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Catalytic activity of dihydride ruthenium complexes in the hydrogenation of nitrogen containing heterocycles

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Abstract

The catalytic activity of the dihydride ruthenium complexes, $RuH_2(CO)_2(P^nBu_3)_2$, $RuH_2(CO)_2(PPh_3)_2$ and $RuH_2(PPh_3)_4$, in the hydrogenation of nitrogen containing heterocycles has been tested by analyzing the influence of reaction parameters such as temperature, hydrogen pressure, catalyst concentration, on the rate and regioselectivity of the reaction.

$RuH_2(PPh_3)_4$ shows a better catalytic activity with an 86.7% conversion of quinoline after 24 h at 100 °C under a hydrogen pressure of 25 bar, while $RuH_2(CO)_2(PPh_3)_2$ and $RuH_2(CO)_2(P^nBu_3)_2$ in the same conditions give a conversion of 37.1% and 35.6%, respectively. These results are confirmed by the reaction rate of the hydrogenation of quinoline, since the K_c in the presence of $RuH_2(PPh_3)_4$ ($1.46 \times 10^{-5}\ s^{-1}$) is higher than others ($6.37 \times 10^{-6}\ s^{-1}$ for $RuH_2(CO)_2(PPh_3)_2$ and $6.36 \times 10^{-6}\ s^{-1}$ for $RuH_2(CO)_2(P^nBu_3)_2$).

Noteworthy is the selectivity of these catalytic systems in the hydrogenation of quinoline: in all tests the three catalysts lead to 1,2,3,4-tetrahydroquinoline as the major product, furthermore this compound is the only formed in the presence of $RuH_2(CO)_2(PPh_3)_2$. The selectivity is affected by the presence of an acid (CH_3COOH) or a base (N^nBu_3) in the reaction media.

The complex $RuH_2(PPh_3)_4$ is catalytically active, even if in a minor extent, in the hydrogenation of isoquinoline, pyridine and 2-methylpyridine.

The basicity of the substrate and steric hindrance around the nitrogen atom show a great influence on the conversion.

The results obtained suggest that the catalytic system activates a heterocyclic ring through the coordination of the heteroatom to the metal centre of the complexes.

Keywords: Homogeneous catalysis; Ruthenium hydride; Hydrogenation; Quinoline; Pyridine

1. Introduction

The regioselective hydrogenation of quinoline and its derivatives is involved in the manufacture of intermediates of considerable industrial interest such as petrochemicals, fine chemicals and pharmaceuticals; furthermore, quinoline and its derivatives are commonly used as model substrates in hydrodenitrogenation (HDN), a reaction of relevant importance in the fossil fuels industries. Therefore, increasing efforts are being paid to set up selective processes to hydrogenate several nitrogen containing heteroaromatic compounds.

Many examples of homogeneous catalytic complexes, mostly based on Rh, Ru, Fe and Co, have been employed after the first application of Jardine and McQuillin for the selective reduction of pyridine to piperidine [1] in the presence of the $Rh(py)_3Cl_3/NaBH_4$ system.

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The activity and selectivity of several rhodium and ruthenium complexes in different reaction conditions have been studied by various authors [2] and extensive studies on homogeneous hydrogenation of nitrogen containing heterocycles by use of Rh(I) and Ru(II) complexes, such as $Rh(PPh_3)_3Cl$, $Ru(PPh_3)_3HCl$ and $[RhCp^*(MeCN)_3]^{2+}$, are due to Fish and co-workers, who also proposed a mechanism for such reactions.

In this paper, we report our studies concerning the hydrogenation of quinoline and some analogous substrates, using the dihydride ruthenium complexes $RuH_2(CO)_2(P^nBu_3)_2$, $RuH_2(CO)_2(PPh_3)_2$ and $RuH_2(PPh_3)_4$. We have tried better conditions to perform the selective reduction of quinoline to 1,2,3,4-THQ (1,2,3,4-tetrahydroquinoline).

The complexes $RuH_2(CO)_2(P^nBu_3)_2$, $RuH_2(CO)_2(PPh_3)_2$ have been chosen in consideration of their good catalytic activity in the hydrogenation of ketones, α,β-unsaturated ketones, alkenes, alkynes, and unsaturated nitrogen containing compounds [3,4], while the specie $RuH_2(PPh_3)_4$ provides an excellent catalytic activity toward the hydrogenation of nitrogen containing compounds [3].

