Fakultät für Mathematik, Informatik und Naturwissenschaften | RWTH AACHEN UNIVERSITY

Boron-Mediated Direct Nitro-Functionalization

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der RWTH Aachen University zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaften genehmigte Dissertation

vorgelegt von

Peter Palchuber, Master of Science

aus

Szolnok, Ungarn

Berichter*:* *Prof. Dr. rer. nat. Meike Niggemann*

Prof. Dr. rer. nat. Markus Albrecht

Tag der mündlichen Prüfung*: 17.04.2024*

Acknowledgements

I am grateful to Prof. Dr. Meike Niggemann for providing me with the opportunity to pursue my doctoral studies in her group. I express my thanks for the various approaches and knowledge that I have gained under her guidance.

Special appreciation goes to Prof. Dr. Markus Albrecht for fulfilling the role of the second reviewer of this work.

I extend my gratitude to Raphael Eckert for being a mentor during my initial days in the group and for the enjoyable moments in the lab. Additionally, I appreciate Sarah Roeb for her assistance on my projects and the positive experiences shared in the lab. I also want to express my appreciation to Max Gerbershagen, Marina Chuchmareva, Christina Strauch, Tillmann Herderich, Niklas Lentelink, Marian Rauser, and Sebastian Schröder for the valuable tips and support they provided.

I would like to acknowledge the contributions of my students: Chris, Lea, Victor, Benjamin, and Orsi.

A special mention goes to Dr. Christoph Räuber for his assistance with NMR measurements and to Cornelia Vermeeren for her insightful advices.

I cannot thank my family enough for their unwavering support, particularly during challenging times.

My deepest gratitude goes to my wife, Anna, for her constant encouragement and support in helping me achieve my goals and dreams.

Abbreviations

Ac	acetyl
acac	acetlyacetonate
Alk	alkyl
Ar	aryl
bipy	2,2'-bipyridine
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
Bz	benzoyl
b.	branched
cat	catechol/1,2-dihydroxybenzene
cat.	catalytic
CPME	cyclopentyl methyl ether
Cp	cyclopentadienyl
Cy	cyclohexyl
dan	naphthalene-1,8-diaminato
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DIPEA	*N*,*N*-Diisopropyethylamine
DMA	*N*,*N*-Dimethylacetamide
DMAP	*N*,*N*-Dimethyaminopyridine
DME	dimethoxyethane
DMF	*N*,*N*-Dimethylformamide
DMG	directed metalation group
DMPU	*N*,*N*'-Dimethylpropyleneurea
E	electrophile
Et	ethyl
EtOAc	ethyl acetate
HMDS	bis(trimethylsilyl)amine
HOMO	highest occupied molecule orbital

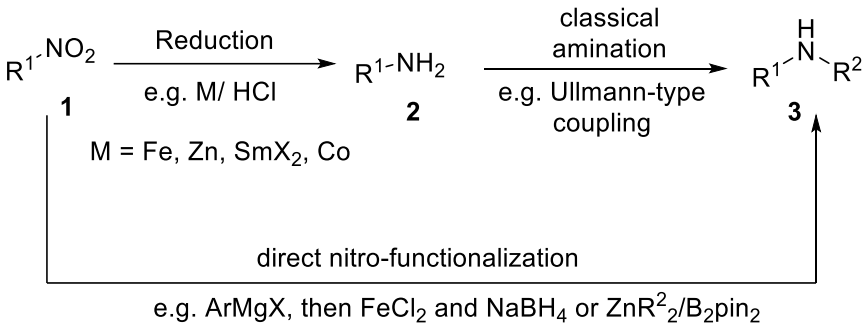
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
IR	infrared spectroscopy
LDA	lithium diisopropylamide
lin.	linear
LUMO	lowest unoccupied molecule orbital
Me	methyl
MOM	methoxymethyl
MS	molecular sieve
MTBE	methyl *tert*-butyl ether
NBS	*N*-bromosuccinimide
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
pin	pinacol
Piv	pivaloyl
Pr	propyl
py	pyridyl
rt	room temperature
SET	single electron transfer
sol	solvated
TBAB	tetra-*n*-butylammonium bromide
TBAF	tetra-*n*-butylammonium fluoride
TMP	2,2,6,6-tetramethylpiperidine
TEMPO	2,2,6,6-tetramethylpiperidin-1-yl)oxyl
Tf	trifluoromethanesulfonate
THF	tetrahydrofuran
TMEDA	*N*,*N*,*N*',*N*'-tetramethylenediamine
TMS	trimethylsilyl
Ts	tosyl

Table of Contents

Introduction: Direct Nitro-Functionalization

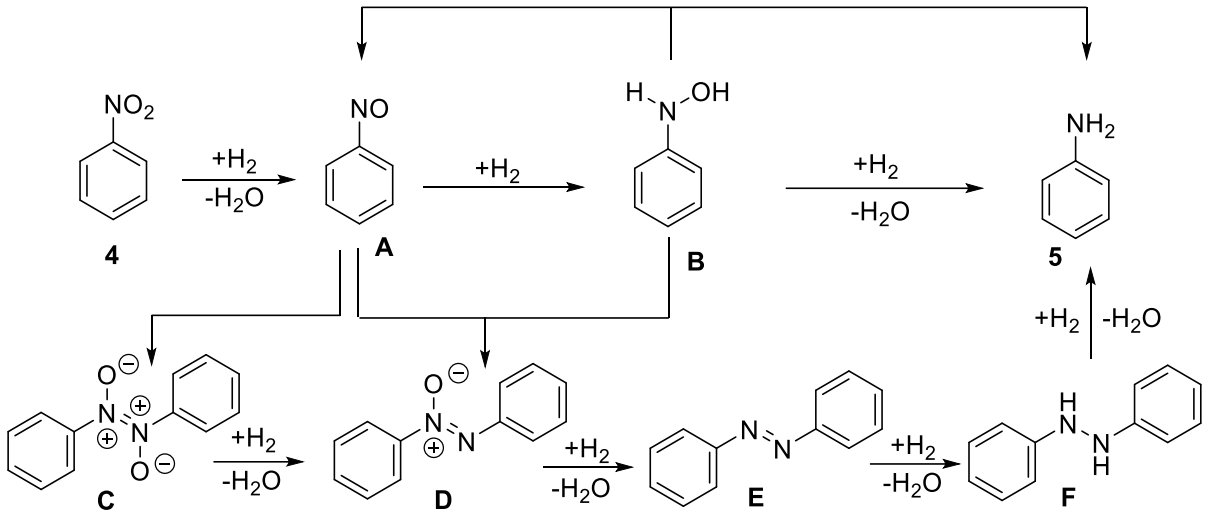
Background

Amines are ubiquitous structures and widely used in many different fields, including medicine and agriculture.[1] The efficient synthesis of functionalized amines is therefore an essential object of the organic chemistry. A classical synthetic way to amines is starting from nitro compounds **1**, where in the first step the nitro group will be reduced to amine function, for instance with metal in acidic milieu or *via* catalytic hydrogenation (Scheme 1).[2] A second step, usually reductive amination or cross-coupling delivers the secondary or tertiary amine **3**.[3] Several methods have also been developed to perform the two steps in a one-pot procedure.[4]



Scheme 1. Classical two-step nitro-functionalization and direct functionalization.

An attractive alternative process is the direct nitro-functionalization, where the nitro moiety will be partially reduced and an intermediate stage of the nitro-reduction cascade is used for the formation of the C-N bond. The most commonly used intermediate in this process is the nitroso compound, as it allows a variety of reactions, such as the nitroso ene reaction, reaction with nucleophiles, or free radicals.[5] One-pot reactions will not be discussed as direct *N*-functionalization, as they differ in the reaction pathway.
The direct transformation of nitro compounds into functionalized amines possesses several advantages, such as improved step economy, cost efficiency, and functional group compatibility.[6] Nitro compounds are usually cheaper and more stable than amines. Despite these benefits, the number of developed reactions is still less developed compared to the classical methods. The reason lies in the nitro reduction cascade (Scheme 2).[7] To functionalize the nitro moiety, it must be reductively activated first. This step is important since the overreduction to amine must be avoided. Also, reduction intermediates are highly reactive for other side reactions, which complicates a selective product formation. For instance, a commonly used nitroso intermediate undergoes dimerization and in the case of aliphatic nitroso compounds will instantly tautomerize to an oxime.[8] Therefore, aliphatic nitroso compounds are usually not tolerated in direct nitro-functionalizations. Another common side reaction is the disproportionation of hydroxylamine **B** to form azoxybenzene **D**, which reacts to azobenzene **E** and hydrazone **F**. Recent research aims to control the selective partial reduction and thereby the reactivity of the intermediates.

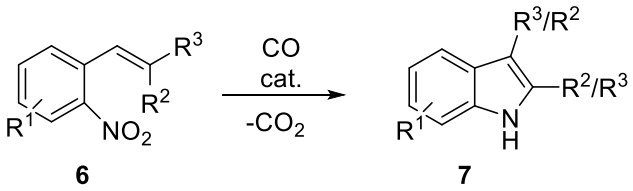


Scheme 2. Reduction cascade of nitrobenzene.

In the following, examples shall illustrate the utility of direct nitro-functionalization, especially the effective and selective activation of the nitro moiety.

Protocols for Direct Functionalization of Nitro Compounds

The direct functionalization of nitro compounds has been in the synthetic toolkit for more than 30 years.[9] The first reported example is a transition metal-catalyzed ($Fe(CO)_5$, $Ru_3(CO)_{12}$ or $Rh_6(CO)_{16}$) indole synthesis from 1986 by *Cenini and co-workers*, applying CO as a reducing agent (Scheme 3).[9a] The performed mechanistic investigations suggest nitroso as intermediate, followed by a cyclization *via* nitroso ene reaction. One of the biggest limitations of this process is the unsuitability of aliphatic nitro compounds.

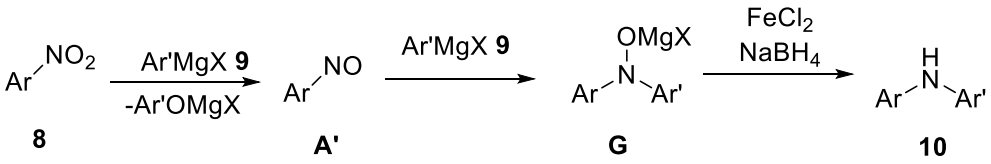


6 **7**

Scheme 3. General synthesis of indoles from *o*-nitrostyrenes with CO as reducing agent.

There were several attempts at the conversion of nitro compounds to functionalized amines, such as *Bartoli et al.*, *Makosza et al.*, and *Bubnov et al.*[10] These methods show either low selectivity or limited applicability.

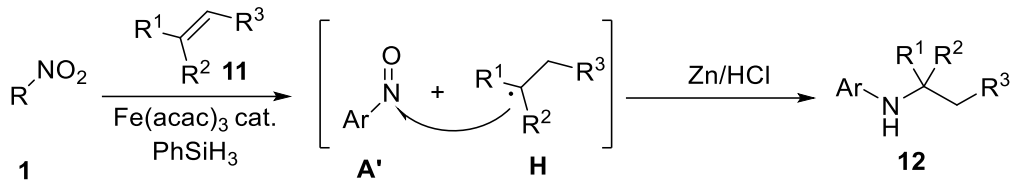
The first procedure for intermolecular secondary amine synthesis, starting directly from nitro compounds, was developed by the *Knochel et al.* in 2002 (Scheme 4).[11] The reaction with the first equivalent Grignard reagent **9** results in the nitroso intermediate **A'**, while the second equivalent provides the functionalized hydroxylamine **G**. The secondary amines **10** are obtained *via* reductive work-up. Aromatic nitro compounds with electron-withdrawing, as well as electron-donating group are suitable substrates, however, the reaction is limited to aryl substituent, due to the nitroso pathway.



8 **A'** **G** **10**

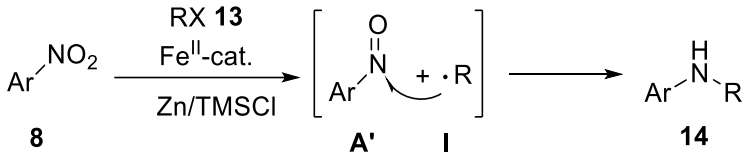
Scheme 4. Reaction pathway of nitro compounds with Grignard-reagents by *Knochel et al.*

The Fe-catalyzed hydroamination protocol of alkenes by *Baran et al.* showed that nitro(hetero)arenes **8** can be transformed into functionalized amines **15** (Scheme 5).[12] According to the mechanistic investigations, nitroso(hetero)arene **A'** forms *via* initial reduction. The most stable tertiary radical **H** reacts with the nitroso species, affording selectively the secondary amines **12**. To avoid the side reaction of the nitroxyl radical, the reductive work-up of the formed bisalkylhydroxylamine is crucial. Despite the presented broad applicability of this process, styrenes, (thio)phenols, pyridines and imidazoles are not tolerated under the reaction conditions. Compared to *Knochel's* procedure, aliphatic nitro compounds are suitable substrates. Yet, only a low yield is achieved, possibly due to the tautomerization of nitroso intermediate **A'** to oxime.



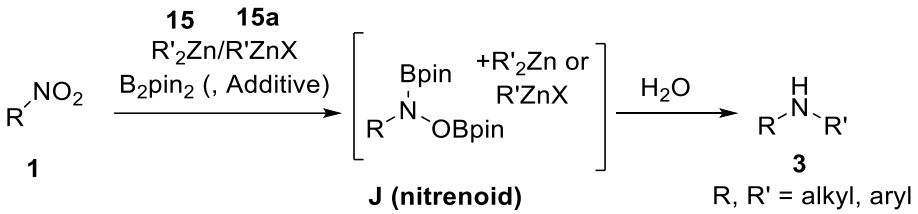
Scheme 5. Formal hydroamination of olefins by *Baran et al.*

Hu and *co-workers* utilized a similar concept, to couple nitro compounds **8** with alkyl halides **13** in an Fe-catalyzed radical reaction (Scheme 6).[6] An alkyl radical **I** is generated from the alkyl halide **13**, which reacts with the simultaneously formed nitroso species **A'**. This approach is the first *N*-functionalization, where the nitro compounds are converted in a reductive coupling to the corresponding amines **14**, by using a second electrophile. Besides the broad applicability, alkyl halides are commercially easily accessible. The applied Zn/TMSCl system is more cost-effective than $PhSiH_3$, used by the *Baran group*.



Scheme 6. Reductive coupling of nitro compounds with alkyl halides by *Hu et al.*

A new photocatalyzed version of this process was published by the *Xue et al.* in 2020.[13] Relating to the halide coupling partner, the approach is orthogonal to Hu's procedure, since only aryl halides are compatible coupling partners. The applicability of the nitro compound side has the same limitation. The role of the Ni-catalyst was not clarified.

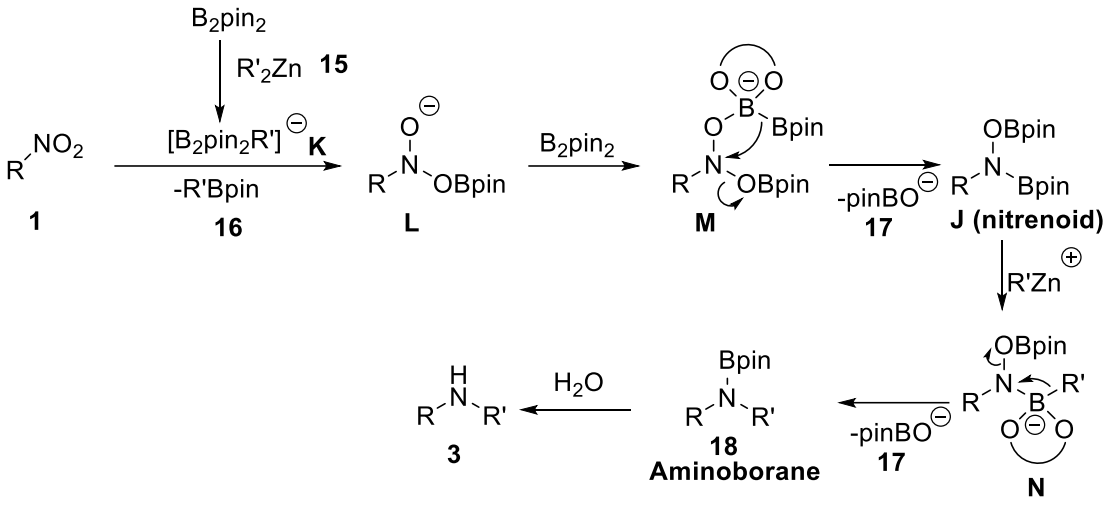


Scheme 7. Overview on the electrophilic amination with nitro compounds by *our group*.

To overcome the limitation of the nitroso intermediate, *our group* developed an electrophilic amination reaction, to utilize the unique reactivity of an electrophilic nitrenoid **J** (Scheme 7).[14] The nitro moiety **1** is converted to this key intermediate in two partial reduction steps, followed by the functionalization with the organozinc reagents **15**/**15a**. Due to the unique reactivity of the nitrenoid **J**, no transition metal catalyst is required and even aliphatic nitro compounds lead to the desired products **3**. The transformation shows high functional group tolerance, phenols, esters and aryl halides are suitable substrates. Based on $^{11}B\{^1H\}$-NMR investigations the following mechanism was proposed:

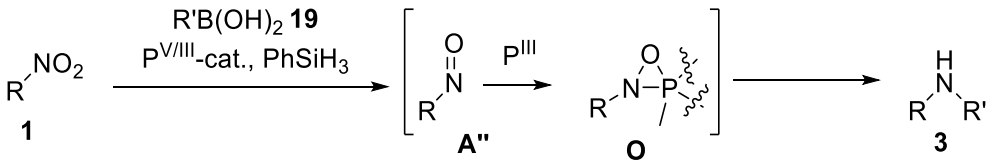
The organozinc compound forms an ate-complex **K** with B_2pin_2, to generate a nucleophilic Bpin moiety, which attacks the oxygen of the nitro compound and partially reduces it to intermediate **L** (Scheme 8).

A second equivalent of B_2pin_2 reacting with intermediate **L** results in nitrenoid **J**, then the boron center of the nitrenoid **J** is attacked by the organozinc species **15** to form **N**. A 1,2-migration and an elimination of an OBpin anion **17** afford the aminoborane **18**. After hydrolysis, the corresponding amine **3** is obtained. The *in situ* trapping of aminoborane **18** with a variety of electrophiles provides tertiary amines and amides. This protocol is the first synthesis of the RR'NBpin type aromatic aminoboranes.



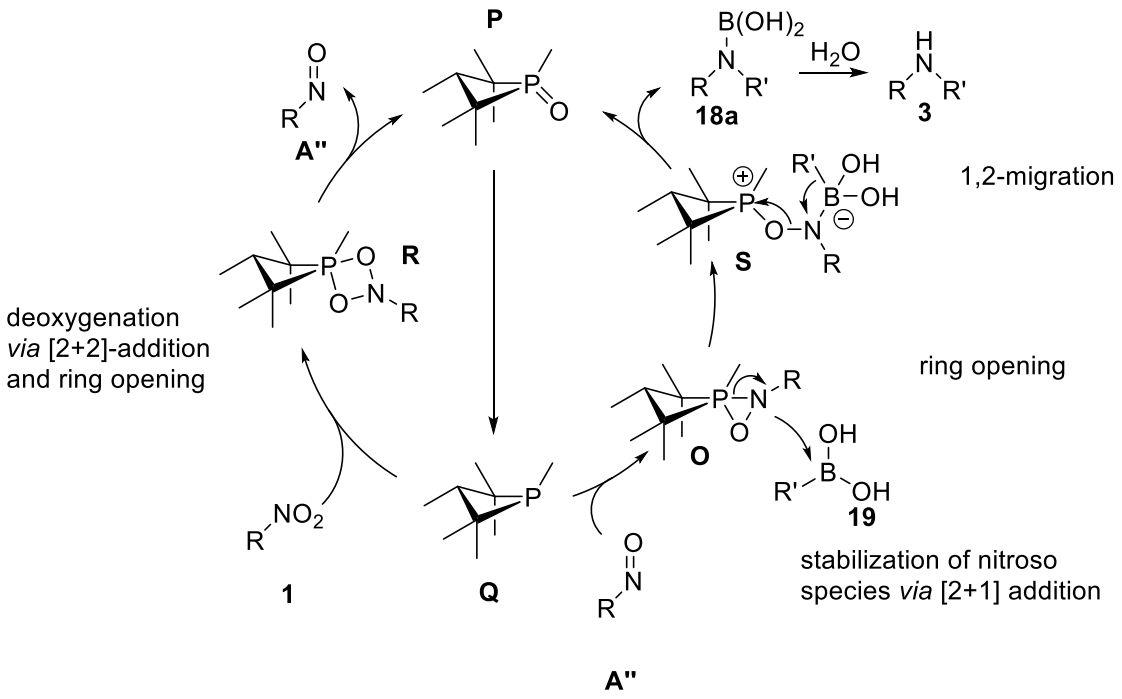
Scheme 8. Proposed mechanism of the electrophilic amination process by our group, based on $^{11}B\{^1H\}$-NMR.

According to the work of the *Radosevich et al.*, arylboronic acids and esters are suitable coupling partners for nitro compounds in the presence of their $P^{V/III}$-catalyst (Scheme 9).[15] Based on the mechanistic investigation and the kinetic experiments, the nitroso intermediate **A"** is stabilized by the active catalyst **Q** (Scheme 10). The active catalytic species is the reduced form of the catalyst **P**. This species is responsible for the reduction of the nitro compound **1** to the nitroso intermediate **A"** as well as the stabilization of the nitroso moiety. As a consequence of this umpolung of the nitrogen, it attacks the boron center of the coupling partner **19**. The C-N bond forms in a 1,2-migration, similar to the reported one by *our group*.[15a]



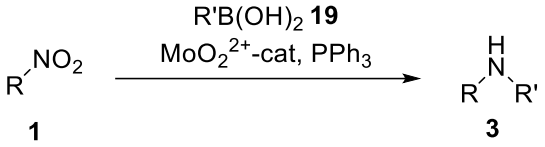
Scheme 9. $P^{V/III}$-catalyzed coupling of nitro compounds with boronic acid derivates by *Radosevich et al.*

Nitro compounds with electron-donating and -withdrawing groups are tolerated, even nitromethane, due to the stabilization of the nitroso intermediate **A"**. The reaction is limited to aromatic boronic acids and esters. The not commercially available catalyst and the expensive phenylsilane may be accounted as a limitation of the applicability. To overcome this drawback, the *same group* invented a catalyst-free method, only applying PEt_3. However, this procedure is restricted to aromatic compounds on both sides of the reaction partners.[15d]



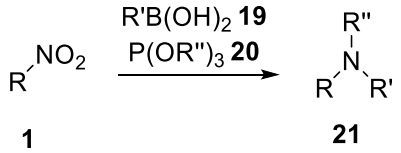
Scheme 10. Proposed mechanism of the $^{V/III}$-catalyzed coupling of nitro compounds with boronic acid derivates by *Radosevich et al.*, based on NMR- and kinetic studies and DFT calculations.

Sanz et al. presented an improved coupling reaction between nitro compounds **1** and boronic acids **19** (Scheme 11).[16] The used Mo-catalyst and PPh_3 as a reductant provide a widely applicable transformation for aliphatic and aromatic nitro compounds with a variety of boronic acids. The authors proposed the reduction of the nitro compound to a nitroso intermediate, which is stabilized by the Mo-catalyst. This may explain the tolerance towards aliphatic nitro compounds. Additionally, PPh_3 may also stabilize the nitroso species, as shown by the *Radosevich group*.



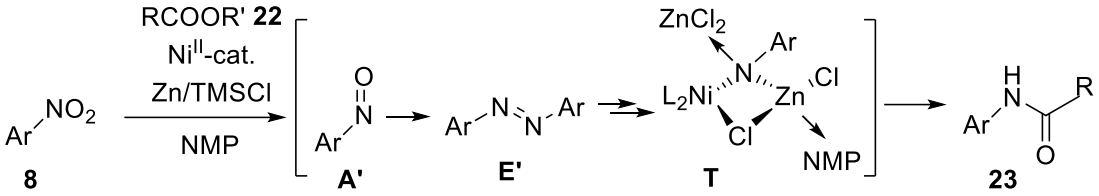
Scheme 11. Mo^{VI}-catalyzed coupling of nitro compounds with boronic acids by *Sanz et al.*

A similar catalyst-free approach was published by the *Csáky group*, using boronic acids **19** as coupling reagents and alkyl phosphite **20** as a reducing agent (Scheme 12).[17] A broad spectrum of tertiary amines **21** can be accessed with this S_N-reaction. The reaction presumably proceeds *via* nitroso intermediate, stabilized by the P^{III}-species, enabling also the conversion of aliphatic nitro compounds.



Scheme 12. Coupling of nitro compounds with boronic acids by *Csáky et al.*

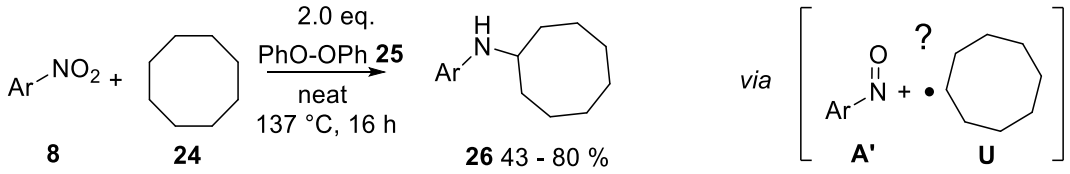
Nitro compounds can also be directly transformed into amides.[18] The first procedure was described by *Hu et al.*, where esters **22** and nitro compounds **8** provide the corresponding amides **23** in a Ni-catalyzed coupling reaction.[18a] According to mechanistic investigations, the nitro group will be first reduced to a nitroso **A'** and then to an azo compound **E'**, which forms a Ni-Zn-nitrene **T** with the catalyst (Scheme 13).[18b] Aliphatic and aromatic esters with diverse functional groups, such as ether, amide, (hetero)aromatic halogen substituent, are suitable substrates. However, aliphatic nitro compounds are not tolerated, due to the lack of stabilizing effects.



Scheme 13. Amidation of ester with nitro compounds by *Hu et al.*

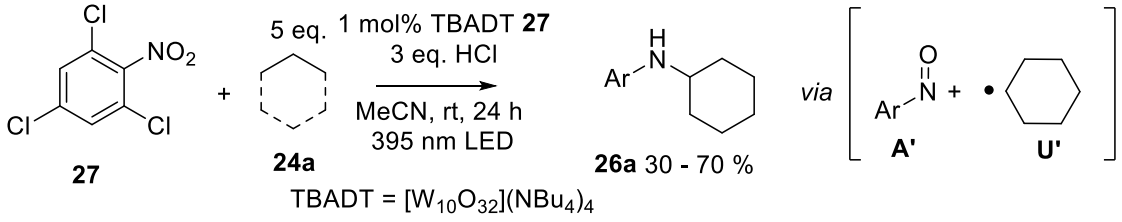
Other approaches for amide synthesis starting from nitro compounds are using a nucleophilic substrate and a carbonyl source, instead of esters.[18c, 18d] In these cases, the reaction is limited on both sides to aromatic compounds.

For C(sp^3)-H amination combined with direct nitro functionalization, three precedents have been reported. *Li et al.* developed a peroxide-mediated amination of cycloalkanes **24** with nitroarenes **8** (Scheme 14).[19]The reaction is limited to cycloalkanes **24** (one alkane as an example with 26% yield) and due to the harsh conditions (presence of 2.0 eq. of peroxide **25** and 137 °C), the yields are only moderate to good. The authors did not comment on the mechanism, therefore, the radical pathway *via* nitroso intermediate **A'** can only be assumed.



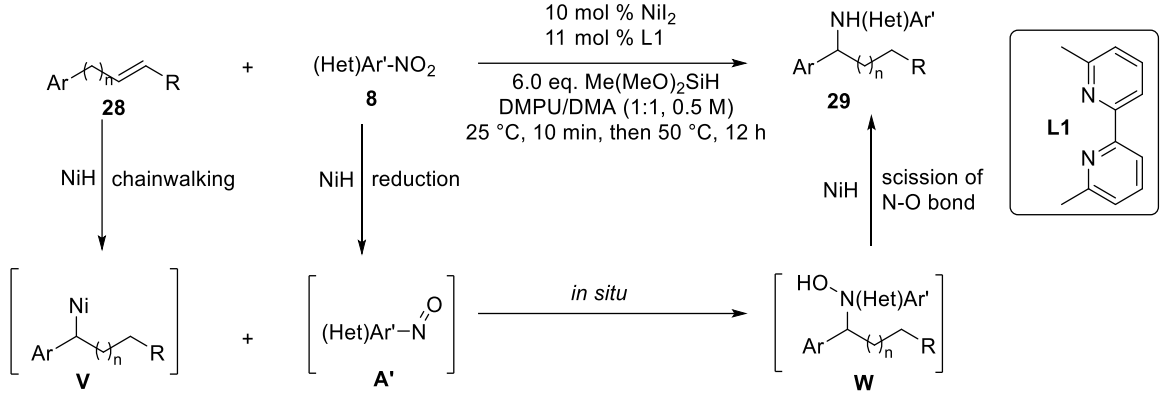
Scheme 14. C(sp^3)-H amination with nitro compounds by *Li et al.*

A photocatalyzed adaptation of this C-H amination was reported by *Pan et al.* in 2022 (Scheme 15).[19b] The presence of the photocatalyst **27** is vital and the application is restricted to specific nitro compounds **27**. The reaction follows a radical pathway and proceeds *via* a nitroso intermediate **A'**.



Scheme 15. C(sp^3)-H amination with nitro compounds by *Pan et al.*

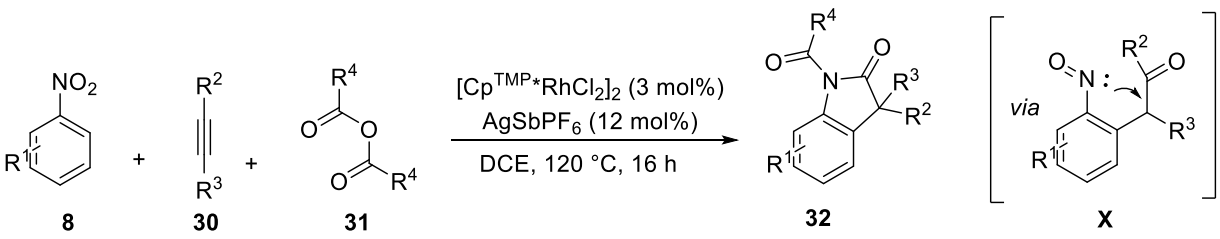
The approach of *Zhu et al.* demonstrates a remote sp^3 C-H amination of alkenes **28** with nitro compounds **8** (Scheme 16).[19c] The reaction tolerates aromatic and heteroaromatic nitro compounds, terminal, unactivated internal olefins and styrenes. The mechanistic investigations revealed that nitroarene **8** is not involved in the chainwalking step and presumable the NiH is responsible for the partial reduction of the nitro group to a nitroso species **A'**. The precise pathway for the formation of hydroxylamine intermediate **W** from the nitroso species and benzylnickel(I) intermediate **V** is not clarified, so it might possible, that it includes radical addition. The reduction of the hydroxylamine affords the desired amine products **29**.



Scheme 16. Remote C(sp^3)-H amination with nitro compounds by *Zhu et al.*

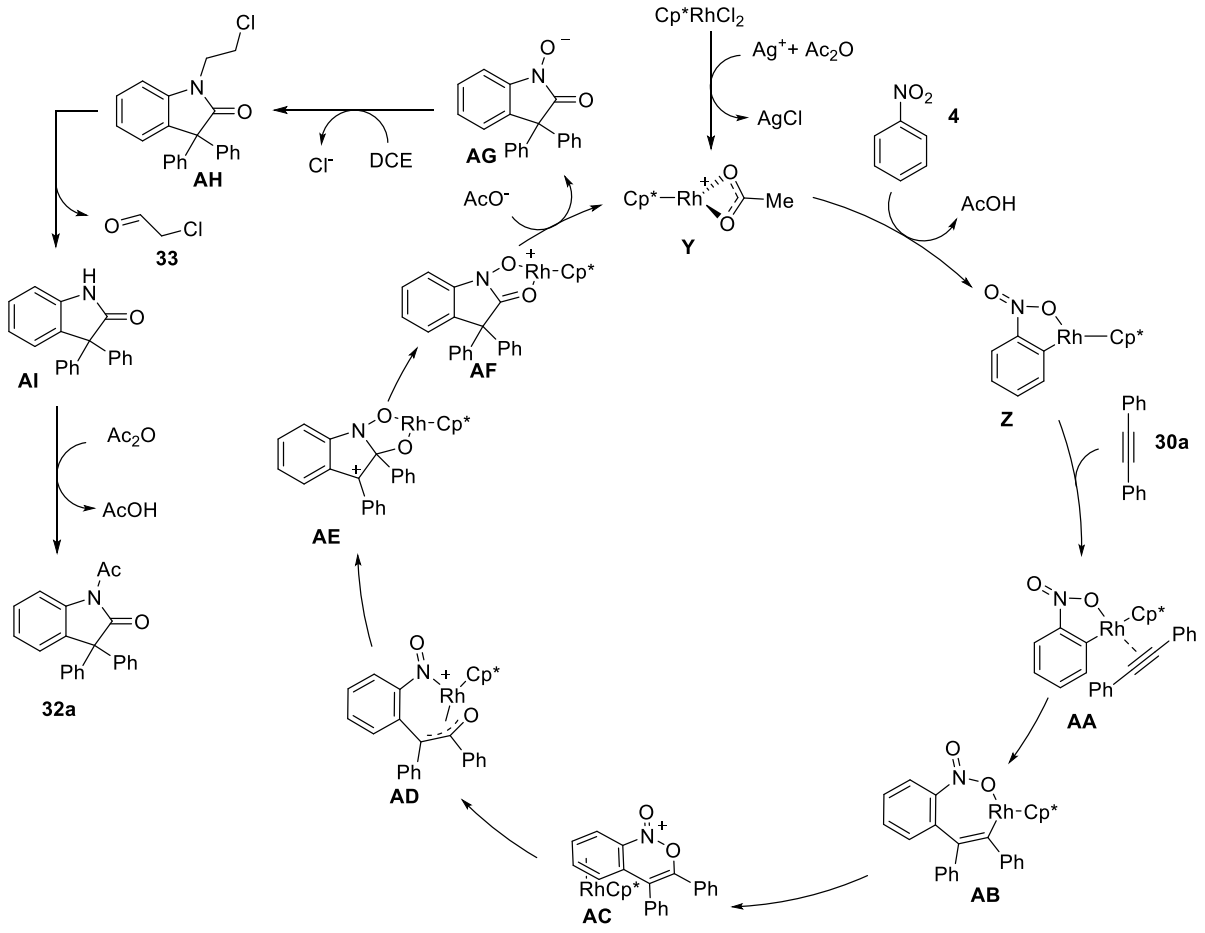
All of the presented approaches are restricted to aliphatic coupling partners and presumably involve radicals in the mechanism. However, in contrast to aliphatic radicals, aryl radicals are highly reactive with many kinds of molecules. These radicals rapidly extract hydrogen atoms from C-H bonds, add to aromatic rings and so on, and rarely carry out a single radical-molecule reaction with high chemoselectivity.[20] Instead, side reactions compete more or less effectively with the primary reaction. There is no precedent for aromatic C-H amination with nitro compounds. Based on these considerations, a non-radical aromatic C-H amination would be a breakthrough and highly beneficial.

During the writing process, a Rh(III)-catalyzed direct nitro-functionalization was reported by *Houk* and *Soulé et al.* (Scheme 17).[19d] The oxindole synthesis from nitroarenes and alkynes is a precedent for a non-radical C-H amination.



Scheme 17. Rh(III)-catalyzed oxindole synthesis form nitro compounds by *Houk* and *Soulé et al.*

Based on density functional theory (DFT) calculations, the catalytically active species is formed by the reaction of $[Cp^*RhCl_2]_2$ with Ac_2O in the presence of $AgSBF_6$. The reaction involves chloride abstraction by Ag^+ and ligand exchange (Scheme 18).



Scheme 18. Proposed mechanism of the Rh-catalyzed oxindole synthesis by *Houk* and *Soulé et al.*

In the following step, a concerted metalation deprotonation (CMP) and dissociation of acetic acid occurs, giving rise to intermediate **Z**. Subsequently, the alkyne **30a** is inserted into the Rh-C bond to form a seven-membered rhodacycle **AB**. The DFT calculations suggest that reductive elimination is followed by oxidative addition to form a Rh(III)-enolate intermediate **AD**. The oxygen atom of the nitroso species attacks the Rh, giving intermediate **AE**. A 1,2-aryl shift results in the formation of the *N*-oxido Rh(III)-complex **AF**. Finally, the active catalytic species **Y** is regenerated through ligand exchange with AcO^-. In the next step, intermediate **AG** reacts with 1,2-dichloroethane *via* nucleophilic attack to form intermediate **AH**. The desired oxindole **32a** is obtained in the final acetylation step.

Summary – Direct Nitro-Functionalization

Direct nitro-functionalization offers a step-economical and practical alternative to classical stepwise amine synthesis. The field has improved since 2015 and demonstrated growing scope of coupling partners. The developed procedures provide successful coupling between olefins, boronic acids, alkyl and aryl halides, organozinc and -magnesium compounds, and aromatic, in some cases aliphatic, nitro compounds. To broaden the applicability, boron- and phosphor-mediated processes have been reported from *our group* and *Sanz et al.* and *Csáky et al.*, respectively. These processes utilize the oxophilicity of the boron and phosphor to stabilize the reactive *N-O* bond-containing intermediates.[21] To fully analyze the activation and stabilization mechanism, further investigations are necessary.

Procedures, combining C-H functionalization with direct nitro-functionalization, are limited to aliphatic nitro compounds, possibly due to their radical reaction mechanism. A non-radical C-H amination reaction with nitro compounds would be beneficial.

The electrophilic amination, reported by *our group*, shows a new effective synthesis for aminoboranes. This process provides easy access to synthetically versatile building blocks and allows the examination of their reactivity. Especially, the direct aminoboration of C-C multiple bonds appears to be a highly attractive approach.[22]

The possibility of a stereoselective C-N bond formation starting from nitro compounds has not been investigated so far. The published methods are focused on the efficient and selective conversion of the nitro compound, especially on the control of background reactions in the reduction cascade. Therefore, no reaction concept has been reported that allows a stereoselective C-N bond formation.

General Perspectives and Aims

Direct nitro-functionalization exhibits the following considerable potential for advancements and diverse applications:

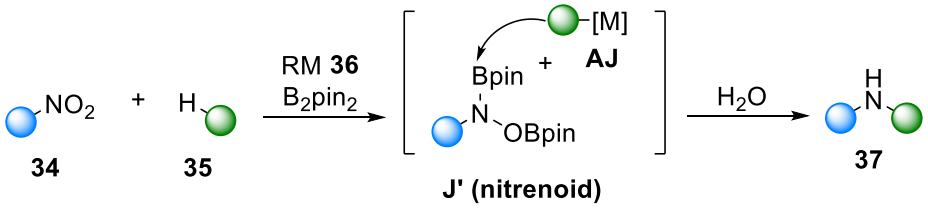
I. The reported examples for direct nitro-functionalization either follow a radical pathway or uses prefunctionalized coupling partners. A protocol for non-radical C-H amination with nitro compounds would be highly attractive. Based on the work of *our group*, a direct nitro-functionalization including a C-H functionalization step is plausible.

II. Introducing a carboamination reaction with nitro compounds presents a step-economic protocol, as hydroxylamines, commonly synthesized from nitro compounds, serve as electrophilic amination reagents. *Our* electrophilic amination approach utilizing nitro compounds employs a nitrenoid intermediate as the electrophilic amination reagent, potentially offering an alternative to hydroxylamines

III. The method developed by *our group* to easily access aminoboranes allows the study of their reactivity, especially in the direct intermolecular aminoboration of C-C multiple bonds.

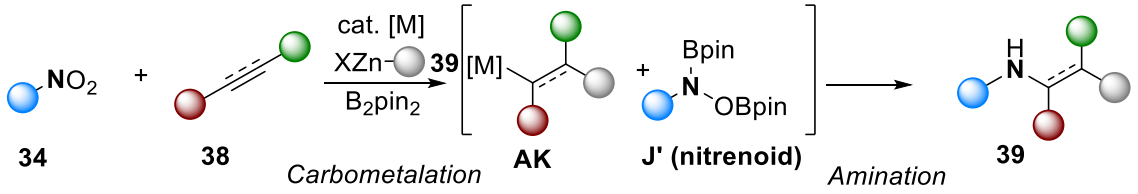
IV. The known concepts for direct nitro-functionalization do not support a stereoselective C-N coupling of nitro compounds. The first step towards such a reaction is the development of a transition metal-catalyzed process, where the catalyst controls the reaction between the partially reduced nitro group and a prochiral substrate.

The reported C-H amination reactions with nitro compounds follow a radical pathway, thereby the substrate scope is limited to aliphatic compounds.[19a,19b,19c] To broaden the spectrum of the applicability, a non-radical reaction may provide a solution. Due to the electronic properties of the nitro compound and its reduction cascade intermediates, a nucleophilic coupling partner seams ideal. According to the protocol of *our group*, nitro compounds react with nucleophilic organozinc reagents in a boron-mediated reaction.[14] However, the synthesis of organozinc compounds requires either organolithium compounds or prefunctionalized halides.[23] The widely used directed *ortho* metalation offers an alternative for the preparation of organozinc reagents.[24] To achieve selective synthesis, the presence of a directing group is vital. The coupling reaction of the nitro group with nucleophiles **AJ**, formed *via* metalation of an unactivated C-H bond, would be a highly step-economic procedure. Hence, the viability of this concept shall be examined, based on the electrophilic amination protocol of *our group* (Scheme 19).



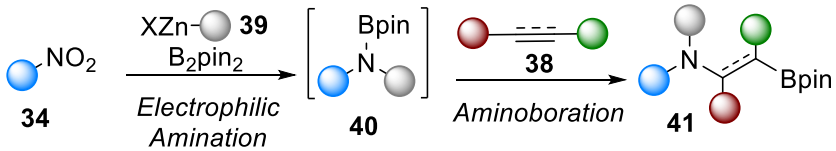
Scheme 19. Boron-mediated C-H amination with nitro compounds.

The current carboamination strategies for alkynes and alkenes involve the use of hydroxylamines as electrophilic amination reagents.[25]However, hydroxylamines are typically synthesized from nitro compounds in advance, leading to a multistep process. The development of a carboamination protocol utilizing nitro compounds would lead to a highly step-economical method (Scheme 20). Based on *our* previously reported electrophilic amination protocol, nitrenoids **J** have been identified as effective electrophilic amination reagents, capable of reacting with a wide range of organozinc compounds.[14] Given the established reactivity of nitrenoids towards organozinc compounds, the introduction of a carbozincation step generates alkyl- or alkenylzinc species **AK**, which may subsequently undergo amination with a nitrenoid **J**. In this work, the feasibility of a carboamination protocol with nitro compounds shall be studied.



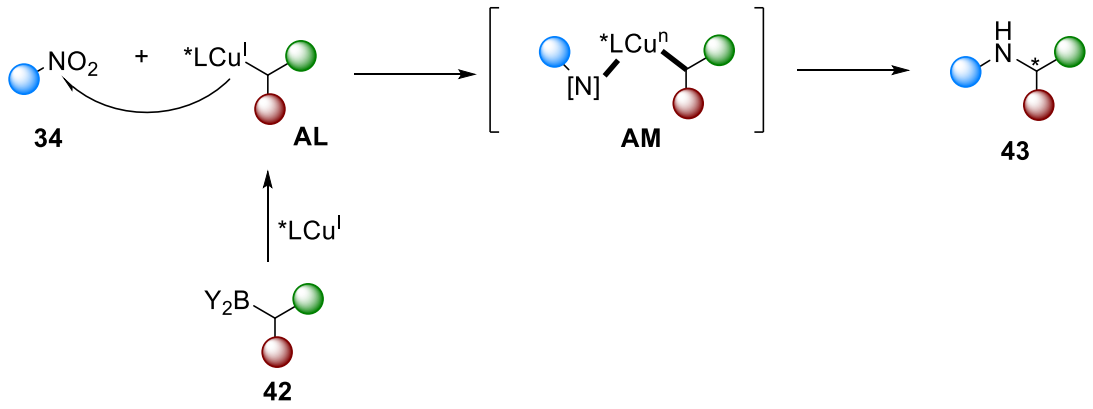
Scheme 20. Carboamination of alkynes and alkenes with nitro compounds.

Aminoboranes are versatile building blocks since they potentially enable the introduction of boron and nitrogen atom to a carbon backbone in a single step.[22] Depending on the reaction partner, they also show orthogonal reactivity to free amines.[26] Their synthetic applications have shown a restricted spectrum since the developed approaches towards aminoboranes have been limited. In particular, access to functionalized, aromatic aminoboranes has been challenging.[27] The electrophilic amination with nitro compounds developed in *our group* is also the first general synthetic method for highly functionalized aminoboranes **40**, allowing the systematic investigation of their reactivity.[14] Above all, the direct aminoboration of multiple bonds, which was first reported by *Blum et al.* is a promising field of application.[22a] The one-step introduction of an amino and a boron moiety to a carbon skeleton for the synthesis of highly functionalized compounds starting from nitro group would be an enormous advancement, compared to previous multistep methods.[28] Therefore, one object of this work, to examine the feasibility of aminoboration of C-C multiple bonds using the conditions established by *our group* (Scheme 21).



Scheme 21. Intermolecular direct aminoboration of C-C multiple bond with aminoboranes.

To date, there has been no successful implementation of a **transition metal-catalyzed coupling of nitro compounds that allows for stereoselective C-N bond formation**. This is primarily due to the need for a reaction design that can induce stereoselectivity. Accordingly, either a chiral substrate and the preservation of its chiral information is necessary or ideally, a chiral catalyst (with a prochiral substrate) is available. The latter must be able to interact with an intermediate from the nitro reduction cascade and control the C-N bond formation. The known procedures are not able to induce chirality. While *Baran et al.* generate a stereocenter in the presented *N*-alkylanilines, the used catalyst might not interact with the nitroso intermediate but rather with the formed radicals, therefore no stereo information can be induced in this case.[12] *Radosevich et al.* manage to efficiently stabilize the nitroso intermediate through the catalyst and then react with the substrate. However, only boronic acids and nitromethane are suitable as coupling partners, leading to achiral products.[15] A catalyst-substrate system, where the catalyst can selectively activate the nitro group and stabilize the intermediates to provide enantiodifferential coupling between the nitro compound and another prochiral substrate, is vital.



Scheme 22. Cu-catalyzed transformation of a nitro compound with a prochiral substrate into a chiral amine.

Copper as catalyst might offer a solution for such a cross-coupling process compared to other common catalysts. C-N cross-coupling chemistry for amines (Ullmann and Chan-Lam-Evans) and oxidized nitrogen derivatives (electrophilic amination) have been extensively studied and provide an important basis for coupling with nitro compounds.[29] Additionally, copper is known for its ability to undergo SET reactions, making it capable of stepwise and controlled activation of the nitro group.[30] Complexes between oxidized nitrogen compounds and copper are also well-known.[31] Boronic acid derivatives show promise as substrates for such a process, as they efficiently transmetalate the carbon residue to the copper.[32] The boron atom may also assist the catalyst in stabilizing reactive intermediates, as previously reported by *our group*.[14] Therefore, this work aims to study a transition metal-catalyzed coupling based on the aforementioned conditions. The results may provide the basis for a future stereoselective reaction of nitro compounds as a nitrogen source (Scheme 22).

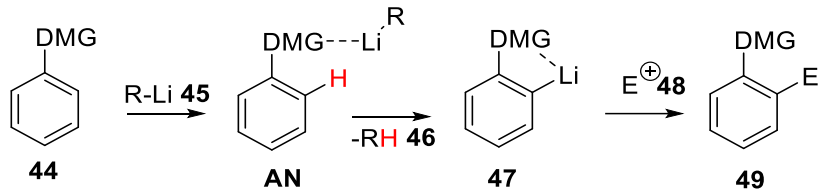
Chapter 1: C-H Amination with Nitro Compounds

Introduction: Directed *Ortho* Metalation

One of the most powerful and step-economic transformations in synthetic chemistry is C-H functionalization.[33] Although this process is known for more than 100 years, it still holds the attention of organic chemists. The first step of this transformation is a cleavage of the C-H bond, which either proceeds *via* radical reaction pathways, with a transition metal catalyst or *via* deprotonation by a strong base. In this chapter, only the deprotonative approach will be discussed.

In 1939-1940, *Gilman* and *Bebb* and *Wittig* and *Fuhrman* independently discovered the *ortho* deprotonation of anisole by ^{n}BuLi.[34] The methoxy group ensure the selective *ortho* deprotonation of anisole, providing a regioselective reaction. These pioneering results initiated the development of the directed *ortho* metalation process (DoM) and the extension to suitable substrates with direct metalation groups (DMG).[24]

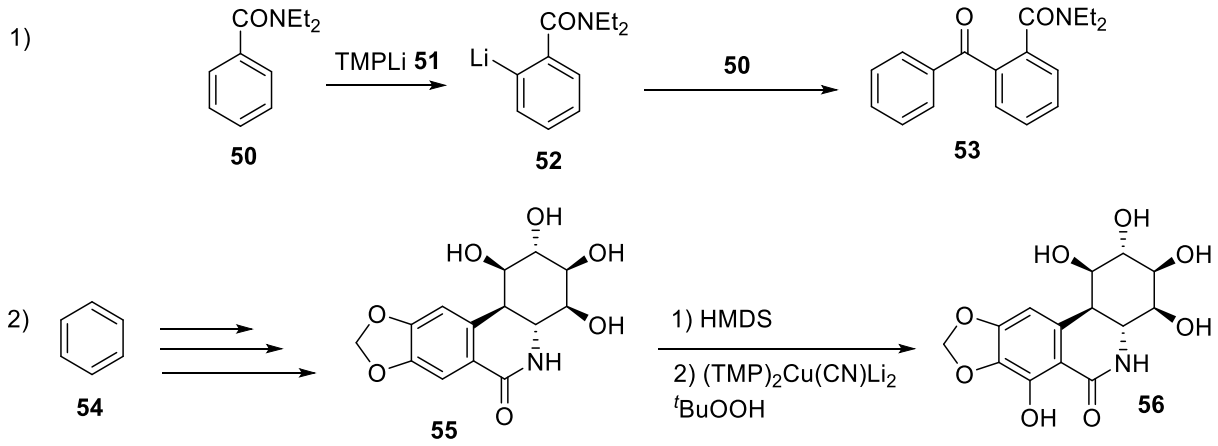
The direct metalation group is typically a Lewis basic moiety that through interaction with the lithium cation allows the selective *ortho* deprotonation (Scheme 23). The resulting organolithium species **47** can be derivatized by trapping with electrophiles **48**.[35]



Scheme 23. Directed *ortho* metalation.

The effective coordination of the alkyl-lithium species to these groups is crucial to establish a complex-induced proximity effect (CIPE).[36] At the same time, they should be poorly electrophilic so as not to react *via* nucleophilic attack by the alkyl-lithium **45**. According to the strength of this interaction, they can be differentiated as strong, moderate, and weak directing groups.

Although the widely used alkyllithium bases are strong and very versatile, they often require low temperature and are considered to be strong nucleophiles.[37] To avoid the nucleophilic addition of the base or rapid self-condensation, bulky, less nucleophilic amine bases can be used, such as TMPLi and LDA.[38] These amine bases have usually higher functional group tolerance than alkyllithium bases while retaining strong basicity.



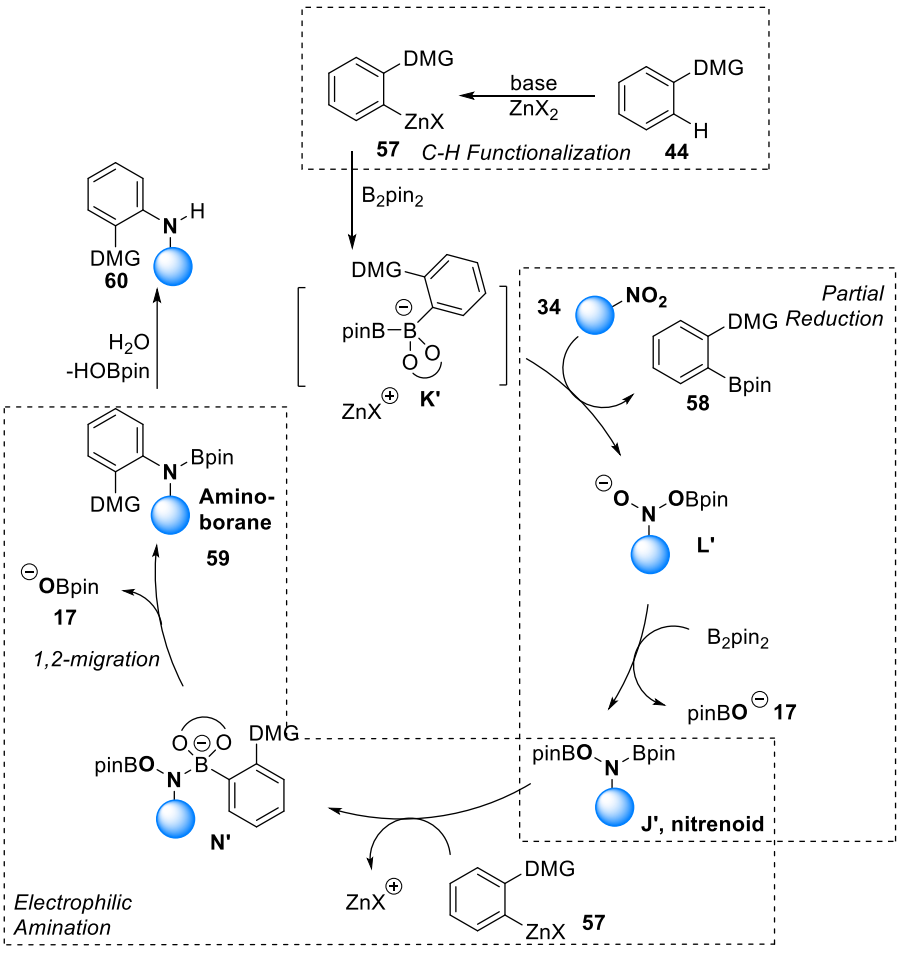
Scheme 24. 1) *ortho* deprotonation of **50** with TMPLi by *Beak et al.*; 2) Late-stage functionalization using a TMP base by *Sarlah et al.*

In the last three decades, the application of the TMP bases has been highly improved from a simple demonstration of selective deprotonation to broad applications, including even late-stage functionalization (Scheme 24).[39]

Chapter 1.1: C(sp^2)-H Amination with Nitro Compounds

Concept

The recently developed electrophilic amination reaction by *our group* allows the conversion of nitro compounds into secondary or tertiary amines with the assistance of an organozinc species.[14] The method shows broad applicability on the side of the organozinc reagent, alkyl, allyl, and even phenyl moiety can be transferred to the amine group. To utilize this process even better, expanding the method to aromatic zinc reagents would be highly beneficial. To do so, a selective synthesis of organozinc compound is required. As it was shown by *Knochel et al.*, an effective synthesis of aromatic organozinc reagent can be achieved by a deprotonation-transmetalation sequence.[40] Based on *our* previous mechanistic investigations, the following working hypothesis was introduced: the sequence starts with a selective deprotonation with a lithium base, followed by a transmetalation step with a zinc salt (Scheme 25). For the selective formation of the arylzinc species **57** the process must be supported by a direct metalation group, therefore the design of the substrate is crucial. The arylzinc reagent **57** then activates B_2pin_2, forming borate complex **K'**, generating a nucleophilic Bpin moiety. This species attacks the oxygen atom of the nitro group forming intermediate **L'**.



Scheme 25. Working hypothesis of an electrophilic C(sp^2)-H amination with nitro compounds.

The next step is an addition of a second equivalent of B_2pin_2, partially reducing intermediate **L'**, to result in the nitrenoid **J'**. The sequence continues with the addition of the organozinc species **57** to the boron center of the nitrenoid **J'** followed by 1,2-migration of the aryl moiety to afford the aminoborane **59**. The corresponding amine **60** is obtained after hydrolysis of the aminoborane **59**.

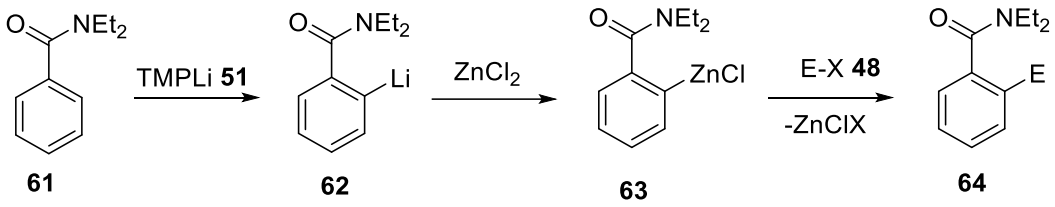
The depicted process would be the first example of a $C(sp^2)$-H amination with nitro compounds.

The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization); *Meike Niggemann* (concept); *Victor Mayerhofer* (optimization).

Results

According to the presented concept, the effective and selective formation of the organozinc reagent is crucial. To investigate the efficiency of this vital step, a test reaction must be designed. Among others, *Knochel et al.* reported a trapping reaction of organozinc compounds with electrophiles.[35] Generally, allyl halides, carbonyl compounds, and iodine are applied. To enhance selective deprotonation, substrates with strong *ortho* direct metalation group (DMG), such as amides, are considered (DMG-substrates). TMPLi was chosen as a base, due to its strong basicity and low nucleophilicity. The investigation started with the deprotonation of diethylbenzamide **61** with TMPLi **51** followed by transmetalation with $ZnCl_2$, then trapping of the organozinc compound **63** with an electrophile **48** (Table 1).

Table 1. Trapping of the organozinc species **63** with electrophiles **48**.

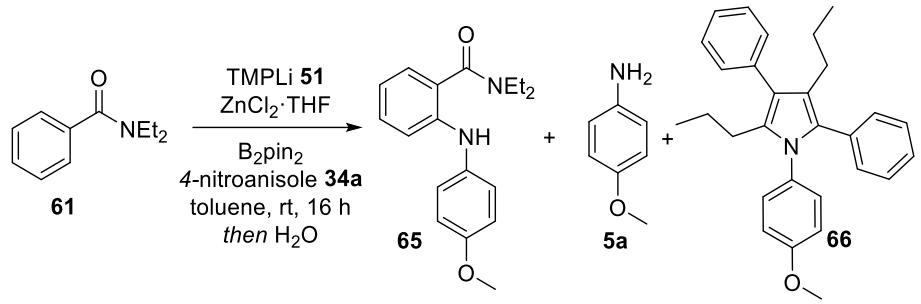


Entry	Electrophile **48**	Temperature [°C]	Time [h]	**64** [%]
1	Benzoyl chloride	-78	0.5	0
2	Iodine	-78	0.5	traces
3	Benzoyl chloride	Rt	1	0
4	Iodine	Rt	16	20

Conditions: *N,N*-diethylbenzamide **61** (0.5 mmol, 89 mg) was dissolved in THF (2 mL), $ZnCl_2$ (0.55 mL, 0.55 mmol, 1.1 eq., 1.0 M in THF) was added. The solution was cooled to -78 °C and TMPLi **51** (1.19 mL, 0.75 mmol, 1.19 mL, 1.5 eq., 0.63 M in THF) was added to the mixture. After 10 min electrophile **48** (0.5 mmol, 1.0 eq.) was added.

The trapping of the organometallic reagent with benzoyl chloride was proved to be ineffective (entries 1 and 3), while applying iodine gave only 20% iodinated product (entry 4). At this point, it was unclear whether the low yield is a result of the ineffective formation of the organometallic reagent or the limitation of the iodine reaction. Therefore, the electrophilic amination reaction with diethylbenzamide **61** was carried out with TMPLi **51** and $ZnCl_2$ in the presence of 4-nitroanisole **34a** and B_2pin_2 in toluene (Table 2).

Table 2. Optimization of C(sp^2)-H amination with 4-nitroanisole **34a**.

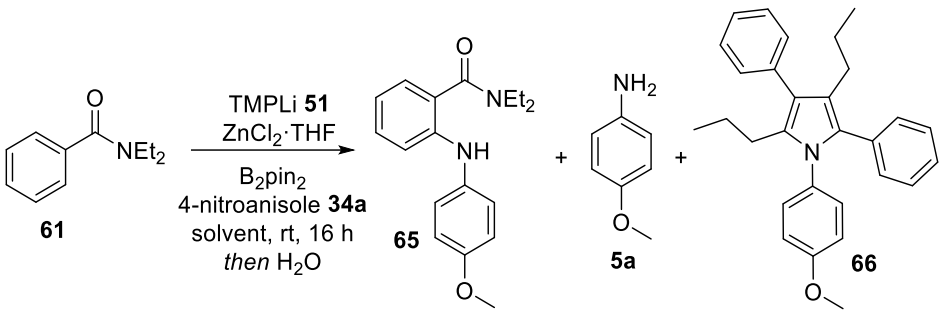


Entry	**61** [eq.]	TMPLi **51** [eq.]	$ZnCl_2$ [eq.]	Conversion [%]	**65** [%]	**5a** [%]	**66** [%]
1[a]	2.0	3.0	2.2	21	0	21	0
2	2.0	4.5	3.0	58	0	58	0
3	2.0	4.5	1.5	49	0	32	17
4	2.0	3.0	3.0	0	0	0	0
5	2.0	3.0	1.0	57	0	57	0
6	3.0	4.5	1.5	0	0	0	0
7	3.0	3.0	1.5	19	0	19	0
8	3.0	2.0	1.5	30	0	30	0
9	3.0	4.5	3.0	28	0	20	8
10[b]	1.5	3.0	2.2	17	0	17	0
11[c]	2.0	3.0	3.0	47	0	32	15

Conditions: benzamide **61** was dissolved in toluene (1 mL), $ZnCl_2$ (1.0 M in THF) was added. The solution was cooled to -78 °C and TMPLi **51** (0.63 M in THF) was added to the mixture. After 30 min 4-nitroanisole **34a** (31 mg, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added and the mixture was stirred overnight at rt; [a] THF instead of toluene; [b] DIPEA (0.4 mmol as additive); [c] Et_3N (0.4 mmol as additive). The reactions were carried out by *Victor Mayerhofer*.

In the first attempt, using 2 equivalents of diethylbenzamide **61**, 3 equivalents of TMPLi **51**, and 2.2 equivalents of $ZnCl_2$ resulted in only a 21% yield of anisidine **5a** and no desired product **65** (entry 1). Increasing the amount of the base did not significantly improve the yield, with 58% of anisidine **5a** was obtained (entry 2). Reducing the amount of $ZnCl_2$ resulted in the formation of a new side product **66**, in addition to the formation of anisidine **5a** (entry 3). Varying the TMPLi/$ZnCl_2$ ratio only resulted in slight changes in the formation of anisidine **5a**, with some cases leading to the formation of the pyrrole **66** in a yield of up to 18%. The mechanism for the formation of pyrrole **66** remains unclarified, although it is possible that the use of ^{n}BuLi in the formation of TMPLi may have an influence.

Table 3. Influence of the solvent on the C(sp^2)-H amination with 4-nitroansiole **34a**.

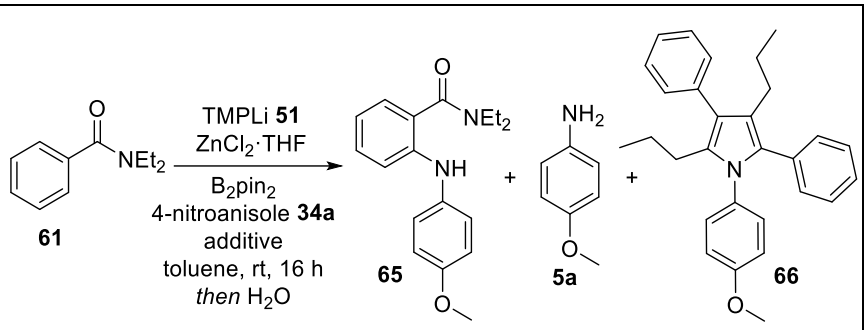


Entry	Solvent	Conversion [%]	**65** [%]	**5a** [%]	**66** [%]
1	CPME	50	0	50	0
2	DME	57	0	43	14
3	Acetonitrile	55	0	45	10
4	Et_2O	46	0	30	16
5	1,4-Dioxane	37	0	28	9

Conditions: *N,N*-diethylbenzamide **61** (71 mg, 0.4 mmol) was dissolved in solvent (1 mL), $ZnCl_2$ (1.0 M in THF, 0.3 mL, 0.3 mmol, 1.5 eq.) was added. The solution was cooled to -78 °C and TMPLi **51** (0.63 M in THF, 1.42 mL, 0.9 mmol, 4.5 eq.) was added to the mixture. After 30 min 4-nitroanisole **34a** (31 mg, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added and the mixture was stirred overnight at rt. The reactions were carried out by *Victor Mayerhofer*.

To improve the efficiency of the deprotonation and the reactivity of the organozinc compound, a variety of solvents were tested (Table 3). Due to the high basicity of the organometallic species, only aprotic solvents were tested. General solvents of deprotonation reactions, such as CPME, DME and Et_2O (entries 1,2 and 4) provided only 4-anisidine **5a** in low to moderate yield and pyrrole **66**, but no desired product. The tested acetonitrile and 1,4-dioxane were also proved unsuccessful, affording only 4-anisidine **5a** and the pyrrole **66** (entries 3 and 5).

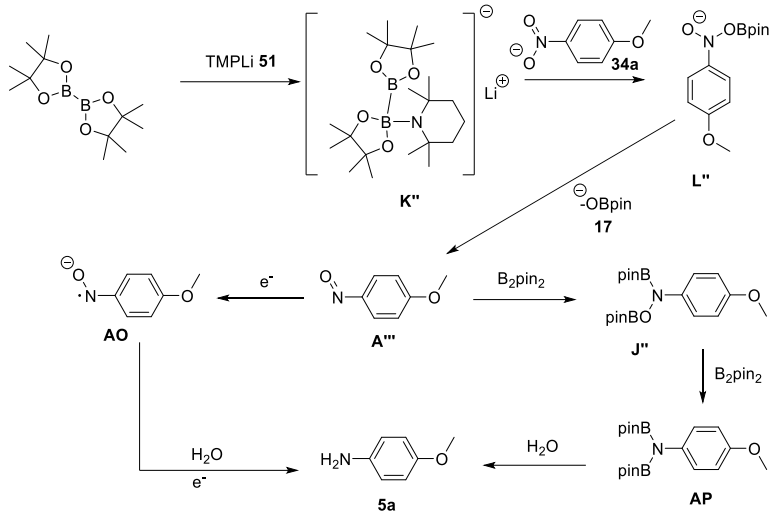
Table 4. Influence of the additives on the C(sp^2)-H amination with 4-nitroansiole **34a**.



Entry	Additive	Conversion [%]	**65** [%]	**5a** [%]	**66** [%]
1	Et_3N	58	0	43	15
2	DIPEA	55	0	39	16
3	DMAP	73	0	63	10
4	LiOMe	50	0	50	0
5[a]	DIPEA	65	0	65	0

Conditions: *N,N*-diethylbenzamide **61** (71 mg, 0.4 mmol, 0.2 eq.) and additive (0.4 mmol, 0.2 eq.) were dissolved in Et_2O (1 mL), $ZnCl_2$ (1.0 M in THF, 0.3 mL, 0.3 mmol, 1.5 eq.) was added. The solution was cooled to -78 °C and TMPLi **51** (0.63 M in THF, 1.42 mL, 0.9 mmol, 4.5 eq.) was added to the mixture. After 30 min 4-nitroanisole **34a** (31 mg, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added and the mixture was stirred overnight at rt; [a] overnight at 50 °C. The reactions were carried out *by Victor Mayerhofer*.

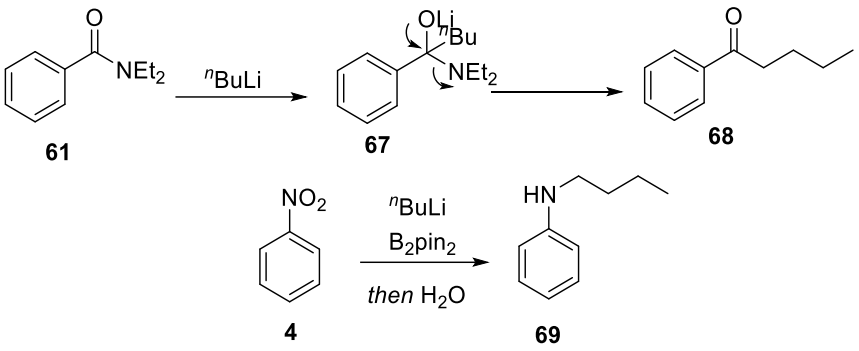
To stabilize the organozinc compound and control its reactivity, several additives were tested (Table 4). Amine bases such as Et_3N, DIPEA, and DMAP gave 4-anisidine **5a** in yields of 43-63% and the pyrrole **66** product 10-16% (entries 1-3). Using LiOMe as an additive, 4-anisidine **5a** in 50% was observed (entry 4). At higher temperature (50 °C) the reaction also favored the formation of 4-anisidine **5a** (entry 5). The used bases are capable of activating B_2pin_2 to form the borate complex **K**", which may reduce the nitro compound **34a** to 4-anisidine **5a,** as shown in Scheme 26.[41] The borate complex **K**" may generate a nucleophilic Bpin moiety, which attacks the oxygen atom of the nitro compound **34a**. The elimination of OBpin anion **17** results in the nitroso compound **A**"'. From this point, two reaction pathways are possible. One is a radical pathway, where two electrons and 1 equivalent of water can lead to 4-anisidine **5a**. In the other pathway, two equivalents of B_2pin_2 with the nitroso **A**"' form the nitrenoid **J**" first, then the diborane **AP**, which may hydrolyzes to 4-anisidine **5a**.



Scheme 26. Proposed mechanism for the formation of 4-anisidine **5a**.

The lack of product formation might have the following explanations: 1) the deprotonation of the DMG-substrate **61** is inefficient, therefore the concentration of the organozinc compound is insufficient to drive the reaction; 2) the large excess of TMPLi induces fast and effective activation of B_2pin_2, thereby reducing the nitro compound **34a** to nitroso species **A'''**, then to the diborane **AP**, resulting in 4-anisidine **5a** after aqueous work-up. In addition, the addition of the organozinc compound to the nitrenoid **J''** and the 1,2-migration of the aryl group might be slower than the reduction of the nitro compound. All in all, both assumptions lead to the conclusion that the designed system and/or substrate are not destined to achieve the desired results.

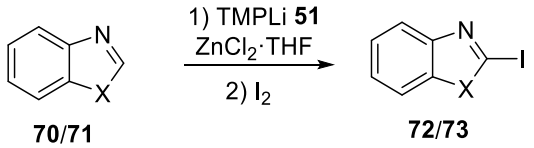
At this point, two options appeared to be adequate, either modification of the deprotonation system or replacement of the DMG-substrate **61**. To improve the efficiency of the *ortho* deprotonation on *N,N*-diethylbenzamide **61**, the substitution of TMPLi **51** with a stronger base seemed to be the straightforward option. The commercially available ^{n}BuLi, ^{sec}BuLi or ^{t}BuLi can be considered as stronger alternatives. However, these bases have increased nucleophilicity compared to TMP-bases, which may lead to undesired side reactions with the DMG-substrates, such as nucleophilic addition to the carbonyl center (forming **68**), formation of alkylated amine **69** (Scheme 27), or cyclization (yielding side product **66**) during electrophilic amination.[37]



Scheme 27. Side reactions of ^{n}BuLi with DMG-substrate or in the electrophilic amination.

These considerations suggested the change of the substrate to an aromatic compound with more acidic hydrogens. The stated criteria match perfectly with heterocyclic compounds, which are widely used in organometallic reactions.[24] These compounds also offer the advantage, that for selective deprotonation, no additional directing group is necessary (heteroatom-facilitated lithiation). For model substrates, benzoxazole **70** and benzothiazole **71** were chosen, due to their mild, selective deprotonation and easy accessibility.[42] The model substrates showed excellent efficiency in the deprotonation test reaction (Table 5. entries 1 and 2).

Table 5. Iodination of organozinc reagents from benzoxazole **70** and -thioazole **71**.



70/71 **72/73**

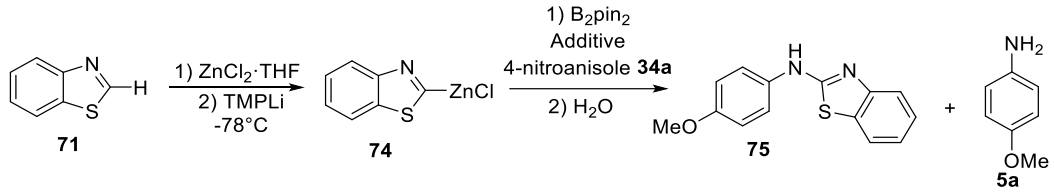
Entry	Base	Zinc salt	Conversion [%]	**72/73** [%]
X=O	TMPLi	$ZnCl_2$	100	99
X=S	TMPLi	$ZnCl_2$	84	84

Conditions: benzoxazole/benzothiazole **70/71** (0.2 mmol, 1.0 eq.) was dissolved in THF (1 mL) and the mixture was degassed three times. $ZnCl_2$ (1.0 M in THF, 0.22 mL, 0.22 mmol, 1.1 eq.) was added at -78 °C and was followed by the addition of TMPLi **51** (0.63 M in THF, 0.475 mL, 0.3 mmol, 1.5 eq.). After 30 min of stirring at -78 °C iodine (51 mg, 0.2 mmol, 1.0 eq.) in THF (0.5 mL) was added. The mixture was let to warm up to rt and was stirred overnight.

The successful trapping of the formed organozinc reagents indicated, that the low concentration of the organozinc compound can no longer be a limiting factor in the electrophilic amination reaction. The prepared organozinc compounds were treated with nitro compound **34a** and B_2pin_2 to obtain the corresponding amines (Table 6). Nevertheless, using THF and toluene as solvents not afforded the desired products (entries 1 and 2), only 4-anisidine **5a** as a side product. Increasing the amount of the organozinc species did not prove to be successful, leading to low conversion of the nitro compound **34a** to 4-anisidine **5a** (entries 3 and 4). Additives, such as LiOMe and TMEDA were inefficient in providing the desired

products (entries 5 and 7). To avoid the rapid consumption of B_2pin_2 and thereby the fast reduction of the nitro compound **34a** to aniline **5a**, the boron reagent was added over time. However, the attempt did not solve the problem, delivering 4-anisidine **5a** as the only product with 95% yield (entry 6).

Table 6. Electrophilic amination of benzothiazole **71** with 4-nitroansiole **34a**.



Entry	Solvent	Additive	Conversion [%]	**75** [%]	**5a** [%]
1	THF	-	15	0	15
2	Toluene	-	10	0	10
3[a]	THF	-	15	0	15
4[b]	THF	-	25	0	25
5	THF	LiOMe	25	0	25
6[c]	THF	-	95	0	95
7	THF	TMEDA	30	0	30
8[d]	THF	-	5	0	5
9	THF	Et_3N	5	0	5
10	THF	KO^{t}Bu	35	0	35
11	THF	NaOMe	25	0	25
12[e]	THF	-	35	0	35
13[f]	THF	-	20	0	20

Conditions: benzothiazole **71** (44 µL, 0.4 mmol, 2.0 eq.) was dissolved in the solvent (1 mL) and the mixture was degassed three times. $ZnCl_2$ (1.0 M in THF, 0.44 mL, 0.44 mmol, 2.2 eq.) was added at -78 °C and was followed by the addition of TMPLi **51** (0.63 M in THF, 0.95 mL, 0.6 mmol, 3.0 eq.). After 30 min of stirring at -78 °C 4-nitroanisole **34a** (31 mg, 0.2 mmol, 1.0 eq.), B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) and additive (0.4 mmol) were added. The mixture was let to warm up to rt and was stirred overnight; [a] 4-nitroanisole **34a** (15.5 mg, 0.1 mmol, 0.5 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 1.0 eq.) were used; [b] 4-nitroanisole **34a** (10 mg, 0.067 mmol) and B_2pin_2 (33 mg, 0.13 mmol) were used; [c] B_2pin_2 was added over 1 h, [d] $ZnCl_2$ (0.7 M in toluene, 0.6 mL, 0.44 mmol, 2.2 eq.) was used; [e] $ZnCl_2$•LiCl (1.0 M in THF, 0.44 mL, 0.44 mmol, 2.2 eq.) was used; [f] LiHMDS (1.0 M in THF, 0.6 mL, 0.6 mmol, 3.0 eq.) was used.

Using commercially available $ZnCl_2$ over the prepared solution resulted in traces of 4-anisidine **5a** (entry 8). Further additives, such as Et_3N, KO^{t}Bu and NaOMe showed no influence on the reaction (entries 9-11). To increase the solubility of the organozinc reagent, and thereby its reactivity, LiCl was added to the reaction.[43] Nevertheless, only a slight increase in the formation of 4-anisidine **5a** was observed (entry 12). Substitution of TMPLi with LiHMDS provided the same result, without any formation of the product **75** (entry 13).

Summary - C(sp^2)-H Amination with Nitro Compounds

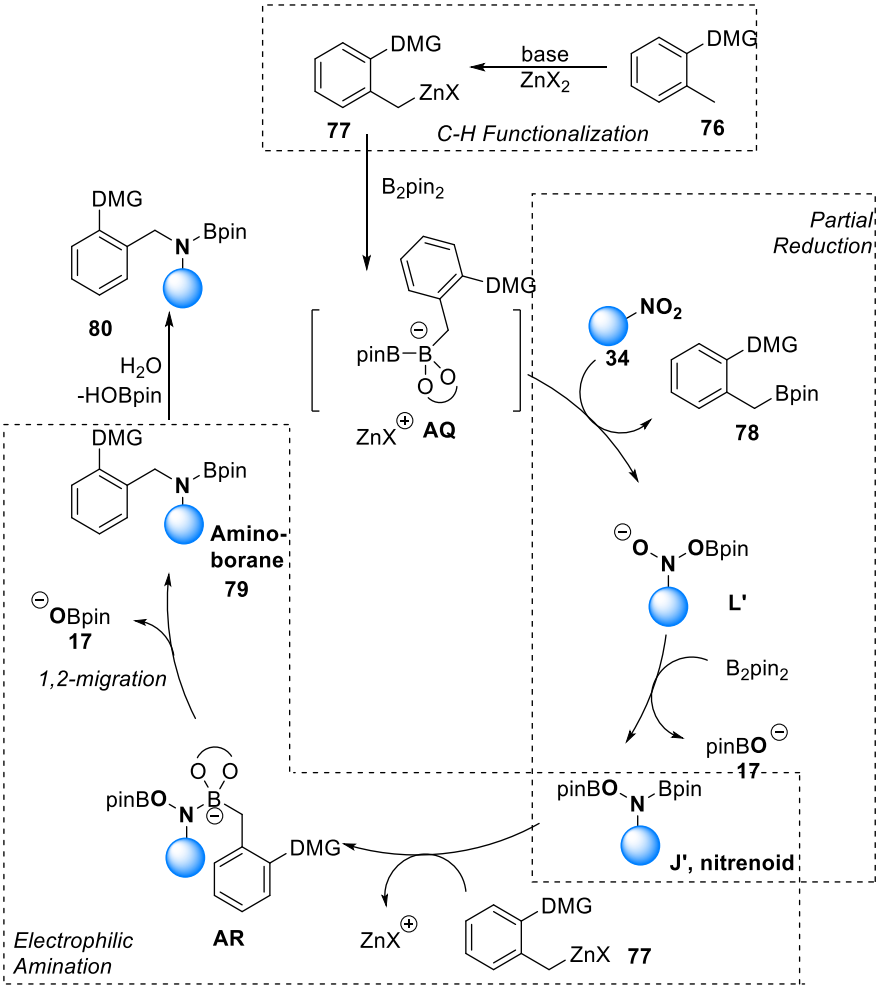
A boron-mediated C(sp^2)-H amination with nitro compounds was investigated. The organozinc coupling partners were prepared *via* deprotonation-transmetalation sequence. For the selective preparation of the organozinc species directed *ortho* metalation was utilized, using TMPLi as strong, non-nucleophilic base. C-H amination of arylzinc compounds has remained unsuccessful, delivering only 4-anisidine **5a** as a product. Presumably, the activation of the B_2pin_2 proceeds faster than the addition of the organozinc species to nitrenoid, resulting in the consumption of the nitro compound and B_2pin_2 and favoring the formation of 4-anisidine. The studied deprotonation system was proved to be efficient on benzoxazole and benzothiazole (Table 5). However, its utilization in C(sp^2)-H amination have not been accomplished since only 4-anisidine was obtained. The similar outcome may be explained with the same assumption that the reaction rate of the activation of B_2pin_2 is significantly higher than the reaction of the addition of the organozinc reagent to nitrenoid. The investigated system and the chosen model substrates may not be suitable for the development of a non-radical C(sp^2)-H amination with nitro compounds.

Chapter 1.2: C(sp^3)-H Amination with Nitro Compounds

Concept

As demonstrated earlier (Chapter 1.1), the C(sp^2)-H amination with nitro compounds has proven to be highly challenging. Nevertheless, a C(**sp^3**)-H amination with nitro compounds *via* a boron-mediated electrophilic amination would be the first precedent for such a non-radical process.

A potential mechanism follows the same pathway as shown in Scheme 25 (Chapter 1.1). The difference is the C(sp^3)-H deprotonation since the starting material **76** has an *ortho*-methyl group to the direct metalation group (DMG) (Scheme 28). The protocol may afford benzylic amines **80** after the hydrolysis of the aminoboranes **79**.



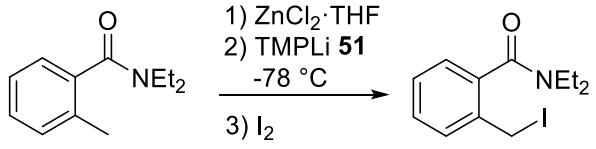
Scheme 28. Concept of a C(sp^3)-H amination with nitro compounds.

The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization); *Meike Niggemann* (concept); *Chris Inger* (scope).

Results

For the synthesis of aliphatic organometallic reagents, α-tolyl derivatives with a strong *ortho* direct metalation group were selected, due to their easy accessibility and frequent application in C-H deprotonation reactions.[24] Respectively, amides and sulfonamides were described as strong *ortho* metalation groups. The reported examples are engaging LDA and TMPLi for these substrates to complete the deprotonation. Firstly, the formation of the organozinc compound was examined. The previously used system, which indicates efficient deprotonation (Table 7), gave the iodinated product **82** in 50% yield (entry 1). By increasing the amount of the base to 2.0 eq., the formation of the iodinated product **82** increased to 60% (entry 2). Applying excess of iodine only slightly improved the yield to 65% (entries 2-4). By inverting the addition of $ZnCl_2$ and TMPLi sequence, the corresponding iodinated product **82** obtained in a yield of 95%.

Table 7. Iodination of benzamide **81**.



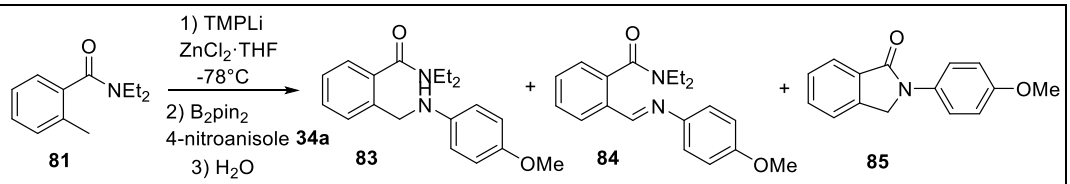
81 **82**

Entry	Base eq.	$ZnCl_2$ eq.	Iodine eq.	Conversion [%]	**82** [%]
1	1.5	1.1	1.0	50	50
2	2.0	1.5	1.0	60	60
3	2.0	1.5	1.5	65	65
4	2.0	1.5	2.0	65	65
5	2.0	1.5	4.0	65	65
6[a]	1.5	1.5	1.5	95	95

Conditions: *N*,*N*-diethyl-2-methylbenzamide (38 mg, 0.2 mmol, 1.0 eq.) was dissolved in THF (1 mL) and the mixture was degassed three times. $ZnCl_2$ (1.0 M in THF) was added at -78 °C and was followed by the addition of TMPLi (0.63 M in THF). After 30 min of stirring at -78 °C iodine was added. The mixture was let to warm up to rt and was stirred overnight; [a] TMPLi at -78 °C than $ZnCl_2$.

After the successful test of the deprotonation system, its utilization in electrophilic amination was investigated. The organozinc species was added to 4-nitroanisole **34a** in the presence of B_2pin_2 (Table 8). Based on the work of *our group*, THF was chosen as a solvent. In this case, 40% conversion was observed with the formation of the desired product **83** in 10% yield (entry 1). Changing the solvent to toluene increased the conversion of the nitro compound **34a** to 70% (entry 2). Under the reaction conditions, an imine **84** and a cyclized isoindolinone side product **85** were obtained. At increased temperature, higher conversion was observed but it changed the ratio of the desired product **83** and the side products **84** and **85** from 3:3:1 to 1:3:3.5 in THF (entry 3). When the reaction was carried out in toluene, full conversion was observed with a ratio of 1:1:1 (entry 4).

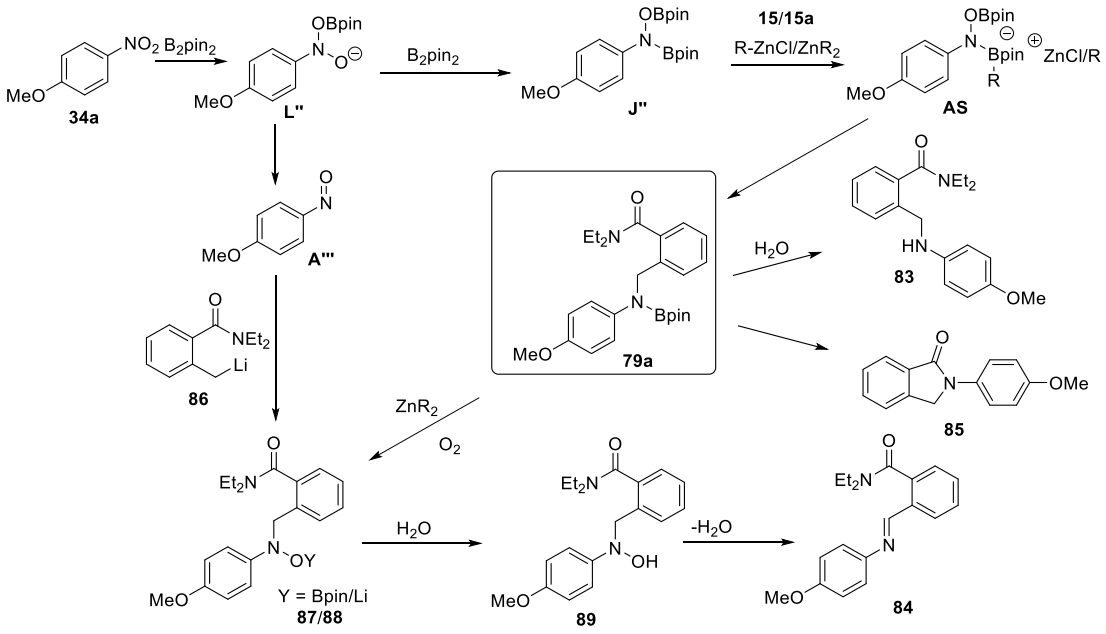
Table 8. Electrophilic amination of benzamide **81** with 4-nitroansiole **34a**.



