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Organocatalysis and Earth-Abundant Transition Metal Catalysis for Sustainable
Borylation and Hydrodefluorination: Catalyst Design and Mechanistic Insights

By
Harleen Kaur

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of
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in
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of the
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Committee in charge:
Prof. Ryan Baxter (Chair)
Prof. Rebeca Arevalo (Advisor)
Prof. Michael Findlater
Prof. Sayantani Ghosh

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Prof. Ryan Baxter

Prof. Rebeca Arevalo

Prof. Michael Findlater

Prof. Sayantani Ghosh

Dedication

To my parents and husband, for their endless love, blessings, and the strength that carried me through this journey.

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List of Abbreviations

Ac - Acetyl
OAc - Acetate
OTf - Triflate (trifluoromethanesulfonate)
HBPin - Pinacolborane
n-BuLi - *n*-Butyllithium
D₂O - Deuterium oxide
KIE - Kinetic Isotope Effect
DHBTa - Dehydrogenative Borylation of Terminal Alkynes
R.T. - Room Temperature
equiv - Equivalent(s)
PDI - Pyridyldiimine
NH₃BH₃ - Ammonia borane
KOtBu - Potassium *tert*-butoxide
NaHBET₃ - Sodium triethylborohydride
THF - Tetrahydrofuran
THF-d₈ - Deuterated tetrahydrofuran
DCM-d₂ - Deuterated dichloromethane
CDCl₃ - Deuterated chloroform
NMR - Nuclear Magnetic Resonance
FT-IR - Fourier-transform infrared spectroscopy
GC - Gas Chromatography
PFAS - Per- and polyfluoroalkyl substances
TON - Turnover Number
PPh₃ - Triphenylphosphine
PMe₃ - Trimethylphosphine
HDF - Hydrodefluorination

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Curriculum Vita

Education

University of California
Ph.D. in organic and organometallic chemistry
Merced, California
May 2026

Panjab University
Master's in chemistry (H.S.)
Chandigarh, India
May 2019

Panjab University
Bachelor's in chemistry (H.S.)
Chandigarh, India
May 2017

Research Experience

Graduate Student Researcher, University of California, Merced 2021-present

- Pioneered silicon-based catalysts for single and sequential hydroboration of terminal alkynes enabling synthesis of C–B bond-containing intermediates relevant to drug discovery and cross-coupling reactions.
- Extended the use of silicon-based catalysts for hydroboration of alkenes, nitriles, ketones, and esters, for synthesis of pharmaceutical and agrochemical intermediates.
- Designed and developed iron catalysts for hydrodefluorination of polyfluoroarenes to access selectively fluorinated arenes, key intermediates in pharmaceuticals, and modified conditions for exhaustive hydrodefluorination.
- Investigated the mechanistic pathways of Mn-Silylene complexes in C–H borylation of terminal alkynes.
- Collaborated with UC campuses and national laboratories through the UC National Laboratory Fees Research (UCNLFR) Program on the conversion of captured CO₂ into synthetically valuable products.
- Evaluated Mo, Ru, Fe, Mn, Co, and Ni complexes with diverse ligands (N-heterocyclic carbenes, bis(silylene)pyridine, xanthphos, diimine, iminopyridine) for small-molecule functionalization, enabling the synthesis of compounds relevant to pharmaceuticals and agrochemicals.

Master's Student Researcher, Panjab University, Chandigarh 2017-2019

- Designed a green, water-mediated protocol for the aerobic homocoupling of thiols to disulfides, relevant in adhesives, coatings, and specialty polymers.
- Developed hands-on experience in TLC, column chromatography, NMR and IR spectroscopy.

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1. **Kaur, H.**; Sharma, D.; Arevalo, R. Bench-Stable Iron Bipyridine Complexes as Long-Lived Catalysts for the Hydrodefluorination of Arenes at Room Temperature *ChemRxiv* **2026**, DOI: 10.26434/chemrxiv.15001775/v1.
2. **Kaur, H.**; Sharma, D.; Arevalo, R. Triethoxysilane-Catalyzed Hydroboration of Alkenes, Nitriles, Ketones and Esters: From Non-Covalent Interactions to a Hydrosilylation/Si-B Exchange Pathway *ChemRxiv* **2026**, DOI: 10.26434/chemrxiv.15000710/v1.
3. Arevalo, R.; Ahuja, H.;‡ Duran Arroyo, V.;‡ **Kaur, H.**‡ Sustainable Catalysis for Borylation: Earth-Abundant Homogeneous Catalysts for C–B Bond Formation in Small Molecules and Their Mechanisms; ACS In Focus; American Chemical Society: Washington, DC, **2025**. 10.1021/acsinfocus.7e9018. ‡ These authors contributed equally.
4. **Kaur, H.**; Ahuja, H.; Arevalo, R. Triethoxysilane-Catalyzed Sequential Regioselective Hydroboration of Terminal Alkynes: Sustainable Access to E-Alkenylboronate and Alkyl Gem-Diboronate Esters *ACS Catal.* **2025**, *15*, 976-981.
5. Ahuja, H.;‡ **Kaur, H.**;‡ Arevalo, R. Chemoselective C(sp)–H Borylation of Terminal Alkynes Catalyzed by a Bis(N-heterocyclicsilylene) Manganese Complex *Inorg. Chem. Front.* **2023**, *10*, 6067-6076. ‡ These authors contributed equally.

Field of Study

Organic and Organometallic Chemistry

Abstract

Catalysis lies at the heart of modern chemical synthesis, underpinning the efficient production of pharmaceuticals, agrochemicals, and advanced materials. As the global scientific community increasingly prioritizes sustainability, there is a growing necessity to move away from catalytic systems that rely on precious metals such as iridium, rhodium, and palladium, elements that are not only scarce and expensive but also associated with significant environmental and supply-chain concerns. Homogeneous and organocatalytic approaches offer a compelling alternative for reducing the ecological footprint of chemical processes. In this context, Earth-Abundant transition metals and main-group elements have emerged as powerful platforms for sustainable catalysis. Despite their enormous potential, their widespread adoption remains hampered by several unresolved challenges, including susceptibility to side reactions, air- and moisture-sensitivity requirements, high catalyst loadings, and harsh reaction conditions.

Moreover, the mechanistic landscapes governing these catalytic cycles remain considerably underexplored compared to their precious metal counterparts, limiting the rational design of improved systems. Against this backdrop, this dissertation explores sustainable homogeneous and organocatalytic strategies employing Earth-Abundant elements (manganese, iron and silicon) for three synthetically valuable transformations: borylation, hydroboration, and hydrodefluorination. Borylation and hydroboration target boronate esters, high-value synthetic intermediates widely utilized in pharmaceutical synthesis, agrochemistry, and cross-coupling reactions. Hydrodefluorination, on the other hand, enables the selective synthesis of fluorinated arenes, privileged structural motifs in drug discovery and medicinal chemistry. Beyond their synthetic value, hydrodefluorination reactions carry broader environmental significance, as selective C–F bond cleavage offers a promising strategy toward the remediation of per- and polyfluoroalkyl substances (PFAS).

The first chapter of this dissertation presents the first manganese-catalyzed chemoselective C(sp)–H borylation of terminal alkynes, employing $[\text{Mn}(\text{SiNSi})\text{Cl}_2]$ ($\text{SiNSi} = 2,6\text{-}[\text{EtNSi}(\text{NtBu})_2\text{CPh}]_2\text{C}_5\text{H}_3\text{N}$), as the precatalyst. Mechanistic studies reveal that the choice of activator critically governs the reaction pathway, dictating chemoselectivity between C–H activation and alkyne insertion. Uniquely, HBPi serves a dual role as both the borylating reagent and an *in situ* activator, directing the catalyst toward the C–H activation pathway and the selective formation of alkynylboronate esters. This chapter thus underscores the pivotal importance of mechanistic understanding in rationalizing and controlling catalytic outcomes.

The second chapter describes the first use of silicon as an organocatalyst for C–B bond formation, employing commercially available triethoxysilane for the chemoselective single and sequential hydroboration of terminal alkynes. This transformation affords alkyl *gem*-diboronate esters, attractive precursors in drugs containing 3D non-flat motifs. Notably, while silicon-catalyzed hydrofunctionalization reactions reported in literature require the silicon center to be activated as a strong Lewis acid, this work demonstrates that a non-

Lewis acidic silicon source is fully competent for catalysis, representing a significant conceptual advance in main-group organocatalysis. Mechanistic insights implicate non-covalent interactions between the multiple bonds of the substrate and the silicon catalyst as key contributors to reactivity. This mechanistic insight directly guided catalyst improvement, wherein a fluorinated analogue of triethoxysilane was identified as a superior catalyst, delivering nearly twice the efficiency of the parent system.

The third chapter extends the application of triethoxysilane as a universal catalyst for the hydroboration of a broad range of unsaturated substrates, including alkenes, nitriles, ketones, and esters. Unlike the alkyne hydroboration described in the preceding chapter, mechanistic studies reveal that the electronic and steric properties of heteroatom-containing aromatic substrates exert distinct effects on catalyst efficiency, highlighting substrate-dependent mechanistic divergence. Notably, a fundamentally different mechanistic pathway is operative for the hydroboration of nitriles, involving a catalytically active species distinct from triethoxysilane itself.

The final chapter presents the first bench-stable iron catalyst, $[\text{Fe}(t\text{Bubipy})(\text{OTf})_2]$ ($t\text{Bubipy}$ = 4,4'-di-tert-butyl-2,2'-bipyridine; $\text{OTf} = \text{CF}_3\text{SO}_3^-$), for the hydrodefluorination of fluoroarenes. The catalyst demonstrates remarkable efficiency, achieving a turnover number (TON) of 31.6 for 2,3,5,6-tetrafluoroanisole at room temperature. The extended catalytic lifetime is attributed to the robust five-membered chelate formed by the $t\text{Bubipy}$ ligand, which stabilizes the catalyst resting state and prevents deactivation through ligand decoordination. At elevated temperatures, the system exhibits enhanced performance, facilitating up to five sequential hydrodefluorination cycles for hexafluorobenzene, underscoring its potential for the exhaustive defluorination of highly fluorinated substrates, a capability of direct relevance to sustainable strategies for PFAS remediation.

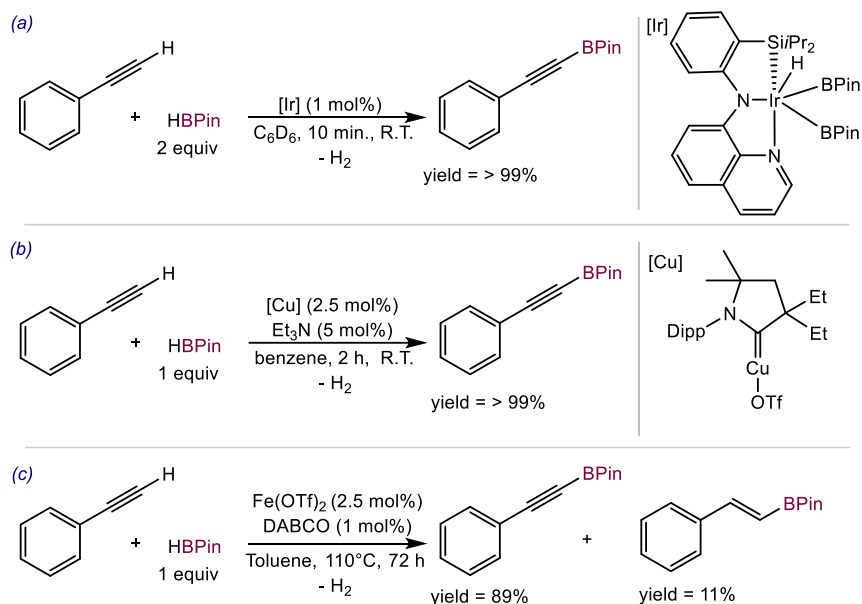
1. Mechanistic Insights into C(sp)–H borylation of terminal alkynes catalyzed by bis(N-heterocyclicsilylene) manganese complex

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<https://doi.org/10.1039/D3QI01033C>
 Himani Ahuja ‡, Harleen Kaur ‡, Rebeca Arevalo*
 ‡ These authors contributed equally

1.1. Introduction

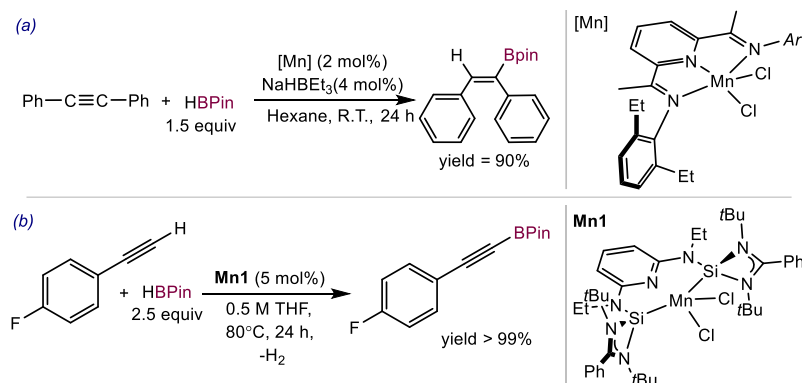
The functionalization of inert bonds catalyzed by transition-metal complexes holds great importance among synthetic routes to access complex organic molecules. Useful compounds can be synthesized from inexpensive feedstocks using these transformations, for instance, feedstock hydrocarbons from petroleum could be upgraded to useful molecular entities. Borylation stands out among several functionalization methods because of the immense significance of the resulting products, namely organoboron compounds.¹ In particular, organoboronate esters have attracted considerable attention due to their reduced toxicity, shelf-stability, ease of preparation and extensive use in pharmaceuticals, agrochemicals, functional materials, and cross-coupling reactions.² Alkynylboronate esters are valuable synthons, not only because of the versatility of the carbon–boron (C–B) bond, but also because of the various reactions that their triple bond (C≡C) could undergo³, for instance, cycloaddition, enyne metathesis and cyclotrimerization. These reactions give access to complex molecular entities that would be difficult to synthesize by late-stage functionalization. The traditional synthesis of alkynylboronate esters involves three steps beginning with deprotonation of the corresponding alkynes by *n*-butyllithium (*n*-BuLi) followed by reaction with a boric ester and finally quenching with anhydrous acid.⁴ However, the conditions are harsh, yielding a low atom economy transformation and limiting the substrate scope. In contrast to this approach, the C(sp)–H borylation of terminal alkynes catalyzed by transition-metal complexes is a more sustainable approach to access alkynylboronate esters in one step. The latter approach employs mild conditions and provides wider substrate scope; with hydrogen (H₂) as the only byproduct. Despite these advantages, the transition-metal catalysis approach suffers from chemoselectivity, yielding a mixture of products from borylation of the C(sp)–H bond and from hydroboration and hydrogenation of the triple bond. Thus, the biggest challenge is to design catalysts chemoselective for C–H borylation rendering alkynylboronate esters as single products.

Catalytic dehydrogenative borylation of terminal alkynes (DHBTA) have been achieved using precious transition-metal catalysts,⁵ the first report employing an iridium (Ir) complex featuring a silyl-amido-quinoline tridentate (SiNN) ligand^{5a} (**Scheme 1.1a**). More recently, C(sp)–H borylation of terminal alkynes,⁶ or tandem processes involving an initial C–H borylation step,⁷ using Earth-Abundant transition metal complexes, including Cu^{6a} and Fe^{6d} (**Scheme 1.1b** and **c**) have also been reported. Using Mn, a non-toxic and the third most abundant transition-metal for catalyzing C(sp)–H borylation of terminal alkynes, would contribute to the sustainability of the process.



Scheme 1.1. Literature examples of C(sp)–H borylation of terminal alkynes, including Ir^{5a}, Cu^{6a} and Fe^{6d} catalysts.

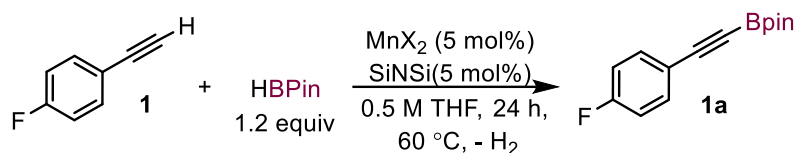
Although, a Mn(II) catalyst with pyridyldiimine (PDI) ligand has been used for hydroboration of internal alkynes (**Scheme 1.2a**),⁸ a Mn catalyst capable of catalyzing DHBTA is unknown. The use of strong field ligands has been leveraged for C–H activation of small molecules using complexes of Co⁹ and Fe¹⁰, a similar approach of using strong field and electron-donating ligand with Mn may promote C(sp)–H activation over hydroboration reactions. Silylenes are among the strongest electron-donating ligands and emerge as promising for efficient transition-metal catalysts,^{9d,e,11} although their applications in C–H functionalization processes remain underexplored. In this work, mechanistic insight into the C(sp)–H borylation of terminal alkynes, catalyzed by the first Mn complex with strong field silylene ligand has been reported (**Scheme 1.2b**).



Scheme 1.2. (a) Mn-catalyzed hydroboration of internal alkynes.⁸ (b) This work: bis(N-heterocyclicsilylene) manganese catalyzed C(sp)–H borylation of terminal alkynes.

Mn(II) complex $[\text{Mn}(\text{SiNSi})\text{Cl}_2]^{11\text{a}}$ ($\text{SiNSi} = 2,6\text{-}[\text{EtNSi}(\text{N}t\text{Bu})_2\text{CPh}]_2\text{C}_5\text{H}_3\text{N}$) (**Mn1**) was found efficient for the catalytic C(sp)–H borylation **1**. Optimization of the reaction conditions revealed 80 °C, a 0.5 M solution of THF and 2.5 equiv. of HBPin using 5 mol% of the catalyst loading as the optimum conditions, affording **1a** in >99% crude yield with a >99% conversion of the starting material. The catalytic efficiency of the in situ generated active species from equimolar mixtures of MnX_2 ($\text{X} = \text{Cl}, \text{CO}_2\text{CH}_3$ or SO_3CF_3) salts and the SiNSi ligand was also evaluated. In all cases the yield of **1a** was significantly lower than when **Mn1** was employed (11% for 5 mol% MnCl_2 + 5 mol% of SiNSi, see **entry 1 in Table 1.1**), pointing toward the inability of these mixtures to generate active species under the catalytic conditions and highlighting the relevance of employing a well-defined precatalyst (**Mn1**) for this transformation.

Table 1.1. Evaluation of catalytic efficiency of in situ synthesized Mn precatalysts



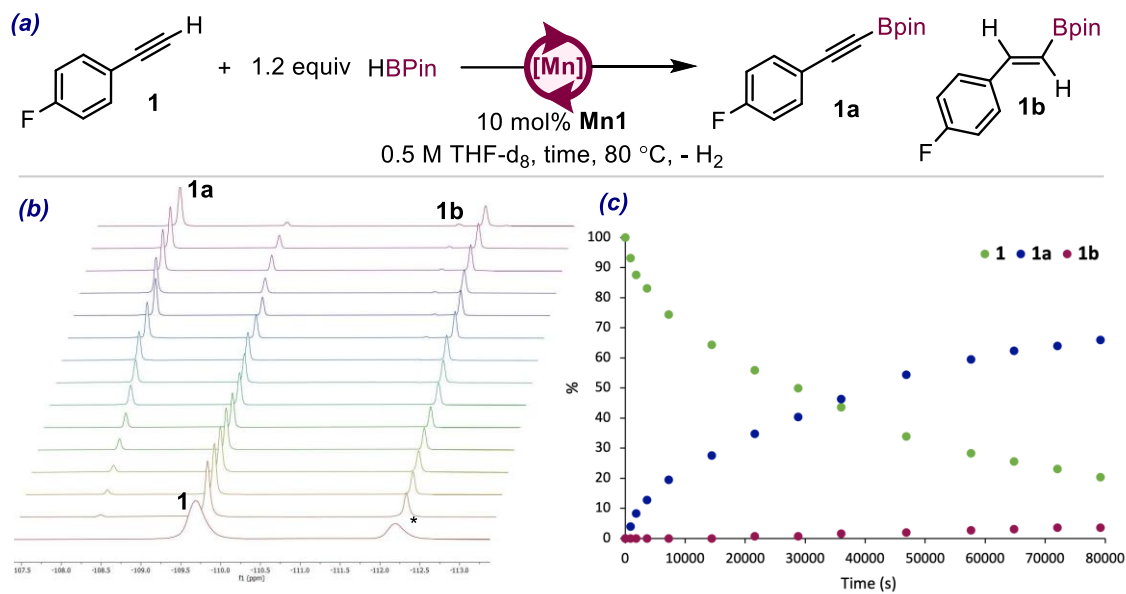
Entry	X	Conversion (%)	Yield 1a (%)
1	Cl	33	11
2	OAc	45	<5
3	OTf	66	<5
4	Mn1	49	47

* <5% of alkenylboronate ester was detected, entry 4 is for the comparison to precatalyst **Mn1** at given conditions.

1.2. Mechanistic insights

Due to the scarce precedents of manganese catalysts for C–H functionalization processes,¹¹ as well as of mechanistic insights for complexes lacking CO ligands, we sought to investigate the mechanism for the C–H borylation of alkynes. Addition of 1 equiv. of TEMPO to the borylation of **1** did not inhibit the catalytic reaction, supporting that a mechanism involving radicals is not operative for this transformation.

To gain insights into the reaction pathway as well as into the identity of the active Mn species, the catalytic C–H borylation of **1** with HBPin in the presence of 10 mol% of **Mn1** at 80 °C was monitored by ^1H , ^{11}B and ^{19}F NMR spectroscopy in THF-d_8 employing fluorobenzene as the internal standard in a J. Young NMR tube where the headspace was evacuated. The ^{19}F (**Scheme 1.3b**) and ^{11}B NMR spectra (**Figure 1.4** in appendix) showed the formation of **1a** (–108 ppm in the ^{19}F NMR spectrum) at the expense of **1** (–110 ppm in the ^{19}F NMR spectrum). A reaction profile accounting for the species present in solution is shown in **Scheme 1.3c**. An induction period was not observed and product **1a** was formed as soon as the reaction mixture was heated to 80 °C.



Scheme 1.3. (a) Reaction pathway for the **Mn1**-catalyzed C(sp)-H borylation of **1** (b) Stacked ^{19}F NMR spectra (c) Quantitative reaction profile.

The ^1H NMR spectra showed a singlet at 4.5 ppm hinting at the presence of H_2 in the reaction mixture. This signal gradually increased in intensity as the reaction proceeded, consistent with the accumulation of the H_2 formed as a byproduct from C-H borylation ((**Figure 1.2** for H_2 evolution). The *E*-alkenyl boronate ester (**1b**, -112 ppm in the ^{19}F NMR spectrum) was detected in trace amounts only after 8 hours, presumably formed by the semihydrogenation of **1a** with H_2 catalyzed by **Mn1**, suggesting that **Mn1** has low efficiency for this process. Neither the ^{19}F nor the ^{11}B spectra showed signals attributable to -BPIn or $-C\equiv CFAr$ ligands in diamagnetic Mn complexes, whereas signals attributable to a SiNSi ligand were not identified in the ^1H NMR spectra (**Figure 1.1**). The signals attributable to the starting materials **1** and HBPIn were broadened when **Mn1** was added to the mixture at room temperature and during the catalytic reaction, suggesting that paramagnetic Mn complexes were responsible for catalysis.

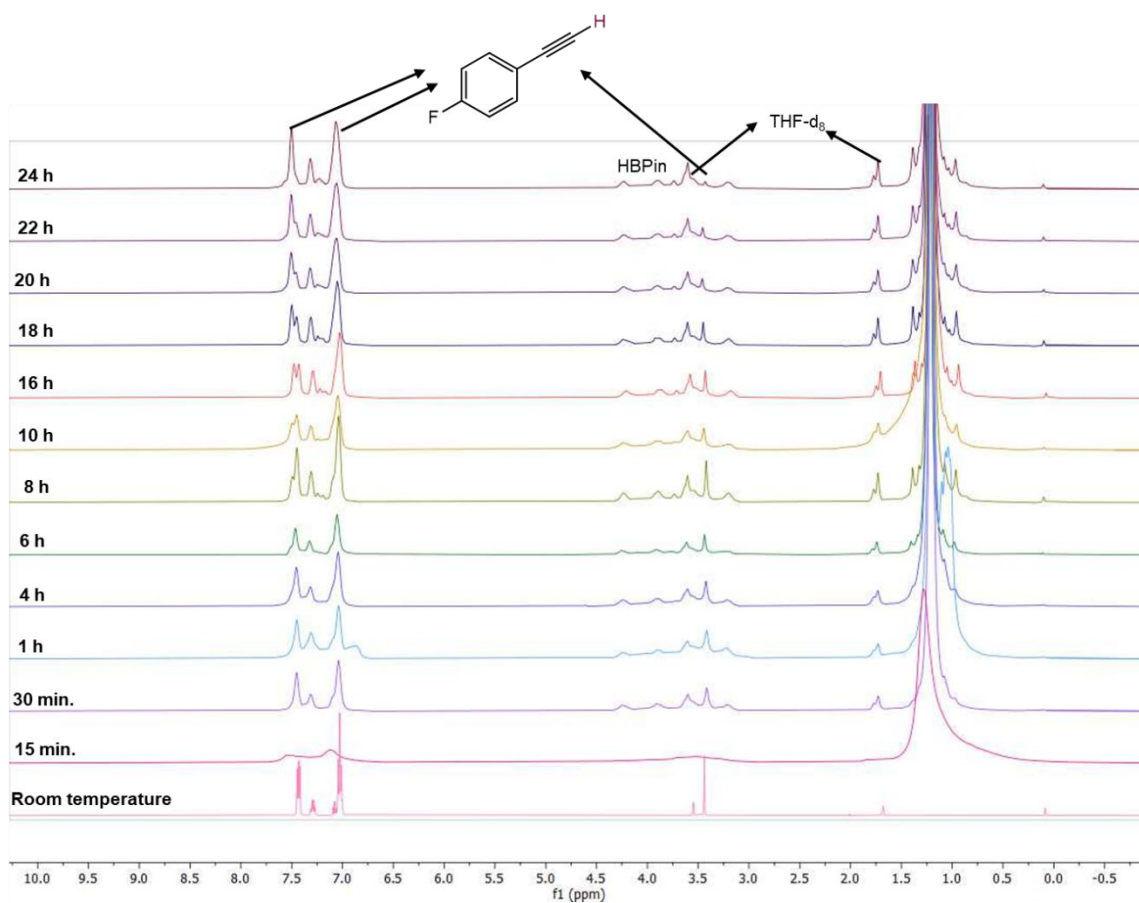


Figure 1.1. ^1H NMR spectra of **Mn1**-catalyzed C(sp)–H borylation of **1** with HBPin in THF- d_8 at 80 °C, using fluorobenzene as internal standard.

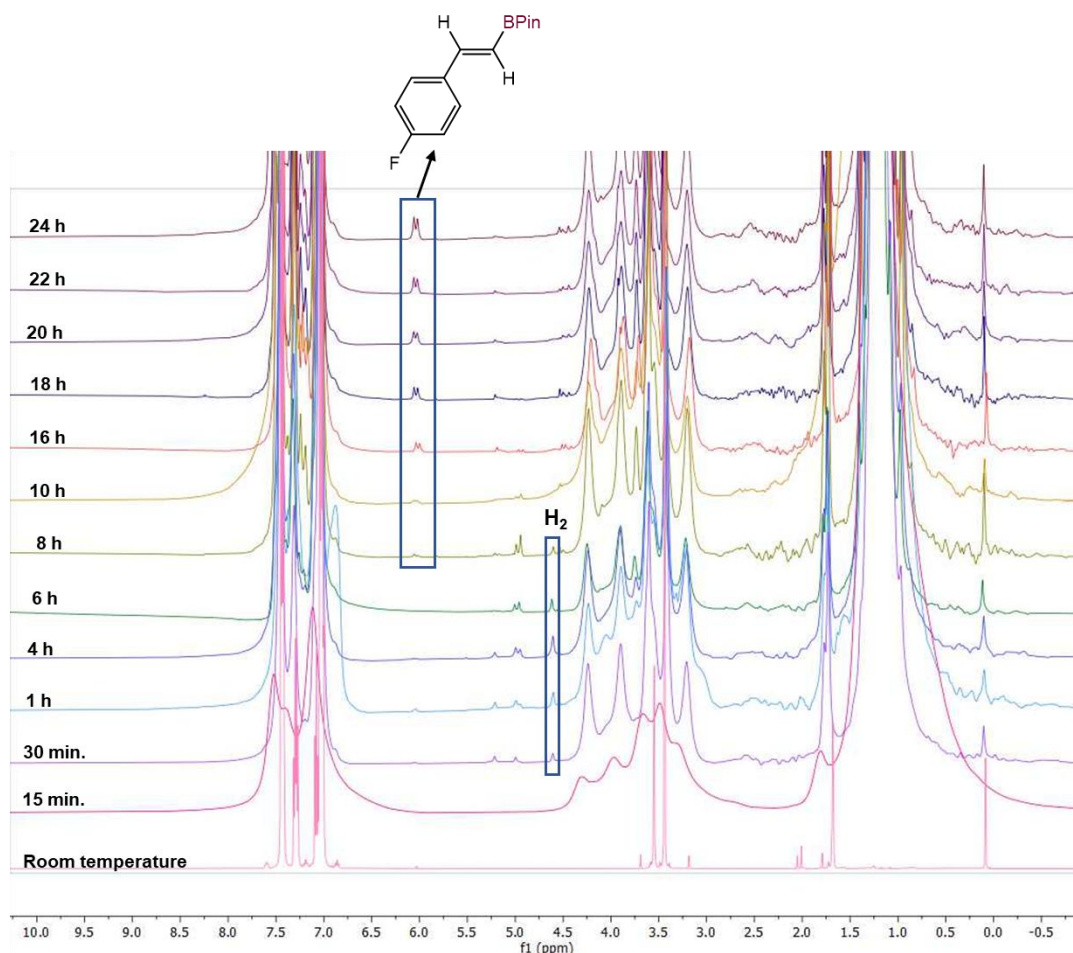


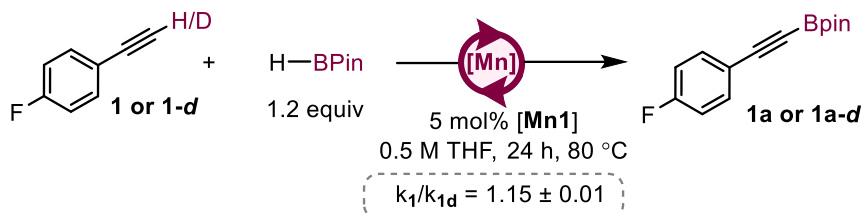
Figure 1.2. ^1H NMR spectra of **Mn1**-catalyzed C(sp)–H borylation of **1** with HBPIn in THF- d_8 at 80 °C, highlighting the formation of H_2 and **1b**.

Attempts to isolate or crystallize any catalytically relevant Mn species from the catalytic reaction mixture after 10 minutes by slow diffusion of hexane into the THF reaction mixture at $-35\text{ }^\circ\text{C}$ failed, and only crystals of the precatalyst **Mn1** could be grown. The fact that only **Mn1** could be isolated from the catalytic reaction suggests that either the activation of the **Mn1** precatalyst was incomplete, or that the Mn active species were in equilibrium with **Mn1** during catalysis. Although catalytically active Mn species were present in the reaction medium after 10 minutes, **Mn1** may be the complex with the lowest solubility under the conditions employed for crystallization.

To gain preliminary insights into the kinetics of the reaction and the identity of the rate-determining step, the KIE for the C–H borylation of **1** was determined employing initial rates in 2 separate vessels (**Figure 1.6** in appendix).^{9b,c,13} The $k_{\text{H}}/k_{\text{D}}$ is 1.15 ± 0.01 (**Table 1.2**) which is consistent with C–H activation of the alkyne not being involved in the rate-determining step, and suggesting a reversible C–H activation step prior to or after the rate-determining step.¹³ This value is lower than that obtained for the C–H borylation of

terminal alkynes catalyzed by an Al complex (1.4),¹⁴ where an asynchronous deprotonation during the rate-determining step was proposed to operate, suggesting that an alternative mechanism for C–H activation could be operative for **Mn1**.

Table 1.2. KIE values for the C–H activation of 4-fluorophenylacetylene and 4-fluorophenylacetylene-d using HBPIn, catalyzed by Mn1 in THF-d₈ at 80 °C, using fluorobenzene as internal standard.



Run	Rate _H (Ms ⁻¹)	Rate _D (Ms ⁻¹)	KIE (K _H /K _D)
1	8 × 10 ⁻⁹	7 × 10 ⁻⁹	1.14
2	7 × 10 ⁻⁹	6 × 10 ⁻⁹	1.16
3	8 × 10 ⁻⁹	7 × 10 ⁻⁹	1.14

Aiming to elucidate how the precatalyst generates the catalytically active species, the reaction of **Mn1** with 10 equivalents of HBPIn was monitored by ¹H and ¹¹B NMR spectroscopy in THF-d₈ in a J. Young NMR tube at room temperature for 16 h. A color change from yellow to orange was observed upon 16 h of reaction, however, the ¹H spectra did not show any signal attributable to a diamagnetic Mn complex, and the ¹¹B NMR spectra only showed the presence of HBPIn with no signals attributable to –BPIn ligands. These observations point toward a paramagnetic Mn complex formed by reaction of **Mn1** and HBPIn. Addition of 10 equiv. of **1** to the reaction mixture at room temperature resulted in the immediate formation of **1a**, as evidenced by the ¹¹B (signal at 26.15 ppm) (**Figure 1.8**) and the ¹⁹F NMR spectrum (signal at –108.24 ppm) (**Figure 1.3**), supporting the formation of a catalytically active species, **Mn5**, upon reaction of **Mn1** with HBPIn (**Scheme 1.4**). Because the formation of product **1a** has not been detected by ¹⁹F NMR spectroscopy when **Mn1**, **1** and HBPIn were mixed at room temperature for 15 minutes in THF-d₈, the formation of **1a** upon addition of **1** at room temperature to the previous reaction mixture must occur upon reaction of complex **Mn5** with **1** and not from a mixture of **Mn1**, **1** and HBPIn.

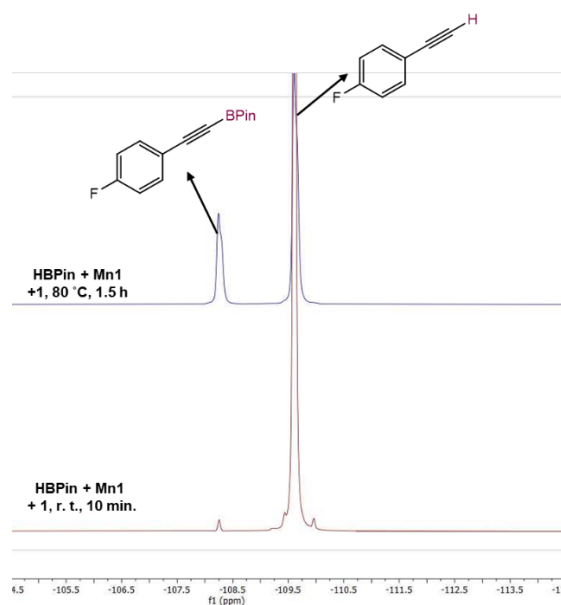
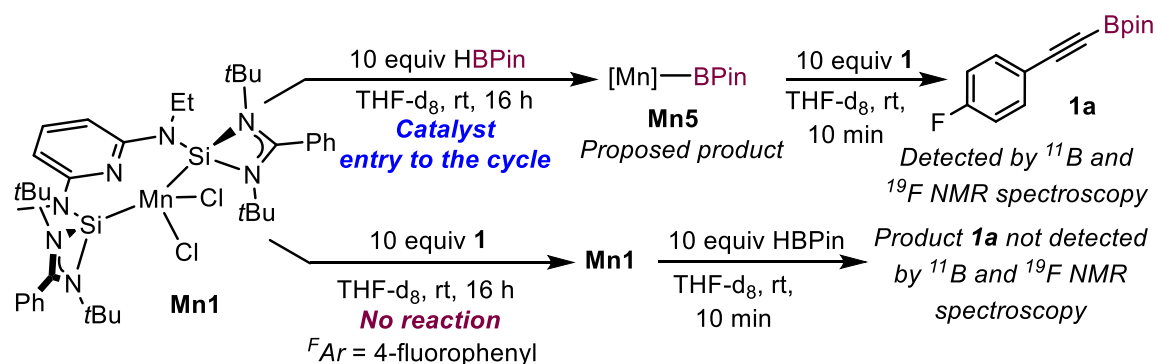


Figure 1.3. ^{19}F NMR spectra of stoichiometric reaction of **Mn1** with HBPIn in THF-d_8 , followed by addition of **1**.

Longer reaction times at room temperature resulted in a slow increase of the peak attributed to **1a** in the ^{19}F NMR spectrum, consistent with the catalytic turnover taking place at slow rates. Upon heating the reaction mixture up to $80\text{ }^\circ\text{C}$, the intensity of the peak attributed to **1a** increased faster over time with a concomitant disappearance of the starting material, supporting the catalytic turnover taking place at a faster rate. This result points toward the reaction of **Mn1** with HBPIn as the precatalyst entry pathway to the cycle.



Scheme 1.4. Reactions of **Mn1** with HBPIn (top) or **1** (bottom) followed by the addition of **1** or HBPIn respectively.

To gain some insights into the identity of **Mn5**, the IR spectrum of the crude product obtained upon reaction of **Mn1** with 10 equiv. of HBPIn in THF at room temperature for 16 hours was registered. The IR spectrum did not match the spectrum for **Mn1**, hinting that **Mn1** reacted with HBPIn, and did not show any stretching band attributable to a Mn–H

stretch, typically in the range of 1900–2000 cm^{-1} .^{11a} Isolation of the product led to the formation of orange oil, the IR spectrum of which matched that of crude product and was different from **Mn1** (Figure 1.9 in appendix). Furthermore, when the reaction of **Mn1** with 2 equiv. of HBPIn in THF- d_8 was conducted and monitored by ^{13}C and ^{11}B NMR spectroscopy, signals attributable to ClBPIn¹⁵ formed as a byproduct were not detected.

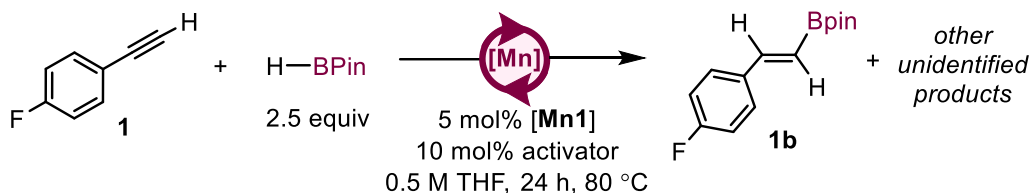
Based on (a) the absence of a signal in the ^{11}B NMR spectrum attributable to ClBPIn upon reaction of **Mn1** with HBPIn and (b) the absence of a Mn–H stretching band in the IR spectrum of the product, Mn hydride complexes can be tentatively ruled out as the product of the reaction of **Mn1** with HBPIn. Based on the evidence presented above, and the fact that upon addition of **1** to **Mn5** product **1a** was formed (Scheme 1.4, top), we propose the formation of a boryl complex (**Mn5**) as the catalytically active species. Transition-metal boryl complexes are well-known intermediates in catalytic C–H borylation,^{9,16} with monoboryl, bisboryl and trisboryl complexes being known and responsible for the C–H activation step.

Aiming to identify other Mn species involved in the catalytic reaction, the reaction of **Mn1** with 10 equiv. of **1** at room temperature was monitored by ^1H , ^{11}B and ^{19}F NMR spectroscopy in THF- d_8 in a J. Young NMR tube for 16 h (Scheme 1.4, bottom). During this time, no significant changes in the color of the solution nor in the ^1H or ^{19}F NMR spectra were observed and no signals attributable to a diamagnetic Mn complex were identified. Addition of 10 equiv. of HBPIn to the reaction mixture at room temperature did not yield signals attributable to product **1a**, however, heating up the reaction mixture to 80 $^\circ\text{C}$ for 1 h and 30 min resulted in the formation of product **1a**, supporting the catalytic turnover (Figures 1.10-1.12). These results support that **Mn1** is not able to activate the C–H bond in **1** at room temperature and only after the addition of HBPIn and heating up the reaction mixture catalytic turnover takes place generating product **1a**. A yellow solid was isolated from the reaction of **Mn1** with 10 equiv. of **1** in THF at room temperature for 16 hours, which did not yield product **1a** upon addition of excess HBPIn and heating up to 80 $^\circ\text{C}$ for 16 h as evidenced by ^{11}B and ^{19}F NMR spectroscopy (the absence of **1** was corroborated by ^{19}F NMR spectroscopy prior to the addition of HBPIn).

The preference of the active species formed upon reaction of **Mn1** with HBPIn for C–H activation versus alkyne insertion is intriguing considering that **Mn1** *in situ* activated with NH_3BH_3 has been previously reported as an efficient catalyst for the semihydrogenation of internal alkynes and is, therefore, capable of alkyne insertion.^{11a} Accordingly, when 5 mol% of the **Mn1** precatalyst were *in situ* activated or preactivated with 10 mol% NH_3BH_3 for the reaction of **1** with HBPIn under the optimized conditions for C–H borylation, the *E*-alkenylboronate ester **1b** was formed in the reaction (Table 1.3, entries 1 and 2), with neither product **1a** nor 4-fluorophenylstyrene formed by semihydrogenation of **1** being detected. These observations support the generation of different active species when **Mn1** is activated with either NH_3BH_3 or HBPIn. Reaction of **Mn1** with NH_3BH_3 yields an active species capable of alkyne insertion leading to the formation of the alkenylboronate ester **1b**, consistent with the reactivity previously observed for the semihydrogenation of internal alkynes.^{11a} In contrast, in the presence of HBPIn, a mechanism involving a C–H activation step is preferred over the one involving alkyne insertion, resulting in the formation of the

alkynylboronate ester **1a**. A Mn hydride is proposed as the active species formed upon reaction of **Mn1** with NH_3BH_3 ,^{11a} although the isolation and characterization of such species are lacking, and its oxidation state is unknown. Either the formation of a boryl complex and/or a different oxidation state at Mn in the catalytically active species upon activation with HBPIn could account for the different chemoselectivity observed in the **Mn1**-catalyzed reaction of terminal alkynes with HBPIn. Furthermore, as evidenced by the trace amount of the alkenylboronate ester **1b** formed in the reaction, the semihydrogenation of **1a** in the presence of the equimolar amount of H_2 formed in the C–H borylation catalyzed by **Mn1**, proceeds to low conversion. Additionally, no diboration products have been identified in the reaction mixtures, supporting that **Mn1** is not efficient for the hydroboration of **1a** with unreacted HBPIn. In fact, when the alkynylboronate ester **1a** was treated with 2.5 equivalents of HBPIn in THF and heated up to 80 °C for 24 h in the presence of 5 mol% of **Mn1**, only signals attributed to the starting material **1a** were identified in the ^1H NMR spectrum of the crude reaction mixture.

Table 1.3. Reaction of **1** with HBPIn employing different Mn active species as catalysts.



Entry	Activator (10 mol%)	Conversion (%)	Yield (%)
1	NH_3BH_3	>99	8
2*	NH_3BH_3	>99	50
3	KO^tBu	>99	9
4	NaHBEt_3	>99	<5
5*	NaHBEt_3	>99	<5

* **Mn1** was preactivated by stirring the THF solution of **Mn1** with activator for 20 min at R.T. before adding other reagents.

The presence of a BPin substituent in **1a** is likely not the origin of this inefficiency toward hydrofunctionalization, because when the hydroboration of the internal alkyne methylphenylacetylene was attempted, only the starting material was recovered and no signals for alkenylboronate esters were detected in the ^1H NMR spectrum of the crude reaction. These results suggest that the barriers for alkyne insertion into the Mn–B bonds of the proposed manganese boryl complex **Mn5** are higher than those for C–H activation, and, therefore, the latter fundamental steps are preferred. Interestingly, using 10 mol% of the strong hydride source NaHBEt_3 as the in situ activator or preactivator with 5 mol% of catalyst loading, only resulted in the formation of a mixture of unidentified products with

1b formed in < 5% yield and neither **1a** nor 4-fluorophenylstyrene being detected in the reaction crude by ^{19}F NMR spectroscopy (Table 1.3, entries 4 and 5). This result suggests that the presence of the strong hydride source precludes catalysis and does not render access to the active species formed upon *in situ* activation by NH_3BH_3 or HBPIn. In contrast, when 10 mol% KO t Bu, well-known for generating a hydride source upon reaction with HBPIn,¹² was employed as the *in situ* activator, an analogous result than when NH_3BH_3 was employed was obtained (Table 1.3, entry 3), suggesting analogous active species involved in catalysis.

