Development of homogeneous catalysts for the selective conversion of levulinic acid to caprolactam

Raoufmoghaddam, S.

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Author: Raoufmoghaddam, Saeed
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General Introduction

Abstract

The aim of this chapter is to introduce the readers to the importance of bio-based products and their potential applications in chemical industries. Alternative routes to the widely used nylon precursor caprolactam are discussed and compared with the current fossil-based synthesis. Furthermore, an overview is given of catalytic C-N bond forming reactions such as reductive amination of aldehydes and hydroaminomethylation of alkenes. Finally, the aim of the research - the development of a novel synthesis route to caprolactam based on biomass - is revealed; the envisaged reaction sequence includes the development of new catalytic chemistry, namely reductive amidation and hydroamidomethylation.

The introduction chapter partially will be submitted as a review paper;
Raoufmoghaddam S.; Drent E.; Bouwman E.; manuscript in preparation

1.1. Biomass

Prior to the discovery of the fossil reserves, society was contingent upon biomass to supply energy demands. The discovery of crude oil, in the nineteenth century, provided a convenient and low-priced liquid fuel resource that promoted industrialization of the world. In recent years, diminishing petroleum reserves combined with an increased demand for energy and rising crude oil price have drawn attention to develop economical and energy-efficient processes for the sustainable production of fuels and chemicals. The global energy demand is predicted to grow up to 50% by 2030, which will have an additional impact on the climate as well as our planet. The recent United Nations Framework Convention on Climate Change has ratified the Kyoto Protocol that is intended to reduce global emissions by at least 20% by 2020 and by 50% - 60% by 2050 relative to the emission level in 2006.[1] Plant biomass is the only current sustainable source of chemicals and bio-fuels.[2-5] A significant advantage of bio-based products is the differences in the green-house gas emissions. The bio-fuels are generally considered to emit less green-house gas than the fossil fuels.[6-9] Nevertheless, there are also growing concerns about the overall sustainability regarding the change in land usage, intensified use of agricultural inputs and limitation on food security.

A number of materials potentially useful as bio-based feedstock such as lignocellulose, proteins, oils, lignin, hemicellulose, cellulose, or starch have been identified.[10] Lignocellulosic biomass is one of the most abundant and attractive sources of biomass for the production of bio-based chemicals.[11-14] One of the drawbacks of lignocellulosic biomass is that it typically contains 40-45 wt% oxygen which decreases the heating value. Lignocellulosic biomass can be converted into liquid fuels by three primary routes, including syngas production by gasification, bio-oil production by pyrolysis or liquefaction, or hydrolysis to produce sugar monomer units. Synthesis gas can be used to produce hydrocarbons (diesel or gasoline), methanol, and other fuels via the classical Fischer-Tropsch process.[15-18]

Cellulose (a crystalline glucose polymer) and hemicellulose (a complex amorphous polymer; the major component is a xylose monomer unit) form 60-90 wt% of terrestrial biomass. Cellulose consists of a linear polysaccharide and the top and bottom of the cellulose chains are essentially hydrophobic.[4] Upon partial acid hydrolysis, cellulose is broken into cellobiose (glucose dimer), cellotriose (glucose trimer), and cellotetrose (glucose tetramer), whereas upon complete acid hydrolysis it forms glucose.[19] Hemicellulose is a sugar polymer that typically constitutes 20-40 wt% of biomass which is a polymer of five different sugars comprising five-carbon sugars (mostly xylose and arabinose) and six-carbon sugars (galactose, glucose, and mannose). The most abundant building block of hemicellulose is xylan (a xylose polymer linked at the 1 and 4 positions).

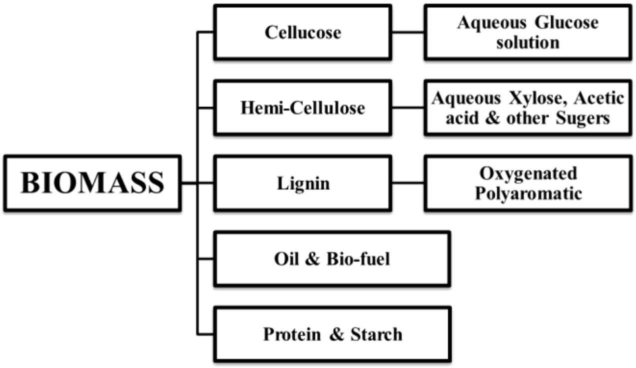
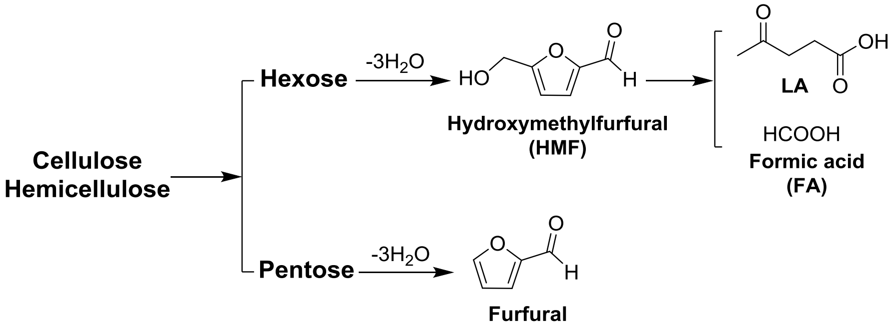


Figure 1.1. Classification of different biomass-derived feedstock

Lignin, a large polyaromatic compound, is the other major component of biomass (10-25 wt%) which is a highly branched, substituted, aromatic polymer. Lignin is often associated with cellulose and hemicellulose forming lignocellulose. Other components called extractives are defined as those compounds that are soluble in solvents such as water, ethers or methanol which involve different types of carbohydrates such as sucrose from sugarcane and amylose from corn grains.[1, 2, 18]

In the biomass conversion process cellulose and hemicellulose can be converted into xylose and glucose. Then, furfural and hydoxymethylfurfural (HMF) can be produced from the remaining sugar stream by acid-catalyzed dehydration (Scheme 1.1).[20]

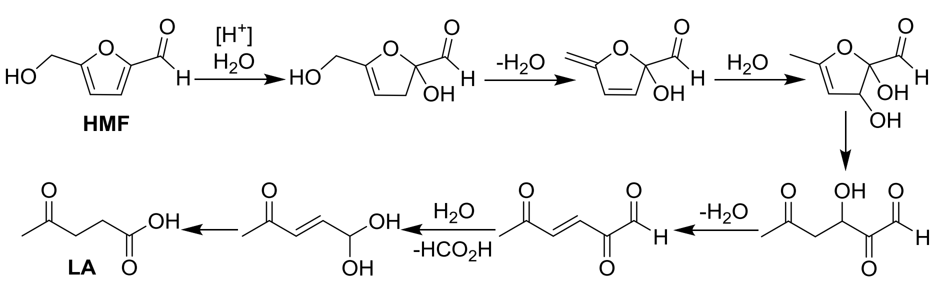
HMF is one of the top building-block chemicals obtained from biomass which can be used to synthesize a broad range of chemicals currently derived from petroleum.[12, 20-23] However, obtaining a highly selective process to produce HMF is still crucial as the current procedure leads to a relatively high manufacturing cost of HMF due to the formation of by-products, thus limiting its potential as a key platform chemical.[24, 25] A number of important compounds can be formed from HMF such as alkoxymethylfurfurals, 2,5-furandicarboxylic acid, 5-(hydroxymethyl)furoic acid, bis(hydroxymethyl)furan, 2,5-dimethylfuran and levulinic acid (LA).[26]



Scheme 1.1. Hydrolysis and degradation of cellulose and hemicellulose to furfural, HMF and levulinic acid (LA)

1.2. Bio-based levulinic acid (LA)

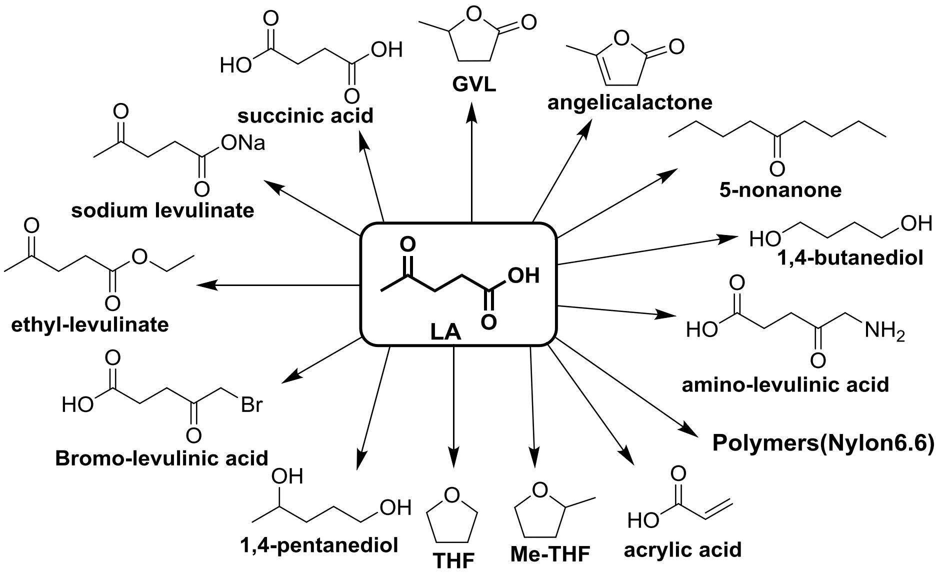
One of the key substances produced from HMF is levulinic acid (LA) which potentially is an important platform molecule for versatile industrial applications such as production of fine chemicals, pharmaceuticals, polymers, solvents and fuels.[27-31] As shown in Scheme 1.2, levulinic acid is the final acid-catalyzed dehydration product formed from cellulose together with formic acid (in a 1:1 molar ratio) and water as co-products.[32-34] The theoretical yield of LA from C6-sugars is 100 mol% or 64.5 wt% due to the coproduction of formic acid.[28, 35] Commonly, LA yields up to two-thirds of the theoretical value are attained, due to side reactions that form undesired black insoluble-materials called humins.[36]



Scheme 1.2. Proposed mechanism for formation of levulinic acid from HMF

The reactivity of the carbonyl functionalities in LA makes it an ideal intermediate for the production of useful chemicals including succinic acid, resins, polymers (nylon precursor, caprolactam), herbicides, pharmaceuticals, flavoring agents, solvents, plasticizers, antifreeze agents and biofuels/oxygenated fuel additives (Scheme 1.3).[37-41]

The current synthetic method for the production of high purity levulinic acid is based upon the conversion of maleic anhydride[42] or hydrolysis of furfuryl alcohol[43, 44] which reactions are more complicated than the acid hydrolysis of biomass. The reasons for restricted manufacturing of levulinic acid production are the cost of raw material used in the synthesis, low yield (due to the formation of undesired side reactions and polymerization of products), equipment costs, high energy input and waste disposal issues.[45]

