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A Sustainable Approach to Selective Hydrogenation of Unsaturated Esters and Aldehydes with Ruthenium Catalysts

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The reduction of esters and aldehydes to alcohols is an important reaction in the chemical industry to produce a wide range of bulk and fine chemicals. Herein, the unexpected behavior of three state-of-the-art, commercially available Ru-catalysts for the hydrogenation of these feedstocks is reported. For ester and aldehydes containing a C=C bond, it was possible to carry out the selective hydrogenation of the ester or

aldehyde functionality while keeping the C=C double-bond essentially untouched. Furthermore, it is demonstrated that these substrates can be reduced under very mild reaction conditions (as low as 40 °C and 5 bar of H₂) and that anisole, a solvent with a high sustainability rank, is suitable for these catalytic hydrogenations.

Introduction

The reduction of esters to alcohols is one of the most important organic transformations due to its application in the syntheses of useful building blocks, and for the industrial production of fatty alcohols, agrochemicals, pharmaceuticals, flavors and fragrances.^[1] The classical reduction methods typically involve the use of stoichiometric amounts of aluminum or boron hydrides, which implies in large amounts of waste, laborious work-up, safety issues and low functional-group tolerance.^[2] In contrast, catalytic hydrogenation is an environmentally benign and atom-economic synthetic approach.^[3]

In the industry, the catalytic hydrogenation of esters to alcohols often employs heterogeneous catalysts. Unfortunately, these catalysts typically require harsh reaction conditions such as high temperature and pressure (typically > 200 °C and > 200 bar of H₂), which may lead to side products.^[4] The alternative of enzyme-based catalysts has some advantages such as not relying on precious metals and presenting a high selectivity under relative mild conditions. However, the current technology cannot yet be applied to the reductions of esters.^[5]

This brings a tremendous opportunity for homogeneous catalysts, which can work under mild conditions (at temperatures as low as 60 °C), with very low catalyst loading and fewer safety issues, as it has been reported, inter alia, by the groups of Beller,^[6] Milstein,^[7] Gusev,^[8] Teunissen,^[9] Clarke,^[3,10] Ikariya,^[11] Kuriama,^[12] Zhou,^[13] Zhang,^[14] and Chianese.^[15] Many of the reported studies employed ruthenium catalysts, however, very efficient osmium-based catalysts have also emerged in recent years. Several recent studies have tested complexes of earth abundant metals^[16] (e.g. Fe,^[6b,17] Co^[7a,18] and Mn^[19]), but the reported catalytic efficiency is still far from that of the best ruthenium and osmium catalysts.^[8a,20]

With respect to the substrate, many existing homogeneous catalysts show high activity in the hydrogenation of carbonyl derivatives such as aldehydes, ketones and imines. However, the reduction of carboxylic acid derivatives such as esters or lactones is typically more challenging to achieve. In this work, we aimed to compare the effectiveness of three state-of-the-art, commercially available Ru-based catalysts shown in Figure 1 for the hydrogenation of a series of aliphatic esters under mild reaction conditions. **Ru-1**, developed at Firmenich and reported by Saudan and co-workers,^[21] is based on a P,N-bidentate ligand. **Ru-2** and **Ru-3**, reported by Gusev et al.,^[8a,b] feature pincer-type NNP and SNS ligands. Additionally, we aimed to replace THF and toluene, solvents commonly used in ester reduction, by anisole, a low-cost alternative with low toxicity and a high sustainability rank.

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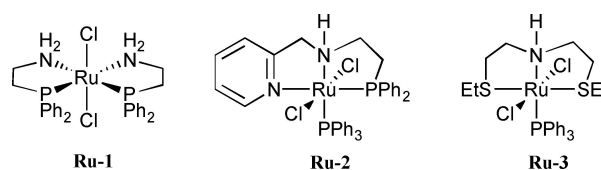
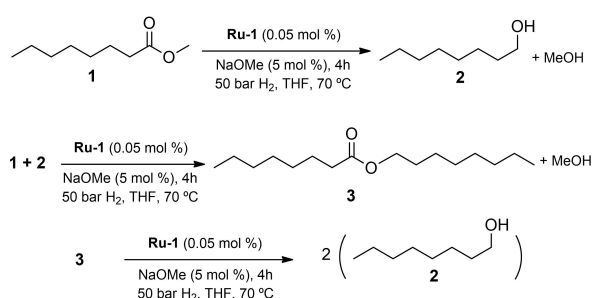


Figure 1. Complexes **Ru-1** (PNNP); **Ru-2** (PNN) and **Ru-3** (SNS).

Results and Discussion

For our initial catalytic investigations, methyl octanoate was chosen as a model substrate because of its ready availability. Furthermore, methyl octanoate does not have other functional group that could be concurrently reduced, allowing us to focus on the activity of the catalysts solely on the reduction of the ester functionality. In the reduction of methyl octanoate, the only possible side-product is octyl octanoate, produced by the transesterification of methyl octanoate with octanol, as depicted in Scheme 1.