2. Results and discussion

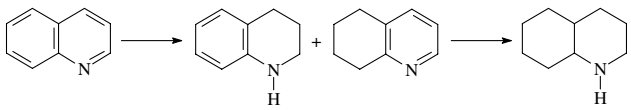
2.1. Synthesis of ruthenium complexes: $RuH_2(PPh_3)_4$, $RuH_2(CO)_2(P^nBu_3)_2$, $RuH_2(CO)_2(PPh_3)_2$

The catalysts $RuH_2(CO)_2(P^nBu_3)_2$ (**1**) [3], $RuH_2(CO)_2(PPh_3)_2$ (**2**) [5] and $RuH_2(PPh_3)_4$ (**3**) [6] have been prepared according to the procedure described in the literature and their spectroscopic characteristics were in agreement with the reported data.

While (**1**) and (**2**) are stable in solution under a nitrogen atmosphere, the complex $RuH_2(PPh_3)_4$ (**3**) is in equilibrium with two species: $RuH_2(PPh_3)_3$ (**4**) and $RuH_2(N_2)(PPh_3)_3$ (**5**), due to a phosphine dissociation and coordination of a nitrogen molecule. The species (**4**) and (**5**) are not present in the solid state. The spectroscopic characteristics of the species present in solution are in agreement with the data reported in the literature [3,5,6].

2.2. Catalytic activity of dihydride ruthenium complexes, $RuH_2(CO)_2(P^nBu_3)_2$, $RuH_2(CO)_2(PPh_3)_2$ and $RuH_2(PPh_3)_4$, in the hydrogenation of quinoline

The catalytic activity of (**1**), (**2**) and (**3**) has been tested by evaluating the influence of reaction parameters on the rate and regioselectivity. In a first step, 1,2,3,4-tetrahydroquinoline (1,2,3,4-THQ) and 5,6,7,8-tetrahydroquinoline (5,6,7,8-THQ) are formed and in a second step decahydroquinoline (DHQ) (Scheme 1) is formed. Other intermediates were not evidenced in the reaction medium.



Scheme 1.

2.2.1. Reaction time

The influence of reaction time has been evaluated in the range among 3–72 h, while the other reaction parameters are kept constant. The conversion of the substrate and the composition of the reaction mixture are reported in Table 1.

In all cases, the conversion increases as the reaction time improves. The $RuH_2(PPh_3)_4$ (**3**) presents a greater catalytic activity with respect to (**1**) and (**2**): just after 3 h the conversion in the presence of (**3**) is 54.4% (entry 11), while it is 5.4% in the presence of (**1**) (entry 1) and 7.5% in the presence of (**2**) (entry 6). After a reaction time of 24 h, the conversion rises up to 86.7% in the presence of (**3**) (entry 14).

It is worthy to note that the hydrogenation is regioselective in the presence of (**1**) and (**2**), since 1,2,3,4-THQ is the sole product even with a high conversion of quinoline (82.1% and 68.2%, respectively, entries 5 and 10).

A lower regioselectivity is obtained in the presence of (**3**): 1,2,3,4-THQ is the major product while 5,6,7,8-THQ and DHQ are formed in lower amounts. By increasing the reaction time, the composition of the reaction mixture changes: basically on increasing the time from 3 to 15 h an increase of 1,2,3,4-THQ and 5,6,7,8-THQ is observed, while the percentage of DHQ remains almost steady (entries 11–13). When the reaction time is prolonged to 24 h, an appreciable increase of 1,2,3,4-THQ and DHQ is observed (entry 14) together with a decrease of 5,6,7,8-THQ, suggesting that DHQ is mainly formed through the reduction of 5,6,7,8-THQ. After a longer reaction time, until 96 h (entries 15–17) the conversion and reaction composition remain constant. These data suggest a deactivation of the catalytically active species due to products formed. It is reasonable to suppose a competition among quinoline and the hydrogenated quinolines for the coordination of the catalytic species to the metal centre, hampering the complete conversion of the substrate. This hypothesis is confirmed by the data obtained from the reaction performed in the presence of a Lewis base (see Section 2.3).

Kinetic analysis of the data reported in Table 1 (entries 1–17), following the procedure reported by Frediani et al. [8], shows a first partial order with respect to reaction time with all the catalysts tested. The kinetic rates (K_c) are in the following order: (**3**) ≫ (**2**) ≅ (**1**) (14.60, 6.37 and 6.36×10^{-6} s^{-1}, respectively) (Table 2).

