Über die Boran-katalysierte Hydrierung von Alkinen und die Reaktion elektrophiler Borane mit Dienen

Inauguraldissertation zur Erlangung des Doktorgrades der Naturwissenschaftlichen Fachbereiche

im Fachgebiet Organische Chemie der Justus-Liebig-Universität Gießen

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Gießen 2024

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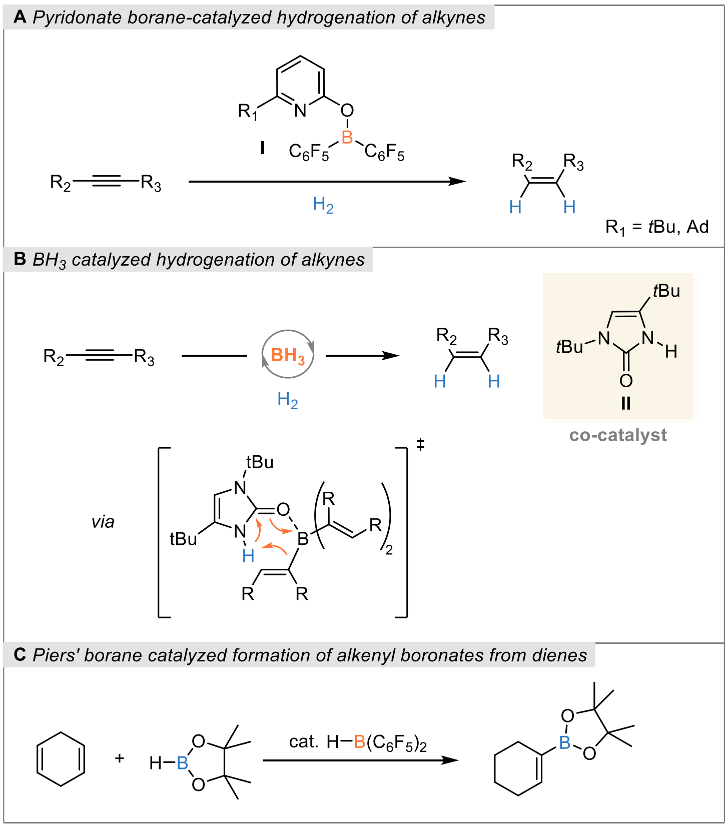
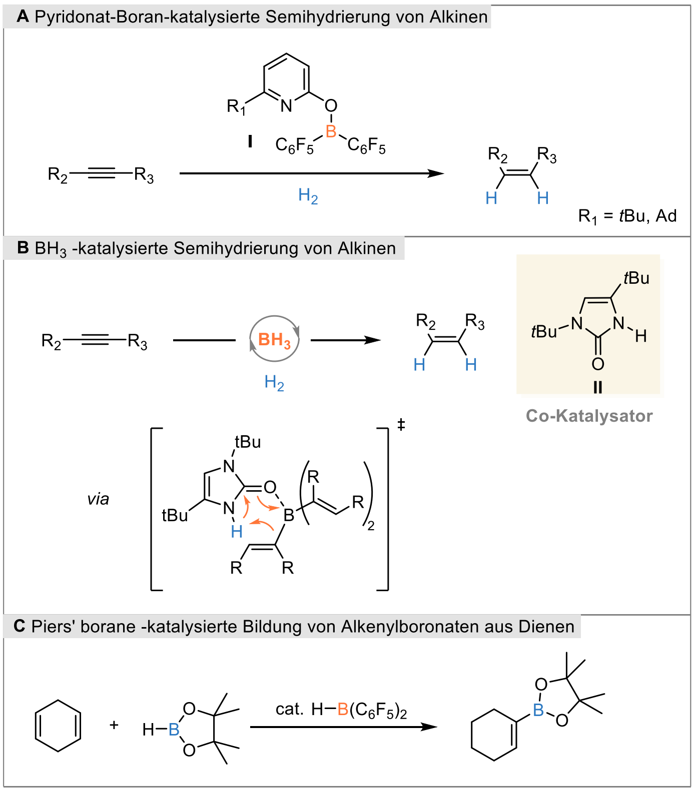
1 Abstract

In 2018, Gellrich and co-workers discovered a pyridonate borane (**I**), which represents an intramolecular frustrated Lewis pair (FLP). This compound can activate H_2 under mild conditions upon which a pyridone-borane complex is obtained that can dissociate to release free $HB(C_6F_5)_2$. This concept has been utilized in a variety of catalytic reactions. In this work, we utilized **I** to catalyze the (*Z*)-selective semihydrogenation of alkynes. By increasing the steric demand of the substituent at the pyridone we were also able to improve the yield of the reaction. Further investigations of structurally related catalysts revealed that the simplest borane, BH_3, in combination with an appropriate co-catalyst (**II**), can efficiently hydrogenate alkynes (*Z*)-selectively. Experimental and computational studies showed that a key step involves the formation of a tris(alkenyl)borane, which, with the help of the co-catalyst, undergoes protodeborylation to release the (*Z*)-alkene. Additionally, the reaction between the electrophilic bis(pentafluorophenyl)borane (Piers' borane) and both cyclic and acyclic dienes was investigated. It was found that, instead of the expected hydroboration product, an alkenylborane is formed. These compounds can react with pinacolborane in a transborylation reaction to yield alkenyl boronates, with the bis(pentafluorophenyl)borane catalyst being regenerated in the process.



2 Zusammenfassung

Gellrich und Mitarbeiter entdeckten 2018 ein Pyridonat Boran (**I**), welches ein intramolekulares frustriertes Lewis-Paar (FLP) darstellt. Dieses ist in der Lage, bereits unter milden Bedingungen H_2 zu aktivieren, wobei ein Pyridon-Boran-Komplex erhalten wird, der durch Dissoziation freies Boran freisetzen kann. Dieses Konzept wurde für verschiedene katalytische Reaktionen verwendet. In dieser Arbeit wurde **I** als Katalysator für die (*Z*)-selektive Semihydrierung von Alkinen eingesetzt. Die Ausbeute der Reaktion konnte dadurch verbessert werden, dass der sterische Anspruch des Substituenten am Pyridon erhöht wurde. Weitere strukturell verwandte Katalysatoren wurden untersucht, wobei gefunden wurde, dass das einfachste Boran, BH_3, in Kombination mit einem geeigneten Co-Katalysator (**II**) in der Lage ist, Alkine effizient (*Z*)-selektiv zu Alkenen zu hydrieren. Experimentelle und computerchemische Untersuchen zeigten, dass ein Schlüsselschritt die Bildung eines Tris(alkenyl)borans ist, welches mithilfe des Co-Katalysators in einer Protodeborylierung das (*Z*)-Alken freisetzt. Zusätzlich wurde die Reaktion zwischen dem elektrophilen Bis(pentafluorphenyl)boran (Piers' Boran) und zyklischen und azyklischen Dienen untersucht. Es zeigte sich, dass sich anstatt des erwarteten Hydroborierungsprodukts ein Alkenylboran bildet. Diese Verbindungen sind in der Lage, mit Pinakolboran in einer Transborylierung zu Alkenylboronaten zu reagieren, wobei der Katalysator Bis(pentafluorphenyl)boran regeneriert wird.



3 Einleitung

Im Jahr 1835 prägte der schwedische Chemiker Jöns Jakob Berzelius den Begriff „Katalyse“, um chemische Reaktionen zu beschreiben, bei denen der Verlauf durch eine Substanz beeinflusst wird, die bei der Reaktion nicht verbraucht wird und somit scheinbar nicht an der Reaktion beteiligt ist.[1] Dieses Phänomen wurde bis zum Ende des 19. Jahrhunderts heftig diskutiert, bis der deutsche Chemiker Wilhelm Ostwald die heute allgemein anerkannte Definition vorschlug: „Ein Katalysator ist eine Substanz, die die Geschwindigkeit einer chemischen Reaktion erhöht, ohne Teil der Endprodukte zu sein.“ Der Katalysator wirkt also, indem er mit den an der Reaktion beteiligten Molekülen Intermediate bildet, die einen alternativen, schnelleren Weg zum Produkt ermöglichen.

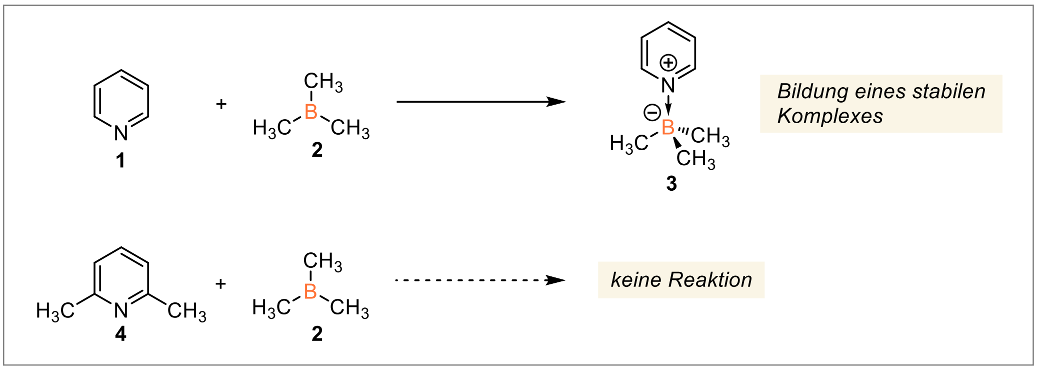
Schon frühe Beispiele bedeutender katalytischer Prozesse beinhalten die Aktivierung von Wasserstoff. Dazu zählen der Sabatier-Prozess, also die Bildung von Methan aus Wasserstoff und CO_2, aber auch das Haber-Bosch Verfahren. Das Haber-Bosch Verfahren ist bis heute einer der bedeutendsten katalytischen Prozesse, der für 1,4% der weltweiten CO_2 Emissionen und ca. 1% des globalen Energieverbrauchs verantwortlich ist.[2] Bei diesem Prozess werden Stickstoff und Wasserstoff über einem Eisenkatalysator unter Bildung von Ammoniak zur Reaktion gebracht. Im Zusammenhang mit diesem Verfahren wurden bereits drei Nobelpreise verliehen: 1918 an den Chemiker Fritz Haber für die grundlegende Entwicklung, 1931 an Carl Bosch für die technische Umsetzung und an Gerhard Ertl, der erst 2007 den Mechanismus der Ammoniakbildung vollständig aufklärte.[3] Durch die nun mögliche industrielle Herstellung von Stickstoff-Dünger trägt das Haber-Bosch Verfahren heute noch signifikant dazu bei, einen Großteil der Weltbevölkerung zu ernähren. Schätzungen zufolge sind 40% des Stickstoffs im menschlichen Körper durch das Haber-Bosch Verfahren aus N_2 generiert worden.[4] Hierbei handelt es sich um einen heterogen katalysierten Prozess, für diese Arbeit ist insbesondere die homogene Katalyse relevant. Es wurden eine ganze Reihe von homogenen katalytischen Konzepten mit dem Nobelpreis für Chemie ausgezeichnet, darunter Metathese-Reaktionen im Jahr 2005[5], Kreuzkupplungen 2010[6], sowie erst 2021 die asymmetrische Organokatalyse.[7] Die enantioselektiven Hydrierungen, für die 2001 Noyori und Knowles, zusammen mit Sharpless, den Nobelpreis für Chemie erhielten, stellten ebenfalls einen großen Meilenstein in der Entwicklung Übergangsmetall-katalysierter Reaktionen dar.[8] Die meisten Katalysatoren für Hydrierungen basieren auf Edelmetallen wie Rh, Ir oder Pd, die teuer und selten sind, und vor allem wegen ihrer Toxizität gemieden werden.[9] Verantwortlich für die Reaktivität homogener Übergangsmetallkatalysatoren ist der geringe Abstand ihrer Grenzorbitale, also des höchsten besetzen Molekülorbitals (HOMO) und des niedrigsten unbesetzten Molekülorbitals (LUMO), wodurch diese gleichzeitig als Elektronenpaardonoren und als Elektronenpaarakzeptoren fungieren können. Diese können dann mit Wasserstoff in einer oxidativen Addition reagieren, wobei das H_2 Molekül heterolytisch am Metallzentrum gespalten wird und im Anschluss auf das Substrat übertragen werden kann. Dieses Verhalten von Übergangsmetallen versuchte man durch die Verwendung reaktiver Hauptgruppenverbindungen nachzuahmen.[10]

Durch die Verwendung eines Alkylaminocarbens konnte die Gruppe von Bertrand das H_2 Molekül an einem einzelnen Kohlenstoff spalten, was hier ebenfalls durch den geringen HOMO/LUMO-Abstand des verwendeten Carbens ermöglicht wird.[11] Ein weiteres faszinierendes Beispiel sind die neu aufgekommenen Arbeiten über die Redoxchemie geometrisch eingeschränkter Phosphine. Obwohl bereits seit den 1980ern bekannt, wurde diese Chemie kürzlich allen voran von der Gruppe von Radosevich wiederentdeckt.[12] Durch geometrisch einschränkende Liganden wird das tetraedrische P(III) in eine T-förmige Geometrie gezwungen, was zu einer Verkleinerung der HOMO/LUMO-Lücke führt. Dies ermöglicht die oxidative Additionen am Phosphor und es konnte kürzlich H_2 an einem einzelnen Phosphoratom gespalten werden.[13] Es konnten eine Vielzahl katalytischer Reaktionen realisiert werden, die auf einem P(III)/P(V)-Redoxpaar basieren.[14] Im Falle von Übergangsmetallkomplexen und den eben genannten metallfreien Beispielen sind HOMO und LUMO an demselben Atom lokalisiert. Es gibt jedoch Beispiele, bei denen die Grenzorbitale an unterschiedlichen Atomen lokalisiert sind und dadurch ambiphilen Charakter aufweisen. Diese sogenannten frustrierten Lewis-Paare (FLPs) sind ebenfalls in der Lage H_2 heterolytisch zu spalten, wodurch eine ganze Reihe neue, metallfreie katalytische Reaktionen zugänglich sind.[15–17] Im Folgenden wird detailliert auf die Chemie von FLPs eingegangen.[18]

Im Rahmen dieser Promotion wurden FLP-katalysierte Semihydrierungen von Alkinen untersucht, wobei eine Reihe neuer Katalysatorsysteme entwickelt wurde. Darüber hinaus waren Reaktionen elektrophiler Borane mit Allenen und Dienen Gegenstand der im Rahmen dieser Arbeit durchgeführten Forschung, wobei ein katalytisches Protokoll entwickelt werden konnte, um aus Dienen und Borsäureestern Alkenylboronate herzustellen, eine Klasse von Verbindungen, die sonst über die katalytische Hydroborierung von Alkinen durch Boronsäureester zugänglich sind.

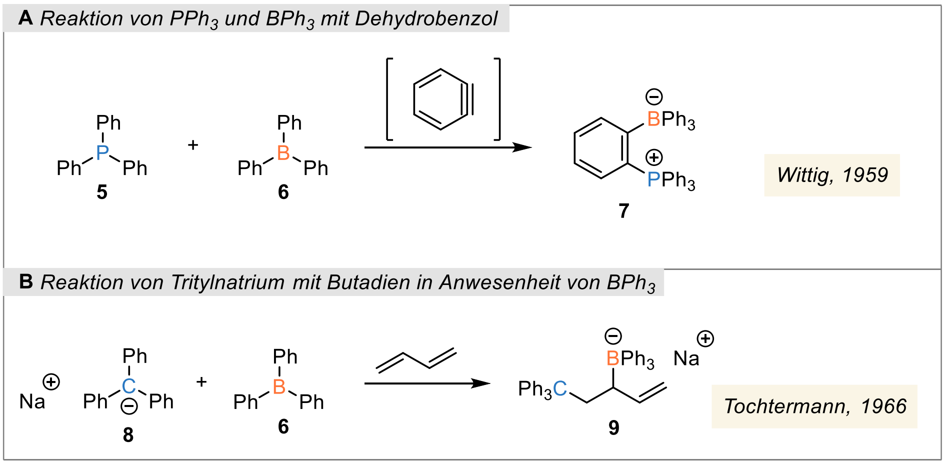
3.1 Frustrierte Lewis–Paare

Im Jahre 1923 wurden Säuren und Basen von J. N. Brönsted als Stoffe definiert, die in der Lage sind Protonen abzuspalten und anzulagern.[19] Im selben Jahr veröffentlichte G. N. Lewis eine erweiterte Definition, wobei Säuren als Elektronenakzeptoren, Basen als Elektronendonoren beschrieben werden.[20] Diese Konzepte sind noch heute Grundsätze in der Chemie und sind wichtig für das Verständnis chemischer Reaktionen im allgemeinen.[19–21] Anfang der 1940er Jahre berichtete H. C. Brown eine Reihe interessanter Beobachtungen zu Lewis Säure–Base Reaktionen.[22] Während Pyridin **1** mit Trimethylboran **2** ein stabiles Lewis Addukt bildet, findet keine Assoziation zwischen Lutidin **4** und Trimethylboran **2** statt (Schema 1).



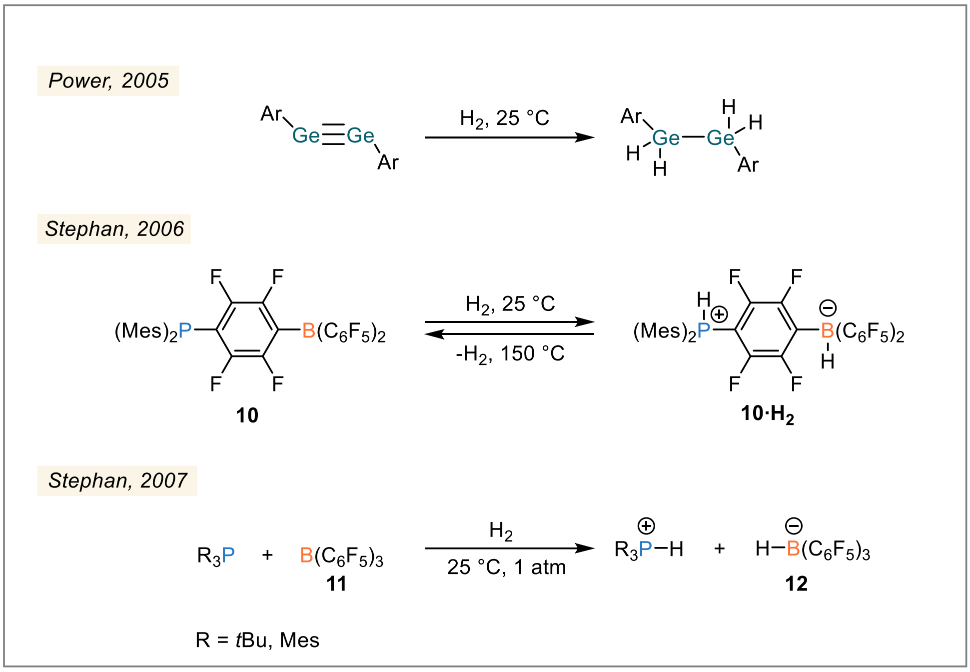
Schema 1. Reaktion von Trimethylboran mit Pyridin und Lutidin nach Brown.

Das sterisch weniger anspruchsvolle Bortrifluorid hingegen reagiert sowohl mit Pyridin als auch mit Lutidin. Brown begründete dies mit der sterischen Abstoßung der *ortho*-methyl Gruppen des Lutidins **4** mit den Methylgruppen des Trimethylborans **2**. Die Reaktivität dieser Komplexe wurde aber nicht weitergehend untersucht. Im Jahre 1959 beschrieb G. Wittig die Reaktion von *in situ* gebildetem Dehydrobenzol mit Triphenylphoshin **5** und Triphenylboran **6** als Lewis-Säure/Base-Paar (Schema 2A). Das hierbei beobachtete Betain **7** resultiert offenbar aus der Addition des Dehydrobenzols an das Triphenylboran **6** und einem anschließendem nukleophilem Angriff des Triphenylphosphins.[23] Einige Jahre später beschrieb Tochtermann Reaktionen mit Triphenylboran **6** und Tritylnatrium **8**.[24] Die Kombination dieser beiden Verbindungen bezeichnete er als antagonistisches Lewis-Base/Lewis-Säure-Paar, die nicht miteinander, aber mit einem geeigneten Reaktionspartner in einem kooperativen Modus reagieren.[25] So initiiert Tritylnatrium **8** die anionische Polymerisation von Butadien, in Anwesenheit von Triphenylboran wird jedoch das anionische Intermediat abgefangen und das Addukt **9** wird gebildet (Schema 2B).



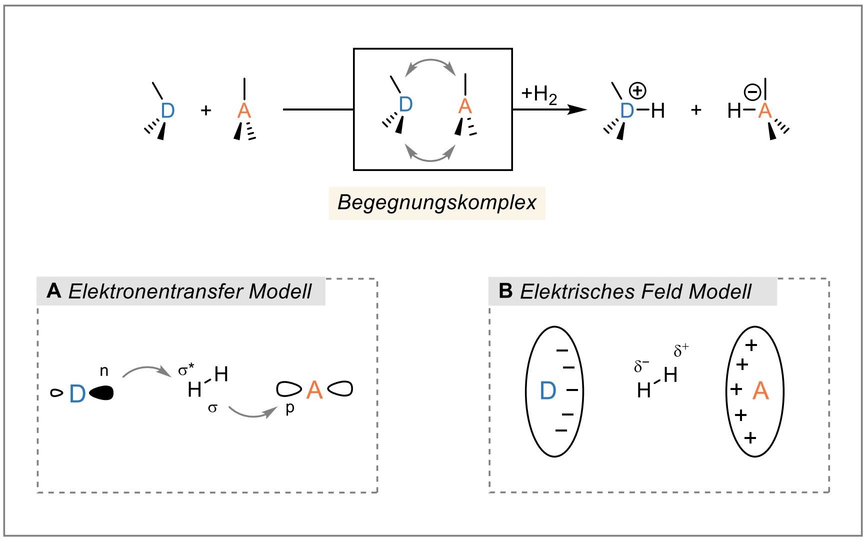
Schema 2. Frühe Beobachtungen zur kooperativen Reaktivität von Lewis-Säure/Base-Paaren.

Diese frühen Beobachtungen zeigten, dass bei sterisch anspruchsvollen Lewis-Paaren eine Adduktbildung verhindert wird und dadurch die Reaktivität der Einzelkomponenten erhalten bleibt. Erst 40 Jahre nach Tochtermanns Bemerkungen zum „antagonistischen Paar“ untersuchte D. W. Stephan intramolekulare Lewis-Säure/Lewis-Base-Paare, bei denen durch räumliche Separation eine gegenseitige Neutralisierung, wie im Falle klassischer Lewis-Paare, ausgeschlossen ist.[26] Bereits einige Jahre zuvor wurden ambiphile Reagenzien beschrieben, die sowohl ein Lewis-basisches als auch ein Lewis-saures Zentrum aufweisen.[27] Es zeigte sich, dass das Zwitterion **10·H₂** bei erhöhter Temperatur Wasserstoff freisetzt und das Phosphinoboran **10** bildet (Schema 3). Bemerkenswerterweise ist **10** bereits unter äußerst milden Bedingungen dazu in der Lage, H_2 heterolytisch zu spalten und das Zwitterion **10·H₂** zurückzubilden. Ein Jahr zuvor stellte P. Power ein Germanium-Alkin-Analogon vor, das in der Lage ist, Wasserstoff irreversibel zu spalten, das FLP **10** ist jedoch das erste metallfreie System, für das eine reversible Wasserstoffaktivierung beobachtet wurde.[28]



Schema 3. Frühe Beispiele für die H_2-Aktivierung durch Hauptgruppenverbindungen.

Die Entdeckung, dass bestimmte Kombinationen von Lewis-Säuren und Lewis-Basen aufgrund sterischer Hinderung keine dative Bindung ausbilden können, führte zur Prägung des Begriffs der „frustrierten Lewis-Paare“ (FLPs)[15,29] und förderte in den darauffolgenden Jahren die Entwicklung einer Vielzahl von intramolekularen[30] und intermolekularen[31] Systemen, die eine vergleichbare Reaktivität aufweisen. Schon früh versuchten Forschungsgruppen den Mechanismus der Wasserstoffaktivierung durch FLPs zu verstehen und aufzuklären. Arbeiten dazu wurden von den Gruppen von Pápai und Grimme veröffentlich.[32–37] Computerchemische und später auch experimentelle Untersuchungen[38] zeigten, dass der Bindungsaktivierung durch FLPs eine Präorganisation des Lewis-Paares vorausgeht. Dieser sogenannte Begegnungskomplex wird durch dispersive Wechselwirkungen der Substituenten stabilisiert (Schema 4).[32,35] Pápai beschreibt dabei die Bindungsaktivierung durch einen simultanen Elektronentransfer, der dem Dewar-Chatt-Duncanson Modell bei der Bindungsaktivierung durch Übergangsmetallkomplexe ähnelt (Schema 4A).[39] Im Falle der FLPs findet eine n→σ* Wechselwirkung des freien Elektronenpaares der Lewis-Base (D, Donor) in das antibindende σ*-Orbital des H_2-Moleküls statt. Außerdem wechselwirkt das bindende σ-Orbitals des H_2-Moleküls mit dem freien p-Orbital der Lewis-Säure (A). Das von Grimme aufgestellte Modell beschreibt ein durch das FLP aufgebautes elektrisches Feld.[35,36] Dieses Feld polarisiert das H_2 Molekül und ist in der Lage, dieses barrierefrei zu spalten (Schema 4B). Das Auftreten einer Aktivierungsbarriere wird durch das Eintreten des H_2 Moleküls in die Kavität des FLPs erklärt, was mit einer geometrischen Verzerrung des Begegnungskomplexes einhergeht.[36]

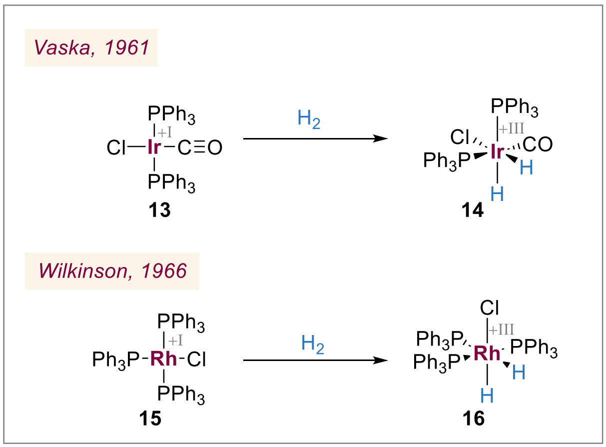


Schema 4. Mechanistische Modelle zur Aktivierung von Wasserstoff durch FLPs.

Jedoch zeigte Pápai in einer darauffolgenden Studie für eine Reihe klassischer FLPs, dass in den untersuchten Fällen die Stärke des elektrischen Feldes nicht ausreicht, um H_2 zu spalten.[40] Eine neuere Studie zeichnet jedoch ein differenziertes Bild und besagt, dass eine elektrostatische Polarisation der σ-Elektronen des H_2-Moleküls durch das FLP eine wichtige Voraussetzung für einen simultanen Elektronenübertrag nach dem Elektronentransfermodell darstellt.[41] Seit ihrer Entdeckung wurden FLPs zur Aktivierung einer Vielzahl kleiner Moleküle eingesetzt, neben H_2 auch SO_2,[42] NO,[43] N_2O,[43] CO_2,[44] oder auch terminale Alkine.[45] Auch Ringöffnungen von Heterozyklen und Cyclopropanen, sowie die Spaltung von Disulfiden wurden durch FLPs realisiert.[46]

3.2 Hydrierungen durch metallhaltige und metallfreie Systeme

Hydrierung beschreibt die Addition von Wasserstoff an ein ungesättigtes Substrat. Dieser Prozess läuft nicht spontan ab und es bedarf eines heterogenen oder homogenen Katalysators. Bereits im frühen 19. Jahrhundert nutze J. W. Döbereiner einen Platinschwamm, um Wasserstoff zu spalten und so kontrolliert mit Sauerstoff zur Reaktion zu bringen, woraus das Döbereiner Feuerzeug entstand.[47] Die Hydrierung von Kohlenwasserstoffen nahm jedoch mit Sabatier ihren Anfang, der erkannte, dass Ethen in Anwesenheit von fein verteiltem Nickel mit Wasserstoff reagiert.[48] Daraus wurde der Sabatier Prozess entwickelt, wofür ihm 1912, zusammen mit Grignard, der Nobelpreis für Chemie verliehen wurde.[49] Die ersten homogen katalysierten Hydrierungen wurden von Calvin und Iguchi beschrieben.[50,51] Calvin beobachtete im Jahre 1938, dass Kupferacetat-Lösungen in Anwesenheit von Wasserstoff organische Substrate wie *p*-Benzochinon reduzieren.[50] Ähnliches Verhalten beobachtete Iguchi mit Rhodium-haltigen wässrigen Lösungen.[51] Eine Voraussetzung für die Wasserstoffaktivierung durch späte Übergangsmetalle wie Ir, Rh oder Ru, ist die oxidative Addition an das Metallzentrum. Einige frühe Studien dazu wurden in den 1960ern von Vaska und Wilkinson veröffentlicht (Schema 5).[52] Wilkinson studierte den Mechanismus und die katalytische Aktivität dieser Komplexe ausführlich. Der Wilkinson-Katalysator **15** ($RhCl(PPh_3)_3$) lässt sich leicht aus $RhCl_3{\cdot}3H_2O$ und PPh_3 in EtOH herstellen, und zeigt außerordentliche und für diese Zeit beispiellose katalytische Aktivität und Selektivität bei der Hydrierung von Olefinen, meist bei Raumtemperatur und Atmosphärendruck.



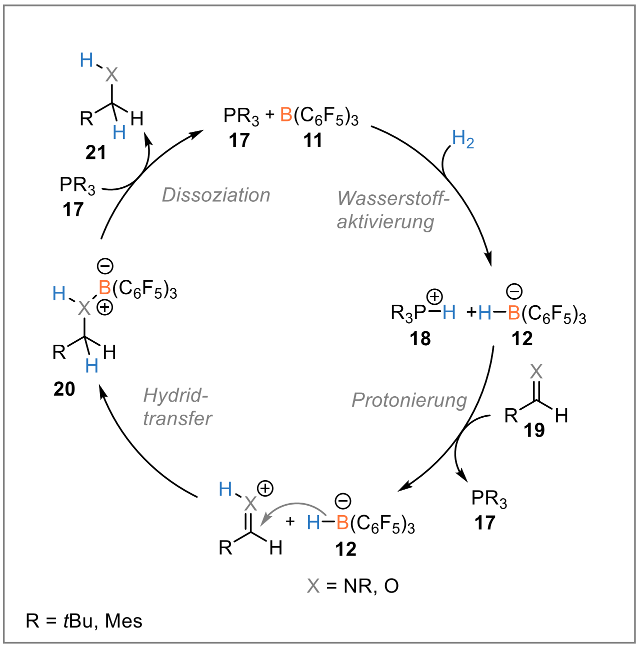
Schema 5. Beispiele früher Hydrierungskatalysatoren.

Dem bemerkenswerten Erfolg dieses Katalysators folgte die Verwendung chiraler Phosphine als Liganden, was wiederum die Geburt der katalytischen enantioselektiven Hydrierung darstellte und zu bahnbrechenden Beiträgen der Gruppen Knowles, Horner und anderer führte.[53–55]

Erste Beobachtungen zur metallfreien Hydrierung ungesättigter Substrate existieren schon seit den 1960er Jahren.[56] Aromatische Substrate konnten auch durch eine Reihe von Supersäuren bei hohen Temperaturen und Drücken reduziert werden.[57] Auch eine Kombination von $NaBH_4/I_2$ wurde auch als Katalysator für Hydrierungen eingesetzt.[58]

Erst die Entdeckung, dass bestimmte Kombinationen sterisch anspruchsvoller Lewis-Basen und Lewis-Säuren in der Lage sind, unter milden Bedingungen reversibel Wasserstoff zu aktivieren, führte zur Entwicklung einer Vielzahl metallfreier katalytischer Hydrierungen.[15,59–62] Wie bereits im vorherigen Kapitel beschrieben, entsteht bei der H_2-Aktivierung durch FLPs eine zwitterionische Spezies, die aus einem Phosphonium-Ion und einem Borhydrid besteht. Dies prädestiniert frustrierte Lewis-Paare als Katalysator zur Hydrierung polarer, ungesättigter Substrate, wie Imine[63], Enamine[64], Silyl

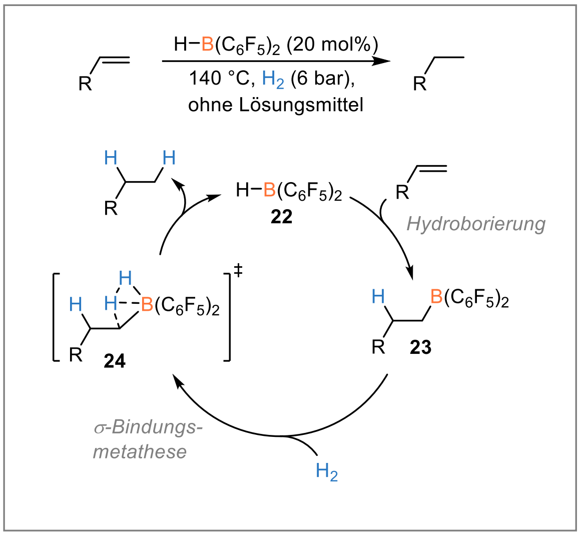
Enolether[65], Enone[66], aktivierte Olefine[67,68], polyzyklischer Aromaten[69] und mehr.[70] Das mechanistische Szenario wird dadurch beschrieben, dass das nach der H_2-Aktivierung durch das FLP entstandenen Phosphonium-Ion **18** das Substrat **19** protoniert und dadurch dessen Elektrophilie gesteigert wird (Schema 6).



Schema 6. Allgemeiner Mechanismus der Hydrierung polarer Substrate durch FLPs.

Nach dem darauffolgenden Hydridtransfer von **12** auf das aktivierte Substrat kann durch Dissoziation von **20** das Produkt freigesetzt und der Katalysator regeneriert werden. Es gibt zahlreiche Beispiele FLP-katalysierter Hydrierungen polarer Substrate, die nach dem hier beschriebenen oder einem ähnlichen Mechanismus ablaufen. Die späten 2000er und frühen 2010er Jahre brachten zahlreiche neue Publikationen hervor und es erschienen bereits viele Übersichtsartikel zu diesem Thema.[15,16,59–62,71] Daneben wurden auch chirale FLP-Katalysatoren für enantioselektive Reduktionen entwickelt.[72]

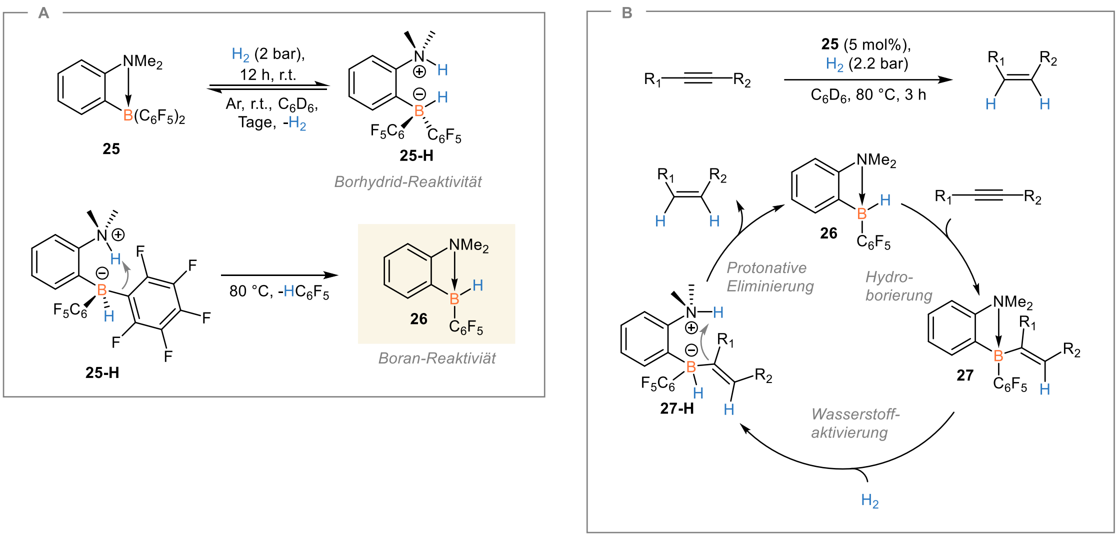
Die Entwicklung metallfreier Hydrierungen apolarer ungesättigter Substrate, wie desaktivierter Olefine und Alkine, stellte jedoch eine größere Herausforderung dar. 2012 publizierten die Gruppen von Paradies und Stephan eine Methode zur FLP-katalysierten Hydrierung einfacher Olefine.[68] Der Schlüssel zum Erfolg lag darin, dass das nach der H_2-Aktivierung entstandene Phosphonium-Ion azide genug ist, um Olefine mit hoher Protonenaffinität, wie 1,1-Diphenylethylen, zu protonieren, woraufhin der Hydridübertrag vom Borhydrid auf das mesomeriestabilisierte Carbeniumion möglich ist. Aliphatische Olefine lassen sich mit dieser Strategie jedoch nicht hydrieren. Bereits in den frühen 1960ern beobachteten DeWitt, Ramp und Trapasso, dass simple Trialkylborane bei 235 °C und 172 bar H_2-Druck in der Lage sind, desaktivierte Olefine katalytisch zu hydrieren.[73] Die Wissenschaftler vermuteten, dass unter den harschen Bedingungen das Trialkylboran H_2 aktiviert und einer der Alyklreste abgespalten wird. Mechanistisch verläuft die H_2-Aktivierung über eine σ-Bindungsmetathese. Das resultierende Dialkylboran ist dadurch in der Lage, das Substrat zu hydroborieren, welches dann auf gleichem Wege H_2 spaltet und das Produkt freisetzt.