1.3. Conclusion

In summary, for **Mn1**-catalyzed C(sp)–H borylation of terminal alkynes with HBPIn, stoichiometric reactions support that the reaction with HBPIn is the precatalyst entry pathway to the cycle, leading to an active species that is proposed to be a boryl complex with no deactivation pathways being identified. The KIE for the reaction points toward C–H activation of the alkyne as not being involved in the rate-determining step. *In situ* activation of the precatalyst by NH_3BH_3 or KO t Bu, resulted in the reduction of the triple bond to afford the alkenylboronate ester, highlighting the key role of HBPIn as an activator of the precatalyst in the chemoselectivity of the reaction, which renders access to active species with a stronger preference for C–H activation.

1.4. Experimental section

1.4.1. General considerations

All air- and moisture-sensitive manipulations were carried out using vacuum line, Schlenk and cannula techniques or in an MBraun inert atmosphere (argon) glovebox unless otherwise noted. All glassware was stored in a pre-heated at 200 °C oven prior to use. All glassware was cleaned using base (KOH, $i\text{PrOH}$) and acid (HCl (aq)) baths. All reported reaction temperatures correspond to external silicone oil bath temperatures. Room temperature (R.T.) was approximately 23 °C. The solvents used for air- and moisture-sensitive manipulations were dried and deoxygenated using literature procedures.¹⁷ MnCl_2 was purchased from Fisher Scientific (99.99%, ultra dry) and dried under high vacuum for 8 h prior to use. Mesitylene, and N,N' -Di-*tert*-butylcarbodiimide were dried over CaH_2 degassed by three freeze-pump-thaw cycles and distilled under vacuum prior to use. NaHBEt_3 (1.0 M solution in THF), KO t Bu (1.0 M solution in THF) and NH_3BH_3 were purchased from Sigma Aldrich and used as received. All other reagents were used as received. SiNSi ,^{11c} 2,6-Diamine- N,N' -diethylpyridine,^{11c,18} $[\text{Mn}(\text{SiNSi})\text{Cl}_2]$ ^{11a} (**Mn1**) were synthesized as reported. 2,6-Diamine- N,N' -diethylpyridine was distilled under vacuum prior to its use. DCM-d_2 , CDCl_3 (Thermo Fisher Scientific) were distilled from CaH_2 under an atmosphere of argon prior to its use and stored over 4 Å molecular sieves. THF- d_8 (Thermo Fisher Scientific) was distilled from sodium metal under an atmosphere of argon and stored under argon. D_2O was purchased from Sigma-Aldrich and used without further purification. ^1H NMR spectra were recorded on either Varian 400 or 500 spectrophotometers operating at 400 MHz, and 500 MHz, respectively. ^{13}C NMR spectra were recorded on Varian 400 or 500 spectrophotometers operating at 101 MHz and 126 MHz, respectively. ^{11}B NMR spectra were recorded on Varian 400 or 500 spectrometers

with 128 MHz and 160 MHz frequencies. ^{19}F NMR spectra were recorded on Varian 400 or 500 spectrometers with 376 MHz and 470 MHz frequencies. All ^1H and ^{13}C NMR chemical shifts are reported in ppm relative to SiMe_4 using the ^1H (chloroform-*d*: 7.26 ppm) and ^{13}C (chloroform-*d*: 77.16 ppm) chemical shifts of the solvent as a standard. ^1H NMR data for diamagnetic compounds are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent, obsc = obscured), coupling constants (Hz), integration, assignment. ^{13}C NMR data for diamagnetic compounds are reported as follows: chemical shift, number of protons attached to carbon (e. g. CH_2), assignment. QC stands for *quaternary carbon*. GC analyses were performed using a Shimadzu GC-2014 gas chromatograph equipped with a Shimadzu AOC-20s autosampler and a Shimadzu capillary column (15m x 250 μm). The instrument was set to a detector temperature of 250 $^\circ\text{C}$. UHP-grade (99.999%) helium was used as carrier gas and further purified employing a He purifier installed prior to the instrument inlet. The temperature program used for GC analyses was as follows: 60 $^\circ\text{C}$, isothermal 1 min; 15 $^\circ\text{C}/\text{min}$ to 250 $^\circ\text{C}$, isothermal 2 min. Infrared spectroscopy was conducted on a ALPHA II Compact FT-IR spectrometer installed in an argon glovebox.

1.4.2. Procedure for evaluation of catalytic efficiency of *in situ* generated catalysts, employing different manganese salts as metal precursors.

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: MnX_2 (for X = Cl, 2 mg, 0.015 mmol; for X = OAc, 3 mg, 0.015 mmol; for X = OTf, 5 mg, 0.015 mmol) and SiNSi (10 mg, 0.015 mmol) in THF (0.3 mL) freshly generated upon stirring the reagents at room temperature for 1 h, 4-fluorophenylacetylene (34 μL , 0.3 mmol), HBPIn (53 μL , 0.36 mmol). The reaction was stirred and heated to 60 $^\circ\text{C}$ for 24 h. After this time, the reaction was brought into the glovebox and fluorobenzene (10 μL , 0.106 mmol) was added as an internal standard. The crude reaction mixture was passed through a plug of Whatman filter paper in a Pasteur pipette and then analyzed by ^{19}F NMR spectroscopy without additional purification.

1.4.3. Procedure for monitoring of the catalytic reactions using NMR spectroscopy

4-Fluorophenylacetylene (20 μL , 0.174 mmol) was added to a solution of **Mn1** (14 mg, 0.0174 mmol) in THF- d_8 (0.30 mL) followed by the addition of HBPIn (30 μL , 0.208 mmol) and fluorobenzene (10 μL , 0.106 mmol) as internal standard in a J. Young NMR tube in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The headspace was evacuated by a freeze-pump-thaw cycle. The reaction was monitored by ^1H , ^{11}B and ^{19}F NMR spectroscopy at 80 $^\circ\text{C}$ for 24 hours. No signals attributable to diamagnetic manganese species were observed in the NMR spectra, however, signals attributable to the C-H borylation product (**1a**) were identified in the ^{11}B and ^{19}F NMR spectra and their intensity grew over time at the expense of those of the starting material. Signals corresponding to H_2 formed as a byproduct were also identified in ^1H NMR.

1.4.4. Procedure of catalytic reaction in the presence of Hg drop

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order- **Mn1** (12 mg, 0.015 mmol), THF (0.52 mL), 4-Fluorophenylacetylene (33 μ L, 0.3 mmol), HBPIn (52 μ L, 0.36 mmol) and a drop of Hg. The tube was sealed, and the resulting mixture was stirred at 80 °C for 24 hours. The reaction was brought into the glovebox and the crude reaction mixture was diluted with THF and passed through a plug of silica gel in a Pasteur pipette and then analyzed by ^{19}F NMR spectroscopy without additional purification. Conversion: 91%; Yield: 51%.

1.4.5. Procedure of catalytic reaction in the presence of TEMPO

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order- **Mn1** (12 mg, 0.015 mmol), THF (0.52 mL), 4-Fluorophenylacetylene (33 μ L, 0.3 mmol), HBPIn (52 μ L, 0.36 mmol) and TEMPO (47 μ L, 0.3 mmol). The tube was sealed, and the resulting mixture was stirred at 60 °C for 24 hours. The reaction was brought into the glovebox and the crude reaction mixture was diluted with THF and passed through a plug of silica gel in a Pasteur pipette and then analyzed by NMR spectroscopy without additional purification. Conversion: 31%; Yield: 31%.

1.4.6. Procedure for the synthesis of 4-fluorophenylacetylene-*d*

4-fluorophenylacetylene-*d* was prepared by dropwise addition of MeLi (3.4 mL of a 1.6 M solution in diethyl ether, 5.39 mmol) to a solution of 4-fluorophenylacetylene (0.55 mL, 4.9 mmol) in diethyl ether (25 mL) at -78 °C. After stirring the contents at -78 °C for 30 min, D₂O (2 mL, 110.8 mmol) was added, and the contents were left for stirring at room temperature for 6 hours followed by separation of organic layer. The organic layer was dried using MgSO₄ and removal of the solvent in vacuo resulted in the formation of the product with >99 % deuterium incorporation.

1.4.7. Procedure for determining the kinetic isotope effect for the C–H borylation of 4-fluorophenylacetylene and 4-fluorophenylacetylene-*d* using Mn1 as the Catalyst (2 Separate Vessels)

In an argon-filled glovebox, a scintillation vial was charged with a solution of **Mn1** (7 mg, 0.008 mmol) in 0.35 mL THF-*d*₈. To this solution, 4-fluorophenylacetylene (20 μ L, 0.174 mmol), fluorobenzene (10 μ L, 0.106 mmol) as the internal standard and HBPIn (30 μ L, 0.208 mmol) were added in the same order. The contents were stirred until a clear solution was formed and then transferred to a J. Young NMR tube. The tube was sealed and brought out of the glovebox. The headspace was evacuated by a freeze-pump-thaw cycle. A separate scintillation vial was charged with a solution of **Mn1** (7.03 mg, 0.008 mmol) in 0.35 mL THF-*d*₈. To this solution, 4-fluorophenylacetylene-*d* (19.1 μ L, 0.174 mmol), fluorobenzene (10 μ L, 0.106 mmol) as the internal standard and HBPIn (30 μ L, 0.208 mmol) were added in the same order. The contents were stirred until a clear solution was formed and then transferred to a J. Young NMR tube. The tube was sealed and brought out of the glovebox. The headspace was evacuated by a freeze-pump-thaw cycle. The reactions were monitored by ^{19}F NMR spectroscopy at 80 °C. Integration of the signal for the internal standard, the

starting material, and the product by ^{19}F NMR spectroscopy afforded the quantitative data reported in **Table 1.2**. The KIE was determined using the initial rates method (up to 10% yield). The rates of the reactions, rate_H and rate_D , correspond to the rates of formation of product **1a** (2-((4-Fluorophenyl)ethynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane) using 4-fluorophenylacetylene and 4-fluorophenylacetylene-*d* as substrates respectively. The overall KIE was calculated by taking the average of the ratios of rate_H and rate_D for all the three runs.

1.4.8. Procedure for monitoring of the stoichiometric reaction of Mn1 with HBPIn, followed by the addition of 1a using NMR spectroscopy.

HBPIn (35 μL , 0.24 mmol) was added to a solution of **Mn1** (20 mg, 0.024 mmol) in THF-d_8 (0.35 mL) in a J. Young NMR tube in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The reaction was monitored by ^1H and ^{11}B NMR spectroscopy at room temperature for 16 hours. After this time, the tube was brought into the glovebox, 4-fluorophenylacetylene (27 μL , 0.24 mmol) was added at room temperature and the ^1H , ^{11}B and ^{19}F NMR spectra were registered at room temperature after 10 min. The resulting mixture was heated up to 80 $^\circ\text{C}$ for 1.5 hours and the reaction was monitored by ^1H , ^{19}F and ^{11}B NMR spectroscopy.

1.4.9. Procedure for the isolation of Mn5.

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar, **Mn1** (70 mg, 0.087 mmol), THF (2.5 mL) and HBPIn (125 μL , 0.87 mmol). The reaction mixture was stirred for 16 h at room temperature. After the completion of the reaction, the reaction mixture was passed through a plug of Whatman filter paper in a Pasteur pipette and solvent was removed under vacuo to obtain orange oil. The product was extracted in hexane and solvent was removed under vacuum to obtain orange oil which was then analyzed by IR spectroscopy.

1.4.10. Procedure for monitoring of the stoichiometric reaction of Mn1 with 1a, followed by the addition of HBPIn, using NMR spectroscopy.

4-fluorophenylacetylene (27 μL , 0.24 mmol) was added to a solution of **Mn1** (20 mg, 0.024 mmol) in THF-d_8 (0.35 mL) in a J. Young NMR tube in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The reaction was monitored by ^1H , ^{11}B and ^{19}F NMR spectroscopy at room temperature for 16 hours. After this time the tube was brought into the glovebox, HBPIn (35 μL , 0.24 mmol) was added at room temperature and the ^1H , ^{11}B and ^{19}F NMR spectra were registered at room temperature. The resulting mixture was heated up to 80 $^\circ\text{C}$ for 1.5 hours and the reaction was monitored by ^1H , ^{19}F and ^{11}B NMR spectroscopy.

1.4.11. Procedure for evaluation of catalytic efficiency of *in situ* generated catalysts, employing different activators with Mn1.

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order- **Mn1** (12 mg, 0.015 mmol), THF (0.46 mL), 4-Fluorophenylacetylene (34 μL , 0.3 mmol), HBPIn (108 μL , 0.75 mmol) and 0.03 mmol of corresponding activator (NH_3BH_3 (0.93 mg) or $\text{KO}t\text{Bu}$ (30 μL of a 1 M solution in THF))

or NaHBET₃ (30 μ L of a 1 M solution in THF)). The tube was sealed, and the resulting mixture was stirred at 80 $^{\circ}$ C for 24 hours. The reaction was brought into the glovebox, and the crude reaction mixture was diluted with THF and passed through a plug of silica gel in a Pasteur pipette and then analyzed by ¹⁹F NMR spectroscopy without additional purification.

1.4.12. Procedure for evaluation of catalytic efficiency of in situ generated catalysts formed by pre-activation using different activators with Mn1.

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar, **Mn1** (12 mg, 0.015 mmol), THF (0.43 mL) and 0.03 mmol of corresponding activator (NH₃BH₃ (0.93 mg) or NaHBET₃ (30 μ L of a 1 M solution in THF)). The contents were stirred at room temperature for 20 min. followed by the addition of 4-Fluorophenylacetylene (33 μ L, 0.3 mmol) and HBPIn (52 μ L, 0.36 mmol). The tube was sealed, and the resulting mixture was stirred at 80 $^{\circ}$ C for 24 hours. The reaction was brought into the glovebox, and the crude reaction mixture was diluted with THF and passed through a plug of silica gel in a Pasteur pipette and then analyzed by ¹⁹F NMR spectroscopy without additional purification.

1.5. Appendix

1.5.1. Monitoring of C–H borylation of **1** catalyzed by Mn1, using NMR spectroscopy.

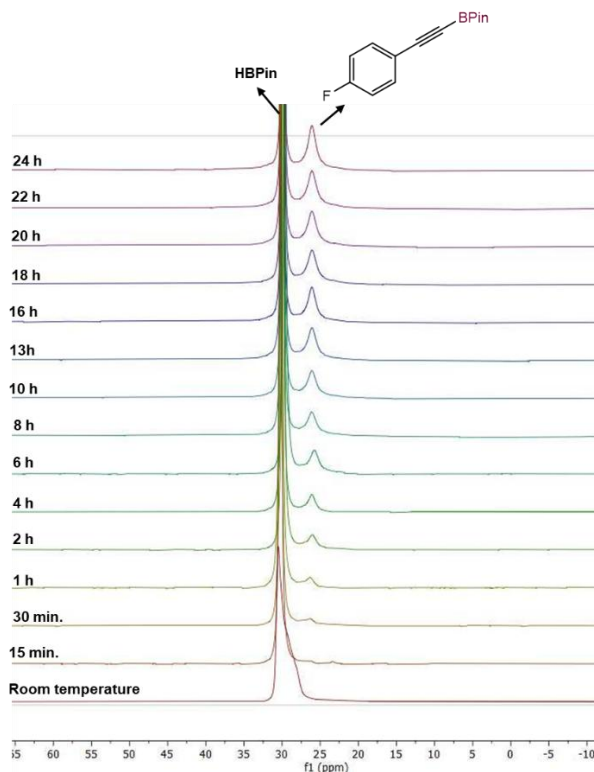


Figure 1.4. ¹¹B NMR spectra of **Mn1**-catalyzed C(sp)–H borylation of **1** with HBPIn in THF-d₈ at 80 $^{\circ}$ C, using fluorobenzene as internal standard.

1.5.2. Determination of KIE.

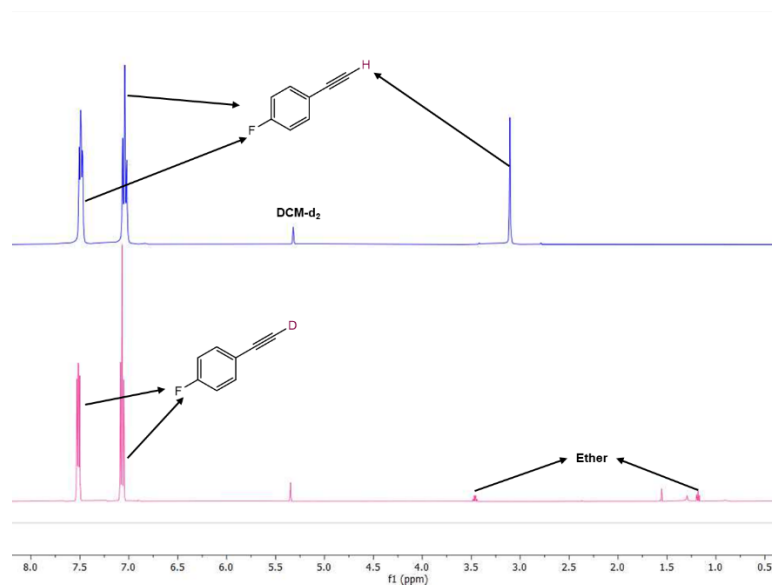
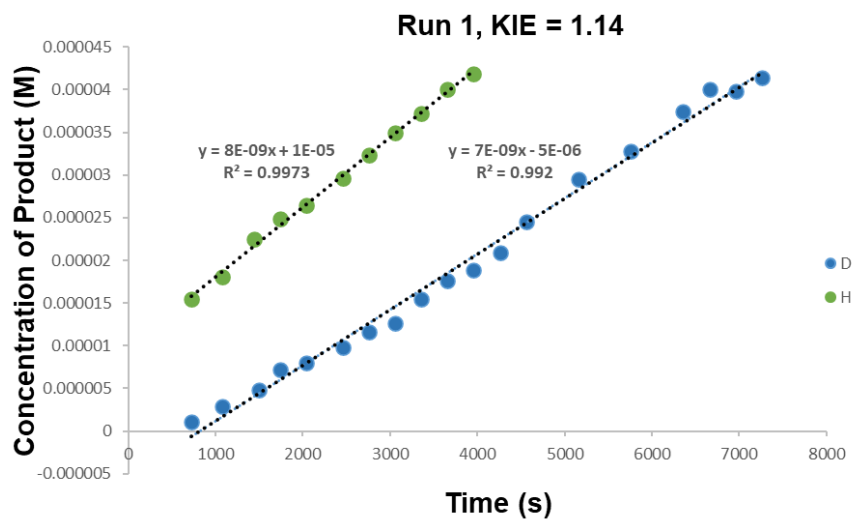


Figure 1.5. Stacked ^1H NMR spectra of 4-fluorophenylacetylene (top) and 4-fluorophenylacetylene- d (down) in DCM-d_2 . (No signal corresponding to alkynyl proton in 4-fluorophenylacetylene- d spectrum).



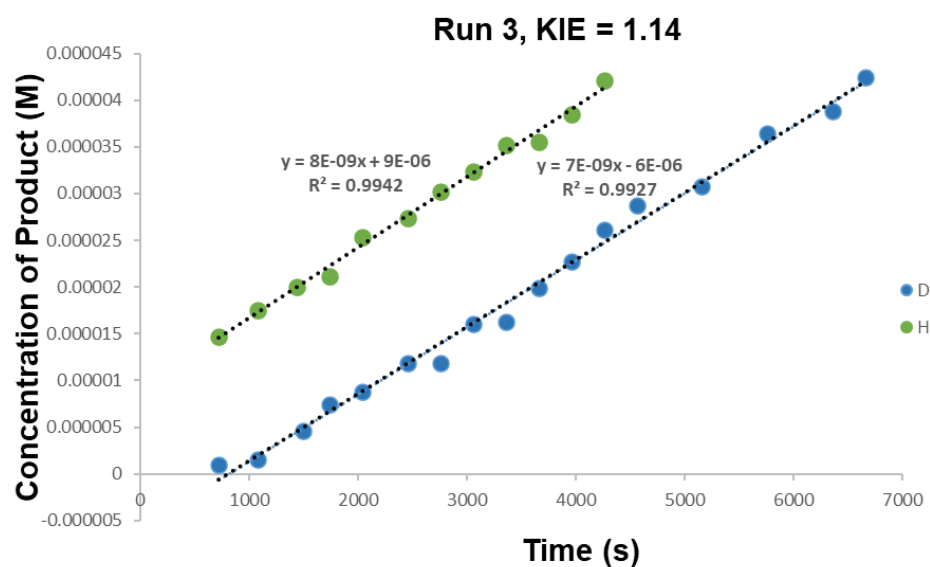
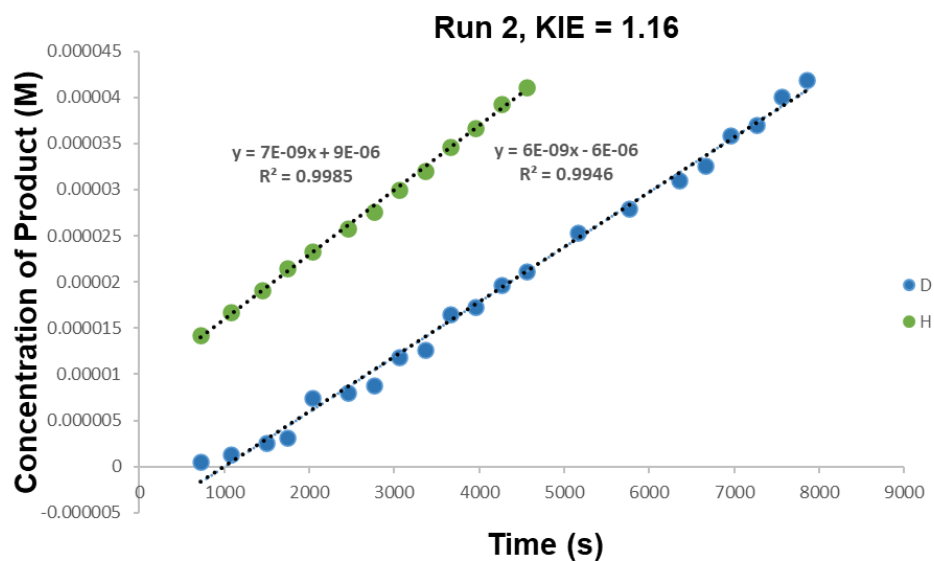


Figure 1.6. Plots of concentration of 2-((4-Fluorophenyl)ethynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (M) vs. time (s) using 4-fluorophenylacetylene and 4-fluorophenylacetylene-*d* as substrates for runs 1-3 using **Mn1** as the precatalyst.

1.5.3. Monitoring of stoichiometric reactions using NMR spectroscopy

NMR monitoring of the reaction of Mn1 with HBPIn at room temperature followed by addition of 4-fluorophenylacetylene.

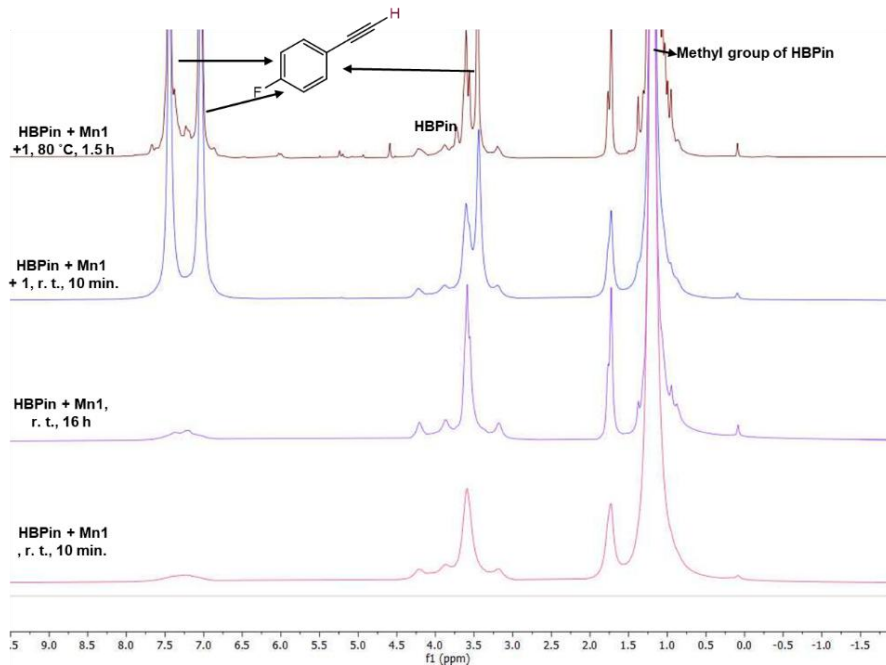


Figure 1.7. ^1H NMR spectra of stoichiometric reaction of **Mn1** with HBPIn in THF- d_8 followed by addition of **1**.

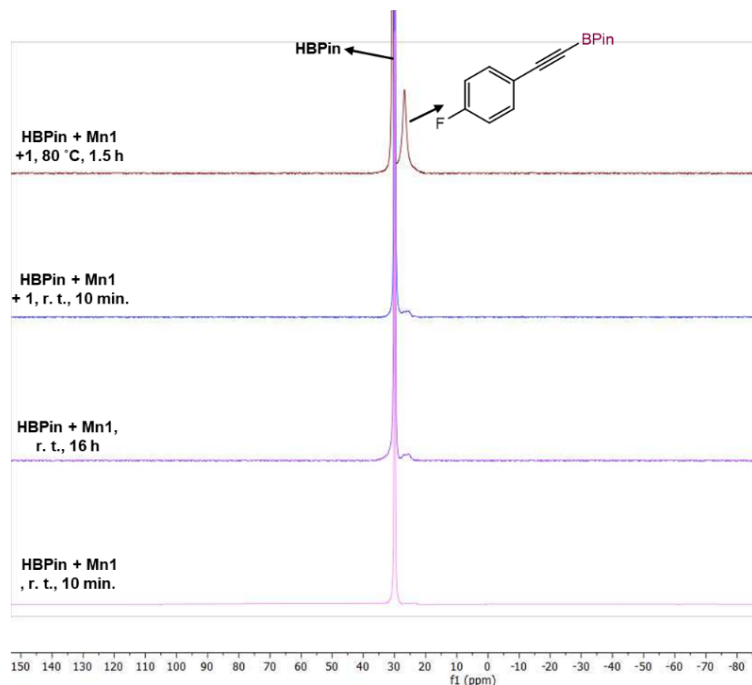


Figure 1.8. ^{11}B NMR spectra of stoichiometric reaction of **Mn1** with HBPIn in THF-d_8 , followed by addition of **1**.

IR spectra of the Mn5 isolated from the stoichiometric reaction of Mn1 and HBPIn:

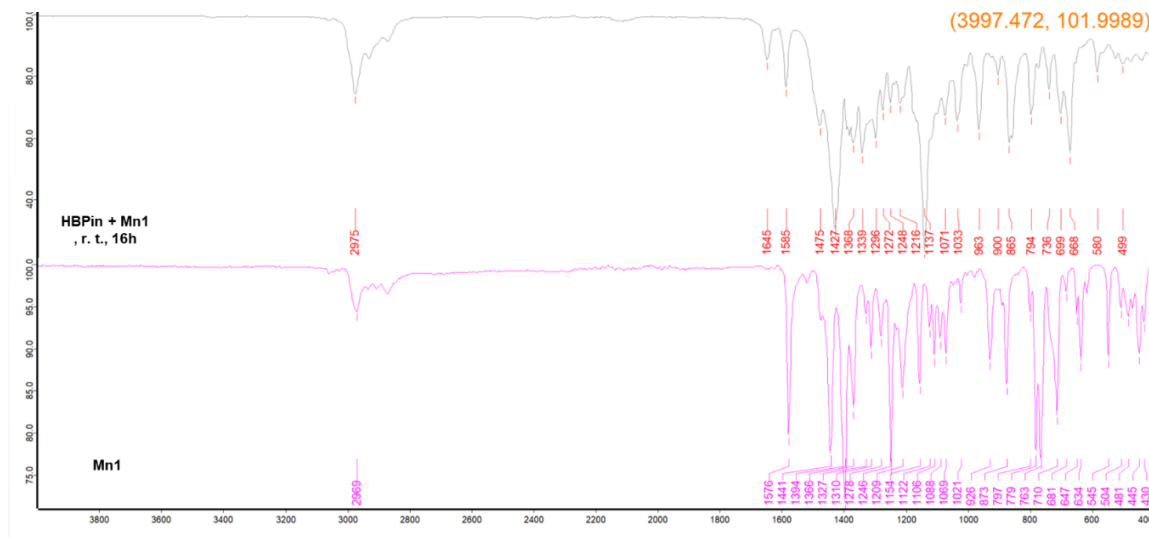


Figure 1.9. Stacked IR spectra of isolated product, **Mn5** (top) and **Mn1**(bottom).

IR of **Mn5** (isolated product): 499(w), 580(w), 668(m), 699(w), 736(w), 794(w), 865(m), 900(w), 963(m), 1033(w), 1071(w), 1137(s), 1216(w), 1248(w), 1272(w), 1296(m), 1339(m), 1368(m), 1427(s), 1475(w), 1585(w), 1645(w), 2975(w).

IR of **Mn1**: 430(w), 445(m), 481(w), 504(w), 545(m), 634(m), 647(w), 681(s), 710(s), 763(s), 779(w), 797(m), 873(m), 926(m), 1021(w), 1069(w), 1088(w), 1106(w), 1122(w), 1154(m), 1209(m), 1246(s), 1278(w), 1310(w), 1327(w), 1366(m), 1394(s), 1441(s), 1576(s), 2969(w).

The spectroscopic data for **Mn1** matched that of previously reported.^{11a}

NMR monitoring of the reaction of Mn1 with 4-fluorophenylacetylene at room temperature followed by addition of HBPIn.

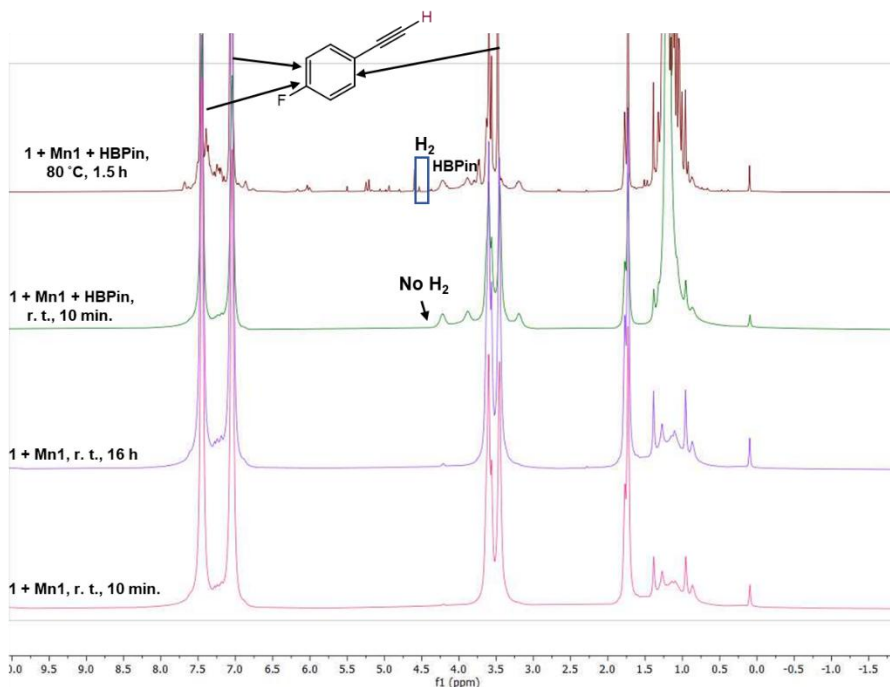


Figure 1.10. ^1H NMR spectra of stoichiometric reaction of **Mn1** with 4-fluorophenylacetylene in THF-d_8 , followed by addition of HBPIn.

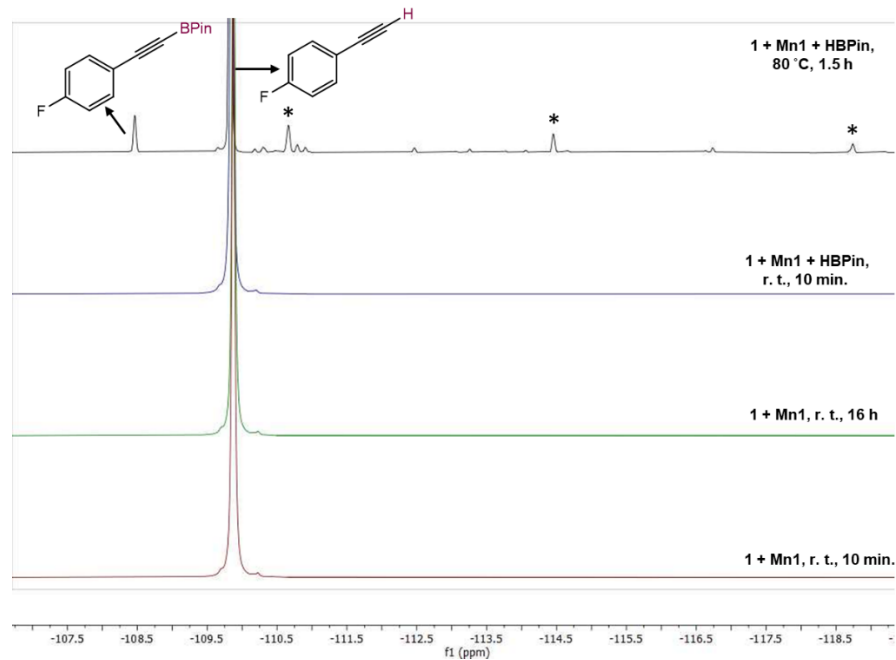


Figure 1.11. ^{19}F NMR spectra of stoichiometric reaction of **Mn1** with 4-fluorophenylacetylene in THF-d_8 , followed by addition of HBPi. (* = unidentified products)

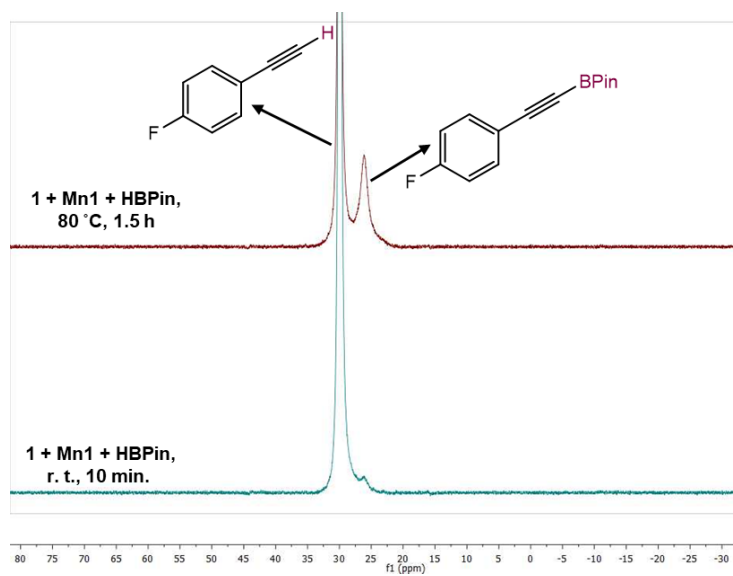


Figure 1.12. ^{11}B NMR spectra of stoichiometric reaction of **Mn1** with 4-fluorophenylacetylene in THF-d_8 , followed by addition of HBPi.

1.6. References

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2. Triethoxysilane-Catalyzed Single and Sequential Regioselective Hydroboration of Terminal Alkynes: Sustainable Access to E-Alkenylboronate and Alkyl *Gem*-Diboronate Esters by NonCovalent Interactions

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 Harleen Kaur, Himani Ahuja, Rebeca Arevalo*

2.1. Introduction

Hydrofunctionalization of inert chemical bonds is a fundamental strategy in modern organic synthesis, enabling efficient access to complex molecular architectures. Among these transformations, hydroboration is particularly valuable due to the broad synthetic utility of the products, organoboronate esters. Alkenylboronate esters are valuable synthetic intermediates due to their dual reactive sites, which enable both simultaneous and sequential functionalization of the carbon-carbon double bond and the boron moiety.¹ This bifunctional reactivity is exemplified by the Rh-catalyzed Michael addition to alkenylboranes reported by Hayashi, which affords chiral β -arylalkylboranes with high enantioselectivity (**Figure 2.1a**).² On the other hand, alkylidiboronate esters containing C(sp³)-B bonds are of particular significance because of their utility as versatile intermediates in the synthesis of pharmaceuticals featuring three-dimensional, non-planar architectures.³ For example, a 1,1-diborylalkane substrate has been shown to undergo two sequential cross-coupling reactions to furnish a key precursor of (*R*)-tolterodine, a clinically used drug for the treatment of urinary incontinence (**Figure 2.1b**).⁴

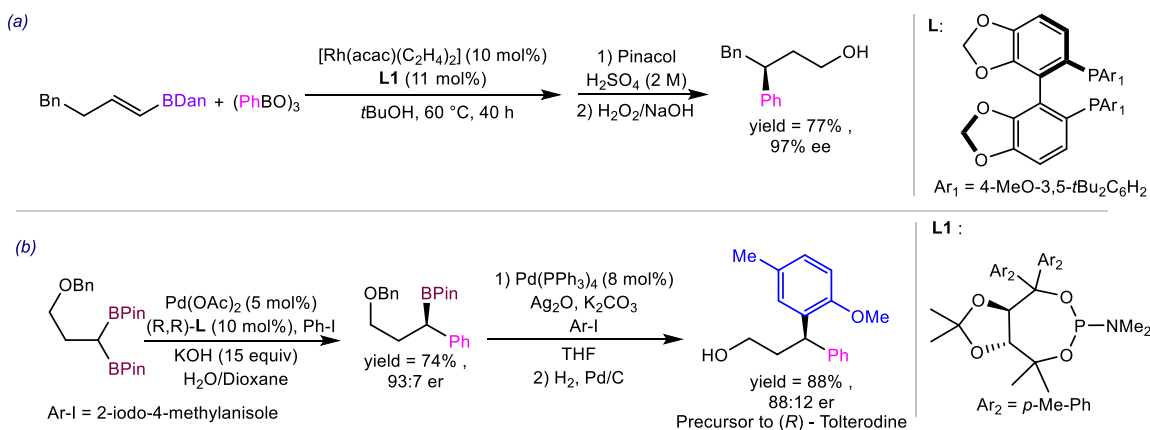


Figure 2.1. Application of boronate esters (a) Dual reactivity of alkenylboronate ester. (b) synthesis of drug intermediate from alkylboronate ester.

Synthesis of these boronate esters has traditionally been limited to homogeneous precious metal catalysis.⁵ More sustainable and greener synthetic approaches involving Earth-Abundant transition metal complexes⁶ or main-group compounds⁷ as catalysts are gaining

momentum in fundamental and applied chemistry, allowing to discover unknown reactivity patterns or overriding precious-metal selectivity.⁸ One of the most convenient transformations to access alkenylboronate and alkylidiboronate esters is the single and sequential hydroboration of terminal alkynes, involving one and two subsequent additions of a H-B bond across the triple bond, respectively. However, enabling the second hydroboration step remains challenging for most catalysts, with precious and Earth-Abundant transition-metal complexes catalyzing a single hydroboration to access *E*-alkenylboronate esters,⁹ and main-group compounds being scarce even for the single hydroboration of terminal alkynes.^{7a,10} Only three transition-metal complexes involving complexes of Co^{11a}, Cu^{11b} and Rh^{11c} have been reported efficient for the double addition of HBPIn across the triple bond of terminal alkynes to yield alkyl *gem*-diboronate esters.

In transitioning toward more sustainable, user-friendly, and affordable catalysts, commercial main-group compounds emerge as a promising alternative to Earth-Abundant transition-metal complexes containing engineered ligands and/or requiring highly air- and moisture-sensitive *in situ* activators. However, main-group catalysts for the single or double hydroboration are scarce,¹⁰ with only the alkylborane (9-BBN)₂ (9-Borabicyclo[3.3.1]nonane dimer) reported efficient for the sequential hydroboration of terminal alkynes with HBPIn (**Figure 2.2a**).¹² However, it suffers from some limitations, mainly, high catalyst loading (20 mol% of the dimer), and high reaction temperatures (120 °C). In this context, silicon catalysis emerges as a promising and more sustainable strategy, by virtue of Si being the second most abundant element in the Earth crust (28%),¹³ and approximately 28,000 times more abundant than B. While neutral silicon catalysis is still in its infancy,¹⁴ covalent bonding between the perfluorinated strong Lewis acid Si(^FCat)₂ (F Cat = perfluorocatecholate)¹⁵ and aldehydes has been reported key for the hydrosilylation of aldehydes (**Figure 2.2b**).^{15a} However, weaker noncovalent interactions promoted by weak Lewis acidic Si compounds, such as siloxanes, are unknown to promote additions across multiple bonds. While promising in catalysis,¹⁶ non-covalent interactions are still restricted to the presence of Lewis basic functional groups in the substrates, such as ketones or esters.¹⁷ Here, we report the first regio- and stereoselective silicon catalyzed single and sequential hydroboration of terminal alkynes affording synthetically valuable *β*-*E*-alkenylboronate and alkyl *gem*-diboronate esters respectively.

