Catalysis LIKAT
Leibniz-Institut für Katalyse e.V.

Development of Novel Pincer Catalysts for the Synthesis of Fine Chemicals Using Hydrogen Autotransfer Reactions

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Summary

This thesis deals with the development of different homogeneous PNP pincer catalysts and their application in hydrogen autotransfer reactions. Herein, a manganese-based catalyst was used for the α-alkylation of ketones with alcohols, a reaction creating new C–C bonds while producing water as sole stochiometric by-product. This reaction was used for the alkylation of a broad scope of ketones including biologically relevant compounds like hormones with various alcohols. Additionally, mechanistic investigations have been conducted implying that the pincer ligand is directly involved in the catalytic cycle, in which the alcohol gets dehydrogenated via an amidate-assisted procedure.

Furthermore, this reaction concept was expanded to a rhenium-based catalyst system. Besides α-alkylation of ketones, this latter catalyst was also applied in the *N*-alkylation of sulfonamides and in a three-component pyrrole synthesis. In all of these reactions, alcohols were employed as alkylating agents, giving potential access to broad substrate scopes and avoiding toxic by-products.

Finally, a new class of ruthenium pincer catalysts is presented, in which the ligand undergoes cyclometallation to the metal center. Thereby, enhanced possibilities are generated to adapt the catalyst's reactivity. To proof reactivity and stability of these complexes, they were applied for alkylating ketones with alcohols. Notably, superior results in comparison to the benchmark catalyst Ru-MACHO were achieved. Furthermore, mechanistic investigation concerning involved catalyst species were conducted. Here, a ruthenium carboxylate complex is predominantly formed under reaction conditions. On top of that, no release of the PNP or the CN ligand was detected which underlines the catalyst's stability.

Zusammenfassung

Die vorliegende Arbeit beschäftigt sich mit der Entwicklung homogener PNP-Pincerkomplexe und deren Einsatz in Hydrogen-Autotransfer-Reaktionen. Dementsprechend wurde ein Magankomplex als Katalysator für die α-Alkylierung von Ketonen mit Alkoholen verwendet. Bei dieser Reaktion werden neue C–C-Bindungen geknüpft, während Wasser das einzige in stöchiometrischen Mengen anfallende Nebenprodukt darstellt. Unter Anwendung dieser Prozedur gelang die Alkylierung zahlreicher Substanzen, unter anderem auch biologisch relevanter Stoffe wie Hormone. Zusätzlich wurden mechanistische Studien durchgeführt, die eine direkte Beteiligung des Pincerliganden an der Reaktion und damit eine Dehydrierung des Alkohols durch einen Amidatkomplex vermuten lassen.

Vergleichbare Reaktionen konnten darauffolgend mit einem Rhenium-basierten System durchgeführt werden. Dieser Katalysator war weiterhin in der Lage, neben der α-Alkylierung von Ketonen auch die *N*-Alkylierung von Sulfonamiden und die Synthese von Pyrrolen aus drei Komponenten zu ermöglichen. Da all diese Reaktionen einfach zugängliche Alkohole als Alkylierungsmittel nutzen, können die untersuchten Reaktionen zur Synthese vielfältiger Produkte genutzt werden, ohne dass dabei giftige oder umweltschädliche Nebenprodukte anfallen.

Des Weiteren wurde eine neue Klasse von Ruthenium-basierten Pincerkomplexen synthetisiert, bei denen das Metallzentrum eine Cyclometallierung zum Liganden ausbildet. Mit diesen homogenen Katalysatoren ergeben sich zusätzliche Möglichkeiten, die Reaktivität des Katalysators zu steuern. Um dies zu demonstrieren, wurden die entwickelten Komplexe erneut für die α-Alkylierung von Ketonen mit Alkoholen verwendet, wo sie bessere Ergebnisse als das Benchmark-System Ru-MACHO zeigten. Abschließend wurden Untersuchungen zur katalytisch aktiven Spezies durchgeführt. Hierbei konnte ein Ruthenium-Carboxylatkomplex als vorherrschende Spezies während der Reaktion identifiziert werden. Die Freisetzung des PNP- oder des CN-Liganden konnte hier wiederum nicht nachgewiesen werden, was die Stabilität des verwendeten Katalysators bestätigt.

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List of Abbreviations

Abbreviation	Meaning
B	billion
BH	borohydride
BINAP	2,2‘-bis(diphenylphosphino)-1,1‘-binaphtyl
DMSO	dimethyl sulfoxide
dippf	1,1‘-bis(diisopropylphosphino)ferrocene
DPEphos	bis[(2-diphenylphosphino)phenyl] ether
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1‘-bis(diphenylphosphino)ferrocene
Et	ethyl
gem	geminal
^{i}Pr	isopropyl
IR	infrared
MACHO	bis(2-(diphenylphosphinoethyl)amine
Mio	million
MLC	metal ligand cooperation
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
p-cym	*para*-cymene
p-tol	*para-tolyl*
Ph	phenyl
rct.	reaction
^{t}Bu	tertiary butyl
THF	tetrahydrofuran

Table 1: List of Abbreviations.

1 Preface

The chemical industry is one of the most important branches of industry in Germany providing jobs for 453,000 people and generating a yearly revenue of 195.5 billion Euro (see Figure 1).[1] Its products find wide application in plastics and rubber production, construction, automotive industry, agriculture, healthcare, and many others enabling the production of many goods available today.[2]

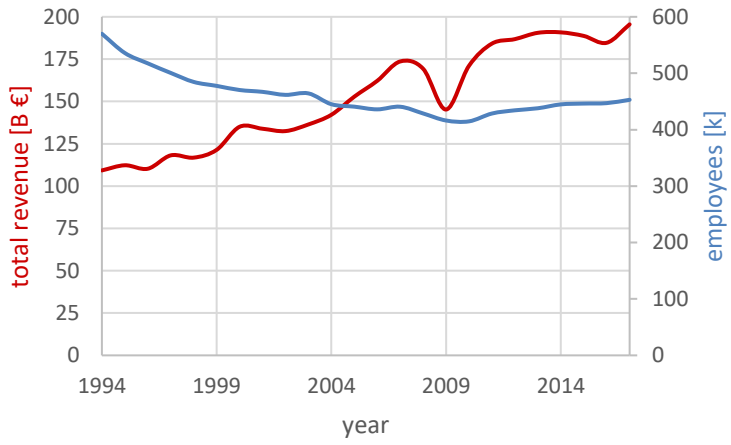


Figure 1: Development of the chemical industry in Germany.[1]

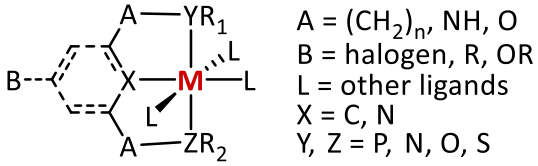
Nevertheless, this large-scale production of diverse chemicals has serious downsides for the environment. The production of chemicals in Germany alone required 20.6 Mio tons of starting materials in 2016.[3] In the same year, 1.3 Mio tons of hazardous waste were emitted by the chemical industry, which accounts for 7.5% of all the hazardous wastes produced in Germany. In line with this, the chemical industry is also responsible for 2.5% of Germany's CO_2 emissions as well as 10.1% of its primary energy consumption.[4]

Therefore, the development of new chemical transformations continues to be important to reduce the output of environmentally harmful substances while still allowing to produce the plethora of bulk and fine chemicals required by modern day society. Without doubt, catalysis is a key technology to achieve this goal by opening energy-efficient pathways for reactions that would otherwise require energy-intensive conditions.[5] While catalysis is already applied in production of approximately 80% of all chemicals,[6] there still is a strong necessity for new catalytic reactions, especially in the very diverse field of fine chemicals and pharmaceuticals that is accounting for 47% of chemical industry's overall revenue by producing a wide variety of different compounds.[1] These compounds are typically synthesized on medium sized scales while containing several functional groups, which make them an ideal target especially for

homogenous catalysis.[5] Herein, finely tunable transition metal complexes are applied at mild reaction conditions to enable a wide range of reactions from hydroformylation for the synthesis of plasticizers[7] to C–C bond formations by cross coupling reactions used in the pharmaceutical industry.[8]

2 Transition Metal Pincer Complexes

For enabling precise tuning of a homogeneous catalyst's reactivity and adjusting it on the substrate's needs, especially the right choice of ligands is crucial. Here, pincer-type ligands offer an enormous potential. These chelating ligands that bind to three coplanar sites on the metal center contain three potentially different donor atoms while rigidly defining the shape of the ligand sphere (see Scheme 1).[9] By that, well defined complexes are obtainable that are unusually stable due to the chelate effect, so that even normally weak or reactive donors like C_6H_5, pyridines or aliphatic amines can be fixed in the middle position of the pincer ligand.



Scheme 1: Common structure of pincer complexes.[9b]

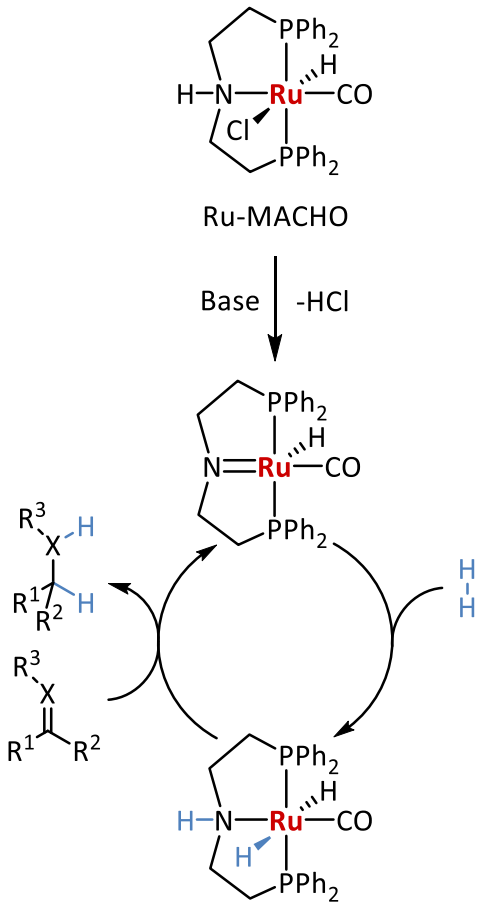
While transition metal pincer complexes have first been reported in the 1970s by the groups of Nelson,[10] Shaw,[11] and van Koten and Noltes[12], mainly platinum-group pincer complexes were studied subsequently for varying applications.[13]

2.1 Ruthenium Pincer Complexes

In the early 2000s it was discovered that the extraordinary stability of pincer complexes allows PNP and PNN pincer ligands to directly participate in chemical reactions without decomposition of the complex.[14] Applying this possibility of metal ligand cooperation

(MLC),[15] especially Ru pincer complexes were found to be very efficient catalysts for reactions involving the transfer of H_2.[16]

One very important example of a ruthenium pincer complex allowing for metal ligand cooperative effects is the so-called Ru-MACHO complex [Ru(HN($CH_2CH_2PPh_2$)$_2$)H(CO)Cl] published and patented by Takasago in 2011 for the hydrogenation of esters.[17] Here, after hydrogen chloride was abstracted from the pre-catalyst (see Scheme 2), the catalyst is able to activate molecular hydrogen by heterolytically cleaving the H–H bond to form a hydridic hydrogen bound to the metal center and a protic hydrogen bound to the amine function of the ligand. By successive transfer of this differently polarized hydrogen atoms, the catalyst is very potent in the hydrogenation especially of polar double bonds.[18]



Scheme 2: General mechanism of hydrogenation reactions by Ru-MACHO.[18]

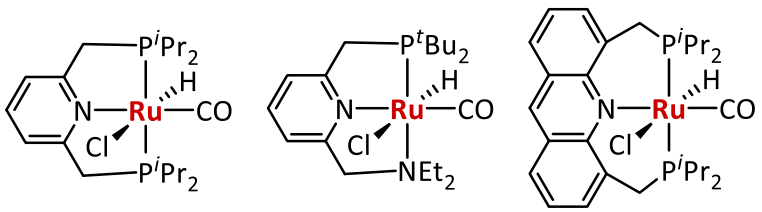
With this principle being discovered, Ru-MACHO was subsequently applied for various hydrogenation reactions[19] including the hydrogenation of various esters like α-fluorinated[20] or perfluorinated ones,[21] fatty acid esters,[22] esters relevant for fragrance production,[23] or ones derived from oxalic acid.[24] For the last reaction a derivative of Ru-MACHO containing a BH_4^- ligand instead of the chloride was used, which allowed for catalyst activation without the addition of base. This catalyst known as Ru-MACHO-BH was also utilized in the hydrogenation of nitriles.[25]

Special attention was paid to the applicability of Ru-MACHO for the hydrogenation of CO_2. In 2012, Ding and co-workers published the hydrogenation of cyclic carbonates to diols and methanol.[18] Because cyclic carbonates can be synthesized from epoxides and CO_2 in the Shell omega process, this reaction depicts an indirect way to hydrogenate CO_2 to methanol. Following another route, Sanford and co-workers enabled carbon dioxide hydrogenation by an amine assisted pathway.[26] Herein, CO_2 is captured by dimethylamine forming dimethyl-

ammonium dimethylcarbamate. This intermediate can then be hydrogenated by Ru-MACHO-BH to form methanol. By improving this concept using pentaethylenehexamine, CO_2 can be captured directly from air to be subsequently hydrogenated into methanol.[27] Further investigations suggest that amine assisted CO_2 hydrogenation can give access to methanol and other carbon-based chemicals in a methanol-based economy independent from petro-chemicals.[28]

On the other hand, Ru-MACHO also is a very potent catalyst for dehydrogenation reactions as was first discovered by Gusev et al. for the acceptorless dehydrogenation of alcohols.[29] This can also be achieved by an *in situ* system forming Ru-MACHO-type catalysts out of $[RuH_2(PPh_3)_3CO]$ and bis(2-(diisopropylphosphinoethyl)amine.[30] This usability of Ru-MACHO for hydrogenation as well as dehydrogenation reactions depicts a good example for the application of the principle of microreversibility of catalytic reactions. Accordingly, also the dehydrogenation of methanol towards hydrogen and carbon dioxide was intensively studied.[31] In 2013, our group published the dehydrogenation of aqueous-phase methanol towards carbon dioxide and three molecules of hydrogen at low temperatures and under atmospheric pressure.[32] By applying this reaction, methanol can be used as liquid energy carrier for fuel cells. A downside of this reaction is the required high base loading, which can be overcome by shifting to a bicatalytic system consisting of Ru-MACHO-BH and $Ru(H)_2(dppe)_2$.[33] Nevertheless, extensive mechanistical and theoretical studies on this reaction pronounced the high importance of base for the catalytic system and also suggested that this reaction follows a solvent-assisted inner-sphere pathway in contrast to the originally proposed outer-sphere mechanisms for Ru-MACHO catalysis (compare Scheme 2).[34] In addition to hydrogen production, dehydrogenation reactions by Ru-MACHO can also be used to synthesize valuable products such as ethyl acetate,[35] amides,[36] carboxylic acid salts,[37] and ureas[38] out of potentially renewable alcohols.

In addition to hydrogenation and dehydrogenation reactions, Ru-MACHO was also applied for other reactions involving the transfer of hydrogen such as transfer hydrogenation,[39] deuterations of alcohols[40] or nitriles,[41] and hydrogen autotransfer reactions,[42] which will be described in depth later on (see chapter 4). Lastly, Ru-MACHO was also applied in reactions involving several reaction steps. By combination with palladium-catalyzed oxycarbonylation, it is for instance possible to convert carbon monoxide into ethylene glycol.[43]



Scheme 3: Important pyridine-based ruthenium pincer complexes.[16a]

Other prominent examples for Ru PNP pincer complexes are the pyridine-based systems introduced by Milstein and co-workers (see Scheme 3).[15a, 16a] While this type of complexes was already known in 1998,[44] interest in them rose significantly when the metal ligand corporative effect in these systems was discovered and applied for the dehydrogenation of alcohols to esters in 2005.[14] Herein, the ligand backbone can be deprotonated leading to a dearomatization of the pyridine unit. By activation of hydrogen or dehydrogenation the aromaticity can be restored, making these catalysts very efficient for hydrogenation and dehydrogenation reactions. In the upcoming years, Milstein's group as well as others have explored broad applicability for these pyridine-based ruthenium PNP and PNN complexes. Accordingly, pyridine-containing pincer complexes were widely used for the dehydrogenation of alcohols into esters,[14, 45] ketones,[46] aldehydes,[47] or acetals[45a] depending on the catalyst and the reaction conditions. In addition to that, methanol can also be dehydrogenated by these pyridine-based systems giving hydrogen and carbonates.[48] Alongside this, dehydrogenation reactions can also be used for coupling of alcohols with other substrates. By this concept of dehydrogenative coupling, alcohols can be reacted with amides using pyridine-based Ru-Pincer catalysts to give amides,[49] which can be applied for the synthesis of polyamides,[50] and alcohols and hydrazines can be coupled giving azines.[51] Additionally, dehydrogenative coupling reactions are applicable for various heterocycle syntheses,[52] which will be discussed in a separate section (see chapter 4.3).

Like Ru-MACHO, pyridine-based pincer systems are potent catalysts for hydrogenation reactions as well. For example, these systems were used for the hydrogenation of amides,[53] carbonates, carbamates, formic acid esters,[54] and nitriles.[55] Furthermore, pyridine-based Ru PNP complexes were intensively studied for the catalytic hydrogenation of carbon dioxide into formate salts.[56]

Interestingly, Milstein and co-workers moreover presented a ruthenium PNN pincer complex capable of overall water splitting by thermal hydrogen liberation combined with light-induced oxygen release.[57] Because of their capability for dehydrogenation and hydrogenation

reactions, Milstein's ruthenium systems are also very interesting catalysts for hydrogen autotransfer reactions,[58] which will be dealt with in a separate segment of this thesis (see chapter 4).

Alongside the widely applied Ru-MACHO and Milstein systems, an array of other ruthenium pincer catalyst was established containing varying heterocycle motifs in PNN ligands[59] as well as NHCs,[60] sulfur,[61] and others as ligating moieties, which were applied for different hydrogenation and dehydrogenation reactions.

2.2 Other Noble Metal Pincer Complexes

Alongside ruthenium, iridium and osmium pincer complexes are known for catalyzing hydrogenation and dehydrogenation reactions. In fact, already in 2006, Milstein and co-workers discovered hydrogen activation by a pyridine-based iridium PNP pincer complex employing metal ligand cooperation.[62] In the following years, related complexes were applied for the hydrogenation of carbon dioxide and the corresponding dehydrogenation of formic acid.[63] The iridium analogues of Ru-MACHO on the other hand have been successfully deployed in the hydrogenation of esters to alcohols[64] and the dehydrogenation of methanol to carbon dioxide.[65]

The corresponding osmium PNP pincer complexes were mainly investigated by Gusev et al. The heavier analogues to Ru-MACHO turned out to be valuable catalysts for the dehydrogenation of alcohols to form esters[29, 66] and the reverse reaction producing alcohols by hydrogenation of esters.[66]

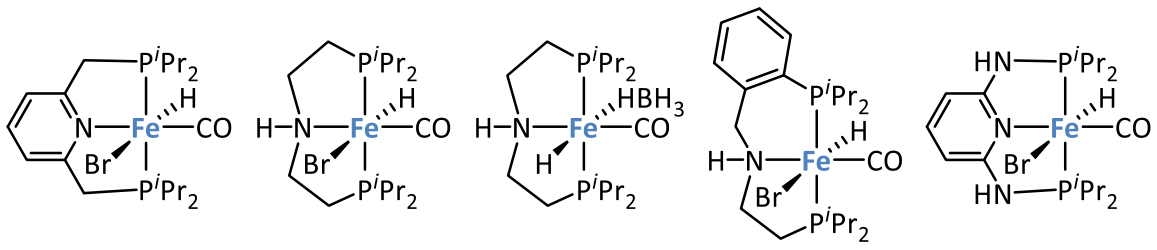
Overall, noble metal pincer complexes have proven to be exceptionally powerful catalysts for a plethora of reactions involving the transfer, activation or release of molecular hydrogen. Moreover, these catalyst systems are highly tunable allowing for variations on several positions in the ligand sphere to adjust the catalyst to the reaction that is performed.

2.3 Non-Noble Metal Pincer Complexes

Because of their direct involvement in the reaction by metal ligand cooperation, pincer ligands have an extraordinarily big influence on the reactivity of a catalyst. This, on the other side, lowers the normally outstanding impact of the metal center on the reactivity of a catalyst. Due to this effect, it was highly desirable to replace rare and expensive noble metals used until then by cheaper and more abundant non-noble metals. In line with this, pincer complexes of a variety of non-noble transition metals have been synthesized and applied as catalysts up to the present day.

2.3.1 Iron Pincer Complexes

Being the cheapest and most abundant transition metal as well as the lighter homologue of ruthenium, iron is a very interesting candidate for replacing noble metals in transition metal pincer complexes.[67] With this aim in mind, Milstein and co-workers prepared the Fe congener of their pyridine-based ruthenium pincer complex (see Scheme 4). And in fact, this complex turned out to be a very active catalyst for the hydrogenation of ketones.[68] Based on these results, modifying the catalyst with sodium borohydride led to a base-free version of the ketone hydrogenation.[69] Alongside this, pyridine-based iron pincer systems were also successfully applied for the hydrogenation of trifluoroacetic acid esters to alcohols,[70] and of CO_2 to formic acid.[71] Contrariwise, the dehydrogenation of formic acid to form carbon dioxide and hydrogen is also possible.[72] Accompanying this, acridine-based iron pincer complexes are able to hydrogenate alkynes selectively to E-alkenes.[73]



Scheme 4: Important iron pincer complexes.[68, 74, 88, 89a]

In addition to that, the iron analogues of Ru-MACHO as well as of Ru-MACHO-BH have been prepared by our group in 2013.[74] While these complexes were first used for the

dehydrogenation of methanol towards carbon dioxide, their field of application soon broadened to hydrogenation reactions including the hydrogenation of nitriles,[75] esters,[76] quinolines,[77] amides,[78] olefins,[79] and carbon dioxide.[80] Besides the initial dehydrogenation of methanol, dehydrogenation of other alcohols to ketones, esters, lactones,[81] or carboxylic acids[82] were reported alongside dehydrogenation of formic acid[83] and hydrazine borane.[84] This reactivity has also been used for the dehydrogenative coupling of alcohols and amines to form amides,[85] and for the hydrogen autotransfer reaction of α,δ-diols to synthesize γ-butyrolactones.[86] By incorporating a phenyl group into one of the arms of the pincer ligand (see Scheme 4), Milstein and co-workers were able to use iron pincer catalysts for the selective hydrogenation of nitriles to symmetric imines[87] and for the cross-coupling of nitriles and amines to asymmetric imines.[88]

An additional type of Fe PNP pincer complexes has been introduced by Kirchner et al. by involving 2,6-diamino pyridine into the ligand backbone.[89] These complexes also turned out to be potent catalysts for hydrogenation reactions including these of ketones, aldehydes,[89a] and carbon dioxide[90] as well as dehydrogenation reactions.[91] Accompanying these, Kirchner's complexes can also be used for dimerization and hydroboration of alkynes.[92]

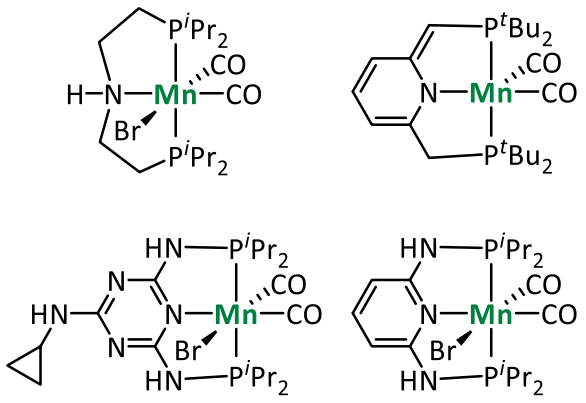
Lastly, asymmetric modifications of the pincer ligand make it possible to apply iron pincer complexes to asymmetric hydrogenations of ketones and imines.[93]

2.3.2 Manganese Pincer Complexes

Besides iron, manganese is a promising candidate for replacing noble metals in pincer catalysts. Following the cross-relationships in the periodic table, Mn(I) complexes should show a comparable behavior to their known Ru(II) analogues. Such manganese(I) PNP pincer complexes have first been prepared in 2009 by the groups of Ozerov and Nocera.[94] Nevertheless, their work was focused on organometallic properties of these complexes and not on their catalytic applicability.

Thus, the potential of these complexes for catalysis was revealed in 2016 by back-to-back publications of our group[43, 95] as well as the groups of Milstein,[96] Kempe,[97] and Kirchner[98] and was broadly applied from thereon.[99]

By this, four major types of Mn PNP pincer complexes with different ligand backbones were established (see Scheme 5). Manganese pincer complexes with an aliphatic backbone were introduced by our group and first applied for the hydrogenation of nitriles, ketones, and aldehydes.[95] Diminishing the steric demand of the ligand by introducing ethyl groups instead of isopropyl groups on the phosphorus atoms led to very efficient hydrogenation of esters as well.[100] In addition to that, aliphatic manganese pincer complexes were also employed for hydrogenations of carbon dioxide via formamide generation[101] and of cyclic carbonates providing diols and methanol.[102] Exchanging one of the phosphorus sidearms by methyl imidazole likewise gave an active catalyst for the hydrogenation of amides.[103] Utilizing this modifiability of the pincer ligand, chiral groups have been introduced at the phosphorus atoms making these catalysts able to hydrogenate ketones enantioselectively.[104] For dehydrogenation oppositely, aliphatic Mn pincer complexes were reported for catalyzing hydrogen abstraction from methanol,[105] formic acid,[106] and other alcohols yielding esters in the latter case.[107] When 1,4-diols are used for dehydrogenation, this can also be applied in the synthesis of pyrroles by coupling with amines.[108]



Scheme 5: First generation of manganese(I) pincer complexes.[99a]

The proven activity of aliphatic Mn pincer complexes in hydrogenations and dehydrogenations make them very interesting candidates for catalyzing hydrogen autotransfer reactions (see chapter 4). In fact, within this thesis it will be shown that these complexes are potent catalysts for the α-alkylation of ketones using alcohols (see chapter 6.1). Besides that, this type of complexes was also applied to the alkylation of amines with alcohols[109] as well as for the Guerbet-type dimerization of ethanol affording 1-butanol.[110]

As was already shown for aliphatic iron pincer complexes, introducing a phenyl group into one arm of the ligand changes the reactivity and in the case of manganese allows for the synthesis of *N*-formamides out of amines and methanol.[111] Additionally, this complex can be used for the α-olefination of nitriles[112] and for the deoxygenation of alcohols involving Wolff-Kishner reduction.[113]

Pyridine-based manganese PNP pincer complexes on the other hand were first synthesized by Milstein and co-workers to be applied for catalytic Michael addition of nitriles to α,β-unsaturated carbonyls.[96a] Further on, these complexes were employed for the dehydrogenative coupling of alcohols and amines to imines,[114] as well as for the hydrogenation of amides giving amines,[115] and – by using ammonia borane as hydrogen source – of alkynes giving alkenes selectively.[116] Testing this type of complexes for hydrogen autotransfer reactions additionally revealed that they are applicable for the methylation of aromatic amines using methanol,[117] and for pyrrole synthesis out of ketones, amines and diols.[118] Introducing acridine into the ligand backbone instead of pyridine, also allows for catalyzing dehydrogenative coupling reactions forming pyrazines, quinoxalines,[119] and amides[120] employing different kinds of alcohols and amines as starting materials.

Moreover, pyridine-based Mn pincer complexes having an amine sidearm were generated. These PNN systems turned out to be good catalysts for the hydrogenation of esters[121] and carbonates forming alcohols and methanol in the latter case.[122] By introducing chiral substituents onto the phosphorus atom of the ligand, asymmetric hydrogenation of ketones can also be conducted.[123] Performing dehydrogenation reactions, these catalysts can furthermore form cyclic imines out of diols and amines,[124] amides out of amines and alcohols or esters,[125] and esters out of alcohols.[126]

While making use of pyridine for his pincer systems, Kirchner et al. included nitrogen groups in the linkers to the phosphorus atoms. With these ligands they were able to generate Mn(I) complexes, which can be applied to the dehydrogenative coupling of alcohols and amines to form imines.[98] Based on this, these so-called PN_3P pincer systems were also utilized for hydrogenating carbon dioxide,[127] ketones,[128] and aldehydes[129] as well as for hydrogen autotransfer reactions enabling the methylation of anilines[130] and ketones,[131] and the aminomethylation of naphthyl alcohols with methanol.[132] In addition to that, pincer ligands can be synthesized employing 2,4-diamino-1,3,5-triazines. By this, Mn PN_5P pincer complexes have been obtained and applied for the hydrogenation of ketones, aldehydes,[97] and imines[133] as well as for the dehydrogenative alkylation of ketones[134] and alkyl-substituted heteroarenes.[135]

On top of that, various other modifications of the pincer ligands are possible. For example, with bis(2-pyridylmethyl)amine as phosphorus-free pincer ligand, transfer hydrogenations can

be conducted,[136] chiral modifications of the ligand allow for enantioselective hydrogenations,[137] and bidentate ligands give access to simple-to-prepare hydrogenation catalysts.[138]

2.3.3 Rhenium Pincer Complexes

With the presented applications known for manganese pincer complexes it should be assumed that its heavier homologue rhenium also can be employed for the herein presented reactions. Nevertheless, until recently, rhenium pincer complexes were scarcely used in homogenous catalysis.[139] In contrast to this, after initial work of Gusev et al.,[140] Schneider and co-workers established Re PNP complexes as potent systems for electrochemical or photolytic nitrogen activation and conversion of dinitrogen into organic compounds.[141] Besides that, pyridine-containing Re PNP complexes have been synthesized by Milstein et al. and were investigated concerning their reactivity towards nitriles,[142] hydrogen and CO_2.[143] Alongside the work presented in this thesis (see chapter 6.2), the group of Sortais prepared aliphatic Re PNP pincer complexes incorporating the previously shown MACHO-ligand[144] as well as a bis(phosphinite) PNP ligand[145] and applied them to the hydrogenation of ketones. Furthermore, rhenium PN_3P pincer complexes were employed for the synthesis of imines and N-containing heterocycles.[146]

2.3.4 Other Non-Noble Metal Pincer Complexes

Besides the beforehand discussed transition metals, pincer complexes of cobalt, nickel, and molybdenum were published as catalysts for reactions involving hydrogenation or dehydrogenation. Of these, cobalt pincer complexes have gained most attention.[99c, 147] Significant work in this field has been realized by the group of Hanson. Their cobalt complexes bearing an aliphatic pincer ligand and a tetramethylsilane-derived ligand were applied as catalysts for the hydrogenation of olefins, ketones, imines,[148] and esters[149] as well as for the dehydrogenation of alcohols towards ketones.[150] On top of that, these complexes catalyze C–N and C–C bond forming reactions via dehydrogenative coupling or hydrogen autotransfer

reactions.[151] In addition to that, Luo, Liu, and co-workers established cobalt dichloride pincer systems, that were subsequently used for the transfer hydrogenation of alkynes,[152] the hydrogenation of nitriles,[153] the dehydrogenation of formic acid,[154] and the isomerization of allylic alcohols.[155] Moreover, cobalt catalysts with phenyl-bridged PNP,[156] PN_3P,[157] and NNS[158] ligands have been reported for hydrogenation reactions.

