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Research paper

Catalytic activity in transfer hydrogenation using ruthenium (II) carbonyl complexes containing two 1,8-naphthyridine as N-monodentate ligands

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ARTICLE INFO

This manuscript is dedicated to Professor Hubert Le Bozec from Rennes University, France, who retired recently. Professor Le Bozec had a long and fruitful collaboration with our group in Chile for 30 years. During that time many Chilean postgraduate students made part of their theses in the University of Rennes, supervised by Prof. Le Bozec. Throughout his collaboration with us, we have not only an excellent co-worker but also a great friend and we are sure that our friendship will last forever.

Keywords:
Ruthenium (II)
1,8-Naphthyridine complexes
Transfer hydrogenation
Acetophenone
Homogeneous catalysis

ABSTRACT

A new series of novel complexes of type *cis*-$[Ru(CO)_2Cl_2(\mathbf{L})_2]$, L = 2-phenyl-1,8-naphthyridine, 2-(4′-nitrophenyl)-1,8-naphthyridine, 2-(4′-bromophenyl)-1,8-naphthyridine, 2-(4′-methylphenyl)-1,8-naphthyridine, 2-(3′-methoxyphenyl)-1,8-naphthyridine, 2-(2′-methoxyphenyl)-1,8-naphthyridine and 2-(4′-methoxyphenyl)-1,8-naphthyridine have been successfully synthesized and characterized. We found that the complexes can be directly synthesized from $[RuCl_2(CO)_2]_2$ with high yield. The crystallographic structures of complex *cis*-$[RuCl_2(CO)_2$(2-(4′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2]$ and *cis*-$[RuCl_2(CO)_2$(2-(2′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2]$ have been established by X-ray single crystal diffraction studies, which indicate an octahedral geometry with two 1,8-naphthyridine ligands coordinated to the metal in a **N**-monodentate fashion. The ruthenium(II) complexes have been studied as catalysts in the transfer hydrogenation of acetophenone. We found that complexes show moderate activities and a 100% selectivity. The best turnover frequency (390 h^{-1}) is found for *cis*-$[RuCl_2(CO)_2$(2-(4′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2]$ when the substrate/catalysis ratio was 1000/1. The catalytic conditions were optimized using different substrate/catalyst and base/catalyst ratios.

1. Introduction

The naphthyridines (NAPs) are a group of diazanaphthalenes that contain a single nitrogen atom in each ring but no nitrogen atom at either of the bridgehead positions [1]. Several structural isomers exist, where the 1,8-NAPs are key components of a number of antibacterial agents [2]. The synthetic procedure are prepared via the Friedländer condensation of 2-aminonicotinaldehyde with the corresponding acyl derivatives [3–6]. In this system, the precursor 2-aminonicotinaldehyde must be freshly prepared and used immediately after isolation to avoid self-condensation side reactions. Indeed, a facile synthesis of 2-aminonicotinaldehyde was reported by Caluwe and co-workers in 1974 [5], with modifications being introduced later by Dunbar et all., Rivera et al. [7,8]. In addition, the preparation of various alkylsubstituted (i.e., 2- and/or 3-position) NAP ligands has also been reported [9–14]. During the formation of mononuclear ruthenium complexes, 1,8-NAP (1) tends to act as either a monodentate or a bidentate ligand. However, chelation is generally disfavored due to the small bite angle of the four-membered chelate ring.

Ruthenium complexes derived from 1,8-NAP have also been applied in homogeneous catalytic reactions as substitutes for 2,2-bipyridine or 1,10-phenanthroline (phen). For example, the catalytic potential of ruthenium complexes containing monodentate 1,8-NAPs, was investigated in the hydroformylation of styrene in dimethylformamide [15].

Ruthenium arene complexes, $[(\eta^6$-p-cymene$)_2Ru_2(L)Cl_2](PF_6)_2$ L = 7-bis(di-2-pyridinyl)-1,8-naphthyridine] was synthesized and

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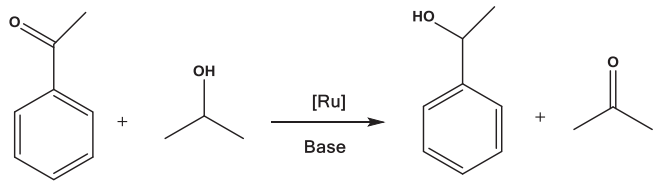


Scheme 1. Hydrogen transfer reaction of ketones (HTR).

characterized by spectroscopic and analytical techniques. The use of these ruthenium complexes as pre-catalysts for oxidative coupling of 1,2-diols/1,2-aminoalcohol with o-phenylenediamines leading to quinoxalines was investigated. [16]. Other ruthenium complexes containing 1,8 NAP derivate have been successfully prepared and used as anticarcer compounds [17].

Other authors found that ruthenium-hydride complexes containing 1,8 NaPs ligands are effective catalysts in the transformation of primary alcohols, including amino alcohols, into the corresponding carboxylic acid in the presence of alkaline water [18]. This work proposed that the 1,8-NAP unit enhances the nucleophilicity of a water molecule through hydrogen bonding, and that the noncoordinated nitrogen atom in the 1,8-NAP unit promotes solvated hydroxide attack through hydrogen bonding with a water molecule of the solvent cage. Alternatively, uncoordinated nitrogen atom may facilitate hydroxide attack by coordination with Na^+.

