Lewis Acid-Lewis Base Mediated Metal-Free Hydrogen Activation and Catalytic Hydrogenation

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Academic Dissertation

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Abstract

Organocatalysis, the use of organic molecules as catalysts, is attracting increasing attention as one of the most modern and rapidly growing areas of organic chemistry, with countless research groups in both academia and the pharmaceutical industry around the world working on this subject.

The literature review of this thesis mainly focuses on metal-free systems for hydrogen activation and organocatalytic reduction. Since these research topics are relatively new, the literature review also highlights the basic principles of the use of Lewis acid-Lewis base pairs, which do not react irreversibly with each other, as a trap for small molecules.

The experimental section progresses from the first observation of the facile heterolytical cleavage of hydrogen gas by amines and $B(C_6F_5)_3$ to highly active non-metal catalysts for both enantioselective and racemic hydrogenation of unsaturated nitrogen-containing compounds. Moreover, detailed studies of structure-reactivity relationships of these systems by X-ray, neutron diffraction, NMR methods and quantum chemical calculations were performed to gain further insight into the mechanism of hydrogen activation and hydrogenation by boron-nitrogen compounds.

Preface

"Great moments are born from great opportunity"

Herbert Paul "Herb" Brooks, Jr.

This work was carried out between 2007 and 2011 at the Laboratory of Inorganic Chemistry, Helsinki University, supported by Academy of Finland (project 123248 and 139550) and Inorganic Materials Chemistry Graduate Program (EMTKO). Also, a considerable part of this work was done during several research visits to the WACKER-Lehrstuhl für Makromolekulare Chemie, Technische Universität München.

I am most grateful to my supervisors, Professors Markku Leskelä and Timo Repo, for providing me the opportunity to work in Finland at the Laboratory of Inorganic Chemistry, for creating all the necessary conditions for efficient research and for their invaluable support for my work. I would like to express my sincere thanks to Professor Timo Repo for giving a feeling of freedom, elation and illumination in my scientific work.

I am most indebted to Professor Bernhard Rieger from the Technical University of Munich, for our successful collaboration and for his valuable contributions to this work. I want to thank Mr. Paul Heinz, Ms. Monika Kellner, Mr. Manuel Winkenstette, Mr. Amir Doroodian from Rieger's group for their warm hospitality, support, and friendliness during my time at the TUM. Especially, I want to say thanks to Dr. Felix Schulz for our friendship and cooperation which has brought many benefits.

I am grateful to Professor Pekka Pyykkö for help with theoretical and computational aspects of the project. I also want to thank his group members: Dr. Michiko Atsumi and Dr. Cong Wang, who have helped me to take this work to a new level.

I want to express my gratitude to all my friends and co-workers at Catlab group, particularly Ms. Sirpa Vuorinen, Ms. Ahlam Sibaouih, Dr. Pertti Elo and Dr. Kirill Axenov. I am grateful to Dr. Sami Heikkinen and Dr. Martin Nieger for help with NMR spectroscopic and X-ray diffraction measurements, respectively. I also want to thank my former students, Ms. Maija Hakola, Mr. Markus Lindqvist and Mr. David Jonson, for being such a good friends and for proofreading my manuscripts. I am especially indebted to my best friends, Dr. Andrej Asachenko and Dr. Konstantin Chernichenko, who have always supported me in my endeavors and been there when I needed them.

I want to express my deepest gratitude to my wife Elena Andreeva for her love and support at the final stage of this work. Last but not least, I want to thank my parents, Victor and Tatyana, for their unconditional love.

List of original publications

This thesis is based on the following publications:

I. Victor Sumerin, Felix Schulz, Martin Nieger, Markku Leskelä, Timo Repo, Bernhard Rieger: Facile Heterolytic H_2 Activation by Amines and $B(C_6F_5)_3$. *Angew. Chem. Int. Ed.* **2008**, 47, 6001-6003.

With Cover Picture: Facile Heterolytic H_2 Activation by Amines and $B(C_6F_5)_3$.

II. Victor Sumerin, Felix Schulz, Michiko Atsumi, Cong Wang, Martin Nieger, Markku Leskelä, Timo Repo, Pekka Pyykkö and Bernhard Rieger: Molecular Tweezers for Hydrogen: Synthesis, Characterization, and Reactivity. *J. Am. Chem. Soc.*, **2008**, 130 (43), 14117–14119.

III. Victor Sumerin, Felix Schulz, Martin Nieger, Michiko Atsumi, Cong Wang, Markku Leskelä, Timo Repo, Pekka Pyykkö and Bernhard Rieger: Experimental and theoretical treatment of hydrogen splitting and storage in boron-nitrogen systems. *J. Organomet. Chem.* **2009**, 694 (17), 2654-2660.

IV. Felix Schulz, Victor Sumerin, Markku Leskelä, Timo Repo, Bernhard Rieger: Frustrated Lewis pairs: reactivities of TMS protected amines and phosphines in the presence of $B(C_6F_5)_3$. *Dalton Trans.*, **2010**, 39, 1920–1922.

V. Felix Schulz, Victor Sumerin, Sami Heikkinen, Björn Pedersen, Cong Wang, Michiko Atsumi, Markku Leskelä, Timo Repo, Pekka Pyykkö, Winfried Petry, Bernhard Rieger: Molecular hydrogen tweezers: Structure and mechanisms by neutron diffraction, NMR, and deuterium labeling studies in solid, and solution. *J. Am. Chem. Soc.*, **2011**, accepted.

VI. Victor Sumerin, Konstantin Chernichenko, Martin Nieger, Markku Leskelä, Bernhard Rieger, Timo Repo: Highly Active Metal-Free Catalysts for Hydrogenation of Unsaturated Nitrogen-containing Compounds. *Adv. Synth. Catal.* **2011**, 353 (11-12), 2093–2110.

Author's contribution

In paper I, the author of this thesis, inspired by previous Felix Schulz's work under the supervision of Prof. Bernhard Rieger, designed TMP-$B(C_6F_5)_3$ system for hydrogen activation, carried out most of experiments and analysis and drafted the manuscript. Felix Schulz helped with the experimental and analytical part of this work and edited the manuscript.

In paper II, the author of this thesis designed the first *ansa*-aminoborane system, which was able to reversibly activate hydrogen, carried out most of experiments and analysis, and drafted the manuscript. Felix Schulz helped with the experimental and analytical part of this work and edited the manuscript. Michiko Atsumi and Cong Wang made DFT calculations.

In paper III, the author of this thesis modified *ansa*-aminoborane system, carried out most of experiments and analysis, and drafted the manuscript. Felix Schulz edited the manuscript.

In paper IV, the author of this thesis and Felix Schulz contributed equally to the experimental and analytical part of this work. Felix Schulz drafted the manuscript. The author of this thesis edited the manuscript.

In paper V, the author of this thesis and Felix Schulz contributed equally to the experimental and analytical part of this work. Felix Schulz together with Dr. Sami Heikkinen drafted the manuscript. The author of this thesis edited the manuscript. Michiko Atsumi and Cong Wang made DFT calculations.

In paper VI, the author of this thesis together with Konstantin Chernichenko designed new *ansa*-aminoborane systems. The author of this thesis designed chiral *ansa*-aminoborane systems, carried out most of experiments and analysis and drafted the manuscript. Konstantin Chernichenko helped with the experimental and analytical part of this work and edited the manuscript.

The author of this thesis together with Felix Schulz was responsible for coordination of this research project.

Dr. Martin Nieger (papers I-III, VI) and Dr. Björn Pedersen (paper V) performed X-ray and neutron diffraction analysis, respectively. Dr. Sami Heikkinen helped with ^{11}B NMR, NOESY NMR and VT NMR measurements (papers I-VI).

Prof. Pekka Pyykkö (papers II, III, V) supervised the theoretical and computational part of the work. Prof. Markku Leskelä, prof. Timo Repo and prof. Bernhard Rieger supervised research project. All authors read and approved the final manuscripts.

Abbreviations

BCF	$B(C_6F_5)_3$, tris(pentafluorophenyl)borane
Bn	Benzyl
BNPA	3,3'- Disubstituted(binaphthyl)phosphoric-acid-catalyzed
n-Bu	Butyl
t-Bu	*tert*-Butyl
DFT	Density functional theory
DHB	Dihydrogen bond
DMDPP	Trans-2,6-dimethyl-2,6-diphenylpiperidine
2D NOESY NMR	Two-dimensional nuclear Overhauser effect spectroscopy
eq.	Equivalent
Et	Ethyl
FLP	Frustrated Lewis pairs
h	Hour
H_2I*t*Bu	1,3-Di-*tert*-butylimidazolidin-2-ylidene
I*t*Bu	1,3-Di-tert-butylimidazolin-2-ylidene
LALB	Lewis acid-Lewis base
Me	Methyl
Mes	Mesityl
NG	Not given
NHC	N-heterocyclic carbene
NMR	Nuclear magnetic resonance
Np	Naphthyl
Ph	Phenyl
PMP	*N*-*p*-methoxyphenyl
i-Pr	Isopropyl
RT	Room temperature
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylenediamine
TMP	2,2,4,4-Tetramethylpiperidinyl
TMS	Trimethylsilyl
Tos	Tosyl, *p*-$CH_3C_6H_4SO_2$-
VT NMR	Variable temperature nuclear magnetic resonance

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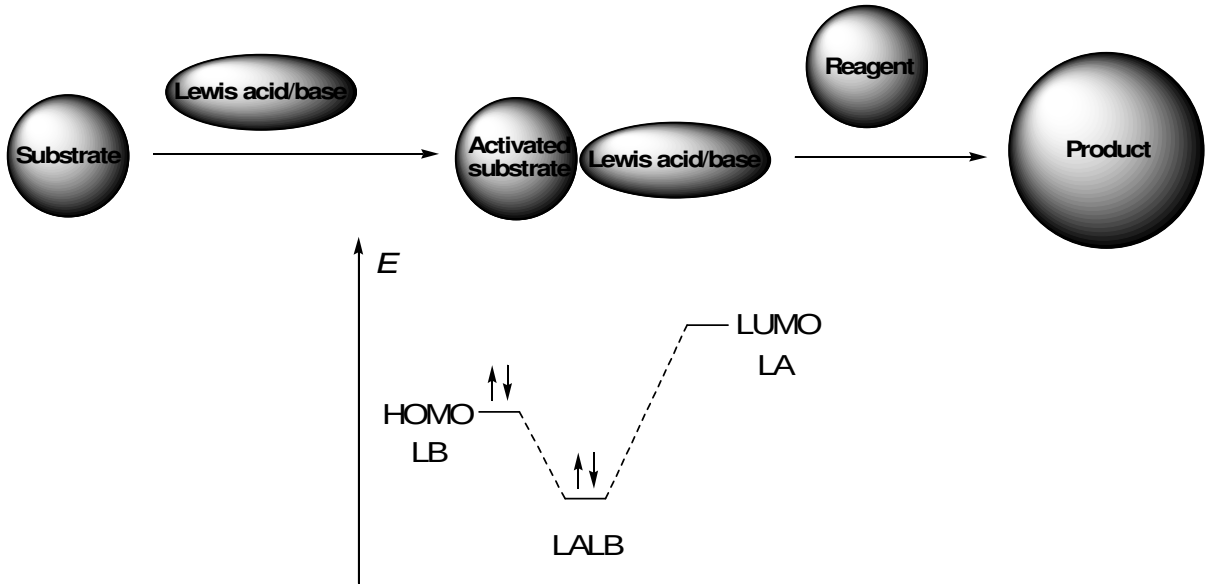
1 Introduction

In 1923 Johannes Brønsted and Thomas Lowry described a new acid-base theory. In it they proposed that any substance that can donate a proton should be classified as an acid and any substance that can accept a proton should be classified as a base, therefore the proton transfer from acid to base is essential feature of the Brønsted-Lowry concept.[1] Although this concept is more general than any that preceded it, it still does not take into account large number of similar acid-base reactions in which no protons are transferred. "The cult of the proton" of Brønsted-Lowry was overthrown by a more general acid-base theory introduced by Gilbert N. Lewis in the same year as Brønsted and Lowry's contribution, but this approach was not widely accepted until the 1930s.[2] According to this concept, a Lewis acid is defined as a substance that has its lowest unoccupied molecular orbitals (LUMOs) act as an electron-pair acceptor from the highest occupied molecular orbitals (HOMOs) of a Lewis base. Simply put, a Lewis acid is an electron-pair acceptor and a Lewis base is an electron-pair donor.

The driving force for the Lewis acid-base interaction is the need to satisfy the octet rule, the rule that states that atoms should have eight valence electrons in order to be stable – in effect having the same electronic configuration as a noble gas. This concept has come to be a primary axiom of chemistry and has a great impact on our understanding of the structure and reactivity of main-group and transition-metal compounds.



Scheme 1. Lewis acid/base mediated reactions.

The Lewis acid-base concept has played a decisive role in the discovery and use of Lewis acids and Lewis bases as reagents and catalysts in many industrially important organic reactions and processes.[3,4] In these transformations the Lewis acid-Lewis base (LALB) adduct between

substrate and Lewis acid/base reagent or catalyst is an essential intermediate (Scheme 1). This is due to the activation of a substrate by either providing (Lewis base) or removing electrons (Lewis acid) which can enhance the chemical reactivity in a number of ways from increasing nucleophilicity or electrophilicity of a substrate to the stabilization of a transition state or a product.

Among the various applications, the use of organic molecules as catalysts, or organocatalysis, is attracting increasing attention as one of the most modern and rapidly growing areas of organic chemistry. There are essentially two different types of organocatalysts: Lewis acids/bases and Brønsted acids/bases. Compared to traditional transition-metal catalysts and enzymes, these systems offer many advantages related to catalysts selectivity, functional-group tolerance, environmental sustainability, cost-efficiency and the fine purification of the final products.[5, 6, 7] Presently both Lewis acid catalysts such as boranes and Lewis base catalysts such as amines and carbenes are widely used in academic laboratories and within industry. However, despite the undeniable achievements obtained in this area in recent decades, there is still a considerable amount of unresolved challenges to be met. Moreover, there is no doubt that even small improvements in the efficiency of these processes can translate into a large monetary saving.

2 The Scope of the Thesis

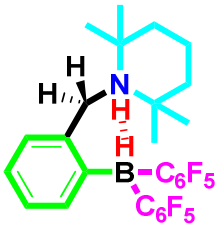
During the past century, hydrogen activation and hydrogenation of unsaturated compounds under mild conditions was an exclusive prerogative of transition metals.[8, 9, 10] While there are countless synthetic and enzymatic complexes having a transition metal at their reactive core that are able to cleave dihydrogen, the H–H bond activation solely by non-metals under mild conditions was unknown until recently.[11] In 2005 Power et al. observed the facile splitting of hydrogen by an unsaturated germanium alkyne analogue ArGeGeAr (where Ar is 2,6-(2,6-*i*-$Pr_2C_6H_3)_2C_6H_3$) to give a mixture of products.[12] In 2006, Stephan and co-workers reported the first example of reversible H_2 activation by intramolecular phosphinoborane *p*-$(Mes)_2PC_6F_4B(C_6F_5)_2$.[13] In an analogous fashion, mixtures of sterically demanding phosphines and boranes were shown to heterolytically cleave H_2, yielding phosphonium-borates of the form $[R_3PH][HB(C_6F_5)_3]$.[14] More recently in 2007, Bertrand and co-workers showed that selected organic carbenes have just enough nucleophilicity to cleave H_2 and NH_3.[15]

During the course of our research, we broadened the family of ”frustrated Lewis pairs“ [16] and demonstrated that not only bulky phosphines and boranes or organic carbenes can cleave H_2, but inexpensive, stable and the most common amines with $B(C_6F_5)_3$ can also perform H_2 activation. The facile heterolytic cleavage of H_2 was readily achieved under mild conditions by cooperative action of the Lewis acid $B(C_6F_5)_3$ and Lewis basic amines such as 2,2,6,6-tetramethylpiperidine and TMS protected amines (Publication I, IV). Later we found that the

product of the heterolytic splitting of hydrogen by *trans*-2,6-dimethyl-2,6-diphenylpiperidine and $B(C_6F_5)_3$ can release dihydrogen upon heating at 110°C. Moreover, the short (less than 1.9 Å) dihydrogen interaction in this system was shown to be one of the key factors in the hydrogen liberating process (Publication III).

Based on the above observation, we designed the first *ansa*-aminoborane *N*-TMP-$CH_2C_6H_4B(C_6F_5)_2$ (**CAT**, where TMP is 2,2,4,4-tetramethylpiperidinyl) which was able to reversibly activate H_2 through an intramolecular mechanism. This new substance made use of the concept of molecular tweezers where the active N and B centers are located close to each other so that one H_2 molecule can fit in this void and be activated. Because of the fixed geometry of this *ansa*-ammonium-borate (Scheme 2), it contains a short N-H···H-B dihydrogen bond of 1.78 Å as determined by X-ray analysis. Moreover, such system was found to release the bound hydrogen upon heating above 100°C. In addition, we demonstrated that *ansa*-ammonium-borate is not only an efficient hydrogen activator, but it also has unprecedented catalytic activity in hydrogenation of different imines and enamines under mild conditions, a task of very broad applicability (Publication II). In this article we also offered one flash of theoretical insight: the energy needed for H_2 splitting can arise from the Coulomb attraction between the resulting ions, or "Coulomb pays for Heitler-London". Quantum chemical calculations were performed to support this idea.

More detailed studies of *ansa*-ammonium-borate **$CATH_2$** system by neutron diffraction and thermogravimetric mass spectroscopic experiments in the solid state as well as by different NMR methods and FT-IR spectroscopy in solution were presented recently (Publication V). The NMR measurements gave strong evidence that the structure of *ansa*-ammonium-borate **$CATH_2$** in solution is similar to that of the solid state. Subsequent isotopic experiments utilizing D_2 and HD gases were also performed. Whereas, the result of these experiments is in agreement with our theoretical results for an intramolecular synchronous mechanism of hydrogen activation, the formation of an η^2-H_2 bound to the Lewis acidic boron center, as the rate-determining step in dihydrogen activation can also explain the observed effects. Therefore, additional experimental studies are needed to enable a conclusion to be drawn between the two mechanisms.



Scheme 2. *ansa*-Ammonium-borate.

Further systematic modification of the amine, borane and benzyl bridge moieties in the original *ansa*-ammonium-borate system resulted in significant improvements. Thus, new highly

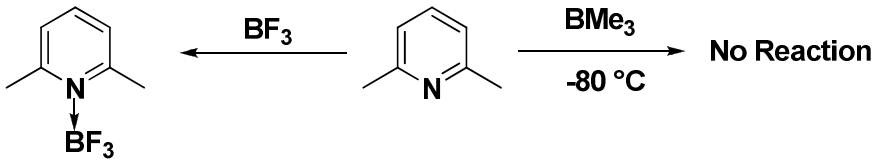
active *ansa*-ammonium-borate catalysts for the direct metal-free hydrogenation of unsaturated nitrogen-containing compounds were prepared by tuning of the basicity and steric bulkiness of their amine moieties. The highest catalytic activity among previously reported organocatalytic systems was shown for a wide range of substrates. Due to the unique properties of new *ansa*-ammonium-borates an effective catalyst recovery procedure was developed. Also, the use of chiral amines instead of the TMP moiety resulted in development of the first example of asymmetric hydrogenation based on an *ansa*-ammonium-borate concept (Publication VI).

In summary, the way from the first observation of facile heterolytic cleavage of hydrogen by amines and $B(C_6F_5)_3$ to highly active non-metal catalysts for both enantioselective and racemic hydrogenation of unsaturated nitrogen-containing compounds are presented.

3 Literature review

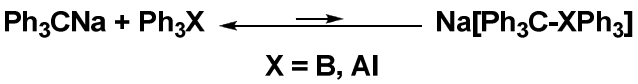
3.1 Early examples of unusual Lewis acid-Lewis base pairs

While much attention was paid to the classical LALB adducts as reagents and intermediates in many industrially important organic reactions and processes, some exceptions to this general rule were observed. In 1942, Brown and co-workers reported that 2,6-lutidine reacted with BF_3 to give a stable LALB adduct in quantitative yield, but did not react with BMe_3 even at low temperature (Scheme 3).[17] This phenomenon was explained by steric constraints between the methyl groups of lutidine and borane, which prevent the classical LALB adduct formation.



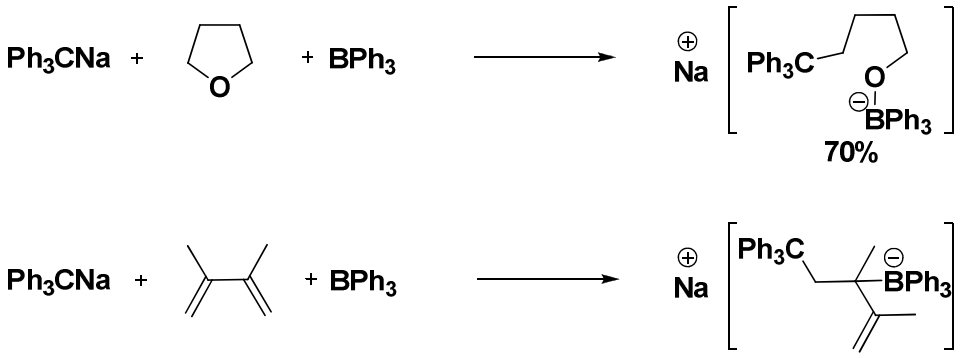
Scheme 3. Reaction of 2,6-lutidine with BF_3 and BMe_3.[17]

However, the subsequent reactivity of such systems with other molecules was unknown until the 1950s, when Wittig and co-workers discovered Lewis acid and Lewis base reagents, which do not bind irreversibly to each other (Scheme 4). For example a mixture of tritylsodium with triphenylborane or triphenylaluminium can attack suitable substrates nucleophilically and electrophilically at the same time to form new organosodium compounds.[18, 19]



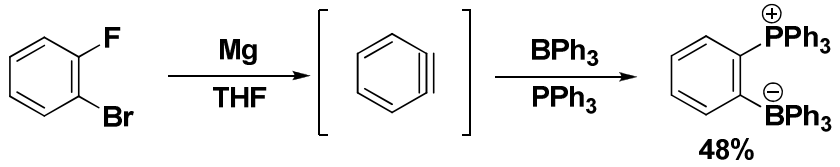
Scheme 4. Reaction of tritylsodium with triphenylborane or triphenylaluminium.[18, 19]

Particularly they found that, while relatively inert tertahydrofuran or 2,3-dimethylbutadiene did not react either with tritylsodium or triphenylborane alone, they can be activated by a stoichiometric mixture of these reagents to afford cleavage of the carbon-oxygen or double carbon-carbon bonds, respectively (Scheme 5).[18, 19, 20, 21]



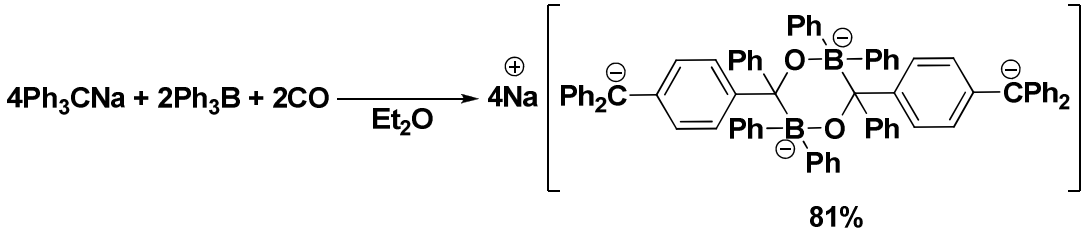
Scheme 5. Activation of tertahydrofuran and 2,3-dimethylbutadiene.[18-20]

Wittig also showed that not only highly reactive organometallic compounds, but also quite stable phosphines can act as a suitable Lewis base in similar reactions.[22] Thus the trapping of benzyne by phenyldibenzophosphole or triphenylphosphine in combination with triphenylborane was observed (Scheme 6).[23]



Scheme 6. Reaction of benzyne with triphenylphosphine/triphenylborane pair.[23]

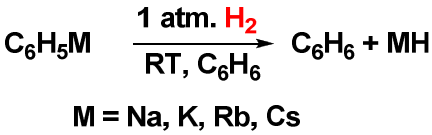
Again, whereas either tritylsodium or triphenylborane could not activate carbon monoxide alone, the original Wittig's LALB system was also able to fixate CO gas at atmospheric pressure and room temperature (Scheme 7).[24]



Scheme 7. Carbon monoxide activation.[24]

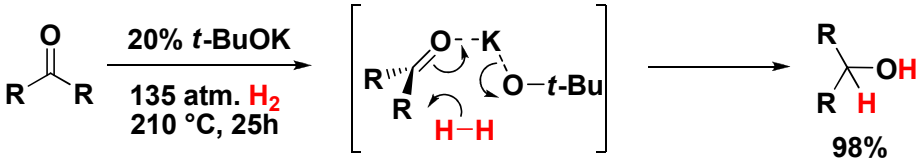
3.2 Early examples of transition metal-free H_2 activation and hydrogenation

In 1938, Gilman and co-workers described the first example of a transition metal-free hydrogen activation under mild conditions.[25] They reported that while phenylsodium, phenylpotassium, phenylrubidium and phenylcesium compounds have enough basicity to cleave molecular hydrogen at room temperature and slightly above atmospheric pressure in a relatively short time (114, 32, 25, 12 minutes, respectively), less basic organolithium compounds required at least 7 atm of hydrogen and a longer reaction time. Exposure times of over 30 hours were needed for the most reactive phenyllithium (Scheme 8). Thus the rate of hydrogenolysis of the metal-carbon bond of organic alkali metal compounds increased in the order: Li, Na, K, Rb, Cs. However, in the presence of an equivalent amount of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as an additive, hydrogen activation by *n*-butyllithium at 30-35°C takes only 30 minutes instead of 61 hours.[26, 27] This method allowed the obtaining of superactive alkali metal hydrides.



Scheme 8. Hydrogen activation by organic alkali metal compounds.[25]

The earliest example of transition metal-free hydrogenation was achieved by Walling and Bollyky in 1961.[28, 29] Unfortunately their method involved extreme reaction conditions (210°C, 135 atm of H_2) and the use of at least 20% of potassium *tert*-butoxide as a base-catalyst. Thus, only robust, nonenolizable ketones such as benzophenone can be reduced with a good yield. For instance, base-catalyzed hydrogenation of nitrobenzene gave only 32% of aniline together with 4% of starting nitrobenzene and unidentified brownish-black residues.

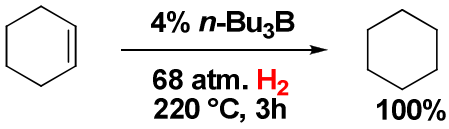


Scheme 9. Proposed mechanism for the base-catalyzed hydrogenation.[28, 29, 30]

Recently, the detailed mechanism of base-mediated hydrogenation was reported to be via a six-membered transition state (Scheme 9). [30] The initial step of the LALB adduct formation between the Lewis-acidic potassium ion and Lewis-basic carbonyl oxygen follows by the joint action of a Lewis-acidic ketone carbonyl-carbon and a Lewis-basic alkoxide anion oxygen on the H_2 molecule.

