Summary

Chemical production helps to sustain the modern society by providing people with energy, medicine and materials. Catalysis plays a central role in chemical processes, as it serves to provide cost-efficient, "green" and selective pathways for otherwise highly energy-consuming, environmentally-hazardous or even inaccessible routes. Hence, catalyst development is one of the main aims of modern chemical research. In the branch of homogeneous catalysis, the development of new catalytic systems strongly relies on the design and synthesis of new organic ligands used to steer the reactivity of transition metal complexes. In conventional organometallic catalysts, ligands usually act as spectators during the reaction, exerting effects mainly by their electronic and steric properties, with the metal center solely interacting with the substrates and mediating the reactions. Bifunctional mechanisms in enzymes, catalysts in nature, that rely on more cooperative and active participation of the organic framework around the metal ion, have inspired chemists to develop new types of ligands that can facilitate chemical processes by directly participating in substrate activation processes, in synergy with the function of the (transition) metal. The cooperative effects of these ligands provide new patterns for catalysis that help to establish more cost-effective and efficient pathways for the synthesis of chemical products. While cooperative ligands functioning as internal (Brønsted) bases/acids in the reactions have been extensively applied and studied and ligands showing radical-type reactivity are currently actively explored in catalysis research by several research groups, ligands that are able to directly assist in hydride (nucleophile group) transfer in substrate activation have remained quite underdeveloped, and only recently attracted attention of chemists. Representative examples of the three types of cooperative ligands in (dehydrogenation)-related catalytic reactions are described in **Chapter 1**. As the development of cooperative ligands capable of facilitating hydride transfer processes could potentially have a profound impact on catalysis, the initial aim of the research described in this thesis was to develop rhodium and iridium complexes containing such cooperative ligand systems and to study their application in (de)hydrogenation-related catalysis. Secondary picolylamine-type ligands coordinated to rhodium and iridium have been described to convert rather easily to the corresponding "electrophilic" imine ligand initiated by N*H* deprotonation. This indicates a quite strong reducing capability of these ligands, presumably associated with their "hydride donating" ability. This was the starting point of the studies described in this Thesis.

In **Chapter 2** the preparation of iridium and rhodium complexes **1** and **2** (Figure 1) based on the *N*-methyl-1-(pyridin-2-yl)methanamine (Me-pma) ligand and their chemistry upon N*H* deprotonation of the ligand are presented. While the iridium amido complex **1a** could be obtained upon treatment with one equivalent of base, the rhodium complex **2a** is probably highly unstable and instantaneously disproportionated into a free pma ligand and dinuclear complex **2b**. Multinuclear NMR spectroscopy and X-ray single crystal structure determination revealed that **2b** adopts a structure with two Rh(I) metal centers hosted by a dianionic $(pma–2H)^{2–}$ ligand, and with the ligand coordinating to Rh2 as an "aza-allyl" fragment (Figure 1). In contrast to previously reported examples, two-electron transfer from the $(pma–H)^{–}$ ligand to rhodium(I) along with a second deprotonation step was not observed for this system. Instead, substantial delocalization of the "excess" electrons over the "aza-allyl" fragment and the pyridine ring occurs. The inability of this system to form a rhodium(-I) complex is proposed to result from the lack of an extra coordinating site on the ligand to stabilize the reduced metal in a

preferred tetrahedral coordination geometry. This study, in combination with previous results from our group, provides useful details about the electron transfer chemistry of these pycolyl-amine-type ligands, not only showing the reducing ability of N*H*-deprotonted pma ligands but also their versatile nature and the subtle dependency of ligand-to-metal electron transfer on a number of factors.