Table 1
Hydrogenation of quinoline: influence of reaction time[a]

Entry	Catalyst code	Reaction time (h)	Conversion (%)	Reaction mixture composition (%)			
				Q	1,2,3,4-THQ	5,6,7,8-THQ	DHQ
1	**1**	3	5.4	94.6	5.4	0	0
2	**1**	6	7.8	92.2	7.8	0	0
3	**1**	24	35.6	64.4	35.6	0	0
4	**1**	48	65.1	34.9	65.1	0	0
5	**1**	72	82.1	17.9	82.1	0	0
6	**2**	3	7.5	92.5	7.5	0	0
7	**2**	6	9.0	91.0	9.0	0	0
8	**2**	9	19.8	80.2	19.8	0	0
9	**2**	24	37.1	62.9	37.1	0	0
10	**2**	48	68.2	31.8	68.2	0	0
11	**3**	3	54.4	45.6	48.0	3.5	2.9
12	**3**	6	68.7	31.3	56.0	9.8	2.9
13	**3**	15	73.9	26.1	59.1	12.4	2.4
14	**3**	24	86.7	13.3	75.2	3.4	8.1
15	**3**	48	84.9	15.1	73.2	3.2	8.5
16	**3**	72	85.8	14.2	74.6	3.4	7.8
17	**3**	96	88.8	11.2	76.4	3.2	9.2

[Cat]: 0.66 mM; [Substrate]: 0.066 M; T: 373 K; $P(H_2)$ 25 bar; THF 20 ml.
[a] Q: quinoline; 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

Table 2
Kinetic and thermodynamic data for the reduction of quinoline in the presence of $RuH_2(CO)_2(P^nBu_3)_2$ (**1**), $RuH_2(CO)_2(PPh_3)_2$ (**2**), and $RuH_2(PPh_3)_4$ (**3**)[a]

Catalyst	Code	$K_c \times 10^6$ (s^{-1})	R^2	$K_p \times 10^7$ (s^{-1} bar^{-1})	R^2	$K_{cat} \times 10^1$ (s^{-1} M^{-1})	R^2	ΔH^{**} (KJ mol^{-1})	R^2	ΔS^{**} (J mol^{-1} K^{-1})	R^2
$RuH_2(CO)_2(P^nBu_3)_2$	**1**	6.36	0.99	1.92	1.00	–	–	1.0	1.00	−334.0	1.00
$RuH_2(CO)_2(PPh_3)_2$	**2**	6.37	0.99	1.80	0.99	–	–	47.1	0.90	−215.0	0.90
$RuH_2(PPh_3)_4$	**3**	14.60	0.94	–	–	1.02	0.97	32.1	1.00	−240.0	1.00

[a] Data from Tables 1, 3 and 4.

2.2.2. Hydrogen pressure

The catalytic activity of the complexes (**1**)–(**3**) has been tested in conditions giving low conversions to evidence how the hydrogen pressure affects the conversion. The catalytic activity is remarkably affected by the hydrogen pressure (Table 3) with an increment of conversion as the hydrogen pressure increases. For instance, the conversion in the presence of (**1**) rises from 5.4% with 25 bar of hydrogen up to 18.9% with 100 bar of hydrogen (entries 1 and 19). It is interesting to point out that working under 25 bar of hydrogen the reaction gives 1,2,3,4-THQ as the sole product (entry 1) even when the conversion is 82.1% (entry 5). However, working with 50 or 100 bar of hydrogen 1,2,3,4-THQ is the main product but 5,6,7,8-THQ and DHQ are also formed, although in a low amount (entries 18 and 19).

Table 3
Hydrogenation of quinoline: influence of hydrogen pressure[a]

Entry	Catalyst code	Catalyst/substrate (molar ratio)	$P(H_2)$ (bar)	Conversion (%)	Reaction mixture composition (%)			
					Q	1,2,3,4-THQ	5,6,7,8-THQ	DHQ
1	**1**	1/100	25	5.4	94.6	5.4	0	0
18	**1**	1/100	50	9.3	90.7	8.5	0.4	0.4
19	**1**	1/100	100	18.9	81.1	17.3	0.9	0.7
6	**2**	1/100	25	7.5	92.5	7.5	0	0
20	**2**	1/100	50	10.5	89.5	10.5	0	0
21	**2**	1/100	100	19.8	80.2	19.8	0	0
22	**3**	1/200	25	40.1	59.9	36.6	1.8	1.7
23	**3**	1/200	50	56.7	43.3	51.8	3.3	1.6
24	**3**	1/200	75	33.6	66.4	29.6	3.4	0.6
25	**3**	1/200	100	36.2	63.8	26.9	9.1	0.2

[Substrate]: 0.066 M; reaction time: 3 h; THF: 20 ml; T: 373 K.
[a] Q: quinoline; 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

Almost the same behaviour is shown in the presence of (**2**) with a slightly greater catalytic activity with respect to (**1**) but, noteworthy, the reaction always gives 1,2,3,4-THQ as the sole product.

