Synthetic Application of Amphoteric Aziridine Aldehydes and α-Boryl Aldehydes

by

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and α-Boryl Aldehydes

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Abstract

A range of N-H alkynylaziridines were prepared from amphoteric unprotected aziridine aldehydes without protecting-group manipulation. Unprotected α-amino allenes can be obtained from these strained propargyl amines via a 9-BBN mediated hydride transfer. ¹ Further transformation of α-amino allenes to 2,4,6-trisubstituted pyridines was realized. We also developed another class of amphoteric molecules – α-boryl aldehydes, equipped with the tetrahedral MIDA boryl group. ² A wide range of boryl-substituted building blocks or functionalized boronic acid derivatives have been accessed from these bench-stable α-borylcarbonyl compounds. Further chemoselective transformations of these α-boryl aldehyde derived building blocks have been conducted, where α-boryl isocyanates, α-aminoboronic acids, ³ acylboronates, and borylated heterocycles were achieved through the decarboxylative functionalization of α-borylcarboxylic acids.

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Chapter One

Background
1. Background

1.1 Amphoteric molecules

The word “amphoteric” originates from the Greek phrase “amphoteroi” literally meaning “both”. In acid/base chemistry, an amphoteric molecule has the capability to react both as an acid and a base. For instance, amino acids are amphoteric molecules in the sense that they can either donate or accept protons. In general, a molecule containing both nucleophilic and electrophilic sites can be considered “amphoteric”. The most well-known examples of amphoteric molecules are isocyanides, which possess a terminal carbon that can attack an electrophile and be attacked by a nucleophile. The amphoteric nature of isocyanides was widely used in multicomponent transformations, such as the Passerini reaction and the Ugi four-component reaction, to generate peptides and other valuable molecules.\(^1\) In these reactions, the terminal carbon of the isocyanide establishes a connection with both the carboxylic acid (nucleophile) and aldehyde or imine (electrophile). Given the fact that orthogonality between nucleophilic and electrophilic reaction centers renders amphoteric molecules capable of forging multiple bonds in a highly chemoselective fashion, demand for constructing complex molecules with high bonding efficiency encourages development of novel amphoteric building blocks.

1.2 Amphoteric unprotected aziridine aldehydes

1.2.1 Unprotected $\alpha$-amino aldehydes

The versatility of nucleophilic amine and electrophilic aldehyde functionalities in chemical interactions and transformations makes amino aldehydes a class of attractive amphoteric building blocks in terms of organic synthesis. However, an amine and an aldehyde cannot coexist for a prolonged period of time without undergoing inter- or intramolecular condensation or decomposition. Interactions between amines and aldehyde functional groups will generate hemiaminals, which in turn transform to imines or enamines (Scheme 1.1),\(^2\) and result in the decomposition of amino aldehydes. As such, the inherent reactivity of amines and aldehydes poses a significant challenge in the preparation and synthetic utility of unprotected amino aldehydes.
Indeed, unprotected amino aldehydes are rare. A thorough literature search revealed few examples of this type of compound (Figure 1.1). Glucosamine, which was discovered in 1902 by Fischer, is believed to be the first example of an unprotected amino aldehyde. The stability of this molecule is attributed to the formation of a cyclic hemiacetal and the non-nucleophilic HCl salt of the amine. Fischer later attempted to synthesize glycinal, the simplest amino aldehyde. This compound can be only characterized through degradation studies due to its instability.

Stable amino aldehydes were also demonstrated by Myers and co-workers through the use of autoprotection of the aldehyde functionality in α-amino aldehydes by trifluoroacetic acid in methanol. The resulting amphoteric molecules were found to be susceptible to self-condensation above pH 5. In another study carried out by Maruoka, it was suggested that self-condensation of amino aldehydes can be suppressed via the installment of a quaternary α-carbon.

Figure 1.1 Examples of unprotected amino aldehydes
As indicated by examples above, the strategy to access stable unprotected amino aldehydes mainly involves using strong acid conditions to diminish the nucleophilicity of the amino group in conjunction with hemiacetal formation to eliminate the electrophilicity of the aldehyde. The possibility of self-condensation could also be eliminated in structural motifs equipped with quaternary α-carbons and secondary amines. Although effective, these methods can only afford a limited number of unprotected amino aldehydes with poor synthetic value. Accordingly, synthetic application of amino aldehydes has been mainly limited to their N- or C-protected derivatives. Such protection disfavors undesired condensation but produces inconvenience for the removal of protecting groups that is usually not trivial. Therefore, in order to realize rapid assembly of complex molecules without recourse to the protecting group manipulation, development of synthetically useful unprotected amino aldehydes is needed.

1.2.2 Stability of unprotected aziridine aldehydes

In contrast to ordinary primary or secondary amines, aziridines, due to their small ring system, might provide a solution to inhibit the formation of imines or iminium ions. The high kinetic barrier to the formation of an aziridinium ion could obstruct the amine/aldehyde condensation (Scheme 1.2), thereby preventing further decomposition in amino aldehyde condensation. Indeed, when aziridines are reacted with aldehydes, stable carbinolamines (hemiaminals) can be isolated by either distillation or recrystallization, without any observable enamine formation. Therefore, we hypothesized that unprotected aziridine and aldehyde functionalites could potentially co-exist in the same molecule.

Based on this hypothesis, our group recently synthetized a new class of bench-stable unprotected α-amino aldehydes - aziridine aldehydes. It was found that these molecules rest as
unsymmetrical dimers under ambient conditions. No evidence of monomers or symmetrical dimers with a 6-membered ring has been observed in solution (Scheme 1.3).

\[
\begin{align*}
\text{monomer} & \quad \text{aziridinium ion} \\
\text{dimer (symmetrical)} & \quad \text{dimer (unsymmetrical)}
\end{align*}
\]

**Scheme 1.3** Dimerization of aziridine aldehydes

Most intriguingly, a crystal structure of the aziridine aldehyde dimer revealed that the compound exists as a single, homochiral diastereomer. A hydrogen bonding interaction between the N-H aziridine and the hemiaminal was observed (Figure 1.2). This interaction is believed to be another contribution, in addition to the intrinsic kinetic barrier of aziridinium ion formation, to the stability of homochiral aziridine aldehyde dimer molecules.
1.2.3 Preparation of unprotected aziridine aldehydes

Unprotected aziridine aldehydes can be prepared from readily available starting materials. N-H aziridine esters serve as general precursors of aziridine aldehydes through DIBAL-H reduction. Three different ways could be implemented to synthesize N-H aziridine ester precursors (Scheme 1.4). Route A employs a lithiation-promoted N-to-C Boc-transfer of the Boc protected aziridine, which can be obtained from the corresponding Boc-protected α-amino acid through a sequence of transformations involving carbamate formation, NaBH$_4$ reduction, tosylation and cyclization. Route B uses serine as the starting material. After converting the α-amino acid to its corresponding ester, a Mitsunobu reaction can be carried out to generate the N-H aziridine ring. Route C starts with the oxiranyl carboxylic esters. The ring-opening of epoxides with sodium azide is followed by the Staudinger reaction to install the aziridine rings.
1.2.4 Reactivity of unprotected aziridine aldehydes

In order to test the reactivity of aziridine aldehyde dimers, a series of transformations were investigated. At the outset, aziridine aldehyde dimers were subjected to reductive amination conditions in the presence of α-amino acid or peptide derivatives (Scheme 1.5). The successful preparation of the aziridine amine demonstrated that the aziridine functional group is orthogonal to the aldehyde functionality in the course of the reaction, allowing selective reactivity with an external amine species. Importantly, no epimerization and overalkylation was observed in this reaction. The absence of epimerization was attributed to energetically uphill enolization of the strained aziridine aldehyde and short lifetime of the “half-opened” imine intermediate. It is hypothesized that the unobservably low concentration of free monomeric aldehydes, due to a fast dimerization, resulted in no overalkylation.
The electrophilic reactivity of the aldehyde function in aziridine aldehyde dimers was further evaluated in an indium(0)-mediated allylation using THF/water as the solvent system.\textsuperscript{13} The reactions afforded a wide range of aziridine alcohols as single diastereomers in excellent isolated yields. DFT analysis of the transition structure of the reaction was consistent with a pocket made out of one nitrogen and two oxygen atoms surrounding the indium center (Scheme 1.6). This highly organized transition structure was believed to account for the high level of diastereoselectivity of the transformation.

Scheme 1.5 Reductive amination of aziridine aldehydes

Scheme 1.6 Indium-mediated diastereoselective allylation of aziridine aldehydes
Another utilization of the aldehyde function of aziridine aldehydes involved the implementation of Horner-Wadsworth-Emmons reaction, which afforded unprotected C-vinyl aziridines successfully (equation 1.1). Treating the aziridine aldehydes with stabilized phosphorous ylide reagents in 2,2,2-trifluoroethane (TFE) resulted in the vinyl aziridines in good yield with high selectivity. TFE has been shown to promote partial dissociation of the aziridine aldehyde dimers due to its weak acidity (pKa 12.4 in DMSO) and capability as hydrogen-bond donor.

\[
\text{R} - \text{N} = \text{CH} - \text{OH} \stackrel{\text{Ph}_3\text{P} = \text{COOEt}}{\text{TFE}} \rightarrow \text{R} - \text{CH} = \text{N} - \text{COOEt}
\]

\[(E/Z > 95:5)\]  

In order to expand the synthetic applications of aziridine aldehydes, reactions involving the nucleophilic aziridine nitrogen were also investigated. Although the basicity of its nitrogen is significantly diminished compared to other secondary amines due to the ring strain and increased s-character of the nitrogen’s lone-pair electrons, aziridine usually still behaves as good nucleophile. This could be explained by the steric availability of the aziridine nitrogen in nucleophilic attacks.

Assisted by initial interaction of the aldehyde functionality with nucleophiles, the aziridine nitrogen could participate in the downstream transformation of a cascade process. It was found that reactions between aziridine aldehyde dimers and N-benzyl tryptamine resulted in complex pentacyclic alkaloid cores through a single cascade transformation in TFE or toluene (Scheme 1.7). The structure of the product implied that an intercepted Pictet-Spengler reaction, initiated by the trapping of aziridine aldehydes by iminium ion formation, has taken place. The electrophilic aromatic addition of the iminium ion to the ipso-position of the indole ring constructed a spiro five membered ring with concomitant generation of a cyclic iminium ion. The nascent unstable iminium ion was subsequently attacked by the aziridine nitrogen intramolecularly to afford the final pentacyclic scaffold.
Besides reactions initiated by the aldehyde functionality, cascade processes starting directly with the nucleophilic attack of the aziridine nitrogen were also developed. It was found that treatment of aziridine aldehyde dimers with phenyl isocyanate in diethyl ether afforded dimeric carbamate derivatives in quantitative yield as a result of simple addition of the aziridine aldehyde dimer to the carbon-nitrogen double bond of the isocyanates (Scheme 1.8). Comparatively, reactions in protic solvent system consisting of a mixture of 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HFIP) and water (8:2) resulted in exclusive formation of an aziridine fused bicycle product (a reduced hydantoin) (Scheme 1.8).\(^{16}\) HFIP, which is analogous to TFE, is also believed to be a good solvent to promote aziridine aldehyde dimer dissociation. The production of the reduced hydantoin product in HFIP/water was hypothesized to result from collapse of the dimeric carbamate intermediate, followed by an intramolecular 5-(enol-endo)-exo-trig cyclization. This hypothesis was supported by the discovery that subjecting dimeric carbamate intermediate, which was isolated from the reaction in diethyl ether, to the same HFIP/water solvent system afforded the same hydantoin product. The monomeric aziridine aldehyde released from the collapse of the intermediate re-dimerized and re-entered the reaction cycle.
Another reaction initiated by the nucleophilic aziridine attack occurred when dimeric aziridine aldehydes were treated with $\alpha,\beta$-unsaturated aldehydes in the presence of benzoic acid and pyrrolidine.\(^{17}\) Formal Baylis-Hillman products were obtained in excellent yields and diastereoselectivities (Scheme 1.9). It is hypothesised that an eight-membered intermediate was formed via the initial Michael addition of the available aziridine nitrogen to the $\alpha,\beta$-unsaturated aldehyde, followed by intramolecular interaction between the enamine and the aldehyde group. Subsequent elimination of the aziridine re-installed the conjugate system, which afforded the final isolated products. The released monomeric aziridine aldehyde, again, re-dimerized to form the starting aziridine aldehyde dimer.
These synthetic applications of aziridine aldehyde dimers demonstrated their amphoteric nature taking effect in complex chemical transformations. The dimeric structures of these unprotected α-amino aldehydes do not inhibit their reactivity. Partial dissociation of aziridine aldehyde dimers and the initial interactions of their nucleophilic or electrophilic reacting sites controlled by solvents, temperature, or acid/base additives and other reagents determine the complexities of the final products and the utility of these amphoteric entities.

1.3 Amphoteric α-metallocarbonyl compounds

Encouraged by the successful synthesis and application of aziridine aldehydes, a versatile amphoteric platform containing nucleophilic nitrogen and electrophilic carbon over the span of three atoms, we are interested in developing new types of stable and valuable amphoteric entities for organic synthesis containing both nucleophilic and electrophilic carbon centers. We envision
that $\alpha$-metallocarbonyl species (C-enolates) would be a good target for such a purpose. In principle, molecules bearing the $\alpha$-metallocarbonyl structures contain the electrophilic carbonyl carbon and the nucleophilic $\alpha$-carbon equipped with electropositive metal or metalloid atoms (Scheme 1.10). However, compared to their $O$-binding tautomers, $\alpha$-metallocarbonyl compounds are normally thermodynamically unstable and cannot survive ambient conditions. Although examples of $\alpha$-metallocarbonyl complexes derived from transition metals, particularly late transition metals, are common, stable ones possessing main-group metals or metalloids are scarce. Developing stable amphoteric main-group $\alpha$-metallocarbonyl building blocks that could be used for day-to-day synthetic production still remains a challenge.

![Scheme 1.10 Equilibrium between C- and O-enolates](image)

1.3.1 $\alpha$-Silylcarbonyl compounds

The relatively stable main group $\alpha$-metallocarbonyl compounds, although rare, are not unknown. The most extensively investigated case is $\alpha$-silylcarbonyl compounds, which can be isolated by silica gel chromatography or distillation. Generally, $\alpha$-silyl aldehydes are the most unstable among all types of $\alpha$-silylcarbonyl compounds (Figure 1.3). The decomposition is mainly attributable to the weakness of carbon-silicon bond, which can be easily cleaved by the attack of nucleophiles at the silicon center. Increasing the steric hindrance around the silicon atom could usually result in higher stability. As indicated in Figure 1.3, the more electron deficient the
carbonyl group is, the weaker the carbon-silicon bond becomes, thus less stable the \( \alpha \)-silylcarbonyl species are. This could be attributable to the considerable hyperconjugative interaction between silicon-carbon bonds and \( \pi^* \)-orbitals of the nearby carbonyl group, which is quite similar to the \( \beta \)-effect. This hyperconjugative interaction can be evidenced in the infrared spectra of \( \alpha \)-silyl esters, which have a characteristic C=O bond stretching band at 1720 to 1735 cm\(^{-1}\) that is 20 to 25 cm\(^{-1}\) lower than that of a normal ester.\(^{22}\)

![Figure 1.3 Stability of \( \alpha \)-silylcarbonyl compounds](image)

1.3.1.1 Synthesis of \( \alpha \)-silylcarbonyl compounds

\( \alpha \)-Silyl carbonyl compounds can be readily prepared by various ways.\(^{19}\) C-Silylation of enolates and derivatives represent a generally applicable route to \( \alpha \)-silyl esters, acids or amides. For instance, the silylation of cyclobutylcarboxylic acid with chloro(methyl)diphenylsilane in the presence of two equivalent of LDA affords the \( \alpha \)-silylcaboxyclic acid product in good yield (Scheme 1.11A). Under similar condition, acetamide can produce the desired \( \alpha \)-silyl amide as the sole product (Scheme 1.11B). These methods are usually not applicable to direct synthesis of \( \alpha \)-silyl aldehydes or ketones, due to the formation of significant amount of \( O \)-silylation by-products. However, treatment of the imine derivatives of corresponding aldehydes or ketones with lithium diisopropylamide (LDA) followed by silyl halides or triflates will produce the \( \alpha \)-silyl imines, which can be transformed to \( \alpha \)-silyl aldehydes or ketones by simple hydrolysis (Scheme 1.11C).
For the preparation of α-silyl aldehydes and ketones, rearrangement of α,β-epoxysilanes probably is the most popular way. The starting α,β-epoxysilanes can be easily prepared by mCPBA epoxidation of readily available vinylsilanes. By treating with protic acids or Lewis acids, the epoxide ring opens at the β-carbon to the silicon center with a concomitant [1,2]-silyl migration to install the carbonyl group. For instance, Maruoka and coworkers reported a preparation of α-silyl aldehydes by using stoichiometric amount of bulky organoaluminum regent (Scheme 1.10A). The epoxide ring opening may also be initiated using transition-metal catalysis. Palladium(0) catalyst has been utilized to rearrange α-silylated β-vinylloxiranes (Scheme 1.10B). The reaction proceeded through a π-allylpalladium complex with a similar [1,2]-silyl migration occurring with complete transfer of chirality. The method is restricted to sterically hindered silicon groups and furnishes α-silylated β,γ-unsaturated aldehydes in good yields.
Another extensively employed methodology to synthesize α-silyl ketones is the addition of α-silyl organometallic species to carboxylic acid derivatives (Scheme 1.13). Due to the α-silicon effect, α-silylated copper, magnesium, or lithium reagents with stabilized α-silyl carbanions can be readily prepared via metal–halogen, metal–sulfur, and metal–tin exchange. Treatment of α-silyl organometallic species to acyl halides, for instance, produced a variety of α-silyl ketones in good yields.\textsuperscript{25} The sterically demanding and electronically stabilizing silicon group is believed to inhibit the addition of a second equivalent of the nucleophile to the carbonyl group of the α-silyl ketone.
1.3.1.2 Reactivity of α-silylcarbonyl compounds

As amphoteric molecules, α-silylcarbonyl compounds can react with either electrophiles or nucleophiles. Desilylation of α-silylcarbonyl compounds in the presence of fluoride ions generates formal enolate ions, which can add to various electrophiles. For instance, addition of α-(trimethylsilyl)acetates to benzaldehyde in the presence of TBAF gave β-hydroxy acids with predominantly syn stereochemistry (Scheme 1.14A).26 On the other hand, based on the reactivity of their carbonyl groups towards nucleophiles, α-silylcarbonyl compounds such as α-silyl aldehydes or ketones readily react with reducing agents (e.g., LiAlH₄, DIBAL-H, NaBH₄),27 Wittig,28 Grignard or organolithium reagents.29 A practical way of synthesizing cis-olefin utilized the nucleophilic reaction of α-silyl aldehydes with n-butyllithium to generate corresponding β-hydroxysilanes, which in turn underwent a stereospecific silyl-Wittig or Peterson elimination30 to install the carbon-carbon double bond under the basic condition (Scheme 1.14B).31 A phenyl α-silyl aldehyde bearing the tert-butylphenylsilyl group was used in this synthesis. The bulky silyl group enhances the stereoselectivity of the silyl alcohol formation, thus providing high yields of stereo-defined alkenes.

