



A pyridyl-triazole ligand for ruthenium and iridium catalyzed C=C and C=O hydrogenations in water/organic solvent biphasic systems

Stefano Paganelli*, Md. Mahbubul Alam, Valentina Beghetto, Alberto Scrivanti, Emanuele Amadio, Matteo Bertoldini, Ugo Matteoli

Department of Molecular Science and Nanosystems, Università Ca' Foscari Venezia, via Torino 155, 30170 Venezia Mestre, Italy

ARTICLE INFO

Article history:

Received 1 July 2014

Received in revised form 2 October 2014

Accepted 10 November 2014

Available online 21 November 2014

Keywords:

Ruthenium

Iridium

Catalytic hydrogenation

Biphasic catalysis

Water

ABSTRACT

The water soluble pyridyl-triazole ligand sodium 2-(1-((pyridin-2-yl)methyl)-1H-1,2,3-triazol-4-yl) ethyl sulfate (Na1) has been successfully employed in combination with ruthenium and iridium for catalytic hydrogenation of C=C and C=O double bonds in water/toluene biphasic systems. Reaction of the ligand with $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})_2]$ affords the new water soluble complex $[\text{RuCl}(\eta^6\text{-}p\text{-cymene})(\mathbf{1})]$ (**2**) which has been found to be catalytically active in the water/organic solvent biphasic hydrogenation using styrene and 2-cyclohexen-1-one as model substrates. Very conveniently, the iridium based catalytic system is prepared by simply stirring in water $[\text{Ir}(\eta^4\text{-COD})\text{Cl}]_2$ with Na1 (Ir:Na1 molar ratio = 1:4), the resulting solution is catalytically active and appears more efficient than **2**. With both the Ru- and Ir-based systems the catalytically active aqueous phases can be used at least three times without loss of activity.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Homogeneous catalysts generally provide very good activities and selectivities, but their application in industrial processes is hampered by their difficult separation from the reaction products. Furthermore, recovery of homogeneous catalysts appears very often a challenging and expensive task. For all these reasons, the development of water soluble catalysts, whose separation from reagents and products could allow a prompt recycle of the catalytically active species, is highly desirable [1–5]. This provides an inexpensive answer to the challenge of preserving resources, making the process more environmentally friendly.

Nowadays water-soluble catalysts are increasingly employed either in water or in water/organic solvent biphasic mixtures.

The most commonly employed catalysts in water/organic phase biphasic systems are metal complexes modified with water soluble phosphines, such as TPPTS (triphenylphosphine-3,3',3''-trisulfonic acid trisodium salt) which, for instance, is employed in the renowned OXEA (former Ruhrchemie/Rhône-Poulenc) hydroformylation process [4–8].

In the last years new species bearing different hydrophilic groups such as $-\text{COOH}$, $-\text{NR}_3^+$, $-\text{OH}$, etc. [1–4] and also natural

compounds, such as aminoacids, peptides, proteins and sugars have been used as ligands in combination with transition metal species in order to obtain catalysts active in water [9–18].

For some time now, our research group has been involved in the synthesis of triazolyl ligands taking advantage of the copper-catalyzed azide-alkyne [3+2] cyclization (Scheme 1) [19–22]. Employing this efficient strategy we have synthesized a small library of N–N or N–S ligands which were successfully employed in palladium catalyzed Suzuki–Miyaura reactions [23,24]. As a part of this ongoing research we have recently reported the synthesis of the water soluble ligand Na1 (Scheme 1) [25], which was successfully employed in aqueous phase palladium catalyzed S–M coupling reactions.

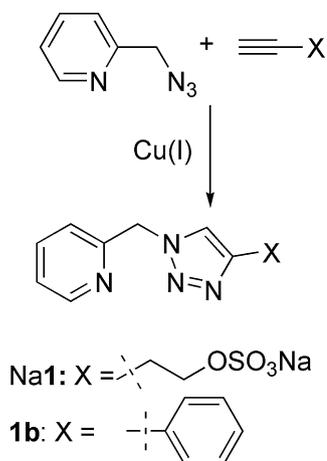
In the present work, we wish to report that Na1 can be successfully employed as the ligand in combination with ruthenium and iridium to catalyze carbon–carbon and carbon–oxygen double bond hydrogenation in biphasic water/organic solvent mixtures.

2. Experimental

2.1. Materials and instrumentation

All reactions were carried out under inert atmosphere (argon) using standard Schlenk techniques. Commercial solvents (Sigma–Aldrich) were purified as described in the literature [26]. Sodium 2-(1-((pyridin-2-yl)methyl)-1H-1,2,3-triazol-4-yl)

* Corresponding author. Tel.: +39 041 2348592; fax: +39 041 2348517.
E-mail address: spag@unive.it (S. Paganelli).



Scheme 1. General synthetic scheme for bidentate pyridyl-triazolyl ligands.

ethyl sulfate (Na1) was prepared as described in the literature [25]. $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})_2]$ [27] and $[\text{Ir}(\eta^4\text{-COD})\text{Cl}]_2$ [28] were prepared according to literature methods. $[\text{Ir}(\eta^4\text{-COD})\text{Cl}]_2$ is also commercially available (Alfa Aesar).

^1H and ^{13}C NMR spectra were recorded in deuterated solvents (Sigma–Aldrich) on a Bruker Avance 300 spectrometer operating at 300.1 and 75.5 MHz, respectively; the chemical shift values are reported in δ units with reference to the residual solvent signal. The proton assignments were performed by standard chemical shift correlations as well as by ^1H 2D COSY experiments. The ^{13}C chemical shift values were assigned through DEPT-135 and 2D-heteronuclear correlation experiments (HMOC and HMBC).