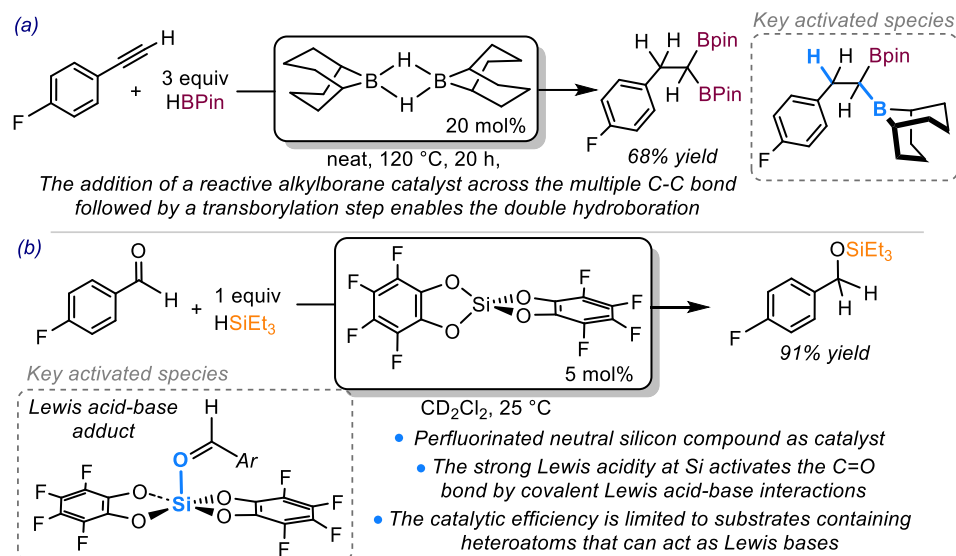
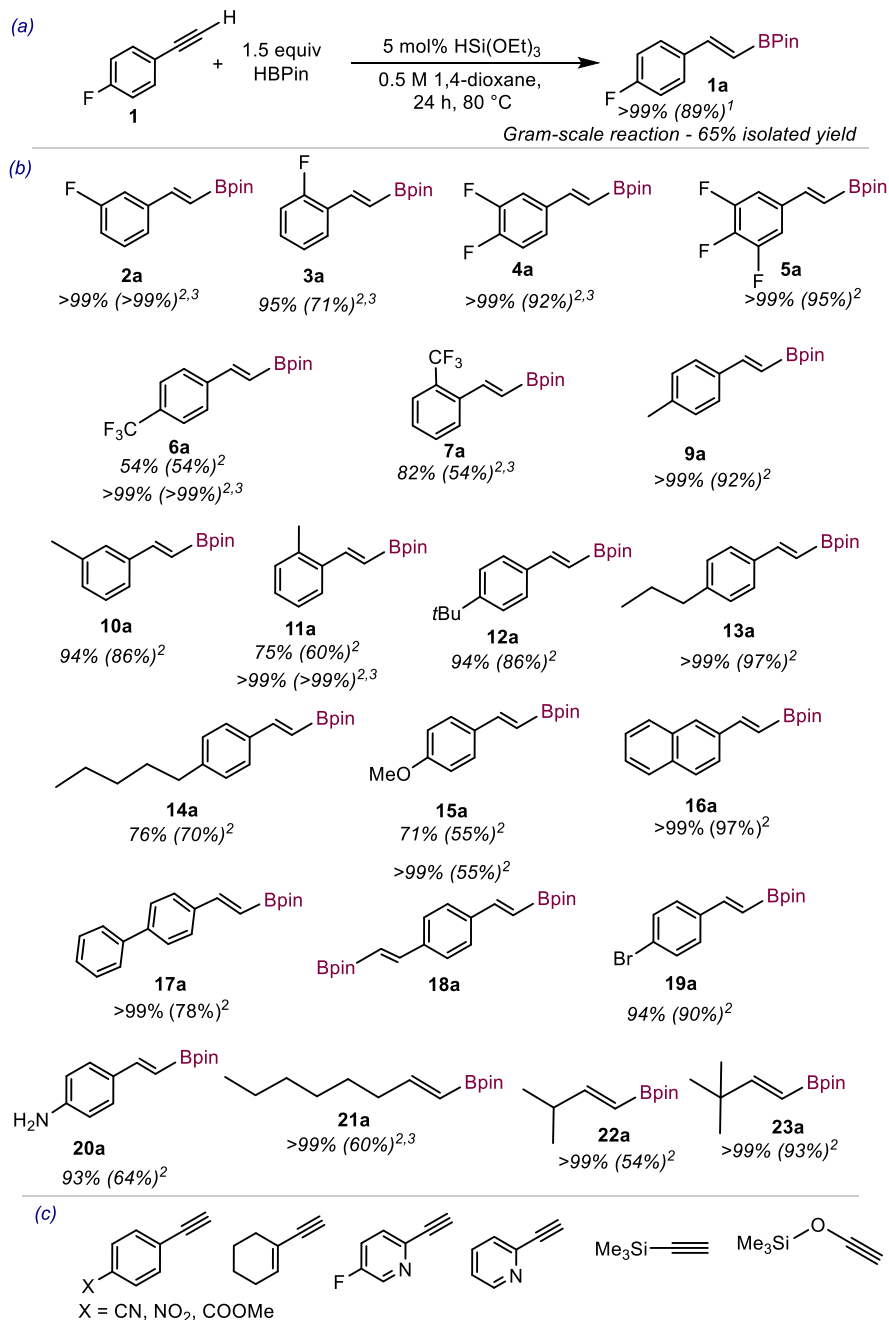


Figure 2.2. (a) Sequential hydroboration of 4-fluorophenylacetylene with HBPIn catalyzed by 9-BBN;¹² (b) hydrosilylation of aldehydes catalyzed by a neutral Si compound;^{15a}

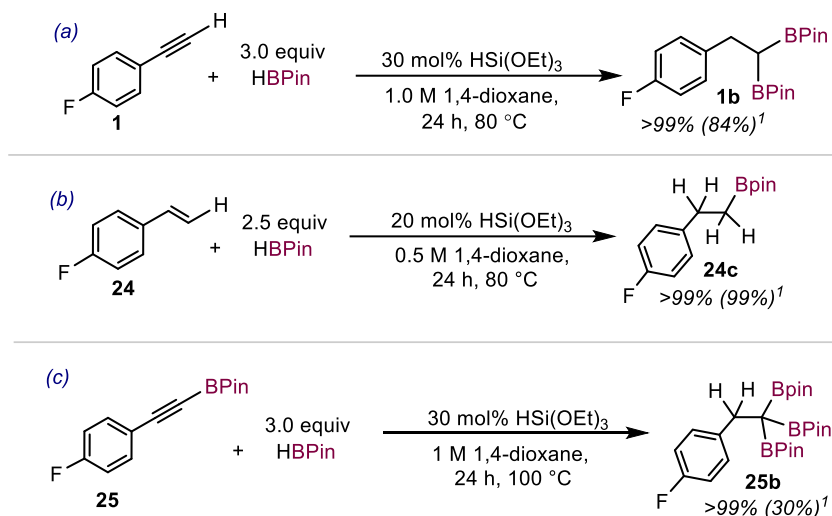
2.2. Results and Discussion

Our research commenced with an assessment of the catalytic efficiency of 30 mol% of HSi(OEt)₃ for the hydroboration of 4-fluorophenylacetylene (**1**) with 3 equiv of HBPIn in a 1.0 M solution of 1,4-dioxane at 80 °C for 2 h. Under these conditions, the *E*-alkenylboronate ester **1a** was formed as an exclusive product in an 80% yield (92% conversion of **1**). In contrast, when the reaction was conducted for 24 h under the same conditions, the diboronate ester **1b** was formed as the exclusive product in 84% yield (>99% conversion of **1**). These results support HSi(OEt)₃ as an efficient catalyst for the hydroboration of **1** with HBPIn, the time being the determining factor for a single or sequential hydroboration yielding **1a** or **1b** respectively. Control experiments supported the need of HSi(OEt)₃ to access **1b** (Table 2.7 in appendix, entry 16) and to access **1a** (Table 2.8 in appendix, entry 8) in a synthetically useful yield. Reaction conditions were optimized for the single hydroboration using 4-fluorophenylacetylene as the model substrate (Table 2.7 in appendix) and the substrate scope was explored at optimized conditions (Scheme 2.1b). Gram-scale reaction under the optimized conditions yielded 65% yield of **1a**. Aromatic alkynes with electron-withdrawing groups afforded products in lower yields than those with electron-donating alkyl groups (*e. g.* 54% for **6a** vs. 92% for **9a**) suggesting that increased electronic density at the aryl ring resulted in more efficient catalysis. However, substituents at the *ortho* position of the aryl ring led to decreased product yields (*e. g.* 60% for **11a** vs. 92% for **9a**), hinting that increased steric hindrance at the C≡C bond resulted in decreased catalyst efficiency. Polyfluorinated aromatic alkynes **4** and **5** as well as the dialkyne **18**, were efficiently hydroborated. HSi(OEt)₃ was also efficient for the aliphatic alkynes **21-23** and was found inefficient for the hydroboration of the alkynes depicted in Scheme 2.1c.



Scheme 2.1. (a) Single hydroboration of 4-fluorophenylacetylene with HBPiN catalyzed by HSi(OEt)₃ under optimized conditions (b) Substrate scope for the single hydroboration (c) Substrates for which HSi(OEt)₃ was inefficient. ¹Conversions and yields (shown in parentheses) are crude calculated by ¹⁹F NMR using fluorobenzene as internal standard. ²Conversion and yields (shown in parentheses) are crude calculated by ¹H NMR using mesitylene as internal standard. ³10 mol% of HSiOEt₃.

Further, conditions were optimized for double hydroboration, using 4-fluorophenylacetylene as the model substrate and 84% of product **1b** was obtained (**Scheme 2.2a**) and substrate scope was evaluated. $\text{HSi}(\text{OEt})_3$ was also found efficient for the single hydroboration of 4-fluorostyrene (**24**, **Scheme 2.2b**) and the sequential hydroboration of the alkynylboronate **25**. (**Scheme 2.2c**)¹⁸



Scheme 2.2. (a) Double hydroboration of 4-fluorophenylacetylene with HBPiñ catalyzed by $\text{HSi}(\text{OEt})_3$ under optimized conditions. (b) Single hydroboration of 4-fluorostyrene under optimized conditions and (c) sequential hydroboration of 4-fluorophenylalkynylboronate ester under non-optimized conditions.

Control experiments employing BH_3 -THF as the precatalyst (**Figure 2.10** in appendix) and trapping BH_3 experiments allowed to rule out hidden-boron catalysis¹⁹ as responsible for observed yields of **1a** and **1b**. However, BH_3 formed at late stages of the reaction could contribute to a minor extent (<11%) to the yield of **1b** (**Figure 2.11** in appendix). The synthetic approach described here presents significant advantages over the reported $\text{Sc}(\text{OTf})_3$ ²⁰ and 9-BBN¹² catalysts for the single and sequential hydroboration of terminal alkynes respectively, mainly the milder temperature and lower catalyst loadings in the absence of a strong hydride source as *in situ* activator.²⁰ Furthermore, unlike $\text{Sc}(\text{OTf})_3$ ²⁰ and 9-BBN,¹² $\text{HSi}(\text{OEt})_3$ is capable of accessing both, alkenyl- and alkyldiboronate esters, under the appropriate conditions.

Screening of commercially available siloxanes indicated that Si-H bond is a must for second hydroboration cycle. However, the presence of a Si-H bond is not the only structural requirement for the siloxane to be efficient for the sequential hydroboration, as evidenced by the poor efficiency of $\text{HSi}(\text{CH}_3)(\text{OEt})_2$ (**Table 2.1, entry 5**) compared to that of $\text{HSi}(\text{OEt})_3$ (**Table 2.1, entry 1**). Therefore, the presence of the 3 OEt groups in $\text{HSi}(\text{OEt})_3$ is also key for catalyst efficiency.

Table 2.1. Optimization of silanes and siloxanes for the hydroboration of terminal alkynes.

Entry	Catalysts [Si]	Conversion (%)	Yield 1a (%)	Yield 1b (%)
1	HSi(OEt) ₃	>99	N.D.	40
2	HSiEt ₃	10	6	N.D.
3	Si(OEt) ₄	83	80	N.D.
4	ClSi(OEt) ₃	>99	84	N.D.
5	HSi(CH ₃)(OEt) ₂	>99	53	11
6	HSi(OiPr) ₃	>99	76	N.D.

Reaction conditions: **1** (0.300 mmol) as the terminal alkyne, HBPIn (0.900 mmol) and 0.060 mmol of the corresponding silicon compound as catalyst, Solvent = 1,4-Dioxane (0.5M) at 80 °C for 24 h. Crude yields and conversion from ¹⁹F NMR using fluorobenzene as internal standard.

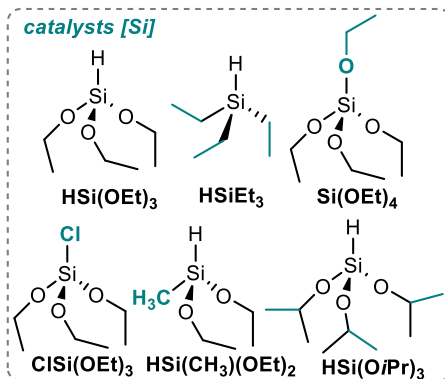
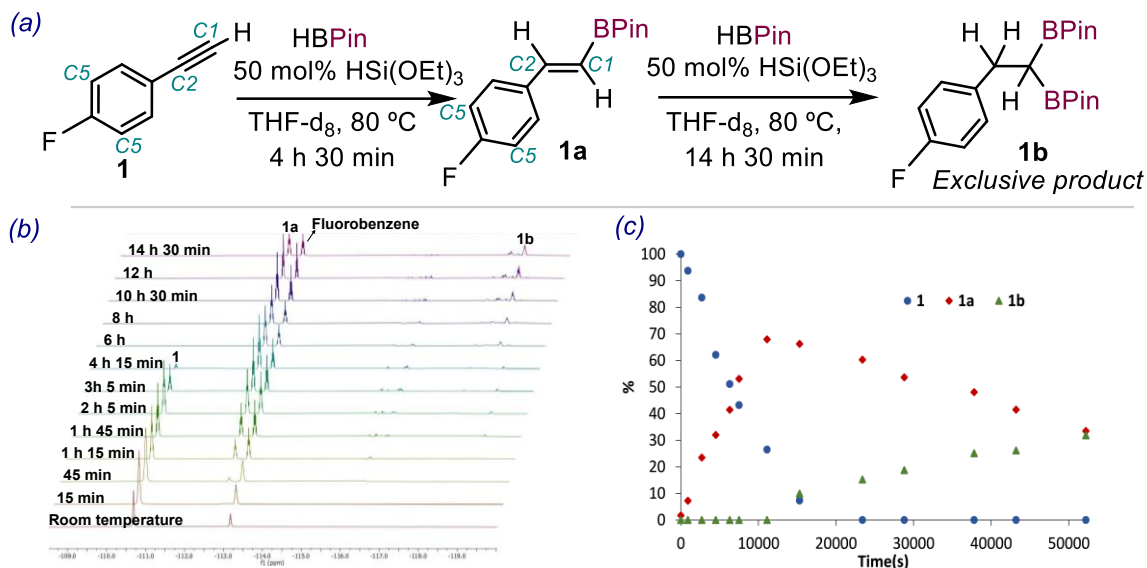


Figure 2.3. Structures of catalysts optimized for double hydroboration of **1**.

2.3. Mechanistic insights into single and double hydroboration of **1**.

To elucidate the keys behind catalyst efficiency, the hydroboration of **1** with 3 equiv of HBPIn in the presence of 50 mol% of HSi(OEt)₃ in THF-d₈ at 80 °C was monitored by ¹H, ¹⁹F, ¹¹B, ¹³C and ²⁹Si NMR spectroscopy. The ¹⁹F and ¹H NMR spectra showed the conversion of **1** into **1a** and of **1a** into **1b**, supporting two sequential hydroboration cycles operative (Schemes 2.3a, b and Figure 2.7).



Scheme 2.3. (a) Reaction pathway for the HSi(OEt)₃-catalyzed double hydroboration of **1** (b) Stacked ¹⁹F NMR spectra (c) Quantitative reaction profile.

The fluorinated analog HSi(OCH₂CF₃)₃²¹ was found more efficient for the transformation, as evidenced by the times required to reach 92% conversion of **1** (2 h and 5 min) and 51% conversion of **1a** (10 h and 30 min), shorter than those when HSi(OEt)₃ was employed (4 h 30 min and 14 h and 30 min respectively (**Figures 2.4 - 2.6**)).

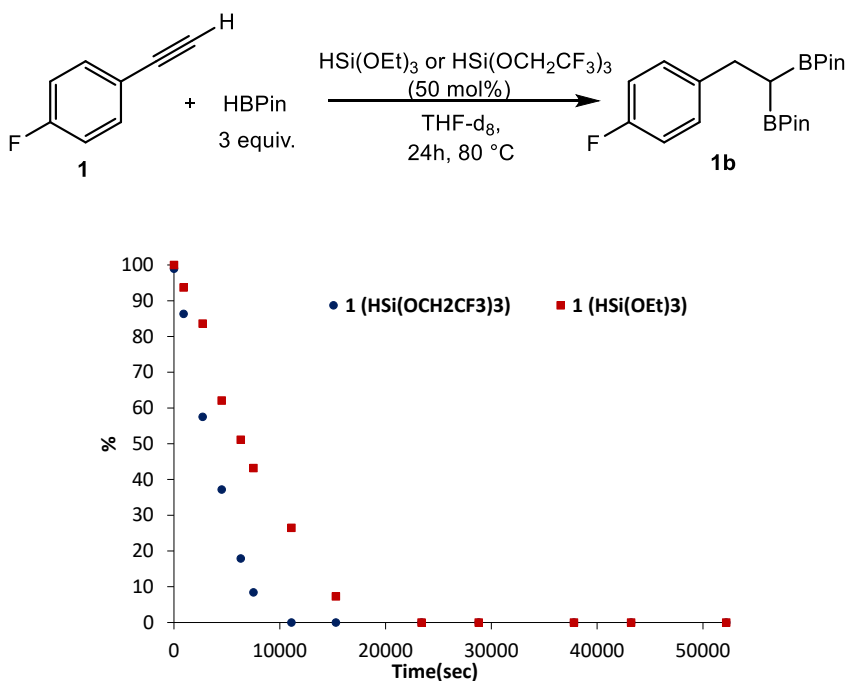


Figure 2.4. Comparison of consumption of **1**.

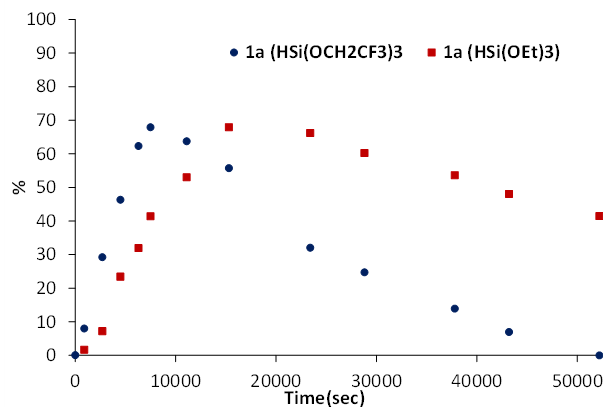


Figure 2.5. Comparison of formation and consumption of **1a**.

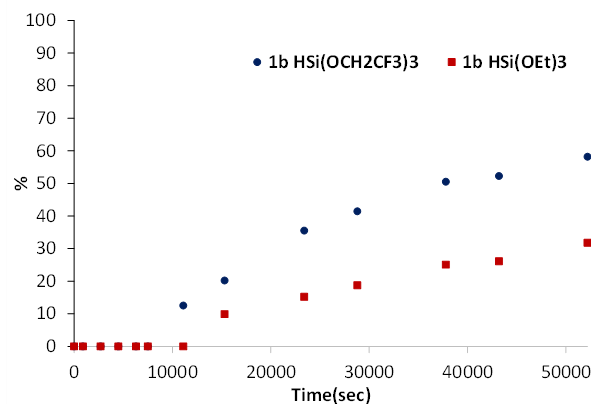


Figure 2.6. Comparison of formation of **1b**.

Furthermore, the times required for the formation of **1b** are longer than those for **1a**, suggesting slower turnover for the second cycle and/or loss of catalyst efficiency over time. In both cases, signals attributable to H₂ in the ¹H NMR spectra and to a mixture of products containing B (broad signals at 22.14 (major) and 35.00 ppm (minor) in the ¹¹B NMR spectra) (**Figure 2.12** in appendix) and Si (-68.55, -40.01, -42.49 ppm in the ²⁹Si NMR spectra) (**Figure 2.8**) were observed, which intensity grew over time. The signal at 22.14 ppm in the ¹¹B NMR spectra was attributed to O(BPin)₂ based on the ¹¹B and ¹³C NMR spectra. The NMR monitoring of the reaction of HSi(OEt)₃ with 1 equiv of HBPIn showed the same signals (**Figures 2.13-2.15** in appendix), supporting reactions involving these species taking place during catalysis. Addition of an equimolar mixture of **1** and HBPIn to the isolated mixture of species and heating at 80 °C for 24 h resulted in recovery of the starting materials, supporting the side reactions involving HBPIn and HSi(OEt)₃ as deactivation pathways that could result in decreased catalyst efficiency over time.

The ¹H NMR spectra of the catalytic reaction did not show any changes in the multiplicity of the signals attributed to **1**, **1a** and HSi(OEt)₃ (**Figure 2.7**) suggesting that covalent

bonding between the substrates and $\text{HSi}(\text{OEt})_3$, including addition of the Si-H bond across the multiple bonds of **1** or **1a**¹², did not take place during catalysis.

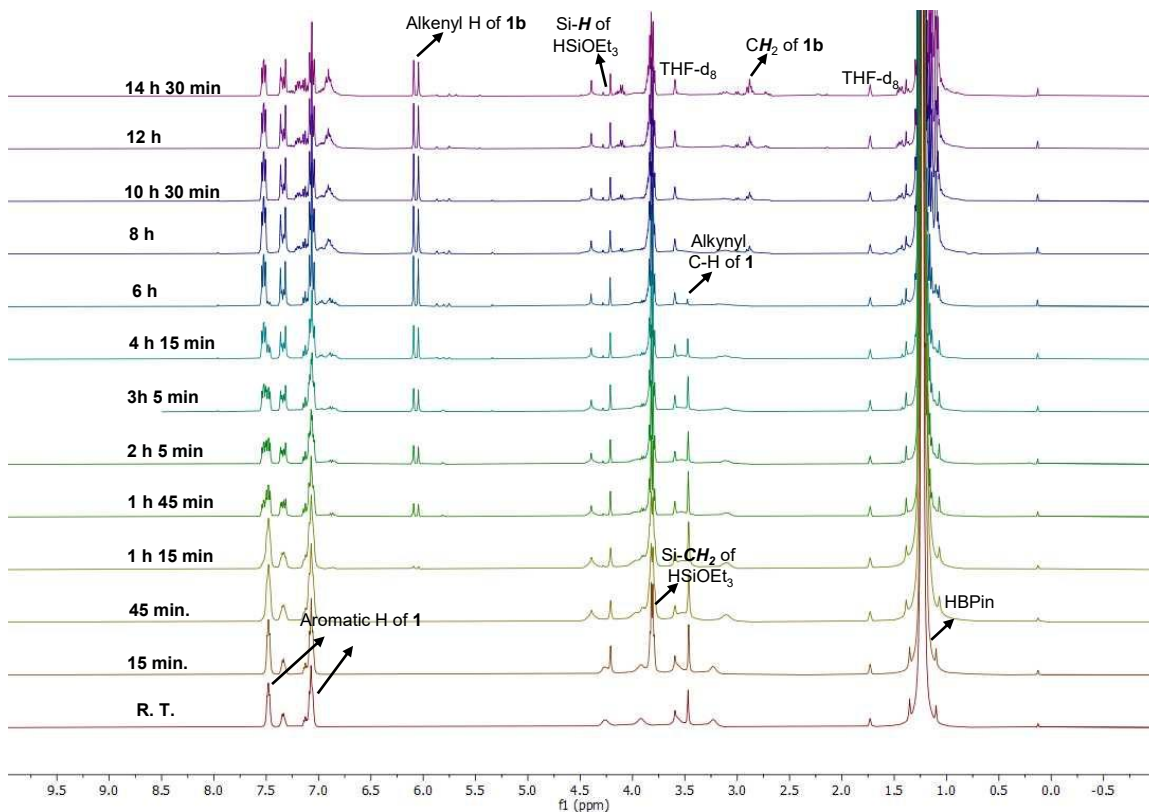
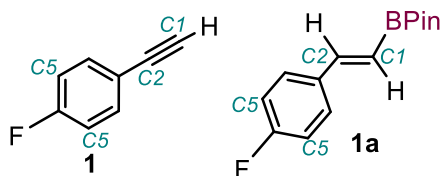


Figure 2.7. ^1H NMR spectra of the sequential hydroboration of **1** with HBPIn employing 50 mol% of $\text{HSi}(\text{OEt})_3$ in THF-d_8 at 80°C , using fluorobenzene as internal standard.

However, the signals attributed to **1**, **1a** and $\text{HSi}(\text{OEt})_3$ shifted from those of samples of the individual reagents in the ^1H , ^{13}C and ^{29}Si NMR spectra throughout catalysis ^1H (e. g. ^1H $\Delta\delta(\text{HSi}(\text{OEt})_3) = +0.013$ ppm; ^{13}C $\Delta\delta(\text{C2 in } \mathbf{1}) = +0.066$ ppm upon mixing the reagents and $\Delta\delta(\text{C2 in } \mathbf{1a}) = +0.012$ ppm at 21% conversion (at 8 h of the reaction time) of **1a**, see **Scheme 2.4** for labelling scheme for **1** and **1a**, and ^{29}Si $\Delta\delta(\text{HSi}(\text{OEt})_3) = -0.062$ ppm upon mixing the reagents and -0.244 ppm at 21% conversion of **1a** (**Tables 2.2** and **2.3**). The shift of the signals suggests that non-covalent interactions between $\text{HSi}(\text{OEt})_3$ and **1** or **1a** are present during the catalytic reaction. The direction of the shifts, downfield for the C2 in **1** and **1a** and upfield for the Si in $\text{HSi}(\text{OEt})_3$, suggest that the non-covalent interactions increase the electronic density on the Si and deplete that of the $\text{C}\equiv\text{C}$ and $\text{C}=\text{C}$ bonds in **1** and **1a** respectively, facilitating the addition of HBPIn.



Scheme 2.4. Number scheme for **1** and **1a**

Table 2.2. ^{13}C NMR $\Delta\delta$ of C2 in **1** and C2 in **1a** during the sequential hydroboration of **1** with HBPIn employing 50 mol% of $\text{HSi}(\text{OEt})_3$ in THF-d_8 at 80°C with respect to those of independently prepared samples of the individual reagents (**1** and **1a**) in THF-d_8 .

Entry	Time	^{13}C NMR $\Delta\delta$ (C2 in 1) (ppm)	^{13}C NMR $\Delta\delta$ (C2 in 1a) (ppm)
1	10 min, R.T.	+0.0656	-
2	1 h 15 min	-	+0.0010
3	3 h 5 min	-	+0.0022
4	6h	-	+0.0065
5	8 h	-	+0.0120

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{C2 in } \mathbf{1}) = ^{13}\text{C}$ NMR $\delta(\text{C2 in } \mathbf{1})_{(\text{catalytic reaction})} - ^{13}\text{C}$ NMR $\delta(\text{C2 in } \mathbf{1})_{(\text{independent sample})}$ for the third column and ^{13}C NMR $\Delta\delta(\text{C2 in } \mathbf{1a}) = ^{13}\text{C}$ NMR $\delta(\text{C2 in } \mathbf{1a})_{(\text{catalytic reaction})} - ^{13}\text{C}$ NMR $\delta(\text{C3 in } \mathbf{1a})_{(\text{independent sample})}$ for the fourth column.

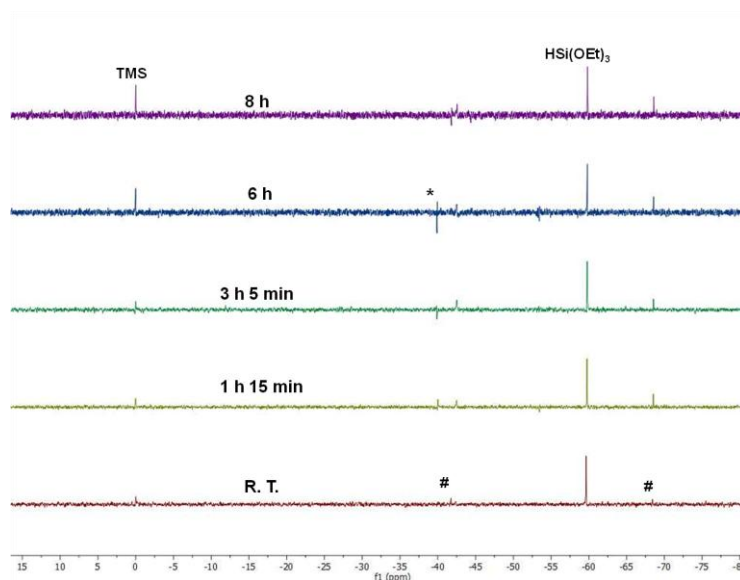


Figure 2.8. ^{29}Si NMR spectra for the sequential hydroboration of 4-fluorophenylacetylene with HBPIn employing 50 mol% of $\text{HSi}(\text{OEt})_3$ in THF-d_8 at 80°C (* = Unidentified product from catalyst deactivation, # = impurities in $\text{HSi}(\text{OEt})_3$)

Table 2.3. ^{29}Si NMR $\Delta\delta$ of Si in $\text{HSi}(\text{OEt})_3$ during the sequential hydroboration of **1** with HBP in employing 50 mol% of $\text{HSi}(\text{OEt})_3$ in THF-d_8 at 80 °C with respect to that of an independently prepared sample of $\text{HSi}(\text{OEt})_3$ in THF-d_8 .

Entry	Time	^{29}Si NMR $\Delta\delta(\text{HSi}(\text{OEt})_3)$
1	10 min, R.T.	-0.0619
2	1 h 15 min	-0.1861
3	3 h 5 min	-0.1993
4	6 h	-0.2123
5	8 h	-0.2436

The $\Delta\delta$ were calculated as follows: ^{29}Si NMR $\Delta\delta(\text{HSi}(\text{OEt})_3) = ^{29}\text{Si}$ NMR $\delta(\text{HSi}(\text{OEt})_3)_{(\text{catalytic reaction})} - ^{29}\text{Si}$ NMR $\delta(\text{HSi}(\text{OEt})_3)_{(\text{independent sample})}$.

To gain some insight into plausible intermediates in the catalytic cycle, stoichiometric reactions between the components of the catalytic system were conducted (**Scheme 2.5**). Addition of 1 equiv of $\text{HSi}(\text{OEt})_3$ to dioxane/ CD_2Cl_2 (12:1) solutions of **1** or **1a** at room temperature resulted in an immediate upfield shift of the signal attributable to $\text{HSi}(\text{OEt})_3$ in the ^{29}Si NMR spectra ($\Delta\delta(\text{HSi}(\text{OEt})_3) = -0.026$ and -0.079 ppm for the mixtures with **1** and **1a** respectively (**Table 2.9** in appendix, entry 1) concomitant with downfield shifts of the signals attributed to **1** (e. g. $\Delta\delta(\text{C2 in } \mathbf{1}) = +0.213$ ppm) or **1a** ($\Delta\delta(\text{C2 in } \mathbf{1a}) = +0.292$ ppm) respectively in the ^{13}C NMR spectra (**Tables 2.4** and **Table 2.5** column 3), in the same direction than those observed during the catalytic reaction. For both **1** and **1a** the ^{13}C NMR $\Delta\delta$ for the aryl C atoms (e. g. $\Delta\delta(\text{C5 in } \mathbf{1}) = +0.053$ ppm and $\Delta\delta(\text{C5 in } \mathbf{1a}) = +0.067$ ppm) were smaller than those of C1 (+ 0.741 ppm for **1**) and C2 (+0.213 ppm for **1** and +0.276 ppm for **1a**) engaged in the $\text{C}\equiv\text{C}$ and $\text{C}=\text{C}$ bonds of **1** and **1a** respectively. This observation points toward the interactions of **1** and **1a** with $\text{HSi}(\text{OEt})_3$ taking place mostly through the multiple C-C bonds.

Table 2.4. $\Delta\delta$ maximum for the ^{13}C NMR signals attributed to the carbon atoms of **1** upon addition of 1 equiv of $\text{HSi}(\text{OEt})_3$.

Entry	Cx in 1	$\Delta\delta(\text{Cx in } \mathbf{1})$ (ppm)
1	C1	+0.7405
2	C2	+0.2182
3	C3	+0.3611
4	C4	+0.0299
5	C5	+0.0528
6	C6	+0.0623

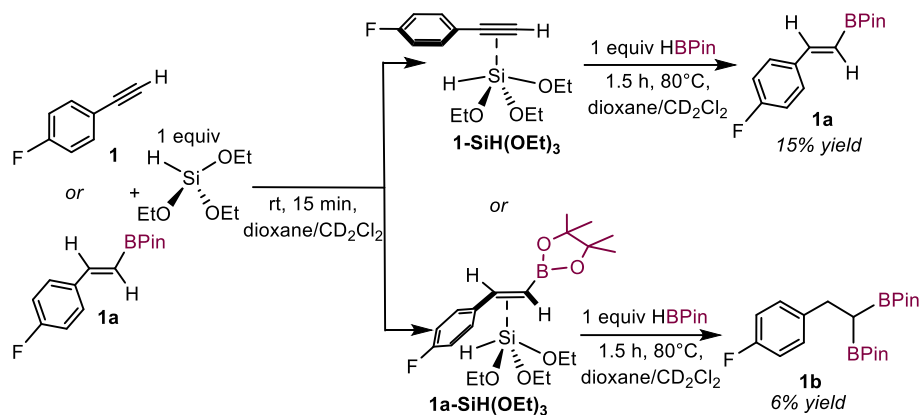
The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{Cx in } \mathbf{1}) = ^{13}\text{C}$ NMR $\delta(\text{Cx})_{(\mathbf{1} + 1 \text{ equiv } \text{HSi}(\text{OEt})_3)} - ^{13}\text{C}$ NMR $\delta(\text{Cx in } \mathbf{1})_{(\text{independent } \mathbf{1})}$.

Table 2.5. ^{13}C NMR $\Delta\delta$ of C_x in **1a** during the stoichiometric reaction of **1a** with $\text{HSi}(\text{OEt})_3$ followed by addition of 1 equiv of HBPIn in dioxane/ DCM-d_2 with respect to that of an independently prepared sample of **1a** in DCM-d_2 .

Entry	Cx in 1a	$\Delta\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\mathbf{1a} + 1 \text{ equiv HSi}(\text{OEt})_3)} \text{ (ppm)}$	$\Delta\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\mathbf{1a} + 1 \text{ equiv HSi}(\text{OEt})_3 + 1 \text{ equiv HBPIn})} \text{ (ppm)}$
1	C2	+0.2924	+0.3077
2	C3	+0.2220	+0.2593
3	C4	+0.0170	+0.0419
4	C5	+0.0838	+0.1089
5	C6	+0.1844	+0.2087

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{C}_x \text{ in } \mathbf{1a}) = ^{13}\text{C}$ NMR $\delta(\text{C}_x)_{(\mathbf{1a} + 1 \text{ equiv HSi}(\text{OEt})_3)} - ^{13}\text{C}$ NMR $\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\text{independent reagent})}$ for third column and ^{13}C NMR $\Delta\delta(\text{C}_x \text{ in } \mathbf{1a}) = ^{13}\text{C}$ NMR $\delta(\text{C}_x)_{(\mathbf{1a} + 1 \text{ equiv HSi}(\text{OEt})_3 + 1 \text{ equiv HBPIn})} - ^{13}\text{C}$ NMR $\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\text{independent reagent})}$ for fourth column.

Titration experiments involving the addition of increasing amounts of $\text{HSi}(\text{OEt})_3$ to CD_2Cl_2 solutions of **1** or **1a** showed analogous shifts of the signals, further supporting non-covalent interactions between the catalyst and the substrates (Tables 2.11 and 2.12 in appendix). Based on these observations, plausible adducts present in solutions of $\text{HSi}(\text{OEt})_3$ and **1** (**1-SiH(OEt)₃**) or **1a** (**1a-SiH(OEt)₃**) are depicted in Scheme 2.5. Addition of 1 equiv of HBPIn to the **1a-SiH(OEt)₃** solution resulted in additional shifts of the signals attributed to **1a** (Table 2.5, column 4) and HBPIn (Table 2.10) in the ^{13}C NMR spectrum, as well as of that of the Si in the ^{29}Si NMR spectrum (Table 2.9 in appendix, entry 2), suggesting that HBPIn interacted with the **1a-SiH(OEt)₃** adduct. Heating the solutions of **1-SiH(OEt)₃** and of **1a-SiH(OEt)₃** after the addition of HBPIn at 80°C for 1.5 hours resulted in the formation of products **1a** and **1b** respectively (Scheme 2.5), supporting the adducts as catalytically competent. The adduct obtained by the addition of 1 equiv of HBPIn to a $\text{HSi}(\text{OEt})_3$ (1 equiv) solution showed analogous results upon addition of **1a** (Table 2.11), suggesting that interaction of any of the substrates, HBPIn, **1** or **1a**, with $\text{HSi}(\text{OEt})_3$ can lead to catalytically active adducts.



Scheme 2.5. Stoichiometric reactions supporting the presence of weak non-covalent interactions in catalysis.

The increased efficiency of $\text{HSi}(\text{OEt})_3$ for alkynes with electron-donating substituents at the *p*-position as well as the increased efficiency of $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ suggests that electron-rich substrates with low steric hindrance, or a more electron-deficient catalyst, render adducts with stronger catalyst-substrate interactions resulting in an increased C-C bond activation toward the addition of HBPIn. The Lewis acidity of $\text{HSi}(\text{OEt})_3$ and $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was examined using the Gutmann-Beckett method, and the results indicate that both siloxanes do not exhibit Lewis acidic behavior.

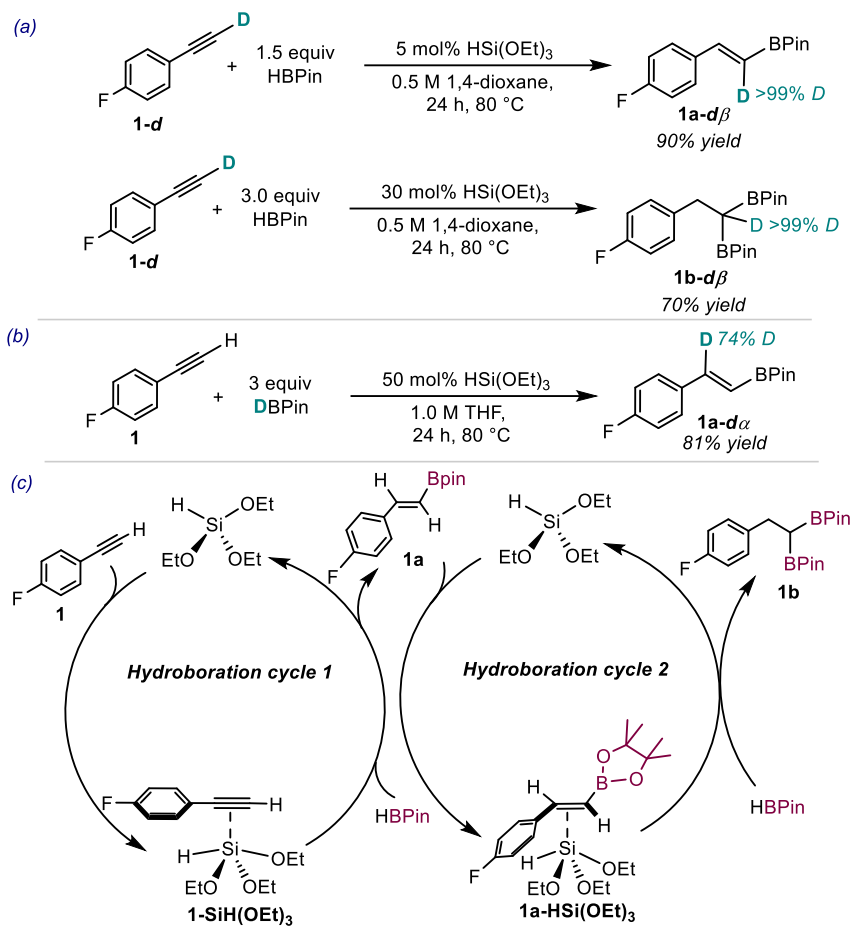
Table 2.6. Assessment of Lewis acidity of $\text{HSi}(\text{OEt})_3$ and $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ by the Gutmann-Beckett method.

Entry	Siloxane	^{31}P NMR $\Delta\delta$ (ppm)
1	$\text{HSi}(\text{OEt})_3$	-0.01 ppm
2	$\text{HSi}(\text{OCH}_2\text{CF}_3)_3$	+0.07 ppm
3	$\text{Si}(\text{FCat})_2^{15a}$	+35.9 ppm

^{31}P NMR $\Delta\delta$ of the signal attributable to OPET_3 upon addition of siloxanes to the solution of OPET_3 in CD_2Cl_2 . The $\Delta\delta$ for the strong Lewis acid $\text{Si}(\text{FCat})_2$ reported in reference 15a is included for comparison (entry 3). ^{31}P NMR $\Delta\delta = ^{31}\text{P}$ NMR $\delta(\text{P})_{(\text{siloxane} + \text{OPET}_3)} - ^{31}\text{P}$ NMR $\delta(\text{P})_{(\text{independent OPET}_3)}$.

Deuterium-labelling experiments employing **1-d** resulted in the formation of products **1a-d β** and **1b-d β** in analogous yields to those of **1a** and **1b** and with >99% D incorporation (**Scheme 2.6a**), supporting that C(sp)–H bond activation of **1** does not take place during catalysis.²² When the catalytic reaction was conducted employing a 1.05 M solution of DBPin in THF under the conditions optimized for the formation of **1b**, only **1a-d α** was formed in 81% yield (**Scheme 2.6b**), suggesting that the cleavage of the D-B bond hinders the formation of **1a** and **1b**. Conducting the reaction for 72 h resulted in the formation of **1a-d β** and **1b-d β** in 24% and 27% yield respectively along with other unidentified products, which hindered calculation of deuterium incorporation due to overlapping

signals. NMR monitoring of the reaction of DBPin and HSi(OEt)₃ supported that H/D exchange took place under the catalytic reaction conditions after 15 minutes (**Figure 2.18** in appendix), accounting for the <99% D incorporation observed in **1a-d α** (**Scheme 2.6b**). When the stoichiometric reactions between **1** or **1a** and DBPin were conducted, no products from deutero-boration were detected under conditions where H/D exchange did not happen (6 hours at room temperature in THF), precluding reliable conclusions from this experiment.



Scheme 2.6. Deuterium labelling experiments employing **1-d** for the single (a, top) and sequential (a, bottom) hydroboration and DBPin (b), and (c) proposed catalytic cycle.

Based on the results presented, catalytic cycles that account for the formation of **1a** and **1b** by the HSi(OEt)₃-catalyzed hydroboration of **1** are depicted in Scheme 4c. In both cycles, HSi(OEt)₃ enters the cycles by interaction of **1** or **1a** to afford the **1-SiH(OEt)₃** and **1a-SiH(OEt)₃** adducts respectively, which promote the H-B bond cleavage of HBPi and its addition across the C≡C and C=C bonds, yielding products **1a** and **1b** respectively.

2.4. Conclusion

In conclusion, $\text{HSi}(\text{OEt})_3$ was found to be an efficient catalyst for the single and sequential hydroboration of alkynes showing a wide substrate scope. Mechanistic experiments supported non-covalent interactions between the multiple C-C bonds of the alkyne or the alkenylboronate ester and $\text{HSi}(\text{OEt})_3$ as responsible for their activation toward the addition of HBPIn.

2.5. Experimental Section

2.5.1. General Considerations

All air- and moisture-sensitive manipulations were carried out using vacuum line, Schlenk and cannula techniques or in an MBraun inert atmosphere (argon) glovebox unless otherwise noted. All glassware was stored in a pre-heated at 200 °C oven prior to use. All glassware was cleaned using base (KOH, *i*PrOH) and acid (HCl (aq)) baths. All reported reaction temperatures correspond to external silicone oil bath temperatures. Room temperature (R.T.) was 23 °C.

The solvents used for air- and moisture-sensitive manipulations were dried and deoxygenated using literature procedures.²³ Mesitylene was dried over CaH_2 , degassed by three freeze-pump-thaw cycles and distilled under vacuum prior to use. The terminal alkynes employed in the substrate scope (**1-23**) were purchased from commercial sources (Thermo Fisher Scientific, AmBeed and Sigma Aldrich), dried over lithium aluminum hydride and distilled prior to use. HBDan,²⁴ 4-fluorophenylacetylene-*d*,²⁵ $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$,²⁶ DBPin²⁷ were synthesized according to literature procedures.

^1H NMR spectra were recorded on either Varian 400 or 500 spectrophotometers operating at 400 MHz, and 500 MHz, respectively. ^{13}C NMR spectra were recorded on Varian 400 or 500 spectrophotometers operating at 101 MHz and 126 MHz, respectively. ^{11}B NMR spectra were recorded on Varian 400 or 500 spectrometers with 128 MHz and 160 MHz frequencies. All the ^{11}B spectra reported are ^1H decoupled ($^{11}\text{B}\{^1\text{H}\}$). ^{19}F NMR spectra were recorded on Varian 400 or 500 spectrometers with 376 MHz and 470 MHz frequencies. ^{29}Si NMR spectra were recorded on Varian 500 with 99 MHz frequency. All ^1H and ^{13}C NMR chemical shifts are reported in ppm relative to SiMe_4 using the ^1H (chloroform-*d*: 7.26 ppm; benzene-*d*₆: 7.16 ppm) and ^{13}C (chloroform-*d*: 77.16 ppm; benzene-*d*₆: 128 ppm) chemical shifts of the solvent as a standard. ^1H NMR data for diamagnetic compounds are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent, obsc = obscured), coupling constants (Hz), integration, assignment. ^{13}C NMR data are reported as follows: chemical shift, number of protons attached to carbon (e. g. CH_2), assignment.

2.5.2. General procedure for the single hydroboration of terminal alkynes:

Synthesis of alkenyl boronate esters

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: terminal alkyne (0.300 mmol), dioxane (0.49 mL), HBPIn

(65 μL , 0.450 mmol) and $\text{HSi}(\text{OEt})_3$ (3 μL , 0.016 mmol). The reaction was exposed to the air after 24 hours fluorobenzene (10 μL , 0.106 mmol) or mesitylene (10 μL , 0.071 mmol) was added as an internal standard. The crude reaction was analyzed by ^{19}F NMR spectroscopy for fluorinated substrates and ^1H NMR spectroscopy for other substrates, without additional purification.