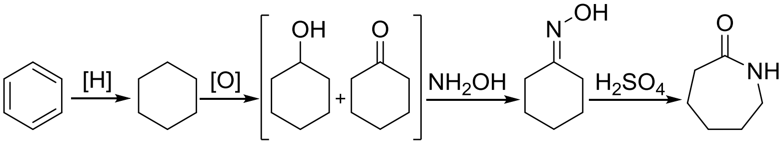


Scheme 1.3. Levulinic acid as an important platform for the production of other chemicals and fuel components

1.3. Synthesis of caprolactam

1.3.1. Industrial production

ε-Caprolactam is the polymer precursor for nylon-6, an extensively used synthetic polymer with an annual production of about four million tons.[46] Caprolactam was first introduced in the late nineteenth century by the cyclization of 1-aminocaproic acid, and then became an important chemical with commercial interest in 1938 by the poly-condensation of caprolactam producing nylon-6.[47] Caprolactam is a monomer for the nylon-6 polyamide which shows excellent properties including high strength-to-weight ratio and good chemical and thermal stability. Nylon-6 is widely used in the manufacture of fishing nets, tires, strings, industrial drive belts, fibers and plastics.[48]



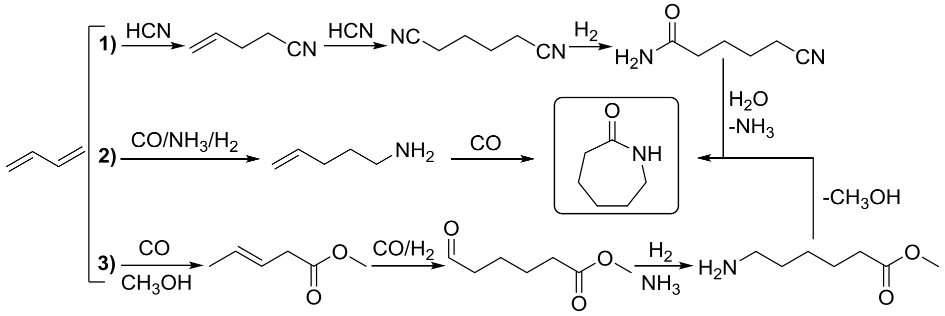
Scheme 1.4. Industrial synthetic route for the production of caprolactam

Several synthetic routes have been reported for the synthesis of caprolactam, which produce relatively large amounts of by-products, mainly ammonium sulfate. This ammonium sulfate can be used as a fertilizer, but in recent years it is being replaced by nitrate or urea fertilizers because of their higher nitrogen content. However, ammonium sulfate is still used as a fertilizer in some countries and on sulfur-poor soils.[48] The synthesis of ε-caprolactam is typically carried out in a four-step procedure[49] including synthesis of cyclohexanone either by oxidation of cyclohexane,[50, 51] or by hydrogenation of phenol,[52, 53] followed by the formation of cyclohexanone oxime.[54, 55] Through a Beckmann rearrangement of this oxime in sulfuric acid ε-caprolactam is obtained.[56-59] In the process water is added for dilution of the acid and purification process which ultimately needs to be evaporated.[60] The increasing demand for ε-caprolactam has provoked the chemical companies to extend their efforts to explore more efficient synthetic routes[61-63] as well as alternative production pathways[64] for this bulk chemical.

1.3.2. Alternative routes

1.3.2.1. Butadiene-based routes

One alternative route for the production of caprolactam comprises the hydrocyanation of butadiene to 1,6-hexanedinitrile which is a process based on homogeneous nickel phosphite catalysts. In the second step the 1,6-hexanedinitrile is hydrogenated with molecular hydrogen in presence of a Raney nickel catalyst with a good yield (conversion: 70-85% and selectivity to 6-aminohexanenitrile: 85-100%).[65, 66] The last step is the hydrolytic cyclization of 6-aminohexanenitrile, either in the gas phase or in the liquid phase with good results (90-99%) using SiO_2 or manganese zirconium oxide phosphate catalysts (Scheme 1.5).[67-71] One major disadvantage of the hydrocyanation route is the high cost of HCN as N source while one mole of N/mole of caprolactam is down-graded to an ammonium salt co-product.



Scheme 1.5. Alternative synthetic routes starting from 1,4-butadiene for the production of caprolactam; 1) via multi-step reaction consisting hydrocyanation, selective hydrogenation and cyclization; 2) via two-step reaction including hydroaminomethylation of butadiene with ammonia and intramolecular aminocarbonylation of aminopentene; 3) via multi-step reaction including methoxycarbonylation, hydroformylation, reductive amination and cyclization

Another route involves hydroaminomethylation of butadiene with ammonia[72] and a subsequent cobalt-catalyzed intramolecular aminocarbonylation to form caprolactam.[73] However, obtaining a very selective hydroaminomethylation with large excess amount of ammonia and high temperature in the first step is challenging (see also Section 1.4). Furthermore, the low selectivity for caprolactam (~40% in the best case) with the formation of different products including nylon-6 oligomers in the second step are still problematic.[73]

The third alternative route producing caprolactam from butadiene is called the hydroesterification route,[74-77] which is based on an initial methoxycarbonylation[78-81] of butadiene to form methyl 3-pentenoate (3-MP).[82, 83] The hydroesterification of butadiene with carbon monoxide and methanol in the presence of a cobalt or palladium catalyst results in high yield with only negligible amounts of by-products like methyl valerate and 4-vinylcyclohexene.[74, 84, 85] For the next step, an isomerization-hydroformylation reaction must be carried out, which results in 30-90% conversion with 65-75% selectivity to methyl 5-formylvalerate.[86] In the third step the methyl 5-formylvalerate can be either reductively aminated to 6-aminohexanoate and then cyclized, or acid hydrolyzed to 5-formylvaleric acid and then reductively aminated and subsequently cyclized (scheme 1.5).[84, 86-93] The first route (reductive amination and cyclization) can be performed in the liquid[75, 94] or the gas phase,[95] both over hydrogenation catalysts in the presence of NH_3, H_2 and NiO–MgO–SiO_2 or ruthenium on Al_2O_3 carrier with 80-95% yield.[75, 93, 95] In the second route, 5-formylvaleric acid is obtained with 74% yield[96] over cation-exchanged resin catalyst; reductive amination to 6-aminohexanoic acid in presence of a Raney Ni catalyst yields 57% of 6-aminohexanoic acid. Finally, this product is cyclized to caprolactam (95-99%) with or without a catalyst at high temperature.[48]

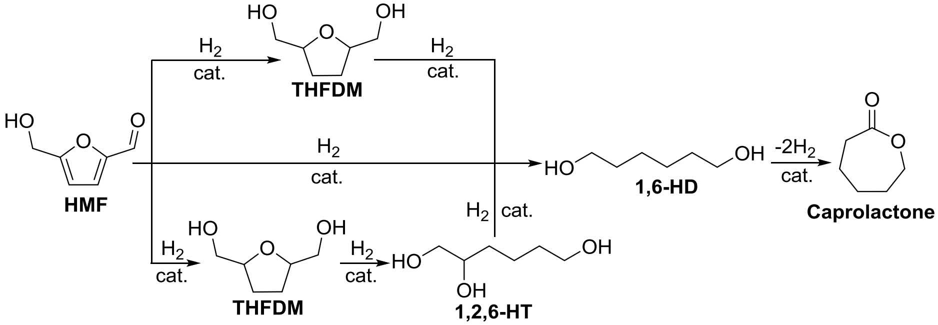
Apart from being fossil-based, the major drawbacks of the butadiene-based caprolactam routes are the necessity of several separations and recycling steps of the products and by-products as well as employing severe conditions with relatively low efficiency.[48]

1.3.2.2. Biomass-based route

Recently, an alternative route to caprolactam has been proposed based upon a multi-step catalytic conversion of hydroxymethylfurfural (HMF) to caprolactone.[64] The demonstrated reaction sequence contains several steps including hydrogenation of HMF to 1,6-hexanediol (1,6-HD) and catalytic conversion of 1,6-HD into caprolactone (Scheme 1.6).[64]

The one-step hydrogenation HMF to 1,6-HD was performed under severe conditions (270 °C, 150 bar H_2) with a mixture of copper chromite and Pd/C (1:0.6). After 16 hours, 100% conversion of HMF to a mixture of products, mainly 2,5-tetrahydrofuran-dimethanol (THFDM) was obtained (less than 4% of desired 1,6-HD). The hydrogenolytic ring opening of THFDM to 1,6-HD using CuCr (consisting of 75%

$Cu_2Cr_2O_5$ and 25% CuO) gave a maximum selectivity of 41% to 1,6-HD with 41% conversion of THFDM. On the other hand, the similar reaction using THFDM as the substrate to form 1,2,6-HT was also investigated using Rh-Re/SiO_2 catalyst. A 97% selectivity to 1,2,6-HT was obtained with only 21% THFDM conversion after 20 hours at 80 °C and 80 bar H_2. The use of higher temperatures and longer reaction time led to a drop in selectivity to 1,2,6-HT. Subsequently, in a two-step reaction, further reduction with the same catalyst in the presence of triflic acid (HOTf) at 125-180 °C and 80 bar H_2 was carried out and 99% selectivity to 1,6-HD at 17% 1,2,6-HT conversion was obtained. The direct formation 1,6-HD from THFDM under optimized condition (Rh-Re/SiO_2, 80 bar H_2, 120 °C, acid catalyst and 20 h) revealed full conversion with 86% selectivity to 1,6-HD. The final step was carried out to form caprolactone from 1, 6-HD using Ru catalyst which turned out to give 99% selectivity to the desired caprolactone.[64]

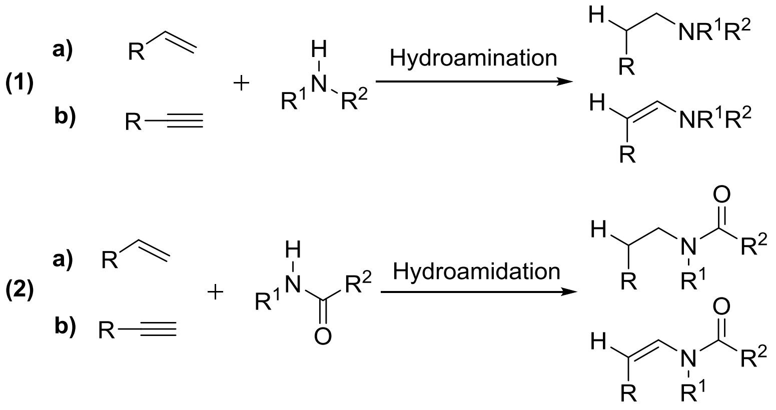


Scheme 1.6. Alternative synthetic routes reported for the conversion of bio-based HMF into caprolactone as a precursor of caprolactam

1.4. Homogeneously-catalyzed C-N bond forming reactions

1.4.1. Hydroamination and hydroamidation of alkenes and alkynes

The catalytic formation of carbon–nitrogen bonds and more importantly amide bonds offer potential advantages over conventional methods of C-N coupling reactions, where large quantities of salts are produced stoichiometrically as by-products. Among the different catalytic methods of carbon-nitrogen bond formation, the most studied and challenging methods are hydroamination and hydroamidation of alkenes and alkynes with amines and amides (Scheme 1.7).[97-106] The hydroamination of alkenes or alkynes is defined as the addition of an H-NR^{1}R^2 bond across an alkene or alkyne providing a next higher substituted alkyl- or alkenylamine, respectively (Scheme 1.7, reaction 1a-b).

