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Modification of bis-Abnormal N-Heterocyclic Carbene Phosphino Ruthenium Complexes and Influences on Transfer Hydrogenation and Oppenauer-type Oxidation Reactions

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"All the world is a laboratory to the inquiring mind."

Martin H. Fischer (1879-1962)

In the hope that, even though I will be leaving my laboratory,

the way of laboratory thinking will never leave me.

Acknowledgements

First and foremost, I express my thanks to my doctoral supervisor

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controls. You bring a lot of fun to the lab. Next, I want to thank **Yogi Büchele** (aka Wolfgang aka Günni). Even though I acted as kind of your co-supervisor during your master thesis, in cooperation with Marco, you usually did most of the work yourself, so that not much supervision was required. I am glad, that the group managed to win you as a colleague and wish you the best for all of your ongoing projects, I am especially interested in completion of the "Yoginator", which you are working on with Alex and Leon. **Shaoheng Qin**, as the newest member of the Kühn group I wish you good luck with your project, which is somewhat of a curiosity compared to the other topics we work on. Even though you have a large language barrier, you always try to take part in group activities, keep up the good work. **Carla Hoefer**, as Greta's master student I enjoyed working with you in the bottom lab. You always retained a positive attitude, even though there were some difficult times during the project. I hope you have a great time during your internship and I wish you all the best for your upcoming doctorate in our group.

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Abstract

The preparation and characterization of *bis*-abnormal *N*-heterocyclic carbene (aNHC) phosphine ruthenium complexes [Ru(OAc)(aNHC-ethyl-PPh$_2$)$_2$)]Br **1** and **3** are described. They are prepared from 1-(2-diphenylphosphino-ethyl)-3-aryl-imidazolium bromide (aryl = phenyl for **1** and di-*iso*-propylphenyl for **3**) and Ru(OAc)$_2$(PPh$_3$)$_2$ as precursor *via* displacement of PPh$_3$ and carbene deprotonation in THF at 60 °C and application of NaOAc as base, similar to a previously reported mesityl analogue **2**. Complex **3** is utilized, due to its higher stability in regards to **1** and **2**, for mechanistic investigations on the formation of this complex class and kinetic and thermodynamic intermediates **3a** and **3b** identified as preceding mono-aNHC species. All complexes are applied as catalysts in both transfer hydrogenation (TH) of acetophenone as well as Oppenauer-type oxidation of *α*-tetralol in a comparative study, exhibiting exceptionally high activities. In TH, **1** shows the highest turn-over frequencies (TOF) of up to 550 000 h^{-1} whilst **3** displays highest TOFs of up to 280 000 h^{-1} in Oppenauer-type oxidation, resulting in a **1** > **2** > **3** trend for TH and **3** > **2** > **1** for the latter. Whilst the activity in TH is likely due to accessibility of the active center, as demonstrated by buried volume calculations based on density functional theory (DFT), the inverse trend for the Oppenauer-type oxidation is rationalized by inversion of the rate determining step (rds) from ketone insertion to the reverse alkoxide *β*-H elimination, facilitated by more bulky wingtip substituents. In a second investigation, a heterobimetallic mixed normal/abnormal *N*-heterocyclic dicarbene (NHDC) rhodium ruthenium complex [Ru(OAc)(Mes-NHC-methyl-PPh$_2$)(Mes-aNHC-methyl-PPh$_2$)RhCl(cod)] **4** is prepared as a comparison to an iridium analogue **5**. The complexes are compared according to their SC-XRD structure, displaying changes in specific carbene-metal bonds and applied as catalysts in the TH of acetophenone, **4** displaying a TOF of 6 700 h^{-1}. By comparison of these complexes, it is concluded that whilst the introduction of a second metal center results in significantly lower catalytic activity compared to monometallic complexes, the nature of the second metal has only a small impact, at least regarding rhodium and iridium.

Zusammenfassung

Die Herstellung und Charakterisierung von *bis*-abnormalen *N*-heterocyclischen Carben (aNHC) Phosphin Ruthenium Komplexen [Ru(OAc)(aNHC-ethyl-PPh$_2$)$_2$)]Br **1** und **3** werden beschrieben. Sie werden aus 1-(2-Diphenylphosphino-ethyl)-3-aryl-imidazoliumbromid (Aryl = Phenyl für **1** und Di-*iso*-propylphenyl für **3**) und Ru(OAc)$_2$(PPh$_3$)$_2$ als Vorstufe durch Verdrängung von PPh$_3$ und Carben-Deprotonierung in THF bei 60 °C und Verwendung von NaOAc als Base hergestellt, ähnlich zu einem zuvor beschriebenen Mesityl-Analogon **2**. Komplex **3** wird aufgrund seiner höheren Stabilität gegenüber **1** und **2** für mechanistische Bildungsuntersuchungen verwendet und die kinetischen und thermodynamischen Zwischenprodukte **3a** und **3b** als vorangehende Mono-aNHC-Spezies identifiziert. Alle Komplexe werden in einer Vergleichsstudie sowohl in der Transferhydrierung (TH) von Acetophenon als auch in der Oppenauer-Oxidation von α-Tetralol als Katalysatoren eingesetzt und zeigen außergewöhnlich hohe Aktivitäten. In TH zeigt **1** die höchsten Wechselzahlen von bis zu 550 000 h^{-1}, während **3** die höchsten Wechselzahlen von bis zu 280 000 h^{-1} in der Oppenauer-Oxidation zeigt, was zu einem **1** > **2** > **3** Trend für TH und **3** > **2** > **1** für letzteres führt. Während die Aktivität in TH wahrscheinlich auf die Zugänglichkeit des aktiven Zentrums zurückzuführen ist, was durch Berechnungen auf Grundlage der Dichtefunktionaltheorie (DFT) gezeigt werden kann, wird der umgekehrte Trend für die Oppenauer-Oxidation durch Inversion des geschwindigkeitsbestimmenden Schritts von der Keton-Insertion zur Alkoxid-β-H-Eliminierung erklärt, welche durch die sperrigeren Wingtip-Substituenten begünstigt wird. In einer zweiten Untersuchung wird ein heterobimetallischer gemischt normaler/abnormaler *N*-heterocyclischer Dicarben (NHDC) Rhodium Ruthenium Komplex [Ru(OAc)(Mes-NHC-Methyl-PPh$_2$)(Mes-aNHC-Methyl-PPh$_2$)RhCl(cod)] **4** als Vergleich mit einem Iridium-Analogon **5** hergestellt. Die Komplexe werden gemäß ihrer SC-XRD Struktur verglichen, welche Abweichungen in spezifischen Carben-Metall-Bindungen zeigt, und als Katalysatoren in der TH von Acetophenon eingesetzt. **4** zeigt eine Wechselzahl von 6 700 h^{-1}. Aus dem Vergleich dieser Komplexe wird geschlossen, dass die Einführung eines zweiten Metallzentrums zwar zu einer deutlich geringeren katalytischen Aktivität führt, verglichen mit monometallischen Komplexen, die Art des zweiten Metalls jedoch nur einen geringen Einfluss hat, zumindest was Rhodium und Iridium betrifft.

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I Introduction

1. Ruthenium

1.1. Discovery

In modern science, chemists have accustomed to the fact, that chemical elements follow a "natural order" in regards to their chemical and physical properties. This periodicity has been known as early as 1869, when Russian Dmitri Ivanovich Mendeleev[1] and German Lothar Meyer[2] independently reported their versions of what is known today as the periodic table of (chemical) elements (PTE, see Figure 1). In a similar fashion, other chemists had also previously attempted to find a "natural order" of elements, examples of which are Newlands octave rule in 1864[3,4] or Döbereiner's triads in 1817.[5,6] In the PTE, elements were ordered according to their mass and grouped regarding their chemical properties. In doing so, they left gaps for yet undiscovered elements, for which Mendeleev went as far as even predicting chemical and physical properties.[7,8] This principle offered an excellent tool and guide for chemists interested in finding new elements, many of which were successfully determined in the following years from these predictions, such as scandium,[9] gallium[10] and germanium.[11]

Reihen	Gruppo I. — R'O	Gruppo II. — RO	Gruppo III. — R'O³	Gruppe IV. RH⁴ RO²	Gruppe V. RH³ R'O⁵	Gruppe VI. RH² RO³	Gruppe VII. RH R'O⁷	Gruppo VIII. — RO⁴
1					H=1			
2	Li=7	Bo=9,4	B=11	C=12	N=14	O=16	F=19	
3	Na=23	Mg=24	Al=27,3	Si=28	P=31	S=32	Cl=35,5	
4	K=39	Ca=40	—=44	Ti=48	V=51	Cr=52	Mn=55	Fo=56, Co=59, Ni=59, Cu=63.
5	(Cu=63)	Zn=65	—=68	—=72	As=75	So=78	Br=80	
6	Rb=85	Sr=87	?Yt=88	Zr=90	Nb=94	Mo=96	—=100	Ru=104, Rh=104, Pd=106, Ag=108.
7	(Ag=108)	Cd=112	In=113	Sn=118	Sb=122	Te=125	J=127	
8	Cs=133	Ba=137	?Di=138	?Co=140	—	—	—	— — — —
9	(—)							
10	—	—	?Er=178	?La=180	Ta=182	W=184	—	Os=195, Ir=197, Pt=198, Au=199.
11	(Au=199)	Hg=200	Tl=204	Pb=207	Bi=208	—	—	
12	—	—	—	Th=231	—	U=240	—	— — — —

Figure 1. Periodic table of the elements (PTE) as presented by Dmitri Ivanovich Mendeleev in 1871. Blank spaces represent predicted element slots. (Creative Commons License)

Prior to this however, elemental "discoveries" or isolations were more random and commonly went hand in hand with new industrial processes and reaction or isolation techniques. One such discovery was during the time of the gold fever. Here, platinum was observed as an impurity in gold ore[12] and finally characterized by Spanish Antonio de Ulloa in 1748.[13] Consequently, palladium and rhodium[14-16] as well as iridium and osmium[17-19] were themselves discovered as impurities in platinum ores by the English chemists William Hyde Wollaston and Smithson Tennant in 1803 and 1804, respectively. Driven by these discoveries, many chemists attempted to isolate further unknown elements from platinum ores as a promising source of new metals.

In 1808, Polish scientist Jędrzej Śniadecki (see Figure 2) reported the potential discovery of a new element, which he had isolated as red needles from platinum ore from South America, which he named vestium (in accordance to the asteroid Vesta).[20] He submitted his discovery to the French and Russian academies of science but neither could verify his results. After not being able to reproduce his own findings, he retracted his claim.[21,22] A decade later, the Swedish and German chemists Jöns Jakob Berzelius and Gottfried Wilhelm Osann (see Figure 2) began their own experiments using platinum ore from newly discovered deposits in the Ural Mountains. In 1828, Osann claimed to have found an unknown metal which he named ruthenium (Latin, *ruthenia*), in accordance to the place of discovery, along with two additional metals pluranium and polinium.[23-25] These claims were however disputed by Berzelius and after Osann was not able to verify his findings, he too retracted his claim.[26] In 1841, Russian-German chemist Karl Ernst Claus (see Figure 2) began attempts to follow up on the experiments performed by Osann and was finally able to isolate ruthenium in 1844.[27] These findings were successfully reproduced and verified by the initially skeptical Berzelius in 1845, which is why Claus is today considered the official discoverer of ruthenium. Whilst he chose to keep the same name as Osann, he did this not in accordance to Russia as the site of ore origin but instead as his motherland, hence why ruthenium is today considered a patriotic element.[25]

Figure 2. From left to right: Jędrzej Śniadecki (1768-1838), Jöns Jakob Berzelius (1779-1848), Gottfried Wilhelm Osann (1796-1866) and Karl Ernst Claus (1796-1864). (Creative Commons Licenses)

Claus was also able to show, that Osann's samples had indeed contained ruthenium, but that the metal Osann had believed to be ruthenium had instead been mainly silicic and titanic acids, iron peroxide and zirconia. He had missed to identify ruthenium as he had been applying hydrochloric acid to his sample without examining the solution.[25] Similarly, Śniadecki had reportedly discovered his vestium in the *aqua-regia* soluble fraction, whilst ruthenium is known today to be insoluble, in addition with additional discrepancies regarding chemical reactivity. Unfortunately, it is unclear what Śniadecki had identified as vestium, as his samples were lost during Russia's annexation of Lithuania.[22] Therefore, Claus is today denoted as the official discoverer of ruthenium, as he was the first to undoubtedly identify, verify and characterize the

chemical properties of his new metal, whilst the previous reports remain speculations.[28] Ruthenium therefore represents the last metal of the platinum metals to be discovered.

1.2. Properties, Production and Application

In the modern periodic table of elements (PTE), the transition metal ruthenium is formally assigned to the iron group 8 together with osmium and hassium. However, ruthenium was not only found together with other platinum metals (both in elemental and combined form) but also shares similar physical and chemical properties such as density (12.45 g·cm⁻³), melting point (2310 °C), boiling point (4150 °C), atom radii and atomization energies to other elements in horizontal configuration in the PTE such as rhodium and palladium.[29] These are also defined as lighter platinum metals, whilst osmium, iridium and platinum count to the heavier platinum metals (see Figure 3). Due to its nature as a noble metal, it is rather unreactive and forms oxides (e.g. RuO_4) or halogenides (e.g. RuF_6 or $RuCl_3$) only at high temperatures. It is also mostly insoluble in acids such as hydrofluoric acid, sulfuric acid, nitric acid and also *aqua regia*.[30]

Group 8 Fe-group	Group 9 Co-group	Group 10 Ni-group	
Fe	Co	Ni	} iron metals
Ru	Rh	Pd	} lighter platinum metals
Os	Ir	Pt	} heavier platinum metals
Hs	Mt	Ds	} hassium metals

Figure 3. Classification of ruthenium (Ru) in the periodic table of elements.[29]

Ruthenium itself is brittle, hard and of silver-white appearance and relatively rare with concentrations of 0.02 ppm in the earth's shell and 100 ppt in the earth's crust.[29,31,32] Minable ore deposits used today are the dunite bodies in the Ural Mountains and South Africa (Bushveld) as well as certain areas in North- and South America (Stillwater, US; Ontario, Canada; Columbia). However, the extraction and purification of ruthenium from these ores is rather complicated and requires a multi-step procedure, relying heavily on oxidizability, volatility and solubility of the various platinum group metals (PGM, see Figure 4).[29]

Initially, the mined ores are ground and the lighter particles separated from the metal containing minerals by flotation and the latter isolated by filtration. Several smelting and reduction/oxidation steps in a furnace involving the formation of a various matte (term in metallurgy for molten metal sulfide phase during smelting) phases finally yield highly concentrated (>30 wt%) PGM, of which base metals are removed by treatment with sulfuric acid and oxygen.[33] In the following steps, the various metals are separated from each other

depending on their solubility, applying selective oxidation and reduction steps, finally resulting in the isolation of RuO_4.
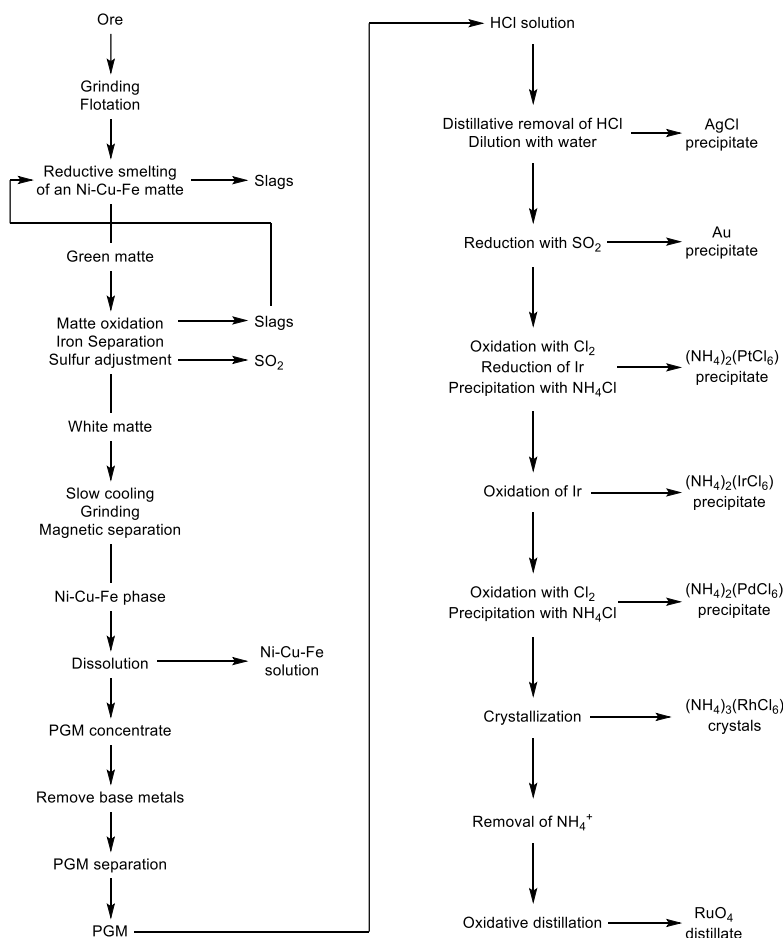
Figure 4. Isolation of platinum group metals (PGM) from ores (left) and separation thereof (right).[33]

This can then be added to an alkali metal hydroxide solution and the precipitated RuO_2 reduced with hydrogen to elemental ruthenium.[29] The worldwide production is estimated at roughly 30 t/year, with 13.8 t applied in electrical devices, 7.7 t in catalysis and 4.6 t in electrochemistry.[34] Specific applications include its use as additive for hardening of Pt metals,[29] as catalyst for hydrogenation,[35] methanation,[36] metathesis,[37] ammonia synthesis,[38] as promoter in the Fischer-Tropsch synthesis[39] and as catalytic converter in the exhaust of motorized vehicles.

For catalytic applications, similar to other transition metals, ruthenium can form a large variety of complexes in a variety of oxidation states, upon binding to soft ligands.[29,40] Although known oxidation states of ruthenium range from -II over zero to +VIII (+II being most common), complexes with both very high (>IV) and low (<II) states are rare.[29] These complexes have been reported with a variety of ligands including phosphines (e.g. first generation Grubbs catalyst, see Figure 5a),[41] halides, cyclopentadienyl (e.g. Shvo catalyst, see Figure 5b),[42]

carbon monoxide, hydride as well as *N*-heterocyclic carbenes (NHCs).[43] Of these, ruthenium NHC complexes have grown in interest, especially for the reduction of functional groups.[44]
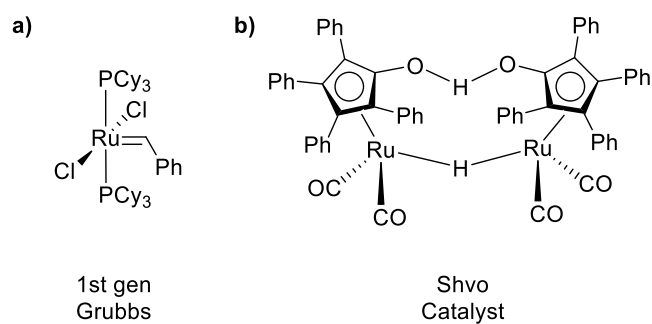
Figure 5. a) First generation Grubbs catalyst and b) Shvo catalyst as examples for Ru complexes.[41,42]

2. *N*-Heterocyclic Carbenes

2.1. History of *N*-Heterocyclic Carbenes

Although *N*-heterocyclic carbenes (NHCs) play an important role in modern transition metal complex chemistry, as shown by a number of publications and reviews, they still represent a relatively young field of research.[45,46] Even though the synthesis of simple (non-*N*-heterocyclic) carbenes has been attempted as early as 1835 by Dumas *et al.*,[47] carbenes in general were thought to be too reactive to isolate and seen as laboratory curiosities representing highly reactive intermediate species.[46,48] Following reports by Breslow from 1957[49] and 1958,[50] in which the involvement of a stable nucleophilic and heterocyclic carbene (described as a thiazol-2-ylidene derivative, see Figure 6) in the catalytic mechanism of vitamin B_1 was suggested, the interest in carbenes as isolatable species increased.[51]
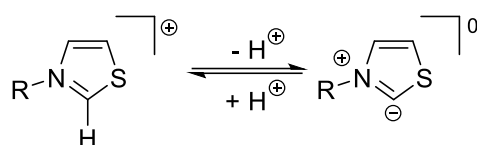
Figure 6. Thiazol-2-ylidene zwitterion intermediate species by proton loss from thiazolium salt under mild conditions as suggested by Breslow in 1957 and 1958.[49,50]

In 1962 Wanzlick investigated the reactivity and stability aspects of nucleophilic carbenes, suggesting potential for a large variety of preparative possibilities.[52] In particular, an equilibrium of carbenes forming dimers was suggested (see Figure 7a). This led to independent reports by Wanzlick *et al.* (see Figure 7b) as well as by Öfele (see Figure 7c) in 1968,[53,54] presenting the first applications of NHCs as ligands in metalorganic complexes.
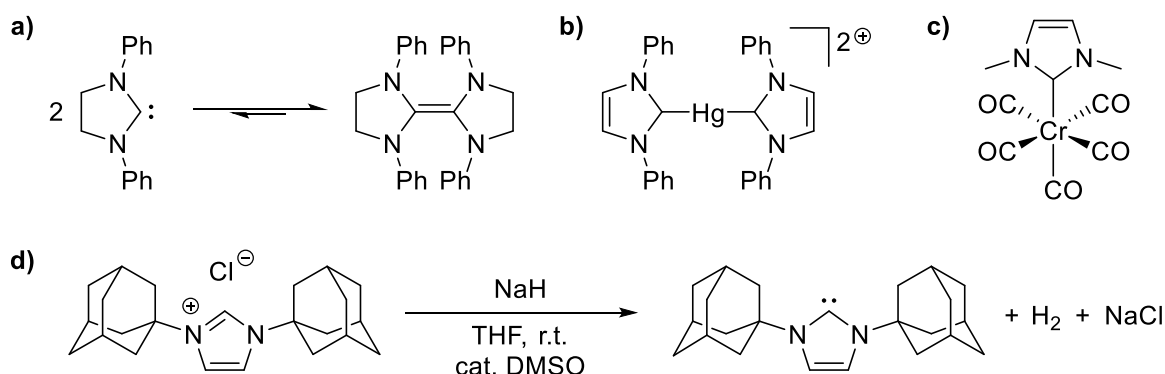
Figure 7. a) Wanzlick equilibrium of 1,3-bisphenyl-4,5-dihydro-imidazol-2-ylidene and its corresponding dimer in 1962,[52] b) Application of an NHC in metalorganic complex by Wanzlick in 1968,[53] c) Application of an NHC in metalorganic complex by Öfele in 1968,[54] d) Preparation of 1,3-di-1-adamantyl-imidazol-2-ylidene as first bench stable NHC by Arduengo in 1991.[55]

However, isolation of the free carbene was not possible until 23 years later, when Arduengo *et al.* were able to fully isolate and characterize bench stable 1,3-di-1-adamantyl-imidazol-2-ylidene as colorless crystals by deprotonation of the imidazolium salt (see Figure 7d).[55] The achieved stabilization, utilizing a π-donor effect from the electron rich NCCN π-system as well

as an σ-electronegativity effect, had been proposed by Wanzlick in 1962. However, the additional steric hindrance induced by the adamantly was reported as crucial for successful preparation, as previous works applying merely electronic effects had been unsuccessful. Due to this achievement, NHCs are today sometimes also referred to as Arduengo carbenes.

