Ruthenium-catalyzed homogeneous hydrogenolysis of esters to alcohols
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Citation for published version (APA):
van Engelen, M. C. (2003). Ruthenium-catalyzed homogeneous hydrogenolysis of esters to alcohols Amsterdam
RUTHENIUM STARTING MATERIAL AND LIGANDS FOR CATALYTIC HYDROGENOLYSIS OF ESTERS

1 Introduction

Ruthenium complexes have been employed in a wide variety of hydrogenation reactions. For example, the hydrogenation of alkynes, alkenes, aldehydes and ketones using ruthenium catalyst precursors is widely established and has been extensively documented in literature. These hydrogenation reactions were achieved in moderate to good yields using a variety of conditions, depending on the substrate used and the availability of hydrogen donors. Hydrogenation was performed either by use of (increased pressures of) dihydrogen gas as the hydrogen source in the direct hydrogenation of the substrate, or by use of other hydrogen donors such as 2-propanol or formic acid in transfer hydrogenations.

Only a few homogeneous systems for the hydrogenolysis of esters to alcohols are available. Furthermore, most of these systems are limited in scope of substrates that they can be applied to; often they are only applicable in the hydrogenolysis of activated esters, such as dimethyl oxalate or fluorinated esters.

It is known that transition metal hydride complexes can facilitate the conversion of ketones and esters to the corresponding alcohols. In most cases, this hydrogenation proceeds via an initial attack of the metal hydride or metal dihydrogen complex on the carbonyl function of an ester or ketone (see the general scheme 1). The lower polarity of the carbonyl function in esters with respect to that of a ketone requires a higher polarity of the M-H fragment than is used for the hydrogenation of ketones. In view of the general problems with, and the lack of, suitable catalysts for the hydrogenolysis of esters, a search towards more active catalysts for the hydrogenolysis of esters to alcohols was initiated.

Interest was directed towards the use of ruthenium complexes having an increased electron density on the ruthenium center, which would enhance the nucleophilicity of the intermediate
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Hydride towards the less polar carbonyl function of the substrate. Furthermore, introducing electron withdrawing groups onto the ester may facilitate the conversion of the ester into the alcohol as was described by Pez et al. These authors also proposed a general mechanism for the hydrogenation of ketones. This mechanism is displayed in scheme 1 and has been extended for the hydrogenolysis of esters.

![Scheme 1: Catalyzed hydrogenation of carbonyl containing substrate](image)

It was shown previously that hydrogenation of carbonyl derivatives is accomplished using ruthenium complexes containing phosphorus-, or nitrogen ligands. In general, complexes bearing phosphorus ligands show a larger activity than the corresponding complexes containing nitrogen ligands.

In this chapter the selection of suitable ruthenium complexes and ligands as catalyst precursor for the hydrogenolysis of esters to alcohols is described. Catalyst precursors were evaluated based on their activity and selectivity in the hydrogenolysis of dimethyl oxalate (1), which due to its structural properties is activated for hydrogenolysis, and can act as an excellent probe (scheme 2). This ester has been used in several instances before, and thus by employing this
substrate, comparison between our newly found catalysts and the systems reported in literature is possible.

Scheme 2: The hydrogenolysis of dimethyl oxalate (1) via methyl glycolate (2) to ethylene glycol (3)

2 Results and Discussion

2.1 Selection of ruthenium precursor

A number of initial experiments, for which general reaction conditions were chosen, were performed to find a suitable ruthenium catalyst precursor for the hydrogenolysis of dimethyl oxalate (1) to the corresponding diol, ethylene glycol (3). It is known from previous experiments that the conversion of the ester proceeds in two steps. In the first step, dimethyl oxalate is converted to methyl glycolate (2), which is subsequently converted to the final product ethylene glycol (3, scheme 2).