The reaction in the presence of (**3**) shows a different behaviour. An increase of the hydrogen pressure in the range from 25 to 50 bar causes an increase of the conversion from 40.1% to 56.7% (entries 22 and 23), as shown in the presence of (**1**) or (**2**). In these reductions, however, 1,2,3,4-THQ is the major product but 5,6,7,8-THQ and DHQ are present; the amount of 5,6,7,8-THQ is higher than DHQ. By increasing the hydrogen pressure up to 75 bar, a surprising lower conversion has been observed: 1,2,3,4-THQ is still the main product but the relative amounts of 5,6,7,8-THQ and DHQ are increased (entry 24). A further improvement of the hydrogen pressure increases the amount of 5,6,7,8-THQ, while the yield of 1,2,3,4-THQ remains almost unchanged (entry 25). Such behaviour could be rationalised suggesting the formation of a dihydrogen complex which at high pressure of hydrogen is not able to activate quinoline. A $RuH_2(H_2)(PPh_3)_3$ has been reported in the literature [6,7]. Nevertheless, it must be noted that $RuH_2(PPh_3)_4$ (**3**) does not show an analogous behaviour in the reduction of other substrates but this behaviour may also be affected by the coordinating ability of the substrates itself. An alternative hypothesis may be the formation of different catalytic species at different hydrogen pressures and the species operating at pressure higher than 50 bar should be less active. This hypothesis is in agreement with the different regio- and chemoselectivity observed in the experiments under different hydrogen pressures.

Kinetic analysis of the data reported in Table 2 (entries 1, 6, 18–21), following the procedure reported by Frediani et al. [8], shows a first partial order with respect to hydrogen pressure for (**1**) and (**2**). The specific rate (K_p) is almost the same with values, respectively, of 1.92×10^{-7} ($s^{-1}\,bar^{-1}$) for (**1**) and 1.80×10^{-7} ($s^{-1}\,bar^{-1}$) for (**2**) (Table 2).

2.2.3. Temperature

The influence of the temperature on the conversion and selectivity of the reactions in the presence of $RuH_2(CO)_2(P^nBu_3)_2$ (**1**), $RuH_2(CO)_2(PPh_3)_2$ (**2**) and $RuH_2(PPh_3)_4$ (**3**) has been investigated among 353 and 393 K. The results are reported in Table 4.

The complex (**3**) shows the best catalytic activity giving a 34.7% conversion at 353 K, with formation of 1,2,3,4-THQ as the main product and 5,6,7,8-THQ and DHQ as secondary products (entry 32). An increase of the temperature causes an appreciable increase of the conversion from 34.7% at 353 K to 76.4% at 393 K (entry 33). In the presence of (**3**), 1,2,3,4-THQ is always the main product. As the temperature increases the amount of DHQ prevails on that of 5,6,7,8-THQ.

Concerning the other catalysts, complex (**1**) does not show any catalytic activity at 353 K, under 100 bar of hydrogen (entry 26) while (**2**) is slightly active with a conversion of 3.9% (entry 29). Working at 393 K the conversion increases up to 20.1% for (**1**) and 20.8% for (**2**) (entries 28 and 31). The temperature does not affect the selectivity of the reaction, since the catalyst (**1**) provides 1,2,3,4-THQ with a high regioselectivity while (**2**) gives exclusively 1,2,3,4-THQ.

The activation parameters [9] have been evaluated using the data reported in Table 3 and the Gibbs equation. Negative activation entropies were found for all catalysts, indicating, in all cases, an associative process in the rate-determining step of the reaction (Table 2).

2.2.4. Catalyst concentration

An increase of the concentration of (**3**) shows a beneficial effect on the conversion that changes from 12.9% to 54.4% when the catalyst/Q ratio changes from 1/1000 to 1/100 (entries 24 and 34–35) (Table 5), while the selectivity of the reaction seems basically unaffected. The kinetic analyses of the data reported in Table 4 show a first partial order with respect to the concentration of the catalyst, with a specific rate of $1.02 \times 10^{-1}\,M^{-1}\,s^{-1}$ (Table 2).

Table 4
Hydrogenation of quinoline: influence of reaction temperature[a]

Entry	Catalyst code	T (K)	$P(H_2)$ (bar)	Conversion (%)	Reaction mixture composition (%)			
					Q	1,2,3,4-THQ	5,6,7,8-THQ	DHQ
26	**1**	353	100	0	100	0	0	0
27	**1**	373	100	18.9	81.1	17.3	0.9	0.7
28	**1**	393	100	20.1	79.9	18.4	1.0	0.7
29	**2**	353	100	3.9	96.1	3.9	0	0
30	**2**	373	100	19.8	80.2	19.8	0	0
31	**2**	393	100	20.8	79.2	20.8	0	0
32	**3**	353	25	34.7	65.3	26.1	6.7	1.9
11	**3**	373	25	54.4	45.6	48.0	3.5	2.9
33	**3**	393	25	76.4	23.6	70.6	2.4	3.5

[Cat]: 0.66 mM; [Substrate]: 0.066 M; THF 20 ml; reaction time: 3 h.

