Main-Group Lewis Acid/Base Pairs: Hydrogen Activation and Hydrogenation Reactions Thereof

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Academic Dissertation

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Abstract

Main-group Lewis acid/base pairs that do not quench each other's reactivity, are able to activate hydrogen and work as catalysts for hydrogenation of various unsaturated substrates. These reactions, which were previously limited to transition metal catalysis, have in just a decade emerged from proof of principle to applicable tools in synthesis.

The thesis focuses on metal-free Lewis acid/base pairs that react with hydrogen through heterolytic splitting and, more importantly, the hydrogenation reactions that consequently are accomplished. The different Lewis acid/base pairs will be discussed and their catalytic activities highlighted.

The results and discussion part is based on the authors publications. Here the first Lewis acid/base pairs utilizing oxygen donors are presented. An additional focus is on synthesizing chiral linked Lewis acid/base pairs and asymmetric hydrogenations. All three papers have a scientific importance in this rapidly developing area and have contributed to the field of metal-free hydrogenation of carbonyls as well as asymmetric reactions.

Preface

This work has been done at the Department of Chemistry, University of Helsinki during the years 2008-2015. I am most grateful to my supervisors, Professor Timo Repo and Professor Markku Leskelä, for giving me the opportunity to work with frustrated Lewis pairs and supporting my choice to study the asymmetric aspect in this field. I am ever so thankful for their guidance during these years.

There is no doubt that this thesis would not exist without the help of my co-authors and therefore I am truly indebted to all of them. Especially I want to express my gratefulness to Dr. Kirill Axenov and Dr. Imre Pápai for their valuable contributions and for showing true interest in the work.

I am thankful to Dr. Victor Sumerin for introducing me to the field of frustrated Lewis pairs and to Dr. Konstantin Chernichenko for the scientific discussions and for sharing both ideas and chemicals. Also, I truly appreciate the contribution of the highly skilled students, Katja Borre and Nina Sarnela, for assisting with the work.

I want to thank Dr. Pertti Elo for encouraging me to enquire for a PhD position in the lab and all co-workers that I had the pleasure to work with. I am especially grateful to Dr. Maija Hakola, Sirpa Vuorinen, Sari Rautiainen, Pauli Wrigstedt, Juha Keskiväli and Kalle Lagerblom for their friendship and support.

I want to thank my parents for always being there for me. Their support has meant the world to me. I can finally also appreciate my brother's interest in my work with his endless enquiries about when my defense will take place.

Most of all I want to thank my wife Elina for always standing by my side with love and support. Last but not least, I want to thank my son Alvar for being the true sunshine in my life.

Helsinki, October 12th

Markus Lindqvist

List of Original Publications

This thesis is based on the following publications:

I. Markus Lindqvist, Nina Sarnela, Victor Sumerin, Konstantin Chernichenko, Markku Leskelä, Timo Repo: Heterolytic dihydrogen activation by $B(C_6F_5)_3$ and carbonyl compounds. *Dalton Trans.* **2012**, *41*, 4310–4312, doi: 10.1039/C2DT12268E

II. Markus Lindqvist, Kirill Axenov, Martin Nieger, Minna Räisänen, Markku Leskelä, Timo Repo: Frustrated Lewis Pair Chemistry of Chiral (+)-Camphor-Based Aminoboranes. *Chem. Eur. J.* **2013**, *19*, 10412–10418, doi: 10.1002/chem.201300462

III. Markus Lindqvist, Katja Borre, Kirill Axenov, Bianka Kótai, Martin Nieger, Markku Leskelä, Imre Pápai, Timo Repo: Chiral Molecular Tweezers: Synthesis and Reactivity in Asymmetric Hydrogenation. *J. Am. Chem. Soc.* **2015**, *137*, 4038–4041, doi: 10.1021/ja512658m

Author's contributions

Paper I: The author preformed the majority of the experimental work and analyses with the help of with Nina Sarnela. Minor experiments performed by Dr. Konstantin Chernichenko and Dr. Victor Sumerin. The work was done under supervision of Prof. Markku Leskelä and Prof. Timo Repo. The author drafted the manuscript and all authors took part in preliminary revision of the paper.

Paper II: The author performed the majority of the experimental work and analyses with the help of Dr. Kirill Axenov. X-ray crystal structures measurements and refinement were performed by Dr. Minna Räisänen and Dr. Martin Nieger. The work was done under the supervision of Prof. Markku Leskelä and Prof. Timo Repo. The author drafted the manuscript and all authors took part in preliminary revision of the paper.

Paper III: The author performed the majority of the experimental work and analyses with the help of Katja Borre and Dr. Kirill Axenov. Computational results were planned and carried out by Bianka Kótai and Dr. Imre Pápai. X-ray crystal structures measurements and refinement were performed by Dr. Martin Nieger. The work was done under the supervision of Prof. Markku Leskelä and Prof. Timo Repo. The author drafted the manuscript and all authors took part in preliminary revision of the paper.

Abbreviations

A	Acceptor
ACN	Acetonitrile
BBN	9-Borabicyclo-[3.3.1]-nonane
D	Donor
d.r.	Diastereomeric ratio
DABCO	1,4-Diazabicyclo[2.2.2]octane
dba	Dibenzylideneacetone
DFT	Density function theory
dppe	1,2-Bis(diphenylphosphino)ethane
EC	Encounter complex
ee	Enantiomeric excess
EF	Electric field
ET	Electron transfer
FLP	Frustrated Lewis pair
HOMO	Highest occupied molecular orbital
HOESY	Heteronuclear Overhauser effect spectroscopy
MIC	Mesoionic *N*-heterocyclic carbene
MTBE	Methyl *tert*-butyl ether
NHC	*N*-heterocyclic carbene
NMR	Nuclear magnetic resonance
NOE	Nuclear Overhauser effect

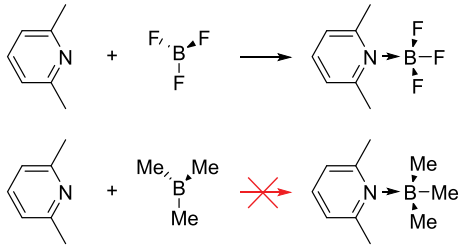
RT	Room temperature
THF	Tetrahydrofuran
TMP	2,2,6,6-Tetramethylpiperidine
TES	Triethylsilyl
TMS	Trimethylsilyl
TS	Transition state
VT	Variable temperature

Table of Contents

1 Introduction

In solution, Lewis acids and bases usually react with each other to form adducts, simultaneously quenching their reactivity. The reaction creates a bonding molecular orbital from the Lewis base's HOMO (highest molecular orbital) and the Lewis acids LUMO (lowest unoccupied molecular orbital) (Scheme 1). By hindering adduct formation the reactivity of both the acid and the base is retained. This was already known over 60 years ago but the unique reactivity was not widely explored until the discovery that main-group compounds were able to activate hydrogen at ambient temperature and pressure.

Scheme 1. Upper: Reaction between a Lewis acid and a Lewis base forming an adduct; Lower: Structures unable to react with each other, thus retaining their reactivities.[1]



The combination of hindered metal-free Lewis acids and bases and their reactivities with small molecules gave rise to a new research area called "Frustrated Lewis Pairs" (FLPs). There are numerous examples of different small molecules reacting with FLPs, hydrogen being the most important due to the possibility of further reactions with the hydrogenated species. Feasible hydrogen activation had been limited to transition metals, as the σ-complex formation involved interactions with partially filled d-orbitals and hydrogen (Figure 1). Later it has been shown that such reactions are possible with main-group compounds that exhibit simultaneous reactivity as a donor (D) and an acceptor (A) (e.g. carbenes and FLPs).

Frustrated Lewis pairs split hydrogen in a heterolytic manner resulting in onium-hydrido ion pairs. Using this species as a reductive agent is possible if the formed proton and hydride can be transferred further. Moreover, unless quenching side reactions occur, the active FLP is restored and catalytic reactions can be achieved.

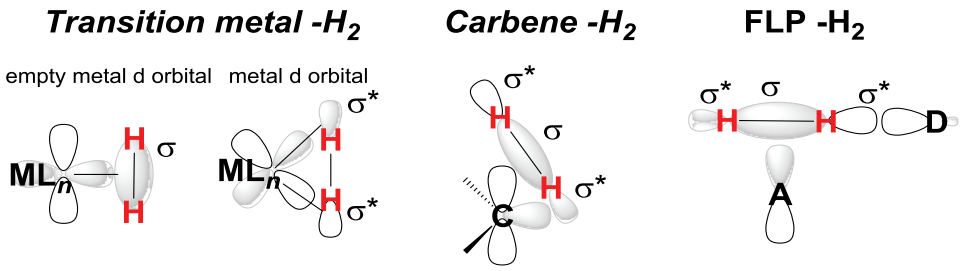


Figure 1. Simplified picture of orbital interactions in transition metals ($\sigma_{H\text{-}H} \rightarrow d_\sigma$ and $d_\pi \rightarrow \sigma^*_{H\text{-}H}$), carbenes and FLPs reacting with hydrogen.

2 Scope of the thesis

The literature review of this thesis will briefly explain how "frustration" is obtained when combining Lewis acids and Lewis bases. This will be followed by a more thorough discussion on how hydrogen activation is thought to occur and how it is experimentally realized. Further chapter division will be made according to the FLP counter Lewis base. Catalytic hydrogenations will be included in the chapters where the specific group of FLPs are discussed, followed by separate sections devoted to hydrogenations of alkenes, alkynes, carbonyls and enantioselective hydrogenations. In this thesis, the focus will be limited to main-group Lewis acid/base pairs, even though the concept of FLPs has expanded to include transition metal compounds. Also, reductions other than hydrogenations are not discussed.

The work done for this thesis is a continuation of the groundbreaking work done in the Laboratory of Inorganic Chemistry at the University of Helsinki. The preceding research in aminoboranes, their *ansa*-linking and catalytic hydrogenations have had a strong influence on the results presented in this thesis.

The results and discussion part will be presented in the chronological order in which the author's papers were published. The discussion will highlight why the study was made and briefly explain what was achieved. More complete accounts of the work can be found in the papers published (attached at the end of the thesis). The first paper is a proof-of-principle type communication for the realization of hydrogen activation with carbonyls as counter bases and the subsequent hydrogenations. These results were novel at the time and reactivity of oxygen-donor/borane FLPs were still unexplored. Later, the author's focus shifted to chiral aminoboranes and asymmetric reactions, presented in the two following papers.

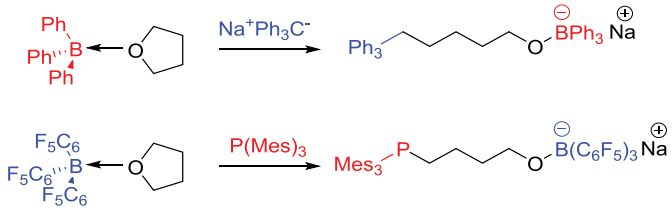
The clear aim of this thesis has been to achieve asymmetric hydrogenations of polarized double bonds. Accordingly, much work has been directed towards catalyst development and the asymmetric synthesis involved. The results included herein have contributed to both FLP catalyst design as well as their catalytic asymmetric hydrogenation reactions.

3 Literature Review

3.1 Concerted Lewis acid-Lewis base reactivity

When Lewis acid-Lewis base adduct formation is hindered, exceptional reactivity is obtained. This was already known long before the concept of FLPs emerged. An example from 1942 is the combination of BF_3 or BMe_3 with 2,6-dimethylpyridine (Scheme 1, page 10).[1] The former forms an adduct while the latter is unable to react due to steric hindrance. It was also shown as early as 1950 that the trityl anion did not displace THF in the BPh_3(THF) adduct, as anticipated, but instead ring-opening and formation of Na^+ $Ph_3B^-O(CH_2)_4CPh_3$ occurred (Scheme 2).[2] This kind of reaction has later been considered archetypal for FLPs.[3-5] Another example of a reaction which resembles the FLP type is the addition of the trityl/BPh_3 pair to one of the double bonds in butadiene.[6] Similarly, triphenylphosphine and triphenylborane were shown to react by intercepting an *in situ* formed benzyne. This resulted in the formation of a zwitterionic phosphonium borate *o*-$(PPh_3)^+C_6H_4(BPh_3)^-$.[7]

Scheme 2. An early example of simultaneous acid-base reactivity resulting in THF ring-opening, a reaction later used as a standard for testing FLP reactivity.[2,3]



The combination of Lewis acids and Lewis bases that do not react nor form reversible adducts with each other are now referred to as "frustrated Lewis pairs".[8-15] Sufficient steric hindrance is needed and the Lewis acidity and basicity has to be tuned for compatibility. This research topic is relatively new and although plenty of progress has been achieved in a short period of

time, there is still room for yearly breakthroughs, e.g. catalytic hydrogenation of alkynes to *cis*-alkenes[16] and ketones to alcohols[17,18] in 2014-2015.

By definition, a FLP is a combination of a Lewis acid and a Lewis base that, due to steric hindrance, cannot react to form an adduct. Yet, similar reactivity can be observed with Lewis acid/base pairs that do not fulfill this criteria. These are still considered as FLPs and at the moment there are three different ways in which this "frustration" can be achieved:

1 The conventional FLP is a combination of a Lewis acid and a Lewis base, both with bulky substituents hindering them from reacting with each other.[8] Even though no acid-base reactions occur, it is likely that some kinds of interactions bringing the pair in vicinity to each other are present, otherwise the termolecular reaction would become very unlikely. Calculations have predicted an "encounter complex" (EC) that is formed by attractive forces other than those of the Lewis acid-base centers.[19] For example, the often-used pentafluorophenyl-groups are known to form hydrogen bonds through the electron-rich fluorines. The Lewis acid and base can also be linked through a backbone in such a way that further reactions are favored due to high concentration of pre-organized reactive species.[20] Detailed discussion can be found in chapter 3.2.

2 A special case of the linked pairs are the ones where adduct formation is hindered or weakened by internal structural strain.[21] This allows usage of less bulky substituents on the Lewis acid and base. Even though internal adducts or dimers can form, adduct break-up to the free Lewis acid/base pair enables reactivity. Detailed discussion can be found in chapter 3.7.

3 Weak Lewis acid/Lewis base adducts can be present in free form in such a concentration that FLP reactivity is achieved.[22] Dissociation into the free Lewis acid and Lewis base might be sufficient at ambient conditions but can also be promoted by heating.[23] Also, encumbering the formation of irreversible adducts might be possible at low

temperatures while FLP reactivity still remains.[24,25] Detailed discussion can be found in chapter 3.3, 3.6 and 3.9.

Frustrated Lewis pairs that are able to heterolytically split hydrogen commonly utilize $B(C_6F_5)_3$ or a $-B(C_6F_5)_2$ group as the Lewis acid. Other boron-containing Lewis acids have also been reported to work as Lewis acids in FLP-induced hydrogen splitting, e.g. partially fluorinated aryl boranes,[26-29] chlorinated aryl boranes,[30,31] boranes,[32] antiaromatic boroles[33] and borenium cations[34,35]. This thesis will focus on these FLPs utilizing boron centers as Lewis acids. It should still be noted that few examples can be found where the closely related alanes are used for this purpose. [36,37] Additionally, FLPs utilizing silylium ions[38-40] and carbon-based[41,42] Lewis acids in hydrogen activation have been reported. Even though not discussed in this thesis, transition metal complexes can show FLP reactivity, broadening their already versatile chemistry.[42-46]

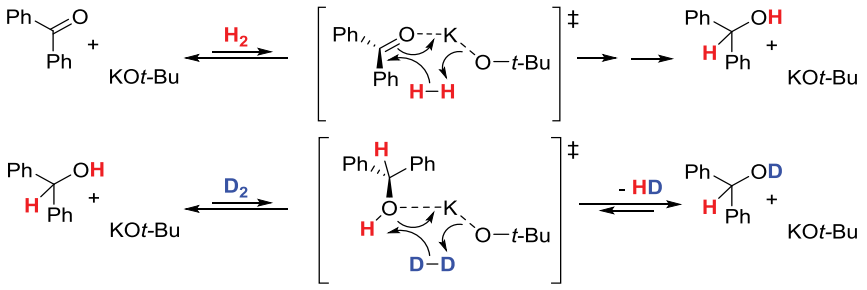
The Lewis base has mainly been varied between four main groups; carbenes, amines, phosphines and oxygen-containing compounds. These have different properties and produce varying reactivity and will thus be thoroughly discussed in the following chapters.

3.2 Heterolytic hydrogen splitting using Frustrated Lewis Pairs

With the exception of beryllium, group 1 and 2 elements are known to react with gaseous hydrogen to form the corresponding hydrides.[47,48] These are powerful reducing agents which nevertheless need to be used in stoichiometric amounts; yet they are still widely used in synthetic chemistry. Hydrogen activation at ambient temperature using main-group elements was achieved quite recently using carbenes[49] and also unsaturated alkyne analogues of germanium (ArGeGeAr) and tin (ArSnSnAr).[50-54] Also, hydrogenation of ketones was known as early as 1964 using a *t*-BuOK catalyst.[55] Unfortunately, the reaction was limited to non-enolizable substrates due to the harsh reaction conditions that were needed.[56] The mechanism proposed for this reaction has a clear resemblance to the one

proposed for FLPs (Scheme 3). The base catalyzed reaction polarizes hydrogen between the carbonyl carbon and the *t*-BuOK oxygen resulting in heterolytic splitting. It was also shown that hydrogen deuterium exchange occurs rapidly, forming HD when D_2 is used (Scheme 3).

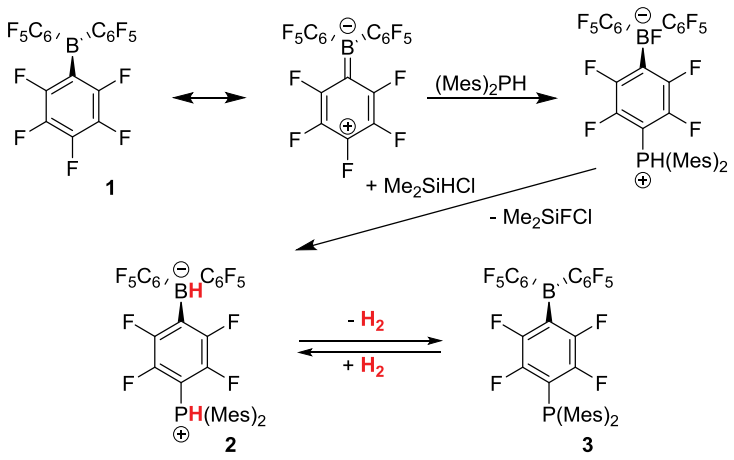
Scheme 3. Base-catalyzed ketone hydrogenation and the corresponding H/D scrambling.[56]



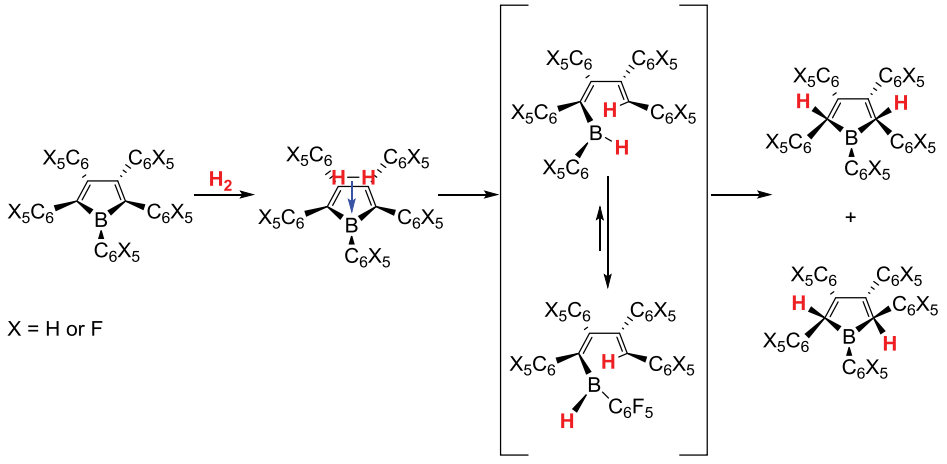
The finding that main-group compounds at ambient temperatures and pressures could activate hydrogen, in some cases even reversibly, gave rise to a new research field called "Frustrated Lewis Pairs".[57] The first reported FLP, phosphinoborane **3**, activated hydrogen at room temperature (RT) and released it back upon heating (Scheme 4). This reactivity, earlier limited to transition metal complexes,[11] quickly emerged in a significant amount of published papers, the majority of which focus on catalytic hydrogenations of unsaturated substrates.[58]

Early plausible mechanisms suggested for hydrogen activation include radical reactions as well as addition to the B-C bond.[59] The former is expected to be present in only subnanomolar concentration but the latter has been experimentally shown to be true for anti-aromatic boroles (Scheme 5).[33] This is a special case and it is unlikely that this mechanism would apply for FLPs in general. Computations show that this kind of activation e.g. with **3** would proceed through an energetically high transition state (TS) (> 50 kcal/mol) that cannot correspond to the rapid hydrogen activation observed (Scheme 4).[59] Additionally it would lead to various by-products not observed experimentally, including B-C bond cleavage.

Scheme 4. The synthesis of the first FLP and its reactivity with hydrogen.[57]



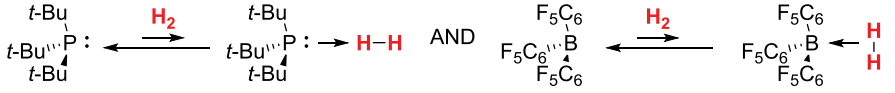
Scheme 5. Hydrogen activation occurs over the B-C bond in anti-aromatic boroles.[33]



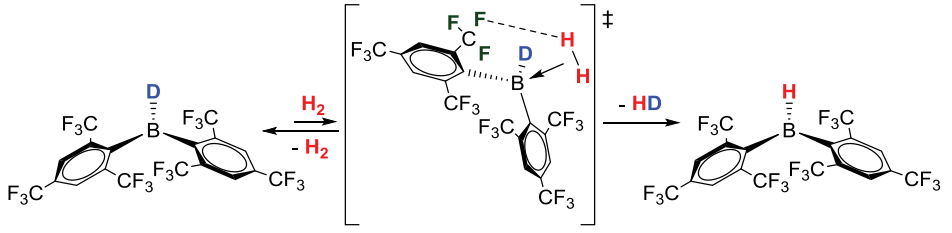
It is now generally accepted that FLP hydrogen activation is proceeding though polarization between the Lewis acid and the Lewis base resulting in heterolytic splitting of dihydrogen. How the molecules are lined up in space

during activation has been up for debate. Lately, orientations permitting end-on donor→H_2 interactions and side-on H_2→acceptor interactions are thought to be decisive (Scheme 6). Whether coordination to the Lewis base or acid initiates the reaction is inconclusive and neither interaction has been experimentally observed, suggesting that it might be a synergetic effect. Deuterium hydrogen exchange experiments have shown that a borohydride is able to exchange the hydride without a counter Lewis base (Scheme 7). Even here, internal CF···H-H interactions might be responsible for the critical stabilization needed. While the final model for hydrogen activation still remains unresolved, most studies suggest a model with a concerted reaction pathway in which both interactions are involved.

