To my beloved grandmother Custódia Catarina

Acknowledgements

First of all, I would like to express my deepest gratitude to my PhD supervisors, Drª. Beatriz Royo and Profª. Maria Miguéns Pereira for the teachings of great value, support, and scientific discussions, and above all for their guidance, commitment and dedication.

I would like to thank CATSUS PhD program and Fundação para a Ciência e Tecnologia for my PhD fellowship, SFRH/BD/52373/2013.

To my laboratory colleagues, current and former colleagues, Mara Pinto, Ana Fernandes, Sofia Friães, Joana Marques, Inês Leitão, Naiára Fernandez, João Cardoso, Patricia Reis and Arturo Baptista, thank you for contributing to a spectacular work environment, always with good disposition, and of our dinners and plans in and outside the ITQB walls.

To my former ITQB colleagues and friends for life, Lorena Postigo and Ana Catarina Coelho, of you I keep the memories of the last 8 years, showered with good doses of joy, complicity, friendship, and support, this thesis is also yours.

In ITQB I would like to acknowledge, Conceição Almeida (Sãozinha), besides an ITQB service, thank you for the right words, support and companionship, also to João Rodrigues, and to the staff of the economato, for the friendship and good atmosphere always on that 1st floor of ITQB. To Sr. Domingos, for the nine years of dedication and friendship.

Also I want to acknowledge the team of the Laboratory of Catalysis and Fine Chemistry in Coimbra my very thank you for the affection and support during my stays.

And finally the most important:

To my boyfriend, João, for all the support, friendship, affection and patience to put up with me in the stresses of writing the thesis and of course for all the love, this thesis is dedicated to you, thank you for being who you are.
To my parents António e Maria and my sister, Ana, for the support and love, without them it would not have been possible, and to them I dedicate this thesis, thank you for always being there.

Thank you for being my life support.
Thank you very much to all!!
This thesis is also yours.

RESUMO

Esta tese descreve a síntese de novos complexos de ferro e de níquel do tipo semi-sanduíche com ligandos carbeno N-heterocíclicos, assim como a sua aplicação na redução catalítica de compostos insaturados e em reações de acoplamento desidrogenativas.

No capítulo 1 é apresentada a introdução geral, onde se destaca o estado-de-arte dos complexos de ciclopentadienilo N-heterocíclico de ferro e níquel aplicados em reações cataliticas de redução. Este capítulo tem especial foco em reduções catalíticas de ligações múltiplas por hidrogenação, transferência de hidrogénio, hidrosililação e hidroboração utilizando complexos de ferro(II) e níquel(II) como catalisadores. Os objetivos da tese também são descritos no capítulo 1.

O Capítulo 2 descreve a coordenação de novos ligandos carbeno N-heterocíclicos funcionalizados com tetrametilciclopentadienilo e diferentes N-substituintes no anel imidazol ao níquel. Os complexos do tipo geral (Cp*-NHC^{R})NiX (X = Cl, I; R = *i*Bu, nBu, Et, Me) foram totalmente caracterizados. Estes complexos de níquel revelaram-se eficientes na catálise seletiva de acoplamento de tióis aromáticos com Et_3SiH, dando origem aos correspondentes sililtioéteres ($RSSiEt_3$). Os complexos de níquel contendo etilo, *iso*-butilo e n-butilo como N-substituintes demonstram uma eficiência catalítica similar, enquanto que o complexo de níquel contendo um grupo metilo como N-substituinte apresenta menor atividade catalítica.

Os novos complexos NHC de níquel(II) podem ser adicionalmente aplicados como catalisadores para a redução de nitroarenos a aminas utilizando fenilsilano como agente redutor. O Capítulo 3 descreve a

aplicação deste sistema catalítico para a preparação de anilinas com diferentes funcionalidades em condições suaves. Os novos complexos NHC de níquel permitem a redução de 5,10,15,20-tetra-(nitrofenil)porfirina(TNPP) e Cu(II) β-nitroporfirina para as aminoporfirinas correspondentes.

A preparação de uma nova série de complexos de ferro(II) com ligandos carbeno N-heterocíclicos com diferentes substituintes alquilo é descrita no capítulo 4. Complexos do tipo geral (Cp* -NHC^R) Fe(CO)I [R = *i*Bu, *n*Bu, Et, CH_2Ph, CH_2CH_2OMe] foram totalmente caracterizados e aplicados como catalisadores em reacções de sililação desidrogenativa de álcoois com silanos. Os complexos metálicos de ferro(II) com N-substituintes de *iso*-butilo e de n-butilo apresentam propriedades catalíticas ligeiramente superiores aos obtidos com os complexos contendo substituintes alquilo mais curtos. Este sistema catalítico baseado em ferro permite obter rendimentos quantitativos dos sililéteres.

O Capítulo 5 descreve a síntese de uma nova família de complexos de NHC de ferro(II) contendo grupos hidroxilo, acetamida e amina no N-substituinte do ligando NHC. Estes novos complexos de ferro-NHC foram aplicados em reacções catalíticas de transferência de hidrogénio, revelando-se catalisadores eficientes na redução de cetonas. O complexo de ferro com o grupo acetamida demonstrou uma atividade catalítica notável na transferência de hidrogenação de cetonas com 2-propanol. Além disso foi também desenvolvido para este complexo, um protocolo no âmbito da química verde para a redução de cetonas usando glicerol como fonte de hidrogénio e aquecimento por microondas. Nestas condições, o sistema catalítico desenvolvido nesta tese permite a síntese de vários álcoois bioativos com elevado rendimento.

Finalmente, o capítulo 6 apresenta as principais conclusões do trabalho.

SUMMARY

This thesis describes the synthesis of new half-sandwich iron and nickel complexes bearing N-heterocyclic carbene ligands and their application in the catalytic reduction of unsaturated compounds, and in dehydrogenative coupling reactions.

The state-of-the-art of iron and nickel N-heterocyclic carbene complexes in catalytic reduction reactions is compiled in a general introduction in chapter 1. Specifically, discussion focus on catalytic reductions of multiple bonds through hydrogenation, transfer hydrogenation, hydrosilylation, and hydroboration using iron and nickel complexes as catalysts. The main aim of the thesis and the specific objectives are described in chapter 1.

Chapter 2 describes the coordination of new tetramethylcyclopentadienyl-functionalized N-heterocyclic carbene ligands incorporating different wingtip substituents to nickel. Complexes of the general type (Cp*-NHC^{R})NiX (X = Cl, I; R = ^{i}Bu, ^{n}Bu, Et, Me) were synthesized and fully characterized. These well-defined nickel complexes selectively catalyze the coupling of aromatic thiols with Et_3SiH to give the corresponding silylthioethers ($RSSiEt_3$). The nickel complexes bearing ethyl, *iso*-butyl and *n*-butyl wingtips displayed comparable catalytic efficiency, while the nickel complex bearing a methyl substituent on the wingtip showed the lowest catalytic activity.

The new nickel(II)-NHC complexes can be further applied as catalysts for the reduction of nitroarenes to amines using phenylsilane as reducing agent. This chemistry is described in chapter 3. Notably, the new nickel NHC complexes allowed the reduction of 5,10,15,20-tetra-(nitrophenyl)porphyrin (TNPP) and Cu(II) β-nitroporphyrin to the corresponding aminoporphyrins.

The preparation of a new series of iron(II) piano-stool complexes with N-heterocyclic carbene ligands bearing different alkyl wingtips is described in chapter 4. Complexes of the general type (Cp*-NHC^R)Fe(CO)I [R = ^{i}Bu, ^{n}Bu, Et, CH_2Ph, CH_2CH_2OMe] were fully characterized and applied as catalysts for the dehydrogenative silylation of alcohols with silanes. Iron(II) metal complexes bearing *iso*-butyl and *n*-butyl wingtips displayed slightly better catalytic performances than complexes bearing shorter alkyl substituents. Gratifyingly, quantitative yields of the corresponding silylethers were obtained using the new iron-based catalytic system.

Chapter 5 describes the synthesis of a new family of iron(II) NHC complexes bearing hydroxyl, acetamide and amine groups on the wingtip of the NHC ligand. These new iron-NHC complexes were applied in catalytic transfer hydrogenation of ketones. Interestingly, the iron complex bearing the acetamide group showed a remarkable catalytic activity in the transfer hydrogenation of ketones with 2-propanol. Furthermore, an interesting green protocol for the reduction of ketones was developed using glycerol as a hydrogen source and microwave heating, in the presence of the iron complex with the acetamide group. Remarkably, under those conditions our catalytic system allowed the synthesis of several bioactive alcohols in high yields.

Finally, chapter 6 presents the main conclusions and the outlook of the work.

LIST OF PUBLICATIONS:

- Iron N-Heterocyclic Carbenes in Reduction Reactions, **R. Lopes**, B. Royo, *Isr. J. Chem*. **2017**, *57*, 1151-1159, DOI: 10.1002/ijch.201700055. Review by invitation Special issue *"Iron Catalysis"*.

- Selective reduction of nitroarenes with silanes catalyzed by nickel N-heterocyclic carbenes, **R. Lopes**, M. M. Pereira, B. Royo, *ChemCatChem,* **2017**, *9*, 1-6. DOI: 10-1002/cctc.201700218.

- Dehydrogenative silylation of alcohols catalysed by half-sandwich iron N-heterocyclic carbene complexes, J. M. S. Cardoso, **R. Lopes**, B. Royo, *J. Organomet. Chem.* **2015**, *775*, 173, DOI: 10.1016/j.jorganchem.2014.06.005. Special Issue "*N-Heterocyclic Carbenes in Applied Organometallic Chemistry*".

- Dehydrogenative Coupling of Thiols and Et_3SiH catalyzed by N-Heterocyclic Carbene Nickel Complexes, L. Postigo, **R. Lopes**, B. Royo, *Dalton Trans.* **2014,** *43*, 853-858**.** DOI: 10.1039/C3DT52052.

LIST OF ABBREVIATIONS:

Et	Ethyl
Bu	Butyl
Cat	Catalyst
Cp	Cyclopentadienyl
Cp*	Pentamethylcyclopentadienyl
NHC	N-heterocyclic carbene
DME	Dimethoxyethane
EA	Elemental Analysis
ESI	Electron-Spray Ionization
FTIR	Fourier Transform Infrared Spectroscopy
GC	Gas Chromatography
i-	*iso-*
Imid	Imidazol
Me	Methyl
MS	Mass spectrometry
NMR	Nuclear Magnetic Resonance
Ph	Phenyl
RI	Alkyl iodide
THF	Tetrahydrofurane
TON	Turnover number
UV	Ultraviolet
X	Generalized anionic ligand (usually halogen)

δ	Chemical shift in ppm (NMR)
v	Frequency (cm^{-1})
Δ	Reflux temperature

CHAPTER 1. INTRODUCTION AND OBJECTIVES

Part of this chapter (Section 1.1) has been published in R. Lopes, B. Royo, *Isr. J. Chem.* **2017**, *57*, 1151-1159.

1. Introduction

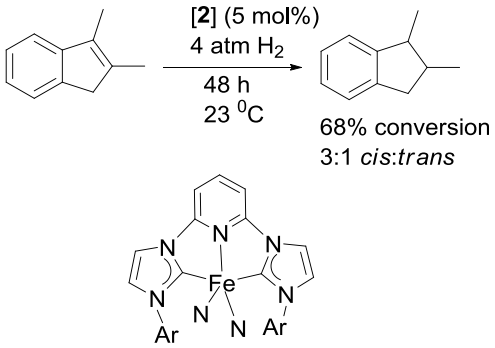
1.1. Iron N-heterocyclic carbene complexes in reduction reactions

N-heterocyclic carbenes (NHCs) have become a unique class of ligands in organometallic chemistry and catalysis. The success of NHCs is attributed to their flexible and easily modulated stereo-electronic properties, and their strong σ-donor capacities.[1] The coordination chemistry of NHCs with late transition metals and their application in catalysis has been intensively studied.[2]In contrast, the NHC chemistry with first-row transition metals has evolved more slowly. In particular, iron-NHC complexes, which are known since the 1970s,[3] have not received much attention until recently. In fact, in a review published by Nolan in 2009, only 10 publications dealing with catalytic applications of iron-NHCs were reported.[4] Currently, the situation is completely different, and an explosion of interest in developing this field of chemistry has been observed in the last decade. The considerable progress that has been made is summarized in several excellent reviews that appeared recently.[5] In particular, the field of catalytic reduction with Fe-NHC catalysts has caught the attention of a number of researchers. Despite this area is still in its infancy, it has proved the considerable potential of Fe-NHCs in catalytic reduction of a variety of unsaturated functionalities, including carbonyls, imines, amides, and alkenes.

Catalytic hydrogenation is one of the most useful and versatile tools used in organic chemistry and in fine chemical industries.[6] In recent years, there has been an increasing interest in developing low-cost catalysts derived from earth-abundant metals for hydrogenation processes. Remarkable advances in this area have been made using Fe, Co-, and Mn-based catalysts for the hydrogenation of a wide

number of functionalities including, carbonyls, imines, amides, esters, alkenes, among others.[7-9] However, the use of N-heterocyclic carbene metal complexes in direct hydrogenation reactions using earth-abundant metals is rather unexplored. Most of the hydrogenation reactions with NHC-metal complexes have been developed using precious metals, namely Ir, Ru, Rh.[10] In particular, the use of iron-NHCs for these transformations remains elusive.

In 2012, Chirik described the catalytic hydrogenation of unfunctionalised alkenes mediated by well-defined Fe-CNC dinitrogen pincer compounds. The pincer complex ($^{i\text{Pr}}$CNC)Fe(N_2)$_2$ (**1**) ($^{i\text{Pr}}$CNC = 2,6-(2,6-^{i}Pr$_2$C$_6$H$_3$-imidazol-2-ylidene)$_2$-C$_5$H$_3$N), previously reported by Danopoulos,[11] displayed remarkable catalytic activity in the hydrogenation of ethyl 3,3-dimethylacrylate, affording complete reduction (95% conversion) in 1 h at 23 °C. The less sterically protected variants of **1**, ($^{\text{Me}}$CNC)Fe(N_2)$_2$ (**2**) and ($^{\text{Mes}}$CNC)Fe(N_2)$_2$ (**3**) ($^{\text{Me}}$CNC = 2,6-(2,6-Me$_2$-C$_6$H$_3$-imidazol-2-ylidene)$_2$-C$_5$H$_3$N, $^{\text{Mes}}$CNC = 2,6-(2,4,6-Me$_3$-C$_6$H$_2$-imidazol-2-ylidene)$_2$-C$_5$H$_3$N), exhibited even better performances, displaying high turnover frequencies for the hydrogenation of challenging substrates, such as unfuctionalised tri- and tetrasubstituted alkenes (Scheme 1).[12] Complexes **1**-**3** bearing strong electron-donating NHC ligands surpassed the catalytic activity of aryl-substituted bis(imino)pyridine iron catalysts previously reported by Chirik.[13,14] Based on these results, a general trend can be established in which more electron donating chelates with smaller 2,6-aryl substituents produces more active hydrogenation catalysts. The iron complexes **1**-**3** reported by Chirik represent the only examples of Fe-NHC complexes known so far for catalytic hydrogenation reactions.

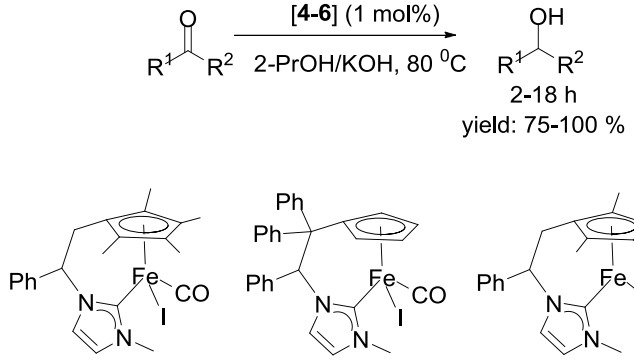


Ar = *i*Pr (**1**), Me (**2**), Mes (**3**)

Scheme 1. Hydrogenation of 2,3-dimethyl-1H-indene using catalyst **2**.

In alternative to direct hydrogenation, transfer hydrogenations (TH) using alcohols or formic acid as hydrogen sources, constitute a valuable reduction procedure for unsaturated organic functionalities, especially for carbonyl groups and imines.[15] Alkenes are more difficult to reduce using TH reactions due to the lower polarity of the C=C bonds. TH offers significant benefits with respect to the conventional hydrogenation reaction because it is operationally simple and intrinsically safe, avoiding pressurised hydrogen, and using alcohols as hydrogen source, which are inexpensive and non-toxic reagents.

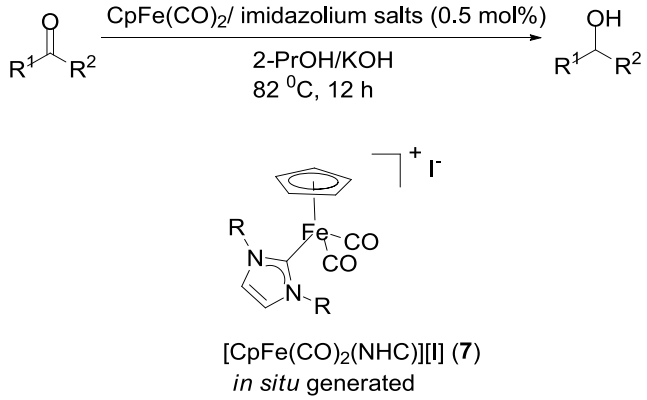
The first examples of iron-NHC complexes catalyzing the reduction of carbonyl groups through TH were reported in 2010 by our group using half-sandwich iron NHC complexes (Cp-NHC)Fe(CO)I (**4, 5**) and (Cp*-NHC)FeCl (**6**) (Cp = η^5-C_5H_4, Cp* = η^5-C_5Me_4) (Scheme 2).[16] Reduction of acetophenone, benzophenone, and cyclohexanone was successfully accomplished using 2-propanol as a hydrogen source and stoichiometric amounts of KOH in the presence of catalysts **4** and **5**. Interestingly, the different substitution on the cyclopentadienyl ring did not seem to affect the catalytic performance in TH. Under the same conditions, the coordinatively unsaturated species **6** displayed comparable catalytic activity.



(Cp*-NHC)Fe(CO)I (**4**) (Cp-NHC)Fe(CO)I (**5**) (Cp*-NHC)FeCl (**6**)

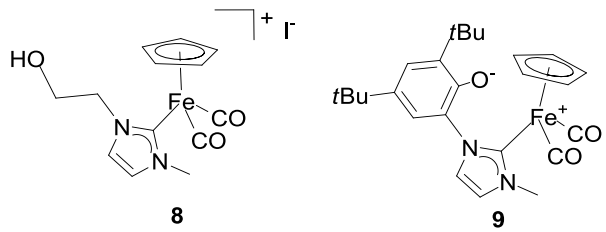
Scheme 2. Transfer hydrogenation of carbonyl groups catalyzed by complexes **4**–**6**.

Later in 2014, Bala and co-workers explored the use of cationic piano-stool iron NHC complexes as *in situ* catalysts for the TH of ketones. Cationic complexes of the general types $[CpFe(CO)_2(NHC)][I]$ (**7**) were prepared *in situ* by the reaction of $CpFe(CO)_2I$ with NHC ligands generated from the corresponding imidazolium salts with KOH. Without further purification, these complexes were directly tested as catalysts for the transfer hydrogenation of ketones using 2-propanol as a hydrogen source (Scheme 3). In this way, a variety of ketones including, aromatic, cyclic and aliphatic were reduced to the corresponding alcohols, reaching turnover numbers up to 200.[17] It was confirmed that the activity of well-defined isolated complexes displayed comparable activities that those obtained for the *in situ* generated catalysts. Despite it was not a clear correlation between the NHC wingtip substitution and the obtained conversions, it was observed that unsymmetrically substituted NHCs afforded less efficient catalysts than symmetrically substituted ones, probably due to catalyst deactivation of the less stable unsymmetrical catalysts.



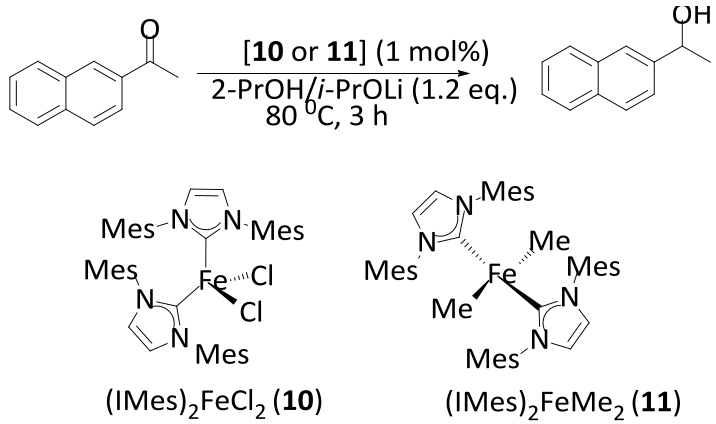
Scheme 3. Transfer hydrogenation of carbonyl groups catalyzed by *in situ* generated iron-NHC species.

More recently, in an effort to exploit the bifunctional cooperativity concept,[18] Chmely prepared two iron piano-stool complexes bearing NHC ligands with hydroxyl-containing pendent arms. It was expected that the presence of hydroxyl groups could assist in proton transfer from 2-propanol via an outer sphere mechanism. Unexpectedly, complexes **8** and **9** (Scheme 4) resulted completely inactive in the reduction of ketones. Even using high catalytic loading (10 mol %) and harsh conditions (light irradiation, 75 °C, 15 h, strong base), reduction of ketones was not observed.[19] The inactivity of complexes **8** and **9** was justified as a consequence of the coordinative saturation around iron, and the instability of these complexes under visible light irradiation.



Scheme 4. Piano-stool iron complexes of iron bearing NHC ligands with hydroxyl-containing pendant arms.

Apart from the studies performed with piano-stool iron NHC complexes, the only other iron–NHC complexes explored in TH are the four-coordinate NHC-iron(II) complexes **10** and **11** synthesized by Glorious, Tatsumi and Ohki, and applied in transfer hydrogenation of 2´-acetonaphthone.[20] Both paramagnetic compounds **10** and **11** resulted active in transfer hydrogenation when stoichiometric amounts of base were used. In the presence of 1.2 equivalents of $KOBu^t$, and using 2-propanol as a hydrogen source, complexes **10** and **11** catalyzed the reduction of 2´-acetonaphthone affording the desired alcohol in moderate yields (48-55% yield). The product yields become excellent (98-99% yield) when $KOBu^t$ was replaced by *i*-PrOLi (Scheme 5).

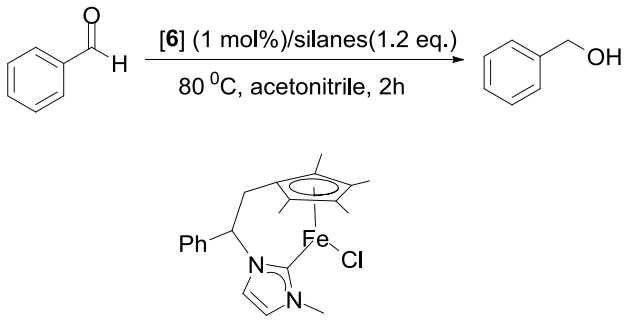


Scheme 5. Transfer hydrogenation of 2'-acetonaphtone catalyzed by **10** and **11**.

Hydrosilylation represents a useful alternative for the reduction of unsaturated molecules. It can be operated under mild conditions and it does not involve hydrogen gas or pressure reactors, so it is often the method of choice for the reduction of unsaturated molecules in small, lab-scale preparations. Hydrosilanes are stable, non-toxic and easy-to-use reagents.[21] On the other hand, the addition of the Si-H bond across C=O bonds is an essential reaction that allows the formation of

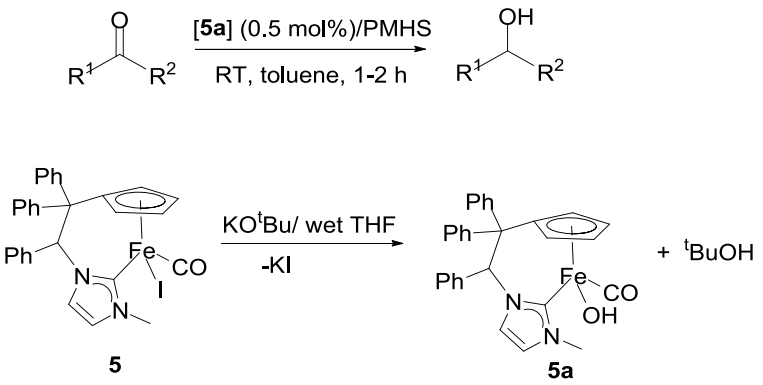
silyl ethers, which have important applications as protecting groups in organic synthesis and in the synthesis of functional organosilicon compounds and polymer chemistry.[22] Despite the progress made in hydrosilylation reactions catalyzed by transition metals, in recent years the toxicity of precious catalysts has pressed the need for the development of more sustainable methods. N-heterocyclic carbene ligands have been exploited in hydrosilylation catalysis mainly with Pt and Rh.[23] In comparison, catalysis with Fe-NHC in hydrosilylation is still in its infancy.

The first example in this field was reported by our group using the well-defined Fe-NHC piano stool complex **6** (Scheme 6), already mentioned before in transfer hydrogenation. Benzaldehyde derivatives were successfully reduced to the corresponding alcohols in the presence of **6** (1 mol %) using different silanes ($PhSiH_3$, Ph_2SiH_2, $(OEt)_2MeSiH$) at 80 °C in acetonitrile. Under similar conditions, ketones were not reduced. Similar results were obtained when the carbonyl complexes (Cp-NHC)Fe(CO)I (**4, 5**) were applied in the hydrosilylation of carbonyl groups. They were capable to reduce benzaldehyde but resulted inactive in the reduction of acetophenone; only a residual conversion of 10% was obtained after 20 h at 100 °C.[16] The group of Darcel and Sortais found similar catalytic activity with the related neutral non–linked piano stool iron complex **12** (Scheme 9), which reduced aldehydes under mild conditions (full reduction at 30 °C in 3 h), but was inactive in the reduction of ketones (100 °C, Ph_2SiH_2).[24]



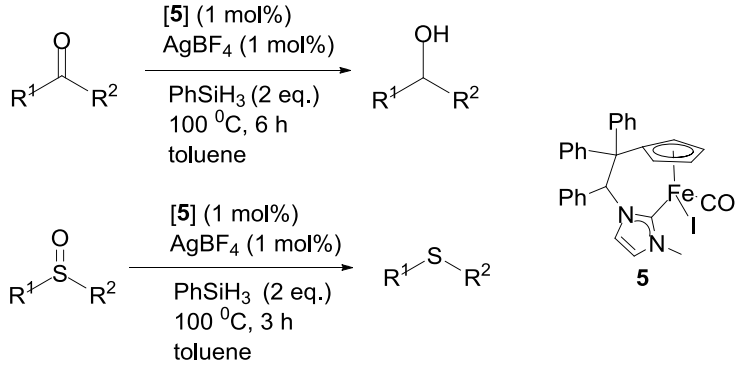
Scheme 6. Reduction of aldehydes catalyzed by **6**.

We observed that addition of catalytic amounts of potassium *tert*-butoxide efficiently activated the neutral complex (Cp-NHC)Fe(CO)I (**5**), which was then capable to reduce ketones quantitatively under mild conditions (25 °C) in short times (1.5 h), and using different silanes, including the less reactive polymeric polymethylhydrosiloxane (PMHS) (Scheme 7).[25] It was proved that treatment of **5** with stoichiometric amounts of potassium *tert*-butoxide afforded an iron-NHC hydroxide complex, which was the active species in the hydrosilylation reaction (Scheme 7).



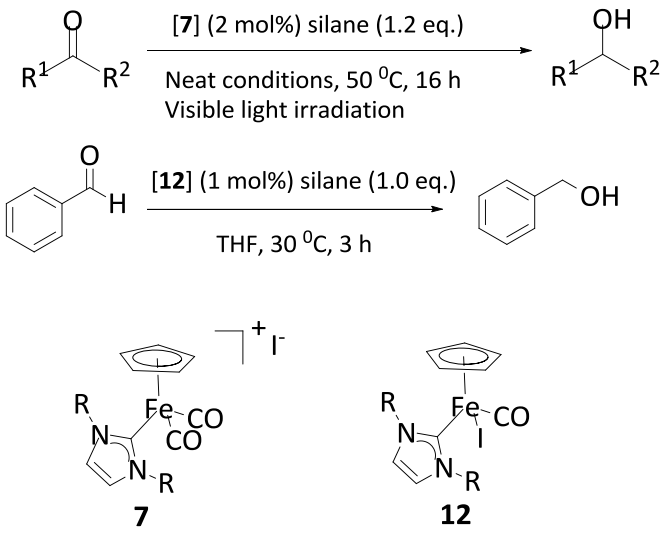
Scheme 7. Reduction of carbonyls using complex **5** activated with potassium *tert*-butoxide.