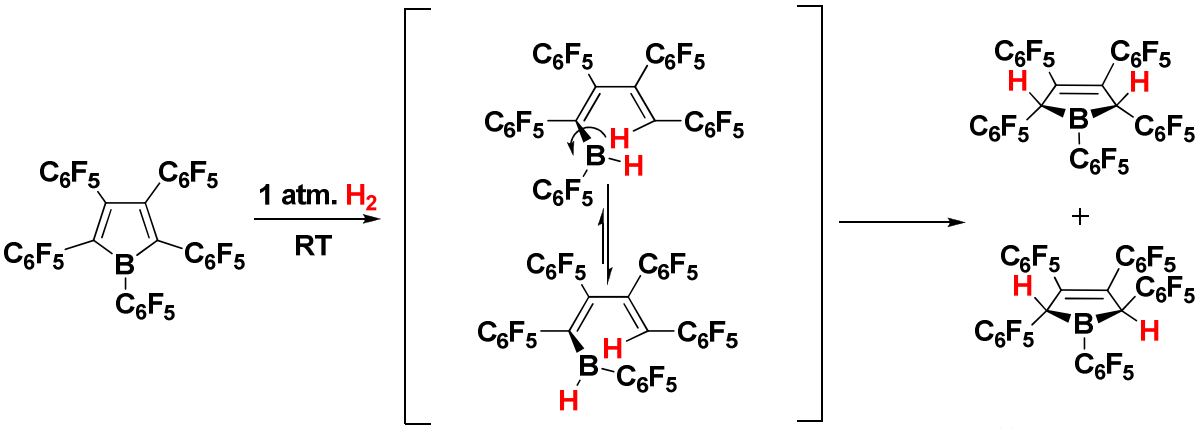
In the same year (1961) Trapasso and co-workers demonstrated that olefins can be quantitatively hydrogenated in 3-5 hours at 220-235°C under 68-170 atm of H_2 by simple alkyl

boranes, such as tri-*n*-butylborane and tri-*i*-butylborane (Scheme 10). [31,32] According to their observations and previously published splitting of hydrogen by tertiary boranes, [33,34] the rate-determining step of this reaction must be associated with hydrogenolysis of the carbon-boron bond. Similarly, tetrapropyldiborane or triethylborane and boron triiodide were used as homogeneous catalysts for the hydrogenation of polycyclic aromatic hydrocarbons (170-200°C and 25-100 atm of H_2) [35, 36] and coal (280-350°C and 148-247 atm of H_2) [37] respectively.



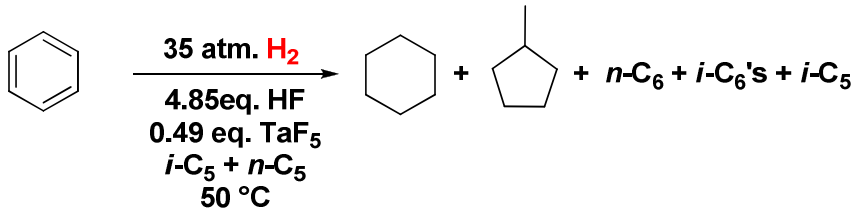
Scheme 10. Borane-catalyzed homogeneous hydrogenation of olefins.[31, 32]

Recently, Piers and Parvez showed that not only the harsh reaction conditions but also the disruption of antiaromaticity upon reaction of the Lewis acidic perfluoropentaphenylborole with H_2 can provide a thermodynamic driving force for the hydrogen activation reaction, followed by C-B bond cleavage. Thus, the antiaromatic borole molecule reacted extremely rapidly with hydrogen gas at room temperature and atmospheric pressure (Scheme 11).[38]



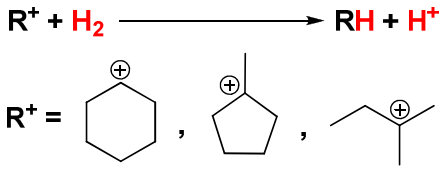
Scheme 11. Hydrogen activation by perfluoropentaphenylborole.[38]

Walling and Bollyky were also the first who proposed the idea to use strong acids as catalysts for hydrogenation of unsaturated aliphatic hydrocarbons.[29] Hydrogenation of cyclohexene with 16% $AlBr_3$ at 150°C and 82 atm pressure of hydrogen gave a mixture of the fully saturated products, consisting of 4% methylcyclopentane and 2% cyclohexane together with many higher-boiling products. Later, by using HF/TaF_5 Siskin accomplished the first superacid-catalyzed hydrogenation of an aromatic hydrocarbon. [39] Detailed study of benzene hydrogenation in presence of HF/TaF_5 by Wristers showed the essential role of an aliphatic solvent in this reaction, since the protonated benzene did not react directly with hydrogen under the experimental conditions (Scheme 12). [40]



Scheme 12. Superacid-catalyzed hydrogenation of benzene.[40]

However in an aliphatic solvent, a hydride transfer occurs from the saturated hydrocarbon to the protonated benzene, yielding an aliphatic carbenium ion, which further reacts with molecular hydrogen to regenerate the starting alkane and give reduced benzene products (Scheme 13). It is noted that an aliphatic carbenium ion is isoelectronic with boranes and a very strong Lewis acid.



Scheme 13. Hydrogen activation by aliphatic carbenium ions.

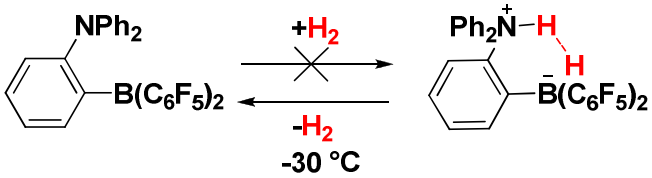
Earlier reports on catalytic transition metal-free hydrogenation of olefins also include processes mediated by single (LiH, NaH, KH and MgH_2)[41] or mixed ($LiAlH_4$)[42] metal hydrides. In all cases, hydrogenation requires harsh reaction conditions (150-225°C, 60-100 atm of H_2), and the use of at least 20% of metal hydride as a catalyst, giving desired products in low yields.

3.3 The first attempt to use LALB system for H_2 activation

The first unusual Lewis acid-Lewis base systems and attempts to use them for small molecule activation were published more than 50 years ago. But only in 2003 did Roesler and Piers prepare the first intramolecular LALB systems, where the active Lewis acidic boron and Lewis basic nitrogen centers were located close to each other and did not form a classical adduct due to the steric hindrance of the bulky amine and borane moieties and the high strain energy of the corresponding four-membered ring.[43]

Roesler and Piers predicted that such "Lewis acid/Lewis base trap", would be suitable for the reversible activation of H_2 (Scheme 14). Particularly, they not only speculated that *ansa*-ammonium-borate might be a "dihydrogen storage device, able to release H_2 upon heating or during a chemical reaction, regenerating" aminoborane *o*-Ph_2N-C_6H_4-$B(C_6F_5)_2$, but also suggested that strong N-$H^{\delta+}$...$^{\delta-}$H-B dihydrogen bond (DHB) interactions would play a key role in this process. Unfortunately Piers' aminoborane was not able to cleave H_2 due to another important observation made in this paper: the significantly reduced basicity of the amino group,

which "would have to be significantly higher in order to thermodynamically favor the formation of a dihydrogen adduct over the elimination of hydrogen". Although the hydrogenated system was never characterized, the *in situ* generated *o*-Ph_2NH^+-C_6H_4-$[HB(C_6F_5)_2]^-$ spontaneously liberated dihydrogen gas even at low temperature.



Scheme 14. Piers' aminoborane and ammonium-borate.[43]

Nevertheless, their unusual LALB system was extremely sensitive to moisture and acids, forming zwitterionic products. Recently, analogous properties of bidentate ammonium and phosphonium boranes were found to be essential for the selective receptors for cyanide and fluorine ions in water at neutral pH.[44, 45, 46]

3.4 Why is it so difficult to activate hydrogen?[9]

The following reasons can be listed as difficulties in hydrogen activation:

I. The hydrogen-hydrogen bond is among the strongest single bonds. The amount of energy needed for homolytic cleavage of the H-H bond is 432 kJ/mol. Thus, since most H-X bonds will be weaker than the H-H bond, there is often little or no thermodynamic driving force for the splitting of dihydrogen gas.

II. Hydrogen is a completely nonpolar molecule, which is a poor target for attack by either electophiles or nucleophiles, resulting in large activation energies required for H_2 activation. Thus, the rates of even thermodynamically favorable direct reactions with hydrogen are often extremely slow.

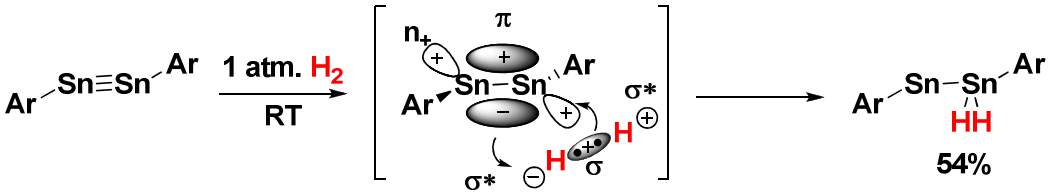
III. The frontier molecular orbitals of hydrogen do not permit the most direct, concerted reactions between dihydrogen and other non-metals.

IV. Due to a nonpolar and remarkably strong H-H bond hydrogen gas is a very poor acid, both kinetically and thermodynamically.[25-27] The pK_a value of 49 in THF places hydrogen among the weakest acids.

However dihydrogen has one great advantage: its small size allows H_2 to react directly with highly reactive systems which cannot quench their reactivity due to the steric hindrance and/or the high strain energy of the corresponding adducts.

3.5 Hydrogen activation by main group elements under mild conditions

In 2005 Power and co-workers reported the first example of the facile splitting of hydrogen by unsaturated germanium alkyne analogue ArGeGeAr (where Ar is 2,6-(2,6-*i*-$Pr_2C_6H_3)_2C_6H_3$) to give a mixture of digermene, digermane and primary germane products at room temperature and 1 atm pressure.[12] The hydrogen activation by digermyne ArGeGeAr is thought to be due in part to the singlet diradical character of the ground state of the corresponding germanium compound. [47] Later, in contrast to digermyne the reactions of tin alkyne analogues ArSnSnAr (where Ar is 2,6-(2,6-*i*-$Pr_2C_6H_3)_2$-4X-C_6H_2 or 2,6-(2,6-*i*-$Pr_2C_6H_3)_2$-3,5-*i*-Pr_2-C_6H and X is H, $SiMe_3$, F) with H_2 were shown to cleanly afford a single tin hydride product (Scheme 15).[48]



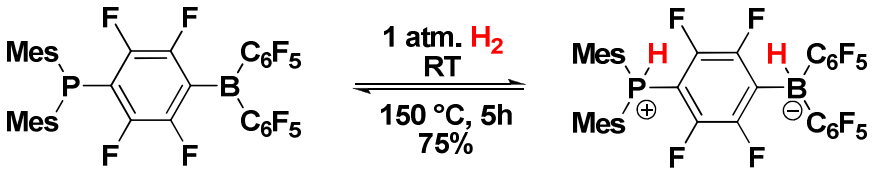
Ar = 2,6-(2,6-*i*-$Pr_2C_6H_3)_2$-3,5-*i*-Pr_2-C_6H

Scheme 15. Possible mechanism of hydrogen splitting by distannynes.[48]

According to the proposed mechanism, hydrogen activation by alkyne analogues involves a synergic interaction of the H-H σ-bond with the LUMO (n_+, virtual lone-pair) of the Sn atom and interaction of the H-H empty σ*-orbital with the HOMO Sn-Sn π-orbital. The energy separation of the π and n_+ levels in distannynes was shown to be related to the singlet diradical character of the ground state of the molecule.

3.6 Hydrogen activation by phosphines and boranes

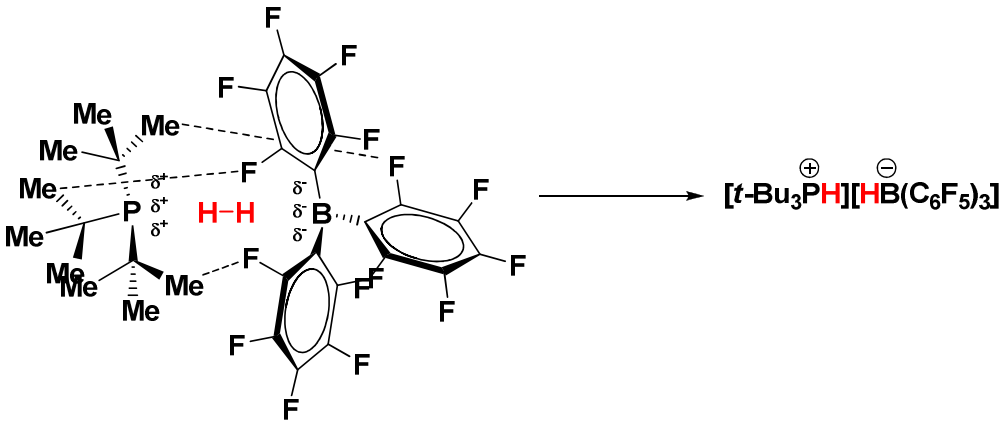
The facile splitting of hydrogen by an unsaturated germanium alkyne analogue was the only example of H_2 activation at nonmetals under mild conditions until 2006. When Piers's concept was successfully implemented in Stephan's group for the reversible hydrogen activation by a nonmetal system based on bulky phosphinoborane "frustrated" Lewis pair (Scheme 16).[13]



Scheme 16. Reversible hydrogen activation by "frustrated" Lewis pair.[13]

The hydrogenated compound *p*-$(Mes)_2PH^+C_6F_4[HB(C_6F_5)_2]^-$ was synthesized in 2 steps with a 72% yield by *para*-nucleophilic aromatic substitution of $B(C_6F_5)_3$ with Mes_2PH followed

by treatment with chlorodimethylsilane. The heating of the phosphonium borate salt solution at 150º C resulted in the liberation of hydrogen gas and formation of the product *p*-$(Mes)_2PC_6F_4B(C_6F_5)_2$, which can further split H_2 at 25º C and 1 atm to reform the original hydrogenated salt in almost quantitative yield. The key to the successful heterolytic cleavage of H_2 under mild conditions by Stephan's phosphinoborane is the use of the Lewis acid-Lewis base pair with correctly matched electronic and steric properties. While steric influences are sufficient to preclude the formation of the phosphine–borane adduct, the Lewis acidity of the boron and the Lewis basicity of the phosphorus atoms are high enough to thermodynamically favor the formation of a hydrogenated product at room temperature. In an analogous fashion, later, mixtures of sterically demanding phosphines and boranes were also shown to heterolytically cleave H_2. The resulted phosphonium-borates $[R_3PH][HB(C_6F_5)_3]$ (R = *t*-Bu, *o*-MeC_6H_4, Mes) were very stable and did not release hydrogen even upon heating at 150º C. [14,49]

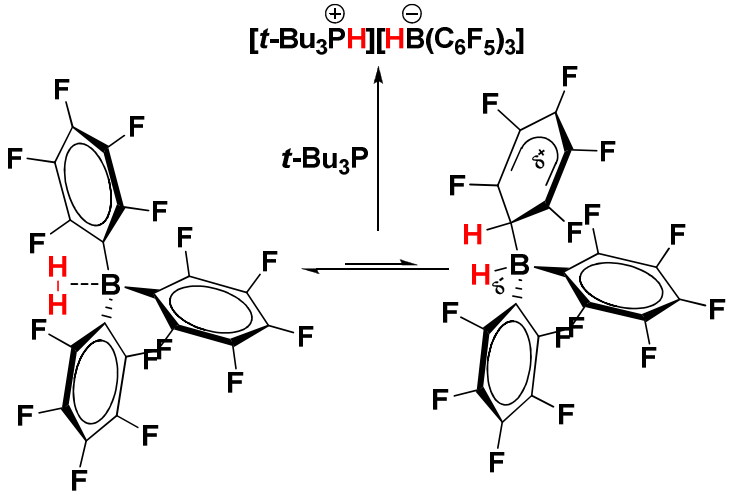


Scheme 17. Possible intermediate in hydrogen activation by FLPs.[50]

The mechanism of reversible hydrogen activation by such systems is still a subject of intense discussions, particularly concerning the initiation step. Two alternative hypotheses have been postulated. The first hypothesis involves a phosphine-borane "encounter complex" stabilized by non-covalent H···F hydrogen bond and/or π-π interactions (Scheme 17). In this "species" the boron and phosphorous atoms are located close to each other but fail to form a dative bond that creates an electric field between two active centers. A hydrogen molecule can easily fit into the void and be polarized by this electric field, leading to cleavage of the H–H bond.[50,51,52,53,54] However, this hypothesis was supported only by computational experiments.

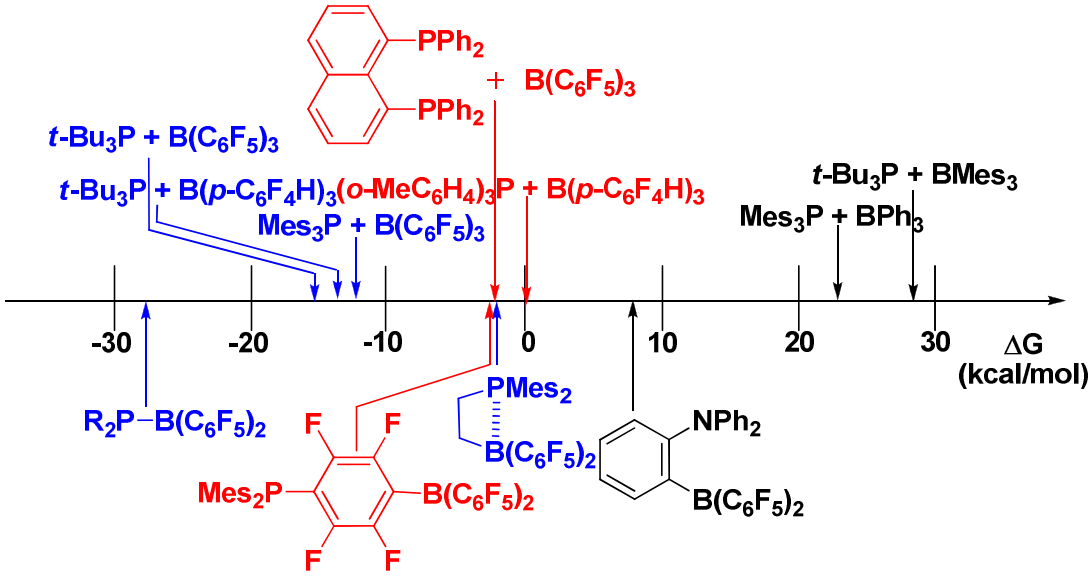
The second hypothesis involves formation of a σ-complex between borane and H_2 (Scheme 18). This intermediate could be deprotonated directly by a Lewis base or undergo heterolytic addition of H_2 across a B–C bond followed by deprotonation with phosphine. To date, all attempts to observe such borane-hydrogen interactions have failed.[14,38] Nevertheless, computational studies[55] and the experimental observation of the hydrogen splitting by Lewis

acidic boranes alone (see chapter 3.2, Scheme 11) suggest that the H_2-$B(C_6F_5)_3$ adduct is not stable but is in fact a possible intermediate in hydrogen activation by FLPs.[33-37,38]



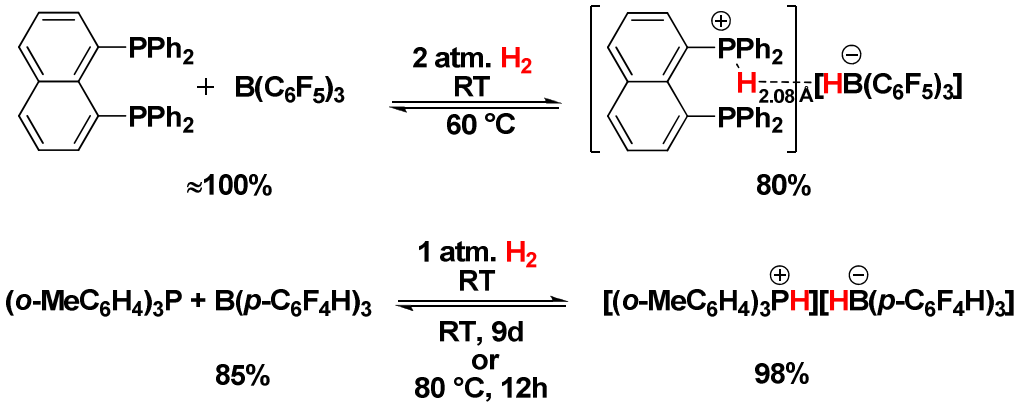
Scheme 18. Possible intermediates in hydrogen activation by FLPs.[38]

Although in the case of phosphonium-borates the liberation of hydrogen is thermodynamically unfavored, it is envisioned that if the reaction is almost thermodynamically neutral, facile hydrogen liberation under mild conditions can take place (Scheme 19).[56]



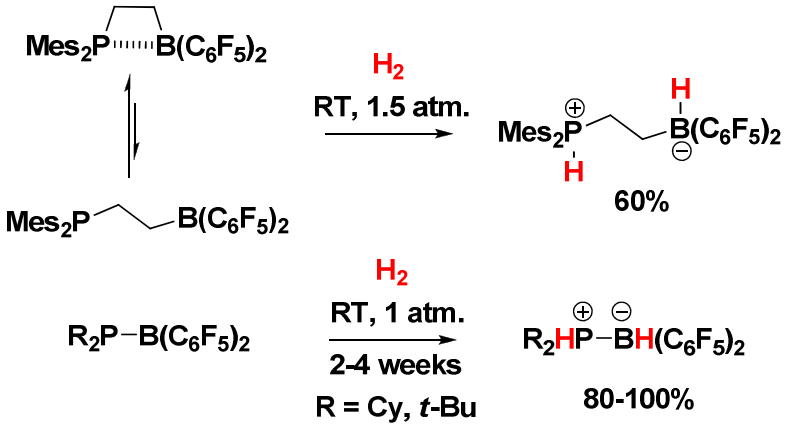
Scheme 19. Calculated Gibbs free energies for the hydrogen splitting reaction by FLPs.[56] (**black** - no reaction; **blue** – H_2 activation; **red** – reversible H_2 activation)

Accordingly, Erker and Stephan recently showed that by lowering the basicity or acidity of the bulky phosphines or boranes, respectively, it is possible to obtain intermolecular systems able to reversibly activate hydrogen even under mild conditions (Scheme 20).[49,57,58]



Scheme 20. Reversible hydrogen activation under mild conditions.[49, 57, 58]

Although, the backbone of such systems contains only lightweight elements, which is an important criterion for hydrogen storage materials,[59,60] their storage capacity is less than 0.25 weight % H_2, still below the targets of 6 to 9 weight %. [61] Nevertheless, these findings further suggested potential for new approaches to H_2 storage.

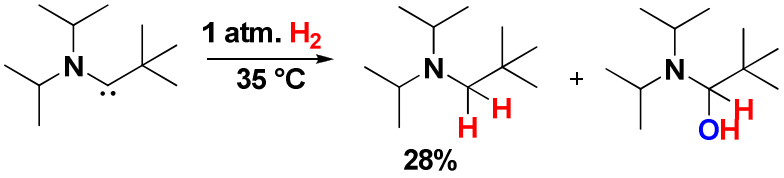


Scheme 21. Hydrogen activation under mild conditions.[64]

During the last four years some intramolecular phosphinoborane systems and different phosphino-metallocenes in combination with $B(C_6F_5)_3$ were shown to non-reversibly activate H_2 and be effective catalysts for the hydrogenation of bulky imines and enamines and nitrogen-containing heterocycles (Scheme 21, also see chapters 3.12 and 3.13).[62, 63, 64, 65, 66, 67, 68]

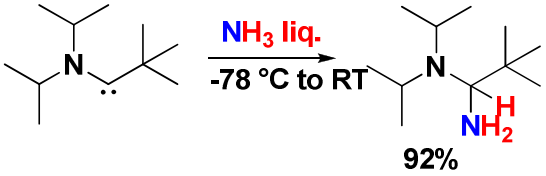
3.7 Hydrogen activation by carbenes and tin(II), germanium(II) carbene analogues

In 2007 Bertrand and co-workers demonstrated that selected organic (alkyl)(amino)carbenes are just nucleophilic enough to cleave H_2 at 35º C and atmospheric pressure. The corresponding saturated compounds were obtained in moderate yield along with the water adduct of the carbenes (Scheme 22).[15]



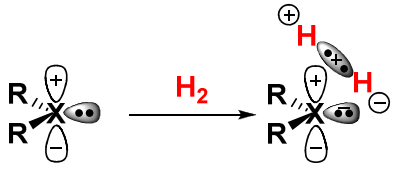
Scheme 22. Hydrogen activation by (alkyl)(amino)carbenes.[15]

Furthermore, while transition-metal complexes (with a few exceptions)[69,70] bind ammonia to give the classical LALB adducts, alkyl(amino)carbenes rapidly react with liquid NH_3, even at -40º C, forming the N-H activation products (Scheme 23).



Scheme 23. Ammonia activation by (alkyl)(amino)carbenes.[15]

Recently Power and co-workers showed that treatment of the tin(II) and germanium(II) carbene analogues, diarylstannylene :$SnAr_2$ and diarylgermylene :$GeAr_2$ (where Ar is 2,6-(2,6-*i*-$Pr_2C_6H_3)_2C_6H_3$), with H_2 and NH_3 also afforded H-H and N-H activation products in high yields.[71,72] Later, the carbene-like gallium monovalent aryl spicies :GaAr (where Ar is 2,6-(2,6-*i*-$Pr_2C_6H_3)_2$-4-$(Me_3Si)C_6H_2$) was shown to react directly with H_2 and NH_3 at room temperature and 1 atm pressure.[73]



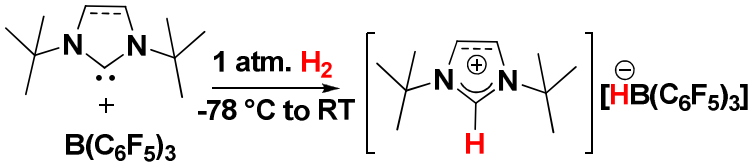
Scheme 24. The initial step of H_2 activation by a divalent group 14 molecule.[71, 72, 73]

The mechanism of hydrogen activation by divalent group 14 molecules is proposed to occur in a manner similar to transition-metal complexes.[15] Singlet carbenes, stannylenes and germylenes have a vacant orbital and a filled nonbonding orbital which are oriented such that the σ-bonding orbital of the hydrogen molecule donates into the vacant orbital and a lone pair

populates the H_2 antibonding σ* orbital, thus polarizing the H-H bond so enabling its cleavage (Scheme 24).

