Metal-free hydrogenations catalyzed by frustrated \textit{ansa}-aminoboranes

Kostiantyn Chernichenko

ACADEMIC DISSERTATION

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Abstract

Frustrated Lewis pairs (FLPs) are powerful, typically nonmetal, Lewis acid/base combinations that can split dihydrogen (H₂) heterolytically, due to their inability to form conventional Lewis adducts (usually as a result of steric repulsion). The H₂ thus activated can be transferred to various substrates in a catalytic fashion. The scope of substrates catalytically hydrogenated with FLPs is rapidly expanding, approaching that of transition-metal-catalyzed hydrogenations. The discovery of FLPs is, perhaps, one of the most remarkable recent findings in the field of main group organometallic compounds.

The literature review part provides a brief critical overview of heterolytic H₂ splitting with FLPs, including the thermodynamic, mechanistic, and catalytic aspects of this process. Particular emphasis is placed on the Lewis acidity of various boranes, since this factor is critical for the ability of FLPs to split H₂ and provides a basis for introducing fluoroaryl-free boranes into the FLP area.

The experimental section of the thesis is devoted to the development of FLP catalysts, based on an ansa-aminoborane core for hydrogenation of various substrates. Within the study, various parts of the ansa-aminoborane molecule were modified:

- an amine group, resulting in highly active ansa-aminoboranes for hydrogenation of imines and other nitrogen-containing compounds, also featuring other unique properties;
- a mutual B/N geometry (changing the nature of the link), resulting in an ansa-catalyst for hydrogenation of unactivated alkynes;
- and a borane part, revealing that lightweight and inexpensive ansa-aminochloroboranes show reactivity to H₂ similar to that of C₆F₅ boranes, including catalytic abilities.

A book chapter covering recent progress in frustrated borane/amine Lewis interaction, involving ansa-systems was included in the thesis.
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I dedicate this work to my beloved wife Diana, my Muse, whose love inspired me in my scientific findings. It was her patience, support, and encouragement that helped me the most to carry this work through.
List of original publications

The thesis is based on the following original publications cited in the text with Roman numbers:


Author's contribution

Paper I: Dr. V. Sumerin and K. Chernichenko performed the syntheses, experiments, and analyses. Dr. M. Nieger performed the X-ray structural analysis. Dr. V. Sumerin drafted the manuscript. Prof. M. Leskelä, Prof. B. Rieger, and Prof. Timo Repo supervised the study. All authors discussed the results and edited the manuscript.

Paper II: M. Lindqvist and N. Sarnela performed the experiments and analyses. K. Chernichenko performed minor experiments and analyses. M. Lindqvist drafted the manuscript. Prof. M. Leskelä and Prof. Timo Repo supervised the study. All authors discussed the results and edited the manuscript.

Paper III: K. Chernichenko performed syntheses, experiments, and analyses. Dr. M. Nieger performed the X-ray structural analysis. K. Chernichenko drafted the manuscript. Prof. M. Leskelä and Prof. Timo Repo supervised the study. All authors discussed the results and edited the manuscript.

Paper IV: K. Chernichenko and Dr. V. Sumerin discussed and planned the review. K. Chernichenko helped to collect the literature. Dr. V. Sumerin drafted the manuscript. All authors edited the manuscript.

Paper V: K. Chernichenko performed the syntheses, experiments, and analyses. Dr. Á. Madarász and Prof. I. Pápai planned and carried out computational studies. K. Chernichenko drafted the manuscript. Prof. M. Leskelä, Dr. M. Nieger, and Prof. Timo Repo supervised the study. All authors discussed the results and edited the manuscript.

Paper VI: K. Chernichenko performed the syntheses, experiments, and analysis. Dr. M. Nieger performed the X-ray structure analysis. Prof. I. Pápai planned and carried out the computational studies. K. Chernichenko drafted the manuscript. Prof. M. Leskelä and Prof. Timo Repo supervised the study. All authors discussed the results and edited the manuscript.
List of abbreviations

Alk – alkyl
Ar – aryl
Bn – benzyl
Bu – butyl
Cy – cyclohexyl
DABCO – 1,4-diazabicyclo[2.2.2]octane
DFT – density functional theory
eq. – equivalent
EW – electron-withdrawing
EWG – electron-withdrawing group
FLP – frustrated Lewis pair
ee – enantiomeric excess
ΔG – Gibbs free energy change
ΔH – enthalpy change
HA – hydride affinity
HOMO – highest occupied molecular orbital
HPLC – high-performance liquid chromatography
HSAB – hard and soft acid and base (principle)
iPr – prop-2-yl
ItBu – N,N-di(tert-butyl)imidazol-2-ylidene
LA – Lewis acid
LB – Lewis base
LUMO – lowest unoccupied molecular orbital
Me – methyl
Mes – mesityl, 2,4,6-trimethylphenyl
MTBE – methyl tert-butyl ether
NMR – nuclear magnetic resonance
NOESY – nuclear Overhauser effect spectroscopy
Np – naphthyl
PA – proton affinity
PES – potential energy surface
PFB – perfluoroarylborane
Ph – phenyl
ppm – part per million
Pr – propyl
RDS – rate determining step
RT – room temperature
sBu – but-2-yl
TBS – tert-butyl(dimethyl)silyl
tBu – tert-butyl
TM – transition metal
TMEDA – N,N,N’,N’-tetramethylethylenediamine
TMP – 2,2,6,6-tetramethylpiperidine or 2,2,6,6-tetramethylpiperid-1-yl
TMS – trimethylsilyl
TS – transition state
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**Introduction**

The concept of frustrated Lewis pairs (FLPs) was introduced\(^1\) by D. Stephan *et al.* soon after the discovery of reversible dihydrogen (H\(_2\)) activation with phosphinoboranes.\(^2\) The main idea is simple: a pair comprising a Lewis acid (LA) and a Lewis base (LB), unable to produce a Lewis adduct or producing a weak adduct\(^*\) due to steric hindrance, has unquenched reactivity. It can be disengaged if a geometrically smaller and electronically suitable molecule can fit in between the acid and base, forming bonds with each other (Fig. 1).

![Diagram of Lewis acid and Lewis base interactions](image)

**Figure 1.** Unlike a classical Lewis pair, a frustrated pair does not produce a stable adduct due to steric repulsion.

Generally, three types of FLP reactivity have been reported to date (Fig. 2):

a) Heterolytic splitting of the substrate's σ-bond. Usually, the substrates are protogenic species resulting in splitting of a sufficiently acidic hydrogen atom as H\(^+\): H\(_2\), HX (\(X = \text{halogen, OH, OR, etc.}\)), terminal alkynes.\(^3\), \(^4\) Examples of heteroatomic bond cleavage in disulfides,\(^5\) ethers,\(^6\) and singlet oxygen\(^7\) were reported.

b) 1,2-Addition of the acid-base pair to the π-bond of the substrate. Not only polar oxygen-containing carbonyl compounds,\(^8\), \(^9\) CO\(_2\),\(^9\), \(^10\) isocyanates,\(^8\), \(^9\) isothiocyanates,\(^9\) nitriles,\(^9\) diazo compounds,\(^11\) nitroso compounds,\(^8\) and SO\(_2\),\(^12\) were activated, but also alkenes\(^13\), \(^14\) and alkynes,\(^3\) including conjugated.\(^15\), \(^16\)

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\(^*\) In this case the 'weak adduct' refers to a dissociation energy low enough to be caused by thermal promotion, thus providing sufficient concentration of free acid and base for further reaction with substrate.
Depending on the conditions, terminal alkynes show amphoteric reactivity: CH-activation or 1,2-addition.\(^4\)

b') A special case of type b is the addition of highly acidic boranes to enamines and imines. Many examples were reported with B(C\(_6\)F\(_5\))\(_3\)\(^{17,18}\) and some with HB(C\(_6\)F\(_5\))\(_3\) recently.\(^{19,20}\)

b'') 1,3-Dipolar addition of the acid-base pair to 1,3-dipoles: reactions with N\(_2\)O.\(^{21,22}\)

c) 1,1-Addition of the acid-base pair to a substrate is presented by activation of NO\(^23\) and azides.\(^8\)

\[
\begin{align*}
R = \text{organic radical} & \quad D = \text{Lewis base (donor)} \\
A = \text{Lewis acid (acceptor)}
\end{align*}
\]

\[
\begin{align*}
a) & \quad D \rightarrow X\downarrow Y \uparrow A \quad \rightarrow \quad [D-X]^+ [Y-A]^- \quad \quad X = H, Y = \text{halogen, OH, -R} \\
& \quad X \cdot Y = R^1 R^2 C=O, OC=O, RN=O, \quad R^1 R^2 C=CR^3 R^4, R^1 C=CR^2 \\
& \quad b) & \quad \quad \quad \rightarrow \quad D^+ \cdot X \downarrow Y \uparrow A \quad \quad D = R^1 R^2 \quad \quad X = R^3 \quad \quad Y = R^4 \quad \quad R^5 \\
& \quad b') & \quad \quad \quad \rightarrow \quad +D^+ \cdot Y \downarrow X \uparrow A \quad \quad Y = X^+ \quad \quad Z = N=\text{N}^+ \quad \quad \text{O}^- \\
& \quad b'') & \quad \quad \quad \rightarrow \quad D \cdot \cdot X \downarrow Y \uparrow A \quad \quad (C\(_6\)F\(_5\))\(_2\) B\(-\text{N}^+\text{(t-Bu)}\)_\(_2\) (C\(_6\)F\(_5\))\(_2\) B\(-\text{N}^+\text{(t-Bu)}\)_\(_2\) \quad \quad \text{N} \cdot \text{NR} \\
& \quad c) & \quad \quad \quad \rightarrow \quad +D^+ \cdot X \downarrow Y \uparrow A
\end{align*}
\]

Figure 2. General reaction types of frustrated Lewis pairs reported to date.

The diversity of small molecule types that can be activated by FLPs, sometimes by a single frustrated pair,\(^8,9\) is unprecedented in main group chemistry and forced some researchers to draw parallels between FLPs and transition metals (TMs).\(^{24}\) The latter have abundant d-orbitals close in energy and with varyiing symmetry. Most often, TM bonding results in simultaneous overlapping of ligand’s both frontier orbitals with the metal center (back donation). In case of reaction between the FLP and substrate (Fig. 3), four orbitals interact: two from the substrate, bonding and antibonding, typically frontier; while a Lewis acidic component participates by its LUMO localized on the central atom and a Lewis
base – by its HOMO localized typically on N or P as a lone pair, i.e. at the nonbonding orbital. As result, a heterolytic cleavage of one substrate’s bond occurs along with formation of two new σ-bonds. This bonding pattern is quite unique and has little in common with TMs. In addition, FLPs, in contrast to TMs, have low capacity for bonding orbitals: simultaneous addition of more than one substrate to the same FLP is implausible. This shortcoming expectedly restricts the potential of FLPs in catalysis. The wide diversity of molecules reacting with FLPs may originate from high reactivity of the latter, since most small molecules are bound irreversibly.

Figure 3. FLP-substrate bonding pattern: the LA participates by its LUMO, the LB by its HOMO, while the substrate participates by its two orbitals (one bond breaks) and two new σ-bonds form.

Although many of the FLP reactivities reported have been unprecedented in metal-free chemistry, few of them can be seen as practically important. The major exception is H<sub>2</sub> activation, which turned into the rapidly growing area of FLP-catalyzed hydrogenation of various organic compounds. The term 'activation' is refers to the transformation of otherwise unreactive molecules into reactive form, especially in a catalytic manner. While this applies to H<sub>2</sub>, it is transformed into reactive onium borohydrides, the vast majority of other small molecules were 'activated' into FLP adducts that were not involved in any further transformations. Therefore, the term 'activation' should be used with care.

Early examples of FLP reactivity were reported in the literature, and many more chemical processes that involve simultaneous presence of a Lewis acid and a
Lewis base are likely to involve FLP mechanisms. Nevertheless, it was perfluoroarylboranates (PFBs), particularly, B(C₆F₅)₃ (1), that made activation of practically important small molecules such as H₂ possible. With few exceptions, such as perfluoroarylaraluminum, zirconium, titanium, silyl, and borenium cations, the Lewis acidic part of FLPs is presented by perfluoroarylboranates. The main features of PFBs are high Lewis acidity (comparable to boron halides, see below) and high hydrolytic stability. They make PFBs unique Lewis acidic catalysts for various organic reactions and efficient non-methylaluminoxane activator of metallocene catalysts for polymerization of α-olefins. On binding of alkyl or other groups to PFB, a weakly coordinating anion is generated, which is crucial to many activation processes.

Usually, sterically encumbered amines or phosphines are used as the basic parts of FLPs. Although more exotic N-heterocyclic carbenes and carbon-based bases were reported, they have not found wide application. Amines and phosphines are equally popular, with some preferences existing in particular research groups. Amines have several advantages over phosphines: the N-C bond length (1.3–1.5 Å) is substantially shorter than in P-C bonds (1.7–1.8 Å), creating significantly more crowded surroundings around N center. Indeed, most of the phosphines used possess at least two tert-butyl or mesityl groups. In contrast, various simple and commercially available amines were used as part of FLPs, including such sterically accessible ones as N,N-dimethylaniline. In addition, tert-butyl-phosphonium group tends towards elimination of isobutene, which can lead to degradation of the FLP adduct. On the other hand, B(C₆F₅)₃ abstracts hydride from many amines containing α-hydrogen atoms. This reaction, however, is reversible, especially, under conditions of H₂ activation.
Scope of the thesis

Several years before Stephan's pioneering studies, the aminoborane system 2 based on the similar principals was published by Piers' group (Fig. 4). The amine and borane parts of this molecule were linked by a phenylene ring, exemplifying the first frustrated ansa-aminoborane, although H₂ activation with 2 was unsuccessful. It was Stephan et al. who demonstrated for the first time that the metal-free system 3 can split dihydrogen heterolytically, opening the intriguing area of frustrated Lewis pairs. Later, Repo et al. showed that simple sterically hindered amines (e.g. 7) can be used as a basic part of FLP. In addition, the catalytic properties of frustrated phosphinoboranes in hydrogenation of imines were demonstrated.

Inspired by these results, previous findings by Stephan's and Piers' groups and rational consideration that the chelating (ansa) configuration of an acid and a base may facilitate H₂ splitting, the ansa-aminoborane CAT was synthesized by Repo et al. This compound demonstrated much faster H₂ uptake than the intermolecular amine/borane system. In addition to kinetic advantages, ansa-configuration of CATH₂ provided additional stabilization due to so-called 'dihydrogen bond' – proximity of NH⁺ and BH⁻ hydrogen atoms at a distance of only 1.67 Å. More remarkably, CAT catalyzed the hydrogenation of imines. At the same time, CAT suffered from some shortcomings, namely, low catalytic activity requiring prolonged heating and inability to catalytically hydrogenate some substrates. Since H₂ activation by CAT is a rapid process, it is the further transfer of H₂ to imine that makes the entire process slow.
Figure 4. Key steps in the development of the FLP area.

Present work was aimed on the development of metal-free catalysts for hydrogenation of various substrates. The core of the CAT molecule was taken as a basis and its various parts were modified (Fig. 5). The resulting new ansa-aminoboranes possess many unprecedented features that were revealed within the study.

Figure 5. Modification of the original CAT system studied in the present work.
Literature review

1. Thermodynamic basis of H₂ splitting by FLPs

Due to the simplicity of the H₂ molecule and the overall process, as well as the availability of some thermodynamic tabular values, H₂ activation can be successfully analyzed, using the formalism of Born-Haber cycle. The process can be separated into five separate hypothetic processes: Lewis acid and Lewis base preparation, heterolytic H₂ dissociation, hydride addition to an LA, protonation of an LB, and eventual aggregation of ions into solid or solvated ionic molecule (Fig. 6). Evaluation of ΔH⁴⁹ and ΔG⁵⁰ for H₂ activation by various FLPs provided data consistent with experimental thermochemical studies (in the case of ΔH) or H₂-splitting ability/reversibility (ΔG). Importantly, the Born-Haber formalism gives theoretical grounds for considering the 'power' of an FLP to a first approximation as an additive of the individual powers of the acid and base. They can be defined as Gibbs free energies (ΔG) of the proton affinity (PA) of the base and hydride affinity (HA) of the base, and are the major negative components in the overall ΔG value. This simple consideration gives ample opportunity for tuning the thermodynamic properties of FLPs with respect to H₂ activation: the weakness of the acid can be compensated for to some extent with the power of the base and vice versa. By tuning the nature of the acid and base, the H₂ splitting can be made energetically neutral and, hence, reversible, if needed. The preparation energy (E_prep) can be varied, but for truly frustrated pairs it is negligible. The association energy can provide additional stabilization of the product and will be discussed in Chapter 5.

\[ D \cdot \cdot A \rightarrow A + D \] Preparation of the Lewis acid (LA) and base (LB), e.g. Lewis adduct dissociation, if any; or the dissociation of the encounter complex (EC).

\[ H_2 \rightarrow H^+ + H^- \] Heterolytic H₂ splitting,
\[ \Delta H = 400.4 \text{ kcal/mol in the gas phase};^55 \]
\[ \Delta G = 128.8 \text{ kcal/mol in toluene};^50 \]

\[ A + H^- \rightarrow AH^- \] Hydride affinity (HA) – H⁻ addition to the LA.
\[ D + H^+ \rightarrow DH^+ \] Proton affinity (PA) – H⁺ addition to the LB.
\[ AH^- + DH^+ \rightarrow [DH]^+[AH]^- \] Association of the ions into an ionic pair.

Figure 6. Partition of the energy of hydrogen splitting by FLPs in terms of Born-Haber cycle formalism.
In most cases conventional amines or phosphines are used as bases, and their proton affinities (PA) are well studied experimentally or can be easily predicted computationally and varied to a large extent. Typical values of the most studied bases, 2,2,6,6-tetramethylpiperidine (TMP) and phosphines, were estimated in the range of \( \Delta G = -60 \) to -50 kcal/mol (toluene solution),\(^{50}\) with TMP and \( \text{Mes}_3\text{P} \) being the weakest and \( \text{Cy}_3\text{P} \) the strongest base. \( \text{H}_2 \) splitting with extremely basic \( N \)-heterocyclic carbenes (PA of \( \text{I} \text{Bu} \) is -80 kcal/mol in toluene) was reported.\(^{36, 37}\) Iminophosphoranes were used recently by Stephan’s group as a basic part of FLPs.\(^{56}\) On the opposite edge of the basicity scale, triarylphosphines with electron withdrawing substituents are located. It was demonstrated that the low basicity of these phosphines plays the key role in an elegant way of alkene hydrogenation catalyzed by FLPs.\(^{57}\)

The crucial role of fluoroarylborane features in \( \text{H}_2 \) splitting was mentioned previously. Increase in Lewis acidity can expectedly cause a rise in FLP reactivity or catalytic activity (in certain cases when FLPs are used as catalysts). The problem of designing powerful LAs was addressed previously in regard to \( \text{\alpha-olefin} \) polymerization\(^{34, 58}\) and revived recently with the discovery of \( \text{H}_2 \) activation with FLPs.

Clearly, the Lewis acidity of any compound cannot be considered apart from a binding base (donor). As a result, affinities for various donors, e.g., fluoride,\(^{59, 60}\) hydride,\(^{61}\) acetonitrile, amines,\(^{44}\) ethyl acetate, carbon monoxide, crotonaldehyde,\(^{62}\) triethylphosphineoxide, etc. have been proposed for ranking Lewis acids. As expected, these scales do not always correlate; in addition, many of them are based on the indirect (usually spectroscopic) methods of affinity determination. The hydride affinity (HA) scale is the most relevant for \( \text{H}_2 \) splitting with FLP. Although calculated HAs are extensively used in FLP chemistry,\(^{50}\) direct experimental measurements of the HAs are complicated.\(^{63}\) In those cases where such studies can be performed, the enthalpies in the gas phase were obtained\(^{55}\) and correlations with free energies in solution are required. As result, other donors are widely used to compare the acidity of boranes. Some insight into the Lewis donor-acceptor bonding of boranes as typical main-group LAs can be provided with the energy decomposition analysis.\(^{64}\) The bond dissociation energy (\( \text{D}_e \)) can be partitioned into two major components, \( \Delta E_{\text{prep}} + \Delta E_{\text{int}} \).

\[
\text{D}_e = \Delta E_{\text{prep}} + \Delta E_{\text{int}} = \Delta E_{\text{prep}} + \Delta E_{\text{elstat}} + \Delta E_{\text{orb}} + \Delta E_{\text{Pauli}}
\]
\( \Delta E_{\text{prep}} \) – preparation energy, required for deformation of acid and base from their ground electronic states and geometries into fragments corresponding to their final condition in the adduct. \( \Delta E_{\text{int}} \) – the actual energy of the deformed fragments interaction which can be partitioned into electrostatic (\( \Delta E_{\text{elstat}} \)) and orbital (\( \Delta E_{\text{orb}} \)) interactions and Pauli repulsion (\( \Delta E_{\text{Pauli}} \)). \( \Delta E_{\text{elstat}} \) and \( \Delta E_{\text{Pauli}} \) are sometimes combined into a steric interaction term \( \Delta E^* \) reflecting non covalent interactions between donor and acceptor fragments.

The utility of the bonding analysis can be demonstrating with the following example: it is well known that the affinity for strong LBs increases in the series BF\(_3\)\(<\)BCl\(_3\)\(<\)BBr\(_3\), while with weak bases (CO, HCN, CH\(_2\)CN, and CH\(_3\)F) the trend is contrasting.\(^{65, 66}\) Since the electronegativity of halogenes falls in the series F>Cl>Br, debates on the origin of the stronger interaction in H\(_3\)N→BCl\(_3\) compared with H\(_3\)N→BF\(_3\) lasted for decades and many explanations were proposed. The more efficient back donation from the 2p orbital of the F than from the 3p of the Cl to the \(p_z\) orbital of boron atom, populating it, is the most popular explanation. However, in the final pyramidal state of the BX\(_3\) fragment, the \(\pi\)-overlapping should be inefficient. It was suggested that the higher charge capacity of BCl\(_3\) due to larger and more polarizable substituents is responsible for the stronger B-N bond.\(^{67}\) Gillespie et al., based on the ligand close-packing model developed, suggested that the stronger B-F bonds require more energy to pyramidize.\(^{65}\) Eventually, energy decomposition analysis recently performed for this case has revealed that a) \( \Delta E_{\text{prep}} \) is nearly the same for both adducts and b) the stronger H\(_3\)N→BCl\(_3\) adduct is caused by a stronger B-N covalent bond (\( \Delta E_{\text{orb}} \) 49.7\% vs 45.9\% in H\(_3\)N→BF\(_3\)), which in turn is caused by the lower LUMO level of BCl\(_3\).\(^{68}\) The reason for the lower LUMO level of BCl\(_3\), however, was not defined. In addition, although the energy decomposition analysis provided meaningful components of the bonding energy, the impact of \( \Delta E_{\text{orb}} \) and \( \Delta E_{\text{elstat}} \) was to some extent equal, while the relative value of the final bond dissociation energy (\( D_e \)) compared with the attracting (\( \Delta E_{\text{orb}} + \Delta E_{\text{elstat}} \)) and repulsive (\( \Delta E_{\text{Pauli}} \)) component was small, making the difference in \( D_e \) of the two adducts negligible compared with the components.\(^{†}\)

\(^†\) For example, in \( D_e(BCl_3-NH_3) \) vs. \( D_e(BF_3-NH_3) \), the difference was only 2.5 kcal/mol or 1.3\%, while \( \Delta E_{\text{Pauli}}(BCl_3-NH_3) = 190.1 \text{ kcal/mol (100\%)} \) and \( \Delta E_{\text{Pauli}}(BF_3-NH_3) = 125.9 \text{ kcal/mol (66.2\%)} \). DFT calculations at the PW91/QZ4P level.\(^{68}\)
Despite such complex bonding pictures of Lewis adduct formation, attempts were made to introduce universal indices of acidity, based on the nature and properties of LA only.\textsuperscript{66} Although most of the indices proposed are based on calculations, the LUMO level of LA is an important molecular characteristic which, on one hand, is correlated with $\Delta E_{\text{orb}}$, and on the other, can be evaluated from electrochemical measurements.

To evaluate the Lewis acidity of boranes, spectroscopic methods are routinely used (Fig. 7). Infrared spectroscopy (IR), namely, vibrational C=O band frequency ($\Delta \nu(C=O)$) of TM carbonyls is heavily used to study the bond strength with this important ligand. Unlike TMs, main group LAs bind CO weakly and the change in IR C=O band frequency ($\Delta \nu(C=O)$) of ethyl acetate upon binding to LA was used. Adducts 11 have shown good qualitative correlation of the acidity of inorganic Lewis acids (LA = BF$_3$, BCl$_3$, BBr$_3$, AlCl$_3$) in comparison with other methods.\textsuperscript{69}

\begin{itemize}
  \item Childs
    \begin{align*}
    \text{H}^3 & \quad \text{O} \\
    \text{LA} & \quad \text{9}
    \end{align*}
    \text{1H NMR: } \Delta(\delta(H^3))
  \end{itemize}

\begin{itemize}
  \item Gutmann
    \begin{align*}
    \text{O} & \quad \text{LA} \\
    \text{Et} & \quad \text{P}^+ \quad \text{Et} \\
    \text{Et} & \quad \text{10}
    \end{align*}
    \text{31P NMR: } \Delta(\delta(P))
  \end{itemize}

\begin{itemize}
  \item Lappert
    \begin{align*}
    \text{O} & \quad \text{Et} \\
    \text{CO} & \quad \text{LA} \\
    \text{11}
    \end{align*}
    \text{IR: } \Delta \nu(C=O)
  \end{itemize}

\textbf{Figure 7.} Spectroscopic methods of Lewis acidity determination.

Due to the abundant use of NMR spectroscopy, two other spectroscopic methods of acidity evaluation are widely used (Fig. 7). The scale of Childs\textsuperscript{62} postulates a linear correlation in the change in chemical shift of the H-3 vinylic proton of crotonaldehyde→LA adducts 9 and their Lewis acidities. This method was theoretically rationalized via a linear correlation found between the change in chemical shift and the calculated level of the lowest $\pi^*$ MO of the Lewis adduct.\textsuperscript{70} Direct calorimetric studies, however, showed only a qualitative correlation between the change in the chemical shift and the enthalpy of the crotonaldehyde adduct formation.\textsuperscript{71} On an analogical scale, the Gutmann number\textsuperscript{72, 73} is based on the change in the $^{31}$P chemical shift in Et$_3$PO upon coordination with LA. Both methods showed good linear correlation over a broad range of inorganic LAs ($R^2 = 0.97$).\textsuperscript{74, 75}
When, however, various organoboranes were compared, using the Gutmann and Childs methods, a strong inconsistency between them was observed. For example, while \( B(OC_6F_5)_3 \) is slightly stronger than \( B(C_6F_5)_3 \) on the Gutmann scale, it is substantially weaker in the Childs method. This contradiction was explained, using the hard and soft acid and base (HSAB) theory: \( B(OC_6F_5)_3 \) and Et₃PO are considered to be a hard LA and a hard LB, respectively, while \( B(C_6F_5)_3 \) and crotonaldehyde are soft, leading to stronger coordination within matching pairs. Particular care should be taken in measuring the acidity of weak LAs by the Gutmann method, since the formation of the adduct in solution can be incomplete. Due to the existing equilibrium between Et₃PO and Et₃PO→LA and their rapid exchange, the \(^{31}P\) chemical shift observed can be substantially lower than the actual shift for Et₃PO→LA. For example, the shift in the 1:1 Ph₃B:Et₃PO mixture is about 5 ppm lower than that in a 5:1 mixture. Since researchers routinely use 3 eq. of Et₃PO, the measured acidity can be very far from the actual acidity. Importantly, sufficiently strong acids such as \((C_6F_5)_3B\), coordinate Et₃PO quantitatively, showing no dependence of the chemical shift on the Et₃PO/LA ratio.

A simple and direct experimental method is based on competing binding of acetonitrile between two acids. Acetonitrile is a small linear molecule that is relatively insensitive to steric factors. Even with strong LAs, such as PFBs, the adducts are kinetically labile, providing rapid equilibrium.
2. Strategies towards design of highly acidic boranes

Attempts to make fluoroarylboranes more Lewis acidic than B(C₆F₅)₃ were made by introducing fused and conjugated perfluoroaryls expected to be stronger electron-withdrawing groups (EWG) than C₆F₅ (Fig. 8). Reported examples include replacement of C₆F₅ with 2-perfluoronaphthyl (12), 2-perfluorobiphenyl (partial, borane 13; complete, 14), bis-3,5-(trifluoromethyl)phenyl, and their acidity measurements are summarized in Table 1. Only in the case of 12 did various methods (calorimetry of reaction with acetonitrile; Childs and Guttmann methods) show evidence for slightly higher acidity than that of B(C₆F₅)₃, while the other boranes demonstrated contradicting trends, which were usually explained in terms of HSAB theory.

![Figure 8.](image)

Interestingly, substitution of a single p-F atom in B(C₆F₅)₃ with a phosphino group did not lead to substantial loss in acidity, while substitution with a cationic phosphonium group (17–20) (e. g. as a result of phosphino group protonation) led to a dramatic rise in acidity (Fig. 8, Table 1). This effect, apparently, plays an important role during H₂ activation with 3 and 16, leading to additional self-stabilization of the H₂ adduct. Thus, introduction of cationic substituents provides another way of designing highly Lewis acidic boranes.
Table 1. Comparative data of Lewis acidic properties of various inorganic and organic boranes.

<table>
<thead>
<tr>
<th>BR₃</th>
<th>Acetonitrile affinity -ΔH°₂⁹₈ kcal/mol, [Kₑq]a)</th>
<th>Crotonaldehyde affinity -ΔH°₂⁹₈ kcal/mol</th>
<th>Childs number, Δ(δ¹H) b)</th>
<th>Et₃PO affinity (Guttman number), δ³¹P c)</th>
<th>Hydride affinity in gas phase -ΔH°₂⁹₈ kcal/mol(d)</th>
<th>Reported H₂ activation (Δ(δ¹H) e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BF₃</td>
<td>14.4 ⁷ 85</td>
<td>1.17 ⁶²</td>
<td>80.₉ ⁷⁵</td>
<td>75.₅ ⁷⁰</td>
<td>70.₅ ⁷⁰</td>
<td></td>
</tr>
<tr>
<td>BCl₃</td>
<td>24.₄ ³(₆) ⁷¹</td>
<td>1.₃₅ ³(₆) ⁶²</td>
<td>88.₇ ⁷⁵</td>
<td>95.₈ ⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BBr₃</td>
<td>1.₄₉ ³(₆)</td>
<td>90.₃ ⁷⁵</td>
<td>104.₉ ⁶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BI₃</td>
<td></td>
<td>92.₉ ⁷⁵</td>
<td>112.₆ ⁶</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BF₃H</td>
<td></td>
<td>63.₂ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCl₃H</td>
<td></td>
<td>80.₉ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BBr₃H</td>
<td></td>
<td>87.₉ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIH₂</td>
<td></td>
<td>94.₃ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BF₃H</td>
<td></td>
<td>60.₀ ³</td>
<td></td>
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<tr>
<td>BCl₃H</td>
<td></td>
<td>88.₁ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BBr₃H</td>
<td></td>
<td>97.₃ ³</td>
<td></td>
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<tr>
<td>BI₂H</td>
<td></td>
<td>106.₀ ³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(C₆F₅)₃</td>
<td>17.₁(₉) ⁷⁹</td>
<td>1.₉₁(₉) ³</td>
<td>78.₁ ⁴²</td>
<td>7₇.₈ ⁴²</td>
<td>11₃.₃ ⁴²</td>
<td>+ ₅₃</td>
</tr>
<tr>
<td>B(p-HC₆F₄)₃</td>
<td>[0.₅(₁)] ⁸²</td>
<td>0.₉₇ [₁.₀₀] ³</td>
<td>7₇.₄ [₇₇.₈] ³²</td>
<td>11₃.₃ ³²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(o-HC₆F₄)₃</td>
<td>[0.₃(₁)] ⁸²</td>
<td>0.₉₆ [₁.₀₀] ³</td>
<td>7₆.₇ [₇₇.₈] ³²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(2,₆-F₂C₆H₃)₃</td>
<td>0.₆₁ [₁.₀₅] ³²</td>
<td>7₂.₆ [₇₈.₁] ³²</td>
<td>11₉.₅ ³²</td>
<td>+ ₈₆</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(2-Np)₃(₁₂)</td>
<td>1₇.₈(₂) ³⁻⁹</td>
<td>1₈(₁) ³⁻⁹</td>
<td>7₆.₈ [₇₇.₈] ³³</td>
<td>+ ₅₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(2-biPh)₃(₁₃)</td>
<td>1.₅₃(₉) ³⁻⁹</td>
<td>1.₉₁(₅) ³⁻⁹</td>
<td>8₉.₆ [₇₇.₀] ³³</td>
<td>+ ₆₄ ₉₉</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C₁₂F₈B(C₆F₅)₂(₂₁)</td>
<td>1.₃₀(₃) ³¹</td>
<td>1.₀₄(3)</td>
<td>8₆.₈ [₇₇.₃] ³³</td>
<td>+ ₃₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B(3,₅-(CF₃)₂PH)₃(₁₅)</td>
<td>0.₆₇ [₁.₀₈] ³³</td>
<td>7₈.₉ [₇₇.₃] ³³</td>
<td>1₂₉.₅ ³³</td>
<td>+ ₃₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2₉</td>
<td>1₈.₅(₂), [₁₇₈(₁)] ³⁻⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rBu₂P(C₆F₅)₂B(C₆F₅)₂(₁₆)</td>
<td>7₃.₁ [₇₈.₁] ³⁴</td>
<td>1₁₇.₁ ³⁴</td>
<td>+ ₃</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mes₂P(C₆F₅)₂B(C₆F₅)₂(₃)</td>
<td>0.₉₇ [₁.₀₀] ³⁴</td>
<td>7₇ [₇₈.₁] ³⁴</td>
<td>1₁₅.₅ ³⁴</td>
<td>+ ²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
\[
\begin{align*}
\text{R}_3\text{P}^+ & & \text{B(C}_6\text{F}_5)_2 & & \text{B(C}_6\text{F}_5)_4 \\
\text{R}_3\text{P} = \text{PPh}_3 & & 1.16 \text{[1.00]}_{\text{exp}} & & 85.6 \text{[78.1]}_{\text{exp}} \\
\text{R}_3\text{P} = \text{Cy}_3\text{P} & & 1.15 \text{[1.00]}_{\text{exp}} & & 85.2 \text{[78.1]}_{\text{exp}} \\
\text{R}_3\text{P} = \text{tBu}_3\text{P} & & 1.12 \text{[1.00]}_{\text{exp}} & & 80.2 \text{[78.1]}_{\text{exp}} \\
\text{R}_3\text{P} = \text{Mes}_3\text{P} & & 1.16 \text{[1.00]}_{\text{exp}} & & 84.6 \text{[78.1]}_{\text{exp}} \\
\text{B(C}_6\text{F}_5)_2\text{(C}_6\text{Cl}_5)_2 & & 0_{\text{exp}} & & 75.8 \text{[77.0]}_{\text{exp}} \\
\text{B(C}_6\text{F}_5)_3\text{(C}_6\text{Cl}_5)_2 & & 0_{\text{exp}} & & 74.5 \text{[77.0]}_{\text{exp}} \\
\text{B(C}_6\text{Cl}_5)_3 & & 0_{\text{exp}} & & 0.0_{\text{exp}} +_{\text{exp}} \\
\text{BPh}_3 & & 0.05_{\text{exp}} & & 65.9 \text{[76.6]}_{\text{exp}} \\
\text{BMes}_3 & & 71.1_{\text{exp}} \\
\text{BH}_2\text{CN} & & 98.2_{\text{exp}} & & 96.3 \pm 3.5(\text{exp.})_{\text{exp}} \text{k} \text{[72.0]}_{\text{exp}} \\
\text{BEt}_3 & & 58.2_{\text{exp}} & & 58.2_{\text{exp}} \\
\text{BH}_3 & & 69.8_{\text{exp}} & & 73.7_{\text{exp}} \text{[72.0]}_{\text{exp}} \\
\text{B(NH}_2)_3 & & 19.8_{\text{exp}} \\
\text{B(NH}_2)_2\text{H} & & 24.0_{\text{exp}} \\
\text{B(NH}_2)\text{H}_2 & & 37.8_{\text{exp}} \\
\text{B(OH)}_3 & & 31.8_{\text{exp}} \\
\text{B(OH)}_2\text{H} & & 36.6_{\text{exp}} \\
\text{B(OH)}\text{H}_2 & & 48.4_{\text{exp}} \\
\text{B(OBu)}_3 & & 38.0_{\text{exp}} \\
\text{B(OSiMe}_3)_3 & & 46.4_{\text{exp}} \\
\text{B(p-O}_2\text{C}_6\text{H}_4\text{OMe})_3 & & 69.9_{\text{exp}} \\
\text{B(Ph)}_3 & & 0.03 \text{[1.05]}_{\text{exp}} & & 69.4 \text{[76.6]}_{\text{exp}} \\
\text{B(OC}_6\text{F}_3)_3 & & 0.40_{\text{exp}} & & 80.9 [76.6]_{\text{exp}} \\
\text{B(C}_6\text{F}_5)_2\text{(OC}_6\text{F}_3)_2 & & 1.00_{\text{exp}} & & 80.0 [76.6]_{\text{exp}} \\
\text{B(C}_6\text{F}_5)_3\text{(OC}_6\text{F}_3)_2 & & 0.50_{\text{exp}} & & 80.5 [76.6]_{\text{exp}} \\
\text{B(SH)}_3 & & 75.2_{\text{exp}} \\
\text{B(SH)}_2\text{H} & & 72.7_{\text{exp}} \\
\text{B(SH)}_2 & & 69.8_{\text{exp}} \\
\text{B(SMe)}_3 & & 69.0_{\text{exp}} \\
\text{B(SPh)}_3 & & 86.9_{\text{exp}} \\
\text{HB(Si}_2\text{C}_6\text{H}_4) & & 74.3_{\text{exp}} \\
\end{align*}
\]

| a) | \( K_{eq} \) – equilibrium constant of the reaction PFB + CH\text{3CN}-B(C\text{6}F\text{5})_3 \leftrightarrow CH\text{3CN}-\text{PFB} + B(\text{C}_6\text{F}_5)_3 \) at RT.
| b) | Difference in chemical shifts of H-3 proton between free crotonaldehyde and its adduct. In square brackets – the respective value for adduct of B(C\text{6}F\text{5})_3 \) under similar conditions. c) The \( ^{31}\text{P} \) chemical shift of Et\text{3}PO→borane adduct. In square brackets – the respective value for adduct of B(C\text{6}F\text{5})_3 \) under similar conditions. d) Calculated value if not otherwise stated. e) In dichloromethane or dichloromethane-d_2 solution. f) In toluene solution. g) Recovered from reported acidity index. h) Ref. 63, DFT, B3LYP/6-311+G** basis set. i) Ref. 63, coupled cluster theory with single and double excitations. |
It is known, that LUMO levels are linearly associated with the species' reduction potential. The reduction potentials of a series of substituted triarylboranes B(Mes)$_n$(C$_6$F$_5$)$_3$-$n$ \(^\text{93}\) and B(C$_6$Cl$_5$)$_n$(C$_6$F$_5$)$_3$-$n$ \(^\text{94}\) ($n = 0–3$) were studied with cyclic voltammetry. The reduction potential of B(C$_6$F$_5$)$_3$ was $-1.79 \pm 0.10$ V (in CH$_2$Cl$_2$ vs. Cp$_2$Fe$^{0/+}$) \(^\text{95}\) or extrapolated to $-1.17$ V (in THF vs. Cp$_2$Fe$^{0/+}$). Replacement of each C$_6$F$_5$ group with Mes or C$_6$Cl$_5$ led to a shift in potential by approx. $-0.5$ mV or $+0.2$ mV, providing more or less electrophilic species, respectively. Although B(C$_6$Cl$_5$)$_3$ is probably much more acidic according to its electronic properties, it shows no interaction with crotonaldehyde and Et$_3$PO by NMR, while mixed boranes B(C$_6$Cl$_5$)$_n$(C$_6$F$_5$)$_3$-$n$ do interact, though more weakly than B(C$_6$F$_5$)$_3$. This effect is attributed to back strain – high preparation energy originating from repulsion of bulky C$_6$Cl$_5$ rings on pyramidalization of the borane. Nevertheless, B(C$_6$Cl$_5$)$_3$ has recently been reported to split H$_2$ with phosphines as bases. \(^\text{90}\)

Incorporation of a boron atom into a rigid antiaromatic 4-electron ring \(^\text{96}\) of perfluoroborafluorene 21 led to slight increase in Lewis acidity in comparison to B(C$_6$F$_5$)$_3$ based on the CH$_3$CN coordination equilibrium constant. The antiaromatic character of 5-membered ring led to diminished overlapping between the boron-fluorene p-π orbitals, simultaneously causing stretching of the C-C bonds of the antiaromatic ring. \(^\text{91}\) Interestingly, H$_2$ activation by boroles 22 alone was reported recently (Fig. 9). \(^\text{97}\)

![Figure 9](image-url)  
**Figure 9.** Borafluorene 21 and boroles 22 containing an antiaromatic ring. Boroles 22 react with H$_2$ in the absence of a base.