2.5.3. General procedure for the isolation of alkenyl boronate esters

After the completion of the reaction, the contents were exposed to air and the volatiles were removed in vacuo. The isolated product was analyzed by ^1H , ^{13}C and ^{11}B NMR spectroscopy.

2.5.4. General Procedure for the double hydroboration of alkynes: Synthesis of alkyl diboronate esters

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: Terminal alkyne (0.300 mmol), dioxane (0.125 mL), HBPIn (130 μL , 0.900 mmol) and $\text{HSi}(\text{OEt})_3$ (16 μL , 0.090 mmol). The reaction was exposed to the air after 24 hours and fluorobenzene (10 μL , 0.106 mmol) or mesitylene (10 μL , 0.071 mmol) was added as an internal standard. The crude reaction was analyzed by ^{19}F NMR spectroscopy for fluorinated substrates and ^1H NMR spectroscopy for other substrates, without additional purification.

2.5.5. Procedure for the hydroboration of 4-fluorostyrene (24). Synthesis of alkyl boronate ester

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: 4-fluorophenylstyrene (36 μL , 0.300 mmol), dioxane (0.40 mL), HBPIn (108 μL , 0.750 mmol) and $\text{HSi}(\text{OEt})_3$ (11 μL , 0.060 mmol). The reaction was exposed to air after 24 hours and fluorobenzene (10 μL , 0.106 mmol) was added as an internal standard. The crude reaction was analyzed by ^{19}F NMR spectroscopy. Crude yield: 99%. Volatiles were removed in vacuo to isolate the product.

2.5.6. Procedure for the double hydroboration of 2-((4-Fluorophenyl)ethynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (25)

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: 2-((4-Fluorophenyl)ethynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (73.8 mg, 0.300 mmol), dioxane (0.125 mL), HBPIn (130 μL , 0.900 mmol) and $\text{HSi}(\text{OEt})_3$ (16 μL , 0.090 mmol). The reaction was exposed to the air after 24 hours and mesitylene (10 μL , 0.071 mmol) was added as an internal standard. The crude reaction was analyzed by ^1H and ^{19}F NMR spectroscopy. Volatiles were removed and ^1H , ^{13}C , ^{11}B and ^{19}F NMR spectra were recorded without further purification.

2.5.7. General procedure for assessment of Lewis acidity by the Gutmann-Beckett method

$\text{HSi}(\text{OEt})_3$ or $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ (0.033 mmol) was added to a J. Young NMR tube containing a solution of OPet_3 (4.4 mg, 0.030 mmol) in CD_2Cl_2 in an argon filled glovebox. The tube

was sealed and brought out of the glovebox. The ^{31}P NMR spectra were recorded before and after the addition of corresponding siloxane employing a capillary with H_3PO_4 as internal standard.

2.5.8. General procedure for monitoring catalytic reactions using NMR spectroscopy

4-Fluorophenylacetylene (34 μL , 0.300 mmol) was added to a J. Young NMR tube followed by the addition THF- d_8 (0.30 mL), HBPIn (130 μL , 0.900 mmol), fluorobenzene (10 μL , 0.106 mmol) as internal standard and $\text{HSi}(\text{OEt})_3$ (27 μL , 0.150 mmol), in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The headspace was evacuated by a freeze-pump-thaw cycle. The reaction was monitored by ^1H , ^{11}B , ^{19}F , ^{13}C and ^{29}Si NMR spectroscopy at 80 $^\circ\text{C}$.

Sample preparation for recording the ^{29}Si and ^{13}C NMR spectra: 4-Fluorophenylacetylene (45 μL , 0.400 mmol) was added to a J. Young NMR tube followed by the addition THF- d_8 (0.30 mL), HBPIn (173 μL , 1.200 mmol), fluorobenzene (10 μL , 0.106 mmol) as internal standard and $\text{HSi}(\text{OEt})_3$ (37 μL , 0.200 mmol), in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The headspace was evacuated by a freeze-pump-thaw cycle. The reaction was monitored by ^{19}F , ^{13}C and ^{29}Si NMR spectroscopy at 80 $^\circ\text{C}$ for 8 hours.

2.5.9. Procedure of NMR monitoring of a 1:1 mixture of $\text{HSi}(\text{OEt})_3$:1 in dioxane/ CD_2Cl_2 followed by addition of HBPIn

$\text{HSi}(\text{OEt})_3$ (92 μL , 0.500 mmol) was added to a solution of 1 (57 μL , 0.500 mmol) in dioxane (0.25 mL) in a J. Young NMR tube in an argon filled glovebox and 20 μL of CD_2Cl_2 was added. The tube was sealed and brought out of the glovebox and ^{13}C and ^{29}Si NMR spectra of the sample were recorded at room temperature after 15 min. (See Figures S48, S49). After recording the ^{13}C and ^{29}Si NMR of the reaction mixture, the tube was brought inside the glovebox and HBPIn (73 μL , 0.500 mmol) was added to the reaction mixture. The ^{19}F NMR spectrum only showed the signal attributable to 1, supporting no product formation at rt. The sample was heated at 80 $^\circ\text{C}$ for 1.5 h and the ^{19}F NMR spectrum was recorded at room temperature.

2.5.10. Procedure for NMR monitoring of a 1:1 mixture of $\text{HSi}(\text{OEt})_3$:1a in dioxane/ CD_2Cl_2 followed by addition of HBPIn

$\text{HSi}(\text{OEt})_3$ (74 μL , 0.400 mmol) was added to a solution of 1a (99 mg, 0.400 mmol) in dioxane (0.25 mL) in a J. Young NMR tube in an argon filled glovebox and 20 μL of CD_2Cl_2 were added as locking solvent. The tube was sealed and brought out of the glovebox and the ^{13}C and ^{29}Si NMR spectra of the sample were recorded at room temperature after 15 min (see Figures S44, S45). After recording the ^{13}C and ^{29}Si NMR of the reaction mixture, the tube was brought inside the glovebox and HBPIn (58 μL , 0.400 mmol) and fluorobenzene as a standard (10 μL , 0.106 mmol) were added to the reaction mixture. The tube was sealed and brought out of the glovebox and the ^{19}F , ^{13}C and ^{29}Si NMR spectra of the sample were recorded after 15 min at room temperature (see Figures S51 and S52). The

reaction mixture was heated at 80 °C for 1 hour and the ^{19}F , ^{13}C and ^{29}Si NMR were recorded at room temperature.

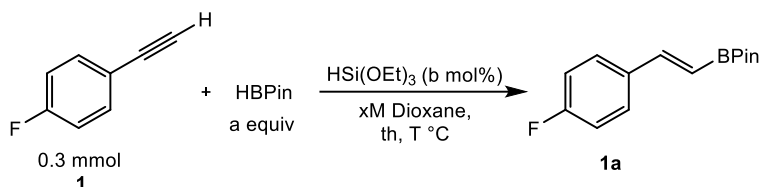
2.5.11. Procedure for NMR titration experiments of 1/1a with $\text{HSi}(\text{OEt})_3$

1 or 1a (0.3600 mmol) was added to a J. Young NMR tube followed by the addition of CD_2Cl_2 (0.30 mL) and the sequential addition of $\text{HSi}(\text{OEt})_3$ (0.1 equiv (6 μL , 0.03 mmol), 0.2 equiv (11 μL , 0.06 mmol), 0.3 equiv (17 μL , 0.09 mmol), 0.5 equiv (28 μL , 0.15 mmol), 0.7 equiv (39 μL , 0.21 mmol), 0.9 equiv (50 μL , 0.27 mmol), 1.0 equiv (55 μL , 0.30 mmol), 1.2 equiv (66 μL , 0.36 mmol), 1.5 equiv (83 μL , 0.45 mmol), 2.0 equiv (111 μL , 0.60 mmol), at room temperature. The ^{13}C NMR spectra was recorded after every addition.

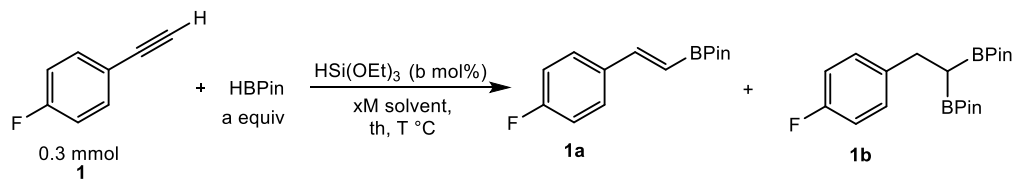
2.6. Appendix

2.6.1. Selected optimizations of reaction conditions for single and sequential hydroboration of 1.

Table 2.7. Selected optimizations of reaction conditions for single hydroboration of 1



Entry	[M] (x)	Equiv of HBpin (a)	Catalyst loading (b) (mol%)	T (°C)	t (h)	Conversion (%)	Yield 1a (%)
1	0.5	1.5	5	80	24	>99	89
2	0.5	1.5	10	80	16	68	62
3	0.5	1.5	10	30	24	6	6
4	0.5	1.5	10	30	16	10	7
5	0.5	1.25	10	80	24	90	84
6	0.5	1.25	5	80	24	48	41
7	1.0	1.0	10	80	24	75	65
8	0.5	1.5	-	80	24	6	<5

Table 2.8. Selected optimizations of reaction conditions for double hydroboration of **1**.

Entry	[M] (x)	Equiv of HBPin (a)	Catalyst loading (mol%) (b)	Solvent	Conversion (%)	Yield 1b (%)	Yield 1a (%)
1 ^a	0.5	2	20	Dioxane	>99	5	84
2 ^b	0.5	2	20	Dioxane	>99	9	70
3	0.5	2.5	20	Dioxane	>99	13	58
4	1	3	30	DCM	>99	54	N. D.
5	0.5	3	30	THF	>99	<5	95
6	0.5	3	50	THF	>99	84	N. D.
7	0.5	2	20	Toluene	>99	15	64
8	0.5	2	20	THP	>99	N. D.	69
9	0.5	2	20	Hexane	>99	5	87
10	-	3	30	Neat	>99	58	N. D.
11	0.5	3	20	Dioxane	>99	40	N. D.
12	1	3	25	Dioxane	>99	75	N. D.
13	1	3	30	Dioxane	>99	84	N. D.
14	1	3.0	30	1,2-DCE	>99	73	N. D.
15	1	3.0	30	ClC_6H_5	>99	57	N. D.
16	0.5	2.5	-	Dioxane	10	N.D.	6

a = Reaction was performed for 16 h, b = Reaction was performed at 60 °C

2.6.2. Hidden Boron Catalysis

Reaction of 4-fluorophenylacetylene (**1**) with HBPin catalyzed by BH_3 -THF under optimized conditions for the sequential hydroboration of **1**.

In an argon-filled glovebox, a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: 4-fluorophenylacetylene (34 μL , 0.300 mmol), dioxane (45 μL), HBPin (130 μL , 0.900 mmol) and BH_3 -THF (90 μL of a 1 M solution in THF, 0.090 mmol). The reaction was exposed to air after 24 hours and fluorobenzene (10 μL , 0.106 mmol) was added as an internal standard and THF-d_8 (10 μL) as locking solvent. The reaction crude was analyzed by ^{19}F NMR spectroscopy (Figure S1) without additional purification. Conversion: >99%. Yield **1a** = 12%, Yield **1b** = 7%

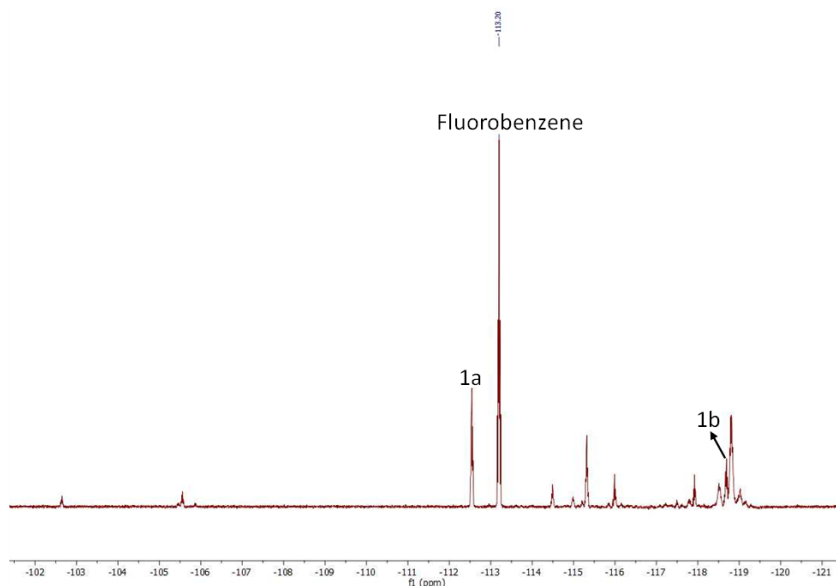


Figure 2.9. ^{19}F NMR spectrum of the reaction of **1** with HBPIn catalyzed by $\text{BH}_3\text{-THF}$ under optimized conditions for the sequential hydroboration of **1**. Unlabeled peaks correspond to unidentified products.

Reaction of **1a** with HBPIn catalyzed by $\text{BH}_3\text{-THF}$.

In an argon-filled glovebox, a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: **1a** (25 mg, 0.100 mmol), dioxane (44 μL), HBPIn (26 μL , 0.180 mmol) and $\text{BH}_3\text{-THF}$ (30 μL of a 1 M solution in THF, 0.030 mmol). The reaction was exposed to air after 24 hours and fluorobenzene (10 μL , 0.106 mmol) was added as an internal standard and THF-d_8 (10 μL) as locking solvent. The reaction crude was analyzed by ^{19}F NMR spectroscopy (Figure S2) without additional purification. Conversion: =95%. Yield **1b** = 11%

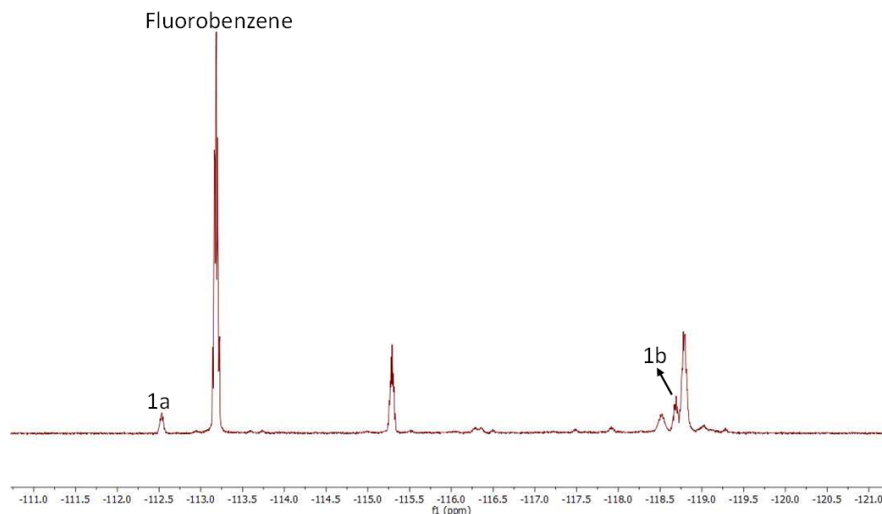


Figure 2.10. ^{19}F NMR spectrum of the reaction of (**1a**) with HBPIn catalyzed by $\text{BH}_3\text{-THF}$. Unlabeled peaks correspond to unidentified products.

Hydroboration of 1 with HBPIn in dioxane (only second hydroboration cycle operative) catalyzed by $\text{HSi}(\text{OEt})_3$ followed by the addition of NEt_3 :

In an argon-filled glovebox, a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: **1** (34 μL , 0.300 mmol), dioxane (0.10 mL), HBPIn (130 μL , 0.900 mmol) and $\text{HSi}(\text{OEt})_3$ (16 μL , 0.090 mmol). After 8 hours, the reaction was brought into the glovebox and NEt_3 (13 μL , 0.090 mmol) and THF-d_8 (0.05 mL) were added to the reaction mixture. The reaction was analyzed by ^{11}B and ^{19}F NMR spectroscopy without additional purification. A signal attributable to the $\text{Et}_3\text{N-BH}_3$ adduct was detected in the ^{11}B NMR spectrum

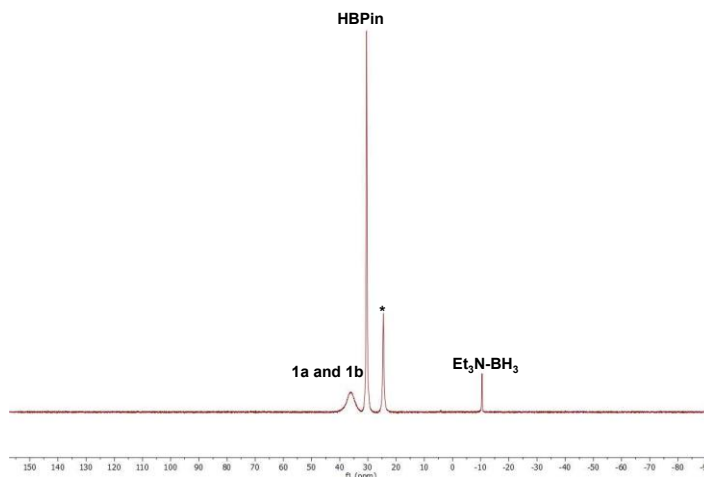


Figure 2.11. ^{11}B NMR spectra of the reaction of the hydroboration of **1a** with HBPIn in dioxane, catalyzed by $\text{HSi}(\text{OEt})_3$ followed by addition of NEt_3 . (* = $\text{O}(\text{BPin})_2$)

2.6.3. NMR Monitoring of the sequential hydroboration of 4-fluorophenylacetylene with HBPIn employing 50 mol% of HSi(OEt)₃ in THF-d₈.

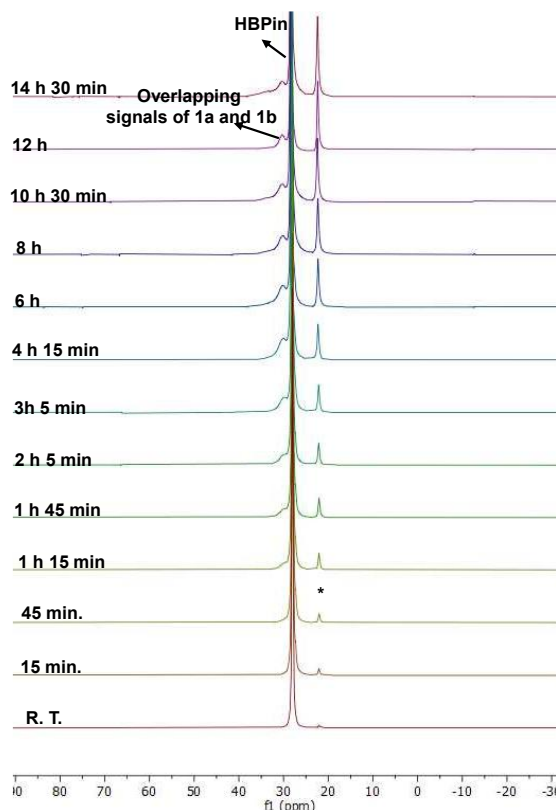
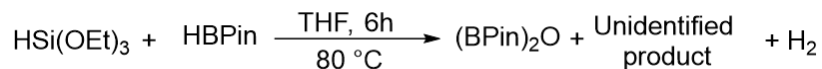


Figure 2.12. ¹¹B NMR spectra of the sequential hydroboration of 4-fluorophenylacetylene (1) with HBPIn employing 50 mol% of HSi(OEt)₃ in THF-d₈ 80 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for given times) (* = (BPin)₂O)

2.6.4. NMR Monitoring of stoichiometric reactions.

NMR monitoring of the reaction of HBPIn with HSi(OEt)₃ (catalyst deactivation pathway):



HBPIn (29 μL, 0.200 mmol) was added to a solution of HSi(OEt)₃ (37 μL, 0.201 mmol) in THF (0.35 mL) in a J. Young NMR tube in an argon filled glovebox and 10 drops of THF-d₈ were added. The tube was sealed and brought out of the glovebox. The reaction was monitored by ¹H, ¹¹B and ²⁹Si NMR spectroscopy at 80 °C for 6h. Signals attributable to an unidentified product were observed in the ¹¹B and ²⁹Si NMR spectra and a singlet at 4.50 ppm attributed to H₂ was observed in ¹H NMR spectra.

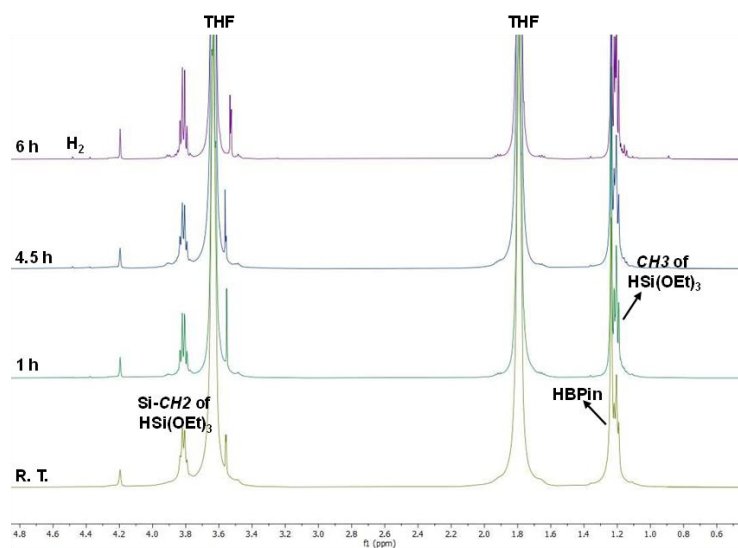


Figure 2.13. ^1H NMR spectra of the stoichiometric reaction of HBPIn with $\text{HSi}(\text{OEt})_3$ in THF/THF- d_8 . All the spectra were recorded at R.T., the bottom spectrum after mixing the reagents at room temperature and the subsequent spectra after heating up to 80°C for the times indicated in each of them.

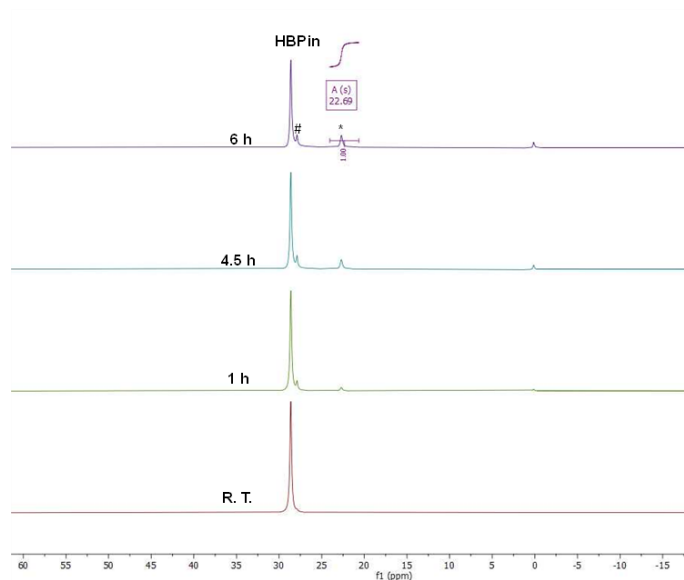


Figure 2.14. ^{29}Si NMR spectra of the stoichiometric reaction of HBPIn with $\text{HSi}(\text{OEt})_3$ in THF/THF- d_8 . All the spectra were recorded at R.T., the first spectrum after mixing the reagents at room temperature and the subsequent spectra after heating up to 80°C for the times indicated in each of them. The bottom spectrum for $\text{HSi}(\text{OEt})_3$ and TMS (employed as internal standard), is shown as a reference. (* = Catalyst deactivation product, # = impurity in $\text{HSi}(\text{OEt})_3$).

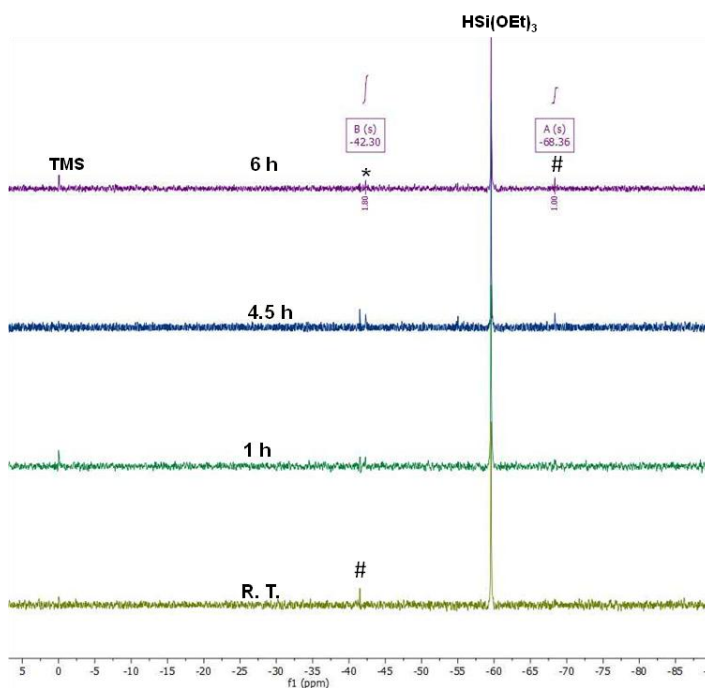


Figure 2.15. ^{29}Si NMR spectra of the stoichiometric reaction of HBPIn with $\text{HSi}(\text{OEt})_3$ in $\text{THF}/\text{THF-d}_8$. All the spectra were recorded at R.T., the first spectrum after mixing the reagents at room temperature and the subsequent spectra after heating up to 80°C for the times indicated in each of them. The bottom spectrum for $\text{HSi}(\text{OEt})_3$ and TMS (employed as internal standard), is shown as a reference. (* = Catalyst deactivation product, # = impurity in $\text{HSi}(\text{OEt})_3$).

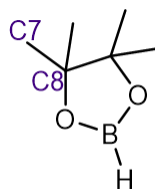
NMR monitoring of a 1:1 mixture of $\text{HSi}(\text{OEt})_3$:1a in dioxane/ CD_2Cl_2 followed by addition of HBPIn:

Table 2.9. ^{29}Si NMR $\Delta\delta$ of Si in $\text{HSi}(\text{OEt})_3$ with respect to that of an independently prepared sample of $\text{HSi}(\text{OEt})_3$ in DCM-d_2 .

Entry	Reagents present	^{29}Si NMR $\Delta\delta(\text{HSi}(\text{OEt})_3)$ (ppm)
1	1a + $\text{HSi}(\text{OEt})_3$	-0.0785
2	1a + $\text{HSi}(\text{OEt})_3$ + HBPIn	-0.1146

The $\Delta\delta$ were calculated as follows: ^{29}Si NMR $\Delta\delta(\text{Si atom of HSi}(\text{OEt})_3) = ^{29}\text{Si}$ NMR $\delta(\text{Si})(1a + 1 \text{ equiv HSi}(\text{OEt})_3) - ^{29}\text{Si}$ NMR $\delta(\text{Si})(\text{independent HSi}(\text{OEt})_3)$ for entry 1 and ^{29}Si NMR $\Delta\delta(\text{Si atom of HSi}(\text{OEt})_3) = ^{29}\text{Si}$ NMR $\delta(\text{Si})(1a + 1 \text{ equiv HSi}(\text{OEt})_3 + 1 \text{ equiv of HBPIn}) - ^{29}\text{Si}$ NMR $\delta(\text{Si})(\text{independent HSi}(\text{OEt})_3)$ for entry 2.

Table 2.10. ^{13}C NMR $\Delta\delta$ of C_X in HBPIn with respect to that of an independently prepared sample of HBPIn in DCM-d_2 .



Entry	Cx in HBPIn	$\Delta\delta(\text{Cx in HBPIn})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3)}$ (ppm)	$\Delta\delta(\text{Cx in HBPIn})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3 + 1 \text{ equiv } \mathbf{1a})}$ (ppm)
1	C7	-0.4198	-0.3623
2	C8	-0.2310	-0.1634

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{Cx in HBPIn}) = ^{13}\text{C}$ NMR $\delta(\text{Cx})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3)} - ^{13}\text{C}$ NMR $\delta(\text{Cx in HBPIn})_{(\text{independent reagent})}$ for third column and ^{13}C NMR $\Delta\delta(\text{Cx in HBPIn}) = ^{13}\text{C}$ NMR $\delta(\text{Cx})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3 + 1 \text{ equiv } \mathbf{1a})} - ^{13}\text{C}$ NMR $\delta(\text{Cx in HBPIn})_{(\text{independent reagent})}$ for fourth column.

NMR monitoring of a 1:1 mixture of HSi(OEt)₃:HBPIn in dioxane/CD₂Cl₂ followed by addition of 1 equiv of **1a:**

HSi(OEt)₃ (74 μL , 0.400 mmol) was added to a solution of HBPIn (58 μL , 0.400 mmol) in dioxane (0.25 mL) in a J. Young NMR tube in an argon filled glovebox and 20 μL of CD₂Cl₂ were added as locking solvent. The tube was sealed and brought out of the glovebox and the ^{13}C and ^{29}Si NMR spectra of the sample were recorded after 15 min at room temperature. After recording the ^{13}C and ^{29}Si NMR of the reaction mixture, the tube was brought inside the glovebox and **1a** (99 mg, 0.400 mmol) and fluorobenzene as internal standard (10 μL , 0.106 mmol) were added to the reaction mixture. The tube was sealed and brought out of the glovebox and the ^{19}F , ^{13}C and ^{29}Si NMR spectra of the resulting mixture were recorded after 15 min at room temperature. The contents were heated at 80 $^{\circ}\text{C}$ for 1 hour and the ^{19}F , ^{13}C and ^{29}Si NMR were recorded at room temperature. Product **1b** was formed in 11% yield (see Figure S56) calculated by ^{19}F NMR spectrum integration.

Table 2.11. ^{29}Si NMR $\Delta\delta$ of Si in HSi(OEt)₃ with respect to that of an independently prepared sample of HSi(OEt)₃ in DCM-d₂.

Entry	Reagents present	^{29}Si NMR $\Delta\delta(\text{HSi(OEt)}_3)$ (ppm)
1	HSi(OEt) ₃ + HBPIn	-0.0713
2	HSi(OEt) ₃ + HBPIn+ 1a	-0.1246

The $\Delta\delta$ were calculated as follows: ^{29}Si NMR $\Delta\delta(\text{Si atom of HSi(OEt)}_3) = ^{29}\text{Si}$ NMR $\delta(\text{Si})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3)} - ^{29}\text{Si}$ NMR $\delta(\text{Si})_{(\text{independent HSi(OEt)}_3)}$ for entry 1 and ^{29}Si NMR $\Delta\delta(\text{Si atom of HSi(OEt)}_3) = ^{29}\text{Si}$ NMR $\delta(\text{Si})_{(\text{HBPIn} + 1 \text{ equiv HSi(OEt)}_3 + 1 \text{ equiv } \mathbf{1a})} - ^{29}\text{Si}$ NMR $\delta(\text{Si})_{(\text{independent HSi(OEt)}_3)}$ for entry 2.

Table 2.12. ^{13}C NMR $\Delta\delta$ of C_x in **1a** during the stoichiometric reaction of HBPIn with $\text{HSi}(\text{OEt})_3$ followed by addition of 1 equiv of **1a** in dioxane/ DCM-d_2 with respect to that of an independently prepared sample of **1a** in DCM-d_2 .

Entry	C_x in 1a	$\Delta\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\mathbf{1a} + 1 \text{ equiv HSi}(\text{OEt})_3 + 1 \text{ equiv HBPIn})}$ (ppm)
1	C7	-0.0366
2	C8	-0.1903
3	C2	+0.3115
4	C3	+0.2598
5	C4	+0.0445
6	C5	+0.1100
7	C6	+0.2080

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{C}_x \text{ in } \mathbf{1a}) = ^{13}\text{C}$ NMR $\delta(\text{C}_x)_{(\mathbf{1} + 1 \text{ equiv HSi}(\text{OEt})_3 + 1 \text{ equiv HBPIn})} - ^{13}\text{C}$ NMR $\delta(\text{C}_x \text{ in } \mathbf{1a})_{(\text{independent reagent})}$.

2.6.5. Titration Experiments

NMR titration of **1** with $\text{HSi}(\text{OEt})_3$ in CD_2Cl_2

Table 2.13. $\Delta\delta$ maximum for the ^{13}C NMR signals attributed to the carbon atoms of **1** upon addition of 2 equiv of $\text{HSi}(\text{OEt})_3$.

Entry	C_x in 1	$\Delta\delta(\text{C}_x \text{ in } \mathbf{1})$ (ppm)
1	C1	+0.0135
2	C2	+0.0414
3	C3	+0.2009
4	C4	+0.0732
5	C5	+0.0755
6	C6	+0.1138

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{C}_x \text{ in } \mathbf{1}) = ^{13}\text{C}$ NMR $\delta(\text{C}_x)_{(\mathbf{1} + 2 \text{ equiv HSi}(\text{OEt})_3)} - ^{13}\text{C}$ NMR $\delta(\text{C}_x \text{ in } \mathbf{1})_{(\mathbf{1} + 0.1 \text{ equiv of HSi}(\text{OEt})_3)}$.

NMR titration of **1a** with $\text{HSi}(\text{OEt})_3$ in CD_2Cl_2

Table 2.14. $\Delta\delta$ maximum for the ^{13}C NMR signals attributed to the carbon atoms of **1a** upon addition of 2 equiv of $\text{HSi}(\text{OEt})_3$.

Entry	C_x in 1a	$\Delta\delta(\text{C}_x \text{ in } \mathbf{1a})$ (ppm)
1	C2	+0.2054
2	C3	+0.1992

3	C4	+0.1368
4	C5	+0.1320
5	C6	+0.1239

The $\Delta\delta$ were calculated as follows: $^{13}\text{C NMR } \Delta\delta(\text{Cx in 1a}) = ^{13}\text{C NMR } \delta(\text{Cx})_{(1\text{a} + 2 \text{ equiv HSi(OEt)}_3)} - ^{13}\text{C NMR } \delta(\text{Cx})_{(1\text{a} + 0.1 \text{ equiv HSi(OEt)}_3)}$.

2.6.6. Deuterium labelling experiments

Synthesis of BD₃-THF:

BD₃-THF was synthesized according to the literature procedure¹⁰ with slight modification. To the stirring suspension of NaBD₄ (1.2 g, 28.7 mmol) in diglyme (5 mL), BF₃·Et₂O (5 mL, 40 mmol) was added over a period of 30 min. The diborane generated was allowed to pass through a cannula into the agitated solution of THF (31 mL) kept at 0 °C. The contents were left under flow of nitrogen until the formation of diborane gas ceased and were stirred for an additional hour. ²H and ¹¹B NMR spectra of the crude sample were recorded in benzene-d₆. The contents were used without further purification for the synthesis of DBPin. ²H NMR (400 MHz, C₆D₆, 23 °C): δ 2.64 (bs). ¹¹B NMR (400 MHz, CDCl₃, 23 °C): δ -0.68.

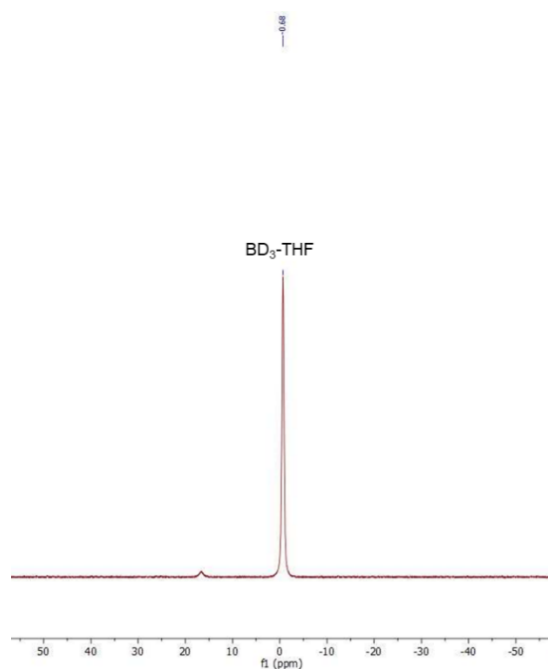


Figure 2.16. ¹¹B NMR of BD₃-THF in C₆D₆

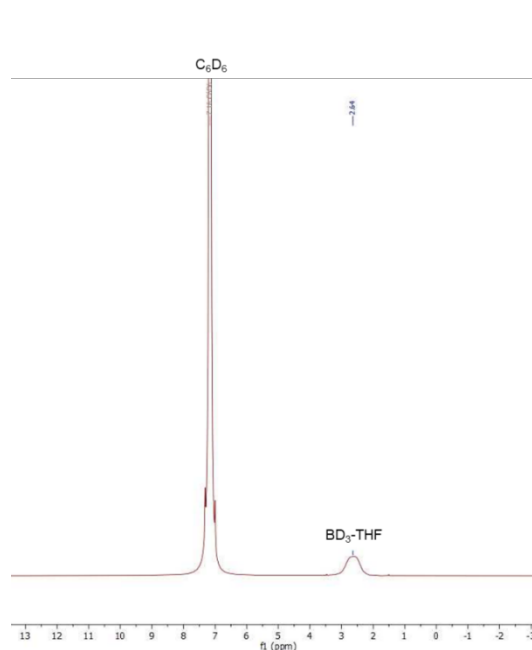


Figure 2.17. ²H NMR of BD₃-THF in C₆D₆

NMR monitoring of the reaction of DBPin with HSi(OEt)₃:

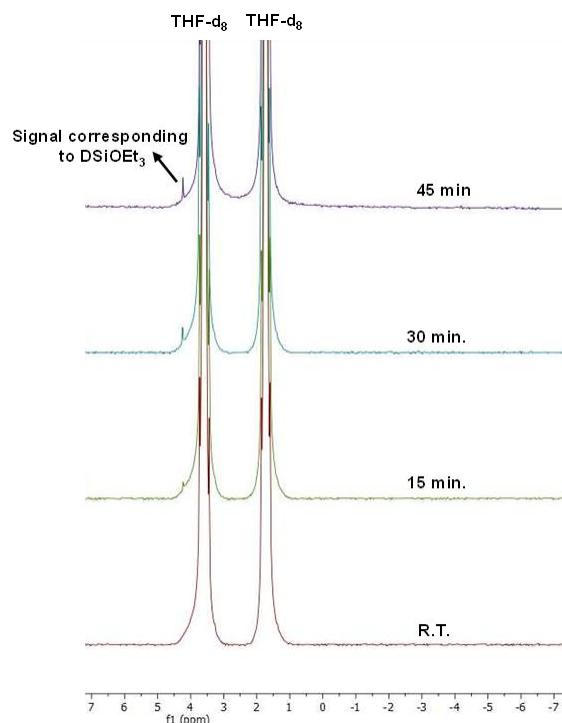


Figure 2.18. ^2H NMR spectra of the reaction between DBPin and $\text{HSi}(\text{OEt})_3$ showing H/D exchange. (The first spectrum was recorded at room temperature, and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for the given times).

Single hydroboration of 4-fluorophenylacetylene-*d* with HBPIn catalyzed by $\text{HSi}(\text{OEt})_3$:

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: 4-fluorophenylacetylene-*d* (33 μL , 0.300 mmol), dioxane (0.50 mL), HBPIn (65 μL , 0.450 mmol) and $\text{HSi}(\text{OEt})_3$ (3 μL , 0.016 mmol). The contents were stirred at 80°C for 24h and then the reaction was exposed to the air. The crude yield and conversion were calculated from ^{19}F NMR spectroscopy using fluorobenzene (10 μL , 0.106 mmol) as an internal standard. The volatiles were removed in vacuo for isolation of the product. The isolated product was analyzed by ^1H , ^2D , ^{13}C , ^{19}F and ^{11}B NMR spectroscopy. Conversion: >99%, Yield **1a-d β** : 90%. Signal corresponding to the $\text{H}\beta$ of **1a** (at 6.06 ppm (1H, d)) was absent in the ^1H NMR spectrum of **1a-d β** , allowing to determine >99% D-incorporation at this position in **1a-d β** .

^1H NMR (400 MHz, CDCl_3 , 23°C): δ 1.13 (12H, s), 6.67 (2H, m), 7.07 (2H, m), 7.55 (1H, s)

^2D NMR (400 MHz, C_6D_6 , 23°C): δ 6.26 (bs)

$^{13}\text{C}\{^1\text{H}\}$ NMR (400 MHz, CDCl_3 , 23°C): δ 24.44, 82.75, 115.20 (d, $J = 21.72$ Hz), 127.53, 128.56 (d, $J = 8.22$ Hz), 133.68, 148.23, 162.95 (d, $J = 248.15$ Hz)

^{11}B NMR (400 MHz, CDCl_3 , 23 °C): δ 30.46.
 ^{19}F NMR (400 MHz, CDCl_3 , 23 °C): δ -112.51.

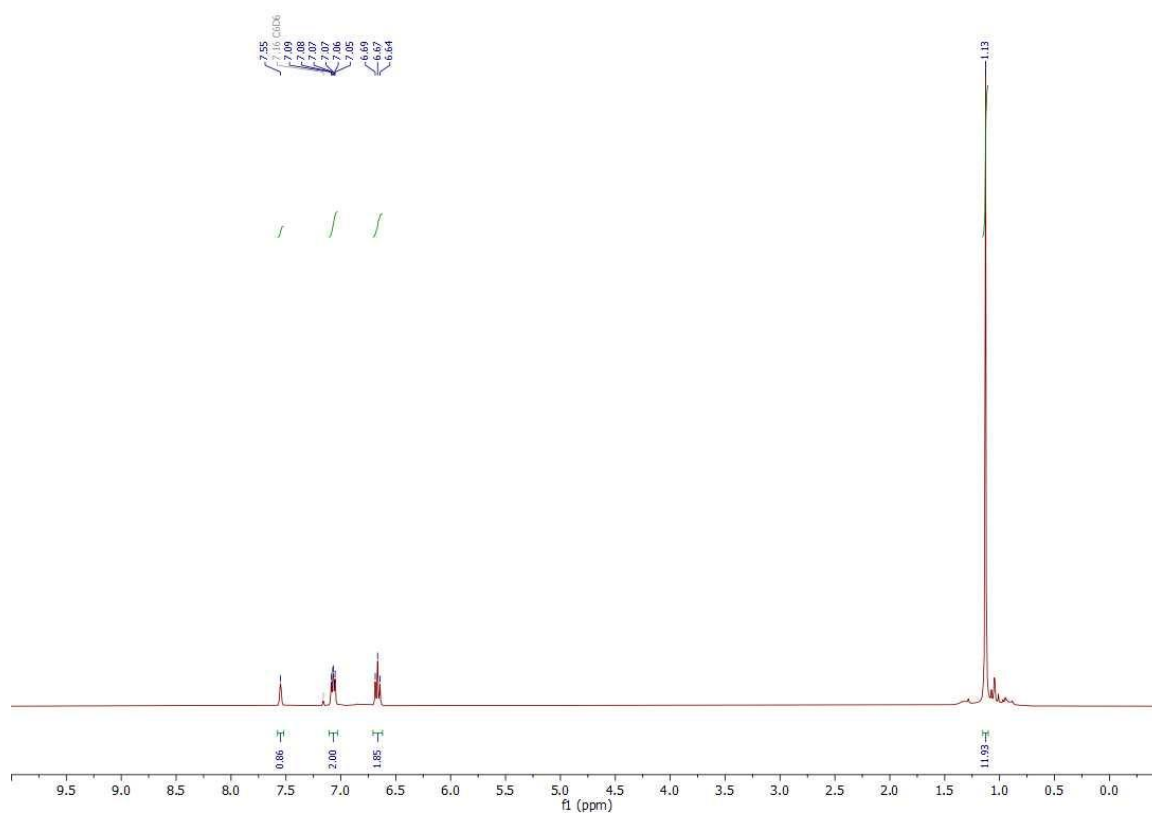


Figure 2.19. ^1H NMR (500 MHz, CDCl_3 , 23 °C) for **1a-d β** .

