TRANSFER HYDROGENATION OF CARBONYL COMPOUNDS AND ALKENES CATALYZED BY RUTHENIUM(II)–N-HETEROCYCLE CARBENE COMPLEXES

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Dedicated to Professor Štefan Toma on the occasion of his 70th birthday in recognition of his outstanding contributions to organic synthesis and transition metal catalysis.

The Ru(II)–N-heterocycle carbene complexes [$RuCl_2(\eta^6$-*p*-cymene)L] (L = 1-butyl-3-methylimidazol-2-ylidene) and [$RuCl(\eta^6$-*p*-cymene)L(pta)]Cl (pta = 1,3,5-triaza-7-phosphaadamantane) showed excellent catalytic activities (with turnover frequencies up to 1116 h^{-1}) in the hydrogen transfer reduction of cinnamaldehyde and several ketones using propan-2-ol/KOH as a H-donor. Similar hydrogenations of *trans*-stilbene and cyclohexene were characterized by low conversions. The hydrogenation of 4-phenylbut-3-en-2-one and cinnamaldehyde proceeded with moderate selectivities of the formation of the saturated alcohol or of the of C=C hydrogenation (giving saturated ketone or saturated aldehyde). In the case of cinnamaldehyde, the unsaturated alcohol is initially formed; however, subsequent redox isomerization to the saturated aldehyde with the same catalyst diminishes its yield. The hydrogen transfer from formate to 4-phenylbut-3-en-2-one in an aqueous-organic two-phase mixture was also demonstrated.

Keywords: Aldehydes; Carbene complexes; Hydrogen transfer; Ketones; Ruthenium; Catalytic hydrogenation; Reductions.

Hydrogenation of unsaturated substrates by hydrogen transfer from suitable H-donors (DH_2) is a valuable alternative to the use of dihydrogen[1]. The most often employed H-donors are propan-2-ol, formic acid (or its azeotrope with triethylamine) and aqueous solutions of formates. All these reagents are liquids, easy to handle; the reaction conditions are generally mild. Several excellent reviews[2] on this topic are available, describing a wide variety of reactions performed with heterogeneous or homogeneous catalysts. Among the latter, ruthenium(II) complexes stand out with their

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catalytic activity and selectivity. In certain cases, prochiral substrates, such as acetophenone were hydrogenated with 100% conversion and 99% e.e. by hydrogen transfer from aqueous formate in the presence of Ru(II) complexes with approriate chiral ligands, successful examples being the monotosylated *N*,*N*′-diphenylethylenediamine and the monotosylated cyclohexane-1,2-diamine[2a,3].

Very importantly, the hydrogen transfer reductions are not simple reproductions of hydrogenations using H_2; in several cases different selectivities have been found. For example, unsaturated aldehydes, such as cinnamaldehyde are hydrogenated at their C=C bonds under catalysis with [$RuCl_2(PPh_3)_3$]. Conversely, aldehydes are easily hydrogenated to alcohols in the presence of the same catalyst by a biphasic hydrogen transfer from aqueous formate[4], and cinnamaldehyde was selectively reduced to cinnamyl alcohol with aqueous Na formate when the water-soluble analog of the above catalyst, [{$RuCl_2$(*m*tppms)$_2$}$_2$] was used (*m*tppms = Na-3-(diphenylphosphanyl)-benzene-1-sulfonate)[5]. The differences between hydrogenations with H_2 and DH_2 originate from the formation of different hydride species in the reactions of the same catalyst precursor and H_2 or DH_2 and due to different mechanisms of the two reaction types[5c–5e].