ESI-MS analyses were performed using a Finnigan LCQ-Duo ion-trap instrument, operating in positive ion mode (sheath gas N_2 , source voltage 4.0 kV, capillary voltage 21 V, capillary temperature 200 °C). Sample solutions were prepared by dissolving the Ru complex (1 mg) in methanol (1 mL) and then further diluting with methanol (1:30). Sample solutions were introduced into the ESI source by a syringe pump at 8 $\mu\text{L}/\text{min}$ flow rate. All mass spectra were recorded on freshly prepared solutions. The ESI-MS data, reported below, have been confirmed by MS/MS experiments and isotope pattern analysis.

The solutions resulting from the catalytic experiments were analyzed by GLC on a 6850 Agilent Technologies gas-chromatograph employing HP-1 capillary column (30 m \times 0.32 mm \times 0.25 μm) or HP-5 capillary column (30 m \times 0.32 mm \times 0.25 μm). GC–MS spectra were recorded on a HP 5890 series II gas-chromatograph interfaced to a HP 5971 quadrupole mass detector employing a HP-5 capillary column (30 m \times 0.25 mm \times 0.25 μm). The reaction products were identified by comparison with commercial samples (Sigma–Aldrich). ICP-MS analyses were performed by using an Agilent 7500a-Series instrument.

2.2. Ruthenium catalyst synthesis 2

In a 50 mL two-neck round-bottomed flask a mixture of sodium 2-(1-((pyridin-2-yl)methyl)-1H-1,2,3-triazol-4-yl)ethyl sulfate (Na1) (118 mg, 0.39 mmol) and $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})_2]$ (118 mg, 0.20 mmol) was stirred in methanol (20 mL) at room temperature for 3 days under nitrogen. Then the mixture was filtered and taken to dryness in vacuo. The resulting yellow-orange solid was extracted with boiling ethanol and filtered; on standing overnight, orange microcrystals (155 mg, 72% yield) precipitate, mp 234 °C (dec). ^1H NMR (300 MHz, CD_3OD , 298 K) δ 9.11 (d, 1H, $J=5.8$, H-1), 8.33 (s, 1H, H-7), 8.06 (td, 1H, $J=7.7$ and 1.3 Hz, H-3), 7.77 (d, 1H, $J=7.2$ Hz, H-4), 7.59 (m, 1H, $J=5.8$ Hz, H-2), 6.10

(d, 1H, $J=15.8$ Hz, H-6_A), 6.08 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.97 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.87 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.81 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.62 (d, 1H, $J=15.8$ Hz, H-6_B), 4.28 (m, 2H, H-10), 3.11 (m, 2H, H-9), 2.92 (spt, 1H, $J=6.9$ Hz, ArCH), 2.01 (s, 3H, ArCH₃), 1.31 (d, 6H, $J=6.9$ Hz, CHCH₃). ^{13}C NMR (75.5 MHz, CD_3OD , 298 K) δ 159.5 (C-1), 154.7 (C-5), 149.7 (C-7), 141.8 (C-3), 130.1 (C-4), 127.4 (C-8 or C-2), 127.3 (C-8 or C-2), 107.9 (*p*-cym), 102.6 (*p*-cym), 89.0 (*p*-cym), 86.3 (*p*-cym), 85.6 (*p*-cym), 84.9 (*p*-cym), 67.1 (C-10), 55.4 (C-6), 32.2 (*p*-cymCH), 27.2 (C-9), 22.6 (CHCH₃), 22.3 (CHCH₃), 18.3 (*p*-cymCH₃). IR (KBr pellet) ν_{max} : 3591, 3461, 3127, 3073, 3022, 2947, 1603, 1468, 1431, 1254, 1218, 1005, 896, 773, 742, 581 cm^{-1} . Anal. Calc. for $\text{C}_{20}\text{H}_{25}\text{ClN}_4\text{O}_4\text{RuS}$ (554.0): C, 43.36; H, 4.55; N 10.11; Cl 6.40%. Found: C, 43.12; H, 4.54, N 9.88; Cl 6.15%.

2.3. Complex 2 aquation

5.5 mg (0.01 mmol) of complex **2** were dissolved in 1.0 mL of D_2O . The following is the description of the ^1H NMR spectrum registered immediately after dissolution. ^1H NMR of complex **2** (300 MHz, D_2O , 298 K) δ 9.03 (d, 1H, $J=5.8$, H-1), 8.33 (s, 1H, H-7), 8.08 (td, 1H, $J=7.8$ and 1.3 Hz, H-3), 7.78 (d, 1H, $J=7.2$ Hz, H-4), 7.59 (m, 1H, $J=5.8$ Hz, H-2), 6.08–6.00 (m, 3H, H-6_A and 2 H of *p*-cym), 5.90 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.88 (d, 1H, $J=6.1$ Hz, *p*-cym), 5.62 (d, 1H, $J=15.8$ Hz, H-6_B), 4.31 (m, 2H, H-10), 3.17 (m, 2H, H-9), 2.81 (spt, 1H, $J=6.9$ Hz, ArCH), 2.07 (s, 3H, ArCH₃), 1.24 (d, 3H, $J=6.9$ Hz, CHCH₃), 1.21 (d, 3H, $J=6.9$ Hz, CHCH₃). On standing the signals relevant to complex **3** develop. The equilibrium is reached after 24 h. The ^1H NMR spectrum displays along with the above reported signals relevant to complex **2**, new signals attributed to the aquo species **3**, according to integration the 2:3 molar ratio is 0.45:0.55, respectively. ^1H NMR of complex **2** (300 MHz, D_2O , 298 K) δ 8.99 (d, 1H, $J=5.8$, H-1), 8.37 (s, 1H, H-7), 8.15 (td, 1H, $J=7.8$ and 1.3 Hz, H-3), 7.84 (d, 1H, $J=7.2$ Hz, H-4), 7.72 (m, 1H, $J=5.8$ Hz, H-2), 6.16–5.86 (overlapping multiplets attributed to 6_A and *p*-cym of **2** and **3**), 5.63 (d, 1H, $J=15.8$ Hz, H-6_B), 4.31 (m, 2H, H-10), 3.17 (m, 2H, H-9), 2.81 (spt, 1H, $J=6.9$ Hz, ArCH), 2.11 (s, 3H, ArCH₃), 1.25–1.19 (overlapping multiplets attributed to CHCH₃ of **2** and **3**).