Entry	Solvent	T [° C]	Additive	Conv. [%]	Yield [%]		
					83	**84**	**85**
1	THF	rt	-	40	10	-	30
2	toluene	rt	-	70	30	30	10
3	THF	50	-	75	10	30	35
4	toluene	50	-	100	30	35	35
5[a]	toluene	50	-	100	traces	40	60
6	toluene	50	KO^{t}Bu	65	50	-	15
7	toluene	50	NaO^{t}Bu	93	58	10	25
8	toluene	50	Et_3N	93	17	32	44
9	toluene	50	DIPEA	80	traces	30	50
10[b]	toluene	rt	-	50	50	-	-

Conditions: benzamide **81** (38 mg, 0.2 mmol, 2.0 eq.) and additive (0.2 mmol, 2.0 eq,) in solvent (0.5 mL), then TMPLi **51** (0.63 M in THF, 0.475 mL, 0.3 mmol, 3.0 eq.) at -78° C, then $ZnCl_2$ (1.0 M in THF, 0.22 mL, 0.22 mmol, 2.2 eq.). After 30 min of stirring at -78 °C 4-nitroanisole **34a** (15.5 mg, 0.1 mmol, 1.0 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 2.0 eq.) were added. The mixture was let to warm up to rt and was stirred overnight; [a] 3 eq. Zn-organyl; [b] $ZnCl_2$·LiCl (1.0 M in THF, 0.22 mL, 0.22 mmol, 2.2 eq.).

All of the observed products might originate from the aminoborane **79a** (Scheme 29). As the depicted mechanism shows, aminoborane **79a** may undergo intramolecular cyclization to form the isoindolinone **85**. For the formation of the imine **84**, two possible pathways were proposed. From borylated hydroxylamine **87**, formed by oxidation of the aminoborane **79a** by zinc peroxides, the corresponding hydroxylamine **89** is liberated during the aqueous work-up, which may provide the imine **84** after the elimination of water. An alternative mechanism proceeds *via* nitroso intermediate **A'''**, which may react with an organolithium reagent **86** that failed to transmetalate, to afford the hydroxylamine salt **88**. Its hydrolysis and the elimination of a water molecule follow the same route as the first predicted pathway.

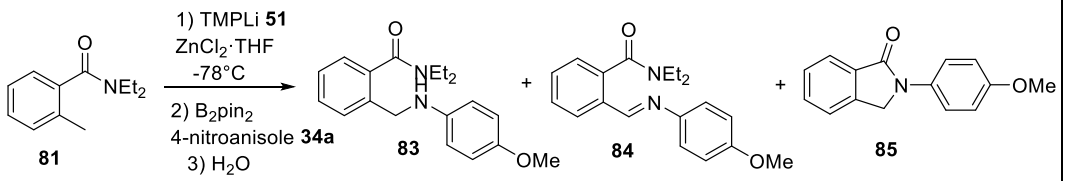


Scheme 29. Proposed pathways of the formation of isoindolinone **85** and imine **84**.

In the case of 3.0 eq. organozinc reagent, the desired product **83** was formed only in traces, shifting the ratio of the side products **84** and **85** to 2:3 (entry 5). Using KO^{t}Bu as an additive gave 50% product and 15% isoindolinone **85** (entry 6). Similar results were achieved with NaO^{t}Bu with a conversion of 93%, with 58% desired and 35% side product (**84**+**85**) formation (entry 7). Amine additives, such as Et_3N and DIPEA favored the formation of the side products **84** and **85** (entries 8 and 9). In the presence of LiCl, the desired amine **83** was obtained selectively with 50% yield (entry 10).

Based on the proposed mechanism (Scheme 29), aminoborane **79a** will be consumed to afford the side product **84** and **85**, therefore the conversion over time shall be examined (Table 9). The first sample after 120 min shows the formation of the desired product **83**, exclusively (entry 1). After 240 min, the two side products **84** and **85** appeared in traces, while the amount of the product **83** slightly increased (entry 2). The turning point occurred after 480 min, when the conversion of the aminoborane **79a** into the side products (**84** and **85**) was observed (entry 4). Running the reaction overnight resulted in 70% conversion of the nitro compound **34a** with 32% desired amine **83**, 18% imine **84** and 20% isoindolinone **85** formation (entry 5).

Table 9. Time-conversion plot of the electrophilic amination of diethyltoluamide with 4-nitroansiole.



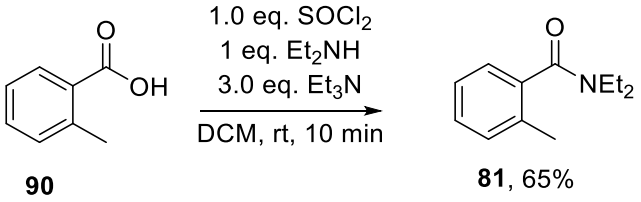
Entry	t [min]	Conversion [%]	Yield [%]		
			83	**84**	**85**
1	120	35	35	-	-
2	240	40	40	traces	traces
3	360	45	45	traces	traces
4	480	55	35	10	10
5	overnight	70	32	18	20

Conditions: benzamide **81** (38 mg, 0.3 mmol, 2.0 eq,) and additive (0.3 mmol, 2.0 eq.) in solvent (0.5 mL), then TMPLi **51** (0.63 M in THF, 0.71 mL, 0.45 mmol) at -78° C, then $ZnCl_2$ (1.0 M in THF, 0.33 mL, 0.33 mmol). After 30 min of stirring at -78 °C 4-nitroanisole (15.5 mg, 0.1 mmol) and B_2pin_2 (51 mg, 0.2 mmol) were added. The mixture was let to warm up to rt.

Synthesis of DMG-substrates

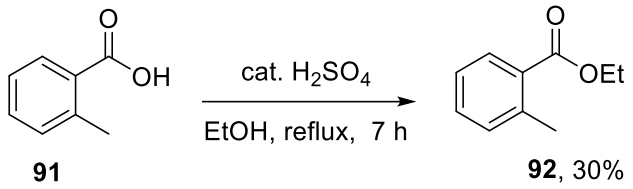
For the investigation of the synthetic utility of the reaction, several substrates were tested. The following substrates were either expensive or commercially not available, therefore they were synthesized according to the shown procedures:

Toluamide **81** was prepared by following the protocol of *Clark et al.*[44] The corresponding carboxylic acid **90** was treated with thionyl chloride and diethyl amine, using Et_3N as a base (Scheme 30). The product was obtained in 65% yield.



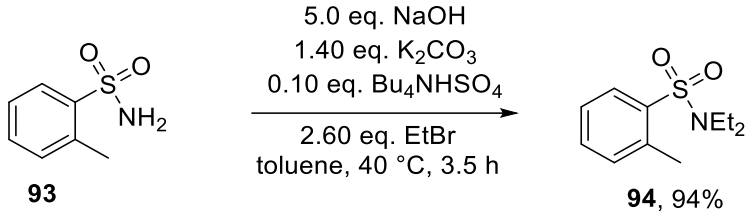
Scheme 30. Synthesis of diethyltoluamide **81** by *Clark et al.*

According to the method of *Kim et al.*, the benzoate **92** was synthesized in the presence of a catalytic amount of sulfuric acid, using ethanol as reaction partner and solvent (Scheme 31).[45]



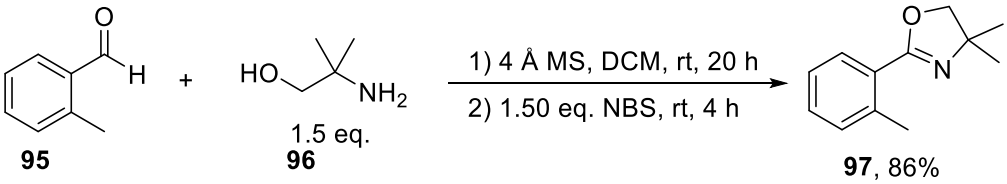
Scheme 31. Synthesis of benzoate **92** by *Kim et al.*

The procedure of *Zwerzak et al.*, using toluenesulfonamide **93** as a starting material, resulted in the sulfonamide **94** in excellent yield (Scheme 32).[46]



Scheme 32. Synthesis of diethylsulfonamide **94** by *Zwerzak et al.*

Synthesis of oxazole **97** was carried out according to *Nachstheim et al*. and the product **97** was obtained in a yield of 86% (Scheme 33).[47]

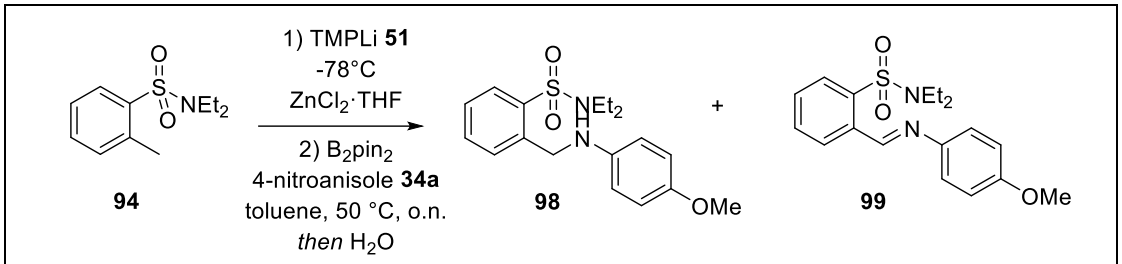


Scheme 33. Synthesis of oxazole **97** by *Nachstheim et al*.

Scope

After achieving full conversion, the applicability and selectivity of various substrates were investigated. Sulfonamide **94** afforded the desired amine **98** in 55% yield in THF while changing the solvent to toluene at 50 °C resulted in 82% yield (Table 10, entries 1 and 2). In both cases, the corresponding imine **99** side product was obtained, without any cyclization.

Table 10. Electrophilic amination of sulfonamide **94**.

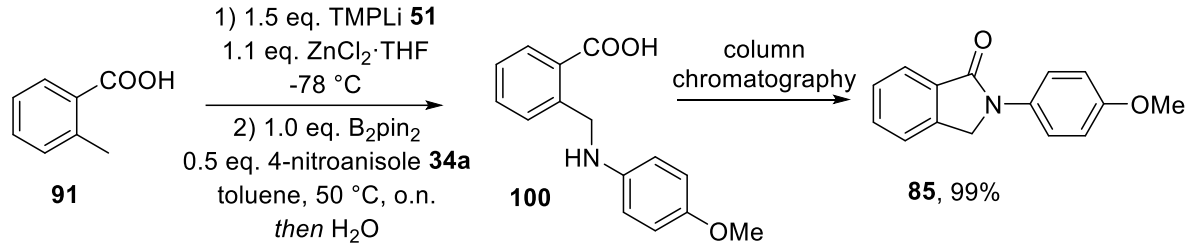


Entry	Solvent	T [°C]	Conv. [%]	Yield [%]	
				98	**99**
1	THF	RT	80	55	25
2	toluene	50	100	82	18

Conditions: sulfonamide **94** (45 mg, 0.2 mmol, 2.0 eq.) in solvent (0.5 mL), then TMPLi **51** (0.63 M in THF, 0.475 mL, 0.3 mmol, 3.0 eq.) at -78° C, then $ZnCl_2$ (1.0 M in THF, 0.22 mL, 0.22 mmol, 2.2 eq.). After 30 min of stirring at -78 °C 4-nitroanisole **34a** (15.5 mg, 0.1 mmol, 1.0 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 2.0 eq.) were added. The mixture was let to warm up to rt and was stirred overnight.

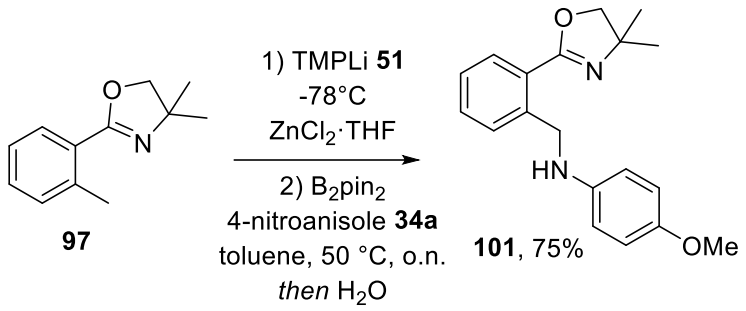
Carbonic acids usually require an increased amount of base in deprotonation reactions, due to the formation of the metal salt, nevertheless, the formed carboxylate is a strong *ortho* direct metalation group.[48] Carboxylic acids are valuable substrates for a variety of transformations.[49] This approach offers a step-economical alternative avoiding a protection-deprotection sequence.[50]

A slight excess of TMPLi proved to be efficient in the transformation of carboxylic acid **91** to the desired product **100**. Yet, after chromatographic purification, the cyclized isoindolinone **85** was obtained in quantitative yield (Scheme 34).



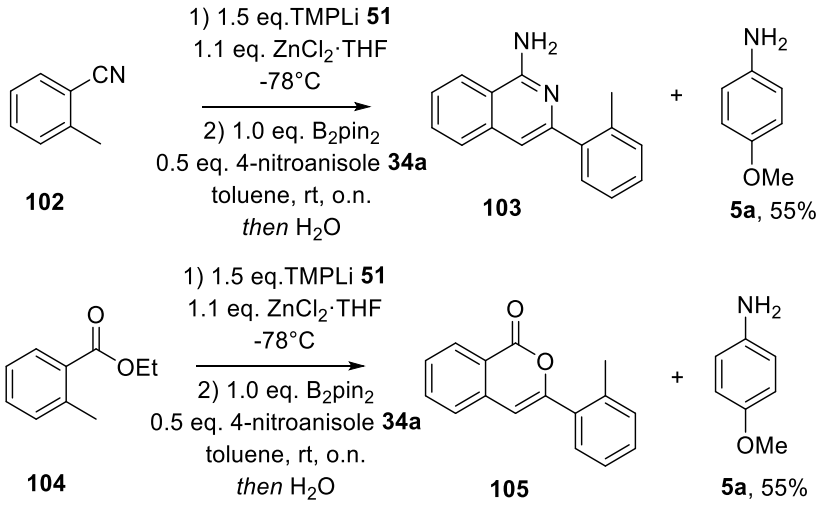
Scheme 34. C-H amination of the benzoic acid **91**.

Compounds, containing oxazoline directing groups, are suitable substrates in DoM reactions.[24] Under the optimized conditions, oxazole **97** afforded the desired product **101** in 75% yield (Scheme 35). The lack of a carbonyl center ensured the selective reaction.



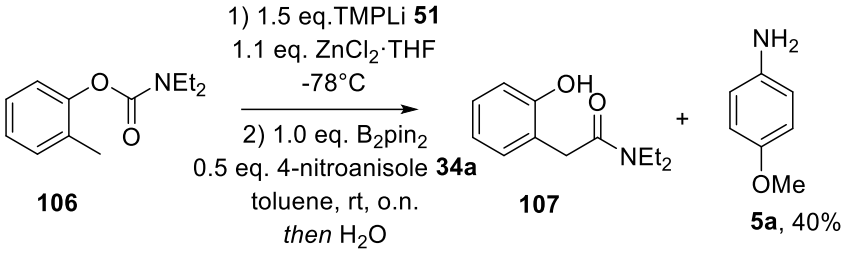
Scheme 35. C-H amination of the oxazole **97**.

Even though the nitrile moiety is considered to be a strong *ortho* direct metalation group, the electrophilic center makes these compounds challenging in organometallic reactions.[51] After the effective deprotonation, the organozinc or -lithium reagent underwent rapid dimerization at room temperature.[52] In the absence of a suitable reaction partner, only 4-anisidine **5a** was formed in the amination reaction (Scheme 36). Presumably, the reduction followed the general boron-mediated pathway (Scheme 26). A similar outcome was observed in the case of the benzoate **104**.



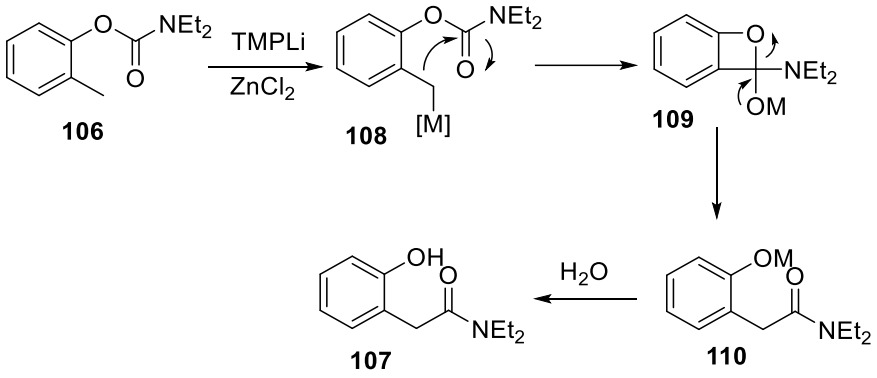
Scheme 36. C-H amination of tolunitrile **102** and benzoate **104**.

Although the carbamate group shows strong *ortho* directing ability in deprotonation reactions, several reported examples indicate its vulnerability towards rearrangement reactions.[53] Under the optimized reaction conditions, carbamate underwent anionic *ortho*-Fries rearrangement (Scheme 37).



Scheme 37. C-H amination reaction of carbamate **106**.

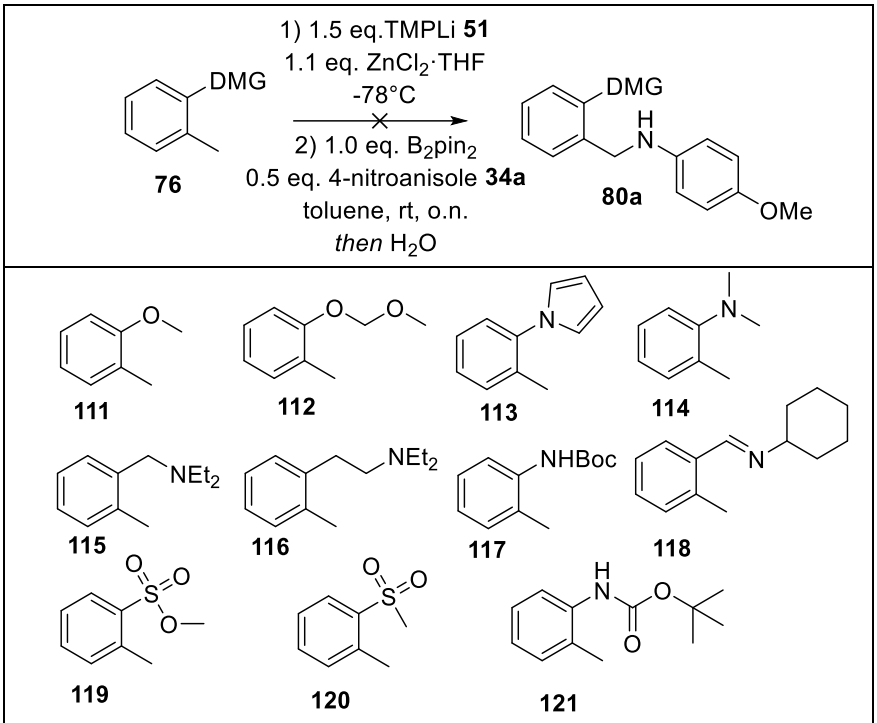
The carbamate group effectively serves as a carrier of the amide function in an anionic *ortho*-Fries rearrangement (Scheme 38). The rearrangement might proceed *via* a tetrahedral intermediate **109**, formed from the organometallic species. As reported, the intramolecular side reaction occurs at room temperature, consuming the organometallic reaction partner, and preventing the designed reaction. 4-anisidine **5a** was observed as the only product of the reaction.



Scheme 38. Anionic *ortho*-Fries rearrangement of carbamate **106**.

Further strong *ortho* direct metalation groups, such as methoxy group, MOM-protected ether, amines, pyrrole moiety, imine, sulfonate, sulfone, and carbamate group were tested under the optimized conditions (Table 11).[24]

Table II. Unsuitable substrates in C-H amination with nitro compound **34a**.



Conditions: DMG-substrate **76** in solvent (0.5 mL), then TMPLi **51** (0.63 M in THF, 0.475 mL, 0.3 mmol, 3.0 eq.) at -78° C, then $ZnCl_2$ (1.0 M in THF, 0.22 mL, 0.22 mmol, 2.2 eq.). After 30 min of stirring at -78 °C 4-nitroanisole **34a** (15.5 mg, 0.1 mmol, 1.0 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 2.0 eq.) were added. The mixture was let to warm up to rt and was stirred overnight.

Unfortunately, none of the examined substrates successfully produced the desired products. Despite the perceived strength of these *ortho* direct metalation groups, it is plausible that the deprotonation step lacked selectivity or was unsuccessful.

Summary - C(sp^3)-H Amination with Nitro Compounds

Although a non-radical C(sp^3)-H amination with nitro compounds has been successfully demonstrated, achieving broad applicability has proven to be challenging. Out of the examined DMG-substrates, only three afforded the desired products, including toluamide **81**, sulfonamide 94, and oxazole 97, with moderate to good yields (**83**, 58%; **98**, 82%; **101**, 75%).

Aminoborane **79a**, which forms from diethyltoluamide **81**, is likely the key intermediate for all observed side products, such as the imine **84** and the isoindolinone **85** (as shown in Scheme 29). Due to presumable instability of the aminoborane **79a**, the desired amine **81** was not selectively obtained. The time-conversion plot indicated that the formation of the side products (**84** and **85**) occurs simultaneously with the formation of the product **83**, resulting in only moderate yield.

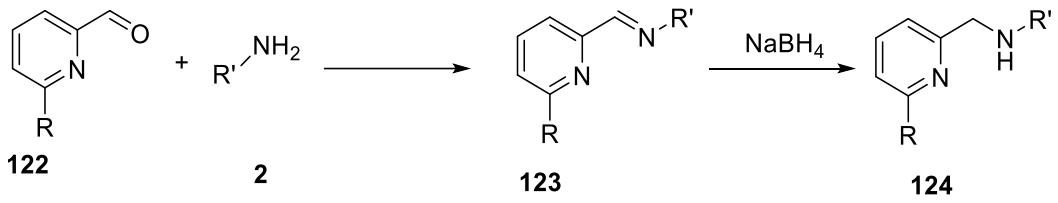
Tolunitrile **102** and benzoate **104** rapidly dimerized under the reaction conditions and failed to produce the corresponding aniline (**103** and **105**). When using diethylcarbamate **106** as a substrate, an anionic *ortho*-Fries rearrangement was observed, resulting in diethylacetamide **107** and no desired product. These observations suggest that these compounds are incompatible with the designed reaction. Furthermore, other substrates with moderate or strong direct metalation groups were unsuitable for the reaction (Table 11).

Although the established method confirms the viability of the presented concept, broad applicability has not yet been achieved. The further optimization of the deprotonation system may solve the formation of the undesired side products.

Chapter 1.3: Synthesis of Azaarylmethylamines

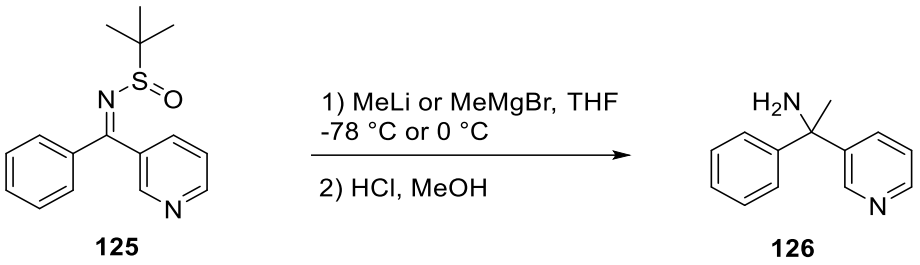
Concept

Azaarylmethylamines are ubiquitous structures in pharmaceuticals, often possessing antitumoral, antiviral, anti-HIV or antihistamine activities.[54] These compounds contain at least two nitrogen atoms, which leads to increased coordination ability, therefore they are also used as ligands and catalysts.[55] Azaarlymethylamines are usually synthesized by the reduction of aldimines.[56] Among others, *Wang et al.* synthesized azaarylmethylamines **124** *via* this pathway.[55a] According to the protocol, the azaarene with aldehyde group **122** forms the aldimine **123** with a primary amine **2**, followed by its reduction with $NaBH_4$ (Scheme 39). The reductive amination *via* imines can also be realized using other hydride reagents, late transition metal complexes and *via* transfer hydrogenation.[56a] The method limited to secondary amine products.



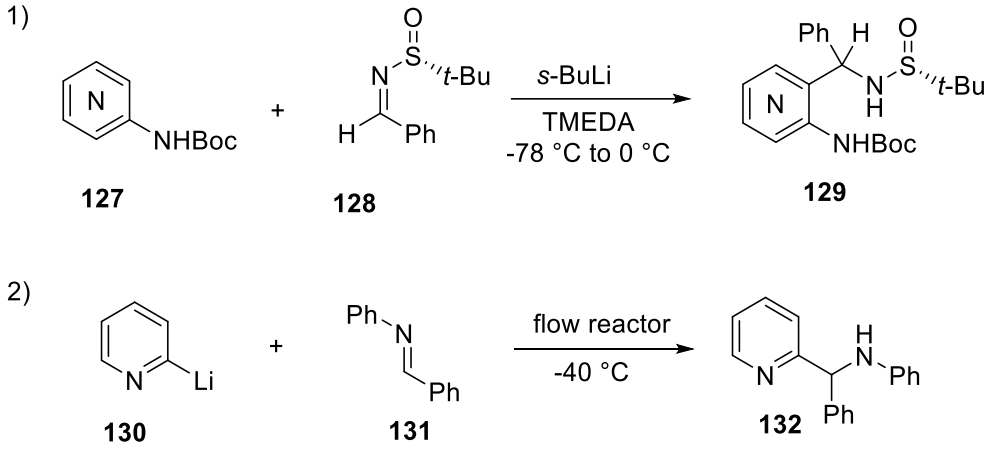
Scheme 39. Reduction of aldimines by *Wang et al.*

To overcome this limitation, several processes have been developed, such as addition of organometallic reagents to imines, which can be distinguished into two categories. When the imine already contains the azaarene moiety **125**, its benzylic position may be functionalized by organomagnesium or organolithium compounds (Scheme 40).[57]



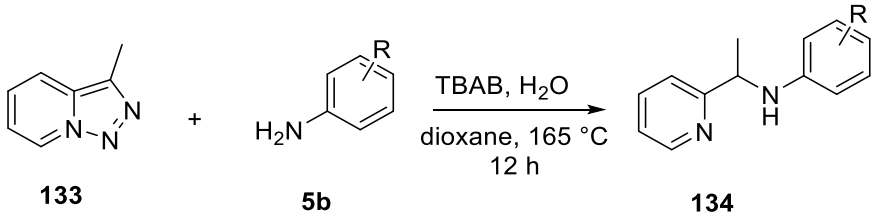
Scheme 40. Selected examples for the addition of organometallic reagent to azaaryl imine **125** by *Shaw* and *deSolms*.

In the second type, the organometallic reagent is generally prepared *via* halogen-lithium exchange or selective *ortho* metalation.[58] In both cases, the formed lithiopyridyl reagent **130** act as a nucleophile, attacking the C-N double bond (Scheme 41). Due to the presence of the highly reactive organolithium compounds, the reaction must be carried out at lower temperature, at -78 °C or -40 °C, respectively and suffers from poor functional group tolerance.



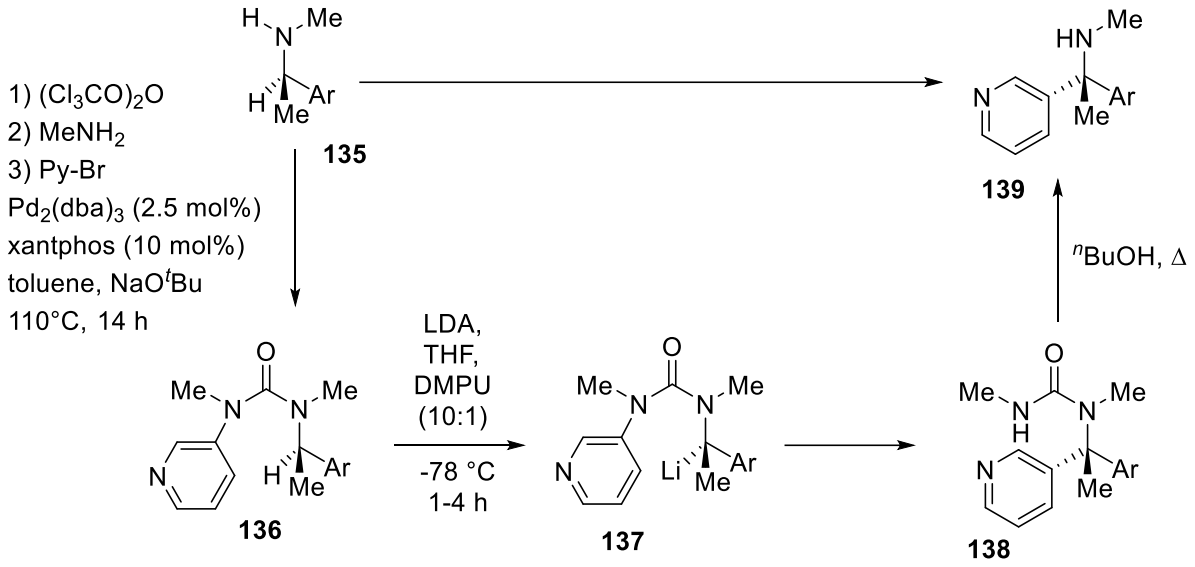
Scheme 41. Addition of lithiopyridyl reagent **130** to imines.

Hamze et al. reported a N-H insertion reaction for the synthesis of azaarlymethylamines (Scheme 42).[59] The unique pyrido-triazole starting material **133** provides a reactive carbene under the reaction conditions. Anilines **5b** are used as reaction partners to afford the desired pyridylalkylamines **134**. Despite the harsh conditions, anilines with ether-, keto-, halide- and hydroxyl group are suitable substrates yielding the corresponding azaarylmethylamines **134** in moderate to good yields.



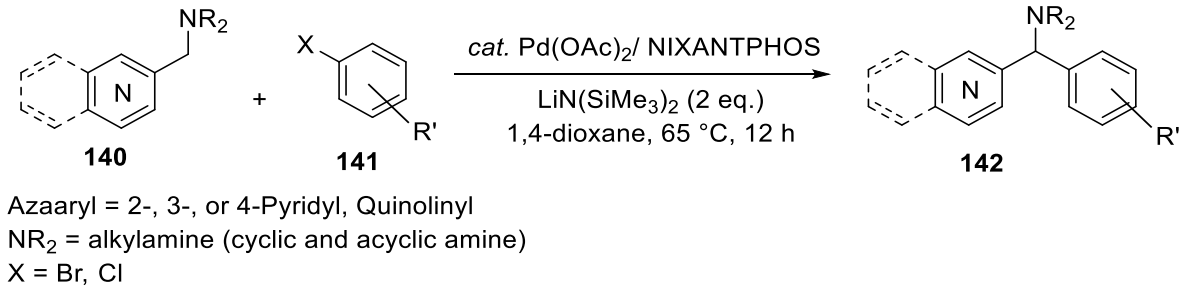
Scheme 42. Synthesis of azaarylmethylamines **134** *via* N-H insertion by *Hamze et al.*

Clayden et al. discovered a process to obtain azaarylmethylamines **139** from chiral amines **135** *via* urea coupling, lithiation and rearrangement sequence (Scheme 43).[60] The ureas **136** are synthesized by treating the amines **135** with triphosgene and subsequently methylamine, followed by palladium-catalyzed coupling. The rearrangement is promoted by with LDA and the desired products **139** are obtained by deprotection. The method shows limited applicability, since only *N*-methyl-substituted amines are suitable substrates, in addition, in some cases dearomatization product is obtained.



Scheme 43. Rearrangement reaction for the synthesis of azaarylmethylamines **139** by *Clayden et al.*

Walsh et al. utilized a deprotonative cross-coupling process (DCCP) in the synthesis of azaarylmethylamines **142** (Scheme 44).[61] In these Pd- or Ni-catalyzed reactions, premade amines **140** react with aromatic chlorides or bromides **141** in the presence of LiHMDS. The process is limited to tertiary amines since the amine function must be installed before the deprotonation reaction since a hydrogen atom of a secondary amine may react with the applied base, consuming LiHMDS or leading to undesired side reactions.

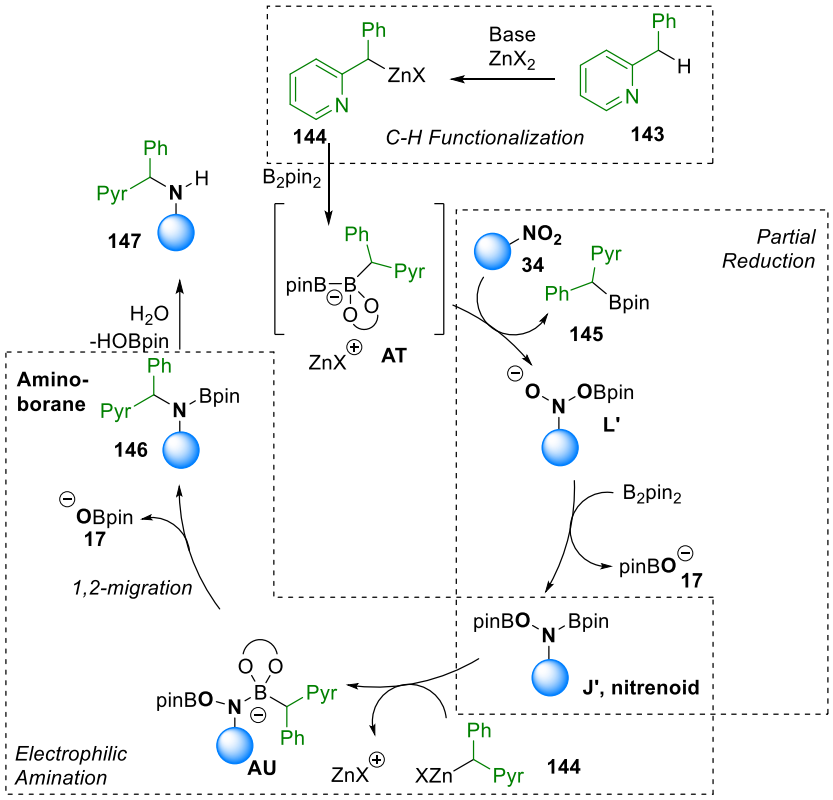


Scheme 44. Synthesis of azaarylmethylamines **142** *via* DCCP by *Walsh et al.*

The reported methodologies involve the functionalization of the benzylic position of premade azaarylmethylamines or the utilization of anilines as reaction partners. In both scenarios, the involvement of amines in the process is indispensable. Amines are commonly derived from nitro compounds due to their commercial availability, and their straightforward reduction, followed by reductive amination or cross-coupling, facilitates the generation of the desired functionalized amine.[2,3] Consequently, the development of a protocol for synthesizing azaarylmethylamines directly from nitro compounds represents an appealing alternative. To eliminate the requirement for prefunctionalized coupling partners and thereby enhancing step-economy, a C-H functionalization step emerges as a promising solution. In this context, azaarylmethanes exhibit potential as viable C-H coupling partners.

The previously reported C(sp^3)-H amination reactions, as discussed earlier (Introduction: Direct Nitro-Functionalization), have predominantly follow a radical pathway and may be insufficient for the synthesis of pyridylmethylamines, due to the side reactions of the C-H coupling partner.[20] Therefore, a novel protocol shall be devised to obtain azaarylmethylamines.

Based on the work of the *Walsh et al.*, a deprotonative cross-coupling process as C-H functionalization step might be a straightforward solution to generate nucleophilic azaarene anions.[61] Although the nitro group is considered to be electrophilic, it remains inert to most reaction conditions, due to the high oxidation state of the N-atom. Recently, *our group* developed an electrophilic amination reaction with nitro compounds, where nitro compounds were transformed into electrophilic nitrenoids, which may act as reaction partners in the designed reaction.[14] According to the working hypothesis, an organozinc compound is generated from azaarylmethanes in a deprotonation-transmetalation sequence (Scheme 45). The reaction might follow the same pathway as discussed in Chapter 1.1 to afford azaarylmethylamines.



Scheme 45. Working hypothesis on the synthesis of azaarylmethylamines **147** *via* C-H amination with nitro compounds **34**.

The transformation of nitroarenes to azarylmethylamines may combine several advantages:

1. No need for prefunctionalized reagents, like halides, triflates, boronic esters or metalorganic reagents.
2. Increased step-economy: by reducing and functionalizing the nitro moiety, the reaction provides azaarenes with amine group in a single step.

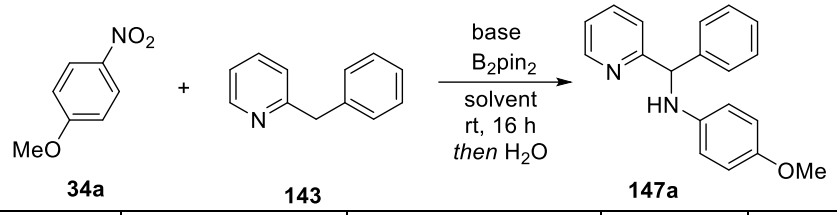
The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization, scope and mechanistic investigations), *Meike Niggemann* (concept), *Sarah Roeb* (scope).

Results

Development and Optimization of the Reaction Conditions

The azaarylmethyl anion was prepared according to the procedure of *Walsh et al.*, using 3.0 eq. KHMDS as a base in CPME.[61c] Unfortunately in the first attempt, by treating the nucleophilic coupling partner with 4-anisole **34a** and B_2pin_2 the 2-bezylpyridyl anion underwent rapid dimerization, consuming the 2-benzylpyridine **143** and providing no desired product (Scheme 46).[62]

Table 12. Optimization of the reaction parameters on the C-H amination with 4-nitroanisole **34a**.

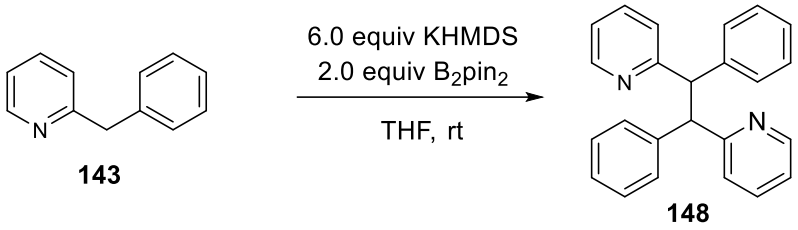


34a **143** **147a**

Entry	Base (eq.)	Zn-salt (eq.)	Solvent	Yield [%]
1	KHMDS (3)	-	CPME	0
2	KHMDS (6)	-	CPME	0
3	KHMDS (3)	$ZnCl_2$*THF (2)	CPME	20
4	**KHMDS (6)**	**$ZnCl_2$*THF (2)**	**CPME**	**95**
5	KHMDS (6)	$ZnCl_2$*THF (2)	THF	95
6	KHMDS (6)	$ZnCl_2$*THF (2)	DME	30
7	KHMDS (6)	$ZnCl_2$*THF (2)	Toluene	60
8	KHMDS (6)	$ZnCl_2$*THF (1)	THF	47
9[a]	KHMDS (6)	$ZnCl_2$*THF (2)	THF	0
10[b]	KHMDS (6)	$ZnCl_2$*THF (2)	THF	0
11	LiHMDS (6)	$ZnCl_2$*THF (2)	CPME	0
12	NaHMDS (6)	$ZnCl_2$*THF (2)	CPME	0

2-benzylpyridine **143** (0.4 mmol, 2.0 eq.) was dissolved in in the solvent (1 mL), the solution was degassed three times. Base and $ZnCl_2$ (1 M in THF) were added. The mixture was treated with nitroarene (0.2 mmol) and B_2pin_2 (0.4 mmol, 2.0 eq.) and stirred for 16 h at rt; [a] without nitroanisole **34a**; [b] without B_2pin_2

Increasing the equivalent of KHMDS to 6.0 eq. also did not provide the desired amine **147a** (Table 12, entry 2). Based on our experience, the most suitable organometallic species in *our* electrophilic amination are organozinc compounds.[14] To convert the organopotassium reagent to the corresponding organozinc species, a simple transmetalation step was inserted, treating the 2-benzylpyrdine **143** with $ZnCl_2$ after the deprotonation process. In the case of 3.0 eq. KHMDS and 2.0 eq. $ZnCl_2$, the desired amine **147a** was formed in 20% yield (entry 3).



143 **148**

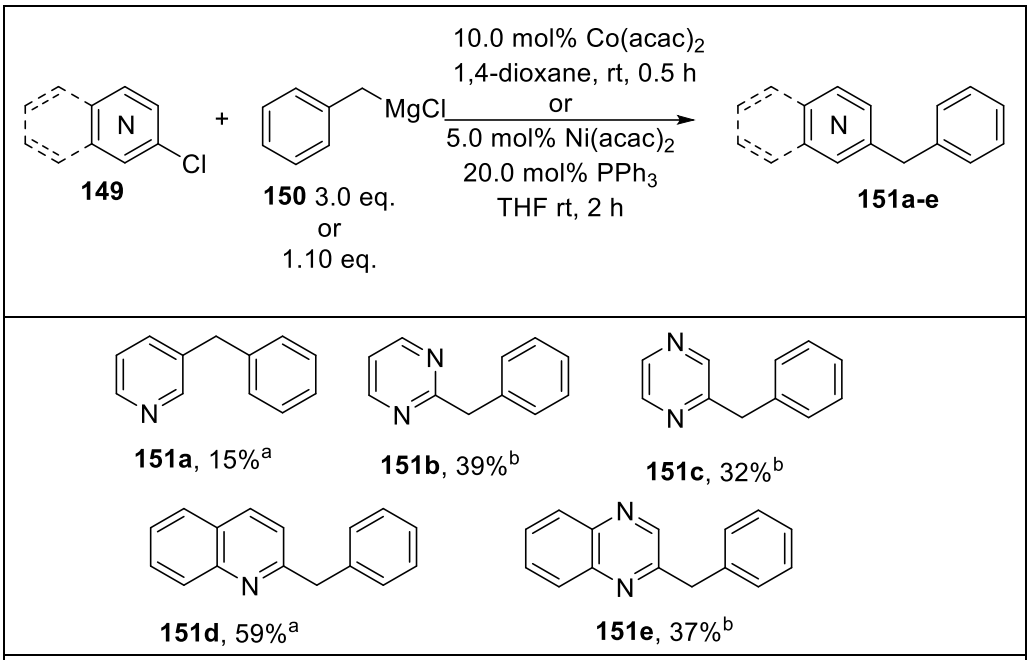
Scheme 46. Dimerization of 2-benzylpyridine **143** in the presence of KHMDS and B_2pin_2.

Using 6.0 equivalents of KHMDS in the presence of $ZnCl_2$ increased the formation of the desired product **147a**, resulting in 95% yield (entry 4). Solvents like DME and toluene produced the desired product **147a** in lower yield, while THF gave the same result as CPME (entries 5-7). Reducing the amount of $ZnCl_2$ to 1 equivalent caused a significant decrease in yield (entry 8). No product was obtained in the absence of either 4-anisole **34a** or B_2pin_2 (entries 9 and 10). Other bases, such as LiHMDS and NaHMDS, were unable to afford the desired product **147a** (entries 11 and 12).

Synthesis of Azaarylmethanes

To test the applicability of the reaction, several azaarylmethanes were tested. The commercially not available compounds were prepared according to the following procedures.

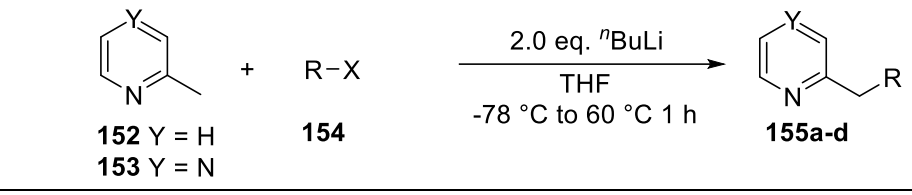
Table 13. Synthesis of azaarylmethanes **151a-e** by *Oshima et al.*

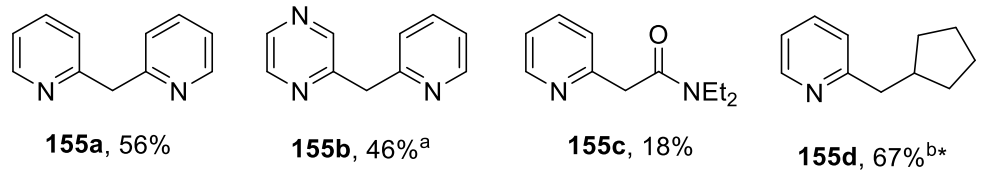


Conditions: [a] Anhydrous cobalt(II) acetylacetonate (51.4 mg, 0.2 mmol, 0.1 eq.) and heterocyclic chloride **149** (2.0 mmol, 1.0 eq.) were placed in a 25 mL flask. Anhydrous dioxane (6 mL) was added and the mixture was cooled to 0 °C. Then benzylmagnesium chloride **150** (6.0 mmol, 3.0 eq., 1.4 M in Et_2O) was added dropwise. The mixture was stirred at rt for 0.5 h. [b] Anhydrous nickel(II) acetylacetonate (128 mg, 0.5 mmol. 0.05 eq.), triphenylphosphine (520 mg, 2.0 mmol, 0.2 eq.) and heterocyclic chloride **149** (10.0 mmol, 1.0 eq.) were placed in a 50 mL flask. Anhydrous THF (20 mL) was added and the mixture was cooled to 0 °C. Then benzylmagnesium chloride 150 (11.0 mmol, 1.1 eq., 1.4 M in Et_2O) was added dropwise. The mixture was stirred at rt for 0.5 h.

The syntheses of azaarylmethanes **151a-e** were carried out according to the procedure of *Oshima et al.* The Co- or Ni-catalyzed cross-coupling reactions provided the products with low to moderate yields (15% to 59%) (Table 13).[63]

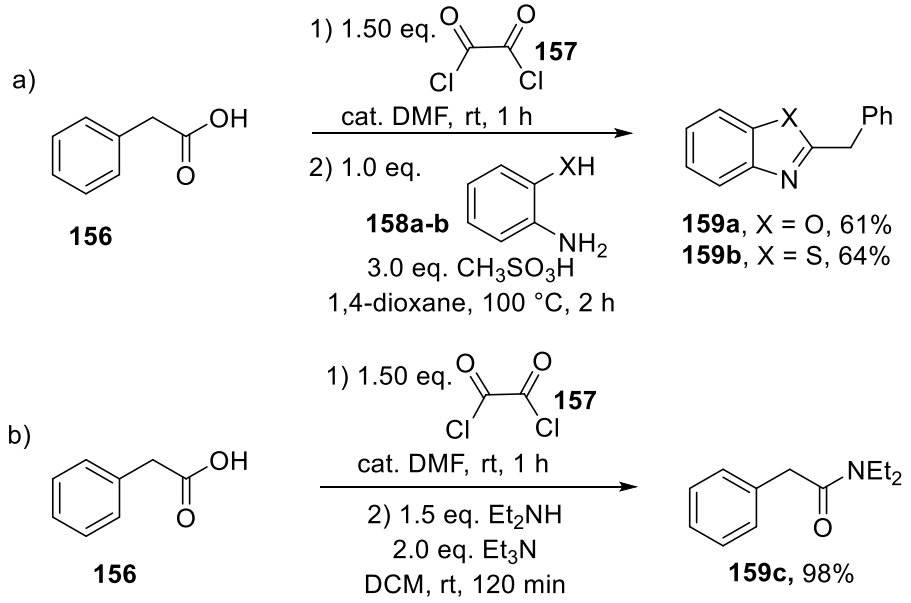
Table 14. Synthesis of azaarylmethanes **155a-d** by *Muth et al.*





Conditions: 2-methylpyridine **152** (0.99 mL, 10 mmol, 2.0 eq.) in THF (10 mL) was cooled to -78 °C, and ^{n}BuLi (6.25 mL, 10.0 mmol, 1.6 M in hexane, 2.0 eq.) was added within 15 min. The reaction mixture was stirred for 30 min at – 78 °C and let it warm up to 0 °C. The corresponding halide **154** (5.0 mmol, 1.0 eq.) was added within 5 min, and the reaction mixture was heated to reflux for 25 min and hydrolysed with ice; [a] 2-methylpyrazine **153** instead of 2-methylpyridine; [b] 1.0 eq. ^{n}BuLi and the reaction mixture was stirred at 0 °C for 2 h; The synthesis was carried out by **Sarah Roeb*.

Following the procedure of *Muth et al.*, several azarylmethanes were synthesized with pyridyl backbone (155a, 56%; 155c, 18%; 155d, 67%) and one with a pyrazine backbone **155b** (Table 14).[64] 2-methylpyridine **152** or 2-methylpyrazine **153** were treated with ^{n}BuLi, to form the corresponding α-pyridyl/pyrazyl anion. The organolithium species were treated with various halides, leading to the functionalized azaarenes with methylene bridge **155a-d**.



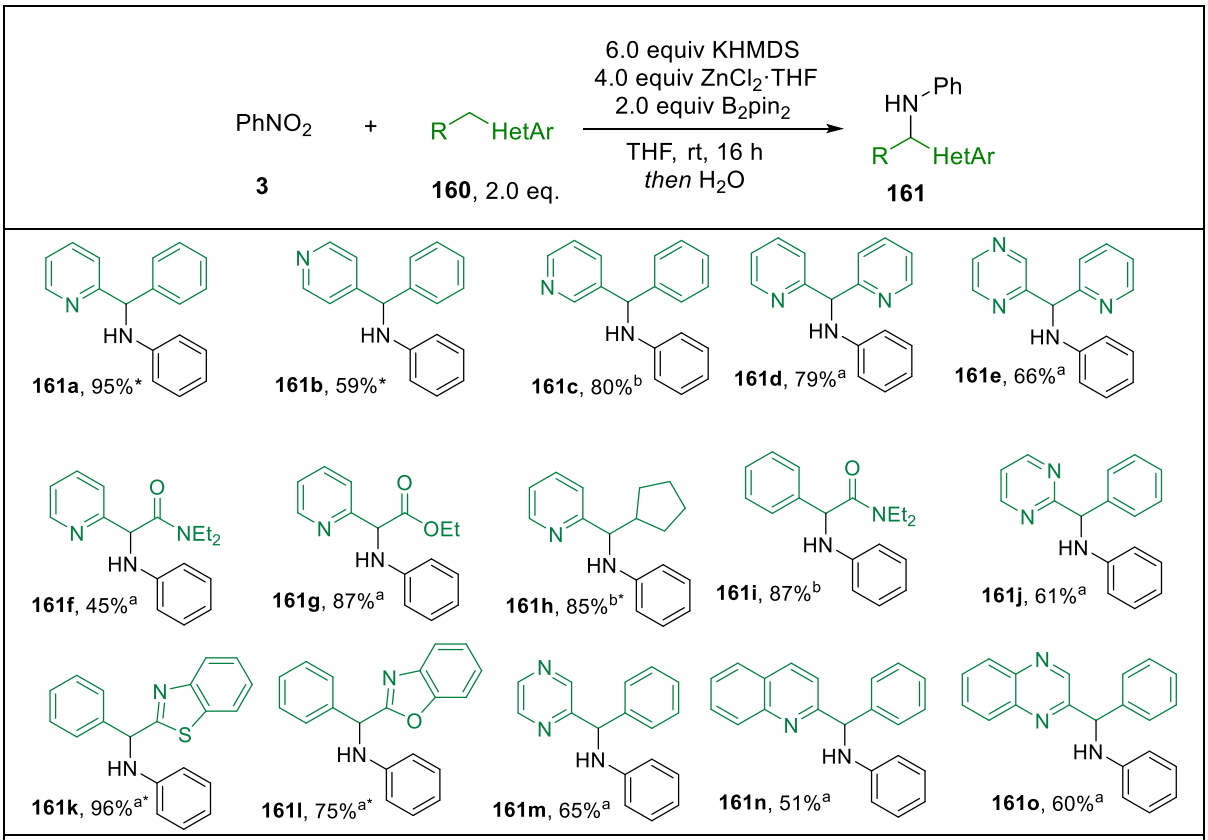
Scheme 47. a) Synthesis of azaarylmethanes **159a** and **159b** by *Chakraborti et al.*, carried out by *Sarah Roeb;* b) Synthesis of amide **159c** by *Baran et al.*

Benzyl benzoxazole **159a** and -benzothiazole **159b** were synthesized following the protocol of *Chakraborti et al.* (Scheme 47 a).[65] The corresponding acid chloride was synthesized by treating 2-phenylacetic acid **156** with oxalyl chloride **157**, then 2-amino(thio)phenol **158a**/**158b** was added to afford the desired products **159a-b**. Following the protocol of *Baran et al.*, amide **159c** was obtained by treating phenylacetic acid **156** with oxalyl chloride **157**, followed by the addition of diethylamine in the presence of triethylamine (Scheme 47 b).[66]

Investigation of the Synthetic Utility

With the optimized conditions in hand, the scope of azaarylmethanes was studied. Since THF and CMPE both provided the desired product in 95% yield, THF was chosen due to its easier accessibility and lower price (Table 15). 4-benzylpyridine afforded the corresponding amine in moderate yield (**161b**, 59%), while 3-benzylpyridine gave the desired product **161c** in 80% yield. A variety of *N*-heterocycles were suitable substrates for the reaction, such as benzoxazole (**161l**, 75%), benzothiazole (**161k**, 96%), pyrimidine (**161j**, 61%), pyrazine (**161m**, 65%), quinoline (**161n**, 51%) and quinoxaline (**161o**, 61%). Bipyridines were transformed into the corresponding amines (**161d**, 79%; **161e**, 66%) with good and moderate yields, respectively. Pyridines with amide function (**161f**, 45%), ester group (**161g**, 87%), and even a cyclopentyl derivate afforded the desired product (**161h**, 85%). The non-heterocyclic phenylacetamide was transformed under the reaction conditions in good yield (**161i**, 87%).

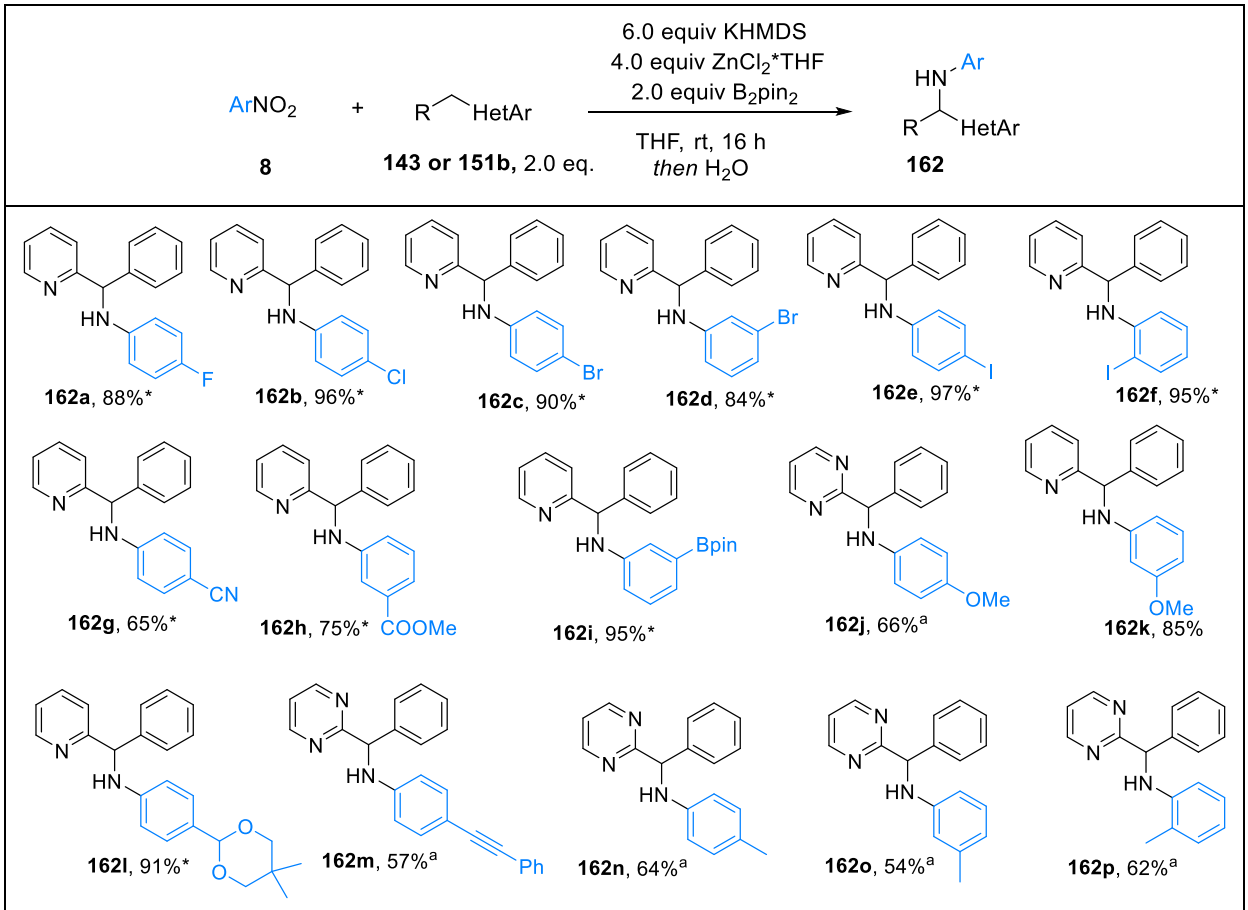
Table 15. Scope of azaarylmethanes.



Azaarylmethane **160** (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) and the mixture was degassed three times. The mixture was charged with $KN(SiMe_3)_2$ (1.7 mL, 1.2 mmol, 6.0 eq., 0.7 m in toluene) followed by $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF). After stirring for 5 min at rt, subsequently nitrobenzene **1** (20 µL, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added. The mixture was stirred at rt for 16 h, [a] $LiN(SiMe_3)_2$ (1.2 mL, 1.2 mmol, 6.0 eq. 1.0 M in THF) as base at 0 °C; [b] TMPLi (1.9 mL, 1.2 mmol, 6.0 eq., 0.63 M in THF) as base at 0 °C; the synthesis was carried out by **Sarah Roeb*

Next, the applicability of the nitro compounds was studied. Nitroaromatics bearing halide group, such as fluoride (**162a**, 88%), chloride (**162b**, 96%), bromides (**162c**, 90%; **162d**, 84%), and iodides (**162e**, 97%; **162f**, 95%) were tolerated in the reaction, resulting in good to excellent yield. Nitro compounds with nitrile (**162g**, 65%) and ester group (**162h**, 75%) were suitable substrates. Boronic esters are usually not tolerated in transition metal-catalyzed reactions, however, the developed transition metal-free approach allowed the transformation of a nitro compound with boronic ester function in excellent yield (**162i**, 95%). Nitroarenes with ether group were successfully converted into the desired amines (**162j**, 85%; **162k**, 66%). A nitro compound bearing an acetal group gave the corresponding amine in excellent yield (**162l**, 91%). Under the reaction conditions, triple bond remained untouched while affording the desired product (**162m**, 57%). Nitrotoluenes, even a relatively bulky *o*-nitrotoluene, reacted smoothly in moderate yields (**162n**, 64%; **162o**, 54%; **162m**, 62%).

Table 16. Scope of Nitroarenes.



Azaarylmethane **143** or **151b** (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) and the mixture was degassed three times. The mixture was charged with $KN(SiMe_3)_2$ (1.7 mL, 1.2 mmol, 6.0 eq., 0.7 M in toluene) followed by $ZnCl_2$ (2 equiv 1.0 M in THF). After stirring for 5 min at rt, subsequently the nitro compound (0.2 mmol) and B_2pin_2 (2 equiv) were added. The mixture was stirred at rt overnight. [a] $LiN(SiMe_3)_2$ (1.2 mL, 1.2 mmol, 6.0 eq., 1.0 M in THF).as base at 0 °C; The synthesis was carried out by **Sarah Roeb*

Mechanistic Investigation

After demonstrating the broad applicability of the reaction, $^{11}B\{^1H\}$-NMR analysis was chosen to examine the mechanism of the reaction.[14]

Analysis of boron signals in the reaction mixture

For the analysis of boron signals in the reaction mixture, the optimized reaction conditions were applied, using 2-benzylpyridine **143** and 4-nitroanisole **34a** as model substrates. 10 minutes after the addition of B_2pin_2 and 4-nitroanisole, the following spectrum was measured (Figure 1). The following boron species were identified:

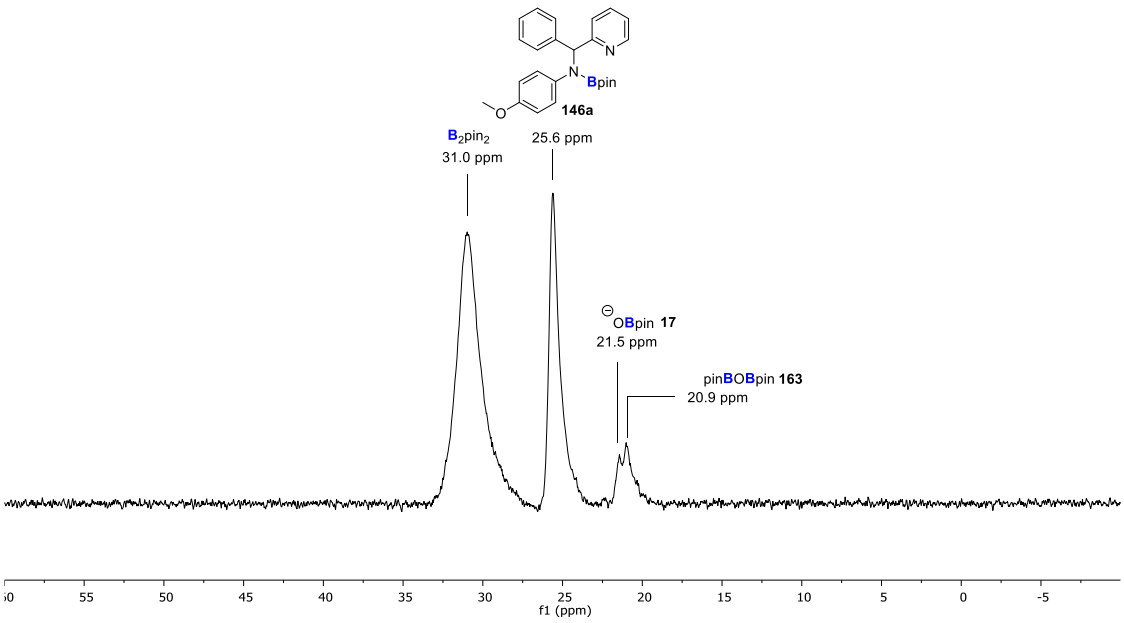


Figure 1. $^{11}B\{^1H\}$-NMR spectrum of the reaction mixture after 10 min.

δ = 31.0 ppm – B_2pin_2

The signal at δ = 31.0 ppm was assigned to B_2pin_2 in accordance with published data. All further spectra have been referenced to this signal.[67]

δ = 25.6 ppm – Aminoborane 146a

The δ = 25.6 ppm signal was assigned to the expected main product since it appears in the typical shift area of aminoboranes.[14]

δ = 20.9 ppm and 21.5 ppm – $pinBO^-$ 17 and pinBOBpin 163

The signals at δ = 20.9 ppm and 21.5 ppm indicate the formation of two pinacol bound Boron-species with an additional B-O bond. Comparison with the literature data for different RO-Bpin compounds allows the

assignment of the signal at 20.9 ppm to pinBO$^-$. The other signal (δ = 21.5 ppm) might be one of the two boron atoms of the pinBOBpin.[68]

To follow the evolution of the boronic species over time, additional spectra by $^{11}B\{^1H\}$-NMR after 30 min, 60 min, and 120 min were recorded. The superimposed spectra are shown in Figure 2.

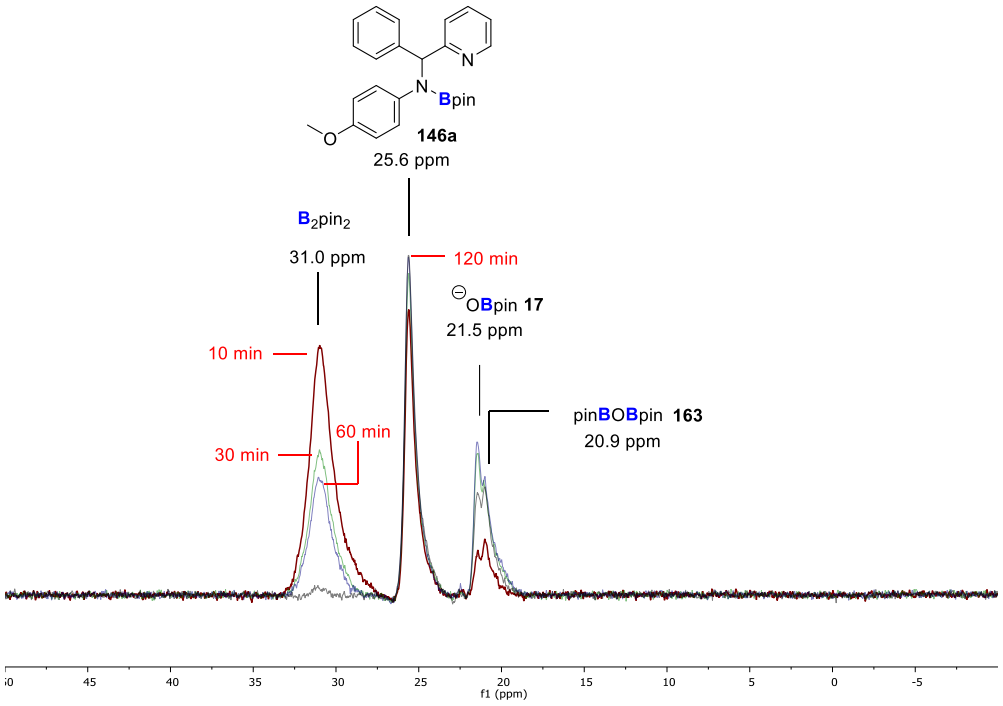
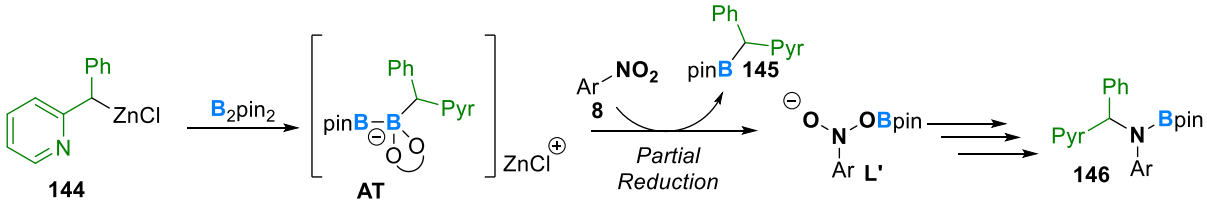


Figure 2. Superimposed $^{11}B\{^1H\}$-NMR spectrum of the reaction mixture.

The superimposed spectra reveal that aminoborane **146a**, the desired product, has already formed to about 80% after only 10 minutes, as indicated by a peak at δ = 25.6 ppm. Subsequently, the formation rate slows down but remains detectable. Meanwhile, B_2pin_2, the starting material, undergoes consumption as evidenced by a decrease in its signal at δ = 31.0 ppm, while the intensity of the pinBO anion signal at δ = 20.9 ppm increases. It is noteworthy that a borate complex **AT** between B_2pin_2 and organozinc compound, and the boronic ester **145** byproduct of the first reduction step were not detected, which contrasts with the findings of *our previous studies* (Scheme 48).[14]



Scheme 48. Formation of borate complex **AT** and boronic ester byproduct **145**.

The detection of the boron atom of a boron species in NMR spectroscopy usually depends on its solubility. A possible explanation of a missing boron signal of the borate complex **AT** is that the formed precipitation could not be analyzed by NMR spectroscopy. Since the developed protocol allows the use of LiHMDS instead of KHMDS, a slightly better soluble borate complex may form, allowing the detection of the boron atoms in the complex. To investigate this case, 2-benzylpyrimidine **151b** was chosen as model substrate since it afforded the desired product in excellent yield in the presence of LiHMDS, B_2pin_2 and nitrobenzene.

The following model reaction was carried out:

In a flame-dried Schlenk tube 2-benzylpyrimidine **151b** (64 µL, 0.4 mmol, 2 eq.) was dissolved in THF (1 mL). The mixture was treated with LiHMDS (1.2 mL, 1.2 mmol, 6 eq., 1.0 M in hexane), after short stirring nitrobenzene (21 mg, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2 eq.) were added. The reaction mixture was transferred to an NMR tube that was dried and kept under argon. The NMR tube was sealed and transferred to an NMR spectrometer.

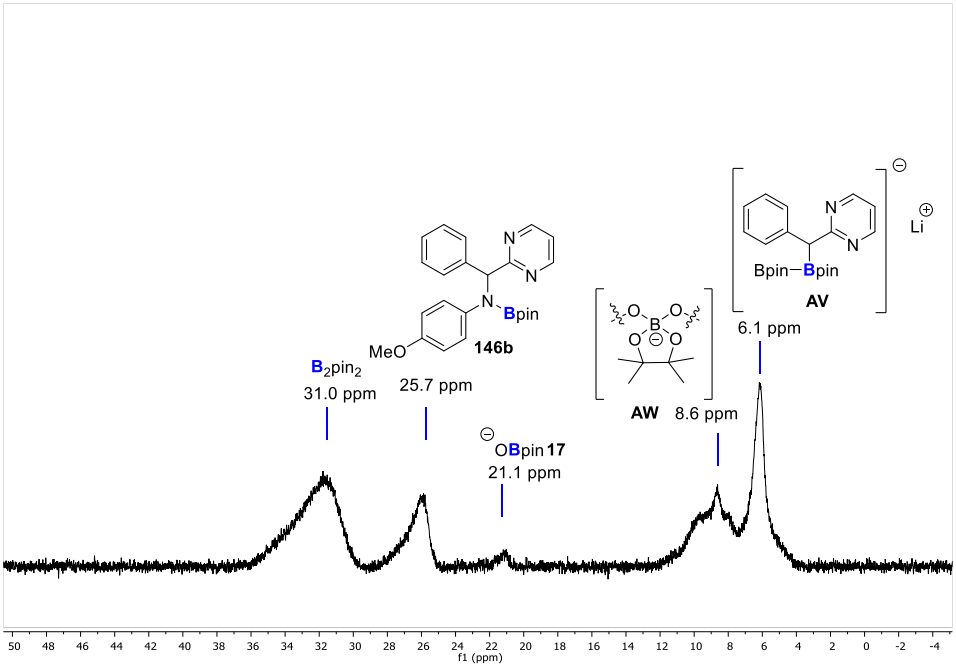


Figure 3. $^{11}B\{^1H\}$-NMR spectrum of the reaction mixture after 10 min with 2-benzylpyrimidine.

The measured $^{11}B\{^1H\}$-NMR spectrum was analyzed and the signals were assigned to the corresponding boron species (Figure 3).

δ = 31.0 ppm – B_2pin_2 and δ = 21.1 ppm – $pinBO^-$ 17

See above.

δ = 25.7 ppm – Aminoborane 146b

The δ = 25.7 ppm signal was assigned to the expected main product, since it appears in the typical shift area of aminoboranes.[14]

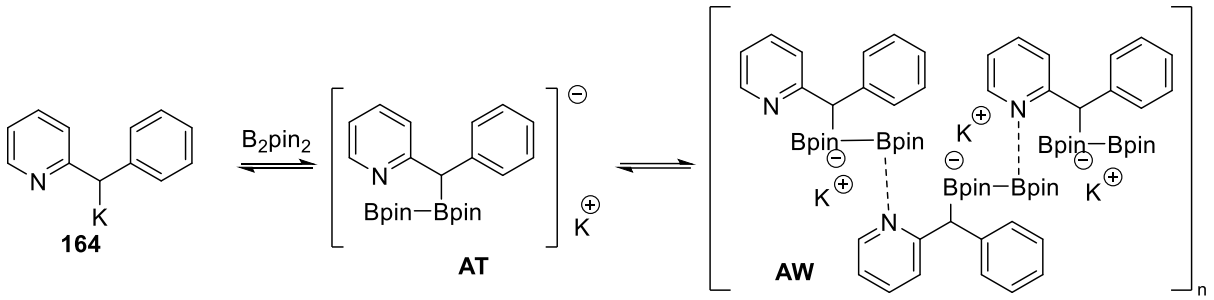
δ = 8.6 ppm – [Bpin$_2$]$^-$ AW

Comparison with the literature data, the signal at δ = 8.6 ppm possibly a decomposition product of B_2pin_2.[69]

δ = 6.1 ppm – [B$_2$pin$_2$•2-benzylpyrimidine]$^-$ AV

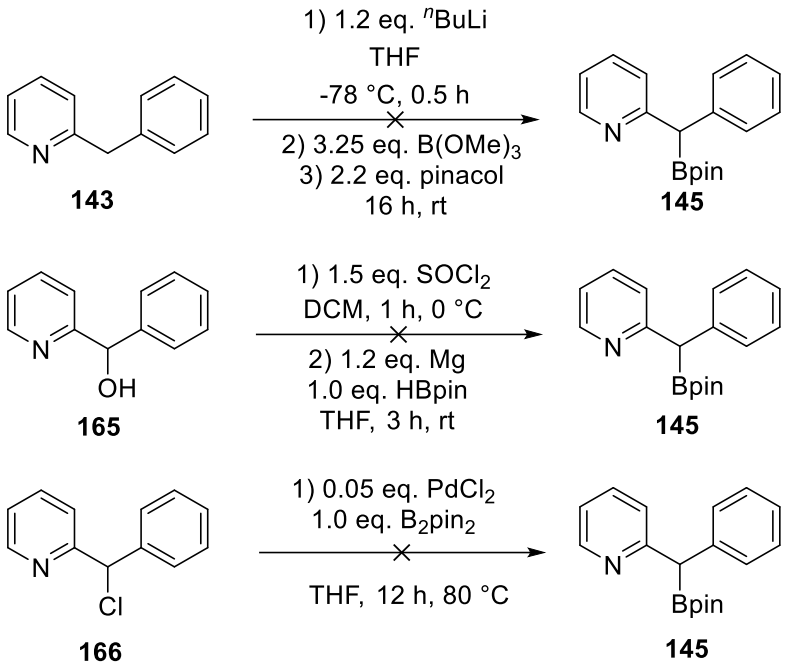
According to the proposed mechanism, in the activation step of B_2pin_2 a borate [Li][B_2pin_2•2-benzylpyrimidine] complex **AV** is generated with both sp^2-hybridized and sp^3-hybridized boron atom. By comparison with *our* previous results the signal at δ = 6.1 ppm can be assigned to the sp^3-hybridized boron atom in B_2pin_2•Bnpyd.[70] The other signal from the sp^2-hybridized boron atom should give a broader and smaller signal at δ = 30 - 35 ppm, which is probably overlapping with the signal of B_2pin_2. Based on the working hypothesis, formation of a 2-benzylpyrimidine boronic ester byproduct (similar to **145)** with a sp^2-hybridized boron atom is expected, however, no signal could be assigned to this compound (typical area δ = 35 - 40 ppm).

Comparing the NMR experiment with KHMDS and LiHDMS (Figure 1 and Figure 3), it can be assumed that the detection of the borate complex **AT** or **AV** in the ^{11}B-NMR spectrum depends on the counter cation. In the case of K^+ the borate complex **AT** is less soluble in THF or oligomerizes (Scheme 49).



Scheme 49. Possible mechanism of an oligomerization of the borate complex **AT**.

The $^{11}B\{^1H\}$-NMR analysis did not show the formation of the boronic ester byproduct **145**. To prove our assignment of the signals in the NMR spectra, several attempts were carried out to synthesize **145**. Unfortunately, every attempt failed to afford this compound (Scheme 50).



Scheme 50. Unsuccessful syntheses to obtain boronic ester **145**.

Boronic ester with a 2-pyridyl group in the α-position has not been reported in the literature. The reported boronate **167** with a 2-pyridyl group in the β-position suggests the influence of the pyridyl group on the ^{11}B-NMR shift of the Bpin moiety since the measured signal at δ = 20.2 ppm is shifted in the upfield, compared to the typical area of an sp^2-hybridized boron atom (δ = 30 - 40 ppm) (Figure 4).[71] At this stage, it was unclear whether the 2-pyridyl group caused the upfield shifting of the ^{11}B-NMR signal of the Bpin group or if the signals from B_2pin_2 obscured the signal in the typical range. If the 2-pyridyl group influenced the signal shifting, one of the two signals at δ = 20.9 ppm and 21.5 ppm might be an OBpin anion **17**, while the other signal might be the byproduct **145**. Due to the lack of evidence, the assignment of these two signals to OBpin anion **17** and pinBOBpin **163** remains more likely.

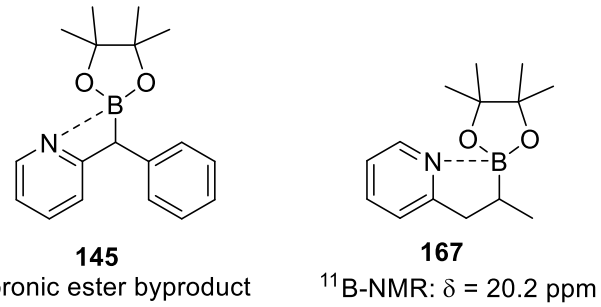


Figure 4. Possible byproduct **145** and a reported boronate **167** with 2-pyridyl group in the β-position.

Conclusions of the mechanistic investigations

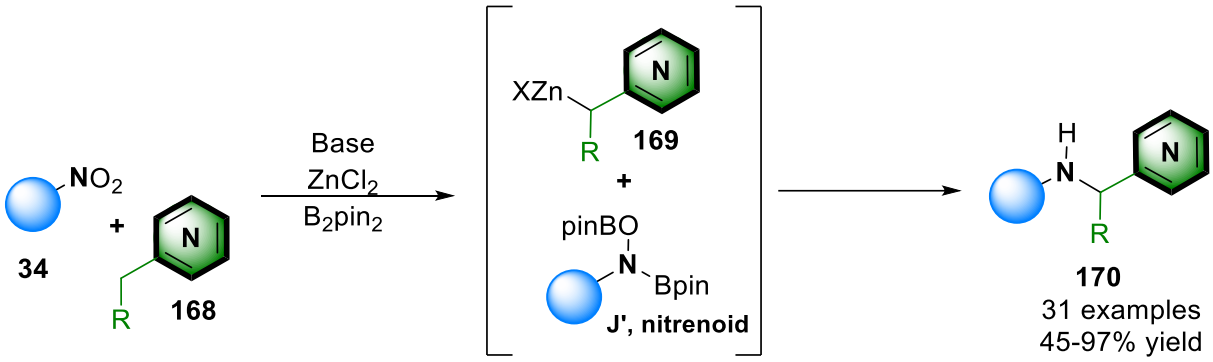
The mechanistic investigations revealed the following aspects:

1) B_2pin_2 is consumed overtime and aminoborane **146a** and OBpin anion **17** are formed.
2) Experiment with 2-benzylpyrimidine as coupling partner and LiHMDS as base showed the formation of $[B_2pin_2 \bullet 2\text{-benzylpyrimidine}]^-$ adduct **AV** while in the presence KHMDS oligomerization may occur (Scheme 49).
3) The presence of the boronic ester byproduct **145** cannot be excluded, but its ^{11}B-NMR signal could not be determined due to the lack of reported data and unsuccessful attempts at its synthesis.

Based on these studies and *our* previous investigations, the reaction mechanism presumable follows the same pathway as *our* reported works.[14]

Summary - Synthesis of Azaarylmethylamines

The reported electrophilic amination by *our group* was successfully adapted for the synthesis of azaarylmethylamines.[14] Thus, the first non-radical boron-mediated C(sp^3)-H amination with nitro compounds was developed, providing an alternative step-economical protocol to access azaarylmethylamines (Scheme 51). The reported deprotonative cross-coupling process (DCCP) by *Walsh et al.* afforded the nucleophilic azaarylmethyl anion coupling partner **169**.[61] The method showed high functional group tolerance since nitro compounds with halide-, ether-, ester-, amide-, acetal-, nitrile- and boronic ester group were suitable substrates. The reaction showed broad applicability, allowing the conversion of numerous *N*-heterocycles to the corresponding amines **170**.



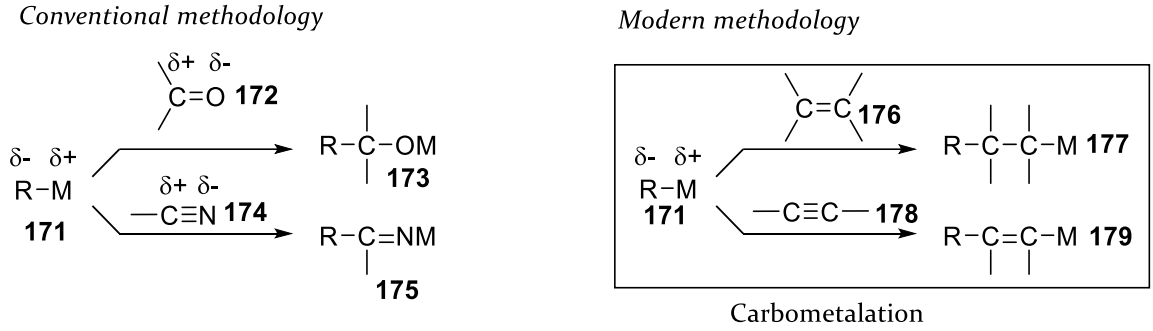
Scheme 51. Synthesis azaarylmethylamines *via* boron-mediated C-H amination with nitro compounds.

Based on the expected similarity with the previously reported approach by *our group*, the mechanism was analyzed *via* $^{11}B\{^1H\}$-NMR spectroscopy. The mechanistic investigations confirmed the formation of aminoborane and the consumption of B_2pin_2 over time while an sp^3-borate complex and OBpin anion species were formed. The $^{11}B\{^1H\}$-NMR experiments and the analogy to the electrophilic amination developed by *our group* indicate a similar reaction pathway as depicted in Scheme 45.

Chapter 2: Electrophilic Amination with Nitro Compounds *via* Carbometalation

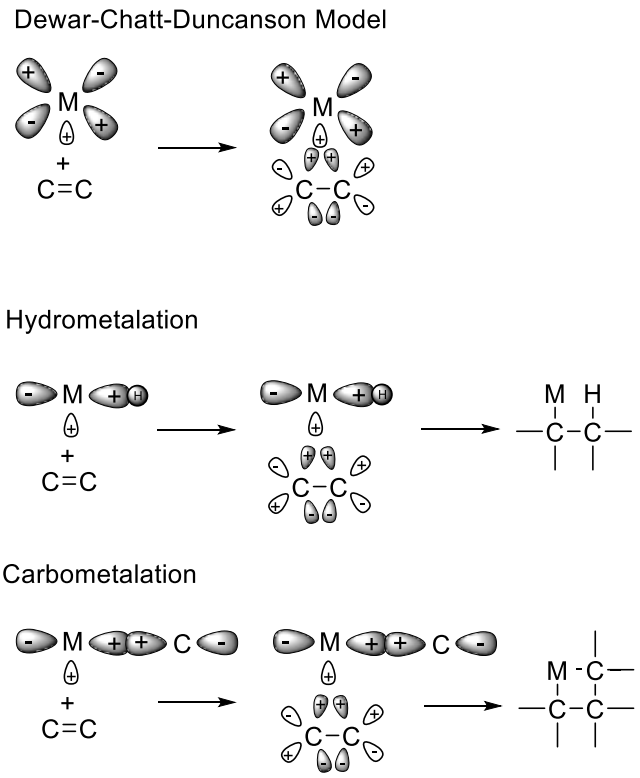
Introduction: Carbometalation

Carbometalation refers to a chemical process in which carbon-metal bonds (C-M bonds) add to carbon-carbon π-bonds.[72] The term was first suggested in 1978, earlier instances of carbometalation were mainly associated with the oligomerization and polymerization of alkenes and alkynes, which are significant in materials chemistry, but have limited use in the synthesis of fine chemicals. An example of well-controlled, single-stage carbometalation is *Normant*'s carbocupration of alkynes, which was reported in the early 1970s.[72b] Essentially, controlled carbometalation is a complementary process to the conventional organometallic C-C bond formation with polar organometals such as Li, Mg, and others, as shown in Scheme 52.



Scheme 52. Conventional and modern methodology of carbometalation.

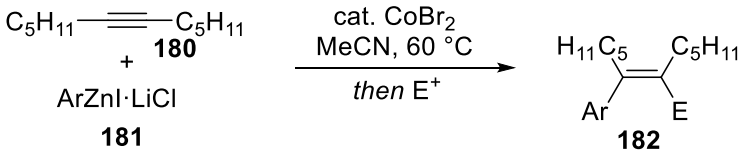
While these processes may seem similar, significant differences have been observed. Conventional reactions are primarily governed by polar processes involving polar sigma C-M and carbon-heteroatom (C-X) bonds, whereas useful and easy carbometallation reactions typically require concerted processes of non-polar π-bonds, specifically C=C and C≡C. Just as the simultaneous existence of a metal-centered empty orbital as a LUMO and a filled non-bonding orbital as a HOMO is critical in π-complexation of metals (or even carbenes, nitrenes, etc.) with π-bonds (Dewar-Chatt-Duncanson model), the concurrent availability of a metal-centered empty orbital and an H-M or a C-M σ-bond acting as a HOMO is believed to be vital for facile, concerted hydrometalation or carbometalation, respectively (Scheme 53).



Scheme 53. Dewar-Chatt-Duncanson model, hydroamination and carbometalation.

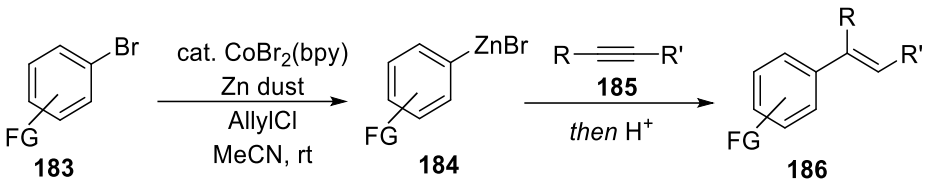
Unfortunately, the framework of this thesis is insufficient to present a comprehensive overview of this field, therefore only several examples will demonstrate the synthetic utility. Specifically, a short insight into carbozincation reaction will be shown.

Usually, carbon-carbon multiple bonds are unreactive towards organozinc reagents.[73] However, activated or strained alkenes and alkynes may react with organozinc compounds in the absence of a catalyst. In general, carbozincation reactions are catalyzed by Co, Cu, Rh, Zr, Fe or Ni.



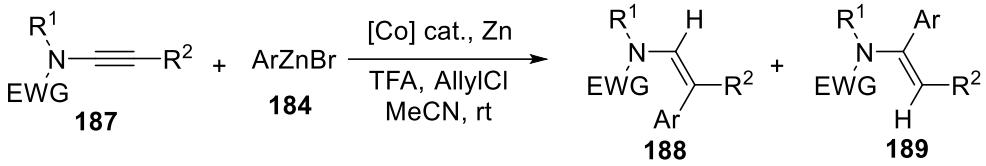
Scheme 54. Carbozincation of alkynes by *Oshima et al.*

Oshima et al. designed a cobalt-catalyzed arylzincation reaction of alkynes (Scheme 54).[74] The organozinc reagents **181** are prepared from aryl iodides in the presence of LiCl. In one hand, the used cobalt catalyst accelerates the formation of the organozinc reagent. On the other hand, after the transmetalation of the zinc to cobalt, the organocobalt species is reactive enough to add to the C-C multiple bond. The developed regioselective protocol provides multisubstituted alkenes **182** in good yields.



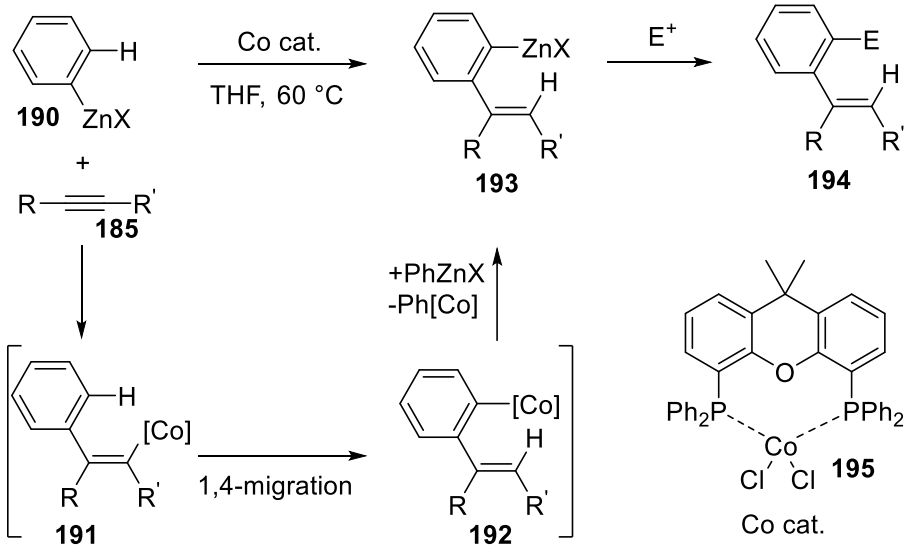
Scheme 55. Carbozincation of alkynes by *Gosmini et al.*

Gosmini et al. developed a procedure to synthesize highly-substituted styrene derivates **186** *via* a cobalt-catalysed arylzincation of alkynes **183** (Scheme 55).[74b] The organozinc reagents **184** are prepared by treating arlybromides with zinc dust in the presence of an allylchloride activator in acetonitrile.