In the following years, a variety of complexes and applications including NHC ligands were reported. In 1995, Herrmann *et al.* introduced Pd/carbene systems (see Figure 8a) as a new type of catalyst for Heck coupling reactions with high thermal and hydrolytic stability, representing the first example of catalytically active NHC catalysts as alternative to phosphines.[56] Following the successful implementation of NHCs in Heck coupling catalysis, their importance in other applications rose immensely. One major issue was the metal catalyzed C-C bond metathesis reaction, relevant both in organic and polymer chemistry as well as in industrial processes. Here, previously applied ruthenium phosphine complexes, such as the 1st generation Grubbs catalyst, could successfully be substituted by the more practical and active NHC catalysts. In 1998, the first alkylidene NHC ruthenium catalyst was successfully applied in the metathesis of olefins (see Figure 8b).[57]
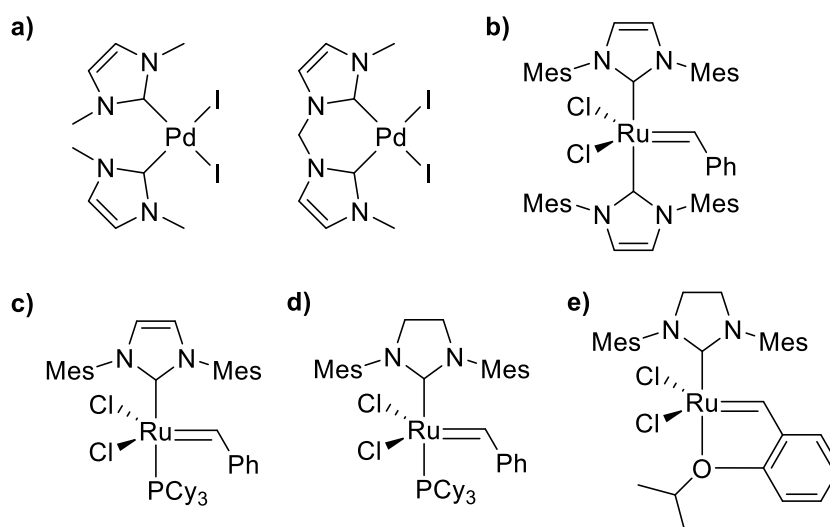
Figure 8. a) First catalytically active Pd/carbene catalysts for Heck coupling by Herrmann *et al.* 1995,[56] b) First alkylidene NHC ruthenium catalyst by Herrmann *et al.* 1998,[57] c) Mono-substituted NHC catalyst independently reported by Nolan *et al.*,[58] Grubbs *et al.*[59] as well as Fürstner and Herrmann *et al.* 1999,[60] d) 2nd generation Grubbs catalyst 1999,[61] e) Hoveyda-Grubbs catalyst 2000.[62]

This was quickly followed by a series of publications in a short time period, indicating the high competitiveness of this field. In March of 1999, Nolan *et al.*[58] and Grubbs *et al.*[59] independently reported the preparation of a mono-substituted NHC complex (see Figure 8c) applying the procedure previously reported by Herrmann *et al.* showing high activity in ring-closing metathesis reactions. In June of the same year, Fürstner and Herrmann *et al.* independently described the same complex as an example of a more comprehensive series of catalysts.[60] In August of 1999, Grubbs *et al.* reported a saturated analogue (see Figure 8d), what is nowadays known as the 2nd generation of Grubbs catalysts.[61] Due to the saturation of the imidazole

ligands, a higher basicity was reasoned, resulting in even higher metathesis activity. These set a milestone for metathesis reactions and are the foundation of modern commercially applied catalysts. In 2000, Hoveyda *et al.* further modified the 2nd generations Grubbs catalysts by a chelating ortho-*iso*-propoxybenzylidene moiety to replace the remaining phosphine ligand, referred to as Hoveyda-Grubbs catalysts (see Figure 8e).[62] This resulted in higher stability, albeit at the cost of activity. The culmination of these works was highlighted by award of the Nobel Prize in Chemistry in 2005 to Chauvin, Grubbs and Schrock for their individual work in the field of metathesis.[63]

The competition for olefin metathesis catalysts was also visible in industry, as indicated by a multi-year lawsuit between Materia Inc., which licensed Grubbs' catalyst, and Evonik Industries AG, applying Herrmann's catMETium® catalysts. In 1998, Herrmann had filed his patents in Germany whilst Materia had licensed Grubbs' catalysts in 2000 and 2001 in the United States. Herrmann's patents were however filed in the United States only in 2002 and 2003, creating a problematic scenario as to the ownership of these patents.[64] In 2009 and 2010 a lawsuit ensued, with Evonik filing against Materia for infringement and violation of their patents, whilst Materia counter-sued for the same. In 2012, the European Patent Office revoked one of Herrmann's patents following the challenge by Materia. The following year, the Federal District Court in Wilmington, Deleware in the United States however ruled in favor of Evonik, accepting the claims that Materia was indeed infringing on their patents, hindering Materia's attempt to broaden the scope of their patent whilst simultaneously narrowing the scope of Evonik's patent.[64,65] Finally, in 2017, the court dispute was settled, confirming the validity of Evonik's patents.[66,67] Materia agreed not to additionally sue Evonik or any of their customers in the future and was also fined 1.5 million US$ plus expenses. However, Evonik also allowed Materia to produce and sell the catalysts covered by the patents, resulting in a mutually beneficial agreement between the two adversaries.[68]

2.2. Reactivity and General Aspects

As previously described, NHCs were historically discovered and applied as ligand alternatives to phosphines in organometallic complexes due to both their relatively simple preparation and tunability for various applications as well as advantageous electronic effects.[45,69,70] In general, NHCs are described as heterocycles containing the following structural features: a carbene moiety, defined as neutral divalent carbon atoms with two unsaturated valence electrons; two (neighboring) nitrogen or heteroatoms; wingtip substituents (also: *N*-substituents) and a backbone structure, either saturated or unsaturated (see Figure 9a,b).[46,71] It is to be noted, that this work will focus on the class of imidazole-based NHCs, other special sub-classes such as triazoles or cyclic alkyl amino carbenes (CAACs) will however not be discussed.
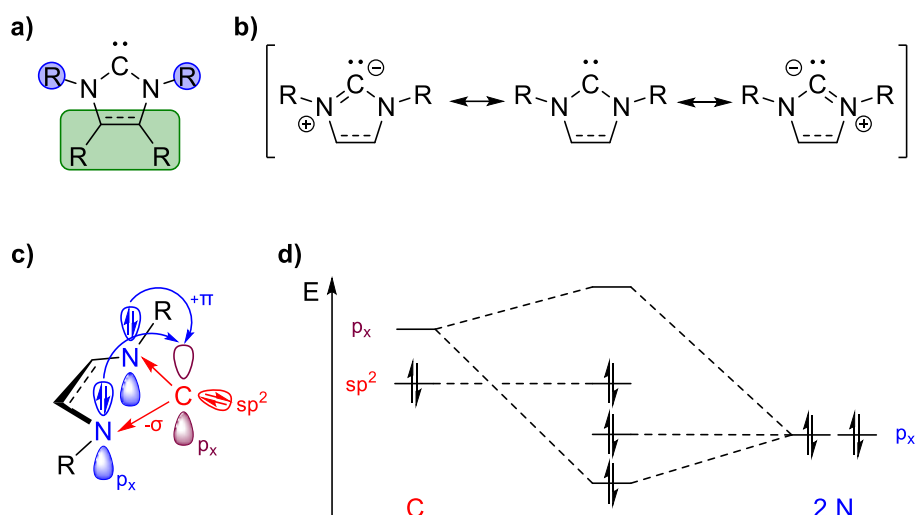
Figure 9. a) General structure of a NHC moiety with divalent carbon, two neighboring nitrogen atoms, wingtip substituents (blue) and backbone (green), b) zwitterionic states of an NHC, c) electronic stabilization within the NHC with π-donation (blue) and σ-withdrawing effect (red), d) molecular orbital diagram of a free NHC regarding the NCN moiety.[72]

Whilst simple carbenes are commonly highly reactive and instable due to their incomplete electron octet, the same does not hold true for NHCs. In these, the instable carbene moiety is stabilized by both a -I and +M effect of neighboring nitrogen or heteroatoms.[46] Whilst the carbene displays a sp^2 orbital occupied by two singlet electrons, the corresponding p_x orbital is electron deficient. The adjacent nitrogen atoms however display electron rich p_x orbitals, which can compensate this *via* π-donation. In addition, the high electronegativity leads to a σ-withdrawing effect from the sp^2 orbital, resulting in stabilization of the carbene (see Figure 9c,d).[72-75] Furthermore, bulky wingtip substituents have been shown to provide kinetic protection to the carbene and unsaturated backbone structures can further increase thermodynamic stability by inducing aromaticity.[76,77] Albeit these effects are negligible regarding NHC stabilization in comparison to the electronic effects of the heteroatoms, these two structural features are responsible for the highly interesting tunability, as they can easily be adjusted according to the required needs, greatly influencing both steric and electronic effects.[78,79] This is highly relevant, as the most common application of NHCs is their utilization as ligands in organometallic complexes. Herein, NHCs exhibit strong σ-donor and π-acceptor influences on the corresponding metal center due to their high energy σ-lone-pair and low energy free π*-orbital.[45,80-82] This results in the formation of very strong bonds with most metals, surpassing phosphines due to higher stability towards oxygen, moisture and elevated temperatures.[46,72,83,84]

Next to high adjustability of the NHC ligands themselves, a multitude of approaches for the preparation of the desired organometallic complexes have been described, with most common approaches being the trans-metalation from an analogous silver complex (see Figure 10a), deprotonation applying a metal complex containing a basic ligand (see Figure 10b), oxidative

addition *via* activation inducing a C-X bond (see Figure 10c) or the *in-situ* deprotonation of an azolium salt (see Figure 10d).[71]
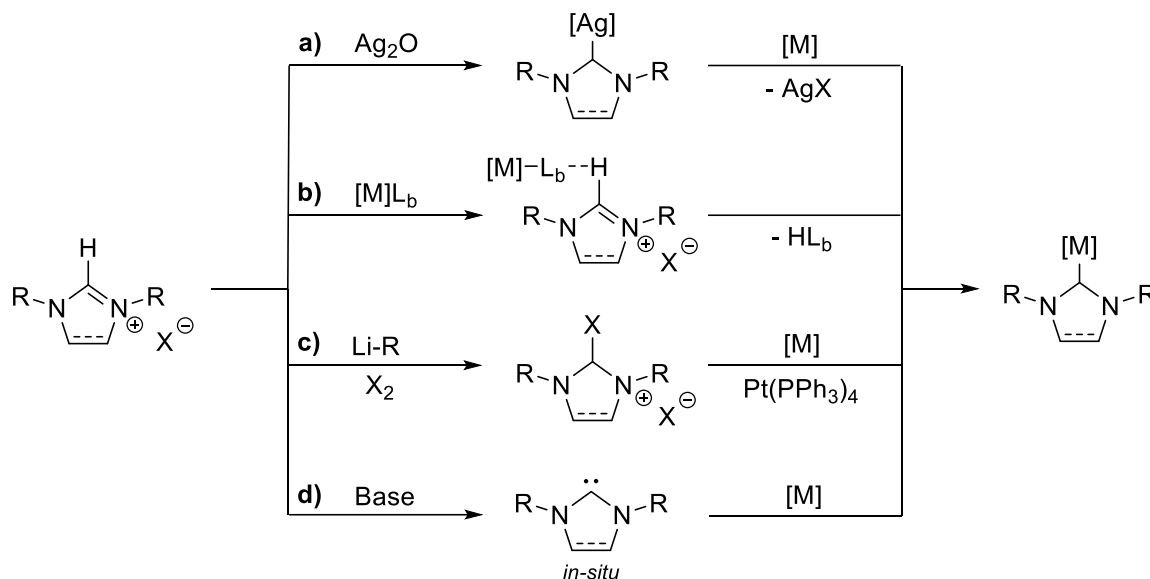
Figure 10. General overview of most common synthesis pathways for organometallic NHC complexes, a) trans-metalation from silver-NHC complex, b) deprotonation with basic ligand (L_b) containing complex, c) oxidative addition *via* bond activation by halogenation of the NCN moiety, d) *in-situ* deprotonation with base *via* free carbene.[71,85-88]

Therefore, due to the distinct advantages over other ligands such as phosphines, namely electronic effects inducing high catalytic activity, stronger stability towards relevant reaction conditions such as oxygen or moisture, simple adjustability and tunability to fit required demands as well as easy synthetic accessibility, the field of NHC complexes has experienced an explosive development in the last decades.[89] It is however vital, to further expand the known classes as well as investigate in-depth their function in various desired applications, as only this will allow for full exploitation of their characteristics and synthetic advantages. Therefore, research towards NHCs remains of great importance up to today.

2.3. Abnormal Carbenes

Up to this point, the herein described NHC structures all display coordination to the metal center at the carbon atom neighbored by the two nitrogen (hetero)atoms. This is commonly described either as the NCN or C^2 position (atom numbering according to IUPAC). However, the definition for NHCs does not necessarily require the heteroatoms to be directly adjacent to the carbene moiety.[46,71] Instead, this can also be formed at any other carbon position of the heterocycle, such as at C^4 or C^5 in the backbone (see Figure 11). These represent a noteworthy subgroup described as either abnormally coordinated NHCs (aNHC) or more general as mesoionic carbenes (MICs).[90] However, carbenes at the backbone positions are considered thermodynamically less stable and energy decomposition analyses have shown energy gaps of about 19 kcal·mol^{-1} to their normal analogues.[91,92]
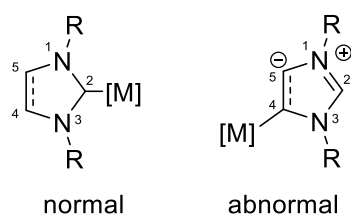
Figure 11. General structure of normal NHC (left) and abnormal NHC (right).

Furthermore, calculations of the acid dissociation constants of imidazolium cations have been reported with pKa values for the C^2 hydrogen of 24.9 in contrast to a pKa of 33.0 for the C^4 (or C^5 depending on nomenclature) hydrogen, indicating a larger acidity for thus more simple preparation of normal carbenes.[93,94] When investigating the electronic effects of aNHCs however, as reported in multiple studies, it could be shown that these exhibit stronger σ-donor properties (see Figure 12) compared to their normal analogues, hence making them highly interesting ligands for catalytic applications.[95-98]
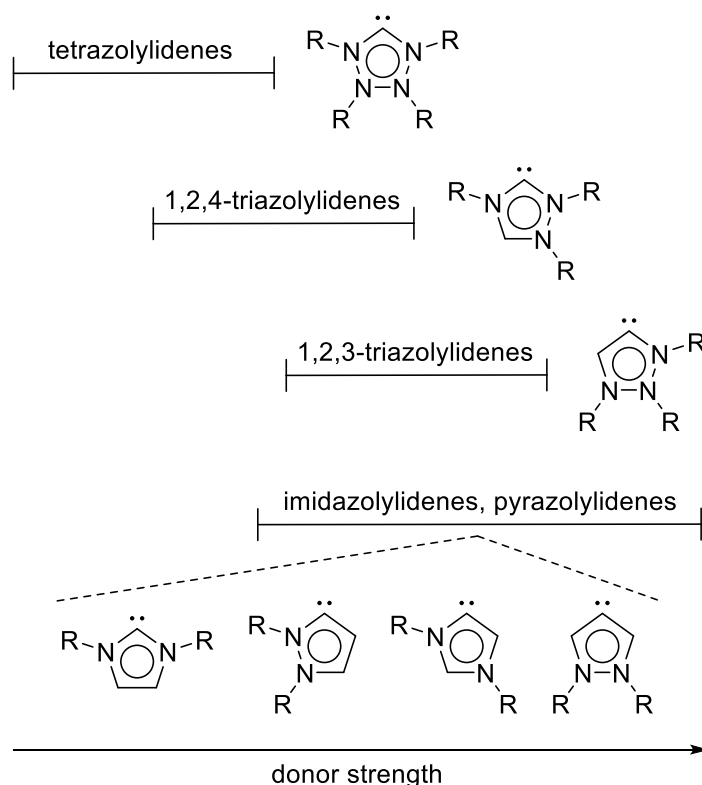
Figure 12. Increasing donor strength of different tetra- and triazolylidenes as well as imidazolylidenes and pyrazolylidined.[99]

To overcome their problematic stability and utilize their interesting properties, the applied synthetic methods have to be specifically tailored. Abnormal coordination can commonly be introduced by bulky wingtip substituents, which inhibit normal coordination by steric hindrance, by a counterion effect or by substitution at the C^2 position as protecting moiety.[100-102] Another strategy is chelate-assisted C-H bond activation, in which the imidazolium moiety is tethered to a donor group such as a phosphine or amine, which initially coordinates to the metal center.

The design of tether length and bite angle then induce abnormal coordination in a bidentate manner.[99,103] Albeit normal NHC complexes were reported as early as 1968, the first aNHC was described only in 2001 by Crabtree *et al.* as an iridium hydride with a methyl bridged NHC-pyridine moiety (see Figure 13a),[104] as well as suggesting a potential transformation of normal to abnormal binding mode. The first example of a novel ruthenium aNHC from a free monodentate carbene was described by Whittlesey *et al.* in 2007 (see Figure 13b).[105] Additional heating lead to the formation of a μ_3-η^2-bridging heterocycle by additional C-H activation at the backbone. The first successful isolation of a free aNHC by Bertrand *et al.* was reported as late as 2009 (see Figure 13c).[106]
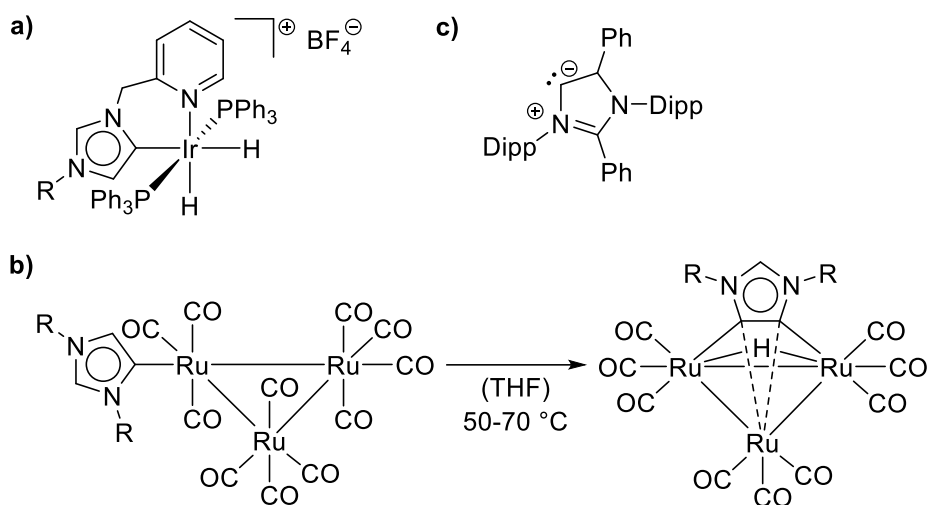
Figure 13. a) First aNHC by Crabtree *et al.* 2001, b) first ruthenium aNHC as well as bridged heterocycle formation by Whittlesey *et al.* 2007 and c) first isolated free aNHC by Bertrand *et al.* 2009.[104-106]

Although aNHC complexes are highly interesting as catalysts due to their enhanced properties compared to normal analogues, immense potential still exists as they are fairly new and have been comparing sparingly reported. Furthermore, only a small number of ruthenium aNHC complexes have been described in comparison to their iridium, rhodium or palladium counterparts. These however exhibit superior catalytic activities, making them highly desirable goals for modern organometallic chemists.[90,99,103]

3. Catalysis

3.1. Definition, History and Modern Industrial Relevance

The definition of catalysis dates back to 1835, as proposed by Jöns Jakob Berzelius (who, as mentioned in chapter 1, was also involved in the discovery of ruthenium): "the property of exerting on other bodies an action […] (to) produce decomposition in bodies and form new compounds into the composition of which they do not enter".[107] He derived the term catalysis from the Greek terms *κατά* (kata, "down") and *λυσις* (lyein, "dissolution").[108] Prior to this, the principle of a catalytic reaction had been reported by Elizabeth Fulhame in 1794, who demonstrated, that certain oxidations take place only with direct involvement of water (in contrast to Berzelius, who worked with heavy metals), which is regenerated following the reaction.[109] In modern day chemistry, a catalyst is defined as a compound that increases the rate of a (chemical) reaction without alteration of the reaction equilibrium.[110] The catalyst itself is hereby not consumed during the reaction but instead allows for the reaction to occur according to an alternative route with a decreased activation energy (see Figure 14). Therefore, catalysts allow for access of new synthetic pathways and the reduced energy consumption is often associated to "green" (sustainable, environmentally friendly) chemistry due to more efficient usage of resources.[111]
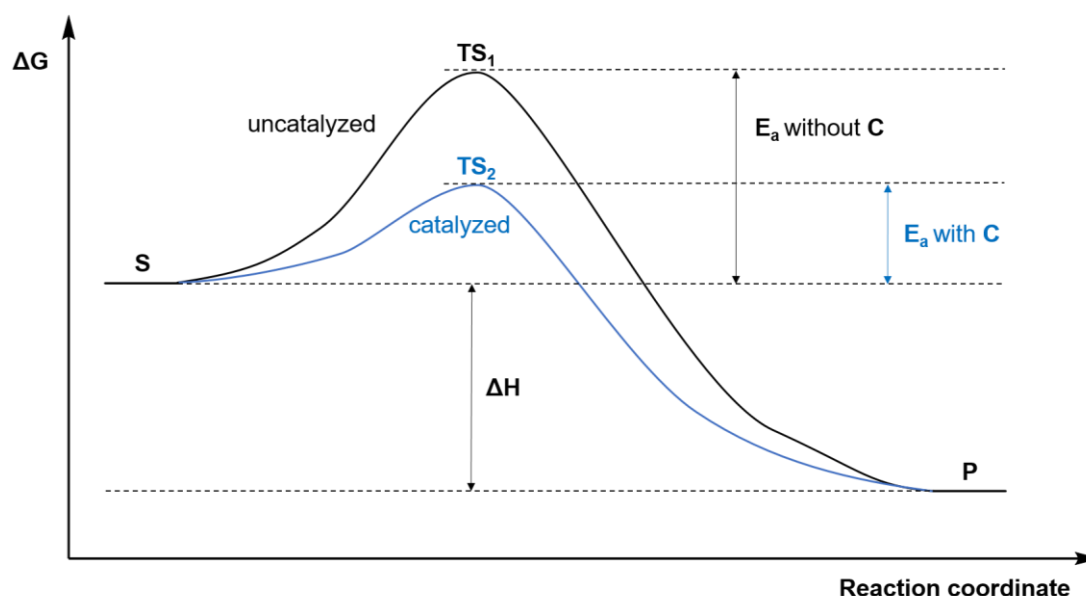
Figure 14. General scheme for the free energy (ΔG) of an uncatalyzed (black) and catalyzed (blue) reaction. Starting from substrates S, the reactions proceed *via* transition states TS_1 or TS_2 (not necessarily at same reaction coordinate) with corresponding activation energies E_a, to form products P with reaction enthalpy (ΔH). Herein, the E_a for the catalyzed reaction is smaller than that of the uncatalyzed reaction.[111]

However, catalytic processes have been applied throughout history even without deepened understanding of the occurring catalytic process. First examples date back to as early as ancient Egypt, where the production of alcohol from yeast *via* fermentation was performed.[108] This represents a biocatalytic process, in which the yeast acts as catalyst. The first inorganic

catalysis was reported by Valerius Cordus in 1575, involving sulfuric acid for the conversion of alcohol to diethylether.[112] In 1823, Johann Wolfgang Döbereiner designed a lighter in which hydrogen was produced by oxidation of zinc with sulfuric acid and ignited using a platinum sponge (see Figure 15). This represented the first practical application of catalysis and due to its practicability quickly spread into households, representing a major industrial relevance.[110,113]

a glass cylinder   e stopcock
b bottle   f nozzle
c wire   g platinum sponge
d zinc

$$Zn + 2\,H^+ \longrightarrow Zn^{2+} + H_2$$

$$2\,H_2 + O_2 \longrightarrow 2\,H_2O$$
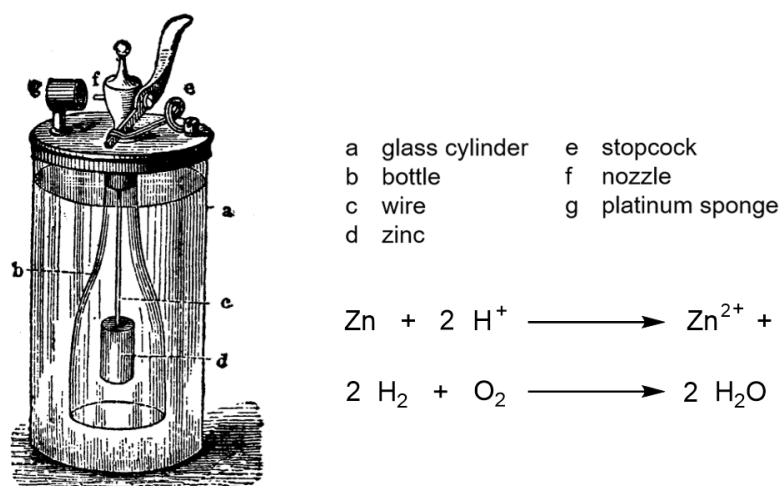
Figure 15. Schematic sketch of Döbereiner's lighter (left, Creative Commons Licenses) and description of components and general reaction (right).[110]

Nowadays, catalysts take up a major role in industry, spanning from large-scale petroleum refining, bulk chemical production and food processing over fine chemical and pharmaceutical preparation to a range of biocatalytic applications. It is estimated, that roughly 90% of all commercially available chemical products today have been produced involving a catalysts at some stage.[114] As of 2020, the global catalyst market was estimated at 35.5 billion US$ with a projected growth reaching 57.5 billion US$ by 2030.[115] Hereof, roughly 27% are assigned to chemical syntheses (Polyolefins, oxidation, hydrogenation), 20% each to petroleum refining (Fluid catalytic cracking, alkylation, hydro processing, reforming) and polymers (Ziegler Natta, reaction initiators). The largest segment is made up by environmental applications with roughly 32% (see Figure 16, left).[116] Whilst most of these processes are catalyzed by heterogeneous catalysts with roughly 80%, homogeneous catalysts also take up a major part of applications with estimated 17%, especially when requiring high (enantio-)selectivity, e.g. during fine-chemical and pharmaceutical production (see Figure 16, right).[117-119] In heterogeneous catalysis, the catalysts are commonly made up of active metals supported on a porous carrier material such as silica or aluminum oxide for increased surface.[120] They are therefore applied as solid-state catalysts reacting with substrates which are brought into contact often in liquid or gaseous form. The reaction conditions applied often describe temperatures of hundreds of degrees Celsius with high pressure, e.g. the synthesis of ammonia, one of the most-produced chemicals in industry *via* the Haber-Bosch process and applied as fertilizer, is produced at

500 °C with 20 MPa or higher.[120-122] On the other hand, detailed mechanistic investigations on the catalyst surface are often not feasible or highly challenging, also due to limiting investigative procedures and models.
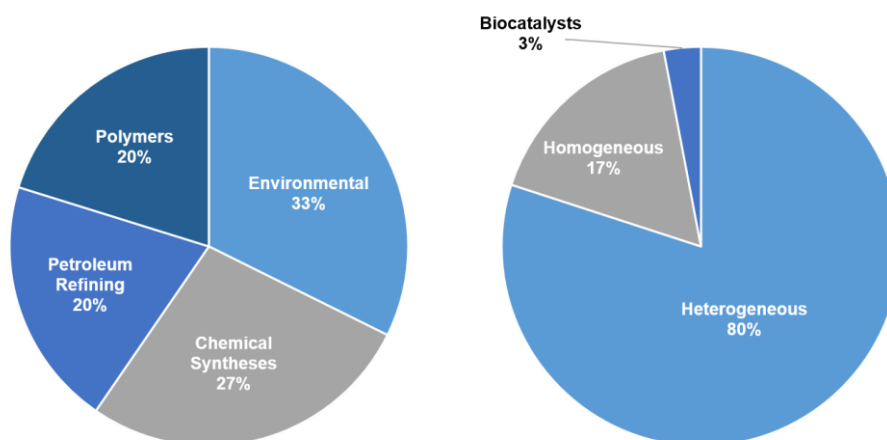
Figure 16. Pie charts of global catalyst market size share by application (left) and proportion of heterogeneous and, homogeneous catalyst applications (right) in industry (biological catalysts, i.e. enzymes, considered separately, however commonly applied in heterogeneous or immobilized form).[116,117]

In contrast, homogeneous catalysts allow for reactions at milder conditions and for more control over the occurring processes (see Table 1). Here, catalysts are made up of active metal centers surrounded by coordinating organic ligands to form defined structures.[123] These can interact with substrates in a lock and key fashion, similar to enzymes in biology, in which the organic ligands make up the geometric structure and additionally modify the reactivity of the active metal. Homogeneous reactions take place with both the catalyst and substrates in the same phase, commonly applying additional solvents. These features allow for high tunability, characterization and performance of mechanistic investigations to deepen the understanding of the underlying processes as well as application in highly selective transformations. Furthermore, every metal center is involved in the catalytic reaction resulting in a high atom efficiency and the utilization of low loadings, whilst heterogeneous catalysts suffer from defects, diffusion limitations and poisoning. A major drawback of homogeneous catalysis is however, next to varying complex stability, the separation of product from the solution media as well as recycling of the catalysts, as tedious steps are required. Furthermore, ligand synthesis represents a multistep and costly process, reducing the advantage of high metal atom economy. Heterogeneous catalysts can be separated and reused applying simple filtration and can be reused multiple times, which is why these are applied for most large-scale industrial applications. Nevertheless, homogeneous catalysts remain of great importance for a multitude of applications.[123-126]

Table 1. Comparison of heterogeneous and homogeneous catalysts regarding various properties.[123-126]

Property	Homogeneous	Heterogeneous
Catalyst	Molecule/complex	Metal on support
Medium	Solution	Solid in gas/liquid
Scale	Small/medium	Large
Structure	Defined	Undefined
Efficiency	High	Varying
Selectivity	High	Varying
Tunability	High	Low
Investigative Methods	Good	Difficult
Conditions	Mild	Harsh
Production	Multistep ligands	Often simple
Stability	Varying	Good
Product Separation	Difficult	Good
Recycling	Difficult	Good

3.2. Transfer Hydrogenation

Out of the large variety of catalytic reactions in industry applying homogeneous catalysts, chemical transformations for the selective synthesis of compounds are of vital importance, especially in pharmaceutical or petrochemical transformations.[127,128] Of these, hydrogenation is an attractive method used in chemistry for reduction of unsaturated compounds applying hydrogen.[69,129] Herein, one typically distinguishes between direct hydrogenation (DH), utilizing molecular hydrogen as source, and transfer hydrogenation (TH) processes which rely on hydrogen containing (organic) molecules such as *iso*-propanol or formic acid as hydrogen sources (see Scheme 1).[69]
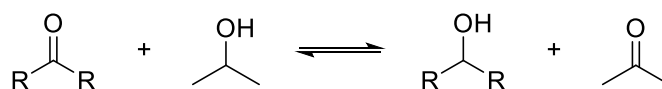
Scheme 1. General scheme of a transfer hydrogenation reaction with *iso*-propanol as hydrogen donor.