![Scheme 1.13 Addition of α-silyl organometallic reagents to carbonyl precursors](image)

![Scheme 1.14 Reaction examples of α-silylcarbonyl compounds](image)
Recently, Lee and co-workers reported a new cyclopropene preparation utilizing both the carbonyl group and carbon-silicon bond of α-silyl ketones (Scheme 1.15). Treatment of the α-silyl ketone with lithiated trimethylsilyldiazomethane afforded an unexpected cyclopropene product resulting from the intramolecular insertion of the alkylidene carbene to the nearby Cα–Si bond. Anticipated products from the Cγ–H bond insertion were not observed. These results indicated a more favorable interaction of the empty p-orbital of the carbenic carbon with the nearby carbon-silicon bond, which is analogous to the β-silicon effect.

\[
\text{Scheme 1.15 Cyclopropenation from α-silyl ketones}
\]

1.3.2 α-Boxylcarbonyl compounds

Due to the diagonal relationship, boron compounds usually have similar chemical or physical properties as silicon compounds. From the stability of α-silylcarbonyl molecules, one can intuitively extrapolate the possibility of stable α-boxylcarbonyl species. However, direct evidence in support of the α-boxylcarbonyl compounds (C-bound boron enolates) is sparse.
despite the fact that they have been proposed as reactive intermediates in many transformations.\(^{34}\)

### 1.3.2.1 Detection of transient $\alpha$-borylcarbonyl species

A few examples of direct identification of reactive $\alpha$-borylcarbonyl intermediates using spectroscopic methods recently emerged. In 2002, Abiko first reported the $^1$H NMR characterization of a transient C-boron enolate of 2,6-diisopropylphenyl acetate when treating the acetate with $c$-Hex$_2$BOTf and triethylamine in deuterated chloroform (Figure 1.3A).\(^{35a}\) Two years later, Marder identified a series of $\alpha$-boryl ester intermediates possessing two pinacolylboryl groups at both $\alpha$- and $\beta$-position of the ester group when carrying out platinum catalyzed 3,4-diboration of $\alpha,\beta$-unsaturated esters (Figure 1.3B).\(^{35b}\) Shea and co-workers recently described a BH$_3$-catalyzed oligomerization of ethyl diazoacetate.\(^{35c}\) The key C-boron enolate intermediate, generated from the treatment of ethyl diazoacetate with BH$_3$·SMe$_2$, was fully characterized with $^1$H, $^{13}$C and $^{11}$B NMR (Figure 1.3C). The intermediate is diethyl 2-borylsuccinate. Its considerable downfield $^{13}$C NMR shift of one of the ester carbonyl group (190.6 ppm) and upfield $^{11}$B NMR shift of the boron center (11.7 ppm) indicated a strong coordination between the carbonyl oxygen and the boron atom forming a five membered ring structure.

**Figure 1.4** Examples of spectroscopically identified $\alpha$-borylcarbonyl (C-boron enolate) intermediates
1.3.2.2 Stable $\alpha$-borylcarbonyl compounds

In general, enolates with $O$-bound boron are much more stable thermodynamically, and isomerizations from $C$-bound enolates to $O$-bound enolates are fast. The typical difference in stability between $O$-bound and $C$-bound boron enolates is estimated as $\sim 20$ kcal/mol.\(^{36}\) The strong affinity of electron-deficient $sp^2$-hybridized boron to oxygen provides the driving force for the isomerization. Hence, it is conceivable that a strategy for stabilizing $\alpha$-borylcarbonyl compounds is to install electron-rich boron centers that have much weak propensity to coordinate to carbonyl oxygen thermodynamically and kinetically.

Indeed, thorough literature search afforded four examples of stable $\alpha$-borylcarbonyl compounds, which were isolated and fully characterized. A class of stable $\alpha$-borylcarboxylic esters with $\beta$-hydrozonyl groups was obtained from the hydroboration of enehydrazones and their derivatives (Scheme 1.16A).\(^{37}\) The strong electron donation from the hydrazone nitrogen to the boron centers leads to stabilization of these molecules. A series of stable $\alpha$-boryl amides with the common structure of dimeric four-membered rings were isolated by Paetzold and co-workers from the reaction between bis(dialkylamino)halaboranes and ketenes (Scheme 1.16B).\(^{38}\) The coordination of the amino group contributed from the second molecule of the $\alpha$-boryl product resulted in a stable cyclic “ate” complex. Another case of stable $\alpha$-borylcarbonyl compounds was discovered by Bürger et al. in treating dimethylaminobis(trifluoromethyl) borane with carbonyl compounds via an ene-type transformation (Scheme 1.16C).\(^{39}\) The reaction produced a family of stable $\alpha$-bis(trifluoromethyl)boryl ketones, esters and amides, which are stabilized by the strong coordination of dimethylamine nitrogen to boron centers. These $\alpha$-borylcarbonyl products can be handled under ambient temperature and purified by sublimation in \textit{vacuo}. The final example of stable $\alpha$-borylcarbonyl species contains a heterocyclic borate complex, which was prepared by Danion-Bougot in 1995 (Figure 1.16D).\(^{40}\) This molecule, in the form of a potassium borate salt, was obtained by the hydroboration of methyl 2-(acetylamino)acrylate.
Scheme 1.16 Examples of isolated and fully characterized \( \alpha \)-borylcarbonyl compounds

These examples of stable \( \alpha \)-borylcarbonyl compounds discussed above demonstrated the pivotal role of the tetracoordinate boron center in stabilizing C-boron enolates. By adding an extra ligand to the \( sp^2 \)-boron centers, the new formed electron-rich \( sp^3 \)-boron will be thermodynamically less prone to undergo the migration to carbonyl oxygen. In addition, the interaction between the empty \( p \)-orbital of trivalent boron and the lone-pair electrons of oxygen, which likely initiates the fast 1,3-sigmatropic shift, will be kinetically (mechanically) no longer available in the case of tetrahedral boron center.
Although stable during isolation and characterization, these amphoteric $\alpha$-borylcarbonyl compounds equipped with tetracoordinate boron centers have no downstream synthetic application, likely because of their inconvenience in handling and preparation. Functional group tolerance might be another problem. Tetracoordinate boryl groups in these molecules, although relatively stabilized, are still vulnerable for most of chemical transformations. As such, new generations of this class of amphoteric molecules which are suitable for further chemical manipulations of are desirable.

1.4 Summary

Unprotected aziridine aldehydes are amphoteric molecules containing a nucleophilic amine nitrogen and an electrophilic aldehyde carbon as two orthogonal reaction centers over the span of three atoms. The dimeric nature of these molecules does not prevent their reactivity towards nucleophiles and electrophiles. A wide range of transformations leading to multi-functionalized compounds have been developed based on aziridine aldehydes, attesting potential and high efficiency of these new building blocks in complex structure construction. New synthetic utilities of aziridine aldehydes will be explored.

Different from aziridine aldehydes, $\alpha$-metallocarbonyl compounds ($C$-bound enolates) are amphoteric entities with nucleophilic and electrophilic carbon centers adjacent to each other. $\alpha$-Silylcarbonyl compounds are the most explored stable molecules of this sort. Reactions involving their electrophilic carbonyl group or nucleophilic carbon-silicon bond demonstrated the potential of these amphoteric reagents in organic synthesis. Unlike $\alpha$-silylcarbonyl compounds, the boron analogues are not so common. $\alpha$-Borylcarbonyl species with electron-deficient trivalent boron are unstable and can be barely detected in-situ with spectroscopic methods. Installation of electron-rich tetracoordinate boron centers supplies solutions to access stable $\alpha$-borylcarbonyl molecules. Considering the great progress in organoboron chemistry in the past decades, the amphoteric $\alpha$-borylcarbonyl compounds will find valuable applications in organic synthesis.
1.5 References


Chapter Two

*N-H Alkynylaziridines and their applications*
2 N-H Alkynylaziridines and their applications

2.1 Introduction

This chapter describes the research toward the synthesis of N-H alkynylaziridines from unprotected aziridine aldehydes. The synthetic utility of these versatile building blocks will also be discussed.

2.1.1 Conjugative interactions between strained rings and $\pi$-systems

In general, strained rings such as cyclopropanes, epoxides and aziridines are known to partake in hyperconjugative interactions with $sp^2$ or $sp$ carbon-containing functional groups, such as carbonyl compounds, alkenes and alkynes.\(^1\) These interactions originate from the overlaps of the Walsh-type orbitals\(^2\) of the three-membered ring and the $\pi$-orbitals of the functional groups (Scheme 1). These interactions are known to stabilize the ground state and assist in lowering the activation barriers of reactions. The stabilization effects are attributed to interactions between the $\pi$-bonding orbitals and $\omega_S$ or $\omega_A$ orbitals of the three membered rings, whereas interactions between the filled $\pi$-bonding orbitals and the anti-bonding orbital $\sigma^*$ (LUMO) of the strained rings destabilize the system and make them active towards ring opening reactions.

\[X = \text{CH}_2, \text{O, NR}\]

\[\omega_S + \pi\]

\[\omega_A + \pi\]

\[\sigma^* + \pi\]

Figure 2.1 Hyperconjugation between three-membered rings and $\pi$-functional groups

We opted to employ this class of interactions as a guide to discovering molecules with useful reactivity. Among the three-membered rings studied, aziridine is one of the most versatile functionalities for nitrogen-containing compounds synthesis. Therefore, molecules with conjugative interactions between aziridine ring and $\pi$-system were of particular interest to us. Specifically, our goal was to evaluate arrangements that contain unprotected aziridine and
acetylene units, namely N-H alkynylaziridines, which have been proven to be extremely useful building blocks for preparation of various types of synthetic or natural compounds. However, despite their apparent simplicity and enormous synthetic potential, methods to synthesize these molecules have remained elusive.

### 2.1.2 Synthesis of alkynylaziridines in literature

Very few procedures for synthesizing alkynylaziridines have been described. Alkynylaziridines had been prepared by ruthenium catalyzed nitrene addition to enynes, Mitsunobu reaction of amino alcohols bearing an ethynyl group or debromination of 2-(1-bromovinyl)aziridines, intramolecular amination of bromoallenes, aziridination of alkynyl aldehydes with guanidinium ylides, and aza-Darzens reaction of propargylic sulfonium ylides, cerium acetylides, lithium acetylides or allenylzincs with imines. While chiral products usually could be obtained in high stereoselectivities by using these methodologies, none of the resulted alkynylaziridines were free of protecting groups on the aziridine nitrogen. A single synthetic example for N-H free alkynylaziridines with an internal carbon-carbon triple bond was demonstrated by Chen and co-workers. However, to the best of our knowledge, no precedent research on direct synthesis of N-H free ethynylaziridines (terminal alkynes) has been reported.

### 2.2 Synthesis of N-H alkynylaziridines from aziridine aldehydes

As aldehyde functionalities are efficient progenitors for carbon-carbon triple bonds, our recent studies in the field of unprotected aziridine aldehydes provide an opportunity to directly achieve the N-H free alkynylaziridines rapidly without protecting-group manipulations. The dimeric nature of aziridine aldehydes does not limit their reactivity towards soft nucleophiles, such as organoindium species or phosphorous ylides. Partial dissociation of aziridine aldehyde dimers enables transformations of the aldehyde functional group and is expected to promote reactions with other potential carbon nucleophiles for the desired carbon-carbon triple bond construction.

#### 2.2.1 N-H Ethynylaziridines via homologation of aziridine aldehydes

We initially used Corey-Fuchs procedure to synthesize the desired terminal N-H ethynylaziridine synthesis (Scheme 2.1). While the first Wittig-type transformation of aziridine aldehyde dimer
2.1a afforded the intermediate dibromoolefin 2.3, the second step of this process, namely, the n-butyllithium promoted conversion of the dibromoolefin to the ethynyl end point, was plagued by rapid formation of intractable tars due to ring-opening.

![Scheme 2.1](image)

**Scheme 2.1** Initial attempt to synthesize N-H ethynylaziridine via Corey-Fuchs procedure

Afterwards, the milder one-step Seyferth-Gilbert homologation\(^{19}\) was alternatively applied. The aziridine aldehyde dimer 2.1a was treated with Bestmann-Ohira reagent\(^{20}\) in dry methanol in the presence of potassium carbonate at room temperature for 5 hours. Satisfactorily, the expected N-H ethynylaziridine 2.2a was furnished as a bench-stable crystal in 95% yield. In order to evaluate the generality of this preparation, a series of aziridine aldehyde dimers with different substituents was tested (Table 2.1). To our delight, the reaction worked well not only with alkyl-substituted aziridine aldehydes (2.1g-h), but also with electron-neutral (2.1a), rich (2.1b), and deficient (2.1c) aryl substituted substrates. The thiophenyl-substituted aziridine aldehyde dimer 2.1d and hindered substrates (2.1e-f) also showed excellent reactivity in this process.

**Table 2.1** N-H Terminal ethynylaziridines from aziridine aldehyde dimers\(^a\)
<table>
<thead>
<tr>
<th>Entry</th>
<th>Aziridine aldehyde dimer</th>
<th>Product</th>
<th>Yield&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td>95%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td>84%</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td>76%</td>
</tr>
</tbody>
</table>
Reactions were carried out using 1.0 equiv of aziridine aldehyde dimer, 2.2 equiv of Bestmann-Ohira reagent and 4.0 equiv of K₂CO₃ in methanol at 25 °C. * Isolated yields.

Interestingly, despite a possibility for decomposition through intermolecular attack of the nucleophilic aziridine nitrogen at the alkyne carbon (causing S₉2’ scission), the unprotected N-H ethynylaziridines were found to be stable up to at least 100 °C. We were curious to examine the molecular structure of these molecules as a way of probing their electronic properties; an X-ray structure of N-H ethynylaziridine 2.2c, shown in Figure 2.2, confirmed the presence of a
stabilizing aziridine/alkyne interaction. The average length of the C3(aziridine)−C2(acetylene) bond is 1.444Å, which is significantly shorter than a typical C(sp3)-C(sp) single bond (1.472Å). The shortening of the carbon-carbon bond demonstrated the existence of hyperconjugative stabilizing effect between the aziridine ring and the acetylene function.

![Figure 2.2 X-ray structure of N-H ethynylaziridine 2.2c](image)

2.2.2 Internal N-H alkynylaziridines via Sonogashira coupling

The facile access to N-H ethynylaziridines from unprotected aziridine aldehyde dimers encouraged us to further explore the possibility of expanding the scope of alkynylaziridines. We worked towards converting the terminal acetylene functionality to internal alkynes equipped with different substituents. We opted to use Sonogashira coupling as a way to achieve this goal. 3-Phenyl substituted N-H ethynylaziridine 2.2a was first selected as the testing ground. By subjecting compound 2.2a to a standard Sonogashira coupling condition (5 mol% Pd(PPh3)2Cl2, 10 mol% CuI, THF/pyrrolidine) in the presence of different aryl iodides or vinyl bromides, a series of aryl or vinyl substituted internal N-H alkynylaziridines 2.4 were prepared without difficulties (Table 2.2). Highly electron-deficient substrates such as p-nitrophenyl or perfluorophenyl substituted alkynes (2.4g and 2.4h) were found unstable. Although mini-scale reaction for these cases generated desired products by TLC analysis, none of them were isolated in later large scale preparation. It could be attributable to the decomposition of these substrates.
during the reaction or purification process via the ring-opening of their vulnerable aziridine rings.