Scheme 6. The orientation of dihydrogen relative to the Lewis base and Lewis acid.



Scheme 7. Deuterium exchange reactions without the use of counter Lewis bases.[27]



For simplicity, the hydrogen activation process can be chopped into separate steps and be presented in a thermodynamic cycle (Figure 2).[20] The first step, heterolytic splitting of dihydrogen into a proton and hydride, is highly endergonic (ΔG_{HH} = +128.8 kcal/mol), which is in common with all FLPs. On the other hand, this is the only energy-consuming step for most FLPs. In cases where the Lewis acid and base form a weak adduct, energy is

also needed for dissociation into the free species (ΔG_d). Protonation of the Lewis base (ΔG_p) and hydride attack (ΔG_r) on the Lewis acid both release energy. These represent the bond energy for the formed D-H^+ and A-H^- (D: donor; A: acceptor).[60] The last step is formation of the ion pair and corresponds to its binding free energy (ΔG_{ip}). Since it has not been possible to find correlations between ΔG_{ip} and the distance between the opposite unit charges for intermolecular systems, this energy is thought to be a result of several factors (electrostatic, dihydrogen bond, steric effects solvation etc.) The Coulomb attraction between the formed cation and anion was proposed to be comparable with the amount of energy lost in scission of the strong Heitler-London covalent H-H bond, thus "Coulomb pays for Heitler-London".[61] This is an insightful but oversimplified picture and it corresponds to homolytic hydrogen splitting.[62] Frustrated Lewis pair induced hydrogen scission is commonly regarded as heterolytic and therefore the endergonicity is higher. Simultaneously, energy is also gained in the association of the newly formed onium and hydrido species.

The thermodynamic cycle for linked FLPs is reasoned in a different way. First of all, these have an entropic advantage over the intermolecular FLPs, not requiring termolecular reactions (donor, acceptor and H_2).[60] Additionally, no entropic penalty is added upon ion pair formation. For the linked pair, ΔG_{ip} quantifies the effect of intramolecular acid-base cooperativity on the thermodynamics, namely how much Lewis acidity increases upon protonation of the donor or how much Lewis basicity increases upon hydride attack on the acceptor. Here, computations reveal a correlation between the donor-acceptor distance where ΔG_{ip} corresponds to the electrostatic interactions between the charges located on the active centers.

It has not been possible to detect donor→H_2 nor H_2→acceptor interactions experimentally.[63] Therefore, the mechanism itself has been extensively studied by computational methods and has given rise to much discussion about two different models (Figure 3). For simplicity, the *t*-$Bu_3P/B(C_6F_5)_3$ pair has often been used as a model.

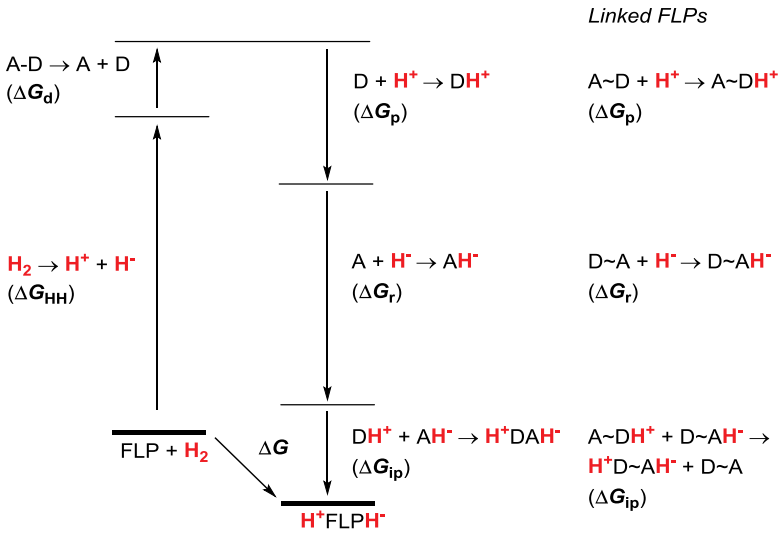


Figure 2. Thermodynamic cycle for hydrogen activation with FLPs (D: donor; A: acceptor).[20]

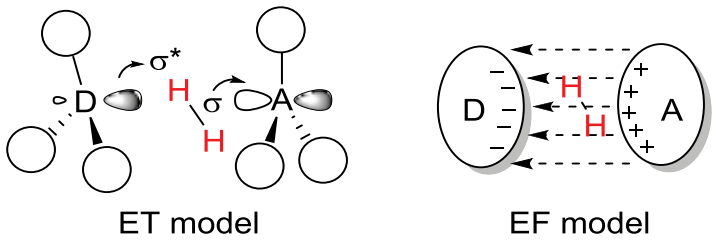


Figure 3. The electron transfer (ET) and electric field (EF) models for hydrogen splitting.

The formation of an "encounter complex" (EC) is required for both models (Figure 4).[19,64] Molecular dynamics simulations predict their existence at a relevant concentration in solution,[65] forming a "reactive pocket"[66] and facilitating the otherwise unreasonable probability of the three molecule reaction. The association energy for the formation of the *t*-$Bu_3P/B(C_6F_5)_3$ EC was calculated to be ΔE = –11.5 kcal/mol and caused by multiple CH···FC type hydrogen bonds.[19] The rigidity of the EC was later questioned due to the

unfavorable alignment of the weak CH···FC interactions.[67] It was also concluded that, despite the frustration of the EC, the P-B interactions are non-negligible. Additionally, interactions between the phosphine lone pair and fluorinated aromatic groups were found. This results in the possibility for the donor to move freely on the borane surface and provide an entrance for hydrogen.

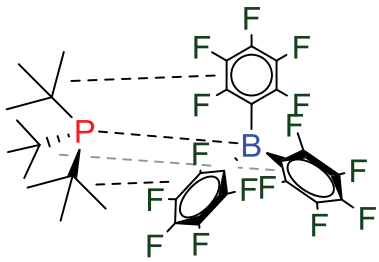


Figure 4. The *t*-$Bu_3P/B(C_6F_5)_3$ "encounter complex" formed by weak CH···FC type hydrogen bonds.[19]

Experimentally there is no definite evidence for the existence of the EC. The change in color has been proposed to be a result of non-covalent intermolecular interactions.[63,68] These interactions have been experimentally studied using ^{19}F, ^{1}H HOESY NMR techniques.[69] The $Mes_3P/B(C_6F_5)_3$ pair was used to determine orientation, which is easier as the methyl groups in the *t*-$Bu_3P/B(C_6F_5)_3$ are homotopic. It was concluded that the results strongly indicate formation of $Mes_3P/B(C_6F_5)_3$ aggregates with random relative orientations. Also, the combined DFT calculations and HOESY NMR results suggest association via weak dispersion interactions rather than interactions between acidic and basic sites.

The first model for hydrogen activation was based on an electron transfer (ET) model and had a nearly linear P···H-H···B configuration.[19] It was proposed that introducing hydrogen between the Lewis acid and the Lewis base would result in polarization of the molecule and eventually lead to heterolytic splitting. The TS was calculated to have a slightly elongated H-H bond, indicating an early TS. The ET process was explained through simultaneous $(t\text{-}Bu)_3P \rightarrow \sigma^*(H_2)$ and $\sigma(H_2) \rightarrow B(C_6F_5)_3$ in a push-pull manner. This heterolytic splitting of hydrogen was predicted to be highly exothermic (ΔE = -26.3 kcal/mol).

The ET model was later criticized for being oversimplified and a result of a computational artifact. The long phosphorous boron distance was claimed to induce a non-existing TS. An alternative model based on the electric field (EF) concept was presented to explain the heterolytic splitting of hydrogen (Figure 3).[64] It was proposed that the close vicinity of the highly Lewis acidic and Lewis basic centers would create a strong electrical field able to polarize hydrogen and split it heterolytically. Similar results were calculated for the *N*-heterocyclic carbene (1,3-di-*tert*-butylimidazolin-2-ylidene, **9**)/$B(C_6F_5)_3$ pair (see chapter 3.3).[24] The entrance of hydrogen into the "reactive pocket" of the *t*-$Bu_3P/B(C_6F_5)_3$ pair was computed to be non-linear and cause a small energy barrier in an otherwise nearly barrierless process. The TS was, much like the ET model, described to have an only slightly elongated H-H bond, the B-H bond forming slightly earlier than the P-H bond.

Recently, with the help of *ab initio* calculations, studies on how the movement of the heavy atoms influence the H-H bond cleavage were done. It was shown that the *t*-$Bu_3P/B(C_6F_5)_3$ pair appears to be frozen in the hydrogen activation time scale.[70] Even though the variation in the P-B distance is small, and mainly caused by the molecular vibrations of the flexible borane, it can still cause noticeable changes in the degree of hydrogen polarization. Calculations even suggest that the use of heavier atomic isotopes in the Lewis acid/base pair would make movement across the reaction coordinates slower and, as a consequence, slow down hydrogen activation.[71] It was also proposed that suitable conditions for hydrogen activation could be initiated already at quite large P-B distances (> 5 Å).[72] Several *t*-$Bu_3P \leftrightarrow H_2$ and $H_2 \leftrightarrow B(C_6F_5)_3$ collisions can either promote the system for development to H-H bond scission or hinder the reaction from occurring.

In summary: the details about hydrogen activation are still up for debate. Even though it is an interesting topic, the outcomes of the models are the same. Resolving the mechanism would likely ease the design of FLPs and explain why some react better than others. The bottom line is that new FLPs are still being invented quite efficiently (Figure 5).

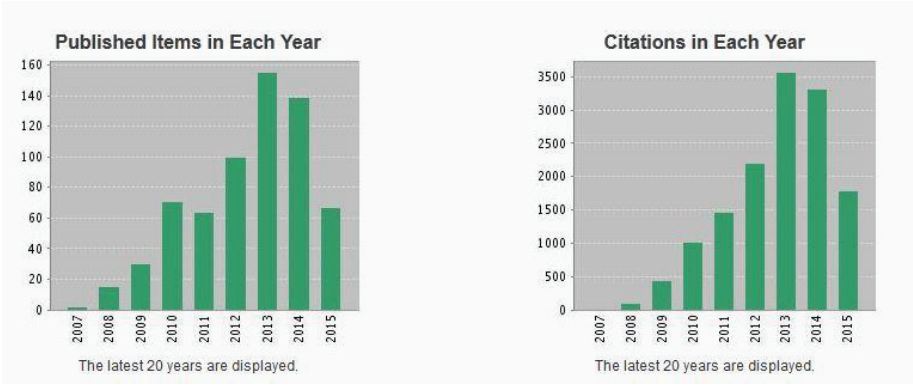


Figure 5 ISI web of science search "frustrated Lewis pairs" (May 12th 2015)

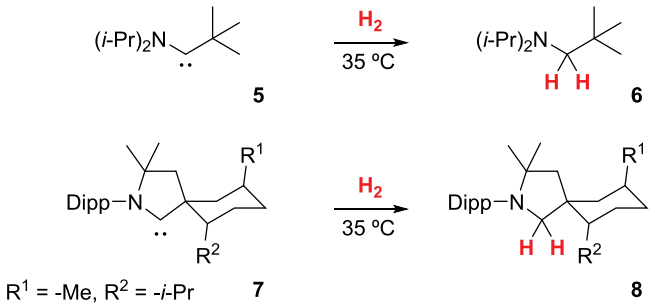
3.3 Carbene Lewis bases in FLP chemistry

In 2007 it was shown that the carbenes **5** and **7** react with hydrogen to form the corresponding amines (Scheme 8).[49] Due to the fact that singlet carbenes have a filled sp hybridized orbital and a vacant p-orbital, their reactivity towards hydrogen resembles that of transition metals (see Introduction, Figure 1). By computational methods it was shown that mono(amino)carbenes, in comparison with di(amino)carbenes, have a HOMO that is energetically higher and a singlet-triplet gap that is significantly lower. This results in a slightly higher nucleophilicity and considerably higher electrophilicity and, as a consequence, hydrogen activation can be achieved, as such, only with mono(amino)carbenes. This reactivity towards hydrogen was experimentally shown by bubbling hydrogen through a solution of the mono(amino)carbene **5** or **7** to form the corresponding amines **6** and **8** in ~ 30% conversions (Scheme 8).

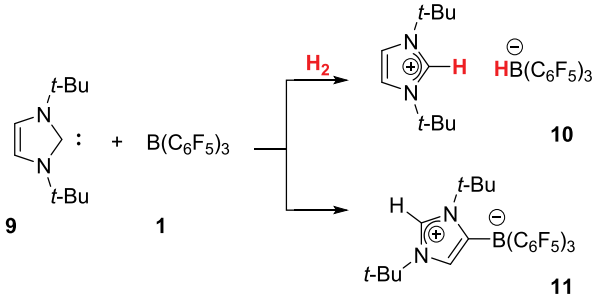
N-heterocyclic carbenes can often replace phosphines in organometallic complexes. While phosphines were known to work in FLP chemistry, the use of highly basic carbenes was a natural continuation in the field of research. There were, in fact, two independent papers reporting hydrogen activation using 1,3-di-*tert*-butyl-1,3-imidazol-2-ylidene **9** in combination with $B(C_6F_5)_3$. This pair is unstable at RT and react irreversibly to form **11** in only 2 h (Scheme 9).[24] Adduct formation could be circumvented by mixing the

carbene and cooling to -60 ˚C, resulting in no detectable reactions.[25] Stirring the cooled reaction under hydrogen resulted in formation of **10**. This reaction could also be carried out at RT when a freshly made toluene solution was purged with hydrogen and reacted for 10 min.[24]

Scheme 8. Hydrogen uptake by reactive singlet carbenes.



Scheme 9. Adduct formation and heterolytic hydrogen splitting with the carbene/$B(C_6F_5)_3$ pair.

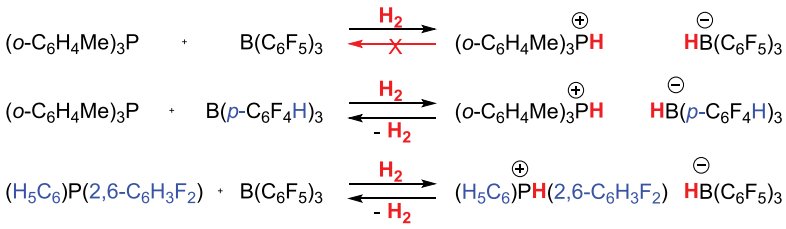


Later other bulky carbenes have been found able to split hydrogen in an analogous way,[73,74] but stability problems limit their applicability. Hydrogen splitting with these pairs is strongly exergonic and thus irreversible, ruling out their use as catalysts.[75]

3.4 FLP catalyzed hydrogenation of C=N double bonds

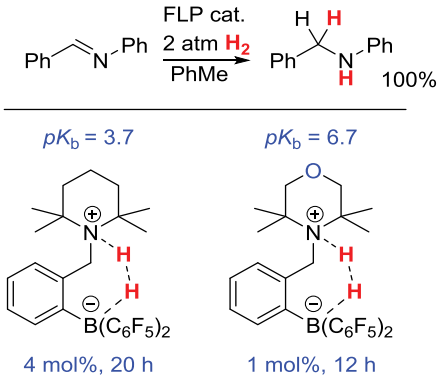
A decisive factor in catalyst design has been to achieve a FLP, with a reaction free energy close to zero, or slightly above, when splitting hydrogen.[20] This way the formed onium-borohydride is not put into a "resting state" but can potentially release hydrogen and more importantly has the ability to react further with substrates. The balance between the Lewis acid and base can be achieved by tuning the electron-withdrawing and electron-donating groups on both parts.[76] This approach has been successful for reducing the basicity of the base[29,77,78] as well as reducing the acidity of the borane,[29] thereby forming a more reactive onium-borohydride species that easily releases hydrogen (Scheme 10) or increases catalytic activity (Scheme 11).

Scheme 10. Tuning the electron withdrawing and donating groups can enable reversible hydrogen activation.[29,79]

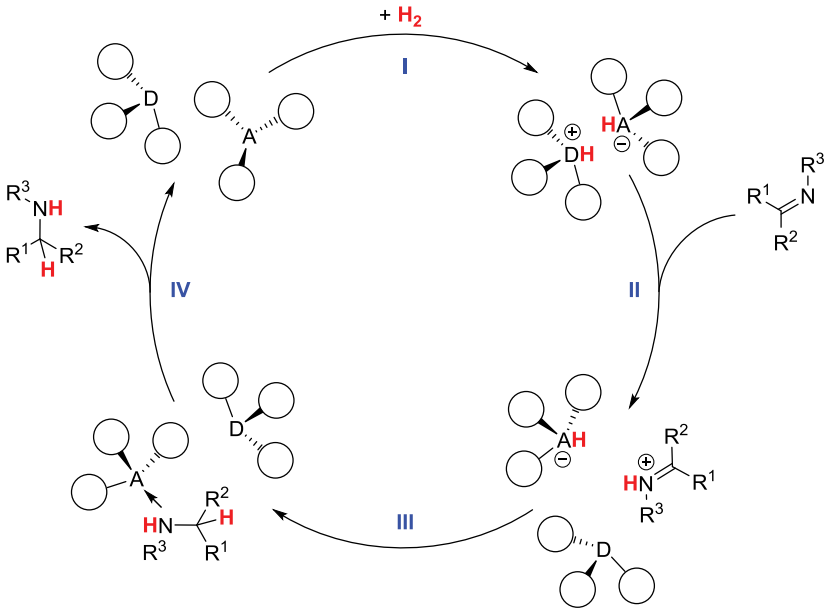


It has been proposed that the catalytic cycle for hydrogenation of imines is initiated by hydrogen activation between the Lewis acid (A: acceptor) and the Lewis base (D: donor) (Scheme 12, **I**).[77] Here, donor substrates and products might contribute as Lewis bases (not depicted). The activation step is followed by proton transfer to the substrate (**II**). This is facilitated by using less basic donors in the catalyst, accordingly producing a more acidic omium species in step **I.** Protonation of the substrate activates the imine for the reductive step which otherwise could not occur.[13] Hydride attack on the iminium carbon produces the product amine (**III**).[77] The reaction might be retarded by amine-Lewis acid adduct formation, in which case this bond needs to be broken before the catalytic cycle is fulfilled (**IV**).

Scheme 11. By reducing donor basicity the catalytic activity can be increased significantly.[77]



Scheme 12. The catalytic cycle proposed for hydrogenation of imines with FLP catalysts.[77]



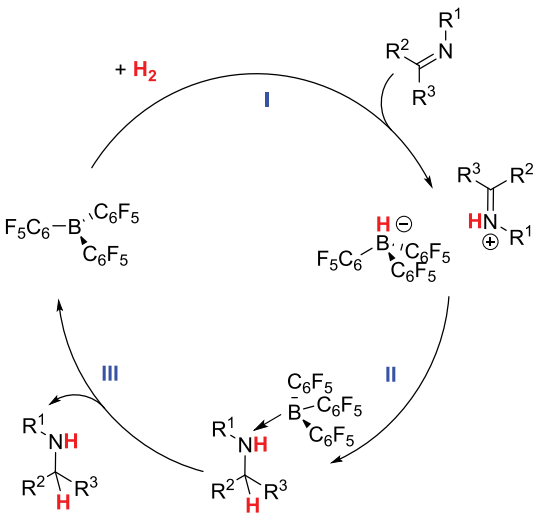
3.5 Catalytic hydrogenations using the substrate as counter base

A simple approach is to utilize the substrate as counter base in the FLP-catalyzed hydrogenations of nitrogen-containing substrates (imines,[80,81] *N*-heterocycles[26,82-84] and aniline derivatives[85]). The use of $B(C_6F_5)_3$ as a catalyst has proven to be highly versatile in these kinds of catalytic reactions. Also, analogues where Lewis acidity and steric bulk are varied have been applied to increase reactivity.

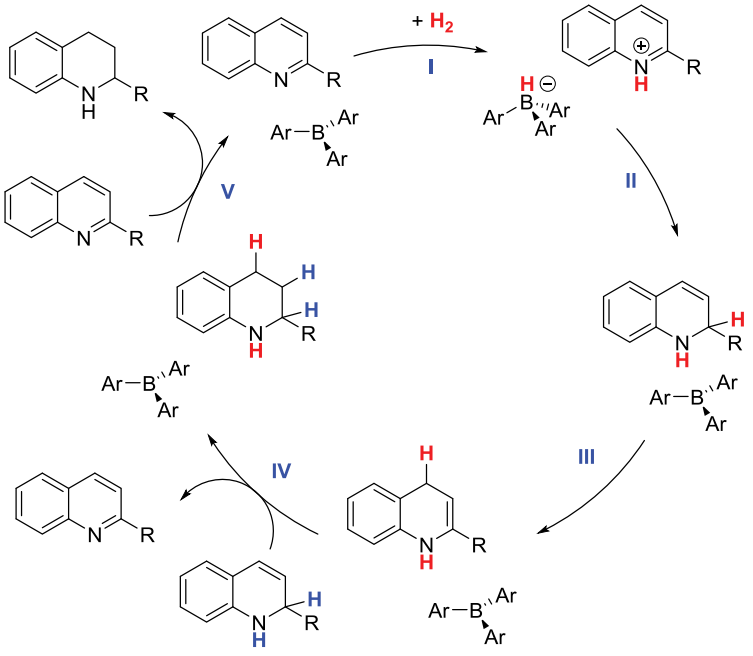
Using $B(C_6F_5)_3$ as catalyst was first introduced for the hydrogenation of bulky imines.[80,81] The mechanism is identical to the one presented above with the exception that no proton transfer is needed. Initiation by hydrogen activation between the Lewis acidic borane and the Lewis basic imine forms the activated iminium species (Scheme 13, **I**). Subsequent hydride attack on the iminium carbon results in the product amine (**II**). The catalytic cycle is accomplished in the case where no product-borane adducts are formed (**II** and **III**). In some special cases when the R^2 and R^3 groups are large, the cycle is intercepted as the hydride attack is hindered, e.g. the formation of the iminium borohydride $[MesN^+(H)=C(Me)t\text{-}Bu][HB^-C_6F_5)_3]$ supports the proposed mechanism.[80]

In comparison with other FLPs known at the time, the $B(C_6F_5)_3$ system performed quite well and high catalytic activity was reported at just 1 atm (Appendix, entry 1-5). This system was later broadened to cover *N*-heteroaromatic substrates.[82] High conversions were obtained in acceptable time scales (<16 h) and at RT, even with substrates that form borane-amine adducts with $B(C_6F_5)_3$ at 50%, due to low steric hindrance. Quinoline substrates were hydrogenated with two equivalents of hydrogen to the respective tetrahydroquinolines (Appendix, entry 6-8). The reaction was carefully studied in experiments with D_2 and the results obtained suggested the mechanism depicted in scheme 14.[26] Hydrogen activation was proposed to occur between the Lewis acidic borane and Lewis basic nitrogen of the heterocycle (Scheme 14, **I**). Subsequently, hydride attack at the 2-position produces the 1,2-dihydro-*N*-heteroaromatic (**II**). These are known to isomerize to imines in the presence on Brønsted acids (**III**)[86] and further disproportionate into the product 1,2,3,4-tetrahydroquinoline and quinoline in step **IV**.