Moreover, treatment of **5** with stoichiometric amounts of $AgBF_4$ yielded the corresponding cationic complex [(Cp-NHC)Fe(CO)][BF_4], [26] which was active in the reduction of ketones[25] and sulfoxides,[27] affording full conversions at 100 °C (Scheme 8). These results demonstrated that smooth changes in the coordination sphere of iron have interesting implications on the catalytic activity of the metal complexes.



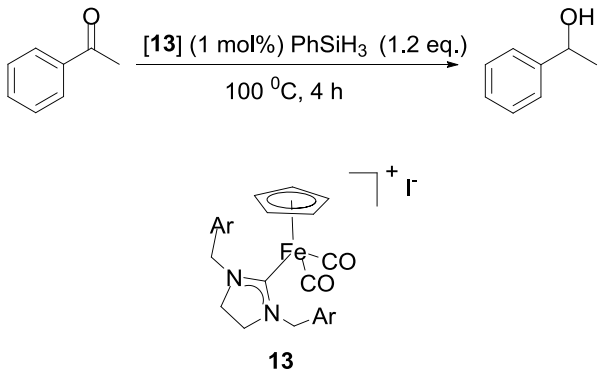
Scheme 8. Reduction of carbonyls and sulfoxides catalized by **5.**

The group of Darcel and Sortais have intensively explored the reactivity of well-defined cationic half-sandwich iron-NHC complexes in the reduction of a variety of unsaturated compounds including not only aldehydes and ketones, but also the reduction of challenging substrates such as amides and imines. They demonstrated that cationic piano stool complexes of the general type [$CpFe(CO)_2$(NHC][I] (**7**) are very efficient catalysts for hydrosilylation reactions.[24] The best catalytic performance for the reduction of aldehydes and ketones was obtained by carrying out the reactions under neat conditions with light irradiation, whereas no reaction occurred in the absence of light (Scheme 9).[28] Despite mechanistic details are scarce, it was demonstrated that the effect of light irradiation plays a crucial role.



Scheme 9. Reduction of carbonyls catalyzed by **7**.

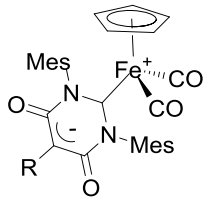
Later, in collaboration with Özdemir group, they reported an improved catalyst, the complex **13** containing benzyl-substituted imidazolidin-2-ylidene, which was able to catalyze the reduction of benzaldehyde in good yield (86%) in the absence of light by heating at 100 °C (Scheme 10).[29]



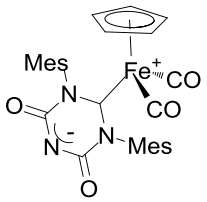
Scheme 10. Catalytic reduction of carbonyls using complex **13**.

An elegant work reported by the groups of Darcel, Sortais and Lavigne proved the effect of the modulation of the electronic properties

of the NHCs on the efficiency of the catalyst. They prepared half-sandwich complexes of Fe bearing malonate (**14**) and imidate (**15**) (Scheme 11) backbone-functionalised anionic carbenes and apply them in the hydrosilylation of carbonyls.[30] The zwitterionic species **14** bearing the malonate-NHC ligand, displayed higher catalytic activity than **15**. The enhanced activity of **14** was rationalized as a consequence of the stronger electron-donating character of the malonate-NHC ligand in comparison with the imidate NHC.

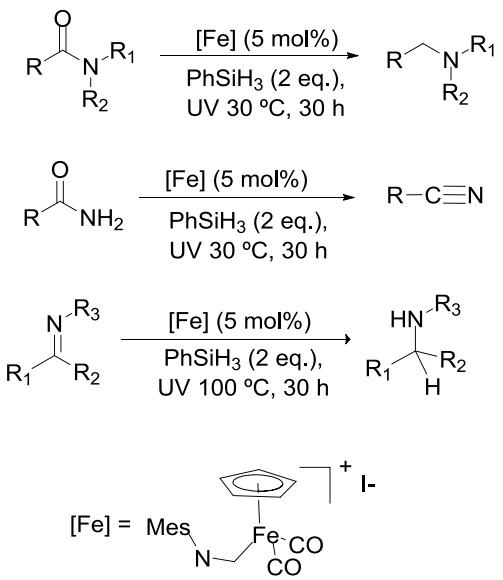


[CpFe(CO)$_2$(malonate-NHC)][I] (**14**)



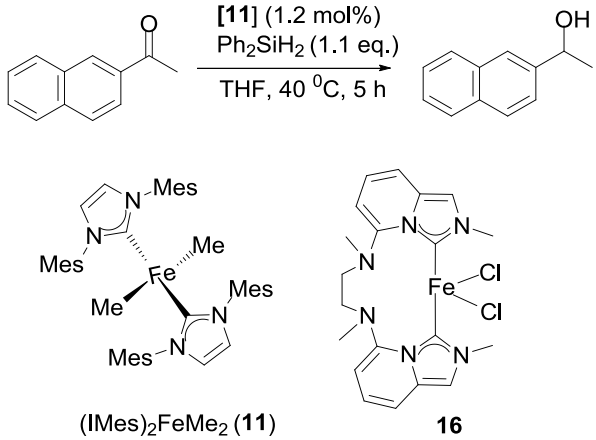
[CpFe(CO)$_2$(imidate-NHC)][I] (**15**)

Scheme 11. Well-defined cyclopentadienyl iron (II) complexes of NHCs bearing a malonate (**14**) and imidate (**15**) backbone.



Scheme 12. Catalytic reduction of amides and imines using [CpFe(IMes)(CO)$_2$][I].

Apart from the intensively explored half-sandwich Fe(II)-NHC complexes, the only other well-defined Fe(II)-NHC complexes able to catalyze the hydrosilylation of ketones are the square-planar *trans*-$(IMes)_2FeMe_2$ (**11**) and the bis-NHC-Fe complex **16** (Scheme 13) described by Glorius.[20,34] Hydrosilylation of 2´-acetonaphthone in good yield (91-96%) was afforded by using 1.2 mol% of **11** and 1.1 equivalent of silanes (Ph_2SiH_2, $(EtO)_3SiH$) at room temperature (Scheme 13).[20] Complex **16** displayed comparable catalytic activity in the reduction of acetophenone although higher temperature (60 °C) was needed to reach high yields.[34]



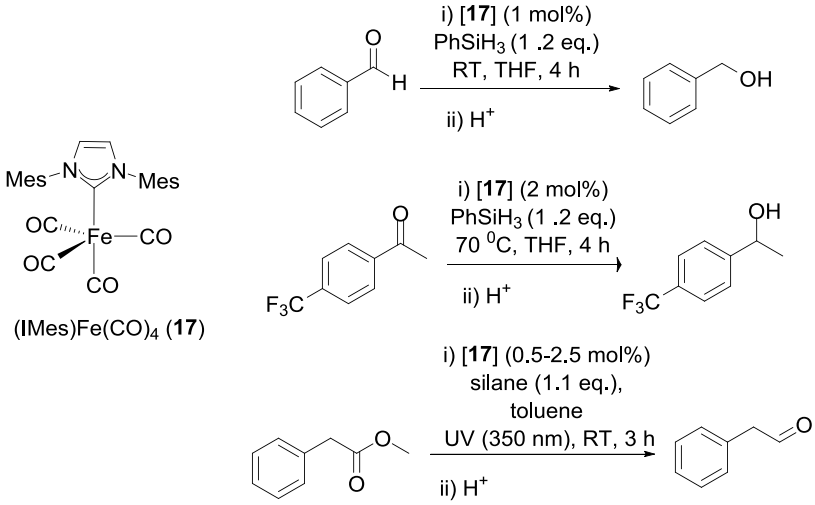
Scheme 13. Reduction of carbonyl groups catalyzed by **11** and **16**.

In addition, Driess *et al.* have reported a bis-NHC stabilised η^6-arene iron(0) complex as an efficient catalyst for the reduction of a number of organic amides to the corresponding tertiary amines in good yields using Ph_2SiH_2 under mild conditions (THF, 70 ^{0}C, 24 h).[35]

Adolfsson has reported the hydrosilylation of carbonyl complexes mediated by an Fe(II)-NHC complex generated *in situ* by using iron(II) acetate as metal precursor and imidazoium salts (IPr.HCl and hydroxyethyl-imidazolium salt) in the presence of strong bases such as *n*-BuLi. The catalytic system was efficient using different silanes as

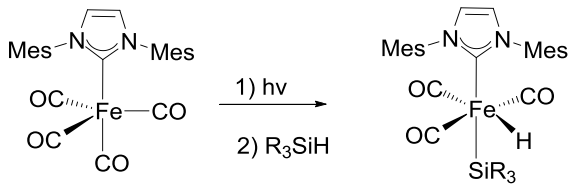
reducing agents, including the less reactive polymethylhydrosiloxane (PMHS).[36,37a] It was assumed that Fe-NHC species were formed under those conditions, although no experimental evidence for their formation was reported. In addition, tertiary amines were efficiently reduced to their corresponding tertiary amines using PMHS as reducing agent and the *in situ* generated iron-NHC complex from iron(II) acetate and 1-(2-hydroxy-2-phenylethyl)-3-methyl-imidazolium triflate.[37b]

Carbonyl Fe(0)-NHC complexes can also be employed as efficient catalysts for the reduction of carbonyls and imine groups. Our group proved the efficiency of $[Fe(CO)_4(NHC)]$ (**17**) complexes in the reduction of benzaldehydes at ambient temperature using phenylsilane as hydrogen source.[38] Ketones can also be reduced using higher temperature (70 °C) (Scheme 14). Interestingly, iron complexes bearing NHCs substituted with bulky aryl groups, such as IMes and IPr ligands displayed better activity than complexes with NHC with alkyl groups. The group of Darcel and Sortais demonstrated that complex **17** is also capable to reduce esters to aldehydes.[39] This challenging reaction was accomplished by using 1 mol% of catalyst **17** in the presence of a secondary silane (diethylsilane or diphenylsilane) as the reducing agent, and under light irradiation at ambient temperature (Scheme 14). They provided experimental evidence that the hydrosilylation occurs by oxidative addition of the hydrosilane to an unsaturated NHC-Fe species to yield a silyl iron hydride complex, which was fully characterized including the X-ray diffraction studies.



Scheme 14. Reduction of carbonyl groups catalyzed by **17**.

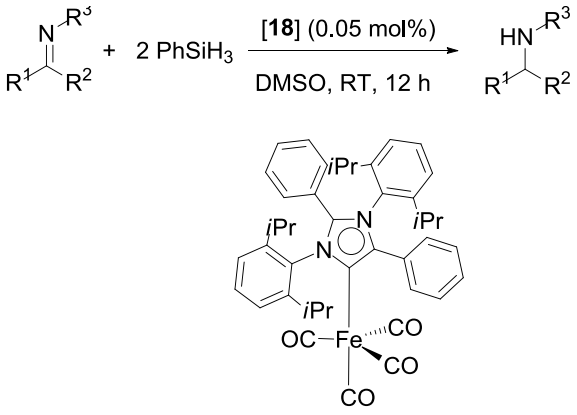
Based on stochiometric reactions, they proposed a catalytic cycle, in which the first step is the generation of a 16-electron species [(IMes)Fe(CO)$_3$] generated by UV activation of [(IMes)Fe(CO)$_4$]. The generated [(IMes)Fe(CO)$_3$] complex reacts then with the hydrosilane to generate by oxidative addition, the silyl-Fe hydride species [(IMes)Fe(H)(SiR$_3$)(CO)$_3$] (Scheme 15).[39]



Scheme 15. Stoichiometric reaction of **16** with silanes under UV light.

In 2016, Mandal described a highly efficient catalytic system for the reduction of imines to amines using the related abnormal *a*NHC-Fe(0) complex **18** depicted in (Scheme 16).[40] Abnormal N-heterocyclic carbenes, which were pioneered by Crabtree and Bertrand,[41] are proved to be better σ-donors than classical NHCs. The strong σ-donor

properties of *a*NHCs often yield improved catalytic systems.[42] In this particular case, the *a*NHC-Fe(0)-based catalyst displayed excellent activity and chemoselectivity in the reduction of imines to amines under very mild conditions with extremely low catalyst loading (less than 0.005 mol%). They attributed the high catalytic performance of **18** as a result of the combination of an electron-rich Fe(0) centre with a strong sigma donor *a*NHC ligand. Among the various silanes tested, phenylsilane performed best, giving TON values of 17000 and yields of 59-96% with extremely low catalyst loading (0.005 ppm) at room temperature. As proposed by Darcel and Sortais in the reduction of esters using [Fe(IMes)$(CO)_4$], Mandal proved that catalyst **18** requires activation by extruding one of the carbonyl ligands, in order to facilitate the oxidative addition of the silane and the generation of an iron hydride species, which has been clearly identified by ^{1}H NMR. It was demonstrated that Fe(0) goes to Fe(II) by oxidative addition of the silane. This process might be facilitated by an electron rich center. In fact, comparing the catalytic efficiency of **18** with **17** bearing a classical NHC in the hydrosilylation of imines, it was observed the better performance of complex **18**. The stronger donating *a*NHC ligand makes the iron(0) center more electron rich, facilitating the oxidative addition of silane.[40]



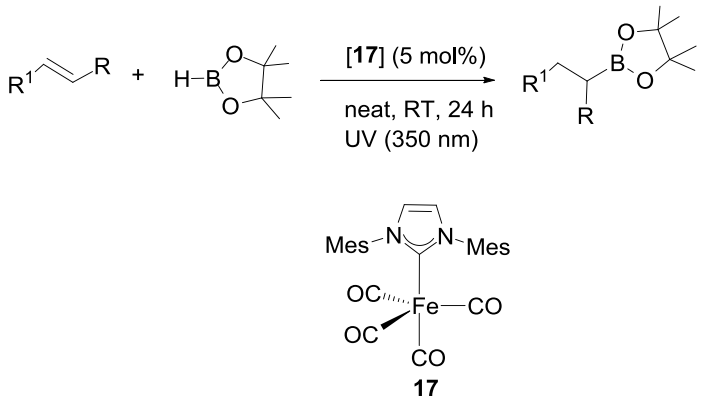
(*a*NHC)Fe(CO)$_4$ (**18**)

Scheme 16. Reduction of imines with silanes catalized by **18**.

Hydroboration, addition of B-H bonds across carbon-carbon multiple bonds, is a well-established method for the synthesis of organoboranes, which can be transformed into a variety of functional groups, and used as synthons in many transformations, including carbon-carbon and carbon-heteroatom bond formation.[43]

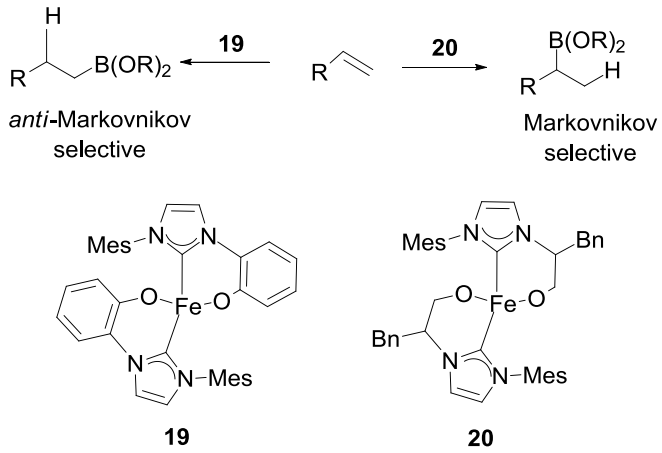
Recently, Darcel and Sortais developed an interesting catalytic system for the hydroboration of functional alkenes with pinacolborane, using the carbonyl Fe-NHC complex **17** as catalyst under visible light irradiation (Scheme 17). Interestingly, the hydroboration of terminal alkenes was chemo- and regio-selective, yielding only *anti*-Markovnikov boronate derivatives in good yields.[44] The reaction was suitable for internal alkenes, which were selectively converted into the linear *anti*-Markovnikov products through a tandem isomerisation/hydroboration process. As it was demonstrated by the same authors for the hydrosilylation reactions with **17**, the mechanism of the catalytic hydroboration implies the oxidative addition of the B-H bond of the hydroboronate on to unsaturated [(IMes)Fe(CO)$_3$] species formed by UV-assisted

decoordination of a CO ligand in **17**. The formation of an iron-hydride-boryl intermediate was identified by NMR spectroscopy.



Scheme 17. Hydroboration of alkenes with pinacolborane catalyzed by **17**.

The group of Thomas has recently described the synthesis and full characterization of a series of alkoxy-tethered NHC Fe(II) complexes, which were catalytically active for the hydroboration of terminal alkenes with controlled and switchable regioselectivity.[45] Ligand design allows to controlling the regioselectivity of the reaction. The alkoxy iron catalyst **19** yielded Markovnikov alkene hydroboration with HBpin while the use of catalyst **20** afforded *anti*-Markonivkov selective hydroboration (Scheme 18). Moreover, successful catalysis was achieved for terminal alkyl- and aryl-alkenes to give the corresponding alcohols following oxidation with basic hydrogen peroxide. This work represents the first example of an iron catalyst achieving Markovnikov selective alkene hydroboration. Significantly, the reaction proceeded in the absence of any external activator. It was proposed the formation of iron-hydride species as plausible intermediates in the reaction, enabling the reaction to occur in short times at ambient temperature.



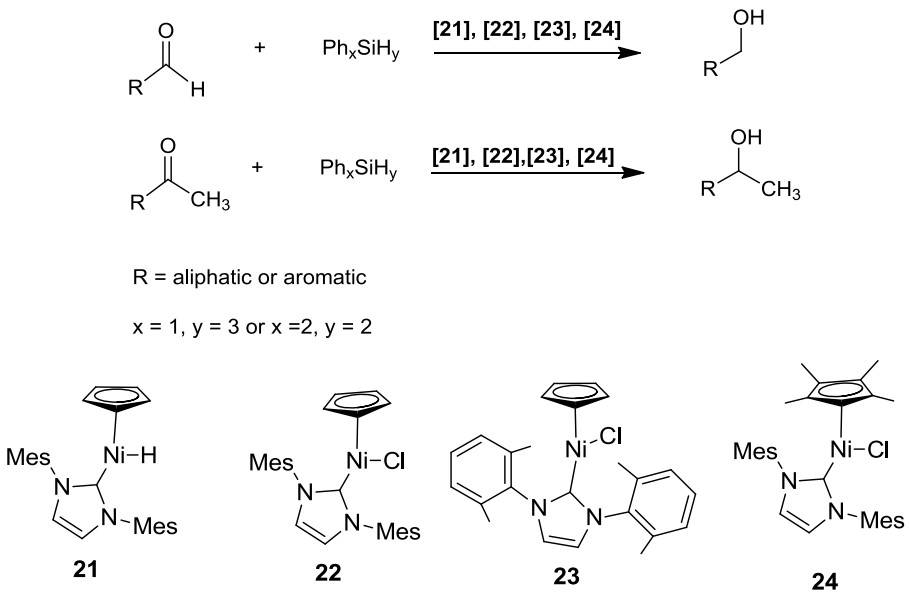
Scheme 18. Switchable Markovnikov and anti-Markovnikov selective hydroboration.

1.2. Nickel N-heterocyclic carbene complexes in reduction reactions

Nickel-NHC complexes have been extensively explored in catalysis, leading to the discovery of an impressive array of chemical transformations, including C-C, C-N, C-S bond forming reactions and oxidation reactions. In contrast, reduction of functional groups catalyzed by well-defined Ni-NHC complexes is poorly developed.

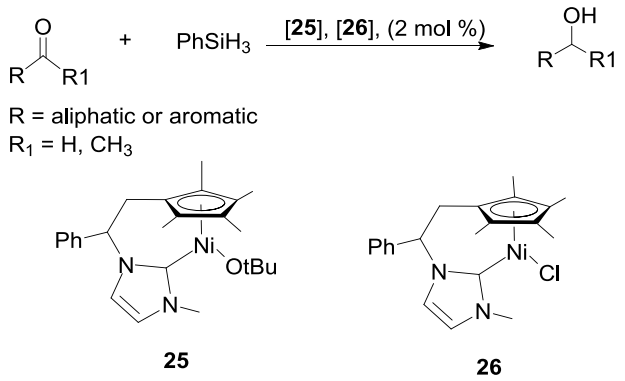
Recently we[46] and Chetcuti´s group[47] independently disclosed two closely related half-sandwich Ni^{II}-NHC complexes capable of performing the reduction of carbonyl compounds by using silane as a reducing agent (Scheme 19 and 20).

The half sandwich nickel-NHC complexes **21**-**24** reported by Chetcuti´s group catalyzed the reduction of aldehydes and ketones to the corresponding alcohols at room temperature in the presence of a catalytic amount of sodium triethylborohydride. The nickel hydride complex **21** was proved to be the intermediate active species (Scheme 19).[47]



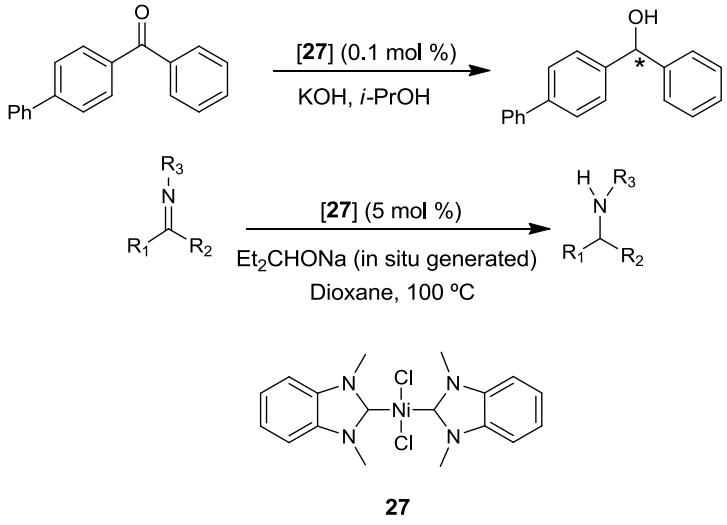
Scheme 19. Reduction of ketones and aldehydes catalyzed by complexes **21**, **22**, **23 and 24**.

Our group disclosed the remarkable catalytic activity of the nickel-alkoxide complex (Cp*-NHC^{Me})Ni(O^{t}Bu) (**25)**, which afforded quantitative reduction of aldehydes to the corresponding alcohols in 5 min at 25 ºC.[46] Mechanistic studies, based on stoichiometric reactions, revealed that the transient nickel hydride (Cp*-NHCMe)NiH complex was the active species in the hydrosilylation of carbonyls (Scheme 20).



Scheme 20. Reduction of ketones and aldehydes catalyzed by complexes **25** and **26**.

Apart from hydrosilylation reactions, reduction of aromatic ketones and imines through hydrogen transfer reactions (TH) has been achieved in good yield by using a combination of **27**/KOH, *i*-PrOH and Ni^0/IMeS.HCl/Et_2CHONa,[49] Scheme 21. In addition, electrocatalytic conversion of CO_2 to CO was performed by using a NHC-isoquinoline nickel complex.[50]



Scheme 21. Transfer hydrogenation of ketones catalysed by $[(NHC)_2NiCl_2]$, **27** complex.

1.3. Objectives

The aim of this thesis was to explore the catalytic activity of Fe and Ni complexes bearing tetramethylcyclopentadienyl functionalized N-heterocyclic carbene ligands in reduction processes, and in dehydrogenative coupling reactions.

Specifically we were interested in developing new catalytic systems for:

(i) dehydrogenative coupling reactions of hydrosilanes with alcohols and thiols;

(ii) reduction of carbonyl groups through transfer hydrogenation processes using alcohols as hydrogen source; and

(iii) reduction of nitrocompounds using silanes as reducing agents;

Metal-ligand cooperativity is an important concept in transition metal catalysis, which implies that both the metal and the ligand are directly involved in both activation processes. The active role of the ligand facilitating the chemical reaction, and working in synergy with the metal, provides new patterns for catalysis. We aimed to combine this concept with the unique properties of NHC ligands by synthesizing new *O*- and *N*-donor functionalized NHC ligands, which upon metalation might facilitate a cooperative catalytic mechanism and result in an enhanced catalytic activity.

1.4. References

[1] a) E. Peris, *Chem. Rev.* **2018**, DOI: 10.1021/acs.chemrev.6b00695; b) D. J. Nelson, S. P. Nolan, *Chem. Soc. Rev*. **2013**, *42*, 6723; c) M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, Nature **2014**, *510*, 485; d) D. Bourissou, O. Gerret, F. P. Gabbai, G. Bertrand, *Chem. Rev*. **2000**, *100*, 39.

[2] a) P. de Fremont, N. Marion, S. P. Nolan, *Coord. Chem. Rev*. **2009**, *253*, 862; b) D. Velazquez, F. Verpoort, *Chem. Soc. Rev*. **2012**, *41*, 7032, c) F. E. Hanh, M. C. Jahnke, *Angew. Chem. Int. Ed*. **2008**, *47*, 3122; d) W. A. Herrmann, C. Kocher, *Angew. Chem. Int. Ed*. **1997**, *36*, 2163.

[3] M. F. Lappert, P. L. Pye, *J. Chem. Soc., Dalton Trans*. **1977**, 2160.

[4] S. Diez-Gonzalez, N. Marion, S. P. Nolan, *Chem. Rev*. **2009**, *109*, 3612.

[5] a) M. J. Ingleson, R. A. Layfield, *Chem. Commun*. **2012**, *48*, 3579; b) D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2013**, *355*, 19; c) K. Riener, S. Haslinger, A. Raba, M. P. Högerl, M. Cokoja, W. A. Herrmann, F. E. Kühn, *Chem. Rev*. **2014**, *114*, 5215.

[6] P. A. Chaloner, M. A. Esteruelas, F. Joó, L A. Oro in Homogeneous Hydrogenations, Series Catalysis by Metal Complexes, Springer Netherlands, 1994, Vol. 15.

[7] a) P. J. Chirik, *Acc. Chem. Res*. **2015**, *48*, 1687-1695; b) Y.-Y. Li, S.-L- Yu, W.-Y. Shen, J.-X. Gao, *Acc. Chem. Res.* **2015**, *48*, 2587.

[8] R. H. Morris, *Acc. Chem. Res*. **2015**, *48*, 1494.

[9] a) S. Elangovan, M. Garbe, H. Jiao, A. Spannenberg, K. Junge, M. Beller, *Angew. Chem. Int. Ed*. **2016**, *55*, 15364; b) F. Kallmeier, T. Irrgang, T. Dietel, R. Kempe, *Angew. Chem. Int. Ed*. **2016**, *55*, 11806.

[10] S. Gülcemal, B. Çentikaya in *N-Heterocyclic Carbenes: from Laboratory Curiosities to Efficient Synthetic Tools*, Ed. S. Díez-González, RSC Catalysis Series, 2017, Chapter 13, pp. 484.

[11] A. A. Danopoulos, J. A. Wright, W. B. Motherwell, *Chem.Commun.* **2005,** 784.

[12] R. P. Yu, J. M. Darmon, J. M. Hoyt, G. W. Margulieux, Z. R. Turner, P. J. Chirik, *ACS Catal*. **2012**, *2*, 1760.

[13] J. M. Darmon, Z. R. Turner, E. Lobkovsky, P. J. Chirik, *Organometallics* **2012**, *31*, 2275.

[14] S. K. Russell, J. M. Darmon, E. Lobkovsky, P. J. Chirik, *Inorg. Chem*. **2010**, *49*, 2782.

[15] D. Wang, D. Astruc, *Chem. Rev.* **2015**, *115*, 6621.

[16] V. V. K. M. Kandepi, J. M. S. Cardoso, E. Peris, B. Royo, *Organometallics* **2010**, *29*, 2777.

[17] M. D. Bala, M. I. Ikhile, *J. Mol. Catal A: Chemical* **2014**, *385*, 98.

[18] O. R. Luca, R. H. Crabtree, *Chem. Soc. Rev*. **2013**, *42*, 1440.

[19] P. Das, T. Elder, W. W. Brennessel, S. C Chmely, *RSC Adv*. **2016**, *6*, 88050.

[20] T. Hashimoto, S. Urban, R. Hoshino, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 4474.

[21] *Modern Reduction Methods*, (Eds: P. G. Andersson, I. J. Munslow), Wiley-VCH, Weinheim **2008**.

[22] P. J. Kociesnki, in *Protecting Groups*, (3rd Ed. P. J. Kociesnki) Thieme, **2005**.

[23] S. Gülcemal, B. Çentikaya in *N-Heterocyclic Carbenes From Laboratory Curiosities to Efficient Synthetic Tools*, (2nd Ed. S. Díez-González) RSC Catalysis Series, **2017**, pp. 504.

[24] L.C. Mistral Castro, D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2011**, *353*, 239.

[25] R. Lopes, J. M. S. Cardoso, L. Postigo, B. Royo, *Catal. Lett.* **2013**, *143*, 1061.