Schema 7. Mechanismus der Piers' Boran-katalysierten Olefinhydrierung.

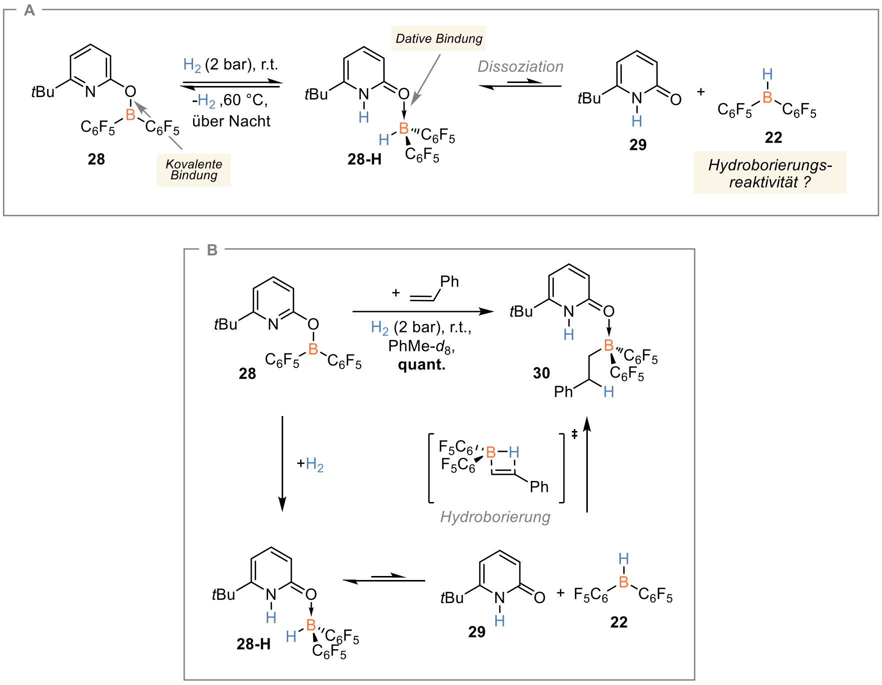
Die Gruppe von Wang entwickelte 2013 eine Bis(pentafluorphenyl)boran (Piers' Boran, **22**)-katalysierte Olefin-Hydrierung (Schema 7).[74] Mechanistische und computerchemische Untersuchungen zeigen, dass nach der initialen Hydroborierung eine Hydrogenolyse der B−C-σ-Bindung stattfindet, wodurch das Produkt freigesetzt und Piers' Boran **22** regeneriert wird. Die experimentell bestimmte freie Aktivierungsenthalpie von 33 kcal·mol^{-1} ist in guter Übereinstimmung mit den berechneten Werten und erklärt die harschen Bedingungen, die für die Reaktion notwendig sind. Bei genauerer Betrachtung erinnert der Übergangszustand der Hydrogenolyse (**24**) an den Übergangszustand der H_2-Aktivierung durch FLPs, wobei der Kohlenstoff in α-Position zum Bor als Lewis-Base fungiert. Die schwache Lewis-Basizität des Kohlenstoffs führt wahrscheinlich zu der hohen Aktivierungsbarriere der H_2-Spaltung durch dieses ungewöhnliche FLP. Die metallfreie Semihydrierung von Alkinen wurde ebenfalls mit Piers' Boran als Katalysator realisiert.[75]

Die Semihydrierung von Alkinen stellt eine wichtige Reaktion in der synthetischen und pharmazeutischen Chemie dar,[76] und wird in der großtechnischen Synthese von verschiedenen Vitaminen eingesetzt.[77] Klassischerweise wird für diese Reaktion die Lindlar-Hydrierung verwendet.[78] Der Lindlar-Katalysator ist ein heterogener Pd-Katalysator, der mit $Pb(OAc)_2$ vergiftet ist. Dies ist notwendig, um eine Überreduktion zum Alkan zu verhindern, wobei diese Nebenreaktion nur schwer zu vermeiden ist. Es ist daher erstrebenswert, neue selektivere Methoden zu entwickeln, die nicht auf die Nutzung toxischer Schwermetalle angewiesen sind. Die Gruppe von Repo berichtete 2013, dass ein intramolekulares FLP in der Lage ist, selektiv unter milden Bedingungen Alkine (*Z*)-selektiv zum Olefin zu hydrieren.[79] Der Schlüssel zum Erfolg liegt in der Eigenschaft des *ansa*-Aminoborans **25**, unter H_2-Atmosphäre und erhöhter Temperatur Pentafluorbenzol abzuspalten (Schema 8A).



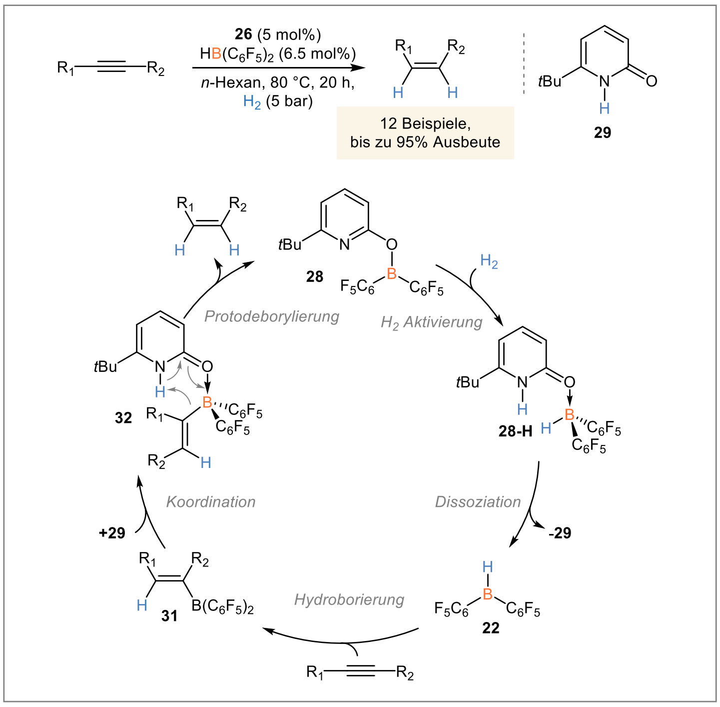
Schema 8. FLP-katalysierte Semihydrierung von Alkinen. A: Zersetzung des Prä-Katalysators **25** führt zur Bildung des Boran-Katalysators **26**. B: Mechanismus der Semihydrierung von Alkinen katalysiert durch **26**.

Während der Prä-Katalysator **25** klassische FLP-Reaktivität aufweist und nach H_2-Aktivierung ein Borhydrid **25-H** bildet, zeigt der Katalysator **26** nach Abspaltung von Pentafluorbenzol Boran-Reaktivität und ist reaktiv hinsichtlich einer Hydroborierung von Alkinen. Die Autoren waren dadurch in der Lage, erstmals metallfrei Alkine katalytisch zu hydrieren, und das schon bei äußerst milden Reaktionsbedingungen. 2018 entwickelte Gellrich ein Pyridonat-Boran (**28**), welches als intramolekulares FLP betrachtet werden kann.[80] Es wurde beobachtet, dass **28** schon bei Raumtemperatur in der Lage ist, reversibel Wasserstoff zu aktivieren. Ein herausstehendes Merkmal dieses intramolekularen FLPs ist der Wechsel des Bindungsmodus während der Wasserstoffaktivierung: Während es sich bei **28** um einen kovalent gebundenen Pyridonat-Substitutenten am Bor handelt, liegt in der hydrierten Form **28-H** ein dativ gebundener Pyridon-Ligand vor. Dieser Wechsel im Bindungsmodus wurde sowohl computerchemisch, als auch experimentell durch die IR Streckschwingung der C=O-Doppelbindung nachgewiesen.[80] Die Beteiligung des Liganden an der Bindungsaktivierung folgt dem Konzept der Bor-Liganden-Kooperation.[81] Die nun dative Bindung zwischen Pyridon und Boran führt dazu, dass die Bindung leicht heterolytisch gespalten werden kann, wobei das trivalente Piers' Boran **22** und freies Pyridon **29** erhalten wird (Schema 9A).



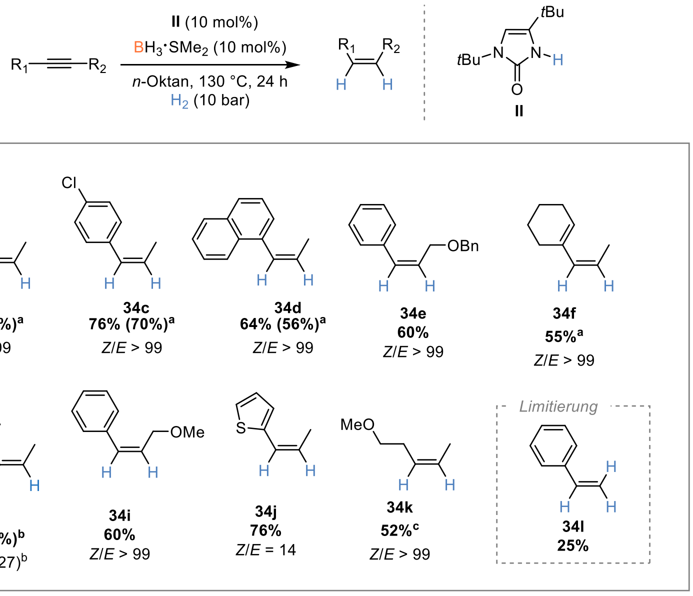
Schema 9. A: Wasserstoffaktivierung durch das Pyridonat-Boran **28**. B: Nachweis der Hydroborierungs-Reaktivität durch Reaktion von **28** mit Styrol in Anwesenheit von H_2.

Dies zeigte sich bei der Reaktion zwischen Pyridonat-Boran **28** und Styrol: Während unter Stickstoffatmosphäre beide Substanzen isoliert nebeneinander vorliegen, zeigt sich unter Wasserstoffatmosphäre quantitative Umsetzung zum Alkylboran-Pyridon-Komplex **30**, der aus einer Sequenz von Wasserstoffaktivierung, Dissoziation und Hydroborierung hervorgeht.[82] Analog zum Konzept des *ansa*-Aminoborans der Gruppe um Repo konnte so auch die Hydrierung von Alkinen realisiert werden (Schema 9).[82] Nach Wasserstoffaktivierung und Bildung des Pyridon-Boran-Komplexes **28-H** dissoziiert dieser unter Freisetzung von Pyridon **29** und freiem Piers' Boran **22**. Nach Hydroborierung des Alkins durch Piers' Boran **22** und Rekoordination des Pyridons **29** kann in einem Protonentransfer ausgehend von **29** das Produkt freigesetzt und der Pyridonat-Boran-Katalysator **28** regeneriert werden. Erstmals konnte so auch die metallfreie Semihydrierung terminaler Alkine realisiert werden, die mit FLPs bislang nicht möglich war, da bisherige Katalysatorsysteme eine irreversible C_{sp}–H-Aktivierung eingehen, was zur Desaktivierung des Katalysators führt.[83] Im Falle des Pyridonat-Borans **28** konnte experimentell gezeigt werden, dass die C_{sp}-H Aktivierung zwar abläuft, unter Reaktionsbedingungen aber reversibel ist, sodass in Anwesenheit von Wasserstoff trotzdem eine katalytische Reaktion erfolgen kann. Die Hydrierung von Alkinen ist nur ein Beispiel einer ganzen Reihe von katalytischen Transformationen, die durch das Pyridonat-Boran **28** realisiert werden konnten.[82,84] Ein Nachteil der FLPs besteht darin, dass sie die Verwendung von stark elektrophilen Boranen erfordern, die oft schwer zu synthetisieren sind und unter inerter Atmosphäre gehandhabt werden müssen.



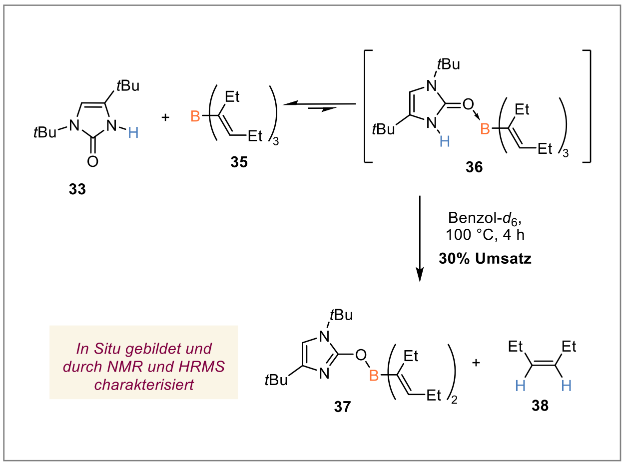
Schema 10. Semihydrierung von Alkinen katalysiert durch Pyridonat-Boran **24**.

Es gibt einige Beispiele „inverser FLPs“, die nicht auf die Nutzung elektrophiler Borane angewiesen sind, jedoch organische Superbasen verwenden.[85] Für großtechnische Anwendungen ist es daher erstrebenswert, simplere und kommerziell erhältliche metallfreie Katalysatoren zu entwickeln. Außerdem ist es von wissenschaftlichem Interesse zu verstehen, ob ein simplifiziertes FLP in der Lage wäre, als Hydrierungskatalysator zu fungieren. Eine im Rahmen dieser Promotion veröffentlichte Arbeit beschäftigte sich mit der Weiterentwicklung der Boran-katalysierten Semihydrierung von Alkinen, wobei gefunden wurde, dass selbst das simpelste Boran, BH_3, zusammen mit Pyridon **29** als Co-Katalysator ein kompetentes Katalysatorsystem für diese Transformation ist.[86] Neben dem Pyridon **29** wurden verschiedene Co-Katalysatoren getestet, wobei gefunden wurde, dass Imidazolon **33** eine effizientere und selektivere Alternative darstellt (Schema 11). In *n*-Oktan bei 130 °C und unter einem moderaten H_2 Druck von 10 bar, konnte eine ganze Reihe interner Alkine selektiv zum (*Z*)-Olefin hydriert werden. Eine Limitierung bei dieser Methode stellten jedoch terminale Alkine dar, so konnte Phenylacetylen nur in 25% Ausbeute zu Styrol hydriert werden, wobei auch die Polymerisation des Startmaterials beobachtet wurde.

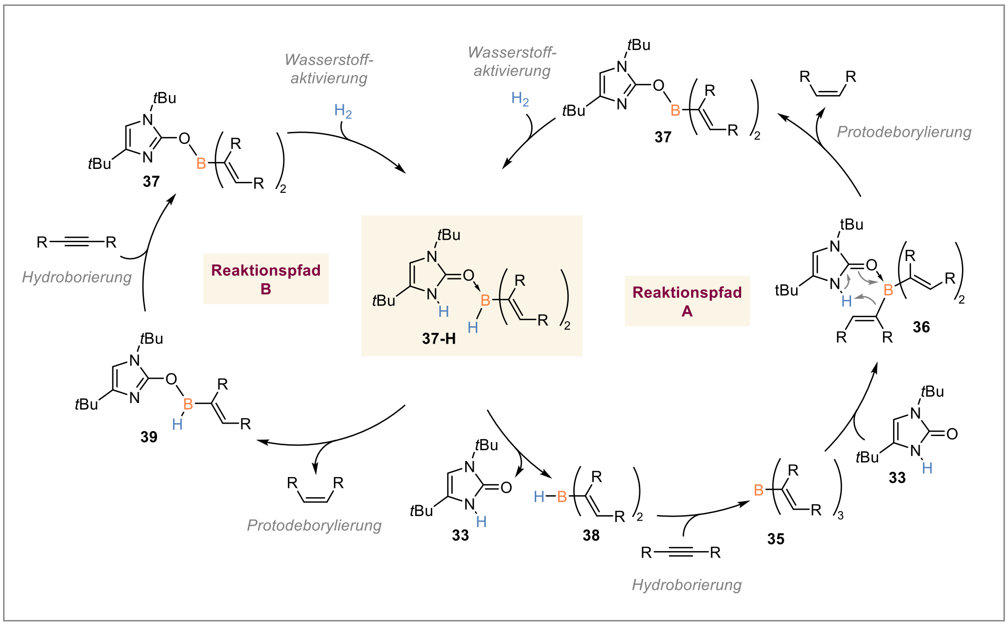


Schema 11. Umfang der BH_3-katalysierten Semihydrierung von Alkinen mit ausgewählten Produkten. Ausbeuten wurden per NMR mit internem Standard bestimmt. [a] Isolierte Ausbeuten in Klammern. [b] 8 h Reaktionszeit. [c] 48 h Reaktionszeit. *Z*/*E* Verhältnis wurde per Gaschromatographie/Massenspektrometrie bestimmt.

Dadurch, dass keine elektrophilen Borane verwendet werden, konnte die Toleranz gegenüber funktionellen Gruppen im Vergleich zu vorherigen FLP-katalysierten Methoden gesteigert werden. Aromatische Amine (**34h**), Thiophene (**34j**) und Methoxy-Gruppen (**34b**, **34k**) wurden toleriert. Wichtig für den Erfolg der Reaktion ist, dass der BH_3-Katalysator erst für eine Zeit mit dem Alkin-Substrat zur Reaktion gebracht wird. Dadurch bildet sich quantitativ ein Trialkenylboran **35**, welches der eigentliche aktive Katalysator in der Reaktion ist (Schema 12). Das Trialkenylboran **35**, welches aus BH_3 und 3-Hexin hergestellt wurde, wurde in einer stöchiometrischen Reaktion mit Imidazolon **33** umgesetzt. Während bei Raumtemperatur keine Assoziation beobachtet werden kann, zeigt sich bei Erwärmen auf 100 °C Umsatz zu einer neuen Spezies, die als Imidazolonat-Boran **37** identifiziert wurde, sowie (*Z*)-3-Hexen als Produkt.



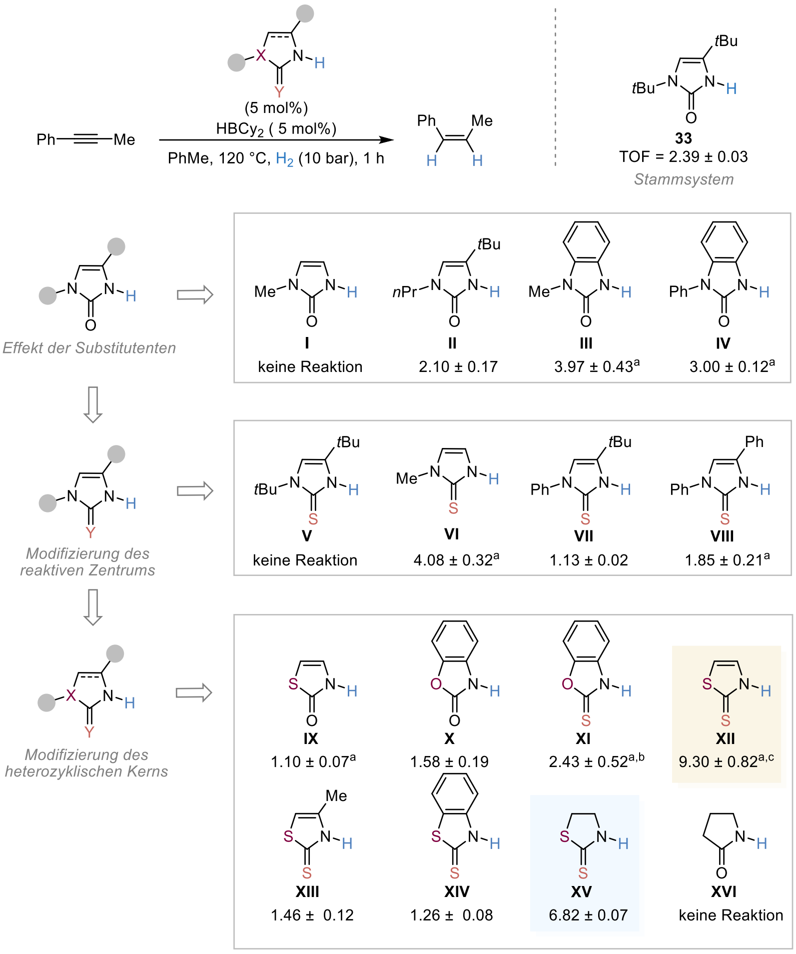
Schema 12. Stöchiometrische Reaktion zwischen Imidazolon **33** und Tris(3-hexenyl)boran **35**.



Schema 13. Mögliche Reaktionsmechanismen für die BH$_3$-katalysierte Semihydrierung von Alkinen.

Die Verbindung **37** ließ sich jedoch nicht isolieren, da bei längerem Erhitzen weitere Äquivalente Produkt abgespalten wurden und eine Mischung erhalten wurde. Das Imidazolonat-Boran **37** ähnelt einem intramolekularem FLP, wie auch das Pyridonat-Boran **28**. Berechnungen basierend auf Dichtefunktional-Theorie (DFT) zufolge ist die H$_2$-Aktivierung durch **37** zwar endergon, jedoch über eine freie Aktivierungsenthalpie von ca. 24 kcal·mol^{-1} bei der Reaktionstemperatur von 130 °C kinetisch zugänglich. Anhand der mechanistischen und computerchemischen Untersuchungen konnten zwei mögliche Mechanismen für die Reaktion vorgeschlagen werden: Im Reaktionspfad A (Schema 13, rechts) kann nach H$_2$-Aktivierung durch **37** zu **37-H** eine Dissoziation stattfinden, wobei freies Boran **38** erhalten wird. Dieses hydroboriert das Alkin, wodurch Trialkenylboran **35** erhalten wird, welches dann wieder an das Imidazolon **33** koordinert und durch eine Protodeborylierung das Produkt freisetzt. Analog zur Übergangsmetallchemie kann dieser Mechanismus auch als *outer sphere* bezeichnet werden.

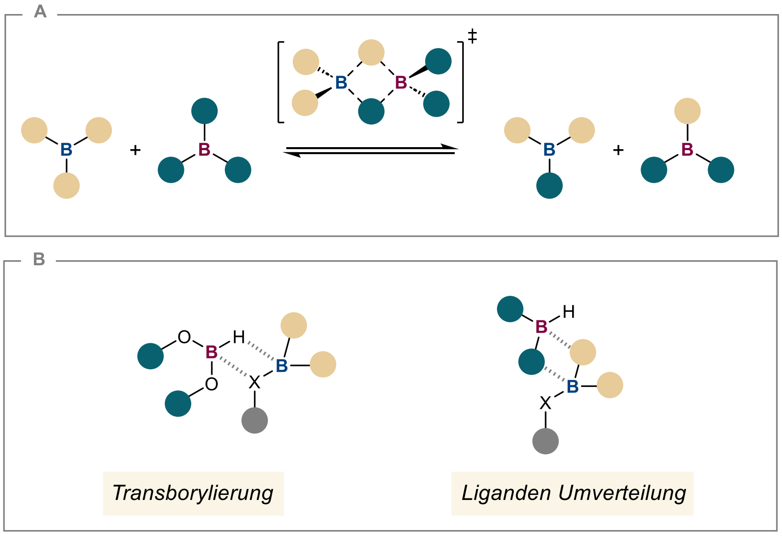
Der zweite Pfad B (Schema 12, links) verläuft so, dass nach H_2-Aktivierung durch **37** ausgehend von **37-H** direkt ein Äquivalent Produkt freigesetzt wird, wodurch das Imidazolonat-Boran **39** erhalten wird. Dieses Imidazolonat-Boran **39** hydroboriert dann das Alkin, um **37** zu erhalten, welches dann erneut H_2 aktivieren kann und so den katalytischen Zyklus schließt. Dieser Pfad kann auch als *inner sphere* Mechanismus bezeichnet werden. Kinetischen Messungen und computerchemischen Rechnungen zufolge ist Reaktionspfad B bevorzugt. Während dieser Katalysator auf kommerziell erhältlichem BH_3 und einem einfachen organischen Co-Katalysator basiert, ist die Effizienz der Reaktion bezüglich der Umsatzfrequenz (TOF) noch weit von vergleichbaren Metallkatalysatoren entfernt.[87] Daher wurde im Rahmen dieser Promotion ein systematisches Schema entwickelt, um eine Struktur-Aktivitätsbeziehung des organischen Co-Katalysators herzustellen und dadurch die Effizienz der Reaktion weiter zu steigern (Schema 14).[88] Um substratspezifische Effekte des Borans zu vermeiden, wurde als Boran-Katalysator Dicyclohexylboran ($HBCy_2$) anstatt $BH_3 \cdot SMe_2$ verwendet, welches sich einfach aus $BH_3 \cdot SMe_2$ und Cyclohexen in einem Schritt ohne Aufreinigung herstellen lässt. In einer standardisierten Reaktionsführung wurden dann mit Phenylpropin als Testsubstrat verschiedene organische Co-Katalysatoren getestet und per Gaschromatographie mit Massenspektrometrie (GC-MS) mit internem Standard die Ausbeute an (*Z*)-*β*-Methylstyrol nach einer Stunde Reaktionszeit und somit die TOF bestimmt. Im ersten Schritt wurden die Substituenten des Stammsystems variiert, während im zweiten Schritt das reaktive Zentrum mitberücksichtigt wurde und auch Thioimidazolon-Derivate mit einbezogen wurden. Im dritten Schritt wurden Modifikationen am heterozyklischen Kern vorgenommen, und andere Heterozyklen wie Oxazole, Thiooxazole, Thiazole, und Mercaptothiazole getestet. Die vorläufigen Ergebnisse dieser noch unveröffentlichten Studie zeigen, dass das einfache, kommerziell erhältliche Mercaptothiazol **XII** und das Mercaptothiazolin **XV** ausgesprochen effiziente Co-Katalysatoren darstellen, und eine TOF von bis zu 9.3 erreicht wurde. Nach weiterer Optimierung der Reaktionsbedingungen konnte die TOF im Vergleich zum Stammsystem um mehr als den Faktor 10 erhöht werden.



Schema 14. Struktur-Aktivitätsbeziehung verschiedener Co-Katalysatoren. TOFs wurden über GC-MS mit internem Standard bestimmt. Die Reaktionen wurden mindestens zwei Mal wiederholt. Sofern nicht anders angegeben wurde nur (*Z*)-Isomer erhalten. [a]Reaktion wurde vier Mal wiederholt. [b]*Z*/*E*=94:6. [c]*Z*/*E*=92:8.

3.3 Transborylierungen

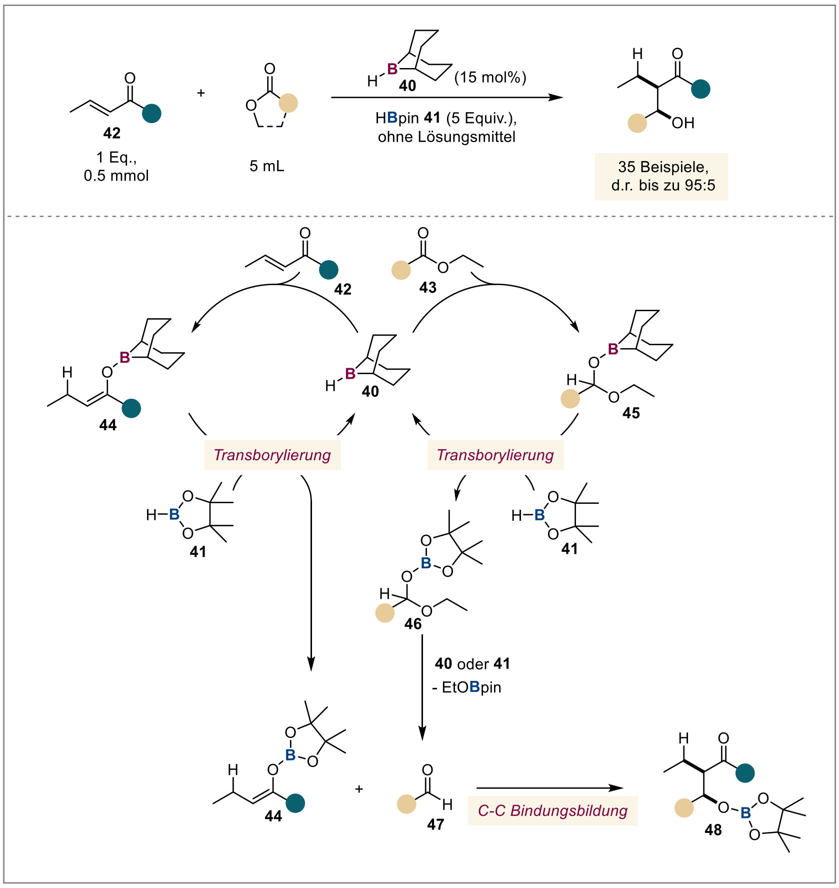
Als Transborylierung wird der kontrollierte Austausch eines Bor-Atoms in einem Molekül durch ein zweites Bor-Atom beschrieben. Dieser Prozess kann auch als Umverteilungsreaktion zwischen zwei Borzentren beschrieben werden und ist bekannt für eine ganze Reihe heteroatomarer Substituenten,[89] aber auch für kohlenstoffhaltige Reste wie Alkyl[90], Alkenyl[91] und Aryl (Schema 15A).[92] Stöchiometrische Boran-Reagenzien sind in der organischen Synthese weit verbreitet, und Reaktionen wie die Allylborierung sind ein unersetzliches Werkzeug für den Aufbau chiraler Moleküle.[93] Die Transborylierung kann als Strategie eingesetzt werden, um katalytischen Umsatz in Boran-katalysierten Reaktionen zu erreichen, indem ein Boran HBR_2 katalytisch eingesetzt wird, während ein weiteres, stöchiometrisch eingesetztes Boran HBR'_2 den Katalysator durch Transborylierung regeneriert. In Konkurrenz zur Transborylierung steht die Liganden-Metathese, wobei nur die Reste von einem Bor auf das andere Bor transferiert werden (Schema 15B).



Schema 15. A: Stöchiometrische Umverteilungsreaktion zwischen Boranen. B: Mechanismen der B/B σ-Bindungsmetathese.

3.3.1 B−H/B−O-Transborylierung

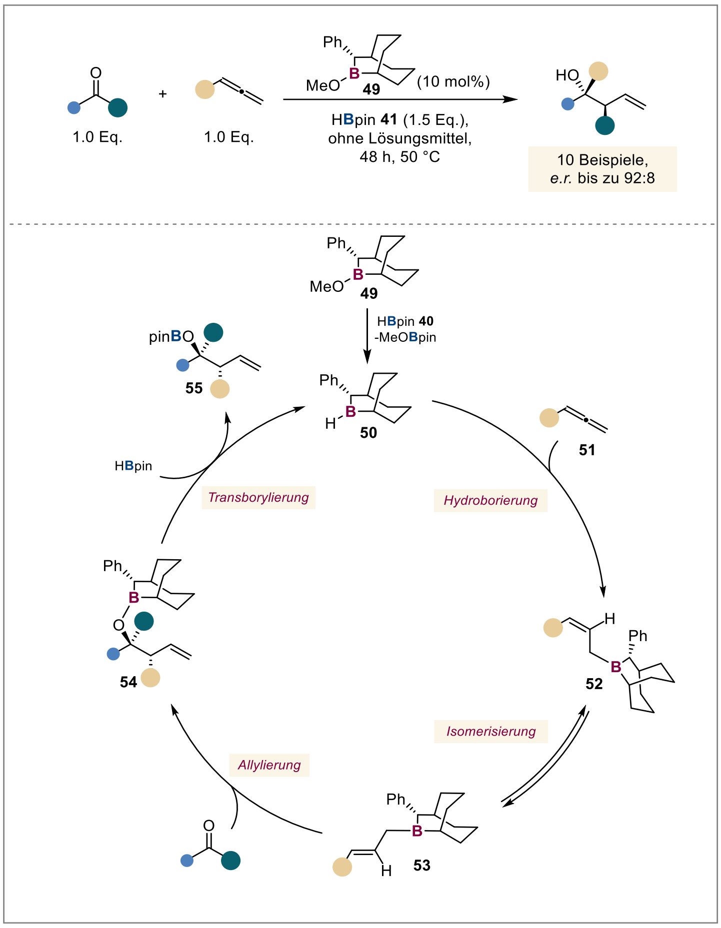
Die in der Katalyse eingesetzten B−H/B−X-Transborylierungen ermöglichen eine ganze Reihe neuer Transformationen. Die B−H/B−O-Transborylierung wird beispielsweise in der katalytischen Reduktion von Ketonen eingesetzt, die mithilfe eines chiralen Boran-Katalysators auch enantioselektiv gelang.[94] Sie wurde auch als Strategie zur katalytischen Hydrofunktionalisierung α,β-ungesättigter Carbonylverbindungen eingesetzt.[95] In einem eleganten Ansatz konnten auch Kreuz-Aldol Produkte katalysiert durch 9-Borabicyclo[3.3.1]nonan **40** (9-BBN) über eine B−H/B−O-Transborylierung mit stöchiometrischen Mengen Pinakolboran **41** (HBpin) diastereoselektiv hergestellt werden.[96]



Schema 16. Diastereoselektive Kreuz-Aldol Reaktion durch Transborylierungs-Katalyse.

Hierbei wird das Enolat **44** nicht durch den stöchiometrischen Einsatz einer starken, sterisch gehinderten Base generiert, sondern durch die Hydroborierung eines Enons **42** mittels 9-BBN **40** und anschließender Transborylierung mit HBpin **41**. In einem dualkatalytischen Ansatz generiert 9-BBN **40** aus Lactonen oder Estern **43** Halbacetale **46**, welche unter den Reaktionsbedingungen zu Aldehyden **47** zerfallen und so für einen nukleophilen Angriff durch das Enolat **44** zur Verfügung stehen.