Nickel pincer complexes on the other hand, while well-known in other areas like cross-coupling reactions,[9b, 9c] were only scarcely applied to hydrogen transfer reactions until today. While pyridine-based PNP pincer systems have been reported for stochiometric CO_2 activation, nickel complexes bearing aliphatic PNP,[159] or aromatic PN_3P[160] were applied to hydrogenation and hydrosilylation reactions.

In parallel to nickel, group six transition metal pincer complexes were only seldomly applied in hydrogenations or related reactions. An interesting exception from this is the pyridine-based molybdenum complex prepared by Nishibayashi's group, which can be employed for catalytic reduction of dinitrogen towards ammonia.[161] Apart from that, aliphatic PNP ligands were used in molybdenum and tungsten complexes catalyzing hydrogenations of nitriles,[162] imines,[163] ketones, and olefins.[164]

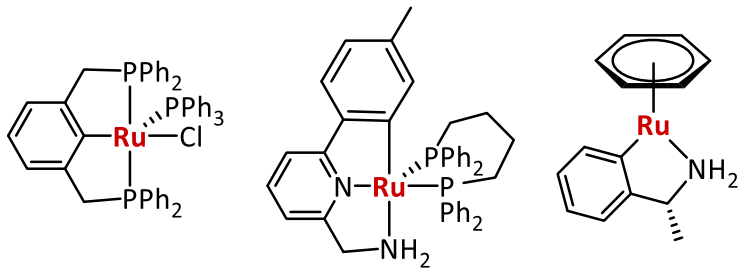
Summing up, transition metal pincer complexes have been proven to be very efficient and versatile catalysts for all sorts of hydrogenation, dehydrogenation, and related hydrogen transfer reactions. The particularly big influence of the ligands, which can take part in the reaction by direct metal ligand cooperation as well as the vast tunability of these systems make transition metal pincer complexes a highly attractive class of catalysts for the synthesis of fine chemicals.

3 Cyclometalated Ruthenium Complexes

While the activity of ruthenium pincer complexes for reactions involving hydrogen transfer has been shown in chapter 2.1, there are other types of Ru complexes that were proven to be efficient catalysts for this kind of reactions, too. Important examples for this are the ruthenium

BINAP complexes established by Noyori[165] as well as the Shvo catalyst bearing cyclopentadienone ligands.[166] Besides these prominent examples, cyclometalated ruthenium complexes have gained significant attention concerning their organometallic properties and their catalytic behavior.[167]

These complexes consist of a direct Ru–C bond whose stability is increased by a classic donor atom like N, O, P, or others making use of the chelate effect forming a relatively stable ruthenacycle.[167b] The ability of adjacent donor atoms to promote and stabilize Ru–C bond formation is widely applied to catalytic C–H activation by ruthenium complexes, which form ruthenacycles in the catalytic cycle and by this, activating otherwise inert C–H bonds.[168] Besides this, cyclometalated ruthenium complexes found applications as photosensitizers[169] and as anticancer agents.[170]



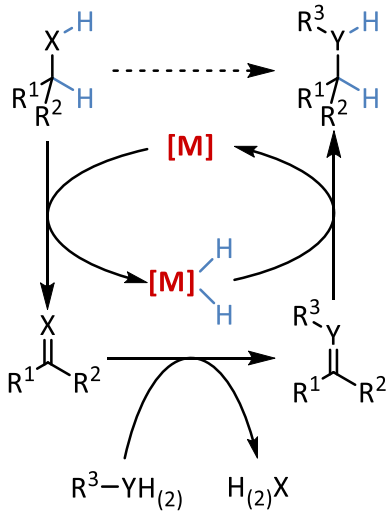
Scheme 6: Assorted ruthenacycles used in catalysis.[174a, 175a, 180a]

In the field of hydrogen transfer catalysis, cyclometalated ruthenium complexes have mainly been employed for transfer hydrogenations of ketones using isopropanol as hydrogen source.[167a] Catalysts used for this reaction are ruthenium half-sandwich complexes bearing bidentate ligands with donors like phosphorus,[171] nitrogen,[172] or NHCs[173] to stabilize the Ru–C bond, ruthenium PCP pincer complexes introduced by van Koten et al.,[174] or ruthenium CNN complexes developed by the group of Baratta.[175] These complexes bearing an additional bidentate phosphine ligand like dppb, are also capable of hydrogenation of ketones and aldehydes with molecular hydrogen[176] as well as deuteration of alcohols.[177] Furthermore, these systems catalyze the amination of alcohols via hydrogen autotransfer (see chapter 4).[178]

When a chiral unit is placed in the backbone of Baratta's CNN pincer ligands, the resulting ruthenium complexes can moreover perform transfer hydrogenations asymmetrically giving access to chiral alcohols.[179] The same reaction can also be catalyzed by half-sandwich ruthenacycles having chiral phenylethylamine ligands.[180]

On top of that, cyclometalated ruthenium complexes were published to catalyze the hydrogenation of olefins[181] and the dehydrogenation of alcohols and N-heterocycles,[182] making this type of complexes an interesting field for finding further applications.

4 Hydrogen Autotransfer Reactions

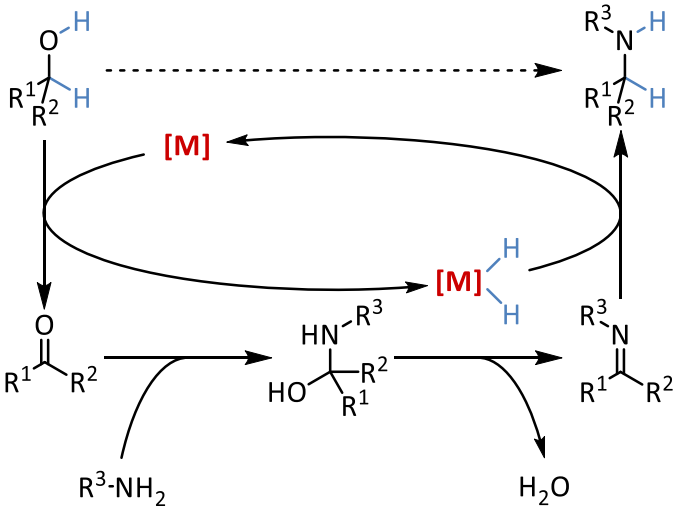


Scheme 7: General principle of hydrogen autotransfer reactions.[183a]

In the previous chapters, highly active transition metal catalysts capable of various reactions involving the transfer of hydrogen have been presented. The combination of these catalysts' abilities for hydrogenation and dehydrogenation reactions opens a broad field of unique reaction sequences. By dehydrogenation, unreactive starting materials like alcohols or amines can be converted to their much more reactive unsaturated counterparts like aldehydes or imines (see Scheme 7). These more reactive molecules in turn can undergo several reactions building up new chemical bonds of various types giving newly functionalized unsaturated molecules. Finally, they could be hydrogenated using the hydrogen abstracted in the first reaction step. Altogether, a reaction sequence like this allows for synthesizing new, otherwise hardly accessible molecules out of simple and relatively inert staring materials mostly generating very few and non-toxic by-products like water. This overall concept of dehydrogenation, functionalization, and hydrogenation is known as hydrogen autotransfer or hydrogen borrowing and was extensively investigated within the last years.[183] As will be shown in the upcoming chapters, applying the principle of hydrogen autotransfer enables a broad scope of reactions forming new C–N, C–C and C–O bonds and therefore giving access to environmentally friendly and highly tunable syntheses of important fine chemicals.

4.1 C–N Bond Formation Reactions

Hydrogen autotransfer was first put into use in the Guerbet reaction dimerizing alcohols towards branched longer-chain alcohols, which is known since the beginning of the 20th century using heterogenous alkoxides.[183d, 184] Besides this early example, the first reactions employing this concept were published by Grigg and Watanabe in 1981.[185] These reactions use the dehydrogenation of alcohols to aldehydes to subsequently form imines which are rehydrogenated giving *N*-alkylated amines as the final product (see Scheme 8). While the first reports were using ruthenium phosphine complexes, this *N*-alkylation of amines has since then been reported using a plethora of different catalysts.[186]



Scheme 8: Amination of alcohols by hydrogen auto-transfer.[186a]

Closely related to the initial works, the reaction was improved by applying different ruthenium phosphine catalysts and *in situ* systems of these from thereon. According to this, ligands like CataCXium A,[187] dppf,[188] DPEphos,[188] triphenyl phosphine,[189] dippf,[178b] or Xanthphos[190] have been used subsequently. Building upon this, the potential of the reaction for the synthesis of pharmaceuticals[191] and for running under continuous flow conditions[192] have been explored.

As discussed above (see chapter 2.1), ruthenium pincer complexes are highly suitable for hydrogen autotransfer reactions as well. Already in 1998, van Koten's group used a pyridine-based Ru pincer catalyst for the *N*-alkylation of amines with diols.[44] This was followed by acridine-based pincer complexes,[58a] which are even able to alkylate ammonia.[58b]

In addition to that, other noble metal complexes were reported catalyzing this reaction. Here, mainly iridium has gained attention, which is usable as pentamethylcyclopentadienyl

complex[193] or as catalyst modified by NHC[194] or phosphine[195] ligands. Besides that, gold[196] and palladium[197] catalysts were published for this reaction.

Nevertheless, in recent years there have been major affords in replacing noble metal catalysts with mostly cheaper and environmentally more benign non-noble metal ones (compare chapter 2.3). In line with this, *N*-alkylation reactions using alcohols as alkylating agents were reported using copper, iron, manganese, cobalt, and nickel catalysts. While copper was applied as simple copper(II) acetate at high temperatures,[198] iron complexes were inserted as more sophisticated Knölker-type cyclopentadienone[199] or PN_3P pincer[98, 200] complexes. For manganese on the other hand, different kinds of pincer complexes including MACHO-type PNP,[109] PNN,[201] and NNS[202] were reported while pyridine-based PNP complexes tend to give imines by dehydrogenative coupling omitting the final hydrogenation step.[98, 114] In addition to that, several cobalt pincer complexes[151a, 203] and some nickel-based systems[204] were published as catalysts for the alkylation of amines. Also, heterogeneous catalysts[205] and biocatalysts[206] were reported for this transformation. On top of that, by using chiral catalysts, some reactions are known giving enantioenriched products in this type of reactions.[207]

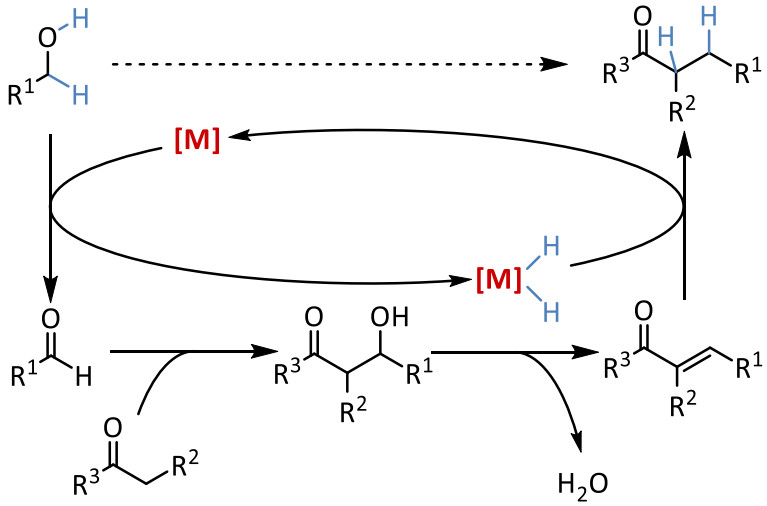
Of special interest, but also of special difficulty is the methylation of amines using methanol as cheap and easy to handle methylating agent. For this, some ruthenium complexes with phosphine ligands[208] and iridium[209] catalysts have been reported and, lately, complexes based on non-noble metals like manganese,[117, 130] cobalt,[210] and iron[211] were found active.

Apart from amines, nitrogen atoms of various other molecules have been alkylated using hydrogen autotransfer protocols. Herein for example, the alkylation of amides,[212] carbamates,[212b] sulfonamides,[188, 213] sulfonamides,[42a] and indoles[214] was reported. It is also possible to use nitriles[215] or nitro compounds[215b, 216] as starting materials, which under reaction conditions first get reduced and then alkylated giving *N*-alkyl amines.

Lastly, while alcohols are by far the most common substrate for activation in hydrogen autotransfer reactions, the use of amines has also been reported. Here, the amine gets dehydrogenated yielding an imine, which subsequently gets attacked by another amine to finally get hydrogenated again. Applying this procedure, alkylated amines can be obtained by the cross-coupling of amines.[217]

4.2 C–C Bond Formation Reactions

In addition to the previously described C–N bond formations, hydrogen autotransfer protocols found wide application in the generation new C–C bonds.[218] Here, the *in situ* generation of aldehydes out of alcohols is used for aldol-type reactivity generating new C–C double bonds, which are hydrogenated to C–C single bonds subsequently (see Scheme 9). After initial works of Guerbet, who used hydrogen autotransfer reactions already at the beginning of the 20th century to dimerize alcohols,[183d, 184] the possibility to form new C–C bonds via hydrogen autotransfer was mainly applied in the α-alkylation of ketones with alcohols. As was the case for C–N bond forming reactions, catalysts were first based on noble metals like ruthenium[219] and iridium.[220] Depending on the catalyst and the reaction conditions, it is also possible to perform an alkylation on already alkylated ketones giving branched products[221] or to use methanol to achieve methylations.[222] As already described, in recent years increasing effort went into replacing the previously required noble metal catalysts with non-noble metal based ones. In the case of ketone alkylation reactions this was achieved by Knölker-type iron catalysts, which turned out to also be applicable for the methylation of ketones,[223] and by cobalt pincer complexes.[151c] On top of that, manganese pincer complexes are very active for this transformation. Besides the MACHO-type ligands that are presented in this thesis (see chapter 6.1), PN_3P[131] and pyridine-linked aliphatic[223c] pincer ligands were employed herein.



Scheme 9: Alkylation of ketones by hydrogen autotransfer.[218b]

Closely related to the α-alkylation of ketones is the β-alkylation of alcohols which involves an additional dehydrogenation step to form ketones out of these alcohols as well as a hydrogenation step in the end giving β-substituted alcohols as final products. Being linked to the beforehand described reactions, the catalysts used here are also similar looking. Mainly ruthenium complexes have been published for this, ranging from $RuCl_2(DMSO)_4$[224] to various

pincer complexes.[225] By using Ru-MACHO in combination with Shvo's catalyst[226] or Ru-MACHO-BH,[227] it is also possible to perform β-methylations of alcohols. In this field of catalysis, the upgrading of simple alcohols like ethanol to higher ones like n-butanol in line with the Guerbet reaction is of special interest since it allows for the generation of longer-chain alcohols interesting for energy storage and for the synthesis of chemicals out of potentially renewable ethanol. For this reaction ruthenium catalysts bearing acridine-based PNP[58c] or NNN[228] pincer ligands have been reported together with manganese-based catalysts,[110] representing the switch toward non-noble metal catalyst.

The opportunity to generate aldehydes out of alcohols *in situ* opens the field for other carbon nucleophiles to attack and generate new C–C bonds as well. Applying this possibility, various carbon atoms in α-position to an electron-withdrawing group can by alkylated by hydrogen autotransfer methodologies. Accordingly, nitriles can be alkylated using alcohols with homogenous catalysts based on metals like iridium,[229] ruthenium,[230] osmium,[231] iron,[232] or manganese[233] and even acetonitrile can be upgraded to heavier nitriles with this method.[234] Additionally, other carboxylic acid derivatives like esters or amides can be alkylated in α-position. Here, mainly ruthenium[58d, 235] and iridium,[236] but also cobalt[237] complexes have been reported.

Furthermore, CH-acidic compounds like α,γ-diketones[229] and barbituric acid derivatives[238] were employed in alkylation reactions and it was shown that alcohols can replace aldehydes in Wittig and Horner-Wadsworth-Emmons reactions under hydrogen autotransfer conditions.[239]

4.3 Syntheses of Heterocycles

As described above, hydrogen autotransfer and dehydrogenative coupling reactions are capable of forming new C–C and C–N bonds utilizing simple starting materials in an efficient manner. When reagents are chosen wisely, these capabilities allow for the generation of various heterocycles via cascade reactions and by this, opening up new synthesis routes for important classes of fine chemicals and pharmaceuticals.

The easiest way to generate heterocycles by hydrogen autotransfer is by double alkylation of amines with diols, which gives saturated heterocycles. This method was already described by Tsuji in the 1980s using ruthenium triphenylphosphine complexes.[240] By selecting heteroatom-containing or unsaturated diols, this pathway can also be used to obtain morpholines, piperazines,[240] or pyrroles.[241] Additionally, when urea derivatives are used instead of amines, 2,3-dihydroimidazol-2-ones are produced.[242]

With catalysts capable of alcohol dehydrogenation, the Friedländer quinoline synthesis is performable with ketones and 2-aminobenzyl alcohol instead of the formerly required aminoaldehydes, which opens up a broader substrate scope for this reaction.[243] Later, it was shown that the ketones applied in this reaction can also be replaced by aldehydes[244] or alcohols.[245] Recently, this transformation has been presented using a manganese PN_3P pincer catalyst.[246] Furthermore, the synthesis of quinoxalines can be achieved from *o*-phenylene-diamine and diols by ruthenium,[247] iridium,[248] or manganese[119] catalysis.

Another very important class of heterocycles are indoles, which have already been synthesized by dehydrogenative cyclization of 2-(2-aminophenyl)ethanol in 1990.[249] More recently, the Fischer indole synthesis was expanded to the use of phenylhydrazines and alcohols.[250] On top of that, indoles were obtained starting from anilines and epoxides via hydrogen autotransfer.[251] Closely related to indoles are benzimidazoles, which can also be produced by the dehydrogenative coupling of *o*-phenylenediamine with alcohols applying ruthenium,[252] iridium,[248] or cobalt[253] complexes.

A lot of natural products and pharmaceuticals contain pyrroles as a structural motif. With this in mind, finding new, improved pyrrole syntheses by hydrogen autotransfer or dehydro-genative coupling has been attempted over the last years. Indeed, amines and diols can be coupled giving pyrroles and releasing hydrogen as a by-product as a resemblance of the classic Parr-Knorr pyrrole synthesis. This reaction has been accomplished using ruthenium,[52d, 254] cobalt,[255] or manganese[108] catalysts. Another way of synthesizing pyrroles is the dehydrogenative coupling of β-aminoalcohols with secondary alcohols. Catalysts reported for this reaction are based on iridium[256] and ruthenium[52b] or more recently, on manganese[257] and cobalt.[258] Moreover, Knölker-type iron complexes were applied for synthesizing pyrroles from amines and unsaturated 1,4-diols.[259] In addition to that, pyrrole synthesis has been reported using a hydrogen autotransfer reaction sequence starting from amines, ketones, and

diols catalyzed by ruthenium,[260] or, very recently, manganese[118] complexes. By using three easily available starting materials, this reaction allows for the synthesis of a many differently substituted pyrroles and will also be highlighted later on in this thesis (see chapter 6.2).

A related transformation to this is the three-component pyrimidine synthesis starting from amidines, primary alcohols, and secondary alcohols. This reaction uses Ir PNP,[261] or more recently, Mn PNP[246, 262] pincer complexes as catalysts. In addition to that, the synthesis of pyrazoles,[263] pyridines,[52c, 264] and pyrazines[52a, 119] out of amines and alcohols was performed via dehydrogenative coupling protocols. Finally, by applying dehydrogenative C–O bond formation, lactones can be obtained from diols.[86]

To sum up, hydrogen autotransfer displays a powerful synthesis concept that puts hydrogenation and dehydrogenation abilities of modern transition metal catalysts into use. Its application allows for the synthesis of various differently substituted fine chemicals including ketones, amines, and heterocycles out of readily available and potentially renewable starting materials like alcohols or amines. Since water, ammonia, or hydrogen are the only stochiometric by-products most of the times, these reactions are environmentally benign and surpassingly sustainable.

5 Objectives of this Work

The presented thesis focusses on the development of novel homogeneous catalysts and their application in hydrogen autotransfer catalysis. Herein, special attention was paid to the scope of applicable transition metals for pincer complexes. This on one the hand benefits the sustainability of the investigated reactions by applying more abundant non-noble metals instead of the previously preferred precious metals and on the other hand shines a light on the versatility of the employed ligand systems, which's outstanding performance can be preserved using various different central atoms in the applied complexes. In addition to that, modifications on the ligand systems have been executed to further increase the tunability of the deployed catalysts and therefore, to provide catalysts that are exactly adjustable to the reaction in which they are employed. More precisely, by exchanging the formerly required carbon monoxide and hydride ligands of ruthenium pincer catalysts, a broadening of the tuning options is presented. This aims at the development of new catalytic systems that are highly adjustable to the necessities of the performed reaction.

On top of that, the transition metal complexes that were investigated within this thesis were used to catalyze various hydrogen autotransfer reactions. This was done to broaden the scope of this concept for cascade reactions and hence, to show its potential to produce a wide array of fine chemicals in an environmentally benign way by using mild reaction conditions typical for homogenous catalysis and producing no stochiometric by-products except of water. In line with this, readily available and potentially renewable alcohols were used as alkylating agents to form a variety of C–C and C–N bonds as well as to build heterocycles out of simple starting materials.

Overall, the focus on catalytic systems and highly efficient and economic reactions targets on making the synthesis of diverse fine chemicals more efficient and sustainable.

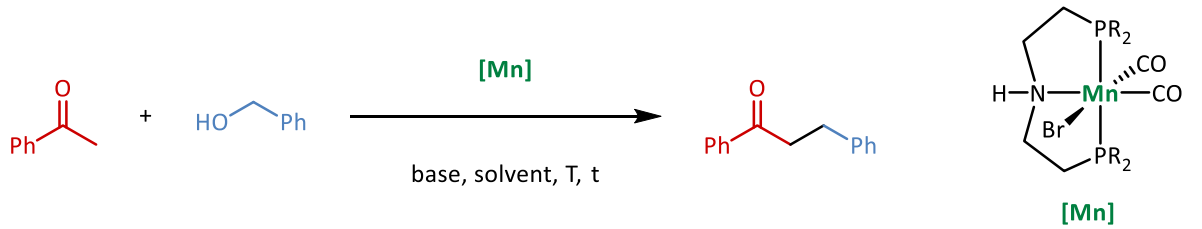
6 Summary of Published Results

6.1 Manganese-Catalyzed Hydrogen-Autotransfer C–C Bond Formation: α-Alkylation of Ketones with Primary Alcohols

As was described in the introduction of this thesis, hydrogen autotransfer depicts a powerful concept for making the synthesis of fine chemicals more sustainable by enabling carbon-carbon bond formations with superior atom-economy (see chapter 4.2). Especially the introduction of non-noble metal catalysts for this type of reactions leads to new, environmentally friendly synthesis protocols. In line with that, finding non-noble metal catalysts for the alkylation of ketones with alcohols was highly anticipated. Herein, the employed alcohol gets dehydrogenated by the catalyst forming an aldehyde in the first reaction step. Further on, this aldehyde undergoes aldol condensation with a ketone yielding an α,β-unsaturated ketone in the second step, that finally gets hydrogenated by the catalyst using the hydrogen abstracted in the first reaction step. While being known with several noble metal catalysts, in the realm of non-noble metal catalysis this reaction has only been reported using Knölker-type iron catalysts prior to our publication.[223a]

Because of this, we became interested in applying MACHO-type manganese catalysts that have recently been prepared by our group[95] to this reaction. Initially, the reaction of acetophenone with benzyl alcohol was tested using three different Mn PNP pincer complexes bearing phenyl, cyclohexyl, or isopropyl groups on the phosphorus atoms. Of these, the isopropyl complex turned out to be the most active one giving 83% of 3-phenyl-propiophenone. Next, different bases were investigated, but neither of the tested ones provided better results than the initially used cesium carbonate, so we focused our attention on lowering the catalyst loading. Here, a decrease to 2 mol% was possible without a loss of overall yield. Similarly, lowering the reaction temperature to 140 °C had no negative effect on the reactivity, but a larger drop in temperature yielded in decreased conversions. While initially 1,4-dioxane was employed as solvent, the use of toluene or *tert*-amyl alcohol had no significant drawback for the reaction outcome. Due to its lower toxicity and higher environmental compatibility,[265] we chose to continue with *tert*-amyl alcohol from thereon. Investigation on the base loading revealed that 5 mol% of Cs_2CO_3 are sufficient to conduct the reaction, so that this together with 2 mol% of catalyst in *tert*-amyl alcohol at 140 °C was

chosen as optimal reaction conditions giving 3-phenylpropiophenone in 88% yield. Control reactions without catalyst or base or with the catalyst's precursor gave no or very poor yields instead.

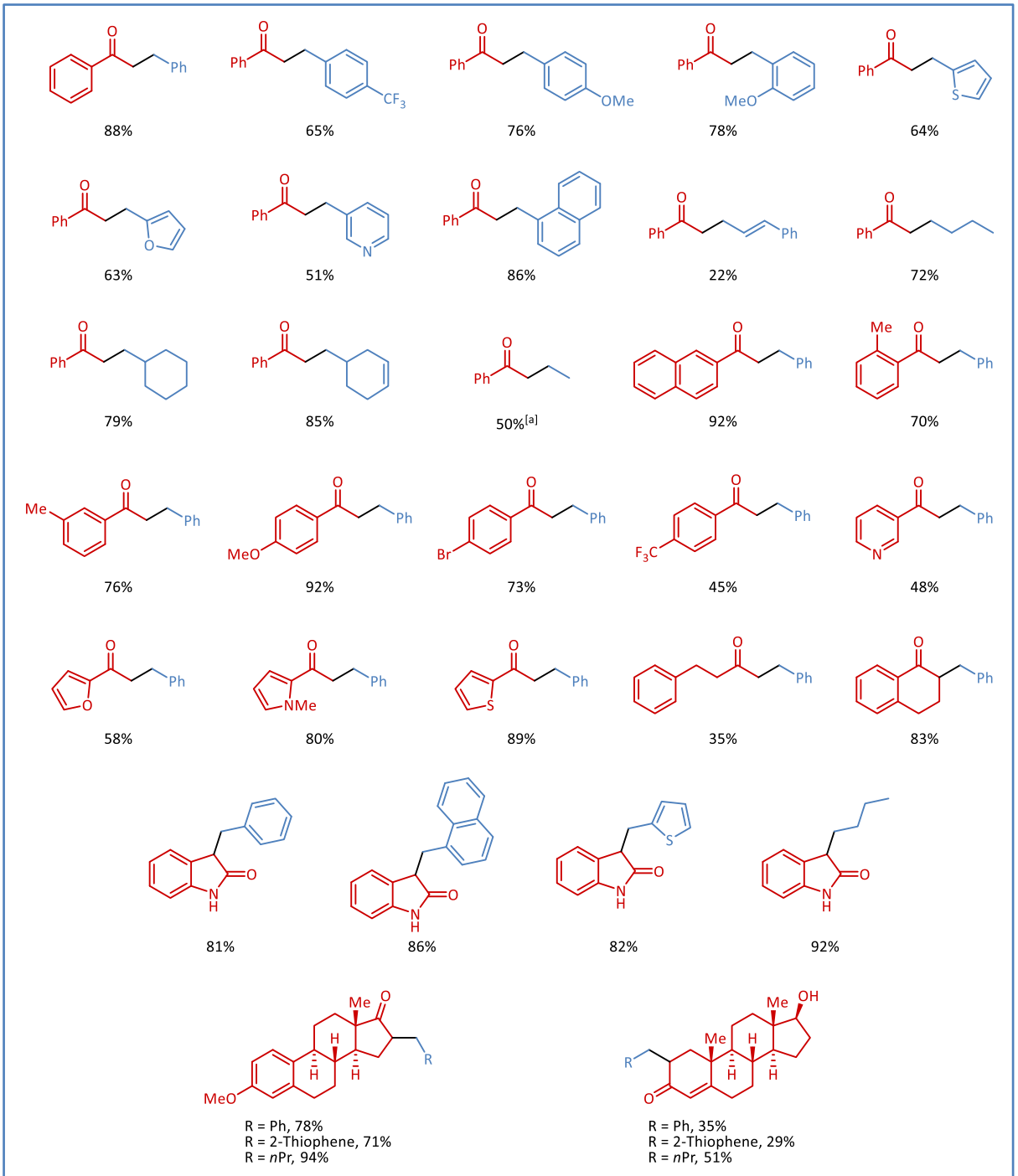


Entry	[Mn]	Base	Base Loading	Solvent	T (°C)	Yield (%)
1	R = phenyl	Cs_2CO_3	10 mol%	1,4-dioxane	150	83
2	R = cyclohexyl	Cs_2CO_3	10 mol%	1,4-dioxane	150	77
3	R = isopropyl	Cs_2CO_3	10 mol%	1,4-dioxane	150	90
4	$Mn(CO)_5Br$	Cs_2CO_3	10 mol%	1,4-dioxane	150	6
5	R = isopropyl	KOH	10 mol%	1,4-dioxane	150	69
6	R = isopropyl	K_2CO_3	10 mol%	1,4-dioxane	150	52
7	R = isopropyl	KO*t*Bu	10 mol%	1,4-dioxane	150	70
8[a]	R = isopropyl	Cs_2CO_3	10 mol%	1,4-dioxane	150	87
9[b]	R = isopropyl	Cs_2CO_3	10 mol%	1,4-dioxane	150	78
10[a]	R = isopropyl	Cs_2CO_3	10 mol%	1,4-dioxane	140	84
11[a]	R = isopropyl	Cs_2CO_3	10 mol%	1,4-dioxane	130	63
12[a]	R = isopropyl	Cs_2CO_3	10 mol%	toluene	140	85
13[a]	R = isopropyl	Cs_2CO_3	10 mol%	*t*-amyl alcohol	140	86
14[a]	R = isopropyl	Cs_2CO_3	5 mol%	*t*-amyl alcohol	140	**88**
15[a]	R = isopropyl	Cs_2CO_3	2 mol%	*t*-amyl alcohol	140	64
16[a]	R = isopropyl	—	—	*t*-amyl alcohol	140	—
17[a]	—	Cs_2CO_3	5 mol%	*t*-amyl alcohol	140	18

Table 2: Optimization of the manganese catalyzed α-alkylation of ketones with alcohols, [a] catalyst loading: 2 mol%, [b] catalyst loading: 1 mol%.

With these optimized conditions in hand, different alcohols were deployed as alkylating agents in this reaction. Herein, substituted benzyl alcohols with a trifluoromethyl or a methoxy group in *para*-position gave the product in good yield. Also, moving the methoxy group from the *para*- to the more sterically demanding *ortho*-position retained a similar yield. Applying heteroaromatic alcohols gave the corresponding alkylated ketones in moderate to good yields as well, while employing 1-naphthyl alcohol gave access to the product in a very good yield of 86%. Cinnamyl alcohol on the other hand was only converted into 22% of the desired product because the final hydrogenation yielded in various partly unsaturated ketones. To our delight, aliphatic alcohols can be utilized, too. Here, 1-butanol and cyclohexanol were tested and gave

the desired products in 72 and 79%, respectively. Even having a double bond in the backbone does not hinder the reaction, which was shown for 3-cyclohexene-1-methanol. Finally, when ethanol is used as solvent for this reaction, it can also provide the ethylated ketone in 50% yield.