Transfer hydrogenation of ketones by propan-2-ol is convenient in large-scale synthesis since there is no need to employ a high hydrogen pressure or to use hazardous reducing agents (Scheme 1). Transition metal complexes containing a coordinative unsaturated metal center and a Brønsted basic π-donor ligand have been reported in homogeneous transfer hydrogenation. Ligands with different transition metals such as amido [19–22], thiolate [23–28], phosphido [29], imido [30–40], oxo [41–46], and sulfido [47] have been investigated for this reaction. The most active and selective catalysts for the transfer hydrogenation reactions are ruthenium [48], iridium [49] and rhodium [50] complexes containing nitrogen, oxygen and N,O-donor ligands [51–58]. We have investigated the synthesis of ruthenium complexes containing polypyridine ligands and their application as potential homogeneous catalysts. We found that the compounds are active in the transfer hydrogenation where the active species is a ruthenium hydride complex containing 2,2-bipyridine, phenanthroline and 1,8-naphthyridine ligands.

Herein, we report the synthesis and the catalytic behavior of ruthenium complexes of the type *cis*-$[Ru(CO)_2Cl_2(\mathbf{L})_2]$ with **L** = 2-phenyl-1,8-naphthyridine; $\mathbf{L_1}$, 2-(4′-nitrophenyl)-1,8-naphthyridine; $\mathbf{L_2}$, 2(4′-bromophenyl)-1,8-naphthyridine; $\mathbf{L_3}$, 2-(4′-methylphenyl)1,8-naphthyridine; $\mathbf{L_4}$, 2-(4′-methoxyphenyl)-1,8-naphthyridine; $\mathbf{L_5}$, 2-(3′-methoxyphenyl)-1,8-naphthyridine; $\mathbf{L_6}$ and 2-(2′-methoxyphenyl)-1,8-naphthyridine, $\mathbf{L_7}$, in hydrogenation reaction of ketones. The X-ray structures of complexes show that two naphthyridines ligands coordinate in an *N*-monodentate fashion to the metal. We will describe detailed studies on their catalytic activities for the hydrogen transfer reaction of ketones (HTR).

2. Experimental part

2.1. Materials and general methods

All the reagents used were chemically pure and analytical grade. Acetophenone was used as supplied from Sigma-Aldrich. $[RuCl_2(CO)_2]_2$ [59] was prepared by refluxing commercial $RuCl_3{\cdot}3H_2O$ in a mixture of 37% hydrochloric acid and 88% formic acid (1:1) during 24 h under nitrogen. The ligands were prepared from 2-aminonicotinaldehyde and substituted acetophenone. The substrates were obtained from Sigma-Aldrich.

The catalytic conversions were determinated by gas chromatography using an Agilent 6890 Series GC System equipped with a flame ionization detector and a (30 m·0.25 mm·0.25 μm) HP-INNOWAX column.

2.2. Crystal structure analysis of complexes

The data were collected at a temperature of 293 ± 2° K on an Oxford Diffraction X calibur Saphir 3 diffractometer equipped with graphite monochromated MoKα radiation (= 0.71069 Å). The structure was solved with SIR-97, which reveals the non-hydrogen atoms of the molecules. The structure was solved in the space group $P2_1/c$ by Patterson or direct method and refined by the full-matrix least-squares fitting on F^2 using SHELXTL-97 with initial isotropic parameters.

3. General procedure

3.1. Synthesis of ligands

A suspension of 2-aminonicotinaldehyde (500 mg; 4.09 mmol), substituted acetophenone (4.09 mmol), and NaOH (200 mg; 5 mmol) in EtOH (40 mL) was refluxed under argon for 4 h. The solvent was removed under vacuum. The residue was extracted from a mixture of CH_2Cl_2/water and the organic layer was dried over magnesium sulfate; the product was purified by column chromatography on silica gel eluting with CH_2Cl_2:EtOAc (6:1). After the solvent was removed, the desired product was obtained as a white solid. (more information about ligands characterization see supplementary material).

3.2. Synthesis of complexes

The ligands **L** (1.316 mmol) and $[RuCl_2(CO)_2]_2$ (0.658 mmol) were mixed in ethanol/H_2O (9/1) (50 mL) The mixture was refluxed for 24 h under nitrogen atmosphere. The precipitate was separated by filtration and the solid was washed with, ethanol, acetone, chloroform and ether ethylic.