2.4. Hydrogenation experiments with catalyst 2

As an example the experimental details relevant to Entry 3 in Table 1 are reported. In a Schlenk tube, a toluene solution of styrene (374 mg, 3.6 mmol in 2.0 mL) was added to an aqueous solution of **2** (4.0 mg, 0.0072 mmol in 2.0 mL of water) under nitrogen atmosphere. The Schlenk tube was then transferred into a 150 mL stainless steel autoclave under nitrogen. The reactor was pressurized at $p(\text{H}_2)=4.0$ MPa and then heated at 80 °C under magnetic stirring. After 6 h the autoclave was cooled to room temperature and the residual gas vented off.

The organic phase was carefully separated, dried on Na_2SO_4 and, after the addition of 0.5 mmol of mesitylene (as the internal GC

Table 1
Biphasic hydrogenation of styrene in the presence of the ruthenium catalyst **2**.^a

Entry	$p(\text{H}_2)$ (MPa)	t (h)	%Conv. ^b (TOF ^c)		
			1st Run	2nd Run	3rd Run
1	4.0	1	25 (125)	64 (320)	60 (300)
2	4.0	3	62 (103)	96 (160)	99 (165)
3	4.0	6	100 (83)	100 (83)	100 (83)
4	3.0	6	98 (81)	99 (82)	99 (82)
5	2.0	6	78 (65)	92 (77)	88 (73)

^a Reaction conditions: $[\text{RuCl}(\eta^6\text{-}p\text{-cymene})(\mathbf{1})]=4.0$ mg (0.0072 mmol), styrene = 374 mg (3.59 mmol), $T=80$ °C, $\text{H}_2\text{O}=2.0$ mL, toluene = 2.0 mL, substrate:Ru (molar ratio) = 500:1.

^b By GLC.

^c Mol of hydrogenated product/mol of catalyst per hour.

standard), analyzed by GC while the catalytic aqueous phase was recycled for further experiments.

2.5. Hydrogenation experiments with the *in situ* prepared iridium catalyst

As an example the experimental details relevant to Entry 3 in Table 4 are reported.

In a Schlenk tube, 3.2 mg (0.0048 mmol) of $[\text{Ir}(\eta^4\text{-COD})\text{Cl}]_2$ and 5.9 mg (0.019 mmol) of ligand Na1 (metal/ligand = 1/2 molar ratio) were stirred under nitrogen in 2 mL of degassed water until complete dissolution of the complex (about 30 min). A solution of 461 mg (4.8 mmol) of 2-cyclohexen-1-one in 2 mL of toluene was then added to the aqueous phase. The Schlenk tube was then transferred into a 150 mL stainless steel autoclave under nitrogen, pressurized with H_2 (0.5 MPa) and magnetically stirred for 6 h at 40 °C. The reactor was then cooled to room temperature and the residual gas vented off. The organic phase was separated, dried on Na_2SO_4 and, after the addition of 0.5 mmol of mesitylene (as the internal GC standard), analyzed by GC while the catalytic aqueous phase was recycled for further experiments.

3. Results and discussion

3.1. Synthesis of the ruthenium catalyst

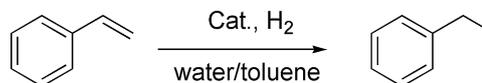
The ruthenium catalyst **2** was prepared by stirring $[\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})]_2$ with Na1 (Ru: Na1 = 1:1) in methanol at room temperature (see Scheme 2).

Recrystallization of the crude product from hot ethanol affords yellow-orange microcrystals which were found to be lamellar aggregates unsuitable for X-ray structure determination. Therefore **2** was formulated on the basis of the elemental analysis, conductivity measurements, ESI-MS, and NMR spectroscopy data.

Methanol or water solutions of **2** are nonconducting ($\Lambda_M < 1 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ for a $1.0 \times 10^{-3} \text{ M}$ solution) in agreement with its zwitterionic nature [29,30].

In the ESI-MS spectrum of **2** the most intense peaks have m/z 1685 (M_3+Na)⁺, 1131 (M_2+Na)⁺, and 577 ($\text{M}+\text{Na}$)⁺, the relative intensity being 100, 40 and 28, respectively. MS/MS scans showed that from the peak at $m/z = 577$ ($\text{M}+\text{Na}$)⁺ arise peaks having $m/z = 519$ ($\text{M}-\text{Cl}$)⁺, 497 ($\text{M}-\text{SO}_3+\text{Na}$), and 439 ($\text{M}-\text{SO}_3-\text{Cl}$)⁺.