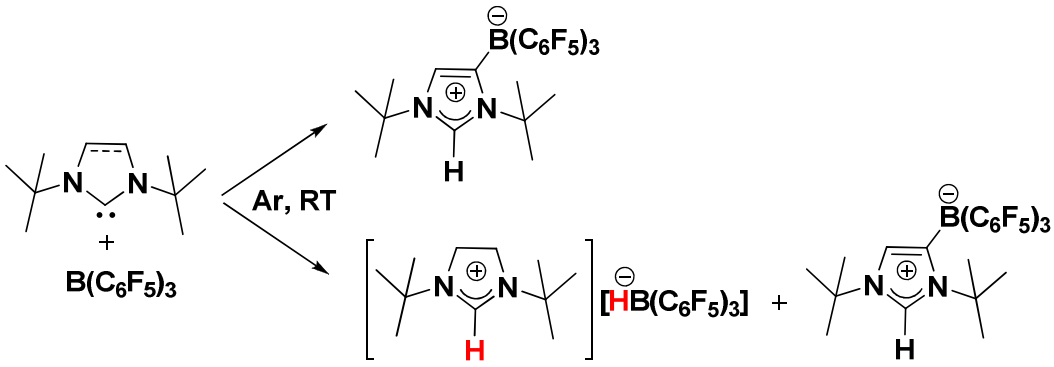
3.8 Hydrogen activation by N-heterocyclic carbenes and $B(C_6F_5)_3$

While alkyl(amino)carbenes and their analogues can cleave hydrogen under mild conditions, both cyclic (N-heterocyclic carbene, NHC) and acyclic diamino carbenes do not react with H_2 without a transition-metal catalyst. [15,74] It was shown in calculations that this fact is due to the slightly higher-lying highest-occupied molecular orbital (HOMO) and the significantly smaller singlet-triplet energy gap in the alkyl(amino)carbenes compared to that of the diamino carbenes. However in presence of a strong Lewis acid, $B(C_6F_5)_3$, 1,3-di-*tert*-butylimidazolidin-2-ylidene (H_2I*t*Bu) and 1,3-di-tert-butylimidazolin-2-ylidene (I*t*Bu) immediately reacted with hydrogen at room temperature and 1 atm pressure to form imidazolinium and imidazolium borohydrides in almost quantitative yields (Scheme 25).[75,76]



Scheme 25. Hydrogen activation by carbenes in combination with $B(C_6F_5)_3$.[75, 76]

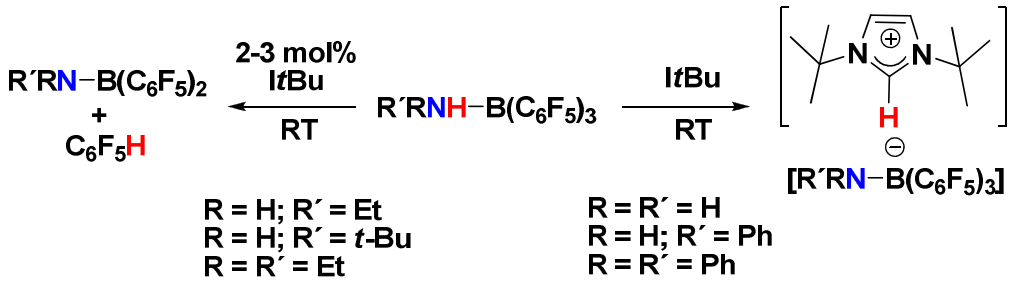
The mechanism of hydrogen splitting by carbenes and boranes is thought to be similar to that proposed for phosphines and boranes (see chapter 3.6).[76] However, in comparison with the energies calculated for phosphine-borane pairs (-14.7 kcal/mol for *t*-Bu_3P-$B(C_6F_5)_3$, Scheme 19) heterolytic dihydrogen cleavage is thermodynamically more favorable for carbene–borane systems (-40.7 kcal/mol for I*t*Bu). This is mainly due to the higher proton affinity of carbenes compared to phosphines, which prevents the use of such systems for reversible hydrogen activation or catalytic hydrogenation.[56]



Scheme 26. Quenching the reactivity of carbene-borane FLPs at RT.[77]

Also, these systems are not sufficiently stable at room temperature. Thus the solutions containing equimolar amounts of N-heterocyclic carbene and $B(C_6F_5)_3$ completely lost their reactivity towards dihydrogen within one hour and gave "abnormal" carbene-borane adducts (Scheme 26). This is a clear limitation for their applicability.[77]

On the other hand, due to the extremely high reactivity of carbene-borane pairs, the reaction with amines resulted in the N-H bond activation and formation of the aminoboranes or imidazolium aminoborates in the case of primary, secondary alkylamines or ammonia, and primary, secondary anilines, respectively (Scheme 27). [75]

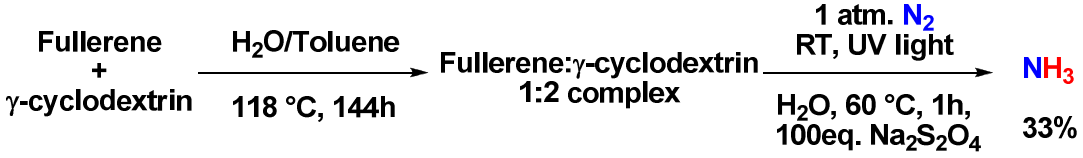


Scheme 27. N-H bond activation by carbene-borane FLP.[75]

Other low-valent carbon systems were shown to also act as Lewis bases in hydrogen activation reactions. Thus, the exposure of a zero-valent carbon (C^0) compound such as hexaphenylcarbodiphosphorane ($Ph_3P{=}C{=}PPh_3$) and $B(C_6F_5)_3$ solution to an atmosphere of H_2 at -78 °C followed by warming to room temperature resulted in the hydrogen activation and formation of the product $[(Ph_3P)_2CH]^+[HB(C_6F_5)_3]^-$ with a 91% yield. [78]

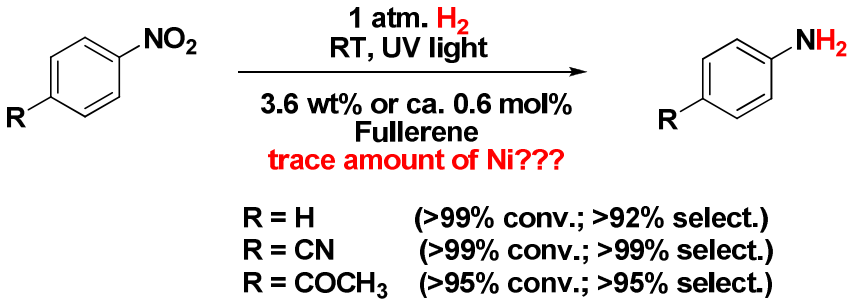
3.9 Reduction by fullerene-based catalysts

In 2004 Nishibayashi et al. described the use of the redox properties of a water-soluble fullerene-γ-cyclodextrin (1:2) complex in the first nonmetal-mediated reduction of nitrogen into ammonia.[79] They showed that the treatment of a fullerene-γ-cyclodextrin complex with 100 equivalents of sodium dithionite as a reducing agent in water under 1 atm of N_2 and with visible light at 60 °C for 1 hour produced NH_3 with a 33% yield (Scheme 28). According to their observations, fullerene in the γ-cyclodextrin complex is readily reduced by $Na_2S_2O_4$ to the corresponding C_{60}^- and C_{60}^{2-} species, which have sufficiently low reduction potentials so as to reduce the coordinated N_2.



Scheme 28. Reduction of N_2 to ammonia by fullerene-γ-cyclodextrin catalyst.[79]

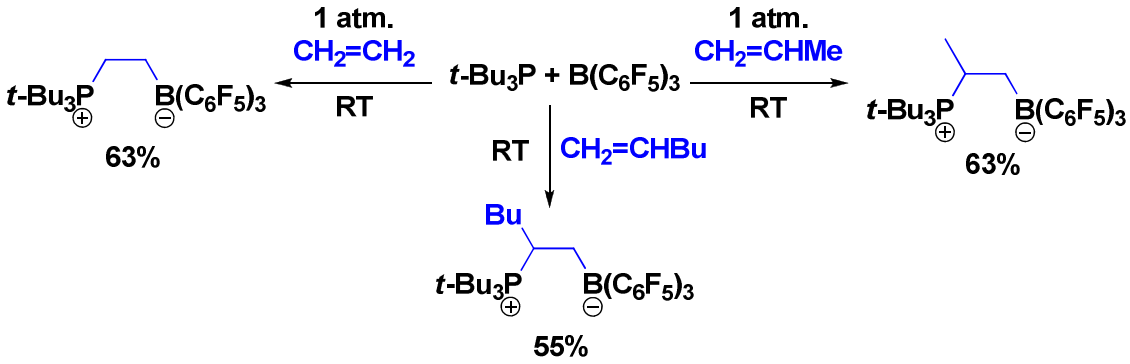
Recently, Li and Xu showed that while fullerene itself was almost inactive in the reduction of nitrobenzene to aniline under forcing conditions (140º C, 49 atm of H_2), [80] the anion C_{60}^- also effectively catalyzed this reaction and at the optimum conditions achieved greater than 99.9% conversion of nitrobenzene with a 88.9% selectivity of aniline (160º C, 49 atm of H_2). Interestingly, employing a mixture of fullerene C_{60} and anione C_{60}^- (1:2) as a catalyst led to the significantly enhanced selectivity (99.9%) with the same conversion >99.9%. Furthermore, irradiation of a THF solution of nitrobenzene and catalytic amount of fullerene under 1 atm pressure of H_2 and at room temperature with UV light gave the corresponding anilines in high yield and high selectivity (Scheme 29).



Scheme 29. Hydrogenation of nitrobenzenes by C_{60}-catalyst.[80, 81]

The exact mechanism of the fullerene-catalyzed hydrogen activation and reduction is still unclear. Moreover, more recent work by van Bokhoven et al. showed that trace amount of nickel is most likely responsible for the observed catalytic hydrogenations.[81]

3.10 Activation and hydrogenation of unsaturated carbon-carbon bonds

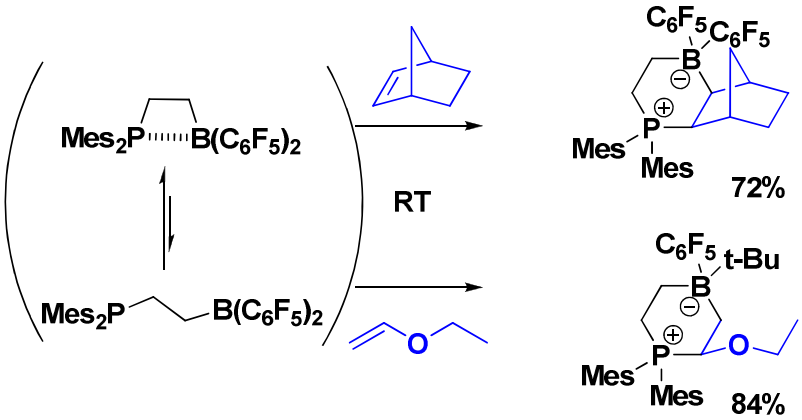


Scheme 30. Activation of alkenes by *t*-Bu_3P and $B(C_6F_5)_3$.[84]

Until recently there were only a few pioneering works [18-21,82,83] on the activation of the carbon-carbon unsaturated bonds by nonmetals under mild conditions. In 2007 Stephan et al. broadened the reactivity of FLP and demonstrated that a system consisting of tri-*tert*-butylphosphine and $B(C_6F_5)_3$ reacts with olefins at room temperature to give alkyl bridged

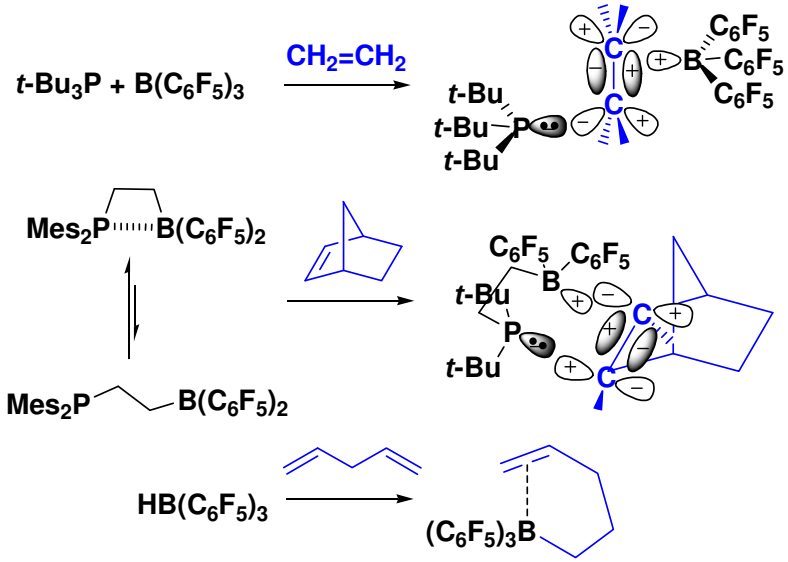
phosphonium borates (Scheme 30).[84] Interestingly, this three-component reaction was regioselective, with the phosphorous and boron atoms adding to the more and less substituted olefinic carbons, respectively.

More recently, Erker and co-workers showed that intramolecular $Mes_2PCH_2CH_2B(C_6F_5)_2$ FLP systems can also cleave the olefinic carbon-carbon double bonds in a similar manner (Scheme 31).[85]



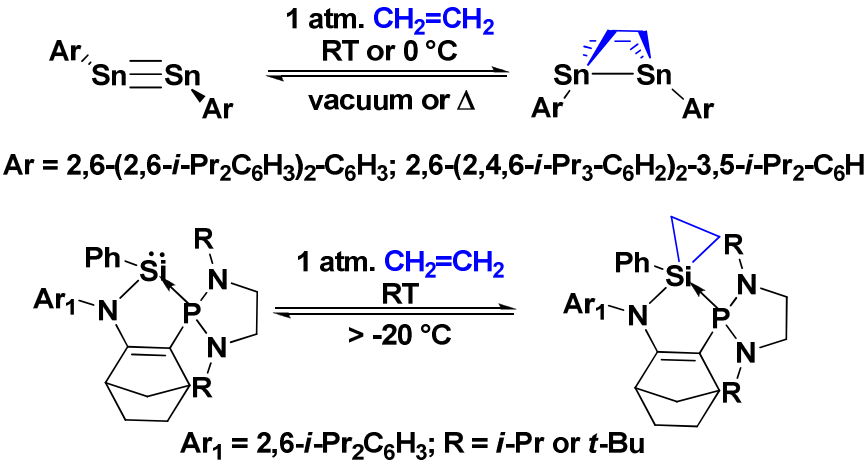
Scheme 31. Alkene activation by intramolecular $Mes_2PCH_2CH_2B(C_6F_5)_2$ FLP.[85]

A detailed theoretical study of the regioselective reaction of boron-phosphorous FLP systems with olefins by Pápai's and Li's groups suggests an asynchronous concerted 1,2-addition mechanism for C=C bond activation through the initial formation of a van der Waals borane–olefin complex (Scheme 32).[86,87]



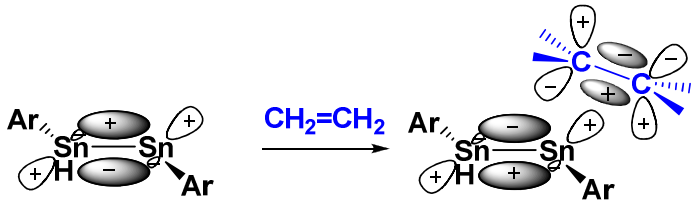
Scheme 32. The initial step of alkene activation by phosphinoborane FLPs.[85]

This point of view was also supported by independent experimental and DFT calculation results of Erker's and Stephan's groups.[85,88] In particular, they showed that the reaction of the intramolecular FLP system $Mes_2PCH_2CH_2B(C_6F_5)_2$ with norbornene gives the kinetic *exo*-2,3-addition product and the existence of a weakly interacted intramolecular borane-olefin van der Waals complex $CH_2{=}CHCH_2CH_2CH_2B(C_6F_5)_2$ at -50°C by NMR (Scheme 32).



Scheme 33. Reversible ethylene activation by distannynes and phosphine–silylene complexes.[89]

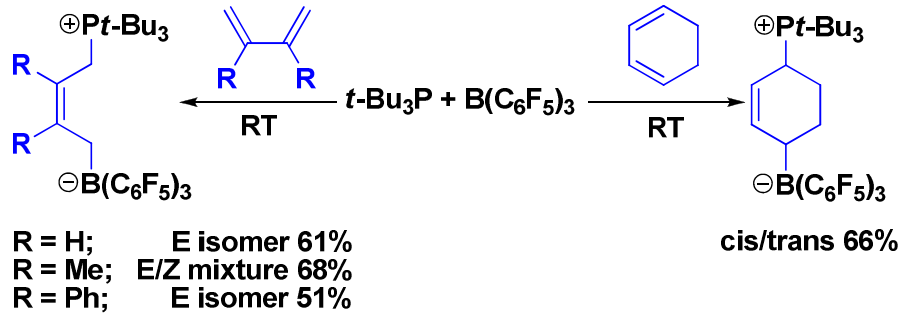
The reversible activation of unsaturated carbon-carbon bonds by main-group compounds is much rarer and until recently was presented only by the reaction of dialkylstannylene $:Sn\{CH(SiMe_3)_2\}_2$ with a strained cyclic acetylene $S(CH_2C(CH_3)_2C)_2$ forming a stannacyclopropene.[82] However, a year ago, Power et al. demonstrated that diarylstannynes analogues to distannynes that can split H_2 under mild conditions (see chapter 3.4) can also reversible activate ethylene at room temperature and 1 atm pressure (Scheme 33).[89] More recently, Baceiredo and Kato et al. showed that bulky phosphine–silylene complexes can undergo reversible [2+1] cycloaddition reaction with ethylene to give the corresponding pentacoordinate siliranes (Scheme 33).[90]



Scheme 34. The initial step of reversible ethylene activation by distannynes.[89]

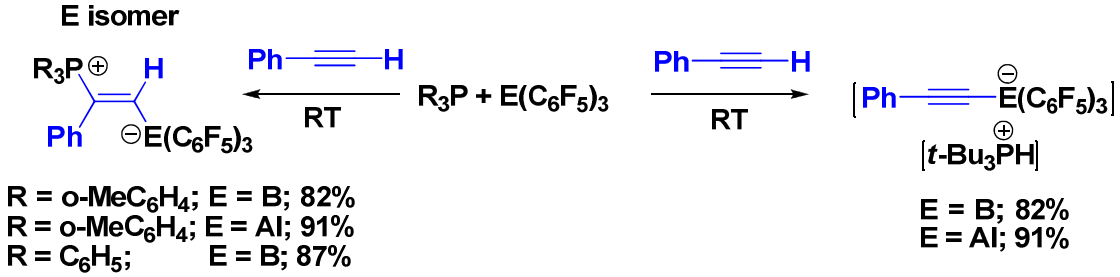
The reversible activation of ethylene by distannynes is possible due to a rare combination of electronic, steric, and thermodynamic effects. According to a proposed mechanism, the initial step of ethylene activation involves a synergic interaction of the C=C π-bond with the LUMO

(virtual lone-pair) of the Sn atom and interaction of the carbon empty π*-orbital with the HOMO Sn-Sn π-orbital (Scheme 34).



Scheme 35. Activation of dienes by Stephan's FLP.[91]

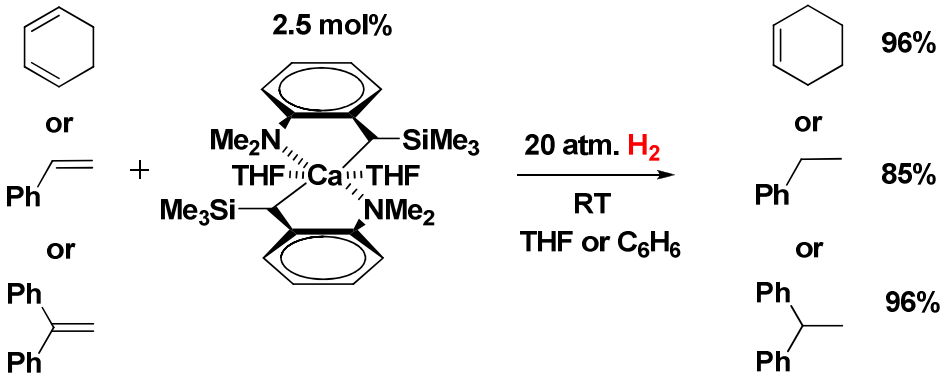
Whereas the early Wittig FLP system consisting of tritylsodium and triphenylborane reacts with 2,3-dimethylbutadiene to give 1,2-addition product,[20] the activation of conjugated dienes by tri-*tert*-butylphosphine and $B(C_6F_5)_3$, lead to 1,4-addition in 50-70% yield together with unidentified byproducts (Scheme 35).[91]



Scheme 36. Activation of phenylacetylene by FLP systems.[92]

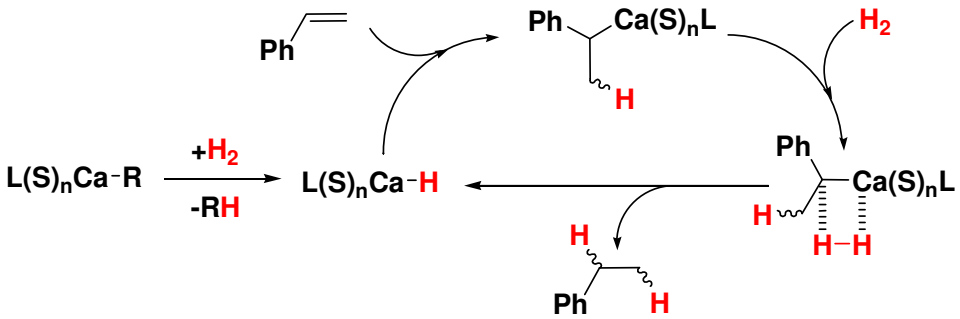
Similarly to alkenes and dienes, the activation of phenylacetylene by FLP systems gave 1,2-addition products in the case of arylphosphines and $B(C_6F_5)_3$ or $Al(C_6F_5)_3$·toluene. However, both trispentafluorophenylborane and trispentafluorophenylaluminum together with the more electron donating *t*-Bu_3P reacted with PhC≡CH to form sp^3-CH bond activation products in almost quantitative yields (Scheme 36).[92]

Besides the undeniable achievements in activation of small molecules by nonmetals, very few reports on the hydrogenation of unsaturated carbon-carbon bonds by main-group compounds are known today.[41,42] Thus, the quest to develop "Cheap Metals for Noble Tasks" is still an attractive goal.[93] A breakthrough in this area was the recent discovery by Harder and co-workers that early main-group metal catalysts having calcium, strontium or potassium at their reactive core can hydrogenate conjugated alkenes even under mild conditions, at 20 atm hydrogen pressure and room temperature (Scheme 37).[94]



Scheme 37. Hydrogenation of conjugated alkenes by an organocalcium catalyst.[94]

Density functional theory calculations have been performed to gain insight into the proposed mechanism for the hydrogenation of conjugated alkenes by early main-group metal catalysts (Scheme 38).[95] In particular, Li and Zeng showed that the hydrogenation reaction proceeds via three steps. The first step is the addition of calcium hydride across a C=C double bond to form organocalcium intermediate. In this intermediate the calcium center acts as a Lewis acid and the carbon atom acts as a Lewis base. Thus the whole system acts as an intramolecular FLP, which can split H_2 heterolytically to produce the hydrogenated product and regenerate the catalyst. The rate-determining step of the hydrogenation process was shown to be the initial hydride transfer step.

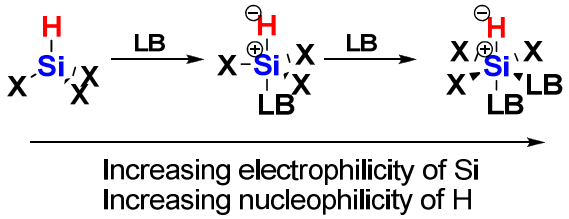


Scheme 38. Hydrogenation of conjugated alkenes by an organocalcium catalyst.[94]

3.11 Nonmetal reduction of imines, enamines and nitrogen-containing heterocycles

The preparation of amines is a fundamental chemical transformation.[96,97] The significant importance of amines and their derivatives such as amides and sulfamides in the chemical, agrochemical, pharmaceutical and polymer industries is well recognized.[98,99] Although countless methods are known for the synthesis of amines, the widely used transition-metal-catalyzed reductions of imines, enamines, nitriles and nitrogen-containing heterocycles are probably the most important.[10,100] Unfortunately, transition-metal catalysts are not only expensive, but also their complete removal from the reaction product can be difficult, but is generally required in the

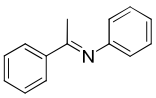
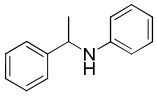
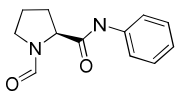
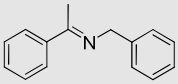
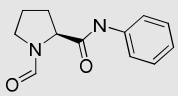
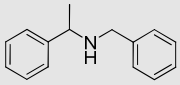
production of pharmaceutical intermediates due to toxicity concerns.[5] Moreover, an alternative stoichiometric reduction by main-group metal hydrides such as $NaBH_4$ and $LiAlH_4$ involves tedious work-up procedures and produces toxic chemical waste.[101] Additionally, there is still a considerable amount of unresolved challenges related to the selectivity and functional-group tolerance of both stoichiometric reducing agents and transition-metal catalysts. Therefore, the use of organocatalyts for the reduction of unsaturated compounds is a promising alternative to the current methods.



Scheme 39. Activation of Lewis acidic siliconhydride by a Lewis base.

In 1982 Benkeser and Snyder reported that trichlorosilane reacted with imines in CH_3CN to give upon workup amines in high yield.[102] Later, Hachiya and co-workers described the use of a dimethylformamide-Cl_3SiH system as an efficient reducing reagent for the reduction of imines, aldehydes and the reductive amination of aldehydes.[103] Additionally, they demonstrated that Lewis basic dimethylformamide coordinates to the Lewis acidic Cl_3SiH forming an active hexacoordinate siliconhydride species (Scheme 39). Further development of Lewis base-promoted hydrosilylation with Cl_3SiH by the Matsumura group revealed the first enantioselective chiral *N*-formylproline-phenylanilide-catalyzed reduction of *N*-aryl- and *N*-benzyl-ketimines (Table 1).[104] However, in both cases only moderate enantioselectivities were obtained.

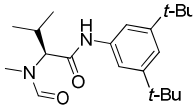
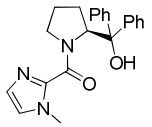
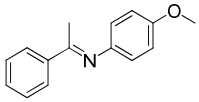
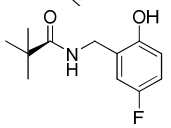
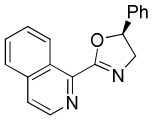
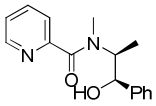
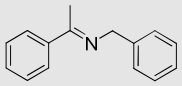
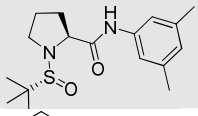
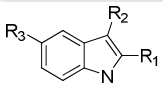
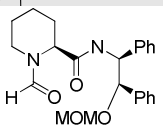
Table 1. Catalytic hydrosilation of imines with 1.5eq Cl_3SiH in CH_2Cl_2 at RT.[104]

Entry	Substrate	Catalyst	Amine	Conv. [%]
1		No catalyst		18[a]
2		20% dimethylformamide		43[a]
3		20% *N*-formylpyrrolidine		79[a]
4				91; 55% ee[b]
5				97; 55% ee[b]

[a] 6h; [b] 10mol% of catalyst, 24h.