Scheme 10: Substrate scope of the Mn-catalyzed alkylation of ketones, [a] EtOH was used as the solvent.

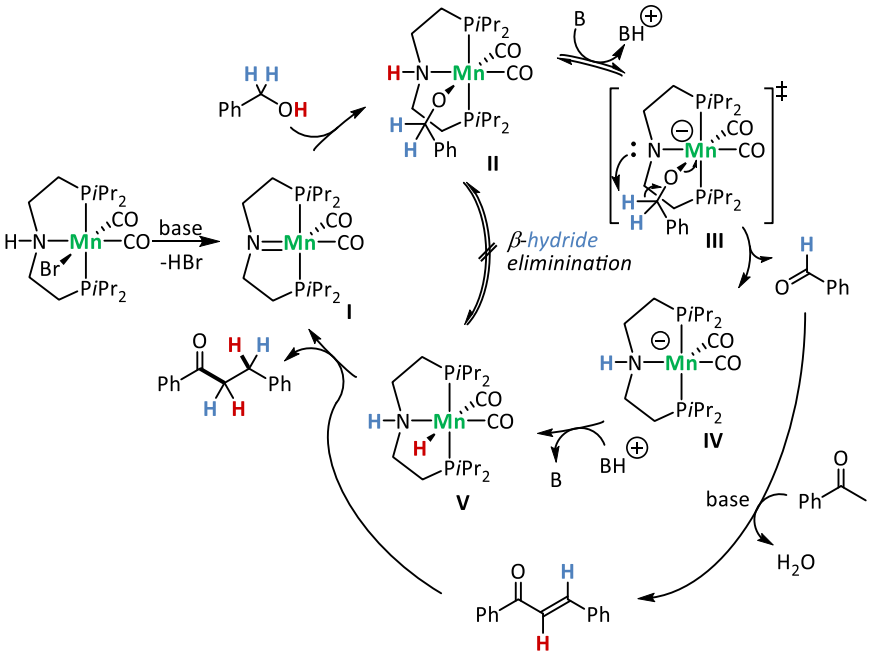
Next, different ketones were applied. In this, exchanging the phenyl group of acetophenone with a naphthyl group gave access to the corresponding product in excellent 92% yield. Increasing the steric demand in comparison to the standard reaction, methyl acetophenones

have been alkylated in good yields as well. Investigation of the electronic influence revealed that electron-rich acetophenones like 4-methoxyacetophenone give better yields than electron-deficient ones like 4-bromo- or 4-trifluoromethylacetophenone. Exchanging acetophenone for heterocycle-containing ketones gave rise to the corresponding products in moderate yields in the case of pyridine- or furan-substituted ketones to very good 89% yield for methyl-2-thienyl ketone. Next, to test the suitability of aliphatic ketones for this reaction, 4-phenyl-2-butanone was applied and gave the corresponding product albeit in lower 35% yield. On top of that, as was shown for α-tetralone, it is also possible to alkylate already substituted α-positions of ketones and by this, generating branched products.

The high selectivity of the reaction was proven for 2-oxindole, which could in principle be alkylated at the nitrogen atom as well, but in our case gave the *C*-alkylated products exclusively and in very good yields for different alcohols. Finally, the presented alkylation method was applied to biologically elevant hormones. Getting substituted derivatives of these is interesting for drug discovery as well as for investigations concerning their mechanism of action in living cells.[266] By putting the investigated manganese catalyst into use, estrone 3-methyl ether was alkylated with different alcohols in very good yields of 71-94%. Testosterone on the other hand was also alkylated albeit in lower yields of 29-51%. Here, the double bond on the other side of the carbonyl group caused side reactions in the terminal hydrogenation step.

To gain more knowledge about the performed reaction, several mechanistic investigations were conducted. As was described previously, MACHO-type ligands can participate in hydrogenation or dehydrogenation reactions directly by abstraction of a proton from the ligand's NH-moiety (see chapter 2). To confirm that this is the case for the herein studied reaction, a complex derivative was prepared where the nitrogen atom of the ligand is blocked by a methyl group which therefor shuts down the described metal ligand cooperativity. When this complex was utilized in the reaction under otherwise optimal conditions, a yield of only 32% instead of 88% was obtained. This shows a strong hindrance of the major reaction pathway as was expected, but on the other hand hints on the existence of a minor reaction route that does not require the direct participation of the ligand. Next, we performed the reaction with [α,α-D_2]benzyl alcohol and investigated the whereabouts of the introduced deuterium atoms by NMR spectroscopy. To avoid scrambling of the hydrogen atoms in protic

media, these reactions were carried out using toluene as solvent. With the originally employed catalyst, the product contained 36% deuterium in α- and 33% in β-position to the carbonyl group. The methylated catalyst on the other hand yielded only 9% α-, but 60% β-deuteration. This again suggests, that the major reaction pathway giving an equal distribution of deuterium between α- and β-position is not accessible for the methylated complex and therefore probably involves metal ligand cooperation.



Scheme 11: Plausible reaction mechanism for the α-alkylation of ketones with alcohols using a manganese pincer catalyst.

With these results in hand, a plausible reaction mechanism was proposed (see Scheme 11). Herein, the pre-catalyst gets activated through abstraction of hydrogen bromide by the employed base. The so-formed amido-complex **I** now reacts with the alcohol giving an alkoxide complex **II**. From here on, β-hydride elimination would be a possibility to directly form hydride complex **V**. This however would have yielded in high deuteration in β-position of the final product in the experiment using deuterated benzyl alcohol. So albeit possible and likely the dominant reaction pathway for the methylated catalyst, we think that the major reaction pathway for the more active NH-catalyst consists of the formation of an amidate-intermediate **III** out of complex **II**, that subsequently abstracts a proton from the α-position of the alkoxide bound to the complex. This yields in the formation of the aldehyde and anionic complex **IV**. While the aldehyde now undergoes aldol condensation giving an α,β-unsaturated ketone, complex **IV** gets protonated therefor becoming hydride complex **V**. In the final reaction step, this complex transfers hydrogen to the unsaturated intermediate and by this forms the final product and finishes the catalytic cycle regenerating complex **I**.

To sum up, a powerful method for the α-alkylation of ketones is presented in this work. The use of alcohols as alkylating agents, the formation of water as sole stochiometric by-product, and the use of a manganese-based catalyst make this transformation environmentally benign and sustainable. A broad substrate scope including biologically relevant compounds is presented and a plausible reaction mechanism including metal ligand cooperation is proposed and backed up by experimental data.

6.2 Hydrogen Autotransfer and Related Dehydrogenative Coupling Reactions using a Rhenium(I) Pincer Catalyst

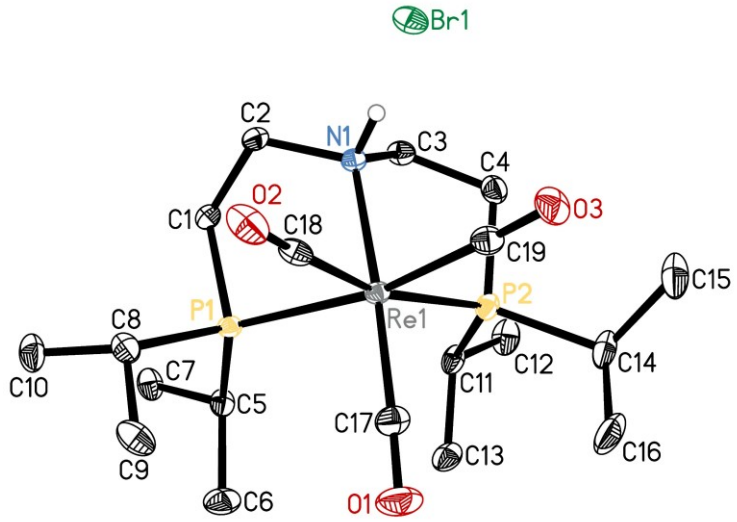
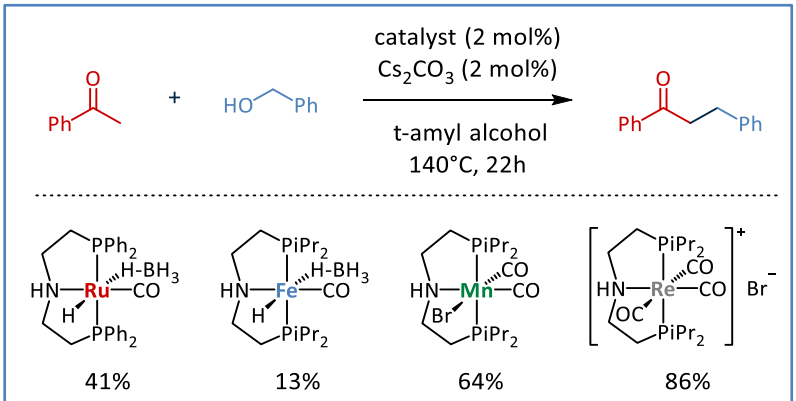


Figure 2: X-ray molecular structure of the applied Re pincer complex. Ellipsoids correspond to 30% probability. Hydrogen atoms are omitted for clarity. There are two molecules in the asymmetric unit of which one is shown.

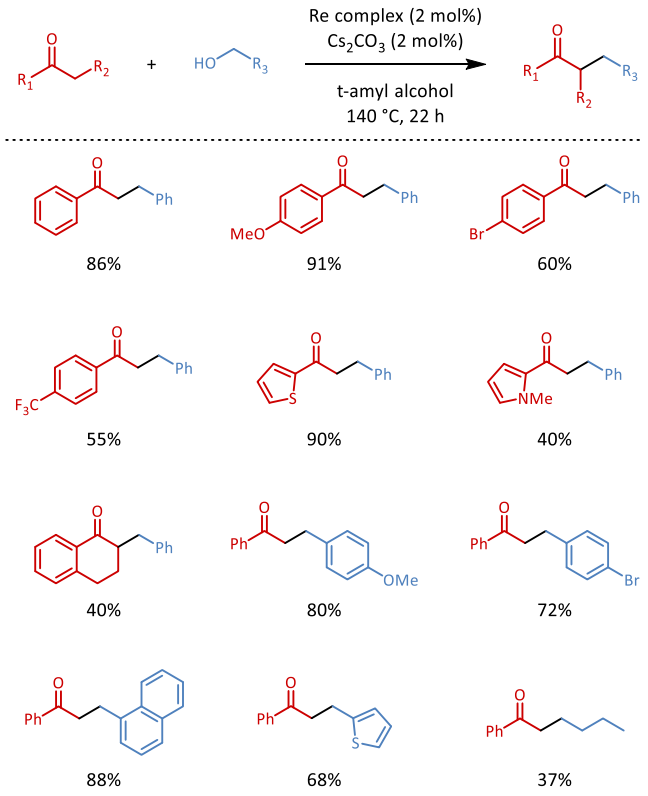
After having established a potent manganese pincer catalyst for the α-alkylation of ketones, we became interested in finding new complexes based on diverse transition metals for hydrogen autotransfer reactions. In line with this, rhenium came into our focus. Being manganese's heavier homologue, comparable chemical behavior can be expected. However, as was described in chapter 2.3.3, rhenium pincer complexes have scarcely been investigated beforehand. With this in mind, a MACHO-type rhenium pincer complex was prepared by combination of the PNP ligand with rhenium pentacarbonyl bromide in toluene and heating to 100 °C for 18 h. As was confirmed by X-ray crystal structure analysis, a rhenium pincer complex was gained by this. In contrast to its manganese analogue, this complex is cationic bearing three CO ligands and a bromide counterion. Furthermore, while pincer ligands are known for preferring an equatorial coordination around a metal center, here, the ligand is

arranged in a facial coordination mode making use of the high flexibility of the aliphatic pincer ligand (see Figure 2).

With a viable synthesis procedure in hand, application of the novel complex in catalysis was tried. Indeed, when the Re PNP complex was used for the previously described α-alkylation of ketones, very good results were obtained. Initially, the catalyst was used in *tert*-amyl alcohol with potassium hydroxide as base for alkylating acetophenone with benzyl alcohol giving 3-phenylpropiophenone in 74% yield. Testing an assortment of bases for this revealed cesium carbonate to be most effective. A lower catalyst loading of 1 mol% instead of the initial 2 mol% slightly diminished the yield while a higher loading did not increase it. Other solvents like 1,4-dioxane or toluene had very little effect on the reaction so that no change was conducted here. Interestingly, investigating the base loading exposed that 2 mol% of Cs_2CO_3 are sufficient for effective catalysis. Having in mind that basic conditions are required for catalyst activation as well as for conducting the aldol condensation reaction step, the here employed one equivalent of base with respect to the catalyst is outstandingly low. Performing the reaction at 130 or 150 °C resulted in lower product quantities than at 140 °C reaction temperature, so that in conclusion, 3-phenylpropiophenone was gained in optimal 86% yield when 2 mol% of the catalyst and cesium carbonate are used, respectively, at 140 °C reaction temperature in *tert*-amyl alcohol. To find out about the activity of the novel rhenium complex it was compared to known MACHO-type complexes with ruthenium, iron, or manganese central atoms. While the rhenium catalyst gave 86% of the product as was stated above, ruthenium and iron only gave poor yields of 41 and 13%, respectively. Even with the previously investigated manganese complex only 64% of 3-phenylpropiophenone were obtained. Conclusively, the presented rhenium complex is the more effective catalyst for the α-alkylation of ketones under given reaction conditions than comparable previously known complexes bearing other metals.



Scheme 12: Reactivity of different pincer catalysts for the α-alkylation of ketones with alcohols.



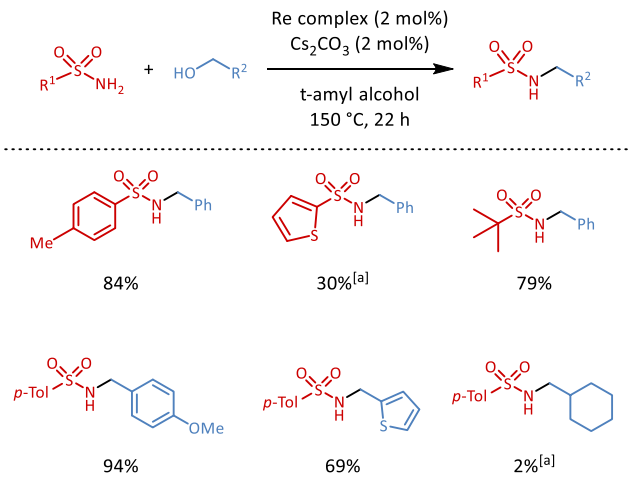
Scheme 13: Substrate scope of the Re-catalyzed α-alkylation of ketones with alcohols.

With the knowledge of having a very effective catalyst in hand, various substrates were surveyed. First, differently substituted acetophenone derivatives were tested. Here, the reaction worked better with more electron donating substrates like 4-methoxyacetophenone, while electron-deficient substrate gave slightly lower yields. Heterocycle-containing ketones were investigated next. In this, 2-acetylthiophene gave very good 88% of the corresponding product while 2-acetyl-*N*-methylpyrrole afforded only 40% of the desired ketone. Lastly, the alkylation of α-tetralone showed that obtaining branched products by the investigated procedure is possible, although in modest 38% yield.

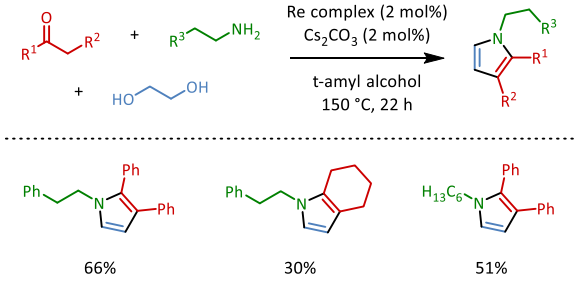
In exchange for benzyl alcohol, other alcohols were tested subsequently. Electron-rich 4-methoxybenzyl alcohol as well as electron-deficient 4-bromobenzyl alcohol gave good yields of 80 or 72%, respectively. Replacing benzyl alcohol's phenyl group with a naphthyl or even a thiophenyl group can also be done giving rise to good yields of the corresponding products. The application of aliphatic alcohols was investigated using n-butanol. Here, hexanophenone was obtained in modest 37% yield.

While it was confirmed that rhenium pincer complexes can be applied in C–C bond formations, we were eager to find out if it can be used for the whole spectrum of hydrogen autotransfer reactions. For achieving this, the C–N bond building reaction between sulfonamides and alcohols was investigated. In this, the alcohol first gets dehydrogenated by a suitable catalyst. Thereafter, the so-formed aldehyde condensates onto the N-atom of the sulfonamide forming a new C–N double bond. This at last gets hydrogenated by the hydrogen abstracted first, so that a C–N single bond was built overall by hydrogen autotransfer catalysis.

Appling this sequence, *para*-toluenesulfonamide was tested for alkylation with benzyl alcohol using the conditions established for the above described C–C bond formation only raising the temperature to 150 °C. By this, *N*-benzyl-*para*-toluenesulfonamide was obtained in very good 84% yield. On top of that, other sulfonamides like *tert*-butylsulfonamide or thiophenesulfonamide were suitable starting materials as well, giving the benzylated product in 79 or 29%, respectively. The latter result is rather modest although a higher base loading of 5 mol% was used here. Varying alcohols can be used for this reaction, too. To give an example, 4-methoxybenzyl alcohol and 2-thiophenemethanol were employed. These gave rise to their corresponding products with good yields of 94 and 69%, respectively. Cyclohexanemethanol, however, only gave traces of the desired product even with higher base loadings.



Scheme 14: Substrate scope of the Re-catalyzed *N*-alkylation of sulfonamides with alcohols, [a] 5 mol% Cs_2CO_3.



Scheme 15: Substrate scope of the Re-catalyzed pyrrole synthesis.

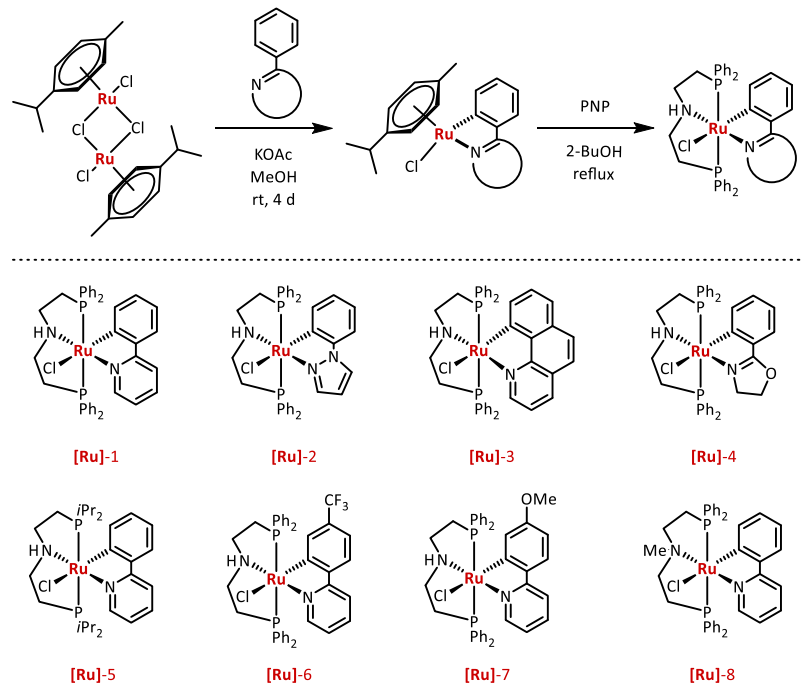
Finally, combining the catalyst's ability for C–C and C–N bond formations, the synthesis of pyrroles starting from ketones, amines, and diols was tried. This reaction proceeds in several steps. First, the amine condensates with the ketone, giving an imine. Simultaneously, the diol gets dehydrogenated twice by the catalyst, so that in the next reaction step an aldol-type condensation between the imine and the *in situ* formed dialdehyde can take place. After partial hydrogenation, intramolecular C–N bond formation can take place, giving rise to the final product while releasing water and hydrogen as only by-products.[260]

When the herein presented rhenium complex catalyzes this reaction, the corresponding pyrrole was obtained out of 1,2-diphenylethanone, 2-phenylethylamine and ethylene glycol in a good yield of 66%, using reaction conditions comparable to the ones used for the *N*-alkylation shown above. The application of hexylamine also gave the desired product in moderate 49% yield. Finally, when cyclohexanone was used as ketone, 1-phenethyl-4,5,6,7-tetrahydroindole was generated in reasonable 30% yield.

Summing up, a novel rhenium PNP pincer complex has been prepared. It was fully characterized by NMR and IR spectroscopy, elemental analysis as well as X-ray crystal structure analysis. The obtained complex was further on applied in a variety of different hydrogen autotransfer reaction. Here, the C–C bond formation by α-alkylation of ketones with alcohols was conducted. This reaction proceeds with very low base loadings and works better with the presented rhenium complexes than with known catalysts bearing ruthenium, iron, or manganese central atoms under tested conditions. Additionally, C–N bond formation has been accomplished to achieve *N*-alkylation of sulfonamides and, on top of that, a three-component pyrrole synthesis applying hydrogen autotransfer was realized giving access to pyrroles out of readily available starting materials.

6.3 Cyclometalated Ruthenium Pincer Complexes as Catalysts for the α-Alkylation of Ketones with Alcohols

As has been shown in the previous chapters, pincer complexes are highly adjustable concerning the applied pincer ligand and even the metal center. Nevertheless, the spectator ligands in this type of complexes are relatively predetermined to be carbon monoxide and/or hydrides (compare Scheme 3). This lack of variability made us think about other ligands replacing CO and H^- in ruthenium pincer systems enhancing their tuneability while conserving their general behavior and reactivity. With this target in mind, we tried to replace the additional ligands in Ru-MACHO-type complexes with cyclometalated phenyl heterocycles. Within these C,N-bidentate ligands, the carbon donor can be compared to the hydride in Ru-MACHO, also being a negatively charged, strong σ-donor, while the aromatic N-donor atom may replace the CO ligand as a charge-neutral, weak σ-donor allowing for interaction with a π-system.



Scheme 16: Synthesis of heterocycle-containing Ru pincer complexes.

To realize this general concept, N-heterocycle-containing Ru complexes were synthesized in the first step starting from air and moisture stable $[Ru(p\text{-cym})Cl_2]_2$ by literature procedures.[267] By stirring this precursor with the respective heterocycle in methanol at room temperature, various N-heterocycle containing ruthenium complexes were obtained as mostly orange solids by acetate-assisted cyclometalation.[167b] In the next step, these complexes were reacted with a pincer ligand in 2-butanol or isopropanol. By this, an assortment of different heterocycle-containing ruthenium pincer complexes was synthesized as colorful solids ranging from bright yellow to ruby red (see Scheme 16). These novel complexes were characterized by NMR and IR spectroscopy, mass spectrometry, and elemental analysis. Additionally, X-ray molecular structure analysis was conducted for representative complexes (for an example see Figure 3).

Next up, these complexes were tested in catalysis and, indeed, we found that they show notable activity in the α-alkylation of ketones with alcohols, whose concept has already been described within this thesis (see chapter 4.2). In initial tests, the novel complexes transform acetophenone and 2-metoxyethanol into 4-methoxy-1-phenylbutan-1-one in moderate yields between 22 and 48%. Remarkably, Ru-MACHO only gives 16% of this rather challenging product under similar conditions. This not only shows that the new catalysts can be superior to Ru-MACHO but also that the attached heterocycle has a strong influence on the catalyst's reactivity allowing for the initially wanted tuneability of these systems.

The best performing catalyst herein was the one bearing benzo[h]quinoline as the cyclometalated ligand (**[Ru]**-3), so that further optimizations were conducted with this complex (see Table 3). First, the reaction temperature was increased. This gave higher product amounts of 58 and 65% for 140 and 150 °C, respectively. Continuing with 150 °C, different bases were tested. Here, other inorganic ones gave lower yields than the beforehand used cesium carbonate while the use of organic NEt_3 gave no product at all. Applying higher amounts of Cs_2CO_3 also did not result in increased yields. Moving on, varying the catalyst loading was tested. Interestingly, the best results were obtained with 1 mol% of **[Ru]**-3, while lower or higher amounts resulted in decreased yields. Additionally, the reaction also takes place in different solvents albeit in lower yields ranging from 10% for water to 53% for THF. Finally, control experiment omitting the catalyst or the base, were performed. In both cases no product was observed. When **[Ru]**-8, the *N*-methylated derivative of the best working catalyst was used, 46% of the product were obtained. This relatively good yield indicates that the dominant reaction pathway here does not require the NH function of the ligand as would be the case for a classical metal-ligand cooperative mechanism. Summing up, optimal conditions for this reaction were set to the use of 1 mol% of **[Ru]**-3 and 10 mol% of cesium carbonate in *tert*-amyl alcohol at 150 °C.

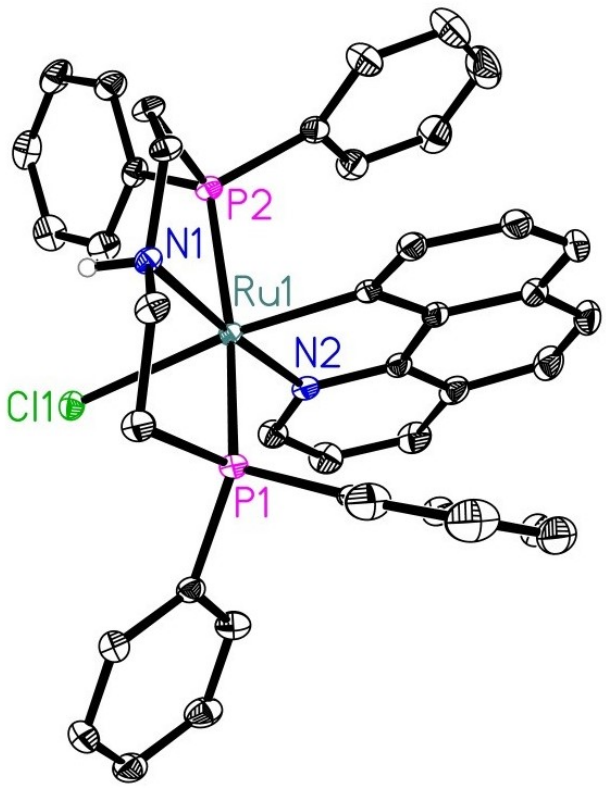
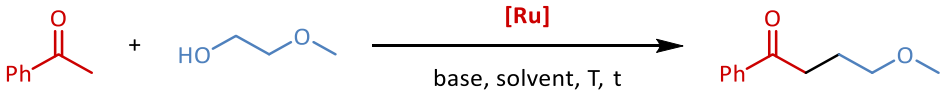


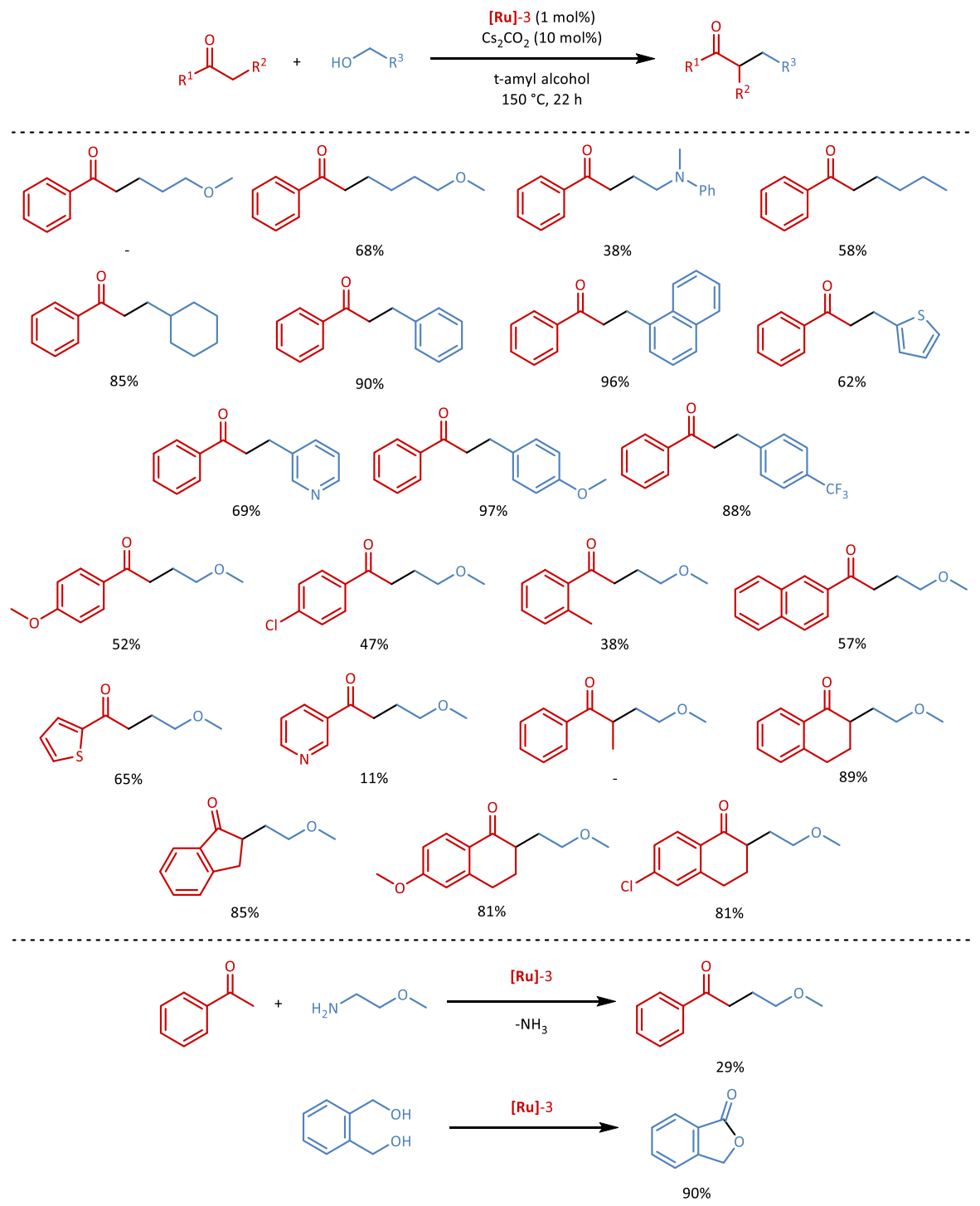
Figure 3: X-ray molecular structure of heterocycle-containing Ru pincer complex **[Ru]**-3. Displacement ellipsoids correspond to 30% probability. Hydrogen atoms (except the N-bound) are omitted for clarity.