The latter are commonly applied as solvents, are commercially available, affordable and most importantly easy to handle, evading the problem of hazardous pressurized hydrogen gas required in DH.[45,69] This has led to a large increase in TH research and makes TH an attractive method for preparation of alcohols from aldehydes or ketones.[130-132] However, it remains limited to small and medium scale applications.

The first report of a hydrogen transfer reaction dates back to 1903, when Knoevenagel demonstrated the disproportionation of dimethyl-1,4-dihydroterephthalate using palladium black which included a hydrogen transfer between two identical molecules.[133,134] In 1925, the Meerwein-Ponndorf-Verley (MPV) reduction (see Scheme 2) utilized aluminum alkoxide as a promotor for the reduction of ketones with *iso*-propanol as hydrogen source.[135-137] This represented the first transfer hydrogenation reaction of carbonyl compounds and found application in large-scale synthesis of fine chemicals and in the fragrance industry.[69] It undergoes hydrogen transfer by formation of a six-membered cyclic transition state, whose mechanism can be attributed to Woodward *et al.*, directly from the *iso*-propanol reductant to the substrate without formation of aluminum hydride species (in contrast to "modern" TH).[138-141] However, both the MPV reduction as well as other established promotors required stoichiometric amounts of aluminum salts,[142] which is why the desire for other catalytic systems arose which could be applied at lower loadings.
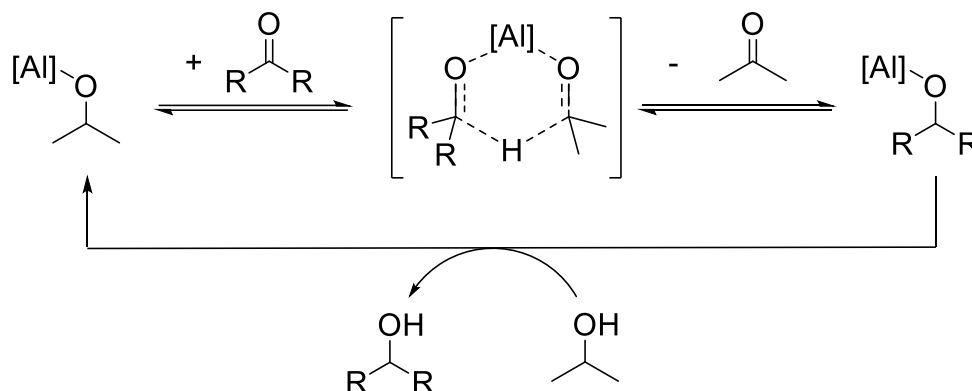
Scheme 2. General scheme for the Meerwein-Ponndorf-Verley reduction *via* a cyclic transition state and regeneration of aluminum alkoxide species.[69]

In the 1960s, the first transition metal catalysts were consequently applied. Here, Henbest and Mitchell *et al.* utilized an iridium hydride complex for the hydrogenation of cyclohexane and α,β-unsaturated ketones under addition of *iso*-propanol.[143,144] Two decades later, in the 1980s, the first successful asymmetric TH was reported applying ruthenium catalysts,[145-149] followed by reports from Bäckvall *et al.* in the 1990s demonstrating that catalytic amounts of base addition can enhance reactivities by multiple orders of magnitude.[150] Finally, the cumulative work of Noyori, Knowles and Sharpless were honored by award of the Nobel Prize in chemistry in 2001 for their work on asymmetric TH,[151] which further underlines the importance of these transformations. Hereby, Noyori *et al.*, among others, applied chiral Ru(II) complexes (see Scheme 3) resulting in enantiomeric excesses of up to 99%.[152,153]
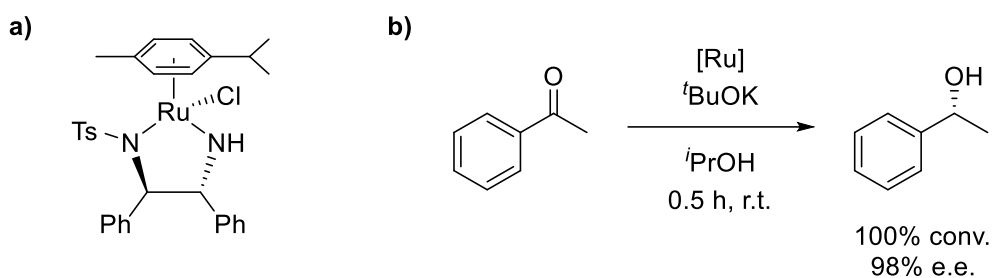
Scheme 3. a) Example of a chiral asymmetric TH pincer catalyst by Noyori *et al.*, b) reaction catalyzed by the Noyori catalyst with acetophenone as substrate and *iso*-propanol as solvent.[153]

Whilst systems containing other platinum group metals such as iridium, rhodium and osmium are of importance in TH reactions,[154-159] as well as more abundant metals such iron,[160,161] the most common metal applied remains ruthenium,[69,162] most likely due to its high versatility in oxidation states and suitable coordination geometries.[163] The highest rates for the enantioselective transformation of a broad substrate scope have been reported by Baratta *et al.* applying CNN pincer Ru complexes, yielding turn-over frequencies of up to 1 000 000 h^{-1} at catalyst loadings of down to 1 mmol%, demonstrating today's most efficient catalytic systems (see Figure 17), to the best of knowledge.[164-166]
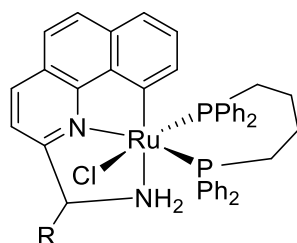
Figure 17. Highly active pincer TH catalyst by Baratta *et al.*[164,165]

3.3. Oppenauer-Type Oxidation

When considering the reduction of ketones to alcohols, as in the TH reaction, the reverse oxidation procedure also occurs as an equilibrium (see Scheme 4a), and applied for oxidation of substrates by careful choice of reaction conditions. In the past, multiple oxidation strategies have been reported, however, these often rely on toxic chromium reagents or dimethylsulfoxide (DMSO), as in the classical Swern-oxidation reaction.[142,167-169] To circumvent this, in 1937, Rupert Viktor Oppenauer reported a gentle and environmentally friendly oxidation procedure, known as Oppenauer-type oxidation. [170] The reaction describes the reverse to the MPV reduction and originally entailed acetone as benign solvent and oxidant using alkaline metals and aluminum *iso*-propoxide. Similar to the MPV reduction, the reaction takes place applying a six-membered cyclic transition state, showing high selectivity towards secondary alcohols, allowing for establishment of chemoselective reactions.[142,171,172] However, the reaction involved stoichiometric amounts of aluminum salts as well as excessive work-up steps, also due to aldol formation as side-reaction (see Scheme 4b) from acetone in combination with strong bases.[142]

a)

b)
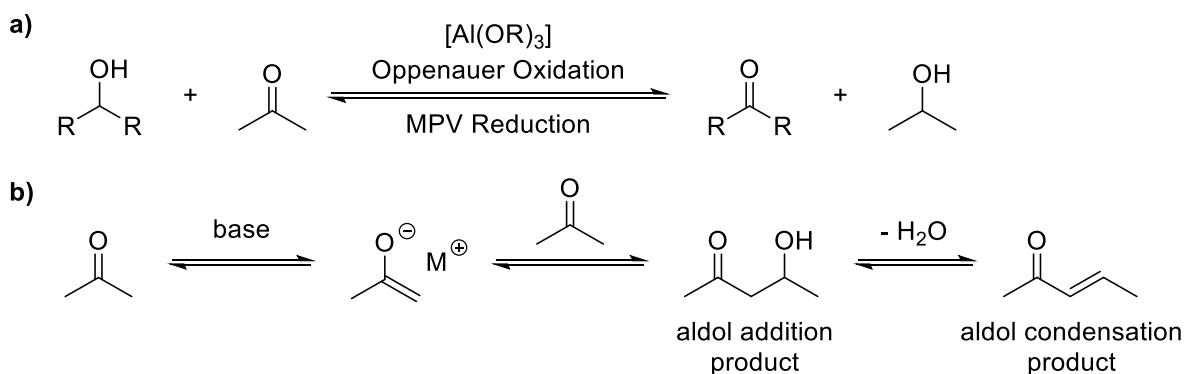
Scheme 4. a) General equilibrium reaction of Oppenauer-type oxidation vs. MPV reduction and b) base induced aldol condensation side reaction with acetone.

In addition, the low boiling point of acetone limited (industrial) applications, which is why many Oppenauer-type oxidation reactions are today performed with a separate solvent such as toluene and by addition of acetone in excess.[173] These drawbacks were however improved over the last years by introduction of transition metal catalysts, most commonly based on ruthenium.[69,150,165] Today, Oppenauer-type oxidation is often applied for acid sensitive substrates due to its basic reaction conditions.[174] Examples include complexes reported by Bäckvall *et al.*, Nolan *et al.* and Yu *et al.* (see Figure 18), reaching TOFs of 1500 h^{-1}, 200 h^{-1} and 11 800 h^{-1}, respectively.[173,175,176] However, catalyst loadings remain higher than those commonly applied in TH reactions, with consequently lower reaction rates.[177]

a)   b)   c)

Bäckvall *et al.*   Nolan *et al.*   Yu *et al.*
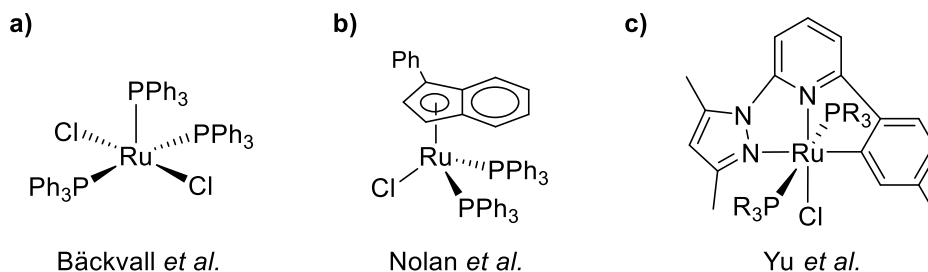
Figure 18. Oppenauer-type oxidation catalysts by a) Bäckvall *et al.*, b) Nolan *et al.*, and c) Yu *et al.*[173,175,176]

3.4. Hydrogenation Reaction Mechanisms

As both the TH and Oppenauer-type reaction represent the corresponding reductive and oxidative pathway of an equilibrium reaction, their mechanistic aspects can also be discussed applying similar mechanistic cycles. In this chapter, this will therefore be done in accordance to the more common TH applying a ketone substrate as well as *iso*-propanol as reducing agent. From a multitude of mechanistic studies performed over the last decades, two main pathways for transition-metal catalyzed hydrogenation have been established, namely the inner sphere (see Scheme 5) and outer sphere (see Scheme 6) mechanism, as proposed by Noyori *et al.* in 1997.[69,152,178,179] Between the two, the first is more prominent, as it is applicable to most complexes, whilst the latter is limited to complexes containing bidentate ligands with a primary

or secondary amino group (albeit bifunctional catalysis with alcohol, thiol or even C-H functionalities have also been reported).[180,181]
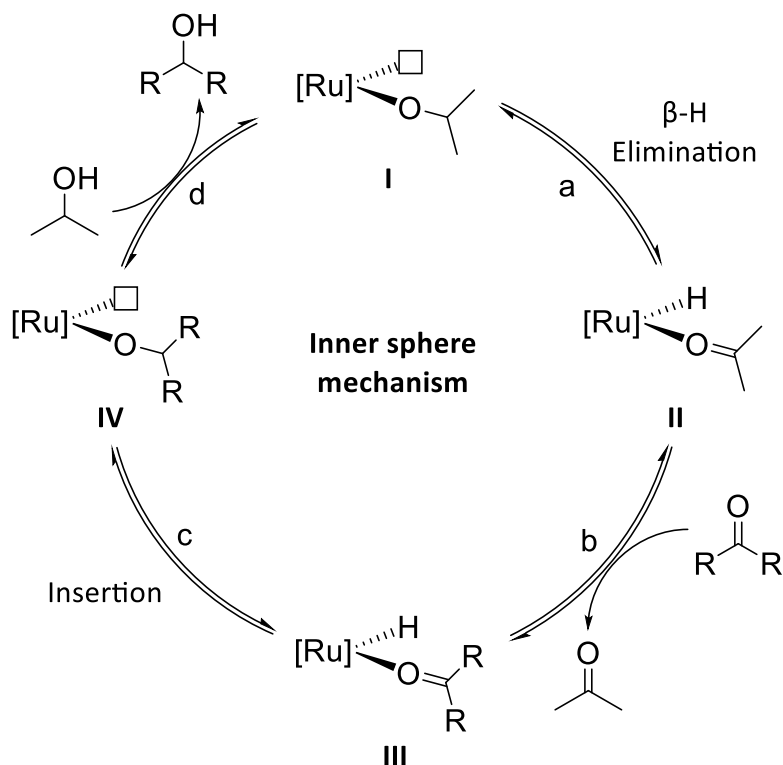
Scheme 5. Catalytic cycle of the inner-sphere ruthenium catalyzed transfer hydrogenation of a ketone substrate with *iso*-propanol as hydrogen donor.[179]

For the inner sphere mechanism (see Scheme 5),[69,179,182] the catalyst requires activation by formation of a free coordination site, which results in *iso*-propoxide species **I**. This allows for a β-hydride elimination step (**a**), in which a hydrogen is transferred from the "β" atom position (assuming the oxygen to be "α", the carbon represents a "β" position) to the free coordination site at the ruthenium complex, forming a metal mono-hydride **II**. Consequently, the formed ketone (here: acetone, as *iso*-propanol is applied as reducing agent) can then be replaced by the substrate carbonyl compound in a ligand exchange reaction (**b**). Species **III** can now undergo an insertion (**c**), in which the hydride is transferred to the β-position of the carbonyl substrate, representing the reverse step in contrast to the previous β-hydride elimination. From **IV**, the product is protonated and eliminated from the system by ligand exchange (**d**) with a fresh *iso*-propanol molecule, forming the alcohol product and rebuilding initial species **I**, from where the catalytic cycle starts anew. As demonstrated, the inner sphere mechanism therefore involves direct coordination of the substrates to the metal center, formation of a metal mono-hydride species and two coordination sites in *cis* position to one another.

In contrast, the outer sphere mechanism (see Scheme 6)[69,179] involves the formation of a bifunctional metal-ligand system in which dihydrogen is transferred in a single intermediate step (see **VI** and **VIII**). First, complex **V** is activated by coordination of *iso*-propanol as reducing

agent (**e**) forming a *syn*-periplanar geometry transition state **VI** of the two hydrogen atoms, induced by the chelating ligand containing a primary amine functionality. Consequently, the ketone (here: acetone) can be eliminated (**f**) from the system forming the hydride species **VII**.[183] Involving the formation of a second *syn*-periplanar transition state **VIII** and the coordination of the carbonyl substrate (**g**), the catalytic cycle is reset (**h**) under formation of alcohol product and initial species **V**.[152] Applying the outer sphere route, only one coordination site on the metal center is required, in contrast to the two required for the inner sphere mechanism, and less reaction steps are required. Therefore, outer sphere catalysts are usually more active than those following the inner sphere route. This is called the amine or N-H effect, which can also be achieved by *in-situ* addition of amine containing ligands such as ethylene diamine or 2-(aminomethyl)-pyridine (ampy).[182]

Scheme 6. Catalytic cycle of the outer-sphere ruthenium-amine catalyzed transfer hydrogenation of a ketone substrate with *iso*-propanol as hydrogen donor.[152,178]

However, both the inner sphere and the outer sphere mechanism include the formation of merely metal mono-hydride species as intermediates.[131] In mono-hydride mechanisms, hydride migration occurs purely from the "β" position of the reducing agent to the "β" position of the substrate, whilst the alcohol proton is not involved.[131] In contrast, some catalysts have been reported which do not follow the common mechanistic pathways such as RuCl$_2$(PPh$_3$)$_3$.[184,185] Here, it was shown that instead of a metal mono-hydride, a metal di-hydride represents the catalytically active species, resulting in the description of an alternative di-hydride mechanistic pathway (see Scheme 7). Here, following the pre-generation of a mono-hydride species **IX**, a β-hydride elimination (**i**) is utilized to form a metal di-hydride complex **X**.

Following a ligand exchange with the desired substrate (**k**) to **XI**, a migratory insertion of one of the two hydrides takes place (**I**), resulting in **XII**. As this insertion occurs at random, the two hydrogen atoms undergo a scrambling. Expulsion of the alcohol product (**m**) with protonation by the second hydride results in an additional scrambling at the alcohol proton position. The catalytic cycle the restarts upon re-coordination (**n**) of the reducing agent and re-formation of the mono-hydride **IX**.[184-186]
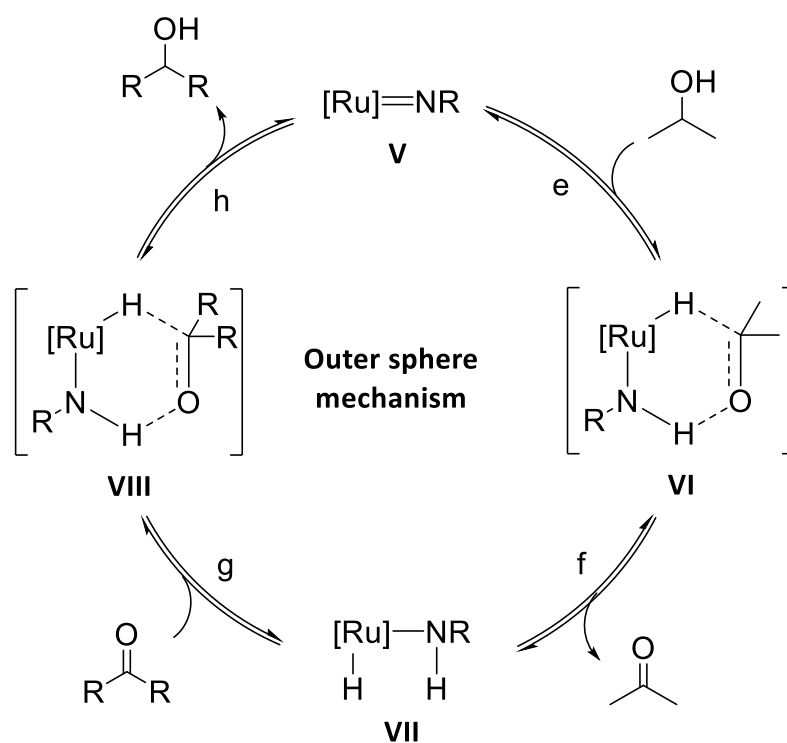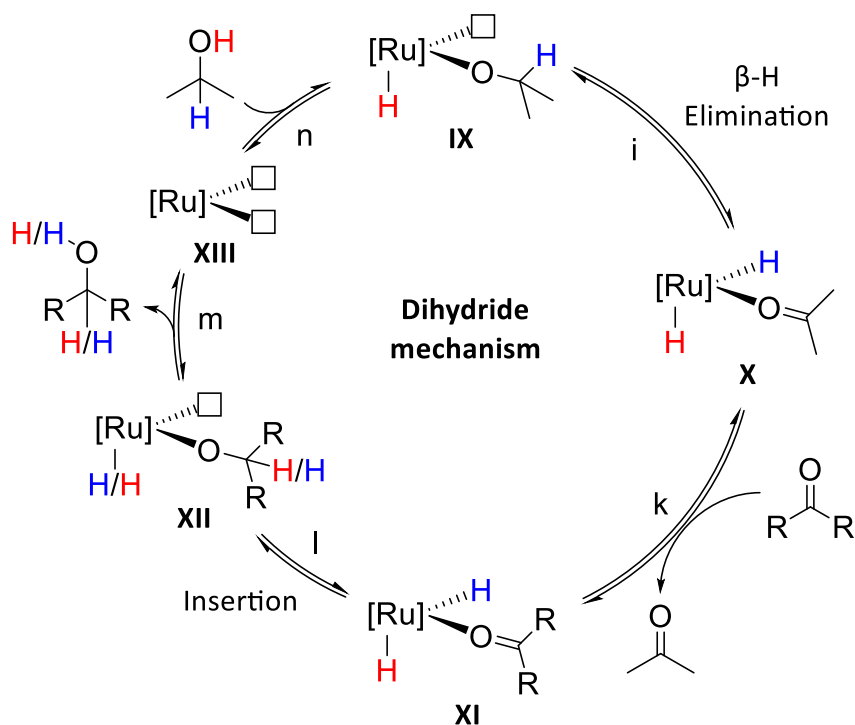

Scheme 7. Catalytic cycle of the di-hydride ruthenium catalyzed transfer hydrogenation of a ketone substrate with *iso*-propanol as hydrogen donor. Proton scrambling at steps **I** and **m** represented by H/H.