Another approach towards highly acidic organoboranes is based on minimization of preparation energy. Binding of the donor changes the geometry of...
the borane from planar to tetrahedral. Steric repulsion between the bulky fluoroaryls causes the so-called 'back strain', preventing optimal configuration. The increased acidity of 21 was also attributed to minimization of back strain. Following an analogical approach, it was proposed that F atoms be replace with smaller H atoms in the positions ortho to boron, since computations predicted stronger coordination between amines or phosphines and these boranes than in B(C₆F₅)₃. Experimental evaluation of CH₃CN, Et₃PO and crotonaldehyde coordination, however, demonstrated a contrasting trend. The acidities were ranked in the order B(o-HC₆F₄)₃/B(p-HC₆F₄)₃/B(C₆F₅)₃ = 0.3:0.5:1 (K_eq for CH₃CN), revealing the inductive and additive electron-withdrawing properties of the fluorine atoms in the C₆F₅-H₅-n groups of tris(fluoroaryl)boranes. This trend was confirmed by studies of the acidity of tris(2,6-difluorophenyl)borane reported recently. Calculations and the H₂-splitting reactivity observed also predicted lower hydridophilicity of B(p-HC₆F₄)₃ than in B(C₆F₅)₃.

![Figure 10](image-url)  
**Figure 10.** Highly acidic fluoroaryl bis-boranes.

Another efficient way to make highly acidic neutral boranes is by using the chelating effect of two boron centers (Fig. 10). Formation of μ-H-diborohydride in treatment of 25 with KBHEt₃ was reported back in 1994. Bis-boranes 26 and 27 were prepared, but showed no cooperation of boron moieties on binding of CH₃CN and THF. Acting as monodendate acids with these donors, the compounds showed acidities similar to that of B(C₆F₅)₃. Nevertheless, 26 was reported to coordinate various small anions, namely, F⁻, HO⁻, MeO⁻, C₆F₅O⁻, Me₂N⁻ in a bidentate fashion. In addition, bis-boranes 26 and 28 form μ-H-diborohydride on H₂ activation with TMP as a base.

Despite the structural similarity, diborantracene 29 stands apart from 26 and 27. Borane 29 has much higher affinity for acetonitrile than B(C₆F₅)₃ according
to calorimetric and equilibrium constant measurements. There is no simple explanation of the elevated affinity for CH$_3$CN; the latter is neither bound in a bidendate mode, nor is the boron atom a part of an antiaromatic ring, as in 21 or 27. Eventually, the phenomenon was attributed to geometric factors diminishing front as well as back strains and minimizing the overlapping of the boron atom p-orbitals with the $\pi$ orbitals of fluorinated areylene groups. Two neighboring o-C$_6$F$_4$ moieties were believed to have strong cumulative electron-withdrawing effects. No data for the hydride affinity of 29 are available.

When are the uniqueness of fluoroarylboran e as catalysts and cocatalysts of various organic transformations are discussed, they are usually compared with inorganic boranes, i.e. classic LAs. In this regard, it is particularly interesting to compare their acidities and B(C$_6$F$_5$)$_3$ (Table 1). Several methods, e.g. Childs, Gutmann, Lappert, and Park (change in $^1$H NMR chemical shifts of $\alpha$- and $\beta$-hydrogens in Me$_3$N$\rightarrow$BX$_3$ and Et$_3$N$\rightarrow$BX$_3$ adducts) showed that the Lewis acidity descends in the series Bl$_3$ > BBr$_3$ > BF$_3$ > B(C$_6$F$_5$)$_3$, with good correlation observed between the methods. In direct calorimetric studies of acetonitrile binding B(C$_6$F$_5$)$_3$ was bound more strongly than BF$_3$. Surprisingly, calculations predicted that the HA of B(C$_6$F$_5$)$_3$ would exceed that of any of the trihaloboranes, particularly the enthalpy of hydride addition of BCl$_3$, which was 24 kcal/mol lower. In addition, the calculated HAs of various monomeric hydrohaloboranes BX$_n$H$_{3-n}$ were additive: the HA decreased gradually on replacement of halogen atoms with hydrogen atoms. Importantly, the hydridophilicity of the lightest borane, BH$_3$, was similar to that of BF$_3$ (app. 70 kcal/mol), making both potentially able to activate H$_2$. Amino- and hydroxyboranes are quite weak hydride acceptors, due to strong electron-donating properties of the substituents. On the other hand, introduction of EWGs as substituents on oxygen atoms led to dramatic rises in hydride affinity; triphenyl and tris(pentafluorophenyl) borates have affinities similar to those of BF$_3$ and BCl$_3$, respectively. These calculated values are also supported by acidity measurements with the Gutmann method, showing good correlation, since both H$^+$ and Et$_3$PO, are considered as hard donors in terms of the HSAB theory. Interestingly, B(SH)$_n$H$_{3-n}$ have HAs comparable to those of BH$_3$ and BF$_3$, making them another promising candidate for H$_2$ splitting. Of particular future interest is the cyano group, a very strong electron acceptor. BH$_2$CN is extremely
hydridophilic; HA 96–98 kcal/mol according to both calculations\textsuperscript{50} and gas-phase mass-spectrometric measurements.\textsuperscript{92}

Examples of H\textsubscript{2} splitting with boranes containing elementary substituents are rare, but known: bis(aryl)boranes \textsuperscript{30, 31} produce respective borohydrides \textsuperscript{32–35} with amines or phosphines as bases (Fig. 11).\textsuperscript{103, 104} Borodihydride [(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}BH\textsubscript{2}]\textsuperscript{−} is unstable with some onium cations and dismutates into a mixture of [(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}BH]\textsuperscript{−} and primary dimeric borane [(C\textsubscript{6}F\textsubscript{5})BH\textsubscript{2}]\textsubscript{2} \textsuperscript{37}. This result demonstrates that \textsuperscript{37} is unable to activate H\textsubscript{2}, at least with the bases reported (Mes\textsubscript{3}P and (\textsuperscript{t}Bu)\textsubscript{3}Py), apparently, due to reduced Lewis acidity and significant stability of hydroborane dimer (in comparison to diarylborane \textsuperscript{30}, which exists as a mixture of monomer and dimer).

![Chemical diagram]

Figure 11. Bis(fluoroaryl)hydro- and bis(fluoroaryl)chloroboranes can activate H\textsubscript{2}, giving various products, depending on the nature of the fluoroaryl and the base.

(C\textsubscript{6}F\textsubscript{5})\textsubscript{2}BCl (\textsuperscript{38}) can split H\textsubscript{2} as well; however, regardless of the base used no chloroborohydride [(C\textsubscript{6}F\textsubscript{5})\textsubscript{2}BClH]\textsuperscript{−} was detected; a dismutation (redistribution of H\textsubscript{2}/Cl\textsubscript{−}) into dichloroborates \textsuperscript{39–41} and \textsuperscript{30} occurred instead. The further fate of \textsuperscript{30} is dependent on the base: coordination with a base (TMP), H\textsubscript{2} activation to give stable [(C\textsubscript{6}F\textsubscript{5})\textsubscript{2}BH\textsubscript{2}]\textsuperscript{−} ((\textsuperscript{t}Bu)\textsubscript{3}P), or hydrogen activation with C\textsubscript{6}F\textsubscript{5}/H redistribution (Mes\textsubscript{3}P). Although it is difficult to distinguish the impacts of fluoroaryl, hydro, and chloro substituents in the total acidity of the boranes mentioned, the results
reported demonstrate important patterns of H/Cl borane reactivity on H\textsubscript{2} activation with FLPs, namely, dismutative redistribution, hydroborane dimerization, etc.
3. **Mechanistic (kinetic) basis of H\textsubscript{2} splitting by FLPs**

Splitting of H\textsubscript{2} by intermolecular FLPs includes interaction of three molecules. Since termolecular reactions are almost improbable, stepwise mechanisms were proposed to explain FLP-H\textsubscript{2} reactivity, comprising association of two reactants prior to interaction with the third.

Using a model reaction tBu\textsubscript{3}P (5) + B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} (1) + H\textsubscript{2}, calculations predicted the preassociation of tBu\textsubscript{3}P + B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} into a so-called 'encounter complex' (EC) 42 as the most probable way (Fig. 12). A pronounced association energy $\Delta E = -11.5$--$-13.1$ kcal/mol originates from noncovalent interactions between the tBu and C\textsubscript{6}F\textsubscript{5} substituents.\textsuperscript{105, 106} The partial concentration of 42 in toluene was estimated to be 0.5%, based on molecular dynamics simulations.\textsuperscript{107} In case of amines the formation of TMP-H···F-C\textsubscript{6}F\textsubscript{4}-B(C\textsubscript{6}F\textsubscript{5})\textsubscript{2} complex 43 was suggested based on colorizing of the FLP mixture.\textsuperscript{46} Calculations for the structurally similar system 2,6-dimethyl-2,6-diphenylpiperidine + B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} + H\textsubscript{2} showed that the formation of the analogical complex 44 was exothermic ($\Delta H = -7.98$ kcal/mol), but endergonic ($\Delta G = 3.63$ kcal/mol).\textsuperscript{51} The encounter complex produced can be considered as a single molecule analogous to ansa-bridged FLPs, with preorganized frontier orbitals slightly different from the original in individual molecules.\textsuperscript{108}

![Figure 12](image)

**Figure 12.** Encounter complex formation between B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} and tBu\textsubscript{3}P (42) or 2,2,6,6-tetra-substituted piperidines (43, 44).
The next step is the actual splitting of $\text{H}_2$, for which various mechanisms were proposed. Initially, based on the transition state (TS) theory, an almost linear $\text{P} \cdots \text{H-H} \cdots \text{B}$ early TS for the $42 + \text{H}_2$ system was calculated by Pápai et al.\textsuperscript{105, 108} This TS was later criticized to be an artifact of the computational method.\textsuperscript{109} However, in a recent article based on calculations of six various FLPs carried out at a higher level of theory, L-shaped TSs were found with the following typical geometry: $\text{H}_2$ stretched up to 0.77–0.85 Å, donor-$\text{H-H}$ was almost linear, while acceptor-$\text{H-H}$ was L-shaped (Fig. 13b). Notably, this geometry is optimal for overlapping between LA’s LUMO and $\sigma(\text{H}_2)$ (HOMO) on one side and LB’s HOMO and $\sigma^*(\text{H}_2)$ (LUMO) on another.\textsuperscript{110} Treatment of the potential energy surface (PES) of the $42 + \text{H}_2$ system by Grimme et al.\textsuperscript{109} revealed that at sufficiently short, but achievable P-B distances, the $\text{H}_2$ splitting can become completely barrierless (Fig. 13, a) and, hence, the kinetics can become controlled by $\text{H}_2$ migration into the cavity of 42. In addition, they proposed that the $\text{H}_2$ molecule can be split solely by the electrostatic field generated between the P and B atoms within the cavity of 42.\textsuperscript{109} However, it was shown recently that the required values of the electrostatic field strength and its anisotropy do not allow such a process.\textsuperscript{110} Nevertheless, Privalov et al. recently studied the molecular dynamics of 42, and concluded that the P-B distance within it can achieve the values required for barrierless splitting, due to thermal oscillations.\textsuperscript{111}

Figure 13. tBu$_3$P + B(C$_6$F$_5$)$_3$ + $\text{H}_2$ system: a) PES cuts at constant P-B distance (Reproduced with permission of John Wiley and Sons from S. Grimme, H. Kruse, L. Goerigk, G. Erker, Angewandte Chemie Int. Ed. 2010, 49, 1402–1405. Copyright 2010 John Wiley and Sons); b) detailed TS (Adapted with permission from T. A. Rokob, I.
Some alternative mechanisms proposed for FLP splitting are worth mentioning as well. Ion-radical intermediates were suggested to form as a result of tBu₃P oxidation with B(C₆F₅)₃, although the concentrations of the active particles estimated, based on redox properties of (tBu)₃P and B(C₆F₅)₃ were too low for reasonable reaction rates (Fig. 14).¹¹²

\[
\text{tBu₃P} + \text{B(C₆F₅)₃} \rightarrow [\text{tBu₃P}]^+ + [\text{B(C₆F₅)₃}]^- + \text{H}_{2} \rightarrow [\text{tBu₃PH}]^+[\text{HB(C₆F₅)₃}]^{-}
\]

**Figure 14.** H₂ splitting via radical-ion mechanism.

Another alternative mechanism includes binding of H₂ to borane or a base (phosphine) prior to interaction with a counterpart. For borole 22a (Fig. 9) reacting with H₂ in the absence of a base, R₃B←H₂ σ-complex formation was suggested as a first elementary step.⁹⁷ The hydroboranes (Mes⁺)₂BD (31-d),¹¹³ BH₃-THF and DB(C₆F₅)₂ (30-d) were reported to exchange D/H upon heating with H₂ in the absence of a base under mild conditions (in the latter case as a step of HB(C₆F₅)₂-catalyzed H/D exchange between deuterated silanes and H₂) (Fig. 15). Computational treatment of the H/H-exchange between 31 or 30 and H₂ revealed 4-centered TSs 46 and 48. However, only for 31 were authors able to locate R₃B←H₂ σ-adduct 45. The latter is very high in energy and resembles the TS of its formation, energetically and geometrically. In addition, the fluorine atom of the CF₃ group interacted with H₂, evidently stabilizing 45.¹¹³ Thus, it is quite likely that formation of the illusive 45, if any, is an exclusive feature of 31, rather than a common occurrence for PFB. Additional calculations suggested that in case of relatively sterically hindered amines (e.g. Et₃N, unlike DABCO), formation of FLP-H₂ adduct 33 (Fig. 11) formation proceeds through R₃B←H₂ σ-adduct 45 as well.
Figure 15. D/H exchange of (MesF)_2BD and DB(C_6F_5)_2 upon heating with H_2.

While the thermodynamic parameters of H_2 activation can be quite reliably predicted computationally, the reaction mechanisms proposed are diverse and many of them seem to be viable. In this regard, one must note surprisingly few articles reporting direct kinetic studies, which can be compared with theoretical models to evaluate them. The main complication arising during these studies is rapid reaction rates and slow H_2 diffusion which may become a rate-limiting step under certain conditions. The system fBu_3P (5) + B(C_6F_5)_3 (1), which was reported to activate H_2 among the first FLPS, is the most popular model for computational analysis. This may be due to the highly symmetric C_3 geometry of their encounter complex 42 (Fig. 12), minimizing the amount of the existing configurations and simplifying calculations. In this respect, precise kinetic data for H_2 splitting with 5 + 1 would be extraordinarily important. A detailed experimental study of this system in an attempt to isolate the encounter complex 42 or detect it spectroscopically led to a finding of in situ formation of a well known bridged phosphinoborane 16. Hydrogen adduct 50, rapidly forming from 16, transfers H_2 to 5 and 1 and, apparently, can catalyze formation of adduct 6 (Fig. 16). This finding makes any results of kinetic measurements of H_2 splitting with 5 and 1 particularly doubtful.
Figure 16. Phosphinoborane 16 produced in situ from 5 and 1 can catalyze formation of 6.
4. Catalytic hydrogenation as the main application of FLPs

The discovery of H$_2$ activation with FLPs quickly addressed the question of the transfer of the thus activated H$_2$ to unsaturated substrates.$^{47}$ The resulting catalytic hydrogenation of various compounds is by far the most important achievement in the FLP area and was comprehensively reviewed recently.$^{25, 26, 27}$

Since H$_2$ is split heterolytically by FLPs, they are naturally suitable mostly as catalysts for the hydrogenation of polar substrates. Initially, the hydrogenation of electron-rich imines and other structurally similar compounds was the main subject of the studies; the hydrogenation of C=N (imines, azines (heterocycles)) and C=C (enamines, silyl ethers, indoles) bonds was reported.$^{25, 26}$ More exotic ring-opening hydrogenolysis of aziridines and hydrogenation of N-monosubstituted anilines into the respective cyclohexylamines$^{115}$ are interesting extensions of the approach (Fig. 17).

![Catalytic hydrogenation diagram](image)

**Figure 17.** Hydrogenation of various electron-rich substrate types catalyzed by FLPs.

FLP-catalyzed hydrogenations of the electron-rich substrates can be divided into three types, depending on whether or not an additional base is used and if used, whether it is linked with the acidic component. B(C$_6$F$_5$)$_3$ (1) alone serves as an efficient catalyst for hydrogenation of nitrogen-containing compounds such as imines,$^{116, 117}$ quinolines,$^{118}$ and indoles,$^{25}$ while the substrate plays the role of a Lewis base during H$_2$ activation. B(C$_6$F$_5$)$_3$ as a catalyst has the advantage of low cost and commercial availability. Bis(borane) 28 was also used as the sole catalyst for hydrogenation of imines, although its catalytic properties were no
better than those of B(C₆F₅)₃.¹⁰² Borane 56 derived from pinene was evaluated as an asymmetric catalyst.¹¹⁷ The catalytic cycle is simple (Fig. 18): the H₂ is split by FLP, consisting of imine 51 and borane 54, followed by a hydride transfer from a boron atom to the iminium carbon atom. At later stages of the process, the amine 57 produced can serve as a Lewis base as well, and a proton transfer between its FLP-H₂ adduct and imine 51 was required to propagate the catalytic cycle. With significantly sterically crowded substrates, the hydride transfer becomes kinetically sluggish and the reaction can stop at the step of the iminium borohydride formation (58).¹¹⁶ The hydride addition step is reversible; in the absence of H₂ 1 can abstract hydride from various amines, producing their respective iminium borohydrides 54.¹⁸ Eventually, both the substrate and the final amine can bind to 54, hampering its reactivity or even completely deactivating it (formation of 52 or 53). This was the main motivation for developing the ‘size-exclusion’ FLP catalysts (see below).

![Figure 18](image-url) Postulated mechanism of hydrogenation of imines catalyzed by solely Lewis acid.

An intermediate case between B(C₆F₅)₃ and bridged FLP systems is presented by intermolecular acid/base pair catalysts (Fig. 19). In comparison to B(C₆F₅)₃-catalyzed hydrogenation, an auxiliary Lewis base 60 can provide optimal conditions for H₂ splitting, regardless of the nature of the substrate 51. Although combinations of B(C₆F₅)₃ with phosphine 63 were successfully used in catalytic hydrogenation of silyl enols,¹¹⁹ the most interesting example of catalysis of this...
type was presented by B(C₆F₅)₂(Mes)/DABCO (61/62). Replacement of the C₆F₅ group with the bulkier mesityl group provides a much more sterically demanding borane 61 than 1. This suppresses formation of adducts 52 and 53 from 61 and leads to extension of the substrate scope to sterically accessible imines and higher functional group tolerance. Sterically accessible DABCO (62) was the optimal base for H₂ splitting with 61, while the reaction with TMP (7) as a base was two orders of magnitude slower. This result is not surprising, since both B(C₆F₅)₂(Mes) and TMP are highly sterically hindered and cannot approximate the B-N distance optimal for H₂ splitting, while compact DABCO or quinuclidine (64) can. This ‘size-exclusion’ concept demonstrates good practice of the rational catalyst design.121

**Figure 19.** a) Postulated mechanism of hydrogenation of imines catalyzed by intermolecular FLP. b) Schematic representation of the ‘size-exclusion’ concept. c) Other bases used in intermolecular FLP-catalyzed hydrogenations.

Bridged systems have the potential advantage of faster H₂ splitting (Fig. 20). Indeed, with comparable activation barriers the concentration of encounter complex 42 of tBu₃P and B(C₆F₅)₃ in toluene was estimated as only 0.5 mol. %, while the bridged system itself can be considered as a 100% encounter complex. On the other hand, the additional step of proton transfer from hydrogenated catalyst 66 to substrate 51 is required. It should be noted that in contrast to
intermolecular FLPs as catalysts (Fig. 19), in which proton transfer from 59 to 51 is assumed to be almost energetically neutral (if the basicities of an auxiliary base 60 and imine 51 are similar), for a bridged system this step is likely to be endergonic, since the H₂ adducts of bridged systems 65 are additionally stabilized by electrostatic interaction and an entropic factor. Charge-separated ionic pair 67 is uphill in energy. Among bridged catalysts, the most known are phosphinoborane 68, developed in the Erker group, and ansa-aminoborane CAT developed in the Repo/Rieger groups. 48

Among bridged catalysts, the most known are phosphinoborane 68, developed in the Erker group, and ansa-aminoborane CAT developed in the Repo/Rieger groups. 48

Asymmetric hydrogenation of imines was performed with FLP catalysts as well (Table 2). According to the postulated mechanisms (Figs. 18–20), it is the step of hydride transfer to the prochiral iminium salt that induces asymmetric excess. Boranes are flat molecules, due to their sp²-hybridized electronic structure. It is possible to design boranes 69 with non-equivalent substituents that could generate enantioenriched chiral borohydride 71 on H₂ splitting with a chiral base, e.g. phosphine 70 (Fig. 21). In practice, however, H₂ splitting requires at least two C₆F₅ groups connected to a boron center to provide sufficient Lewis acidity. Chiral borane 72 was prepared, but no catalytic hydrogenation or H₂ activation was reported with it. 123

Figure 20. Postulated mechanisms for hydrogenation of imines catalyzed by a bridged FLP.
Figure 21. Hypothetical generation of chiral borohydride 71 induced by a chiral base 70. Chiral borane 72.

As a result, with the few exceptions developed within this thesis, reported examples of asymmetric FLP catalysts were prepared by hydroboration of chiral alkenes with HB(C₆F₅)₂. In the works by Klankermeyer¹²⁴,¹²⁵ and Du¹²⁶ boranes derived from camphor (56, 73, 74) or binaphthodienes (75) provided typical ee values of 70–85% when used as catalysts of N-aryl-arylethanimine hydrogenation under 20–25 bar H₂, 25-65 °C and 5 mol% catalyst loading (Table 2). Interestingly, bridged phosphonium borohydride 74 not only could be recovered from the reaction mixture, but could also be used in successive hydrogenations up to five times without loss of asymmetric induction.¹²⁵

Table 2. Selected results of asymmetric hydrogenation of imines 51 catalyzed by chiral boranes 56, and 73–75.

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Catalyst</th>
<th>ee, [yield] %</th>
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</thead>
<tbody>
<tr>
<td>Ph</td>
<td>Me</td>
<td>Ph</td>
<td>56</td>
<td>13 [99]¹¹⁷</td>
</tr>
<tr>
<td>73</td>
<td>79</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>72</td>
<td>70</td>
<td></td>
<td></td>
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<tr>
<td>75</td>
<td>78</td>
<td>98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>Me</td>
<td>4-MeOPh</td>
<td>73</td>
<td>81 [99]</td>
</tr>
<tr>
<td>74</td>
<td>73</td>
<td>99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-MeOPh</td>
<td>Me</td>
<td>Ph</td>
<td>74</td>
<td>70 [99]</td>
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<tr>
<td>75</td>
<td>84</td>
<td>99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-Np</td>
<td>Me</td>
<td>Ph</td>
<td>73</td>
<td>80 [93]</td>
</tr>
<tr>
<td>74</td>
<td>76</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>74</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-BnOPh</td>
<td>Me</td>
<td>Ph</td>
<td>75</td>
<td>89 [91]</td>
</tr>
</tbody>
</table>

³
It was also shown that chiral imines can be diastereoselectively hydrogenated, using 1 as a catalyst.\textsuperscript{127} Notably, imines 76 and 77, derived from chiral ketones (camphor and menthone), were reduced almost diastereospecifically, unlike 78, which was derived from chiral amines (Fig. 22). This could have resulted from the partial racemization of amines produced from 78 as the results of \( \alpha \)-hydrogen abstraction by 1 upon prolonged heating.\textsuperscript{128}

![Figure 22](image)

\[ R^1, R^2 = \text{Bn, Ph: de} = 95-99\% \]

**Figure 22.** Imines hydrogenated diastereoselectively with 1 as a catalyst.

The hydrogenation of electron-rich compounds discussed above is the most common and studied application of FLPs. At the same time, polar unsaturated bonds of electron-deficient compounds were catalytically hydrogenated as well (Fig. 23). Regioselective hydrogenation of the conjugated C=C bond of (\(+\))-carvone 79 was the first reported instance of this type of reaction.\textsuperscript{120} The electron-poor allenes 81 and alkenes 86 were hydrogenated at 60 bar \( \text{H}_2 \) with a combination of \( \text{B}([\text{C}_6\text{F}_5])_3 \) and DABCO (10–15 mol\%).\textsuperscript{129} The conjugated enones 83 and ynones 88 were hydrogenated at 10–40 bar \( \text{H}_2 \) and elevated temperatures, using the catalysts 84 derived from addition of \( \text{B}([\text{C}_6\text{F}_5])_3 \) to alkynes.\textsuperscript{130, 131} The nitroolefins 91 and acrylates 86 were hydrogenated under mild conditions, using a combination of novel borane \( \text{B}(2,6-\text{F}_2\text{C}_6\text{H}_3)_3 \) and pyridine bases.\textsuperscript{88}
Figure 23. Reported examples of FLP-catalyzed hydrogenation of electron-deficient substrates.

Saturated ester 87a-d (Fig. 24) is produced during stoichiometric reduction of substrate 86a with isotope-labeled borohydride 93, presumably as the result of borohydride attack on the ammonium-activated substrate (via 94). This mechanism is supported by formation of adduct 95 on exposure of the stoichiometric mixture of nitroalkene 91a, TMP, and THF→B(2,6-F₂C₆H₃)₃ to H₂. Sluggish hydrogenation of the various substrates catalyzed by the B(C₆F₅)₃/DABCO pair in comparison to the less Lewis acidic boranes MesB(C₆F₅)₂ and B(2,6-F₂C₆H₃)₃ can be explained by excessive stability of the DABCO→B(C₆F₅)₃ adduct barely dissociating into FLP.
Figure 24. Formation of deuterated product 87a-d and intermediate 95 as evidence of borohydride attack on β-carbon to as elementary step in the hydrogenation of electron-deficient multiple C-C bonds.

Due to the heterolytic nature of FLP-H₂ adducts, the latter are naturally suitable mostly for hydrogenation of polar unsaturated bonds. Hence, one of the most challenging problems until recently has been the hydrogenation of nonpolar multiple C-C bonds, such as in conventional alkenes and alkynes. Indeed, regardless of whether a proton or a hydride addition to the substrate should be the first elementary step of this reaction, these processes are very unlikely with nonpolarized C-C bonds. Despite the seeming infeasibility of this process, low basic phosphines 98–100 or amines (101) in combination with B(C₆F₅)₃ efficiently catalyze hydrogenation of selected alkenes 96, easily producing carbocations (Fig. 25).⁵⁷ Moreover, polycyclic aromatic hydrocarbons 103 were partially hydrogenated with the same approach as well.¹³² A recent modification of this approach exploits Et₂O as a base instead of phosphines and amines.¹³³
Figure 25. FLP-catalyzed hydrogenation of unactivated unsaturated C-C bonds: in alkenes 96 and anthracenes 103.
5. **Ansä-aminoboranes among FLPs**

Frustrated B/N systems, including ansä-aminoboranes, were comprehensively reviewed by us recently.\textsuperscript{IV} Nevertheless, some aspects are worth mentioning. The Repo/Rieger groups were the first to publish that simple amines such as 2,2,6,6-tetramethylpiperidine (TMP) together with B(C\(_6\)F\(_5\))\(_3\) can split H\(_2\) heterolytically.\textsuperscript{46} Based on the initial finding, the ansä-system CAT was proposed, in which TMP and a boryl groups were linked together. This new compound was able to activate H\(_2\) reversibly, producing the respective ammonium borohydride CATH\(_2\).\textsuperscript{48} The barrier for H\(_2\) splitting was calculated to be 14.4 kcal/mol,\textsuperscript{48} and the geometry of the transition state was recently reported.\textsuperscript{110}

![Diagram of CAT and CATH\(_2\)](image)

**Figure 26.** Reversible H\(_2\) uptake by CAT and neutron diffraction structure of CATH\(_2\). d\((H1-H8) = 1.67\) Å.

**CAT** has several distinct features. From the thermodynamic standpoint, the ansä-B/N junction has a pronounced stabilization effect on the H\(_2\) adduct, arising from an entropic factor (in comparison to the bimolecular FLPS) and electrostatic interaction of NH\(^+\) and BH\(^-\) hydrogen atoms. The latter approximate each other at a distance of 1.67 Å, producing the so-called `dihydrogen bond` and contracting 7-membered CCCBHNN cycle (Fig. 26).\textsuperscript{134} The \(\Delta G\) value estimated for the process of H\(_2\) activation by CAT ranges from -12\textsuperscript{50} to -7.3\textsuperscript{48} kcal/mol. Even though these values are compatible with the reversibility observed, they seem to be overestimated.
The energy arising from association of the separate ions \([\text{H-LA}]^+\) and \([\text{H-LB}]^-\) into ionic an pair \([\text{H-LA}]^+[\text{H-LB}]^-\) is the third stabilizing component appearing on partition of the energy of \(\text{H}_2\) splitting by any FLP (along with the energies of the proton and hydride attachments to an LB and LA, respectively). The value of the association energy is dependent on the distance between the centers of the LA and LB distance in the final \(\text{H}_2\) adduct.\(^{50}\) For linked systems the association energy calculated is proportional to \(1/d(\text{LA-LB})\), reflecting the electrostatic character of this free energy's component (Fig. 27). Accordingly, for intermolecular FLPs the values lie within the range of -14 to -25 kcal/mol, while for CATH\(_2\) this value is -34.2 kcal/mol \((d_{\text{BN}} = 3.25 \text{ Å})\). Notably, phenylene-bridged Piers' aminoborane (2, Fig. 4) has a shorter B-N distance \((2.87 \text{ Å})\), resulting in even higher (-44.5 kcal/mol) association energy, while for phosphine-borane \(t\text{Bu}_2\text{HP-BH(C}_6\text{F}_5)_2\) \((\text{the H}_2 \text{ adduct of } t\text{Bu}_2\text{P-B(C}_6\text{F}_5)_2)\), an extremely high value of -65.6 kcal/mol was calculated.

\[
y = -116.64x - 4.5434
\]

Figure 27. \(\Delta G\) of association of separate ions \([\text{HLB}]^+\) and \([\text{HLA}]^-\) into ionic pairs \([\text{HLB}]^+[\text{HLA}]^-\) in toluene solution.\(^{50}\)

The CATH/CATH\(_2\) system is a metal-free catalyst for hydrogenation of various imines under typical conditions: 4 mol\% CATH\(_2\), 110 °C, 12 h, 1 bar \(\text{H}_2\). Although the splitting of \(\text{H}_2\) with CAT is rapid, the catalytic properties of CATH\(_2\) in hydrogenation of imines are relatively poor. Moreover, substrates 51b and 51h
were hydrogenated under standard conditions in 37% and 4% conversions, respectively, due to inefficient H₂ transfer to imine (Fig. 29). Proton transfer from CATH₂ to imine results in formation of charge-separated particles 67 (Fig. 20) from neutral reactants. The intrinsic stability of ansa-ammonium borate makes this process unfavorable and can be demonstrated by the high endergonicity of the relevant reactions (Fig. 28). The reaction of proton transfer from CATH₂ to an imine is strongly unfavored and hindered by a large barrier (up to 40 kcal/mol), suggesting that a typical imine being reduced has a basicity similar to that of TMP or lower. It should be noted that exact ΔG values can be extracted only for the formation of separate ions, rather than an associated ion pair; however, the calculated association energy of a broad range of intermolecular onium borohydrides does not typically exceed -25 kcal/mol.⁵⁰

\[
\text{CATH}_2 + \text{TMP} \xrightarrow{\Delta G = +68.0 \text{ kcal/mol}} [\text{CATH}]^- + [\text{TMPH}]^+ \\
\text{CATH}_2 + \text{B(C}_6\text{F}_5)_3 \xrightarrow{\Delta G = +55.8 \text{ kcal/mol}} [\text{CATH}]^+ + [\text{HB(C}_6\text{F}_5)_3]^-
\]

**Figure 28.** Estimated Gibbs free energies for proton transfer to TMP and hydride transfer to B(C₆F₅)₃ from CATH₂ in toluene.

While substrates 5₁b and especially 5₁h were slowly reduced, due to the basicity issue, sterically accessible 5₁e–5₁g (Fig. 29) were not reduced with CATH₂, presumably due to inhibition of the catalyst via formation of adducts 5₂a or 5₃a (Fig. 20).

**Figure 29.** Substrates showing problems on hydrogenation with CATH₂: sterically accessible (5₁e–5₁g) and low basic 5₁b, 5₁h.
Results and discussion

Hydrogenation of unsaturated bonds is one of the principal reactions in organic chemistry. A recent approach to the activation of H₂, using powerful but sterically ‘frustrated Lewis acid-Lewis base pairs (FLPs) has opened a new way to catalytic hydrogenation.²

The present work was focused mostly on the development of highly efficient FLP catalysts for hydrogenation of various substrates, based on the ansa-aminoborane backbone initially developed in the Repo and Rieger groups.⁴⁸ The association of the Lewis acidic and basic parts within a single molecule allows separating H₂ splitting from other stages of the catalytic cycle, with further optimization of this process. In addition, most of the H₂ adducts produced are isolable compounds, allowing easy separation of a pure catalyst, separate studies of the H₂ activation processes, etc.