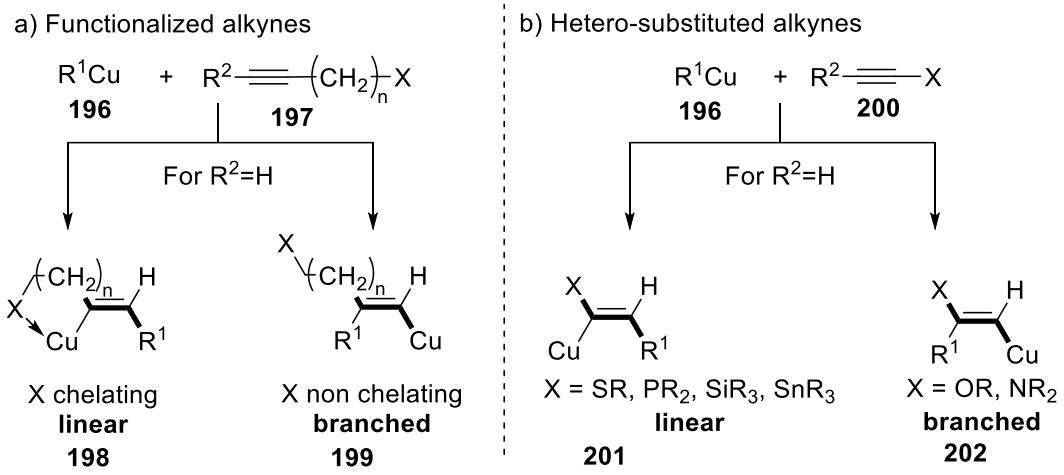
Scheme 56. Carbozincation of ynamides **187** by *Gosmini et al.*

The *same group* also reported a highly regioselective carbozincation of ynamides **187** in 2017 (Scheme 56).[74c] Despite the short reaction time and mild conditions, the yields remain moderate and the steric and electronic effects have a high influence on the selectivity.



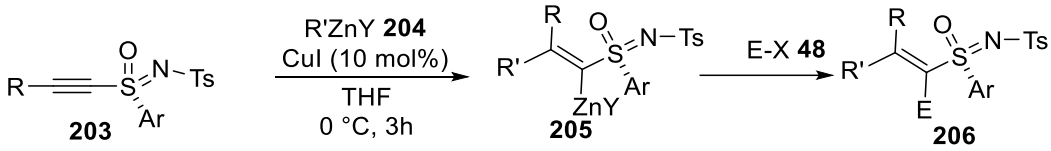
Scheme 57. Carbozincation of alkynes by *Yoshikai et al.*

According to the approach of *Yoshikai et al.*, *ortho*-alkenylaryl-zinc species **193** is obtained after the addition of an arlyzinc reagent **190** to alkynes **185** followed by 1,4-migration and cobalt-to-zinc transmetalation (Scheme 57).[74d] The combined C-C bond formation and C-H functionalization are a representation of a synthetically useful 1,2-functionalization.



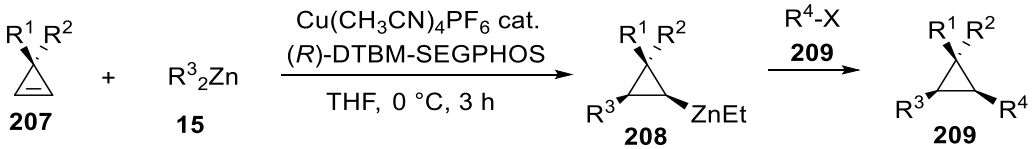
Scheme 58. Cu-catalyzed carbozincation of alkynes.

Alongside the cobalt-catalyzed processes, numerous procedures have been developed using Cu as a catalyst.[75] Although dialkylsubstituted alkynes tend to have a low reactivity towards organocopper reagents, alkynes that are mono- or disubstituted and contain heteroatoms **200** or functional groups **197** may undergo a smooth reaction.[76] Alkynes with chelating groups or hetero-substituted alkynes offer the solution to control the regioselectivity (Scheme 58).



Scheme 59. Cu-catalyzed carbozincation of alkynes by *Marek et al.*

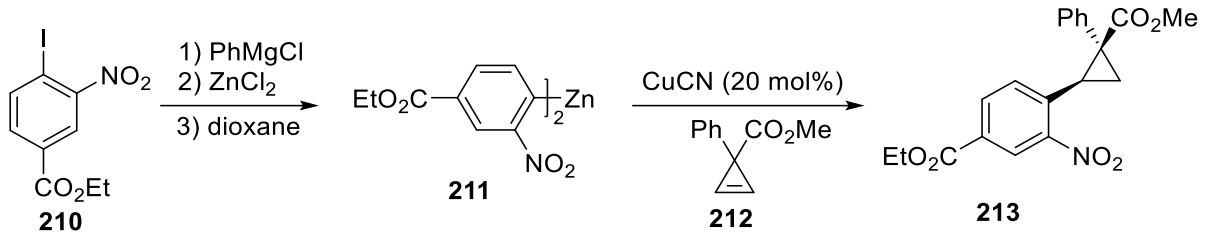
Especially attractive substrates are chiral sulfur-containing molecules, such as sulfoxides and sulfoximines, due to the opportunity to generate chiral products. Among others, *Marek et al.* synthesized chiral polysubsituted vinyl sulfoximines and sulfones as unique isomers with total regio- and stereoselectivity.[76d] After the *syn* addition of mono- or diorganozinc compounds **204**, a reaction with classical electrophiles is feasible (Scheme 59).



Scheme 60. Cu-catalyzed carbozincation of cyclopropenes by *Marek et al.*

By replacing alkynes with alkenes, the two-dimensional space (E/Z selectivity) can be translated into the three-dimensional space (formation of stereocenters).[77] Among alkenes, cyclopropenes are especially attractive motifs, due to their symmetry features and strain release-driven reactivity, and they provide cyclopropanes in regio-, diastereo- and enantioselective synthesis.[78] From the numerous procedures, two examples were chosen for the Cu-catalyzed carbozincation of cyclopropenes. *Marek et al.* developed a diastereoselective method to obtain enantioenriched and configurationally stable cyclopropylzinc species,

which can be trapped with various electrophiles to provide tetrasubstituted cyclopropanes (Scheme 60).[78a]

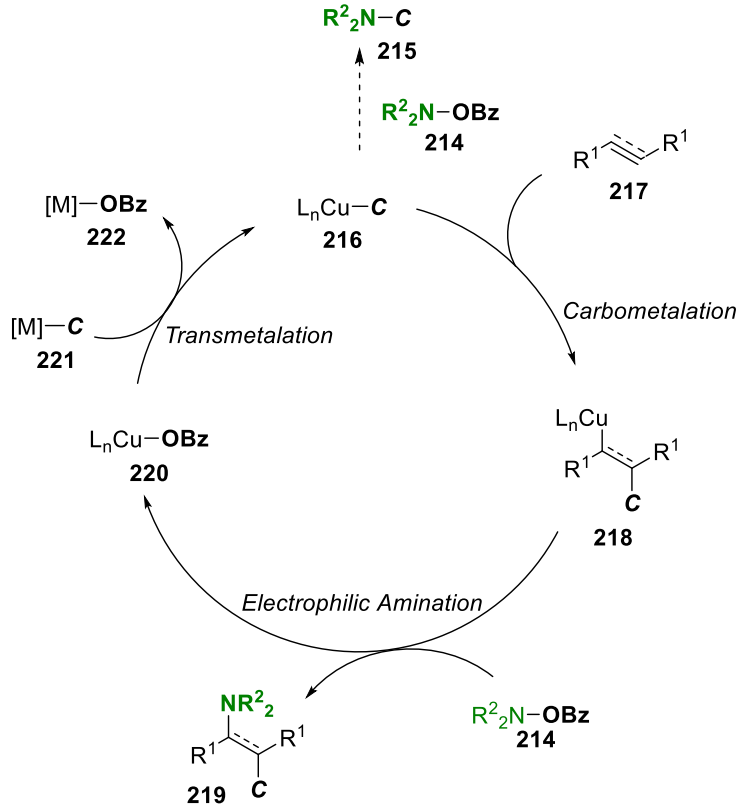


Scheme 61. Cu-catalyzed carbozincation of cyclopropenes by *Fox et al.*

The work of *Fox et al.* demonstrates, that diastereoselective carbozincation of cyclopropene **212** can be carried out by using various organozinc reagents **211** (Scheme 61).[78e] For the high diastereoselectivity it is vital to remove the magnesium halide salt by complexation with dioxane.

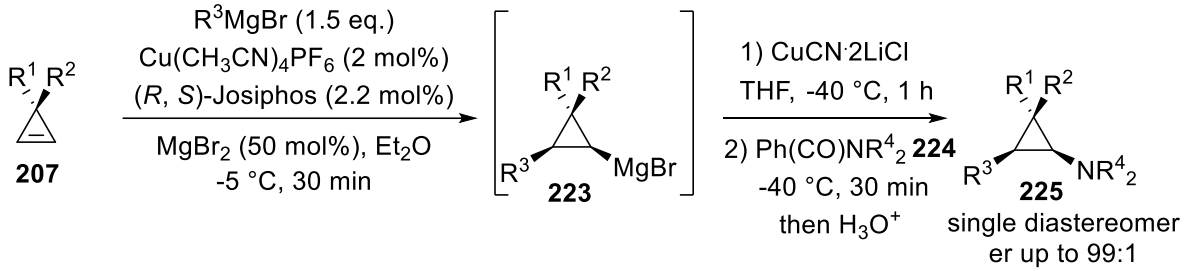
Concept

While carbometalation reactions have demonstrated broad applicability in the formation of carbon-carbon (C-C) and carbon-oxygen (C-O) bonds, their utility in carbon-nitrogen (C-N) bond formation reactions has remained limited.[75a] Among the reported carbometalation-amination sequences (carboamination), the catalytic carbometalation step is typically facilitated by copper (Cu), cobalt (Co), nickel (Ni), palladium (Pd), or rhodium (Rh). Subsequently, the construction of a C-N bond necessitates the presence of an electrophilic amination reagent.[28d] In the case of a Cu-catalyzed carboamination, the sequential formation of a new C-C bond and C-N bond poses significant challenges. This arises from the inherent reactivity of the organocopper species **216**, which readily engages with the electrophilic amination reagent **214**, thus impeding the desired carbometalation step (Scheme 62).[79] Consequently, the selection of alkene/alkyne substrates becomes critical for achieving success, with strained alkenes and benzynes being the most amenable options.[28d] The used hydroxylamines can be synthesized from nitro compounds *via* a reduction step to amines followed by a partial oxidation and an acylation.



Scheme 62. Plausible mechanism of a Cu-catalyzed carboamination of alkynes or alkenes.

Among the limited number of examples, *Marek et al.* showcased the efficacy of a Cu-catalyzed carboamination in the synthesis of cyclopropylamines (Scheme 63).[78a] The subsequent treatment of cyclopropylmagnesium compounds **223** with CuCN and *O*-benzoyl hydroxylamines **224** afforded the cyclopropylamines **225** as single diastereomers. It is worth noting, that the scope of hydroxylamines is limited to aliphatic substituents.

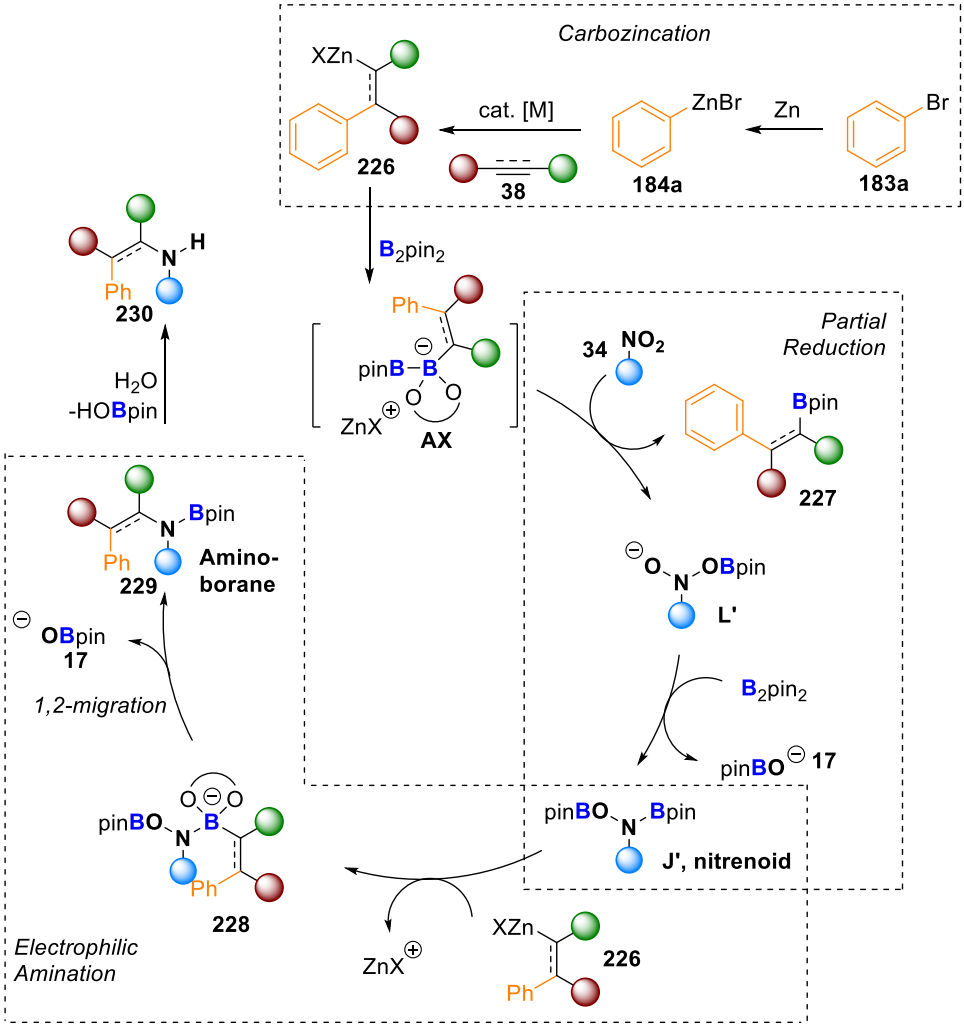


Scheme 63. Carboamination of cyclopropenes by *Marek et al.*

The current state of carboamination reactions primarily relies on hydroxylamines as electrophilic amination reagents. Hydroxylamines are typically prepared from nitro compounds through a reduction-partial oxidation sequence.[79] Since a hydroxylamine moiety is a partially reduced form of the nitro group, using a nitro species directly as an electrophilic coupling partner might be feasible. However, to date, no established carboamination protocol utilizing nitro compounds has been developed. Such an approach would offer significant advantages in terms of step economy and cost-effectiveness.

Recently, *our research group* has reported an electrophilic amination with nitro compounds. This boron-mediated transformation harnesses the reactivity of nitrenoids as effective electrophilic amination reagents, demonstrating their reactivity towards a wide range of organozinc compounds.[14] Exploiting the unique reactivity of nitrenoids offers a promising avenue for achieving carboamination of alkenes or alkynes using nitro compounds. Moreover, *our* methodology enables the generation of aromatic nitrenoids, thereby expanding the scope of amination reactions beyond those restricted to aliphatic substituents.

Based on our working hypothesis, the procedure begins with the treatment of an aryl halide **183a** with zinc, leading to the formation of the corresponding organozinc reagent **184a** (Scheme 64). Subsequently, the carbozincation reaction of an alkene or alkyne substrate affords an alkyl- or alkenylzinc compound **226**. This organometallic species activates B_2pin_2, thereby initiating the pathway as discussed in Chapter 1.1, ultimately leading to the formation of an aminoborane **229**. Upon hydrolysis, the desired amine product is obtained **230**.



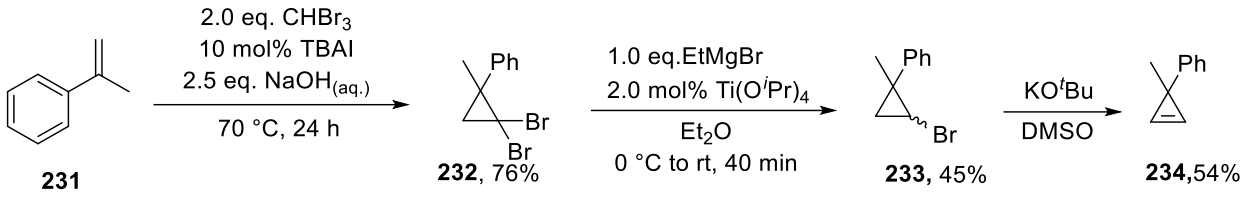
Scheme 64. The proposed mechanism of a carboamination with nitro compounds.

The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization); *Meike Niggemann* (concept).

Results

Synthesis of Cyclopropenes and Acetylenes

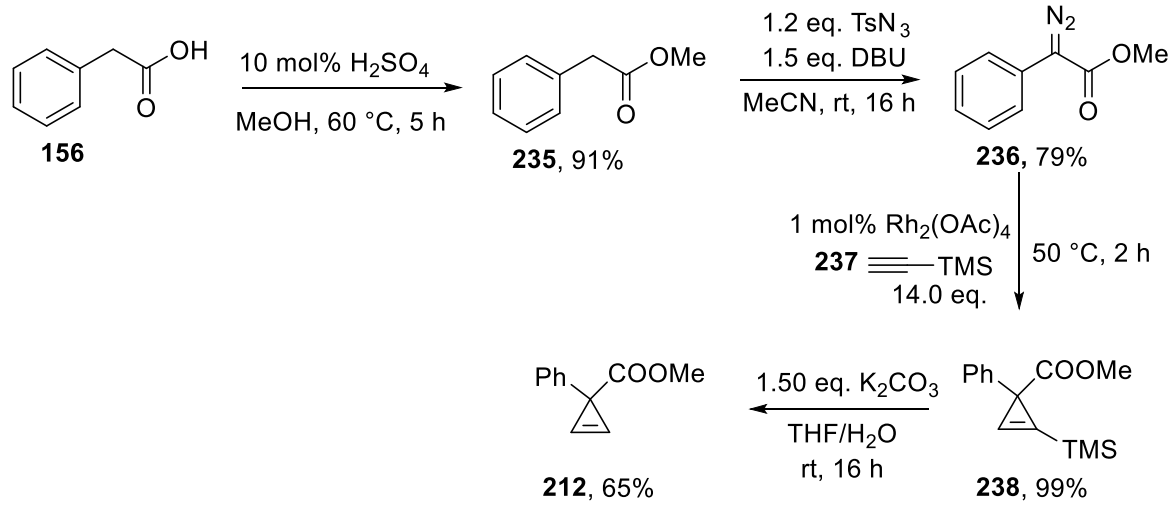
While most of the alkynes are commercially easily accessible, the cyclopropenes must be synthesized.



Scheme 65. Synthesis of cyclopropene **234** by *Gevorgyan et al.*

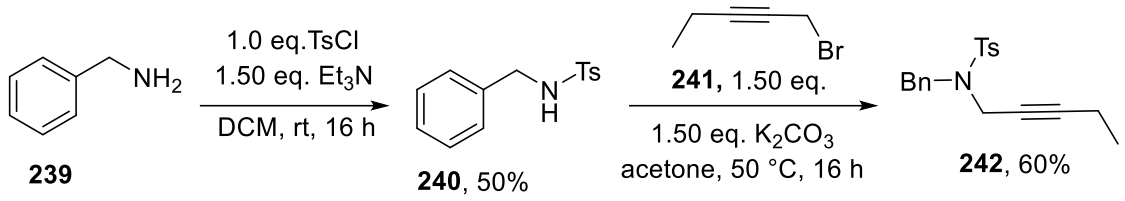
Cyclopropene **234** was synthesized according to the procedure of *Gevorgyan et al.* (Scheme 65).[80] Treating α-methylstyrene **231** with bromoform in the presence of a catalytic amount of TBAI in a basic milieu, provided the cyclized dibromocyclopropane **232** in 76% yield. The bromocyclopropane **233** occurred in 45% yield in a Ti-catalyzed selective reduction. The final elimination step afforded the desired product **234** in 54% yield (18% over the three steps).

The synthesis of cyclopropene **212** was carried out following the 4-step synthesis of *Gevorgyan et al.* (Scheme 66).[80] The first esterification reaction provided phenylacetate **235** in excellent yield. In the next step, the ester **235** was treated with tosyl azide, forming the azide **236**, which cyclized in a Rh-catalyzed reaction. The TMS group was removed by treating the mixture with K_2CO_3 and the product **212** was obtained with an overall yield of 46% over the 4 steps.



Scheme 66. Synthesis of cyclopropene **212** by *Gevorgyan et al.*

Based on the work of *Jana et al.*, benzylamine **239** was reacted with tosyl chloride to afford sulfonamide **240** (Scheme 67).[81] Following the protocol of *Maestri et al.*, the alkylation was carried out at 50 °C with pentyne **241** in the presence of K_2CO_3, achieving 60% yield (30% over the two steps).[82]

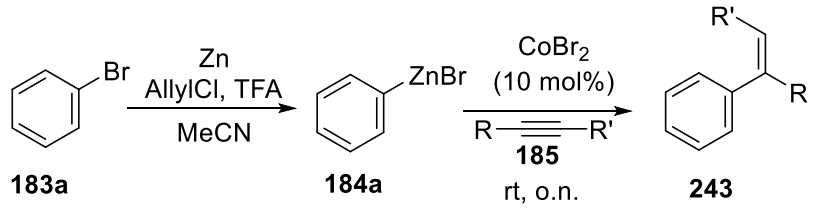


Scheme 67. Synthesis of sulfonamide **242** by *Maestri et al.*

Investigation of Carbozincation and Electrophilic Amination of Alkynes

To test our hypothesis, the effective formation of the alkenyl-metal reagent shall be first examined as the presence of the desired organozinc reagent is crucial for the transformation of nitro compounds into the corresponding amines. The investigation began by studying the carbometalation reaction of alkynes with organozinc compounds in the presence of a cobalt catalyst. Following the protocol established by *Gosmini et al.*, arylzinc bromide was efficiently formed from bromobenzene using zinc dust in the presence of allyl chloride and TFA as activating agents in acetonitrile.[74b] The carbometalation reaction was conducted using the $CoBr_2$ catalyst with arlyzinc reagent **184a** on different alkynes **185a-f** (Table 17). After the carbometalation reaction, the mixture was hydrolyzed, and the resulting products were analyzed using ^{1}H-NMR spectroscopy. The observed yields after protonation served as indicators of the efficiency of alkenylzinc species formation. Among the tested alkynes, only 3-hexyne **185a** yielded the desired product in 40% yield (entry 1), while the other substrates did not provide the desired products (entries 2-6).

Table 17. Test of the carbozincation of alkynes according to *Gosmini et al.*



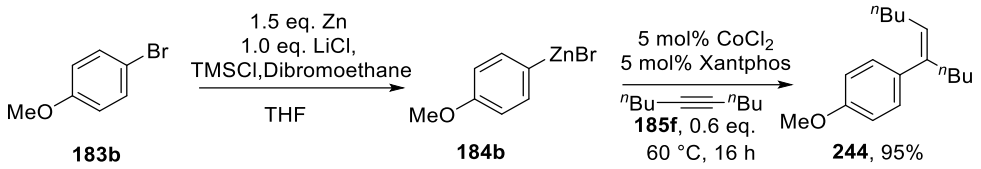
183a 184a 243

Entry	Alkyne	Conversion [%]	**243** [%]
1	R=R'=Et **185a**	40	40
2	R=Ph, R'=Et **185b**	5	5
3	R=R'=Ph **185c**	5	5
4	R=PhEt, R'=H **185d**	5	5
5	R=*p*-OMePh, R'=H **185e**	5	5
6	R=R'=^{n}Bu **185f**	5	5

Conditions: Schlenk tube was charged with $CoBr_2$ (8.7 mg, 0.04 mmol, 10 mol%)) and zinc powder (52 mg, 0.8 mmol, 2.0 eq.), then acetonitrile (2 mL) was added. Subsequently allylchloride (0.01 mL, 0.12 mmol) and 1 drop trifluoroacetic acid were added. This caused a rise in temperature and a change of color of the mixture from blue to green to orange to grey. Once the orange tinge of the mixture disappeared bromobenzene (0.042 mL, 0.4 mmol, 1.0eq.) was added. After 30 min stirring the mixture was treated with alkyne (0.13 mmol, 0.33 eq.) at 0 °C. The mixture was let to warm up to rt and was stirred overnight.

Since the previous attempts to achieve successful carbometalation with good yields were unsuccessful, an alternative method was sought to accomplish the first step effectively. As mentioned earlier, the procedure

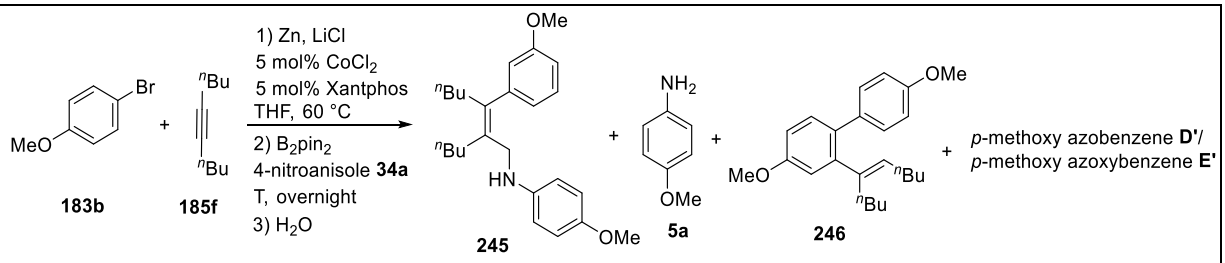
described by *Yoshikai et al.* offers an efficient carbozincation approach in which aryl halides are transformed into the corresponding organozinc reagents in the presence of zinc, LiCl, and TMSCl, and dibromoethane as activators.[74d] $CoCl_2$ was used as catalyst to facilitate the desired alkene formation in the carbozincation reaction. By adapting this procedure, the conversion of 5-decyne **185f** resulted in the desired product **244** in an excellent yield of 95% (Scheme 68).



Scheme 68. Carbozincation of 5-decyne according to the protocol of *Yoshikai et al.*

The carbozincation of 5-decyne **185f**, following the procedure of *Gosmini et al.*, only provided the desired product in a low yield of 5% (Table 17). In contrast, the method of *Yoshikai et al.* demonstrated excellent yield for the same transformation (Scheme 68). Once the successful carbozincation step was validated, the alkenyl-zinc species was tested in the direct nitro-functionalization reaction using 4-nitroanisole **34a** and B_2pin_2(Table 18). In THF as the solvent, the reaction resulted in only traces of 4-anisidine **5a** and an ortho-functionalized side product **246** derived from the alkenylaryl-zinc compound **248**, without yielding the desired amine **245** (entry 1). A similar outcome was observed when toluene was used as the solvent, with the formation of azobenzene **D'** and azoxybenzene **E'** (entry 2). Increasing the reaction temperature led to increased amounts of the 4-anisidine **5a** and side product **246** (entries 3-5). Furthermore, the addition of Et_3N resulted in a higher yield (43%) of the side product **246** (entry 6). Unfortunately, none of the attempts successfully afforded the desired product **245.**

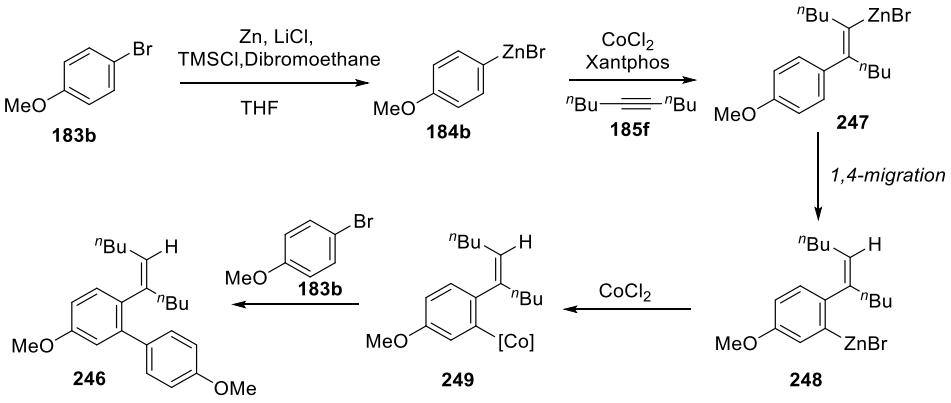
Table 18. Electrophilic amination of the alkenyl-zinc reagent according to *Yoshikai et al.*



Entry	Solvent	T [°C]	Conversion [%]	**245** [%]	**5a** [%]	**D'** [%]	**E'** [%]	**246** [%][a]
1	THF	rt	5	0	traces	0	0	traces
2	THF+toluene	rt	20	0	traces	11	9	traces
3	THF	60	77	0	48	15	14	30
4	THF+toluene	60	70	0	40	17	13	30
5[b]	THF+toluene	60	70	0	40	15	15	43

Conditions: Schlenk tube was charged with LiCl (18 mg, 0.4 mmol) and zinc powder (40 mg, 0.6 mmol), then 1 mL THF was added. Subsequently one drop of dibromoethane and TMSCl were added and the solution was heated to reflux after each addition. $CoCl_2$ (2.6 mg, 0.02 mmol), Xantphos (12 mg, 0.02 mmol) and 4-bromoanisole **183b** (0.05 ml, 0.4 mmol) was added and the mixture was stirred for 10 min. The mixture was charged with 5-decyne **185f** (0.043 ml, 0.24 mmol) and stirred overnight at 60 °C. Then B_2pin_2 (122 mg, 0.48 mmol) and 4-nitroanisole **34a** (37 mg, 0.24 mmol) were added and the mixture was stirred overnight; [a] Compared to the side product X; [b] Et_3N (0.48 mmol, 2.0 eq.) as additive.

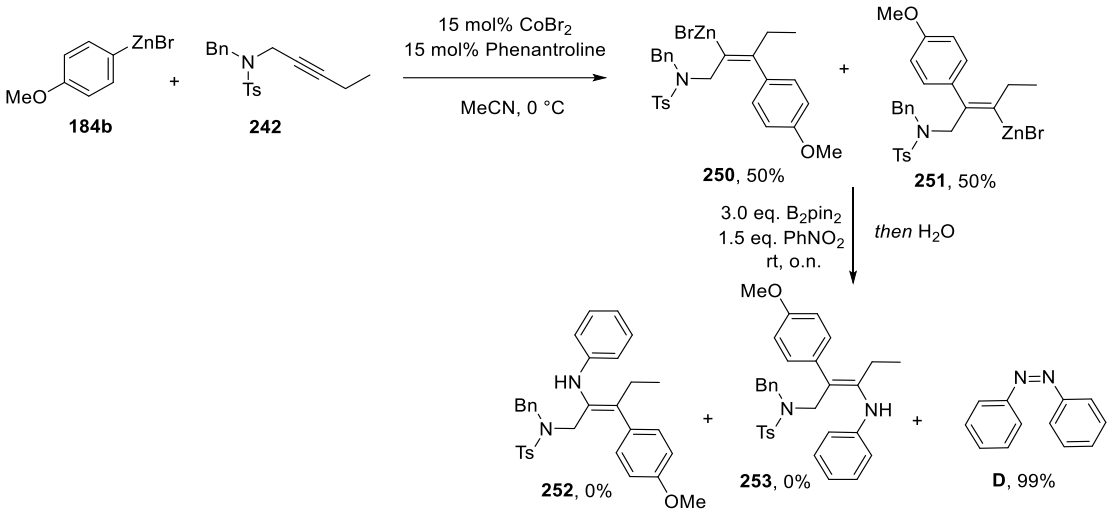
The observed *ortho*-functionalization may be the result of the previously mentioned reaction between the alkenylaryl-cobalt reagent **249**, which is formed after the 1.4-migration and zinc-to-cobalt transmetalation, and the unreacted arylbromide **183b** (Scheme 69).



Scheme 69. Possible reaction mechanism leading to the side product **246**.

After successfully adapting the protocol of *Yoshikai et al.* for the first step, the investigated electrophilic amination reactions have failed to afford the desired product. To avoid the formation of the unreactive alkenylarylzinc compound **248**, an alternative method was tested. With the above mentioned protocol of *Gosmini et al*. ynamide **242** was transformed into the corresponding alkenyl-zinc species **250** and **251** in

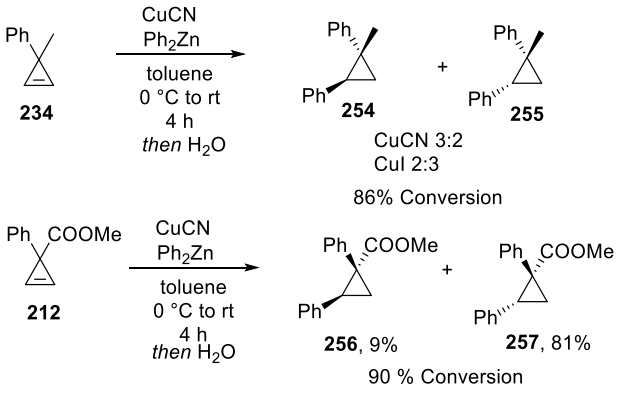
the presence of $CoBr_2$ and phenantroline (Scheme 70).[74c] The isomers were formed in a 1:1 ratio, showing low regioselectivity. Despite the low regioselectivity of the first step, the reactivity of the alkenyl-zinc reagent **250** and **251** was examined in the boron-mediated electrophilic amination reaction with nitrobenzene. Unfortunately, no desired product formation (**252** and **253**) was observed, only azobenzene **D** was obtained in quantitative yield, alongside the protonated alkenyl-zinc reagent as side products.



Scheme 70. Carbozincation of ynamide **242**, followed by boron-mediated electrophilic amination with nitrobenzene.

Investigation of Carbozincation and Electrophilic Amination of Cyclopropenes

Since the investigated alkynes and ynamide did not lead to the desired products, the focus shifted to the study of cyclopropenes, which are known to be more reactive. Taking inspiration from the work of *Fox et al.* [78d], cyclopropene **234** and its carboxylate derivative **212** were examined in a Cu-catalyzed carbozincation reactions. These substrates demonstrated high conversion (86% for **234** and 90% for **212**) with low (3:2 ratio) and high diastereoselectivity (9:1 ratio), respectively (Scheme 71).

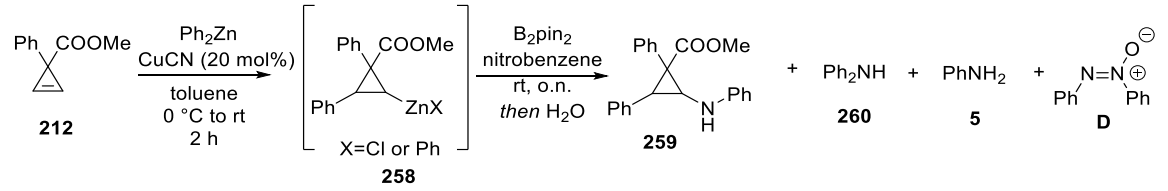


Scheme 71. Cu-catalyzed carbozincation of cyclopropenes (**234** and **212**).

After successfully synthesizing the cyclopropanyl-zinc reagents, their application in the boron-mediated electrophilic amination with nitro compounds was investigated (Table 19). In the first experiment (entry 1), when the cyclopropyl-zinc reagent **258** was prepared using 1.5 equivalents of Ph_2Zn, the desired product

259 was not obtained. Instead, diphenylamine **260** and azoxybenzene **D** were produced in 71% and 29% yield, respectively. The formation of diphenylamine **260** as a side product was expected because the excess of Ph_2Zn can react with nitrobenzene **4** in the presence of B_2pin_2. In the second experiment (entry 2), using a 1:1 ratio of Ph_2Zn and cyclopropene **212**, the yield of diphenylamine **260** decreased to 25%, while aniline **5** was obtained in 35% yield. Increasing the amount of Ph_2Zn resulted in complete conversion of nitrobenzene **4** to diphenylamine **260** (entries 3 and 4). Furthermore, a modified procedure involving the preparation of Ph_2Zn using ZnI_2 selectively yielded diphenylamine **260** in 74% yield (entry 5).

Table 19. Electrophilic amination of cyclopropylzinc species **258** with nitrobenzene.

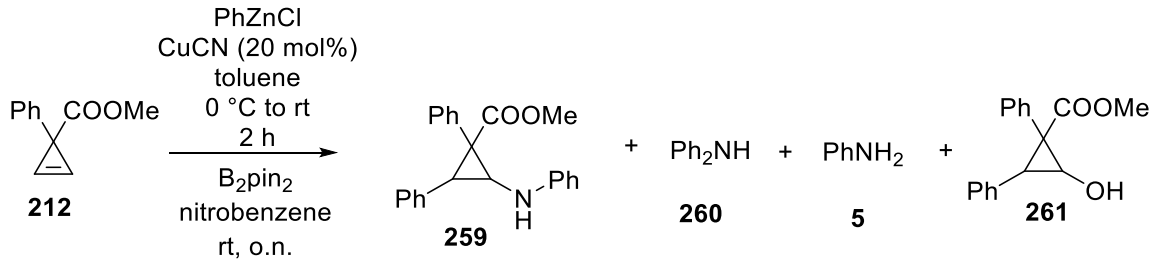


Entry	Zn-organyl	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**D** [%]
1	Ph_2Zn (1.5)	100	0	71	0	29
2	Ph_2Zn (1)	66	0	25	35	5
3	Ph_2Zn (2)	100	0	100	0	0
4[a]	Ph_2Zn (2)	100	0	100	0	0
5[b]	Ph_2Zn (2)	74	0	74	0	0

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol, 20 mol%) in toluene (0.5 mL) Ph_2Zn was added, then at 0 °C a solution of cyclopropene (35 mg, 0.2 mmol, 1.0 eq. in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C, then nitrobenzene (0.01 mL, 0.1 mmol, 0.5 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 1.0 eq.) were added and the mixture was stirred overnight at rt; [a] 0.4 mmol cyclopropene and LiCl (8.5 mg, 0.2 mmol, 1.0 eq.); [b] 0.4 mmol cyclopropene and Ph_2Zn from ZnI_2 was prepared.

Considering that diphenylamine **260** in a 66% yield was formed even at a 1:1 ratio of Ph_2Zn and cyclopropene **212**, its origin cannot solely be the side reaction between the unconsumed Ph_2Zn and nitrobenzene. It is likely that the formed cyclopropyl-zinc compound **258** contains a phenyl residue on the zinc, which can also react with nitrobenzene. This assumption leads to two possible solutions The first solution involves replacing diarylzinc with arylzinc halide to generate an organozinc species with both a cyclopropyl and a halide residue. To explore this possibility, PhZnCl and PhMgBr were employed as organometallic reagents (Table 20). Although 2.0 eq. of PhZnCl suppressed the formation of diphenylamine **260**, the desired product **259** was not obtained, and only aniline **5** was produced in 33% yield (entry 1). The lower reactivity of PhZnCl compared to Ph_2Zn may explain this result. Using 3.0 eq. of PhZnCl resulted in exclusively aniline **5** in traces, and the cyclopropanol side product **261** was obtained in 40% yield (entry 2). Its origin can be explained, that oxygen contamination may have occurred since the reaction was not carried out in a glovebox, leading to the oxidation of the organozinc compound **258**.[78a] The attempt with PhMgBr only gave aniline **5** in 50% yield and no desired product **259** (entry 3).

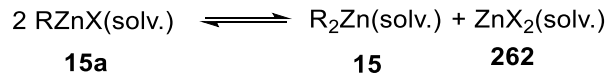
Table 20. Influence of the applied organozinc compound on the electrophilic amination of cyclopropene **212**.



Entry	Organyl	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**261**[a] [%]
1	PhZnCl (2)	33	0	0	33	0
2[b]	PhZnCl (3)	5	0	0	traces	40
3	PhMgBr (2)	50	0	0	50	0

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol) in 0.5 mL toluene organyl was added, then at 0 °C a solution of cyclopropene **212** (35 mg, 0.2 mmol in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C, then nitrobenzene (0.01 mL, 0.1 mmol) and B_2pin_2 (51 mg, 0.2 mmol) were added and the mixture was stirred overnight at rt. a) yield from cyclopropane intermediate; b) 0.3 mmol cyclopropene **212**.

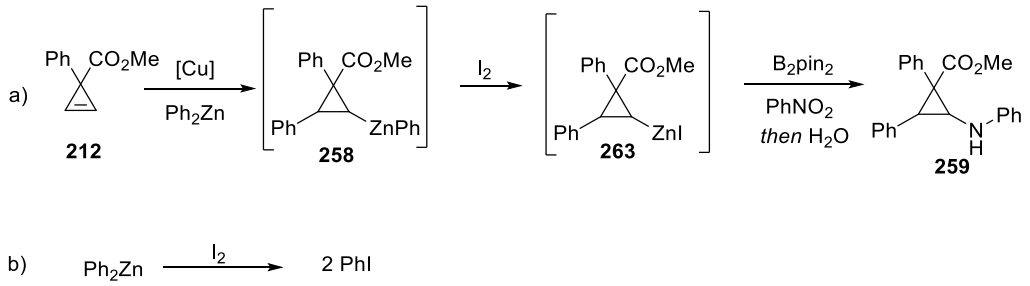
It is worth mentioning that a Schlenk equilibrium occurs between the organozinc halide species **15a** and the diorganozinc reagent **15** (Scheme 72). However, the reported studies state that the spontaneous ionic disproportion of RZnX **15a** is not favorable, and therefore the formation of Ph_2Zn from PhZnCl is unlikely, which aligns with the results.[83]



Scheme 72. Zinc Schlenk equilibrium.

Although numerous methods have been developed for the copper-catalyzed carbozincation of cyclopropenes, they mainly focus on improving the stereoselectivity rather than on the mechanistic aspects of the transformation and investigating the Schlenk equilibrium of the formed cyclopropylzinc and copper species. These systems are complex, involving several Schlenk equilibria and transmetalations between copper and zinc. Consequently, a comprehensive exploration of the nature of the organozinc(copper) species necessitates extensive experimentation and/or calculation. Unfortunately, due to the lack of such investigations, addressing the undesired reactivity of the organozinc compounds has remained an elusive challenge.

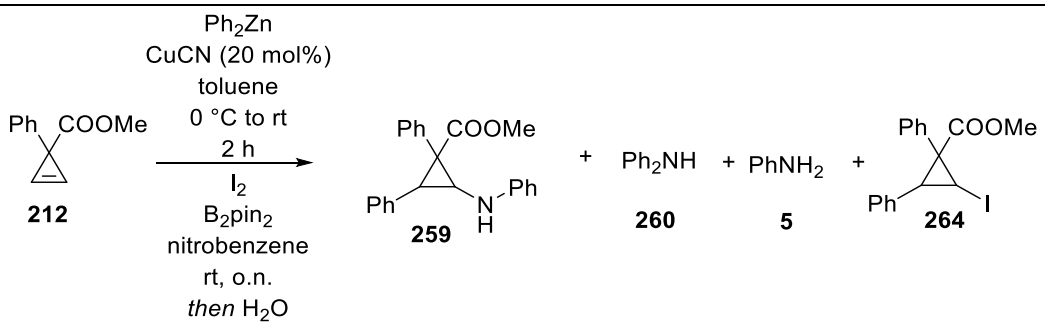
An alternative approach to prevent the concurrent formation of diphenylamine involves two simultaneous steps: the conversion of diorganozinc to organozinc halide and the elimination of the unreacted Ph_2Zn (Scheme 73). One possible strategy for achieving this is the addition of iodine, which is commonly employed in the titration of organozinc compounds, as it reacts with Ph_2Zn (Scheme 73b).[84]



Scheme 73. Possible strategy to eliminate the formation of diphenylamine **260**.

The addition of 1.0 equivalent of iodine did not affect the side reaction, as diphenylamine **260** was still obtained in a yield of 71% (Table 21, entry 1). However, a small amount (13% yield) of iodinated cyclopropane **261** was observed. Increasing the amount of iodine completely stopped the reactions, yielding only **264** with no conversion of the nitrobenzene (entry 2). When 4.0 equivalents of iodine were used, the cyclopropylzinc reagent **258** was fully converted to the iodide **264**, but no desired product **259** was formed (entry 3). The detection of PhI was complicated due to multiple aromatic signals in the NMR spectra.

Table 21. Influence of iodine on the electrophilic amination of cyclopropene **212**.



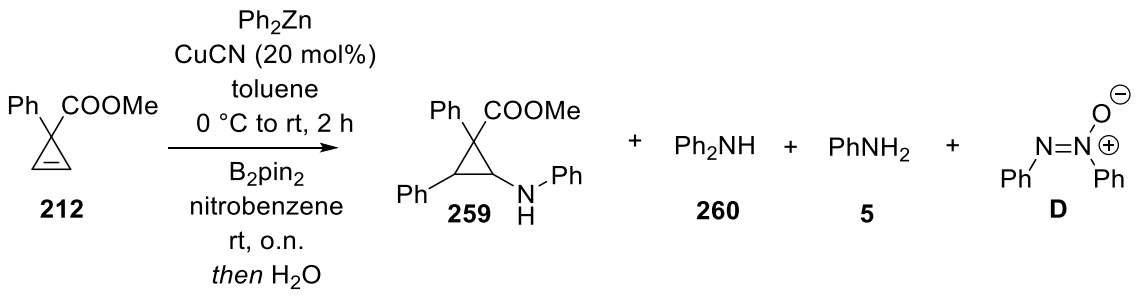
Entry	Iodine eq.	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**264**[a] [%]
1	1	93	0	71	22	13
2	2	0	0	0	0	63
3	4	20	0	0	20	100

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol, 20 mol%) in toluene (0.5 mL) Ph_2Zn (0.83 mL, 0.4 mmol, 2.0 eq.) was added, then at 0 °C a solution of cyclopropene **212** (35 mg, 0.2 mmol, 1.0 eq. in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C, then iodine was added. After 30 min the mixture was treated with nitrobenzene (0.01 mL, 0.1 mmol, 0.5 eq.) and B_2pin_2 (51 mg, 0.2 mmol, 1.0 eq.) and was stirred overnight at rt; [a] yield from the cyclopropene **212**.

To address the side reaction involving the consumption of nitrobenzene and B_2pin_2, it would be practical to use an excess of these compounds (Table 22). However, increasing the amount of B_2pin_2 to 4 equivalents and nitrobenzene to 2 equivalents did not lead to the formation of the desired product **259** (entry 1). Instead, diphenylamine **260** was obtained in a yield of 23%, aniline **5** in 18% yield, and azoxybenzene **D** in 7% yield. Since an excess of B_2pin_2 results in a lower concentration of the borate complex **AX**, an additional activator was employed. Nonetheless, the reaction exclusively produced aniline **5** in a yield of

58% (entry 2). When only a slight excess of B_2pin_2 and nitrobenzene was used, diphenylamine **260** was obtained in a yield of 33%, while aniline **5** and azoxybenzene **D** were also formed (entry 3).

Table 22. Influence of the excess of nitrobenzene and B_2pin_2 on the electrophilic amination of cylopropene **212**.

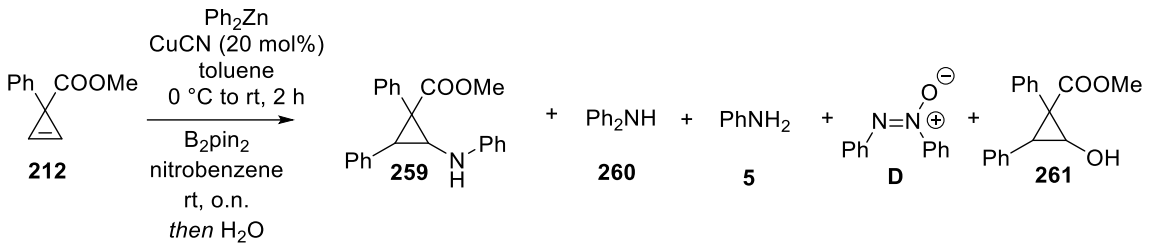


Entry	B_2pin_2 eq.	Nitrobenzene eq.	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**D** [%]
1	4	2	48	0	23	18	7
2[a]	4	2	58	0	0	58	0
3	3	1.5	71	0	33	22	16

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol, 20 mol%) in toluene (0.5 mL) Ph_2Zn (0.83 mL, 0.4 mmol, 2.0 eq.) was added, then at 0 °C a solution of cyclopropene **212** (35 mg, 0.2 mmol, 1.0 eq. in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C. Then nitrobenzene and B_2pin_2 were added and the mixture was stirred overnight at rt; [a] NaO^tBu (38 mg, 0.4 mmol, 2.0 eq.) as additive.

Various additives were tested to enhance the reactivity of the cyclopropylzinc species **258** (Table 23). Addition of Et_3N led to complete conversion to diphenylamine **260** (entry 1). A similar outcome was observed with the use of LiCl, resulting in full conversion of nitrobenzene to diphenylamine **260** and the formation of cyclopropanol **261** as a side product (entry 2). When TMEDA was employed, it favored the formation of aniline **5** and azoxybenzene **D** over diphenylamine **260**, yielding 79% alcohol **261** as well (entry 3). On the other hand, Et_2O and DME inhibited the reaction, resulting in low yields of aniline **5** (entries 4 and 5). In the case of THF as a cosolvent, 79% conversion was observed with 60% diphenylamine **260** and 19% aniline **5** formation (entry 6).

Table 23. Influence of the additives on the electrophilic amination of cyclopropene.

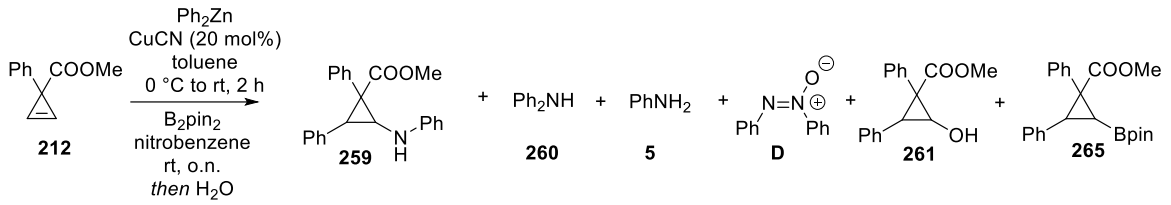


Entry	Additive	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**D** [%]	**261**[a] [%]
1	Et_3N (2)	100	0	100	0	0	0
2	LiCl (2)	100	0	100	0	0	46
3	TMEDA (1)	79	0	24	29	26	79
4	Et_2O (1 mL)	26	0	0	26	0	38
5	DME (1 mL)	10	0	5	5	0	5
6	THF (1 mL)	79	0	60	19	0	0

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol) and additive in 0.5 mL toluene Ph_2Zn (0.83 mL, 0.4 mmol) was added, then at 0 °C a solution of cyclopropene **212** (35 mg, 0.2 mmol in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C. Then the mixture was treated with nitrobenzene (0.01 mL, 0.1 mmol) and B_2pin_2 (51 mg, 0.2 mmol) and was stirred overnight at rt. a) yield from the cyclopropene **212**.

The addition of ligands plays a crucial role in metal-catalyzed reactions as they can significantly influence reactivity and selectivity by virtue of their electronic, steric, and topological properties. In carbozincation reactions, particularly in Cu-catalyzed versions, *N*- and *P*-ligands are commonly employed.[75] Therefore, a range of representative ligands was tested in the carboamination of cyclopropene **212** (Table 24). When DPEphos was used as the ligand, only diphenylamine **260** was obtained in a yield of 50% (entry 1). Bipy as a ligand resulted in diphenylamine **260** in 55% yield, azoxybenzene **D** in 19% yield, and the formation of cyclopropanol **261** in 37% yield (entry 2). The addition of Diphos provided diphenylamine **260** in 72% yield and azoxybenzene **D** in 5% yield (entry 3). However, a significant decrease in conversion was observed when Xantphos was applied, affording the borylated cyclopropane **265** in a yield of 24% (entry 4). In the presence of phenanthroline, full conversion was achieved, yielding diphenylamine **260** in 57% yield, aniline **5** in 33% yield, and azoxybenzene **D** in 10% yield (entry 6). However, no product formation was detected in this case as well, similarly to the previous attempts.

Table 24. Influence of the ligands on the carboamination of cyclopropene

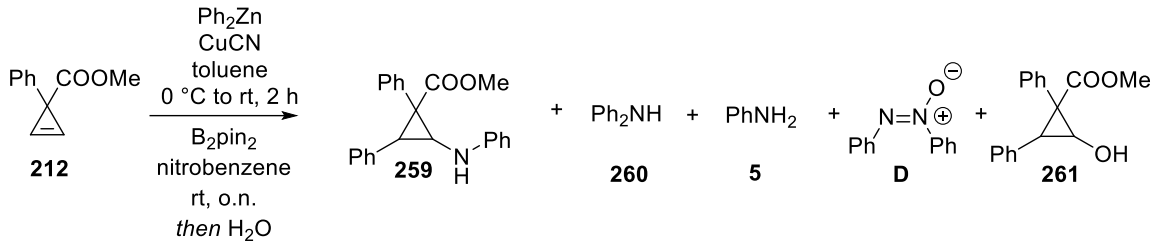


Entry	Ligand	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**D** [%]	**261**[a] [%]	**265**[a] [%]
1	DPEphos	50	0	50	traces	0	0	0
2	Bipy	74	0	55	0	19	37	0
3	Diphos	77	0	72	0	5	0	0
4	Xantphos	10	0	10	0	0	0	24
5	Phenantroline	100	0	57	33	10	39	0

Conditions: to a solution of CuCN (3.6 mg, 0.02 mmol) and ligand (0.02 mmol) in 0.5 mL toluene Ph_2Zn (0.83 mL, 0.4 mmol) was added, then at 0 °C a solution of cyclopropene **212** (35 mg, 0.2 mmol in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C. Then the mixture was treated with nitrobenzene (0.01 mL, 0.1 mmol) and B_2pin_2 (51 mg, 0.2 mmol) and was stirred overnight at rt. a) yield calculated from the cyclopropene **212**.

In the Cu-catalyzed carboamination of the cyclopropene **212**, where no desired product was formed, additional experiments were conducted by increasing the amount of Cu to explore the possible formation and reactivity of cyclopropylcopper species (Table 25). When the catalyst loading was reduced to 5 mol% Cu, only 83% conversion was achieved compared to the 20 mol% catalyst (entry 2). Using a stoichiometric amount of Cu resulted in lower conversion, with 40% diphenylamine **260** and 20% aniline **5** formation, while 62% of the cyclopropene **212** was transformed into the cyclopropanol **261** (entry 3). $CoBr_2$ as a catalyst yielded diphenylamine **260** in 20% yield and aniline **5** in 40% yield (entry 4). In the absence of a catalyst, diphenylamine **260** was formed in 26% yield, along with 37% aniline **5** and 47% cyclopropanol **261** (entry 5).

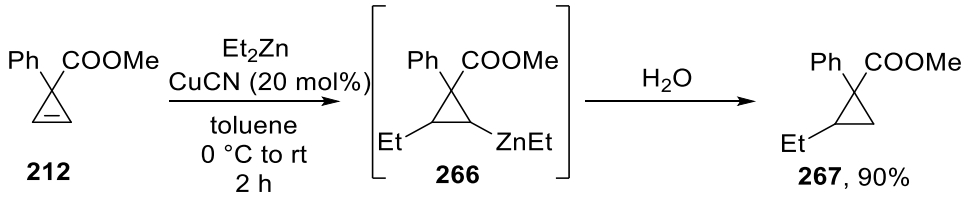
Table 25. Influence of the catalyst loading on the electrophilic amination of the cyclopropene **212**.



Entry	Catalyst	Conversion [%]	**259** [%]	**260** [%]	**5** [%]	**D** [%]	**261**[a] [%]
1	CuCN (0.2)	100	0	100	0	0	0
2	CuCN (0.05)	83	0	52	10	21	10
3	CuCN (1)	60	0	40	20	0	62
4	$CoBr_2$ (0.2)	60	0	20	40	0	traces
5	-	66	0	26	35	5	47

Conditions: to a solution of catalyst in 0.5 mL toluene Ph_2Zn (0.83 mL, 0.4 mmol) was added, then at 0 °C a solution of cyclopropene (35 mg, 0.2 mmol in 0.5 mL toluene) was added. The mixture was stirred 2 hours at 0 °C. Then the mixture was treated with nitrobenzene (0.01 mL, 0.1 mmol) and B_2pin_2 (51 mg, 0.2 mmol) and was stirred overnight at rt. a) yield from the cyclopropene **212**.

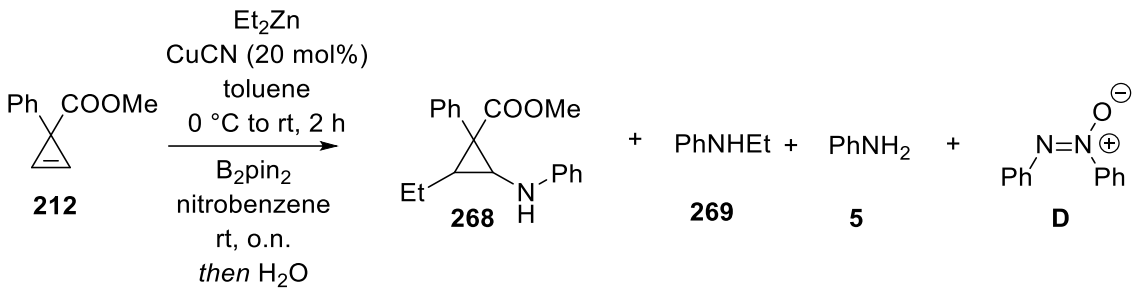
Since the previous attempts to obtain the desired product using the phenylcyclopropylzinc reagent **258** were unsuccessful, exploring a different organozinc species might lead to the formation of the cyclopropylamine product. It was presumed that in the carbozincation of cyclopropene, both residues of the resulting cyclopropylzinc reagent can react with the nitrenoid. Using a smaller alkyl substituent might prevent blocking of the cyclopropyl side and enable the desired reaction. Thus, it was proposed to employ Et_2Zn instead of Ph_2Zn. To begin, the efficient formation of the cyclopropylzinc reagent was tested. The Cu-catalyzed carbozincation of cyclopropene was examined, resulting in the desired cyclopropane **267** in 90% yield (Scheme 74), indicating the successful formation of the cyclopropylzinc reagent **266**.



Scheme 74. Cu-catalyzed carbozincation of the cyclopropene **212** using Et_2Zn.

The cyclopropyl zinc reagent **266** was employed in the electrophilic amination reaction with nitrobenzene in the presence of B_2pin_2, as detailed in Table 26. When 2.0 equivalents of Et_2Zn were used, *N*-ethylaniline **269** was obtained in a yield of 90% (entry 1), indicating a similar reaction pathway as the Ph_2Zn reaction. In the case of using 3 equivalents of Et_2Zn, *N*-ethylaniline **269** was formed in 33% yield, while azoxybenzene **D** was obtained in 20% yield (entry 2).

Table 26. Influence of the organozinc reagent on the electrophilic amination of the cyclopropene **212**.



Entry	Organozinc compound	Conversion [%]	**268** [%]	**269** [%]	**5** [%]	**D** [%]
1	Et_2Zn (2)	90	0	90	0	0
2	Et_2Zn (3)	53	0	33	0	20

Although the test systems have demonstrated efficient carbozincation of cyclopropene **212** and successful synthesis of cyclopropylzinc compounds **258** and **266** (Scheme 71 and Scheme 74), their application in direct nitro-functionalization has proven to be unsuccessful. To gain control over the reactivity of the cyclopropylzinc species, it is crucial to develop a comprehensive understanding of their nature.

Summary – Electrophilic Amination with Nitro Compounds *via* Carbometalation

A three-component-coupling-type carboamination reaction of alkynes and alkenes using organozinc reagents and nitro compounds was investigated. Nitro compounds were transformed into nitrenoids according to *our* protocol and used as electrophilic amination reagents.[14] The carboamination reactions involve two essential steps: carbometalation and amination, both of which were separately investigated.

Although alkynes and cyclopropenes successfully underwent a carbometalation reaction and generated organozinc species, they were proven to be unsuitable coupling partners for nitrenoids. According to *Yoshikai et al.*, the alkenyl zinc compound **247** underwent 1,4-migration, forming an unreactive alkenylaryl zinc compound **248** for the electrophilic amination reaction.[74d] Arylzinc compounds already showed no reactivity in the C(sp^2)-H amination reaction with nitro compounds (see Chapter 1.1), and similar results were observed with the rapid formation of the activated borate complex **AT**, providing only aniline **5** and azoxybenzene **D'** as products.

The investigated strained and more reactive cyclopropene **212** yielded cyclopropylzinc compounds **258** and **266** in excellent conversion in a Cu-catalyzed carbometalation reaction. However, the organozinc compounds (Ph_2Zn and Et_2Zn) used for the carbometalation step appeared to be more reactive towards nitrenoids, favoring the concurrent electrophilic amination reaction.[14a] Therefore, only the diphenylamine **260** or the ethylaniline **269** were obtained, respectively. Several solutions were investigated to suppress this side reaction. Monozinc and organomagnesium reagents afforded the diphenylamine **266**, while the trapping of the unconsumed Ph_2Zn with iodine also resulted in a negative outcome. Experiments testing a variety of ligands and additives remained unsuccessful. Variations in the stoichiometry of nitrobenzene, B_2pin_2, and the Cu-catalyst showed no effect on the outcome.

While unsuccessful carboaminations were primarily attributed to side reactions, the observations might have confirmed the reduced reactivity of nitrenoids toward cyclopropylcopper/zinc compounds compared to hydroxylamines.[78a]

In summary, all of the tested systems were unable to successfully achieve carboamination of cyclopropenes or alkynes using organozinc reagents and nitro compounds.

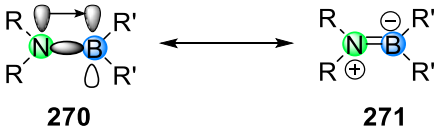
Chapter 3: Investigation of the Reactivity of Aminoboranes

Chapter 3.1: Aminoboration of C-C Multiple Bonds with Nitro Compounds

Introduction

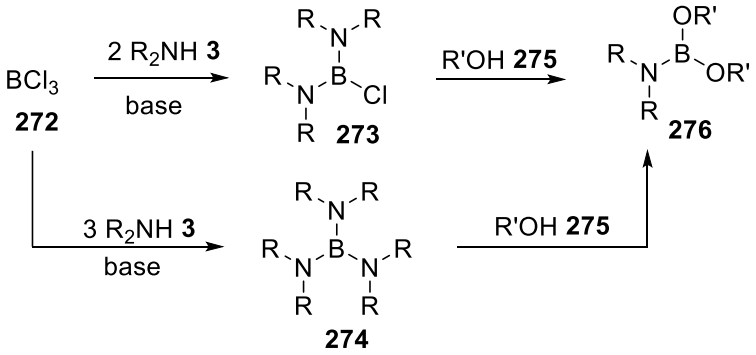
Aminoboranes

Compounds with nitrogen-boron bonds can be distinguished into two classes: aminoboranes, when the bond has a covalent character and amine boranes, which are Lewis-acid-Lewis-base-adducts (e.g.: $H_3N{\bullet}BH_3$).[85] The N-B bond in aminoboranes shows partial double bond properties, due to the delocalization of the free electron pairs of nitrogen on the empty p-orbital of the boron (Scheme 75). Due to their air- and moisture sensitivity, aminoboranes can only be synthesized in solution and are not suitable for isolation.



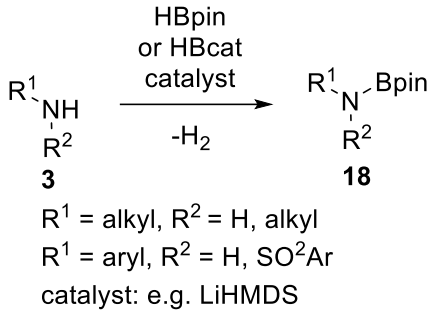
Scheme 75. Mesomeric structure of aminoborane.

One of the initial syntheses involved a stepwise substitution of BCl_3 with a secondary amine **3** (Scheme 76).[27b] The stability of the resulting aminoboranes **273** and **274** can be enhanced by adding alcohol. However, the application of this reaction is limited, and the handling and storage of BCl_3 pose clear disadvantages.



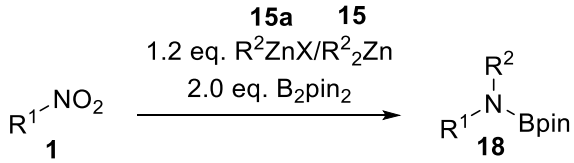
Scheme 76. Synthesis of aminoboranes **276** from BCl_3.

Another approach involves the use of boranes in dehydrocoupling reactions with amines **3**, in the presence of alkali or alkaline earth metal catalysts, to generate aminoboranes **18** (Scheme 77).[27c] While this process offers improved applicability and higher functional group tolerance, it also has its limitations. It only produces the desired product with primary or secondary aliphatic amines, as well as primary anilines or sulfonamides.



Scheme 77. Dehydrocoupling for the synthesis of aminoboranes **18** with pinacolborane.

As discussed in previous chapters, significant progress has been made by *our group* in the synthesis of aminoboranes through a boron-mediated reaction using organozinc compounds.[14] This method provides a distinct advantage in the production of diverse aminoboranes and enables the exploration of their reactivity. In contrast to the moisture-sensitive BCl_3, B_2pin_2 serves as a bench-stable alternative source of boron.

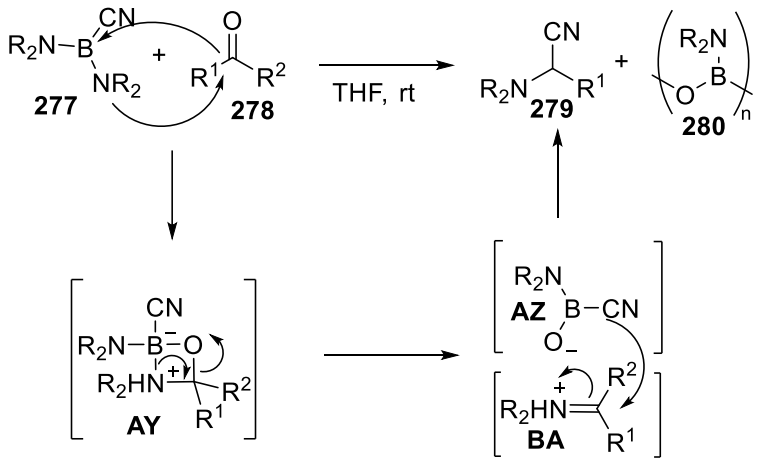


Scheme 78. Synthesis of aminoboranes *via* electrophilic amination with nitro compounds.

Applications of Aminoboranes

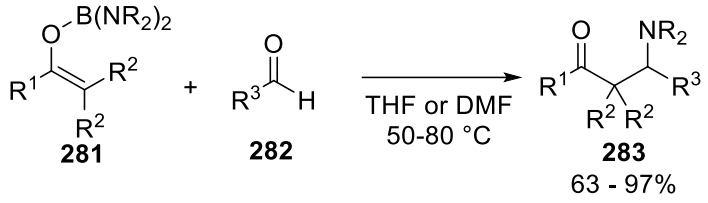
Aminoboranes demonstrate dual reactivity: the amino group can act as a nucleophile, participating in nucleophilic substitution reactions with electrophiles to form new carbon-nitrogen bonds. Additionally, the boron atom in an aminoborane acts as a Lewis acid, accepting electrons from Lewis bases to form coordinate covalent bonds. Despite its versatile reactivity, only a limited number of transformations involving aminoboranes have been reported.

A notable example of aminoborane's reactivity is its ability to serve as an iminium ion generator in amination reactions, as demonstrated by *Suginome et al.*[86] In the Strecker-type aminative cyanation process, the applied aminoboranes react with carbonyl compounds (Scheme 79). The authors propose the formation of a four-membered ring intermediate **AY** that generates the iminium ion **BA**. Subsequently, the boron-bound cyano group attacks the iminium ion, resulting in the formation of α-aminonitrile **279**.



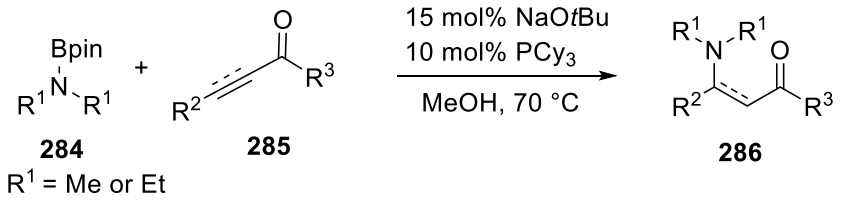
Scheme 79. Strecker-type aminative cyanation with aminoboranes by *Suginome et al*.

Utilizing the reactivity of iminium ions, the same research group reported a Mannich-type reaction (Scheme 80).[86b] The use of bis(dialkylamino)boron enolates **281** affords the β-amino ketones **283** with good to high yields, while the corresponding aldol products were not observed.



Scheme 80. Mannich-type reaction with aminoboranes **281** by *Suginome et al.*

In another study, *Fernández et al.* successfully employed aminoboranes **284** for the amination of α,β-unsaturated carbonyl compounds **285** (Scheme 81).[26b] To enhance the nucleophilic attack of the amine moieties on electron-deficient α,β-unsaturated carbonyl compounds, the activation of aminoboranes **284** is achieved by combining alkoxide and phosphine. Notably, electron-deficient alkynes, including olefins, proved to be suitable substrates even in the absence of phosphine.



Scheme 81. Amination of C-C multiple bonds by *Fernández et al.*

Additionally, the formation of anionic adducts **BB** and **BC** between aminoborane and alkoxylate was confirmed by ^{11}B-NMR measurements (Figure 5).

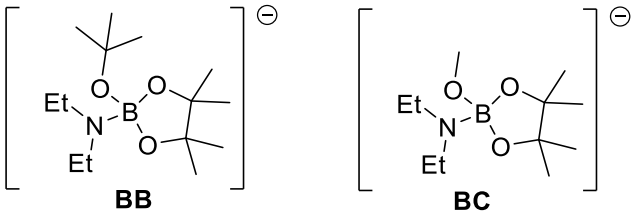
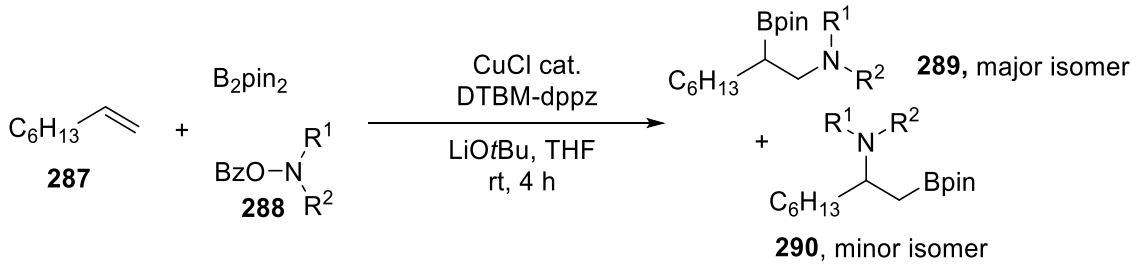


Figure 5. Detected borate complexes **BB** and **BC** by *Fernández et al.*

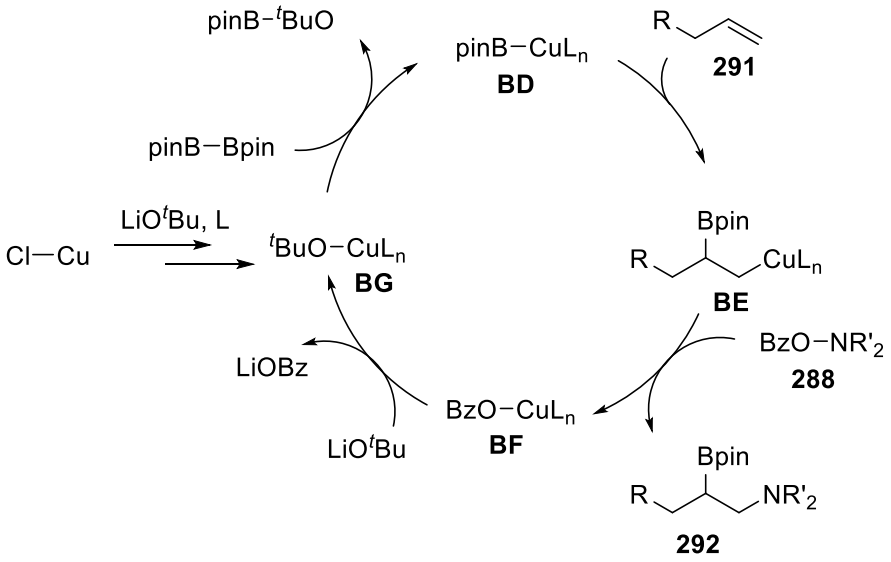
Intermolecular Aminoboration

Aminoboration offers a powerful strategy for the introduction of both amine and boron functionalities into organic molecules enabling the preparation of synthetically important building blocks. Due to the versatile derivatization of the boryl group, such as Suzuki cross-coupling, oxidation and halogenation.[87] In the last two decades, some procedures have been developed for the aminoboration of the C-C multiple bonds.[28d] These can be distinguished between intermolecular aminoboration with external *N*-source and intramolecular aminoboration with amines as substrates. The majority of the reported examples utilize premade, substituted hydroxylamines, while applying diboron compounds as boron sources. The first reported example of intermolecular simultaneous addition of an amino group and boryl group to C-C double bonds was developed by *Hirano* and *Miaura*.[28j] This copper-catalyzed intermolecular aminoboration affords various β-aminoalkylboranes (**289** and **290**) in a regioselective reaction of unactivated terminal alkenes, using bis(pinacolato)diboron and *O*-benzoylhydroxylamines **288** (Scheme 82).



Scheme 82. Cu-catalyzed aminoboration of styrenes **287** by *Hirano* and *Miaura et al.*

The proposed mechanism suggests that the active Cu alkoxide species is generated through a salt metathesis reaction between CuCl and LiO^{t}Bu (Scheme 83). This alkoxide species then undergoes a σ-bond metathesis with B_2pin_2, resulting in the formation of the borylcopper **BD** species. Subsequently, the alkene **291** undergoes a migratory insertion into the borylcopper intermediate **BD**, resulting in the formation of the borylated alkylcopper intermediate **BE**. The overall regioselectivity of the reaction can be controlled in this insertion step. An electrophilic amination with a *O*-benzoylhydroxylamine **288** is then performed, affording the aminoboronated product **292**. The catalytic cycle is completed by regenerating the Cu alkoxide through ligand exchange with LiO^{t}Bu.



Scheme 83. The proposed catalytic cycle of the Cu-catalyzed aminoboration of alkenes by *Hirano* and *Miaura et al.*

This pioneering work was followed by several protcols to extend the applicability of the umpolung-enabled aminoboration catalysis. Strained alkenes such as cyclopropenes, methylencyclopropenes, benzylidenecyclopropenes were transformed into the corresponding borylated cyclopropane-containing alkylamines (**293**, **294**, **295**) (Figure 6).[28e, 28f, 78b] Bicyclic alkenes were also suitable substrates.[28c] Good to high stereochemical control was achieved in the transformation of vinylsilanes and vinylboranes to β-borylated α-aminosilanes and -boranes (**297** and **298**).[28g, 28h]

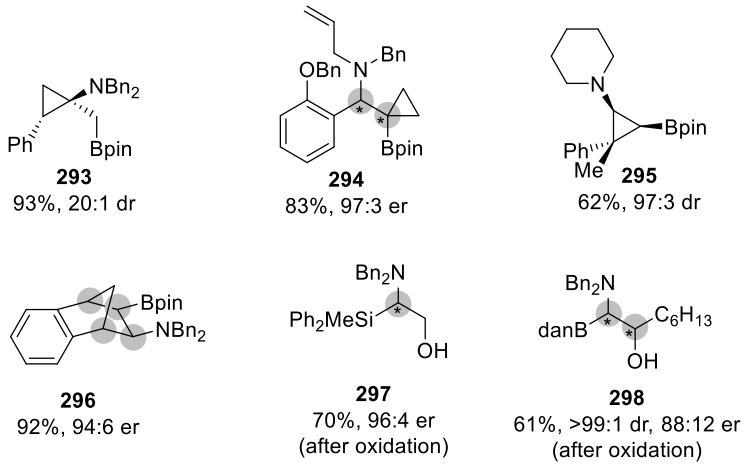
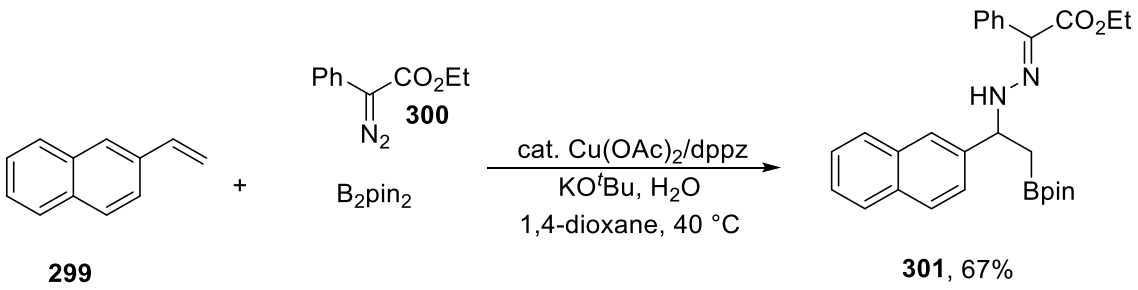


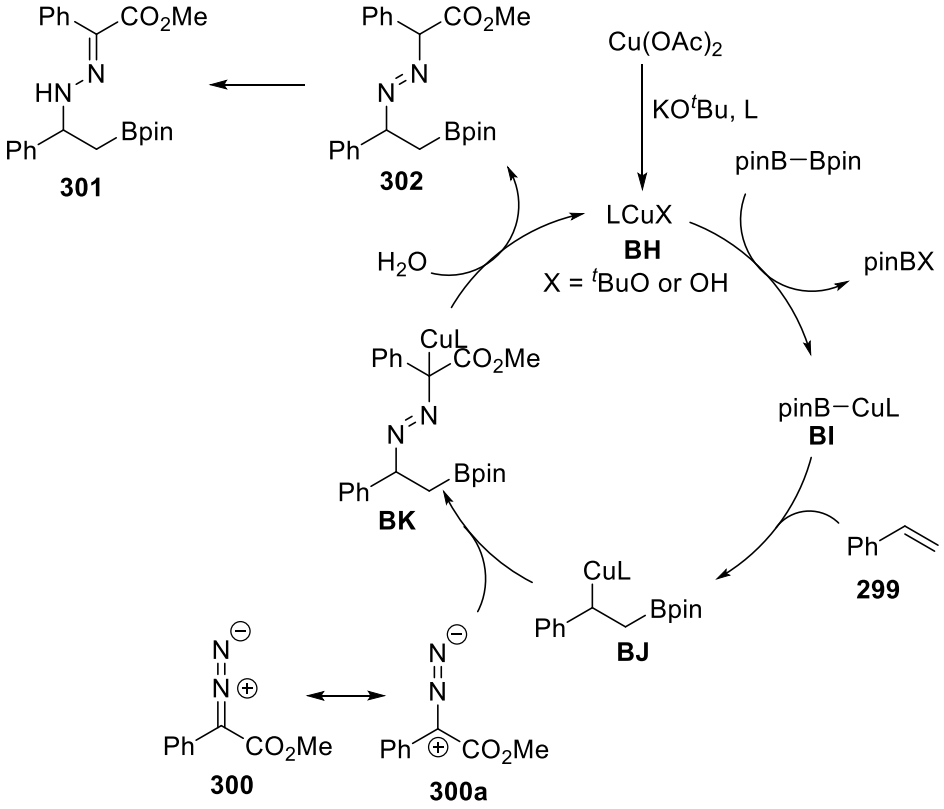
Figure 6. Products of the reported examples for aminoboration.

The majority of the reported copper-catalyzed umpolung-enabled aminoboration reactions have utilized *O*-acylated hydroxylamines **288** as the electrophilic amination reagents. However, there is one exception where diazo ester is combined with B_2pin_2, although the substrates are restricted to electronically activated and sterically accessible terminal styrenes (Scheme 84).[28l]



Scheme 84. Aminoboration of alkenes with diazo esters as electrophilic *N*-source by *Wang et al.*

According to the proposed mechanism, $Cu(OAc)_2$ is first reduced to the active catalyst **BH** in the presence of a ligand and KO^tBu (Scheme 85). The resulting active Cu(I) species **BH** then undergoes transmetalation with B_2pin_2, forming a borylcopper(I) intermediate **BI**. In the subsequent step, styrene **299** inserts into the Cu-B bond, resulting in the formation of the benzylcopper species **BJ**. This intermediate **BJ** is then trapped by the diazo compound **300a**, leading to the formation of intermediate **BK**. Through subsequent protonation and rapid isomerization, the borylated hydrazone product **301** is obtained.



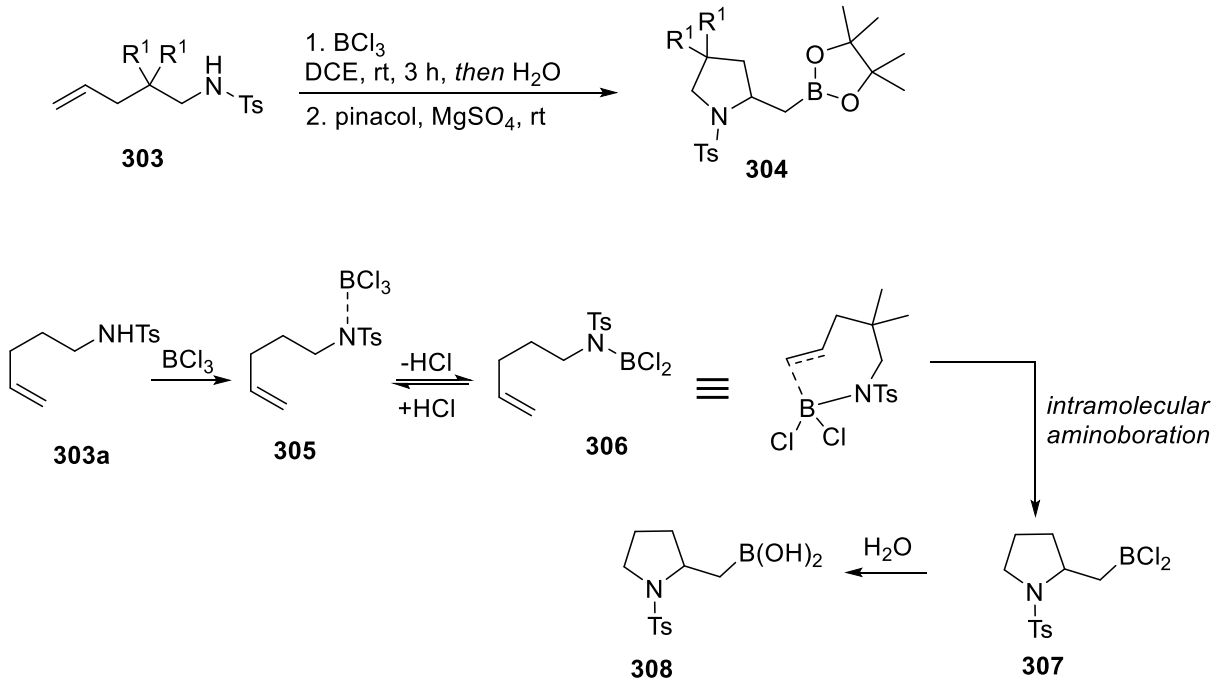
Scheme 85. Proposed mechanism of the aminoboration of alkenes with diazo esters by *Wang et al.*

In the last decades several intermolecular aminoborations have been developed.[28d] However, in all cases, the scope of the hydroxylamines is limited to aliphatic substituents and several challenges remain unsolved, e.g., internally borylated enantioselective aminoboration of terminal alkenes.

Intramolecular Aminoboration

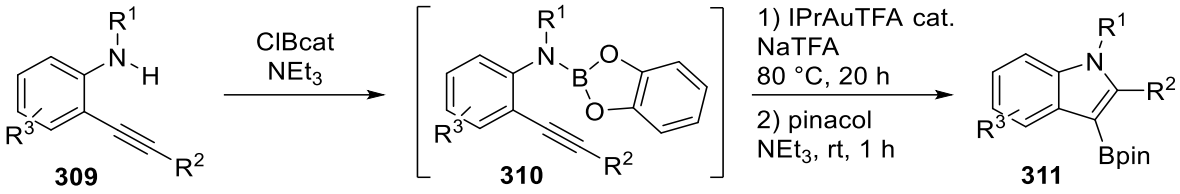
The above discussed studies have explored aminoboration reactions using external electrophilic amine sources. On the other hand, it is also possible to employ alkenes containing amine functionalities as substrates for aminoboration.[22] Nevertheless, only a limited number of intramolecular aminoborations have been reported in the literature. These reactions typically involve amines or hydrazones as substrates, and chlorinated boron compounds are used to introduce the boryl group.

An illustrative example of intramolecular aminoboration is the aminoboration of unactivated olefins, as demonstrated by *Li et al.* (Scheme 86).[22e] In this particular reaction, sulfonamides **303** are transformed into *N*-heterocyclic boronic acids **308** and boronates **304** *via* the proposed reaction pathway. The sulfonamide substrate's nitrogen atom interacts with BCl_3, leading to the formation of an intermediate B-Cl_2 **306** species after HCl elimination. Subsequently, an intramolecular aminoboration, resembling a hydroboration reaction, takes place to provide **307**. Hydrolysis of **307** results in the desired aminoboration product **308**. To enhance product stability, a pinacol ester **304** can be conveniently prepared by treating **308** with pinacol.



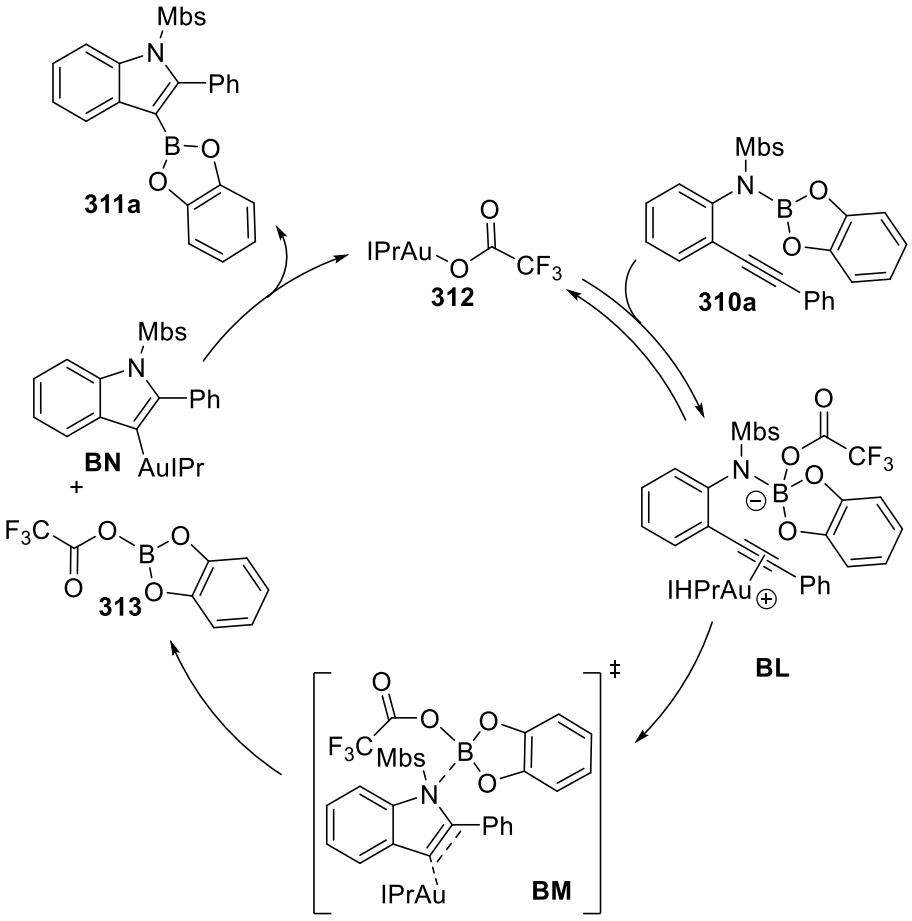
Scheme 86. Intramolecular aminoboration by *Li et al.*

The *Blum group* in 2015 introduced a procedure for intramolecular aminoboration of alkynes in the presence of a gold catalyst (Scheme 87).[22a] The extended tolerance of functional groups is provided by the use of carbophilic gold catalyst and mildly basic medium.