Table 2.2 Preparation of internal N-H alkynylaziridines via Sonogashira coupling$^a$

![Chemical Reaction Diagram]

$^a$ Reaction conditions: 5 mol% Pd(PPh$_3$_2Cl$_2$, 10 mol% CuI, THF-pyridine (3:1) r.t. 0.5 - 3.0 hr.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Halide</th>
<th>Product</th>
<th>Yield$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="I.png" alt="I-" /></td>
<td><img src="Ph-NH-Ph.png" alt="Ph-NH-Ph" /></td>
<td>95%</td>
</tr>
<tr>
<td>2</td>
<td><img src="I-Me.png" alt="I-Me" /></td>
<td><img src="Ph-NH-Ph.png" alt="Ph-NH-Ph" /></td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td><img src="I-OMe.png" alt="I-OMe" /></td>
<td><img src="Ph-NH-Ph.png" alt="Ph-NH-Ph" /></td>
<td>84%</td>
</tr>
<tr>
<td>4</td>
<td><img src="I-Br.png" alt="I-Br" /></td>
<td><img src="Ph-NH-Ph.png" alt="Ph-NH-Ph" /></td>
<td>76%</td>
</tr>
</tbody>
</table>
5. \[
\begin{align*}
I \quad & \quad F \\
\text{Ph} & \quad \text{Ph} \quad \text{NH} \quad \text{NH} \\
\text{F} & \quad \text{F} \quad \text{C} \quad \text{C} \\
\text{74%} & 
\end{align*}
\]

6. \[
\begin{align*}
\text{Br} & \quad \text{C} \\
\text{Ph} & \quad \text{NH} \quad \text{NH} \\
\text{80%} & 
\end{align*}
\]

7. \[
\begin{align*}
\text{Me} & \quad \text{C} \\
\text{Br} & \quad \text{Ph} \quad \text{NH} \quad \text{NH} \\
\text{90%} & 
\end{align*}
\]

8. \[
\begin{align*}
\text{Br} & \quad \text{C} \\
\text{Ph} & \quad \text{Ph} \quad \text{NH} \quad \text{NH} \\
\text{72%} & 
\end{align*}
\]

9. \[
\begin{align*}
\text{F} & \quad \text{F} \\
\text{I} & \quad \text{F} \\
\text{F} & \quad \text{F} \\
\text{decomp.} & 
\end{align*}
\]

10. \[
\begin{align*}
\text{I} & \quad \text{NO}_2 \\
\text{Ph} & \quad \text{Ph} \quad \text{NH} \quad \text{NH} \\
\text{decomp.} & 
\end{align*}
\]
Reactions were carried out using 1.0 equiv of ethynylaziridine and 1.2 equiv of aryl iodides or vinyl bromides in the presence of 5 mol% of Pd(PPh$_3$)$_2$Cl$_2$ and 10 mol% of CuI in THF/pyrrolidine (3:1) at 25 ºC. Isolated yields.

It is worth mentioning that Sonogashira coupling of 2-phenyl-substituted ethynylaziridine 2.2f with aryl iodide was also tested and resulted in decomposition under a variety of temperature and base conditions (Equation 2.1). In reactions involving secondary amine bases, such as diethylamine or pyrrolidine, ESI-MS analysis of the crude reaction mixture confirmed the disappearance of the starting ethynylaziridine 2.2f within 30 min and showed a mass of the ring-opened products by the base. It appeared that the high stability of a carbocation on the quaternary carbon of the starting material resulted in a very nucleophile-labile substrate that could not withstand metal-catalyzed coupling conditions. Indeed, further experiments on this system showed that CuI and base alone were sufficient to decompose compound 2.2f.

\[ \text{PhH} \rightarrow \left( \begin{array}{c}
\text{Ph-} \\
5 \text{ mol} \% \ Pd(PPh$_3$)$_2$Cl$_2$ \\
10 \text{ mol} \% \ CuI \\
\text{THF/base, 30 min, r.t.} \\
\text{Decomposition}
\end{array} \right) \]

(base screened: Et$_2$NH, Pyrrolidine, Et$_3$N, DIPEA, K$_2$CO$_3$)

2.3 Synthetic applications of N-H alkynylaziridines

With both terminal and internal N-H alkynylaziridines in hand, we decided to further explore the synthetic utilities of these multi-functionalized building blocks. We envisioned that electronic interactions between the two adjacent functional groups in these molecules, namely the unprotected aziridine and the carbon-carbon triple bond, would supply efficient access to valuable compounds that are difficult to prepare via other established methodologies.

2.3.1 Synthesis of α-amino allenes

In recent years, much attention has been paid to allenes as useful building blocks possessing axial chirality and unique reactivity for advanced organic synthesis. With regard to their preparation, propargylic derivatives are well known precursors to access allenes via $S_N2'$-type
substitution. For example, ring-opening reactions can afford α-hydroxy allenes by treating alkynyloxiranes with metal hydride or other organometallic reagents. As the aza-analogues of alkynyloxiranes, alkynylaziridines are envisioned as potential precursors of α-amino allenes, a class of versatile building blocks for constructing nitrogen-containing heterocycles. The transformation can be achieved via the aforementioned S$_{N}2'$ ring-opening reaction. However, a literature survey revealed a surprising paucity of methods that facilitate the synthesis of α-amino allenes from alkynylaziridines. In particular, no precedent examples demonstrating direct transformation of inactivated N-H alkynylaziridines to unprotected α-amino allenes were reported. Thus, using N-H alkynylaziridines as starting material, we wished to find out a practical one-step procedure to facilitate the direct synthesis of unprotected α-amino allenes without any extra protecting/activating group manipulation.

2.3.1.1 Reaction of alkynylaziridine with 9-BBN

Inspired by Reddy’s recent development of metal hydride reduction of propargylic alcohols to generate allenes and other works of α-hydroxy alene preparation from alkynyloxiranes, we treated N-H ethynylaziridine 2.2g with different commercially available metal hydride reagents, such as NaBH$_4$, LiAlH$_4$, DIBAL-H, 9-borabicyclo[3,3,1]nonane (9-BBN), [(Ph$_3$P)CuH]$_6$ (Stryker’s reagent) and Cp$_2$Zr(H)Cl (Schwartz reagent) in THF at room temperature (Table 2.3). To our delight, the expected α-amino allene 2.5g was isolated from most of these reactions, except in the case of LiAlH$_4$ and [(Ph$_3$P)CuH]$_6$. Reduction of 2.2g using LiAlH$_4$ only resulted in the alkenylaziridine by-product 2.6 that could be formed via a simple reduction of the acetylene moiety, whereas NaBH$_4$ and [(Ph$_3$P)CuH]$_6$ showed no reactivity to the alkynylaziridine starting material. Of all the hydride transfer reagents tested, 9-BBN demonstrated the optimal reactivity, giving the desired α-amino allene 2.5g exclusively in high isolated yield within one hour. Remarkably, the alkyne hydroboration by-product was not observed from this reaction. After identifying 9-BBN as the best reducing agent for unprotected α-amino allene formation, we subsequently evaluated the generality of this transformation with
different N-H ethynylaziridines prepared from aziridine aldehyde dimers. As summarized in Table 2.4, a range of α-amino allenes can be obtained in good to excellent yields.

**Table 2.3 Reduction of N-H ethynylaziridines by metal hydrides**

<table>
<thead>
<tr>
<th>Metal hydride</th>
<th>Time (hrs)</th>
<th>Conversion (%)</th>
<th>Selectivity (2.5g:2.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaBH₄</td>
<td>48</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>LiAlH₄</td>
<td>0.5</td>
<td>100</td>
<td>&lt; 5:95</td>
</tr>
<tr>
<td>9-BBN</td>
<td>1.0</td>
<td>100</td>
<td>&gt; 95:5</td>
</tr>
<tr>
<td>DIBAL-H</td>
<td>12</td>
<td>85</td>
<td>50:50</td>
</tr>
<tr>
<td>Cp₂Zr(H)Cl</td>
<td>3.0</td>
<td>100</td>
<td>25:75</td>
</tr>
<tr>
<td>[(Ph₃P)CuH]</td>
<td>48</td>
<td>0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

a Reactions were carried out using 1.0 equiv of ethynylaziridine 2.2g and 1.0 equiv of metal hydrides in THF at room temperature. b Conversion and selectivity were determined by ¹H NMR analysis of the crude reaction mixture after aqueous workup.

**Table 2.4 Synthesis of unprotected α-amino allenes from N-H ethynylaziridines**
<table>
<thead>
<tr>
<th>Entry</th>
<th>N-H Ethynylaziridine</th>
<th>Product</th>
<th>Yield&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="2.2a" /></td>
<td><img src="image" alt="2.5a" /></td>
<td>84%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="2.2b" /></td>
<td><img src="image" alt="2.5b" /></td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="2.2c" /></td>
<td><img src="image" alt="2.5c" /></td>
<td>76%</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="2.2d" /></td>
<td><img src="image" alt="2.5d" /></td>
<td>75%</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="2.2e" /></td>
<td><img src="image" alt="2.5e" /></td>
<td>88%</td>
</tr>
</tbody>
</table>
Reactions were carried out using 1.0 equiv of N-H ethynylaziridines and 1.0 equiv of 9-BBN in THF at 25 °C.  

Isolated yields.

It is highly possible that the above 9-BBN mediated reduction was initiated by a pre-coordination of the boron species to the basic aziridine nitrogen, which accordingly resulted in a highly regioselective hydride transfer leading to the α-amino allene products. The coordination not only activated the N-H aziridine for ring-opening, but also increased the capability of 9-BBN to donate its hydride. This hypothesis found support from the reaction between N-tosylated ethynylaziridine 2.7 with 9-BBN. It was found that compound 2.7 remained intact after exposed to 9-BBN in THF at room temperature for more than 12 hours (Equation 2.2). This observation unambiguously indicated the crucial role of pre-coordination of 9-BBN to aziridine nitrogen in the formation allene products. Additionally, it is noteworthy that compound 2.7 was also inactive towards direct hydroboration of the acetylene function by 9-BBN. This could be attributed to the deactivation of the carbon-carbon triple bond by electron-withdrawing effects of the tosyl group through hyperconjugative interactions between the alkyne and the aziridine ring.
In order to further evaluate the mechanism of the 9-BBN mediated hydride transfer reaction, and to gain insight into the stereochemistry of this process, we opted to subject the internal alkynylaziridine 2.4a to the 9-BBN reduction (Scheme 2.2A). Gratifyingly, the desired α-amino allene 2.8a was obtained as a predominant diastereomer (dr = 92:8). The product was subsequently converted to a dihydropyrrole 2.9 upon treatment with AuCl with complete transfer of chirality. Afterwards, the crystal structure of the tosylated derivative 2.10 was obtained. The anti-relationship of the two phenyl groups in 2.10 indicated the anti-configuration of the internal allenes 2.8a. This result is consistent with a highly selective syn-hydride transfer directed by the pre-coordination of 9-BBN to the aziridine nitrogen (Scheme 2.2B). It is conceivable that a distorted six-membered ring transition state was involved in the transformation.

Scheme 2.2 Relative stereochemistry and mechanism evaluation of α-amino allene formation
Other internal alkynylaziridines were also tested in the 9-BBN reduction and showed similar reactivity to produce the corresponding anti-configured α-amino allenes with good to excellent diastereoselectivities (Table 2.5). It is noteworthy that vinyl substituted alkynylaziridines afforded the corresponding conjugated vinyl allenes with high isolated yields and excellent diastereoselectivities (Table 2.5, entries 6-8), while the vinyl groups remained intact during the reduction. The lack of hydroboration of these substrates demonstrates the power of the pre-coordination between aziridine nitrogen and the 9-BBN boron in the highly regio- and chemoselective synthesis of α-amino allenes.

**Table 2.5** Synthesis of internal α-amino allenes from aryl or vinyl N-H ethynylaziridines

![Diagram of reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Halide</th>
<th>Product</th>
<th>Yield</th>
<th>d.r.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="2.4a" /></td>
<td><img src="image" alt="2.8a" /></td>
<td>89%</td>
<td>92:8</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="2.4b" /></td>
<td><img src="image" alt="2.8b" /></td>
<td>74%</td>
<td>&gt;95:5</td>
</tr>
</tbody>
</table>
Reactions were carried out using 1.0 equiv of internal N-H alkynylaziridine and 1.0 equiv of 9-BBN in THF at 25 °C. Isolated yields. Diastereoisomeric ratios (d.r.) were determined by 1H NMR analysis of crude reaction mixture.

### 2.3.1.2 Reaction of N-H alkynylaziridine with borane THF complex

Although the reactions of alkynylaziridines with 9-BBN to prepare α-amino allenes resulted in excellent selectivity and yields, the purification of the reaction mixture sometimes was troublesome. The cyclooctane-1,5-diol residue from the oxidative cleavage of 9-BBN has similar polarity with the α-amino allene products in some cases, which makes the column chromatography separation difficult.

We envision that the commercially available borane THF complex (BH$_3$·THF) would be an alternative choice in the α-amino allene preparation in terms of purification issue. We thus tested the reaction between ethynylaziridine 2.2a and borane THF complex in anhydrous THF at room temperature. Encouragingly, the desired α-amino allene 2.5a was formed after aqueous workup, as indicated by TLC and crude 1H NMR analysis. However, a much less polar by-product was also observed. Upon silica gel chromatography, the non-polar by-product was isolated, which was found to be stable in air. 1H NMR and 13C NMR spectra of the by-product have similar peak patterns with the desired α-amino allene, indicating a similar molecular skeleton, yet slightly different chemical shift at certain peaks was observed. Most intriguingly, 11B NMR of the by-product revealed a strong quartet signal at -20 ppm ($J_{BH} = 94$ Hz), indicating that this molecule contains a highly electron-rich boron center equipped with three hydrogen atoms. Based on the spectroscopic information, we concluded that the by-product was consistent with the structure of a borane-amine adduct 2.11, in which the α-amino allene was complexed with a BH$_3$ molecule at its amino nitrogen. This compound was found to be quite stable towards varies of aqueous treatment in subsequent investigation. Upon stirring at room temperature for 12 hours, strong basic solution such as 10% NaOH or 10% NaOH/30% H$_2$O$_2$ (1:1) was found surprisingly ineffective to destroy the borane adduct. In contrast, weakly basic, acidic, or neutral hydrogen peroxide solution smoothly converted the adduct 2.11 to free α-amino allene without difficulties.
Attempts to decrease the yield of the borane-amine adduct were made. It is noteworthy that lowering the reaction temperature would significantly suppressed the formation of the by-product (Table 2.6). Considering the reaction time, reactions carried out at around -25 to -30 °C would be optimal. The reaction was completed within 3 hours at this temperature and afforded the expected α-amino allene product 2.5a exclusively.

Table 2.6 The borane-amine adduct formation at different temperatures

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction temperature</th>
<th>Ratio (2.5a : 2.11)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65 °C</td>
<td>45:55</td>
</tr>
<tr>
<td>2</td>
<td>25 °C</td>
<td>50:50</td>
</tr>
<tr>
<td>3</td>
<td>0 °C</td>
<td>85:15</td>
</tr>
<tr>
<td>4</td>
<td>-25 °C</td>
<td>&gt; 95:5</td>
</tr>
<tr>
<td>5</td>
<td>-78 °C</td>
<td>&gt; 95:5</td>
</tr>
</tbody>
</table>

² Reactions were carried out using 1.0 equiv of N-H ethynylaziridine 2.2a and 1.0 equiv of borane THF complex in THF. Product ratios were determined by ¹H NMR analysis of the crude product mixture after basic hydrogen peroxide workup.

The clean formation of the α-amino allene through the reduction of terminal N-H ethynylaziridine with borane THF complex encouraged us to test this procedure with internal N-H alkynylaziridines. Surprisingly, unlike 9-BBN, which converted all internal alkynylaziridines to the corresponding α-amino allenes in every case, borane THF complex resulted in a series of
highly substrate-dependent outcomes (Table 2.7). When vinyl-substituted alkynylaziridines 2.4f was exposed to the borane reagent (Table 2.7, entry 1), the 1,4-reduction product, α-amino allene 2.8f, was obtained predominantly, although trace of the 1,2-reduction product homopropargyl amines 2.12 were found by crude ¹H NMR analysis. Strikingly, the desired α-amino allenes were not observed in the cases of aryl-substituted substrates (Table 2.7, entries 3-5), whereas the corresponding homopropargyl amines 2.12 were found to be the major product along with a small amount of over-reduced homoallylic amines 2.13. It is noteworthy that the phenylvinyl-substituted compound 2.4h, a "hybrid" of 2.4f and 2.4a with regard to their structures, afforded accordingly an intermediate outcome in relation to the results from 2.4f and 2.4a (Table 2.7 entry 2). These substrate-dependent regioselective outcomes were likely attributable to the electronic property of these starting internal N-H alkynylaziridines. Two possible mechanisms were posited to account for the formation of the homopropargyl amines: A) a direct 1,2-reduction of the alkynylaziridines by the attack of hydride at 3-position; B) isomerization from the pre-formed α-amino allenes in the presence of Lewis acidic species (boron species) (Scheme 2.3). It appears that mechanism A is highly possible since conjugative stabilization of carbocation on the propargyl position by terminal aromatic substituents could result in vulnerable aziridine ring towards direct borane hydride attack at 3-position. The reaction between 2.4a with BH₃·THF was monitored using crude ¹H NMR analysis. No trace of α-amino allene product was observed during the course of the reaction over 3 hours. Moreover, a reaction between α-amino allene 2.8a and BH₃·THF was carried out to test the hypothesis that BH₃ was responsible for the isomerization of allenes to alkynes in mechanism B. However, the expected homopropargyl amine 2.12a was not observed. These preliminary results implied the faint possibility of forming homopropargyl amines 2.12 through isomerization from the pre-formed α-amino allenes in mechanism B.