The first experiments were conducted using readily available and stable ruthenium starting materials such as RuCl2(PPh3)4. RuCl2(PPh3)4 is known to be an excellent catalyst precursor used in the transfer hydrogenation of ketones and aldehydes.5 When RuCl2(PPh3)4 was applied as catalyst precursor for the hydrogenolysis of dimethyl oxalate, 37% conversion of the starting ester (1) was observed using THF.6 The catalyst precursor, however, showed poor selectivity and only a 12% yield of the product, methyl glycolate (2), was isolated after 16 hours, no formation of ethylene glycol was observed; the remainder are unidentified side-products. The newly formed substrate, methyl glycolate, is less susceptible to undergo hydrogenolysis, because its ester function is no longer activated by the presence of a strong electron withdrawing group nearby like was present in substrate 1. The electron withdrawing character of the α-hydroxygroup is insufficient to render the ester function activated for hydrogenolysis. It is

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known that for further hydrogenolysis of the α-hydroxy ester to the diol, increased reaction temperatures (180 °C instead of 120 °C) and reaction times are required. For this active catalyst, reaction conditions were varied. First, the focus was at the solvent for the reaction. An interesting solvent to perform the conversion of dimethyl oxalate to ethylene glycol and methanol would be methanol itself. Matteoli et al. found for their catalyst that hydroxylated solvents increased selectivity for ethylene glycol. When methanol was used, 51% of the starting ester (1) is converted to 2. Yet, the hydrogenolysis is again halted at the stage of the intermediate product 2. Further hydrogenolysis to 3 was not observed under the standard conditions using RuCl₂(PPh₃)₄. Experiments showed that conversion of the substrate is influenced by the presence of water in the reaction medium. When commercial methanol was used in the catalytic reaction, conversions and yields are lower compared to use of dry methanol. The presence of water may lead to hydrolysis of the ester resulting in the formation of the corresponding acids that in turn can lead to inactive carbonyl species formed by decarbonylation in the presence of ruthenium.

Table 1: Selected ruthenium precursors for the hydrogenolysis of dimethyl oxalate (1)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Solvent</th>
<th>Conv. 1 (%)</th>
<th>Yield 2 (%)</th>
<th>Yield 3 (%)</th>
<th>T.O.F. (mol mol⁻¹ h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 RuCl₂(PPh₃)₄</td>
<td>THF</td>
<td>37</td>
<td>12</td>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>2 RuCl₂(PPh₃)₄</td>
<td>MeOH</td>
<td>51</td>
<td>20</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>3 RuCl₃ + PPh₃</td>
<td>MeOH</td>
<td>44</td>
<td>15</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>4 Ru(acac)₃ + PPh₃</td>
<td>MeOH</td>
<td>73</td>
<td>36</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>5 Ru(CO)₃(OAc)₂(PBu₃)₂</td>
<td>MeOH</td>
<td>100</td>
<td>18</td>
<td>82</td>
<td>0.9</td>
</tr>
</tbody>
</table>

† General conditions: pH₂ = 80 bar, T=120 °C; T.O.F. = Turnover Frequency = amount of ester converted (mmol) per hour / amount of catalyst (mmol). T.O.F. is determined as an average value after 16 hours.
‡ T=180 °C, pH₂=200 bar; t= 144 h, reference 7.

All reactions conducted thus far were performed using a well-defined ruthenium(II) precursor. Although conversion of the substrate is observed, catalyst activity is low and only partial hydrogenolysis to 2 is observed (maximum conversion of the starting ester 51%, entry 2) and other (undefined) side-products are formed; in all cases the hydrogenolysis is stopped at methyl glycolate and no formation of ethylene glycol was observed. In order to increase the conversion of the substrate 1 and to facilitate the formation of ethylene glycol (3), other new and readily available ruthenium starting materials that can act as a pre-catalyst were screened. An appealing route towards an active catalyst is the formation of the catalyst in situ by reduction of a
ruthenium(III) starting material in the presence of a suitable ligand under catalytic conditions, thus forming an active system. It was previously reported by Hara et al. that an in situ prepared catalyst derived from Ru(acac)₃ and phosphine type ligands was suitable in the hydrogenation of γ-lactones to α,ω-diols (scheme 3). ⁹

![Scheme 3: The hydrogenation of succinic anhydride via γ-butyrolactone to 1,4-butanediol](image)