[26] J. M. S. Cardoso, A. Fernandes, B. de P. Cardoso, M. D. Carvalho, L. P. Ferreira, M. J. C. Calhorda, B. Royo, *Organometallics* **2014**, *33*, 5670.

[27] J. M. S. Cardoso, B. Royo, *Chem. Commun.* **2012**, *48*, 4944.

[28] D. Bézier, F. Jiang, T. Roisnel, J.-B. Sortais, C. Darcel, *Eur. J. Inorg. Chem.* **2012**, 1333.

[29] S. Demir, Y. Gökçe, N. Kaloğlu, J.-B. Sortais, C. Darcel, İ. Özdemir, *Appl. Organomet. Chem*. **2013**, *27*, 459.

[30] V. César, L. C. Mistral Castro, T. Dombray, J.-B. Sortais, C. Darcel, S. Labat, K. Miqueu, J.-M. Sotiropoulos, R. Brousses, N. Lugan, G. Lavigne, *Organometallics* **2013**, *32*, 4643.

[31] A. V. Dubrovskiy, N. A. Markina, R. C. Larock, *Org. Biomol. Chem.* **2013**, *11*, 191.

[32] D. Bézier, G. T. Venkanna, J.-B. Sortais, C. Darcel, *ChemCatChem.* **2011**, *3*, 1747.

[33] L. C. M. Castro, J.-B. Sortais, C. Darcel, *Chem. Commun.* **2012**, *48*, 151.

[34] C. Grohmann, T. Hashimoto, R. Fröhlich, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 8047.

[35] B. Blom, G. Tan, S. Enthaler, S. Inoue, J. D. Epping, M. Driess, *J. Am. Chem. Soc*. **2013**, *135*, 18108.

[36] E. Buitrago, L. Zani, H. Adolfsson, *Appl. Organomet. Chem*. **2011**, *25*, 748.

[37] a) E. Buitrago, F. Tinnis, H. Adolfsson, *Adv. Synth. Catal*. **2012**, *354*, 217; b) A. Volkov, E. Buitrago, H. Adolfsson, *Eur. J. Org. Chem* **2013**, 2066.

[38] S. Warrat, L. Postigo, B. Royo, *Organometallics* **2013**, *23*, 893.

[39] H. Li, L.C. Mistral Castro, J. Zheng, T. Roisnel, V. Dorcet, J.-B. Sortais, C. Darcel, *Angew. Chem. Int. Ed.* **2013**, *52*, 1.

[40] M. Bhunia, P. K. Hota, G. Vijaykumar, D. Adhikari, S. K. Mandal, *Organometallics* **2016**, *35*, 2930.

[41] a) S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller, R. H. Crabtree, *Chem. Commun*. **2001**, 2274; b) E. Aldeco-Perez, A. J. Rosenthal, B. Donnadieu, P. Parameswaran, G. Frenking, G. Bertrand, *Science* **2009**, *326*, 556.

[42] M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485.

[43] R. Jana, T. P. Pathak, M. S. Sigman, *Chem. Rev*. **2011**, *111*, 1417.

[44] J. Zheng, J.-B. Sortais, C. Darcel, *ChemCatChem*. **2014**, *6*, 763.

[45] A. J. MacNair, C. R. P. Millet, G. S. Nichol, A. Ironmonger, S. P. Thomas, *ACS Catal*. **2016**, *6*, 7217.

[46] L. Postigo, B. Royo, *Adv. Synth. Catal*. **2012**, *354*, 2613.

[47] L. P. Bheeter, M. Henrion, L. Brelot, C. Darcel, M. J. Chetcuti, J-B. Sortais and V. Ritleng, *Adv. Synth. Catal*. **2012**, *354*, 2619.

[48] A.P. Prakasham, P. Ghosh, *Inorganica Chimica Acta,* **2015**, *431*, 61

[49] S. Kuhl, R. Schneider, Y. Fort, *Organometallics* **2003**, *22*, 4184.

[50] V. S. Thoi, N. Kornienko, C. G. Margarit, P. Yang, C. J. Chang, *J. Am. Chem. Soc.* **2013**, *135*, 14413.

CHAPTER 2. DEHYDROGENATIVE COUPLING OF AROMATIC THIOLS WITH Et_3SiH CATALYZED BY N-HETEROCYCLIC CARBENE NICKEL COMPLEXES

This chapter has been published in L. Postigo, R. Lopes, B. Royo, *Dalton Trans,* **2014**, *43*, 853-858.

2.1. Summary

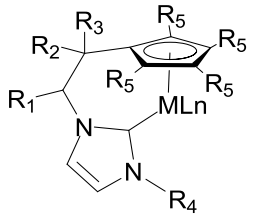
This chapter describes the coordination of new tetramethylcyclopentadienyl-functionalized N-heterocyclic carbene ligands with different wingtip substituents to nickel affording complexes of the general type (Cp*-NHC^R)NiX (X = Cl, I; R = ^{i}Bu, ^{n}Bu, Et, Me). These well-defined nickel complexes selectively catalyzed the coupling of aromatic thiols with Et_3SiH to give the corresponding silylthioethers ($RSSiEt_3$). The nickel complexes bearing ethyl, *iso*-butyl and *n*-butyl wingtips displayed comparable catalytic efficiency, while the nickel complex bearing a methyl substituent on the wingtip was the worst performing catalyst.

All new compounds were fully characterized by mass spectrometry, elemental analysis, and NMR spectroscopy.

2.2. Introduction

During the last decade, there has been much interest in the development of new catalysts based on inexpensive, non-toxic and abundant first-row transition metals.[1] Among them, nickel is an attractive metal for catalysis since it can adopt flexible number of oxidation states, Ni(0), Ni(I), Ni(II), Ni(III), Ni(IV) offering unique reactivity pathways.[2]

Some years ago, our group developed a new family of bidentade cyclopentadienyl ligands tethered to N-heterocyclic carbenes (NHCs) (**A**, Scheme 2.1).[3]



A

Scheme 2.1. Functionalised-cyclopentadienyl N-heterocyclic carbenes, **A**.

Related indenyl-functionalised NHCs have been described by us[4] and by Danopolous,[5] Wang,[6] and others.[7] An important feature of these Cp-NHC chelating ligands is the possibility of independently varying their structure components, namely the cyclopentadienyl ring, the spacer, and the imidazolium ring in order to fine tune the steric and electronic properties of the ligand. The introduction of chelating NHC ligands to the coordination sphere of a metal catalyst has interesting consequences in terms of the enhancement of thermal stability and rigidity. In addition, the introduction of chirality elements into this system may assist in controlling the stereochemistry of reactions taking place at the metal center. The versatile coordination chemistry

of these new ligands to a variety of metals ranging from early to late transition metals is also an interesting feature that we are exploring in our group.[3f]

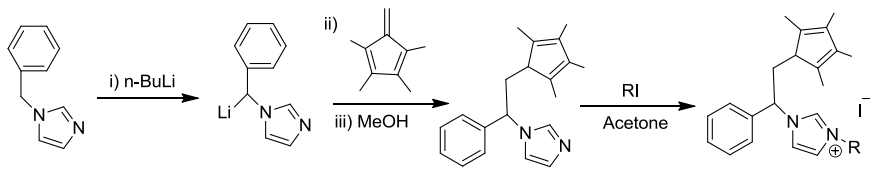
One of the structural parameters that can be modified to tune the stereoelectronic properties of the Cp-NHC ligand is the N-substituent of the imidazolium ring. In this work, we have prepared a new series of bidentate Cp-NHC ligands containing different substituents in the wingtip (R_4) of the imidazolium ring with the aim of investigating the consequences that smooth modifications may have on catalysis.

Thus, we decided to prepare a series of (Cp*-NHC^R)NiI (R=^{i}Bu, ^{n}Bu, Et, Me) complexes and apply them as catalysts for the dehydrogenative coupling of thiols with silanes.

2.3. Results and discussion

2.3.1. Synthesis and characterization of the imidazolium proligands

Compound **1** was prepared following the procedure previously described by us.[3a] Alkylation of **1** with the appropriate alkyl halide in acetone at 25 ºC affords the corresponding imidazolium proligands **2**-**6** with an overall yield of 70-87% (Scheme 2.2). Compounds **2**-**6** were obtained as a mixture of tautomers resulting from the different position of the double bonds in the cyclopentadienyl ring. Alkylation of **1** was limited to primary alkyl halides as secondary and tertiary alkyls gave unwanted elimination reactions. This is a general limitation for the synthesis of unsymmetrical NHC´s.[8]



1

R = ^{t}Bu (**2**)
R = ^{n}Bu (**3**)
R = Et (**4**)
R = Me (**5**)[3]
R = CH_2Ph (**6**)

Scheme 2.2. Synthesis of proligands **2**-**6**.

As illustrated in Figure 2.1 (^{1}H NMR of **1**), Compound **1** displays a complex NMR spectrum due to the presence of several region-isomers. The most representative signals of the ^{1}H NMR spectra are:
(i) the doublet at approximately 0.8 ppm that corresponds to the resonance of the methyls of the cyclopentadienyl group that couples with the proton of the Cp ring, (ii) the three singlet resonances at 1.8–1.2 ppm due to the protons of the three inequivalent methyl groups of the Cp*-ring, (iii) the signals at 2.6–2.2 ppm, that resonate as triplets, and correspond to the proton of the Cp*-ring resulting from the regio-isomers formed of substituted Cp*, (iv) the resonances at 3.2–2.8 ppm resulting from the CH_2 of the linker, (v) the triplet resonances at 5.2–4.8 ppm resulting from the CH of the linker, (vi) the protons from the imidazole ring, the NC*H*N, and finally (vii) the protons of the phenyl ring of the linker which display resonances in the region of 7.5-6.7 ppm.

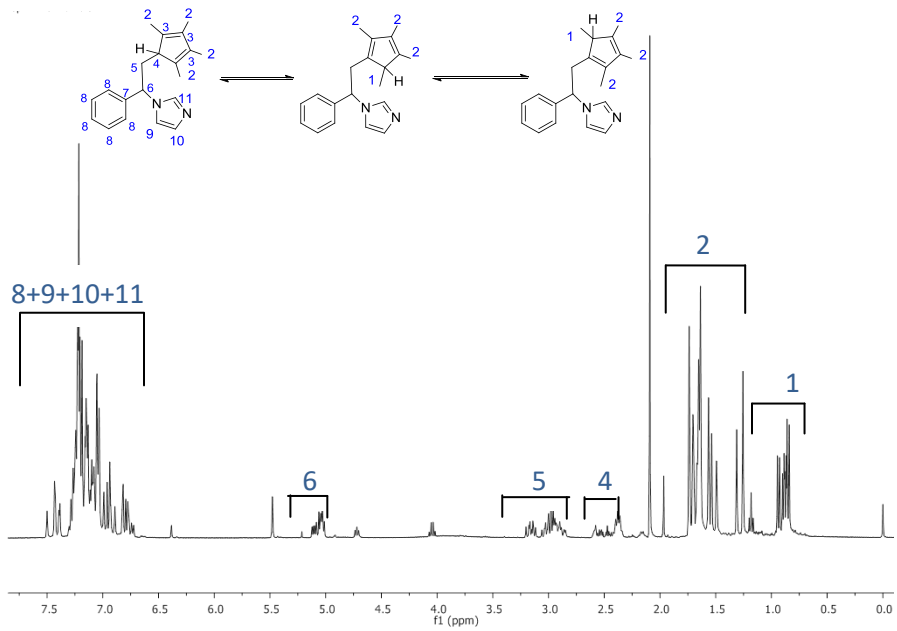


Figure 2.1. ^{1}H NMR spectrum of **1** (400 MHz, $CDCl_3$, 300K).

After alkylation of the wingtip, the imidazolium salts of general type Cp*-NHC^R [R = ^{i}Bu (**2**), ^{n}Bu (**3**), Et (**4**) $(CH_2)_2Ph$ (Bn) (**6**)], were isolated as yellow solids. Formation of the corresponding imidazolium salt is corroborated by the appearance in the ^{1}H-NMR of the typical resonances at 11 - 10 ppm (Figure 2.2).

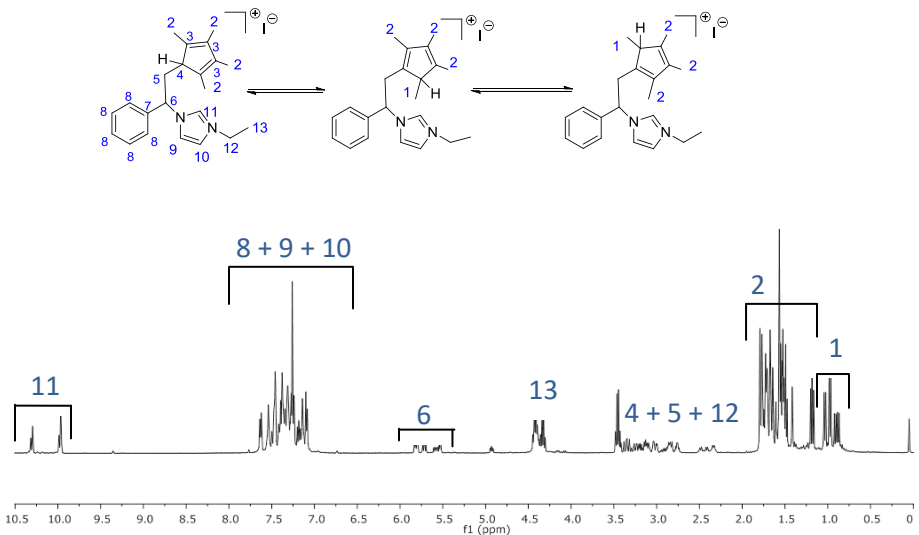
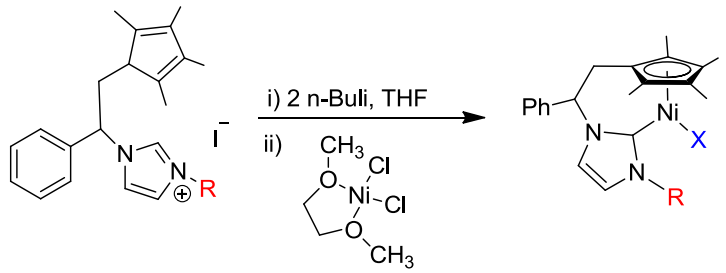


Figure 2.2. ^{1}H NMR spectrum of **4** (400 MHz, $CDCl_3$, 300K).

2.3.2. Synthesis and characterization of the nickel complexes

Proligands **2**-**4** were coordinated to nickel following a method similar to that described for the synthesis of (Cp*-NHC^{Me})NiCl (**10**) (Scheme 2.3), reported by our group.[8b] Treatment of **2**–**4** with two equivalents of *n*-BuLi generated *in situ* the corresponding (Cp*-NHC^{R})Li (R = ^{i}Bu, ^{n}Bu, Et) lithium salts, which were subsequently reacted with $NiCl_2$(DME) (DME = dimethoxyethane) to afford the novel complexes (Cp*-NHC^{R})NiI [R =^{i}Bu (**7**), ^{n}Bu (**8**), Et (**9**)], which were isolated as red solids in good yields (Scheme 2.3).



Imidazolium salt	R	Complex	X	Yield (%)
2	^{i}Bu	**7**	I	74
3	^{n}Bu	**8**	I	78
4	Et	**9**	I	72
5	Me	**10**	Cl	75
		11	I	65
6	CH_2Ph(Bn)	-	-	-

Scheme 2.3. Synthesis of (Cp*-NHC^{R})NiI complexes **7**- **11**.

The identity of all compounds was established by analytical and spectroscopic methods. The ^{1}H NMR spectra of **7, 8** and **9** show the signals due to the non-equivalent protons of the methyl substituents of the cyclopentadienyl ring at resonances 2.02, 1.93, 1.70, and 1.08

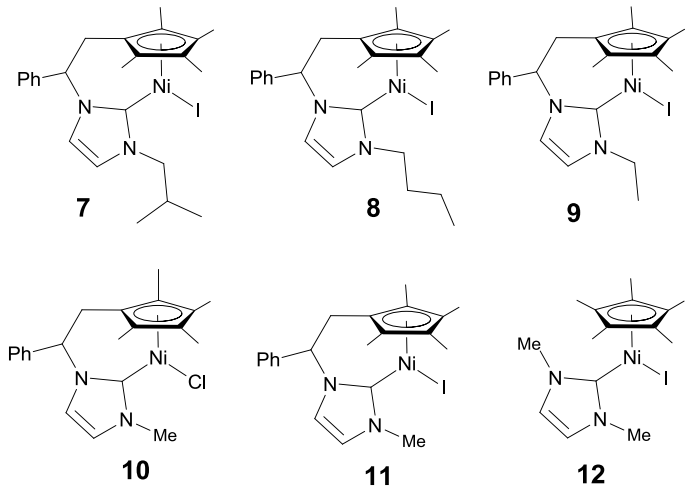
ppm for **7**, (similar set of signals are displayed for **7** and **8**) confirming that coordination of the cyclopentadienyl ring has occurred. Their ^{13}C NMR spectra provide a direct evidence of metalation as seen by the signal at resonances 174 ppm for **7,** (similar set of signals are displayed for **8** and **9**), assigned to the Ni-$C_{carbene}$, which is in the region of the previously reported (Cp*-NHCMe)NiCl complex, (176 ppm), and other half sandwich Ni-NHC complexes described in the literature.[9] Elemental analysis indicated that the corresponding iodide complexes **7**–**9** were formed. The formation of the iodides instead of the chlorides was unexpected because similar reaction of proligand **5** with $NiCl_2$(DME) afforded the chloride complex (Cp*-NHC^{Me})NiCl (**10**) instead of the corresponding iodide.[3i] However this halide exchange has been already observed by us in the coordination reaction of proligand **5** to other transition metals.[3c] The iodide complex (Cp*-NHC^{Me})NiI (**11**) was obtained by treating **10** with KI in THF under reflux for several hours.

Attempts to coordinate proligand **6** to nickel failed. The reaction of proligand **6** with two equivalents of BuLi did not afford the expected imidazolium salts as a pure sample. A mixture of undentified compounds was obtained, probably as a consequence of deprotonation of CH_2 protons of the benzyl wingtip, revealing that **6** is not tolerant to strong bases such as BuLi.

2.3.3. Catalytic dehydrogenative coupling of aromatic thiols with Et_3SiH

With the nickel complexes in our hands, we decided to explore the catalytic efficiency of complexes **7-9** and **11** (Scheme 2.4) in the dehydrogenative coupling of thiols (RSH) with triethylsilane (Et_3SiH). This reaction represents a useful catalytic process for the preparation of thiosilanes ($RSSiEt_3$).[10]

To date, there are only a few reported examples of metal complexes catalyzing the coupling of thiols with silanes.[11] In 2011, Nakazawa described the unprecedented dehydrogenative coupling of thiol with silanes catalyzed by an iron complex, the half sandwich $CpFe(CO_2)Me$.[11h] In view of these results, we became interested in exploring the reactivity of our half-sandwich Ni-NHC complexes in this reaction.



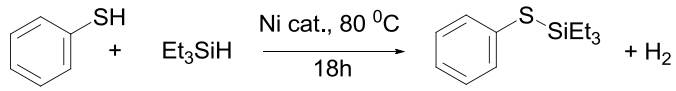
Scheme 2.4. Nickel complexes investigated as catalysts for the dehydrogenative coupling of thiols with Et_3SiH.

The catalytic activity of the complexes **7-9** and **11** (Scheme 2.4) was explored using thiophenol (PhSH) as a model substrate with Et_3SiH. The reaction was carried out in toluene at 80 ºC over 18 hours, in the presence of 1 mol % of catalyst, and using an Et_3SiH: substrate ratio of 4:1.

As shown in Table 2.1, the nickel complexes **7-9** and **11** catalyzed the dehydrogenation of thiophenol affording the corresponding silylthioether ($PhSSiEt_3$) in good yields. The reaction was selective to

the formation of the silylthiother; no homo-dehydrogenative coupling products such as disulfide or disilane were detected in the reaction. No coupling was observed in the absence of catalyst. The catalytic activity of complexes, **7, 8** and **9** containing the ^{i}Bu, ^{n}Bu and Et wingtips displayed very similar catalytic activity, achieving good yields of the corresponding $PhSSiEt_3$ after 18 hours at 80 ºC (Table 2.1, entries 1-3). In contrast, the nickel complex **11** containing the methyl group in the wingtip, resulted to be less active, affording 45 % yield of the corresponding silylthioether under similar reaction conditions.

Table 2.1. Dehydrogenative coupling of PhSH with Et_3SiH catalysed by nickel catalysts **7–12**.[a]



Entry	Catalyst	% Yield[b]	TON[c]
1	**7**	**84**	84
2	**8**	**81**	81
3	**9**	**82**	82
4	**10**	**42**	42
5	**11**	**45**	45
6	**12**	**62**	62

[a]All reactions were carried out with 1.0 mmol of PhSH and 4 mmol of Et_3SiH using 1 mol % of catalyst in toluene at 80 ºC for 18h.

[b]Yield determined by ^{1}H NMR spectroscopy using Ph_2CH_2 (0.5 mmol) as internal standard. [c]TON (turnover number) calculated from mol product/mol catalyst.

In order to investigate the effect of linking the cyclopentadienyl ring to the NHC in the catalytic performance, the catalytic activity of the related non-linked Cp*Ni(NHC^{Me})I[9a] (**12**) was determined using similar reaction conditions (in toluene at 80 ºC, 18h). Complex **12** displayed

moderate catalytic activity (62% yield, Table 2.1, entry 6), slightly higher than the obtained by **11** (45% yield).

Additionally, the chloride complex (Cp*NHC^{Me})NiCl (**10**) was applied as catalyst under the same catalytic conditions to check the influence of the halide in the performance of the catalyst. As shown in Table 2.1, entries 4 and 5, no influence of the halide was observed.

Under similar reaction conditions, the catalyst loading of complex **7** could be lowered to 0.1 mol % achieving turnover numbers of 650 (Table 2.2, entry 4), showing better catalytic performance than the previously reported iron complex $CpFe(CO)_2Me$ (TON 5.8 after 24 h in toluene at 80 ºC and using 1:10 PhSH:Et_3SiH ratio).[11h]

Table 2.2. Dehydrogenative coupling of PhSH with Et_3SiH catalysed by (Cp*-NHC^{iBu})NiI (**7**).[a]

Entry	% mol cat.	% Yield[b]	TON[c]
1	1	84	84
2	0.5	80	160
3	0.25	78	312
4	0.1	65	650

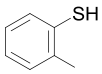
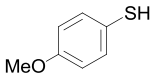
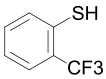
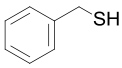
[a]All reactions were carried out with 1.0 mmol of PhSH and 4 mmol of Et_3SiH using 1 mol % of catalyst in toluene at 80ºC for 18h.

[b]Yield determined by ^1H NMR spectroscopy using Ph_2CH_2 (0.5 mmol) as internal standard. [c]TON (turnover number) calculated from mol product/mol catalyst.

The catalytic scope was evaluated with catalysts **7** and **8** using different aromatic thiols (Table 2.3). Thiophenol derivates containing functional groups such as methyl (Table 2.3, entries 3 and 4) and methoxy (Table 2.3, entries 5 and 6) were well tolerated for both **7** and **8** catalysts. A detrimental in the yield was observed for the coupling of 2-(trifluoromethyl)benzenethiol with silane, showing that thiols having electron-withdrawing groups display lower yields than those containing

electron-donating groups (Table 2.3, entries 7 and 8). Low yields, were obtained in the coupling of cyclohexanethiol (26%) and benzyl mercaptan (14%) (Table 2.3, entries 9 and 10). Similar findings were reported for the iron catalyst $CpFe(CO_2)Me$.[11h]

Table 2.3. Dehydrogenative coupling of thiols with Et_3SiH catalysed by (Cp*-NHC^R)NiI (R = ^{i}Bu (**7**), ^{n}Bu (**8**)).[a]

Entry	Substrate	Catalyst	%Yield[b]
1		**7**	84
2		**8**	81
3		**7**	80
4		**8**	75
5		**7**	73
6		**8**	96
7		**7**	60
8		**8**	38
9		**7**	26
10		**7**	14

[a]All reactions were carried out with 1.0 mmol of PhSH and 4 mmol of Et_3SiH using 1 mol % of catalyst in toluene at 80 ºC for 18h. [b]Yield determined by ^{1}H NMR spectroscopy using Ph_2CH_2 (0.5 mmol) as internal standard.

2.4. Conclusions

In summary, this chapter describes the preparation of new bidentate Cp*-NHC ligands and their coordination to nickel. A series of (Cp*-NHC^R)NiX (X = Cl, I) complexes bearing different substituents on the wingtip have been applied as catalysts for the dehydrogenative coupling of aromatic thiols with Et_3SiH. Interestingly, nickel complexes bearing ethyl, *iso*-butyl and *n*-butyl wingtips displayed comparable

catalytic activity, while the nickel complex containing the methyl substituent on the wingtip resulted to be the worst performing catalyst. This is the first report of well-defined nickel(II) complexes catalyzing the coupling of thiols with Et_3SiH.

2.5. Experimental Procedures

2.5.1. Materials and methods

Compounds **1**[3a], **10**[3i] and **12**[9a] were synthesized according to the methods described in the literature. All other reagents were used as received from commercial suppliers without further purification. All manipulations were carried out under a nitrogen atmosphere using standard Schlenck techniques and solvents were purified from appropriate drying agents.

Deuterated solvents were degassed and stored over molecular sieves. ^{1}H, ^{13}C, and ^{29}Si NMR spectra were recorded on a Bruker Avance III 400 MHz. Assigment of resonances was made from HSQC and HMBC experiments. Electrospray mass spectra (ESIMS) were recorded on a Micromass Quatro LC instrument; nitrogen was employed as drying and nebulising gas. A QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface (Micromass Manchester, UK) was used for high-resolution mass spectrometry (HRMS). The drying gas was used as nebulizing gas nitrogen at a flow of 400 and 80L/h, respectively.Elemental analyses were performed in our laboratories at ITQB.

2.5.2. Synthesis and characterization of proligands 2-4 and 6

Synthesis of (Cp*-NHC^{iBu}I) (2). 1-Iodo-2-methylpropane (1 mL, 8.54 mmol) was added to a solution of Cp*-NHC (**1**) (0.56 g, 1.19 mmol) in 10 mL of acetone. The mixture was stirred at room

temperature for 4 days. All volatiles were removed under vacuum to afford a yellow solid which was washed several times with ethyl ether and hexane to yield compound **2** as a yellow solid. Yield: 648 mg (81%). ^{1}H-NMR ($CDCl_3$): 10.68-10.16 (s, N=C*H*-N), 7.66-7.01 (m, CH_{Ph}, CH_{Imid}), 5.97-5.73 (m, CH_{linker}), 4.23-4.00 (m, C$H_{2linker}$, CH_{2iBu})), 3.46- 2.98 (m, C$H_{2linker}$, CH_{2iBu}), 2.15 (m, CH_{Cp*}, CH_{iBu}), 2.15 (m, CH_{Cp*}, CH_{iBu}), 1.82-1.76 (C_5Me_4), 1.05-0.84 (C_5Me_4, ^iBu). ^{13}C{^{1}H}-NMR ($CDCl_3$): 140.0 (N=*C*H-N), 131.3-128.1 (*C*H$_{Ph}$, *C*H$_{Imid}$), 63.9 (*C*H$_{linker}$) 57.2 (*C*H$_{2linker}$, *C*H$_{2iBu}$), 49.0 (*C*H, ^iBu), 31.6 (*C*H$_{2linker}$, *C*H$_{2iBu}$), 29.7-29.6 (*C*H$_{Cp*}$, *C*H$_{iBu}$), 19.5-10.8 (C_5Me_4, ^iBu). Anal. Calc for $C_{24}H_{33}N_2I$ (476.44): C, 60.50; H, 6.98; N, 5.88. Found: C, 60.70; H, 6.97; N, 5.81. HRMS (ESI-TOF): *m*/*z* [M-I]$^+$ calcd for $C_{24}H_{33}N_2$, 349.2644; found: 349.2642 [M-I]$^+$.