However, as octyl octanoate is an intermediate that ultimately evolves into octanol, its formation does not represent a significant problem. For screening and optimization of the reaction conditions, **Ru-1** was used as the catalyst. In Table 1, three parameters were initially assessed: catalyst loading (entries 1–3), H₂ pressure (c.f. entries 3, 6, and 9), reaction temperature (c.f. entries 3, 12, 13 and 14). We chose a catalyst loading of 0.05 mol%, H₂ pressure of 50 bar and temperature of 70 °C for further studies. The base is necessary to activate the



Scheme 1. Methyl octanoate (**1**) hydrogenation to octanol (**2**).

Table 1. Screening of reaction conditions for the hydrogenation of **1** with **Ru-1** as catalyst.^[a]

Entry	Cat. Loading [mol %]	T [°C]	<i>p</i> (H ₂) [bar]	Conversion [%] ^[b]	Product Distribution [%] ^[b,c]	
					2	3
1	0.005	100	30	7	4	96
2	0.01	100	30	34	23	77
3	0.05	100	30	78	69	31
4	0.005	100	50	5	3	97
5	0.01	100	50	42	29	71
6	0.05	100	50	98	97	3
7	0.005	100	80	24	12	88
8	0.01	100	80	79	69	31
9	0.05	100	80	>99	0	100
10 ^[d]	0.05	100	50	61	44	56
11 ^[e]	0.05	100	50	96	93	7
12	0.05	30	50	59	38	62
13	0.05	50	50	84	74	26
14	0.05	70	50	95	93	7

[a] Conditions: methyl octanoate (**1**) (4.0 mmol); THF (2.0 mL); **Ru-1**; NaOMe (0.2 mmol; 5 mol%); 4 h. [b] Conversion and product distribution obtained by GC using undecane (1.9 mmol) as internal standard. [c] Based on moles of **1** incorporated in the product. [d] NaOMe (0.04 mmol; 1 mol%). [e] NaOMe (0.4 mmol; 10 mol%).

catalyst, and in this initial study, we tested sodium methoxide at different concentrations.

Comparing base loadings of 1%, 5%, and 10% (Table 1, entries 10, 6, and 11, respectively), the best result was obtained with 5 mol% base, and this amount was used in the subsequent experiments.

Pressure and temperature are important parameters to be considered in an industrial process. These two parameters are included in the top four major process parameters (MPP) because high temperature and/or pressure involve high operational costs and higher potential safety risks. Thus, we focused our efforts on reducing the temperature and pressure necessary for the hydrogenation, which would allow more sustainable processes by sparing energy and increasing the safety. A series of hydrogenation experiments were performed at 30, 50 and 80 bar, while the reaction temperature ranged from 30 to 100 °C. In the literature, temperatures as high as 100 °C are commonly used in catalytic ester reduction.^[6a,22] Even higher temperatures (120–130 °C) are not rare.^[6b,7a,18]

Analyzing the data in Table 1, it appears that the catalyst loading of 0.05 mol%, with 5 mol% sodium methoxide, at 70 °C, under 50 bar H₂ are suitable reaction parameters to compare **Ru-1**, **Ru-2**, and **Ru-3** catalysts in the reduction of methyl octanoate. These reaction conditions allowed 95% conversion of the ester with **Ru-1**, with good selectivity for octanol (93%), as shown in entry 14.

The time-dependent reaction profiles for methyl octanoate reduction under the chosen reaction conditions for the three catalysts are presented in Figure 2. The transesterification product **3** is formed as an intermediate, which is subsequently converted to **2**. Among the catalysts, **Ru-2** proved to be the most efficient and resulted in 90% substrate conversion in 1 h. Octyl octanoate intermediate **3** was also readily converted into **2** by **Ru-2**, and the reaction was complete in 3 h (Figure 2b). **Ru-1** was the least efficient of the three catalysts tested, despite being more active than **Ru-3** in the first hour, when the conversions reached 60% and 30%, respectively. **Ru-3** seems to be more efficient than **Ru-1** for the conversion of intermediate **3** into **2**, probably due to a lower steric hindrance around the metal center. While the three catalysts have an amino group coordinated to the metal center, regarded as fundamental for the selective C=O hydrogenation (Noyori-type catalysts), **Ru-2** has a pincer ligand which contribute to the catalyst stability and a hemilabile moiety (pyridyl group) that facilitates the substrate coordination. **Ru-3** has a pincer-type ligand containing sulfide arms which confer both stability and reactivity due to a greater hemi-lability of this ligand. The mechanism for hydrogenation catalyzed by **Ru-3** is discussed in a previous work,^[8b] and the formation of a six-membered ring involving the amino group and the Ru center seems to be the responsible for the selective hydrogenation of esters. As **Ru-2** showed the best catalytic performance in the comparative study (Figure 2), we decided to explore it under operationally friendlier reaction conditions, *i.e.* under lower H₂ pressures and in a green solvent. In Figure 2, the extrapolation of the curves for shorter reaction times suggests induction periods of few minutes for the catalysts under these conditions.