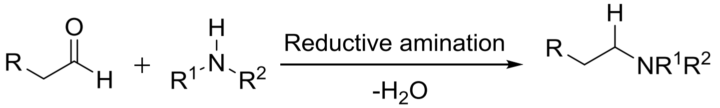


Scheme 1.7. Hydroamination; hydroamidation reactions

This reaction, which can be catalyzed both by transition metal complexes or by strong base, has been mostly studied with secondary and primary amines rather than ammonia; due to the need of high ratio of ammonia/alkene as well as the subsequent reactivity of the primary reaction product.[104, 107] The catalytic hydroamination reaction of olefins is further characterized by low rates and low catalyst turnover numbers, as the thermodynamic driving force for the intermolecular version of hydroamination is close to zero or even negative at the elevated temperatures generally required for the reaction to proceed. The related hydroamidation reaction, involving the addition of an amide's N-H bond to an alkene (Scheme 1.7, reaction 2a-b) has also been studied; application of this reaction in an intermolecular fashion suffers from similar problems as mentioned for intermolecular hydroamination, in particular with alkenes as substrate.

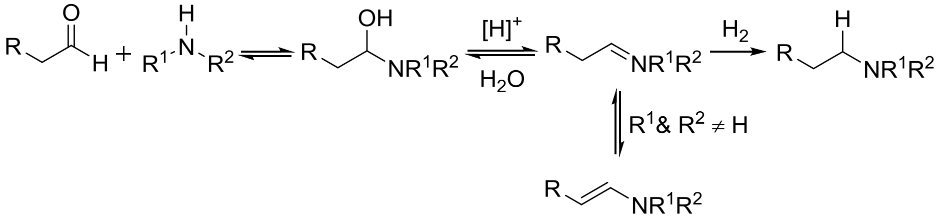
1.4.2. Reductive amination of aldehydes

The reductive amination of carbonyl compounds is of great importance in synthetic organic chemistry (Scheme 1.8).[108-111] In principle, this reaction can be performed with high atom efficiency, with very limited waste formation, fulfilling one of the requirements of green chemistry.



Scheme 1.8. Reductive amination of aldehydes

The reductive amination of aldehydes typically proceeds in several consecutive steps. Generally, the reaction progresses via the initial formation of an intermediate carbinolamine by nucleophilic addition of an amine to an aldehyde; this carbinolamine is dehydrated to form an imine, which is then reduced to form the amine product (Scheme 1.9).[108, 112-114] Some reports provided evidence suggesting a direct reduction of the carbinolamine.[108, 115] The main side reaction in the reductive amination concerns the formation of an alcohol from the competing hydrogenation of the unreacted aldehyde. Another side reaction comprises the aldol condensation of aldehyde which can be suppressed by optimizing the process.[108]



Scheme 1.9. Separate steps of the catalytic reductive amination of aldehydes

In the reductive amination the choice of reducing agent play an important role to the success of the reaction in which the imine intermediates need to be reduced selectively over the aldehydes. Traditionally, the reductive amination of aldehydes is carried out using stoichiometric amounts of reducing agents such as borohydrides,[116-119] formates,[120-123] silanes[124, 125] and many other different reagents.[126, 127] However, all of these methods are not atom efficient.

The use of heterogeneous catalysts in the reductive amination such as Raney-nickel, Pt/C, Pd/C, Pd/Al_2O_3, Pd/$CaCO_3$, $Pd(OH)_2$ and metal nanoparticles in presence of dihydrogen gas as reducing agent have also been reported.[112, 128-131]

A few homogeneously-catalyzed reductive amination reactions have been reported using transition metals (Pd, Pt, Ir, Ru and Rh) in combination with different ligands,[111, 113, 126, 132-136] as well as iron complexes[137-139] and cobalt complexes in presence of an alcoholic solvent as a source of hydrogen.[140, 141]

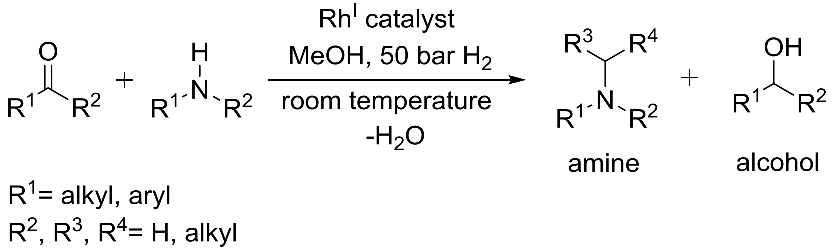
A more practical method is to employ molecular hydrogen as a reducing agent in the reaction in the presence of a catalyst. Clearly, the use of molecular hydrogen in the catalytic reductive amination is the most atom-economic and environmentally friendly, particularly in large-scale reactions.[111, 131, 142-145]

Some examples concerning the catalytic reductive amination of aldehydes using molecular hydrogen are collected in Table 1.1. The success of this procedure requires the reduction of the carbonyl compound to be relatively slower than the reduction of imine intermediate.

Table 1.1. Overview of different reaction conditions used in the catalytic reductive amination of aldehydes in presence of molecular hydrogen

aldehyde	amine	reagent	conditions	amine selectivity	research group
bezaldehyde derivatives	aniline derivatives	5 mol% $Cu(OAc)_2$, molecular Sieves	Toluene, 50 bar H_2, 120°C, 24h	75-85%	Beller (Green Chem., **2012**, 14, 2371
bezaldehyde derivatives	aniline derivatives	4 mol% $Fe_3(CO)_{12}$	Toluene, 50 bar H_2, 65°C, 24h	65-95%	Beller (Chem. Asian J. **2011**, 6, 2240)
bezaldehyde	ammonia	1 mol% Pd/C,	MeOH, 40 bar H_2, 90°C, 10h	sec. >80%	Gu (Chem.Commun. **2012**, 48, 9631)
alkyl aldehydes	Secondary amines	5 mol% $[Fe^{II}]$, Me_3NO (5 mol%)	EtOH, 5 bar H_2, 85°C, 12h	35-90%	Renaud (Angew. Chem. Int. Ed. **2012**, 51, 4976)
aliphatic aldehydes	Secondary amines	0.2 mol% $[Rh(dppb)(cod)]BF_4$	MeOH, 50 bar H_2, 25°C, 20h	40-90%	Börner (Chem. Commun. **2000**, 1867; Adv. Synth. Catal. **2002**, 344, 200)
benzaldehyde derivatives	ammonia	0.5 mol% [Rh], 1.3 mol% TPPTS	H_2O/THF, 65 bar H_2, 135°C, 2h	33-86%	Beller (Org. Lett. **2002**, 4, 2055)

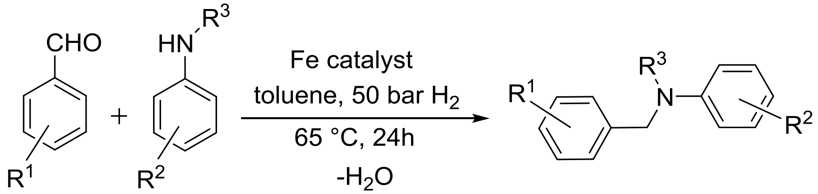
The reductive amination of aldehydes with secondary amines (like piperidine) has been reported employing a rhodium precursor in combination with bidentate phosphane ligands (Scheme 1.10).[111] The best results revealed nearly full conversions with the relatively high amine/alcohol ratios (3-12); however, the amine/alcohol ratios for the benzaldehyde derivatives were rather low (< 2).



Scheme 1.10. Reductive amination of aldehydes with secondary amines using rhodium (I) catalyst

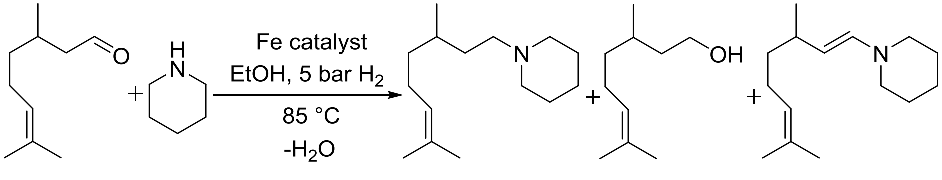
The use of chelating phosphane ligands (like dppb) for the reaction appeared to be necessary for high selectivity to the amine. Furthermore, a good correlation between the selectivity of the reaction and the basicity and steric hindrance of the amine substrate was shown. Use of more basic amines as a substrate resulted in higher selectivity and higher amine/alcohol ratios.

Beller and co-workers recently reported the use of iron carbonyl complexes in the reductive amination of carbonyl compounds with aromatic amines (Scheme 1.11).[137] The inexpensive iron catalyst gave good to excellent yields of 68–97% of alkylated amines for a range of aryl, alkyl, and heterocyclic ketones as well as aldehydes with primary and secondary anilines.



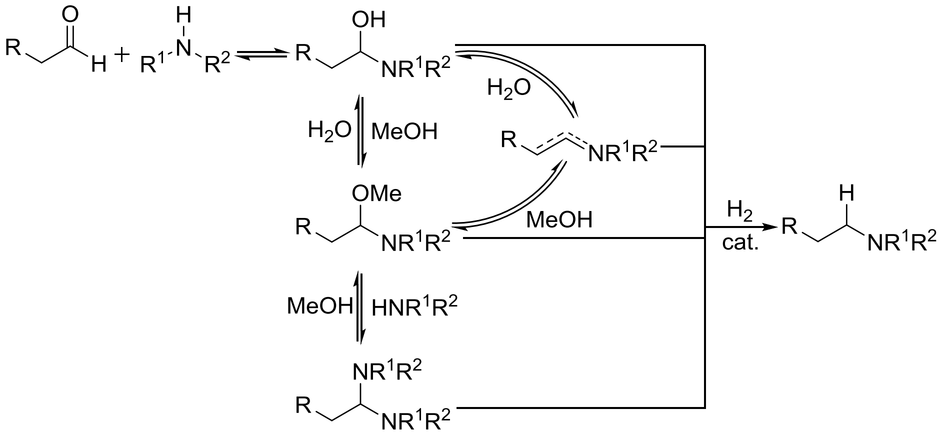
Scheme 1.11. Reductive amination of aldehydes with various aniline derivatives using Fe catalyst

More recently, the reductive amination of 3,7-dimethyl-6-octenal (citronellal) with piperidine catalyzed by iron complexes under low hydrogen pressure (5 bar H_2) and in mild reaction conditions (85 °C) in ethanol was reported (Scheme 1.12).[138] The scope of the reaction using citronellal with different amines revealed moderate to good yields (38-94%) under optimized conditions.