In comparison to the mono-hydride mechanisms, this pathway requires access to three coordination sites. In addition, the scrambling effect results in the loss of identity of the hydrogen atoms, as was shown by Bäckvall *et al.* applying a deuteration procedure (see Scheme 8).[131]
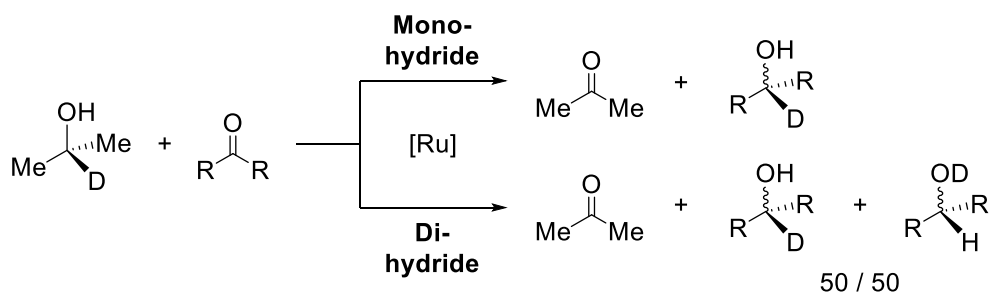
Scheme 8. Bäckvall deuteration procedure showing the influence of the monohydride (inner-sphere) pathway (top) versus the dihydride pathway (bottom) resulting in scrambling with a ratio of 50/50.[131]

3.5. Ruthenium Carbene Complexes in Hydrogenation Reactions

As described, a large variety of compounds has been reported for the TH and Oppenauer-type oxidation reactions of alcohols and ketones applying organometallic complexes,[187] with ruthenium being the most commonly applied active metal.[44] Hereof, ruthenium NHC complexes represent the group of most widely studied compounds due to their activity and tunability regarding these reactions.[188] Whilst the first NHC complex applied for TH reactions was reported only in 2001 by Nolan *et al.* (see Figure 19a),[189] describing an iridium cyclooctadiene (cod) pyridine NHC complex and achieving 100% conversion of cyclohexanone after 4.5 h with a TON of 44 h^{-1} (0.5 mol% cat., *iso*-propanol, 80 °C), the first ruthenium NHC complexes for TH were described by Danopoulos *et al.* (see Figure 19b)[190] and Peris *et al.* (see Figure 19c)[191] in the following years. These showed (full) conversion of acetophenone after 12 h (0.015 mol% cat., *iso*-propanol, 80 °C) and after 6 h with a TOF of 117 h^{-1} and TON of 700 h^{-1} (0.07 mol% cat., *iso*-propanol, 80 °C), respectively.
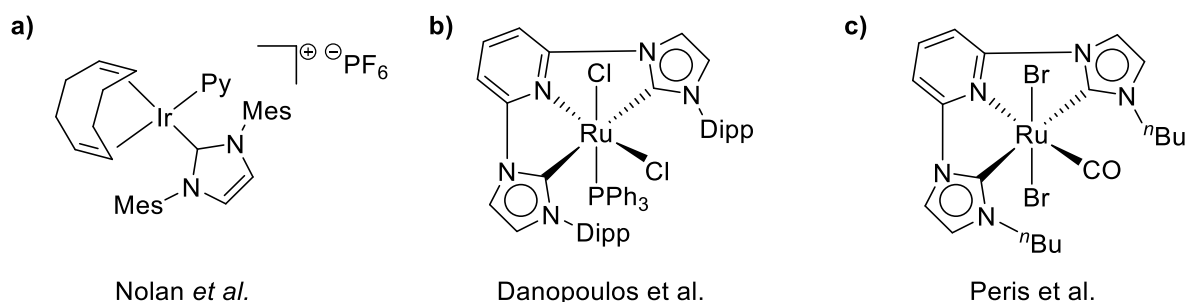
Figure 19. a) First NHC complex applied in TH, b) and c) first ruthenium NHC complexes in TH.[189-191]

In 2013 Kühn, Baratta *et al.* reported the synthesis and characterization of the first aNHC phosphine ruthenium complex (see Figure 20a).[192] This complex showed high activities in the hydrogenation of acetophenone, achieving 97% conversion after 2 h (0.05 mol% cat., *iso*-propanol, reflux) and a TOF of 38 000 h^{-1}. Yasar *et al.* reported a monodentate complex showing a TOF of 256 h^{-1} and 96% conversion after 30 min for the transformation of acetophenone (0.75 mol% cat., *iso*-propanol, 80 °C).[193] In 2015 and 2016, Kühn, Baratta *et al.* described the preparation of the first examples of anionic *N*-heterocyclic dicarbene (NHDC) complexes with two different d-block elements (see Figure 20c).[194,195]
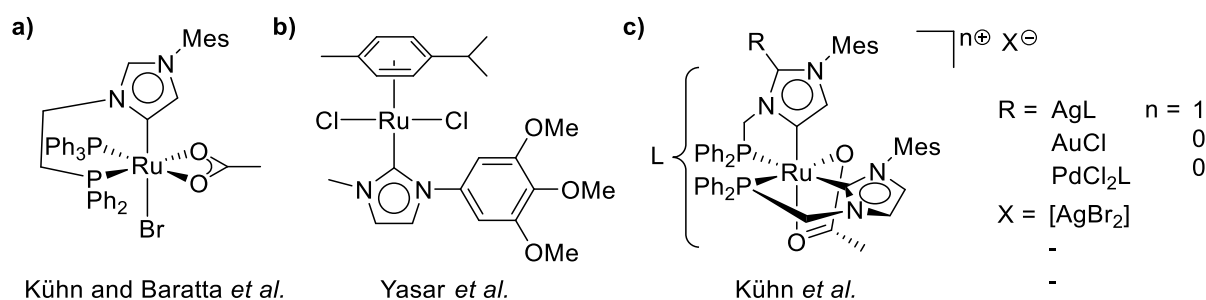
Figure 20. a) First aNHC phosphine ruthenium complex, b) monodentate complex by Yasar *et al.* and c) first examples of anionic NHDC complexes.[192-195]

In 2016 Kühn, Albrecht *et al.* reported the first XRD solid state structure of a mixed normal/abnormal NHC ruthenium complex (see Figure 21a).[196] It achieved a TOF of up to 1100 h⁻¹ with 98% conversion within 80 min in the TH of acetophenone (0.5 mol% cat., *iso*-propanol, 82 °C). This report was shortly followed by the first ruthenium (II) open chain tetra-NHC complex, whose differing coordination geometry could be influenced by the length of the alkyl chain, displaying both sawhorse and equatorial coordination (see Figure 21b, left vs. right) coordination.[197] Both geometries displayed high catalytic activity, reaching 98% and 94% conversion within 1 min and 30 min, respectively, with a TOF of up to 110 000 h⁻¹ (0.1 mol% cat., *iso*-propanol, reflux). In 2017, Ramaiah *et al.* prepared a half-sandwich ruthenium(II) complex bearing an pyridyl-imidazolylidene ligand (see Figure 21c).[198] Quantitative yields were obtained within 1 h (0.5 mol% cat., *iso*-propanol, 80 °C). The preparation of a neutral pincer complex was reported by Bezuidenhout *et al.* in 2018 with a TOF of 2500 h⁻¹ in the TH of acetophenone (0.01 mol% cat., *iso*-propanol, 80 °C), reaching 74% conversion after 3 h.[199]
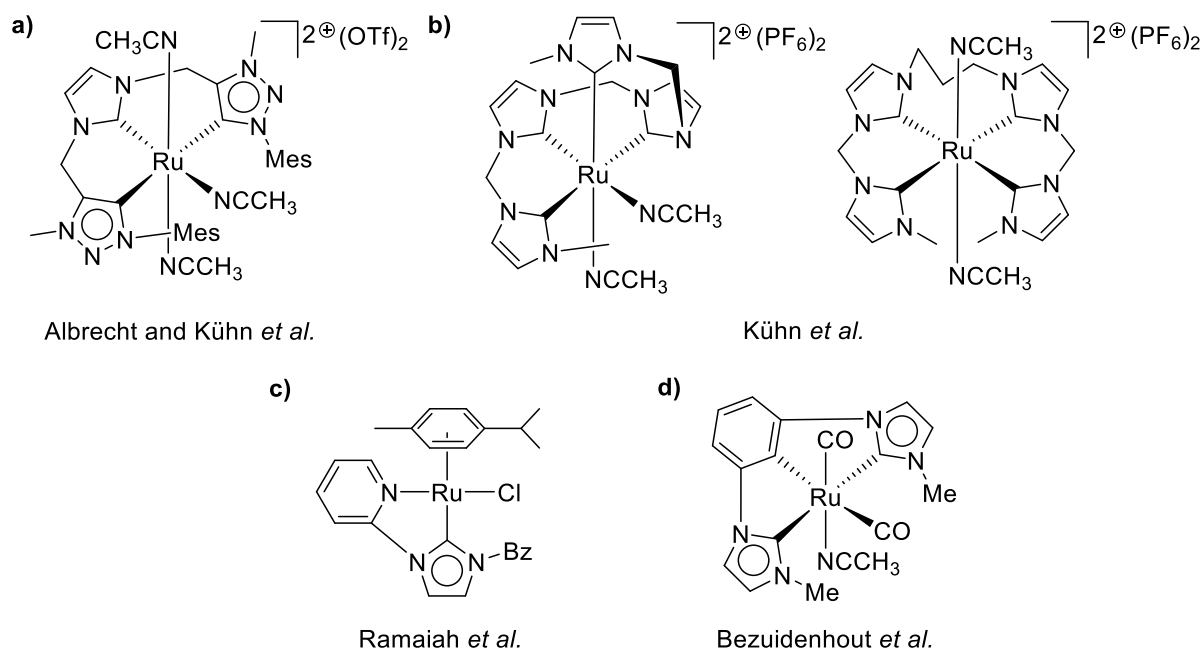
Figure 21. Various ruthenium NHC complexes for TH.[196-199]

In 2019, Kühn, Baratta *et al.* described the first example of a ruthenium complex containing two aNHC phosphine ligands (see Figure 22a).[200] This displayed unprecedented activity in both TH and Oppenauer-type oxidation reactions, representing the most active carbene (NHC) ruthenium catalyst for TH to date, to the best of knowledge, with TOFs of up to 600 000 h⁻¹ with 99% conversion in the TH of acetophenone after 1 min (0.01 mol% cat., *iso*-propanol, reflux) and 550 000 h⁻¹ with 98 % conversion in the Oppenauer-type oxidation of α-tetralol after 2 min (0.01 mol% cat., neat, 50 °C). In comparison, the most efficient system for TH today, to the best of knowledge, was described by Baratta *et al.* with a CNN pincer complex without any NHC ligand (see Figure 22b), displaying a TOF of 1 000 000 h⁻¹ at a loading of 1 mmol%.[164,165]

However, when comparing these two catalysts, one must take into consideration, that the latter can facilitate an outer-sphere mechanism, thus profiting from the amine effect for increased activity (see chapter 3.4), whilst the NHC complex shows no clear possibility for this kind of mechanism, making it an interesting candidate for further investigations.

a)

b)

Kühn, Baratta *et al.*   Baratta *et al.*
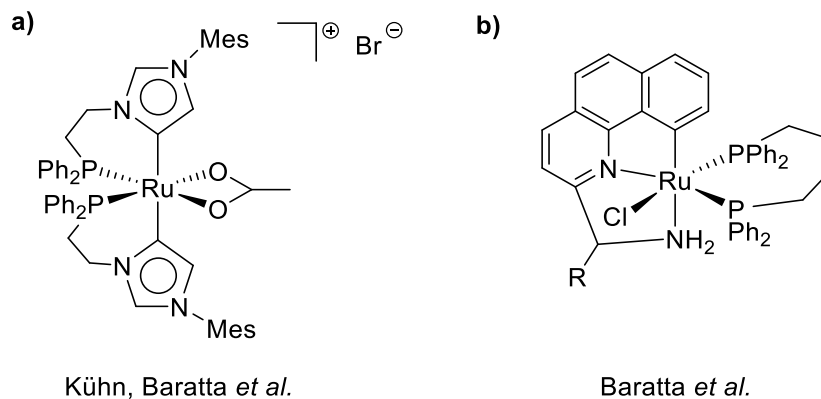
Figure 22. a) Most active carbene (NHC) ruthenium TH catalyst and b) most active Ru TH complex.[164,165,200]

II Objective

As described above, abnormally coordinating, *N*-heterocyclic carbene ruthenium complexes are of special interest as homogeneous catalysts for transfer hydrogenation (TH) reactions due to their excellent activities and adjustable ligand design. This work is therefore divided into two chapters dealing with alteration and investigation of different components of such aNHC complexes for catalytic transformations. The first example of a *bis*-aNHC phosphine ruthenium system described by Kühn, Baratta *et al.* in 2019[200] has demonstrated unprecedented high turn-over frequencies (TOFs) in both TH and Oppenauer-type oxidation reactions with a variety of substrates (600 000 h^{-1} in TH of acetophenone and 550 000 h^{-1} in Oppenauer-type oxidation of *α*-tetralol). However, catalytic experiments were designed aiming at an initial investigation as well as stability towards functional groups. In addition, only little was reported regarding mechanistic insights and the precise influence of ligand design on activity remained unclear. In the first chapter, the aim of this work is therefore to further investigate how such complexes can be designed and optimized by considering the formation intermediates and the steric influence of wingtip substituents on catalytic activity. Adding to the initial investigation, the catalytic conditions require a more fine-tuned approach and design for better compatibility of various catalysts applying the same substrates. Supported by computational methods an aim is also to gain further insight into the fundamental mechanisms. In the second chapter, the NHC subgroup of heterobimetallic NHC complexes (NHDC) containing a second metal center at the NCN position of the abnormal NHC ligands is discussed. Here, a mixed normal/abnormal bis-NHC ruthenium iridium complex has also previously been reported by Kühn, Baratta *et al.* in 2019.[201] However, the influence of the second metal on catalytic activity and complex structure remained unclear. Therefore, another aim of this work is the alteration of the second metal from iridium to rhodium to investigate if this has a significant influence on catalytic activity.

a) ⟹ 1. Formation study
2. Wingtip sterics
3. Catalytic influence

b) ⟹ 1. Alteration Ir to Rh
2. (XRD) structure analysis
3. Catalytic influence
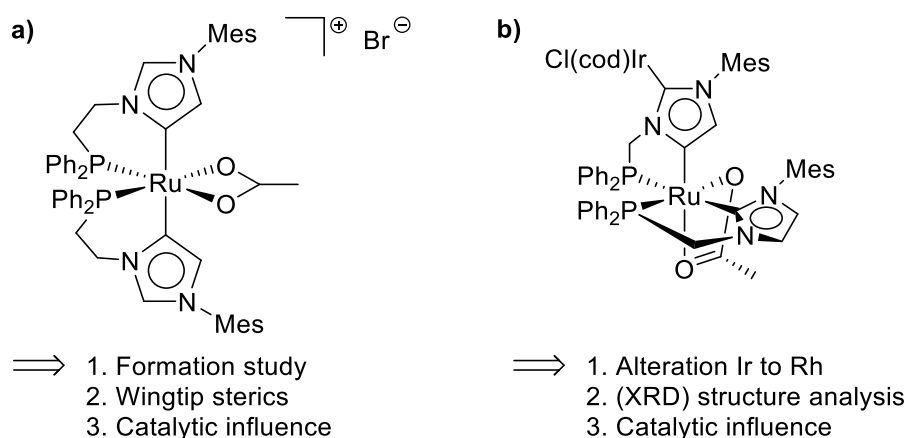
Figure 23. a) General bis-aNHC phosphine ruthenium complex structure and aims for investigation of formation and effect of wingtip substituents and b) structure of NHDC complex for investigation of catalytic influence of second metal center.

III Results and Discussion

4. Abnormal NHC Ruthenium Catalysts: Mechanistic Investigations of their Preparation and Steric Influence on Catalytic Performance

The results of this chapter have been published in

4.1. Publication Summary

In this manuscript, the synthesis and characterization of a family of bis-abnormal NHC ruthenium diphenylphosphino complexes are described. Of these, the wingtip substituents are varied from phenyl **1** over mesityl **2** (as previously described by Kühn, Baratta *et al.* in 2019[200]) to di-*iso*-propylphenyl **3**, representing an increase in steric bulk, respectively. Both complexes **1** and **3** are characterized and their successful preparation verified by NMR, elemental analysis, and LIFDI-MS spectrometry. In addition, the structure of complex **3** is also confirmed by SC-XRD experiments (see Figure 24).
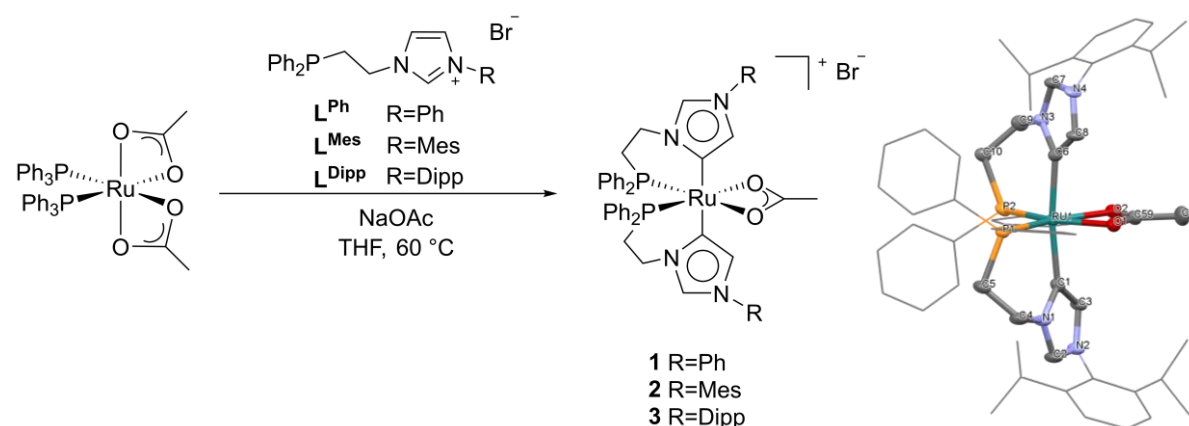
Figure 24. Synthetic procedure for the preparation of aNHC ruthenium complexes **1**, **2** and **3** (left) and SC-XRD structure of **3** (right).

During preparation, complex **3** is shown to be more stable in solution in comparison to **1** and **2**. As the elucidation of complex formation could reveal important information for future complex design and preparation of more optimized catalysts, mechanistic studies were performed on **3** on account of its higher stability. Following reaction of the ligand **L^Dipp** in THF without base addition and at room temperature, formation of a pink intermediate is observed. Following an NMR study, both a kinetic and thermodynamic intermediate, **3a** and **3b** respectively, are successfully identified. Therefore, the formation of final complex **3** is proposed according to following reaction pathway, in which initially a single NHC moiety coordinates

abnormally, whilst the other remains dangling followed by a coordination switch of the coordinating NHC from a *mer* to *fac* arrangement (see).
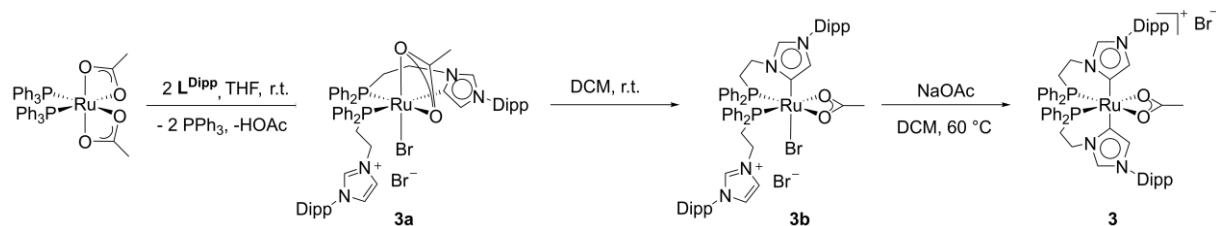
Figure 25. Proposed reaction pathway for preparation of **3** *via* kinetic and thermodynamic intermediates **3a** and **3b**, respectively.

Following the formation study, all complexes are applied as catalysts in both TH and Oppenauer-type oxidation reactions to investigate the influence of the wingtip substituents on catalytic activity. Whilst TH follows the row of **1** > **2** > **3**, the reverse is surprisingly observed for Oppenauer-type oxidation, with activity decreasing from **3** > **2** > **1**. Whilst the reactivity order in TH is rationalized by lower accessibility to the active center and thus in line with steric hindrance and supported by computational buried volume calculations, the reverse trend in the Oppenauer-type oxidation is rationalized by a change in the rate determining step from ketone insertion to the reverse alkoxide β-H elimination, facilitated by the increased steric bulkiness (see Figure 26). In accordance to the previous report, normal NHC di-hydride formation is also suggested as deactivation pathway.
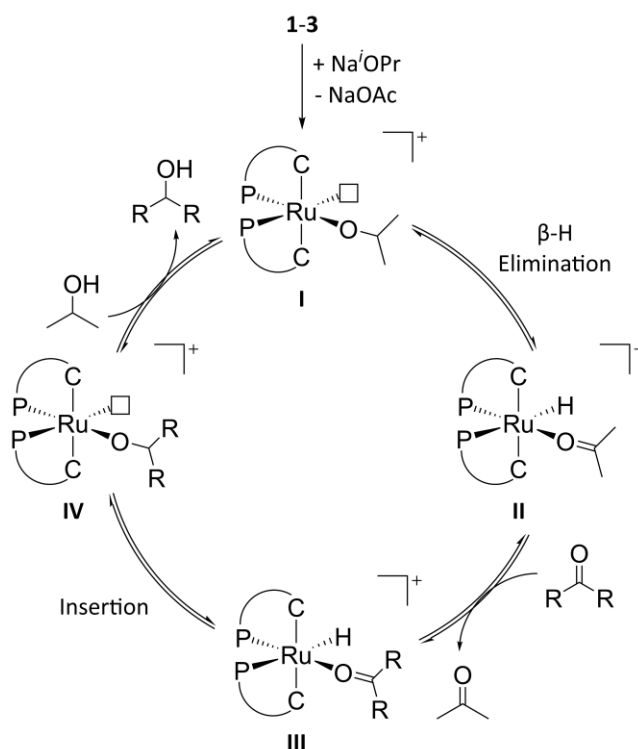
Figure 26. General mechanistic scheme proposed according to the inner-sphere mechanism for TH and Oppenauer-type oxidation. Bis-NHC-phosphine ligands abbreviated as P-C. Bromide counterion excluded for clarity.

4.2. Publication Reprint

Check for updates

Abnormal NHC ruthenium catalysts: mechanistic investigations of their preparation and steric influence on catalytic performance†

Alexander D. Böth, [ID][a] Michael J. Sauer,[a] Walter Baratta [ID] *[b] and Fritz E. Kühn [ID] *[a]

The bis-abnormal N-heterocyclic carbene (aNHC) ruthenium complexes [Ru(OAc)(aNHC-ethyl-PPh$_2$)$_2$]Br **1** and **3** are obtained from Ru(OAc)$_2$(PPh$_3$)$_2$ with the ligands 1-(2-diphenylphosphino-ethyl)-3-aryl-imidazolium bromide (aryl = phenyl, di-iso-propylphenyl) L^{Ph} and L^{Dipp} in THF at 60 °C and in the presence of NaOAc *via* displacement of PPh$_3$ and carbene deprotonation. Mechanistic studies on the formation of the di-iso-propylphenyl derivative **3** reveal the preceding generation of mono-aNHC intermediate isomers **3a** and **3b** as kinetic and thermodynamic products. Complexes **1** and **3** exhibit exceptionally high activity in the transfer hydrogenation (TH) of acetophenone and Oppenauer-type oxidation of α-tetralol, **1** showing turn-over frequencies (TOF) of up to 550 000 h^{-1} in the TH of acetophenone and **3** showing TOFs up to 280 000 h^{-1} in the Oppenauer-type oxidation of α-tetralol. The comparison of the catalytic activity of the phenyl **1**, mesityl **2** and di-iso-propylphenyl **3** complexes follows the order **1 > 2 > 3** for TH, likely due to accessibility of the active center, whilst following the inverse **3 > 2 > 1** order in Oppenauer-type oxidation. This inversion appears to be dependent on steric influences. These observations are in line with buried volume calculations based on density functional theory (DFT) optimized structures.

Introduction

In the syntheses of organic compounds, such as fine-chemicals or pharmaceutical products, highly specific tools are required for the designed transformation of functional groups.[1–3] Of these, transfer hydrogenation (TH) of carbonyl compounds, classically performed *via* the Meerwein–Ponndorf–Verley reduction, is a key reaction for the preparation of alcohols, using iso-propanol as a nonhazardous and environmentally friendly solvent and hydrogen donor, favoring the product formation due to a shift of the reaction equilibrium (Scheme 1).[4–7] In addition, the reverse Oppenauer-type oxidation of alcohols to ketones is an attractive reaction entailing acetone as an environmentally benign solvent and oxidant, in place of toxic chromium reagents or the classical Swern-oxidation (Scheme 1).[8] These transformations,[9–11] originally carried out using alkaline metals as well as Al iso-propoxide and resulting in excessive work-up steps, have been improved in the last decades by

employment of transition metal catalysts.[12–23] Outstanding systems for the hydrogenation and TH reactions such as those developed by Noyori are based on ruthenium catalysts containing diphosphine and arene ligands in combination with an amine N–H function.[24–26] The presence of the N–H motif in 18-electron complexes allows for fast and robust catalysts operating *via* an outer sphere mechanism.[27] Conversely, efficient coordinatively unsaturated catalysts can also be obtained using suitable polydentate ligands, which may retard deactivation. In addition to phosphines, which have been extensively employed in homogeneous catalysis because of the easy formation of catalytically active metal hydride species, N-heterocyclic carbenes (NHCs) have been used as suitable ligands for ruthenium catalysts in olefin-metathesis[28] and TH reactions.[29–39] In these complexes, the NHC ligands can also coordinate to the ruthenium *via* the less acidic C^4 or C^5 positions, affording the mesoionic or abnormal NHC (aNHC) complexes, favored by introduction of bulky wingtip substituents at the N atom.[40,41] The aNHC

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† Electronic supplementary information (ESI) available. CCDC 2163076. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d2cy01036d
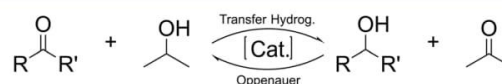
Scheme 1 General scheme of a transfer hydrogenation (TH) reaction using iso-propanol (left to right) and reverse Oppenauer-type oxidation (right to left).

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ligands generally exhibit stronger σ-donor properties compared to their related NHC analogues, resulting in a higher basicity at the metal center, making them good candidates for achieving highly active homogeneous catalysts for TH and Oppenauer-type oxidations.[42–47] Recently, we have reported the synthesis of the first example of a ruthenium complex (**2**) containing two aNHC ligands with a mesityl wingtip substituent. This compound displays catalytic activity in TH and Oppenauer-type oxidations, with unprecedented high activities in both reactions (Fig. 1).[48] Whilst further investigations are required to fully rationalize and optimize this system, the abnormal coordination of the NHC ligand appears to be crucial for the high performances.

In this work the preparation of two further highly active bis-aNHC ruthenium catalysts **1** and **3** with different wingtip substituents (phenyl and di-iso-propylphenyl, respectively), as well as the characterization of two intermediate species, **3a** and **3b**, involved in the dicarbene formation are described. The influence of the steric bulkiness of wingtip substituents is investigated for both the TH of acetophenone and the Oppenauer type oxidation of α-tetralol. The results are evaluated with additional DFT studies on the buried volume and the steric maps for accessibility and deactivation.