NMR spectroscopy indicates that in **2** the pyridyl-triazolyl ligand chelates ruthenium through the N-pyridyl atom and the central N atom of the triazole ring (see Scheme 2 for the relevant numbering scheme). In fact, in the ¹H NMR spectrum (CD_3OD , 298 K) of **2** both the H(1) doublet and the H(7) singlet are found significantly downfield with respect to the free ligand ($\Delta\delta = 0.57$ and 0.33 ppm, respectively) as found for other pyridyl-triazole ligands when chelating to a metal centre [23,31,32]. Definitive evidence for chelation of **1** at ruthenium comes from the AB spin pattern found for the methylene bridge protons. This pattern is due to



Scheme 3. Catalytic hydrogenation of styrene.

the lack of any element of symmetry in the six-membered ring which forms upon ligand chelation. Hence, the axial and the equatorial protons of the methylene moiety become non-equivalent and give two separate resonances with a geminal coupling constant of 15.8 Hz. Owing to the lack of symmetry, the aromatic protons of the coordinated *p*-cymene give four separate resonances (two AB spin systems) in the 6.1–5.8 ppm range, about 1 ppm upfield with respect to the free ligand. The chemical shifts of the isopropyl and the methyl moieties are almost unchanged with respect to the starting ruthenium complex; in this connection it is worth noting that the two methyls of isopropyl moiety which are accidentally equivalent in the ¹H NMR spectrum give two separate signals in the ¹³C NMR spectrum.

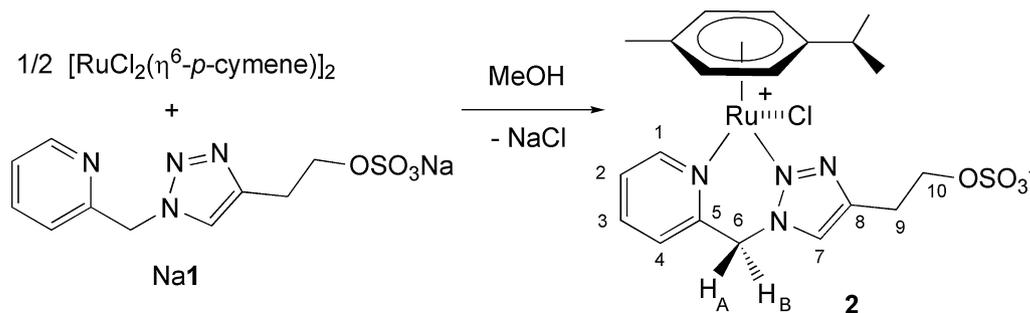
Ligand chelation is also indicated by the ¹³C NMR spectrum in which both C(1) and C(7) resonate at lower fields with respect to free ligand Na1, the $\Delta\delta$ s being 3.9 and 3.5 ppm, respectively. It is worth remarking that both the ¹H and the ¹³C NMR spectra are in good agreement with those reported by Kösmrlj and co-workers for the strictly related species $[\text{RuCl}(\eta^6\text{-}p\text{-cymene})(\mathbf{1b})\text{Cl}]$ (for the chemical structure of ligand **1b** see Scheme 1) the structure of which has been determined by X-ray crystallography [32,33].

3.2. Catalysis with ruthenium complex **2**

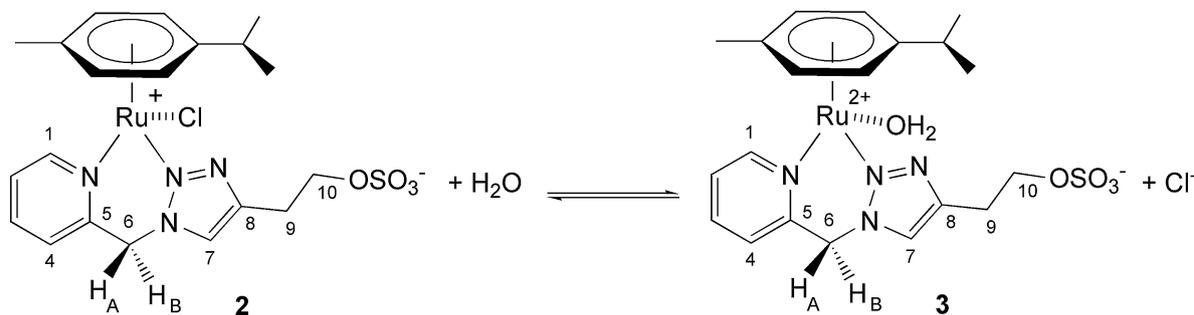
In order to test the applicability of Na1 in biphasic hydrogenation, a first set of experiments was carried out employing the ruthenium complex **2**. Styrene was chosen as the exploratory model substrate (see Scheme 3), the relevant results are gathered in Table 1.

The reactions were carried out in a water/toluene system at 80 °C. A first experiment carried out at $p(\text{H}_2) = 4.0 \text{ MPa}$ showed that **2** has a moderately good catalytic activity as 25% of the substrate is hydrogenated to ethyl benzene in 1 h (Entry 1). Most importantly, a recycle experiment not only shows that the recovered aqueous phase remains catalytically active, but also that its activity increases affording 67% of substrate conversion under the same conditions (column 5 in Entry 1); furthermore, this enhanced catalytic activity is maintained in a second recycle experiment.