[a] Q: quinoline; 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

Table 5
Hydrogenation of quinoline in the presence of $RuH_2(PPh_3)_4$ (**3**): influence of catalyst concentration[a]

Entry	Catalyst concentration (mM)	Conversion (%)	Reaction mixture composition (%)			
			Q	1,2,3,4-THQ	5,6,7,8-THQ	DHQ
34	0.0822	12.9	87.1	12.9	0	0
24	0.3300	40.1	59.9	36.6	1.8	1.7
35	0.6600	54.4	45.6	48.0	3.5	2.9

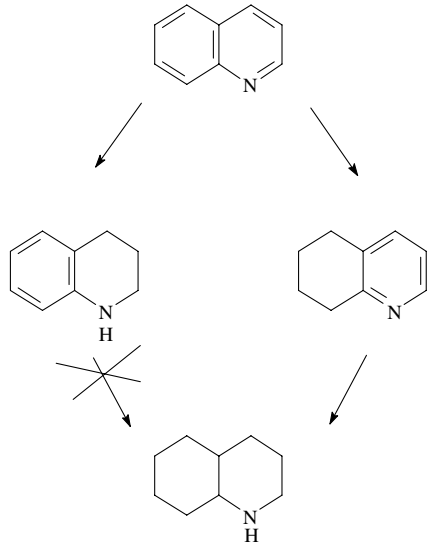
[Substrate]: 0.066 M; THF 20 ml; $P(H_2)$: 25 bar; reaction time: 3 h; T: 373 K.
[a] Q: quinoline; 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

2.3. Hydrogenation of 1,2,3,4-tetrahydroquinoline and 5,6,7,8-tetrahydroquinoline in the presence of $RuH_2(PPh_3)_4$

We have reported in Section 2.2.1 that $RuH_2(PPh_3)_4$ provides an appreciable amount of DHQ in the hydrogenation of Q. Its formation is attributed to the hydrogenation of 5,6,7,8-THQ (Scheme 2). In order to verify this hypothesis, we have tested the catalytic activity of the complex (**3**) in the hydrogenation of 1,2,3,4-THQ or 5,6,7,8-THQ, respectively. The reaction parameters have been chosen in order to compare the data of these reactions with those of the reduction of Q (Table 6).

The complex (**3**) shows a greater catalytic activity in the hydrogenation of the carbocyclic ring rather than the heterocyclic one: in fact there is no conversion of 1,2,3,4-THQ after 3 h (entry 36), while the conversion of 5,6,7,8-THQ is 7.5% (entry 37). A 2.1% conversion of 1,2,3,4-THQ may be obtained only after 24 (entry 38).

We may conclude that DHQ is formed from Q through the hydrogenation of the 5,6,7,8-THQ intermediate. The different reactivity of 5,6,7,8-THQ with respect to 1,2,3,4-THQ may be attributed to the presence of a more electronegative nitrogen atom on 5,6,7,8-THQ favouring the attack of the reducing agent on the heterocyclic ring.



Scheme 2.

2.4. Influence of an acid or a basic media

In the literature, several studies are reported on the possibility to modify the regioselectivity of the catalytic hydrogenation of quinoline using an acid or a basic media. Vierhapper and Eliel [10] obtained the prevalent hydrogenation of Q to 5,6,7,8-THQ working in the presence of HCl, in heterogeneous phase with PtO_2 as catalyst.

Campanati et al. [11] reported the use of a sterically hindered Lewis base to favour the formation of DHQ in the presence of heterogeneous catalytic systems (Ru/Al_2O_3 5 wt.%). They report that the products of partial hydrogenation of the heterocyclic ring of Q, formed during the reaction, are able to coordinate the active sites of the metal causing a progressive decrease of activity. This inhibition is a general behaviour in many catalytic reactions in which the products are stronger bases than reactants. The amine N^nBu_3, added to the media, should compete for the active sites of the catalytic system, hampering change in causing its deactivation.

On this basis, we have carried out some experiments in the presence of bases or acids such as NaOH, N^nBu_3, CH_3COOH or HCl in order to evaluate their influence on the rate and regioselectivity of the reaction. $RuH_2(PPh_3)_4$ (**3**) has been chosen as catalyst in consideration of its better catalytic activity. Different ratios between catalyst and base or acid were employed. The results are collected in Table 7.