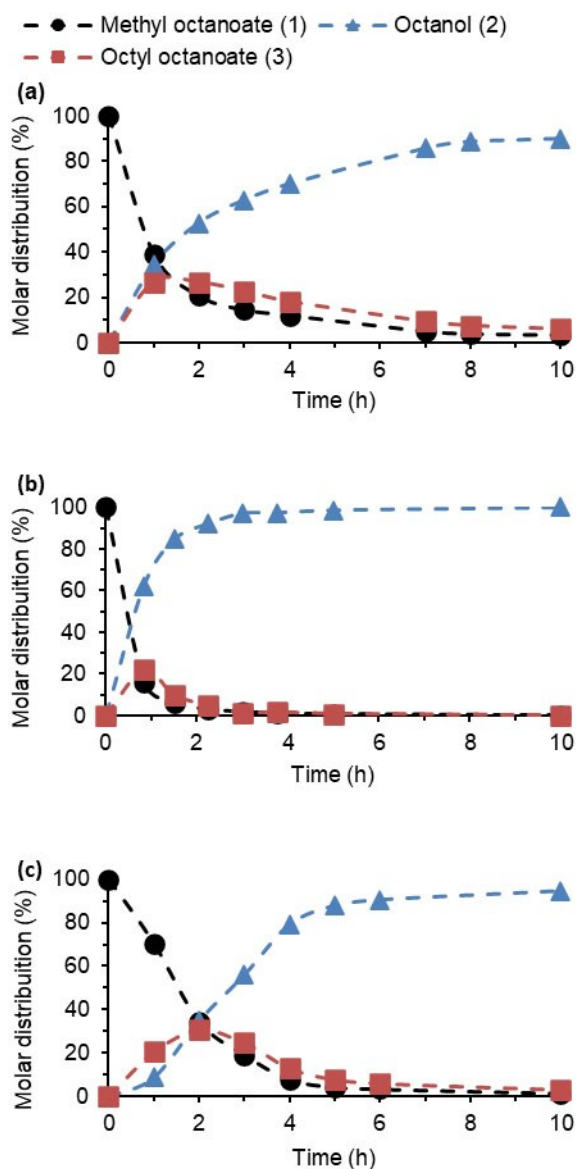


Figure 2. Molar distribution based on the initial amount of 1 as a function of reaction time. (a) **Ru-1**; (b) **Ru-2**; (c) **Ru-3**; reaction conditions: 1 (12.0 mmol); NaOMe (6.0×10^{-1} mmol, 5.0 mol%), THF (6.0 mL); **Ru-cat** (6.0×10^{-3} mmol, 0.05 mol%), 70 °C, 50 bar (H_2). The dashed lines are a mere guide to the eye and do not represent a fit to the data.

Solvents have a major impact on the sustainability of industrial chemical processes. The most common solvent used for ester hydrogenation is tetrahydrofuran (THF),^[6b,7a, 17–18] which presents major sustainability issues according to the GSK sustainable solvent guide.^[22] The most common alternative found in the literature is toluene, which is more recommended than THF in sustainability guides, but still has a considerable number of issues. In our search for greener processes, motivated by the world trend on green chemistry, we decided to test anisole, one of the most recommended solvents according to the GSK guide.^[22]

We compared THF, toluene and anisole under the same reaction conditions for the hydrogenation of methyl octanoate

employing **Ru-2** as catalyst. Our results showed that when anisole is used as solvent, the production of 2 is larger than that obtained in toluene, and comparable with that obtained when THF was used. **Ru-2** presented lower activity in methanol, ethanol and isopropanol. The transesterification products with the solvent were added together with the substrate and the transesterification with the solvent reduced the amount of the transesterification product 2 in the product distribution (Table S5, Supporting Information).

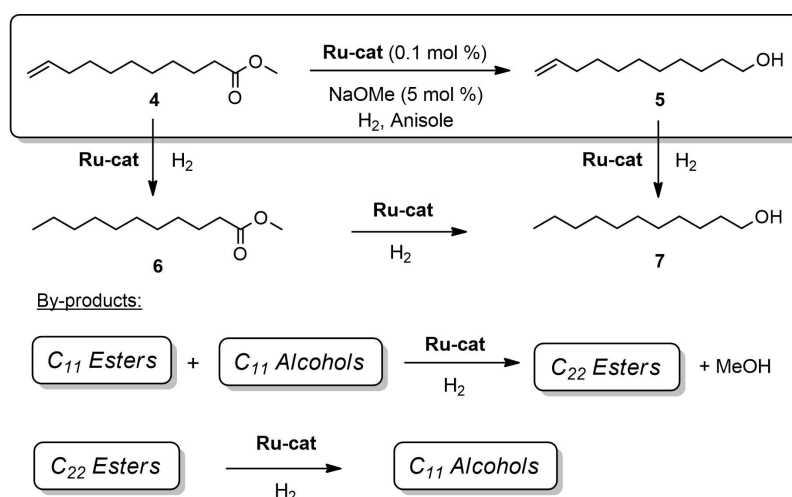
The use of a base is necessary to promote metal halide catalysts. In addition to sodium methoxide, we tested potassium *tert*-butoxide and potassium carbonate. Our studies showed that when **Ru-2** was used as catalyst, sodium methoxide gave the best performance. (Table S6, Supporting Information)