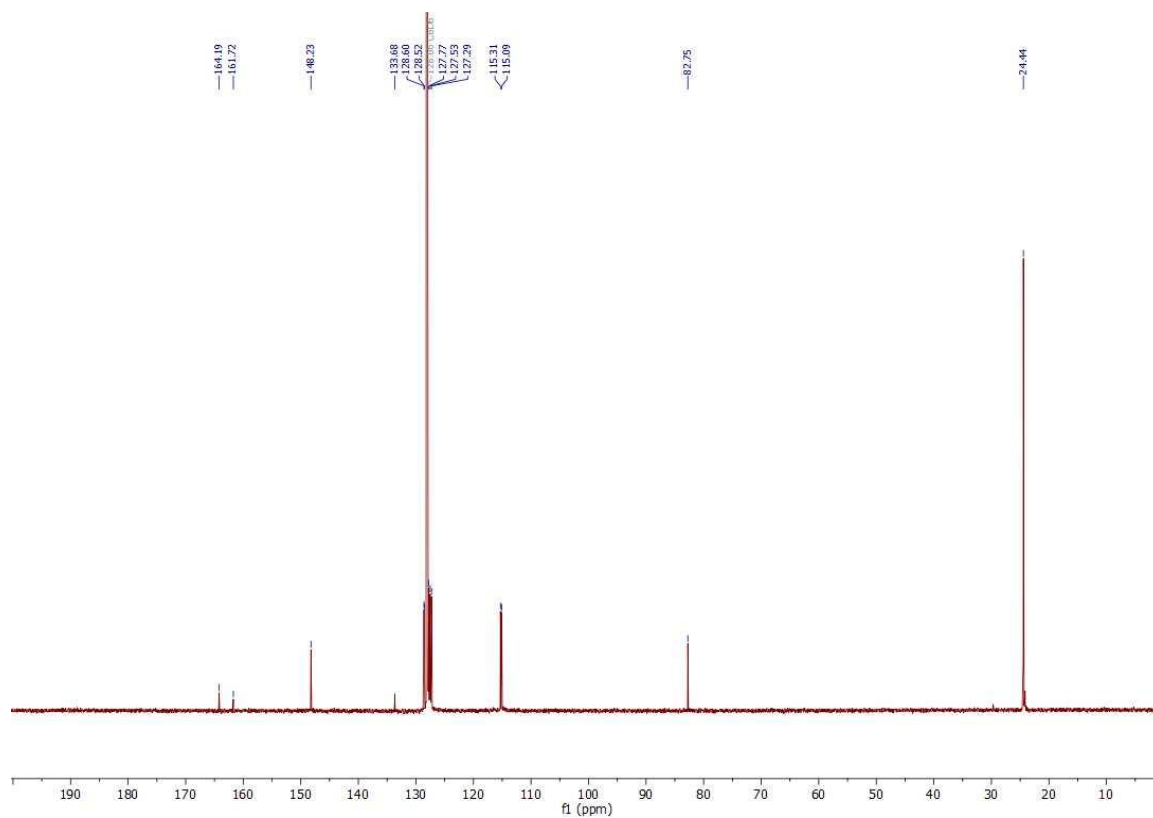


Figure 2.20. ^{13}C NMR (500 MHz, CDCl_3 , 23 °C) for **1a-d β** .

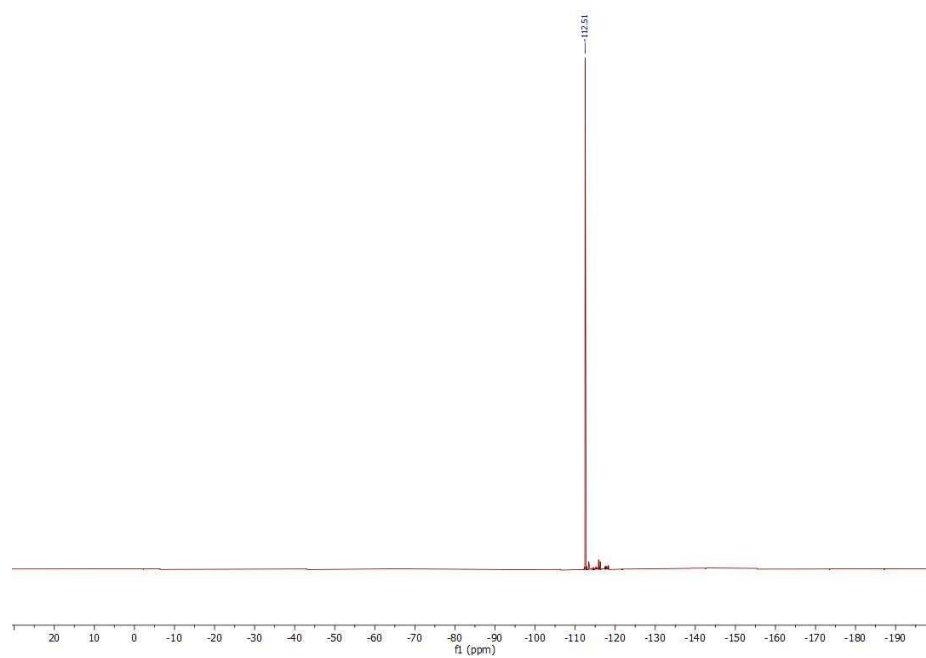
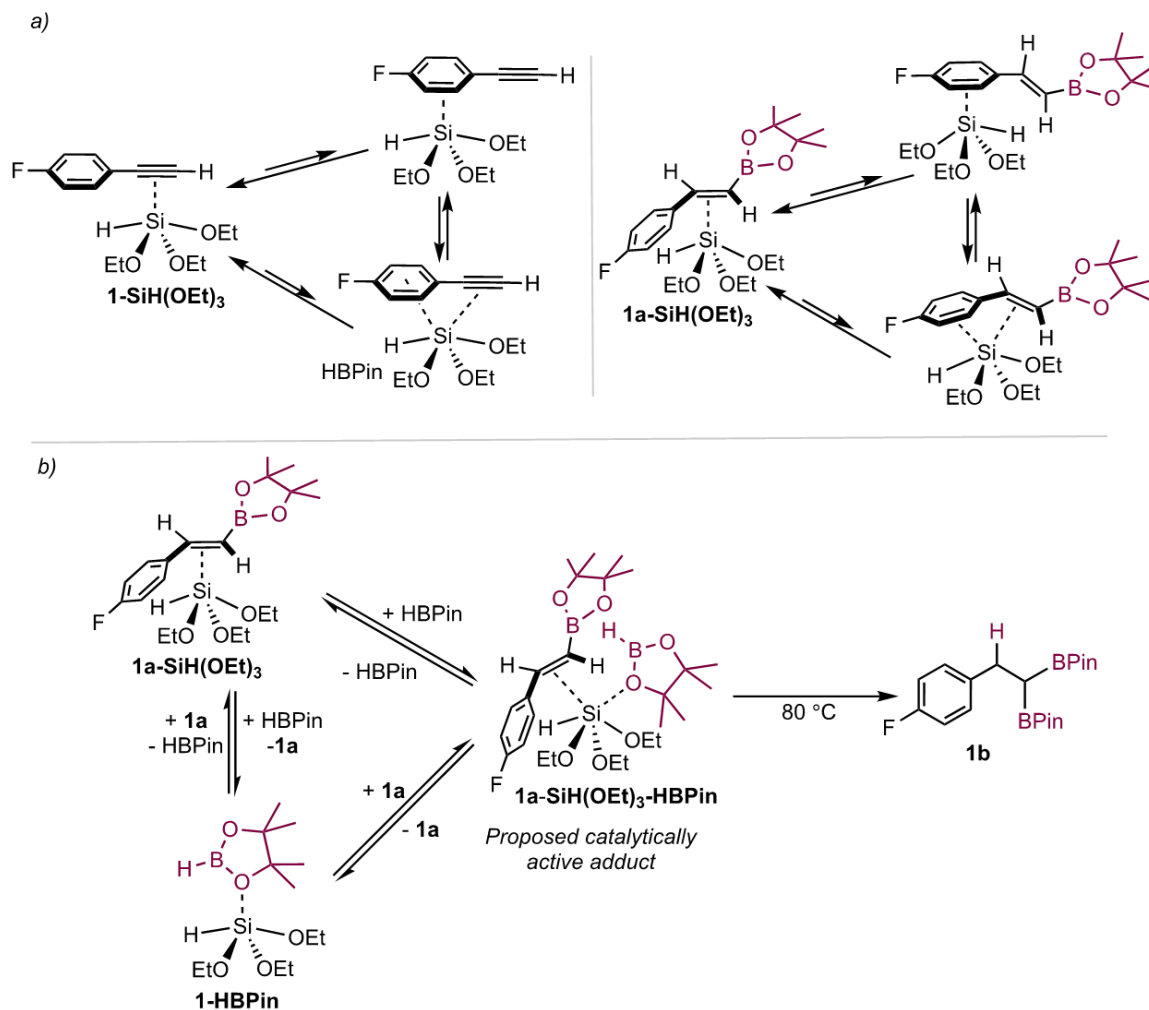


Figure 2.21. ^{19}F NMR (500 MHz, CDCl_3 , 23 °C) for **1a-d β** .

2.5.7. Proposed adducts present in the reaction medium: a) plausible adducts in equilibria with **1**-HSi(OEt)₃ and **1a**-HSi(OEt)₃ and b) plausible adducts engaging HBPin and leading to efficient catalysis



Similar adducts engaged in analogous equilibria are expected to be present in the reaction medium involving **1** instead of **1a** leading to the formation of **1a**.

Note that adducts involving dioxane may be present in the reaction medium and in equilibria with the **1a**-SiH(OEt)₃, **1**-HBPin and **1a**-SiH(OEt)₃-HBPin adducts but would not be catalytically active as they would not lead to the formation of products **1a** or **1b**.

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3. Triethoxysilane-Catalyzed Hydroboration of Alkenes, Nitriles, Ketones and Esters: From Non-Covalent Interactions to a Hydrosilylation/Si-B Exchange Pathway

<https://chemrxiv.org/doi/full/10.26434/chemrxiv.15000710/v1>

Harleen Kaur, Diksha Sharma, Rebeca Arevalo*

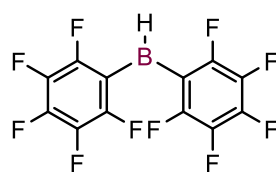
3.1. Introduction

The hydroboration of C–C and C–X (X = O, N) multiple bonds in organic molecules is among the most convenient methods for accessing synthetically useful boronate esters. In efforts to develop more sustainable approaches, catalysts based on main group elements¹ and organocatalysts² have attracted increasing attention. In general, such catalysts tend to display high efficiency toward a specific class of functional groups, and catalysts capable of catalyzing the hydroboration of different substrates classes are scarce. Boron compounds are well-established catalysts for the hydroboration of alkenes, nitriles, ketones, and esters,³ with fluorinated Lewis acidic boranes such as BH₂(C₆F₅)-SMe₂^{3a} or Piers' borane^{3c} (**Scheme 3.1a**, left) being well-known to catalyze these transformations, along with borenium and boronium catalysts.⁴ However, the catalytic efficiency of non-Lewis acidic neutral boranes is less documented, with 9-BBN (**Scheme 3.1a**, right) being the only alkyl borane found efficient for the sequential hydroboration of terminal alkynes with pinacolborane (HBPin).⁵ Whereas the strong acidity at boron activates the C–C or C–X multiple bonds toward the addition of HBPin in Lewis acidic boranes, Thomas and coworkers reported that 9-BBN operates through a distinct mechanism involving an initial addition of the H–B bond of the catalyst across the multiple bond, followed by a B–B exchange step with HBPin. More recently, this catalyst has been also demonstrated efficient for the sequential hydroboration of nitriles.⁶

Although reactive silicon compounds, such as silylenes and silylium cations are known to catalyze hydroboration reactions,⁷ catalysis by neutral silicon compounds remains rare. Neutral silicon catalysis has recently emerged as a highly active area of research, attracting growing interest due to its unique reactivity and has seen significant expansion in recent years. Reported examples are typically restricted to Lewis superacidic silicon compounds⁸ for the hydrofunctionalization of substrates bearing heteroatoms, where adduct formation enables efficient activation of the multiple bonds (**Scheme 3.1b**, top). Seminal work by Tilley and Bergman demonstrated that a strongly Lewis-superacidic silicon compound can catalyze the hydrosilylation of aldehydes through coordination of the carbonyl oxygen to silicon, resulting in significant activation of the C=O bond toward silane addition.⁹ This report paved the way for the discovery of other Lewis superacidic Si compounds efficient as catalysts for hydrofunctionalization reactions, such as those reported by Greb and coworkers for the hydroboration of pyridines¹⁰ and by Inoue and coworkers for the reduction of P=O bonds employing H₃SiPh.¹¹

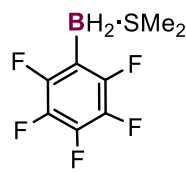
(a) *B-catalyzed hydroboration*

Strong Lewis acids (well-known)



Stephan, 2016

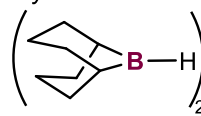
Hydroboration of alkynes



Vasko and Repo, 2025

Hydroboration of alkenes

Weaker Lewis acidic
alkylboranes: Rare



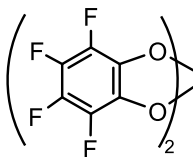
Thomas, 2020

Gunanathan, 2022

Hydroboration of
alkynes and nitriles

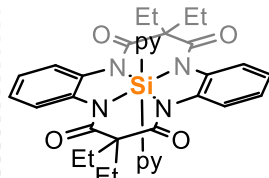
(b) *Si-catalyzed hydrofunctionalization*

Lewis superacids (well-known)



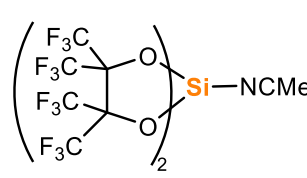
Tilley and
Bergman, 2015

Hydrosilylation
of aldehydes



Greb, 2024

Hydroboration of
pyridines

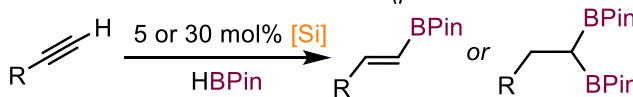


Inoue, 2026

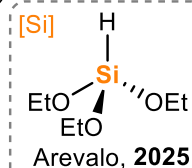
Reduction of P=O bonds
with H₃SiPh

- Operate through Lewis acid-base adducts
- Require a heteroatom in the substrate

Non-Lewis acidic siloxanes: Rare (previous work in our lab)

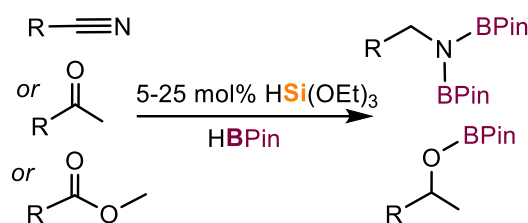


- Single and sequential hydroboration of terminal alkynes
 - Operates through non-covalent interactions
 - Does not require a heteroatom in the substrate

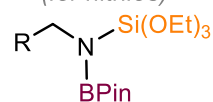


Arevalo, 2025

(c) *This work: HSi(OEt)₃ and HBPIn synergy in the HSi(OEt)₃-catalyzed hydroboration of heteroatom containing substrates (unknown)*



Catalytic intermediates
(for nitriles)



Hydrosilylation + Si-B bond
exchange mechanism

- Non-Lewis acidic commercially available HSi(OEt)₃ as the catalyst
 - Efficient for nitriles, ketones and esters
- Si-H bond addition across C-N and C-O bonds facilitates hydroboration

Scheme 3.1. a) Borane catalysts for the hydroboration of alkenes and alkynes, b) Lewis superacidic Si catalysts for the hydrofunctionalization of multiple bonds containing heteroatoms (top) and non-Lewis acidic HSi(OEt)₃ as catalyst for the single and sequential hydroboration of alkynes (previous work in our lab, bottom) and c) this work: HSi(OEt)₃-catalyzed hydroboration of nitriles, ketones and esters through a mechanism involving hydrosilylation and Si-B bond exchange steps.

The ability of the non-Lewis acidic $\text{HSi}(\text{OEt})_3$ to catalyze this type of transformations was unknown until we disclosed that $\text{HSi}(\text{OEt})_3$ was efficient for the single and sequential hydroboration of terminal alkynes with HBPIn affording *E*-alkenylboronate and alkyldiboronate esters as exclusive products in good to excellent yields.¹² Non-covalent interactions between multiple $\text{C}\equiv\text{C}$ and $\text{C}=\text{C}$ bonds and the Si in $\text{HSi}(\text{OEt})_3$ were proposed to be key to trigger HBPIn addition across the multiple bonds (**Scheme 3.1b**, bottom). We hypothesized that $\text{HSi}(\text{OEt})_3$ could similarly engage in interactions with a broader range of substrates, leading to the activation of their multiple bonds toward the addition of HBPIn, and thereby paving the way for the discovery of a general catalyst for the hydroboration of multiple bonds across diverse substrate classes. Given the novelty of $\text{HSi}(\text{OEt})_3$ as a catalyst, its substrate preferences and the influence of substrate identity on the underlying reaction mechanism remain unexplored. Gaining this knowledge is essential to obtain fundamental insights into the factors governing the catalytic behavior of $\text{HSi}(\text{OEt})_3$ and to develop sustainable hydroboration methodologies that enable straightforward access to boronate esters using readily available commercial compounds. Moreover, such insights are expected to inform the rational design of neutral silicon catalysts for other small-molecule functionalization processes, a field that remains in its infancy.

In this work, we demonstrate that the catalytic activity of $\text{HSi}(\text{OEt})_3$ extends beyond the hydroboration of terminal alkynes, enabling the efficient hydroboration of alkenes, nitriles, ketones, and esters to afford the corresponding products with high selectivity and excellent yields under sustainable conditions (**Scheme 3.1c**). The efficiency of $\text{HSi}(\text{OEt})_3$ was strongly dependent on substrate identity, with steric and electronic effects exerting distinct influences depending on the substrate class. Our mechanistic studies indicate that the presence of heteroatoms in the substrate leads to pronounced differences in catalytic efficiency relative to alkyne hydroboration. It also significantly influences the effects of substitution on substrates and Lewis acidity at Si on the catalyst performance. For nitriles, these differences can be attributed to weaker non-covalent interactions between the substrate and $\text{HSi}(\text{OEt})_3$ compared to those with alkynes, resulting in a mechanism that involves the addition of the Si-H bond across the multiple CN bond followed by a Si-B exchange step.

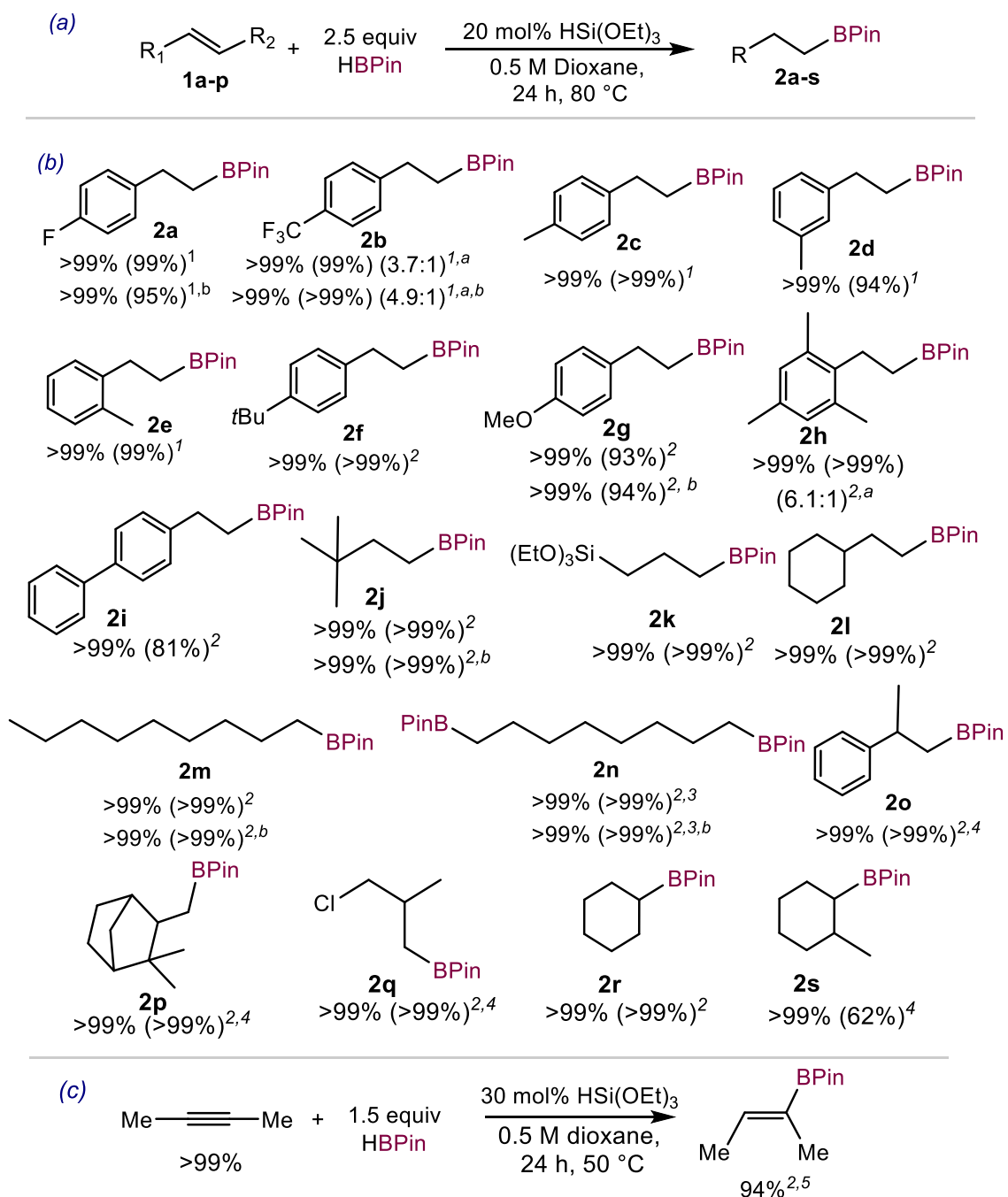
3.2. Results and Discussion

3.2.1. $\text{HSi}(\text{OEt})_3$ -catalyzed hydroboration of alkenes

In our previous work we disclosed that $\text{HSi}(\text{OEt})_3$ was efficient for the hydroboration of 4-fluorostyrene (**1a**) and at 20 mol% $\text{HSi}(\text{OEt})_3$ and 2.5 equiv of HBPIn in a 0.5 M solution of dioxane at 80 °C for 24 h affording the corresponding alkylboronate ester (**2a**) in >99% yield (**Schemes 3.2a and b**).¹² Control experiments confirmed the need of $\text{HSi}(\text{OEt})_3$ to access excellent yields of the alkylboronate esters,¹² with BH_3 -trapping experiments allowing to rule out borane hidden catalysis as responsible for the formation of **2a** during the initial 10 h of reaction (60% yield of **2a**). However, after 10 h of reaction, BH_3 was detected in the reaction medium, suggesting that BH_3 catalysis could be contributing to

some extent to the formation of product **2a** at high substrate conversion. Our initial efforts focused on determining whether the efficiency of $\text{HSi}(\text{OEt})_3$ translated to alkenes other than **1a** and on how the substrate identity impacted the efficiency of the system. To that end, we explored the efficiency of the system for the hydroboration of 17 terminal alkenes under the optimized conditions depicted in **Scheme 3.2a**. The results depicted in **Scheme 3.2b** suggest that the system was highly efficient and regioselective for the single hydroboration of terminal aliphatic and aromatic alkenes affording the corresponding linear alkylboronate esters in excellent yields and as the exclusive products in virtually all cases. For aromatic terminal alkenes (**1a-i**) the system was tolerant of electron-donating and withdrawing substituents in the aryl ring with the identity of the substituent playing a minor role in catalyst efficiency. Whereas the presence of a F, CF_3 , CH_3 , *t*Bu or a OMe group at the *para* position of the aryl ring afforded the products in 93% (for **2g**) to >99% yield (for **2a-c** and **2f**), the presence of a Ph group slightly decreased the yield to 81% (**2i**). This trend contrasts with that observed in the single hydroboration of alkynes, where the presence of electron-withdrawing substituents at any position of the aryl ring led to lower product yields.¹² For methyl substituted aromatic alkene, the position of the methyl group (*p* in **1c**, *m* in **1d** and *o* in **1e**) did not significantly impact the efficiency of the system, all the products being formed in excellent yields (94 to >99%). This trend also contrasts with the efficiency of the system for methyl substituted aromatic alkynes, where the yields of the *E*-alkenylboronate ester products were lower the closer the methyl substituent was to the $\text{C}\equiv\text{C}$ bond (92% yield starting from *p*-methylphenylacetylene, 86% yield starting from *m*-methylphenylacetylene and 60% yield starting from *o*-methylphenylacetylene). These results suggest that, for the hydroboration of alkenes, the electronic and steric profile of the substrate is less critical than for that of alkynes. Instead, the trigonal planar geometry at the C atoms in the $\text{C}=\text{C}$ bond arising from the sp^2 hybridization, as well as the non-cylindrical π -electron cloud, could be playing the largest role in catalyst efficiency, rendering the electronic and steric factors largely negligible. In line with this interpretation, a higher catalyst loading is required for alkene hydroboration (20 mol%) compared to the single hydroboration of alkynes (5 mol%), indicating that alkenes, regardless of the identity of the substituents, are more challenging substrates for $\text{HSi}(\text{OEt})_3$. Whereas products **2a**, **2c-g** and **2i** were obtained exclusively as the linear regioisomer, the presence of a CF_3 group in **1b** impacted the stereoselectivity of the system affording product **2b** as a mixture of the linear:branched isomers in a 3.7:1 ratio. An analogous result was observed when three methyl groups were present at the 2, 4 and 6 positions of the aryl ring (**1h**), product **2h** being formed as a linear:branched isomer mixture in a 6.1:1 ratio. These results also stand in contrast with that for the single hydroboration of alkynes, where the presence of a CF_3 substituent at the *para* position of the aryl ring did not impact the regioselectivity of the system and the linear alkenylboronate ester was obtained as the exclusive product. The aliphatic alkenes **2j-n** underwent hydroboration affording the corresponding products in >99% in all cases. This comparable efficiency of $\text{HSi}(\text{OEt})_3$ toward aliphatic and aromatic alkenes also contrasts with that reported for alkynes,¹² where the nature of the substituent (aromatic vs aliphatic) significantly impacted the efficiency of the system, with aliphatic alkynes being more challenging substrates than their aromatic counterparts. This observation further supports the notion that, in the case of alkenes, the role of electronic

effects is less relevant than in alkynes as a result of the trigonal planar geometry the C=C bond compared to the linear of the C≡C bond.



Scheme 3.2. a) Optimized conditions for the HSi(OEt)₃-catalyzed hydroboration of terminal alkenes with HBPin; b) Substrate scope for HSi(OEt)₃ catalyzed hydroboration of alkenes. c) Hydroboration of but-2-yne under unoptimized conditions. ¹Conversions and yields (shown in parentheses) are crude calculated by ¹⁹F NMR using fluorobenzene as

internal standard. ²Conversion and yields (shown in parentheses) are crude calculated by ¹H NMR using mesitylene as internal standard. ³5 equiv of HBPIn, 40 mol% of HSi(OEt)₃, ⁴Reaction time = 48 h; Conversion is crude and yield (shown in parentheses) is isolated, calculated by ¹H NMR using mesitylene as internal standard, ^aratio of linear to branched product, ^b2-MeTHF was used as the solvent. ⁵The *Z*-isomer was formed in 5% yield.

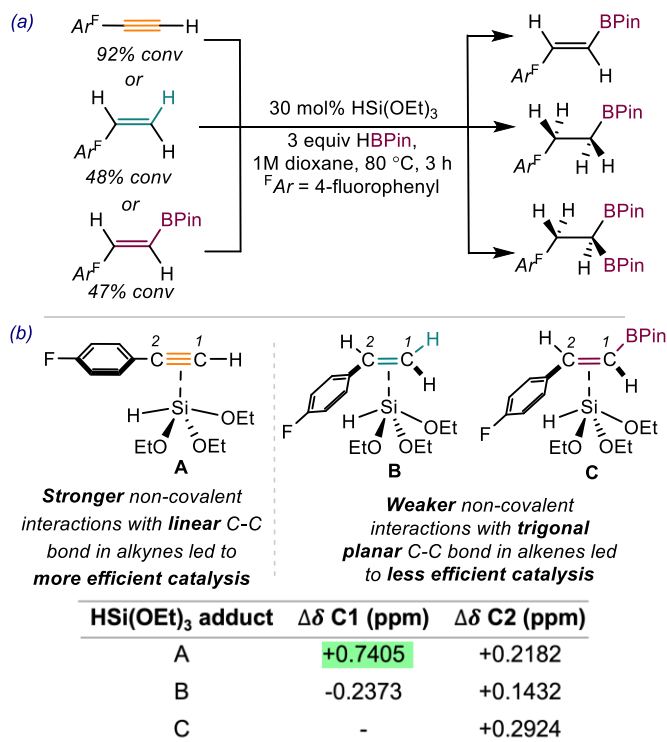
Additionally, as previously observed for terminal alkynes, the system tolerated a Si(OEt)₃ substituent (product **2k**) and could catalyze the double hydroboration of the diene **1n** employing a 40 mol% of catalyst loading, which rendered access to an alkyldiboronate ester with a BPin group at each of the terminal carbon atoms (**2n**). Interestingly, products from hydroboration of the more sterically hindered 1,1-disubstituted terminal alkenes **2o-q** and the disubstituted internal alkene **2r** were also formed in >99% yield as the exclusive products, although the 1,1-disubstituted alkenes required 48 h of reaction time. An analogous result was observed for the trisubstituted internal alkene **1s** which afforded the alkylboronate ester **2s** in a lower yield (62%) than the disubstituted internal alkenes, consistent with the increased steric hindrance at the C=C bond for this substrate.

Encouraged by the efficiency of the system for internal alkenes, we aimed to determine if such efficiency translated to internal alkynes. Remarkably, when dimethylacetylene was employed as the substrate, the reaction proceeded to >99% conversion of the starting material affording the product in 99% yield with the *E* isomer as the major (94% yield) and the *Z* isomer only formed in 5% yield (**Scheme 3.2c**). The fact that the system has an excellent regioselectivity toward the *E* isomer, suggests that the addition of HBPIn occurred in a *cis* fashion, aligning well with the *cis* addition reported for the single hydroboration of terminal alkynes¹² which resulted in the formation of the *E*-alkenylboronate esters as the exclusive products, supporting that the position of the C≡C bond (terminal vs internal) does not impact the stereoselectivity of the system. Unfortunately, although the hydroboration of prop-1-yn-1-ylbenzene proceeded to full conversion, the system was found to be non-selective, since a mixture of the four possible regio- and stereoisomers in equimolar amounts was obtained. On the other hand, attempts to hydroborate diphenylacetylene and 4-octyne led to mixtures of unidentified products. These results suggest that the system is highly sensitive toward the nature of the substituents at the C≡C bond in internal alkynes, with only non-sterically hindered CH₃-substituted alkynes resulting in efficient catalysis and the presence of a phenyl group resulting in a loss of the regio- and stereoselectivity of the system.

Aiming to develop a more sustainable system for the hydroboration of alkenes, our efforts focused on discovering if the reaction could be conducted under greener conditions than those described in our original report. To that end, we assess the efficiency of HSi(OEt)₃ for the hydroboration of **1a** employing the greener solvent 2-MeTHF and under neat conditions under the same conditions as when the reaction was conducted in dioxane (**Scheme 3.2b**). Remarkably, the reaction proceeded to >99% conversion of **1a** in both cases and product **2a** was obtained in 95% (2-MeTHF) and 96% (neat) yields, supporting the efficiency of HSi(OEt)₃ for the hydroboration of this substrate under more sustainable conditions than those reported in our original manuscript.¹² Aiming to identify whether the

efficiency of $\text{HSi}(\text{OEt})_3$ in 2-MeTHF translated to substrates other than **1a**, a substrate scope including the terminal alkenes **2a**, **2b**, **2g**, **2j**, **2m** and **2n** was conducted (**Scheme 3.2b**). In all cases the yields obtained for the corresponding alkenylboronate esters were comparable to those when the reaction was conducted in dioxane. Interestingly, the use of 2-MeTHF as a solvent resulted in a higher linear to branched product ratio (4.9:1) for product **2b** than when THF was employed (3.7:1), suggesting that the identity of the solvent played a role in the regioselectivity of the system for this substrate, which could be attributed to the lower coordinating ability of 2-MeTHF compared to THF which can impact the identity and, therefore, the kinetic barriers and energies of the intermediates involved in the cycles for substrates where the barriers for the formation of each regioisomer are relatively close.

In our previous work our mechanistic studies supported that the hydroboration of an *E*-alkenylboronate ester proceeded through a mechanism involving non-covalent interactions, where the interaction of the double C=C bond with the Si atom of $\text{HSi}(\text{OEt})_3$ activated the alkene toward the addition of HBPIn.¹² Therefore, we propose that the hydroboration of terminal and internal alkenes proceeds through an analogous mechanism. However, $\text{HSi}(\text{OEt})_3$ was found less efficient for the hydroboration of alkenes than for that of alkynes, as evidenced by the fact that the conversion of 4-fluorophenylacetylene was 92% after 2 h of reaction in dioxane at 80 °C (80% yield of the *E*-alkenylboronate ester), whereas that of the analogous terminal alkene, **1a**, was only 48% (48% yield of **2a**) under the same conditions (see **Scheme 3.3a**). This difference in efficiency between alkenes and alkynes can be traced back to the strength of the non-covalent interactions established between each of the substrates and $\text{HSi}(\text{OEt})_3$. When the equimolar amount of $\text{HSi}(\text{OEt})_3$ was added to a CD_2Cl_2 solution of **1a** and the ^1H and ^{13}C NMR spectra were registered, the ^{13}C NMR signals attributed to the C atoms engaged in the C=C bond underwent smaller shifts ($\Delta\delta$ (ppm) = -0.2373 and +0.1432 for C1 and C2 respectively, see adduct **B** in Scheme 3.3b) than those observed for the C(sp) atoms in the C≡C bond of 4-fluorophenylacetylene ($\Delta\delta$ (ppm) = +0.7405 and +0.2182 for C1 and C2 respectively, see adduct **A** in Scheme 3.3b) in the presence of the equimolar amount of $\text{HSi}(\text{OEt})_3$. These results support that **1a** engages in weaker non-covalent interactions with $\text{HSi}(\text{OEt})_3$ than 4-fluorophenylacetylene, resulting in a lower degree of activation of the C=C bond toward the addition of HBPIn. These weaker interactions could be a result of the non-cylindrical distribution of the π -electron cloud in the alkene C=C bond as well as the trigonal planar geometry at the C(sp²) atoms, which would result in an increased steric hindrance between the alkene and the $\text{HSi}(\text{OEt})_3$. The presence of a BPin substituent at the alkene in the *E*-4-fluorophenylalkenyl boronate ester resulted in only a slight increase in the strength of the interactions between this substrate and $\text{HSi}(\text{OEt})_3$ ($\Delta\delta$ (ppm) = +0.2924 for C2, see adduct **C** in **Scheme 3.3b**), consistent with the comparable catalyst efficiency for alkenylboronate esters and alkenes, and further suggesting that the geometry around the C atoms and the distribution of the π -electron cloud in the C-C multiple bond are the main factors determining the strength of the interactions between the substrate and $\text{HSi}(\text{OEt})_3$.

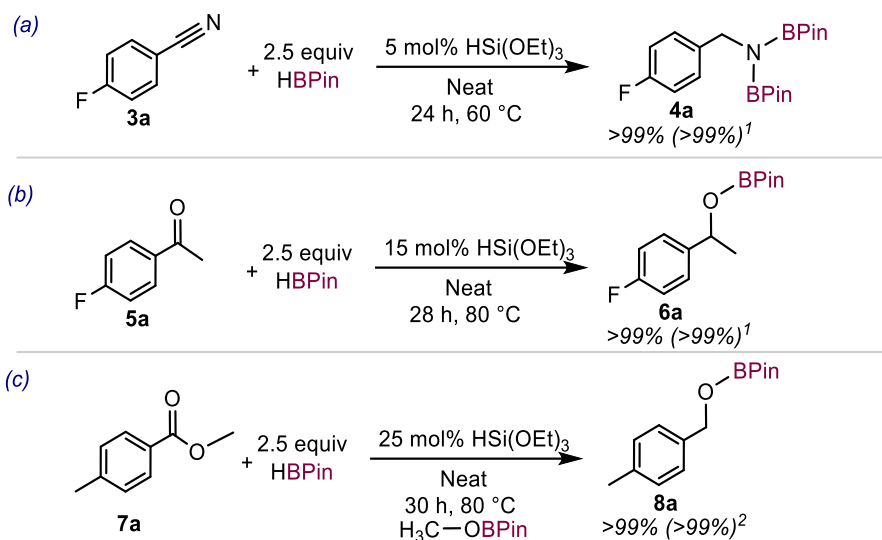


Scheme 3.3. a) Conversion of 4-fluorophenylacetylene (top), 4-fluorophenylethylene (middle) and *E*-4-fluorophenylethynyl boronate ester (bottom) in the $\text{HSi}(\text{OEt})_3$ catalyzed hydroboration with HBPi ; b) $\Delta\delta$ (ppm) of the C1 and C2 of 4-fluorophenylacetylene, 4-fluorophenylethylene and *E*-4-fluorophenylethynyl boronate ester in a 1:1 mixture with $\text{HSi}(\text{OEt})_3$ in CD_2Cl_2 . $\Delta\delta$ were calculated with respect to the chemical shifts of the corresponding starting materials in a CD_2Cl_2 solution with the same concentration.

3.2.2. $\text{HSi}(\text{OEt})_3$ -catalyzed hydroboration of nitriles, ketones and esters

Encouraged by the efficiency of $\text{HSi}(\text{OEt})_3$ as a catalyst for hydroboration of alkynes and alkenes, we next sought to determine the impact that the presence of a heteroatom in the multiple bonds has on catalyst efficiency. To this end, we assessed the efficiency of the system for the hydroboration of multiple bonds other than C-C, mainly $\text{C}\equiv\text{N}$ in nitriles. Gratifyingly, $\text{HSi}(\text{OEt})_3$ was found to efficiently catalyze the sequential hydroboration of the $\text{C}\equiv\text{N}$ bond in 4-fluorobenzonitrile (**3a**) under milder conditions than those employed for the hydroboration of alkenes and alkynes (5 mol%, 2.5 equiv HBPi , 60°C, 24 h, 1 M dioxane) affording the corresponding diborylamine **4a** in >99% yield (**Scheme 3.4a**). Remarkably, the system afforded product **4a** in the same yield when the reaction was conducted under more sustainable conditions, either employing 2-MeTHF as the solvent or under neat conditions. Interestingly, the catalyst was also efficient in the poorly coordinating solvent dichloromethane affording product **4a** in a >99% yield. This result stands in contrast with that obtained in the hydroboration of alkynes,¹² which required a coordinating solvent (THF or dioxane) to afford the products in excellent yields and suggests that the coordinating ability of the nitrile through the N atom can be playing an analogous role to coordinating solvents in the hydroboration of alkynes. Control

experiments conducted in the absence of $\text{HSi}(\text{OEt})_3$ supported the need of this reagent for product formation and borane-trapping experiments allowed to rule out BH_3 -hidden catalysis as responsible for product formation. When the hydroboration of **3a** was conducted employing HBCat (Cat = catecholate) rather than HBPIn, the starting material was recovered. This result stands in contrast to what was observed for the $\text{HSi}(\text{OEt})_3$ hydroboration of alkynes, where employing HBCat resulted in efficient catalysis and highlights that the identity of the borane is key for the efficient hydroboration of nitriles.

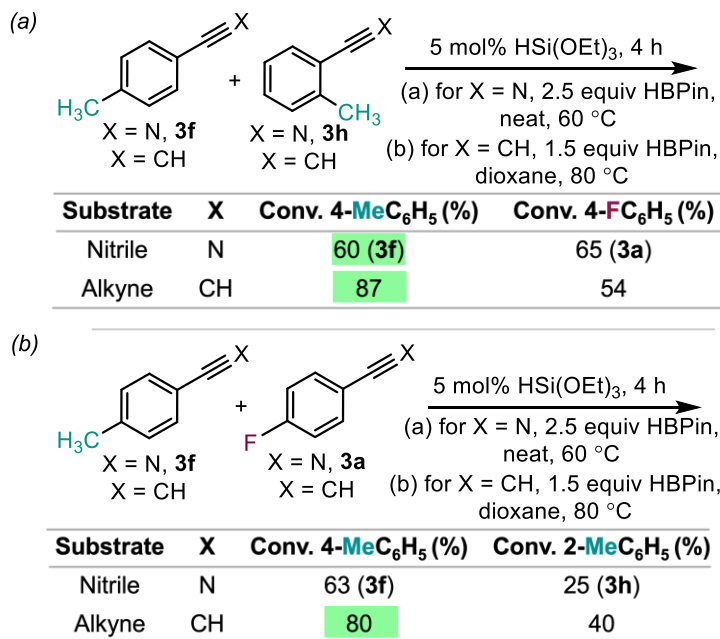


Scheme 3.4. (a) Double hydroboration of 4-fluorobenzonitrile (b) Hydroboration of 4-fluoroacetophenone (c) Hydroboration of methyl p-toluate, with HBPIn catalyzed by $\text{HSi}(\text{OEt})_3$ under optimized conditions.

Encouraged by the efficiency of the system for the hydroboration of nitriles, we set to explore its efficiency for the hydroboration of ketones and esters. When 4-fluoroacetophenone (**5a**) was employed as the substrate, the corresponding boronate ester **6a** was obtained in 95% yield, at harsher conditions than for the hydroboration of nitriles, mainly higher catalyst loading (15 mol%) and temperature (80 °C) and longer reaction time (28 h) (**Scheme 3.4b**). When the ester methyl p-toluate (**7a**) was employed as the starting material, product **8a** was obtained in >99% yield, however, the transformation required harsher conditions (**Scheme 3.4c**) than those employed for the hydroboration of nitriles and ketones. As observed for nitriles, for both ketones and esters the role of the solvent was negligible, and 2-MeTHF, 1,4-dioxane, toluene and CH_2Cl_2 afforded comparable yields of product **6a** and **8a**, respectively. Borane-trapping experiments supported the absence of BH_3 during the first 24 h of the reaction of **5a** (87% yield of **6a**), with BH_3 being detected upon completion of the reaction in trace amount, which could only contribute to a minor extent to the overall observed yield of **6a** (95%) during the final stages of the reaction. Additionally, BH_3 was only detected at the end of the reaction (after 30 h) and in trace amount, supporting that the formation of **8a** is due to $\text{HSi}(\text{OEt})_3$ catalysis.