**Table 2.7** Reactions between internal alkynylaziridines and borane THF complex

```
# Table 2.7 Reactions between internal alkynylaziridines and borane THF complex

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Product 1</th>
<th>Product 2</th>
<th>Product 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.4f → BH₃·THF</td>
<td>2.12f</td>
<td>2.13f</td>
<td>2.12f</td>
</tr>
</tbody>
</table>

1H NMR analysis.
<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkynylaziridine</th>
<th>Product ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="2.4f" /></td>
<td>95:5:0</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="2.4h" /></td>
<td>75:25:0</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="2.4a" /></td>
<td>0:80:20</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="2.4c" /></td>
<td>0:75:25</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="2.4e" /></td>
<td>0:70:30</td>
</tr>
</tbody>
</table>

*Reactions were carried out using 1.0 equiv of alkynylaziridine and 1.0 equiv of borane THF complex in THF at -30 °C. *a* product ratios were determined by 1H NMR analysis of the crude product mixture after aqueous workup.*
Scheme 2.3 Proposed mechanism for the formation of homopropargyl amines 2.12

Based on the above investigation, we can conclude that BH₃·THF complex is only suitable for the preparation of terminal α-amino allenes. 9-BBN is still necessary in the cases of internal α-amino allenes synthesis.

2.3.2 From α-amino allenes to 2,4,6-trisubstituted pyridines

The facile synthesis of α-amino allenes prompted us to pursue their new synthetic applications. The enormous synthetic potential of α-amino allenes by combining the reactivities of both amine and allene functionalities supplied opportunities to establish new transforamtions for efficent heterocycle construction.

Among all heterocyclic compounds, pyridines are of great significance. They are not only found in cores of numerous pharmaceutical compounds and natural alkoloids, but also widely used as building blocks in the preparation of chiral ligands and new materials with important photo- or electrochemical properties. Consequently, efficient preparation of highly substituted pyridine derivatives represents a worthwhile goal of organic synthesis. The majority of synthetic routes to pyridine rings are based on condensations of amines with carbonyl compounds, Diels–Alder reactions with 1-azadienes, and other metal-catalyzed cycloaddition reactions. Despite the numerous studies and applications that have appeared in the literature, most methods...
are still suffer from one or more important limitations, including the lack of generality or selectivity, use of harsh reaction conditions, and poor chemical yields. New or improved synthetic methods to gain easy access to pyridine derivatives are therefore much sought after.

It is known that allenyl aldehydes, ketones or imines can undergo efficient intramolecular 5-\textit{exo} cyclization through allylic intermediates generated from palladium-mediated arylation of the allene moiety (Scheme 2.4A).\textsuperscript{34} These transformations are usually assisted by another extra metal, such as indium(0), in order to promote a transmetallation with the initially formed $\pi$-allylpalladium intermediate to form the more reactive allylindium species for the final cyclization process. Based on these reaction patterns, we envisioned that $\alpha$-(N-alkylideneamino)allenes, simply derived from combination of a $\alpha$-amino allene and an aldehyde, could have the possibility to undergo a palladium-catalyzed 6-\textit{endo} cyclization to construct the six-membered nitrogen-containing heterocycles (Scheme 2.4B). This resulting heterocyclic precursor could potentially undergo a subsequent aromatization process to create the pyridine ring.

\begin{center}
\includegraphics[width=\textwidth]{Scheme_2.4.png}
\end{center}

\textbf{Scheme 2.4} Palladium-catalyzed allylic cyclization of allene derivatives

Although the 5-\textit{exo} mode cyclizations have generally been observed to be dominant ring closure pathway when substrates can cyclize via either process, various examples of the less favored 6-
endo cyclization have been reported.\textsuperscript{35} For instance, Larock has reported a preparation of quinoline derivative A by a palladium-catalyzed annulation of internal acetylenes via the 6-endo addition of vinylpalladium intermediates across the carbon-nitrogen double bond of imines (Scheme 2.5).\textsuperscript{36} An indole-type by-product B was also isolated as the minor product, which is believed to be generated alternatively via a 5-exo attack of the vinylpalladium nucleophile to the nitrogen of C=N double bond. These results strongly support our envisioned synthetic strategy for constructing six-membered ring heterocycle via the 6-endo attack of allylpalladium nucleophiles.

In order to test the feasibility of our planned transformation, we chose $\alpha$-(N-alkylideneamino) allene 2.14a, which was prepared from $\alpha$-amino allene 2.5a and benzaldehyde, as the testing substrate (Scheme 2.5). The reaction was initially carried out with phenyl iodide under N\textsubscript{2} in the presence of Pd(OAc)\textsubscript{2} (10 mol%), LiCl (1.0 equiv), and Na\textsubscript{2}CO\textsubscript{3} (2.5 equiv) in DMF at 100 °C
for 12 hours. Gratifyingly, the desired 2,4,6-triphenyl pyridine product 2.15a was detected by TLC and crude $^1$H NMR analysis. Not surprisingly, considerable amount of dihydropyridine precursors were also observed.

**Scheme 2.6** Pyridine formation via palladium-catalyzed 6-endo-trig cyclization

The catalytic cycle (Scheme 2.6) was believed to involve an allylpalladium intermediate C generated from the addition of phenylpalladium(II) species to the allene function. It is conceivable that a strong coordination of the imine nitrogen to the palladium center not only activated the imine C≡N bond towards nucleophilic attack, but also facilitated the nucleophilic
$\eta^1$-allylpalladium character of the intermediate. The allylpalladium intermediate could subsequently undergo the 6-endo-trig cyclization with the imine double bond, forming the six-membered intermediate D (pathway a, scheme 2.6), followed by $\beta$-Hydride eliminations to furnish a mixture of dihydropyridines. Alternatively, the allylpalladium intermediate C could also undergo a $\beta$-hydride elimination to generate the conjugate imine intermediate E (pathway b, Scheme 2.6), which subsequent underwent the thermal electrocyclization to afford the dihydropyridine intermediate. The formation of pyridine is likely attributable to a palladium-catalyzed oxidative aromatization process. Exposure of the reaction mixture to air for an additional 12 hours at 100 °C resulted in full conversion of the dihydropyridine intermediates to the desired pyridine product.

Further condition screenings revealed that a simple combination of 10 mol% tetrakis(triphenylphosphine)palladium and 2.5 equiv of sodium acetate at 80 °C in the absence of other additives, followed by a subsequent stirring under air at the same temperature, gave optimal yields of the pyridine product. The pre-formation of $\alpha$-(N-alkylideneamino) allene starting material before the palladium-catalysis step was found necessary. Attempts at one-pot reactions directly using $\alpha$-imino allene 2.5a, benzaldehyde and phenyl iodide to prepare pyridine 2.15a resulted in considerable decomposition and very low yield of the product. The decomposition might be attributable to the undesired coordination of the palladium catalyst with the free amino group at $\alpha$-imino allene.

In order to evaluate the generality of this methodology for the preparation of 2,4,6-trisubstituted pyridines, we employed a series of $\alpha$-(N-alkylideneamino) allenes, which were first prepared from $\alpha$-amino allene 2.5a and different aldehydes, and a variety of aryl iodides (Scheme 2.7). The procedure worked well with a wide range of aromatic aldehydes, including those possessing heterocyclic substituents such as pyridinyl, furanyl and thiophenyl groups. Different aryl iodide reagents with electron-deficient, electron-rich or heterocyclic aromatic rings were all found effective in this transformation.
Scheme 2.7 Preparation of 2,4,6-trisubstituted pyridines from \( \alpha-(N\text{-alkylideneamino}) \) allenes\(^a\)

\[ \begin{array}{c}
\text{Scheme 2.7 Preparation of 2,4,6-trisubstituted pyridines from } \alpha-(N\text{-alkylideneamino}) \text{ allenes}\(^a\)} \\
\end{array} \]

\[ \begin{array}{c}
\text{Step 1: Reactions were carried out using 1.0 equiv of } \alpha\text{-amino allene, 1.0 equiv of aldehyde, and anhydrous } \\
\text{MgSO}_4 \text{ (100 mg per 1 mmol starting } \alpha\text{-amino allenes) in anhydrous DCM at 23 °C for 8 hr. Step 2: Reactions were} \\
carried out using 1.0 equiv of } \alpha-(N\text{-alkylideneamino}) \text{ allene, 1.1 equiv of aryl iodide, 10 mo% of } \\
Pd(PPh_3)_4, \\
\text{and 2.5 equiv of NaOAc in anhydrous DMF under N}_2 \text{ atmosphere at 80 °C for 12 hr, then exposed to air at 80 °C for another } \\
12 \text{ hr.} \(^b\) \text{ All yields in parentheses are isolated yields after silica gel chromatography.} \\
\end{array} \]

An interesting result was observed when using \( \alpha-(N\text{-alkylideneamino}) \) allene 2.16 as the starting material (Scheme 2.8). A symmetrical \( N\)-benzyl pyrrole 2.17 was formed instead of the desired pyridine. This result revealed the possible involvement of the 5-\( \text{exo} \) cyclization of the allylpalladium intermediate, which could find support from Larock’s synthesis of indole derivative \( \text{B} \) described in Scheme 2.5. Subsequent protonation and oxidative aromatization of the cyclized five-membered ring intermediate resulted in the generation of final pyrrole product. It is conceivable that the absence of the bulky phenyl group at the \( \alpha \)-position could allow free C\(_\alpha\)--N
bond rotation in intermediate \( E \) (Scheme 2.8), promoting conformations prone to 5-exo cyclization.

![Scheme 2.8 Pyrrole formation via palladium-catalyzed 5-exo-trig cyclization](image)

### 2.3.3 Other reactions of N-H alkynylaziridines

Encouraged by the facile synthesis of \( \alpha \)-amino allenes via 9-BBN mediated \( S_N2' \) hydride transfer, we have further investigated the extent of regiocontrol by way of nitrogen-mediated nucleophilic attack at the carbon-carbon triple bond. For instance, N-H ethynylaziridine 2.2a and 2.2f were subjected to the reaction with acetone in DMSO in the presence of LiOH/CsF base combination (Scheme 2.9). Interestingly, the starting ethynylaziridines readily furnished fused bicycles 2.18 and 2.19, respectively. It is expected that the unique feature of aziridine nitrogen prevents formation of the energetically uphill iminium ion from the intermediate oxyanion after the attack at acetone, enabling a subsequent 5-exo-dig ring closure to afford the cyclic enol ether products. In contrast to the boron reagents, no intramolecular \( S_N2' \) attack, which could form a cyclic allene species, was initiated in this case.
Scheme 2.9 Annulation of N-H ethynylaziridines with acetone

Beside reactions involving both aziridine and alkyne units, we have also collected evidence for regio- and chemoselective oxidation of the aziridine moiety in N-H ethynylaziridine without touching the alkyne functionality. Using the conditions normally prescribed for the Swern oxidation, alkynylaziridine 2.2a and 2.2g afforded the corresponding bench-stable 2H-azirines 2.20 and 2.21, respectively (Scheme 2.10A). It is intriguing that the newly formed carbon-nitrogen double bonds in the azirines were always exclusively at the distant side relative to the acetylene group. The structure of the products was confirmed by NMR spectroscopy and X-ray crystallography (Scheme 2.10B).

Scheme 2.10 2H-azirine synthesis from N-H ethynylaziridines
A close examination of the possible mechanism for the Swern oxidation revealed that the regioselectivity of the above reaction could be attributed to the formation of the sulfur ylide intermediate $G$ via the interaction between the aziridine nitrogen and the chlorosulfonium species at the same face of the less sterically hindered acetylene group, whereas the sulfur ylide intermediate $F$ was not formed due to the stronger steric hindrance of alkyl or aryl groups. (Scheme 2.11).

Scheme 2.11 A rationale for the regioselectivity of 2H-azirine formation

2.4 Summary

A new class of unprotected terminal N-H ethynylaziridines has been directly prepared from amphoteric aziridine aldehyde dimers via Seyferth-Gilbert homologation. Further Sonogashira coupling of these terminal alkynes with vinyl or aryl halides afforded a series of internal N-H alkynylaziridines. Given the recent interest in structural characterization of the unusual interactions involving unprotected amines and acetylenes, molecules of this sort are noteworthy. N-H alkynylaziridines can be directly converted into unprotected $\alpha$-amino allenes.
by a 9-BBN mediated highly diastereoselective syn hydride delivery. The condensation between α-amino allenes and aldehydes generates valuable α-(N-alkylideneamino) allene intermediates, which were found to be capable of creating 2,4,6-trisubstituted pyridines through a palladium-catalyzed 6-endo cyclization and aromatization. N-H terminal ethynylaziridines are also distinguished by their chemo- and regioselective transformations into bicyclic aziridine/enol ethers and highly strained ethynyl-2H-azirine. The ongoing renaissance in alkyne chemistry should render these readily available building blocks synthetically useful. On the basis of the dissected reactivity patterns, we anticipate that myriad possibilities await these molecules.

2.5 Experimental details
2.5.1 General information

General: Anhydrous methylene chloride (DCM), anhydrous toluene and anhydrous methanol (MeOH) were purchased and used as received. Anhydrous tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. All other solvents were of reagent grade quality.

Chromatography: Flash column chromatography was carried out using Silicycle 230-400 mesh silica gel and thin-layer chromatography (TLC) was performed on Macherey Nagel pre-coated glass backed TLC plates (SIL G/UV254, 0.25 mm) and visualized using a UV lamp (254 nm) or by using either KMnO₄ or phosphomolybdic acid (PMA) stain in case of no UV activity.

Nuclear magnetic resonance spectra: ¹H NMR and ¹³C NMR spectra were recorded on Varian 400 MHz spectrometer. ¹H NMR spectra were referenced to TMS (0 ppm) and ¹³C NMR spectra were referenced to CDCl₃ (77.2 ppm). Peak multiplicities are designated by the following abbreviations: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets; dq, doublet of quartet; sxt, sextet.

Mass Spectroscopy: High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities.


2.5.2 Preparation of aziridine aldehyde dimers

The aziridine aldehyde dimers 2.1a, 2.1d, 2.1f were synthesized by using our reported procedures.\(^{41}\)

The aziridine aldehyde dimers 2.1b, 2.1c, 2.1e were synthesized by a sequence outlined below:

\[
\begin{align*}
\text{R}^1\text{R}^2\text{O} + \text{Cl}\text{COOEt} & \xrightarrow{t-\text{BuOK, THF}} \text{R}^1\text{R}^2\text{O}\text{COOEt} \\
& \xrightarrow{1. \text{NaN}_3, \text{NH}_4\text{Cl, EtOH}} \text{R}^1\text{R}^2\text{NHCOOEt} \\