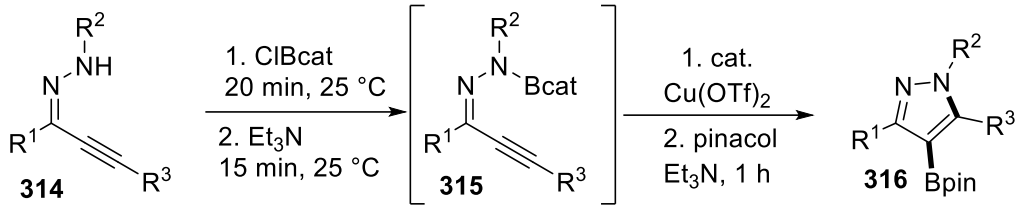
Scheme 87. Gold-catalyzed aminoboration with aminoboranes by *Blum et al.*

The authors claim that, in the catalytic cycle, the potentially bifunctional Lewis acidic/basic catalyst IPrAuTFA **312** and substrate **310a** associate to generate intermediate **BL**, which contains a tetracoordinate borate. Simultaneous activation of the B-N bond and cyclization result in the release of the organogold intermediate **BN** and *B*-(trifluoroacetyl)-catecholborane **313** (Scheme 88). Subsequently, the organogold **BN** species and *B*-(trifluoroacetyl)-catecholborane **313** undergo a Au-B transmetalation to produce the 3-borylated indole product **311a** and regenerate the IPrAuTFA **312** catalyst.



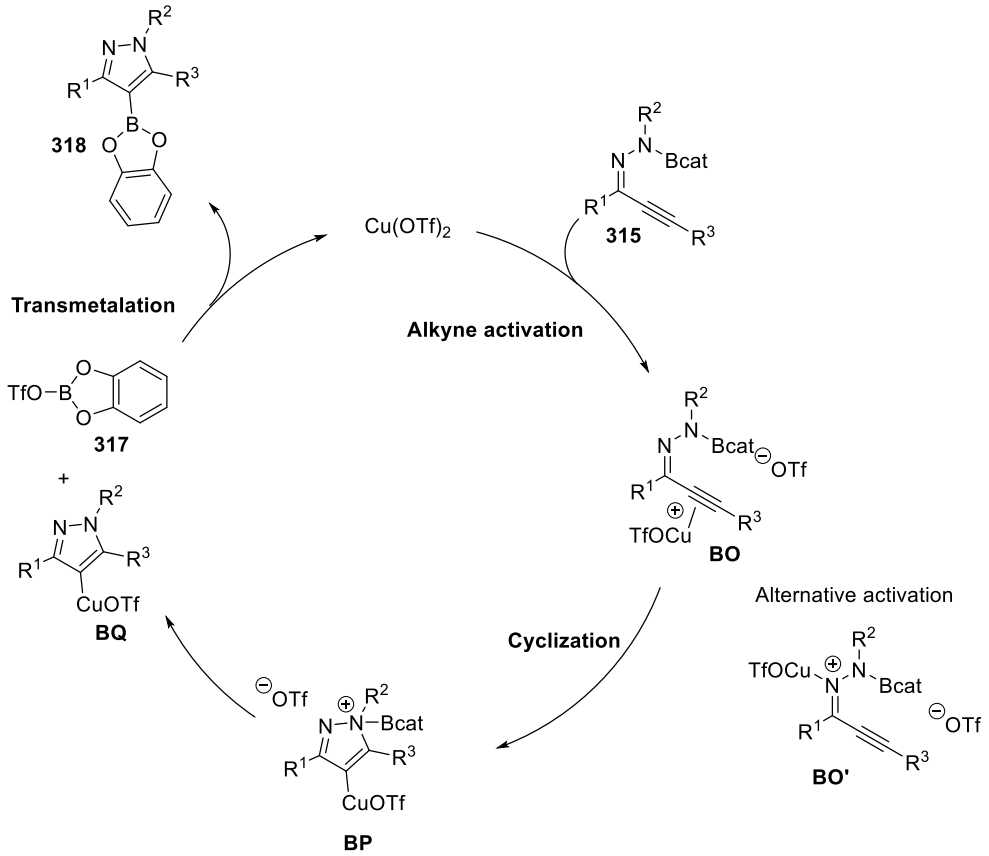
Scheme 88. Postulated mechanism of aminoboration by *Blum et al.*

The *same group* has developed a Cu-catalyzed intramolecular direct aminoboration of hydrazones, leading to the synthesis of borylated pyrazoles (Scheme 89).[22d] The reaction demonstrates high tolerance towards functional groups, such as bromides and thiophenes, that are typically incompatible with other methods and exhibits exclusive formation of a single regioisomer.



Scheme 89. Cu-catalyzed aminoboration to synthesize borylated pyrazoles by *Blum et al.*

In the catalytic cycle, $Cu(OTf)_2$, acting as a Lewis acid, activates the C-C π-bond, to generate the intermediate **BO** (Scheme 90). Subsequently, the N-B σ-bond adds to the C-C triple bond, to form intermediate **BP**. This intermediate **BP** then undergoes separation into a neutral organocopper **BQ** species and an electrophilic boron intermediate **317**. The organocopper species **BQ** is primed for transmetalation with the electrophilic boron compound **317** in the following step, leading to the desired boronate **318** and the regeneration of $Cu(OTf)_2$. Finally, the transesterification of boronate **318** with pinacol affords the corresponding pinacol boronic ester **316**.

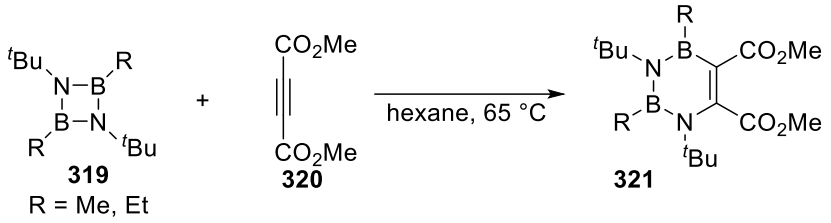


Scheme 90. Proposed mechanism for the Cu-catalyzed aminoboration by *Blum et al.*

In the reported intramolecular aminoboration protocols, the B-N bond is directly added to the C-C double bond. These protocols involve the reaction of amines or hydrazones with chlorinated boron reagents, leading to the formation of aminoboranes. However, it is worth noting that these boron reagents present inherent challenges, primarily due to their high toxicity and sensitivity to moisture. Furthermore, their utilization can impose limitations on the tolerance of functional groups in the reaction.

Concept

As discussed earlier, *Blum et al.* have successfully employed aminoboranes for the direct intramolecular aminoboration of C-C multiple bonds. However, only one intermolecular protocol has been developed for the direct addition of a B-N σ-bond to a C-C π-bond (Scheme 91). This protocol involves the [4+2] cycloaddition of a strained diazaboretidine **319** with dimethylacetylenedicarboxylate **320**, resulting in a heterocycle **321** with limited synthetic utility for subsequent functionalization.[88] In addition, the diazaboretidine aminoboration reagents are synthesized through the cyclodimerization of metastable iminoboranes.[89]



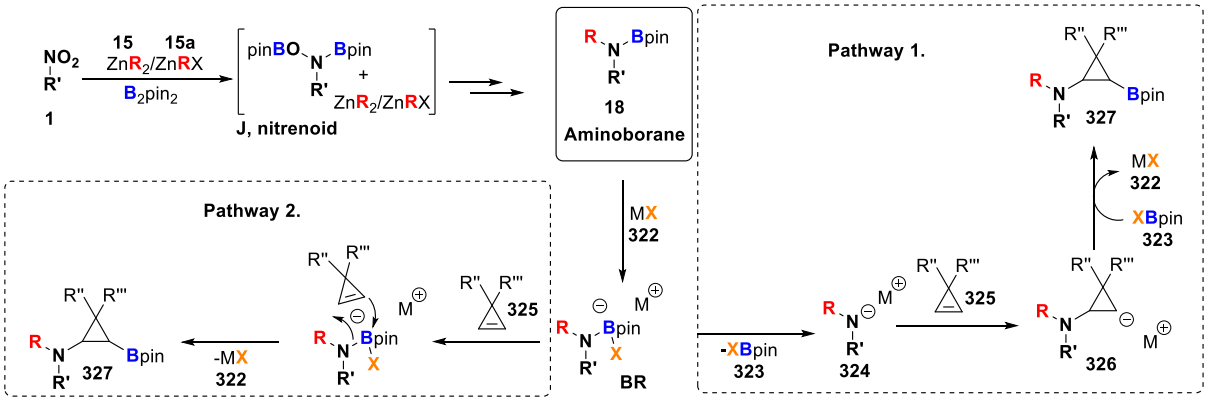
Scheme 91. Addition of B-N σ-bond to C-C π-bond by *Paetzold et al*.

Intermolecular aminoboration methods typically involve the transformation of alkenes or alkynes into borylcopper species, followed by an electrophilic amination step (Scheme 83). However, the electrophilic amination reagents, such as hydroxylamines or diazo esters, are often not commercially available and require synthesis. The hydroxylamines are generally prepared from commercially accessible nitro compounds. Therefore, designing a direct aminoboration method utilizing nitro compounds would be highly advantageous.

Our group has recently made significant progress by developing an electrophilic amination reaction with nitro compounds, leading to the desired amines through the hydrolysis of reactive aminoborane species.[14] This approach may offer a promising opportunity to utilize aminoboranes as both the *N*-source and *B*-source in aminoboration reactions, eliminating the need for additional synthesis of electrophilic amination reagent and relying solely on inexpensive and readily available nitro compounds and B_2pin_2. While nitro compounds were selected as potential coupling partners, cyclopropenes may provide suitable acceptors since they have already been successfully utilized in intermolecular aminoboration reactions.[78b]

The aminoboration protocol described by *Blum et al.* activates both the N-B bond and the C-C multiple bond, facilitating the introduction of the amine and boryl moieties into the alkyne (Scheme 88 and 90). The C-C multiple bond activation is achieved using a Au or a Cu catalyst, while a Lewis acid activator, a metal alkoxide, is employed to activate the B-N bond. Although the proposed mechanism for the addition of the B-N bond suggests the subsequent formation of an organometallic adduct followed by transmetalation with the electrophilic boron reagent, the exact mechanism of the addition is not firmly established.

In analogy, two plausible reaction pathways were proposed (Scheme 92). According to *our protocol* (Chapter I.1), aminoboranes can be obtained from nitro compounds. In the subsequent step, a metal alkoxide **322** can activate the B-N bond of the aminoborane **18**, to form intermediate **BR**. In one possible pathway, intermediate **BR** releases an XBpin moiety **323**, resulting in the formation of the species **324**. This species **324** may then add to the cyclopropene, generating **326**. The XBpin species **323** can subsequently transmetalate with the organometallic species **326**, providing the aminoboration product **327** and regenerating **322**. In an alternative pathway, the nitrogen atom of the adduct **BR** may attack the double bond of the cyclopropene **325**, while simultaneously forming the C-B bond, leading to the desired product **327**. It is worth noting that a strained cyclopropene may serve as a sufficiently reactive alkene partner, potentially eliminating the need for double bond activation. However, employing a catalyst for the activation of the C-C multiple bond may still be necessary.



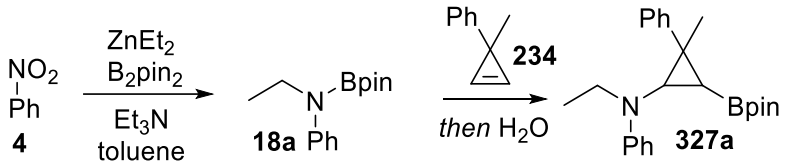
Scheme 92. Proposed aminoboration of cyclopropenes using nitro compounds, organozinc reagents and B_2pin_2.

The utilization of highly functionalized aminoboranes would represent a significant advancement in direct intermolecular aminoboration. This protocol may enable the synthesis of borylated cyclopropylamines using nitro compounds, B_2pin_2, and cyclopropenes.

The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization), *Meike Niggemann* (concept).

Results

The preparation of aminoboranes was carried out according to the protocol of *our group's* protocol.[14] Phenylethylaminoborane **18a** was chosen as the model substrate (Scheme 93), due to the commercially availability of Et_2Zn. The aminoboration of cyclopropene **234** was investigated by treating the *in situ* formed aminoborane **18a** with cyclopropene **234** (Table 27). After aqueous work-up, the mixture was analyzed by ^{1}H-NMR spectroscopy.



Scheme 93. The model substrate and the desired aminoboration product.

In the absence of an additional activator or catalyst, 86% conversion of the nitrobenzene **4** was observed (entry 1), however, only ethylaniline **269** was obtained in 72% yield and the cyclopropylamine **328** in 14% yield. The formation of ethylaniline **269** is not surprising since it easily forms from the hydrolysis of aminoborane **18a**. The presence of the cyclopropylamine **328**, however, may indicate the formation of the desired product **327a**, as it might have been obtained through protodeboronation of **327a**.[90] To avoid the protodeboronation, aminoboration protocols often include the oxidation of the boronic ester moiety to an alcohol, directly converting the aminoboranes into the more stable aminoalcohols.[28] When the reaction mixture was treated with $NaBO_3$ to form the corresponding aminoalcohol, the NMR spectrum was complex and did not provide any evidence for the successful aminoboration.

Since direct aminoboration protocols typically require the activation of the C-C multiple bond, the influence of a Cu-catalyst was examined. The addition of 20 mol% CuCN resulted in full conversion of the nitrobenzene, affording ethylaniline **269** in 78% yield and aniline **5** in 22% yield (entry 2). Despite the full consumption of the nitro compound, not even cyclopropylamine **328** was formed.

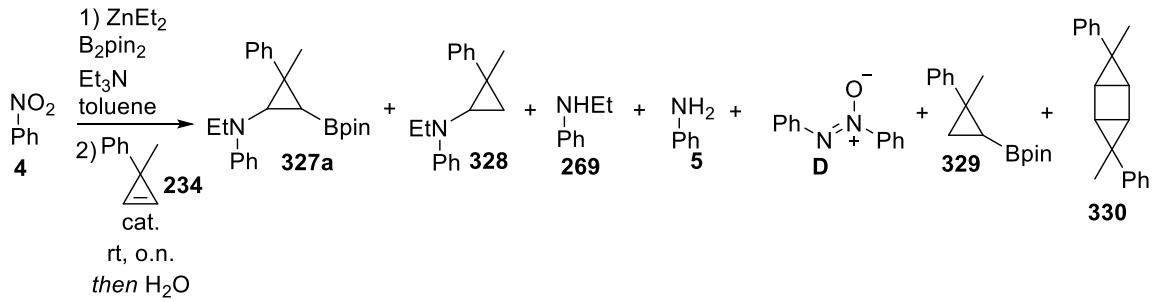
The activation of the B-N bond in aminoboration approaches is usually induced by an alkoxide, such as KO^{t}Bu, NaO^{t}Bu or LiO^{t}Bu.[41] Although Et_3N and the organozinc reagent can activate the B-N bond, the impact of additional activators was investigated. The presence of additional KO^{t}Bu only slightly decreased the yield of ethylaniline **269** but did not produce the desired product **327a** (entry 3). Other Lewis acids, including CsF, NaOMe, and LiOMe, were unsuccessful in facilitating the aminoboration of cyclopropene **234** (entries 4-7). When the reaction was carried out in the presence of NaOMe and Cu-catalyst no desired product **327a** was obtained, only the formation of ethylaniline **269** in 46% yield and azoxybenzene **D** in 20% yield was observed (entry 8).

Increasing the temperature to 50 °C provided cyclopropylamine **328** in 19% yield, also ethylaniline **269** in 70% yield and traces of azoxybenzene **D** (entry 9). Under these reaction conditions, the hydroboration of cyclopropene **234** occurred.[91] At 100 °C, nitrobenzene was fully converted into cyclopropylamine **328** (18% yield) and ethylaniline **269** (82% yield) (entry 10). The higher temperature favored the hydroboration

of the cyclopropene since at 100 °C 80% of the cyclopropene **234** was converted into cyclopropylboronate **329**.

In comparison to the catalyst-free attempts, the addition of CuCN did not affect the reaction at 50 °C (entry 6). Similar outcomes were observed when 2 and 3 equivalents of cyclopropene **234** was used, as the additional substrates impaired the electrophilic amination. This resulted in the cyclopropylamine **328** in 18% yield, ethylaniline **269** in 52% yield and 62% yield, respectively (entries 12 and 14). Implementing a one-pot procedure increased the yield of cyclopropylamine **327a** to 25% and decreased the yield of ethylaniline **269** to 35% (entry 13). However, the conversion reached a plateau at 61%.

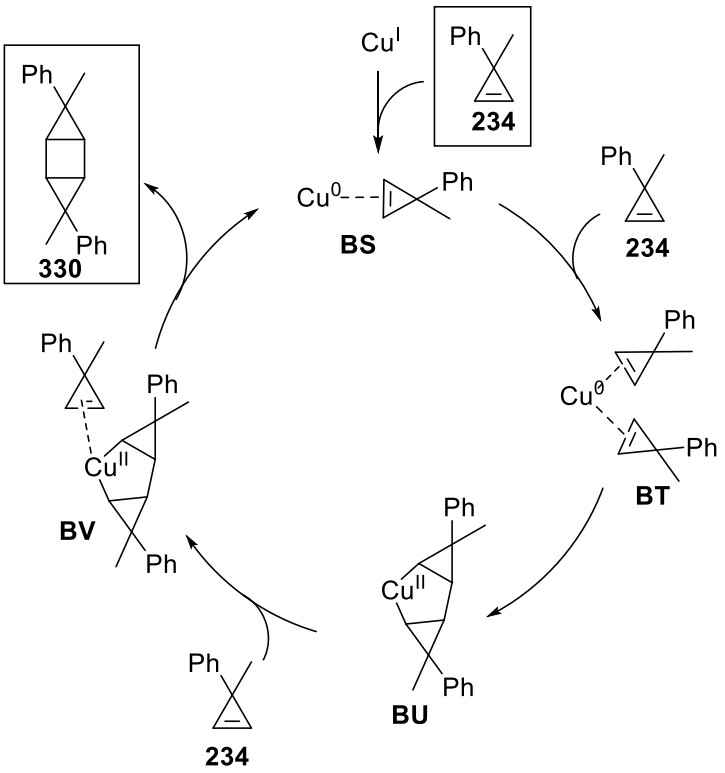
Table 27. Optimization of the aminoboration of the cyclopropene **234**.



Entry	Eq. **234**	Catalyst	Additive/ Ligand	Conv. [%]	**327a** [%]	**328** [%]	**269** [%]	**5** [%]	**D** [%]	**329**[a] [%]	**330**[a] [%]
1	1	-	-	86	0	14	72	0	0	5	86
2	1	CuCN (0.2)	-	100	0	0	78	22	0	0	70
3	1	-	KO^{t}Bu (2)	76	0	0	54	22	0	0	17
4	2	-	CsF (2)	55	0	5	55	0	0	5	90
5	2	-	KO^{t}Bu (2)	95	0	0	95	0	0	0	90
6	2	-	NaOMe (2)	99	0	0	99	0	0	0	0
7	2	-	LiOMe (2)	72	0	19	53	0	0	0	10
8	2	CuCN (0.2)	NaOMe (2)	66	0	0	46	0	20	0	10
9[b]	1	-	-	93	0	19	70	0	4	13	33
10[c]	1	-	-	100	0	18	82	0	0	80	9
11[b]	1	CuCN (0.2)	-	97	0	11	72	0	15	13	58
12	2	-	-	70	0	18	52	0	0	0	45
13[d]	2	-	-	61	0	25	35	0	3	17	5
14	3	-	-	80	0	18	62	0	0	0	8
15[b]	1	CuCl (0.2)	Xantphos (0.2)	87	0	12	75	0	0	74	14
16	2	CuCN (0.2)	-	100	0	17	70	0	13	5	42
17	2	CuI (0.2)	-	70	0	15	52	0	4	29	45
18	2	CuCN (0.2)	Phenantroline (0.2)	88	0	23	50	0	18	40	40
19	2	CuCN (0.2)	Bipy (0.2)	100	0	17	83	0	0	42	42

Conditions: nitrobenzene (0.02 mL, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were dissolved in 1 mL toluene. The mixture was degassed three times and flushed with argon. Et_3N (0.06 mL, 0.4 mmol, 2.0 eq.) and Et_2Zn (1 M solution in hexane, 0.24 mL, 0.24 mmol, 1.2 eq.) were added and the mixture was stirred for 5 hours. Then a solution of cyclopropene (35 mg, 0.2 mmol, 1.0 eq. in 0.5 mL toluene) was added. The mixture was stirred overnight at rt; [a] conversion from cyclopropene; [b] after addition of cyclopropene 50 °C; [c] after addition of cyclopropene 100 °C; [d] cyclopropene from the beginning.

The use of other Cu-salts, such as CuCl and CuI, did not result in the desired product **327a** or improved the yield of cyclopropylamine **328** (entries 15-19). Instead, the tested Cu-catalysts with the ligands increased the yield of the borylated cyclopropane **329** and had only a slight effect on the aminoboration reaction.

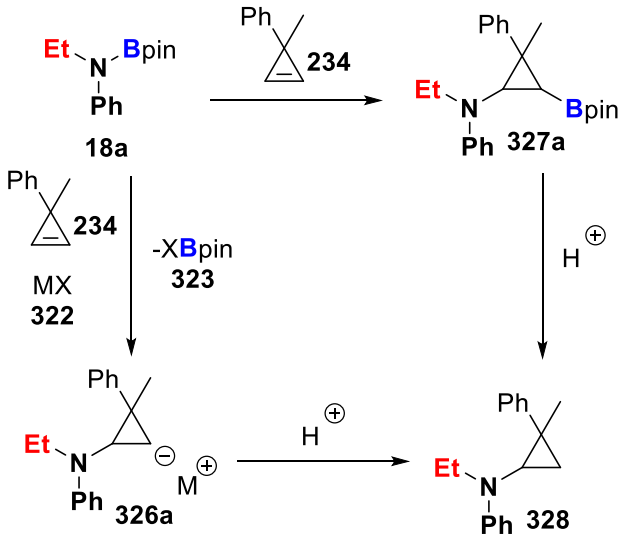


Scheme 94. Proposed mechanism for the formation of side product **330** *via* Cu-catalyzed formal [2+2] cycloadditon.

In most cases, the dimerization of cyclopropene **234** occurred, likely *via* a Cu-catalyzed formal [2+2] cycloaddition (Scheme 94).[92] Dimerization is one of the most common side reactions in transition metal-catalyzed reactions with cyclopropenes.[78c] Typically, this challenge is overcome by performing reactions at lower temperatures and with the addition of MeOH. However, this solution was not feasible for the designed system because aminoboranes are highly reactive towards protic solvents and undergo rapid hydrolysis.

Summary – Direct Aminoboration of C-C Multiple Bonds

In this study, a direct aminoboration of C-C double bonds using aminoboranes has been investigated. The protocol of *our group* was applied to afford the aminoborane **18a** from nitrobenzene in a boron-mediated electrophilic amination, while cyclopropene **234** served as an acceptor. Although, direct aminoboration procedures often require the activation of the B-N bond and/or the C-C multiple bond, the examined aminoborane **18a** readily reacted with cylopropene **234** in the absence of an additional activator or a catalyst. While in several cases cyclopropylamine **328** was obtained, the exact origin of this species has not been clarified. One possibility is the protodeboronation of the desired cyclopropylaminoboronate product **327a**, as the reaction mixture was analyzed after aqueous work-up. Despite the reported stability of these compounds during aqueous work-up and column chromatography, their potential to undergo protodeboronation cannot be excluded. Another hypothesis suggests the formation of an intermediate **324** from the aminoborane **18a**, which subsequently reacts with cyclopropene **234** without further borylation of **326** (Scheme 95).



Scheme 95. Plausible pathways for the formation of the cyclopropylamine **328**.

The tested metal-alkoxides as activators of the B-N bond and Cu-salts did not provide the desired aminoboration product **327a**, only resulting in the formation of the cyclopropylamine **328**. In some cases, a Cu-catalyzed hydroboration of cyclopropene **234** was obtained.[91] As commonly observed in transition-metal catalyzed reactions involving cyclopropenes, the dimerization of a cyclopropene poses a significant challenge. The mechanism of this dimerization is typically a formal [2+2] cycloaddition in the presence of a transition-metal catalyst (Scheme 94), while the uncatalyzed generation of the dimer **330** remained unclarified.

Chapter 3.2: Synthesis of α-Borylated Amines

Introduction: α-Borylated Amines

Organoboron compounds play a pivotal role in various fields, including organic synthesis, material science, and drug discovery.[93] Among them, the α-aminoboronic acids and their derivatives represent a unique class of compounds that serve as analogs of α-amino acids.[94] Bortezomib **331**, the first boronic acid-containing compound and proteasome inhibitor, gained FDA approval in 2004 for the treatment of multiple myeloma and mantle cell lymphoma (Figure 7).[94a] Additionally, certain α-aminoboronic acids have exhibited antibacterial activity, while others show selective and potent inhibition of dipeptidyl peptidase.[94b,94c,94d,94e] The intramolecular coordination of boron with nearby heteroatoms has been found to play a crucial role in determining biologically active conformations.[94f] The coordination of the nitrogen atom to boron atom negatively impacts binding affinity to biological targets, which can be attributed to conformational changes and the mediation of Lewis acidity.

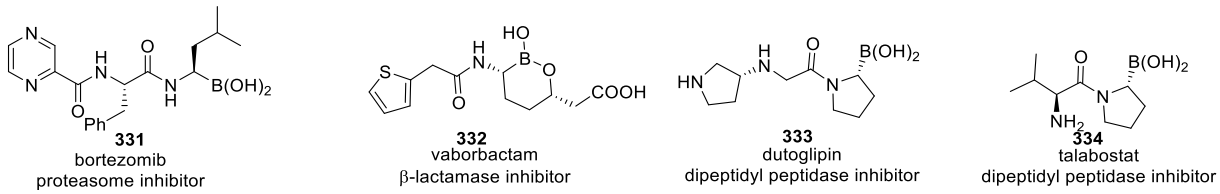


Figure 7. Examples for biologically active α-aminoboronic acids.

The significant role of α-aminoboronic acids was also reported in material science by the *Wang* group.[95]These first water-soluble and stable α-aminoboronic acid carbohydrate sensors showed significant fluorescence change upon binding with glucose, sorbitol and fructose (Figure 8).

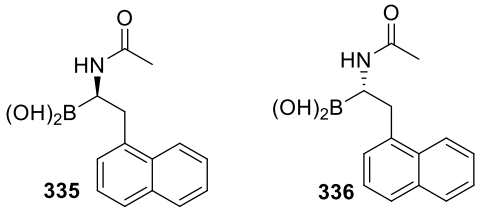
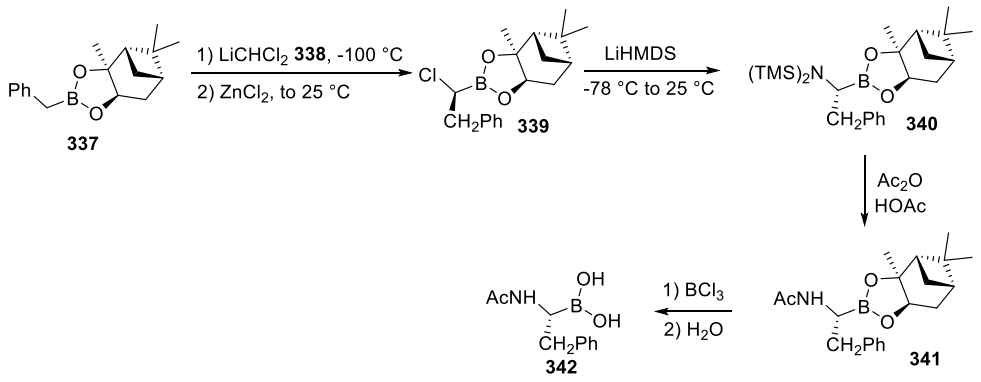


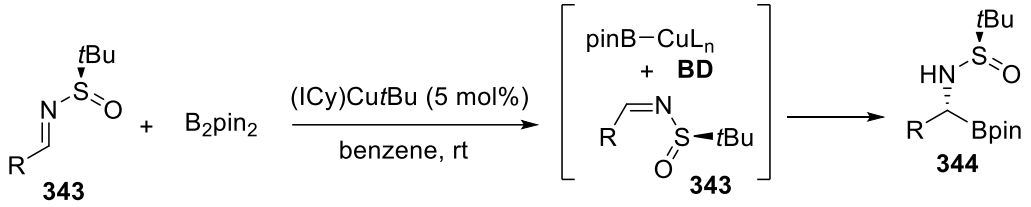
Figure 8. α-aminoboronic acids that serve as carbohydrate sensor.

Considering the demonstrated activity of α-aminoboronic acids, several procedures have been developed for their synthesis and the production of their derivatives. The initial preparation of α-aminoboronic acids was reported by *Matteson et al.* and has since found widespread use in both industry and academia.[96] According to the protocol, enantioenriched α-chloroboronates **339** are generated from boronic esters with a chiral pinandiol auxiliary **337** *via* diastereoselective homologation (Scheme 96). The α-chloroboronates **339** are then treated with LiHMDS to yield the α-aminoboronates **341**. This approach was also employed in the enantioselective synthesis of Bortezomib **331** from isobutylboronic acid.



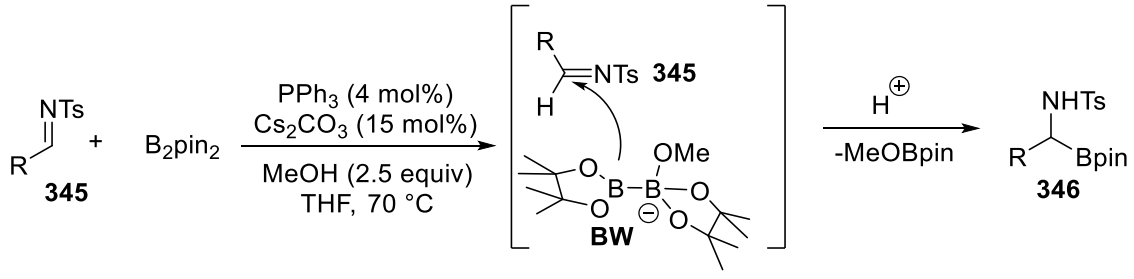
Scheme 96. Diastereoselective homologation by *Matteson et al.*

An alternative method widely employed for the preparation of α-aminoboronates involves the formation and use of a nucleophilic boron species, such as hydroboration, hydroamination and aminoboration. [28,97,98] The reported procedures transform imines, alkenes and alkynes into α-aminoboronates. The following examples shall represent the concept of these methods. *Ellmann et al.* reported a copper-catalyzed hydroboration protocol, wherein *N*-tert-butanesulfinyl aldimines **343** are converted into α-amino boronates **345** through an asymmetric synthesis (Scheme 97).[97b] The proposed mechanism follows the conventional hydroboration pathway of multiple bonds. Initially, a borylcopper(I) **BD** species is formed, followed by imine insertion into the Cu-B bond. After hydrolysis, the desired α-amino boronate **344** is obtained.



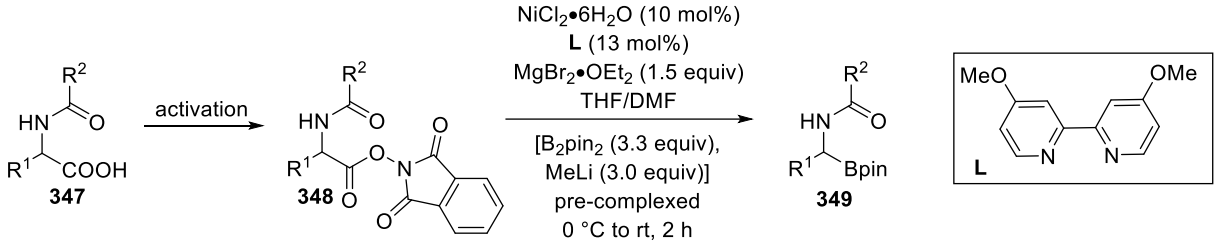
Scheme 97. A Cu-catalyzed hydroboration of aldimines **343** by *Ellmann et al.*

Furthermore, *Fernández et al.* reported a transition metal-free reaction for the hydroboration of imines (Scheme 98).[97d] In this method, the *in situ* activation of B_2pin_2 is achieved by adding an alkoxide anion to form **BW**. Tosylaldimines **345** are then transformed into the corresponding α-amino boronates **346** through an organocatalytic process.



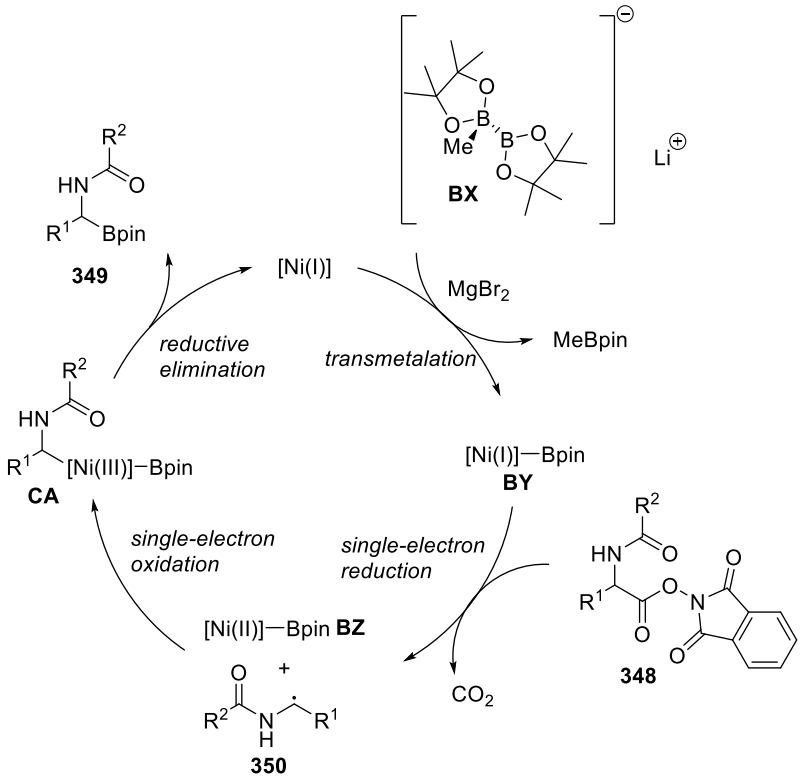
Scheme 98. Hydroboration of imines by *Fernández et al.*

Baran et al. developed a unique and conceptually different synthesis for α-aminoboronates through a Ni-catalyzed decarboxylative borylation of *N*-hydroxyphthalimides **348**, to afford valuable alkyl boronic esters **349**.[99] When native peptides are used as substrates, a range of diverse α-aminoboronates, including biologically active compounds like bortezomib and ixazomib, can be obtained (Scheme 99).



Scheme 99. Synthesis of α-aminoboronates *via* decarboxylative borylation by *Baran et al.*

Although the authors did not provide a detailed mechanism, a plausible catalytic cycle can be proposed based on the Ni-catalyzed Miyaura borylation of alkyl halides and the Ni-catalyzed C-C cross-coupling of alkyl NHPI esters (Scheme 100).[100,101,102]



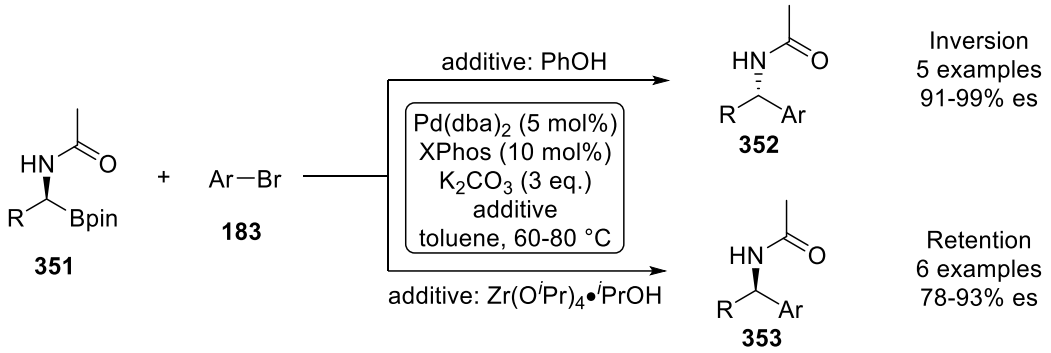
Scheme 100. Plausible mechanism for the decarboxylative borylation by *Baran et al.*

The process likely involves the transient Ni^{I} species interacting with activated $[MeB_2pin_2]Li$ **BX** in the presence of Lewis acid $MgBr_2$, completing the transmetalation process and resulting in the formation of $[Ni^{I}]$-Bpin species **BY**. Subsequently, the alkyl radical **350** may be generated *via* a single-electron reduction of alkyl NHPI esters, leading to the concomitant formation of $[Ni^{II}]$-Bpin species **BZ** and CO_2. A subsequent single-electron oxidative process may enable the recombination of the alkyl radical **350** with

[Ni^{II}]-boryl species **BZ**, generating the alkyl-[Ni^{II}]-Bpin complex **CA**. This complex may then undergo reductive elimination, producing the α-aminoboronate product **349** and regenerating the active [Ni^{I}] catalyst.

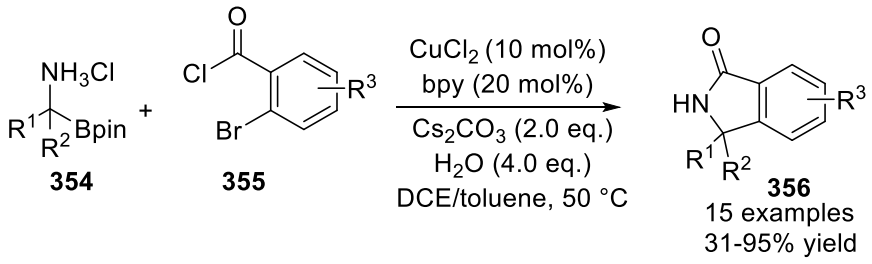
Synthetic Applications

α-Aminoboronic acids and their derivatives have proven to be highly valuable building blocks in organic synthesis due to their versatility.[103] The presence of two easily modifiable functional groups (N- and B-side) in α-aminoboronic acids and their ester analogs has expanded their application in synthetic chemistry over the past few decades. Ohmura, Suginome, and co-workers reported a stereoselective Suzuki-Miyaura coupling of enantiopure α-aminoboronates (**352** or **353**) with aryl bromides or chlorides (Scheme 101).[103a] By selecting the right additives, it is possible to achieve either retention or inversion of the configuration during the coupling process.



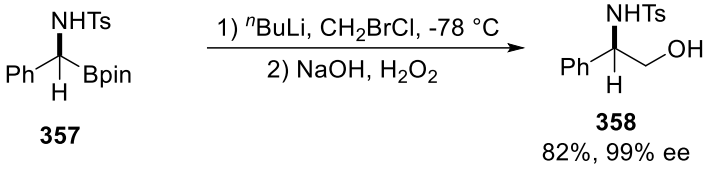
Scheme 101. Pd-catalyzed asymmetric Suzuki-Miyaura coupling of α-(acylamino)boronic esters **351** by *Ohmura* and *Suginome et al.*

α-Aminoboronates are highly intriguing compounds, primarily due to their distinctive feature of possessing geminal nucleophilic centers. Leveraging the inherent bis-nucleophilicity arising from both the nitrogen atom and the C–B bond, *Dumas et al.* accomplished a domino amination/arylation reaction utilizing α-aminoboronates **354** in conjunction with 2-bromobenzoyl chlorides **355** (Scheme 102).[103b] This coupling leads to the efficient synthesis of isoindolinones **356**, showcasing the synthetic utility and potential applications of α-aminoboronates in complex molecular transformations.



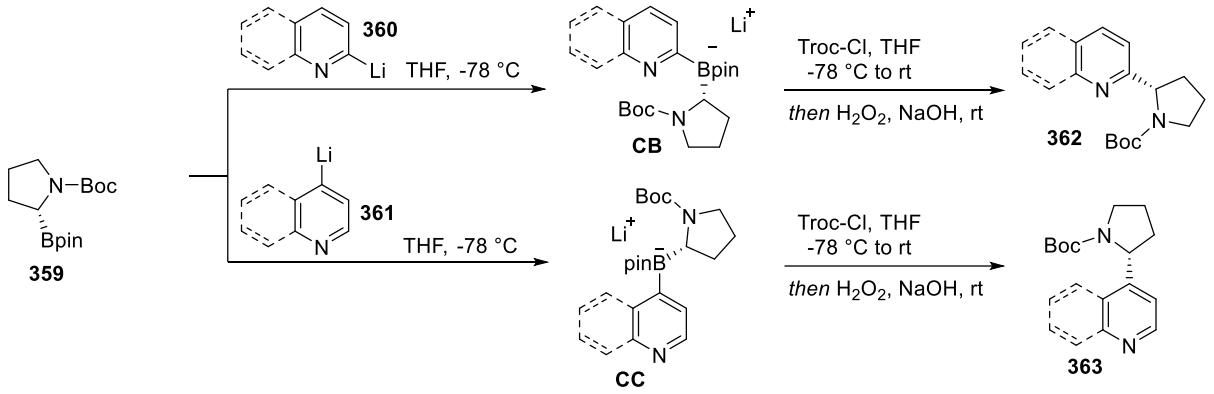
Scheme 102. α-aminoboronic esters as bis-nucleophiles in the synthesis of isoindolinones **356** by *Dumas et al.*

Fernández et al. described a protocol wherein α-aminoboronates **357** are converted into 1,2-aminoalcohols **358** (Scheme 103).[97d] The synthesis involves a homologation step using ^{n}BuLi and bromochloromethane, followed by an oxidation using NaOH/H_2O_2.



Scheme 103. Homologation for the synthesis of 1,2-aminoalcohols **358** by *Fernández et al.*

Aggarwal et al. developed a transition metal-free stereospecific coupling method for chiral cyclic α-aminoboronic esters **359** with lithiated *N*-heteroaromatic compounds **360** or **361** (Scheme 104).[103c] When the formed boronate complexes (**CB** and **CB**) are treated with 2,2,2-trichloroethyl chloroformate (Troc-Cl) a 1,2-migration occurs. Subsequent oxidative work-up leads to the formation of coupling products (**362** and **363**) with excellent stereospecificity.

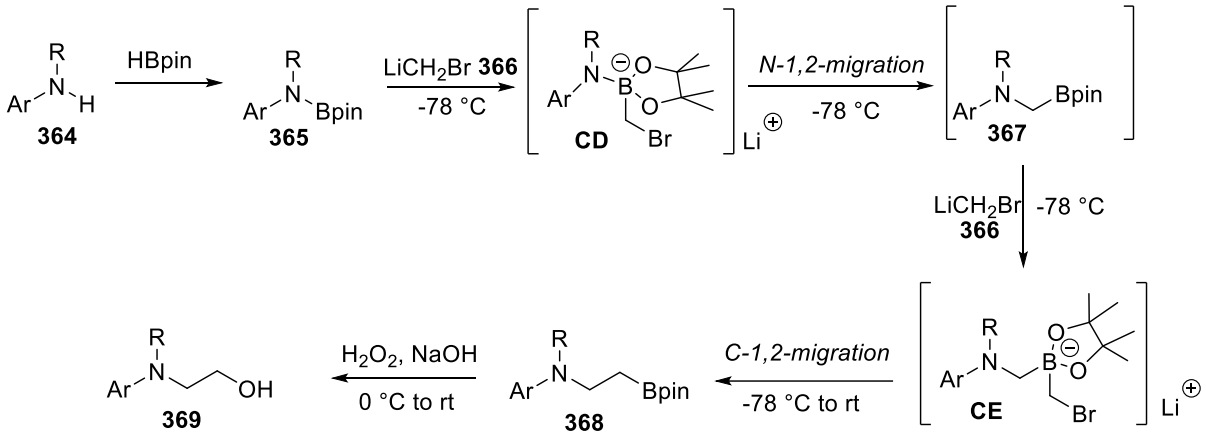


Scheme 104. Enantioselective coupling of α-aminoboronic esters with *N*-heteroaromatic compounds by *Aggarwal et al.*

While C-4 lithiated pyridines exhibit broad applicability in the coupling reaction, the use of 2-lithiopyridine **360** is somewhat restricted to tertiary boronic esters. This limitation may be attributed to increased steric hindrance around the nitrogen of the boronate complex **CB**, which may inhibit the acylation process and leads to unsuccessful transformations.

Concept

As previously discussed, α-aminoboronates hold significant importance in the fields of material science and pharmaceuticals.[87c] Moreover, they are emerging as valuable precursors in organic synthesis, owing to their bifunctional nature that allows for a wide range of transformations. While α-aminoboronates and aminoboranes share similarities in terms of containing amino and boryl groups, their distinction lies in the relative positioning of these functional groups. Aminoboranes possess a B-N bond, whereas α-aminoboronates feature an N-C-B skeleton. Exploiting this distinction, aminoboranes present promising candidates for the synthesis of α-aminoboronates, as the insertion of a methylene group into the B-N bond (homologation) of an aminoborane may provide the desired α-aminoboronate. Recently, *Xie* and *Dong* reported an aza-Matteson homologation reaction of aminoboranes (Scheme 105).[104] Aminoboranes **365** are prepared by treating anilines **364** with HBpin at 120 °C. According to the proposed mechanism, the boron center of aminoborane **365** is attacked by $LiCH_2Br$, forming borate complex **CD**. This intermediate undergoes *N*-1,2-migration to afford the mono insertion species **367**. A second homologation occurs using $LiCH_2Br$, while the mono insertion product is obtained with $LiCH_2Cl$ in the presence of $MgBr_2$. Following the second addition of the organometallic reagent to the boryl moiety and C-1,2-migration, β-aminoboronates **368** are formed. Due to their sensitivity to air and moisture, further transformations of these compounds, such as oxidation, amination, or Suzuki coupling with aryl halides, are required.



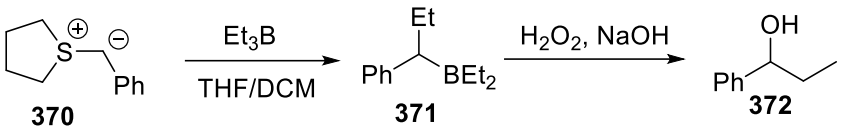
Scheme 105. Aza-Matteson homologation by *Xie* and *Dong*.

Despite the elegant and efficient synthesis of α-aminoboronates, the current protocol remains limited to glovebox conditions due to the relatively unstable nature of the products. Moreover, the synthesis of aminoboranes from anilines and HBpin adds complexity and reduces step economy, as anilines are typically derived from nitro compounds. To address these limitations and enhance step economy, a synthesis of α-aminoboronates directly from nitro compounds would be highly advantageous, leveraging the appealing homologation strategy developed by *Xie* and *Dong*.

Recently *our group* reported an electrophilic amination involving the formation of aminoboranes from nitro compounds in the presence of an organozinc species and B_2pin_2.[14] Instead of utilizing CH_2BrLi/CH_2ClLi as a carbenoid, which may lead to undesired side reactions due to its concurrent

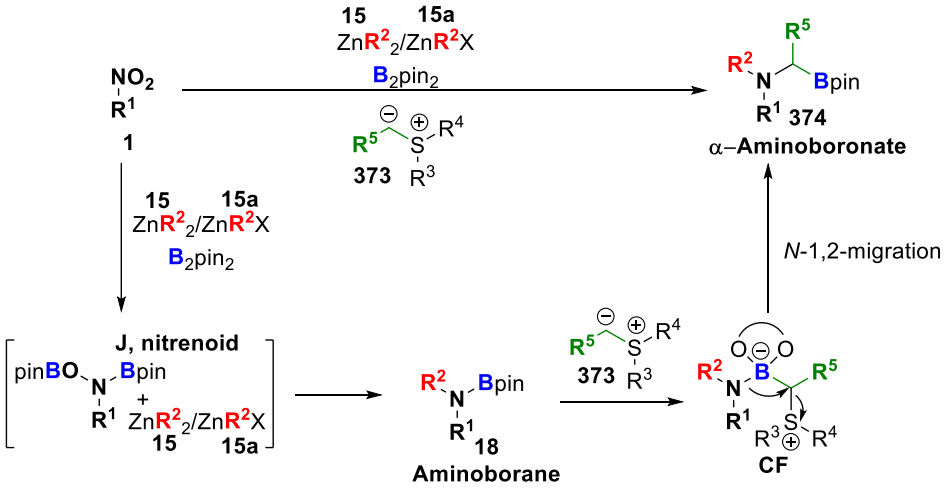
reactivity with the organozinc reagent in electrophilic amination, the use of ylides as a homologation reagent was envisioned.[105] Ylides possess nucleophilic character and exhibit a favorable leaving group on the nucleophilic carbon atom, enabling a 1,2-metalate rearrangement. Among the various types of ylides (S-, N-, and P-ylides), sulfur ylides demonstrate the most suitable leaving group for an efficient 1,2-metalate rearrangement.[106]

Among others, *Aggarwal et al.* have reported a homologation reaction of boranes using aryl-stabilized sulfur ylides (Scheme 106).[105a] The protocol involves the reaction of trialkyl/triaryl borane with the sulfur ylide **370**, leading to the formation of homologated borane **371**, which can subsequently be converted into the corresponding alcohol **372**.



Scheme 106. Homologation of boranes with sulfur ylide **370** by *Aggarwal et al.*

According to our working hypothesis, the transformation of a nitro compound into an aminoborane **18** is followed by a potential homologation step using a sulfur ylide **373**, which may lead to the formation of an α-aminoboronate **374** (Scheme 107). In more detail, the nucleophilic carbon center of the sulfur ylide **373** may attack the electrophilic boron center of the aminoborane **18**, resulting in the formation of borate intermediate **CF**. However, the repulsion between the lone pair of electrons on the nitrogen atom and the vicinal formal negative charge on the boron atom may destabilize the borate intermediate **CF**. Exploiting the favorable leaving group properties of the sulfur ylide **373**, the borate **CF** may undergo a spontaneous *N*-1,2-migration, facilitating the generation of the desired α-aminoboronate **374**.



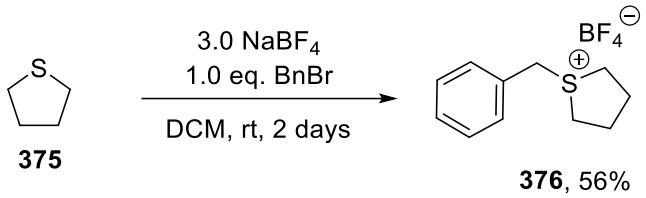
Scheme 107. Proposed mechanism for the synthesis of α-aminoboronates *via* electrophilic amination with nitro compounds followed by a homologation.

The following people have contributed to this research: *Peter Palchuber* (concept, development, optimization), *Meike Niggemann* (concept).

Results

Synthesis of the Sulfonium Salt

The *in situ* preparation of ylides proceeds *via* deprotonation of a sulfonium salt. The sulfonium salt was prepared prior according to the procedure of *Aggarwal et al*. The benzylation of tetrahydrothiophene **375** was achieved by applying benzyl bromide and sodium tetrafluoroborate with 56% yield (Scheme 108).[107]



Scheme 108. Synthesis of the sulfonium salt **376** by *Aggarwal et al.*

Optimization of the Reaction Parameters

In order to address the limitations of Xie and Dong's approach[104], which necessitates the direct transformation of α- and β-aminoboronates under glovebox conditions, the selection of a suitable nitro compound and/or organozinc reagent is crucial. The stability of α-aminoboronates relies on the nature of their substituents, wherein a carbonyl or a sulfoxide group can contribute to the internal stabilization by donating electrons to the vacant p-orbital of the boron center in the boronate **351** and **341** (Figure 9).[97b, 98a] Alternatively, the presence of an *N*-heterocycle at the α-position of the amine moiety can offer stabilization through coordination.[97c]

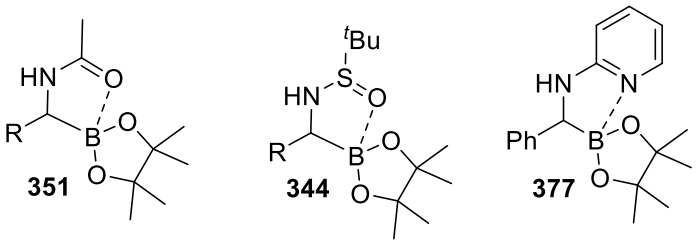
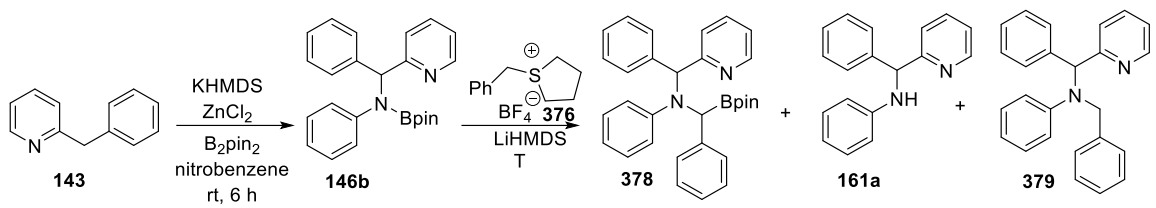


Figure 9. Stabilization of α-aminoboronates.

In order to obtain aminoboranes with heterocyclic substituents, the C-H amination protocol developed in Chapter 1.3 seemed to be ideal. As a model substrate, 2-benzylpyridine **143** was selected to serve as the precursor for the organozinc reagent, while nitrobenzene was utilized as the nitrogen source. The sulfur ylide **370** was employed as a reagent for the homologation reaction (Table 28). To generate the sulfur ylide **370** *in situ*, the sulfonium salt **376** was treated with LiHMDS.[105a] Subsequently, the aminoborane, is obtained *via* the boron-mediated electrophilic amination reactions (Chapter 1.3), was subjected to reaction with the sulfur ylide **370** at a temperature of -78 °C. To prevent potential protodeboronation, the reaction mixture was carefully filtered through a short plug of Celite after the specified reaction time, and the resulting mixture was further analyzed using ^{1}H-NMR spectroscopy.

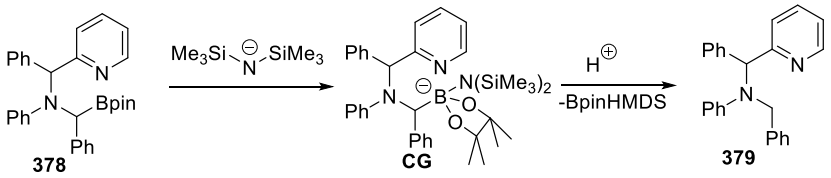
Table 28. Optimization of the α-aminoboronate synthesis.



Entry	T [°C]	Solvent	Conversion [%]	**378** [%]	**161a** [%]	**379** [%]
1	-78	THF	100	0	100	0
2	rt	THF	94	0	21	73
3[a]	rt	THF	92	0	20	72
4[b]	rt	THF	93	0	22	73
5[c]	rt	THF	84	0	45	39
6[d]	rt	THF	100	0	13	87
7[e]	rt	THF	100	0	5	95
8[e]	rt	CPME	100	0	5	95
9[f]	rt	CPME	100	0	0	100

Conditions: mixture A: 2-benzylpyridine (0.064 mL,0.4 mmol, 2.0 eq.) was dissolved in solvent (1 mL), the solution was degassed three times. Subsequently KHMDS (1.7 mL, 1.2 mmol, 6.0 eq., 0.7 M in toluene) and $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF) were added. After 10 min stirring at rt, nitrobenzene (0.02 mL, 0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added and the mixture was stirred for 16 hours. Mixture B: the solution of sulfonium salt (106 mg, 0.4 mmol, 2.0 eq. in 1 mL DCM) at -78 °C was treated with LiHMDS (0.48 mL, 0.48 mmol, 2.4 eq., 1.0 M in hexane). After 30 min, the mixture B was added to mixture A and stirred for 3 h at rt. Work-up with filtration over Celite; a) treatment with $NaBO_3$ (280 mg, 14.0 eq.) in THF/H_2O (1 mL/1 mL) for 1.5 h before work-up; b) treatment with NaOH (1 mL, 2.0 M in H_2O) and H_2O_2 (0.5 mL, 30% in H_2O) for 1.5 h before work-up; c) no LiHMDS; d) sulfonium salt from the beginning, no DCM; e) work-up after 6 hours; f) sulfonium salt with nitrobenzene and B_2pin_2, work up after 6 hours.

In the initial trial (entry 1), the reaction provided exclusively hydrolyzed aminoborane product **161a**, with no formation of the desired product **378**. Notably, when the reaction mixture was stirred at room temperature following the addition of the ylide **370**, the aniline **379** was obtained in 73% yield, indicating the successful formation of the desired product **378** (entry 2). It is important to note that while aminoborane **146b**, with its pyridine backbone, was chosen for its potential to stabilize the boronic ester group, the presence of a basic environment may have already triggered the protodeboronation of the desired product **378**, as depicted in Scheme 109.[91]



Scheme 109: Plausible mechanism of the formation of the protodeboronation product **379**.

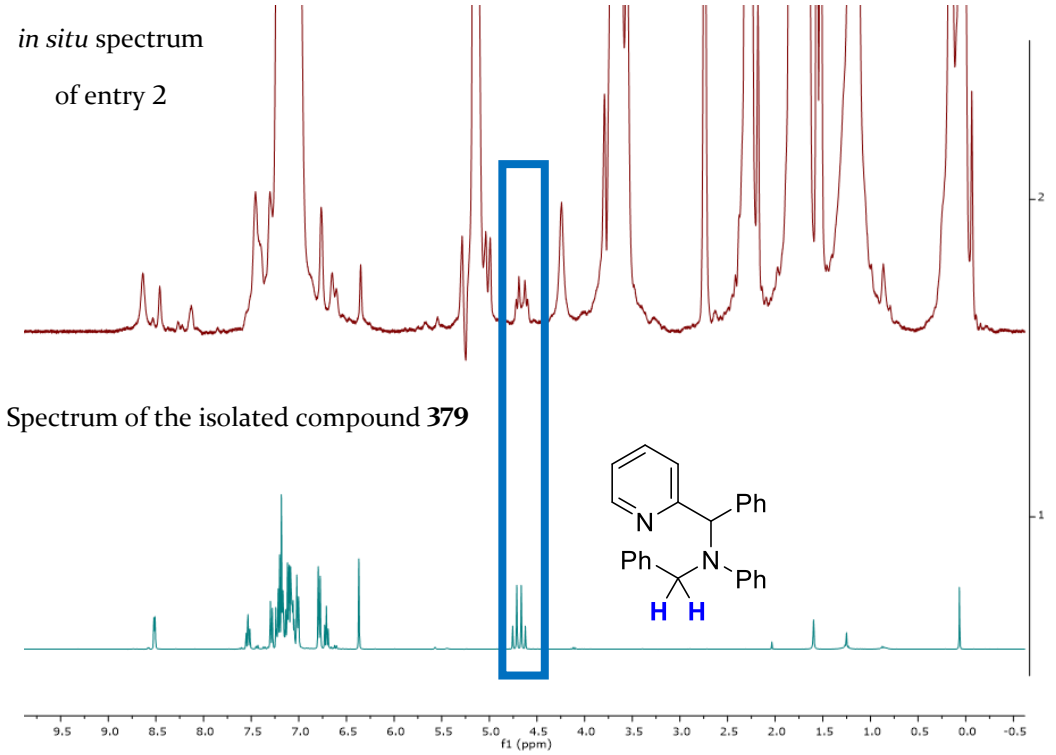


Figure 10: In situ measured ^{1}H-NMR spectrum of entry 2 and the spectrum of the isolated protodeboronation product **379**.

To investigate the potential formation of the desired product, *in situ* ^{1}H- and ^{11}B-NMR spectra were measured. However, the presence of non-deuterated THF and toluene resulted in signal overlapping and broadening in the ^{1}H-NMR spectrum, hindering accurate analysis of the sample (Figure 10). Nevertheless, the presence of **379** was discernible. The obtained ^{11}B-NMR spectrum resembled the spectrum obtained in Chapter 1.3 (Figure 1), where no S-ylide was added. Analysis of the spectrum indicated the presence of aminoborane **146b** (δ = 25.6 ppm) and OBpin anion **17** (δ = 20.8 ppm), suggesting the persistence of B_2pin_2 (δ = 33.2 ppm) in the mixture (Figure 11). Typically, boronic esters exhibit signals between δ = 30 ppm and δ = 40 ppm in ^{11}B-NMR, while α-aminoboronates with a pyridine backbone have been reported to display signals at δ = 9-12 ppm due to the interaction between the empty p-orbital of the boron atom and the lone pair of the nitrogen atom in the pyridine backbone.[97c] Unfortunately, no signal was observed within the range of δ = 9-12 ppm, suggesting the absence of the desired product **378**.

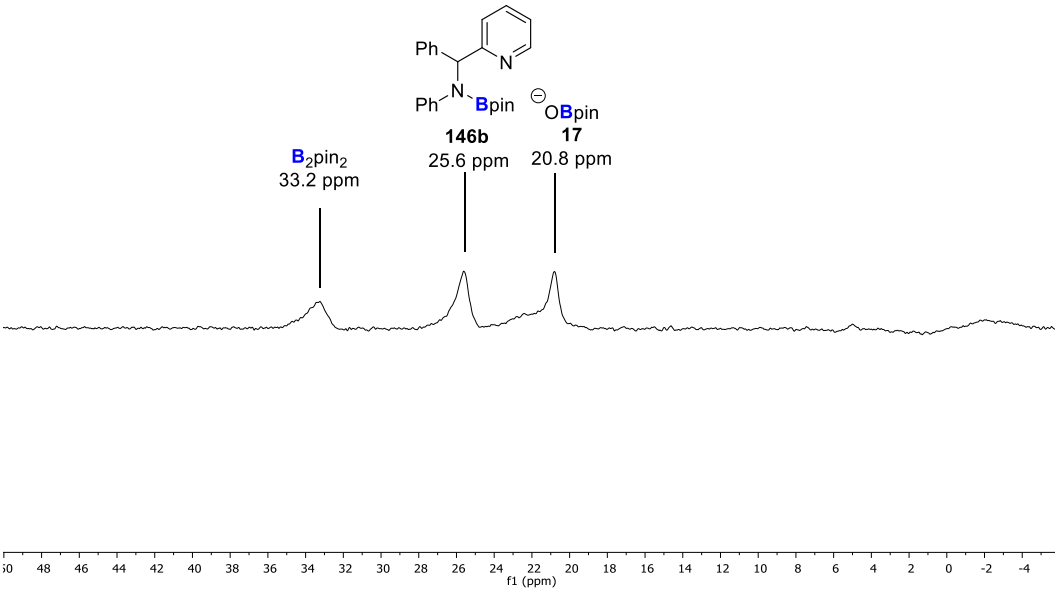


Figure 11: *In situ* measured ^{11}B-NMR spectrum of entry 2.

Despite the unsuccessful attempts to generate and isolate the desired α-aminoboronate **378**, an investigation was carried out to convert it into a more stable aminoalcohol.[78] However, the use of $NaBO_3$ or H_2O_2 as reagents only led to the formation of the protodeboronated product **379** (entries 3 and 4). Direct addition of the sulfonium salt **376** to the aminoborane **146b** resulted in a 45% yield of the aniline **161a** and a 39% yield of **379** (entry 5). Employing a one-pot procedure with the sulfonium salt **376** from the beginning yielded 13% of the hydrolyzed aminoborane and 87% of the protodeboronated product **379** (entry 6). Extended reaction time of 6 hours led to nearly complete conversion to the protodeboronated product **379** (entry 7). Using CPME as the solvent produced similar results, with full conversion of the nitro compound into the side product **379**. In the case of the one-pot protocol with a 6-hour reaction time, a 95% yield of the protodeboronated side product **379** was obtained (entry 9). When the reaction was carried out in a glovebox, the measured ^{1}H-NMR spectrum exhibited a comparable complex pattern as shown in Figure 11, while the ^{11}B-NMR spectrum did not show any indication of the desired product.

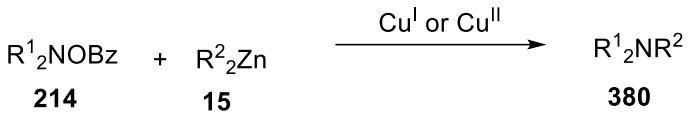
Summary – Synthesis of α-Aminoboronates

A new synthetic route was investigated to convert nitro compounds into α-aminoboronates. According to developed C-H amination protocol (Chapter 1.3), nitrobenzene was transformed into the aminoborane **146b**. This reaction utilized 2-benzylpyridine and KHMDS in the presence of B_2pin_2. The aminoborane **146b** was subsequently subjected to a homologation reaction with the S-ylide **370**. However, instead of obtaining the desired product **378**, the side product **379** was observed. This compound likely formed *via* protodeboronation of the desired product. The *in situ* NMR measurements suggested that the protodeboronation may occur during the reaction, as no traces of the desired product were found, even when the reaction and filtration were performed in a glovebox. One possible pathway for this protodeboronation is a base-mediated process. Since the presence of a base is crucial for the formation of the aminoborane and S-ylide, it suggests that the tested system may not be feasible for synthesizing the desired α-aminoboronate.

Chapter 4: Cu-Catalyzed Coupling of Nitro Compounds with Allylboronates

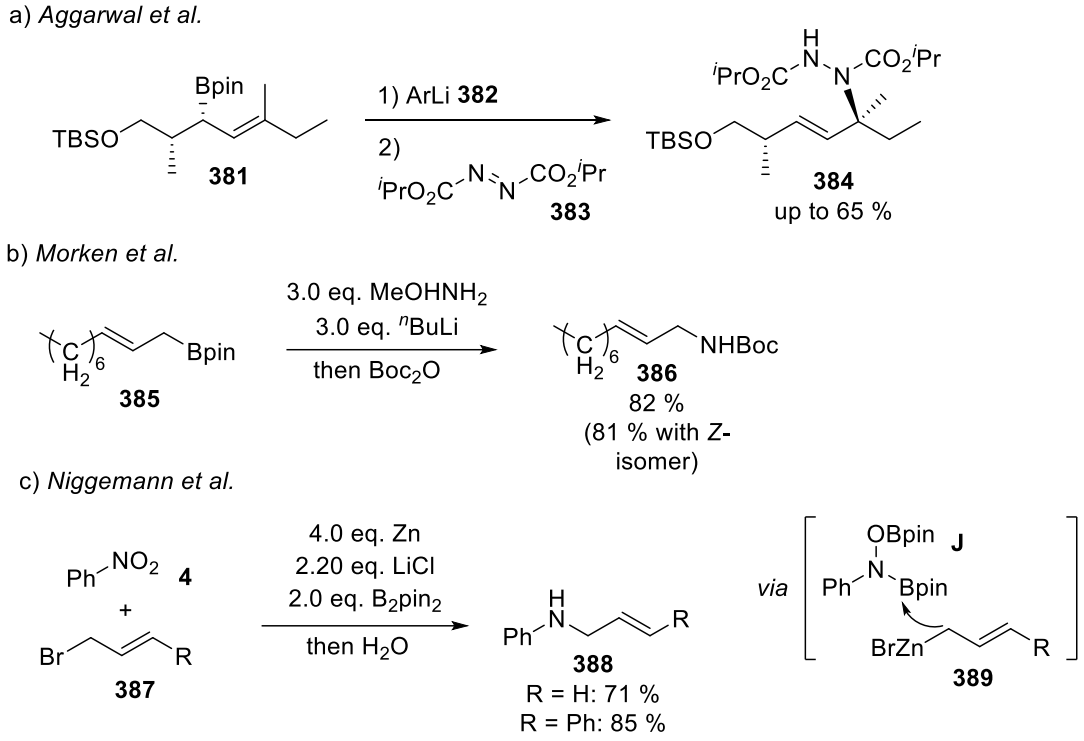
Introduction – Electrophilic Amination

Electrophilic amination reagents offer effective strategies for constructing C-N bonds. Unlike classical amination reactions involving nucleophilic nitrogen reacting with an electrophile (e.g., reductive amination or Buchwald-Hartwig coupling) or a nucleophile (e.g., Chan-Lam or C-H amination), electrophilic amination involves the transformation of an electrophilic nitrogen source with a nucleophile. A key advantage of these processes is the prevention of a multiple alkylation, making them highly beneficial.[29a,b,c,f]



Scheme 110. Electrophilic amination of organozinc compounds by *Johnson et al.*

The development of transition metal-catalyzed methods has significantly enhanced the applicability and popularity of this strategy. Earlier procedures focused on transforming highly reactive organoalkali and organo earth alkaline compounds using nitrogen electrophiles. However, the new processes, inspired by the work of *Johnson et al.* (Scheme 110)[29a,b], can convert even bench-stable organoboron compounds. These methods exhibit tolerance towards primary, secondary, and aromatic residues, although allylic nucleophiles are not suitable substrates. Notably, there have been no reports of transition metal-catalyzed electrophilic amination reactions with allylic nucleophiles.[108] On the other hand, allylic nucleophilic reagents have been employed under metal-free conditions, although the reaction is limited to highly reactive organometallic compounds.[109] For more practical precursors like boronic acid derivatives, only a limited number of examples have been reported by *Aggarwal et al.* (Scheme 111 a) (racemic procedure by *Minakata et al.*), *Morken et al.* (Scheme 111 b), and *our group*'s protocol of a reductive coupling (Scheme 111 c).[110] However, it is important to note that all these approaches require activation of the boronic ester. Examples (a) and (b) are particularly restricted in terms of functional group tolerance due to the necessary presence of an organolithium species.



Scheme 111. Examples for allylation of *N*-electrophiles by a) *Aggarwal et al.* b) *Morken et al.* c) *Niggemann et al.*

The limited success of electrophilic amination with allylic nucleophiles may be attributed to the chemistry of metal allyl complexes. The formation of π-allyl complexes prior to the reductive elimination step can impose constraints on α,γ-selectivity and limit the applicability of substituted allyl groups.[111] This limitation is also observed in the related Chan-Lam reaction, where a Cu-catalyzed coupling of nucleophilic boronic acid derivatives with amines is involved.[29d,e]

In electrophilic amination, compounds with at least one σ-bond to a heteroatom of higher electronegativity, typically oxygen, are commonly used as amination reagents (Figure 12).[112] Benzoyl hydroxylamines **288** and chloramines **390** are frequently employed as such reagents. However, the intricate synthesis of these compounds poses a significant drawback, resulting in limited application in various protocols.[113] Interestingly, nitrogen-containing compounds with higher oxidation states, such as nitro compounds **1**, are readily available but are seldom utilized (see Introduction: Direct Nitro Functionalization).[10,11,14,15]

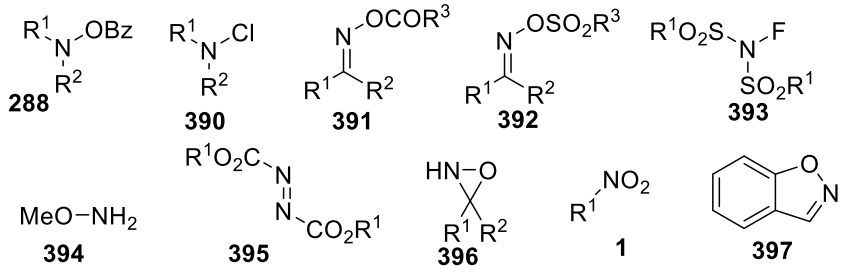
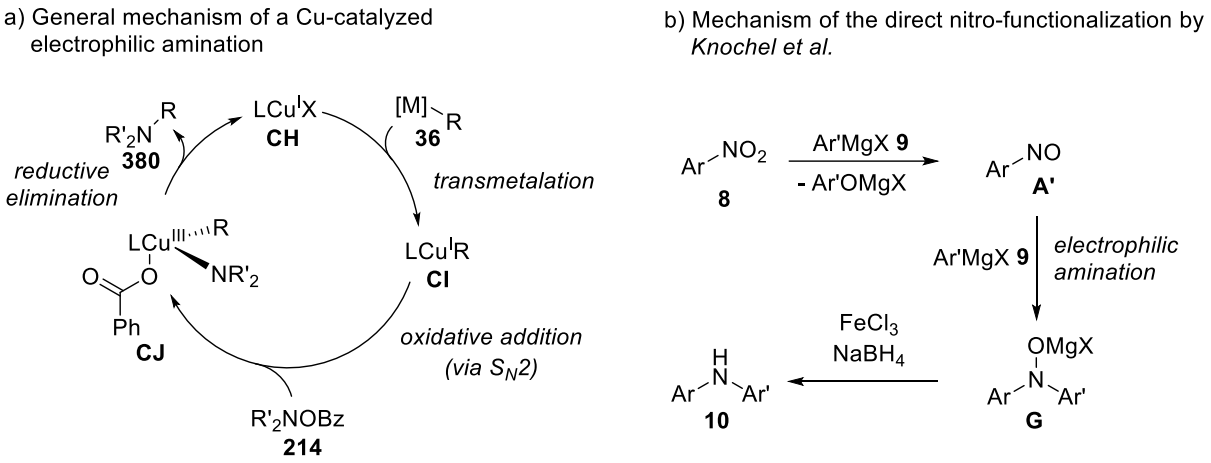


Figure 12. Examples for electrophilic amination reagents.

From a mechanistic standpoint, two types of electrophilic amination can be distinguished (Scheme 112 a and 112 b). Firstly, the classical transition metal-catalyzed approach is illustrated in Scheme 112 a).[29a,b,c,f] In this example, a Cu-catalyzed electrophilic amination is demonstrated, where the organocopper compound **CI** is generated through transmetalation. This species then adds to the electrophilic amination reagent **214**. The formation of the C-N bond occurs through reductive elimination, similar to the amination reaction of nucleophilic nitrogen precursors.[114]



Scheme 112. a) General reaction mechanism of a Cu-catalyzed electrophilic amination; the oxidation states of Cu are strictly formal; b) mechanism of electrophilic amination with nitroso intermediates by *Knochel et al.*

A precedent for the second type is the direct nitro-functionalization with a Grignard reagent, as demonstrated by *Knochel et al.* (Scheme 112 b).[11] This catalyst-free electrophilic amination involves the nucleophilic substrate **9** directly attacking the nitrogen center of the nitroso intermediate **A'**. The reaction leads to the formation of the hydroxylamine anion **G**, which is subsequently hydrolyzed to afford the desired amine **10**.

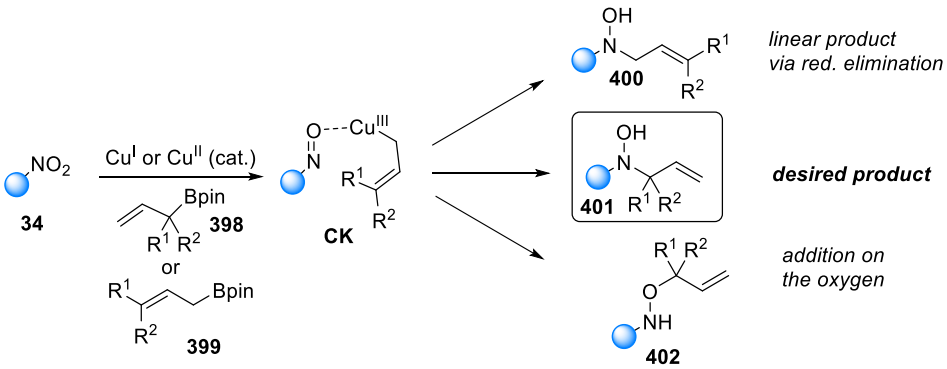
Concept

Despite significant advancements in direct nitro-functionalization and extensively studied C-N coupling methods, a comprehensive concept for utilizing nitro compounds as electrophilic amination reagents in transition metal-catalyst-controlled reactions is still missing. Such a concept may provide the basis for achieving stereoselective C-N bond formation reactions starting from nitro compounds by precisely controlling the C-N bond formation with an appropriate catalyst.

As mentioned in the Aims of this work, the catalyst for this transformation must fulfill three requirements: 1) activation of the nitro group to enable the functionalization of the typically inert nitro group, 2) stabilization of the generated species and 3) control over the C-N bond formation. Copper emerges as an excellent candidate for the catalyst, as it satisfies all three criteria. Based on the redox potential of nitro compounds and Cu-salts, activation of the nitro group through single-electron transfer (SET) may be feasible.[30] The weakly coordinating nitro group can be transformed into a nitro radical-anion, allowing more efficient interaction with the catalyst. The structural aspects of complexes involving oxidized nitrogen species such as nitroso and nitroxyl compounds have been extensively studied. Among these, nitroso species appear to be the most promising candidates for interaction with Cu, considering the nitro reduction cascade.[31] Furthermore, the well-established Cu-catalyzed cross-coupling chemistry provides a fundamental understanding of the coupling with nitro compounds, with the C-N bond-forming step typically described as a reductive elimination originating from a Cu(III) complex.[29a,d,e,f]

Despite the wide utilization of Cu-catalyzed electrophilic amination and the Chan-Lam-Evans reaction, the application of allyl nucleophiles for these reactions remains unexplored.[29a,d,e,f] Therefore, the development of a coupling reaction between allylic substrates and nitro compounds would be highly valuable. Based on the versatility of transmetalation to Cu and *our knowledge* of the stabilizing properties of boron compounds for reduced nitro compounds, allylic pinacolboronates appear to be ideal coupling partners.[14]

Taking all these factors into consideration, a Cu-catalyzed direct *N*-allylation of nitro compounds **34** via a nitroso intermediate in a Cu^{III}-complex **CK** represents an attractive approach (Scheme 113, where all copper oxidation states are strictly formal and are only depicted to illustrate the shown reactivity).

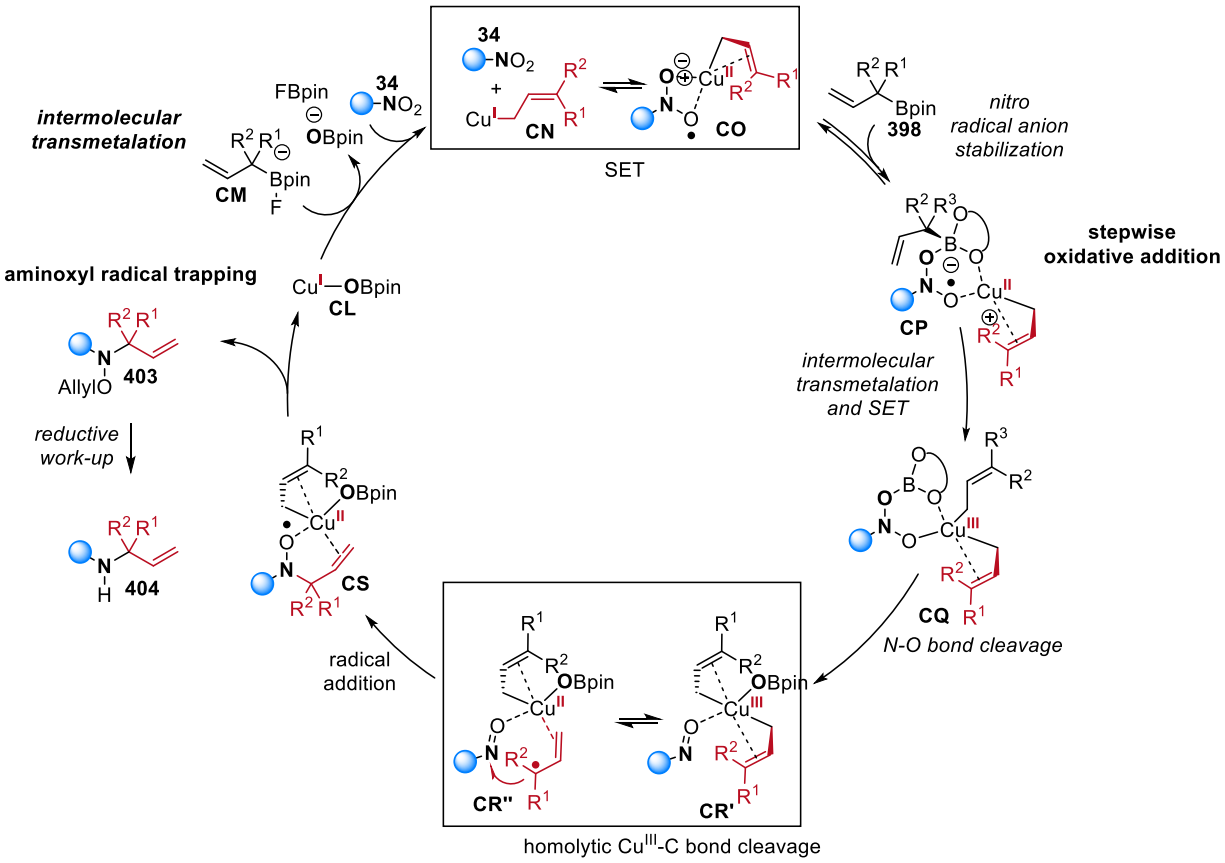


Scheme 113. Potential concurrent reaction pathway in the designed reaction.

The concept involves the following challenges (Scheme 113):

1. The selective generation of the nitroso species is generally difficult, due to the possible side reactions on the way to this intermediate, if it is not bound to a catalyst or an additional stabilizer.[6,7]
2. Based on the work of *Studer et al.* and *Morken et al.*, the nucleophilic addition of allylboronates to nitroso compounds prefers oxygen over nitrogen.[115]
3. The formed hydroxylamines are often unstable, especially when bearing α-hydrogen atoms.[11]

The following concept may provide solutions for the stated challenges (Scheme 114):



Scheme 114. Detailed concept for the Cu-catalyzed coupling of allylboronates with nitro compounds.

To achieve selective *N*-addition to the most highly branched isomer, the formation of the C-N bond should occur via a radical pathway rather than reductive elimination. This radical addition to nitroso compounds is commonly employed in EPR studies.[5d,f] In order to prevent concurrent side reactions involving the free allyl radical, these radicals must be generated from a Cu^{III}-nitroso-allyl complex **CR'**. The feasibility of this elementary step within the catalytic cycle is supported by the microscopic reversibility of radical addition to Cu^{II}, which has been extensively utilized in recent radical relay reactions, as well as studies on halogen radical elimination from Cu^{III}-X complex **CX** (Figure 13 a and b).[116] It is not favorable for both allyl residues to undergo reductive elimination, as this process occurs relatively slowly in the absence of a strong donor ligand.[111]

If the complex **CR'** cleaves an allyl radical, it will attack the nitrogen atom with the carbon atom that is the most stabilized and closest to the nitroso ligand to form an aminoxyl radical **CS**.

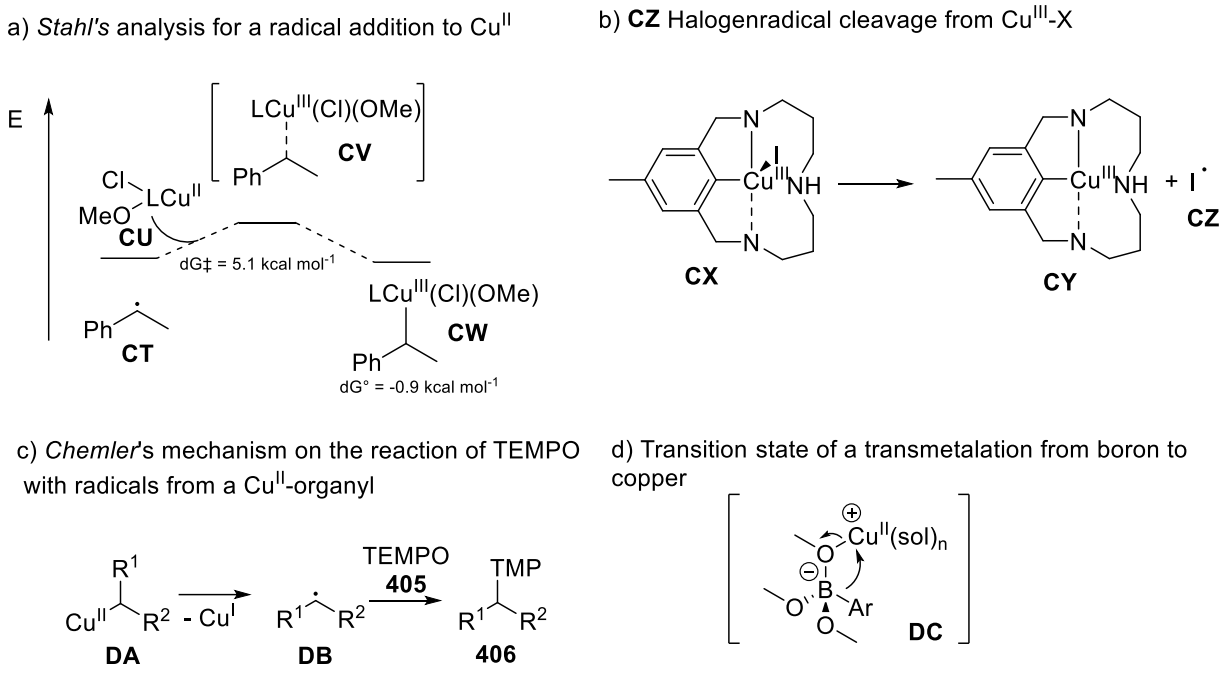


Figure 13. Reported precedents for the hypothesis of reaction pathways of the reaction between Cu-catalyst, nitro compounds and allylboronates.

Analogously to the reaction of TEMPO **405** with Cu^{II}-organyl **DA** (Figure 13 c), the aminoxyl radical **CS** then undergoes recombination with the second allyl residue, resulting in the release of Cu^{I}.[117] Finally, a reductive work-up of the thus stabilized hydroxylamine **403** provides the desired amine **404**.[11,12]

To address the handling difficulty associated with the nitroso compound during the formation of complex **CR'**, it should be generated directly on the catalyst. If the nitroso intermediate were free and not stabilized, the conversion of aliphatic nitro compounds would be impossible from the beginning.[6,11,12,13,15,18a] Additionally, the catalyst could not control the stereochemistry since it would not be bound to the nitroso intermediate and unable to regulate the C-N bond formation step. Consequently, in the first step, the nitro group should be activated by a single electron transfer (SET) from the Cu-allyl species **CN**, which should be feasible based on the redox potentials.[30,32] The resulting complex **CO** from Cu^{II}-allyl and nitro radical anion exists in equilibrium with the nitro compound **34** and organocopper(I) species **CN**, as long as no suitable reaction partner is available. As mentioned earlier, boronic esters can stabilize reduced nitro species. Hence, the complex **CP** may be formed by coordinating a second allylic substrate to the oxygen. The quaternized boron atom is expected to undergo intermolecular transmetalation to the positively charged copper center (Figure 13 d).[118] Due to the increased electron density at the copper center, it likely recombines with an aminoxyl radical. The N-O bond of the resulting bishydroxylamine species **CQ** cleaves off, forming the key intermediate **CR'**.[7] The formed Cu^{III} species **CR'** does not undergo reductive elimination but instead undergoes radical relay to facilitate the desired bond formation from Cu^{III}. In the

final step, a Cu-organyl reacts with an aminoxyl radical to form the C-O bond and releases a Cu(I) species **CL** and an allylhydroxylamine **403**. The desired amine **404** is obtained after reductive work-up.

In the following, it shall be examined whether the described concept is synthetically applicable.

This work is a cooperation of the following people: *Raphael Eckert* (concept, development/optimization, scope, mechanistic investigation), *Meike Niggemann* (concept), *Peter Palchuber* (scope), *Max Gerbershagen* (optimization of α,α-disubstituted allylboronates, scope), *Sarah Roeb* (scope).

Results

My contribution to this work was the scope of the reaction, therefore only these experiments will be discussed.