Scheme 13. Catalytic cycle utilizing the substrate as a counter base.[80]



Scheme 14. The catalytic cycle for FLP catalyzed hydrogenation of quinolines.[26]



The (Mes)B(p-$C_6F_4H)_2$ catalyst was designed to tolerate functional groups and hinder coordination to non-bulky heterocycles.[26] Unlike $B(C_6F_5)_3$, this Lewis acid proved not to form dative bonds with the non-substituted quinoline and could thus be used as a hydrogenation catalyst for unhindered quinolines (Appendix, entry 9-13). In fact, this bulky borane is stable enough to be exposed to air without affecting its catalytic performance.

The hydrogenation of aromatics has also been reported for combinations of $B(C_6F_5)_3$ and *N*-phenyl amines.[85] Unless forcing conditions are used, one will end up with the corresponding ammonium borohydrides. Harsh conditions and prolonged reactions times will drive the reaction further through the anilinium intermediate and end up as cyclohexyl ammonium-borohydrides (Appendix, entry 14-15). This total hydrogenation of the aromatic ring is namely stoichiometric, but the reaction mediates the uptake of four equivalents of hydrogen.

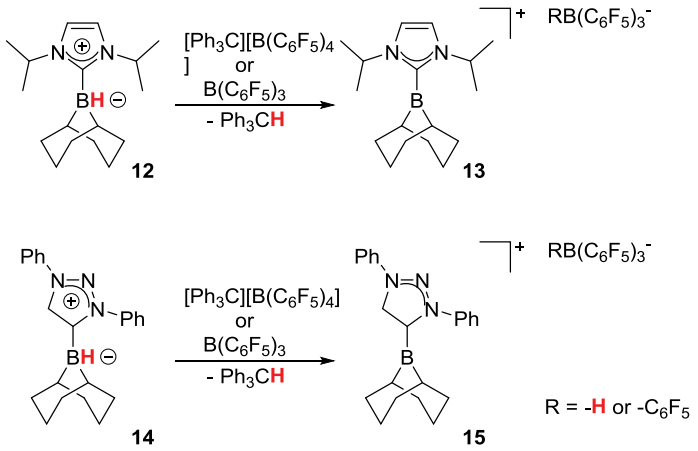
Similar stoichiometric reactions are observed with polycyclic aromatic *N*-heterocycles.[87] As it was already known that $B(C_6F_5)_3$ is able to catalytically hydrogenate some *N*-heterocycles (discussed above)[88] and stoichiometrically hydrogenate anilines, the logical next step was to combine these reactions. As a result, when polycyclic aromatic *N*-heterocycles and $B(C_6F_5)_3$ are reacted at elevated temperatures and pressures it will ultimately lead to hydrogenation of both the *N*-heterocyclic ring as well as the aniline heterocyclic ring (Appendix, entry 16). This stoichiometric reaction could also be utilized with substituted pyridine substrates leading to substituted piperidenes (Appendix, entry 17).

Using Piers' borane [$HB(C_6F_5)_2$] in combination with the electron-deficient alkene ($C_6F_5CH_2{=}CH_3$) as Lewis acid makes it possible to catalytically hydrogenate substituted pyridines to selectively give the corresponding *cis*-piperidines (Appendix, entry 18 and 19).[84] Even though this reaction requires forcing conditions, it should be noted that such reactivity has not been reported with other boranes. Later, the same reaction was achieved utilizing a borenium cation catalyst (discussed below).

Regarding the attempts to get rid of the perfluoro groups, borenium cations have shown the most promising results. The reactions of borenium cations are much studied in the literature and they are known to e.g. catalyze reductions of alkanes,[89] ketones[90,91] and imines[92]; their synthesis can be

tailored to fulfil the chemical properties needed. More recent progress concerned the borenium-catalyzed hydrogenation of imines, enamines and heterocycles (Appendix, entry 20-25).[34,35] So far the activation from the carbeneborane adduct to the borenium cation has been done using the non-coordinating trityl tetrakis(pentafluorophenyl)borate or $B(C_6F_5)_3$ (Scheme 15), which in practice means that there is no direct benefit in terms of avoiding perfluoro groups. This also indicates the higher hydricities of **12** and **14** in comparison with $HB(C_6F_5)_3^-$ and as a consequence also higher reducing power.[34] The mesoionic *N*-heterocyclic carbenes (MIC) are, due to the increased σ-donor capacity, superior to their *N*-heterocyclic carbene (NHC) analogues in terms of borenium ion stabilization[93] and reducing power, resulting in higher activity at lower pressure (Scheme 15, **13** and **14**; Appendix, cf. entry 20 and 23).[35] Also, these borenium cations showed similar inherent Lewis acidity but lower hydride affinity than $B(C_6F_5)_3$, resulting in better catalytic activity at ambient conditions (Appendix, cf. entry 8, 21 and 24).

Scheme 15. Activation of the carbeneborane adduct to form a borenium catalyst.[34,35]



The proposed mechanism is identical to the one for $B(C_6F_5)_3$ (Scheme 13) and thus also the substrate scope. Substrates with steric bulk are easily hydrogenated but the ones able to coordinate to the catalyst might lead to catalyst inhibition. The catalytic hydrogenation of substituted pyridines is

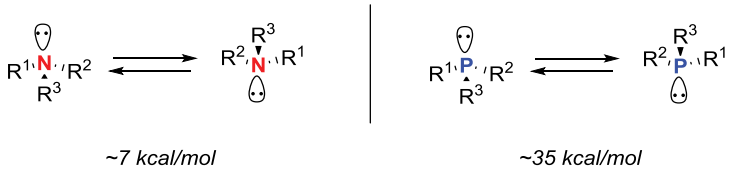
attainable with borenium catalyst **15**, yet the reaction is sluggish, (Appendix, entry 25).

Reactions utilizing the product as counter base are effective as long as the substrates have the required basicity and steric properties. While many substrates are easily hydrogenated this way, others require the addition of a Lewis base for making hydrogen activation possible. Also, by varying the Lewis base, different reactivities are achieved. This is obviously not possible when the substrate is used for this purpose.

3.6 Highly versatile amino- and phosphinoborane FLPs

Amines and phosphines, both being group 15 elements, have several similarities yet they are also different in many ways. Phosphorous is a heavier element and thus also less electronegative than nitrogen (P: 2.2; N 3.0).[94] Consequently, P-C bonds are longer than the corresponding N-C ones, 1.84 Å and 1.70 Å respectively. This creates a difference in the steric environment for amine and phosphine analogues. Additionally, they have different basicities, phosphines being less basic than the corresponding amines. In FLP chemistry these features are all very important. It is also possible, although not yet utilized in FLP chemistry, to create optically active phosphines, as the pyramidal inversion energy barrier is typically around 35 kcal/mol. The corresponding value for amines is 7 kcal/mol and therefore isomers cannot be isolated at RT unless structural constraints are present (Scheme 16).

Scheme 16. Common inversion energies for amines and phosphines.



Amino- and phosphinoboranes are by far most studies FLPs. They have also exhibited the best applicability in catalysis. In the following chapter

amino- and phosphinoboranes and their catalytic properties are presented. Their enantioselective reactions will be discussed separately in chapter 3.8.

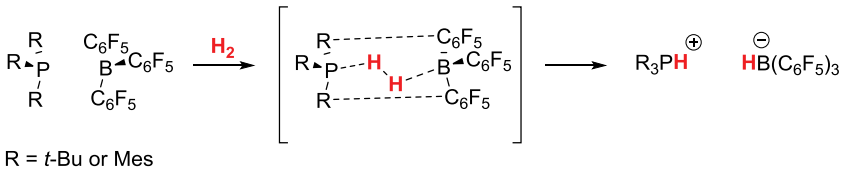
The first FLP discovered, $Mes_2P(p\text{-}C_6F_4)B(C_6F_5)_2$ (Scheme 4, **3**), was in fact highly advanced.[57] It is still one of the few that are reported to activate hydrogen reversibly and it also exhibits catalytic activity (Appendix, entry 26-30).[95] The phosphine linked to the electron withdrawing -(p-$C_6F_4)B(C_6F_5)_2$ reduces its basicity but simultaneously increases the acidity of the borane. The t-Bu_3P-analogue of **3** was also reported, but it showed no clear benefit in reactivity (Appendix, entry 31 and 32).[95] In fact, it was not reported to release hydrogen, probably because it is a stronger base and thus the reversibility is less favored.[20]

The generality of hydrogen activation with phosphinoboranes was later presented in a subsequent paper. Bimolecular pairs of commercial phosphines P(t-Bu)$_3$ or P(Mes)$_3$) and $B(C_6F_5)_3$ were reported to activate hydrogen, although not reversibly (Scheme 17).[63] Speculation has been raised regarding whether the (t-Bu)$_3$P/$B(C_6F_5)_3$ pair is activating hydrogen or hydrogenated by **3** that is also formed in small quantities in solution.[96] It was later shown that P(t-Bu)$_3$ attack on *para*-carbon can be hampered by using B(p-$C_6F_4H)_3$ as a borane.[97] This pair readily activates hydrogen demonstrating the attainable termolecular reaction. The (t-Bu)$_3$P/$B(C_6H_5)_3$ pair was also reported to cleave hydrogen but due to the high calculated free energy (ΔG = +18.2 kcal/mol) its reactivity has been questioned and the results probably need to be revisited.[60]

The use of a proton sponge, 1,8-bis(diphenylphosphino)naphthalene, in combination with $B(C_6F_5)_3$ yielded a phosphonium borohydride salt with a dynamic behavior at the cationic species.[98] This salt readily released hydrogen back when heated to 60 ˚C. Furthermore, it was possible to hydrogenate silyl enol ethers under mild conditions (Appendix, entry 35 and 36).

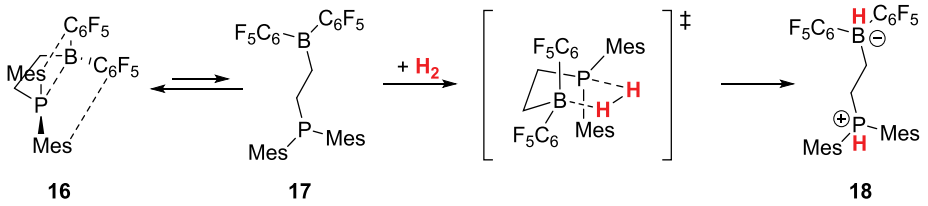
Even though $B(C_6F_5)_3$ alone is reported to work as a catalyst in hydrogenation of imines (Chapter 3.5), it should be noted that the use of phosphines can assist the reactions. This was evident when hydrogenation of electron-poor imines and protected nitriles was attempted.[80] These are not able to work as counter bases and therefore the catalytic hydrogenation require the presence of the Lewis acid/base pair (Appendix, entry 33 and 34).

Scheme 17. Hydrogen activation is possible with the combination of simple phosphines and $B(C_6F_5)_3$.[63]

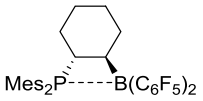


Linking the phosphinoborane through an ethylene bridge[22] resulted in the active catalyst (**16**).[99] The increased activity in comparison to **3** has been attributed to the fact that the Lewis acidity is reduced by the exchange of the electron withdrawing –(*p*-C_6F_4)- linker to –$(CH_2)_2$- (Appendix, entry 37 and 38).[13] Although the most stable form is the datively bound one (Scheme 18, **16**), the open *gauche*-**17** and *trans*-**17** forms are readily attainable at RT being only ~7 kcal/mol higher in energy.[64] This creates the active FLP that is pre-organized so the phosphine and borane are in close vicinity making hydrogen activation very rapid.[22] The produced zwitterion **18** is however not able to release hydrogen.[12]

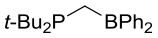
Scheme 18. Hydrogen activation with the ethylene-bridged phosphinoborane adduct.[22]



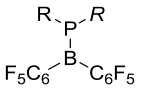
1,2-Linking was also achieved with a cyclohexyl backbone giving the phosphinoborane **19** (Figure 6). The synthesis using hydroboration with Piers' borane $[HB(C_6F_5)_2]$[100] resulted in *syn* addition putting the phosphine and borane *anti,* and in equatorial orientation, to each other.[101] The restricted rotation of the phosphine and borane favors adduct formation but the dissociation energy is (~12 kcal/mol) low enough for hydrogen activation to be achieved. However, neither hydrogen release nor catalytic activity was reported for **19**.



19



20

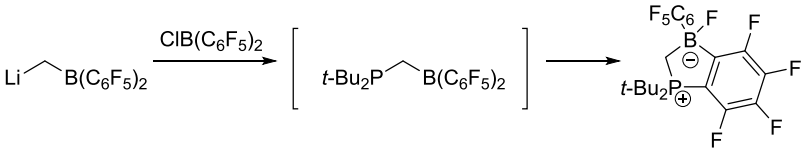


21 R = *t*-Bu
22 R = Cy

Figure 6. Different phosphinoborane linking modes that have been successful in achieving hydrogen activating compounds.

Attempts to use propylene and butylene bridges resulted in formation of five- and six-membered rings due to strong P-B dative bonds.[102] A more promising approach was to reduce the linker length. A computational study revealed potential in the use of 1,1-linking.[103] Initially, this was problematic experimentally as these structures underwent intramolecular C-F bond activation (Scheme 19).[104] The problem was circumvented by the use of less basic -$P(C_6F_5)_2$ groups but, presumably as a result of the decreased basicity, these compounds did not react with hydrogen. [105,106] Later, it was shown that substituting the borane perfluoro groups with phenyls made it possible to use the -*t*-Bu_2 group without internal nucleophilic attack occurring.[107] Surprisingly, this compound (**20**) was in fact reacting with hydrogen at ambient conditions resulting in low yield (28%, 5 h) of the corresponding zwitterionic compound. This demonstrates the importance of pre-organizing the active sites in the intermolecular structure when the aim is achieving heterolytic hydrogen activation.

Scheme 19. Intramolecular C-F activation in 1,1-linked phosphinoboranes.[104]



Real peculiarities are the zero-atom linkers (**21** and **22**) where phosphorous and boron are directly bound to each other.[108] The P-B distance for **21** is short (1.79 Å) compared to the average value (2.06 Å). Also the phosphorous and boron centers remain pseudo trigonal planar. The short

Lewis acid-Lewis base distance results in a high stabilizing effect upon reaction with hydrogen[60] and both **21** and **22** were shown to react even at RT. As a consequence, the reaction is highly exothermic (-43 kcal/mol)[108] and thus not reversible nor suitable for catalytic application.

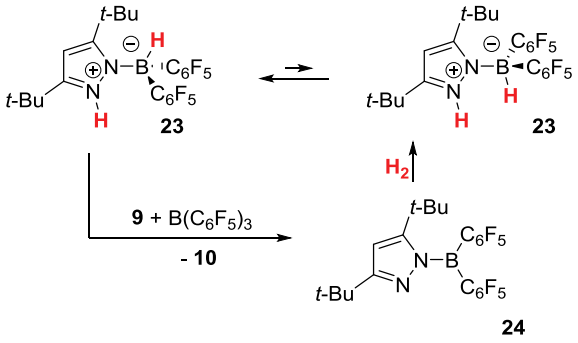
"Frustration" is preserved due to the mismatch in energy of the phosphorous lone pair and the vacant p-orbital on boron, resulting in a polarized π-bond. This kind of reactivity was first suggested in a computational paper for amine-borane adducts,[109] yet experimentally it has not been verified. An experimental study revealed that *i*-$Pr_2N(H)\cdot(H)B(C_6F_5)_2$ is indeed able to slowly release hydrogen in toluene solution at elevated temperatures (23%, 100˚C, 70 h).[110] The hydrogenation reaction, on the other hand, was not achieved even under forcing conditions nor with transition metal assisted catalysis. This was attributed to the strength of the π-bond that is much stronger when phosphorous is substituted with nitrogen (ΔH_π^P = -16.6 kcal/mol; ΔH_π^N = 29.7 kcal/mol).

The B-N linking does not quench reactivity even though "zero-linked" aminoboranes were not able to activate hydrogen. It has been reported possible within pyrazolylborane (**24**)[111] which is generated through dehydrogenation of **23**. Unlike its 9-borabicyclo-[3.3.1]-nonane (BBN) analogue, **23** does not lose hydrogen instantly upon preparation,[112] but activation with **9**/$B(C_6F_5)_3$ resulted in formation of **10** and the active species **24** (Scheme 20).[111] The unactivated substance **23** was reported to have catalytic activity in hydrogenation of *N*-(benzylidene)benzylamine giving 63% conversion (Appendix, entry 39).

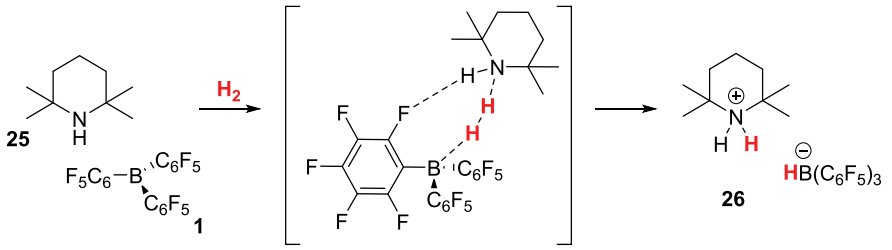
In FLP chemistry, the use of amines as donors has proven to be as effective as phosphines, if not more so. The availability and easy synthesis of amines with various sterics and basicities have resulted in a number of new FLPs. The first report combined the hindered amines, diisopropylamine or 2,2,6,6-tetramethylpiperidine **25** (TMP) with $B(C_6F_5)_3$.[68] Combining *i*-Pr_2NH and $B(C_6F_5)_3$ in solution resulted in formation of the salts [i-Pr_2NH_2][$HB(C_6F_5)_3$ and [*i*-$PrN^+{=}C(CH_3)CH_2$][$HB^-(C_6F_5)_3$]. The reverse reaction occurs at elevated temperatures, releasing the free amine and borane and simultaneously facilitating hydrogen activation. Being truly "frustrated", the TMP/$B(C_6F_5)_3$ pair reacts with hydrogen at RT and it has been proposed to occur through an "encounter-like species" held together by weak NH···FC interactions (Scheme 21). It is worth mentioning that the [$TMPH^+$][$H^-B(C_6F_5)_3$] salt reacts

with CO_2 to produce the corresponding formato borate complex.[113] This can be convert all the way to methanol by adding three additional equivalents of the ammonium borohydride and prolonged heating (Appendix, entry 40).

Scheme 20. Hydrogen activation with an N-B linked pyrazoleborane.[111]



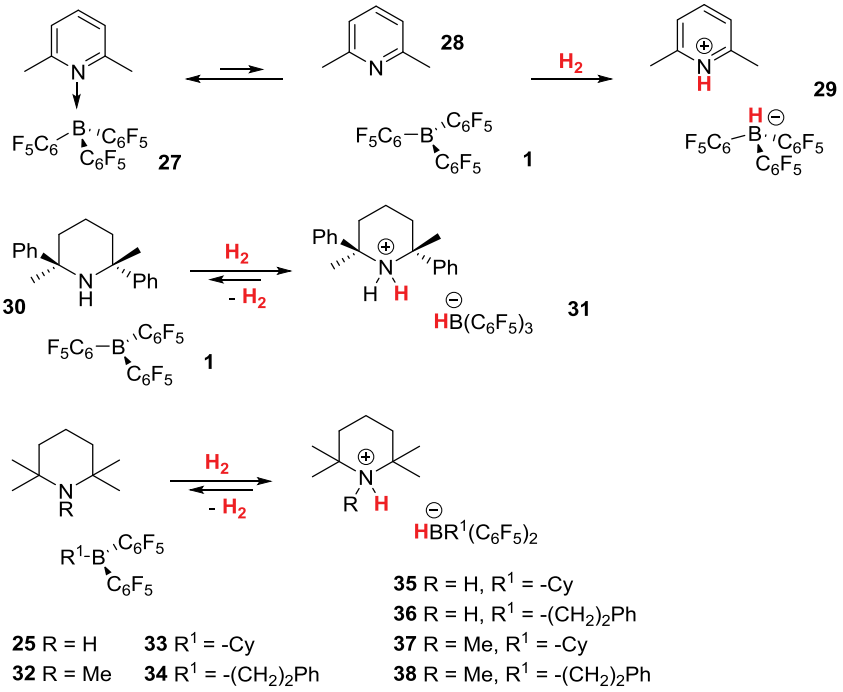
Scheme 21. Hydrogen activation with the TMP/$B(C_6F_5)_3$ pair occurs through an intermediate "encounter complex".[68]



Even though combination of 2,6-lutidine (**28**) and $B(C_6F_5)_3$ forms a weak adduct, the free amine and borane is present in high enough concentration to be able to activate hydrogen at RT (Scheme 22).[88] In addition to the moderate steric hindrance of 2,6-lutidine, its low basicity is likely to facilitate adduct break-up. Despite the low basicity, no hydrogen release was reported. Conversely, the combination of $B(C_6F_5)_3$ with the less basic analogue of TMP, trans-2,6-dimethyl-2,6-diphenylpiperidine (**30**) was shown to activate and release hydrogen back upon prolonged heating.[114] It was later shown that a more decisive factor for reversibility is the Lewis acidity of the borane.[115] Replacing one $-C_6F_5$ group in $B(C_6F_5)_3$ with cyclohexyl (**33**) or $-(CH_2)_2Ph$ (**34**) resulted in readily reversible hydrogen activation when combined with TMP

(**25**) or *N*-MeTMP (**32**). Furthermore, the combination of the considerably less Lewis acidic THF•B(2,6-$C_6H_3F_2)_3$ and 2,6-lutidine (**27**) did not even form onium borohydrides under hydrogen. Surprisingly, the Lewis acid in combination with substituted pyridines proved to be active catalysts for the hydrogenation of nitroalkenes and acrylates (Appendix, entry 41 and 42).[28] The reduced Lewis acidity and basicity results in the inability to form a stable ammonium borohydride yet preserving its activity as a catalyst. The THF adduct was used for convenience as the reactivity was the same as for the free borane.