In situ formation was applied in the hydrogenolysis of 1 by starting from RuCl₃ and PPh₃ (activated zinc was added to facilitate the reduction of the ruthenium). This initial attempt proved to be successful, and indeed an active catalyst was formed, however, the activity of this catalyst system was lower than the activity obtained from RuCl₂(PPh₃)₄. Presumably, the formation of the catalyst is not optimum under these conditions (15% yield with a turnover frequency of only 0.2 per hour) and the chlorides introduced with RuCl₂(PPh₃)₄ and RuCl₃ may be hampering the reaction. To prevent the presence of chlorides in the reaction mixture, the ruthenium(III) complex Ru(acac)₃, a succesful catalyst precursor for the hydrogenation of cyclic esters,⁹ was used as the starting material. Indeed with this catalyst precursor, a large increase in activity was observed (entry 4). This experiment showed that the formation of the catalyst in situ from Ru(acac)₃ provides an easier and more efficient route towards the active species that is involved in catalysis. Using Ru(acac)₃ and PPh₃, already 73% of the starting material 1 was converted to methyl glycolate; hydrogenolysis of the resulting α-hydroxy ester 2 to the diol 3 was, again, not observed.

The highest catalytic activity was thus obtained from a phosphine ligand and Ru(acac)₃ as catalyst precursor in the presence of zinc as an additive. The role of the additive zinc can be ascribed to two influences. Metallic zinc acts as a reducing agent in the conversion of the RuIII starting material to RuII, furthermore, the formed ZnII acts as a Lewis acid and can activate the
ester carbonyl function by coordinating to it, hence rendering it more prone to attack by the ruthenium catalyst.\textsuperscript{3}

\[ M^+O \overset{\text{HRu}}{\text{C}} \]

\textbf{Figure 3: Activation of the carbonyl group by a Lewis acid}

At this point it was assumed that the formation of the actual catalyst is initiated by the hydrogenation of the acetyl acetonate ligands on the ruthenium center to 2,4-pentanediol. Indeed, amounts of 2,4-pentanediol were recovered in a separate experiment, confirming the hydrogenation of the acetyl acetonate ligands.

\subsection{2.2 Ligand Selection}

Having identified a suitable source of ruthenium in the complex Ru(acac)$_3$, focus was shifted towards the optimization of the system by careful selection of the ligand. Common ligands such as mono, di- and tridentate ligands based on N- and P- donor systems were selected, as displayed in chart 1.

The chemistry of ruthenium complexes containing these types of ligands is generally well documented and a wide range of catalyst precursors is available, some examples are the hydrogenation of olefins (for 1,10-phenanthroline (7) and trispyrazolylborate (10))\textsuperscript{10,11} and the transfer hydrogenation of ketones and aldehydes (for 1,10-phenanthroline (7),\textsuperscript{11} bis(diphenylphosphine)ethane (9)\textsuperscript{12} and 2,2',6',2''-terpyridine (11)\textsuperscript{13}). Other examples can be found for triphenylarsine (5), PhP(CH$_2$CH$_2$PPh$_2$)$_2$ (12), CH$_3$C(CH$_2$PPh$_2$)$_3$ (13),\textsuperscript{14} and (PPh$_2$C$_2$H$_4$PPhCH$_2$)$_2$ (14).\textsuperscript{15}
Table 2 summarizes the activity of the catalytic system with these ligands in the \textit{in situ} hydrogenolysis of dimethyl oxalate (1) to ethylene glycol (3) with \textit{Ru(acac)}\textsubscript{3} as the ruthenium source. A first screening of ligands revealed that best results were obtained for phosphine type ligands. Although ligands containing nitrogen donor atoms such as 1,10-phenanthroline or 2,2′,6′,2″-terpyridine (Ligands 7 and 11 respectively) have proven to be active in the hydrogenation of ketones, they show no activity in the hydrogenolysis of dimethyl oxalate, even at higher temperatures and pressures no conversion of the ester was observed.
Monodentate Ligands

Using simple monodentate coordinating phosphine ligands gave rise to the formation of only the mono-hydrogenated α-hydroxy ester methyl glycolate (2). For example in the case of PPh₃ (4), 73% of the starting material is converted with a selectivity of 50% for methyl glycolate (2) (other products are unidentified by-products). It was thought that an increased electron density on the ruthenium catalyst would enhance the attack of the catalyst on the electrophilic carbonyl carbon atom of the ester, thus increasing the rate of conversion to the alcohol. For this reason, the ligand was changed to the more basic PCy₃. With this ligand, however, catalyst activity was found to decrease, presumably as a result of its stronger donor-acceptor properties; the more basic ligand stabilizes the ruthenium complex too much.