Scheme 1.12. Reductive amination of citronellal with piperidine using Fe catalyst

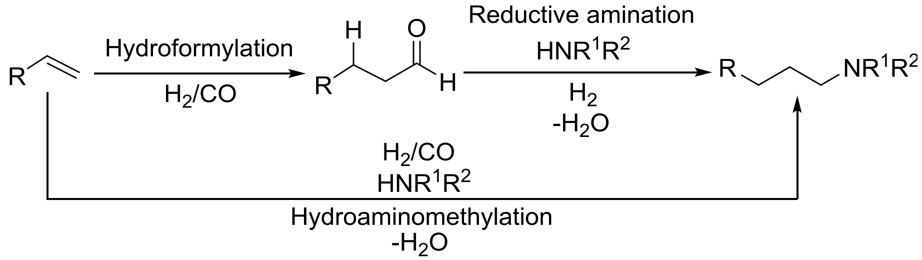
It is imperative to note that alcohol as a solvent typically has a positive role in the hydrogenolysis step and promotes the hydrogenation activity. It has been postulated that the mechanism contains several equilibrium reactions in which the intermediates ultimately undergo hydrogenation to form amine products (Scheme 1.13).[145]



Scheme 1.13. Proposed mechanism for the reductive amination of aldehydes using molecular hydrogen

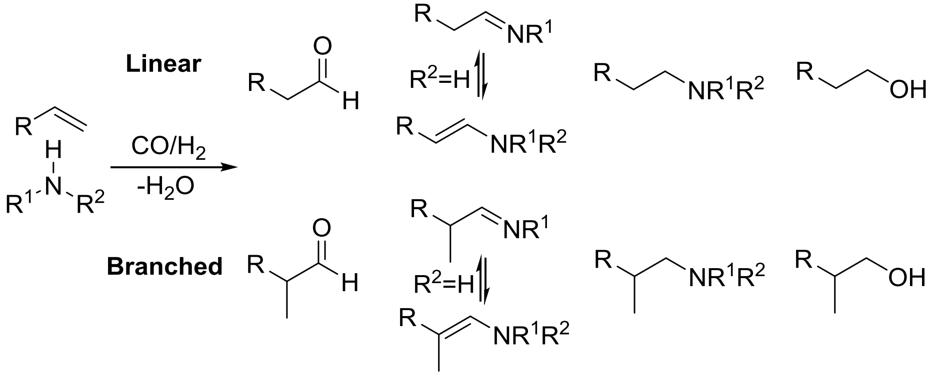
1.4.3. Hydroaminomethylation of Alkenes

The hydroaminomethylation of alkenes is a cascade reaction of two consecutive reactions. The alkene substrate first undergoes a hydroformylation reaction[146] to form an aldehyde; and then the reductive amination of the resulting aldehyde with an amine produces an N-alkylated amine (Scheme 1.14).[108-111]



Scheme 1.14. Hydroaminomethylation reaction

Despite the fact that the hydroaminomethylation reaction was originally discovered by Reppe in the early 1950s at BASF using $Fe(CO)_5$ in nearly stoichiometric amounts,[147, 148] intensive research on this topic only started in the past fifteen years. Research on this reaction until the mid-1990s revealed that relatively harsh conditions (> 150 °C) were required to give the desired amines in good yield.[149-157] Generally, the cascade hydroaminomethylation results in the formation of various intermediates and products depending on the reaction conditions and the type of catalyst used in the reaction (Scheme 1.15).



Scheme 1.15. Overview of hydroaminomethylation of alkenes; formation of various products

In the following years, most of the reports described the hydroaminomethylation as a versatile, selective and atom-efficient tool for the synthesis of a range of organic compounds, including fatty amines from unsaturated fatty acid esters,[158-161] pharmaceuticals compounds[162, 163] and heterocyclic rings *via* ring-closing intramolecular hydroaminomethylation reaction.[164-169]

The critical step in this reaction sequence is the hydrogenation of the intermediate imino compounds, which is generally hampered by the presence of carbon monoxide; however, over the last decade significant progress has been made and the problem was reduced by using alcoholic and polar solvents.[162, 170-175] In recent years, the focus has been on catalyst development to obtain the desired chemo- and regioselectivity for the reaction.

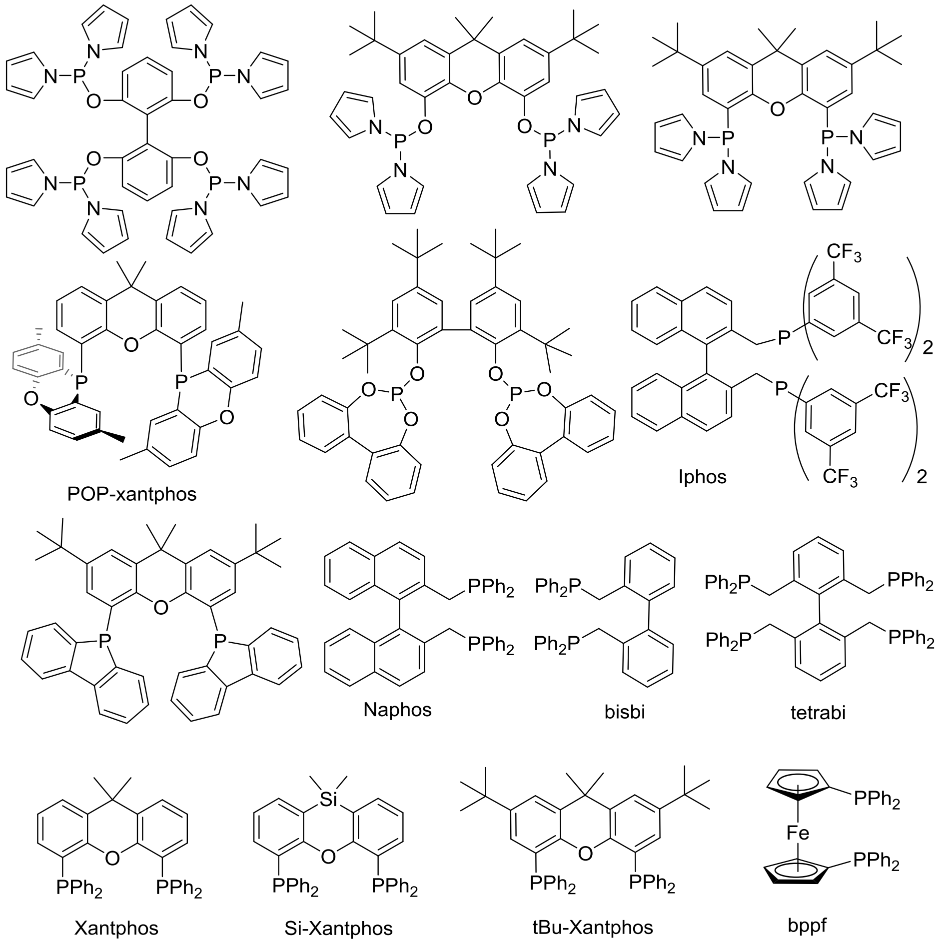
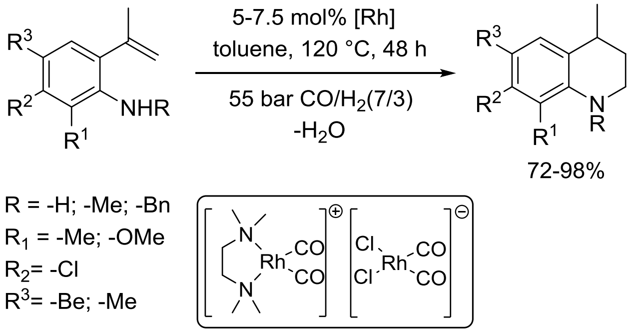


Figure 1.2. Selected ligands used in hydroaminomethylation of alkenes

To achieve good regioselectivity for the hydroformylation step the use of ligands with large bite angle (β_n) is important for obtaining good regioselectivity, promoting the formation of linear aldehydes.[146, 176, 177] The electronic properties of a ligand influences on the activity and regioselectivity of the catalytic system.[178, 179] The π-acidic ligands are known to afford high activities in rhodium-catalyzed hydroformylation.[146]

The ligands shown in Figure 1.2 are particularly adapted to produce the linear aldehyde in the hydroformylation step, even when starting from an internal alkene.[146, 176, 180-183] It has also been reported that the use of these bidentate phosphite ligands give good results in the hydrogenation step.[184, 185] Although the phosphite ligands are seemingly attractive for the hydroaminomethylation reaction, they have often been considered as unsuitable due to their sensitivity to hydrolysis.[175]

The use of bidentate phosphane ligands, such as xantphos, Naphos, Iphos, POP-xantphos bisbi and tetrabi has been reported mainly for hydroaminomethylation of aliphatic alkenes (Figure 1.2).[170, 171, 173, 186] Di-pyrrolylphosphane ligands in combination with Rh have also been introduced for the hydroaminomethylation reaction and resulted in satisfactory selectivity of amine.[172] Furthermore, the use of nitrogen-containing ligands in combination with a rhodium precursor has recently been reported showing a good selectivity, but with large catalyst loading (Scheme1.16).[168, 169, 187]



Scheme 1.16. Rhodium catalyzed intramolecular hydroaminomthylation of 2-isopropylanilines

The use of other ligands in the catalytic systems, such as bis-pyrazolylmethane (bpm),[188] mixed phosphane-amine[189, 190] and N-heterocyclic carbene (NHC) ligands [162, 167, 191] have been reported to give satisfactory selectivities (Table 1.2).The group of Beller was the first to report rhodium based catalytic systems to transform both terminal and internal alkenes into linear amines with very high regioselectivities (Table 1.2).[170, 171, 175, 192]