Scheme 22. Hydrogen activation with various amine/borane pairs.[88,114,115]



The use of the hydride sponge, 1,8-bis(dipentafluorophenylboryl) naphthalene, in combination with TMP (**25**), resulted in hydrogen activation of one hydrogen molecule.[116] This bulky bisborane was not hampered by product-catalyst N→B adduct formation but instead the hydrogen activation was the limiting factor. Under forcing conditions the borane could still be

used for imine hydrogenation with the substrate working as a counter base (Appendix, entry 43).

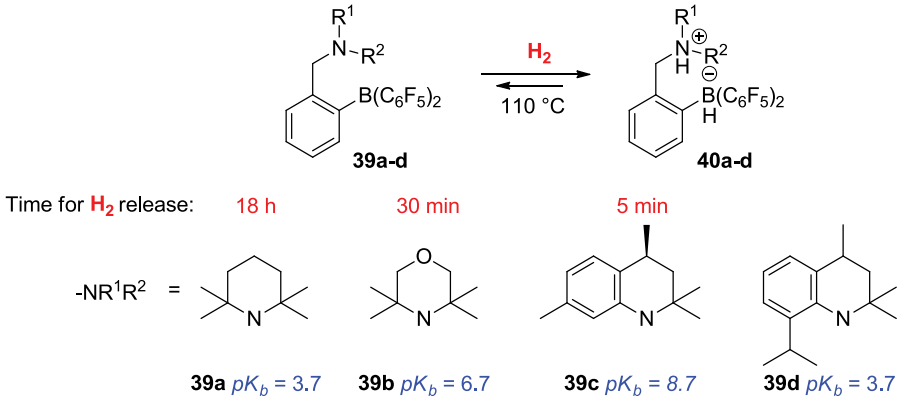
The bulky borane $MesB(C_6F_5)_2$ was synthesized to fulfill the size exclusion idea.[117] Here the strategy was to increase the steric bulk around boron to gain functional group tolerance. One should notice the diminished Lewis acidity when the $-C_6F_5$ group is substituted with the Mes-group. Hydrogen activation using the borane was probed with amines of different sterics and basicities as counter bases. It was noticed that bulky groups around the Lewis base had to be made smaller to achieve optimal conditions for hydrogen activation. The unhindered 1,4-diazabicyclo[2.2.2]octane (DABCO) proved to be of appropriate size.

The $MesB(C_6F_5)_2$/DABCO pair was an active catalyst for the hydrogenation of imines and enamines (Appendix, entry 44 and 45). Quite surprisingly it also enabled the selective hydrogenation of the α,β-unsaturated double bond in carvone, leaving the carbonyl group and the unactivated double bond untouched (Appendix, entry 45). DABCO has also been used in combination with $B(C_6F_5)_3$ for the hydrogenation of allenes and alkylidene malonates under quite harsh conditions (Appendix, entry 47 and 48).[118] Activation of the substrates are suggested to occur through a $[DABCO]H^+$ hydrogen bond to the malonate keto group. The reaction could be improved by using the less Lewis acidic $B(2,3,4\text{-}C_6H_2F_3)_3$, allowing reactivity in milder conditions and also broadening the substrate scope to nitroalkenes (Appendix, entry 49 and 50).[119]

The TMP/$B(C_6F_5)_3$ combination was further developed in a linked structure **39a** which the authors called an *ansa*-compound.[61] This linking brought the active centers close to each other, resulting in a pre-organized dynamic structure. This results in much faster hydrogen activation (Scheme 23). The structure of **40a** was determined by both X-ray and neutron diffraction[120] and it revealed a short BH···HN distance, 1.78 Å and 1.67Å respectively, indicating the presence of a partially covalent bond. Additionally calculations (1.51 Å) and NOE NMR experiments (1.6—1.8 Å in solution) suggest similar distances. At elevated temperature **40a** slowly released hydrogen to restore the aminoborane **39a** in full conversion (110 ˚C, 18 h). The authors emphasize the importance of the partially covalent dihydrogen bond being a key factor in hydrogen release.[114] Catalytic activity was also observed with various bulky imines and enamines (Appendix, entry

51-54).[61] Like in most FLP catalyzed hydrogenations, unhindered substrates/products coordinated to borane, inhibiting catalytic activity (Appendix, entry 53).

Scheme 23. Tuning the basicity significantly affects the reversibility.[77]



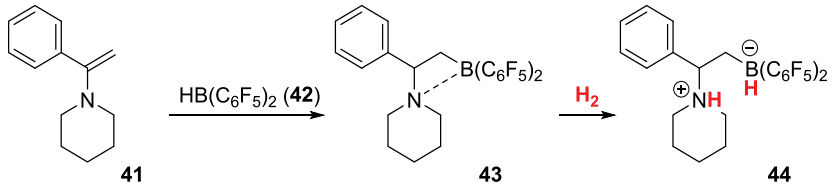
It was later realized that decreasing the basicity of the amine has a substantial effect on both hydrogen release and catalytic activity (Scheme 23).[77] The dehydrogenative reaction became 36 times faster by increasing pK_b from 3.7 for the original **39a** to 6.7 for structure **39b**. The release of hydrogen was additionally six times faster and quantitative in only 5 min for **39c**, having pK_b 8.7. Interestingly, this had no effect on hydrogen activation and all aminoboranes **39a-d** reacted fully to the ammonium borohydrides in only 5 min at RT. The fast activation and reversibility made **39c** interesting for parahydrogen-induced polarization in NMR experiments.[121] This technique made it possible to prove that hydrogen activation indeed occurs within **39c** and not in an intermolecular manner, something that was hard to prove earlier.

The seemingly small change of reducing the basicity had a huge effect on catalytic activity. Taking the catalytic cycle into account, proton transfer can be the rate determining step when the substrate has low basicity. This is clearly visible in the hydrogenation of *N*-aryl imine substrates which are easily catalyzed by **39c** whereas both **39a** and **39b** fail to produce full conversions (Appendix, entry 54-56). It is also important to notice that the steric bulk enables catalytic hydrogenation of unhindered *N*-methyl imines

that can only be hydrogenated catalytically with **39d** (Appendix, entry 57 cf. entry 53). The low basicity of the catalyst **39c** enables hydrogenation of electron-poor substrates (Appendix, entry 58). Additionally, it is possible to catalyze hydrogenation of a heterocycle (Appendix, entry 59). Here it should be noted that the use of methyl *tert*-butyl ether (MTBE) instead of toluene allows hydrogenation reactions at RT (Appendix, cf. entry 56 and 60).

The 1,2-linking of aminoboranes in manner to alkyl structures has had variable success. Such linked aminoboranes have been synthesized through enamine hydroboration with $HB(C_6F_5)_2$ (Scheme 24).[122] Many formed internal adducts and showed no reactivity with hydrogen. Surprisingly, the structure **43** reacted to form the corresponding ammonium borohydride **44** and even exhibited catalytic activity in hydrogenation of enamine substrates (Appendix, entry 61). Attempts to make a chiral 1,2-linked aminoborane catalyst using camphor backbones will be discussed in chapter 4.3.

Scheme 24. Synthesis of a 1,2-linked aminoborane and its reaction with hydrogen.[122]

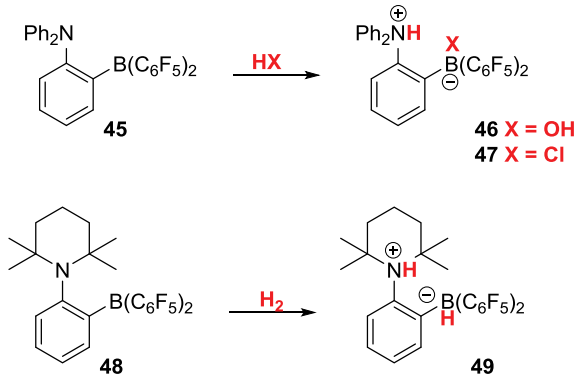


3.7 *o*-Phenylene FLPs and hydrogenation of alkynes and alkenes

The aminoborane **45** was already prepared before the FLP concept emerged.[123] This was an early attempt to produce aminoboranes that would react with $A^{\delta+}$–$X^{\delta-}$ species, including hydrogen. The authors state that "*The aminoborane* **45** *has also the potential to act as a "trap" for reactive molecules or fragments through the synergetic effects of the neighboring electron donor and electron acceptor sites*". This is how we define FLPs today but unfortunately **45** did not react with hydrogen (Scheme 25). It was later

shown that the -NPh_2 group was not basic enough to form a stable ammonium borohydride. If the amine is substituted with TMP (**48**) the reaction with hydrogen occurs rapidly forming a very stable zwitterionic salt **49**.[21] The *ortho*-phenylene linked aminoboranes experience significant electrostatic stabilization upon hydrogen activation due to the short Lewis acid-Lewis base distance.

Scheme 25. *ortho*-Phenylene linked aminoboranes with amines of different basicites.[21,123]

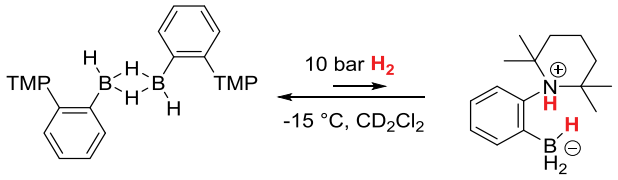


This kind of linking is in fact so rigid that even the –BH_2 group can be used as a Lewis acid in the structure, still maintaining the ability to activate hydrogen (Scheme 26). This is surprising as it exists in several different quenched states (internal adduct, *cis* and *trans*-dimers), of which the *trans*-dimer **50** is the most stable.[32] Even though the Lewis acidities of BX_3 groups are comparable with that of $B(C_6F_5)_3$, their hydride affinity in solution phase is weaker. Also the size of the group causes severe challenges in producing FLP activity. Despite the difficulties, the hindered amine in combination with the strain in the four-membered ring results in an open form lying low enough for heterolytic hydrogen splitting to occur. The reaction could be forced to 72% conversion in CD_2Cl_2 under 10 bar pressure at -15 ˚C. The polarity of the solvent was crucial for stabilizing the product and reactions in toluene under similar conditions resulted in 1.8% conversion.

The analogue *o*-$Me_2N(C_6H_4)B(C_6F_5)_2$ **52** exhibits versatile applicability. Due to the lack of amine steric bulk it exists as an internal adduct, yet it reacts with hydrogen. Evidently, adduct break-up has to occur to produce the

reactive species and thus the reaction is not very fast. The driving force for dissociation is the strained four membered ring as no bulky groups are present on the amine. On the other hand, adduct formation is the key factor for facilitating hydrogen release. Catalytic hydrogenations were also accomplished with an enamine and an unhindered imine (Appendix, entry 62 and 63).

Scheme 26. Hydrogen activation with the small $-BH_2$ borane Lewis acid.[32]



50 **51**

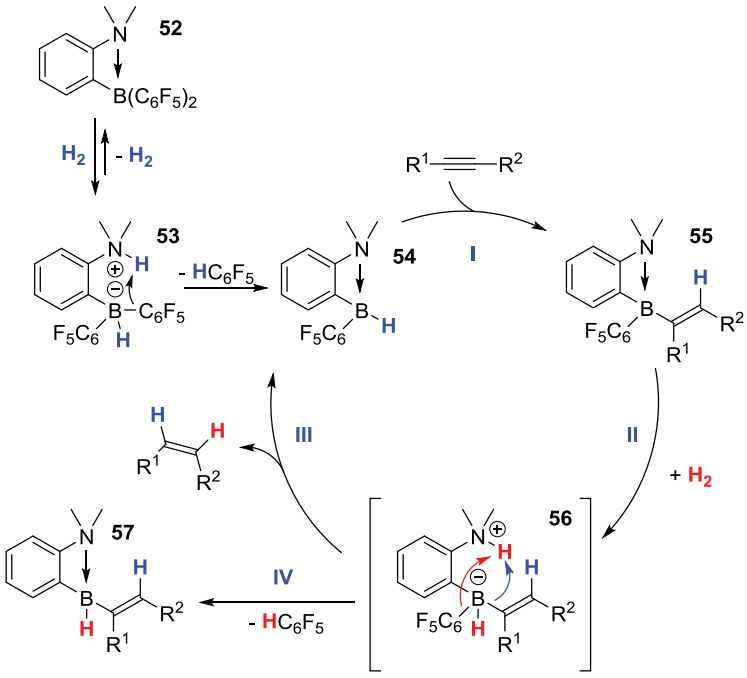
More importantly, protolysis of one $-C_6F_5$ group occurs when **52** is heated under hydrogen.[16] The close vicinity of the ammonium group facilitates elimination of HC_6F_5 and yields **54**. This resulting aminoborane, which can either be generated *in situ* or prepared in advance, turned out to be a catalyst for the hydrogenation of alkynes to *cis*-alkenes.

The catalytic cycle is initiated by hydroboration of the alkyne (**I**) with subsequent hydrogen activation (**II**) (Scheme 27).[16] The formed ammonium borohydride **56** now reacts through internal protolysis, which is equivalent to what occurred in preparation of **54**. Here the two competing reactions, elimination of HC_6F_5 (**IV**) or the alkene (**III**) (23.0 kcal/mol vs. 19.1 kcal/mol for 2-butyne), either deactivate the catalyst or complete the catalytic cycle. The energy difference is high enough for feasible catalytic reactions but limits the turnover number to 91. The *cis*-selectivity has its origins in the *syn*-hydroboration leading to a configuration that is retained through the catalytic cycle.

Hydrogenation with **54** covers a variety of different alkynes (Appendix, entry 64-68). The main limitation is terminal alkene functional groups that are hydroborated irreversibly (Appendix, entry 68). Moreover, terminal alkynes react through deprotonative deborylation and thus cannot react further; but this can be circumvented by trialkylsilyl protection (Appendix, entry 66). The reaction is also very selective to alkene formation, and no over

hydrogenation is observed for the reason that protolysis releasing the corresponding alkane is too high in energy. Nonetheless, alkanes can be hydroborated but the reaction is slow and reversible (unless they are terminal) and thus does not quench the catalyst.

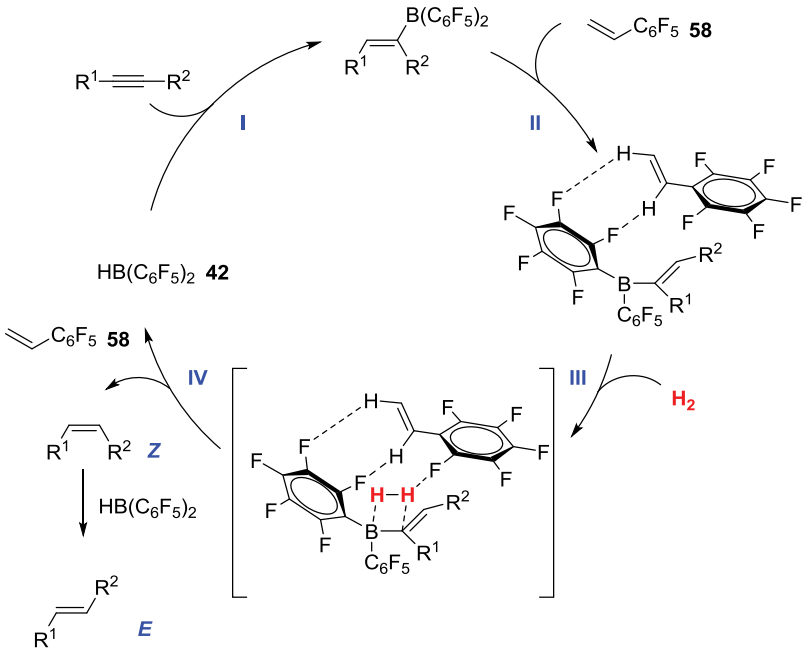
Scheme 27. Catalytic hydrogenation of alkynes using an *ortho*-phenylene linked aminoborane.[16]



Alkyne hydrogenation has also been achieved using borane $HB(C_6F_5)_2$ (**42**) in combination with pentafluorostyrene (**58**) (Scheme 28).[124] The hydroboration of alkynes are shown to be favored over the competing reaction with the electron-poor alkene **58**. Even though this reaction also occurs, it can retro-hydroborate back to the alkene and borane. In the catalytic cycle **58** is proposed to work as an encounter complex with the hydroborated alkyne intermediate (Scheme 28, **III**). This reaction requires considerably harsher conditions than the aforementioned, catalyzed by **54**, and the rate-determining step is likely to be the hydrogenolytic hydrogen activating step. Under kinetic control, this reaction yields the *Z*-product with various alkynes (Appendix, entry 69-71). The *E*-product is also attainable

through thermodynamic control as borane **42** isomerizes the alkene to the more stable product (Appendix, entry 72 and 73). Over-hydrogenation was also found to be inhibited by the addition of **58** and only small amounts of alkanes could be detected in some cases.

Scheme 28. Catalytic alkyne hydrogenation with Piers' borane catalyst and pentafluorostyrene as co-catalyst.[124]



Bases (e.g. $P(Ar)_3$[78] and Et_2O[125]) that produce highly acidic onium species upon hydrogen activation with $B(C_6F_5)_3$ have been used as catalysts for the hydrogenation of styrene derivatives and conjugated dienes (Appendix, entry 74-76). The reaction is initiated by protonation of the substrate, forming a cation, and therefore the intermediate stabilization through e.g. adjacent aryl groups in required. Dimerization was also shown to be a competing reaction and thus a balance between protonation and rapid nucleophilic attack was suggested as crucial.[78] Some conjugated dienes could also be hydrogenated to alkenes (Appendix, entry 76). As a result of a more easily accessible double bond, 2-methyl-butadiene is hydrogenated to 2-methyl-butene with 82% selectivity.

The examples above represent electron rich alkenes, and so far the hydrogenation of simple olefins need harsh conditions. It has been shown that trialkylboranes form dialkyl borohydrides and alkanes through hydrogenolysis under very forcing conditions.[126] This could be utilized for catalytic hydrogenation of alkenes, still under harsh conditions (3 mol% B(*i*-Bu)$_3$, 172 bar, 235 ˚C).[127,128] A similar approach was much later adopted with borane HB(C_6F_5)$_2$ (**42**) as catalyst.[129] The reaction conditions were much less forcing (6 bar, 140 ˚C), but quite high catalyst loading had to be used (20 mol%). They were able to hydrogenate several different alkenes, including terminal ones (Appendix, entry 77-78). Additionally, phenyl substituted olefins could be hydrogenated in high yield but the use of styrene as substrate caused problems, resulting in partial oligomerization (Appendix, entry 79-80). Mechanistics and further details for this reaction are still unclear.

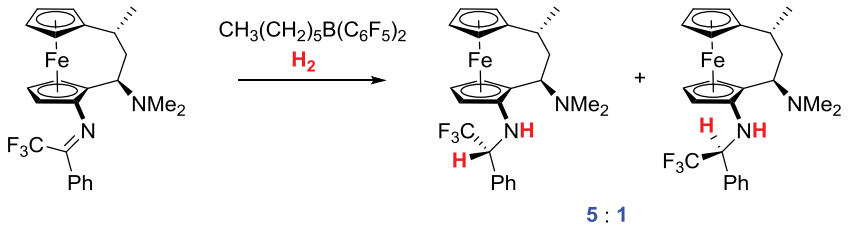
3.8 Enantioselective hydrogenations producing chiral amines

The main application of FLPs has been as catalysts in hydrogenations of imines and enamines, yet there are only few reports of such asymmetric reactions. Taking a closer look at the catalytic cycle for hydrogenation of imines (described in chapters 3.4 and 3.5) one can conclude that hydride transfer is the crucial step for asymmetric induction. Thus the preferred position of chirality would be on boron. This is not possible as boranes are trigonal planar and can only be prochiral. In this sense, it is possible to synthesize a borane that, upon formation of the corresponding borohydride, would become chiral. In practice, this would mean that the reaction should be restricted to one side of the borane, resulting in formation of just one enantiomer. This is hard to realize because without configurational restrictions the borane bonds are freely rotating and limiting reactivity to one side would be, from a synthetic point of view, very hard to achieve.

There are some reports of substrate-induced diastereoselectivity using achiral FLP catalysts. The Mes$B(C_6F_5)_3$/DABCO pair was reported to hydrogenate (+)-carvone with a diastereoselectivity of 4.3/1 (Appendix, entry 46).[117] Similar selectivity was achieved for ferroceno-based imines that were catalytically hydrogenated with $CH_3(CH_2)_5B(C_6F_5)_3$ (Scheme 29).[130]

Using $B(C_6F_5)_3$ to hydrogenate a variety of imines possessing chirality adjacent to the C=N group was studied.[131] Accordingly, when the chirality was next to the functional group carbon, high selectivity was observed even though the reaction was heated (Appendix, entry 81). However, when the substrate chirality was next to the imine nitrogen, the diastereoselectivity remained low (Appendix, entry 82). Additionally, if the *N*-alkyl group was bulky, selectivity was lost altogether (Appendix, entry 83). This highlights the importance of the proximity of the chirality inducing group when asymmetric hydrogenations are desired.

Scheme 29. Chiral substrate-induced diastereoselectivity in hydrogenation reactions.[130]



In practice, all chiral FLPs used for catalytic asymmetric hydrogenations utilize some form of chiral backbone or chiral donor to induce stereoselectivity. Screening chiral commercial phosphines resulted in weak product enantiomeric excess, 25% ee at best (eg. Appendix, entry 84).[83] These reactions were heated which probably also reduced the enantioselectivity. Chiral *ansa*-aminoboranes (e.g. Scheme 23, **39c**) were also tried out, but even though the reactivity was good with different substrates and the reactions worked at RT, the product ee's remained less than 40% (Appendix, entry 59 and 60).[77] The low selectivity is likely to be a result of low interactions and remote distances between the Lewis base and the substrate upon the chirality-determining hydride attack.