Der B−H/B−O-Austausch wurde auch zur asymmetrischen Allylierung von Ketonen eingesetzt.[97] Mit 5 mol% 9-BBN **40** als Katalysator gelingt die Reaktion diastereoselektiv für 32 Beispiele mit moderaten bis sehr guten Ausbeuten, und teilweise sehr guter Diastereoselektivität. Es wurde auch ein chirales 9-BBN-Derivat **50** als Katalysator eingesetzt. Die Allylierung von Ketonen durch das chirale Allylboran **53** erfolgt dann enantioselektiv, während durch anschließende Transborylierung mit HBpin **41** das chirale Boran regeneriert und das Produkt **55** freigesetzt wird (Schema 17). Neben den hier gezeigten Beispielen für B-H/B-O-Transborylierungen gibt es noch viele weitere B−H/B−X-Austauschreaktionen, sowie Austauschreaktionen von anderen Elementen der Gruppe 13.[98]

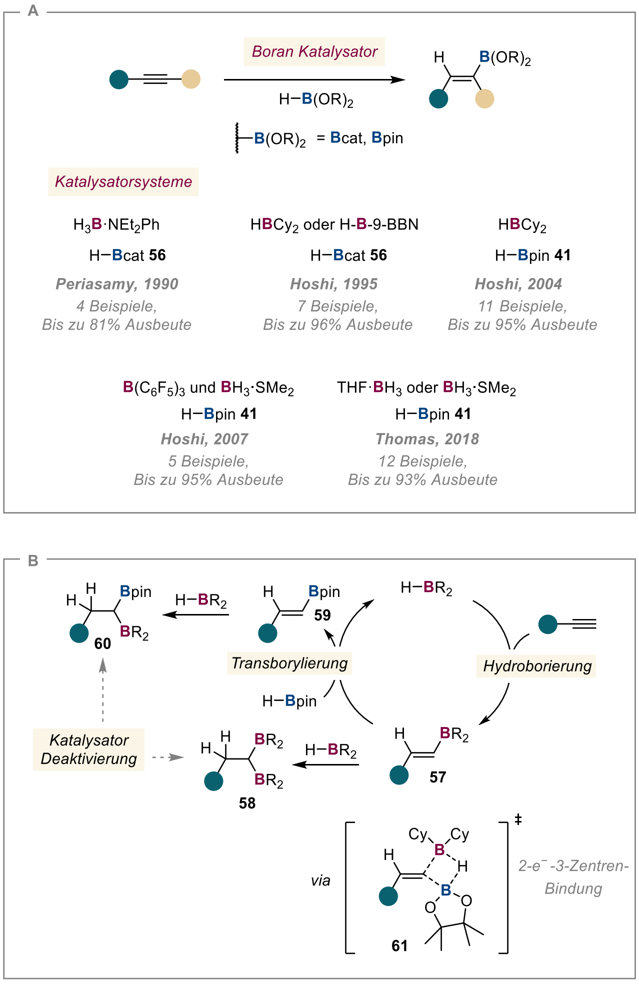


Schema 17. Enantioselektive Boran-katalysierte Allylierung von Ketonen.

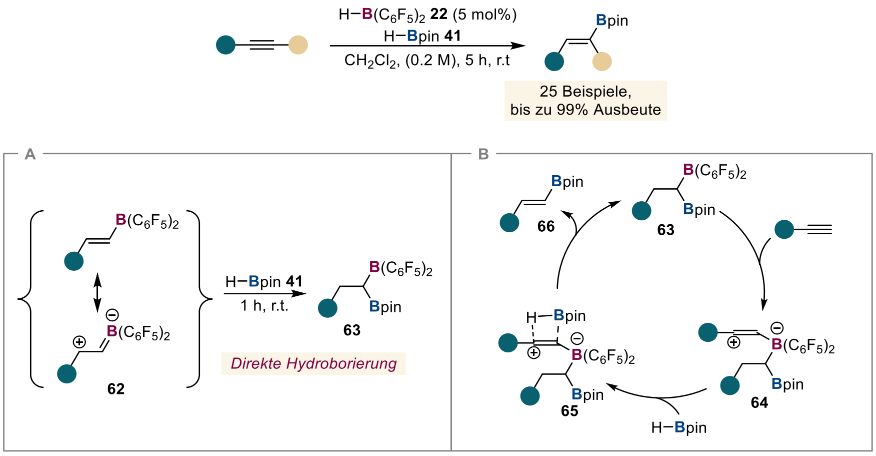
3.3.2 B−H/B−C-Transborylierungen

Die B−H/B−C-Transborylierungen wird vor allem zur Synthese von Alkenylboronaten verwendet, eine Klasse von Verbindungen, die wichtige Substrate für die Suzuki-Miyaura Reaktion sind. Die erste katalytische Variante dieser Reaktion wurde von Periasamy berichtet.[99] Die Forscher erkannten, dass ein $BH_3 \cdot NEt_2Ph$-Komplex die Hydroborierung von Alkinen durch Catecholboran **56** (HBcat) katalysiert (Schema 18A). Es wird vermutet, dass das Alkin durch $BH_3 \cdot NEt_2Ph$ hydroboriert wird und das gebildete Alkenylboran mit HBcat in einem Ligandenaustausch reagiert, was den Katalysator regeneriert und das Alkenylboronat als Produkt bildet. Einige Jahre später entdeckten Arase und Hoshi, dass auch einfache Alkylborane wie $HBCy_2$ und 9-BBN diese Reaktion katalysieren, wobei der gleiche Mechanismus vermutet wird, wie er von Periasamy beschrieben wurde.[100] Hoshi erweiterte den Umfang der Reaktion auf HBpin und erklärte, dass katalytischer Umsatz für verzweigte Alkenylborane schwierig ist, was auch bereits von Brown für stöchiometrische Umverteilungsreaktionen an Boranen beobachtet wurde.[101] Hoshi entwickelte ein alternatives Katalysatorsystem für die Hydroborierung von Alkinen, das aus $BH_3 \cdot SMe_2$ und $B(C_6F_5)_3$ als Prä-Katalysatoren besteht.[102] Daraus bildet sich *in situ* durch B−H/B−C-Transborylierung $Me_2S \cdot BH(C_6F_5)_2$, was als eigentlicher Katalysator fungiert. Thomas untersuchte diese Reaktion weiter und konnte auch $THF \cdot BH_3$ Komplex oder $BH_3 \cdot SMe_2$ direkt als Katalysator einsetzen.[103] Der BH_3-Katalysator kann auch *in situ* aus einem Überschuss HBpin und substöchiometrischen Mengen KO*t*Bu generiert werden kann.[104,105]

Während die Arase-Hoshi Reaktion bereits seit 1990 bekannt ist und über die Jahre sukzessive weiterentwickelt wurde, beschäftigten Thomas und Lloyd-Jones sich erst 2019 mit dem Mechanismus der $HBCy_2$- und 9-BBN-katalysierten Reaktion (Schema 18B).[106] Isotopenexperimente unterstützt durch kinetische und computerchemische Untersuchungen zeigten eine konzertierte B−H/C(sp^2)−H-Transborylierung als umsatzgenerierenden Schritt. Wenn isotopenmarkiertes H^{10}Bpin mit Alkenylboran umgesetzt wurde, zeigte sich die exklusive Bildung von ^{10}B markiertem Alkenylboronat, was die Vermutung der Transborylierung gegenüber eines Ligandenaustauschs unterstützt. Auch konnte die experimentelle freie Reaktionsenthalpie bestimmt werden ($\Delta G^{\ddagger} = 20.3$ kcal mol^{-1}), welche gut mit der berechneten Barriere übereinstimmt ($\Delta G^{\ddagger} = 19.7$ kcal mol^{-1}).



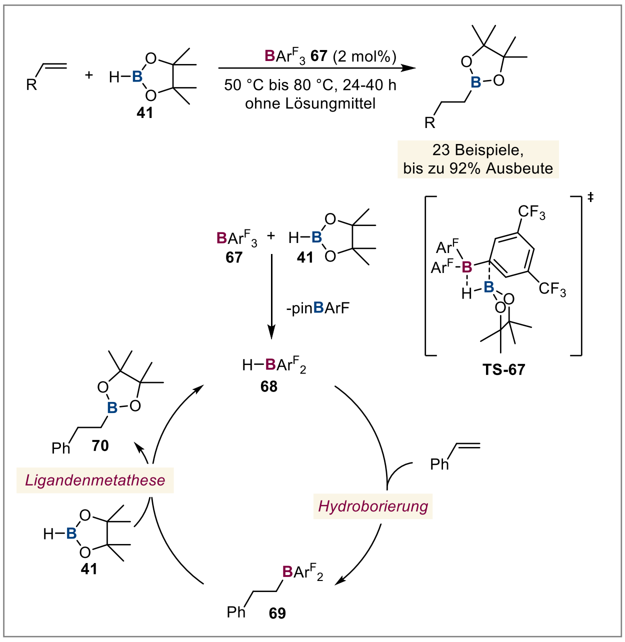
Schema 18. A: Beispiele zur Synthese von Alkenylboronaten aus Alkinen durch B−H/B−C-Transborylierung. B: Vorgeschlagener Mechanismus und Pfade zur Katalysator-Deaktivierung.



Schema 19. Piers' Boran-katalysierte Hydroborierung von Alkinen durch HBpin. A: Direkte Hydroborierung des Alkenylborans durch HBpin (dunkler Kreis: Aryl-Rest). B: Möglicher Mechanismus der Reaktion.

Piers' Boran wurde ebenfalls verwendet, um die Hydroborierung von Alkinen durch HBpin zu katalysieren (Schema 19).[107] Nach der Hydroborierung des Alkins durch Piers' Boran entsteht ein Alkenylboran, welches durch die stark elektronenziehenden Substituenten des Bors polarisiert ist. Die Autoren vermuten, dass dadurch eine direkte Hydroborierung des Alkenylborans **62** durch HBpin stattfinden kann, um eine *gem*-diborylierte Spezies **63** zu bilden. Tatsächlich ist ein alternativer Mechanismus denkbar, wobei erst eine B−H/B−C-Transborylierung zwischen Alkenylboran **62** und HBpin stattfindet, wobei Alkenylboronat **66** gebildet und Piers' Boran freigesetzt wird. Das Alkenylboronat **66** wird dann durch Piers' Boran hydroboriert, was zur *gem*-diborylierten Spezies **63** führt. Die Autoren vermuten, dass **63** der eigentliche Katalysator der Reaktion ist und an das Substrat koordiniert, was zum zwitterionischen Intermediat **64** führt. Dieses kann durch HBpin direkt hydroboriert werden, was zur Produktbildung und Regeneration des *gem*-diborylierten Katalysators führt. Mit dieser Methode konnte eine Vielzahl terminaler und auch interner Alkine in exzellenten Ausbeuten unter milden Bedingungen zu den korrespondierenden Alkenylboronaten umgesetzt werden.

Die Boran-katalysierte Hydroborierung von Olefinen durch HBpin gestaltet sich schwieriger als für Alkine, da die Barrieren für eine Transborylierung am sp^3 Kohlenstoff deutlich höher sind. Die Gruppe von Oestreich berichtete 2016 die Boran-katalysierte Hydroborierung von Olefinen.[108] Das stöchiometrisch eingesetzte Reagenz ist hier HBpin **41**, während Tris(3,5-trifluormethylphenyl)boran **67** (BAr^F_3) als Katalysator eingesetzt wird. Es konnte durch NMR-Untersuchungen gezeigt werden, das BAr^F_3 **67** eine Ligandenaustauschreaktion mit HBpin **41** eingeht, wobei sich verschiedene Boran Spezies ($HBAr^F_2$ **68** und H_2BAr^F) bilden, die in der Lage sind, das Substrat zu hydroborieren (Schema 20). Das nun erhaltene Alkylboran **69** kann dann einen weiteren Ligandenaustausch mit HBpin **41** durchführen, um das Produkt **70** freizusetzen.

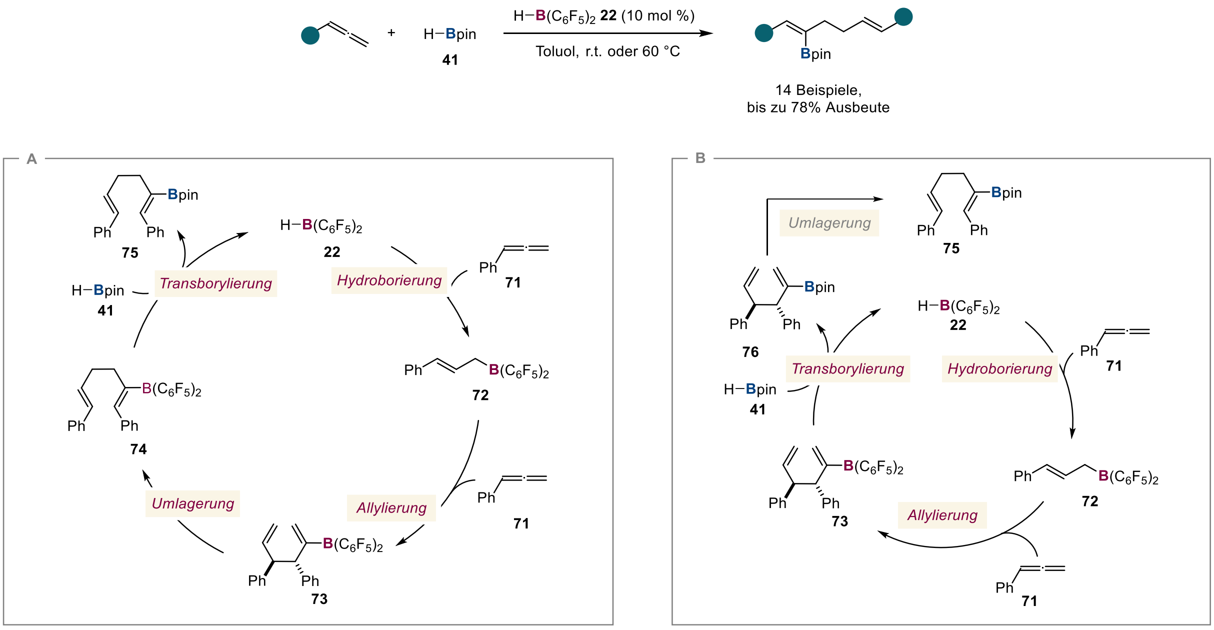


Schema 20. Möglicher Mechanismus der $\mathrm{BAr^F_3}$-katalysierten Hydroborierung von Olefinen.

Die Autoren zeigten auch, dass neben *in situ* gebildetem $\mathrm{HBAr^F_2}$ **68** und $\mathrm{H_2BAr^F}$ auch Piers' Boran als Katalysator geeignet ist.

Die Gruppe von Ingleson erreichte eine formale *trans*-Hydroborierung von Alkinen mittels eines Boran-NHC-Komplexes und $\mathrm{B(C_6F_5)_3}$ als Katalysator.[109] Die Gruppe von Thomas konnte die Hydroborierung von Alkinen durch HBpin durch katalytische Mengen $\mathrm{B(C_6F_5)_3}$ erreichen.[110] In stöchiometrischen Kontrollexperimenten zeigte sich hier, dass $\mathrm{B(C_6F_5)_3}$ mit Alkinen zu einer zwitterionischen Zwischenstufe reagiert. Ein ähnliches Intermediat wurde auch bereits charakterisiert und kristallisiert.[111] In der katalytischen Reaktion wird dieses dann durch eine direkte Hydroborierung von HBpin abgefangen.

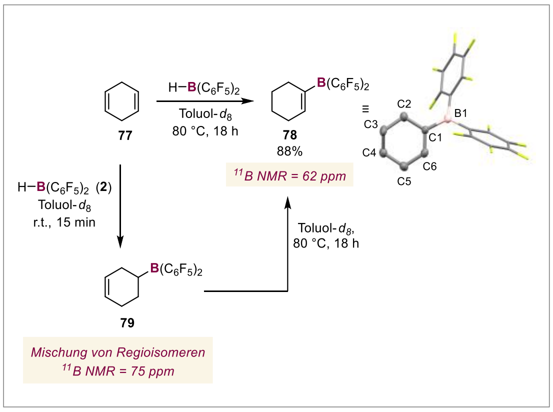
Eine weitere Anwendung findet die B−H/B−C-Transborylierung in der Piers' Boran-katalysierten Dimerisierung von Allenen.[112] Eine stöchiometrische Variante dieser Reaktion wurde bereits von Erker berichtet.[113] Die Reaktion startet mit der Hydroborierung des Allens durch Piers' Boran (Schema 21). Das entstandene Allylboran **72** reagiert dann mit einem zweiten Äquivalent Arylallen **71**, wobei das Dimer **73** entsteht. Das Dimer **73** enthält ein Alkenylboran, welches in einer B-H/B-C-Transborylierung mit HBpin **41**, HBcat **56** und anderen Boronsäureestern reagieren kann, wobei Piers' Boran als Katalysator regeneriert wird. Es sind hierbei zwei mögliche mechanistische Szenarien denkbar: Im ersten Fall wird das nach der Allylierung des Allens gebildete Alkenylboran **73** erst zum thermodynamisch stabileren Isomer **74** umlagert. Dieses unterzieht sich dann einer Transborylierung durch HBpin **41** um das Produkt **75** freizusetzen (Schema 21A).



Schema 21. Piers' Boran-katalysierte Allen-Dimerisierung und anschließende Transborylierung.

Im zweiten Fall findet nach der Allylierung direkt die Transborylierung statt und der intermediär gebildete Boronsäureester **76** wird zum Produkt **75** umgelagert (Schema 21B). Um die Mechanismen zu unterscheiden, wurde **73** unabhängig hergestellt und die Umlagerung zu **74** untersucht. In einem zweiten Versuch wurde der Reaktion ein Äquivalent HBpin **41** zugesetzt, wobei gezeigt werden konnte, dass dies keinen Einfluss auf die Reaktionsgeschwindigkeit hatte. Dies ist ein Hinweis darauf, dass die Transborylierung nach der Umlagerung stattfindet und somit über Mechanismus A verläuft. Piers' Boran **22** wird nicht nur zur katalytischen Hydroborierung von Alkinen eingesetzt, sondern kann auch Olefine katalytisch isomerisieren.[114] Die Hydroborierung durch Piers' Boran **22** ist exergon und weist geringe Barriere auf. Dadurch ist bereits bei Raumtemperatur die Rückreaktion kinetisch zugänglich und eine *retro*-Hydroborierung kann ablaufen. Dies führt im Falle von terminalen Olefinen dazu, dass diese zu thermodynamisch stabileren internen Olefinen isomerisiert werden.

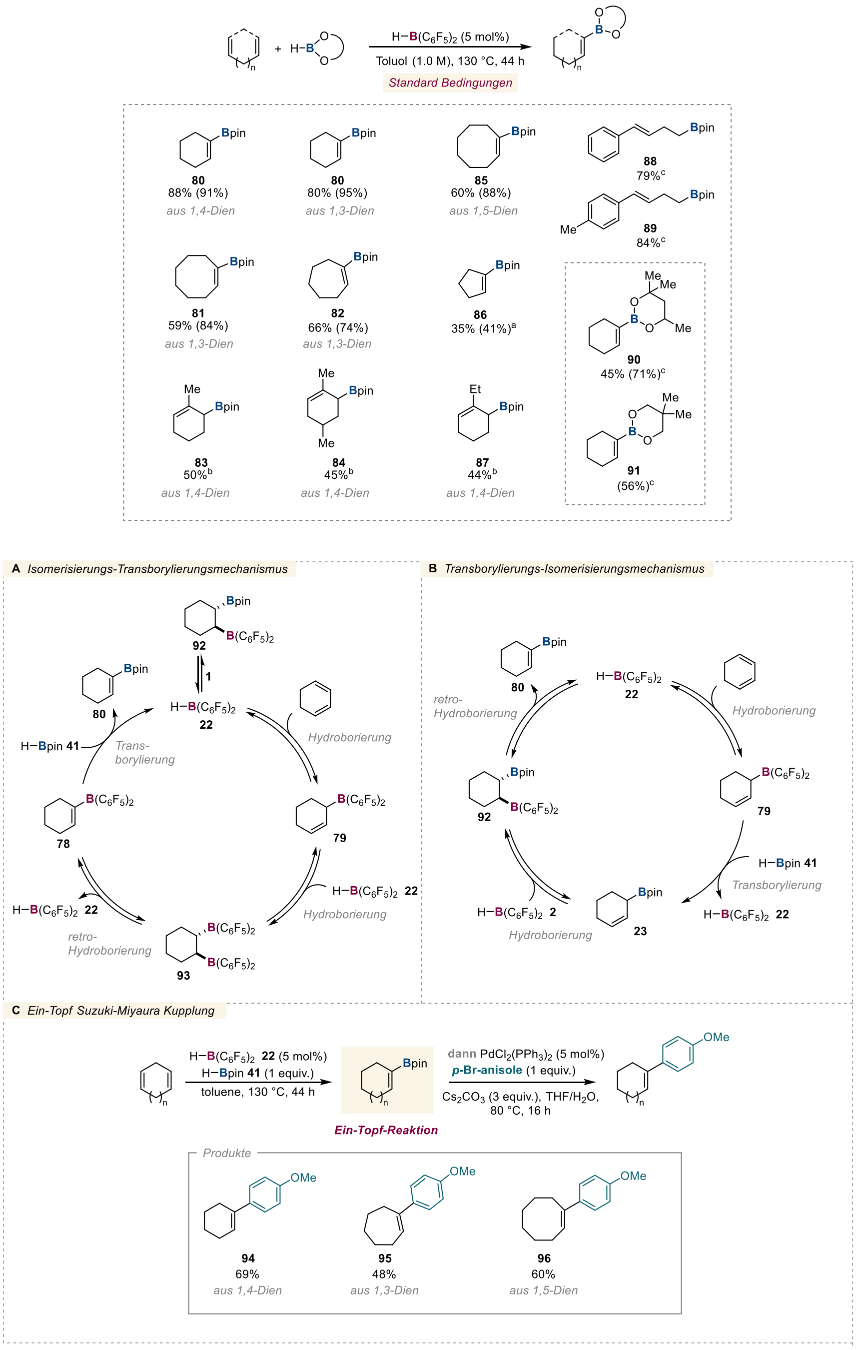
Im Rahmen dieser Studie wurde nun gefunden, dass zyklische Diene, wie Cyclooctadien und Cyclohexadien **77**, mit Piers' Boran **22** nicht wie erwartet zu Alkylboranen, sondern zu Alkenylboranen (**78**) reagieren (Schema 22).[115] Im Falle von 1,4-Cyclohexadien **77** bildet sich nach Zugabe von Piers' Boran eine Mischung von Hydroborierungsprodukten (**79**), welche ein gemeinsames ^{11}B NMR-Signal bei 75 ppm aufweisen. Dies ist charakteristisch für Alkylborane und in guter Übereinstimmung mit dem ^{11}B NMR-Signal für $CyB(C_6F_5)_2$.[116] Nach erhitzen dieser Mischung bildet sich sauber das Alkenylboran **78** in 88% Ausbeute, welches auch durch Einkristallstrukturanalyse charakterisiert wurde.



Schema 22. Initiale Beobachtungen. 1,4-Cyclohexadien **77** regiert mit Piers‘ Boran **22** zu Alkenylboran **78**.

Dies führte zu der Hypothese, dass durch Transborylierung mit HBpin **41** aus diesen Alkenylboranen wieder Piers' Boran **22** freigesetzt werden könnte und dadurch katalytischer Umsatz erzielt werden kann.[117] Tatsächlich war es möglich, durch Zugabe von HBpin **41** eine katalytische Reaktion zu entwickeln. Mit katalytischen Mengen Piers' Boran **22** konnten verschiedene Boronsäureester synthetisiert werden (Schema 23). Unsubstituierte zyklische Diene konnten in guten bis sehr guten Ausbeuten umgesetzt werden, wobei 1,4-Cyclohexadien im Grammmaßstab zum Cyclohexenylboronat **80** umgesetzt werden konnte. Zudem konnte gezeigt werden, dass neben HBpin **41** auch weitere $HB(OR)_2$ Derivate als Reagenz eingesetzt werden konnten. Im Falle substituierter zyklischer Diene wurden Allylboronate erhalten, wahrscheinlich weil eine Isomerisierung zur thermodynamisch stabileren Doppelbindung stattfindet. Phenylbutadien und 1-(4-Methylphenyl)butadien ergeben die Homoallylboronate **88** und **89** als Produkte, wobei auch hier die Doppelbindung zur benzylischen Position isomerisiert. Es wurde auch gezeigt, dass nach vollständigem Umsatz zum Alkenylboronat direkt in einem One-Pot Ansatz eine Suzuki-Miyaura-Kupplung durchgeführt werden kann, wobei die Produkte **94**–**96** erhalten wurden (Schema 23C). Durch stöchiometrische und katalytische Kontrollexperimente konnten wir zwei mögliche Mechanismen für die Reaktion ableiten (Schema 23A und 23B). Wenn **78** als Katalysator eingesetzt wird, ist die Ausbeute der Reaktion vergleichbar mit der Reaktion unter Standardbedingungen. Durch Reaktion von **78** mit HBpin **41** konnte das potenzielle Intermediat **92** synthetisiert und als Addukt per Einkristallstrukturanalyse und NMR charakterisiert werden. **92** konnte ebenfalls erfolgreich als Katalysator eingesetzt werden.

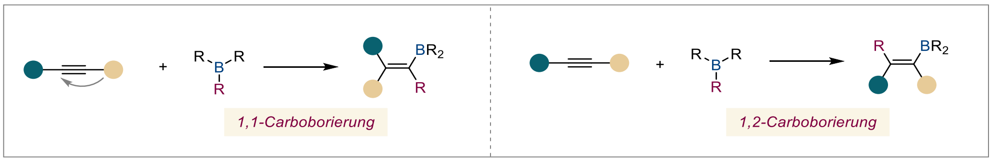
Die hier gezeigte Methode ermöglichte einfachen und atomökonomischen Zugang zu zyklischen Alkenylboronaten, die wichtige Substrate für die Suzuki-Miyaura-Reaktion darstellen. Während azyklische Alkenylboronate leicht über die katalytische Hydroborierung von Alkinen zugänglich sind, werden zyklische Alkenylboronate klassischerweise über mehrstufige, übergangsmetallkatalysierte Synthesen hergestellt.[118]



Schema 23. Piers' Boran-katalysierte Bildung von Alkenylboronaten aus Boronsäure Estern und Dienen, sowie vermutete Mechanismen (A und B); C: Anwendung in einer Ein-Topf-Reaktion. Isolierte Ausbeuten sind angegeben und *in situ* Ausbeuten in Klammern (bestimmt über NMR mit *p*-Xylol als internem Standard). [a]10 mol% $HB(C_6F_5)_2$, 24 h; [b]80 °C, 2 h; [c]80 °C, 22 h.

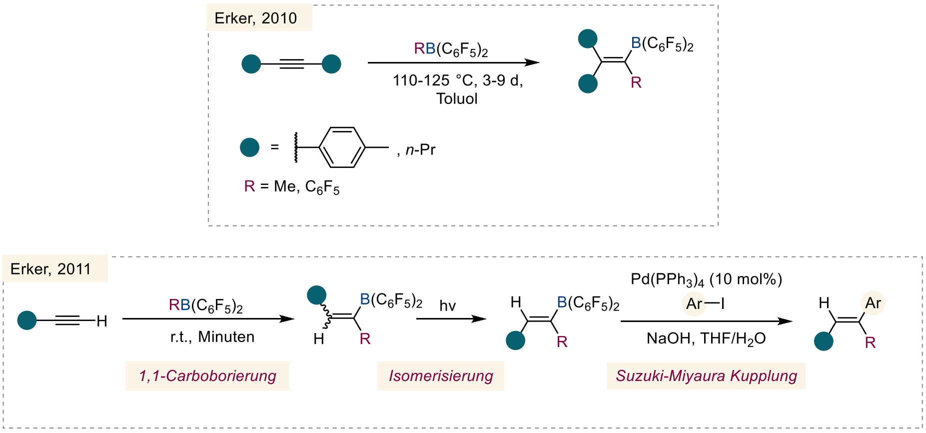
3.4 Carboborierungen

Eine weitere Reaktion, die Borane mit C–C-Mehrfachbindungen eingehen können, ist die Carboborierung. Dies führt zum Bruch einer C–C-π-Bindung und einer B–C-σ-Bindung, und zur Bildung einer neuen C–C-σ und B–C-σ-Bindung. Es wird also ein Kohlenstoffrest vom Boran auf das Substrat übertragen (Schema 24). Man unterscheidet dabei zwischen 1,1-Carboborierungen, bei denen Bor und Rest auf den gleichen Kohlenstoff übertragen werden, und 1,2-Carboborierungen, die analog zur Hydroborierung verlaufen. Im Folgenden soll nur auf 1,1-Carboborierungen eingegangen werden, für 1,2-Carboborierungen sei auf weiterführende Literatur verwiesen.[119,120]



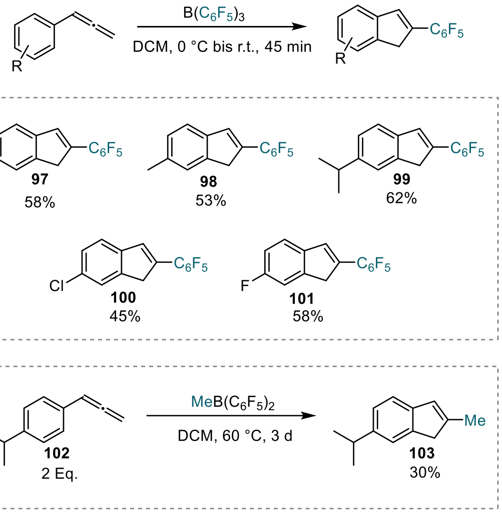
Schema 24. Die Carboborierung von Alkinen.

Für Carboborierungen werden meist Übergangsmetallkatalysatoren eingesetzt.[121] Seit mit dem Aufkommen von FLPs in den 2000ern vermehrt Reaktionen Lewis-saurer Borane untersucht wurden, wurde gefunden, dass durch den Einsatz stark Lewis-saurer Borane, wie $B(C_6F_5)_3$, Carboborierungen auch unkatalysiert ablaufen können.[120,122] Unkatalysierte Carboborierungen wurden bereits seit den 1970ern von Wrackmeyer untersucht.[123] Bei der Wrackmeyer-Reaktion reagieren Borane mit Alkinyl-Zinn Verbindungen in einer 1,1-Carboborierung. In den frühen 2010ern entdeckten die Gruppen von Erker und Berke, dass diese Reaktion auch mit unsubstituierten Alkinen abläuft, wenn elektrophile Borane des Typs $R–B(C_6F_5)_2$ verwendet werden.[124] Die dabei entstandenen Alkenylborane können anschließend in einer Ein-Topf Suzuki-Miyaura-Kupplung mit Arylhalogeniden umgesetzt werden.[125] Hashmi und Stephan nutzten die Aktivierung von Alkinen durch $B(C_6F_5)_3$ für Tandem Zyklisierungs-/Carboborierungs-Reaktionen.[126]



Schema 25. 1,1-Carboborierung von unsubstituierten Alkinen durch elektrophile Borane.

Arylallene reagieren auch mit $B(C_6F_5)_3$ in einer 1,1-Carboborierung. Dabei findet nach der Aktivierung des Allens durch $B(C_6F_5)_3$ eine intramolekulare Friedel-Crafts-Reaktion statt, anschließend wird ein C_6F_5-Rest übertragen (Schema 26).[127] Dadurch konnten aus fünf verschiedenen Arylallenen C_6F_5-substituierte Inden-Derivate synthetisiert werden. Durch Verwendung von $MeB(C_6F_5)_2$ gelang es, bei erhöhter Temperatur und längerer Reaktionszeit selektiv die Methylgruppe auf den Inden-Ring zu übertragen. Dabei war der Einsatz von elektronenreichem, *p*-Isopropyl-substituiertem Arylallen **102** wichtig für den Erfolg der Reaktion. Das Produkt **103** konnte dennoch nur in moderaten 30% Ausbeute erhalten werden. Die hohe Sensitivität der Reaktion gegenüber den Substituenten am Phenylring veranlasste uns, eine Hammett-Analyse durchzuführen, wobei die Geschwindigkeitskonstante der Reaktion für verschiedene Reste bestimmt und gegen den Hammett-Parameter σ_p aufgetragen wurde. Die resultierende Gerade wies eine stark negative Steigung auf, was ein Indikator für die Bildung einer positiven Ladung in benzylischer Position im geschwindigkeitsbestimmenden Übergangszustand ist. Dies ist auch im Einklang mit dem berechneten Reaktionsmechanismus. Einzigartig für dieses Beispiel einer 1,1-Carboborierung ist, dass das Bor nicht im Endprodukt verbleibt, sondern in der Form von Piers' Boran **22** in einer *retro*-Hydroborierung wieder freigesetzt wird.



Schema 26. Boran-induzierte Zyklisierung von Arylallenen (Nur das Hauptisomer ist dargestellt).

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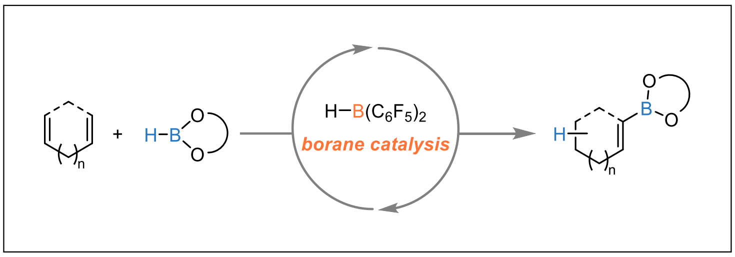
5 Veröffentlichte Projekte

5.1 Bis(pentafluorphenyl)borane catalyzed atom-economic formation of alkenyl- and (homo)allyl boronates from dienes and boronic esters



We described a bis(pentafluorophenyl)borane-catalyzed reaction to synthesize alkenyl- and (homo)allyl boronates from dienes. This is based on the finding, that cyclic dienes do not react with bis(pentafluorphenyl)borane to the expected alkyl borane, but yield an alkenyl borane, which can undergo transborylation with HBpin. This then yields an alkenyl boronate, which enabled us to synthesize normal and medium cyclic unsubstituted alkenyl boronates in good to excellent yields with catalytic amounts of $HB(C_6F_5)_2$. When substituted cyclohexadienes are employed, allyl boronates are obtained since the remaining double bond isomerizes to the thermodynamically more stable position. The same was observed for phenylbutadienes, where homoallyl boronates are obtained since the double bond isomerizes to the benzylic position. Catalytic and stoichiometric control experiments allowed us to identify potential intermediates of the catalytic reaction, which were also employed as catalysts.