& \xrightarrow{2. \text{Ph}_3\text{P, MeCN}} \text{DIBAL-H toluene} \\
2.1b: R^1 = p\text{-MeO-}C_6\text{H}_4, R^2 = H \\
2.1c: R^1 = p\text{-F-}C_6\text{H}_4, R^2 = H \\
2.1e: R^1 = C_6\text{H}_5, R^2 = \text{Me} \\
\end{align*}
\]

To a solution of starting aldehyde/ketone (10 mmol) and chloroethylacetate (13 mmol) in 20 ml of anhydrous THF was added t-BuOK (15 mmol) over a period of 30 min. The solution was allowed to stir overnight at room temperature. The reaction mixture was then filtered and the filtrate was partitioned between water and diethyl ether. The ether layer was extracted and washed with water, brine, dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The crude oxirane-2-carboxylic acid ester was carried over to the next step without column chromatography.

In a round bottom flask equipped with a magnetic stirring bar and a reflux condenser was added oxirane-2-carboxylic acid ethyl ester from above and NaN\(_3\) (30 mmol) in 20 ml of absolute ethanol. NH\(_4\)Cl (30 mmol) was then added and the reaction mixture was heated to 80 °C and stirred for 8 hours. The reaction mixture was then concentrated under reduced pressure and the residue was diluted with ethyl acetate and washed with water and brine, dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The crude azidoalcohol was carried over to the next step without column chromatography.
The azidoalcohol from above was dissolved in 30 mL acetonitrile and heated to 50 °C in a round bottom flask. Triphenylphosphine (10 mmol) was added slowly (N₂ evolved) and then the flask was fitted with a condenser and heated to 83 °C for 5 hours. The resulting mixture was filtered and the filtrate concentrated under reduced pressure. To the residue was added 10% Et₂O in hexanes and the precipitate was filtered off. The filtrate was then concentrated and subjected to silica gel column chromatography using 10% EtOAc in hexanes to afford the pure aziridine-2-carboxylic acid ester as oil and subjected to the next step.

In a flame dried 100 ml round-bottom flask equipped with a magnetic stirring bar was placed aziridine-2-carboxylic acid ester from above (5 mmol) in 10 ml toluene. The solution was cooled to –78 °C and a 1.5M solution of DIBAL in toluene (10 mmol) was added dropwise along the wall of the vessel. Once the addition was complete, the reaction was allowed to stir at –78 °C for additional 2 hours at which point ESI MS showed the lack of starting material. MeOH (1 mL) was slowly added along the wall of the vessel at –78 °C. The reaction mixture was then allowed to stir for 30 minutes while warming to room temperature. Saturated Na₂SO₄ (2 mL) was then added and the solution was allowed to stir for another 2 hours. The reaction mixture was then filtered; the aluminum salt was washed with dichloromethane. To the combined filtrate was added water and ether. The organic later was extracted from the partition three times, washed with brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to afford the desired aziridine aldehyde as a foam, which was pure enough by NMR for use in subsequent transformations.

6-(4-methoxyphenyl)-2-(3-(4-methoxyphenyl)aziridin-2-yl)-3-oxa-1-aza-bicyclo[3.1.0]hexan-4-ol (2.1b)

White foam; yield 55% (from aziridine ester). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, J = 11.0 Hz, 1H), 7.17 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.89-6.84 (m, 4H), 5.48 (d, J = 10.7 Hz, 1H), 5.23 (s, 1H), 3.79 (s, 6H), 3.01 (bs, 1H), 2.75-2.85 (m, 2H), 2.43 (d, J = 2.8 Hz, 1H), 1.12 (bs, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 159.3, 129.6, 127.6, 127.2,
114.6, 114.2, 114.1, 97.1, 94.9, 55.6, 53.1, 40.6, 36.2 ppm. HRMS (ESI) [M+H]^+ calcd. For C_{20}H_{23}N_{2}O_{4} 355.1652, found 355.1646.

**6-(4-fluorophenyl)-2-(3-(4-fluorophenyl)aziridin-2-yl)-3-oxa-1-aza-bicyclo[3.1.0]hexan-4-ol (2.1c)**

White foam; yield 75% (from aziridine ester). Mp = 60-62 °C

^1H NMR (400 MHz, CDCl$_3$) δ 7.79 (br.d, J = 7.2 Hz, 1H), 7.24-7.13 (m, 4H), 7.05-6.99 (m, 4H), 5.49 (d, J = 8.3 Hz, 1H), 5.24 (s, 1H), 3.05 (bs, 1H), 2.83-2.78 (m, 2H), 2.47 (d, J = 2.8 Hz, 1H), 1.23 (bs, 1H) ppm. 

^13C NMR (100 MHz, CDCl$_3$) δ 162.6 (d, J$_{CF}$ = 247.0 Hz), 162.5 (d, J$_{CF}$ = 245.8 Hz), 133.2(5), 133.2(2), 128.1 (d, J$_{CF}$ = 8.0 Hz), 127.7 (d, J$_{CF}$ = 8.2 Hz), 116.1 (d, J$_{CF}$ = 21.8 Hz), 115.6 (d, J$_{CF}$ = 21.7 Hz), 97.0, 94.7, 53.3, 40.8, 40.3, 36.1 ppm. HRMS (ESI) [M+H]^+ calcd. For C$_{18}$H$_{17}$N$_2$O$_2$F$_2$ 331.1252, found 331.1262.

**6-methyl-2-(3-methyl-3-phenylaziridin-2-yl)-6-phenyl-3-oxa-1-aza-bicyclo[3.1.0]hexan-4-ol (2.1e)**

Yellowish foam; yield 70% (from aziridine ester). 

^1H NMR (400 MHz, CDCl$_3$) δ 7.43-7.22 (m, 10H), 5.45 (s, 1H), 5.27 (s, 1H), 2.93 (bs, 1H), 2.82 (s, 1H), 2.73 (d, J = 1.2 Hz, 1H), 1.74 (s, 3H), 1.57 (s, 3H) ppm. 

^13C NMR (100 MHz, CDCl$_3$) δ 145.2, 144.3, 128.9, 128.6, 127.5, 127.1, 126.7, 125.9, 96.4, 92.2, 55.6, 45.1, 43.6, 18.8, 13.4 ppm. HRMS (ESI) [M+H]^+ calcd. For C$_{20}$H$_{23}$N$_2$O$_2$ 323.1754, found 323.1751

Aziridine aldehyde **2.1g** was synthesized by a sequence of procedures shown below:
3,4-epoxybutyl benzene

The title compound was synthesized using literature method. To a solution of 4-phenylbutene (42.30 g, 0.32 mol) in 700 mL chloroform was added mCPBA (75.30 g, 77%, 0.34 mol) at 0 °C. The mixture was stirred at room temperature overnight. The reaction solution was washed with 10% NaOH (100 mL×3) and water (100 mL). The organic layer was then separated and concentrated to dryness, giving the title compound 47.4 g (TLC Rf = 0.50, 10% EtOAc in Hexanes), which was carried over to the next step without further purification.

tert-butyl 2-phenethylaziridine-1-carboxylate

To the solution of epoxide (47.4 g, 0.32 mol) from above in 500 mL methanol, was added NaN₃ (62.4 g, 0.96 mol) and NH₄Cl (51.3 g, 0.96 mol). The mixture was refluxed for 6 hours, cooled to room temperature and was concentrated to remove most of the solvent. The residue was diluted by 500 mL diethyl ether and washed with water (100 mL). The organic layer was then concentrated to dryness, giving the crude azidoalcohol as a brownish oil. The oil was dissolved in 500 mL acetonitrile and warmed to 50 °C. Triphenylphosphine (83.9 g, 0.32 mol) was slowly added in portions to avoid vigorous N₂ formation. Afterwards, the reaction mixture was refluxed for 5 hours and cooled to 0 °C. Triethylamine (49 mL, 0.35 mol), DMAP (0.5 g) and Boc₂O (69.8 g, 0.32 mol) were added to the solution. The reaction was warmed up to room temperature and stirred for overnight. The reaction mixture was then concentrated to remove most of the solvent, and 10% Et₂O in hexanes (500 mL in total) was added to precipitate the triphenylphosphine oxide. The solid was filtered and the filtrate was concentrated to dryness. The residue was purified by flash column
chromatography to afford the title compound (32.25 g) as a colorless oil (TLC $R_f = 0.75$, 20% EtOAc in Hexanes), yield 41% over 4 steps.

**trans-tert-butyl 3-phenethylaziridine-2-carboxylate**

The title compound was synthesized using literature method.\(^\text{43}\) To a solution of 2,2,6,6-tetramethyl piperidine (66 mL, 0.39 mol) in 700 mL anhydrous THF was added $n$-BuLi (1.6 M in hexanes, 244.5 mL, 0.39 mol) at -78 °C over 1 hour. The mixture was allowed to warm to room temperature and stirred for additional 30 min, then cooled back to -78 °C. A solution of Boc protected aziridine (32.25 g, 0.13 mol) from above in 100 mL THF was added dropwise over 30 min and stirred at -78 °C for 2 hours. The reaction was then quenched by adding 200 mL saturated NH$_4$Cl and extracted with diethyl ether (150 mL × 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered, concentrated, and the residue was subjected to flash column chromatography to afford the title compound 23.4 g as a white solid (TLC $R_f = 0.45$, 20% EtOAc in Hexanes), yield 73%.

**6-phenethyl-2-(3-phenethylaziridin-2-yl)-3-oxa-1-aza-bicyclo[3.1.0]hexan-4-ol (2.1g)**

To a toluene solution of the above $t$-butyl ester (23.4 g, 0.095 mol) was added DIBAL-H in toluene (1.5M, 132 mL, 0.198 mol) slowly along the wall of a flask maintained at –78 °C. Then the mixture was stirred for additional 2 hours at –78 °C. Methanol (10 mL) was added slowly along the flask wall at –78 °C. The reaction mixture was then allowed to stir for 30 min while warming to room temperature. Saturated Na$_2$SO$_4$ (20 mL) was then added and the solution was stirred overnight. The mixture was filtered; the filter cake was washed with dichloromethane. To the combined organic filtrate was added water and ether for extraction. The organic layer was separated, dried with anhydrous Na$_2$SO$_4$, concentrated to dryness, affording the title compound (9.71 g) as a white solid, yield 60%, which was pure enough by NMR analysis and was used in subsequent transformations. Mp = 103-105 °C. $^1$H
NMR (400 MHz, CDCl₃) δ 7.31-7.26 (m, 4H), 7.23-7.16 (m, 6H), 5.18 (s, 1H), 4.73 (s, 1H), 2.83-2.65 (m, 4H), 2.36 (d, J = 2.9 Hz, 1H), 2.02-1.98 (m, 2H), 1.89-1.80 (m, 1H), 1.77-1.65 (m, 3H), 1.36 (td, J = 6.8, 2.9 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 141.5, 141.1, 128.8, 128.7, 128.6(3), 128.5(8), 126.5, 126.2, 96.5, 94.5, 50.5, 38.8, 38.7, 35.7, 34.1, 34.0, 33.6, 33.0 ppm. HRMS (ESI) [M+H]⁺ calcd. For C₂₂H₂₇N₂O₂ 351.2067, found 351.2058.

The aziridine aldehyde 2.1h was synthesized by a sequence of procedures shown below:

\[
\begin{align*}
\text{NH-Boc} & \quad \text{N-methyl morpholine} \quad \text{THF} \\
\text{O} & \quad \text{N-HBoc} \\
\text{COOH} & \quad \text{NaBH₄, water} \\
\text{N-Boc-L-leucine} & \quad \text{TsCl, KOH} \quad \text{Et₂O} \\
\text{N} & \quad \text{Li} \\
\text{N} & \quad \text{THF} \\
\text{DIBAL} & \quad \text{toluene} \\
\text{NH} & \quad \text{COMtBu} \\
\end{align*}
\]

\[2.1h\]

\[N\text{-Boc-}\text{-L-leucinol}\]

To a solution of \(N\text{-Boc-}\text{-L-leucine}\) (23.1 g, 100 mmol) in 100 ml of THF at –10°C was added \(N\)-methyl morpholine (11 ml, 100 mmol) and isobutyl chloroformate (13.1 ml, 100 mmol). After stirring at –10°C for 15 minutes the reaction was filtered to remove the precipitate and the filtrate was then cooled back to –10°C. \(\text{NaBH}_4\) (5.67 g, 150 mmol) dissolved in 50 ml of water was added to the reaction mixture over 5 minutes. After the addition was complete, the reaction was then diluted with water and extracted three times with ethyl acetate. The organic extracts were dried over anhydrous \(\text{Na}_2\text{SO}_4\), filtered, and concentrated under reduced pressure to afford 18.8g (87%) of the title compound as a colourless oil which was subjected to the next step without further purification.
(S)-N-Boc-2-isobutylaziridine

The title compound was synthesized using literature method.\textsuperscript{44} To a solution of N-Boc-L-leucinol (12.5 g, 58 mmol) dissolved in 1000 ml of anhydrous Et\textsubscript{2}O was added finely ground KOH (13.02 g, 232 mmol) and tosyl chloride (13.27 g, 69.6 mmol). The reaction mixture was then heated to reflux for 16 hours. The reaction was then cooled to room temperature and water was added to the mixture and the organic phase was extracted three times with diethyl ether. The combined organic phases were dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure to afford a slightly yellow oil, which was subjected to Kugelrohr distillation to afford the title compound in (8.77 g, 76\%) as a colourless oil.

(2R,3S)-tert-butyl 3-isobutylaziridine-2-carboxylate

The title compound was synthesized using literature method.\textsuperscript{43} In a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added 2,2,6,6-tetramethyl piperidine (5 ml, 15 mmol) in 75 ml of THF. The mixture was cooled to –78°C and then n-BuLi (36 ml, 15 mmol) was added dropwise along the wall. The reaction was then allowed to warm to room temperature and stirred for 30 minutes. The reaction was then cooled down to –78°C and (S)-N-Boc-2-isobutylaziridine (1.99 g, 10 mmol) from above was added along the wall of the flask over a period of one minute. The reaction was stirred for two hours at –78°C. Saturated aqueous NH\textsubscript{4}Cl was added to quench the reaction, and the mixture was allowed to warm to room temperature. The mixture was extracted three times with ethyl acetate, and the extracts were dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated under reduced pressure. The product was then subjected to silica gel flash column chromatography to yield the title compound (1.40 g, 70\% yield) as colourless oil. (TLC R\textsubscript{f} = 0.15, 20\% EtOAc in hexanes).

(2S,4S,5R,6S)-6-isobutyl-2-((2R,3S)-3-isobutylaziridin-2-yl)-3-oxa-1-aza-bicyclo[3.1.0]hexan-4-ol (2.1h)

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added aziridine tert-butyl ester (2.94 g, 14.75 mmol) from above and 50 ml of anhydrous toluene. The reaction was cooled to –78°C after which DIBAL-H (1.5M in toluene, 19.67 ml, 29.5 mmol) was added
along the wall of the vessel over a period of 45 minutes. The reaction was stirred at –78°C for an additional two hours and then methanol (2 mL) was added along the wall of the vessel over a period of 30 minutes. The reaction was allowed to warm to room temperature and then saturated aqueous Na₂SO₄ (4 mL) was added to the mixture. After stirring for 2 hours, the white precipitate was filtered, and the filter cake was washed with dichloromethane. Water was added to the filtrate from which the organic layer was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and then concentrated under reduced pressure to afford the title compound as a pale yellow solid (1.61 g, 86% yield). 

\(^1\)H NMR (400 MHz, CDCl₃) δ 7.94 (bs, 1H), 5.26 (s, 1H), 4.95 (s, 1H), 2.41 (d, J = 2.9 Hz, 1H), 2.12 (d, J = 2.9 Hz, 1H), 2.00-1.96 (m, 1H), 1.82-1.71 (m, 2H), 1.44-1.40 (m, 1H), 1.38-1.31 (m, 2H), 1.30-1.21 (m, 1H), 0.97-0.93 (m, 12H), 0.51 (bs, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl₃) δ 96.5, 94.5, 50.6, 43.2, 40.2, 38.9, 38.0, 33.0, 27.7, 27.2, 23.0, 22.9(7), 22.6, 22.5 ppm. HRMS (ESI) [M+H]⁺ calcd. for C₁₀H₃₅N₂O₄ 355.2597, found 355.2605.

### 2.5.3 General procedure for synthesis of terminal N-H ethynylaziridine

![Diagram](attachment:image.png)

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added aziridine aldehyde dimer (10 mmol) in 100 mL of anhydrous methanol. Anhydrous K₂CO₃ (40 mmol) and dimethyl 1-diazo-2-oxopropylphosphate (Bestmann-Ohira reagent) (22 mmol) were subsequently added. The reaction mixture was stirred under N₂ at room temperature for around 8 hours until the reaction was complete as indicated by ESI MS. The mixture was concentrated under reduced pressure to remove most of the solvent. The residue was diluted with 100 mL of diethyl ether, washed with 5% NaHCO₃ and dried over anhydrous Na₂SO₄, filtered, and
concentrated under reduced pressure. The crude product was purified using flash column chromatography on silica eluting with 20% ethyl acetate in hexanes.

**trans-2-ethynyl-3-phenylaziridine (2.2a)**

![Structure of trans-2-ethynyl-3-phenylaziridine (2.2a)](structure.png)

White solid; 95% yield; $R_f = 0.47$, 20% EtOAc in hexanes. Mp = 53-55 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34-7.23 (m, 5H), 3.32 (bs, 1H), 2.37 (bs, 1H), 2.19 (s, 1H), 1.29 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.2, 128.8, 127.9, 126.1, 83.5, 69.0, 41.3, 29.1 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{10}$H$_{10}$N 144.0809, found 144.0808.