Entry	[Ru]	Base	Base Loading	Solvent	T (°C)	Yield (%)
1	**[Ru]**-1	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	42
2	**[Ru]**-2	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	44
3	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	48
4	**[Ru]**-4	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	32
5	**[Ru]**-5	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	22
6	**[Ru]**-6	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	38
7	**[Ru]**-7	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	43
8	Ru-MACHO	Cs_2CO_3	10 mol%	*t*-amyl alcohol	130	16
9	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	140	58
10	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	65
11	**[Ru]**-3	KO*t*Bu	10 mol%	*t*-amyl alcohol	150	44
12	**[Ru]**-3	NaO*t*Bu	10 mol%	*t*-amyl alcohol	150	45
13	**[Ru]**-3	NaOH	10 mol%	*t*-amyl alcohol	150	38
14	**[Ru]**-3	K_2CO_3	10 mol%	*t*-amyl alcohol	150	36
15	**[Ru]**-3	NEt_3	10 mol%	*t*-amyl alcohol	150	-
16	**[Ru]**-3	Cs_2CO_3	20 mol%	*t*-amyl alcohol	150	66
17	**[Ru]**-3	Cs_2CO_3	30 mol%	*t*-amyl alcohol	150	64
18[a]	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	57
19[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	68
20[c]	**[Ru]**-3	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	60
21[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	heptane	150	41
22[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	toluene	150	38
23[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	THF	150	53
24[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	1,4-dioxane	150	37
25[b]	**[Ru]**-3	Cs_2CO_3	10 mol%	water	150	10
26[b]	**[Ru]**-3	-	-	*t*-amyl alcohol	150	-
27	-	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	-
28[b]	**[Ru]**-8	Cs_2CO_3	10 mol%	*t*-amyl alcohol	150	46

Table 3: Optimization of the ruthenium catalyzed α-alkylation of ketones with alcohols, [a] catalyst loading: 0.5 mol%, [b] catalyst loading: 1 mol%, [c] catalyst loading: 3 mol%.

Applying these optimized conditions, we started testing different substrates (see Scheme 17). First, 3-methoxypropan-1-ol was employed. Surprisingly, this gave no product at all, while with 4-methoxybutan-1-ol 68% of the corresponding product were received. When an alcohol substituted with a tertiary amine is used instead of the beforehand used methoxyalcohols, the desired product was gained in 38% yield. Moving on to unsubstituted alcohols, 1-butanol and



Scheme 17: Substrate scope of the Ru-catalyzed alkylation of ketones with alcohols and related reactions.

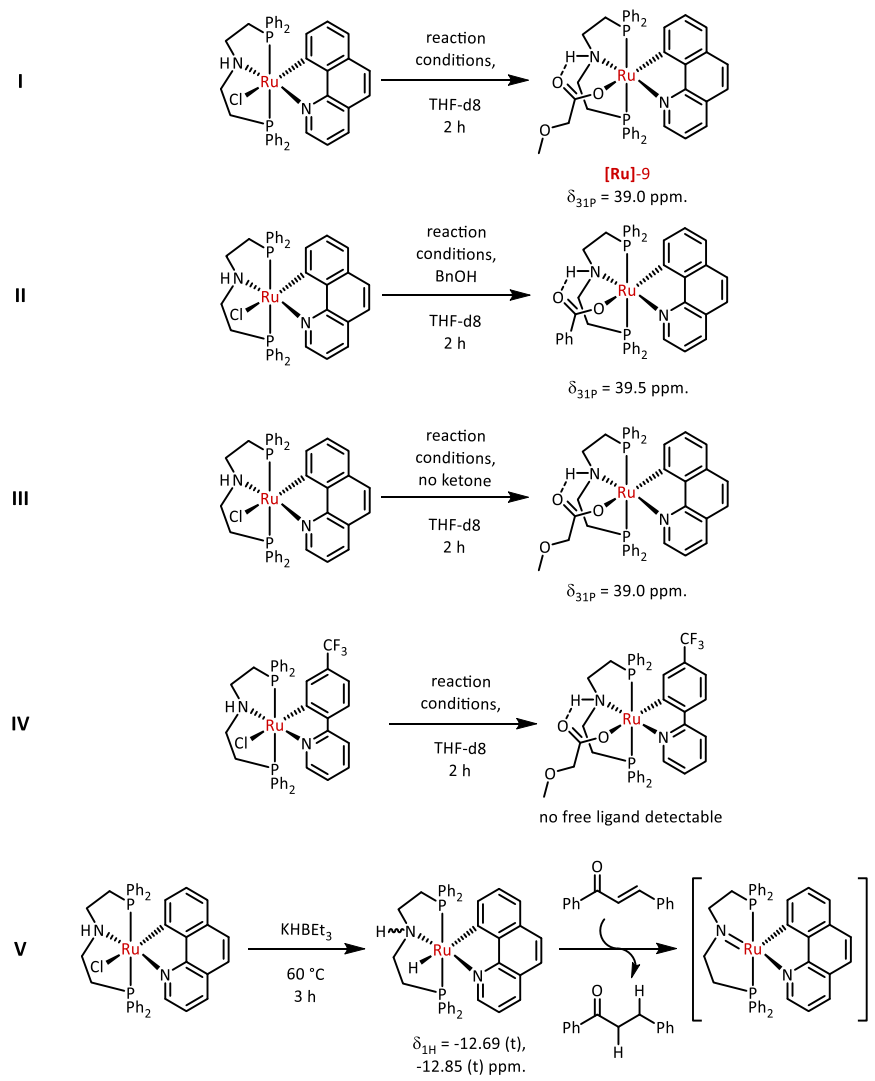
cyclohexanemethanol have been employed giving the corresponding products in 58 and 85% yield, respectively. With benzyl alcohol the alkylated ketone can be obtained in very good 90%. Employing 1-naphtalenemethanol, the yield can further be raised to excellent 96%. The application of 2-thiophenemethanol or 3-pyridylmethanol gave access to the desired products in 62 to 69% yield. Having a look at the influence of the electronic situation in benzyl alcohol derivatives, electron-rich 4-methoxybenzyl alcohol was converted into the corresponding

product in outstanding 97% yield, while electron-poor 4-trifluoromethylbenzyl alcohol gave the alkylated ketone in good 88% yield.

After testing varying alcohols in the reaction, we were interested in the alkylation of other ketones than acetophenone. For this, first, acetophenone-derivatives like electron-rich 4-methoxyacetophenone, electron-poor 4-chloroacetophenone, and sterically demanding 2-methylacetophenone have been employed. These gave rise to the corresponding products in 38 to 52% yield. With other acetylarenes like 2'-acetonaphthone or 2-acetylthiophene, the alkylation can be performed with mediocre yields of 57 and 65%, respectively. 3-Acetyl-pyridine, however, only gave the desired product in poor 11%. Interestingly, while the alkylation of propiophenone was not successful due to its less accessible α-position, α-tetralone was converted into the desired product in very good 89% yield. This preference for cyclic ketones was confirmed when 1-indanone was applied. Here, α-alkylation gave 85% of the corresponding product. On top of that, substituted tetralone derivatives like 6-methoxy- and 6-chlorotetralone were converted in good yields of 81% in both cases.

Remarkably, the catalyst is not limited to the α-alkylation of ketones with alcohols. Instead, when 2-methoxyethylamine was used instead of an alcohol, the similarly alkylated ketones can be generated by dissociation of ammonia. For the investigated example, this yielded in the formation of 29% of the product without any further optimization. Additionally, diols like 1,2-benzenedimethanol can undergo C–O bond formation yielding lactones. Here, the product was obtained in very good 90% yield.

With a comprehensive substrate scope in hand, we tried investigating the catalyst's species present during the reaction. For this, the reaction was performed in a pressure resistant NMR tube. Here, the conditions were adjusted by using THF-d8 as solvent, higher catalyst loadings and shorter reaction times. Doing this, one major signal was detected by ^{31}P NMR performed directly after the reaction (rct. **I** in Scheme 18). To identify this species, the reaction was repeated applying benzyl alcohol instead of 2-methoxyethanol (rct. **II**). This resulted in a slightly shifted ^{31}P signal, implying the involvement of the used alcohol in the examined species. Because of this, the ketone was omitted in the next reaction (rct. **III**). Here, the same species than in rct. **I** was observed, so that the ketone cannot play a role in its formation. Additionally, by filtration and vapor diffusion of pentane into the reaction solution, crystals suitable for X-ray crystallography have been obtained. Surprisingly, this revealed that the



Scheme 18: Experiments concerning the mechanism and the catalyst's species involved in the Ru-catalyzed alkylation of ketones with alcohols.

investigated complex is a ruthenium pincer complex bearing the phenylheterocycle ligand and methoxyacetate as additional donor. The methoxyacetate probably stems from dehydrogenation of the alcohol followed by the addition of water forming a *gem*-diol that subsequently gets dehydrogenated again yielding methoxyacetic acid. The required water for this is either formed as by-product of the aldol condensation or introduced with the alcohol which was applied without further drying. As known in literature,[34a, 268] carboxylates form very stable species with MACHO-type complexes due to hydrogen bonding between the acid's oxygen atom and the NH function of the pincer ligand. Because of this, the question arose if this species depicts a catalyst resting state or a dead end of the catalytic cycle. To learn about this, we attempted synthesizing **[Ru]**-8 independently. However, it was only possible to obtain a sample containing 78% of it and some **[Ru]**-3, which could not be further purified. When this mixture was applied as catalyst in the standard reaction, 68% of the product were obtained, confirming that **[Ru]**-8 can be activated by base and form the active catalyst in a similar way than **[Ru]**-3 does.

Furthermore, experiments were conducted concerning the stability of the cyclometalation. Here, the NMR-scale reaction was carried out with **[Ru]**-6. The trifluoromethyl group of this

catalyst allows for investigation by ^{19}F NMR. By this, it was found that no free ligand is detectable after two hours reaction time, confirming the stability of the newly applied ligands (rct. **IV**). On top of that, we investigated, how hydrogen is transferred by our catalyst. For this, ruthenium hydride species were synthesized by treatment of **[Ru]**-3 with potassium triethylborohydride (rct. **V**). This led to the formation of two different species generating a hydride signal in ^{1}H NMR. Interestingly, these species are stable for several days when kept under inert conditions although spontaneous reductive elimination of the hydride and the phenyl heterocycle formally would be possible. Nevertheless, when an α,β-unsaturated ketone is added to the reaction solution, one of the hydrides reacts very fast even at room temperature yielding in its transformation and the formation of the corresponding saturated ketone in analogy to the last step of the investigated hydrogen autotransfer reaction.

Overall, a novel method for modifying ruthenium pincer complexes has been established by the application of ligands allowing for cyclometalation. With this procedure, a variety of active catalysts for hydrogen autotransfer reactions was synthesized. They have subsequently been applied in the α-alkylation of ketones with alcohols, in which superior performances in comparison to Ru-MACHO were achieved. Mechanistic investigations revealed that the newly applied ligands remain bound to the complex during catalysis even when metal hydrides are formed. Ruthenium carboxylate complexes were found to be the dominant catalyst resting state that can re-enter the catalytic cycle when activated by base.

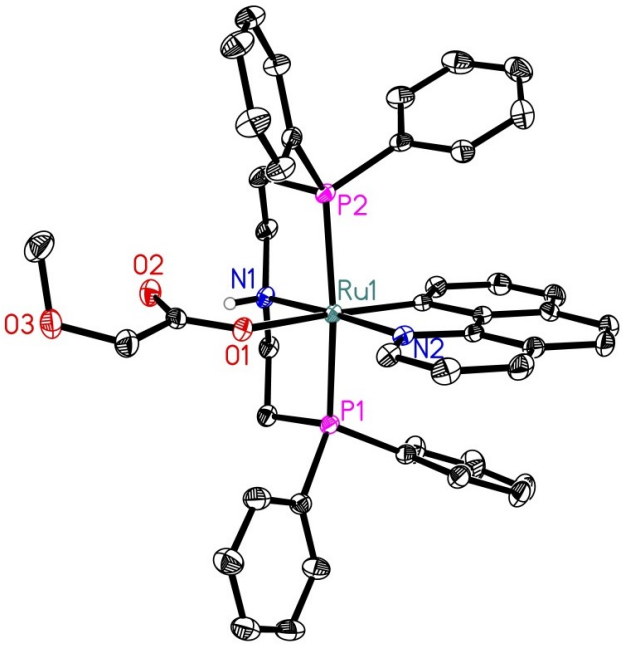


Figure 4: X-ray molecular structure of ruthenium carboxylate complex **[Ru]**-8. Displacement ellipsoids correspond to 30% probability. Only one molecule of the asymmetric unit is shown. Hydrogen atoms (except the N-bound) are omitted for clarity.

6.4 Summary

Summing up, within this thesis new catalysts for hydrogen autotransfer reactions have been developed. Initially, a manganese pincer complex was applied for the α-alkylation of ketones with alcohols. By this, cheap and environmentally benign manganese was first used for hydrogen autotransfer reactions leading to an atom-economical and sustainable reaction sequence. Applying this, a broad scope of α-alkylated ketones was produced including biologically relevant hormone derivatives and selective procedures for the *C*-alkylation of oxindoles. Furthermore, mechanistic investigations have been conducted suggesting an amidate-assisted reaction pathway including metal ligand cooperation.

Secondly, a novel rhenium pincer complex has been synthesized. This cationic complex was found to be an efficient catalyst for diverse hydrogen autotransfer reactions including the α-alkylation of ketones, the *N*-alkylation of sulfonamides and the synthesis of pyrroles out of ketones, diols, and amines. By expanding the reactivity of MACHO-type complexes in hydrogen autotransfer reactions to rhenium, the universality of this concept for metal ligand cooperative hydrogen transfer has been underlined and the usability of otherwise scarcely applied rhenium(I) catalysts was demonstrated.

Lastly, by introducing cyclometalated phenyl heterocycle ligands into ruthenium pincer complexes, a new class of catalyst has been established. By replacing of the formerly applied carbon monoxide and hydride ligands, further adjustments at the catalyst are possible, therefore enabling novel reactivity. These complexes were successfully applied in the α-alkylation of ketones with alcohols showing better yields than Ru-MACHO herein. By mechanistic investigations, the stability of the ligand system under reaction conditions was confirmed and a ruthenium carboxylate complex was found to be the predominant catalyst resting state.

Overall, novel catalysts were developed within this thesis that expand the scope of transition metal pincer complexes usable in hydrogen autotransfer reactions. By this, environmentally benign and highly adjustable synthesis procedures for fine chemicals are displayed within this work.

7 Publications

7.1 Manganese-Catalyzed Hydrogen-Autotransfer C–C Bond Formation: α-Alkylation of Ketones with Primary Alcohols

Miguel Peña-López, Patrick Piehl, Saravanakumar Elangovan, Helfried Neumann, and Matthias Beller*, *Angew. Chem. Int. Ed.* **2016**, 55, 14967-14971.

Contribution

For this publication, most of the experiments for the optimization and the substrate scope were conducted by me. In addition to that, I assisted in planning these experiments and in writing the manuscript. Overall, my share of this work sums up to approximately 35%.

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Manganese-Catalyzed Hydrogen-Autotransfer C–C Bond Formation: α-Alkylation of Ketones with Primary Alcohols

*Miguel Peña-López, Patrick Piehl, Saravanakumar Elangovan, Helfried Neumann, and Matthias Beller**

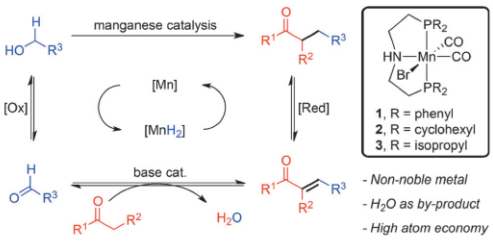
Abstract: *A novel catalytic hydrogen-autotransfer protocol for the atom-efficient α-alkylation of ketones with readily available alcohols is presented. The use of manganese complexes bearing non-innocent PNP pincer ligands enabled the functionalization of a broad range of valuable ketones, including 2-oxindole, estrone 3-methyl ether, and testosterone. Mechanistic investigations suggest the participation of an intramolecular amidate-assisted alcohol-dehydrogenation process.*

Transition-metal-catalyzed hydrogen autotransfer—also called borrowing hydrogen—has become an important synthetic strategy in organic chemistry as a result of its efficiency, low cost, and versatility. It allows the formation of C–N and C–C bonds through the reaction of non-activated alcohols with amines or C-nucleophiles, respectively,[1] as well as the synthesis of valuable heterocycles by domino processes.[2] The availability of starting materials from renewable resources, the operational simplicity, and the generation of H_2O as the only stoichiometric by-product make this process sustainable, atom-economical, and environmentally benign.

Applications of this methodology include the formation of new carbon–carbon bonds. More specifically, the α-functionalization of carbonyl compounds with simple alcohols as electrophiles provides several advantages as compared to classical procedures involving enolates. In the latter reactions, relevant amounts of waste are formed as a result of the use of stoichiometric bases and halides.[3] Hydrogen autotransfer, which is commonly performed with noble metals, such as ruthenium and iridium, constitutes a greener alternative.[4] Besides different reactivity, catalysis with nonprecious metals has economic and ecological benefits. In this regard, the report of a general iron-catalyzed α-alkylation of ketones with Knölker-type complexes is notable.[5]

Apart from iron, manganese is attracting increasing interest in synthesis, since it is cheap and toxicologically benign in comparison to most other transition metals. It is also an abundant element on Earth's crust and is capable of existing in several oxidation states. A wide variety of derivatives are readily available, and the number of manganese-catalyzed transformations has increased considerably during the last few years.[6] Despite all this progress, the use of manganese in dehydrogenative coupling processes is scarce,[7] and to the best of our knowledge no catalytic hydrogen-autotransfer C–C bond-forming processes in the presence of defined molecular manganese complexes have been described previously.[8]

On the basis of our recent study on the iron-catalyzed α-alkylation of ketones with alcohols,[5] we became interested in the catalytic application of manganese(I) pincer complexes for such transformations (Scheme 1). We therefore prepared precatalysts **1–3** by the treatment of the corresponding



Scheme 1. Manganese-catalyzed α-alkylation of ketones with alcohols.

tridentate ligands with $[Mn(CO)_5Br]$ (see the Supporting Information for a general procedure). In accordance with the outer-sphere mechanism established for related processes with ruthenium-based complexes,[9] the active catalytic species would be formed through base-mediated dehydrobromination of the precatalyst. Then, the in situ dehydrogenation of the alcohol would afford the corresponding carbonyl compound. Subsequent aldol condensation with the starting ketone should provide the α,β-unsaturated intermediate, which would finally be reduced by the hydrogen extracted in the first step. Water would be formed as the only by-product in a reaction which avoids the use of stoichiometric reagents for both redox processes.

As a model system, the manganese-catalyzed alkylation of acetophenone (**4a**) with benzyl alcohol (**5a**) was optimized (Table 1). To our delight, the use of 3 mol% of pincer complexes **1–3** for the reaction of **4a** (1 mmol) with **5a** (1.2 mmol) in the presence of Cs_2CO_3 (10 mol%) in 1,4-dioxane at 150°C allowed the alkylated ketone **6a** to be obtained selectively in good yields (77–90%; Table 1, entries 1–3). The diisopropylphosphine derivative **3** was the most effective precatalyst, whereas $[Mn(CO)_5Br]$, the precursor in the preparation of the pincer complexes, only

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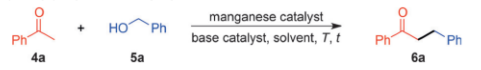
Table 1: Optimization of the reaction conditions for the synthesis of 1,3-diphenylpropan-1-one (**6a**).[a]



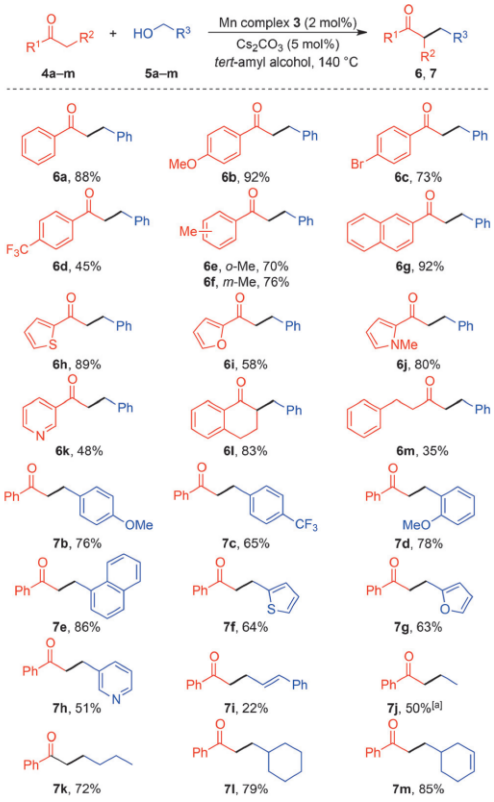
4a **5a** **6a**

Entry	Mn catalyst	Base	Solvent	T [°C]	Yield [%][b]
1	Mn complex **1**	Cs_2CO_3	1,4-dioxane	150	83
2	Mn complex **2**	Cs_2CO_3	1,4-dioxane	150	77
3	Mn complex **3**	Cs_2CO_3	1,4-dioxane	150	90
4	$[Mn(CO)_5Br]$	Cs_2CO_3	1,4-dioxane	150	6
5	Mn complex **3**	KOH	1,4-dioxane	150	69
6	Mn complex **3**	K_2CO_3	1,4-dioxane	150	52
7	Mn complex **3**	KO*t*Bu	1,4-dioxane	150	70
8[c]	Mn complex **3**	Cs_2CO_3	1,4-dioxane	150	87
9[d]	Mn complex **3**	Cs_2CO_3	1,4-dioxane	150	78
10[c]	Mn complex **3**	Cs_2CO_3	1,4-dioxane	140	84
11[c]	Mn complex **3**	Cs_2CO_3	1,4-dioxane	130	63
12[c]	Mn complex **3**	Cs_2CO_3	toluene	140	85
13[c]	Mn complex **3**	Cs_2CO_3	*tert*-amyl alcohol	140	86
14[c,e]	Mn complex **3**	Cs_2CO_3	*tert*-amyl alcohol	140	88
15[c,f]	Mn complex **3**	Cs_2CO_3	*tert*-amyl alcohol	140	64
16[c]	Mn complex **3**	–	*tert*-amyl alcohol	140	–
17[c,e]	–	Cs_2CO_3	*tert*-amyl alcohol	140	20

[a] Unless otherwise specified, reactions were carried out with **4a** (1 mmol), **5a** (1.2 mmol), the Mn catalyst (0.03 mmol), and the base (0.10 mmol) in 1 mL of the solvent at the indicated temperature for 22 h. [b] Yield of the isolated product. [c] Catalyst loading: 2 mol%. [d] Catalyst loading: 1 mol%. [e] Base: 5 mol%. [f] Base: 2 mol%.

afforded the desired product in 6% yield (Table 1, entry 4). The relevance of the basic medium for both catalyst activation and aldol condensation led us to analyze different bases. We obtained the best result when using cesium carbonate (Table 1, entries 5–7). For further optimization, we examined other critical parameters, such as the catalyst loading, solvent, base concentration, and temperature (Table 1, entries 8–15). Finally, we selected the reaction of **4a** (1 mmol), **5a** (1.2 mmol), **3** (0.02 mmol), and Cs_2CO_3 (0.05 mmol) in *tert*-amyl alcohol at 140 °C for 22 h as optimal conditions, which gave **6a** in 88% yield (Table 1, entry 14). An experiment without a base showed no conversion, and a reaction in the absence of a manganese complex led to the coupling product in 20% yield (Table 1, entries 16 and 17). As reported previously, such processes can be promoted in a basic medium under metal-free conditions.[10] The selectivity of the transformation is notable, since by-product formation is completely avoided.

Having developed a reliable procedure, we analyzed the reaction of benzyl alcohol (**5a**) with structurally diverse ketones **4a–l** (Scheme 2). An aryl ketone substituted with a methoxy group was converted into **6b** in excellent 92% yield, whereas the presence of electron-withdrawing substituents, such as Br and CF_3, led to a slight decrease in efficiency (products **6c**,**d**, 73 and 45%, respectively). This reaction could also be carried out with 2- and 3-acetyltoluene as well as 2-acetylnaphthalene as starting materials (products **6e–g**, 70–92%). Gratifyingly, heterocyclic ketones containing thiophene, furyl, pyrrole, and pyridine moieties were transformed into the desired products **6h–k** in moderate to good yields (48–89%). A cyclic substrate with a secondary α-carbon atom



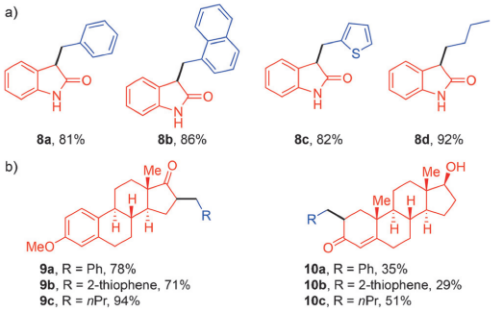
Scheme 2. Manganese-catalyzed reaction of ketones **4** with primary alcohols **5**. Yields are for the isolated product. [a] EtOH (1 mL) was used as the solvent. The yield was determined by GC with hexadecane as an internal standard.

was also functionalized. Thus, the reaction of benzyl alcohol with **4l** afforded the product **6l** in 83% yield. Interestingly, the aliphatic ketone **4m** also showed reactivity, although in this case the alkylated compound **6m** was obtained in lower 35% yield.

We also studied the reaction of acetophenone (**4a**) with differently substituted primary alcohols **5a–m** (Scheme 2). The electron-rich derivative **5b** afforded ketone **7b** in good yield (76%), and the reaction with 4-(trifluoromethyl)benzyl alcohol (**5c**) took place in a similar manner (65%). An experiment with more hindered 2-methoxybenzyl alcohol gave rise to **7d** in 78% yield, and 1-naphthylmethanol reacted with **4a** to give the desired product **7e** in high yield (86%). Heteroaromatic substrates were also efficiently applied to the alkylation of **4a**, although in moderate yields (products **7f–h**, 51–64% yield). Moreover, the reaction with cinnamyl alcohol (**5i**) gave the desired ketone **7i** but in low 22% yield. Next, we studied the reactivity of aliphatic alcohols. The alkylation of acetophenone (**4a**) with ethanol, used as the solvent, pro-

vided **7j** in 50% yield (as determined by GC), whereas 1-butanol afforded the corresponding ketone **7k** in good 72% yield. Cyclohexanemethanol (**5l**) was also used effectively as the electrophile (79%). Interestingly, the reaction with cyclohex-3-en-1-ylmethanol (**5m**) provided **7m** in 85% yield. In this case, unlike in some ruthenium-catalyzed hydrogen-autotransfer applications,[11] reduction of the C–C double bond present in the starting alcohol did not take place.

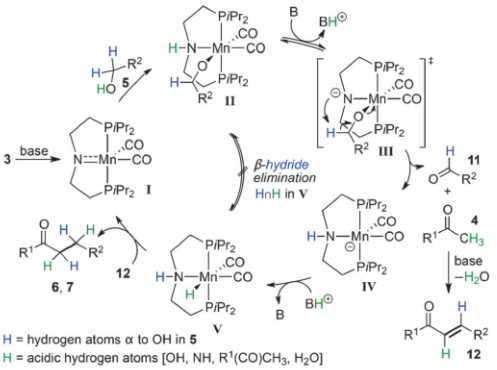
To increase the versatility of this catalytic protocol, we applied it to the functionalization of other interesting carbonyl compounds (Scheme 3). Initially, we studied the α-alkylation of 2-oxindole, a relevant heterocycle found in many biologically active molecules.[12] Such compounds often present substituents at the 3-position, which are normally introduced by the use of organic halides. Owing to the presence of a free amine in this cyclic amide, carbon–carbon bond formation by the method described herein must be performed selectively to avoid the amination reaction.[13] The manganese-catalyzed reaction of 2-oxindole with alcohols bearing aryl, heteroaryl, and alkyl groups under the previously optimized conditions provided the C–C coupled products **8a–d** in excellent yields (81–92%, Scheme 3a).



Scheme 3. Manganese-catalyzed α-alkylation of a) 2-oxindole and b) estrone 3-methyl ether and testosterone with alcohols. Yields are for the isolated product.

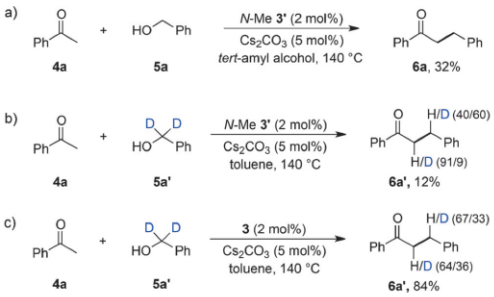
The modification of natural products allows for structure–activity relationship (SAR) studies with the aim of exploring their full drug potential.[14] Along this line, we applied our catalytic strategy to the derivatization of hormones. Indeed, estrone and testosterone derivatives could be readily functionalized by using simple alcohols as starting materials (Scheme 3b). In this way, estrone 3-methyl ether was effectively alkylated at the carbon atom adjacent to the carbonyl group with benzyl alcohol, 2-thiophenemethanol, and 1-butanol to afford products **9a–c** in 71–94% yield. Despite the presence of a free secondary alcohol in the D ring of testosterone, the α-position of the six-membered cyclic ketone was smoothly substituted with the same alcohols. In this case, lower product yields were observed (products **10a–c**, 29–51%) owing to the formation of two main side products.[15]

Finally, we propose a plausible mechanism depicted in Scheme 4 for this manganese-catalyzed transformation. Initially, the precatalyst **3** is activated by reaction with a base in a dehydrobromination reaction to give species **I**. In agreement with related complexes based on other transition metals,[16] coordination of the deprotonated alcohol **5** then provides an alkoxo-type complex **II**. At this point, a dehydrogenation reaction might take place by β-hydride elimination, despite the lack of free coordination sites at the metal center. However, we do not think that this option is very probable and instead propose that the basic medium promotes the formation of an amidate, which undergoes abstraction of the β-hydrogen atom, as shown in transition state **III**. Such an intramolecular ligand-assisted mechanism leads to aldehyde **11** and the intermediate **IV**, which is protonated to form the manganese hydride **V**. An aldol condensation between **11** and the enolate resulting from the starting ketone **4** affords the α,β-unsaturated compound **12** with the release of a molecule of H_2O. Finally, hydrogenation by species **V** yields the desired ketone **6**/**7** and regenerates the catalytic active species **I**. Previously, organometallic hydride complexes (e.g. Ru, Ir, as well as Fe) with pincer ligands have been shown to reduce polarized multiple bonds.[17] Thus, we assume that our reaction proceeds through Mn–H hydride transfer from complex **V** to the β-position in a Michael-type process followed by N–H proton transfer to the corresponding enolate.[4f]



Scheme 4. Plausible mechanism for the manganese-catalyzed α-alkylation of ketones with alcohols.

To confirm the participation of the N–H moiety of the pincer ligand in this transformation, we performed the alkylation of acetophenone (**4a**) with benzyl alcohol (**5a**) in the presence of the corresponding N-methylated manganese complex **3′** (Scheme 5a). When the optimal conditions were applied, ketone **6a** was isolated in only 32% yield (88% yield was observed with **3** as the catalyst). This observation indicates the possibility of different pathways with the prevalence of an NH-assisted outer-sphere mechanism. Deuterium-labeling experiments were also carried out with [α,α-D_2]benzyl alcohol (**5a′**). In this case, the aprotic solvent toluene was used instead of *tert*-amyl alcohol to avoid additional H/D exchange. An experiment with the *N*-Me complex **3′** provided the desired ketone **6a′** in low yield



Scheme 5. Control experiments. Yields are for the isolated product.