6. Experimental details

The ansa-aminoboranes were prepared by reaction between the respective aryllithium and the chloroboryl compounds. Ansa-aminoboranes are moisture-sensitive compounds and were handled in an inert atmosphere. The structures and purity of the ansa-aminoboranes were confirmed by various methods: NMR and mass-spectrometry, elemental analysis, single-crystal X-ray diffraction, etc. High purity (5.5 or 6.0 grade) H₂ was used in the H₂ activation and hydrogenation reactions. Further experimental details of the starting material purchase and purifications, syntheses and analyses of the target compounds, their reactivities, and catalytic properties can be found in the experimental sections of the publications attached and in the supplementary materials in the publications on the Internet.
7. **New ansa-aminoboranes as efficient catalysts for the hydrogenation of nitrogen-containing compounds**

The initial goal of this work was to implement asymmetric FLP-catalyzed hydrogenations of imines with the existing CAT ansa system. Prior to moving in this direction, we needed to resolve several disadvantages, from which the existing catalyst suffered. First, we needed to make the catalyst work at room temperature, since elevated temperatures are not compatible with high asymmetric induction. Second, we had to resolve substrate restrictions to make the catalyst universal with respect to the substrate scope (see literature review).

Both goals were achieved with a family of new ansa-catalysts, which were designed rationally, based on evaluation of the previously proposed catalytic cycle. Slow hydrogenation of imines by CAT/CATH\(_2\) catalyst was attributed to excessive stability of the CATH\(_2\) adduct. To shift the protonation equilibrium towards the products, the basicity of the amine part in the series of newly prepared ansa-aminoboranes was reduced (Fig. 30).
Figure 30. *ansa*-Ammonium borate catalyst with reduced basicity of the amine part (estimated with ACD Labs package (Advanced Chemistry Development Inc., Toronto, Ontario, Canada) for the respective *N*-benzylamines in water) and the catalytic cycle.\(^1\)

Gradual change in the amine part basicity enhanced the catalytic activity; full conversions of most of the substrates were achieved with the catalyst loadings reduced to 1 mol% (Table 3). The difference in activities was most pronounced with imines 51b and 51h. The turnover frequency (TOF) value for 51b increases in the order CATH\(_2\) – 0.77 h\(^{-1}\) (110 °C), MCATH\(_2\) – 1.75 h\(^{-1}\) (110 °C), QCATH\(_2\) ≥ 33.3 h\(^{-1}\) (80 °C). QCATH\(_2\) was chosen as a catalyst of choice due to commercial availability of the starting 2,2,4,7-tetramethyltetrahydroquinoline. With this catalyst in hand, further optimizations were conducted. Ethereal solvents (THF, Et\(_2\)O, MTBE) were not only compatible with the catalyst (QCAT) for the first time in FLP.
chemistry, but also had a dramatic acceleration effect. During optimizations of the hydrogenation of 51b catalyzed by QCATH\textsubscript{2}, a TOF of \(\sim 100 \text{ h}^{-1}\) was detected in Et\(_2\)O at 50 °C. To the best of our knowledge, this value is still the highest among FLP catalysts developed for imine hydrogenation. Although the substrate 51h achieved only partial conversion on hydrogenation with QCATH\textsubscript{2}, the overstoichiometric reduction reflects the large progress achieved in \textit{ansa}-catalyst development.

**Table 3.** Catalytic hydrogenation of imines.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Catalyst, mol%</th>
<th>Time [h]</th>
<th>Conv. [%]</th>
<th>Substrate</th>
<th>Catalyst, mol%</th>
<th>Time [h]</th>
<th>Conv. [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Ph} \equiv \text{N} \equiv \text{Ph}) 51i</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>20</td>
<td>100\textsuperscript{c}</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>MCATH\textsubscript{2}</td>
<td>1</td>
<td>12</td>
<td>100</td>
<td>MCATH\textsubscript{2}</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>QCATH\textsubscript{2}</td>
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<td>15</td>
<td>QCATH\textsubscript{2}</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>iPrICATH\textsubscript{2}</td>
<td>1</td>
<td>12</td>
<td>100</td>
<td>iPrICATH\textsubscript{2}</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>(\text{Ph} \equiv \text{N} \equiv \text{Ph}) 51j</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>6</td>
<td>100\textsuperscript{c}</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>MCATH\textsubscript{2}</td>
<td>1</td>
<td>12</td>
<td>100</td>
<td>MCATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>QCATH\textsubscript{2}</td>
<td>1</td>
<td>5</td>
<td>100</td>
<td>QCATH\textsubscript{2}</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>iPrICATH\textsubscript{2}</td>
<td>2</td>
<td>12</td>
<td>100</td>
<td>iPrICATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>(\text{Ph} \equiv \text{N}) 51k</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
<td>100\textsuperscript{c}</td>
<td>CATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>MCATH\textsubscript{2}</td>
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<td>12</td>
<td>100</td>
<td>MCATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
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<tr>
<td></td>
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<td>2</td>
<td>12</td>
<td>100</td>
<td>QCATH\textsubscript{2}</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>iPrICATH\textsubscript{2}</td>
<td>2</td>
<td>12</td>
<td>100</td>
<td>iPrICATH\textsubscript{2}</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>QCATH\textsubscript{2}</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>iPrICATH\textsubscript{2}</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

\textsuperscript{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). \textsuperscript{b) Determined by \(^1\text{H}\) NMR spectroscopy. \textsuperscript{c) Ref. \textsuperscript{48}. \textsuperscript{d) 80 °C. \textsuperscript{e) Et\(_2\)O (3 ml) at room temperature. \textsuperscript{f) 25 °C, 4 atm H\(_2\), ref. \textsuperscript{11d}}}

Another important feature of the new catalysts is the much easier release of H\(_2\) in comparison to CATH\textsubscript{2} (110 °C, 24 h). QCATH\textsubscript{2} already begins to dehydrogenate at room temperature on standing in solution and completes this process in less than 5 min at 110 °C, demonstrating energetically neutral H\(_2\) uptake (Fig. 31).
Figure 31. Reduced basicity of the amine part in *ansa*-aminoboranes makes H$_2$ uptake energetically neutral.

The reduced basicity of the amine part decreases the stability of adducts not only of H$_2$, but of other protic molecules as well. This opens the way to highly efficient methods of catalyst recovery (Fig. 32). After completion of the hydrogenation, the amine produced is extracted with aqueous HCl. The catalyst in the form of H$_2$O adduct remains in the organic phase, and is converted into hydrogen bromide (HBr) adducts on treatment with TMSBr. The latter product is fairly unstable, similar to the H$_2$ adduct, and rapidly releases HBr on heating in a vacuum. Resulting aminoborane, QCAT, was converted into QCATH$_2$ in a conventional way for an overall yield of 80%.

Figure 32. Recovery of the QCATH$_2$ from the reaction mixture via HBr adduct.

Imine 51f was reduced only stoichiometrically with CATH$_2$. After formation of the aminoborane, it is believed to be blocked by coordination of either the starting imine or the target amine to the boron center of CAT. To cope with this problem a highly sterically hindered analogue of QCATH$_2$, iPrQCATH$_2$, was prepared. Imine 51f was successfully hydrogenated with iPrQCATH$_2$, thus substantially extending the scope of the reaction to sterically accessible substrates (Table 4).
Table 4. Hydrogenation of imine 51f catalyzed by *ansa*-ammonium borates vs iPrQCATH$_2$.\(^{a)}\)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>mol%</th>
<th>Time [h]</th>
<th>Conv. [%](^{b)}</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CATH$_2$</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>MCATH$^2$</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>QCATH$_2$</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>iPrICAT</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>iPrQCA</td>
<td>4</td>
<td>12</td>
<td>82</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a)}\) *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.

Eventually, after the problems of activity and substrate scope were successfully resolved, asymmetric hydrogenations were attempted with *ansa*-catalysts (Table 5). For this purpose, a chiral version of QCATH$_2$, Q*CATH$_2$, was prepared along with chiral *ansa*-catalyst CarCAT derived from the terpene carvone. The highest ee values of 35–37% were reached with Q*CATH$_2$ catalyst under mild conditions (room temperature). This result is quite surprising, since the chiral center of Q*CATH$_2$ is located on the periphery of the molecule relative to the B center, which induces asymmetry in the amine produced. In addition, X-ray diffraction analysis showed that Q*CATH$_2$ exists as a mixture of two diastereomers, thus even in H$_2$ splitting, which is believed to be a synchronous process, the chiral center has very weak asymmetric induction. The ee values achieved demonstrate that even under such unfavorable conditions, the chiral amine in the *ansa*-aminoborane moiety has high potential for asymmetric induction. The H$_2$ transfer to substrate is likely to proceed as a close-contact ionic pair, causing higher differences between diastereomeric transition states.
Table 5. Asymmetric catalytic hydrogenation.\textsuperscript{a)} Structures of $S$-CarCAT and diastereomers of $Q^*\text{CATH}_2$.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time, h</th>
<th>Temperature, °C</th>
<th>Conversion, [%]</th>
<th>ee, [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>Toluene</td>
<td>1</td>
<td>80</td>
<td>100</td>
<td>4</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>Hexane</td>
<td>1</td>
<td>80</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>1</td>
<td>60</td>
<td>100</td>
<td>12</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>1</td>
<td>20</td>
<td>100</td>
<td>19</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>MTBE</td>
<td>1</td>
<td>20</td>
<td>100</td>
<td>26</td>
</tr>
<tr>
<td><img src="51j.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>1</td>
<td>60</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td><img src="51j.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>31</td>
</tr>
<tr>
<td><img src="51j.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>MTBE</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>35</td>
</tr>
<tr>
<td><img src="51l.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>1</td>
<td>60</td>
<td>100</td>
<td>18</td>
</tr>
<tr>
<td><img src="51l.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>$Et_2O$</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>31</td>
</tr>
<tr>
<td><img src="51l.png" alt="image" /></td>
<td>$Q^*\text{CATH}_2$</td>
<td>MTBE</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>37</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>CarCAT</td>
<td>Toluene</td>
<td>20</td>
<td>80</td>
<td>70</td>
<td>8</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>CarCAT</td>
<td>Hexane</td>
<td>20</td>
<td>80</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td><img src="51b.png" alt="image" /></td>
<td>CarCAT</td>
<td>$Et_2O$</td>
<td>20</td>
<td>60</td>
<td>35</td>
<td>17</td>
</tr>
</tbody>
</table>

\textsuperscript{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. \textsuperscript{b)} Determined by $^1$H NMR spectroscopy. \textsuperscript{c)} Determined by chiral-HPLC.
8. **2-Boryl-\(N, N\)-dialkylanilines – *ansa*-aminoboranes with a reduced bridge**

Low asymmetric induction during hydrogenation with \(Q^\ast\text{CAT}\) was attributed to excessive flexibility of the aminoborane molecule (Fig. 33). Two identical \(\text{C}_6\text{F}_5\) groups possessed by the boron center together with a flexible chiral amine moiety create too weak a chiral surrounding.

![Diagram of aminoborane molecules](image)

**Figure 33.** New (\textit{SCAT}) and previously reported (2) 2-boryl-\(N, N\)-dialkylanilines.

We envisioned that more rigid aminoboranes can be prepared by removing the methylene bridge between the phenylene and the amine part. Two model achiral aminoboranes (\textit{SCAT} and \textit{DMCAT}) were synthesized (Fig. 34) to evaluate the potential catalytic properties of this reduced system in hydrogenation of imines. This type of \textit{ortho}-junction aminoborane (Fig. 33, 2) was reported back in 2003 in an unsuccessful attempt to activate \(\text{H}_2\).\(^{45}\) Although the authors distinctly described the approach, later called FLP, emphasizing the importance of using highly Lewis acidic \(\text{C}_6\text{F}_5\) groups and simultaneous presence of the base, \(\text{H}_2\) was not activated, due to insufficient basicity of the diphenylamino group, as the authors suggested. Hence, the subgoal within these studies was to elucidate whether \(\text{H}_2\) activation was unsuccessful due to low basicity, or other issues, e.g., mutual B/N geometry.
Figure 34. Synthesis of the 2-boryl-\textit{N,N}-dialkylanilines SCAT and DMCAT and their reaction with H$_2$.

Both compounds were prepared in good to excellent yields from the respective organolithiums and ClB(C$_6$F$_5$)$_2$ in non-coordinating solvent. X-ray diffraction analysis revealed that DMCAT exists as the intermolecular N→B adducts ($d$(N-B) = 1.771(3) and 1.741(3) Å), while SCAT is truly frustrated, evidently due to the highly sterically bulky TMP group.

Despite their structural difference, both aminoboranes activated H$_2$ at ambient temperature and 2 bar partial pressure. SCAT produced the extremely stable adduct SCATH$_2$ which did not release H$_2$, even on prolonged heating. The intrinsic stability of SCATH$_2$ was attributed to the rigidity of the phenylene bridge and mutual B/N geometry, giving rise to a 6-membered C-N-H-H-B-C ring (rather than 7-membered as in CATH$_2$). DMCAT reversibly reacts with H$_2$, already releasing it back at room temperature on venting off the vessel. Apparently, intramolecular B-N bonding in DMCAT plays a crucial role in the slow kinetics observed during H$_2$ addition, as well as in the near-neutral energetics of this process.
SCAT and DMCAT (or respective H₂ adducts) were tested as catalysts for hydrogenation of imines (Table 6). We found that SCATH₂ is unable to transfer H₂ to any substrate, even benzaldehyde, catalytically or stoichiometrically. DMCATH₂ showed more promising results; however, of the substrates tested (used previously with CATH₂, QCATH₂, etc.) only two, 51f and 106, were hydrogenated. Since these substrates are the least sterically hindered (51f was a model substrate during development of iPrQCATH₂, while for enamine 109 protonation proceeds at the C-2 rather than the N atom), we suggested the extreme steric hindrance of DMCATH₂ makes sluggish or prevents H₂ transfer to substrates 51b, 51g, 51j, and 51l. However, further studies of the reactivity of the ortho-(dimethylamino)phenylboryl core (see Chapter 9) revealed easy cleavage of the B-C₆F₅ bond as the result of intramolecular protonolysis. On heating of the DMCAT with dibenzylamine (115) and indoline (117), mono- and disubstituted aminoboranes 110 and 111 formed (Fig. 35). Enamines, 109 in particular, produce tertiary amines on hydrogenation, which are not protogenic in contrast to secondary amines.¹³⁵

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Table 6. Substrates used in attempted catalytic hydrogenations with SCAT/SCATH₂ or DMCAT/DMCATH₂. Hydrogenation of 51f and 106 catalyzed by DMCAT

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Loading of DMCAT, mol%</th>
<th>T, °C</th>
<th>Time, h</th>
<th>Conversion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>51f</td>
<td>4</td>
<td>110</td>
<td>36</td>
<td>30</td>
</tr>
<tr>
<td>51f</td>
<td>10</td>
<td>80</td>
<td>18</td>
<td>70</td>
</tr>
<tr>
<td>51f</td>
<td>10</td>
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<td>18</td>
<td>81</td>
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<td>51f</td>
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<td>109</td>
<td>5</td>
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</tr>
<tr>
<td>109</td>
<td>5</td>
<td>80</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>

a) 0.25 mmol of substrate, catalytic amount of DMCAT and 0.5 ml of C₆D₆ were placed in a Schlenk tube and stirred under 2 bar H₂ under respective conditions. Conversions were determined by ¹H NMR of crude reaction mixtures.
Figure 35. DMCAT degradation during heating with secondary (protogenic) amines.

In summary, both SCAT and DMCAT activate H₂ under ambient conditions. Although they show poor catalytic properties in the hydrogenation of imines, they have many distinctive features, which are disclosed in subsequent chapters.

9. Hydrogenation of unactivated multiple C-C bonds

FLP-catalyzed hydrogenation of unactivated C-C bonds is a challenging goal, due to existing natural mechanistic limitations (Fig. 36a). FLPs split H₂ in a heterolytic way, generating onium borohydrides. At the respective step of the catalytic cycle, proton transfer from onium borohydride 123 to substrate 124 should occur. This proton transfer proceeds very easily in the case of relatively highly basic imines as substrates, but is a very unlikely process for hydrocarbons, due to the high level of acidity of the carbocations. Decrease in the basicity of the amine 122 to make it able to protonate a wider variety of substrates may lead to inability to split H₂. Despite the seeming infeasibility of this approach, it was successfully implemented recently, using combinations of B(C₆F₅)₃ with finely selected low-basic phosphines, amines⁵⁷ or, recently, Et₂O,¹³³ as catalysts. This method is still restricted to alkenes with high proton affinity though. The hydrogenation of dienes (to monoenues), α-methylstyrenes, 1,1-diphenylethylene, and trimethyl(2-
methylprop-2-enyl)silane was reported. Polyarenes having an anthracene core were reduced under similar conditions as well.\textsuperscript{132}

**Figure 36.** Two potential mechanisms of unactivated C-C bond hydrogenation: traditional approach via sequential addition of proton and hydride (and vice versa) from FLP-H\textsubscript{2} and novel approach via preceding hydroboration of C-C bond (substrate activation).

To circumvent this natural limitation, we proposed an FLP-based catalytic cycle (Fig. 36 b), in which H\textsubscript{2} activation is preceded by a substrate activation step via hydroboration, a well-known reaction from organoboron chemistry. Hence, the Lewis acidic component of an FLP should be presented not by a tertiary borane, but by a secondary one 125 (hydroborane). Another essential step is the protonation of the alkyl or alkenyl group (substrate bound to B center) within the ionic pair 127. Initially, Piers borane ((C\textsubscript{6}F\textsubscript{5})\textsubscript{2}BH) was attempted as a catalyst to bring about this new approach. A recent article and our trials showed that although (C\textsubscript{6}F\textsubscript{5})\textsubscript{2}BH smoothly hydrogenates various alkynes and alkenes, and the resulting alkylboranes are able to split H\textsubscript{2} in a heterolytic way, no production of reduced hydrocarbons was observed; the reaction gave only starting FLP via a reverse dehydrogenation process.\textsuperscript{54}

In studying the thermal behavior of DMCATH\textsubscript{2}, we observed surprisingly easy cleavage of C\textsubscript{6}F\textsubscript{5} group, producing the unique ansa-aminohydroborane hydroCAT (Fig. 37). This reaction is unprecedented in FLP chemistry and calculations predicted a low barrier (\(\Delta G^f = 18.1 \text{ kcal/mol}\)) for this process. It proceeds as a direct protodeborylation of the sp\textsubscript{2}-carbon atom of the C\textsubscript{6}F\textsubscript{5} group rather than involving carbocationic intermediates. Apparently, the favorable B/N geometry in the ortho-
Me₂N-phenylboryl core is responsible for facile protonation of substituents on boron. This finding allowed us to perform highly selective metal-free semihydrogenation of *unactivated* internal alkynes into cis-alkenes. It should be noted that DMCAT is a crystalline compound that is stable indefinitely under Ar and can be loaded into a reaction vessel, generating the active catalytic species hydro-CAT *in situ*.

![DMCAT and hydro-CAT](image)

**Figure 37. Formation of hydro-CAT.**

Various dialkyl-, diaryl-, and arylalkylacetylenes were successfully hydrogenated under standard conditions: 5 mol% of DMCAT in C₆D₆, 2 bar of H₂, 80 °C, 3 h (Table 7), demonstrating the generality of the approach and providing exceptional cis-stereoselectivity. Enynes, diynes, silyl-protected ynols and esters (Table 7, entries 10, 13, 12, 9) were successfully hydrogenated as well. The products were isolated in excellent yields in experiments scaled up to 10 mmol of substrate. Some of the substrates required prolonged reaction time and/or higher temperature and catalyst loading, while some were not hydrogenated at all. There are essentially two classes of alkynes that are not reduced with the current method: terminal alkynes and alkynes comprising a terminal double bond. Nevertheless, terminal alkynes have been silylated, using conventional methods, and the silylacetylenes obtained were smoothly hydrogenated (Table 7, entries 11, 16).
Table 7. Hydrogenation of alkynes, using DMCAT as a precatalyst.\textsuperscript{v a)}

\[ \text{R}^1\equiv\text{R}^2 \xrightarrow{\text{cat. - DMCAT}} 2.2 \text{ bar } \text{H}_2 \xrightarrow{\Delta} \text{C}_6\text{D}_6, \Delta \]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate(s)</th>
<th>Product(s)</th>
<th>DMCAT Time, T, ( \text{mol%} ), ( \text{h} ), ( ^\circ \text{C} )</th>
<th>Conversion\textsuperscript{b)} [isolated yield], ( % ) (product)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>128a</td>
<td>128b</td>
<td>7 3 80 100</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>129a</td>
<td>129b</td>
<td>5 3 80 100</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>130a</td>
<td>-</td>
<td>5 15 80 n.r.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>129b : 130b</td>
<td>= 1:1</td>
<td>5 3 80 n.r.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>: 130a</td>
<td>= 1:1</td>
<td>5 3 80 n.r.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>131a</td>
<td>131b</td>
<td>7 3 80 100</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>132a</td>
<td>132b</td>
<td>10 3 80 100</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>133a</td>
<td>133b</td>
<td>5 3 80 100 [80]</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>134a</td>
<td>134b</td>
<td>5 3 80 100 [98]</td>
<td></td>
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<tr>
<td>10</td>
<td>135a</td>
<td>135b</td>
<td>5 3 80 100</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>136a</td>
<td>136b</td>
<td>5 3 80 100 [95]</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>137a</td>
<td>137b</td>
<td>5 3 80 100</td>
<td></td>
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<tr>
<td>13</td>
<td>138a</td>
<td>138b</td>
<td>5 3 80 100 [94]</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>139a</td>
<td>139b</td>
<td>5 3 80 52</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>139a</td>
<td>139b</td>
<td>9 80 100 [91]</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>140a</td>
<td>140b</td>
<td>5 3 80 88 (140b) 12 (140c)</td>
<td></td>
</tr>
</tbody>
</table>
Catalytic activity up to 31.6 h⁻¹ was estimated, using DMCAT or hydro-CAT as the catalyst under standard conditions and 129a or 133a as substrates. Remarkably, the catalytic hydrogenation proceeds at room temperature, although 20 times more slowly than at 80 °C. Conversely, high pressure of H₂ (30 bar) causes an almost 10-fold acceleration of hydrogenation: up to 296 h⁻¹.

No overreduction to alkanes was detected. Under standard conditions, cis-alkenes were produced exclusively; traces of other products, such as trans-alkenes, have been barely detected by ¹H NMR. The only exception found was 1-trimethylsilyl-2-phenylacetylene 140a; a substantial amount of trans-alkene 140c was produced (12 mol%) independently of the conversion level (Table 7, entries 16, 17). 140c is likely to be produced directly during hydrogenation. Accumulation of trans-alkenes as a result of isomerization was observed when prolonged heating and/or high temperature (120 °C) were applied to force hydrogenation of poorly reactive substrates (Table 7, entries 19, 21).

Further mechanistic studies and their computational evaluation support the reaction to follow the general mechanism depicted at Fig. 38, b. In addition, various details of the reaction are revealed:

1. Calculations (for but-2-yn 128a as a model substrate) predict that the activation barriers of all elementary steps have similar values $\Delta G^\ddagger = 14$–16

---

<table>
<thead>
<tr>
<th>17</th>
<th>140c</th>
<th>1.5 80</th>
<th>30.5 (140b) 4.3 (140c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>141b</td>
<td>5 3 80</td>
<td>&lt;20</td>
</tr>
<tr>
<td>19</td>
<td>141c</td>
<td>10 15 120</td>
<td>71 (141b) 9.5 (141c)</td>
</tr>
<tr>
<td>20</td>
<td>142b</td>
<td>20 18 80</td>
<td>44 (142b) 26 (other alkenes)</td>
</tr>
<tr>
<td>21</td>
<td>142d</td>
<td>15 10 120</td>
<td>42 (142b) 10 (142c)</td>
</tr>
<tr>
<td>22</td>
<td>142e</td>
<td>10.5 (142d) 10.2 (142e)</td>
<td></td>
</tr>
</tbody>
</table>

a) 0.25–0.5 mmol of alkyne, catalytic amount of DMCAT, and 0.5 ml of C₆D₆ were placed in a Schlenk tube and stirred under 2 bar H₂ under respective conditions. b) Cis-alkene if not otherwise stated. Defined by crude sample analysis with ¹H/¹³C NMR. c) No reaction. d) Including bound to the catalyst.
kcal/mol (Fig. 40). This means that, depending on the substrate and conditions, any of the barriers can be a rate-determining step (RDS).

2. Internal alkynes are irreversibly hydroborated by hydro-CAT, producing their respective adducts 145, of which some were isolated. The rate of the hydroboration is controlled by steric and electronic factors. The rate greatly varies from instant reaction of hex-3-yne 129a at room temperature (the highest rate of the substrates tested) to negligible for diphenylacetylene 139a (requires heating at 80 °C).
Figure 38. a) Mechanism of the hydro-CAT-catalyzed hydrogenation of alkynes and of the catalyst degradation process. b) Solution-phase Gibbs free energy diagram computed for the hydrogenation of but-2-yne (128a). Optimized structures of transition states identified for hydroboration (TS\text{hydr}), heterolytic hydrogen splitting (TS\text{split}), and protonation (TS\text{prot}) steps are shown in the upper part of the figure. The energetics of the elementary steps identified computationally is consistent with the proposed reaction mechanism.

3. For hex-3-yne having the highest hydroboration rate, the splitting of H\textsubscript{2} is assumed to be the RDS, since a 15-fold increase in H\textsubscript{2} pressure (from 2 to 30 bar) causes a 10-fold acceleration of the reaction rate (TOF increased from 31.6 to 296 h\textsuperscript{-1}).

4. The active catalyst hydro-CAT is unstable under the reaction conditions, decomposing through protonative cleavage of the remaining C\textsubscript{6}F\textsubscript{5} group. For hex-3-yne as a substrate, formation of 147 is about 100 times slower than the hex-3-en-2-yl cleavage, leading to propagation of the catalytic cycle. This limits the maximum turnover number values and the minimal catalyst loading, ideally, is required to be at least 1 mol%.

5. Reaction of hydroboration of alkenes with hydro-CAT is much less exergonic than of alkynes. Terminal alkenes react irreversibly, cis-1,2-di-(n-alkyl)ethylene...
reversibly, while the more hindered 1,2-disubstituted ethylenes do not react at all. The result of the irreversible hydroboration of terminal alkenes is inhibition of the reaction by substrates with a terminal double bond (Table 7, entry 22).

6. Calculations predict that the analogical catalytic cycle for hydrogenation of alkenes can be brought about as well. However, the calculated barrier for the intramolecular protonative cleavage (protodeborylation) of the alkyl group is substantially higher than that of C₆F₅, resulting in the following stability against protonation: alkenyl < C₆F₅ < alkyl. In practice, this means that under standard conditions (2 bar H₂, 80 °C, 5 h) terminal alkenes, which are irreversibly hydroborated by hydro-CAT, block the catalyst due to inability to propagate the catalytic cycle via protodeborylation. Under forcing conditions (40 bar H₂, 80 °C, >15 h) full cleavage of C₆F₅ group is observed with no evidence of alkane formation.

7. Terminal alkynes are not hydrogenated with the current system, since they tend to react via the C-H activation pathway (deprotoborylation) with the catalyst (Fig. 39), reacting further via protonative cleavage of the C₆F₅ group, leading to rapid degradation of the catalyst and loss of H₂-splitting reactivity.

![Figure 39](image)

**Figure 39.** Terminal alkyne addition to DMCAT and further catalyst degradation.

8. The mechanism proposed was supported by several isotope-labeling experiments with alkyne 148a (Fig. 40). On reaction with HD all four possible isotopomers 148b-e were produced in a ratio similar to statistic (1:1:1:1). When 148a reacted with hydro-CAT, two regioisomeric vinylboranes, 145d and 145e, were formed. When this mixture was then treated with D₂, two isotopomers were observed in the same ratio, demonstrating selective deuterative cleavage the of B-C bond.
Figure 40. Scrambling of the isotopes upon reaction of alkyne 148a with HD in a similar to the statistic ratio (1:1:1:1) and selective deuteration of the B-C bond upon reaction of the regioisomeric vinylboranes 145d,e with $D_2$.

In conclusion, a new approach to unactivated multiple C-C bond hydrogenation was proposed. Using the catalytic system developed (precatalyst DMCAT, the actual catalyst hydro-CAT formed in situ), this approach was implemented as semihydrogenation of internal alkynes under mild conditions with exceptional cis-selectivity.
10. Hydrogen activation and catalytic properties of frustrated ansa-aminochloroboranes

The storage of hydrogen with FLPs was proposed in 2003, in the paper mentioned above, by Piers et al. Although they were unable to activate $\text{H}_2$ with their B/N system, afterwards, frustrated Lewis pairs were reported to feature direct, rapid, and noncatalytic $\text{H}_2$ uptake. Moreover, changing the nature of the counterparts provides ample opportunity for tuning the thermodynamic properties of hydrogen activation process, making it reversible under desired conditions, if needed. The major problem of FLPs as hydrogen storage materials is their high molecular weight making their capacity for absorbed $\text{H}_2$ very low. For instance, canonical FLPs, such as $\text{B(C}_6\text{F}_5)_3/$TMP or $\text{B(C}_6\text{F}_5)_3/$P$\text{Bu}_3$ can absorb app. 0.3 wt% of $\text{H}_2$ while 70-77% of weight falls in the $\text{C}_6\text{F}_5$ groups. In addition, high costs of FLPs originate mostly from that of the fluorinated aryls.

It was shown in a literature review that the hydride affinities of many inorganic boranes approach that of $\text{B(C}_6\text{F}_5)_3$. Of particular interest are the inexpensive commercially available boron halides and BH$_3$ (as diborane or Lewis adducts). Activation of $\text{H}_2$ with fluoroaryl-free boranes can provide low-cost catalytic applications, while the low molar weight of these compounds shows a promising approach to hydrogen storage. A previous attempt to use mixed $\text{C}_6\text{F}_5/\text{Cl}$ type borane $(\text{C}_6\text{F}_5)_2\text{BCl}$ as an FLP part for $\text{H}_2$ splitting demonstrated an important pattern of reactivity: the tendency towards Cl/H exchange leading to subsequent reactions (Fig. 11). We reasoned that the ansa-system can help to stabilize the $\text{H}_2$ adduct due to a dihydrogen bond and other factors, as discussed previously. We prepared analogues of the aminoborane SCAT, in which the perfluorophenyl group was partially or completely replaced with a simple chlorine atom (Fig. 41). The chlorine atom is substantially smaller than the $\text{C}_6\text{F}_5$ group and the sterically bulky $\text{ortho}$-$\text{TMP}$-phenyl backbone was chosen to prevent inter- as well as intramolecular B-N bonding similar to those found in DMCAT. Indeed, the new aminoboranes CI-CAT and diCl-CAT are truly frustrated, as evident from their typically neutral borane $^{11}\text{B}$ NMR shifts: 63.1 and 55.8 ppm, respectively. Both compounds were isolated in yields close to quantitative, similar to SCAT. Apparently, formation of side products is suppressed by the high steric hindrance of the TMP group, preventing addition of the second equivalent of 107 to the aminoborane.
Figure 41. Preparation of ansa-aminochloroboranes and their reaction with hydrogen.

Upon exposure of the Cl-CAT or diCl-CAT solutions to hydrogen (2 bar), it is absorbed instantly, producing the respective chloroborohydrides Cl-CATH₂ and diCl-CATH₂ quantitatively. Cl-CATH₂ and diCl-CATH₂ are white crystalline solids that are stable indefinitely under Ar at room temperature. These unique compounds were characterized comprehensively; their structures were additionally studied with single crystal X-ray diffraction method in the solid state and 2D NOESY ¹H NMR in solution, showing consistency. For the first time among the ansa-aminoboranes, the NH⁺ hydrogen atom was attached to the Cl atom in Cl-CATH₂ unlike other structures, including diCl-CATH₂, containing dihydrogen bond (Fig. 42). There is no solid explanation for this finding, although gas-phase calculations predict preference of the chlorohydrogen over the dihydrogen bond in the ionic pair [NH₄][HBCl₃].

Figure 42. Structures of the chloroborohydrides in the solid state and solution based on X-ray diffraction and NOESY ¹H NMR, respectively.

This result opens the way to potential materials for H₂ storage, based on FLP principles, since a chlorine atom with a molecular weight of 35.5 is substantially
lighter than a conventional C₆F₅ group with a weight of 167. **DiCl-CAT** with a molecular weight 298 is the lightest FLP reported to date that is able to activate H₂ with capacity of 0.6 wt%, which is more than twice as high as conventional FLPs (Fig. 41).

The H₂ adducts **diCl-CATH₂** and **Cl-CATH₂** were heated at 120 °C for 24 h to attempt H₂ release. As a result, HCl adducts of aminochloroboranes 150 and 151 formed, rather than the starting chloroboranes. Presumably, these compounds (Fig. 43) were derived from dismutation of H₂ adducts via H⁺/Cl⁻ exchange. Other products of dismutation, the respective di- or trihydroborates 152 and 153, were, presumably unstable and decomposed. During heating of **Cl-CATH₂**, C₆F₅H was formed in amounts nearly equimolar to 151, as evidenced by ¹⁹F NMR. We suggest that pentafluorobenzene resulted from intramolecular protonative cleavage of B-C₆F₅, similar to the formation of **hydro-CAT**.

![Diagram of thermal decomposition of chloroborohydrides into chloroborates and their X-ray structures.](image)

**Figure 43.** Thermal decomposition of chloroborohydrides into chloroborates and their X-ray structures.

Inability to achieve reversibility of H₂ uptake was attributed to easy exchange of chlorine atoms between borane compounds and intrinsic stability of dichloroborates (HCl adducts). Evidently, the latter are stabilized additionally by
intra-molecular hydrogen H⁺-ClB bond distinctly detected by X-ray diffraction (Fig. 43).

Eventually, the chloroborane DMCl, the chloro-analogue of the precatalyst DMCAT, was prepared and catalyzed the hydrogenation of alkynes. DMCl can be prepared in one-pot synthesis from inexpensive starting materials: N,N-dimethylaniline, boron trichloride and butyllithium (Table 8).

Table 8. Synthesis of DMCl and hydrogenation of alkynes catalyzed by DMCl.a)

![Diagram of DMCl synthesis](image)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>p(H₂), bar</th>
<th>DMCl, mol%</th>
<th>T, °C</th>
<th>Time, h</th>
<th>Conversion b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>129a</td>
<td>40</td>
<td>5</td>
<td>80</td>
<td>3</td>
<td>65</td>
</tr>
<tr>
<td>129a</td>
<td>2</td>
<td>10</td>
<td>80</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>133a</td>
<td>2</td>
<td>10</td>
<td>80</td>
<td>18</td>
<td>34</td>
</tr>
<tr>
<td>133a</td>
<td>2</td>
<td>10</td>
<td>80</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>133a</td>
<td>40</td>
<td>5</td>
<td>80</td>
<td>3</td>
<td>73 c)</td>
</tr>
<tr>
<td>133a</td>
<td>2</td>
<td>10</td>
<td>80</td>
<td>24</td>
<td>90 c)</td>
</tr>
<tr>
<td>136a</td>
<td>40</td>
<td>5</td>
<td>80</td>
<td>3</td>
<td>52</td>
</tr>
<tr>
<td>136a</td>
<td>2</td>
<td>10</td>
<td>80</td>
<td>48</td>
<td>13</td>
</tr>
</tbody>
</table>

a) 0.25–0.5 mmol of alkyne, catalytic amount of DMCl, and 0.5 ml of C₆D₆ or CD₂Cl₂ were placed in a Schlenk tube (2 bar H₂) or an autoclave (40 bar H₂) and stirred at 80 °C. b) Conversions were determined by ¹H NMR of crude reaction mixtures. c) 10 mol% of MeTMP added.
11. Hydrogen activation by carbonyl compounds and B(C$_6$F$_5$)$_3$"}

Progress in the FLP area is increasing. FLPs catalyze hydrogenation of polar electron-rich and electron-deficient compounds, nonpolar multiple C-C bonds, perform asymmetric hydrogenation of imines, etc. However, catalytic hydrogenation of carbonyl compounds is still the challenge. The reduction of ketones and aldehydes, using only stoichiometric amounts of prepreparted onium borohydrides was reported. Due to the intrinsic stability of the B-O bond and relatively high acidity of alcohols produced the final product exists as a very stable FLP product of the heterolytic cleavage of RO$^-$-H$^+$ bond (Fig. 44 a). Following the idea of QCAT recovery, we reasoned that it is possible to find such a weak base that the respective FLP-ROH adduct will be labile enough to provide sufficient concentration of FLP for the propagation of the catalytic cycle.

Eventually, we found that carbonyl compounds, namely benzaldehyde $155a$ and benzophenone $155b$, on heating with equimolar amounts of B(C$_6$F$_5$)$_3$ under H$_2$, are reduced to toluene and diphenylmethane, respectively (Fig. 44 b). The intermediate formation of adducts $156$ is evidenced by condensation with toluene-$d_8$ when the latter is used as a solvent. In addition, the incorporation of gaseous hydrogen into reduced species was evident in the experiments with D$_2$.

Apparently, carbonyl compounds serve as bases during H$_2$ splitting with B(C$_6$F$_5$)$_3$. Analogous to the hydrogenation of imines catalyzed by B(C$_6$F$_5$)$_3$, the intermediate onium borohydrides instantly turns into the products $156$. Adducts $156$
quickly dismutate into 157 and starting 155, which occurs in an independent experiment on mixing of the respective alcohols with B(C₆F₅)₃. This reactivity can open the way towards FLP-catalyzed hydrogenation of carbonyl compounds.
Conclusions

Figure 45. New ansa-aminoboranes developed in the present work and their properties.