Presently, chiral amide, sulfonamide and oxazoline-catalyzed hydrosilylation with trichlorosilane is a well-established strategy for the enantioselective reduction of *N*-alkyl-[105], *N*-aryl-ketimines[106,107,108,109,110] and indoles[111] giving both high yields and *ee*'s (Table 2). However, all these methods usually require a relatively high loading of the catalyst (10-20%), and only in the case of the most active amides (Table 2, entries 1,2) 1 mol% of catalyst was also shown to be highly effective.[112,113]

Table 2. Enantioselective catalytic hydrosilation of imines with 2-3 eq Cl_3SiH.

Entry	Substrate	Catalyst	Conditions	Conv. [%]	ee [%]
1			1-5 mol%, RT, 24h	92-95	93-94[112]
2			1 mol%, 0 ºC, 4h	96	87[113]
3			20 mol%, -20 ºC, 48h	97	91[108]
4			20 mol%, -20 ºC, 24h	60	85[106]
5			20 mol%, -10 ºC, 24h	90	93[109]
6			10 mol%, 0 ºC, 24h	98	96[105]
7			10 mol%, -20 ºC, 72h, 1eq. H_2O	78-91	46-93 (d.r.99:1)[111]

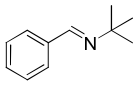
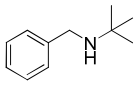
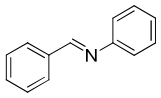
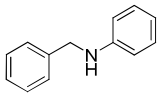
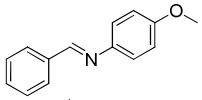
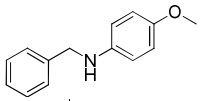
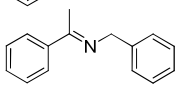
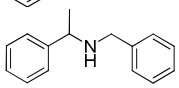
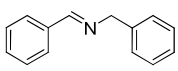
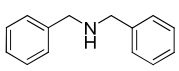
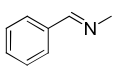
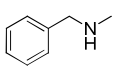
Until recently the lack of a highly desirable catalyst recovery procedure was one of the main drawbacks of such systems. Nevertheless, the development of a methyl-substituted analogue of Sigamide (Table 2, entry 1) with fluorous tag (*p*-O-$CH_2CH_2C_6F_{13}$), different polymers (*p*-O-CH_2Polymer) or gold nanoparticles attached to phenyl ring helped to overcome this disadvantage.[114,115,116] The separation of the fluorous catalyst from the reaction mixture was readily achieved by column chromatography on fluorous silica, while polymer-supported or gold

nanoparticle-immobilized catalysts can be easily separated by decantation of the mother liquor. Fluorinated, polymer-supported and immobilized chiral catalysts could be recovered and reused up to 5 times with minimal losses of activity and enantioselectivity. However, the higher catalyst loading (typically 15 mol %) is required in the case of organocatalysts immobilized on a solid (heterogeneous) support.

Whereas Lewis base-catalyzed hydrosilylation require an excess of Cl_3SiH as a hydrogen source, trichlorosilane is relatively easy to handle under an anhydrous atmosphere and is a cheap industrial product (Sigma-Aldrich, 26.6€ per 1 mol). Moreover, the aqueous $NaHCO_3$ workup procedure produces only non-toxic NaCl and SiO_2 as side products. Therefore, today this method is one of the most promising organocatalytic approaches for the practical synthesis of chiral amines.

In the case of more reactive transition-metal catalysts, during hydrosilylation Cl_3SiH can generate the highly toxic and pyrophoric gas, silane (SiH_4).[117, 118, 119] Thus, the large-scale reduction with trichlorosilane should be undertaken with great caution.

Table 3. Catalytic hydrosilation[a] of imines in the presence of 5-10 mol% $B(C_5F_6)_3$.[125]

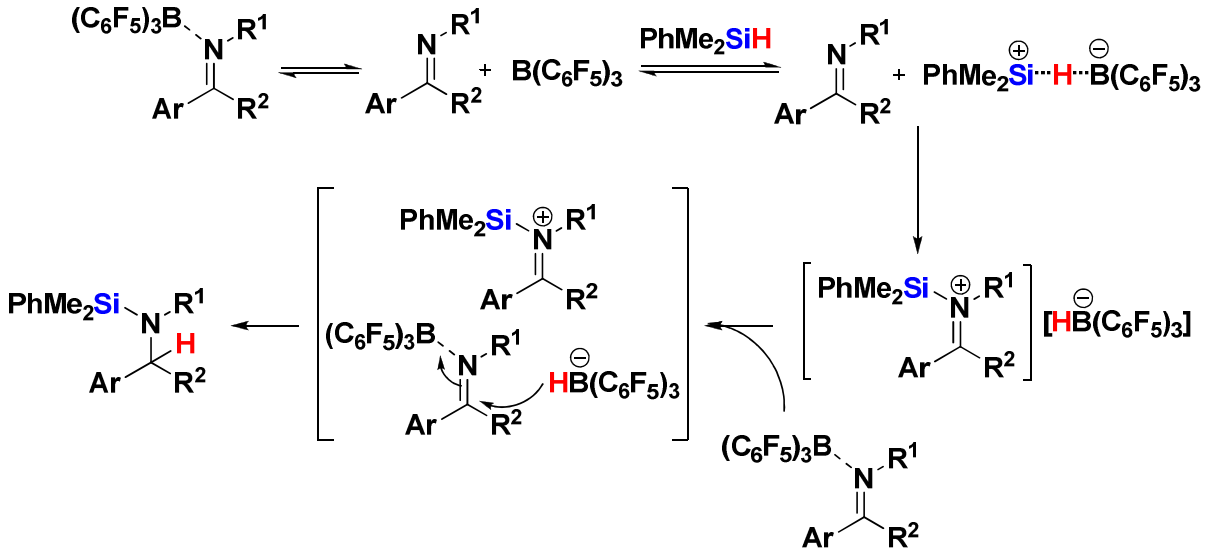
Entry	Substrate	Conditions	Amine	Conv. [%]
1		RT, 0.5h		80
2		RT, 1h		95
3		70 ºC, 1.5h		95
4		RT, 4h		95
5		70 ºC, 3h		91
6		70 ºC, 48h		NR

[a] 1.1eq $PhMe_2SiH$.

In contrast to Lewis base-catalyzed hydrosilylation, Lewis acid-mediated organocatalytic protocols with silanes are less developed.[120,121,122,123,124] The first example of transition metal-free reduction of imines by an organic Lewis acid was a $B(C_5F_6)_3$-catalyzed hydrosilylation with $PhMe_2SiH$ developed recently by the Piers group.[125] In this study a wide range of aldimines and ketimines were reduced to their corresponding amines with excellent yields (Table 3). The

comprehensive mechanistic studies by Piers suggested that Lewis acid-mediated hydrosilation proceeds via intermolecular attack of boronhydride anione by silyliminium cation, which is formed via abstraction of a hydride from silane by $B(C_6F_5)_3$ with a further attack of "$PhMe_2Si^+$" on the imine.[126]

However, based on the recent results of imines hydrosilylation with stereogenic silane, Oestreich and Hog proposed an improved reaction mechanism, in which in contrast to the reduction of ketones and Piers's mechanism for the reduction of imines,[127] boronhydride can not directly transfer a hydride onto a hindered silylated cationе (Scheme 40). Instead, it attacks the less bulky and more reactive imine-borane complex.



Scheme 40. Lewis acid-catalyzed hydrosilation of imines.[125]

An important feature of Lewis acid-catalyzed hydrosilylation is the suppression of the activity of the catalyst by the formation of amine- and imine-borane adducts. Thus, the reduction of less bulky imines usually requires more time at higher temperatures compared to that for more bulky substrates (Table 3, entries 4, 5), and non-bulky *N*-methyl aldimine does not react even at 70 ºC (Table 3, entry 6). Due to the higher basicity of the amines and as a consequence the higher energy needed for LALB adduct dissociation, the reduction of imines with electron donating *N*-aryl substitutions also requires higher temperatures (Table 3, entries 2, 3).

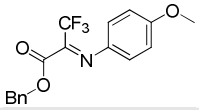
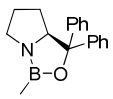
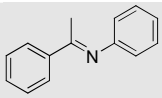
Recently, Zhang has reported an improved Lewis acid-catalyzed hydrosilylation protocol utilizing more active phenyl and diphenylsilanes in the presence of 2 mol% of $B(C_6F_5)_3$ for the reduction of enamines and indoles.[128] However, this method is still relatively new and undeveloped.

Another useful system for the reduction of unsaturated compounds is the well known Et_3SiH-CF_3CO_2H reagent.[129,130] Since trifluoroacetic acid is a Brønsted acid of medium strength with pK_a=0.23, it has strong ionization and solvation properties but does not react with silanes. Therefore CF_3CO_2H acid can serve as a "proton source", while the silane can act as a hydride donor in ionic hydrogenation reactions. Thus, the reagent combination of silane and trifluoroacetic acid is as an efficient stoichiometric reducing system for the direct hydrogenation of different imines[131] and indoles,[132] and for the reductive amination of aldehydes.[133,134]

Not only silanes, but also borane-based reducing agents have been found to be successful in organocatalytic approaches. Different Lewis base-borane complexes such as BH_3-pyridine, BH_3-Me_2N and BH_3-*t*-$BuNH_2$ were shown to be a cheap, readily available and chemoselective alternative to sodium boronhydride and cyanoboronhydride for the reduction of imines and reductive amination.[135,136,137,] However, all these compounds have been found to be less reactive than BH_3-THF and BH_3-Me_2S. As a result, the reduction can only be performed in the presence of an excess amount of acetic or methansulfonic acid, which activate the amine-borane complex. Furthermore, besides the unwanted health risk associated with pyridine, the BH_3-pyridine reagent is quite unstable to heat, thus large-scale use should be undertaken with extreme care.[138]

New amine-borane complexes that alleviate or eliminate the above-mentioned problems were recently introduced. Thereby α-picoline-borane,[139] *N*-ethyl-*N*-isopropylaniline[140] and *N*-*t*-butyl-*N*-*i*-propyl-*N*-methylamine[141] were found to be highly reactive and environmentally benign borane carriers for the reduction of imines and nitriles, and reductive amination of aldehydes and ketones. The reactions were carried out in THF, MeOH-AcOH (10:1), H_2O-AcOH (10:1) or neat conditions at room temperature giving superior yields to those obtained with other aminoborane complexes. A simple decaborane $B_{10}H_{14}$ (30 mol%) promoted reductive amination at room temperature in methanol was also reported to give the corresponding amines in high yields.[142]

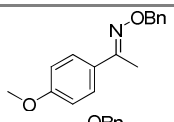
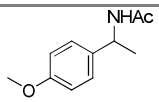
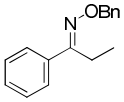
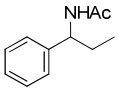
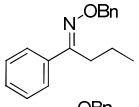
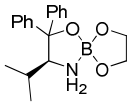
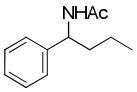
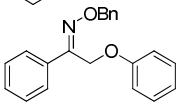
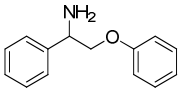
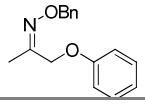
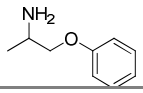
Table 4. Enantioselective catalytic hydroboration of imines in the presence of 10mol% (S)-methyl-CBS-oxazaborolidine in THF at RT.[152]

Entry	Substrate	Catalyst	Reducing agent	Conv. [%]	ee [%]
1			Catecholborane	95	68
2			BH_3-THF	69	87 (*R*)
3			Catecholborane	98	47 (*S*)

Chiral oxazaborolidines have found wide application as catalysts for asymmetric ketone reductions with boranes.[143] However, their use in the reduction of imines has not been as extensive, and until recently has been limited to the stoichiometric hydroboration of *N*-

arylimines and oximes ethers with excess of borane.[144,145,146,147,148,149,150] Presently there is only one chiral oxazaborolidine able to catalyze the enantioselective reduction of *N*-arylimines[151] and *N*-aryl-α-imino ethers[152] (Table 4) and one chiral spiroborate ester able to catalyze the enantioselective reduction of oximes ethers (Table 5).[153,154] Both of these methods require 10 mol% of catalyst and excess of BH_3-THF as the hydrogen source (1.15-4 equiv.) to give the corresponding amines in high yields and high *ee*'s.

Table 5. Enantioselective catalytic hydroboration of oxime ethers with 4 eq BH_3-THF in the presence of 10 mol% spiroborate esters at 0 ºC.[153, 154]

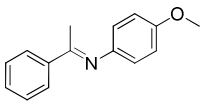
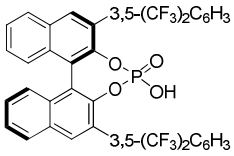
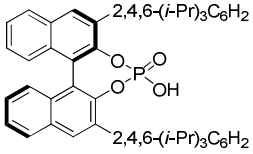
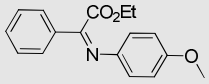
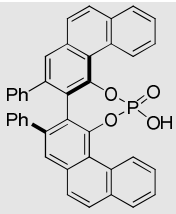
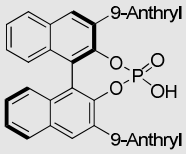
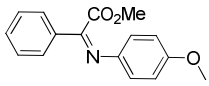
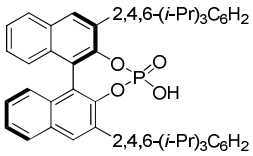
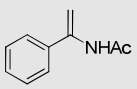
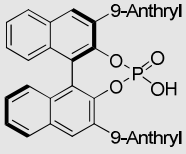
Entry	Substrate	Catalyst	Amine	Conv. [%]	ee [%]
1				90	85[a]
2				89	83[a]
3				71	99[a]
4				84	97
5				83	94

[a] The produced amines were *in situ* protected with an acetyl group for the determination of their enantiomeric ratio by chiral-GC analysis.

Despite recent achievements in enantioselective catalytic hydroboration, this method is still far from a practical application. Specifically, the low concentration and the high cost of the reducing agent (1M BH_3-THF, Sigma-Aldrich, 186.2€ per 1 mol) strictly limits it. Moreover the BH_3-THF complex itself is not stable over long periods.

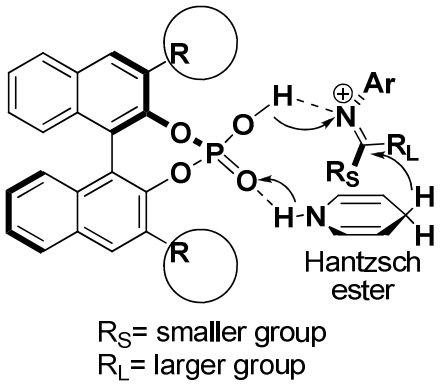
Recently, alternative approaches for the enantioselective organocatalytic reduction of imines using analogues of nicotinamide adenine dinucleotide cofactor (NADH) as hydride donors such as Hantzsch esters[155,156] or benzothiazolines[157] were developed. In 2005 Rueping and co-workers demonstrated the first example of chiral 3,3'-disubstituted(binaphthyl)-phosphoric-acid-catalyzed (BNPA) asymmetric reduction of ketimines by a Hantzsch ester (HEH) (Table 6, entry 1). [158] However, this method required the use of 20% of chiral Brønsted acids.

Table 6. Asymmetric catalytic reduction of imines with Hantzsch esters (HEH) or 2-arylbenzothiazoline (Ph-BTH; 2-Np-BTH) in the presence of a Brønsted acid.

Entry	Substrate	Catalyst	Conditions	Conv. [%]	ee [%]
1			20 mol%, 1.4eq. HEH,60 ºC, 3d	76	74[158]
2			1mol%, 1.4eq. HEH, 35 ºC, 45h	96	88[159]
3			2 mol%, 1.4eq. 2-Np-BTH, 50 ºC, 26h	90	98[157]
4			5 mol%, 1.4 eq HEH, 50 ºC, 19h	93	96[160]
5			1 mol%, 1.4 eq HEH, 60 ºC, 48h	88	92[161]
6			1 mol%, 1.6 eq Ph-BTH, 50 ºC, 24h	95	98[162]
7			1 mol%, 1.4 eq HEH, 50 ºC, 15h, 10% AcOH	97	91[163]

Almost simultaneously with the work of Rueping, a slightly different enantioselective imine reduction protocol was reported by List et al.[159] They found that bulky 3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate (TRIP) was a superior BNPA-

type catalyst for the ketimine reduction by Hantzsch esters. A series of *N*-arylketimines was reduced in the presence of only 1 mol% of TRIP-acid with good yields and high enantioselectivities (80-93% ee) (Table 6, entry 2). Moreover, *in situ* imine generation in the presence of molecular sieves followed by TRIP-catalzyed reduction with Hantzsch esters was reported by List's group (Table 7, entry 1). More recently, Akiyama and Zhu achieved the highest *ee* (>98%) reported so far for the reduction of *N*-PMP-imines by employing benzothiazolines as a hydrogen source in combination with 2 mol% of TRIP acid (Table 6, entry 3).[157] Subsequently, Antilla's, You's and Akiyama's groups reported an enantioselective transfer hydrogenation of *N*-PMP-protected α-imino esters affording chiral *N*-PMP-α-amino esters (*ee* of 92-98%) in high yields (Table 6, entries 4-6).[160,161,162] Surprisingly, while 1 mol% of chiral-phosphoric-acid was generally required for the reduction of methyl and ethyl α-imino esters, a loading of the chiral phosphoric acid as low as 0.1 mol% showed almost the same activity and enantioselectivity as 1 mol% in the case of sterically demanding isopropyl esters. The Antilla's group also developed the highly enantioselective reduction of acetyl-protected imines with Hantzsch ester using 1 mol% of chiral phosphoric and 10 mol% of acetic acids (Table 6, entry 7). The main advantage of this method is that in contrast to PMP-protected amines, the corresponding *N*-acylamines can be easily deprotected by hydrolysis.[163]



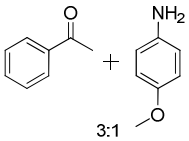
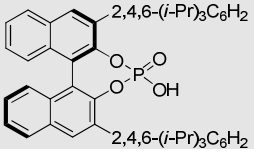
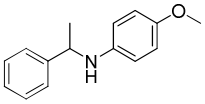
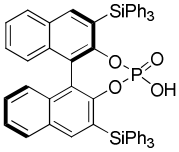
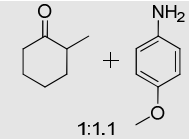
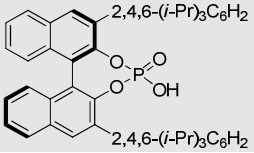
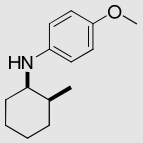
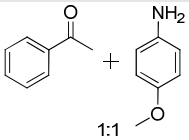
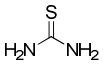
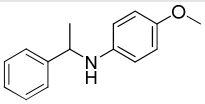
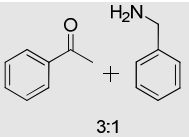
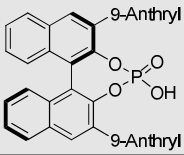
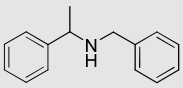
Scheme 41. The hydride transfer transition state in imine reduction by Hantzsch ester.[164, 165]

The detailed theoretical investigations by Goodman and Himo revealed a simultaneous three-component transition state in which the ketimine is protonated by the phosphoric acid, and the Hantzsch ester is activated by a hydrogen bond formed between the Lewis basic oxygen of the phosphoryl group and NH group of the dehydropyridine (Scheme 41).[164,165] Following hydride transfer and phosphate protonation, the *N*-arylamine and the Hantzsch pyridine are released and the phosphoric acid is regenerated. Thereby diarylphosphoric acids act as a bifunctional Lewis base/Brønsted acid catalyst.

Recently, MacMillan and co-workers developed the first, and to date only, organocatalytic enantioselective reductive amination employing 3,3′-bis(triphenylsilyl)-

binaphthyl phosphoric acid as a catalyst (10 mol%) and Hantzsch esters as a reducing agent in the presence of 5Å molecular sieves.[166] (Table 7, entry 2). This procedure has a significant advantage over standard methods, namely avoiding isolation of the imine during synthesis. However, there is a strong restriction on the type of amines that can be used in such a reduction. Thus, only for different *N*-aryl- and *N*-hetarylamines equally high reactivity and enantioselectivity in the reductive amination of aryl-alkyl and dialkyl ketones were shown.

Table 7. Asymmetric catalytic reductive amination with Hantzsch esters [HEH].

Entry	Substrate	Catalyst	Conditions	Amine	Conv. [%]	ee [%]
1	 3:1		5Å MS, 9h; then 5 mol%, 1.4 eq HEH, 35 ºC, 45h		>81	88[159]
2			10 mol%, 1.2 eq HEH, 50 ºC, 5Å MS, 24h		87	94[166]
3	 1:1.1		1 mol%, 1.4 eq HEH, 50 ºC, 5Å MS, 72h		82	86 (d.r.5:1) [169]
4	 1:1		10 mol%, 1.5 eq HEH, 50 ºC, 5Å MS, 2d		88	-[167]
5	 3:1		5 mol%, 1.4 eq HEH, 167 mbar, 57 ºC, 5d		96	88[168]

A similar racemic version of the organocatalytic reductive amination of ketones with *N*-aryl- and *N*-hetarylamines requires only a catalytic amount (10 mol%) of thiourea as a hydrogen bond donor and 1.5 equivalents of Hantzsch ester as a hydrogen source (Table 7, entry 4)[167] More recently, the List's group has extended the chiral-BNPA-catalyzed approach to reductive amination with *N*-benzylamines (Table 7, entry 5)[168] and dynamic kinetic reductive amination of α-branched ketones (Table 7, entry 3).[169]

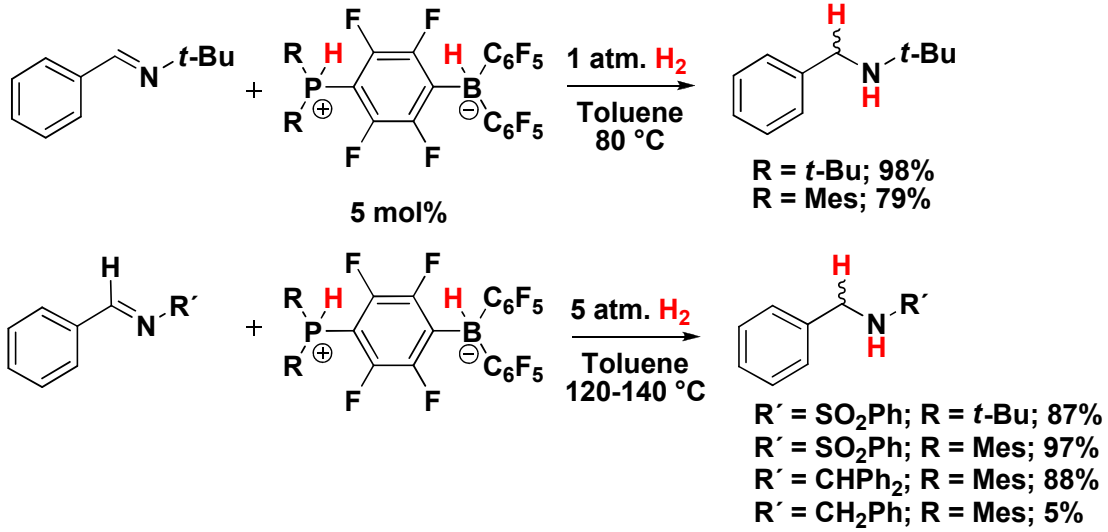
The methodology for the immobilization of chiral BNPA on polymers has been developed.[170] Such polymer-supported chiral Brønsted acid catalysts were found to be as

effective as their homogeneous counterparts. Furthermore, they can simply be removed from the reaction mixture and reused in several catalytic cycles without any loss of enantioselectivity and reactivity.

In summary, so far there are two main well-established organocatalytic approaches for the reduction of imines, enamines and nitrogen-containing heterocycles. The first being a Lewis base catalyzed hydrosilylation with trichlorosilane and the second a Brønsted acid catalyzed reduction with Hantzsch esters or benzothiazolines. Both of these methods give the corresponding amines in high yields and high enantioselectivities, but require the use of at least a stoichiometric amount of a hydrogen source as a reducing agent.

3.12 Hydrogenation by boranes and phosphinoboranes

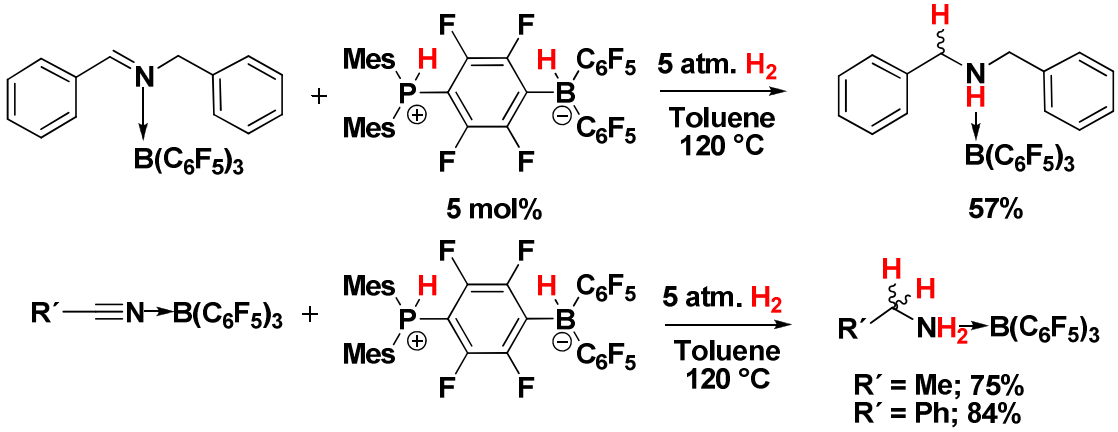
While the hydrogenation of alkenes without transition-metal complexes is still rather limited (see chapters 3.10), phosphinoboranes were recently shown to catalyze the direct hydrogenation of bulky aldimines and ketimines under mild conditions.[171]



Scheme 42. Hydrogenation of imines by phosphinoboranes.[171]

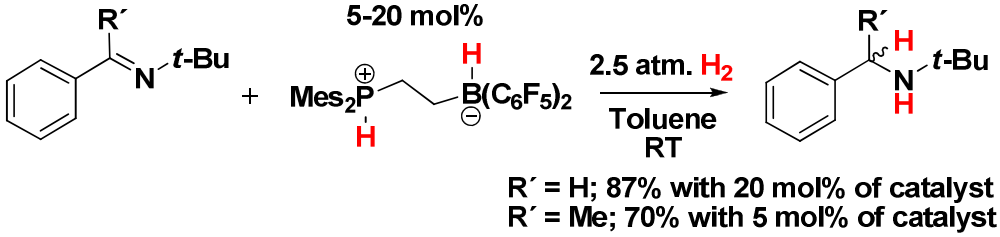
For instance, heating of the toluene solution of *N*-*tert*-butylbenzaldimine in the presence of 5 mol % of phosphonium-borates under 1 atm of H_2 led to the rapid formation of *tert*-butylbenzylamine in an almost quantitative yield at 80 ºC (Scheme 42). However, even small changes in the steric hindrance of the imine have dramatic impacts on the hydrogenation process. Therefore less bulky substrates such as the imine from benzaldehyde and benzylamine could only be reduced stoichiometrically (Scheme 42), which is due to the inhibition of the catalyst activity through the formation of LALB adduct with the resulting amine. Nevertheless, in the presence of a stoichiometric amount of $B(C_6F_5)_3$ as an additive, phosphinoboranes can even

hydrogenate methyl and phenyl-nitriles to give LALB adduct of corresponding primary amine with $B(C_6F_5)_3$ in good yields (Scheme 43).