**trans-2-ethynyl-3-(4-methoxyphenyl)aziridine (2.2b)**

![Structure of trans-2-ethynyl-3-(4-methoxyphenyl)aziridine (2.2b)](structure.png)

Colorless oil; 70% yield; $R_f = 0.35$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.5$ Hz, 2H), 3.79 (s, 3H), 3.30 (dd, $J = 9.5$, 2.2 Hz, 1H), 2.25 (d, $J = 7.6$ Hz, 1H), 2.18 (s, 1H), 1.17 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.4, 130.1, 127.1, 114.1, 83.5, 68.8, 55.4, 40.7, 28.9 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{11}$H$_{12}$NO 174.0913, found 174.0914.

**trans-2-ethynyl-3-(4-fluorophenyl)aziridine (2.2c)**

![Structure of trans-2-ethynyl-3-(4-fluorophenyl)aziridine (2.2c)](structure.png)

Pale yellow solid; 70% yield; $R_f = 0.50$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25-7.15 (m, 2H), 7.05-6.95 (m, 2H), 3.34 (d, $J = 8.1$ Hz, 1H), 2.24 (bs, 1H), 2.20 (s, 1H), 1.22 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 162.5 (d, $^1J_{CF} = 245.9$ Hz), 133.9 (d, $^4J_{CF} = 3.0$ Hz), 127.7 (d, $^3J_{CF} = 8.2$ Hz), 115.6 (d, $^2J_{CF} = 21.6$ Hz), 83.2, 69.1, 40.5, 29.1 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{10}$H$_9$NF 162.0713, found 162.0719.

**trans-2-ethynyl-3-(thiophen-2-yl)aziridine (2.2d)**

![Structure of trans-2-ethynyl-3-(thiophen-2-yl)aziridine (2.2d)](structure.png)

White solid; 76% yield; $R_f = 0.48$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.17 (d, $J = 5.0$ Hz, 1H), 7.03 (d, $J = 3.6$ Hz, 1H), 6.95 (dd, $J = 5.0$, 3.6 Hz, 1H), 3.57 (bs, 1H), 2.42 (bs, 1H), 2.21 (s, 1H), 1.37 (bs, 1H) ppm. $^{13}$C NMR (100
MHz, CDCl$_3$) $\delta$ 142.6, 127.0, 124.8, 124.1, 82.6, 69.3, 37.5, 30.0 ppm. HRMS (EI) [M]$^+$ calcd. For C$_8$H$_7$NS 149.0299, found 149.0302.

**trans-3-ethynyl-2-methyl-2-phenylaziridine (2.2e)**

![Structure](image)

Colorless oil; 74% yield; $R_f = 0.51$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.38-7.30 (m, 4H), 7.27-7.23 (m, 1H), 2.51 (bs, 1H), 2.26 (d, $J = 1.5$ Hz, 1H), 1.76 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.8, 128.7, 127.5, 126.3, 81.9, 71.1, 43.4, 33.2, 22.2 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{11}$H$_{12}$N 158.0964, found 158.0970.

**2-ethynyl-2-phenylaziridine (2.2f)**

![Structure](image)

Colorless oil; 80% yield; $R_f = 0.47$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (d, $J = 7.6$, 2H), 7.33 (dd, $J = 7.6$, 7.2 Hz, 2H), 7.28-7.24 (m, 1H), 2.69 (d, $J = 10.7$ Hz, 1H), 2.33 (s, 1H), 1.97 (d, $J = 9.0$ Hz, 1H), 1.31 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 139.1, 128.6, 127.7, 126.0, 85.5, 69.5, 39.7, 30.8 ppm. HRMS (EI) [M]$^+$ calcd. For C$_{10}$H$_9$N 143.0735, found 143.0737.

**trans-2-ethynyl-3-phenethylaziridine (2.2g)**

![Structure](image)

Colorless oil; 90% yield; $R_f = 0.20$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.30-7.26 (m, 2H), 7.20-7.17 (m, 3H), 2.83-2.68 (m, 2H), 2.26 (bs, 1H), 2.07 (s, 1H), 2.02 (bs, 1H), 1.78-1.60 (m, 2H), 0.64 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.5, 128.6(8), 128.6(6), 126.3, 84.0, 68.4, 39.6, 34.8, 33.5, 24.9 ppm. HRMS (EI) [M-H]$^+$ calcd. For C$_{12}$H$_{12}$N 170.0970, found 170.0974.

**(2S,3S)-2-ethynyl-3-isobutylaziridine (2.2h)**

![Structure](image)

Colorless oil; 72% yield; $R_f = 0.60$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.25 (td, $J = 6.3$, 2.9 Hz, 1H), 2.08 (d, $J = 1.8$ Hz, 1H), 2.04 (t, $J = 2.3$ Hz, 1H), 1.85-1.75 (m, 1H), 1.37-1.31 (m, 1H), 1.26-1.19 (m, 1H), 0.98 (d, $J = 2.33$ Hz, 3H), 0.96 (d, $J = 2.35$ Hz, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 84.1, 68.2, 42.6, 39.0, 27.3, 24.9, 23.0, 22.5 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{8}$H$_{14}$N 124.1120, found 124.1121. The
enantiomeric excess of this compound was measured to be 98% after conversion into the corresponding Mosher’s amide by using (S)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid according to the previously described procedure.\textsuperscript{45} \textsuperscript{19}F NMR analysis was performed (external standard: TFA \( \delta \) 0.00), major diastereomer (\( \delta \) 5.76, CF\(_3\)), minor diastereomer (\( \delta \) 5.89, CF\(_3\)).

2.5.4 General procedure for synthesis of internal N-H alkynylaziridines

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{2.2a} & \quad \text{Ar} \quad \text{R} \\
\text{or} & \quad \text{Br} \\
\text{Ph} & \quad \text{NH} \quad \text{R'}
\end{align*}
\]

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added THF (3 mL) and pyrrolidine (1 mL). The solvent mixture was bubbled with N\(_2\) for 15 min to eliminate O\(_2\). Terminal N-H ethynylaziridine \textbf{2.2a} (100 mg, 0.698 mmol), aryl iodide or vinyl bromide (0.838 mmol), Pd(PPh\(_3\))\(_2\)Cl\(_2\) (25 mg, 0.035 mmol) and CuI (13 mg, 0.070 mmol), were subsequently added under N\(_2\). The reaction mixture was stirred at room temperature under N\(_2\) for 0.5-3 hours complete as indicated by TLC. The reaction was then cool to 0 °C and quenched by adding 10 mL of saturated NH\(_4\)Cl, extracted with Et\(_2\)O (5 mL×3), dried over anhydrous Na\(_2\)SO\(_4\), concentrated under reduced pressure. The crude product was purified using flash column chromatography on silica eluting with 20% EtOAc in hexanes, afforded the desired internal ethynylaziridines.

\textit{trans-2-phenyl-3-(phenylethynyl)aziridine (2.4a)}

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{2.4} & \quad \text{Ph}
\end{align*}
\]

Colorless oil; 93% yield; R\(_f\) = 0.60, 20% EtOAc in hexanes. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.45-7.42 (m, 2H), 7.35-7.26 (m, 8H), 3.43 (d, \( J \) = 7.7 Hz, 1H), 2.51 (d, \( J \) = 4.7 Hz, 1H), 1.33 (bs, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 138.3, 131.7, 128.4(4), 128.3(9), 127.6, 125.9, 122.5, 88.7, 80.5, 41.3, 30.1 ppm. HRMS (ESI) [M+H]\(^+\) calcd. For C\(_{16}\)H\(_{14}\)N 220.1120, found 220.1119.
trans-2-phenyl-3-(o-tolylethynyl)aziridine (2.4b)

Colorless oil; 83% yield; $R_f = 0.62$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.38 (m, 1H), 7.34-7.24 (m, 5H), 7.22-7.17 (m, 2H), 7.14-7.10 (m, 1H), 3.41 (dd, $J = 9.3$, 2.3 Hz, 1H), 2.54 (dd, $J = 7.8$, 2.3 Hz, 1H), 2.42 (s, 3H), 1.32 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 140.6, 138.6, 132.3, 129.7, 128.7, 127.8, 126.2, 125.8, 122.5, 92.9, 79.7, 41.8, 30.6, 20.9 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{16}$N 234.1277, found 234.1274.

trans-2-((4-methoxyphenyl)ethynyl)-3-phenylaziridine (2.4c)

Colorless oil; 92% yield; $R_f = 0.38$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36 (d, $J = 8.7$ Hz, 2H), 7.34-7.23 (m, 5H), 6.82 (d, $J = 8.7$ Hz, 2H), 3.78 (s, 3H), 3.40 (d, $J = 8.2$ Hz, 1H), 2.48 (d, $J = 6.3$ Hz, 1H), 1.31 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.9, 138.6, 133.4, 128.7, 127.7, 126.2, 114.8, 114.2, 87.6, 80.7, 55.5, 41.5, 30.5 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{16}$NO 125.1226, found 125.1227.

trans-2-((3-bromophenyl)ethynyl)-3-phenylaziridine (2.4d)

Colorless oil; 90% yield; $R_f = 0.52$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58 (s, 1H), 7.44 (d, $J = 8.3$ Hz, 1H), 7.35-7.24 (m, 6H), 7.2 (t, $J = 7.9$ Hz, 2H), 3.42 (dd, $J = 9.3$, 2.2 Hz, 1H), 2.49 (dd, $J = 7.8$, 2.2 Hz, 1H), 1.35 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.3, 134.7, 131.8, 130.5, 130.0, 128.7, 127.9, 126.2, 124.7, 122.4, 90.4, 79.3, 41.6, 30.2 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{16}$H$_{13}$NBr 298.0225, found 298.0234.

trans-2-((2-fluorophenyl)ethynyl)-3-phenylaziridine (2.4e)

Colorless oil; 85% yield; $R_f = 0.50$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.45-7.40 (m, 1H), 7.37-7.21 (m, 6H), 7.10-7.03 (m, 2H), 3.45 (d, $J = 7.1$ Hz, 1H), 2.53 (d, $J = 6.5$ Hz, 1H), 1.40 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 163.2 (d, $^{1}J_{CF} = 251.5$ Hz), 138.4, 133.8, 132.3 (d, $^{3}J_{CF} = 9.9$ Hz),
130.3 (d, $^3J_{CF} = 8.0$ Hz), 128.7, 127.8, 126.2, 124.2 (d, $^4J_{CF} = 3.7$ Hz), 115.8 (d, $^2J_{CF} = 20.9$ Hz), 111.3 (d, $^2J_{CF} = 15.7$ Hz), 94.2 (d, $J = 3.2$ Hz), 74.2, 41.7, 30.2 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{16}$H$_{13}$NF 238.1026, found 238.1031.

**trans-2-(but-3-en-1-yn-1-yl)-3-phenylaziridine (2.4f)**

Colorless oil; 77% yield; $R_f = 0.62$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25-7.33 (m, 5H), 5.80 (ddd, $J = 17.5, 11.0, 1.6$ Hz, 1H), 5.66 (dd, $J = 17.5, 2.2$ Hz, 1H), 5.50 (dd, $J = 11.0, 2.2$ Hz, 1H), 3.35 (d, $J = 7.9$ Hz, 1H), 2.40 (d, $J = 4.8$ Hz, 1H), 1.24 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 135.4, 128.7, 127.8, 126.1, 116.8, 89.7, 79.4, 41.5, 30.2 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{12}$H$_{12}$N 170.0964, found 170.0961.

**trans-2-(3-methylbut-3-en-1-yn-1-yl)-3-phenylaziridine (2.4g)**

Colorless oil; 82% yield; $R_f = 0.62$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33-7.25 (m, 5H), 5.3 (s, 1H), 5.24 (q, $J = 1.6$ Hz, 1H), 3.33 (bs, 1H), 2.40 (bs, 1H), 1.89 (t, $J = 1.3$ Hz, 1H), 1.23 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.5, 128.6, 127.7, 126.4, 126.1, 122.6, 88.0, 81.9, 41.5, 30.2, 23.6 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{13}$H$_{14}$N 184.1120, found 184.1120.

**trans-2-phenyl-3-((E)-4-phenylbut-3-en-1-yn-1-yl)aziridine (2.4h)**

Colorless oil; 88% yield; $R_f = 0.60$, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37-7.22 (m, 10H), 6.95 (d, $J = 16.3$ Hz, 1H), 6.14 (dd, $J = 16.3, 1.7$ Hz, 1H), 3.34 (d, $J = 8.5$ Hz, 1H), 2.45 (d, $J = 6.7$ Hz, 1H), 1.29 (bs, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.2, 138.5, 136.3, 129.0, 128.7, 127.8, 126.5, 126.1, 107.7, 91.3, 80.1, 41.8, 30.5 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{18}$H$_{16}$N 246.1277, found 246.1275.

### 2.5.5 General procedure for synthesis of α-amino allenes

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added N-H alkynylaziridine (0.4 mmol) in anhydrous THF (3 mL). 0.5 M 9-BBN in THF solution (0.4
mmol) was added at 0 °C. The reaction mixture was then warm to room temperature and stirred under N₂ at room temperature for 1 hour until the reaction was complete as indicated by TLC. The reaction was cooled to 0 °C again. 0.6 mL of 10% NaOH and 0.2 mL of 30% H₂O₂ was added. The mixture was vigorously stirred for 2 hours at room temperature. Additional 5 mL of 5% NaOH solution was added and the mixture was extracted with diethyl ether (5 mL×3). The combined ether layer was dried with Na₂SO₄, concentrated under reduced pressure. The crude product was purified using flash column chromatography on silica gel eluted with 2%−5% methanol (containing 2.0 M ammonia) in dichloromethane.

**1-phenylbuta-2,3-dien-1-amine (2.5a)**

![1-phenylbuta-2,3-dien-1-amine](image)

Colorless oil; 84% yield; Rₜ = 0.48, 5% MeOH (containing 2M ammonia) in DCM. ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.31 (m, 4H), 7.28-7.23 (m, 1H), 5.40 (q, J = 6.4 Hz, 1H), 4.90 (dd, J = 6.6, 3.0 Hz, 2H), 4.59-4.54 (m, 1H), 1.92 (bs, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 207.2, 144.9, 128.8, 127.5, 126.8, 96.7, 78.2, 54.6 ppm. HRMS (EI) [M-H]⁺ calcd. For C₁₀H₁₀N 144.0813, found 144.0814.

**1-(4-methoxyphenyl)buta-2,3-dien-1-amine (2.5b)**

![1-(4-methoxyphenyl)buta-2,3-dien-1-amine](image)

Colorless oil; 70% yield; Rₜ = 0.40, 5% MeOH (containing 2M ammonia) in DCM. ¹H NMR (400 MHz, CDCl₃) δ 7.30 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.31 (q, J = 6.3 Hz, 1H), 4.90 (dd, J = 6.6, 2.9 Hz, 2H), 4.52 (m, 1H), 3.80 (s, 3H), 1.64 (bs, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ 207.0, 159.0, 137.0, 127.9, 114.1, 96.8, 78.2, 55.5, 53.9 ppm. HRMS (ESI) [(M+H)-NH₃]⁺ calcd. For C₁₁H₁₁O 159.0804, found 159.0802.

**1-(4-fluorophenyl)buta-2,3-dien-1-amine (2.5c)**

![1-(4-fluorophenyl)buta-2,3-dien-1-amine](image)

Colorless oil; 76% yield; Rₜ = 0.45, 5% MeOH (containing 2M ammonia) in DCM. ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.32 (m, 2H), 7.05-6.99 (m, 2H), 5.37 (q, J = 5.37, 1H), 4.90 (dd, J = 6.6, 3.0 Hz, 2H), 4.59-4.54 (m,
1H), 1.63 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 207.1, 162.2 (d, $^1J_{CF} = 245.0$ Hz), 140.6 (d, $^3J_{CF} = 3.1$ Hz), 128.4 (d, $^3J_{CF} = 7.8$ Hz), 115.4 (d, $^2J_{CF} = 21.4$ Hz), 96.7, 78.3, 53.9 ppm. HRMS (ESI) [(M+H)-NH$_3$]$^+$ calcd. For C$_{10}$H$_{11}$NF 147.0604, found 147.0884.

1-(thiophen-2-yl)buta-2,3-dien-1-amine (2.5d)

Colorless oil; 75% yield; R$_f$ = 0.47, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.22 (dd, J = 4.9, 1.4 Hz, 1H), 6.98-6.94 (m, 2H), 5.48 (q, J = 6.5 Hz, 1H), 4.93 (dd, J = 6.4, 2.5 Hz, 2H), 4.83-4.80 (m, 1H), 1.72 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 207.1, 149.7, 126.9, 124.5, 123.7, 96.6, 78.6, 50.8 ppm. HRMS (EI) [M-H]$^+$ calcd. For C$_8$H$_8$NS 150.0377, found 150.0379.

2-phenylpenta-3,4-dien-2-amine (2.5e)

Colorless oil; 88% yield; R$_f$ = 0.45, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.55-7.52 (m, 2H), 7.36-7.31 (m, 2H), 7.26-7.21 (m, 1H), 5.52 (t, J = 6.6 Hz, 1H), 4.96-4.88 (m, 2H), 1.85 (bs, 2H), 1.57 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 206.0, 148.3, 128.4, 126.9, 125.6, 102.3, 78.8, 54.9, 31.3 ppm. HRMS (ESI) [(M+H)-NH$_3$]$^+$ calcd. For C$_{11}$H$_{11}$N 143.0855, found 143.0854.

2-phenylbuta-2,3-dien-1-amine (2.5f)

Colorless oil; 77% yield; R$_f$ = 0.48, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.39-7.32 (m, 4H), 7.26-7.21 (m, 1H), 5.22 (t, J = 3.4 Hz, 2H), 3.70 (bs, 2H), 1.45 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 207.5, 128.8, 127.8, 127.2, 126.2, 108.4, 80.6, 41.6 ppm. HRMS (EI) [M-H]$^+$ calcd. For C$_{10}$H$_{10}$N 144.0813, found 144.0811.

1-phenylhexa-4,5-dien-3-amine (2.5g)

Colorless oil; 77% yield; R$_f$ = 0.40, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.29-7.26 (m, 2H), 7.20-7.16 (m, 3H), 5.21 (q, J = 6.5 Hz, 1H), 4.83 (dd, J = 6.6, 2.6 Hz, 2H), 3.40-3.34 (m,
1H), 2.77-2.65 (m, 2H), 1.86-1.72 (m, 2H), 1.46 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 207.3, 142.2, 128.6(4), 128.5(9), 126.0, 96.5, 77.4, 50.1, 40.1, 32.7 ppm. HRMS (EI) [M]$^+$ calcd. For C$_{12}$H$_{15}$N 173.1204, found 173.1207.

(S)-6-methylhepta-1,2-dien-4-amine (2.5h)

\[
\begin{align*}
\text{Colorless oil; 55% yield; } R_f = 0.38, 5\% \text{ MeOH (containing 2M ammonia)} \text{ in DCM. } \text{H NMR (400 MHz, CDCl}_3\text{)} & \text{ δ 5.16 (q, } J = 6.5 \text{ Hz, 1H), 4.80 (dd, } J = 6.6, 2.5 \text{ Hz, 2H), 3.45-3.38 (m, 1H), 1.85 (bs, 2H), 1.79-1.69 (m, 1H), 1.39-1.28 (m, 2H), 0.91 (d, } J = 1.1 \text{ Hz, 3H), 0.92 (d, } J = 1.0 \text{ Hz, 3H) ppm. } \text{C NMR (100 MHz, CDCl}_3\text{)} & \text{ δ 207.2, 96.7, 77.6, 48.7, 47.6, 25.2, 22.9, 22.7 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_8$H$_{16}$N 126.1277, found 126.1282. The enantiomeric excess of this compound was measured to be 98% after conversion to the corresponding Mosher’s amide by using (S)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid according to the previously described procedure. $^{45}$ $^{19}$F NMR analysis was performed (external standard: TFA δ 0.00), major diastereomer (δ 6.79, CF$_3$), minor diastereomer (δ 6.57, CF$_3$).
\end{align*}
\]

anti-1,4-diphenylbuta-2,3-dien-1-amine (2.8a)

\[
\begin{align*}