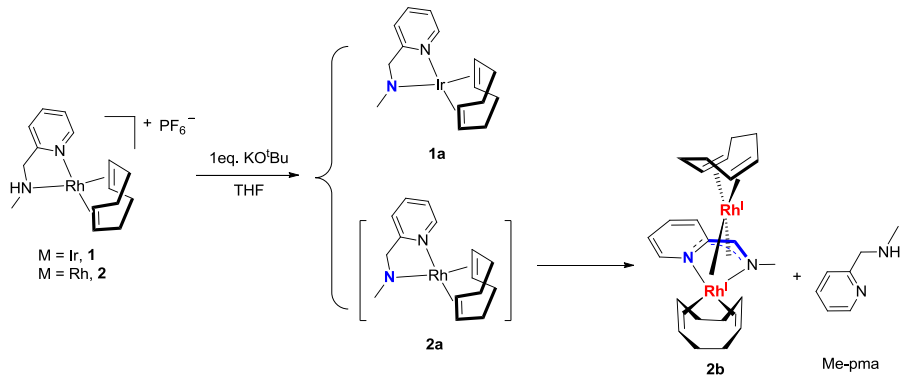
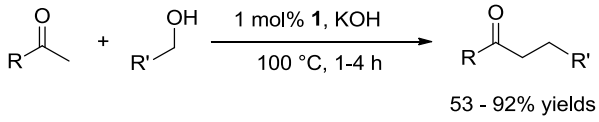


Figure 1. Transformations of **1a** and **1b** upon N*H* deprotonation.

In **Chapter 3**, catalytic activity of the iridium complex **1**(synthesis described in Chapter 2) in a series of transfer hydrogenation (TH) related reactions was studied, which showed high activity for especially α-alkylation of ketones with alcohols via a hydrogen auto-transfer process (Scheme 1), while the rhodium complex **2** showed no activity. A mechanism involving the Me-pma ligand assisting in hydride transfer between substrates via *pseudo*-Meerwein–Ponndorf–Verley (MPV) type transition states was proposed (Figure 2) and examined with experimental model studies and DFT calculations. Labelling experiments indicated that hydride transfer from the substrate (*iso*propanol) to the corresponding imine ligand can readily occur under mild conditions, and the reverse process was indirectly proven by substrate (acetophenone and *trans*-chalcone) reduction by complex **1a** in the presence of a protic reagent. DFT calculations reveal that the TH reaction pathway can proceed via "reversible hydride-storage" at the imine ligand, and the corresponding substrate-to-ligand and ligand-to-substrate hydride transfer steps both proceed with moderate barriers (Figure 2). This new ligand cooperative pathway can be competitive with other mechanisms proposed in earlier studies (e.g. traditional inner-sphere TH mechanisms).



Scheme 1. α-alkylation of ketones with alcohols catalyzed by **1**.

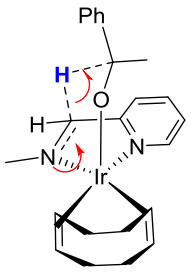


Figure 2. Proposed *pseudo*-MPV transition state.

Summary

In **Chapter 4**, the preparation of a new PNN ligand is described, which is derived from a unique combination of the well-known "proton responsive" 2-(phosphinomethyl)pyridine structure with the pma type ligand fragment studied in **Chapter 2** and **3**. This PNN pincer ligand was further used to prepare the corresponding rhodium carbonyl complex **3**. Complex **3** is able to undergo sequential deprotonation and "hydride-loss" (or proton loss combined with two-electron oxidation) to form complex **4**, which bears a very interesting ligand structure incorporating both a nucleophilic phosphine arm and an electrophilic imine arm (Figure 3). Complex **4** shows interesting "Janus-type" ligand reactivity in the splitting of sulfonamide substrate *o*TsNH$_2$, leading to formation of a (fully characterized) rare hemi-aminal complex **5**, where the proton and the sulfonamido group are each stored at one of the two arms of ligand. Notably, the sulfonamide N atom replaced the aniline atom as the coordinating donor bound to rhodium (Scheme 2). Further reaction of complex **5** with iodomethane (believed to occur on the metal center via oxidative addition) leads to formation of the methylated sulfonamine *o*TsNHMe and imine complex **7**. Subsequent deprotonation of complex **7** regenerates compex **4**.