Synthesizing boranes from terpenes has been the most popular choice for making chiral borane catalysts. The first example was the pinene borane **59**, which catalyzed asymmetric hydrogenation in high yield but with only 13% ee, even though relatively mild conditions were applied (Appendix, entry 85).[81] The chiral borane used as a catalyst was reported to rearrange through

retrohydroboration to form regioisomers which may affect the enantioselectivity.[132]

This concept was later improved using boranes with derivatized camphor backbones (Figure 7, **60** and **61**).[133] Synthesis through hydroboration with $HB(C_6F_5)_2$ produces both of the *trans*-diastereomers, **60a** and **60b**. These are separated quite elegantly by kinetically controlled hydrogen activation where the product **60a** is formed faster than the diastereomer **60b**. Some enantioselectivity was obtained even when the racemate **60** was used as a hydrogenation catalyst, due to the rate difference in hydrogen activation (ee 20%). Surprisingly, catalysis with **60a** results in lower enantioselectivity and therefore **60b** was chosen for further studies. The substrate scope for the catalytic reactions compromised of different *N*-aryl acetophenone imine derivatives for which the yields and enantioselectivities were high (75–83% ee, Appendix, entry 86 and 87). In general, the conversions were high but introducing steric hindrance on the *N*-aryl group encumbered the reaction.

Furthermore, the camphor backbone was utilized in the linked structure **61**.[134] The donor–acceptor distance is large and hence the typical advantage of linked structures is lost. In contrast to its predecessor, **61** yields only one diastereomer in the preparative hydroboration step and quite surprisingly the hydrogenated zwitterionic salt is stable enough to be purified by column chromatography. In catalysis, its performance was poorer than the unlinked pair, needing longer reaction times and still giving lower yields and slightly lower ee's (Appendix, entry 88). Yet, the unique stability made it possible to recycle the catalyst without loss in activity (Appendix, entry 89).

Two clear attempts to make linked camphor-based aminoboranes failed to work as hydrogenation catalysts. These will be discussed further in chapter 4.3.[135,136]

In a recent paper, chiral binaphthyl dienes were used for the *in situ* preparation of diboranes (Figure 7, **62**; notice the varying Ar groups in Appendix, entry 90–95 and 97) through hydroboration with $HB(C_6F_5)_2$.[137] As the hydroboration is a clean reaction, no purification of the borane is needed. This is a clear advantage, yet the synthesis of the diene is a multistep synthesis, starting from 1,1'-bi-2-naphthol and requiring tedious synthetic work.[138-140] Bulky aryl groups at the 3-position in the catalyst framework (**62**) proved to be optimal in hydrogenation reactions. Different *N*-aryl

acetophenone imine substrates, possessing both electron-withdrawing and donating groups, were hydrogenated with high yields and ee's (Appendix, entry 90 and 91). The hydrogenation proceeded smoothly at room temperature but 20 bar pressure was still needed. Interestingly, alkyne functional groups that often deprotonate to form alkynylborates, were tolerated (Appendix, entry 92). Yet, *ortho*-substitution of the substrate *N*-aryl group resulted in lowered selectivity (< 40% ee), apparently because of steric factors. Also, an attempt to hydrogenate a dialkyl ketimine resulted in high yield but total loss of chiral induction (Appendix, entry 93). The addition of P(*t*-Bu)$_3$ as a counter base for **62** broadened the reaction scope to include aryl or conjugated silyl enol ethers, which were hydrogenated in high yield and with ee's ranging between 88-99% (Appendix, entry 94 and 95).[141] It is noteworthy that silyl enol ethers cannot be hydrogenated with metal catalysts.

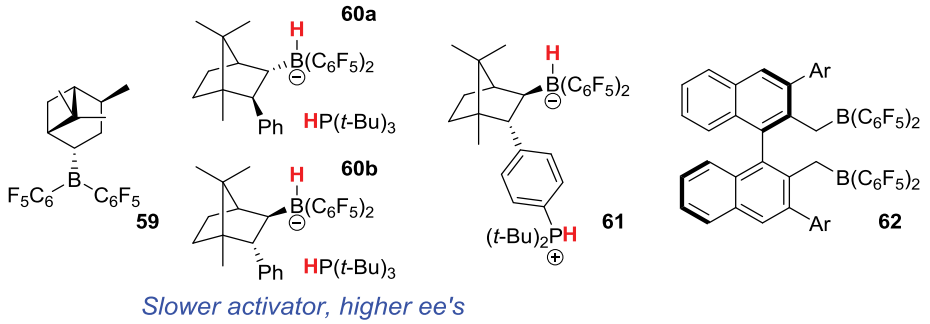


Figure 7. Chiral FLP catalysts for asymmetric hydrogenation of imines.[81,133,134,137]

Asymmetric hydrogenations of heterocycles have also been studied. The hydrogenation of 2,3-disubstituted quinoxalines with achiral catalysts was shown to be *cis*-selective reaching very high diastereomeric ratios (d.r.) in controlled reaction conditions (Appendix, entry 96).[142] When the quinoxalines were 2,3-alkyl-aryl-substituted, this reaction could be made enantioselective using **62** as catalyst. The reaction gave both high d.r. as well as ee's for a variety of substrates (Appendix, entry 97). Unfortunately, alkyl-alkyl or aryl-aryl substitution resulted in low ee's. Also, the asymmetric induction was reduced when 5-substituted quinoxalines were hydrogenated (67% ee).

As there are only a few papers on asymmetric hydrogenation catalyzed by FLPs, there will very likely be several papers concerning the topic in a near future. There is also plenty of room for further development in the field of asymmetric hydrogenation of imines, enamines, *N*-heterocycles and silyl enol ethers. Even though the hydrogenation reactions of alkenes, alkynes and alcohols are known, no reports have been published for the corresponding asymmetric hydrogenations.

Further discussion on the topic of catalytic asymmetric hydrogenation of imines and enamines can be found in chapter 4.3.

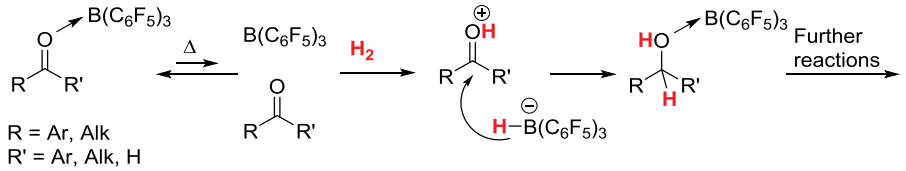
3.9 Utilization of carbonyls and ethers as counter bases

It was thought that the Lewis acidic boron, being highly oxophilic, makes reactions with oxygen containing compounds extremely challenging. The coordination of oxygen lone pairs increases electron density in the borane and simultaneously decreases the Lewis acidity. It was known that reversible adducts could be formed with the highly Lewis acidic $B(C_6F_5)_3$ and a variety of carbonyl compounds, aldehydes, ketones esters and amides.[143] The association energies of the borane and the carbonyl decreases with the carbonyl basicity, reaching -5.8 kcal mol^{-1} for benzaldehyde and -4.1 kcal mol^{-1} for acetophenone at RT. While these are reasonable values for formation of FLPs through dissociation, the low basicity of the carbonyls in comparison to the corresponding nitrogen analogues create highly acidic onium ions upon hydrogen activation.

Catalytic hydrogenation of carbonyls using the FLP created by dissociation of the substrate working as counter base, together with a catalytic amount of $B(C_6F_5)_3$, was first proposed in a computational paper.[144] Hydrogen activation itself was later attained experimentally but only sub-stoichiometric hydrogenations were achieved. This was first shown with aromatic, non-enolizable carbonyls.[23] Later the substrate scope was broadened to aliphatic ketones.[145] Surprisingly, no side reactions due to substrate enolization were observed for these substrates.[145] In contrast, the reactions between $B(C_6F_5)_3$ and the aldehyde Et_2CHCHO gave a clean product of the boron enolate $Et_2C{=}C(H)OB(C_6F_5)_2$ and HC_6F_5 and attempts to hydrogenate other aliphatic aldehydes led to complex mixtures.

Unfortunately, attempts to realize catalytic reactions with carbonyl substrates failed due to side reactions with the product alcohols (Scheme 30). Strong alcohol-borane coordination and dehydrations quench further reactivity. It has also been suggested that the carbonyl onium ion formed upon hydrogen activation is acidic enough to break the B-C bond in $B(C_6F_5)_3$.[17] Thus, catalytic reactions going through activation between carbonyl moiety and boranes have not been successful as they decompose into HC_6F_5 and $ROB(C_6F_5)_2$.[23]

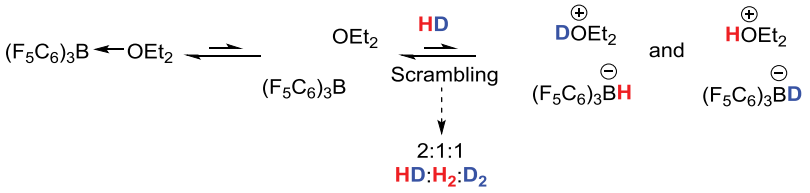
Scheme 30. Stoichiometric hydrogenations with carbonyl→$B(C_6F_5)_3$.[23,145]



More recently it has been shown that activation between boranes and ethers is possible. Calculation show that the $Et_2O/B(C_6F_5)_3$ pair is thermally accessible,[125] even though hydrogen activation in CH_2Cl_2 is calculated to be clearly less exothermic than that of the *t*-$Bu_3P/B(C_6F_5)_3$ pair, corresponding to the lower basicity of ether. The solvation effect by addition of ether molecules lowers the energy (ΔE) significantly but the increase in entropy ends up being similar, ΔG ~10 kcal/mol. Hints of FLP reactivity were experimentally revealed in VT NMR experiments showing ether oxygen lone pair inversion with a 2:1 mixture of diethyl ether and $B(C_6F_5)_3$ in CD_2Cl_2 solution. This corresponds to reversible adduct formation and even though the zwitterionic species couldn't be detected, activation was confirmed by reaction with HD at ambient temperature under 4 atm pressure. In only 15 min, the statistical mixture of $HD/H_2/D_2$ in proportions 2:1:1 was observed (Scheme 31). This pair was also able to reduce 1,1-diphenylethylene to 1,1-diphenylethane in high yield. The proposed mechanism was analogous to other FLP catalyzed hydrogenation of polarized double bonds. Hence, the carbocation produced upon protonation of 1,1-diphenylethylene is stable enough for further reduction to occur with the borohydride while less stable intermediates mainly undergo Friedel-Crafts dimer formation.

Ring-opening of THF was one of the first reported reactions for FLPs and thus ethereal solvents have not been widely used in FLP-catalyzed hydrogenation reactions.[3] Recently, heterolytic hydrogen activation of the THF/$B(C_6Cl_5)(C_6F_5)_2$ pair was detected spectroscopically, utilizing VT NMR techniques.[4] Substitution of one perfluorophenyl group with a perchlorophenyl one increases electrophilicity but at the same time Lewis acidity is reduced due to increased steric hindrance.[146] Thus THF and even water binds weakly and reversibly to it, making it air and moisture stable. The adduct THF→$B(C_6Cl_5)(C_6F_5)_2$ is too electron-rich to work as a counter acid in FLP reactions. Therefore, dissociation to the active FLPs is needed to activate the catalyst from its resting state. This equilibrium is strongly shifted towards adduct formation and thus this is the borderline between a classical adduct and FLP.

Scheme 31. Ethers working as donors in FLP-induced hydrogen-deuterium scrambling.[125]



Nevertheless, the THF→$B(C_6Cl_5)(C_6F_5)_2$ adduct could be used for reduction of imines using THF as solvent (Appendix, entry 98).[4] It is worth noting that these weakly basic imines could not be hydrogenated catalytically with $B(C_6Cl_5)(C_6F_5)_2$ alone in non-donor solvents. As activation cannot occur between the Lewis acid and the substrate due to its low basicity, the importance of forming a highly Brønsted acidic protonated THF becomes relevant.

3.10 Catalytic hydrogenation of carbonyls in ethereal solvents

Potassium *t*-butoxide was the first example of a main-group catalyst being able to hydrogenate benzophenone.[55] Even though this study was done decades ago, the catalysis itself has many similarities to what is thought to be peculiar for FLPs. The mechanism proposed for this is heterolytic spitting of hydrogen between the carbonyl carbon working as a Lewis acid and the alkoxide as a base.[56] Forcing conditions are required and the strongly basic medium limits the substrates to non-enolizable ketones. Catalytic hydrogenation of carbonyls was one of the most challenging reactions for FLPs and were not unveiled until 2014. Before this, several attempts were made to hydrogenate various carbonyl substrates, all resulting in stoichiometric reactions (Discussed in chapter 3.9).

Recently, two parallel studies on catalytic hydrogenation of ketones were reported utilizing ethers as counter bases. The two studies have close to identical results with the main difference that one uses diethyl ether[17] and the other one 1,4-dioxane[18] (Appendix, entry 99-104). It is proposed that the decisive advantage, in comparison to the use of the carbonyl group as donor, is the lesser acidity of the ether onium ion not being able to break the B-C bond.[17] Also, the competing coordination of the polar solvent dissociating the product alcohols might be important.[18] The THF→$B(C_6Cl_5)$-$(C_6F_5)_2$ adduct was already known to activate hydrogen[7] but gave only slightly catalytic reactions due to quenching water release in the side reaction forming ether from the product alcohol.[18] Increasing steric bulk on the Lewis acid resulted in a less reactive borohydride and consequently $B(C_6F_5)_3$ was tried. To improve the reaction, 1,4-dioxane was chosen as counter base. It is a weaker donor and, as a direct consequence, coordination to Lewis acids is not as strong as for THF. Due to the lower polarity of 1,4-dioxane, proton solvation is thought to be suppressed and the reaction medium is less favorable for dehydrative ether formation. This resulted in better selectivity and cleaner reactions. The 1,4-dioxane→$B(C_6F_5)_3$ system still struggles with electron-rich compounds and hydrogenation of acetophenone leads, through dehydration, to styrene with low conversion (Appendix, entry 103). Ether, on the other hand, being even less polar and forming a less acidic onium species, is able to hydrogenate acetophenone in combination with $B(C_6F_5)_3$ to form 1-phenylethanol in high yield (Appendix, entry 100).[17] Surprisingly, the first

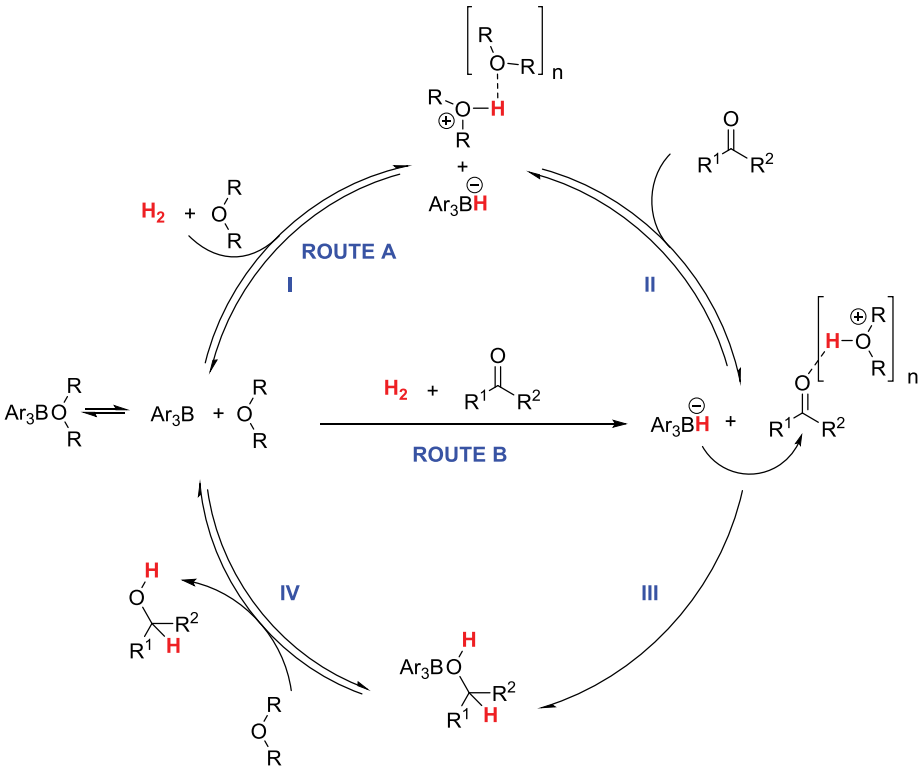
results of FLP-catalyzed hydrogenation of an alkyl aldehyde is reported for the ether→$B(C_6F_5)_3$ system (Appendix, entry 101). Catalytic hydrogenation of electron-poor aryl aldehydes is also possible with the 1,4-dioxane→$B(C_6F_5)_3$ system (Appendix, entry 104).[18]

The mechanism suggested for both systems is the same and analogous to what is typical for FLPs (cf. scheme 32 and scheme 12). Hydrogen activation is proposed to occur as described above, between the ether/Lewis acid pair (Scheme 32; route a, **I**). This is followed by Brønsted acid activation of the carbonyl substrate (**II**) and subsequent hydride attack producing the corresponding alcohol (**III**). The huge excess of the donor solvent results in competitive coordination to the Lewis acid, simultaneously releasing the alcohol (**IV**). One cannot fully rule out the possibility of activation between the carbonyl moiety and $B(C_6F_5)_3$ (route b), even though it seems unlikely as the solvent (working as donor) is present in huge excess.[17]

Further studies on the mechanism show that activation of the carbonyl substrate through a solvated proton is likely to occur prior to hydride attack on the carbonyl carbon. Using Jutzi's acid $[Et_2O)H][B(C_6F_5)_4]$[147] and 1-phenyl-2-butanone in *i*-Pr_2O made it possible to create the activated carbonyl species, where the onium *i*-Pr_2O is hydrogen bound to the carbonyl ([*i*-$Pr_2OH]\cdots O=C(CH_2Ph)CH_2CH_3$).[17] The importance of the proton-mediated activation was further proven by trying to react [*n*-$Bu_4N][HB(C_6F_5)_3]$ with ketones in 1,4-dioxane. As no reaction occurred, further attempts adding $B(C_6F_5)_3$ to the reaction mixture were studied. This resulted in slow reduction but not rapid enough to account for the activity observed in the hydrogenation reaction. Aldehydes, on the other hand, reacted rapidly under these conditions. From this it can be concluded that aldehydes and ketones react through different activation modes. Here aldehydes are activated by Lewis acids whereas ketones are reliant on Brønsted acid activation.

Enabling catalytic hydrogenation of carbonyl compounds is an important discovery. Here, the issue of alcohol group tolerance is circumvented by using ether solvents that competitively coordinate to the Lewis acid. Also, the formed onium species is less acidic than the corresponding species obtained in hydrogen activation with the carbonyl moiety, so no B-C bond cleavage occurs. So far only two papers have been published concerning this topic but most certainly these reactions will be further developed, e.g. towards asymmetric reactions.

Scheme 32. The catalytic cycle for hydrogenation of carbonyls utilizing $B(C_6F_5)_3$ in ethereal solvents.[18]



4 Results and Discussion

4.1 Experimental notes

Moisture and air-sensitive reactions were performed under an inert atmosphere using Schlenk techniques or with an argon glovebox (MBraun Unilab). Scientific Hydrogen 6.0 was purchased from Oy Aga Ab and used as such through a double manifold H2/vacuum line. Solvents were dried using a Vacuum Atmospheres Company VAC solvent purifier or according to published procedures and distilled under an argon atmosphere. Reagents were purchased from Sigma-Aldrich, Acros Organics or Strem and used as such. NMR experiments were performed on a Varian Mercury 300 MHz or Varian Inova 500 MHz instrument. HPLC chromatograms were recorded on a Hewlett-Packard 1100 using a Daicel Chiralcel OJ-H or OD-H 0.46 cm x 25 cm columns with equivalent guard columns. Specific rotations were measured on a JASCO DIP-1000 polarimeter. Absolute configurations were determined by comparison of reported retention times, unless otherwise mentioned.

Detailed experimental procedures can be found in the papers attached and as supporting material for the publications via publisher homepages: http://pubs.rsc.org; http://onlinelibrary.wiley.com/ and http://pubs.acs.org/.

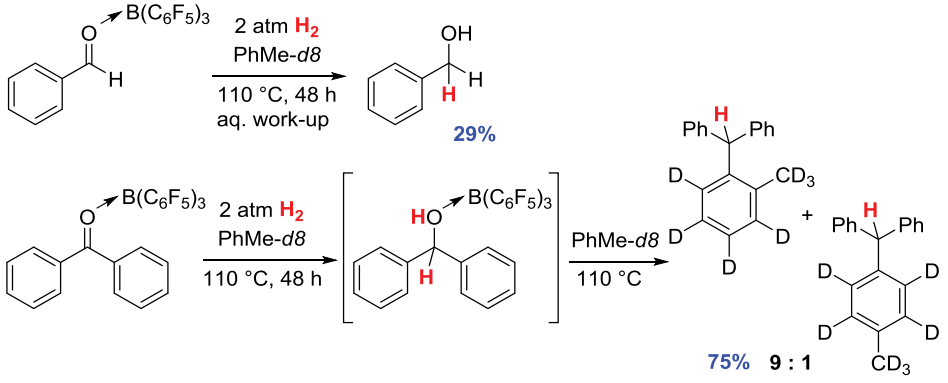
4.2 Carbonyl compounds and $B(C_6F_5)_3$ for hydrogen activation

At the time of the study there were no experimental reports on hydrogen activation using oxygen as counter base in FLP chemistry. There was a theoretical paper suggesting the possibility of hydrogen activation between such pairs.[144] It was proposed that catalytic hydrogenation of carbonyl moieties would be possible with $B(C_6F_5)_3$. Nyhlén and Privalov found that the HOMOs of ketones are close in energy to the HOMO of *t*-BuN(H)CH_2Ph which was known to work as a donor. The expected energy for hydrogen activation

was calculated to be higher due to fact that carbonyls are weaker bases. It had also been shown experimentally that carbonyl→$B(C_6F_5)_3$ adducts dissociate relatively easily, e.g. 5.8 kcal/mol for the benzaldehyde→$B(C_6F_5)_3$ adduct at RT.[143] Boranes tend to be extremely oxophilic and the dissociative step is very important for hydrogen activation to be possible.