3.2.3. Competition experiments

To understand the impact of the steric and electronic profile of the nitrile on the catalyst preference, competition experiments under non-optimized conditions (60 °C, 4 h, 5 mol% HSi(OEt)₃, 2.5 equiv HBPIn) were conducted (**Scheme 3.5**). When the hydroboration of an equimolar mixture of **3f** and **3h**, containing methyl groups in the *para* and *ortho* positions of the aryl ring respectively, was conducted, the conversion of **3f** was 63%, significantly higher than that of **3h** (25%), hinting a decreased catalytic efficiency of

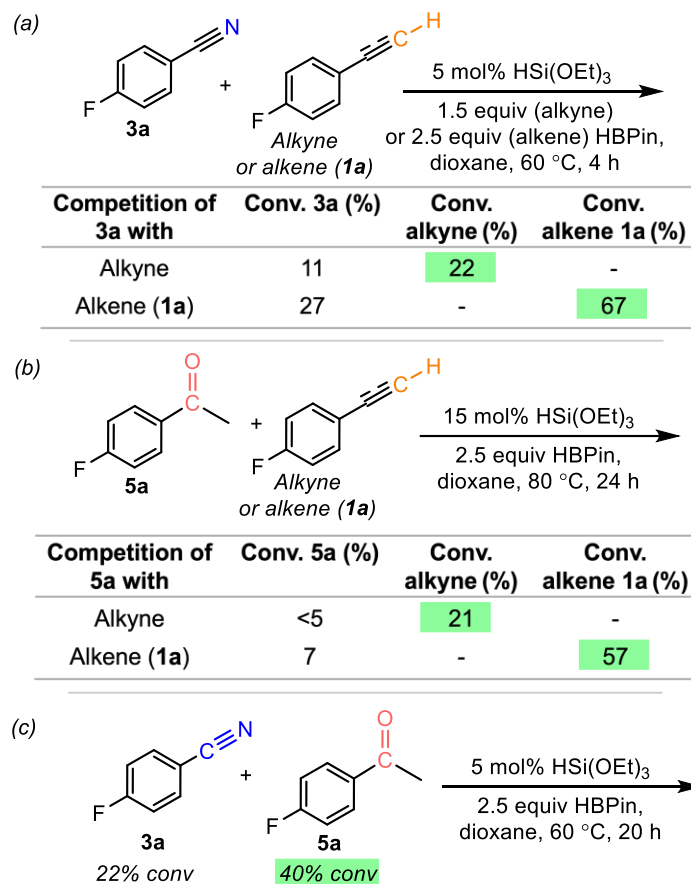


Scheme 3.5. Competition experiments allowing to rationalize a) impact of the steric profile of the substrate in catalyst efficiency for nitriles and alkynes; b) impact of the electronic profile of the substrate in catalyst efficiency for nitriles and alkynes.

HSi(OEt)₃ as the steric hindrance at the C≡N bond increased (**Scheme 3.5a**). An analogous result was obtained when the competition experiment was conducted employing an equimolar mixture of 4-methylphenylacetylene (80% conversion) and 2-methylphenylacetylene (40% conversion) as the starting material at 80 °C, hinting that for both substrates alkynes and nitriles, an increased steric hindrance at the multiple bond results in decreased catalyst efficiency. In contrast, when the reaction was conducted employing an equimolar mixture of nitriles **3a** and **3f**, containing a fluorine or a methyl group at the *para* position of the phenyl ring respectively, the conversion for both substrates was virtually identical (65% and 60% for **3a** and **3f** respectively, **Scheme 3.5b**) suggesting that the decreased or increased electron-density at the phenyl ring does not impact catalyst efficiency. This result stands in contrast to the conversion obtained when the analogous competition experiment was conducted employing the analogous alkynes 4-fluoro- or 4-methyl-phenyl acetylene, for which conversions of 54% and 87% respectively were obtained (**Scheme 3.5b**). This result highlights a stark difference in the impact of the

electron- density at the phenyl ring on catalyst efficiency depending on substrate identity, the fact that the catalyst is sensitive to the electronic profile of alkynes could be attributed to an increased or decreased electron-density at the $C\equiv C$ bond that results in stronger or weaker non-covalent interactions with Si respectively.¹² However, the fact that the catalyst is not sensitive to the electronic profile of nitriles could be hinting that a mechanism different from that for the hydroboration of alkynes could be operative for nitriles or that the rate-determining step is different for nitriles and the electron density at the $C\equiv N$ bond does not impact the rate of this step (see below).

To determine whether possible differences in the reaction mechanisms for nitriles and alkynes play a role in the barriers of the cycles for each substrate that can be reflected in catalyst preference for one substrate over the other, a competition experiment between an alkyne and a nitrile was conducted. When the hydroboration reactions of equimolar mixtures of **3a** and 4-fluorophenylacetylene or **1a** were conducted at 60 °C for 4 h employing 5 mol% of $HSi(OEt)_3$, the conversions of the alkyne (22%) or the alkene (67%) were higher than those of **3a** (11% and 27% respectively) (**Scheme 3.6a**). Analogous results were observed when equimolar mixtures of 4-fluorophenylacetylene or **1a** and the ketone **5a** were employed as the starting materials, with the conversion for the alkyne (21%) and **1a** (57%) being higher than those for the ketone (<5% and 7% respectively) (**Scheme 3.6b**). These results suggest that the hydroboration of **3a** and **5a** feature higher barriers than those of 4-fluorophenylacetylene and **1a**, either due to higher barriers in an analogous mechanism involving non-covalent interactions or due to change in the reaction mechanism. To establish the catalyst preferences for heteroatom-containing substrates, an equimolar mixture of the nitrile **3a** and the ketone **5a** was used as the substrate, the conversion of the ketone was found to be higher (40%) than that of the nitrile (22%) (**Scheme 3.6c**), allowing to rationalize the catalyst preference for ketone hydroboration before nitrile hydroboration in substrate **5a**. Additionally, this result suggests that the geometry around the carbon (linear $C(sp)$ vs. trigonal planar $C(sp^2)$) as well as the symmetry of the π -electron cloud in the multiple bond do not play the same role than for alkenes and alkynes, where $HSi(OEt)_3$ showed a higher efficiency for the hydroboration of the linear $C(sp)$ $C-C$ bond of alkynes. These results establish the catalyst preference for the hydroboration of the different substrates as alkyne > alkene > ketone > nitrile and further points toward significant mechanistic differences for the $HSi(OEt)_3$ catalyzed hydroboration when heteroatoms are present in the substrates.



Scheme 3.6. Competition experiments to rationalize catalyst preference for a) nitrile vs. alkyne or alkene; b) ketone vs. alkyne or alkene; c) nitrile vs. ketone.

3.2.4. Insights into the reaction pathway operative for the hydroboration of nitriles

To determine whether the different results for the competition experiments in alkynes and nitriles arose from a significantly different mechanism for the hydroboration of these substrates, the hydroboration of **3a** with 2.5 equiv of HBPIn in the presence of 5 mol % of $\text{HSi}(\text{OEt})_3$ in CD_2Cl_2 at 60 °C for 16 h and 30 min was monitored by ^1H , ^{19}F , ^{11}B and ^{13}C NMR spectroscopy. The ^{19}F and ^1H NMR spectra showed signals attributable to **3a** (−103.5 ppm in the ^{19}F NMR spectrum) decreasing their intensity as the reaction proceeded and supporting its conversion into **4a** (−118 ppm in the ^{19}F NMR spectrum and 4.20 ppm for the new CH_2 group in the ^1H NMR spectrum) (see **Figure 3.1** for ^{19}F NMR spectra and **Figure 3.2. and 3.3.** in the appendix for ^1H and ^{13}C NMR spectra). Additionally, a signal at −107 ppm in the ^{19}F NMR spectrum was present during catalytic turnover until all the **3a** was converted into **4a**, which initially grew and started decreasing at higher substrate conversion, but was minor compared to the signals attributed to **3a** and **4a** throughout all

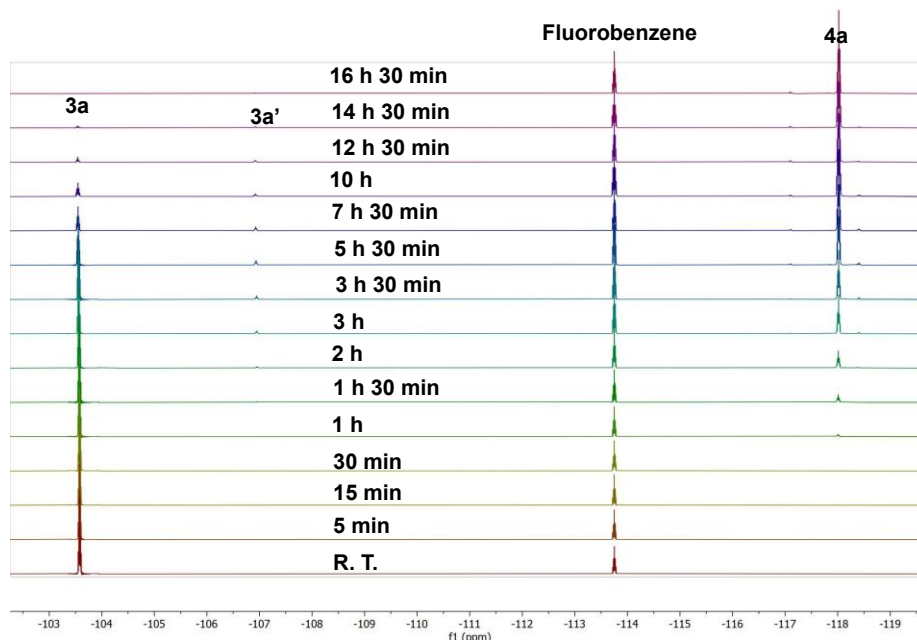
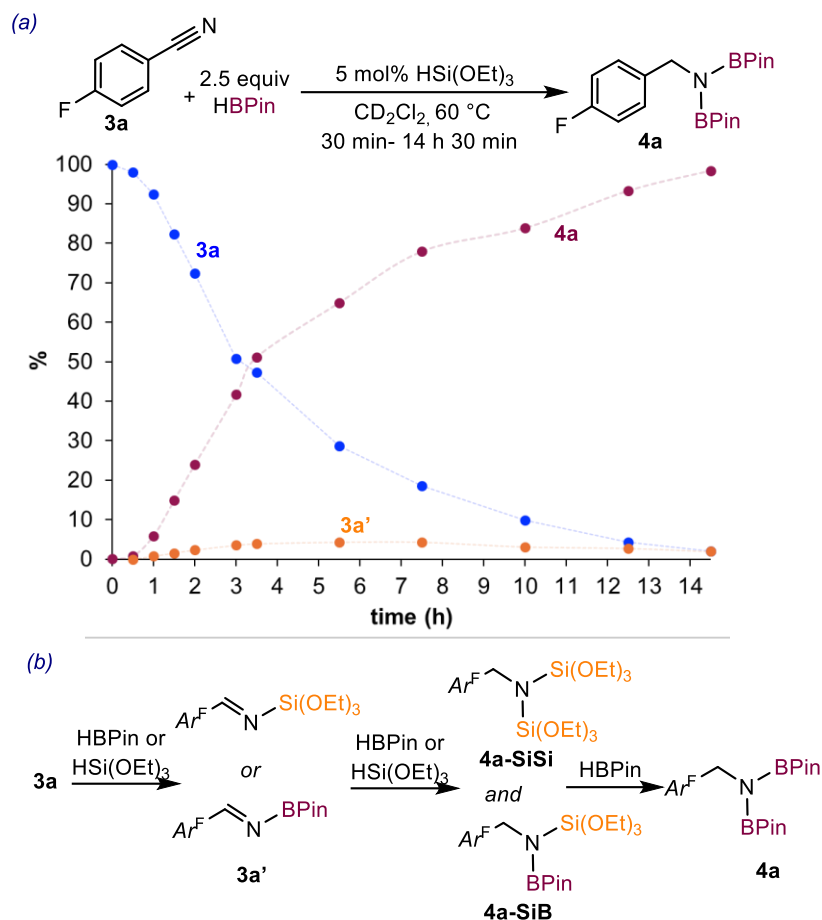


Figure 3.1. ^{19}F NMR spectra of the double hydroboration of 4-fluorobenzonitrile (**3a**) with HBPIn employing 5 mol% of $\text{HSi}(\text{OEt})_3$ in CD_2Cl_2 at 60 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 60°C for given times) **3a'** = Proposed intermediate formed from single hydroboration or hydrosilylation formed *in situ*.

catalytic turnovers. This change in intensity suggests an intermediate (**3a'**) was present in the reaction medium and was eventually consumed at high substrate conversion (see **Scheme 3.7a** for the reaction profile). This signal could be tentatively attributed to either the imine from single hydroboration or hydrosilylation of **3a** (**Scheme 3.7b**). However, a diagnostic signal for the $\text{CH}=\text{N}$ in the ^1H NMR spectrum at 9.30 ppm (for the silylated imine) or at 10.21 ppm (for the borylated imine) was not present in the ^1H NMR spectra of the catalytic monitoring, presumably the low concentration of this species prevented its observation in the ^1H NMR spectrum. The fact that the imine **3a'** was present in trace amount throughout the overall catalytic reaction, suggests that the transformation of **3a'** into **4a** is faster than that of **3a** into **3a'**, and, therefore, that the first hydroboration cycle to access the imine is slower than the second which affords the amine. The relative rates for the hydroboration cycles for nitriles stand in contrast to those observed in the sequential hydroboration of alkynes, where the first cycle involving the hydroboration of the alkyne was faster than the second involving the hydroboration of the alkenylboronate ester, which was attributed to the trigonal planar geometry at the C in the $\text{C}=\text{C}$ bond of the alkenylboronate ester that resulted in weaker non-covalent interactions with $\text{HSi}(\text{OEt})_3$ than those of the alkyne (see above). In contrast, the trigonal planar geometry at the $\text{C}=\text{N}$ group of imine **3a'** does not seem to be the main factor determining the rate of the second cycle in the hydroboration of **3a**.



Scheme 3.7. Sequential hydroboration of 3a; a) Reaction profile employing HSi(OEt)₃ as catalyst; b) proposed intermediates for the hydroboration detected by ¹⁹F and ¹³C NMR spectroscopy.

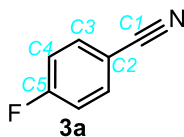
In stark contrast to what was observed in the sequential hydroboration of alkynes,¹² the signals attributed to HSi(OEt)₃ in the ¹H and ¹³C NMR spectra were shifted due to non-covalent interactions with the substrates only during the initial 30 min of the reaction, coinciding with an induction period where no product was formed. After these 30 min, the signals attributed to the Si-bonded H (at 4.23 ppm) and those to the CH₂O-Si groups (q, 3.82 ppm) in the ¹H NMR spectrum gradually decreased their intensity until they completely vanished after 3 h of reaction. Additionally, there was a concomitant appearance of a new quadruplet attributable to a CH₂ group in the OEt substituents (at 3.87 ppm, q) in the ¹H NMR spectrum and two new signals in the ¹³C NMR spectrum that could be attributed to CH₃CH₂O groups (at 60.7 (CH₂) and 17.6 (CH₃) ppm), which grew in intensity at the expense of the signals of HSi(OEt)₃. All these observations are consistent with the consumption of HSi(OEt)₃ within the initial 3 h of the reaction to afford a catalytically active species which does not contain a Si-H bond. Further efforts are ongoing in our laboratory to fully identify and characterize this species.

Additionally, the ^{13}C NMR spectra of the catalytic reaction showed the presence of minor signals close to those of product **4a**, along with minor signals attributable to OEt groups (59.0 ppm for the OCH_2 and 18.6 for the CH_3) close to those of $\text{HSi}(\text{OEt})_3$. These signals can be tentatively attributed to an amine containing two $\text{Si}(\text{OEt})_3$ groups (**4a-SiSi**) or one $\text{Si}(\text{OEt})_3$ and one BPin (**4a-SiB**, see **Scheme 3.7b**). Moreover, these signals disappeared upon complete conversion of the starting material **3a**, suggesting that they transformed into product **4a** and supporting their identity as intermediates in the catalytic cycle. The presence of **4a-SiB** or **4a-SiSi** as intermediates during catalysis suggest that the addition of the Si-H bond in $\text{HSi}(\text{OEt})_3$ across the multiple C-N bonds of **3a** and of **3a'** takes place during catalysis. Further efforts are ongoing in our lab to fully characterize these species.

Taken altogether, these observations suggest that the sequential hydroboration of nitriles could proceed through a mechanism that involves the addition of the Si-H bond of $\text{HSi}(\text{OEt})_3$ across the $\text{C}\equiv\text{N}$ bond and compound **4a-SiB** as an intermediate, either through sequential steps of hydrosilylation and Si-B bond exchange or through a sequential hydrosilylation/hydroboration followed by a Si-B bond exchange step to render access to the diboryl amine **4a**, the Si-B bond exchange steps being driven by the formation of the N-B bonds, stronger than N-Si. A mechanism involving the addition of the H-B bond of 9-BBN followed by B-B exchange with HBPIn has been proposed for the sequential hydroboration of alkynes with HBPIn catalyzed by 9-BBN.⁵ However, this type of mechanism has not been reported involving siloxanes as catalysts and highlights the impact of substrate identity on $\text{HSi}(\text{OEt})_3$ -catalyzed sequential hydroboration. Whereas non-covalent interactions were operative for the sequential hydroboration of alkynes, a mechanism involving the bond cleavage of the Si-H bond could be operative for nitriles. In line with this hypothesis, employing $\text{Si}(\text{OEt})_4$ or $\text{ClSi}(\text{OEt})_3$, which were efficient for the single hydroboration of alkynes, as catalysts for the hydroboration of **3a**, resulted in full recovery of the starting material (for $\text{Si}(\text{OEt})_4$), or formation of the product in poor yield (12% for $\text{ClSi}(\text{OEt})_3$). This result is in agreement with the need of a Si-H bond for the formation of the catalytically active species as well as for the addition across the $\text{C}\equiv\text{N}$ bond, which is required for efficient hydroboration, and suggests a more energetically demanding pathway (inaccessible for $\text{Si}(\text{OEt})_4$) for a direct addition of HBPIn. This pathway involving the cleavage of the Si-H bond in $\text{HSi}(\text{OEt})_3$ for the hydroboration of **3a** seems to be more energetically demanding than the mechanism engaging non-covalent interactions for the hydroboration of alkynes, as suggested by the fact that $\text{HSi}(\text{OEt})_3$ preferentially hydroborates 4-fluorophenylacetylene rather than **3a** in the competition experiment described above (**Scheme 3.6a**).

When an equimolar mixture of **3a** and $\text{HSi}(\text{OEt})_3$ was heated to 60 °C for 24 hours, the starting materials were recovered, suggesting that the presence of HBPIn is key to promote the addition of the Si-H bond across the $\text{C}\equiv\text{N}$ bond of **3a**. When the equimolar amount of $\text{HSi}(\text{OEt})_3$ was added to a CD_2Cl_2 solution of **3a** and the ^1H , ^{13}C and ^{29}Si NMR spectra were registered at room temperature all the ^{13}C NMR signals attributed to **3a** showed immediate downfield shifts (see **table 3.1**), with the signal attributed to the C atom in the CN group undergoing a $\Delta\delta$ (*CI*) of +0.0013 ppm. This shift is significantly smaller than those observed for the C atoms in the $\text{C}\equiv\text{C}$ bond of 4-fluorophenylacetylene in adduct **A**

Table 3.1. $\Delta\delta$ maximum for the ^{13}C NMR signals attributed to the carbon atoms of **3a** upon addition of 1 equiv of $\text{HSi}(\text{OEt})_3$.



Entry	Cx in 3a	$\Delta\delta(\text{Cx in } \mathbf{3a})$ (ppm)
1	C1	+0.0013
2	C2	+0.2291
3	C3	+0.1086
4	C4	+0.1342
5	C5	+0.1599

The $\Delta\delta$ were calculated as follows: ^{13}C NMR $\Delta\delta(\text{Cx in } \mathbf{3a}) = ^{13}\text{C}$ NMR $\delta(\text{Cx})_{(\mathbf{3a} + 1 \text{ equiv } \text{HSi}(\text{OEt})_3)} - ^{13}\text{C}$ NMR $\delta(\text{Cx in } \mathbf{3a})_{(\text{independent } 1)}$.

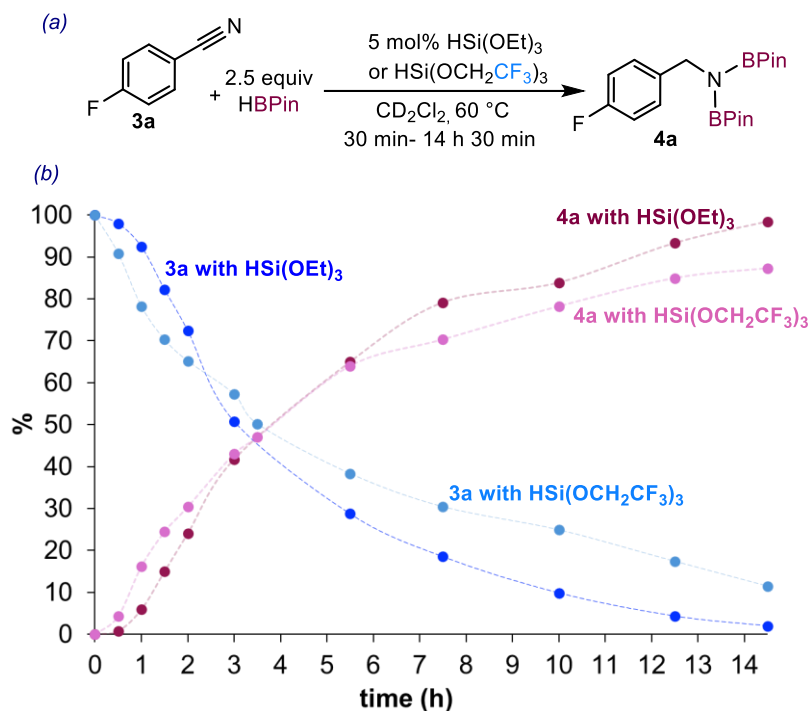
($\Delta\delta$ of +0.7405 and +0.2182 ppm, see **Scheme 3.3b**) and than those observed in the C=C atoms of adducts **B** and **C** ($\Delta\delta$ of -0.2373 and +0.1432 ppm for adduct **B** and +0.2924 ppm for adduct **C**, see **Scheme 3.3b**), hinting that the interactions of $\text{HSi}(\text{OEt})_3$ with **3a** are weaker than those with the alkyne, the alkene and the alkenylboronate ester, and further suggesting that non-covalent interactions between the nitrile and $\text{HSi}(\text{OEt})_3$ are not responsible for catalysis.

Analogous results were obtained when the hydroboration of ketone **5a** and ester **7b** with HBPIn were monitored by ^1H , ^{19}F , ^{11}B , and ^{13}C NMR spectroscopy, respectively (see **Figures 3.5 - 3.8** for ketone **5a** and **Figures 3.9 - 3.11** for ester **7b** in the appendix). Further efforts are ongoing in our laboratory to support the identity of the intermediates engaged in these hydroboration reactions.

3.2.5. Impact of Lewis acidity at Si on catalyst efficiency in the hydroboration of nitriles

Aiming to gain more insights in the factors that govern the catalyst efficiency in the hydroboration of nitriles, the fluorinated analog of $\text{HSi}(\text{OEt})_3$, $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$,¹² was employed as catalyst for the hydroboration of **3a** under the conditions depicted in **Scheme 3.8a**, which afforded **4a** in a slightly lower yield (70%) than when $\text{HSi}(\text{OEt})_3$ was employed as the catalyst (80%). In our previous work, we have reported that the acidity at Si center of $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ is slightly higher than that of $\text{HSi}(\text{OEt})_3$ ($\Delta\delta$ ^{31}P NMR (POEt_3)) for $\text{HSi}(\text{OEt})_3$ was -0.01 ppm vs. ($\Delta\delta$ ^{31}P NMR (POEt_3)) for $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was +0.07 ppm P). This subtle increase in Lewis acidity at Si resulted in a dramatic increased efficiency of $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ in the sequential hydroboration of alkynes as a result of a faster reaction, with the first hydroboration cycle proceeding 2.1 times faster and the second 2.3 times faster than when $\text{HSi}(\text{OEt})_3$ was employed as the catalyst.¹² This trend stands in stark

contrast with the slightly lower yield observed when $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was employed as catalyst and supports that the increase of Lewis acidity at Si did not result in an increased efficiency for the hydroboration of **3a**.



Scheme 3.8. Comparison of the reaction profiles of sequential hydroboration of **3a** with HBPIn employing $\text{HSi}(\text{OEt})_3$ or $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ as catalysts.

To dig into the origin of this observation, the hydroboration of **3a** catalyzed by 5 mol% of $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was monitored by ^1H , ^{19}F and ^{11}B , NMR spectroscopy in CD_2Cl_2 at 60°C and the reaction profiles were compared to those of the reaction catalyzed by $\text{HSi}(\text{OEt})_3$ (**Schemes 3.8a and b**). In contrast to what was observed for alkynes, the rates of **3a** consumption and of **4a** formation at initial stages of the reaction (up to 5 h 30 min, 65% yield of **4a**) were virtually the same when $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ or $\text{HSi}(\text{OEt})_3$ were employed as catalysts. However, the reaction profile suggests that $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ deactivates earlier than $\text{HSi}(\text{OEt})_3$, resulting in a slower reaction after 5 h and 30 min, this earlier deactivation being the origin of the observed slightly lower yield for **4a** when $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was employed as the catalyst rather than an initial slower rate. This significantly different trend in catalyst efficiency when the Lewis acidity at Si is increased between nitriles and alkynes further supports a significant change in the nature of the mechanism operative for these substrates. For alkynes, where a mechanism involving non-covalent interactions was operative, an increased Lewis acidity at Si led to stronger interactions between the siloxane and the alkyne which resulted in more efficient catalysis. The fact that the Lewis acidity at Si does not significantly impact the rate of hydroboration suggests that the strength of non-covalent interactions is not governing the rate of the reaction. A mechanism involving the addition of Si-H bond across the C-N bond followed by Si-B exchange steps, would align

well with the Lewis acidity at Si not significantly impacting the barriers of these fundamental steps, which will be governed by the strength of the Si-H, B-H, N-Si and N-B bonds breaking and forming.

Additionally, the ^{19}F NMR spectra (see **Figure 3.4** in the appendix) for the monitoring of the reaction employing $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ as precatalyst further supported the reaction of $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ during catalysis, showing an analogous disappearance of the signals attributed to the precatalyst in all the spectra. This can be further confirmed by the disappearance of the signal attributed to the CF_3 group in the ^{19}F NMR spectra (at -77.24 ppm) concomitant with the formation of a new major species at -76.88 ppm. This new species can be identified as the catalytically active species, along with another two minor species (at -77.41 and -77.11 ppm) tentatively identified as the trifluoromethyl analogs of **4a-SiSi** and **4a-SiB**, which intensity increased at early stages of the reaction and decreased at high substrate conversion, consistent with their transformation into **4a**. Additionally, the signal at -107 ppm was also present, which could be attributed to the trifluoromethylated analog of **3a'**. Interestingly, the induction period when $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was employed as the catalyst was also 30 minutes, and the full disappearance of the signals attributed to $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was observed after 1 h (from ^{19}F NMR spectra), whereas those of $\text{HSi}(\text{OEt})_3$ remained in the reaction medium for 3 h. These results support that the formation of the catalytically active species from $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ was faster than from $\text{HSi}(\text{OEt})_3$, allowing to rationalize the fact that product **4a** was formed in higher amounts in 30 min, than in the $\text{HSi}(\text{OEt})_3$ -catalyzed reaction.

3.3. Conclusions

In conclusion, we have demonstrated that $\text{HSi}(\text{OEt})_3$ is a general and sustainable catalyst for the hydroboration of alkenes, nitriles, ketones and esters. The catalyst showed a wide substrate scope including aromatic and aliphatic substrates affording the products from hydroboration in good to excellent yields. Unlike in the $\text{HSi}(\text{OEt})_3$ -catalyzed hydroboration of alkynes, which required the coordinating THF or 1,4-dioxane solvents, the system was efficient in the presence of coordinating or non-coordinating solvents as well as under neat conditions for heteroatom-containing substrates. The steric and electronic profile of the substrates impacted the catalytic efficiency differently than for alkynes, with the electronic profile not impacting the catalyst efficiency in the hydroboration of nitriles. Competition experiments allowed to establish the catalyst preference for the different class of substrates as alkyne > alkene > ketone > nitrile. The slight increase in the Lewis acidity at Si in $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ did not result in a significantly increased catalyst efficiency, unlike in the hydroboration of alkynes, where employing $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$ as catalyst increased the reaction rate two times compared to that with $\text{HSi}(\text{OEt})_3$. Mechanistic studies for the sequential hydroboration of 4-fluorobenzonitrile allowed to trace back the significant differences between the catalytic hydroboration of alkynes and nitriles to a different mechanism operative, where the addition of the Si-H bond in $\text{HSi}(\text{OEt})_3$ across the C-N bond in nitriles is a fundamental step. Additionally, a catalytically active species different from $\text{HSi}(\text{OEt})_3$ was found to be present in the reaction medium throughout catalysis in the hydroboration of nitriles, ketones and esters. Further

experiments are ongoing in our lab to fully identify and characterize the catalytically active species in this transformation.

3.4. Experimental section

3.4.1. General considerations

All air- and moisture-sensitive manipulations were carried out using vacuum line, Schlenk and cannula techniques or in an MBraun inert atmosphere (argon) glovebox unless otherwise noted. All glassware was stored in a pre-heated at 200 °C oven prior to use. All glassware was cleaned using base (KOH, iPrOH) and acid (HCl (aq)) baths. All reported reaction temperatures correspond to external silicone oil bath temperatures. Room temperature (rt) was 23 °C.

The solvents used for air- and moisture-sensitive manipulations were dried and deoxygenated using literature procedures.¹³ Mesitylene and fluorobenzene were dried over CaH₂, degassed by three freeze-pump-thaw cycles and distilled under vacuum prior to use. The terminal alkenes employed in the substrate scope (**1a-1s**) were purchased from commercial sources (Thermo Fisher Scientific, AmBeed and Sigma Aldrich), dried over CaH₂ or MgSO₄, and distilled prior to use. HSi(OCH₂CF₃)₃¹⁴ was synthesized according to literature procedure.

¹H NMR spectra were recorded on either Varian 400 or 500 spectrophotometers operating at 400 MHz, and 500 MHz, respectively. ¹³C NMR spectra were recorded on Varian 400 or 500 spectrophotometers operating at 101 MHz and 126 MHz, respectively. ¹¹B NMR spectra were recorded on Varian 400 or 500 spectrometers with 128 MHz and 160 MHz frequencies. All the ¹¹B spectra reported are ¹H decoupled (¹¹B{¹H}). ¹⁹F NMR spectra were recorded on Varian 400 or 500 spectrometers with 376 MHz and 470 MHz frequencies. ²⁹Si NMR spectra were recorded on Varian 500 with 99 MHz frequency. All ¹H and ¹³C NMR chemical shifts are reported in ppm relative to SiMe₄ using the ¹H (chloroform-*d*: 7.26 ppm; benzene-*d*₆: 7.16 ppm) and ¹³C (chloroform-*d*: 77.16 ppm; benzene-*d*₆: 128 ppm) chemical shifts of the solvent as a standard. ¹H NMR data for diamagnetic compounds are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent, obsc = obscured), coupling constants (Hz), integration, assignment. ¹³C NMR data are reported as follows: chemical shift, number of protons attached to carbon (e. g. CH₂), assignment.

3.4.2. General procedure for the hydroboration of alkenes

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: alkene (0.300 mmol), 2-MeTHF or Dioxane (0.40 mL), HBPin (109 µL, 0.750 mmol) and HSiOEt₃ (11 µL, 0.060 mmol). The reaction was stirred at 80 °C for 24 hours or 48 hours (for substrates **2o-2s**) and then exposed to air. Fluorobenzene (10 µL, 0.106 mmol) or mesitylene (10 µL, 0.072 mmol) was added as an internal standard and the crude reaction was analyzed by ¹⁹F NMR spectroscopy for

fluorinated substrates or ^1H NMR spectroscopy for other substrates, without additional purification.

General procedure for the isolation of alkylboronate esters

After the completion of the reaction, the contents were exposed to air, and the volatiles were removed in vacuo. The isolated product was analyzed by ^1H , ^{13}C , and ^{11}B NMR spectroscopy.

3.4.3. General procedure for competition experiments

In an argon-filled glovebox, a J. Young flask equipped with a magnetic stir bar was charged with the appropriate pair of substrates (0.150 mmol each), HBPIn (0.45-0.75 mmol), and $\text{HSi}(\text{OEt})_3$ (0.015-0.045 mmol). Dioxane (0.2-0.5 mL) was added as solvent in the required reaction. The sealed flask was removed from the glovebox and stirred at 60-80 °C for 4-24 h. After completion, the reaction mixture was returned to the glovebox, and fluorobenzene (10 μL , 0.106 mmol) or mesitylene (10 μL , 0.072 mmol) was added as an internal standard and the crude reaction was analyzed by ^{19}F NMR spectroscopy for fluorinated substrates or ^1H NMR spectroscopy for other substrates, without additional purification.

3.4.4. General procedure for monitoring catalytic reactions using NMR spectroscopy

In an argon-filled glovebox, a J. Young NMR tube was charged with the appropriate substrate (0.300 mmol), HBPIn (0.75–1.05 mmol), siloxane ($\text{HSi}(\text{OEt})_3$ or $\text{HSi}(\text{OCH}_2\text{CF}_3)_3$) (0.015–0.075 mmol), and fluorobenzene (0.106 mmol) as an internal standard. CD_2Cl_2 (0.30 mL) was added, and the tube was sealed and brought out of the glove box. The headspace of the tube was degassed via three freeze-pump-thaw cycles. The reaction was then monitored by ^1H , ^{11}B , and ^{19}F NMR spectroscopy at 60–80 °C over the specified time. Product formation was confirmed by characteristic signals observed in the corresponding NMR spectra.

3.5. Appendix

3.5.1. NMR Monitoring of the double hydroboration of 4-fluorobenzonitrile (**3a**) with HBPIn employing 5 mol% of HSi(OEt)₃ in CD₂Cl₂.

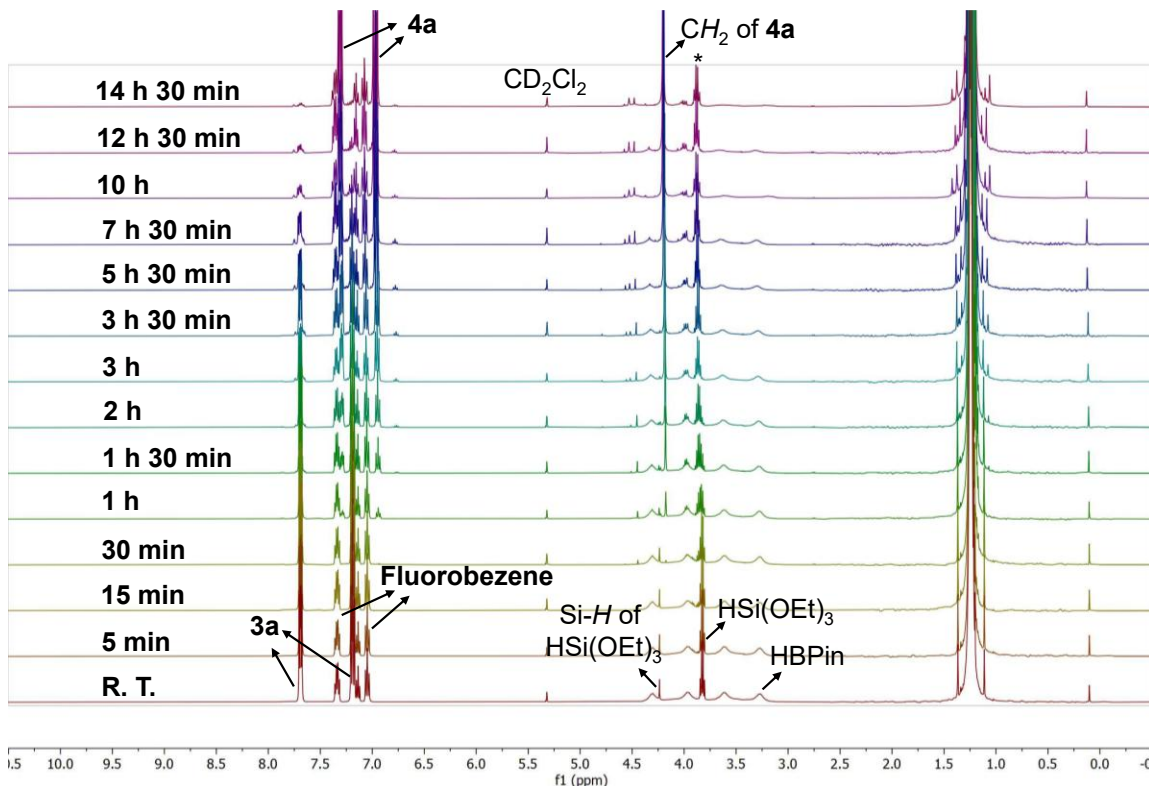


Figure 3.2. ¹H NMR spectra of the double hydroboration of 4-fluorobenzonitrile (**3a**) with HBPIn employing 5 mol% of HSi(OEt)₃ in CD₂Cl₂ at 60 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 60°C for given times). * = New silicon containing species formed *in situ*.

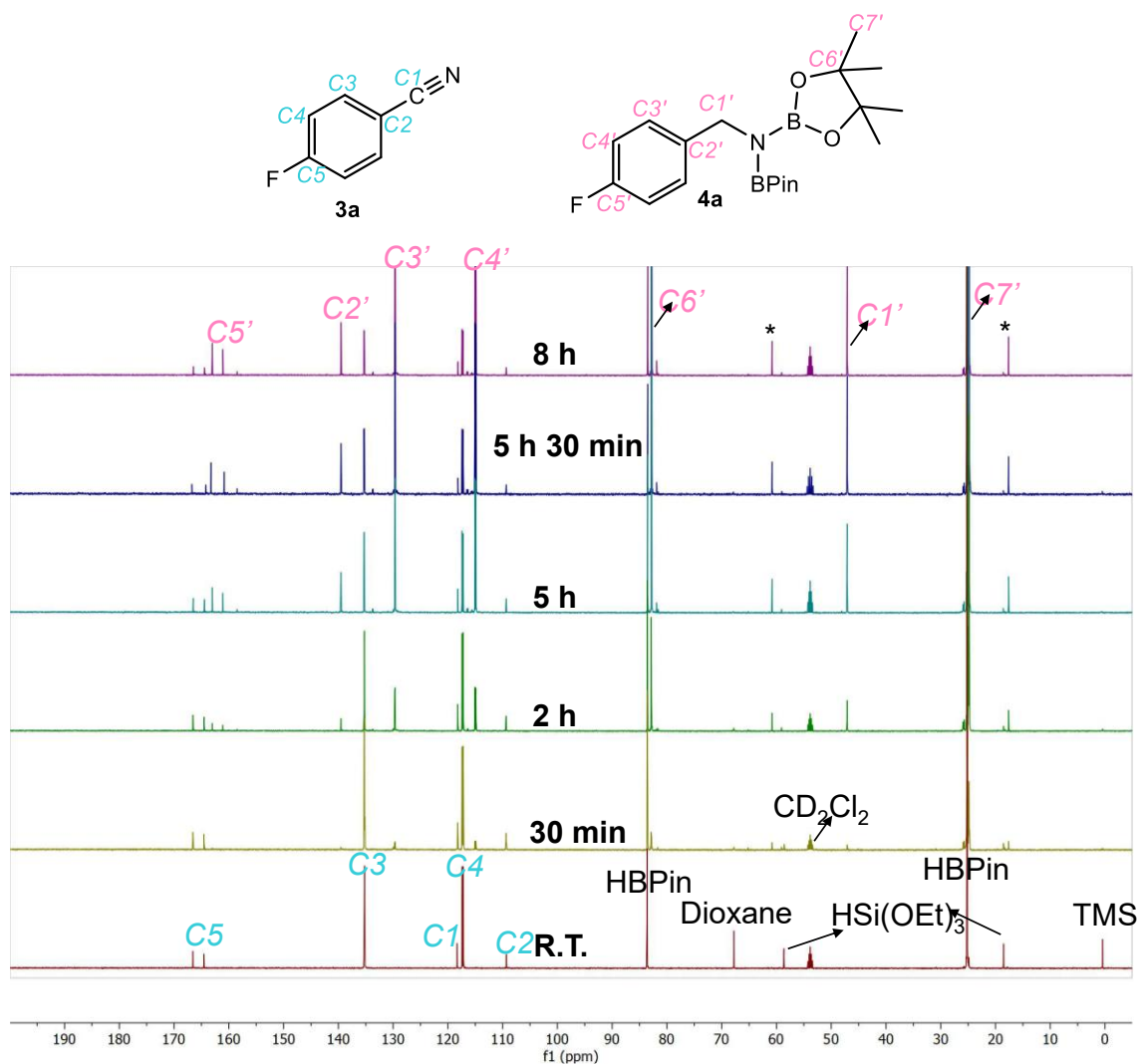


Figure 3.3. ¹³C NMR spectra of the double hydroboration of 4-fluorobenzonitrile (3a) with HBPIn employing 5 mol% of HSi(OEt)₃ in CD₂Cl₂ at 60 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 60°C for given times). TMS = Tetramethylsilane, * = New silicon containing species formed *in situ*.

3.5.2. NMR Monitoring of the double hydroboration of 4-fluorobenzonitrile(3a) with HBPIn employing 5 mol% of HSi(OCH₂CF₃)₃ in CD₂Cl₂.

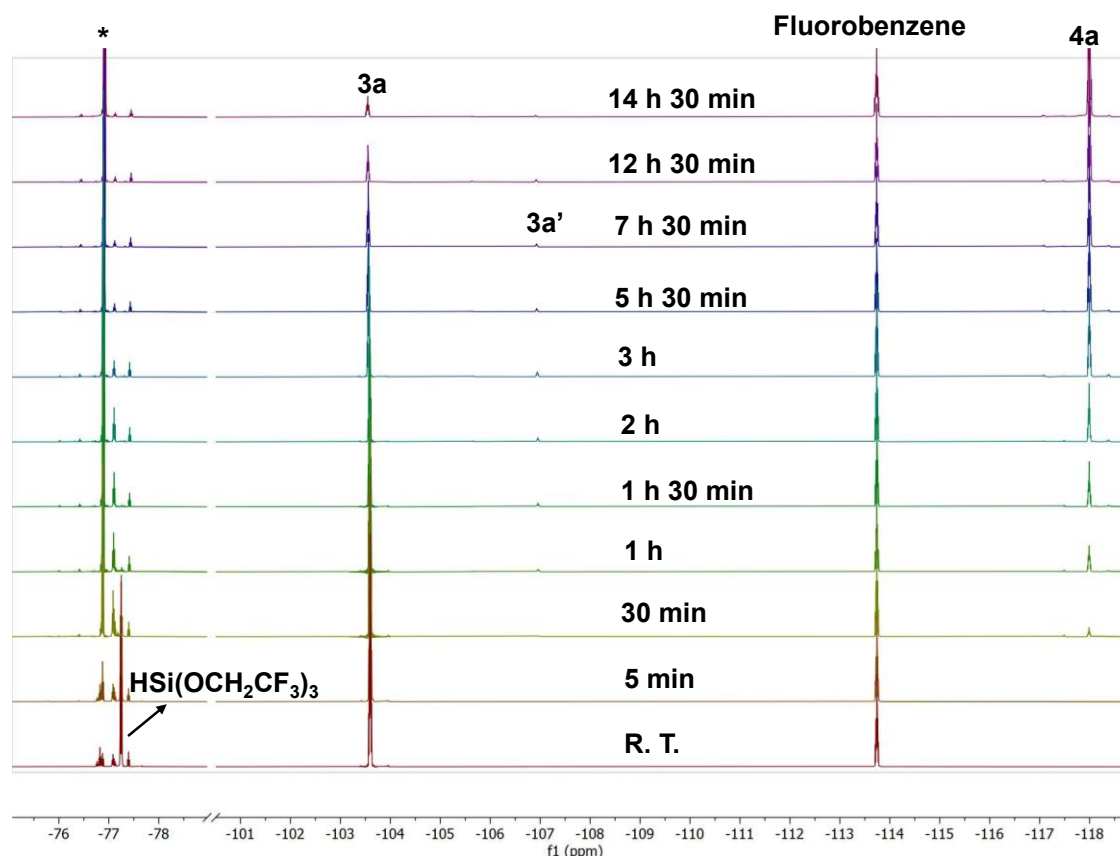


Figure 3.4. ¹⁹F NMR spectra of the double hydroboration of 4-fluorobenzonitrile (**3a**) with HBPIn employing 5 mol% of HSi(OCH₂CF₃)₃ in CD₂Cl₂ at 60 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 60°C for given times) **3a'**= Proposed intermediate from single hydrosilylation or hydroboration formed *in situ*. * = New silicon containing species formed *in situ*.

3.5.3. NMR Monitoring of the hydroboration of 4-fluoroacetophenone(5a) with HBPIn employing 15 mol% of HSi(OEt)₃ in CD₂Cl₂.