Results and discussion

Synthesis and characterization

The aNHC ruthenium complexes **1** and **3** (31% and 81% yield, respectively) are obtained by reaction of the ruthenium precursor $Ru(OAc)_2(PPh_3)_2$ with the phenyl imidazolium ligand $\mathbf{L^{Ph}}$ or the analogous di-iso-propylphenyl ligand $\mathbf{L^{Dipp}}$ in THF at 60 °C in the presence of NaOAc, following the procedure described for the mesityl complex **2** (85% yield) using $\mathbf{L^{Mes}}$ (Scheme 2).[48,49]

While the ligand $\mathbf{L^{Dipp}}$ was obtainable in accordance to the procedure reported for the mesityl $\mathbf{L^{Mes}}$, a slightly different synthetic protocol (ESI†) has been followed for the synthesis of $\mathbf{L^{Ph}}$, due to its high solubility in polar solvents (*i.e.* water). Both complex **1**, which displays lower stability in solution compared to **2**, and complex **3** have been successfully isolated and characterized by NMR, elemental analysis and LIFDI-MS spectrometry (ESI†). In the ^1H NMR spectrum of complex **1**, the resonances at δ 1.36, 1.89, 3.98 and 5.58 ppm represent the bridging CH_2 hydrogens, with the resonance at δ 1.89 ppm overlapping with that at δ 1.92
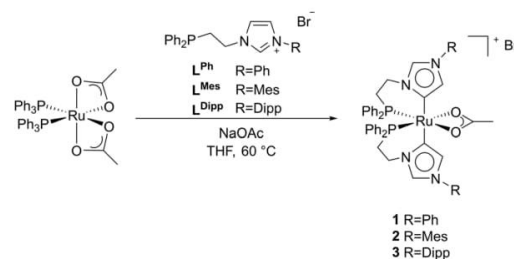
Scheme 2 Syntheses of the aNHC ruthenium complexes **1–3**.

ppm of the acetate methyl group. The doublet at δ 9.38 ppm (^4J = 1.9 Hz) corresponds to the two imidazolium NC*H*N protons of the abnormal carbene coordination, in agreement with the analogous mesityl derivative **2**. A characteristic singlet can be observed in the ^{13}C NMR spectrum at δ 184.7 ppm for the acetate, as well as a signal at δ 165.3 ppm, representing the abnormal carbene carbons. The ^{31}P NMR spectrum of **1** shows a singlet at δ 55.8 ppm, consistent with the C_2 symmetry of the complex, with the two phosphorus atoms in *cis* position, as observed for **2**. In the ^1H NMR spectrum of **3**, the resonances at δ 0.43, 1.20 and 1.78 ppm (6 : 18 : 3 ratio) correspond to the eight di-iso-propylphenyl and the acetate methyl groups. Two heptets are observed at δ 2.29 and 2.48 ppm (ratio 1 : 1), representing the two tertiary di-iso-propylphenyl hydrogens, whilst the doublet at δ 8.59 ppm (^4J = 1.8 Hz) corresponds to the NC*H*N protons.[48] The ^{13}C NMR singlet at δ 184.2 ppm and the triplet at δ 165.1 ppm ($^2J_{CPcis}$ = 12.5 Hz) represent the acetate and the two abnormal carbene carbons, respectively, while the ^{31}P NMR spectrum shows a singlet at δ 56.1 ppm.[48] The structure of **3** has additionally been confirmed through an SC-XRD experiment carried out on a single crystal obtained by layering a solution of **3** in dichloromethane (adding 1 drop of benzene) with *n*-pentane at room temperature (Fig. 2).

Formation of complex 3

Mechanistic studies have been carried out to elucidate the intermediate complexes involved in the formation of the bis-abnormal complexes, relevant for complex design and preparation. The synthesis of the di-iso-propylphenyl derivative **3** has been examined on account of its higher stability with respect to **1** and **2**. The reaction of the diacetate $Ru(OAc)_2(PPh_3)_2$ with two equivalents of $\mathbf{L^{Dipp}}$ in THF at room temperature and without base results in the formation of the pink intermediate **3a** as precipitate, which has been isolated in 78% yield (Scheme 3). Control ^{31}P NMR experiments of the reaction solution, indicate that the diacetate precursor $Ru(OAc)_2(PPh_3)_2$ undergoes substitution of the two PPh_3 ligands at room temperature in THF by addition of the two equivalents of $\mathbf{L^{Dipp}}$, one of which is easily deprotonated by the acetate ligand acting as an internal base and resulting in the formation of the abnormal carbene (ESI,† Fig. S27). The ^{31}P NMR spectrum of **3a** in CD_2Cl_2 shows two doublets at δ
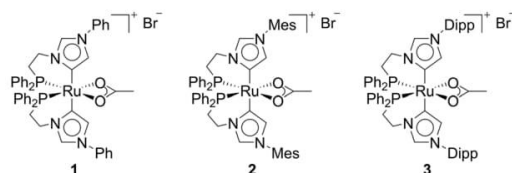

Fig. 1 Overview of bis-aNHC complexes **1**, **2** and **3** with steric demand of wingtip substituents increasing from phenyl (Ph) over mesityl (Mes) to di-iso-propylphenyl (Dipp), respectively.

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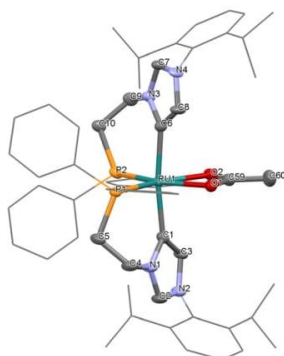

Fig. 2 ORTEP style molecular structure representation of complex **3**. Thermal ellipsoids are given at a 50% probability level. Hydrogen atoms, the counterion (bromide), solvent and all disorders are omitted for clarity. Phenyl and di-iso-propylphenyl substituents are depicted in wireframe style for clarity. Gray = carbon, blue = nitrogen, yellow = phosphorous, red = oxygen and turquoise = ruthenium. Selected bond lengths (Å) and angles (°): C1 Ru1 2.094(5), C6 Ru 2.089(5), O1 Ru 2.226(4), O2 Ru 2.229(4), P1 Ru 2.2300(13), P2 Ru 2.2259(13), C1 Ru C6 172.0(2), C1 Ru P1 91.53(14), C6 Ru P2 91.49(14), C1 Ru P2 94.09(15), C6 Ru P1 94.03(15), P1 Ru P2 92.18(5), O1 Ru O2 58.57(15), P2 Ru O2 104.29(11), P1 Ru O1 104.98(10).

Fig. 3 ^{31}P NMR study showing the transformation of complex **3a** (red) to complex **3b** (orange) in dichloromethane without base at room temperature. Measurements performed after 1 h, 5 h, 17 h and 24 h. Low formation of complex **3** (yellow) from complex **3a**, as latter is formed *in situ*.

56.9 ppm and δ 24.6 ppm with a relatively small J_{PP} = 24.6 Hz, consistent with a *cis* configuration of the two P atoms, one of them shifted at high field due to the presence of a carbene ligand displaying a high *trans* influence and resulting in a *mer* arrangement of the Ru(κ^2-L$_{Dipp}$)(κ^1-L$_{Dipp}$) fragment. In the ^{13}C NMR spectrum the doublet of doublets signal at δ 164.4 ppm, with a large and small J_{PC} = 101.3 Hz and 15.8 Hz, represents a carbene coordinated in an abnormal way and *trans* and *cis* to the two P atoms, while the singlet at δ 184.5 ppm represents the carbonyl acetate ligand. The singlet at δ 46.3 ppm and the doublet at δ 31.6 ppm (with J_{PC} = 30.6 Hz) represent the CH$_2$N and CH$_2$P backbone of the six membered ring, respectively, in agreement with related carbene complexes.[48,49] The dangling moiety gives two doublets at δ 44.4 ppm (J_{PC} = 8.6 Hz) and δ 29.2 ppm (J_{PC} = 16.8 Hz) for CH$_2$N and CH$_2$P, rather similar to those of the free ligand. However, compound **3a** is not stable in solution at room temperature and slowly isomerizes to **3b**, as observed *in situ via* NMR measurements carried out in CD$_2$Cl$_2$ within 24 h (Fig. 3). In the ^{31}P NMR spectrum, the species **3b** shows two close doublets at δ 50.1 and 49.6 ppm, with a J_{PP} = 43.3

Hz, in agreement with two *cis* P atoms *trans* to acetate, which displays a weak *trans* influence. Based on ^{13}C NMR measurements showing a triplet at δ 158.1 ppm (J_{PC} = 14.6 Hz) for the ruthenium-carbene, while the non-coordinated imidazolium moiety is observed at δ 146.4 ppm, complex **3b** displays a *fac* Ru(κ^2-L$_{Dipp}$)(κ^1-L$_{Dipp}$) arrangement. In addition, the singlet and doublet at δ_C 45.9 and 32.9 ppm (J_{PC} = 21.5 Hz), represent the CH$_2$N and CH$_2$P backbone of the six membered ring respectively,[48,49] whereas the dangling CH$_2$-CH$_2$ moiety gives two doublets at δ_C 47.8 (J_{PC} = 7.5 Hz) and 28.9 ppm (J_{PC} = 13.4 Hz), for the CH$_2$N and CH$_2$P, respectively. A small amount of **3** (δ_P 56.1 ppm, <5%) is also observed in solution and full conversion to **3** can be easily achieved by addition of one equivalent of NaOAc as external base. According to this study, the formation of **3** from Ru(OAc)$_2$(PPh$_3$)$_2$ most likely follows the reaction pathway reported in Scheme 3, affording the kinetic product **3a**, *via* PPh$_3$ substitution and C–H activation *trans* to the phosphorus, followed by thermal isomerization to the more stable species **3b**. Its geometry is the same as that of the mesityl mono-aNHC complex.[49] Subsequent deprotonation of **3b** in the presence of external base NaOAc gives quantitatively the bis-aNHC derivative **3**. Thus, the identification and characterization of kinetic and thermodynamic products should be taken into account for the design and efficient synthesis of abnormal NHC catalysts.
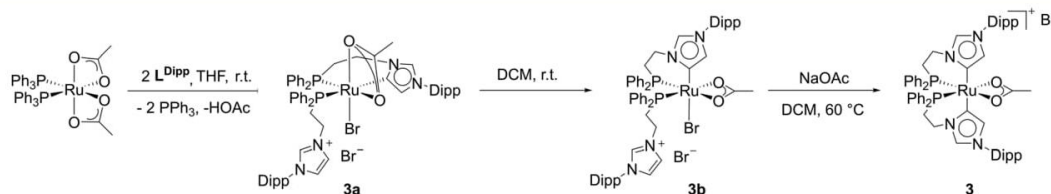
Scheme 3 Proposed mechanistic pathway for the formation of complex **3** *via* intermediates **3a** and **3b** from Ru(OAc)$_2$(PPh$_3$)$_2$.

Transfer hydrogenation

Since mesityl complex **2** has been proven to be an extremely efficient catalyst in TH of carbonyl compounds to alcohols, the derivatives **1** and **3** are applied in the catalytic TH of acetophenone as a model substrate to evaluate the influence of the wingtip substituent on the activity and the stability by varying the catalyst loadings and temperatures (Tables 1 and 2). Applying an S/C ratio of 1000, the sterically least demanding **1**, with NaO^{i}Pr (2.00 mol%) in iso-propanol, achieves a TOF of 120 000 h^{-1} with 97% conversion after 0.5 min at 80 °C (Table 1, entry 1), which is a value roughly twice as high as the one obtained for mesityl derivative **2** (TOF of 60 000 h^{-1}) affording 97% conversion after 1 min (entry 2). By comparison, the more sterically hindered **3** shows a TOF of 25 000 h^{-1} and requires 5 min to achieve 97% conversion (entry 3). However, at this catalyst concentration, overloading likely occurs, so that the kinetic curves do not allow for a realistic comparison (ESI,† Fig. S31). In contrast, the precursor Ru(OAc)$_2$(PPh$_3$)$_2$ shows merely 38% conversion as catalyst after 8 h under the same reaction conditions.[50]

The TH has therefore been carried out with a lower amount of catalyst. At S/C of 2000, **1** leads to 97% conversion after 0.5 min with a TOF of 230 000 h^{-1} (entry 4), whereas **2** and **3** achieve TOFs of 140 000 and 50 000 h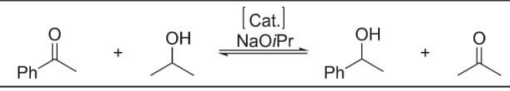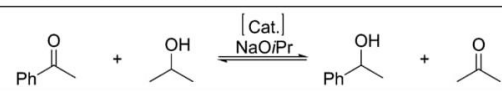$^{-1}$, respectively, with 97% conversion after 5 min (entries 5 and 6). On account of the extremely high activity of **1**, the catalysis has been performed at even lower loading with an S/C of 10 000. Complex **1** affords quantitative reduction of acetophenone in 3 min with a TOF of 500 000 h^{-1} (entry 7), while **2** and **3** give TOFs of 300 000 and 120 000 h^{-1} after 5 and 15 min, respectively (entries 8 and 9). Conversely, at S/C = 20 000 a drastic loss of conversion is observed, indicating that under these conditions a deactivation occurs possibly due to the presence of traces of solvent impurity or oxygen during catalysis. Therefore, a S/C of 10 000 has been chosen as optimal loading without major catalyst overloading

Table 1 Catalytic TH of acetophenone with catalysts **1**, **2** and **3** (Ph, Mes, Dipp, respectively) at 80 °C with NaO^{i}Pr (2.00 mol%) in iso-propanol at varying catalyst loadings

Entry	Cat.	S/C	Conv.^{a}/%	t/min	TOF^b/h^{-1}
1	**1**	1000	97	0.5	120 000
2	**2**	1000	97	1	60 000
3	**3**	1000	97	5	25 000
4	**1**	2000	97	0.5	230 000
5	**2**	2000	97	5	140 000
6	**3**	2000	97	5	50 000
7	**1**	10 000	96	3	500 000
8	**2**	10 000	97	5	300 000
9	**3**	10 000	95	15	120 000

^{a} The conversion was determined by GC, values represent maximal conversion. ^{b} Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion as "initial" TOF values (see ESI†).

Table 2 Effect of temperature on catalytic TH of acetophenone with catalysts **1**, **2** and **3** (Ph, Mes, Dipp, respectively) at S/C = 10 000 with NaO^{i}Pr (2.00 mol%) in iso-propanol

Entry	Cat.	T/°C	Conv.^{a}/%	t/min	TOF^b/h^{-1}
1	**1**	90	98	3	550 000
2	**2**	90	97	3	500 000
3	**3**	90	98	5	480 000
4	**1**	70	97	10	150 000
5	**2**	70	94	15	95 000
6	**3**	70	77	20	50 000

^{a} The conversion was determined by GC, values represent maximal conversion. ^{b} Turnover frequency (moles of ketone converted to alcohol per mole of catalyst per hour) at 50% conversion as "initial" TOF values (see ESI†).

or (significant) catalyst deactivation for the further studies at different temperatures. At a bath temperature of 90 °C, least hindered phenyl complex **1** converts acetophenone in 3 min (98% conversion) with a TOF of 550 000 h^{-1} (Table 2, entry 1).

This value is higher than that obtained with the mesityl derivative **2** (TOF of 500 000 h^{-1}) (entry 2) and higher than those, observed for other previously described NHC ruthenium catalysts (ESI,† Table S2).[35,36,38,39,49] With the sterically more demanding di-iso-propylphenyl complex **3** a slightly lower rate (TOF of 480 000 h^{-1}) is attained, leading to quantitative conversion after 5 min (entry 3). Albeit a clear trend is observed and it is in line with the steric hindrance of the aryl substituents of the aNCH ligand, it is worth pointing out that these catalysts are all extremely active, also in absence of an N–H function, and show TOF values of the same order of magnitude with full conversion of the substrate within 5 min. As reported in the previous part at 80 °C the complexes **1**, **2** and **3** display TOF values of 500 000, 300 000 and 120 000 h^{-1}, respectively (Table 1, entries 7–9). Conversely, at 70 °C, the derivatives **1**, **2** and **3** give TOFs of 150 000, 95 000 and 50 000 h^{-1}, respectively, with **3** showing a significant decrease of activity and incomplete conversion even after 20 min (Table 2, entries 4–6). In summary, the highest performances for these complexes in the TH are observed at 90 °C with S/C = 10 000 and with a rate, which quickly declines by lowering the temperature and also decreases with increasing the steric effect of the aryl groups of the carbene ligand. At 70 °C the complexes **1**, **2** and **3** show a TOF of 27, 19 and 11% with respect to the values at 90 °C, with the more sterically hindered catalyst **3** displaying a marked decrease of the rate. This is consistent with a higher enthalpy of activation on account of the lesser accessibility of the substrate to the catalytic site by the increase of the bulkiness of the wingtip substituents of the aNHC carbene ligand.

Oppenauer-type oxidation

Interestingly, when investigating the reverse Oppenauer-type oxidation reaction with α-tetralol as model substrate (Table 3),

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Table 3 Effect of temperature on catalytic Oppenauer-type oxidation of α-tetralol (1 eq.) with complexes **1**, **2** and **3** (Ph, Mes, Dipp, respectively) at S/C = 10 000 with KO^{t}Bu (2 mol%) and acetone (6.00 eq.) in ^{t}BuOH

Entry	Cat.	T/°C	Conv.^{a}/%	t/min	TOF^b/h^{-1}
1	**1**	40	4	20	2000
2	**2**	40	42	20	18 000
3	**3**	40	58	20	29 000
4	**1**	50	13	20	8000
5	**2**	50	76	20	37 000
6	**3**	50	96	20	83 000
7	**1**	60	19	20	13 000
8	**2**	60	97	20	85 000
9	**3**	60	97	10	280 000

^{a} The conversion was determined by GC, values represent maximal conversion. ^{b} Turnover frequency (moles of alcohol initially converted to ketone per mole of catalyst per hour) as "initial" TOF values (see ESI†).

applying a S/C of 10 000, as for TH, using 6 eq. of acetone with KO^{t}Bu (2 mol%) in ^{t}BuOH, the previously most active catalyst **1** merely achieves a TOF of 2000 h^{-1} and 4% conversion after 20 min (Table 3, entry 1). Catalysts **2** and **3** on the other hand are more active, with TOFs of 18 000 and 29 000 h^{-1} with 42 and 58% conversion after 20 min (Table 3, entries 2–3), respectively, thus showing an inversion of the activity trend in comparison to the TH of acetophenone. Increasing the temperature to 50 °C the complexes **1**, **2** and **3** show 13, 76 and 96% conversion of α-tetralol after 20 min, affording TOF values of 8000, 37 000 and 83 000 h^{-1}, respectively (Table 3, entries 4–6). At 60 °C, **1**, **2** and **3** give 19, 97 (20 min) and 97% (10 min) conversion with TOFs of 13 000, 85 000 and 280 000 h^{-1}, respectively (Table 3, entries 7–9). These are among the highest values for the Oppenauer-type ruthenium catalysts (ESI,† Table S3).[51–56] These results show that increasing catalytic performance is observed with increasing bulk of the wingtip substituents of the abnormal carbene.

TH vs. Oppenauer-type oxidation reaction

The catalytic activities observed for complexes **1**, **2** and **3** in the TH of acetophenone as well as in the Oppenauer-type oxidation of α-tetralol show an activity decrease in the row **1** > **2** > **3** for TH and in the opposite direction **3** > **2** > **1** for the Oppenauer-type oxidation. For the TH it is likely that the catalysis occurs through an inner-sphere mechanism (Scheme 4).[57] The ruthenium dicarbene complex reacts with sodium iso-propoxide, affording **I**, which converts to the hydride species **II** via β-H elimination. Coordination of the incoming ketone substrate, followed by insertion into the Ru–H bond of **III**, affords the species **IV**. Displacement of the alkoxide by iso-propoxide in the iso-propanol media results in the alcohol product. In agreement with the experimental data, it is likely that the rate determining step for the TH

involves the reduction of the incoming ketone substrate to the alkoxide at the metal center, a process which is affected by the bulkiness of the wingtip substituent of the carbene ligand. To shed more light on the catalytic pathway, calculations on the buried volume %V_{Bur} of the active center of DFT optimized structures of **1–3**, as well as the generation of steric maps (ESI,† Tables S10–S15 and Fig. S54–S56), have been performed. The buried volume increases from 79.7%V_{Bur} over 79.9%V_{Bur} to 80.1%V_{Bur}, as well as from 69.4%V_{Bur} over 70.5%V_{Bur} to 71.8%V_{Bur} from complex **1** over **2** to **3**, for sphere radii of 3.5 Å and 5.0 Å, respectively (Fig. 4). Hence, the increase in buried volume occupying the active center is in line with lower substrate accessibility to the active center, resulting in a lower catalytic activity. Thus, the least bulky complex **1** shows the highest catalytic activity.

The Oppenauer-type oxidation reaction may occur through the same mechanistic pathway, representing the reverse
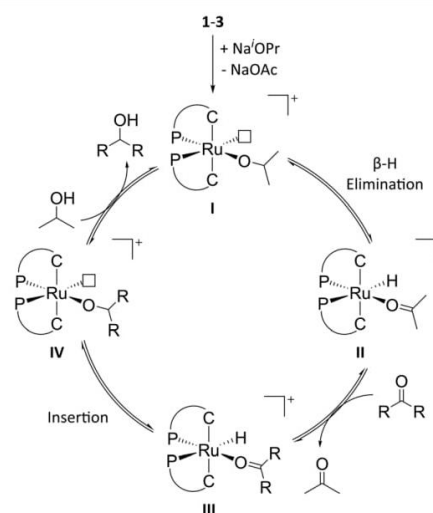
Scheme 4 General scheme for the inner-sphere mechanism for the transfer hydrogenation reaction. Bis-NHC–phosphine ligands abbreviated as P–C. Bromide counterion excluded for clarity.
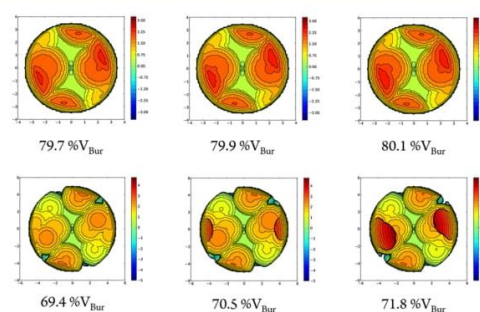

Fig. 4 Steric maps for complexes **1** (left), **2** (center) and **3** (right) at 3.5 Å (top) and 5.0 Å (bottom). The relative values for buried volume given below each map.

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equilibrium reaction to the TH, with the alcohol as substrate. In the TH both the protonation reaction and the dehydrogenation of iso-propanol (β-H elimination) and in the Oppenauer-type oxidation the hydrogenation of acetone (insertion) are likely to occur at higher rate, on account of their higher concentration and less steric constrains. The observed trend for the catalytic Oppenauer-type oxidation with **1–3**, where **3** is most active, is therefore consistent with a rate determined step involving the β-H elimination of the alkoxide **IV** (*i.e.* the reverse rate determined step of the TH), affording the ketone product. This process can be explained by better extrusion of the formed ketone from the catalytic system facilitated by the presence of bulky ligands due to their steric influence, in contrast to the TH where the rate determining insertion is facilitated by less bulky ligands, allowing for better accessibility.

Conclusions

In summary, the preparation of ruthenium complexes with two abnormal aNHC phosphine ligands is reported, expanding this class of highly active catalysts by alternation of the wingtip substituents (phenyl *vs.* mesityl *vs.* di-iso-propylphenyl). The formation of the more stable complex **3**, containing the bulkier di-iso-propylphenyl ligand, has been mechanistically investigated, affording the characterization of two mono-abnormal carbene intermediates **3a** and **3b** as kinetic and thermodynamic products, yielding insights for the design of efficient catalysts. The catalysts **1**, **2** and **3** are applied in the transfer hydrogenation (TH) of acetophenone and the Oppenauer-type oxidation of α-tetralol, showing that the activity for the two reactions depends on the bulkiness of the aryl-wingtip substituents. The phenyl derivative **1** shows extremely high activity in TH with TOFs up to 550 000 h^{-1}, while the di-iso-propylphenyl derivative **3** displays the best activity in Oppenauer-type oxidation with TOFs up to 280 000 h^{-1}. Buried volume calculations and steric maps, performed using DFT optimized structures, are performed to help explain the activity. For the TH, the insertion of the incoming ketone substrate to the Ru–H bond was identified as potential rate determining step, inhibited by bulky ligands. Conversely, in the Oppenauer-type oxidation the rate determined step is likely due to the reverse alkoxide β-H elimination leading to an inversion of activity, favored by the bulky ligands. Further studies are currently ongoing to further elucidate the catalytic mechanisms of both reactions regarding the here observed inversion of activity and to extend applications of the abnormal carbene complexes in other organic transformations.

Author contributions

Alexander D. Böth: synthesis, computational chemistry, catalysis, manuscript preparation; Michael J. Sauer: X-ray diffraction measurements/analysis; Walter Baratta: project design and experimental strategy planning; Fritz E. Kühn: project design and controlling.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

References

1 G. Rothenberg, *Catalysis: Concepts and Green Applications*, Wiley-VCH, 2008.

2 P. Atkins, T. Overton, T. Overton, J. Rourke, M. Weller and F. Armstrong, *Shriver and Atkins Inorganic Chemistry*, Oxford, 2010.