The addition of NaOH to the reaction solution completely inhibits the Q conversion, in agreement to that reported by Campanati et al. [11]. Also, the presence of N^nBu_3 reduces the conversion from 54.4% (entry 11) to 41.7% (entry 40) and causes a change in the selectivity: 1,2,3,4-THQ still remains the prevailing product but the yield of DHQ significantly increases and overwhelms that of 5,6,7,8-THQ. Therefore, the base has a beneficial effect on the hydrogenation of Q to DHQ. It may be likely that in the absence of an added base the DHQ formed during the reaction competes with the substrate for the active sites of the catalyst reducing its activity. To confirm this hypothesis, it is worthy to note that the hydrogenation of quinoline in the presence of (**3**) carried out for 48 h, and longer (entries 15–17), does not show any remarkable increase of the conversion

Table 6
Hydrogenation of tetrahydroquinolines in the presence of $RuH_2(PPh_3)_4$ (**3**)[a]

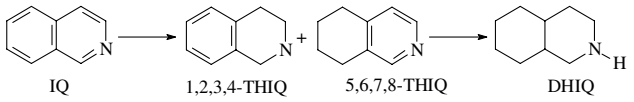
Entry	Substrate	Conversion (%)	Reaction time (h)	Reaction mixture composition (%)	
				Substrate	DHQ
36	1,2,3,4-THQ	0	3	100	0
37	5,6,7,8-THQ	7.5	3	92.5	7.5
38	1,2,3,4-THQ	2.1	24	97.9	2.1

$[RuH_2(PPh_3)_4]$: 0.66 mM; [Substrate]: 0.066 M; THF: 20 ml; $P(H_2)$: 25 bar; T: 373 K.
[a] 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

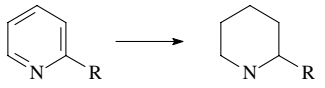
with respect to the reaction carried out for 24 h (entry 14); this may be attributed to the inhibiting effect of DHQ on the catalytic species.

Also, the presence of CH_3COOH causes a decrease of the conversion from 54.4% (entry 11) to 39.6% (entry 41), and affects the regioselectivity favouring the hydrogenation of the carbocyclic ring of the quinoline: 1,2,3,4-THQ and 5,6,7,8-THQ are obtained in similar amount, while DHQ remains lower. This behaviour may be ascribed to a different co-ordination of protonated quinoline, which can determinate a remarkable change in the selectivity.

Using a strong acid, that is a THF solution saturated with HCl, no reaction has been observed (entry 42).



Scheme 3.



R = H, PY R = H, PP

R = Me, MPY R = Me, MPP

Scheme 4.

2.5. Hydrogenation of isoquinoline, pyridine and 2-methylpyridine in the presence of $RuH_2(PPh_3)_4$

In order to evaluate the influence of different electronic and steric characteristics of the substrate on the conversion and selectivity, the hydrogenation of isoquinoline (IQ) (Scheme 3) has been performed and the results are reported in Table 8.

The complex (**3**) hydrogenates IQ with a lower catalytic activity than Q: the conversion is 36.3% (entry 43) but surprisingly an opposite selectivity is obtained since the reaction gives exclusively 5,6,7,8-tetrahydroquinoline (5,6,7,8-THIQ).

Table 7
Hydrogenation of quinoline in the presence of $RuH_2(PPh_3)_4$ (**3**): influence of the presence of a base or an acid[a]

Entry	Acid or base	Concentration (mM)	Conversion (%)	Reaction mixture composition (%)			
				Q	1,2,3,4-THQ	5,6,7,8-THQ	DHQ
11	//	//	54.4	45.6	48.0	3.5	2.9
39	NaOH	3.96	0	100	0	0	0
40	N^nBu_3	66.00	41.7	58.3	38.6	0.8	2.3
41	CH_3COOH	3.96	39.6	60.4	21.9	15.8	1.9
42	HCl	saturated sol.	0	100	0	0	0

$[RuH_2(PPh_3)_4]$: 0.66 mM; [Substrate]: 0.066 M; THF: 20 ml; $P(H_2)$: 25 bar; T: 373 K; reaction time: 3 h.
[a] Q: quinoline; 1,2,3,4-THQ: 1,2,3,4-tetrahydroquinoline; 5,6,7,8-THQ: 5,6,7,8-tetrahydroquinoline; DHQ: decahydroquinoline.

Table 8
Hydrogenation of the nitrogen containing heterocycles in the presence of $RuH_2(PPh_3)_4$ (**3**)[a]

Entry	Substrate	Conversion (%)	Reaction mixture composition (%)					
			Substrate	1,2,3,4-TH	5,6,7,8-TH	DH	PP	MPP
11	Q	54.4	45.6	48.0	3.5	2.9	–	–
43	IQ	36.3	63.7	0	36.3	0	–	–
44	PY	36.3	63.7	–	–	–	36.3	–
45	MPY	4.1	95.9	–	–	–	–	4.1

$[RuH_2(PPh_3)_4]$: 0.66 mM; [Substrate]: 0.066 M; THF 20 ml; $P(H_2)$: 25 bar; T: 373 K; reaction time: 3 h.
[a] Q: quinoline; 1,2,3,4-TH: 1,2,3,4-tetrahydroquinoline or 1,2,3,4-tetrahydroisoquinoline; 5,6,7,8-TH: 5,6,7,8-tetrahydroquinoline or 5,6,7,8-tetrahydroisoquinoline; DH: decahydroquinoline or decahydroisoquinoline; PY: pyridine; MPY: 2-methylpyridine; PP: piperidine; MPP: 2-methylpiperidine.