3.2.1. Cis-$[RuCl_2(CO)_2$(2-phenyl-1,8-naphthyridine-κN8)$_2]$(**Ru-1**)

^{1}H NMR (200 MHz, $CDCl_3$) 10.44 (dd, H_7,J = 5.4 Hz, J = 2.0 Hz,1H), 8.98 (dd, $H_{7'}$, J = 5.3 Hz, 1.9 Hz,1H), 8.83 (dd, H_5, J = 8.0 Hz, J = 2.0 Hz, 1H), 8.75 (m, o-Ph, m-Ph, 2H), 8.65 (d, H_4, J = 8.4 Hz,1H), 8.45 (d, $H_{4'}$, J = 8.8 Hz,1H), 8.43 (d, $H_{3'}$, J = 8.8 Hz, 1H), 8.29 (dd, $H_{5'}$, J = 8.0 Hz, J = 1.9 Hz, 1H), 8.10 (d, H_3, J = 8.4 Hz, 1H), 8.01 (dd, H_6, J = 8.0 Hz, J = 5.4 Hz, 1H), 7.78 (m, m-Ph, 1H), 7.70 (m, p-Ph, 1H), 7.37 (m, m-Ph, 1H), 7.35 (m, o-Ph, 1H), 7.24 (m, o-Ph, 1H), 7.09 (dd, $H_{6'}$, J = 8.0 Hz, J = 5.3 Hz, 1H), 6.95 (m, o-Ph, 1H). Yield 65%. MP 340 °C (d). IR (KBr, cm^{-1}) M-CO 2044.7; 1983.2. Anal. Calcd. (%) for: $C_{30}H_{20}Cl_2N_4O_2Ru$ C, 56.26; H, 3.15; N, 8.75. Found (%): C, 55.95; H, 2.95; N, 8.76.

3.2.2. Cis-$[RuCl_2(CO)_2$(2-(4′-nitrophenyl)-1,8-naphthyridine-κN8)$_2]$ (**Ru-2**)

^{1}H NMR (200 MHz, $CDCl_3$) 10.93 (dd, H_7, J = 5.3 Hz, J = 1.8 Hz, 1H), 8.98 (m, $H_{7''}$, Ph′ 3H), 8.91 (dd, H_5, J = 8.1, J = 1.8, 1H), 8.71 (m, 2H, Ph), 8.69 (d, H_4, J = 8.4 Hz, 1H), 8.56 (d, $H_{4'}$, J = 8.6 Hz, 1H), 8.49 (d, $H_{3'}$,J = 8.6, 1H), 8.32 (dd, $H_{5'}$, J = 8.0 Hz , J = 1.6 Hz, 1H), 8.15 (d, H_3, J = 8.4 Hz, 1H), 8.1 (dd, H_6, J = 8.1, J = 5.3, 1H), 7.82 (m. Ph', 2H), 7.57 (m, Ph, 2H), 7.09 (dd, $H_{6'}$, J = 8.0 Hz, J = 5.2 Hz, 1H). Yield 57%. MP 328 °C (d). IR (KBr, cm^{-1}): M-CO 2051.6; 1987.6. Anal. Calcd. (%) for $C_{30}H_{18}Cl_2N_6O_6Ru$: C, 49.33; H, 2.48; N, 11.50. Found (%): C, 48.96; H, 2.32; N, 11.26.

3.2.3. Cis-$[RuCl_2(CO)_2$(2-(4′-bromophenyl)-1,8-naphthyridine-κN8)$_2]$ (**Ru-3**)

^{1}H NMR (200 MHz, $CDCl_3$) 10.05 (dd, H_7, J = 5.4 Hz, J = 1.8 Hz, 1H), 9.76(dd, $H_{7'}$, J = 5.4 Hz , J = 1.8 Hz, 1H), 8.52 (dd, H_5, J = 8.1 Hz, J = 1.8 Hz, 1H), 8.47(d, H_3, J = 8.6 Hz, 1H), 8.36 (dd, $H_{5'}$,

J = 8.1 Hz, 1.8 Hz, 1H), 8.35 (d, H_4, J = 8.9 Hz, 1H), 8.17(d, $H_{3'}$, J = 8.6 Hz, 1H), 8.09 (d, H_3, J = 8.9 Hz, 1H), 8.05 (m, Ph, Ph′, 3H), 7.82 (dd, H_6, J = 8.1 Hz, J = 5.4 Hz), 7.79 (d, Ph′, J = 8.7 Hz), 2H), 7.64 (dd. $H_{6'}$, J = 8.1 Hz, J = 5.4 Hz). Yield 67%. MP 368 °C (d). IR (KBr, cm^{-1}) M-CO 2050.2; 1985.6. Calcd. (%) for $C_{30}H_{18}Br_2N_4O_2Ru$: C, 45.14; H, 2.27; N, 7.02. Found (%): C, 44.96; H, 2.37; N, 6.79.

3.2.4. Cis-[$RuCl_2(CO)_2$(2-(4′-methylphenyl)-1,8-naphthyridine-κN8)$_2$] (Ru-4)

^{1}H NMR (200 MHz, $CDCl_3$) 10.47 (dd, H_7, J = 5.5 Hz, J = 1.9 Hz, 1H), 8.85 (dd, $H_{7'}$, J = 5.4 Hz, J = 1.0 Hz), 8.46 (d, Ph,1H), 8.38 (dd, H_5, J = 7.8 Hz , J = 1.9 Hz, 1H), 8.20 (d, H_4, $H_{4'}$, J = 8.4 Hz, 2H), 8.05 (d, H_3, J = 8.5 Hz, 1H), 7.78 (m,$H_{5'}$,H_6, 2H,), 7.70 (d, Ph, J = 7.50 Hz, 1H), 7.69 (d, $H_{3'}$, J = 8.4 Hz, 1H), 7.50 (m, Ph, 2H), 7.07 (d, Ph′, 1H), 6.72 (dd, $H_{6'}$, J = 7.8 Hz, J = 5.4 Hz, 1H), 6.66 (d, Ph′, J = 8.0 Hz, 1H), 6.60 (d, Ph′, J = 8.0 Hz), 2.52 (s, Me), 2,25 (s, Me). Yield 69%. MP 341 °C (d). IR (KBr, cm^{-1}) M-CO 2055.0, 1988.9. Anal.Calcd. (%) for $C_{32}H_{24}Cl_2N_4O_2Ru$: C, 57.49; H, 3.62; N, 8.38. Found (%): C, 57.20; H, 4.00; N, 8.28.