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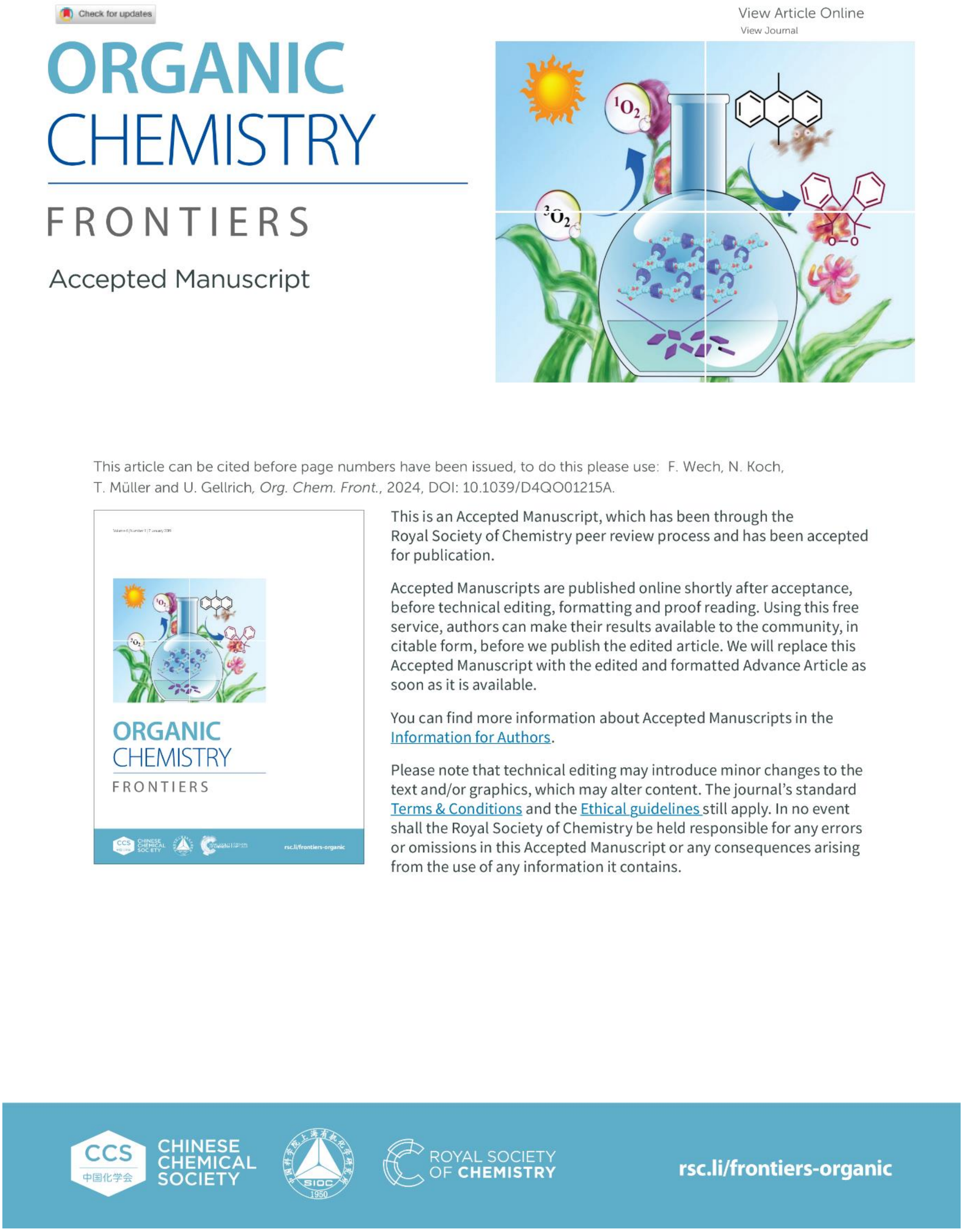
Org. Chem. Front. **2024**, *Accepted Manuscript*

DOI: 10.1039/D4QO01215A

Akzeptiertes Manuskript: 26. August 2024

Online veröffentlicht: 30. August 2024



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DOI: 10.1039/D4QO01215A

ARTICLE

Bis(pentafluorophenyl)borane catalyzed atom-economic formation of alkenyl- and (homo)allyl boronates from dienes and boronic esters

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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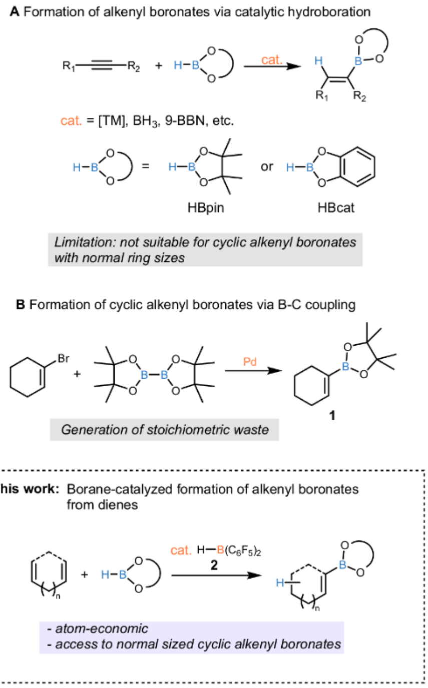
Based on the finding that bis(pentafluorophenyl)borane reacts with dienes at elevated temperatures to alkenyl boranes, contrary to the expected alkyl boranes, we developed a scalable and atom-economic bis(pentafluorophenyl)borane-catalyzed process for the synthesis of alkenyl and (homo)allyl boronates from dienes and boronic esters. This method enables the synthesis of cyclic alkenyl boronates with normal ring size that were previously inaccessible via the catalyzed hydroboration of alkynes.

Introduction

Alkenyl boronates are valued as stable reagents for transition metal-catalyzed, stereospecific C–C couplings, which are preeminent in synthetic medicinal chemistry.[1] The classic approach for the synthesis of these reagents relies on the hydroboration of alkynes.[2] However, dioxaborolanes such as pinacolborane (HBpin) and catecholborane (HBcat) are inert to hydroboration. Therefore, a variety of transition metal complexes that catalyze the hydroboration of alkynes with pinacolborane or catecholborane have been developed.[3] Moreover, carboxylic acids, amides, hydroxides and various main-group compounds have been found to be effective in catalyzing this reaction.[4] In the early 1990s, Periasamy and co-workers demonstrated that BH_3 complexes have a catalytic effect in the formation of alkenyl boronates from alkynes and catecholborane.[5] Further research by Arase and Hoshi revealed that alkylboranes such as 9-BBN and dicyclohexylborane efficiently catalyze the *Z*-selective hydroboration of alkynes with pinacolborane and catecholborane under mild conditions in a stereospecific manner (Scheme 1A).[6] This method has been widely used for the synthesis of bioactive compounds, noteworthy also on kilogram-scale in an industrial setting.[7] Detailed mechanistic investigations by Thomas and Llyod-Jones showed that the Arase-Hoshi reaction proceeds by transborylation via a B-C/B-H σ-bond metathesis.[8] Moreover, in situ prepared or isolated bis(pentafluorophenyl)borane **2**, also known as Piers' borane, was shown to be an effective catalyst for alkyne hydroboration with pinacolborane.[9]



Scheme 1. The context of this work.

However, the formation of alkenyl boronates via catalyzed hydroboration of alkynes has a major limitation: It cannot be applied routinely for the synthesis of alkenyl boronates if the corresponding alkyne precursor is inaccessible or difficult to

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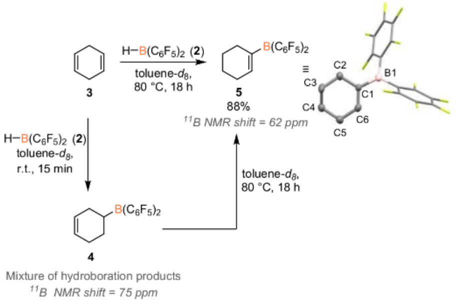
Supplementary Information available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x synthezise, as it is the case for normal and medium sized rings. For example, cyclohexyne, which has been studied since the early 1960s, can be produced in situ but cannot be isolated, and no reaction of this alkyne with boranes has been reported.[10] Therefore, cyclic alkenyl boronates with normal ring sizes such as cyclohexenylboronic acid pinacol ester **1** are usually prepared via transition metal-catalyzed B–C coupling reactions which mandate the stoichiometric formation of by-products (Scheme 1B).[11] In another method ruthenium or molybdenum-based catalysts are used for ring-closing metathesis of linear alkenyl boronates to form cyclic alkenyl boronates.[12] More recently, elegant organocatalyzed methods for the synthesis of **1** involving radical pathways have been reported.[13] However, these methods require an excess of bis(pinacolato)diboron and use stoichiometric leaving groups. Since cycloalkenyl boronates are used for the derivatization of drug candidates, the development of new atom-economic methods for their preparation is of interest for pharmaceutical chemistry.[14]

Results and discussion

As part of our studies on the bis(pentafluorophenyl)borane (**2**)-catalyzed isomerization of olefins, we investigated the stoichiometric reaction of 1,4-cyclohexadiene **3** with $HB(C_6F_5)_2$ (Piers' borane) **2** (Scheme 2).[15] At r.t. and short reaction times, a mixture of hydroboration products is obtained in addition to unreacted 1,4-diene and isomerized 1,3-diene. Therefore, we assume that a mixture of mono- and di-borylated compounds is obtained with **4** as the major product. A new peak in the ^{11}B NMR spectrum at 75 ppm appeared, which is indicative of an alkylborane and in agreement with the ^{11}B NMR shift of bis(pentafluorophenyl)cyclohexylborane.[16] However, at 80 °C the ^{11}B NMR signal at 75 ppm vanishes and a new signal at 62 ppm emerges, which hints to the formation of an alkenyl borane species. Removal of the solvent gave the product **5** in 88% yield. The identity of **5** was substantiated by single crystal X-ray diffraction (SCXRD), which allowed the double bond to be unequivocally localized based on the C–C bond lengths (Scheme 2).



Scheme 2. Initial finding: Stoichiometric reaction of $HB(C_6F_5)_2$ (**2**) with 1,4-cyclohexadiene (3). Molecular structure of **5** derived from SCXRD. Thermal ellipsoids drawn at 50% probability level. Selected bond lengths of **5**: d(C1-C6) = 1.369 Å, d(C5-C6) = 1.482 Å, d(B1-C1) = 1.580 Å. Note that the reaction at r.t. gives a mixture of 1,3-diene, 1,4-diene and hydroboration products.

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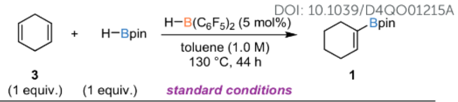
Table 1. Selected observations during reaction optimization.



entry	Deviations from standard conditions	yield **4** [%][a,b]
1	none	91 (88)
2	reaction at 80 °C (22 h)	traces
3	0.1 M concentration	19
4	no $HB(C_6F_5)_2$	0
5	$HB(2,6\text{-}C_6F_2H_3)_2$ instead of $HB(C_6F_5)_2$	33
6	$HBCy_2$ instead of $HB(C_6F_5)_2$	0
7	9-BBN instead of $HB(C_6F_5)_2$	0

[a]Yield determined by NMR using *p*-xylene as internal standard. [b]Yield of isolated product after column chromatography in parenthesis.

NMR spectroscopic studies by Oestreich and co-workers, as well as experimental and computational investigations by our group, have shown that Lewis acidic boranes with fluorinated aryl substituents undergo transborylations with pinacolborane (HBpin).[15,17] We now hypothesized that such a transborylation of **5** would release Piers' borane **2** and allow a catalytic reaction to obtain cyclohexenyl boronate **1**. Pleasingly, this is the case: In toluene at 130 °C and with only 5 mol% **2**, the reaction of 1,4-cyclohexadiene **3** with pinacolborane forms **1** in 91% yield, as determined by ^1H NMR using *p*-xylene as an internal standard (Table 1). The yield of the isolated product is comparable at 88%. We further observed that a high diene concentration is critical for the reaction to proceed, since the 0.1 M reaction gave only minor amounts of product. A yield of only 32% was observed with the less Lewis acidic $HB(2,6\text{-}C_6F_2H_3)_2$ and no product was formed with dialkylboranes $HBCy_2$ and 9-BBN as catalysts (Table 1). We then attempted to expand the scope of the reaction towards different dienes (Scheme 3A). 1,3-Cyclohexadiene gave the product **1** in a comparable yield of 80% under the same conditions as 1,4-cyclohexadiene **3**. We were pleased that upscaling the reaction works equally well, as we were able to synthesize **1** on gram scale under similar conditions. The reaction also works with medium sized rings: The alkenyl boronate **6** was isolated in 60% and 59% yield for 1,5-cyclooctadiene and 1,3-cyclooctadiene as substrates, respectively. 1,3-Cycloheptadiene reacts under the same conditions to the corresponding alkenyl boronate **7** in 66% yield. The alkenyl boronate **8** derived from cyclopentadiene was isolated in 35% yield. This reaction required lower temperatures and a lower concentration to prohibit dimerization of the cyclopentadiene substrate. Using 1-methyl-1,4-cyclohexadiene and 1-ethyl-1,4-cyclohexadiene as substrates, the corresponding 2-borylated allyl boronates **9** and **11** could be isolated in 50% and 44% yield after 2 h at 80 °C. Longer reaction times gave inseparable mixtures.

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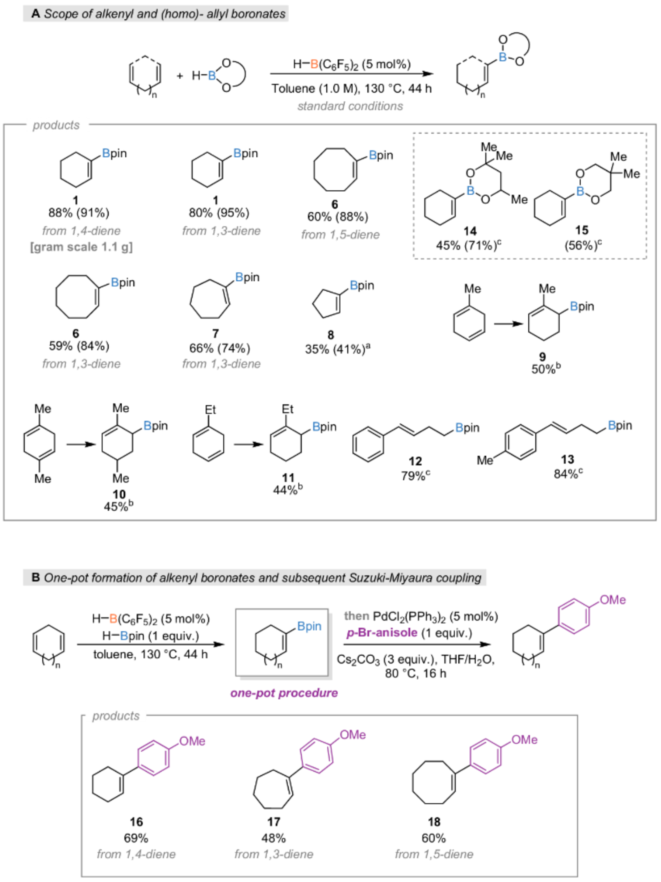

Scheme 3. Scope of the borane catalyzed reaction of dienes with boronic esters and one-pot Suzuki-Miyaura coupling of alkenyl boronates. Isolated yields are given. In situ yields were determined by ^{1}H NMR using *p*-xylene as an internal standard and are given in parenthesis. ^{a}Carried out using 10 mol% catalyst at 0.1 M concentration. ^{b}Reaction was run for 2 h at 80 °C. ^{c}Reaction was run for 22 h at 80 °C.

These products likely form by isomerization under thermodynamic control. Under the same conditions, 1,4-dimethyl-1,4-cyclohexadiene gave the corresponding allyl boronate **10** in 45% yield. When using 1-phenyl-1,3-butadiene as a substrate, the reaction gave homoallyl boronate **12** in 79% yield after 22 h at 80 °C. The methylated derivative gave **13** in 84% yield. Employing 4,4,6-trimethyl-1,3,2-dioxaborinane instead of HBpin at 80 °C for 22 h, the alkenyl boronate 14 was observed in 71% yield and isolated in 45% yield. Under the same conditions, 5,5-dimethyl-1,3,2-dioxoborinane gave the borylated product 15 in 56% yield. We further developed a one-pot procedure for a Suzuki-Miyaura coupling. In the first step, we conducted the catalytic reaction using standard conditions for 1,4- cyclohexadiene, 1,3-cycloheptadiene and 1,5-cyclooctadiene (Scheme 3B). Without isolation of the product or solvent removal, we added bis(triphenylphosphine)-palladium chloride, *p*-bromo anisole and a THF/H_2O mixture, together with Cs_2CO_3 as a base. After additional 16 h at 80 °C,

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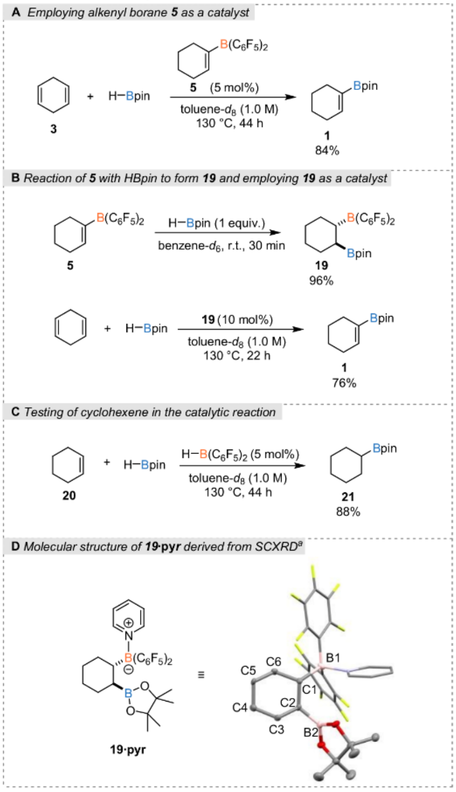
we were able to isolate the corresponding coupling products **16** to **18** in 69% to 48% yield. We then became interested in the mechanism of the reaction. Our mechanistic hypothesis involves hydroboration of the diene to alkylborane species **4**, followed by isomerization of the remaining double bond by free Piers' borane to form the alkenyl borane **5**. To test if alkenyl borane **5** is a likely intermediate in the catalytic reaction, we isolated **5** and employed it as a catalyst (Scheme 4A). Under authentic conditions 5 shows similar catalytic activity as Piers' borane (**2**). Therefore, we conclude that under the reaction conditions **5** can indeed undergo transborylation and release the Piers' borane catalyst.



Scheme 4. Catalytic and stoichiometric control experiments. In situ yields are given and were determined by ^{1}H NMR using an internal standard. ^{a} Drawn at 50% probability level: Selected bond lengths for **19·pyr**: d(C1-C2) = 1.553(6) Å, d(C1-C6) = 1.550(6) Å, d(B1-C1) = 1.644(7) Å, d(B2-C6) = 1.561(6) Å.

We further considered the possibility that after transborylation of **5** with pinacolborane, the alkenyl boronate **1** can react with the released Piers' borane (**2**) in a hydroboration reaction. Therefore, we reacted **5** with pinacolborane in a stoichiometric reaction. After 30 minutes at r.t. **5** is fully consumed, as determined by ^{1}H NMR, since the olefinic signal of **5** vanished. We assume that the new and almost quantitatively formed species is the vicinal diborylated compound **19** (Scheme 4B). We successfully isolated the product as a pyridine adduct and confirmed the trans-configuration of the cyclohexyl ring through SCXRD (Scheme 4D). However, we could not isolate **19** in the absence of additional Lewis base. Oestreich and co-workers described for the catalytic hydroboration of olefins and alkynes with pinacolborane a transborylation step at an alkylborane, and noted that allyl benzene and pinacolborane react in the presence of catalytic amounts of Piers' borane.[17] Since these findings suggest that transborylation can occur at a sp^3 carbon, we also tested cyclohexene as a substrate to elucidate whether transborylation on a secondary alkylborane is a plausible mechanistic hypothesis for the formation of **1**.

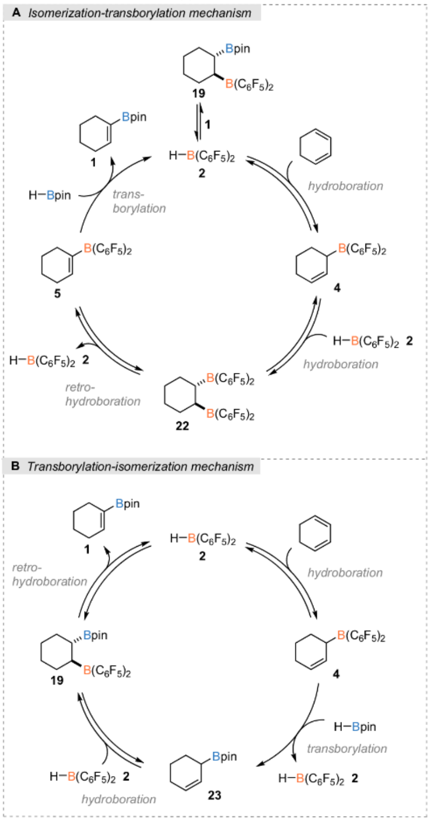


Figure 1. Proposed catalytic cycles for the reaction.

Indeed, we found that cyclohexyl boronate **21** forms in 88% yield under standard conditions (Scheme 4C). When testing cyclohexene with HBCy$_2$ as a catalyst under the same conditions, only 12% of **21** was obtained. Based on our findings and the previous mechanistic work of the groups of Thomas and Oestreich, we derived two plausible mechanistic scenarios. Since 1,4-cyclohexadiene is rapidly isomerised to 1,3-cyclohexadiene under the reaction conditions, we show the mechanism only for 1,3-cyclohexadiene (Figure 1). In both catalytic cycles, the reaction commences with a hydroboration of a double bond by Piers' borane (**2**) to form the alkylborane species **4**. In the first case (Figure 1A), a second equivalent of **2** undergoes hydroboration of the second double bond to form the vicinal diborylated intermediate **22**. Retro-hydroboration of **22** can then lead to alkenyl borane **5** which can undergo rapid transborylation under the reaction conditions to regenerate the catalyst **2** and release the product **1**. We assume that the hydroborations are reversible and therefore small amounts of free Piers' borane are always present, which can act as a catalyst. Note that **1** and **19** are linked via a hydroboration/retro-hydroboration by **2** and therefore mechanism A is also accessible starting from **19**. In the second catalytic cycle, after hydroboration by Piers' borane **2** a direct transborylation of **4** could take place to form allyl boronate **23** as an intermediate (Figure 1B). Transborylation at secondary C(sp^3) has been previously reported by Thomas and co-workers.[18] The released Piers' borane could then hydroborate the allyl boronate **23** to form the vicinal diborylated compound **19**. *Retro*-hydroboration by Piers' borane **2** releases the product **1** and closes the catalytic cycle. We independently synthesised **23** and indeed observed the formation of **19** upon treatment with Piers' borane **2**, further supporting the possibility of this mechanistic pathway (see supplementary information).

Conclusions

In summary, we present a catalytic method for preparing a class of alkenyl and allyl boronic esters, specifically cyclic alkenyl boronates of normal ring size, which are not accessible by hydroboration of a triple bond followed by transborylation. This method provides a facile and atom-economic route to alkenyl boronates, utilizing Piers' borane ($HB(C_6F_5)_2$) catalyzed hydroboration of dienes with pinacolborane or related boronic acid esters. The key to the reaction's success is the electrophilic Piers' borane's ability to rapidly and reversibly hydroborate double bonds, allowing for the isomerization of the dienes double bonds.[19] However, this process consistently yields the thermodynamic product, which for substituted phenylbutadienes and cyclohexadienes are homoallyl boronates and cyclic allyl boronates, the latter being typically synthesized *via* metal-catalyzed hydroboration or coupling reactions.[20] We anticipate that the method reported herein will be widely applied in the preparation of cyclic alkenyl boronates, which are valuable starting materials for further synthetic transformations.

Author contributions

Felix Wech, Niklas Koch, and Tizian Müller: Investigation, Data curation. Urs Gellrich: Conceptualization, Funding acquisition, Supervision. Felix Wech and Urs Gellrich: Writing – original draft, Writing – review & editing.

Conflicts of interest

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There are no conflicts of interest to declare.

Data availability

The data supporting this article have been included as part of the supplementary information.

Acknowledgements

This work was supported by the DFG (Emmy-Noether program, GE 3117/1-1). The authors thank Dr. H. Hausmann for assistance with NMR experiments.

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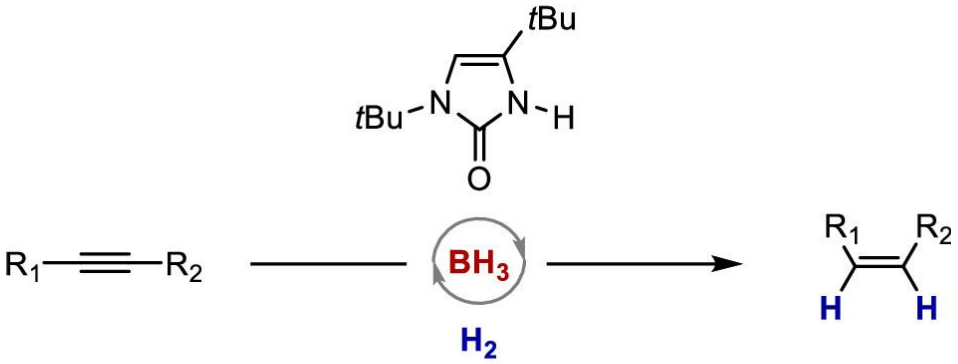
- The data supporting this article have been included as part of the Supplementary Information.
- Crystallographic data for **5** and **19·pyr** has been deposited at the Cambridge Crystallographic Data Centre under CCDC 2364438 and CCDC 2364453 and can be obtained from https://www.ccdc.cam.ac.uk/

5.2 In situ Formation of an Efficient Catalyst for the Semihydrogenation of Alkynes from Imidazolone and BH_3



- *Catalytic amounts of the simplest borane*
- *Bench-stable organic co-catalyst*
- *In situ formation of an FLP-type catalyst from BH_3*

The (*Z*)-selective semihydrogenation of alkynes catalyzed by BH_3 and an organic co-catalyst was studied. Kinetic studies revealed that the reaction is dependent of the alkyne concentration, but independent of the H_2 pressure. Thus, the reaction can be operated at low pressure. Mechanistic experiments hint that a tris(alkenyl)borane is formed which reacts with the co-catalyst in a protodeborylation forming an imidazolonate borane. Computational studies show that H_2 activation by the imidazolonate borane is endergonic but kinetically accessible allowing for catalytic turnover.

Felix Wech, Urs Gellrich

ACS Catal. **2022**, *12*, 5388–5396.

DOI: 10.1021/acscatal.2c00722

Final veröffentlichte Version online: 20. April 2022

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In Situ Formation of an Efficient Catalyst for the Semihydrogenation of Alkynes from Imidazolone and BH_3

Felix Wech and Urs Gellrich*

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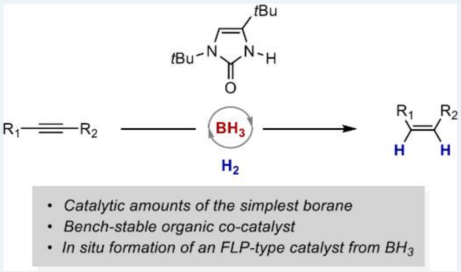
ABSTRACT: We herein report the finding that a sterically encumbered imidazolone turns the simplest borane, i.e., BH_3, into a potent catalyst for the semihydrogenation of alkynes. The efficiency of this catalyst system was demonstrated by the successful semihydrogenation of 15 different alkynes with excellent *Z*-selectivity. Kinetic studies show that the reaction rate depends on the alkyne concentration but is independent of the hydrogen pressure. Thus, the catalytic reaction can be operated at low hydrogen pressures (2 bar). Further mechanistic investigations and dispersion-corrected double-hybrid density functional theory (DFT) computations revealed that the imidazolone undergoes an initial protodeborylation with a trialkenylborane, formed in situ by hydroboration of the alkyne with BH_3. The protodeborylation yields an imidazolonate borane that resembles a frustrated Lewis pair and is capable of activating dihydrogen.



- *Catalytic amounts of the simplest borane*
- *Bench-stable organic co-catalyst*
- *In situ formation of an FLP-type catalyst from BH_3*

KEYWORDS: *frustrated Lewis pairs, hydrogenation, borane, alkyne, main-group catalysis*

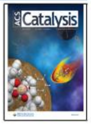
INTRODUCTION

The stereoselective semihydrogenation of alkynes is of utmost importance for the industrial synthesis of insect pheromones, pharmaceuticals, and fine chemicals.[1] Furthermore, this reaction is used for industrial polymerization processes to remove alkyne residues from olefin feedstocks.[2] One prevalent method for the *Z*-selective semihydrogenation of alkynes uses Lindlars's catalyst.[3] The catalyst relies on a poisoned palladium catalyst to prohibit over-reduction to the alkane. Disadvantages of this process are the use of toxic lead as catalyst poison and *Z*/*E* isomerization.[3c] Therefore, various other heterogeneous and homogeneous noble transition-metal-based catalysts for this reaction have been developed.[4] Furthermore, the last decade has witnessed a proliferation of reports on first-row transition-metal complexes that effectively catalyze this synthetically relevant transformation.[5] Other established methods for the semireduction of alkynes make use of stoichiometric amounts of boranes.[6] Motivated by the seminal finding from Stephan and co-workers that certain combinations of sterically encumbered Lewis bases and highly Lewis acidic boranes, referred to as frustrated Lewis pairs (FLP), are able to activate dihydrogen, Repo et al. devised a protocol for an FLP-catalyzed semihydrogenation of alkynes (Scheme 1).[7,8] This finding fueled the development of different FLP-catalyzed reductions of alkynes.[9] We have recently reported that an FLP-type catalyst formed in situ by coordination of pyridone to Piers' borane, i.e., $HB(C_6F_5)_2$, is also capable of catalyzing this reaction.[10,11] Classic FLPs usually contain Lewis acidic boranes with fluorinated aryl substituents, such as Piers' borane or $B(C_6F_5)_3$.[12] The synthesis of these boranes requires sophisticated techniques executed under an inert gas atmosphere.[13] However, more recently, Repo and co-workers demonstrated that a carefully designed FLP with the smallest boryl site, BH_2, also splits dihydrogen.[14,15] We now became interested in elucidating whether an appropriate organic co-catalyst transforms simple BH_3 into an effective FLP-type catalyst for the semihydrogenation of alkynes, which is potentially suited for large-scale applications.

RESULTS AND DISCUSSION

Our attempts commenced by assessing the efficacy of several organic co-catalysts for the semihydrogenation of 1-phenyl-1-propyne with $BH_3 \cdot SMe_2$ complex (Table 1). The first co-catalyst we tested was 6-*tert*-butyl-2-pyridone (**1a**), which was used previously in conjunction with Piers' borane for the hydrogenation of alkynes in our group.[11,16] After a 24 h reaction time at 130 °C under 10 bar H_2 pressure, the Z-alkene was obtained in 38% yield. We then tested 6-*tert*-butyl-2-thiopyridone (**1b**), which gave the alkene in 84% yield under

Received: February 10, 2022
Revised: April 5, 2022
Published: April 20, 2022



https://doi.org/10.1021/acscatal.2c00722
ACS Catal. 2022, 12, 5388−5396

Scheme 1. Context of This Work: Hydrogen Activation by a Phosphine-Borane FLP, the First FLP-Type Catalyst for the Semihydrogenation of Alkynes, and the Imidazolone/BH_3 Catalyzed Semihydrogenation Reported Herein

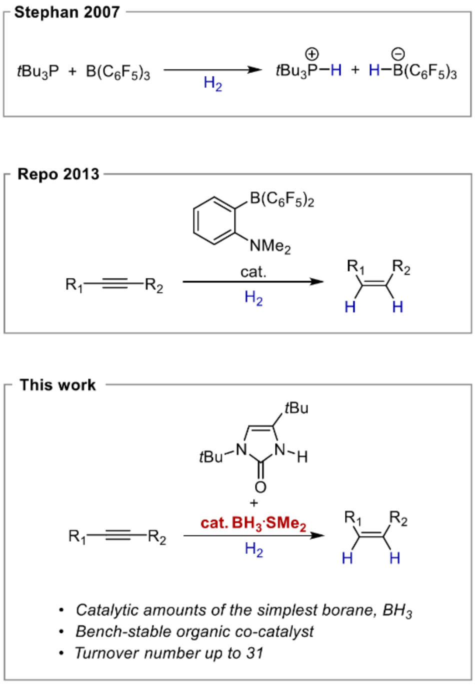
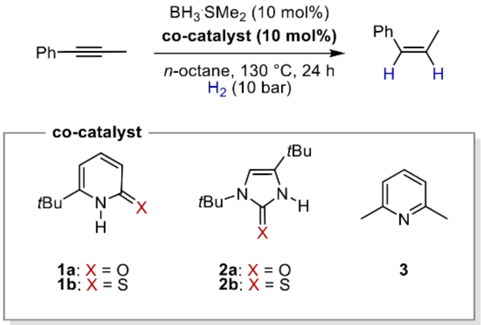


Table 1. Assessment of Organic Co-Catalysts for the Semihydrogenation of 1-Phenyl-1-Propyne



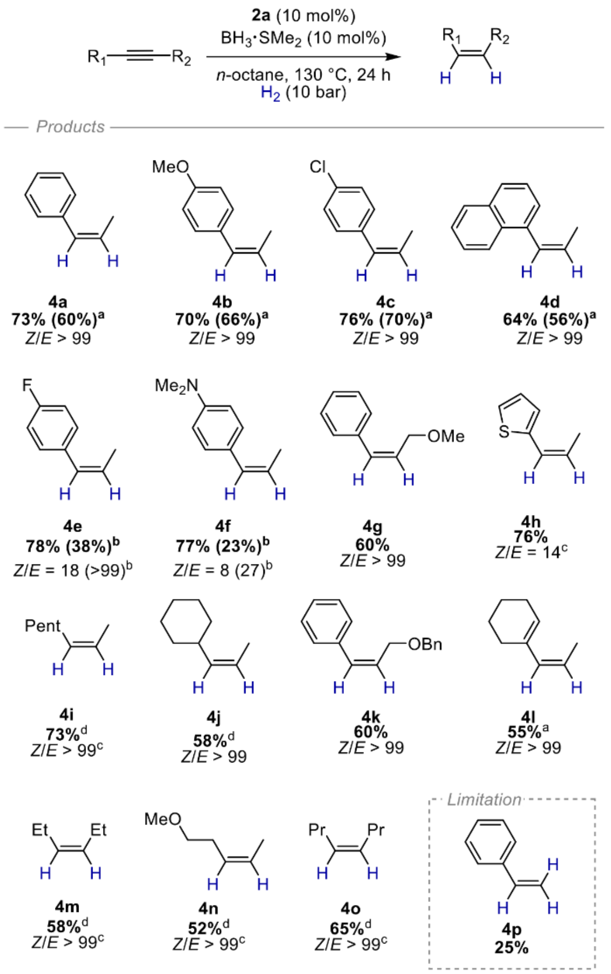
entry	co-catalyst	yield[a] (%)	Z/E[b]	TON
1	**1a**	38		3.8
2	**1b**	84	2.6	8.4
3	**2a**	73	>99	7.3
4	**2b**	8		0.8
5	**3**	4		0.4
6	none	8		0.8

[a] Yield determined by NMR using 1,3,5-trimethoxybenzene as internal standard. [b] Z/E ratio determined by GC–MS.

the same conditions. However, *Z*/*E* isomerization was observed and a 2.6:1 mixture of both isomers was obtained. Next, the catalytic performance of the more basic 1,4-di-*tert*-butylimidazolone (**2a**) was evaluated.[17] Pleasingly, after 24 h reaction time, Z-alkene was obtained as the major product in 73% yield. The *E*-isomer was only detected in traces by GC–MS. When using 1,4-di-*tert*-butyl-thioimidazolone (**2b**) as a co-catalyst, only 8% of the alkene was detected, indicating that no catalytic reaction was achieved. Furthermore, we tested lutidine (**3**) as a co-catalyst, a base that is commonly used in FLP chemistry.[18] The hydrogenation with **3** yielded only 4% of the olefin. This result indicates that the bifunctionality of **2a** that can act as Lewis base and (weak) Brønsted acid is indeed important for its catalytic activity. A reaction with $BH_3{\cdot}SMe_2$ without co-catalyst yielded 8% of the alkene, likely formed by direct hydrogenolysis of the B–C bond, which is less than one turnover.[9b,c] Thus, the addition of **2a** transformed the simple $BH_3{\cdot}SMe_2$ complex that is by itself not catalytically competent, into an efficient and selective hydrogenation catalyst. With this promising result in hand, we explored the scope and the limitations of the semihydrogenation of alkynes catalyzed by $BH_3{\cdot}SMe_2$ and **2a**. Using this simple catalyst system, we were able to hydrogenate a variety of different internal alkynes to the corresponding Z-alkene (Scheme 2). As mentioned above, at 130 °C and under 10 bar of hydrogen, the hydrogenation of 1-phenyl-1-propyne to *Z*-*β*-methylstyrene **4a** proceeded in 73% yield. 2-Propynylthiophene gave the olefin **4h** in 79% yield, and the reaction with (4-*N*,*N*-dimethylaminophenyl)propyne gave **4f** in 77% yield, which shows that coordinating groups are tolerated in this reaction. Aromatic and aliphatic ethers are suitable substrates, as demonstrated by the formation of **4g**, **4k**, and **4n**. Furthermore, the successful hydrogenation of 4-chlorophenylpropyne and 4-fluorophenylpropyne shows that electron-poor aromatic substituents are tolerated (**4c** and **4e**).