It was shown within this work that (Fig. 45):

1. Frustrated ansa-aminoboranes are efficient catalysts for metal-free hydrogenation of polar (imines, enamines, quinolines) as well as nonpolar (alkynes) unsaturated compounds under mild conditions.

2. Different parts of ansa-aminoboranes, the amine moiety, the boryl group, and the link can be easily modified, resulting in compounds featuring new unprecedented properties.

3. Reduction of the basicity of the amine part of the initial CAT system resulted in a family of highly active ansa-aminoboranes for hydrogenation of imines and other nitrogen-containing compounds, featuring high activity under mild conditions (TOF up to 100 h⁻¹), broad substrate scope, catalyst recovery, compatibility with ethereal solvents, and asymmetric induction (ee up to 37%).

4. Two new ansa-aminoboranes SCAT and DMCAT, were prepared as analogues of the original CAT system with a linker reduced (ortho-phenylene). Although DMCAT has an intramolecular B-N bond and SCAT is truly frustrated, both aminoboranes activate H₂ under ambient conditions.

5. DMCAT is an efficient precatalyst of cis-stereoselective semihydrogenation of internal alkynes. The active catalyst species hydro-CAT is produced in situ via hydrogenolysis of the B-C₆F₅ bond.

6. The alkyne hydrogenation developed demonstrates a new approach towards metal-free hydrogenation of unsaturated unactivated C-C bonds. This approach combines hydroboration of substrate (substrate binding) and H₂ splitting via an
FLP mechanism and results in mild reaction conditions and high hydrogenation rates. The mechanism of the alkyne hydrogenation is well supported by experimental and computational studies. In addition, calculations predict that the method can be extended to hydrogenation of alkenes.

7. The *ansa*-aminochloroboranes Cl-CAT and diCl-CAT were prepared as analogues of SCAT, in which the C₆F₅ groups were partially or completely replaced with chlorine atoms. They activate H₂ in a manner similar to that of SCAT, producing stable chloroborohydrides.

8. This finding opens the way to lightweight FLP-based applications, since diCl-CAT absorbs by weight two times more H₂ than SCAT. To demonstrate this, a simple aminoborane DMCl, a dichloroboryl analogue of DMCAT, was prepared and showed catalytic properties in hydrogenation of alkynes.

9. The *ansa* junction was essential in all cases mentioned, providing rapid H₂ splitting. The *ortho*-phenylene junction was crucial to hydrogenation of alkynes with hydro-CAT. Optimal B/N geometry facilitates protodeborylation, which proceeds as a synchronous mechanism according to calculations. This allows not only release of the reduced substrate from the catalyst core, but also in situ production of hydro-CAT from DMCAT. The *ansa* junction stabilizes chloroborohydrides Cl-CATH₂ and diCl-CATH₂, which are indefinitely stable at ambient temperature, unlike intermolecular systems.

10. Not only amines, phosphines, and other highly basic compounds can split H₂ with B(C₆F₅)₃, but simple carbonyl compounds as well. Benzaldehyde and benzophenone can be hydrogenated into their respective alcohols or hydrocarbons under 2 bars of H₂ pressure in the presence of equimolar amounts of B(C₆F₅)₃.
References

135 Unpublished results
Highly Active Metal-Free Catalysts for Hydrogenation of Unsaturated Nitrogen-Containing Compounds

Victor Sumerin, Konstantin Chernichenko, Martin Nieger, Markku Leskelä, Bernhard Rieger, and Timo Repo

Abstract: New highly active ansa-amination borane catalysts for the direct metal-free hydrogenation of imines 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 nitrogen-containing substrates. The first example of asymmetric imine hydrogenation based on the ansa-amination borane concept was demonstrated. Furthermore, effective catalyst recovery by extraction of the acidic solution with an organic solvent followed by dehydration with TMSBr was elaborated. The initial findings highlight the development of more effective chiral ansa-amination borates for enantioselective hydrogenation. Therefore, the progress achieved in the ansa-amination borate concept makes it very promising for further elaboration with the aim to obtain industrially applicable catalysts.

Keywords: amines; boranes; homogeneous catalysis; hydrogenation; organocatalysis

Introduction

During the past century, hydrogen activation and catalytic hydrogenation of unsaturated nitrogen-containing compounds under mild conditions was an exclusive prerogative of transition metal catalysts. Despite the undeniable achievements obtained in this area in recent decades, there is still a considerable amount of unresolved challenges related to catalyst selectivity, functional group tolerance, environmental sustainability, cost-efficiency and fine purification of the reaction products. Among the various alternative methods, the fast growing area of enantioselective organocatalytic reduction of imines, enamines and nitrogen-containing heterocycles is attracting increasing attention. Presently, there are essentially two well-established asymmetric organocatalytic approaches for this transformation. The first method is a Lewis base-catalyzed hydrosilylation with trichlorosilane with the second being 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.

An alternative atom-economical metal-free enantioselective imine hydrogenation is less developed. To date, there are only two non-metal systems based on the bis(perfluorophenyl)boranyl [B(CF₃)₂] moiety substituted with a chiral alkyl chain 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 H₂ pressure showed complete conversion of the imine but with only 13% ee (Scheme 1).

Scheme 1. Chiral alkyl-bis(perfluorophenyl)borane-based catalysts.
More recently, tris(tert-butyl)phosphonium [(1R,2R,3R,4S)-4,7,7-trimethyl-3-phenylbicyclo[2.2.1]-heptan-2-yl bis(perfluorophenyl)hydroborate prepared from (1R)-(+) -camphor catalyzed (5 mol%) the reduction of different N-arylketimines at 65 °C under 25 atm pressure of H₂ to give the corresponding amines in high yields and good ees (up to 83%).] In contrast to achiral systems based on triarylboranes, I a higher pressure of hydrogen is required in the case of chiral-alkylidiboranes. Moreover, such nonmetal catalysts cannot be recovered and/or reused, which is an important requirement for large-scale applications.

We recently showed that the ansa-aminoborane N-TMP-CH₂C₅H₃B(C₅F₅)₂ (where TMP is 2,2,6,6-tetramethylpiperidinyl) can rapidly activate hydrogen at 20 °C and 1 atm pressure to give the ansa-aminium borate CATH₁, which can release dihydrogen upon heating at 100 °C. Besides providing a reversible H₂ activation, CATH₁ was found to be an efficient catalyst for the reduction of imines and enamines (Scheme 2). However, much like other organocatalytic systems with the bis(perfluorophenyl)boranyl moiety, it has significant drawbacks and limitations with respect to the reactivity.

Herein we report new efficient catalysts for the metal-free hydrogenation of a broad palette of unsaturated nitrogen-containing compounds. By tuning the basicity of the amine moiety a 100-fold increase in activity was achieved. Also a simple procedure for the recovery of the highly moisture-sensitive catalysts after quenching the reaction with aqueous acidic solution is described. Furthermore, the first results on the enantioselective ansa-aminoborane/ansa-aminium borate-catalyzed hydrogenation of nitrogen-containing compounds are reported.

**Results and Discussion**

**Synthesis of ansa-Ammonium Borate Catalysts**

One disadvantage of the previously developed CATH₁ is the sensitivity to steric factors around the nitrogen atom of the imine. Non-bulky amines or/and corresponding imines inhibit the catalyst by coordination to its Lewis acidic boron centre. As a result conversions in these cases did not exceed the ansa-aminium borate loading. Another is CATH₁’s low ability to reduce less basic N-arylketimines in comparison with other more basic N-alkyl- and N-benzylketimines. Thus the reduction of N-(4-methoxy)phenyl-1-phenylethylideneamine 1d with 4 mol% of CATH₁ afforded only 37% yield of the desired amine in 12 h (toluene, 100 °C) (Table 1, entry 13). These observations support a proposed mechanism in which any one or more steps may be rate-determining depending on the substrate and catalyst structures (Scheme 2). The proton transfer (Scheme 2, stage II) seems to be a primary and rate-controlling step for the reaction of bulky imines. For instance, the reduction of N-aryl-α-amino ester 1e which has the lowest basicity in the series of imines proceeded with a low conversion percentage (Table 2, entry 5). The fact that the conversion of non-bulky imines does not exceed the catalyst loading highlights another important step in the hydrogenation mechanism: the inhibition of the catalytic
Table 1. Catalytic hydrogenation of imines.[4]  

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<th>Entry</th>
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[a] *ansa*-Ammonium borate catalyst (0.01 mmol, 1-4%), substrate (0.25-1.0 mmol) in toluene (5.0 mL) were refluxed (110$^\circ$C) under 2 atm of H$_2$ pressure (56 mL, 2.5 mmol).

[b] Determined by $^1$H NMR spectroscopy.

[c] Ref.$^{[34]}$

[d] At 80$^\circ$C.

Table 2. Catalytic hydrogenation of imines.[5]  

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<td>B(C$_6$H$_5$)$_3$</td>
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[a] *ansa*-Ammonium borate catalyst (0.01 mmol, 4%), substrate (0.25 mmol) in toluene (5.0 mL) were refluxed (110$^\circ$C) under 2 atm of H$_2$ pressure (56 mL, 2.5 mmol).

[b] Determined by $^1$H NMR spectroscopy.

[c] In Et$_2$O (3 mL) at room temperature.

[d] At 25$^\circ$C, 4 atm H$_2$, ref.$^{[34]}$.

Interestingly, lowering the basicity of the starting amines had no significant effect on the hydrogen cleavage process by *ansa*-aminoboraborates MCAT$_3$, QCAT$_3$ and iPfICATH$_3$. However, reduced basicity dramatically decreased the temperature and the time required for hydrogen liberation (Scheme 5).

While *ansa*-aminoborane CATH$_3$ released H$_2$ quantitatively in toluene after 18 h at 110$^\circ$C, less basic MCATH$_3$ liberated hydrogen in 30 min under the same conditions. Even the less basic QCAT$_3$ and iPfICATH$_3$ either slowly decomposed in CDCl$_3$ solution at room temperature or gave starting *ansa*-aminoboraborates QCAT$_3$ and iPfICATH$_3$ after 5-10 min at 110$^\circ$C in toluene.$^{[20]}$ Accordingly, the less basic *ansa*-aminoboraborates lost hydrogen much faster than the original CATH$_3$, mainly due to the lower energy needed to cleave the weaker N$^+$--H bonds to form hydrogen gas. Therefore, QCAT$_3$ and iPfICATH$_3$ exhibited excellent kinetics (a few minutes) in both activation and liberation of hydrogen.$^{[21]}$

Catalytic Hydrogenation by *ansa*-Ammonium Boron Catalysts

Because of weaker N$^+$--H interactions the catalytic activity of the new MCATH$_3$, QCAT$_3$ and iPfICATH$_3$ in the hydrogenation of imines also increased dramatically (Table 1 and Table 2). Full conversions were achieved with either lower catalyst loading and/
basicity of the corresponding N-benzylamines

Scheme 3. Rational design of the new anusa-ammonium borate catalysts.\cite{1-2}

or shorter reaction time and/or lower temperature than with CATH\textsubscript{2} (Table 1). Thus, the proton transfer seems to be a rate-controlling step for the reaction of imines 1a–d. One should note that these experiments were performed under standard conditions, optimization of which can lead to further increases of catalytic activity (Table 2 and Table 3).
Scheme 5. Reversible \( \text{II} \) activation by \( \text{ansa-amineboranes} \).

Table 3. Catalytic hydrogenation of imine \( \text{1d} \) by \( \text{ansa-amineborane QCAH}_3 \).[4]

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[4] Catalyst QCAH₃ (0.01 mmol, 1%) and \( \text{1d} \) (1.0 mmol) were stirred in solvent (5.0 mL) under 2 atm of \( \text{H}_2 \) pressure (56 mL, 2.5 mmol).


The most expressive example is \( N \)-aryl-\( \alpha \)-imino ester \( \text{1e} \) which has the lowest basicity in the series of imines proceeded. Whilst CATH₁ and generally more active MCATH₂ provided only stoichiometric reduction, hydrogenation with QCAH₃ and iPrCATH₂ led to low, but over-stoichiometric conversions (Table 2, entries 3 and 4). Additionally QCAH₃ and iPrCATH₂ were able to hydrogenate 2-phenylquinoline catalytically to give 2-phenyl-1,2,3,4-tetrahydroquinoline in an almost quantitative yield (Table 2, entries 10–15).

As we have mentioned above the dissociation of a Lewis acid-Lewis base adduct between the \( \text{ansa-amineboranes} \) and product amine is the rate-determining step in the case of sterically benign substrates (Scheme 2, Stage IV). Therefore, the generally more active non-metal systems MCATH₂, QCAH₃ and iPrCATH₂ (4 mol%) could provide only a stoichiometric reduction of non-bulky imine \( \text{1f} \) (Table 2, entries 6–8) evidently due to catalyst inhibition by the substrate.

Figure 1. X-ray structure of \( \text{ansa-ammonium borate iPrQCAH}_3 \).[10] Hydrogen atoms were omitted for clarity, except those of the NHHB fragment. Atoms of the \( \text{ansa} \) fragment are labelled and coloured with black. The structural disorder of the C-11 and C-23 atom is caused by the presence of diastereomers.

To overcome this obstacle a special catalyst iPrQCAH₃ based on the more bulky 8-isopropyl-2,2,4-tri-methyl-1,2,3,4-tetrahydroquinoline moiety was used (Figure 1). Although iPrQCAH₃ exhibited a catalytic activity lower than those of MCATH₂, QCAH₃ and iPrCATH₂ for most of the substrates, hydrogenation of imine \( \text{1f} \) was performed in 82% yield under the standard conditions.

Inspired by the high activity of QCAH₃ we focused on the reduction of imine \( \text{1d} \) in different solvents and temperatures with 1 mol% of catalyst (Table 3). Overall, the best results were obtained using a solvent such as toluene and hexane at 80°C (2.5 h) or Et₂O at 50°C (1 h).

Thus the rational design of highly active MCATH₂, QCAH₃, iPrCATH₂ and iPrQCAH₂ catalysts was achieved simply by fine tuning of the electronic and steric properties of the amine moiety. To date reported substrates for FLP-catalyzed hydrogenation can be divided with small exceptions on two main groups: sterically hindered \( (N\text{-}r\text{-Bu})_{11a,b,c} \) \( N \)-Dipp,[11b] \( N \)-benzhydryl[11a,b,c] imines and enamines[11d] and low-basic \( (N\text{-}aryl)[9] \) \( N \)-arylsulfonyl[9,11a,b,c] imines and quinolines[11d] unsaturated nitrogen-containing compounds. Both of these aforementioned factors facilitate dissociation of the Lewis adducts between catalyst and substrates or fully prevent formation of those providing catalytic activity of triarylimines. In this respect new \( \text{ansa-ammonium borates} \) substantially extend the substrate scope of non-metal catalytic hydrogenation. A striking example is hydrogenation of \( \text{1f} \) with the particularly effective catalyst iPrQCAH₂. For substrates hydrogenated by both \( \text{ansa-} \) and other...
systems, the first provide superior \(1a^{[14,6]}\) and \(1d^{[15]}\) or comparable catalytic activity \(1g^{[1c]}\).

After the optimized conditions were determined, we then investigated the possibility of recovering the catalyst. It is a well known fact that the free forms of the catalytic systems based on the frustrated Lewis acid-Lewis base concept are very sensitive towards water.\(^{[22]}\) Thus, in spite of the fact that most of \(ansa\)-ammonium borates are air- and moisture-stable, the corresponding \(ansa\)-aminoboranes easily react with \(\text{H}_2\text{O}\) from the air affording water activation products. This indicates that the presence of accidental traces of water in the reaction system not only inhibits the catalyst activity in the hydrogenation reaction, but also suggests that water activation products would form during the quenching of the reaction mixture. Thus, the dehydration of such compounds is a key transformation in the catalyst recovery process. Surprisingly, after the solution of water-activated \(ansa\)-ammonium borate in benzene had been refluxed with excess of TMSBr (5 equiv.) for 5 min. and then evaporated under vacuum, the starting \(ansa\)-aminoborane QCAT was obtained in almost quantitative yield.\(^{[18]}\) Finally, based on the above results the hydrogenation of \(N-(4\text{-methoxy})\text{phenyl-1-phenylethyldieneamine} 1d\) \(\times 25\) times, 5.632 g) by \(ansa\)-ammonium borate QCATH\(_4\) (1 mol%) was scaled up, with the corresponding amine being isolated in 97% yield. Furthermore, 80% of the catalyst was recovered by extraction of the acidic solution with toluene followed by dehydration with TMSBr at 80°C. This procedure was successful due to the high hydrophobic effect of the perfluorophenyls of the catalyst.

**Chiral \(ansa\)-Ammonium Borate Catalysts**

So far, the \(ansa\)-ammonium borates QCATH\(_4\) and iPrICATH\(_4\) are the most active catalysts in the hydrogenation of imines among the previously reported B-

![Figure 2](image2.png)

**Figure 2.** X-ray structure of \(ansa\)-ammonium borate QCATH\(_4\).\(^{[15]}\) Hydrogen atoms were omitted for clarity, except those of the NHHB fragment. Atoms of the \(ansa\) fragment are labelled and coloured with black.

![Figure 3](image3.png)

**Figure 3.** X-ray structure of \(ansa\)-ammonium borate iPrICATH\(_4\).\(^{[16]}\) Hydrogen atoms were omitted for clarity, except those of the NHHB fragment. Atoms of the \(ansa\) fragment are labelled and coloured with black. A distinct \(\pi\)-\(\pi\) stacking between phenyl and perfluorophenyl groups is noticeable.

(C\(_6\)F\(_3\))\(_2\)-based systems. Both of them have a tertiary carbon stereocentre.

Additionally, due to the fixed conformation of \(ansa\)-ammonium borates\(^{[23]}\) nitrogen atoms present in these compounds are stereoic as well. According to NMR and X-ray diffraction studies, QCATH\(_4\) and iPrICATH\(_4\) exist as a mixture of diastereomers (5.7:1) and a single diastereomer, respectively (Figure 2 and Figure 3). Thus the stereochemistry of the tertiary carbon in these systems has a strong influence on the configuration of the tertiary ammonium nitrogen centre.

Due to the above-mentioned results, we attempted to prepare enantioenriched catalysts QCATH\(_4\) and iPrICATH\(_4\) containing enantiopure amine moieties and test them as catalysts for enantioselective hydrogenation. The starting 7-isopropyl-3,3-dimethyl-2-phenyl-3\(H\)-indole \(\text{II}\) and 2,2,4,7-tetramethyl-1,2-dihydroquinoline \(\text{Ij}\) were prepared according to the standard procedures.\(^{[18,24]}\) The 7-isopropyl-3,3-dimethyl-2-phenylindoline was synthesized by a similar method to that recently elaborated by Rueping et al.\(^{[7b,25]}\) The reduction of 3\(H\)-indole with Hantzsch ester catalyzed by enantiopure phosphoric acid (\(R\)-TRIP)\(^{[26]}\) showed the same enantioselectivity of 99% as previously reported with 3,3-bis(9-anthracenyl)-substituted phosphoric acid (Scheme 6).

To date no direct enantioselective approach to 4-substituted tetrahydroquinolines from 2,2-substituted-1,2-dihydroquinolines has been described.\(^{[7b,27]}\) Moreover, the only known example of asymmetric reduction of 4-substituted quinolines by a chiral Brønsted acid with a Hantzsch ester as hydrogen source postulates the first step of the mechanism to be hydride attack on the 4-position of protonated quinoline with

Subsequent formation of 1,4-dihydroquinoline. Whereas such a mechanism cannot be realized in the case of 2,2-substituted-1,2-dihydroquinolines, the corresponding 2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline was prepared in high yield and good ee (86.5%, Scheme 6) by a similar organocatalytic procedure. We believe that prior formation of the ortho-quinone tautomer followed by 1,4-reduction could be a possible explanation for this observation. Notably, >99% ee was achieved after one recrystallization of the hydrochloride salt. Therefore, our method provides a simple route to the synthesis of valuable enantiopure 2,2,4-substituted-1,2,3,4-tetrahydroquinolines.[24]

The anusa-aminonion borates Q*CATH₂, and iPrI*CATΗ were synthesized by a standard two-step procedure from corresponding enantiopure amines (Scheme 4). The $^1$H, $^11$B, $^13$C and $^{19}$F NMR spectroscopic data of Q*CATH₂ were in agreement with the proposed structure. However, in contrast to the racemic compound Q*CATH₂ exist as a mixture of diastereomers at a lower ratio (1:5:1) at the ammonium nitrogen atom. This is probably due to the longer time period needed for crystallization of the enantiopure anusa-aminonion borate compared to that of the racemic system and the previously observed slow decomposition of QCATH₂ to QCAT in solution at room temperature even under an atmosphere of hydrogen.

The $^1$H, $^11$B, $^13$C and $^{19}$F NMR spectroscopic data of iPrI*CATΗ were identical to those of racemic anusa-aminonion borate iPrICATΗ. Furthermore, the X-ray crystal structure study of PrI*CATΗ revealed the same P1 space group.[16] Thus, in spite of the absence of $\beta$-protons[25] in the starting amine and the high steric hindrance of the iPrICAT, the Lewis acidic boron centre can abstract the $\alpha$-proton of the amine fragment to form the intramolecular iminium borohydride species, which is in equilibrium with the starting anusa-aminoborane (Scheme 7).

To evaluate the catalytic activity of B(CF₃)$_3$ and anusa-aminonion borates in the racemization of enantioenriched amines, illustrative examples are collected in Table 4. Under standard conditions (heating for 15 h with 10 mol% of the catalyst at 110 °C in toluene) B(CF₃)$_3$ was found to be superior, providing full racemization. Among the tested anusa-aminonion borates, only QCATH₂ showed activity comparable to that of B(CF₃)$_3$. The inactivity of CATH₂ can be explained by slow dehydrogenation into the corresponding anusa-aminoborane which is considered to be the actual catalyst. The anusa-aminoborane iPrICAT is unable to abstract hydrogen from substrate amine as it exists in zwitterionic form (Scheme 7).

Table 4. Catalytic racemization of amines.[a]

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</table>

[a] Substrate (0.1 mmol), B(CF₃)$_3$ (0.01 mmol, 10% mol) were heated (110 °C) in toluene (2.0 mL) under an argon atmosphere for 15 h.
[b] Determined by chiral-HPLC.
[c] Under 2 atm of hydrogen pressure.
Scheme 8. Synthesis of CarCAT.

A hydrogen atmosphere (2 atm) fully suppresses racemization with B(C₆F₅)₃ as the catalyst (Table 4, entry 2). These results provide an important mechanistic datapoint for extending our understanding of hydrogen/hydride exchange between amines/imines and catalysts.

Therefore, only the enantiomeric amines without α-protons can be applied in the backbone of chiral ansa-ammonium borates. Additionally, the steric hindrance around the nitrogen centre must be sufficient to preclude a Lewis acid-Lewis base adduct formation. Due to this reason, the less bulky ansa-aminoborane ICATH₁, without the isopropyl group at the 7-position forms a stable intramolecular Lewis acid-Lewis base adduct, which is totally inactive in hydrogen activation.

Based on the above observations, the 4a,9a-substituted 2,3,4,4a,9,9a-hexahydro-1H-carbazole skeleton was chosen for the further evaluation. The starting enantiopure (2R,4aR)-2-isopropyl-4a-methyl-2,3,4,4a-tetrahydro-1H-carbazole was prepared according to the literature procedure.⁷⁻⁸ The subsequent addition of PhLi in toluene gave only the cis isomer (2R,4aR,9aS)-2-isopropyl-4a-methyl-9a-phenyl-2,3,4,4a,9,9a-hexahydro-1H-carbazole in high yield.⁹ The final ansa-ammonium borate CarCAT was synthesized by the standard procedure (Scheme 8). Interestingly, while ansa-ammonium borates QCATH₂ and iPR-CATH₂ slowly decomposed in solution at room temperature, CarCAT did not react with hydrogen even at -20°C. Since the hexahydrocarbazole has the lowest basicity in the series of investigated amines, the hydrogen activation equilibrium shifts to the left and the corresponding ansa-ammonium borate CarCAT cannot be isolated.

**Asymmetric Hydrogenation by ansa-Ammonium Borate Catalysts**

To gain insight into the reactivity of the ansa-ammonium borate QCATH₂ and ansa-ammonium borate CarCAT, their catalytic activity in the asymmetric hydrogenation of nitrogen-containing compounds at different temperatures and solvents was investigated (Table 5). The reduction of the model imine 1d with 4 mol% of ansa-ammonium borate QCATH₂ in toluene, hexane, diethyl ether or methyl tert-butyl ether (MTBE) at 20–80°C under 2 atm of H₂ pressure (56 mL, 2.5 equiv.) gave N-(4-methoxy)phenyl-1-phe-nyl-ethylamine in a quantitative yield in one hour (Table 4, entries 1–5). Thus, the enantiopure ansa-ammonium borate QCATH₂ exhibited the same unpre-

<table>
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<th>Temp. [°C]</th>
<th>Conv. [%] [b]</th>
<th>ee [%] [c]</th>
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[a] Catalyst (0.01 mmol, 4%) and imine (0.25 mmol) were stirred in solvent (3.0 mL) under 2 atm of H₂ pressure.
[b] Determined by "H NMR spectroscopy.
[c] Determined by chiral HPLC.
cedently high activity as its racemic version. However, the enantioselectivities were low. The best ee of 26% was obtained using MTBE as a solvent at 20°C (1 h). Repeating the reduction of N-benzylketimine 1b or 2-phenylquinoline 1g with 4 mol% of ansa-ammonium borate $Q^\ast$CATH$_2$ gave the corresponding amine in quantitative yields (12 h). The best ee values (35–37%) were also achieved in MTBE at room temperature (Table 5, entries 6–11).

The reduction of the model imine 1d with CarCAT resulted in low enantioselectivities of 8–17% (Table 5, entries 12–14), and low to moderate conversions (30–70%) after 20 h. This observation supports the idea that the hydrogenation became the rate-determining step in the hydrogenation of imines when the Lewis acidity or Lewis basicity of ansa-aminoborane is not high enough.

Accordingly, ansa-aminoborane CarCAT showed the low activity, mainly because of the too low basicity of the active nitrogen centre.

Conclusions

In summary, new catalysts for the direct hydrogenation of nitrogen-containing compounds were designed based on the ansa-ammonium boronate concept previously reported by our research group. Decreasing the basicity of the amine moiety causes a growth in catalytic activity by two orders of magnitude. Moreover, relatively low basicity allowed the elaboration of a simple and elegant catalyst recovery procedure. An efficient fine-tuning of the steric surroundings of the nitrogen catalyst atom allows hydrogenation of a wide substrate range, including sterically hindered and benign, N-aryl- and N-alkyl imines, quinolines, and others. Therefore, the newly designed catalysts are considered to be promising a toolkit for large-scale applications. Furthermore, the approach to the synthesis of enantiopure ansa-ammonium borates using organocatalytic reduction was elaborated, 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. Further studies on ansa-ammonium borate concept are ongoing.

Experimental Section

4-(2-Bromobenzyl)-3,3,5,5-tetramethylmorpholine

$[PK_c = 6.61(0.7)]^{[14]}$

A dry 25-mL Schlenk tube was charged with 1.432 g (10 mmol) 3,3,5,5-tetramethylmorpholine, 2.499 g (10 mmol) 2-bromobenzyl bromide, 1.6 g (11.6 mmol) K$_2$CO$_3$, and 0.166 g KI (1 mmol) in 18 mL of dry acetonitrile. The mixture was heated at 95°C for 24 h. The Schlenk tube was cooled and the content filtered. The solvent present filtrate was heated under reduced pressure. The crude product was purified by flash chromatography (silica gel was washed with 100 mL of hexane to remove unreacted 2-bromo benzyl bromide and then with 150 mL of CH$_2$Cl$_2$). The resulting CH$_2$Cl$_2$ fraction was rotovap to give 4-(2-bromobenzyl)-3,3,5,5-tetramethylmorpholine as white crystals; yield: 2.617 g (84%).$^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ = 7.83 (s, 1H, $J_{HH}$ = 7.7 Hz), 7.46 (dd, 1H, $J_{HH}$ = 7.5 Hz, $J_{HH}$ = 1.1 Hz), 7.27 (pseudo t, $J_{HH}$ = 7.7 Hz), 7.04 (pseudo t, $J_{HH}$ = 7.7 Hz), 3.73 (s, 2H), 3.48 (s, 4H), 1.00 (br, s, 12H);$^1$C NMR (CDCl$_3$, 75 MHz): $\delta$ = 142.69 (s), 131.95 (s), 129.80 (s), 127.43 (s), 126.72 (s), 122.26 (s), 79.13 (s), 35.88 (s), 48.08 (s), 23.96 (br, s); HR-MS (ESI$^+$-TOF): m/z = 312.0946, calcd. for C$_9$H$_{14}$NO$_2$Br$^+$: 312.0958, m/z = 314.0929, calcd. for C$_9$H$_{14}$NO$_2$Br$^+$: 314.0938.

1-(2-Bromobenzyl)-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline

$[PK_c = 4.67 (0.6)]$

A dry 25-mL Schlenk tube was charged with 1.893 g (10 mmol) 1,2,3,4-tetrahydro-2,2,4,7-tetramethylquinoline, 2.499 g (10 mmol) 2-bromobenzyl bromide, 1.6 g (11.6 mmol) K$_2$CO$_3$, and 0.166 g KI (1 mmol) in 18 mL of dry acetonitrile. The mixture was heated at 110°C for 12 h. The Schlenk tube was cooled and the content filtered. The solid residue was washed with 100 mL of CH$_2$Cl$_2$ and the combined organic solution evaporated under reduced pressure. The crude product was dissolved in mixture of hexane 150 mL and CH$_2$Cl$_2$ 30 mL, passed through a short column with silica gel. The solvent was removed under reduced pressure, and the resulting oil was crystallized from hexane 5 mL to give 1-(2-bromobenzyl)-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline as white crystals; yield: 2.52 g (70%).$^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ = 7.58 (dd, 1H, $J_{HH}$ = 7.6 Hz, $J_{HH}$ = 1.2 Hz), 7.34 (d, 1H, $J_{HH}$ = 7.7 Hz), 7.23 (pseudo t, 1H, $J_{HH}$ = 7.7 Hz), 7.11 (m, 2H), 6.51 (d, 1H, $J_{HH}$ = 7.7 Hz), 6.02 (s, 1H), 4.64 (d, 1H, $J_{HH}$ = 18.4 Hz), 4.21 (d, 1H, $J_{HH}$ = 18.4 Hz), 3.06 (m, 1H), 2.14 (s, 3H), 1.81 (m, 2H), 1.39 (d, 3H, $J_{HH}$ = 6.6 Hz), 1.29 (s, 3H), 1.23 (s, 3H);$^1$C NMR (CDCl$_3$, 75 MHz): $\delta$ = 144.99 (s), 138.85 (s), 136.56 (s), 132.34 (s), 128.80 (s), 128.01 (s), 127.40 (s), 126.12 (s), 124.29 (s), 122.02 (s), 116.96 (s), 112.84 (s), 54.50 (s), 50.54 (s), 46.94 (s), 29.56 (s), 26.95 (s), 24.10 (s), 21.54 (s), 20.50 (s); HR-MS (ESI$^+$-TOF): m/z = 358.1120, calcd. for C$_{17}$H$_{21}$NO$_2$Br$^+$: 358.1165, m/z = 360.1095, calcd. for C$_{17}$H$_{21}$NO$_2$Br$^+$: 360.1146.

8-Isopropyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline

Reactions were performed in 20-mL glass vials sealed with caps. Three Biotage vials were charged with 2.7 g (20.0 mmol) 2-isopropylaniline, 0.51 g (2 mmol) I$_2$ in 15 mL of acetonitrile. The mixtures were heated in a microwave at 150°C (40 W) for 1 h. Vials were cooled and the contents were combined and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane-CH$_2$Cl$_2$, 1:1). After evaporation of solvent the obtained product was hydrogenated under 1.5 atm of H$_2$ and...
room temperature with 0.5 g 5% Pd/C in 80 mL MeOH for 16 h. The content was filtered through silica gel and evaporated under reduced pressure to give 8-isopropyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline as an yellow oil; yield: 8.47 g (65%). 1H NMR (CDCl3, 300 MHz): δ = 7.09 (d, 1H, JHH = 7.7 Hz), 7.01 (d, 1H, JHH = 7.4 Hz), 6.69 (t, 1H, JHH = 7.6 Hz), 3.62 (brs, 1H), 2.96 (m, 1H), 2.82 (m, 1H), 1.77 (dd, 1H, JHH = 12.8 Hz, JHH = 5.6 Hz), 1.47 (m, 1H), 1.37 (d, 3H, JHH = 6.9 Hz), 1.30 (s, 3H), 1.27 (d, 3H, JHH = 7.4 Hz), 1.25 (d, 3H, JHH = 7.7 Hz), 1.21 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ = 119.8 (s), 130.78 (s), 125.25 (s), 124.36 (s), 122.61 (s), 116.24 (s), 49.23 (s), 44.22 (s), 31.95 (s), 28.24 (s), 28.01 (s), 27.09 (s), 22.62 (s), 21.98 (s), 20.63 (s).

1-(2-Bromobenzyl)-8-isopropyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline [pKs = 4.96 (0.6)]

A dry 25-mL Schlenk tube was charged with 2.17 g (10 mmol) 8-isopropyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline, 2.50 g (10 mmol) 2-bromobenzyl bromide, 1.6 g (11.6 mmol) K2CO3, and 0.166 g KI (1 mmol) in 18 mL of dry acetonitrile. The mixture was heated at 95°C for 12 h, then 0.5 g (2 mmol) 2-bromobenzyl bromide and 0.5 g (3.6 mmol) K2CO3 were added and the resulting suspension was refluxed at 95°C for an extra 12 h. The Schlenk tube was cooled and the content filtered. The solid residue was washed with 100 mL of CH2Cl2 and the combined organic solution evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel in hexane to give 1-(2-bromobenzyl)-8-isopropyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline as yellow crystals; yield: 2.2 g (57%). 1H NMR (CDCl3, 300 MHz): δ = 8.02 (d, 1H, JHH = 8.0 Hz), 7.48 (d, 1H, JHH = 8.0 Hz), 7.33 (t, 1H, JHH = 7.6 Hz), 7.11 (m, 3H), 7.02 (t, 1H, JHH = 7.4 Hz), 4.32 (d, 1H, JHH = 18.4 Hz), 3.78 (d, 1H, JHH = 18.4 Hz), 3.31 (septet, 1H, JHH = 6.9 Hz), 2.98 (m, 1H), 1.80 (m, 1H), 1.63 (dd, 1H, JHH = 13.7 Hz, JHH = 8.0 Hz), 1.40 (d, 3H, JHH = 6.9 Hz), 1.12 (s, 3H), 1.09 (d, 3H, JHH = 6.6 Hz), 0.99 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ = 147.88 (s), 146.64 (s), 141.43 (s), 135.33 (s), 132.23 (s), 129.97 (s), 127.65 (s), 126.51 (s), 124.96 (s), 123.90 (s), 123.13 (s), 122.00 (s), 59.34 (s), 54.46 (s), 38.11 (s), 29.60 (s), 29.25 (s), 27.28 (s), 26.73 (s), 24.95 (s), 22.71 (s), 22.07 (s); HR-MS (ESI+-TOF): m/z = 384.1326, calc. for C28H26BrNBr+: 384.1321, m/z = 384.1455, calc. for C28H26BrNBr+H+: 388.1460.

7-Isopropyl-3,3-dimethyl-2-phenyl-3H-indole

A solution of 2-isopropylphenylhydrazine (7.511 g, 50 mmol) and isopropyl phenyl ketone (7.41 g, 50 mmol) in acetic acid (50 mL) was refluxed under reflux (140°C oil bath) for 25 h. After cooling down to room temperature, the solution was evaporated. The crude product was dissolved in 100 mL of CH2Cl2, washed with 1 M K2CO3 (3×50 mL). The organic phase was dried (K2CO3) and concentrated under reduced pressure. The residue was crystallized from petroleum ether to give 7-isopropyl-3,3-dimethyl-2-phenyl-3H-indole as white crystals; yield: 8.5 g (65%). 1H NMR (CDCl3, 300 MHz): δ = 8.18 (m, 2H), 7.49 (m, 3H), 7.23 (m, 3H), 3.90 (septet, 1H, JHH = 6.9 Hz), 1.59 (s, 6H), 1.43 (d, 6H, JHH = 6.9 Hz); 13C NMR (CDCl3, 75 MHz): δ = 181.41 (s), 150.65 (s), 147.58 (s), 141.49 (s), 133.85 (s), 130.06 (s), 128.47 (s), 128.25 (s), 125.95 (s), 124.43 (s), 118.16 (s), 53.45 (s), 28.92 (s), 24.82 (s), 23.54 (s); HR-MS (ESI+-TOF): m/z = 264.1753, calc. for C16H14N2O+: 264.1747, m/z = 286.1567, calc. for C16H14N2ONa+: 286.1566.