3.2.5. Cis-[$RuCl_2(CO)_2$(2-(4′-metoxyphenyl)-1,8-naphthyridine-κN8)$_2$] (Ru-5)

^{1}H NMR (200 MHz, $CDCl_3$) 10.54 (dd, H_7, J = 5.5 Hz, J = 2.2 Hz,1H), 9.03 (dd, $H_{7'}$, J = 5.7 Hz, J = 1.8 Hz, 1H), 8.93 (m,H_5, Ph, 2H), 8.71 (d, H_4, J = 8.8 Hz, 1H), 8.68 (d, $H_{4'}$, J = 8.6 Hz, 1H), 8.59 (d,$H_{3'}$, J = 8.6 Hz, 1H), 8.42 (dd, $H_{5'}$, J = 8.1 Hz, J = 1.8 Hz, 1H), 8.21 (d, H_3, J = 8.8 Hz), 8.1 (dd, H_6, J = 8.2 Hz, J = 5.5 Hz, 1H), 7.50 (m, Ph′,2H), 7.21 (dd, $H_{6'}$, J = 8.1 Hz, J = 5.7 Hz, 1H), 6.58 (m, Ph′,2H), 4.14 (OMe), 3.91 (OMe). Yield 68%. MP 337 °C (d). IR (KBr, cm^{-1}) M-CO 2050.0, 1988.2. Anal. Calcd. (%) for $C_{32}H_{24}Cl_2N_4O_4Ru$: C, 54.86; H, 3.45; N, 8.00. Found (%): C, 54.09; H, 3.95; N, 7.98.

3.2.6. Cis-[$RuCl_2(CO)_2$(2-(3′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2$] (Ru-6)

^{1}H NMR (200 MHz, $CDCl_3$) 10.47 (dd, H_7, J = 5.4 Hz, J = 1.8 Hz, 1H), 8.80 (dd, $H_{7'}$, J = 5.3 Hz, J = 1,8 Hz, 1H), 8.41 (dd,H_5, J = 7.9 Hz, J = 1.8 Hz, 1H), 8.23 (m , Ph, 2H), 7.98 (m, $H_{4'}$, H_4, 2H), 7.79 (m, $H_{3'}$,$H_{5'}$, H_3, 3H), 7.58 (m, H_6, Ph, 2H), 7.18 (m, Ph, 1H), 6.91 (m, Ph′,1H), 6.68 (m ,H_6, Ph′, Ph, 4H), 4.05 (s, m-OMe), 3.35 (s, m-OMe). Yield 62%. MP 358 °C (d). IR (KBr, cm^{-1}) M-CO 2055.5, 1986. Anal. Calcd. (%) for $C_{32}H_{24}Cl_2N_4O_4Ru$: C, 54.86; H, 3.45; N, 8.00. Found (%): C, 54.06; H, 3.53; N, 8.10.

3.2.7. Cis-[$RuCl_2(CO)_2$(2-(2′-methoxiphenyl)-1,8-naphthyridine-κN8)$_2$] (Ru-7)

^{1}H NMR (200 MHz, $CDCl_3$) 10.54 (dd, H_7, J = 5.5 Hz, J = 2.0 Hz, 1H), 9.03 (dd, $H_{7'}$, J = 5.7 Hz, J = 1,8 Hz,1H), 8.93 (m,H_5, Ph, 3H), 8.68 (d, $H_{4'}$, J = 8.6 Hz, 1H), 8.71 (d, H4, J = 8.8 Hz, 1H), 8.59 (d, $H_{3'}$, J = 8.6 Hz, 1H), 8.42 (dd, $H_{5'}$, J = 8.1 Hz, J = 1.8 Hz, 1H), 8.21 (d, H_3, J = 8.8 Hz, 1H), 8.10 (dd, H_6, J = 8.2 Hz, J = 5.5 Hz, 1H), 7.50 (m, Ph, Ph′, 4H), 7.21 (d ,$H_{6'}$, 1H, J = 8.1 Hz, J = 5.7 1 Hz, 1H), 6.58 (m, Ph′. 2H), 4.14 (s, o-OMe), 3.91 (s, o-OMe). Yield 50%. MP 287 °C (d). IR (KBr, cm^{-1}) M-CO; 2056.0, 1989.0. Anal. Calcd. (%) for $C_{32}H_{24}Cl_2N_4O_4Ru$: C, 54.86; H, 3.45; N, 8.00. Found (%): C, 54.04; H, 3.91; N, 7.89.