Synthesis of Cp*-NHC^{nBu}I (3): Iodobutane (0.98 mL, 8.54 mmol) was added to a solution of Cp*-NHC (**1**) (0.50 g, 1.70 mmol)) in 10 mL of acetone The mixture was stirred at room temperature for 4 days. All volatiles were removed under vacuum to afford a yellow solid which was washed several times with ethyl ether and hexane to yield compound **3** as a yellow solid. Yield: 722 mg (91 %). ^{1}H-NMR ($CDCl_3$): 10.55-9.58 (s, N=C*H*-N), 7.80-7.01 (C*H*$_{Ph}$, C*H*$_{Imid}$), 5.90-5.57 (C*H*$_{linker}$), 4.37-3.99 (m, C*H*$_{2nBu}$), 3.43- 2.98 (m, C*H*$_{2linker}$, C*H*$_{2iBu}$, C*H*$_{Cp*}$), 1.80-0.88 (C_5Me_4, ^nBu). ^{13}C{^{1}H}-NMR ($CDCl_3$): 135.2 (N=*C*H-N), 131.0-120.3 (*C*H$_{Ph}$, *C*H$_{Imid}$), 64.5-62.1 (*C*H$_{linker}$) 51.8-48.9 (*C*H$_{Cp*}$), 49.9-49.7 (*C*H$_{2linker}$, *C*H$_{2nBu}$), 32.3-31.7 (*C*H$_{2linker}$, *C*H$_{2nBu}$), 14.7-10.8 (C_5Me_4, ^nBu). Anal. Calc for $C_{24}H_{33}N_2I$ (476.44): C, 60.50; H, 6.68; N, 5.78. Found: C, 60.20; H, 6.19; N, 5.32. MS (ESI-TOF): *m*/*z* [M-I]$^+$ calcd for $C_{24}H_{33}N_2$, 349; found: 349 [M-I]$^+$.

Synthesis of Cp*-NHC^{Et}I (4): Iodoethane (0.55 mL, 6.84 mmol) was added to a solution of Cp*-NHC (**1**) (0.40 g, 1.36 mmol) in 10

mL of acetone. The mixture was stirred at room temperature for 2 days. All volatiles were removed under vacuum and then washed several times with ethyl ether and hexane to yield the compound **4** as a yellow solid. Yield: 444 mg (74 %). %). ^{1}H-NMR ($CDCl_3$): 10.47-9.43 (s, N=C*H*-N), 7.75-7.01 (m, CH_{Ph}, CH_{Imid}), 5.83-5.53 (m, CH_{linker}), 4.43-4.10 (m, CH_{2Et}), 3.47- 2.29 (m, C$H_{2linker}$, CH_{Cp*}), 1.81-0.83 (C_5Me_4, *Et*). ^{13}C{^{1}H}-NMR ($CDCl_3$): 140.0 (N=*C*H-N), 131.3-119.5 (*C*H$_{Ph}$, *C*H$_{Imid}$), 69.4-64.0 (*C*H$_{linker}$) 57.2-49.1 (*C*H$_{Cp*}$), 45.6-45.4 (*C*H$_{2Et}$), 32.6-31.4 (*C*H$_{2linker}$), 15.7-11.5 (C_5Me_4, *Et*). Anal. Calc for $C_{22}H_{29}N_2I$ (448.38): C, 58.93; H, 6.51; N, 6.24. Found: C, 58.61; H, 6.24; N, 5.86.

Synthesis of Cp*-NHC^{Bn}I (6): Benzylbromide (1.05 mL, 8.85 mmol), NaI (1.32 g, 8.85 mmol) was added to a solution of Cp*-NHC (**1**) (0.52 g, 1.77 mmol)) in 10 mL of acetone. The mixture was stirred at room temperature for 4 days. All volatiles were removed under vacuum to afford a yellow solid which was washed several times with diethyl ether and hexane to yield the compound **5** as a yellow solid. Yield: 806 mg (90 %). ^{1}H NMR ($CDCl_3$): 10.50-9,81 (s, N=C*H*-N), 7.63-6.92 (CH_{Ph}, CH_{Imid}), 5.74-5.40 (CH_{linker}, CH_{2Bz}), 3.46-2.20 (m, C$H_{2linker}$, CH_{Cp*}), 1.82-0.81 (C_5Me_4). ^{13}C{^{1}H}-NMR ($CDCl_3$): 136.4 (N=*C*H-N), 133.2-120.2 (*C*H$_{Ph}$, *C*H$_{Imid}$), 64.5 (*C*H$_{linker}$), 53.8-51.8 (*C*H$_{2Bz}$), 49.0 (*C*H$_{Cp*}$), 31.8-31.4 (C$H_{2linker}$), 15.2-10.9 (C_5Me_4). Anal. Calc for $C_{27}H_{31}N_2I$ (510.15): C, 63.53; H, 6.12; N, 5.49. Found: C, 63.20; H, 5.84; N, 5.25. MS (ESI-TOF): (*m*/*z*) $[M-I]^+$ calcd for $C_{27}H_{31}N_2$ 383; found: 383 $[M-I]^+$.

2.5.3. Synthesis and characterization of nickel complexes 7-9 and 11

Synthesis of (Cp*-NHC^{iBu})NiI (7). Two equivalents of *n*-BuLi (0.86 mL, 1.36 mmol) were added to a solution of **2** (0.30 g, 0.62 mmol) in THF (10 mL) at -60 ºC. The mixture was stirred for 1h at room temperature, and a suspension of $NiCl_2$(DME) (0.14 g, 0.62 mmol) in THF (5 mL) was added at once. The reaction mixture was stirred overnight at room temperature. The solvent was removed under vacuum, and the remaining solid was extracted in a mixture of toluene/hexane (15 mL/5 mL), yielding complex **7** as a red crystalline solid. Yield: 200 mg (74 %). ^{1}H-NMR (C_6D_6): 7.07-6.90 (m, 5 H, C*H*$_{Ph}$), 6.05 (s, 1 H, C*H*$_{Imid}$), 5.85 (s, 1 H, C*H*$_{Imid}$), 5.19 (dd, 1 H, C*H*$_{linker,}$ ^2J = 8.84 Hz, ^3J = 5.60 Hz), 5.08 (dd, 1 H, *^{i}Bu, ^2J = 13 Hz, ^3J = 6 Hz*), 3.59 (dd, 1 H, *^{i}Bu, ^2J = 13 Hz, ^3J = 6 Hz*), 2.90 (m, 1 H, *^{i}Bu*), 2.12 (s, 1 H, C_5*Me$_4$*), 2.02 (m, 2 H, C*H$_{2linker}$*) 1.93 (s, 3 H, C_5*Me$_4$*), 1.70 (s, 3 H, C_5*Me$_4$*), 1.08 (s, 3 H, C_5*Me$_4$*), 0.99 (d, 3 H, ^{3}J = 7.2 Hz, *^{i}Bu*), 0.80 (d, 3 H, ^{3}J = 7.2 Hz, *^{i}Bu*). ^{13}C{^{1}H}-NMR (C_6D_6): 174.5 (Ni-*C*$_{Carbene}$), 137.9 (*C*$_{iPh}$), 130.8 (*C*H$_{Ph}$), 129.5 (*C*H$_{Ph}$), 128.4 (*C*H$_{Ph}$), 126.1 (*C*H$_{Ph}$), 122.9 (*C*H$_{Imid}$), 119.7 (*C*H$_{Imid}$), 105.1 (C_5Me$_4$), 104.4 (C_5Me$_4$), 102.8 (C_5Me$_4$), 101.2 (C_5Me$_4$), 89.1 (C_5Me$_4$), 66.6 (*C*H$_{linker}$), 60.1 (*C*H$_2$, *^{i}Bu*), 30.2 (*C*H$_{2linker}$), 30.1 (*C*H, *^{i}Bu*), 20.1 (*Me*, *^{i}Bu*), 20.0 (*Me*, *^{i}Bu*), 12.4 (C_5*Me$_4$*), 10.7 (C_5*Me$_4$*), 10.6 (C_5*Me$_4$*), 10.0 (C_5*Me$_4$*). Anal. Calc for $C_{24}H_{31}N_2NiI$ (533.11): C, 54.07; H, 5.86; N, 5.25. Found: C, 53.80; H, 5.52; N, 4.86 . HRMS (ESI-TOF): *m*/*z* [M-I]$^+$ calcd for $C_{24}H_{31}N_2Ni$, 405.1841; found: 405.1841 [M-I]$^+$.

Synthesis of (Cp*-NHC^{nBu})NiI (8). A procedure similar to that used for the preparation of complex **7** was applied by using proligand **3** (0.30 g, 0.62 mmol), *n*-BuLi (0.86 mL, 1.36 mmol), and $NiCl_2$(DME) (0.14 g, 0.62 mmol). Yield: 210 mg (78%). ^{1}H-NMR (C_6D_6): 7.17-

6.94 (m, 5 H, C*H*$_{Ph}$), 6.05 (s, 1 H, C*H*$_{Imid}$), 5.85 (s, 1 H, C*H*$_{Imid}$), 5.19 (m, 1 H, C*H*$_{linker}$), 5.08 (m, 1 H, *Bu*), 4.04 (m, 1 H, *Bu*), 2.02 (s, 3 H, C_5*Me*$_4$), 2.01 (m, 2 H, C*H*$_{2linker}$), 1.97 (s, 3 H, C_5*Me*$_4$), 1.90 (m, 2 H, *Bu*), 1.70 (s, 3 H, C_5*Me*$_4$), 1.08 (s, 3 H, C_5*Me*$_4$), 1.29 (m, 2 H, *Bu*), 0.97 (m, 3 H, *Bu*). $^{13}C\{^1H\}$-NMR (C_6D_6): 174.3 (Ni-*C*$_{Carbene}$), 137.9 (*C*$_{iPh}$), 129.8 (*C*H$_{Ph}$), 128.35 (*C*H$_{Ph}$), 127.2 (*C*H$_{Ph}$), 121.9 (*C*H$_{Imid}$), 120.2 (*C*H$_{Imid}$), 104.9 (*C*$_5$Me$_4$), 104.4 (*C*$_5$Me$_4$), 102.7 (*C*$_5$Me$_4$), 100.8 (*C*$_5$Me$_4$), 89.2 (*C*$_5$Me$_4$), 66.7 (*C*H$_{linker}$), 52.7 (*C*H$_2$, *Bu*), 33.5 (*C*H$_{2linker}$), 30.2 (*C*H, *Bu*), 19.7 (Me, *Bu*), 12.4 (Me, *Bu*), 11.9 (C_5*Me*$_4$), 11.3 (C_5*Me*$_4$), 11.1 (C_5*Me*$_4$), 10.7 (C_5*Me*$_4$). Anal. Calc for $C_{24}H_{31}N_2NiI.C_7H_8$ (625.25): C, 59.55; H, 6.29; N, 4.48. Found: C, 59.30; H, 6.27; N, 4.48 . HRMS (ESI-TOF): *m*/*z* $[M\text{-}I]^+$ calcd for $C_{24}H_{31}N_2Ni$, 405.1841; found: 405.1836 $[M\text{-}I]^+$.

Synthesis of (Cp*-NHC^{Et})NiI (9). A procedure similar to that used for the preparation of complex **7** was applied by using proligand **4** (0.20 g, 0.44 mmol), *n*-BuLi (0.63 mL, 0.98 mmol), and $NiCl_2$(DME) (0.10 g, 0.44 mmol). Yield: 150 mg (72%). ^{1}H-NMR (C_6D_6): 7.08-6.88 (m, 5 H, C*H*$_{Ph}$), 6.97 (s, 1 H, C*H*$_{Imid}$), 5.82 (s, 1 H, C*H*$_{Imid}$), 5.22 (dd, 1 H, ^3J = 10.6 Hz, ^3J = 3.5 Hz, C*H*$_{linker}$), 4.85 (sex, 1 H, C*H*$_2^{Et}$), 4.17 (sex, 1 H, C*H*$_2^{Et}$), 2.10 (m, 2 H, C*H*$_{2linker}$), 2.07 (s, 3 H, C_5*Me*$_4$), 1.99 (s, 3 H, C_5*Me*$_4$), 1.73 (s, 3 H, C_5*Me*$_4$), 1.30 (t, 3 H, C*H*$_3^{Et}$), 1.05 (s, 3 H, C_5*Me*$_4$).$^{13}C\{^1H\}$-NMR (C_6D_6): 174.5 (Ni-*C*$_{Carbene}$), 137.7 (*C*$_{iPh}$), 129.8 (*C*H$_{Ph}$), 129.1 (*C*H$_{Ph}$), 128.9 (*C*H$_{Ph}$), 128.5 (*C*H$_{Ph}$), 121.0 (*C*H$_{Imid}$), 120.4 (*C*H$_{imid}$), 105.0 (*C*$_5$Me$_4$), 104.85 (*C*$_5$Me$_4$), 102.8 (*C*$_5$Me$_4$), 100.2 (*C*$_5$Me$_4$), 89.3 (*C*$_5$Me$_4$), 66.3 (*C*H$_{linker}$), 47.8 (*C*H$_2$, *Et*), 30.2 (*C*H$_{2linker}$), 16.4 (Me, *Et*), 12.4 (C_5*Me*$_4$), 11.1 (C_5*Me*$_4$), 10.7 (C_5*Me*$_4$), 9.9 (C_5*Me*$_4$). Anal. Calc for $C_{22}H_{27}N_2NiI$ (505.05): C, 52.31; H, 5.39; N, 5.55. Found: C, 51.97; H, 5.08; N, 5.16.

Synthesis of (Cp*-NHC^{Me})NiI (11). Complex **10** (0.15 g, 0.37 mmol) was treated with KI (0.31 g, 1.88 mmol) and the mixture refluxed in THF (15 mL) mixture for 16 h. After cooling, all volatiles were removed in vacuum and the remaining solid was extracted in a mixture of toluene/hexane (10 mL/5 mL), yielding complex **11** as a red solid. Yield: 120 mg (65%). ^{1}H-NMR (C_6D_6): 7.09-6.87 (m, 5 H, C*H*$_{Ph}$), 5.91 (d, 1 H, ^{3}J = 1.8 Hz, C*H*$_{Imid}$), 5.79 (d, 1 H, ^{3}J = 1.8 Hz, C*H*$_{Imid}$), 5.22 (dd, 1 H, ^{3}J = 10.8 Hz, ^{3}J = 3.3 Hz, C*H*$_{linker}$), 3.80 (s, 3 H, N*Me*), 2.07-2.05 (m, 2 H, C*H*$_{2linker}$), 2.06 (s, 3 H, C_5Me_4), 2.00 (s, 3 H, C_5Me_4), 1.73 (s, 3 H, C_5Me_4), 1.04 (s, 3 H, C_5Me_4).^{13}C{^{1}H}-NMR (C_6D_6): 176.1 (Ni-*C*$_{Carbene}$), 137.7 (*C*$_{iPh}$), 129.0 (*C*H$_{Ph}$), 128.9 (*C*H$_{Ph}$), 128.3 (*C*H$_{Ph}$), 122.4 (*C*H$_{Imid}$), 120.2 (*C*H$_{imid}$), 104.8 (*C*$_5$Me$_4$), 104.5 (*C*$_5$Me$_4$), 103.1 (*C*$_5$Me$_4$), 100.0 (*C*$_5$Me$_4$), 89.0 (*C*$_5$Me$_4$), 66.8 (*C*H$_{linker}$), 40.9 (N*Me*), 30.3 (*C*H$_{2linker}$), 12.4 (C_5Me_4), 10.8 (C_5Me_4), 10.6 (C_5Me_4), 9.7 (C_5Me_4). Anal. Calc for $C_{21}H_{25}N_2NiI.C_7H_8$ (582.10): C, 57.67; H, 5.70; N, 4.80. Found: C, 57.60; H, 5.52; N, 5.15.

2.5.4. Catalytic dehydrogenative coupling of thiols with Et_3SiH.

Toluene (0.5 mL), (Cp*-NHC^R)NiCl (1 mol %), thiol (1 mmol), Et_3SiH (4 mmol), and Ph_2CH_2 (0.5 mmol) used as internal standard, were charged in a vial, and the solution was heated at 80 ºC for 18 h. All volatiles were removed under vacuum, and the residue was dissolved in $CDCl_3$. The amount of the corresponding triethylsilylthioether formed was determined by ^{1}H NMR by the relative intensity of signals of the product and the Ph_2CH_2 used as internal standard. The triethylsilylthioether produced was identified by comparison of the NMR spectra with reported data.

2.6. Acknowledgements

We gratefully acknowledge financial support from FCT of Portugal, POCI 2010 and FEDER through projects PTDC/QUI-QUI/110349/2009 and PTDC/QUI-QUI/099389/2008. We thank FC&T for REDE/1517/RMN/2005 and REDE/1504/REM/2005.
We thank the Analytical Services at ITQB for elemental analyses, and the UniMS-Mass Spectrometry Unit, ITQB/IBET. The NMR spectrometers are part of the national NMR facility supported by FCT (RECI/BBB-BQB/0230/2012).
The work described in the present chapter was done in collaboration with Drª Lorena Postigo, a postdoc researcher in our group, who performed part of the synthetic and catalytic essays.

2.7 References

[1] a) M. Albrecht, R. Bedford, B. Plietker, *Organometallics* **2014**, *33*, 5619; b) P. J. Chirik, T. B. Gunnoe, *ACS Catalysis* **2015**, *5*, 5584.
[2] a) M. I. Lipschutz, T. D. Tilley, *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 7290; b) J. R. Bour, N. M. Camasso, M. S. Sanford, *J. Am. Chem. Soc.* **2015**, *137*, 8034; c) J. Hao, B. Vabre, D. Zargarian, *J. Am. Chem. Soc.* **2015**, *137*, 15287; d) B. Vabre, Y. Canac, C. Lepetit, C. Duhayon, R. Chauvin, D. Zargarian, *Chem. Eur. J.* **2015**, *21*, 17403; e) M. Mastalir, B. Stoger, E. Pittenauer, G. Allmaier, K. Kirchner, *Org. Lett.* **2016**, *18*, 3186.
[3] a) A. P. da Costa, M. Viciano, M. Sanau, S. Merino, J. Tejeda, E. Peris, B. Royo, *Organometallics*, **2008**, *27*, 1305; b) A. P. da Costa, M. Sanau, E. Peris, B. Royo, *Dalton Trans*, **2009**, 6960; c) V. Kandepi, J. M.S. Cardoso, E. Peris, B. Royo, *Organometallics*, **2010**, *29*, 2777; d) A. P. da Costa, J. A. Mata, B. Royo, E. Peris, *Organometallics* **2010**, *29*, 1832; e) V. Kandepi, J. M. S. Cardoso, E. Peris, B. Royo,

Organometallics, **2011**, *30*, 4437; f) B. Royo, E. Peris, *Eur. J. Inorg. Chem.* **2012**, 1309; g) L. P. Bheeter, M. Henrion, L. Brelot, C. Darcel, M. J. Chetcuti, J-P. Sortais, V. Ritleng, *Adv. Synth. Catal.* **2012**, *354*, 2619; h) J. M. S. Cardoso, B. Royo, *Chem. Commun.* **2012**, *48*, 4944; i) L. Postigo, B. Royo, *Adv. Synth. Catal.* **2012**, *354*, 2613.

[4] a) S. Conde-Guadano, A. A. Danopoulos, R. Pattacini, M. Hanton, R. P. Tooze, *Organometallics* **2012**, *31*, 1643; b) S. P. Downing, P. J. Pogorzelec, A. A. Danopoulo, D. J. Cole-Hamilton, *Eur. J. Inorg. Chem.* **2009**, 1816.

[5] a) D. Wang, *Organometallics* **2007**, *26*, 3167; b) D. Wang, *Dalton Trans.* **2009**, 8963; c) D. Wang, *Macromolecules* **2008**, 1983.

[6] a) H.-M. Sun, D.-M. Hu, Y.-S. Wang, Q. Shen, Y. Zhang, *J. Organomet. Chem.* **2007**, *692*, 903; b) W. Zhang, *Dalton Trans* **2009**, 7230; c) D. Takaki, T. Okayama, H. Shuto, S. Matsumoto, Y. Yamaguchi, *Dalton Trans.* **2011**, *40*, 1445.

[7] S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299-309.

[8] O. Kühl, Functionalized N-Heterocyclic carbene complexes, 1, *Wiley*, UK, **2010**.

[9] a) V. Ritleng, C. Barth, E. Brenner, S. Milosevic, M. J. Chetcutti, *Organometallics* **2008**, *27*, 4223; b) *J. Am. Chem. Soc.* **2010**, *132*, 13588; c) V. R. A. M. Oertel, M. J. Chetcutti, L. F. Veiros, *J. Am. Chem. Soc.* **2010**, 8153; d) V. Ritleng, A. M. Oertel, M. J. Chetcuti, *Dalton Trans.* **2010**, *39*, 8153; e) A. M. Oertel, V. Ritleng, M. J. Chetcuti, *Organometallics* **2012**, *31*, 2829.

[10] G. Sartori, R. Balini, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199.

[11] a) I. Ojima, M. Nihonyanagi, *J. Organomet. Chem.* **1973**, *50*, C26; b) I. Ojima, M. Nihonyanagi, *J. Organomet. Chem.* **1973**, *57*, C42; c) B. P. S. Chauhan, P. Boudjouk, *Tetrahedron Lett.* **2000**, *41*; d) J. B. Brauah, K. Osakada, T. Yamamoto, *J. Mol. Catal. A: Chem.* **1995**, *101*,

17; e) C. K. Toh, H. T. Poh, C. S. Lim, W. Y. Fan, *J. Organomet. Chem.* **2012**, *717*, 9; f) M.-K. Chung, M. Schlaf, *J. Am. Chem. Soc.* **2004**, *126*, 7386; g) D. J. Harrison, D. R. Edwards, R. McDonald, L. Rosenberg, *Dalton Trans.* **2008**, 3401; h) K. Fukumoto, M. Kasa, T. Oya, M. Itazaki, H. Nakazawa, *Organometallics* **2011**, *30*, 3461.

CHAPTER 3. SELECTIVE REDUCTION OF NITROARENES WITH SILANES CATALYZED BY NICKEL N-HETEROCYCLIC CARBENES

This chapter has been published in R. Lopes, M. M. Pereira, B. Royo, *ChemCatChem* **2017**, *9*, 3073.

3.1. Summary:

This chapter describes an efficient catalytic system for the reduction of nitroarenes to amines using a well-defined nickel-NHC complex as catalyst and phenylsilane as reducing agent. The excellent activity of the catalyst provides access to anilines containing a wide array of reactive functionalities at 20 ºC, and without using any base or additive. Notably, the catalytic system allows the reduction of 5,10,15,20-tetra-(nitrophenyl)porphyrin (TNPP) and Cu(**II**) β-nitroporphyrin to the corresponding aminoporphyrins.

3.2. Introduction:

Functionalized anilines are valuable building blocks for the synthesis of dyes, pigments, pharmaceutical and agrochemicals.[1] One of the most general methods for the synthesis of anilines is by catalytic hydrogenation of nitroarenes. Well-established hydrogenation methods for industrial-scale production are based on the use of heterogeneous catalysts, generally based on precious metals, under high temperatures and also high pressure of H_2 gas.[2] However, selective hydrogenation of the nitro group in the presence of other reducible groups under mild conditions remains a challenging task. An alternative method to direct hydrogenation is the use of hazardous pressurized H_2 gas. At laboratory scale, the catalytic reduction of nitroarenes through hydrosilylation processes is an interesting approach since hydrosilanes are readily available and easy to handle. Currently, methods for hydrosilylation of nitroarenes have mainly been developed using precious metals as catalysts[3], and few catalytic systems using cheap metals are described in the literature.[4,5]

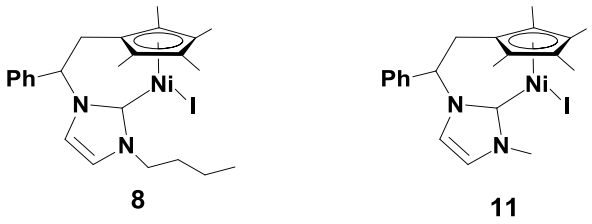
Herein we also present the use of well-definied Ni(II)-NHC complexes as catalysts for the reduction of a set of nitroarenes, including the value added nitroporphyrins, using phenylsilane as reducing agent under mild conditions.

3.3. Results and Discussion

3.3.1. Selective reduction of nitroarenes with silanes

The catalytic activity of half-sandwich complexes **8**[6a] and **11**[6b](Scheme 3.1) in the reduction of nitroarenes was tested using a primary silane, phenylsilane ($PhSiH_3$), as reducing agent and 1-chloro-4-nitrobenzene as a model substrate. Initially, the reaction was carried out in toluene at 60 ºC in the presence of 2 mol % of catalyst and using

a $PhSiH_3$: substrate ratio of 5:1. Under these conditions, an interesting effect of the wingtips substituents of the NHC ligands in complexes **8** and **11**[6] was observed (Table 3.1, entries 1 and 3).



Scheme 3.1. Nickel NHC complexes **8** and **11**.

Complex **8**, possessing a larger N-chain, is more active than **11**, affording 95% yield of 4-chloro-aniline in just 3 hours. The reaction profile is depicted in Figure 3.1. As shown in this profile, complex **8** displayed higher reaction rate than **11**. Progressively, the reaction rate increases to reach selective conversion to 4-chloroaniline in 3 hours, while the reaction catalyzed by complex **11** reached just a 62% of aniline in 3 h.

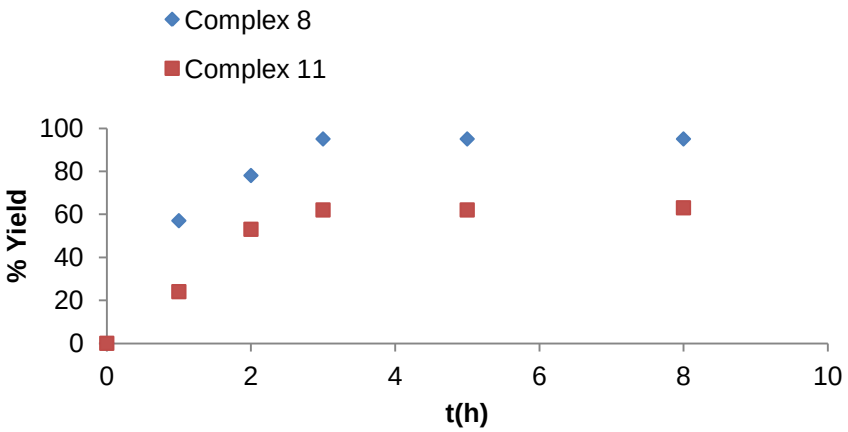


Figure 3.1. Time-dependent profile of the reaction of 1-chloro-4-nitrobenzene with phenylsilane using complexes **8** and **11**. Reaction conditions: 1-chloro-4-nitrobenzene (1 mmol), catalyst (2 mol %), $PhSiH_3$ (5 mmol), toluene (0.4 mL), 60 ºC.

We observed that the catalytic reduction of 1-chloro-4-nitrobenzene could be conducted at 20 ºC by increasing the catalyst loading to 10 mol %. A high yield (83%) of 4-chloroaniline was obtained in 15 hours using 10 mol % of **8** (Table 3.1, entry 4).

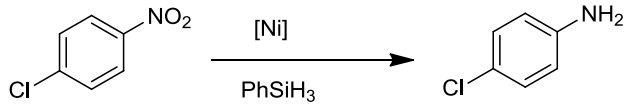
When the amount of **8** is reduced to 5 mol %, a 69% yield of 4-chloroaniline was obtained under those conditions (Table 3.1, entry 5).

The solvent had a significant influence on the reaction in terms of reactivity. Replacing toluene with acetonitrile, THF or dichloromethane produced a significant drop in conversion (Table 3.1, entries 6-8). The reaction can be performed under neat conditions affording high yield (85%) of the corresponding amine (Table 3.1, entry 9).

Full conversion of 1-chloro-4-nitrobenzene to 4-chloroaniline was obtained with a primary silane ($PhSiH_3$) at 60 ºC using **8** as catalyst (Table 3.1, entry 3). However secondary silanes, diphenylsilane (Ph_2SiH_2), alkyl silanes and alkoxysilanes, such as triethylsilane (Et_3SiH) and triethoxysilane [$(EtO)_3SiH$] showed no reactivity.

As expected, no reaction took place in the absence of catalyst (Table 3.1, entries 10 and 11). Complex **8** displayed slightly higher activity than the nickel complex Ni(*a*NHC)$_2$Cl$_2$ bearing an abnormal NHC ligand recently reported by Mandal and co-workers, which needed higher temperature (90 ºC) to afford 78% yield of the corresponding amine.[7]

Table 3.1. Reduction of 1-chloro-4-nitrobenzene with $PhSiH_3$ using catalysts **8** and **11.**[a]

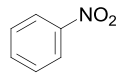
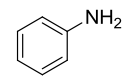
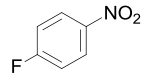
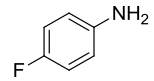
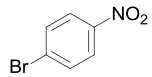
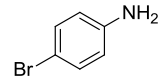
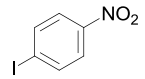
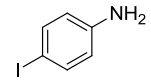
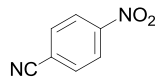
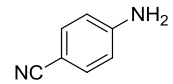


Entry	Catalyst	Loading (mol %)	Solvent	T (ºC)	t (h)	% Yield[b]
1	**11**	2	toluene	60	3	62
2	**11**	10	toluene	20	15	72
3	**8**	2	toluene	60	3	95
4	**8**	10	toluene	20	15	83
5	**8**	5	toluene	20	15	69
6	**8**	2	MeCN	60	3	25
7	**8**	2	THF	60	3	34
8	**8**	2	CH_2Cl_2	60	3	27
9	**8**	2	neat	60	3	85
10	none	--	toluene	60	3	0
11	none	--	toluene	20	15	0

[a] Reaction conditions: substrate (1 mmol), catalyst, $PhSiH_3$ (5 mmol), solvent (0.4 mL). [b] Isolated yield after column chromatography.