Pyridine (PY) and 2-methylpyridine (MPY) are also hydrogenated in the presence of $RuH_2(PPh_3)_4$ (**3**) (Table 8) (Scheme 4). A lower catalytic activity with respect to the hydrogenation of Q has been observed also in these reductions with conversions, respectively, of 36.3% (entry 44) and 4.1% (entry 45). These data are in agreement with those reported by Fish et al. [12], who noted a decrease of the conversion as the basicity and steric hindrance around the nitrogen atom increase.

3. Conclusion

The dihydride ruthenium complexes, $RuH_2(CO)_2(P^nBu_3)_2$ (**1**), $RuH_2(CO)_2(PPh_3)_2$ (**2**) and $RuH_2(PPh_3)_4$ (**3**) are catalytically active in the hydrogenation of quinoline (Q). The best performance has been obtained with $RuH_2(PPh_3)_4$ (**3**), which allows a 86.7% conversion at 373 K while $RuH_2(CO)_2(P^nBu_3)_2$ (**1**) and $RuH_2(CO)_2(PPh_3)_2$ (**2**) give lower conversions (35.6% and 37.1%, respectively) but higher selectivities.

The catalytic activity is significantly affected by the hydrogen pressure. The reaction in the presence of $RuH_2(CO)_2(P^nBu_3)_2$ (**1**) or $RuH_2(CO)_2(PPh_3)_2$ (**2**) shows a first partial order with respect to hydrogen pressure. The $RuH_2(PPh_3)_4$ (**3**) catalyst shows a singular trend: the conversion rises when increasing the hydrogen pressure up to 50 bar, but at higher pressure (75 and 100 bar) the conversion decreases, and the selectivity changes suggesting the presence of different catalytically active species as the amount of hydrogen changes.

A first partial order with respect to the catalyst concentration has been detected in the presence of $RuH_2(PPh_3)_4$ (**3**).

The regioselectivity of the hydrogenation of Q is complete using $RuH_2(CO)_2(PPh_3)_2$ (**2**) as catalyst, while in the presence of $RuH_2(CO)_2(PBu_3)_2$ or $RuH_2(PPh_3)_4$ an appreciable amount of 5,6,7,8-THQ and DHQ is formed. Also, the presence of a weak acid or base in the reaction medium changes the selectivity. It is interesting to note that in the presence of acetic acid the products of partial reduction (1,2,3,4-THQ and 5,6,7,8,-THQ) are formed in equal amount, therefore, the presence of acetic acid favours the hydrogenation of the carbocyclic ring with respect to heterocyclic one.

The complex (**3**) is also catalytically active in the hydrogenation of isoquinoline (IQ), although in a less extent than quinoline (Q), with a complete and unusual regioselectivity towards 5,6,7,8-THIQ [13]. A different coordination mode of the substrate to the metal centre may be claimed in agreement with the result obtained for the hydrogenation of Q in acid media.

Pyridine (PY) and 2-methylpyridine (MPY) may be hydrogenated in the presence of the complex (**3**). The conversions are lower confirming a strong influence of steric and electronic factors, as reported by Fish's studies [12–15].[1]

In conclusion, the three complexes (**1**)–(**3**) are catalytically active in the hydrogenation of nitrogen containing heterocycles giving results comparable with those reported in the literature for other ruthenium systems like $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_4H_4(CO)_{12}$, but operating under milder reaction temperatures (353–373 K against 453 K) and lower catalyst/substrate ratio (1/100 against 1/10) [15].

The data collected are not sufficient to propose a mechanism of the reaction but the negative value of the activation entropy indicates with all catalysts an associative rate-determining step. Further studies are in progress to collect new evidences on the mechanism of these reactions.

4. Experimental

4.1. Instruments and materials

Quantitative analysis was performed by GC using a Shimadzu GC-14A chromatograph coupled with a computer Shimadzu C-R4A, equipped with a FID detector, using 2-m packed columns filled with a CW 20 M + KOH (Chromosorb W) as stationary phase. *p*-Xylene was used as internal standard and calibration curves for quinoline (Q) and 1,2,3,4-tetrahydroquinoline (1,2,3,4-THQ) were calculated 5,6,7,8-tetrahydroquinoline (5,6,7,8-THQ), decahydroquinoline (DHQ), isoquinoline (IQ) and 5,6,7,8-tetrahydroisoquinoline (5,6,7,8-THIQ) were assumed to have the same response factor than 1,2,3,4-THQ. Pyridine (PY), 2-methylpyridine (MPY), piperidine (PP) and 2-methylpiperidine (MPP) were assumed to have the same response factors.