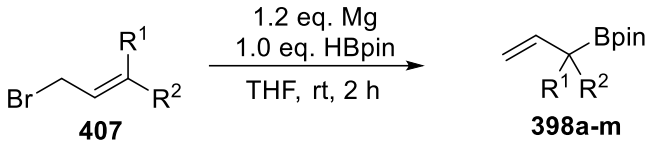
Investigation of the Applicability

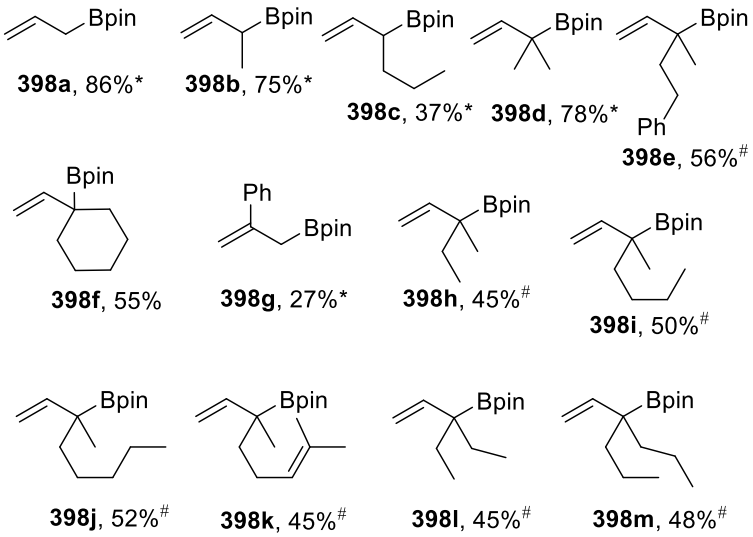
Synthesis of the Starting Materials

Allylpinacol boronates

In order to assess the range of applications, particularly with regard to the α,γ-selectivity of non-symmetrically substituted allyl substrates, the synthesis of these allyl boronates was necessary. The α- or β-substituted substrates were synthesized using pinacolborane in the presence of Mg turnings following the procedure by *Morken et al.* (Table 29).[119] In most cases, moderate yields were achieved (**398c**, 37%; **398e**, 56%; **398f**, 55%; **398g**, 27%; **398h**, 45%; **398i**, 50%; **398j**, 52%; **398k**, 45%; **398l**, 45%; **398m**, 48%), with a few exceptions (**398a**, 86%; **398b**, 75%; **398d**, 78%). The use of column chromatography for purification posed a limitation on the achievable yield, leading to partial protodeboronation of the product. Although the commonly employed Kugelrohr distillation is a solution to this issue, it was not available at the time of the study. When the required bromides **407** were not commercially accessible, they were synthesized by vinylation of the corresponding ketones followed by bromination. Due to their photosensitivity and sensitivity to air, the resulting bromides were used directly without further purification.[119]

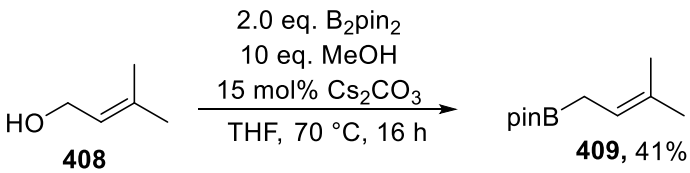
Table 29. Synthesis of allyl pinacol boronates **398a-m** with HBpin and magnesium.





Conditions: activated Mg chips (1.2 eq.) in THF, then HBpin (1.0 eq.), then the corresponding allylbromide (1.0 eq.) added dropwise; 30 min at rt; then allylbromide (1.0 eq.) added dropwise; 1.5 h at rt; reaction was stopped by adding pentane and HCl (0.05 M) at 0 °C; synthesized by **Raphael Eckert #Max Gerbershagen.*

Following the procedure of *Fernández et al.*, the prenyl substrate **409** was synthesized in a based-catalyzed borylation of prenol **408** in a moderate yield of 41% (Scheme 115).[120]

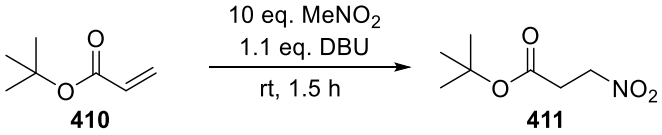


Scheme 115. Synthesis of prenyl pinacol boronate by *Fernandez et al.*

Nitro compounds

The majority of the tested nitro compounds were commercially accessible. Of the commercially unavailable nitro substrates, the following was synthesized.

A nitro alkane with an ester group **411** was obtained in a satisfactory yield of 27% in a modified reaction of *Jirgensons et al.* (Scheme 116).[121]

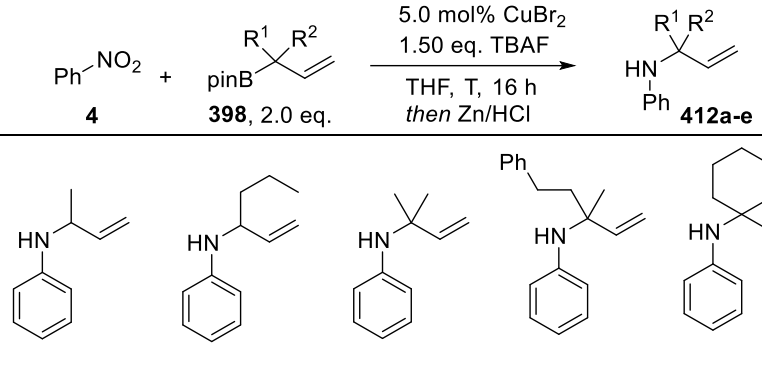


Scheme 116. Synthesis of an ester-substituted nitroalkane **411**.

Investigation on the Regioselectivity of Various Allyl Boronates

After a short optimization of the reaction conditions, it was discovered that nitrobenzene **4** and 2.0 eq. of the allyl boronate **398b,** in the presence of 5.0 mol% $CuBr_2$ and 1.50 eq. TBAF in THF, selectively provide aniline **412a** in an excellent yield of 87%. Ensuring regioselective transformation of the allyl group is a critical aspect of the applicability. Therefore, the suitability of the optimized approach for the methyl-substituted allyl boronate **398a** was primarily assessed for other substrates (Table 30). To demonstrate the applicability of the developed procedure in the synthesis of (sterically hindered) allylamines, a reductive work-up was performed.

Table 30. Investigation of the regioselectivity on different allyl boronates.



412a, 87%[a*]	**412b,** 90%[a,b#]	**412c,** 93%[c°]	**412d,** 70%[c,d,e‡]	**412e,** 70%[c,d,e‡]
no lin. det.	14.5/1 (b/l)	no lin. det.	no lin. det.	no lin. det.

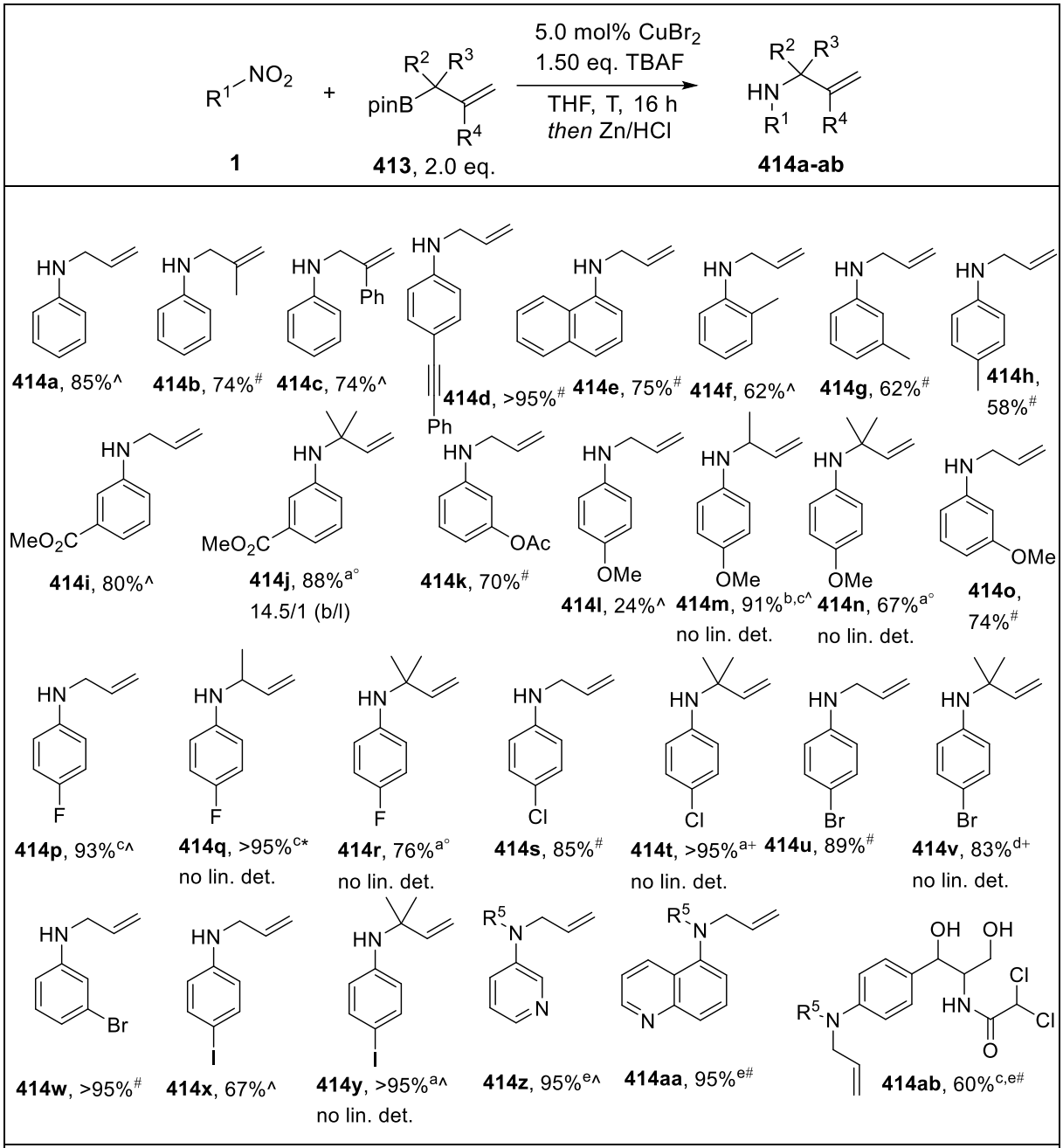
Conditions: Schlenk technique, Cu-salt (5 mol%) and TBAF (1.5 eq., 1.0 M in THF) were dissolved in THF (2 mL), then degassed (brought to T), PhNO2 (0.2 mmol, 1.0 eq.) and allyl boronate (2.0 eq.) was added, 16 h; then Zn (20 eq.) and HCl (4.0 M in dioxane, 2 mL), 4 h, rt. [a] 0 °C; [b]Cu(OAc)2; [c] -40 °C; [d] 10 mol% CuBr2; [e] 3.0 eq. of allyl boronate. Ratio between branched and linear products was determined per crude-NMR (no lin. det. = no linear isomer detected). Synthesized by **Raphael Eckert*. Pre-evaluation of the hydroxylamine synthesis by *Raphael Eckert* and amine synthesis by #*Peter Palchuber*/°*Sarah Roeb*, carried out by ‡*Max Gerbershagen*.

While a longer side-chain in the α-position resulted in minor selectivity losses (**412b**, 90%, b/l = 14.5/1), α,α-disubstituted allyl boronates exclusively provided highly congested branched products in good to excellent yields (**412c**, 93%; **412d**, 70%; **412e**, 70%). The requirement for a lower temperature can be attributed to the increased reactivity of the substituted allyl boronate, likely due to the enhanced electron density in the allyl group, which raises the redox potential of the Cu-allyl species. Consequently, both the two transmetalations and the reduction of the nitro group by the Cu-organyl species are favored.

Investigation of the Functional Group Tolerance

To explore the substrate scope with various functional groups, a wide range of substituted nitro compounds was tested with diverse allyl boronates, demonstrating broad applicability. The regioselectivity for the formation of branched amines was confirmed for all substrates, with only one exception (Table 31).

Table 31. Scope of Cu-catalyzed coupling of nitroarenes with allyl boronates.



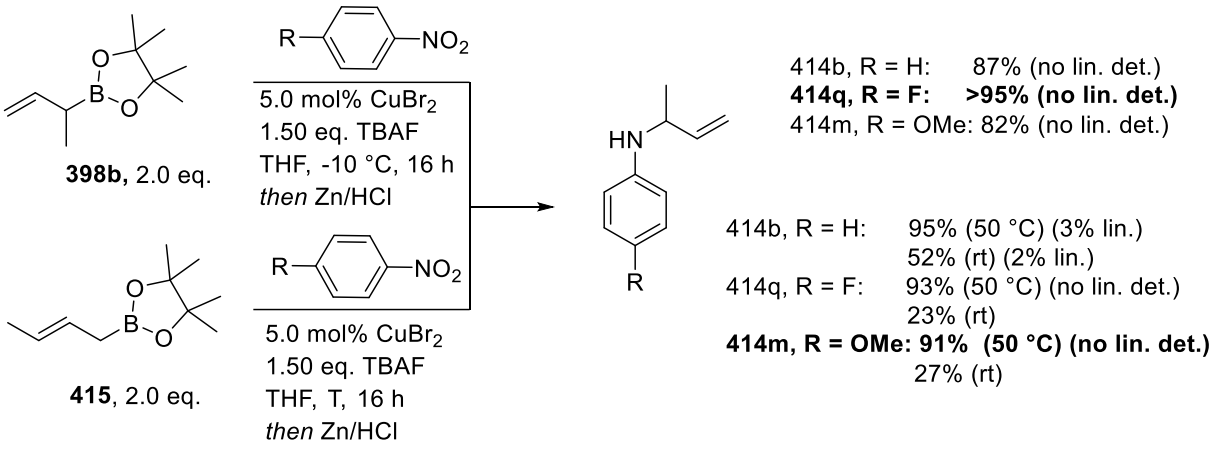
Conditions: Cu-salt (5.0 mol%) and TBAF (1.0 M in THF, 1.50 eq.) were dissolved in THF (2.0 mL), then the mixture was degassed (and brought to T), $PhNO_2$ (0.10 mmol, 1.0 eq.) and allyl boronate (2.0 eq.) were added, 16 h at T; [a] -40 °C; [b] with crotyl boronate; [c] 0 °C; [d] -20 °C; [e] isolated before reductive work-up, R^5 = OAllyl. Ratio between branched and linear isomer was determined per crude-NMR (no lin. det. = no linear isomer detected). Pre-evaluation of the hydroxylamine formation by *Raphael Eckert* and amine synthesis by °*Sarah Roeb*/^*Peter Palchuber*, carried out by **Raphael Eckert* +*Sarah Roeb* #*Peter Palchuber*

Nitrobenzene was successfully converted to allyl aniline in a good yield (**4l4a**, 85%). Substituents in the β-position were well tolerated, providing good yields (**4l4b**, 74%; **4l4c**, 74%). Conjugated systems also showed similar results, with high conversion rates (**4l4d**, >95%; **4l4e**, 75%). Electron-rich methyl nitrobenzenes yielded the desired products with non-substituted allyl boronates, although in slightly lower yields (**4l4f**, 62%; **4l4g**, 62%; **4l4h**, 58%). However, when a more electron-rich para-methoxy substituent was present, a lower yield was obtained (**4l4l**, 24%). On the other hand, substituted allyl boronates gave good to very good yields (**4l4m**, 91%; **4l4n**, 67%). This difference may be attributed to the decreased electron affinity of the electron-rich para-methoxy nitrobenzene, which can be compensated by the enhanced reactivity of the alkylated allyl substrate.[122] The electronic properties played a minor role when the methoxy group was in the meta-position, resulting in a good yield (**4l4o**, 74%).

Electrophilic substituents are well-suited for reactions with nucleophilic reagents like the employed allyl boronates in the presence of TBAF.[123] Various ester substituents were found to be well-tolerated, yielding good results (**4l4i**, 80%; **4l4j**, 88%; **4l4k**, 70%). The use of substituted allyl boronates led to slightly lower yields. Halogen-substituted aromatic compounds are generally challenging in transition metal-catalyzed reactions due to their susceptibility to cleavage from the aromatic backbone through oxidative metal insertion.[29e] Moreover, iodo-substituted aromatic nitro compounds tend to undergo dehalogenation upon reduction to the radical anion.[124] Despite these difficulties, fluoro- (**4l4p**, 93%; **4l4q**, >95%; **4l4r**, 76%), chloro- (**4l4s**, 85%; **4l4t**, >95%), bromo- (**4l4u**, 89%; **4l4v**, 83%; **4l4w**, >95%), and iodo-substituents (**4l4x**, 67%; **4l4y**, >95%) were well-tolerated, resulting in good to excellent yields and selectivity. Heterocycles are similarly challenging substrates in transition metal-catalyzed reactions due to their strong metal complexation and subsequent catalyst deactivation. However, nitrogen heterocycles proved to be efficient substrates in the coupling with allyl boronates (**4l4z**, 95%; **4l4aa**, 95%). Additionally, the acetylated chloramphenicol was obtained in a moderate yield (**4l4ab**, 60%). Due to the high polarity of the backbone, amines derived from heterocyclic nitro compounds and chloramphenicol were isolated with insufficient purity. Therefore, the Cu-catalyzed coupling reaction was demonstrated by isolating the hydroxylamines (**4l4z**, **4l4aa** and **4l4ab**).

To explore the further synthetic utility of regioconvergence, an electron-deficient and an electron-rich nitroarene were reacted with the respective allyl boronate (Scheme 117).

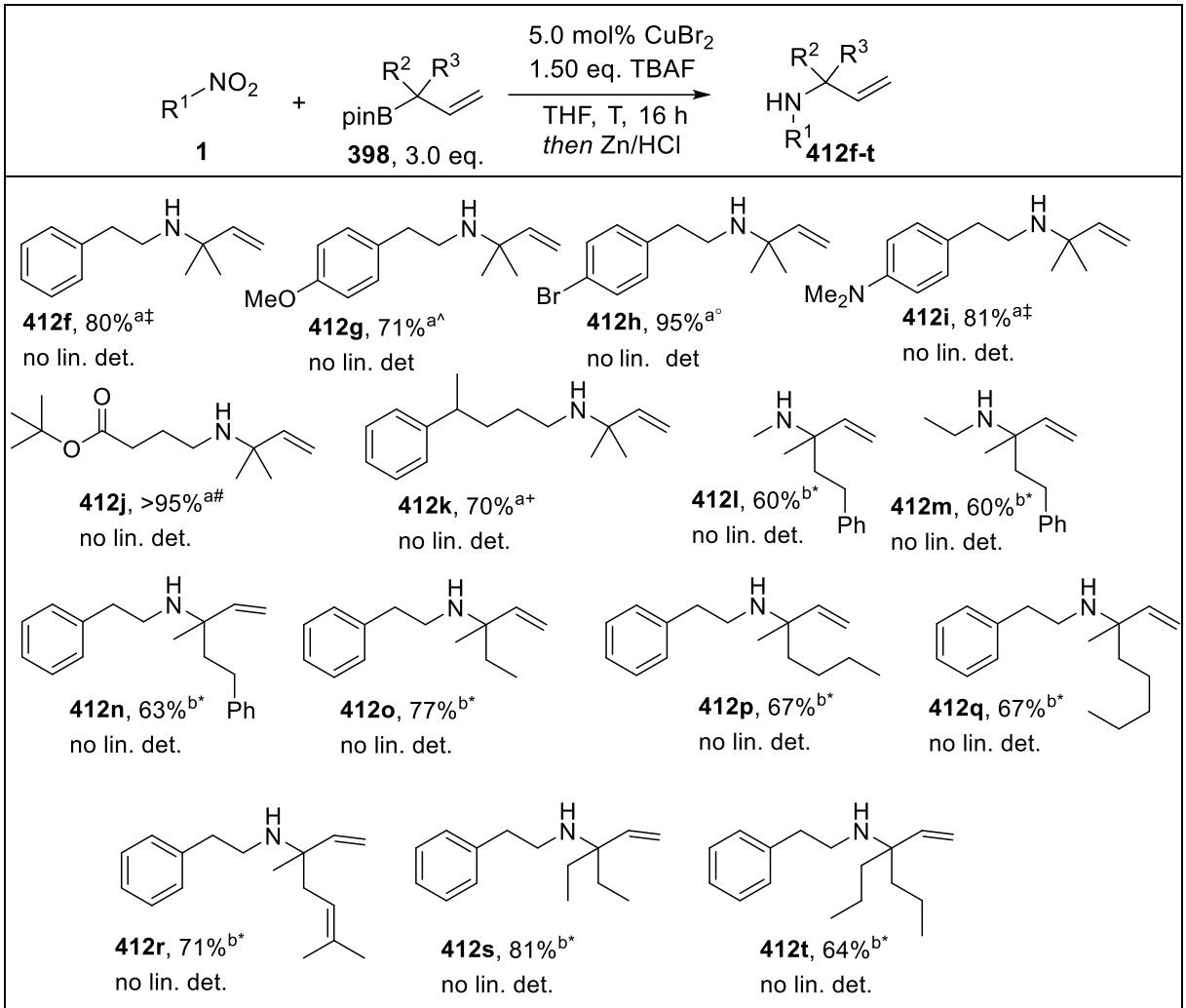
It was previously observed that the optimal temperature for the crotyl substrate is significantly higher than its branched isomer. However, para-methoxy nitrobenzene reacted with crotyl boronate, resulting in an improved yield and an excellent selectivity at a lower temperature (**4l4m**, 91%). Therefore, in the optimization of the reaction conditions for preparing amines with substituted allyl side chains, it is promising to test both isomers of the boronates to achieve an ideal result.



Scheme 117. Synthetic application of regioselectivity, carried out by *Raphael Eckert*.

After aromatic nitro compounds showed a wide range of applications, the investigation was extended to aliphatic nitro compounds. As previously mentioned, aliphatic nitro compounds are often challenging substrates for direct nitro-functionalization due to their propensity to undergo tautomerization in the nitroso intermediate stage to form oxime.[6,9,10,11,12,15c,15d,18] However, the tested aliphatic nitro compounds, when reacted with various allyl boronates, yielded the desired branched products in good to excellent yields. This observation suggests the absence of free nitroso intermediates, thus aligning with the underlying concept for controlling reactive nitro reduction intermediates. Similarly, the tolerance towards different functional groups was consistent with the earlier findings. The scope of tolerated carbon frameworks encompassed linear and branched chains (**412t**, 80%; **412k**, 70%), ether (**412g**, 71%), halogen (**412h**, 95%), amine (**412i**, 81%), ester-substituted compound (**412j**, >95%), and short-chain nitroalkanes (**412l**, 60%; **412m**, 60%). The examination of variously substituted allyl boronates consistently resulted in good yield and excellent selectivity. The substrate scope included both short- and long-chain substrates (**412o**, 77%; **412p**, 67%; **412q**, 67%), phenyl-substituted compounds (**412n**, 63%), those with an olefinic side chain (**412r**, 71%), and sterically hindered amines (**412s**, 81%; **412t**, 64%).

Table 32. Scope of Cu-catalyzed coupling of nitroaliphatic compounds with allyl boronates.



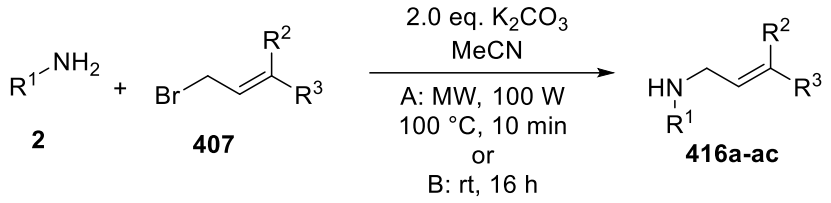
Conditions: Cu-salt (5.0 mol%) and TBAF (1.0 M in THF, 1.50 eq.) were dissolved in THF (2.0 mL), then the mixture was degassed (and brought to T), $PhNO_2$ (0.10 mmol, 1.0 eq.) and allyl boronate (2.0 eq.) were added, 16 h at T; [a] 0 °C; [b] -78 °C, 10 mol% $CuBr_2$; [c] 0 °C; Ratio between branched and linear isomer was determined per crude-NMR (no lin. det. = no linear isomer detected). Pre-evaluation of the hydroxylamine formation by *Raphael Eckert* and amine synthesis by °*Sarah Roeb*/^*Peter Palchuber*, carried out by ‡*Raphael Eckert* **Max Gerbershagen* +*Sarah Roeb* #*Peter Palchuber*

The investigation focused on tertiary allylic boronates as primary and secondary allylic boronic esters did not yield products with aliphatic nitro compounds. This limited scope may be attributed to their lower reactivity. Even with tertiary allylic boronates, the reaction required the presence of 3.0 equivalents of boronates. Notably, 2-nitropropane, a secondary nitroalkane, failed to undergo conversion to the corresponding amine. This may be attributed to its increased steric hindrance and lower electron affinity, which likely hindered the reaction.[30a]

Method for Determining the Regioselectivity

The regioselectivity analysis was conducted by comparing the crude ^{1}H-NMR spectra of the reaction with the isolated spectra of the branched and linear products. To establish a reference, linear compounds were synthesized. This involved the reaction of the corresponding primary amines with the respective allyl bromides. For commercially unavailable amines, crude products from the allylation reaction were utilized. A similar approach was followed for the synthesis of allyl bromides. Microwave-assisted reactions at 100°C were employed for short-chain bromides, while longer-chain bromides or those with bromine or iodine substituents were stirred at room temperature for 16 hours. The nucleophilic amination reaction generally yielded the desired products in moderate to satisfactory yields. Notably, short-chain allyl bromides exhibited lower yields compared to their long-chain counterparts. This discrepancy may be attributed to increased bisallylation of the amines, as evidenced by the crude NMR spectra in cases involving prenyl and crotyl bromides. However, such observations were less frequent with more sterically hindered substrates. Importantly, the formation of amines with branched carbon centers on nitrogen *via* S_N2' reactions was not observed in any of the cases, highlighting the effectiveness of the presented transformation for the synthesis of amines with highly branched carbon centers.

Table 33. Synthesis of reference amines.



2 **407** **416a-ac**

416a, 36%[a#] **416b**, 42%[a] **416c**, 26%[a#] **416d**, 65%[b*] **416e**, 63%[b*] **416f**, 21%[b#]

416g, 18%[a#] **416h**, 25%[a#] **416i**, 14%[a#] **416j**, 31%[a#] **416k**, 29%[a#] **416l**, 18%[a#]

416m, 18%[b#] **416n**, 15%[a#] **416o**, 23%[a#] **416p**, 24%[a]

416q, 25%[b+] **416r**, 10%[b#]

416s, 12%[a] **416t**, 23%[b+] **416u**, 23%[b*]

416v, 59%[b*] **416w**, 61%[b*] **416x**, 60%[b#]

416y, 47%[b+] **416z**, 59%[b#] **416ac**, 66%[b*]

416aa, 64%[b*] **416ab**, 60%[b*]

Conditions: amine (0.625 mmol, 1.20 eq.), bromide (0.5 mmol, 1.0 eq.) and K_2CO_3 (1.0 mmol, 2.0 eq.) were dissolved in MeCN, then [a] MW, 100 W, 100 °C, 10 min or [b] rt, 16 h. carried out by **Raphael Eckert *Max Gerbershagen [+]Sarah Roeb [#]Peter Palchuber*

As mentioned above, to determine the selectivity, the crude ^{1}H-NMR spectra were compared to the spectra of the products. A representative example is depicted in Figure 14.

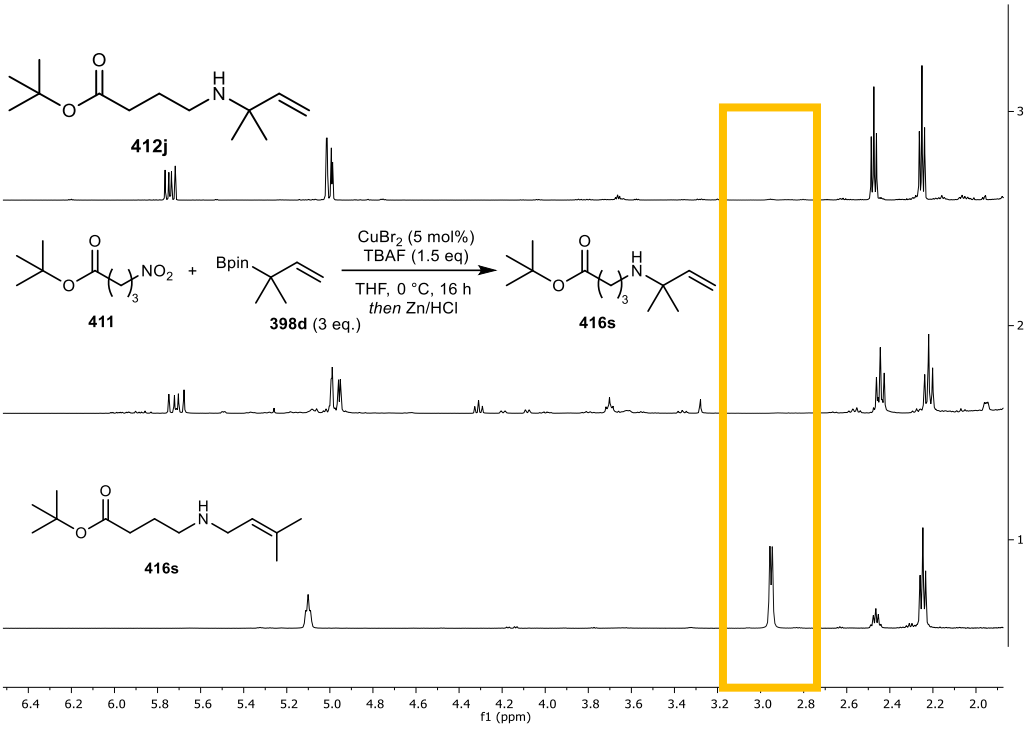


Figure 14. Determination of the regioselectivity of the reaction with nitro compound **411** and prenylboronate **398d** *via* ^{1}H-NMR.

This example presents the reaction between the aliphatic nitro compound **411** and prenyl boronate **398d** and both isomers of prenylamine. The missing signal of the CH_2 next to the amine function indicates that linear substituted product was below the limit detection (5%). The method was applied identically to substrates with potential regioisomer formation.

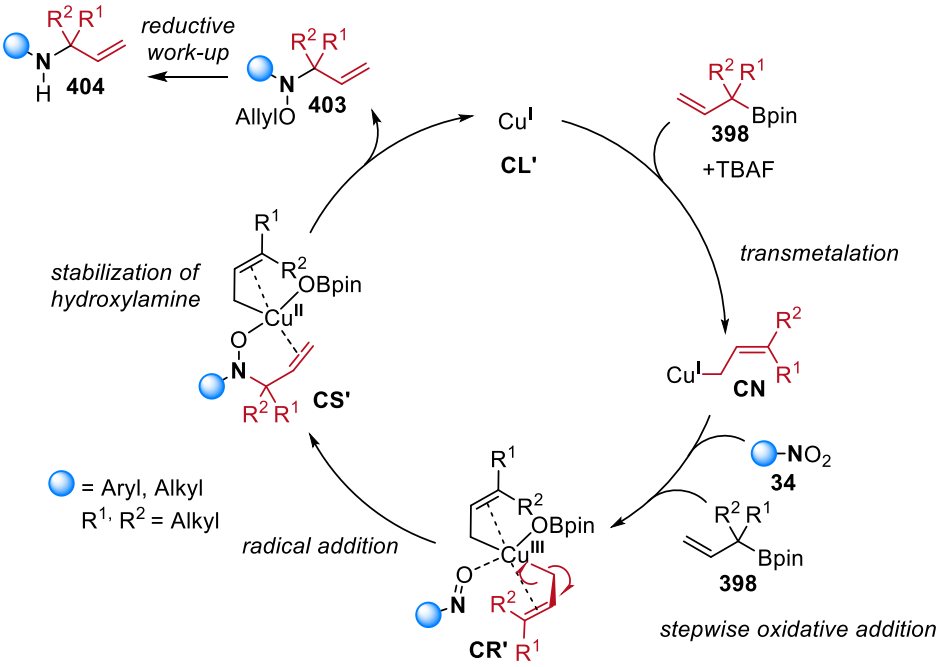
Summary – Cu-Catalyzed Coupling of Nitro Compounds with Allyl Boronates

In the course of this work, a Cu-catalyzed cross-coupling of nitro compounds with allyl boronates was realized (Scheme 118). The reaction is the first reported transition metal-catalyzed coupling of its type and combines the following advantages:

I. The unique type of C-N bond formation on Cu^{III} allowed the first application of allyl nucleophiles in a transition metal-catalyzed C-N cross-coupling reaction.

II. The central role of the Cu-catalyst for the activation, stabilization and functionalization of the nitro function may enable future investigations of a stereoselective C-N cross-coupling with nitro compounds.

III. Due to the efficient control of the stepwise reduction of the nitro group both aromatic and aliphatic compounds were suitable substrates for the reaction.



Scheme 118. Simplified catalytic cycle of the Cu-catalyzed coupling of nitro compounds with allyl boronates.

The reaction design relies on the stepwise oxidative addition of Cu^{I}-allyl organyl to the nitro group to form a Cu-coordinated nitroso species **CN**. A second allyl boronate **398** provides additional stabilization of the reactive intermediate. The nitroso group will be then allylated on the nitrogen with excellent selectivity for the most substituted carbon atom. After stabilization of the forming hydroxylamine through *O*-allylation and a reductive work-up, the desired amines **404** were obtained. In the reaction, a variety of functional groups were tolerated, particularly those commonly used as substrates in Cu-catalyzed cross-coupling reactions, such as aryl halides. Due to the efficient generation of the nitroso species on the Cu,

aliphatic nitro compounds can also be converted. On the allyl coupling partner side, primary, secondary and a variety of different substituted tertiary allyl boronates reacted selectively with the electrophilic nitrogen. The utilization of allyl nucleophiles in a C-N coupling demonstrated here was previously not reported.

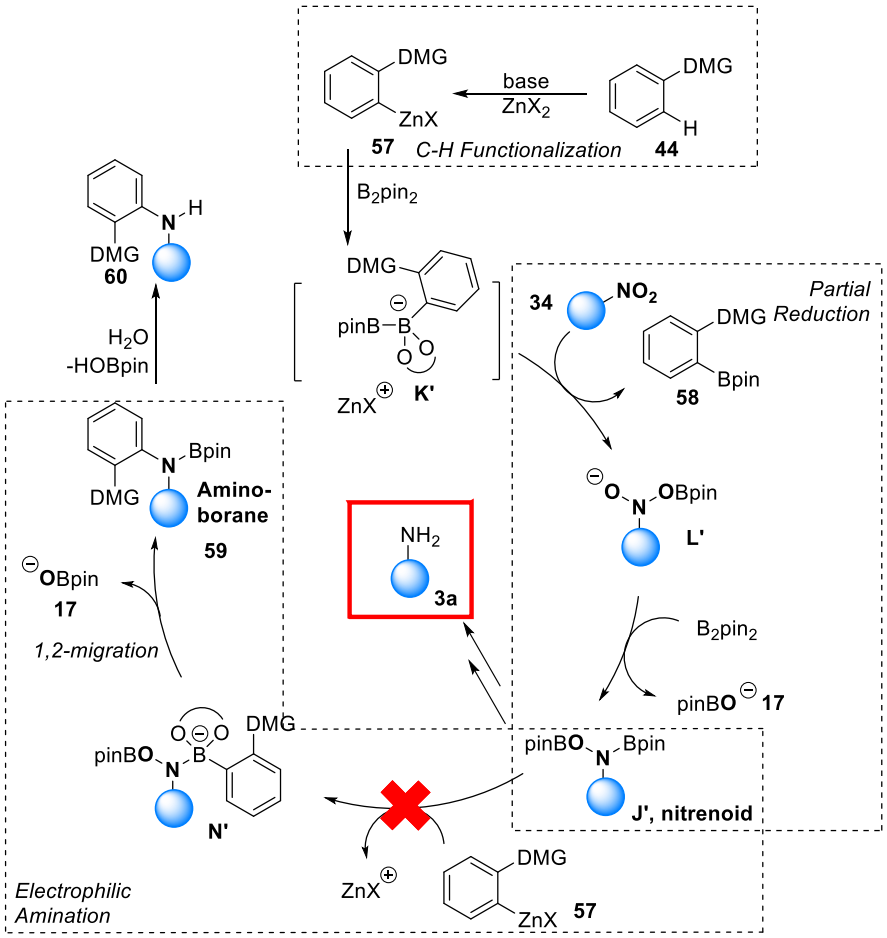
Based on these results, it is promising to study the stereoselective coupling between nitro compounds and allyl boronates in the future. The influence of a ligand on the Cu catalyst is likely to play a key role.

Summary – Boron-Mediated Direct Nitro-Functionalization

The utilization of direct nitro-functionalization in amine synthesis has garnered significant interest in recent decades due to its simplicity and improved step-economy compared to traditional methods. While several protocols have been developed for direct nitro-functionalization, only three examples utilize C-H functionalization to directly convert C-H bonds to C-N bonds. However, these reported reactions follow a radical pathway and are not applicable for converting C(sp^2)-H bonds to C(sp^2)-N bonds due to the uncontrollable reactivity of the corresponding aryl radical.

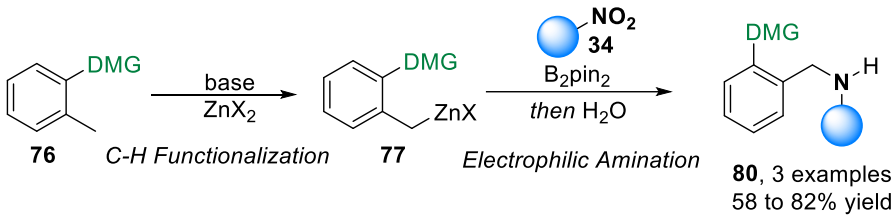
To explore the feasibility of an electrophilic C-H amination reaction with nitro compounds, our previously reported electrophilic amination protocol was employed. In this procedure, nitro compounds were transformed into nitrenoids through partial reduction, and (hetero)aromatic compounds with direct metalation groups served as coupling partners. Organozinc reagents were obtained through a deprotometalation step.

In the case of C(sp^2)-H amination, the reaction rate of the desired organozinc addition to a nitrenoid appeared to be slower compared to the activation of B_2pin_2. Consequently, a side reaction occurred, resulting in the formation of aniline as the primary product, while the desired product was not observed (Scheme 119).



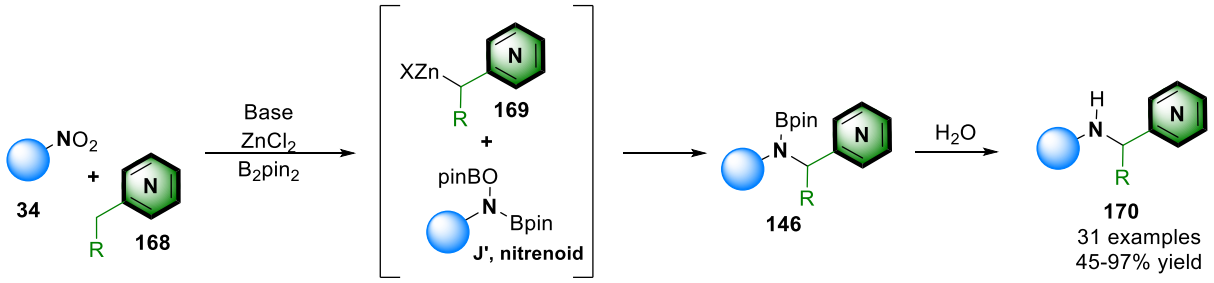
Scheme 119. The proposed C(sp^2)-H amination with nitro compounds leading to aniline **3a** as product.

The examined system exhibited limited success when applied to aromatic organozinc compounds; however, it was successfully employed in C(sp^3)-H amination. The formed benzylzinc species demonstrated excellent performance in affording the desired amines with good to excellent yields (Scheme 120). The presence of a suitable direct metalation group proved crucial for achieving favorable outcomes. Out of the 19 tested direct metalation groups, only 3 were successful. Some instances involved undesired side reactions, such as rearrangement or dimerization of the organozinc compound, while in other cases, the deprotonation system proved inefficient for the formation of the corresponding organozinc species.



Scheme 120. C(sp^3)-H amination with nitro compounds with limited applicability.

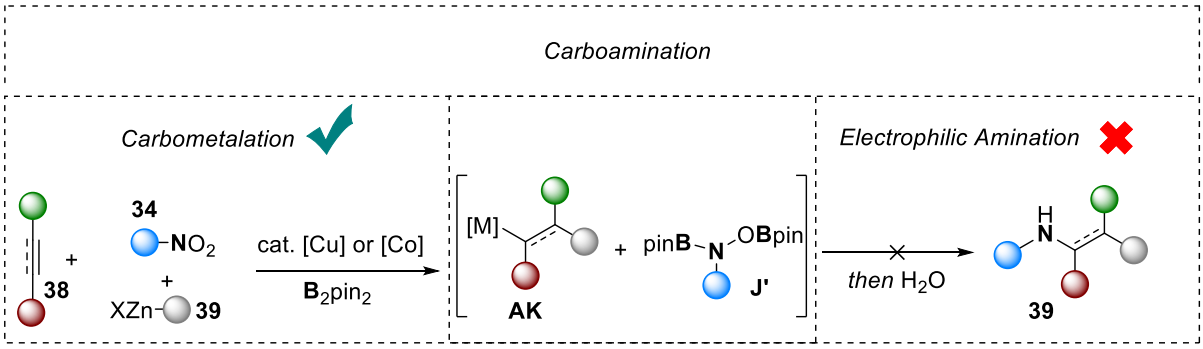
The protocol demonstrated a broad applicability when azaarylmethanes **168** were employed as substrates (Scheme 121). Various heterocyclic coupling partners **169** proved to be suitable substrates for the synthesis of highly functionalized azaarylmethylamines **170**. Notably, the reaction exhibited excellent functional group tolerance, enabling the transformation of nitro compounds containing ether-, ester-, amide-, nitrile-, halide-, and boronic ester groups. Mechanistic investigations revealed that the reaction follows a similar pathway as *our* previous protocol, involving the partial reduction of a nitro compound and subsequent formation of an aminoborane **146** through 1,2-migration.



Scheme 121. Synthesis of azaarylmethylamines *via* boron-mediated C(sp^3)-H amination with nitro compounds.

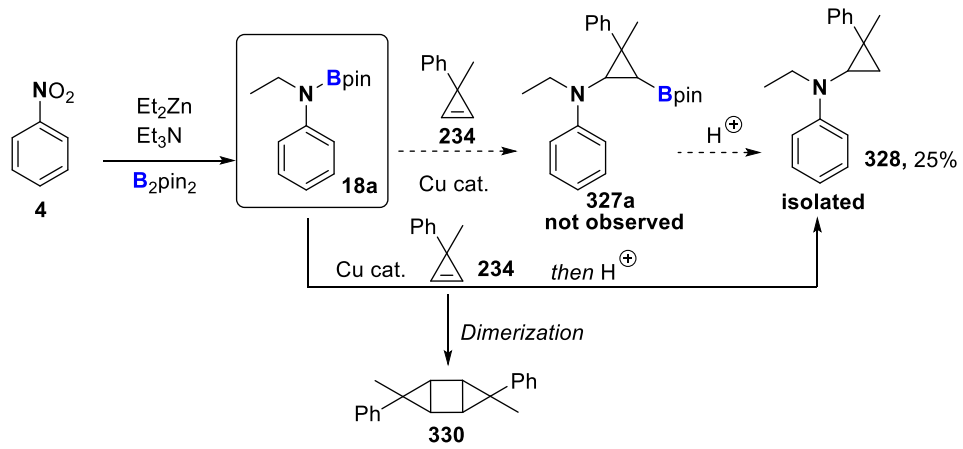
In the presented C(sp^3)-H amination reactions, a nitrenoid **J'** was successfully utilized as an electrophilic amination reagent. To expand the applicability of this species, a carboamination reaction of alkynes and alkenes was envisioned (Scheme 122). According to the working hypothesis, in the presence of a Cu or Co catalyst, the organozinc species adds to the C-C multiple bond, while also playing a crucial role in the partial reduction of nitro compounds to form a nitrenoid **J'**. Although the carbometalation step proceeded successfully, the electrophilic amination did not occur. This observation suggests that the nitrenoids **J'** may not have been suitable coupling partners for the generated alkyl- and alkenylzinc species **AK**.

Notably, in the case of alkynes, the resulting alkenylzinc **AK** compounds underwent 1,4-migration, leading to the formation of unreactive arylzinc species. When cyclopropenes were employed, the necessary presence of highly reactive organozinc compounds resulted in side reactions that consumed the nitro compounds. Unfortunately, the investigated systems were unable to achieve carboamination and provide the desired amines **39**.



Scheme 122. Designed carboamination of alkynes and alkenes with organozinc reagents and nitro compounds.

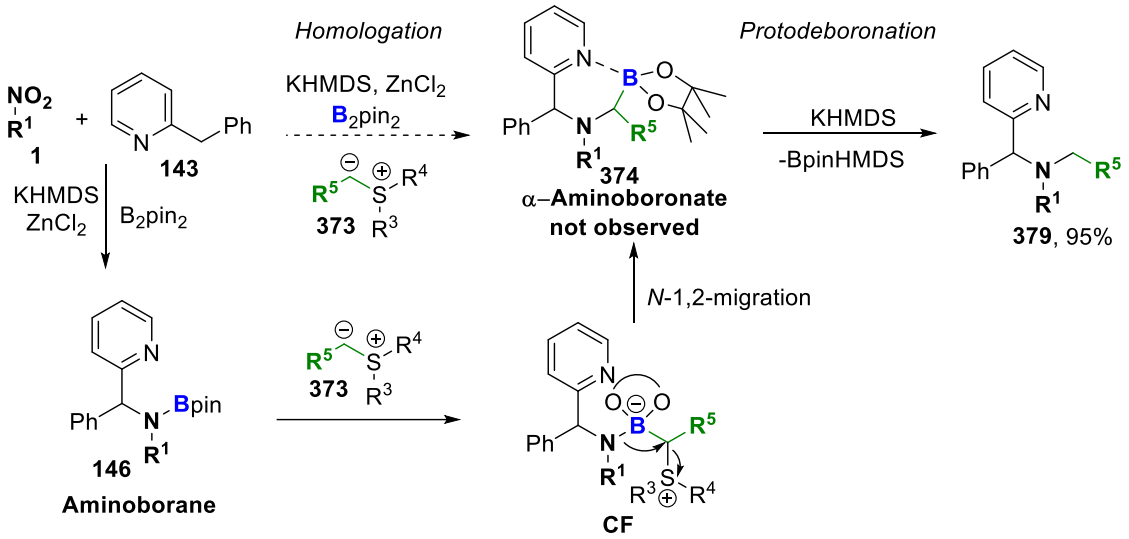
The investigated methods have primarily focused on expanding the applicability of *our* direct nitro-functionalization through the formation of diverse aminoboranes. To obtain the desired amines, aminoboranes were straightforwardly hydrolyzed. Despite *our* recent work showcasing the reactivity of aminoboranes towards electrophiles, there are only a limited number of reported examples concerning the reactivity of these compounds. One such example is the intramolecular aminoboration of C-C multiple bonds. However, the extension of direct aminoboration of C-C multiple bonds to intermolecular reactions remains unresolved. Given that *our* protocol enables the generation of various aminoboranes, their potential for direct intermolecular aminoboration was investigated. Unfortunately, in the designed system no aminonoboration of cyclopropene **234** was observed (Scheme 123). Although it is possible that the desired product **327a** may have formed during the reaction, protodeboronation likely occurred since **328** was isolated. It is worth mentioning that the highest yield of **328** was 25%, which may be attributed to the rapid dimerization and consumption of cyclopropene **234**, an issue that remained unresolved.



Scheme 123. Concept for a direct aminoboration of the cyclopropene **234** and a presumed protodeboronation.

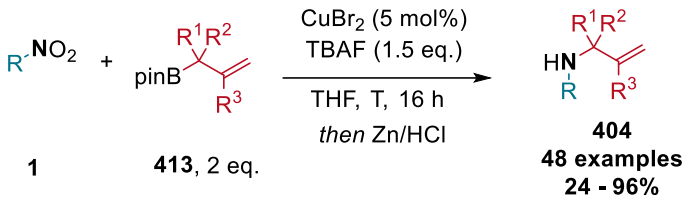
While limited success was achieved in the direct aminoboration of cyclopropenes using aminoboranes, their potential utilization in synthesis emerged through their transformation into α-aminoboronates. Given that α-aminoboronates differ from aminoboranes by only one methylene group, a straightforward homologation reaction may provide the desired α-aminoboronates (Scheme 124). To obtain stable and isolable α-aminoboronates, internal stabilization via functional groups such as carbonyl groups or N-containing heterocycles is crucial. The developed C-H amination reaction (Chapter 1.3) was ideal for synthesizing such stabilized α-aminoboronates, as the protocol allows the preparation of aminoboranes with an *N*-heterocyclic backbone.

Despite the complete consumption of the aminoborane in the reaction with a S-ylide as a homologation reagent, the desired product was not obtained; only the protodeboronation product was observed. Although protodeboronation may have occurred through a base-catalyzed reaction, the presence of the base was essential for generating the aminoborane.



Scheme 124. The designed synthesis of α-aminoboronates **374** and a plausible protodeboronation of the desired product.

In the last part of this work, the first Cu-catalyzed coupling of nitro compounds was presented, in particular the first utilization of allyl nucleophiles in C-N cross-coupling (Scheme 125). My contribution to this work was the investigation of the applicability of this protocol, therefore only this part was discussed. The method showed high-functional group tolerance and even usually problematic aliphatic nitro compounds were suitable substrates. The protocol may provide the basis of a future stereoselective introduction of the nitro group's nitrogen into a carbon skeleton.



Scheme 125. Cu-catalyzed C-N coupling of nitro compounds with allyl boronates.

Overall, the utilization of direct nitro-functionalization has been successfully employed in the synthesis of highly functionalized azaarylmethylamines. This strategy offers a straightforward protocol for coupling nitro compounds with unfunctionalized azaarylmethanes *via* C-H amination. Additionally, a Cu-catalyzed method utilizing allyl boronates as nucleophilic coupling partners has been developed for the direct transformation of nitro compounds. However, certain challenges remain unresolved, such as C(sp^2)-H amination or carboamination with nitro compounds and the application of aminoboranes in direct intermolecular aminoboration of C-C multiple bonds.

Experimental Part

Generals

General Techniques

Air- and moisture-sensitive reactions were carried out under Schlenk conditions under argon. The Schlenk tubes and flasks were dried in oven at least for one night before use. Degassing the solvents was performed by evacuating the reaction vessel until boiling the solvent, followed by the refilling with argon. This process was repeated three times.

Solvents and Reagents

Solvents for the reactions without air and moisture exclusion, extraction and isolation of the products (e.g., *n*-pentane, EtOAc and DCM) were distilled prior. THF, toluene, DMF and Et_2O for the reaction under Schlenk conditions were dried in a MB-SPS-800 solvent purification system from the company *MBraun*. The solvents were purchased from *Honeywell*. Commercially available chemicals were used without further purification and were purchased from the following suppliers: *Acros Organics, Sigma Aldrich, ChemPUR, Alfa Aesar, J&K Scientific, TCI, abcr* and *Roth*.

Chromatography

The way of the column chromatographic purification was designed according to the batch size. The newly developed reactions (usually 0.2 mmol batch size) were usually purified by semi-preparative *HPLC* (instrument: *Knauer*, column: *Hibar@250-25* with *Smartline UV detector 2500* and a *Smartline pump 1000)*. Starting materials and products of the C-H amination reactions and coupling reactions were purified by Kieselgel 60 (particle size: 0.04-0.063) by the company *Machery-Nagel*. The solvent mixtures were given in volume ratio.

Thin-Layer Chromatography

The thin-layer chromatography was carried out with *Machery-Nagel* ALUGRAM Xtra SIL G/UV254 aluminum plates. The analysis was proceeded via UV light radiation (λ = 254 nm), oxidation by $KMnO_4$ solution (13.1 g K_2CO_3, 2.0 g $KMnO_4$, 0.2 g KOH, 200 mL H_2O), ceric ammonium molybdate solution (2.5 g ammonium molybdate tetrahydrate, 1 g cerium ammonium sulfate dihydrate, 10 mL sulfuric acid, 90 mL H_2O) or ninhydrin solution (1.5 g ninhydrin, 3.0 mL acetic acid, 100 mL ethanol).

NMR Spectroscopy

NMR spectra were measured on the following instruments: *Varian* VNMRS-400, VNMRS-600 or *Mercury* 300, *Bruker* Advance Neo 400 and 600. All spectra were measured decoupled in the given deuterated solvent. In the case of ^1H- or ^{13}C-NMR was referenced to the residue signal of the NMR solvent. The multiplicity of the signals was given as the following: s (singlet), d (doublet), t (triplet), dt (doublet of triplets), td (triplet of doublets), q (quartet), quint (quintett) and m (multiplet).

Mass Spectrometry

A FINNIGAN SSQ 7000 was used for the measurements of mass spectra by electron ionization (MS-EI: EV 70). The detected masses were given as dimensionless numbers in the mass-to-charge ratio m/z, where the relative intensity was given in parentheses. High-resolution mass spectra (HRMS) were either measured by FINNIGAN MAT 95 or THERMO SCIENTIFIC LTQ ORBITRAP XL spectrometer.

IR Spectroscopy

The measurements of the IR spectra (ATR) were carried out on a PERKIN-ELMER 1760 SERIES FT-IR. Characteristic bands for important functional groups were given.

Chapter 1: C-H Amination with Nitro Compounds

General Procedures

Preparation of $ZnCl_2$•THF (1 M)

According to the procedure of *Knochel et al.*, $ZnCl_2$ (4.08 g, 0.3 mmol) was dried in a Schlenk flask at 150 °C for 5 hours *in vacuo* (1.0 mbar). The flask was let to cool off to rt, then was charged with THF (30 mL). The solution was stirred until the all of the $ZnCl_2$ was dissolved. NOTE: after 1 or 2 days, precipitation was formed at the bottom of the flask, possibly $ZnCl_2$ THF complex (1:2), which did not influence the efficiency of the reagent. The solution was stored under argon.

Preparation of TMPLi (0.63 M in THF)

According to the procedure of *Knochel et al.*, in a Schlenk flask, freshly distilled 2,2,6,6-tetramethylpiperidine (0.21 mL, 1.25 mmol) was dissolved in THF (1 mL). The flask was brought to -40 °C and ^{n}BuLi (1.6 M in hexanes, 0.78 mL, 1.25 mmol) was added to the mixture. The mixture was stirred at -40 °C for 0.5 h.

General procedure A1 for electrophilic amination *via* C(sp^2)-H deprotonation

In a Schlenk tube, DMG substrate (0.4 mmol, 2.0 eq.) was dissolved in THF (1 mL), then $ZnCl_2$ solution (1.0 M in THF, 0.3 mL, 0.3 mmol, 1.5 eq.) was added and the mixture was brought to -78 °C. The mixture was treated with TMPLi (0.63 M, 1.42 mL, 0.9 mmol, 4.5 eq.). After 30 mins, 4-nitroanisole (31 mg, 0.2 mmol) and B_2pin_2 (102 mg, 0.4 mmol) were added and the mixture was stirred at rt. After 16 hours, water (1 mL) was added and the aqueous layer was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure A2 for the electrophilic amination *via* C(sp^3)-H deprotonation

In a Schlenk tube, 2-methylphenyl DMG substrate (0.4 mmol, 2.0 eq.) was dissolved in THF (1 mL) and the mixture was brought to -78 °C. The mixture was subsequently treated with TMPLi (0.63 M, 0.95 mL, 0.6 mmol, 3.0 eq.) and $ZnCl_2$ solution (1.0 M in THF, 0.44 mL, 0.44 mmol, 2.2 eq.). After 30 mins, 4-nitroanisole (31 mg, 0.2 mmol) and B_2pin_2 (102 mg, 0.4 mmol) were added and the mixture was stirred at rt. After 16 hours, water (1 mL) was added and the aqueous layer was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B1 for coupling of nitro compounds with azaarylmethanes

Azaarylmethane (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) in a flame dried Schlenk tube and the mixture was degassed three times. The mixture was charged with $KN(SiMe_3)_2$ (1.7 mL, 1.2 mmol, 6.0 eq., 0.7 M in toluene) followed by $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF). After stirring for 5 min at rt, nitro compound (0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were subsequently added. The mixture was stirred at rt overnight, stopped with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of Na_2SO_4 and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude product was purified *via* flash column chromatography.

General procedure B2 for coupling of nitro compounds with azaarylmethanes

Azaarylmethane (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) in a flame dried Schlenk tube and the mixture was degassed three times. The mixture was cooled to 0 °C, charged with $LiN(SiMe_3)_2$ (1.2 mL, 1.2 mmol, 6.0 eq., 1.0 M in THF) followed by $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF). After stirring for 5 min at 0 °C, nitro compound (0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were subsequently added. The mixture was stirred at rt overnight, stopped with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of Na_2SO_4 and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude product was purified *via* flash column chromatography.

General procedure B3 for coupling of nitro compounds with azaarylmethanes

Azaarylmethane (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) in a flame dried Schlenk tube and the mixture was degassed three times. The mixture was cooled to -78 °C, charged with freshly prepared TMPLi (0.95 mL, 0.6 mmol, 3.0 eq., 0.63 M in THF) followed by $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF). After stirring for 5 min at -78 °C, nitro compound (0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were subsequently added. The mixture was stirred at rt overnight, stopped with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of Na_2SO_4 and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude product was purified *via* flash column chromatography.

General procedure B4 for synthesis of azaarylmethanes

The reaction was carried out according to the literature.[63]

Anhydrous cobalt(II) acetylacetonate (51.4 mg, 0.2 mmol, 0.1 eq.) and heterocyclic chloride (2.0 mmol, 1.0 eq.) were placed in a 25 mL flask. Anhydrous dioxane (6 mL) was added and the mixture was cooled to 0 °C. Then benzylmagnesium chloride (6.0 mmol, 3.0 eq., 1.4 M in Et_2O) was added dropwise. The mixture warmed up to rt. After 30 min H_2O (6ml) was added and the reaction was extracted with ethyl acetate three times. The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure B5 for synthesis of azaarylmethanes

The reaction was carried out according to the literature.[63]

Anhydrous nickel(II) acetylacetonate (128 mg, 0.5 mmol, 0.05 eq.), triphenylphosphine (520 mg, 2.0 mmol, 0.2 eq.) and heterocyclic chloride (10.0 mmol, 1.0 eq.) were placed in a 50 mL flask. Anhydrous THF (20 mL) was added and the mixture was cooled to 0 °C. Then benzylmagnesium chloride (11.0 mmol, 1.4 M in Et_2O) was added dropwise. The mixture was let to warm up to rt. After 30 min H_2O (6 ml) was added and the reaction was extracted with ethyl acetate three times. The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure B6 for synthesis of azaarylmethanes

The reaction was carried out according to the literature.[63]

Anhydrous nickel(II) acetylacetonate (128 mg, 0.5 mmol, 0.05 eq.), triphenylphosphine (520 mg, 2.0 mmol, 0.2 eq.) and heterocyclic chloride (10.0 mmol, 1.0 eq.) were placed in a 50 mL flask. Anhydrous THF (20 mL) was added and the mixture was cooled to 0 °C. Then benzylmagnesium chloride (30.0 mmol, 3.0 eq., 1.4 M in Et_2O) was added dropwise. The mixture was let to warm up to rt. After 16 h H_2O (6 ml) was added and the reaction was extracted with ethyl acetate three times. The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure B7 for synthesis of azaarylmethanes

The reaction was carried out according to the literature.[64]

A solution of 2-methylpyridine (0.99 mL, 10.0 mmol) in dry THF (10 mL) was cooled to -78 °C, and *n*-butyllithium (6.25 mL, 10.0 mmol, 1.6 M in hexane) was added within 15 min. The reaction mixture was stirred for 30 min at – 78 °C and warmed up to 0 °C. 2-fluoropyridine (0.43 mL, 5.0 mmol) was added within 5 min, and the reaction mixture was heated to reflux for 25 min and hydrolysed with ice. The aqueous phase was extracted three times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by vacuum distillation or column chromatography.

General procedure B8 for the synthesis azaarylmethanes

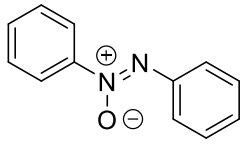
The reaction was carried out according to the modified procedure of *Chakraborti et al.*[65]

Phenylacetic acid (0.68 g, 5 mmol, 1.0 eq.) was dissolved in DCM (15 mL) and two drops of DMF were added. To the mixture was added oxalyl chloride (0.95 g, 7.5 mmol, 1.5 eq.) dropwise and the mixture was stirred for 1 hour at rt. Then the solvent and the remaining oxalyl chloride were evaporated. The residue was dissolved in 1,4-dioxane (10 mL). To the reaction mixture were added 2-aminophenol (0.545 g, 5 mmol, 1.0 eq.) and methanesulfonic acid (1.48 g, 15 mmol, 3.0 eq.) and the mixture was stirred at 100 °C. After 2 hours, the mixture was concentrated. The residue was diluted with EtOAc and saturated $NaHCO_3$ was added. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography (Pentane: EtOAc).

Chapter 1.1: C(sp^2)-H Amination with Nitro Compounds

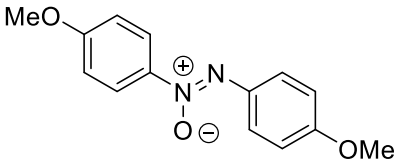
Isolated Compounds

1,2-diphenyldiazene 1-oxide (azoxybenzene) (D)



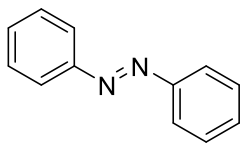
Following the general procedure B13 compound **D** was isolated by flash column chromatography (Pentane: EtOAc = 19:1) ; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.36 – 8.29 (m, 2H), 8.21 – 8.15 (m, 2H), 7.60 – 7.46 (m, 5H), 7.42 – 7.37 (m, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 144.0, 131.6, 129.6, 128.8, 128.7, 125.5, 122.3 ppm; m/z (EI) (%): 199.1 (25), 198.0 (100), 170.1 (17), 169.0 (34), 141.0 (18), 105.0 (24), 91.1 (26), 77.2 (88), 65.1 (23), 64.1 (17), 51.2 (37), 50.2 (10); HRMS-ESI: calcd. For $C_{12}H_{11}N_2O$ $[M+H]^+$: 199.08659, found.: 199.08600; IR (KBr): 3066, 1774, 1477, 1437, 1299, 1163, 1071, 1024, 924, 761, 682 cm^{-1}.
The spectral data are in accordance with the literature.[125]

(*Z*)-1,2-bis(4-methoxyphenyl)diazene 1-oxide (*p*-methoxy azoxybenzene) (D')



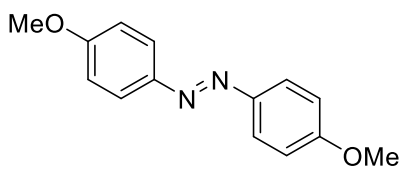
Following the general procedure B13, using 4-nitroanisole, compound **D'** was isolated by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.26 (dd, *J* = 19.7, 9.2 Hz, 4H), 6.97 (dd, *J* = 10.4, 9.2 Hz, 4H), 3.88 (d, *J* = 4.1 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.84, 160.18, 138.00, 127.79, 123.76, 113.72, 113.58, 55.67, 55.47 ppm.
The spectral data are in accordance with the literature.[125]

1,2-diphenyldiazene (azobenzene) (E)



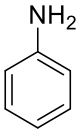
Following the general procedure B13 compound **E** was isolated by flash column chromatography (Pentane: EtOAc = 19:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.93 – 7.82 (m, 4H), 7.55 – 7.35 (m, 6H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 152.7, 131.0, 129.1, 122.8 ppm; m/z (EI) (%): 182.0 (100), 152.1 (14), 105.1 (13), 77.2 (33), 51.2 (49), 50.2 (18); HRMS-ESI: calcd. for $C_{12}H_{11}N_2$ $[M+H]^+$: 183.09167, found: 183.09120; IR (KBr): 3061, 1480, 1452, 1069, 923, 771, 683 cm^{-1}.
The spectral data are in accordance with the literature.[47]

(*E*)-1,2-bis(4-methoxyphenyl)diazene (*p*-methoxy azobenzene) (E')



Following the general procedure B13, using 4-nitroanisole, compound **E'** was isolated by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.9 Hz, 4H), 7.00 (d, *J* = 9.0 Hz, 4H), 3.89 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.57, 148.99, 126.87, 115.16, 57.23 ppm.
The spectral data are in accordance with the literature.[126]

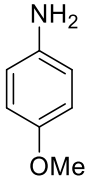
Aniline (5)



Following the general procedure B13 compound **5** was isolated by flash column chromatography (Pentane: EtOAc = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.16 (dd, *J* = 8.4, 7.3 Hz, 2H), 6.81 – 6.74 (m, 1H), 6.69 (d, *J* = 7.3 Hz, 2H), 3.60 (br s, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.3, 129.3, 118.6, 115.1 ppm; HRMS-ESI: calcd. for C_6H_8N $[M+H]^+$: 94.06513, found: 94.06491; IR (KBr): 3430, 1602 cm^{-1}.

The spectral data are in accordance with the literature.[127]

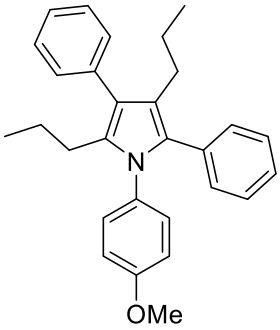
4-methoxyaniline (5a)



Following the general procedure A1 compound **5a** was isolated by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.75 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.7 Hz, 2H), 3.75 (s, 3H), 3.40 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.8, 139.8, 116.4, 114.8, 55.7.

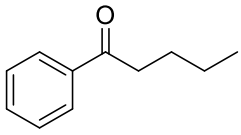
The spectral data are in accordance with the literature.[127]

1-(4-methoxyphenyl)-2,4-diphenyl-3,5-dipropyl-1H-pyrrole (66)



Following the general procedure A1 compound **66** was isolated by semi-preparative HPLC(Pentane:EtOAc = 10:1 to 2:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 (d, *J* = 4.9 Hz, 4H), 7.22 – 7.19 (m, 1H), 7.12 – 7.08 (m, 2H), 7.05 – 7.02 (m, 3H), 7.01 – 6.97 (m, 2H), 6.73 – 6.69 (m, 2H), 3.70 (s, 3H), 2.43 – 2.34 (m, 4H), 1.17 – 1.11 (m, 2H), 1.11 – 1.04 (m, 2H), 0.57 (t, *J* = 7.3 Hz, 3H), 0.51 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 158.15, 137.45, 133.53, 132.33, 131.59, 130.62, 130.30, 129.76, 127.94, 127.55, 125.84, 125.65, 122.57, 120.68, 113.61, 55.29, 27.15, 27.09, 24.40, 23.38, 14.24, 13.96 ppm; IR (KBr): ν= 3054, 2956, 2930, 2867, 1603, 1511, 1451, 1378, 1294, 1244, 1173, 1101, 1072, 1031, 913, 833, 757, 698 cm^{-1}; m/z (EI) (%): 410.2 (34), 409.1 (100), 381.1 (21), 380.1 (79), 108.1 (26), 91.1 (10), 78.1 (19), 77.1 (17); HRMS (m/z): $[M+H]^+$ calcd. for $C_{29}H_{32}ON$: 410.24784; found: 410.24695.

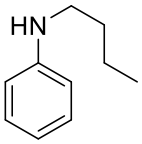
1-phenylpentan-1-one (68)



Following the general procedure A1 compound **68** was isolated by flash column chromatography (Pentane:EtOAc = 50:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 – 7.82 (m, 2H), 7.49 – 7.44 (m, 1H), 7.42 – 7.31 (m, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 1.68 – 1.61 (m, 2H), 1.33 (h, *J* = 7.4 Hz, 2H), 0.87 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 200.56, 137.13, 132.85, 128.55, 128.41, 128.16, 128.06, 38.33, 26.50, 22.50, 22.49, 13.95, 13.94 ppm; IR (KBr): ν= 2957, 2933, 2870, 1683, 1596, 1450, 1352, 1321, 1263, 1207, 1106, 1010, 967, 749, 690 cm^{-1}; m/z (EI) (%): 163.1 (21), 162.1 (28), 120.1 (55), 150.1 (100), 77.1 (35), 51.2 (11); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{11}H_{14}ONa$: 185.09369; found: 185.09360.

The spectral data are in accordance with the literature.[128]

***N*-butylaniline (69)**



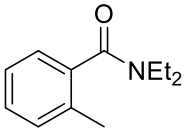
Following the general procedure A1 compound **69** was isolated by flash column chromatography (Pentan:EtOAc = 20:1) as colorless liquid; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.20 – 7.14 (m, 2H), 6.68 (td, *J* = 7.3, 1.1 Hz, 1H), 6.63 – 6.58 (m, 2H), 3.60 (s, 1H), 3.11 (t, *J* = 7.1 Hz, 2H), 1.60 (p, *J* = 6.6 Hz, 2H), 1.43 (h, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 148.5, 129.2, 117.0, 112.7, 43.7, 31.7, 20.3, 13.9 ppm; m/z (EI) (%): 182.1 (20), 84.3 (10), 77.2 (10), 71.3 (29), 69.3 (20), 57.2 (100), 55.3 (51); HRMS-ESI: calcd. for $C_{10}H_{16}N$ $[M+H]^+$: 150.12773, found: 157.12773; IR (KBr): 3407, 1600, 1259 cm^{-1}.

The spectral data are in accordance with the literature.[129]

Chapter 1.2: C(sp^2)-H Amination with Nitro Compounds

Synthesis of the Starting Materials

_N,N_-diethyl-2-methylbenzamide (81)

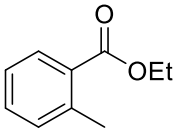


The synthesis was carried out according to the procedure of *Clark et al.*[44]

Toluic acid (2.5 g, 18 mmol, 1.0 eq.) was dissolved in DCM (30 mL). Et_3N (7.6 mL, 55.0 mmol, 3.0 eq.) and Et_2NH (1.85 mL, 18 mmol, 1.0 eq.) were added and the mixture was cooled to 0 °C. Freshly distilled $SOCl_2$ (1.3 mL, 18 mmol, 1.0 eq.) was added dropwise, then the mixture was stirred at rt. After 10 min, the solvent and the remaining $SOCl_2$ were removed in vacuo. The residue was dissolved in DCM (30 mL) and was subsequently washed with 1 M HCl, 1 M NaOH and brine. The solvent was evaporated in vacuo and the product was obtained after column chromatography (Pentane: EtOAc = 3:1) as a colorless liquid (2.57 g, 13.5 mmol, 75%)

The spectral data are in accordance with the literature.[44]

ethyl 2-methylbenzoate (92)

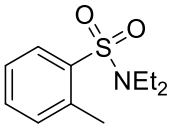


The synthesis was carried out according to the procedure of *Kim et al.*[45]

Toluic acid (2.5 g, 18 mmol, 1.0 eq.) was dissolved in 10 mL ethanol, then sulfuric acid (0.25 mL, 4.7 mmol) was added and the mixture was stirred at 80 °C. After 7 hours the solvent was evaporated. Then H_2O (12 mL) and Et_2O (5 mL) were added and the organic phase was subsequently washed twice with H_2O and Na_2CO_3 solution (5 mol%). The organic phase was dried over Na_2SO_4 and the solvent was removed in vacuo. The crude product was distilled *in vacuo*. The product was isolated as colorless liquid (0.88 g, 5.4 mmol, 30%).

The spectral data are in accordance with the literature.[45]

_N,N_-diethyl-2-methylbenzenesulfonamide (94)

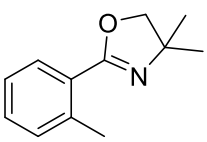


The synthesis was carried out according to the procedure of *Zwerzak et al.*[46]

2-methylbenzenesulfonamide (1.7 g, 10 mmol, 1.0 eq.), NaOH (2.0 g, 50 mmol, 5.0 eq.), K_2CO_3 (2.0 g, 14 mmol, 1.4 eq.) and Bu_4NHSO_4 (0.34 g, 1.0 mmol, 0.1 eq.) were dissolved in toluene (15 mL). To this mixture ethyl bromide (2.81 g, 1.46 mL, 26 mmol. 2.6 eq.) in 10 mL toluene was added dropwise at 40 °C. Then the mixture was stirred at 40 °C for 3.5 h. The mixture was cooled to rt and was filtered. The solid residue was washed three times with 10 mL toluene. The filtrate was washed three times with 10 mL H_2O and once with 10 mL brine. The organic phase was dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was obtained after recrystallization from ethanol (20 mL) as colorless solid (2.1 g, 9.4 mmol, 94%)

The spectral data are in accordance with the literature.[46]

4,4-dimethyl-2-(o-tolyl)-4,5-dihydrooxazole (97)



The synthesis was carried out according to the protocol of *Nachstheim et al.*[47]

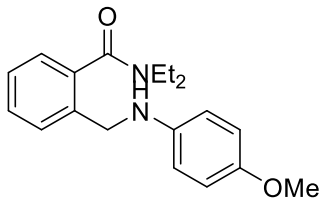
2-methylbenzaldehyde (1.2 g, 1.16 mL, 10 mmol, 1.0 eq.) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15 mmol, 1.5 eq.) were dissolved in 25 mL DCM. Then 4 Å molecular sieve (10 g) was added and the mixture was stirred at rt. After 20 h, the mixture was treated with *N*-bromosuccinimide (2.67 g, 15 mmol, 1.5 eq.) and was stirred at rt. After 4 hours, the solid residue was filtered off. The organic phase was washed three times with saturated $NaHCO_3$ solution. The aqueous phase was extracted two times with DCM. The combined organic phase was washed with saturated $Na_2S_2O_3$ solution, were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was obtained as brown oil (1.62 g, 8.6 mmol, 86%); ^1H NMR (600 MHz, $CDCl_3$): δ 7.75 (d, J = 8.3 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.20 – 7.14 (m, 2H), 4.01 (s, 2H), 2.56 (s, 3H), 1.36 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 162.5, 138.3, 130.9, 130.2, 129.6, 127.6, 125.3, 78.3, 67.7, 28.3, 21.3 ppm; IR (KBr): ν=

3026, 2967, 2928, 2890, 2328, 2085, 1717, 1642, 1490, 1456, 1350, 1308, 1278, 1246, 1186, 1132, 1039, 966, 921, 869, 820, 773, 728, 689, 665 cm^{-1}; m/z (EI) (%): 191.0 (11), 190.0 (86), 189.0 (100), 173.9 (42), 146.0 (16); HRMS (m/z): $[M]^+$ calcd. for $C_{12}H_{15}ON$: 189.11482; found: 189.11491.

The spectral data are in accordance with the literature.[47]

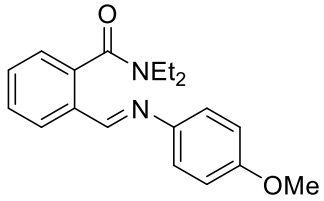
Isolated Compounds

_N,N_-diethyl-2-(((4-methoxyphenyl)amino)methyl)benzamide (83)



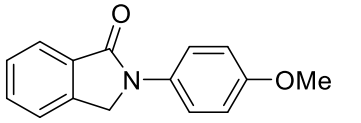
Following the general procedure A2 compound **83** was isolated by flash column chromatography (Pentane:EtOAc = 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 - 7.41 (m, 1H), 7.30 (td, *J* = 7.0 Hz, *J* = 1.3 Hz, 2H), 7.22 – 7.17 (m, 1H), 6.75 (d, *J* = 9.1 Hz, 2H), 6.63 - 6.57 (m, 2H), 4.26 (s, 2H), 3.82 (s, 1H), 3.72 (s, 3H), 3.20 - 3.03 (m, 4H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 170.71, 152.11, 142.27, 136.50, 136.48, 128.93, 128.90, 127.11, 125.78, 114.75, 114.23, 55.74, 47.16, 42.93, 38.76, 13.96, 12.72.ppm; IR (KBr): ν= 3351, 2975, 2934, 2832, 1619, 1511, 1432, 1376, 1289, 1233, 1177, 1037, 946, 878, 819, 775, 747 cm^{-1}; m/z (EI) (%): 313.2 (20), 312.2 (100), 240.1 (24), 239.1 (90), 238.1 (20), 224.1 (31), 212.1 (13), 211.1 (80), 210.1 (17), 196.1 (31), 74.2 (14); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{19}H_{24}O_2N_2Na$: 355.17300; found: 355.17300.

_N,N_-diethyl-2-(((4-methoxyphenyl)imino)methyl)benzamide (84)



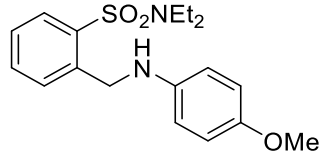
Following the general procedure A2 compound **84** was isolated by flash column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.20 – 8.12 (m, 1H), 7.47 (dd, *J* = 5.7, 3.3 Hz, 2H), 7.32 – 7.28 (m, 1H), 7.21 – 7.17 (m, 2H), 6.92 – 6.88 (m, 2H), 3.82 (s, 3H), 3.65 – 3.57 (m, 2H), 3.15 (q, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.69, 158.47, 155.29, 144.56, 138.38, 132.67, 130.68, 128.93, 127.64, 126.26, 122.27, 114.35, 77.21, 55.47, 43.06, 39.08, 13.95, 12.92 ppm; IR (KBr): ν= 2972, 2933, 2839, 1625, 1501, 1459, 1430, 1374, 1289, 1244, 1188, 1106, 1080, 1031, 879, 831, 765 cm^{-1}; m/z (EI) (%): 311.0 (22), 309.9 (100), 281.9 (10), 280.9 (69), 252.8 (33), 239.0 (21), 237.9 (91), 210.9 (32), 208.9 (17), 195.9 (14), 166.9 (14), 129.9 (11), 72.2 (16); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{19}H_{22}O_2N_2Na$: 333.15735; found: 333.15668.

2-(4-methoxyphenyl)isoindolin-1-one (85)



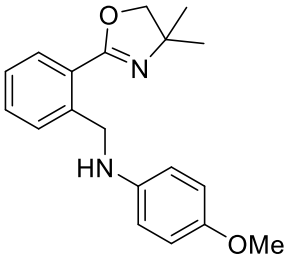
Following the general procedure A2 compound **85** was isolated by flash column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 – 7.90 (m, 1H), 7.76 – 7.71 (m, 2H), 7.58 (td, *J* = 7.4, 1.2 Hz, 1H), 7.53 – 7.48 (m, 2H), 6.98 – 6.93 (m, 2H), 4.82 (s, 2H), 3.83 (s, 4H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 167.23, 156.62, 140.11, 133.28, 132.63, 131.78, 128.30, 124.03, 122.52, 121.51, 114.33, 55.49, 51.17 ppm; IR (KBr): ν= 3006, 2927, 2838, 1680, 1624, 1506, 1463, 1437, 1388, 1296, 1238, 1184, 1156, 1096, 1063, 1032, 952, 878, 827, 792, 736, 680 cm^{-1}; m/z (EI) (%): 240.0 (16), 238.9 (100), 223.9 (58), 195.9 (11); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{15}H_{13}O_2NNa$: 262.08385; found: 262.08389.
The spectral data are in accordance with the literature.[130]

_N,N_-diethyl-2-(((4-methoxyphenyl)amino)methyl)benzenesulfonamide (98)



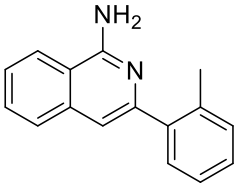
Following the general procedure A2, using *N,N*-diethyl-2-methylbenzenesulfonamide (91 mg, 0.4 mmol, 2.0 eq.) as DMG-substrate, compound **98** was isolated by flash column chromatography (Pentane:EtOAc = 5:1) as colorless oil (57 mg, 0.16 mmol, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.62 - 6.56 (m, 2H), 4.67 (s, 2H), 3.84 (s, 1H), 3.73 (s, 3H), 3.37 (q, *J* = 7.1 Hz, 4H), 1.17 (t, *J* = 7.1 Hz, 6H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ 152.32, 141.8, 139.5, 136.9, 132.2, 129.4, 127.8, 121.5, 115.1, 113.6, 56.1, 42.7, 38.8, 10.2 ppm.

_N_-(2-(3,3-dimethylcyclopent-1-en-1-yl)benzyl)-4-methoxyaniline (101)



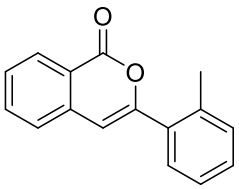
Following the general procedure A2, using 4,4-dimethyl-2-(o-tolyl)-4,5-dihydrooxazole (76 mg, 0.4 mmol, 2.0 eq.) as DMG-substrate, compound **101** was isolated by flash column chromatography (Pentane:EtOAc: Et_3N = 2:1:0.01) as yellow oil (47 mg, 0.15 mmol, 75%). ^1H NMR (600 MHz, $CDCl_3$): δ 8.25 – 8.14 (m, 1H), 7.76 – 7.70 (m, 1H), 7.34 – 7.24 (m, 1H), 7.20 (ddt, *J* = 7.7, 1.4, 0.7 Hz, 2H), 6.99 – 6.91 (m, 2H), 4.06 (d, *J* = 1.8 Hz, 2H), 3.89 (s, 2H), 2.54 (s, 3H), 1.38 (d, *J* = 1.8 Hz, 6H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 165.4, 151.7, 141.6, 136.9, 135.9, 130.8, 130.1, 129.0, 121.9, 115.1, 113.3, 79.1, 72.7, 55.8, 44.0, 27.8 ppm; IR (KBr): ν= 3288, 2966, 2930, 2112, 1638, 1511, 1451, 1354, 1304, 1240, 1192, 1125, 1033, 962, 822, 777, 746, 698 cm^{-1}; HRMS (m/z): $[M+H]^+$ calcd. for $C_{19}H_{23}O_2N_2$: 311.17540; found: 311.17640.

3-(o-tolyl)isoquinolin-1-amine (103)



Following the general procedure A2, using 2-methylbenzonitrile as DMG-substrate, compound **103** was isolated by semi-preparative HPLC (Pentane:EtOAc: Et_3N = 4:1:0.01). ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (dq, *J* = 8.4, 1.0 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.67 – 7.63 (m, 1H), 7.51 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.44 (dt, *J* = 6.3, 1.5 Hz, 1H), 7.30 – 7.27 (m, 2H), 7.11 (d, *J* = 0.9 Hz, 1H), 5.36 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.28, 151.99, 141.55, 138.07, 136.07, 130.58, 130.06, 129.60, 127.87, 127.35, 126.02, 125.75, 122.62, 112.24, 20.38.
The spectral data are in accordance with the literature.[52]

3-(o-tolyl)-1H-isochromen-1-one (105)



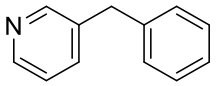
Following the general procedure A2, using ethyl 2-methylbenzoate as DMG-substrate, compound **105** was isolated by flash column chromatography (Pentane:EtOAc = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.6, 1.2 Hz, 1H), 7.60 – 7.48 (m, 3H), 7.36 – 7.31 (m, 1H), 7.29 (d, *J* = 7.6 Hz, 2H), 6.60 (s, 1H), 2.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.75, 155.62, 137.65, 137.09, 135.02, 133.1, 130.92, 126.06, 129.89, 129.12, 128.45, 126.13, 126.01, 120.57, 106.19, 20.92. HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{13}O_2$ $[M+H]^+$: 237.09102; found: 237.09176

The spectral data are in accordance with the literature.[131]

Chapter 1.3: Synthesis of Azaarlymethylamines

Synthesis of Starting Materials

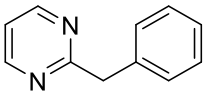
3-benzylpyridine (151a)



According to the general procedure B4 compound **151a** was synthesized as yellow liquid (195 mg, 1.153 mmol, 57%). Purification by flash column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 – 8.44 (m, 1H), 7.50 – 7.45 (m, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.19 (m, 3H), 7.18 (d, *J* = 7.4 Hz, 2H), 3.98 (s, 2H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 149.9, 147.4, 139.7, 136.5, 128.8, 126.5, 123.5, 39.0 ppm;IR (KBr): ν= 3027, 2082, 1703, 1575, 1479, 1450, 1422, 1189, 1102, 1074, 1026, 828, 779, 740, 703 cm^{-1}; m/z (EI) (%): 339.0 (22), 260.0 (14), 170.0 (78), 169.0 (100), 168.0 (86), 167.0 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{12}N$: 170.09643; found: 170.09686.

The spectral data are in accordance with the literature.[132]

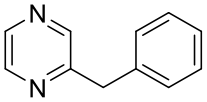
2-benzylpyrimidine (151b)



According to the general procedure B5 on a 10.0 mmol scale compound **151b** was synthesized as yellow liquid (663 mg, 3.890 mmol, 39%). Purification by flash column chromatography (Pentane:EtOAc = 1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 – 8.66 (s, 2H), 7.36 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 4.9 Hz, 1H), 4.30 (s, 2H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 170.0, 157.3, 138.2, 129.1, 128.5, 126.6, 118.6, 46.0 ppm;IR (KBr): ν= 3032, 2103, 1562, 1494, 1417, 1181, 1029, 993, 806, 742, 698 cm^{-1}; m/z (EI) (%): 171.1 (18), 170.1 (53), 169.1 (100), 168.0 (10); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{11}N_2$: 171.09167; found: 171.09148.

The spectral data are in accordance with the literature.[63b]

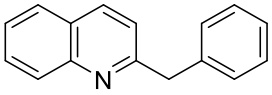
2-benzylpyrazine (151c)



According to the general procedure B5 compound **151c** was synthesized as brown liquid (550 mg, 3.233 mmol, 32%). Purification by flash column chromatography (Pentane:EtOAc = 1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.47 (s, 1H), 8.42 (s, 1H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.22 (m, 3H), 4.18 (s, 2H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 156.5, 144.7, 144.0, 142.3, 138.0, 128.8, 126.8, 41.9 ppm; IR (KBr): ν= 3058, 3030, 2921, 2325, 2109, 1892, 1601, 1577, 1525, 1494, 1472, 1453, 1430, 1400, 1310, 1229, 1126, 1056, 1017, 841, 806, 744, 698 cm^{-1}; m/z (EI) (%): 171.0 (10), 170.0 (65), 169.0 (100); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{11}N_2$: 171.09167; found: 171.09180.

The spectral data are in accordance with the literature.[133]

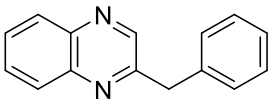
2-benzylquinoline (151d)



According to the general procedure B4 compound **151d** was synthesized as yellow liquid (258 mg, 1.178 mmol, 59 %). Purification by flash column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.32 (ddt, *J* = 7.9, 1.8, 0.5 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.67 – 7.02 (m, 3H), 7.40 – 7.21 (m, 5H), 4.18 (s, 2H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 161.4, 147.9, 139.2, 136.5, 129.7, 129.3, 129.2, 128.7, 127.6, 126.9, 126.5, 126.0, 121.6, 45.8 ppm; IR (KBr): ν= 3057, 3029, 2917, 1589, 1562, 1499, 1452, 1425, 1310, 1219, 1142, 1115, 1073, 1026, 956, 839, 810, 747, 712 cm^{-1}; m/z (EI) (%): 220.1 (30), 219.1 (77), 218.0 (100), 217.0 (35); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{14}N$: 220.11208; found: 220.11177.

The spectral data are in accordance with the literature.[63b]

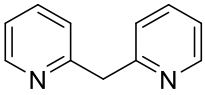
2-benzylquinoxaline (151e)



According to the general procedure B6 compound **151e** was synthesized as yellow liquid (164 mg, 0.745 mmol, 37 %). Purification by flash column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.72 (s, 2H), 8.07 (t, *J* = 9.2 Hz, 2H), 7.77 – 7.70 (m, 1H), 7.34 – 7.29 (m, 4H), 7.27 – 7.21 (m, 1H), 4.38 (s, 2H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 155.8, 145.9, 141.9, 141.2, 137.8, 130.1, 129.1, 128.9, 126.9, 42.9 ppm; IR (KBr): ν= 3061, 3027, 2920, 1558, 1491, 1453, 1410, 1364, 1290, 1203, 1118, 1073, 1014, 982, 935, 874, 758, 714 cm^{-1}; m/z (EI) (%): 221.1 (25), 220.1 (88), 219.1 (100), 218.1 (11); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{15}H_{12}N_2Na$: 243.08927; found: 243.08964.