Then, we decided to investigate the catalytic activity of **8** with various nitroarenes, and we found that the reductions proceed with high yields and selectivities when other functional groups such as halogen and cyano are present. Notably, halogenated nitroarenes (Br, F, I) were chemoselectively reduced to the corresponding anilines; no dehalogenated product was observed in any case. When the reactions are performed at 60 ºC using 2 mol % of **8**, high yields are obtained in 3 hours (Method A). The reactions can be performed at 20 ºC using higher catalyst loading (10 mol %) and longer reaction times (15 h), Method B. Results are summarized in Table 3.2.

Table 3.2. Reduction of nitrobenzenes to amines with $PhSiH_3$ using catalyst **8**.[a]

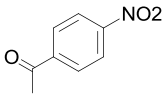
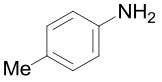
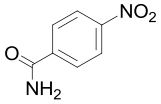
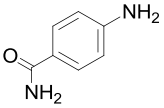
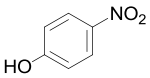
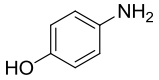
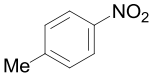
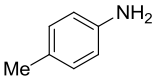
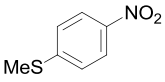
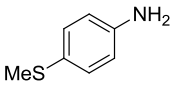
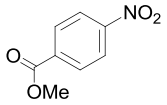
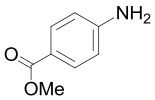
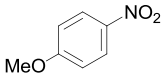
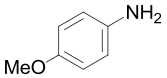
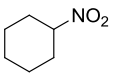
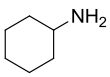
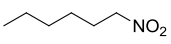
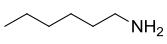
Entry	Substrate	Product	Method	%Yield[b]
1			**A**	87
2			**B**	91
3			**A**	79
4			**B**	91
5			**A**	70
6			**B**	80
7			**A**	88
8			**B**	90
9			**A**	74
10			**B**	82

[a] Reaction conditions: Method A: substrate (1 mmol), catalyst **8** (2 mol%), $PhSiH_3$ (5 mmol), solvent (0.4 mL), 60 ºC, 3 h; Method B: substrate (1 mmol), catalyst **8** (10 mol%), $PhSiH_3$ (5 mmol), solvent (0.4 mL), 20 ºC, 15 h. [b] Isolated yield.

Moreover, the present catalytic system also showed remarkable chemoselectivity in the reduction of a variety of substrates bearing other easily reducible functional groups such as ketone (Table 3.3, entry 1), amide (Table 3.3, entry 2), hydroxyl (table 4.3, entry 3), methyl (Table 3.3, entry 4), methylthio (Table 3.3, entry 5), ester (Table 3.3, entry 6), and methoxy (Table 3.3, entry 7). In all cases high yields (up to 81%) have been obtained. Exceptions are the reduction of nitrobenzenes substituted by amide and methylthio groups, where moderate yields were obtained (entries 2 and 5, Table 3.3).

Furthermore, the reduction of nitrobenzene substituted with an aldehyde or alkene gave, in both cases, a mixture of compounds attributed to the reducing of both functionalities. In addition, nitrocyclohexane and 1-nitrohexane were reduced to corresponding amines in good yield (entries 8 and 9, Table 3.3).

Table 3.3. Reduction of nitrobenzenes to amines with $PhSiH_3$ using catalyst **8**.[a]

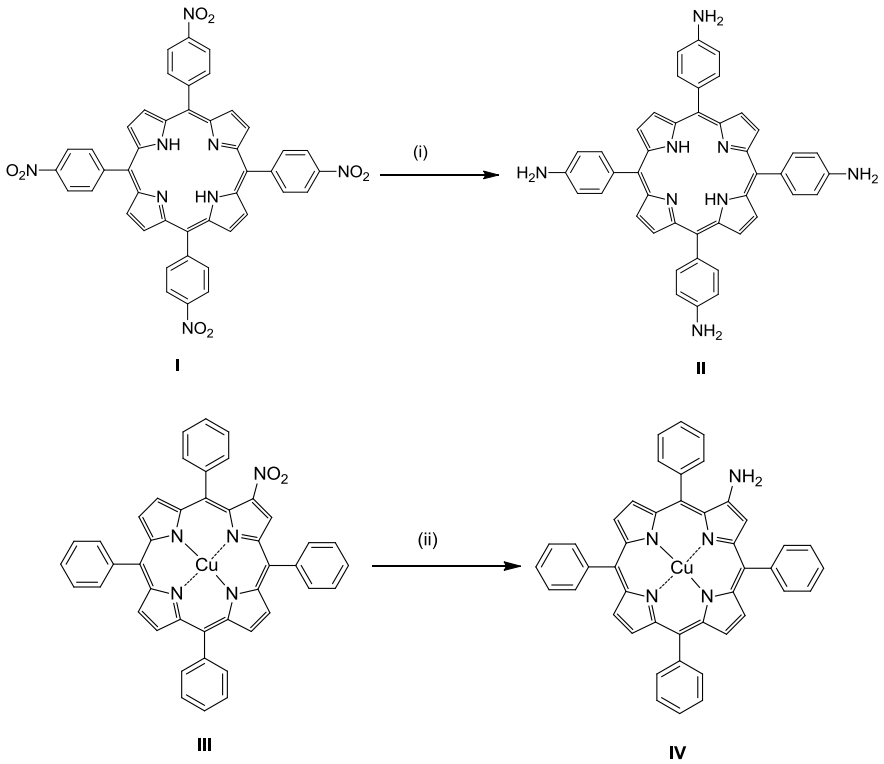
Entry	Substrate	Product	%Yield[b]
1			96
2			59
3			97
4			94
5			67
6			88
7			81
8			81
9			77

[a] Reaction conditions: Method B: substrate (1 mmol), catalyst **8** (10 mol%), $PhSiH_3$ (5 mmol), solvent (0.4 mL), 20 ºC, 15 h. [b] Isolated yield.

Finally, another relevant example to demonstrate the scope of this new catalytic system, is the highly efficient reduction of 5,10,15,20-tetra-(nitrophenyl)porphyrin (TNPP, **I**) and Cu(II) β-nitroporphyrin (**III**), Scheme 3.2. In a typical reaction, to a toluene solution of nitro-porphyrins **I** or **III**, the catalyst **8** and phenylsilane were added, and the

reaction was maintained along 15 hours at 20 ºC. After easy work-up and chromatographic purification, the desired porphyrinic amino compounds **II** and **IV** have been obtained with isolated yields of 86% and 94%, respectively.

This is a quite remarkable result that opens the way for the large scale preparation on amino-porphyrins, which are very important for the preparation of new functionalized materials,[7] without the use of highly toxic Sn/HCl approaches.[7- 9]



Scheme 3.2. Reduction of 5,10,15,20-tetra-(nitrophenyl)porphyrin, TNPP (**I**) and Cu(II) β-nitroporphyrin (**III**). Reaction conditions: (i) catalyst **8** (10 mol %) $PhSiH_3$ (20 mmol), toluene (0.4 mL), 20 ºC, 15 h; (ii) catalyst **8** (10 mol %), $PhSiH_3$ (5 mmol), toluene (0.4 mL), 20 ºC, 15 h.

In order to get an insight into the reaction mechanism, we performed the stoichiometric reaction of complex **8** with one equivalent of 1-

chloro-4-nitrobenzene in C_6D_6. The reaction mixture was heated at 60 ºC and monitored by ^{1}H NMR.

Complex **8** did not react with the substrate after being heated for 6 h. We also explored the stoichiometric reaction of **8** with $PhSiH_3$. The reaction was performed in a J. Young valve NMR tube. Phenylsilane was added to a solution of **8** in deuterated benzene (C_6D_6), and the reaction was heated to 60 ºC and monitored by ^{1}H NMR and ^{29}Si NMR during a period of 24 hours. Complex **8** did not react with phenylsilane. This result contrast with those reported by Mandal, who reported that a Ni complex bearing an abnormal NHC reacted with a stoichiometric amount of $PhSiH_3$ forming a Ni-silyl complex.[5] A similar result was observed by Shimada on reacting a (salicylaldiminato)Ni(II) complex with an stoichiometric amount of Ph_2SiH_2.[4i] They proposed the formation of an intermediary silyl complex based on ^{29}Si NMR experiments. In 2012, our group reported the formation of the silyl Ni complex (Cp*-NHC^{Me})Ni-SiH_2Ph formed by stoichiometric reaction of the Ni alkoxide (Cp*-NHC^{Me})Ni-OBu^t with $PhSiH_3$.[6a] The silyl complex displayed a resonance at -18.7 ppm in its ^{29}Si NMR spectrum, and the silyl hydrogen resonances at 4.67 and 4.44 ppm in its ^{1}H NMR spectrum. Therefore, if complex **8** were reacted with $PhSiH_3$ forming the expected silyl complex (Cp*-NHC^{nBu})Ni-SiH_2Ph, a resonance close to -18 ppm would be observed in the ^{29}Si NMR spectrum. Nevertheless, we only observed a resonance at -59.5 ppm, which corresponds to free $PhSiH_3$.

We believe that complex **8** reacts with phenylsilane under catalytic conditions in which a large excess of silane is present. We have attempted to explore the nature of the Ni species that remained after catalysis. We isolated a brown residue, which corresponds to a complex mixture as showed by its ^{1}H NMR. The ^{29}Si NMR of the residue did not display any resonance characteristic of a Ni-silyl species. The kinetic profile of complex **8** indicates the rapid formation

of the active species, since 29% yield of the corresponding product is formed after 15 min of reaction (Figure 3.1).

3.4. Conclusions:

A new catalytic system capable to perform the selective reduction of functionalized nitroarenes at 20 ºC was developed. The half-sandwich Ni-NHC complex **8** catalyzed the reduction of nitroarenes to anilines with phenylsilane without adding any bases or additives. Under the optimized conditions, the reduction of nitroarenes was chemoselective, displaying tolerance to a wide variety of functional groups including halogens, cyano, hydroxyl, ketone, amide, methoxy, and ester groups. Notable, nitroporphyrins were selectively reduced to the corresponding aminoporphyrins. The described catalytic system represents a synthetically useful method for the reduction of nitroarenes.

3.5. Experimental Procedures

3.5.1. Typical procedure for catalytic reduction of nitroarenes

Method A: In a closed vessel under nitrogen atmosphere, a mixture of catalyst (2 mol %), nitroarene (1 mmol), phenylsilane (5 mmol), and toluene (0.4 mL) was heated at 60 ºC for 3 hours. All volatiles were removed under vacuo and the remaining residue was purified by column chromatography (with a mixture ethyl acetate:hexane:methanol 1:4:1). The NMR spectra produced was compared with the reported data for identification of products.

Method B: In a closed vessel, under nitrogen atmosphere, a mixture of catalyst (10 mol %), nitroarene (1 mmol), phenylsilane (5 mmol), and toluene (0.4 mL) was stirred at 20 ºC for 15 hours. All volatiles were removed under vacuo and the remaining residue was purified by

column chromatography (with a mixture ethyl acetate:hexane:methanol 1:4:1). The NMR spectra produced was compared with the reported data for identification of products.

3.5.2. Catalytic reduction of 5,10,15,20-tetra-(nitrophenyl)porphyrin (TNPP, I) : Under nitrogen atmosphere, a 5 mL screw-capped vial was charged with compound **I** (1.0 mmol), $PhSiH_3$ (20.0 mmol), catalyst **8** (10 mol %), and toluene (0.4 mL). After being stirred for 15 hours at room temperature, all volatiles were evaporated, and the remaining residue was purified by column chromatography (with a mixture of MeOH/ACN/Acetone/Et_3N) to yield 5,10,15,20-tetra-(aminophenyl)porphyrin (**II**). **Yield: 66 mg (88%)** ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.91 (s, 8H, β - pirrol), 8.00 (d, *J* = 8.2 Hz, 8H), 7.07 (d, *J* = 8.3 Hz, 8H), 4.03 (s, 8H, -Ar-NH_2), -2.70 (s, 2H, NH - pirrol); UV-Vis (THF): ʎ = 430; 526; 565 nm

3.5.3. Catalytic reduction of Cu (II) β-nitroporphyrin (III): Under nitrogen atmosphere, a 5 mL screw-capped vial was charged with compound **II** (1.0 mmol), $PhSiH_3$ (20.0 mmol), catalyst **8** (10 mol %), and toluene (0.4 mL). After being stirred for 15 hours at room temperature, all volatiles were evaporated, and the remaining residue was purified by column chromatography (with a mixture of MeOH/ACN/Acetone/Et_3N) to yield Cu (II) β-aminoporphyrin (**IV**).

3.6. Acknowledgments:

We gratefully aknowledge financial suppot from FCT of Portugal (UID/Multi/04551/2013), grant fellowship SFRH/BD/52372/2013 (RL) and IF consolidation contract IF/00346/2013 (BR).
We thank the Analytical Services at ITQB for elemental analyses, and the UniMS-Mass Spectrometry Unit, ITQB/IBET. The NMR

spectrometers are part of the national NMR facility supported by FCT (RECI/BBB-BQB/0230/2012).

3.7. References

[1] S. P. Downing, *Catalysis Today* **1997**, *37*, 121.

[2] a) A. Corma, *Science* **2006**, *313*, 332; b) H.-U. Blaser, H. Steiner, M. Studer, *ChemCatChem* **2009**, *1*, 210.

[3] a) P. Lara, K.Philippot, *Catal. Sci. Technol.* **2014**, *4*, 2445; b) A. Corma, C. Gonzalez-Arellano, M. Iglesias, F. Sanchez, *Appl. Catal. A: Gen*. **2009**, *356*, 99; c) P. K. Verma, M. Bala, T. Thakur, U. Sharma, N. Kumar, B. Singh, *Catal. Lett.* **2014**, *144*, 1258; (d) D. Damodara, R. Arundhathi, T. V. R. Babu, M. K. Legan, H. J. Kumpaty, P. R. Likhar, *RSC Adv.* **2014**, *4*, 22567; e) S. Park, I. S. Lee, L. Park, *Org. Biomol. Chem.* **2013**, *11*, 395; f) N. Sakai, K. Fuji, S. Nabeshima, R. Ikeda, T. Konakahara, *Chem. Commun*. **2010**, *46*, 3173; g) R. G. Noronha, C. C. Romão, A. C. Fernandes, *J. Org. Chem*. **2009**, *74*, 6960.

[4] a) K. Junge, B. Wendt, N. Shaikh, M. Beller, *Chem. Commun*. **2010**, *46*, 1769; b) L. Pehlivan, E. Métay, S. Laval, W. Dayoub, P. Demonchaux, G. Mignani, M. Lemaire, *Tetrahedron* **2011**, *67*, 1971.

c) L. Pehlivan, E. Métay, S. Laval, W. Dayoub, P. Demonchaux, G. Mignani, M. Lemaire, *Tetrahedron Lett.* **2010**, *51*, 1939; d) E. Pedrajas, I. Sorribes, K. Junge, M. Beller, R. Llusar, *ChemCatChem* **2015**, *7*, 2675; e) D. Rey, N. Mukherjee, S. Ahammed, B. C. Ranu, *Chem. Commun.* **2012***, 48*, 7982; f) G. Wiennhöfer, I. Sorribes, A. Boddien, F. Westerhaus, K. Junge, H. Junge, R. Llusar, M. Beller, *J. Am. Chem. Soc.* **2011**, *133*, 12875; g) P. M. Reis, B. Royo, *Tetrahedron Lett.* **2009**, *50*, 949; h) M. Baron, M. Lemaire, F. Popowycz, *Green Chem.* **2013**, *15*, 1006; i) S. Sun, Z. Quan, X. Wang, *RSC Adv.* **2015**, *5*, 84574.

[5] G. Vijaykumar, S. K. Mandal, *Dalton Trans.* **2016**, *45*, 7421.

[6] a) L. Postigo and B. Royo, *Adv. Synth. Catal.* **2012**, *354*, 2613; b) L. Postigo, R. Lopes, B. Royo, *Dalton Trans* **2014,** *43*, 853.

[7] C. A. Henriques, A. Fernandes, L. M. Rossi, M. F. Ribeiro, M. J. F. Calvete, M. M. Pereira, *Adv. Funct. Mat*. **2016**, *26*, 3359; b) V. I. V. Serra, S. M. G. Pires, C. M. A. Alonso, M. G. P. M. S. Neves, A. C. Tomé, J. A. S. Cavaleiro, *Top Heterocycl. Chem*. **2014**, *33*, 35.

[8] X. L. Xu, F. W. Lin, W. Xu, J. Wu, K. Xu, *Chem. Eur. J*. **2015**, *21*, 984.

[9] H. K. Hombrecher, V. M. Gherdan, S. Ohm, J. A. S. Cavaleiro, M. G. P. M. S. Neves, M. F. Condesso, *Tetrahedron*, **1993**, *49*, 8569.

[15] a) X.-J. Yang, B. Chen, L.-Q. Zheng, L.-Z Wu, C.-H.Tung, *Green Chem*. **2014**, *16*, 1082; b) S. Park, I. S. Lee, J. Park, *Org. Biomol. Chem.* **2013**, *11*, 395; c) R. Dey, N. Mukherjee, S. Ahammed, B. C. Ranu, *Chem. Commun.* **2012**, *48*, 7982; d) R. J. Rahaim, R. E. Maleczka, *J. Org. Lett.* **2015***, 7*, 5087.

CHAPTER 4. DEHYDROGENATIVE SILYLATION OF ALCOHOLS CATALYZED BY HALF-SANDWICH IRON N-HETEROCYCLIC CARBENE COMPLEXES

This chapter has been published in J. M. S. Cardoso, R. Lopes, B. Royo, *J. Organomet. Chem*. **2015**, *775*, 17-22.

4.1. Summary

This chapter describes the synthesis of a new series of tetramethylcyclopentadienyl-functionalised N-heterocyclic carbene complexes of iron bearing different wingtips of general type (Cp*-NHC^{R})Fe(CO)I [R = ^{i}Bu (**14**), ^{n}Bu (**15**), Et (**16**), CH_2CH_2OMe (**17),** CH_2Ph(Bn) (**18**)]. Complexes **14-18** were prepared by direct reaction of $Fe_3(CO)_{12}$ and the corresponding imidazolium proligands. These new iron-NHC complexes have been found to be efficient catalysts for the dehydrogenative silylation of alcohols with silanes. Iron metal complexes bearing *iso*-butyl and *n*-butyl wingtips displayed slightly better catalytic performances than related complexes, affording quantitative yields of the corresponding silylethers in 8 h at 70 °C in acetonitrile.

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4.2. Introduction

In recent years, significant efforts have been devoted to developing catalytic applications of iron N-heterocyclic carbene (NHC) complexes.[1] The low price and high abundance of iron, along with the great popularity of N-heterocyclic carbene ligands in catalysis have motivated the growing interest in this area of research.[2] Notable examples of catalytic applications of Fe-NHCs are C-C bond formation reactions[3], polymerization[4], C-H activation and arene borylation[5], and reduction of functional groups by hydrosilylation and hydrogen transfer processes.[6-12]

Recently, our research group disclosed a simple synthetic pathway for the preparation of iron NHC complexes by direct reaction of the corresponding imidazolium proligands with commercially available $Fe_3(CO)_{12}$.This procedure allowed us to prepare Fe-NHC complexes bearing monodentate NHCs[9] and cyclopentadienyl-functionalised NHC ligands, Cp-NHC (Cp = η^5-C_5H_4, η^5-C_5Me_4) in high yield.[7] This advance precludes the requirement for the strong bases traditionally employed in the synthesis of similar complexes.[4d,13,14]

In this work, we extended our studies to the preparation of a new series of iron pentamethylcyclopentadienyl-functionalized NHCs containing different substituents in the wingtip (R) of the imidazolium ring (Figure 4.1). As part of our ongoing research into the development of new catalytic applications of first-row transition metal-NHC complexes with silanes[6-9,15,16], we decided to explore the activity of the iron complexes containing the fragment "(Cp*-NHC^R)Fe" in the dehydrogenative silylation of alcohols.

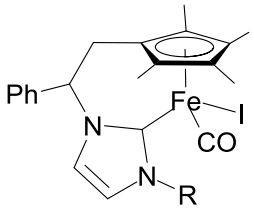


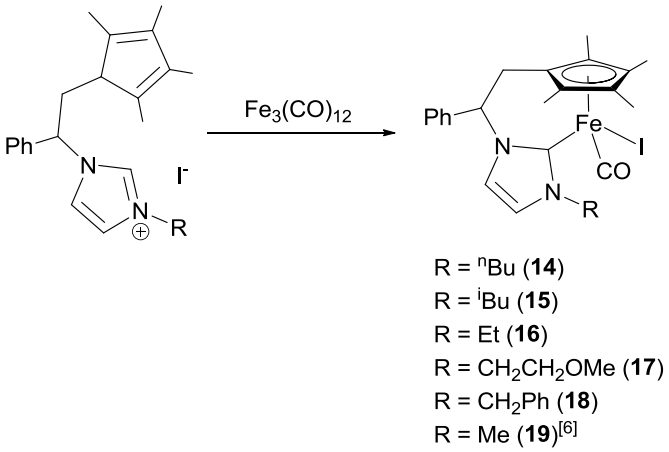
Figure 4.1. Iron complexes bearing functionalized-cyclopentadienyl N-heterocyclic carbene ligands.

4.3. Results and Discussion

Compounds **14**-**18** were prepared by an extension of a method recently reported in our research group.[10] Direct reaction of the iron cluster $Fe_3(CO)_{12}$ with the appropriate proligand (Cp*-NHC^R)I (R = ^{n}Bu, ^{i}Bu, Et, CH_2CH_2OMe, CH_2Ph) in refluxing toluene afforded complexes **14**-**18** in high yield (Scheme 4.1). Complexes **14**-**18** were isolated as air stable green crystalline solids. The identity of all compounds was established by analytical and spectroscopic methods. The successful metalation is confirmed by the appearance of the characteristic carbene signal at 195 ppm (for complexes **14**-**17**) and 197 ppm (for **18**) in ^{13}C NMR, which is the region of previously reported half-sandwich Fe-NHC complexes.[7g,6,12,21] The length of the alkyl substituents of the wingtip has not detectable impact on the Fe-$C_{carbene}$ resonance frequency. Introduction of a benzyl group at the wingtip decreases the upfield shift by 2 ppm. The formation of the new complexes is further verified by the carbonyl signal at 227 ppm and by the four resonances for the methyl groups of the cyclopentadienyl in ^{13}C NMR.

The infrared spectra of **14**-**18** display the expected strong carbonyl band in the region 1905-1902 cm^{-1}. The similar stretching band frequency for all complexes **14**-**18** is indicative of similar donor

capacity of the imidazolium ring which is not influenced by the wingtip substituents.

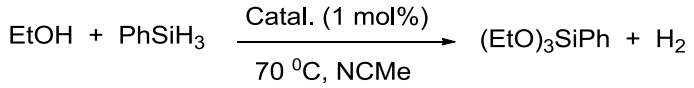


R = ^{n}Bu (**14**)
R = ^{i}Bu (**15**)
R = Et (**16**)
R = CH_2CH_2OMe (**17**)
R = CH_2Ph (**18**)
R = Me (**19**)[6]

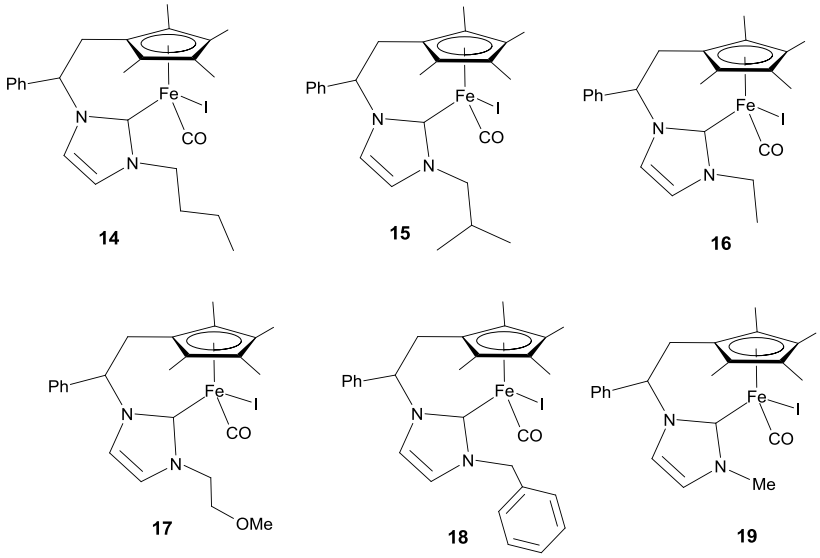
Scheme 4.1. Synthesis of iron complexes **14-18**.

With these complexes in our hands, we decided to explore their catalytic activity in the dehydrogenative silylation of alcohols. Silylether formation is a fundamental process in the synthesis of functional organosilicon compounds and polymer chemistry.[22] Moreover, silylethers are widely used as protecting groups for the hydroxyl functionality in organic synthesis.[23] The catalytic dehydrogenative silylation of alcohols is a very convenient method for the preparation of silylethers from an atom economy point of view, being H_2 the only by-product formed in the coupling reaction. Metal-catalysed dehydrogenative coupling of silanes with alcohols have been described in the literature.[24] However, to the best of our knowledge, iron-NHC complexes have not been successfully employed in this coupling reaction. Dehydrogenative coupling of thiols with hydrosilanes catalyzed by CpFe(CO)Me was recently disclosed by Nakazawa.[25]

The half-sandwich iron-NHC complexes **14**-**19** (Scheme 4.3) were applied as catalysts for the dehydrogenative silylation of alcohols. Their catalytic activity was initially explored using ethanol and $PhSiH_3$ as model substrates. The reaction was carried out in acetonitrile at 70 °C in the presence of 1 mol% of catalyst (Scheme 4.2). All complexes **14**-**19** were active catalysts in the dehydrogenative silylation of ethanol with $PhSiH_3$, affording high yields (91-99%) of triethoxyphenylsilane in 16 h (Table 4.1). Complexes **14** and **15**, bearing the ^{n}Bu and ^{i}Bu wingtips respectively, displayed the highest activities affording quantitative yields of the silylether in 8 h (Table 4.1, entries 1 and 2, respectively), while longer reaction times (12-16 h) were needed for complexes **16**-**19** to afford similar yields (Table 4.1, entries 3-6). No coupling was observed when the reaction was performed at room temperature. For all catalysts, the reaction was selective to the formation of triethoxyphenylsilane, and no other coupling products were formed in the reaction. It seems that variation of the wingtip substituents at R (Figure 4.1) has some impact on the catalytic performance.



Scheme 4.2. Catalytic dehydrogenative silylation of ethanol with phenylsilane.



Scheme 4.3. Iron complexes applied in the catalytic dehydrogenative silylation of ethanol with phenylsilane.

Table 4.1. Dehydrogenative silylation of alcohol with silanes using iron complexes **14**-**19** as catalysts.[a]

Entry	Catalyst	Silane	Alcohol	Product	Time	Yield[b] (%)
1	**14**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	8	99 (92)
2	**15**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	8	91 (87)
3	**16**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	12	99 (93)
4	**17**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	16	95 (87)
5	**18**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	12	99 (91)
6	**19**	$PhSiH_3$	EtOH	$PhSi(OEt)_3$	16	96 (87)
7	**14**	Ph_2SiH_2	EtOH	$Ph_2Si(OEt)_2$	8	82 (77)
8	**14**	$PhMe_2SiH$	EtOH	-	8	0
9	**14**	Ph_3SiH	EtOH	-	8	0

10	**14**	$(EtO)_3SiH$	EtOH	$Si(OEt)_4$	8	98 (91)
11	**14**	$PhSiH_3$	^{i}PrOH	$PhSi(O^{i}Pr)_3$	8	66 (62)
12	**14**	$PhSiH_3$	$Bu^{t}CH(Me)OH$	$PhSiH[OCH(Me)Bu^{t}]_2$	16	69 (60)
13	**14**	$PhSiH_3$	PhCH(Me)OH	$PhSiH[OCH(Me)Ph]_2$	16	71 (65)

[a]Reaction conditions: alcohol (3 mmol), silane (1 mmol), catalyst (1 mol%) in NCMe at 70 °C. [b]Yield determined by ^{1}H NMR spectroscopy using Ph_2CH_2 as internal standard. Isolated yields in parentheses.