N-heterocycle carbenes (NHC) are now widely used in homogeneous catalysis[6]. Usually, the transition metal complexes of these ligands are robust and withstand decomposition under catalytic conditions better than complexes of tertiary phosphines. As part of our earlier studies, we have synthesized[7] the half-sandwich Ru–NHC complex, [$RuCl_2$(η^6-*p*-cymene)L] (**1**) (L = 1-butyl-3-methylimidazol-2-ylidene) from the easily available [{$RuCl_2$-(η^6-*p*-cymene)}$_2$] by transmetallation with the silver carbene complex obtained from 1-butyl-3-methylimidazolium chloride and Ag_2O. Reaction of **1** with the water-soluble 1,3,5-triaza-7-phosphaadamantane (pta) afforded [RuCl(η^6-*p*-cymene)L(pta)]Cl (**2**), containing both NHC and tertiary phosphine ligands. Complexes **1** and **2** showed moderate activity in the hydrogenation[7] of alkenes, aldehydes and ketones (10 bar H_2, 80 °C, turnover frequencies, TOF, in the range 39–139 h^{-1}) as well as in the oligomerization[8] of alkynes. Interestingly, these complexes also catalyzed the redox isomerization of allylic alcohols[9] to the corresponding oxo compounds (e.g. oct-1-en-3-ol to octan-3-one) with TOF up to 125 h^{-1}.

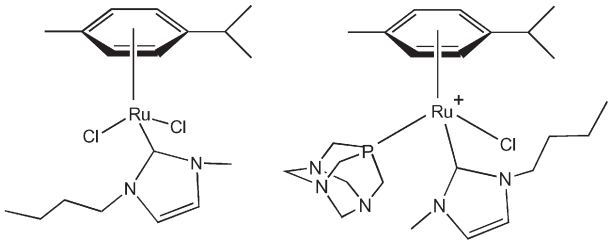
Of the possible mechanisms of the redox isomerization of allylic alcohols, both the η^3-allyl[10] and the η^3-oxo-allyl[11,12] mechanisms consider initial dehydrogenation of the allylic alcohol with the concomitant formation of a hydrido complex; the hydride ligand is transferred to the C=C bond in the next steps of the reaction, thereby closing the catalytic cycle. In other

words, such redox isomerizations are internal transfer hydrogenations. The pronounced ability of **1** and **2** to catalyze the isomerization of allylic alcohols prompted us also to investigate their catalytic properties in more widely employed intermolecular hydrogen transfer reactions, and the first results of these studies are described herein.

EXPERIMENTAL

The products were identified and the catalytic reactions were followed by ^{1}H NMR spectroscopy (Bruker Avance 360) or by gas chromatography (HP5890 Series II, Chrompack WCOT Fused Silica CP WAX 52 CB 30 m × 0.32 mm, FID, carrier gas argon).

[$RuCl_2(\eta^6$-*p*-cymene)L] (**1**) and [$RuCl(\eta^6$-*p*-cymene)L(pta)]Cl (**2**) (Scheme 1) were prepared as described earlier[7]. All other reagents were obtained from Aldrich, Fluka and Merck and used as received after purity check by GC and ^{1}H NMR.



SCHEME 1
Structures of [$RuCl_2(\eta^6$-*p*-cymene)L] (**1**) and of [$RuCl(\eta^6$-*p*-cymene)L(pta)]Cl (**2**) (L = 1-butyl-3-methylimidazol-2-ylidene; pta = 1,3,5-triaza-7-phosphaadamantane)

All manipulations were run under oxygen-free argon atmosphere. A representative example of a catalytic transfer hydrogenation is as follows: **1** (4.5 mg, 0.01 mmol) and benzylideneacetone (296 mg, 2.0 mmol) were placed into a Schlenk tube closed with a rubber septum. The tube was then evacuated and filled with argon several times. Propan-2-ol (10 ml), containing KOH (56 mg, 1 mmol) was injected through the septum. The tube was immersed into a thermostatted bath (80 °C) and the reaction mixture was stirred vigorously for the desired reaction (or sampling) time. Samples were filtered through a small silica gel plug and analyzed by gas chromatography. In the case of the aqueous-organic biphasic transfer hydrogenation of benzylideneacetone, the reaction mixture was extracted twice with $CHCl_3$ (1.5 ml), the combined extracts were dried over anhydrous $MgSO_4$ and analyzed by GC.