While the hydrogenation of aryl-substituted alkynes readily proceeded within 24 h, the hydrogenation of alkynes with an aliphatic residue required a longer reaction time of 48 h. Under these conditions, 2-octyne was hydrogenated to give **4i** in 73% yield, as well as 4-octyne and 3-hexyne to give **4o** and **4m** in 65 and 58% yields, respectively. Note that the lower yield in the case of 3-hexyne is possibly due to the low boiling point of this substrate. Moderate yields were obtained for aliphatic ethers, such as 1-methoxy-3-pentyne and 1-methoxy-3-phenylpropyne. The hydrogenation of 1-propynylcyclohexene shows that in the presence of olefinic double bonds, the alkyne is selectively hydrogenated to the *Z*-olefin. The reaction shows an excellent *Z*-selectivity for most substrates. While in the case of the unsubstituted phenylpropyne trace amounts of *E*-product were detected, only a single isomer was obtained for most other substrates. However, the olefins **4e**, **4f**, and **4h** were obtained with lower *Z*-selectivities of 18:1, 8:1, and 14:1, respectively. To elucidate whether the lower selectivity originates in these cases from an isomerization during the hydrogenation, the catalytic reactions with 4-fluorophenlpropyne and 4-(*N*,*N*-dimethylaminophenyl)propyne were run for 8 h with a doubled concentration of alkyne. Under these conditions, **4e** and **4f** were indeed obtained with improved *Z*-selectivities of 99:1 and 27:1. A limitation of the catalytic protocol described herein is the hydrogenation of terminal alkynes; under standard conditions, the reaction with phenylacetylene yielded only 24% styrene (**4p**).

Scheme 2. Scope of the Semihydrogenation of Alkynes Catalyzed by 2a and $BH_3·SMe_2$[e]



[a] Isolated yields in parentheses. [b] 8 h reaction time and 5 mol % catalyst loading. [c] Z/E ratio determined by NMR. [d] 48 h reaction time. [e] Yields are determined by NMR using 1,3,5-trimethoxy-benzene as internal standard and are the average of two runs. Unless otherwise noted, Z/E ratios were determined by GC−MS.

To gain mechanistic insights into this transformation, we conducted a series of kinetic experiments. First, we determined the turnover frequency (TOF) of the hydrogenation of 1-phenyl-1-propyne with **2a** and $BH_3·SMe_2$ at different alkyne concentrations (Figure 1, top). A linear relationship between the TOF and the starting concentration of the alkyne was observed. This indicates that the alkyne enters the productive catalytic cycle between the resting state and the rate-determining transition state.[19] We then evaluated if the hydrogen concentration affects the reaction rate. Therefore, we investigated the reaction applying different hydrogen pressures (Figure 1, bottom). When lowering the hydrogen pressure, no significant change in the reaction rate could be observed. Even at a 2 bar H_2 pressure, the TOF does not decrease within the error of the measurement. Therefore, we concluded that hydrogen does not participate in the rate-determining states of the underlying mechanism. With the results of these experiments in hand, we performed the hydrogenation of phenylpropyne at a low hydrogen pressure (2 bar) under standard conditions for 24 h (Scheme 3, top). The *Z*-*β*-methylstyrene **4a** was obtained in 60% yield compared to 73% at 10 bar. This drop in yield is likely due to a lower internal temperature that is reached at a lower H_2 pressure since the catalytic reaction is operated at a temperature that is slightly above the boiling point of *n*-octane (125.6 °C). However, this experiment shows that the catalytic procedure

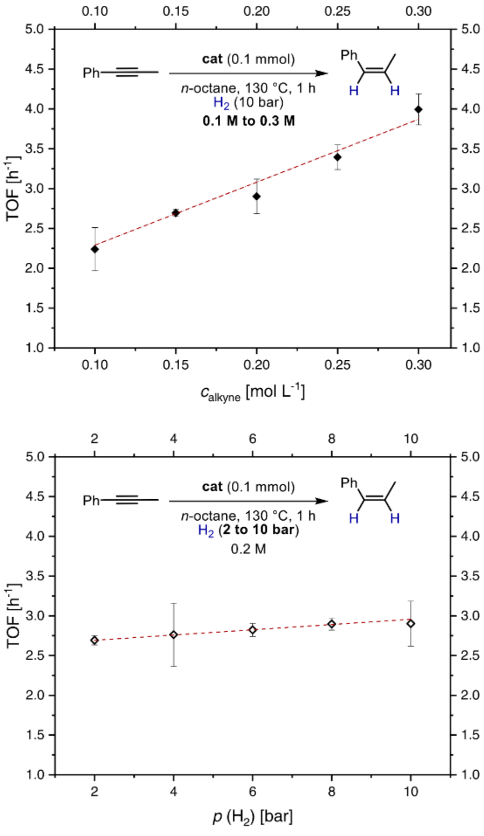


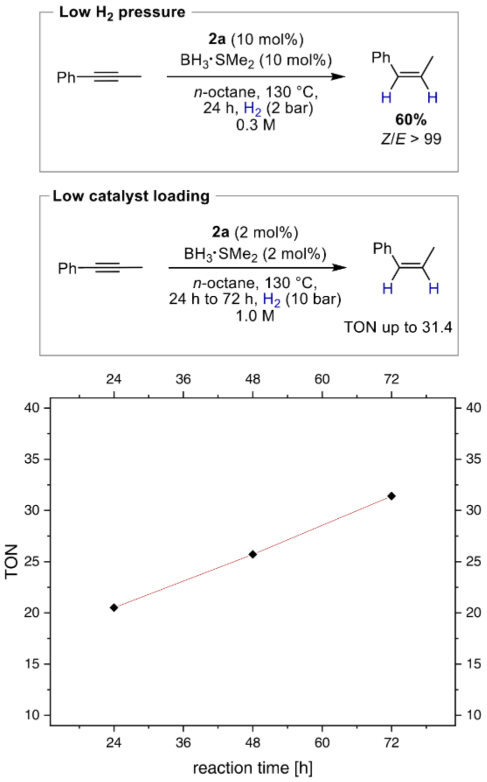
Figure 1. Investigation of the hydrogenation of 1-phenyl-1-propyne catalyzed by **2a** and $BH_3 \cdot SMe_2$ at different alkyne concentrations at 10 bar H_2 pressure *n*-octane (5 mL) (top). Hydrogenation of 1-phenyl-1-propyne with **2a** and $BH_3 \cdot SMe_2$ at different H_2 pressures at a 0.2 M alkyne concentration in *n*-octane (5 mL) (bottom).

described herein can be conveniently conducted at low hydrogen pressures.

As the reaction rate increases with alkyne concentration, we envisioned that the catalytic reaction can be run at a higher alkyne concentration using a low catalyst loading to achieve a high turnover number (TON). Therefore, the reaction was run at a 1 M concentration of 1-phenyl-1-propyne, which corresponds to 2 mol % catalyst loading (Scheme 3, bottom). TONs of 20.7, 25.7, and 31.4 were observed after 24, 48, and 72 h, respectively. Thus, up to 31 equivalents of substrate were converted per BH_3 as a catalytic entity. We then focused our attention on elucidating the nature of the actual catalyst formed under the reaction conditions. During our initial reaction optimization, we noticed that it is important that the $BH_3 \cdot SMe_2$ is first reacted with the alkyne in the absence of the co-catalyst for 30 min at r.t. Within the 30 min preformation, the $BH_3 \cdot SMe_2$ hydroborates the alkyne and forms a tri-alkenylborane.[20] Therefore, we assume that the catalytic reaction commences with a protodeborylation of one of the alkenyl substituents, which is initiated by **2a**. To substantiate the importance of a protodeborylation for the catalytic reaction, we synthesized *N*-methyl imidazolone **5** and used it as a co-catalyst for the semihydrogenation of 1-phenyl-1-propyne (Scheme 4A). Under standard conditions, only 3% olefin and no catalytic turnover were observed. This result indicates that the NH group is indeed vital for the catalytic reaction. To prove whether **2a** is capable of mediating a protodeborylation, we reacted tri-((Z)-3-hexenyl)borane **6**, obtained from hydroboration of 3-hexyne with $BH_3 \cdot SMe_2$, with **2a** (Scheme 4B). At r.t., **2a** does not coordinate to **6**, as deducible from the ^1H and ^{11}B NMR. However, upon heating to 100 °C, protodeborylation and formation of (*Z*)-3-hexene were observed. Furthermore, a new borane species emerged that we tentatively assigned to imidazolonate borane **7**.[20] We assume that **7**, which can be regarded as an intramolecular FLP, is responsible for the hydrogen activation during the catalytic transformation.

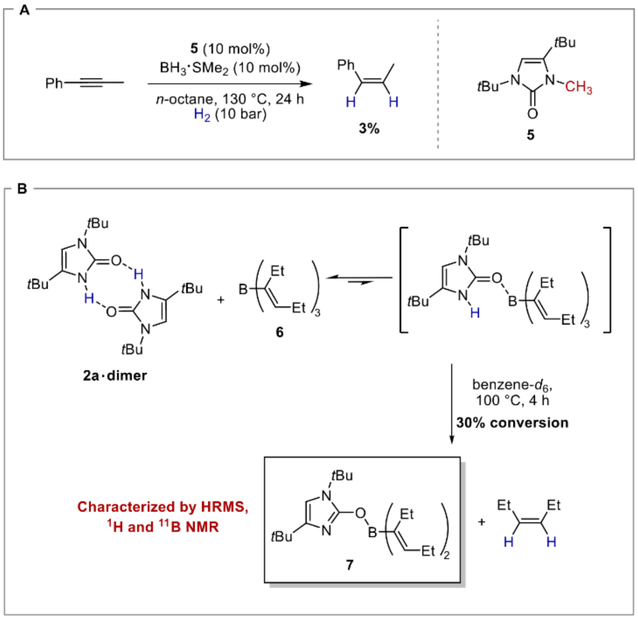
To test this hypothesis, we studied the hydrogen activation with model compound **8** (methyl instead of ethyl groups at the alkenyl substituents) with the spin-component scaled,

Scheme 3. Catalytic Experiments Run at Low H_2 Pressures and Low Catalyst Loading[a]



[a] Yields and TONs were determined by ^1H NMR with 1,3,5-trimethoxy-benzene as the internal standard. *Z/E* ratios were determined by GC−MS and are >99:1 in all cases.

Scheme 4. (A) Semihydrogenation of Phenylpropyne with 5 as an Organic Co-Catalyst and (B) Protodeborylation of Tri-((Z)-3-Hexenyl)borane 6 by 2a and Formation of the Bis-Alkenyl Imidazolonate Borane 7



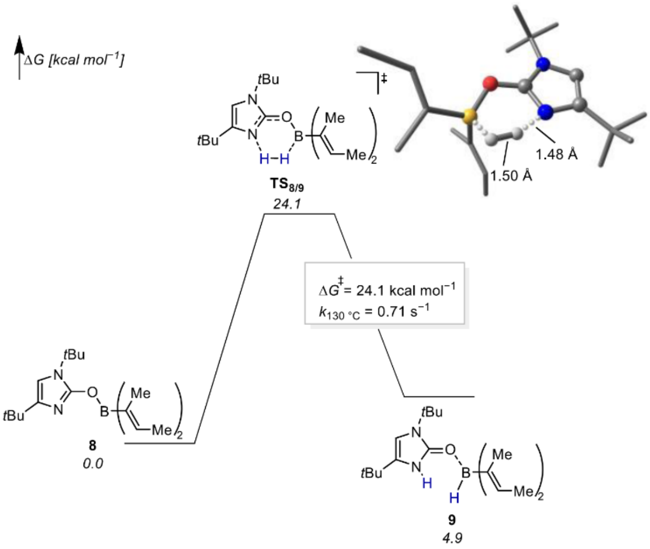


Figure 2. Gibbs free energies of the H_2 activation by **8** computed at revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c. The SMD model for *n*-octane was used to implicitly account for solvent effects.

dispersion-corrected double-hybrid functional revDSD-PBEP86-D4 and the large def2-QZVPP basis set (Figure 2).[21] For structure optimizations, the PBEh-3c composite method was used.[22] Solvent effects were considered implicitly

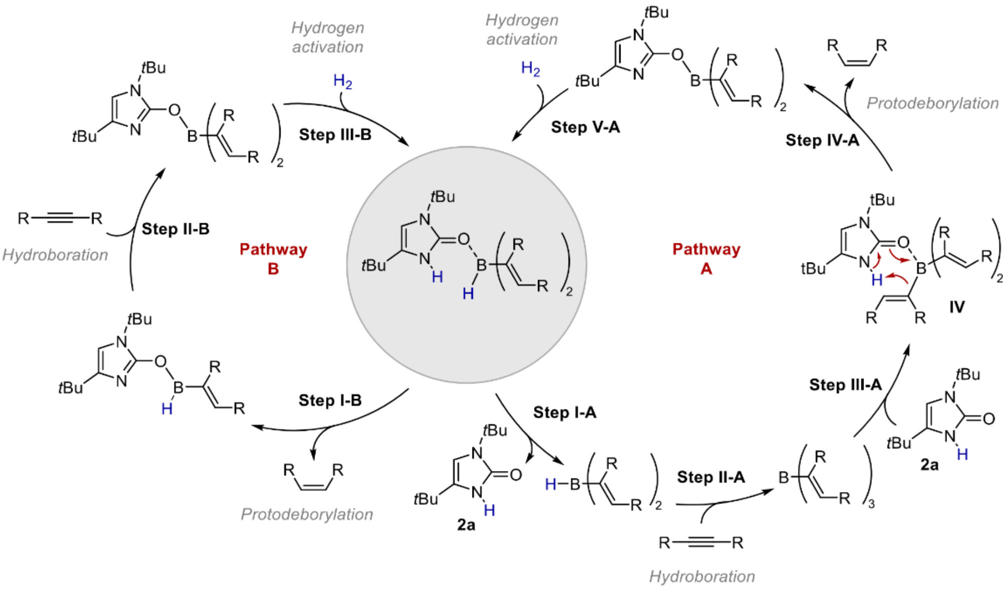


Figure 3. Two plausible pathways for the hydrogenation of an internal alkyne: Pathway A consists of an initial dissociation, followed by hydroboration of an alkyne (Step I-A and II-A). This leads to the formation of a tri-alkenylborane. Coordination of **2a** initiates a protodeborylation that releases imidazolonate borane and the product (Step III-A and IV-A). The imidazolonate borane can now activate hydrogen in an FLP-like manner (Step V-A). Pathway B starts with an initial protodeborylation to release the product (Step I-B). The product can then hydroborate the substrate to give an imidazolonate borane which can then activate hydrogen (Step II-B and III-B).

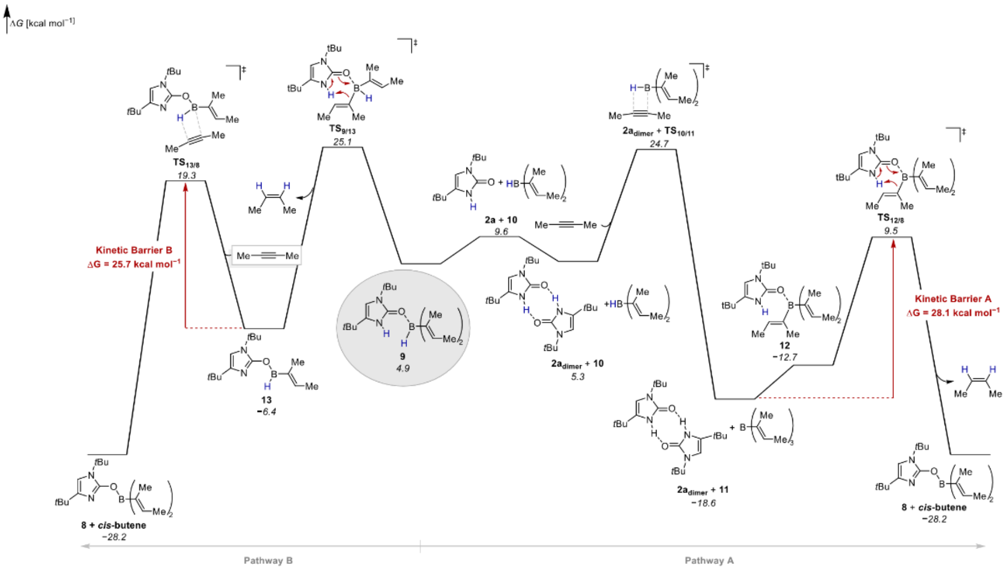


Figure 4. Two possible pathways for the hydrogenation of 2-butyne starting from the imidazolone borane complex **9** computed at revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c. Gibbs free energies are given with respect to the separated reactants. The SMD model for *n*-octane was used to implicitly account for solvent effects.

using the SMD model for *n*-octane.[23] According to the computations, hydrogen activation by **8** and the formation of the imidazolone borane complex **9** is endergonic. However, hydrogen activation via $\mathbf{TS_{8/9}}$ is kinetically accessible. The computed barrier of 24.1 kcal mol^{-1} corresponds to a rate constant of 0.71 s^{-1} at 130 °C. Upon the formation of the imidazolone borane complex, the product of the hydrogen activation, two catalytic pathways seemed plausible (Figure 3).

An initial dissociation of the imidazolone borane complex could form a bis-alkenylborane that can undergo hydroboration of the alkyne substrate, forming a tri-alkenylborane (Figure 3, Step I-A, and II-A). The imidazolone (**2a**) can reenter the cycle and coordinate back to the tri-alkenylborane (Step III-A). After protodeborylation, Z-olefin, the product of the catalytic reaction, is released (Step IV-A). The imidazolonate borane that is formed can again activate hydrogen, which closes the catalytic cycle (Step V-A). Besides pathway A, a second productive pathway seems plausible (Figure 3, pathway B). This pathway is initiated by protodeborylation of the imidazolone borane complex, forming the trivalent borane species (Step I-B). The borane can then hydroborate the alkyne, which leads to an imidazolonate borane, which can again activate hydrogen (Step II-B and III-B). To elucidate which of the reaction paths is kinetically preferred, both pathways were investigated computationally (Figure 4).

Starting from **9**, the dissociation into **2a** and hydroborane **10** is almost thermoneutral if the dimerization of **2a** is considered (Figure 4). The free borane **10** can then hydroborate the alkyne via $\mathbf{TS_{10/11}}$. This exergonic reaction yields then tri-alkenylborane **11**. According to the computations, the coordination of imidazolone to the tri-alkenylborane is endergonic. This is in favorable agreement with our experimental NMR investigations that revealed that imidazolone **2a** and tri-((*Z*)-3-hexenyl)borane **4** do not associate. However, the endergonic coordination of **2a** to **11** can initiate a protodeborylation via $\mathbf{TS_{12/8}}$ that liberates the *Z*-olefin as the product of the catalytic reaction. The imidazolonate borane **8** that is deemed as the FLP-type catalyst reenters the catalytic cycle and can activate dihydrogen again (Figure 2). The kinetic barrier for this pathway is 28.1 kcal mol^{-1}. It is important to emphasize that this barrier must be surpassed initially to generate imidazolonate borane from tri-alkenylborane that is formed upon catalyst preformation (see Scheme 4). Pathway B commences with the protodeborylation of one alkenyl substituent of **9**, which yields the trivalent mono-alkenylborane **13** (Figure 4, Pathway B). Hydroboration of the alkyne by **13** via $\mathbf{TS_{13/8}}$ then regenerates **8**. The hydroboration also resembles the kinetic barrier of Pathway B, which is 25.7 kcal mol^{-1}. Thus, Pathway B is kinetically preferred over Pathway A. However, the barriers to enter Pathway A via $\mathbf{TS_{10/11}}$ and Pathway B via $\mathbf{TS_{9/13}}$ are similar. Therefore, $\mathbf{2a_{dimer}}$ + **11** and **13** are formed in similar proportions and the regeneration of catalyst **8** via protodeborylation of **11** ($\mathbf{TS_{12/8}}$) contributes to the overall barrier of the catalytic reaction. The assumption that Pathway B is the main productive pathway is substantiated by the kinetic experiments: Since the alkyne enters this catalytic cycle between the resting state and the rate-determining transition state, a dependency of the reaction rate from the alkyne concentration is expected (Figure 4). This agrees with the experimentally observed rate enhancement at high alkyne concentrations (Figure 1). However, for each substrate that is used, the identity of the catalyst differs due to the substrate being involved in the formation of the tri-alkenylborane.

■ CONCLUSIONS

In summary, we present a new protocol for the catalytic semihydrogenation of internal alkynes using simple $BH_3{\cdot}SMe_2$ complex and 1,4-di-*tert*-butylimidazolone (**2a**) as an organic co-catalyst. Using this catalytic system, a variety of different internal alkynes were hydrogenated in synthetically useful yields with excellent Z-selectivity. Mechanistic investigations indicate that the catalytically active species is an imidazolonate borane formed in situ by a protodeborylation. This imidazolonate borane resembles an FLP that is able to activate dihydrogen. The study reported herein is a curiosity-driven exploration of to what extent an FLP can be simplified and still operate as a hydrogenation catalyst. However, by essentially using the simplest borane, i.e., BH_3, as a hydrogenation catalyst for alkynes, the devised protocol might be suitable for large-scale applications. We expect the finding reported herein to stimulate further developments of FLP-type catalysts that rely on simple boranes.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.2c00722.

Detailed experimental procedures, copies of NMR spectra and GC traces, Cartesian coordinates, and energies of computed structures (PDF)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the German Research Foundation (DFG; Emmy-Noether Program, GE 3117/1-1). The authors thank Max Hasenbeck and Arthur Averdunk for initial experiments and Beyza Iltir for alkyne synthesis. Furthermore, continuous support by Prof. Dr. P. R. Schreiner, Prof. Dr. H. A. Wegner, and Prof. Dr. R. Göttlich is acknowledged.

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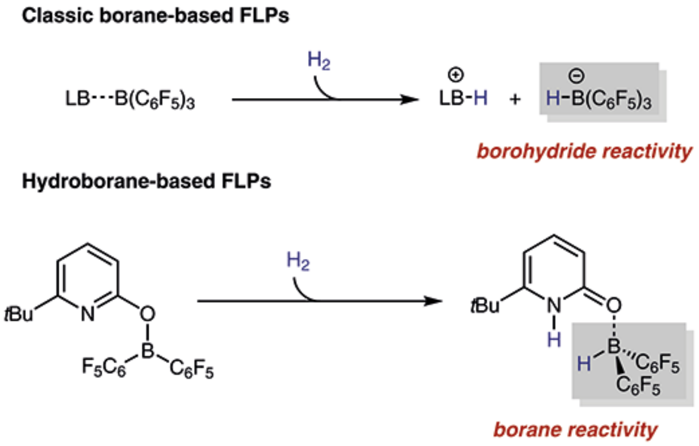
5.3 Hydrogenation of Olefins, Alkynes, Allenes, and Arenes by Borane-Based Frustrated Lewis Pairs



Frustrated Lewis-pairs (FLPs) that utilize H_2 activation to reduce unsaturated substrates have long been used. These catalysts are limited to substrates that are reactive towards borohydrides. This work highlights reactions of borane-based FLPs that exhibit hydroboration reactivity upon H_2 activation.

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Synthesis, **2022**, *54*, 3421-3431.

DOI: 10.1055/a-1684-5552

Akzeptiertes Manuskript online: 02. November 2021

Final veröffentlichte Version online: 22. Dezember 2021

Hydrogenation of Olefins, Alkynes, Allenes, and Arenes by Borane-Based Frustrated Lewis Pairs

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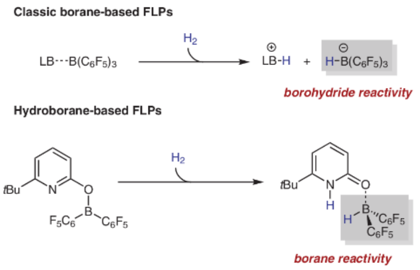
Published as part of the
Bürgenstock Special Section 2021 – Future Stars in Organic Chemistry



Received: 14.10.2021
Accepted after revision: 02.11.2021
Published online: 02.11.2021
DOI: 10.1055/a-1684-5552; Art ID: ss-2021-r0616-st

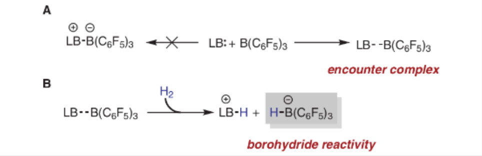
Abstract In recent years, borane-based frustrated Lewis pairs have proved to be efficient hydrogenation catalysts and they have become an alternative to transition-metal-based systems. The hydrogen activation by classic FLPs leads to a protonated Lewis base and a borohydride. Consequently, hydrogenations catalyzed by classic FLPs consist of stepwise hydride transfer reactions and protonations (or vice versa). More recently, systems that operate via an initial hydroboration have allowed the substrate scope for FLP-catalyzed hydrogenations to be extended. In this review, hydrogenations of organic substrates catalyzed by borane-based frustrated Lewis pairs are discussed. Emphasis is given to the mechanistic aspects of these catalytic reactions.

Key words frustrated Lewis pair, hydrogenation, hydrogen activation, hydroboration, pyridone–borane, metal-free catalysis

1 Introduction

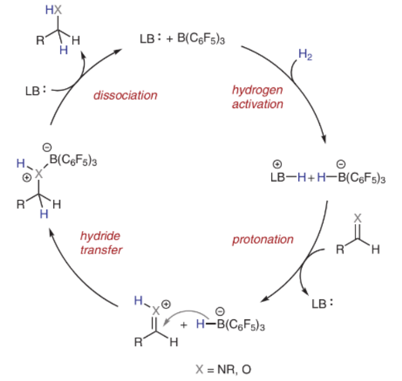
While the transition-metal-catalyzed hydrogenation of acetylene to ethylene has been known since the late 19th century,[1,2] the field of main group element catalyzed hydrogenations was discovered much later. The use of transition metal complexes to activate hydrogen and hydrogenate unsaturated substrates has been an extensively studied research topic in the last few decades.[2,3] Hydrogenations catalyzed by main group metals were discovered around the 1960s.[4] Using sub-stoichiometric amounts of $LiAlH_4$ at high temperatures and hydrogen pressures, olefins could be catalytically hydrogenated. However, the harsh reaction conditions made this reaction unfavorable in comparison to the transition-metal-catalyzed variants. The first metal-free hydrogenation came with the discovery of frustrated Lewis pairs (FLPs).

One of the most fascinating features of FLPs is their unique reactivity towards small molecules, especially molecular hydrogen.[5] This allowed the development of metal-free hydrogenation strategies employing H_2 instead of stoichiometric reducing agents, such as Hantzsch esters,[6] dihydrothiazoles,[7] or cyclohexadienes.[8] The key to this concept is that upon mixing of a sterically encumbered Lewis base (LB) with a highly Lewis acidic borane, such as $B(C_6F_5)_3$, a datively bound 'encounter complex' forms rather than a classic ionic Lewis adduct (Scheme 1A).[9–11] This encounter complex preserves the reactivity of both the Lewis acidic and Lewis basic sites and allows the system to activate hydrogen. Suitable Lewis bases are bulky phosphines such as $P(Mes)_3$, or nitrogen-based alternatives such as 2,2,6,6-tetramethylpiperidine (TMP), or 2,6-lutidine.[12,13] From a mechanistic point of view, the hydrogen bond is cleaved heterolytically by protonation of the Lewis base and hydride transfer to the Lewis acid.[14] An ion pair (or a zwitterionic species in the case of an intramolecular FLP) is formed that consists of a borohydride and the protonated Lewis base (Scheme 1B). The mechanisms for hydrogen activation by FLPs have been extensively studied and discussed in the literature.[9,10,15] This mode of bond activation pioneered the way for the first metal-free catalytic hydrogenation reactions, especially of polar substrates that can be readily reduced by common borohydride-based methods. These metal-free hydrogenations have been broadly reviewed in previous works.[5,14–17]



Scheme 1 (A) General concept of a frustrated Lewis pair (FLP) consisting of a Lewis base (LB) and the strong Lewis acid $B(C_6F_5)_3$. (B) Hydrogen activation by the FLP leads to the protonated LB and a borohydride species.

2 FLP-Catalyzed Hydrogenation of Polarized Double Bonds

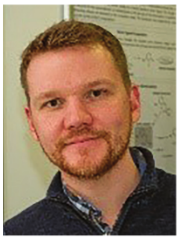


Scheme 2 General catalytic cycle for the FLP-catalyzed hydrogenation of a polarized double bond, such as in imines, aldehydes, or ketones.

The borohydride that forms upon hydrogen activation by the FLP can transfer a hydride to polar organic substrates. The first example of a metal-free catalytic hydrogenation is the FLP-catalyzed reduction of imines by the Stephan group (Scheme 2).[18] After H_2 activation the substrate is protonated which enhances its electrophilicity. Afterwards, the hydride is transferred to the iminium ion. The borane product complex can dissociate, which closes the catalytic cycle and releases the product. While this transformation works for imines,[18] as well as enamines[19] and a variety of other substrates, such as silyl enol ethers,[11,12,20,21] the catalytic reduction of aldehydes and ketones turned out to be more challenging. This is due to the lower basicity of oxygen compared to nitrogen which prevents protodeborylation. Furthermore, the oxygen can bind irreversibly to the boron center. This eventually leads to the deactivation of the catalyst.[15] However, work by the Stephan group and Ashley and co-workers showed that the reduction of aldehydes and ketones is possible when using $B(C_6F_5)_3$ in an ethereal solvent under high hydrogen pressure.[22] Both, aldehydes and ketones can be transformed into their corresponding primary and secondary alcohols in good to excel-

Biographical Sketches

Felix Wech studied chemistry at Justus Liebig University in Giessen and obtained his B.Sc. in 2017. He then joined the research group of Dr. Urs Gellrich for an internship in 2019 and obtained his M.Sc. in 2020, for his work on the pyridone-borane-catalyzed hydrogenation of alkynes. Currently, he is a doctoral student in the group of Urs Gellrich, investigating the application of pyridone borane complexes for metal-free catalysis.

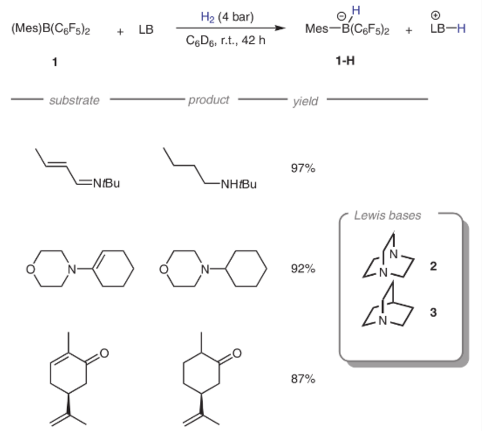


Urs Gellrich studied chemistry at the University of Freiburg in Germany where he obtained his doctorate in 2013 for the work on supramolecular ligands under the guidance of Prof. Bernhard Breit. In 2014, he moved to Israel and joined the group of Prof. David Milstein at the Weizmann Institute of Science as a postdoc. In 2017, Urs Gellrich started his independent career as a Liebig Fellow of the *Fonds der chemischen Industrie* (FCI) at the Justus Liebig University Giessen where he is currently Emmy Noether Group Leader. His research focuses on the *in silico* design of novel metal-free systems for bond activation and catalysis. For his work on the concept of boron-ligand cooperation, he was awarded the ADUC Prize 2020.

lent yields. The key to this transformation is that the ether functions as the Lewis base and participates during hydrogen activation. The corresponding Brønsted acid that forms from the ether upon hydrogen activation is now acidic enough to promote the protodeborylation which enables the catalytic reaction.

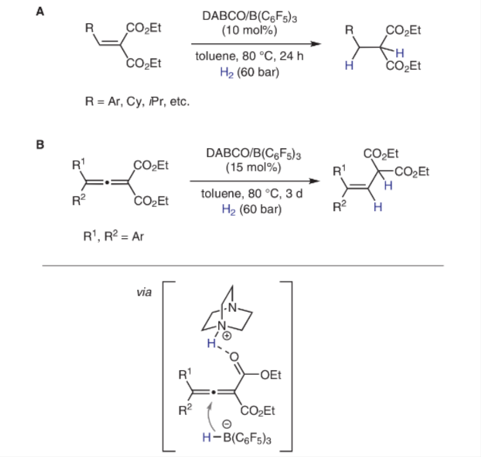
2.1 Hydrogenation of Michael Acceptors by FLPs

The hydrogenation of double bonds attached electron-withdrawing groups is challenging because of their strong binding to Lewis acidic boranes. By fine-tuning the steric bulk of the Lewis acid to weaken the binding between oxygen and boron, Soós and co-workers achieved the catalytic reduction of the C=C bond of α,β-unsaturated imines, ketones, as well as enamines at room temperature (Scheme 3).[13] The mesityl substituent on the Lewis acid **1** shields the boron center so that it is not coordinating to a Lewis basic site within the substrate. Noticeably, they achieved the selective catalytic hydrogenation of the activated C=C double bond in carvone (Scheme 3, bottom) in good yield, where classic transition-metal-based catalytic methods also reduced the less reactive terminal C=C bond.[13,23]



Scheme 3 Catalytic hydrogenation of activated olefins by a modified FLP system consisting of a sterically more shielded Lewis acid.

Using a similar approach and a catalyst system consisting of $B(C_6F_5)_3$ and 1,4-diazabicyclo[2.2.2]octane (DABCO, **2**), Alcarazo and co-workers hydrogenated electron-deficient allenes and olefins (Scheme 4).[24] While the hydrogenation of α,β-unsaturated malonates at 80 °C takes place within 24 h, allenes required longer reaction times. The activation of the substrate occurs in a similar fashion as in the previous examples: protonation of the ester function allows the electron-deficient central carbon of the allene to react as a hydride acceptor (Scheme 4B).



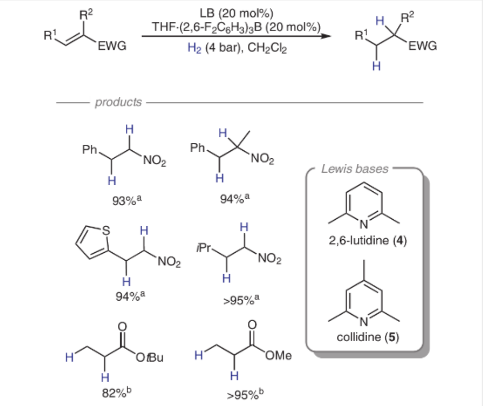
Scheme 4 Catalytic hydrogenation of electron-poor olefins and allenes by the $B(C_6F_5)_3$/DABCO FLP system.

Melen, Morrill, and co-workers discovered a related procedure to hydrogenate aza-Morita–Baylis–Hillman adducts in a diastereoselective fashion.[25]

Another advance regarding the hydrogenation of α,β-unsaturated compounds was made by the Paradies group.[26] They achieved the hydrogenation of nitroolefins and acrylates (Scheme 5). Instead of modifying the Lewis base, the Lewis acid was changed to $B(2,6\text{-}F_2C_6H_3)_3$. Although $B(2,6\text{-}F_2C_6H_3)_3$ has lower Lewis acidity compared to $B(C_6F_5)_3$, it is still capable of activating hydrogen under mild conditions using common Lewis bases such as 2,6-lutidine (**4**) or collidine (**5**).[26] Because the Lewis acid is weaker, the borohydride that forms upon hydrogen activation is a stronger nucleophile and thus able to undergo 1,4-addition to nitroolefins or acrylates. The products are obtained in good to excellent yields at room temperature or at 40 °C in dichloromethane.

2.2 Asymmetric Hydrogenation of Polarized Double Bonds

The field of transition-metal-catalyzed enantioselective hydrogenations has been extensively studied.[27] The development of FLP-catalyzed hydrogenations sparked the interest in using this concept for enantioselective reactions. The first enantioselective hydrogenation by FLPs was developed in 2010 by the Klankermeyer group .[28] Other early examples



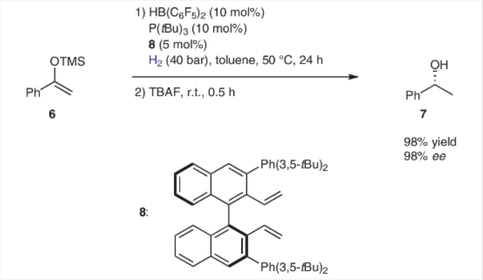
Scheme 5 Hydrogenation of nitroolefins and acrylates by FLP systems; ^{a} Using **4** (as LB), 40 °C. ^{b} Using **5** (as LB), 25 °C.

were developed by Repo and co-workers.[29] However, this reaction was still limited to imines as substrates.