We investigated the scope of the dehydrogenative silylation of alcohols, using catalyst **14**, EtOH and different silanes. In each case, reactions were performed under optimized conditions heating at 70 °C in NCMe. As shown in Table 1, phenylsilane, diphenylsilane, and triethoxysilane were all very efficient substrates when reacted with ethanol, giving high yields (85-99%) of the corresponding silylethers in 8 hours (Table 4.1, entries 1, 7, and 10, respectively). In all cases, the reaction led to conversion of all Si-H groups to tetra-, tri-, and bis-alkoxyl silanes. The coupling reaction did not occur when dimethylphenylsilane and triphenylsilane were used as substrates in their reaction with ethanol (Table 4.1, entries 8 and 9, respectively). The dehydrogenative silylation of bulkier alcohols such as 2-propanol, 1-phenylethanol, and 3,3-dimethyl-butan-2-ol in the presence of catalyst **14**, and under similar reaction conditions afforded the corresponding tri(alkoxy)silane and bis(alkoxy)silanes, respectively in moderate yield (Table 4.1, entries 11-13).

4.4. Conclusions

A series of new (Cp*-NHC^{R})Fe(CO)I complexes bearing different wingtips have been prepared and fully characterized. We have demonstrated that these half-sandwich iron-NHC complexes are efficient catalysts for the dehydrogenative coupling of alcohols with silanes. Better catalytic performances were exhibited by the iron complexes bearing *iso*-butyl and n-butyl wingtips, indicating that smooth modifications on metal complexes have consequences in their catalytic activity. This is the first report of well-defined iron(II) complexes catalyzing the coupling of alcohols with hydrosilanes.

4.5. Experimental Procedures

The corresponding proligands (Cp*-NHC^{R})I (R = ^{i}Bu (**2**), ^{n}Bu (**3**), Et (**4**), CH_2Ph (**6**), were prepared according to the method reported by our research group[16,17] and described in Chapter 2. All other reagents were used as received from the commercial suppliers without further purification. All manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques, and solvents were purified from appropriate drying agents. Deuterated solvents were degassed and stored over molecular sieves. NMR spectra were recorded using a Bruker Avance III 400 MHz. Elemental analyses and Electrospray mass spectra were performed in our laboratories at ITQB. Infrared (IR) spectra was recorded on samples as KBr pellets using a Bruker IFS 66/S ATR-FTIR spectrometer.

4.5.1. <u>Preparation of compound 13:</u> 1-Bromo-2-methoxyethane (0.80 mL, 8.5 mmol), and NaI (1.26 g, 8.5 mmol) were added to a solution of Cp*-NHC (**1**) (500 mg, 1.7 mmol) in 10 mL of acetone. The mixture was stirred at room temperature for 4 days. Then all volatiles were

removed under vacuum to afford a yellow solid, which was washed several times with diethyl ether and hexane to yield the compound **13** as a yellow solid. Yield: 714 mg (89%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.40, 10.33, 10.31, 10.00, 9.98, 9.92 (s, N=C*H*-*N*), 7.59-6.95 (m, C*H*$_{Phenyl}$, C*H*$_{Imid}$), 5.69-5.26 (m, CH_{linker}), 4.64-4.50 (m, NCH_2), 3.81-3.70 (m, CH_{2OMe}) 3.39-3.33 (OCH_3), 3.27-3.03 (m, $CH_{2linker}$), 2.78-2.33 (m, CH_{Cp^*}), 1.80-1.35 (CH_{3Cp^*}), 1.07-0.84 (CH_{3Cp^*}). ^{13}C {1H} NMR (100 MHz, $CDCl_3$): δ 140.33 (N=*C*H-N), 136.47-119.54 (C_{Phenyl}, C_{Imid}), 70.35-64.29 (CH_{linker}), 59.05 (CH_{Cp^*}), 53.85-49.11 (NCH_2, CH_{2OMe}), 31.94-29.71 ($CH_{2linker}$), 14.67-10.90 (OCH_3, CH_{3Cp^*}). MS (ESI-TOF) *m/z* for $[C_{23}H_{31}N_2OI\text{- }I]^+$ 351.24; found, 350.98.

4.5.2. General preparation of complexes 14-18

A mixture of the appropriate proligand (Cp*-NHC^{R})I [R = ^{i}Bu (**2**), ^{n}Bu (**3**), Et (**4**), CH_2Ph (**6**), CH_2CH_2OMe (**13**)], (1.38 mmol) and $Fe_3(CO)_{12}$ (0.46 mmol) was refluxed in toluene (15 mL) overnight. Filtration and removal of toluene under vacuum gave a green solid, which was washed with hexane to afford the corresponding iron complexes **14**-**18**.

Characterization of (Cp*-NHC^{nBu})Fe(CO)I (**14**)

Yield of **14:** 86%. ^{1}H NMR (400 MHz, acetone-d_6): δ 7.63-7.52 (m, 5 H, C*H*$_{Ph}$), 7.11 (s, 1 H, C*H*$_{Imid}$), 6.47 (s, 1 H, C*H*$_{Imid}$), 6.06 (d, *J* = 12 Hz, 1 H, C*H*Ph$_{linker}$), 4.21-4.19 (m, 1 H, C*H*$_{linker}$), 4.27 (q, NC*H*$_{2Bu}$), 3.11-3.05 (m, C*H*$_{2Bu}$), 2.50 (s, 3 H, C*H*$_{3Cp^*}$), 2.15 (s, 3 H, C*H*$_{3Cp^*}$), 1.90 (s, 3 H, C*H*$_{3Cp^*}$), 1.49 (t, 3 H, C*H*$_3$*Bu*), 1.04 (s, 3 H, C*H*$_{3Cp^*}$). ^{13}C {1H} NMR (100 MHz, acetone-d_6): δ 226.8 (CO), 194.9 ($C_{carbene\text{-}Fe}$), 138.8 ($C_{ipso\text{-}phenyl}$), 130.0 (CH_{phenyl}), 129.9 (CH_{phenyl}), 123.0 (CH_{Imid}), 121.0 (CH_{Imid}), 104.7 (C_{Cp^*}), 91.6 (C_{Cp^*}), 90.3 (C_{Cp^*}), 84.2 (C_{Cp^*}), 81.0 (C_{Cp^*}), 67.0 ($CH_{Ph\text{-}linker}$), 51.1 (NCH_2), 34.0 (CH_{2nBu}), 29.8 ($CH_{2linker}$), 20.4 (CH_{2nBu}), 14.0 (CH_{3nBu}) 13.4 (CH_{3Cp^*}), 10.4 (CH_{3Cp^*}), 9.6 (CH_{3Cp^*}), 9.5 (CH_{3Cp^*}). Selected IR

data (KBr): ν(CO) 1905 vs cm^{-1}. Anal. Calcd. for $C_{25}H_{31}N_2OFeI$ (558.08): C, 53.78; H, 5.60; N, 5.02. Found: C, 53.50; H, 5.86; N. 5.23.

Characterization of (Cp*-NHC^{iBu})Fe(CO)I (**15**)

Yield of **15**: 84%. ^1H NMR (400 MHz, acetone-d_6): δ 7.64-7.54 (m, 5H, CH_{Ph}), 7.06 (s, 1 H, CH_{Imid}), 6.48 (s, 1H, CH_{Imid}), 6.08 (d, *J* = 12 Hz, 1H, CHPh$_{linker}$), 3.97 (d, J = 8 Hz, 2H, NCH_2); 3.02-2.97 (m, 2H, $CH_{2linker}$), 2.39 (s, 3H, CH_{3Cp*}), 2.27-2.19 (m, 1H, CH_{iBu}, 1.80 (s, 3H, CH_{3Cp*}), 1.75 (s, 3H, CH_{3Cp*}), 0.95 (s, 3H, CH_{3Cp*}), 0.94 (t, *J* = 8, 3H, CH_{3nBu}). $^{13}C\{^1H\}$ NMR (100 MHz, acetone-d_6): δ 226.8 (CO), 195.2 (Fe-$C_{carbene}$), 138.8 (C_{ipsoPh}), 130.8 (CH_{Ph}), 129.9 (CH_{Ph}), 128.8 (CH_{Ph}), 128.3 (CH_{Ph}), 127.6 (CH_{Ph}), 124.0 (CH_{Imid}), 121.7 (CH_{Imid}), 104.7 (C_{Cp*}), 91.6 (C_{Cp*}), 90.4 (C_{Cp*}), 84.3 (C_{Cp*}), 81.0 (C_{Cp*}), 67.1 (CH_{linker}), 58.3 (NCH_{2Bu}), 29.8 (CH_{iBu}), 29.1 ($CH_{2linker}$), 20.0 (CH_{3iBu}), 19.8 (CH_{3iBu}), 13.4 (CH_{3Cp*}), 10.4 (CH_{3Cp*}), 9.6 (CH_{3Cp*}), 9.5 (CH_{3Cp*}). Anal. Calc. for $C_{25}H_{31}N_2OFeI$ (558.26): C, 53.78; H, 5.60; N, 5.02. Found: C, 53.40; H, 5.50; N, 4.87. Selected IR data (KBr): ν(CO) 1905 vs cm^{-1}. MS (ESI-TOF) m/z for $[C_{25}H_{31}N_2OFeI\text{-}I]^+$ calcd for $C_{25}H_{31}N_2OFeI$, 431.17; found 430.96.

Characterization of (Cp*-NHC^{Et})Fe(CO)I (**16**)

Yield of **16**: 81%. ^1H NMR (400 MHz, acetone-d_6): δ 7.63-7.53 (m, 5H, CH_{Ph}), 7.13 (s, 1H, CH_{Imid}), 6.48 (s, 1H, CH_{Imid}), 6.06 (d, *J* = 12 Hz, 1H, CH_{linker}), 4.35-4.23 (m, 2H, CH_{2Et}), 3.05-2.92 (m, 2H, C$H_{2linker}$), 2.40 (s, 3H, CH_{3Cp*}), 1.81 (s, 3H, CH_{3Cp*}), 1.76 (s, 3H, CH_{3Cp*}), 1.35 (t, *J* = 8 Hz, 3H, CH_{3Et}), 0.96 (s, 3H, CH_{3Cp*}). $^{13}C\{^1H\}$ NMR (100 MHz, acetone-d_6): δ 226.8 (CO), 194.8 (Fe-$C_{carbene}$), 138.8 (C_{iPh}), 130.1 (CH_{Ph}), 130.0 (CH_{Ph}), 129.9 (CH_{Ph}), 122.3 (CH_{Imid}), 121.3 (CH_{Imid}), 104.7 (C_{Cp*}), 91.7 (C_{Cp*}), 90.4 (C_{Cp*}), 84.1 (C_{Cp*}), 81.3 (C_{Cp*}), 67.1 (CH_{linker}), 46.1 (NCH_{2Et}), 28.9 ($CH_{2linker}$), 16.9 (CH_{3Et}), 13.4 (CH_{3Cp*}), 10.4 (CH_{3Cp*}), 9.7 (CH_{3Cp*}), 9.5 (CH_{3Cp*}). Anal. Calc. for $C_{23}H_{27}N_2OFeI$ (530.05): C, 52.10; H, 5.13;

N, 5.28. Found: C; 52.30 H, 5.29; N, 4.91. Selected IR data (KBr): ν(CO) 1904 vs cm^{-1}. MS (ESI-TOF) m/z for $[C_{23}H_{27}N_2OFeI\text{-}I\text{-}CO]^+$ 375.15; found 375.09.

Characterization of (Cp*-NHC^{CH2CH2OMe})Fe(CO)I (**17**)

Yield of **17**: 76%. ^{1}H-NMR (400 MHz, acetone-d_6): δ 7.64-7.56 (m, 5H, Ph), 7.05 (s, 1H, CH_{Imid}), 6.45 (s, 1H, CH_{Imid}), 6.05 (d, *J* = 12, 1H, C$H_{Ph\text{-}linker}$), 4.48-4.29 (m, 2H, NCH_2), 3.69-3.67 (m, 2H, CH_{2OMe}), 3.25 (s, 3H, OCH_3), 3.02-2.97 (m, 2H, C$H_{2linker}$), 2.40 (s, 3H, CH_{3Cp*}), 1.81 (s, 3H, CH_{3Cp*}), 1.75 (s, 3H, CH_{3Cp*}), 0.97 (s, 3H, CH_{3Cp*}). ^{13}C {1H} NMR (100 MHz, acetone-d_6): δ 227.0 (*C*O), 195.3 ($C_{carbene\text{-}Fe}$), 138.9 ($C_{ipso\text{-}phenyl}$), 130.3 (*C*H$_{phenyl}$), 127.2 (*C*H$_{phenyl}$), 129.0 (*C*H$_{phenyl}$), 127.7 (*C*H$_{phenyl}$), 127.2 (*C*H$_{phenyl}$), 124.3 (*C*H$_{Imid}$), 120.9 (*C*H$_{Imid}$), 104.9 (C_{Cp*}), 92.0 (C_{Cp*}), 90.7 (C_{Cp*}), 84.3 (C_{Cp*}), 81.5 (C_{Cp*}), 72.7 (*C*H$_{2OMe}$), 67.3 (*C*H$_{Ph\text{-}linker}$), 58.9 (O*C*H$_3$), 51.2 (N*C*H$_2$), 29.40 (*C*H$_{2linker}$), 13.5 (*C*H$_{3Cp*}$), 10.5 (*C*H$_{3Cp*}$), 9.8 (*C*H$_{3Cp*}$), 9.6 (*C*H$_{3Cp*}$). Anal. Calc. for $C_{24}H_{29}N_2O_2FeI$ (560.06): C: 51.45, H: 5.22, N: 5.00; found, C: 51.20, H: 5.31, N: 4.97. Selected IR data (KBr): *v*(CO) 1902 vs cm^{-1}. MS (ESI-TOF) *m/z* for $[C_{24}H_{29}N_2O_2FeI - I]^+$ 433.16; found, 432.89.

Characterization of (Cp*-NHC^{CH2Ph})Fe(CO)I (**18**)

Yield of **18**: 74%. ^{1}H NMR (400 MHz, acetone-d_6): δ 7.65-7.51 (m, 5H, CH_{Ph}), 7.37-7.27 (m, 5H, CH_{CH2Ph}), 7.06 (s, 1 H, CH_{Imid}), 6.54 (s, 1H, CH_{Imid}), 6.17 (d, *J* = 1 2 Hz, 1H, CH_{linker}), 5.51 (dd, *J* = 14 Hz, 2H, NCH_2), 3.07-2.93 (m, 2 H, C$H_{2linker}$), 2.42 (s, 3H, CH_{3Cp*}), 1.76 (s, 3H, CH_{3Cp*}), 1.71 (s, 3H, CH_{3Cp*}), 0.86 (s, 3H, CH_{3Cp*}). ^{13}C{^{1}H} NMR (100 MHz, acetone-d_6): δ 226.6 (*C*O), 197.1 (Fe-$C_{carbene}$), 138.9 (C_{iPh}), 130.2 (*C*H$_{Ph}$), 130.0 (*C*H$_{Ph}$), 129.3 (*C*H$_{Ph}$), 129.0 (*C*H$_{Ph}$), 128.4 (*C*H$_{Ph}$), 122.9 (*C*H$_{Imid}$), 122.1 (*C*H$_{Imid}$), 104.8 (C_{Cp*}), 91.7 (C_{Cp*}), 90.1 (C_{Cp*}), 84.8 (C_{Cp*}), 81.7 (C_{Cp*}), 69.2 (*C*H$_{linker}$), 54.4 (N*C*H$_2$Ph), 28.9 (*C*H$_{2linker}$), 13.5 (*C*H$_{3Cp*}$), 10.4 (*C*H$_{3Cp*}$), 9.7 (*C*H$_{3Cp*}$), 9.6 (*C*H$_{3Cp*}$). Anal. Calc. for

$C_{28}H_{29}N_2OFeI$ (592.06): C, 56.78; H, 4.94; N, 4.74. Found: C, 56.47; H, 5.08; N, 4.52. Selected IR data (KBr): ν(CO) 1904 vs cm^{-1}. MS (ESI-TOF): m/z for $[C_{28}H_{29}N_2OFeI\text{-}I]^+$ 465.16; found 464.91.

4.5.3. Catalytic dehydrogenative silylation of alcohols

Acetonitrile (1 mL), (Cp*-NHC^R)Fe(CO)I (1 mol %), alcohol (3 mmol), silane (1 mmol) were charged in a vial. The vial was tightly closed under nitrogen, and the solution was heated at 70 °C for 8-16 h depending on the silane and the alcohol. All volatiles were evaporated under vacuum, the residue was dissolved in $CDCl_3$, and Ph_2CH_2 (1 mmol) was added to the mixture as an internal standard. The ^1H NMR was measured at room temperature and the amount of the corresponding silylether produced was evaluated by the relative intensity of the signals of the product and internal standard. Isolation of the silylethers was carried out by removing all the volatiles under vacuum. The residue was diluted with hexanes (ca. 2 mL), loaded directly on to a silica gel column and chromatographed with the appropriate mixture of hexanes and acetone to give the corresponding silylethers. The silylethers produced were identified by comparison of the NMR data with the reported data: $PhSi(OEt)_3$, $PhSi(O^iPr)_3$[18], $Ph_2Si(OEt)_2$[19], $PhSiH[OCH(Me)Ph]_2$[20]. The obtained silylether $Si(OEt_3)_4$ was compared with an authenticate sample (commercially available).

4.6. Acknowledgements

We gratefully acknowledge financial support from FCT Portugal, POCI 2010 and FEDER through projects PTDC/QUI-QUI/110349/2009 and PTDC/QEQ-QIN/0565/2012. We thank FCT for REDE/157/RMN/2005.

We wish to acknowledge M. C. Almeida for providing data from the Elemental Analyses and Mass Spectrometry Services at ITQB.
The work described in this chapter was developed in collaboration with João Cardoso, who performed the catalytic essays.

4.7. References

[1] D. Bézier, J.-B. Sortais, C. Darcel*, Adv. Synth. Catal.* **2013**, *355*, 19.
[2] M. J. Ingleson, R. A. Layfield, *Chem. Commun*. **2012**, *48*, 3579.
[3] (a) H.-H. Gao, C.-H. Yan, X.-P. Tao, Y. Xia, H.-M. Sun, Q. Shen, Y. Zhang, *Organometallics* **2010**, *29*, 4189; (b) S. Meyer, C. M. Orben, S. Demeshko, S. Dechert, F. Meyer, *Organometallics* **2011**, *30*, 6692; (c) J. Wu, W. Dai, J. H. Farnaby, N. Hazari, J. J. Le Roy, V. Mereacre, M. Murugesu, A.K. Powell, M.K. Takase, *Dalton Trans.* **2013**, *42*, 7404.
[4] (a) J. Louie, R. H. Grubbs, *Chem. Commun.* **2000**, 1479; (b) D. S. McGuinness, V. C. Gibson, J. W. Steed, *Organometallics* **2004**, *23*, 6288; (c) M. -Z. Chen, H. -M. Sun, W. -F. Li, Z. -G. Wang, Q. Shen,Y. Zhang J *Organomet Chem* **2006**, *69*, 12489; (d) V. Lavallo, R. H. Grubbs, *Science* **2009**, *326,* 559; (e) L. Xiang, J. Xiao, L. Deng, *Organometallics* **2011**, *30*, 2018; (f) H. Gao, C. Yan, X. Tao, Y. Xia, H. Sun, Q. Shen, Y. Zhang, *Organometallics* **2010**, *29*, 4189.
[5] (a) Y. Ohki, T. Hatanaka , K. Tatsumi, *J. Am. Chem. Soc.* **2008**, *130*, 17174; (b) T. Hatanaka, Y. Ohki, K. Tatsumi, *Chem. Asian J.* **2010**, *5*, 1657.
[6] V. V. K. M. Kandepi, J. M. S. Cardoso, E. Peris, B. Royo, *Organometallics* **2010**, *29*, 2777.
[7] J. M. S. Cardoso, B. Royo, *Chem. Commun.* **2012**, *48*, 4944.
[8] R. Lopes, J. M. S. Cardoso, L. Postigo, B. Royo, *Catal. Lett.* **2013**, *14*, 31061.
[9] S. Warratz, L. Postigo, B. Royo, *Organometallics* **2013**, *32*, 893.

[10] (a) V. César, L.C.M. Castro, T. Dombray, J. -B. Sortais, C. Darcel, S. Labat, K. Miqueu, J. -M. Sotiropoulos, R. Brousses, N. Lugan, G. Lavigne, *Organometallics* **2013**, *32*, 4643; (b) H. Li, L. C. M. Castro, J. Zheng, T. Roisnel, V. Dorcet, J. -B. Sortais, C. Darcel, *Angew. Chem. Int. Ed.* **2013**, *52*, 1; (c) L. C. M. Castro, D. Bézier, J, -B Sortais, C Darcel, *Adv. Synth. Catal.* **2011**, *353*, 1279; (d) D. Bézier, F. Jiang, T. Roisnel, J. -B. Sortais, C. Darcel, *Eur. J. Inorg. Chem.* **2012**, 1333; (e) D. Bézie, G. T. Venkanna, L.C.M. Castro, J. Zhen, T. Roisnel, J. -B Sortais, Darcel C, *Adv. Synth. Catal.* **2012**, *354*, 1879; (f) L. C. M. Castro, J. -B. Sortais, C. Darcel, *Chem Commun* **2012**, *48*, 151; (g) D. Bézier, G. T. Venkanna, J. -B. Sortais, C. Darcel, *ChemCatChem* **2011**, *3*, 1747; (h) S. Demir, Y. Gökçe, N. Kaloğlu, J. -B. Sortais, C. Darcel, Í. Özdemir, *Appl. Organomet. Chem.* **2013**, *27*, 459; (i) B. Blom, G. Tan, S. Enthaler, S. Inoue, J.D. Epping, M. Driess, *J. Am. Chem. Soc.* **2013**, *135*, 18108.

[11] (a) C. Grohmann, T. Hashimoto, R. Frohlich, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 8047; (b) T. Hashimoto, S. Urban, R. Hoshino, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 4474.

[12] (a) E. Buitrago, L. Zani, H. Adolfsson, *Appl. Organomet. Chem.* **2011**, *25*, 748; (b) E. Buitrago , F. Tinnis , H. Adolfsson, *Adv. Synth. Catal.* **2012**, *354*, 217.

[13] P. Buchgraber, L. Toupet, V. Guerchais, *Organometallics* **2003**, *22*, 5144.

[14] Selected references: (a) D. S. McGuinness, V. C. Gibson, J. W. Steed, *Organometallics* **2004**, *23*, 6288; (b) J. A. Przyojski, H. D. Arman, Z. J. Tonzetich, *Organometallics* **2012**, *31*, 3264; (c) S. A. Cramer, D. M. Jenkins, *J. Am. Chem. Soc.* **2011**, *133*, 19342.

[15] (a) L. Postigo, B. Royo, *Adv. Synth. Catal.* **2012**, *354*, 2613. (b) L. P Bheeter, M. Henrion, L. Brelot, C. Darcel, M. J. Chetcuti, J. -B. Sortais, V. Ritleng, *Adv. Synth. Catal*. **2012,** *354*, 2619.

[16] L. Postigo, R. Lopes, B. Royo, *Dalton Trans.* **2014**, *43*, 853.

[17] A.P da Costa, M. Viciano, M. Sanaú, S. Merino, J. Tejeda, E. Peris B. Royo, *Organometallics* **2008**, *27*, 1305.

[18] W. Sattler, G. Parkin *J. Am. Chem. Soc*. **2012**, 134, 17462.

[19] J. Y. Corey, C. S. John, M. C. Ohmsted, L. H. S. Chang, *J. Organomet. Chem.* **1986**, *304*, 93.

[20] A. Y. Khalimon, S. K. Ignatov, R. Simionescu, L. G. Kuzmina, J. A. K. Howard, G. I Nikonov, *Inorg. Chem.* **2012**, *51*, 754.

[21] L. Mercs, G. Labat, A. Neels, A. Ehlers, M. Albrecht, *Organometallics* **2006**, *25*, 5648.

[22] G. W. Parshall, S. D. Itell, Homogeneous Catalysts: The Applications and Chemistry by Soluble Transition Metal Complexes, Wiley, New York, **1992**.

[23] P. J. Kocienski, Protecting Groups, Springer, Stuttgart, **1994**.

[24] For recent references, see: (a) A. Krüger, M. Albrecht, *Chem. Eur. J.* **2012**, *18*, 652;(b) D. Mukherjee, R. R. Thompson, A. Elern, A. D. Sadow, *ACS Catal.* **2011**, *1*, 698; (c) A. Weickgenannt, M. Mewald, T.W.T. Muesmann, M. Oestreich, Angew. *Chem. Int. Ed.* **2010**, *49*, 2223; (c) R. A. Corbin, E. A. Ison, M. M. Abu-Omar, *Dalton Trans.* **2009**, 2850; (c) H. Ito, A. Watanabe, M. Sawamura, *Org. Lett*. **2005**, *7*, 1869; (c) P. M. Reis, B. Royo, *Catal. Commun.* **2007**, *8*, 1057; (f) D. Gao, C. Cui, *Chem. Eur. J.* **2013**, *19*, 11143; (g) C. K. Toh, H. T. Poh, C. S. Lim, W. Y. Fan, *J. Organomet. Chem.* **2012**, *717*, 9.

[25] K. Fukumoto, M. Kasa, T. Oya, M. Itazaki, H. Nakazawa, *Organometallics* **2011**, *30*, 3461.

CHAPTER 5. TRANSFER HYDROGENATION OF KETONES CATALYZED BY HALF-SANDWICH IRON N-HETEROCYCLIC CARBENE COMPLEXES

5.1. Summary

This chapter describes the synthesis of a new series of tetramethylcyclopentadienyl-functionalized N-heterocyclic carbene complexes of iron bearing different wingtips of general type (Cp*-NHC^R)Fe(CO)I [R = $(CH_2)_2OH$ (**24**), $(CH_2)_3OH$ (**25**), CH_2CONEt_2 (**26**), $CH_2CH_2NEt_2$ (**27**)] prepared by direct reaction of $Fe_3(CO)_{12}$ with the corresponding imidazolium proligands **20**-**23**. The new iron-NHC complexes **24**-**27** have been found to be efficient catalysts for the transfer hydrogenation of ketones. Complex **26**, bearing the acetamide group on the wingtip displayed the best catalytic performance. Interestingly, a highly efficient catalytic system was developed using glycerol as a hydrogen source and microwave heating with **26**. Quantitative conversions of the corresponding alcohols were obtained in 15 min by using 0.5 mol % of **26** in the presence of catalytic amounts of base (KOH). Notable, under those conditions our catalytic system allowed the synthesis of several bioactive alcohols in high yields.

All compounds were fully characterized by analytical and spectroscopic methods. Crystals suitable for X-ray diffraction studies were obtained for iron complex **26**. Complexes **14**, **19** and **25**-**27** have been studied by electrochemical methods.

5.2. Introduction

In this chapter we report a new class of Cp*-NHC iron complexes outfitted with pendant arms containing hydroxyl, acetamide and amine groups. We demonstrate, through IR spectroscopy and cyclic voltammetry experiments, that the introduction of some of these functionalities have a measurable effect on the electronic situation of the metal center.[1,4-7] This work was inspired by the recent publication reported by Chmley and co-workers describing the synthesis of piano-stool iron complexes bearing NHC ligands with hydroxyl pendant arms and their application in transfer hydrogenation of benzaldehyde and acetophenone.[1] It was expected that the presence of hydroxyl in the NHC wingtips could assist in proton transfer from 2–propanol via an outer sphere mechanism. Surprisingly, these complexes resulted completely inactive towards the reduction of carbonyl groups. These results contrast with bifunctional Ir-NHC complexes reported in the literature[2] in which the introduction of hydroxyl groups has a positive effect in the catalytic performance of the catalyst. Chmely and co-workers explained the inactivity of the piano-stool iron complexes [CpFe(NHC)$(CO)_2$I], as a result of the coordinative saturation around iron. Related iron complexes have been described by Darcel and Sortais as effective catalysts in transfer hydrogenation under visible light, which allows *in situ* formation of the active catalytic species [CpFe(NHC)(CO)I] by liberation of a CO ligand. However, the iron complexes reported by Chmely suffered decomposition under light irradiation conditions, which could explain the lack of reactivity.

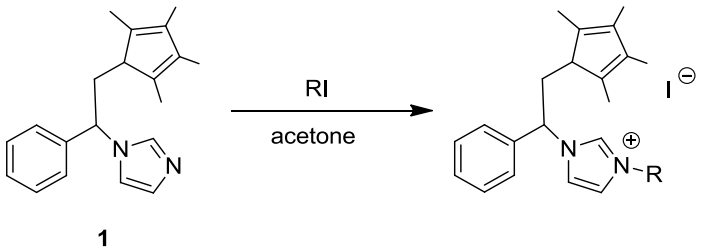
Intrigued by these results, we decided to prepare a series of Cp*-NHC iron complexes outfitted with pendant arms containing hydroxyl, acetamide and amine pendant arms, and explore their catalytic activity in the reduction of ketones. The advantage of our functionalized Cp-NHC ligands is that their metal complexes [(Cp-NHC)FeCOI] are

conveniently accessible through direct reaction of the imidazolium proligands with $Fe_3(CO)_{12}$ without need of light irradiation.