Low hydrogen pressures (below 10 bar) have been rarely used in ester hydrogenation. Even rarer are the examples in which low pressures are combined with low temperatures. For pressures of about 10 bar, temperatures above 100 °C are usually employed.^[6a,19b] If low temperatures are used, then H_2 pressures above 50 bar are commonly used.^[6–7,17–18] To the best of our knowledge, the use of pressures below 10 bar combined with temperatures below 80 °C has not been reported before. Thus, we performed catalytic studies using hydrogen pressures ranging from 5–20 bar at a fixed temperature of 70 °C for the hydrogenation of 1 to 2. After 24 h, with a catalyst loading of 0.05 mol%, a good yield for 2 (86%) was obtained under 20 bar of H_2 . Lowering the pressure to 10 bar reduced the product yield to 68%. For the reaction performed under 5 bar of H_2 , the yield dropped to 35%. (Table S8–S9, Supporting Information). Although the yields were not optimal, they indicated that the catalysts could be used under mild conditions, which may facilitate their industrial application in the fine chemicals segment. **Ru-1**, **Ru-2**, and **Ru-3** were tested for several classes of substrates. For instance, **Ru-3** was tested for unsaturated esters, lactones, ketones, imines and even olefins.^[8b]

In this work we expanded the scope for challenging substrates, including a ω -unsaturated ester (methyl 10-undecenoate), which is prone to concurrent C=C isomerization, and α,β -unsaturated aldehydes (myrtenal and cinnamaldehyde), which, besides C=C isomerization can give rise to base-catalyzed condensations. These substrates are interesting from an economic point of view, because the related alcohols obtained from the hydrogenation of their carbonyl or carboxylic groups are at least twice as valuable as the original substrates.

Methyl 10-undecenoate has two sites that can be potentially reduced by catalytic hydrogenation: the carboxylic moiety and the terminal C=C bond. It is worth noting that terminal C=C bonds are more amenable to reduction than internal C=C bonds. In addition, C=C bonds are prone to migration and isomerization, resulting in undesirable side-products (Scheme 2).

Besides the hydrogenation of methyl 10-undecenoate (4) into 10-undecenol (5), methyl undecanoate (6) can be formed if the hydrogenation of the double bond of 4 takes place before the hydrogenation of the ester. Both 5 and 6 can be doubly hydrogenated to form undecanol (7). The transesterification of



Scheme 2. Hydrogenation of methyl 10-undecenoate (**4**) into methyl 10-undecanol (**5**).

C_{11} -esters with C_{11} -alcohols leads to C_{22} -esters, which can also be reduced to C_{11} -alcohols. (For a more detailed reaction scheme, see Scheme S3 in the Supporting Information).

We studied the selective hydrogenation of **4** ($p(H_2) = 5$ –50 bar, $T = 40$ and 100°C , 3–72 h) with **Ru-1**, **Ru-2**, and **Ru-3** catalysts, and the results are presented in Table 2. Once again, the results indicate that **Ru-2** is the most active catalyst under these reaction conditions. However, the reaction with **Ru-2**, under 5 bar of H_2 and 100°C , resulted in only 1% of **5** after 24 h (Table 2, entry 1), despite 99% conversion of **4**, due to the formation of the side products depicted in Scheme 2. The loss of selectivity seems to correlate with the concurrent $C=C$ bond isomerization both for the reactant and the products. After 48 h (entry 2) the C_{22} -esters are converted into unsaturated alcohols, but the amount of the saturated alcohol does not raise in the same proportion. When the reaction was carried out under 20 atm H_2 in the presence of **Ru-2**, almost all C_{22} -esters were converted into C_{11} -alcohols.

The comparison of the three catalysts was also performed under $p(H_2) = 50$ bar (entries 6–8). Under these harsher conditions, even **Ru-1** was able to reduce C_{22} -esters to C_{11} -alcohols

in 3 h. **Ru-2** and **Ru-3** produced significant amounts of the fully hydrogenated alcohol **7** under these conditions. On attempt to increase the selectivity, we associated low pressure with a lower temperature (40°C), using a longer reaction time (72 h), as in entries 9–11. Then, **Ru-1** reached 82% conversion; however, most of the product was a mixture of C_{22} -esters, which is consistent with the relatively low reactivity of this catalyst. **Ru-2** showed good activity for ester reduction, but the $C=C$ bond isomerization was highly competitive. Furthermore, a fair amount (49%) of the fully hydrogenated alcohol was formed. **Ru-3** exhibited a much better yield for **5** (81%) under these conditions, suggesting a good activity for ester hydrogenation and a lower activity for the $C=C$ bond isomerization.