The spectral data are in accordance with the literature.[134]

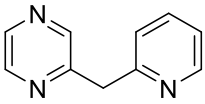
di(pyridin-2-yl)methane (155a)



According to the general procedure B8 compound **155a** was synthesized as orange liquid (952 mg, 5.597 mmol, 56%). Purification by vacuum distillation. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.57 – 8.51 (m, 2H), 7.60 (td, *J* = 7.7, 1.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.13 (dd, *J* = 7.3, 5.1 Hz, 2H), 4.34 (s, 2H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 159.3, 149.4, 136.7, 123.6, 121.5, 47.2 ppm; IR (KBr): ν= 3381, 3057, 3009, 2928, 1587, 1471, 1431, 1211, 1148, 1094, 1050, 995, 753 cm^{-1}; m/z (EI)(%): 171.0 (16), 170.0 (35), 169.0 (100), 168.0 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{11}N_2$: 171.09167; found: 171.09203.

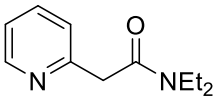
The spectral data are in accordance with the literature.[64]

2-(pyridin-2-ylmethyl)pyrazine (155b)



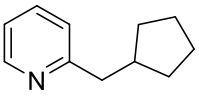
According to the general procedure B5 compound **155b** was synthesized as brown liquid (390 mg, 2.280 mmol, 46%). Purification by flash column chromatography (DCM: MeOH: Et_3N = 100:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.55 (d, *J* = 4.8 Hz, 1H), 8.50 (d, *J* = 4.0 Hz, 1H), 8.43 (d, *J* = 2.5 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.5, 4.9 Hz, 1H), 4.36 (s, 2H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 158.1, 155.1, 149.6, 145.2, 144.1, 142.6, 136.8, 123.6, 44.5 ppm; IR (KBr): ν= 3412, 3053, 3010, 2930, 2331, 1665, 1591, 1525, 1473, 1433, 1402, 1308, 1217, 1150, 1128, 1089, 1056, 1018, 865, 818, 759 cm^{-1}; m/z (EI) (%): 172.0 (20), 171.0 (60), 170.0 (100), 117.0 (18); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{10}N_3$: 172.08692; found: 172.08640.

***N*,*N*-diethyl-2-(pyridin-2-yl)acetamide (155c)**



According to the general procedure B7 using diethylacetamide instead of 2-methylpyridine at 0 °C instead of 60 °C, compound **155c** was synthesized as yellow liquid (102 mg, 0.531 mmol, 18%). Purification by flash column chromatography (DCM: MeOH = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.51 (d, *J* = 4.7 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.16 (dd, *J* = 7.2, 5.2 Hz, 1H), 3.90 (s, 2H), 3.44 – 3.35 (m, 4H), 1.11 (q, *J* = 6.9 Hz, 6H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.1, 156.1, 149.0, 136.7, 123.7, 121.8, 77.2, 43.6, 42.4, 40.2, 14.2, 12.9 ppm; IR (KBr): ν= 2973, 2933, 1636, 1591, 1459, 1431, 1377, 1273, 1217, 1129, 1090, 948, 753 cm^{-1}; m/z (EI) (%): 284.0 (11), 194.0 (16), 193.0 (100), 192.0 (36), 93.0 (25), 92.0 (11), 72.1 (18); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{11}H_{16}ON_2Na$: 215.11548; found: 215.11549.

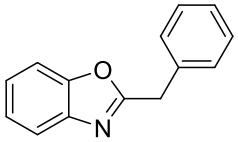
2-(cyclopentylmethyl)pyridine (155d)



According to the general procedure B6, using 1-iodocyclopentane and rt instead of reflux, compound **155d** was synthesized as yellow liquid (540 mg, 3.35 mmol, 67 %). Purification by flash column chromatography (Pentane: EtOAc = 92:8). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.52 (dt, *J* = 4.9, 1.3 Hz, 1H), 7.58 (tt, *J* = 7.7, 1.5 Hz, 1H), 7.13 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.11 – 7.08 (m, 1H), 2.79 (d, *J* = 7.5 Hz, 2H), 2.27 (hept, *J* = 7.7 Hz, 1H), 1.75 – 1.60 (m, 4H), 1.57 – 1.49 (m, 2H), 1.28 – 1.19 (m, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.3, 149.3, 136.5, 123.4, 121.2, 44.7, 41.0, 32.7, 25.3 ppm; IR (KBr): ν= 3064, 3006, 2946, 2865, 1590, 1472, 1434, 1299, 1149, 1049, 993, 751 cm^{-1}; m/z (EI) (%): 93.1 (100), 52.1 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{16}N$: 162.12773; found: 162.12845.

The spectral data are in accordance with the literature.[135]

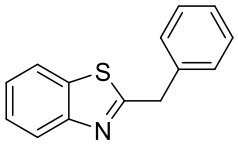
2-benzylbenzo[d]oxazole (159a)



According to the general procedure B7, compound **159a** was synthesized as yellow liquid (628 mg, 3.05 mmol, 61%). Purification by flash column chromatography (Pentane: EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.70 – 7.68 (m, 1H), 7.48 – 7.45 (m, 1H), 7.40 – 7.37 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.27 (m, 3H), 4.28 (s, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.5, 151.4, 141.6, 135.1, 129.3, 129.1, 127.6, 125.0, 124.5, 120.1, 110.8, 35.6 ppm; IR (KBr): ν= 3061, 3032, 2322, 2112, 1894, 1610, 1568, 1494, 1453, 1426, 1349, 1274, 1240, 1141, 1104, 1075, 1002, 954, 922, 841, 745, 719 cm^{-1}; m/z (EI) (%): 299.9 (7), 209.9 (27), 209.1 (100), 207.9 (31), 206.9 (18), 179.9 (23), 90.9 (40); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{14}H_{11}NNaO$: 232.07329; found: 232.07371.

The spectral data are in accordance with the literature.[65]

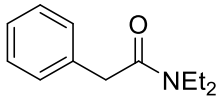
2-benzylbenzo[d]thiazole (159b)



According to the general procedure B7, using 2-amino-thiophenol, compound **159b** was synthesized as yellow liquid (721 mg, 3.20 mmol, 64%). Purification by flash column chromatography (Pentane: EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.46 (td, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.39 – 7.32 (m, 5H), 7.31 – 7.28 (m, 1H), 4.45 (s, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.3, 153.3, 137.3, 135.7, 129.3, 129.0, 127.5, 126.1, 124.9, 122.9, 121.6, 40.7 ppm; IR (KBr): ν= 3061, 3029, 2116, 1597, 1513, 1432, 1309, 1241, 1201, 1108, 1061, 1013, 937, 860, 758, 702 cm^{-1}; m/z (EI) (%): 227.0 (10), 226.0 (43), 225.0 (100), 224.0 (88), 223.0 (13), 91.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{12}NS$: 226.06850; found: 226.06841.

The spectral data are in accordance with the literature.[136]

***N,N*-diethyl-2-phenylacetamide (159c)**



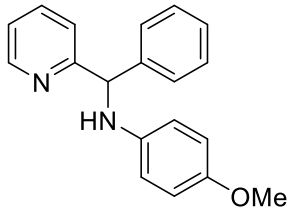
The synthesis was carried out according to the modified procedure of *Baran et al*.[66]

Phenylacetic acid (0.68 g, 5 mmol, 1.0 eq.), one drop of DMF were dissolved in 15 mL DCM. Oxalyl chloride (0.95 g, 7.5 mmol, 1.5 eq.) was added dropwise. The mixture was stirred at rt. After 1 hour, the solvent and the remaining oxalyl chloride was removed and the residue was dissolved in DCM (10 mL). To the reaction mixture were added triethylamine (1.01 g, 1.4 mL, 10 mmol, 2.0 eq.) and diethylamine (0.55 g, 0.77 mL, 7.5 mmol, 1.5 eq.), and the reaction mixture was stirred at rt for 2 hours. The reaction was stopped by the addition of 1 M HCl, and was washed with DCM and water. The aqueous layer was extracted with DCM. The organic layer was washed with saturated $NaHCO_3$, brine and was dried over Na_2SO_4 and concentrated. The product was obtained as colorless liquid (936 mg, 4.897 mmol, 98 %). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.21 (m, 3H), 3.70 (s, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 3.29 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 170.1, 135.5, 128.6, 126.6, 42.3, 40.9, 40.1, 14.2, 12.9 ppm; IR (KBr): ν= 3029, 2973, 2933, 2326, 2108, 1633, 1454, 1429, 1376, 1313, 1261, 1220, 1130, 1076, 1027, 948, 792, 725, 696 cm^{-1}; m/z (EI) (%): 383.2 (22), 292.2 (13), 291.2 (59), 282.1 (24), 193.1 (17), 192.1 (100), 191.1 (91), 100.1 (71), 91.1 (26), 72.1 (19); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{12}H_{17}ONNa$: 214.12024; found: 214.11961.

The spectral data are in accordance with the literature.[66]

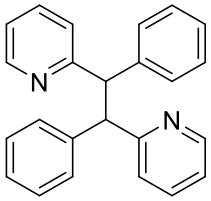
Isolated Compounds

4-methoxy-*N*-(phenyl(pyridin-2-yl)methyl)aniline (147a)



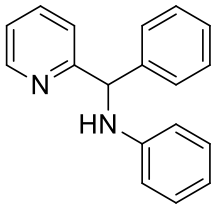
According to the general procedure B1 compound **147a** was synthesized as yellow liquid (55.1 mg, 0.190 mmol, 95 %). Purification by flash column chromatography (Pentane: EtOAc: DCM = 10:1:1). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.61 (td, *J* = 7.7, 1.8 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.37 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.27 – 7.21 (m, 1H), 7.15 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H), 6.74 – 6.68 (m, 2H), 6.60 – 6.55 (m, 2H), 5.52 (s, 1H), 3.70 (s, 4H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.22, 152.06, 149.19, 142.62, 141.31, 136.84, 128.81, 127.49, 127.41, 122.17, 121.86, 114.80, 114.74, 64.19, 55.71 ppm; IR (KBr): ν= 3379, 3056, 3003, 2933, 2831, 1589, 1509, 1468, 1435, 1406, 1317, 1236, 1178, 1124, 1033, 997, 818, 749, 699 cm^{-1}; m/z (EI) (%): 427.3 (35), 413.3 (19), 339.1 (17), 301.1 (67), 168.1 (100); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{19}H_{18}ON_2Na$: 313.13113; found: 313.13071.
The spectral data are in accordance with the literature.[137]

1,2-diphenyl-1,2-di(pyridin-2-yl)ethane mixture of isomers (148)



According to the general procedure B1, in the absence of $ZnCl_2$, compound **148**was synthesized as colorless solid. Purification by flash column chromatography (Pentane: EtOAc = 5:1). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.47 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 8.42 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.41 – 7.31 (m, 4H), 7.24 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.14 – 7.07 (m, 5H), 7.03 – 6.98 (m, 2H), 6.92 – 6.86 (m, 2H), 5.29 (s, 1H), 5.26 (s, 1H) ppm; ^{13}C-NMR (151 MHz, $CDCl_3$) δ 162.48, 162.04, 149.19, 148.83, 142.15, 136.07, 135.97, 128.80, 128.63, 128.01, 127.99, 126.12, 126.06, 124.24, 123.93, 121.00, 57.72, 57.54 ppm; IR (KBr): ν= 3031, 3005, 2923, 2326, 1586, 1493, 1469, 1430, 1148, 1072, 1048, 992, 746, 696 cm^{-1}; HRMS (m/z): $[M+H]^+$ calcd. for $C_{24}H_{21}N_2$: 337.16993; found: 337.16974.
The spectral data are in accordance with the literature.[138]

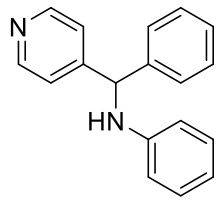
***N*-(phenyl(pyridin-2-yl)methyl)aniline (161a)**



According to the general procedure B1 compound **161a** was synthesized as yellow liquid (49.4 mg, 0.190 mmol, 95%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 2:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.24 (m, 1H), 7.17 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 2H), 6.70 – 6.66 (m, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 5.60 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.9, 149.2, 147.1, 142.5, 137.0, 129.2, 127.6, 127.5, 122.3, 122.0, 117.6, 113.7, 63.3 ppm; IR (KBr): ν= 3387, 3052, 3022, 1596, 1500, 1428, 1317, 1262, 1179, 1151, 1122, 1074, 1028, 994, 908, 870, 835, 747, 695 cm^{-1}; m/z (EI) (%): 262.1 (10), 261.1 (50), 260.0 (100), 259.1 (6), 183.0 (9), 182.1 (26), 168.0 (27), 167.0 (15); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{16}N_2Na$: 283.12057; found: 283.11971.

The spectral data are in accordance with the literature.[137]

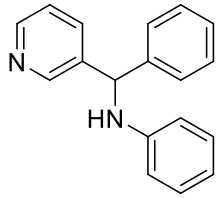
***N*-(phenyl(pyridin-4-yl)methyl)aniline (161b)**



According to the general procedure B1 compound **161b** was synthesized as yellow liquid (30.7 mg, 0.118 mmol, 59%). Purification by flash column chromatography (Pentane: EtOAc: Et_3N = 8:2:0.01). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (d, *J* = 6.2 Hz, 2H), 7.37 – 7.33 (m, 4H), 7.33 – 7.28 (m, 3H), 7.17 – 7.10 (m, 2H), 6.74 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.52 (d, *J* = 7.6 Hz, 2H), 5.46 (d, *J* = 3.0 Hz, 1H), 4.23 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.3, 149.9, 146.8, 141.5, 129.3, 129.2, 128.3, 127.8, 122.5, 118.4, 113.6, 62.5 ppm; IR (KBr): ν= 3270, 3029, 1597, 1497, 1451, 1414, 1314, 1267, 1183, 1112, 1067, 1028, 994, 908, 873, 837, 793, 733, 695 cm^{-1}; m/z (EI) (%): 429.1 (7), 428.0 (28), 262.0 (6), 261.0 (41), 260.0 (100), 183.0 (5), 182.0 (15), 169.0 (8), 168.0 (55), 167.0 (31), 77.1 (8), 51.1 (6); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{17}N_2$: 261.13862; found: 261.13806.

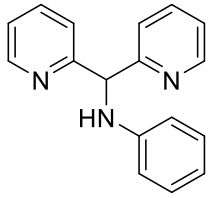
The spectral data are in accordance with the literature.[139]

***N*-(phenyl(pyridin-3-yl)methyl)aniline (161c)**



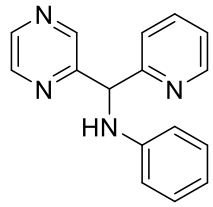
According to the general procedure B3 compound **161c** was synthesized as colorless liquid (41.6 mg, 0.160 mmol, 80%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 5:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.65 (d, *J* = 2.3 Hz, 1H), 8.52 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.70 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.38 – 7.32 (m, 4H), 7.32 – 7.25 (m, 2H), 7.13 (dd, *J* = 8.6, 7.2 Hz, 2H), 6.73 (td, *J* = 7.4, 1.1 Hz, 1H), 6.57 – 6.53 (m, 2H), 5.55 (s, 1H), 4.23 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 149.1, 148.5, 146.8, 141.8, 138.4, 135.1, 129.2, 129.0, 127.9, 127.4, 123.7, 118.2, 113.6, 60.9 ppm; IR (KBr): ν= 3269, 3029, 2093, 1599, 1498, 1451, 1424, 1314, 1268, 1180, 1108, 1070, 1026, 909, 833, 790, 746, 697 cm^{-1}; m/z (EI) (%): 428.1 (32), 261.1 (34), 260.1 (100), 169.0 (15), 168.0 (98), 167.0 (33); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{17}N_2$: 261.13863; found: 261.13823.

***N*-(di(pyridin-2-yl)methyl)aniline (161d)**



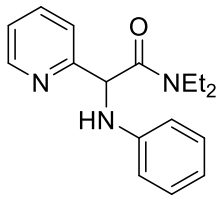
According to the general procedure B2 compound **161d** was synthesized as yellow liquid (41.3 mg, 0.158 mmol, 79 %). Purification by flash column chromatography (Pentane: EtOAc: DCM = 2:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58 (ddd, *J* = 5.0, 1.9, 1.0 Hz, 2H), 7.59 (td, *J* = 7.6, 1.7 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.17 – 7.10 (m, 4H), 6.70 – 6.64 (m, 3H), 6.24 (bs, 1H), 5.76 (s, 1H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 160.4, 148.9, 146.6, 137.0, 129.2, 122.4, 121.9, 117.3, 113.5, 63.8 ppm; IR (KBr): ν= 3382, 3051, 3012, 1594, 1502, 1472, 1428, 1319, 1257, 1146, 1088, 1047, 994, 870, 840, 748, 692, 665 cm^{-1}; m/z (EI) (%): 262.1 (36), 261.1 (100), 184.0 (13), 183.0 (84), 169.0 (19); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{15}N_3Na$: 284.11582; found: 284.11548.

***N*-(pyrazin-2-yl(pyridin-2-yl)methyl)aniline (161e)**



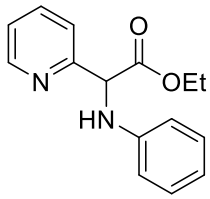
According to the general procedure B2 compound **161e** was synthesized as brown liquid (34.6 mg, 0.132 mmol, 66%). Purification by flash column chromatography (Pentane:EtOAc:DCM:Et_3N = 1:1:1:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.60 (d, *J* = 4.4 Hz, 1H), 8.52 (s, 1H), 8.45 (s, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.20 – 7.17 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 2H), 6.72 – 6.60 (m, 3H), 6.10 (bs, 1H), 5.83 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 159.2, 156.1, 149.2, 146.2, 144.5, 143.4, 143.4, 137.1, 129.3, 122.8, 121.9, 117.8, 113.5, 62.1 ppm; IR (KBr): ν= 3354, 3055, 2924, 2855, 1683, 1629, 1589, 1495, 1436, 1398, 1314, 1285, 1247, 1153, 1091, 1052, 1016, 995, 947, 859, 802, 750, 682 cm^{-1}; m/z (EI) (%): 261.1 (18), 260.1 (89), 259.0 (100), 185.1 (23), 182.1 (14), 181.1 (30), 79.2 (12), 78.2 (19), 77.2 (12), 52.2 (40), 51.2 (39); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{16}H_{14}N_4Na$: 285.11107; found: 285.11047.

***N,N*-diethyl-2-(phenylamino)-2-(pyridin-2-yl)acetamide (161f)**



According to the general procedure B2 compound **161f** was synthesized as colorless liquid (25.5 mg, 0.090 mmol, 45 %). Purification by flash column chromatography (Pentane:EtOAc:DCM = 1:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 (ddd, *J* = 5.0, 1.8, 0.9 Hz, 1H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.17 (ddd, *J* = 7.4, 5.0, 1.2 Hz, 1H), 7.13 – 7.08 (m, 2H), 6.71 – 6.67 (m, 2H), 6.64 (td, *J* = 7.3, 1.1 Hz, 1H), 5.76 (bs, 1H), 5.45 (s, 1H), 3.87 (dq, *J* = 14.3, 7.1 Hz, 1H), 3.42 (ddt, *J* = 18.6, 14.1, 7.1 Hz, 2H), 3.33 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.07 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.1, 159.5, 148.3, 146.1, 137.4, 129.2, 122.7, 121.7, 117.4, 113.3, 60.6, 41.6, 40.8, 13.9, 12.6 ppm; IR (KBr): ν= 3327, 2971, 2929, 2870, 1635, 1599, 1507, 1458, 1430, 1361, 1315, 1273, 1250, 1213, 1130, 1090, 990, 956, 864, 805, 754, 695 cm^{-1}; m/z (EI) (%): 285.1 (15), 284.1 (83), 283.1 (39), 184.0 (15), 183.0 (100); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{21}ON_3Na$: 306.15768; found: 306.15712.

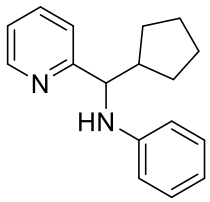
ethyl 2-(phenylamino)-2-(pyridin-2-yl)acetate (161g)



According to the general procedure B2 compound **161g** was synthesized as colorless liquid (44.6 mg, 0.174 mmol, 87 %). Purification by flash column chromatography (Pentane:EtOAc:DCM = 5:1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.69 (td, *J* = 7.7, 1.8 Hz, 1H), 7.49 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.19 – 7.10 (m, 2H), 6.72 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.68 – 6.62 (m, 2H), 5.27 (s, 1H), 4.27 – 4.11 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 171.0, 156.3, 149.1, 145.9, 137.4, 129.3, 123.2, 122.1, 118.3, 113.5, 61.9, 14.1 ppm; IR (KBr): ν= 3387, 3054, 2982, 2931, 1736, 1597, 1502, 1436, 1370, 1312, 1226, 1196, 1091, 1020, 954, 750, 691 cm^{-1}; m/z (EI) (%): 256.0 (19), 255.0 (10), 254.0 (22), 183.0 (63), 182.0 (20), 181.0 (100), 77.1 (12); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{15}H_{16}O_2N_2Na$: 279.11040; found: 279.11018.

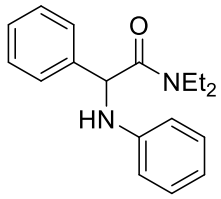
The spectral data are in accordance with the literature.[140]

***N*-(cyclopentyl(pyridin-2-yl)methyl)aniline (161h)**



According to the general procedure B3 compound **161h** was synthesized as yellow liquid (42.9 mg, 0.170 mmol, 85%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 4:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (dd, *J* = 5.1, 1.7 Hz, 1H), 7.59 (td, *J* = 7.6, 1.8 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.13 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.10 – 7.05 (m, 2H), 6.62 (td, *J* = 7.3, 1.1 Hz, 1H), 6.57 (d, *J* = 7.3 Hz, 2H), 4.29 (d, *J* = 8.2 Hz, 1H), 2.34 (h, *J* = 8.3 Hz, 1H), 1.85 (ddt, *J* = 12.4, 7.7, 3.9 Hz, 1H), 1.68 – 1.48 (m, 5H), 1.44 – 1.33 (m, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.4, 149.2, 147.9, 136.9, 129.4, 122.3, 122.0, 117.5, 113.7, 64.0, 46.8, 30.0 (d, *J* = 12.6 Hz), 25.6 (d, *J* = 7.8 Hz) ppm; IR (KBr): ν= 3265, 3031, 2947, 2861, 1596, 1521, 1496, 1435, 1308, 1277, 1180, 1151, 1113, 1057, 996, 853, 787, 748, 693 cm^{-1}; m/z (EI) (%): 254.1 (12), 253.1 (60), 252.1 (33), 184.0 (16), 183.0 (100), 182.0 (6); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{21}N_2$: 253.16993; found: 253.17051.

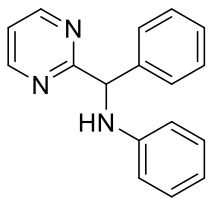
***N,N*-diethyl-2-phenyl-2-(phenylamino)acetamide (161i)**



According to the general procedure B3 compound **161i** was synthesized as colorless liquid (49 mg, 0.174 mmol, 87 %). Purification by flash column chromatography (Pentane: EtOAc: DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48 – 7.43 (m, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 2H), 6.67 (dd, *J* = 7.8, 5.4 Hz, 3H), 5.23 (s, 1H), 3.50 – 3.40 (m, 2H), 3.30 (ddq, *J* = 29.4, 14.6, 7.2 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 169.8, 146.4, 138.8, 129.1, 128.9, 127.9, 127.8, 117.8, 113.7, 58.3, 41.5, 40.7, 13.9, 12.7 ppm; IR (KBr): ν= 3409, 3052, 2973, 2930, 1623, 1600, 1500, 1465, 1420, 1374, 1303, 1243, 1215, 1185, 1105, 1029, 990, 965, 874, 810, 781, 748, 701 cm^{-1}; m/z (EI) (%): 565.2 (15), 284.1 (14), 283.1 (70), 282.1 (35), 183.0 (17), 182.0 (100); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{22}ON_2Na$: 305.16243; found: 305.16142.

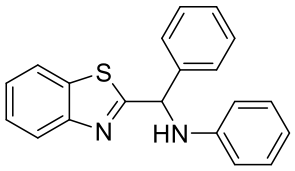
The spectral data are in accordance with the literature.[141]

***N*-(phenyl(pyrimidin-2-yl)methyl)aniline (161j)**



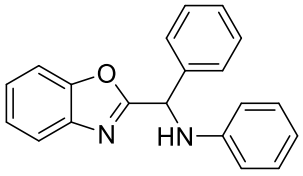
According to the general procedure B2 compound **161j** was synthesized as colorless liquid (31.9 mg, 0.122 mmol, 61%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.71 (d, *J* = 4.9 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.16 (t, *J* = 4.9 Hz, 1H), 7.12 (t, *J* = 7.9 Hz, 2H), 6.67 (dd, *J* = 12.7, 7.7 Hz, 3H), 5.79 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.5, 157.3, 146.4, 141.1, 129.1, 128.7, 127.6, 127.3, 119.4, 117.6, 113.7, 63.4 ppm;IR (KBr): ν= 3380, 3048, 2924, 1702, 1602, 1566, 1503, 1448, 1414, 1316, 1257, 1179, 1132, 1075, 1027, 994, 867, 804, 748, 694 cm^{-1}; m/z (EI) (%): 262.0 (23), 261.0 (100), 184.0 (12), 183.0 (12), 182.0 (76), 169.0 (39), 168.0 (16), 77.1 (15); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{16}N_3$: 262.13387; found: 262.13371.

***N*-(benzo[d]thiazol-2-yl(phenyl)methyl)aniline (161k)**



According to the general procedure B2 compound **161k** was synthesized as yellow liquid (60.7 mg, 0.192 mmol, 96%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 7:0.01:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.32 – 7.22 (m, 4H), 7.08 (t, *J* = 7.7 Hz, 2H), 6.68 (t, *J* = 7.4 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 5.81 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 176.0, 153.8, 146.8, 140.7, 135.5, 129.6, 129.5, 128.8, 127.8, 126.3, 125.3, 123.4, 122.1, 119.2, 114.2, 62.4 ppm; IR (KBr): ν= 3398, 3057, 1735, 1596, 1500, 1436, 1309, 1220, 1169, 1074, 1051, 1011, 906, 732, 693 cm^{-1}; m/z (EI) (%): 318.0 (9), 317.0 (31), 316.0 (100), 314.0 (5), 226.0 (8), 225.0 (22), 224.0 (88), 223.0 (36), 182.0 (10), 180.0 (6); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{20}H_{16}N_2NaS$: 339.09264; found: 339.09103.

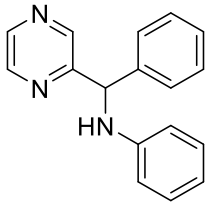
***N*-(benzo[d]oxazol-2-yl(phenyl)methyl)aniline (161l)**



According to the general procedure B2 compound **161l** was synthesized as yellow liquid (45.1 mg, 0.150 mmol, 75%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 7:0.08:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 – 7.71 (m, 1H), 7.59 (dd, *J* = 7.2, 1.5 Hz, 2H), 7.52 – 7.46 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.36 – 7.28 (m, 3H), 7.16 (dd, *J* = 8.6, 7.3 Hz, 2H), 6.74 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 2H), 5.85 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.9, 151.0, 146.2, 140.8, 138.3, 129.4, 129.2, 128.6, 127.4, 125.2, 124.6, 120.2, 118.7, 113.7, 110.9, 57.2 ppm; IR (KBr): ν= 3401, 3326, 3056, 3027, 1600, 1560, 1501, 1452, 1312, 1240, 1159, 1070, 1001, 973, 934, 874, 844, 778, 740, 691 cm^{-1}; m/z (EI) (%): 301.0 (27), 300.0 (96), 209.0 (18), 208.0 (100), 207.0 (11), 182.0 (8), 180.0 (17), 151.9 (5), 77.0 (8); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{20}H_{16}N_2NaO$: 323.11548; found: 323.11456.

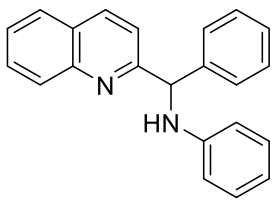
The spectral data are in accordance with the literature.[142]

***N*-(phenyl(pyrazin-2-yl)methyl)aniline (161m)**



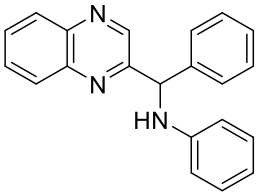
According to the general procedure B2 compound **161m** was synthesized as yellow liquid (33.9 mg, 0.130 mmol, 65%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 5:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.54 (s, 1H), 8.46 (d, *J* = 2.2 Hz, 1H), 7.45 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.16 – 7.10 (m, 2H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 2H), 5.67 (s, 1H) ppm;^{13}C NMR (151 MHz,$CDCl_3$): δ 156.5, 146.4, 144.0, 143.8, 143.3, 141.2, 129.2, 129.1, 127.9, 127.3, 118.1, 113.7, 61.5 ppm; IR (KBr): ν= 3391, 3054, 1599, 1500, 1434, 1401, 1316, 1266, 1149, 1113, 1058, 1018, 907, 863, 809, 749, 694 cm^{-1}; m/z (EI) (%): 366.0 (11), 262.0 (29), 261.0 (100), 183.0 (14), 182.0 (85), 169.0 (47), 168.0 (10), 77.1 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{16}N_3$: 262.13387; found: 262.13399.

***N*-(phenyl(quinolin-2-yl)methyl)aniline (161n)**



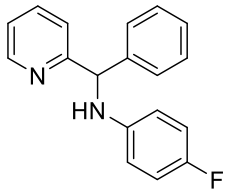
According to the general procedure B2 compound **161n** was synthesized as colorless liquid (31.6 mg, 0.102 mmol, 51%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 20:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.79 – 7.76 (m, 1H), 7.74 (t, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.59 – 7.51 (m, 3H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27 – 7.22 (m, 1H), 7.17 – 7.11 (m, 2H), 6.77 – 6.71 (m, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.15 (bs, 1H), 5.75 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 160.4, 147.0, 142.4, 136.9, 129.7, 129.1, 128.9, 127.6, 127.5, 127.3, 126.5, 120.0, 117.4, 113.6, 63.3 ppm; IR (KBr): ν= 3372, 3057, 2923, 2855, 1661, 1597, 1500, 1424, 1314, 1255, 1157, 1112, 1071, 1027, 968, 921, 843, 805, 779, 745, 691 cm^{-1}; m/z (EI) (%): 311.1 (33), 310.0 (100), 233.0 (13), 218.0 (33), 217.0 (16), 182.0 (26); HRMS (m/z): $[M+H]^+$ calcd. for $C_{22}H_{19}N_2$: 311.15428; found: 311.15375.

_N_-(phenyl(quinoxalin-2-yl)methyl)aniline (161o)



According to the general procedure B2 compound **161o** was synthesized as colorless liquid (37.3 mg, 0.120 mmol, 60%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 10:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.16 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.08 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.79 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.74 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.18 – 7.12 (m, 2H), 6.75 – 6.68 (dd, *J* = 19.9, 7.7 Hz, 3H), 5.84 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.3, 146.5, 144.8, 141.7, 141.4, 141.1, 130.3, 129.7, 129.2, 129.2, 129.1, 128.1, 127.5, 61.8 ppm; IR (KBr): ν= 3392, 3056, 3026, 1600, 1499, 1453, 1431, 1366, 1313, 1260, 1175, 1105, 1074, 991, 908, 732, 695 cm^{-1}; m/z (EI) (%): 312.1 (35), 311.0 (100), 219.0 (33), 182.0 (43); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{21}H_{17}N_3Na$: 334.13147; found: 334.13120.

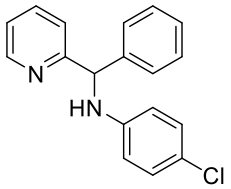
4-fluoro-_N_-(phenyl(pyridin-2-yl)methyl)aniline (162a)



According to the general procedure B1 compound **162a** was synthesized as yellow liquid (48.9 mg, 0.176 mmol, 88%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 6:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.63 (td, *J* = 7.6, 1.8 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.38 – 7.30 (m, 3H), 7.28 – 7.24 (m, 1H), 7.17 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.86 – 6.80 (m, 2H), 6.60 – 6.53 (m, 2H), 5.53 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 160.7, 156.7, 155.1, 149.1, 143.5, 142.4, 137.0, 129.0, 127.7, 127.4, 122.4, 122.1, 115.7, 115.5, 114.5, 114.4, 63.8 ppm; IR (KBr): ν= 3383, 1590, 1508, 1474, 1433, 1402, 1316, 1262, 1216, 1154, 1095, 818, 781, 749, 699 cm^{-1}; m/z (EI) (%): 279.1 (25), 278.1 (100), 201.0 (10), 200.0 (31), 168.0 (39), 167.0 (19); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{15}FN_2Na$: 301.11115; found: 301.11110.

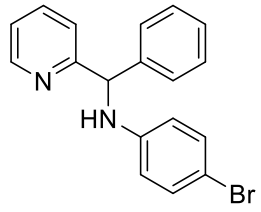
The spectral data are in accordance with the literature.[59]

4-chloro-_N_-(phenyl(pyridin-2-yl)methyl)aniline (162b)



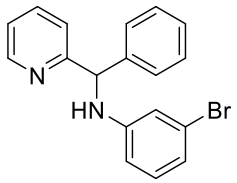
According to the general procedure B1 compound **162b** was synthesized as yellow liquid (56.6 mg, 0.192 mmol, 96%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 5:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.59 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.46 – 7.42 (m, 2H), 7.35 – 7.30 (m, 3H), 7.27 – 7.22 (m, 1H), 7.17 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 7.07 – 7.03 (m, 2H), 6.57 – 6.53 (m, 2H), 5.54 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.3, 149.1, 145.6, 142.1, 137.0, 129.0 (d, *J* = 2.6 Hz), 127.8, 127.3, 122.4, 122.1, 114.8, 63.1 ppm; IR (KBr): ν= 3379, 1594, 1496, 1465, 1428, 1399, 1312, 1253, 1175, 1147, 1085, 1049, 996, 813, 751, 698 cm^{-1}; m/z (EI) (%): 297.0 (14), 296.0 (45), 295.0 (42), 294.0 (100), 218.0 (8), 217.0 (8), 216.0 (24), 169.0 (6), 168.0 (40), 167.0 (18); HRMS (m/z): [M] calcd. for $C_{18}H_{15}ClN_2$: 294.09238; found: 294.09139.

4-bromo-_N_-(phenyl(pyridin-2-yl)methyl)aniline (162c)



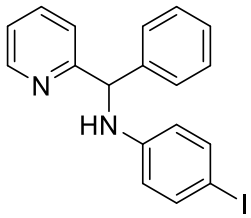
According to the general procedure B1 compound **162c** was synthesized as yellow liquid (61.1 mg, 0.180 mmol, 90%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 6:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58 (dd, *J* = 5.0, 1.7 Hz, 1H), 7.61 (td, *J* = 7.7, 3.8 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.34 – 7.30 (m, 3H), 7.26 – 7.24 (m, 1H), 7.20 – 7.15 (m, 3H), 6.51 (d, *J* = 8.8 Hz, 2H), 5.52 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.3, 149.2, 146.0, 142.1, 137.0, 131.9, 129.0, 127.8, 127.3, 122.4, 122.1, 115.3, 109.2, 63.0 ppm; IR (KBr): ν= 3378, 2922, 2854, 1591, 1494, 1428, 1396, 1314, 1253, 1175, 1147, 1069, 1025, 996, 925, 809, 749, 699 cm^{-1}; m/z (EI) (%): 342.0 (8), 341.0 (47), 339.9 (91), 339.0 (51), 337.9 (100), 336.9 (5), 262.9 (9), 261.8 (30), 260.9 (11), 259.9 (33), 181.9 (5), 181.0 (6), 180.0 (5), 169.0 (16), 168.0 (65), 167.0 (38), 166.0 (6), 154.9 (6); HRMS (m/z): [M] calcd. for $C_{18}H_{15}BrN_2$: 338.04186; found: 338.04112.

3-bromo-*N*-(phenyl(pyridin-2-yl)methyl)aniline (162d)



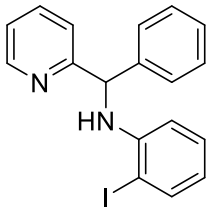
According to the general procedure B1 compound **162d** was synthesized as yellow liquid (56.9 mg, 0.168 mmol, 84%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 5:0.5:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.61 (d, *J* = 4.0 Hz, 1H), 7.67 (td, *J* = 7.8, 3.5 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.38 – 7.32 (m, 3H), 7.30 – 7.27 (m, 1H), 7.21 (dt, *J* = 7.5, 3.5 Hz, 1H), 6.97 (t, *J* = 8.0 Hz, 1H), 6.83 – 6.78 (m, 2H), 6.56 (dd, *J* = 8.2, 2.2 Hz, 1H), 5.58 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.1, 149.0, 148.3, 142.0, 137.2, 130.5, 129.0, 127.8, 127.3, 123.2, 122.5, 122.2, 120.3, 116.4, 112.2, 62.7 ppm; IR (KBr): ν= 3376, 3059, 1591, 1489, 1430, 1322, 1280, 1258, 1165, 1123, 1068, 986, 905, 847, 754, 697cm^{-1}; m/z (EI) (%): 342,0 (6), 341.0 (38), 339.9 (93), 339.0 (45), 337.9 (100), 336.9 (6), 262.9 (9), 261.9 (33), 260.9 (11), 259.9 (37), 169.0 (9), 168.0 (49), 167.0 (25); HRMS (m/z): [M] calcd. for $C_{18}H_{15}BrN_2$: 338.04186; found: 338.04056.

4-iodo-*N*-(phenyl(pyridin-2-yl)methyl)aniline (162e)



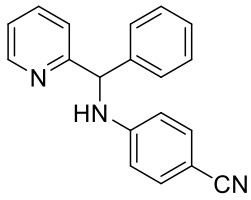
According to the general procedure B1 compound **162e** was synthesized as yellow liquid (74.9 mg, 0.194 mmol, 97%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 5:1:0.2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.67 – 7.60 (m, 1H), 7.43 (d, *J* = 7.3 Hz, 2H), 7.38 – 7.30 (m, 5H), 7.27 – 7.22 (m, 1H), 7.21 – 7.15 (m, 1H), 6.42 (d, *J* = 6.5 Hz, 2H), 5.55 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.2, 148.9, 146.5, 141.9, 137.8, 137.3, 129.0, 127.8, 127.3, 122.5, 122.2, 116.0, 78.4, 62.8 ppm; IR (KBr): ν= 3335, 2922, 2323, 2083, 1861, 1743, 1589, 1492, 1429, 1393, 1318, 1295, 1257, 1180, 1148, 1052, 996, 924, 893, 802, 749, 698, 671 cm^{-1}; m/z (EI) (%): 387.0 (20), 385.9 (100), 308.9 (7), 307.9 (26), 168.0 (27), 167.0 (13); HRMS (m/z): [M+Na]$^{+}$ calcd. for $C_{18}H_{15}IN_2Na$: 409.01721; found: 409.01698.

2-iodo-*N*-(phenyl(pyridin-2-yl)methyl)aniline (162f)



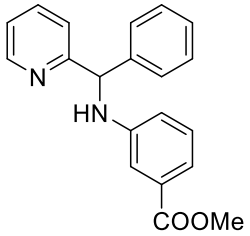
According to the general procedure B1 compound **162f** was synthesized as yellow liquid (73.4 mg, 0.190 mmol, 95%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 6:3:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.1 Hz, 1H), 7.71 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.66 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (d, *J* = 7.3 Hz, 2H), 7.40 – 7.33 (m, 3H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.21 – 7.18 (m, 1H), 7.11 – 7.05 (m, 1H), 6.47 – 6.42 (m, 2H), 6.16 (s, 1H), 5.67 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.4, 149.2, 146.2, 141.9, 139.1, 137.1, 129.3, 129.0, 127.8, 127.2, 122.4, 121.8, 118.9, 112.1, 85.8, 63.5 ppm; IR (KBr): ν= 3343, 3060, 3020, 2329, 1885, 1585, 1495, 1425, 1312, 1145, 1088, 1070, 1047, 1002, 907, 835, 740, 700 cm^{-1}; m/z (EI) (%): 388.0 (9), 387.0 (51), 385.9 (97), 308.9 (8), 307.9 (36), 260.1 (32), 259.0 (100), 181.0 (10), 180.0 (13), 169.0 (8), 168.0 (40), 167.0 (25); HRMS (m/z): [M+Na]$^{+}$ calcd. for $C_{18}H_{15}IN_2Na$: 409.01721; found: 409.01639.

4-((phenyl(pyridin-2-yl)methyl)amino)benzonitrile (162g)



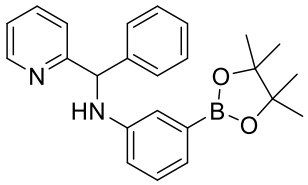
According to the general procedure B1 compound **162g** was synthesized as yellow liquid (37.1 mg, 0.130 mmol, 65%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 5:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.59 (dt, *J* = 5.0, 1.2 Hz, 1H), 7.65 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.37 – 7.28 (m, 5H), 7.29 – 7.23 (m, 1H), 7.21 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 6.62 (d, *J* = 8.8 Hz, 2H), 5.60 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.0, 150.0, 148.8, 141.3, 137.4, 133.7, 129.2, 128.1, 127.1, 122.8, 122.4, 120.5, 113.3, 99.1, 61.8 ppm; IR (KBr): ν= 3360, 3059, 2212, 1602, 1519, 1471, 1428, 1335, 1265, 1172, 1091, 997, 909, 823, 729, 700 cm^{-1}; m/z (EI) (%): 287.0 (6), 286.0 (40), 285.0 (100), 208.0 (7), 207.0 (19), 169.0 (7), 168.0 (47), 167.0 (15); HRMS (m/z): [M+Na]$^{+}$ calcd. for $C_{19}H_{15}N_3Na$: 308.11582; found: 308.11587.

***N*-(phenyl(pyridin-2-yl)methyl)naphthalen-1-amine (162h)**



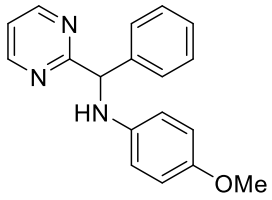
According to the general procedure B1 compound **162h** was synthesized as yellow liquid (47.7 mg, 0.150 mmol, 75%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 5:1:2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (d, *J* = 4.1 Hz, 1H), 7.64 (tt, *J* = 8.0, 2.2 Hz, 1H), 7.46 (d, *J* = 6.9 Hz, 2H), 7.36 – 7.30 (m, 5H), 7.25 – 7.22 (m, 1H), 7.20 – 7.13 (m, 2H), 6.79 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 5.64 (s, 1H), 3.85 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.7, 160.5, 149.1, 147.2, 142.3, 137.5, 131.2, 129.4, 129.2, 128.0, 127.6, 118.9, 118.1, 114.9, 63.0, 52.3 ppm; IR (KBr): ν= 3378, 3059, 3027, 2950, 1714, 1598, 1492, 1434, 1328, 1246, 1193, 1105, 995, 908, 869, 803, 749, 698 cm^{-1}; m/z (EI) (%): 320.0 (5), 319.0 (34), 318.0 (100), 317.0 (8), 287.0 (6), 241.0 (17), 240.0 (64), 169.0 (10), 168.0 (58), 167.0 (36), 166.0 (5); HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{19}N_2O_2$: 319.14410; found: 319.14388.

***N*-(phenyl(pyridin-2-yl)methyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (162i)**



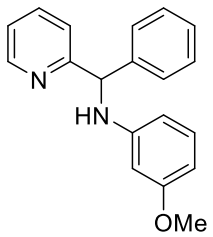
According to the general procedure B1 compound **162i** was synthesized as yellow liquid (73.4 mg, 0.190 mmol, 95%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 6:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.58 (d, *J* = 4.0 Hz, 1H), 7.63 (td, *J* = 7.6, 1.7 Hz, 1H), 7.46 – 7.43 (m, 2H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.20 (m, 2H), 7.18 – 7.15 (m, 1H), 7.11 (d, *J* = 7.0 Hz, 2H), 6.63 (dt, *J* = 6.8, 2.5 Hz, 1H), 5.64 (s, 1H), 1.32 (s, 12H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.9, 148.9, 146.4, 142.5, 137.2, 128.9, 128.7, 127.6, 127.5, 123.9, 122.3, 122.1, 121.0, 115.6, 83.7, 63.0, 24.9 (d, *J* = 5.6 Hz) ppm; IR (KBr): ν= 3384, 2979, 2930, 1581, 1503, 1474, 1428, 1358, 1318, 1273, 1211, 1143, 1076, 993, 964, 910, 853, 789, 732, 702 cm^{-1}; m/z (EI) (%): 388.1 (11), 387.1 (52), 386.0 (100), 385.0 (19), 309.1 (12), 308.1 (42), 307.0 (10), 168.0 (17), 167.0 (7); HRMS (m/z): $[M+H]^+$ calcd. for $C_{24}H_{28}BN_2O_2$: 387.22384; found: 387.22467.

4-methoxy-*N*-(phenyl(pyrimidin-2-yl)methyl)aniline (162j)



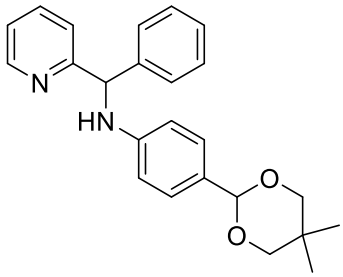
According to the general procedure B2 compound **162j** was synthesized as colorless liquid (38.4 mg, 0.132 mmol, 66%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 2:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.69 (d, *J* = 4.9 Hz, 2H), 7.56 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.30 (t, *J* = 8.4, 7.0 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.15 – 7.13 (m, 1H), 6.73 – 6.70 (m, 2H), 6.69 – 6.65 (m, 2H), 5.73 (s, 1H), 3.70 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.6, 157.2, 128.6, 127.6, 127.4, 119.4, 115.4, 114.8, 64.5, 55.7 ppm; IR (KBr): ν= 3369, 3033, 2928, 2834, 1621, 1565, 1508, 1405, 1317, 1238, 1179, 1135, 1107, 1033, 997, 826, 803, 751, 698 cm^{-1}; m/z (EI) (%): 292.1 (22), 291.1 (100), 212.1 (31), 169.1 (22); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{17}ON_3Na$: 314.12638; found: 314.12601.

3-methoxy-N-(phenyl(pyridin-2-yl)methyl)aniline (162k)



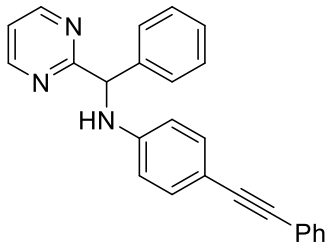
According to the general procedure B1 compound **162k** was synthesized as colorless liquid (48.0 mg, 0.166 mmol, 83%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 5:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.22 (m, 1H), 7.18 – 7.14 (m, 1H), 7.03 (t, *J* = 8.1 Hz, 1H), 6.28 – 6.23 (m, 2H), 6.19 (d, *J* = 2.3 Hz, 1H), 5.59 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 160.6, 149.0, 148.4, 142.4, 136.9, 129.8, 128.9, 127.5, 127.3, 122.2, 121.9, 106.7, 102.9, 99.5, 63.2, 54.9 ppm; IR (KBr): ν= 3384, 3058, 3005, 2936, 2834, 1592, 1497, 1455, 1432, 1338, 1301, 1264, 1209, 1159, 1044, 994, 910, 826, 751, 694 cm^{-1}; m/z (EI) (%): 291.0 (46), 290.0 (100), 212.0 (29), 168.0 (25), 167.0 (13); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{19}H_{18}ON_2Na$: 313.12113; found: 313.13080.

4-(5,5-dimethyl-1,3-dioxan-2-yl)-*N*-(phenyl(pyridin-2-yl)methyl)aniline (162l)



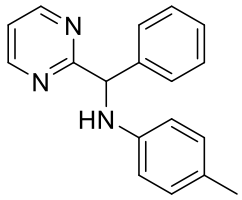
According to the general procedure B1 compound **162l** was synthesized as yellow liquid (68.2 mg, 0.182 mmol, 91%). Purification by flash column chromatography (Pentane: EtOAc: DCM = 4:1:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.57 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.60 (td, *J* = 7.7, 1.8 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.19 (m, 3H), 7.15 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 2H), 5.61 (s, 1H), 5.25 (s, 1H), 3.71 (d, *J* = 10.2 Hz, 2H), 3.59 (d, *J* = 10.8 Hz, 2H), 1.27 (s, 3H), 0.76 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.7, 149.2, 147.4, 142.3, 137.0, 128.9, 127.8, 127.6, 127.4, 127.1, 122.3, 122.1, 113.4, 102.2, 77.7, 63.0, 30.2, 23.1, 22.0 ppm; IR (KBr): ν= 3366, 2957, 2848, 2801, 1615, 1592, 1526, 1470, 1430, 1408, 1379, 1307, 1259, 1213, 1177, 1097, 1017, 991, 932, 805, 751, 699 cm^{-1}; m/z (EI) (%): 376.1 (10), 375.1 (45), 374,0 (100), 373.1 (12), 297.1 (10), 296.0 (33), 289.0 (7), 288.0 (31), 210.0 (11), 168.0 (19), 167.0 (8); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{24}H_{26}N_2NaO_2$: 397.18865; found: 397.18854.

N-(phenyl(pyrimidin-2-yl)methyl)-4-(phenylethynyl)aniline (162m)



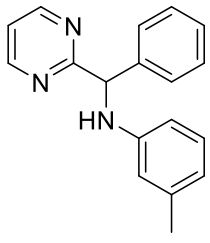
According to the general procedure B2 compound **162m** was synthesized as yellow solid (41.2 mg, 0.114 mmol, 57%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.72 (d, *J* = 4.9 Hz, 2H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.48 – 7.45 (m, 2H), 7.33 – 7.28 (m, 5H), 7.28 – 7.21 (m, 3H), 7.17 (t, *J* = 4.9 Hz, 1H), 6.63 (d, *J* = 8.6 Hz, 2H), 6.02 (s, 1H), 5.80 (s, 1H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.0, 157.3, 146.5, 140.7, 132.9, 131.3, 128.7, 128.2, 127.7, 127.5, 127.2, 124.0, 119.5, 113.3, 111.4, 90.4, 87.2, 62.9 ppm; IR (KBr): ν= 3369, 3032, 2924, 2854, 1708, 1604, 1566, 1514, 1406, 1321, 1289, 1245, 1178, 1137, 1105, 1070, 1026, 995, 908, 811, 753, 695 cm^{-1}; m/z (EI) (%): 362.1 (27), 361.0 (100), 282.0 (26), 192.1 (14), 169.1 (51), 168.0 (20); HRMS (m/z): $[M+H]^+$ calcd. for $C_{25}H_{20}N_3$: 362.16517; found: 362.16554.

4-methyl-*N*-(phenyl(pyrimidin-2-yl)methyl)aniline (162n)



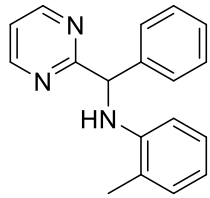
According to the general procedure B2 compound **162n** was synthesized as colorless liquid (35.2 mg, 0.128 mmol, 64%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (dd, *J* = 4.9, 1.1 Hz, 2H), 7.58 (dt, *J* = 8.1, 1.3 Hz, 2H), 7.30 (td, *J* = 7.6, 1.3 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.14 (td, *J* = 4.9, 1.1 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.64 – 6.60 (m, 2H), 5.78 (s, 1H), 2.20 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.6, 157.2, 143.9, 141.1, 129.7, 128.6, 127.6, 127.3, 119.4, 113.9, 63.8 ppm;IR (KBr): ν= 3376, 3026, 2917, 2857, 1615, 1566, 1518, 1483, 1449, 1421, 1402, 1303, 1247, 1182, 1135, 1068, 1031, 994, 832, 805, 749, 696, 666 cm^{-1}; m/z (EI) (%): 276.1 (45), 275.1 (100), 196.1 (43), 169.0 (23); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{17}N_3Na$: 298.13147.; found: 298.13124.

3-methyl-*N*-(phenyl(pyrimidin-2-yl)methyl)aniline (162o)



According to the general procedure B2 compound **162o** was synthesized as orange liquid (34.1 mg, 0.124 mmol, 62%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (dd, *J* = 4.9, 1.4 Hz, 2H), 7.59 – 7.57 (m, 2H), 7.33 – 7.29 (m, 2H), 7.22 (td, *J* = 7.3, 1.4 Hz, 1H), 7.14 (td, *J* = 4.9, 1.4 Hz, 1H), 7.04 – 6.97 (m, 1H), 6.55 (s, 1H), 6.49 (dd, *J* = 10.8, 7.4 Hz, 2H), 5.79 (s, 1H), 2.23 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.6, 157.2, 146.4, 141.2, 138.9, 129.0, 128.6, 127.6, 127.3, 119.4, 118.6, 114.7, 110.7, 63.4, 21.6 ppm; IR (KBr): ν= 3392, 3037, 2919, 2856, 1602, 1564, 1513, 1450, 1413, 1330, 1308, 1281, 1256, 1187, 1126, 1069, 1028, 993, 885, 840, 810, 774, 695 cm^{-1}; m/z (EI) (%): 276.0 (40), 275.0 (100), 196.0 (46), 169.0 (21); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{18}N_3$: 276.14952; found: 276.14919.

2-methyl-*N*-(phenyl(pyrimidin-2-yl)methyl)aniline (162p)



According to the general procedure B2 compound **162p** was synthesized as orange solid (29.7 mg, 0.108 mmol, 54%). Purification by flash column chromatography (Pentane:EtOAc:DCM = 4:1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.74 – 8.70 (m, 2H), 7.61 – 7.58 (m, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 7.09 – 7.06 (m, 1H), 6.99 (td, *J* = 7.8, 1.5 Hz, 1H), 6.62 (td, *J* = 7.3, 1.1 Hz, 1H), 6.52 (dd, *J* = 8.2, 1.1 Hz, 1H), 5.84 (s, 1H), 2.36 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 169.6, 157.2, 144.4, 141.3, 130.0, 128.6, 127.6, 127.2, 126.9, 122.4, 119.4, 117.1, 111.1, 63.2, 17.7 ppm; IR (KBr): ν= 3414, 3034, 2969, 2918, 1603, 1566, 1507, 1450, 1411, 1316, 1274, 1176, 1140, 1050, 1029, 989, 911, 849, 806, 746, 699 cm^{-1}; m/z (EI) (%): 276.1 (45), 275.0 (100), 196.0 (51), 169.0 (39), 168.0 (14); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{18}H_{17}N_3Na$: 298.13147; found: 298.13115.

Chapter 2. Electrophilic Amination with Nitro Compounds *via* Carbometalation

General Procedures

General procedure B9 for the carbozincation of alkynes

According to the procedure of *Gosmini et al.*, to a solution of $CoBr_2$ (8.7 mg, 0.04 mmol, 0.1 eq.) and Zn dust (52 mg, 0.8 mmol, 2.0 eq.) in MeCN (2 mL) were added AllylCl (0.01 mL, 0.12 mmol, 0.3 eq.) and one drop TFA under vigorous stirring. This caused a rise of temperature and change of the color of the mixture from blue to orange to dark grey. Once the orange tinge of the mixture had disappeared, aryl bromide (0.4 mmol, 1.0 eq.) was added. The reaction mixture was stirred for 0.5 h and was charged with alkyne (0.13 mmol, 0.33 eq.). The mixture was stirred at rt. After 8 hours, aqueous HCl (1.0 M, 2 mL) was added and the phases were separated. The aqueous phase was extracted three times with Et_2O. The combined organic phases were dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B10 for the carbozincation of alkynes

According to the procedure of *Yoshikai et al.*, anhydrous LiCl (18 mg, 0.4 mmol, 2.0 eq.) was placed in a Schlenk tube, dried under vacuum (1 mbar) at 150 °C for 5 min, and cooled down to room temperature under argon. To the Schlenk tube was added zinc dust (40 mg, 0.6 mmol, 3.0 eq.) and the heterogeneous mixture of Zn and LiCl was dried under vacuum (1 mbar) at 150 °C for 5 min. While cooling to room temperature, the reaction tube was evacuated and backfilled with argon for three times. The mixture was suspended in THF (1 mL), followed by the activation of zinc with 1,2-dibromoethane (one drop) and TMSCl (one drop) and stirring for 5 min. Then Xantphos (11 mg, 0.02 mmol, 0.1 eq.) and $CoCl_2$ (2.6 mg, 0.02 mmol, 0.1 eq.) were added sequentially. After stirring for additional 5 min, aryl halide (0.4 mmol, 2.0) was added in one portion. The reaction was stirred at room temperature for 30 min. Then alkyne (0.2 mmol, 1.0 eq.) was added to the arylzinc reagent. The resulting solution was stirred at 60 °C. After 16 hours, the mixture was allowed to cool to room temperature and saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL). The aqueous layer was extracted three times with EtOAc and the combined organic layer was dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B11 for the carbometalation of cyclopropenes

According to the procedure of *Fox et al.*, Schlenk tube was charged with $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0eq, 1.0 M in THF). Then phenyllithium (0.45 mL, 0.8 mmol, 4.0 eq., 1.9 M in dibutyl ether) was added dropwise at 0 °C. The mixture was stirred at rt for 0.5 h, then CuCN (2.6 mg, 0.04 mmol, 0.2 eq.) was added. To the mixture was added cyclopropene (0.2 mmol, 1.0 eq., in 1 mL toluene) and the mixture was stirred at rt. After 16 hours, saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL) were added. The aqueous layer was extracted three times with EtOAc and the combined organic layer was dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B12 for the electrophilic amination *via* carbometalation with alkynes

Anhydrous LiCl (18 mg, 0.4 mmol, 2.0 eq.) was placed in a Schlenk tube, dried under vacuum (1 mbar) at 150 °C for 5 min, and cooled down to room temperature under argon. To the Schlenk tube was added zinc dust (40 mg, 0.6 mmol, 3.0 eq.) and the heterogeneous mixture of Zn and LiCl was dried under vacuum (1 mbar) at 150 °C for 5 min. While cooling to room temperature, the reaction tube was evacuated and backfilled with argon for three times. The mixture was suspended in THF (1 mL), followed by the activation of zinc with 1,2-dibromoethane (one drop) and TMSCl (one drop) and stirring for 5 min. Then Xantphos (11 mg, 0.02 mmol, 0.1 eq.) and $CoCl_2$ (2.6 mg, 0.02 mmol, 0.1 eq.) were added sequentially. After stirring for additional 5 min, aryl halide (0.4 mmol, 2.0) was added in one portion. The reaction was stirred at room temperature for 30 min. Then alkyne (0.2 mmol, 1.0 eq.) was added to the arylzinc reagent. The resulting solution was stirred at 60 °C. After 16 hours, the mixture was allowed to cool to room temperature and nitro compound (0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were

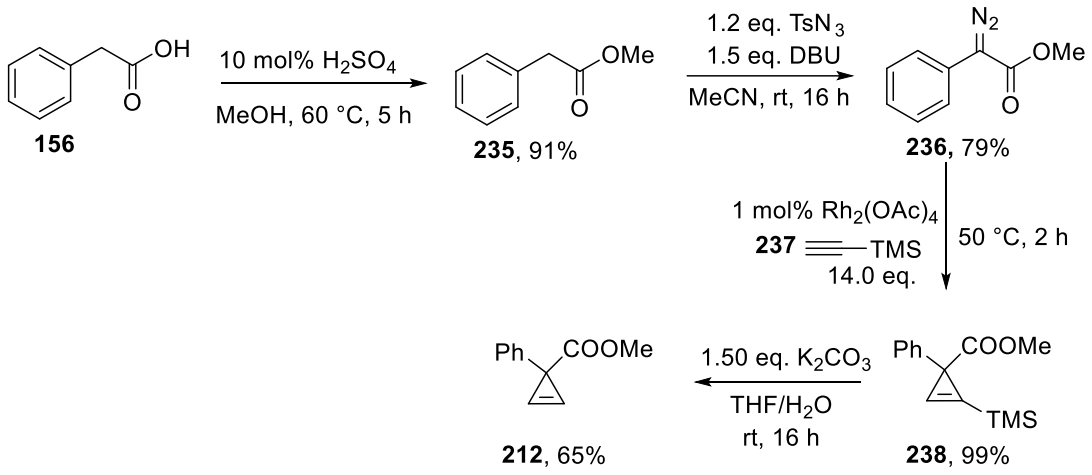
subsequently added. The mixture was stirred at rt for 16 hours, then saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL). The aqueous layer was extracted three times with EtOAc and the combined organic layer was dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B13 for the electrophilic amination *via* carbometalation with cyclopropenes

According to the procedure of *Fox et al.*, Schlenk tube was charged with $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0eq, 1.0 M in THF). Then phenyllithium (0.45 mL, 0.8 mmol, 4.0 eq., 1.9 M in dibutyl ether) was added dropwise at 0 °C. The mixture was stirred at rt for 0.5 h, then CuCN (2.6 mg, 0.04 mmol, 0.2 eq.) was added. To the mixture was added cyclopropene (0.2 mmol, 1.0 eq., in 1 mL toluene) and the mixture was stirred at rt. After 4 hours, nitro compound (0.2 mmol, 1.0 eq.) and B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) were added in solution of toluene (0.5 mL). The mixture was stirred for 16 hours, then saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL) were added. The aqueous layer was extracted three times with EtOAc and the combined organic layer was dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

Synthesis of Starting Materials

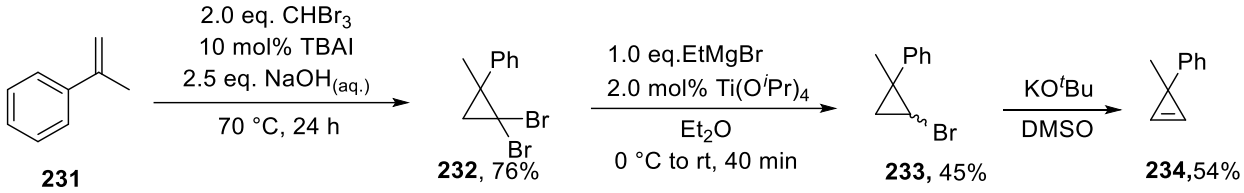
methyl 1-phenylcycloprop-2-ene-1-carboxylate (212)



The synthesis was carried out according to the procedure of *Gevorgyan et al.*[80]
Phenylacetic acid **156** (4.08 g, 30 mmol, 1.0 eq.) was dissolved in 30 mL MeOH. To the mixture was added sulfuric acid (1.68 mL) and was stirred at 60 °C for 5 hours. The reaction mixture was then cooled off to rt, was diluted with saturated $NaHCO_3$ solution and was extracted three times with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated. The product **235** was obtained as white solid (4.1 g, 27.3 mmol, 91%) and was used without further purification in the next step.
Methyl 2-phenylacetate **235** (0.75 g, 5 mmol, 1.0 eq.) was dissolved in acetonitrile (20 mL). To the mixture were added subsequently tosyl azide (1.1 g, 6 mmol, 1.2 eq.) and 1,8-diazabicyclo(5.4.0)undec-7-ene (1.1 g, 7.5 mmol, 1.5 eq.). The reaction mixture was stirred at rt. After 16 hours, saturated NH_4Cl solution was added. The mixture was extracted with EtOAc and was washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The product **236** was obtained after column chromatography (Pentane: EtOAc = 100:1) as orange oil (0.695 g, 3.95 mmol, 79%) and was used in the next step.
Methyl 2-diazo-2-phenylacetate **236** (0.350 g, 2 mmol, 1.0 eq.) was dissolved in trimethylsilylacetylene **237** (2.4 mL) and was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.02 mmol, 0.01 eq.) in trimethylsilylacetylene (1.7 mL) at 50 °C under argon atmosphere over 1 hour. The mixture was stirred for 2 hours at 50 °C. The mixture was then concentrated. The residue was dissolved in EtOAc and filtered through a short plug of silica. The product **238** was obtained as yellow oil (0.5 g, 1.99 mmol, 99%) and was used without further purification.
Methyl 1-phenyl-2-(trimethylsilyl)cycloprop-2-ene-1-carboxylate **238** (0.49 g, 2 mmol, 1.0 eq.) was dissolved in THF (10 mL). A K_2CO_3 solution (0.414 g in 3.5 mL H_2O) was added dropwise at 0 °C. The mixture was stirred 16 hours at rt. The mixture was then extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The product **239** was obtained after column

chromatography (Pentane: EtOAc = 7:1) as colorless liquid (226 mg, 1.3 mmol, 65%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 – 7.29 (m, 2H), 7.27 (dd, *J* = 8.9, 2.1 Hz, 2H), 7.24 – 7.23 (m, 1H), 3.71 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 175.54, 141.41, 128.16, 128.13, 126.60, 107.70, 52.28, 30.60 ppm; IR (KBr): ν= 3155, 3113, 3058, 3025, 2951, 1720, 1659, 1601, 1493, 1436, 1284, 1218, 1111, 1009, 890, 963, 790, 759, 738, 698, 664 cm^{-1}; m/z (EI) (%): 310.2 (10), 296.2 (43), 293.3 (47), 268.3 (13), 265.3 (16), 256.4 (14), 237.3 (13), 219.3 (13), 194.3 (10), 178.3 (14), 167.2 (20), 165.2 (10), 159.2 (13), 151.3 (11), 150.2 (14), 149.2 (83), 129.3 (35), 127.3 (15), 125.3 (16), 123.3 (14), 121.3 (10), 115.2 (78), 113.3 (17), 112.3 (14), 111.3 (31), 109.3 (17), 105.2 (21), 103.3 (17), 99.3 (12), 98.3 (16), 97.3 (44), 96.3 (17), 95.3 (26), 91.3 (13), 85.3 (47), 84.3 (20), 83.3 (51), 82.3 (15), 81.3 (28), 77.3 (15), 73.3 (25), 71.4 (69Ö, 70.4 (24), 69.4 (62), 67.3 (14), 60.3 (13), 59.3 (17), 57.4 (100), 56.4 (21), 55.4 (57); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{11}H_{10}O_2Na$: 197.05730; found: 197.05684.
The spectral data are in accordance with the literature.[80]

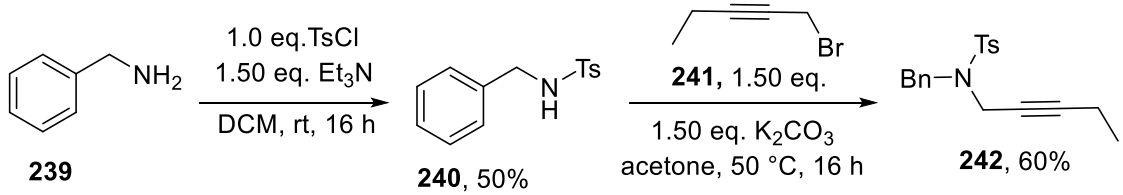
(1-methylcycloprop-2-en-1-yl)benzene (234)



231 **232**, 76% **233,** 45% **234,**54%

The synthesis was carried out according to the procedure of *Gevorgyan et al*.[80]
Prop-1-en-2-ylbenzene **231** (11.8 g, 0.1 mol. 1.0 eq.) was dissolved in bromoform (17.5 mL, 0.2 mol, 2.0 eq.). To the mixture TBAI (3.2 g, 0.01 mol, 0.1 eq.) and aqueous NaOH (50% solution in H_2O, 0.25 mol, 2.5 eq.). The reaction mixture was stirred at 70 °C for 24 hours. Then the mixture was concentrated. The residue was dissolved in pentane and filtered through a short column of silica. The product **232** was obtained as red liquid (21.8 g, 0.076 mol, 76%) and was used without further purification in the next step.
Under argon atmosphere, (2,2-dibromo-1-methylcyclopropyl)benzene **232** (5.8 g, 0.02 mol, 1.0 eq.) was dissolved in Et_2O (25 mL). To the solution was added titanium isopropoxide (0.11 g, 0.4 mmol, 0.02 eq.). Ethylmagnesium bromide (10 mL, 0.03 mol, 1.5 eq., 3N in Et_2O) was added at 0 °C over 30 minutes. The mixture was stirred for additional 40 minutes at rt. The reaction was stopped by the addition of 1 M HCl (30 mL) at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was then washed with saturated $NaHCO_3$ solution and brine. The product **233** was obtained as yellow solid (1.89 g, 9 mmol, 45%) and was used without further purification in the next step.
Potassium tert-butoxide (0.12 g, 1.08 mmol, 1.2 eq.) was in DMSO (1 mL) at 60 °C. To this mixture was added dropwise di(2-bromo-1-methylcyclopropyl)benzene **233** (0.19 g, 0.9 mmol, 1.0 eq.) at rt. The mixture was stirred for 16 hours at rt. The reaction mixture was poured to ice and was extracted with pentane. The organic layer was washed with water, brine and was concentrated. The crude product was distilled in vacuo (97 °C, 19 mbar) to afford the product **234** as colorless liquid (63 mg, 0.49 mmol, 54%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33 – 7.28 (m, 2H), 7.25 – 7.21 (m, 2H), 7.19 – 7.14 (m, 1H), 1.64 (s, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 149.92, 127.80, 126.01, 124.96, 115.46, 25.40 ppm; IR (KBr): ν= 3467, 3057, 3025, 2967, 2867, 1638, 1600, 1492, 1446, 1381, 1196, 1155, 1075, 1026, 994, 788, 743, 698, 615, 537, 496 cm^{-1}; m/z (EI) (%): 203.2 (11), 189.2 (35), 161.2 (11), 159.2 (15), 154.1 (32), 153.1 (13), 148.1 (55), 147.2 (14), 145.2 (12), 143.2 (29), 141. (11), 133.1 (24), 131.2 (33), 130.1 (53), 129.1 (100), 128.1 (55), 119.2 (33), 118.2 (10), 117.2 (23), 116.1 (14), 115.1 (95), 106.2 (11), 105.2 (27), 103.1 (16), 103.1 (16), 91.2 (48), 78.2 (11), 77.2 (24), 73.2 (58), 57.2 (44), 51.2 (19), 45.2 (36); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{11}$: 131.08553; found: 131.08512.
The spectral data are in accordance with the literature.[80]

***N*-benzyl-4-methyl-N-(pent-2-yn-1-yl)benzenesulfonamide (242)**



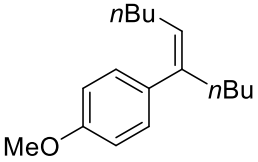
239 **240**, 50% **242**, 60%

The synthesis was carried out according to the procedure of *Maestri et al.*[82]
Benzylamine **239** (2.1 g, 2.1 mL, 20 mmol, 1.0 eq.) and Et_3N (3.0 g, 4.1 mL, 30 mmol, 1.5 eq.) were dissolved in DCM (100 mL). Tosyl chloride (3.8 g, 20 mmol, 1.0 eq.) was added to the mixture in smaller portions

at 0 °C and the mixture was stirred at rt. After 16 hours, the reaction was stopped by the additon of H_2O (40 mL) and the mixture was extracted with DCM. The organic layer was dried over Na_2SO_4 and was concentrated. After recrystallization from DCM/Pentane (1:5), the product **240** was obtained as white solid (2.6 g, 10 mmol, 50%).
Under argon atmosphere, *N*-benzyl-4-methylbenzenesulfonamide **240** (1.0 g, 4 mmol, 1.0 eq.) and K_2CO_3 (0.82 g, 6 mmol, 1.5 eq.) were dissolved in acetone (20 mL). To the mixture was added dropwise 1-bromopent-2-yne **241** (0.88 g, 0.6 mL, 6 mmol, 1.5 eq.) and the mixture was stirred at 50 °C. After 16 hours, saturated NH_4Cl solution was added at rt and the mixture was extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated. The product **242** was obtained after column chromatography (Pentane: EtOAc = 4:1) as orange solid (0.79 g, 2.4 mmol, 60%); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 – 7.77 (m, 2H), 7.38 – 7.28 (m, 8H), 4.33 (s, 2H), 3.90 (t, *J* = 2.2 Hz, 2H), 2.44 (s, 3H), 1.91 (qt, *J* = 7.5, 2.2 Hz, 2H), 0.90 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 143.27, 136.24, 135.27, 129.32, 128.77, 128.59, 127.95, 127.93, 87.85, 71.52, 49.76, 36.11, 21.51, 13.53, 12.10 ppm; IR (KBr): ν= 3031, 2976, 2921, 1717, 1598, 1494, 1451, 1344, 1158, 1093, 1054, 897, 812, 762, 729, 700, 658 cm^{-1}; m/z (EI): 236.2 (46), 173.3 (13), 172.3 (100), 171.3 (13), 156.2 (16), 155.1 (18), 143.2 (10), 92.3 (12), 91.3 (73), 65.3 (14); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{19}H_{21}O_2NaS$: 350.11852; found: 350.11684.
The spectral data are in accordance with the literature.[82]

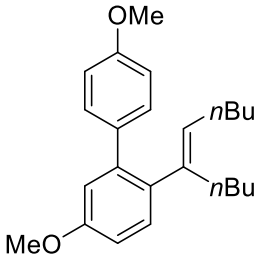
Isolated Compounds

1-(dec-5-en-5-yl)-4-methoxybenzene (244)



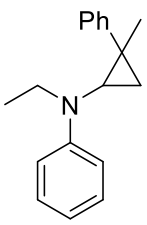
Following the general procedure B9, using 4-bromoanisole and 5-decyne, compound **244** was isolated by flash column chromatography (Pentane:EtOAc = 100:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 – 7.22 (m, 2H), 6.90 – 6.80 (m, 2H), 5.58 (t, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 2.52 – 2.41 (m, 2H), 2.18 (t, *J* = 7.2 Hz, 2H), 1.46 – 1.36 (m, 4H), 1.35 – 1.28 (m, 4H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.91 – 0.85 (m, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 158.29, 139.36, 136.04, 127.74, 127.26, 113.48, 55.23, 32.20, 30.97, 29.49, 28.24, 22.70, 22.49, 14.06, 13.99 ppm; IR (KBr): ν= 2957, 2928, 2862, 1607, 1511, 1461, 1252, 1177, 1012, 865, 791, 695 cm^{-1}; m/z (EI) (%): 247.2 (19), 246.2 (100), 204.2 (13), 203.2 (34), 189.2 (55), 175.1 (10), 161.1 (18), 149.1 (11), 148.1 (93), 147.1 (59), 121.1 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{26}O$: 246.19837; found: 247.20544.
The spectral data are in accordance with the literature.[74b]

2-(dec-5-en-5-yl)-4',5-dimethoxy-1,1'-biphenyl (246)



According to the general procedure B10 compound **246** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 – 7.30 (m, 2H), 7.26 (d, *J* = 1.3 Hz, 1H), 7.12 – 7.06 (m, 1H), 6.90 – 6.85 (m, 2H), 6.82 – 6.77 (m, 2H), 5.39 (td, *J* = 7.3, 1.2 Hz, 1H), 3.84 (d, *J* = 1.3 Hz, 3H), 3.82 (d, *J* = 1.3 Hz, 3H), 2.09 – 2.02 (m, 2H), 1.79 (t, *J* = 7.6 Hz, 2H), 1.39 – 1.29 (m, 4H), 1.11 – 0.99 (m, 4H), 0.90 (dtd, *J* = 17.5, 7.2, 1.3 Hz, 5H), 0.72 (td, *J* = 7.2, 1.3 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 158.52, 158.17, 141.45, 140.30, 136.21, 134.69, 131.40, 130.98, 129.96, 115.14, 113.26, 111.84, 55.26, 55.22, 31.92, 30.56, 30.38, 27.83, 22.55, 22.38, 14.05, 13.89 ppm; IR (KBr): ν= 2928, 2859, 1605, 1565, 1513, 1463, 1289, 1244, 1216, 1175, 1107, 1039, 871, 829, 731, 691 cm^{-1}; m/z (EI) (%): 353.2 (12), 352.2 (41), 296.1 (22), 295.1 (100), 239.1 (42), 224.1 (12).

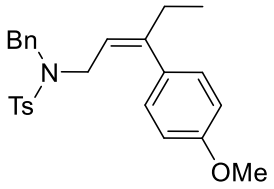
***N*-ethyl-*N*-(2-methyl-2-phenylcyclopropyl)aniline (248)**



Following the general procedure B14 compound **248** was isolated by flash column chromatography (Pentane:EtOAc:Et_3N = 50:1:0.1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 – 7.25 (m, 3H), 7.24 – 7.15 (m, 4H), 6.85 – 6.77 (m, 2H), 6.72 (td, *J* = 7.2, 1.1 Hz, 1H), 3.56 (ddd, *J* = 44.0, 14.8, 7.3 Hz, 2H), 2.67 (dd, *J* = 7.8, 5.0 Hz, 1H), 1.52 – 1.46 (m, 1H), 1.41 (d, *J* = 0.6 Hz, 3H), 1.16 (td, *J* = 7.1, 0.8 Hz, 3H), 1.01 (t, *J* = 5.3 Hz, 1H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$): δ 155.0, 146.6, 129.6, 128.3, 125.6, 125.0, 121.9, 114.3, 53.4, 41.1, 26.8, 22.1, 20.6, 10.2 ppm; IR (KBr): ν= 3059, 3028, 2970, 2930, 2872, 2328, 2075, 1920, 1664, 1598, 1497, 1447, 1372, 1341,

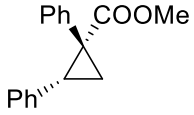
1300, 1259, 1194, 1130, 1074, 1031, 995, 843, 752, 694 cm^{-1}; HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{21}N$: 251.1665; found: 251.16687.

(E/Z)-*N*-benzyl-*N*-(3-(4-methoxyphenyl)pent-2-en-1-yl)-4-methylbenzenesulfonamide mixture (250a)



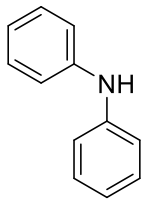
According to the general procedure B9 compound **250a** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.81 – 7.74 (m, 2H), 7.59 – 7.52 (m, 2H), 7.36 – 7.29 (m, 5H), 7.25 – 7.16 (m, 5H), 7.12 – 7.08 (m, 2H), 7.00 – 6.93 (m, 4H), 6.81 – 6.74 (m, 2H), 6.74 – 6.68 (m, 2H), 5.53 (td, *J* = 7.3, 1.2 Hz, 1H), 5.19 – 5.15 (m, 1H), 4.38 (s, 2H), 4.27 (s, 2H), 4.14 (s, 2H), 3.95 (d, *J* = 6.8 Hz, 2H), 3.81 – 3.77 (m, 6H), 2.44 (s, 6H), 2.21 (q, *J* = 7.7 Hz, 2H), 1.85 (td, *J* = 7.4, 0.9 Hz, 2H), 0.86 (td, *J* = 7.5, 1.0 Hz, 3H), 0.80 (td, *J* = 7.5, 1.0 Hz, 3H) ppm; ^{13}C NMR (151 MHz,$CDCl_3$): δ 158.85, 158.70, 144.78, 143.22, 142.97, 137.63, 137.08, 136.44, 136.30, 135.79, 133.30, 133.02, 129.73, 129.46, 128.55, 128.33, 128.18, 127.86, 127.81, 127.69, 127.33, 127.27, 127.24, 127.21, 119.81, 113.49, 113.40, 55.25, 50.75, 50.73, 44.98, 44.91, 22.64, 21.51, 21.44, 14.15, 13.38 ppm; IR (KBr): ν= 3031, 2963, 2874, 1604, 1510, 1455, 1336, 1289, 1246, 1155, 1093, 1033, 923, 896, 809, 766, 733, 698, 658 m^{-1}; m/z (EI): 436.1 (11), 435.1 (33), 281.2 (10), 280.2 (48), 279.2 (23), 278.1 (57), 274.1 (32), 250.1 (14), 188.1 (18), 176.2 (21), 175.1 (25), 174.1 (100), 173.1 (11), 161.1 (12), 159.1 (24), 149.1 (15), 148.1 (12), 92.1 (10), 91.1 (91); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{26}H_{29}O_3NNaS$: 458.17604; found: 458.17580.

methyl (1R,2R)-1,2-diphenylcyclopropane-1-carboxylate (257)



According to the general procedure B13 compound **257** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.32 – 7.27 (m, 3H), 7.23 (dt, *J* = 9.3, 7.6 Hz, 3H), 7.18 – 7.14 (m, 1H), 3.22 (s, 2H), 2.79 (t, *J* = 8.2 Hz, 1H), 2.26 (dd, *J* = 7.5, 5.1 Hz, 1H), 1.54 (dd, *J* = 9.0, 5.0 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.05, 140.32, 136.56, 130.23, 129.02, 128.35, 128.07, 127.36, 126.83, 51.97, 38.17, 33.21, 18.31 ppm; IR (KBr): ν= 3057, 3027, 2950, 1724, 1601, 1495, 1440, 1310, 1278, 1209, 1161, 1111, 1073, 1028, 960, 927, 867, 796, 770, 730, 696 cm^{-1}; m/z (EI) (%): 253.1 (22), 252.1 (100), 221.1 (13), 220.1 (48), 193.1 (42), 192.1 (23), 191.1 (33), 178.0 (12), 121.0 (19), 115.0 (31), 91.1 (10); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{16}O_2Na$: 275.10425; found: 275.10428.
The spectral data are in accordance with the literature.[143]

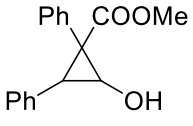
Diphenylamine (260)



Following the general procedure B13 compound **260** was isolated by flash column chromatography (Pentane:EtOAc = 40:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 4H), 7.08 (dt, *J* = 8.7, 1.6 Hz, 4H), 6.94 (ddt, *J* = 8.4, 7.4, 1.0 Hz, 2H), 5.70 (s, 1H); ^{13}C NMR (151 MHz, CDCl3) δ 143.2, 129.6, 129.5, 121.1, 117.9. *m/z* (EI) (%): 170.3(16), 169.2(100), 168.2(32), 167.2(17). IR (KBr): ν = 3383, 3039, 2329, 2103, 1738, 1588, 1485, 1417, 1311, 1231, 1163, 1080, 1021, 989, 874, 741, 687 cm^{-1}.

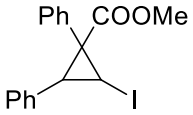
The spectral data are in accordance with the literature.[14a]

methyl 2-hydroxy-1,3-diphenylcyclopropane-1-carboxylate (mixture of isomers) (261)



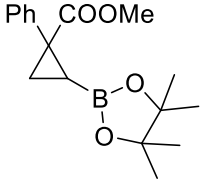
According to the general procedure B13 compound **261** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 100:1 to 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 8.1, 1.2 Hz, 2H), 7.52 – 7.47 (m, 2H), 7.44 (dt, *J* = 8.1, 1.2 Hz, 2H), 7.39 – 7.33 (m, 4H), 7.33 – 7.25 (m, 5H), 7.25 – 7.20 (m, 3H), 7.19 – 7.12 (m, 2H), 3.63 (s, 3H), 3.56 (s, 3H), 3.24 – 3.19 (m, 1H), 3.03 (dd, *J* = 6.8, 2.7 Hz, 1H), 2.78 – 2.72 (m, 1H), 2.41 (dd, *J* = 6.8, 2.7 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.27, 171.18, 141.63, 141.46, 135.52, 135.21, 130.25, 130.04, 129.77, 129.46, 128.39, 128.24, 128.21, 128.16, 52.10, 52.08, 39.82, 39.36, 36.91, 36.29, 29.51, 29.05 ppm; IR (KBr): ν= 3062, 3025, 2996, 2947, 1721, 1601, 1496, 1434, 1313, 1218, 1188, 1143, 1056, 1028, 932, 913, 811, 768, 728, 695 cm^{-1}; HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{16}O_3Na$: 291.09917; found: 291.09883.

methyl 2-iodo-1,3-diphenylcyclopropane-1-carboxylate (264)



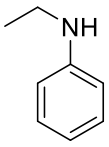
According to the general procedure B13 compound **264** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 100:1). Isomer 1: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.32 (m, 1H), 7.29 (ddt, *J* = 8.4, 6.5, 1.5 Hz, 2H), 7.24 – 7.21 (m, 1H), 7.17 – 7.11 (m, 5H), 6.86 – 6.83 (m, 2H), 4.25 (d, *J* = 9.3 Hz, 1H), 3.64 (s, 3H), 3.27 (d, *J* = 9.4 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.89, 134.30, 132.90, 131.46, 130.86, 127.91, 127.63, 127.07, 127.05, 53.38, 37.20, 35.22 ppm; IR (KBr): ν= 3033, 1714, 1601, 1496, 1437, 1318, 1249, 1136, 1077, 997, 957, 907, 761, 734, 698 cm^{-1}; m/z (EI) (%): 251.1 (30), 248.5 (11), 220.2 (27), 219.1 (100), 217.6 (37), 216.6 (16), 192.1 (21), 191.1 (87), 189.2 (22), 165.0 (12); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{15}O_2NaI$: 401.00089; found: 401.00085; isomer 2: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 – 7.48 (m, 2H), 7.44 – 7.36 (m, 6H), 7.36 – 7.31 (m, 2H), 3.70 – 3.68 (m, 1H), 3.56 (d, *J* = 1.2 Hz, 3H), 2.85 (dt, *J* = 8.9, 1.1 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.25, 140.32, 134.73, 129.40, 129.14, 128.70, 127.96, 127.88, 127.32, 52.26, 38.83, 34.17, 1.92 ppm; IR (KBr): ν= 3056, 3028, 2949, 1732, 1600, 1494, 1440, 1306, 1212, 1151, 1059, 1028, 963, 937, 881, 734, 696 cm^{-1}; m/z (EI) (%): 251.3 (25), 236.1 (18), 221.0 (14), 220.3 (21), 219.1 (100), 192.1 (15), 191.0 (67), 190.0 (28), 189.1 (15); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{17}H_{15}O_2NaI$: 401.00089; found: 401.00047.

methyl 1-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropane-1-carboxylate (265)



According to the general procedure B13 compound **265** was synthesized. Purification by flash column chromatography (Pentane: EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.19 (m, 5H), 3.61 – 3.57 (s, 3H), 1.74 – 1.68 (m, 1H), 1.66 – 1.61 (m, 1H), 1.29 (ddd, *J* = 16.0, 10.4, 8.0 Hz, 1H), 1.05 (s, 6H), 0.82 (s, 6H), 0.70 (dd, 8.0 Hz, 3.6 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.86, 137.72, 131.14, 131.10, 127.82, 127.78, 127.06, 83.29, 52.47, 33.77, 24.85, 24.81, 24.41, 24.37, 18.72, 18.69 ppm; IR (KBr): ν= 2981, 1723, 1408, 1374, 1330, 1261, 1223, 1192, 1142, 1103, 1064, 1004, 968, 941, 857, 780, 740, 697, 668 cm^{-1}; m/z (EI) (%): 305.6 (31), 304.6 (12), 303.2 (17), 301.9 (100), 292.2 (42), 278.9 (17), 202.0 (20), 144.0 (83), 143.0 (21), 116.0 (39), 115.0 (32), 83.1 (11), 48.2 (20), 46.7 (21);HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{23}BO_4$: 303.17622; found: 303.17658.
The spectral data are in accordance with the literature.[144]

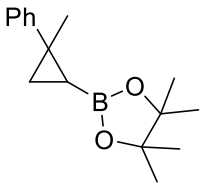
***N*-ethylaniline (269)**



Following the general procedure B14 compound **269** was isolated by flash column chromatography (Pentane: EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2H), 6.75 (tt, J = 7.3, 1.1 Hz, 1H), 6.67 – 6.64 (m, 2H), 3.57 (s, 1H), 3.20 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 148.6, 129.3, 117.3, 112.8, 38.5, 15.0; *m/z* (EI) (%): 278.1 (47), 277.1 (100), 201.1 (11), 199.1 (14), 183.1 (10), 106.1 (19); HRMS-ESI calcd. for $C_8H_{12}N$: 122.09643 ($[M+H]^+$); found: 122.09646; IR (KBr): ν = 3402, 3051, 3021, 2969, 2871, 1601, 1504, 1430, 1378, 1318, 1257, 1177, 1147, 1098, 1063, 1028, 991, 868, 823, 746, 690, 618, 528 cm^{-1}.