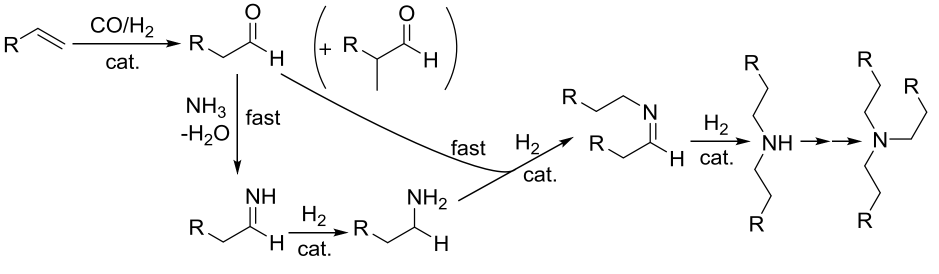
Table 1.2. Overview of different reaction conditions used in the hydroaminomethylation of alkenes

alkene	amine	reagent	condition	amine selectivity	group
1-dodecene	morpholine	1 mol% Rh, BISBIS	[Bmim][p-$CH_3C_6H_4SO_3$],CO /H_2, 130°C, 5h	45-75%	Luo (Green Chem., **2006**, 8, 545)
Intramolecular (alkene and secondary amine)		2.5-7.5 mol% Rh	toluene,CO/H_2, 120°C, 48h	60-90%	Alper (Org. Lett., **2008**,10, 485; Chem. Commun., **2007**, 2710)
1-alkenes	piperidine	0.02-0.09 mol% Rh, sulfoxantphos	[PMIM][BF_4], CO/H_2,125°C,17h	>90%	Vogt (Adv. Synth. Catal. **2008**, 350, 332)
1,1-diphenyl-ethene	piperidine	0.2 mol% Rh, carbene ligand (NHC)	toluene, CO/H_2, 125°C, 24h	11-99%	Beller (Chem. Eur. J. **2007**, 13, 1594; Tet.Lett.44, **2003**,1679)
alkenes	amine derivatives	0.4 mol% Rh, POP-xantphos or Iphos or Naphos	tol/MeOH(1/1), CO/H_2, 125°C, 16-24h	50-90%	Beller(Chem.Eur.J.**2006**,12,79; J.Am.Chem.Soc.**2003**,125,10311;Science**2002**,297,1676)
limonene	amine derivatives	1.25 mol% Rh, PPh_3	THF, CO/H_2, 100°C, 10-19h	0-90%	Rosa (Catal. Commun. 9, **2008**,1066)
1-alkenes	amine derivatives	1 mol% Rh, biphephos	[bmim][BF_4], CO/H_2, 110°C, <1h, MW	55-90%	Taddei (Tet. Lett. 48, **2007**, 8501)
N-methylallyl-phthalimide	amine derivatives	1 mol% Rh	toluene or dioxane, CO/H_2, 100-140°C, 72h	44-96%	Elibracht (Org. Biomol. Chem., **2006**, 4, 826)
allyl alcohols	secondary amines	0.5 mol% Rh, biphephos	toluene or dioxane, CO/H_2, 120°C, 45-65h	>95%	Eilbracht (Tetrahedron 60, **2004**,11487; Tetrahedron 59, **2003**, 8265)
allyl alcohols	secondary amines	0.2 mol% Rh, biphosphite	THF, CO/H_2, 75°C, 18h	>65%	Whiteker (Org. Lett., 7, **2005**, 4795)
alkenes	secondary amines	0.1 mol% Rh, tetrabi	iPrOH/EtOH(2/1) or iPrOH, CO/H_2, 125-135°C, 12-36h	80-99%	Zhang(Chem.Eur.J.**2011**,17,14559;Org.Lett.,14,**2012**,102; Adv.Synth.Catal.**2011**,2665; Chem.Eur.J. **2010**, 16, 4938; Org. Lett., 15, **2013**, 1036)
Styrene derivatives	aryl hydrazine	0.5 mol% Rh	toluene, CO/H_2, 100°C, 48-72h	23-57%	Eilbracht (Org. Lett., 5, **2003**, 3213)
1-octene	piperidine	0.1 mol% Rh, Xanthene-pyrrolo Ligand	tol/MeOH(1/1), CO/H_2,110°C,17h	>85%	Vogt (ChemCatChem **2009**, 1, 103)
1-alkenes	secondary amines	5-10 mol% In or Ti	toluene, CO/H_2, 80-160°C, 24-96h	5-95%	Doye (Angew. Chem. Int. Ed. **2010**, 49, 2626)

As shown in Table 1.2, the hydroaminomethylation of various alkenes (mostly terminal) with different (mostly secondary) amines has been studied using rhodium precursor in combination with phosphane ligands (or NHC ligand). The use of other metal precursors such as indium or titanium has been rarely studied and very high temperature (160 °C) must be employed in the reaction to obtain to a high conversion (Table 1.2).

The impact of solvents in the hydroaminomethylation reaction is quite considerable specifically on the hydrogenation activity. The acidity of the alcohol (for instance in a toluene/alcohol (1/1) solvent mixture) influences the catalytic performances in the hydrogenation reaction. The highest combined activity, regio- and chemoselectivity values were achieved for the reactions performed in toluene/EtOH using rhodium/bidentate phosphane catalyst (95% conversion, n/iso>200, >90% selectivity) or toluene/n-BuOH (88% conversion, n/iso=160, >98% selectivity) mixtures. The use of more acidic alcohols led to higher activities, but side-reactions like aldol condensation also occurred.[172]

The main drawback of the hydroaminomethylation reaction is that it is mostly limited to the use of secondary amines; for primary amines and more specifically ammonia the selectivity generally is particularly low because of over-alkylation.[72, 193, 194]

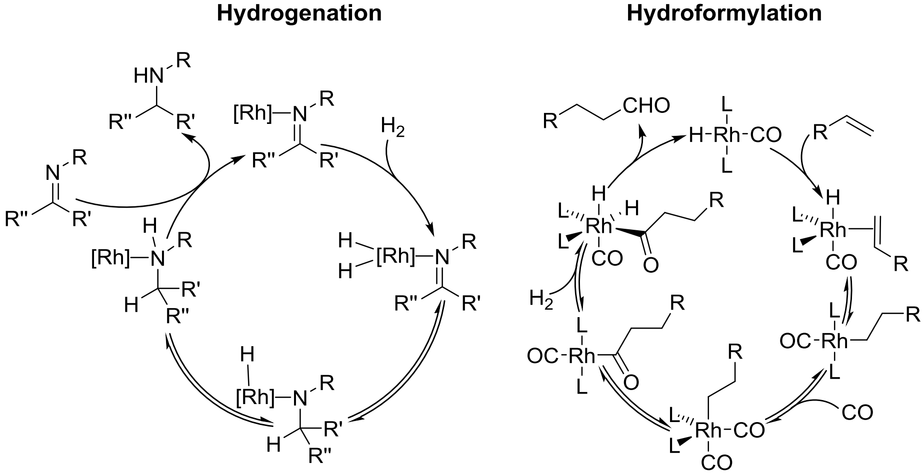


Scheme 1.17. Hydroaminomthylation of alkenes with ammonia; formation of primary, secondary and tertiary amines

The study on hydroaminomethylation with ammonia is still rarely undertaken. One of the difficulties is that the initially produced primary amine is more reactive than ammonia, and reacts preferentially to form secondary and tertiary amines. Moreover, the large excess of ammonia, which is necessary for the reductive amination step, blocks the catalytic species and as a consequent lowers the catalytic activity, specifically for the hydrogenation step, yielding large amounts of unwanted by-products (Scheme1.17).

The mechanistic aspects of the first step of the hydroaminomethylation reaction, the hydroformylation of the alkene, is already well-established.[146] It generally involves the substitution of a CO by the alkene, hydride transfer and coordination of CO followed by migratory CO insertion in the alkyl moiety, leading to the acyl-rhodium species. Oxidative addition of dihydrogen and reductive elimination provides the aldehyde in either the linear or branched isomeric form and recovers the catalyst species.

The resulting aldehydes then react with the primary or secondary amines to generate the corresponding imines or enamines, respectively. No particular studies have been presented to understand if the rhodium complex plays a unique role in the condensation reaction. It has been observed that the linear aldehyde reacts faster with the amine than the branched aldehyde. A general proposal has been presented suggesting that the hydrogenation of the enamine or the imine takes place on the rhodium metal center, and involves coordination, oxidative addition of dihydrogen, hydride transfer providing an alkyl or an amido moiety and reductive elimination eventually leading to the product amine (Scheme 1.18).[174, 195, 196]



Scheme 1.18. General schematic catalytic cycle for hydroformylation and imine hydrogenation

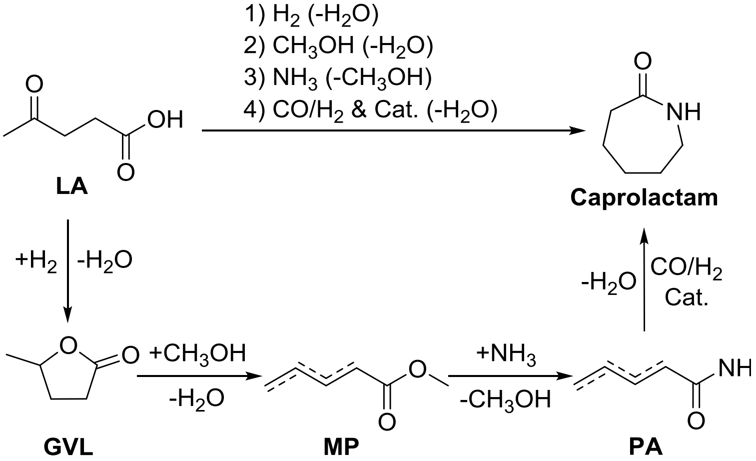
The hydrogenation step is indeed challenging and requires higher temperatures and higher partial dihydrogen pressures. The presence of large quantities of amine in the reaction supposedly modifies significantly the coordination sphere of the metal center.

1.5. Aim and outline of this thesis

1.5.1. Levulinic acid to caprolactam

As discussed in section 1.3, the current industrially applied route to produce caprolactam is based on fossil feedstock. Finding an alternative route to produce caprolactam from renewable resources like levulinic acid is highly desirable as it may reduce the environmental footprint of nylon. So far, the only report on the development of a synthetic route to bio-based caprolactam is based upon the use of hydroxymethylfurfural (HMF) as feedstock via a multi-step reaction technology.[64] Apart from the disadvantage of a multistep process, which will involve several product separation steps, this process is also energy demanding due to the requirement of significant amounts of (expensive) high pressure hydrogen.