7-Isopropyl-3,3-dimethyl-2-phenylindole

A dry 25-mL Schlenk tube was charged with 2.91 g (11 mmol) 7-isopropyl-3,3-dimethyl-2-phenylindoline, 2.74 g (11 mmol) 2-bromobenzyl bromide, 1.8 g (13.0 mmol) K2CO3 and 0.2 g KI (1.2 mmol) in 18 mL of dry acetonitrile. The mixture was heated at 95°C for 6 h. The Schlenk tube was cooled and the content filtered. The solid residue was washed with 100 mL of CH2Cl2 and the combined organic solution evaporated under reduced pressure. The crude product was dissolved in mixture of hexane (150 mL) and CH2Cl2 (30 mL), then passed through a short column with silica gel. The solvent was removed under reduced pressure, and the resulting oil was crystallized from hexane (20 mL) to give 1-(2-bromobenzyl)-7-isopropyl-3,3-dimethyl-2-phenylindoline as white crystals; yield: 4.14 g (87%). 1H NMR (CDCl3, 300 MHz): δ = 7.58 (pseudot, 2H, JHH = 7.7 Hz), 7.25 (brs, 5H), 7.17 (pseudot, 1H, JHH = 7.4 Hz), 7.10 (dd, 1H, JHH = 7.7 Hz, JHH = 1.4 Hz), 7.06 (pseudot, 1H, JHH = 7.4 Hz), 6.92 (dd, 1H, JHH = 7.1 Hz, JHH = 1.4 Hz), 6.85 (t, 1H, JHH = 7.4 Hz), 4.64 (d, 1H, JHH = 18.1 Hz), 4.41 (d, 1H, JHH = 18.1 Hz), 4.34 (s, 11H), 2.97 (septet, 1H, JHH = 6.6 Hz), 1.44 (s, 3H), 1.16 (d, 1H, JHH = 6.9 Hz), 1.14 (d, 1H, JHH = 6.9 Hz), 0.80 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ = 147.20 (s), 139.68 (s), 139.62 (s), 138.85 (s), 132.59 (s), 130.83 (s), 128.63 (s), 128.01 (s), 128.00 (s), 127.99 (s), 127.31 (s), 127.18 (s), 125.55 (s), 122.42 (s), 119.96 (s), 119.74 (s), 81.35 (s), 55.39 (s), 44.55 (s), 30.22 (s), 27.28 (s), 25.50 (s), 24.73 (s), 23.51 (s); HR-MS (ESI+-TOF): m/z = 432.1376, calc. for C20H18N2Br+: 432.1365.
Chiral 7-Isopropyl-3,3-dimethyl-2-phenylindoline

7-Isopropyl-3,3-dimethyl-2-phenyl-3H-indole (3.5 g, 13.3 mmol), Hantzsch dihydropyridine (4.2 g, 16.6 mmol, 1.25 equiv) and 1 mol% of (R)-3'-bis(2,6-trisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (R-TRIP 0.1 g, 0.113 mmol) were suspended in CHCl₃ (25 mL). The resulting mixture was stirred vigorously at room temperature for 20 h. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexane-ethyl acetate, 20:1) to give 7-isopropyl-3,3-dimethyl-2-phenylindoline as a colourless oil with 99% ee; yield: 3.53 g (100%). 1H NMR (CDCl₃, 300 MHz): δ = 7.50 (m, 2H), 7.36 (m, 3H), 7.04 (d, 1H, JHH = 7.7 Hz), 6.95 (dd, 1H, JHH = 7.3 Hz, JHJ = 1.2 Hz), 6.82 (t, 1H, JHH = 6.8 Hz), 4.63 (s, 1H), 4.05 (brs, 1H), 2.90 (septet, 1H, JHH = 6.9 Hz), 1.46 (s, 3H), 1.33 (d, 3H, JHH = 6.9 Hz), 1.31 (d, 3H, JHH = 6.9 Hz), 0.77 (s, 3H). 13C NMR (CDCl₃, 75 MHz): δ = 146.63 (s), 140.28 (s), 137.61 (s), 129.12 (s), 128.04 (s), 127.45 (s), 127.43 (s), 123.55 (s), 119.90 (s), 119.14 (s), 74.38 (s), 65.46 (s), 27.58 (s), 26.76 (s), 19.48 (s), 22.18 (s), 22.10 (s). HPLC (% 2-propanol in n-hexane, flow rate = 0.7 mL/min⁻¹): major enantiomer: τₚ = 7.3 min, minor enantiomer: τₚ = 9.4 min (the absolute configuration was not determined). HIR-MS (ESI⁺-TOF): m/z = 264.1778, calcd. for [C₈H₇N⁺]: 264.1747, m/z = 266.1937, calcd. for C₈H₇N⁺: 266.1903.

Chiral 1-(2-Bromobenzyl)-7-isopropyl-3,3-dimethyl-2-phenylindoline [Pₖ = 4.16 (0.6)]

A dry 25-mL Schlenk tube was charged with 2.91 g (11 mmol) (2R)-7-isopropyl-3,3-dimethyl-2-phenylindoline, 2.74 g (11 mmol) 2-bromobenzyl bromide, 1.8 g (13.0 mmol) K₂CO₃ and 0.2 g KI (1.2 mmol) in 15 mL of dry acetonitrile. The mixture was heated at 95°C for 65 h. The Schlenk tube was cooled and the content filtered. The solid residue was washed with 100 mL of CH₂Cl₂ and the combined organic solution evaporated under reduced pressure. The crude product was dissolved in mixture of hexane (150 mL) and CH₂Cl₂ (30 mL), then passed through a short column with silica gel. The solvent was removed under reduced pressure, and the resulting oil was crystallized from hexane (20 mL) to give chiral-1-(2-bromobenzyl)-7-isopropyl-3,3-dimethyl-2-phenylindoline with >99% ee as white crystals; yield: 4.14 g (87%). 1H NMR (CDCl₃, 300 MHz): δ = 7.58 (pseudo t, 2H, JHH = 7.7 Hz), 7.25 (brs, 5H), 7.17 (pseudo t, 1H, JHH = 7.4 Hz), 7.10 (dd, 1H, JHH = 7.7 Hz, JHJ = 1.4 Hz), 7.06 (pseudo t, 1H, JHH = 7.4 Hz), 6.92 (dd, 1H, JHH = 7.1 Hz, JHJ = 1.4 Hz), 6.85 (t, 1H, JHH = 7.4 Hz), 4.64 (d, 1H, JHH = 18.1 Hz), 4.41 (d, 1H, JHH = 18.1 Hz), 4.34 (s, 1H), 2.97 (septet, 1H, JHH = 6.6 Hz), 1.44 (s, 3H), 1.16 (d, 1H, JHH = 6.9 Hz), 1.14 (d, 1H, JHH = 6.9 Hz), 0.80 (s, 3H), 13C NMR (CDCl₃, 75 MHz): δ = 147.20 (s), 139.68 (s), 139.62 (s), 138.85 (s), 132.59 (s), 130.83 (s), 128.63 (s), 128.01 (s), 128.01 (s), 127.99 (s), 127.31 (s), 127.18 (s), 125.55 (s), 122.42 (s), 119.96 (s), 119.74 (s), 81.55 (s), 55.39 (s), 44.55 (s), 30.22 (s), 27.28 (s), 25.50 (s), 24.73 (s), 23.51 (s); HPLC (0.5% 2-propanol in n-hexane, flow rate = 0.7 mL/min⁻¹): major enantiomer: τₚ = 9.036 min; minor enantiomer: τₚ = 9.411 min; HIR-MS (ESI⁺-TOF): m/z = 432.1376, calcd. for [C₈H₇N⁺]: 432.1369, m/z = 436.1493, calcd. for [C₈H₇N⁺]: 436.1461.
CH₂Cl₂ and the combined organic solution evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel in hexane-CH₂Cl₂ 5:1 to give (2R,4aR,9aS)-9-(2-bromobenzyl)-2-isopropyl-4a-methyl-9a-phenyl-2,3,4,4a,9,9a-hexahydro-1H-carbazole as yellow crystals; yield: 3.42 g (72%). ¹³C NMR (CDCl₃, 300 MHz): δ = 75.5 (d, 1H, J₂₃ = 8.0 Hz), 7.48 (d, 1H, J₃₄ = 7.7 Hz), 7.27-7.14 (m, 4H), 7.11-7.05 (m, 4H), 6.91 (d, 1H, J₂₃ = 7.1 Hz), 6.71 (t, 1H, J₅₆ = 7.3 Hz), 6.26 (d, 1H, J₃₄ = 7.7 Hz), 4.25 (d, 1H, J₃₄ = 18.1 Hz), 4.14 (d, 1H, J₃₄ = 18.1 Hz), 2.39 (m, 2H), 2.06 (m, 1H), 1.69-1.29 (m, 6H), 1.05 (s, 3H), 0.87 (d, 3H, J₃₄ = 3.0 Hz), 0.84 (d, 3H, J₃₄ = 3.0 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ = 150.38 (s), 142.82 (s), 139.56 (s), 138.03 (s), 132.47 (s), 128.92 (s), 128.11 (s), 127.95 (s), 127.87 (s), 127.38 (s), 127.28 (s), 127.63 (s), 124.99 (s), 120.70 (s), 117.71 (s), 105.51 (s), 77.85 (s), 49.16 (s), 48.39 (s), 45.45 (s), 39.24 (s), 32.41 (s), 29.35 (s), 25.56 (s), 19.67 (s), 19.41 (s). HR-MS (ESI⁺-TOF): m/z = 472.1726, calcd. for C₂₆H₂₅N₅Br⁺: 472.1634, m/z = 476.1826, calcd. for C₂₆H₂₅N₅Br⁺H⁺: 476.1775.

Hydroxy[bis(pentafluorophenyl)][(2-[3,3,5,5-tetramethylmorpholin-4-ium-4-yl)methyl]phenyl]borate(1−) (MCATH)

To a solution of 4-(2-bromobenzoyl)-3,3,5,5-tetramethylmorpholinol (0.937 g, 3 mmol) in toluene (15 mL) t-BuLi (3.8 mL, 6.1 mmol, 1.6 M solution in pentane) was added dropwise at −70°C. The solution was allowed to warm up to room temperature in about 30 min and stirred for additional 1 hour. Without further purification the resultant lithium salt suspension was recooled to −80°C and a precooled solution (−70°C) of (CF₃O)₂BCI (1.414 g, 3 mmol) in toluene (5 mL) was added in one portion. Immediately, an intense bright yellow colouration indicated formation of the product. The reaction mixture was stirred overnight at room temperature and the contents were filtered. The present in the filtrate was removed to give the crude product 1-[2-[bis(pentafluorophenyl)]boronyl]benzyl]-2,2,6,6-tetramethylpyperidinedine as an yellow oil; yield: 1.7 g.

Without further purification the product was dissolved in toluene (10 mL) and the resultant solution was degassed once with a freeze-pump-thaw cycle and refilled with H₂ (1.5 atm). The reaction mixture was stirred at 1000 rpm at room temperature for 1 hour, a short period (5 min) of intense precipitation was observed. The reaction mixture was filtered, washed with toluene (3 x 3 mL) to give the final product [hydroxy[bis(pentafluorophenyl)]][(2-[3,3,5,5-tetramethylmorpholin-4-ium-4-yl)methyl]phenyl]borate(1−)] as a white solid; yield: 0.960 g (55%). ¹³C NMR (CDCl₃, 300 MHz): δ = 8.53 (br.s, 1H), 7.18 (m, 4H), 4.43 (s, 1H), 4.41 (s, 1H), 3.73 (d, 2H, J₂₃ = 12.9 Hz), 3.72 (br.q, 1H, J₂₃ = 74 Hz), 3.62 (d, 2H, J₃₄ = 12.9 Hz), 1.62 (s, 6H), 0.97 (s, 6H). ¹²B NMR (CDCl₃, 128 MHz): δ = −20.74 (d, J₂₃ = 75 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ = 147.88 (dm, JCF₂ = 236 Hz), 138.30 (dm, JCF₂ = 245 Hz), 136.82 (dm, JCF₂ = 253 Hz), 136.72 (s), 132.22 (s), 129.96 (s), 129.18 (s), 125.55 (s), 77.63 (s), 64.30 (s), 54.81 (s), 24.18 (s), 20.73 (s), quaternary carbons of CF₂ ring and (CF₃O)₂BCI were not observed.

¹⁷F NMR (CDCl₃, 282 MHz): δ = −132.83 (d, 4F, JCF₂ = 22 Hz, ortho-F), −161.62 (t, 2F, JCF₂ = 20 Hz, para-F), −165.37 (m, 4F, meta-F); HR-MS (ESI⁺-TOF): m/z =

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Hydrodi[bis(pentafluorophenyl)][2-(2,2,4,7-tetramethyl-3,4-dihydroquinolinium-1(2H)-yl) methylpheny]borate(1−) (QCATH2)

To a solution of 1-(2-bromobenzyl)-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline (1.075 g, 3 mmol) in toluene (15 mL) t-BuLi (3.8 mL, 6.1 mmol, 1.6 M solution in pentane) was added dropwise at −80°C. The solution was allowed to warm up to room temperature in about 30 min and stirred for additional 30 min. The resultant lithium salt suspension was recooled to −80°C and a precooled solution (−70°C) of (CF3)3BCl (1.141 g, 3 mmol) in toluene (5 mL) was added in one portion. The reaction mixture was stirred overnight at room temperature and the contents were filtered. The solvent present in the filtrate was removed to give the crude product 1-[bis(pentafluorophenyl)borylbenzyl]-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline as a red oil; yield: 1.8 g.

Without further purification the product was dissolved in mixture of hexane (10 mL) and toluene (10 mL). The resultant solution was degassed once with a freeze-pump-thaw cycle and refilled with H2 (1.5 atm). The reaction mixture was stirred at 1000 rpm at room temperature for 24 h. The reaction mixture was filtered, washed with hexane (3 × 3 mL) to give the final product [hydrodi[bis(pentafluorophenyl)][2-(2,2,4,7-tetramethyl-3,4-dihydroquinolinium-1(2H)-yl)methylpheny]borate(1−)] as a white solid; yield: 0.815 of 43%.1H NMR (CDCl3, 300 MHz) major isomer: δ = 8.93 (br. s, 1H), 7.09−7.32 (m, 4H), 6.81 (pseudo t, 1H, JHH = 7.4 Hz), 6.17 (d, 1H, JHH = 7.4 Hz), 6.34 (dd, 1H, JHH = 10.7 Hz, JHF = 9.1 Hz), 7.44 (1H, 5.10 (d, 3H, JHH = 6.9 Hz), 4.24 (2H, 3H).13C NMR (CDCl3, 128 MHz); δ = -21.16 (d, JHF = 69 Hz).13C NMR (CDCl3, 75 MHz); δ = 148.14 (dm, JCFC = 247 Hz).13C NMR (CDCl3, 128 MHz); δ = 173.17 (s), 136.81 (dm, JCFC = 240 Hz), 136.24 (s), 132.52 (s), 131.43 (s), 130.88 (s), 130.46 (s), 129.87 (s), 129.21 (s), 128.70 (s), 126.21 (s), 124.75 (s), 63.96 (d, s), 57.51 (s), 27.37 (s), 25.39 (s), 25.32 (s), 22.21 (s), 20.29 (s), quaternary carbons of CF3 ring and (CF3)2BCl2 were not observed;19F NMR (CDCl3, 282 MHz); δ = -131.80 (d, 2F, JCF = 21.4 Hz, ortho-F, -134.01 (d, 2F, JCF = 21.4 Hz, ortho-F, -161.95 (t, 2F, JCF = 21.4 Hz, para-F, -165.35 (m, 2F, meta-F, -165.85 (m, 2F, meta-F); HR-MS (ESI+TOF); m/z = 624.1944, calculated for [C6H5B(NF3)2]+: 624.1920; HR-MS (ESI-TOF); m/z = 624.1967, calculated for [C6H5B(NF3)2]+: 624.1926.

Chiral Hydrodi[bis(pentafluorophenyl)][2-(2,2,4,7-tetramethyl-3,4-dihydroquinolinium-1(2H)-yl)methylpheny]borate(1−) (Q+CATH1)

To a solution of chiral 1-(2-bromobenzyl)-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline (1.075 g, 3 mmol) in toluene (15 mL) t-BuLi (3.8 mL, 6.1 mmol, 1.6 M solution in pentane) was added dropwise at −80°C. The solution was allowed to warm up to room temperature in about 30 min and stirred for additional 30 min. The resultant lithium salt suspension was recooled to −80°C and a precooled solution (−70°C) of (CF3)3BCl (1.141 g, 3 mmol) in toluene (5 mL) was added in one portion. The reaction mixture was stirred overnight at room temperature and the contents were filtered. The solvent present in the filtrate was removed to give the crude product 1-[bis(pentafluorophenyl)borylbenzyl]-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline as a red oil; yield: 1.8 g.

Without further purification the product was dissolved in mixture of hexane (10 mL) and toluene (10 mL). The resultant solution was degassed once with a freeze-pump-thaw cycle and refilled with H2 (1.5 atm). The reaction mixture was stirred at 1000 rpm at room temperature for 1 hour, a
The resultant solution was concentrated to 10 mL, degassed once with a freeze-pump-thaw cycle and refilled with H₂ (1.5 atm). The reaction mixture was stirred at 1000 rpm at room temperature for 12 hours, a short period (5 min) of intense precipitation was observed. The reaction mixture was filtered, washed with hexane (3x10 mL) to give the final product hydroxy[2-[7-isopropyl-3,3-dimethyl-2-phenyl-2,3-dihydro-1H-indolium-1-yl]methylphenyl]bis(pentafluorophenyl)borate(1−) as a white solid; yield: 1.250 g (76%).

**rac-Hydroxy[2-[7-isopropyl-3,3-dimethyl-2-phenyl-2,3-dihydro-1H-indolium-1-yl]methylphenyl]bis(pentafluorophenyl)borate(1−) (rPr(iCATH)₂)**

To a solution of 1-(2-bromobenzoyl)-7-isopropyl-3,3-dimethyl-2-phenylindoline or ||2R||-1-(2-bromobenzyl)-7-isopropyl-3,3-dimethyl-2-phenylindoline (1.303 g, 3 mmol) in toluene (15 mL) t-BuLi (4.1 mL, 6.1 mmol, 1.5M solution in pentane) was added dropwise at −80°C. The solution was allowed to warm up to room temperature in about 30 min and stirred for additional 30 min. The resultant lithium salt suspension was recooled to −80°C and a precooled solution (−70°C) of (C₆F₅)₂BCl (1.141 g, 3 mmol) in toluene (5 mL) was added in one portion. The reaction mixture was stirred overnight at room temperature and the contents were filtered. The solvent present in the filtrate was removed to give the crude product 1-[2-[bis(pentafluorophenyl)boronyl]benzyl]-7-isopropyl-3,3-dimethyl-2-phenylindoline as a red oil; yield: 2.2 g.

The product was dissolved in hexane (40 mL). After 6 h stirring at ambient temperature, the mixture was filtered.
1-[2-[(Pentafluorophenyl)boryl]benzyl]-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline (QCATH)

In a glass box, a 25-mL flame-dried Schlenk tube equipped with a stir bar, a Teflon stopcock and a glass stopper (Glindemann® sealing rings were used for conical joints instead of grease) was charged with ansa-ansaammonium borate QCATH (0.1 mmol, 62.5 mg) and 1.0 mL dry toluene. The reaction mixture was degassed once with a freeze-pump-thaw cycle, stirred at 1000 rpm and 80°C for 15 h or 110°C for 5 min. All volatiles were removed under vacuum to give 1-[2-[(pentafluorophenyl)boryl]benzyl]-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline as a red oil; yield: 62.3 mg (100%). 1H NMR (CDCl3, 300 MHz): δ = 7.52 (d, JHH = 7.7 Hz), 7.16 (m, 2H), 7.05 (m, 2H), 6.59 (d, JHH = 7.4 Hz), 6.32 (s, 1H), 4.69 (d, JHH = 17.6 Hz), 4.24 (d, JHH = 17.6 Hz), 2.75 (m, 1H), 2.15 (s, 3H), 1.51 (m, 2H), 1.22 (d, JHH = 6.6 Hz), 1.00 (s, 3H), 0.85 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ = 147.67 (d, JCFP = 247 Hz). 146.64 (s), 144.01 (dm, JCFP = 247 Hz), 145.44 (s), 137.78 (dm, JCFP = 254 Hz), 136.82 (s), 134.16 (s), 133.77 (s), 128.06 (s), 126.84 (s), 126.79 (s), 118.65 (s), 114.15 (s), 54.80 (s), 51.12 (s), 47.02 (s), 29.23 (s), 27.283 (s), 23.69 (s), 21.42 (s), 20.56 (s); quaternary carbons of CF3 ring and (CF3)2BCl2 were not observed: 19F NMR (CDCl3, 282 MHz): δ = 129.15 (d, JFF = 17 Hz, ortho-CF3), 146.28 (t, JFF = 19 Hz, para-CF3), 161.01 (m, 4F, meta-CF3); HR-MS (ESI-TOF): m/z = 646.1748, calcd. for C24H21BFN2Na*Na+. 644.1740.

1-[2-[(Pentafluorophenyl)boryl]benzyl]-7-iso-propyl-3,3-dimethyl-2-phenylindoline (iPrQCAT)

In a glass box, a 25-mL flame-dried Schlenk tube equipped with a stir bar, a Teflon stopcock and a glass stopper (Glindemann® sealing rings were used for conical joints instead of grease) was charged with ansa-ansaammonium borate iPrQCAT (0.1 mmol, 70.1 mg) and 1.0 mL dry toluene. The reaction mixture was degassed once with a freeze-pump-thaw cycle, stirred at 1000 rpm and 110°C for 5 min. All volatiles were removed under vacuum to give (2R)-1-[2-[[pentafluorophenyl]boryl]benzyl]-7-iso-propyl-3,3-dimethyl-2-phenylindoline as a red oil; yield: 69.9 mg (100%). 1H NMR (CDCl3, 300 MHz): δ = 7.67 (d, JHH = 7.4 Hz), 7.27-8.67 (m, 11H), 4.79 (d, JHH = 17.6 Hz), 4.45 (d, JHH = 17.6 Hz), 4.36 (s, 1H), 3.15 (m, 1H), 1.29 (s, 3H), 1.21 (m, 3H), 1.07 (s, 3H), 0.74 (s, 3H); 13C NMR (CDCl3, 128 MHz): δ = 63.44 (br. s); 19F NMR (CDCl3, 75 MHz): δ = 147.23 (dm, JCFP = 254 Hz). 146.64 (s), 144.00 (dm, JCFP = 254 Hz), 139.46 (s), 139.06 (s), 137.61 (dm, JCFP = 254 Hz), 134.91 (s), 133.64 (s), 130.37 (s), 128.19 (s), 127.85 (s), 126.81 (s), 126.36 (s), 126.13 (s), 120.59 (s), 120.56 (s), 81.02 (s), 53.95 (s), 44.30 (s), 29.69 (s), 27.63 (s), 25.80 (s), 25.35 (s), 23.22 (s), quaternary carbons of CF3 ring and (CF3)2BCl2 were not observed: 19F NMR (CDCl3, 282 MHz): δ = 129.35 (d, JFF = 21.4 Hz, ortho-CF3), 146.52 (t, JFF = 21.4 Hz, para-CF3), 161.00 (m, 4F, meta-CF3); HR-MS (ESI-TOF): m/z = 722.2054, calcd. for C24H21BFN2Na*Na+. 722.2002.

(2R,4aR,9aS)-9-[2-[Pentafluorophenyl]boryl]benzyl]-2-isopropyl-4a-methyl-9a-phanyl-2,3,4,4a,9a-hexahydro-1H-carbazole (S-CarCAT)

To a solution of (2R,4aR,9aS)-9-(2-bromobenzyl)-2-isopropyl-4a-methyl-9a-phanyl-2,3,4,4a,9a-hexahydro-1H-carbazole (0.797 g, 1.68 mmol) in toluene (10 mL) t-BuLi (2.2 mL, 3.5 mmol, 1.6 M solution in pentane) was added dropwise at -80°C. The solution was allowed to warm up to room temperature in about 30 min and stirred for additional 30 min. The resultant lithium salt suspension was recooled to -80°C and a precooled solution (-70°C) of (CF3)2BCl (0.640 g, 1.68 mmol) in toluene (5 mL) was added in one portion. The reaction mixture was stirred overnight at room temperature and the contents were filtered. The solvent present in the filtrate was removed to give the crude product (2R,4aR,9aS)-9-[2-[pentafluorophenyl]boryl]benzyl]-2-isopropyl-4a-methyl-9a-phanyl-2,3,4,4a,9a-hexahydro-1H-carbazole as a red oil; yield: 1.03 g.

The product was dissolved in hexane (10 mL). After 1 h stirring at ambient temperature, the mixture was filtered.

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The resultant solution was cooled to -80°C and allowed to warm up to room temperature in about 30 min. The reaction mixture was filtered and this procedure was repeated twice to give the final product as a red oil; yield: 0.590 g (47%). 

^1H NMR (CDCl₃, 300 MHz): δ = 7.69 (d, 1H, J₆,H₇ = 7.7 Hz), 7.57 (pseudo t, 1H, J₆,H₇ = 7.6 Hz), 7.42 (d, 1H, J₆,H₇ = 7.0 Hz). 7.32 (pseudo t, 1H, J₆,H₇ = 7.7 Hz), 7.20-7.00 (m, 6H), 6.90 (pseudo t, 1H, J₆,H₇ = 7.0 Hz), 6.73 (t, 1H, J₆,H₇ = 7.7 Hz), 6.72 (d, 1H, J₆,H₇ = 7.7 Hz), 3.90 (s, 2H), 2.40-2.20 (m, 1H), 1.90-1.28 (m, 7H), 1.27 (s, 3H), 0.88 (d, 3H, J₆,H₇ = 7.2 Hz), 0.88 (d, 3H, J₆,H₇ = 7.2 Hz). 13C NMR (CDCl₃, 128 MHz): δ = 151.01 (s), 147.15 (s), 146.30 (dm, J₁C=245 Hz), 142.56 (s), 140.11 (dm, J₁C=245 Hz), 137.34 (s), 137.27 (dm, J₁C=245 Hz), 135.13 (s), 128.01 (s), 127.82 (s), 127.54 (s), 127.44 (s), 127.26 (s), 126.84 (s), 126.70 (s), 120.69 (s), 118.13 (s), 117.33 (s), 105.52 (s), 77.58 (s), 50.42 (s), 48.64 (s), 46.01 (s), 39.16 (s), 32.38 (s), 29.68 (s), 25.68 (s), 19.73 (s), 19.50 (s), quaternary carbons of C₂F₅ ring and (C₂F₅)₂B(C₆H₅) were not observed. 

^27Al NMR (CDCl₃, 282 MHz): δ = -129.70 (d, 2F, J₆,F = 24.4 Hz, ortho-F), -129.73 (d, 2F, J₆,F = 24.4 Hz, ortho-F). 

Typical Hydrogenation Procedure

In a glove box, a 25-mL flame-dried Schlenk tube equipped with a stir bar, a Teflon stopcock and a glass stopper (Glim- demann®-sealing rings were used for conical joints instead of grease) was charged with ansa-ammotonin borate (0.01 mmol), 5 mL dry toluene and imine (0.25-1 mmol). The reaction mixture was degassed once with a freeze-pump-thaw cycle and refilled with H₂ (2 atm). The reaction mixture was stirred at 1000 rpm and a suitable temperature for a suitable time. All volatiles were removed under vacuum to give the product (Table 1). The amimes were not purified from residual catalyst but identified by comparison of their ^1H NMR spectra with literature values.

Scaled-Up Hydrogenation of N-(4-Methoxyphenyl)-1-phenylethylidenecaine

In a glove box, a 1-L flame-dried, round-bottom Schlenk flask equipped with a stirrer bar, a Teflon stopcock and a glass stopper (Glimdemann®-sealing rings were used for conical joints instead of grease) was charged with ansa-ammotonin borate QCATIH (1 mol-\%, 156 mg, 0.25 mmol), 125 mL dry Et₂O and N-(4-methoxyphenyl)-1-phenylethylidenecaine Id (5.632 g, 25 mmol). The reaction mixture was degassed once with a freeze-pump-thaw cycle and refilled with H₂ (1.6 atm). The reaction mixture was stirred at 700 rpm and at 50°C for 2 h. The Et₂O solution was extracted with warm 1 N HCl (3 × 150 mL). The aqueous solution was basified to pH 12 with NaOH and extracted with CH₂Cl₂ (3 × 50 mL). The resulting organic layer was stirred over K₂CO₃, passed through a short column with silica gel and evaporated to give N-(4-methoxyphenyl)-1-phenylethylidenecaine as white crystals; yield: 5.535 g (97%); mp 65-66°C. The ^1H NMR and ^13C NMR data were identical to literature values. 

^1H NMR (CDCl₃, 300 MHz): δ = 7.26-7.39 (m, 5H), 6.70 (d, 2H, J₆,H₇ = 8.9 Hz), 6.48 (d, 2H, J₆,H₇ = 8.9 Hz), 4.42 (q, 1H, J₆,H₇ = 6.6 Hz), 3.79 (br. s, 1H), 3.70 (s, 3H), 1.51 (d, 3H, J₆,H₇ = 6.9 Hz); 13C NMR (CDCl₃, 75 MHz): δ = 151.86 (s), 145.45 (s), 141.54 (s), 128.55 (s), 126.75 (s), 125.84 (s), 114.73 (s), 114.51 (s), 55.67 (s), 53.45 (s), 25.05 (s).

Catalyst Recovery Procedure under an Argon Atmosphere

The organic solution obtained after extraction of the amine with warm 1 M HCl was evaporated. The obtained solid was dissolved in 150 mL of CH₂Cl₂, basified to pH 12 with aqueous NaOH, and heated to 40°C. The resulting organic layer was separated, dried over Na₂SO₄ and evaporated. The product was dissolved in 2 mL of dry benzene and TMSBr (191 mg, 1.25 mmol). After the solution had been refluxed for 5 min. and then evaporated under vacuum, the crude ansa-aminoborane QCAT was obtained; yield: 95% yield.

Without further purification the product was dissolved in a mixture of hexane (1 mL) and toluene (1 mL). The resulting solution was degassed once with a freeze-pump-thaw cycle and refilled with H₂ (1.5 atm). The reaction mixture was stirred at 1000 rpm at room temperature for 1 hour, and a short period (5 min) of intense precipitation was observed. The reaction mixture was filtered, washed with hexane (3 × 1 mL) to give the final product QCATH yield: 125 mg (80%).

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References


[14] The pKₐ values of the corresponding N-benzylamines were predicted by ACD/Labs software version 5.11 software, see Supporting Information.


[16] According to H NMR and X-Ray diffraction studies, iPrQCAH, exists as a mixture of diastereomers at the C-4 atom of the tetrahydroquinoline ring (2.1:1 cis/trans).

[17] According to ²⁷F NMR of QCAH, iPrQCAH, and iPrICAH, their perfluorophenyl rings are not equal, presumably due to a significant barrier of rotation.

[18] The X-ray crystal structure studies of MCAH and QCAH showed that the N–H–H–B dihydrogen bonds (DHB) presented in the structures were extremely short, in the order of 1.65 Å. While DHBs in iPrQCAH, iPrICAH, are much longer: 1.93 Å and 1.96 Å, respectively. See Supporting Information. Crystallographic data (excluding structure factors) for the structure reported in this work have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 804254 (MCATH), CCDC 804255 (QCAH), CCDC 804256 (iPrQCAH), and CCDC 804257 (iPrICAH). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif or on application to The Director, CCDC, 12 Union Road, Cambridge DB2 1EZ, UK (Fax: int.code: +(1223)–336–033; e-mail: deposit@ccdc.cam.ac.uk).

[19] It is noted that the real N–H⋯H–B dihydrogen bond distance in ansa-ammonium borates should be 10–15% shorter than those observed by X-ray diffraction. Due to the tendency of the X-ray technique to give too short X–H bonds, compared to neutron scattering; see: T. Steiner, *Angew. Chem. 2002*, 114, 50–80; *Angew. Chem. Int. Ed.* **2002**, 41, 48–76.

[20] Ansa-ammonium borates are only slightly soluble in toluene at room temperature.


[23] Two sets of different perfluorophenyl signals were observed in solution by ²⁷F NMR in the case of QCAH, iPrQCAH and iPrICAH. These findings highlight a significant barrier of rotation of B(CF₃)₂ moiety around the B–C bond, which caused a fixed conformation of ansa-ammonium borates. Moreover, the X-ray structures of all ansa-ammonium borates exhibited the presence of additional hydrogen bonds between methyl or phenyl C–H and perfluorophenyl F–C atoms. Additionally, in the X-ray structure of iPrICAH, a strong intramolecular phenyl-perfluorophenyl π–π stacking of 3.7 Å was found.


[26] (R)-3,3′-Bis(2,4,6-trisopropylphenyl)-1,1′-binaphthyl-2,2′-dil hydrogen phosphate.

[27] M. Rueping, M. Stöckel, T. Theissmann, announced manuscript.


Heterolytic dihydrogen activation by B(C₆F₅)₃ and carbonyl compounds†

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Aromatic carbonyl compounds in combination with B(C₆F₅)₃ are able to activate H₂ heterolytically. The reactivity of the carbonyl-B(C₆F₅)₃ adduct is initiated by its thermal dissociation into components. After H₂ addition, aromatic carbonyl compounds convert into aryl-substituted methanes or alcohols.

Metal-free activation of small molecules, such as NH₃, C₂H₄, CO, CO₂ and especially H₂, has in the last few years attracted an increasing scientific and practical interest.¹ Main-group compounds consisting of merely lightweight elements could serve as potential hydrogen storage materials and hydrogenation catalysts.² The first example of H–H bond activation under mild conditions by a non-metal compound (ArGeGeAr) was published by Power and co-workers in 2005.³ Later, it has been shown that certain bulky alkylaminocarbene⁴ and antiaromatic boroles⁵ react with hydrogen gas leading to H–H bond cleavage.

A real breakthrough in hydrogen activation was the discovery of frustrated Lewis pairs (FLPs).⁶ Unquenched reactivity existing between bulky and strongly acidic perfluoropolyboranes and hindered phosphines,⁷,⁸ amines⁹ or even carbenes as well as other low-valent carbon bases¹⁰,¹¹ enable facile splitting of H₂ and other small molecules. The products of H₂ activation, the respectiveoniumborohydrides, are powerful reducing agents and effective catalysts for the hydrogenation of silyl enol ethers,¹² imines, enamines, and nitrogen-containing heterocycles¹³–¹⁴ as well as stoichiometric hydrogenation of benzaldehyde¹⁵ and CO₂.¹⁶

To the best of our knowledge, all experiments to employ oxygen-containing Lewis bases in the presence of Lewis acidic boranes as components of FLPs for the splitting of molecular hydrogen have failed so far. The high affinity of boron to oxygen and low basicity of ethers or carbonyl compounds favour the formation of classical Lewis adducts instead. Nevertheless, we show that aromatic carbonyl compounds can act as non-classical Lewis bases in H₂-splitting mediated by oxygen–boron FLPs.¹⁷ In combination with B(C₆F₅)₃, they are able to activate H₂, resulting in hydrogenation of the carbonyl group.

In the first experiments, stoichiometric amounts of benzaldehyde 1 and B(C₆F₅)₃ were mixed in toluene-d₈, forming a classical Lewis acid–base adduct. No change was observed upon heating this solution at 110 °C under an inert atmosphere. However, when argon was substituted with hydrogen gas (2 atm), heating of the same solution of components showed the occurrence of a chemical reaction in the mixture. Upon an aqueous work-up, the ¹H-NMR spectrum of the obtained organic residue featured signals at 6 7.35–7.13 and 4.62 ppm belonging to benzyl alcohol 3 in addition to the ¹H-NMR pattern of the starting benzaldehyde at 6 10.03, 7.89, 7.65 and 7.55 ppm. Formation of benzyl alcohol 3 indicated that splitting of the H–H bond occurred, subsequently proceeding to hydrogenation of the benzaldehyde carbonyl group (Scheme 1). The conversion to benzyl alcohol 3 was calculated to be 29%.