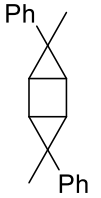
The spectral data are in accordance with the literature.[14a]

4,4,5,5-tetramethyl-2-(2-methyl-2-phenylcyclopropyl)-1,3,2-dioxaborolane (329)



Following the general procedure B14 compound **329** was isolated by flash column chromatography (Pentane:EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.28 (m, 2H), 7.27 – 7.23 (m, 3H), 7.14 (t, *J* = 7.2 Hz, 1H), 1.49 (s, 3H), 1.28 (s, 6H), 1.26 (s, 6H), 1.18 (dd, *J* = 9.7, 3.6 Hz, 1H), 1.00 (dd, *J* = 7.2, 3.6 Hz, 1H), 0.36 (dd, *J* = 9.7, 7.2 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 148.09, 128.07, 127.00, 125.55, 83.16, 26.74, 25.15, 24.55, 22.91, 20.23 ppm; IR (KBr): ν= 3061, 2978, 2930, 2869, 2165, 1664, 1600, 1539, 1491, 1408, 1377, 1318, 1214, 1146, 1114, 1027, 967, 855, 816, 756, 699 cm^{-1}; m/z (EI) (%): 158.2 (13), 143.1 (14), 131.2 (13), 130.1 (17), 129.1 (12), 115.1 (16), 105.2 (11), 91.2 (20), 85.2 (27), 84.2 (53), 83.2 (10), 77.2 (21), 69.3 (12), 61.2 (20), 59.6 (17), 58.0 (24), 56.2 (11), 54.7 (13), 48.3 (89), 46.7 (100), 45.3 (21); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{16}H_{23}BO_2Na$: 281.16833; found: 281.16758.
The spectral data are in accordance with the literature.[145]

3,6-dimethyl-3,6-diphenyltricyclo[3.1.0.02,4]hexane (330)



Following the general procedure B14 compound **330** was isolated by flash column chromatography (Pentane:EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.35 (m, 1H), 7.31 – 7.27 (m, 5H), 7.21 – 7.13 (m, 2H), 7.10 – 7.05 (m, 2H), 1.85 (s, 1H), 1.79 – 1.75 (m, 1H), 1.61 (s, 3H), 1.60 (s, 3H), 1.45 – 1.41 (m, 1H), 1.23 (s, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.55, 145.48, 143.11, 129.46, 128.22, 128.11, 128.02, 127.78, 127.58, 126.06, 125.88, 47.47, 44.75, 44.63, 29.98, 29.11, 28.60, 24.72, 16.86, 16.56 ppm; IR (KBr): ν= 3023, 2976, 2944, 2920, 2867, 1600, 1493, 1445, 1372, 1264, 1065, 1022, 903, 860, 759, 696 cm^{-1}; m/z (EI) (%): 261.1 (19), 260.0 (100), 257.6 (49), 255.1 (14), 253.4 (24), 246.1 (11), 245.1 (52), 244.2 (62), 241.7 (16), 240.0 (19), 230.7 (50), 230.1 (19), 229.1 (20), 228.2 (37), 226.6 (37), 217.3 (30), 216.1 (20), 215.0 (52), 213.3 (22), 204.1 (15), 203.1 (11), 201.9 (21), 169.1 (15), 168.1 (10), 167.0 (44), 166.1 (10), 165.0 (22), 156.1 (17), 155.0 (59), 154.1 (13), 153.1 (16), 152.1 (19), 143.1 (18), 142.0 (69), 141.0 (34), 131.1 (36), 130.1 (12), 129.1 (31), 128.1 (36), 127.0 (12), 117.1 (14), 116.1 (11), 114.9 (55), 105.0 (64), 103.0 (18), 91.0 (46), 78.1 (12), 77.1 (28), 54.6 (21); HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{20}$: 260.15595; found: 260.15601.

Chapter 3. Investigation of the Reactivity of Aminoboranes

General Procedures

General procedure B14 for aminoboration of cyclopropenes

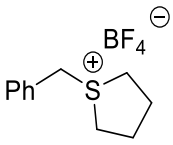
Nitrobenzene (21 mg, 0.2 mmol, 1.0 eq.), B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) and Et_3N (60µL, 0.4 mmol, 2.0 eq.) were dissolved in toluene (1 mL) and the solution was degassed three times. To the mixture was added Et_2Zn (0.265 mL, 0.24 mmol, 1.2 eq., 0.9 M in hexane). The reaction mixture was stirred at room temperature and cyclopropene (0.2 mmol, 1.0 eq.) was added. The mixture was stirred for additional 16 hours. Then saturated aqueous NH_4Cl (1 mL) and H_2O (1 mL) were added. The aqueous layer was extracted three times with EtOAc and the combined organic layer was dried over Na_2SO_4 and concentrated to afford the crude material, which was purified by flash column chromatography (SiO_2, Pentane: EtOAc).

General procedure B15 for synthesis of α-amino boronates

Azaarylmethane (0.4 mmol, 2.0 eq.) was dissolved in THF (1.0 mL) in a flame dried Schlenk tube and the mixture was degassed three times. The mixture was charged with $KN(SiMe_3)_2$ (1.7 mL, 1.2 mmol, 6.0 eq., 0.7 M in toluene) followed by $ZnCl_2$ (0.4 mL, 0.4 mmol, 2.0 eq., 1.0 M in THF). After stirring for 5 min at rt, nitro compound (0.2 mmol, 1.0 eq.), B_2pin_2 (102 mg, 0.4 mmol, 2.0 eq.) and sulfonium salt (106 mg, 0.4 mmol, 2.0 eq.) were subsequently added. The mixture was stirred at rt overnight, stopped with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of Na_2SO_4 and silica. The pad was rinsed with additional ethyl acetate, and the solution was concentrated *in vacuo*. The crude product was purified *via* flash column chromatography.

Synthesis of Starting Materials

_S_-benzyltetrahydrothiophenium tetrafluoroborate (376)



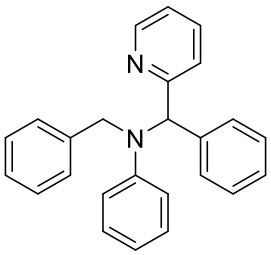
The synthesis was carried out according to the procedure of *Aggarwal et al.*[107]

Tetrahydrothiophene (1.51 g, 12 mmol, 3.0 eq.) and benzyl bromide (0.68 g, 4 mmol, 1.0 eq.) were dissolved in DCM (4 mL). To the mixture saturated $NaBF_4$ solution (1.37g, 12 mmol, 3.0 eq. in 1.4 mL H_2O) was added and the mixture was stirred at rt. After 2 days, the mixture was diluted with DCM (30 mL) and the organic and aqueous and organic layer were separated. The organic layer was dried over Na_2SO_4. The crude product was recrystallized from ethanol (5 mL) and the product was obtained as white solid (0.6 g, 6.7 mmol, 56%).

The spectral data are in accordance with the literature.[107]

Isolated Compounds

_N_-benzyl-_N_-(phenyl(pyridin-2-yl)methyl)aniline (379)



Following the general procedure B15 compound **379** was isolated by flash column chromatography (Pentane:EtOAc: Et_3N = 20:1:0.1). ^1H NMR (600 MHz, $CDCl_3$) δ 8.55 – 8.51 (m, 1H), 7.55 (td, *J* = 7.7, 1.9 Hz, 1H), 7.30 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.25 – 7.21 (m, 2H), 7.19 (d, *J* = 7.2 Hz, 3H), 7.16 – 7.10 (m, 4H), 7.10 – 7.06 (m, 2H), 7.05 – 7.00 (m, 2H), 6.83 – 6.78 (m, 2H), 6.73 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.38 (s, 1H), 4.78 – 4.63 (m, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.71, 149.56, 139.61, 139.34, 136.35, 129.27, 128.94, 128.29, 127.83, 127.34, 126.53, 126.11, 123.55, 122.05, 117.85, 114.90, 68.70, 52.43 ppm; IR (KBr): ν= 3056, 2962, 2920, 1591, 1496, 1451, 1432, 1352, 1250, 1200, 1152, 1091, 1025, 992, 947, 802, 746, 693 cm^{-1}; m/z (EI) (%): 182.1 (27), 170.1 (14), 169.1 (100), 168.2 (37), 167.1 (23), 91.1 (11), 83.1 (11); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{25}H_{22}N_2Na$: 373.16752; found: 373.16599.

Chapter 4. Cu-Catalyzed Coupling of Nitro Compounds with Allyl Boronates

General Procedures

General procedure C1 for the coupling of nitro compounds with allyl boronates (no reductive work-up)

$CuBr_2$ (2.23 mg, 0.01 mmol, 5.0 mol%) was added to a flame dried Schlenk tube under argon. After dissolving the salt in THF (2.0 mL) TBAF (300 µL, 1.50 eq., 1.0 M in THF) was added and the mixture was degassed three times. Subsequently the nitro compound (0.20 mmol, 1.0 eq.) and allyl boronic pinacol ester (0.40 mmol, 2.0 eq.) were added. The mixture was stirred at rt overnight. After filtration over a silica plug (Et_2O) and evaporation of the solvents the crude product was purified *via* column chromatography.

NOTE: When carried out at other temperatures than rt the degassed $CuBr_2$-TBAF-solution was brought to the desired temperature before the addition of $PhNO_2$. Then the reaction mixture was allowed to warm to rt overnight.

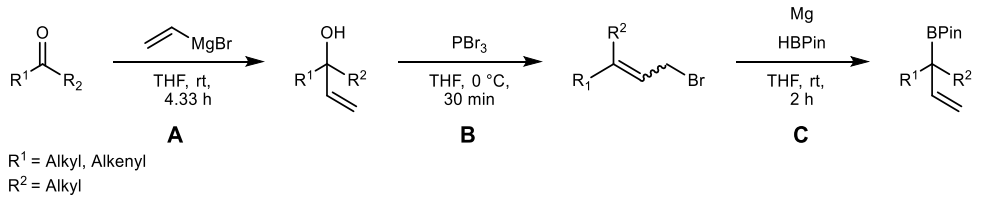
General procedure C2 for the coupling of nitro compounds with allyl boronates (reductive work-up)

$CuBr_2$ (2.23 mg, 0.01 mmol, 5.0 mol%) was added to a flame dried Schlenk tube under argon. After dissolving the salt in THF (2.0 mL) TBAF (300 µL, 1.50 eq., 1.0 M in THF) was added and the mixture was degassed three times. Subsequently the nitro compound (0.20 mmol, 1.0 eq.) and allyl boronic pinacol ester (0.40 mmol, 2.0 eq.) were added. The mixture was stirred at rt overnight after which Zn (262 mg, 20.0 eq.) and HCl (2.0 mL, 4.0 M in dioxane) were added (NOTE: the addition of acid needs to be done in a dropwise or portionwise manner). After TLC showed consumption of the hydroxyl amine (approx. 4 h) the mixture was neutralized with $NaHCO_3$ (sat. aq.) and extracted with DCM (3x). Column chromatography was used for purification of the crude products.

NOTE 1: When carried out at other temperatures than rt the degassed $CuBr_2$-TBAF-solution was brought to the desired temperature before the addition of $PhNO_2$.

NOTE 2: When coupling *aliphatic nitro compounds* 3.0 eq. of allyl boronate were used and the reductive work-up was done with aqueous HCl (2.0 mL, 4.0 M). To facilitate isolation the reaction mixture can be filtered through silica (pentane/EtOAc (9/1, 30 mL) then Et_2O (3.0 mL)) before reductive work-up to remove any TBA or boric acid salts. After evaporation of the solvents the crude mixture is dissolved in THF (2.0 mL), then Zn and HCl were added. Work-up and purification as stated above.

General procedure C3 for the synthesis of allyl pinacol boronates



Part A: The ketone (1.0 eq.) was dissolved in THF (3.0 mL per mmol) and the solution was cooled to 0°C. Then a solution of vinylmagnesium bromide (1.2 eq., 1.0 M in THF) was added dropwise under vigorous stirring. After 20 minutes the mixture was allowed to warm up to room temperature and was stirred for another 4 hours. The reaction mixture was cooled to 0°C and then quenched by the addition of saturated NH_4Cl solution (2.0 mL per mmol). The mixture was extracted with three portions of diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to yield the allyl alcohol. Occasionally, residues of the ketone were removed by flash chromatography.

Part B: The resulting tertiary allyl alcohol (1.0 eq.) was dissolved in THF (2.0 mL per mmol) and the solution was cooled to 0°C. Under stirring PBr_3 was added dropwise. After 30 minutes the reaction mixture was poured into ice water, followed up by extraction with three portions of diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product

was filtered through silica (pentane). The solvent was removed under reduced pressure. The product was subjected to the following step without further purification. (NOTE: the disubstituted allyl bromides are very sensitive towards silica and therefore should not be purified by flash chromatography. A complete consumption of the starting material needs to be ensured.)

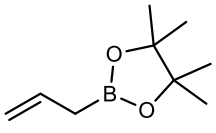
Part C: A Schlenk flask was charged with magnesium turnings (1.2 eq.), THF (2.0 mL per mmol pinacolborane) and pinacolborane (1.0 eq.). Then, the allyl bromide (1.0 eq.) was added dropwise over a period of 5 minutes under stirring at room temperature. After 30 minutes a second portion of the allyl bromide (1.0 eq) was added over a period of 5 minutes. The mixture was stirred for another 2 hours or until the magnesium turnings were completely consumed. Then the mixture was cooled to 0 °C, diluted with pentane and quenched with HCl (0.5 mL per mmol, 1.0 M solution in H_2O) (NOTE: careful addition of HCl is mandatory). After 10 minutes the mixture was extracted with pentane (3x), the organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo* (not below 200 mbar at 40 °C). The product was purified by flash column chromatography (NOTE: short columns are preferred since the products can be unstable on silica).

General procedure C4 for the synthesis of reference compounds

Aniline (0.625 mmol, 1.25 eq.), bromide (0.50 mmol, 1.0 eq.), K_2CO_3 (1.3 mmol, 135 mg, 2.0 eq.) and MeCN (2.0 mL) were added to a microwave vial. After the reaction was conducted in a microwave reactor (10 min, 100 °C, 100 W) the mixture was filtered through silica (Et_2O or EtOAc). The desired product was isolated using column chromatography.

Synthesis of Boronic Pinacol Esters

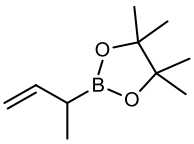
2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (398a)



According to the general procedure **C3** compound **398a** was isolated as a colorless liquid (1445 mg, 8,60 mmol, 86%). Purification by vacuum distillation (20 mbar, ~ 90 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91–5.82 (m, 1H), 5.02–4.9 (m, 2H), 1.73 (d, *J* = 8.0 Hz, 2H), 1.25 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 134.2; 115.0; 83.4; 24.9; 18.1; IR (KBr): 2979; 2935; 1637; 1457; 1346; 1323; 1273; 1214; 1142; 969; 900; 876; 674 cm^{-1}; m/z (EI) (%): 57 (100), 67 (21), 85 (94), 101 (10), 109 (16), 125 (24), 140 (10), 153 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{18}BO_2$, 169.1394; found, 169.1392.

The spectral data are in accordance with the literature.[146]

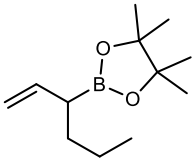
2-(but-3-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (398b)



According to general procedure **C3** compound **398b** was isolated as a colorless liquid (1365 mg, 7,50 mmol, 75%). Purification by column chromatography (Pentane:Et_2O = 98:2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.97–5.91 (m, 1H), 4.98–4.84 (m, 2H), 1.90 (d, *J* = 7.4 Hz, 1H), 1.23 (s, 12H), 1.09 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 140.9, 111.9, 83.1, 24.6, 14.1; IR (KBr): 2977, 1633, 1460, 1348, 1320, 1271, 1208, 1142, 966, 898, 852, 726 cm^{-1}, m/z (EI) (%): 270.0 (26), 256.0 (12), 255.0 (100), 254.0 (50), 197.0 (14), 128.9 (25), 84 (10), 83.0 (15), 59.0 (25), 58.0 (13), 57.0 (20), 55.0 (45); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{20}BO_2$; 183.15509; found, 183.18468.

The spectral data are in accordance with the literature.[147]

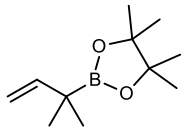
2-(hex-1-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (398c)



According to general procedure **C3** compound **398c** was isolated as a colorless liquid (777 mg, 3.7 mmol, 37%). Purification by column chromatography (Pentane:Et_2O = 99:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.85–5.57 (m, 1H), 5.23–4.87 (m, 2H), 1.83 (q, *J* = 7.9 Hz, 1H), 1.64–1.49 (m, 2H), 1.49–1.25 (m, 2H), 1.23 (s, 12H), 0.88 (t, *J* = 7.3 Hz, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 139.7, 113.3, 83.1, 32.4, 24.6 (d, *J* = 13.3 Hz), 22.0, 14.1; IR (KBr): 2959, 2928, 2869, 1736, 1459, 1366, 1321, 1258, 1143, 1099, 1017, 969, 899, 857, 803 cm^{-1}; m/z (EI)

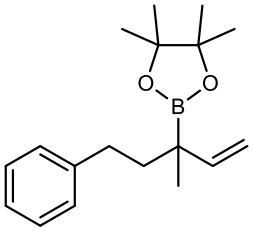
(%): 281.2 (12), 209.0 (35), 207.0 (34), 199.2 (19), 198.1(22), 197.1 (43), 181.1 (19), 179.1 (13), 163.0 (16), 161.0 (14), 138.1 (41), 137.1 (45), 109.1 (11),97.2 (17), 95.1 (13), 83.1 (42), 82.1 (13), 81.1 (28), 69.1 (18), 67.2 (17), 57.1 (19), 55.2 (100), 54.2 (15), 53.1 (13); HRMS (m/z): [M] calcd. for $C_{12}H_{23}O_2B$, 210.17856; found, 210.17868. The spectral data are in accordance with the literature.[148]

4,4,5,5-tetramethyl-2-(2-methylbut-3-en-2-yl)-1,3,2-dioxaborolane (398d)



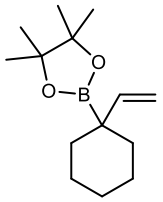
According to general procedure **C3** compound **398d** was isolated as a colorless liquid (1484 mg, 7,57 mmol, 78%). Purification by column chromatography (Pentane:Et_2O = 50:1). ^1H NMR (600 MHz, $CDCl_3$): δ 6.00–5.90 (m, 1H), 4.94–4.92 (m, 1H), 4.90–4.87 (m, 1H), 1.22 (s, 12H), 1.06 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.6 140.18; 120.7, 110.0, 83.3, 24.5, 23.4; IR (KBr): 297, 1629, 1467, 1315, 1213, 1133, 966, 900, 846, 709, 668 cm^{-1}, m/z (EI) (%): 69 (100), 83 (66), 95 (43), 123 (47), 135 (67), 137 (58), 163 (48), 185 (64), 203 (41), 205 (36); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{11}H_{21}O_2BNa$, 219.15268; found, 219.15224. The spectral data are in accordance with the literature.[147]

4,4,5,5-tetramethyl-2-(3-methyl-5-phenylpent-1-en-3-yl)-1,3,2-dioxaborolane (398e)



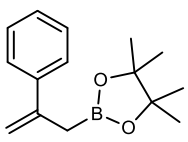
According to general procedure **C3** borane **398e** was synthesized as a colorless liquid (913 mg, 3.19 mmol, 56%). Purification by column chromatography (Pentane:Et_2O = 100:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.26 (t, *J* = 7.6 Hz, 2H), 7.20–7.13 (m, 3H), 5.96 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.04–4.95 (m, 2H), 2.61–2.51 (m, 2H), 1.84–1.77 (m, 1H), 1.71–1.65 (m, 1H), 1.24 (s, 12H), 1.14 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.0, 143.4, 128.4, 128.2, 125.5, 111.5, 83.3, 40.5, 32.1, 24.7, 24.6, 19.5; IR (KBr): 3875, 3402, 3074, 2975, 2931, 2865, 2662, 2331, 2106, 1994, 1924, 1740, 1623, 1455, 1315, 1266, 1203, 1143, 1106, 1004, 965, 902, 851, 745, 698 cm^{-1}; m/z (EI) (%): 287.3 (18), 286.3 (37), 285.3 (11), 201.2 (10), 195.2 (67), 194.2 (19), 159.1 (17), 105.0 (14), 101.1 (11), 95.0 (12), 91.0 (100), 84.0 (11), 83.0 (34), 65.0 (12), 55.1 (17); HRMS (m/z): $[M]^+$ calcd. for $C_{18}H_{27}BO_2$, 286.20986; found, 286.20924.

4,4,5,5-tetramethyl-2-(1-vinylcyclohexyl)-1,3,2-dioxaborolane (398f)



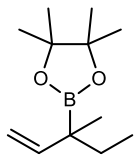
According to general procedure **C3** compound **398f** was isolated as a colorless liquid (337 mg, 1.42 mmol, 55%). Purification by column chromatography (Pentane:Et_2O = 100:1). ^1H NMR (600 MHz, $CDCl_3$): δ 5.81–5.74 (m, 1H), 4.94–4.90 (m, 2H), 1.98–1.93 (m, 2H), 1.69–1.64 (m, 2H), 1.34–1.26 (m, 2H), 1.24–1.21 (m, 16H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.6, 111.1, 83.0, 33.7, 26.4, 25.0, 24.6; IR (KBr): 2978, 2924, 2852, 1625, 1451, 1364, 1311, 1229, 1139, 1007, 968, 900, 855, 805, 695 cm^{-1}; m/z (EI) (%): 346.3 (14), 345.3 (29), 344.2 (86), 343.2 (23), 324.3 (17), 261.2 (40), 260.1 (15), 248.2 (26), 236.2 (28), 235.2 (100), 234.1 (34), 217.3 (26), 216.2 (22), 203.2 (21), 179.2 (13), 135.2 (39), 134.1 (12), 122.2 (21), 109.2 (22), 108.1 (12), 107.2 (20), 101.2 (14), 85.2 (22), 84.2 (10), 83.2 (13), 79.2 (13), 67.2 (19), 55.2 (17); HRMS (m/z): [M] calcd. for $C_{14}H_{25}O_2B$, 236.19421; found, 236.19454. The spectral data are in accordance with the literature.[147]

4,4,5,5-tetramethyl-2-(2-phenylallyl)-1,3,2-dioxaborolane (398g)



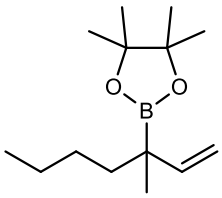
According to general procedure **C3** compound **398g** was isolated as a colorless liquid (330 mg, 1.35 mmol, 27%). Purification by column chromatography (Pentane:EtOAc = 99:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.65 Hz, 2H), 7.31–7.19 (m, 3H), 5.35 (s, 1 H), 5.09 (s, 1H), 2.15 (s, 2 H), 1.15 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.2; 141.7; 127.9; 127.1; 125.7; 112.1; 83.3; 24.5; IR (KBr): 2978, 1327, 1141, 878, 846, 776, 697 cm^{-1}; m/z (EI) (%): 91 (65), 105 (36), 115 (38), 129 (33), 231 (74), 232 (100), 233 (48); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{22}BO_2$, 245.17128; found, 247.17175. The spectral data are in accordance with the literature.[147]

4,4,5,5-tetramethyl-2-(3-methylpent-1-en-3-yl)-1,3,2-dioxaborolane (398h)



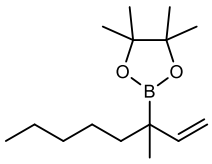
According to general procedure **C3** borane **398h** was synthesized as a colorless liquid (598 mg, 2.26 mmol, 45%). Purification by column chromatography (Pentane:Et_2O = 200:1). ^1H NMR (600 MHz, $CDCl_3$): δ 5.89 (dd, *J* = 17.5, 10.7 Hz, 1H), 4.98–4.91 (m, 2H), 1.56 (dq, *J* = 13.2, 7.4 Hz, 1H), 1.38 (dq, *J* = 13.3, 7.4 Hz, 1H), 1.22 (d, *J* = 1.7 Hz, 12H), 1.03 (s, 3H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 111.0, 83.1, 30.8, 24.6, 24.6, 19.1, 9.9; IR (KBr): 2971, 2929, 2877, 2097, 1628, 1459, 1372, 1347, 1312, 1263, 1213, 1141, 1004, 965, 898, 851 cm^{-1}; m/z (EI) (%): 663.4 (30), 662.4 (68), 648.4 (26), 647.4 (56), 441.2 (17), 317.1 (17), 316.2 (57), 284.2 (15), 256.2 (16), 239.2 (11), 220.2 (10), 219.2 (14), 211.2 (11), 197.2 (12), 193.1 (10), 191.1 (16), 183.2 (11), 179.1 (10), 169.2 (13), 167.2 (1), 165.1 (18), 163.1 (18), 155.1 (17), 153.1 (18), 151.1 (12), 149.0 (22), 141.1 (15), 139.1 (14), 138.1 (13), 137.1 (17), 135.1 (15), 129.1 (13), 127.1 (23), 125.1 (17), 123.1 (17), 121.1 (11), 113.1 (18), 111.1 (25), 110.1 (10), 107.1 (11), 99.1 (20), 97.1 (28), 95.1 (21), 91.1 (10), 85.1 (41), 84.1 (18), 83.1 (47), 82.1 (12), 81.1 (16), 73.2 (11), 71.1 (45), 70.1 (12), 69.1 (34), 67.1 (15), 59.1 (17), 57.2 (100), 56.1 (13), 55.1 (60); HRMS (m/z): $[M]^+$ calcd. for $C_{12}H_{23}O_2B$, 210.17856; found, 210.17869. The spectral data are in accordance with the literature.[147]

4,4,5,5-tetramethyl-2-(3-methylhept-1-en-3-yl)-1,3,2-dioxaborolane (398i)



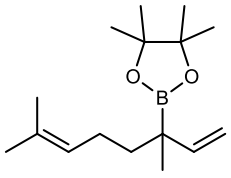
According to general procedure **C3** borane **398i** was synthesized as a colorless liquid (480 mg, 2.01 mmol, 50%). Purification by column chromatography (Pentane:Et_2O = 150:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.89 (dd, *J* = 17.4, 10.8 Hz, 1H), 4.99–4.80 (m, 2H), 1.48 (dd, *J* = 17.0, 12.0 Hz, 1H), 1.37–1.22 (m, 5H), 1.20 (s, 12H), 1.02 (s, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3): δ 145.7, 110.7, 83.1, 38.0, 27.9, 24.6, 24.5, 23.4, 19.5, 14.1; IR (KBr): 3274, 3083, 2963, 2930, 2866, 2174, 2026, 1988, 1810, 1627, 1462, 1373, 1347, 1311, 1216, 1140, 1083, 1003, 966, 900, 852, 803, 716, 670 cm^{-1}; m/z (EI) (%): 505.1 (14), 504.1 (19), 503.0 (38), 431.1 (26), 430.0 (37), 429.0 (88), 415.1 (11), 401.0 (10), 369.2 (18), 357.1 (21), 356.1 (32), 355.0 (100), 341.1 (20), 295.2 (24), 282.1 (13), 281.1 (44), 222.2 (12), 221.2 (53), 207.1 (18), 147.1 (27); HRMS-ESI (m/z): $[M+K]^+$ calcd. for $C_{14}H_{27}BKO_2^+$, 261.19963; found, 261.19971.

4,4,5,5-tetramethyl-2-(3-methyloct-1-en-3-yl)-1,3,2-dioxaborolane (398j)



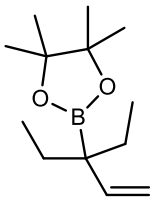
According to general procedure **C3** borane **398j** was synthesized as a colorless liquid (823 mg, 3.26 mmol, 52%). Purification by column chromatography (Pentane:Et_2O = 100:1). ^1H NMR (600 MHz, $CDCl_3$): δ 5.84 (dd, *J* = 17.4, 10.7 Hz, 1H), 4.89–4.81 (m, 2H), 1.45–1.39 (m, 1H), 1.29–1.16 (m, 7H), 1.15 (d, *J* = 2.6 Hz, 12H), 0.97 (s, 3H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.8, 110.8, 83.1, 38.3, 32.6, 25.3, 24.7, 24.6, 22.6, 19.6, 14.1; IR (KBr): 2961, 2928, 2861, 2325, 2086, 2012, 1807, 1628, 1462, 1372, 1347, 1311, 1269, 1210, 1140, 1002, 966, 899, 853, 718, 670 cm^{-1}; m/z (EI) (%): 253.2 (48), 252.2 (83), 251.2 (26), 237.1 (20), 196.1 (16), 195.1 (65), 194.1 (19), 167.1 (15), 166.1 (23), 153.0 (15), 152.1 (14), 151.1 (24), 139.0 (43), 138.0 (14), 125.0 (21), 124.1 (48), 123.0 (16), 110.0 (11), 109.0 (19), 101.0 (23), 97.0 (11), 96.0 (19), 95.0 (26), 85.0 (27), 84.0 (100), 83.0 (43), 81.0 (15), 69.1 (27), 67.0 (19), 59.0 (15), 57.1 (19), 56.1 (11), 55.0 (59), 53.0 (15); HRMS (m/z): $[M]^+$ calcd. for $C_{15}H_{29}O_2B$, 252.22551; found, 252.22463.

2-(3,7-dimethylocta-1,6-dien-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (398k)



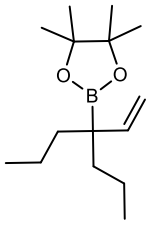
According to general procedure **C3** borane **398k** was synthesized as a colorless liquid (598 mg, 2.26 mmol, 45%). Purification by column chromatography (Pentane:Et_2O = 200:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.84 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.09–5.00 (m, 1H), 4.91–4.82 (m, 2H), 1.86 (d, *J* = 6.8 Hz, 2H), 1.60 (s, 3H), 1.52 (s, 3H), 1.50–1.38 (m, 1H), 1.29 (dd, *J* = 23.7, 6.6 Hz, 1H), 1.15 (s, 12H), 1.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.4, 131.0, 125.1, 111.0, 83.2, 38.3, 25.7, 24.7, 24.6, 24.4, 19.5, 17.6; IR (KBr): 3873, 3384, 3082, 2972, 2923, 2662, 2329, 2096, 1994, 1895, 1627, 1457, 1313, 1213, 1143, 1011, 965, 901, 849, 804, 709, 672 cm-1; m/z (EI) (%): 265.3 (10), 264.3 (19), 221.2 (55), 220.1 (16), 195.1 (26), 137.1 (22), 136.1 (42), 135.0 (12), 123.1 (17), 121.0 (18), 109.0 (25), 101.0 (31), 95.0 (35), 93.0 (11), 85.1 (23), 84.1 (33), 83.0 (100), 82.0 (13), 81.0 (17), 69.1 (48), 67.0 (21), 57.1 (17), 55.0 (42), 53.0 (14), 43.1 (28), 41.1 (66), 39.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{30}BO_2$, 265.23334; found, 265.23409. The spectral data are in accordance with the literature.[147]

2-(3-ethylpent-1-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (398l)



According to general procedure **C3** borane **398l** was synthesized as a colorless liquid (504 mg, 2.25 mmol, 45%). Purification by column chromatography (Pentane:Et_2O = 150:1). ^1H NMR (600 MHz, $CDCl_3$): δ 5.73 (dd, *J* = 17.7, 10.9 Hz, 1H), 5.12–4.80 (m, 2H), 1.52 (q, *J* = 7.4 Hz, 4H), 1.23 (s, 12H), 0.82 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 143.8, 112.8, 83.0, 26.5, 24.7, 9.4; IR (KBr): 3404, 3083, 2968, 2931, 2876, 2182, 2029, 1822, 1628, 1459, 1375, 1309, 1261, 1213, 1140, 1029, 1005, 968, 903, 855, 802, 691, 669 cm^{-1}; m/z (EI) (%): 505.1 (16), 504.1 (21), 503.0 (42), 431.1 (29), 430.0 (40), 429.0 (97), 415.0 (11), 401.0 (11), 369.2 (14), 357.1 (22), 356.0 (33), 355.0 (100), 341.1 (18), 295.2 (21), 282.1 (13), 281.1 (42), 222.2 (10), 221.2 (43), 207.1 (15), 147.1 (27), 73.2 (19); HRMS-ESI (m/z): $[M+Na]^+$ calcd. for $C_{13}H_{25}BNaO_2$, 247.18398; found, 247.18403.

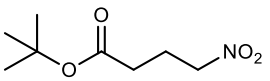
4,4,5,5-tetramethyl-2-(4-vinylheptan-4-yl)-1,3,2-dioxaborolane (398m)



According to general procedure **C3** borane **398m** was synthesized as a colorless liquid (812 mg, 3.21 mmol, 48%). Purification by column chromatography (Pentane:Et_2O = 150:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.02–4.92 (m, 2H), 1.48–1.39 (m, 4H), 1.21 (s, 16H), 0.87 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.30, 112.2, 83.0, 37.0, 24.7, 18.4, 15.0; IR (KBr): 3413, 3081, 2957, 2930, 2871, 2323, 2091, 1989, 1877, 1627, 1461, 1373, 1343, 1309, 1272, 1239, 1139, 1001, 972, 900, 861, 790, 741, 670 cm^{-1}; m/z (EI) (%): 429.2 (30), 355.2 (38), 281.2 (13), 252.3 (42), 251.3 (10), 237.3 (12), 195.2 (25), 151.2 (12), 124.2 (26), 85.2 (17), 84.2 (100), 83.1 (52), 69.2 (20), 57.2 (37), 55.2 (64); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{15}H_{29}BNaO_2$, 275.21528; found, 275.21539.

Synthesis of Nitro Compounds

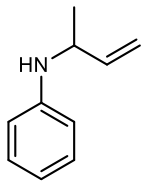
tert-butyl 4-nitrobutanoate (411)



Compound **411** was synthesized according to the literature.[121] ^1H NMR (600 MHz, $CDCl_3$): δ 4.46 (t, *J* = 6.7 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 2.26 (p, *J* = 6.9 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.1, 81.2, 74.5, 31.6, 28.0, 22.6; IR (KBr): 1724, 1551, 1152 cm^{-1}; m/z (EI) (%): 206.0 (26), 188.0 (44), 159.0 (16), 141.0 (12), 59.1 (11), 57.1 (100), 56.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_8H_{15}O_4NNa$, 212.08933; found, 212.08932. The spectral data are in accordance with the literature.[121]

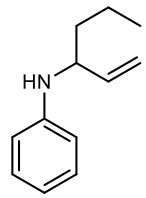
Isolated Compounds

_N_-(but-3-en-2-yl)aniline (412a)



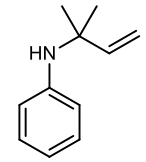
According to general procedure **C2** compound **412a** was synthesized at 0 °C as a colorless liquid (25.6 mg, 0.174 mmol, 87%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17 (dd, *J* = 8.6, 7.3 Hz, 2H), 6.70 (t, *J* = 7.5 Hz, 2H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.02–5.80 (m, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 5.09 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.03–3.96 (m, 1H), 1.32 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 147.0, 141.0, 129.1, 117.5, 114.3, 113.6, 51.3, 21.5; IR (KBr): 3404, 1600 cm^{-1}; m/z (EI) (%): 147.0 (64), 133.0 (18), 132.0 (100), 130.0 (16), 120.0 (25), 118.9 (12), 117.9 (19), 93.0 (12), 55.1 (16); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11224. The spectral data are in accordance with the literature.[149]

_N_-(hex-1-en-3-yl)aniline (412b)



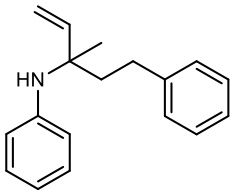
According to general procedure **C2** compound **412b** was synthesized as a colorless liquid (31.5 mg, 0.180 mmol, 90%) at 0 °C. Purification by column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.19–7.13 (m, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 2H), 5.74–5.71 (m, 1H), 5.24–5.09 (m, 2H), 3.81 (q, *J* = 6.6 Hz, 1H), 1.66–1.53 (m, 2H), 1.51–1.37 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.9, 139.7, 129.1, 117.6, 115.3, 113.7, 56.1, 37.7, 19.1, 13.9; IR (KBr): 3408, 1600, 1257 cm^{-1}; m/z (EI) (%): 176.1 (16), 175.1 (50), 133.0 (12), 132.0 (100), 130.0 (19), 117.0 (29), 77.0 (22), 51.1 (10); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{18}N$, 176.14338; found, 176.14347. The spectral data is in accordance with the literature.[150]

_N_-(2-methylbut-3-en-2-yl)aniline (412c)



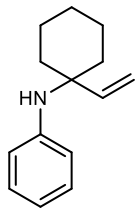
According to general procedure **C2** compound **412c** was synthesized at -40 °C as a colorless liquid (29.0 mg, 0.180 mmol, 90%). Purification by column chromatography (Pentane:Et_3N, 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18–7.11 (m, 2H), 6.89–6.75 (m, 3H), 6.04 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.17 (d, *J* = 17.5 Hz, 1H), 5.12 (d, *J* = 10.4 Hz, 1H), 1.41 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.7, 146.3, 128.8, 117.7, 115.9, 112.9, 54.8, 28.4; IR (KBr): 3343, 1600, 1259 cm^{-1}; m/z (EI) (%): 161.2 (85), 146.1 (81), 130.1 (10), 93.1 (100), 77.1 (10), 69.2 (16), 65.1 (10), 51.2 (10); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{16}N$, 162.12773; found, 162.12800. The spectral data are in accordance with the literature.[151]

_N_-(3-methyl-5-phenylpent-1-en-3-yl)aniline (412d)



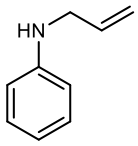
According to general procedure **C2** compound **412d** was synthesized at -40 °C as a colorless liquid (35.2 mg, 0.140 mmol, 70%). Purification by column chromatography (Pentane:Et_2O:NEt_3 = 40:1:1). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.20 (t, *J* = 7.4 Hz, 2H), 7.14–7.02 (m, 3H), 6.98 (t, *J* = 7.9 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 6.48 (t, *J* = 7.2 Hz, 1H), 5.95 (dd, *J* = 17.9, 10.4 Hz, 1H), 5.41 (s, 1H), 5.10 (d, *J* = 2.9 Hz, 2H), 2.57 (ddd, *J* = 27.5, 14.0, 4.9 Hz, 2H), 1.88 (dtd, *J* = 71.0, 13.1, 4.9 Hz, 2H), 1.32 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.8, 146.2, 142.8, 128.8, 128.7, 128.6, 126.0, 116.2, 115.1, 113.6, 56.9, 42.2, 29.9, 25.1; IR (KBr): 3338, 1599, 1257 cm^{-1}; m/z (EI) (%): 252.0 (11), 251.0 (47), 146.9 (12), 145.9 (100), 129.9 (11), 92.9 (12), 90.9 (41), 77.0 (12), 65.0 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{22}N$, 252.17468; found, 252.17405. The spectral data are in accordance with the literature.[152]

***N*-(1-vinylcyclohexyl)aniline (412e)**



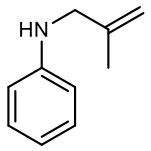
According to general procedure **C2** compound **412e** was synthesized at -40 °C as a colorless liquid (28.2 mg, 0.140 mmol, 70%). Purification by column chromatography (Pentane:Et_2O:NEt_3 = 50:1:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.14–7.04 (m, 2H), 6.67 (dd, *J* = 18.9, 7.6 Hz, 3H), 5.93 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.24–5.08 (m, 2H), 1.91 (d, *J* = 12.6 Hz, 2H), 1.53 (dtd, *J* = 27.4, 13.6, 12.2, 8.5 Hz, 7H), 1.35–1.24 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.0, 145.7, 128.6, 117.1, 115.8, 113.3, 56.2, 35.3, 25.6, 21.6; IR (KBr): 3421, 1599, 1254 cm^{-1}; m/z (EI) (%): 202.1 (29), 201.1 (100), 173.1 (14), 158.1 (25); HRMS (m/z): $[M+H]^+$ calcd. for, $C_{14}H_{20}N$; found, 202.15849. The spectral data are in accordance with the literature.[153]

***N*-allylaniline (414a)**



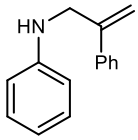
According to general procedure **C2** compound **414a** was synthesized as a colorless liquid (22.7 mg, 0.170 mmol, 85%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.23–7.18 (m, 2H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.77–6.73 (m, 2H), 6.00–5.94 (m, 1H), 5.32–5.17 (m, 2H), 4.16 (bs, 1H), 3.79 (dt, *J* = 5.7, 1.6 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.3, 134.3, 129.2, 119.0, 117.3, 114.3, 47.5; IR (KBr): 3350, 1600, 1260 cm^{-1}; m/z (EI) (%): 134.0 (25), 133.0 (100), 132.0 (57), 130.0 (11), 116.9 (15), 106.0 (64), 103.9 (17), 77.0 (23), 65.0 (13), 51.1 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{12}N$, 134.09643; found, 134.09638. The spectral data are in accordance with the literature.[154]

***N*-(2-methylallyl)aniline (414b)**



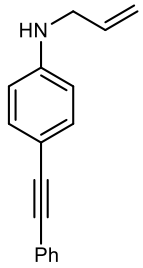
According to general procedure **C2** compound **414b** was synthesized as a colorless liquid (21.8 mg, 0.148 mmol, 74%). Purification by column chromatography (Pentane:EtOAc = 10:1 v/v). ^1H NMR (600 MHz, $CDCl_3$): δ 7.19–7.14 (m, 2H), 6.70 (td, *J* = 7.3, 1.1 Hz, 1H), 6.64–6.61 (m, 2H), 5.84 (ddd, *J* = 17.1, 10.3, 5.6 Hz, 1H), 5.22 (dt, *J* = 17.3, 1.4 Hz, 1H), 5.09 (dt, *J* = 10.4, 1.4 Hz, 1H), 4.03–3.96 (m, 1H), 3.85 (br, 1H), 1.32 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.1, 141.0, 129.1, 117.4, 114.2, 113.5, 51.2, 21.5; IR (KBr): 3405, 1600, 1253 cm^{-1}; m/z (EI) (%): 147.2 (28), 132.1 (47), 120.2 (12), 119.1 (13), 93.1 (10), 77.0 (48), 66.1 (18), 65.1 (46), 64.1 (14), 63.0 (23), 57.2 (13), 55.2 (100), 54.0 (13), 53.1 (23), 52.0 (20), 51.0 (70), 50.0 (23); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11221. The spectral data are in accordance with the literature.[154]

***N*-(2-phenylallyl)aniline (414c)**



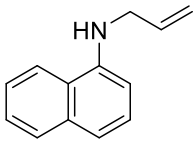
According to general procedure **C2** compound **414c** was synthesized as a colorless liquid (30.9 mg, 0.148 mmol, 74%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.49–7.46 (m, 2H), 7.39–7.35 (m, 2H), 7.34–7.31 (m, 1H), 7.22–7.18 (m, 2H), 6.76–6.72 (m, 1H), 6.68–6.64 (m, 2H), 5.50 (d, *J* = 1.1 Hz, 1H), 5.36 (q, *J* = 1.4 Hz, 1H), 4.18 (t, *J* = 1.2 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.7, 144.5, 139.1, 129.2, 128.5, 127.9, 126.1, 117.7, 113.8, 113.0, 48.1; IR (KBr): 3430, 1601 cm^{-1}; m/z (EI) (%): 210.0 (23), 209 (100), 106.0 (73), 102.9 (11), 77.0 (32), 51.1 (14); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{16}N$, 210.12773; found, 210.12785. The spectral data are in accordance with the literature.[155]

***N*-allyl-4-(phenylethynyl)aniline (414d)**



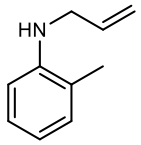
According to general procedure **C2** compound **414d** was synthesized as a colorless liquid (44.8 mg, 0.190 mmol, 95%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.50–7.48 (m, 2H), 7.37–7.35 (m, 2H), 7.33–7.30 (m, 2H), 7.30–7.26 (m, 1H), 6.60–6.56 (m, 2H), 5.98–5.91 (m, 1H), 5.32–5.17 (m, 2H), 4.00 (bs, 1H), 3.80 (dt, *J* = 5.4, 1.6 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.9, 134.7, 132.9, 131.3, 128.2, 127.5, 124.0, 116.6, 112.6, 111.4, 90.4, 87.2, 46.2; IR (KBr): 3413, 1601, 1262 cm^{-1}; m/z (EI) (%): 234.1 (22), 233.1 (100), 232.1 (10), 206.0 (19), 192.0 (34), 164.9 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{16}N$, 234.12773; found, 234.12778.

***N*-allylnaphthalen-1-amine (414e)**



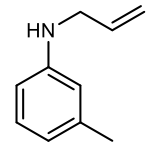
According to general procedure **C2** compound **414e** was synthesized as a colorless liquid (27 mg, 0.15 mmol, 75%). Purification by column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88–7.78 (m, 2H), 7.50–7.42 (m, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.31–7.25 (m, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.13–6.07 (m, 1H), 5.43–5.22 (m, 2H), 4.54 (bs, 1H), 3.97 (dt, *J* = 5.6, 1.7 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 134.9, 134.3, 128.7, 126.5, 125.7, 124.8, 123.5, 119.9, 117.9, 116.9, 46.9; IR (KBr): 3437, 1580, 1279 cm^{-1}; m/z (EI) (%): 184.1 (19), 183.1 (100), 182.0 (20), 168.0 (20), 167.0 (10), 154.0 (11), 142.0 (16), 115.0 (32); HRMS-ESI (m/z): $[M+H]^+$ calcd. for $C_{13}H_{14}N$, 184.11208; found, 184.11186. The spectral data are in accordance with the literature.[156]

***N*-allyl-2-methylaniline (414f)**



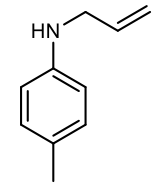
According to general procedure **C2** compound **414f** was synthesized as a colorless liquid (18.2 mg, 0.124 mmol, 62%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.12 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 1H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 8.1 Hz, 1H), 6.04–5.97 (m, 1H), 5.33–5.17 (m, 2H), 3.83 (dt, *J* = 5.4, 1.6 Hz, 2H), 3.69 (bs, 1H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.9, 135.5, 130.0, 127.1, 121.9, 117.1, 116.2, 110.0, 46.5, 17.5; IR (KBr): 3431, 1603 cm^{-1}; m/z (EI) (%): 397.3 (100), 292.3 (18), 291.2 (61), 287.2 (60), 163.2 (15), 261.2 (12), 172.2 (11), 171.1 (23), 170.1 (26), 168.1 (10), 160.2 (23), 158.1 (16), 157.1 (16), 156.1 (11), 146.1 (11), 145.1 (16), 144.1 (89), 143.0 (18), 142.1 (10), 134.1 (98), 132.1 (10), 130.1 (15), 120.1 (29), 119.1 (14), 118.1 (58), 117.0 (11), 107.1 (53), 106.1 (51), 91.1 (43), 77.1 (12), 65.1 (13), 57.2 (16), 55.2 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11187. The spectral data are in accordance with the literature.[157]

***N*-allyl-3-methylaniline (414g)**



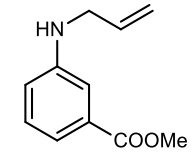
According to general procedure **C2** compound **414g** was synthesized as a colorless liquid (18.2 mg, 0.124 mmol, 62%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 6.47 (d, *J* = 8.2 Hz, 2H), 6.00–5.93 (m, 1H), 5.31–5.15 (m, 2H), 4.12 (bs, 1H), 3.77 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.7, 139.0, 135.3, 129.1, 118.8, 116.3, 114.0, 110.4, 46.8, 21.6; IR (KBr): 3408, 1602 cm^{-1}; m/z (EI) (%): 148.0 (14), 147.0 (100), 146.0 (41), 132.0 (29), 131.0 (18), 130.0 (16), 91.0 (24), 77.0 (14), 65.1 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11185. The spectral data are in accordance with the literature.[158]

***N*-allyl-4-methylaniline (414h)**



According to general procedure **C2** compound **414h** was synthesized as a colorless liquid (17.1 mg, 0.116 mmol, 58%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.01–6.98 (m, 2H), 6.60–6.56 (m, 2H), 6.00–5.93 (m, 1H), 5.32–5.13 (m, 2H), 4.07 (bs, 1H), 3.76 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 135.4, 129.7, 127.1, 116.3, 113.4, 47.1, 20.4; IR (KBr): 3408, 1616 cm^{-1}; m/z (EI) (%): 321.3 (22), 320.2 (100), 292.3 (22), 279.2 (22), 186.2 (45), 174.1 (28), 146.1 (18), 144.2 (17); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11186. The spectral data are in accordance with the literature.[154]

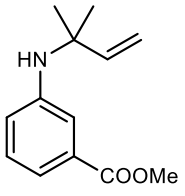
Methyl 3-(allylamino)benzoate (414i)



According to general procedure **C2** compound **414i** was synthesized as a colorless liquid (30.6 mg, 0.160 mmol, 80%). Purification by column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.29 (dd, *J* = 2.6, 1.6 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.80 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 5.98–5.91 (m, 1H), 5.32–5.17 (m, 2H), 3.88 (s, 3H), 3.81 (dt, *J* = 5.5, 1.7 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.5, 147.9, 134.8, 130.9, 129.1, 118.7, 117.5, 116.6, 113.6, 52.0, 46.4; IR (KBr): 3398, 1603,

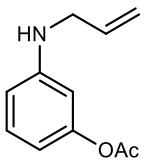
1282, 1237 cm^{-1}; m/z (EI) (%): 192.1 (39), 191.0 (100), 190.0 (19), 164.0 (39), 160.0 (14), 158.0 (11), 132.0 (17), 130.0 (18); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{14}O_2N$, 192.10191; found, 192.10124.

methyl 3-((2-methylbut-3-en-2-yl)amino)benzoate (414j)



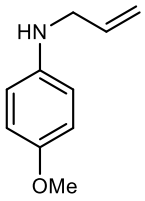
According to general procedure **C2** compound **414j** was synthesized at -40 °C as a colorless liquid (37.0 mg, 0.170 mmol, 88%). Purification by HPLC (Pentane:EtOAc = 11:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.42–7.36 (m, 2H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.97-6.90 (m, 1H), 6.00 (dd, *J* = 17.6, 10.7, 1H), 5.20 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.15 (dd, *J* = 10.6, 1.0 Hz, 1H), 3.87 (s, 3H), 1.41 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.3, 144.9, 130.6, 128.6, 119.0, 117.1, 113.5, 52.0, 27.9; IR (KBr): 3394, 1600, 1237 cm^{-1}; m/z (EI) (%): 220.0 (12), 219.0 (72), 205.0 (13), 204.0 (87), 192.0 (14), 188.0 (18), 151.9 (10), 150.9 (100), 143.9 (21), 119.9 (31), 91.9 (12), 90.9 (10), 69.0 (39); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{18}NO_2$, 220.13321; found, 220.13303.

***N*-allyl-3-methoxyaniline (414k)**



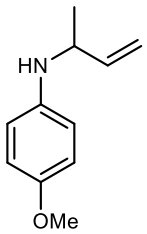
According to general procedure **C2** compound **414k** was synthesized as a colorless liquid (26.8 mg, 0.140 mmol, 70%). Purification by column chromatography (Pentane:EtOAc = 3:1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.15 (t, *J* = 8.1 Hz, 1H), 6.47 (dddd, *J* = 40.1, 8.0, 2.2, 0.9 Hz, 2H), 6.36 (t, *J* = 2.2 Hz, 1H), 5.97–5.90 (m, 1H), 5.31–5.15 (m, 2H), 3.75 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.5, 151.8, 148.8, 134.6, 129.9, 116.8, 110.9, 110.7, 106.2, 46.7, 21.2; IR (KBr): 3408, 1611, 1258, 1211 cm^{-1}; m/z (EI) (%): 192.0 (18), 191.0 (100), 150.0 (13), 149.0 (94), 148.0 (62), 134.0 (22), 122.0 (52), 120.0 (20); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{14}O_2N$, 192.10191; found, 192.10193.

***N*-allyl-4-methoxyaniline (414l)**



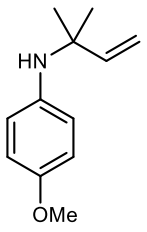
According to general procedure **C2** compound **414l** was synthesized as a colorless liquid (7.80 mg, 0.048 mmol, 24%). Purification by column chromatography (Pentane:EtOAc = 5:1). ^1H NMR (600 MHz, $CDCl_3$): δ 6.80–6.78 (m, 2H), 6.68–6.65 (m, 2H), 6.00–5.93 (m, 1H), 5.31–5.14 (m, 2H), 3.75 (s, 3H), 3.74–3.73 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.5, 141.6, 135.4, 116.5, 114.8, 114.7, 55.8, 47.9; IR (KBr): 1510, 1235 cm^{-1}; m/z (EI) (%): 164.1 (12), 163.0 (100), 149.0 (14), 148.0 (40), 136.1 (16), 122.0 (44); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}ON$, 164.10699; found, 164.10707. The spectral data are in accordance with the literature.[154]

***N*-(but-3-en-2-yl)-4-methoxyaniline (414m)**



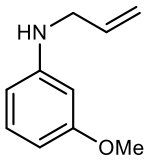
According to general procedure **C2** compound **414m** was synthesized at 50 °C as a colorless liquid (32.2 mg, 0.182 mmol, 91%) with crotyl pinacol boronate. Purification by column chromatography (Pentane:EtOAc = 5:1). ^1H NMR (600 MHz, $CDCl_3$): δ 6.77 (d, *J* = 8.9 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 5.89–5.72 (m, 1H), 5.18 (d, *J* = 1.4 Hz, 1H), 5.08 (dd, *J* = 10.3, 1.3 Hz, 1H), 3.91 (p, *J* = 6.5 Hz, 1H), 3.74 (s, 3H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 152.4, 141.3, 115.4, 114.8, 114.4, 55.8, 52.5, 21.5; IR (KBr): 3391, 1234 cm^{-1}; m/z (EI) (%): 178.1 (14), 177.0 (100), 162.0 (72), 150.0 (14), 130.0 (10), 122.0 (36), 108.0 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{16}NO$, 178.12264; found, 178.12234. The spectral data are in accordance with the literature.[159]

4-methoxy-*N*-(2-methylbut-3-en-2-yl)aniline (414n)



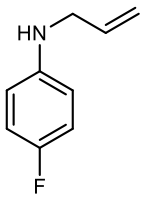
According to general procedure **C2** compound **414n** was synthesized at -40 °C as a colorless liquid (25.6 mg, 0.134 mmol, 67%). Purification by column chromatography (Pentane:EtOAc:Et_3N = 5:1:0.1). ^1H NMR (600 MHz, $CDCl_3$): δ 6.65 (s, 4H), 5.94 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.09–4.98 (m, 2H), 3.66 (s, 3H), 1.26 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.0, 145.5, 139.0, 118.2, 113.1, 111.4, 54.5, 54.2, 27.0; IR (KBr): 1237 cm^{-1}; m/z (EI) (%): 192.1 (15), 191.1 (100), 176.0 (45), 123.0 (73), 122.0 (26), 108.0 (66); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{18}ON$, 192.13829; found, 192.13895. The spectral data are in accordance with the literature.[115]

***N*-allyl-3-methoxyaniline (414o)**



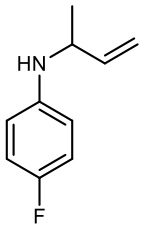
According to general procedure **C2** compound **414o** was synthesized as a colorless liquid (24.1 mg, 0.148 mmol, 74%). Purification by column chromatography (Pentane:EtOAc = 5:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.28 (dddd, *J* = 16.1, 8.1, 2.2, 0.9 Hz, 2H), 6.21 (t, *J* = 2.3 Hz, 1H), 5.99–5.92 (m, 1H), 5.31–5.15 (m, 2H), 3.77 (s, 3H), 3.77–3.76 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.8, 149.1, 135.1, 129.9, 116.5, 106.4, 102.9, 99.2, 55.1, 46.7; IR (KBr): 3407, 1604, 1206 cm^{-1}; m/z (EI) (%): 164.1 (14), 163.0 (100), 162.0 (34), 148.0 (23), 136.0 (41), 134.0 (10); HRMS-ESI (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}ON$, 164.10699; found, 164.10666. The spectral data are in accordance with the literature.[160]

***N*-allyl-4-fluoroaniline (414p)**



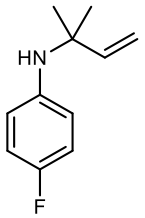
According to general procedure **C2** compound **414p** was synthesized as a colorless liquid (28.1 mg, 0.186 mmol, 93%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.91–6.88 (m, 2H), 6.67–6.60 (m, 2H), 5.98–5.92 (m, 1H), 5.31–5.16 (m, 2H), 3.74 (d, *J* = 5.2 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.1, 155.5, 143.4, 134.7, 116.9, 115.8, 115.6, 114.6, 114.6, 47.7; IR (KBr): 1509, 1216 cm^{-1}; m/z (EI) (%): 152.0 (22), 151.0 (100), 150.0 (39), 134.9 (11), 124.0 (63), 122.0 (19), 109.9 (12), 94.9 (14), 83.0 (16), 75.0 (10); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{11}NF$, 152.08700; found, 152.08693. The spectral data are in accordance with the literature.[161]

***N*-(but-3-en-2-yl)-4-fluoroaniline (414q)**



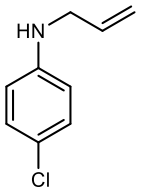
According to general procedure **C2** compound **414q** was synthesized at 0 °C as a colorless liquid (31.4 mg, 0.191 mmol, 95%). Purification by column chromatography (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.86 (t, *J* = 8.7 Hz, 2H), 6.61–6.42 (m, 2H), 5.94–5.71 (m, 1H), 5.20 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dd, *J* = 10.4, 1.4 Hz, 1H), 3.90 (q, *J* = 6.0 Hz, 1H), 3.55 (br s, 1H), 1.30 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.5, 154.9, 143.6, 141.1, 115.5, 114.3, 51.8, 21.6; IR (KBr): 3411, 1611 cm^{-1}; m/z (EI) (%): 235.2 (11), 227.1 (23), 220.3 (23), 205.2 (27), 165.1 (72), 150.2 (100), 148.1 (18), 138.1 (29), 137.1 (61), 135.1 (14), 124.1 (13), 122.1 (11), 111.2 (11), 55.2 (22); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{13}N$, 166.10265; found, 166.10224. The spectral data are in accordance with the literature.[162]

4-fluoro-*N*-(2-methylbut-3-en-2-yl)aniline (414r)



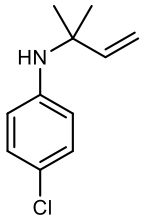
According to general procedure **C2** compound **414r** was synthesized at -40 °C as a colorless liquid (27.0 mg, 0.150 mmol, 76%). Purification by column chromatography (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.86–6.81 (m, 2H), 6.76–6.70 (m, 2H), 6.00 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.15 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.11 (dd, *J* = 10.7, 1.1 Hz, 1H), 1.36 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.8, 129.1, 118.7, 115.6, 115.5, 113.6, 56.1, 28.1; IR (KBr): 3413, 1216 cm^{-1}; m/z (EI) (%): 180.1 (10), 179.1 (84), 164.1 (60), 152.1 (11), 148.1 (12), 111.1 (100), 69.2 (16); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}FN$, 180.11830; found, 180.11845. The spectral data are in accordance with the literature.[162]

***N*-allyl-4-chloroaniline (414s)**



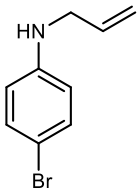
According to general procedure **C2** compound **414s** was synthesized as a colorless liquid (28.4 mg, 0.170 mmol, 85%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.16–7.09 (m, 2H), 6.63–6.52 (m, 2H), 5.96–5.90 (m, 1H), 5.31–5.13 (m, 2H), 3.89 (bs, 1H), 3.75 (dt, *J* = 5.4, 1.6 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.2, 134.7, 129.0, 122.3, 116.6, 114.2, 46.7; IR (KBr): 3419, 1598, 1258, 812 cm^{-1}; m/z (EI) (%): 169.1 (31), 168.1 (20), 167.0 (100), 166.0 (34), 142.1 (18), 140.1 (62), 138.1 (17), 132.1 (17), 131.1 (12), 130.1 (20); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{11}NCl$, 168.05745; found, 168.05704. The spectral data are in accordance with the literature.[163]

4-chloro-*N*-(2-methylbut-3-en-2-yl)aniline (414t)



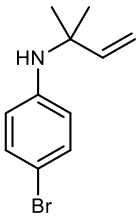
According to general procedure **C2** compound **414t** was synthesized at -40 °C as a colorless liquid (37.0 mg, 0.190 mmol, 95%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.07–7.03 (m, 2H), 6.65–6.61 (m, 2H), 5.97 (dd, *J* = 17.5, 10.6 Hz, 1H), 5.17 (dd, *J* = 17.5, 1.1 Hz, 1H), 5.12 (dd, *J* = 10.7, 1.1 Hz, 1H), 1.38 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 129.2, 128.6, 116.9, 113.2, 54.9, 28.0; IR (KBr): 3415, 1255, 816 cm^{-1}; m/z (EI) (%): 197.0 (33), 196.0 (14), 195.0 (90), 181.9 (12), 179.9 (35), 144.0 (24), 129.9 (12), 128.9 (35), 127.9 (11), 126.9 (100), 69.1 (33); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}ClN$, 196.08875; found, 196.08893. The spectral data are in accordance with the literature.[152]

***N*-allyl-4-bromoaniline (414u)**



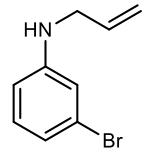
According to general procedure **C2** compound **414u** was synthesized at -40 °C as a colorless liquid (37.6 mg, 0.178 mmol, 89%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.27–7.23 (m, 2H), 6.55–6.50 (m, 2H), 5.95–5.89 (m, 1H), 5.31–5.15 (m, 2H), 4.08 (bs, 1H), 3.74 (dt, *J* = 5.4, 1.7 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.7, 134.7, 131.9, 116.6, 114.7, 109.3, 46.6; IR (KBr): 3415, 1593, 1253 cm^{-1}; m/z (EI) (%): 214.0 (16), 213.0 (92), 212.0 (32), 211.0 (100), 209.9 (15), 185.9 (42), 183.9 (49), 181.9 (12), 132.0 (22), 131.0 (13), 130.0 (39), 116.9 (10), 104.9 (16), 91.0 (14); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{11}NBr$, 212.00694; found, 212.00679. The spectral data are in accordance with the literature.[154]

4-bromo-*N*-(2-methylbut-3-en-2-yl)aniline (414v)



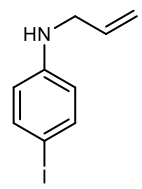
According to general procedure **C2** compound **414v** was synthesized at -20 °C as a colorless liquid (38.0 mg, 0.160 mmol, 83%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21–7.17 (m, 2H), 6.59 (d, *J* = 8.2 Hz, 2H), 5.96 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.17 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.12 (dd, *J* = 10.6, 1.0 Hz, 1H), 1.38 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 131.6, 117.5, 113.4, 55.1, 28.2; IR (KBr): 3412, 1256, 694 cm^{-1}; m/z (EI) (%): 240.9 (57), 238.9 (58), 225.9 (28), 223.9 (30), 172.8 (100), 170,8 (95), 143,9 (35), 129.9 (13), 69.1 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}BrN$, 240.03824; found, 240.03857.

***N*-allyl-3-bromoaniline (414w)**



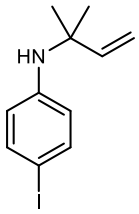
According to general procedure **C2** compound **414w** was synthesized as a colorless liquid (41.4 mg, 0.196 mmol, 98%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.01 (t, *J* = 8.0 Hz, 1H), 6.82 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.76 (t, *J* = 2.1 Hz, 1H), 6.54 (dd, *J* = 8.2, 2.3 Hz, 1H), 5.95–5.89 (m, 1H), 5.30–5.16 (m, 2H), 4.11 (bs, 1H), 3.75 (dt, *J* = 5.4, 1.7 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.0, 134.5, 130.4, 123.2, 120.4, 116.7, 115.6, 111.8; IR (KBr): 3417, 1593, 1255, 679 cm^{-1}; m/z (EI) (%): 214.0 (23), 213.0 (92), 212.0 (47), 211.0 (100), 210.0 (31), 185.9 (37), 183.9 (46), 132.0 (33), 131.0 (20), 130.0 (45), 117.0 (16), 104.0 (11), 63.0 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{11}NBr$, 212.00694; found, 212.00639. The spectral data are in accordance with the literature.[164]

***N*-allyl-4-iodoaniline (414x)**



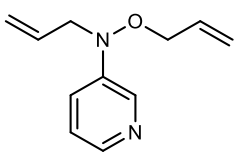
According to general procedure **C2** compound **414x** was synthesized as a colorless liquid (34.7 mg, 0.134 mmol, 67%). Purification by column chromatography (Pentane:EtOAc = 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48–7.39 (m, 2H), 6.49–6.38 (m, 2H), 5.95–5.88 (m, 1H), 5.33–5.12 (m, 2H), 3.89 (bs, 1H), 3.74 (dt, *J* = 5.5, 1.7 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.8, 137.8, 134.3, 116.9, 115.7, 46.7; IR (KBr): 3413, 1588, 1316 cm^{-1}; m/z (EI) (%): 259.9 (11), 258.9 (100), 257.9 (11), 231.9 (25), 129.9 (16); HRMS (m/z): $[M+H]^+$ calcd. for $C_9H_{11}NI$, 259.99307; found, 259.99302. The spectral data are in accordance with the literature.[165]

4-iodo-*N*-(2-methylbut-3-en-2-yl)aniline (414y)



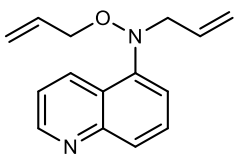
According to general procedure **C2** compound **414y** was synthesized as a colorless liquid (55.0 mg, 0.190 mmol, 95%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.8 Hz, 2H), 6.49 (d, *J* = 8.3 Hz, 2H), 5.95 (dd, *J* = 17.5 Hz, 10.6 Hz, 1H), 5.17 (d, *J* = 17.5 Hz, 1H), 5.12 (d, *J* = 10.6 Hz, 1H), 1.37 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.3, 137.5, 118.0, 113.4, 76.9, 55.0, 28.2; IR (KBr): 3407, 1255, 1182, 693 cm^{-1}; m/z (EI) (%): 288.0 (13), 287.0 (96), 271.9 (33), 218.9 (100), 144.0 (24), 130.0 (10), 92.0 (12), 69.1 (24); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}IN$, 288.02437; found, 288.02313.

***N*,*O*-diallyl-N-(pyridin-3-yl)hydroxylamine (414z)**



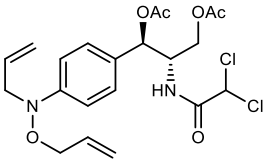
According to general procedure **C1** compound **414z** was synthesized as a colorless liquid (36.1 mg, 0.190 mmol, 95%). Purification by column chromatography (EtOAc:Et_3N = 1:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (d, *J* = 2.7 Hz, 1H), 8.21 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.40–7.31 (m, 1H), 7.20 (ddd, *J* = 8.4, 4.7, 0.7 Hz, 1H), 5.96 (dddt. *J* = 16.7, 14.5, 10.3, 6.2 Hz, 2H), 5.37–5.15 (m, 4H), 4.32 (dt, *J* = 6.2, 1.3 Hz, 2H), 3.97 (dt, *J* = 6.3, 1.3 Hz, 2H); ^{13}C NMR (151 MHz, CDCl3): δ 147.2, 143.1, 138.8, 133.0, 132.6, 123.6, 123.3, 119.1, 74.8, 60.6; IR (KBr): 3342, 1576, 925 cm^{-1}; m/z (EI) (%): 241.1 (33), 240.0 (43), 200.0 (14), 169.0 (44), 168.0 (20), 127.9 (29); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}N_2O$, 191.11789; found, 191.11784.

***N*,*O*-diallyl-N-(quinolin-5-yl)hydroxylamine (414aa)**



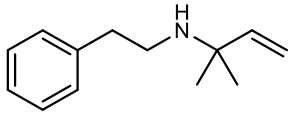
According to general procedure **C1** compound **414aa** was synthesized as a colorless liquid (45.6 mg, 0.190 mmol, 95%). Purification by column chromatography (Pentane:EtOAc:Et_3N = 5:1:0.1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.41 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.83 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.67–7.57 (m, 2H), 7.32 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.10–5.98 (m, 1H), 5.92–5.81 (m, 1H), 5.23–5.03 (m, 4H), 4.18 (dt, *J* = 6.1, 1.3 Hz, 2H), 3.69 (dt, *J* = 6.3, 1.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.3, 148.7, 147.9, 133.9, 133.7, 131.5, 129.3, 126.2, 123.0, 120.5, 118.2, 118.0, 116.5, 74.4, 63.9; IR (KBr): 1572, 923, 802 cm^{-1}; m/z (EI) (%): 268.1 (14), 232.0 (11), 192.2 (11), 191.1 (86), 190.1 (100), 149.1 (31), 48.2 (14), 47.2 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{17}N_2O$, 241.13354; found, 241.13310.

(1R,2S)-1-(4-(allyl(allyloxy)amino)phenyl)-2-(2,2-dichloroacetamido)propane-1,3-diyl di-acetate (414ab)



According to general procedure **C1** compound **414ab** was isolated at 0 °C as a colorless liquid (56.8 mg, 0.120 mmol, 60%). Purification by column chromatography (Pentane:EtOAc:Et_3N = 1:1:0.01). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.18 (m, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 9.3 Hz, 1H), 6.06–5.85 (m, 4H), 5.36 –5.13 (m, 3H), 4.59–4.52 (m, 1H), 4.29 (d, 2H), 4.10 (dd, *J* = 11.7, 4.2 Hz, 2H), 3.97–3.88 (m, 3H), 2.09 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 170.4, 151.9, 133.3, 133.2, 128.9, 127.7, 118.5, 118.5, 116.5, 74.7, 73.6, 66.2, 62.7, 60.6, 53.3, 21.1, 20.7; IR (KBr): 3313, 1739, 1689 cm^{-1}; m/z (EI) (%): 474.0 (12), 472.0 (17), 433.0 (47), 432.0 (14), 305.0 (14), 304.0 (79), 260.0 (11), 220.0 (23), 218.0 (29), 178.0 (100), 176.9 (21), 162.0 (12); HRMS (m/z): $[M+Na]^+$ calcd. for $C_{21}H_{26}N_2O_6Cl_2Na$, 495.10601; found, 495.10538.

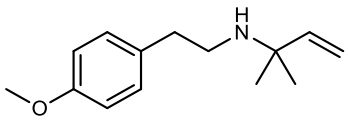
***N*-(phenethyl)-2-methylbut-3-en-2-amine (412f)**



According to general procedure **C1** compound **412f** was synthesized at 0 °C as a colorless liquid (30.2 mg, 0.160 mmol, 80%). Purification by column chromatography (EtOAc:Et_3N, 1:0.01). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21 (t, *J* = 7.5 Hz, 2H), 7.15–7.12 (m, 3H), 5.75–5.55 (m, 1H), 4.96–4.85 (m, 2H), 2.73–2.68 (m, 4H), 1.09 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.8, 140.0, 128.7, 128.4, 126.1, 112.2, 54.5, 44.4, 37.0, 26.8; IR (KBr): 3371, 1607 cm^{-1}; m/z (EI) (%): 104.9 (16), 97.9 (23), 90.9

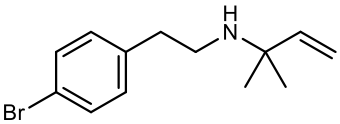
(91), 83.0 (13), 81.9 (22), 76.9 (19), 71.0 (28), 70.0 (19), 69.0 (100), 67.0 (16), 65.0 (25), 57.0 (60), 55.0 (52), 54.0 (10), 51.0 (19); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{15}N^+$, 190.15903; found, 190.15888.

***N*-(4-methoxyphenethyl)-2-methylbut-3-en-2-amine (412g)**



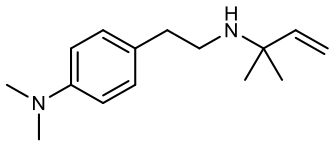
According to general procedure **C2** compound **412g** was synthesized at 0 °C as a colorless liquid (31.1 mg, 0.140 mmol, 70%). Purification by column chromatography (EtOAc:Et_3N = 1:0.01). ^1H NMR (600 MHz, $CDCl_3$): δ 7.16–7.07 (m, 2H), 6.85–6.80 (m, 2H), 5.71 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.02–4.93 (m, 2H), 3.78 (s, 3H), 2.72 (s, 4H), 1.16 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.9, 145.7, 132.0, 129.6, 113.8, 112.2, 55.2, 54.4, 44.5, 35.9, 26.8; IR (KBr): 1511, 1244, 1176 cm^{-1}; m/z (EI) (%): 221.2 (16), 220.1 (100), 135.0 (24), 122.0 (10), 121.0 (73), 98.0 (71), 91.0 (14), 82.0 (24), 78.0 (16), 77.0 (14), 69.1 (31); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}NO$, 220.16959; found, 220.16940.

***N*-(4-bromophenethyl)-2-methylbut-3-en-2-amine (412h)**



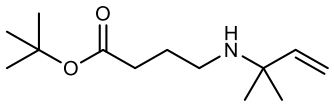
According to general procedure **C2** compound **412h** was synthesized at 0 °C as a colorless liquid (51.0 mg, 0.190 mmol, 95%). Purification by column chromatography (EtOAc:MeOH:Et_3N = 19:0.4:0.1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 5.72 (ddd, *J* = 17.5, 10.8, 1.3 Hz, 1H), 5.03 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.00 (dd, *J* = 17.5, 1.2 Hz, 1H), 2.77–2.71 (m, 4H), 1.18 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 139.0, 131.6, 130.6, 120.1, 112.8, 54.9, 44.2, 36.3, 26.7; IR (KBr): 1638, 687 cm^{-1}; m/z (EI) (%): 270.0 (36), 268.0 (40), 253.9 (22), 251.9 (20), 184.9 (16), 182.9 (17), 170.8 (30), 168.8 (31), 104,0 (18), 98.0 (100), 90.0 (20), 89.0 (17), 82.0 (27), 69.1 (47), 53.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{19}BrN$, 268.06954; found, 268.06935.

***N,N*-dimethyl-4-(2-((2-methylbut-3-en-2-yl)amino)ethyl)aniline (412i)**



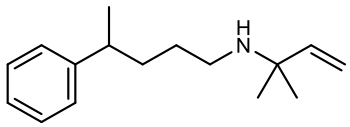
According to general procedure **C2** compound **412i** was synthesized at 0 °C as a yellow liquid (37.6 mg, 0,162 mmol, 81%). Purification by column chromatography (EtOAc:Pentane:Et_3N = 9:1:0.1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.6 Hz, 2H), 5.72 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.05 – 4.93 (m, 2H), 2.89 (s, 6H), 2.70 (s, 4H), 1.16 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.3, 145.6, 129.3, 127.9, 113.0, 112.3, 54.6, 44.6, 40.9, 35.6, 26.7, IR (KBr): 3357, 1614 cm^{-1}; m/z (EI) (%): 232.1 (19), 136.0 (10), 135.0 (100), 133.9 (58), 119.9 (12), 117.9 (17), 69.0 (21); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{15}N$, 233.20123; found, 233.20106.

tert-butyl 4-((2-methylbut-3-en-2-yl)amino)butanoate (412j)



According to general procedure **C2** compound **412j** was synthesized at 0 °C as a colorless solid (43.2 mg, 0.190 mmol, 95%). Purification by column chromatography (Pentane:EtOAc:Et_3N = 5:1:0.01). ^1H NMR (600 MHz, $CDCl_3$): δ 5.77–5.72 (m, 1H), 5.04–4.95 (m, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.25 (t, *J* = 7.4 Hz, 3H), 1.71 (p, *J* = 7.3 Hz, 2H), 1.43 (s, 9H), 1.15 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.9, 146.1, 111.9, 80.1, 54.3, 42.2, 33.6, 28.1, 26.9, 26.4; IR (KBr): 1726, 1148 cm^{-1}; m/z (EI) (%): 358.1 (28), 286.1 (15), 230.1 (21), 228.1 (28), 214.0 (16), 200.0 (17), 174.0 (40), 172.0 (24), 158.0 (39), 156.0 (11), 140.0 (11), 128.0 (12), 102.0 (28), 84.0 (11), 71.0 (22), 59.1 (13), 57.1 (100), 56.1 (15), 55.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{26}O_2N$, 228.19581; found, 228.19555.

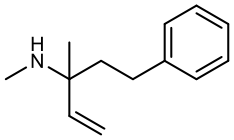
***N*-(2-methylbut-3-en-2-yl)-4-phenylpentan-1-amine (412k)**



According to general procedure **C2** compound **412k** was synthesized at 0 °C as a colorless liquid (32.0 mg, 0.140 mmol, 70%). Purification by column chromatography (EtOAc:MeOH:Et_3N = 19:0.2:0.1). ^1H NMR (600 MHz, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.16 (m, 3H), 5.75 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.02 (d, *J* = 8.5 Hz, 1H), 5.00 (d, *J* = 12.8 Hz, 1H), 2.67 (h, *J* = 7.1 Hz, 1H), 2.47–2.38 (m, 2H), 1.61–1.56 (m, 2H), 1.48–1.29 (m, 2H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.16 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.6,

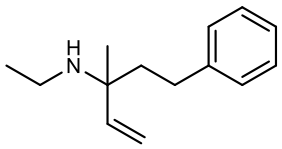
145.8, 128.4, 127.1, 126.0, 112.4, 54.7, 43.1, 40.0, 36.4, 28.9, 26.8, 22.3; IR (KBr): 1452, 1181 cm^{-1}; m/z (EI) (%): 232.1 (24), 321.1 (37), 217.1 (16), 216.1 (100), 204.1 (13), 145.0 (10), 104.9 (55), 102.9 (11), 90.9 (13), 84.9 (22), 82.9 (33), 82.0 (18), 77.0 (12), 69.0 (12), 47.0 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}N$, 232.20598; found, 232.20532.

***N*,3-dimethyl-5-phenylpent-1-en-3-amine (412l)**



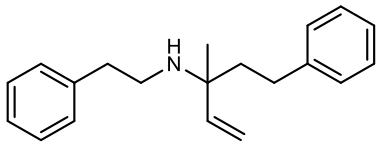
According to general procedure **C2** compound **412l** was synthesized at –78 °C as a colorless liquid (33.3 mg, 0.176 mmol, 88%). Purification by column chromatography (Et_2O:MeOH:NEt_3 = 100:10:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (dd, *J* = 8.3, 7.1 Hz, 2H), 7.18 (d, *J* = 7.2 Hz, 3H), 5.76 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.20 – 5.08 (m, 2H), 2.62 – 2.52 (m, 2H), 2.31 (s, 3H), 1.81 – 1.73 (m, 2H), 1.22 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.0, 142.6, 128.4, 128.3, 125.7, 113.9, 57.4, 41.7, 30.3, 28.8, 22.4; IR (KBr): 3320 cm^{-1}; m/z (EI) (%): 302.2 (16), 219.2 (13), 91.1 (17), 84.2 (100), 56.2 (11), 55.2 (15); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{20}N$, 190.15903; found, 190.15874.

***N*-ethyl-3-methyl-5-phenylpent-1-en-3-amine (412m)**



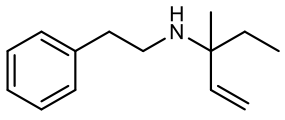
According to general procedure **C2** compound **412m** was synthesized at –78 °C as a colorless liquid (37.8 mg, 0.186 mmol, 93%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.19 (m, 2H), 7.16 (d, *J* = 7.3 Hz, 3H), 5.76 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.17 – 5.00 (m, 2H), 2.62 – 2.47 (m, 4H), 1.81 – 1.68 (m, 2H), 1.20 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.1, 142.8, 128.3, 128.3, 125.6, 112.9, 56.9, 42.1, 36.5, 30.3, 23.5, 15.9; IR (KBr): 3326 cm^{-1}; m/z (EI) (%): 204.1 (37), 203.1 (13), 188.0 (24), 176.0 (14), 98.1 (100), 91.1 (25), 83.0 (10), 48.1 (14), 47.1 (17); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}N$, 204.17468; found, 204.174398.

3-methyl-*N*-phenethyl-5-phenylpent-1-en-3-amine (412n)



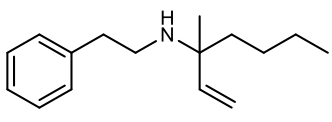
According to general procedure **C2** compound **412n** was synthesized at –78 °C as a colorless liquid (43.0 mg, 0.154 mmol, 77%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.19 (m, 7H), 7.15 (dd, *J* = 12.6, 7.2 Hz, 3H), 5.69 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.10 (d, *J* = 10.7 Hz, 1H), 5.01 (d, *J* = 17.6 Hz, 1H), 2.77 (s, 4H), 2.48 (dd, *J* = 12.8, 6.6 Hz, 2H), 1.73 (d, *J* = 7.5 Hz, 2H), 1.18 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 142.7, 140.1, 128.7, 128.4, 128.3, 128.3, 126.2, 125.7, 113.2, 56.9, 43.8, 42.0, 37.0, 30.2, 23.5; IR (KBr): 3320 cm^{-1}; m/z (EI) (%): 280.1 (23), 189.0 (12), 188.0 (79), 175.0 (14), 174.0 (100), 159.0 (12), 104.9 (23), 90.9 (82), 65.0 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{25}N$, 280.20598; found, 280.20523.

3-methyl-*N*-phenethylpent-1-en-3-amine (412o)



According to general procedure **C2** compound **412o** was synthesized at -40 °C as a colorless liquid (32.1 mg, 0.158 mmol, 79%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.23 (m, 2H), 7.19 (d, *J* = 7.4 Hz, 3H), 5.60 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.04 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 17.6 Hz, 1H), 2.81–2.67 (m, 4H), 1.42 (p, *J* = 7.1, 6.7 Hz, 2H), 1.07 (s, 3H), 0.74 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.9, 140.2, 128.7, 128.3, 126.1, 112.9, 57.0, 43.8, 37.0, 32.7, 22.5, 7.9; IR (KBr): 3324 cm^{-1}; m/z (EI) (%): 188.0 (12), 175.0 (14), 174.0 (100), 112.0 (37), 104.9 (33), 90.9 (49), 83.0 (19), 82.0 (16), 65.0 (10), 55.0 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}N$, 204.17468; found, 204.17397.

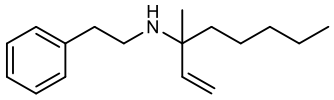
3-methyl-*N*-phenethylhept-1-en-3-amine (412p)



According to general procedure **C2** compound **412p** was synthesized at -78 °C as a colorless liquid (38.9 mg, 0.168 mmol, 84%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.24–7.17 (m, 2H), 7.14 (d, *J* = 7.2 Hz, 3H), 5.56 (dd, *J* = 17.6, 10.8 Hz, 1H), 4.97 (d, *J* = 10.8 Hz, 1H), 4.87 (d, *J* = 17.6 Hz, 1H), 2.73–2.62 (m, 4H), 1.32 (q, *J* = 8.4, 8.0 Hz, 2H),

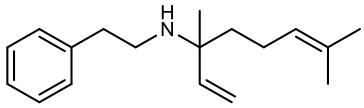
1.19 (q, *J* = 7.3 Hz, 2H), 1.11–1.04 (m, 2H), 1.03 (s, 3H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.3, 140.2, 128.7, 128.4, 126.1, 112.7, 56.8, 43.9, 40.2, 37.1, 25.8, 23.3, 23.1, 14.1; IR (KBr): 3325 cm^{-1}; m/z (EI) (%): 233.2 (19), 232.1 (100), 216.1 (10), 175.0 (13), 174.0 (99), 140.0 (25), 105.0 (27), 90.9 (81), 82.9 (19), 82.0 (29), 69.1 (11), 55.1 (14), 48.0 (13), 47.0 (17); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}N$, 232.20598; found, 232.20544.

3-methyl-*N*-phenethyloct-1-en-3-amine (412q)



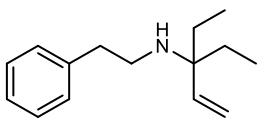
According to general procedure **C2** compound **412q** was synthesized at -78 °C as a colorless liquid (45.6 mg, 0.186 mmol, 93%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.24 (m, 2H), 7.20 (d, *J* = 6.3 Hz, 3H), 5.63 (dd, *J* = 17.5, 10.8 Hz, 1H), 4.99 (dd, *J* = 30.1, 14.7 Hz, 2H), 2.74 (dt, *J* = 10.4, 5.0 Hz, 4H), 1.45–1.34 (m, 2H), 1.33–1.12 (m, 6H), 1.10 (s, 3H), 0.85 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.1, 140.1, 128.7, 128.4, 126.1, 112.8, 57.0, 43.8, 40.2, 37.0, 32.4, 23.3, 23.0, 22.6, 14.0; IR (KBr): 3321 cm^{-1}; m/z (EI) (%): 246.1 (17), 175.1 (15), 174.0 (100), 105.0 (21), 91.0 (27); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{28}N$, 246.22163; found, 246.22124.

3,7-dimethyl-*N*-phenethylocta-1,6-dien-3-amine (412r)



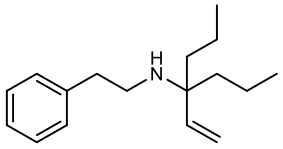
According to general procedure **C2** compound **412r** was synthesized at –78 °C as a colorless liquid (45.3 mg, 0.176 mmol, 88%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.24 (m, 2H), 7.21 (d, *J* = 7.1 Hz, 3H), 5.66 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.11–4.92 (m, 3H), 2.85–2.70 (m, 4H), 1.92–1.81 (m, 2H), 1.65 (s, 3H), 1.56 (s, 3H), 1.47–1.39 (m, 2H), 1.13 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.9, 140.1, 131.4, 128.7, 128.4, 126.2, 124.4, 113.1, 57.2, 43.9, 40.1, 36.9, 25.7, 23.1, 22.5; IR (KBr): 3402 cm^{-1}; m/z (EI) (%): 258.0 (13), 175.0 (15), 173.9 (100), 166.0 (22), 104.9 (17), 90.9 (35); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{28}N$, 258.22163; found, 258.22104.

3-ethyl-*N*-phenethylpent-1-en-3-amine (412s)



According to general procedure **C2** compound **412s** was synthesized at -78 °C as a colorless liquid (26.1 mg, 0.120 mmol, 60%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.17 (m, 2H), 7.18–7.08 (m, 3H), 5.52 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.06 (d, *J* = 10.9 Hz, 1H), 4.91 (d, *J* = 17.7 Hz, 1H), 2.74 (t, *J* = 7.0 Hz, 2H), 2.61 (t, *J* = 7.3 Hz, 2H), 1.38 (q, *J* = 7.3 Hz, 7H), 0.65 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.4, 140.3, 128.7, 128.3, 126.1, 113.6, 59.4, 43.2, 37.0, 27.5, 7.3; IR (KBr): 3333 cm^{-1}; m/z (EI) (%): 189.1 (16), 188.0 (100), 126.0 (17), 104.9 (26), 95.9 (10), 90.9 (27), 55.0 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{15}H_{24}N$, 218.19033; found, 218.18961.

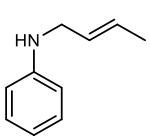
***N*-phenethyl-4-vinylheptan-4-amine (412t)**



According to general procedure **C2** compound **412t** was synthesized at -78 °C as a colorless liquid (34.8 mg, 0.140 mmol, 71%). Purification by column chromatography (Pentane:NEt_3 = 100:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24–7.17 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 3H), 5.53 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.01 (d, *J* = 10.9 Hz, 1H), 4.88 (d, *J* = 17.7 Hz, 1H), 2.70 (d, *J* = 6.7 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 1.33–1.24 (m, 4H), 1.07 (dq, *J* = 14.9, 7.3 Hz, 4H), 0.79 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.8, 140.3, 128.7, 128.4, 126.1, 113.2, 59.3, 43.3, 38.2, 37.0, 16.3, 14.6; IR (KBr): 2956, 1458 cm^{-1}; m/z (EI) (%): 246.2 (14), 203.1 (23), 202.1 (100), 105.1 (12), 91.1 (21); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{28}N$, 246.22163; found, 246.22104.