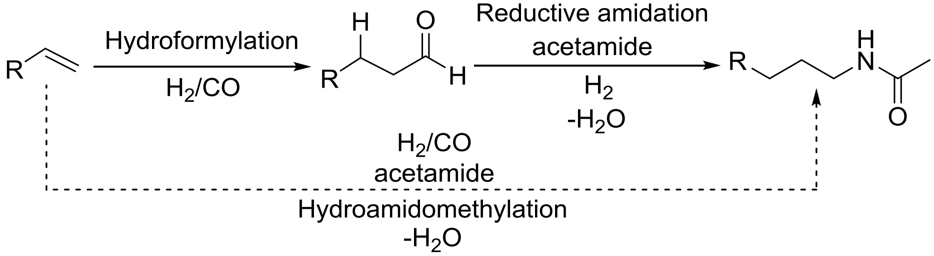
The aim of the research described in this thesis is to investigate an alternative bio-based pathway to synthesize caprolactam.



Scheme 1.19. Proposed synthetic route for the conversion of levulinic acid to caprolactam

Our proposed pathway is to obtain caprolactam from biomass-based levulinic acid starting from γ-valerolactone (GVL, derived from levulinic acid). The conversion of levulinic acid into GVL by a hydrogenation reaction, using mostly ruthenium catalysts, is reported to occur in high efficiency (>95%).[197-199] The proposed route proceeds via the acid-catalyzed reactive distillation of GVL with methanol to a mixture of isomeric methyl pentenoates (MPs), reaction of MPs with ammonia to the corresponding pentenamides (PAs), which then eventually are converted to caprolactam through a rhodium-catalyzed intramolecular hydroamidomethylation reaction (Scheme 1.19).

To reach this goal we need to study new catalytic reactions such as reductive amidation and hydroamidomethylation using transition metal catalysts. The reductive amidation is a reaction of aldehydes with amides affording alkylated amides. The envisaged hydroamidomethylation reaction comprises a cascade reaction of hydroformylation and reductive amidation (Scheme 1.20). Whereas reductive amidation and hydroamidomethylation with amides are related to the above mentioned reductive amination and hydroaminomethylation amines discussed in section 1.4.3, they do appear to display profoundly different reaction characteristics.



Scheme 1.20. Hydroamidomethylation and reductive amidation reactions

1.5.2. Contents of this thesis

In **Chapter 2**, our investigation of the homogeneously catalyzed reductive amidation of aldehydes with amides is described. The study of this novel reaction has been carried out making use of the model substrates hexanal and acetamide.

In **Chapter 3**, the direct chemo- and regioselective homogeneous rhodium-catalyzed hydroamidiomethylation of alkenes with amides is reported. The hitherto unknown hydroamidomethylation reaction comprises a cascade reaction of hydroformylation and catalytic reductive amidation. Finding an active and selective alkene hydroamidomethylation catalyst involves the development of a catalytic system that is not only active for hydroformylation of alkenes, but under the prevailing syngas conditions also possesses the ability for a selective hydrogenation.

In **Chapter 4**, the reductive amidation of aldehydes with formamide as well as hydoamidomethylation of alkenes with formamide is described, aiming for the formation of primary amines via the subsequent decarbonylation of the resulting alkylated formamides. The investigations focus on efficiency and selectivity of the reactions to the desired alkylated formamide over alcohol as well as the decarbonylation of N-alkylformamide to form the primary amine.

In **Chapter 5**, our study of the possible conversion of γ-valerolactone (GVL) in three atom-efficient steps into the important polymer precursor ε-caprolactam is reported. GVL can be converted to a mixture of isomeric methyl pentenoates (MP) via trans-esterification with methanol. In the second step, subsequent aminolysis with ammonia leads to a mixture of pentenamides (PA). The resulting pentenamides are ultimately converted into ε-caprolactam via the rhodium-catalyzed intramolecular hydroamidomethylation reaction.

Finally, in **Chapter 6**, a detailed summary of the most significant findings of this research, followed by a general conclusion and an outlook on future perspectives is presented.

Parts of this thesis have been published;[200, 201] have been submitted for publication[202, 203] and/or are soon to be submitted.

1.6. References

[1] A. K. Dalai, A. Bassi, *Energy & Fuels* **2010**, *24*, 4627.
[2] D. L. Klass, *Biomass for Renewable Energy, Fuels and Chemicals*, Academic Press, San Diego, **1998**.
[3] D. L. Klass, in *Encyclopedia of Energy, Vol. 1*, Elsevier, London, **2004**.
[4] C. E. Wyman, S. R. Decker, M. E. Himmel, J. W. Brady, C. E. Skopec, L. Viikari, *Polysaccharides*, New York, **2005**.
[5] E. L. Kunkes, D. A. Simonetti, R. M. West, J. C. Serrano-Ruiz, C. A. Gartner, J. A. Dumesic, *Science* **2008**, *322*, 417.
[6] L. R. Lynd, J. H. Cushman, R. J. Nichols, C. E. Wyman, *Science* **1991**, *251*, 1318.
[7] C. E. Wyman, *Appl. Biochem. Biotechnol.* **1994**, *45-6*, 897.
[8] C. E. Wyman, N. D. Hinman, *Appl. Biochem. Biotechnol.* **1990**, *24-5*, 735.
[9] G. W. Huber, J. N. Chheda, C. J. Barrett, J. A. Dumesic, *Science* **2005**, *308*, 1446.
[10] J. P. Lange, *Biofpr* **2007**, *1*, 39.

[11] J. B. Binder, R. T. Raines, *J. Am. Chem. Soc.* **2009**, *131*, 1979.
[12] A. Corma, S. Iborra, A. Velty, *Chem. Rev.* **2007**, *107*, 2411.
[13] J. P. Lange, R. Price, P. M. Ayoub, J. Louis, L. Petrus, L. Clarke, H. Gosselink, *Angew. Chem. Int. Ed.* **2010**, *49*, 4479.
[14] V. Menon, M. Rao, *Prog. Energy Combust. Sci.* **2012**, *38*, 522.
[15] Z. W. Miao, Y. Shastri, T. E. Grift, A. C. Hansen, K. C. Ting, *Biofpr* **2012**, *6*, 351.
[16] J. Y. Zhu, X. S. Zhuang, *Prog. Energy Combust. Sci.* **2012**, *38*, 583.
[17] S. P. S. Chundawat, G. T. Beckham, M. E. Himmel, B. E. Dale, in *Annual Review of Chemical and Biomolecular Engineering, Vol. 2* (Ed.: J. M. Prausnitz), **2011**, pp. 121.
[18] C. H. Zhou, X. Xia, C. X. Lin, D. S. Tong, J. Beltramini, *Chem. Soc. Rev.* **2011**, *40*, 5588.
[19] T. A. Hsu, C. S. Gong, G. T. Tsao, *Biotechnol. Bioeng.* **1980**, *22*, 2305.
[20] M. E. Zakrzewska, E. Bogel-Lukasik, R. Bogel-Lukasik, *Chem. Rev.* **2011**, *111*, 397.
[21] F. W. Lichtenthaler, *Acc. Chem. Res.* **2002**, *35*, 728.
[22] J. N. Chheda, G. W. Huber, J. A. Dumesic, *Angew. Chem. Int. Ed.* **2007**, *46*, 7164.
[23] C. Moreau, M. N. Belgacem, A. Gandini, *Top. Catal.* **2004**, *27*, 11.
[24] A. D. Patel, J. C. Serrano-Ruiz, J. A. Dumesic, R. P. Anex, *Chem. Eng. J.* **2010**, *160*, 311.
[25] J. C. Serrano-Ruiz, D. Wang, J. A. Dumesic, *Green Chem.* **2010**, *12*, 574.
[26] R. J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, J. G. de Vries, *Chem. Rev.* **2013**, *113*, 1499.
[27] E. I. Gurbuz, S. G. Wettstein, J. A. Dumesic, *Chemsuschem* **2012**, *5*, 383.
[28] R. H. Leonard, *Ind. Eng. Chem.* **1956**, *48*, 1331.
[29] J. O. Metzger, *Angew. Chem. Int. Ed.* **2006**, *45*, 696.
[30] T. Runge, C. H. Zhang, *Ind. Eng. Chem. Res.* **2012**, *51*, 3265.
[31] R. Weingarten, W. C. Conner, G. W. Huber, *Energy Environ. Sci.* **2012**, *5*, 7559.
[32] J. Horvat, B. Klaic, B. Metelko, V. Sunjic, *Tet. Lett.* **1985**, *26*, 2111.
[33] G. W. Huber, S. Iborra, A. Corma, *Chem. Rev.* **2006**, *106*, 4044.
[34] D. J. Hayes, S. Fitzpatrick, M. H. B. Hayes, R. J. R. H., in *Biorefineries-Industrial Processes and Products: Status Quo and Future Directions*, Wiley-VCH, **2008**.
[35] R. Weingarten, J. Cho, R. Xing, W. C. Conner, G. W. Huber, *Chemsuschem* **2012**, *5*, 1280.
[36] D. W. Rackemann, W. O. S. Doherty, *Biofpr* **2011**, *5*, 198.
[37] B. Girisuta, K. G. Kalogiannis, K. Dussan, J. J. Leahy, M. H. B. Hayes, S. D. Stefanidis, C. M. Michailof, A. A. Lappas, *Bioresour. Technol.* **2012**, *126*, 92.
[38] H. F. Lin, J. Strull, Y. Liu, Z. Karmiol, K. Plank, G. Miller, Z. H. Guo, L. S. Yang, *Energy Environ. Sci.* **2012**, *5*, 9773.
[39] D. W. Rackemann, W. O. S. Doherty, *Int. Sugar J.* **2013**, *115*, 28.
[40] J. J. Bozell, L. Moens, D. C. Elliott, Y. Wang, G. G. Neuenscwander, S. W. Fitzpatrick, R. J. Bilski, J. L. Jarnefeld, *Resour. Conserv. Recy.* **2000**, *28*, 227.
[41] J. C. Shen, C. E. Wyman, *AlChE J.* **2012**, *58*, 236.
[42] M. G. Al-Shaal, W. R. H. Wright, R. Palkovits, *Green Chem.* **2012**, *14*, 1260.
[43] A. M. R. Galletti, C. Antonetti, V. De Luise, M. Martinelli, *Green Chem.* **2012**, *14*, 688.
[44] S. Van de Vyver, J. Geboers, S. Helsen, F. Yu, J. Thomas, M. Smet, W. Dehaen, B. F. Sels, *Chem. Commun.* **2012**, *48*, 3497.
[45] S. M. Sen, C. A. Henao, D. J. Braden, J. A. Dumesic, C. T. Maravelias, *Chem. Eng. Sci.* **2012**, *67*, 57.
[46] J. Ritz, H. Fuchs, W. C. Kieczka, in *Morgan in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2002**.

[47] J. Ritz, H. Fuchs, H. Kieczka, W. C. Moran, in *Caprolactam, Ullmann's Encyclopedia of Industrial Chemistry*, 6th ed. (Ed.: Weinheim), VCH, **2001**.

[48] G. Dahlhoff, J. P. M. Niederer, W. F. Hoelderich, *Cat. Rev. - Sci. Eng.* **2001**, *43*, 381.