Serendipitously, during our attempts to use $B(C_6F_5)_3$ and the proton sponge, 1,8-dimethoxynaphthalene, for hydrogen activation with subsequent reduction of benzaldehyde, we noticed sub-stoichiometric product benzyl alcohol formation. On further investigation, we found that the reaction proceeded better without the proton sponge. The stoichiometric reaction with $B(C_6F_5)_3$ and benzaldehyde in deuterotoluene under 2 atm H_2 for 48 h at 110 ˚C followed by aqueous work up resulted in 29% conversions to benzyl alcohol (Scheme 33). The analogous reaction with benzophenone resulted in 75% conversion of diphenyltolylmethane, in which the tolyl group was deuterated. Reaction with D_2 in toluene confirmed the origin of the reductive hydride, as it resulted in deuteration of the methane trityl group. While this was still not the anticipated product, we speculated that a diphenylmethanol→$B(C_6F_5)_3$ intermediate could react through Friedel-Crafts alkylation with the solvent. This assumption was confirmed by heating diphenylmethanol with $B(C_6F_5)_3$ under the same conditions, leading to the exact same products (Scheme 33).

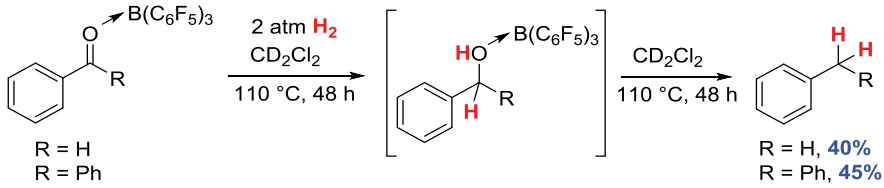
Scheme 33. Hydrogenation reactions with the carbonyl/$B(C_6F_5)_3$ pair.[23]



To avoid Friedel-Crafts alkylation these reactions were performed in CD_2Cl_2. In the case of benzaldehyde the hydrogenation resulted in 40%

conversion to toluene (Scheme 34). The corresponding reaction with benzophenone resulted in 45% conversion to diphenylmethane. To establish the reaction pathway, as the deoxygenation can occur both through hydrogenation or disproportionation, we performed a reaction with the diphenylmethanol→$B(C_6F_5)_3$ adduct under argon. This reaction also resulted in a one-to-one mixture of benzophenone and diphenylmethane, verifying the disproportionation pathway. Attempts to make full conversions failed. Increasing the amount of Lewis acid facilitated other unwanted side reactions. All of these reactions resulted in various $B(C_6F_5)_3$ decomposition products, e.g. HC_6F_5 and $(C_6F_5)_2BOH$.

Scheme 34. Deoxygenative hydrogenations facilitated by $B(C_6F_5)_3$.[23]



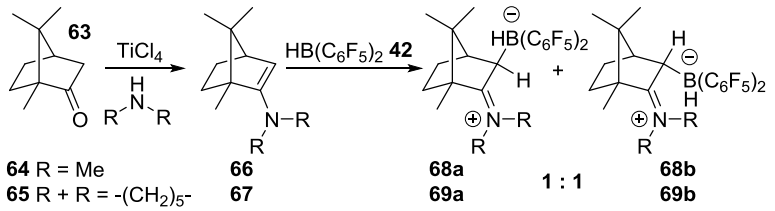
Even though e.g. benzaldehyde had been reduced with FLPs before,[22,68,95] this was the first example of hydrogen activation with an oxygen counter base and subsequent hydrogenation of carbonyls. For a long time after this paper, there were no reports on FLP-induced carbonyl hydrogenations. Recently the topic became interesting again as the first stoichiometric hydrogenations of alkyl substituted ketones were reported.[145] This paper was followed by two papers reporting catalytic hydrogenation of carbonyl compounds (described in chapters 3.9 and 3.10).[17,18]. These reactions were considered, if not impossible, then very hard to realize due to the high affinity of boron to oxygen.

4.3 Different behavior of (+)-Camphor based amino-boranes

Inspired by the 1,2-linked aminoboranes[122] and the terpene based asymmetric catalysts[81,133,134], our vision was to prepare chiral (+)-camphor-

based aminoboranes. The approach was straightforward, as enamines prepared from camphor were known to form in good yields when using $TiCl_4$ as a water scavenger (Scheme 35).[148] Subsequent hydroboration with borane, $HB(C_6F_5)_2$ **42** was thought to form the expected aminoborane. This was also the strategy of Erker and co-workers who published parallel results slightly before us. Here both results will be discussed, but it should be noted that only the results corresponding to **68** are published by us (Scheme 35).

Scheme 35. The synthesis of iminium borohydrides with camphor backbones.[135,136]



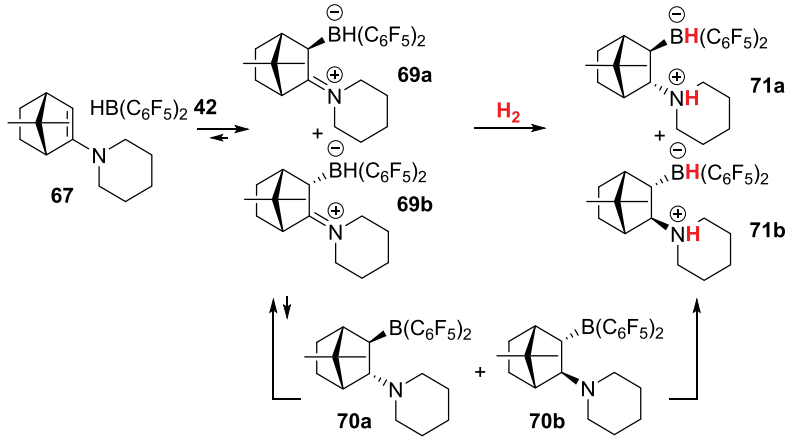
Quite surprisingly, the hydroboration of imines **66** and **67** did not occur but instead a one-to-one mixture of the zwitterionic species **68a/68b** or **69a/69b** were produced. The unexpected selectivity is likely to be a result of electrophilic attack instead of hydroboration, followed by hydride abstraction. The first impression was that hydrogen activation with these zwitterionic species, "invisible FLPs", would not be possible, but in fact both **68** and **69** reacted, although resulting in different products.

The zwitterionic diastereomers **69a-b** were reacted with hydrogen in pentane at RT for 20 h to form the corresponding ammonium borohydride (**71a-b**) in >70% yield.[135] This was clearly a result of intermediate aminoborane (**70a-b**) formation after which hydrogen activation occurred (Scheme 36). Further proof was obtained with D_2 reactions, yielding the deuterated product on the ammonium and borohydride. An interesting observation is that products **71a-b** are formed in the ratio 1:5, indicating that the formation of **69a-b** is reversible and that the corresponding aminoboranes **70a-b** have different formation rates or reactivities with hydrogen.

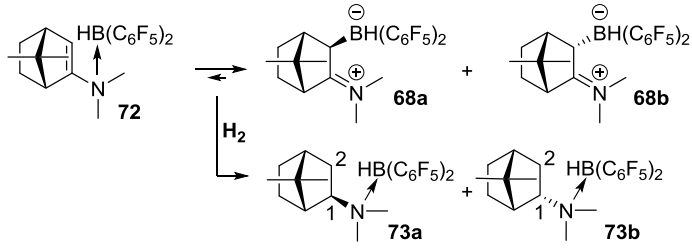
In contrast, when the zwitterionic dimethyl analogue **68a-b** was exposed to hydrogen it resulted in the corresponding diastereomeric aminoborane

adduct (**73a-b**) in the ratio 1:1 (Scheme 37). Studying the starting zwitterionic pair more closely, an equilibrium was found where the borane also could be coordinated to nitrogen **72**. The N→B adduct formation could be favored by heating, (1:8 ratio at 27 ˚C to 1:5 at 75 ˚C). This equilibrium was thought to induce intermolecular FLP reactivity between the enamine and borane. This was confirmed by performing the experiments with D_2 which yielded four diastereomers, where the most important proof was the 50% deuteration of C-1, corresponding to the statistical probability of hydride attack from the formed $HDB{\cdot}(C_6F_5)_2$.

Scheme 36. Hydrogen activation obtained through intermediate hydroboration.[135]

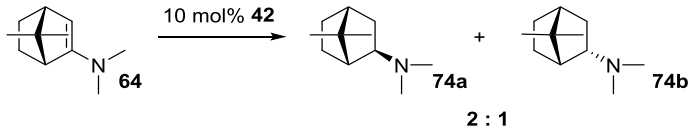


Scheme 37. Adduct equilibrium promoted FLP reactivity with hydrogen.[136]



Catalytic hydrogenation of the camphor enamine was attempted as the borane **42** was restored in the reaction (Scheme 38). Surprisingly, although the quite unhindered amine was formed, no quenching N→B adduct formation occurred and the reaction proceeded smoothly with 10 mol% $HB(C_6F_5)_2$ in benzene at 80 ˚C for 16 h (conversion 98%). Also some selectivity was observed as the bornyl- and isobornyldimethylamine were attained in a 1:2 ratio. Surprisingly, the major product is the opposite to what is obtained when formic acid is used as reductant.[149]

Scheme 38. Catalytic hydrogenation with Piers' borane.



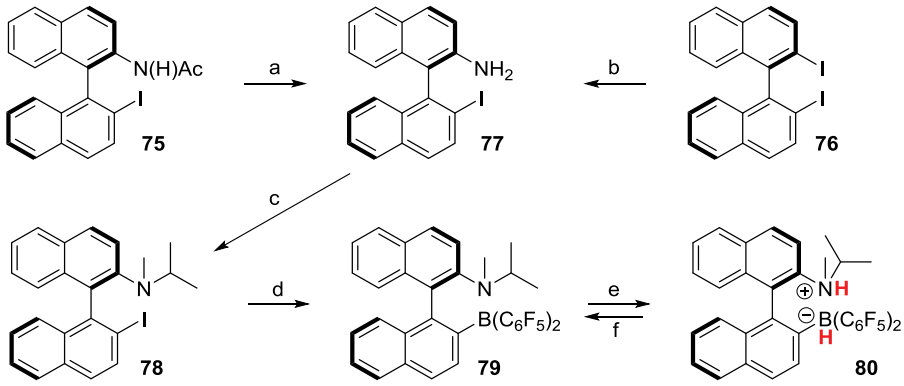
Unfortunately, neither of these iminium borohydrides **68a-b** nor **69a-b** could be used as catalysts for hydrogenation reactions. These results are still interesting as "invisible FLPs" can function as FLPs and react with hydrogen. Also, despite the obvious similarity of **68** and **69**, they react in completely different ways with hydrogen. The tunability of FLPs is what makes them as versatile as they are but, at the same time, predictability is difficult and much is based on trial and error.

4.4 Catalytic asymmetric hydrogenations with a chiral binaphthyl aminoborane

Striving for asymmetric hydrogenations, our vision was to combine the advantages of having a linked acceptor-donor structure and an aryl backbone.[150] With the results from our previous work in mind we were convinced that aryl linking would be a much better approach. The obvious choice was to go for biaryl structures. Though this seems easy enough, it took us numerous unsuccessful attempts to make such FLPs, finally ending up with a 2,2'-linked aminoborane catalyst (**79**). Here, it is worth mentioning that we were unable to synthesize the $-NMe_2$ analogue and the $-N(i\text{-}Pr)_2$ equivalent was a less active hydrogen activator and catalyst than **79**.

Even though the synthesis of **80** requires several steps the reactions were simple, giving relatively good yields and, more importantly, no racemization occurred (Scheme 39). Preparation of **78** through route b and c (Scheme 39) was known in the literature but yielded product with 82% ee, as compound **76** has a tendency to racemize in palladium catalyzed reactions.[151] Also, we were not able to enrich enantiopurities of the intermediate compounds by diastereomeric crystallization.

Scheme 39. Synthesis of the enantiopure binaphthyl ammonium-borohydride.



(a) EtOH, conc. HCl, 2 h, reflux. (b) $Ph_2C{=}NH$, NaO*t*-Bu, cat. $Pd_2(dba)_3$ + dppe, PhMe, 16 h, 100 °C. (c) (1) *i*-PrI (2 equiv.), K_2CO_3 (2 equiv.), ACN, 48 h, 120 °C; (2) MeI (2 equiv.), K_2CO_3 (2 equiv.), ACN, 16 h, 60 °C. (d) (1) −78 °C to RT, PhMe, *n*-BuLi (1 equiv.), 3 h; (2) −78 °C to RT, $B(C_6F_5)_2Cl$ (1 equiv.), PhMe, 16 h. (e) H_2 (2 bar), PhMe, 1 min, RT. (f) C_6D_6, 15 min, 80 °C.

The commercially readily available and also easily preparable[152,153] enantiopure 2,2'-diaminobinaphthyl could be used to synthesize **75** in two steps.[151] Subsequent deprotection and alkylation resulted in the enantiopure amino iodo compound **78** (Scheme 39, a and c). This was easily converted to the aminoborane (**79**) that rapidly reacted with hydrogen to form the zwitterionic ammonium borohydride **80** (Scheme 39, d). The reaction with hydrogen was extremely fast and full conversions were obtained within a minute (Scheme 39, e). Surprisingly, hydrogen release was also fast and full

conversion back into **79** was obtained in 15 min at 80 ˚C (Scheme 39, f). These results prompted us to further investigate the catalytic activity of **80**.

To our surprise the hydrogenations were successful with structurally quite different substrates. Acetophenone *N*-alkyl and benzyl imines were hydrogenated in high yields and ee's ranged from 75-83% (Appendix, entry 105-106). The reactions worked better with non-bulky substrates, in contrast to what is the usual trend with FLPs. This is thought to be a result of the very bulky environment around boron. Unfortunately, the commonly used acetophenone *N*-aryl imines needed heating and still only ~50% conversions could be obtained (Appendix, entry 107). As a result of heating, the ee's remained low.

Alkyl amines tend to be hard to hydrogenate in high ee's due to the chemically similar groups on both sides of the imine carbon. Catalysis with **80** proved to be no different and ee's remained at ~30% level (Appendix, entry 108). In comparison with other FLP catalysts, these are still noteworthy results (Appendix, entry 93 and 108).

Remarkably, *N,N*-symmetric imines were quantitatively hydrogenated in extremely high ee's (Appendix, entry 109). Also the alkyl enamine could be hydrogenated in relatively high enantiopurity (85% ee) (Appendix, entry 110). Using two different *N*-alkyl groups decreased the ee, most likely because of non-selective iminium intermediate formation leading to different enantiomers (< 50% ee). These are important results, as enamines are among the most challenging substrates in catalytic enantioselective hydrogenation.[154]

It is likely that catalyst **80** could be used for other substrates as well, e.g. silyl enol ethers. The similarity of enamines and silyl enol ethers also implies that these enantiopurities could be high. The easy synthesis of the catalyst enables further modification, which may improve it further. This might lead to even better catalytic activity and higher enantioselectivities.

Conclusions

Frustrated Lewis pairs and their reactivity with hydrogen have, in a short period of time, evolved from the proof-of-principle stage to catalysts for hydrogenation of various unsaturated substrates. Reactivity and functional group tolerance is not yet comparable with transition metal catalysts, but great progress has been achieved. The earlier dependence on metal catalysts has been so strong that reactions where their use can be avoided is already a huge improvement.

So far most reports concerning FLPs have dealt with hydrogen activation and catalytic hydrogenation of imines and enamines. Recent advances have made it possible to use FLPs as catalysts in hydrogenation of alkenes, alkynes and carbonyl substrates and also to produce asymmetric hydrogenations. Future challenges involve development of better functional group tolerance and also selective hydrogenations. Furthermore, FLPs catalyzing reactions other than hydrogenations would be desirable areas for further research.

In this work it has been shown that hydrogen activation using FLPs with a carbonyl counter base is possible. Oxygen counter bases were considered very challenging in FLP chemistry and this was the first report where it was experimentally achieved. The hydrogenations resulted in intermediate alcohols that reacted further with the strong Lewis acid $B(C_6F_5)_3$, quenching further reactivity. Recently, further developments by other groups have resulted in FLP catalyzed hydrogenations of carbonyl compounds. This is a highly important achievement in the field, as alcohols have been very challenging functional groups for the oxophilic boranes.

Later the author focused on asymmetric reactions and the synthesis of chiral (+)-camphor based iminium borohydrides was presented. Terpene boranes were known to work well as catalysts in asymmetric hydrogenation of imines and thus incorporation of Lewis acid/base linking was a desired goal. The outcome was a (+)-camphor based iminium borohydride with a "hidden reactivity" going through intermediate FLP formation and resulting in hydrogen activation. Additionally it was shown how small differences in the steric bulk result in completely changed reactivity – in one case, a FLP was formed through hydroboration; in another case, through a Lewis acid-base equilibrium.

The development of a chiral binaphthyl-based aminoborane and its reactivity as a catalyst in asymmetric hydrogenation of imines and enamines was also reported. The catalyst preparation was realized with readily available starting materials and the synthesis route designed so the highly enantiopure product was obtained. The simplicity of the catalyst structure gives room for easy modification to fit other demands. The catalytic activity was different to what is usual for FLPs and high yields could be obtained with unhindered substrates. Also, structurally quite different substrates were hydrogenated under ambient conditions and high yields and ee's could be obtained for most of them. Exceptional catalytic activity was achieved with *N*,*N*-symmetrically substituted enamines that were rapidly hydrogenated in high enantiomeric excesses.

The applicability of the results and interest by fellow scientists is a good measurement of their scientific significance. The results presented in the papers have already resulted in further development by other groups, e.g. the catalytic hydrogenation of carbonyls. Also, the achievements in asymmetric catalysis will most certainly be utilized in future studies.

References

(1) Brown, H. C.; Schlesinger, H. I.; Cardon, S. Z. *J. Am. Chem. Soc.* **1942**, *64*, 325.

(2) Wittig, G.; Rückert, A. *Liebigs Ann. Chem.* **1950**, *566*, 101.

(3) Welch, G. C.; Masuda, J. D.; Stephan, D. W. *Inorg. Chem.* **2006**, *45*, 478.

(4) Scott, D. J.; Fuchter, M. J.; Ashley, A. E. *Angew. Chem., Int. Ed.* **2014**, *53*, 10218.

(5) Birkmann, B.; Voss, T.; Geier, S. J.; Ullrich, M.; Kehr, G.; Erker, G.; Stephan, D. W. *Organometallics* **2010**, *29*, 5310.

(6) Tochtermann, W. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 351.

(7) Wittig, G.; Benz, E. *Chem. Ber.* **1959**, *92*, 1999.

(8) Stephan, D. W. *Org. Biomol. Chem.* **2008**, *6*, 1535.

(9) Stephan, D. W. *Dalton Trans.* **2009**, 3129.

(10) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 46.

(11) Power, P. P. *Nature* **2010**, *463*, 171.

(12) Erker, G. *C. R. Chim.* **2011**, *14*, 831.

(13) Stephan, D. W. *Org. Biomol. Chem.* **2012**, *10*, 5740.

(14) Hounjet, L. J.; Stephan, D. W. *Org. Process Res. Dev.* **2014**, *18*, 385.

(15) Paradies, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 3552.

(16) Chernichenko, K.; Madarász, Á.; Pápai, I.; Nieger, M.; Leskelä, M.; Repo, T. *Nat. Chem.* **2013**, *5*, 718.

(17) Mahdi, T.; Stephan, D. W. *J. Am. Chem. Soc.* **2014**, *136*, 15809.

(18) Scott, D. J.; Fuchter, M. J.; Ashley, A. E. *J. Am. Chem. Soc.* **2014**, *136*, 15813.

(19) Rokob, T. A.; Hamza, A.; Stirling, A.; Soós, T.; Pápai, I. *Angew. Chem., Int. Ed.* **2008**, *47*, 2435.

(20) Rokob, T. A.; Hamza, A.; Pápai, I. *J. Am. Chem. Soc.* **2009**, *131*, 10701.

(21) Chernichenko, K.; Nieger, M.; Leskela, M.; Repo, T. *Dalton Trans.* **2012**, *41*, 9029.

(22) Spies, P.; Erker, G.; Kehr, G.; Bergander, K.; Frohlich, R.; Grimme, S.; Stephan, D. W. *Chem. Commun.* **2007**, 5072.

(23) Lindqvist, M.; Sarnela, N.; Sumerin, V.; Chernichenko, K.; Leskela, M.; Repo, T. *Dalton Trans.* **2012**, *41*, 4310.

(24) Holschumacher, D.; Bannenberg, T.; Hrib, C. G.; Jones, P. G.; Tamm, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7428.

(25) Chase, P. A.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 7433.

(26) Erős, G.; Nagy, K.; Mehdi, H.; Pápai, I.; Nagy, P.; Király, P.; Tárkányi, G.; Soós, T. *Chem.—Eur. J.* **2012**, *18*, 574.
(27) Lu, Z.; Cheng, Z.; Chen, Z.; Weng, L.; Li, Z. H.; Wang, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 12227.
(28) Greb, L.; Daniliuc, C.-G.; Bergander, K.; Paradies, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 5876.
(29) Greb, L.; Tussing, S.; Schirmer, B.; Ona-Burgos, P.; Kaupmees, K.; Lokov, M.; Leito, I.; Grimme, S.; Paradies, J. *Chem. Sci.* **2013**, *4*, 2788.
(30) Zhao, H.; Reibenspies, J. H.; Gabbai, F. P. *Dalton Trans.* **2013**, *42*, 608.
(31) Travis, A. L.; Binding, S. C.; Zaher, H.; Arnold, T. A. Q.; Buffet, J.-C.; O'Hare, D. *Dalton Trans.* **2013**, *42*, 2431.
(32) Chernichenko, K.; Kótai, B.; Pápai, I.; Zhivonitko, V.; Nieger, M.; Leskelä, M.; Repo, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 1749.
(33) Fan, C.; Mercier, L. G.; Piers, W. E.; Tuononen, H. M.; Parvez, M. *J. Am. Chem. Soc.* **2010**, *132*, 9604.
(34) Farrell, J. M.; Hatnean, J. A.; Stephan, D. W. *J. Am. Chem. Soc.* **2012**, *134*, 15728.
(35) Eisenberger, P.; Bestvater, B. P.; Keske, E. C.; Crudden, C. M. *Angew. Chem., Int. Ed.* **2015**, *54*, 2467.
(36) Ménard, G.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2012**, *51*, 8272.
(37) Menard, G.; Tran, L.; Stephan, D. W. *Dalton Trans.* **2013**, *42*, 13685.
(38) Schäfer, A.; Reißmann, M.; Schäfer, A.; Saak, W.; Haase, D.; Müller, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 12636.
(39) Herrington, T. J.; Ward, B. J.; Doyle, L. R.; McDermott, J.; White, A. J. P.; Hunt, P. A.; Ashley, A. E. *Chem. Commun.* **2014**, *50*, 12753.
(40) Schäfer, A.; Reißmann, M.; Schäfer, A.; Schmidtmann, M.; Müller, T. *Chem.—Eur. J.* **2014**, *20*, 9381.
(41) Alcarazo, M.; Gomez, C.; Holle, S.; Goddard, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 5788.
(42) Boone, M. P.; Stephan, D. W. *J. Am. Chem. Soc.* **2013**, *135*, 8508.
(43) Chapman, A. M.; Haddow, M. F.; Wass, D. F. *J. Am. Chem. Soc.* **2011**, *133*, 18463.
(44) Chapman, A. M.; Wass, D. F. *Dalton Trans.* **2012**, *41*, 9067.
(45) Kalz, K. F.; Brinkmeier, A.; Dechert, S.; Mata, R. A.; Meyer, F. *J. Am. Chem. Soc.* **2014**, *136*, 16626.
(46) Forrest, S. J. K.; Clifton, J.; Fey, N.; Pringle, P. G.; Sparkes, H. A.; Wass, D. F. *Angew. Chem., Int. Ed.* **2015**, *54*, 2223.
(47) Greenwood, N. N.; Earnshaw, A. In *Chemistry of the Elements (2nd Edition)*; Elsevier, p 68.
(48) Greenwood, N. N.; Earnshaw, A. In *Chemistry of the Elements (2nd Edition)*; Elsevier, p 107.