In a second set of experiments the reaction time was increased to 3 h; this allowed to obtain a substrate conversion of 62% in the first run and almost complete conversion in the two following recycle experiments, confirming that the catalyst becomes more active after the first catalytic run. When the reaction time is extended to 6 h, styrene conversion is complete in the presence of both fresh and recycled catalyst (Entry 3).



Scheme 2. Synthesis of the ruthenium catalyst.



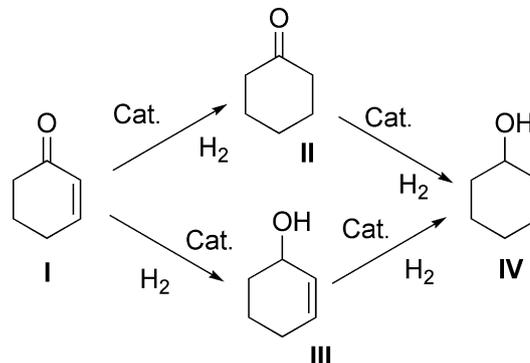
Scheme 4. Complex 2 aquation.

Owing to the good activity displayed by the catalytic system, an experiment was carried out by lowering the hydrogen pressure to 3.0 MPa. Again, a practically complete olefin hydrogenation is obtained after 6 h, and the recovered catalyst maintains its activity unchanged in two consecutive recycle experiments (Entry 4). A further decrease of $p(\text{H}_2)$ to 2.0 MPa brings to a moderate decrease of the substrate conversion (78%) in the first run, but the catalyst, when recycled, shows a remarkable increase of efficiency affording ethylbenzene in about 90% yield (Entry 5).

As far as the observed catalyst activation is concerned, it is to recall that in organoruthenium arene complexes such as **2**, the Ru–Cl bond is quite reactive and, in particular, can be easily cleaved by water to give the corresponding aquo complex (see Scheme 4). For instance, the aquation reaction is thought to play an important role in setting the anticancer activity displayed by some ruthenium arene complexes [34]. Aquation of complex **2** can be inferred by ^1H NMR spectroscopy and conductivity measurements. In fact, the ^1H NMR spectrum of **2** in D_2O , which immediately after dissolution is almost identical to the one registered in CD_3OD , slowly changes on standing. After 24 h, the ^1H NMR spectrum is the superimposition of the signals relevant to complex **2** and the aquo complex **3** in 0.45/0.55 molar ratio, respectively. In this connection it is to point out that $[\text{RuCl}(\eta^6\text{-}p\text{-cymene})(\mathbf{1b})]\text{Cl}$ displays the same behaviour [33]. In keeping with partial breaking of the Ru–Cl bond and formation of the charged aquo complex **3**, the Λ_{M} value of a 10^{-3} M water solution of **2** upon standing increases from about 0.9 to $40 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$, value which agrees with a partial formation of a 1:1 electrolyte [35].

In order to substantiate the involvement of the aquo species **3** in the catalyst activation, we carried out a hydrogenation experiment employing a sample of catalyst which was previously “pre-activated” by stirring in water under H_2 ($p(\text{H}_2)=4.0$ MPa) at 80°C for 1 h. Employing such “pre-activated” catalyst, a styrene conversion of 34% was obtained (result not reported in Table 1). Accordingly, it appears that aquation alone cannot account for the catalyst activation observed.

When employing ruthenium catalysts in homogeneous or biphasic hydrogenation, the reaction rate can be improved by introducing a base which acts as promoter by scavenging the acid which forms upon heterolytic hydrogen activation [36]. Thus, some experiments were carried out in the presence of inorganic bases. When we tried to carry out the reaction in 0.1 M of aqueous KOH, we observed immediate decomposition of the catalyst to ruthenium black. Thus, attributing catalyst decomposition to the strong basic medium, we resolved to use K_2CO_3 as basic promoter in a 1:1 molar ratio with the catalyst. In this case we did not observe immediate metal precipitation, and the aqueous phase could be employed in styrene hydrogenation. As surmised, the presence of the base led to a significantly higher reaction rate affording ethylbenzene in 80% yield. However, at the end of the reaction, extensive formation of ruthenium black in the water phase was noticed. According to these observations, we are brought to believe that also the substrate plays



Scheme 5. Hydrogenation of 2-cyclohex-1-ene (I).

Table 2

Biphasic hydrogenation of 2-cyclohexen-1-one (I) in the presence of the ruthenium catalyst **2**.^a

Entry	<i>t</i> (h)	Run	%Conv. ^b (TOF ^c)	%Selectivity ^d	
				II	IV
1	6	1st	17 (14)	94	6
2	24	1st	100 (21)	96	4
3	24	2nd	100 (21)	95	5
4	24	3rd	100 (21)	95	5
5	24	1st	36 (7.5)	98	2

^a Reaction conditions: $[\text{RuCl}(\eta^6\text{-}p\text{-cymene})(\mathbf{1})]=4.0$ mg (0.0072 mmol), 2-cyclohexen-1-one = 345 mg (3.59 mmol), $T=80^\circ\text{C}$, $p(\text{H}_2)=2.0$ MPa, $\text{H}_2\text{O}=2.0$ mL, toluene = 2.0 mL, substrate:Ru (molar ratio) = 500:1.

^b By GLC.

^c Moles of hydrogenated products/mol of catalyst per hour.