[49] I. Dodgson, K. Griffin, G. Barberis, F. Pignataro, G. Tauszik, *Chem. Ind.* **1989**, 830.

[50] L. Liu, Y. Li, H. B. Wei, M. Dong, J. G. Wang, A. M. Z. Slawin, J. P. Li, J. X. Dong, R. E. Morris, *Angew. Chem. Int. Ed.* **2009**, *48*, 2206.

[51] Y. Wang, J. S. Zhang, X. C. Wang, M. Antonietti, H. R. Li, *Angew. Chem. Int. Ed.* **2010**, *49*, 3356.

[52] M. Chatterjee, H. Kawanami, M. Sato, A. Chatterjee, T. Yokoyama, T. Suzuki, *Adv. Synth. Catal.* **2009**, *351*, 1912.

[53] Y. Z. Chen, C. W. Liaw, L. I. Lee, *Appl. Catal., A* **1999**, *177*, 1.

[54] Y. Ishii, S. Sakaguchi, *Catal. Today* **2006**, *117*, 105.

[55] K. Suzuki, T. Watanabe, S. I. Murahashi, *Angew. Chem. Int. Ed.* **2008**, *47*, 2079.

[56] M. Anilkumar, W. F. Hoelderich, *Catal. Today* **2012**, *198*, 289.

[57] A. B. Fernandez, M. Boronat, T. Blasco, A. Corma, *Angew. Chem. Int. Ed.* **2005**, *44*, 2370.

[58] K. I. Min, T. H. Lee, C. P. Park, Z. Y. Wu, H. H. Girault, I. Ryu, T. Fukuyama, Y. Mukai, D. P. Kim, *Angew. Chem. Int. Ed.* **2010**, *49*, 7063.

[59] J. S. Zhang, K. Wang, Y. C. Lu, G. S. Luo, *AlChE J.* **2012**, *58*, 925.

[60] W. B. Fisher, L. Crescentini, in *Caprolactam, Kirk-Othmer Encyclopedia of Chemical Technology*, Wiley, **2004**.

[61] S. G. Lee, J. Y. Shin, J. D. J., *ACS Catal.* **2013**, *3*, 525.

[62] R. Turgis, J. Estager, M. Draye, V. Ragaini, W. Bonrath, J. M. Leveque, *Chemsuschem* **2010**, *3*, 1403.

[63] J. Zhang, Y. Lu, K. Wang, L. G., *Ind. Eng. Chem. Res.* **2013**, *52*, 6377.

[64] T. Buntara, S. Noel, P. H. Phua, I. Melian-Cabrera, J. G. de Vries, H. J. Heeres, *Angew. Chem. Int. Ed.* **2011**, *50*, 7083.

[65] K. M. Sanches, in *US Patent 5,296,628*, **1992**.

[66] J. B. Sieja, *US Patent 5,192,399*, **1993**.

[67] L. Gilbert, N. Laurain, P. Leconte, C. Nedez, *Eu Patent 748797 A1*, **1998**.

[68] G. Achhammer, E. Fuchs, *US Patent 5,874,575*, **1999**.

[69] E. Eiermann, T. Narbeshuber, *WO Patent 9928296*, **1999**.

[70] J.-P. Brunelle, A. Seigneurin, L. Sever, *WO Patent 0005203 A1*, **2000**.

[71] P. Bassler, H. Luyken, G. Achhammer, T. Witzel, E. Fuchs, R. Fischer, W. Schnurr, in *US Patent 5,717,090*, **1998**.

[72] B. Zimmermann, J. Herwig, M. Beller, *Angew. Chem. Int. Ed.* **1999**, *38*, 2372.

[73] S. S. Liu, A. Sen, R. Parton, *J. Mol. Catal. A: Chem.* **2004**, *210*, 69.

[74] H. Hovenkamp, O. E. Sielcken, *US Patent 5,693,851*, **1998**.

[75] R. Fischer, F. Merger, H. J. Gosch, *US Patent 4,906,769*, **1990**.

[76] J. G. DeVries, O. J. Gelling, C. Lensink, A. J. J. M. Teunissen, in *US Patent 5,811,589*, **1998**.

[77] E. Drent, *Eu Patent, EP0457386B1*, **1994**.

[78] M. Beller, A. Krotz, W. Baumann, *Adv. Synth. Catal.* **2002**, *344*, 517.

[79] O. Diebolt, P. van Leeuwen, P. C. J. Kamer, *ACS Catal.* **2012**, *2*, 2357.

[80] D. Milstein, J. L. Huckaby, *J. Am. Chem. Soc.* **1982**, *104*, 6150.

[81] A. Seayad, S. Jayasree, K. Damodaran, L. Toniolo, R. V. Chaudhari, *J. Organomet. Chem.* **2000**, *601*, 100.

[82] L. T. Mika, T. Robert, I. Toth, S. Pitter, I. T. Horvath, *Organometallics* **2011**, *30*, 4751.

[83] A. J. Rucklidge, G. E. Morris, D. J. Cole-Hamilton, *Chem. Commun.* **2005**, 1176.

[84] W. Bertleff, R. Fischer, R. Kummer, F. Merger, H. W. Schneider, in *US Patent 5,003,102*, **1991**.
[85] W. Bertleff, G. Kuhn, R. Markel, P. Panitz, G. Schluch, P. Stops, in *EP Patent 351616*, **1990**.
[86] F. Merger, H. Horler, W. F. Hoelderich, T. Witzel, *Eu Patent 338 427 B1*, **1993**.
[87] X. M. Li, Y. J. Ding, G. P. Jiao, J. W. Li, L. Yan, H. J. Zhu, *J. Nat. Gas Chem.* **2008**, *17*, 351.
[88] O. J. Gelling, P. C. Borman, P. W. N. M. Van Leeuwen, *US Patent 6153800*, **2000**.
[89] O. E. Sielcken, F. P. Agterberg, N. F. Haasen, *US Patent 5495041*, **1996**.
[90] J. C. Tsai, H. H. Tai, T. T. Su, B. P. Wang, *US Patent 6017843*, **2000**.
[91] W. F. Holderich, H. Aichinger, F. Naeumann, R. Fischer, *Eu Patent 0266689 B1*, **1987**.
[92] F. Naeumann, W. F. Holderich, F. Merger, in *EP Patent 0295552 B1*, **1988**.
[93] W. Buijs, N. F. Haasen, F. E. Ferkes, S. L. Lane, H. F. W. Wolters, *US Patent 5,700,934*, **1997**.
[94] F. J. Broecker, R. Fischer, R. Harder, H. M. Hutmacher, F. Merger, C. U. Priester, H. W. Schneider, U. Vagt, in *US Patent 4,730,041*, **1988**.
[95] R. Fischer, W. Harder, F. Merger, C. U. Priester, U. Vagt, *US Patent 5,068,398*, **1991**.
[96] U. Vagt, R. Fischer, F. Merger, H. M. Hutmacher, *US Patent 4,730,040*, **1988**.
[97] S. Ko, H. Han, S. Chang, *Org. Lett.* **2003**, *5*, 2687.
[98] S. Obika, Y. Yasui, R. Yanada, Y. Takemoto, *J. Org. Chem.* **2008**, *73*, 5206.
[99] N. T. Patil, Z. B. Huo, G. B. Bajracharya, Y. Yamamoto, *J. Org. Chem.* **2006**, *71*, 3612.
[100] Y. S. Salprima, Y. Kuninobu, K. Takai, *Org. Lett.* **2007**, *9*, 5609.
[101] Y. Yu, G. A. Stephenson, D. Mitchell, *Tet. Lett.* **2006**, *47*, 3811.
[102] I. Kadota, A. Shibuya, L. M. Lutete, Y. Yamamoto, *J. Org. Chem.* **1999**, *64*, 4570.
[103] L. M. Lutete, I. Kadota, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 1622.
[104] T. E. Muller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem.Rev.* **2008**, *108*, 3795.
[105] M. Utsunomiya, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 14286.
[106] M. Utsunomiya, R. Kuwano, M. Kawatsura, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 5608.
[107] W. F. Holderich, G. Heitmann, *Catal. Today* **1997**, *38*, 227.
[108] S. Gomez, J. A. Peters, T. Maschmeyer, *Adv. Synth. Catal.* **2002**, *344*, 1037.
[109] A. W. Heinen, J. A. Peters, H. van Bekkum, *Eur. J. Org. Chem.* **2000**, 2501.
[110] B. C. Ranu, A. Majee, A. Sarkar, *J. Org. Chem.* **1998**, *63*, 370.
[111] V. I. Tararov, R. Kadyrov, T. H. Riermeier, A. Borner, *Chem. Commun.* **2000**, 1867.
[112] P. N. Rylander, *Hydrogenation Methods*, Academic Press, London, **1985**.
[113] T. Gross, A. M. Seayad, M. Ahmad, M. Beller, *Org. Lett.* **2002**, *4*, 2055.
[114] P. B. Quynh, T. H. Kim, *Tet. Lett.* **2011**, *52*, 5004.
[115] J. Tadanier, R. Hallas, J. R. Martin, R. S. Stanaszek, *Tetrahedron* **1981**, *37*, 1309.
[116] J. H. Billman, J. W. McDowell, *J. Org. Chem.* **1962**, *27*, 2640.
[117] R. J. Mattson, K. M. Pham, D. J. Leuck, K. A. Cowen, *J. Org. Chem.* **1990**, *55*, 2552.
[118] A. F. Abdel-Magid, S. J. Mehrman, *Org. Process Res. Dev.* **2006**, *10*, 971.
[119] R. O. Hutchins, N. R. Natale, *Org. Prep. Proced. Int.* **1979**, *11*, 201.
[120] R. Kadyrov, T. H. Riermeier, *Angew. Chem. Int. Ed.* **2003**, *42*, 5472.
[121] M. Kitamura, D. Lee, S. Hayashi, S. Tanaka, M. Yoshimura, *J. Org. Chem.* **2002**, *67*, 8685.
[122] D. O'Connor, A. Lauria, S. P. Bondi, S. Saba, *Tet. Lett.* **2011**, *52*, 129.
[123] S. Ogo, K. Uehara, T. Abura, S. Fukuzumi, *J. Am. Chem. Soc.* **2004**, *126*, 3020.

[124] O.-Y. Lee, K.-L. Law, C.-Y. Ho, D. Yang, *J. Org. Chem.* **2008**, *73*, 8829.

[125] T. Mizuta, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **2005**, *70*, 2195.

[126] D. Gnanamgari, A. Moores, E. Rajaseelan, R. H. Crabtree, *Organometallics* **2007**, *26*, 1226.

[127] A. F. AbdelMagid, C. A. Maryanoff, in *Reductions in Organic Synthesis: Recent Advances and Practical Applications, Vol. 641* (Ed.: A. F. AbdelMagid), **1996**, pp. 201.