3 J. M. Thomas and D. M. Harris, *Energy Environ. Sci.*, 2016, **9**, 687–708.

4 H. Meerwein and R. Schmidt, *Justus Liebigs Ann. Chem.*, 1925, **444**, 221–238.

5 W. Ponndorf, *Angew. Chem.*, 1926, 138.

6 A. Verley, *Bull. Soc. Chim. Fr.*, 1925, **37**, 537.

7 H. Adkins, R. M. Elofson, A. G. Rossow and C. C. Robinson, *J. Am. Chem. Soc.*, 1949, **71**, 3622–3629.

8 R. V. Oppenauer, *Recl. Trav. Chim. Pays-Bas*, 1937, **56**, 137–144.

9 C. R. Graves, B.-S. Zeng and S. T. Nguyen, *J. Am. Chem. Soc.*, 2006, **128**, 12596–12597.

10 T. Ooi, T. Miura, Y. Itagaki, H. Ichikawa and K. Maruoka, *Synthesis*, 2002, **2002**, 279–291.

11 C. F. de Graauw, J. A. Peters, H. van Bekkum and J. Huskens, *Synthesis*, 1994, 1007–1017.

12 D. Wang and D. Astruc, *Chem. Rev.*, 2015, **115**, 6621–6686.

13 F. Foubelo, C. Nájera and M. Yus, *Tetrahedron: Asymmetry*, 2015, **26**, 769–790.

14 J.-i. Ito and H. Nishiyama, *Tetrahedron Lett.*, 2014, **55**, 3153–3166.

15 W. Baratta and P. Rigo, *Eur. J. Inorg. Chem.*, 2008, 4041–4053.

16 T. C. Johnson, G. J. Clarkson and M. Wills, *Organometallics*, 2011, **30**, 1859–1868.

17 A. Quintard and J. Rodriguez, *Angew. Chem., Int. Ed.*, 2014, **53**, 4044–4055.

18 S. A. Moyer and T. W. Funk, *Tetrahedron Lett.*, 2010, **51**, 5430–5433.

19 F. Hanasaka, K.-i. Fujita and R. Yamaguchi, *Organometallics*, 2006, **25**, 4643–4647.

20 M. G. Coleman, A. N. Brown, B. A. Bolton and H. Guan, *Adv. Synth. Catal.*, 2010, **352**, 967–970.

21 D. Zhao, L. Candish, D. Paul and F. Glorius, *ACS Catal.*, 2016, **6**, 5978–5988.

22 J. Ito and H. Nishiyama, *Tetrahedron Lett.*, 2014, **55**, 3133–3146.

23 D. A. Hey, P. J. Fischer, W. Baratta and F. E. Kühn, *Dalton Trans.*, 2019, **48**, 4625–4635.

Paper

24 H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya and R. Noyori, *Angew. Chem., Int. Ed.*, 1998, **37**, 1703–1707.

25 K.-J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya and R. Noyori, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 285–288.

26 W. Baratta, E. Herdtweck, K. Siega, M. Toniutti and P. Rigo, *Organometallics*, 2005, **24**, 1660–1669.

27 K. J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya and R. Noyori, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 285–288.

28 R. H. Grubbs, A. G. Wenzel, D. J. O'Leary and E. Khosravi, *Handbook of Metathesis*, Wiley-VCH, 2015.

29 R. H. Morris, *The Handbook of Homogeneous Hydrogenation*, Wiley-VCH, 2008.

30 L. Schwartsburd and M. K. Whittlesey, *Ruthenium N-Heterocyclic Carbene Complexes for the Catalysis of Nonmetathesis Organic Transformations*, Wiley-VCH, 2014.

31 J. S. M. Samec, J. E. Bäckvall, P. G. Andersson and P. Brandt, *Chem. Soc. Rev.*, 2006, **35**, 237–248.

32 D. A. Hey, R. M. Reich, W. Baratta and F. E. Kühn, *Coord. Chem. Rev.*, 2018, **374**, 114–132.

33 S. Gauthier, R. Scopelliti and K. Severin, *Organometallics*, 2004, **23**, 3769–3771.

34 C. Cesari, A. Cingolani, C. Parise, S. Zacchini, V. Zanotti, M. C. Cassani and R. Mazzoni, *RSC Adv.*, 2015, **5**, 94707–94718.

35 M. Hollering, M. Albrecht and F. E. Kühn, *Organometallics*, 2016, **35**, 2980–2986.

36 G. Kleinhans, G. Guisado-Barrios, E. Peris and D. I. Bezuidenhout, *Polyhedron*, 2018, **143**, 43–48.

37 L. Pardatscher, M. J. Bitzer, C. Jandl, J. W. Kück, R. M. Reich, F. E. Kühn and W. Baratta, *Dalton Trans.*, 2019, **48**, 79–89.

38 M. Viji, N. Tyagi, N. Naithani and D. Ramaiah, *New J. Chem.*, 2017, **41**, 12736–12745.

39 S. Yasar, S. Cekirdek and I. Ozdemir, *J. Coord. Chem.*, 2014, **67**, 1236–1248.

40 J. B. Waters and J. M. Goicoechea, *Coord. Chem. Rev.*, 2015, **293**, 80–94.

41 O. Schuster, L. R. Yang, H. G. Raubenheimer and M. Albrecht, *Chem. Rev.*, 2009, **109**, 3445–3478.

42 L. Benhamou, J. Wolf, V. César, A. S. Labande, R. Poli, N. L. Lugan and G. Lavigne, *Organometallics*, 2009, **28**, 6981–6993.

43 S. Saha, T. Ghatak, B. Saha, H. Doucet and J. K. Bera, *Organometallics*, 2012, **31**, 5500–5505.

44 A. Prades, E. Peris and M. Albrecht, *Organometallics*, 2011, **30**, 1162–1167.

45 P. Mathew, A. Neels and M. Albrecht, *J. Am. Chem. Soc.*, 2008, **2008**, 13534–13535.

46 F. P. Malan, E. Singleton, P. H. van Rooyen, M. Albrecht and M. Landman, *Organometallics*, 2019, **38**, 2624–2635.

47 L. Bernet, R. Lalrempuia, W. Ghattas, H. Mueller-Bunz, L. Vigara, A. Llobet and M. Albrecht, *Chem. Commun.*, 2011, **47**, 8058.

48 L. Pardatscher, B. J. Hofmann, P. J. Fischer, S. M. Hölzl, R. M. Reich, F. E. Kühn and W. Baratta, *ACS Catal.*, 2019, **9**, 11302–11306.

49 J. Witt, A. Pöthig, F. E. Kühn and W. Baratta, *Organometallics*, 2013, **32**, 4042–4045.

50 D. A. Hey, M. J. Sauer, P. J. Fischer, E. M. H. J. Esslinger, F. E. Kühn and W. Baratta, *ChemCatChem*, 2020, **12**, 3537–3544.

51 M. L. S. Almeida, M. Beller, G. Z. Wang and J. E. Bäckvall, *Chem. – Eur. J.*, 1996, **2**, 1533–1536.

52 A. Mukherjee and S. Bhattacharya, *RSC Adv.*, 2021, **11**, 15617–15631.

53 F. Saleem, G. K. Rao, S. Kumar, M. P. Singh and A. K. Singh, *Dalton Trans.*, 2015, **44**, 19141–19152.

54 Q. Wang, W. Du, T. Liu, H. Chai and Z. Yu, *Tetrahedron Lett.*, 2014, **55**, 1585–1588.

55 S. Gauthier, R. Scopelliti and K. Severin, *Organometallics*, 2004, **23**, 3769–3771.

56 S. Manzini, C. A. Urbina-Blanco and S. P. Nolan, *Organometallics*, 2013, **32**, 660–664.

57 S. Gladiali and R. Taras, *Modern Reduction Methods*, Wiley-VCH, 2008.

35

5. Synthesis and Characterization of a Heterobimetallic *N*-heterocyclic Carbene Rhodium Ruthenium Complex as Catalyst for Transfer Hydrogenation

The results of this chapter have been published in

5.1. Publication Summary

In this manuscript, the preparation of a new mixed normal/abnormal NHC dicarbene complex **4** with both rhodium and ruthenium metal centers (see Figure 27) is described as a comparison to a previously reported heterobimetallic iridium ruthenium NHDC **5** to investigate the influence of the second metal center on catalytic performance and complex structure.[201] It is characterized by NMR, elemental analysis and SC-XRD experiments. In accordance to its iridium analogue **5**, complex **4** is obtained as an isomeric mixture.
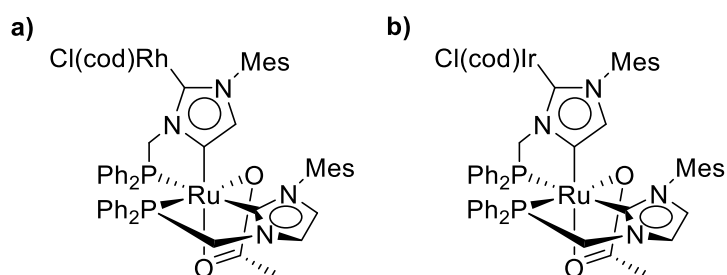
Figure 27. a) New heterobimetallic rhodium ruthenium NHDC complex **4** and b) previously reported iridium ruthenium analogue **5**.

Upon comparison of the SC-XRD structures of **4** (see Figure 28) and **5**, both are observed with their second metal center (rhodium or iridium, respectively) in square planar coordination whilst the coordination at the ruthenium center is described as distorted octahedral. However, complex **5** displays a significantly longer carbene-iridium bond with a value of 2.059(3) Å and a shorter iridium-chloride bond of 2.3693(9) Å, whilst the new rhodium complex has a carbene-rhodium bond with a value of 2.042(2) Å and a rhodium-chloride bond of 2.3756(7) Å. Whilst the abnormal carbene-ruthenium bonds are of similar magnitude in both **4** and **5**, the normal carbene-ruthenium bond in **4** is larger than in **5**, with 2.090(2) Å and 2.071(3) Å, respectively. Following the structural comparison of both compounds, complex **4** is also applied as catalyst in the TH of acetophenone. Similar to other complexes of this structure, a minor initiation phase is observed. Here, a TOF of 5 700 h^{-1} is achieved with 80% conversion after 25 min. In comparison, the iridium analogue **5** was reported to show a TOF of 6 700 h^{-1}. However, under

similar catalytic conditions, monometallic complexes have been reported to achieve near to full conversion after merely 5 min with TOFs of four times as high (26 000 h^{-1}).[194] It is therefore concluded, that whilst introduction of a second metal center results in significantly lower catalytic activity, the nature of the second metal has only a small impact, at least regarding rhodium and iridium. However, other structural changes have been shown to have a much larger impact on catalytic activity with several orders of magnitude, so that the small influence might be ascribed to the remoteness of the second metal center.
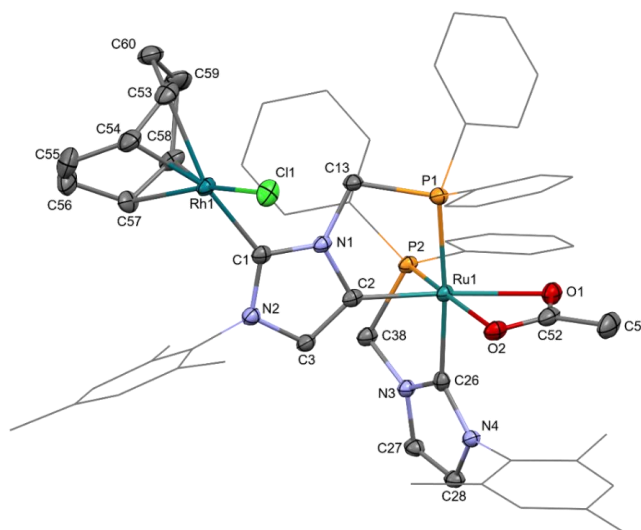

Figure 28. SC-XRD structure of rhodium ruthenium NHDC complex **4**.

5.2. Publication Reprint

Synthesis and Characterisation of a Heterobimetallic *N*-heterocyclic Carbene Rhodium Ruthenium Complex as Catalyst for Transfer Hydrogenation[☆]

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ABSTRACT

The heterobimetallic *N*-heterocyclic dicarbene (NHDC) rhodium ruthenium complex [Ru(OAc)(Mes-NHC-methyl-PPh$_2$)(Mes-aNHC-methyl-PPh$_2$)RhCl(cod)] (**4**) is obtained from a mixed normal/abnormal bis-NHC ruthenium complex *via* transmetallation by addition of [RhCl(cod)]$_2$ in THF at 40 °C, applying Ag$_2$O as base. Crystallization is achieved by layering a solution of **4** in THF with Et$_2$O. The complex is applicable as a catalyst in the transfer hydrogenation (TH) reaction of acetophenone, exhibiting a turnover frequency (TOF) of 6 700 h^{-1} with 80% conversion after 25 min (0.10 mol% catalyst, ^{i}PrOH, 80 °C, 2.00 mol% Na^{i}OPr). These results are compared to an analogous iridium ruthenium NHDC complex.

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1. Introduction

In coordination and organometallic chemistry, *N*-heterocyclic carbenes are applied as ligands for a large number of complexes in various research fields, among them, for example, medicinal chemistry [1], water splitting [2] and olefin metathesis [3]. An additional of the many areas of catalytic application is transfer hydrogenation (TH), especially for ruthenium based complexes [4–7] due to their strong σ-donor and weak π-acceptor capabilities and straightforward synthetic design [8]. Following the first report of a benchstable free NHC in 1991 by Arduengo *et al.* [9], research towards NHC complexes increased greatly. Among many other subgroups, abnormally coordinated NHC (aNHC) complexes have gained interest due to the exhibition of even stronger σ-donor effects compared to normal NHCs [10]. The first aNHC complex, an iridium hydride diphosphine with a bridged aNHC-pyridine ligand, was reported by Crabtree *et al.* in 2001 [11]. However, NHCs also allow for

deprotonation at several sites simultaneously, i.e. attainable due to the free *NCN* coordination site exhibited by the abnormal ligand, allowing for the coordination of a second metal centre. Such compounds, which are a relatively uncommon subgroup of NHCs, are described as carbanionic *N*-heterocyclic dicarbenes (NHDCs), often displaying electronic interactions of the metal centres across the π-system of the NHC ligand [12]. However, despite them representing a still comparatively rare NHC subgroup, various types of NHDC complexes have already been reported and summarized in reviews [13–19]. In 2006, an amido-tethered NHC lanthanide complex was treated with potassium naphthalenide for the generation of the first examples of NHC ligands with a C,C' bridge between two metals, as a heterobimetallic complex [20]. The first anionic *N*-heterocyclic dicarbene polymeric complex containing both normal and abnormal carbene in the same five-membered imidazole ring was prepared by Robinson *et al.* in 2010 [21]. A rare example of a mixed normal/abnormal NHC ruthenium complex (**1**, Fig. 1) was reported in 2015 [22]. Such ruthenium NHC complexes were shown to be highly active in TH reactions. Furthermore, the first examples of heterobimetallic imidazolyl-phosphine based NHDC complexes with two different d-block elements (**2**, **3**) were reported. These belong to the class of Janus-type di-NHC complexes [23].

This work reports the preparation and structure of [Ru(OAc)(Mes-NHC-methyl-PPh$_2$)(Mes-aNHC-methyl-PPh$_2$)RhCl(cod)] (**4**, cod = 1,5-cycloocta-diene) as a rare example for such transition metal heterobimetallic NHDCs. It is applied in the TH of acetophenone and compared to an analogous iridium ruthenium NHDC (**5**) [24].

2. Experimental

2.1. General Methods and Materials

All reactions were carried out under oxygen free, dry conditions in an argon atmosphere using standard Schlenk and glovebox conditions. The solvents used were purified, degassed, and dried according to standard purification techniques [25] or prior obtained from an MBraun solvent purification system (SPS). Mesitylimidazole [26], hydroxomethyl diphenylphosphine oxide [27], Ru(OAc)$_2$(PPh$_3$)$_2$ [28] and complexes **1** and **2** were obtained according to literature procedures [22]. All further chemicals were purchased and used from Sigma-Aldrich, VWR and abcr as received. NMR spectra were recorded on a Bruker Avance Ultrashield 400 MHz and a Bruker DPX 400 MHz spectrometer. All ^{1}H chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak serving as internal reference [29]. ^{31}P{1H} NMR spectra are referenced to 85% H$_3$PO$_4$ as external standard. Abbreviations for NMR multiplicities are singlet (s), doublet (d), triplet (t), septet (sept), and multiplet (m). Coupling constants are given in Hz. Elemental analysis was performed at the microanalytical laboratory of the Catalysis Research Center, Technische Universität München. Single crystals were measured in the SC-XRD laboratory of the Catalysis Research Center at Technische Universität München, Germany.

2.2. Synthesis and Characterization

Complex **2** (100 mg, 88.0 μmol, 1.00 eq.), [RhCl(cod)]$_2$ (43.5 mg, 88.0 μmol, 1.00 eq.), and Ag$_2$O (40.6 mg, 176 μmol, 2.00 eq.) are suspended in THF (10 ml) and stirred at 40 °C for 2 h under exclusion of light. The suspension is filtered off with a cannula and concentrated to less than 4 ml under reduced pressure. The product is precipitated upon slow addition of *n*-pentane. The solvent is removed by a cannula and the crude product is washed with *n*-pentane (3 × 3 mL) and subsequently dried *in vacuo*, affording complex **4** as light-yellow powder. In accordance to literature, the product is obtained as an isomeric mixture (ratio 1.00:0.70). Yield: 78% (82.2 mg, 68.6 μmol). Single crystals suitable for X-ray diffraction (XRD) analysis are obtained by layering of a solution of **4** in THF with Et$_2$O. The crystals are fixed on the top of a Kapton micro sampler with perfluorinated ether and transferred to the diffractometer. ^{1}H NMR (400 MHz, CD$_2$Cl$_2$, 298 K, major isomer): δ 7.94–7.80 (m, 2H, Ar–H), 7.67–7.55 (m, 2H, Ar–H), 7.48–7.26 (m, 5H, Ar–H), 7.25–6.81 (m, 14H, Ar–H), 6.62 (s, 1H, Ar–H), 6.37–6.28 (m, 2H, Ar–H), 5.58 (s, 1H, Ar–H), 5.62 (dd, ^2J = 9.8, 14.6 Hz, 1H, CH$_2$P), 4.72 (dd, ^2J = 12.5 Hz 1H, CH$_2$P), 4.51–4.41 (m, 1H, CH$_{cod}$), 4.10 (t, 1H, CH$_2$P), 4.13–4.05 (m, 1H, CH$_{cod}$), 3.15 (dd, ^2J = 14.0 Hz, 1H, CH$_2$P), 3.02–2.90 (m, 2H, CH$_{cod}$), 2.51 (s, 3H, CH$_3$), 2.38 (s, 3H, CH$_3$), 2.22 (s, 3H, CH$_3$), 2.17 (s, 3H, CH$_3$), 1.97 (s, 3H, CH$_3$), 1.86–1.46 (m, 8H, CH$_{cod}$), 0.52 (s, 3H, CH$_3$). ^{1}H NMR (400 MHz, CD$_2$Cl$_2$, 298 K, minor isomer): δ 7.94–7.80 (m, 2H, Ar–H), 7.67–7.55 (m, 2H, Ar–H), 7.48–7.26 (m, 5H, Ar–H), 7.25–6.81 (m, 14H, Ar–H), 6.66 (s, 1H, Ar–H), 6.37–6.28 (m, 2H, Ar–H), 5.90 (dd, ^2J = 10.1, 13.9 Hz, 1H, CH$_2$P), 5.50 (s, 1H, Ar–H), 4.72 (dd, ^2J = 12.5 Hz 1H, CH$_2$P), 4.51–4.41 (m, 1H, CH$_{cod}$), 4.10 (t, 1H, CH$_2$P), 4.01–4.05 (m, 1H, CH$_{cod}$), 3.39 (m, 1H, CH$_2$P), 3.33–3.20 (m, 2H, CH$_{cod}$), 2.38 (s, 3H, CH$_3$), 2.27 (s, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 2.17 (s, 3H, CH$_3$), 2.07 (s, 3H, CH$_3$), 1.86–1.46 (m, 8H, CH$_{cod}$), 0.49 (s, 3H, CH$_3$). ^{31}P{1H} NMR (162 MHz, CD$_2$Cl$_2$, 298 K, major isomer): δ 80.3 (d, 1P, $^2J_{PP}$= 24.7 Hz), 56.9 (d, 1P, $^2J_{PP}$ = 23.4 Hz). ^{31}P{1H} NMR (162 MHz, CD$_2$Cl$_2$, 298 K, minor isomer): δ 80.7 (d, 1P, $^2J_{PP}$ = 23.7 Hz), 59.1 (d, 1P, $^2J_{PP}$ = 23.7 Hz). Elemental analysis anal. calcd for **4**: C, 60.34; H, 5.94; N, 4.85%. Found: C, 59.85; H, 5.41; N, 4.55%.

2.3. Crystallisation and Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. Hydrogen atoms could not be located in the difference Fourier maps and were calculated in ideal positions (riding model) with C-H = 0.95 Å (aromatic), 0.98 Å (methyl), 0.99 Å (methylene) and 1.00 Å (methine) and with U$_{iso}$(H) = 1.5·U$_{eq}$(C) for methyl groups and 1.2·U$_{eq}$(C) otherwise.

The rhodium bound 1,5-cyclooctadiene (cod) ligand was found to be partially disordered over two positions. The site-occupancy factors of the disordered parts were refined by means of a free variable and result in a ratio of 0.516(9) to 0.484(9). The displacement parameters of the carbon atoms of the cod moiety were restrained using SIMU with a standard uncertainty (s.u.) of 0.04 Å^2 and RIGU with an s.u. of 0.004 Å^2. Furthermore, C53B and C58B were isotropically restrained using ISOR (s.u. = 0.005 Å^2). CCDC 2194285 contains the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

2.4. Catalytic Procedure

A Schlenk tube (25.0 mL) is charged with catalyst stock solution (1.00 mL, 1.00 mM in ^{i}PrOH). Acetophenone (117 μL, 1.00 mmol) and ^{i}PrOH (8.68 mL) are added. A syringe (1.00 mL) is inserted through a septum *via* a cannula. The argon valve (0.30 bar) is left open during the entire reaction for a constant overpressure. The mixture is stirred and heated to 80 °C for 2 min. The reaction is initiated by addition of a 0.1 M solution of NaO^{i}Pr in ^{i}PrOH (200 μL, 0.02 mmol, 2.00 mol%). Samples (0.30 mL) are taken at defined intervals using the syringe without removing the cannula from the septum. The syringe is detached from the cannula and a fresh syringe is used for every sample. The samples are quenched in a cooling solution (0 °C) of Et$_2$O and filtered over a short pad of silica. Analysis is performed *via* gas chromatography. Blanc experiments without catalyst or without base show no conversion.

3. Results and Discussion

3.1. Synthesis and NMR Analysis

Applying a literature procedure [24], the heterobimetallic silver NHDC complex **2** is prepared from the monometallic precursor complex **1** (Scheme 1). From here, a transmetallation reaction with [RhCl(cod)]$_2$ is performed with Ag$_2$O [24]. This results in the isolation of the heterobimetallic Rh-Ru complex **4** as yellow powder. The NMR results support the structure obtained from the X-ray diffraction analysis and propose that complex **4** is retained in CD$_2$Cl$_2$ solvent. The ^{1}H NMR spectrum shows characteristic peaks for all hydrogen atoms in the structure of the complex. According to the spectrum, the signal of the NCHN proton of the abnormal carbene is extremely deshielded (δ = 9.76 ppm), close to the approximately acidic proton of the ligand precursor P-NHC·HBr (10.33 ppm) [22,39]. The results indicate that the transmetallation reaction occurs efficiently in the presence of extra equivalent Ag$_2$O to avoid the formation of trace amounts of complex **1** with chloride or bromide as counter-ion. The ^{31}P{1H} NMR measurements of Rh-Ru complex in CD$_2$Cl$_2$ reveal *cis* RuP$_2$ configuration for both

2

III Results and Discussion

Table 1
Crystallographic data and details of structure refinement of **4**.

Crystal data	
Chemical formula	$C_{60}H_{64}ClN_4O_2P_2RhRu$
M_r	1174.53
Crystal system, space group	Triclinic, $P1$
Temperature (K)	100
a, b, c (Å)	11.1016 (11), 15.8900 (16), 17.1242 (18)
α, β, γ (°)	70.164 (3), 73.100 (3), 75.893 (3)
V (Å^3)	2683.3 (5)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.75
Crystal size (mm)	$0.18 \times 0.16 \times 0.04$
Data collection	
Diffractometer	Bruker D8 Venture
Absorption correction	Multi-scan
SADABS 2016/2	
T_{min}, T_{max}	0.666, 0.745
No. of measured, independent And observed [$I > 2\sigma(I)$] reflections	115490, 10310, 9460
R_{int}	0.036
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.613
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.023, 0.058, 1.07
No. of reflections	10310
No. of parameters	720
No. of restraints	348
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.44, −0.60

Computer programs: *APEX* 4 Control Software [30], *SAINT* [31], SHELXT [32], *SHELXL* [33], SHELXLE [34], *PLATON* [35], enCIFer [36], Mercury [37], SADABS 2016/2 [38].
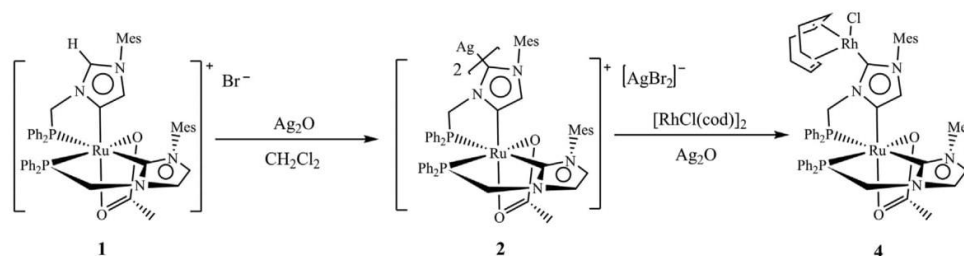
Scheme 1. Synthetic pathway for preparation of NHDC complex **4** from precursor **1**, applying the silver trans-metalation route over complex **2** as intermediate.
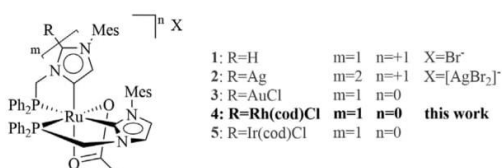
Fig. 1. Mono- and heterobimetallic mixed normal/abnormal NHC ruthenium(II) complexes. (**1-3** [22] and **5** [24] as well as this work).

isomers, illustrated by the presence of four doublets at 80.4, 57.1 ($^2J_{PP}$ = 24 Hz) and 80.7, 59.1 ppm ($^2J_{PP}$ = 24 Hz), respectively, for two isomers which is comparable to the coupling constants reported for the analogous iridium ruthenium complex **5** in this family [24]. It should be noted that the signal splitting between the major and minor isomer peaks in rhodium ruthenium complex **4** is bigger than complex **5**.