Analogous heating of benzophenone 4 together with B(C₆F₅)₃ in toluene-d₈ led to rather unexpected results. Whereas the appearance of diphenylmethanol as a result of hydrogenation

Scheme 1 Hydrogenations using benzaldehyde–B(C₆F₅)₃ and benzophenone–B(C₆F₅)₃ adducts in toluene-d₈.
was anticipated, diphenyl(tolyl)methane was found to be an ultimate product of the reaction (Scheme 1). A detailed study of the obtained 1H-NMR data showed that 75% of starting benzophenone 4 was converted into an isomeric mixture of diphenyl(p-tolyl-d₄)-methane 6a and diphenyl(o-tolyl-d₄)-methane 6b obtained in a 9:1 ratio. The products 6a and 6b featured 1H-NMR signals of the CH protons at δ 5.50 and 5.60 ppm and phenyl groups in the region of δ 7.33–6.95 ppm that were easily distinguished from benzophenone 4 (1H-NMR, CDCl₃: δ 7.80, 7.61, 7.49 ppm). Presumably, diphenyl(p-tolyl-d₄)-methanes were produced in Friedel–Crafts alkylation of the solvent, toluene-d₄, with an intermediately formed diphenylmethanol-B(C₆F₅)₃ adduct 5. Elimination of the hydroxyl group from 5 might be facilitated by the formation of the Ph₂CH⁺ cation, which reacted further with toluene-d₄ to give the compounds 6a and 6b. Other products of the reaction were C₆F₅H (7) and (C₆F₅)₂BOH (8) (see below). In order to prove the proposed reaction sequence, a diphenylmethanol-B(C₆F₅)₃ mixture was heated in toluene-d₄ under similar conditions giving the isomeric products 6a and 6b in the same ratio. Diphenyl(tolyl)methanes 6-D substituted with deuterium at the former carbonyl carbon atom were produced from a stoichiometric benzophenone-B(C₆F₅)₃ mixture by the splitting of deuterium gas in analogous conditions, using toluene as solvent. These results showed that hydrogenation of the carbonyl group in the substrates 1 and 4 was provided by hydrogen gas, and not by the solvent. However, the ultimate product output depended on the used solvent. Whereas hydrogenation of 1 and 4 in toluene gave either benzyl alcohol 3 or a mixture of triarylmethanes 6 (see above), hydrogenations carried out in CDCl₃ gave different products (Scheme 2). A stoichiometric mixture of benzaldehyde 1 and B(C₆F₅)₃ in CDCl₃ produced toluene 9 as the final product of hydrogenation upon heating at 110 °C in the presence of hydrogen gas (2 atm). Signals, corresponding to the formed toluene, were found in the 1H-NMR spectrum of the resulting mixture (1H-NMR, CDCl₃: δ 7.32–7.05 and 2.34 ppm), alongside signals belonging to the starting material. Hydrogenation of benzophenone 4 at the same conditions provided diphenylmethane 10, which was identified by a characteristic 1H-NMR singlet of the CH₂ group at δ 3.97 ppm. The conversion of 1 and 4 into the fully hydrogenated products 9 and 10 was 40% and 45%, respectively. In these reactions, FLP-mediated hydrogenation initially led to the corresponding alcohol-B(C₆F₅)₃ adducts. Besides the products 9 and 10, the presence of C₆F₅H was also detected in the resulting mixtures. This points out that further deoxygenation of the initially formed alcohol-B(C₆F₅)₃ adducts occurred with active participation of the B(C₆F₅)₃ species. Two reaction pathways might be proposed for this reaction step, either direct elimination of the hydroxyl group by an electrophilic B(C₆F₅)₃ attack or dissipation of the intermediate diphenylmethanol-B(C₆F₅)₃ adduct onto benzophenone and diphenylmethane. The former mechanism can be realized only in the presence of hydrogen gas, while the second route does not require a hydrogen atmosphere. In a control experiment, the heating of a 1:1 diphenylmethanol-B(C₆F₅)₃ mixture at 110 °C under argon gave a 1:1 mixture of benzophenone and diphenylmethane. Based on this fact, B(C₆F₅)₃-mediated dissipation of diphenylmethanol could be accepted as a plausible route to fully hydrogenated arylalkane 10. It is worth mentioning here that hydrogenation of 1 and 4 did not occur in heptane, possibly due to the low ability of non-polar solvents to stabilize the zwitter-ionic intermediate species. Only the intact adducts were observed after heating the starting mixtures at 110 °C under 2 atm of H₂ for 48 h.

Neither benzaldehyde nor benzophenone could be fully reduced by prolonged heating, because all B(C₆F₅)₃ was decomposed or deactivated within the first 48 hours. In another approach, by simply increasing the amount of B(C₆F₅)₃, side-reactions began to dominate, which did not improve the yield of the partly or fully hydrogenated products.

As was mentioned already above, C₆F₅H (7), (C₆F₅)₂BOH (8) and the B(C₆F₅)₃-H₂O adduct were identified by ¹H and ¹⁹F-NMR spectroscopy and mass spectrometry as the major fluorine-containing products of the hydrogenation reaction.¹⁵ In the presence of water traces, B(C₆F₅)₃ hydrolyzes into C₆F₅H and boronic acids, (C₆F₅)₂BOH acid being the first product of hydrolysis. It has been shown earlier that B(C₆F₅)₃ works as a H₂O scavenger when added to (C₆F₅)₂BOH, promoting formation of boric acid anhydride and a B(C₆F₅)₃-H₂O adduct.¹⁶

In general, catalytic reduction of carbonyl compounds with H₂ by main group elements has proven to be a difficult task. To the best of our knowledge, there is only one catalytic transition metal-free system able to hydrogenate ketones. This purely base-catalyzed reaction works under extremely harsh conditions (210 °C, 135 atm of H₂) with at least 20% mol of potassium tert-butoxide and is limited to non-nucleophilic ketones.²⁰

The successful stoichiometric reduction of benzaldehyde under ambient conditions with both phosphonium and ammonium borohydrides, encouraged the use of such compounds as hydrogen transfer reagents.¹⁵ However, the successful catalytic hydrogenation of carbonyl compounds with hydrogen gas mediated by FLP systems could still not be achieved, probably due to the high affinity of boron to oxygen.¹⁰

On the other hand, it has been shown that the dissociation energy of carbonyl-B(C₆F₅)₃ adducts is quite small even at room temperature. For instance, the energy required for dissociation of the benzaldehyde-B(C₆F₅)₃ adduct is only about 5.8 kcal mol⁻¹.²¹ Even so, heating of the reaction mixture is required to promote dissociation of this classical Lewis adduct into a frustrated Lewis pair. No H₂ activation could be detected for the benzaldehyde-B(C₆F₅)₃ system at ambient temperature by ¹H NMR spectroscopy, even though a significant peak corresponding to molecular hydrogen was recorded in the solution.²²
According to the computational study by Nyhlén and Privolov,23 HOMOs of ketones are quite close in energy to the HOMO of $\beta$BuN(H)CH$_2$Ph, which has been reported to cleave H$_2$ together with B(C$_6$F$_{13}$)$_3$ at 4 atm pressure and 80 °C. Nevertheless, due to the fact that the carbonyl oxygen is a much weaker base than previously studied amines and phosphines,24 a higher energy for activation of H$_2$ is to be expected.23

In conclusion, aromatic carbonyl compounds mixed with B(C$_6$F$_{13}$)$_3$ activate H$_2$. Initially, the carbonyl compounds and B(C$_6$F$_{13}$)$_3$ give classical Lewis acid–base coordination adducts at ambient temperature. Based on the calculated results23 and the products observed in the experiments, the reaction is likely to occur at elevated temperatures through heterolytic splitting of the H–H bond by a dissociated carbonyl–B(C$_6$F$_{13}$)$_3$ system, which is thermally promoted in an equilibrium with the classical coordination adduct. This was not detected directly, but was evidently established by an observed subsequent hydrogenation of the carbonyl moiety. The reaction outcome depends on the substrate and solvent used. In contrast to earlier described phosphorus- or nitrogen-based FLPs, the basicity of carbonyl compounds is much lower and the corresponding oxonium borohydride species should be an extremely unstable intermediate and cannot be detected by conventional methods. Nevertheless, the reactions seem to be pushed forward by the formation of the thermodynamically stable alcohol–B(C$_6$F$_{13}$)$_3$ adducts and their subsequent transformations into hydrogenated species.

The experimental evidence that Lewis basicity of carbonyl compounds is sufficient in cooperation with B(C$_6$F$_{13}$)$_3$ for hydrogen splitting extends the concept of small molecule activation with frustrated Lewis pairs. Further studies on forming catalytic systems by keeping the FLP system intact during the reaction are underway.

Acknowledgements
We are grateful for the financial support from the Academy of Finland (139550).

Notes and references
16. No reactions were observed with dihydrogen and B(C$_6$F$_{13}$)$_3$ adducts of hindered bulky diaxylketones, such as diadamantyl ketone, 2,2,4,4-tetramethyl-2-pentanone and furfural. It was also found that they could not be reduced even with highly active TMP'HB(C$_6$F$_{13}$)$_3$' (TMP is 2,2,6,6-tetramethylpiperidine).
17. C$_2$H$_4$: NMR (300 MHz toluene-d$_8$): δ 1.75 (m, 3H, C$_2$H$_4$); $^1$H NMR (300 MHz toluene-d$_8$): δ -139.66 (dt, 2F, m-F); δ-154.71 (t, 1F, p-F), δ-162.97 (m, 2F, m-F); (C$_6$F$_{13}$)$_3$BOH: HRMS (ESI, $^+$ CHCl$_3$) $m/z$ [(C$_6$F$_{13}$)$_3$BOH] $^+$ obs 360.989; calc 360.988; error 1.993 ppm; B (C$_6$F$_{13}$)$_3$: $^1$H NMR (ESI, $^+$ CHCl$_3$) $m/z$ [(C$_6$F$_{13}$)$_3$H$_2$] $^+$ obs 528.989; calc 528.988; error 0.552 ppm.
23. It was shown recently that some quinolines can be effectively hydrogenated with B(C$_6$F$_{13}$)$_3$ even though they produce weak Lewis acid–base adducts: S. J. Geier, P. A. Chase and D. W. Stephan, Chem. Commun., 2010, 46, 4884.
Hydrogen activation by 2-boryl-N,N-dialkylnilines: a revision of Piers’ ansa-aminoborane†

Konstantin Chernichenko, Martin Niegę, Markku Leskelä and Timo Repo*

Two 2-[bis(pentafluorophenyl)boryl]-N,N-dialkylnilines reported here exemplify a new class of intramolecular frustrated B/N Lewis pairs. A structure closely related to this class structure was synthesized in 2003 by Piers et al. but was unable to activate H₂. The new aminoboranes can activate hydrogen at near ambient conditions; besides, one of them can hydrogenate imines and enamines in a catalytic fashion demonstrating the validity of the original Piers’ approach to hydrogen activation with ansa-aminoboranes.

Frustrated Lewis pairs (FLPs) is a rapidly developing concept in contemporary chemistry and catalysis.¹ The idea of the substrate activation by a mutual action of both a Lewis acid and base is not new and has been successfully used in transition metal catalysis.² On the other hand, the frustrated Lewis pairs comprising lightweight main-group elements and their reactivity have been known for decades.³ Nevertheless, a real breakthrough in this area was brought by Stephan et al. in 2006 in their pioneering work on the activation of elemental hydrogen with phosphinoborane (C₅F₅)₃BC₅F₅PMe₅.⁴ This initial finding boosted research activity in this field leading to more than two hundred papers on activation of hydrogen and other small molecules.⁵ Whereas a variety of small molecules have been activated by FLPs, the most important achievement and practical application is FLP-catalyzed hydrogenation of polar double bonds.⁶,⁷

In 2003, Piers et al. described an approach for hydrogen activation by a bridged frustrated aminoborane, emphasizing the importance of the highly Lewis acidic bis(pentafluorophenyl)boryl group. As an example, aminoborane 1 was synthesized (Fig. 1).⁸ Attempts to activate hydrogen with 1 were unsuccessful. This paper has presumably therefore been sparingly cited in later publications.

Herein we report two new compounds closely related to the original ansa-aminoborane 1. In these molecules the diphenylamino moiety was substituted with more basic 2,2,6,6-tetramethylpiperidine-1 (TMP) (2) or dimethylamino (3) groups. Both 2 and 3 readily activate H₂ at ambient conditions, demonstrating that Piers et al. were very close to successful hydrogen activation using a solely main-group compound (Fig. 1).

Recently, we have reported the ansa-aminoboranes 4 and 5, which efficiently transfer molecular hydrogen to imines and other nitrogen-containing compounds in a catalytic fashion.⁸,⁹ Asymmetric hydrogenations have been attempted by introducing chiral amines into frameworks of the catalysts (e.g. (S)-5) but only fair enantioselective inductions (up to 38% ee) were achieved. We attributed this to excessive conformational freedom of the catalyst molecules (Fig. 1). In this regard removal of the methylene junction between the phenylene ring and the amino groups may lead to more rigid molecules with superior asymmetric effectiveness. To the best of our knowledge, 1 is the only 2-[bis(pentafluorophenyl)boryl]-aniline that has been aimed for H₂ activation, although some other structures with nitrogen-containing groups in the ortho-position to the bis(pentafluorophenyl)boryl moiety are known.¹⁰ Hence, the achiral ansa-aminoboranes 2 and 3 were prepared to test their reactivity towards hydrogen and evaluate potential catalytic activity in hydrogenations.

Results

The ansa-aminoboranes 2 and 3 were prepared in high yield by the standard approach⁸,⁹ from bis(pentafluorophenyl)boron chloride 1¹¹ and o,N,N-dialkylnilinophenyllithiums 9 and 10 (Scheme 1). A one-step synthesis starting from iodobenzene and LTMP was previously reported to give 1-(2-iodophenyl)-2,2,6,6-tetramethylpiperidine 7 in 81% yield.¹² Since no exact
procedure was reported for 7, we were able to synthesize it in ca. 30% reproducible yield only. The respective lithium compounds 9 and 10 were isolated from the reaction of 7 or N,N-dimethyl-2-bromoaniline 8 with butyllithium in hexane at 0 °C. It is worth noting that isolation of pure 9 and 10 is beneficial as the subsequent reaction with (C₆F₅)₂BCl 11 gives 3 in high yield, and 2 almost quantitatively.

The aminoborane 2 was isolated as deeply coloured yellow crystals. NMR data, especially the $^{19}$F-NMR spectrum, which contains resonances at -127.2, -149.3 and -162.1 ppm, are consistent with three-coordinated boron species and reveal the “frustration” between the B and N centres. Colours from yellow to deep bloody red are typical for bridged phosphino- and aminoboranes, and the aminoborane 2 is not an exception in this respect. In contrast, the N,N-dimethylaminoborane 3 was isolated as white crystals. In addition, NMR measurements (in ppm $^{13}$C: δ = 47.9 (N(CH₃)₂); $^{11}$B: δ = 9.0; $^{19}$F: δ = -156.6 (p-F), -163.4 (m-F)) evidence a B-N bonding. It was not clear from the NMR data whether the B-N bonding is intra- or intermolecular, taking into account that the dimethylamino group is sterically benign. Both structures, 2 and 3, were determined using the X-ray diffraction method (Fig. 2). A four-membered ring with the B-N bond lengths of 1.771(3) and 1.741(3) Å for two different molecules of 3 in a unit cell was found. The formation of four-membered B-N rings was recently reported for the products of hydroboration of enantiomers with Piers’ borane HB(C₆F₅)₂. In contrast to 3, the X-ray diffraction method showed no evidence of the B-N bonding in 2. Evidently, extreme steric hindrance of the 2,2,6,6-tetramethylpiperidinyl moiety is responsible for this effect.

Though both 2 and 3 activate molecular hydrogen under 2 bar pressure and at room temperature, they do this in a different fashion. The “truly frustrated” 2 absorbs H₂ instantly upon exposure. The resultant borohydride 2H₂ was produced in toluene and isolated as white crystals, from which the crystal structure was determined (Scheme 2). Attempts to dehydrogenate 2H₂ back to 2 were unsuccessful; heating it for 4 days at 110 °C in toluene-d₈ led to formation of a minute (2.6 mol% by $^{19}$F NMR) amount of 2. The irreversible activation of hydrogen by 2 is in sharp contrast with the previously reported 4, whose corresponding hydrogen aduct 4H₂ starts to release hydrogen within minutes at 110 °C and is fully converted to 4 upon heating for 24 h in an open system. The structure of 2H₂ in a solid state represents the zwiterionic structure typical for those ansa-ammonium borohydrides reported previously by us and Erker et al. The counterparts of the intramolecular ion pair are oriented towards each other forming an almost plain 6-membered pseudo-ring with the 1.65(3) Å H–H distance (Scheme 2, Table 2).

The aminoborane 3, containing the four-membered B–N ring, slowly produces the respective intramolecular ammonium borohydride 3H₂ in C₆D₆ at the constant rate of about 8 mol% h⁻¹ upon exposure to 2 bar of hydrogen. Thus 3 was totally converted into 3H₂ within 12 h. When hydrogen is vented off and the solution of 3H₂ is left standing under Ar in an open system, it slowly dehydrogenates back to 3 with the rate of about 10% per day. Thus 3 exhibits reversibility of hydrogen uptake at room temperature without any need of thermal promotion for dehydrogenation of 3H₂. The thermal behaviour of the borohydride 3H₂ is more complicated and is a subject of a separate study which will be published elsewhere.

Catalytic activity of the prepared aminoboranes/ammonium borohydrides in the hydrogenation of imines and enamines was studied. No reaction occurred in an attempted hydrogenation of...
Table 1 Hydrogenation of 16 and 17 catalyzed by the aminoborane 3

<table>
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<th>Substrate</th>
<th>Loading of 3, %mol</th>
<th>Temperature, °C</th>
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<th>Conversion, %</th>
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<td>17</td>
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<td>80</td>
<td>1</td>
<td>100</td>
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</table>

*a 0.25 mmol of the substrate and a catalytic amount of 3 were placed in a Schlenk tube and stirred under 2 bar H2 and respective conditions. Conversions were determined by 1H-NMR of crude reaction mixtures.

Table 2 Comparison of geometries of the B–C≡C–N frames of 2, 2H2 and 3, based on X-ray diffraction data

<table>
<thead>
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<th>2H2</th>
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<td>1.771(3)</td>
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<td>α(C–C=B) °</td>
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*a Angle between the least squares planes of the phenylene bridge and the TMP (NCC) or B(C6F5)3 (BCC) groups. A reorientation of hydrogen atoms from the B–C≡C–N plane. Values for the second crystallographically independent molecule are in brackets.

Fig. 3 Substrates used in the attempted catalytic hydrogenation with the aminoboranes 2, 3 or ammonium borohydrides 2H2, 3H2.

iminines 12–16 (Fig. 3) using 2 or 2H2 as the catalyst (5 mol%, toluene, 110 °C, 2 bar H2, 16 h). Moreover, no reactivity was observed when equimolar amounts of the borohydride 2H2 and benzaldehyde or benzonitrile were heated for 24 h at 110 °C in C6D6.

The aminoborane 3 was tried as a catalyst for the hydrogenation of imines 12–16 and an enamine 17 (4 mol%, toluene, 110 °C, 2 bar H2, 36 h). As a result, only 16 and 17 were catalytically hydrogenated (Table 1, Fig. 3). To figure out the reason for such a strong difference in reactivity, 12–17 were mixed with equimolar amounts of the ammonium borohydride 3H2 in C6D6. No reaction occurred between 3H2 and imines 12–15 at room temperature or upon heating for 3 h at 50 °C. In contrast, 16 and 17 react instantly at room temperature, though with different outcome. The enamine 17 produces smoothly N-cyclohexylpiperidine (17H2) and the aminoborane 3. No interactions were found between 3 and the starting enamine 17 or the product amine 17H2 by NMR. On the other hand, as complete consumption of the borohydride 3H2 occurred upon mixing with imine 16 (1 : 1), the complex mixture comprising the reduced imine 16H2 coordinated to aminoborane 3 was produced. The coordination between 3 and the amine 16H2 or the imine 16 explains the longer reaction times (compared to 17) and the requirement of thermal promotion to break the Lewis acid–base adduct (Table 1).

Discussion

Experimental results reported herein and published by Piers et al. represent three different examples of 2-[bis(perfluorophenyl)boranyl]anilines. The aminoborane 1 does not produce an intramolecular B–N bonding and does not activate hydrogen. While frustration of the borane and amine parts is caused, apparently, by steric reasons, the inability to split hydrogen was attributed by Piers and lately by Pápai to a low basicity of the diphenylamino group. The power of a frustrated Lewis pair stems from the basicity of the basic and the acidity of the acidic counterparts, of which both are crucial for activation of H2. This has been studied theoretically.15 Besides, in our recent paper we have systematically studied a series of structurally homological intramolecular frustrated Lewis pairs. It was shown that gradual decreasing of the basicity of the amino group (from 4 to 5) makes the respective ammonium borohydride less stable and hydrogen liberation more facile. This translates into a dramatic rise of the catalytic activity of the respective aminoboranes, for example 5. Eventually, we have reached the point on the basicity scale of the amine part where the respective ammonium borohydride, the product of H2 activation, was no longer stable at ambient conditions.16 A relation between the acidity of boranes and reversibility of hydrogen uptake was a matter of an experimental study as well.16 On the other hand, the mutual geometry of the acid and base counterparts can substantially improve not only kinetic parameters of hydrogen splitting,15 but also thermodynamic stability of hydrogen adducts. Thus enhanced thermodynamic stability of ortho-anilinium borohydrides was emphasized by Pápai et al.; the calculated ΔG value for hydrogenation of 1 is +7.1 kcal mol−1. This value is much lower than expected based on evaluation of the Lewis acid and base strengths apart from their intramolecular nature and the mutual geometry. Similarly, surprisingly high thermodynamic stability was calculated for the ansa-amination borohydride 4H2.15 In addition, other frustrated ansa-B/N systems containing an ethylene or ethynylene bridge and constrained geometry were theoretically designed and claimed to be promising candidates for activation of small molecules, particularly methane.17

The ansa-amination boronate 2 exemplifies the exceptionally reactive frustrated Lewis pair. Possessing the extremely hindered TMP-moiety, the aminoborane 2 does not form the B–N bond ring, revealing FLP reactivity in full strength. Other structurally close compounds have either partially quenched reactivity due to the B–N bond formation caused by less hindered amino substituents (3 or reported by Erker et al.)14 or diminished reactivity due to a lower basicity of the diphenylamino group in 1. Therefore, aminoborane 2 activates H2 producing the extremely stable adduct 2H2. Comparison of the structures of 2 and 2H2 in a solid state revealed that activation of H2 causes a minor change in geometry of the B–C≡C–N frame (Table 2). Thus the rigid
geometry of 2 is optimal for H₂ activation, making 2H₂ particularly stable due to a large contribution of the entropic factor to the free energy. The formation of the 6-membered pseudo-ring of 2H₂ is thermodynamically more favourable than the respective 7-membered ring as evident by different dehydrogenation behaviour of 2H₂ and 4H₂, mentioned previously. This suggestion requires further experimental verification by direct calorimetric studies which are in progress. Additional stability of the resultant ammonium borohydride 2H₂ is supported by its inability to hydrogenate imines or even benzaldehyde. Apparently, an important step in the hydrogenation with *ansa*-ammonium borohydrides is the breaking of the "dihydrogen" bond and the resultant ring-opening of the six-membered pseudo-ring. In the case of 2H₂ this step is complicated by rigidity of the B–C–N–C–N frame and strong electrostatic attraction between counterparts of the intramolecular ion pair. Nevertheless, there are some differences between 2 and 2H₂ in orientation of the amine and boryl parts. Due to steric repulsion, the TMP- and (C₅H₅)₂B-groups have a sliding orientation in 2 and are turned by 76° and 49° respectively relative to the plane of the bridging CₓHᵧ ring (Table 2). In the borohydride 2H₂ these angles are 86° and 74° respectively, demonstrating geometry close to Cₓ-symmetric.

The N,N-dimethylaminoborane 3 is an example of a sterically benign *ortho*-borylaniline. The absence of steric repulsion facilitates formation of a four-membered B–N ring. Though the basicity of the dimethylamino group is substantially lower than that of the TMP, and some reactivity is quenched by the intramolecular Lewis B–N adduct, 3 is still able to activate H₂ at near ambient conditions. The progress of hydrogen uptake was found to be linear with time under constant pressure, perhaps due to the rate-limiting character of the B–N ring dissociation. The formation of four-membered (C₅H₅)₂B–N adducts was reported previously by Erker et al. and the B–N ring dissociation energy was measured to be 13–14 kcal mol⁻¹. The ease of hydrogen release from the ammonium borohydride 3H₂ is remarkable. Evidently, the formation of the B–N bond facilitates the shift of the equilibrium to 3.

Reversibility of hydrogen uptake by 3 at room temperature resembles that of 5, which was found to be the most active FL-P catalyst for the hydrogenation of various imines (TOF ca. 100 h⁻¹). While imines 12–15 were smoothly hydrogenated with the *ansa*-aminoboranes 4 and 5 as catalysts, the imine 16 was not hydrogenated catalytically due to coordination of the substrate to the catalyst. In contrast, the *ansa*-aminoborane 3 was able to hydrogenate 16 but not 12–15, demonstrating the opposite selectivity to non-hindered imines. Even though the dimethylamino group is one of the smallest possible secondary amino-groups, 3H₂ is much more hindered than 4H₂ containing the TMPCH₂ group; the diminished accessibility of the ammonium borohydride catalyst 3H₂ for a substrate is caused by the tighter *ortho*-connection of the amine and boryl parts and by constrained geometry of the 6-membered pseudo-ring in comparison to the 7-membered one in 4H₂. In this respect the smooth hydrogenation of the quite hindered imine 17 is remarkable. A possible explanation is the influence of steric factors during proton transfer from the catalyst (3H₂) to a substrate, which is considered to be the first step in the catalytic cycle. Indeed, while in the case of imines the protonation occurs at the nitrogen atom and hence the proximity of the catalyst's NHMe₂⁺ group to the substrate’s –N=C– bond is required, in the case of enamines the catalyst protonates the β-carbon, which is much more accessible. This consideration requires further experimental and theoretical support.

In conclusion, two new *ansa*-aminoboranesbridged with a phenylene ring were prepared. The aminoborane 2 containing a highly basic and sterically hindered 2,2,6,6-tetramethylpiperidine moiety instantly activates H₂ at ambient conditions producing the extremely stable and unreactive ammonium borohydride 2H₂. The *ansa*-aminoborane 3 containing a smaller N,N-dimethylamino group produces an intramolecular Lewis adduct comprising a four-membered B–N ring. It features reversible H₂ activation at room temperature, which is remarkable. 3 or the respective ammonium borohydride 3H₂ efficiently catalyzes hydrogenation of some imines and enamines, demonstrating selectivity to non-hindered substrates. The aminoboranes 2 and 3 exemplify the validity of the approach to hydrogen activation by the first intramolecular B/N frustrated pair proposed by Piers et al. back in 2003.

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Notes and references

5. On the moment of writing, 237 publications containing the concept “frustrated Lewis pair” can be found through SciFinder.
Amine-Borane Mediated Metal-Free Hydrogen Activation and Catalytic Hydrogenation

Victor Sumerin, Konstantin Chernichenko, Felix Schulz, Markku Leskelä, Bernhard Rieger, and Timo Repo

Abstract The use of frustrated Lewis pairs (FLPs) as hydrogenation catalysts is attracting increasing attention as one of the most modern and rapidly growing areas of organic chemistry, with many research groups around the world working on this subject. Since the pioneering studies of the groups of Stephan and Piers on the Lewis acid–base pairs, which do not react irreversibly with each other and act as a trap for small molecules, numerous FLPs for hydrogen activation have been reported. Among others, intra- and intermolecular systems based on phosphines, organic carbenes, amines as Lewis bases, and boranes or alanes as Lewis acids were studied. This review 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 and also internal alkenes.

Keywords Amines · Aminoboranes · Boranes · FLP · Homogeneous catalysis · Hydrogenation · Organocatalysis

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Abbreviations

1D NOE One-dimensional nuclear Overhauser effect spectroscopy
2D NOESY Two-dimensional nuclear Overhauser effect spectroscopy
9-BBN 9-Borabicyclo[3.3.1]nonane
BCF Tris(pentafluorophenyl)borane
Bn Benzyl
Bu Butyl
d Day(s)
DABCO 1,4-Diazabicyclo[2.2.2]octane
DFT Density functional theory
DHB Dihydrogen bond
DMDPP trans-2,6-Dimethyl-2,6-diphenylpiperidine
ee Enantiomer excess
equiv. Equivalent(s)
Et Ethyl
FLP Frustrated Lewis pair
FT-IR Fourier transform infrared spectroscopy
h Hour(s)
iPr Isopropyl
IrBu 1,3-Di-tert-butylimidazolin-2-ylidene
LAB Lewis acid–base
Me Methyl
Mes Mesityl 2,4,6-trimethylphenyl (not methanesulfonyl)
min Minute(s)
MTBE Methyl tert-butyl ether
NHC N-Heterocyclic carbene
NMR Nuclear magnetic resonance
Np Naphthyl
α-Tol o-Methylphenyl
Ph  Phenyl
PMP  \textit{p}-Methoxyphenyl
Pr  Propyl
RT  Room temperature
\textit{t}Bu  \textit{tert}-Butyl
THF  Tetrahydrofuran
TMP  2,2,6,6-Tetramethylpiperidine
TMS  Trimethylsilyl
Tos  Tosyl 4-toluenesulfonyl
TRIP  3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate

1 Introduction

During the past century, hydrogen activation and hydrogenation of unsaturated compounds under mild conditions was an exclusive prerogative of transition metals [1–3]. While there are countless synthetic and enzymatic complexes which contain a transition metal at their reactive core and that are able to cleave dihydrogen and catalytically reduce organic substrates, the H–H bond activation solely by non-metals under mild conditions was unknown until recently [4, 5]. In 2005–2007 different main group systems capable of hydrogen activation were reported and the “frustrated Lewis pairs (FLPs)” concept was introduced (Scheme 1) [6–9]. According to this concept, steric and/or electronic properties of the Lewis acid and the Lewis base prevent the irreversible classical Lewis acid–base (LAB) adduct formation. Recently, several metal-free FLP catalysts for the direct metal-free catalytic hydrogenation of imines, enamines, nitrogen-containing heterocycles, and non-terminal alkynes were developed.

Compared to traditional transition metal catalysts and enzymes, these systems offer many advantages related to catalyst selectivity, functional-group tolerance, environmental sustainability, cost-efficiency, and the fine purification of the final products [10–12]. This review concentrates on hydrogen activation and catalytic hydrogenation by intra- and inter-molecular amine-borane FLPs. The capabilities and limitations of such systems are described and compared to each other.

2 Pioneering Studies

Like many other organocatalytic methods, the FLP concept took a long time to mature. Remarkably, the first example of an unusual LAB pair, comprising amine and borane, dates back to 1942, when Brown and co-workers reported that
2,6-lutidine reacts with BF₃ to give a stable classical LAB adduct in quantitative yield, but does not react with BMe₃ even at low temperature (Scheme 1) [13]. Moreover, the subsequent reactivity of unusual LAB pairs with other molecules had already been discovered by Wittig and co-workers in the 1950s. For instance, they showed that a mixture of tritylsodium (Ph₃CNa) with triphenylborane (Ph₃B) can attack suitable substrates like tetrahydrofuran, 2,3-dimethylbutadiene, and carbon monoxide nucleophilically and electrophilically at the same time to form new organosodium compounds [14–18]. However, as with other metal-free catalytic transformations, FLPs required a key discovery – reversible hydrogen activation by a nonmetal system based on bulky phosphinoborane in 2006 – to boost the research activity in this field (Scheme 2) [6].

The key to the successful heterolytic cleavage of H₂ under mild conditions by Stephan’s phosphinoborane is the use of the LAB pair with correctly matched electronic and steric properties. While steric repulsion is 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 favor thermodynamically the formation of a hydrogenated product at room temperature. When the reaction is almost thermodynamically neutral, facile hydrogen liberation takes place at elevated temperature [19]. In an analogous fashion, later, mixtures of sterically demanding phosphines and B(C₆F₅)₃ were also shown to cleave H₂ heterolytically. However, the resulting phosphonium-borates [R₃PH][HB(C₆F₅)₃] (R = tBu, o-MeC₆H₄, Mes) were more stable and did not release hydrogen even upon heating at 150°C [7].

Looking back now, 3 years before Stephan’s “frustrated” phosphinoborane, there was an important prerequisite for the discovery of FLPs. In 2003 Roessler and Piers published “synthesis, structural characterization and reactivity of the
Amino borane 1-(NPh₂)-2-[B(C₆F₅)₂]C₆H₄⁺, invited paper in Journal of Organometallic Chemistry, which is a specialized journal and as a result their work was not recognized at that time. In this article, they described the first “frustrated” intramolecular LAB system, where the active Lewis acidic boron and Lewis basic nitrogen centers were located close to each other and did not form a classical LAB adduct due to the steric hindrance of the bulky amine and borane moieties and the high strain energy of the corresponding four-membered ring [20].

Roesler and Piers also predicted that such a “Lewis acid/Lewis base trap” would be suitable for the reversible activation of H₂ (Scheme 3). Specifically, they not only speculated that ammonium borate o-Ph₂NH⁺···C₆H₄⁻[HB(C₆F₅)₂]⁻ might be a “dihydrogen storage device, able to release H₂ upon heating or during a chemical reaction, regenerating” amino borane o-Ph₂N–C₆H₄–B(C₆F₅)₂, but also suggested that strong N–H–H–B dihydrogen bond (DHB) interactions would play a key role in this process. Unfortunately, Piers’ amino borane was unable to cleave H₂ 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, attempts to generate ammonium borate in situ led to spontaneous liberation of dihydrogen gas even at low temperature.

Nevertheless, their “frustrated” amino borane was extremely sensitive to moisture and acids or, in other words, was able to activate H₂O and HCl forming zwitterionic products. Recently, analogous properties of ammonium and phosphonium boranes were found to be essential for the selective receptors for cyanide and fluorine ions in water at neutral pH [21–23]. Moreover, as we showed recently, a simple replacement of the diphenylamino moiety by the more electron-donating dimethylamino group led to amino borane o-Me₂N–C₆H₄–B(C₆F₅)₂, which is indeed able to activate reversibly hydrogen gas [24].

3 Hydrogen Activation by Amines and Boranes

The FLP concept states that steric and/or electronic properties of the corresponding Lewis acid and Lewis base should be appropriate to preclude the irreversible LAB adduct formation [25]. Indeed, the first examples of FLP systems, which were able to cleave hydrogen in a facile manner, consisted of extremely bulky phosphines and
tris(pentafluorophenyl)borane [6, 7]. This was due to the fact that less sterically hindered phosphines can react with B(C₆F₅)₃ forming stable LAB adducts or can undergo nucleophilic substitution of the para-fluorine atom, giving intramolecular phosphonium-borates [26]. Thus, there are only a few commercially available bulky phosphines, such as Mes₃P, o-Tol₃P, tBu₃P, that can be used for hydrogen activation in combination with highly Lewis acidic boranes [7, 27]. Even then, in some cases, despite the seeming simplicity of such FLPs, the mechanistic picture is rather complex and includes the in situ formation of phosphinoboranes p-R₂PC₆F₅B(C₆F₅)₂, which can further catalyze phosphonium-borate formation, for example [tBu₃PH][HB(C₆F₅)₃] [28].

A logical development of the FLP systems, but still significant, was the implementation of bulky amines as Lewis basic components [29]. Since the carbon–nitrogen bond is shorter than the carbon–phosphorus bond, a much broader variety of sterically hindered amines is readily and commercially available. Furthermore, in contrast to bulky phosphines, such amines are air-stable and inexpensive.

Similarly to non-bulky phosphines and B(C₆F₅)₃, the binary mixtures of amines and boranes can undergo different transformations depending on their steric, electronic, and chemical properties [30–33]. These transformations can be classified into two categories: the classical LAB adduct formation and the abstraction of an α-hydride from an amine by the Lewis acidic B(C₆F₅)₃ (Schemes 4 and 5). In the first case, whilst sterically accessible amines and pyridines react with boranes forming stable LAB adducts (Scheme 4, 1a), the reactions of more sterically hindered amines or pyridines with B(C₆F₅)₃ are fully reversible either at room or elevated temperature (Scheme 4, 1b). In addition, no interaction between the most bulky amines and B(C₆F₅)₃ can be detected via NMR spectroscopy, even at low temperature (Scheme 4, 1c). Generally, in this case the steric effects prevail over electronic effects.

However, if the steric effects are large enough to prevent irreversible LAB adduct formation, then, depending on their electronic properties, amines and anilines that contain an aliphatic chain with α- or α- and β-protons next to each

\[
\begin{align*}
1a) & \quad \text{R}_3\text{N} + \text{B(C}_6\text{F}_5)_3 \quad \rightarrow \quad \text{R}_3\text{N} \cdots \text{B(C}_6\text{F}_5)_3 \\
\text{R}_3\text{N} = \text{NH}_3, \; \text{tBuNH}_2, \; \text{BnNH}_2, \; \text{BnNHMe, Bn}_2\text{NH, Me}_3\text{N, Pyridine} \\
1b) & \quad \text{R}_3\text{N} + \text{B(C}_6\text{F}_5)_3 \quad \rightarrow \quad \text{R}_3\text{N} \cdots \text{B(C}_6\text{F}_5)_3 \\
\text{R}_3\text{N} = \text{tBuNHBn, PhNMe}_2, \; \text{BnNMe}_2, \; 2,6\text{-Lutidine} \\
1c) & \quad \text{R}_3\text{N} + \text{B(C}_6\text{F}_5)_3 \quad \rightarrow \quad \text{No reaction} \\
\text{R}_3\text{N} = \text{TMP, N-MeTMP, DMDPP, 2,4,6-t-butyl-pyridine}
\end{align*}
\]

Scheme 4  LAB interactions between amines and B(C₆F₅)₃
other (like Me, Bn or Et, n-Pr, iPr groups) may exhibit completely different reactivities towards tris(pentafluorophenyl)borane. In this case, the reaction of various amines with B(C₆F₅)₃ results in an α-hydride abstraction by the Lewis acidic borane from an amine, followed by the reversible formation of iminium borohydride (Scheme 5, 2a). The racemization of enantioenriched amines catalyzed by B(C₆F₅)₃ is an example of this type of reaction [34, 35]. When both α and β protons are present in the alkyl chain of an amine, the reaction can proceed further to produce, in either an irreversible or a reversible manner, a mixture of zwitterion iminium borate and ammonium borohydride (Scheme 5, 2b and 2c). In some cases, as with N-isopropylaniline and B(C₆F₅)₃, both LAB adduct formation and abstraction of an α-hydride pathways were observed (Scheme 5, 3a).

The above examples demonstrate a wide range of possible interactions between amines and B(C₆F₅)₃. Nevertheless, in most of the cases (1b, 2a, 2c, 3a) the free amine and tris(pentafluorophenyl)borane are in equilibrium with the products of the reaction or do not react with each other at all (1c), and can be used in the subsequent activation of small molecules.