5.3. Results and Discussion

5.3.1. Synthesis of proligands 20-23

The proligands **20-23** were synthesized according to a method previously described by us (Scheme 5.1).[8] Alkylation of **1** with the appropriate alkyl halide, RI, [R = $(CH_2)_2OH$, $(CH_2)_3OH$, CH_2CONEt_2 and $CH_2CH_2NEt_2$] in acetone at 25 ºC, affords the corresponding imidazolium proligands **20**-**23,** which were isolated as yellow solids with moderate to good yields 63-85%. All the proligands were fully characterized by analytical and spectroscopic methods.



1

R = $(CH_2)_2OH$ (**20**)
R = $(CH_2)_3OH$ (**21**)
R = CH_2CONEt_2 (**22**)
R = $CH_2CH_2NEt_2$ **(23)**

Scheme 5.1. Synthesis of pro-ligands **20-23**.

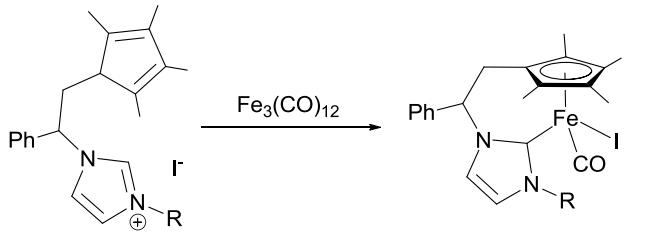
Compounds **20**-**23** were obtained as a mixture of tautomers resulting from the different position of the double bonds on the cyclopentadiene ring. Alkylation of **1** with the respective alkyl halides is corroborated by the appearance in the ^{1}H-NMR of the typical resonances at 11-9 ppm for the imidazolium proton. In addition, the ^{1}H NMR of **20** showed two

triplets at 4.42-4.40 (t, N-CH_2) ppm, and 3.91-3.81 (t, CH_2) ppm, corresponding to the methylene groups (CH_2) from the *N*-alkyl substituent, and compound **21** showed the characteristic resonances at 4.55-4.44 (t, N-CH_2) ppm, 3.62-3.18 (t, CH_2) ppm, 2.11-2.03 (q, CH_2) ppm from the *N*-alkyl chain.

Compound **22**, displayed the expected resonances for the acetamide group: a triplet at 5.24 (t, N-CH_2) ppm, a quintuplet resonance at 3.43-3.39 (q, CH_2) ppm, and a triplet at 1.24-1.06 (t, CH_3) ppm. Its ^{13}C NMR of **22**, showed a resonance for the CO of the group acetamide at 163.27 ppm. Compound **23,** showed in its ^{1}H-NMR spectrum resonances at 4.70-4.26 (t, N-CH_2) ppm, 3.99-3.69 (t, N-CH_2-CH_2) ppm, at 2.87-2.40 (q, CH_2N) ppm and a resonance as a triplet at 0.79-0.69 (t, C$H_3$$CH_2$N) for the protons of the amine group, confirming the *N*-alkylation of the imidazole ring.

5.3.2. Synthesis of Fe-NHC iron complexes 24-27

The iron complexes **24**-**27** were conveniently accessible following the procedure previously described by us, by direct reaction of $Fe_3(CO)_{12}$ with the appropriate proligands in refluxing toluene.[7] (Scheme 5.2). Complexes **24-27** were isolated as green crystalline solids in high yields 74-82%, and were fully characterized by IR, ^{1}H and ^{13}C NMR spectroscopy, MS spectrometry and elemental analysis. Additionally, the molecular structure of **26** was determined by X-ray diffraction studies.



R = $(CH_2)_2OH$ (**24**)
R = $(CH_2)_3OH$ (**25**)
R = CH_2CONEt_2 (**26**)
R = $CH_2CH_2NEt_2$ (**27**)
R = ^{n}Bu (**14**)[14]

Scheme 5.2. Synthesis of Cp*-NHC iron complexes **24-27**.

The successful metalation is confirmed by the appearance of the characteristic carbene signal at 195 ppm (for complexes **24** and **25**), 198 ppm (for **26**), and 196 ppm (for **27**) in the ^{13}C NMR, which is in the region of previously reported half sandwich Fe-NHC complexes.[4,9-10] The length of the alkyl substituents and the introduction of different functionalities has not detectable impact on the Fe-$C_{Carbene}$ resonance frequency. In addition the ^{13}C NMR spectra of **24**-**27** show the characteristic resonance for the carbonyl group at 227 ppm (for complexes **24**-**26**) and 226 ppm (for **27**).

The infrared spectra of **24** and **25** display the expected strong carbonyl resonance at 1900-1901 cm^{-1}. Their similar value is indicative of an analogous electron donor capacity of the N-heterocylic carbene ligand, which is not influenced by the length of the alkyl wingtip. In contrast, compound **26**, displays a strong carbonyl resonance at 1924 cm^{-1}, indicating a lower electronic density around the metal centre. The introduction of the amine group in **27** has no detectable impact in the CO stretching band frequency (see Table 5.1).[7,14]

The IR values correlate well with the redox potentials obtained from the cyclic voltammetry studies. Compound **26** which displayed the highest CO stretching frequency band at 1924 cm^{-1} gives the highest redox potential $E_{1/2}$ = 1.28 V (Fe/Fe^{+}) (see Table 5.1 and Figure 5.1)

indicating a poor π back-donation from iron and thus higher Lewis acidity of the metal center.

Table 5.1. Selected IR frequencies, ^{13}C NMR chemical shifts and redox potential of complexes **24**–**27**.

	IR[a]	^{13}C NMR[b]		$E_{1/2}$
complex	$\nu_{CO\ (cm^{-1})}$	C_{NHC}	CO	vs Fe/Fe^+ (V)[c]
24	1900	195	227	--
25	1901	195	227	0.61
26	1924	198	227	1.28
27	1902	196	226	0.73

[a] In KBr pellets; [b] In C_6D_6, 300 MHz, 300 K. All chemical shifts are reported in ppm.

[C]In V *vs* SCE ($E_{1/2}$ Fc^+/Fc at +0.46 V), measured in CH_2Cl_2, 0.1 M $[Bu_4N][PF_6]$ electrolyte, sweep rate 100 mV s^{-1}.

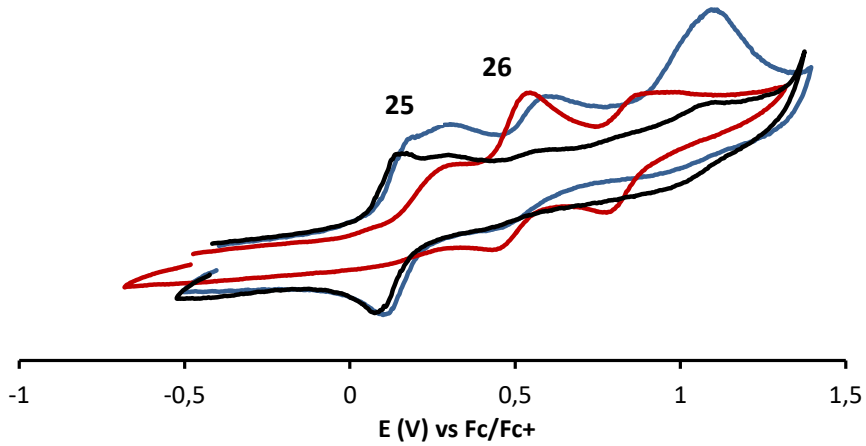


Figure 5.1. Cyclic voltammograms of [(Cp*-NHC$^{(CH2)3OH}$]Fe(CO)I (**25**) (in blue), [Cp*-NHC^{CH2CONEt}]Fe(CO)I (**26**) (in red), and [(Cp*-NHC$^{(CH2)3Me}$]Fe(CO)I (**14) (in black)** in CH_2Cl_2/0.2 M $[Bu_4N][PF_6]$ and at the voltage sweep rate v = 100 mV s^{-1}.

The molecular structure of complex **26** was confirmed by X-ray diffraction studies. Table 5.2 shows the selected bond, distances and angles, and the molecular diagram of complex **26** (Figure 5.2). Crystals of complex **26** suitable for single crystal X-ray diffraction were obtained from a mixture of toluene and hexane at 2 ºC. The structure crystallizes in the triclinic system, P-1 space group, with two chemically similar, but crystallographically independent molecules in the asymmetric unit. One of the molecules presents positional disorder involving the iodide and carbonyl ligands. The molecular structure shows a piano-stool arrangement, characteristic of half-sandwich iron complexes, with a distance of 1.720(1) Å between the Fe atom and the Cp centroid. The Fe-$C_{carbene}$ [1.953 (4) Å], Fe-I [2.626 (1) Å] and Fe-C_{CO} [1.747 (5) Å] bond distances compare well with those of related Fe-NHC complexes.[15-18]

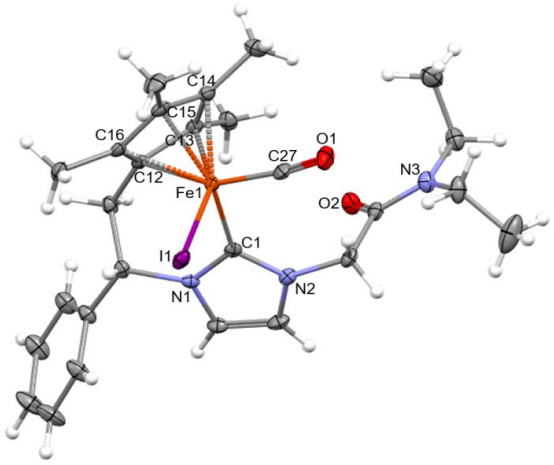


Figure 5.2. Molecular structure of complex **26** using 30% probability level ellipsoids.

Table 5.2. Selected bond lengths [Å] and angles [º] for complex **26**.

Fe(1)-I(1)	2.626 (1)	Fe(1)-C(12)	2.107 (4)
Fe(1)-C(27)	1.747 (5)	Fe(1)-C(13)	2.068 (4)
O(1)-C(27)	1.142 (5)	Fe(1)-C(14)	2.075 (4)
Fe(1)-C(1)	1.953 (4)	Fe(1)-C(15)	2.112 (4)
Fe-Cp(centroid)	1.720(1)	Fe(1)-C(16)	2.163 (4)
C(27)-Fe(1)-C(1)	102.1 (2)	C(12)-Fe(1)-C(15)	66.2 (2)
C(27)-Fe(1)-C(13)	114.5 (2)	C(27)-Fe(1)-C(16)	138.6 (2)
C(1)-Fe(1)-C(13)	93.7 (2)	C(1)-Fe(1)-C(16)	119.3 (2)
C(27)-Fe(1)-C(14)	88.7 (2)	C(13)-Fe(1)-C(16)	66.2 (2)
C(1)-Fe(1)-C(14)	130.6 (2)	C(14)-Fe(1)-C(16)	65.8 (2)
C(13)-Fe(1)-C(14)	40.0 (2)	C(12)-Fe(1)-C(16)	38.6 (2)
C(27)-Fe(1)-C(12)	154.1 (2)	C(15)-Fe(1)-C(16)	38.9 (2)
C(1)-Fe(1)-C(12)	88.6 (2)	C(27)-Fe(1)-I(1)	89.1 (2)
C(13)-Fe(1)-C(12)	40.5 (2)	C(1)-Fe(1)-I(1)	89.7 (1)
C(14)-Fe(1)-C(12)	66.9 (2)	C(13)-Fe(1)-I(1)	154.7 (1)
C(27)-Fe(1)-C(15)	100.9 (2)	C(14)-Fe(1)-I(1)	139.1 (1)

C(1)-Fe(1)-C(15)	154.8 (2)	C(12)-Fe(1)-I(1)	114.8 (1)
C(13)-Fe(1)-C(15)	67.2 (2)	C(15)-Fe(1)-I(1)	100.9 (1)
C(14)-Fe(1)-C(15)	40.0 (2)	C(16)-Fe(1)-I(1)	90.3 (1)

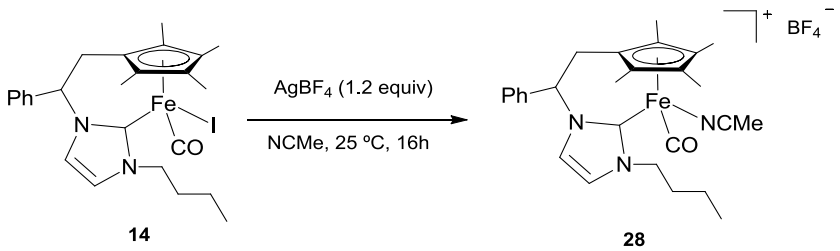
The Fe-C_{NHC} (1.95 Å) and the Fe-$Cp_{centroid}$ (1.72 Å) distances are in the expected range for half-sandwich iron complexes and in agreement with the related and already published Cp*-NHC(Fe)(CO)I complexes.[4,11-13]

5.3.3. Synthesis of Fe-NHC cationic complex 28

In order to compare the catalytic activity of the neutral compounds **24**–**27** with cationic species, we decided to synthesize the cationic iron(II) carbonyl complex [(Cp*-$NHC^{n\text{-}Bu}$)Fe(CO)$(NCMe)^{+}$][BF_4^{-}] **(28).** Complex **28** was prepared in high yield (99%) by stoichiometric reaction of **14** with silver tetrafluorborate $AgBF_4$ in acetonitrile (Scheme 5.3), and it was fully characterized by analytical and spectroscopic methods. The NMR characterization of complex **28** revealed the presence of two diastereomers in a 3:1 ratio. The presence of diastereomers was rationalized by the existence of two stereogenic centers in the molecule, at the metal center and at the aliphatic linker between the NHC and the cyclopentadienyl ring. Therefore, two sets of signals corresponding to the coordinated cyclopentadienyl-NHC ligand were observed in the NMR spectra.

The ^{13}C NMR of **28** shows the characteristic carbene signal (Fe-$C_{carbene}$) at 187.05 ppm for the major isomer (minor isomer at 186 ppm), shifted upfield in comparison to the neutral complex **14** (194.9 ppm). As expected, related cationic piano-stool iron-NHC complexes containing the unsubstituted Cp ligand display resonances for the carbene signal shifted to higher field (182-174 ppm).

The infrared vibrational spectrum of **28** shows an intense absorption band at 1934 cm^{-1}, indicative of the terminal carbonyl ligand. As expected, the carbonyl stretching band frequency is shifted to higher wavenumber in comparison to that of the neutral complex **14** (ν_{CO} 1905 cm^{-1}), indicating less π back-donation from iron to NHC fragment and thus higher Lewis acidity of the metal.



14 **28**

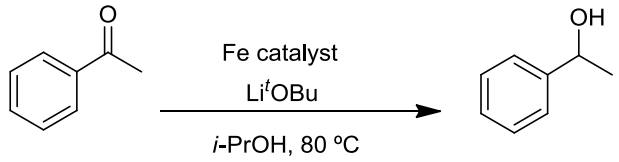
Scheme 5.3. Synthesis of [Cp*-NHC$^{n\text{-}Bu}$Fe(CO)(NCMe)$^{+}$][BF_4^{-}], (**28)**.

5.3.4. Transfer hydrogenation of ketones

5.3.4.1. Transfer hydrogenation of ketones using 2-propanol and Li^{t}OBu as base

The catalytic activity of iron complexes **14**, **19**, **24**-**29** (Scheme 5.4) in transfer hydrogenation was initially explored using acetophenone as a substrate model and 2-propanol as a hydrogen source, in the presence of 0.5 mol % catalyst and 20 mol % of base (Li^{t}OBu). Other bases such as KOH and KO^{t}Bu afforded unwanted base-promoted hydrogen transfer reaction under the same experimental conditions (20 mol % of KOH and KO^{t}Bu afforded 75% and 80% of 1-phenylethanol in 12 h, respectively). These results are in agreement with published work.[26] The progress of the reaction was monitored by gas chromatography. The results are summarized in Table 5.4.

Table 5.4. Transfer hydrogenation of acetophenone.[a]



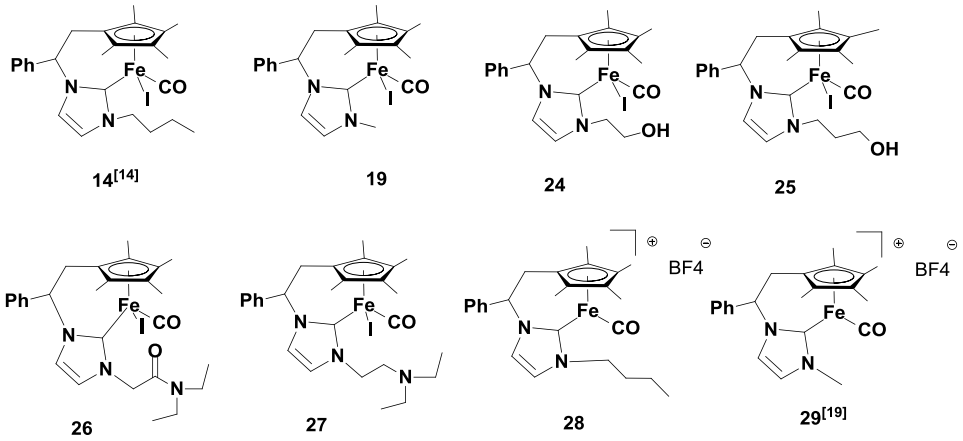
Entry	Catalyst	Yield (%)[b]
1	**14**	61
2	**19**	53
3	**24**	39
4	**25**	62
5	**26**	84
6	**27**	63
7	**28**	77
8	**29**	59

[a] The reactions were carried out using substrate (2.0 mmol), catalyst (0.5 mol %), Li^{t}OBu (0.4 mmol) and 2-propanol (4 mL) at 80 ºC, for 24 hours. [b] Yield determined by GC chromatography.

All complexes depicted in Scheme 5.4 resulted active in transfer hydrogenation of acetophenone (Figure 5.3).

Complexes **14, 25** and **27** present a comparable catalytic activity, indicating that the introduction of the hydroxyl and amine functionalities has not consequences in the catalytic performance of the iron complexes. We observed that the presence of longer alkyl chains induce slightly better performance than shorter ones (**14** versus **19**). In addition, the cationic complex [Cp*-NHC^{nBu}Fe(CO)(NCMe)$^+$][BF_4^-] **(28)**, performed better than the neutral complex (**28** *versus* **14**).

Interestingly, complex **26**, bearing an acetamide group on the wingtip, displayed the highest catalytic activity affording 84% yield in 24 hours.



Scheme 5.4. Iron-NHC complexes used for catalytic transfer hydrogenation of acetophenone.

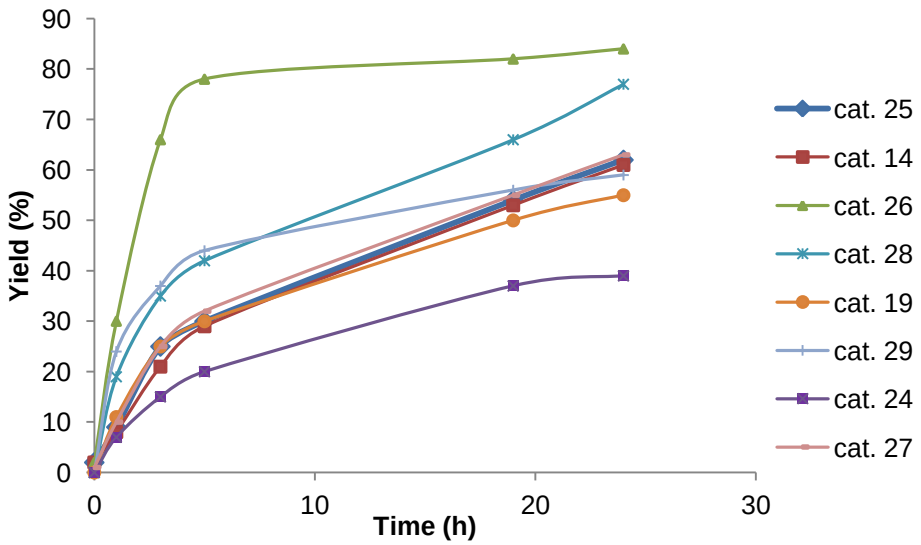
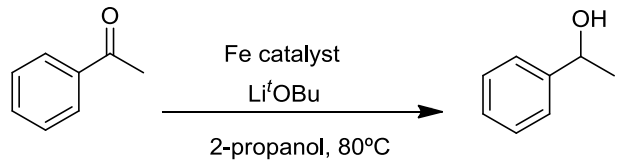


Figure 5.3. Kinetic profile of the reduction of acetophenone in 2-propanol. Catalytic conditions: 0.5 mol % catalyst, acetophenone (2 mmol), Li^{t}OBu (0.4 mmol), 2-propanol (4 mL) at 80 °C in 24 ºC. Yields were determined by GC.

Encouraged by the efficiency of complex **26** in transfer hydrogenation of acetophenone, we decided to optimize the reaction conditions and

investigate its activity using different catalytic amounts. Under same reaction conditions, catalyst loading of **26** could be lowered to 0.05 mol %, achieving a TON of 1340 (Table 5.5, entry 7).

Table 5.5. Transfer hydrogenation of acetophenone with **26**.[a]



Entry	Cat. amount (mol %)	T (ºC)/t (h)	Yield (%)[b]	TON
1	5	80/24	85	17
2	2	80/24	83	42
3	1	80/24	82	82
4	0.5	80/24	84	168
5	0.2	80/31	80	400
6	0.1	80/35	78	780
7	0.05	80/40	67	1340

[a]Reactions were carried out using substrate (2.0 mmol), catalyst (0.5 mol %), Li^{t}OBu (0.4 mmol) and 2-propanol (4 mL) at 80 ºC for 24 hours. [b] Yield determined by GC.

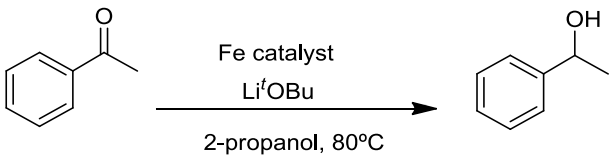
As shown in Figure 5.3, catalyst **26** bearing the acetamide group displays the best catalytic performance, surpassing the catalytic activity of the cationic species **28**.

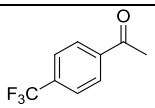
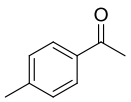
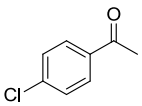
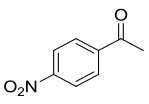
Based on these data, we believe that the higher catalytic efficiency of **26** can not be explained by electronic factors, and it is most probably

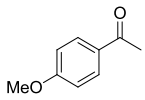
due to a metal-ligand cooperativity induced by the presence of the acetamide group. There are two types of bifunctional behavior that could be considered, hemilability, implying the direct coordination of the acetamide group to the iron center through its oxygen atom, or by remote metal-ligand cooperation, both cases involving the active participation of the acetamide group in reversible protonation/deprotonation processes. Mechanistic investigations have to be performed to elucidate the role of the acetamide group.

Under similar reaction conditions, the scope of the reaction was evaluated using different *p*-substituted aromatic ketones in the presence of complex **26** (Table 5.6.).

Table 5.6. Transfer hydrogenation of *p*-substituted ketones.[a]



Entry	Substrate	Yield (%)[b]	TON
1		73	146
2		83	166
3		22	44
4[c]		5	10

5[c]		76	152

[a] The reactions were carried out using substrate (2.0 mmol), catalyst (0.5 mol %), Li[t]OBu (0.4 mmol) and 2-propanol (4 mL) at 80 ºC for 24 hours. [b] Yield determined by GC.[c] conversions determined by ^{1}H-NMR.

Ketones bearing functional groups such as CF_3, Me and OMe were fully reduced and the corresponding alcohols were obtained in good yields (73-83%).[20,21] In contrast, chloro- and nitro- functional groups were not well tolerated.

5.3.4.2. Transfer hydrogenation of carbonyl groups using glycerol as a hydrogen source and microwave (MW) heating

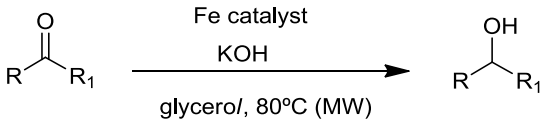
The use of glycerol as a solvent in transfer hydrogenation is very attractive, since glycerol is cheap and readily available.[22,23] There are few reports in the literature of transfer hydrogenation of carbonyl groups in glycerol. An interesting example was recently reported by Peris and Azua,[24,25] where they described a series of iridium and ruthenium NHC based catalysts for the reduction of a variety of substrates using glycerol as a hydrogen source. Both Ru and Ir catalysts proved to be very active in the reduction of aromatic ketones and aldehydes and also moderately active in the reduction of a selected set of olefins and acetylenes.

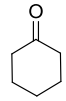
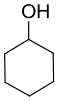
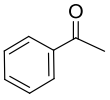
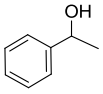
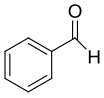
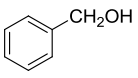
Based on these results, we decided to explore the activity of our iron complex **26** in the reduction of ketones using 0.5 mmol of KOH at 80 ºC in MW. As shown in Table 5.7, cyclohexanone, acetophenone and benzaldehyde were converted into the corresponding alcohols in quantitative yields in 15 minutes.

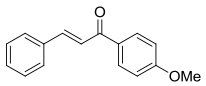
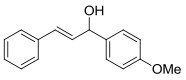
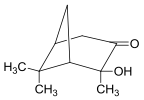
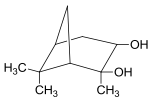
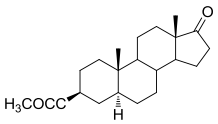
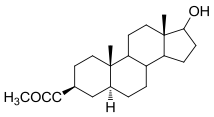
Interestingly, the catalytic system was applied for the chemoselective reduction of biological substrates (Table 5.7, entries 4-6).

Comparing our results with those obtained by Peris and Azua, we observe that complex **26** was capable to reduce acetophenone using less amount of catalyst (0.5 mol % *vs* 2.5 mol %) at lower temperatures (80 ºC *vs* 80-120 ºC) and in less reaction time (15 min *vs* 1-2 hours).[24, 25]

Table 5.7. Transfer hydrogenation of ketones using glycerol as the hydrogen source and MW heating in the presence of iron complex **26**.



entry	substrate	product	Yield (%)[b,c]
1			96[b]
2			98[b]
3			97[b]

4			75[c]
5			80[c]
6			82[c]

[a] All reactions were carried out with substrate (1 mmol), compound **26** (0.5 mol%), KOH (0.5 mmol) in glycerol (0.8 mL) at 80 ºC with MW heating; [b] Yields were determined by ^{1}H NMR using *n*-tetradecane as internal standard; [c] isolated yields.

5.4. Conclusions

As conclusion, in this chapter, we have described the preparation and characterization of a series of Cp*-functionalized NHC iron complexes bearing, hydroxyl, acetamide and amine groups, and explored their catalytic activity in the reduction of ketones through transfer hydrogenation processes.

Interestingly complex **26**, bearing the acetamide group, exhibited the best catalytic performance when the reactions were performed using 2-propanol as hydrogen source. Furthermore, we have developed a green protocol for the reduction of ketones using glycerol as a hydrogen source and microwave heating in the presence of catalytic amounts of **26** and KOH.

5.5. Experimental Procedures

5.5.1. Materials and methods: All reagents were used as received from commercial suppliers without further purification. All manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques, and solvents were purified from appropriate drying agents. Deuterated solvents were degassed and stored over molecular sieves. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker Avance III 400 MHz. Elemental analyses and Electrospray mass spectra were performed in our laboratories at ITQB. Infrared (IR) spectra were recorded on samples as KBr pellets using a Bruker IFS 66/S ATR-FTIR spectrometer.

5.5.2. Electrochemical Experiments: The electrochemical experiments were performed on an EG&G Princeton Applied Research Model 273A potentiostat/galvanostat and monitored with a personal computer loaded with Electrochemistry PowerSuite v2.51 software from Princeton Applied Research. Cyclic voltammograms were obtained in 1 mM solutions of anhydrous dichloromethane with tetrabutylammonium hexafluorophosphate (0.2 M) as supporting electrolyte, using a homemade three-electrode configuration cell with a platinum-disk working electrode (1.0 mm diameter), a silver-wire pseudo-reference electrode and a Pt wire as the auxiliary electrode. All the experiments were performed under a nitrogen atmosphere at room temperature. The redox potentials of the complexes were measured against the ferrocene/ferrocenium redox couple as the internal standard with $E_{1/2}(Fc/Fc^{+})$ *vs* SCE = +0.46 V. The supporting electrolyte was purchased from Aldrich Chemical Co. and dried under vacuum for several hours prior to the experiments.