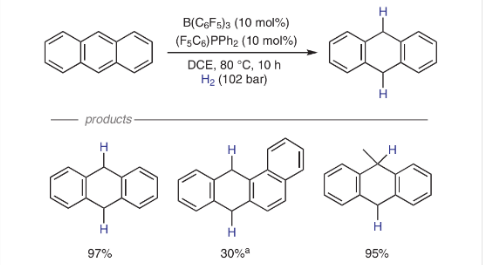
The first hydrogenation of silyl enol ethers was reported by the Erker group in 2008;[30] an enantioselective variant was reported in 2014 by the Du group.[31] They found that reacting Piers' borane [HB(C_6F_5)$_2$] in situ with the chiral bis-olefin **8** gave a chiral Lewis acid that is a potent catalyst for enantioselective hydrogenations (Scheme 6). The olefin **8** employed in this reaction is derived from the (*S*)-binaphthyl scaffold and carries vinyl groups in the 2- and 2′-positions. The vinyl groups are hydroborated by the Piers' borane to give the active chiral catalyst. In conjunction with tri-*tert*-butylphosphine the chiral Lewis acid can activate hydrogen. The substrate is then at first protonated to give a cation that is stabilized by the silyl ether. The stereoinduction proceeds via hydride transfer from the chiral borohydride. After deprotection using TBAF, the alcohols are obtained with 88% to 99% ee and in excellent yields. This reaction is efficient and shows good functional group tolerance. While the asymmetric metal-free reduction of unprotected ketones has not been achieved using molecular hydrogen, examples of FLP-catalyzed reductions that rely on the use of stoichiometric amounts of silane were reported.[32]

2.3 Hydrogenation of Arenes and N-Heterocycles

Using classic FLP hydrogenation chemistry, it is not only possible to reduce substrates such as imines, silyl enol ethers, or α,β-unsaturated malonates, but also different arenes and N-heterocyclic compounds.[20,33,34] The Stephan group used B(C_6F_5)$_3$ in conjunction with a triarylphosphine to selectively hydrogenate polyaromatic hydrocarbons (PAHs) to the corresponding dihydro derivatives (Scheme 7). While the central ring is hydrogenated, the terminal cycles preserve their aromaticity. The initial protonation step takes place in the 10-position of the anthracene scaffold. The hydride is then transferred to the opposing carbon in the 9-position which then leads to product formation. An overreaction does not take place due to the aromaticity of the remaining rings which prevents further protonation under the reaction conditions.

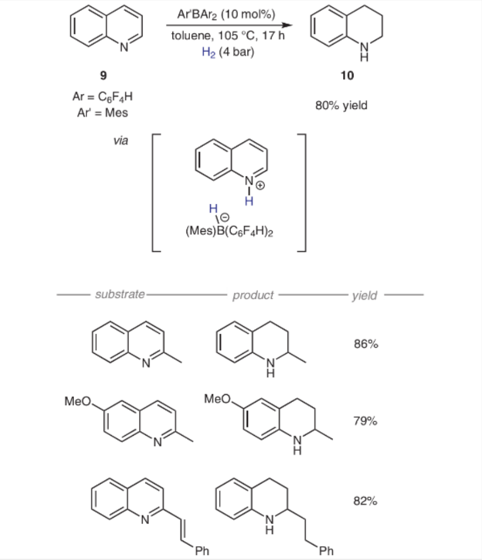


Scheme 6 Enantioselective hydrogenation of silyl enol ethers.



Scheme 7 Hydrogenation of PAHs by a frustrated Lewis pair und selected scope. ^{a} Reaction time 48 h.

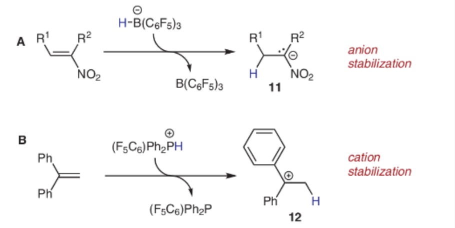
Soós and co-workers were able to hydrogenate different quinoline derivatives using sterically more demanding and less Lewis acid (Mes)B(C_6F_5)$_2$. No additional Lewis base was needed because the substrate itself reacts as a Lewis base (Scheme 8). By reducing the Lewis acidity of the Lewis acid by exchanging the C_6F_5 groups to C_6F_4H groups, the conversion was increased significantly [from 24% for (Mes)B(C_6F_5)$_2$ to 99% for (Mes)B(C_6F_4H)$_2$].[20] When employing the classic and readily available B(C_6F_5)$_3$, no reaction was observed. However, the quinoline substrate with a methyl group in 2-position leads to 29% conversion with B(C_6F_5)$_3$ as the catalyst. This is attributed to the fact that stronger Lewis acids irreversibly form dative adducts with the quinoline substrates which leads to inhibition of the catalytic reaction. With weaker Lewis acids, the quinoline adducts form reversibly, which preserves their ability to activate hydrogen. Using this protocol, Soós and co-workers were able to hydrogenate a variety of differently substituted quinoline derivatives to their corresponding tetrahydroquinoline (Scheme 8). Furthermore, the Stephan group used $B(C_6F_5)_3$ to hydrogenate a variety of different N-heterocycles, such as pyridine or acridines.[33,35]



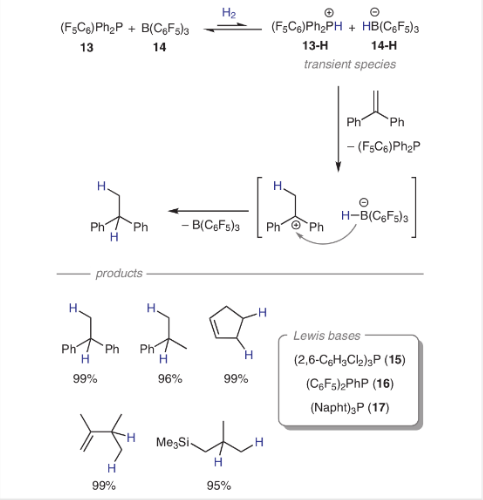
Scheme 8 Catalytic hydrogenation of quinoline derivatives and selected substrate scope.

3 Hydrogenation of Unactivated Olefins and Alkynes

The hydrogenation of non-activated olefins is more challenging for FLP catalysts. The Alcarazo group showed that olefins can react as hydride acceptors if the resulting carbanion **11** is stabilized by resonance (Scheme 9A).



Scheme 9 (A) Stabilization of an anion after the initial hydride transfer step. (B) Stabilization of a cation after the initial protonation step.



Scheme 10 FLP-catalyzed hydrogenation of olefins enabled by an initial protonation step with selected substrate scope. Napht = Naphthyl. *Reagents and conditions*: Lewis base (20 mol%), $B(C_6F_5)_3$ (20 mol%), 25 °C to 70 °C, 12 h to 240 h.

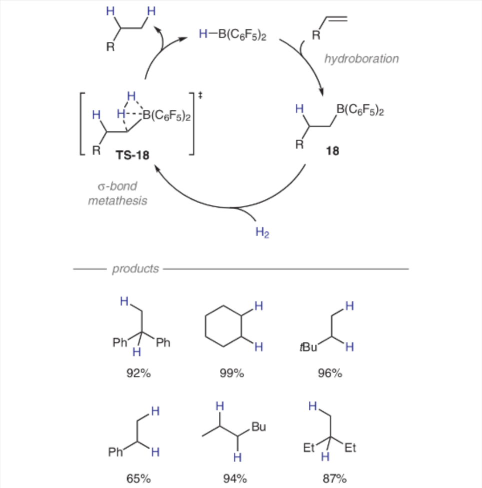
In analogy to that concept, it is also possible to achieve an initial protonation of the substrate if the resulting cation **12** is stabilized in a similar fashion (Scheme 9B). In contrast to the work by the Alcarazo group, the Paradies group developed a method to hydrogenate olefins with high proton affinity by an initial protonation step (Scheme 9B).[36] The use of a modified FLP system with the weaker Lewis base $(F_5C_6)Ph_2P$ (**13**) in conjunction with $B(C_6F_5)_3$ (**14**) facilitates this transformation (Scheme 10). The weaker Lewis base provides a stronger Brønsted acid after hydrogen activation which can now protonate olefins such as 1,1-diphenylethylene. While the hydrogen activation product of this FLP is not detectible at room temperature, the ^{31}P NMR spectra at low temperature suggest the formation of a phosphonium ion which is consistent with the observations in the ^{11}B and ^{19}F spectra. At –80 °C, the equilibrium lies entirely on the side of the phosphonium ion **13-H** and borohydride **14-H**. When slowly heated to room temperature, gradual loss of hydrogen is observed, and the starting materials are regenerated, indicating a low barrier for hydrogen activation. This system was used for the hydrogenation of olefins that can form tertiary carbocations or ones that are stabilized by benzylic or allylic resonance upon protonation (Scheme 10).

3.1 Hydrogenation of Olefins and Alkynes by an Initial Hydroboration

While olefins that can be activated by an initial proton or hydride transfer step are readily hydrogenated by FLP systems, aliphatic olefins cannot be reduced in such a way. In the early 1960s, DeWitt, Ramp, and Trapasso utilized the ability of simple dialkylboranes to hydroborate such simple olefins to develop a catalytic procedure.[37] At temperatures of 235 °C and 172 bar H_2 pressure, aliphatic alkenes were catalytically reduced to the corresponding alkanes. The hydrogenation of 1,2-di(1-naphthyl)ethane and pyrene catalyzed by $NaBH_4/I_2$ is also likely to include a hydroboration of the organic substrate.[38] The widely used Piers' borane[39] $[HB(C_6F_5)_2]$ is far more reactive in hydroboration reactions compared to classic dialkylboranes and is commonly used in the synthesis of novel FLP systems.[15,40]

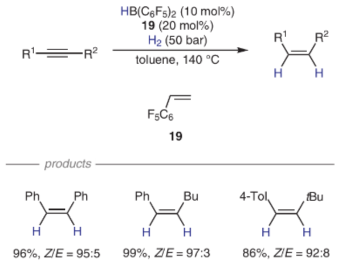
Wang and co-workers used the reactivity of Piers' borane for hydroborations and its strong electrophilicity for the catalytic hydrogenation of unactivated olefins (Scheme 11).[41] Using 20 mol% Piers' borane at 140 °C under 6 bar of hydrogen, a variety of terminal and internal alkenes were hydrogenated. In contrast to classic FLP hydrogenation methods that rely on hydride transfer, the initial activation of the olefin proceeds via hydroboration. Under the reaction conditions, the newly formed bis(perfluorophenyl)alkylborane **18** can split hydrogen by σ-bond metathesis (**TS-18**) regenerating the Piers' borane and releasing the product. The low-lying p-orbital of the electrophilic borane is crucial for this transformation, as suggested by DFT computations. When using the less electrophilic 9-BBN instead of Piers' borane, no reaction was observed which supports this computational finding.[41] The experimental activation parameters are in good agreement with the computations and suggest a free activation energy of around 33 kcal mol^{-1}. It is noteworthy that the bond activation by the alkylborane **18** is reminiscent of an intramolecular frustrated Lewis pair, where the carbon center reacts as the Lewis base. The weak Lewis basicity of the carbon in the α-position to the boron probably leads to the high activation barrier for this transformation.

The metal-free semihydrogenation of alkynes to the corresponding olefins is a synthetically attractive variant to the Lindlar hydrogenation.[42] First attempts to realize this transformation were made by the Erker group in 2011, when they hydrogenated ynones to the corresponding α,β-unsaturated ketones using FLP chemistry.[40] Their method also relies on an initial hydride transfer step. Using a similar approach to Wang and co-workers, the Du group realized the semihydrogenation of alkynes using catalytic amounts of Piers' borane and (perfluorophenyl)ethylene **19** as a co-catalyst (Scheme 12).[43] At 140 °C and under 50 bar of hydrogen they readily converted aromatic alkynes into the corresponding alkenes with high *Z* selectivity and excellent yields (Scheme 12). The Du group propose that favorable H–F interactions between the alkene and the substrate in the transition state for the hydrogen activation promote this transformation.[43] When using non-fluorinated styrene or different olefins as additives, the conversion is not enhanced which supports this claim. A computational investigation of this reaction shown that the transition state for the σ-bond metathesis of molecular hydrogen is lowered by 1.3 kcal mol^{-1} considering H–F interactions with (perfluorophenyl)ethylene. Interestingly, the *Z*-selectivity was reversed by using prolonged reaction times to give *E*-alkenes almost exclusively. Compared to the Piers' borane catalyzed hydrogenation of olefins, this alkyne hydrogenation requires harsher reaction conditions. In the case of the alkyne semihydrogenation, the carbon atom involved in the H_2 splitting is sp^2 hybridized and back-donation of the π-electrons to the empty p-orbital of the borane takes place. Therefore, the borane becomes less electrophilic which leads to a larger activation barrier for H_2 splitting. This might also be the reason why additives are required in this case.



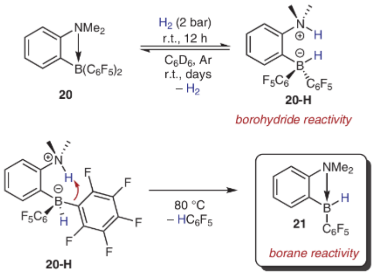
Scheme 11 Hydrogenation of olefins catalyzed by Piers' borane with selected substrate scope. *Reagents and conditions*: $HB(C_6F_5)_2$ (20 mol%), 140 °C, 6 bar H_2, C_6D_6; NMR yields are given.

A notable approach for the catalytic semihydrogenation of internal alkynes is the work by Repo and co-workers, who used their molecular tweezer-like FLP **20**.[19,44] Their catalyst is capable of hydrogen activation at room temperature (Scheme 13, top). Upon standing at room temperature under an argon atmosphere, the hydrogenated form **20-H** slowly loses hydrogen to regenerate the amino borane **20**. However, when heating the catalyst under hydrogen atmosphere, a decomposition pathway is accessible where



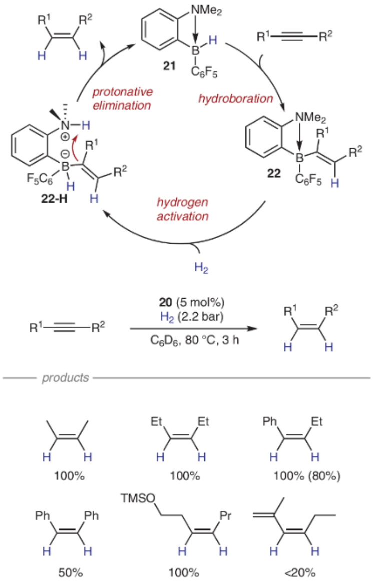
Scheme 12 Semihydrogenation of internal alkynes catalyzed by Piers' borane and selected scope. Note that the selectivity was reversed by changing the reaction conditions to give *E* product only. NMR yields are given.

protodeborylation of one of the pentafluorophenyl rings on the borane of **20-H** occurs and pentafluorobenzene is eliminated giving **21** (Scheme 13, bottom). This decomposition product now resembles the reactivity of a trivalent borane and is a potent hydroboration reagent.

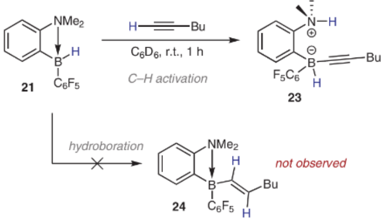


Scheme 13 Reversible hydrogen activation by an *ansa*-amino borane to give a classic FLP species and the catalyst decomposition pathway leading to an *ansa*-amino borane with activity that resembles borane reactivity.

Using **20** as a pre-catalyst, Repo and co-workers were able to hydrogenate a variety of internal alkynes and obtained excellent conversions and mostly very good yields (Scheme 14). One advantage is that this reaction[44] worked under much milder conditions than the Piers' borane catalyzed semihydrogenation by the Du group.[43] This makes the reaction much more feasible in the lab. One disadvantage is that the species **22-H** (Scheme 14) can not only release the product but can also eliminate the remaining pentafluorophenyl on the boron center. This leads to deactivation of the catalyst because it is no longer capable of hydrogen activation. In contrast to the Piers' borane catalyzed semihydrogenation of alkynes[43] no isomerization to the *E* product was observed and *Z*-alkenes were obtained exclusively. While internal alkynes are hydrogenated efficiently by the two described methods, the semihydrogenation of terminal alkynes to the corresponding terminal olefin could not be realized using these systems. In the case of the *ansa*-amino borane, the reaction of **21** with one equivalent of terminal alkyne leads solely to the C–H activation product **23** (Scheme 15) and hydroboration product **24** is not observed.



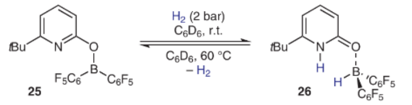
Scheme 14 Semihydrogenation of internal alkynes catalyzed by an *ansa*-amino borane. Conversions are given for selected products, isolated yield in parenthesis.



Scheme 15 Attempts for the hydroboration of terminal alkynes with an *ansa*-amino borane; irreversible CH activation is observed.

In 2018, our group showed that upon mixing Piers' borane with 6-*tert*-butyl-2-pyridin-2(1*H*)-one, a pyridone–borane complex **26** forms that reversibly loses hydrogen at room temperature (Scheme 16).[45] Heating under passive vacuum shifts the equilibrium towards the (pyridin-2-

oxy)borane **25**, while pressurizing the sample with 2 bar of hydrogen leads to the clean formation of the pyridone–borane complex **26**. This is in good agreement with the computations that suggest a free activation energy barrier of 19.6 kcal mol^{-1} at DLPNO-CCSD(T) level of theory. Additionally, according to the computations, the reaction is almost thermoneutral which matches the experimental observations. Note that upon hydrogen activation by **25**, the C–O bond shortens which indicates the formation of a double bond during the H_2 activation process (Figure 1). Furthermore, the B–O bond elongates by almost 0.2 Å indicating the switch from a covalently bound oxypyridine to a datively bound pyridone ligand. This is analogous to the concept of metal-ligand cooperation and was therefore named boron-ligand cooperation.[45–47] Computations of the nuclear independent chemical shifts (NICS) suggest the loss of aromaticity in the pyridone ring upon hydrogen activation.



Scheme 16 Reversible hydrogen activation by (6-*tert*-butylpyridin-2-oxy)bis(perfluorophenyl)borane.

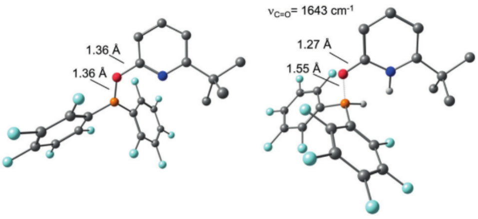
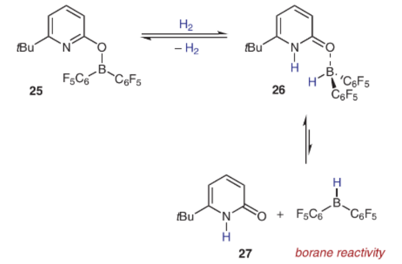
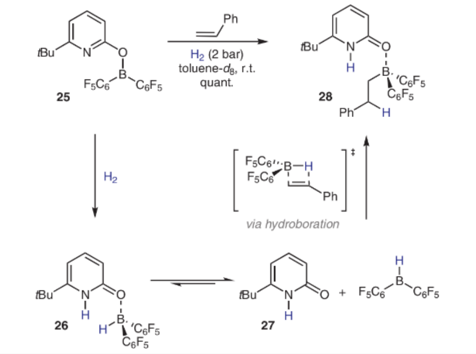


Figure 1 Computed molecular structures of (6-*tert*-butylpyridin-2-oxy)-bis(perfluorophenyl)borane (**25**) (left) and 6-*tert*-butylpyridin-2(1*H*)-one–bis(perfluorophenyl)borane (**26**) (right); optimized at PBE0/def2-TZVP level.

Notably, the existence of a C=O stretching vibration in the IR spectrum of **26** strongly supports the change in the bonding mode during hydrogen activation. We anticipated that this change in the coordination mode from a covalently bound substituent to a datively bound ligand enables the 6-*tert*-butylpyridin-2(1*H*)-one–bis(perfluorophenyl)borane (**26**) to dissociate into 6-*tert*-butylpyridin-2(1*H*)-one (**27**) and Piers' borane (Scheme 17). The release of free Piers' borane could then facilitate hydroboration reactions. To prove this concept, the dehydrogenated complex **25** was mixed with styrene in deuterated toluene at room temperature (Scheme 18).[48] No reaction was observed as the NMR signals are indistinguishable from the independent species. However, when the sample was pressurized with 2 bar of hydrogen, the olefinic signals vanished and quantitative conversion to the pyridone–borane complex **26** was observed. This supports the hypothesis that the pyridone–borane complex **26** can indeed dissociate into pyridin-2(1*H*)-one **27** and the trivalent Piers borane which then hydroborates the styrene. Recoordination of the pyridin-2(1*H*)-one **27** forms then the 6-*tert*-butylpyridin-2(1*H*)-one–alkylbis(perfluorophenyl)borane complex **28**.



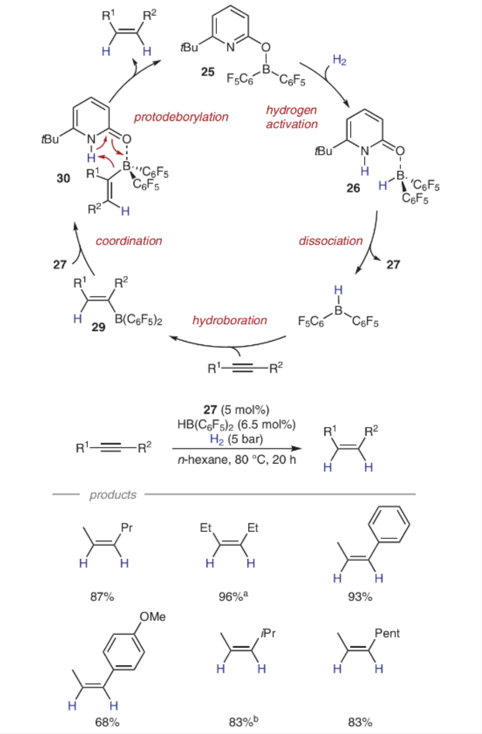
Scheme 17 Hydrogen activation by (6-*tert*-butylpyridin-2-oxy)bis(perfluorophenyl)borane (**25**) and dissociation of 6-*tert*-butylpyridin-2(1*H*)-one–bis(perfluorophenyl)borane (**26**) into 6-*tert*-butylpyridin-2(1*H*)-one (**27**) and free Piers' borane.



Scheme 18 Hydroboration of styrene starting from (6-*tert*-butylpyridin-2-oxy)bis(perfluorophenyl)borane (**25**).

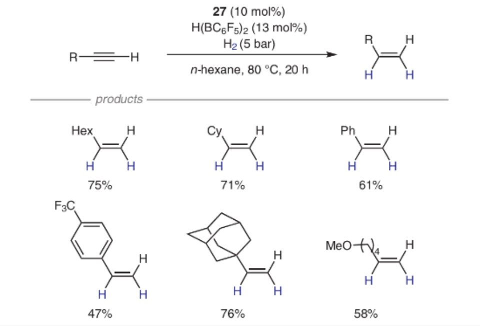
For a corresponding alkenylborane that results from alkyne hydroboration by the Piers' borane, we anticipated that a protodeborylation pathway might be accessible. We, therefore, envisioned a catalytic cycle for the hydrogenation of alkynes to their corresponding *cis* alkene (Scheme 19). In the first step, **25** activates hydrogen to form the datively bound pyridone–borane complex **26**, which can now dissociate to release free Piers' borane. The alkyne then enters the catalytic cycle and is readily hydroborated by the borane. The formed alkenylborane **29** can coordinate back to the free pyridin-2(1*H*)-one **27** to form the complex **30**.

This complex can then undergo a protodeborylation to release the *cis*-alkene and regenerate the (pyridin-2-oxy)borane catalyst **25**. Indeed, we were able to hydrogenate a variety of aliphatic and aromatic alkynes in good to excellent yields. Furthermore, the selectivity towards the *E*- or *Z*-isomer could be controlled by changing the reaction time. The proof of this concept also led to the development of differently substituted pyridin-2(1*H*)-one derivatives that react in a similar fashion.[49]



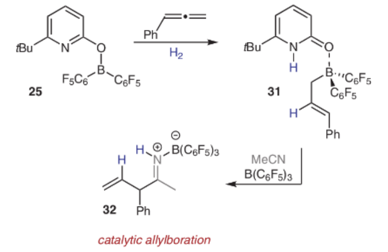
Scheme 19 Catalytic cycle and products of the pyridone–borane catalyzed semihydrogenation of alkynes. [a] Reaction time 16 h. [b] Reaction time 8 h. Yields were determined by quantitative NMR using trimethoxybenzene as internal standard.

One drawback of this reaction is the functional group tolerance. While ethers and aryl substituents are tolerated, alcohols and amines led to a mixture of decomposition products. We anticipated that for terminal alkynes irreversible Csp–H cleavage occurs as observed for Repo's *ansa*-amino borane catalyst. However, in the case of (pyridin-2-oxy)-borane catalyst **25** the Csp–H activation of terminal alkynes is reversible, as shown by exchange experiments with different terminal alkynes. Therefore, we were able to devise a protocol for the hydrogenation of terminal alkynes (Scheme 20). This is to the best of our knowledge the first protocol for the metal-free hydrogenation of terminal alkynes.



Scheme 20 Protocol for the pyridone–borane catalyzed hydrogenation of terminal alkynes.

Another application of **25** is the generation of a nucleophilic allylborane from dihydrogen and an allene (Scheme 21).[45] After hydrogen activation by **25** and dissociation of the pyridone–borane complex **26**, the allene is hydroborated by Piers' borane which leads to the pyridone–allylborane complex **31**. Complex **31** can then allylate acetonitrile. In the presence of $B(C_6F_5)_3$ the reaction could be conducted catalytically leading to allyl imine–borane complex **32** as a product and the first catalytic allylboration reaction. The introduction of boron-ligand cooperation to the concept of frustrated Lewis pair chemistry enabled us to use dihydrogen in a synthetically new way.



Scheme 21 In situ formation of a nucleophilic allylborane from H_2 and an allene.

4 Summary and Outlook

The pool of FLP-catalyzed hydrogenations has been growing since the first works by Stephan.[18] Since hydrogenations catalyzed by classic FLPs consist of an initial hydride transfer or protonation step, the scope of such reactions is limited. Substrates that act as hydride acceptors, such as imines,[18] are easily reduced, as well as Michael acceptors such as α,β-unsaturated carbonyl compounds[24,25] or nitro olefins.[26] Olefins that are easily protonated by stronger Brønsted acids are also suitable substrates for classic FLP-catalyzed hydrogenations. In such cases, the emerging positive charge is stabilized by allylic or benzylic resonance as shown in the work by the Paradies group.[36] A major advance was made more recently by Wang and co-workers who used solely Piers' borane for the hydrogenation of unfunctionalized olefins.[41] In this case, the activation of the substrate is not achieved by an initial hydride or proton transfer, but rather through hydroboration of the double bond. The hydrogen activation does not take place in a classic FLP-like manner where an ion pair or a zwitterion is generated. However, it can be argued that the hydrogen activation proceeds in a way in which the α-carbon atom to the boron reacts as a Lewis base. This new concept of substrate activation through hydroboration then led to the development of methods for the semihydrogenation of alkynes, such as the seminal work by Repo and co-workers,[44] as well as the work by the Du group.[43] The alkenyl borane requires harsh reaction conditions to split molecular hydrogen by itself, as shown by the Du group. We could show that the introduction of pyridin-2(1*H*)-one facilitates the protodeborylation and aids the Piers' borane to activate hydrogen in the manner of an intramolecular FLP. The combination of this aspect of frustrated Lewis pair chemistry with the concept of boron-ligand cooperation then allowed us to use a pyridone–Piers' borane complex for the hydrogenation of internal and terminal alkynes,[48] but also for the unprecedented generation of allylboranes from molecular hydrogen and allenes.[50] Since FLP-catalyzed hydrogenations are primarily based on electrophilic boranes that require multistep syntheses and are moisture sensitive[51] there is a great interest in using simpler boranes for catalysis. Furthermore, these highly reactive boranes are prone to side reactions and have mostly poor thermal stability which leaves room for future developments.

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

This work was supported by the Deutsche Forschungsgemeinschaft (DFG; German Research Foundation) (GE 3117/1-1).

Acknowledgment

Continued support from Prof. Dr. P. R. Schreiner, Prof. Dr. R. Göttlich, and Prof. Dr. H. A. Wegner is acknowledged.

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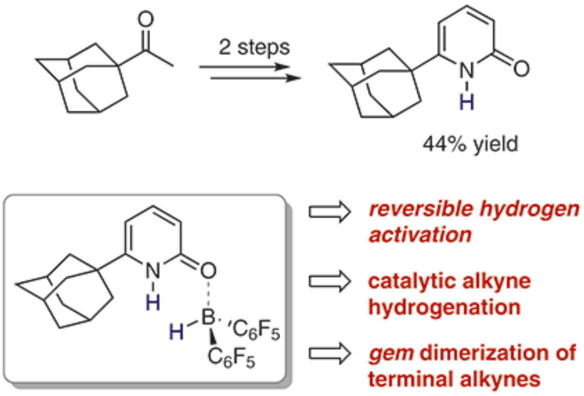
5.4 Synthesis of 6-Adamantyl-2-pyridone and Reversible Hydrogen Activation by the Corresponding Bis(perfluorophenyl)borane Complex



A new 6-adamantyl substituted pyridone was synthesized. Its bis(pentafluorphenyl)borane complex was studied which is capable of reversible hydrogen activation. This complex was then used as a catalyst in the catalytic hydrogenation of alkynes, as well as in the dimerization of terminal alkynes.

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Synthesis, **2021**, *53*, 666–672.

DOI: 10.1055/s-0040-1705970

Final veröffentlichte Version online: 10. November 2020

Synthesis of 6-Adamantyl-2-pyridone and Reversible Hydrogen Activation by the Corresponding Bis(perfluorophenyl)borane Complex

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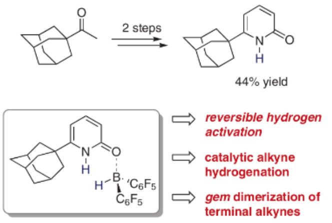


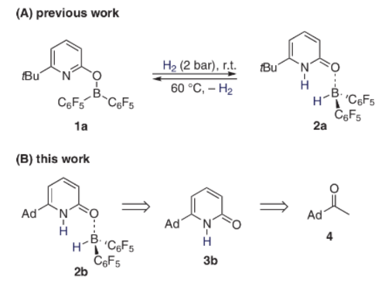
Received: 27.08.2020
Accepted after revision: 05.10.2020

DOI: 10.1055/s-0040-1705970; Art ID: ss-2020-z0457-fa

Abstract We herein describe the two-step synthesis of 6-adamantyl-2-pyridone from 1-acetyladamantane. The borane complex derived from 6-adamantyl-2-pyridone and the Piers borane liberates dihydrogen at 60 °C. The reverse reaction, hydrogen activation by the formed pyridonate borane is accomplished under mild conditions. The mechanism of the hydrogen activation is studied by DFT computations.

Key words frustrated Lewis Pair, hydrogen activation, pyridones, boron-ligand cooperation, DFT

In 2006, Stephan and co-workers reported the seminal finding that specific combinations of sterically encumbered Lewis bases and highly Lewis acidic boranes are able to activate dihydrogen.[1] The unique reactivity of these Lewis pairs was attributed to the fact that they do not form classic Lewis adducts. Therefore, the term frustrated Lewis pairs (FLP) was coined to describe these reactive Lewis pairs.[2] Recently, we reported the reversible activation of dihydrogen by the pyridonate borane **1a**, that can be described as an intramolecular FLP (Scheme 1).[3] A characteristic aspect of hydrogen activation by **1a** is that the covalently bound pyridonate substituent becomes a datively bound pyridone ligand upon bond activation. This change in the coordination sphere of the borane is reminiscent of metal-ligand cooperation and was therefore referred to as boron-ligand cooperation.[4] This mode of action allows **2a** to dissociate into 6-*tert*-butyl-2-pyridone and HB(C_6F_5)$_2$ (Piers' borane). This dissociation enables the hydroboration of an alkyne. A subsequent protodeborylation yields the corresponding *cis* alkene and regenerates the pyridonate borane **1a**. In this way, the catalytic *semi*-hydrogenation of alkynes was realized (Scheme 2).[4] Classic FLPs undergo irreversible C_{sp}–H activations with terminal alkynes.[5] Likewise, pyridonate borane **1a** reacts with terminal alkynes to give a pyridone alkynyl borane complex **5**.



Scheme 1 (A) Reversible hydrogen activation by a 6-*tert*-butyl-2-pyridonate borane **1a** described previously. (B) A working hypothesis of the research project described herein: Synthesis of 6-adamantyl-2-pyridone borane complex and reversible hydrogen activation by a corresponding pyridonate borane (Ad = adamantyl).

However, we were able to show that C_{sp}–H activation of terminal alkynes by **1a** is reversible and thus competes with dihydrogen activation. Therefore, we were able to realize the first metal-free *semi*-hydrogenation of terminal alkynes (Scheme 2, bottom).[6] In the absence of H_2, the alkynyl borane complex formed upon C_{sp}–H activation reacts at elevated temperatures with a second equivalent of the alkyne to yield the *gem*-dimerization product of the terminal alkyne (Scheme 2, top). This reaction regenerates **1a** (Scheme 2).[7] Thus, we were able to devise a protocol for the metal-free dimerization of terminal alkynes catalyzed by **1a**. The *tert*-butyl group at the 6-position of the pyridine ring is required to suppress the dimerization of **1a**. Thus we

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became interested in how the replacement of this *tert*-butyl group by a sterically more demanding and electron-rich adamantyl group would affect the properties of the pyridonate borane (Scheme 1).

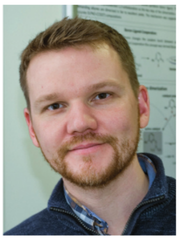
To synthesize the required 6-adamantyl-2-pyridone **3b**, we followed a procedure of Hintermann and co-workers that we had successfully applied for the synthesis of **1a**.[8] We first prepared the sodium enolate **6** from commercially available 1-acetyladamantane (**4**) (Scheme 3). Next, the enolate **6** was used to generate a phosphonium ylide in situ from the phosphonium salt **7** to initiate a Wittig olefination. The addition of acetic acid enabled the condensation that furnished the adamantyl pyridone **3b** in 52% yield (Scheme 3). Single-crystal X-ray diffraction (SCXRD) analysis revealed that **3b** crystallizes as a lactam dimer in the space group $P\bar{1}$ (Figure 1).

Biographical Sketches

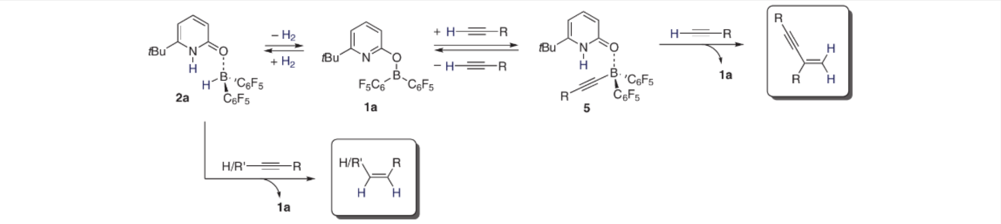
Felix Wech studied chemistry at Justus-Liebig-Universität Gießen and obtained his B.Sc. in 2017. He then joined the research group of Dr. Urs Gellrich for an internship in 2019 and obtained his M.Sc. in 2020 for his work on the pyridone-borane-catalyzed hydrogenations of alkynes. Currently, he is a doctoral student in the group of Urs Gellrich, investigating the application of pyridine-borane complexes for metal-free catalysis.