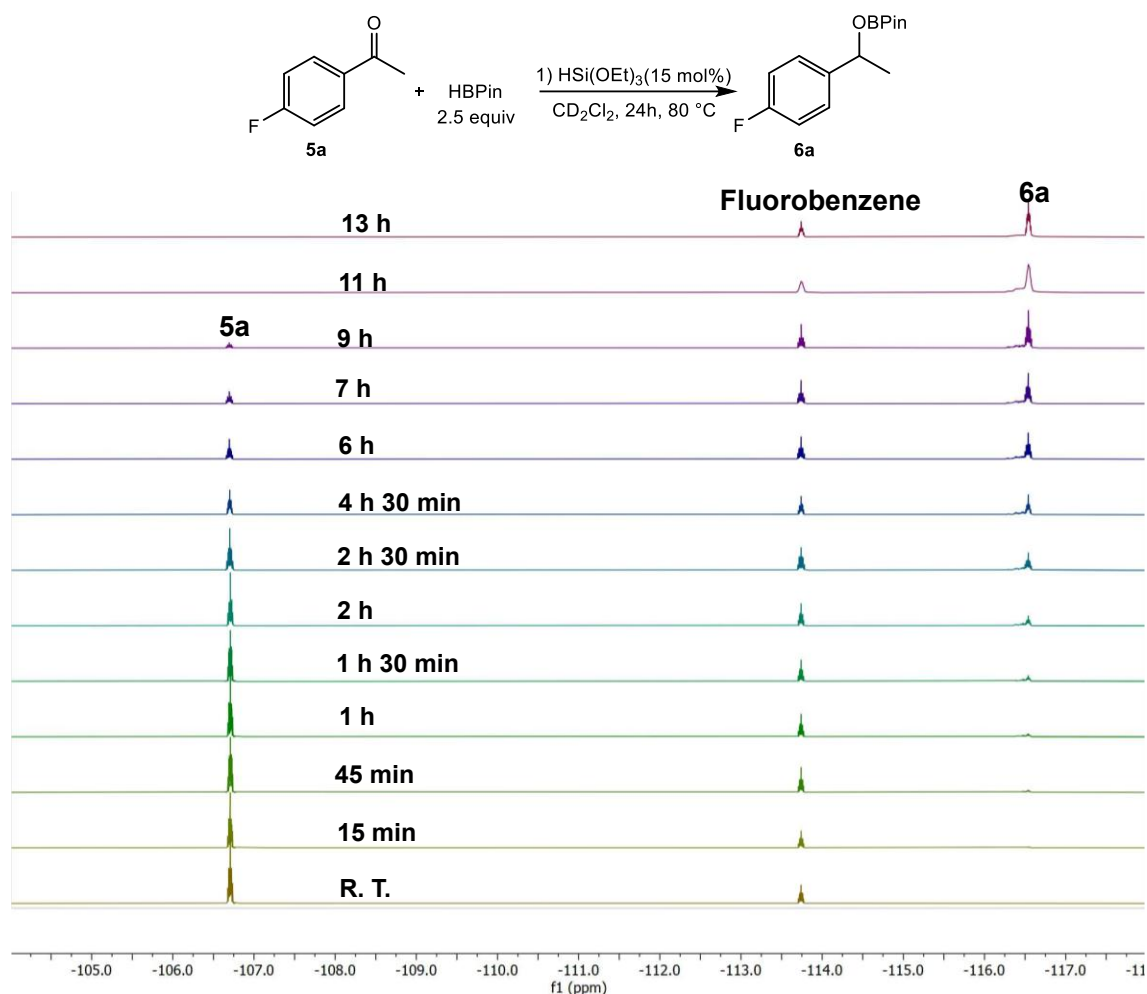


Figure 3.5. ¹⁹F NMR spectra of the hydroboration of 4-fluoroacetophenone (5a) with HBPIn employing 15 mol% of HSi(OEt)₃ in CD₂Cl₂ at 80 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for given times).

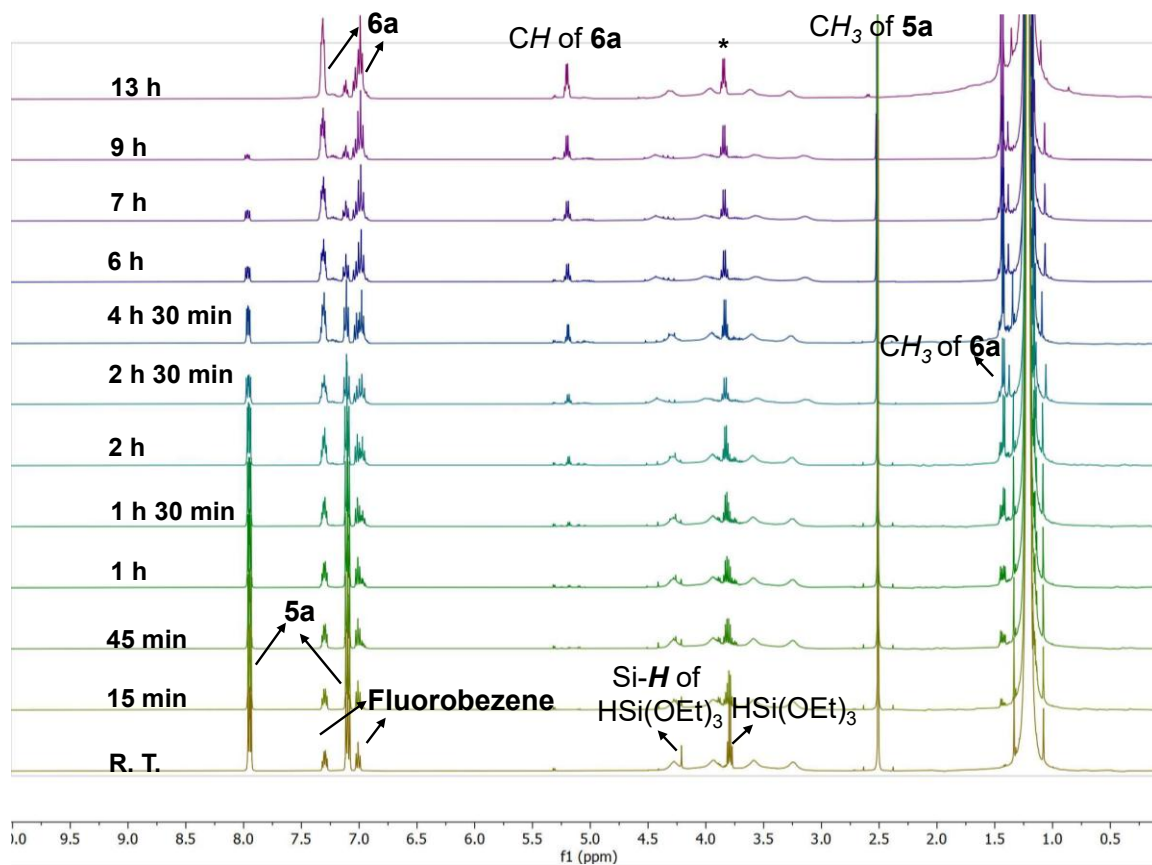


Figure 3.6. ¹H NMR spectra of the double hydroboration of 4-fluoroacetophenone (**5a**) with HBPIn employing 15 mol% of HSi(OEt)₃ in CD₂Cl₂ at 80 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80 °C for given times). * = New silicon containing species formed *in situ*.

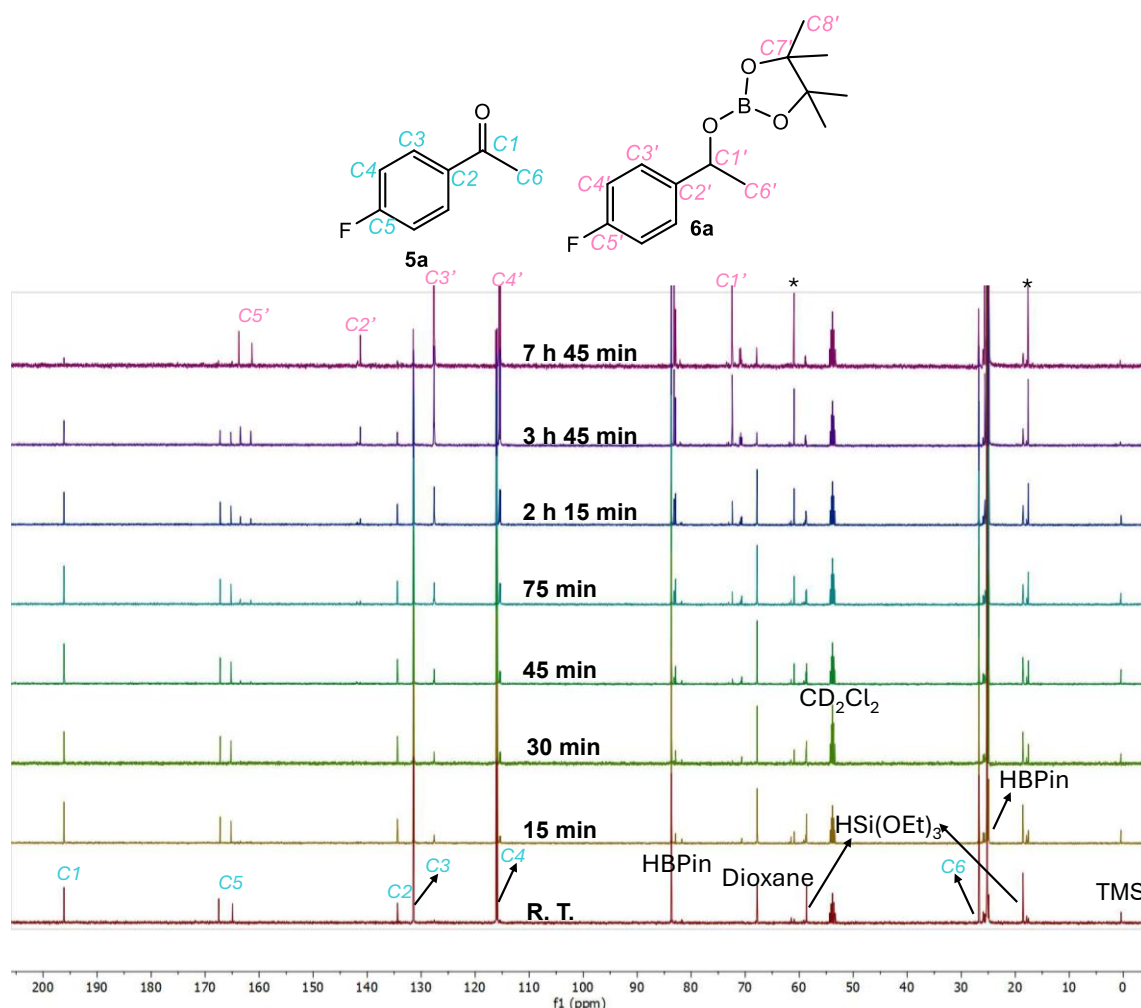
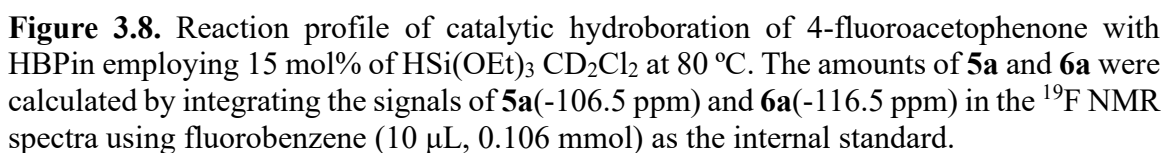


Figure 3.7. ¹³C NMR spectra of the double hydroboration of 4-fluoroacetophenone (**5a**) with HBPi employing 15 mol% of HSi(OEt)₃ in CD₂Cl₂ at 80 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for given times. * = New silicon containing species formed *in situ*).



Reaction scheme showing the conversion of 7b to 8b and 9a:

7b + HBPIn (3.5 equiv) $\xrightarrow[\text{CD}_2\text{Cl}_2, 80^\circ\text{C}]{\text{HSi}(\text{OEt})_3 (25 \text{ mol}\%)}$ 8b + 9a

Chemical structures: 7b is 4-fluorobenzyl acetate, 8b is 4-fluorobenzyl pinacolboronate, and 9a is pinacolboronic acid.

Stacked ^1H NMR spectra (f1 (ppm)) showing the reaction progress over time (R.T., 30 min, 1 h 30 min, 3 h, 5 h, 7 h 15 min, 9 h 15 min, 12 h 15 min, 16 h 15 min, 20 h, 24 h). The spectra show the disappearance of 7b and the appearance of 8b and 9a.

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internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for given times).

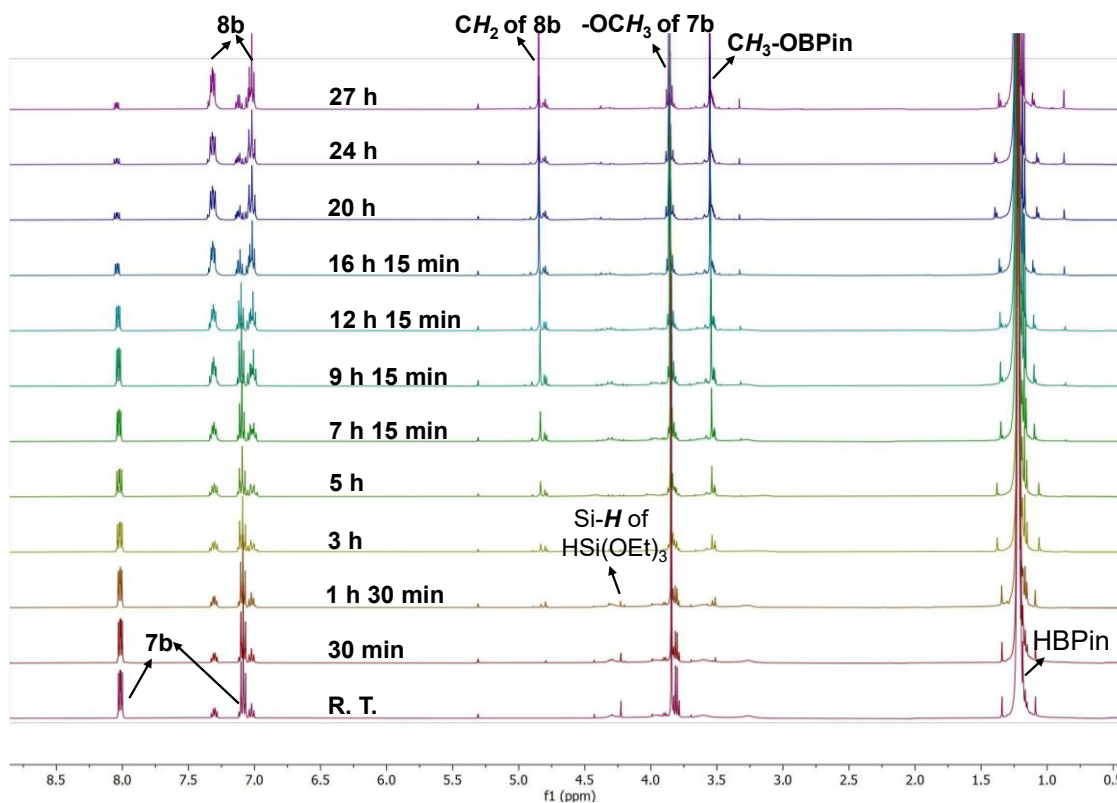


Figure 3.10. ¹H NMR spectra of the double hydroboration of Methyl 4-fluorobenzoate (**7b**) with HBPi employing 25 mol% of HSi(OEt)₃ in CD₂Cl₂ at 80 °C, using fluorobenzene as internal standard. (First spectrum was recorded at room temperature and the subsequent spectra were recorded at room temperature after heating the reaction at 80°C for given times).

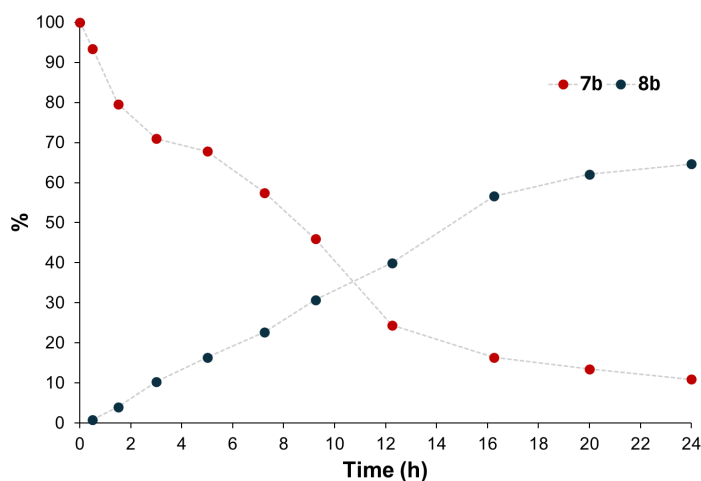


Figure 3.11. Reaction profile of catalytic double hydroboration of Methyl 4-fluorobenzoate (**7b**) with HBPi employing 25 mol% of $\text{HSi}(\text{OEt})_3$ CD_2Cl_2 at 80 °C. The amounts of **7b** and **8b** were calculated by integrating the signals of **7b** (-106.8ppm) and **8b** (-115.9ppm) in the ^{19}F NMR spectra using fluorobenzene (10 μL , 0.106 mmol) as the internal standard.

3.6. References

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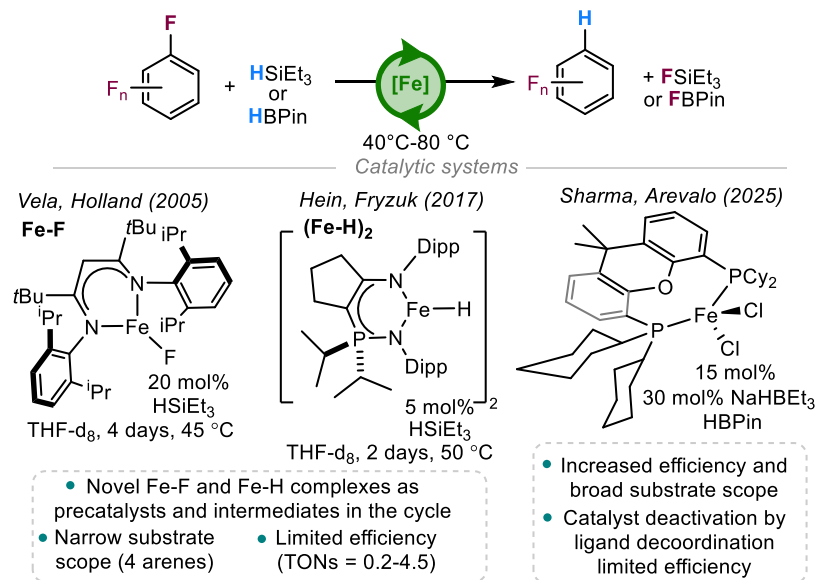
4. Bench-Stable Iron Bipyridine Complexes as Long-Lived Catalysts for the Hydrodefluorination of Arenes at Room Temperature

<https://chemrxiv.org/doi/full/10.26434/chemrxiv-2025-4599v>

Harleen Kaur, Diksha Sharma, Rebeca Arevalo*

4.1. Introduction

The hydrodefluorination (HDF) of small molecules is a key process with applications in the synthesis of pharmaceuticals, agrochemicals, and advanced materials, as well as for the remediation of perfluoroalkyl substances (PFAS).¹ Homogeneous catalysis has proven to be key in developing sustainable methods for HDF, with Ni complexes efficiently catalyzing the HDF of C(sp²)-F and C(sp³)-F bonds in polyfluorinated arenes with broad substrate scope.² In the pursuit of more sustainable systems, Fe complexes emerge as an appealing alternative, however, they remain scarce with their ability and mechanisms to catalytically activate C-F bonds being largely unexplored. Pioneering work by Holland³ and Fryzuk⁴ demonstrated the potential of Fe(II) complexes for this transformation and established a mechanistic framework, but were constrained by a narrow substrate scope, limited to only three and two fluoroarenes respectively. In both cases, well-defined Fe(II)-F and Fe(II)-H species were employed as precatalysts and identified as catalytic intermediates (**Scheme 4.1**). The use of bulky, monoanionic bidentate N-donor ligands forming six-membered chelates was key to stabilizing low-coordinate (CN = 3) intermediates in the cycle, which were proposed to underpin catalytic efficiency.

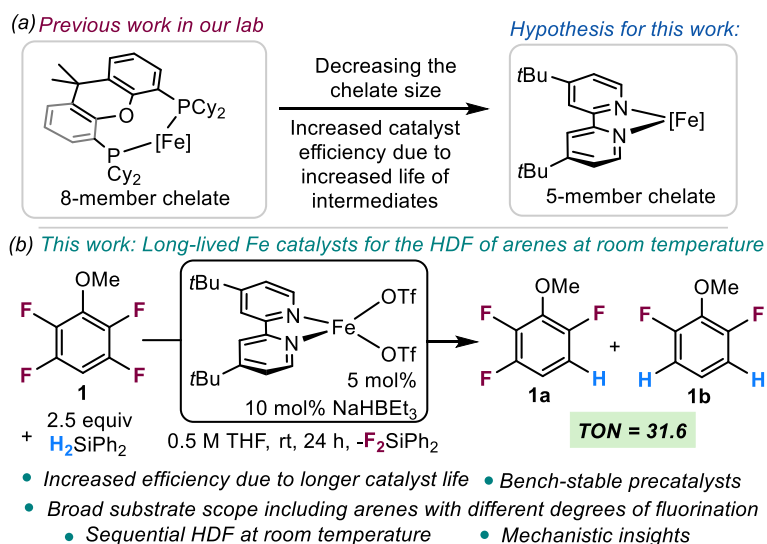


Scheme 4.1. Previously reported Fe catalysts for the HDF of arenes.

As part of our efforts to unlock efficiency of Fe complexes for this process, our group recently reported the first Fe(II) complex bearing the neutral, wide bite-angle ^{Cy}Xanthphos

(4,5-bis(di-cyclohexylphosphino)-9,9-dimethylxanthene) ligand that is efficient for the HDF of fluoroarenes upon *in situ* activation with NaHBEt_3 or NaOtBu using HBPIn as the H source (**Scheme 4.1**).⁵ This system exhibited significantly improved efficiency relative to previously reported catalysts, together with a broad substrate scope encompassing both perfluorinated arenes and substrates with lower degrees of fluorination. Mechanistic studies identified a putative Fe–H species as the active intermediate responsible for C–F bond activation. However, efficient catalysis required elevated temperatures (80 °C), and catalyst deactivation was observed under turnover conditions, primarily by Xantphos decooordination. While the wide bite angle of the Xantphos and the bulky cyclohexyl substituents could contribute to catalytic performance by providing steric protection to the Fe center and stabilizing low-coordinate intermediates, the formation of a large, eight-membered chelate could facilitate ligand dissociation, ultimately compromising catalyst robustness.

Aiming to further increase catalytic efficiency, we envisioned that reducing the size of the chelate could enhance the stability of key intermediates while minimizing catalyst deactivation by ligand decooordination (**Scheme 4.2a**). 2,2'-Bipyridine (bipy) ligands form robust five-membered chelates with transition metals and are ubiquitous in Earth-Abundant transition metal catalysts due to their commercial availability and their ability to stabilize metal centers across different oxidation states under harsh reaction conditions. However, despite extensive studies of 18-electron complexes such as $[\text{Fe}(\text{bipy})_3]^{2+}$ as Earth-Abundant photosensitizers, the catalytic potential of electronically unsaturated Fe complexes bearing a single bipy ligand remains largely unexplored,⁶ and their underlying fundamental chemistry poorly understood.



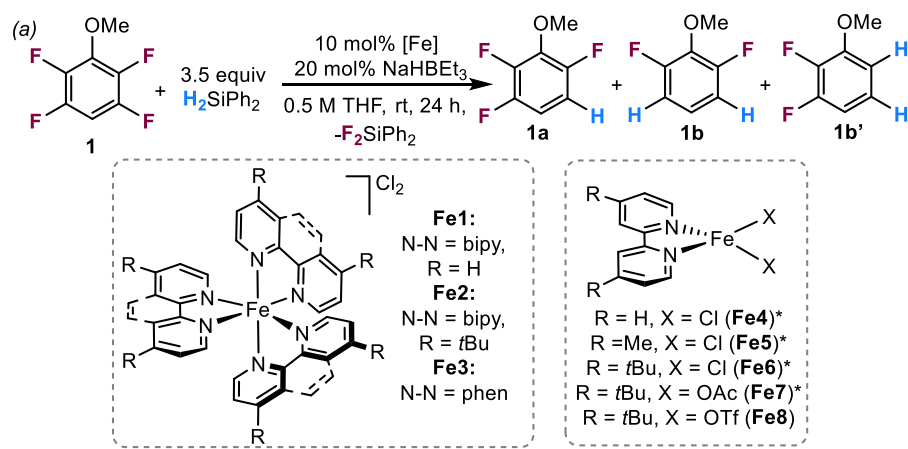
Scheme 4.2. (a) Fe(II) catalyst for the HDF of arenes containing a wide bite-angle phosphine (previous work in our lab); (b) This work: a bench-stable Fe(II) bipy complex as an efficient catalyst for the HDF of polyfluorinated arenes at room temperature.

Herein we report the first bench-stable Fe precatalyst for the HDF of polyfluorinated arenes that works at room temperature. The $[\text{Fe}(\text{}^t\text{Bu}^{\text{bipy}})\text{OTf}_2]$ ($\text{}^t\text{Bu}^{\text{bipy}} = 4,4'$ -di-*tert*-butyl-2,2'-bipyridine, $\text{OTf} = \text{CF}_3\text{SO}_3^-$) complex is an efficient precatalyst for the HDF of fluorinated arenes employing NaHBEt_3 as *in situ* activator (**Scheme 4.2b**). The catalytic system was efficient at room temperature and in the presence of the commercially available silane H_2SiPh_2 . We report insights on how the substitution at the 4 and 4' positions of the bipy ligand as well as the identity of the X-type ligand in the precatalyst impact catalytic efficiency. The Fe complexes reported in this work are the first Fe complexes that show catalytic efficiency for the HDF of arenes at room temperature. The catalytic system exhibited a remarkable efficiency for tetra- and trifluorinated arenes, with slightly lower activity observed for per- and difluorinated substrates. The catalyst displayed a pronounced preference for F atoms between C–F and C–H bonds, with the number of F atoms in this environment being the primary determinant of efficiency, while the positions of the remaining F atoms exerted a secondary influence. Mechanistic studies indicated that different Fe complexes act as resting states for first and second HDF cycle and allowed to identify the formation of a Fe–H upon precatalyst activation with NaHBEt_3 that reacted with H_2SiPh_2 to enter the catalytic cycle.

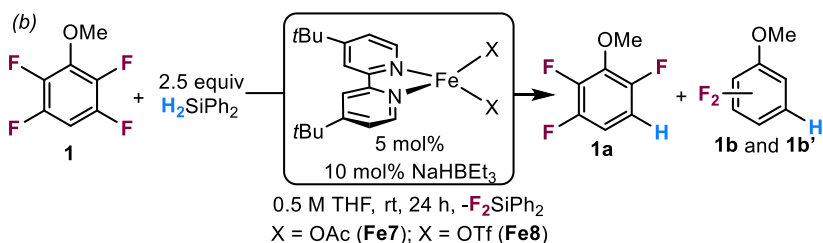
4.2. Results and Discussion

4.2.1. Catalyst discovery and optimization of the reaction conditions

Since iron(II) trisbipy complexes have been extensively studied due to their potential applications as photosensitizers, our research commenced with the synthesis of the iron(II) complexes $[\text{Fe}(\text{NN})_3]\text{Cl}_2$ [$\text{NN} = \text{}^R\text{bipy} = 2,2'$ -bipyridine ($\text{R} = \text{H}$ (**Fe1**),⁷ $\text{R} = \text{}^t\text{Bu}$ (**Fe2**);⁸ $\text{NN} = \text{phen}$ (**Fe3**)]⁹ by the procedures reported in the literature and the evaluation of their catalytic efficiency for the HDF of 2,3,5,6-tetrafluoroanisole (**1**) employing H_2SiPh_2 as the H source and NaHBEt_3 as the *in situ* activator. Under the conditions in **Scheme 4.3a** the starting material was fully recovered in all cases (see entries 1-3 in table in **Scheme 4.3a**), with products from HDF of **1** not being detected in the reaction crude by ^{19}F NMR spectroscopy, suggesting that the precatalysts were not capable of generating a Fe–H efficient for HDF. We reasoned that the lack of catalytic efficiency in these complexes could be due to the presence of three N–N ligands that resulted on the electronic saturation of the complexes preventing the formation of a Fe–H upon reaction with NaHBEt_3 . Accordingly, we envisioned that the presence of only one bipyridine ligand in the precatalyst could render access to a catalytically efficient Fe–H for the HDF of **1**. To this end, the Fe(II) complex $[\text{Fe}(\text{bipy})\text{Cl}_2]$ (**Fe4**) was synthesized by slightly modifying the reported procedure¹⁰ and was found to catalyze the HDF of **1** (33% conversion) affording product **1a** from single HDF in 21% yield (see entry 4 in table in **Scheme 4.3a**) resulting in a TON of 2.1 (calculated assuming quantitative precatalyst activation by reaction with NaHBEt_3). This result supports that the presence of only one bipy ligand in the precatalyst was key to enable catalysis.



Entry	[Fe]	Conv 1 (%)	Yield 1a (%)	Yield 1b (%)	Yield 1b' (%)
1	Fe1	-	N. D.	N. D.	N. D.
2	Fe2	-	N. D.	N. D.	N. D.
3	Fe3	-	N. D.	N. D.	N. D.
4	Fe4	33	21	N.D.	N.D.
5	Fe5	28	16	N.D.	N.D.
6	Fe6	56	56	N.D.	N.D.
7	Fe7	95	85	7	N.D.
8	Fe8	>99	21	45	34



Entry	[Fe]	Deviation from Conditions	Conv 1 (%)	Yield 1a (%)	Yield 1b (%)	Yield 1b' (%)	TON
1	Fe7	None	60	38	5	N. D.	9.6
2	Fe7	Hexane	50	44	N. D.	N. D.	8.8
3	Fe7	Et ₂ O	49	35	N. D.	N. D.	7.0
4	Fe8	3 equiv H_2SiPh_2	97	54	22	19	27.2
5	Fe8	3 equiv H_2SiPh_2 , 16 h	95	64	14	11	22.8
6	Fe8	3.5 equiv H_2SiPh_2	>99	42	32	26	31.6

Scheme 4.3. (a) Assessment of catalytic efficiency of $[\text{Fe}(\text{N-N})_3]\text{Cl}_2$ (N-N = bipy or phen) and $[\text{Fe}(\text{Rbipy})\text{X}_2]$ (Rbipy = 4,4'-dialkyl-2,2'-bipyridine) complexes for the HDF of **1** employing H_2SiPh_2 as the H source and NaHBEt_3 as the *in situ* activator. (b) optimization of the conditions for the HDF of **1** employing **Fe7** or **Fe8** as precatalysts. Conversions and yields were determined by ^{19}F NMR spectroscopy with (trifluoromethyl)benzene as

internal standard. N. D. stands for Not Detected. *Monomers of complexes **Fe4-Fe7** are depicted for simplicity, however, these complexes can exist as dimers containing Cl^- or OAc^- bridging ligands in the solid-state.^{6b,10b}

Aiming to increase the efficiency of the catalytic system, the impact of the presence of electron-donating substituents at the 4 and 4' positions of the bipy ligands in the precatalysts was evaluated. The Fe(II) complex $[\text{Fe}(\text{Me}^{\text{bipy}})\text{Cl}_2]$ (Me^{bipy} = 4,4'-dimethyl-2,2'-bipyridine, **Fe5**)¹¹ showed an analogous efficiency to **Fe4** for the HDF of **1** (see entry 5 in table in **Scheme 4.3a**), however, the presence of a *tert*-butyl group at the 4 and 4' positions of the bipy ligand in $[\text{Fe}(\text{t}^{\text{Bu}}\text{bipy})\text{Cl}_2]$ ($\text{t}^{\text{Bu}}\text{bipy}$ = 4,4'-ditertbutyl-2,2'-bipyridine, **Fe6**, see appendix for synthetic details) resulted in a significant increase in catalyst efficiency, **Fe6** affording **1a** in 56% yield (TON = 5.6, see entry 6 in table in **Scheme 4.3a**). Employing the $[\text{Fe}(\text{t}^{\text{Bu}}\text{bipy})\text{OAc}_2]$ (**Fe7**) complex, with OAc X-type ligands instead of Cl, led to a remarkable increase in the catalyst efficiency, the reaction proceeding to 95% conversion of **1** and affording **1a** in 85% yield. More interesting, **Fe7** afforded access to product **1b** from sequential HDF of **1** in 7% yield, resulting in a TON of 10 for this precatalyst.

Control experiments supported the need of all the reagents for efficient catalysis, the starting material being recovered when at least one of the components was missing. Furthermore, the identity of the silane was key to enable efficient HDF, when HSiEt_3 or HSiMe_2Ph were employed as the H source, the starting material was recovered (for HSiEt_3) or low conversion of **1** (22%) and yield of **1a** (22%) were obtained (for HSiMe_2Ph). In contrast, H_2SiEt_2 and $\text{HSi}(\text{OEt})_3$ afforded full conversion of starting material, however, **1a** was formed in only 60% and 50% yields respectively, along with multiple unidentified products. The presence of the strong hydride source MHBET_3 (M = Na, K) as the precatalyst activator was key to enable catalysis, with the weaker hydride source LiAlH_4 resulting in full recovery of the starting material. Employing other nucleophiles, mainly *tert*butoxides or amides, resulted in full recovery of **1**, supporting that the presence of a strong hydride source is key to generate the catalytically active species.

Interestingly, the triflate analog of **Fe7**, $[\text{Fe}(\text{t}^{\text{Bu}}\text{bipy})\text{OTf}_2]$ (**Fe8**),^{6a} showed a remarkable higher efficiency for the process, the reaction proceeding to full conversion of **1**, affording **1a** in 21% yield, and the two regioisomers from sequential HDF, **1b** and **1b'** (**Scheme 4.3a**) in 45% and 34% yields respectively (entry 8 in table in **Scheme 4.3a**), which resulted in a 17.9 TON for **Fe8**, the highest TON reported to date for Fe catalysts for the HDF of arenes.^{3,4} The fact that **1a** was formed as the exclusive product in the first HDF cycle supports that the catalyst is highly regioselective toward the F atoms that have a C-H group right next to them (at the 3 and 5 positions). Along these lines, the ratio of the regioisomers obtained in the second HDF cycle (**1b**:**1b'** ratio of 1.3:1) suggests that when 2,3,6-trifluoroanisole (**1a**) was the starting material, the system showed a similar preference and only targeted the two F atoms with C-H groups next to them (at the 3 and 6 positions). A slight preference for the F in position 3 (in between the C-H and the C-F bond) than for the one in position 6 (in between the C-H and the C-O bond), was observed, with no preference for the F atom in position 2 which did not have a C-H group next to it.

More interestingly, **Fe8** was found to be air- and moisture-stable for 24 hours, showing a significant practical advantage over **Fe7**, which decomposed immediately after exposure to air and moisture, and being the first bench-stable precatalyst reported for the HDF of arenes. After an optimization of the reaction conditions a >99% conversion of **1** at room temperature employing 5 mol% of **Fe8** (entry 6 in table in **Scheme 4.3b**, TON 31.6) whereas our previously reported system, $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$,⁵ required 80 °C and 24 h to reach to a 75% conversion of **1** with a 15 mol% of catalyst loading. Additionally, whereas $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ afforded **1a** from single HDF as the exclusive product, **Fe8** was capable of catalyzing the sequential HDF of **1**, affording a mixture of the two regioisomers **1b** and **1b'** from sequential HDF. Overall, these results highlight the increased efficiency of **Fe8** compared to the $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ precatalyst.

4.2.2. Mechanistic insights: NMR monitoring of the catalytic reaction catalyzed by FeOTfbipy

To gain insight into the nature of the catalytic reaction, the HDF of **1** was conducted in the presence of one drop of Hg employing 10 mol% **Fe7** and 3.5 equiv of H_2SiPh_2 . This reaction afforded an analogous conversion of **1** and yield of **1a** (85% conversion of **1** and 80% yield of **1a**) than that in the absence of Hg (93% conversion of **1** and 85% yield of **1a**, entry 7 in **Scheme 2a**), supporting homogeneous catalysis operative for the process.

To identify any species present in the catalytic reaction, the HDF of **1** with 3 equiv of H_2SiPh_2 catalyzed by 10 mol% of **Fe8** *in situ* activated with 20 mol% of NaHBET_3 was monitored by ^1H and ^{19}F NMR spectroscopy at room temperature (25 °C) for 23 h and 30 min. The ^{19}F NMR spectra showed signals attributable to **1** (at -156.9 and -139.2 ppm) which intensity decreased over time, and signals attributable to **1a** (at -132.1, -140.1 and -150.8 ppm), **1b** (at -128 ppm) and **1b'** (at -137.3 and -159.6 ppm) (see **Figure 4.1**). The intensity of the signals attributed to **1a** increased their intensity at early stages of the reaction at the expense of the signals attributed to **1** and started decreasing their intensity after 7 h (92% conversion of **1**). These observations support a first HDF cycle that converts **1** into **1a** and another two HDF cycles that convert **1a** into **1b** and **1b'** respectively (see **Scheme 4.4b** for the reaction profile). The fact that signals attributable to **1b** could be detected after 30 minutes of reaction (20% conv of **1**) and those attributed to **1b'** after 1 h of reaction (32% conv of **1**), supports that three HDF cycles were operative simultaneously throughout most of the catalytic turnover, and that the HDF of **1a** proceeded as soon as the substrate was present in the reaction medium. The decrease in the concentration of **1a** due to its HDF was only apparent after 7 h, when most **1** was consumed and the cycles for the HDF of **1a** started being operative to a larger extent. Although the three cycles are operative at the same time, the first cycle starting from **1** is 8.2 times faster than the two second cycles for the HDF of **1a** (see **Scheme 4.4b**). Accordingly, the first cycle afforded **1a** in 46% yield and the second **1b** in only 5% yield in 2 hours, consistent with a marked decreased reaction rate as the number of F in the substrate decreased, rather than as a result of catalyst deactivation. This result allows to rationalize why the catalytic system afforded the product from single HDF as the major for most of the substrates depicted in **Scheme 3**. Additionally, a signal attributable to 1,2-fluoroanisole (**1c**, at -133.9 ppm), from the HDF of **1b** and **1b'**, could not be observed until late stages of the reaction (98% conversion of **1**, 16 h and 30

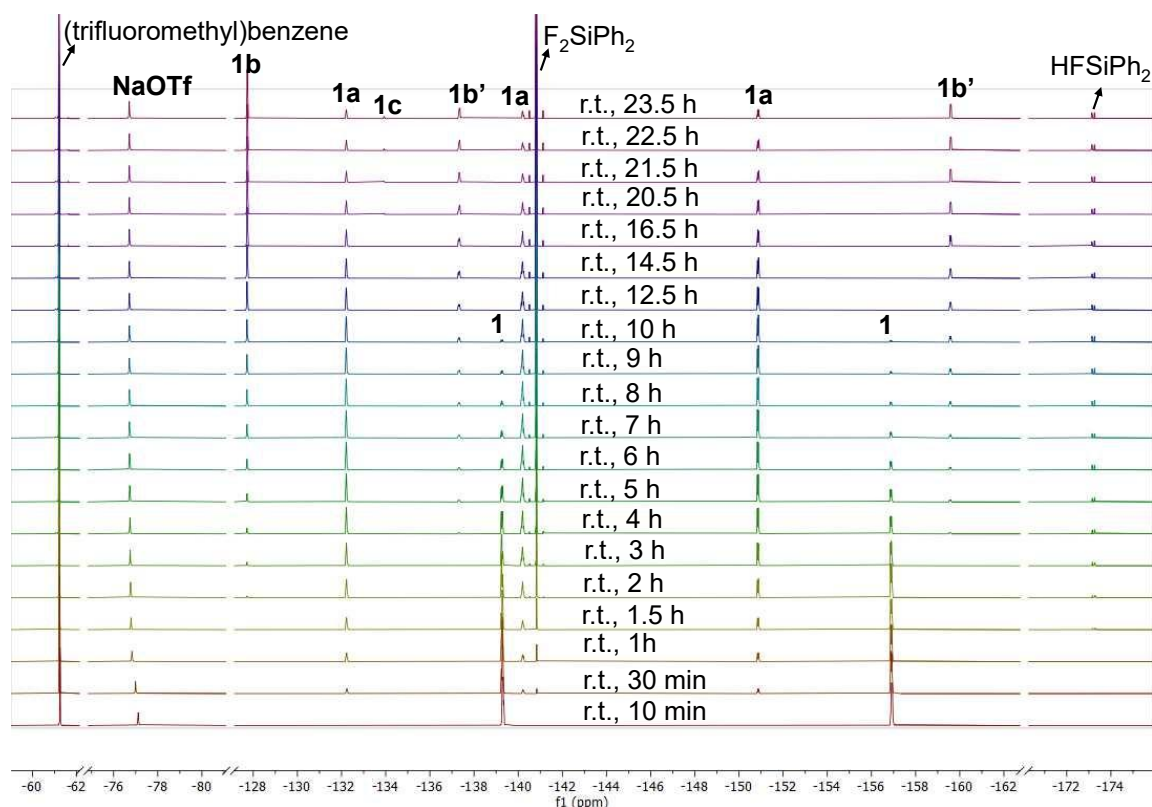
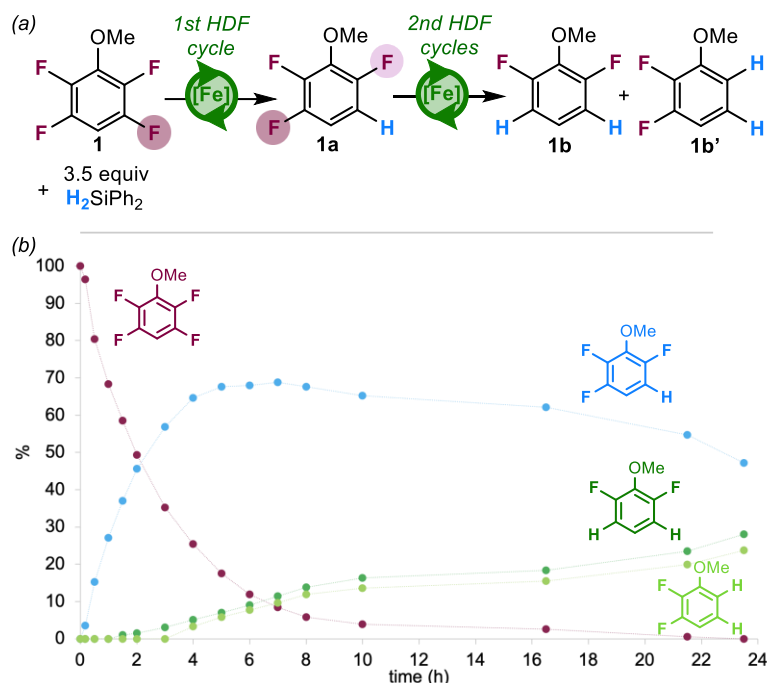


Figure 4.1. ^{19}F NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe8** at room temperature in THF- d_8 , using (trifluoromethyl)benzene as internal standard.

min), and was formed in trace amount, supporting a remarkable decreased efficiency for the HDF of difluoroarenes **1b** and **1b'**. As observed in the substrate scope evaluation, the system was regioselective for the HDF of **1**, targeting the F atoms in the 3 and 5 positions to access **1a**, however, the fact that **1b'** starts forming only 30 min later than **1b** as well as the analogous rates for the formation of **1b** and of **1b'** supported that the system only had a slight preference for the F atom in the 3 position (in between a C-H and a C-F bond) than for that in the 6 position (in between a C-H and the C-O bond) in the HDF of **1a**.



Scheme 4.4. (a) Reaction pathway and (b) profile for the HDF of **1** employing **Fe8** as precatalyst.

A signal at -141.0 ppm, which intensity grew over time could be attributed to the presence of SiF_2Ph_2 in increasing amounts as the reaction proceeded, suggesting that H_2SiPh_2 was capable of transferring both the H to the substrates in the HDF process. A minor signal attributable to SiHFPh_2 (-173.0 ppm, d) was also present, which remained minor compared to that of SiF_2Ph_2 throughout catalytic turnover, further supporting the transfer of both H from H_2SiPh_2 . Signals attributable to Fe-bonded F ligands were not identified in the ^{19}F NMR spectra.