In the ruthenium-catalyzed hydrogenation of aldehydes, it was suggested that the initial step in hydrogenation is the reversible dissociation of a phosphine ligand \textit{trans} to a hydride.\textsuperscript{16} Since arsines bind less strongly to transition metals than do the corresponding phosphines, the dissociation of the ligand and catalysis should be favored using AsPPh₃. Despite favorable dissociation of the ligand, electron density on the metal is diminished and catalyst activity is reduced to zero using AsPPh₃.

Didentate Ligands

Polyphosphines have favorable behavior over their comparable monodentate phosphines and often exhibit excellent bonding activity to metals leading to an increased basicity or nucleophilicity at the metal. Furthermore they often can be used in the formation of stable complexes in a variety of metal oxidation states giving detailed structural and bonding information.\textsuperscript{14}

Didentate phosphine ligands of the type \( R_2PCH_2CH_2PR_2 \) (\( R=\text{alkyl and aryl} \)), have proven to be a useful class of supporting ligands in organometallic complexes and catalysis. Significant research efforts have been devoted to the investigation of ruthenium hydrides bearing didentate phosphines.\textsuperscript{17}
**Table 2: Ligand variations in the homogeneous hydrogenolysis of dimethyl oxalate**

<table>
<thead>
<tr>
<th>Ligand/Ru</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
<th>T.O.N. (T.O.F.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.0</td>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td><strong>Monodentate phosphine ligands</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPh3 (4)</td>
<td>15.9</td>
<td>73</td>
<td>36</td>
</tr>
<tr>
<td>PCy3 (6)</td>
<td>4.6</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td><strong>Didentate phosphine ligands</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thixanthphos (8)#</td>
<td>0.0c</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ph3PC2H4PPH2 (9)</td>
<td>3.0</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td><strong>Tritendentate phosphine ligands</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PhP(C2H4PPH2)2 (12)</td>
<td>1.7</td>
<td>76</td>
<td>67</td>
</tr>
<tr>
<td>CH3C(CH2PPH2)3 (13)</td>
<td>1.4</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td><strong>Tetradentate phosphine ligands</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CH2PPh2C2H4PPH2)2 (14)</td>
<td>1.0</td>
<td>91</td>
<td>85</td>
</tr>
<tr>
<td><strong>Other ligands / catalysts</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AsPh3 (5)</td>
<td>8.9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1,10-Phenanthroline (7)</td>
<td>6.4</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Trispyrazolylborate (10)</td>
<td>2.3</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>2,2':6',2&quot;:-Terpyridine (11)</td>
<td>1.8</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>K2[Ru3H4(Ph3P3)(Ph2P)]*2C6H14O3#</td>
<td>---</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>Ru(CO)2(OAc)2(PBu3)2##</td>
<td>---</td>
<td>100</td>
<td>18</td>
</tr>
</tbody>
</table>

General conditions: Ru(acac)3 10 μmol, in 15 ml methanol pH2 = 80 bar, T=120 °C. Cy= Cyclohexyl, C6H11:

T.O.N. = Turnover number = amount of ester converted (mmol) / amount of catalyst (mmol);
T.O.F. = Turnover Frequency = amount of ester converted (mmol) per hour / amount of catalyst (mmmol).
T.O.N. and T.O.F. were determined as an average after the standard reaction time of 16 hours.

#)Was applied as the complex (thioxanthphos)_2RuH2 see reference 3 see reference 7.

Several didentate ligands were applied in the hydrogenolysis of dimethyl oxalate (1). The application of the ligand dppe (9, R=C6H5) proved successful, and 18% of the ester is converted with the formation of only a small amount of undefined side-products.
The phosphine ligand thioxanthphos (8)18 was available as its ruthenium hydride complex (thioxanthphos)_2RuH2 and was used as such, contrary to the other ligands that were applied in the in situ generation of the catalyst. This complex showed no activity.
Multidentate Ligands

For the hydrogenation of aldehydes, Sung et al.\textsuperscript{14,19} showed that ruthenium(II) complexes containing diphosphines that form larger chelate ring sizes exhibit better catalytic activities. Chelate ring opening was regarded as the rate determining step in similar catalytic processes. In complexes containing larger chelate rings, this opening should be faster, and enhance activity. Moreover, since polyphosphine complexes usually have two or more chelate rings, the chelate effect is augmented and the number of undesired isomers which often appear in complexes of monodentate or didentate ligands was considered to be diminished. Tridentate ligands for catalysis are well documented and have been used in a variety of catalytic experiments (such as hydrogenation of aldehydes and ketones) using different ruthenium complexes.\textsuperscript{14,20}