[128] T. C. Nugent, D. E. Negru, M. El-Shazly, D. Hu, A. Sadiq, A. Bibi, M. N. Umar, *Adv. Synth. Catal.* **2011**, *353*, 2085.

[129] P. N. Rylander, *Catalytic Hydrogenation in Organic Synthesis*, Academic Press, New York, **1979**.

[130] E. Byun, B. Hong, K. A. De Castro, M. Lim, H. Rhee, *J. Org. Chem.* **2007**, *72*, 9815.

[131] B. Sreedhar, P. S. Reddy, D. K. Devi, *J. Org. Chem.* **2009**, *74*, 8806.

[132] Y. X. Chi, Y. G. Zhou, X. M. Zhang, *J. Org. Chem.* **2003**, *68*, 4120.

[133] D. Imao, S. Fujihara, T. Yamamoto, T. Ohta, Y. Ito, *Tetrahedron* **2005**, *61*, 6988.

[134] R. Kadyrov, T. H. Riermeier, U. Dingerdissen, V. Tararov, A. Borner, *J. Org. Chem.* **2003**, *68*, 4067.

[135] A. Robichaud, A. N. Ajjou, *Tet. Lett.* **2006**, *47*, 3633.

[136] T. C. Nugent, M. El-Shazly, *Adv. Synth. Catal.* **2010**, *352*, 753.

[137] S. Fleischer, S. L. Zhou, K. Junge, M. Beller, *Chem. -an Asian J.* **2011**, *6*, 2240.

[138] A. Pagnoux-Ozherelyeva, N. Pannetier, M. D. Mbaye, S. Gaillard, J. L. Renaud, *Angew. Chem. Int. Ed.* **2012**, *51*, 4976.

[139] S. Enthaler, *Chemcatchem* **2010**, *2*, 1411.

[140] U. Sharma, P. Kumar, N. Kumar, V. Kumar, B. Singh, *Adv. Synth. Catal.* **2010**, *352*, 1834.

[141] V. Kumar, U. Sharma, P. K. Verma, N. Kumar, B. Singh, *Adv. Synth. Catal.* **2012**, *354*, 870.

[142] C. Li, B. Villa-Marcos, J. Xiao, *J. Am. Chem. Soc.* **2009**, *131*, 6967.

[143] T. Bunlaksananusorn, F. Rampf, *Synlett* **2005**, 2682.

[144] L. Rubio-Perez, F. J. Perez-Flores, P. Sharma, L. Velasco, A. Cabrera, *Org. Lett.* **2009**, *11*, 265.

[145] V. I. Tararov, R. Kadyrov, T. H. Riermeier, A. Borner, *Adv. Synth. Catal.* **2002**, *344*, 200.

[146] P. W. N. M. van Leeuwen, C. Claver, *Rhodium Catalyzed Hydroformylation*, Kluwer Academic Publishers, **2000**.

[147] W. Reppe, *Experietia* **1949**, *5*, 93.

[148] W. Reppe, H. Vetter, *Leibigs Ann. Chem.* **1953**, *582*, 133.

[149] T. Baig, P. Kalck, *J. Chem. Soc., Chem. Comm.* **1992**, 1373.

[150] T. Baig, J. Molinier, P. Kalck, *J. Organomet. Chem.* **1993**, *455*, 219.

[151] B. Breit, *Tet. Lett.* **1998**, *39*, 5163.

[152] J. J. Brunet, D. Neibecker, F. Agbossou, R. S. Srivastava, *J. Mol. Catal.* **1994**, *87*, 223.

[153] A. F. M. Iqbal, *Helv. Chim. Acta* **1971**, *54*, 1440.

[154] F. Jachimowicz, J. W. Raksis, *J. Org. Chem.* **1982**, *47*, 445.

[155] K. Murata, A. Matsuda, T. Masuda, *J. Mol. Catal.* **1984**, *23*, 121.

[156] S. Toros, I. Gemespecsi, B. Heil, S. Maho, Z. Tuba, *J. Chem. Soc., Chem. Comm.* **1992**, 858.

[157] P. Eilbracht, L. Barfacker, C. Buss, C. Hollmann, B. E. Kitsos-Rzychon, C. L. Kranemann, T. Rische, R. Roggenbuck, A. Schmidt, *Chem. Rev.* **1999**, *99*, 3329.

[158] A. Behr, A. Westfechtel, *Chem. Ing. Tech.* **2007**, *79*, 621.

[159] A. Behr, M. Fiene, C. Buss, P. Eilbracht, *Eur. J. Lipid Sci. Technol.* **2000**, *102*, 467.

[160] C. Buch, R. Jackstell, D. Buhring, M. Beller, *Chem. Ing. Tech.* **2007**, *79*, 434.

[161] E. Nagy, B. Heil, S. Toros, *J. Organomet. Chem.* **1999**, *586*, 101.

[162] M. Ahmed, C. Buch, L. Routaboul, R. Jackstell, H. Klein, A. Spannenberg, M. Beller, *Chem. Eur. J.* **2007**, *13*, 1594.

[163] J. R. Briggs, J. Klosin, G. T. Whiteker, *Org. Lett.* **2005**, *7*, 4795.

[164] G. Angelovski, P. Eilbracht, *Tetrahedron* **2003**, *59*, 8265.

[165] C. S. Graebin, V. L. Eifler-Lima, R. G. da Rosa, *Catal. Commun.* **2008**, *9*, 1066.

[166] K. S. Muller, F. Koc, S. Ricken, P. Eilbracht, *Org. Biomol. Chem.* **2006**, *4*, 826.

[167] A. M. Seayad, K. Selvakumar, M. Ahmed, M. Beller, *Tet. Lett.* **2003**, *44*, 1679.

[168] T. O. Vieira, H. Alper, *Chem. Commun.* **2007**, 2710.

[169] T. O. Vieira, H. Alper, *Org. Lett.* **2008**, *10*, 485.

[170] M. Ahmed, R. P. J. Bronger, R. Jackstell, P. C. L. Kamer, P. W. N. M. van Leeuwen, M. Beller, *Chem. Eur. J.* **2006**, *12*, 8979.

[171] M. Ahmed, A. M. Seayad, R. Jackstell, M. Beller, *J.Am.Chem.Soc.* **2003**, *125*, 10311.

[172] B. Hamers, E. Kosciusko-Morizet, C. Muller, D. Vogt, *Chemcatchem* **2009**, *1*, 103.

[173] G. D. Liu, K. X. Huang, C. X. Cai, B. N. Cao, M. X. Chang, W. J. Wu, X. M. Zhang, *Chem. Eur. J.* **2011**, *17*, 14559.

[174] D. Crozet, M. Urrutigoity, P. Kalck, *Chemcatchem* **2011**, *3*, 1102.

[175] A. Seayad, M. Ahmed, H. Klein, R. Jackstell, T. Gross, M. Beller, *Science* **2002**, *297*, 1676.

[176] R. P. J. Bronger, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **2003**, *22*, 5358.

[177] L. A. van der Veen, P. H. Keeven, G. C. Schoemaker, J. N. H. Reek, P. C. J. Kamer, P. W. N. M. van Leeuwen, M. Lutz, A. L. Spek, *Organometallics* **2000**, *19*, 872.

[178] C. A. Tolman, *J. Am. Chem. Soc.* **1970**, *92*, 2953.

[179] P. W. N. M. Van Leeuwen, *Homogeneous Catalysis: Understanding the Art*, Springer, **2004**.

[180] R. P. J. Bronger, J. P. Bermon, J. Herwig, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Adv. Synth. Catal.* **2004**, *346*, 789.

[181] L. A. van der Veen, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Angew. Chem. Int. Ed.* **1999**, *38*, 336.

[182] E. Zuidema, P. E. Goudriaan, B. H. G. Swennenhuis, P. C. J. Kamer, P. W. N. M. van Leeuwen, M. Lutz, A. L. Spek, *Organometallics* **2010**, *29*, 1210.

[183] R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals* 5ed., Wiley, **2009**.

[184] M. Dieguez, A. Ruiz, C. Claver, *J. Org. Chem.* **2002**, *67*, 3796.

[185] L. A. Oro, D. Carmona, J. de Vries, C. J. Elsevier, *Handbook of Homogeneous Hydrogenation*, Wiley-VCH, **2007**.

[186] G. D. Liu, K. X. Huang, B. N. Cao, M. X. Chang, S. K. Li, S. C. Yu, L. Zhou, W. J. Wu, X. M. Zhang, *Org. Lett.* **2012**, *14*, 102.

[187] J. J. Kim, H. Alper, *Chem. Commun.* **2005**, 3059.

[188] E. Teuma, M. Loy, C. Le Berre, M. Etienne, J. C. Daran, P. Kalck, *Organometallics* **2003**, *22*, 5261.

[189] I. D. Kostas, *J. Chem. Res.* **1999**, 630.

[190] I. D. Kostas, C. G. Screttas, *J. Organomet. Chem.* **1999**, *585*, 1.

[191] A. S. Veige, *Polyhedron* **2008**, *27*, 3177.

[192] J. F. Hartwig, *Science* **2002**, *297*, 1653.

[193] H. Klein, R. Jackstell, M. Kant, A. Martin, M. Beller, *Chem. Eng. Technol.* **2007**, *30*, 721.

[194] J. F. Knifton, J. J. Lin, *J. Mol. Catal.* **1993**, *81*, 27.

[195] A. Fabrello, A. Bachelier, M. Urrutigoity, P. Kalck, *Coord. Chem. Rev.* **2010**, *254*, 273.

[196] D. Crozet, A. Gual, D. McKay, C. Dinoi, C. Godard, M. Urrutigoity, J. C. Daran, L. Maron, C. Claver, P. Kalck, *Chem. Eur. J.* **2012**, *18*, 7128.

[197] D. M. Alonso, S. G. Wettstein, J. A. Dumesic, *Green Chem.* **2013**, *15*, 584.

[198] X. L. Du, L. He, S. Zhao, Y. M. Liu, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem. Int. Ed.* **2011**, *50*, 7815.

[199] X. Hu, C. Z. Li, *Green Chem.* **2011**, *13*, 1676.

[200] S. Raoufmoghaddam, E. Drent, E. Bouwman, *Adv. Synth. Catal.* **2013**, *355*, 717.

[201] S. Raoufmoghaddam, E. Drent, E. Bouwman, *ChemSusChem* **2013**, *6,* 1759.

[202] S. Raoufmoghaddam, M. T. M. Rood, F. K. W. Buijze, E. Drent, E. Bouwman, *Chem. Eur. J.* **2013**, *Submitted.*

[203] S. Raoufmoghaddam, E. Drent, E. Bouwman, *EP 13162426*, **2013**.