5.5.3. Crystallographic data for complex 26. Crystals of complex **26** suitable for single-crystal X-ray analysis were grown from a mixture of

toluene and hexane at 2 ºC. Selected crystals were covered with Fomblin (polyfluoroether oil) and mounted on a nylon loop. The data were collected at 110(2) K on a Bruker D8 Venture diffractometer equipped with a Photon 100 CMOS detector and an Oxford Cryosystems gaseous nitrogen stream Cooler, using graphite monochromated Mo-Kα radiation (ʎ = 0.71073 Å). Data were processed using APEX2 suite software package, which includes integration and scaling (SAINT), absorption corrections (SADABS) and space group determination (XPREP). Structure solution and refinement were done using direct methods with the programs SHELXS-16 inbuilt in APEX and WinGX-Version 2014.1[20] software packages. All non-hydrogen atoms were refined anisotropically and all the hydrogen atoms were inserted in idealized positions and allowed to refine riding on the parent carbon atom. The molecular diagrams were drawn with ORTEP-3 for windows[21] and Mercury,[22] included in the software package. Table 1 contains crystallographic experimental data and structure refinement parameters.

5.5.4. Synthesis and characterization of proligands 20-23

Cp*-NHC^{R} [(R=$(CH_2)_2OH$ (**20**), $(CH_2)_3OH$ (**21**), CH_2CONEt_2 (**22**), $CH_2CH_2NEt_2$ (**23**)]

Proligand **20**: 2-Iodoethanol (0.71 mL; 9.1 mmol) was added to a solution of proligand **1** (0.529; 1.8 mmol) in acetone (10 mL), and the mixture was stirred at room temperature for 4 days. The suspension was filtered and the filtrate was evaporated to dryness to yield a yellow solid which was washed with diethyl ether and hexane and dried under vacuum. Proligand **20** was isolated as a yellow solid. Yield: 532 mg (63%). ^{1}H-NMR (400 MHz, $CDCl_3$): mixture of isomers: δ 9.66-9.37 (s, N=C*H*-*N*), 7.53-6.98 (m, CH_{Phenyl}, C*H*Imid), 5.65-5.39 (m. CH_{linker}), 4.42-4.40 (t, N-CH2), 3.91-3.81 (t, CH2), 3.31-3.03 (m, C$H_{2linker}$), 2.76-

2.48 (m,CH_{Cp^*}), 1.88-1.38 (s,CH_{3Cp^*}), 1.15-0.86 (d, CH_{3Cp^*}).^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.32 (N=CH-N), 136.39-120.24 (C_{Phenyl}, C_{Imid}), 70.48-62.41 (CH_{linker}), 59.50 (CH_{Cp^*}), 53.82-49.31 (NCH_2, CH_2OH), 32.15-31.73 ($CH_{2Linker}$), 15.40-11.95 (CH_{3Cp^*}). MS (ESI-TOF) m/z $[M-I]^+$ calcd for $C_{22}H_{29}N_2O$: 337; found 337 $[M-I]^+$.

Proligand **21:** 1-Iodo-3-propanol (0.71 mL; 7.4 mmol) was added to a solution of proligand **1** (0.533; 1.5 mmol) in acetone (10 mL), and the mixture was stirred at room temperature for 4 days. The suspension was filtered and the filtrate was evaporated to dryness to yield a yellow solid which was washed with diethyl ether and hexane, and dried under vacuum. Proligand **21** was obtained as a yellow solid. Yield: 456 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$) mixture of isomers: δ 10.08-9.69 (s, N=C*H-N*), 7.52-7.05 (m, CH_{Phenyl}, C*H*Imid), 5.87-5.69 (m. CH_{linker}), 4.55-4.44 (t, N-CH2), 3.62-3.18 (t, CH2), 2.78 (m, C$H_{2linker}$), 2.15 (m,CH_{Cp^*}), 2.11-2.03 (q, CH2), 1.80-1.43 (s,CH_{3Cp^*}), 1.23-0.91 (d, CH_{3Cp^*}). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.04 (N=CH-N), 133.57-120.23 (C_{Phenyl}, C_{Imid}), 64.96-62.48 (CH_{linker}), 56.91 (CH_{Cp^*}), 56.91-49.60 (NCH_2, CH_2OH), 47.79 (CH2), 32.45-31.69 ($CH_{2Linker}$), 14.20-10.76 (CH_{3Cp^*}). MS (ESI-TOF) m/z $[M-I]^+$ calcd for $C_{22}H_{29}N_2O$: 351; found 351 $[M-I]^+$.

Proligand **22**: 2-Chloro-N,N-diethylacetamide (1.48 mL; 11 mmol) and KI (1.84g; 11 mmol) was added to a solution of proligand **1** (0.640; 2.2 mmol) in acetone (10 mL), the mixture was stirred at room temperature for 4 days. The suspension was filtered and the filtrate was evaporated to dryness to yield a yellow solid which was washed with diethyl ether and hexane, and dried under vacuum. Proligand **22** was isolated as a yellow solid. Yield: 801 mg (69%). ^{1}H NMR (400 MHz, $CDCl_3$) mixture of isomers: δ 9.88-9.60 (s, N=C*H-N*), 7.61-6.99 (m, CH_{Phenyl}, C*H*Imid), 5.67-5.46 (m. CH_{linker}), 5.24 (t, N-CH2), 3.43-3.39 (q, CH2), 2.78 (m,

C*H*$_{2linker}$), 2.39 (m,C*H*$_{Cp*}$), 1.71-1.59 (t, CH2), 1.58-1.40 (s,C*H*$_{3Cp*}$), 1.23-0.78 (d, C*H*$_{3Cp*}$). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.27 (C=O), 143.68 (N=CH-N), 140.13-120.18 (C_{Phenyl}, C_{Imid}), 64.91-62.56 (CH_{linker}), 53.52 (CH_{Cp*}), 50.53 (NCH_2), 41.67 (CH_{2acet}), 32.90-32.70 ($CH_{2Linker}$), 14.0-11.36 (CH_{3Cp*}). MS (ESI-TOF) m/z [M-I]$^+$ calcd for $C_{26}H_{36}N_3O$: 406; found 406 [M-I]$^+$. Anal. Calcd for $C_{26}H_{36}N_3OI$: C: 52.70; H: 5,57; N: 6.83; Found: C: 53.00; H: 5.90; N: 6.58.

Proligand **23**: 2-Chloro-N,N-diethylamine was prepared from the neutralization of 1g of 2-Chloro-N,N-diethylamine hydrochloride with crushed ice (2.32 g), ice-cold ether (5.8 mL) and ice-cold 20 % aqueous sodium hydroxide (1.16 mL) and the ether layer was decanted and the aqueous layer extracted with ice-cold ether (2 x 15 mL). The combined extracts were dried at 4ºC over $MgSO_4$. Drying agent was removed by filtration, and ether removed in vacuum to yield the respective product in quantitative conversion. Then 2-chloro-N,N-diethylamine (0.951 g; 5.52 mmol) and KI (0.92 g; 5.52 mmol) were added to a solution of **1** (0.400; 1.1 mmol) in acetone (10 mL), and the mixture was stirred at room temperature for 4 days. The suspension was filtered, and the filtrate was evaporated to dryness, washed with diethyl ether and hexane, and dried under vacuum. Proligand **22** was isolated as a yellow solid. Yield 635 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$) mixture of isomers: δ 10.50-9.66 (s, N=C*H-N*), 7.55-7.04 (m, C*H*$_{Phenyl}$, C*H*$_{Imid}$), 5.58-5.28 (m, C*H*$_{linker}$), 4.70-4.26 (t, N-CH_2), 3.99-3.69 (t, N-CH_2-C$\underline{H}_2$), 3.33 (m, C*H*$_{2linker}$), 3.99-3.69 (m, CH_2), 2.87-2.40 (q, CH_2N), 2.22 (m,C*H*$_{Cp*}$), 1.68-1.33 (s,C*H*$_{3Cp*}$), 0.88 (d, C*H*$_{3Cp*}$), 0.79-0.69 (t, C$\underline{H}_3$CH_2N). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.68 (N=CH-N), 133.13-127.50 (C_{Phenyl}), 122.24-120.14 (C_{Imid}), 65.24-64.23 (CH_{linker}), 57.19 (N-CH_2), 52.61 (CH_{Cp*}), 48.76 ($NCH_2\underline{C}H_2$), 46.62 (CH_{2amine}), 31.99 ($CH_{2Linker}$), 14.14-9.23 (CH_{3Cp*+} CH_{3amine}). Anal. Calcd

for $C_{26}H_{38}N_3I$: C: 60.11; H: 7,37; N: 8.09; Found: C: 60.01; H: 7.80; N: 8.25.

5.5.5. Synthesis and characterization of iron complexes 24–28

General procedure: A mixture of the appropriate proligand (Cp*-NHC^R)I [R=$(CH_2)_2OH$, $(CH_2)_3OH$, CH_2CONEt_2, $CH_2CH_2NEt_2$ (1.38 mmol) and $Fe_3(CO)_{12}$ (0.46 mmol) was refluxed in toluene (15 mL) for 16 h. Filtration and removal of toluene under vacuum gave a green solid, which was washed with hexane to afford the corresponding iron complexes isolated as green solids **24-27**.

Complex **24:** Yield: 74%. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.59-7.53 (m, 5H,CH_{Ph}), 7.07 (s, 1H, CH_{imid}), 6.46 (s, 1H, CH_{imid}), 6.06 (m, 1H, C$H_{Phlinker}$), 4.5-4.4 (m, 2H N-CH_2), 3.88-3.86 (m, 2H, CH_2) 3.0-2.92 (m, 2H, C$H_{2linker}$) 2.39 (s, 3H, CH_{3Cp*}), 1.82 (s, 3H, CH_{3Cp*}), 1.7 (s, 3H, CH_{3Cp*}), 0.94 (s, 3H, CH_{3Cp*}). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 226.8 (CO), 194.9 ($C_{carbene-Fe}$), 138.8 ($C_{ipso-phenyl)}$, 129 (CH_{Phenyl}), 124 (CH_{imid}), 120 (CH_{imid}), 104 (C_{Cp*}), 91.6 (C_{Cp*}), 90.4 (C_{Cp*}), 84.3 (C_{Cp*}), 81.2 (C_{Cp*}), 69 (CH_2-N), 67.1 ($CH_{Ph-linker}$), 61 (CH_{linker}), 52 ($CH_{2linker}$), 21 (CH_2), 13 (CH_{3Cp*}), 11 (CH_{3Cp*}),10 (CH_{3Cp*}), 9.5 (CH_{3Cp*}). Selected IR data (KBr): ν (CO) 1901 vs cm^{-1}. MS (ESI-TOF^+) m/z $[M-I]^+$ calcd for $C_{24}H_{27}N_2O_2Fe$: 419 ; found 419 $[M-I]^+$. Anal. Calcd for $C_{23}H_{27}N_2O_2FeI$ (546): C: 50.57; H: 4,98; N: 5.13; Found: C: 50.35; H: 4.77; N: 5.00.

Complex **25**: Yield: 76%. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.62-7.42 (m, 5H,CH_{Ph}), 7.17 (s, 1H, CH_{imid}), 6.48 (s, 1H, CH_{imid}), 6.07(m, 1H, C$H_{Phlinker}$), 4.32 (m, 2H N-CH_2), 3.59 (m, 2H, C$H_{2)}$ 3.05-2.93 (m, 2H, C$H_{2linker}$) 2.40 (s, 3H, CH_{3Cp*}), 2.04 (CH_2) 1.81 (s, 3H, CH_{3Cp*}), 1.75 (s, 3H, CH_{3Cp*}), 0.95 (s, 3H, CH_{3Cp*}).^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 226.8 (CO), 195.1 ($C_{carbene-Fe}$), 138.49 ($C_{ipso-phenyl)}$, 129 (CH_{Phenyl}), 123

(CH_{imid}), 121 (CH_{imid}), 104.7 ($C_{Cp^*)}$, 91.7 ($C_{Cp^*)}$, 90.4 ($C_{Cp^*)}$, 84.3 ($C_{Cp^*)}$, 81.2 ($C_{Cp^*)}$, 67 (CH_{linker}), 58.9 (CH_2), 48.02 (CH_2), 34.7 ($CH_{2linker}$), 13 (CH_{3Cp^*}), 10 ($CH_{3Cp^*)}$, 9.6 (CH_{3Cp^*}), 1.4 (CH_{3Cp^*}). Selected IR data (KBr): v (CO) 1900 vs cm^{-1}. MS (ESI-TOF) m/z [M-I]+ calcd for $C_{24}H_{29}N_2O_2Fe$: 433; found 433 [M-I]+. Anal. Calcd for $C_{24}H_{29}N_2O_2FeI$ (560): C: 51.45; H: 5.22; N: 5.00; Found: C: 51.90; H: 5.78; N: 4.82.

Complex **26**: Yield: 76%. ^1H NMR (400 MHz, C_6d_6) δ 7.22-7.16 (m, 5H,CH_{Ph}), 6.28 (s, 1H, CH_{imid}), 6.23 (s, 1H, CH_{imid}), 6.05 (m, 1H, C$H_{Phlinker}$), 5.43 (d, J = 2.16 Hz, 1H, N-CH_2CO), 3.87 (d, J = 1.54 Hz, 1H, N-CH_2CO), 3.46 (m, 2H, COCH_2), 2.92 (m, 2H, C$H_{2linker}$), 2.77 (m, 2H, COCH_2), 2.59 (m, 2H, COCH_2), 2.40 (s, 3H, CH_{3Cp^*}), 1.81 (s, 3H, CH_{3Cp^*}), 1,72 (s, 3H, CH_{3Cp^*}), 1.15 (s, 3H, CH_{3Cp^*}), 1.02 (t, J = 0.41 Hz, 3H, $COCH_2CH_3$), 0.77 (t, J = 0.30 Hz, 3H, $COCH_2CH_3$). ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ 227.3 (CO), 198.3 ($C_{carbene\text{-}Fe}$), 166 (CO), 138.52 ($C_{ipso\text{-}phenyl}$), 129 (CH_{Phenyl}), 123 (CH_{imid}), 120 (CH_{imid}), 102.7 (C_{Cp^*}), 92.7 (C_{Cp^*}), 90.6 (C_{Cp^*}), 83.3 (C_{Cp^*}), 82.2 (C_{Cp^*}), 66 (CH_{linker}), 52 (NCH_2CO), 41 ($COCH_2CH_3$), 40 ($COCH_2CH_3$), 29.1 ($CH_{2linker}$), 13 (CH_{3Cp^*}), 13 ($COCH_2CH_3$), 10 (CH_{3Cp^*}), 10 ($COCH_2CH_3$), 9.9 (CH_{3Cp^*}), 1.6 (CH_{3Cp^*}). Selected IR data (KBr): v (CO) 1924 vs cm^{-1} MS (ESI-TOF) m/z [M-I]+ calcd for $C_{27}H_{34}N_3O_2Fe$: 488; found 488 [M-I]+. Anal. Calcd for $C_{27}H_{34}N_3O_2FeI$ (615): C: 52.70; H: 5.57; N: 6.83; Found: C: 53.00; H: 5.90; N: 6.58.

Complex **27**: Yield: 82% (0.187g). ^1H NMR (400 MHz, C_6d_6) δ 7.28-7.12 (m, 5H,CH_{Ph}), 6.51 (s, 1H, CH_{imid}), 6.27 (s, 1H, CH_{imid}), 6.22 (m, 1H, C$H_{Phlinker}$), 4.32 (t, J = 1.73 Hz, 1H, N-CH_2), 3.90 (t, J = 1.56 Hz, 1H, N-CH_2), 2.81 (t, J = 1.12 Hz, 1H, N-CH_2CH_2) 2.68 (t, J = 1.1 Hz, 1H, N-CH_2CH_2), 2.41 (s, 3H, CH_{3Cp^*}), 2.31 (m, C$H_{2linker}$), 1.81 (s, 3H, CH_{3Cp^*}), 1,72 (s, 3H, CH_{3Cp^*}), 1.15 (s, 3H, CH_{3Cp^*}), 1.12 (t, J = 1.1 Hz, 3H, $COCH_2CH_3$), 0.82 (t, J = 0.33 Hz, 3H, $COCH_2CH_3$). ^{13}C {^1H} NMR

(100 MHz, $CDCl_3$): δ 226 (CO), 195.5 ($C_{carbene-Fe}$), 137.8 ($C_{ipso-phenyl}$), 129.1 (CH_{Phenyl}), 122.1 (CH_{imid}), 119.6 (CH_{imid}), 104.2 (C_{Cp^*}), 91.6 (C_{Cp^*}), 89.2 (C_{Cp^*}), 83.3 (C_{Cp^*}), 81 (C_{Cp^*}), 66 (CH_{linker}), 54.2 (N-CH_2), 47.8 (N-CH_2), 54 (NCH_2CH_2), 50.3 (N-CH_2CH_2), 29.3 ($CH_{2linker}$), 13.9 (CH_{3Cp^*}), 12.5 ($COCH_2CH_3$), 10.9 (CH_{3Cp^*}), 10 ($COCH_2CH_3$), 9.9 (CH_{3Cp^*}), 1.6 (CH_{3Cp^*}). Selected IR data (KBr): v (CO) 1902 vs cm^{-1}. Anal. Calcd for $C_{27}H_{36}N_3OFeI$: C: 53.92; H: 6.03; N: 6.99; Found: C: 53.55; H: 6.41; N: 7.10;

Complex **28**: A mixture of **14** (0.070 g, 0.13 mmol) and 1.2 equivalents of $AgBF_4$ (0.029 g, 0.15 mmol) in acetonitrile (5 mL) was stirred for 3 hours at room temperature. The solution was filtered and the filtrate was concentrated to dryness affording an orange solid, which was washed with diethyl ether and dried under vacuum. Complex **28** was isolated as a crystalline brown solid. Yield: 99% (0.077 g).

Data for the major isomer are as follows: ^{1}H NMR (400 MHz, CD_3CN) δ 7.64-7.23 (m, 5H,CH_{Ph}), 7.11 (s, 1H, CH_{imid}), 6.58 (s, 1H, CH_{imid}), 5.38-5.35 (d, J=5.45 Hz, 1H, C$H_{Phlinker}$), 4.13 (t, 2H, N-CH_{2Bu}), 3.41 (q, 2H, CH_{2Bu}), 3.07-2.72 (m, 2H, C$H_{2linker}$ + CH_{2Bu}), 2.23 (s, 3H, NCCH_3), 1.96 (s, 3H, CH_{3Cp^*}), 1.86 (s, 3H, CH_{3Cp^*}), 1.84 (s, 3H, CH_{3Cp^*}), 1.41 (s, 3H, CH_{3Cp^*}), 1.15 (m, 2H, CH_{3Bu}), 0,93 (t, J=8.3 Hz, CH_{3nBu}). ^{13}C {^{1}H} NMR (100 MHz, CD_3CN): δ 222.22 (CO), 187.05 (N*C*N), 138.19 (N*C*CH_3), 130.34 (6x*C*H_{phenyl}), 124.28 (*C*HImid), 122.48 (*C*H_{Imid}), 106.4-88.24 (5xC_{Cp^*}), 67.15 (*C*$H_{Ph\ linker}$), 51.85 (N*C*H_2), 34.94 (*C*H_2), 28.60 (*C*$H_{2linker}$), 20.37 (*C*H_2), 10.22−8.92 (*C*H_{3Cp^*} + NC*C*H_3).

Data for the minor isomer are as follows: ^{1}H NMR (400 MHz, CD_3CN): δ 7.63−7.09 (m, 5H, CH_{Ph}), 7.12 (s, 1H, CH_{Imid}), 6.62 (s, 1H, CH_{Imid}), 4.85-4.82 (dd, J = 4.96 Hz, 1H, C$H_{Ph\ linker}$), 3.90 (t, 2H, N-CH_{2Bu}), 3.41 (q, 2H, CH_{2Bu}), 2.54-2.40 (m, 2H, C$H_{2linker}$ + CH_{2Bu}), 2.21 (s, 3H, NCCH_3), 1.85 (s, 3H, CH_{3Cp^*}), 1.63 (s, 3H, CH_{3Cp^*}), 1.60 (s, 3H,

C*H*$_{3Cp^*}$), 1.39 (s, 3H, C*H*$_{3Cp^*}$), 1.09 (m, 2H, C*H*$_{3Bu}$), 0,78 (t, J=8.3 Hz, C*H*$_{3nBu}$).

Anal.Calcd for $C_{27}H_{34}N_3FeOBF_4$ (559.07): C, 57.98; H, 6.13; N, 7.52. Found: C, 58.02; H, 6.15; N, 7.57. Selected IR data (KBr): ν (CO) 1934 vs cm^{-1}.

5.5.6. General procedure for the transfer hydrogenation of ketones in 2-propanol

The samples were typically prepared as follows: the appropriate ketone (2.0 mmol), iron complex (0.5 mol %), Li^{t}OBu (0.4 mmol) and 2-propanol (4 mL) were introduced into a vial at 80 °C. The reaction was then monitored by GC. The identity of the alcohol was assessed by comparison with commercially available pure samples.

5.5.7. General procedure for the transfer hydrogenation of carbonyl groups in glycerol

The samples were typically prepared as follows: the appropriate substrate (1.0 mmol), iron complex (0.5 mol %), KOH (0.5 mmol) and glycerol (0.8 mL) were heated under microwave irradiation at 80 ºC for 15 minutes. The reaction was then stopped and the product was isolated by extraction of the organic phase with ethyl acetate and dried under vacuum to obtain the derivated alcohols from the chalcone, steroid and pinone as pure isolated compounds. In the case of phenylethanol, cyclohexanol and benzyl alcohol the yields were determinate by ^{1}H NMR with the addition of an internal standard *n*-tetradecane.

5.6. Acknowledgements:

We gratefully acknowledge Drª Maria Paula Robalo (Instituto Superior Técnico, IST, Lisbon, Portugal) for the cyclic voltammetry studies of

the iron complexes and to Carolina Vinagreiro for the purification of the steroid alcohol. We wish to acknowledge Analytical Services and UniMS-Mass Spectrometry Unit at ITQB/IBET for elemental analysis and mass spectra. The NMR data was acquired at CERMAX, ITQB-NOVA, Oeiras, Portugal with equipment funded by FCT-Fundação para a Ciência e Tecnologia, project AAC 01/SAICT/2016 and finally we gratefully acknowledge the crystallography services of University Nova of Lisbon (Project RECI/BBB-BEP/0124/2012 from FCT-MCTES).

5.7. References:

[1] P. Das, T. Elder, W. W. Brennesser and S. C. Chmely, *RSC. Adv.,* **2016**, *6*, 88056.

[2] M. V. Jiménez, J. Fernández-Tornos, J. J. Pérez-Torrente, F. J. Modrego, S. Winterle, C. Cunchillos, F. J. Lahoz, and L. A. Oro, *Organometallics* **2011**, *30*, 5493.

[3] A. Iturmendi, N. García , E. A. Jaseer , J. Munárriz , P. J. Sanz Miguel , V. Polo , M. Iglesias, L. A. Oro, *Dalton Trans.*, **2016**, *45***,** 12835.

[4] V. V. K. M. Kandepi, J. M. S. Cardoso, E. Peris, B. Royo, *Organometallics* **2010**, 29, 2777.

[5] C. Johnson, M. Albrecht, *Coord. Chem. Rev.*, **2017**, *352*, 1–14.

[6] M. D. Bala, M. I. Ikhile, *J. Mol. Catal. A: Chem*. **2014**, *385*, 98.

[7] J. M. S. Cardoso, B. Royo, *Chem. Commun.*, **2012**, *48*, 4944.

[8] A. P. da Costa, M. Viciano, M. Sanau, S. Merino, J. Tejeda, E. Peris, B. Royo, *Organometallics* **2008**, *27*, 1305.

[9] V. Cesar, L. C. Mistral Castro, T. Dombray, J.-B. Sortais, C. Darcel, S. Labat, K. Miqueu, J.-M. Sotiropoulos, R. Brousses, N. Lugan, G. Lavigne, *Organometallics* **2013**, *32*, 4643.

[10] S. Demir, Y. Gokçe, N. Kaloglu, J.-B. Sortais, C. Darcel, I. Ozdemir, *Appl. Organomet. Chem*. **2013**, *27*, 459.

[11] P. Buchgraber, L. Toupet, V. Guerchais, *Organometallics* **2003**, *22*, 5144.

[12] L. Mercs, G. Labat, A. Neels, A. Ehlers, M. Albrecht, *Organometallics* **2006**, *25*, 5648.

[13] Y. Ohki, T. Hatanaka, K. Tatsumi, *J. Am. Chem. Soc.* **2008**, *130*, 17174.

[14] J. M. S. Cardoso, R. Lopes, B. Royo, *J. Organomet. Chem*. **2015**, *775*, 173.

[15] L. J. Farrugia, *J. Appl. Cryst.* **2012**, *45*, 849.

[16] L. J. Farrugia, *J. Appl. Cryst.* **1997**, *30*, 565.

[17] C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, Towler and van der Streek, *J. Appl. Crystallogr.* **2006**, *39*, 453.

[18] a) P. Buchgraber, L. Toupet, V. Guerchais, *Organometallics*, **2003**, *22*, 5144; b) S. A. Llewellyn, M. L. H. Green, J. C. Green, A. R. Cowley, *Dalton Trans.* **2006**, 2535; c) L. Mercs, G. Labat, A Neels, A Ehlers, M. Albrecht, *Organometallics*, **2006**, *25*, 5648.

[19] J. M. S. Cardoso, A. Fernandes, B de P. Cardoso, M. D. Carvalho, L. P. Ferreira, M. J. Calhorda, B. Royo, *Organometallics* **2014***, 33*, 5670.

[20] I. Yamada, R. Noyori, *Org. Lett.* **2000**, *2*, 3425.

[21] M. J. Palmer, M. Wills, *Tetrahedron: Asymmetry* **1999**, *10*, 2045.

[22] L. Y. Gu, F. Jerome, *Green Chem.* **2010**, *12*, 1127.

[23] M. B. Gawande, A. K. Rathi, P. S. Branco, I. D. Nogueira, A. Velhinho, J. J. Shrikhande, U. U. Indulkar, R. V. Jayaram, C. A. A. Ghumman, N. Bundaleski, *Chem. Eur. J.* **2012**, *18*, 12628.

[24] A. Azua, J. A. Mata, E. Peris, *Organometallics* **2011**, *30*, 5532.

[25] A. Azua, J. A. Mata, E. Peris, F. Lamaty, J. Martinez, E. Colacino, *Organometallics* **2012**, *31*, 3911.

[26] (a) I. A. Ouali, J.-P. Majoral, A.-M. Caminade, M. Taillefer, *ChemCatChem* **2009**, *1*, 504; (b) V. Polshttiwar, R. S. Varma, *Green Chem.* **2009**, 11, 1313.

CHAPTER 6. CONCLUSIONS AND OUTLOOK

We have described the first well-defined nickel(II) NHC complexes capable to catalyze the dehydrogenative coupling of aromatic thiols with Et_3SiH. The catalytic system was based on the use of half-sandwich nickel complexes bearing N-heterocyclic carbene ligands. In order to explore the effect of the alkyl NHC substituents in the catalytic performance of the catalysts, a new family of complexes (Cp*-NHC^R)NiX (X = Cl, I) bearing different wingtips was prepared and fully characterized. Interestingly, nickel complexes bearing ethyl, *iso*-butyl and *n*-butyl wingtips displayed comparable catalytic activity, while the nickel complex containing the methyl substituent on the wingtip resulted to be the worst performing catalyst.

These new nickel NHC complexes were further applied in the reduction of nitroarenes to anilines with phenylsilane. The reduction of nitroarenes was chemoselective, displaying tolerance to a wide variety of functional groups including halogens, cyano, hydroxyl, ketone, amide, methoxy, and ester groups. In addition, nitroporphyrins were selectively reduced to the corresponding aminoporphyrins.

A second part of the thesis was dedicated to the development of new iron-based catalytic systems. A new series of (Cp*-NHC^R)Fe(CO)I complexes bearing different wingtips was prepared and fully characterized. We demonstrated that iron metal complexes of the general type (Cp*-NHC^R)Fe(CO)I were efficient catalysts for the dehydrogenative coupling of alcohols with silanes. Better catalytic performances were exhibited by the iron complexes bearing *iso*-butyl and *n*-butyl wingtips, indicating that smooth modifications on metal complexes have consequences in their catalytic activity. This work

represents the first report of well-defined iron(II) complexes catalyzing the coupling of alcohols with hydrosilanes.

In addition, we have explored the effect on the introduction of hydroxyl, acetamide and amine groups on the wingtips of the NHC in half-sandwich iron(II) complexes. Interestingly, we observed a significant enhancement of their catalytic activity in transfer hydrogenation of ketones when the acetamide group was present in the NHC ligand. Using the iron complex bearing the acetamide group, an attractive green protocol for the reduction of the ketone functionality of a series of biorelevant substrates were developed, using glycerol as a hydrogen source with microwave heating.

In summary, we have contributed to expand the area of catalytic reductions using iron and nickel NHCs as catalysts. Currently, we are performing mechanistic studies of TH with the iron complex bearing the acetamide group on the NHC fragment. Metal ligand cooperativity has proved to be essential in the development of efficient iron catalysts. Understanding the mechanistic details of this reaction will allow us to develop new catalytic systems for transfer hydrogenation reactions with improved efficiencies.