First, PhP(CH\textsubscript{2}CH\textsubscript{2}PPh\textsubscript{2})\textsubscript{2} (12) was attempted as a possible ligand. This ligand has the capability to coordinate in a facial, as well as in a meridional fashion to a transition metal such as ruthenium. This ligand was previously applied in the complex RuHCl(CO)(PhP(CH\textsubscript{2}CH\textsubscript{2}PPh\textsubscript{2})\textsubscript{2}) (figure 1), which was used as a catalyst for the hydrogenation of alkenes as cyclohexene and ketones like cyclohexanone and propanal.\textsuperscript{14}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{coordination modes for the ligand etp in RuHCl(CO)(etp) (etp=PPh(CH\textsubscript{2}CH\textsubscript{2}PPh\textsubscript{2})\textsubscript{2}}14
\caption{Coordination modes for the ligand etp in RuHCl(CO)(etp) (etp=PPh(CH\textsubscript{2}CH\textsubscript{2}PPh\textsubscript{2})\textsubscript{2}}}
\end{figure}

With this ligand (12) in combination with Ru(acac)\textsubscript{3}, catalyst activity increased appreciably and the ester is fully converted to the \(\alpha\)-hydroxy ester. Although the coordination mode of 12 in the hydrogenolysis of the ester has not been determined, this experiment showed that in the hydrogenolysis of the ester, a tridentate ligand is preferred over didentate or monodentate ligands.

Forcing a tridentate ligand into a facially coordinating fashion, as for example with the tripod ligand triphos (13), suddenly the catalyst displays unforeseen activity and selectivity in the hydrogenolysis of the ester, and almost full selectivity towards ethylene glycol (3) is observed.
Furthermore, it appeared that, depending on the ligand chosen the hydrogenolysis could be tuned to either produce methyl glycolate as almost the sole product or to produce ethylene glycol (3). The high activity can be explained according to Sung; by the forcing conformation of the ligand compared to mono-, or didentate ligands formation of different coordination isomers that are possibly inactive in catalysis is greatly diminished, and the formation of the active species is almost exclusive.

Application of tetradentate ligands as in 14, however, again changes selectivity to the mono hydrogenated product.

3 Conclusions

A valuable and easily available catalyst precursor for the hydrogenolysis of dimethyl oxalate (1) to ethylene glycol (3) has been obtained. The catalytic system appeared to be most efficient when Ru(acac)$_3$ was used in combination with the facially coordinating tripod ligand triphos (CH$_3$C(CH$_2$PPh$_2$)$_3$, 13). Compared to the known catalyst reported in literature by Matteoli et al." (the only homogeneous catalyst able to hydrogenate dimethyl oxalate to ethylene glycol), this catalyst is far more active. For the first time, a catalyst was found that enabled the full conversion of esters into the corresponding alcohols in high yields and selectivities using relatively mild conditions.

By selecting different ligands, the product of the reaction can be chosen. For example, when using the meridional coordinating ligand PhP(C$_2$H$_4$PPh)$_2$, dimethyl oxalate is almost exclusively converted to methyl glycolate (2) whereas the use of MeC(CH$_2$PPh$_2$)$_3$ leads to the exclusive formation of ethylene glycol (3).

4 Experimental section

4.1 Equipment

Gas Chromatography

Analysis was carried out using a Varian 3300 gas chromatograph equipped with a DB-5 capillary column (length = 30 m, internal diameter Φ = 0.32 mm, film thickness 1μm)
and a FID detector. Injection and detection temperatures were set at 250 °C. After injection, the temperature of the GC was kept at 70 °C for a period of 2 minutes. After two minutes, the GC was warmed to 230 °C with a gradient of 20 °C per minute; afterwards the GC was allowed to remain at 230 °C for 5 minutes before cooling down to 70 °C.