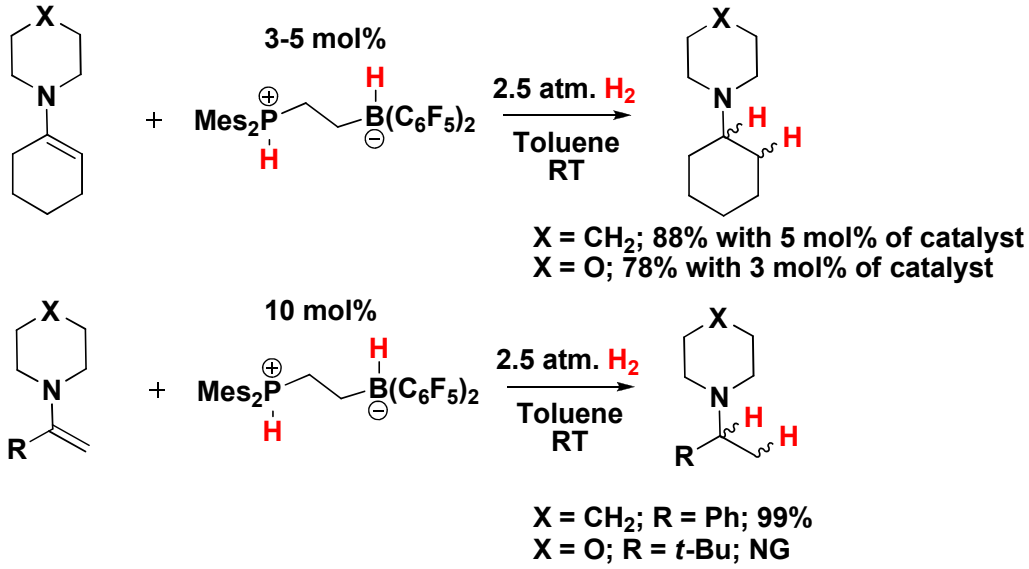
Scheme 43. Hydrogenation of imines- and nitriles-$B(C_6F_5)_3$ complexes by phosphinoboranes.[171]

Later, simple trispentafluorophenylborane and 1,8-bis(dipentafluorophenylboryl) naphthalene [172,173,174,175] as well as some other triarylboranes[176] and intramolecular phosphonium-borates [64,177] were also shown to be effective catalysts for the hydrogenation of bulky imines and nitrogen-containing heterocycles under mild conditions. Despite the fact that strong substrate limitations are still the major drawback of these catalytic systems, some of them have high activity and can reduce the bulky imines and N-heterocycles in high yields even at room temperature (Scheme 44). However, a considerable amount of phosphonium-borate or borane catalyst is still needed in order to obtain a good conversion in a reasonable time.



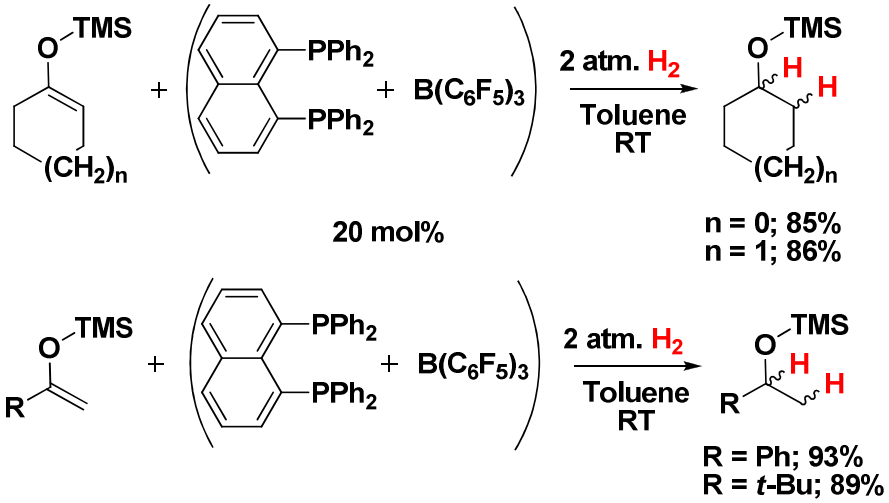
Scheme 44. Hydrogenation of imines by $Mes_2PHCH_2CH_2HB(C_6F_5)_2$.[177]

The intramolecular phosphonium-borate $Mes_2PH^+CH_2CH_2[HB(C_6F_5)_2]^-$ was shown to be a very active catalyst for the hydrogenation of enamines at room temperature and 2.5 atm pressure of H_2.[177] The corresponding amines were achieved with high yields under mild conditions in 20 hours (Scheme 45).



Scheme 45. Hydrogenation of enamines by $Mes_2PHCH_2CH_2HB(C_6F_5)_2$.[177]

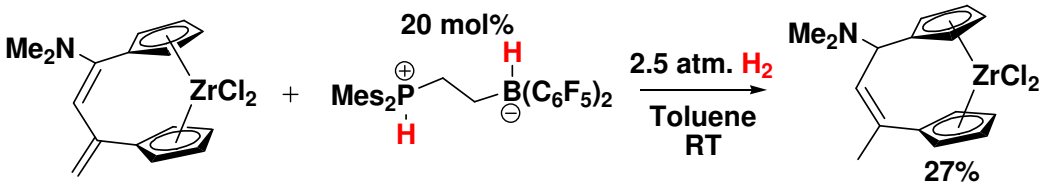
While phosphonium-borates can reduce carbonyl compounds only stoichiometrically[171] the intermolecular 1,8-$[(C_6H_5)_2P]_2C_{10}H_6/B(C_6F_5)_3$ system was successfully applied as a catalyst (20 mol %) for the hydrogenation of TMS-protected enol ethers at nearly ambient conditions (Scheme 46).[57]



Scheme 46. Hydrogenation of silyl enol ethers by 1,8-$[(C_6H_5)_2P]_2C_{10}H_6$/ $B(C_6F_5)_3$.[57]

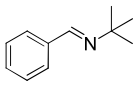
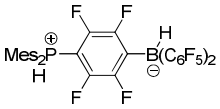
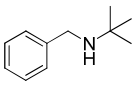
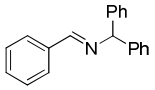
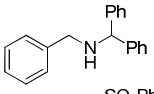
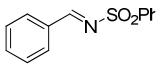
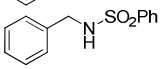
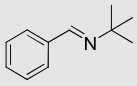
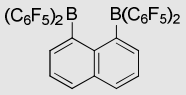
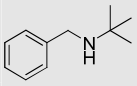
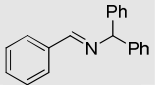
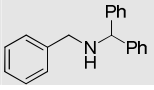
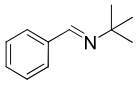
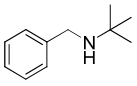
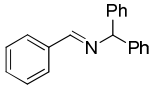
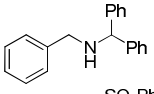
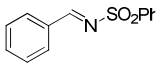
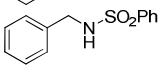
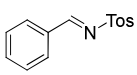
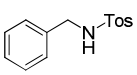
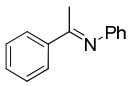
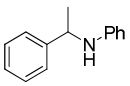
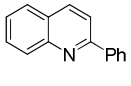
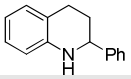
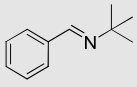
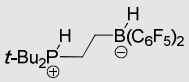
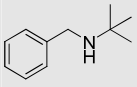
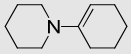
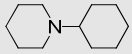
Additionally, intramolecular phosphonium-borate systems were used as hydrogenation catalysts for quite sensitive ferro- and zirconocene compounds.[178] 1,4-Hydrogenation of more stable ferrocene framework gave corresponding products in high yields. However, the reduction of the less stable zirconocene framework in the presence of 20% of the catalyst resulted in an

isolated yield of only 27% (Scheme 47).



Scheme 47. Hydrogenation of zirconocene by $Mes_2PHCH_2CH_2HB(C_6F_5)_2$.[178]

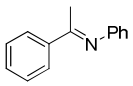
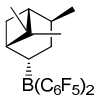
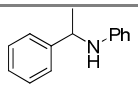
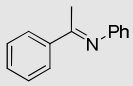
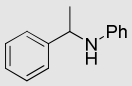
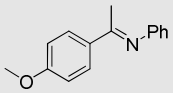
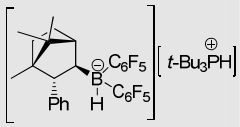
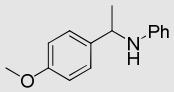
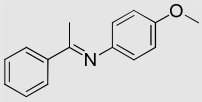
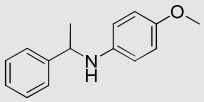
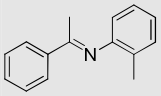
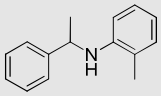
Table 8. Catalytic hydrogenation by boranes and phosphinoboranes.

Entry	Substrate	Catalyst	Conditions	Amine	Conv. [%]	Ref.
1			5 mol%, 5 atm H_2, 80 °C, 1h		79	171
2			5 mol%, 5 atm H_2, 140 °C, 1h		88	171
3			5 mol%, 5 atm H_2, 120 °C, 10.5h		97	171
4			10 mol%, 15 atm H_2, 120 °C, 1h		99	174
5			5 mol%, 15 atm H_2, 120 °C, 1h		99	174
6		$B(C_6F_5)_3$	5 mol%, 1 atm H_2, 80 °C, 2h		89	172
7			5 mol%, 5 atm H_2, 120 °C, 1h		99	172
8			5 mol%, 5 atm H_2, 120 °C, 41h		98	172
9			10 mol%, 30 atm H_2, 100 °C, 15h		99	173
10			5 mol%, 20 atm H_2, 80 °C, 15h		99	173
11			5 mol%, 4 atm H_2, 25 °C, 1h		80	175
12			20 mol%, 2.5 atm H_2, 20 °C, 45min		87	177
13			5 mol%, 2.5 atm H_2, 20 °C, 20h		88	177

In summary different organic compounds based on the Lewis acidic bis(perfluorophenyl)boranyl ($B(C_6F_2)_2$) moiety were shown to be effective catalysts for the direct hydrogenation of bulky imines, enamines and nitrogen-containing heterocycles (Table 8). All reported substrates for borane- and phosphinoborane-catalyzed hydrogenation can be divided with small exceptions into two main groups: sterically hindered (*N*-*t*-Bu-,[171-177] *N*-Dipp-,[172] *N*-benzhydryl[171-174] imines; enamines[177]) and low-basic (*N*-aryl,[173] *N*-arylsulfonyl[171-173] imines and quinolines[175]) unsaturated nitrogen-containing compounds (Table 8). Both of these aforementioned factors facilitate dissociation of the Lewis adducts between the catalyst and the substrates or fully prevent formation of those providing catalytic activity of boranes and phosphinoboranes. For instance, such nonmetal systems have shown only stoichiometric reductions of the non-bulky imine $PhCH_2N{=}C(H)Ph$. Only in the case of sterically hindered borane $MesB(C_6F_5)_2$ in combination with quinuclidine was a 49% yield of dibenyzlamine recently achieved.[176]

3.13 Enantioselective catalytic hydrogenation of *N*-arylketimine by boranes

Table 9. Enantioselective catalytic hydrogenation by boranes.

Entry	Substrate	Catalyst	Conditions	Amine	Conv. [%]	ee [%]
1			10 mol%,20 atm H_2, 65 ºC, 15h		>99	13[173]
2			5 mol%, 25 atm H_2, 65 ºC, 15h		95	79[179]
3			5 mol%, 25 atm H_2, 65 ºC, 15h		96	81[179]
4			5 mol%, 25 atm H_2, 65 ºC, 15h		>99	81[179]
5			5 mol%, 25 atm H_2, 65 ºC, 15h		37	74[179]

Presently there are only two chiral non-metal systems able to catalyze asymmetric *N*-arylketimine hydrogenation. In an early experiment, hydrogenation of *N*-(1-phenylethylidene)aniline with 10 mol% of 3-pinanyl-bis(perfluorophenyl)borane at 65 °C under 20 atm of H_2 exhibited a complete conversion of the imine but with only 13% *ee* (Table 9, entry 1). [173] More recently, tris(*tert*-butyl)phosphonium/chiral-alkyl-bis(perfluorophenyl)hydroborate prepared from (*1R*)-(+)-camphor catalyzed the hydrogenation of different *N*-arylketimines to give the corresponding amines in good yields and good enantioselectivities (Table 9, entries 2-

5).[179] In contrast to achiral systems based on triarylboranes,[171-177] higher pressures of hydrogen (25 atm) is required in the case of chiral-alkyl-bis(perfluorophenyl)boranes.[180]

3.14 Conclusions

So far the different organic compounds based on the bis(perfluorophenyl)boranyl ($B(C_6F_5)_2$) moiety are the most promising systems for the metal-free reversible hydrogen activation and direct hydrogenation of a wide array of substrates, such as bulky imines, enamines, nitrogen-containing heterocycles and silyl enol ethers. However, all these systems have disadvantages, including: 1) strong substrate limitation to bulky starting materials; 2) requirement of the presence of a considerable amount of catalyst (5-20 mol%), which cannot be recovered and/or reused, owing to its sensitivity to the moisture; 3) as well as the lack of efficient enantioselective catalytic methods for the preparation of desired chiral amines.

Therefore, the further development of new and highly active main-group catalysts without the above-mentioned drawbacks for the direct hydrogenation of a wide range of substrates under mild conditions is a very challenging task.

4 Results and discussion

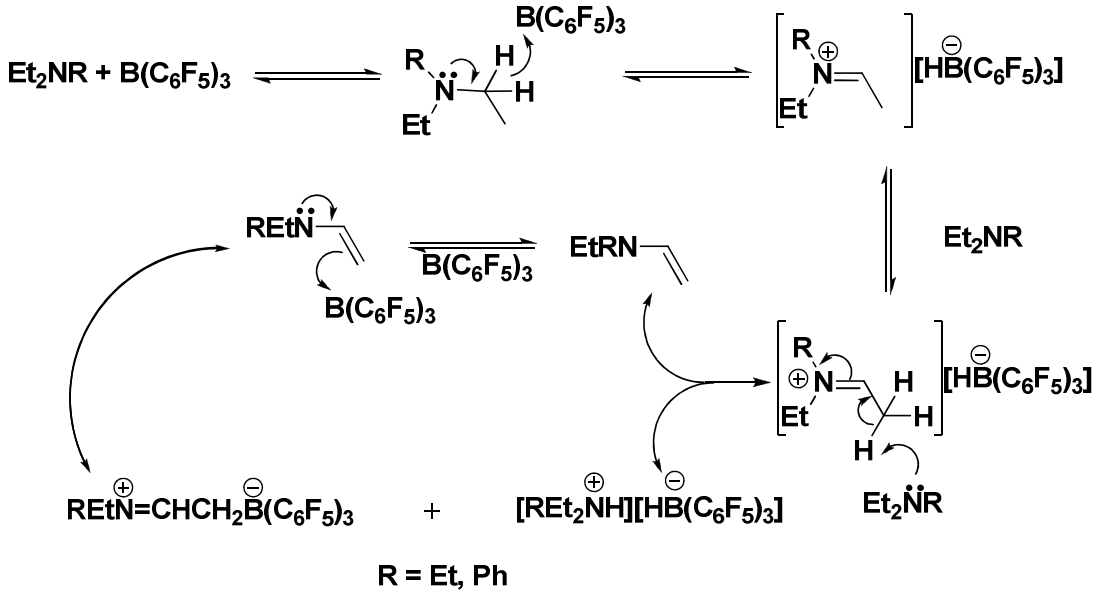
4.1 Experimental notes

All solvents, including deuterated solvents for NMR analysis were dried and distilled under argon before use by employing appropriate drying agents. Hydrogen gas was purchased from AGA Ab and passed through a drying unit prior to use. All organic reagents were purchased from Acros Organics, Sigma-Aldrich or Strem and purified by conventional methods. All air and moisture sensitive syntheses were performed on a double-manifold (H_2 or Ar and vacuum lines) using standard Schlenk techniques or in an argon-filled glove-box. NMR (^{1}H, ^{11}B, ^{13}C, ^{19}F, ^{31}P), ESI^{+} TOF-MS, EI-GCMS, chiral-HPLC, X-ray diffraction, neutron-diffraction techniques were used to analyze and characterize the products. The detailed information about the purification of the solvents, hydrogen gas and starting materials, synthesis of catalysts, analyses, as well as metal-free hydrogen activation and hydrogenation procedures can be found in the experimental part of the attached original publications.

4.2 Hydrogen activation by amines and $B(C_6F_5)_3$ [I, III, IV]

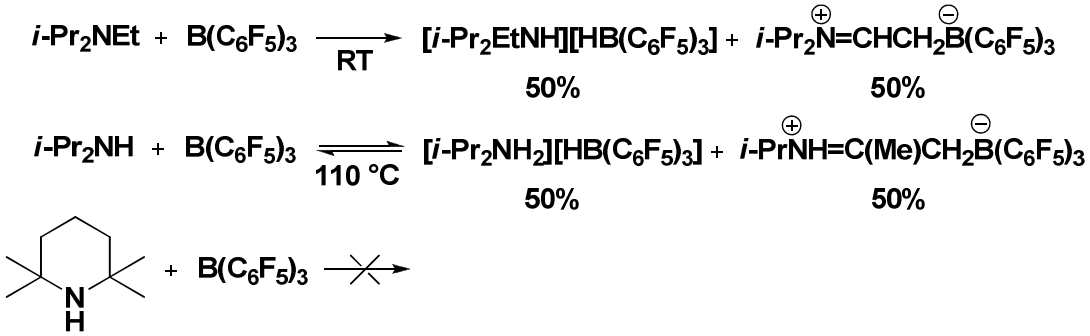
This research started in 2007 in collaboration with Prof. Bernhard Rieger's group. At that time, countless synthetic complexes and enzymes, with transition metals at their reactive core, able to cleave hydrogen gas and hydrogenate unsaturated organic molecules were well known. However, hydrogen activation solely by nonmetals was an absolutely new research field, pioneered by only a few systems: the germanium alkyne analogue $[2,6\text{-}(2,6\text{-}i\text{-}Pr_2C_6H_3)_2C_6H_3Ge]_2$, the intramolecular phosphino-borane system $p\text{-}(Mes)_2PC_6F_4B(C_6F_5)_2$ and (alkyl)(amino)carbenes $i\text{-}Pr_2NC{:}t\text{-}Bu$.[12,13,15] Later, mixtures of highly sterically hindered

phosphines, like *t*-Bu_3P or Mes_3P, with $B(C_6F_5)_3$ were also shown to heterolytically cleave hydrogen gas under mild conditions (see chapter 3.6).[14]



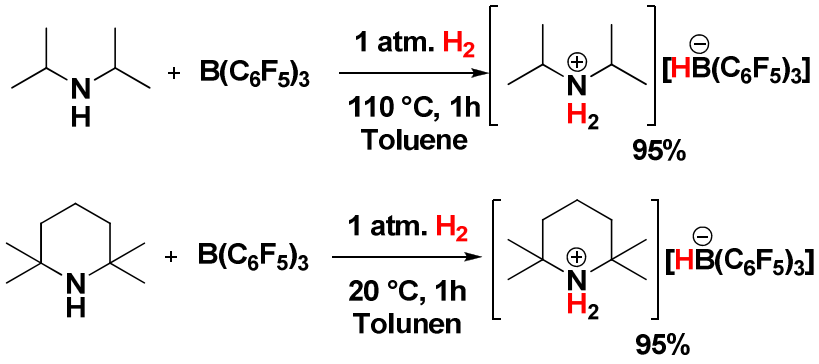
Scheme 45. Interactions of triethylamine and *N*,*N*-diethylaniline with $B(C_6F_5)_3$.[182]

It is a well known that classical Lewis bases such as simple amines and phosphines react with $B(C_6F_5)_3$ forming LALB adducts.[181,182] Additionally, some bulky secondary and tertiary phosphine-$B(C_6F_5)_3$ adducts can undergo nucleophilic substitution of the *para*-fluorine atom giving intramolecular phosphonium-borates at temperatures over 125 ºC. In contrast to more nucleophilic phosphines, amines that contain an aliphatic chain with α and β-protons next to each other exhibit totally different reactivity towards trispentafluorophenylborane. Thus, the reaction of various amines with $B(C_6F_5)_3$ results in formation of a mixture of zwitterion iminium borate compound and ammonium boronhydride salt (Scheme 45).[182,183] In some cases, like with *N*,*N*-diethylaniline, this reaction is fully reversible even at room temperature giving the mixture of starting materials (40%) and products (60%).



Scheme 46. Interactions between bulky amines and $B(C_6F_5)_3$.

We started our research with the investigation of stoichiometric mixtures of diisopropylethylamine, diisopropylamine and 2,2,6,6-tetramethylpiperidine in combination with $B(C_6F_5)_3$ in toluene by ^1H, ^{11}B, and ^{19}F NMR spectroscopy. While the reactions of diisopropylethylamine and diisopropylamine with $B(C_6F_5)_3$ followed a predictable path giving accordingly a mixture of iminium borate and ammonium boronhydride, no reaction was observed in case of 2,2,6,6-tetramethylpiperidine (Scheme 46). This fact was in a good agreement with the proposed mechanism for the reaction of amines with trispentafluorophenylborane in which the first step is believed to be an α-proton abstraction by the Lewis acidic borane from amine.



Scheme 47. Hydrogen activation by bulky amines and $B(C_6F_5)_3$.

Exposure of these toluene solutions to an atmosphere of H_2 at room temperature afforded the product $[R_2NH_2]^+[HB(C_6F_5)_3]^-$ only in the case of 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ (Scheme 47).[I] However, since the reaction of diisopropylamine with $B(C_6F_5)_3$ is slightly reversible at elevated temperatures, facile hydrogen activation by this system was obtained at 110°C. At the same time a thermally stable mixture of iminium borate and ammoinum boronhydride from diisopropylethylamine and $B(C_6F_5)_3$ showed no reactivity towards hydrogen (2 atm) after 24 hours at temperatures up to 110°C. Furthermore, under the same conditions no reactions were observed between different amines and less Lewis acidic triphenylborane (BPh_3), while more Lewis acidic 1,2-bis(pentafluorophenylboryl)benzene $[(C_6F_5)_2B]_2C_6H_4$ in combination with TMP gave almost quantitative yield of the hydrogenated product in less than 5 minutes.[184] All of these results suggested that the hydrogen activation requires amines and boranes with fine-tuned steric and electronic properties. In addition to hydrogen activation, the 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ system by analogy to tri-*tert*-butylphosphine and $B(C_6F_5)_3$[84] was tested for the reactivity to ethylene affording ethylene bridged ammonium-borate at 110 ºC and 1 atm pressure in 80% yield.[184]

Both isolated hydrogenated products having the formula $[R_2NH_2]^+[HB(C_6F_5)_3]^-$ were characterized by ^1H, ^{11}B, ^{13}C, ^{19}F NMR spectroscopy. The structure of $[TMPH_2]^+[HB(C_6F_5)_3]^-$ was also confirmed by X-ray diffraction (Figure 1). According to this data, the ammonium and

borhydride ions in this compound were connected only by a network of N–H···F and C–H···F hydrogen bonds, with the shortest N–H···H–B distance being about 2.97 Å.

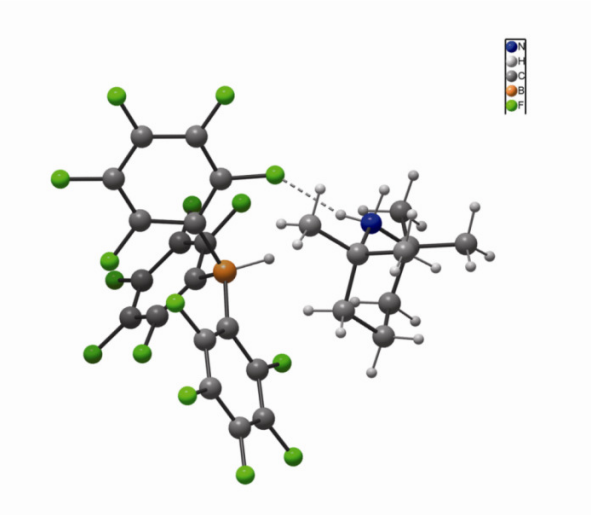
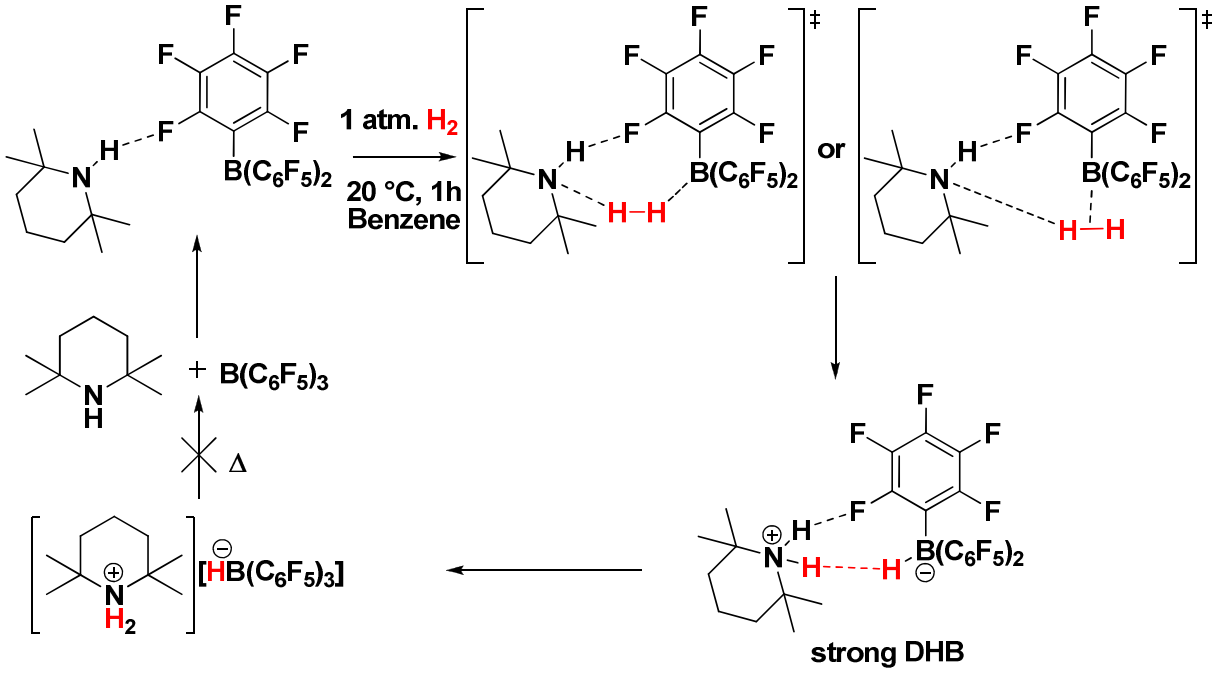


Figure 1. X-ray structure of $[TMPH_2]^+[HB(C_6F_5)_3]^-$.