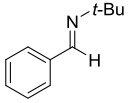
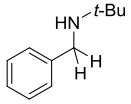
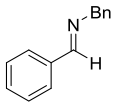
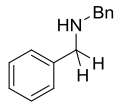
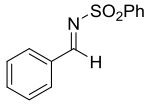
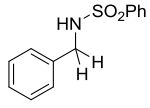
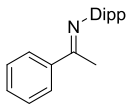
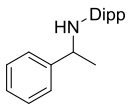
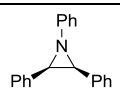
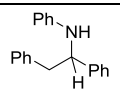
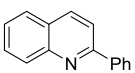
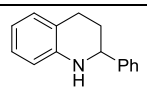
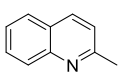
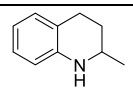
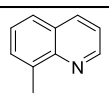
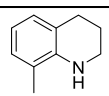
(49) Frey, G. D.; Lavallo, V.; Donnadieu, B.; Schoeller, W. W.; Bertrand, G. *Science* **2007**, *316*, 439.
(50) Spikes, G. H.; Fettinger, J. C.; Power, P. P. *J. Am. Chem. Soc.* **2005**, *127*, 12232.
(51) Peng, Y.; Brynda, M.; Ellis, B. D.; Fettinger, J. C.; Rivard, E.; Power, P. P. *Chem. Commun.* **2008**, 6042.
(52) Peng, Y.; Ellis, B. D.; Wang, X.; Power, P. P. *J. Am. Chem. Soc.* **2008**, *130*, 12268.
(53) Peng, Y.; Guo, J.-D.; Ellis, B. D.; Zhu, Z.; Fettinger, J. C.; Nagase, S.; Power, P. P. *J. Am. Chem. Soc.* **2009**, *131*, 16272.
(54) Zhao, L.; Huang, F.; Lu, G.; Wang, Z.-X.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **2012**, *134*, 8856.
(55) Walling, C.; Bollyky, L. *J. Am. Chem. Soc.* **1964**, *86*, 3750.
(56) Berkessel, A.; Schubert, T. J. S.; Müller, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 8693.
(57) Welch, G. C.; Juan, R. R. S.; Masuda, J. D.; Stephan, D. W. *Science* **2006**, *314*, 1124.
(58) Stephan, D. W. *Acc. Chem. Res.* **2014**.
(59) Piers, W. E.; Marwitz, A. J. V.; Mercier, L. G. *Inorg. Chem.* **2011**, *50*, 12252.
(60) Rokob, T.; Pápai, I. In *Frustrated Lewis Pairs I*; Erker, G., Stephan, D. W., Eds.; Springer Berlin Heidelberg: 2013; Vol. 332, p 157.
(61) Sumerin, V.; Schulz, F.; Atsumi, M.; Wang, C.; Nieger, M.; Leskelä, M.; Repo, T.; Pyykkö, P.; Rieger, B. *J. Am. Chem. Soc.* **2008**, *130*, 14117.
(62) Pyykko, P.; Wang, C. *Phys. Chem. Chem. Phys.* **2010**, *12*, 149.
(63) Welch, G. C.; Stephan, D. W. *J. Am. Chem. Soc.* **2007**, *129*, 1880.
(64) Grimme, S.; Kruse, H.; Goerigk, L.; Erker, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 1402.
(65) Bako, I.; Stirling, A.; Balint, S.; Papai, I. *Dalton Trans.* **2012**, *41*, 9023.
(66) Hamza, A.; Stirling, A.; András Rokob, T.; Pápai, I. *Int. J. Quantum Chem.* **2009**, *109*, 2416.
(67) Kim, H. W.; Rhee, Y. M. *Chem.—Eur. J.* **2009**, *15*, 13348.
(68) Sumerin, V.; Schulz, F.; Nieger, M.; Leskelä, M.; Repo, T.; Rieger, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 6001.
(69) Rocchigiani, L.; Ciancaleoni, G.; Zuccaccia, C.; Macchioni, A. *J. Am. Chem. Soc.* **2013**, *136*, 112.
(70) Pu, M.; Privalov, T. *J. Chem. Phys.* **2013**, *138*, 154305.
(71) Pu, M.; Privalov, T. *ChemPhysChem* **2014**, *15*, 2936.
(72) Pu, M.; Privalov, T. *ChemPhysChem* **2014**, *15*, 3714.
(73) Holschumacher, D.; Taouss, C.; Bannenberg, T.; Hrib, C. G.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Dalton Trans.* **2009**, 6927.
(74) Kronig, S.; Theuergarten, E.; Holschumacher, D.; Bannenberg, T.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Inorg. Chem.* **2011**, *50*, 7344.

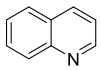
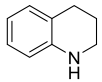
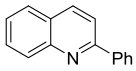
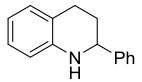
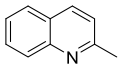
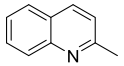
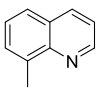
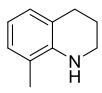
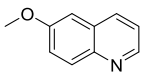
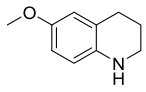
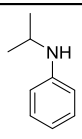
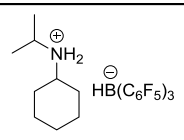
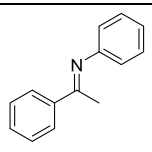
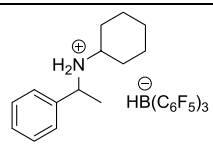
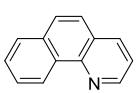
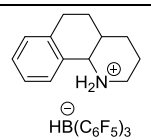
(75) Kolychev, E.; Theuergarten, E.; Tamm, M. In *Frustrated Lewis Pairs II*; Erker, G., Stephan, D. W., Eds.; Springer Berlin Heidelberg: 2013; Vol. 334, p 121.
(76) Nyhlén, J.; Privalov, T. *Eur. J. Inorg. Chem.* **2009**, *2009*, 2759.
(77) Sumerin, V.; Chernichenko, K.; Nieger, M.; Leskelä, M.; Rieger, B.; Repo, T. *Adv. Synth. Catal.* **2011**, *353*, 2093.
(78) Greb, L.; Oña-Burgos, P.; Schirmer, B.; Grimme, S.; Stephan, D. W.; Paradies, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 10164.
(79) Ullrich, M.; Lough, A. J.; Stephan, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 52.
(80) Chase, P. A.; Jurca, T.; Stephan, D. W. *Chem. Commun.* **2008**, 1701.
(81) Chen, D.; Klankermayer, J. *Chem. Commun.* **2008**, 2130.
(82) Geier, S. J.; Chase, P. A.; Stephan, D. W. *Chem. Commun.* **2010**, *46*, 4884.
(83) Stephan, D. W.; Greenberg, S.; Graham, T. W.; Chase, P.; Hastie, J. J.; Geier, S. J.; Farrell, J. M.; Brown, C. C.; Heiden, Z. M.; Welch, G. C.; Ullrich, M. *Inorg. Chem.* **2011**, *50*, 12338.
(84) Liu, Y.; Du, H. *J. Am. Chem. Soc.* **2013**, *135*, 12968.
(85) Mahdi, T.; Heiden, Z. M.; Grimme, S.; Stephan, D. W. *J. Am. Chem. Soc.* **2012**, *134*, 4088.
(86) Forrest, T. P.; Dauphinee, G. A.; Deraniyagala, S. A. *Can. J. Chem.* **1985**, *63*, 412.
(87) Mahdi, T.; del Castillo, J. N.; Stephan, D. W. *Organometallics* **2013**, *32*, 1971.
(88) Geier, S. J.; Stephan, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 3476.
(89) Prokofjevs, A.; Boussonnière, A.; Li, L.; Bonin, H.; Lacôte, E.; Curran, D. P.; Vedejs, E. *J. Am. Chem. Soc.* **2012**, *134*, 12281.
(90) Denmark, S. E.; Ueki, Y. *Organometallics* **2013**, *32*, 6631.
(91) Chen, J.; Lalancette, R. A.; Jakle, F. *Chem. Commun.* **2013**, *49*, 4893.
(92) Eisenberger, P.; Bailey, A. M.; Crudden, C. M. *J. Am. Chem. Soc.* **2012**, *134*, 17384.
(93) de Oliveira Freitas, L. B.; Eisenberger, P.; Crudden, C. M. *Organometallics* **2013**, *32*, 6635.
(94) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley: New York, 2000.
(95) Chase, P. A.; Welch, G. C.; Jurca, T.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 8050.
(96) Marwitz, A. J. V.; Dutton, J. L.; Mercier, L. G.; Piers, W. E. *J. Am. Chem. Soc.* **2011**, *133*, 10026.
(97) Ullrich, M.; Lough, A. J.; Stephan, D. W. *Organometallics* **2010**, *29*, 3647.

(98) Wang, H.; Frohlich, R.; Kehr, G.; Erker, G. *Chem. Commun.* **2008**, 5966.
(99) Spies, P.; Schwendemann, S.; Lange, S.; Kehr, G.; Fröhlich, R.; Erker, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7543.
(100) Parks, D. J.; von H. Spence, R. E.; Piers, W. E. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 809.
(101) Axenov, K. V.; Mömming, C. M.; Kehr, G.; Fröhlich, R.; Erker, G. *Chem.—Eur. J.* **2010**, *16*, 14069.
(102) Spies, P.; Fröhlich, R.; Kehr, G.; Erker, G.; Grimme, S. *Chem.—Eur. J.* **2008**, *14*, 333.
(103) Wang, Z.; Lu, G.; Li, H.; Zhao, L. *Chin. Sci. Bull.* **2010**, *55*, 239.
(104) Zhao, X.; Gilbert, T. M.; Stephan, D. W. *Chem.—Eur. J.* **2010**, *16*, 10304.
(105) Stute, A.; Kehr, G.; Frohlich, R.; Erker, G. *Chem. Commun.* **2011**, *47*, 4288.
(106) Rosorius, C.; Kehr, G.; Fröhlich, R.; Grimme, S.; Erker, G. *Organometallics* **2011**, *30*, 4211.
(107) Bertini, F.; Lyaskovskyy, V.; Timmer, B. J. J.; de Kanter, F. J. J.; Lutz, M.; Ehlers, A. W.; Slootweg, J. C.; Lammertsma, K. *J. Am. Chem. Soc.* **2012**, *134*, 201.
(108) Geier, S. J.; Gilbert, T. M.; Stephan, D. W. *J. Am. Chem. Soc.* **2008**, *130*, 12632.
(109) Staubitz, A.; Besora, M.; Harvey, J. N.; Manners, I. *Inorg. Chem.* **2008**, *47*, 5910.
(110) Robertson, A. P. M.; Whittell, G. R.; Staubitz, A.; Lee, K.; Lough, A. J.; Manners, I. *Eur. J. Inorg. Chem.* **2011**, *2011*, 5279.
(111) Theuergarten, E.; Schluns, D.; Grunenberg, J.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Chem. Commun.* **2010**, *46*, 8561.
(112) Yalpani, M.; Boese, R.; Köster, R. *Chem. Ber.* **1990**, *123*, 1275.
(113) Ashley, A. E.; Thompson, A. L.; O'Hare, D. *Angew. Chem., Int. Ed.* **2009**, *48*, 9839.
(114) Sumerin, V.; Schulz, F.; Nieger, M.; Atsumi, M.; Wang, C.; Leskelä, M.; Pyykkö, P.; Repo, T.; Rieger, B. *J. Organomet. Chem.* **2009**, *694*, 2654.
(115) Jiang, C.; Blacque, O.; Fox, T.; Berke, H. *Dalton Trans.* **2011**, *40*, 1091.
(116) Jiang, C.; Blacque, O.; Berke, H. *Chem. Commun.* **2009**, 5518.
(117) Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G.; Soós, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 6559.
(118) Inés, B.; Palomas, D.; Holle, S.; Steinberg, S.; Nicasio, J. A.; Alcarazo, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 12367.
(119) Nicasio, J. A.; Steinberg, S.; Inés, B.; Alcarazo, M. *Chem.—Eur. J.* **2013**, *19*, 11016.

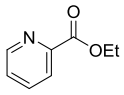
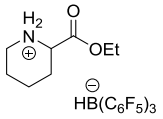
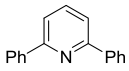
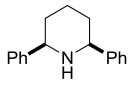
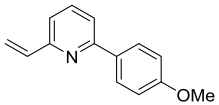
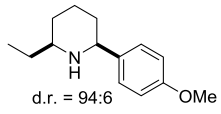
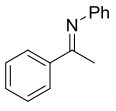
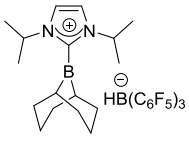
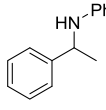
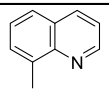
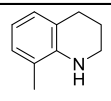
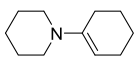
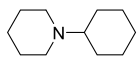
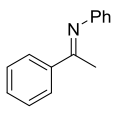
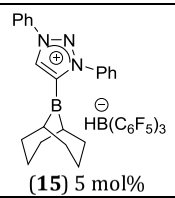
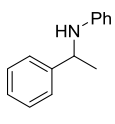
(120) Schulz, F.; Sumerin, V.; Heikkinen, S.; Pedersen, B.; Wang, C.; Atsumi, M.; Leskelä, M.; Repo, T.; Pyykkö, P.; Petry, W.; Rieger, B. *J. Am. Chem. Soc.* **2011**, *133*, 20245.
(121) Zhivonitko, V. V.; Telkki, V.-V.; Chernichenko, K.; Repo, T.; Leskelä, M.; Sumerin, V.; Koptyug, I. V. *J. Am. Chem. Soc.* **2014**, *136*, 598.
(122) Schwendemann, S.; Frohlich, R.; Kehr, G.; Erker, G. *Chem. Sci.* **2011**, *2*, 1842.
(123) Roesler, R.; Piers, W. E.; Parvez, M. *J. Organomet. Chem.* **2003**, *680*, 218.
(124) Liu, Y.; Hu, L.; Chen, H.; Du, H. *Chem.—Eur. J.* **2015**, *21*, 3495.
(125) Hounjet, L. J.; Bannwarth, C.; Garon, C. N.; Caputo, C. B.; Grimme, S.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2013**, *52*, 7492.
(126) Köster, R.; Bruno, G.; Binger, P. *Liebigs Ann. Chem.* **1961**, *644*, 1.
(127) DeWitt, E. J.; Ramp, F. L.; Trapasso, L. E. *J. Am. Chem. Soc.* **1961**, *83*, 4672.
(128) Ramp, F. L.; DeWitt, E. J.; Trapasso, L. E. *J. Org. Chem.* **1962**, *27*, 4368.
(129) Wang, Y.; Chen, W.; Lu, Z.; Li, Z. H.; Wang, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7496.
(130) Unverhau, K.; Lübbe, G.; Wibbeling, B.; Fröhlich, R.; Kehr, G.; Erker, G. *Organometallics* **2010**, *29*, 5320.
(131) Heiden, Z. M.; Stephan, D. W. *Chem. Commun.* **2011**, *47*, 5729.
(132) Parks, D. J.; Piers, W. E.; Yap, G. P. A. *Organometallics* **1998**, *17*, 5492.
(133) Chen, D.; Wang, Y.; Klankermayer, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 9475.
(134) Ghattas, G.; Chen, D.; Pan, F.; Klankermayer, J. *Dalton Trans.* **2012**, *41*, 9026.
(135) Schwendemann, S.; Oishi, S.; Saito, S.; Fröhlich, R.; Kehr, G.; Erker, G. *Chem. Asian J.* **2013**, *8*, 212.
(136) Lindqvist, M.; Axenov, K.; Nieger, M.; Räisänen, M.; Leskelä, M.; Repo, T. *Chem.—Eur. J.* **2013**, *19*, 10412.
(137) Liu, Y.; Du, H. *J. Am. Chem. Soc.* **2013**, *135*, 6810.
(138) Ohta, T.; Ito, M.; Inagaki, K.; Takaya, H. *Tetrahedron Lett.* **1993**, *34*, 1615.
(139) Ooi, T.; Uematsu, Y.; Maruoka, K. *J. Org. Chem.* **2003**, *68*, 4576.
(140) Cao, Z.; Du, H. *Org. Lett.* **2010**, *12*, 2602.
(141) Wei, S.; Du, H. *J. Am. Chem. Soc.* **2014**, *136*, 12261.
(142) Zhang, Z.; Du, H. *Angew. Chem., Int. Ed.* **2015**, *54*, 623.
(143) Parks, D. J.; Piers, W. E.; Parvez, M.; Atencio, R.; Zaworotko, M. J. *Organometallics* **1998**, *17*, 1369.
(144) Nyhlen, J.; Privalov, T. *Dalton Trans.* **2009**, 5780.
(145) Longobardi, L. E.; Tang, C.; Stephan, D. W. *Dalton Trans.* **2014**, *43*, 15723.

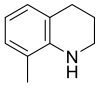
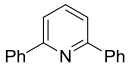
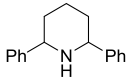
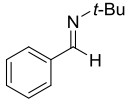
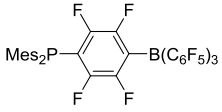
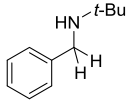
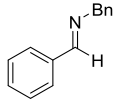
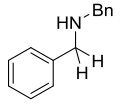
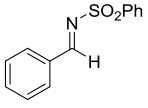
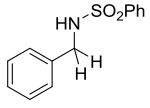
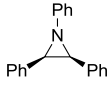
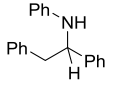
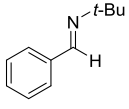
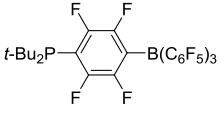
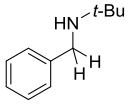
(146) Ashley, A. E.; Herrington, T. J.; Wildgoose, G. G.; Zaher, H.; Thompson, A. L.; Rees, N. H.; Krämer, T.; O'Hare, D. *J. Am. Chem. Soc.* **2011**, *133*, 14727.
(147) Jutzi, P.; Müller, C.; Stammler, A.; Stammler, H.-G. *Organometallics* **2000**, *19*, 1442.
(148) Carlson, R.; Nilsson, Å. *Acta Chem. Scand.* **1984**, *38b*, 49.
(149) Carlson, R.; Nilsson, Å. *Acta Chem. Scand.* **1985**, *39b*, 181.
(150) Lindqvist, M.; Borre, K.; Axenov, K.; Kótai, B.; Nieger, M.; Leskelä, M.; Pápai, I.; Repo, T. *J. Am. Chem. Soc.* **2015**, *137*, 4038.
(151) Mešková, M.; Putala, M. *Tetrahedron Lett.* **2011**, *52*, 5379.
(152) Yamamoto, Y.; Sakamoto, A.; Nishioka, T.; Oda, J.; Fukazawa, Y. *J. Org. Chem.* **1991**, *56*, 1112.
(153) Brown, K. J.; Berry, M. S.; Murdoch, J. R. *J. Org. Chem.* **1985**, *50*, 4345.
(154) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713.