^d Formation of **III** was never observed.

a role in activating the catalyst, however we were unable to find evidences supporting this hypothesis and the actual mechanism of catalyst activation remains uncertain.

It is worth noting that in all the experiments carried out using complex **2**, no catalyst leaching was observed. As a matter of fact, the organic phase recovered after the first hydrogenation reaction (Entry 1, Table 1) was used as catalyst in the homogeneous hydrogenation of undec-1-ene in toluene, after 6 h at 80°C and 2.0 MPa of H_2 undecane was not formed at all. Furthermore, the toluene phases recovered from a few different experiments were analyzed by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) in order to determine the content of ruthenium: in no case the ruthenium content was found to be greater than 1 ppm.

In order to test the chemoselectivity of the catalyst we studied the hydrogenation of 2-cyclohexen-1-one (I, see Scheme 5), the relevant data are collected in Table 2.

In a first experiment carried out at 80°C and $p(\text{H}_2)=2.0$ MPa the catalyst activity appeared modest as only 17% of the substrate was hydrogenated in 6 h (Entry 1). On the other hand, the experiment showed that the catalyst is endowed with a good

chemoselectivity. In fact, only small amounts of cyclohexanol (**IV**) are formed in addition to cyclohexanone (**II**) which is by far the most abundant product, while 2-cyclohexen-1-ol (**III**) does not form at all.

We were delighted to find that when the reaction time is increased to 24 h, complete substrate hydrogenation is obtained. This result can be explained only by admitting that the catalyst undergoes an activation process during the reaction. Once the catalyst has been activated it maintains its activity for at least two recycle experiments (Entries 3 and 4 of Table 2). In this connection it is worth noting that activation process does not change the chemoselectivity of the catalyst.

The high selectivity towards formation of the saturated ketone is noteworthy since most commonly with ruthenium catalysts the opposite selectivity is found, i.e. the unsaturated alcohol selectively forms. Nevertheless, exceptions are known [37], and, in particular, it is to remind that Joó [38] demonstrated that the pH of the aqueous phase may strongly influence the hydrogenation selectivity.

Since water solutions of complex **2** are almost neutral (pH = 6.2) and in basic solutions the catalyst decomposes to ruthenium black, we have carried out an experiment under acidic conditions in order to ascertain if the pH could change the hydrogenation selectivity. The experiment was carried out at pH = 3 dissolving the catalyst in a 10⁻³ M HCl solution, while all the other reaction conditions were unchanged (Entry 5 of Table 2). Not surprisingly, under acidic conditions the reaction rate is strongly depressed and only 36% substrate conversion is obtained by 24 h. Moreover, it appears that the pH has no influence on the selectivity since no formation of unsaturated alcohol is observed.

According to these results it must be concluded that the unusual selectivity could be attributed to the N,N-bidentate nature of our ligand.

Summing up, complex **2** appears endowed with an interesting catalytic activity which does not appear to be far from that of the most employed biphasic hydrogenation catalysts based on sulphonated mono- and diphosphines [38,39] and compares favourably with that of water soluble nitrogen ligands [37b].

3.3. Catalytic hydrogenations with the in situ prepared system [Ir(η^4 -COD)Cl]₂/Na1

To further explore the scope of our ligand in aqueous biphasic hydrogenation, we studied the catalytic activity of a system prepared by combining in situ Na1 with [Ir(η^4 -COD)Cl]₂ (COD: 1,5-cyclooctadiene) which is a commercially available iridium precursor widely used in hydrogenation reactions [40,41]. For the sake of comparison the efficiency of the system was tested with the same substrates employed with ruthenium.

Plain stirring of Na1 with the iridium precursor in degassed water at room temperature affords in about 30 min a clear catalytically active solution. Preliminary experiments showed that the catalytic activity depends on the ligand to iridium ratio, the best results being obtained using 4 moles of ligand for mole of [Ir(η^4 -COD)Cl]₂ (Na1/Ir = 2/1), therefore such ratio was used in all the hydrogenation experiments. The most significant results obtained in styrene hydrogenation (Scheme 2) are reported in Table 3.

A first experiment carried out under mild conditions affords a modest ethylbenzene yield (26%, Entry 1), but when the temperature is increased to 60 °C and the hydrogen pressure to 4.0 MPa complete substrate conversion is obtained in only 1 h. Most importantly, the recovered aqueous phase can be reused four times (Entries 2a–d). ICP-MS analyses indicates that the organic phases recovered after the hydrogenation reaction contain small amounts of iridium (about 8 ppm). According to these results it may be

Table 3
Styrene hydrogenation in water/toluene using the iridium/Na1 system.^a

Entry (recycle)	T (°C)	t (h)	%Conv. ^b (TOF ^c)
1 ^d	40	3	26 (43)
2	60	1	100 (500)
2a (1st)	60	1	98 (490)
2b (2nd)	60	1	96 (480)
2c (3rd)	60	1	95 (475)
2d (4th)	60	1	93 (465)

^a Reaction conditions: [Ir(η^4 -COD)Cl]₂ = 3.2 mg (0.0048 mmol), p(H₂) = 4.0 MPa, styrene = 500 mg (4.8 mmol), toluene = 2.0 mL, H₂O = 2.0 mL, Na1 = 5.9 mg (0.019 mmol), ligand:Ir (molar ratio) = 2:1, styrene:Ir (molar ratio) = 500:1.

^b By GLC.

^c Mol of hydrogenated product/mol of catalyst per hour.

^d p(H₂) = 1.0 MPa.