(12%) with 9% deuteration at the α-position and 60% at the β-position (Scheme 5b). The lower yield is caused by the absence of an alcoholic solvent (alkoxide formation in basic medium) or the different reactivity of **5a′**. Alternatively, the reaction of **4a** with **5a′** under the catalysis of the N–H complex **3** led to **6a′** in 84% yield with deuterium atoms equally distributed in the C2 and C3 positions (36 and 33% D, respectively, Scheme 5c). Deuterium incorporation at the α-position of **6a′** implies the formation of "D^+" from deuterated benzyl alcohol. As shown in Scheme 4, the amidate-assisted pathway offers the possibility of transforming the C–D bonds in the benzyloxy intermediate **II** to give an N-deuterated complex **IV**, which acts as a source of "D^-". On the other hand, with complex **3′** such transition state cannot be formed, thereby explaining the high incorporation of H^+ at the α-position in this experiment (91%). Notably, the observed H/D ratios in both reactions suggest the possibility of alternative pathways for this manganese-catalyzed transformation.

In conclusion, we have developed the first manganese-catalyzed alkylation of ketones and related compounds with primary alcohols. This straightforward transformation takes place with an air- and water-stable manganese(I) PNP pincer precatalyst. A low base concentration and broad applicability are notable features of this hydrogen-autotransfer methodology.

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[1] For reviews on hydrogen autotransfer, see: a) Q. Yang, Q. Wang, Z. Yu, *Chem. Soc. Rev.* **2015**, *44*, 2305–2329; b) Y. Obora, *ACS Catal.* **2014**, *4*, 3972–3981; c) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 249–260; d) S. Pan, T. Shibata, *ACS Catal.* **2013**, *3*, 704–712; e) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681–703; f) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* **2010**, *110*, 1611–1641; g) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555–1575; h) K.-I. Fujita, R. Yamaguchi, *Synlett* **2005**, 560–571.

[2] For selected references on hydrogen autotransfer and the dehydrogenative synthesis of heterocycles, see: a) M. Peña-López, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 7826–7830; *Angew. Chem.* **2016**, *128*, 7957–7961; b) M. Peña-López, H. Neumann, M. Beller, *Chem. Commun.* **2015**, *51*, 13082–13085; c) M. Peña-López, H. Neumann, M. Beller, *ChemCatChem* **2015**, *7*, 865–871; d) N. Deibl, K. Ament, R. Kempe, *J. Am. Chem. Soc.* **2015**, *137*, 12804–12807; e) M. Peña-López, H. Neumann, M. Beller, *Chem. Eur. J.* **2014**, *20*, 1818–1824; f) A. Monney, M. Peña-López, M. Beller, *Chimia* **2014**, *68*, 231–234; g) S. Michlik, R. Kempe, *Nat. Chem.* **2013**, *5*, 140–144; h) D. Srimani, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2013**, *52*, 4012–4015; *Angew. Chem.* **2013**, *125*, 4104–4107; i) S. Michlik, R. Kempe, *Angew. Chem. Int. Ed.* **2013**, *52*, 6326–6329; *Angew. Chem.* **2013**, *125*, 6450–6454; j) R. Yamaguchi, K.-I. Fujita, M. Zhu, *Heterocycles* **2010**, *81*, 1093–1140; k) K.-I. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett.* **2004**, *6*, 3525–3528.

[3] For reviews on the α-alkylation of ketones with classical electrophiles, see: a) F. A. Carey, R. J. Sundberg, *Advanced Organic Chemistry Part B: Reactions and Synthesis*, 5th ed., Springer, New York, **2007**, pp. 1–62; b) *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, **2000**; c) D. Caine in *Comprehensive Organic Chemistry, Vol. 3* (Eds.: B. M. Trost, I. Fleming, G. Pattenden), Pergamon, Oxford, **1991**, pp. 1–63.

[4] a) F. Huang, Z. Liu, Z. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 862–875; *Angew. Chem.* **2016**, *128*, 872–885; b) F. Li, J. Ma, N. Wang, *J. Org. Chem.* **2014**, *79*, 10447–10455; c) L. K. M. Chan, D. L. Poole, D. Shen, M. P. Healy, T. J. Donohoe, *Angew. Chem. Int. Ed.* **2014**, *53*, 761–765; *Angew. Chem.* **2014**, *126*, 780–784; d) D. Wang, K. Zhao, P. Ma, C. Xu, Y. Ding, *Tetrahedron Lett.* **2014**, *55*, 7233–7235; e) T. Kuwahara, T. Fukuyama, I. Ryu, *Org. Lett.* **2012**, *14*, 4703–4705; f) R. Martínez, D. J. Ramón, M. Yus, *Tetrahedron* **2006**, *62*, 8988–9001; g) K.-I. Fujita, C. Asai, T. Yamaguchi, F. Hanasaka, R. Yamaguchi, *Org. Lett.* **2005**, *7*, 4017–4019.

[5] S. Elangovan, J.-P. Sortais, M. Beller, C. Darcel, *Angew. Chem. Int. Ed.* **2015**, *54*, 14483–14486; *Angew. Chem.* **2015**, *127*, 14691–14694.

[6] For reviews on manganese-catalyzed reactions, see: a) D. A. Valyaev, G. Lavigne, N. Lugan, *Coord. Chem. Rev.* **2016**, *308*, 191–235; b) R. I. Khusnutdinov, A. R. Bayguzina, U. M. Dzhemilev, *Russ. J. Org. Chem.* **2012**, *48*, 309–348; c) C. Cahiez, C. Duplais, J. Buendia, *Chem. Rev.* **2009**, *109*, 1434–1476.

[7] For the synthesis of imines from alcohols, see: a) A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben-David, N.-A. Espinosa-Jalapa, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 4298–4301; for the MnO_2-catalyzed N-alkylation of amines with alcohols, see: b) S. R. Takkellapati, M. N. Nadagouda, *Curr. Org. Chem.* **2013**, *17*, 2332–2337; c) X. Yu, C. Liu, L. Jiang, Q. Xu, *Org. Lett.* **2011**, *13*, 6184–6187.

[8] For a C–C bond-forming reaction catalyzed by a manganese pincer complex, see: A. Nerush, M. Vogt, U. Gellrich, G. Leitus, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 6985–6997.

[9] a) M. Nielsen, E. Alberico, W. Baumann, H.-J. Drexler, H. Junge, S. Gladiali, M. Beller, *Nature* **2013**, *495*, 85–89; b) M. Nielsen, H. Junge, A. Kammer, M. Beller, *Angew. Chem. Int. Ed.* **2012**, *51*, 5711–5713; *Angew. Chem.* **2012**, *124*, 5809–5811; c) M. Nielsen, A. Kammer, D. Cozzula, H. Junge, S. Gladiali, M.

Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 9593 – 9597; *Angew. Chem.* **2011**, *123*, 9767 – 9771; d) J. I. Van der Vlugt, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2009**, *48*, 8832 – 8846; *Angew. Chem.* **2009**, *121*, 8990 – 9004.

[10] a) Q. Xu, J. Chen, H. Tian, X. Yuan, S. Li, C. Zhou, J. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 225 – 229; *Angew. Chem.* **2014**, *126*, 229 – 233; b) Y.-F. Liang, X.-F. Zhou, S.-Y. Tang, Y.-B. Huang, Y.-S. Feng, H.-J. Xu, *RSC Adv.* **2013**, *3*, 7739 – 7742; c) Q. Xu, J. Chen, Q. Liu, *Adv. Synth. Catal.* **2013**, *355*, 697 – 704; d) L. J. Allen, R. H. Crabtree, *Green Chem.* **2010**, *12*, 1362 – 1364.

[11] a) S. Muthaiah, S. H. Hong, *Adv. Synth. Catal.* **2012**, *354*, 3045 – 3053; b) S. Shahane, C. Fischmeister, C. Bruneau, *Catal. Sci. Technol.* **2012**, *2*, 1425 – 1428; c) T. J. Donohoe, T. J. O'Riordan, C. P. Rosa, *Angew. Chem. Int. Ed.* **2009**, *48*, 1014 – 1017; *Angew. Chem.* **2009**, *121*, 1032 – 1035.

[12] a) S. R. S. Rudrangi, V. K. Bontha, V. R. Manda, S. Bethi, *Asian J. Res. Chem.* **2011**, *4*, 335 – 338; b) J. J. Badillo, N. V. Hanhan, A. K. Franz, *Curr. Opin. Drug Discov. Devel.* **2010**, *13*, 758 – 776; c) B. Volk, J. Barkóczy, E. Hegedus, S. Udvari, I. Gacsályi, T. Mezei, K. Pallagi, H. Kompagne, G. Levay, A. Egyed, L. G. Harsing, Jr., M. Spedding, G. Simig, *J. Med. Chem.* **2008**, *51*, 2522 – 2532.

[13] For examples of the catalytic α-alkylation of 2-oxindole with alcohols, see: a) A. E. Putra, Y. Oe, T. Ohta, *Eur. J. Org. Chem.* **2015**, 7799 – 7805; b) C. Chaudhari, S. M. A. H. Siddiki, K. Kon, A. Tomita, Y. Tai, K.-I. Shimizu, *Catal. Sci. Technol.* **2014**, *4*, 1064 – 1069; c) T. Jensen, R. Madsen, *J. Org. Chem.* **2009**, *74*, 3990 – 3992; d) R. Grigg, S. Whitney, V. Sridharan, A. Keep, A. Derrick, *Tetrahedron* **2009**, *65*, 4375 – 4383.

[14] a) O. Robles, D. Romo, *Nat. Prod. Rep.* **2014**, *31*, 318 – 334; b) F. Hasdenteufel, S. Luyasu, N. Hougardy, M. Fisher, M. Boisbrun, P. M. Mertes, G. Kanny, *Curr. Clin. Pharmacol.* **2012**, *1*, 15 – 27; c) J. D. McKinney, A. Richard, C. Waller, M. C. Newman, F. Gerberick, *Toxicol. Sci.* **2000**, *56*, 8 – 17.

[15] 2-Substituted 4,5-dihydrotestosterones and 2-alkylidene testosterones were detected as major side products.

[16] a) J. R. Khusnutdinova, D. Milstein, *Angew. Chem. Int. Ed.* **2015**, *54*, 12236 – 12273; *Angew. Chem.* **2015**, *127*, 12406 – 12445; b) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, *114*, 12024 – 12087; c) S. Chakraborty, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2014**, *136*, 8564 – 8567; d) E. A. Bielinski, P. O. Lagaditis, Y. Zhang, B. Q. Mercado, C. Würtele, W. H. Bernskoetter, N. Hazari, S. Schneider, *J. Am. Chem. Soc.* **2014**, *136*, 10234 – 10237; e) C. Gunanathan, D. Milstein, *Acc. Chem. Res.* **2011**, *44*, 588 – 602.

[17] a) R. Xu, S. Chakraborty, S. M. Bellows, H. Yuan, T. R. Cundari, W. D. Jones, *ACS Catal.* **2016**, *6*, 2127 – 2135; b) C. Bornschein, S. Werkmeister, B. Wendt, H. Jiao, E. Alberico, W. Baumann, H. Junge, K. Junge, M. Beller, *Nat. Commun.* **2014**, *5*, 4111; c) D. Spasyuk, S. Smith, D. G. Gusev, *Angew. Chem. Int. Ed.* **2012**, *51*, 2772 – 2775; *Angew. Chem.* **2012**, *124*, 2826 – 2829; d) E. Balaraman, B. Gnanaprakasam, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2010**, *132*, 16756 – 16758.

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7.2 Hydrogen Autotransfer and Related Dehydrogenative Coupling Reactions using a Rhenium(I) Pincer Catalyst

Patrick Piehl, Miguel Peña-López, Anna Frey, Helfried Neumann, and Matthias Beller*, *Chem. Commun.* **2017**, 53, 3265-3268.

Contribution

For this publication, the synthesis and characterization of the catalyst was conducted by me. In addition to that, the experiments for optimization and substrates scope were planned and often performed by me. On top of that, the first draft for the manuscript was written by me and I took part in the revision thereof. Overall, my share of this work sums up to approximately 70%.

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Hydrogen autotransfer and related dehydrogenative coupling reactions using a rhenium(I) pincer catalyst†

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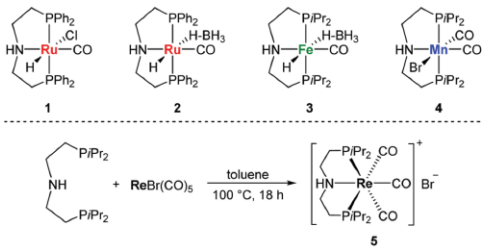
A novel rhenium complex bearing a non-innocent PNP pincer ligand was prepared. This novel catalyst is active in hydrogen autotransfer reactions to form new C–C and C–N bonds. More specifically, valuable alkylations of ketones and sulfonamides with primary alcohols are herein presented. In addition, the first examples of rhenium-catalysed synthesis of pyrroles are described by dehydrogenative coupling of diols, amines and ketones.

Compared to other transition metals, molecularly defined rhenium complexes[1] have remained largely unexplored in catalysis.[2] Selected examples for reductive processes and C–C bond formation include the dehydration of alcohols,[3] hydrosilylation reactions,[4] as well as coupling of propargylic alcohols.[5] Most recently, some rhenium-pincer complexes have been also described for the stoichiometric activation of nitrogen.[6] In addition, several rhenium catalysts were applied for the dehydrogenative coupling of carbonyl compounds with alcohols,[7] as well as the alkylation of primary amines with the same substrates, in the latter case to give the corresponding imines[8] or secondary amines.[9]

Transition metal-catalyzed hydrogen autotransfer (also called borrowing hydrogen) of alcohols are atom economical, operational simple and eco-friendly methodologies where water is formed as the only stoichiometric residue.[10] Mechanistically, readily available alcohols are initially dehydrogenated to afford more reactive carbonyl compounds. Further condensation with an appropriate nucleophile provides the corresponding unsaturated intermediates, which are finally reduced with the hydrogen extracted in the first step, regenerating the active species. This strategy has been widely used to form new C–C and C–N bonds. More specifically, the alkylation of amines or ketones with non-activated, cheap and abundant alcohols continues to be challenging. Furthermore, a plethora of relevant heterocyclic compounds can be synthesised using such methodologies or related dehydrogenative coupling processes.[11] So far, such protocols are mainly performed using ruthenium and iridium complexes, although recently significant attention has been paid to use alternative metals. For example, a variety of complexes bearing PNP pincer ligands have been developed using several metals such as ruthenium,[12] iron,[13] cobalt[14] and lately manganese (Scheme 1).[15]

All these complexes showed reactivity in hydrogenation and dehydrogenation reactions, as well as hydrogen autotransfer processes. Notably, the reactivity for individual catalytic steps can be tuned by varying the metal centre and not the ligand scaffold. Hence, we are interested in the preparation of novel related complexes. Following our previous experience on this topic, we herein describe the synthesis of a rhenium-based pincer complex and its application in hydrogen autotransfer reactions, which are barely known in the presence of rhenium. Initially, the reaction of $Re(CO)_5Br$ with the PNP pincer ligand in toluene at 100 °C overnight, provided the cationic complex **5** quantitatively (Scheme 1). Crystallisation from chloroform/heptane provided the X-ray molecular structure shown in Fig. 1. To our delight, **5** showed a good reactivity in the α-alkylation of ketones with alcohols,[15d,16] a greener alternative for the carbon–carbon formation compared to classical enolate procedures.

More specifically, we optimised the reaction of acetophenone (**6a**) with benzyl alcohol (**7a**) to form 3-phenylpropiophenone (**8a**)



Scheme 1 Ruthenium, iron and manganese PNP pincer complexes. Synthesis of cationic rhenium(I) pincer complex **5**.

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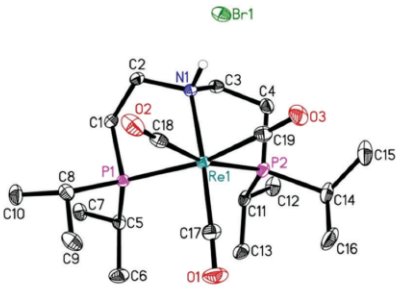
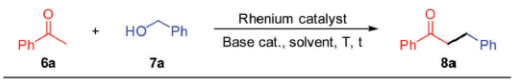


Fig. 1 X-ray molecular structure of rhenium complex **5** (ellipsoids correspond to 30% probability. Hydrogen atoms except the NH-proton and solvent molecules are omitted for clarity. There are two molecules in the asymmetric unit of which one is shown).

(Table 1). By testing different bases (Table 1, entries 1–4), we found Cs_2CO_3 to be the most effective one for this transformation. Lowering the amount of catalyst led to a slight drop in yield while a higher amount does not improve the reaction (Table 1, entries 6 and 7).

Different solvents do not have a strong influence on the reaction (Table 1, entries 8 and 9). To our delight, it was possible to reduce the base loading to only 2 mol% without a significant decrease of the yield (Table 1, entry 10). This is an important improvement compared to most other catalysts known for such transformations. Advantageously, the reaction takes places with only one equivalent of base with respect to the

Table 1 Rhenium-catalysed α-alkylation of acetophenone (**6a**) with benzyl alcohol (**7a**): variation of reaction conditions[a]



6a **7a** **8a**

Entry	Re catalyst	Base	Solvent	T (°C)	Yield[b] (%)
1	Re complex **5**	KOH	*t*-Amyl alcohol	140	74
2	Re complex **5**	KO*t*Bu	*t*-Amyl alcohol	140	81
3	Re complex **5**	K_2CO_3	*t*-Amyl alcohol	140	65
4	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	140	84
5	$Re(CO)_5Br$	Cs_2CO_3	*t*-Amyl alcohol	140	—
6[c]	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	140	81
7[d]	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	140	88
8	Re complex **5**	Cs_2CO_3	1,4-Dioxane	140	86
9	Re complex **5**	Cs_2CO_3	Toluene	140	85
10[e]	**Re complex 5**	**Cs_2CO_3**	***t*-Amyl alcohol**	**140**	**86**
11[f]	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	140	86
12[e]	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	130	72
13[e]	Re complex **5**	Cs_2CO_3	*t*-Amyl alcohol	150	75
14	Re complex **5**	—	*t*-Amyl alcohol	140	—
15[e]	—	Cs_2CO_3	*t*-Amyl alcohol	140	4
16[e]	Ru complex **2**	Cs_2CO_3	*t*-Amyl alcohol	140	41
17[e]	Fe complex **3**	Cs_2CO_3	*t*-Amyl alcohol	140	13
18[e]	Mn complex **4**	Cs_2CO_3	*t*-Amyl alcohol	140	64

[a] Unless otherwise specified, all reactions were carried out with **6a** (1 mmol), **7a** (1.2 mmol), Re catalyst (0.02 mmol), base (0.05 mmol) in a solvent (1 mL) at indicated temperature for 22 h. [b] Isolated yields. [c] Catalyst loading: 1 mol%. [d] Catalyst loading: 5 mol%. [e] Base: 2 mol%. [f] Base: 10 mol%.

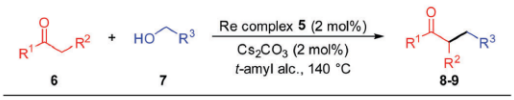
catalyst although the activation of the catalyst as well as the product formation require basic conditions. Finally, we chose the reaction of **6a** (1 mmol) with **7a** (1.2 mmol), rhenium complex **5** (2 mol%) and Cs_2CO_3 (2 mol%) as base in *tert*-amyl alcohol at 140 °C as model system, giving the product **8a** in a good 86% yield.

With optimised conditions in hand, we compared the activity of our novel rhenium complex with previously described ruthenium-, iron- and manganese-pincer complexes **2–4** (Scheme 1).[11g,h,15d,17] Reaction of acetophenone (**6a**) with benzyl alcohol (**7a**) catalysed by **2** and **3** (2 mol%) under the same conditions provided **8a** in lower yield (41 and 13%, respectively; Table 1, entries 16 and 17). Similarly, the manganese complex **4**, recently reported to catalyse this alkylation of ketones,[15d] gave the desired product in 64% yield (Table 1, entry 18). Comparing all the product yields in the presence of the different pincer complexes showed clearly the superiority of the rhenium system (86% yield). These results suggest that this catalyst is more reactive than analogous complexes bearing other metals at low concentration of base.

Next, the versatility and generality of the method was studied (Table 2). Initially, differently 4-substituted acetophenones were tested in the rhenium-catalysed reaction with benzyl alcohol. The synthesis of methoxy-, bromo- and trifluoromethyl-substituted 3-phenylpropiophenones (**8b–d**) was possible in moderate to very good yields (53–91%, Table 2, entries 2–4). Moreover, heteroaryl derivatives such as 2-acetylthiophene (**6e**) and 2-acetyl-*N*-methylpyrrol (**6f**) were applied affording the desired products in 88 and 40% yield, respectively (**8e–f**, Table 2, entries 5 and 6). Tetralone was also α-alkylated in secondary carbon to give compound **8g** in a moderate 38% yield (Table 2, entry 7). On the other hand, structurally diverse alcohols **7** were assayed in the reaction with acetophenone (**6a**). Electron-rich 4-methoxybenzyl and electron-deficient 4-bromobenzyl alcohol were effectively used affording products **9b** and **9c** in good yields (80 and 72%, respectively, Table 2, entries 8 and 9). In addition, 1-naphthalenemethanol and 2-thiophenemethanol were applied as alkylating agents giving the corresponding coupled products in 83 and 68% yields (Table 2, entries 10 and 11). Finally, we found that aliphatic alcohols such as *n*-butanol can also be used, obtaining the desired ketone in modest yield (Table 2, entry 12).

After studying the rhenium-catalysed *C*-alkylation of ketones, we focused our interest on *N*-alkylation processes using hydrogen autotransfer methodology, which had been described earlier.[18] In this reaction, a new carbon–nitrogen bond is formed using simple and easily available alcohols as electrophiles. In this line, we found that sulfonamides can be efficiently *N*-functionalised using the rhenium complex **5** as catalyst (Scheme 2).[18d,19] Applying the aforementioned developed conditions although increasing the reaction temperature to 150 °C, *p*-toluenesulfonamide (**10a**) was *N*-alkylated with benzyl alcohol affording *N*-benzyl-*p*-toluenesulfonamide (**11a**) in 84% yield. Likewise, *N*-benzyl-*tert*-butylsulfonamide (**11b**) was obtained in 79% yield, whereas 2-thiophenesulfonamide (**10c**) was also functionalised, albeit in lower yield. In addition, higher base concentration was required in the latter case to get a modest

Table 2 Rhenium-catalysed reaction of ketones (**6**) with primary alcohols (**7**)[a]

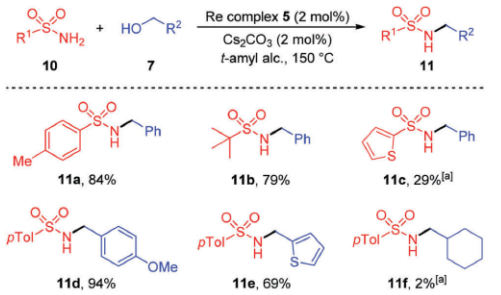


6 7 8-9

Entry	Ketone	Alcohol	Product	Yield[b] (%)
1	6a	7a	8a	86
2	6b	7a	8b	91
3	6c	7a	8c	60
4	6d	7a	8d	53
5	6e	7a	8e	88
6	6f	7a	8f	40
7	6g	7a	8g	38
8	6a	7b	9b	80
9	6a	7c	9c	72
10	6a	7d	9d	83
11	6a	7e	9e	68
12	6a	7f	9f	37

[a] Unless otherwise specified, all reactions were carried out with **6** (1 mmol), **7** (1.2 mmol), Re catalyst **5** (0.02 mmol), Cs_2CO_3 (0.02 mmol) in *t*-amyl alcohol (1 mL) at 140 °C for 22 h. [b] Isolated yields.

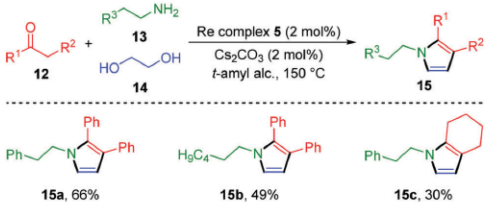
29% yield. Gratifyingly, different alcohols can be used as alkylating agents in this transformation. For example, 4-methoxybenzyl alcohol and 2-thiophenemethanol were applied for the alkylation of *p*-toluenesulfonamide (**10a**) giving the desired products **11d** and **11e** in 94 and 69% yield, respectively (Scheme 2). Finally, the reaction of **10a** with cyclohexanemethanol gave only traces of product **11f**, even in presence of higher amounts of caesium carbonate.



Scheme 2 Rhenium-catalysed reaction of sulfonamides (**10**) with primary alcohols (**7**). Unless otherwise specified, all reactions were carried out with **10** (1 mmol), **7** (1.2 mmol), Re catalyst **5** (0.02 mmol), Cs_2CO_3 (0.02 mmol) in *t*-amyl alcohol (1 mL) at 150 °C for 22 h, isolated yields. [a] 5 mol% Cs_2CO_3.

Besides the formation of new C–C and C–N bonds, one of the most relevant applications of the hydrogen autotransfer methodology is the synthesis of heterocycles. In this case, related dehydrogenative coupling processes have been also described to obtain unsaturated heterocyclic compounds. Here, in addition to water, hydrogen gas is obtained as by-product. As an example, the multistep ruthenium-catalysed synthesis of pyrroles from ketones, amines and diols was recently developed by our research group.[11d,c] With the aim of extending the scope of the novel cationic rhenium catalyst, we also assayed such a three-component reaction (Scheme 3). Indeed, the reaction of 1,2-diphenylethanone, ethylene glycol and phenethylamine provided *N*-phenethyl-2,3-diphenylpyrrole (**15a**) in 66% yield. It is worth mentioning that two C–C and one C–N bonds are sequentially formed in this domino reaction. Using hexylamine allowed to obtain the corresponding *N*-hexyl-2,3-diphenylpyrrole (**15b**, 49% yield), while the reaction with cyclohexanone as ketone gave rise to 1-phenethyl-4,5,6,7-tetrahydroindole (**15c**) in modest yield.

In conclusion, we have synthesised a new cationic rhenium(I) pincer complex and demonstrated for the first time that such complexes can be conveniently used in several hydrogen autotransfer reactions. More specifically, the α-alkylation of ketones, the *N*-functionalisation of sulfonamides with non-activated



Scheme 3 Rhenium-catalysed reaction of ketones **12** with amines **13** and alcohol **14**. Unless otherwise specified, all reactions were carried out with **6** (0.5 mmol), **13** (1.0 mmol), **14** (5.0 mmol), Re catalyst **5** (0.01 mmol), Cs_2CO_3 (0.01 mmol) in *t*-amyl alcohol (1 mL) at 150 °C for 22 h, isolated yields.

alcohols and the synthesis of pyrroles by dehydrogenative coupling of ketones, diols and amines were developed. Notably, these transformations take place in good to moderate yields in presence of very low concentrations of base. Under such conditions, the new complex has proven to be more efficient than other comparable PNP pincer complexes.

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Notes and references

1 The complex was independently reported very recently in the following publication: D. Wei, T. Roisnel, C. Darcel, E. Clot and J.-B. Sortais, *ChemCatChem*, 2017, **9**, 80–83.

2 (*a*) G. Mao, B. Jia and C. Wang, *Youji Huaxue*, 2015, **35**, 284–293; (*b*) R. Hua and J.-L. Jiang, *Curr. Org. Synth.*, 2007, **4**, 477–498; (*c*) M. C. Lipke, A. L. Liberman-Martin and T. D. Tilley, *Angew. Chem., Int. Ed.*, 2017, **129**, 2260–2294.

3 (*a*) T. J. Korstanje, E. F. de Waard, J. T. B. H. Jastrzebski and R. J. M. Klein Gebbink, *ACS Catal.*, 2012, **2**, 2173–2181; (*b*) T. J. Korstanje, J. T. B. H. Jastrzebski and R. J. M. Klein Gebbink, *ChemSusChem*, 2010, **3**, 695–697.

4 J. J. Kennedy-Smith, K. A. Nolin, H. P. Gunterman and F. D. Toste, *J. Am. Chem. Soc.*, 2003, **125**, 4056–4057.

5 (*a*) J. J. Kennedy-Smith, L. A. Young and F. D. Toste, *Org. Lett.*, 2004, **6**, 1325–1327; (*b*) M. R. Luzung and F. D. Toste, *J. Am. Chem. Soc.*, 2003, **125**, 15760–15761; (*c*) Y. Kuninobu, H. Ueda and K. Takai, *Chem. Lett.*, 2008, **37**, 878–879; (*d*) Y. Kuninobu, E. Ishii and K. Takai, *Angew. Chem., Int. Ed.*, 2007, **46**, 3296–3299.

6 (*a*) I. Klopsch, M. Kinauer, M. Finger, C. Würtele and S. Schneider, *Angew. Chem., Int. Ed.*, 2016, **55**, 4786–4789; (*b*) I. Klopsch, M. Finger, C. Würtele, B. Milde, D. B. Werz and S. Schneider, *J. Am. Chem. Soc.*, 2014, **136**, 6881–6883; (*c*) M. J. Bezdek and P. J. Chirik, *Angew. Chem., Int. Ed.*, 2016, **55**, 7892–7896.

7 (*a*) P. P. M. Schleker, R. Honeker, J. Klankermayer and W. Leitner, *ChemCatChem*, 2013, **5**, 1762–1764; (*b*) H. Jin, J. Xie, C. Pan, Z. Zhu, Y. Cheng and C. Zhu, *ACS Catal.*, 2013, **3**, 2195–2198.

8 M. Vogt, A. Nerush, M. A. Iron, G. Leitus, Y. Diskin-Posner, L. J. W. Shimon, Y. Ben-David and D. Milstein, *J. Am. Chem. Soc.*, 2013, **135**, 17004–17018.

9 A. Abdukader, H. Jin, Y. Cheng and C. Zhu, *Tetrahedron Lett.*, 2014, **55**, 4172–4174.

10 (*a*) A. J. A. Watson and J. M. J. Williams, *Science*, 2010, **329**, 635–636; (*b*) S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann and M. Beller, *ChemCatChem*, 2011, **3**, 1853–1864; (*c*) C. Gunanathan and D. Milstein, *Science*, 2013, **341**, 1229712; (*d*) Y. Obora, *ACS Catal.*, 2014, **4**, 3972–3981; (*e*) Q. Yang, Q. Wang and Z. Yu, *Chem. Soc. Rev.*, 2015, **44**, 2305–2329; (*f*) F. Huang, Z. Liu and Z. Yu, *Angew. Chem., Int. Ed.*, 2016, **55**, 862–875; (*g*) J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland and R. Newton, *Org. Process Res. Dev.*, 2015, **19**, 1400–1410.

11 (*a*) S. Michlik and R. Kempe, *Nat. Chem.*, 2013, **5**, 140–144; (*b*) D. Srimani, Y. Ben-David and D. Milstein, *Angew. Chem., Int. Ed.*, 2013, **52**, 4012–4015; (*c*) M. Zhang, X. Fang, H. Neumann and M. Beller, *J. Am. Chem. Soc.*, 2013, **135**, 11384–11388; (*d*) M. Zhang, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.*, 2013, **52**, 597–601; (*e*) A. Monney, M. Peña-López and M. Beller, *Chimia*, 2014, **68**, 231–234; (*f*) M. Peña-López, H. Neumann and M. Beller, *Chem. – Eur. J.*, 2014, **20**, 1818–1824; (*g*) M. Peña-López, H. Neumann and M. Beller, *ChemCatChem*, 2015, **7**, 865–871; (*h*) M. Peña-López, H. Neumann and M. Beller, *Chem. Commun.*, 2015, **51**, 13082–13085; (*i*) M. Peña-López, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.*, 2016, **55**, 7826–7830.