3.3. Catalytic procedure

In a glass reactor fitted with a condenser, NaOH (0.475 mmol) was added to propan-2-ol (5 mL) and stirred for 1 h at 80 °C under nitrogen. Next, the ruthenium complex (0.0125 mmol), propan-2-ol (4 mL) and a solution (1 mL) of *p*-cymene as internal standard (1.92 mmol) were added to the corresponding substrate (2.56 mmol) dissolved in propan-2-ol completing a total volume of 10 mL. Identities of reaction components were determined by comparison with commercial samples by gas chromatography.

4. Results and discussion

A series of ruthenium (II) complexes with different substituted naphthyridine ligands have been prepared and characterized. The ligands **L1-L7** were synthesized from 2-aminonicotinaldehyde and the corresponding substituted acetophenone (Scheme 2).

Then, the Ru(II) complexes **Ru-1-Ru-7** were readily prepared by reaction of the carbonyl precursor $[RuCl_2(CO)_2]_2$ and the naphthyridine derivatives L by the procedures reported in the literature [56–60] (Scheme 3).

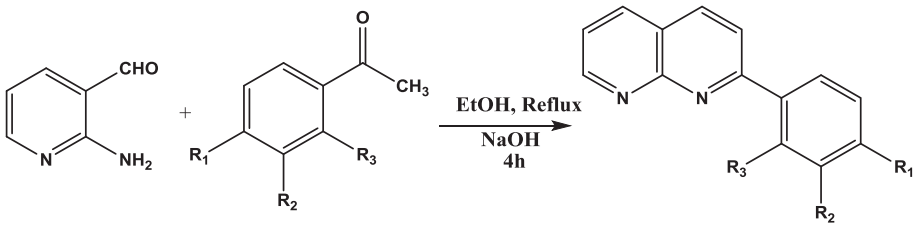
All the complexes $RuCl_2(CO)_2(\mathbf{L})_2$ were isolated in good yield. Two 1,8-naphthyridine ligands **L** coordinate to the metal center in a *N*-monodentate fashion. Whatever the reaction conditions, we do not observe the formation complexes containing *N*,*N*-bidentate **L** ligands. Examples of *N*,*N*-bidentate coordination of naphthyridines have been reported in the case of the phosphine complex $Ru(\mathbf{L})(PPh_3)_2Cl_2$ [57].

The chemical structure of the complexes, **Ru-5**, and **Ru-7** were confirmed by X-ray crystallographic studies (Figs. 1 and 2). Table 1 presents selected bond lengths and Table 2 selected bond angles. The two complexes have an octahedral geometry, in which the two naphthyridine ligands are *cis* to each other, one is *trans* to a chloride and the second one is *trans* to a carbonyl. The high sterical hindrance of phenyl substituted naphthyridine ligands does not preclude a *cis* configuration.

The bond distances and bond angles are similar to those found in related complexes reported by us [53].

4.1. Catalytic results

Table 3 summarizes the catalytic activity in the transfer hydrogenation of acetophenone shown by the ruthenium (II) complexes **Ru-1** to **Ru-5** in the presence of NaOH. In all cases, only one product, 1-

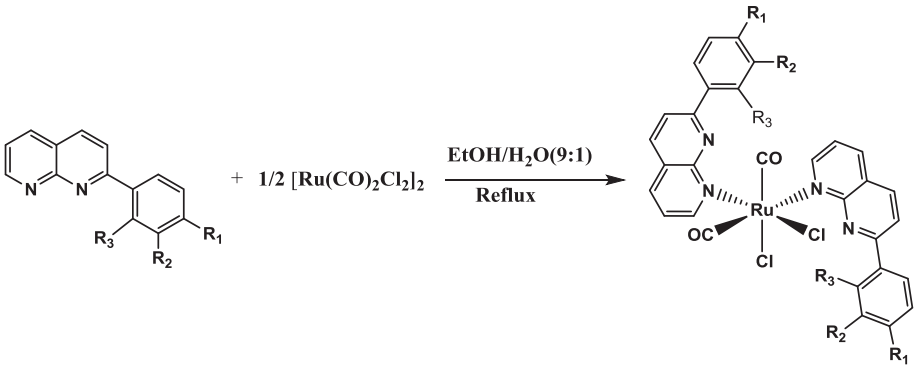


L_1: R_1=H, R_2=H, R_3=H ; L_2: R_1=NO_2, R_2=H, R_3=H ; L_3: R_1=Br, R_2=H, R_3=H

L_4: R_1=CH_3, R_2=H, R_3=H ; L_5: R_1=OCH_3, R_2=H, R_3=H ; L_6: R_1=H, R_2=OCH_3, R_3=H

L_7: R_1=H, R_2=H, R_3=OCH_3

Scheme 2. Synthesis of 1,8-naphthyridine ligands (1,8 NAPs).



Ru-1: R_1=H, R_2=H, R_3=H ; Ru-2: R_1=NO_2, R_2=H, R_3=H ; Ru-3: R_1=Br, R_2=H, R_3=H

Ru-4: R_1=CH_3, R_2=H, R_3=H ; Ru-5: R_1=OCH_3, R_2=H, R_3=H ; Ru-6: R_1=H, R_2=OCH_3, R_3=H

Ru-7: R_1=H, R_2=H, R_3=OCH_3

Scheme 3. Synthesis of ruthenium complexes containing naphthyridine ligands.