3.2. X-ray Diffraction Crystallography

In the heterobimetallic title compound **4** (Fig. 1) rhodium is found in square planar coordination by cod, chloride and a ligand moiety, while ruthenium is coordinated by acetate and two ligand moieties that are all binding in bidentate fashion. The coordination geometry is best described as distorted octahedral. The main reason for this is the small binding angle of acetate with a O1-Ru1-O2 angle of 59.03(5)°. The abnormal NHC is bound to ruthenium with a C2-Ru1 distance of 2.035(2) Å, while C26-Ru1 amounts to 2.090(2) Å for the NCN coordinating imidazolyl. The ruthenium bound carbenes thereby span an angle of 93.23(8)°. The stronger trans-influence of the carbenes with respect to O- and P-donors manifests in significantly longer Ru1-O1 (2.2586(15) Å; trans to abnormal NHC, C2) and Ru1-P1 (2.2951(7) Å; trans normal NHC, C26) compared to Ru1-O2 (2.2042(15) Å; trans P2) and Ru1-P2 (2.2196(7) Å; trans O2). The bond distances between rhodium and the NHC and rhodium and chloride are 2.042(2) Å and 2.3756(7) Å, respectively, resulting in an almost perfect rectangular C1-Rh1-Cl1 angle of 89.60(6)° (Fig. 2).
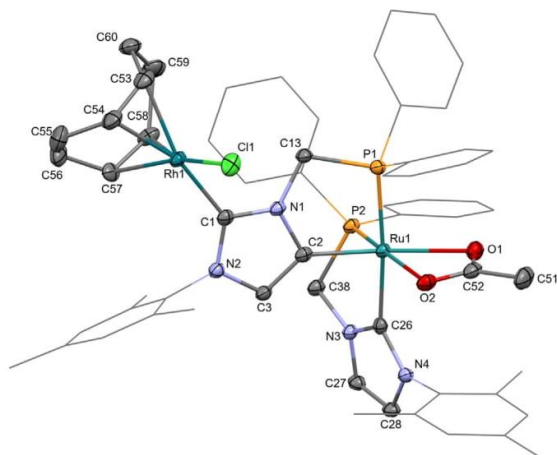
Fig. 2. View of **4** with the atom numbering scheme. H atoms and the disordered cod part have been omitted and the mesityl and phenyl substituents are drawn in wireframe representation for clarity. Displacement ellipsoids are drawn at a 50% probability level.

Fig. 3. Kinetic profile of the catalytic TH of acetophenone to acetophenol applying the Rh-Ru NHDC complex **4** at 80 °C with NaO^{i}Pr (2.00 mol%) in ^{i}PrOH at 0.10 mol% catalyst loading.

Structurally related compounds have been reported in literature with NCN bound Au-Cl (**3**) and Ag (**2**), which gives a positively charged silver bound dimer, where [AgBr$_2$]$^-$ interacts with the silver bridge. However, direct comparison of the crystallographic data to the monometallic ruthenium complex (**1**) is not feasible as no suitable crystals for SC-XRD could be obtained [22]. The closest related compound with an Ir(cod)Cl moiety (**5**) [24] shows a significantly longer carbene-iridium bond with 2.059(3) Å, whilst the Ir1-Cl1 distance is significantly shortened to 2.3693(9) Å. The C1-Ir1-Cl1 angle is significantly larger than for the rhodium compound with a value of 90.68(9)° Å. The abnormal C2-Ru1 and the normal C26-Ru1 distances are 2.026(3) Å and 2.071(3) Å, respectively. Only the normal carbene-ruthenium bond is significantly shorter in the iridium compound in comparison to the rhodium compound, whilst the abnormal carbene-ruthenium bond does not deviate in terms of statistical relevance. With respect to the rhodium compound, the C2-Ru1-C26 angle is significantly smaller in the iridium compound with a value of 88.19(12)°.

3.3. Transfer Hydrogenation Catalysis

Complex **4** has been applied as catalyst in transfer hydrogenation (TH) as similar literature-known complexes are usually very potent in this field. Applying a catalyst loading of 0.10 mol% in regard to the substrate at 80 °C in ^{i}PrOH and applying 2.00 mol% Na^{i}OPr as base, a turnover frequency (TOF) of 5 700 h^{-1} with 80% conversion after 25 min was achieved (Fig. 3). Similar to other complexes [40], complex **4** also shows a minor initiation phase, indicating the necessity of activation. More strictly speaking, compound **4** has therefore to be considered a pre-catalyst, not as the catalyst itself.

In contrast, the analogous iridium ruthenium catalyst **5** has been reported to display a TOF of 6 700 h^{-1}, whilst the monometallic complex **1** achieves near to full conversion after 5 min with a TOF about four times as high (26 000 h^{-1}) under similar catalytic conditions. Therefore, in comparison to the monometallic complex, introduction of a second metal centre (Rh, Ir) results in significantly lower catalytic activity. However, alteration of the second metal itself apparently has only a small impact on the catalytic activity. Whilst the Rh catalyst **4** shows a TOF about 15 % lower than that of the Ir analogue **5**, other (e. g. structural) changes have been
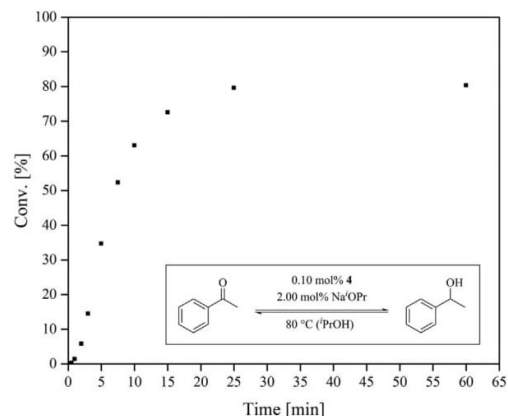
shown to have a much greater impact on catalytic activity (several orders of magnitude), hence the influence of the second metal appears to be comparatively small [24,40]. This observation might be ascribed to the remoteness of the second metal with respect to the active center.

4. Summary

Preparation of a new hetero-bimetallic rhodium ruthenium mixed normal/abnormal NHC complex is reported as well as its characterization. It has been applied as catalyst in the transfer hydrogenation reaction of acetophenone at 80 °C in *iso*-propanol utilizing NaO^{i}Pr as base, resulting in a TOF of ca. 5 700 h^{-1}. The results were rationalized in comparison to an iridium and monometallic analogue and discussed regarding the effect of the second metal on catalyst activity.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2022.122498.

References

[1] I. Ott, Metal N-heterocyclic carbene complexes in medicinal chemistry, in: 2020: pp. 121–148. doi:10.1016/bs.adioch.2019.10.008.

[2] S. Kaufhold, L. Petermann, R. Staehle, S. Rau, Transition metal complexes with N-heterocyclic carbene ligands: From organometallic hydrogenation reactions toward water splitting, Coord. Chem. Rev. 304–305 (2015) 73–87, doi:10.1016/j.ccr.2014.12.004.

[3] R.H. Grubbs, A.G. Wenzel, D.J. O'Leary, E. Khosravi, Handbook of Metathesis, WILEY-VCH, 2015.

[4] D.A. Hey, R.M. Reich, W. Baratta, F.E. Kühn, Current advances on ruthenium(II) N-heterocyclic carbenes in hydrogenation reactions, Coord. Chem. Rev. 374 (2019) 11302–11306, doi:10.1016/j.ccr.2018.06.005.

III Results and Discussion

[5] L. Pardatscher, B.J. Hofmann, P.J. Fischer, S.M. Hölzl, R.M. Reich, F.E. Kühn, W. Baratta, Highly Efficient Abnormal NHC Ruthenium Catalyst for Oppenauer-Type Oxidation and Transfer Hydrogenation Reactions, ACS Catal 9 (2019) 11302–11306, doi:10.1021/acscatal.9b03677.

[6] D. Wang, D. Astruc, The Golden Age of Transfer Hydrogenation, Chem. Rev. 115 (2015) 6621–6686, doi:10.1021/acs.chemrev.5b00203.

[7] J. Witt, A. Pöthig, F.E. Kühn, W. Baratta, Abnormal N-Heterocyclic Carbene-Phosphine Ruthenium(II) Complexes as Active Catalysts for Transfer Hydrogenation, Organometallics 32 (2013) 4042–4045, doi:10.1021/om400400w.

[8] E. Peris, Smart N-Heterocyclic Carbene Ligands in Catalysis, Chem. Rev. 118 (2018) 9988–10031, doi:10.1021/acs.chemrev.6b00695.

[9] A.J. Arduengo, R.L. Harlow, M. Kline, A stable crystalline carbene, J. Am. Chem. Soc. 113 (1991) 361–363, doi:10.1021/ja00001a054.

[10] R.H. Crabtree, Abnormal, mesoionic and remote N-heterocyclic carbene complexes, Coord. Chem. Rev. 257 (2013) 755–766, doi:10.1016/j.ccr.2012.09.006.

[11] S. Gründemann, A. Kovacevic, M. Albrecht, J.W. Faller Robert, H. Crabtree, Abnormal binding in a carbene complex formed from an imidazolium salt and a metal hydride complex, Chem. Commun. (2001) 2274, doi:10.1039/b107881j.

[12] J.B. Waters, J.M. Goicoechea, Coordination chemistry of ditopic carbanionic N-heterocyclic carbenes, Coord. Chem. Rev. 293–294 (2015) 80–94, doi:10.1016/j.ccr.2014.09.020.

[13] J.A. Mata, F.E. Hahn, E. Peris, Heterometallic complexes, tandem catalysis and catalytic cooperativity, Chem. Sci. 5 (2014) 1723–1732, doi:10.1039/C3SC53126K.

[14] E. Mas-Marzá, J.A. Mata, E. Peris, Triazolediylidenes: A Versatile Class of Ligands for the Preparation of Discrete Molecules of Homo- and Hetero-Binuclear Complexes for Improved Catalytic Applications, Angew. Chemie Int. Ed. 46 (2007) 3729–3731, doi:10.1002/anie.200700535.

[15] A. Zanardi, J.A. Mata, E. Peris, Well-Defined Ir/Pd Complexes with a Triazolyldiylidene Bridge as Catalysts for Multiple Tandem Reactions, J. Am. Chem. Soc. 131 (2009) 14531–14537, doi:10.1021/ja906028g.

[16] S. Sabater, J.A. Mata, E. Peris, Heterobimetallic Iridium–Ruthenium Assemblies through an Ambidentate Triazole-Diylidene Ligand: Electrochemical Properties and Catalytic Behavior in a Cascade Reaction, Organometallics 31 (2012) 6450–6456, doi:10.1021/om300675p.

[17] R. Maity, H. Koppetz, A. Hepp, F.E. Hahn, Heterobimetallic Carbene Complexes by a Single-Step Site-Selective Metalation of a Tricarbene Ligand, J. Am. Chem. Soc. 135 (2013) 4966–4969, doi:10.1021/ja401546h.

[18] M.T. Zamora, M.J. Ferguson, R. McDonald, M. Cowie, Unsymmetrical Dicarbenes Based on N-Heterocyclic/Mesoionic Carbene Frameworks: A Stepwise Metalation Strategy for the Generation of a Dicarbene-Bridged Mixed-Metal Pd/Rh Complex, Organometallics 31 (2012) 5463–5477, doi:10.1021/om3004543.

[19] S. Gonell, M. Poyatos, J.A. Mata, E. Peris, Y-Shaped Tris-N-Heterocyclic-Carbene Ligand for the Preparation of Multifunctional Catalysts of Iridium, Rhodium, and Palladium, Organometallics 31 (2012) 5606–5614, doi:10.1021/om300569w.

[20] P.L. Arnold, S.T. Liddle, Deprotonation of N-Heterocyclic Carbenes to Afford Heterobimetallic Organolanthanide Complexes, Organometallics 25 (2006) 1485–1491, doi:10.1021/om050895u.

[21] Y. Wang, Y. Xie, M.Y. Abraham, P. Wei, H.F. Schaefer, P.v.R. Schleyer, G.H. Robinson, A Viable Anionic N-Heterocyclic Dicarbene, J. Am. Chem. Soc. 132 (2010) 14370–14372, doi:10.1021/ja106631r.

[22] M.J. Bitzer, A. Pöthig, C. Jandl, F.E. Kühn, W. Baratta, Ru–Ag and Ru–Au dicarbene complexes from an abnormal carbene ruthenium system, Dalt. Trans. 44 (2015) 11686–11689, doi:10.1039/C5DT01914A.

[23] M. Poyatos, E. Peris, Insights into the past and future of Janus-di-N-heterocyclic carbenes, Dalt. Trans. 50 (2021) 12748–12763, doi:10.1039/D1DT02035H.

[24] L. Pardatscher, M.J. Bitzer, C. Jandl, J.W. Kück, R.M. Reich, F.E. Kühn, W. Baratta, Cationic abnormal N-heterocyclic carbene ruthenium complexes as suitable precursors for the synthesis of heterobimetallic compounds, Dalt. Trans. 48 (2019) 79–89, doi:10.1039/C8DT03713B.

[25] W.L.F. Armarego, C. li lin Chai, Purification of Laboratory Chemicals, 5th ed., Butterworth-Heinemann, Oxford, 2003.

[26] D.-H. Lee, J.-H. Kim, B.-H. Jun, H. Kang, J. Park, Y.-S. Lee, Macroporous Polystyrene-Supported Palladium Catalyst Containing a Bulky N-Heterocyclic Carbene Ligand for Suzuki Reaction of Aryl Chlorides, Org. Lett. 10 (2008) 1609–1612, doi:10.1021/ol8003047.

[27] E.M. Schuster, M. Botoshansky, M. Gandelman, Pincer Click Ligands, Angew. Chemie Int. Ed. 47 (2008) 4555–4558, doi:10.1002/anie.200800123.

[28] R.W. Mitchell, A. Spencer, G. Wilkinson, Carboxylato-triphenylphosphine complexes of ruthenium, cationic triphenylphosphine complexes derived from them, and their behaviour as homogeneous hydrogenation catalysts for alkenes, J. Chem. Soc. Dalt. Trans. 846 (1973), doi:10.1039/dt9730000846.

[29] G.R. Fulmer, A.J.M. Miller, N.H. Sherden, H.E. Gottlieb, A. Nudelman, B.M. Stoltz, J.E. Bercaw, K.I. Goldberg, NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist, Organometallics 29 (2010) 2176–2179, doi:10.1021/om100106e.

[30] APEX suite of crystallographic software, (2021).

[31] SAINT, Bruker AXS Inc.: Madison, Wisconsin, USA, (2019).

[32] G.M. Sheldrick, Crystal structure refinement with SHELXL, Acta Crystallogr. Sect. C Struct. Chem. 71 (2015) 3–8, doi:10.1107/S2053229614024218.

[33] G.M. Sheldrick, SHELXL2018/3, University of Göttingen, Germany, 2018.

[34] C.B. Hübschle, G.M. Sheldrick, B. Dittrich, ShelXle : a Qt graphical user interface for SHELXL, J. Appl. Crystallogr. 44 (2011) 1281–1284, doi:10.1107/S0021889811043202.

[35] A.L. Spek, PLATON, A Multipurpose Crystallographic Tool (2011).

[36] F.H. Allen, O. Johnson, G.P. Shields, B.R. Smith, M. Towler, CIF applications, XV. enCIFer : a program for viewing, editing and visualizing CIFs, J. Appl. Crystallogr. 37 (2004) 335–338, doi:10.1107/S0021889804003528.

[37] C.F. Macrae, I. Sovago, S.J. Cottrell, P.T.A. Galek, P. McCabe, E. Pidcock, M. Platings, G.P. Shields, J.S. Stevens, M. Towler, P.A. Wood, Mercury 4.0 : from visualization to analysis, design and prediction, J. Appl. Crystallogr. 53 (2020) 226–235, doi:10.1107/S1600576719014092.

[38] SADABSVersion 2016/2, Bruker AXS Inc., Madison, Wisconsin, USA, 2016.

[39] T. Guo, S. Dechert, F. Meyer, Dinuclear Palladium Complexes of Pyrazole-Bridged Bis(NHC) Ligands: A Delicate Balance between Normal and Abnormal Carbene Coordination, Organometallics 33 (2014) 5145–5155, doi:10.1021/om500351j.

[40] A.D. Böth, M.J. Sauer, W. Baratta, F.E. Kühn, Abnormal NHC ruthenium catalysts: mechanistic investigations of their preparation and steric influence on catalytic performance, Catal. Sci. Technol. (2022) Advance Article, doi:10.1039/D2CY01036D.

IV Conclusion and Outlook

In this work, two types of modified aNHC ruthenium complexes were prepared and their corresponding influences on their catalytic activities in transfer hydrogenation and Oppenauer-type oxidation reactions investigated.

In the first modification, a row family of *bis*-aNHC ruthenium diphenylphosphino complexes of the type [Ru(OAc)(aNHC-ethyl-PPh$_2$)$_2$)]Br is described, with increasing steric bulk of their wingtip substituents, from phenyl **1** over mesityl **2** to di-*iso*-propylphenyl **3**. It could be shown, that the stability of these complexes in solution increases with larger steric bulk, **3** being the most stable. This could then be utilized for a mechanistic formation study, revealing complexes **3a** and **3b** as kinetic and thermodynamic mono-NHC intermediates. This finding is of interest for the complex design when preparing further compound of this class, as they can be adapted to suit the conditions and transformations required for the formation of the final complexes. Complexes **1**, **2** and **3** were then applied in a comparative study in TH and Oppenauer-type oxidation reactions, with acetophenone and *α*-tetralol as substrates, respectively. Here, the varying steric demand of the wingtip substituents resulted in increasing activity following the order **1** > **2** > **3** for TH and the reverse **3** > **2** > **1** for Oppenauer-type oxidation, with **1** achieving an exceptionally high TOF of 550 000 h^{-1} in TH and **3** a TOF of up to 280 000 h^{-1} in the latter. This trend was rationalized according to buried volume calculations, computational results and mechanistic insights. Whilst in the TH, increased activity is in-line with decreased steric demand of the wingtip substituent, which corresponds to ketone H insertion from the substrate into the active center being the rate determining step, the Oppenauer-type oxidation most likely displays a change of the rate determining step to the *β*-H elimination of the alkoxide product, facilitated by the larger bulk. The results of this mechanistic investigation therefore open up the field for further studies regarding the catalytic cycle of *bis*-aNHC ruthenium complexes as well as further potential modifications. For one, the herein described mechanism remains a suggestion based on literature results. Therefore, further experiments are required to gain a better understanding of its nature. A specific experiment aimed at strengthening the suggested inner-sphere mechanism is performance of NMR experiments with deuterated substrates, similar to Bäckvalls deuteration procedure (see Scheme 8), albeit still hindered by possible scrambling of the protons. Furthermore, as catalytic results and the observation of induction periods under certain conditions indicate the formation of an active catalytic species from complexes **1-3** (hence acting as pre-catalysts), isolation and characterization of these species is highly desirable. Possibly, ^{31}P NMR experiments applying low (or slowly increasing) temperatures under catalytic conditions could yield insight into the nature of this active species. However, these require careful design, as fast decomposition of the catalyst is likely to occur upon near to full conversion within minutes. Changing the solvent from *iso*-propanol (which

also acts as reagent) to a solvent that does not facilitate *β*-H elimination, normal NHC di-hydride formation and thus deactivation could represent a promising approach. Normal NHC di-hydride formation and thus deactivation could also be inhibited by blocking the normal NHC carbene position, thus only facilitating aNHC coordination. Here, modification of the NCN carbene position by addition of a methyl substituent or switching from imidazole to triazole based ligands could be promising approaches. These could then additionally be utilized for characterization of the active species. Should the problem of complex stability be overcome, inclusion of enantioselectivity, i.e. by backbone modification, would represent the next step towards industrial application for this class of complexes.

For the second modification, a new heterobimetallic mixed normal/abnormal NHDC rhodium ruthenium complex **4** was prepared in accordance to an iridium analogue **5**. Comparison of SC-XRD structures revealed a significantly shorter carbene-rhodium bond of **4** compared to the analogous carbene-iridium bond of **5**, whilst the rhodium-chloride bond of **4** was observed to be larger than the iridium-chloride bond of **5**. In addition, whilst the abnormal NHC-ruthenium bonds are of similar order of magnitude for both **4** and **5**, the normal NHC-ruthenium is larger for **4** than **5**. Regarding catalytic activity in the TH of acetophenone, both **4** (5 700 h^{-1}) and **5** (6 700 h^{-1}) are also in the same order of magnitude, whilst comparable monometallic complexes have been reported to display TOFs four times as high (26 000 h^{-1}). Hence, application of heterobimetallic complexes in catalysis does not seem promising in TH and will require identification of other specifically tailored transformations.

V References

(1)   Mendeleev, D. I. *Zh. Russ. Fiz.-Khim. Obsch.* **1869**, 60.
(2)   Meyer, L. *F. Wöhler, J. Liebig, H. Kopp (Eds.) Annalen der Chemie und Pharmacie: Supplementband, C. F. Winter'sche Verlagshandlung* **1869**, 354.
(3)   Newlands, J. A. R. *Chemical News* **1864**, *10*, 94.
(4)   Newlands, J. A. R. *Chemical News* **1865**, *12*, 83.
(5)   Wurzer, F. *Annalen der Physik* **1817**, *56*, 331.
(6)   Döbereiner, J. W. *Annalen der Physik* **1829**, *91*, 301.
(7)   Spronsen, J. W. v. *J. Chem. Educ.* **1969**, *46*, 136.
(8)   Constable, E. C. *Dalton Trans.* **2019**, *28*, 9408.
(9)   Nilson, F. L. *Chem. Ber.* **1879**, *12*, 554.
(10)   Boisbaudran, P. E. L. d. *C. R. Acad. Sci.* **1875**, *81*, 493.
(11)   Winkler, C. *Chem. Ber.* **1886**, *19*, 210.
(12)   D. McDonald, L. B. H. *A History of Platinum and its Allied Metals*; Johnson Matthey Plc: London, **1982**.
(13)   Weeks, M. E. *Discovery of the Elements*; Journal of Chemical Education, **1956**.
(14)   Griffith, W. P. *Platin. Met. Rev.* **2003**, *47*, 175.
(15)   Wollaston, W. H. *Philos. Trans. R. Soc.* **1804**, *94*, 419.
(16)   Wollaston, W. H. *J. Nat. Philos., Chem. Arts* **1805**, *10*, 3.
(17)   Griffith, W. P. *Platin. Met. Rev.* **2004**, *48*, 182.
(18)   Tennant, S. *Philos. Trans. R. Soc.* **1804**, *94*, 411.
(19)   Tennant, S. *J. Nat. Philos., Chem. Arts* **1805**, *10*, 24.
(20)   Śniadecki, J. *Rozprawa o nowym metalu w surowej platynie odkrytym* Wilno, **1808**.
(21)   Emsley, J. *Nature's Building Blocks. An A-Z Guide to the Elements*; Oxford University Press: Oxford, **2001**.
(22)   Marshall, J. L.; Marshall, V. R. *Bull. Hist. Chem.* **2010**, *35*, 33.
(23)   *The Philosophical Magazine* **1827**, *2*, 391.
(24)   Osann, G. *Poggendorffs Annalen der Physik und Chemie* **1828**, *14*, 329.
(25)   Weeks, M. E. *J. Chem. Educ.* **1932**, *9*, 1017.
(26)   Osann, G. *Poggendorffs Annalen der Physik und Chemie* **1829**, *15*, 158.
(27)   Claus, K. E. *Annalen der Physik und Chemie* **1845**, *140*, 192.
(28)   Pitchkov, V. N. *Platin. Met. Rev.* **1996**, *40*, 181.
(29)   Hollemann, A. F.; Wiberg, E.; Wiberg, N. *Lehrbuch der Anorganischen Chemie*; 102. ed.; Walter de Gruyter & Co.: Berlin, **2007**.
(30)   Rard, J. A. *Chem. Rev.* **1985**, *85*, 1.
(31)   Binder, H. H. *Lexikon der chemischen Elemente*; S. Hirzel Verlag: Stuttgart, **1999**.
(32)   Greenwood, N. N.; Earnshaw, A. *Chemistry of the elements*; Butterworth-Heinemann: Oxford, **1997**.
(33)   Renner, H.; Schlamp, G.; Kleinwächter, I.; Drost, E.; Lüschow, H. M.; Tews, P.; Panster, P.; Diehl, M.; Lang, J.; Kreuzer, T.; Knödler, A.; Starz, K. A.; Dermann, K.; Rothaut, J.; Drieselmann, R.; Peter, C.; Schiele, R. *Platinum Group Metals and Compounds*; Wiley-VCH: Weinheim, **2001**.
(34)   Loferski, P. J.; Ghalayini, Z. T.; Singerling, S. A. *Minerals Yearbook*; United States Geological Survey: Reston, United States, **2016**.
(35)   Kluson, P.; Cerveny, L. *Appl. Catal. A Gen.* **1995**, *128*, 13.
(36)   B., G. C. *Platin. Met. Rev.* **1968**, *12*, 19.
(37)   Ogba, O. M.; Warner, N. C.; O'Leary, D. J.; Grubbs, R. H. *Chem. Soc. Rev.* **2018**, *47*, 4510.
(38)   Bielawa, H.; Hinrichsen, O.; Birkner, A.; Muhler, M. *Angew. Chem. Int. Ed.* **2001**, *40*, 1061.
(39)   Schulz, H. *Appl. Catal. A Gen.* **1999**, *186*, 3.
(40)   Barthazy, P.; Stoop, R. M.; Wörle, M.; Togni, A.; Mezzetti, A. *Organometallics* **2000**, *19*, 2844.