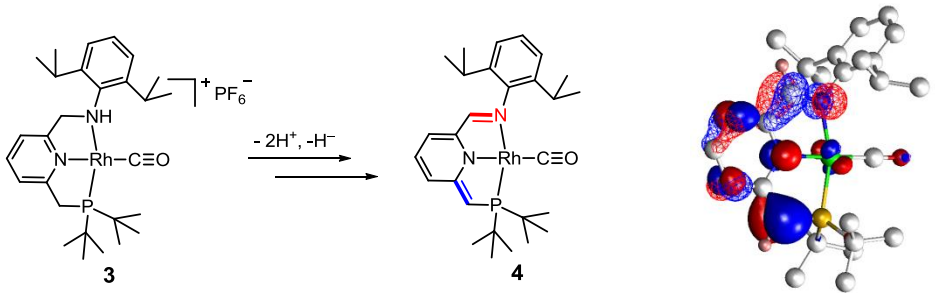
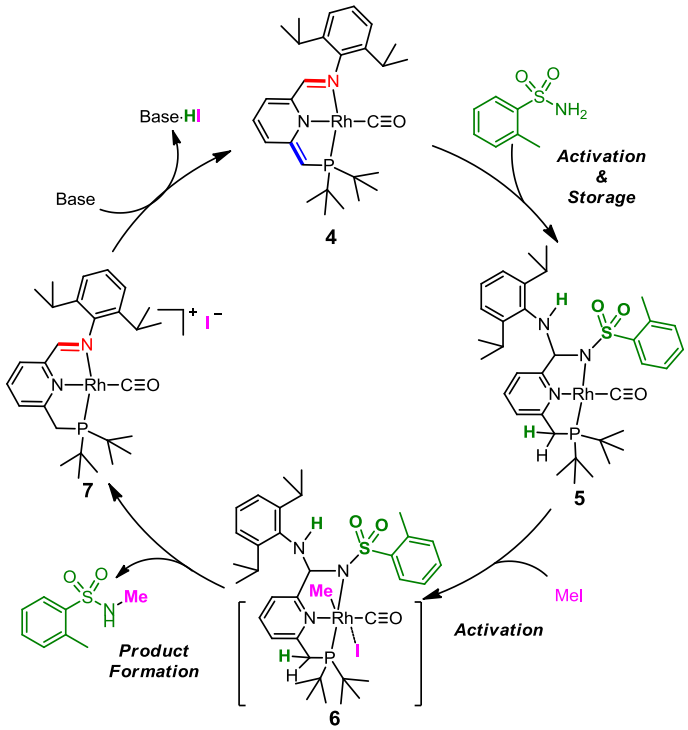


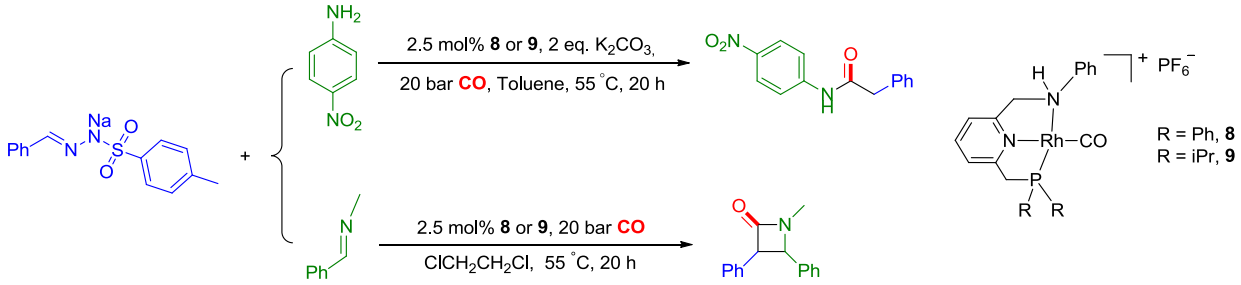
Figure 3. Synthesis of complex **4** from complex **3** via sequential deprotonation and "hydride-loss". The figure on the right shows the HOMO (solid surface) and LUMO (wireframe) of complex **4**.