To get a better understanding of the selectivity of the three catalysts in the hydrogenation of **4**, we studied the time-dependent profiles of the catalytic reactions carried out with **Ru-1**, **Ru-2**, and **Ru-3**. The results are shown in Figure 3. The analysis of the conversion profile in shorter reaction times suggests an induction period of ca. 3 h for **Ru-2** and **Ru-3** (Figure 3b and 3c, respectively) under the reported reaction conditions. The corresponding analysis for **Ru-1** does not

Table 2. – Comparative study with **Ru-1**, **Ru-2** an **Ru-3** for the hydrogenation of methyl 10-undecenoate.^[a]

Entry	Catalyst	$p(H_2)$ [bar]	t [h]	Conversion [%] ^[b]	Product Distribution [%] ^[b,c]			
					5	7	C_{11} -alcohol isomers	Others
1	Ru-2	5	24	99	1	11	20	68
2	Ru-2	5	48	>99	2	18	70	11
3	Ru-1	20	24	97	2	18	8	72
4	Ru-2	20	24	>99	2	44	53	1
5	Ru-3	20	24	99	2	11	43	44
6	Ru-1	50	3	>99	<1	13	85	1
7	Ru-2	50	3	>99	1	61	37	1
8	Ru-3	50	3	>99	1	59	39	0
9 ^[d]	Ru-1	5	72	82	24	9	12	55
10 ^[d]	Ru-2	5	72	>99	2	49	47	1
11 ^[d]	Ru-3	5	72	>99	81	5	13	1

[a] Reaction conditions: Methyl 10-undecenoate (**4**) (2 mmol); anisole (1 mL), catalyst loading (0.1 mol%), NaOMe (0.1 mmol; 5 mol %); 100°C . [b] Conversion and Yield obtained by GC using undecane (0.95 mmol) as internal standard. [c] Based on moles of **4** incorporated in the product. [d] 40°C

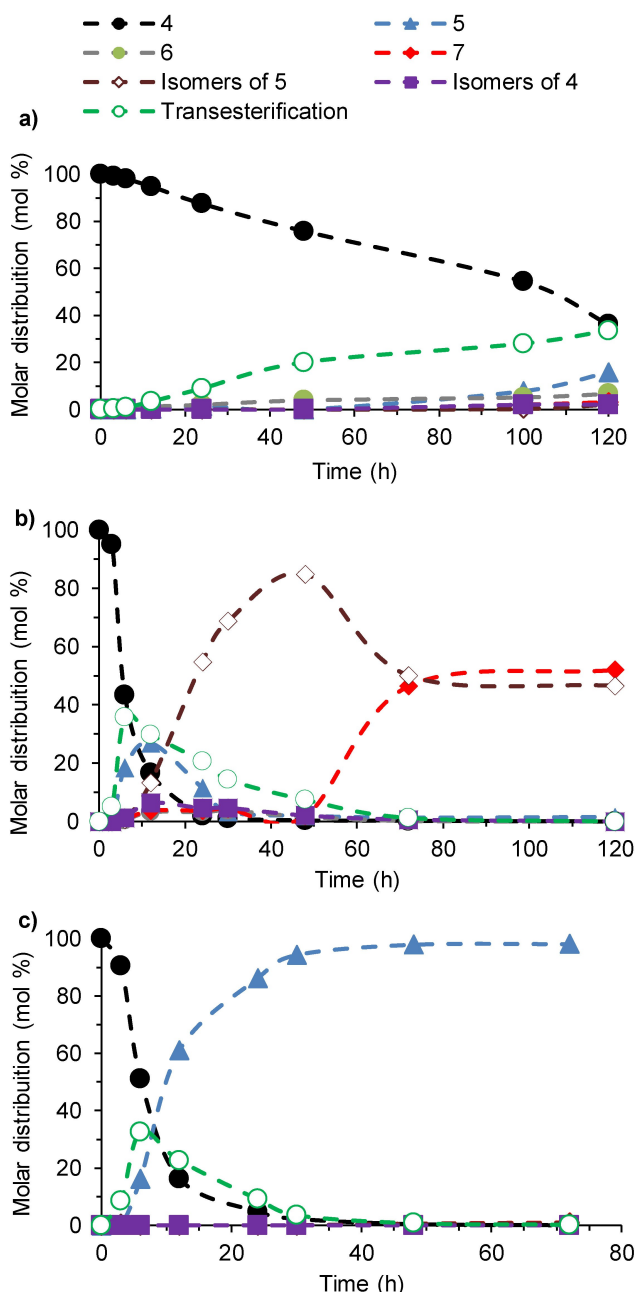


Figure 3. Molar distribution of methyl 10-undecenoate (**4**) into products as a function of time. **4** (10 mmol), catalyst (0.1 mol%), sodium methoxide (5 mol%), anisole (5 mL), 10 bar (H_2), 40 °C. (a) **Ru-1**, (b) **Ru-2**, (c) **Ru-3**. The dashed lines are a mere guide to the eye and do not represent a fit to the data.

indicate such a long induction period, but the catalyst is clearly less active.