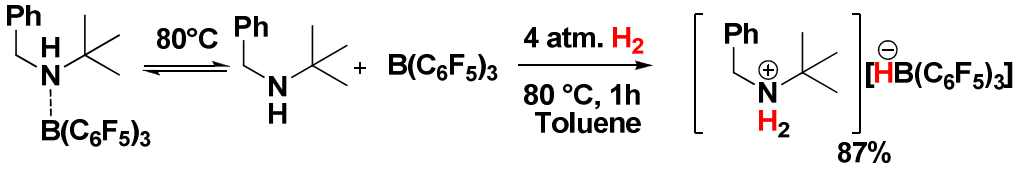


Scheme 48. Possible mechanism for the heterolytic cleavage of H_2 by TMP and $B(C_6F_5)_3$.

In order to gain further insight into the mechanism of hydrogen activation by amines and $B(C_6F_5)_3$ the deuterobenzene-*d6* solution of 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ under an atmosphere of H_2 was monitored by ^1H and ^{19}F NMR spectroscopy. The different chemical shifts

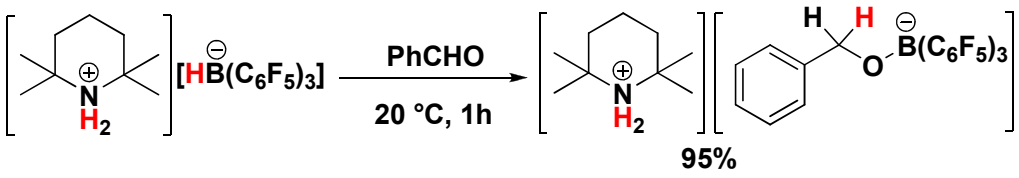
for NH and BH species as well as the presence of the second set of three fluorine peaks with the same coupling constant were observed. However, evaporating, storing at room temperature for one day or heating of the resulted solution led to only the hydrogenated product $[TMPH_2]^+[HB(C_6F_5)_3]^-$ in an almost quantitative yield. Thereby these NMR data could only be attributed to the presence of an intermediate, which contains a strong N–H···H–B dihydrogen bond interaction between the cation and the anion analogous to the NH_3*BH_3 complex (Scheme 48).[185] The successful detection of such an intermediate was presumably possible due to the appropriate choice of solvent – benzene, which led to the intermediate stabilization by the solvation effects. Later, the incorporations of deuterobenzene-*d6* in the crystal lattice of most late-synthesized ammonium-borates were observed.

A similar example of hydrogen activation by Stephan and co-workers using *tert*-butylbenzylamine and $B(C_6F_5)_3$ appeared during the preparation of our first manuscript.[172] Particularly they discovered that heating of the adduct of *tert*-butylbenzylamine and $B(C_6F_5)_3$ at 80 ºC and 4 atm pressure of H_2 resulted in thermal dissociation of the B-N bond and splitting of the hydrogen forming $[t\text{-Bu(Bn)}NH_2]^+[HB(C_6F_5)_3]^-$ (Scheme 49). Thus, our study of hydrogen activation by amines and boranes was broader in scope and our 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ system was much more active. An X-ray crystal structure study of $[t\text{-Bu(Bn)}NH_2]^+[HB(C_6F_5)_3]^-$ showed a presence of a strong N–H···H–B dihydrogen bond of 1.87 Å. Although, this system has a shorter N–H···H–B contact than ours (2.97 Å), both of them were not able to liberate hydrogen upon heating.



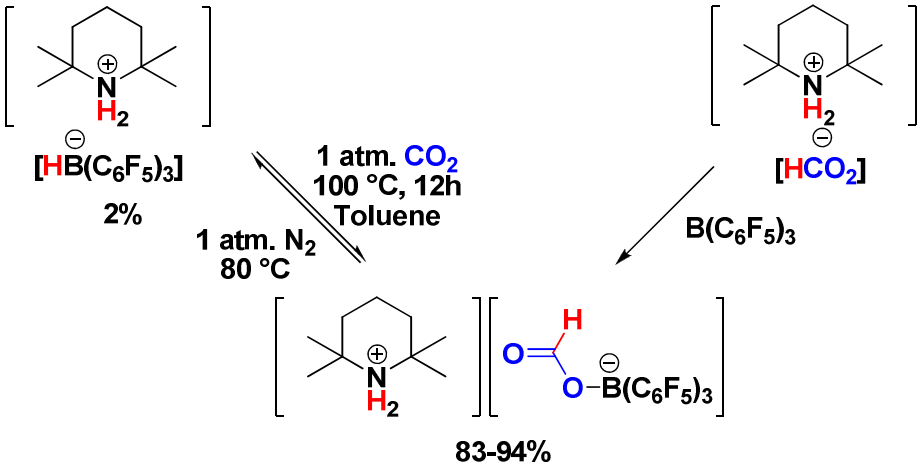
Scheme 49. Hydrogen activation by bulky amines and $B(C_6F_5)_3$.[172]

To get more information on the reactivity of our ammonium-borate system, a benzaldehyde reduction was undertaken. The toluene solution of equimolar amounts of benzaldehyde and $[TMPH_2]^+[HB(C_6F_5)_3]^-$ was stirred at room temperature for 1 hour giving a product with the molecular formula $[TMPH_2]^+[PhCH_2OB(C_6F_5)_3]^-$ with a 95% yield (Scheme 50).



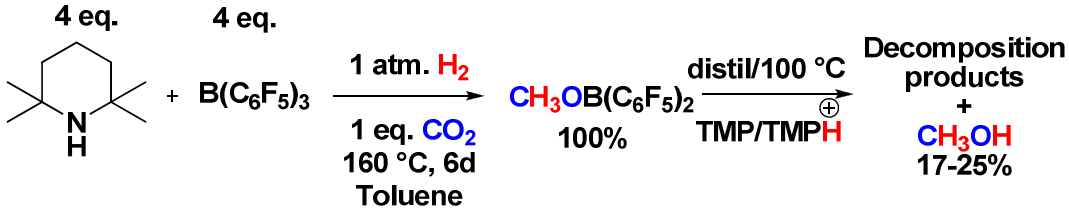
Scheme 50. Stoichiometric reduction of benzaldehyde with $[TMPH_2]^+[HB(C_6F_5)_3]^-$.

This experiment highlighted the possibility to use ammonium-borate systems as reducing agents. However, all our attempts towards the catalytic hydrogenation of carbonyl compounds by such amine-borane pairs failed, presumably due to the high bond energy of the B-O bond (560-790 kJ/mol) which makes it hard to break.[186] Nevertheless, our original $[TMPH_2]^+[HB(C_6F_5)_3]^-$ system was successfully applied by others for the stoichiometric fixation of CO_2, which is a promising C1 feedstock for the production of many chemical products (Scheme 51).[187] Moreover, because of the zwitterionic NHC adduct with CO_2 was recently considered as the key intermediate in the deoxygenative hydrosilylation of CO_2 by diphenylsilane to CH_3OH upon workup,[188] this finding foreshadowed the potential of ammonium-borate system to act as CO_2 activator in further reduction processes.



Scheme 51. CO_2 fixation by $[TMPH_2]^+[HB(C_6F_5)_3]^-$.

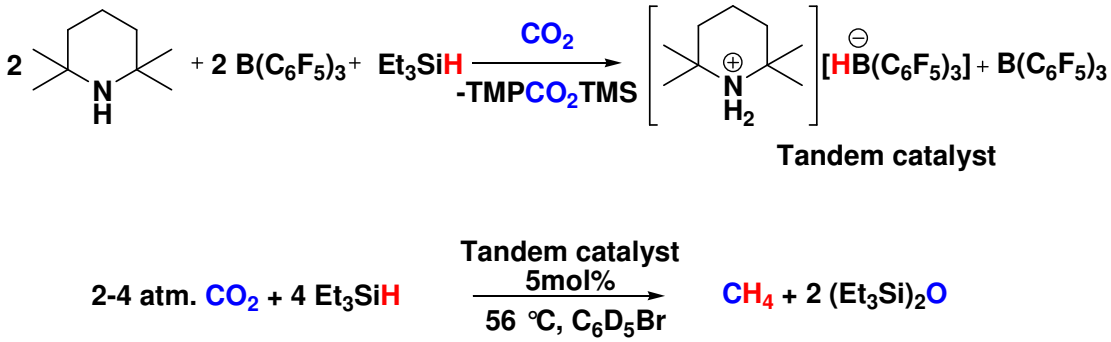
Indeed, a procedure for the quantitative hydrogenation of CO_2 to methoxy-bispentafluorophenylborane with a four times excess of amine-borane FLP under mild conditions was also reported by O'Hare and co-workers.[187] However, further cleavage of the B-O bond was still rather difficult and the desired methanol product was obtained in a very low yield (Scheme 52).



Scheme 52. Reduction of CO_2 to methanol by TMP-$B(C_6F_5)_3$ FLP.[188]

More recently, Piers et al. reported that a tandem catalyst based on our system together with trispentafluorophenylborane in the presence of excess of triethylsilane as a reducing and

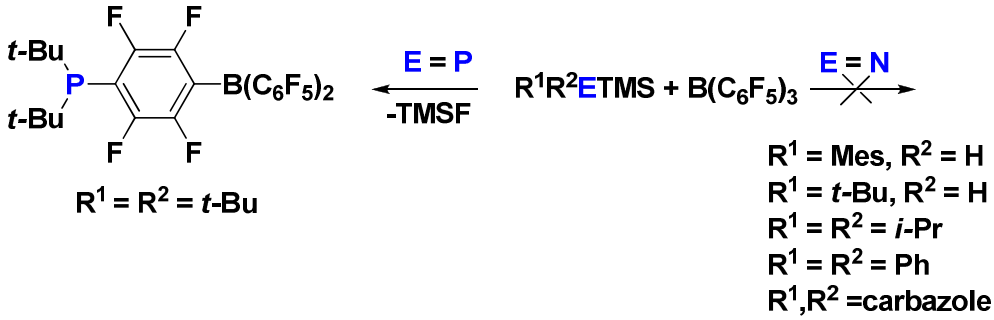
deoxygenative agent can convert carbon dioxide to methane under mild conditions (Scheme 53). [189] The ammonium-borate $[TMPH_2]^+[HB(C_6F_5)_3]^-$ reacted with CO_2 (2–4 atm) in the presence of Et_3SiH (18 equiv) at 56 °C in C_6D_5Br to afford the previously reported ammonium formatoborate $[TMPH_2]^+[HCO_2B(C_6F_5)_3]^-$ (see Scheme 51). Further addition of a stoichiometric amount of $B(C_6F_5)_3$ to the reaction mixture resulted in the immediate and complete conversion of ammonium formatoborate back into the starting ammonium-borate and the appearance of CH_4 along with two equivalents of $(Et_3Si)_2O$ as the final reaction products.



Scheme 53. Tandem TMP-$B(C_6F_5)_3$/$B(C_6F_5)_3$ catalyzed deoxygenative hydrosilylation of CO_2.[189]

Thus, our simple 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ system for hydrogen activation not only became a popular target for further research, but also showed quite a different behavior compared to Stephan's and Erker's intermolecular phosphine-borane systems.[190, 191]

In continuation of our work on the facile heterolytic cleavage of hydrogen by bulky amines and $B(C_6F_5)_3$, we became interested in the behavior of trimethylsilyl- amines and phospines as a Lewis base in the hydrogen activation process. [IV] The usage of TMS protected Lewis bases has a couple of advantages. Firstly, most TMS protected amines and phosphines are just bulky enough and should not form stable adducts with $B(C_6F_5)_3$. And secondly, they are easily synthesized or commercially available.

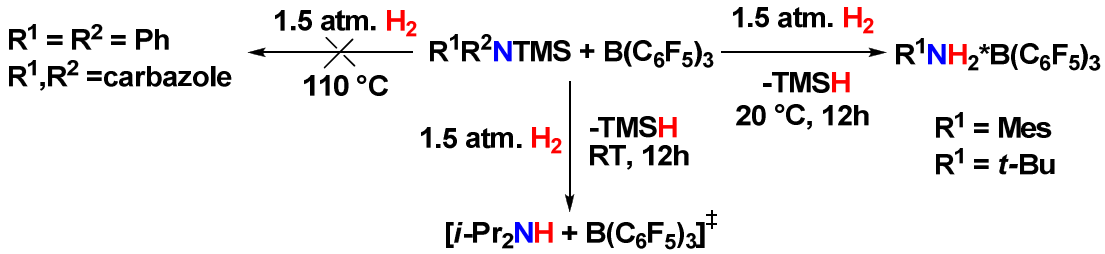


Scheme 54. Interactions between bulky TMS-amines and TMS-phospines with $B(C_6F_5)_3$.

At the outset, we investigated the interaction of different amine and phosphine variations of TMS with $B(C_6F_5)_3$ in toluene solution using ^1H, ^{11}B, and ^{19}F NMR spectroscopy. While the amines in combination with $B(C_6F_5)_3$ did not form LALB adducts even at low temperature, a *para*-nucleophilic aromatic substitution reaction of the fluorine atom in the case of *t*-Bu_2PTMS and $B(C_6F_5)_3$ was observed to give the previously reported intramolecular phosphinoborane compound in almost quantitative yield (Scheme 54).[16] In contrast to the previously reported method for the synthesis of such compounds, which were prepared in a two-step sequence with only 44-62% yields, our procedure offered a simple and efficient way to synthesize intramolecular frustrated Lewis pairs having the formula $R_2PC_6F_4B(C_6F_5)_2$.

Further exposing toluene solutions of TMS-amines and $B(C_6F_5)_3$ to an atmosphere of H_2 (1.5 atm) showed different reactivity of such systems. While less Lewis basic trimethylsilyldiphenylamine or trimethylsilylcarbazole together with trispentafluorophenylborane did not react with H_2 at 110°C (Scheme 55), more basic MesNHTMS or *t*-BuNHTMS and $B(C_6F_5)_3$ cleaved hydrogen even at room temperature in a facile manner. In addition to the previous study of the influence of Lewis acidity on the hydrogen activation (see page 46),[184] this finding indicates that the Lewis basicity of the amine should also be strong enough to thermodynamically favor the cleavage of the H_2 bond.

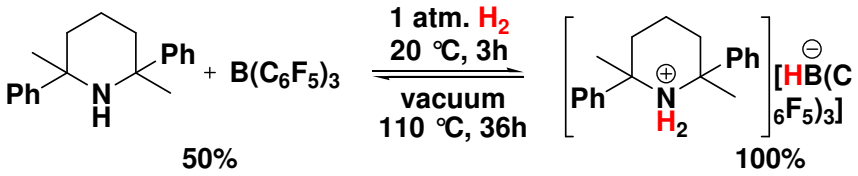
Based on real-time NMR studies we assumed that hydrogen splitting by MesNHTMS, *t*-BuNHTMS and *i*-Pr_2NTMS in combination with $B(C_6F_5)_3$ resulted in TMS-ammonium borohydrides. However, the formed salts were not stable and spontaneously liberated TMSH gas (bp = 6.7 °C). The stable LALB adducts were formed as the ultimate reaction products in the cases of mesetylaniline and *tert*-butylamine. The reaction of more bulky diisopropyltrimethylsilylamine and $B(C_6F_5)_3$ with H_2 afforded the expected 1:1 mixture of the salt $[i\text{-}Pr_2NH_2]^+[HB(C_6F_5)_3]^-$ and the zwitterion $iPrN^+H{=}C(CH_3)CH_2B^-(C_6F_5)_3$ (Scheme 55). As described earlier, the two former compounds are in an equilibrium with the free diisopropylamine/$B(C_6F_5)_3$ at 110°C, and can further split hydrogen upon heating (see Schemes 46, 47).



Scheme 55. Hydrogen activation by bulky TMS-amines and $B(C_6F_5)_3$.

Since alkyl- and aryl hydrosilanes are promising reducing and deoxygenative agents for the metal-free conversion of carbon dioxide to methane or methanol,[188,189] the heterolytic

splitting of hydrogen by *N*-TMS amines and $B(C_6F_5)_3$ with the simultaneous generation of TMSH highlights the possible application of these systems in such processes.



Scheme 56. Reversible hydrogen activation by DMDPP and $B(C_6F_5)_3$.

Later, we also performed the hydrogen activation by *trans*-2,6-dimethyl-2,6-diphenylpiperidine and $B(C_6F_5)_3$.[III] This reaction led to the formation of the hydrogenated product $[DMDPPH_2]^+[HB(C_6F_5)_3]^-$ in quantitative yield within 3 h at room temperature and 1 atm pressure of H_2. The longer time needed for the cleavage of hydrogen compared to that of the TMP-$B(C_6F_5)_3$ system is thought to be due to the lower basicity of the amine. Interestingly, the final $[DMDPPH_2]^+[HB(C_6F_5)_3]^-$ compound was found to be able to liberate H_2 gas upon heating under reflux at 110°C to give the mixture (1:1) of the remaining ammonium-borate and starting materials after 36 hours (Scheme 56).

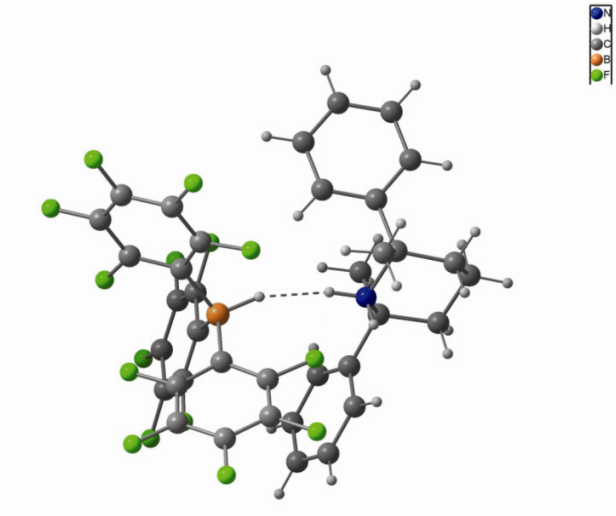


Figure 2. X-ray structure of $[DMDPPH_2]^+[HB(C_6F_5)_3]^-$ with shortest N–H···H–B distance of 1.89 Å.

At that time and now, there are only a few examples of FLPs known to release hydrogen after activation.[13,49,57,58,II,VI] All of such intra- and intermolecular systems (except our *ansa*-ammonium-borates, which will be discussed later in chapter 4.3),[II,VI] are characterized by the presence of a phenylated cation and a fluorophenylated anion. To explain this phenomenon, the structure of $[DMDPPH_2]^+[HB(C_6F_5)_3]^-$ was determined by X-ray crystallography. The strong phenyl-perfluorophenyl π– π stacking interactions as well as additional N–H···F (2.34 Å), C–

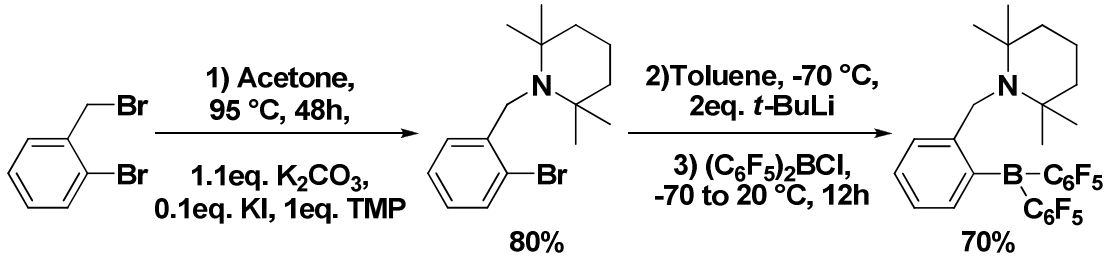
H···F (2.52 Å) hydrogen bonds and the DHB interaction of 1.89 Å were observed (Figure 2). The similar short N-H···H-B dihydrogen bond of 1.87 Å was also detected in the previous reported ammonium-borate [*t*-Bu(Bn)NH_2]$^+$[$HB(C_6F_5)_3$]$^-$.[172] However, in contrast to our system [*t*-Bu(Bn)NH_2]$^+$[$HB(C_6F_5)_3$]$^-$ was not able to liberate hydrogen upon heating.

Thus, it seems that phenyl rings connected to the Lewis base not only form a strong π– π interactions with perfluorophenyl rings of Lewis acid in order to kinetically promote the H_2 liberation process through the stabilization of the transition state, but also lower the basicity of the amine or phosphine in order to thermodynamically favor the elimination of hydrogen gas.[192] Accordingly, binding together through a covalent bridge the fine-tuned FLP system should give a new intramolecular compound with extraordinary properties.

4.3 Hydrogen activation by the first intramolecular *ansa*-aminoborane[II, V]

The observations described above and previously in Piers's work [43] inspired us to attempt the synthesis of an intramolecular system where active B and N centers are located close to each other. In this respect we designed the *ansa*-aminoborane *o*-*N*-TMP$CH_2C_6H_4B(C_6F_5)_2$ and developed an effective and common procedure for the preparation of dual intramolecular Lewis acid–Lewis base systems.

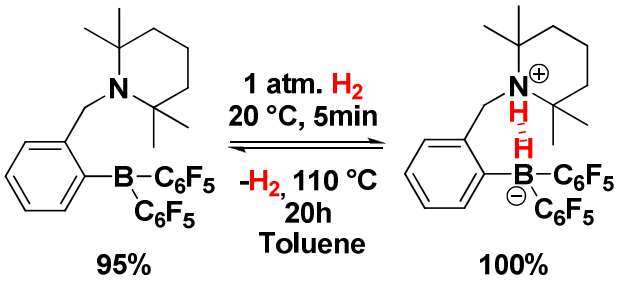
o-Bromobenzyl bromide was alkylated with TMP in the presence of K_2CO_3 as a base and 10 mol% of KI as catalyst to afford 1-(2-bromobenzyl)-2,2,6,6-tetramethylpiperidine in 80% yield. Further lithiation with 2 equivalents of *t*-BuLi at -70°C in toluene followed by addition of a precooled solution of $(C_6F_5)_2BCl$ gave the crude product *o*-*N*-TMP$CH_2C_6H_4B(C_6F_5)_2$ **CAT** in a total yield of 55% as a bright yellow oil (Scheme 57).



Scheme 57. Synthesis of *ansa*-aminoborane **CAT**.

Without further purification the *ansa*-aminoborane was exposed to an atmosphere of H_2 at room temperature to give the *ansa*-ammonium-borate **$CATH_2$** in quantitative yield in 5 minutes as a white solid (Scheme 58). Thus, the first air- and moisture-stable *ansa*-ammonium-borate **$CATH_2$** has been prepared on a gram scale by an efficient three-step procedure from readily available precursors. Next, we examined the possible liberation of hydrogen gas from the new intramolecular system. A toluene solution of *ansa*-ammonium-borate **$CATH_2$** (0.1M) was refluxed at 110 °C in a closed system under reduced pressure to give a 50% conversion to the

starting *ansa*-aminoborane **CAT** in 3 hours. A prolongation of the reaction time up to 20 hours caused almost quantitative recovery of the non-hydrogenated intramolecular system *o*-*N*-$TMPCH_2C_6H_4B(C_6F_5)_2$. Accordingly, the new *ansa*-ammonium-borate **$CATH_2$** lost hydrogen gas during heating much faster than our previous non-bridged system $[DMDPPH_2]^+[HB(C_6F_5)_3]^-$.



Scheme 58. Reversible hydrogen activation by *ansa*-aminoborane **CAT**.

In order to gain further insight into the mechanism of reversible hydrogen activation by *ansa*-aminoborane *o*-*N*-$TMPCH_2C_6H_4B(C_6F_5)_2$ (**CAT**), the structure of the corresponding *ansa*-ammonium-borate **$CATH_2$** was studied by X-ray, neutron-diffraction and thermogravimetric mass spectroscopic experiments in the solid state and by NMR and FT-IR in solution. Additionally, the structure, reaction path and energetics were studied theoretically.

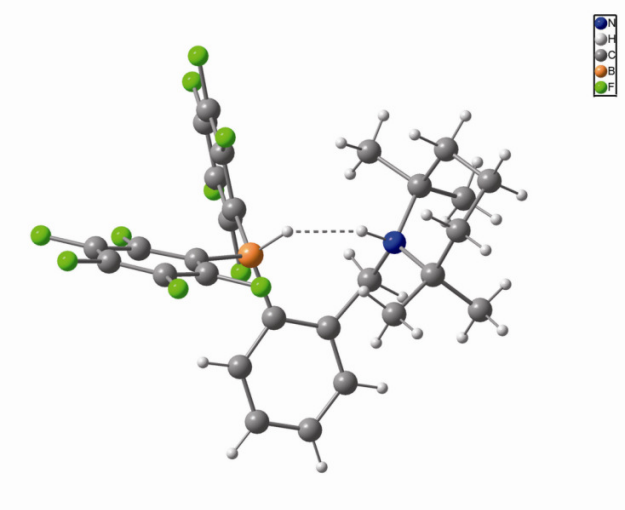


Figure 3. X-ray structure of *ansa*-ammonium-borate **$CATH_2$** with N–H···H–B distance of 1.78Å.

The X-ray data of *ansa*-ammonium-borate **$CATH_2$** showed the presence of C–H···F (2.52 Å, 2.73 Å) hydrogen bonds and a strong dihydrogen bond interaction of 1.78 Å between the ammonium cation and boron hydride anion (Figure 3). Additionally ab initio DFT calculations performed by ourselves and others[56] on the PBE/6-31G(d) and the M05-2X/6-31G(d) levels of

theory for geometry optimizations in solution and gas phase, respectively, were in good agreement with X-ray results overall. However, the values found for the intramolecular N–H···H–B dihydrogen bond distance were significantly shorter (1.51 and 1.53 Å, Table 10).

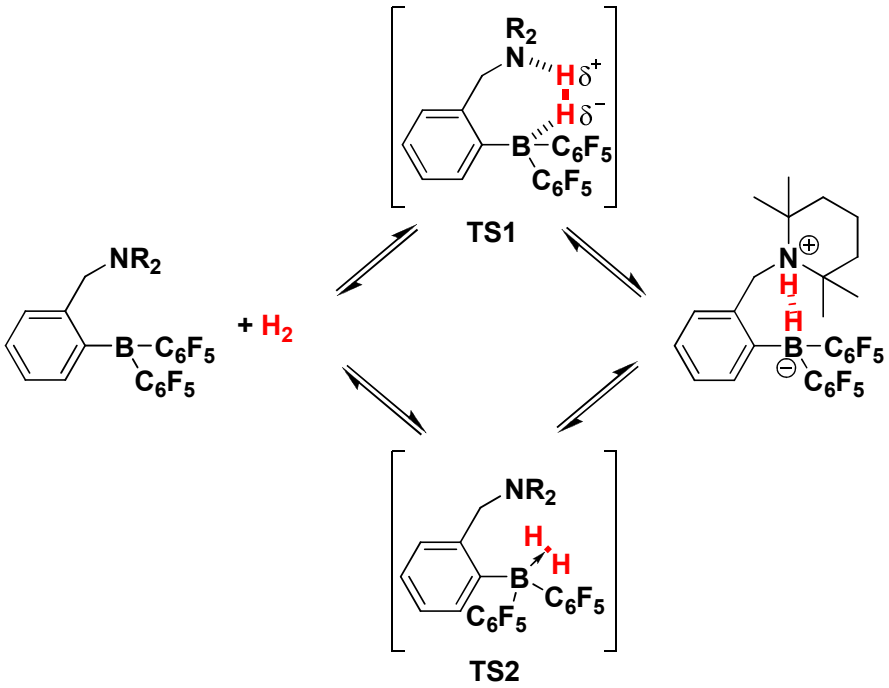
Table 10. Comparison of structural data of *ansa*-ammonium-borate **CATH$_2$** obtained by different methods.