(41) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **1995**, *34*, 2039.

(42) Shvo, Y.; Czarkie, D.; Rahamim, Y.; Chodosh, D. F. *J. Am. Chem. Soc.* **1986**, *108*, 7400.

(43) Bruneau, C.; Dixneuf, P. H. *Ruthenium in Catalysis*; Springer Verlag: Berlin, Germany, **2014**.

(44) Morris, R. H. *The Handbook of Homogeneous Hydrogenation*; Wiley-VCH, **2008**.

(45) Hey, D. A.; Reich, R. M.; Baratta, W.; Kühn, F. E. *Coord. Chem. Rev.* **2018**, *374*, 114.

(46) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. *Nature* **2014**, *510*, 485.

(47) J. B. Dumas, E. P. *Annales de Chimie et de Physique* **1835**, *58*, 5.

(48) Cesar, V.; Gade, L. H.; Bellemin-Laponnaz, S. *NHC-Cobalt, Rhodium and Iridium Complexes in Catalysis in N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*; Royal Society of Chemistry, **2011**.

(49) Breslow, R. *Chem. Ind. (London)* **1957**, *80*, 893.

(50) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.

(51) Skouta, R. *Chem.* **2018**, *4*, 654.

(52) Wanzlick, H. W. *Angew. Chem. Int. Ed.* **1962**, *74*, 129.

(53) Wanzlick, H. W.; Schönherr, H. J. *Angew. Chem. Int. Ed.* **1968**, *7*, 141.

(54) Öfele, K. *J. Organomet. Chem.* **1968**, *12*, P42.

(55) Arduengo, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361.

(56) Herrmann, W. A.; Elison, M.; Fischer, J.; Kocher, C.; Artus, G. R. J. *Angew. Chem. Int. Edit.* **1995**, *34*, 2371.

(57) Weskamp, T.; Schattenmann, W. C.; Spiegler, M.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 2490.

(58) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674.

(59) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247.

(60) Ackermann, L.; Fürstner, A.; Weskamp, T.; Kohl, F. J.; Herrmann, W. A. *Tetrahedron Lett.* **1999**, *40*, 4787.

(61) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.

(62) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.

(63) Nobel Prize in Chemistry 2005, www.nobelprize.org/prizes/chemistry/2005/summary, accessed on 10th November **2020**.

(64) Schulz, W. G.; Heidari, N. *Chemical & Engineering News* **2013**, *91*, 8.

(65) Press Release: U.S. Court Confirms the Scope of Evonik's Patent Rights in Metathesis Catalysts Patent, https://catalysts.evonik.com/en/us-court-confirms-the-scope-of-evoniks-patent-rights-in-metathesis-catalysts-patent-100682.html, accessed on 9th June **2022**.

(66) Evonik gewinnt US Patentverletzungsverfahren, https://www.chemie.de/news/161692/evonik-gewinnt-us-patentverletzungsverfahren.html, accessed on 9th June **2022**.

(67) Press Release: Evonik prevails in US patent litigation against Materia Inc., https://catalysts.evonik.com/en/evonik-prevails-in-us-patent-litigation-against-materia-inc-100679.html, accessed on 9th June **2022**.

(68) Materia, Inc. and Evonik Reach Agreement on Catalyst License, https://www.prnewswire.com/news-releases/materia-inc-and-evonik-reach-agreement-on-catalyst-license-300536710.html, accessed on 9th June **2022**.

(69) Wang, D.; Astruc, D. *Chem. Rev.* **2015**, *115*, 6621.

(70) Öfele, K.; Herrmann, W. A.; Mihalios, D.; Elison, M.; Herdtweck, E.; Scherer, W.; Mink, J. *J. Organomet. Chem.* **1993**, *459*, 177.

(71) Hahn, F. E.; Jahnke, M. C. *Angew. Chem. Int. Ed.* **2008**, *47*, 3122.

(72) Jha, B. N.; Singh, N.; Raghuvanshi, A. *Catalytic Activity of Iron N-Heterocyclic Carbene Complexes in Organic Synthesis - A Nascent Relook*; IntechOpen: London, **2020**.

(73)   Bellotti, P.; Koy, M.; Hopkinson, M. N.; Glorius, F. *Nat. Rev. Chem.* **2021**, *5*, 711.

(74)   N-heterocyclische Carbene, https://roempp.thieme.de/lexicon/RD-08-03197, accessed on 10th June **2022**.

(75)   Nelson, D. J.; Nolan, S. P. *N-heterocyclic Carbenes*; Wiley-VCH Verlag, **2014**.

(76)   Arduengo, A. J.; Dias, H. V. R.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1992**, *114*, 5530.

(77)   Arduengo, A. J.; Goerlich, J. R.; Marshall, W. J. *J. Am. Chem. Soc.* **1995**, *117*, 11027.

(78)   Kuhl, O. *Chem. Soc. Rev.* **2007**, *36*, 592.

(79)   Droge, T.; Glorius, F. *Angew. Chem. Int. Ed.* **2010**, *49*, 6940.

(80)   Jacobsen, H.; Correa, A.; Costabile, C.; Cavallo, L. *J. Organomet. Chem.* **2006**, *691*, 4350.

(81)   Tukov, A. A.; Normand, A. T.; Nechaev, M. S. *Dalton Trans.* **2009**, 7015.

(82)   Mathew, P.; Neels, A.; Albrecht, M. *J. Am. Chem. Soc.* **2008**, *130*, 13534.

(83)   Crudden, C. M.; Allen, D. P. *Coord. Chem. Rev.* **2004**, *248*, 2247.

(84)   Garrou, P. E. *Chem. Rev.* **1985**, *85*, 171.

(85)   Fehlhammer, W. P.; Bliss, T.; Kernbach, U.; Brudgam, I. *J. Organomet. Chem.* **1995**, *490*, 149.

(86)   Hayes, J. M.; Viciano, M.; Peris, E.; Ujaque, G.; Lledos, A. *Organometallics* **2007**, *26*, 6170.

(87)   McGuinness, D. S.; Cavell, K. J.; Yates, B. F.; Skelton, B. W.; White, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 8317.

(88)   Waters, J. B.; Goicoechea, J. M. *Coord. Chem. Rev.* **2015**, *293*, 80.

(89)   Schuster, O.; Yang, L. R.; Raubenheimer, H. G.; Albrecht, M. *Chem. Rev.* **2009**, *109*, 3445.

(90)   Crabtree, R. H. *Coord. Chem. Rev.* **2013**, *257*, 755.

(91)   Sini, G.; Odile, E.; Crabtree, R. H. *Inorg. Chem.* **2002**, *41*, 602.

(92)   Tonner, R.; Heydenrych, G.; Frenking, G. *Chem. Asian J.* **2007**, *2*, 1555.

(93)   Magill, A. M.; Cavell, K. J.; Yates, B. F. *J. Am. Chem. Soc.* **2004**, *126*, 8717.

(94)   Magill, A. M.; Yates, B. F. *Aust. J. Chem.* **2004**, *57*, 1205.

(95)   Bazinet, P.; Yap, G. P. A.; Richeson, D. S. *J. Am. Chem. Soc.* **2003**, *125*, 13314.

(96)   Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem.* **2002**, *649*, 219.

(97)   Mayr, M.; Wurst, K.; Ongania, K.-H.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 1256.

(98)   Sau, S. C.; Hota, P. K.; Mandal, S. K.; Soleilhavoup, M.; Bertrand, G. *Chem. Soc. Rev.* **2020**, *49*, 1233.

(99)   Malan, F. P.; Singleton, E.; van Rooyen, P. H.; Albrecht, M.; Landman, M. *Organometallics* **2019**, *38*, 2624.

(100)   Kovacevic, A.; Grundemann, S.; Miecznikowski, J. R.; Clot, E.; Eisenstein, O.; Crabtree, R. H. *Chem. Commun.* **2002**, 2580.

(101)   Grundemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 10473.

(102)   Chianese, A. R.; Kovacevic, A.; Zeglis, B. M.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2004**, *23*, 2461.

(103)   Arnold, P. L.; Pearson, S. *Coord. Chem. Rev.* **2007**, *251*, 596.

(104)   Gründemann, S.; Kovacevic, A.; Albrecht, M.; Faller Robert, J. W.; Crabtree, H. *Chem. Commun.* **2001**, 2274.

(105)   Ellul, C. E.; Mahon, M. F.; Saker, O.; Whittlesey, M. K. *Angew. Chem. Int. Ed.* **2007**, *46*, 6343.

(106)   Aldeco-Perez, E.; Rosenthal, A. J.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Science* **2009**, *326*, 556.

(107)   Berzelius, J. J. *Jahres-Bericht* **1835**, *14*, 237.

(108)   Wisniak, J. *Educ. Quimica* **2010**, *21*, 60.

(109)   Rayner-Canham, M.; Rayner-Canham, G. W. *Women in Chemistry: Their Changing Roles from Alchemical Times to the Mid-Twentieth Century*; American Chemical Society: Chemical Heritage Foundation: Washington DC, **2001**.

(110)   van Santen, R. A. *Modern Heterogeneous Catalysis: An Introduction*; Weinheim, Germany: Wiley VCH-Verlag, **2017**.

(111) Reschetilowski, W. *Einführung in die heterogene Katalyse*; Berlin, Germany: Springer-Verlag, **2015**.

(112) Cordus, V. *Le Guidon des Apotiquaires: C'est à dire, la Vraye Forme et Maniere de Composer les Médicamens*; L. Cloquemin, E. Michel: Lyons, France, **1575**.

(113) Döbereiner, J. W. *Journal für Chemie und Physik* **1823**, *38*, 321.

(114) *Recognizing the Best in Innovation: breakthrough Catalyst*; R&D Magazine, **2005**.

(115) Catalyst Market by Type (Zeolites, Metals, Chemical Compounds, Enzymes, and Organometallic Materials), Process (Recycling, Regeneration, and Rejuvenation), and Application (Petroleum Refining, Chemical Synthesis, Polymer Catalysis, and Environmental): Global Opportunity Analysis and Industry Forecast, 2021–2030 accessed on 28th July 2022.

(116) Catalyst Market Size, Share & Trends Analysis Report, accessed on 28th July 2022.

(117) Thomas, J. M.; Harris, D. M. *Energy Environ. Sci.* **2016**, *9*, 687.

(118) Atkins, P.; Overton, T.; Rourke, J.; Weller, M.; Armstrong, F. *Shriver and Atkins Inorganic Chemistry*; Oxford, **2010**.

(119) Rothenberg, G. *Catalysis: Concepts and Green Applications*; Wiley-VCH, **2008**.

(120) Dumesic, J. A.; Huber, G. W.; Boudart, M. *Handbook of Heterogeneous Catalysis*; Wiley VCH Verlag: Weinheim, Germany, **2008**.

(121) Appl, M. *The Haber-Bosch Process and the Development of Chemical Engineering in A Century of Chemical Engineering*; Plenum Press: New York, USA, **1982**.

(122) Appl, M. *Ammonia in Ullmann's Encyclopedia of Industrial Chemistry*; Wiley VCH Verlag: Weinheim, Germany, **2006**.

(123) Herrmann, W. A.; Cornils, B. *Angew. Chem. Int. Ed.* **1997**, *36*, 1048.

(124) Cornils, B.; Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds*; Wiley VCH Verlag: Weinheim, Germany, **2008**.

(125) Gheorghe, D. *Homogeneous Catalysis with Metal Complexes - Fundamentals and Applications*; Springer-Verlag: Berlin, **2012**.

(126) Hanefeld, U.; Lefferts, L. *Catalysis - An Integrated Textbook for Students*; Wiley VCH Verlag: Weinheim, Germany, **2018**.

(127) Andersson, P. G.; Munslow, I. J. *Modern Reduction Methods*; Wiley-VCH, **2008**.

(128) Magano, J.; Dunetz, J. R. *Org. Process Res. Dev.* **2012**, *16*, 1156.

(129) Hudlicky, M. *Reductions in Organic Chemistry*; American Chemical Society, **1996**.

(130) Ikariya, T.; Blacker, A. J. *Acc. Chem. Res.* **2007**, *40*, 1300.

(131) Samec, J. S. M.; Bäckvall, J. E.; Andersson, P. G.; Brandt, P. *Chem. Soc. Rev.* **2006**, *35*, 237.

(132) Ito, J.; Nishiyama, H. *Tetrahedron Lett.* **2014**, *55*, 3133.

(133) Knoevenagel, E.; Bergdolt, B. *Chem. Ber.* **1903**, *36*, 2857.

(134) Wieland, H. *Chem. Ber.* **1912**, *45*, 484.

(135) Meerwein, H.; Schmidt, R. *Justus Liebigs Ann. Chem.* **1925**, *444*, 221.

(136) Ponndorf, W. *Angew. Chem.* **1926**, *39*, 138.

(137) Verley, A. *Bull. Soc. Chim. Fr.* **1925**, *37*, 537.

(138) Kurti, L.; Czako, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier Science, **2005**.

(139) Screttas, C. G.; Cazianis, C. T. *Tetrahedron* **1978**, *34*, 933.

(140) Klomp, D.; Maschmeyer, T.; Hanefeld, U.; Peters, J. A. *Chem. Eur. J.* **2004**, *10*, 2088.

(141) Laue, T.; Plagens, A. *Namen- und Schlagwort-Reaktionen der Organischen Chemie*; Vieweg+Teubner Verlag: Braunschweig, Germany, **2004**.

(142) De Graauw, C. F.; Peters, J. A.; Van Bekkum, H.; Huskens, J. *Synthesis* **1994**, *1994*, 1007.

(143) Haddad, Y. M. Y.; Henbest, H. B.; Husbands, J.; Mitchell, T. R. B. *Proc. Chem. Soc.* **1964**, 361.

(144) Trocha-Grimshaw, M. J.; Henbest, H. B. *Chem. Commun.* **1967**, 544.

(145) Bianchi, M.; Matteoli, U.; Menchi, G.; Frediani, P.; Pratesi, S.; Piacenti, F.; Botteghi, C. *J. Organomet. Chem.* **1980**, *198*, 73.

(146) Matteoli, U.; Frediani, P.; Bianchi, M.; Botteghi, C.; Gladiali, S. *J. Mol. Catal.* **1981**, *12*, 265.

(147)   Pugin, B.; Blaser, H. U. *Top. Catal.* **2010**, *53*, 953.
(148)   Vaclavik, J.; Sot, P.; Vilhanova, B.; Pechacek, J.; Kuzma, M.; Kacer, P. *Molecules* **2013**, *18*, 6804.
(149)   Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051.
(150)   Chowdhury, R. L.; Bäckvall, J. E. *J. Chem. Soc.* **1991**, 1063.
(151)   Nobel Prize in Chemistry 2001, www.nobelprize.org/prizes/chemistry/2001/summary, accessed on 3rd August **2022**.
(152)   Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97.
(153)   Yamada, I.; Noyori, R. *Org. Lett.* **2000**, *2*, 3425.
(154)   Sluijter, S. N.; Elsevier, C. J. *Organometallics* **2014**, *33*, 6389.
(155)   Bolje, A.; Hohloch, S.; Van Der Meer, M.; Kosmrlj, J.; Sarkar, B. *Chem. Eur. J.* **2015**, *21*, 6756.
(156)   Gülcemal, S. *Appl. Organomet. Chem.* **2012**, *26*, 246.
(157)   Akinci, P. A.; Gülcemal, S.; Kazheva, O. N.; Alexandrov, G. G.; Dyachenko, O. A.; Cetinkaya, E.; Cetinkaya, B. *J. Organomet. Chem.* **2014**, *765*, 23.
(158)   Putignano, E.; Bossi, G.; Rigo, P.; Baratta, W. *Organometallics* **2012**, *31*, 1133.
(159)   Chelucci, G.; Baldino, S.; Baratta, W. *Acc. Chem. Res.* **2015**, *48*, 363.
(160)   Baidilov, D.; Hayrapetyan, D.; Khalimon, A. Y. *Tetrahedron* **2021**, *98*, 132435.
(161)   Zuo, W.; Morris, R. H. *Nat. Protoc.* **2015**, *10*, 241.
(162)   Jagadeesh, R. V.; Wienhöfer, G.; Westerhaus, F. A.; Surkus, A.-E.; Junge, H.; Junge, K.; Beller, M. *Chem. Eur. J.* **2011**, *17*, 14375.
(163)   Tyagi, N.; Borah, G.; Patel, P.; Ramaiah, D. *IntechOpen* **2022**.
(164)   Facchetti, S.; Jurcik, V.; Baldino, S.; Giboulot, S.; Nedden, H. G.; Zanotti-Gerosa, A.; Blackaby, A.; Bryan, R.; Boogard, A.; McLaren, D. B.; Moya, E.; Reynolds, S.; Sandham, K. S.; Martinuzzi, P.; Baratta, W. *Organometallics* **2016**, *35*, 277.
(165)   Baratta, W.; Rigo, P. *Eur. J. Inorg. Chem.* **2008**, *2008*, 4041.
(166)   Chelucci, G.; Baldino, S.; Baratta, W. *Coord. Chem. Rev.* **2015**, *300*, 29.
(167)   House, H. O. *Modern Synthetic Reactions (The Organic Chemistry Monograph Series)*; W. A. Benjamin, **1972**.
(168)   Graves, C. R.; Zheng, B.-S.; Nguyen, S. T. *J. Am. Chem. Soc.* **2006**, *128*, 12596.
(169)   Ooi, T.; Miura, T.; Itagaki, Y.; Ichikawa, H.; Maruoka, K. *Synthesis* **2002**, *2002*, 279.
(170)   Oppenauer, R. V. *Rec. Trav. Chim. Pays Bas* **1937**, *56*, 137.
(171)   Corey, E. J.; Nicolaou, K. C. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier, **2005**.
(172)   Otvos, L.; Gruber, L.; Meisel-Agoston, J. *Acta Chim. Acad. Sci. Hung.* **1965**, *43*, 149.
(173)   Manzini, S.; Urbina-Blanco, C. A.; Nolan, S. P. *Organometallics* **2013**, *32*, 660.
(174)   Djerassi, C. *The Oppenauer Oxidation in: Organic Reactions* John Wiley & Sons, Inc., **2011**.
(175)   Almeida, M. L. S.; Kocovsky, P.; Bäckvall, J. E. *J. Org. Chem.* **1996**, *61*, 6587.
(176)   Du, W. M.; Wang, L. D.; Wu, P.; Yu, Z. K. *Chem-Eur J* **2012**, *18*, 11550.
(177)   Pardatscher, L., Technische Universität München, 2019.
(178)   Haack, K. J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem. Int. Ed.* **1997**, *36*, 285.
(179)   Gladiali, S.; Taras, R. *Modern Reduction Methods*; Wiley-VCH, **2008**.
(180)   Klomp, D.; Hanefeld, U.; Peters, J. A. *The Handbook of Homogeneous Hydrogenation*; Wiley-VCH, **2008**.
(181)   Peris, E. *Chem. Rev.* **2018**, *118*, 9988.
(182)   Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2201.
(183)   Noyori, R. *Angew. Chem. Int. Edit.* **2002**, *41*, 2008.
(184)   Aranyos, A.; Csjernyik, G.; Szabo, K. J.; Bäckvall, J.-E. *Chem. Commun.* **1999**, 351.
(185)   Bäckvall, J.-E. *J. Organomet. Chem.* **2002**, *652*, 105.
(186)   Laxmi, Y. R. S.; Bäckvall, J.-E. *Chem. Commun.* **2000**, 611.
(187)   Böth, A. D.; Sauer, M. J.; Reich, R. M.; Kühn, F. E. *Ruthenium and Osmium Complexes containing NHC and pi-Acid Ligands in Comprehensive Organometallic Chemistry IV*; Elsevier, **2022**.

(188)   Schwartsburd, L.; Whittlesey, M. K. *Ruthenium N-Heterocyclic Carbene Complexes for the Catalysis of Nonmetathesis Organic Transformations*; Wiley-VCH, **2014**.

(189)   Hillier, A. C.; Lee, H. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2001**, *20*, 4246.

(190)   Danopoulos, A. A.; Winston, S.; Motherwell, W. B. *Chem. Commun.* **2002**, 1376.

(191)   Poyatos, M.; Mata, J. A.; Falomir, E.; Crabtree, R. H.; Peris, E. *Organometallics* **2003**, *22*, 1110.

(192)   Witt, J.; Pöthig, A.; Kühn, F. E.; Baratta, W. *Organometallics* **2013**, *32*, 4042.

(193)   Yasar, S.; Cekirdek, S.; Ozdemir, I. *J. Coord. Chem.* **2014**, *67*, 1236.

(194)   Bitzer, M. J.; Pöthig, A.; Jandl, C.; Kühn, F. E.; Baratta, W. *Dalton Trans.* **2015**, *44*, 11686.

(195)   Bitzer, M. J.; Kühn, F. E.; Baratta, W. *J. Catal.* **2016**, *338*, 222.

(196)   Hollering, M.; Albrecht, M.; Kühn, F. E. *Organometallics* **2016**, *35*, 2980.

(197)   Hollering, M.; Weiss, D. T.; Bitzer, M. J.; Jandl, C.; Kühn, F. E. *Inorg. Chem.* **2016**, *55*, 6010.

(198)   Viji, M.; Tyagi, N.; Naithani, N.; Ramaiah, D. *New. J. Chem.* **2017**, *41*, 12736.

(199)   Kleinhans, G.; Guisado-Barrios, G.; Peris, E.; Bezuidenhout, D. I. *Polyhedron* **2018**, *143*, 43.

(200)   Pardatscher, L.; Hofmann, B. J.; Fischer, P. J.; Hölzl, S. M.; Reich, R. M.; Kühn, F. E.; Baratta, W. *ACS Catal.* **2019**, *9*, 11302.

(201)   Pardatscher, L.; Bitzer, M. J.; Jandl, C.; Kück, J. W.; Reich, R. M.; Kühn, F. E.; Baratta, W. *Dalton Trans.* **2019**, *48*, 79.

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Figure 1.   Dmitry Ivanovich Mendeleev's "Periodic Table of the Elements from 1871". From https://commons.wikimedia.org/wiki/File:Mendelejevs_periodiska_system_1871.png accessed on the 10th of May 2022. In agreement with the creative commons license (CC BY 4.0), this work is in the public domain in its country of origin and other countries where the copyright term is the author's life plus 100 years or fewer. The author of this work does not claim any authorship over the figure.

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Figure 15.   Schematic drawing of a gadget that makes fire, invented by Johann Wolfgang Döbereiner (Döbereiner's lighter) from 1907. From https://commons.wikimedia .org/wiki/File:D%C3%B6bereiner_fire_gadget.png, copied from Projekt Runeberg, accessed on the 28th of July 2022. In agreement with the creative commons license (CC BY 4.0), this work is in the public domain in its country of origin and other countries where the copyright term is the author's life plus 70 years or fewer. The author of this work does not claim any authorship over the figure. The component descriptions and reactions on the right were added manually.

Main Publication 1:

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VII Appendix

Complete List of Publications and Scientific Contributions

"Abnormally Coordinated NHC Ruthenium Complexes for Catalytic Transfer Hydrogenation"

Poster Presentation, TUM AC Get-Together 2019, 26-28th July 2019, Raitenhaslach.

"Activation of Molecular Oxygen by a Cobalt(II) tetra-NHC Complex"

Jonas F. Schlagintweit,[§] Philipp J. Altmann,[§] Alexander D. Böth, Benjamin J. Hofmann, Christian Jandl, Clemens Kaußler, Linda Nguyen, Robert M. Reich, Alexander Pöthig, Fritz E. Kühn*

Chem. Eur. J. **2020**, *27*, 1311-1315.

https://doi.org/10.1002/chem.202004758

"Tuning the electronic properties of tetradentate iron-NHC complexes: Towards stable and selective epoxidation catalysts"

Marco A. Bernd,[§] Florian Dyckhoff,[§] Benjamin J. Hofmann, Alexander D. Böth, Jonas F. Schlagintweit, Jens Oberkofler, Robert M. Reich, Fritz E. Kühn*

J. Catal. **2020**, *391*, 548-561.

https://doi.org/10.1016/j.jcat.2020.08.037

"Mimicking reactive high-valent diiron-μ2-oxo intermediates of nonheme enzymes by an iron tetracarbene complex"

Tim P. Schlachta,[§] Markus R. Anneser,[§] Jonas F. Schlagintweit, Christian H. G. Jakob, Carolin Hintermeier, Alexander D. Böth, Stefan Haslinger, Robert M. Reich, Fritz E. Kühn*

Chem. Commun. **2021**, *57*, 6644-6647.

https://doi.org/10.1039/D1CC02027G

"Ruthenium and Osmium Complexes containing NHC and π-Acid Ligands"

Alexander D. Böth,[§] Michael J. Sauer,[§] Robert M. Reich, Fritz E. Kühn*

Book chapter, *Comprehensive Organometallic Chemistry IV* **2022**, *7*, 444-527.

https://doi.org/10.1016/B978-0-12-820206-7.00142-6

"Abnormal NHC Ruthenium Catalysts: Mechanistic Investigations of their Preparation and Steric Influence on Catalytic Performance"

Alexander D. Böth, Michael J. Sauer, Walter Baratta,* Fritz E. Kühn*

Cat. Sci. Tech. **2022**, *12*, 5597-5603.

"Synthesis and Characterisation of a Heterobimetallic N-heterocyclic Carbene Rhodium Ruthenium Complex as Catalyst for Transfer Hydrogenation"

Mohammad Kaikhosravi,[§] Alexander D. Böth,[§] Michael J. Sauer, Robert M. Reich and Fritz E. Kühn*

J. Organometall. Chem. **2022**, *979*, 122498.

Annotations

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