In Figure 3a, the product evolution with **Ru-1** indicates that, under mild conditions, the catalyst shows low activity for ester reduction. Alcohol **5** formed is transesterified to the C_{22} -esters, which are slowly reduced to alcohol **5** at longer reaction times. It is noteworthy that the $C=C$ bond isomerization is not significant under these conditions and the reduction of $C=C$ bond is not significant either.

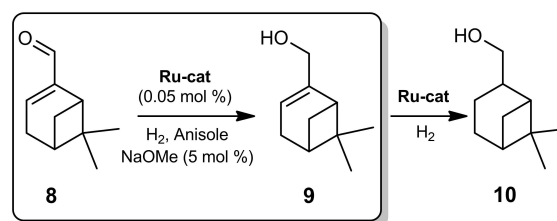
For the reaction performed using catalyst **Ru-2**, Figure 3b, after an induction period of ca. 3 hours, the catalyst becomes highly active forming primarily product **5** and its transesterification product. After 6 h, the $C=C$ bond isomerization takes place along with the conversion of **4** to **5** and C_{22} -ester to C_{11} -alcohols. As a result, the amount of 10-undecenoate **5** does not increase. Interestingly, only after 48 h the amount of the saturated alcohol **7** showed an increase at the expense of C_{11} -alcohols containing an isomerized $C=C$ bond. These observations suggest that the direct reduction of the $C=C$ bond is not a major route for this catalyst. One can speculate that the $C=C$ bond walks along the carbon chain until it reaches the enolic position. The enol isomerizes to aldehyde, which is then reduced by the catalyst.

For catalyst **Ru-3**, Figure 3c, after an induction period of ca. 3 hours, the catalyst becomes highly active, forming alcohol **5** and the corresponding transesterification product, which is subsequently converted to **5**. To our delight, under these conditions the $C=C$ bond isomerization does not occur, and the desired product is formed in an almost quantitative yield after 30 h. Although such high selectivity has been reported,^[23] to the best of our knowledge, this is the first time that the hydrogenation of an ester containing a terminal double bond is achieved with this high selectivity under very mild conditions such as 5 bar of H_2 and 40 °C. This result is even more remarkable if we take into account that the SNS ligand of **Ru-3** is easier to synthesize than the phosphorus ligands of catalyst **Ru-1** and **Ru-2**, while employing less toxic reactants.

Since the selective hydrogenation of the $C=O$ bond of α,β -unsaturated aldehydes is an important route to allylic alcohols of industrial interest,^[23b] we decided to test the selectivity of catalysts **Ru-1**, **Ru-2**, and **Ru-3** in the reduction of (1R)-(–)-myrtenal (**8**) and (E)-cinnamaldehyde (**11**) as model substrates. To the best of our knowledge, the selective hydrogenation of myrtenal (**8**) to myrtenol (**9**) has not been previously reported. Conversely, cinnamaldehyde is used as a model for the selective hydrogenation of α,β -unsaturated aldehydes, and is described in a large number of works, some with excellent selectivity for cinnamyl alcohol (**12**, Scheme 4).^[24] It was included in this study to place the catalysts **Ru-1**, **Ru-2**, and **Ru-3**, which were underexploited on the selective reduction of aldehydes.

In myrtenal, both the $C=C$ and $C=O$ bonds can undergo hydrogenation, although the former is sterically encumbered, as depicted in Scheme 3.

The catalytic reactions were performed at different pressures (5, 20 and 50 bar of H_2), as shown in Table 3.



Scheme 3. Hydrogenation of myrtenal (**8**) into myrtenol (**9**).

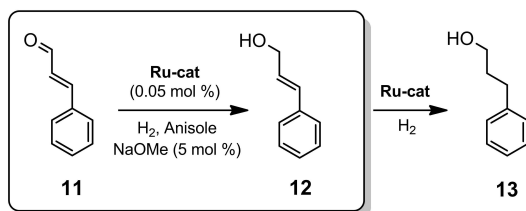
Table 3. – Comparative studies of the different catalysts at different pressures in the hydrogenation of myrtenal (**8**).^[a]

Entry	Cat.	$p(H_2)$ [bar]	t [h]	Conversion, [%] ^[b]	Product Distribution [%] ^[b,c]		
					9	10	Others
1	Ru-1	5	24	48	35	39	26
2	Ru-2	5	24	98	69	21	9
3	Ru-3	5	24	>99	40	5	55
4 ^[d]	Ru-1	20	24	>99	87	11	2
5	Ru-1	50	4	>99	90	7	3
6	Ru-2	50	4	>99	90	8	2
7	Ru-3	50	4	>99	89	8	3

[a] Reaction conditions: **8** (4 mmol); anisole (2 mL), catalyst (0.05 mol%), NaOMe (5 mol%); 100 °C; [b] Conversion and product distribution obtained by GC using undecane (1.9 mmol) as an internal standard. [c] Based on mol of **8** incorporated in the product. [d] 70 °C.