Property	Crystal structure (neutron diffraction)	Crystal structure (X-ray diffraction)	PBE/6-31G(d) with PCM model (in C_6H_6)	M05-2X/6-31G(d) (in gas phase)[56]
d(NH–HB)		1.78 Å	1.51 Å	1.53 Å
d(N–H)		0.94 Å	1.06 Å	1.04 Å
d(B–H)		1.19 Å	1.24 Å	1.23 Å
d(N–B)		3.36 Å	3.34 Å	3.25 Å
ψ(∠N–H¨H)		154.2º	150.3º	159.7º
θ(∠B–H¨H)		125.2º	132.5º	122.9º

Since this DHB interaction was the most interesting in view of understanding the mechanism of reversible hydrogen activation by intramolecular aminoboranes, we performed a neutron diffraction measurement. In contrast to the X-ray technique, neutron diffraction locates the nuclei more clearly. Thus, the actual dihydrogen bond length was determined to be even shorter, or one of the shortest DHB interactions reported in literature so far for.[III, V] Together with the experimental topological parameters such as the N–H···H (154°) and B–H···H (125°) angles this observation suggested that the dihydrogen bond interaction in the *ansa*-ammonium-borate **CATH$_2$** is partially covalent in nature.[III, 193] However, although a presence of a short DHB interaction seems to be an important structural prerequisite for the hydrogen liberation by "non-phenylated" systems (see pages 52-53), one should note that this is a necessary but not a sufficient condition and first of all the reaction needs to be almost thermodynamically neutral (see page 20).[56]

Both hydrogen activation and liberation take place in organic solvents therefore in addition to the solid state studies, multinuclear solution NMR experiments were performed.[V] Dilution, variable temperature and 2D NOESY NMR measurements of *ansa*-ammonium-borate **CATH$_2$** in CD_2Cl_2 solution showed that it consists of two conformers which are in dynamic equilibrium. In order to determine the intramolecular N–H···H–B dihydrogen bond distance in CD_2Cl_2 solution we carried out ^{1}H NMR T_1 relaxation and selective 1D NOE measurements.

Two independent measurements of the H···H distance showed that the DHB length is very close to the value determined in the solid state by neutron diffraction or even shorter at elevated temperatures. Therefore, the NMR measurements gave strong evidence that the structure of *ansa*-ammonium-borate **CATH$_2$** in solution is similar to that of the solid state.



Scheme 59. Possible intermediates in hydrogen activation by *ansa*-aminoboranes.

Interestingly, H/D stable-isotope labeled experiments were not in contrast to the earlier reported theoretical calculation, which suggested **TS1** as the possible transition state (Scheme 59, see also pages 19-20). In this structure the H–H bond is only slightly elongated and the corresponding Zero-Point Energy (ZPE) values and Gibbs free-energy isotopic differences are quite small. Although after the B–H and N–H bonds are formed simultaneously, they become larger for the products. This supports the idea that the early transition state does not produce a NMR visible isotope effect.

At the same time, the coordination of H_2 to the Lewis acidic boron center and formation of an η^2-bound adduct **TS2** followed by the fast intramolecular deprotonation with the Lewis basic nitrogen atom can also explain the absence of a kinetic isotope effect. Whereas our theoretical calculations support the simultaneous mechanism for the hydrogen activation, the formation of a σ-complex between borane and H_2 cannot be ruled out at this point. Further experimental studies are needed to favor one of the mechanisms.

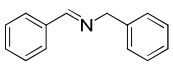
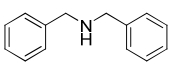
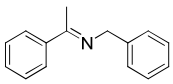
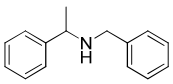
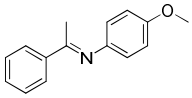
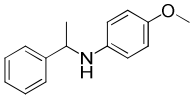
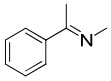
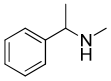
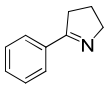
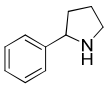
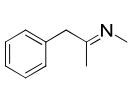
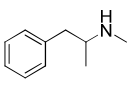
In addition, our theoretical studies of the reaction pathway and energetics showed that the extra Coulomb attraction between the resulting ammonium cationic and boron hydride anionic

fragments at 3.32 Å (the calculated B–N distance for **CAT**) would produce an attraction energy of 413 kJ/mol. This would be comparable with the amount of energy required for the heterolytic cleavage of H_2, 432 kJ/mol.[9] According to this calculation, the 'Coulomb pays for Heitler-London' hypothesis was enounced; however this was only an order-of-magnitude estimate.

4.4 Hydrogenation by the first intramolecular *ansa*-ammonium-borate[II]

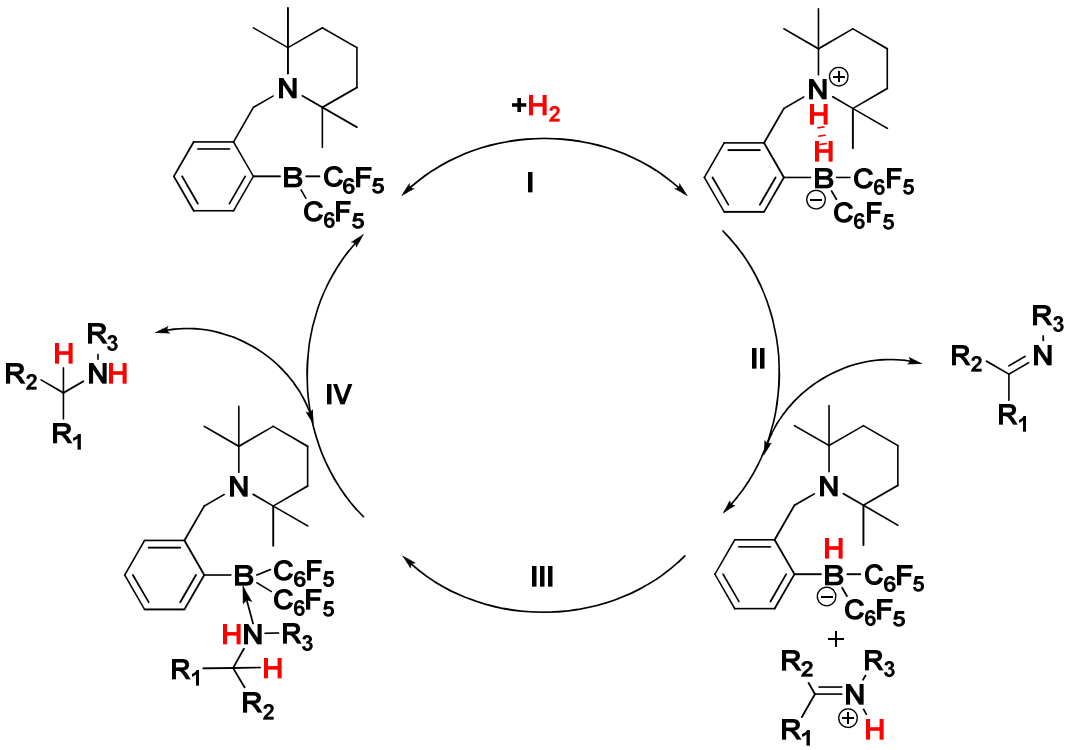
To continue our experimental investigation, we examined the reduction of imines with the *ansa*-ammonium-borate **CATH$_2$**. Among previously reported non-metal systems based on the bis(perfluorophenyl)boranyl moiety ($B(C_6F_5)_2$, see chapter 3.12 and table 8) the *ansa*-ammonium-borate **CATH$_2$** has shown high catalytic activity in the hydrogenation of a wide range of imines and enamines (Table 11). However, much like other FLP systems, **CATH$_2$** has significant drawbacks and limitations with respect to the reactivity. The first disadvantage is the sensitivity to steric factors at the α-positions of the imine, due to the suppression of the catalyst's activity by formation of an amine-borane Lewis acid-base adduct. Thus, conversions in these cases usually did not exceed the *ansa*-ammonium-borate loading (Table 11, entries 5, 6). Another disadvantage is **CATH$_2$** low ability to reduce less basic imines (Table 11, entry 3).

Table 11. Catalytic hydrogenation of imines by *ansa*-ammonium-borate **CATH$_2$**.[a]

Entry	Substrate	Time [h]	Amine	Conv. [%][b]
1		20		100
2		6		100
3		12		37
4		12		100
5		12		4[c]
6		12		4[c]

[a] Catalyst **CATH$_2$** (0.01 mmol, 4%) and substrate (0.25 mmol) were refluxed in toluene (1.0 mL, 110°C) under 2 atm of H_2 pressure (56 mL, 2.5 mmol). [b] Determined by ^{1}H NMR spectroscopy. [c] Toluene (5.0 mL)

The results from the catalytic hydrogenation experiments (Table 11) further support a proposed mechanism in which any one or more steps may be the rate-determining point, depending on the structure of both substrates and catalysts (Scheme 60).

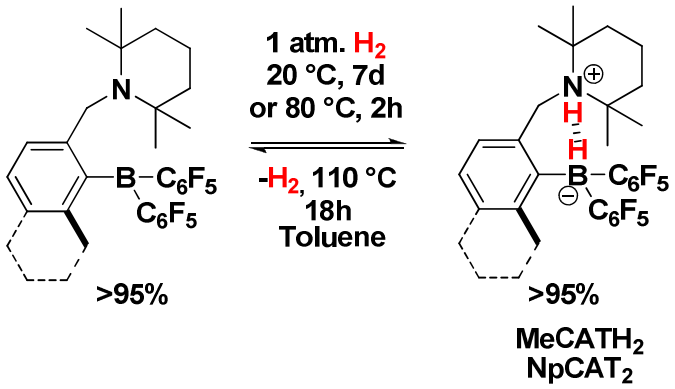


Scheme 60. Proposed mechanism for the catalytic hydrogenation of imines by *ansa*-ammonium-borates.

Thus, the proton-transfer equilibrium seems to be a primary and rate controlling step in the reduction of bulky *N*-arylketimines (Scheme 60, Stage II and Table 11, entry 3). The inhibition of the catalyst activity by Lewis acid–Lewis base adduct formation seems to be a rate-determining step in the reduction of non-bulky imines (Scheme 60, Stage IV and Table 11, entries 5, 6).

4.5 Tuning of the Lewis acidic component of *ansa*-aminoboranes[III]

On the basis of the above results, we proposed that the further reduction of Lewis acidity at the active boron centre should not only lower the temperature needed for the hydrogen liberation process, but should also lead to an increase in the activity of our catalyst in hydrogenation reactions. In this respect, the new *ansa*-aminoboranes **MeCAT** and **NpCAT** with more sterically hindered and electron donating benzyl bridges between Lewis acid and Lewis base were synthesized in a similar manner to the original *ansa*-aminoboranes **CAT** (Scheme 57).



Scheme 61. Reversible hydrogen activation by *ansa*-aminoborane **MeCAT**.

Interestingly, while the time needed for the hydrogen splitting by new *ansa*-aminoboranes dramatically increased (one week instead of a few minutes), the corresponding *ansa*-ammonium-borates **MeCATH$_2$** and **NpCATH$_2$** lost molecular dihydrogen gas only slightly faster than **CATH$_2$** upon heating (Schemes 58 and 61). Thus, in contrast to Stephan's intermolecular phosphine-borane systems,[49] the reduction of the Lewis acidity of the borane moiety in the case of the *ansa*-aminoboranes had no prospects. However, increasing the bulkiness around the active boron center (Figure 4) together with fine-tuning the Lewis acidity by introducing electron withdrawing groups may extend the substrate scope of catalytic hydrogenation. Unfortunately, all our attempts towards synthesis of such *ansa*-aminoboranes through modification of either the benzyl bridge or C_6F_5 groups have failed so far.

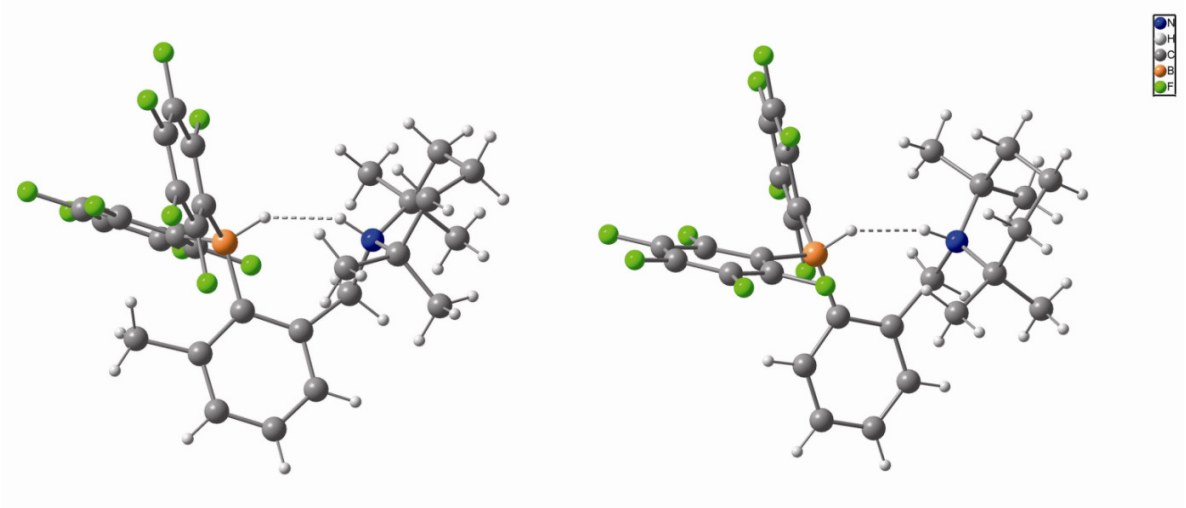
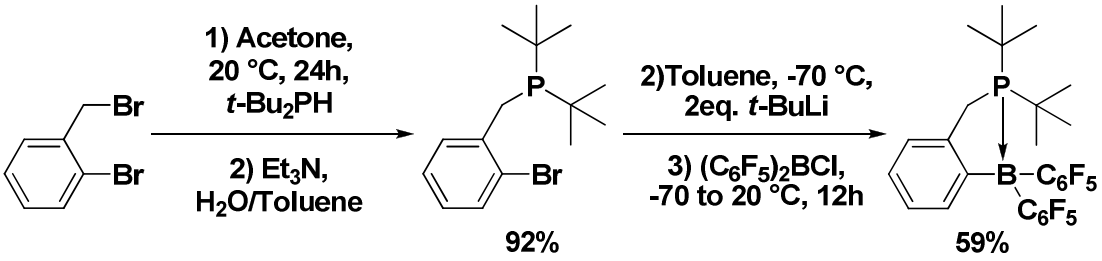


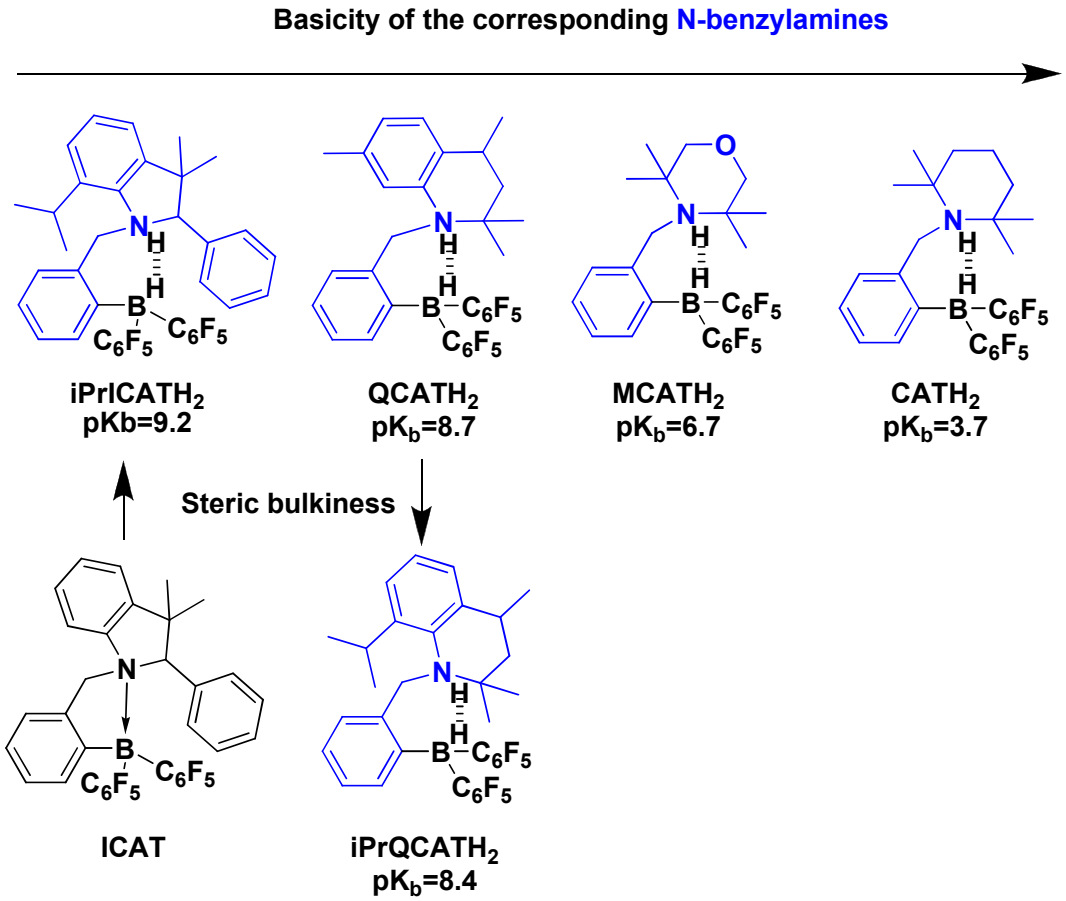
Figure 4. X-ray structures of *ansa*-ammonium-borates **MeCATH$_2$** (left) and **CATH$_2$** (right).

4.6 Tuning of the Lewis basic component of *ansa*-aminoboranes[VI]



Scheme 62. Synthesis of *ansa*-phosphinoborane **PCAT**.

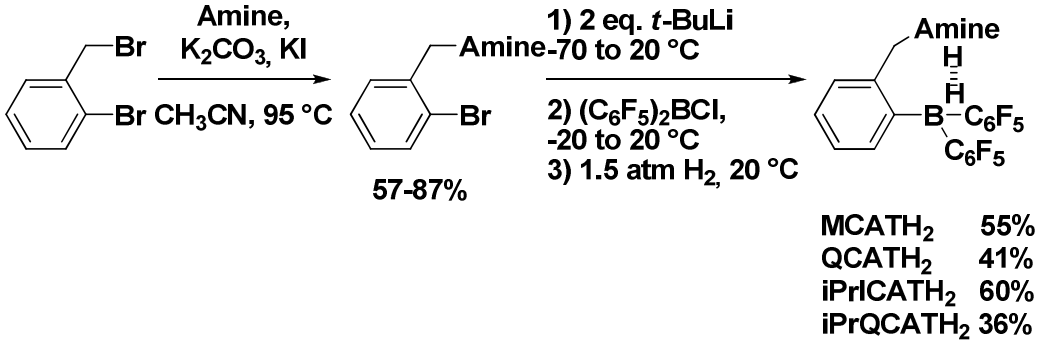
After generally unsuccessful efforts to decrease the time needed for the hydrogen liberation from *ansa*-ammonium-borate systems by modification of the Lewis acidic component, systematic studies on the Lewis basic amine moiety were performed. At first, TMP moiety in the *ansa*-aminoborane **CAT** was replaced by bulky secondary di-*tert*-butylphosphine (Scheme 62).



Scheme 63. Tuning of the amine moiety of the new *ansa*-ammonium-borate catalysts.

The corresponding *ansa*-phosphinoborane **PCAT** was synthesized by a standard two-step procedure in 54% total yield. However, **PCAT** formed a stable intramolecular Lewis acid-base complex, which was not able to activate H_2 even at elevated temperature as was shown by us and later by others.[184,194]

During further investigation, based on the above results two general approaches for modification of the *ansa*-ammonium-borates were proposed: decreasing the basicity of the amine moiety to facilitate hydrogen liberation and proton transfer to imines by weakening the N–H bond; and increasing the sterical hindrance around the active boron center to prevent Lewis acid-base adduct formation between the catalyst and substrate/product by introducing more bulky amines to *ansa*-ammonium-borate's framework (Scheme 63). The corresponding *ansa*-ammonium-borates **MCATH$_2$**, **QCATH$_2$**, **iPrQCATH$_2$** and **iPrICATH$_2$** were synthesized on a gram scale by a standard two-step procedure from readily or commercially available starting materials, followed by facile H_2 activation (Scheme 64). However, the less bulky *ansa*-aminoborane **ICAT** without the isopropyl group at 7-position formed a stable intramolecular Lewis acid-Lewis base adduct.



Scheme 64. Synthesis of the new *ansa*-ammonium-borate catalysts.

The structures of all new *ansa*-ammonium-borates were additionally confirmed by X-ray diffraction (Figures 5 and 6). The X-ray crystal structure of **MCATH$_2$** and **QCATH$_2$** (Figure 5) showed that the N–H···H–B dihydrogen bonds (DHB) presented in the structures are extremely short, in the order of 1.65 Å.[195] While DHBs in the previous **CATH$_2$**, **MeCATH$_2$** systems (Figure 4) and new **iPrQCATH$_2$**, **iPrICATH$_2$** *ansa*-ammonium-borates (Figure 6) are much longer, 1.78 Å, 1.90 Å, 1.93 Å and 1.96 Å, respectively. The X-ray structures of all *ansa*-ammonium-borates exhibited the presence of additional hydrogen bonds between methyl or phenyl C–H and perfluorophenyl C–F groups. Moreover, the X-ray structure of **iPrICATH$_2$** showed a strong intramolecular phenyl-perfluorophenyl π-π stacking of 3.7 Å. Additionally, two sets of different perfluorophenyl signals were observed in solution by ^{19}F NMR in the case of **QCATH$_2$**, **iPrQCATH$_2$** and **iPrICATH$_2$**. Thus, such *ansa*-ammonium-borates have a fixed

conformation, due to a significant barrier of rotation of the $B(C_6F_5)_2$ moiety around the $B–C_6H_4$ bond.

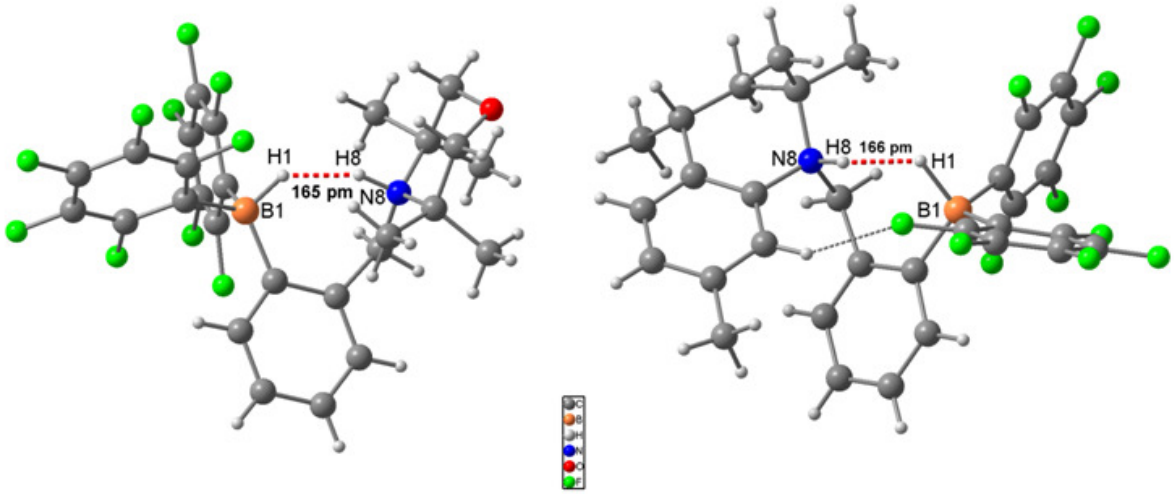


Figure 5. X-ray structures of *ansa*-ammonium-borates **MCATH$_2$** (left) and **QCATH$_2$** (right).

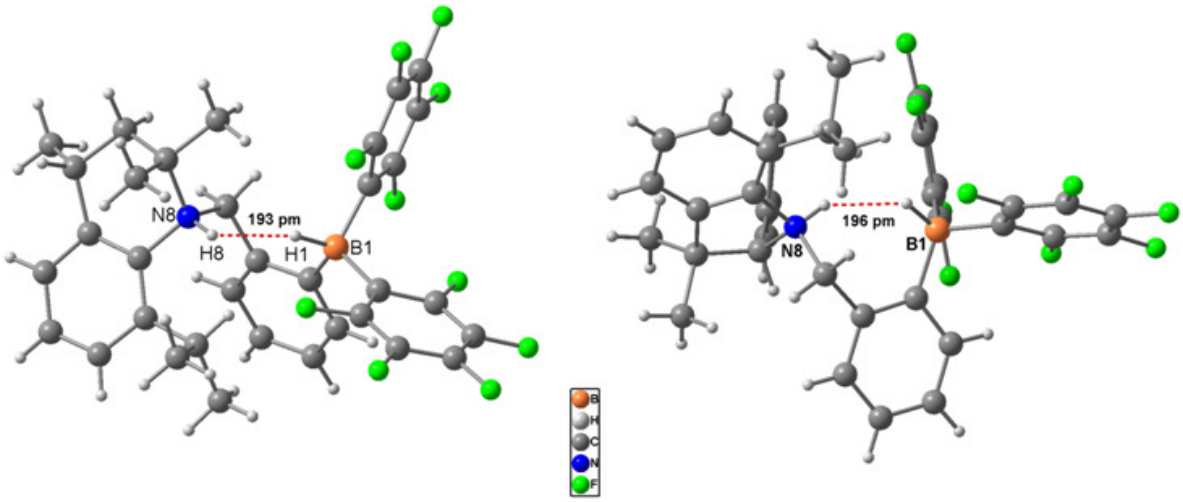
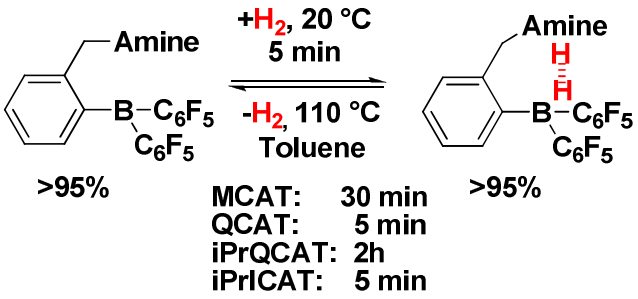


Figure 6. X-ray structures of *ansa*-ammonium-borates **iPrQCATH$_2$** (left) and **iPrICATH$_2$** (right).