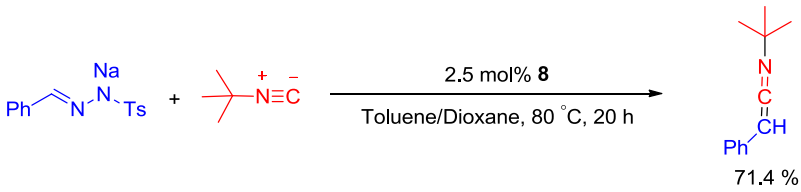
Scheme 2. Hypothetical catalytic cycle composed of stoichiometric steps (one turnover) involving mono-methylation of ***o*-TsNH$_2$** with MeI mediated by complex **4**.

Summary

In **Chapter 5**, the activity of a series of PNN rhodium carbonyl complexes (based on similar PNN scaffolds as those described in Chapter 4) in catalytic synthesis of ketenes and ketene imines from carbene precursors is described. The purpose of using rhodium-based catalysts for these reactions is to develop a catalyst that can both catalyze ketene formation from carbene precursors *and* mediate the following coupling reactions, as this might eventually allow the development of enantioselective protocols in follow-up studies. Rhodium is expected to have a higher affinity to bind ketenes compared to the reported catalysts for this reaction, and is thus expected to give rise to inner-sphere coupling reactions between the *in situ* formed ketene and the nucleophile/imine. In the catalytic reactions described in Chapter 5, ketenes were generated *in situ* by carbonylation of a diazo compound or a sodium *N*-tosyl hydrazone salt as the carbene precursor, mediated by the PNN rhodium carbonyl complexes **8** and **9** under basic conditions (Scheme 3). Trapping of the thus formed ketenes with an amine or imine in one-pot reactions leds to formation of amides and β-lactams, respectively, in moderate to high yields. A similar reaction using an isocyanide instead of carbon monoxide led to formation of a ketene imine, providing the first catalytic example for the synthesis of ketene imines from a carbene precursors (Scheme 4). The ketene formation and the subsequent [2+2] Staudinger reaction steps were evaluated with DFT, showing that diazo activation to form the metallocarbene species is the rate-determining-step, with the neutral amido form of the complex being more active than the cationic amine form, in agreement with experimental observations. Outer-sphere CO insertion is computed to be slightly favored over the inner-sphere mechanism, but follow-up coupling mechanisms are very similar in energy for both pathways.



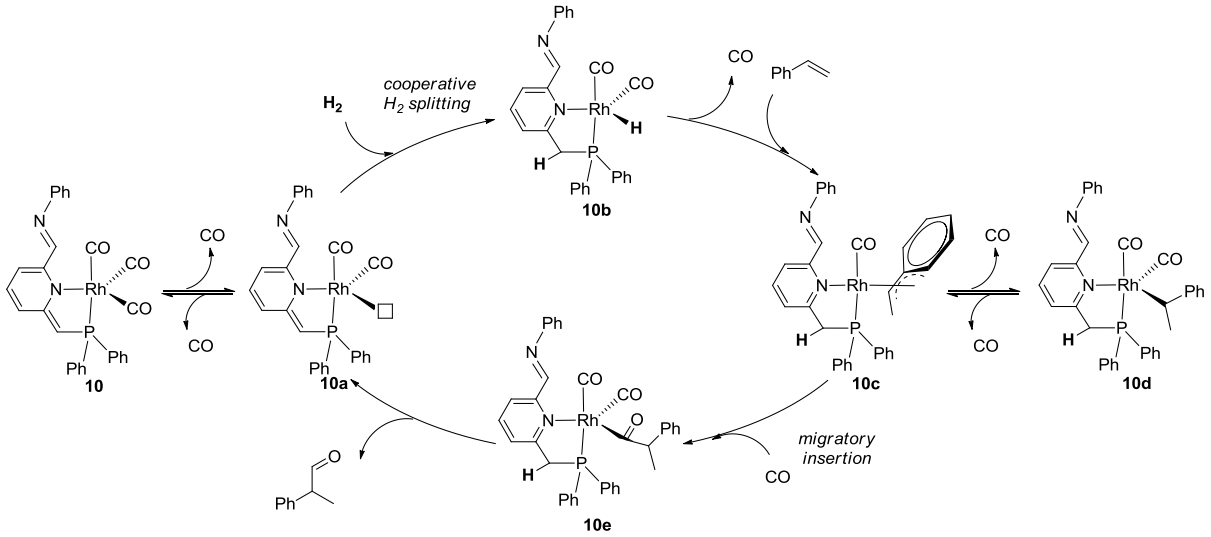
Scheme 3. Amide and β-lactam synthesis from *in situ* generated ketenes generated by Rh-mediated carbonylation of carbene precursors using the PNN rhodium carbonyl complexes **8** and **9**.