12 (*a*) W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo and T. Saito, *Org. Process Res. Dev.*, 2012, **16**, 166–171; (*b*) J. Neumann, C. Bornschein, H. Jiao, K. Junge and M. Beller, *Eur. J. Org. Chem.*, 2015, 5944–5948; (*c*) A. Monney, E. Barsch, P. Sponholz, H. Junge, R. Ludwig and M. Beller, *Chem. Commun.*, 2014, **50**, 707–709; (*d*) M. Nielsen, H. Junge, A. Kammer and M. Beller, *Angew. Chem., Int. Ed.*, 2012, **51**, 5711–5713.

13 E. Alberico, P. Sponholz, C. Cordes, M. Nielsen, H.-J. Drexler, W. Baumann, H. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2013, **52**, 14162–14166.

14 (*a*) G. Zhang, K. V. Vasudevan, B. L. Scott and S. K. Hanson, *J. Am. Chem. Soc.*, 2013, **135**, 8668–8681; (*b*) G. Zhang, B. L. Scott and S. K. Hanson, *Angew. Chem., Int. Ed.*, 2012, **51**, 12102–12106.

15 (*a*) S. Elangovan, M. Garbe, H. Jiao, A. Spannenberg, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2016, **55**, 15364–15368; (*b*) S. Elangovan, C. Topf, S. Fischer, H. Jiao, A. Spannenberg, W. Baumann, R. Ludwig, K. Junge and M. Beller, *J. Am. Chem. Soc.*, 2016, **138**, 8809–8814; (*c*) A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben-David, N.-A. Espinosa-Jalapa and D. Milstein, *J. Am. Chem. Soc.*, 2016, **138**, 4298–4301; (*d*) M. Peña-López, P. Piehl, S. Elangovan, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.*, 2016, **55**, 14967–14971.

16 (*a*) R. Martínez, D. J. Ramón and M. Yus, *Tetrahedron*, 2006, **62**, 8988–9001; (*b*) S. Elangovan, J.-B. Sortais, M. Beller and C. Darcel, *Angew. Chem., Int. Ed.*, 2015, **54**, 14483–14486.

17 N. J. Oldenhuis, V. M. Dong and Z. Guan, *J. Am. Chem. Soc.*, 2014, **136**, 12548–12551.

18 (*a*) S. Bähn, S. Imm, K. Mevius, L. Neubert, A. Tillack, J. M. J. Williams and M. Beller, *Chem. – Eur. J.*, 2010, **16**, 3590–3593; (*b*) K.-I. Fujita, A. Komatsubara and R. Yamaguchi, *Tetrahedron*, 2009, **65**, 3624–3628; (*c*) C. Gunanathan and D. Milstein, *Angew. Chem., Int. Ed.*, 2008, **47**, 8661–8664; (*d*) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson and J. M. J. Williams, *J. Am. Chem. Soc.*, 2009, **131**, 1766–1774; (*e*) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn and M. Beller, *Eur. J. Org. Chem.*, 2008, 4745–4750; (*f*) T. Yan, B. L. Feringa and K. Barta, *Nat. Commun.*, 2014, **5**, 5602.

19 (*a*) A. Martínez-Asencio, D. J. Ramón and M. Yus, *Tetrahedron Lett.*, 2010, **51**, 325–327; (*b*) A. Martínez-Asencio, D. J. Ramón and M. Yus, *Tetrahedron*, 2011, **67**, 3140–3149; (*c*) A. J. A. Watson, A. C. Maxwell and J. M. J. Williams, *J. Org. Chem.*, 2011, **76**, 2328–2331.

7.3 Cyclometalated Ruthenium Pincer Complexes as Catalysts for the α-Alkylation of Ketones with Alcohols

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Contribution

For this publication, the presented catalysts were developed, synthesized, and characterized by me. Moreover, optimization and substrate scope of the presented reaction was planned and partly conducted by me. Furthermore, experiments concerning the mechanism and the catalytically active species were mainly planned and conducted by me. Also, the publication's first draft was written by me and I took part in the revision thereof. Overall, my share of this work sums up to approximately 65%.

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RESEARCH ARTICLE

Cyclometalated Ruthenium Pincer Complexes as Catalysts for the α-Alkylation of Ketones with Alcohols

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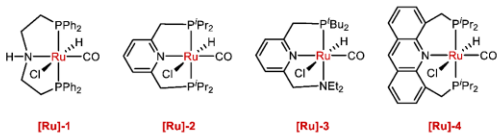
Supporting information for this article is given via a link at the end of the document.

Abstract: Ruthenium PNP pincer complexes bearing supplementary cyclometalated C,N-bound ligands have been prepared and fully characterized for the first time. By replacing CO and H^- as ancillary ligands in such complexes, additional electronic and steric modifications of this actual class of catalysts are possible. The advantages of the new catalysts are demonstrated in the general α-alkylation of ketones with alcohols following a hydrogen autotransfer protocol. Herein, various aliphatic and benzylic alcohols were applied as green alkylating agents for ketones bearing aromatic, heteroaromatic or aliphatic substituents as well as cyclic ones. Mechanistic investigations revealed that during catalysis Ru carboxylate complexes are predominantly formed while neither the PNP nor the CN ligand are released from the catalyst in significant amounts.

Introduction

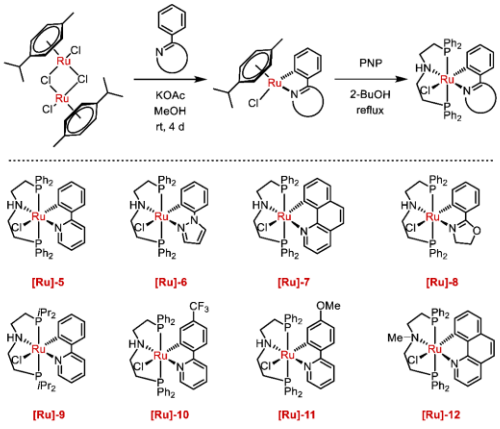
In the past two decades, metal pincer complexes have proven to be exceptionally powerful catalysts for hydrogenation and dehydrogenation reactions.[1] Especially ruthenium complexes such as Ru-MACHO (**[Ru]-1** in Scheme 1) were introduced for the catalytic hydrogenation of esters,[2] organic carbonates,[3] nitriles,[4] and others as well as for dehydrogenation reactions of compounds like methanol[5] or ethanol.[6] In addition to that, specifically **[Ru]-1** was applied in hydrogen autotransfer reactions producing γ-butyrolactones[7] and chiral N-alkyl sulfinamides.[8] Furthermore, pyridine-based Ru pincer complexes **[Ru]-2** and **-3** were developed by Milstein and co-workers and have been applied as efficient catalysts for numerous (de)hydrogenation reactions.[9] Based on that, manifold variations concerning the nature of the pincer ligand have been performed and the so obtained complexes have shown to be interesting catalysts as well.[1e]



Scheme 1. Frequently used Ru PNP pincer complexes.[1e]

Looking at the popular pincer complexes, it is evident that most of them rely on a similar set of ligands. Typically, besides the pincer unit, carbon monoxide and hydride ligands are employed herein. While this arrangement is generally known to be crucial for reactivity and stability,[1d] obviously it does not allow for any further variations. Hence, we had the idea to introduce alternative ligands mimicking the behavior of CO and H^- ligands. More specifically, cyclometalation of N-heterocycles should provide an active metal center due to the strongly σ-donating C-donor (H^- analogue) and the π-back bonding interaction with the heterocycle (CO analogue).

Although neglected for a long time, in the past years cyclometalated ruthenium complexes became of interest as redox catalysts.[10] For example, Ru half-sandwich complexes bearing



Scheme 2. Preparation of ruthenium pincer complexes bearing C,N-bound heterocycle ligands.

bidentate ligands with a C and a P,[11] N,[12] or NHC[13] donor were used for the transfer hydrogenation of ketones. Additionally, ruthenacycles have been applied in the direct hydrogenation of olefins,[14] the dehydrogenation of alcohols,[15] and the α-alkylation of amides by a hydrogen autotransfer protocol.[16] In addition to that, complexes bearing a carbon donor as part of the pincer ligand were applied as catalysts for transfer hydrogenations,[17] direct hydrogenations,[18] and acceptorless dehydrogenations.[19]

In line with this, Baratta and co-workers established highly efficient Ru CNN complexes for the transfer hydrogenation of ketones[20] or aldehydes,[21] the direct hydrogenation of ketones,[22] and the racemization or deuteration of alcohols.[23]

Results and Discussion

Following our concept *vide supra*, we attempted the synthesis of **[Ru]-5** via cyclometalation of [Ru(*p*-cym)Cl_2]$_2$ with 2-phenylpyridine.[24] Next, an array of other heterocycles was employed to prepare the corresponding intermediates, which were reacted with aliphatic pincer ligands in 2-butanol. The desired complexes **[Ru]-5-12** precipitated during this reaction, giving powdery solids ranging from bright yellow to ruby red in color (see Scheme 2). All of them were subsequently characterized by NMR, IR, and MS analyses and for representative examples, X-ray structural analyses were performed (see Figure 1 and SI).

Having these novel complexes in hand, we were interested to apply them in hydrogen autotransfer – also called hydrogen borrowing – reactions.[25] In these cascade reactions, first, hydrogen gets abstracted from an unreactive substrate, mostly an alcohol, generating a more reactive intermediate like an aldehyde. By this activation step, a variety of transformations is now accessible, for instance forming new C–C or C–N double bonds under elimination of water. Finally, the newly formed double bond gets hydrogenated using the hydrogen abstracted in the first step. More specifically, the α-alkylation of ketones with alcohols was of interest.[26]

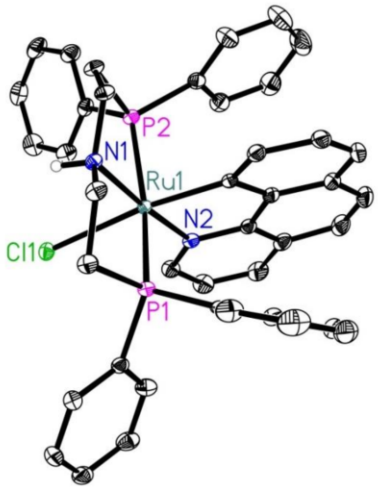
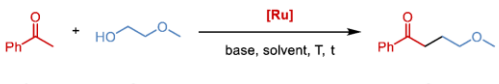


Figure 1. Crystal structure of **[Ru]-7**. Displacement ellipsoids correspond to 30% probability. Hydrogen atoms (except the N-bound) and co-crystallized solvent are omitted for clarity.

Table 1: Catalyst comparison and optimization for α-alkylation of acetophenone with 2-methoxyethanol.

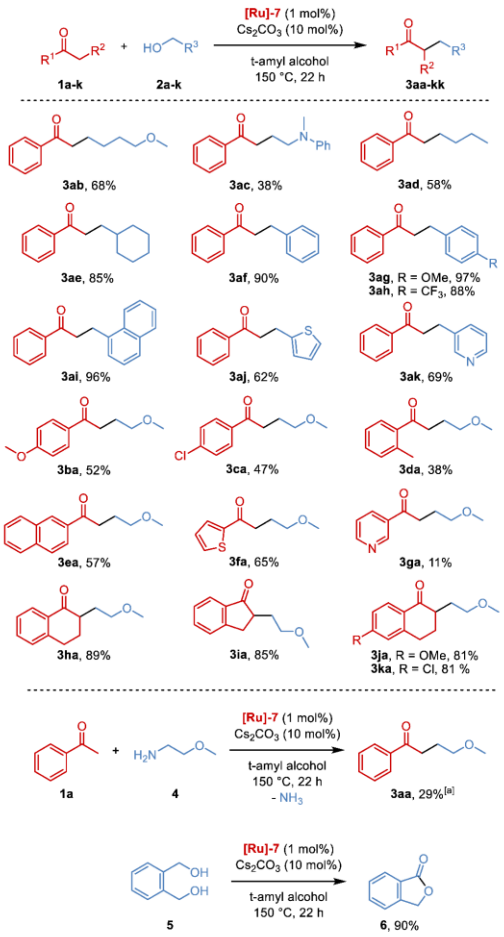


1a **2a** **3aa**

#	[Ru]	Base	Base Loading	Solvent	T (°C)	Yield (%)
1	[Ru]-1	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	16
2	[Ru]-5	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	42
3	[Ru]-6	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	44
4	[Ru]-7	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	48
5	[Ru]-8	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	32
6	[Ru]-9	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	22
7	[Ru]-10	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	38
8	[Ru]-11	Cs_2CO_3	10 mol%	*t*-amyl alc.	130	43
9	[Ru]-7	Cs_2CO_3	10 mol%	*t*-amyl alc.	140	58
10	[Ru]-7	Cs_2CO_3	10 mol%	*t*-amyl alc.	150	65
11	[Ru]-7	KO*t*Bu	10 mol%	*t*-amyl alc.	150	44
12	[Ru]-7	NaO*t*Bu	10 mol%	*t*-amyl alc.	150	45
13	[Ru]-7	NaOH	10 mol%	*t*-amyl alc.	150	38
14	[Ru]-7	K_2CO_3	10 mol%	*t*-amyl alc.	150	36
15	[Ru]-7	NEt_3	10 mol%	*t*-amyl alc.	150	-
16	[Ru]-7	Cs_2CO_3	20 mol%	*t*-amyl alc.	150	66
17	[Ru]-7	Cs_2CO_3	30 mol%	*t*-amyl alc.	150	64
18[a]	[Ru]-7	Cs_2CO_3	10 mol%	*t*-amyl alc.	150	57
19[b]	**[Ru]-7**	**Cs_2CO_3**	**10 mol%**	***t*-amyl alc.**	**150**	**68**
20[c]	[Ru]-7	Cs_2CO_3	10 mol%	*t*-amyl alc.	150	60
21[b]	[Ru]-7	Cs_2CO_3	10 mol%	heptane	150	41
22[b]	[Ru]-7	Cs_2CO_3	10 mol%	toluene	150	38
23[b]	[Ru]-7	Cs_2CO_3	10 mol%	THF	150	53
24[b]	[Ru]-7	Cs_2CO_3	10 mol%	1,4-dioxane	150	37
25[b]	[Ru]-7	Cs_2CO_3	10 mol%	water	150	10
26[b]	[Ru]-7	-	-	*t*-amyl alc.	150	-
27	-	Cs_2CO_3	10 mol%	*t*-amyl alc.	150	-
28	[Ru]-12	Cs_2CO_3	10 mol%	*t*-amyl alc.	150	46

Unless otherwise specified, reactions were carried out with **1a** (1.0 mmol), **2a** (1.2 mmol), the catalyst (0.02 mmol), and the base (0.1 mmol) in 1 ml of solvent at the indicated temperature for 22 h; [a] catalyst loading: 0.5 mol%; [b] catalyst loading: 1 mol%; [c] catalyst loading: 3 mol%; yields determined by GC using n-hexadecane as internal standard.

To compare the reactivity of the novel catalysts with the parent Ru-MACHO system, the reaction of acetophenone with 2-methoxyethanol was investigated in *tert*. amyl alcohol at 130 °C in the presence of catalytic amounts of cesium carbonate as base. Under these conditions, **[Ru]-1** only yielded in 16% of the desired product (see Table 1, entry 1). In contrast, when the newly synthesized catalysts are applied under identical conditions higher yields up to 48% were obtained (Table 1, entries 2-8). Thus, having confirmed that the introduced phenyl heterocycle ligands can be beneficial for catalysis, we started optimizing the reaction conditions using **[Ru]-7**, which bears benzo[h]quinoline as additional ligand. Proceeding with this catalyst, an optimal yield of 68% could be obtained (Table1, entry 19). Notably, performing the reaction without any catalyst or without base yielded in no product formation at all. Interestingly, the application of **[Ru]-12**, in which the NH is replaced by a *N*-methyl group gave 46% of the desired product. This comparably high yield suggests that the NH proton of the pincer ligand should not be directly involved in the catalytic cycle. Ultimately, we performed the reaction with **1a**



Scheme 3. Substrate scope of the Ru-catalyzed α-alkylation of ketones and related reactions. Isolated yields; [a] yield determined by GC using hexadecane as internal standard.

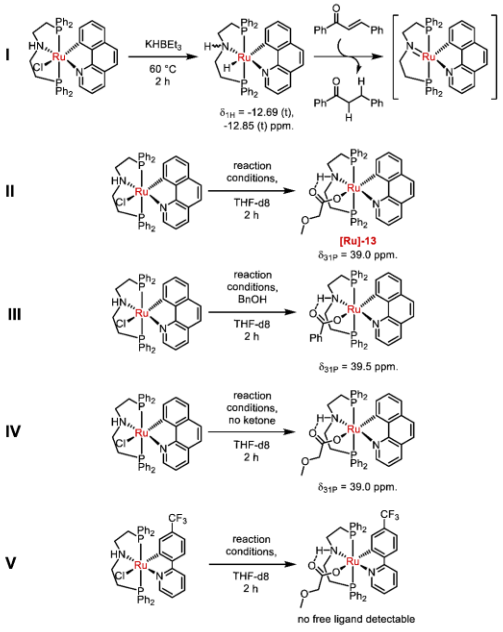
(1.0 mmol), **2a** (1.2 mmol), **[Ru]-7** (0.01 mmol), and Cs_2CO_3 (0.1 mmol) in 1 ml of *t*-amyl alcohol at 150 °C and chose these optimal conditions for testing different substrates.

Reaction of 4-methoxybutanol (**2b**) gave 68% of the desired product **3ab** and exchanging the ether group for a tertiary amine, the corresponding product **3ac** was obtained in 38% yield. Additionally, starting from simple, aliphatic alcohols like 1-butanol **2d** or cyclohexanemethanol **2e**, acetophenone was alkylated in satisfying yields (58 and 85%, respectively). Pleasingly, when benzyl alcohol **2f** is applied, the yield rises to 90%. Similarly, substituted benzyl alcohols were used to give alkylated ketones **3ag** and **3ah** in 97 and 88% yield, respectively, and moreover, 1-naphthyl methanol **2i** was converted to give the desired product **3ai** in excellent 96% yield. Finally, 2-thiophenemethanol **2j** and 3-pyridylmethanol **2k** were applied as representatives of heterocycle-bearing alcohols. Here, the corresponding products were obtained in 62% and 69% yield, respectively.

Next, differently substituted acetophenone derivatives were alkylated. Here, reactions preceded smoothly affording 38 to 58% of the corresponding products **3ba** to **3da**. In line with this, 2-acetonaphthone was converted into **3ea** in 57% yield and 2-acetyl heterocycles **1f** and **1g** gave 65 and 11%, respectively. Furthermore, using α-tetralone **1h** or 1-indanone **1i**, the desired products can be obtained in good yields of 89 and 85%, respectively. In line with this, when substituted tetralone-derivates **1j** and **1k** are employed, the corresponding products are generated in 81% yield in both cases.

This new class of complexes is not merely limited to the beforehand discussed reactions, but they are as well able to dehydrogenate amines allowing for their application in alkylating ketones. To demonstrate this, 2-methoxyethylamine **4** was used instead of the alcohol **2a**, giving **3aa**. In addition to that, diols like 1,2-benzenedimethanol **5** undergo cyclization to give the corresponding cyclic lactone **6** under C-O bond formation in a very good yield of 90%.

After having established a gratifying substrate scope, investigations concerning the reaction mechanism were carried out. First, we wanted to find out, if the applied complex is capable of forming stable ruthenium hydride species. In principle, it would be possible that these species spontaneously release the hydride and the aryl heterocycle ligand via reductive elimination. However, when **[Ru]-7** is treated with $KHBEt_3$, two hydridic species can be obtained and detected by ^1H NMR spectroscopy (compare Scheme 4, rct. **I** and SI). In a follow up experiment, one of these hydride complexes is able to promptly hydrogenate benzylideneacetophenone which corresponds to the last step of the alkylation of ketones with alcohols.



Scheme 4. Experiments to investigate the catalyst species involved in the reaction.

Subsequently, we wanted to find out, which catalyst species are actually present under reaction conditions. For this, the reaction was carried out in a pressure resistant NMR tube (reaction conditions were adjusted to this by using THF-d8 as solvent, shortened reaction times and higher catalyst loadings). Here, besides starting complex **[Ru]-7**, one major species was detected in ^{31}P NMR (rct. **II**). To verify the nature of this species, the NMR scale reaction was carried out using benzyl alcohol instead of 2-methoxyethanol (rct. **III**). This resulted in a slightly shifted ^{31}P NMR signal suggesting that a different complex is formed herein, when a different alcohol is deployed. Additionally, the experiment was repeated without addition of the ketone (rct. **IV**). Here, a similar species was detected by ^{31}P NMR, while it was not observed in a comparison experiment without alcohol or ketone (see SI). The species formed in this reaction was further characterized by NMR spectroscopy as well as X-ray structural analysis. By this, it was revealed that the complex predominantly present during catalysis is ruthenium carboxylate complex **[Ru]-13** (see Figure 2). Under reaction conditions, this species is probably generated by hydration of the *in situ* formed aldehyde followed by catalytic dehydrogenation of the so-formed *gem*-diol.[5c, 27] The required water for this likely stems from the aldol condensation taking place during catalysis or from moisture present in the alcohols as these have not been dried prior to use. Attempts to synthesize **[Ru]-13** independently in the best case yielded in a mixture of 78% of it and the starting complex **[Ru]-7** (see SI for details). However, when this mixture was applied in the standard reaction, the product was obtained in similar 68%. Due to this, **[Ru]-13** likely depicts a catalyst reservoir and can be activated by base in a similar manner than pre-catalyst **[Ru]-7**.

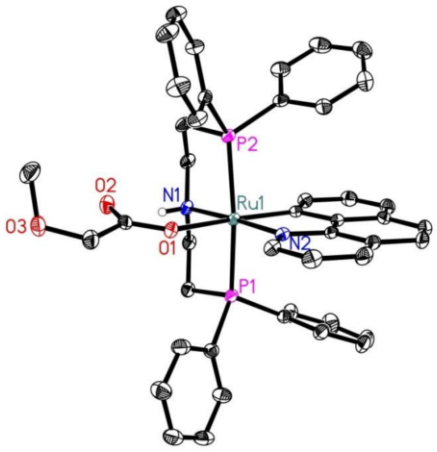


Figure 2. Crystal structure of **[Ru]-13**. Displacement ellipsoids correspond to 30% probability. Only one molecule of the asymmetric unit is shown. Hydrogen atoms (except the N-bound) and co-crystallized solvent are omitted for clarity.

Finally, experiments were performed concerning the stability of the phenyl heterocycle ligand during catalysis. For this, the NMR reaction was carried out under use of **[Ru]-10** as catalyst to investigate species involving this ligand by ^{19}F NMR. Here again, a species fitting to the corresponding carboxylate complex and the starting material were observed. Besides this, only small traces of other fluorine-containing species were detected, indicating that the applied cyclometalated ligands in fact remain bound to the complex during catalysis.

Conclusion

Summing up, cyclometalated aryl heterocycles can be used as a tunable mimic of carbonyl and hydride ligands in popular ruthenium pincer complexes. Following this concept, a series of novel potent catalysts for (de)hydrogenations have been obtained. The general advantage of such catalysts compared to the parent complex is demonstrated for the green α-alkylation of ketones with alcohols. Plausible reaction intermediates were investigated for this, all still involving the intact phenyl heterocycle and the pincer ligand. We believe this catalyst design can be used as a guideline for the creation of a variety of other pincer complexes, too; thus, opening the door for more effective catalysis.

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Keywords: Ruthenium • Metallacycles • Pincer Complexes • Hydrogen Autotransfer • C-C Bond Formation

[1] a) E. Peris, R. H. Crabtree, *Chem. Soc. Rev.* **2018**, *47*, 1959-1968; b) M. A. W. Lawrence, K.-A. Green, P. N. Nelson, S. C. Lorraine, *Polyhedron* **2018**, *143*, 11-27; c) H. Valdés, M. A. García - Eleno, D. Canseco - Gonzalez, D. Morales - Morales, *ChemCatChem* **2018**, *10*, 3136-3172; d) H. A. Younus, W. Su, N. Ahmad, S. Chen, F. Verpoort, *Adv. Synth. Catal.* **2015**, *357*, 283-330; e) S. Werkmeister, J. Neumann, K. Junge, M. Beller, *Chem. - Eur. J.* **2015**, *21*, 12226-12250; f) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, *114*, 12024-12087; g) D. Benito-Garagorri, E. Becker, J. Wiedermann, W. Lackner, M. Pollak, K. Mereiter, J. Kisala, K. Kirchner, *Organometallics* **2006**, *25*, 1900-1913; h) D. Benito-Garagorri, K. Kirchner, *Acc. Chem. Res.* **2008**, *41*, 201-213.

[2] W. Kuriyama, T. Matsumoto, Y. Ino, O. Ogata (Takasago International Corporation), WO20110487227, **2011**.

[3] Z. Han, L. Rong, J. Wu, L. Zhang, Z. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2012**, *51*, 13041-13045.

[4] J. Neumann, C. Bornschein, H. Jiao, K. Junge, M. Beller, *Eur. J. Org. Chem.* **2015**, *2015*, 5944-5948.

[5] a) M. Nielsen, E. Alberico, W. Baumann, H.-J. Drexler, H. Junge, S. Gladiali, M. Beller, *Nature* **2013**, *495*, 85-89; b) A. Monney, E. Barsch, P. Sponholz, H. Junge, R. Ludwig, M. Beller, *Chem. Commun.* **2014**, *50*, 707-709; c) E. Alberico, A. J. J. Lennox, L. K. Vogt, H. Jiao, W. Baumann, H.-J. Drexler, M. Nielsen, A. Spannenberg, M. P. Checinski, H. Junge, M. Beller, *J. Am. Chem. Soc.* **2016**, *138*, 14890-14904.

[6] M. Nielsen, H. Junge, A. Kammer, M. Beller, *Angew. Chem. Int. Ed.* **2012**, *51*, 5711-5713.

[7] M. Peña-López, H. Neumann, M. Beller, *Chem. Commun.* **2015**, *51*, 13082-13085.

[8] N. J. Oldenhuis, V. M. Dong, Z. Guan, *J. Am. Chem. Soc.* **2014**, *136*, 12548-12551.

[9] a) J. Zhang, M. Gandelman, L. J. W. Shimon, H. Rozenberg, D. Milstein, *Organometallics* **2004**, *23*, 4026-4033; b) J. Zhang, G. Leitus, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2005**, *127*, 10840-10841; c) H. Zeng, Z. Guan, *J. Am. Chem. Soc.* **2011**, *133*, 1159-1161; d) P. Hu, Y.

Diskin-Posner, Y. Ben-David, D. Milstein, *ACS Catal.* **2014**, *4*, 2649-2652; e) E. Khaskin, M. A. Iron, L. J. W. Shimon, J. Zhang, D. Milstein, *J. Am. Chem. Soc.* **2010**, *132*, 8542-8543; f) E. Balaraman, C. Gunanathan, J. Zhang, L. J. W. Shimon, D. Milstein, *Nat. Chem.* **2011**, *3*, 609; g) C. Gunanathan, M. Hölscher, W. Leitner, *Eur. J. Inorg. Chem.* **2011**, 3381-3386; h) C. A. Huff, M. S. Sanford, *ACS Catal.* **2013**, *3*, 2412-2416.

[10] a) M. Albrecht, *Chem. Rev.* **2010**, *110*, 576-623; b) J.-P. Djukic, J.-B. Sortais, L. Barloy, M. Pfeffer, *Eur. J. Inorg. Chem.* **2009**, 817-853; c) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879-5918.

[11] R. Sun, X. Chu, S. Zhang, T. Li, Z. Wang, B. Zhu, *Eur. J. Inorg. Chem.* **2017**, 3174-3183.

[12] a) N. U. Din Reshi, D. Senthurpandi, A. G. Samuelson, *J. Organomet. Chem.* **2018**, *866*, 189-199; b) W.-G. Jia, T. Zhang, D. Xie, Q.-T. Xu, S. Ling, Q. Zhang, *Dalton Trans.* **2016**, *45*, 14230-14237.

[13] a) S. Bauri, S. N. R. Donthireddy, P. M. Illam, A. Rit, *Inorg. Chem.* **2018**, *57*, 14582-14593; b) G. Balamurugan, R. Ramesh, J. G. Malecki, *ChemistrySelect* **2017**, *2*, 10603-10608.

[14] a) L. N. Lewis, *J. Am. Chem. Soc.* **1986**, *108*, 743-749; b) S. M. Islam, C. R. Saha, *J. Mol. Catal. A: Chem.* **2004**, *212*, 131-140; c) B. Bagh, A. M. McKinty, A. J. Lough, D. W. Stephan, *Dalton Trans.* **2015**, *44*, 2712-2723.

[15] D. Gong, B. Hu, D. Chen, *Dalton Trans.* **2019**, *48*, 8826-8834.

[16] D. Gong, B. Hu, W. Yang, D. Chen, *ChemCatChem* **2019**, *11*, 4841-4847.

[17] a) P. Dani, T. Karlen, R. A. Gossage, S. Gladiali, G. van Koten, *Angew. Chem. Int. Ed.* **2000**, *39*, 743-745; b) M. Gagliardo, P. A. Chase, S. Brouwer, G. P. M. van Klink, G. van Koten, *Organometallics* **2007**, *26*, 2219-2227.

[18] E. Fogler, E. Balaraman, Y. Ben-David, G. Leitus, L. J. W. Shimon, D. Milstein, *Organometallics* **2011**, *30*, 3826-3833.

[19] a) S. Tang, N. von Wolff, Y. Diskin-Posner, G. Leitus, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2019**, *141*, 7554-7561; b) Q. Wang, H. Chai, Z. Yu, *Organometallics* **2018**, *37*, 584-591.

[20] a) W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando, P. Rigo, *Angew. Chem. Int. Ed.* **2005**, *44*, 6214-6219; b) W. Baratta, M. Bosco, G. Chelucci, A. Del Zotto, K. Siega, M. Toniutti, E. Zangrando, P. Rigo, *Organometallics* **2006**, *25*, 4611-4620; c) W. Baratta, M. Ballico, S. Baldino, G. Chelucci, E. Herdtweck, K. Siega, S. Magnolia, P. Rigo, *Chem. - Eur. J.* **2008**, *14*, 9148-9160; d) W. Baratta, F. Benedetti, A. Del Zotto, L. Fanfoni, F. Felluga, S. Magnolia, E. Putignano, P. Rigo, *Organometallics* **2010**, *29*, 3563-3570.

[21] W. Baratta, K. Siega, P. Rigo, *Adv. Synth. Catal.* **2007**, *349*, 1633-1636.