Table 4
2-Cyclohexen-1-one hydrogenation in water/toluene using the iridium/1 system.

Entry (recycle)	p(H ₂) (MPa)	T (°C)	t (h)	%Conv. ^b (TOF ^c)	Selectivity	
					II	IV
1	4.0	60	21	100 (23)	4	96
2	4.0	60	1	100 (500)	80	20
2a (1st)	4.0	60	1	100 (500)	81	19
2b (2nd)	4.0	60	1	100 (500)	83	17
3	0.5	40	6	100 (83)	100	0
3a (1st)	0.5	40	6	100 (83)	95	5
3b (2nd)	0.5	40	6	100 (83)	97	3

^a Reaction conditions: [Ir(η^4 -COD)Cl]₂ = 3.2 mg (0.0048 mmol), H₂O = 2 mL, toluene = 2 mL, ligand = 5.9 mg (0.019 mmol), 2-cyclohexen-1-one = 461 mg (4.8 mmol), Ir/ligand (molar ratio) = 1/2, substrate/Ir (molar ratio) = 500/1.

^b By GLC.

^c Moles of hydrogenated products/mol of catalyst per hour.

concluded that the iridium/Na1 system is significantly more active than the ruthenium catalyst **2**, while this latter appears more robust.

To shed some light on the ligand role, an hydrogenation experiment (not reported in Table 3) was carried out under the conditions of Entry 2 in the absence of Na1. In the absence of the ligand, the iridium precursor dissolves in the organic phase giving a pale yellow solution and although styrene is completely hydrogenated, extensive decomposition of [Ir(η^4 -COD)Cl]₂ to iridium black occurs. This finding demonstrates the key role played by the ligand which not only immobilizes the metal in the water phase, but also stabilizes it against reduction to metal. In this connection it is to point out that no ligand is detected by ¹H NMR spectroscopy in the organic phase after the catalytic experiments.

The results of 2-cyclohexen-1-one hydrogenation (Scheme 5) are collected in Table 4.

Under the same reaction conditions employed for styrene hydrogenation (60 °C and p(H₂) = 4.0 MPa), complete substrate conversion is achieved by 21 h leading to a mixture of **IV** and **II** in 96/4 molar ratio (Entry 1). Accordingly, the reaction time was reduced to 1 h in order to understand through which reaction sequence the final products form (i.e. if the reaction path is **I** → **II** → **IV**, or if **I** → **III** → **IV**). The experiment showed that the actual reaction sequence is the former, and that the hydrogenation of the endocyclic C=C is much faster than C=O hydrogenation resulting in a moderate selectivity towards the formation of cyclohexanone. The aqueous phase remains catalytically active and may be reused two times without loss of efficiency. Complete chemoselectivity towards cyclohexanone was finally obtained by further decreasing the temperature to 40 °C and the p(H₂) to 0.5 MPa. Under these very mild conditions, complete C=C double bond hydrogenation is achieved by 6 h, cyclohexanone being the only product observed; moreover, it is possible to recycle at least two times the aqueous phase with only a negligible loss of chemoselectivity.

4. Conclusions

Summing up, the present work demonstrates the usefulness of the pyridyl-triazole Na1 as ligand for hydrogenation in water/organic solvent biphasic systems. Na1 can be successfully employed in combination with both ruthenium and iridium. Reaction of Na1 with ruthenium affords a well defined species (complex 2) which displays a fairly good catalytic activity; the catalyst is robust and no metal leaching in the organic phase has been detected, so that the aqueous phase can be reused at least three times without loss of activity. A peculiar feature of the ruthenium catalyst is represented by its activation occurring during the first catalytic run; studies devoted to rationalize this facet are in progress. The practical usefulness of Na1 is even more evident when we consider that the highly active iridium system is promptly prepared by simply stirring an aqueous solution of the ligand with the commercially available $[\text{Ir}(\eta^4\text{-COD})\text{Cl}]_2$. Notwithstanding the small amounts of iridium leaching in the organic phase, the system retains its activity almost unchanged and the catalytically active aqueous phase can be reused at three times without drawbacks.