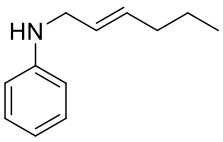
Synthesis of Reference Substrates

(*E*)-*N*-(but-2-en-1-yl)aniline (416a)



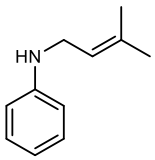
According to general procedure **C4** compound **416a** was isolated as a colorless liquid (26.7 mg, 0.182 mmol, 36%). Purification by column chromatography (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.19 (d, *J* = 7.2 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 2H), 5.76–5.70 (m, 1H), 5.66 – 5.55 (m, 1H), 3.70 (d, *J* = 5.9 Hz, 2H), 1.72 (dd, *J* = 6.5, 1.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 148.1, 129.2, 128.0, 128.0, 117.5, 113.1, 46.1, 17.8; IR (KBr): 3410, 1601 cm^{-1}; m/z (EI) (%): 147.1 (100), 146.0 (11), 132.0 (38), 106.0 (19), 93.0 (28), 84.9 (11), 82.9 (15), 77 (13), 55.1 (16); HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{14}N$, 148.11208; found, 148.11191. The spectral data are in accordance with the literature.[166]

***N*-(hex-2-en-1-yl)aniline (416b)**



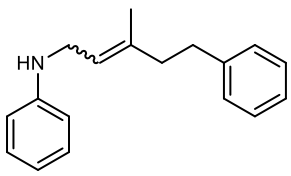
According to general procedure **C4** compound **416b** was isolated as a colorless liquid (37.1 mg, 0.211 mmol, 42%). Purification by column chromatography (Pentane:EtOAc = 50:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24–7.17 (m, 2H), 6.71–6.74 (m, 1H), 6.68–6.63 (m, 2H), 5.74–5.68 (m, 1H), 5.57–5.62 (m, 1H), 3.71–3.72 (m, 2H), 2.04 (q, *J* = 6.0 Hz, 2H), 1.42 (sext, *J*=6.0 Hz, 2H), 0.92 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 148.1, 133.3, 129.2, 126.8, 117.5, 113.1, 46.2, 34.4, 22.4, 13.7; IR (KBr): 3411, 1601, 1254 cm^{-1}; m/z (EI) (%): 176.1 (22), 175.1 (100), 146.0 (12), 132.0 (54), 106.0 (21), 104.0 (12), 93.0 (68), 77.0 (20), 65.0 (12), 55.1 (19); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{18}N$, 176.14338; found, 176.14338. The spectral data are in accordance with the literature.[167]

***N*-(3-methylbut-2-en-1-yl)aniline (416c)**



According to general procedure **C4** compound **416c** was isolated as a colorless liquid (21.2 mg, 0.132 mmol, 26%). Purification by column chromatography (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.10 (t, *J* = 7.7 Hz, 2H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 2H), 5.29 – 5.21 (m, 1H), 3.61 (d, *J* = 6.8 Hz, 2H), 1.65 (d, *J* = 24.6 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 148.2, 135.8, 129.2, 121.5, 117.6, 113.1, 42.2, 25.7, 18.0; IR (KBr): 3406, 1601 cm^{-1}; m/z (EI) (%): 349.3 (22), 348.3 (100), 280.3 (20), 279.2 (52), 251.2 (14), 229.3 (59), 212.2 (10), 177.2 (19), 162.1 (19), 161.2 (62), 160.2 (59), 93.1 (40), 69.2 (24); HRMS (m/z): $[M]^+$ calcd. for $C_{11}H_{16}N$, 162.12773; found, 162.12742. The spectral data are in accordance with the literature.[167]

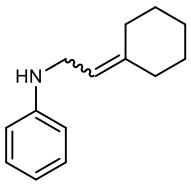
***N*-(3-methyl-5-phenylpent-2-en-1-yl)aniline (416d)**



According to general procedure **C4** compound **416d** was synthesized as a colorless liquid (32.7 mg, 0.130 mmol, 65%). Purification by HPLC (Pentane:EtOAc = 40:1). ^{1}H NMR (Major isomer, 400 MHz, $CDCl_3$): δ 7.25–7.17 (m, 2H), 7.17–7.06 (m, 5H), 6.66 (tt, *J* = 7.4, 1.2 Hz, 1H), 6.54–6.49 (m, 2H), 5.28 (td, *J* = 7.0, 1.6 Hz, 1H), 3.40 (dd, *J* = 7.0, 1.2 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.71 (s, 3H); ^{13}C NMR (Major isomer, 101 MHz, $CDCl_3$): δ 141.7, 138.5, 129.2, 128.6, 128.4, 126.0, 122.4, 118.3, 113.8, 42.1, 34.1, 23.3; IR (KBr): 3407 cm^{-1}; m/z (EI) (%): 252.1 (25), 251.1 (100), 160.1 (14), 146.0 (26), 104.0 (13), 93.0 (81), 91.0 (71) 77.0 (13) 65.0 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{22}N$, 252.17468; found, 252.17425.

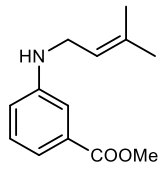
***N*-(2-cyclohexylideneethyl)aniline (416e)**

According to general procedure **C4** compound **416e** was synthesized as a yellow liquid (25.4 mg, 0.126 mmol, 63%). Purification by HPLC (Pentane:EtOAc = 40:1). ^{1}H NMR (Major isomer, 300 MHz, $CDCl_3$): δ 7.23–7.15 (m, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 5.30 (t, *J* = 6.9 Hz, 1H), 3.71 (d, *J* = 6.9 Hz, 2H), 2.16 (d, *J* = 26.0 Hz, 4H), 1.57 (s, 6H); ^{13}C NMR (Major isomer, 151 MHz, $CDCl_3$): δ 147.2, 144.4, 129.2, 118.3, 117.4, 113.9, 41.8, 37.0, 29.0, 28.4, 27.7, 26.7; IR (KBr): 3401 cm^{-1}; m/z (EI) (%): 429.3 (36), 428.2 (100), 321.1 (12), 320.1 (48), 319.1 (68), 303.1 (12), 212.1 (38), 201.2 (25), 200.1 (49), 109.2 (14),



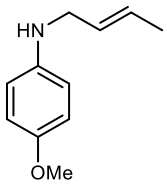
106.2 (16), 93.2 (46), 77.2 (12), 67.3 (32), 55.3 (16); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{19}N$, 202.15903; found, 202.15827. The spectral data are in accordance with the literature.[168]

methyl 3-((3-methylbut-2-en-1-yl)amino)benzoate (416f)



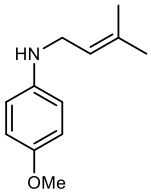
According to general procedure **C4** compound **416f** was isolated as a colorless liquid (22.6 mg, 0,103 mmol, 21%). Purification by HPLC (Pentane:EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.8 Hz, 1H), 7.30–7.26 (m, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.82 – 6.77 (m, 1H), 5.36–5.27 (m, 1H), 3.89 (s, 3H), 3.72 (d, *J* = 6.8 Hz, 2H), 1.73 (d, *J* = 20.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.5, 148.1, 136.2, 131.0, 129.1, 120.9, 118.6, 117.6, 113.5, 52.0, 42.1, 25.7, 18.0; IR (KBr): 3395, 1713, 1602, 1280, 1237 cm^{-1}; m/z (EI) (%): 220.2 (15), 219.1 (96), 204.1 (36), 188.1 (15), 164.1 (12), 152.1 (10), 151.0 (100), 120.0 (32), 69.2 (25); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{18}NO_2$, 220.13321; found, 220.13348.

(*E*)-*N*-(but-2-en-1-yl)-4-methoxyaniline (416g)



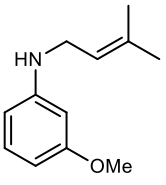
According to general procedure **C4** compound **416g** was isolated as a colorless liquid (16.0 mg, 0.090 mmol, 18%). Purification by HPLC (Pentane:EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.9 Hz, 2H), 6.61 (d, *J* = 8.9 Hz, 2H), 5.79–5.64 (m, 1H), 5.64 – 5.56 (m, 1H), 3.75 (s, 3H), 3.64 (dt, *J* = 5.9, 1.3 Hz, 2H), 1.70 (dd, *J* = 6.4, 1.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 152.2, 142.2, 128.2, 128.0, 114.8, 114.5, 55.8, 47.1, 17.8; IR (KBr): 3384, 1243 cm^{-1}; m/z (EI) (%): 232.1 (19), 231.1 (100), 177.0 (43), 176.0 (19), 162.0 (11), 136.0 (15), 133.9 (13), 122.0 (20), 55.1 (18); HRMS (m/z): $[M]^+$ calcd. for $C_{11}H_{15}NO$, 177.11482; found, 178.11458. The spectral data are in accordance with the literature.[169]

4-bromo-*N*-(3-methylbut-2-en-1-yl)aniline (416h)



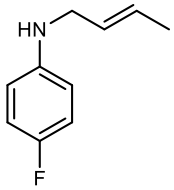
According to general procedure **C4** compound **416h** was isolated as a colorless liquid (24.1 mg, 0.126 mmol, 25%). Purification by HPLC (Pentane:EtOAc = 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.79 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 5.35–5.31 (m, 1H), 3.75 (s, 3H), 3.65 (d, *J* = 6.8 Hz, 2H), 1.72 (d, *J* = 25.4 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 152.2, 142.5, 135.4, 121.8, 114.9, 114.4, 55.8, 43.1, 25.7, 18.0; IR (KBr): 3386, 1235 cm^{-1}; m/z (EI) (%): 192.1 (16), 191.1 (100), 123.0 (31), 122.0 (20), 108.0 (29); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{18}ON$,192.13829; found, 192.13760.

3-methoxy-*N*-(3-methylbut-2-en-1-yl)aniline (416i)



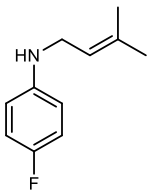
According to general procedure **C4** compound **416i** was isolated as a colorless liquid (13.7 mg, 0,072 mmol, 14%). Purification by HPLC (Pentane:EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.07 (t, *J* = 8.1 Hz, 1H), 6.25 (m, 2H), 6.17 (t, *J* = 2.3 Hz, 1H), 5.39 – 5.22 (m, 1H), 3.76 (s, 3H), 3.67 (d, *J* = 6.8 Hz, 1H), 1.72 (d, *J* = 15.9 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.8, 149.6, 135.8, 129.9, 121.4, 106.2, 102.6, 98.9, 55.1, 42.1, 25.7, 18.0 ppm; IR (KBr): 3400, 1607, 1207 cm^{-1}; m/z (EI) (%): 192.0 (20), 192.0 (100), 175.9 (23), 122.9 (43), 93.9 (15), 69.0 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{12}H_{18}NO$, 192.13829; found, 192.13850.

(*E*)-*N*-(but-2-en-1-yl)-4-fluoroaniline (416j)



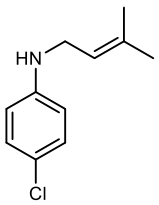
According to general procedure **C4** compound **416j** was isolated as a colorless liquid (25.7 mg, 0.156 mmol, 31%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.89 (t, *J* = 8.8 Hz, 2H), 6.58–6.56 (m, 2H), 5.79–5.67 (m, 1H), 5.61–5.56 (m, 1H), 3.65 (d, *J* = 6.0 Hz, 2H), 1.71 (d, *J* = 6.4, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.7, 155.2, 144.3, 128.2, 127.8, 115.6, 114.0, 46.8, 17.7; IR (KBr): 3412, 1611 cm^{-1}; HRMS (m/z): $[M+H]^+$ calcd. for $C_{10}H_{13}NF$, 166.10265; found, 166.10233.

4-fluoro-*N*-(3-methylbut-2-en-1-yl)aniline (416k)



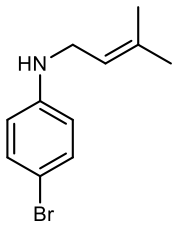
According to general procedure **C4** compound **416k** was isolated as a colorless liquid (25.6 mg, 0.143 mmol, 29%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.80 (t, *J* = 8.7 Hz, 2H), 6.5–6.4 (m, 2H), 5.3–5.2 (m, 1H), 3.56 (d, *J* = 6.7 Hz, 2H), 1.64 (d, *J* = 24.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 156.6, 155.1, 144.7, 135.7, 121.5, 115.6, 113.7, 42.7, 25.7, 18.0.; IR (KBr): 3411, 1611 cm^{-1}; m/z (EI) (%): 180.1 (21), 179.0 (100), 164.0 (19), 123.9 (11), 112.0 (12), 111.0 (58), 94.9 (10), 69.1 (27); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}NF$, 180.11830; found, 180.11835.

4-chloro-*N*-(3-methylbut-2-en-1-yl)aniline (416l)



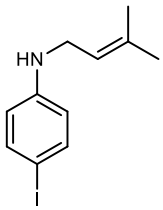
According to general procedure **C4** compound **416l** was isolated as a colorless liquid (18.0 mg, 0.092 mmol, 18%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 5.37–5.24 (m, 1H), 3.66 (d, *J* = 6.8 Hz, 2H), 1.73 (d, *J* = 26.4 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 146.8, 136.1, 129.0, 121.9, 121.1, 114.0, 42.2, 25.7, 18.0; IR (KBr): 3414, 1599 cm^{-1}; m/z (EI) (%): 197.0 (38), 196.1 (16), 195.0 (100), 180.0 (13), 139.9 (18), 128.9 (20), 126.9 (57), 69.1 (26); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}NCl$, 196.08875; found, 196.08855.

4-bromo-*N*-(3-methylbut-2-en-1-yl)aniline (416m)



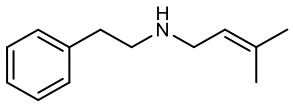
According to general procedure **C4** compound **416m** was isolated as a colorless liquid (22.0 mg, 0.092 mmol, 18%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 5.37–5.24 (m, 1H), 3.66 (d, *J* = 6.8 Hz, 2H), 1.73 (d, *J* = 26.4 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 146.8, 136.1, 129.0, 121.9, 121.1, 114.0, 42.2, 25.7, 18.0; IR (KBr): 3412, 1594 cm^{-1}; m/z (EI) (%): 242.0 (17), 241.0 (100), 240.0 (17), 239.0 (99), 185.9 (20), 183.8 (25), 144.0 (15), 129.9 (16), 116.9 (10), 104.9 (10), 91.9 (14), 90.9 (21), 76 (13), 74.9 (10), 65.0 (20), 64.0 (11), 63.0 (17), 53.0 (19), 51.0 (13), 50.0 (13); HRMS (m/z): [M] calcd. for $C_{11}H_{14}NBr$, 239.03041; found, 239.02953.

4-bromo-*N*-(3-methylbut-2-en-1-yl)aniline (416n)



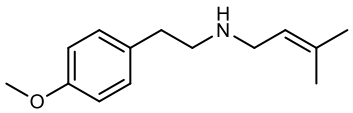
According to general procedure **C4** compound **416n** was isolated as a colorless liquid (21.3 mg, 0.074 mmol, 15%). Purification by HPLC (Pentane:EtOAc = 19:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.8 Hz, 2H), 6.41 (d, *J* = 8.8 Hz, 2H), 5.30–5.28 (m, 1H), 3.65 (d, *J* = 6.8 Hz, 2H), 1.72 (d, *J* = 28.4 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 147.5, 137.8, 136.3, 120.9, 115.4, 78.2, 42.1, 25.7, 18.0; IR (KBr): 3408, 1589 cm-1; m/z (EI) (%): 288.0 (14), 287.0 (100), 218.9 (37), 69.1 (19); HRMS (m/z): $[M+H]^+$ calcd. for $C_{11}H_{15}NI$, 288.02437; found, 288.02307.

3-methyl-*N*-phenethylbut-2-en-1-amine (416o)



According to general procedure **C4** compound **416o** was isolated as a colorless liquid (22.0 mg, 0.120 mmol, 23%). Purification by column chromatography (EtOAc:Et_3N = 99:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.20 (t, *J* = 7.5 Hz, 2H), 7.12–7.09 (m, 3H), 5.22–5.19 (m, 1H), 3.05 (d, *J* = 6.9 Hz, 2H), 2.78–2.66 (m, 2H), 2.66–2.55 (m, 2H), 1.66 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 139.8, 133.5, 127.7, 127.3, 124.8, 120.7, 54.5, 50.3, 32.6, 24.9, 17.0; IR (KBr): 3314, 1603 cm^{-1}; m/z (EI) (%): 190.1 (15), 105.1 (12), 98.1 (100), 91.1 (28), 69.2 (54), 65.1 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{20}N$, 190.15903; found, 190.15888.

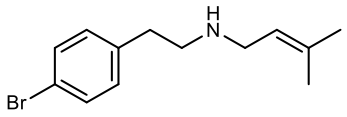
***N*-(4-methoxyphenethyl)-3-methylbut-2-en-1-amine (416p)**



According to general procedure **C4** compound **416p** was synthesized as a colorless liquid (21.0 mg, 0.095 mmol, 24%). Purification by column chromatography (Pentane:EtOAc:Et_3N = 5:1:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.13–7.11 (m, 2H), 6.84–6.82 (m, 2H), 5.22 (tdt, *J* = 6.9, 2.9, 1.4 Hz, 1H), 3.78 (s, 3H), 3.21 (d, *J* = 6.9, 2H), 2.83 (td, *J* = 7.1, 1.0 Hz, 2H), 2.75 (t, *J* = 7.1 Hz, 2H), 1.70 (s, 3H),

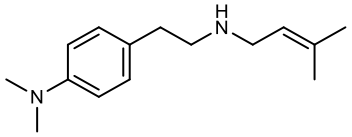
1.62 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.9, 134.2, 132.1, 129.6, 122.9, 113.9, 55.2, 50.9, 47.1, 35.4, 25.7, 17.9; IR (KBr): 1509, 1245, 1176 cm^{-1}; m/z (EI) (%): 166.2 (39), 135.0 (86), 121.1 (32), 105.1 (13), 91.0 (32), 79.1 (15), 78.1 (20), 77.0 (28), 69.1 (100), 65.1 (15), 53.2 (21), 51.1 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}NO$, 220.16959; found, 220.16943.

***N*-(4-bromophenethyl)-3-methylbut-2-en-1-amine (416q)**



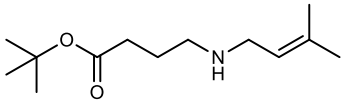
According to general procedure **C4** compound **416q** was synthesized as a colorless liquid (13.6 mg, 0.051 mmol, 25%). Purification by column chromatography (EtOAc:Et_3N = 19:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 7.9 Hz, 2H), 5.15 (t, *J* = 7.2 Hz, 1H), 3.16 (d, *J* = 7.0 Hz, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 2.71 (t, *J* = 7.2 Hz, 2H), 1.64 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 139.1, 134.9, 131.6, 130.6, 122.4, 120.1, 50.4, 47.2, 35.8, 25.9, 18.1; IR (KBr): 2924, 806 cm^{-1}; m/z (EI) (%): 269.8 (59), 267.9 (64), 170.8 (55), 170.1 (28), 168.8 (60), 103.9 (17), 102.9 (11), 101.9 (12), 97.9 (82), 90.9 (12), 89.9 (33), 88.9 (32), 81.9 (19), 76.9 (11), 69.0 (100), 68.0 (24), 67.0 (15), 62.9 (11), 57.0 (12), 56.0 (13), 55.0 (15), 53.0 (23), 51.0 (12); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{19}BrN$, 268.06954; found, 268.06949.

***N,N*-dimethyl-4-(2-((3-methylbut-2-en-1-yl)amino)ethyl)aniline (416r)**



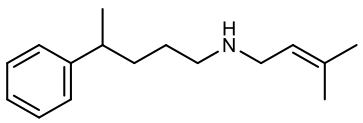
According to general procedure **C4** compound **416r** was synthesized as a colorless liquid (11.6 mg, 0.050 mmol, 10%). Purification by column chromatography (EtOAc:Et_3N = 19:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 5.23 (t, *J* = 6.6 Hz, 1H), 3.24 (d, *J* = 6.9 Hz, 2H), 2.91 (s, 6H), 2.83 (d, *J* = 5.9 Hz, 2H), 2.76 (d, *J* = 6.6 Hz, 2H), 1.70 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.2, 134.3, 129.3, 128.0, 122.7, 113.0, 50.9, 47.1, 40.8, 35.2, 25.7, 17.9; IR (KBr): 3309, 1615 cm^{-1}; m/z (EI) (%): 233.2 (14), 232.2 (26), 136.1 (11), 135.1 (100), 124.1 (50), 120.1 (17), 119.1 (14), 60.3 (18); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}N_2$, 233.20123; found, 233.20125.

tert-butyl 4-((3-methylbut-2-en-1-yl)amino)butanoate (416s)



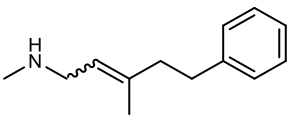
According to general procedure **C4** compound **416s** was synthesized as a colorless liquid (8.20 mg, 0.036 mmol, 12%). Purification by column chromatography (Pentane:EtOAc = 20:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.13–5.06 (m, 1H), 2.95 (d, *J* = 6.7 Hz, 2H), 2.25 (t, *J* = 7.7 Hz, 2H), 1.76–1.70 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.52–1.46 (m, 1H), 1.44 (s, *J* = 1.1 Hz, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.44, 133.4, 123.9, 79.9, 57.5, 46.6, 33.2, 28.1, 25.8, 24.8, 17.9; IR (KBr): 1727, 1149 cm^{-1}; m/z (EI) (%): 424.1 (22), 355.1 (16), 354.1 (79), 350.1 (26), 295.1 (19), 294.1 (100), 242.0 (17), 238.0 (37), 169.9 (14), 57.0 (53); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{26}NO_2$, 228.19581; found, 228.19691.

***N*-(3-methylbut-2-en-1-yl)-4-phenylpentan-1-amine (416t)**



According to general procedure **C4** compound **416t** was synthesized as a colorless liquid (10.6 mg, 0.046 mmol, 23%). Purification by column chromatography (EtOAc:Et_3N = 19:0.1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30–7.25 (m, 3H), 7.19–7.15 (m, 2H), 5.25 (s, 1H), 3.10 (s, 2H), 2.67 (p, *J* = 7.0 Hz, 1H), 2.45 (s, 2H), 1.72 (s, 3H), 1.62–1.53 (m, 4H), 1.58 (s, 3H), 1.24 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.4, 140.3, 128.5, 127.1, 126.0, 51.0, 39.9, 36.2, 29.8, 26.1, 22.5, 18.1, 14.2; IR (KBr): 2924, 1450, 699 cm^{-1}; m/z (EI) (%): 231.1 (22), 230.1 (36), 167.1 (14), 166.1 (100), 105.1 (22), 98.2 (21), 69.2 (23); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}N$, 232.20598; found, 232.20566.

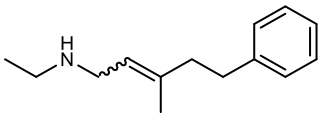
***N*,3-dimethyl-5-phenylpent-2-en-1-amine (416u)**



According to general procedure **C4** with NEt_3 replacing K_2CO_3 as a base compound **416u** was synthesized as a yellow liquid (7.57 mg, 0.04 mmol, 20%). Purification by column chromatography (Et_2O:MeOH:NEt_3 = 100:10:3). ^{1}H NMR (1:1 mixture of (E)-/(Z)-isomers, 400 MHz, $CDCl_3$): δ

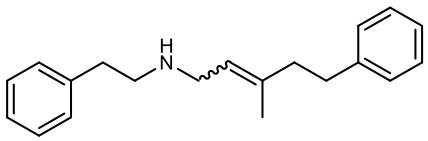
7.29–7.22 (m, 4H), 7.20–7.12 (m, 5H), 5.28–5.21 (m, 2H), 3.17 (d, *J* = 6.8 Hz, 2H), 2.96 (d, *J* = 7.0 Hz, 2H), 2.69 (ddd, *J* = 13.1, 9.3, 7.2 Hz, 4H), 2.39–2.24 (m, 9H), 1.76 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (1:1 mixture of (E)-/(Z)-isomers, 151 MHz, $CDCl_3$): δ 142.1, 141.9, 137.9, 137.3, 128.5, 128.3, 128.3, 128.3, 125.9, 125.7, 125.5, 123.8, 122.5, 48.8, 48.7, 41.5, 35.7, 35.5, 34.4, 34.2, 34.0, 30.3, 23.4, 16.4; IR (KBr): 3425 cm^{-1}; m/z (EI) (%): 313.2 (12), 98.3 (29), 91.2 (100), 84.3 (23), 82.3 (13), 65.3 (21), 51.3 (10); HRMS (m/z): $[M+H]^+$ calcd. for $C_{13}H_{20}N$, 190.15903; found, 190.15863.

_N_-ethyl-3-methyl-5-phenylpent-2-en-1-amine (416v)



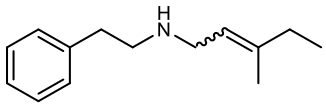
According to general procedure **C4** with NEt_3 replacing K_2CO_3 as a base compound **416v** was synthesized as a yellow liquid (24.0 mg, 0.171 mmol, 59%). Purification by column chromatography (Et_2O:MeOH:NEt_3 = 100:10:3). ^{1}H NMR (5:3 mixture of (E)-/(Z)-isomers, 400 MHz, $CDCl_3$): δ 7.23–7.17 (m, 4H), 7.10 (ddd, *J* = 8.5, 4.5, 2.1 Hz, 6H), 5.24–5.17 (m, 2H), 3.15 (d, *J* = 6.8 Hz, 2H), 2.94 (d, *J* = 6.8 Hz, 1H), 2.68–2.59 (m, 4H), 2.54 (q, *J* = 7.1 Hz, 2H), 2.44 (q, *J* = 7.1 Hz, 1H), 2.28 (t, *J* = 7.7 Hz, 1H), 2.25-2.20 (m, 2H), 1.70 (s, 2H), 1.62 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR (5:3 mixture of (E)-/(Z)-isomers, 151 MHz, $CDCl_3$): δ 142.2, 142.0, 137.0, 136.5, 128.5, 128.4, 128.3, 128.3, 125.9, 125.7, 124.6, 123.4, 47.0, 46.8, 43.6, 41.5, 34.5, 34.3, 34.1, 23.4, 16.4, 15.3, 15.2; IR (KBr): 3455, 3308 cm^{-1}; m/z (EI) (%): 341.2 (28), 203.3 (15), 91.2 (100), 65.3 (10), 58.3 (26), 56.3 (14), 55.3 (13); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}N$, 204.17468; found, 204.17468.

3-methyl-_N_-phenethyl-5-phenylpent-2-en-1-amine (416w)



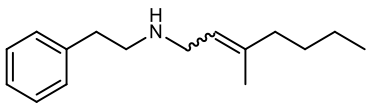
According to general procedure **C4** compound **416w** was synthesized as a colorless liquid (34.1 mg, 0.122 mmol, 61%). Purification by column chromatography (EtOAc:NEt_3 = 100:3). ^{1}H NMR (3:2 mixture of (E)-/(Z)-isomers, 400 MHz, $CDCl_3$): δ 7.36–7.10 (m, 10H), 5.37–5.18 (m, 1H), 3.30–2.99 (m, 2H), 2.98–2.53 (m, 6H), 2.33 (q, *J* = 10.5, 9.5 Hz, 2H), 1.85–1.66 (m, 3H); ^{13}C NMR (mixture of isomers, 101 MHz, $CDCl_3$): δ 142.1, 142.1, 141.9, 140.7, 140.1, 140.0, 137.6, 137.4, 137.3, 137.2, 136.8, 128.7, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 126.1, 125.9, 125.7, 124.4, 123.2, 123.2, 122.1, 55.5, 55.4, 51.2, 51.2, 51.1, 50.8, 50.6, 47.0, 46.8, 41.6, 41.5, 36.4, 36.4, 34.5, 34.4, 34.6, 34.3, 34.3, 34.1, 33.6, 33.5, 23.8, 23.6, 23.4, 16.6, 16.4; IR (KBr): 3316 cm^{-1}; m/z (EI) (%): 281.1 (20), 280.0 (74), 187.9 (60), 158.9 (30), 116.9 (16), 104.9 (17), 90.9 (100), 65.0 (15); HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{26}N$, 280.20598; found, 280.20575.

3-methyl-_N_-phenethylpent-2-en-1-amine (416x)



According to general procedure **C4** compound **416x** was synthesized as a colorless liquid (24.4 mg, 0.120 mmol, 60%). Purification by column chromatography (EtOAc:NEt_3 = 100:3). ^{1}H NMR (1:1 mixture of (E)-/(Z)-isomers, 400 MHz, $CDCl_3$): δ 7.33–7.12 (m, 5H), 5.25–5.13 (m, 1H), 3.22 (t, *J* = 7.6 Hz, 2H), 2.89–2.75 (m, 4H), 2.08–1.90 (m, 2H), 1.64 (d, *J* = 30.4 Hz, 3H), 0.95 (dt, *J* = 17.3, 7.5 Hz, 3H); ^{13}C NMR (1:1 mixture of (E)-/(Z)-isomers, 151 MHz, $CDCl_3$): δ 140.0, 128.7, 128.4, 126.1, 121.0, 50.6, 47.0, 36.3, 32.2, 24.9, 22.9, 16.2, 12.5; IR (KBr): 3314 cm^{-1}; m/z (EI) (%): 204.0 (13), 111.9 (26), 90.9 (100), 84.8 (15), 82.9 (56), 65.0 (15), 55.0 (33), 49.0 (10), 48.0 (28), 47.0 (34); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{22}N$, 204.17468; found, 204.17447.

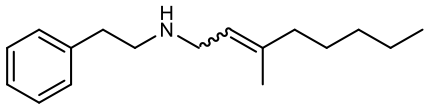
3-methyl-_N_-phenethylhept-2-en-1-amine (416y)



According to general procedure **C4** compound **416y** was synthesized as a colorless liquid (21.8 mg, 0.094 mmol, 47%). Purification by column chromatography (EtOAc:Et_3N = 19:0.1). ^{1}H NMR (2:1 mixture of (E)-/(Z)-isomers, 600 MHz, $CDCl_3$): δ 7.22 (t, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 3H), 5.15 (q, *J* = 6.7, 6.3 Hz, 1H), 3.16 (dd, *J* = 12.8, 6.9 Hz, 2H), 2.88–2.69 (m, 4H), 1.95–1.88 (m, 2H), 1.62 (s, 1H), 1.53 (s, 2H), 1.34–1.16 (m, 4H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (2:1 mixture of (E)-/(Z)-isomers, 151 MHz, $CDCl_3$): δ 140.1, 140.1, 138.2, 128.7, 128.4, 126.1, 122.3, 50.6, 47.1, 39.3, 36.4, 29.9, 22.3, 16.2, 13.9; IR (KBr): 2926, 1452, 1108 cm^{-1}; m/z (EI) (%): 233.1 (17), 232.1 (94), 231.1 (16), 230.1 (18), 141.0 (11),

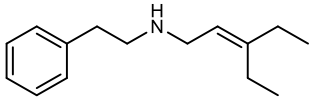
140.0 (100), 111.0 (34), 105.0 (26), 91.0 (86), 77.0 (10), 69.1 (44), 68.0 (11), 65.0 (16), 55.1 (43); HRMS (m/z): $[M+H]^+$ calcd. for $C_{16}H_{26}N$, 232.20598; found, 232.20514.

3-methyl-*N*-phenethyloct-2-en-1-amine (416z)



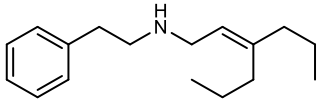
According to general procedure **C4** compound **416z** was synthesized as a colorless liquid (29.0 mg, 0.118 mmol, 59%). Purification by column chromatography (EtOAc:NEt_3 = 99:1). ^1H NMR (2:1 mixture of (E)-/(Z)-isomers, 600 MHz, $CDCl_3$): δ 7.22 (t, *J* = 7.4 Hz, 2H), 7.14 (d, *J* = 7.5 Hz, 3H), 5.15 (t, *J* = 6.4 Hz, 1H), 3.17 (dd, *J* = 13.0, 6.8 Hz, 2H), 2.85–2.72 (m, 4H), 1.92 (dt, *J* = 16.0, 7.6 Hz, 2H), 1.62 (s, 1H), 1.54 (s, 2H), 1.35–1.11 (m, 8H), 0.81 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (2:1 mixture of (E)-/(Z)-isomers, 151 MHz, $CDCl_3$): δ 140.0, 138.7, 138.5, 128.7, 128.5, 126.1, 122.9, 122.1, 50.6, 50.6, 47.0, 46.8, 39.6, 36.3, 33.0, 31.8, 31.5, 30.3, 27.8, 27.4, 23.4, 22.6, 16.2, 14.1; IR (KBr): 3319, 1613 cm^{-1}; m/z (EI) (%): 246.1 (20), 245.1 (10), 155.1 (13), 154.1 (100), 125.1 (18), 105.1 (19), 91.1 (29), 69.2 (50), 57.2 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{28}N$, 246.22163; found, 246.22115.

3-ethyl-*N*-phenethylpent-2-en-1-amine (146aa)



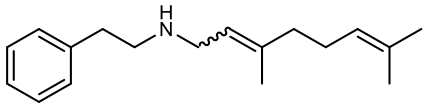
According to general procedure **C4** compound **416aa** was synthesized as a colorless liquid (27.8 mg, 0.129 mmol, 64%). Purification by column chromatography (EtOAc:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.26–7.19 (m, 2H), 7.17 (d, *J* = 6.1 Hz, 3H), 5.27 (t, *J* = 7.2 Hz, 1H), 3.49 (d, *J* = 7.2 Hz, 2H), 3.10–2.95 (m, 4H), 2.06–1.94 (m, 4H), 0.91 (dt, *J* = 15.5, 7.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.5, 128.8, 126.9, 114.2, 48.3, 45.1, 33.5, 29.2, 23.7, 13.2, 12.5; IR (KBr): 2964, 1606, 1027 cm^{-1}; m/z (EI) (%): 363.1 (17), 273.0 (11), 218.1 (48), 217.1 (17), 216.0 (24), 126.0 (100), 104.9 (27), 97.0 (74), 90.9 (42), 79.0 (11), 76.9 (10), 65.0 (12), 55.0 (87); HRMS (m/z): $[M+H]^+$ calcd. for $C_{14}H_{20}N$, 218.19033; found, 218.12961.

***N*-phenethyl-3-propylhex-2-en-1-amine (416ab)**



According to general procedure **C4** compound **416ab** was synthesized as a colorless liquid (29.4 mg, 0.120 mmol, 60%). Purification by column chromatography (EtOAc:NEt_3 = 100:3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.31–7.24 (m, 2H), 7.17 (dd, *J* = 17.9, 7.8 Hz, 3H), 5.24 (dt, *J* = 22.2, 6.7 Hz, 1H), 3.23 (d, *J* = 6.8 Hz, 2H), 2.91–2.78 (m, 4H), 1.96 (dt, *J* = 15.3, 8.3 Hz, 4H), 1.38 (ddt, *J* = 28.8, 15.1, 7.5 Hz, 4H), 0.91–0.81 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.3, 141.9, 140.8, 140.1, 128.7, 128.4, 128.3, 126.1, 125.8, 123.0, 122.0, 55.5, 51.2, 50.7, 46.9, 39.1, 38.9, 36.4, 33.6, 32.5, 32.4, 30.3, 21.7, 21.7, 21.1, 21.1, 14.2, 14.1, 13.9, 13.9; IR (KBr): 3322 cm^{-1}; m/z (EI) (%): 147.0 (21), 145.9 (100), 143.8 (11), 119.8 (29), 103.9 (32), 90.9 (19), 76.9 (35); HRMS (m/z): $[M+H]^+$ calcd. for $C_{17}H_{28}N$, 246.22163; found, 246.22133.

3,7-dimethyl-*N*-phenethylocta-2,6-dien-1-amine (416ac)



According to general procedure **C4** compound **416ac** was synthesized as a colorless liquid (34.1 mg, 0.132 mmol, 66%). Purification by column chromatography (EtOAc:NEt_3 = 100:3). ^1H NMR (major isomer, 400 MHz, $CDCl_3$): δ 7.31–7.25 (m, 2H), 7.21 (d, *J* = 7.5 Hz, 3H), 5.34 (t, *J* = 7.7 Hz, 1H), 5.00 (t, *J* = 5.5 Hz, 1H), 3.48 (d, *J* = 7.3 Hz, 2H), 3.03 (q, *J* = 4.3 Hz, 4H), 2.10–1.99 (m, 4H), 1.64 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (major isomer, 101 MHz, $CDCl_3$): δ 137.8, 131.9, 128.7, 126.7, 123.5, 117.0, 48.5, 45.5, 39.6, 33.9, 26.2, 25.6, 17.7, 16.5; IR (KBr): 3425 cm^{-1}; m/z (EI) (%): 90.9 (86), 82.0 (11), 81.0 (18), 76.9 (11), 69.0 (100), 68.0 (18), 65.0 (21), 55.0 (17), 53.0 (34), 51.0 (11); HRMS (m/z): $[M+H]^+$ calcd. for $C_{18}H_{28}N$, 258.22163; found, 258.22113.

References

[1] a) Y. Ponomaryov, V. Krasikova, A. Lebedev, D. Chernyak, L. Varacheva, A. Chernobroviy, *Chem Heterocycl Comp* **2015**, *51*, 133; b) L. Zhu, L. Chen, *Cellular & molecular biology letters* **2019**, *24*, 40; c) I. Volovych, M. Neumann, M. Schmidt, G. Buchner, J.-Y. Yang, J. Wölk, T. Sottmann, R. Strey, R. Schomäcker, M. Schwarze, *RSC Adv.* **2016**, *6*, 58279.

[2] a) A. J. Béchamp **1854**, 186; b) H.-U. Blaser, H. Steiner, M. Studer, *ChemCatChem* **2009**, *1*, 210; c) *Synfacts* **2011**, *2011*, 1371; d) H. K. Kadam, S. G. Tilve, *RSC Adv.* **2015**, *5*, 83391; e) B. Li, Z. Xu, *Journal of the American Chemical Society* **2009**, *131*, 16380; f) A. M. Tafesh, J. Weiguny, *Chemical reviews* **1996**, *96*, 2035; g) S. Wu, G. Wen, B. Zhong, B. Zhang, X. Gu, N. Wang, D. Su, *Chinese Journal of Catalysis* **2014**, *35*, 914.

[3] a) A. F. Abdel-Magid, S. J. Mehrman, *Org. Process Res. Dev.* **2006**, *10*, 971; b) E. W. Baxter, A. B. Reitz in *Organic Reactions*, John Wiley & Sons, Inc, Hoboken, NJ, USA, **2004**, pp. 1–714; c) R. F. Borch, M. D. Bernstein, H. D. Durst, *J. Am. Chem. Soc.* **1971**, *93*, 2897; d) S. Gomez, J. A. Peters, T. Maschmeyer, *Advanced Synthesis & Catalysis* **2002**, *344*, 1037; e) J. F. Hartwig, *Accounts of chemical research* **2008**, *41*, 1534; f) L. Huang, M. Arndt, K. Gooßen, H. Heydt, L. J. Gooßen, *Chemical reviews* **2015**, *115*, 2596; g) V. I. Isaeva, L. M. Kustov, *Top Catal* **2016**, *59*, 1196; h) S. V. Ley, A. W. Thomas, *Angewandte Chemie (International ed. in English)* **2003**, *42*, 5400; i) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chemical reviews* **2008**, *108*, 3795; j) D. S. Surry, S. L. Buchwald, *Angewandte Chemie (International ed. in English)* **2008**, *47*, 6338.

[4] a) E. Byun, B. Hong, K. A. de Castro, M. Lim, H. Rhee, *The Journal of organic chemistry* **2007**, *72*, 9815; b) R. Cano, D. J. Ramón, M. Yus, *The Journal of organic chemistry* **2011**, *76*, 5547; c) A. M. Jadhav, S. Bhunia, H.-Y. Liao, R.-S. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 1769; d) T. B. Nguyen, L. Ermolenko, A. Al-Mourabit, *J. Am. Chem. Soc.* **2013**, *135*, 118; e) B. Sreedhar, P. S. Reddy, D. K. Devi, *The Journal of organic chemistry* **2009**, *74*, 8806; f) K. Natte, H. Neumann, M. Beller, R. V. Jagadeesh, *Angewandte Chemie (International ed. in English)* **2017**, *56*, 6384; g) L. Wang, H. Neumann, M. Beller, *Angew. Chem.* **2019**, *131*, 5471.

[5] a) W. Adam, O. Krebs, *Chemical reviews* **2003**, *103*, 4131; b) M. Baidya, H. Yamamoto, *Synthesis* **2013**, *45*, 1931; c) D. J. Fisher, G. L. Burnett, R. Velasco, J. Read de Alaniz, *J. Am. Chem. Soc.* **2015**, *137*, 11614; d) E. G. Janzen, *Acc. Chem. Res.* **1971**, *4*, 31; e) H. Kaur, K. H. W. Leung, M. J. Perkins, *J. Chem. Soc., Chem. Commun.* **1981**, 142; f) C. Lagercrantz, *J. Phys. Chem.* **1971**, *75*, 3466; g) J. Ouyang, X. Mi, Y. Wang, R. Hong, *Synlett* **2017**, *28*, 762; h) S. Roscales, A. G. Csákÿ, *Organic letters* **2018**, *20*, 1667; i) F. Tripoteau, L. Eberlin, M. A. Fox, B. Carboni, A. Whiting, *Chemical communications (Cambridge, England)* **2013**, *49*, 5414; j) A. van der Werf, M. Hribersek, N. Selander, *Organic letters* **2017**, *19*, 2374; k) H. Yamamoto, N. Momiyama, *Chemical communications (Cambridge, England)* **2005**, 3514; l) Y. Yamamoto, N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 5962; m) M. Kawasaki, H. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 16482; n) Y. Yu, J. Srogl, L. S. Liebeskind, *Organic letters* **2004**, *6*, 2631.

[6] C. W. Cheung, X. Hu, *Nature communications* **2016**, *7*, 12494.

[7] a) C. Paradisi, G. Scorrano, *Acc. Chem. Res.* **1999**, *32*, 958; b) P. Zuman, B. Shah, *Chem. Rev.* **1994**, *94*, 1621.

[8] a) D. Beaudoin, J. D. Wuest, *Chem. Rev.* **2016**, *116*, 258; b) J. A. Long, N. J. Harris, K. Lammertsma, *The Journal of organic chemistry* **2001**, *66*, 6762.

[9] a) F. Ferretti, D. R. Ramadan, F. Ragaini, *ChemCatChem* **2019**, *11*, 4450; b) F. Ragaini, S. Cenini, E. Gallo, A. Caselli, S. Fantauzzi, *COC* **2006**, *10*, 1479.

[10] a) L. Barboni, G. Bartoli, E. Marcantoni, M. Petrini, R. Dalpozzo, *J. Chem. Soc., Perkin Trans. 1* **1990**, 2133; b) N. Moskalev, M. Mąkosza, *Chem. Commun.* **2001**, 1248; c) Y. N. Bubnov, D. G. Pershin, A. V. Ignatenko, M. E. Gurskii, *Mendeleev Communications* **2000**, *10*, 108.

[11] I. Sapountzis, P. Knochel, *J. Am. Chem. Soc.* **2002**, *124*, 9390.

[12] J. Gui, C.-M. Pan, Y. Jin, T. Qin, J. C. Lo, B. J. Lee, S. H. Spergel, M. E. Mertzman, W. J. Pitts, T. E. La Cruz et al., *Science (New York, N.Y.)* **2015**, *348*, 886.

[13] G. Li, L. Yang, J.-J. Liu, W. Zhang, R. Cao, C. Wang, Z. Zhang, J. Xiao, D. Xue, *Angewandte Chemie (International ed. in English)* **2021**, *60*, 5230.

[14] a) M. Rauser, C. Ascheberg, M. Niggemann, *Angewandte Chemie (International ed. in English)* **2017**, *56*, 11570; b) M. Rauser, C. Ascheberg, M. Niggemann, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2018**, *24*, 3970; c) M. Rauser, R. Eckert, M. Gerbershagen, M. Niggemann, *Angewandte Chemie (International ed. in English)* **2019**, *58*, 6713.

[15] a) G. Li, T. V. Nykaza, J. C. Cooper, A. Ramirez, M. R. Luzung, A. T. Radosevich, *J. Am. Chem. Soc.* **2020**, *142*, 6786; b) G. Li, Z. Qin, A. T. Radosevich, *J. Am. Chem. Soc.* **2020**, *142*, 16205; c) T. V. Nykaza, J. C. Cooper, G. Li, N. Mahieu, A. Ramirez, M. R. Luzung, A. T. Radosevich, *J. Am. Chem. Soc.* **2018**, *140*, 15200; d) T. V. Nykaza, J. Yang, A. T. Radosevich, *Tetrahedron* **2019**, *75*, 3248.

[16] S. Suárez-Pantiga, R. Hernández-Ruiz, C. Virumbrales, M. R. Pedrosa, R. Sanz, *Angew. Chem.* **2019**, *131*, 2151.

[17] S. Roscales, A. G. Csáky, *Advanced Synthesis & Catalysis* **2020**, *362*, 111.

[18] a) C. W. Cheung, M. L. Ploeger, X. Hu, *Nature communications* **2017**, *8*, 14878; b) M. L. Ploeger, A. Darù, J. N. Harvey, X. Hu, *ACS Catal.* **2020**, *10*, 2845; c) N. Shen, C. W. Cheung, J.-A. Ma, *Chem. Commun.* **2019**, *55*, 13709; d) F. Zhou, D.-S. Wang, X. Guan, T. G. Driver, *Angewandte Chemie (International ed. in English)* **2017**, *56*, 4530.

[19] a) G. Deng, W. Chen, C.-J. Li, *Advanced Synthesis & Catalysis* **2009**, *351*, 353; b) Q. Wang, S. Ni, X. Wang, Y. Wang, Y. Pan, *Sci. China Chem.* **2022**, *65*, 678; c) J. Xiao, Y. He, F. Ye, S. Zhu, *Chem* **2018**, *4*, 1645; d) M. Peng, C.-S. Wang, P.-P. Chen, T. Roisnel, H. Doucet, K. N. Houk, J.-F. Soulé, *J. Am. Chem. Soc.* **2023**, *145*, 4508.
[20] A. Studer, D. P. Curran, *Angewandte Chemie (International ed. in English)* **2016**, *55*, 58.
[21] K. P. Kepp, *Inorganic chemistry* **2016**, *55*, 9461.
[22] a) E. Chong, S. A. Blum, *J. Am. Chem. Soc.* **2015**, *137*, 10144; b) A. Issaian, K. N. Tu, S. A. Blum, *Acc. Chem. Res.* **2017**, *50*, 2598; c) J. Lv, B. Zhao, L. Liu, Y. Han, Y. Yuan, Z. Shi, *Advanced Synthesis & Catalysis* **2018**, *360*, 4054; d) K. N. Tu, S. Kim, S. A. Blum, *Organic letters* **2019**, *21*, 1283; e) C.-H. Yang, Y.-S. Zhang, W.-W. Fan, G.-Q. Liu, Y.-M. Li, *Angewandte Chemie (International ed. in English)* **2015**, *54*, 12636.
[23] a) P. Knochel, J. J. Almena Perea, P. Jones, *Tetrahedron* **1998**, *54*, 8275; b) F. M. Piller, A. Metzger, M. A. Schade, B. A. Haag, A. Gavryushin, P. Knochel, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2009**, *15*, 7192.
[24] a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; b) H. W. Gschwend, H. R. Rodriguez in *Organic Reactions*, John Wiley & Sons, Inc, Hoboken, NJ, USA, **2004**, pp. 1–360; c) R. D. Clark, A. Jahangir in *Organic Reactions*, John Wiley & Sons, Inc, Hoboken, NJ, USA, **2004**, pp. 1–314.
[25] a) S.-L. Niu, J. Hu, K. He, Y.-C. Chen, Q. Xiao, *Organic letters* **2019**, *21*, 4250; b) Z. Li, M. Zhang, Y. Zhang, S. Liu, J. Zhao, Q. Zhang, *Organic letters* **2019**, *21*, 5432; c) S. Lee, T. Rovis, *ACS Catal.* **2021**, *11*, 8585; d) V. A. van der Puyl, J. Derosa, K. M. Engle, *ACS Catal.* **2019**, *9*, 224; e) A. Lerchen, T. Knecht, C. G. Daniliuc, F. Glorius, *Angewandte Chemie (International ed. in English)* **2016**, *55*, 15166; f) T. Kang, N. Kim, P. T. Cheng, H. Zhang, K. Foo, K. M. Engle, *J. Am. Chem. Soc.* **2021**, *143*, 13962; g) T. Piou, T. Rovis, *Nature* **2015**, *527*, 86.
[26] a) M. Rauser, D. P. Warzecha, M. Niggemann, *Angewandte Chemie (International ed. in English)* **2018**, *57*, 5903; b) C. Solé, E. Fernández, *Angew. Chem.* **2013**, *125*, 11561; c) M. Suginome, L. Uehlin, M. Murakami, *J. Am. Chem. Soc.* **2004**, *126*, 13196.
[27] a) M. Arrowsmith, M. S. Hill, G. Kociok-Köhn, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2013**, *19*, 2776; b) P. Y. Chavant, M. Vaultier, *Journal of Organometallic Chemistry* **1993**, *455*, 37; c) J. D. Erickson, T. Y. Lai, D. J. Liptrot, M. M. Olmstead, P. P. Power, *Chem. Commun.* **2016**, *52*, 13656; d) A. Harinath, S. Anga, T. K. Panda, *RSC Adv.* **2016**, *6*, 35648; e) D. J. Liptrot, M. Arrowsmith, A. L. Colebatch, T. J. Hadlington, M. S. Hill, G. Kociok-Köhn, M. F. Mahon, *Angewandte Chemie (International ed. in English)* **2015**, *54*, 15280; f) D. J. Liptrot, M. S. Hill, M. F. Mahon, A. S. S. Wilson, *Angewandte Chemie (International ed. in English)* **2015**, *54*, 13362; g) E. A. Romero, J. L. Peltier, R. Jazzar, G. Bertrand, *Chem. Commun.* **2016**, *52*, 10563; h) Z. Yang, M. Zhong, X. Ma, K. Nijesh, S. De, P. Parameswaran, H. W. Roesky, *J. Am. Chem. Soc.* **2016**, *138*, 2548.
[28] a) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2013**, *135*, 4934; b) R. Sakae, K. Hirano, M. Miura, *J. Am. Chem. Soc.* **2015**, *137*, 6460; c) R. Sakae, K. Hirano, T. Satoh, M. Miura, *Angewandte Chemie (International ed. in English)* **2015**, *54*, 613; d) K. Hirano, M. Miura, *J. Am. Chem. Soc.* **2022**, *144*, 648; e) R. Sakae, N. Matsuda, K. Hirano, T. Satoh, M. Miura, *Organic letters* **2014**, *16*, 1228; f) H.-C. Jiang, X.-Y. Tang, M. Shi, *Chem. Commun.* **2016**, *52*, 5273; g) K. Kato, K. Hirano, M. Miura, *Angewandte Chemie (International ed. in English)* **2016**, *55*, 14400; h) D. Nishikawa, K. Hirano, M. Miura, *Organic letters* **2016**, *18*, 4856; i) K. Kato, K. Hirano, M. Miura, *The Journal of organic chemistry* **2017**, *82*, 10418; j) K. Kato, K. Hirano, M. Miura, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2018**, *24*, 5775; k) J. Huo, Y. Xue, J. Wang, *Chem. Commun.* **2018**, *54*, 12266.
[29] a) X. Dong, Q. Liu, Y. Dong, H. Liu, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2017**, *23*, 2481; b) E. Erdik, M. Ay, *Chem. Rev.* **1989**, *89*, 1947; c) K. M. Korch, D. A. Watson, *Chem. Rev.* **2019**, *119*, 8192; d) I. Munir, A. F. Zahoor, N. Rasool, S. A. R. Naqvi, K. M. Zia, R. Ahmad, *Molecular diversity* **2019**, *23*, 215; e) M. J. West, J. W. B. Fyfe, J. C. Vantourout, A. J. B. Watson, *Chem. Rev.* **2019**, *119*, 12491; f) Z. Zhou, L. Kürti, *Synlett* **2019**, *30*, 1525.
[30] a) F. G. Bordwell, Y. Zhao, *The Journal of organic chemistry* **1995**, *60*, 6348; b) N. G. Connelly, W. E. Geiger, *Chem. Rev.* **1996**, *96*, 877; c) D. Formenti, F. Ferretti, F. K. Scharnagl, M. Beller, *Chem. Rev.* **2019**, *119*, 2611; d) R. E. Kyne, M. C. Ryan, L. T. Kliman, J. P. Morken, *Organic letters* **2010**, *12*, 3796; e) G. Tabbì, A. Giuffrida, R. P. Bonomo, *Journal of Inorganic Biochemistry* **2013**, *128*, 137.
[31] a) M. S. Askari, F. Effaty, F. Gennarini, M. Orio, N. Le Poul, X. Ottenwaelder, *Inorganic chemistry* **2020**, *59*, 8678; b) K. A. Emhoff, L. Balaraman, A. M. Salem, K. I. Mudarmah, W. C. Boyd, *Coordination Chemistry Reviews* **2019**, *396*, 124; c) K. D. Karlin (Ed.) *Progress in Inorganic Chemistry*, John Wiley & Sons, Inc, Hoboken, New Jersey, **2014**.
[32] a) L. Dang, Z. Lin, T. B. Marder, *Organometallics* **2010**, *29*, 917; b) H. A. Duong, P. B. Huleatt, Q.-W. Tan, E. L. Shuying, *Organic letters* **2013**, *15*, 4034; c) E. M. Vieira, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 3332; d) R. Wada, T. Shibuguchi, S. Makino, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2006**, *128*, 7687.
[33] a) H. M. L. Davies, D. Morton, *The Journal of organic chemistry* **2016**, *81*, 343; b) W. R. Gutekunst, P. S. Baran, *Chemical Society reviews* **2011**, *40*, 1976; c) L. McMurray, F. O'Hara, M. J. Gaunt, *Chemical Society reviews* **2011**, *40*, 1885; d) P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz, L. Ackermann, *Chem. Rev.* **2019**, *119*, 2192.
[34] a) H. Gilman, R. L. Bebb, *J. Am. Chem. Soc.* **1939**, *61*, 109; b) G. Wittig, G. Fuhrmann, *Ber. dtsch. Chem. Ges. A/B* **1940**, *73*, 1197.

[35] a) J.-M. L'Helgoual'ch, A. Seggio, F. Chevallier, M. Yonehara, E. Jeanneau, M. Uchiyama, F. Mongin, *The Journal of organic chemistry* **2008**, *73*, 177; b) C. J. Rohbogner, S. H. Wunderlich, G. C. Clososki, P. Knochel, *Eur J Org Chem* **2009**, *2009*, 1781; c) M. Á. Fuentes, A. R. Kennedy, R. E. Mulvey, J. A. Parkinson, T. Rantanen, S. D. Robertson, V. Snieckus, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2015**, *21*, 14812; d) M. Uzelac, A. R. Kennedy, E. Hevia, R. E. Mulvey, *Angewandte Chemie (International ed. in English)* **2016**, *55*, 13147; e) R. McLellan, M. Uzelac, A. R. Kennedy, E. Hevia, R. E. Mulvey, *Angew. Chem.* **2017**, *129*, 9694.
[36] P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356.
[37] a) C. Einhorn, J. Einhorn, J.-L. Luche, *Tetrahedron Letters* **1991**, *32*, 2771; b) R. E. Ludt, J. S. Griffiths, K. N. McGrath, C. R. Hauser, *The Journal of organic chemistry* **1973**, *38*, 1668; c) M. G. E. Din, E. E. Knaus, C.-S. Giam, *Can. J. Chem.* **1982**, *60*, 1821.
[38] T. D. Krizan, J. C. Martin, *J. Am. Chem. Soc.* **1983**, *105*, 6155.
[39] a) P. Beak, G. R. Brubaker, R. F. Farney, *J. Am. Chem. Soc.* **1976**, *98*, 3621; b) T. W. Bingham, L. W. Hernandez, D. G. Olson, R. L. Svec, P. J. Hergenrother, D. Sarlah, *J. Am. Chem. Soc.* **2019**, *141*, 657.
[40] A. Frischmuth, M. Fernández, N. M. Barl, F. Achrainer, H. Zipse, G. Berionni, H. Mayr, K. Karaghiosoff, P. Knochel, *Angewandte Chemie (International ed. in English)* **2014**, *53*, 7928.
[41] E. C. Neeve, S. J. Geier, I. A. I. Mkhalid, S. A. Westcott, T. B. Marder, *Chem. Rev.* **2016**, *116*, 9091.
[42] a) R. R. Fraser, T. S. Mansour, S. Savard, *Can. J. Chem.* **1985**, *63*, 3505; b) H. Chikashita, M. Ishibaba, K. Ori, K. Itoh, *BCSJ* **1988**, *61*, 3637.
[43] C. Feng, D. W. Cunningham, Q. T. Easter, S. A. Blum, *J. Am. Chem. Soc.* **2016**, *138*, 11156.
[44] M. Buswell, I. Fleming, U. Ghosh, S. Mack, M. Russell, B. P. Clark, *Organic & biomolecular chemistry* **2004**, *2*, 3006.
[45] S. H. Kim, H. S. Lee, K. H. Kim, J. N. Kim, *Tetrahedron Letters* **2009**, *50*, 6476.
[46] A. Koziara, S. Zawadzki, A. Zwierzak, *Synthesis* **1979**, *1979*, 527.
[47] D. Göbel, N. Clamor, E. Lork, B. J. Nachtsheim, *Organic letters* **2019**, *21*, 5373.
[48] P. L. Creger, *J. Am. Chem. Soc.* **1970**, *92*, 1396.
[49] S. D. Roughley, A. M. Jordan, *Journal of medicinal chemistry* **2011**, *54*, 3451.
[50] P. G. M. Wuts, T. W. Greene, *Greene's Protective Groups in Organic Synthesis*, Wiley, **2006**.
[51] A. Nagaki, H. Kim, H. Usutani, C. Matsuo, J. Yoshida, *Organic & biomolecular chemistry* **2010**, *8*, 1212.
[52] J.-B. Feng, X.-F. Wu, *Advanced Synthesis & Catalysis* **2016**, *358*, 2179.
[53] a) M. Korb, H. Lang, *Chemical Society reviews* **2019**, *48*, 2829; b) M. A. J. Miah, M. P. Sibi, S. Chattopadhyay, O. B. Familoni, V. Snieckus, *Eur J Org Chem* **2018**, *2018*, 447.
[54] a) M. Liu, M. S. Bryant, J. Chen, S. Lee, B. Yaremko, Z. Li, J. Dell, P. Lipari, M. Malkowski, N. Prioli et al., *Cancer chemotherapy and pharmacology* **1999**, *43*, 50; b) L.-J. Yang, S.-H. Wang, S.-Y. Zhou, F. Zhao, Q. Chang, M.-Y. Li, W. Chen, X.-D. Yang, *Materials science & engineering. C, Materials for biological applications* **2017**, *76*, 1136; c) J.-H. Chern, K.-S. Shia, T.-A. Hsu, C.-L. Tai, C.-C. Lee, Y.-C. Lee, C.-S. Chang, S.-N. Tseng, S.-R. Shih, *Bioorganic & medicinal chemistry letters* **2004**, *14*, 2519; d) V. Summa, A. Petrocchi, V. G. Matassa, C. Gardelli, E. Muraglia, M. Rowley, O. G. Paz, R. Laufer, E. Monteagudo, P. Pace, *Journal of medicinal chemistry* **2006**, *49*, 6646; e) H. Anagnostopulos, R. R. Bartlett, U. Elben, P. Stoll, *European Journal of Medicinal Chemistry* **1989**, *24*, 227; f) R. S. Upadhayaya, J. K. Vandavasi, N. R. Vasireddy, V. Sharma, S. S. Dixit, J. Chattopadhyaya, *Bioorganic & medicinal chemistry* **2009**, *17*, 2830.
[55] a) C. Jing, L. Wang, Q. Mahmood, M. Zhao, G. Zhu, X. Zhang, X. Wang, Q. Wang, *Dalton transactions (Cambridge, England : 2003)* **2019**, *48*, 7862; b) C. Jing, L. Wang, G. Zhu, H. Hou, L. Zhou, Q. Wang, *Organometallics* **2020**, *39*, 4019.
[56] a) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069; b) G. Chelucci, S. Baldino, S. Chessa, G. A. Pinna, F. Soccolini, *Tetrahedron: Asymmetry* **2006**, *17*, 3163.
[57] a) S. D. Kuduk, R. M. DiPardo, R. K. Chang, C. Ng, M. G. Bock, *Tetrahedron Letters* **2004**, *45*, 6641; b) M. T. Robak, M. A. Herbage, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 3600; c) J. C. Lanter, H. Chen, X. Zhang, Z. Sui, *Organic letters* **2005**, *7*, 5905; d) J. C. Barrow, P. L. Ngo, J. M. Pellicore, H. G. Selnick, P. G. Nantermet, *Tetrahedron Letters* **2001**, *42*, 2051; e) A. W. Shaw, S. deSolms, *Tetrahedron Letters* **2001**, *42*, 7173; f) G. Liu, P. J. Walsh, J. Mao, *Organic letters* **2019**, *21*, 8514.
[58] a) H. A. Rajapakse, M. B. Young, H. Zhu, S. Charlton, N. N. Tsou, *Tetrahedron Letters* **2005**, *46*, 8909; b) I. Gómez, E. Alonso, D. J. Ramón, M. Yus, *Tetrahedron* **2000**, *56*, 4043; c) N. Weidmann, R. H. V. Nishimura, J. H. Harenberg, P. Knochel, *Synthesis* **2021**, *53*, 557.
[59] D. Lamaa, H.-P. Lin, T. Bzeih, P. Retailleau, M. Alami, A. Hamze, *Eur J Org Chem* **2019**, *2019*, 2602.
[60] J. Clayden, U. Hennecke, *Organic letters* **2008**, *10*, 3567.
[61] a) B.-S. Kim, J. Jiménez, F. Gao, P. J. Walsh, *Organic letters* **2015**, *17*, 5788; b) G. Gao, Y. Fu, M. Li, B. Wang, B. Zheng, S. Hou, P. J. Walsh, *Advanced Synthesis & Catalysis* **2017**, *359*, 2890; c) S. Duan, M. Li, X. Ma, W. Chen, L. Li, H. Zhang, X. Yang, P. J. Walsh, *Advanced Synthesis & Catalysis* **2018**, *360*, 4837.
[62] E. KLEMM, D. KLEMM, H. H. HÖRHOLD, *Synthesis* **1977**, *1977*, 342.
[63] a) H. Ohmiya, H. Yorimitsu, K. Oshima, *Chem. Lett.* **2004**, *33*, 1240; b) T. Niwa, H. Yorimitsu, K. Oshima, *Organic letters* **2007**, *9*, 2373.
[64] G. Dyker, O. Muth, *Eur J Org Chem* **2004**, *2004*, 4319.
[65] D. Kumar, S. Rudrawar, A. K. Chakraborti, *Aust. J. Chem.* **2008**, *61*, 881.

[66] K. Hayashi, J. Griffin, K. C. Harper, Y. Kawamata, P. S. Baran, *J. Am. Chem. Soc.* **2022**, *144*, 5762.
[67] S. R. Tamang, M. Findlater, *Dalton transactions (Cambridge, England : 2003)* **2018**, *47*, 8199.
[68] a) S. Bagherzadeh, N. P. Mankad, *J. Am. Chem. Soc.* **2015**, *137*, 10898; b) S. Hawkeswood, D. W. Stephan, *Dalton transactions (Cambridge, England : 2003)* **2005**, 2182; c) S. Sueki, Y. Kuninobu, *Organic letters* **2013**, *15*, 1544.
[69] C. Kleeberg, A. G. Crawford, A. S. Batsanov, P. Hodgkinson, D. C. Apperley, M. S. Cheung, Z. Lin, T. B. Marder, *The Journal of organic chemistry* **2012**, *77*, 785.
[70] a) C. Pubill-Ulldemolins, A. Bonet, C. Bo, H. Gulyás, E. Fernández, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2012**, *18*, 1121; b) R. B. Bedford, P. B. Brenner, E. Carter, T. Gallagher, D. M. Murphy, D. R. Pye, *Organometallics* **2014**, *33*, 5940.
[71] a) R. L. Reyes, T. Iwai, S. Maeda, M. Sawamura, *J. Am. Chem. Soc.* **2022**, *144*, 10659; b) S. Bera, X. Hu, *Angewandte Chemie (International ed. in English)* **2019**, *58*, 13854.
[72] a) *Topics in Organometallic Chemistry*, Springer Berlin Heidelberg, Berlin, Heidelberg, **2005**; b) J. F. Normant, M. Bourgain, *Tetrahedron Letters* **1971**, *12*, 2583; c) J. F. Normant, A. Alexakis, *Synthesis* **1981**, *1981*, 841.
[73] a) K. Murakami, H. Yorimitsu, *Beilstein journal of organic chemistry* **2013**, *9*, 278; b) E. Lorthiois, C. Meyer in *PATAI'S Chemistry of Functional Groups* (Ed.: Z. Rappoport), John Wiley & Sons, Ltd, Chichester, UK, **2009**.
[74] a) K. Murakami, H. Yorimitsu, K. Oshima, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2010**, *16*, 7688; b) M. Corpet, C. Gosmini, *Chem. Commun.* **2012**, *48*, 11561; c) R. Sallio, M. Corpet, L. Habert, M. Durandetti, C. Gosmini, I. Gillaizeau, *The Journal of organic chemistry* **2017**, *82*, 1254; d) B.-H. Tan, J. Dong, N. Yoshikai, *Angewandte Chemie (International ed. in English)* **2012**, *51*, 9610.
[75] a) D. S. Müller, I. Marek, *Chemical Society reviews* **2016**, *45*, 4552; b) A. B. Flynn, W. W. Ogilvie, *Chem. Rev.* **2007**, *107*, 4698; c) B. H. Lipshutz, S. Sengupta in *Organic Reactions*, John Wiley & Sons, Inc, Hoboken, NJ, USA, **2004**, pp. 135–631.
[76] a) S. Casson, P. Kocienski, *Contemp. Org. Synth.* **1995**, *2*, 19; b) A. Basheer, I. Marek, *Beilstein journal of organic chemistry* **2010**, *6*; c) Y. Minko, M. Pasco, H. Chechik, I. Marek, *Beilstein journal of organic chemistry* **2013**, *9*, 526; d) G. Sklute, C. Bolm, I. Marek, *Organic letters* **2007**, *9*, 1259.
[77] A. Alexakis, N. Krause, S. Woodward in *Copper-Catalyzed Asymmetric Synthesis* (Eds.: A. Alexakis, N. Krause, S. Woodward), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, **2014**, pp. 33–68.
[78] a) M. Simaan, I. Marek, *Beilstein journal of organic chemistry* **2019**, *15*, 752; b) A. Parra, L. Amenós, M. Guisán-Ceinos, A. López, J. L. García Ruano, M. Tortosa, *J. Am. Chem. Soc.* **2014**, *136*, 15833; c) W. M. Sherrill, M. Rubin, *J. Am. Chem. Soc.* **2008**, *130*, 13804; d) V. Tarwade, X. Liu, N. Yan, J. M. Fox, *J. Am. Chem. Soc.* **2009**, *131*, 5382; e) V. Tarwade, R. Selvaraj, J. M. Fox, *The Journal of organic chemistry* **2012**, *77*, 9900.
[79] N. Matsuda, K. Hirano, T. Satoh, M. Miura, *Angewandte Chemie (International ed. in English)* **2012**, *51*, 3642.
[80] M. Rubin, V. Gevorgyan, *Synthesis* **2004**, *2004*, 796.
[81] A. Polley, G. Bairy, P. Das, R. Jana, *Advanced Synthesis & Catalysis* **2018**, *360*, 4161.
[82] G. Cera, M. Lanzi, F. Bigi, R. Maggi, M. Malacria, G. Maestri, *Chem. Commun.* **2018**, *54*, 14021.
[83] a) J. Boersma, J. G. Noltes, *Tetrahedron Letters* **1966**, *7*, 1521; b) D. F. Evans, I. Wharf, *J. Chem. Soc., A* **1968**, 783; c) D. F. Evans, G. V. Fazakerley, *J. Chem. Soc., A* **1971**, 182; d) J. E. Fleckenstein, K. Koszinowski, *Organometallics* **2011**, *30*, 5018; e) K. Koszinowski, P. Böhrer, *Organometallics* **2009**, *28*, 100.
[84] A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *2006*, 890.
[85] a) K. Niedenzu, H. Beyer, J. W. Dawson, H. Jenne, *Chem. Ber.* **1963**, *96*, 2653; b) K. Niedenzu, J. W. Dawson in *Anorganische und Allgemeine Chemie in Einzeldarstellungen* (Eds.: M. Becke-Goehring, K. Niedenzu, J. W. Dawson), Springer Berlin Heidelberg, Berlin, Heidelberg, **1965**, pp. 5–7.
[86] a) M. Suginome, A. Yamamoto, Y. Ito, *Chem. Commun.* **2002**, 1392; b) M. Suginome, L. Uehlin, A. Yamamoto, M. Murakami, *Organic letters* **2004**, *6*, 1167.
[87] a) X. Li, D. G. Hall, *Advanced Synthesis & Catalysis* **2021**, *363*, 2209; b) G. F. S. Fernandes, W. A. Denny, J. L. Dos Santos, *European Journal of Medicinal Chemistry* **2019**, *179*, 791; c) W. Ming, H. S. Soor, X. Liu, A. Trofimova, A. K. Yudin, T. B. Marder, *Chemical Society reviews* **2021**, *50*, 12151.
[88] P. Schreyer, P. Paetzold, R. Boese, *Chem. Ber.* **1988**, *121*, 195.
[89] P. Paetzold in *Advances in Inorganic Chemistry*, Elsevier, **1987**, pp. 123–170.
[90] H. L. D. Hayes, R. Wei, M. Assante, K. J. Geogheghan, N. Jin, S. Tomasi, G. Noonan, A. G. Leach, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **2021**, *143*, 14814.
[91] B. Tian, Q. Liu, X. Tong, P. Tian, G.-Q. Lin, *Org. Chem. Front.* **2014**, *1*, 1116.
[92] P. Binger, M. J. Doyle, *Journal of Organometallic Chemistry* **1978**, *162*, 195.
[93] a) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890; b) D. G. Hall, *Preparation and Applications in Organic Synthesisand Medicine - Boronic Acids*, **2006**; c) E. Fernández, *Synthesis and Application of Organoboron Compounds*, **2015**.
[94] a) K. C. Anderson, P. G. Richardson, I. M. Ghobrial, *Bortezomib in the treatment of multiple myeloma*, Springer, Basel, **2011**; b) S. J. Hecker, K. R. Reddy, M. Totrov, G. C. Hirst, O. Lomovskaya, D. C. Griffith, P. King, R. Tsivkovski, D. Sun, M. Sabet et al., *Journal of medicinal chemistry* **2015**, *58*, 3682; c) O. Lomovskaya, D. Sun, D. Rubio-Aparicio, K. Nelson, R. Tsivkovski, D. C. Griffith, M. N. Dudley, *Antimicrobial agents and chemotherapy* **2017**, *61*; d) J. H. Lai, W. Wu, Y. Zhou, H. H. Maw, Y. Liu, L. J. Milo, S. E. Poplawski, G. D. Henry, J. L. Sudmeier, D. G. Sanford et al., *Journal of medicinal chemistry* **2007**, *50*, 2391; e) W. Wu, Y. Liu, L. J. Milo, Y. Shu, P. Zhao, Y.

Li, I. Woznica, G. Yu, D. G. Sanford, Y. Zhou et al., *Bioorganic & medicinal chemistry letters* **2012**, *22*, 5536; f) S. J. Coutts, T. A. Kelly, R. J. Snow, C. A. Kennedy, R. W. Barton, J. Adams, D. A. Krolikowski, D. M. Freeman, S. J. Campbell, J. F. Ksiazek et al., *Journal of medicinal chemistry* **1996**, *39*, 2087.
[95] S. Jin, C. Zhu, M. Li, B. Wang, *Bioorganic & medicinal chemistry letters* **2009**, *19*, 1596.
[96] a) N. Di Ferrante, R. D. Leachman, P. Angelini, P. V. Donnelly, G. Francis, A. Almazan, G. Segni, C. Franzblau, R. E. Jordan, *Birth defects original article series* **1975**, *11*, 31; b) D. S. Matteson, T.-C. Cheng, *The Journal of organic chemistry* **1968**, *33*, 3055; c) D. S. Matteson, K. M. Sadhu, G. E. Lienhard, *J. Am. Chem. Soc.* **1981**, *103*, 5241; d) D. S. Matteson, K. M. Sadhu, *Organometallics* **1984**, *3*, 614; e) D. S. Matteson, P. K. Jesthi, K. M. Sadhu, *Organometallics* **1984**, *3*, 1284; f) D. S. Matteson, T. J. Michnick, R. D. Willett, C. D. Patterson, *Organometallics* **1989**, *8*, 726; g) D. S. Matteson, *Chem. Rev.* **1989**, *89*, 1535.
[97] a) K. Hong, J. P. Morken, *J. Am. Chem. Soc.* **2013**, *135*, 9252; b) M. A. Beenen, C. An, J. A. Ellman, *J. Am. Chem. Soc.* **2008**, *130*, 6910; c) W. Ming, X. Liu, A. Friedrich, J. Krebs, T. B. Marder, *Organic letters* **2020**, *22*, 365; d) C. Solé, H. Gulyás, E. Fernández, *Chem. Commun.* **2012**, *48*, 3769.
[98] a) N. Hu, G. Zhao, Y. Zhang, X. Liu, G. Li, W. Tang, *J. Am. Chem. Soc.* **2015**, *137*, 6746; b) D.-W. Gao, Y. Gao, H. Shao, T.-Z. Qiao, X. Wang, B. B. Sanchez, J. S. Chen, P. Liu, K. M. Engle, *Nature catalysis* **2020**, *3*, 23; c) Q. Qi, X. Yang, X. Fu, S. Xu, E. Negishi, *Angewandte Chemie (International ed. in English)* **2018**, *57*, 15138.
[99] C. Li, J. Wang, L. M. Barton, S. Yu, M. Tian, D. S. Peters, M. Kumar, A. W. Yu, K. A. Johnson, A. K. Chatterjee et al., *Science (New York, N.Y.)* **2017**, *356*.
[100] L. Xu, *Eur J Org Chem* **2018**, *2018*, 3884.
[101] P. Liu, Y. Zhao, R. Qin, S. Mo, G. Chen, L. Gu, D. M. Chevrier, P. Zhang, Q. Guo, D. Zang et al., *Science (New York, N.Y.)* **2016**, *352*, 797.
[102] a) A. S. Dudnik, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 10693; b) F. Toriyama, J. Cornella, L. Wimmer, T.-G. Chen, D. D. Dixon, G. Creech, P. S. Baran, *J. Am. Chem. Soc.* **2016**, *138*, 11132.
[103] a) T. Awano, T. Ohmura, M. Suginome, *J. Am. Chem. Soc.* **2011**, *133*, 20738; b) A. M. Dumas, A. J. Sieradzki, L. J. Donnelly, *Organic letters* **2016**, *18*, 1848; c) J. Llaveria, D. Leonori, V. K. Aggarwal, *J. Am. Chem. Soc.* **2015**, *137*, 10958.
[104] Q. Xie, G. Dong, *J. Am. Chem. Soc.* **2021**, *143*, 14422.
[105] a) G. Y. Fang, O. A. Wallner, N. Di Blasio, X. Ginesta, J. N. Harvey, V. K. Aggarwal, *J. Am. Chem. Soc.* **2007**, *129*, 14632; b) P. R. Blakemore, M. S. Burge, *J. Am. Chem. Soc.* **2007**, *129*, 3068; c) P. R. Blakemore, S. P. Marsden, H. D. Vater, *Organic letters* **2006**, *8*, 773.
[106] V. K. Aggarwal, J. N. Harvey, R. Robiette, *Angewandte Chemie (International ed. in English)* **2005**, *44*, 5468.
[107] V. K. Aggarwal, G. Y. Fang, A. T. Schmidt, *J. Am. Chem. Soc.* **2005**, *127*, 1642.
[108] C. García-Ruiz, J. L.-Y. Chen, C. Sandford, K. Feeney, P. Lorenzo, G. Berionni, H. Mayr, V. K. Aggarwal, *J. Am. Chem. Soc.* **2017**, *139*, 15324.
[109] R. Lasch, M. R. Heinrich, *The Journal of organic chemistry* **2015**, *80*, 10412.
[110] a) E. K. Edelstein, A. C. Grote, M. D. Palkowitz, J. P. Morken, *Synlett* **2018**, *29*, 1749; b) K. Kiyokawa, S. Kainuma, S. Minakata, *Chem. Lett.* **2019**, *48*, 1116; c) I. P. Klimenko, A. F. Medvedev, V. A. Korolev, G. D. Kolomnikova, Y. V. Tomilov, Y. N. Bubnov, *Journal of Organometallic Chemistry* **2009**, *694*, 2106; d) S. N. Mlynarski, A. S. Karns, J. P. Morken, *J. Am. Chem. Soc.* **2012**, *134*, 16449.
[111] a) C. Diner, K. J. Szabó, *J. Am. Chem. Soc.* **2017**, *139*, 2; b) P. Schäfer, M. Sidera, T. Palacin, S. P. Fletcher, *Chem. Commun.* **2017**, *53*, 12499; c) N. Yoshikai, E. Nakamura, *Chem. Rev.* **2012**, *112*, 2339.
[112] S. Guo, J. C. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **2018**, *140*, 15976.
[113] Y. Yang, S.-L. Shi, D. Niu, P. Liu, S. L. Buchwald, *Science (New York, N.Y.)* **2015**, *349*, 62.
[114] a) M. J. Campbell, J. S. Johnson, *Organic letters* **2007**, *9*, 1521; b) S. Tobisch, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2016**, *22*, 8290; c) S. Tobisch, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2017**, *23*, 17800; d) S. Tobisch, *Chemical science* **2017**, *8*, 4410.
[115] Y. Li, S. Chakrabarty, A. Studer, *Angewandte Chemie (International ed. in English)* **2015**, *54*, 3587.
[116] a) H. Hu, S.-J. Chen, M. Mandal, S. M. Pratik, J. A. Buss, S. W. Krska, C. J. Cramer, S. S. Stahl, *Nature catalysis* **2020**, *3*, 358; b) H.-M. Huang, M. H. Garduño-Castro, C. Morrill, D. J. Procter, *Chemical Society reviews* **2019**, *48*, 4626; c) Z.-L. Li, G.-C. Fang, Q.-S. Gu, X.-Y. Liu, *Chemical Society reviews* **2020**, *49*, 32; d) K. L. Vikse, P. Chen, *Organometallics* **2015**, *34*, 1294; e) F. Wang, P. Chen, G. Liu, *Acc. Chem. Res.* **2018**, *51*, 2036.
[117] a) L. Belding, S. R. Chemler, T. Dudding, *The Journal of organic chemistry* **2013**, *78*, 10288; b) M. C. Paderes, J. B. Keister, S. R. Chemler, *The Journal of organic chemistry* **2013**, *78*, 506.
[118] a) A. E. King, B. L. Ryland, T. C. Brunold, S. S. Stahl, *Organometallics* **2012**, *31*, 7948; b) Q. Zhang, Y. Liu, T. Wang, X. Zhang, C. Long, Y.-D. Wu, M.-X. Wang, *J. Am. Chem. Soc.* **2018**, *140*, 5579.
[119] M. J. Ardolino, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 7092.
[120] N. Miralles, R. Alam, K. J. Szabó, E. Fernández, *Angewandte Chemie (International ed. in English)* **2016**, *55*, 4303.
[121] S. S. Kher, M. Penzo, S. Fulle, P. W. Finn, M. J. Blackman, A. Jirgensons, *Bioorganic & medicinal chemistry letters* **2014**, *24*, 4486.
[122] H. Shalev, D. H. Evans, *J. Am. Chem. Soc.* **1989**, *111*, 2667.
[123] a) H.-M. Huang, P. Bellotti, P. M. Pflüger, J. L. Schwarz, B. Heidrich, F. Glorius, *J. Am. Chem. Soc.* **2020**, *142*, 10173; b) M. S. Kharasch, G. Sosnovsky, *J. Am. Chem. Soc.* **1958**, *80*, 756; c) C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, *53*, 5481.

[124] I. Gallardo, S. Soler, *Journal of Electroanalytical Chemistry* **2017**, *799*, 9.
[125] J. R. Hwu, A. R. Das, C. W. Yang, J.-J. Huang, M.-H. Hsu, *Organic letters* **2005**, *7*, 3211.
[126] E. Paris, F. Bigi, D. Cauzzi, R. Maggi, G. Maestri, *Green Chem.* **2018**, *20*, 382.
[127] U. Sharma, P. Kumar, N. Kumar, V. Kumar, B. Singh, *Advanced Synthesis & Catalysis* **2010**, *352*, 1834.
[128] J. Wu, X. Yang, Z. He, X. Mao, T. A. Hatton, T. F. Jamison, *Angewandte Chemie (International ed. in English)* **2014**, *53*, 8416.
[129] Z. Wang, S. Chen, C. Chen, Y. Yang, C. Wang, *Angewandte Chemie (International ed. in English)* **2023**, *62*, e202215963.
[130] S. Maiti, S. Roy, P. Ghosh, A. Kasera, D. Maiti, *Angewandte Chemie (International ed. in English)* **2022**, *61*, e202207472.
[131] S. Chaudhary, B. R. K. Shyamlal, L. Yadav, M. K. Tiwari, K. Kumar, *RSC Adv.* **2018**, *8*, 23152.
[132] J. D. St Denis, C. C. G. Scully, C. F. Lee, A. K. Yudin, *Organic letters* **2014**, *16*, 1338.
[133] T. Niwa, H. Yorimitsu, K. Oshima, *Angewandte Chemie (International ed. in English)* **2007**, *46*, 2643.
[134] D. N. Mai, R. D. Baxter, *Organic letters* **2016**, *18*, 3738.
[135] J. J. Gladfelder, S. Ghosh, M. Podunavac, A. W. Cook, Y. Ma, R. A. Woltornist, I. Keresztes, T. W. Hayton, D. B. Collum, A. Zakarian, *J. Am. Chem. Soc.* **2019**, *141*, 15024.
[136] Y. Sun, H. Jiang, W. Wu, W. Zeng, X. Wu, *Organic letters* **2013**, *15*, 1598.
[137] D. J. van As, T. U. Connell, M. Brzozowski, A. D. Scully, A. Polyzos, *Organic letters* **2018**, *20*, 905.
[138] S. Bank, M. Gernon, *The Journal of organic chemistry* **1987**, *52*, 5105.
[139] G. Wang, J. Cao, L. Gao, W. Chen, W. Huang, X. Cheng, S. Li, *J. Am. Chem. Soc.* **2017**, *139*, 3904.
[140] Y. Shi, A. V. Gulevich, V. Gevorgyan, *Angewandte Chemie (International ed. in English)* **2014**, *53*, 14191.
[141] L. Cardinale, M.-O. W. S. Schmotz, M. O. Konev, A. Jacobi von Wangelin, *Organic letters* **2022**, *24*, 506.
[142] J. Kumar, E. Suresh, S. Bhadra, *The Journal of organic chemistry* **2020**, *85*, 13363.
[143] W. A. Starmans, L. Thijs, B. Zwanenburg, *Tetrahedron* **1998**, *54*, 629.
[144] A. Edwards, M. Rubina, M. Rubin, *Chemistry (Weinheim an der Bergstrasse, Germany)* **2018**, *24*, 1394.
[145] M. Sayes, G. Benoit, A. B. Charette, *Angewandte Chemie (International ed. in English)* **2018**, *57*, 13514.
[146] L. Mao, K. J. Szabó, T. B. Marder, *Organic letters* **2017**, *19*, 1204.
[147] C. A. Incerti-Pradillos, M. A. Kabeshov, A. V. Malkov, *Angewandte Chemie (International ed. in English)* **2013**, *52*, 5338.
[148] P. Zhang, I. A. Roundtree, J. P. Morken, *Organic letters* **2012**, *14*, 1416.
[149] C. S. Yi, S. Y. Yun, *Organic letters* **2005**, *7*, 2181.
[150] A. Leitner, S. Shekhar, M. J. Pouy, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 15506.
[151] I. T. Alt, C. Guttroff, B. Plietker, *Angewandte Chemie (International ed. in English)* **2017**, *56*, 10582.
[152] J. S. Arnold, G. T. Cizio, H. M. Nguyen, *Organic letters* **2011**, *13*, 5576.
[153] S. Hayashi, H. Yorimitsu, K. Oshima, *Angewandte Chemie (International ed. in English)* **2009**, *48*, 7224.
[154] J. B. Sweeney, A. K. Ball, P. A. Lawrence, M. C. Sinclair, L. J. Smith, *Angewandte Chemie (International ed. in English)* **2018**, *57*, 10202.
[155] A. Bunrit, S. Sawadjoon, S. Tšupova, P. J. R. Sjöberg, J. S. M. Samec, *The Journal of organic chemistry* **2016**, *81*, 1450.
[156] K.-H. Gan, C.-J. Jhong, Y.-J. Shue, S.-C. Yang, *Tetrahedron* **2008**, *64*, 9625.
[157] D. Ghorai, À. Cristòfol, A. W. Kleij, *Euro J of Inorganic Chem* **2022**, *2022*.
[158] M. T. Barros, S. S. Dey, C. D. Maycock, *Eur J Org Chem* **2013**, *2013*, 742.
[159] L. E. Overman, C. E. Owen, M. M. Pavan, C. J. Richards, *Organic letters* **2003**, *5*, 1809.
[160] S. Ge, R. A. Green, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 1617.
[161] F. C. Sequeira, M. T. Bovino, A. J. Chipre, S. R. Chemler, *Synthesis* **2012**, *44*, 1481.
[162] S. W. Kim, L. A. Schwartz, J. R. Zbieg, C. E. Stivala, M. J. Krische, *J. Am. Chem. Soc.* **2019**, *141*, 671.
[163] B. Schmidt, S. Krehl, E. Jablowski, *Organic & biomolecular chemistry* **2012**, *10*, 5119.
[164] S. B. Larsen, B. Bang-Andersen, T. N. Johansen, M. Jørgensen, *Tetrahedron* **2008**, *64*, 2938.
[165] Y. Ma, Z.-Y. Tian, S.-Y. Zheng, C.-P. Zhang, *Synthesis* **2022**, *54*, 2350.
[166] Z. Niu, W. Zhang, P. C. Lan, B. Aguila, S. Ma, *Angewandte Chemie (International ed. in English)* **2019**, *58*, 7420.
[167] R. K. Everett, J. P. Wolfe, *The Journal of organic chemistry* **2015**, *80*, 9041.
[168] H. Chen, A. Kaga, S. Chiba, *Organic letters* **2014**, *16*, 6136.
[169] A. D. Worthy, C. L. Joe, T. E. Lightburn, K. L. Tan, *J. Am. Chem. Soc.* **2010**, *132*, 14757.

Fakultät für Mathematik, Informatik und Naturwissenschaften | RWTH AACHEN UNIVERSITY

Eidesstattliche Erklärung

Ich, Peter Palchuber (geb. 14.11.1993 in Szolnok, Ungarn)

erkläre hiermit, dass diese Dissertation und die darin dargelegten Inhalte die eigenen sindund selbstständig, als Ergebnis der eigenen originären Forschung, generiert wurden.

Hiermit erkläre ich an Eides statt

1. Diese Arbeit wurde vollständig oder größtenteils in der Phase als Doktorand dieser Fakultät und Universität angefertigt;

2. Sofern irgendein Bestandteil dieser Dissertation zuvor für einen akademischen Abschlussoder eine andere Qualifikation an dieser oder einer anderen Institution verwendet wurde, wurde dies klar angezeigt;

3. Wenn immer andere eigene- oder Veröffentlichungen Dritter herangezogen wurden,wurden diese klar benannt;

4. Wenn aus anderen eigenen- oder Veröffentlichungen Dritter zitiert wurde, wurde stets die Quelle hierfür angegeben. Diese Dissertation ist vollständig meine eigene Arbeit, mit der Ausnahme solcher Zitate;

5. Alle wesentlichen Quellen von Unterstützung wurden benannt;

6. Wenn immer ein Teil dieser Dissertation auf der Zusammenarbeit mit anderen basiert, wurde von mir klar gekennzeichnet, was von anderen und was von mir selbst erarbeitetwurde;

7. Kein Teil dieser Arbeit wurde vor deren Einreichung veröffentlicht.

Aachen, 03.01.2024