The ^1H NMR spectra showed signals consistent with the presence of diamagnetic Fe(II) complexes as the resting-states of the HDF cycles of **1** and **1a**. After 10 min of reaction, a diagnostic signal at -1.14 ppm was present in the ^1H NMR spectrum which vanished after 30 min of reaction. Diagnostic signals at -33.87, -7.98 and -2.41 ppm were present throughout the catalytic turnover. The intensity of -2.41 ppm signal decreases over time, while the signals at -7.98 and -33.87 ppm increase correspondingly (see **Figure 4.2**). When the catalytic reaction was conducted using 10 mol% of **Fe7** as the precatalyst, only signals attributable to **1a** were observed in the ^{19}F NMR spectrum (see **Figures 4.6–4.8** in appendix), indicating that only a single HDF cycle was operative. This observation is consistent with the lower catalytic efficiency associated with this precatalyst. Under these conditions, the ^1H NMR spectrum displayed only a signal at -1.14 ppm during the initial 10 minutes of the reaction. This species did not promote conversion of **1** within this time frame, suggesting the presence of an approximately 10-minute induction period, which was not observed when **Fe8** was employed as the precatalyst. Signals at -2.41 ppm and -33.87 ppm were identified as diagnostic, with the -2.41 ppm signal disappearing after 4 hours,

coinciding with the plateau in conversion of **1**. This behavior suggests that the -2.41 ppm signal corresponds to the catalyst resting-state during the first HDF cycle.

In contrast, when **Fe8** is used as the catalyst, the signal at -7.98 ppm appears only after the initial 10 minutes, consistent with the availability of **1a** after the first HDF cycle. Its subsequent increase in intensity as the reaction progressed indicates its involvement in the second HDF cycle, and it is therefore assigned to the catalyst resting-state of this cycle. Further, the absence of the -7.98 ppm signal in reactions catalyzed by **Fe7**, where only the first cycle is operative, further supports that this species is not involved in the first cycle. Finally, the signal at -33.87 ppm is observed under conditions where both the first and second HDF cycles occur and its intensity increased slightly over time. This indicates that the corresponding resting-state was common to both catalytic cycles and could be attributed to catalyst deactivation or an off-cycle species that keeps on accumulating as the reaction proceeded. Further efforts are ongoing in our laboratory to identify and characterize the catalyst resting-states.

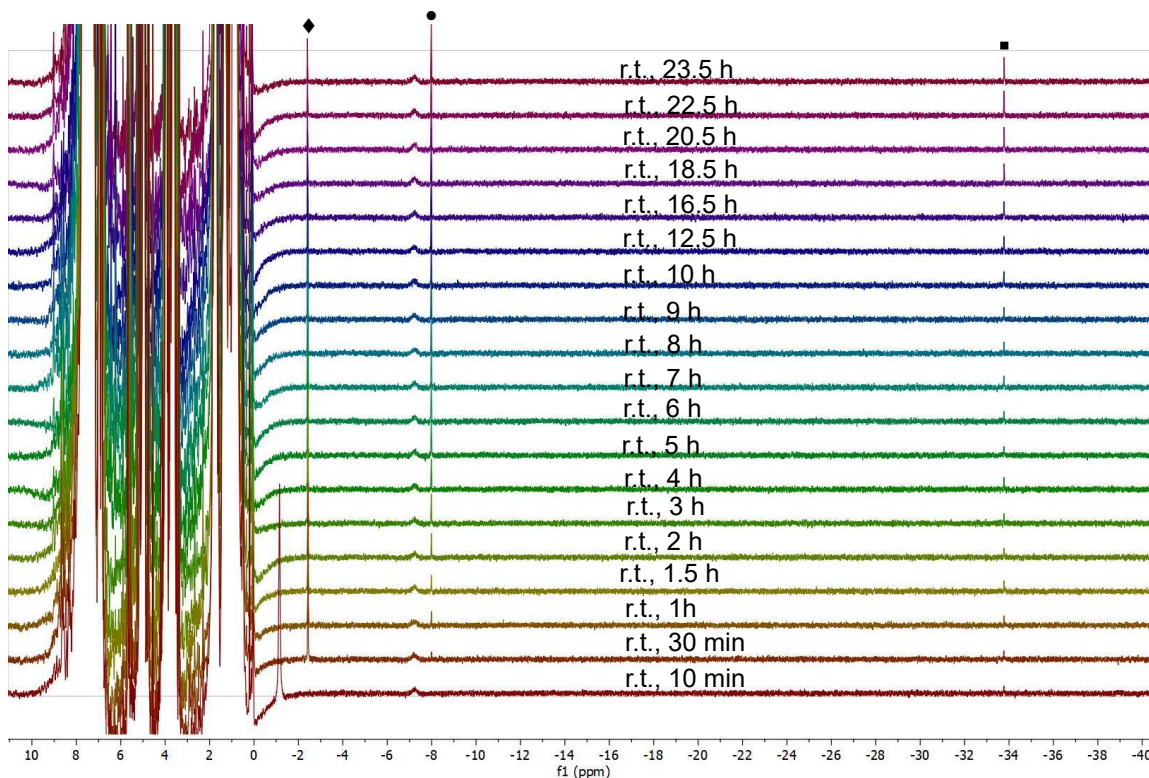
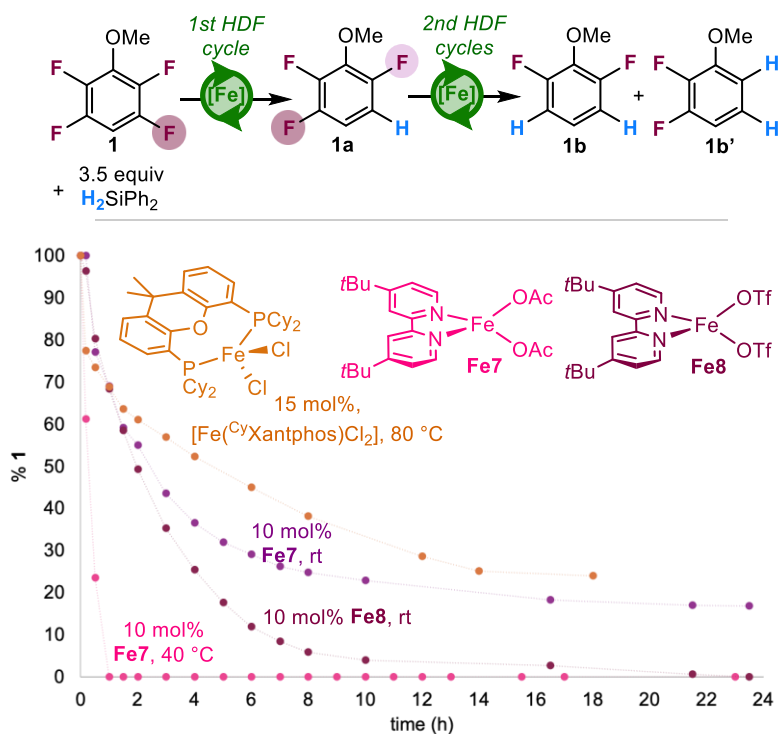


Figure 4.2. Wide-range ppm ^1H NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by 10 mol% of **Fe8** at room temperature in THF-d_8 , using (trifluoromethyl)benzene as internal standard. ♦ = proposed catalyst resting-state for the first HDF cycle. • = proposed catalyst resting-state for the second HDF cycle ▪ = proposed catalyst deactivation or off cycle species.

A comparison of the reaction profiles for the % of **1** employing **Fe7** as precatalyst at rt or at 40 °C (**Scheme 4.5**) showed that at 40 °C full conversion of **1** was reached within 1 h, whereas at rt only a 30% was accessed, supporting an increase of 2.8 times in the reaction rate as a result of the increase in temperature. As a result of a faster first HDF cycle when the reaction was conducted at 40 °C, sequential HDF resulting in the formation of **1b** and **1b'** was observed, whereas only single HDF was operative at rt. Comparing the reaction profiles for the % of **1** employing **Fe7** and **Fe8** as precatalysts at rt (**Scheme 4.5**) revealed that both precatalysts showed a comparable efficiency during the initial 2 h of the reaction (up to 50% conversion of **1**). However, as mentioned above, when **Fe7** was employed as the precatalyst, an induction period of 10 min was observed, suggesting that **Fe7** required a longer time than **Fe8** to generate the catalytically active species. Although the efficiency of both catalytic systems was comparable up to 2 h, the reaction profile employing **Fe7** as precatalyst suggests that the reaction became slower than that employing **Fe8** after the initial 2 h, with the conversion of **1** plateauing at 83% for **Fe7**, whereas full conversion of **1** was achieved with **Fe8**. This result rationalizes the higher efficiency of **Fe8** relative to **Fe7** and suggests that the increased efficiency of **Fe8** arises primarily from the earlier catalyst deactivation of **Fe7**, indicating that the X-type ligand in the Fe precatalyst may participate in the catalyst deactivation pathway.

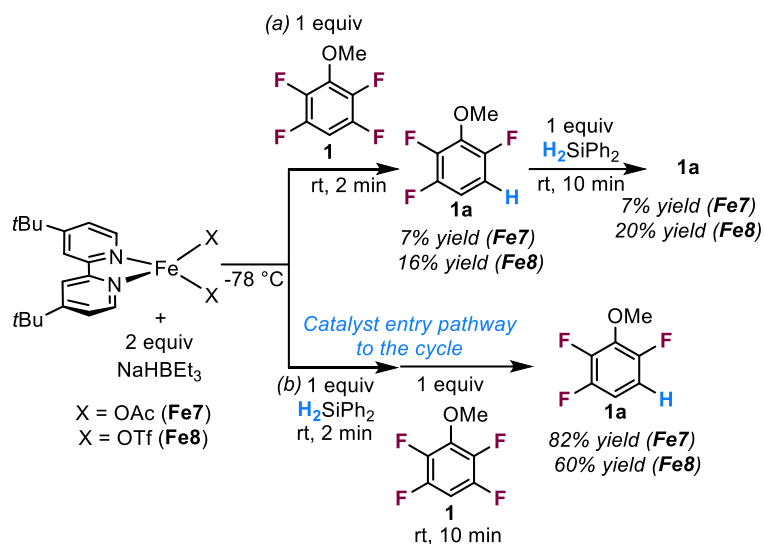


Scheme 4.5. Comparison of the reaction profiles (% **1**) for the HDF of **1** employing (i) **Fe7** at rt or (ii) at 40 °C, (iii) **Fe8** at rt with H_2SiPh_2 as H source or (iv) $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ at 80 °C with HBPIn as H source.

The comparison of the reaction profiles (% of **1**) for the HDF of **1** employing **Fe7** or **Fe8** to that employing our previously reported complex $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ *in situ* activated with NaHBEt_3 depicted in **Scheme 4.5**, supported the higher efficiency of **Fe7** and **Fe8** than $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$. **Fe8** achieved 94% conversion of **1** in 8 h under milder conditions (10 mol% and rt) whereas $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ achieved only 62% conversion during the same time but under harsher conditions (15 mol% and 80 °C). The ^{31}P NMR spectra of the catalytic reaction employing $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ as the precatalyst showed the disappearance of the signals attributed to the catalyst resting states and the emergence of unidentified deactivation products after 14 h, coinciding with a plateau in the conversion of **1**.⁵ Additionally, a signal attributable to free CyXantphos was observed after only 30 min, consistent with catalyst deactivation by ligand decooordination. In contrast, when **Fe8** was employed as the precatalyst, the conversion of **1** did not plateau, and the signals attributable to the catalyst resting states were present in the ^1H NMR spectrum after 24 h (full conversion of **1**). Remarkably, the ^1H NMR spectra of the catalytic reaction employing **Fe7** or **Fe8** as precatalysts did not show any signal attributable to decoordinated *t*^{Bu}bipy ligand up to 23.5 h, the catalyst resting-states being the only species present throughout the catalytic turnover, allowing to rule out catalyst deactivation by ligand decooordination. Therefore, the higher efficiency of **Fe7** and **Fe8** compared to $[\text{Fe}(\text{CyXantphos})\text{Cl}_2]$ can be attributed to the longer lifetime of the catalytically active species in the former systems. This enhanced longevity likely arises from the greater robustness of the five-membered chelate formed by the *t*^{Bu}bipy ligand relative to the eight-membered chelate formed by the CyXantphos ligand, which presumably stabilizes catalytic intermediates and suppresses catalyst deactivation by ligand dissociation.

4.2.3. Insights into the catalyst entry pathway into the cycle

Aiming to elucidate the catalyst entry pathway to the cycle, stoichiometric reactions were conducted (**Scheme 4.6**). When 2 equiv of NaHBEt_3 were added to THF-*d*₈ solutions of **Fe7** or **Fe8** at -78 °C followed by the addition of 1 equiv of **1**, the ^{19}F NMR spectrum supported the formation of **1a** in 7% yield (for **Fe7**) and 16% yield (for **Fe8**) (**scheme 4.6a**). Since the reaction of **1** with NaHBEt_3 resulted in the recovery of **1**, this result suggests that the reactions of **Fe7** or **Fe8** with NaHBEt_3 afforded a Fe-H complex capable of transferring the hydride to **1** to afford **1a** presumably generating a Fe-F complex as the byproduct. However, the putative Fe-H was not highly efficient in transferring the hydride, because **1a** was formed in low yield starting from either **Fe7** or **Fe8**. Addition of 1 equiv of H_2SiPh_2 to the reaction mixtures only increased the yield of **1a** to 20% (for **Fe8**) and did not result in an increase of the yield when **Fe7** was employed, suggesting that the putative Fe-F complex formed after hydride transfer to **1** did not react with H_2SiPh_2 to regenerate the active Fe-H. The low yields of **1a** in these reactions allow to rule out the reaction of the Fe-H with **1** as the catalyst entry pathway to the cycle.



Scheme 4.6. Single-turnover experiments involving addition of NaHBET₃ to the **Fe7** or **Fe8** precatalysts followed by addition of (a) **1** and H₂SiPh₂ and (b) H₂SiPh₂ and **1**.

Our attempts to isolate and characterize the Fe-H complex by reaction of **Fe8** with 2 equiv of NaHBET₃ failed due to the thermal instability of this complex at room temperature. Analogous results were obtained when the addition of NaHBET₃ to **Fe8** was conducted in the presence of PPh₃ or PMe₃ to stabilize the putative Fe-H, where mixtures of unidentified products were detected in the ³¹P and ¹H NMR spectra.

In contrast, when 1 equiv of H₂SiPh₂ was added to a solution of **Fe7** or of **Fe8** and 2 equiv of NaHBET₃ followed by the addition of 1 equiv of **1**, the ¹⁹F NMR spectrum showed signals attributable to **1a** formed in 82% yield (for **Fe7**) and 60% yield (for **Fe8**) (Scheme 4.6b). The formation of **1a** in higher yield than when **1** was added to the putative Fe-H complex before H₂SiPh₂ supports the reaction of the putative Fe-H with H₂SiPh₂ as the catalyst entry pathway to the cycle. Additionally, the ¹H NMR spectrum showed a diagnostic signal at -33.87 ppm after the addition of **1**, hinting that the catalyst resting-state observed in catalysis was formed upon addition of **1**. This entry pathway stands in contrast to that found for our previously reported system [Fe(^{Cy}Xantphos)Cl₂], where the putative Fe-H generated *in situ* by reaction of the precatalyst with NaHBET₃ reacted with the fluoroarene to enter the cycle, the putative Fe-F being formed as a byproduct being capable of regenerating the active Fe-H by reaction with HBPIn. Further efforts are ongoing in our laboratory to fully rationalize these differences as well as to identify and characterize the Fe complex responsible for C-F activation.

4.3. Conclusions

In conclusion, we have discovered the first Fe catalyst efficient for the hydrodefluorination of arenes at room temperature. The HDF of 2,3,5,6-tetrafluoroanisole afforded the highest TON reported to date for Fe HDF catalysts, rendering access to products from single and sequential HDF. The system also delivered superior TONs for the HDF of perfluorinated arenes at room temperature. Notably, its efficiency increased with temperature, enabling

access to products arising from four- and five-fold HDF of C₆F₆ under more forcing conditions. Mechanistic studies allowed to identify different diamagnetic Fe complexes as the resting-states for the sequential HDF cycles of 2,3,5,6-tetrafluoroanisole. The presence of a 4,4',*tert*-butyl-2,2'-bipyridine ligand in the catalyst was found to be key for the high efficiency of the system, the robustness of the 5-membered ring chelate preventing catalyst deactivation through ligand decoordination which resulted in a longer catalyst lifetime. Single-turnover experiments supported that the H₂SiPh₂ not only acted as the H source but also played a relevant role in generating the C-F activating species.

4.4. Experimental section

4.4.1. General considerations

All air- and moisture-sensitive manipulations were carried out using vacuum line, Schlenk and cannula techniques or in an MBraun inert atmosphere (argon) glovebox unless otherwise noted. All glassware was stored in a pre-heated at 200 °C oven prior to use. All glassware was cleaned using base (KOH, *i*PrOH) and acid (HCl (aq)) baths. All reported reaction temperatures correspond to external silicone oil bath temperatures. Room temperature (rt) was 23 °C. The solvents used for air- and moisture-sensitive manipulations were dried and deoxygenated using literature procedures.¹²

(Trifluoromethyl)benzene was dried over CaH₂, degassed by three freeze-pump-thaw cycles and distilled under vacuum prior to use. FeCl₂, Fe(OTf)₂, Fe(OAc)₂, 2,2'-bipyridine, 4,4'-Dimethyl-2,2'-bipyridine, 4,4'-Ditertbutyl-2,2'-bipyridine and 1,10-phenanthroline ligands, H₂SiPh₂, HBPIn, HSiEt₃ and HSi(OEt)₃ were purchased from commercial sources (Thermo Fisher Scientific, AmBeed and Sigma-Aldrich) and used without further purification. Complexes **Fe1**,⁷ **Fe2**,⁸ **Fe3**,⁹ **Fe4**,¹⁰ **Fe5**¹¹ and **Fe8**^{6a} were synthesized according to literature procedures.

¹H NMR spectra were recorded on either Varian 400 or 500 spectrophotometers operating at 400 MHz, and 500 MHz, respectively. ¹³C NMR spectra were recorded on Varian 400 or 500 spectrophotometers operating at 101 MHz and 126 MHz, respectively. ¹¹B NMR spectra were recorded on Varian 400 or 500 spectrometers with 128 MHz and 160 MHz frequencies. All the ¹¹B spectra reported are ¹H decoupled (¹¹B{¹H}). ¹⁹F NMR spectra were recorded on Varian 400 or 500 spectrometers with 376 MHz and 470 MHz frequencies. ²⁹Si NMR spectra were recorded on Varian 500 with 99 MHz frequency. All ¹H and ¹³C NMR chemical shifts are reported in ppm relative to SiMe₄ using the ¹H (chloroform-*d*: 7.26 ppm; benzene-*d*₆: 7.16 ppm) and ¹³C (chloroform-*d*: 77.16 ppm; benzene-*d*₆: 128 ppm) chemical shifts of the solvent as a standard. ¹H NMR data for diamagnetic compounds are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent, obsc = obscured), coupling constants (Hz), integration, assignment. ¹³C NMR data are reported as follows: chemical shift, number of protons attached to carbon (e. g. CH₂), assignment.

4.4.2. Procedure for synthesis of Fe4

Fe4 was synthesized by slightly modifying the procedure reported in the literature.¹⁰ A solution of bipyridine ligand (184.3 mg, 1.18 mmol) in 5 mL of THF was added dropwise to a THF (5 mL) solution of FeCl₂ (150 mg, 1.18 mmol) at room temperature. The resulting red solution was stirred for 16 hours at room temperature, and the volatiles were removed under vacuum. The red solid formed was washed with 15 mL (5 mL × 3) ether and **Fe4** was obtained as a red solid in 82% yield (267 mg). The ¹H NMR spectrum matched as previously reported.¹⁰

¹H NMR (500 MHz, CD₃CN, 25°C): δ 8.46 (d, 2H, py BiPy), 8.09 (s, 2H, py BiPy), 7.39 (s, 4H, py BiPy).

4.4.3. Procedure for synthesis of Fe6

A solution of 4,4'-Ditertbutyl-2,2'-bipyridine (318 mg, 1.18 mmol) in 5 mL of ethanol was added dropwise to an ethanol (5 mL) solution of FeCl₂ (150 mg, 1.18 mmol) at room temperature. The resulting red solution was stirred for 16 hours at 80°C and the volatiles were removed under vacuum. The red solid formed was washed with 15 mL (5 mL × 3) ether and **Fe6** was obtained as a red solid in 80% yield (372 mg).

¹H NMR (500 MHz, CD₃CN, 25°C): δ 8.39 (s, 2H, py ^tBuBiPy), 7.37 (s, 2H, py ^tBuBiPy), 7.20 (s, 2H, py ^tBuBiPy), 1.36 (s, 18H, ^tBuBiPy).

4.4.4. Procedure for synthesis of Fe7

A solution of 4,4'-Ditertbutyl-2,2'-bipyridine (230 mg, 0.86 mmol) in 5 mL of THF was added dropwise to a THF (5 mL) solution of Fe(OAc)₂ (150 mg, 0.86 mmol) at room temperature. The resulting solution was stirred for 16 hours at 60°C, followed by filtration. The volatiles were removed from the filtrate in vacuo resulting in the formation of maroon-pink solid. The maroon-pink solid formed was washed with 15 mL (5 mL × 3) hexane and **Fe7** was obtained in 87% yield (332 mg).

¹H NMR (500 MHz, CD₃CN, 25°C): δ 8.49 (s, 2H, py ^tBuBiPy), 7.36 (s, 2H, py ^tBuBiPy), 7.15 (s, 2H, py ^tBuBiPy), 2.02 (bm, 6H, -OAc), 1.39 (s, 18H, ^tBuBiPy).

4.4.5. General procedure for hydrodefluorination of fluoroarenes.

In an argon-filled glovebox a J. Young flask was charged with a magnetic stir bar and the reagents in the following order: THF (0.40 mL), **Fe8** (9 mg, 0.015 mmol), fluoroarene (0.300 mmol), H₂SiPh₂ (139 μL, 0.750 mmol) and NaHBET₃ (10 μL of a 1 M solution in THF, 0.010 mmol). The reaction was stirred at room temperature for 24 hours and then exposed to air. (Trifluoromethyl)benzene (10 μL, 0.106 mmol) was added as an internal standard and the crude reaction was analyzed by ¹⁹F NMR spectroscopy without additional purification.

4.4.6. General procedure for NMR monitoring of hydrodefluorination of **1** using H₂SiPh₂, employing Fe7 or Fe8 as catalyst.

2,3,5,6-tetrafluoroanisole (**1**) (42 μ L, 0.300 mmol) was added to a solution of respective iron catalyst (0.030 mmol) in THF-*d*₈ (0.30 mL) followed by the addition of H₂SiPh₂ (195 μ L, 1.050 mmol), (trifluoromethyl)benzene (10 μ L, 0.082 mmol) as internal standard and NaHBET₃ (60 μ L of a 1 M solution in THF, 0.020 mmol)) in a J. Young NMR tube in an argon filled glovebox. The tube was sealed and brought out of the glovebox. The reaction was monitored by ¹H and ¹⁹F NMR spectroscopy at room temperature for given time.

4.5. Appendix

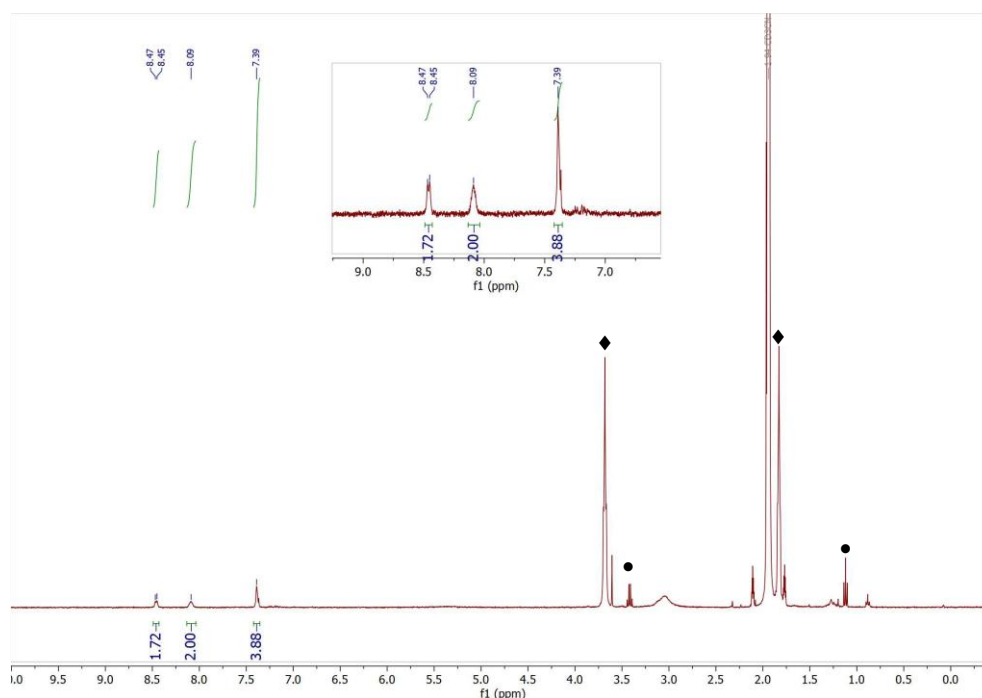


Figure 4.3. ¹H NMR (500 MHz, CD₃CN, 23 °C) spectra for **Fe4**. ♦ = residual THF, • = residual ether.

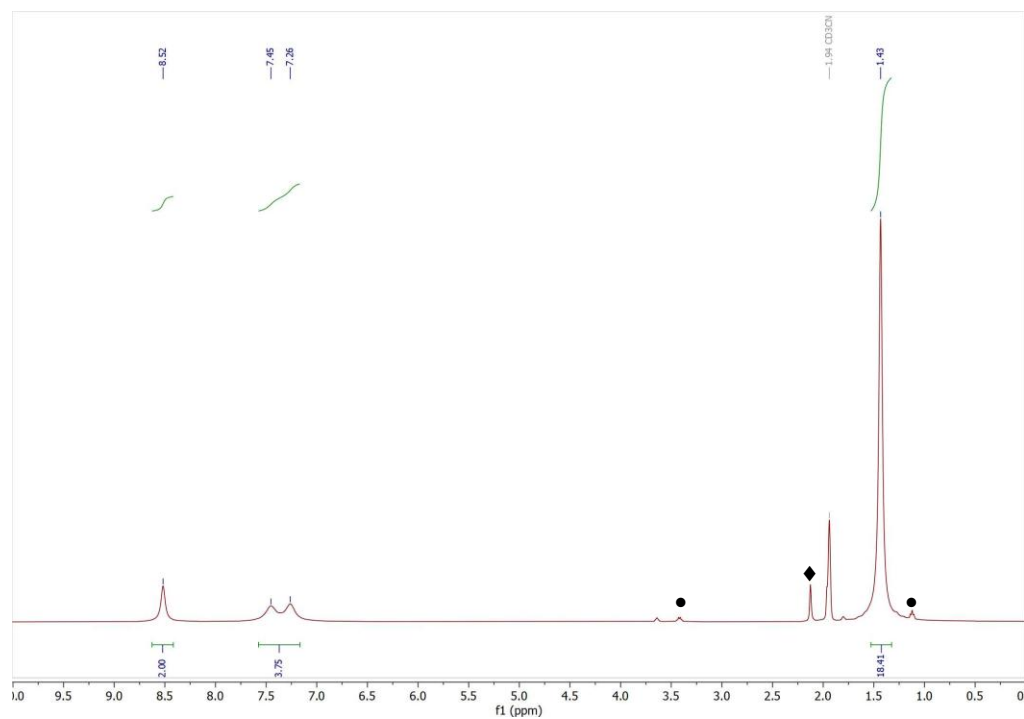


Figure 4.4. ^1H NMR (500 MHz, CD_3CN , 23 $^\circ\text{C}$) spectra for **Fe6**. ♦ = water, • = residual ether.

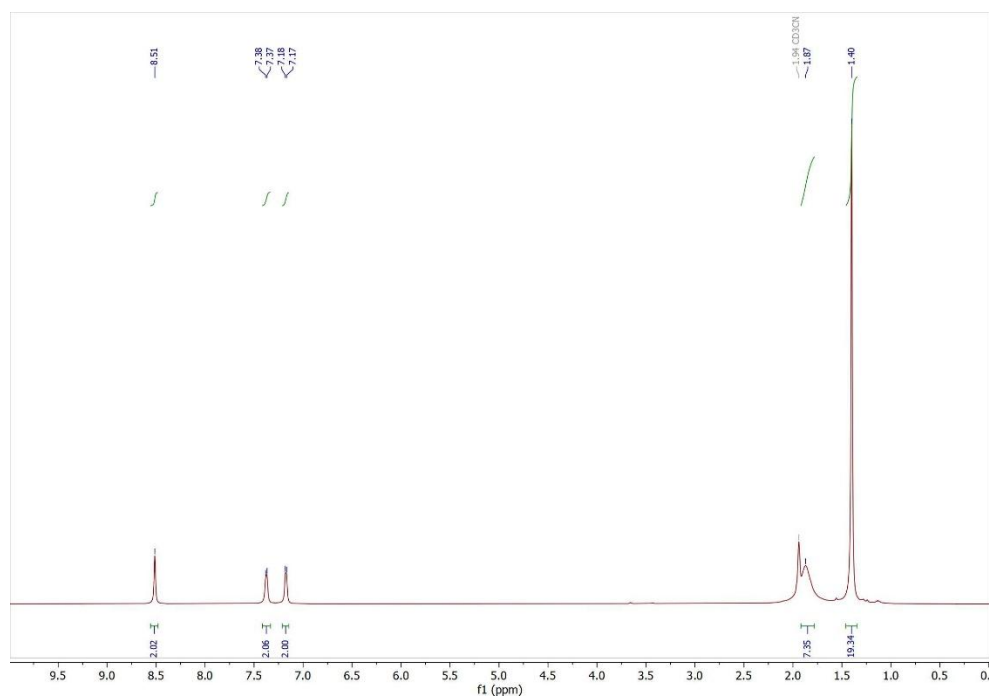


Figure 4.5. ^1H NMR (500 MHz, CD_3CN , 23 $^\circ\text{C}$) spectra for **Fe7**.

4.5.1. NMR monitoring of hydrodefluorination of **1 using H₂SiPh₂, Fe7 as catalyst at room temperature.**

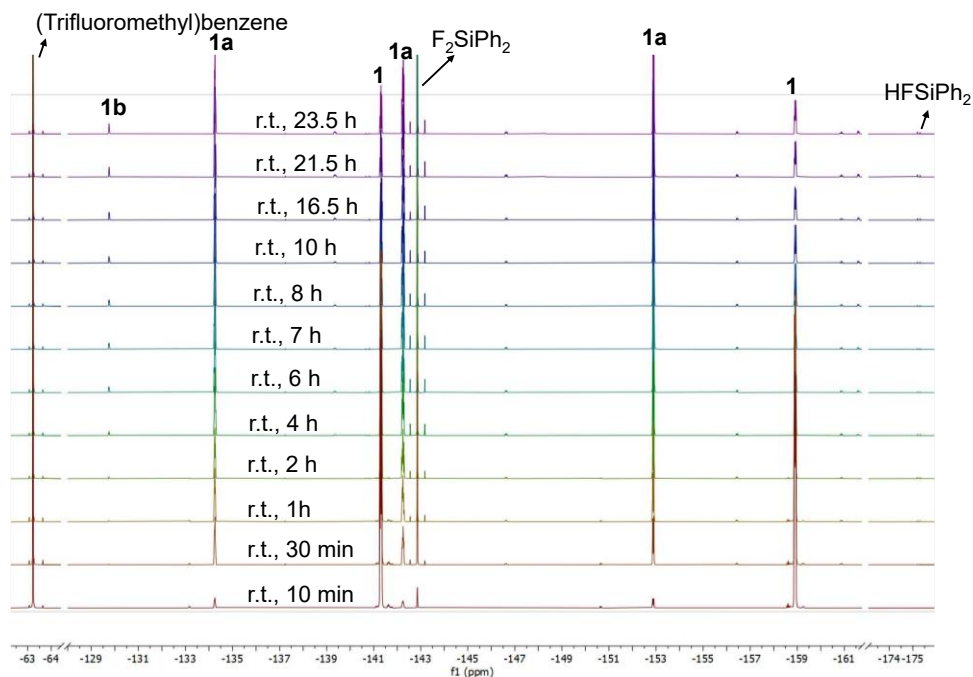


Figure 4.6. ¹⁹F NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe7** at room temperature in THF-d₈, using (trifluoromethyl)benzene as internal standard.

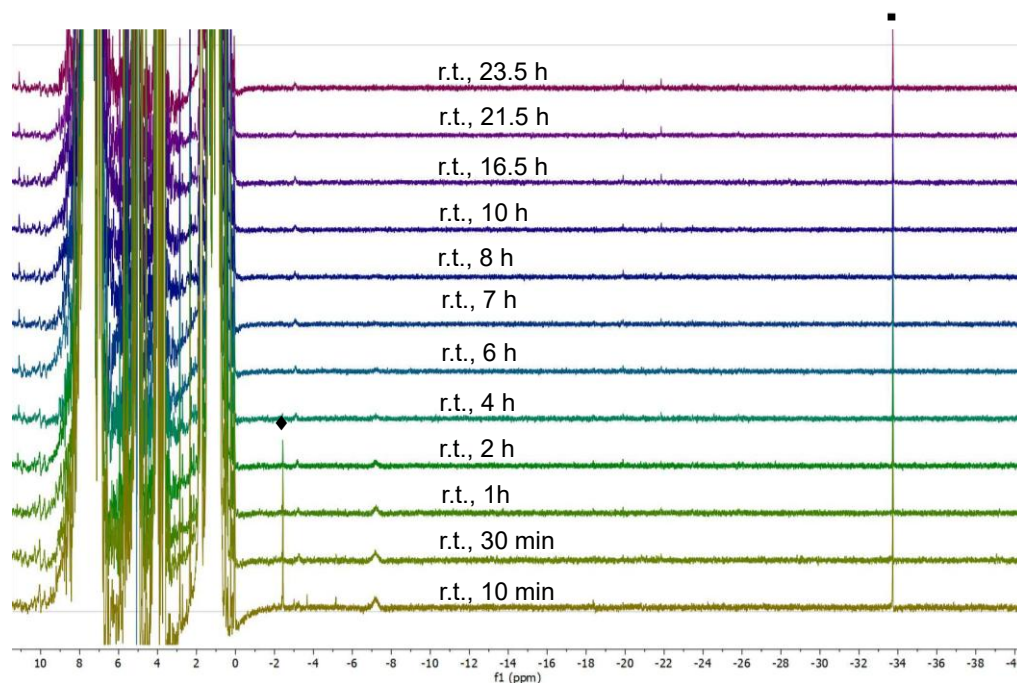


Figure 4.7. Wide-range ppm ^1H NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe7** at room temperature in THF-d_8 , using (trifluoromethyl)benzene as internal standard. ♦ = proposed catalyst resting-state for the first HDF cycle. ▪ = proposed catalyst deactivation or off-cycle species.

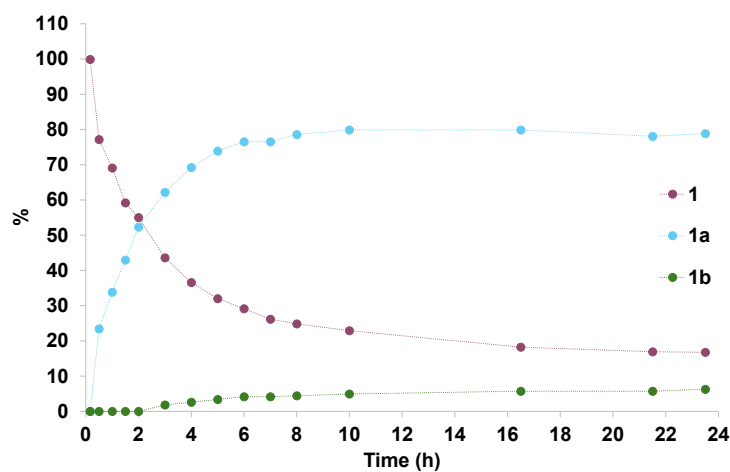


Figure 4.8. Reaction profile of hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe7** at room temperature in THF-d_8 , using (trifluoromethyl)benzene as internal standard.

4.5.2. NMR monitoring of hydrodefluorination of **1 using H_2SiPh_2 , Fe7 as catalyst 40 °C.**

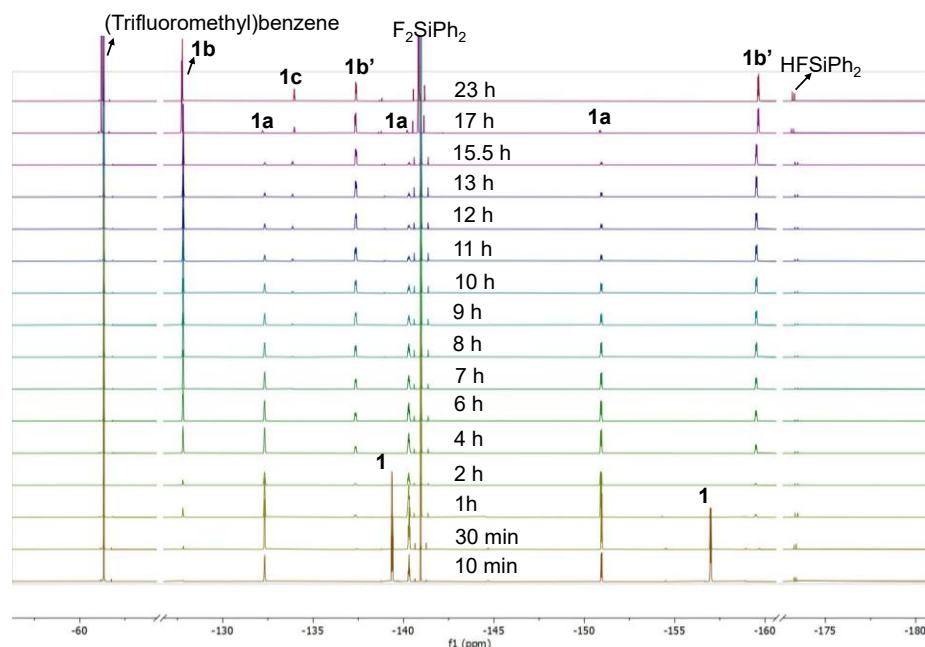


Figure 4.9. ^{19}F NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by Fe7 at 40 °C in THF-d_8 , using (trifluoromethyl)benzene as internal standard. The spectra were recorded at room temperature after heating the sample at 40 °C for required time.

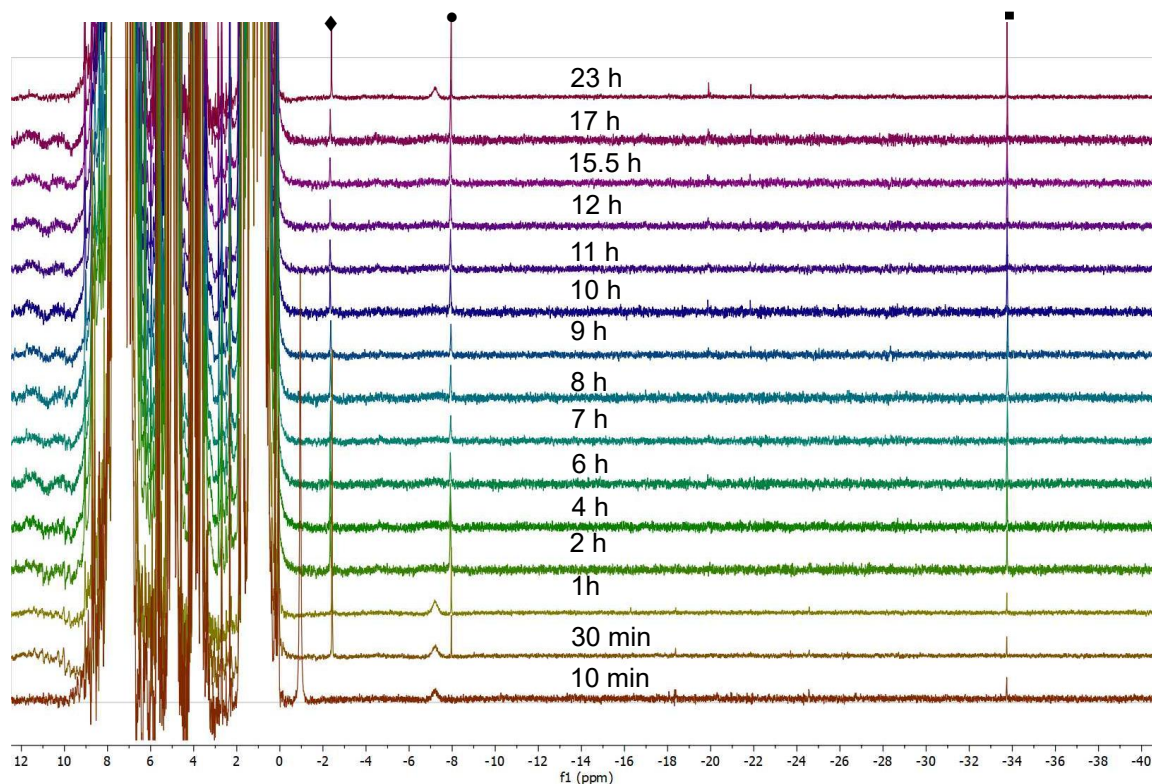


Figure 4.10. Wide-range ppm ^1H NMR spectra of the hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe7** at 40 °C in THF- d_8 , using (trifluoromethyl)benzene as internal standard. The spectra were recorded at room temperature after heating the sample at 40 °C for required time. ♦ = proposed catalyst resting-state for the first HDF cycle. ● = proposed catalyst resting-state for the second HDF cycle ■ = proposed catalyst deactivation or off-cycle species.

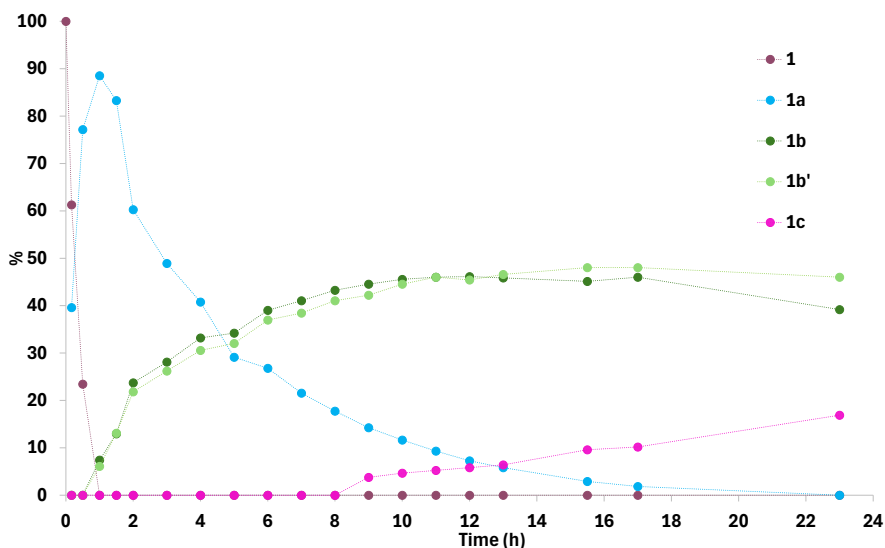


Figure 4.11. Reaction profile of hydrodefluorination of **1** using diphenylsilane, catalyzed by **Fe7** at 40 °C in THF- d_8 , using (trifluoromethyl)benzene as internal standard.

4.6. References

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Chemoselective C(sp)-H borylation of terminal alkynes catalyzed by a bis(N-heterocyclicsilylene) manganese complex

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Triethoxysilane-Catalyzed Single and Sequential Regioselective Hydroboration of Terminal Alkynes: Sustainable Access to E-Alkenylboronate and Alkyl Gem-Diboronate Esters by Non-Covalent Interactions



Author: Harleen Kaur, Himani Ahuja, Rebeca Arevalo

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