Tizian Müller studied chemistry at Justus-Liebig-Universität Gießen and received his B.Sc. in 2016. He joined the research group of Dr. Urs Gellrich in 2018 and obtained his M.Sc. in 2019. Currently, he is working on the activation of molecular hydrogen through self-association of frustrated Lewis pairs, both experimentally and computationally.

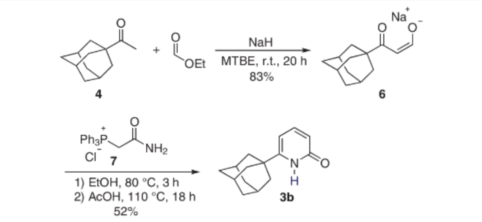
Jonathan Becker studied chemistry at Justus-Liebig-Universität Gießen and received a 'Dr. rer. Nat' degree working in the group of Professor Siegfried Schindler. He then worked as a postdoctoral fellow with Dr. Peter Müller at the Massachusetts Institute of Technology (USA). After returning to Germany and Justus-Liebig-Universität Gießen, he now works on crystallographic problems in the group of Professor Müller-Buschbaum at the Institute of Inorganic and Analytical Chemistry.



Urs Gellrich studied chemistry at the University of Freiburg in Germany where he obtained his doctorate in 2013 for his work on supramolecular ligands under the guidance of Prof. Bernhard Breit. In 2014, he moved to Israel and joined the group of Prof. David Milstein at the Weizmann Institute of Science as a postdoctoral researcher. In 2017, Urs started his independent career as a Liebig Fellow of the *Fonds der Chemischen Industrie* (FCI) at Justus-Liebig-Universität Gießen, where he is currently an Emmy Noether Group Leader. His research focuses on the *in silico* design of novel metal-free systems for bond activation and catalysis. For his work on the concept of boron-ligand cooperation, he was awarded the ADUC Prize in 2020.



Scheme 2 Using pyridonate borane complex **1a** as a catalyst for the *semi*-hydrogenation of alkynes and the *gem*-dimerization of terminal alkynes



Scheme 3 Synthesis of 6-adamantyl-2-pyridone **3b** from 1-acetyladamantane (**4**)

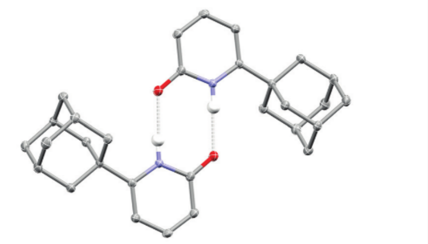
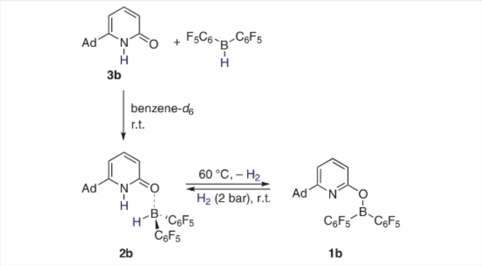


Figure 1 Molecular structure of **3b** (CCDC 2024101) derived from SCXRD (50% probability ellipsoids, all hydrogens attached to carbons are omitted).[9] Selected bond lengths and angles: N–C2: 1.3788(10) Å, C2–O: 1.2509(10) Å, N–O: 2.8021(10) Å, N–H–O: 175.7(12)°, N–C2–O: 119.91(7)°.

The N–O distance is 2.8021(10) Å and thus elongated compared to that in a non-substituted 2-pyridone (2.76 Å).[10] At the next stage, we added **3b** to a solution of Piers' borane in benzene-d_6 (Scheme 4). As expected, the immediate formation of the pyridone borane complex **2b** was observed (Figure 2). The ^{1}H NMR spectrum shows that hydrogen loss already occurs at room temperature (Figure 2, bottom). When heating the sample at 60 °C for 20 hours, full conversion of **2b** into the pyridonate borane **1b** was observed (Figure 2, middle). When pressurizing the reaction mixture with 2 bar of hydrogen, re-formation of **2b** was observed at r.t. within 24 hours (Figure 2, top). Thus, we demonstrated that the pyridonate borane **1b** is indeed capable of H_2 activation. Although **2b** is formed as the major product upon mixing of **3b** and Piers' borane, a minor impurity was observed by NMR analysis (Figure 2, signals marked with asterisks). It is known that upon formation of pyridonate borane **1a** in the presence of free 6-*tert*-butyl-2-pyridone (**3a**) a bispyridone complex is formed that contains a second equivalent of the pyridone **3a**.[3] As described for the *tert*-butyl analogue, the adamantyl-derived bispyridone complex **8b** was prepared from addition of two equivalents of **3b** to the Piers' borane at r.t. (Scheme 5).[11] After crystallization from *n*-hexane and DCM, **8b** was isolated as colorless crystals in 84% yield. As expected, the NMR signals of **8b** matched the signals of the impurity that had been observed during the hydrogen activation experiments. Crystallization of **8b** enabled us to further investigate its molecular structure by SCXRD (Figure 3). Compound **8b** crystallizes in the space group $P2_1/c$. The molecular structure of **8b** was then compared with the structure of the 6-*tert*-butyl-2-pyridone-derived bispyridone complex **8a** that was described previously.[11]



Scheme 4 Synthesis of **2b** and reversible hydrogen activation by **2b** (Ad = adamantyl)

Compound **8a** crystallized in the space group *Cc* and contains two independent molecules in the unit cell. Therefore, the averaged structural parameters of **8a** are displayed (Table 1). The bispyridone complexes **8a** and **8b** show relat-

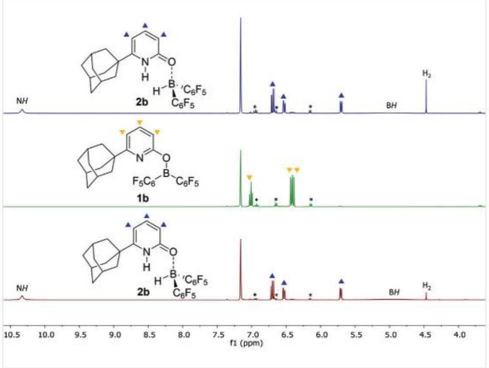
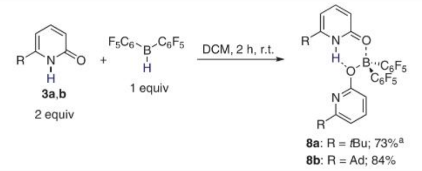


Figure 2 ^1H NMR spectrum obtained after mixing Piers' borane with **3b** at r.t. Traces of **1b** are already observable (bottom). ^1H NMR spectrum after heating at 60 °C under a passive vacuum for 20 hours (middle). ^1H NMR spectrum after pressurizing the NMR tube with 2 bar of hydrogen and keeping the mixture at r.t. overnight (400 MHz, benzene-d_6, top).



Scheme 5 Synthesis of bispyridone complex **8b** derived from 6-adamantyl-2-pyridone **3b** and Piers' borane. The 6-*tert*-butyl-2-pyridone-derived bispyridone complex **8a** was characterized in previous work (Ad = adamantyl). [a] From reference 3.

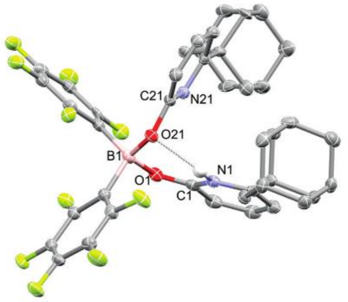


Figure 3 Molecular structure of bispyridone complex **8b** (CCDC 2024102) derived from SCXRD (50% probability ellipsoids, all hydrogens attached to carbons are omitted)[9]

ed structural features. The bond lengths associated with the pyridone that serves as a hydrogen bond donor show little difference when comparing both structures. Interestingly, the N–O distance associated with the hydrogen bond is slightly contracted for the adamantyl derivative **8b** compared to the *tert*-butyl derivative **8a**. Furthermore, the O–B–O bond angle for the *tert*-butyl system is widened.

Table 1 Selected Bond Lengths and Angles of **8a** and **8b** Derived from SCXRD

	tert-Butyl bispyridone **8a**[a]	Adamantyl bispyridone **8b**
N1–O21	2.718 Å	2.697(2) Å
B1–O21	1.471 Å	1.475(2) Å
B1–O1	1.522 Å	1.524(2) Å
C1–O1	1.292 Å	1.292(2) Å
C21–O21	1.362 Å	1.366(2) Å
O1–B1–O21	113.5°	112.8(1)°
O21–H1–N1	137°	136(1)°
B1–O1–C1–N1	3.3°	0.4(2)°

[a] Values are the average of the two independent molecules in the unit cell.

Hydrogen activation by **1b** was further investigated computationally at the rev-DSD-PBEP86-D4/def2-QZVPP//PBEh-3c level (Figure 4).[12,13] The SMD model for benzene was used to implicitly account for solvent effects (Figure 4).[14] The activation barrier for hydrogen activation is 19.3 kcal mol^{-1} for the adamantyl derivative and thus 0.5 kcal mol^{-1} lower in Gibbs free energy compared to the 6-*tert*-butyl pyridonate borane system. This is expected because of the more electron-rich pyridine ring of the adamantyl derivative that leads to a higher Lewis basicity. The hydrogen activation is exergonic for both derivatives by 1.4 and 1.5 kcal mol^{-1}, respectively. The dissociation of the pyridone borane complexes into pyridone and Piers' borane is endergonic by 18.0 kcal mol^{-1} for the adamantyl-substituted system and 18.1 kcal mol^{-1} for the *tert*-butyl-substituted system, respectively. The formation of the bispyridone complex is exergonic for both systems. For the adamantyl-substituted system the gain in Gibbs free energy is almost 1 kcal mol^{-1} higher compared to the *tert*-butyl pyridone system. This might be due to the shorter and thus stronger hydrogen bond.

To gain first insights regarding the catalytic activity of **2b**, we tested it as a catalyst for the *gem*-selective dimerization of terminal alkynes and the hydrogenation of internal and terminal alkynes (see Scheme 2). The results for a prototypical substrate are compared to those obtained with **2a** as the catalyst.[5,7] The adamantyl pyridone borane complex **2b** indeed catalyzed the *gem* dimerization of phenylacetylene. However, the activity of **2b** was inferior compared to that of **2a** (Scheme 6). The pyridone borane system **2a** was

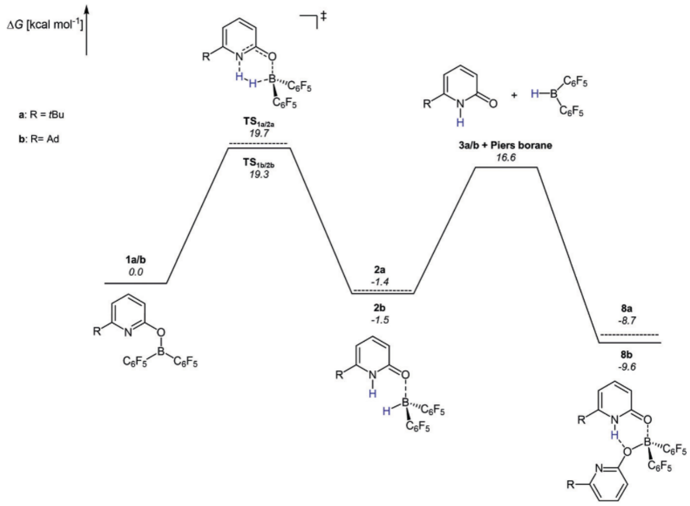
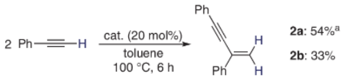
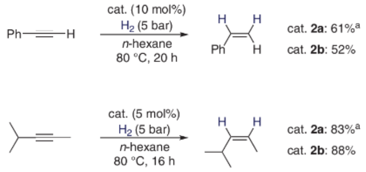


Figure 4 Gibbs free energy profile for the hydrogen activation by *tert*-butyl- and adamantyl-substituted pyridonate borane complexes **1a** and **1b** and formation of bispyridone complexes **7a** and **7b** computed at the revDSD-PBEP86/def2-QZVPP//PBEh-3c level of theory. Bulk solvation was considered implicitly using the SMD model for benzene.

able to hydrogenate terminal alkynes in the presence of hydrogen due to reversible C_{sp}–H activation which competes with hydrogen activation.[5] Therefore, we attempted the hydrogenation of phenylacetylene using **2b** as the catalyst, which gave styrene as the product in a slightly lower yield than that reported when using **2a** (Scheme 7, top). In addition, we used **2b** as the catalyst for the hydrogenation of 2-methyl-3-pentyne (Scheme 7, bottom). The reaction gave the corresponding *cis* alkene exclusively after a reaction time of 16 hours in a slightly higher yield compared to that obtained with **2a**.



Scheme 6 Dimerization of phenylacetylene using the pyridone borane complexes **2a** and **2b** as catalysts under previously reported optimized conditions.[7] The reported yields are the average of two runs. [a] From reference 7.



Scheme 7 Hydrogenation of phenylacetylene and 2-methyl-3-pentyne using the pyridone borane complexes **2a** and **2b** under previously reported optimized conditions.[5] Note that for the formation of the respective pyridone borane complex, a slight excess of Piers' borane was used (1.3 equiv). The reported yields are the average of two runs. [a] From reference 5.

In summary, we have synthesized the novel 6-adamantyl-2-pyridone **3b** from commercially available 1-acetyladamantane in 44% yield over two steps. This pyridone derivative can form pyridonate borane complex **1b** on loss of hydrogen. The pyridonate borane **1b** can reactivate hydrogen at room temperature under 2 bar of hydrogen. We were also able to synthesize a bispyridone complex **8b** that is an adduct of pyridonate borane complex **1b** with another equivalent of pyridone. The molecular structure of **8b**, derived from SCXRD, revealed a shortened hydrogen bond compared to the *tert*-butyl-derived bispyridone complex that was described previously.[11] Additionally, we have shown that **3b** in conjunction with Piers' borane is a suitable catalyst for the *gem* dimerization of terminal alkynes and the hydrogenation of terminal and internal alkynes.

All manipulations involving air- or moisture-sensitive compounds were performed using standard Schlenk or glovebox techniques. All dry, non-deuterated solvents were, if commercially available, purchased from Acros Organics or Sigma-Aldrich in sealed bottles with a septum. Deuterated solvents were distilled under inert conditions and kept in a glovebox over 4 Å molecular sieves or were degassed using the freeze/pump/thaw method and stored over 4 Å molecular sieves for at least one day prior to use. $B(C_6F_5)_3$ was synthesized from boron trifluoride–diethyl etherate according to a literature procedure.[15] Piers' borane was synthesized from $B(C_6F_5)_3$ according to a modified literature procedure:[16] $B(C_6F_5)_3$ (2.0 g, 3.9 mmol) and Et_3SiH (623 µL, 3.9 mmol) were dissolved in benzene (20 mL) in a pressure tube and stirred for 4–5 d at 60 °C. The reaction mixture was cooled to r.t., causing precipitation of the product. The supernatant was removed, and the residue was washed with benzene (3 × 3 mL) and *n*-pentane (2 × 2–3 mL). 2-Triphenylphosphonium-acetamide chloride was synthesized according to a literature procedure.[8] Flash column chromatography was performed using Macherey-Nagel silica gel (0.04–0.063 mm). TLC analyses were performed using standard silica TLC plates purchased from Macherey-Nagel. Melting points were measured on an A. Krüss Optotronics melting point meter. IR spectra were recorded on a Bruker Optics VERTEX70 Platinum ATR spectrometer. NMR spectra were recorded on Bruker Avance II 200 MHz, Bruker Avance III HD 400 MHz, Bruker Avance II 400 MHz or Bruker Avance III HD 600 MHz spectrometers. ^1H and ^{13}C NMR chemical shifts are referenced to residual solvent resonance signals. Mass spectra were recorded on an ESI-MS Bruker Micro-TOF mass spectrometer. Samples were dissolved in methanol. In positive ion detection mode the capillary current was set to 4500 V with an end plate offset of –500 V, and in negative mode the capillary current was set to 3000 V with an end plate offset of 500 V. Elemental analysis was performed with a Thermo FlashEA 1112 instrument.

Sodium Enolate 6

Sodium hydride (60% dispersion, 0.84 g, 21 mmol) was suspended in MTBE (15 mL). EtOH (0.1 mL) was added slowly with gas evolution at r.t. Next, a solution of ethyl formate (1.37 g, 18.5 mmol) and 1-acetyladamantane (**4**) (2.99 g, 16.8 mmol) in MTBE (5.0 mL) was added dropwise over 2 h. The resulting yellow slurry was diluted with MTBE (5 mL) and the suspension was stirred overnight at r.t. The mixture was filtered, and the yellow residue was washed multiple times with *n*-pentane. After drying *in vacuo*, the product was obtained as a pale yellow solid (3.2 g, 83%). No NMR data were obtained because of the insolubility of the product. The product was used without further purification.

IR (ATR): 2892, 2850, 1698, 1586, 1446, 1360, 1224, 774 cm^{-1}.

HRMS (ESI): *m*/*z* [M – Na]$^-$ calcd for $C_{13}H_{17}O_2$: 205.1234; found: 205.1233.

6-Adamantyl-2-pyridone (3b)

Sodium enolate **6** (1.07 g, 5.00 mmol) was suspended in EtOH (25 mL). 2-Triphenylphosphonium-acetamide chloride (**7**) (1.78 g, 5.00 mmol) was added and the mixture was heated at 80 °C for 3 h. Acetic acid (10 mL) was then added and the mixture was refluxed at 110 °C for 18 h. The solvent was then removed and the residual acetic acid was co-evaporated with toluene. The product was purified by column chromatography on silica gel using *n*-hexane/EtOAc/AcOH (3:1:0.01). The product was isolated as a white crystalline solid (600 mg, 52%).

R_f = 0.24; mp 219.5 °C

^1H NMR (400 MHz, $CDCl_3$): δ = 11.1 (s, 1 H, N*H*), 7.36 (dd, *J* = 9.1 Hz, 7.1 Hz 1 H, Pyr*H*), 6.38 (dd, *J* = 9.1 Hz, 0.8 Hz, 1 H, Pyr*H*), 6.03 (dd, *J* = 7.0 Hz, 0.7 Hz, 1 H, Pyr*H*), 2.13–2.08 (m, 3 H), 1.96–1.88 (m, 6 H), 1.79–1.71 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9 (C_q), 157.1 (C_q), 141.6 (Pyr-*C*H), 117.6 (Pyr-*C*H), 101.6 (Pyr-*C*H), 40.6 (3 *C*H_2), 36.6 (C_q), 36.4 (3 *C*H_2), 28.2 (3 *C*H).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NONa$: 252.1358; found: 252.1360.

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.18; H, 8.08; N 6.11.

6-Adamantyl-2-pyridone Borane Complex 2b

In a nitrogen-filled glovebox, 6-adamantyl-2-pyridone (**3b**) (6.8 mg, 0.03 mmol) and Piers' borane (10.6 mg, 0.031 mmol) were dissolved in benzene-d_6 (0.3 mL) in a vial. The solution was transferred to an NMR tube via a J. Young valve and the vial was washed with benzene-d_6 (0.1 mL). NMR spectra were recorded immediately, showing the formation of pyridone borane complex **2b** and bispyridone complex **8b**.

^1H NMR (400 MHz, benzene-d_6): δ = 10.33 (s, 1 H, N*H*), 6.69 (dd, *J* = 8.9 Hz, 7.5 Hz, 1 H, Pyr-*H*), 6.53 (ddd, *J* = 8.9 Hz, 2.2 Hz, 0.9 Hz, 1 H, Pyr-*H*), 5.70 (ddd, *J* = 7.5 Hz, 1.9 Hz, 1.0 Hz, 1 H, Pyr-*H*), 5.01 (br s, 1 H, B*H*), 1.66–1.59 (m, 3 H, C*H*), 1.43–1.35 (m, 3 H, CH_2), 1.30–1.21 (m, 3 H, CH_2), 1.15–1.09 (m, 6 H, CH_2).

^{13}C NMR (100 MHz, benzene-d_6): δ = 161.9 (C_q), 156.9 (C_q), 145.8 (Pyr-*C*H), 114.3 (Pyr-*C*H), 109.4 (Pyr-*C*H), 40.1 (*C*H_2), 36.7 (C_q), 35.7 (*C*H_2), 28.0 (*C*H).

^{11}B NMR (128 MHz, benzene-d_6): δ = –7.1.

^{19}F NMR (377 MHz, benzene-d_6): δ = –134.4 (dd, *J* = 22.1 Hz, 7.7 Hz), –158.6 (t, *J* = 20.5 Hz), –164.3 (ddd, *J* = 24.3 Hz, 19.8 Hz, 9.4 Hz) (F integration 2:1:2).

6-Adamantyl-2-pyridonate Borane Complex 1b

In a nitrogen-filled glovebox, 6-adamantyl-2-pyridone (**3b**) (6.8 mg, 0.03 mmol) and Piers' borane (10.8 mg, 0.031 mmol) were dissolved in benzene-d_6 (0.4 mL) in a vial. The solution was transferred to an NMR tube via a J. Young valve and the vial was washed with benzene-d_6 (0.1 mL). The NMR tube was degassed three times using the freeze/pump/thaw technique and placed in a 60 °C oil bath for 20 h. Afterwards, it was again degassed via freeze/pump/thaw and NMR spectra were recorded. The formation of pyridonate borane **1b** and bispyridone complex **8b** were observed.

^1H NMR (400 MHz, benzene-d_6): δ = 7.01 (t, *J* = 8.0 Hz, 1 H, Pyr-*H*), 6.43 (dd, *J* = 7.7 Hz, 0.4 Hz, 1 H, Pyr-*H*), 6.40 (dd, *J* = 8.2 Hz, 0.6 Hz, 1 H, Pyr-*H*) 1.85–1.78 (m, 3 H, C*H*), 1.60–1.44 (m, 12 H, CH_2).

^{13}C NMR (100 MHz, benzene-d_6): δ = 166.6 (C_q), 163.4 (C_q), 142.4 (Pyr-*C*), 114.5 (Pyr-*C*), 108.2 (Pyr-*C*), 41.2 (*C*H_2), 38.7 (C_q), 36.6 (*C*H_2), 28.7 (*C*H).

^{11}B NMR (128 MHz, benzene-d_6): δ = 29.7.

^{19}F NMR (377 MHz, benzene-d_6): δ = –132.3 (dd, *J* = 24.0, 9.2 Hz), –150.8 (s), –162.0 to –162.1 (m) (F integration 2:1:2).

Adamantyl Bispyridone Complex 8b

In a nitrogen-filled glovebox, 6-adamantyl-2-pyridone (**3b**) (22.9 mg, 0.1 mmol) and Piers' borane (17.3 mg, 0.05 mol) were suspended in DCM (0.7 mL). The solution was stirred for 2 h at r.t. and then *n*-hexane (5 mL) was added. Upon evaporation of the DCM, the product crystallized as colorless crystals (33.7 mg, 84%).

^{1}H NMR (400 MHz, benzene-d_6): δ = 12.8 (s, 1 H, N*H*), 6.93 (dd, *J* = 8.4 Hz, 7.6 Hz, 2 H, Pyr*H*), 6.65 (d, *J* = 8.4 Hz, 2 H, Pyr*H*), 6.14 (d, *J* = 7.5 Hz, 2 H, Pyr*H*), 1.83 (s, 6 H, 6 C*H*), 1.58–1.49 (m, 24 H, 12 CH_2).

^{13}C NMR (100 MHz, benzene-d_6): δ = 162.6 (C_q), 162.5 (C_q), 142.2 (Pyr-CH), 113.6 (Pyr-CH), 110.9 (Pyr-CH), 40.9 (CH_2), 37.9 (C_q), 36.5 (CH_2) 28.6 (CH).

^{11}B NMR (128 MHz, benzene-d_6): δ = 4.93.

^{19}F NMR (377 MHz, benzene-d_6): δ = –137.1 (dd, *J* = 24.4, 9.3 Hz), –158.1 (t, *J* = 20.6 Hz), –164.5 to –164.7 (m) (F integration 2:1:2).

Catalytic Experiments

Dimerization of Phenylacetylene

The *gem* dimerization was performed according to a previously reported procedure.[7] Under a nitrogen atmosphere, 6-adamantyl-2-pyridone (**3b**) (7.0 mg, 0.03 mmol) and Piers' borane (11.5 mg, 0.033 mmol) were dissolved in toluene (1 mL). The solution was transferred to a Schlenk tube and phenylacetylene (16.5 μL, 0.15 mmol) was added. The tube was placed in a pre-heated oil bath at 100 °C and the contents stirred for 6 h. The solvent was removed *in vacuo* and trimethoxybenzene (8.4 mg, 0.05 mmol) was added. The residue was dissolved in chloroform-*d* and NMR spectra were recorded (see Figures SI 29 and SI 30 in the Supporting Information).

Hydrogenation of Alkynes

The hydrogenations were performed according to a previously reported procedure.[5] Under a nitrogen atmosphere, 6-adamantyl-2-pyridone (**3b**) (6.9 mg, 0.03 mmol) and Piers' borane (13.5 mg, 0.039 mmol) were dissolved in *n*-hexane (5 mL) in a Fisher–Porter type reactor bomb. The respective alkyne [phenylacetylene (0.3 mmol) or 2-methyl-3-pentyne (0.6 mmol] was added and the vessel sealed. It was then connected to a H_2 bomb cylinder with a gas hose that had been rinsed several times with hydrogen. The vessel was pressurized with 5 bar hydrogen and placed in an 80 °C pre-heated oil bath for 20 h or 16 h. Finally, trimethoxybenzene (8.4 mg, 0.05 mmol) was added and NMR spectra were recorded (see Figures SI 25–28 in the Supporting Information).

Funding Information

This work was supported by the Deutsche Forschungsgemeinschaft (DFG; German Research Foundation) (GE 3117/1-1).

Acknowledgment

Continued support from Prof. Dr. P. R. Schreiner, Prof. Dr. R. Göttlich, and Prof. Dr. H. A. Wegner is acknowledged.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1705970.

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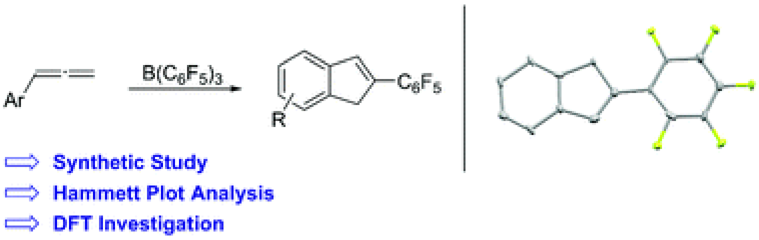
5.5 Indene formation upon borane-induced cyclization of arylallenes, 1,1-carboboration, and retro hydroboration



The reaction of tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) with aryl allenes was investigated. Mechanistic studies showed that coordination of $B(C_6F_5)_3$ to the allene facilitates a Friedel-Crafts-like cyclization to the indene. Subsequent 1,1-carboboration and retro-hydroboration yields the C_6F_5-substituted indenes.

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Chem. Commun. **2021**, *57*, 5518-5521.

DOI: 10.1039/d1cc01750k

ChemComm

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View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2021, 57, 5518

Received 2nd April 2021,
Accepted 29th April 2021

DOI: 10.1039/d1cc01750k

rsc.li/chemcomm

Indene formation upon borane-induced cyclization of arylallenes, 1,1-carboboration, and retro-hydroboration†

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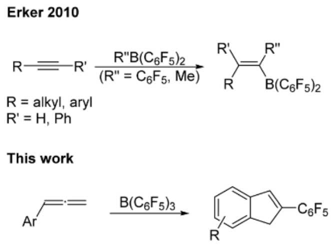
We herein report the reaction of arylallenes with tris(pentafluorophenyl)borane that yields pentafluorophenyl substituted indenes. The tris(pentafluorophenyl)borane induces the cyclization of the allene and transfers a pentafluorophenyl ring in the course of this reaction. A Hammett plot analysis and DFT computations indicate a 1,1-carboboration to be the C–C bond-forming step.

In 2010, Erker and co-workers reported that the reaction of the strongly Lewis acidic tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) with terminal alkynes leads to a 1,1-carboboration of the alkyne.[1] The substrate scope of the 1,1-carboboration was extended to phosphinyl substituted alkynes, yielding alkenyl-bridged frustrated Lewis pairs.[2] Furthermore, the 1,1-carboboration of internal alkynes with concomitant C–C cleavage was demonstrated.[3,4] More recently, Melen *et al.* reported the 1,2-carboboration of allenyl ketones.[5]

We found now that the reaction of $B(C_6F_5)_3$ with phenylallene **1** leads to the formation of the pentafluorophenyl-substituted indene **2** (Scheme 1).[6] Our initial finding was that the addition of **1** to a solution of $B(C_6F_5)_3$ in dichloromethane-d$_2$ (DCM-d$_2$) leads to the formation of indene **2** in 48% NMR-yield within 45 minutes (Scheme 2).

Hence, the $B(C_6F_5)_3$ induces a ring closure and transfers a pentafluorophenyl ring to the allene.[7] As a side product of this reaction, we observed the allylborane **3** that is likely formed by hydroboration of the phenylallene **1**.[8] Besides, minor amounts of a vinylborane, originating from the hydroboration of the internal double bond, and a 2-boryl-hexa-1,5-dien, formed by Piers' borane induced dimerization of the allene, were detected (for details, see the ESI†). The detection of **3** gives a direct hint to the intermediate formation of Piers' borane $HB(C_6F_5)_2$ in the course of the reaction.[9] Accordingly, the reaction constitutes a formal exchange of a pentafluorophenyl group of the $B(C_6F_5)_3$ with hydrogen. The reaction was subsequently performed on a preparative scale and the indene **2** was isolated and fully characterized. The structural assignment is further supported by SCXRD (Scheme 2). We then investigated the scope of this transformation by reacting different aryl allenes with $B(C_6F_5)_3$. As the hydroboration observed in the initial experiment consumes some of the allene, these reactions were performed with two equivalents of the allene. Under these conditions, **2** was isolated in 68% yield with respect to $B(C_6F_5)_3$, the limiting reagent (Scheme 3). The same reaction with one equivalent phenylallene and norbornene as sacrificial olefine to capture Piers' borane yielded **2** in 58% yield. The benzindene **4** is obtained in 65% yield from the reaction of 1-naphthylallene with $B(C_6F_5)_3$. However, it was isolated as a mixture of isomers that differ regarding the position of the benzylic double bond. Likewise, the reaction of *p*-tolylallene and *p*-(isopropyl)phenylallene gives the indenes **5** and **6** as a mixture of regioisomers.



Scheme 1 The context of this work: the 1,1-carboboration of alkynes described by Erker and the borane-induced ring closure with concomitant aryl group transfer described herein.

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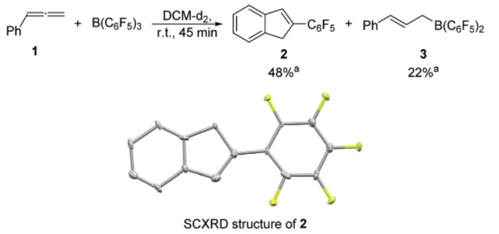
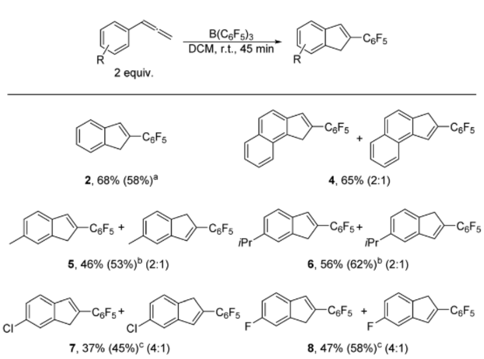
† Electronic supplementary information (ESI) available: Experimental and computational details, spectroscopic and crystallographic data, copies of NMR spectra. CCDC 2059168. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1cc01750k



Scheme 2 Formation of the pentafluorophenyl-substituted indene **2** upon the reaction of **1** with $B(C_6F_5)_3$. [a]Yields determined by qNMR with 1,3,5-trimethoxybenzene as internal standard. The inset shows the molecular structure of **2** derived from SCXRD (50% probability ellipsoids, all hydrogen atoms are omitted for clarity).



Scheme 3 Scope of the $B(C_6F_5)_3$ mediated formation of indenes from allenes. Yields of products isolated by column chromatography are given. (a) With one equivalent phenylallene and one equivalent norbornene. (b) Reaction temperature 0 °C. (c) Oil bath temperature 60 °C.

A better yield was obtained when the reactions with these substrates were run at 0 °C, presumably because of side reactions at r.t. In contrast, the reactions with *p*-(chloro)phenylallene and *p*-(fluoro)phenylallene required an elevated reaction temperature to give **7** and **8** in moderate yields. These findings indicate that electron-rich arylallenes undergo a faster cyclization whereas electron-withdrawing substituents slow down the reaction.

The effect of the substituents on the phenyl ring on the reaction rate was further assessed by a Hammett analysis (Fig. 1).[10] The negative slope of the Hammett plot and the rho value of -3.9 ± 0.7 indicate that in the rate-determining transition state of this reaction positive charge is built up in the benzylic position of the arylallene.

The increased reactivity of electron-rich allenes was used for a cyclization with a less Lewis acidic borane. The reaction of *p*-(isopropyl)phenylallene with $MeB(C_6F_5)_2$ leads to cyclization of the allene and transfer of the methyl group (Scheme 4). However, the formation of methylindene **9** required a prolonged reaction time.

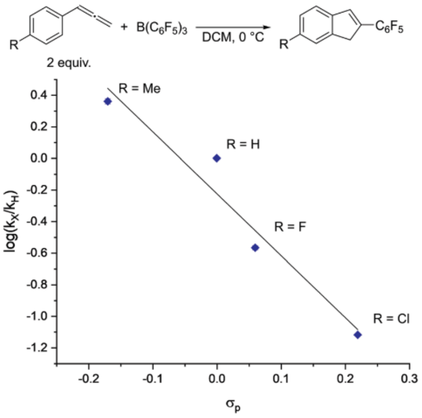
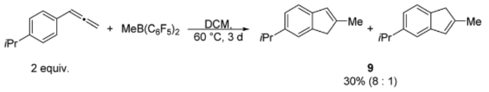


Fig. 1 Hammett plot analysis of the $B(C_6F_5)_3$- mediated formation of indenes from aryl allenes. Note that only the major isomer is shown in the scheme.



Scheme 4 Formation of the methyl indene 9 upon reaction of *p*-(isopropyl)phenylallene with $MeB(C_6F_5)_2$.

The mechanism of the $B(C_6F_5)_3$-mediated indene formation was further investigated computationally by DFT at the revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c level of theory (Fig. 2).[11–13] As zwitterionic intermediates are likely involved in the reaction, the SMD solvent model for DCM was used for the structure optimizations and the single point computations.[14] We assume that the reaction commences with the addition of $B(C_6F_5)_3$ to the π-system of **1**. This step yields the zwitterion **INT-1**. The positive charge in this intermediate is stabilized by allyl and benzyl resonance. An intramolecular Friedel–Crafts alkylation *via* **TS-2** closes the five-membered ring of the indene core. We further assume that an intermolecular proton shift leads to a re-aromatization and the intermediate **INT-3** (Scheme 5). However, all attempts to optimize the structure of **INT-3** resulted in a pentafluorophenyl transfer and lead to **INT-4**. Relaxed potential energy surface scans further showed that the pentafluorophenyl transfer is a barrierless process. This finding agrees with computational studies of the 1,1-carboboration of alkynes by Erker, Grimme, and co-workers that showed that once a carbocation is formed in α-position to the $B(C_6F_5)_3$ moiety, the pentafluorophenyl transfer is barrierless.