Scheme 4. Catalytic ketene imine synthesis by coupling of a carbene precursor and an isocyanide catalyzed by PNN rhodium carbonyl complex **8**.

In **Chapter 6**, catalytic studies of a series of PNN rhodium carbonyl complexes in the hydroformylation of styrene and 1-octene is presented. Complexes **8** and **9** (see also Chapter 5) show

good activity and regioselectivity (*branched* over *linear*; *b/l*) in the hydroformylation of styrene. The presence of a base is critical for achieving good catalytic performance. Very high selectivity of the branched aldehyde product (*b*/*l* ratio > 99) was obtained with 1 eq. of KO^{t}Bu as the base. When K_2CO_3 was used as the base, the aldehyde yields were somewhat higher, while the selectivity is still high but lower than obtained with KO^{t}Bu as the base. A catalytically active intermediate **10** was spectroscopically observed using **8** as the precatalyst, which is even able to catalyze the reaction at room temperature with high regioselectivity, showing the unusual coordination chemistry of the PNN ligand scaffold. High pressure NMR spectroscopy suggested that species **10** exists in a monomeric Rh^I form hosted by a pyridine-dearomatized PNN ligand or in a dimeric Rh^0 form with a *P*,*N*-bidentate ligand. High pressure FT-IR spectroscopy and DFT calculations suggested that species **10** is a mononuclear [Rh^I(CO)$_3$(κ^2-*P*,*N*-PNN*)$^{-1}$] species, probably adopting a trigonal bipyramidal coordination geometry with the phosphorus donor and the pyridine nitrogen donor occupying an axial and an equatorial position, respectively. A mechanism was proposed based on the structure of species **10**, in which the cooperative ligand assists in the H_2 activation step (Scheme 5).



Scheme 5. Proposed mechanism for the PNN-Rh catalyzed hydroformylation of styrene, featuring ligand cooperativity in the H_2 splitting step.

Overall this Thesis shows that cooperative ligands provide versatile reactivity platforms, thus stimulating follow-up research. The unusual ligand assisted hydride transfer mechanism proposed in Chapter 3 for transfer hydrogenation and hydrogen auto-transfer-type substrate activation processes mediated by pma Rh/Ir complexes is noteworthy in this perspective, and application of related complexes with similar ligand structures might well lead to unexplored new reactivity patterns in organic synthesis. Also the unusual “Janus-type” PNN-ligands described in Chapter 4 provide interesting possibilities. The combination of an electrophilic and a nucleophilic ligand arm in one cooperative ligand was shown to provide a versatile ligand-based reactivity platform for the activation of a sulfonamide substrate, and the cooperative ligand allowed reversible “storage” of the activated substrate in the ligand backbone to enable a subsequent metal-based substrate activation proces. A *pseudo*-catalytic reaction was achieved based on integration of the multiple processes involved, thereby demonstrating that similar dual-mode ligand reactivity patterns in general may be a viable

approach in organometallic catalysis. The catalytic activity of similar Rh-PNN complexes in ketene and ketene imine synthesis from carbenes, as well as in styrene hydroformylation, further underlines the versatility of the PNN-Rh platform in homogeneous catalysis. We therefore believe that further mechanistic studies and ligand modifications will lead to further improvements of catalytic efficiencies and development of new catalytic reactions.