\text{Colorless oil; 89% yield; } R_f = 0.47, 5\% \text{ MeOH (containing 2M ammonia)} \text{ in DCM. } \text{H NMR (400 MHz, CDCl}_3\text{)} & \text{ δ 7.42-7.40 (m, 2H), 7.36-7.31 (m, 2H), 7.30-7.23 (m, 5H), 7.21-7.16 (m, 1H), 6.34 (dd, } J = 6.3, 2.5 \text{ Hz, 1H), 5.82 (t, } J = 6.1 \text{ Hz, 1H), 4.70 (d, } J = 3.3 \text{ Hz, 1H), 1.76 (bs, 2H) ppm. } \text{C NMR (100 MHz, CDCl}_3\text{)} & \text{ δ 203.9, 144.8, 134.4, 128.9(2), 128.8(7), 127.6, 127.4, 127.0, 126.8, 101.7, 97.9, 55.4 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{16}$H$_{16}$N 222.1277, found 222.1290.
\end{align*}
\]

anti-1-phenyl-4-(o-tolyl)buta-2,3-dien-1-amine (2.8b)

\[
\begin{align*}
\text{Colorless oil; 74% yield; } R_f = 0.47, 5\% \text{ MeOH (containing 2M ammonia)} \text{ in DCM. } \text{H NMR (400 MHz, CDCl}_3\text{)} & \text{ δ 7.44-7.41 (m, 2H), 7.37-7.33 (m, 3H), 7.29-7.25 (m, 1H), 7.16-7.10 (m, 3H), 6.55 (dd, } J = 6.4, 2.5 \text{ Hz, 1H), 5.80 (dd, } J = 6.4, 5.8 \text{ Hz, 1H), 5.71 (dd, } J = 5.8, 2.5 \text{ Hz, 1H), 2.35 (s, 3H), 1.88 (bs, 2H) ppm. } \text{C}
\end{align*}
\]
NMR (100 MHz, CDCl$_3$) $\delta$ 204.4, 144.5, 135.0, 126.5, 127.1, 127.0, 126.6, 126.1, 100.5, 94.9, 55.1, 19.9 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{18}$N 236.1433, found 236.1428

**anti-4-(4-methoxyphenyl)-1-phenylbuta-2,3-dien-1-amine (2.8c)**

Colorless oil; 81% yield; $R_f = 0.38$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44-7.41 (m, 2H), 7.38-7.33 (m, 2H), 7.29-7.24 (m, 1H), 7.20 (d, $J = 8.8$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 6.31 (dd, $J = 6.3$, 2.5 Hz, 1H), 5.80 (dd, $J = 6.3$, 6.0 Hz, 1H), 4.69 (dd, $J = 6.0$, 2.5 Hz, 1H), 3.79 (s, 3H), 1.78 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 203.2, 159.2, 144.9, 128.8, 128.1, 127.5, 126.8, 126.7, 114.4, 101.6, 97.4, 55.5(4), 55.4(7) ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{18}$NO 252.1382, found 252.1372

**anti-4-(3-bromophenyl)-1-phenylbuta-2,3-dien-1-amine (2.8d)**

Colorless oil; 75% yield; $R_f = 0.45$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.43-7.25 (m, 7H), 7.20-7.12 (m, 2H), 6.27 (dd, $J = 6.3$, 2.5 Hz, 1H), 5.87 (t, $J = 6.1$ Hz, 1H), 4.73 (dd, $J = 5.8$, 2.5 Hz, 1H), 1.79 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 204.0, 144.3, 136.5, 130.1, 130.0, 129.5, 128.7, 127.5, 126.5, 125.3, 122.8, 102.0, 96.6, 55.1 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{16}$H$_{15}$NBr 300.0382, found 300.0395.

**trans-4-(2-fluorophenyl)-1-phenylbuta-2,3-dien-1-amine (2.8e)**

Colorless oil; 84% yield; $R_f = 0.45$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.45-7.25 (m, 6H), 7.20-7.14 (m, 1H), 7.11-6.99 (m, 2H), 6.57 (dd, $J = 6.4$, 2.5 Hz, 1H), 5.85 (t, $J = 6.2$ Hz, 1H), 4.73 (dd, $J = 6.1$, 2.5 Hz, 1H), 1.69 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 204.7 (d, $^4$J$_{CF} = 1.9$ Hz), 159.9 (d, $^1$J$_{CF} = 249.9$ Hz), 144.6, 128.8, 128.6 (d, $^3$J$_{CF} = 8.2$ Hz), 128.3 (d, $^4$J$_{CF} = 3.4$ Hz), 127.6, 126.8, 124.4 (d, $^3$J$_{CF} = 3.7$ Hz), 122.0 (d, $^2$J$_{CF} = 11.9$ Hz), 115.9 (d, $^2$J$_{CF} =
21.5 Hz), 101.5, 90.3 (d, $^3J_{CF} = 6.4$ Hz), 55.3 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{16}$H$_{15}$NF 240.1183, found 240.1190.

**anti-1-phenylhexa-2,3,5-trien-1-amine (2.8f)**

\[
\begin{array}{c}
\text{Ph} \quad \text{H} \\
\text{NH}_2 \\
\end{array}
\]

Colorless oil; 83% yield; $R_f = 0.48$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39-7.31 (m, 4H), 7.28-7.23 (m, 1H), 6.19 (ddt, $J = 17.0, 10.2, 0.8$ Hz, 1H), 6.02 (ddt, $J = 10.4, 6.0, 0.8$ Hz, 1H), 5.59 (m, 1H), 5.21 (ddt, $J = 17.0, 1.4, 0.8$ Hz, 1H), 5.01 (ddt, $J = 10.0, 1.5, 0.8$ Hz, 1H), 4.59 (dd, $J = 6.0, 2.6$ Hz, 1H), 1.86 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 206.0, 144.6, 132.8, 128.8, 127.5, 126.8, 116.5, 99.0, 97.9, 55.1 ppm. HRMS (ESI) [(M+H)-NH$_3$]$^+$ calcd. For C$_{12}$H$_{11}$ 155.0855, found 155.0851.

**anti-5-methyl-1-phenylhexa-2,3,5-trien-1-amine (2.8g)**

\[
\begin{array}{c}
\text{Ph} \quad \text{Me} \\
\text{NH}_2 \\
\end{array}
\]

Colorless oil; 79% yield; $R_f = 0.48$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.32 (m, 4H), 7.28-7.23 (m, 1H), 6.11 (dd, $J = 6.2, 2.5$ Hz, 1H), 5.66 (m, 1H), 4.94 (m, 1H), 4.85 (m, 1H), 4.61 (dd, $J = 6.1, 2.5$ Hz, 1H), 1.75 (m, 3H), 1.69 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 204.4, 144.8, 139.0, 128.8, 127.5, 126.7, 114.3, 100.9, 100.5, 55.4, 19.9 ppm. HRMS (ESI) [(M+H)-NH$_3$]$^+$ calcd. For C$_{13}$H$_{13}$ 169.1011, found 169.1005.

**anti-(E)-1,6-diphenylhexa-2,3,5-trien-1-amine (2.8h)**

\[
\begin{array}{c}
\text{Ph} \quad \text{Ph} \\
\text{NH}_2 \\
\end{array}
\]

Colorless oil; 82% yield; $R_f = 0.48$, 5% MeOH (containing 2M ammonia) in DCM. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42-7.19 (m, 10H), 6.61 (ddd, $J = 15.7, 9.8, 0.9$ Hz, 1H), 6.53 (d, $J = 15.7$ Hz, 1H), 6.20 (ddd, $J = 9.8, 6.0, 2.4$ Hz, 1H), 5.68 (t, $J = 6.0$ Hz, 1H), 4.64 (dd, $J = 6.0, 2.4$ Hz, 1H), 1.75 (bs, 2H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 206.8, 144.7, 137.4, 131.3, 128.8, 127.7, 127.6, 126.8, 126.5, 124.6, 99.3, 98.0, 55.3 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{18}$H$_{18}$N 248.1433, found 248.1413.
2.5.6 Transformation of internal α-amino allene for stereochemistry assessment

\[
\text{NH}_2 \quad \begin{array}{c}
\text{Ph} \\
\text{H} \\
\text{Ph}
\end{array} \quad \begin{array}{c}
\text{Ph} \\
\text{H} \\
\text{Ph}
\end{array} \quad \text{AuCl} \quad \begin{array}{c}
\text{Ph} \\
\text{H} \\
\text{Ph}
\end{array} \quad \begin{array}{c}
\text{Ph} \\
\text{H} \\
\text{Ts}
\end{array} \quad \text{Et}_3\text{N}
\]

\[2.8a \quad 2\% \text{AuCl} \quad \text{DCM} \quad 2.9 \quad 2.10\]

\textit{anti-2,5-diphenyl-2,5-dihydro-1H-pyrrole (2.9)}

The title compound was synthesized using literature method.\(^{46}\) AuCl (1.7 mg, 0.0072 mmol) was added at room temperature under N\(_2\) to a solution of α-amino allene 5a (80 mg, 0.36 mmol) in 2 mL anhydrous DCM. The mixture was stirred overnight. The solvent was removed in \textit{vacuo} and the crude product was purified using flash column chromatography on silica gel eluting with 5% MeOH in DCM, affording 66 mg (83%) of the title compound as a white solid. R\(_f\) = 0.50, 5% MeOH in DCM. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.36-7.31 (m, 8H), 7.27-7.23 (m, 2H), 5.97 (s, 2H), 5.29 (s, 2H), 2.48 (bs, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 144.6, 132.6, 128.9, 127.6, 127.2, 69.6 ppm. HRMS (ESI) [M+H]\(^+\) calcd. For C\(_{10}\)H\(_{16}\)N 222.1277, found 222.1276.

\textit{anti-2,5-dihydro-2,5-diphenyl-1-tosyl-1H-pyrrole (2.10)}

To a solution of the dihydropyrrole 2.9 (66 mg, 0.298) in 2 mL anhydrous DCM was added triethylamine (62 μL, 0.447 mmol) and TsCl (85 mg, 0.447 mmol). The reaction was stirred under N\(_2\) at room temperature overnight. The solvent was removed in \textit{vacuo} and the crude product was purified using flash column chromatography on silica gel eluting with 10% EtOAc in hexanes, affording 79 mg (71%) of the title compound as a white crystal. R\(_f\) = 0.25, 10% EtOAc in hexanes. The structure of compound 2.10 was verified using X-ray crystallography, shown as below:

\textbf{X-ray structure of anti-2,5-Dihydro-2,5-diphenyl-1-tosyl-1H-pyrrole (2.10)}
2.5.7 General procedure for synthesis of 2,4,6-trisubstituted pyridines

![Reaction Scheme]

To a oven-dried small vial containing a solution of α-amino allene 2.5a (1.0 mmol) in anhydrous DCM (2 mL) was added MgSO₄ (100 mg) and aldehyde (1.0 mmol). The reaction was stirred at room temperature for approximately 2 hr, at which point the complete conversion of starting material to imine was confirmed by crude ¹H NMR. The resulting mixture was filtered through celite then concentrated to obtain the α-(N-alkylideneamino) allene 2.14 as an orange oil which was carried over to the next step without further purification.

To a flame-dried round-bottom flask equipped with rubber septum and N₂ line was added DMF (2 mL), imine (0.689 mmol), and aryl iodide (0.758 mmol). N₂ was bubbled through the solution for 30 min to eliminate O₂. Pd(PPh₃)$_4$ (0.069 mmol) and NaOAc (2.067 mmol) were then added. The reaction was stirred at 80 °C for 12 hr under N₂ then exposed to air and stirred for another 12 hr, maintaining a temperature of 80 °C. Subsequently, the mixture was cooled to room temperature. 10 mL of H₂O were added and the product was extracted with Et₂O (10 mL x 3). The organic layer was concentrated to yield a crude mixture which was purified via flash column chromatography on silica gel with 0 to 10% EtOAc in hexanes gradient elution system to obtain the pyridine product 2.15.
2,4,6-triphenylpyridine (2.15a)

![Image of 2,4,6-triphenylpyridine (2.15a)]

Off-white waxy solid; 84% yield; \(R_f = 0.62\), 10% EtOAc in hexanes. \(^1^H\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) 8.2 (dd, \(J = 8.3, 1.3\) Hz, 4H), 7.8 (s, 2H), 7.7 (dd, \(J = 8.2, 1.3, 2H\)), 7.4-7.6 (m, 9H) ppm; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 157.8, 150.4, 139.9, 139.3, 129.4, 129.3, 129.2, 129.0, 127.5, 127.4, 117.4 ppm.

2,6-diphenyl-4-(p-tolyl)pyridine (2.15b)

![Image of 2,6-diphenyl-4-(p-tolyl)pyridine (2.15b)]

Yellow waxy solid; 63% yield; \(R_f = 0.67\), 10% EtOAc in hexanes. \(^1^H\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) 8.2 (dd, \(J = 8.5, 1.1\) Hz, 4H), 7.8 (s, 2H), 7.7 (d, \(J = 8.1\) Hz, 2H), 7.3-7.6 (m, 8H), 2.4 (s, 3H) ppm; \(^{13}\)C NMR (CDCl\(_3\), 400 MHz) \(\delta\) 157.7, 150.3, 140.0, 139.3, 136.3, 130.1, 129.3, 129.0, 127.4, 127.3, 117.1, 21.5 ppm.

4-(4-methoxyphenyl)-2,6-diphenylpyridine (2.15c)

![Image of 4-(4-methoxyphenyl)-2,6-diphenylpyridine (2.15c)]

Yellow solid; 50% yield; \(R_f = 0.55\), 10% EtOAc in hexanes. \(^1^H\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) 8.2 (m,4H), 7.8 (s, 2H), 7.7 (d, \(J = 8.9\)Hz, 2H), 7.4-7.6 (m, 6H), 7.0 (d, \(J = 8.8\)Hz, 2H), 3.8 (s, 3H) ppm; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 160.7, 157.7, 149.9, 140.0, 131.5, 129.2, 128.9, 128.6, 127.4, 116.8, 114.8, 55.7 ppm.

2-(4-fluorophenyl)-6-phenyl-4-(p-tolyl)pyridine (2.15d)

![Image of 2-(4-fluorophenyl)-6-phenyl-4-(p-tolyl)pyridine (2.15d)]

White solid; 67% yield; \(R_f = 0.70\), 10% EtOAc in hexanes; \(^1^H\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) 8.18-8.13 (m, 4H), 7.82 (d, \(J = 1.4\) Hz, 1H), 7.77 (d, \(J = 1.4\) Hz, 1H), 7.60 (d, \(J = 8.2\) Hz, 2H), 7.51-7.46 (m, 2H), 7.44-7.39 (m, 1H), 7.29 (d, \(J = 7.8\) Hz, 2H), 7.18-7.13 (m, 2H), 2.40 (s, 3H) ppm; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 163.8 (d, \(1J_{CF} = 248.3\) Hz), 157.7, 156.6, 150.4, 139.8, 139.4, 136.2, 136.0 (d, 4\(^J_{CF} = 2.9\) Hz), 130.1, 129.3, 129.2 (d, \(^3J_{CF} = 8.3\) Hz), 129.0, 127.4, 127.2, 117.0, 116.7, 115.8 (d, \(^2J_{CF} = 21.6\) Hz), 21.5 ppm.
4-(4-fluorophenyl)-2,6-diphenylpyridine (2.15e)

White solid; 79% yield; R_f = 0.60, 10% EtOAc in hexanes. ^1H NMR (CDCl_3, 400 MHz) δ 8.19-8.16 (m, 4H), 7.79 (s, 2H), 7.69-7.66 (m, 2H), 7.52-7.48 (m, 4H), 7.45-7.41 (m, 2H), 7.21-7.16 (m, 2H) ppm; ^13C NMR (CDCl_3, 100 MHz) δ 163.6 (d, ^3J_{CF} = 248.8 Hz), 157.7, 149.3, 139.6, 135.3 (d, ^4J_{CF} = 3.3 Hz), 129.3, 129.1 (d, ^2J_{CF} = 8.3 Hz), 128.9, 127.3, 117.0, 116.3 (d, ^2J_{CF} = 21.6 Hz) ppm.

4,6-diphenyl-2,2'-bipyridine (2.15f)

White solid; 86% yield; R_f = 0.40, 10% EtOAc in hexanes; ^1H NMR (CDCl_3, 400 MHz) δ 8.72-8.64 (m, 3H), 8.22-8.18 (m, 2H), 7.97 (d, J = 1.7 Hz, 1H), 7.85 (dd, J = 7.8, 1.7 Hz, 1H), 7.83-7.80 (m, 2H), 7.54-7.43 (m, 6H), 7.32 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H) ppm; ^13C NMR (CDCl_3, 100 MHz) δ 157.3, 156.6, 156.5, 150.5, 149.2, 139.7, 139.0, 137.0, 129.3, 129.2, 128.9, 127.5, 127.3, 124.0, 121.7, 118.7, 117.7 ppm.

2',6'-diphenyl-2,4'-bipyridine (2.15g)

White solid; 29% yield; R_f = 0.12, 5% EtOAc in hexanes; ^1H NMR (CDCl_3, 400 MHz) δ 8.80 (ddd, J = 4.8, 1.8, 1.0 Hz, 1H), 8.31 (s, 2H), 8.27-8.24 (m, 4H), 7.93 (dt, J = 7.9, 1.1 Hz, 1H), 7.86 (ddd, J = 7.5, 6.1, 1.8 Hz, 1H), 7.54-7.50 (m, 4H), 7.47-7.43 (m, 2H), 7.38 (ddd, J = 7.4, 4.8, 1.2 Hz, 1H) ppm; ^13C NMR (CDCl_3, 100 MHz) δ 157.9, 155.6, 150.3, 148.4, 139.7, 137.3, 129.3, 128.9, 127.4, 124.0, 121.3, 116.6, 77.2 ppm.

2-(4-methoxyphenyl)-6-phenyl-4-(p-tolyl)pyridine (2.15h)

Yellow solid; 48% yield; R_f = 0.55, 10% EtOAc in hexanes; ^1H NMR (CDCl_3, 400 MHz) δ 8.19-8.13 (m, 4H), 7.79 (dd, J = 4.2, 1.4 Hz, 2H), 7.61 (ddd, J = 8.2, 2.0, 1.8 Hz, 2H), 7.51-7.47 (m, 2H), 7.43-7.39 (m, 1H), 7.29 (d, J = 7.8 Hz, 2H), 7.01 (ddd, J = 8.9, 2.9, 2.1 Hz, 2H),
3.84 (s, 3H), 2.41 (s, 3H) ppm; $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 160.7, 157.4, 157.2, 150.1, 140.0, 139.1, 136.4, 132.5, 130.0, 129.1, 128.8, 128.6, 127.3, 127.1, 116.4, 116.3, 114.2, 55.5, 21.4 ppm.

4,6-diphenyl-2,3'-bipyridine (2.15i)

Yellow solid; 58% yield; $R_f = 0.22$, 20% EtOAc in hexanes; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 9.39 (s, 1H), 8.68 (d, $J = 3.8$ Hz, 1H), 8.51 (ddd, $J = 8.0, 2.0, 1.8$ Hz, 1H), 8.19 (ddd, $J = 7.0, 2.3, 1.5$ Hz, 2H), 7.93 (d, $J = 1.4$ Hz, 1H), 7.88 (d, $J = 1.4$ Hz, 1H) 7.74 (ddd, $J = 6.8, 2.4, 1.6$ Hz, 2H), 7.56-7.42 (m, 7H) ppm; $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 158.1, 155.1, 150.7, 150.1, 148.6, 139.3, 138.8, 135.3, 134.8, 129.5, 129.4, 129.0, 127.4, 127.3, 123.8, 118.0, 117.3 ppm.

2,4-diphenyl-6-(thiophen-3-yl)pyridine (2.15j)

Yellow-pale solid; 62% yield; $R_f = 0.73$, 10% EtOAc in hexanes; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 8.18-8.15 (m, 2H), 8.06 (dd, $J = 3.0, 1.3$ Hz, 1H), 7.82 (dd, $J = 5.0, 1.3$ Hz, 1H), 7.81 (d, $J = 1.4$ Hz, 1H), 7.74 (d, $J = 1.4$ Hz, 1H), 7.72-7.69 (m, 2H), 7.53-7.39 (m, 7H) ppm; $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 157.7, 153.8, 150.3, 142.7, 139.7, 139.2, 129.3, 129.2, 129.2, 128.9, 127.3, 127.3, 126.7, 126.3, 124.0, 117.0, 117.0 ppm.

2-(furan-2-yl)-4,6-diphenylpyridine (2.15k)

Thick oil; 68% yield; $R_f = 0.70$, 10% EtOAc in hexanes; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 8.14-8.11 (m, 2H), 7.86 (d, $J = 1.5$ Hz, 1H), 7.79 (d, $J = 1.5$ Hz, 1H), 7.74-7.71 (m, 2H), 7.55-7.40 (m, 7H), 7.24 (dd, $J = 3.4, 0.7$ Hz, 1H), 6.56 (dd, $J = 3.4, 1.8$ Hz, 1H) ppm; $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 157.9, 154.4, 150.2, 149.9, 143.4, 139.5, 138.9, 129.2(8), 129.2(6), 129.2(3), 128.9, 127.3, 127.3, 117.1, 115.2, 112.3, 109.2 ppm.

2,6-diphenyl-4-(thiophen-2-yl)pyridine (2.15l)
White solid; 55% yield; Rf = 0.50, 5% EtOAc in hexanes; 1H NMR (CDCl₃, 400 MHz) δ 8.19-8.13 (m, 4H), 7.86 (s, 2H), 7.60 (dd, J = 3.7, 1.1 Hz, 1H), 7.53-7.42 (m, 7H), 7.16 (dd, J = 5.1, 3.7 Hz, 1H) ppm; 13C NMR (CDCl₃, 100 MHz) δ 157.9, 143.2, 139.6, 137.7, 129.3, 128.9, 128.6, 127.3, 127.2, 125.5, 115.5 ppm.

2.5.8 General procedures for synthesis of aziridine-fused bicycles

![Diagram](image)

To a mixture of CsF (53 mg, 0.35 mmol) and LiOH (8.4 mg, 0.35 mmol) in DMSO (2 mL) was added N-H ethynylaziridine (0.35 mmol) and acetone (30 mg, 0.52 mmol). The mixture was stirred at 80 °C in a sealed vial for 1 hour. After cooling to room temperature, water (5 mL) was added and extracted with ether (2 mL × 5). The combined extract was concentrated and purified with flash column chromatography on silica eluting with 10% EtOAc in hexanes, afforded the aziridine-fused bicyclic compound.

**trans-2,2-dimethyl-4-methylene-6-phenyl-3-oxa-1-azabicyclo[3.1.0]hexane (2.18)**

![Structure](image)