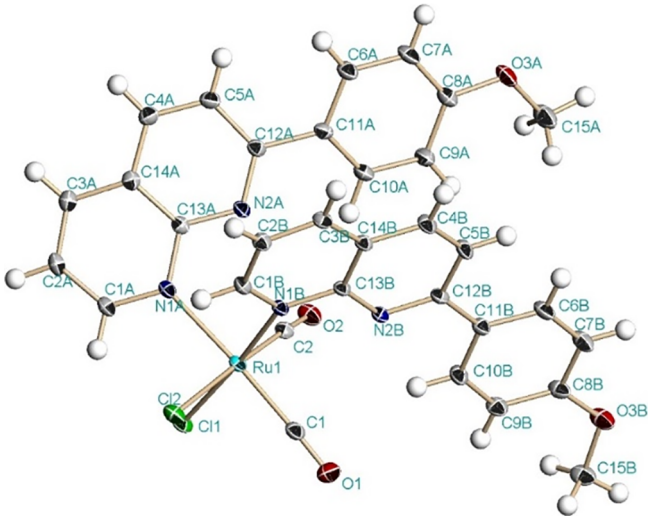


Fig. 1. Molecular view of the complex *cis*-[$RuCl_2(CO)_2$(2-(4′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2$], **Ru-5** showing the labeling scheme.

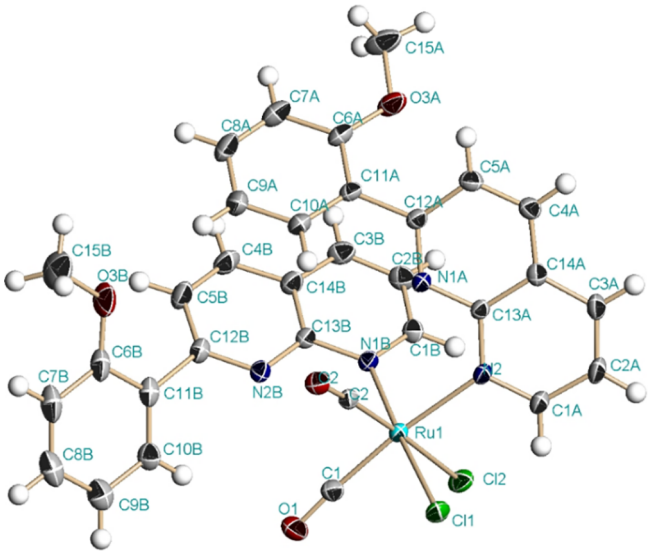


Fig. 2. Molecular view of the complex *cis*-[$RuCl_2(CO)_2$(2-(2′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2$], **(Ru-7)** showing the labeling scheme.

Table 3
Catalytic activities in the hydrogen transfer reaction of acetophenone with ruthenium complexes containing naphthyridine ligands.

Run	Conversion (%) *Complexes*					
	Time(min)	Ru-1	Ru-2	Ru-3	Ru-4	Ru-5
1	5	32	23	28	36	39
2	10	35	23	29	38	41
3	15	35	29	33	40	45
4	30	42	31	36	56	53
5	45	53	35	45	63	67
6	60	57	35	53	66	70
7	185	78	74	79	84	79
8	300	87	85	88	91	95

Reaction conditions: acetophenone (2.56 mmol), catalyst (0.0125 mmol), NaOH (0.475 mmol), p-cymene (1.92 mmol), propan-2-ol (10 mL), 80 °C, N_2. Substrate/catalyst ratio = 205/1. *cis*-[$RuCl_2(CO)_2$(2-phenyl-1,8-naphthyridine-κN8)$_2$] **(Ru-1),** *cis*-[$RuCl_2(CO)_2$(2-(4′-nitrophenyl)-1,8-naphthyridine-κN8)$_2$] **(Ru-2)**, cis-[$RuCl_2(CO)_2$(2-(4′-bromophenyl)-1,8-naphthyridine-κN8)$_2$] **(Ru-3)**, *cis*-[$RuCl_2(CO)_2$(2-(4′-methylphenyl)-1,8-naphthyridine-κN8)$_2$] **(Ru-4)**, *cis*-[$RuCl_2(CO)_2$(2-(4′-methoxyphenyl)-1,8-naphthyridine-κN8)$_2$] **(Ru-5)**.

phenyl ethanol, is obtained with 100% selectivity. Entry 6 shows that the best activity (66% and 70% of conversion) after 1 h of reaction is observed for **Ru-4** and Ru-**5** respectively. The lesser is found for **Ru-2** (R_1 = NO_2). In the hydrogen transfer reaction, the first ten minutes of reaction is very important since the reaction of the precatalyst with propan-2-ol allows the formation of the actives species of the reaction, during this time the metal hydride is formed. The proposed mechanism of the hydrogen transfer reaction suggests that the ruthenium hydride is the active species in this reaction (Fig. 3).