The identity of the products was confirmed by GC–MS using a Shimadzu apparatus (GCMS-QP5050A) equipped with a capillary column SP™-1 (length 30 m, i.d. 0.25 mm, film thickness 0.1 μm).

Elemental analyses were performed with a Perkin–Elmer Analyser model 2400 Series II CHNS/O. IR spectra were recorded with a Perkin-Elmer mod. 1760 FTIR spectrometer.

^1H, ^{13}C and ^{31}P NMR spectra were recorded using a Varian VXR300 spectrometer operating at 299.987 MHz for ^1H, at 75.429 MHz for ^{13}C and at 121.421 MHZ for ^{31}P NMR, using solutions in appropriate solvents. $SiMe_4$ was used as external standard for ^1H and ^{13}C NMR, H_3PO_4 (85%) for ^{31}P NMR (signals reported as positive downfield to the standard). ^{13}C

[1] The p*K*a of the substrates are: Q 4.94, IQ 5.10, PYR 5.23, MePYR 5.97; The steric hindrance are in the following order: PYR ≅ IQ < MePYR ≅ Q.

and ^{31}P NMR spectra were acquired using a broadband decoupler.

All manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques. Reagents and solvents were purified and dried as reported. Tetrahydrofuran (J.T. Baker pure at 99%) was dried and deoxygenated by refluxing and distilling over sodium/potassium amalgam under nitrogen atmosphere, immediately before its use (bp 66 °C). $Ru_3(CO)_{12}$ (Aldrich pure at 99%) was purified by crystallisation from methanol under a 20 bar of CO pressure. Pyridine (Carlo Erba pure at 99.6%) was refluxed over KOH for 2 h, then distilled under nitrogen, immediately before its use (bp 115 °C). 2-Methylpyridine (Aldrich pure at 98%) was distilled at reduced pressure, immediately before its use (bp 25 °C/5 mm Hg). Other solvents and reagents were obtained from commercial suppliers and employed without further purification.

The following catalysts were prepared according to the literature and their spectroscopic characteristics were in agreement with the data reported: $Ru(CO)_2(CH_3COO)_2(P^nBu_3)_2$ [16], $Ru(CO)_2(CH_3COO)_2(PPh_3)_2$ [17], $RuH_2(CO)_2(P^nBu_3)_2$ (**1**) [3], $RuH_2(CO)_2(PPh_3)_2$ (**2**) [5], and $RuH_2(PPh_3)_4$ (**3**) [1].

4.2. Catalytic hydrogenation

A typical hydrogenation experiment was reported for each ruthenium catalyst: the same procedure was employed for all substrates.

4.2.1. Hydrogenation in the presence of $RuH_2(CO)_2(P^nBu_3)_2$ (1), $RuH_2(CO)_2(PPh_3)_2$ (2)

Each catalyst was prepared immediately before its use from the corresponding acetate complex, following the procedure reported in the literature [3,5]. $Ru(CO)_2(CH_3COO)_2(PR_3)_2$, ($1.32 \times 10^{-5}$ mol), 4 mL of dry THF, and Na_2CO_3 (0.5 g) were introduced in a glass vial inserted in a stainless steel autoclave, then hydrogen up to 100 bar was added. The vessel was heated at 100 °C for 14 h in a thermostated oil bath. The reactor was cooled, the gas vented out and the yellow solution filtered and transferred in a Schlenk tube containing the substrate (1.32×10^{-3} mol) and *p*-xylene (1.131×10^{-3} mol) as internal standard. A further amount of THF was added up to a total volume of 20 mL. The solution was introduced in a high-pressure vessel under nitrogen atmosphere, then hydrogen was added up to the pressure required. The vessel was rocked in an oil bath, heated at the prefixed temperature, for the time required.

At the end of the reaction, the vessel was cooled down, the gas vented out and the solution analysed by GC and GC–MS techniques.

4.2.2. Hydrogenation in the presence of $RuH_2(PPh_3)_4$ (3)

In a Schlenk tube, $RuH_2(PPh_3)_4$ (**3**) (1.32×10^{-5} mol), substrate (1.32×10^{-3} mol), and *p*-xylene (1.131×10^{-3} mol) as internal standard were dissolved in THF (20 mL). The solution was transferred by suction in a Parr autoclave model 4759 (150 mL) electrically heated, with a magnetic drive stirrer. After addition of hydrogen up to the pressure required, the reactor was stirred at the established temperature.

At the end of the reaction, the vessel was cooled down, the gas vented out and the solution analysed by GC and GC–MS techniques.

The same procedure was followed for the catalytic hydrogenations in the presence of NaOH, CH_3COOH, and N^nBu_3. The hydrogenation in the presence of HCl was carried out using a saturated HCl solution prepared by bubbling gaseous HCl in THF.

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