A retro-hydroboration, *i.e.* the liberation of $HB(C_6F_5)_2$ from **Int-4**, forms product **2**. According to the computations, this step requires only a moderate activation energy of 16.7 kcal mol^{-1}. Notably, the retro-hydroboration is computed to be exergonic by 2.2 kcal mol^{-1}. According to the computations, **TS-1**, the

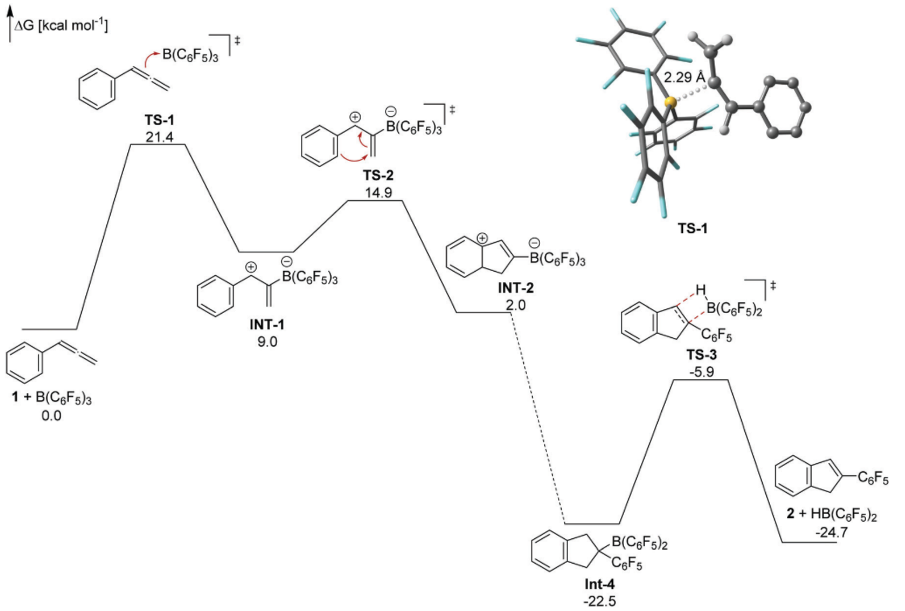
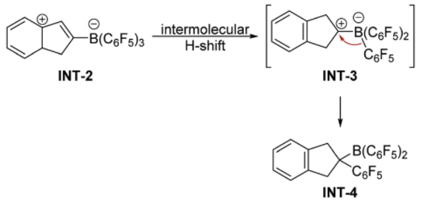


Fig. 2 Gibbs free energies of the B$(C_6F_5)_3$-mediated indene formation computed at the revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c level of theory. The SMD solvent model for DCM was used for the structure optimizations and the single point computations. The inset shows the optimized structure of **TS-1**.



Scheme 5 Proposed mechanism for the pentafluorophenyl transfer.

addition of the phenyl allene to B$(C_6F_5)_3$, is the rate-determining transition state. In this transition state, a positive charge is built up in the benzylic position that is stabilized by electron-donating groups in the para position. Thus, the computations are in favorable agreement with the Hammett analysis. In summary, we have documented that the reaction of arylallenes with B$(C_6F_5)_3$ leads to pentafluorophenyl substituted indenes. A plausible mechanistic scenario consists of a B$(C_6F_5)_3$-induced cyclization, a pentafluorophenyl transfer, and a retro-hydroboration. This reaction is a rare example of a metal-free C_{sp^2}–C_{sp^2} bond formation.[15] The results reported herein might inspire the development of synthetic methods that rely on 1,1-carboboration and retro-hydroboration reactions.

We thank the German research foundation (DFG) for financial support (GE 3117/1-1).

Conflicts of interest

There are no conflicts to declare.

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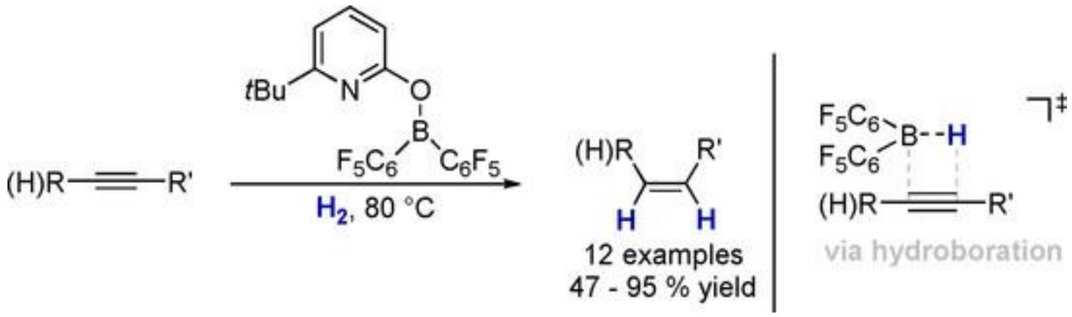
5.6 Semihydrogenation of Alkynes Catalyzed by a Pyridone Borane Complex: Frustrated Lewis Pair Reactivity and Boron–Ligand Cooperation in Concert



A pyridonate-borane complex, which can reversibly activate hydrogen, was used as a catalyst for the (*Z*)-selective semihydrogenation of alkynes. We found that this pyridonate-borane complex acts as an intramolecular frustrated Lewis-pair (FLP) but can dissociate after hydrogen activation. This releases a free, trivalent borane, which exhibits hydroboration reactivity. After hydroboration of the alkyne, the pyridone can recoordinate, and after proton transfer the product is obtained. As the first example for a metal-free system, this system is capable to hydrogenate not only internal, but also terminal alkynes. This is possible, because the C_{sp}-H activation of the alkyne by the FLP is reversible and thus in the presence of hydrogen, the hydrogenation pathway is kinetically accessible.

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Chem. Eur. J. **2020**, *26*, 13445–13450.

DOI: 10.1002/chem.202001276

Final veröffentlichte Version online: 03. April 2020

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Chemistry–A European Journal | Full Paper
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Homogeneous Catalysis

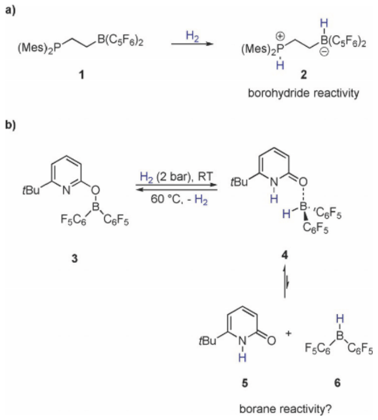
Semihydrogenation of Alkynes Catalyzed by a Pyridone Borane Complex: Frustrated Lewis Pair Reactivity and Boron–Ligand Cooperation in Concert

Felix Wech, Max Hasenbeck, and Urs Gellrich*[a]

Abstract: The metal-free *cis* selective hydrogenation of alkynes catalyzed by a boroxypyridine is reported. A variety of internal alkynes are hydrogenated at 80 °C under 5 bar H_2 with good yields and stereoselectivity. Furthermore, the catalyst described herein enables the first metal-free semihydrogenation of terminal alkynes. Mechanistic investigations, substantiated by DFT computations, reveal that the mode of action by which the boroxypyridine activates H_2 is reminiscent of the reactivity of an intramolecular frustrated Lewis pair. However, it is the change in the coordination mode of the boroxypyridine upon H_2 activation that allows the dissociation of the formed pyridone borane complex and subsequent hydroboration of an alkyne. This change in the coordination mode upon bond activation is described by the term boron-ligand cooperation.

Introduction

The seminal finding that specific combinations of sterically encumbered Lewis bases and Lewis acids, named „frustrated Lewis pairs“ (FLPs), can activate hydrogen, stimulated the development of catalytic metal-free hydrogenations.[1] Early examples included the hydrogenation of (di)imines, nitriles, aziridines, silyl enol ethers, and enamines, but the scope of FLP catalyzed hydrogenations was extended to heterocycles, alkenes, allenes, and aromatic hydrocarbons.[2,3] The heterolytic hydrogen cleavage by the FLP yields a tetravalent borohydride species. Therefore, hydrogenations by FLPs consist of a hydride and a subsequent proton transfer step (or *vice versa*) and require activated alkenes.[3] A notable exception is the semihydrogenation of alkynes catalyzed by an intramolecular FLP that was reported by Repo et al.[4] In that case, mechanistic investigations showed that the protolysis of the FLP under the reaction conditions yields an amine-hydroborane that initiates the catalytic cycle by hydroboration of the alkyne.[5] A protodeborylation of the alkenylborane yields then, in a highly stereoselective reaction, the *cis*-alkene.[6] We recently reported reversible H_2 activation by the boroxypyridine **3**.[7] A distinguishing feature of this system is that the H_2 activation is associated with a transition of the covalently bound oxypyridine substituent to a neutral pyridone donor ligand (Scheme 1). This mode of action was, in analogy to the concept of metal-ligand cooperation, termed boron-ligand cooperation. The change in the coordination mode of the pyridone substituent might enable the dissociation of the pyridone borane complex **4** in the ligand 6-*tert*-butylpyridone **5** and Piers borane **6**. Piers borane has been shown to display the typical reactivity of a trivalent borane, for example, it effects the hydroboration of alkenes and alkynes. Such dissociation is not possible for classic FLPs that, as aforementioned, therefore rather display borohydride reactivity upon H_2 activation (Scheme 1).



Scheme 1. A classic intramolecular FLP that displays borohydride reactivity and reversible H_2 activation by the boroxypyridine **3** that might display borane reactivity upon H_2 activation and dissociation.

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https://doi.org/10.1002/chem.202001276.

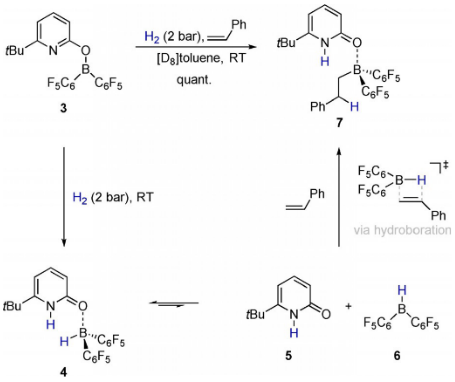
Results and Discussion

We envisioned the hydroboration of an alkene to be a valid test reaction to elucidate whether **3** displays borane reactivity upon hydrogen activation, since hydroboration requires the presence of a trivalent borane. Indeed, when **3** was reacted with one equivalent of styrene under moderate H_2-pressure at RT, the formation of the alkyl borane **7** was observed (Scheme 2). The alkylborane **7** is also formed when styrene is reacted with the pyridone borane **4**, which supports the assumption that **4** is an intermediate in the formation of **7** starting from **3**.

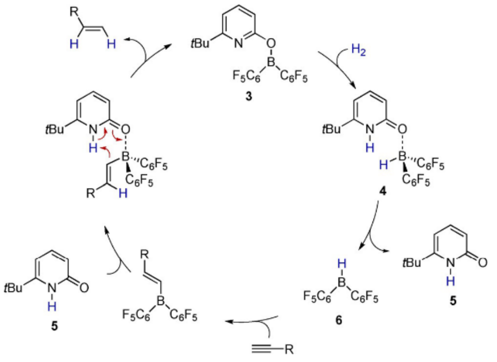
The alkylborane **7** does not undergo a protodeborylation. However, we envisioned that an analogous alkenylborane, originating from a reaction sequence consisting of H_2 activation and hydroboration of an alkyne might succumb to protonolysis. This reaction would regenerate the boroxypyridine **3** and close a catalytic cycle for the hydrogenation of alkynes that consists of H_2 activation by **3**, hydroboration of an alkyne and protonolysis of the alkenylborane (Scheme 3).

Indeed, 2-hexyne was stereoselectively converted to *cis*-2-hexene in 87% yield in the presence of catalytic amounts of **4** at 80 °C under 5 bar H_2 pressure (Scheme 4). The catalyst **4** was generated in situ by coordination of **5** to Piers borane **6**. An initial screening of reaction conditions showed that a slight excess of Piers borane **6** (1.3 equivalents with respect to **5**) is beneficial to obtain reproducible good yields. Under the same conditions, *cis*-2-octene is obtained in very good yields from the hydrogenation of 2-octyne. Likewise, *cis*-3-hexene is formed upon hydrogenation of 3-hexyne in excellent yield after only 8 h reaction time. The hydrogenation of 4-methyl-2-pentyne leads to the corresponding *cis* alkene in a very good yield after 16 h reaction time. Upon hydrogenation of the respective alkyne, 1-phenyl-1-propene is obtained in an excellent yield of 93%. Ethers are suitable substrates, as proven by the successful hydrogenation of 1-(*para*-methoxyphenyl)-propyne.

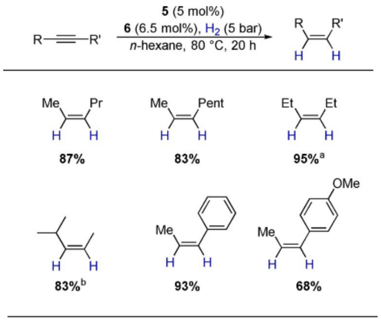
While 3-hexyne is obtained after 8 h exclusively as *cis* isomer, a prolonged reaction time of 16 h led to a 1:1 mixture of the *cis* and the *trans* isomer (Scheme 5). After 20 h, the *trans* isomer is the major product. Liu et al. reported that Piers borane can isomerize *cis*-alkenes via reversible hydroboration.[5] We, therefore, assume that the catalytic reaction yields first *cis*-3-hexene that is then subsequently isomerized by the Piers borane **6** that is present in the reaction mixture. Thus, both stereoisomers are accessible with the catalytic protocol described herein.



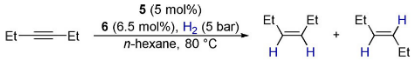
Scheme 2. Hydroboration of styrene upon H_2 activation by **3**.



Scheme 3. Envisioned mechanism of the hydrogenation of alkynes catalyzed by **3**: H_2 activation yields the pyridone borane complex **4** that undergoes a dissociation. Piers borane **6** hydroborates an alkyne, formation of the pyridone alkenylborane complex and its protolysis are closing the catalytic cycle.



Scheme 4. Substrate scope of the semihydrogenation of internal alkynes. Yields were determined by ^1H NMR with trimethoxybenzene as internal standard and are given as the average of two runs a) 8 h reaction time; b) 16 h reaction time.



8 h reaction time: 95% yield	100	:	0
16 h reaction time: 96% yield	49	:	51
20 h reaction time: 95% yield	20	:	80

Scheme 5. Stereoselectivity of the hydrogenation of 3-hexyne in dependence of the reaction time.

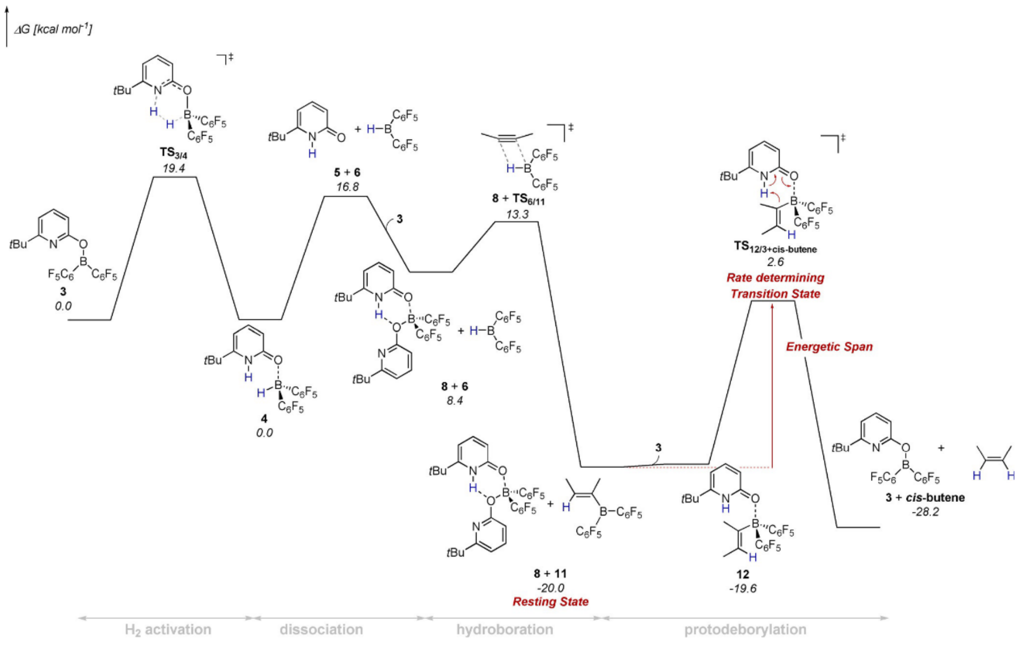
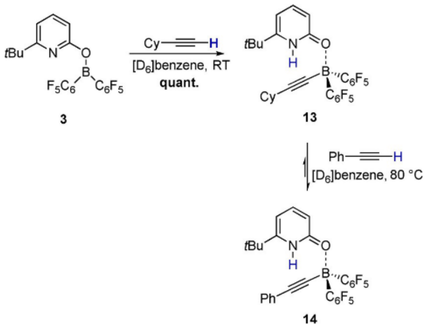


Figure 2. Gibbs free energy profile for the hydrogen activation by **3** computed at revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c. Bulk solvation was considered implicitly with the SMD model for hexane.

gen activation by **3** requires a free activation energy of 19.4 kcal mol^{-1}. This elementary step is according to our computations thermoneutral, which agrees with the previously observed facile reversibility of the hydrogen activation.[7] The free energy change that is associated with the dissociation of **4** into Piers borane **6** and the pyridone **5** is 16.8 kcal mol^{-1}. Relaxed potential energy surface scans indicate that the dissociation is barrierless. As the experimental results indicate that the bispyridone complex **8** is the resting state of the transformation, we considered the coordination of the free pyridone **5** to the boroxypyridine **3**. Indeed, the formation of **8** is according to the computations exergonic. The hydroboration of the model substrate 2-butyne requires a moderate activation energy of 4.9 kcal mol^{-1} and yields the alkenylborane **11**. The bispyridone complex **8** together with **11** is the resting state of the catalytic transformation.[13] The pyridone **5**, that is bound in complex **8**, coordinates than to **11** forming the pyridone alkenylborane complex **12**.

Note that pyridone exchange between **8** and the pyridone alkenylborane complex **10** was observed experimentally by EXSY NMR. The activation barrier for the protodeborylation is 22.2 kcal mol^{-1}, which corresponds to a half-life time of **12** of 35.8 minutes at 25 °C.[14] This agrees with the experimental observation that the protodeborylation takes place at RT (Scheme 9). The „Energetic Span“, that is the kinetic barrier of the catalytic transformation, is between the resting state (**8** and **11**) and the transition state of the protodeborylation.[15] Classic FLP type catalysts are not suitable for the hydrogenation of terminal alkynes, presumably because they are deactivated by an irreversible C_{sp}–H cleavage.[3] To understand why the catalyst system described herein tolerates terminal alkynes, **3** was reacted with cyclohexylacetylene at RT. As previously reported, this reaction led to the formation of the alkynylborane complex **13** (Scheme 10).[16] Upon addition of phenylacetylene



Scheme 10. C_{sp}–H cleavage of cyclohexylacetylene by **3** and exchange with phenylacetylene upon heating to 80 °C.

The known metal-free protocols for the hydrogenation of alkynes are limited to internal alkynes. We were pleased to find that the catalyst described herein is capable to hydrogenate 1-octyne in good yield with a catalyst loading of 10 mol% (Scheme 6). The catalytic protocol can also be used for the hydrogenation of other aliphatic alkynes such as cyclohexyl- and adamantly acetylene. While aromatic rings are tolerated, the hydrogenation of phenylacetylene and *para*-(trifluoromethyl)-phenylacetylene yielded the corresponding alkenes in lower yields. Again, ethers are suitable substrates, as demonstrated by the hydrogenation of 6-methoxy-1-hexylacetylene.

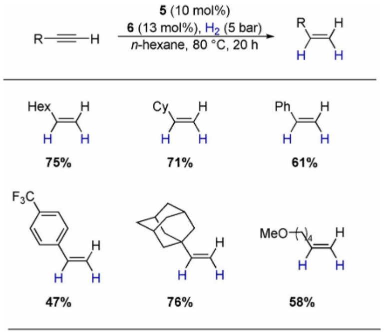
With these results in hand, we aimed for a mechanistic understanding of the catalytic reaction. To verify that the pyridone **5** is indeed vital for the reaction, we attempted the hydrogenation of 2-hexyne only with Piers borane **6** as catalyst (Scheme 7). Less than 1% product was formed under reaction conditions that are identical to those reported in Scheme 4, clearly indicating that the presence of the pyridone **5** is essential for the reaction outcome.

We then focused on the identification of the resting state of the catalytic reaction. For this purpose, the catalytic hydrogenation of 3-hexyne was monitored by NMR (Scheme 8). Under 4 bar H_2-pressure, rapid formation of *cis*-3-hexene was observed at 70 °C in [D$_6$]benzene, which implies that the observations made by this experiment are meaningful regarding the catalytic transformation.

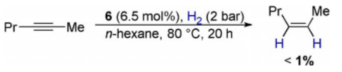
The bispyridone complex **8** that was previously described and characterized in detail was observed by ^{1}H NMR as the resting state of the catalytic reaction (Figure 1).[8] Furthermore, ^{1}H and ^{11}B NMR proved formation of boroxypyridine **3** with progressing reaction and hydrogen consumption. This finding strongly supports the assumption that **3** is part of the catalytic cycle.[9]

To elucidate whether the envisioned protonolysis of the alkenylborane can be assumed to be part of the catalytic reaction, **5** was added to the borane **9**, derived from the reaction of Piers borane **6** and 3-hexyne. The reaction progress at RT was monitored by NMR spectroscopy (Scheme 9). Within 30 minutes, the formation of the expected pyridone alkenylborane complex **10** was observed. Furthermore, signals that were assigned to *cis*-3-hexene, the product of the protonolysis, were detected. The presence of *cis*-3-hexene implies that boroxypyridine **3**, originating from the protonolysis must be present. Indeed, the formation of the bispyridone complex **8** that contains one equivalent of **3** was observed.

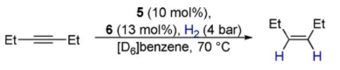
EXSY NMR spectroscopy shows an exchange of the pyridone **5** between **10** and **8** at RT, which further supports that **8** is not an unreactive, irreversibly formed species but rather a resting state. The mechanism of the catalytic reaction was further investigated computationally at revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c (Figure 2).[10,11] The SMD model for *n*-hexane was used to implicitly account for solvent effects.[12] The hydro-



Scheme 6. Substrate scope of the semihydrogenation of terminal alkynes. Yields were determined by ^{1}H NMR with trimethoxybenzene as internal standard and are given as the average of two runs.



Scheme 7. Attempted hydrogenation with Piers borane **6** as the catalyst.



Scheme 8. NMR monitoring of the catalytic hydrogenation of 3-hexyne.

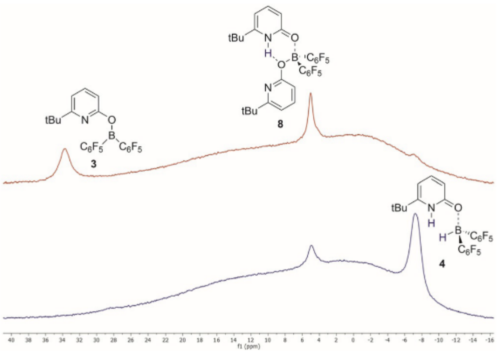
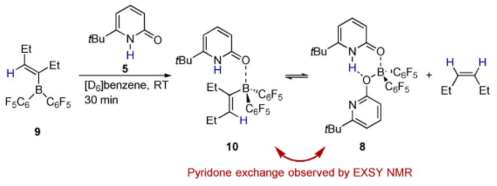


Figure 1. ^{11}B NMR spectra (193 MHz, [D$_6$]benzene) obtained by monitoring of the catalytic reaction (Scheme 8) before heating (blue) and after 15 h at 60 °C (red).



Scheme 9. Stoichiometric reaction of the alkenylborane **9** with the *tert*-butylpyridone **5**.

and heating to 80 °C, **13** was partially converted to the phenylalkynylborane complex **14**.

After 1 h at 80 °C, the ratio of **14** to **13** was 4:1. This experiment indicates that the C_{sp}–H cleavage is reversible under the reaction conditions. The assumption that the formation of the alkynylborane is reversible is further supported by DFT computations (Figure 3). According to the computations, the liberation of cyclohexyacetylene from **13** requires a free Gibbs activation energy of 24.1 kcal mol^{-1}, which corresponds to a half-life time of 79 seconds at 80 °C. The formation of the phenyl alkynyl borane complex **14** is kinetically and thermodynamically favored.

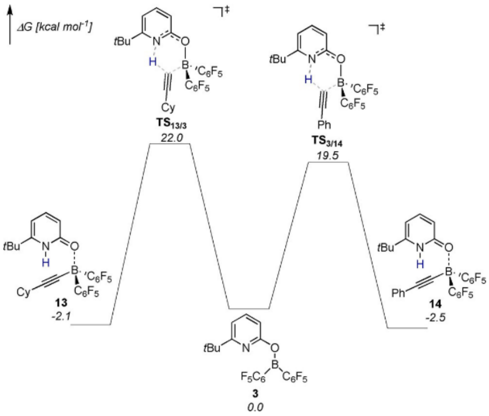


Figure 3. Gibbs free energy profile for the C_{sp}–H activation of cyclohxylacetylene and phenylacetylene by **3** computed at revDSD-PBEP86-D4/def2-QZVPP//PBEh-3c. Bulk solvation was considered implicitly with the SMD model for hexane.

The computed Gibbs free energy difference of 0.4 kcal mol^{-1} corresponds to a ratio of 2:1, which is in reasonable agreement with the experimentally observed proportion of the two alkynyl borane complexes. It is certainly the reversibility of the C_{sp}–H cleavage that allows H_2 activation in the presence of terminal alkynes and thus the first metal-free hydrogenation of terminal alkynes.

Conclusions

We have documented the efficient semihydrogenation of internal and terminal alkynes by a boroxypyridine that displays frustrated Lewis pair reactivity and is, therefore, able to activate hydrogen. However, the change in the coordination mode of the pyridonate substituent enables hydroboration as the initial step of the hydrogenation and is thus vital for the catalytic reaction. We expect this finding to pave the way for novel metal-free catalytic reactions that rely on this mode of action.

Experimental Section

General Procedure for hydrogenation of alkynes: Piers borane **6** (13.5 mg, 0.039 mmol) and 6-*tert*-butyl-2-pyridone **5** (4.5 mg, 0.030 mmol) were dissolved in *n*-hexane (5 mL) in a Fisher-Porter type 150 mL reaction vessel equipped with a stirring bar. The respective alkyne (0.60 mmol or 0.30 mmol) was added. The reaction vessel was closed and connected to an H_2 bomb with a gas hose. The hose was rinsed with H_2 several times and the reaction vessel pressurized with H_2 (5 bar). The reaction vessel was placed inside an 80 °C preheated oil bath and stirred at 1000 rpm. After 20 h, the reaction mixture was cooled to room temperature and the excess H_2 gas was released. An aliquot was taken, and the yield determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard.

Acknowledgements

This work was financially supported by the FCI and the DFG. The authors thank Dr. H. Hausmann for assistance with NMR experiments. Continuous and generous support by Prof. Dr. P. R. Schreiner, Prof. Dr. R. Göttlich, and Prof. Dr. H. A. Wegner is acknowledged. Open access funding enabled and organized by Projekt DEAL.

Conflict of interest

The authors declare no conflict of interest.

Keywords: alkynes · boron–ligand cooperation · density functional calculations · frustrated Lewis pair · hydrogenation

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Manuscript received: March 14, 2020
Revised manuscript received: April 1, 2020
Accepted manuscript online: April 3, 2020
Version of record online: September 18, 2020

6 Zusammenfassung und Schlussfolgerung

Im Rahmen dieser Arbeit wurden neue metallfreie Katalysatoren zur (*Z*)-selektiven Semihydrierung von Alkinen entwickelt. Klassische FLPs zeichnen sich durch ihre Borhydrid-Reaktivität aus und sind daher geeignete Katalysatoren für die Reduktion polarer, ungesättigter Substrate. Ein Merkmal der hier eingesetzten FLPs ist es, dass nach der H_2 Aktivierung durch Dissoziation ein Boran freigesetzt wird, welches in der Lage ist Alkine zu hydroborieren. Nach Koordination der Lewis-Base kann durch einen Protonentransfer das (*Z*)-Alken als Produkt freigesetzt und der Katalysator regeneriert werden. Wir fanden heraus, dass die C_{sp}–H Aktivierung terminaler Alkine durch das Pyridonat Boran **28** reversibel ist, wodurch die erste metallfreie Semihydrierung von terminalen Alkinen realisiert werden konnte. Durch Modifizierung des sterischen Anspruchs des Substituenten am Pyridon **29** konnten wir außerdem ein ebenfalls effizientes Katalysatorsystem entwickeln und die Ausbeuten der Reaktion erhöhen.

Zusätzlich fanden wird heraus, dass selbst einfaches $BH_3 \cdot SMe_2$, aber auch Alkylborane wie $HBCy_2$, als Katalysator eingesetzt werden können, wodurch wir das hoch elektrophile $HB(C_6F_5)_2$ durch synthetisch leicht zugängliche und kommerziell erhältliche Alternativen ersetzen konnten. Es zeigte sich, dass der gebildete Katalysator unter Reaktionsbedingungen äußerst stabil ist, und wir so mit niedrigen Katalysatorladungen hohe Umsatzzahlen erreichen konnten.

Im Rahmen dieser Arbeit wurden auch die für die Semihydrierung von Alkinen eingesetzten Lewis-Basen systematisch modifiziert und als Co-Katalysator eingesetzt, und dadurch versucht eine Struktur-Aktivitätsbeziehung abzuleiten. Während Änderungen an den Substituenten und dem reaktiven Zentrum einen nur geringen Einfluss auf die TOF hatten, zeigte sich eine Kernmodifikation, der Wechsel des Imidazolons zu einem Mercaptothiazol, als ausschlaggebend für eine drastische Erhöhung der katalytischen Aktivität. Es sind jedoch weitere Studien zu diesem Thema notwendig, doch diese initialen Ergebnisse demonstrieren, dass die Effizienz der metallfreien Semihydrierung von Alkinen entscheidend zu erhöhen, um diese kompetitiv zu Übergangsmetall-katalysierten Alternativen zu machen.

Zusätzlich wurde noch die Reaktion elektrophiler Borane mit Allenen und Dienen untersucht. Wir haben gezeigt, dass $B(C_6F_5)_3$ mit Allenen in einer intramolekularen Friedel-Crafts-Reaktion reagiert. Im Anschluss wird ein C_6F_5-Ring übertragen und es wurden verschiedene C_6F_5-substituierte Indene durch diese 1,1-Carboborierung erhalten. Durch den Einsatz von $MeB(C_6F_5)_2$ konnte auch selektiv die Methylgruppe übertragen werden, auch wenn die Reaktion durch die verringerte Elektrophilie weniger effizient ablief. Dennoch ist dies eines der wenigen Beispiele für 1,1-Carboborierungen, und das erste Beispiel, bei dem das Bor in Form von Piers' Boran in einer *retro*-Hydroborierung wieder freigesetzt wird und nicht im Endprodukt enthalten ist.

Wir beobachteten auch, dass sich aus der Reaktion zyklischer Diene mit $HB(C_6F_5)_2$ nicht wie erwartet ein Alkylboran bildet, sondern ein Alkenylboran. Dies erlaubte uns durch Zugabe stöchiometrischer Mengen HBpin eine katalytische Reaktion zu realisieren, die auf einer Transborylierung basiert. Dabei ist besonders herauszustellen, dass sich durch diese Methode atomökonomisch Alkenylboronate aus Dienen und HBpin herstellen lassen, für die klassischerweise Mehrstufige Synthesen notwendig sind, die stöchiometrische Mengen Abfallprodukte generieren. Durch stöchiometrische Kontrollexperimente konnten wir mögliche Zwischenstufen isolieren und als Katalysator einsetzen und daraus mechanistische Hypothesen ableiten.

7 Danksagung

Zuletzt möchte ich noch einigen Menschen danken, ohne die es nicht möglich gewesen wäre, diese Arbeit abzuschließen:

Allen voran möchte ich Prof. Dr. Urs Gellrich meinen herzlichen Dank aussprechen, der mich während meiner gesamten Promotionszeit unterstützt und gefördert hat. Seine fachliche Unterstützung, wertvollen Ratschläge und konstruktives Feedback haben maßgeblich zum Fortschritt und zur Fertigstellung dieser Arbeit beigetragen. Ich habe sowohl professionell als auch persönlich sehr viel gelernt und konnte mich kontinuierlich weiterentwickeln.

Prof. Dr. Wegner für die Übernahme des Zweitgutachtens und die Unterstützung unserer Arbeitsgruppe in Gießen.

Prof. Dr. Schreiner für die Aufnahme und die Möglichkeit der Teilnahme am Gruppenseminar, sowie für die ebenfalls kontinuierliche Unterstützung.

Ich möchte der gesamten Arbeitsgruppe Gellrich danken: Dr. Max Hasenbeck für die Betreuung während meines Masters, sowie Dr. Sebastian Ahles, von dem ich vor Allem in meiner Anfangszeit sehr viel lernen konnte. Mein besonderer Dank gilt auch Prof. Dr. Ravindra Phatake, von dem ich viel lernen konnte, sowohl was die Laborarbeit betrifft als auch persönlich. Ich danke auch Dr. Tizian Müller, Jama Ariai, Arthur Averdunk, Niklas Koch und John Liebig für das stets produktive und positive Arbeitsumfeld und den tatkräftigen Beistand während zahlreicher Kaffeepausen und Feierabendbiere. Vielen Dank auch an meine ehemaligen Studenten Matthis Wittke und Beyza Iltir.

Ich möchte auch der Arbeitsgruppe Prof. Dr. Göttlich danken für die stets gute Zusammenarbeit und Hilfsbereitschaft.

Ich danke auch allen Mitarbeitern des Instituts, die mir mit ihrer technischen und administrativen Expertise stets geholfen haben. Allen voran danke ich den Mitarbeiterinnen der NMR-Abteilung, Anika Bernhardt, Anja Platt und Inna Klein, für die Messung aller NMR-Spektren und die vielen Stunden Messzeit, die für diese Arbeit notwendig waren. Dr. Heike Hausmann für ihre große NMR-Expertise und Hilfe bei komplexen Messungen und Auswertungen und dass sie immer Zeit für einen Messtermin finden konnte. Außerdem Danke ich Dr. Raffael Wende, Stefan Bernhardt, Steffen Wagner und Edgar Reitz, für ihre Expertise in der OC-Analytik. Ohne die Mitarbeiter der Chemikalienausgabe wäre diese Arbeit ebenfalls nicht möglich gewesen: Mario Dauber, Eike Santowski. Ich danke auch Dr. Jörg Neudert, der mich stets bei Problemen aller Art unterstützte. Danke auch an die Mitarbeiter der Materialausgabe und der Glasbläserei Jana Küchenmeister und Anja Beneckenstein.

Dr. Jonathan Becker, Dr. Christian Würtele und Lisa-Marie Wagner für die Unterstützung bei der Messung und Lösung von Kristallstrukturen.

Michaela Richter, Anika Jäger und Maurice Monnard, die mir bei allen administrativen und verwaltungstechnischen Fragen und Problemen geholfen haben.

Ein großer Dank gilt meinen Eltern und meiner Familie: Christina Wech, Klaus-Peter Wech, Philipp Wech, sowie meinen Großeltern Hilde Wech, Heidi Lotz und Reinhold Lotz, und Nicole, Jochen, Quentin und Joscha. Durch ihre ständige Unterstützung war es mir erst möglich Chemie zu studieren und nun meine Promotion abzuschließen. Ich danke auch all meinen Freunden, auf die ich mich immer verlassen konnte. Ich danke Jannis Volkmann für die stetige und gegenseitige Motivation sich sportlich zu betätigen.

Meiner Freundin Katha möchte ich besonders danken, ohne ihre Unterstützung und ihr Verständnis hätte ich diesen Weg so nicht einschlagen können.