The results reported here (Table 3) show that the formation of the active species (the dihydride complex) (see (Fig. 3) could depend on the nature of the ligand L. The presence of the electron-withdrawing group into the ligand (L_3) (NO_2 and Br) could be disfavor the dihydride complex formation showing a lower conversion during the first thirty minutes of reaction. When the ruthenium hydride active species is formed the conversion for all catalysts become similar (Entry 8), where all catalysts converge to a maximum conversion between 80 and 95%. With the aim of optimizing the catalyst activity of **Ru-4** that showed the larger activity, we did comparative studies using two types of base: NaOH and *t*-BuOK. The role of the base is essential as it activates the coordinated isopropanoxy leading to the formation of the hydride species (Fig. 3). The results are summarized in Table 4. During the course of the reaction, the TOF fluctuates, due to the decrease in

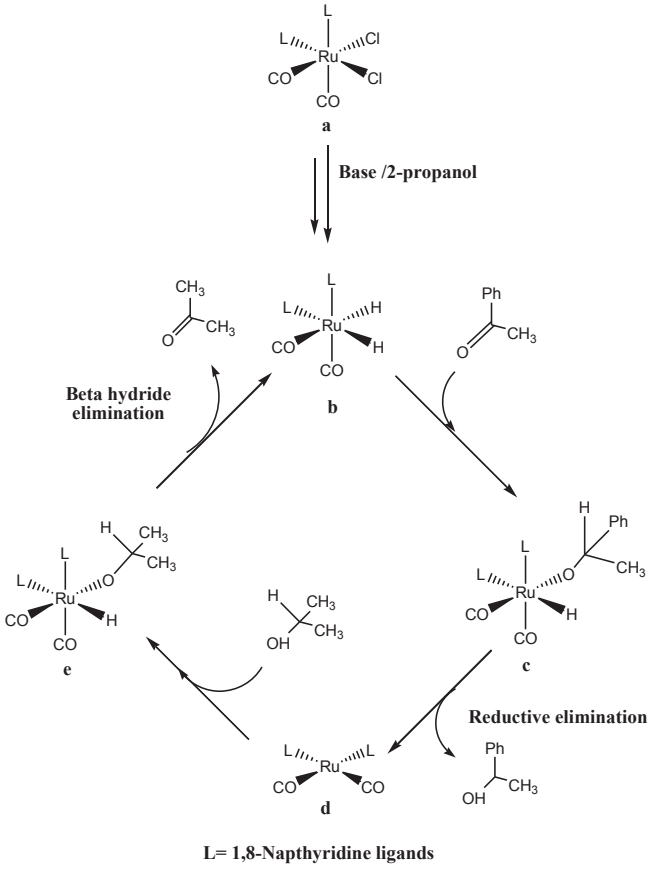


Fig. 3. Proposed mechanism for the hydrogen transfer reaction of acetophenone.

Table 4
Effect of the base in the transfer hydrogenation of acetophenone using the complex *cis*-[$RuCl_2(CO)_2$(2-(4′-methylphenyl)-1,8-naphthyridine-κN8)$_2$], (**Ru-4)** as precatalyst.

Time (min)	Base NaOH		Base *t*-BuOK	
	Conversion (%)	TOF (h^{-1})	Conversion %	TOF(h^{-1})
5	36	886	44	1082
10	38	467	44	542
15	40	328	44	361
30	56	230	44	180
45	63	172	50	137
60	66	135	50	103

Reaction conditions: acetophenone (2.56 mmol), catalyst (0.0125 mmol), base (0.475 mmol), p-cymene (1.92 mmol), propan-2-ol (10 mL), 80 °C, N_2. Substrate/catalyst ratio = 205/1.

substrate concentration during the catalytic reaction, affecting the conversion rate.

Using the inorganic base (NaOH) as a co-catalyst and after 1 h of reaction, the activity of catalyst **Ru-4** is 66% and the turnover frequency (TOF) is 135 h^{-1}, this activity is similar for catalyst **Ru-5**. This latter value is greater that than obtained by employing of *t*-BuOK. Our group have been studied the hydrogen transfer using different ruthenium complexes containing polypyridine ligands which showed that the complex containing polypiridine ligands are active catalysts in this reaction [53,55]. The catalyst loading was also studied with the goal of optimizing the maximum substrate concentration at which the catalyst shows good performance.

Table 5 shows the conversion and the turnover frequencies obtained using different substrate/catalyst ratio for 1 h of reaction. If the

Table 5
Effect of the substrate/catalyst ratio in the transfer hydrogenation of acetophenone with the complex *cis*-[$RuCl_2(CO)_2$(2-(4′-methylphenyl)-1,8-naphthyridine-κN8)$_2$], (**Ru-4**).

Substrate/catalyst	Conversion %	TOF(h^{-1})
205/1	66	135
500/1	47	235
700/1	42	294
1000/1	39	390

Reaction conditions: substrate acetophenone, catalyst (0.0125 mmol), NaOH (0.475 mmol), p-cymene (1.92 mmol), propan-2-ol (10 mL), 80 °C, N_2. Reaction time:1 h.

substrate/catalyst ratio is larger, the TOF value increases. Thus, in the case of a ratio of 1000/1, the TOF value is 390 h^{-1}. We consider that this ratio is optimal, although the conversion, down to 39%, is only 3% lesser than that obtained when the substrate catalyst ratio is 700/1. Although the conversion diminishes as the concentration of catalyst increases, the turnover frequency is higher. By contrast, when the reaction is performed between 3 and 5 h, the conversions were close to 95% whatever the substrate/catalyst ratio used. The mechanism of hydrogen transfer reaction has been reported by several authors. Van Leeuwen [61,62] reported a detailed mechanism for this reaction. In a first stage, the dichloro precursor is converted into the metal dihydride complex (**b**) following the reported mechanism.