RESULTS AND DISCUSSION

In the presence of KOH, both **1** and **2** catalyzed the hydrogen transfer from propan-2-ol to ketones (acetophenone, benzophenone, benzylideneacetone), cinnamaldehyde, stilbene and cyclohexene. The time course of the reaction of acetophenone is shown in Fig. 1. The linear phase of the

conversion-vs-time function (between 2 and 7 h) is characterized by a TOF of 19 h^{-1}. Under the experimental conditions used, the highest conversion was 85% (total number of turnovers, TON = 120), indicating the equilibrium position of the reaction acetophenone + propan-2-ol $\rightleftharpoons$ 2-phenylethan-1-ol + acetone in the closed Schlenk tube. As seen from the data in Table I (note that experimental conditions are somewhat different from those in Fig. 1), both catalysts were highly active even in the case of sterically more hindered benzophenone, leading to close-to-quantitative conversions. On the other hand, *trans*-stilbene and cyclohexene underwent conversions in the 7–4% range with catalyst **1**, and cyclohexene showed hardly any conversion (1%) with catalyst **2**. These low conversions are not unexpected as propan-2-ol is generally more efficient in transfer hydrogenations of aldehydes and ketones than in those of alkenes or alkynes[1].

The possible products of hydrogenation of benzylideneacetone and cinnamaldehyde are shown in Scheme 2. With both catalysts, the transfer hydrogenation of the unsaturated ketone proceeded with 100% conversion; however, **1** and **2** showed different selectivities. While with **1** the major product (82%) was the saturated alcohol (4-phenylbutan-2-ol), with **2** the reaction afforded mainly the saturated ketone (4-phenylbutan-2-one). Conversely, in the hydrogenation of cinnamaldehyde **1** was found less active than **2**; nevertheless, the saturated aldehyde was the major product with both complexes.

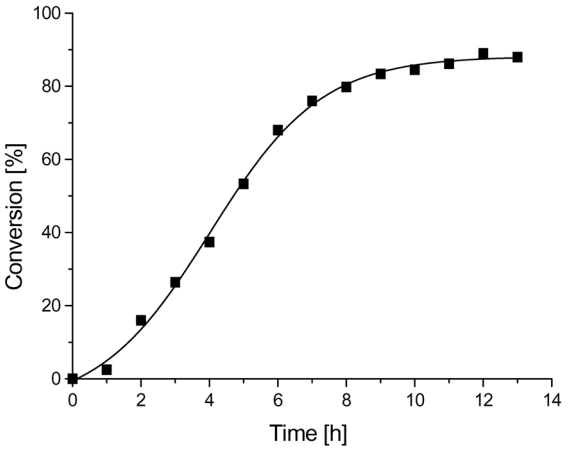
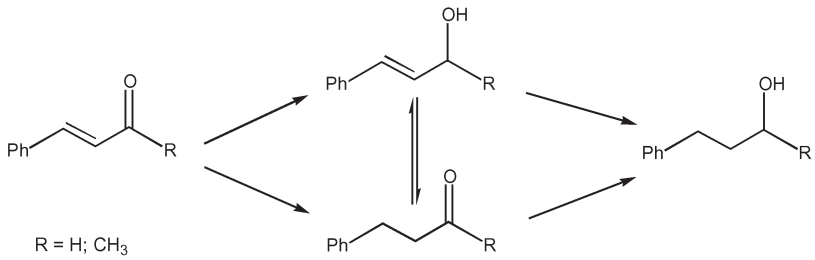


FIG. 1
Time course of transfer hydrogenation of acetophenone to 2-phenylethan-1-ol with propan-2-ol/KOH catalyzed with [$RuCl_2(\eta^6$-*p*-cymene)L] (**1**). Conditions: 0.0095 mmol catalyst, 1.334 mmol substrate, 2 ml propan-2-ol, 1 mmol KOH, 80 °C



SCHEME 2
Possible products of hydrogen transfer reduction of cinnamaldehyde (R = H) and benzylideneacetone (R = CH_3)

The catalytic transfer hydrogenation of 4-phenylbut-3-en-2-one with propan-2-ol with **1** as the catalyst is a fast reaction. When run with a relatively small [substrate]/[catalyst] ratios ([S]/[C] ≤ 100), the substrate fully reacted in a few minutes and only the hydrogenation of the intermediate

TABLE I
Reduction product yields (in %) of various substrates by hydrogen transfer from propan-2-ol catalyzed with [$RuCl_2(\eta^6$-*p*-cymene)L] (**1**) and [$RuCl(\eta^6$-*p*-cymene)L(pta)]Cl (**2**) (L = 1-butyl-3-methylimidazol-2-ylidene; pta = 1,3,5-triaza-7-phosphaadamantane)