While previously studied *ansa*-ammonium-borates **CATH$_2$** and **MeCATH$_2$** released H_2 almost quantitatively after 18 hours at 110 °C (Schemes 58 and 61), under the same conditions less basic **MCATH$_2$** lost hydrogen in just 30 minutes. Moreover, even less basic **QCATH$_2$** and **iPrICATH$_2$** slowly decomposed in solution at room temperature and could be quantitatively converted to starting *ansa*-aminoboranes **QCAT** and **iPrICAT** after 5-10 min at 110 °C (Scheme 65). Accordingly, new, less basic *ansa*-ammonium-borates exhibited excellent kinetics (a few

minutes) in both hydrogen activation and liberation processes mainly due to a rare combination of steric, electronic and thermodynamic effects, which were tuned by a simple modification of the amine moieties.



Scheme 65. Reversible H_2 activation by new *ansa*-aminoboranes.

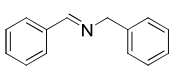
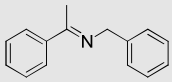
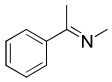
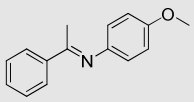
4.7 Hydrogenation by new *ansa*-ammonium-borates.[VI]

In order to gain further insight into the reactivity of the new *ansa*-ammonium-borates, their catalytic activity in the hydrogenation of imines was investigated (Table 13 and 14). The reduction of the model imine **1a** with 1 mol% of *ansa*-ammonium-borates **MCATH$_2$** or **iPrICATH$_2$** in toluene at 110°C under 2 atm of H_2 pressure (56 mL, 2.5 eq.) gave corresponding dibenzylamine in a quantitative yield (Table 13, entries 2,4). However, the reduction of **1a** with either **QCATH$_2$** or **iPrQCATH$_2$** resulted in only 12-15% yields (Table 13, entries 3,5). This fact may be explained by the additional stabilization of catalyst-amine adducts possibly through π–π stacking and/or hydrogen bond interactions.

The reductions of more bulky ketimines **1b** and **1c** with 1-2 mol% of **MCATH$_2$**, **QCATH$_2$** and **iPrICATH$_2$** afforded *N*-benzyl-α-methylbenzylamine and *N*-methyl-α-methylbenzylamine in quantitative yields (Table 13, entries 7-9 and 12-14). The hydrogenation of such imines by more bulky **iPrQCATH$_2$** proceeded to only partial conversion and/or required a higher catalyst loading (4 mol%) (Table 13, entries 10, 15). The hydrogenation of the less basic and more bulky imine **1d** led to a significant increase in the reaction time (40 hours) and gave a lower product yield (70-80%) in the case of *ansa*-ammonium-borates **MCATH$_2$** (1 mol%) and **iPrQCATH$_2$** (4 mol%), respectively (Table 13, entries 17, 20). However, the less basic and less sterically demanding catalysts **QCATH$_2$** (1 mol%) and **iPrICATH$_2$** (2 mol%) reduced the imine **1d** quantitatively after 3 hours at 80°C and 12 hours at 110°C (Table 13, entries 18,19).

Thus, due to a weaker N–H bond new *ansa*-ammonium-borates **MCATH$_2$**, **QCATH$_2$** and **iPrICATH$_2$** showed higher activity than the original **CATH$_2$** (Table 1). Full conversions were achieved with lower catalyst loading and/or shorter reaction time and/or lower temperature. Moreover, further optimization of the reaction conditions can lead to further increase in catalytic activity (Tables 14 and 15).

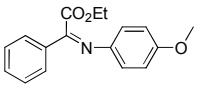
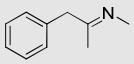
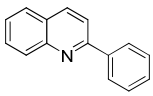
Table 13. Catalytic hydrogenation of imines.[a]

Entry	Substrate	Catalyst	[mol%]	Time [h]	Conv. [%][b]
1	 **1a**	**$CATH_2$**	4	20	100
2		**$MCATH_2$**	1	12	100
3		**$QCATH_2$**	1	12	15
4		**iPrI$CATH_2$**	1	12	100
5		**iPrQ$CATH_2$**	1	12	12
6	 **1b**	**$CATH_2$**	4	6	100
7		**$MCATH_2$**	1	12	100
8		**$QCATH_2$**	1	5	100
9		**iPrI$CATH_2$**	2	12	100
10		**iPrQ$CATH_2$**	4	12	52
11	 **1c**	**$CATH_2$**	4	12	100
12		**$MCATH_2$**	2	12	100
13		**$QCATH_2$**	2	12	100
14		**iPrI$CATH_2$**	2	12	100
15		**iPrQ$CATH_2$**	4	12	100
16	 **1d**	**$CATH_2$**	4	12	37
17		**$MCATH_2$**	1	40	70
18		**$QCATH_2$**	1	3	100[c]
19		**iPrI$CATH_2$**	2	12	100
20		**iPrQ$CATH_2$**	4	12	80

[a] *ansa*-Ammonium-borate catalyst (0.01 mmol, 1-4%), substrate (0.25-1.0 mmol) in toluene (5.0 mL) were refluxed (110 °C) under 2 atm of H_2 pressure (56 mL, 2.5 mmol). [b] Determined by ^{1}H NMR spectroscopy. [c] 80 °C.

Despite the significantly reduced basicity of new *ansa*-ammonium-borates (Scheme 63) the reduction of *N*-aryl-α-imino ester **1e** (which has the lowest basicity in the series of imines) proceeded only with low, but over-stoichiometric, conversions (Table 14, entries 3, 4).

Table 14. Catalytic hydrogenation of imines.[a]

Entry	Substrate	Catalyst	[mol%]	Time [h]	Conv. [%][b]
1	 **1e**	**$CATH_2$**	4	12	4
2		**$MCATH_2$**	4	12	4
3		**$QCATH_2$**	4	40	21
4		**iPrI$CATH_2$**	4	12	15
5		**iPrQ$CATH_2$**	4	12	4
6	 **1f**	**$CATH_2$**	4	12	4
7		**$MCATH_2$**	4	12	4
8		**$QCATH_2$**	4	12	4
9		**iPrI$CATH_2$**	4	12	4
10		**iPrQ$CATH_2$**	4	12	82
11	 **1g**	**$CATH_2$**	4	12	4
12		**$MCATH_2$**	4	12	4
13		**$QCATH_2$**	4	40	80
14		**iPrI$CATH_2$**	4	12	100
15		**iPrQ$CATH_2$**	4	12	97
16		**$QCATH_2$**	4	6	100[c]
17		**iPrI$CATH_2$**	4	6	94[c]
18		**$B(C_6F_5)_3$**	5	4	80[d]

[a] *ansa*-Ammonium-borate catalyst (0.01 mmol, 4%), substrate (0.25 mmol) in toluene (5.0 mL) were refluxed (110 °C) under 2 atm of H_2 pressure (56 mL, 2.5 mmol). [b] Determined by ^{1}H NMR spectroscopy. [c] Et_2O (3 mL) at room temperature. [d] 25 °C, 4 atm H_2.[175]

While generally more active non-metal systems **$MCATH_2$**, **$QCATH_2$** and **iPrI$CATH_2$** (4 mol%) could provide only a stoichiometric reduction of non-bulky imine **1f** (Table 14, entries 7-9). The more sterically demanding **iPrQ$CATH_2$** catalyzed the hydrogenation of the imine **1f** with a yield of 82% (Table 14, entry 10). These observations support a proposed mechanism in which either the proton-transfer equilibrium or dissociation of an amine-catalyst adduct may be the rate-determining step (Scheme 60). Additionally, the *ansa*-ammonium-borates **$QCATH_2$** and **iPrI$CATH_2$** showed high catalytic activity in hydrogenation of 2-phenylquinoline under mild

conditions and gave 2-phenyl-1,2,3,4-tetrahydroquinoline in an almost quantitative yield (Table 14, entries 16, 17).

Inspired by the high activity of **QCATH$_2$**, we further focused on optimizing conditions for the reduction of imine **1d** (Table 15). Overall, the best results were obtained using 1 mol% of catalyst in toluene and hexane at 80°C (2.5 h) or Et_2O at 50°C (1h), respectively (Table 15 entries 8, 13).

Table 15. Catalytic hydrogenation of imine **1d** by *ansa*-ammonium-borate **QCATH$_2$**.[a]

Entry	Solvent	Time [h]	Temperature [°C]	Conv. [%][b]	TOF [h^{-1}]
1	CH_2Cl_2	1	25	10	10
2	CH_2Cl_2	2.5	60	51	20.4
3	$CDCl_3$	1	25	22	22
4	$CDCl_3$	2.5	80	92	36.8
5	Hexane	1	25	2	2
6	Hexane	2.5	80	100	≥40
7	Toluene	1	25	31	31
8	Toluene	2.5	80	99	39.6
9	Et_2O	1	25	17	17
10	Et_2O	2.5	60	100	≥40
11	THF	1	25	2	2
12	THF	2.5	80	42	16.8
13	Toluene	1	50	89	89
14	Et_2O	1	50	97	97

[a] Catalyst **QCATH$_2$** (0.01 mmol, 1%) and **1d** (1.0 mmol) were stirred in solvent (5.0 mL) under 2 atm of H_2 pressure (56 mL, 2.5 mmol). [b] Determined by ^{1}H NMR spectroscopy.

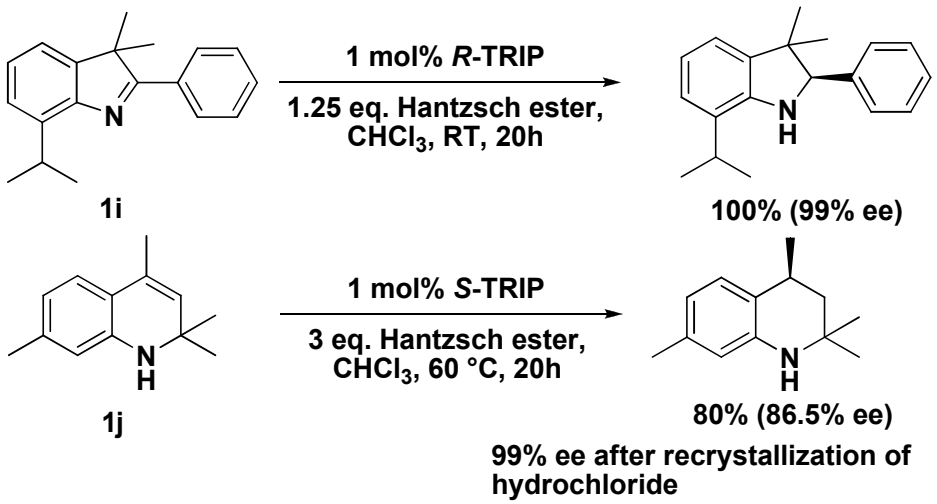
After optimal conditions were found, the possibility of catalyst recovery was investigated. The sensitivity of FLPs towards traces of water is a well known fact.[14,43,I] The presence of accidental traces of water in H_2 gas or the reaction mixture poisons the *ansa*-aminoborane catalyst during the imine hydrogenation, and also forms water adducts of the *ansa*-aminoborane during the quenching of the reaction mixture. Therefore, the dehydration of *ansa*-ammonium-borates containing the highly energetic boron-oxygen bonds is a key transformation for the catalyst recovery procedure. Since the Si–O bond is even more stable than the B–O, and because the B–Br bond is much weaker than the B–Cl, trimethylsilyl bromide was chosen as a dehydrating agent. Surprisingly, after the benzene solution of water-activated *ansa*-ammonium-

borate was treated with an excess of TMSBr (5 eq.) at 80 ºC for 5 minutes and then evaporated under vacuum, *ansa*-aminoborane **QCAT** was isolated in an almost quantitative yield.

Based on the above results the gram-scale hydrogenation of *N*-(4-methoxy)phenyl-1-phenylethylideneamine **1d** (5.632g) by *ansa*-ammonium-borate **QCATH$_2$** (1mol%) was performed to give the corresponding amine in a 97% isolated yield. Moreover, 80% of the catalyst was recovered by a simple extraction of the acidic solution with toluene followed by dehydration with TMSBr at 80 °C. The successful extraction of the water adducts of the *ansa*-aminoborane from the acidic solution was possible due to the high hydrophobic effect of the perfluorophenyl rings.

4.8 Synthesis of chiral *ansa*-ammonium-borates[VI]

The *ansa*-ammonium-borates **QCATH$_2$** and **iPrICATH$_2$** were found to be the most active catalysts in the hydrogenation of imines among previously reported *bis*(perfluorophenyl)boranyl-based systems. Moreover, both of catalysts have a tertiary carbon and nitrogen stereocenters. According to NMR and X-ray diffraction studies, the stereochemistry of the tertiary carbon in these systems has a strong influence on the configuration of the tertiary ammonium nitrogen centre due to a fixed conformation. Thus, **QCATH$_2$** and **iPrICATH$_2$** were shown to be a mixture of diastereomers (5.7:1) and a single diastereomer, respectively (Figure 5 and 6).

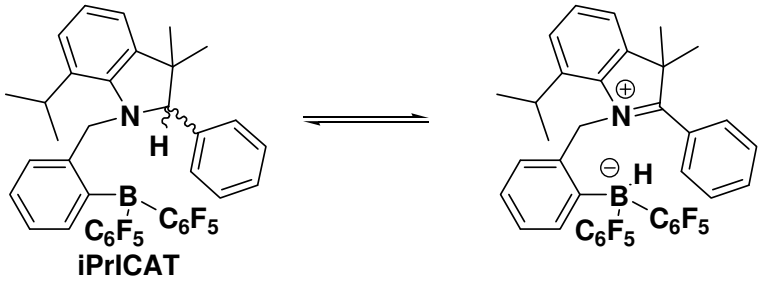


Scheme 66. Synthesis of enantiopure amines.

Due to the above mentioned results, chiral **Q*CATH$_2$** and **iPrI*CATH$_2$** were chosen for further studies. The previously unpublished enantiopure amines were prepared by a phosphoric acid (*R*)-TRIP[196] catalyzed reduction with Hantzsch esters with high yield and high enantioselectivities (Scheme 66). Notably, at that time there was no direct enantioselective

approach to 4-substituted tetrahydroquinolines from 2,2-substituted-1,2-dihydro-quinoline.[155,197] Therefore, our method provided a first and also simple route for the synthesis of such enantiopure amines.

The corresponding chiral *ansa*-ammonium-borates **Q*CATH$_2$**, and **iPrI*CATH$_2$** were prepared by a standard procedure from corresponding enantiopure amines (Scheme 64). In contrast to racemic- **QCATH$_2$**, chiral-**Q*CATH$_2$** exists as a mixture of diastereomers at a lower ratio (1.5:1). This was probably due to the different solubility of chiral and racemic forms and also equilibrium between the hydrogenated **QCATH$_2$** and free **QCAT** form in solution.



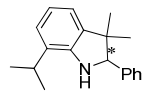
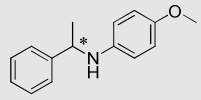
Scheme 67. Racemization of the enantiopure **iPrI*CAT**.

Unfortunately, the X-ray crystal structure study of **PrI*CATH$_2$** revealed the P-1 space group. This meant that in spite of the absence of β-protons in the starting phenylindoline and high steric hindrances around the nitrogen centre, the Lewis acidic borane moiety could abstract the α-proton of the amine fragment and formed the intramolecular iminium borohydride (Scheme 67). Thus, starting from the chiral amine, the racemic *ansa*-ammonium-borate **PrICATH$_2$** was obtained. Therefore, only chiral indolines without α-protons can be applied in the backbone of chiral *ansa*-ammonium-borates.

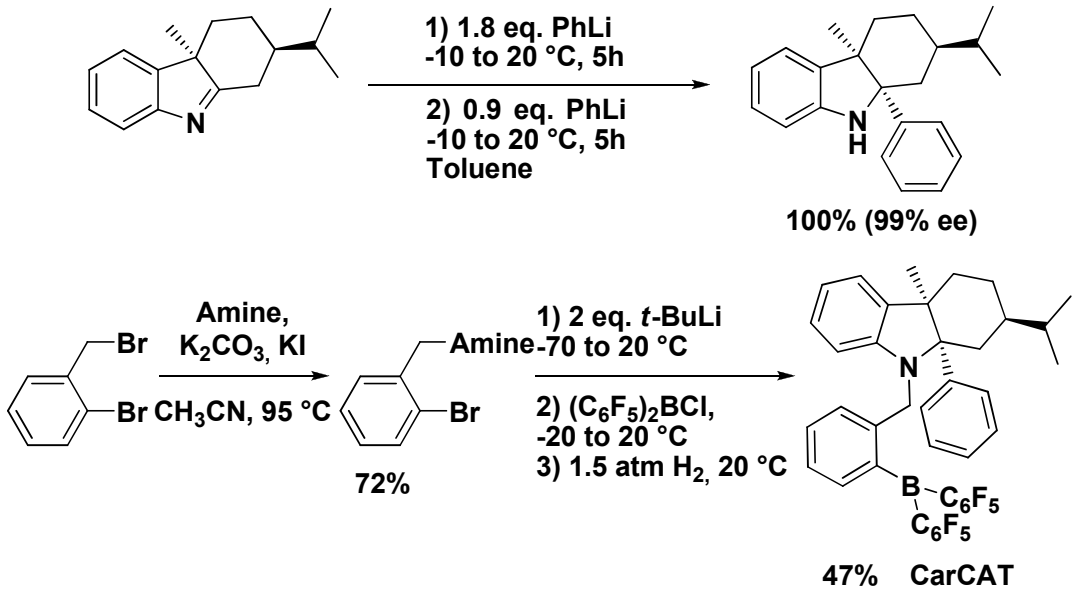
Later, the catalytic activity of $B(C_6F_5)_3$ and *ansa*-ammonium-borates in the intermolecular racemization of chiral amines was evaluated. Among the tested catalysts only $B(C_6F_5)_3$ and **QCATH$_2$** showed reasonable activity at 110 ºC under an argon atmosphere (Table 12). Interestingly, an atmosphere of H_2 (2 atm) fully suppressed the racemization of chiral indoline with $B(C_6F_5)_3$ (Table 12, entry 2).

Next, the 4a,9a-substituted-2,3,4,4a,9,9a-hexahydro-1*H*-carbazole skeleton was examined as a promising amine moiety for chiral *ansa*-ammonium-borates. The enantiopure (2*R*,4a*R*,9a*S*)-2-isopropyl-4a-methyl-9a-phenyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazole was synthesized according to literature procedures (Scheme 68).[198,199,200] The final *ansa*-aminoborane **CarCAT** was prepared by a standard procedure in 34% total yield (Scheme 68). However, since the corresponding carbazole had the lowest basicity in the series of investigated amines, the equilibrium in hydrogen activation by **CarCAT** shifted to the left and the corresponding *ansa*-ammonium-borate **CarCATH$_2$** could not be isolated even at -20 °C.

Table 12. Catalytic racemization of amines.[a]

Entry	Substrate	Catalyst	Initial ee [%][b]	Final ee [%][b]
1		**$B(C_6F_5)_3$**	>97	0
2		**$B(C_6F_5)_3$**		>97 [c]
3		**$CATH_2$**		96.8
4		**$QCATH_2$**		13
5		**$iPrICATH_2$**		86.6
6		**$B(C_6F_5)_3$**	89.5	<0.8
7		**$CATH_2$**		87.6
8		**$QCATH_2$**		42.5
9		**$iPrICATH_2$**		86.2

[a] Substrate (0.1 mmol), $B(C_6F_5)_3$ (0.01 mmol, 10% mol.) were heated (110°C) in toluene (2.0 mL) under argon atmosphere for 15 h. [b] Determined by chiral-HPLC. [c] Under 2 atm of hydrogen pressure.



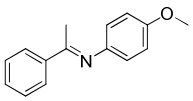
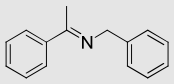
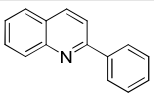
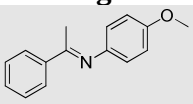
Scheme 68. Synthesis of **CarCAT**.

4.9 Asymmetric hydrogenation by chiral *ansa*-aminoboranes[VI]

The catalytic activity of chiral *ansa*-ammonium-borate **$QCATH_2$** and *ansa*-aminoborane **CarCAT** in the asymmetric hydrogenation of nitrogen-containing compounds at different temperatures and solvents was investigated (Table 16). The chiral *ansa*-ammonium-borate

Q*CATH$_2$ exhibited the same unprecedentedly high activity as its racemic version. Thus, substrates **1b**, **1d**, **1g** were reduced in quantitative yields in 1-12 hours. However, the achieved enantioselectivities were low. The best *ee*s for all substrates were obtained using MTBE as a solvent at room temperature (Table 16, entries 5, 8, 11).

Table 16. Asymmetric catalytic hydrogenation.[a]

Entry	Substrate	Catalyst	Solvent	Time [h]	Temp. [° C]	Conv. [%][b]	ee [%][c]
1	 **1d**	**Q*CATH$_2$**	Toluen	1	80	100	4
2		**Q*CATH$_2$**	Hexane	1	80	100	1
3		**Q*CATH$_2$**	Et_2O	1	60	100	12
4		**Q*CATH$_2$**	Et_2O	1	20	100	19
5		**Q*CATH$_2$**	MTBE	1	20	100	26
6	 **1b**	**Q*CATH$_2$**	Et_2O	1	60	100	21
7		**Q*CATH$_2$**	Et_2O	12	20	100	31
8		**Q*CATH$_2$**	MTBE	12	20	100	35
9	 **1g**	**Q*CATH$_2$**	Et_2O	1	60	100	18
10		**Q*CATH$_2$**	Et_2O	12	20	100	31
11		**Q*CATH$_2$**	MTBE	12	20	100	37
12	 **1d**	**CarCAT**	Toluen	20	80	70	8
13		**CarCAT**	Hexane	20	80	30	17
14		**CarCAT**	Et_2O	20	60	35	17

[a] Catalyst (0.01 mmol, 4%) and imine (0.25 mmol) were stirred in solvent (3.0 mL) under 2 atm of H_2 pressure. [b] Determined by ^1H NMR spectroscopy. [c] Determined by chiral-HPLC.

The repeating of asymmetric hydrogenation of the imine **1d** with **CarCAT** resulted in low to moderate conversions (30-70%) after 20 hours and low *ee*s of 8-17% (Table 16, entries 12-14). The *ansa*-aminoborane **CarCAT** exhibited the low activity, mainly because the very low basicity of the active nitrogen centre. As a result, the hydrogen activation became the rate-determining step of mechanism (Scheme 60).

5 Conclusions

This study presents a progression from the first observation of the facile heterolytical cleavage of hydrogen gas by amines and $B(C_6F_5)_3$ to highly active non-metal catalysts for both enantioselective and racemic hydrogenation of unsaturated nitrogen-containing compounds.

In contrast to bulky diisopropylethylamine and diisopropylamine with α and β-protons the sterically hindered 2,2,6,6-tetramethylpiperidine in combination with $B(C_6F_5)_3$ or $[(C_6F_5)_2B]_2C_6H_4$ was shown to activate dihydrogen gas at room temperature at 1 atm pressure to form ammonium borohydrides in almost quantitative yields. The corresponding $[TMPH]^+[HB(C_6F_5)_3]^-$ system was successfully applied by us and others for the stoichiometric reduction of benzaldehyde, fixation of CO_2, deoxygenative hydrosilylation of CO_2 by diphenylsilane to CH_3OH and together with trispentafluorophenylborane for the deoxygenative reduction of carbon dioxide by triethylsilane to methane. Thus, our first non-metal TMP-$B(C_6F_5)_3$ system for hydrogen activation showed quite a different reactivity compared to classical frustrated Lewis pairs based on phosphines and boranes.

Additionally, the facile heterolytic cleavage of H_2 was readily achieved by different amines, with reduced basicity, and $B(C_6F_5)_3$ under mild conditions. Whilst in the case of the TMS protected amines, the resulting ammonium borohydrides were not stable and liberated TMSH spontaneously, the hydrogenated product $[DMDPPH]^+[HB(C_6F_5)_3]^-$ was found to liberate H_2 gas upon heating at 110°C to give the starting *trans*-2,6-dimethyl-2,6-diphenylpiperidine and $B(C_6F_5)_3$ with a 50% conversion after 36 hours.

The above observations led to the development of the *ansa*-aminoborane *o*-*N*-$TMPCH_2C_6H_4B(C_6F_5)_2$, where the active B and N centers are located close to each other. An effective and common procedure for the preparation of such dual intramolecular Lewis acid–Lewis base systems was also developed. Due to the favorable steric and electronic properties, this nonmetal system can rapidly activate hydrogen at room temperature and 1 atm pressure to give *ansa*-ammonium-borate **$CATH_2$**, which can release dihydrogen gas upon heating at 110 °C. The structure of the *ansa*-ammonium-borate **$CATH_2$** was determined by X-ray and neutron scattering in the solid state, revealing a short intramolecular N–H···H–B dihydrogen bond of 1.78 Å (X-ray value). The short H···H contact and the N–H···H (154°) and B–H···H (125°) angles support the argument that the corresponding dihydrogen interaction is partially covalent in nature. In addition, the dynamic nature of the *ansa*-ammonium-borate **$CATH_2$** in solution was studied by different NMR techniques, showing the existence of an equilibrium between two conformational diastereomers. However, the structure of the most stable conformer in solution was found to be similar to that in the solid state.

To gain further insight into the intramolecular mechanism of reversible hydrogen activation the structure, reaction path, and energetics were studied theoretically by quantum

chemical methods. It was found that the energy needed for splitting H_2 can arise from the Coulomb attraction between the resulting ionic fragments, or "Coulomb pays for Heitler–London". However, this was only an estimate within an order-of-magnitude. In addition, whereas our theoretical and experimental results support the simultaneous mechanism for the hydrogen activation, the formation of a σ-complex between borane and H_2 cannot be ruled out at this point. Further experimental studies are needed to enable a conclusion to be drawn between the two mechanisms.

Aside from the reversible activation of H_2, **CATH$_2$** was also shown to be an efficient catalyst in the direct hydrogenation of different imines and enamines under mild conditions (110 °C and 2 atm of H_2) to give the corresponding amines in high yields. Further rational design of the amine moiety of the *ansa*-ammonium-borate **CATH$_2$** revealed new nonmetal systems with the highest catalytic activity among previously reported organocatalysts. An efficient fine-tuning of the steric surrounding of the nitrogen catalyst atom allowed hydrogenation of a wide substrate range, including sterically hindered and benign, *N*-aryl and *N*-alkyl imines, quinolines, and others. A simple and elegant catalyst recovery procedure was also elaborated. Therefore, the general and simple *ansa*-ammonium-borate concept was developed.[201] The newly designed catalysts were also considered to be a promising toolkit for large-scale applications.

Furthermore, the approach to the synthesis of enantiopure *ansa*-ammonium-borates was developed, and the first example of the enantioselective hydrogenation based on the *ansa*-ammonium-borate concept was demonstrated. These initial findings provide essential information for the further rational design of efficient *ansa*-ammonium-borates for asymmetric hydrogenation

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