[22] a) W. Baratta, S. Baldino, M. J. Calhorda, P. J. Costa, G. Esposito, E. Herdtweck, S. Magnolia, C. Mealli, A. Messaoudi, S. A. Mason, L. F. Veiros, *Chem. - Eur. J.* **2014**, *20*, 13603-13617; b) S. Facchetti, V. Jurcik, S. Baldino, S. Giboulot, H. G. Nedden, A. Zanotti-Gerosa, A. Blackaby, R. Bryan, A. Boogaard, D. B. McLaren, E. Moya, S. Reynolds, K. S. Sandham, P. Martinuzzi, W. Baratta, *Organometallics* **2016**, *35*, 277-287; c) S. Giboulot, S. Baldino, M. Ballico, R. Figliolia, A. Pöthig, S. Zhang, D. Zuccaccia, W. Baratta, *Organometallics* **2019**, *38*, 1127-1142.

[23] G. Bossi, E. Putignano, P. Rigo, W. Baratta, *Dalton Trans.* **2011**, *40*, 8986-8995.

[24] B. Li, T. Roisnel, C. Darcel, P. H. Dixneuf, *Dalton Trans.* **2012**, *41*, 10934-10937.

[25] a) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555-1575; b) G. Guillena, D. J. Ramón, M. Yus, *Angew. Chem. Int. Ed.* **2007**, *46*, 2358-2364; c) T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Dalton Trans.* **2009**, 753-762; d) K. Krüger, A. Tillack, M. Beller, *ChemSusChem* **2009**, *2*, 715-717; e) A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635-636; f) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* **2010**, *110*, 1611-1641; g) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681-703; h) S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann, M. Beller, *ChemCatChem* **2011**, *3*, 1853-1864; i) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 1229712; j) Y. Obora, *ACS Catal.* **2014**, *4*, 3972-3981; k) F. Huang, Z. Liu, Z. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 862-875; l) Q. Yang, Q. Wang, Z. Yu, *Chem. Soc. Rev.* **2015**, *44*, 2305-2329; m) G. Chelucci, *Coord. Chem. Rev.* **2017**, *331*, 1-36; n) A. Corma, J. Navas, M. J. Sabater, *Chem. Rev.* **2018**, *118*, 1410-1459; o) T. Irrgang, R. Kempe, *Chem. Rev.* **2019**, *119*, 2524-2549.

[26] a) R. Martínez, G. J. Brand, D. J. Ramón, M. Yus, *Tetrahedron Lett.* **2005**, *46*, 3683-3686; b) R. Martínez, D. J. Ramón, M. Yus, *Tetrahedron* **2006**, *62*, 8988-9001; c) C. Schlepphorst, B. Maji, F. Glorius, *ACS Catal.* **2016**, *6*, 4184-4188; d) C. Xu, X.-M. Dong, Z.-Q. Wang, X.-Q. Hao, Z. Li, L.-M. Duan, B.-M. Ji, M.-P. Song, *J. Organomet. Chem.* **2012**, *700*, 214-218; e) F. Li, J. Ma, N. Wang, *J. Org. Chem.* **2014**, *79*, 10447-10455; f) D. Wang, K. Zhao, P. Ma, C. Xu, Y. Ding, *Tetrahedron Lett.* **2014**, *55*, 7233-7235; g) S. Elangovan, J.-B. Sortais, M. Beller, C. Darcel, *Angew. Chem. Int. Ed.* **2015**, *54*, 14483-14486; h) C. Seck, M. D. Mbaye, S. Coufourier, A. Lator, J. F. Lohier, A. Poater, T. R. Ward, S. Gaillard, J. L. Renaud, *ChemCatChem* **2017**, *9*, 4410-4416; i) L. Bettoni, C. Seck, M. D. Mbaye, S. Gaillard, J.-L. Renaud, *Org. Lett.* **2019**, *21*, 3057-3061; j) M. Peña-López, P. Piehl, S. Elangovan, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 14967-14971; k) A. Bruneau-Voisine, L. Pallova, S. Bastin, V. César, J.-B. Sortais, *Chem. Commun.* **2019**, *55*, 314-317; l) D. Banerjee, L. M. Kabadwal, J. Das, *Chem. Commun.* **2018**, *54*, 14069-14072; m) G. Zhang, J. Wu, H. Zeng, S. Zhang, Z. Yin, S. Zheng, *Org. Lett.* **2017**, *19*, 1080-1083; n) P. Piehl, M. Pena-Lopez, A. Frey, H. Neumann, M. Beller, *Chem. Commun.* **2017**, *53*, 3265-3268.

[27] a) J. Kothandaraman, M. Czaun, A. Goeppert, R. Haiges, J.-P. Jones, R. B. May, G. K. S. Prakash, G. A. Olah, *ChemSusChem* **2015**, *8*, 1442-1451; b) Y. Zhang, A. D. MacIntosh, J. L. Wong, E. A. Bielinski, P. G. Williard, B. Q. Mercado, N. Hazari, W. H. Bernskoetter, *Chem. Sci.* **2015**, *6*, 4291-4299.

8 References

[1] *Chemiewirtschaft in Zahlen 2018*, Verband der Chemischen Industrie e.V. (VCI), Frankfurt am Main, **2018**.

[2] *Facts & Figures of the European Chemical Industry*, European Chemical Industry Council - Cefic aisbl, Brussels, **2018**.

[3] *Energiestatistik für die Chemie- und Pharmaindustrie*, Verband der Chemischen Industrie e.V. (VCI), Frankfurt am Main, **2019**.

[4] Umweltbundesamt, *Strukturdaten: Chemikalien und chemisch-pharmazeutische Industrie*, https://www.umweltbundesamt.de/daten/chemikalien/strukturdaten-chemikalien-chemisch-pharmazeutische, Accessed 22.07.2019.

[5] B. M. Trost, in *Transition Metals for Organic Synthesis, Vol. 1*, 2 ed. (Eds.: M. Beller, C. Bolm), Wiley VCH, Weinheim, **2004**, pp. 3-14.

[6] S. Enthaler, K. Junge, M. Beller, *Angew. Chem. Int. Ed.* **2008**, *47*, 3317-3321.

[7] R. Franke, D. Selent, A. Börner, *Chem. Rev.* **2012**, *112*, 5675-5732.

[8] A. Dumrath, C. Lübbe, M. Beller, in *Palladium-Catalyzed Coupling Reactions: Practical Aspects and Future Developments* (Ed.: Á. Molnár), Wiley VCH, Weinheim, **2013**, pp. 445-489.

[9] a) G. van Koten, *J. Organomet. Chem.* **2013**, *730*, 156-164; b) E. Peris, R. H. Crabtree, *Chem. Soc. Rev.* **2018**, *47*, 1959-1968; c) M. A. W. Lawrence, K.-A. Green, P. N. Nelson, S. C. Lorraine, *Polyhedron* **2018**, *143*, 11-27.

[10] W. V. Dahlhoff, S. M. Nelson, *J. Chem. Soc. A* **1971**, 2184-2190.

[11] C. J. Moulton, B. L. Shaw, *J. Chem. Soc., Dalton Trans.* **1976**, 1020-1024.

[12] G. van Koten, K. Timmer, J. G. Noltes, A. L. Spek, *J. Chem. Soc., Chem. Commun.* **1978**, 250-252.

[13] a) M. Albrecht, G. van Koten, *Angew. Chem. Int. Ed.* **2001**, *40*, 3750-3781; b) M. E. van der Boom, D. Milstein, *Chem. Rev.* **2003**, *103*, 1759-1792.

[14] J. Zhang, G. Leitus, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2005**, *127*, 10840-10841.

[15] a) D. Milstein, *Top. Catal.* **2010**, *53*, 915-923; b) J. R. Khusnutdinova, D. Milstein, *Angew. Chem. Int. Ed.* **2015**, *54*, 12236-12273; c) B. Zhao, Z. Han, K. Ding, *Angew. Chem. Int. Ed.* **2013**, *52*, 4744-4788.

[16] a) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, *114*, 12024-12087; b) H. A. Younus, N. Ahmad, W. Su, F. Verpoort, *Coord. Chem. Rev.* **2014**, *276*, 112-152; c) S. Werkmeister, J. Neumann, K. Junge, M. Beller, *Chem. - Eur. J.* **2015**, *21*, 12226-12250; d) H. A. Younus, W. Su, N. Ahmad, S. Chen, F. Verpoort, *Adv. Synth. Catal.* **2015**, *357*, 283-330; e) H. Valdés, M. A. García-Eleno, D. Canseco-Gonzalez, D. Morales-Morales, *ChemCatChem* **2018**, *10*, 3136-3172; f) H. Li, T. P. Gonçalves, D. Lupp, K.-W. Huang, *ACS Catal.* **2019**, 1619-1629.

[17] a) W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo, T. Saito, *Org. Process Res. Dev.* **2012**, *16*, 166-171; b) W. Kuriyama, T. Matsumoto, Y. Ino, O. Ogata (Takasago International Corporation), WO20110487227, **2011**.

[18] Z. Han, L. Rong, J. Wu, L. Zhang, Z. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2012**, *51*, 13041-13045.

[19] a) S. Werkmeister, K. Junge, M. Beller, *Org. Process Res. Dev.* **2014**, *18*, 289-302; b) P. A. Dub, T. Ikariya, *ACS Catal.* **2012**, *2*, 1718-1741.
[20] T. Otsuka, A. Ishii, P. A. Dub, T. Ikariya, *J. Am. Chem. Soc.* **2013**, *135*, 9600-9603.
[21] D. Lazzari, M. C. Cassani, M. Bertola, F. C. Moreno, D. Torrente, *RSC Adv.* **2013**, *3*, 15582-15584.
[22] N. T. Fairweather, M. S. Gibson, H. Guan, *Organometallics* **2015**, *34*, 335-339.
[23] J. Deutsch, J. Jiménez Pinto, S. Doerfelt, A. Martin, A. Köckritz, *Flavour Fragrance J.* **2015**, *30*, 101-107.
[24] C. Ziebart, R. Jackstell, M. Beller, *ChemCatChem* **2013**, *5*, 3228-3231.
[25] J. Neumann, C. Bornschein, H. Jiao, K. Junge, M. Beller, *Eur. J. Org. Chem.* **2015**, *2015*, 5944-5948.
[26] N. M. Rezayee, C. A. Huff, M. S. Sanford, *J. Am. Chem. Soc.* **2015**, *137*, 1028-1031.
[27] J. Kothandaraman, A. Goeppert, M. Czaun, G. A. Olah, G. K. S. Prakash, *J. Am. Chem. Soc.* **2016**, *138*, 778-781.
[28] a) S. Kar, R. Sen, A. Goeppert, G. K. S. Prakash, *J. Am. Chem. Soc.* **2018**, *140*, 1580-1583; b) S. Kar, A. Goeppert, G. K. S. Prakash, *J. Am. Chem. Soc.* **2019**, *141*, 12518-12521; c) G. A. Olah, A. Goeppert, G. K. Surya Prakash, *Beyond Oil and Gas: The Methanol Economy*, Wiley VCH, Weinheim, **2006**.
[29] M. Bertoli, A. Choualeb, A. J. Lough, B. Moore, D. Spasyuk, D. G. Gusev, *Organometallics* **2011**, *30*, 3479-3482.
[30] M. Nielsen, A. Kammer, D. Cozzula, H. Junge, S. Gladiali, M. Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 9593-9597.
[31] E. Alberico, M. Nielsen, *Chem. Commun.* **2015**, *51*, 6714-6725.
[32] M. Nielsen, E. Alberico, W. Baumann, H.-J. Drexler, H. Junge, S. Gladiali, M. Beller, *Nature* **2013**, *495*, 85-89.
[33] A. Monney, E. Barsch, P. Sponholz, H. Junge, R. Ludwig, M. Beller, *Chem. Commun.* **2014**, *50*, 707-709.
[34] a) E. Alberico, A. J. J. Lennox, L. K. Vogt, H. Jiao, W. Baumann, H.-J. Drexler, M. Nielsen, A. Spannenberg, M. P. Checinski, H. Junge, M. Beller, *J. Am. Chem. Soc.* **2016**, *138*, 14890-14904; b) V. Sinha, N. Govindarajan, B. de Bruin, E. J. Meijer, *ACS Catal.* **2018**, 6908-6913.
[35] M. Nielsen, H. Junge, A. Kammer, M. Beller, *Angew. Chem. Int. Ed.* **2012**, *51*, 5711-5713.
[36] N. J. Oldenhuis, V. M. Dong, Z. Guan, *Tetrahedron* **2014**, *70*, 4213-4218.
[37] Z. Lei, N. D. Hanh, R. Guillaume, T. Xavier, C. Frédéric, D. Simon, P. Sébastien, D. Franck, G. R. M., *ChemSusChem* **2016**, *9*, 1413-1423.
[38] S. H. Kim, S. H. Hong, *Org. Lett.* **2016**, *18*, 212-215.
[39] S. H. Kim, S. H. Hong, *ACS Catal.* **2014**, *4*, 3630-3636.
[40] B. Chatterjee, C. Gunanathan, *Org. Lett.* **2015**, *17*, 4794-4797.
[41] V. Krishnakumar, C. Gunanathan, *Chem. Commun.* **2018**, *54*, 8705-8708.
[42] a) N. J. Oldenhuis, V. M. Dong, Z. Guan, *J. Am. Chem. Soc.* **2014**, *136*, 12548-12551; b) M. Peña-López, H. Neumann, M. Beller, *Chem. Commun.* **2015**, *51*, 13082-13085.
[43] K. Dong, S. Elangovan, R. Sang, A. Spannenberg, R. Jackstell, K. Junge, Y. Li, M. Beller, *Nat. Commun.* **2016**, *7*, 12075.
[44] R. A. T. M. Abbenhuis, J. Boersma, G. van Koten, *J. Org. Chem.* **1998**, *63*, 4282-4290.
[45] a) C. Gunanathan, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2009**, *131*, 3146-3147; b) J. Zhang, E. Balaraman, G. Leitus, D. Milstein, *Organometallics* **2011**, *30*, 5716-5724.

[46] J. Zhang, M. Gandelman, L. J. W. Shimon, H. Rozenberg, D. Milstein, *Organometallics* **2004**, *23*, 4026-4033.
[47] M. Montag, J. Zhang, D. Milstein, *J. Am. Chem. Soc.* **2012**, *134*, 10325-10328.
[48] P. Hu, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *ACS Catal.* **2014**, *4*, 2649-2652.
[49] D. Srimani, E. Balaraman, P. Hu, Y. Ben-David, D. Milstein, *Adv. Synth. Catal.* **2013**, *355*, 2525-2530.
[50] H. Zeng, Z. Guan, *J. Am. Chem. Soc.* **2011**, *133*, 1159-1161.
[51] J. O. Bauer, G. Leitus, Y. Ben-David, D. Milstein, *ACS Catal.* **2016**, *6*, 8415-8419.
[52] a) B. Gnanaprakasam, E. Balaraman, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2011**, *50*, 12240-12244; b) D. Srimani, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2013**, *52*, 4012-4015; c) D. Srimani, Y. Ben-David, D. Milstein, *Chem. Commun.* **2013**, *49*, 6632-6634; d) P. Daw, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2018**, *140*, 11931-11934.
[53] E. Balaraman, B. Gnanaprakasam, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2010**, *132*, 16756-16758.
[54] E. Balaraman, C. Gunanathan, J. Zhang, L. J. W. Shimon, D. Milstein, *Nat. Chem.* **2011**, *3*, 609.
[55] C. Gunanathan, M. Hölscher, W. Leitner, *Eur. J. Inorg. Chem.* **2011**, 3381-3386.
[56] a) C. A. Huff, M. S. Sanford, *ACS Catal.* **2013**, *3*, 2412-2416; b) G. A. Filonenko, M. P. Conley, C. Copéret, M. Lutz, E. J. M. Hensen, E. A. Pidko, *ACS Catal.* **2013**, *3*, 2522-2526; c) G. A. Filonenko, R. van Putten, E. N. Schulpen, E. J. M. Hensen, E. A. Pidko, *ChemCatChem* **2014**, *6*, 1526-1530.
[57] S. W. Kohl, L. Weiner, L. Schwartsburd, L. Konstantinovski, L. J. W. Shimon, Y. Ben-David, M. A. Iron, D. Milstein, *Science* **2009**, *324*, 74-77.
[58] a) C. Gunanathan, D. Milstein, *Angew. Chem. Int. Ed.* **2008**, *47*, 8661-8664; b) X. Ye, P. N. Plessow, M. K. Brinks, M. Schelwies, T. Schaub, F. Rominger, R. Paciello, M. Limbach, P. Hofmann, *J. Am. Chem. Soc.* **2014**, *136*, 5923-5929; c) Y. Xie, Y. Ben-David, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 9077-9080; d) M. B. Chaudhari, G. S. Bisht, P. Kumari, B. Gnanaprakasam, *Org. Biomol. Chem.* **2016**, *14*, 9215-9220.
[59] a) D. Spasyuk, D. G. Gusev, *Organometallics* **2012**, *31*, 5239-5242; b) C. Hou, J. Jiang, Y. Li, C. Zhao, Z. Ke, *ACS Catal.* **2016**, 786-795; c) R. Adam, E. Alberico, W. Baumann, H.-J. Drexler, R. Jackstell, H. Junge, M. Beller, *Chem. - Eur. J.* **2016**, *22*, 4991-5002; d) J. R. Cabrero-Antonino, E. Alberico, H.-J. Drexler, W. Baumann, K. Junge, H. Junge, M. Beller, *ACS Catal.* **2016**, *6*, 47-54.
[60] a) L. Le, J. Liu, T. He, D. Kim, E. J. Lindley, T. N. Cervarich, J. C. Malek, J. Pham, M. R. Buck, A. R. Chianese, *Organometallics* **2018**, *37*, 3286-3297; b) X. He, Y. Li, H. Fu, X. Zheng, H. Chen, R. Li, X. Yu, *Organometallics* **2019**, *38*, 1750-1760.
[61] D. Spasyuk, S. Smith, D. G. Gusev, *Angew. Chem. Int. Ed.* **2013**, *52*, 2538-2542.
[62] E. Ben-Ari, G. Leitus, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2006**, *128*, 15390-15391.
[63] a) R. Tanaka, M. Yamashita, K. Nozaki, *J. Am. Chem. Soc.* **2009**, *131*, 14168-14169; b) R. Tanaka, M. Yamashita, L. W. Chung, K. Morokuma, K. Nozaki, *Organometallics* **2011**, *30*, 6742-6750.
[64] K. Junge, B. Wendt, H. Jiao, M. Beller, *ChemCatChem* **2014**, *6*, 2810-2814.
[65] C. Prichatz, E. Alberico, W. Baumann, H. Junge, M. Beller, *ChemCatChem* **2017**, *9*, 1891-1896.

[66] a) M. Bertoli, A. Choualeb, D. G. Gusev, A. J. Lough, Q. Major, B. Moore, *Dalton Trans.* **2011**, *40*, 8941-8949; b) D. Spasyuk, S. Smith, D. G. Gusev, *Angew. Chem. Int. Ed.* **2012**, *51*, 2772-2775.
[67] T. Zell, D. Milstein, *Acc. Chem. Res.* **2015**, *48*, 1979-1994.
[68] R. Langer, G. Leitus, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2011**, *50*, 2120-2124.
[69] R. Langer, M. A. Iron, L. Konstantinovski, Y. Diskin-Posner, G. Leitus, Y. Ben-David, D. Milstein, *Chem. - Eur. J.* **2012**, *18*, 7196-7209.
[70] T. Zell, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2014**, *53*, 4685-4689.
[71] R. Langer, Y. Diskin-Posner, G. Leitus, L. J. W. Shimon, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2011**, *50*, 9948-9952.
[72] T. Zell, B. Butschke, Y. Ben-David, D. Milstein, *Chem. - Eur. J.* **2013**, *19*, 8068-8072.
[73] D. Srimani, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2013**, *52*, 14131-14134.
[74] E. Alberico, P. Sponholz, C. Cordes, M. Nielsen, H.-J. Drexler, W. Baumann, H. Junge, M. Beller, *Angew. Chem. Int. Ed.* **2013**, *52*, 14162-14166.
[75] C. Bornschein, S. Werkmeister, B. Wendt, H. Jiao, E. Alberico, W. Baumann, H. Junge, K. Junge, M. Beller, *Nat. Commun.* **2014**, *5*, 4111.
[76] a) S. Werkmeister, K. Junge, B. Wendt, E. Alberico, H. Jiao, W. Baumann, H. Junge, F. Gallou, M. Beller, *Angew. Chem. Int. Ed.* **2014**, *53*, 8722-8726; b) S. Chakraborty, H. Dai, P. Bhattacharya, N. T. Fairweather, M. S. Gibson, J. A. Krause, H. Guan, *J. Am. Chem. Soc.* **2014**, *136*, 7869-7872; c) S. Elangovan, B. Wendt, C. Topf, S. Bachmann, M. Scalone, A. Spannenberg, H. Jiao, W. Baumann, K. Junge, M. Beller, *Adv. Synth. Catal.* **2016**, *358*, 820-825.
[77] S. Chakraborty, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2014**, *136*, 8564-8567.
[78] N. M. Rezayee, D. C. Samblanet, M. S. Sanford, *ACS Catal.* **2016**, 6377-6383.
[79] R. Xu, S. Chakraborty, S. M. Bellows, H. Yuan, T. R. Cundari, W. D. Jones, *ACS Catal.* **2016**, *6*, 2127-2135.
[80] E. M. Lane, Y. Zhang, N. Hazari, W. H. Bernskoetter, *Organometallics* **2019**, *38*, 3084-3091.
[81] S. Chakraborty, P. O. Lagaditis, M. Förster, E. A. Bielinski, N. Hazari, M. C. Holthausen, W. D. Jones, S. Schneider, *ACS Catal.* **2014**, *4*, 3994-4003.
[82] D. H. Nguyen, Y. Morin, L. Zhang, X. Trivelli, F. Capet, S. Paul, S. Desset, F. Dumeignil, R. Gauvin, *ChemCatChem* **2017**, *9*, 2652-2660.
[83] E. A. Bielinski, P. O. Lagaditis, Y. Zhang, B. Q. Mercado, C. Würtele, W. H. Bernskoetter, N. Hazari, S. Schneider, *J. Am. Chem. Soc.* **2014**, *136*, 10234-10237.
[84] R. Knitsch, D. Han, F. Anke, L. Ibing, H. Jiao, M. R. Hansen, T. Beweries, *Organometallics* **2019**, *38*, 2714-2723.
[85] E. M. Lane, K. B. Uttley, N. Hazari, W. Bernskoetter, *Organometallics* **2017**, *36*, 2020-2025.
[86] M. Peña-López, H. Neumann, M. Beller, *ChemCatChem* **2015**, *7*, 865-871.
[87] S. Chakraborty, D. Milstein, *ACS Catal.* **2017**, *7*, 3968-3972.
[88] S. Chakraborty, G. Leitus, D. Milstein, *Angew. Chem. Int. Ed.* **2017**, *56*, 2074-2078.
[89] a) N. Gorgas, B. Stöger, L. F. Veiros, E. Pittenauer, G. Allmaier, K. Kirchner, *Organometallics* **2014**, *33*, 6905-6914; b) N. Gorgas, K. Kirchner, *Acc. Chem. Res.* **2018**, *51*, 1558-1569.

[90] F. Bertini, N. Gorgas, B. Stöger, M. Peruzzini, L. F. Veiros, K. Kirchner, L. Gonsalvi, *ACS Catal.* **2016**, *6*, 2889-2893.
[91] I. Mellone, N. Gorgas, F. Bertini, M. Peruzzini, K. Kirchner, L. Gonsalvi, *Organometallics* **2016**, *35*, 3344-3349.
[92] N. Gorgas, L. G. Alves, B. Stöger, A. M. Martins, L. F. Veiros, K. Kirchner, *J. Am. Chem. Soc.* **2017**, *139*, 8130-8133.
[93] a) R. Huber, A. Passera, A. Mezzetti, *Chem. Commun.* **2019**, *55*, 9251-9266; b) P. O. Lagaditis, P. E. Sues, J. F. Sonnenberg, K. Y. Wan, A. J. Lough, R. H. Morris, *J. Am. Chem. Soc.* **2014**, *136*, 1367-1380.
[94] a) A. T. Radosevich, J. G. Melnick, S. A. Stoian, D. Bacciu, C.-H. Chen, B. M. Foxman, O. V. Ozerov, D. G. Nocera, *Inorg. Chem.* **2009**, *48*, 9214-9221; b) D. Bacciu, C.-H. Chen, P. Surawatanawong, B. M. Foxman, O. V. Ozerov, *Inorg. Chem.* **2010**, *49*, 5328-5334.
[95] S. Elangovan, C. Topf, S. Fischer, H. Jiao, A. Spannenberg, W. Baumann, R. Ludwig, K. Junge, M. Beller, *J. Am. Chem. Soc.* **2016**, *138*, 8809-8814.
[96] a) A. Nerush, M. Vogt, U. Gellrich, G. Leitus, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 6985-6997; b) A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben David, N. A. Espinosa Jalapa, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 4298-4301.
[97] F. Kallmeier, T. Irrgang, T. Dietel, R. Kempe, *Angew. Chem. Int. Ed.* **2016**, *55*, 11806-11809.
[98] M. Mastalir, M. Glatz, N. Gorgas, B. Stöger, E. Pittenauer, G. Allmaier, L. F. Veiros, K. Kirchner, *Chem. - Eur. J.* **2016**, *22*, 12316-12320.
[99] a) M. Garbe, K. Junge, M. Beller, *Eur. J. Org. Chem.* **2017**, 4344-4362; b) R. Kempe, F. Kallmeier, *Angew. Chem. Int. Ed.* **2018**, *57*, 46-60; c) A. Mukherjee, D. Milstein, *ACS Catal.* **2018**, 11435-11469.
[100] S. Elangovan, M. Garbe, H. Jiao, A. Spannenberg, K. Junge, M. Beller, *Angew. Chem. Int. Ed.* **2016**, *55*, 15364-15368.
[101] S. Kar, A. Goeppert, J. Kothandaraman, G. K. S. Prakash, *ACS Catal.* **2017**, 6347-6351.
[102] A. Kaithal, M. Holscher, W. Leitner, *Angew. Chem. Int. Ed.* **2018**, *57*, 13449-13453.
[103] V. Papa, J. R. Cabrero-Antonino, E. Alberico, A. Spanneberg, K. Junge, H. Junge, M. Beller, *Chem. Sci.* **2017**, *8*, 3576-3585.
[104] a) M. Garbe, K. Junge, S. Walker, Z. Wei, H. Jiao, A. Spannenberg, S. Bachmann, M. Scalone, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 11237-11241; b) M. Garbe, Z. Wei, B. Tannert, A. Spannenberg, H. Jiao, S. Bachmann, M. Scalone, K. Junge, M. Beller, *Adv. Synth. Catal.* **2019**, *361*, 1913-1920; c) A. Passera, A. Mezzetti, *Adv. Synth. Catal.* **2019**, *361*, 4691-4706.
[105] M. Anderez-Fernandez, L. K. Vogt, S. Fischer, W. Zhou, H. Jiao, M. Garbe, S. Elangovan, K. Junge, H. Junge, R. Ludwig, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 559-562.
[106] A. M. Tondreau, J. M. Boncella, *Organometallics* **2016**, *35*, 2049-2052.
[107] D. H. Nguyen, X. Trivelli, F. Capet, J.-F. Paul, F. Dumeignil, R. M. Gauvin, *ACS Catal.* **2017**, 2022-2032.
[108] J. C. Borghs, Y. Lebedev, M. Rueping, O. El-Sepelgy, *Org. Lett.* **2018**, *21*, 70-74.
[109] S. Elangovan, J. Neumann, J.-B. Sortais, K. Junge, C. Darcel, M. Beller, *Nat. Commun.* **2016**, *7*, 12641.
[110] a) S. Fu, Z. Shao, Y. Wang, Q. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 11941-11948; b) N. V. Kulkarni, W. W. Brennessel, W. D. Jones, *ACS Catal.* **2017**, 997-1002.
[111] S. Chakraborty, U. Gellrich, Y. Diskin-Posner, G. Leitus, L. Avram, D. Milstein, *Angew. Chem. Int. Ed.* **2017**, *56*, 4229-4233.

[112] S. Chakraborty, U. K. Das, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2017**, *139*, 11710-11713.
[113] J. O. Bauer, S. Chakraborty, D. Milstein, *ACS Catal.* **2017**, *7*, 4462-4466.
[114] A. Mukherjee, A. Nerush, G. Leitus, L. J. W. Shimon, Y. Ben-David, N.-A. Espinosa-Jalapa, D. Milstein, *J. Am. Chem. Soc.* **2016**, *138*, 4298-4301.
[115] Y.-Q. Zou, S. Chakraborty, A. Nerush, D. Oren, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *ACS Catal.* **2018**, 8014-8019.
[116] A. Brzozowska, L. M. Azofra, V. Zubar, I. Atodiresei, L. Cavallo, M. Rueping, O. El-Sepelgy, *ACS Catal.* **2018**, 4103-4109.
[117] J. Neumann, S. Elangovan, A. Spannenberg, K. Junge, M. Beller, *Chem. - Eur. J.* **2017**, *23*, 5410-5413.
[118] J. C. Borghs, L. M. Azofra, T. Biberger, O. Linnenberg, L. Cavallo, M. Rueping, O. El-Sepelgy, *ChemSusChem* **2019**, *12*, 3083-3088.
[119] P. Daw, A. Kumar, N. A. Espinosa-Jalapa, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *ACS Catal.* **2018**, 7734-7741.
[120] P. Daw, A. Kumar, N. A. Espinosa-Jalapa, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2019**, *141*, 12202-12206.
[121] N. A. Espinosa-Jalapa, A. Nerush, L. J. W. Shimon, G. Leitus, L. Avram, Y. Ben-David, D. Milstein, *Chem. - Eur. J.* **2017**, *23*, 5934-5938.
[122] A. Kumar, T. Janes, N. A. Espinosa-Jalapa, D. Milstein, *Angew. Chem. Int. Ed.* **2018**, *57*, 12076-12080.
[123] L. Zhang, Y. Tang, Z. Han, K. Ding, *Angew. Chem. Int. Ed.* **2019**, *58*, 4973-4977.
[124] N. A. Espinosa-Jalapa, A. Kumar, G. Leitus, Y. Diskin-Posner, D. Milstein, *J. Am. Chem. Soc.* **2017**, *139*, 11722-11725.
[125] D. Milstein, A. Kumar, N.-A. Espinosa-Jalapa, G. Leitus, Y. Diskin-Posner, L. Avram, *Angew. Chem. Int. Ed.* **2017**, *56*, 14992-14996.
[126] U. K. Das, Y. Ben-David, G. Leitus, Y. Diskin-Posner, D. Milstein, *ACS Catal.* **2018**, 479-484.
[127] F. Bertini, M. Glatz, N. Gorgas, B. Stöger, M. Peruzzini, L. F. Veiros, K. Kirchner, L. Gonsalvi, *Chem. Sci.* **2017**, *8*, 5024-5029.
[128] A. Bruneau-Voisine, D. Wang, T. Roisnel, C. Darcel, J.-B. Sortais, *Catal. Commun.* **2017**, *92*, 1-4.
[129] M. Glatz, B. Stöger, D. Himmelbauer, L. F. Veiros, K. Kirchner, *ACS Catal.* **2018**, 4009-4016.
[130] A. Bruneau-Voisine, D. Wang, V. Dorcet, T. Roisnel, C. Darcel, J.-B. Sortais, *J. Catal.* **2017**, *347*, 57-62.
[131] A. Bruneau-Voisine, L. Pallova, S. Bastin, V. César, J.-B. Sortais, *Chem. Commun.* **2019**, *55*, 314-317.
[132] M. Mastalir, E. Pittenauer, G. Allmaier, K. Kirchner, *J. Am. Chem. Soc.* **2017**, *139*, 8812-8815.
[133] F. Freitag, T. Irrgang, R. Kempe, *J. Am. Chem. Soc.* **2019**, *141*, 11677-11685.
[134] S. S. Gawali, B. K. Pandia, C. Gunanathan, *Org. Lett.* **2019**, *21*, 3842-3847.
[135] Z. Guoying, I. Torsten, D. Thomas, K. Fabian, K. Rhett, *Angew. Chem. Int. Ed.* **2018**, *57*, 9131-9135.
[136] M. Perez, S. Elangovan, A. Spannenberg, K. Junge, M. Beller, *ChemSusChem* **2017**, *10*, 83-86.