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
1		$B(C_6F_5)_3$ (**1**) 5 mol%	2	1	80	PhMe		89		80
2	 Bn = $PhCH_2$-	$B(C_6F_5)_3$ (**1**) 5 mol%	1	5	120	PhMe		99	 Bn = $PhCH_2$-	80
3		$B(C_6F_5)_3$ (**1**) 5 mol%	41	5	120	PhMe		94		80
4	 dipp = 2,6-(*i*-Pr)$_2$C$_6$H$_3$-	$B(C_6F_5)_3$ (**1**) 5 mol%	8	5	120	PhMe		94	 dipp = 2,6-(*i*-Pr)$_2$C$_6$H$_3$-	80
5		$B(C_6F_5)_3$ (**1**) 5 mol%	2	5	120	PhMe		95		80
6		$B(C_6F_5)_3$ (**1**) 5 mol%	4	~4 (1 at 78K)	25	PhMe		80		82
7		$B(C_6F_5)_3$ (**1**) 5 mol%	16	~4 (1 at 78K)	50	PhMe		74		82
8		$B(C_6F_5)_3$ (**1**) 10 mol%	6	~4 (1 at 78K)	80	PhMe		88		82

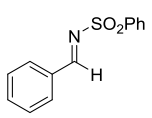
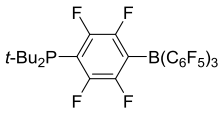
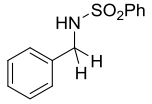
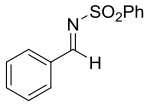
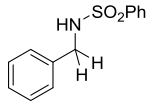
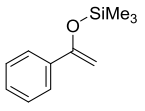
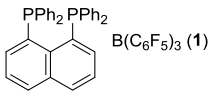
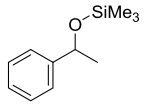
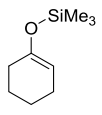
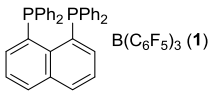
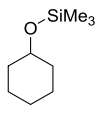
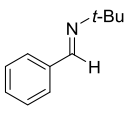
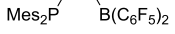
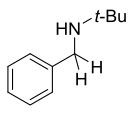
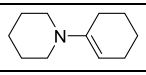
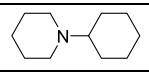
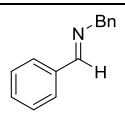
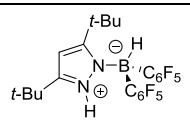
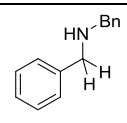
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
9		MesB(p-C_6F_4H)$_2$ 10 mol%	17	~4 (1 at 78K)	105	PhMe-*d8*		80		26
10		MesB(p-C_6F_4H)$_2$ 10 mol%	17	~4 (1 at 78K)	105	PhMe-*d8*		93		26
11		MesB(p-C_6F_4H)$_2$ 10 mol%	17	~4 (1 at 78K)	105	PhMe-*d8*		86		26
12		MesB(p-C_6F_4H)$_2$ 10 mol%	17	~4 (1 at 78K)	105	PhMe-*d8*		84		26
13		MesB(p-C_6F_4H)$_2$ 10 mol%	17	~4 (1 at 78K)	105	PhMe-*d8*		63		26
14		$B(C_6F_5)_3$ (**1**) 1 equiv.	36	4 at 77 K	110	PhMe		93		85
15		$B(C_6F_5)_3$ (**1**) 1 equiv.	96	4 at 77 K	110	PhMe		57		85
16		$B(C_6F_5)_3$ (**1**) 1 equiv.	48	4 at 77 K	115	PhMe		55		87

[3]

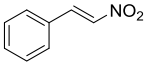
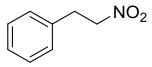
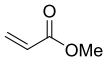
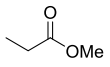
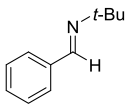
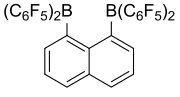
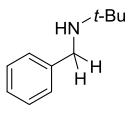
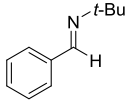
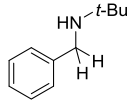
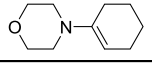
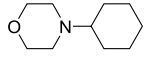
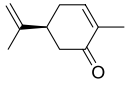
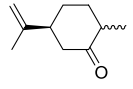
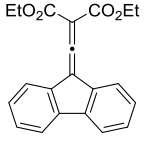
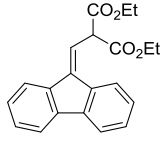
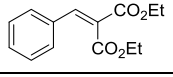
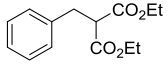
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
17		$B(C_6F_5)_3$ (**1**) 1 equiv.	36	4 at 77 K	115	PhMe		74		87
18		$HB(C_6F_5)_2$/ $C_6F_5CHC{=}H_2$ 10 mol%	20	49	100	PhMe		98	 d.r. = 98:2	84
19		$HB(C_6F_5)_2$/ $C_6F_5CHC{=}H_2$ 10 mol%	20	49	100	PhMe		96	 d.r. = 94:6	84
20		 (**13**) 5 mol%	4	102	RT	CH_2Cl_2	100	90		34
21		(**13**) 5 mol%	4	102	RT	PhCl	27			34
22		(**13**) 5 mol%	4	102	RT	CH_2Cl_2	100	85		34
23		 (**15**) 5 mol%	23	1	RT	CH_2Cl_2	100			35

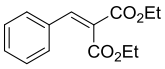
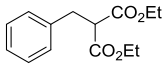
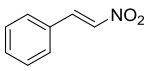
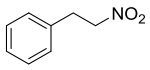
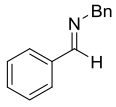
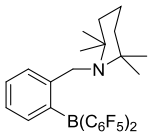
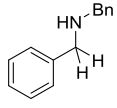
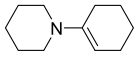
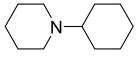
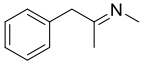
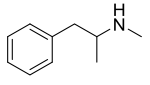
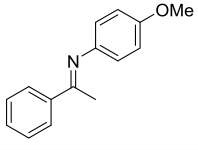
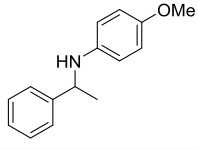
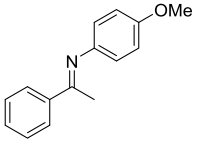
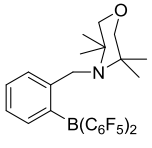
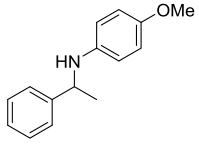
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
24		(**15**) 10 mol%	18	5	RT	CH_2Cl_2		87		35
25		(**15**) 10 mol%	48	5	RT	CH_2Cl_2	55			35
26		 (**3**) 5 mol%	1	1	80	PhMe		79		95
27	 Bn = $PhCH_2$-	(**3**) 5 mol%	1	~5	140	PhMe		88	 Bn = $PhCH_2$-	95
28		(**3**) 5 mol%	10.5	~5	120	PhMe		97		95
29		(**3**) 5 mol%	1.5	~5	120	PhMe		98		95
30	PhCN → $B(C_6F_5)_3$	(**3**) 5 mol%	24	~5	120	PhMe		84	$PhCH_2NH_2$ → $B(C_6F_5)_3$	95
31		 5 mol%	1	1	80	PhMe		98		95

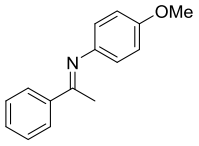
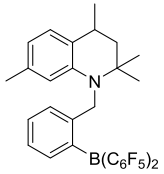
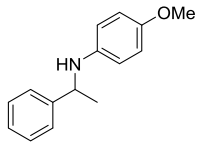
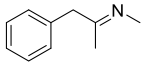
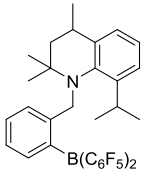
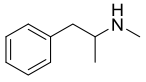
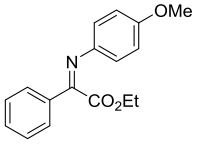
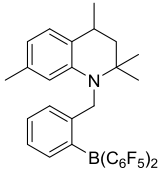
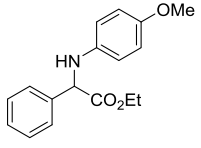
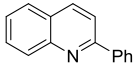
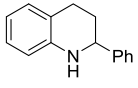
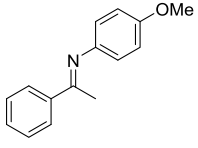
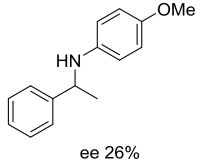
[4]

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
32		 5 mol%	16	~5	120	PhMe		87		95
33		$Mes_3P/B(C_6F_5)_3$ 5 mol%	8	5	120	PhMe		98		80
34	PhCN → $B(C_6F_5)_3$	$Mes_3P/B(C_6F_5)_3$ 5 mol%	48	5	120	PhMe		94	$PhCH_2NH_2$ → $B(C_6F_5)_3$	80
35		 20 mol%	20	2	RT	C_6D_6	>99	93		98
36		 20 mol%	20	2	RT	C_6D_6	>99	86		98
37		 (**16**) 20 mol%	0.75	1.5	RT	PhMe		87		22
38		(**16**) 5 mol%	20	2.5	RT	PhMe		88		22
39	 Bn = $PhCH_2$-	 (**23**) 8 mol%	14	2	110	PhMe	63		 Bn = $PhCH_2$-	111

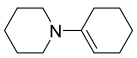
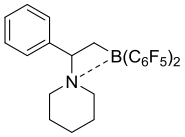
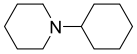
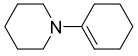
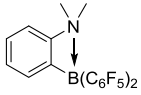
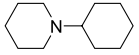
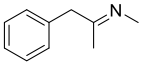
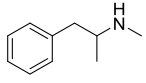
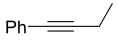
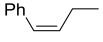
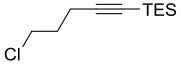
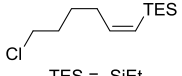
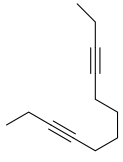
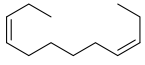
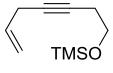
[5]

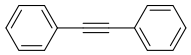
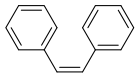
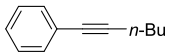
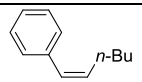
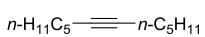
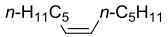
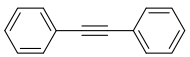
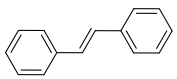
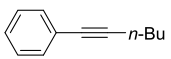
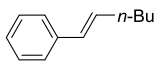
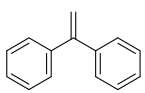
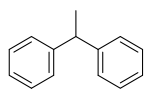
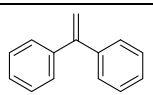
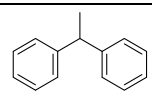
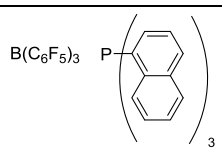
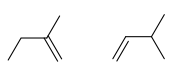
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
40	CO_2	TMP/$B(C_6F_5)_3$ (**25/1**) 4 equiv.	144	1	160	PhMe-*d8*	17-25		$MeOB(C_6F_5)_2$	113
41		2,6-Lutidine/ THF•$B(2,6\text{-}C_6H_3F_2)_3$ 20 mol%	24	4	40	CH_2Cl_2	>95			28
42		Collidine (unknown isomer)/ THF•$B(2,6\text{-}C_6H_3F_2)_3$ 20 mol%	48	4	25	CH_2Cl_2	>95			28
43		 10 mol%	1	15	120	C_6D_6	>99			116
44		$MesB(C_6F_5)_2$/DABCO 10 mol%	24	~4	20	C_6D_6	100			117
45		$MesB(C_6F_5)_2$/DABCO 10 mol%	42	~4	20	C_6D_6	92			117
46		$MesB(C_6F_5)_2$/DABCO 20 mol%	42	~4	20	C_6D_6	87		 d.r. = 4.3:1	117
47		$B(C_6F_5)_3$/DABCO 20 mol%	72	59	80	PhMe		93		118
48		$B(C_6F_5)_3$/DABCO 10 mol%	24	59	80	PhMe		92		118

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
49		$B(2,3,4\text{-}C_6H_2F_3)_3$/DABCO 5 mol%	24	5	50	PhMe	>98			119
50		$B(2,3,4\text{-}C_6H_2F_3)_3$/DABCO 5 mol%	24	5	50	PhMe		95		119
51	 Bn = $PhCH_2$-	 (**39a**) 8 mol%	12	2	110	PhMe	99		 Bn = $PhCH_2$-	61
52		(**39a**) 4 mol%	12	2	110	PhMe	85			61
53		(**39a**) 4 mol%	24	2	110	PhMe	4			61
54		(**39a**) 4 mol%	12	2	110	PhMe	37			77
55		 (**39b**) 1 mol%	40	2	110	PhMe	70			77

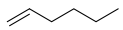
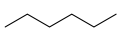
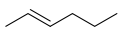
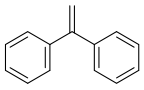
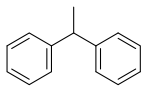
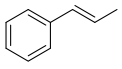
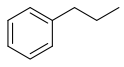
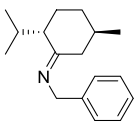
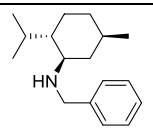
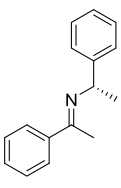
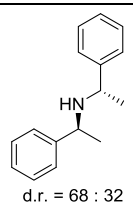
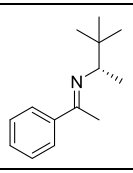
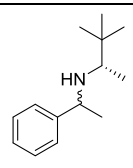
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
56		 (**39c**) 1 mol%	3	2	110	PhMe	100			77
57		 (**39d**) 4 mol%	12	2	110	PhMe	82			77
58		 (**39c**) 4 mol%	40	2	110	PhMe	21			77
59		(**39c**) 4 mol%	12	2	20	MTBE	100		 ee 37%	77
60		(**39c**) 4 mol%	20	2	20	MTBE	100		 ee 26%	77

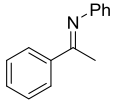
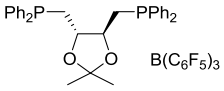
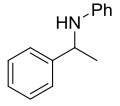
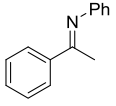
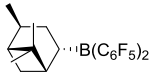
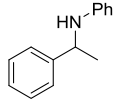
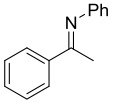
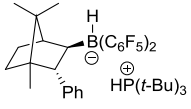
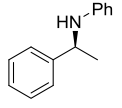
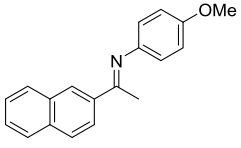
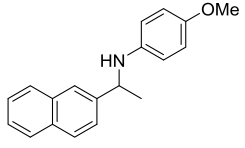
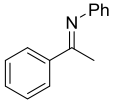
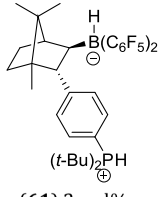
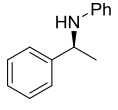
[8]

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
61		 (**43**) 5 mol%	3	60	RT	PhMe	100	56		122
62		 (**52**) 5 mol%	1	2	80	PhMe	100			21
63		(**52**) 15 mol%	22	2	80	PhMe	100			21
64		(**54**) 5 mol%	3	2,2	80	C_6D_6	100			16
65		(**54**) 5 mol%	3	2,2	80	C_6D_6	100	80		16
66	 TES = -$SiEt_3$	(**54**) 5 mol%	3	2,2	80	C_6D_6	100	95	 TES = -$SiEt_3$	16
67		(**54**) 5 mol%	3	2,2	80	C_6D_6	100	94		16
68	 TMS = -$SiMe_3$	(**54**) 5 mol%	3	2,2	80	C_6D_6			No reaction	16

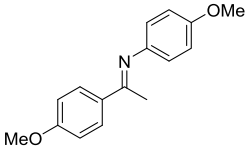
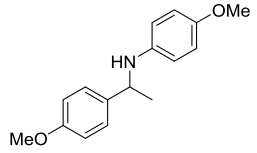
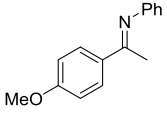
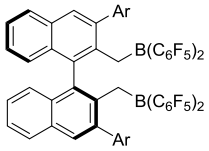
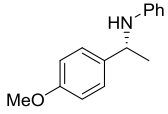
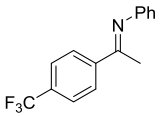
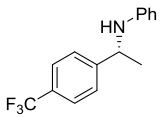
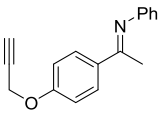
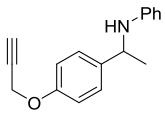
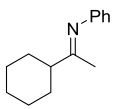
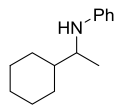
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
69		$HB(C_6F_5)_2/C_6F_5CH=CH_2$ (**42/58**) 10 mol% / 20 mol%	6	49	140	PhMe	>99	96	 *E*/*Z* =95/5	124
70		$HB(C_6F_5)_2/C_6F_5CH=CH_2$ (**42/58**) 10 mol% / 20 mol%	6,5	49	140	PhMe	93	99	 *E*/*Z* =97/3	124
71		$HB(C_6F_5)_2/C_6F_5CH=CH_2$ (**42/58**) 10 mol% / 20 mol%	10	49	140	PhMe	91	93	 *E*/*Z* =96/4	124
72		$HB(C_6F_5)_2/C_6F_5CH=CH_2$ (**42/58**) 12.5 mol% / 20 mol%	24	49	140	PhMe		97	 *E*/*Z* =1/99	124
73		$HB(C_6F_5)_2/C_6F_5CH=CH_2$ (**42/58**) 15 mol% / 20 mol%	24	49	140	PhMe		89	 *E*/*Z* =5/95 (Including 24–30% C=C bond migration isomers.)	124
74		$B(C_6F_5)_3$ (**1**)/Et_2O 10 mol% / 30 mol%	96	4	50	CD_2Cl_2	96			125
75		$B(C_6F_5)_3$ (**1**)/$Ph_2P(C_6F_5)$ 20 mol%	24	5	RT	CD_2Cl_2	99			78
76		 (**1**)/P(1-Np)$_3$ 20 mol%	240	5	50	CD_2Cl_2	100		 10 : 1	78

[10]

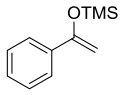
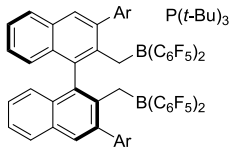
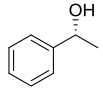
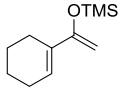
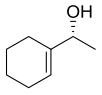
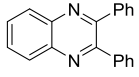
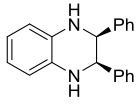
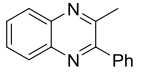
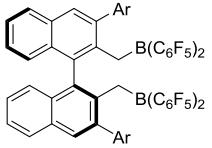
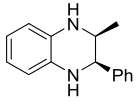
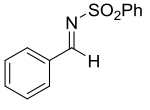
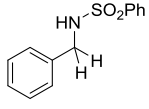
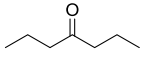
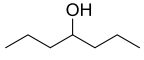
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
77		$HB(C_6F_5)_2$ (**42**) 20 mol%	72	6	140	C_6D_6	99			129
78		$HB(C_6F_5)_2$ (**42**) 20 mol%	72	6	140	C_6D_6	99			129
79		$HB(C_6F_5)_2$ (**42**) 20 mol%	120	6	140	C_6D_6	92			129
80		$HB(C_6F_5)_2$ (**42**) 20 mol%	120	6	140	C_6D_6	94			129
81		$B(C_6F_5)_3$ (**1**) 10 mol%	120	5	115	PhMe	100		 d.r. = 100 : 0	131
82		$B(C_6F_5)_3$ (**1**) 10 mol%	48	5	80	PhMe	72		 d.r. = 68 : 32	131
83		$B(C_6F_5)_3$ (**1**) 10 mol%	48	5	80	PhMe	100			131

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
84		 (*S*,*S*)-DIOP (**1**)/(*S*,*S*)-DIOP 20 mol%	96	4	100	PhMe	99		 ee 25%	83
85		 (**59**) 10 mol%	15	20	65	PhMe	>99		 ee 13%	81
86		 (**60b**) 5 mol%	15	25	65	PhMe	95		 ee 79% (*R*)	133
87		(**60b**) 5 mol%	15	25	65	PhMe	96		 ee 83% (+)	133
88		 (**61**) 2 mol%	48	25	65	PhMe	70	63	 ee 72% (*R*)	134

[12]

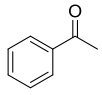
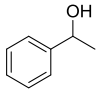
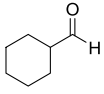
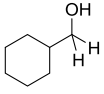
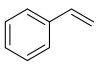
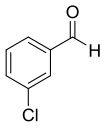
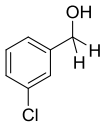
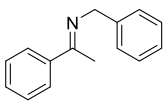
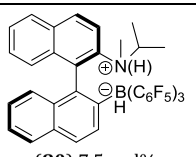
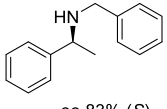
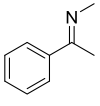
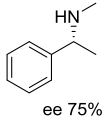
Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
89		(**61**) 2.5 mol%	24	25	65	PhMe	>99		 ee 76% (+) Four consecutive runs	134
90		 Ar = 3,5-(*t*-Bu)$_2$C$_6$H$_3$- (**62a**) 2.5 mol%	15	20	RT	Mesitylene		98	 ee 84% (*R*)	137
91		(**62a**) 2.5 mol%	15	20	RT	Mesitylene		97	 ee 85% (*R*)	137
92		(**62a**) 2.5 mol%	15	20	RT	Mesitylene		95	 ee 85% (-)	137
93		(**62a**) 2.5 mol%	15	20	60	Mesitylene		97	 ee 5%	137

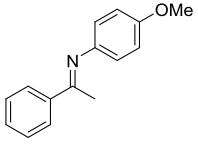
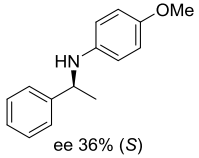
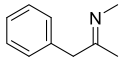
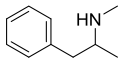
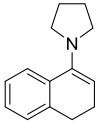
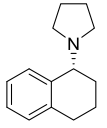
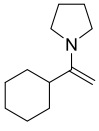
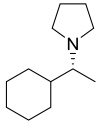
[13]

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
94	 TMS = Me_3Si-	 Ar = 3,5-(t-Bu)$_2$C$_6$H$_3$- (**62a**/P(t-Bu)$_3$) 5 mol%	24	40	50	PhMe		98	 ee 98% (*R*)	141
95	 TMS = Me_3Si-	(**62a**/P(t-Bu)$_3$) 5 mol%	24	40	50	PhMe		98	 ee 99% (*R*)	141
96		$B(C_6F_5)_3$ (**1**) 10 mol%	24	20	100	PhMe	95		 *cis*/*trans* 99: 1	142
97		 Ar = 2-MeO-(t-Bu)C$_6$H$_3$- (**62b**) 5 mol%	24	20	RT	n-Hexane		82	 *cis*/*trans* 99: 1 ee 89%	142
98		$THF{\rightarrow}B(C_6Cl_5)(C_6F_5)_2$ 5 mol%	3	4	60	THF	>99			4
99		$Et_2O{\rightarrow}B(C_6F_5)_3$ 5 mol%	12	12	70	Et_2O	>99	91		17

[14]

[15]

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
100		$Et_2O \rightarrow B(C_6F_5)_3$ 5 mol%	12	12	70	Et_2O	90			17
101		$Et_2O \rightarrow B(C_6F_5)_3$ 5 mol%	12	12	70	Et_2O	32			17
102		1,4-dioxane→$B(C_6F_5)_3$ 5 mol%	6	12-13	100	1,4-dioxane	99			18
103		1,4-dioxane→$B(C_6F_5)_3$ 5 mol%	30	5	100	1,4-dioxane	14			18
104		1,4-dioxane→$B(C_6F_5)_3$ 5 mol%	90	5	80	1,4-dioxane	78			18
105		 (**80**) 7.5 mol%	20	2	RT	MTBE	94	83	 ee 83% (*S*)	150
106		(**80**) 2.5 mol%	16	2	RT	MTBE	99	92	 ee 75% (*R*)	150

Entry	Substrate	Catalyst	Time [h]	H_2 [atm]	Temp. [°C]	Solvent	NMR Yield/ Conversion [%]	Yield [%]	Product	[Ref]
107		(**80**) 10 mol%	64	2	60	MTBE	53	34	 ee 36% (*S*)	150
108		(**80**) 5 mol%	16	2	RT	MTBE	97	72	 ee 32%	150
109		(**80**) 2.5 mol%	0.5	2	RT	MTBE	99	95	 ee 99% (*R*)	150
110		(**80**) 2.5 mol%	16	2	RT	MTBE	99	42	 ee 85% (*S*)	150

[16]