**Nuclear magnetic resonance spectroscopy**

The characterization of the compounds was based mainly on NMR techniques. $^1$H and $^{31}$P NMR spectra were recorded on a Varian Mercury 300 or a Bruker AMX 300 spectrometer. $^1$H NMR spectra were referenced to tetramethylsilane (TMS), and $^{31}$P-NMR spectra to 85% H$_3$PO$_4$. All samples were measured at room temperature with deuterated chloroform (99.8 atom % D, Cambridge Isotope Laboratories, Inc.) as the solvent.

**Autoclave setup**

All experiments were conducted in a homebuilt stainless steel batch reactor (autoclave) designed for reactions under pressures up to 130 bar. The autoclave consisted of a thick-walled (1.5 cm) beaker of approximately 200 ml (4, figure 2). The beaker was attached to a wider stainless steel ring in which an deeper lying opening allowed for the placement of a Viton® O-ring (5) to ensure an air-tight seal with the lid (6) of the autoclave. The lid was attached to the beaker by tightening six bolts in a crosswise manner.

On the lid of the autoclave were three openings that connected to a manometer (8) combined with the gas inlet (7), a connector for the thermocouple (2); the third opening allowed for the introduction of a sample via a sample inlet valve (10). The entire autoclave system was protected against overpressure by the variable relief valve (9). Mixing of the contents of the autoclave was achieved by a magnetic stirring bar. To heat the contents of the autoclave, the autoclave was placed in an electrically heated oven that was regulated by a Jumo dTRON controller with feedback from the PT-100 thermocouple (2).

* Since high gas pressures were involved, safety precautions had to be taken at all stages of studies involving high pressure equipment.
4.2 Chemicals

All manipulations were carried out using standard Schlenk techniques in a dried nitrogen atmosphere. Solvents were obtained from Acros Organics, and dried on the appropriate drying agent.\textsuperscript{21} Solvents were distilled prior to use and stored in a dried nitrogen atmosphere. Hydrogen gas (purity 5.0, 99.999\%) was obtained in 10 m\textsuperscript{3} cylinders from Hoek Loos B.V. Holland, and used without additional purification or drying.

Ru(acac)\textsubscript{3} was purchased from Acros Organics and used without further purification. RuCl\textsubscript{3}.xH\textsubscript{2}O was obtained from Johnson and Matthey and used as received. RuCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{4} was prepared according to literature procedures.\textsuperscript{22,23} Ligands and substrates were obtained commercially from Acros Organics. All solid ligands were purified by recrystallization from a boiling hexanes solution. Liquid compounds were distilled under reduced pressures prior to use.
4.3 General hydrogenolysis experiment

All hydrogenolysis experiments were standardized with respect to temperature, pressure and reaction time in order to facilitate comparison of the data obtained.

In a typical experiment, a solution was prepared using a Schlenk vessel. Solid materials were weighed in air and transferred to a Schlenk vessel that was closed afterwards using a rubber septum. A syringe was used to introduce solvents, liquid substrates and additives under exclusion of air. The catalytic mixture consisted of a 15 ml solution of the catalyst precursor (usually 0.5% with respect to the substrate (10-15 μmol for 30 mmol substrate), although it may differ in individual experiments). In addition to the ruthenium precursor, 4.5 equivalents of a monodentate ligand were added (in the case of didentate ligands, 2 equivalents and for tri-, and tetridentate ligands 1.5 equivalents were used). In some cases, additional heating was required to dissolve all the starting materials and to obtain a homogeneous solution. To this solution (if necessary the mixture was allowed to cool to room temperature before addition), the substrate (30 mmol) was added using a syringe.

Before introducing the solution into the autoclave, the autoclave was evacuated and flushed with dry nitrogen three times. Because of the large volume, this should be done slowly. The mixture was then introduced in the autoclave by connecting a syringe to one of the available Swagelok™ connectors. By reducing the pressure inside the autoclave, the solution, that was previously prepared, was introduced in the autoclave. While stirring, the autoclave was flushed three times with 25 bar of hydrogen gas before applying the final pressure of 80 bar. The autoclave was heated to 120 °C and left stirring over a period of 16 hours. The autoclave was allowed to reach room temperature after which the pressure was slowly released to 1 bar. The contents in the autoclave were transferred to a round-bottomed flask, and the solvent was removed in vacuo. A sample from the remaining mixture was taken for NMR and GC analysis.

5 References

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