[137] a) M. B. Widegren, G. J. Harkness, A. M. Z. Slawin, D. B. Cordes, M. L. Clarke, *Angew. Chem. Int. Ed.* **2017**, *56*, 5825-5828; b) L. Gade, H. Wadepohl, V. Vasilenko, C. K. Blasius, *Angew. Chem. Int. Ed.* **2017**, *56*, 8393-8397.
[138] a) R. van Putten, E. A. Uslamin, M. Garbe, C. Liu, A. Gonzalez-de-Castro, M. Lutz, K. Junge, E. J. M. Hensen, M. Beller, L. Lefort, E. A. Pidko, *Angew. Chem. Int. Ed.* **2017**, *56*, 7531-7534; b) A. Dubey, L. Nencini, R. R. Fayzullin, C. Nervi, J. R. Khusnutdinova, *ACS Catal.* **2017**, 3864-3868.
[139] a) R. Hua, J.-L. Jiang, *Curr. Org. Synth.* **2007**, *4*, 477-498; b) G. Mao, B. Jia, C. Wang, *Youji Huaxue* **2015**, *35*, 284-293; c) M. C. Lipke, A. L. Liberman-Martin, T. D. Tilley, *Angew. Chem. Int. Ed.* **2016**, *56*, 2260-2294.
[140] A. Choualeb, A. J. Lough, D. G. Gusev, *Organometallics* **2007**, *26*, 3509-3515.
[141] a) I. Klopsch, M. Finger, C. Würtele, B. Milde, D. B. Werz, S. Schneider, *J. Am. Chem. Soc.* **2014**, *136*, 6881-6883; b) I. Klopsch, M. Kinauer, M. Finger, C. Würtele, S. Schneider, *Angew. Chem. Int. Ed.* **2016**, *55*, 4786-4789; c) F. Schendzielorz, M. Finger, J. Abbenseth, C. Würtele, V. Krewald, S. Schneider, *Angew. Chem. Int. Ed.* **2019**, *58*, 830-834.
[142] M. Vogt, A. Nerush, M. A. Iron, G. Leitus, Y. Diskin-Posner, L. J. W. Shimon, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2013**, *135*, 17004-17018.
[143] M. Vogt, A. Nerush, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *Chem. Sci.* **2014**, *5*, 2043-2051.
[144] D. Wei, T. Roisnel, C. Darcel, E. Clot, J.-B. Sortais, *ChemCatChem* **2017**, *9*, 80-83.
[145] H. Li, D. Wei, A. Bruneau-Voisine, M. Ducamp, M. Henrion, T. Roisnel, V. Dorcet, C. Darcel, J.-F. Carpentier, J.-F. Soulé, J.-B. Sortais, *Organometallics* **2018**, *37*, 1271-1279.
[146] M. Mastalir, M. Glatz, E. Pittenauer, G. Allmaier, K. Kirchner, *Org. Lett.* **2019**, *21*, 1116-1120.
[147] V. Papa, K. Junge, M. Beller, *Chem. - Eur. J.* **2019**, *25*, 122-143.
[148] G. Zhang, B. L. Scott, S. K. Hanson, *Angew. Chem. Int. Ed.* **2012**, *51*, 12102-12106.
[149] J. Yuwen, S. Chakraborty, W. W. Brennessel, W. D. Jones, *ACS Catal.* **2017**, 3735-3740.
[150] G. Zhang, K. V. Vasudevan, B. L. Scott, S. K. Hanson, *J. Am. Chem. Soc.* **2013**, *135*, 8668-8681.
[151] a) G. Zhang, Z. Yin, S. Zheng, *Org. Lett.* **2016**, *18*, 300-303; b) Z. Yin, H. Zeng, J. Wu, S. Zheng, G. Zhang, *ACS Catal.* **2016**, *6*, 6546-6550; c) G. Zhang, J. Wu, H. Zeng, S. Zhang, Z. Yin, S. Zheng, *Org. Lett.* **2017**, *19*, 1080-1083.
[152] S. Fu, N.-Y. Chen, X. Liu, Z. Shao, S.-P. Luo, Q. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 8588-8594.
[153] J. Schneekönig, B. Tannert, H. Hornke, M. Beller, K. Junge, *Catal. Sci. Technol.* **2019**, *9*, 1779-1783.
[154] W. Zhou, Z. Wei, A. Spannenberg, H. Jiao, K. Junge, H. Junge, M. Beller, *Chem. - Eur. J.* **2019**, *25*, 8459-8464.
[155] B. Spiegelberg, A. Dell'Acqua, T. Xia, A. Spannenberg, S. Tin, S. Hinze, J. G. de Vries, *Chem. - Eur. J.* **2019**, *25*, 7820-7825.
[156] P. Daw, S. Chakraborty, G. Leitus, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *ACS Catal.* **2017**, 2500-2504.
[157] H. Li, A. Al-Dakhil, D. Lupp, S. S. Gholap, Z. Lai, L.-C. Liang, K.-W. Huang, *Org. Lett.* **2018**, *20*, 6430-6435.
[158] P. Puylaert, A. Dell'Acqua, F. El Ouahabi, A. Spannenberg, T. Roisnel, L. Lefort, S. Hinze, S. Tin, J. G. de Vries, *Catal. Sci. Technol.* **2019**, *9*, 61-64.
[159] K. V. Vasudevan, B. L. Scott, S. K. Hanson, *Eur. J. Inorg. Chem.* **2012**, 4898-4906.

[160] K.-W. Huang, H. Li, T. P. Goncalves, Q. Zhao, D. Gong, Z. Lai, Z.-X. Wang, J. Zheng, *Chem. Commun.* **2018**, *54*, 11395-11398.
[161] a) K. Arashiba, Y. Miyake, Y. Nishibayashi, *Nat. Chem.* **2010**, *3*, 120; b) S. Kuriyama, K. Arashiba, K. Nakajima, H. Tanaka, N. Kamaru, K. Yoshizawa, Y. Nishibayashi, *J. Am. Chem. Soc.* **2014**, *136*, 9719-9731.
[162] S. Chakraborty, H. Berke, *ACS Catal.* **2014**, *4*, 2191-2194.
[163] S. Chakraborty, O. Blacque, T. Fox, H. Berke, *Chem. - Asian J.* **2014**, *9*, 328-337.
[164] T. Leischner, A. Spannenberg, K. Junge, M. Beller, *Organometallics* **2018**, *37*, 4402-4408.
[165] R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.* **2001**, *40*, 40-73.
[166] B. L. Conley, M. K. Pennington-Boggio, E. Boz, T. J. Williams, *Chem. Rev.* **2010**, *110*, 2294-2312.
[167] a) J.-P. Djukic, J.-B. Sortais, L. Barloy, M. Pfeffer, *Eur. J. Inorg. Chem.* **2009**, 817-853; b) M. Albrecht, *Chem. Rev.* **2010**, *110*, 576-623.
[168] a) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879-5918; b) J. A. Leitch, C. G. Frost, *Chem. Soc. Rev.* **2017**, *46*, 7145-7153; c) F. F. Khan, S. K. Sinha, G. K. Lahiri, D. Maiti, *Chem. - Asian J.* **2018**, *13*, 2243-2256; d) S. De Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, *Adv. Synth. Catal.* **2014**, *356*, 1461-1479.
[169] J.-F. Yin, M. Velayudham, D. Bhattacharya, H.-C. Lin, K.-L. Lu, *Coord. Chem. Rev.* **2012**, *256*, 3008-3035.
[170] C. Gaiddon, M. Pfeffer, *Eur. J. Inorg. Chem.* **2017**, 1639-1654.
[171] a) R. Sun, X. Chu, S. Zhang, T. Li, Z. Wang, B. Zhu, *Eur. J. Inorg. Chem.* **2017**, 3174-3183; b) W. Baratta, P. Da Ros, A. Del Zotto, A. Sechi, E. Zangrando, P. Rigo, *Angew. Chem. Int. Ed.* **2004**, *43*, 3584-3588.
[172] N. U. Din Reshi, D. Senthurpandi, A. G. Samuelson, *J. Organomet. Chem.* **2018**, *866*, 189-199.
[173] a) W. Baratta, J. Schütz, E. Herdtweck, W. A. Herrmann, P. Rigo, *J. Organomet. Chem.* **2005**, *690*, 5570-5575; b) G. Balamurugan, R. Ramesh, J. G. Malecki, *ChemistrySelect* **2017**, *2*, 10603-10608; c) S. Bauri, S. N. R. Donthireddy, P. M. Illam, A. Rit, *Inorg. Chem.* **2018**, *57*, 14582-14593.
[174] a) P. Dani, T. Karlen, R. A. Gossage, S. Gladiali, G. van Koten, *Angew. Chem. Int. Ed.* **2000**, *39*, 743-745; b) M. Gagliardo, P. A. Chase, S. Brouwer, G. P. M. van Klink, G. van Koten, *Organometallics* **2007**, *26*, 2219-2227.
[175] a) W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando, P. Rigo, *Angew. Chem. Int. Ed.* **2005**, *44*, 6214-6219; b) W. Baratta, M. Bosco, G. Chelucci, A. Del Zotto, K. Siega, M. Toniutti, E. Zangrando, P. Rigo, *Organometallics* **2006**, *25*, 4611-4620; c) W. Baratta, K. Siega, P. Rigo, *Adv. Synth. Catal.* **2007**, *349*, 1633-1636; d) W. Baratta, M. Ballico, S. Baldino, G. Chelucci, E. Herdtweck, K. Siega, S. Magnolia, P. Rigo, *Chem. - Eur. J.* **2008**, *14*, 9148-9160; e) S. Giboulot, S. Baldino, M. Ballico, R. Figliolia, A. Pöthig, S. Zhang, D. Zuccaccia, W. Baratta, *Organometallics* **2019**, *38*, 1127-1142.
[176] a) W. Baratta, S. Baldino, M. J. Calhorda, P. J. Costa, G. Esposito, E. Herdtweck, S. Magnolia, C. Mealli, A. Messaoudi, S. A. Mason, L. F. Veiros, *Chem. - Eur. J.* **2014**, *20*, 13603-13617; b) S. Facchetti, V. Jurcik, S. Baldino, S. Giboulot, H. G. Nedden, A. Zanotti-Gerosa, A. Blackaby, R. Bryan, A. Boogaard, D. B. McLaren, E. Moya, S. Reynolds, K. S. Sandham, P. Martinuzzi, W. Baratta, *Organometallics* **2016**, *35*, 277-287.
[177] G. Bossi, E. Putignano, P. Rigo, W. Baratta, *Dalton Trans.* **2011**, *40*, 8986-8995.

[178] a) S. Agrawal, M. Lenormand, B. Martín-Matute, *Org. Lett.* **2012**, *14*, 1456-1459; b) W. Baratta, R. Figliolia, S. Baldino, H. G. Nedden, A. Zanotti-Gerosa, *Chem. - Eur. J.* **2017**, *23*, 14416-14419.
[179] W. Baratta, F. Benedetti, A. Del Zotto, L. Fanfoni, F. Felluga, S. Magnolia, E. Putignano, P. Rigo, *Organometallics* **2010**, *29*, 3563-3570.
[180] a) J.-B. Sortais, V. Ritleng, A. Voelklin, A. Holuigue, H. Smail, L. Barloy, C. Sirlin, G. K. M. Verzijl, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, M. Pfeffer, *Org. Lett.* **2005**, *7*, 1247-1250; b) J.-B. Sortais, L. Barloy, C. Sirlin, H. M. de Vries André, G. de Vries Johannes, M. Pfeffer, in *Pure Appl. Chem., Vol. 78*, **2006**, p. 457; c) N. Pannetier, J.-B. Sortais, P. S. Dieng, L. Barloy, C. Sirlin, M. Pfeffer, *Organometallics* **2008**, *27*, 5852-5859.
[181] a) L. N. Lewis, *J. Am. Chem. Soc.* **1986**, *108*, 743-749; b) B. Bagh, A. M. McKinty, A. J. Lough, D. W. Stephan, *Dalton Trans.* **2015**, *44*, 2712-2723.
[182] Q. Wang, H. Chai, Z. Yu, *Organometallics* **2018**, *37*, 584-591.
[183] a) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555-1575; b) T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Dalton Trans.* **2009**, 753-762; c) A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635-636; d) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681-703; e) R. H. Crabtree, *Organometallics* **2011**, *30*, 17-19; f) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 1229712; g) A. Corma, J. Navas, M. J. Sabater, *Chem. Rev.* **2018**, *118*, 1410-1459.
[184] M. Guerbet, *C. R, Acad. Sci. Paris* **1908**, 129-132.
[185] a) R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc., Chem. Commun.* **1981**, 611-612; b) Y. Watanabe, Y. Tsuji, Y. Ohsugi, *Tetrahedron Lett.* **1981**, *22*, 2667-2670.
[186] a) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* **2010**, *110*, 1611-1641; b) S. Bähn, S. Imm, L. Neubert, M. Zhang, H. Neumann, M. Beller, *ChemCatChem* **2011**, *3*, 1853-1864; c) M. Pera-Titus, F. Shi, *ChemSusChem* **2014**, *7*, 720-722; d) Q. Yang, Q. Wang, Z. Yu, *Chem. Soc. Rev.* **2015**, *44*, 2305-2329.
[187] a) D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. - Asian J.* **2007**, *2*, 403-410; b) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn, M. Beller, *Eur. J. Org. Chem.* **2008**, *2008*, 4745-4750.
[188] M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc.* **2009**, *131*, 1766-1774.
[189] G. W. Lamb, A. J. A. Watson, K. E. Jolley, A. C. Maxwell, J. M. J. Williams, *Tetrahedron Lett.* **2009**, *50*, 3374-3377.
[190] L. Jia, M. Makha, C.-X. Du, Z.-J. Quan, X.-C. Wang, Y. Li, *Green Chem.* **2019**, *21*, 3127-3132.
[191] a) J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland, R. Newton, *Org. Process Res. Dev.* **2015**, *19*, 1400-1410; b) A. P. Taylor, R. P. Robinson, Y. M. Fobian, D. C. Blakemore, L. H. Jones, O. Fadeyi, *Org. Biomol. Chem.* **2016**, *14*, 6611-6637.
[192] R. Labes, C. Mateos, C. Battilocchio, Y. Chen, P. Dingwall, G. R. Cumming, J. A. Rincon, M. J. Nieves-Remacha, S. V. Ley, *Green Chem.* **2018**, *21*, 59-63.
[193] O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Angew. Chem. Int. Ed.* **2009**, *48*, 7375-7378.
[194] A. Prades, R. Corberán, M. Poyatos, E. Peris, *Chem. - Eur. J.* **2008**, *14*, 11474-11479.
[195] S. Ruch, T. Irrgang, R. Kempe, *Chem. - Eur. J.* **2014**, *20*, 13279-13285.
[196] H. Yang, R. Mao, C. Luo, C. Lu, G. Cheng, *Tetrahedron* **2014**, *70*, 8829-8835.

[197] a) H. Hikawa, T. Koike, K. Izumi, S. Kikkawa, I. Azumaya, *Adv. Synth. Catal.* **2016**, *358*, 784-791; b) H. Hikawa, H. Imamura, S. Kikkawa, I. Azumaya, *Green Chem.* **2018**, *20*, 3044-3049.
[198] A. Martínez-Asencio, D. J. Ramón, M. Yus, *Tetrahedron Lett.* **2010**, *51*, 325-327.
[199] a) T. Yan, B. L. Feringa, K. Barta, *Nat. Commun.* **2014**, *5*, 5602; b) A. J. Rawlings, L. J. Diorazio, M. Wills, *Org. Lett.* **2015**, *17*, 1086-1089; c) H.-J. Pan, T. W. Ng, Y. Zhao, *Chem. Commun.* **2015**, *51*, 11907-11910; d) T. Yan, B. L. Feringa, K. Barta, *ACS Catal.* **2016**, *6*, 381-388.
[200] M. Mastalir, B. Stöger, E. Pittenauer, M. Puchberger, G. Allmaier, K. Kirchner, *Adv. Synth. Catal.* **2016**, *358*, 3824-3831.
[201] L. Homberg, A. Roller, K. C. Hultzsch, *Org. Lett.* **2019**, *21*, 3142-3147.
[202] K. Das, A. Mondal, D. Pal, H. K. Srivastava, D. Srimani, *Organometallics* **2019**, *38*, 1815-1825.
[203] a) S. Rösler, M. Ertl, T. Irrgang, R. Kempe, *Angew. Chem. Int. Ed.* **2015**, *54*, 15046-15050; b) M. Mastalir, G. Tomsu, E. Pittenauer, G. Allmaier, K. Kirchner, *Org. Lett.* **2016**, *18*, 3462-3465.
[204] a) M. Vellakkaran, K. Singh, D. Banerjee, *ACS Catal.* **2017**, 8152-8158; b) A. Afanasenko, S. Elangovan, M. C. A. Stuart, G. Bonura, F. Frusteri, K. Barta, *Catal. Sci. Technol.* **2018**, *8*, 5498-5505.
[205] a) R. Martínez, D. J. Ramón, M. Yus, *Org. Biomol. Chem.* **2009**, *7*, 2176-2181; b) Y. Takahashi, R. Kondo, M. Utsunomiya, T. Suzuki, H. T. Takeshita, Y. Obora, *ChemCatChem* **2019**, *11*, 2432-2437.
[206] N. J. Turner, S. Montgomery, J. Mangas-Sanchez, M. Thompson, G. Aleku, B. Dominguez, *Angew. Chem. Int. Ed.* **2017**, *56*, 10491-10494.
[207] a) D. Hollmann, *ChemSusChem* **2014**, *7*, 2411-2413; b) L. Zhang, Z. Han, X. Zhao, Z. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2015**, *54*, 6186-6189; c) Z.-Q. Rong, Y. Zhang, R. H. B. Chua, H.-J. Pan, Y. Zhao, *J. Am. Chem. Soc.* **2015**, *137*, 4944-4947; d) L.-C. Yang, Y.-N. Wang, Y. Zhang, Y. Zhao, *ACS Catal.* **2016**, 93-97.
[208] a) T. T. Dang, B. Ramalingam, A. M. Seayad, *ACS Catal.* **2015**, *5*, 4082-4088; b) O. Ogata, H. Nara, M. Fujiwhara, K. Matsumura, Y. Kayaki, *Org. Lett.* **2018**, *20*, 3866-3870.
[209] D. Deng, B. Hu, M. Yang, D. Chen, *Organometallics* **2018**, *37*, 3353-3359.
[210] Z. Liu, Z. Yang, X. Yu, H. Zhang, B. Yu, Y. Zhao, Z. Liu, *Adv. Synth. Catal.* **2017**, *359*, 4278-4283.
[211] A. Lator, S. Gaillard, A. Poater, J.-L. Renaud, *Org. Lett.* **2018**, *20*, 5985-5990.
[212] a) Y. Watanabe, T. Ohta, Y. Tsuji, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2647-2651; b) K.-I. Fujita, A. Komatsubara, R. Yamaguchi, *Tetrahedron* **2009**, *65*, 3624-3628.
[213] A. J. A. Watson, A. C. Maxwell, J. M. J. Williams, *J. Org. Chem.* **2011**, *76*, 2328-2331.
[214] S. Bähn, S. Imm, K. Mevius, L. Neubert, A. Tillack, J. M. J. Williams, M. Beller, *Chem. - Eur. J.* **2010**, *16*, 3590-3593.
[215] a) C. Feng, Y. Liu, S. Peng, Q. Shuai, G. Deng, C.-J. Li, *Org. Lett.* **2010**, *12*, 4888-4891; b) X. Cui, Y. Zhang, F. Shi, Y. Deng, *Chem. - Eur. J.* **2011**, *17*, 2587-2591.
[216] B. Paul, S. Shee, D. Panja, K. Chakrabarti, S. Kundu, *ACS Catal.* **2018**, 2890-2896.
[217] a) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Angew. Chem. Int. Ed.* **2007**, *46*, 8291-8294; b) D. Deng, B. Hu, Z. Zhang, S. Mo, M. Yang, D. Chen, *Organometallics* **2019**, *38*, 2218-2226.
[218] a) G. Guillena, D. J. Ramón, M. Yus, *Angew. Chem. Int. Ed.* **2007**, *46*, 2358-2364; b) Y. Obora, *ACS Catal.* **2014**, *4*, 3972-3981; c) F. Huang, Z. Liu, Z. Yu, *Angew. Chem. Int. Ed.* **2016**, *55*, 862-875.

[219] a) R. Martínez, G. J. Brand, D. J. Ramón, M. Yus, *Tetrahedron Lett.* **2005**, *46*, 3683-3686; b) R. Martínez, D. J. Ramón, M. Yus, *Tetrahedron* **2006**, *62*, 8988-9001.
[220] a) G. Onodera, Y. Nishibayashi, S. Uemura, *Angew. Chem. Int. Ed.* **2006**, *45*, 3819-3822; b) C. Xu, X.-M. Dong, Z.-Q. Wang, X.-Q. Hao, Z. Li, L.-M. Duan, B.-M. Ji, M.-P. Song, *J. Organomet. Chem.* **2012**, *700*, 214-218; c) F. Li, J. Ma, N. Wang, *J. Org. Chem.* **2014**, *79*, 10447-10455; d) D. Wang, K. Zhao, P. Ma, C. Xu, Y. Ding, *Tetrahedron Lett.* **2014**, *55*, 7233-7235.
[221] a) C. Schlepphorst, B. Maji, F. Glorius, *ACS Catal.* **2016**, *6*, 4184-4188; b) W. M. Akhtar, C. B. Cheong, J. R. Frost, K. E. Christensen, N. G. Stevenson, T. J. Donohoe, *J. Am. Chem. Soc.* **2017**, *139*, 2577-2580.
[222] D. Shen, D. L. Poole, C. C. Shotton, A. F. Kornahrens, M. P. Healy, T. J. Donohoe, *Angew. Chem. Int. Ed.* **2015**, *54*, 1642-1645.
[223] a) S. Elangovan, J.-B. Sortais, M. Beller, C. Darcel, *Angew. Chem. Int. Ed.* **2015**, *54*, 14483-14486; b) C. Seck, M. D. Mbaye, S. Coufourier, A. Lator, J. F. Lohier, A. Poater, T. R. Ward, S. Gaillard, J. L. Renaud, *ChemCatChem* **2017**, *9*, 4410-4416; c) S. Chakraborty, P. Daw, Y. Ben David, D. Milstein, *ACS Catal.* **2018**, 10300-10305.
[224] R. Martínez, D. J. Ramón, M. Yus, *Tetrahedron* **2006**, *62*, 8982-8987.
[225] a) J. Shi, B. Hu, P. Ren, S. Shang, X. Yang, D. Chen, *Organometallics* **2018**, *37*, 2795-2806; b) C. Zhang, J.-P. Zhao, B. Hu, J. Shi, D. Chen, *Organometallics* **2019**, *38*, 654-664; c) S. Thiyagarajan, C. Gunanathan, *J. Am. Chem. Soc.* **2019**, *141*, 3822-3827.
[226] Y. Li, H. Li, H. Junge, M. Beller, *Chem. Commun.* **2014**, *50*, 14991-14994.
[227] A. Kaithal, M. Schmitz, M. Hölscher, W. Leitner, *ChemCatChem* **2019**, DOI: 10.1002/cctc.201900788.
[228] K.-N. T. Tseng, S. Lin, J. W. Kampf, N. K. Szymczak, *Chem. Commun.* **2016**, *52*, 2901-2904.
[229] P. J. Black, G. Cami-Kobeci, M. G. Edwards, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Org. Biomol. Chem.* **2006**, *4*, 116-125.
[230] S. Thiyagarajan, C. Gunanathan, *ACS Catal.* **2017**, *7*, 5483-5490.
[231] M. L. Buil, M. A. Esteruelas, J. Herrero, S. Izquierdo, I. M. Pastor, M. Yus, *ACS Catal.* **2013**, *3*, 2072-2075.
[232] W. Ma, S. Cui, H. Sun, W. Tang, D. Xue, C. Li, J. Fan, J. Xiao, C. Wang, *Chem. - Eur. J.* **2018**, *24*, 13118-13123.
[233] A. Jana, C. B. Reddy, B. Maji, *ACS Catal.* **2018**, 9226-9231.
[234] a) T. Sawaguchi, Y. Obora, *Chem. Lett.* **2011**, *40*, 1055-1057; b) B. Anxionnat, D. Gomez Pardo, G. Ricci, J. Cossy, *Org. Lett.* **2011**, *13*, 4084-4087.
[235] T. Kuwahara, T. Fukuyama, I. Ryu, *RSC Adv.* **2013**, *3*, 13702-13704.
[236] a) Y. Iuchi, Y. Obora, Y. Ishii, *J. Am. Chem. Soc.* **2010**, *132*, 2536-2537; b) L. Guo, Y. Liu, W. Yao, X. Leng, Z. Huang, *Org. Lett.* **2013**, *15*, 1144-1147; c) L. Guo, X. Ma, H. Fang, X. Jia, Z. Huang, *Angew. Chem. Int. Ed.* **2015**, *54*, 4023-4027; d) Y. Tsukamoto, S. Itoh, M. Kobayashi, Y. Obora, *Org. Lett.* **2019**, *21*, 3299-3303.
[237] N. Deibl, R. Kempe, *J. Am. Chem. Soc.* **2016**, *138*, 10786-10789.
[238] A. E. Putra, Y. Oe, T. Ohta, *Tetrahedron Lett.* **2017**, *58*, 1098-1101.
[239] a) M. G. Edwards, J. M. J. Williams, *Angew. Chem. Int. Ed.* **2002**, *41*, 4740-4743; b) M. G. Edwards, R. F. R. Jazzar, B. M. Paine, D. J. Shermer, M. K. Whittlesey, J. M. J. Williams, D. D. Edney, *Chem. Commun.* **2004**, 90-91.
[240] Y. Tsuji, K. T. Huh, Y. Ohsugi, Y. Watanabe, *J. Org. Chem.* **1985**, *50*, 1365-1370.
[241] Y. Tsuji, Y. Yokoyama, K.-T. Huh, Y. Watanabe, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3456-3458.

[242] T. Kondo, S. Kotachi, Y. Watanabe, *J. Chem. Soc., Chem. Commun.* **1992**, 1318-1319.
[243] a) C. S. Cho, B. T. Kim, T.-J. Kim, S. C. Shim, *Chem. Commun.* **2001**, 2576-2577; b) K. Taguchi, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **2005**, *46*, 4539-4542.
[244] C. S. Cho, W. X. Ren, S. C. Shim, *Bull. Korean Chem. Soc.* **2005**, *26*, 2038-2040.
[245] C. S. Cho, B. T. Kim, H.-J. Choi, T.-J. Kim, S. C. Shim, *Tetrahedron* **2003**, *59*, 7997-8002.
[246] M. Mastalir, M. Glatz, E. Pittenauer, G. Allmaier, K. Kirchner, *J. Am. Chem. Soc.* **2016**, *138*, 15543-15546.
[247] C. S. Cho, S. G. Oh, *Tetrahedron Lett.* **2006**, *47*, 5633-5636.
[248] T. Hille, T. Irrgang, R. Kempe, *Chem. - Eur. J.* **2014**, *20*, 5569-5572.
[249] Y. Tsuji, S. Kotachi, K. T. Huh, Y. Watanabe, *J. Org. Chem.* **1990**, *55*, 580-584.
[250] A. Porcheddu, M. G. Mura, L. De Luca, M. Pizzetti, M. Taddei, *Org. Lett.* **2012**, *14*, 6112-6115.
[251] M. Peña-López, H. Neumann, M. Beller, *Chem. - Eur. J.* **2014**, *20*, 1818-1824.
[252] A. J. Blacker, M. M. Farah, M. I. Hall, S. P. Marsden, O. Saidi, J. M. J. Williams, *Org. Lett.* **2009**, *11*, 2039-2042.
[253] P. Daw, Y. Ben-David, D. Milstein, *ACS Catal.* **2017**, 7456-7460.
[254] N. D. Schley, G. E. Dobereiner, R. H. Crabtree, *Organometallics* **2011**, *30*, 4174-4179.
[255] P. Daw, S. Chakraborty, J. A. Garg, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2016**, *55*, 14373-14377.
[256] S. Michlik, R. Kempe, *Nat. Chem.* **2013**, *5*, 140-144.
[257] F. Kallmeier, B. Dudziec, T. Irrgang, R. Kempe, *Angew. Chem. Int. Ed.* **2017**, *56*, 7261-7265.
[258] S. P. Midya, V. G. Landge, M. K. Sahoo, J. Rana, E. Balaraman, *Chem. Commun.* **2018**, *54*, 90-93.
[259] a) T. Yan, K. Barta, *ChemSusChem* **2016**, *9*, 2321-2325; b) B. Emayavaramban, M. Sen, B. Sundararaju, *Org. Lett.* **2016**, *19*, 6-9.
[260] a) M. Zhang, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2013**, *52*, 597-601; b) M. Zhang, X. Fang, H. Neumann, M. Beller, *J. Am. Chem. Soc.* **2013**, *135*, 11384-11388.
[261] N. Deibl, K. Ament, R. Kempe, *J. Am. Chem. Soc.* **2015**, *137*, 12804-12807.
[262] N. Deibl, R. Kempe, *Angew. Chem. Int. Ed.* **2017**, *56*, 1663-1666.
[263] D. C. Schmitt, A. P. Taylor, A. C. Flick, R. E. Kyne, *Org. Lett.* **2015**, *17*, 1405-1408.
[264] S. Michlik, R. Kempe, *Angew. Chem. Int. Ed.* **2013**, *52*, 6326-6329.
[265] K. Alfonsi, J. Colberg, P. J. Dunn, T. Fevig, S. Jennings, T. A. Johnson, H. P. Kleine, C. Knight, M. A. Nagy, D. A. Perry, M. Stefaniak, *Green Chem.* **2008**, *10*, 31-36.
[266] O. Robles, D. Romo, *Nat. Prod. Rep.* **2014**, *31*, 318-334.
[267] B. Li, T. Roisnel, C. Darcel, P. H. Dixneuf, *Dalton Trans.* **2012**, *41*, 10934-10937.
[268] a) J. Kothandaraman, M. Czaun, A. Goeppert, R. Haiges, J.-P. Jones, R. B. May, G. K. S. Prakash, G. A. Olah, *ChemSusChem* **2015**, *8*, 1442-1451; b) Y. Zhang, A. D. MacIntosh, J. L. Wong, E. A. Bielinski, P. G. Williard, B. Q. Mercado, N. Hazari, W. H. Bernskoetter, *Chem. Sci.* **2015**, *6*, 4291-4299.