Under 5 bar of H_2 , Ru-1 was the least active catalyst, rendering 48% conversion in 24 h. Noteworthy is the low selectivity of the reaction with Ru-1 (entry 1). Ru-2 led to almost complete conversion and better selectivity for **9**. Ru-3 also gave full conversion, however the selectivity to the desired product **9** was poor (entry 3). Increasing the pressure to 20 bar with simultaneous decrease in temperature to 70 °C (entry 4) gave full conversion and a better selectivity for **9** with Ru-1. Under $p(H_2) = 50$ bar (entries 5–7), the desired product **9** was obtained in good yields with all three catalysts (90%). Taking into account that the reactant disappearance corresponded to the formation of the same amount of products by proper GC quantification, the formation of significant amounts of high boiling condensation products can be ruled out. Under low H_2 pressure (5 bar, entries 1–3) the proportion of the fully saturated product **10** is higher than under high pressure (50 bar, entries 5–7). A plausible explanation is that, since the reaction time is longer under 5 bar H_2 , the C=C bond isomerization in **9** may lead to the corresponding enol, which in turn isomerizes to the saturated aldehyde. The latter is hydrogenated by the catalysts to give **10**.

Cinnamaldehyde broadens the scope of investigation because the C=C bond is conjugated with the phenyl ring and the C=C bond in cinnamaldehyde (**11**) is not as sterically hindered as in myrtenal (**8**). Again, the reduction of **11** can give the desired product **12**, which can be further hydrogenated to **13** (Scheme 4).


Scheme 4. Hydrogenation of cinnamaldehyde (**11**) into cinnamyl alcohol (**12**).

The catalytic reaction depicted in Scheme 4 was carried at different pressures (5, 20 and 50 bar of H_2) as shown in Table 4. It is worth mentioning that with the Wilkinson's catalyst or Pd/C, the C=C bond of cinnamaldehyde is hydrogenated preferentially.^[25] However, with the catalysts tested in this work, 3-phenylpropanol (**13**) was not observed in significant amounts.

The comparison of entries 1–3 on Table 2 and 3, suggests that cinnamaldehyde is less reactive than myrtenal under these conditions since the conversions are much lower for the former at the same reaction time. The order of activity of the three catalysts for cinnamaldehyde is: Ru-2 > Ru-1 ~ Ru-3. The selectivity for **12** was higher with Ru-2. Raising the H_2 pressure to 20 bar (entries 4–6) led to an increase in conversion, but only Ru-2 gave a high conversion of the substrate (91%) and an excellent selectivity for **12** (97%). The minimal formation of **13** (Scheme 4) is in agreement with the proposed mechanism of full reduction via enol intermediate, which formation is less likely in **12** since the isomerization requires disrupting the conjugation with the aromatic ring. At $p(H_2) = 50$ bar (entries 7–9), Ru-1 gave only 20% conversion in 4 h, while Ru-2 and Ru-3 resulted in nearly quantitative conversion and selectivity for **12**. These results highlight the excellent potential of Ru-2 and Ru-3 for the selective hydrogenation of α,β -unsaturated aldehydes.

Conclusions

This work endeavors for the first time a rigorous comparison among three state-of-the-art, commercially available catalyst (Ru-1, Ru-2, and Ru-3, Figure 1) and discloses their different patterns in reactivity for the selective hydrogenation of esters and α,β -unsaturated aldehydes into alcohols. For the reduction of methyl octanoate, the order of catalytic activity was Ru-2 > Ru-3 > Ru-1. For the selective reduction of methyl-10-undecenoate to the corresponding ω -unsaturated alcohol, Ru-3 gave excellent selectivity and good activity under mild reaction conditions (10 bar of hydrogen and 40 °C). Ru-2, although more active, led to a concurrent C=C bond isomerization, which drastically reduced the selectivity for the ω -unsaturated alcohol

Table 4. – Comparative studies at different pressures in the hydrogenation of cinnamaldehyde (**11**).^[a]

Entry	Cat	$p(H_2)$ [bar]	t [h]	Conversion, [%] ^[b]	Product Distribution [%] ^[b,c]		
					12	13	others
1	Ru-1	5	24	16	85	2	13
2	Ru-2	5	24	24	90	3	7
3	Ru-3	5	24	14	78	4	18
4	Ru-1	20	24	37	92	1	7
5	Ru-2	20	24	91	97	0	3
6	Ru-3	20	24	36	91	1	8
8	Ru-1	50	4	20	94	0	6
9	Ru-2	50	4	98	98	0	2
10	Ru-3	50	4	98	99	0	1

[a] Reaction conditions: **11** (4 mmol); anisole (2 mL), catalyst (0.05 mol%), NaOMe (5 mol%); 100 °C. [b] Conversion and yield obtained by GC using undecane (1.9 mmol) as an internal standard. [c] Based on mol of **11** incorporated in the product.