The first examples of hydrogen activation by intermolecular amine-borane based FLP systems were reported in 2008 by us and others (Scheme 6) [29, 36]. Specifically, the facile heterolytic cleavage of H₂ was readily achieved by the cooperative action of the Lewis basic 2,2,6,6-tetramethylpiperidine, diisopropylamine, and tert-butylbenzylamine with Lewis acidic tris(pentafluorophenyl)borane at 20°C, 100°C, and 80°C, respectively, to afford the corresponding [R₂NH₂⁺][HB(C₆F₅)₃]⁻ products (Scheme 6). Since less bulky diisopropylamine or tert-butylbenzylamine react with B(C₆F₅)₃ to give a mixture of iminium borate and ammonium borohydride or the LAB adduct, the higher temperatures were required in order to shift equilibriums toward the free amines and borane. The more sterically hindered
Scheme 6  Hydrogen activation by bulky amines and B(\text{C}_6\text{F}_5)_3 [29, 36]

2,2,6,6-tetramethylpiperidine without α-protons does not react with B(\text{C}_6\text{F}_5)_3 even at low temperature, meaning that the TMP/B(\text{C}_6\text{F}_5)_3 system is capable of splitting H_2 at temperature as low as −80°C [37].

Later, hydrogen activation by the FLPs of TMP and different boranes was also studied (Scheme 7). Similar to the reaction with B(\text{C}_6\text{F}_5)_3, bis(pentafluorophenyl) chloroborane CIB(\text{C}_6\text{F}_5)_2 reacted with TMP under an atmosphere of H_2 to yield initially [TMPH]^+[\text{ClHB}(\text{C}_6\text{F}_5)_2]^−, which was not stable in the presence of CIB (\text{C}_6\text{F}_5)_2 and dismutates subsequently into [TMPH]^+[\text{Cl}_2\text{B}(\text{C}_6\text{F}_5)_2]^− and HB(\text{C}_6\text{F}_5)_2 [37]. While, in combination with more Lewis acidic 1,2-bis(pentafluorophenylboryl) benzene [(\text{C}_6\text{F}_5)_2\text{B}]_2\text{C}_6\text{H}_4 an almost quantitative yield of the hydrogenated product was achieved in less than 5 min instead of 1 h with B(\text{C}_6\text{F}_5)_3, the reaction with more bulky 1,8-bis(dipentafluorophenylboranyl)naphthalene required prolonged heating at 80°C and gave a low product yield (unpublished results) [38]. Even at elevated temperatures the less sterically hindered Piers’ bis(pentafluorophenyl)borane HB (\text{C}_6\text{F}_5)_2 reacted with TMP to give a very stable LAB adduct [37].

In order to extend the family of FLPS based on amines and borane, we investigated the behavior of simple N-trimethylsilyl protected amines as Lewis bases in combination with B(\text{C}_6\text{F}_5)_3 [39]. The usage of TMS substituted amines has a couple of advantages. First, most N-TMS-aminos are bulky enough and should not form stable adducts with B(\text{C}_6\text{F}_5)_3. Second, they are easily synthesized or commercially available.

In contrast to bulky P-TMS-phosphines that undergo nucleophilic aromatic substitution reaction of the para-fluorine atom, the less nucleophilic N-TMS-aminos do not react with B(\text{C}_6\text{F}_5)_3 (Scheme 8). Exposing toluene solutions of N-TMS-aminos and B(\text{C}_6\text{F}_5)_3 to an atmosphere of H_2 (1.5 atm) showed different reactivity of such FLPS. Whilst less Lewis basic trimethylsilyldiphenylamine or trimethylsilylcarbazole together with trispentafluorophenylborane did not react with H_2 at 110°C, more basic MesNH-TMS, tBuNHTMS, or iPr_2NTMS and B(\text{C}_6\text{F}_5)_3 cleaved hydrogen even at
Scheme 7  Hydrogen activation by TMP and boranes (unpublished results) [37, 38]

Scheme 8  Interactions between bulky N-TMS-amines and P-TMS-phosphines with B(C₆F₅)₃ [39]

room temperature in a facile manner (Scheme 9). In addition to the previous study on the influence of Lewis acidity on the hydrogen activation (Scheme 7), this finding suggests that the Lewis basicity of the amine should also be high enough to favor thermodynamically the cleavage of the H₂ bond.

Based on real-time NMR studies we assumed that hydrogen splitting by MesNHTMS, tBuNHTMS, and iPr₂NTMS in combination with B(C₆F₅)₃ resulted in N-TMS-ammonium borohydrides. However, the formed salts were not stable and
Scheme 9  Hydrogen activation by bulky TMS-amines and B(C₆F₅)₃ [39]

Scheme 10  Relative steric hindrance phenomenon in hydrogen activation by amines and boranes

spontaneously liberated TMSH gas (bp = 6.7°C). The stable LAB adducts were formed as the ultimate reaction products in the cases of mesitylamine and tert-butylamine. The reaction of more bulky diisopropyltrimethylsilylamine and B(C₆F₅)₃ with H₂ afforded the expected 1:1 mixture of the salt [(iPr₂NH)⁺[HB(C₆F₅)₃]]⁻ and the zwitterion iPrN⁺H=CH₂CH₂B⁻(C₆F₅)₃. As described earlier, the two former compounds are in an equilibrium with the free diisopropylamine and B(C₆F₅)₃ at 110°C, and can further split hydrogen upon heating (Scheme 9).

In 2010 Soós and co-workers demonstrated that steric hindrance required for H₂ activation in FLPs is a complementary phenomenon (Scheme 10) [40, 41]. They found that further increase of the steric bulk of the ortho-substituted aryl groups of the active boron center leads to Lewis acids with a remarkably high tolerance to the nature of the corresponding Lewis bases. Thus, in contrast to B(C₆F₅)₃ (Schemes 4 and 5), even non-bulky amines with α- and β-protons next to each other can be used as a Lewis basic part of FLPs in combination with more sterically hindered MesB(C₆F₅)₂. For instance, FLP consisting of quinuclidine or DABCO and MesB(C₆F₅)₂ showed faster H₂ splitting than the bulky TMP/MesB(C₆F₅)₂ system (Scheme 11).
Scheme 11  Hydrogen activation by amines and MesB(C₆F₅)₂ [40]

Scheme 12  Hydrogen activation by amines and (2,4,6-(CF₃)₃C₆H₂)₂BH [42]

More recently, Li and Wang et al. also reported that the secondary borane with extremely bulky and electron-withdrawing 2,4,6-tris(trifluoromethyl)phenyl groups, together with simple sterically benign amines, can activate hydrogen under mild conditions (Scheme 12) [42].

Unfortunately, none of the amine-borane FLP systems described above was able to liberate hydrogen upon heating. However, as it was shown by us and others to facilitate the hydrogen release reaction, the activation of H₂ by FLP should be almost thermodynamically neutral [19, 43–45]. Thus, the FLP systems derived from less Lewis basic amines and B(C₆F₅)₃ or less Lewis acidic boranes and TMP can heterolytically cleave hydrogen under ambient conditions to form ammonium borohydrides, which can liberate hydrogen at higher temperatures (Scheme 13).

While the main factor for the reversible hydrogen activation by intermolecular amine-borane FLP systems was shown to be the reduced Lewis acidity of the boron center, the changes in the Lewis basicity of amines turned out to be of secondary importance. Specifically, the ammonium borohydrides prepared from TMP and cyclohexylbis(pentafluorophenyl)borane or 1-phenyl-2-[(bis(pentafluorophenyl)boryl)ethane, exhibiting 15% and 10% lower acidity than B(C₆F₅)₃, easily liberate hydrogen at 50°C or 65°C, respectively [44]. In contrast to that, the hydrogen release reaction from the hydrogenated FLP system based on B(C₆F₅)₃ and trans-2,6-dimethyl-2,6-diphenylpiperidine, which is about 15% less basic than TMP, required a higher temperature and longer time (110°C and 36 h) to yield 50% of the free amine and borane [43]. Moreover, if the Lewis acidity of the borane is too low, the corresponding FLP, for instance triphenylborane (BPh₃) and 2,2,6,6-tetramethylpiperidine, may not form a stable ammonium borohydride [29].
Scheme 13  Reversible hydrogen activation by amines and boranes [29, 43, 44]

The structures of different ammonium borohydrides were determined by X-ray diffraction crystallography. It was found that the ammonium and borohydride ions in these compounds are usually connected by a network of N–H···F and C–H···F hydrogen bonds (Fig. 1, left). Additionally, a strong N–H···H–B dihydrogen bond the length of which is less than 2.0 Å can be present (Fig. 1, right) [36, 43, 44]. However, the ability to liberate hydrogen by intermolecular ammonium borohydrides was shown to correlate mainly with the strength of the B–H and N–H bonds rather than with a close interaction between the protonic and hydridic hydrogen atoms [44].

All of these results support the idea that the reversible hydrogen activation requires amines and boranes with fine-tuned steric and electronic properties. First, the steric constraints between the Lewis acid and Lewis base and their electronic properties must be sufficient to provide at least the equilibrium amounts of free amine and borane. Second, the power of the FLP, which depends on the basicity of the Lewis base and the acidity of the Lewis acid counterparts, should be high enough to favor thermodynamically the formation of a hydrogenated product at mild temperature, but not too high to facilitate hydrogen liberation at elevated temperature. Although the detailed mechanisms of hydrogen activation solely by boranes or by FLPS have been investigated in some detail, they are still a subject of debate and not the focus of this review [19, 42, 46–53].
4 Hydrogenation by Amines and Boranes

The subsequent reactivity of ammonium borohydrides obtained through hydrogen activation by amine-borane FLP systems was investigated. In a preliminary experiment, benzaldehyde was selectively and rapidly reduced at room temperature to a product with the molecular formula \( [\text{TMPH}]^+\text{[HB}(C_6F_5)_3]^- \) in 95% yield by employing \([\text{TMPH}]^+\text{[HB}(C_6F_5)_3]^-\) as a stoichiometric reducing agent (Scheme 14) [29].

Later, different ammonium borohydrides were also successfully applied in the stoichiometric fixation of CO\(_2\), which is a promising C1 feedstock for the production of many chemicals (Scheme 15) [31, 54, 55]. Moreover, because the zwitterionic \( N \)-heterocyclic carbene adduct with CO\(_2\) was recently considered as the key intermediate in the deoxynative hydroxylation of CO\(_2\) by diphenylsilane to CH\(_3\)OH upon workup, this initial finding foreshadowed the potential of ammonium borohydrides to act as CO\(_2\) activator for its further reduction [56].

Indeed, a procedure for the in situ quantitative hydrogenation of CO\(_2\) to methoxy-(bispentafluorophenyl)borane with a four times excess of the TMP/B(C\(_6\)F\(_5\))\(_3\) pair was reported by O’Hare and co-workers (Scheme 16) [54]. Unfortunately, further cleavage of the B–O bond was rather difficult due to the high bond energy of the B–O bond (560–790 kJ/mol) which makes it hard to break, and the desired methanol product was obtained in very low yield (Scheme 16) [57].

More recently, Piers et al. demonstrated that a tandem catalyst, based on \([\text{TMPH}]^+\text{[HB}(C_6F_5)_3]^-\) together with B(C\(_6\)F\(_5\))\(_3\) and in the presence of excess of triethylsilane as a reducing and deoxynative agent, can convert carbon dioxide
Scheme 15  CO$_2$ fixation by ammonium and lutidinium borohydrides [31, 54, 55]

Scheme 16  Reduction of CO$_2$ to methanol by TMP/B(C$_6$F$_5$)$_3$ FLP [54]

directly to methane under mild conditions [58]. The TMP/B(C$_6$F$_5$)$_3$ FLP reacts with CO$_2$ (2–4 atm) in the presence of Et$_3$SiH at 56°C in C$_6$D$_5$Br to afford ammonium borohydride [TMPH]$^+[$HB(C$_6$F$_5$)$_3$]$^-$ which further reacts with CO$_2$ to give the previously reported ammonium formateborate [TMPH]$^+[$HCO$_2$B(C$_6$F$_5$)$_3$]$^-$ (Scheme 17).

Further addition of a catalytic amount of B(C$_6$F$_5$)$_3$ to the reaction mixture results in the immediate and complete conversion of ammonium formateborate back into the starting ammonium borohydride and the appearance of CH$_4$ along with 2 equiv. of (Et$_3$Si)$_2$O as the final reaction products (Scheme 18).

Whilst the reduction of carbonyl compounds by FLPS is still rather limited, simple trispentafluorophenylborane, 1,8-bis(dipentafluorophenylboryl)naphthalene, and others were recently shown to catalyze the direct hydrogenation of bulky amines, anilines, and quinolines (Table 1) (unpublished results) [36, 59–62].

The initiation step in this transformation involves heterolytic splitting of H$_2$ by the imino-borane FLP to generate an iminium borohydride, which can be further reduced by nucleophilic attack of a hydride ion on the iminium carbon atom to afford the corresponding amine in the form of an LAB adduct with B(C$_6$F$_5$)$_3$. 
Scheme 17 Formation of the key ammonium formatoborate intermediate [58]

Scheme 18 Catalytic deoxygenative hydrosilylation of CO₂ [58]

In some cases, if the starting imine is too bulky for the nucleophilic attack, an intermediate iminium borohydride can be isolated (Scheme 19) [36]. Moreover, as discussed above, the addition of a hydride ion to the iminium double bond is a reversible reaction and the same intermediate iminium borohydride is responsible for the racemization of enantioenriched amines catalyzed by B(C₆F₅)₃ (Scheme 5).

The main disadvantage of perfluorophenylboranes as catalysts for the reduction of unsaturated nitrogen-containing compounds is their strong sensitivity to the nature of the substrates. Therefore, only sterically hindered (Table 1, entries 1, 2, 5–9) and low-basic (Table 1, entries 3–6, 9) imines and quinolines can be catalytically reduced. Both of these factors facilitate dissociation of the LAB adducts between borane and the final amine, which inhibits borane’s catalytic activity. For instance, the stoichiometric reaction between tBuN≡C(H)Ph and B(C₆F₅)₃ under hydrogen at room temperature gives a stable LAB adduct of tert-butylbenzylamine and tris(pentafluorophenyl)borane (Scheme 20). However, heating of the toluene solution of N-tert-butylbenzaldimine in the presence of only 5 mol% of B(C₆F₅)₃ under 1 atm of H₂ at 80°C leads to the rapid formation of tert-butylbenzylamine in an almost quantitative yield (Table 1, entry 1) due to the fast thermal dissociation of the B–N bond forming free borane at elevated temperatures.
Table 1  Catalytic hydrogenation of imines and quinolines by boranes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst</th>
<th>Conditions</th>
<th>Amine</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Substrate" /></td>
<td>5 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>1 atm $\text{H}_2$, 80°C, 2 h</td>
<td><img src="image2" alt="Amine" /></td>
<td>89 [36]</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Substrate" /></td>
<td>5 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>5 atm $\text{H}_2$, 120°C, 1 h</td>
<td><img src="image4" alt="Amine" /></td>
<td>99 [36]</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Substrate" /></td>
<td>5 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>5 atm $\text{H}_2$, 120°C, 41 h</td>
<td><img src="image6" alt="Amine" /></td>
<td>98 [36]</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Substrate" /></td>
<td>10 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>30 atm $\text{H}_2$, 100°C, 15 h</td>
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<td>99 [36]</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Substrate" /></td>
<td>5 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>20 atm $\text{H}_2$, 80°C, 15 h</td>
<td><img src="image10" alt="Amine" /></td>
<td>99 [36]</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Substrate" /></td>
<td>5 mol% $\text{B(C}_6\text{F}_5)_3$</td>
<td>4 atm $\text{H}_2$, 25°C, 1 h</td>
<td><img src="image12" alt="Amine" /></td>
<td>80 [59]</td>
</tr>
</tbody>
</table>
7. 10 mol% MesB(C₆F₅H)₂, 4 atm H₂, 105°C, 17 h, 99 [60]

8. 10 mol% MesB(C₆F₅H)₂, 4 atm H₂, 105°C, 17 h, 99 [60]

9. 10 mol% (C₆F₅)₂B, 15 atm H₂, 120°C, 1 h, 99 (unpublished results)

10. 5 mol% (C₆F₅)₂B, 15 atm H₂, 120°C, 1 h, 99 (unpublished results)

11. 10 mol% (C₆F₅)₂B, 20 atm H₂, 65°C, 15 h, 99 [61]
Scheme 19  Hydrogen activation by bulky imine and B(C₆F₅)₃ [36]

Scheme 20  Ammonium borohydride formation via hydrogen activation by imine and B(C₆F₅)₃ [36]

Since both free amine and borane are also present in the reaction mixture during catalytic hydrogenation, they can compete with the imine-borane FLP in the cleavage of H₂ to form an ammonium borohydride (Scheme 20), which can act as a reducing agent in the subsequent transfer hydrogenation of imine. Additionally, because the corresponding amines are more basic than starting imines, the rate of the hydrogen activation by amine-borane FLPs is higher than those for imine-borane FLPs.

Indeed, recently, Soós and co-workers confirmed that the addition of a catalytic amount of a properly chosen amine to borane accelerates the hydrogenation of imines (Table 2) [40, 41]. Specifically, they showed that intermolecular amine-borane FLPs with well-matched steric and electronic properties are highly active hydrogenation catalysts even at room temperature (Table 3).

However, despite the significantly improved activity of the new amine-borane FLPs, a strong substrate limitation is still the major drawback of these catalytic systems [35]. For instance, even with a mixture of sterically hindered borane MesB(C₆F₅)₂ and quinuclidine as a catalyst, only 49% conversion of non-bulky imine PhCH₂N=C(H)Ph to dibenzylamine was achieved (Table 3, entry 5).
Table 2  Catalytic hydrogenation of imines by amines and MesB(C₆F₅)₂ [40]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amine</th>
<th>Conv. (%)a</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
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<td>5</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>2</td>
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<tr>
<td>4</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

a Determined by GC analysis

5  Hydrogen Activation by Intramolecular ansa-Aminoboranes

After our initial discovery of the first intermolecular TMP/B(C₆F₅)₃ FLP system for hydrogen activation under ambient conditions, we designed intramolecular ansa-aminoborane \( o-N\)-TMPCH₂C₆H₄B(C₆F₅)₂ where active B and N centers are located close to each other [63]. We also developed an effective and common procedure for the preparation of such dual Lewis acid–base systems using commercially available 2-bromobenzylbromide, amine, and (C₆F₅)₂BCl (Scheme 21).

The first step of the synthesis was N-alkylation of TMP with \( o \)-bromobenzyl bromide in the presence of K₂CO₃ as a base and 10 mol% of KI as a catalyst to produce 1-(2-bromobenzyl)-2,2,6,6-tetramethylpiperidine in 80% yield. The corresponding intermediate product readily underwent halogen–lithium exchange with \( tert \)-butyllithium at \(-70^\circ C\) in diethyl ether, after which a pre-cooled solution of (C₆F₅)₂BCl was added to give the crude product CAT in 70% yield as a bright
Table 3  Catalytic transfer hydrogenation of imines and enamines by amines with MesB(C₆F₅)₂ [40]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Amine</th>
<th>Conv. (%)(^a)</th>
</tr>
</thead>
<tbody>
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<td><img src="image1" alt="Image" /></td>
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<td>49</td>
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<tr>
<td>6</td>
<td><img src="image11" alt="Image" /></td>
<td><img src="image12" alt="Image" /></td>
<td>16</td>
</tr>
</tbody>
</table>

\(^a\) Determined by \(^3\)H NMR spectroscopy

Scheme 21  Synthesis of *ansa*-aminoborane CAT [63]
yellow oil. In the next step, the *ansa*-aminoborane CAT reacted rapidly with H₂ at room temperature and 1 atm pressure to give the *ansa*-ammonium borate CATH₂ in almost quantitative yield in 5 min (Scheme 22). In contrast to the starting *ansa*-aminoborane CAT, CATH₂ is an air- and moisture-stable solid compound. Therefore, this method allowed successful preparation of CATH₂ in good yield on a gram scale.

The possibility of hydrogen gas liberation from CATH₂ was also examined. When a toluene solution of *ansa*-ammonium borate CATH₂ (0.1 M) was refluxed at 110°C in a closed system under reduced pressure for 3 h, a 50% conversion of CATH₂ was observed. An extension of the reaction time up to 20 h resulted in almost quantitative recovery of the starting *ansa*-aminoborane CAT, exemplifying the first non-metal FLP-based system able to activate hydrogen reversibly through an intramolecular mechanism.

To gain further insight into the mechanism of reversible hydrogen activation by intramolecular *ansa*-aminoborane CAT, the structure of the corresponding *ansa*-ammonium borate CATH₂ 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 [64].

The neutron diffraction data of *ansa*-ammonium borate CATH₂ showed the presence of C–H···F (2.36 and 2.82 Å) hydrogen bonds and a strong, partially covalent, dihydrogen bond interaction N–H···H–B of 1.67 Å between the ammonium cation and borohydride anion (Fig. 2) [65]. Ab initio DFT calculations performed by ourselves and others 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 the neutron diffraction results [19, 63]. However, the values found for the intramolecular N–H···H–B dihydrogen bond distance were significantly shorter (1.51 and 1.53 Å, Table 4).

Since both hydrogen activation and liberation occurred in organic solvents and in solid state studies, multinuclear solution NMR experiments of CATH₂ and its deuterated isotopomers were performed [64]. It could be shown that, in contrast to the B–H hydride, the N–H proton can be exchanged easily in solution. These experiments also showed that no rotation of H₂ within the molecule takes place even at elevated temperatures. Dilution, variable temperature, and 2D NOESY NMR measurements of *ansa*-ammonium borate CATH₂ in CD₂Cl₂ solution.
showed that it consists of two conformers which are in dynamic equilibrium (Scheme 23). Both of them have the N–H proton in an axial position and differ only in the orientation of the axial methyl groups adjacent to the nitrogen center. Based on the chemical NMR shifts of N–H and CH₂ groups and the X-ray crystal structure of CATH₂, the more stable conformer was assumed to have the methyl groups in an axial position pointed away from the N–H group. Thus, the subsequent conformer equilibrium was shifted to the right side with \( k_1/k_2 \approx 9:1 \) (Scheme 23).

To determine the intramolecular N–H···H–B dihydrogen bond distance in CD₂Cl₂ solution \(^1\)H NMR T₁ relaxation and selective 1D NOE measurements were carried out. These independent experiments showed that the DHB length is very close to the value determined in the solid state by neutron diffraction in the range of approximately 1.6–1.8 Å and becomes even shorter at elevated temperatures. Therefore, the NMR data gave strong evidence that the structure of *ansa*-ammonium borate CATH₂ in solution is similar to that in the solid state, which was also supported by independent FT-IR measurements.
Scheme 23  TMP ring inversion in the \textit{ansa}-ammonium borate CATH$_2$ [64]

![Scheme 23](image)

Scheme 24  Possible intermediates in hydrogen activation by \textit{ansa}-aminoborane CAT [64]

Although our theoretical calculations support the synchronous mechanism for the hydrogen activation with N–H$_2$–B as an intermediate, the formation of a \sigma-complex between borane and hydrogen NB–H$_2$ cannot be ruled out at this point (Scheme 24). Further experimental studies are needed to favor one of the mechanisms.

As a continuation of our work, we proposed that the reduction of Lewis acidity of the active boron center of \textit{ansa}-aminoboranes should not only lower the temperature needed for hydrogen liberation but should also lead to an increase in their catalytic activity in hydrogenation reactions, which will be discussed in the next section. In this respect, the new \textit{ansa}-aminoboranes MeCAT and NpCAT, with more sterically hindered and electron donating benzyl bridges between Lewis acid and base, were synthesized in a similar manner as the original \textit{ansa}-aminoborane CAT (Scheme 21) (unpublished results) [43].

While the time required for the splitting of hydrogen by MeCAT and NpCAT dramatically increased compared to the \textit{ansa}-aminoborane CAT (1 week instead of
Scheme 25  Reversible hydrogen activation by *ansa*-aminoboranes MeCAT and NpCAT (unpublished results) [43]

![Scheme 25](image)

**Scheme 26**  Synthesis of *ansa*-phosphinoborane PCAT (unpublished results)

a few minutes), the corresponding *ansa*-ammonium borates MeCATH₂ and NpCATH₂ were losing hydrogen gas only slightly faster than CATH₂ upon heating (Schemes 22 and 25). Thus, in contrast to intermolecular phosphine-borane and amine-borane systems, the further reduction of the Lewis acidity of the borane moiety turned out to be of minor importance in the case of the *ansa*-aminoboranes [27, 44].

After 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 by us. At first, the TMP moiety in the *ansa*-aminoborane CAT was replaced by a bulky secondary di-tert-butylphosphine (Scheme 26). The corresponding *ansa*-phosphinoborane PCAT, which was synthesized by a standard two-step procedure in 54% total yield, exists as a stable intramolecular LAB adduct and cannot cleave H₂ even at elevated temperature (unpublished results) [66].

During further investigations a general approach for the modification of *ansa*-ammonium borates was considered: basicity of the nitrogen atom can be reduced to facilitate proton transfer by weakening the N–H bond. The corresponding *ansa*-ammonium borates containing less basic amine moieties than TMP – MCATH₂, QCATH₂, iPrQCATH₂, and iPrICATH₂ – were synthesized on a gram scale by a standard three-step procedure from readily or commercially available starting materials (Scheme 27) [34].

Interestingly, lowering the basicity of the starting amines had no significant effect on the rate of hydrogen activation, but dramatically decreased the temperature and the time required for hydrogen liberation. While the original *ansa*-ammonium borate CATH₂ system liberated H₂ almost quantitatively only after 20 h at 110°C
Scheme 27  Synthesis of the new ansa-ammonium borates [34]

The estimated basicity of the corresponding N-benzylamines

(Schemes 22 and 28), under the same conditions MCATH$_2$, produced with less basic 3,3,5,5-tetramethylmorpholine instead of TMP, released hydrogen in less than 30 min. Furthermore, the ansa-ammonium borates QCATH$_2$ and iPrICATH$_2$, containing amine moieties with even lower basicity than former ones, slowly decomposed in solution even at room temperature and can be quantitatively converted to starting ansa-aminoboranes QCAT and iPrICAT after 5–10 min at 110°C. Thereby, new ansa-ammonium borates exhibited excellent kinetics (a few minutes) for the hydrogen activation and liberation. This is believed to be mainly due to a rare combination of steric, electronic, and thermodynamic effects, which were tuned by a simple modification of the amine moieties.
A different approach for the synthesis of *ansa*-aminoboranes by hydroboration of enamines with Piers’ bis(pentafluorophenyl)borane HB(C₆F₃)₂ was recently developed by Erker and co-workers [67]. The corresponding C₂-bridged *ansa*-aminoboranes were isolated in good yields of 46–70% as intramolecular LAB adducts. Some of these four-membered *ansa*-aminoboranes with correctly matched electronic and steric properties can dissociate to the “unquenched” Lewis pairs and subsequently activate hydrogen to form *ansa*-ammonium borates (Scheme 29).

In contrast to the previously reported *ansa*-aminoboranes with benzyl bridges between Lewis acid and Lewis base centers, Erker’s *ansa*-aminoboranes undergo different reversible transformations even at room temperature and fully decompose upon heating (Scheme 30). The above-mentioned side reactions considerably limit further applications of C₂-bridged *ansa*-aminoboranes.

Recently we also reported new C₂-bridged *ansa*-aminoboranes with a 1,2-phenylene fragment between the N and B active centers [24]. The *ansa*-aminoboranes TMPCAT and DMACAT were prepared in high yield by the standard procedure from *o*-N,N-dialkylaminophenyllithiums and bis(pentafluorophenyl)chloroborane (Scheme 31). While dimethylamine-based DMACAT exists as an intramolecular LAB adduct, in TMPCAT Lewis acidic and Lewis basic centers remain “unquenched” due to the steric hindrance between the bulky 2,2,6,6-tetramethylpiperidine and bis(pentafluorophenyl)borane moieties.

Both TMPCAT and DMACAT activated hydrogen under mild conditions and gave the corresponding *ansa*-ammonium borates in almost quantitative yields. However, *ansa*-aminoborane TMPCAT was much more reactive towards hydrogen than DMACAT and formed the *ansa*-ammonium borate TMPCATH₂ instantly upon exposure to hydrogen (Scheme 32). On the other hand, all attempts to dehydrogenate TMPCATH₂ back to the starting *ansa*-aminoborane were unsuccessful and only trace amounts of TMPCAT could be detected by ¹⁹F NMR, while *ansa*-ammonium borate DMACATH₂ containing a less basic dimethylamine moiety was able to release hydrogen even at room temperature.
Scheme 30 Possible side reactions of Erker’s *ansa*-aminoboranes [67]

Scheme 31 Synthesis of *ansa*-aminoboranes TMPCAT and DMACAT [24]

The exceptional stability of TMPCATH₂ (pKₐ = 5.7) compared to the “more basic” CATH₂ (pKₐ = 3.7) with an additional CH₂ group between active centers can be explained by the fact that the formation of the six-membered H–B–C₂–N–H pseudo-ring is thermodynamically more favorable than the respective H–B–C₃–N–H seven-membered ring. The comparison of the structures of *ansa*-aminoborane TMPCAT and *ansa*-ammonium borate TMPCATH₂ in a solid state, revealed that hydrogen activation results in a minor change in the geometry of the B–C=C–N frame (Fig. 3). Thus the rigid geometry of TMPCAT is optimal for the activation of hydrogen.

These new results on the effect of the basicity of amine moiety on the stability of *ansa*-ammonium borates are in a good agreement with those obtained by Piers for the first *ansa*-aminoborane DPhACAT (Schemes 3 and 32) [20]. Specifically, while DPhACAT was unable to activate hydrogen due to the significantly reduced basicity of the diphenylamino group, in situ generated *ansa*-ammonium borate DPhACATH₂ was not detected even at low temperatures and only liberation of hydrogen was observed.
Scheme 32. The effect of the basicity of amine moiety on the reversible H₂ activation by ansa-aminoboranes [24]

Fig. 3. Crystal structures of ansa-aminoborane TMPCAT and ansa-ammonium borate TMPCATH₂ determined by X-ray [24]

Another example of intramolecular ansa-aminoboranes able to cleave hydrogen heterolytically is pyrazolylboranes recently reported by Tamm et al. (Scheme 33) [68]. They showed that the direct reaction of the bulky 3,5-di-tert-butyl-1H-pyrazole with secondary boranes leads to the corresponding pyrazolylboranes and pyrazoliumborates depending on the Lewis acidity of the borane. Thus, while highly Lewis acidic Piers’ bis(pentafluorophenyl)borane HB(C₆F₅) reacted with 3,5-di-tert-butyl-1H-pyrazole to afford pyrazolium-borate trans-PyrCATH₂ in high yield, the reaction
Scheme 33  Synthesis of pyrazolylboranes and pyrazolium-borates [68, 69]

with less Lewis acidic 9-borabicyclo[3.3.1]nonane (9-BBN) proceeded with evolution of $\text{H}_2$ and gave pyrazolylborane BBNCAT as a final product [69]. Since 3,5-di-tert-butyl-1H-pyrazole is much more basic than the N-phenyl-2,2,6,6-tetramethylpiperidine moiety in TMPCATH$_2$, the corresponding pyrazolium-borate trans-PyrCATH$_2$ can even be sublimed at 100°C/0.05 mbar without noticeable decomposition. However, the dehydrogenation of trans-PyrCATH$_2$ to pyrazolylborane PyrCAT was successfully achieved only by employing extremely reactive carbene–borane FLP consisting of 1,3-di-tert-butylimidazolin-2-ylidene (IBrit) and B(C$_6$F$_5$)$_3$ [19, 70]. In contrast to BBNCAT, the obtained pyrazolylborane PyrCAT could easily react with hydrogen under mild conditions to give a mixture of trans and cis isomers (81:19) of PyrCATH$_2$ in almost quantitative yield.

6  Catalytic Hydrogenation of Unsaturated Nitrogen-Containing Compounds by Intramolecular ansa-Ammonium Borates

While the hydrogenation of unactivated alkenes and alkynes without transition metals is still rather limited (see Chap. 8), boranes (see Chap. 4) and phosphinoboranes were recently shown to catalyze the direct hydrogenation of bulky imines and enamines under mild conditions (Table 5) [71, 72].

The main disadvantages of boranes and phosphinoboranes as metal-free catalysts for hydrogenation are their low substrate tolerance and low activity. For instance, only sterically hindered (Table 5, entries 1, 2, 5, 7, 8) and low-basic (Table 5, entries 3, 6) unsaturated nitrogen-containing compounds can be
### Table 5  Catalytic hydrogenation of imines and enamines by intramolecular phosphonium-borates

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst</th>
<th>Conditions</th>
<th>Amine</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![Entry 1 Image]</td>
<td>5 mol% Mes$_2$PH$_2$Mes</td>
<td>5 atm H$_2$, 80°C, 1 h</td>
<td>![Entry 1 Amine Image]</td>
<td>79 [71]</td>
</tr>
<tr>
<td>2</td>
<td>![Entry 2 Image]</td>
<td>![Entry 2 Catalyst Image]</td>
<td>5 atm H$_2$, 140°C, 1 h</td>
<td>![Entry 2 Amine Image]</td>
<td>88 [71]</td>
</tr>
<tr>
<td>3</td>
<td>![Entry 3 Image]</td>
<td>5 atm H$_2$, 120°C, 10.5 h</td>
<td>![Entry 3 Amine Image]</td>
<td>97 [71]</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>![Entry 4 Image]</td>
<td>5 atm H$_2$, 120°C, 48 h</td>
<td>![Entry 4 Amine Image]</td>
<td>5 [71]</td>
<td></td>
</tr>
</tbody>
</table>
catalytically hydrogenated with 5–20 mol% of phosphonium-borates. Both of these above-mentioned factors facilitate dissociation of the LAB adducts between the catalyst and the substrate/product or fully prevent their formation. The unsaturated nitrogen-containing compounds that do not fulfill the required criteria, for instance the sterically open imine from benzaldehyde and benzylamine, can only be reduced stoichiometrically with such systems (Table 5, entry 4).

As a continuation of our investigations on the intramolecular ansa-aminoboranes, we examined the reduction of unsaturated nitrogen-containing compounds with the original CATH$_2$ and later with its low basic analogues: MCATH$_2$, QCATH$_2$, iPrICATH$_2$, iPrQCATH$_2$ (Table 6) [34, 63]. Among previously reported non-metal systems for catalytic hydrogenation based on the bis(perfluorophenyl)boranyl moiety (Table 5) the ansa-ammonium borates have shown high activity and high substrate tolerance in the hydrogenation of a wide range of imines, enamines, and quinolines.

These results (Table 6) further support a proposed mechanism for the catalytic hydrogenation by FLPs in which any one, or more, of the equilibrium steps may be the rate-determining step, depending on the structure of both substrates and catalysts (Scheme 34).

First, ansa-aminoboranes MeCAT and NpCAT with decreased Lewis acidity showed extremely low activity in the hydrogenation of imines, due to the longer time required for the splitting of dihydrogen compared to CAT (1 week instead of a few minutes; Scheme 34, Stage I).

Second, the “less basic” ansa-ammonium borates MCATH$_2$, QCATH$_2$, iPrICATH$_2$, and iPrQCATH$_2$ showed higher catalytic activity than the original CATH$_2$ due to a facilitated proton transfer. Full conversions were achieved with lower catalyst loadings and/or shorter reaction times and/or lower temperatures. Thus the proton-transfer equilibrium seems to be a primary and rate controlling step in the reduction of bulky N-aryketimines and quinolines (Scheme 34, Stage II and Table 6, entries 16–25 and 31–35).

Third, when both the starting unsaturated nitrogen-containing compound and the catalyst are bulky enough (e.g., N-benzyl-α-methylbenzylamine and iPrQCATH$_2$; Table 6, entry 10), the nucleophilic attack of a hydride ion to the protonated double bond can also be suppressed and becomes the rate-limiting step (Scheme 34, Stage III and Table 6, entries 10, 20, 25).

Finally, the inhibition of the catalyst activity by LAB adduct formation seems to be a rate-determining step in the reduction of non-bulky imines (Scheme 34, Stage IV and Table 6, entries 3, 26–29, 31–32). While generally more active ansa-ammonium borates MCATH$_2$, QCATH$_2$, and iPrICATH$_2$ could provide only a stoichiometric reduction of non-bulky phenylacetone-N-methylamine (Table 6, entries 26–29), the more sterically hindered iPrQCATH$_2$-catalyzed hydrogenation gave the corresponding amine in 82% yield (Table 6, entry 30).