Substrate	Product(s)[a]	Catalyst	
		1	**2**
Acetophenone	2-phenylethan-1-ol	95	96
Benzophenone	diphenylmethanol	98	97
trans-4-Phenylbut-3-en-2-one (benzylideneacetone)	4-phenyl-3-buten-2-ol	0	0
	4-phenylbutan-2-one	17	77
	4-phenylbutan-2-ol	82	23
trans-Cinnamaldehyde	cinnamyl alcohol	17	2
	3-phenylpropanal	39	77
	3-phenylpropan-1-ol	2	23
trans-Stilbene	1,2-diphenylethane	7	7
Cyclohexene	cyclohexane	4	1

Conditions: 0.02 mmol catalyst, 2.0 mmol substrate, 10 ml propan-2-ol, 1 mmol KOH, 80 °C, 4 h.
[a] When product yields do not sum up to 100%, the rest is unreacted substrate.

4-phenylbutan-2-one to 4-phenylbutan-2-ol could be followed. However, as shown in Fig. 2, at high substrate loadings the unsaturated alcohol intermediate, 4-phenylbut-3-en-2-ol was also observed in the first few minutes of the reaction. Under the conditions in Fig. 2, the transfer hydrogenation of 4-phenylbut-3-en-2-one was over in 30 min, i.e. the catalyst showed TOF = 704 h^{-1}.

The transfer hydrogenation of cinnamaldehyde catalyzed by **1** showed some peculiar features (Fig. 3). The total conversion of the substrate reached 93% (TOF = 1116 h^{-1}) within the first 10 min and did not change significantly in the next 50 min. At the same time, the amount of the totally reduced product, 3-phenylpropan-1-ol, slowly decreased from 5 to 3%. These two phenomena refer to the possibility of the reverse hydrogen transfer, i.e. from 3-phenylpropan-1-ol to acetone (the product of the dehydrogenation of propan-2-ol). An obvious and significant change in the product distribution accompanied the transformation of cinnamyl alcohol to dihydrocinnamaldehyde (3-phenylpropanal). It seems that the catalyst is also active in the redox isomerization (the internal hydrogen transfer) of cinnamyl alcohol, as can be expected from our earlier findings[9]. From the data in Fig. 3 it can be concluded that in the very fast first phase of the reaction, cinnamyl alcohol and dihydrocinnamaldehyde are formed inde-

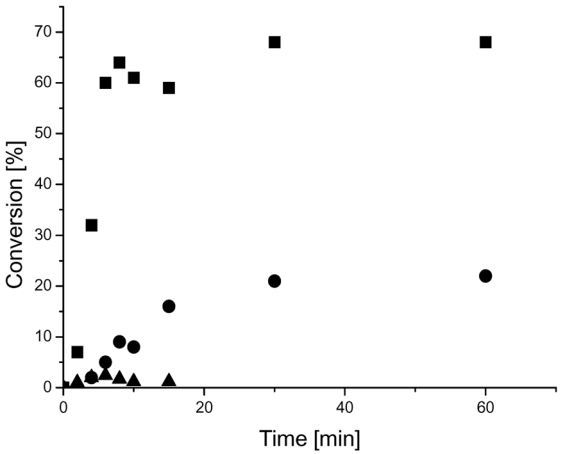


FIG. 2

Time course of transfer hydrogenation of 4-phenylbut-3-en-2-one to 4-phenylbut-3-en-2-ol (▲), 4-phenylbutan-2-one (■) and 4-phenylbutan-2-ol (●) with propan-2-ol/KOH catalyzed with [$RuCl_2(\eta^6$-*p*-cymene)L] (**1**). Conditions: 0.01 mmol catalyst, 4.0 mmol substrate, 10 ml propan-2-ol, 2 mmol KOH, 80 °C