5. For α,β -unsaturated aldehydes, the order of activity was essentially the same, and the efficient selective hydrogenation to allylic alcohols was reached under moderate reaction conditions (20–50 bar of hydrogen and 100 °C) for myrtenal. Cinnamaldehyde proved to be a less reactive substrate, but its selective reduction to cinnamyl alcohol was efficiently achieved employing catalysts **Ru-2** and **Ru-3**. The reaction profiles suggest a mechanism of double-bond isomerization until enol formation, which is in equilibrium with the corresponding aldehyde, the latter being readily reduced with these catalysts to form the fully saturated product. It is worth mentioning that such transformations can be carried out under environmentally friendly conditions, employing hydrogen pressures as low as 5 bar and temperatures as low as 40 °C, in anisole as solvent.

Experimental Section

General Procedures

All experiments and manipulations of air or water-sensitive compounds were carried out under argon atmosphere using a glove box (MBRAUN UNILAB PRO) or using standard Schlenk techniques. NMR (^1H , 400 MHz, ^{13}C , 100 MHz) spectra were recorded on a Bruker NanoBay spectrometer and referenced to residual solvent. GC analyses were performed on samples diluted with untreated toluene on a Shimadzu GC2010 Plus instrument equipped with an auto-sampler, fitted with polar Carbowax column (30 m, 0.25 mm internal diameter, 0.25 μm film thickness) and a flame ionization detector (FID). Qualitative analyses were performed on a Shimadzu GC2010/QP2010-PLUS equipment operating at 70 eV. Conversion and selectivity were determined using undecane as internal standard. THF (Tetrahydrofuran) ($\geq 99.9\%$, anhydrous, Sigma-Aldrich), anisole ($\geq 99.7\%$, anhydrous, Sigma-Aldrich) and toluene ($\geq 99.8\%$, anhydrous, Sigma-Aldrich) were opened inside a glove box. Methyl octanoate (99%, Sigma-Aldrich), methyl 10-undecenoate (96%, Sigma-Aldrich), (E)-cinnamaldehyde (99%, Sigma-Aldrich), (1R)-(–)-myrtenal (98%, Sigma-Aldrich), undecane (≥ 99 , Sigma-Aldrich), were treated with Magnesol® (5% m/m) and alumina (5% m/m), and heated to 80 °C under vigorous stirring for 2 h, then distilled in a Kugelrohr distillation apparatus at 2×10^{-2} mbar, collected under argon atmosphere and stored in a glove box prior to use to eliminate peroxides. **Ru-1** was purchased from Sigma Aldrich (95%) and used as received. **Ru-2** and **Ru-3** (also available in Sigma Aldrich) were synthesized according to reported procedures.

Hydrogenation Reactions

In a typical experiment, three 4 mL vial containing a magnetic stirring bar was loaded with the catalyst (2.0 μmol), NaOMe (0.2 mmol), substrate (4.0 mmol), undecane (1.9 mmol), and solvent (2.0 mL) in a glove box. The vials were closed with a cap containing a septum and removed from the glove box. On a Schlenk line, the septa were punctured with hypodermic needles under argon flow and the vials were placed in a stainless-steel autoclave adapted with a 3-well aluminium block, which was subsequently closed and purged with three quick cycles of vacuum/argon. The autoclave was then pressurized with hydrogen (5–50 bar) and introduced in a aluminium block pre-heated to the desired temperature reaction over a PID-controlled hot plate with magnetic stirring. After the desired reaction time, the autoclave was cooled to room temperature and slowly vented in a fume hood. Trifluoroacetic acid

(0.2 mmol) was added to neutralize the base in each vial, and the products were analysed by gas chromatography. For the kinetic follow-up, the reaction was carried in a larger scale (5 times) directly in the autoclave. The progress was monitored by taking liquid samples through a valved 1/16" tube without depressurizing the reactor. For further details, please refer to the Supporting Information.

Supporting Information

Additional references cited within the Supporting Information.^[12a,21,26]

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: chemoselectivity · homogeneous catalysis · renewable feedstock

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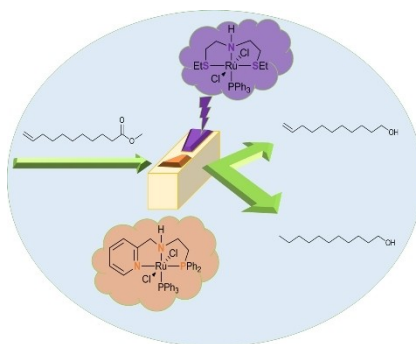
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RESEARCH ARTICLE

Selectivity under mild conditions: three state-of-the-art, commercially available Ru catalysts are compared for the selective hydrogenation of esters and aldehydes containing C=C at 40 °C and 5 bar of hydrogen in anisole as solvent.



L. H. R. Passos, Dr. V. Martínez-Agramunt, Prof. D. G. Gusev, Prof. E. Peris, Prof. E. N. dos Santos**

1 – 9

A Sustainable Approach to Selective Hydrogenation of Unsaturated Esters and Aldehydes with Ruthenium Catalysts