References

- [1] F. Joó, *Aqueous Organometallic Catalysis*, Kluwer Academic Publishers, Dordrecht, 2001.
- [2] B. Cornils, W.A. Herrmann, *Aqueous-Phase Organometallic Catalysis*, second ed., Wiley-VCH, Weinheim, 2004.
- [3] B. Cornils, W.A. Herrmann, I.T. Horváth, W. Leitner, S. Mecking, H. Olivier-Bourbigou, D. Vogt, *Multiphase Homogeneous Catalysis*, Wiley-VCH, Weinheim, 2005.
- [4] D.J. Cole-Hamilton, R.P. Tooze, *Catalyst Separation, Recovery and Recycling*, Springer, Dordrecht, 2006.
- [5] P.H. Dixneuf, V. Cadierno, *Metal-Catalyzed Reactions in Water*, Wiley-VCH, Weinheim, 2013.
- [6] E.G. Kuntz, *Chem. Tech.* 17 (1987) 570–575.
- [7] B. Cornils, E.G. Kuntz, *J. Organomet. Chem.* 502 (1995) 177–186.
- [8] B. Cornils, *Org. Process Res. Dev.* 2 (1998) 121–127.
- [9] N. Zhang, F. Li, Q.J. Fu, S.C. Tsang, *React. Kinet. Catal. Lett.* 71 (2000) 393–404.
- [10] E. Guibal, *Prog. Polym. Sci.* 30 (2005) 71–109.
- [11] J. Steinreiber, T.R. Ward, *Coord. Chem. Rev.* 252 (2008) 751–766.
- [12] M. Marchetti, F. Minello, S. Paganelli, O. Piccolo, *Appl. Catal. A: Gen.* 373 (2010) 76–80.
- [13] H. Mao, X. Liao, B. Shi, *Catal. Commun.* 16 (2011) 210–214.
- [14] M. Marchetti, G. Mangano, S. Paganelli, C. Botteghi, *Tetrahedron Lett.* 41 (2000) 3717–3720.
- [15] M. Marchetti, S. Paganelli, *Chim. Ind.* 10 (2005) 44–46.
- [16] C. Bertucci, C. Botteghi, D. Giunta, M. Marchetti, S. Paganelli, *Adv. Synth. Catal.* 344 (2002) 556–562.
- [17] S. Paganelli, M. Marchetti, M. Bianchin, C. Bertucci, *J. Mol. Catal. A: Chem.* 269 (2007) 234–239.
- [18] S. Di Dio, M. Marchetti, S. Paganelli, O. Piccolo, *Appl. Catal. A: Gen.* 399 (2011) 205–210.
- [19] C.W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* 67 (2002) 3057–3064.
- [20] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, *Angew. Chem. Int. Ed.* 41 (2002) 2596–2599.
- [21] V.D. Bock, H. Hiemstra, J.H. van Maarseveen, *Eur. J. Org. Chem.* (2006) 51–68.
- [22] M. Meldal, C.W. Tornøe, *Chem. Rev.* 108 (2008) 2952–3015.
- [23] E. Amadio, A. Scrivanti, G. Chessa, U. Matteoli, V. Beghetto, M. Bertoldini, M. Rancan, A. Dolmella, A. Venzo, R. Bertani, *J. Organomet. Chem.* 716 (2012) 193–200.
- [24] E. Amadio, A. Scrivanti, M. Bortoluzzi, M. Bertoldini, V. Beghetto, U. Matteoli, G. Chessa, *Inorg. Chim. Acta* 405 (2013) 188–195.
- [25] E. Amadio, A. Scrivanti, V. Beghetto, M. Bertoldini, M.M. Alam, U. Matteoli, *RSC Adv.* 3 (2013) 21636–21640.
- [26] W.L.F. Armarego, D.D. Perrin, *Purification of Laboratory Chemicals*, fourth ed., Butterworth-Heinemann, Oxford, 1996.
- [27] M.A. Bennett, A.K. Smith, *J. Chem. Soc. Dalton Trans.* (1974) 233–241.
- [28] J.L. Herde, J.C. Lambert, C.V. Senoff, M.A. Cushing, *Inorg. Synth.* 15 (1974) 18–20.
- [29] R.R. Schrock, J.A. Osborn, *Inorg. Chem.* 9 (1970) 2339–2343.
- [30] H.J. Nolte, G. Gafner, L.M. Haines, *J. Chem. Soc. Chem. Commun.* (1969) 1406–1407.
- [31] E. Amadio, M. Bertoldini, A. Scrivanti, G. Chessa, V. Beghetto, U. Matteoli, R. Bertani, A. Dolmella, *Inorg. Chim. Acta* 370 (2011) 388–393.
- [32] D. Urankar, B. Pinter, A. Pevec, F. De Proft, I. Turel, J. Kósmrlj, *Inorg. Chem.* 49 (2010) 4820–4829.
- [33] I. Bratsos, D. Urankar, E. Zangrando, P. Genova-Kalou, J. Košmrlj, E. Alessio, I. Turel, *Dalton Trans.* 40 (2011) 5188–5199.
- [34] F. Wang, H. Chen, S. Parsons, I.D.H. Oswald, J.E. Davidson, P.J. Sadler, *Chem. Eur. J.* 9 (2003) 5810–5820.
- [35] W.J. Geary, *Coord. Chem. Rev.* 7 (1971) 81–122.
- [36] Selected references:
 - (a) G.S. Forman, T. Ohkuma, W.P. Hems, R. Noyori, *Tetrahedron Lett.* 41 (2000) 9471–9475;
 - (b) D. Jantke, M. Cokoja, M. Drees, F.E. Kühn, *ChemCatChem* 5 (2013) 3241–3248.
- [37] Selected references:
 - (a) A. Andriollo, J. Carrasquel, J. Marifio, F.A. Lopez, D.E. Paez, I. Rojas, N. Valencia, *J. Mol. Catal. A: Chem.* 116 (1997) 157;
 - (b) C. Stangel, G. Charalambidis, V. Varda, A.G. Coutsolelos, I.D. Kostas, *Eur. J. Inorg. Chem.* (2011) 4709–4716;
 - (c) L.G. Melean, M. Rodriguez, A. González, B. González, M. Rosales, P.J. Baricelli, *Catal. Lett.* 141 (2011) 709–716.
- [38] F. Joó, J. Kovács, Cs.A. Bényei, Á. Kathó, *Angew. Chem. Int. Ed.* 37 (1998) 969–970.
- [39] F. Joó, *Acc. Chem. Res.* 35 (2002) 738–745.
- [40] G.-H. Hou, J.-H. Xie, P.-C. Yan, Q.-L. Zhou, *J. Am. Chem. Soc.* 131 (2009) 1366–1367.
- [41] G. Hou, R. Tao, Y. Sun, X. Zhang, F. Gosselin, *J. Am. Chem. Soc.* 132 (2010) 2124–2125.