Further optimization of the reaction conditions for the hydrogenation of bulky unsaturated nitrogen-containing compounds revealed (Table 7) that the best results can be obtained by using 1 mol% of QCATH$_2$ as a catalyst in toluene and hexane at 80°C (2.5 h) or Et$_2$O at 50°C (1 h), respectively (Table 7, entries 4, 5, 10).
Table 6 Catalytic hydrogenation of imines by ansa-ammonium borates [34, 63]

![Chemical Structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst</th>
<th>mol%</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
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<td><img src="image1" alt="Substrate 1" /></td>
<td>CATH₂</td>
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<td>20</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Substrate 2" /></td>
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<td>12</td>
<td>100</td>
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<td><img src="image3" alt="Substrate 3" /></td>
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<td><img src="image5" alt="Substrate 5" /></td>
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<td><img src="image6" alt="Substrate 6" /></td>
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<td>12</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td><img src="image8" alt="Substrate 8" /></td>
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<td>5</td>
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<tr>
<td>9</td>
<td><img src="image9" alt="Substrate 9" /></td>
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<td><img src="image11" alt="Substrate 11" /></td>
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<td>14</td>
<td><img src="image14" alt="Substrate 14" /></td>
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<td>100</td>
</tr>
<tr>
<td>15</td>
<td><img src="image15" alt="Substrate 15" /></td>
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<td>12</td>
<td>100</td>
</tr>
<tr>
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<td><img src="image16" alt="Substrate 16" /></td>
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<td>3</td>
<td>100&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>12</td>
<td>100</td>
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<tr>
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<td>12</td>
<td>80</td>
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<td><img src="image21" alt="Substrate 21" /></td>
<td>CATH₂</td>
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<td>4</td>
</tr>
<tr>
<td>22</td>
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<td>12</td>
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</tr>
<tr>
<td>26</td>
<td><img src="image26" alt="Substrate 26" /></td>
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<td><img src="image27" alt="Substrate 27" /></td>
<td>MCATH₂</td>
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<td><img src="image28" alt="Substrate 28" /></td>
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<td>29</td>
<td><img src="image29" alt="Substrate 29" /></td>
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<td><img src="image31" alt="Substrate 31" /></td>
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<td>iPrQCATH₂</td>
<td>4</td>
<td>12</td>
<td>97</td>
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</tbody>
</table>

<sup>a</sup>80°C
Scheme 34 Proposed mechanism for the catalytic hydrogenation of imines by *ansa*-ammonium borates [34]

Table 7 Optimization of the conditions for catalytic hydrogenation by *ansa*-ammonium borate QCATH₂ [34]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Temperature (°C)</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
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<td>CH₂Cl₂</td>
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<td>60</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>Et₂O</td>
<td>2.5</td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>CDCl₃</td>
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<td>80</td>
<td>92</td>
</tr>
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<td>4</td>
<td>Hexane</td>
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<td>80</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>Toluene</td>
<td>2.5</td>
<td>80</td>
<td>99</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>2.5</td>
<td>80</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>Toluene</td>
<td>1</td>
<td>25</td>
<td>31</td>
</tr>
<tr>
<td>8</td>
<td>Et₂O</td>
<td>1</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>Toluene</td>
<td>1</td>
<td>50</td>
<td>89</td>
</tr>
<tr>
<td>10</td>
<td>Et₂O</td>
<td>1</td>
<td>50</td>
<td>97</td>
</tr>
</tbody>
</table>
Scheme 35  Regeneration of *ansa*-aminoborane QCAT from hydrated adduct QCATH$_2$O [34]

The sensitivity of FLPs towards traces of water is a well known fact [7, 20, 29]. The presence of accidental H$_2$O in the reaction mixture poisons the *ansa*-aminoborane FLP catalyst via adduct formation; the same hydrated adduct is also formed during the quenching of the reaction mixture (Scheme 35). Therefore the dehydration of *ansa*-ammonium borates, containing the highly energetic boron–oxygen bonds, is a key transformation in the catalyst recovery procedure. Surprisingly, after the benzene solution of QCATH$_2$O was treated with an excess of TMSBr (5 equiv.) at 80°C for 5 min and then evaporated under vacuum, *ansa*-aminoborane QCAT was isolated in almost quantitative yield. This procedure was successful mainly because the Si–O bond is even more stable than the B–O bond. However, this protocol is not applicable to the recovery of CAT from the corresponding water adduct, since the decreased basicity of the amine part plays a key role, facilitating elimination of HBr upon heating.

As a result of the above-mentioned observations, the hydrogenation of a model compound, *N*-(4-methoxy)phenyl-1-phenylethylideneamine, by *ansa*-ammonium borate QCATH$_2$ (1 mol%) was scaled up to gram quantities (5.632 g) giving the corresponding amine in 97% isolated yield. Moreover, 80% of the catalyst QCATH$_2$ was recovered by a simple extraction of the acidic solution with toluene followed by dehydration with TMSBr at 80°C and hydrogen activation at room temperature.

7  Enantioselective Hydrogenation of Unsaturated Nitrogen-Containing Compounds by Intramolecular *ansa*-Aminoboranes

The enantioselective hydrogenation of unsaturated nitrogen-containing compounds catalyzed by FLP systems is a less developed topic and until recently was possible only by the asymmetric hydrogenation of *N*-arylketimine with 3-pinanyl-bis(perfluorophenyl)borane and tris(tert-butyl)phosphonium/chiral-alkyl-bis
Table 8  Enantioselective catalytic hydrogenation of N-arylketimines by chiral-borane and phosphonium-chiral-borate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst</th>
<th>Conditions</th>
<th>Conv. (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Chemical Structure" /></td>
<td>10 mol% ($\text{C}_6\text{F}_5\text{B}$)</td>
<td>20 atm $\text{H}_2$, 65°C, 15 h</td>
<td>&gt;99</td>
<td>13 [61]</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2.png" alt="Chemical Structure" /></td>
<td>5 mol% ($\text{C}_6\text{F}_5\text{B}$)</td>
<td>25 atm $\text{H}_2$, 65°C, 15 h</td>
<td>95</td>
<td>79 [73]</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3.png" alt="Chemical Structure" /></td>
<td>25 atm $\text{H}_2$, 65°C, 15 h</td>
<td>96</td>
<td>81 [73]</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="image4.png" alt="Chemical Structure" /></td>
<td>25 atm $\text{H}_2$, 65°C, 15 h</td>
<td>&gt;99</td>
<td>81 [73]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="image5.png" alt="Chemical Structure" /></td>
<td>25 atm $\text{H}_2$, 65°C, 15 h</td>
<td>37</td>
<td>74 [73]</td>
<td></td>
</tr>
</tbody>
</table>

(performophenyl)hydroborate (Table 8) [61, 73]. The phosphonium-chiral-borate catalyzed the hydrogenation of different N-arylketimines giving the corresponding amines in good yields and good enantioselectivities (Table 8, entries 2–5). However, in contrast to achiral systems based on triarylboranes (unpublished results) [36, 59, 60, 71], higher pressure of hydrogen (25 atm) were required in the case of chiral-alkyl-bis(performophenyl)borane-based FLP, probably to prevent retro-hydroboration see [74].

Since, in contrast to boranes, a much broader variety of chiral amines is readily and commercially available, chiral ansa-ammonium borates are promising candidates for asymmetric hydrogenation. Indeed, we demonstrated that ansa-ammonium borates with chiral-amine moieties can also be used as catalysts for the asymmetric hydrogenation of unsaturated nitrogen-containing compounds [34]. The standard procedure for the preparation of chiral ansa-ammonium borates $\text{Q}^*\text{CATH}_2$, and $\text{iPrI}^*\text{CATH}_2$ from the corresponding enantiopure secondary
Amine-Borane Mediated Metal-Free Hydrogen Activation and Catalytic Hydrogenation

Scheme 36  Racemization of the enantiopure iPrICAT

[34]

amines was applied (Scheme 27). Unfortunately, in the case of chiral-7-isopropyl-3, 3-dimethyl-2-phenylindoline the racemic ansa-ammonium borate iPrICATH$_2$ was obtained as a final product (Scheme 36). A possible mechanism for the racemization of ansa-aminoborane iPrICAT involves the abstraction of an α-hydride from the amine fragment by the Lewis acidic borane moiety and formation of the intramolecular iminium borohydride (Scheme 37).

Later, a similar racemization phenomenon was also observed for intermolecular FLP systems consisting of catalytic amounts of B(C$_6$F$_5$)$_3$ and chiral amines (Scheme 38) [34, 35]. Interestingly, heating of the chiral 7-isopropyl-3,3-dimethyl-2-phenylindoline with 10 mol% of B(C$_6$F$_5$)$_3$ at 110°C and 1 atm of argon led to full racemization in 15 h. However, no racemization occurred under an atmosphere of H$_2$ but otherwise identical conditions.

Therefore, only amines with a chiral tertiary carbon atom adjacent to the nitrogen atom can be applied in the backbone of chiral ansa-ammonium borates. For this reason, another enantiopure ansa-aminoborane Car*CAT based on 4a,9a-substituted-2,3,4,4a,9,9a-hexahydro-1H-carbazole skeleton was prepared according to the standard procedure in 34% total yield (Scheme 38). However, because the starting hexahydrocarbazole had the lowest basicity in the series of investigated amines, the equilibrium in hydrogen activation between Car*CAT and Car*CATH$_2$ is shifted to the left and the corresponding ansa-ammonium borate could not be isolated even at low temperature.

The asymmetric hydrogenation of nitrogen-containing compounds with chiral ansa-ammonium borate Q*CATH$_2$ and ansa-aminoborane Car*CAT was investigated (Table 9). While the enantiopure ansa-ammonium borate Q*CATH$_2$ exhibited the same unprecedentedly high activity as its racemic version (Table 9), hydrogenation with “low basic” ansa-aminoborane Car*CAT resulted in low to moderate conversions (Table 9, entry 4). In all cases the best ees were obtained in MTBE as a solvent at room temperature (Table 9, entries 3, 7, 10). Although the achieved enantioselectivities were low with both ansa-ammonium borate Q*CATH$_2$ and ansa-aminoborane Car*CAT, these experiments clearly proved the feasibility of using chiral amines as a part of intramolecular FLP systems for the chiral induction during catalytic hydrogenation. The highest ees achieved with Q*CATH$_2$ are in the range of about 35–40% (ee ~70:30). This is remarkable, taking into account the large distance between the chiral center at the 4-position of the tetrahydroquinoline moiety and the active stereogenic boron center.
Scheme 37 Interactions of chiral 7-isopropyl-3,3-dimethyl-2-phenylindoline with B(C₆F₅)₃ under an atmosphere of hydrogen or nitrogen [34]

Scheme 38 Synthesis of enantiopure ansa-aminoborane Car*CAT [34]
Table 9  Enantioselective catalytic hydrogenation by \textit{ansa}-ammonium borate $\text{Q}^*\text{CATH}_2$ and \textit{ansa}-aminoborane $\text{Car}^*\text{CAT}$ [34]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Temp. (°C)</th>
<th>Conv. (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
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<td>Et$_2$O</td>
<td>1</td>
<td>20</td>
<td>100</td>
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<td></td>
<td>$\text{Q}^*\text{CATH}_2$</td>
<td>Et$_2$O</td>
<td>1</td>
<td>60</td>
<td>100</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>$\text{Q}^*\text{CATH}_2$</td>
<td>Et$_2$O</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>31</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>$\text{Q}^*\text{CATH}_2$</td>
<td>MTBE</td>
<td>12</td>
<td>20</td>
<td>100</td>
<td>37</td>
</tr>
</tbody>
</table>

8  Catalytic Hydrogenation of Unactivated Triple C–C Bonds by Intramolecular \textit{ansa}-Aminoboranes

The metal-free hydrogenation of unactivated alkenes (220–235°C and 68–170 atm of H$_2$) [75, 76], polycyclic aromatic hydrocarbons (170–200°C and 25–100 atm of H$_2$) [77, 78] and coal (280–350°C and 148–247 atm of H$_2$) [79] under harsh reaction conditions with simple trialkylboranes, tetraalkyldiborane and boron triiodide is well known. Until recently, due to the heterolytic nature ofonium borohydrides, there were only a few examples of 1,4-conjugated hydrogenation of enone, ynone, dienes, and styrenes catalyzed by FLPs [40, 80, 81].

A breakthrough in this area was the recent discovery by us that \textit{ansa}-aminohydroboranec \text{DMACATBH} can hydrogenate internal alkynes even under mild conditions at 2 atm hydrogen pressure and 80°C (Table 10) [82].

The \textit{ansa}-aminohydroborane \text{DMACATBH} was prepared by heating of either \text{DMACAT} at 80°C under 2 atm of hydrogen or \text{DMACATH}_2 under an atmosphere of argon via hydrogenolysis of the B–C bond (Scheme 39).

The mechanisms of hydrogenation of alkynes by \text{DMACATBH} have been investigated in some detail. It involves the sequence of hydroboration followed by hydrogen activation and hydrogenolysis of the B–C bond accompanied by the liberation of alkene (Scheme 40).
Table 10  Catalytic hydrogenation of unactivated alkenes by **DMACATBH** [81]

![Catalytic hydrogenation reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>3</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>3</td>
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<td>80</td>
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<tr>
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<td></td>
<td>100</td>
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<td>4</td>
<td></td>
<td>3</td>
<td></td>
<td>78</td>
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<tr>
<td>5</td>
<td>![Cl-substituted substrate]</td>
<td>3</td>
<td>![Cl-substituted product]</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>![O-substituted substrate]</td>
<td>3</td>
<td>![O-substituted product]</td>
<td>100</td>
</tr>
<tr>
<td>7</td>
<td>![Ph-enylalkyne]</td>
<td>3</td>
<td>![Ph-enylalkyne product]</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td>![Biphenylalkyne]</td>
<td>3</td>
<td>![Biphenylalkyne product]</td>
<td>52</td>
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<tr>
<td></td>
<td></td>
<td>9</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>
9 Conclusions

The use of FLPs as metal-free hydrogenation catalysts is a rapidly expanding field in modern organic chemistry. Since the pioneering studies on the reversible hydrogen activation by phosphinoboranes, numerous FLP systems for hydrogenation have been reported. Among others the *ansa*-aminoborane concept is one of the most promising for further elaboration with the aim of obtaining industrially applicable catalysts. Specifically, this approach allows the performance of hydrogenation of unsaturated nitrogen-containing compounds and internal alkenes under mild conditions with low catalyst loadings. Furthermore, recently the first example of
the enantioselective hydrogenation with chiral ansa-ammonium borates was demonstrated. Given the wide range of ansa-aminoboranes with different structures and properties, we anticipate new transformations will arise in the near future. Therefore over the next few years, many new exciting developments within this field are expected.

References

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A frustrated-Lewis-pair approach to catalytic reduction of alkynes to cis-alkenes

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Frustrated Lewis pairs are compounds containing both Lewis acidic and Lewis basic moieties, where the formation of an adduct is prevented by steric hindrance. They are therefore highly reactive, and have been shown to be capable of heterolysis of molecular hydrogen, a property that has led to their use in hydrogenation reactions of polarized multiple bonds. Here, we describe a general approach to the hydrogenation of alkynes to cis-alkenes under mild conditions using the unique ansa-aminohydroborane as a catalyst. Our approach combines several reactions as the elementary steps of the catalytic cycle: hydroboration (substrate binding), heterolytic hydrogen splitting (typical frustrated-Lewis-pair reactivity) and facile intramolecular protodeborylation (product release). The mechanism is verified by experimental and computational studies.

Recently, a new approach to dihydrogen activation known as the frustrated Lewis pairs (FLPs) concept has been introduced1-4. A combination of highly Lewis-acidic boranes and sterically hindered bases can split hydrogen heterolytically to generate onium (for example, phosphonium, ammonium) borohydrides. These compounds demonstrate reduction activities resembling those of inorganic borohydrides such as NaBH4 that is, they are suitable predominantly for the reduction of polarized multiple bonds. Amines, enamines, silyl ethers5-8, 6,8-8, 6,8-2-oxazolines7, yrones4 and N-alkylpyridines2 have been hydrogenated using stoichiometric or catalytic amounts of FLPs. Owing to the heterolytic nature of FLP-H2 adducts, the hydrogenation of unsaturated multiple C-C bonds using FLPs has some natural limitations, because during the relevant step of the catalytic cycle a proton transfer from catalyst to substrate should take place (Fig. 1a). Although Greb et al. have implemented this approach in the hydrogenation of alkynes under ambient conditions, this method is predictably restricted to alkynes with high proton affinity9.

Combining the FLP approach and previous knowledge about borane-catalyzed hydrogenation of alkene10-14 and polyalkenes10-14, we propose herein a new general catalytic pathway to the hydrogenation of unsaturated hydrocarbons (Fig. 1b) and demonstrate its validity by the highly selective hydrogenation of alkynes into cis-alkenes. Stereoselective hydrogenation of alkenes is an important protocol in the synthesis of natural and industrially relevant compounds15-23. Heterogeneous as well as homogeneous metal catalysts for this stereoselective hydrogenation are known24-26; however, metal-free catalytic hydrogenation of unsaturated alkenes into alkynes has not been reported previously.

In contrast to classical FLP-catalyzed reactions, the substrate is bound to catalyst 1 by hydroboration before hydrogen activation (Fig. 1b). The resulting borane 3, together with a Lewis base co-catalyst, can activate hydrogen, producing adduct 4. In this onium borohydride 4, a proton transfer can occur, liberating the initial borane 1, the Lewis base and hydrogenated substrate 5. To the best of our knowledge, this approach has not been studied experimentally or theoretically.

Initially, we attempted to use Piers’ borane, (C5F5)2BH (ref. 29), as a catalyst. (C5F5)2BH smoothly hydroborates different alkenes and alkynes30,31. Moreover, it has been shown that the resulting bis(pentafluorophenyl)alkylboranes as well as (C5F5)2BH itself32, together with the properly chosen Lewis bases, can split hydrogen heterolytically to give the respective onium borohydrides33. However, upon heating of these compounds, only hydrogen release was observed, demonstrating the reversibility of H2 uptake by these FLPs. Our numerous attempts to realize the approach depicted in Fig. 1b using (C5F5)2BH together with different bases and additives were unsuccessful (Supplementary Section S47).

Recently, we have reported 2-[bis(pentafluorophenyl)borolyl]-N,N-diarylalanilines, exemplifying a new class of bridged frustrated B/N Lewis pairs24. Interestingly, compound 6 exists as an intramolecular Lewis adduct, containing a strained four-membered C-N – B-C cycle. Owing to strain, the B-N bond in 6 is relatively weak, because at room temperature 6 reversibly reacts with hydro- gen to give ammonium borohydride 7 (Fig. 2).

Results and discussion

New ansa-aminohydroborane as a catalyst. In this work we report that, upon heating of aminoborane 6 at 80 °C under 2 bar H2, new signals (different from those of 6 or 7) appear in the 1H, 13C and 19F NMR spectra, together with the formation of C5F5H (9). The new species was isolated as a greenish oil and identified as hydroborane 8 (Fig. 2), producing in the 1H NMR spectrum a characteristic partially relaxed quadruplet (6 = 4.35 ppm, J = 105 Hz) attributed to BH2 signal. This reactivity is unprecedented, because neither inter- nor intramolecular FLPs have been reported to undergo B-C5F5 hydrogenolysis as a result of hydrogen activation35-37.

Because 8 is a potentially hydroborating BH2 species and can be produced in situ from 6, we attempted to use 8 as a catalyst in the hydrogenation of unsaturated alkenes and alkynes following the strategy depicted in Fig. 1b. Hex-1-ene (12b), hex-1-yne (12a) and hex-3-yne (11a) were heated separately together with 10 mol% of precatalyst 6 in C6D6 under 2 bar H2 at 80 °C. After 15 h, no products of hex-1-ene and hex-1-yne hydrogenation were detected by NMR. In the case of 11a, no evidence of starting alkyne was found; instead, a complex mixture of alkenes was observed, mostly comprising cis-hex-3-ene 11b. Minor amounts of trans-hex-3-ene and other hexenes were attributed to...
Figure 1 | FLP-catalysed hydrogenation of multiple C-C bonds. a, Traditional approach including heterolytic hydrogen splitting by the catalyst followed by protonation of the substrate as the key steps. b, In the novel approach, substrate activation via hydroboronation precedes hydrogen activation. Reduced substrate is then released via protonation of the formed H₂ adduct.

Figure 2 | Mechanism of catalytic hydrogenation of alkynes into cis-alkenes. Formation of the active catalyst species 8 proceeds through H₂ addition to the precatalyst 6, followed by intramolecular protonative cleavage of the CsF₃ ring. Produced catalyst 8 hydroborates alkene (substrate binding), producing vinylborane 27. The latter activates hydrogen by the FLP mechanism. Intramolecular protonation of vinyl carbon in 28 causes cycle propagation, while CsF₃ group cleavage leads to active catalyst degradation. Reaction of hydroboration intermediates 27 with D₂ results in selective formation of monodeuterated cis-alkenes 21c, 26-d and catalyst 8-d. Deuterium occurs selectively to the 8–C carbon, giving solid support to the proposed mechanism.

isomerization of the initially produced cis-hex-3-ene via a hydroboronation/rehydroboronation sequence, catalysed either by 8 or other hydroborane species. When hydrogenation of 11a was repeated for 3 h with 5 mol% 6, cis-hex-3-ene 11b was produced almost exclusively (according to NMR).

Various dialkyl-, diaryl-, arylalkylacetylenes were successfully hydrogenated under standard conditions—5 mol% 6 in CsD₃, 2 bar H₂, 80 °C, 3 h (Table 1)—demonstrating the generality of the approach and providing exceptional cis-stereoselectivity. Silyl-protected esters, ethers, silyl-protected ynoles and diynes (Table 1, entries 9, 10, 19, 12, 13) were also successfully hydrogenated. The products were isolated in excellent yields in experiments scaled up to 10 mmol of substrate. Some of the substrates required prolonged reaction times and/or higher temperatures and catalyst
Table 1 | Catalytic hydrogenation of alkynes using 6 as a precatalyst.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Conversion: isolated yield (%)</th>
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<tr>
<td>1*</td>
<td>10a</td>
<td>10b</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>11a</td>
<td>11b</td>
<td>100</td>
</tr>
<tr>
<td>3†</td>
<td>12a</td>
<td>-</td>
<td>n.r.†</td>
</tr>
<tr>
<td>4</td>
<td>11a + 12b</td>
<td>13b</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>11a + 12a</td>
<td>13b</td>
<td>100</td>
</tr>
<tr>
<td>6*</td>
<td>14a</td>
<td>15a</td>
<td>100</td>
</tr>
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<td>7</td>
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<tr>
<td>9</td>
<td>16a</td>
<td>16b</td>
<td>100 (98%)</td>
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<tr>
<td>10</td>
<td>17a</td>
<td>17b</td>
<td>100</td>
</tr>
<tr>
<td>11</td>
<td>18a</td>
<td>18b</td>
<td>100 (95%)</td>
</tr>
<tr>
<td>12</td>
<td>19a</td>
<td>19b</td>
<td>100</td>
</tr>
<tr>
<td>13</td>
<td>20a</td>
<td>20b</td>
<td>100 (94%)</td>
</tr>
<tr>
<td>14</td>
<td>21a</td>
<td>21b</td>
<td>50</td>
</tr>
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<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product(s)</th>
<th>Conversion: product (%)</th>
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<tbody>
<tr>
<td>16</td>
<td>Ph</td>
<td>22a, TMS</td>
<td>88 (22b) 12 (22c)</td>
</tr>
<tr>
<td>17†</td>
<td>22a</td>
<td>22b, TMS</td>
<td>30.5 (22b) 4.3 (22c)</td>
</tr>
<tr>
<td>18</td>
<td>23a</td>
<td>23b, TMS</td>
<td>&lt;20 (23b)</td>
</tr>
<tr>
<td>19**</td>
<td>23a</td>
<td>23c</td>
<td>71 (23b) 9.5 (23c)</td>
</tr>
<tr>
<td>20††</td>
<td>24a</td>
<td>24b, Bu</td>
<td>44 (24b) 26 (other alkenes)</td>
</tr>
</tbody>
</table>

1) 10 mol% of 6; 2) Reaction time: 15 h; 3) No reaction; 4) 10 mol% of 6; 5) Reaction time: 15 h; 6) 10 mol% of 6, 120 °C; 7) 20 mol% of 6, 18 h; 8) 15 mol% of 6, 120 °C, 10 h; 9) D2 was used instead of H2; 10) 10 mol% of 6, 5 h; 11) H2 gas was used instead of H2; 12) Low conversion (60%) is due to insufficient pressure of available H2 (1.2 bar); 13) Isolated yield in 15% ratio, Bu, butyl; Ph, phenyl; Pr, propyl; p-Tol, 4-methylphenyl; TBS, tert-butyldimethylsilyl; TES, trimethylsilyl; TMS, trimethylsilyl.

loading, and some were not hydrogenated at all. There are essentially two substrate classes that are unreactive using the current method: terminal alkynes and alkynes comprising a terminal double bond. Nevertheless, terminal alkynes can be silylated using conventional methods and the obtained silylacetylenes were smoothly hydrogenated (Table 1, entries 11, 16). Catalytic activity up to 31.6 h⁻¹ was estimated using 6 or 8 as the catalyst under standard conditions and 11a or 15a as substrates. Remarkably, the
catalytic hydrogenation proceeds at room temperature, although 20 times slower than at 80 °C. Meanwhile, high-pressure H2 (30 bar) causes almost tenfold acceleration of hydrogenation up to 296 h⁻¹ (Supplementary Section S7).

No over-reduction to alkanes was detected. Under standard conditions cis-alkenes were produced exclusively, with traces of other products such as trans-alkenes barely detected by ¹H NMR. The only exception was 1-trimethylsilyl-2-pentynylacetylene 22a, where a substantial amount of trans-alkene 22c was produced (12 mol%), independently of the conversion level (Table 1, entries 16, 17). Product 22c is likely to be produced directly during hydrogenation. Accumulation of trans-alkenes as a result of isomerization was observed when prolonged heating and/or high temperature (120 °C) was applied to force hydrogenation of poorly reactive substrates (Table 1, entries 19, 21).

Mechanistic insight into the catalytic cycle. The reaction mechanism for the catalytic hydrogenation of alkynes was investigated in a combined experimental/theoretical study. The basic steps of the envisioned catalytic cycle are depicted in Fig. 2, and are consistent with the new concept outlined in Fig. 1b.

The initial step of the catalytic cycle, that is, the hydroboration of alkynes with 8, was verified by the isolation of respective intermediates 27b–e. Additionally, relative rates of hydroboration of different alkynes and alkenes by 8 were measured in competitive experiments. The rate of the reaction is descending in the order hex-3-yne > hex-1-yne > but-2-yne > hex-1-ene > cis-hex-3-ene > prop-1-yn-1-ylbenzene (α-β-positions) > prop-1-yn-1-ylbenzene (α-position) > diphenylacetylene: cis-but-1-en-1-yl benzene = 136 : 109 : 57 : 44 : 35 : 4 : 1: no reaction (25 °C); no reaction (80 °C) (Supplementary Section S31). These rates are in agreement with common rules of hydroboration. Hydroboration of 10a appears instantly at room temperature. Replacement of a methyl group with a phenyl substituent leads to 14-fold retardation of hydroboration to the sterically less hindered site of prop-1-yn-1-ylbenzene and 57-fold to the more hindered site. Eventually, diphenylacetylene 21a remains intact with 8 at room temperature and requires heating at 80 °C, apparently making the hydroboration the rate-limiting step in the overall slow hydrogenation of this substrate.

Density functional theory (DFT) calculations (Supplementary Section S49) carried out for the reaction of catalyst 8 with but-2-yne (10a) predict a relatively small activation barrier (16.2 kcal mol⁻¹) for the hydroboration process, and point to the high exergonicity of this step (Fig. 3). These results suggest that alkyne hydroboration is irreversible, so compound 8 can be recovered only upon completion of the catalytic cycle. This irreversibility has also been demonstrated experimentally (Supplementary Section S32).

The zwitterionic reaction intermediates 28b–e formed in the hydrogen activation step were not detectable, which can be rationalized in light of the computed energetics. Although the formation of 28a takes place via a low barrier (TS_pret, π ≈ 5.8 kcal mol⁻¹ above 27a + H₂ in free energy), this step is found to be slightly endergonic. Notably, heterolytic H₂ splitting with B/N FLPs containing only one electron-withdrawing C₆F₅ group on the Lewis acceptor site is unprecedented due to the reduced acidity of the resulting borane. However, as pointed out previously, the ortho-phenylene linker between the B/N centres provides significant electrostatic stabilization in the zwitterionic species formed upon H₂ cleavage.

The calculations predict facile intramolecular protonation of the vinyl substituent in 28a, which proceeds as direct protodeborylation, leading to the elimination of cis-alkene 10b and regeneration of the catalyst. The barrier to product elimination is rather low (14.8 kcal mol⁻¹ relative to 28a) and is thermodynamically favoured. The mutual position of the B/N sites of the catalyst core plays a crucial role in this process because it determines the feasibility of the proton shift. In this particular case, a low-lying isomer of 28a could be identified computationally with the NH bond oriented towards the alpha carbon atom of the vinyl group (Supplementary Section S49).

Protodeborylation of 28, resulting in B-C₆F₅ cleavage and degration of the active catalyst into inactive vinylborane 29 and C₆F₅H, is an alternative reaction pathway in this phase of the catalytic cycle (Fig. 2), which has also been explored computationally. The calculated barrier of αr elimination is notably higher than that of alkene formation (19.1 kcal mol⁻¹ relative to 28a), but this process is still feasible at the applied reaction conditions. The protodeborylation of 28a is analogous to that taking place in the generation of 8 from precatalyst 6, for which computations predict an

Figure 4 | Reaction of 6 and 8 with alkynes. Alkynes hydroboration outcome depends on the level of steric crowding of the double bond: rapid and irreversible for terminal alkynes (12b); slow and reversible for cis-d-(n-alkyl)ethenes (10b, 11b), no reaction for 15b, 18b, 21b. Alternatively, alkylboranes 30 are produced from alkynes or alkenes and 6 under hydrogenation conditions. The one-pot reaction includes formation of 8 in situ, followed by hydroboration of the alkene loaded as is or produced in situ from the respective alkyne.

Figure 3 | Solution-phase Gibbs free energy diagram computed for the hydrogenation of but-2-yne (10a). Optimized structures of transition states identified for hydroboration (TS_hyb), heterolytic hydrocarbon splitting (TS_prep), and protonation (TS_prep) steps are shown in the upper part of the figure. The energetics of the elementary steps identified computationally is consistent with the proposed reaction mechanism. A detailed description of the structure and energetics of species involved in the catalytic cycle is given in Supplementary Section S49.

12b: rapid, irreversible
10b, 11b: slow, reversible
15b, 19b, 21b: no reaction
even higher barrier (23.0 kcal mol⁻¹; Supplementary Section S48). Assuming the C₂F₅H elimination to be the only catalyst degradation pathway, the ratio of the reaction rates of these two intramolecular protonation pathways corresponds to the maximum turnover number, which was found to be 91 for hydrogenation of hex-3-yne (Supplementary Section S9). Eventually, the exceptional cis-selectivity observed in the hydrogenation reactions results from exclusive syn-hydroboration and the configuration is retained during subsequent elementary steps, particularly protodeborylation.

Additional experimental support for the proposed mechanism was collected in isolation-labeling experiments. 1-Methyl-4-propyl-1-nitrobenzene-α₂, 26a, a model substrate, was hydrogenated with H₂, resulting in all four possible isomeric cis-styrenes 26b–e in nearly equal ratio (Table 1, entry 25). Isotope scrambling is in full accordance with the proposed mechanism, because the B(H)D hydrogen in 8 originates from a preceding catalytic cycle (Fig. 2). In addition, when 26a was treated with an equimolar amount of 8, products of hydroboration were isolated as a 79:21 mixture of regioisomers 27d and 27e. Upon treatment with D₂, a mixture of 26d and 26e in the ratio 79:21 was produced, together with an equimolar amount of deuterated 8-d (Fig. 2). Thus, deuteration of alkynes appears exclusively at the carbon adjacent to the boron atom in the alkynyl borane intermediate 27. A similar experiment performed with diphenylacetylene led to exclusive formation of monodeuterated cis-stilbene-d 21c (Fig. 2).

**Alkenes under hydrogenation conditions.** In an attempt to apply the new synthetic approach (Fig. 1b) to alkene hydrogenation, the reactivities of various terminal and cis-disubstituted alkenes with 6, 8 and H₂ were examined, however, no alkane products were detected (Supplementary Section S8). In stoichiometric reactions, terminal alkene 12b is hydroborated rapidly and irreversibly by catalyst 8, cis-di-(r-alkyl)alenes (10b, 11b) react at a slower rate and reversibly, whereas 8 remains intact with more sterically hindered cis-alkenes (Fig. 4). Alkyboranes 30a–c can be produced directly via hydrogenolysis of 6 in the presence of 12b or alkynes 10a, 11a (Fig. 4) and found to be particularly stable to further hydrogenolysis: 30c is the major boron-containing component of the reaction mixture after 15 h at 2 bar H₂. As a result, alkynes that contain a terminal double bond cause partial or complete deactivation of the catalyst via formation of alkyl-boranes, which are unable to propagate the catalytic cycle (in Table 1 compare entry 2 and 4, 10 and 18, 12 and 22; Supplementary Sections S24, S25). Although at the end of 11a hydrogenation the catalyst is present as alkylborane 30c, the latter can easily dissociate to give active catalyst species 8, pointing again to the reversibility of hydroboration in the reactions with cis-di-(r-alkyl)alenes (Supplementary Section S33).

These results can be interpreted readily in terms of the free energy profiles computed for the hydroboration of cis-but-2-ene and ethylene as model substrates for internal and terminal alkenes (Supplementary Sections S50, S51). Calculations predict rather different exergonicities for these substrates (−11.9 and −20.5 kcal mol⁻¹ for cis-but-2-ene and ethylene, respectively), which is in qualitative agreement with the observed reactivity. The subsequent heterolytic hydrogen cleavage is a kinetically and thermodynamically allowed elementary step; however, the intramolecular protonation of the alkyl substituent in alkylborohydride intermediate is hindered by a large activation barrier. Actually, this step represents the only limiting factor towards the hydrogenation of alkenes using the present approach, and it is associated with the lack of a σ-system in the zwiterionic intermediate formed in the H₂ activation step.

The limitation of the current approach to non-terminal alkynes also required additional studies. It is known from previous publications that FLPs react with terminal alkynes via deprotonative borylation pathway, producing the respective onium alkynylboronates 34a–b. Indeed, 6 reacts with hex-1-yne giving the respective adduct 31 (Fig. 5). Upon heating 6 with excess hex-1-yne at 80 °C under 2 bar H₂, 31 remains the major product after 1 h. However, after 3 h three new aminoborane species were formed in the ratio 3.3:2, each containing the hex-1-ynyl group, as evident from ¹H and ¹¹B NMR. The ¹¹B NMR spectrum revealed complete cleavage of the C₂F₅ group into C₆F₆H. Evidently, the inability to hydrogenate terminal alkynes is a result of catalyst degradation into species inert to hydrogen due to complete elimination of the perfluorophenyl groups.

**Conclusion.** In conclusion, we have developed a new strategy for the catalytic metal-free hydrogenation of unactivated multiple C=C bonds using frustrated Lewis pairs. Using catalyst 8, formed in situ from aminoborane 6, the approach was implemented as highly chemoselective and stereoselective hydrogenation of internal alkynes into the respective cis-alkenes under mild conditions (2 bar H₂, 80 °C). The catalytic pathway includes three steps: hydroboration of alkyne (substrate binding), heterolytic H₂ cleavage with formed vinylborane, followed by intramolecular protodeborylation of vinyl substituent, recovering 8 and releasing cis-alkene. High cis-selectivity is a result of exclusive syn-hydroboration, and is retained during subsequent steps, particularly the intramolecular protonation. Mutual ansa-B/N geometry plays a key role in all elementary steps, especially during protodeborylation, which proceeds in a single step, rather than including carbocation intermediates. The mechanism was supported by isolation of some intermediates, including the active catalyst species 8, isotope-labeling studies and quantum-chemical calculations. Substrate restrictions associated with the presence of the terminal double bond and triple bond were studied and rationalized. The computational analysis provides solid support for the proposed mechanism as all elementary steps could be identified and the obtained energetics is in full accordance with experimental findings. In principle, alkynes could be hydrogenated using the current approach; however, at the final stage of the catalytic cycle the C₂F₅ group is cleaved more easily than an alkyl group, causing catalyst degradation rather than alkene release. Some early examples of the catalytic hydrogenation of unactivated alkynes were reported by us as part of a review and are included again as entries 2, 6–8 and 11–15 in Table 1). Compared to other ansa-aminoboranes discussed there, 8 is unique enabling the catalytic hydrogenation of unactivated alkynes.

**Methods.**

**Standard protocol.** A quantity of 0.2–0.5 mmol of an alkyne were placed into a 25 ml Schlenk tube, followed by 5 mol% of 6 and 0.7 ml of C₂D₅H. The tube was filled with 2–2.2 bar of hydrogen by two freeze-pump–thaw cycles and vigorously stirred at 80 °C for 3 h, or longer if needed. The reaction mixture was transferred into an NMR tube and analysed.

**Computational details.** DFT, with the dispersion-corrected, range-separated hybrid functional (ωB97X-D exchange-correlation functional), was used to examine possible reaction pathways relevant to the title reaction. For geometry optimizations, vibrational
analysis and the estimation of solvent effects, the 6-311G(d,p) polarized triple-ζ basis set was used, and additional single-point energy calculations were carried out for each located stationary point with the larger 6-311+G(3dpd) basis set. The energy values in the paper correspond to solution-phase Gibbs free energies. Additional computational details are provided in the Supplementary Information (Computational Protocol).

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References


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Author contributions

K.C. and T.R. conceived and K.C. carried out the experiments. A.M. and I.P. designed and performed the DFT studies. All authors discussed the work.

Additional information

Supplementary information and chemical compound information are available in the online version of the paper. Reprints and permissions information is available online at www.nature.com/reprints. Correspondence and requests for materials should be addressed to T.R. and those related to computational studies to I.P.

Competing financial interests

The authors declare no competing financial interests.