Then addition of the ketone gives rises to the formation of the [Ru]-$OC(CH_3)(H)(Ph)$ (**c**) species. The species (**c**) undergoes reductive elimination to form a tetracoordinate metal complex (**d**) together with a molecule of the hydrogenated product which leaves the cycle. Then this tetracoordinate intermediate reacts with propanol-2-ol to generate the metal hydride complex (**e**). Finally, species (**e**) through a β-elimination produces acetone regenerating the dihydride hexacoordinate complex (**b**), thus closing the catalytic cycle.

Correlation between Hammet parameters for the substrate substituent and conversion, is shown in Table 6, when the catalyst **Ru-4** was studied in the hydrogen transfer reaction. When a chloride is incorporated in the *para*-position of the phenyl group, the conversion improves by 20% with respect to the unsubstituted substrate. By contrast, when an electron-donating group, a *p*-methyl or *p*-methoxy is introduced into the substrate, the activity decreases considerably. Based on the mechanism proposed for this reaction, the presence of an electron-withdrawing on the substrate favors hydride attack (step (**c**) → (**d**), (Fig. 3). The hydrogen transfer to the substrate is favored by the presence of the chloride substituent on the phenyl ring, as illustrated by Fig. 4 which shows good correlation between Hammet parameters and TOF values. This suggests that the step (**c**) → (**d**), is the determining step in the transfer hydrogenation reaction of acetophenone by ruthenium(II) complexes incorporating naphthyridine ligands. Additionally, the study of the activity *vs.* time (Table 3) confirms that the formation of a metal hydride (**b**) depends on the nature of the naphthyridine ligand.

Table 6
Effect of the substrate in hydrogen transfer reaction of acetophenone using the *cis*-[$RuCl_2$(2-(4′-methylphenyl)-1,8-naphthyridine-κN8)$_2(CO)_2$] complex, **Ru-5**.

Substrate	Conversion %	Hammett parameter
p-ClC_6H_4-C(O)-CH_3	77	0,23
C_6H_4C(O)-CH_3	57	0,0
p-CH_3-C_6H_4-C(O)-CH_3	35	-0,17
p-CH_3O-C_6H_4-C(O)-CH_3	23	-0,27

Reaction conditions: substrate (2.56 mmol), pre-catalyst (0.0125 mmol), NaOH (4.75 mmol), p-cymene (1.92 mmol), propanol-2-ol (10 mL), 80 °C, N_2. Substrate/catalyst ratio = 205/1.

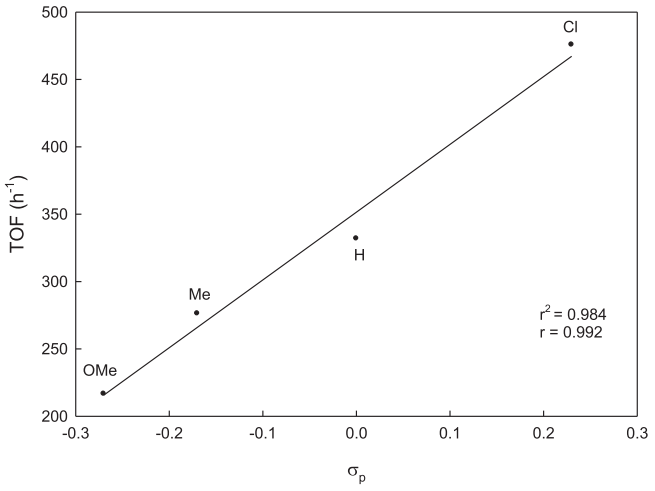


Fig. 4. Correlation between Hammett parameter and the turnover frequency for different substrates in hydrogen transfer reaction of **Ru-5**.

5. Conclusions

A series of ruthenium(II) complexes of the general molecular formula Ru $(CO)Cl_2(\mathbf{L})_2$ (where **L** = substituted naphthyridine ligands) were successfully synthesized and characterized. The characterization of the complexes was accomplished by standard analytical and spectral methods. Single crystal X-ray diffraction analysis confirms the coordination of two naphthyridine ligands to the metal, showing that they are bonded to the metal through a monodentate *N*-coordination mode, generating a distorted octahedral structure.

We have demonstrated that all complexes exhibit a moderate catalytic activity in the transfer hydrogenation of acetophenone in the presence of a base. It is noteworthy that these complexes exhibit 100% selectivity, the corresponding alcohol being formed and a low load of the base (NaOH) is required in order to achieve the observed activities.

The catalyst (**Ru-5**) shown turnover frequency value between 135 and 390 h^{-1}, depending the substrate/catalyst ratio. In addition, the catalyst is active for various acetophenone derivatives. The reaction is sensitive to the nature of the substituent on the phenyl ring. The best activity is obtained when the ring was substituted by Cl in *para* position, indicating that the rate-determining step is the reductive elimination.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ica.2018.10.037.

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