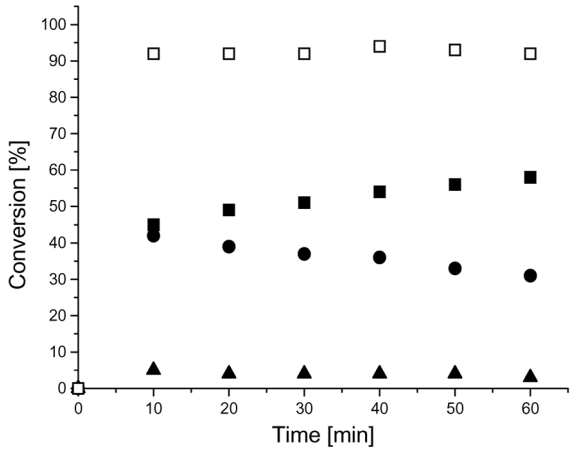


FIG. 3
Time course of transfer hydrogenation of cinnamaldehyde (□ total conversion) to 3-phenylpropanal (■), cinnamyl alcohol (●) and 3-phenylpropan-1-ol (▲) with propan-2-ol/KOH catalyzed with [$RuCl_2(\eta^6$-*p*-cymene)L] (**1**). Conditions: 0.01 mmol catalyst, 2.0 mmol substrate, 10 ml propan-2-ol, 1 mmol KOH, 80 °C

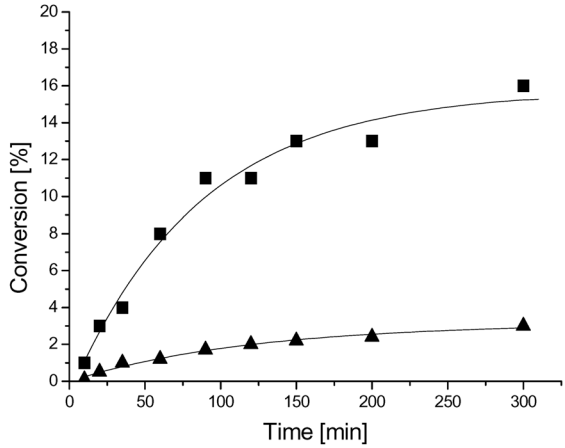


FIG. 4
Time course of the transfer hydrogenation of 4-phenylbut-3-en-2-one to 4-phenylbutan-2-one (■) and 4-phenylbut-3-en-2-ol (▲) with HCO_2Na/H_2O catalyzed with [$RuCl_2(\eta^6$-*p*- cymene)L] (**1**). Conditions: 0.01 mmol catalyst, 2.0 mmol substrate, 1.0 mmol HCO_2Na, 3 ml 0.1 M phosphate buffer (pH 7.0), 80 °C

pendently and at about the same rate (after 10 min, their concentrations were 43 and 45%, respectively) and it is only the almost total lack of further reactivity of the saturated aldehyde, which makes the redox isomerization of cinnamyl alcohol observable.

An attempt was also made to exploit the water solubility of **1** and run the catalytic transfer hydrogenation of 4-phenylbut-3-en-2-one in an aqueous-organic system using an aqueous solution of Na formate as the H-donor. At the reaction temperature, the substrate melts and forms a separate organic phase. Figure 4 shows that under such conditions, a slow reaction (TOF = 18 h^{-1}) took place affording 4-phenylbutan-2-one as the major product accompanied by only a small amount of the unsaturated alcohol. This selectivity is opposite to that observed with propan-2-ol/KOH as the H-donor (Table I), while the low reaction rate may be (partly) due to the mass transfer limitations in the two-phase mixture. The unreacted substrate and the products can be separated from the catalyst-containing aqueous phase by extraction; however, the possibility of recycling the catalyst and the ways to improve the catalytic efficiency of hydrogen transfer need further investigations.

CONCLUSIONS

The Ru(II)–N-heterocycle carbene complexes **1** and **2** showed excellent catalytic activities (with turnover frequencies up to 1116 h^{-1}) in the hydrogen transfer reduction of cinnamaldehyde and several ketones using propan-2-ol/KOH as the H-donor. Similar hydrogenations of *trans*-stilbene and cyclohexene were characterized by low conversions. The hydrogenation of an unsaturated ketone (4-phenylbut-3-en-2-one) and unsaturated aldehyde (cinnamaldehyde) showed only moderate selectivities in the formation of the saturated alcohol or the product of C=C hydrogenation (saturated ketone or saturated aldehyde) while the yield of the product of selective C=O hydrogenation (unsaturated alcohol) never exceeded 20%. The possibility of hydrogen transfer from formate to 4-phenylbut-3-en-2-one in an aqueous-organic two-phase mixture was also demonstrated.

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