Colorless oil; 75% yield; Rf = 0.75, 20% EtOAc in hexanes. 1H NMR (400 MHz, CDCl₃) δ 7.33-7.23 (m, 5H), 4.41 (d, J = 1.6 Hz, 1H), 4.19 (d, J = 1.6 Hz, 1H), 3.00 (d, J = 2.1 Hz, 1H), 3.82 (d, J = 2.1 Hz, 1H), 1.51 (s, 3H), 1.47 (s, 3H) ppm. 13C NMR (100 MHz, CDCl₃) δ 157.4, 137.8, 128.6, 127.6, 126.6, 101.2, 83.3, 49.6, 42.4, 27.8, 23.0 ppm. HRMS (ESI) [M+H]+ calcd. For C₁₃H₁₆NO 202.1226, found 202.1224.

**2,2-dimethyl-4-methylene-5-phenyl-3-oxa-1-azabicyclo[3.1.0]hexane (9)**

![Structure](image)

Colorless oil; 71% yield; Rf = 0.60, 20% EtOAc in hexanes. 1H NMR (400 MHz, CDCl₃) δ 7.46-7.43 (m, 2H), 7.38-7.30 (m, 3H), 4.44 (d, J = 1.9 Hz, 1H), 3.90 (d, J =
1.9 Hz, 1H), 2.23 (s, 1H), 2.12 (s, 1H), 1.57 (s, 3H), 1.49 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 160.5, 136.0, 129.1, 128.6, 128.3, 99.0, 85.2, 52.4, 34.7, 28.3, 22.7 ppm. HRMS (ESI) [M+H]$^+$ calcd. For C$_{13}$H$_{16}$NO 202.1226, found 202.1224.

2.5.9 General procedure for the synthesis of ethynyl-$2H$-azirines

![Reaction Scheme](image)

To a solution of oxalyl chloride (0.782g, 6.16 mmol) in 20 mL anhydrous DCM at -78 °C, was added anhydrous DMSO (0.984g, 12.60 mmol) and stirred for 5 min. The ethynylaziridine (2.80 mmol) solution in 5 mL anhydrous DCM was then added dropwise, and stirred for additional 10 min at -78 °C. Afterwards, triethylamine (2.27g, 22.4 mmol) was added dropwise at the same temperature and stirred for another 5 min. Then, the reaction mixture was gradually warmed to room temperature and stirred for 4 hours. The reaction was quenched by adding 40 mL water, extracted with diethyl ether (20 mL × 3). The combined ether layers were dried over anhydrous Na$_2$SO$_4$, and concentrated to dryness. The crude product was purified using flash column chromatography on silica eluting with 5% EtOAc in hexanes, affording the ethynyl-$2H$-azirine.

2-ethynyl-3-phenyl-$2H$-azirine (2.20)

![Structure](image)

Colorless solid; 87% yield; R$_f$ = 0.74, 20% EtOAc in hexanes. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.95-7.92 (m, 2H), 7.67-7.57 (m, 3H), 2.66 (d, J = 1.5 Hz, 1H), 1.97 (d, J = 1.5 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.8, 133.9, 130.2, 129.5, 123.3, 84.2, 66.6, 18.7 ppm.

X-ray quality crystals were grown by slowly evaporating a solution of 2.20 in DCM:
2-ethynyl-3-phenethyl-2H-azirine (2.21)

Brown oil; 80% yield; Rf = 0.50, 10% EtOAc in hexanes. 1H NMR (400 MHz, CDCl3) δ 7.33-7.21 (m, 5H), 3.16-3.06 (m, 4H), 2.23 (d, J = 1.5 Hz, 1H), 1.92 (d, J = 1.5 Hz, 1H) ppm. 13C NMR (100 MHz, CDCl3) δ 167.4, 139.7, 128.9, 128.5, 126.9, 84.6, 66.5, 30.4, 29.3, 18.1 ppm.

2.6 References

1 The theoretical basis for the strained ring/π interactions has been extensively studied by Rademacher. For reviews see: Rademacher, P. Chem. Rev. 2003, 103, 933–975.


Chapter Three

$\alpha$-Boryl aldehydes and their applications
3. α-Boryl aldehydes and their applications

3.1 Introduction

Unlike α-silylcarbonyl compounds, α-borylcarbonyl species are extremely unstable due to the fast rearrangement to their O-bound isomers. Installation of electron-rich $sp^3$-hybridized boron centers proved to be a feasible strategy to obtain stable α-borylcarbonyl compounds. In this chapter, we will discuss the discovery, synthesis and application of a new class of bench-stable α-boryl aldehydes equipped with a tetrahedral $sp^3$-boryl group possessing the trivalent ligand, $N$-methyliminodiacetic acid (MIDA).

3.2 Discovery and synthesis of stable α-boryl aldehydes

As part of a project directed towards new classes of amphoteric molecules, we became interested in the preparation of aziridinyl boronic acids from oxiranyl MIDA boronates (Scheme 3.1). The latter molecules can be made by $m$CPBA epoxidation of vinyl MIDA boronates, which were recently developed by Burke and co-workers. Since the MIDA-derived tetrahedral boryl groups are known to be well-tolerant to a wide range of chemical conditions, we predicted we would be able to achieve the subsequent two-step transformations containing the preparation of azidoalcohols and aziridines, respectively, while retaining of the MIDA boryl group.

Scheme 3.1 From oxiranyl MIDA boronates to aziridinyl boronic acids
During our initial attempts to make the azidoalcohol precursor to the target aziridinyl boronate, the starting oxiranyl MIDA boronate 3.1a was reacted with excess TMSN₃ in the presence of BF₃ etherate at -30 °C (Equation 3.1). Surprisingly, in addition to the expected epoxide ring-opening product, a white solid was isolated in 10% yield. Spectroscopic analysis (¹H, ¹³C, ¹¹B NMR and IR) indicated that this material has the structure consistent with α-boryl aldehyde 3.2a. This molecule was found to be surprisingly stable, and could be purified by silica gel chromatography and stored at room temperature under air for months. It is conceivable that compound 3.2a was generated from the epoxide rearrangement promoted by the Lewis acid BF₃. In order to confirm this transformation, we further exposed the starting oxiranyl MIDA boronate 3.1a to BF₃ etherate at -30 °C in anhydrous dichloromethane in the absence of any nucleophilic reagents. Indeed, the same α-boryl aldehyde product was obtained in nearly quantitative yield.

Encouraged by the serendipitous discovery of the stable α-(MIDA)boryl aldehyde 3.2a, we tested the generality of this procedure to access other α-boryl aldehydes of this type. Gratifyingly, a variety of α-boryl aldehydes were obtained in excellent yields by treating the corresponding starting oxiranyl MIDA boronates with BF₃ etherate (Table 3.1). The reaction was found to work well not only with electron-neutral (entry 1) and electron-rich (entry 2) aryl substrates, but also with electron-deficient (entry 3) aryl derivatives. The primary and secondary alkyl substituted oxiranyl MIDA boronates (entry 4–8) also cleanly afforded the desired aldehyde products. All of these α-boryl aldehydes proved to be stable at ambient conditions.
Table 3.1 Preparation of α-boryl aldehydes via rearrangement of oxiranyl MIDA boronates

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxiranyl MIDA boronate</th>
<th>Product</th>
<th>Yield $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="3.1a" /></td>
<td><img src="image" alt="3.2a" /></td>
<td>98%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="3.1b" /></td>
<td><img src="image" alt="3.2b" /></td>
<td>97%</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="3.1c" /></td>
<td><img src="image" alt="3.2c" /></td>
<td>98%</td>
</tr>
</tbody>
</table>
4  
\[
\begin{align*}
\text{3.1d} & \quad \text{3.1e} \\
\text{Ph} & \quad \text{MeN} \\
\end{align*}
\]

5  
\[
\begin{align*}
\text{3.1e} & \quad \text{3.1f} \\
\text{Ph} & \quad \text{MeN} \\
\end{align*}
\]

6  
\[
\begin{align*}
\text{3.1f} & \quad \text{3.2f} \\
\text{MeN} & \quad \text{B} \\
\end{align*}
\]

7  
\[
\begin{align*}
\text{3.1g} & \quad \text{3.2g} \\
\text{MeN} & \quad \text{B} \\
\end{align*}
\]

8  
\[
\begin{align*}
\text{3.1h} & \quad \text{3.2h} \\
\text{MeN} & \quad \text{B} \\
\end{align*}
\]

76\%  

69\%  

94\%  

80\%  

66\%
Reactions were carried out using 1.0 equiv of epoxide and 1.0 equiv of BF$_3$-Et$_2$O in anhydrous CH$_2$Cl$_2$ at –30 °C to 0 °C for 30 min. Isolated yields after silica gel chromatography.

However, some limitations of this BF$_3$-promoted rearrangement process were also observed (Figure 3.1). A complex mixture of intractable materials was obtained while tert-butyl substituted oxiranyl MIDA boronate 3.1i was exposed to BF$_3$ etherate. This could be attributed to the strong tendency of cationic intermediates toward unexpected isomerization promoted by the tertiary alkyl group. The unsubstituted oxiranyl MIDA boronate 3.1j was also tested in the reaction. However, no rearrangement took place, even under elevated temperature and prolonged reaction time (40 °C, 24 hr). The difficulties in generating stabilized carbocations may have inhibited the ring opening of the epoxide. Oxiranyl boronate 3.1k with a benzyloxyl group also resulted in no reactivity during the treatment with BF$_3$ etherate in DCM. This might imply the notorious effect of extra heteroatoms in Lewis acid catalyzed process: the relatively more basic oxygen on benzyloxyl group could compete with the oxygen on epoxide ring to coordinate with Lewis acid BF$_3$, thus inhibiting the occurrence of the desired rearrangement.

![Substrates that are not working in the α-boryl aldehyde preparation](image)

**Figure 3.1** Substrates that are not working in the α-boryl aldehyde preparation

In principle, the α-boryl aldehyde formation could take place via the migration of either the boryl group or the aryl/alkyl groups (Scheme 3.2). In order to clarify the mechanism, 1-deuterated oxiranyl MIDA boronates 3.3a and 3.3b, equipped with aryl and alkyl substituents respectively, were subjected to the BF$_3$-promoted rearrangement (Scheme 3.3). It was found that, strikingly, the deuterium label was both exclusively incorporated at the carbonyl carbon of the resulting α-boryl aldehydes 3.4a and 3.4b. These results unambiguously indicate that a 1,2-boryl migration has taken place during the rearrangement leading to the aldehyde products (Scheme 3.4A). Taking the deuterium labeling experiment results and the fact that no ketone by-product
was observed in these rearrangement reactions into account, we can conclude that the migratory attitude of electron-rich MIDA boryl groups is much higher than that of alkyl, aryl groups and hydrogen (hydride). While similar phenomenon can be seen in the generation of $\alpha$-silyl aldehydes from oxiranylsilanes via the silyl group migration, to the best of our knowledge, the boron version of this process is unprecedented. It is conceivable that a stabilization interaction from the electron-rich boron center to the nascent $\beta$-carbocation might take into effect in this rearrangement process, which can be considered analogous to the well-known silicon $\beta$-effect (Scheme 3.4B).

![Scheme 3.2](image)

**Scheme 3.2** Two possible rearrangement pathways to form $\alpha$-boryl aldehydes

![Scheme 3.3](image)

**Scheme 3.3** Deuterium labeling experiments for BF$_3$-promoted $\alpha$-boryl aldehyde generation
Scheme 3.4 1,2-Boryl migration and stabilization of β-cation by MIDA boryl groups

This BF₃-mediated epoxide rearrangement was also found to be stereospecific. Studies in the Burke group have revealed a very similar rearrangement of the diastereomerically pure oxiranyl PIDA boronate to the corresponding α-boryl aldehyde product promoted by Mg(ClO₄)₂ with complete maintenance of stereochemical purity (Equation 3.2).²

In addition to 2-substituted oxiranyl MIDA boronates, a representative 1-substituted substrate 3.5 was also tested in the BF₃-promoted epoxide rearrangement. Interestingly, the same α-boryl aldehyde 3.2a, which was obtained from 2-substituted oxiranyl boronates 3.1a, was isolated here (Equation 3.3). This result indicated that a 1,2-hydride migration, instead of the 1,2-boryl migration, had taken place. The migration could be initiated by the generation of more stabilized positive charge at the carbon connecting to boryl group. Although the rearrangement is likely concerted, the involvement of transient boryl-substituted cationic species during the rearrangement of 3.5 has not been ruled out.
3.3 Reactivity of $\alpha$-boryl aldehydes

In order to demonstrate the potential of amphoteric $\alpha$-boryl aldehydes in synthesis, we evaluated their chemical reactivity under a variety of conditions.

3.3.1 Attempts to prepare $\alpha$-boryl imines

Encouraged by the stability of $\alpha$-boryl aldehydes, we turned our attention to $\alpha$-boryl imines.\textsuperscript{4} Since boron-nitrogen bonds are generally weaker than boron-oxygen bonds,\textsuperscript{5} a $\alpha$-boryl imine molecule is expected to be relatively more stable than its oxygen analogue, and thus more feasible to be obtained. In order to prepare $\alpha$-boryl imines, we mixed different classes of amines/amides, including benzylamine, aniline, $p$-toluenesulfonamide and tert-butanesulfinamide, with $\alpha$-boryl aldehyde 3.2a in the presence of dehydrating agents and/or Lewis acids (Scheme 3.5). However, the majority of amines tested can only afford $N$-boryl enamines, which were found to be stable and isolable using silica gel chromatography. It is interesting that only in the case of tert-butanesulfinamide, the desired $\alpha$-boryl imine 3.7c was isolated as the major product along with a small amount of $N$-boryl enamine isomer 3.6c. Although stable in solid state, prolonged storage of $\alpha$-boryl imine 3.7c in solution (DMSO-d$_6$) over a week resulted in slow conversion to the enamine isomer 3.6c.
Reasons for the difficulty in obtaining stable α-boryl imines are still elusive. The general B-O/B-N bonding energy trend seems to be irrelevant to the relative stability of α-boryl aldehydes and imines, thus cannot be used as a guide in real cases. An intuitive explanation for the instability of α-boryl imines is the more accessible imine nitrogen lone-pair electrons, which might promote the 1,3-sigmatropic shift of the tetrahedral MIDA boryl group from α-carbon to nitrogen.

### 3.3.2 Nucleophilic attack on the aldehyde

In order to demonstrate the electrophilic reactivity of the aldehyde functional group in α-boryl aldehydes, we first tested the Wittig-type transformations. Using compound 3.2a as the model substrate, several commercially available phosphorous ylide reagents were evaluated (Figure 3.2) in a range of solvents such as DCM, THF or toluene at different temperatures. It is interesting that only phosphoranes with ester group were found reactive and afforded the desired allyl boronate products. For instance, (E)-γ-boryl-α,β-unsaturated ester 3.8 was obtained exclusively as E-isomer in good isolated yield by using ethyl 2-(triphenylphosphoranylidene)propanoate

*Scheme 3.5 Attempts to prepare α-amino imines*
(Equation 3.4). Meanwhile, α-boryl aldehydes 3.2a and 3.2d were also subjected to Ramirez olefination condition in the presence of tetrabromocarbon and triphenylphosphine. The anticipated gem-dibromoallyl boronates 3.9a and 3.9b were obtained without difficulties (Equation 3.5). These allyl boron reagents have not been reported to date. Since the utility of gem-dihaloalkene intermediates in metal catalysis is well documented, one can anticipate interesting possibilities for these novel dibromoallyl boronates in tandem reactions.

Figure 3.2 Phosphorous ylides tested with α-boryl aldehydes

We later decided to examine the reactivity of aldehyde function in α-boryl aldehyde towards organometallic reagents. Compound 3.2a was initially reacted with allylmagnesium bromide in THF at 0 °C. $^1$H NMR analysis of the crude reaction mixture indicated a considerable decomposition of the starting boryl aldehyde, likely due to the instability of the MIDA boryl
group towards hard nucleophiles. We thus opted to utilize milder organoindium reagents. Gratifyingly, treatment of \(\alpha\)-boryl aldehyde 3.2a with allylbromide in the presence of indium metal, which would generate the allylindium intermediate in situ, resulted in a highly diastereoselective formation of the boryl alcohol 3.10a (\(\text{syn:anti} = 93:7\)) with good isolated yields (Scheme 3.6A), whereas similar transformation using alkyl-substituted \(\alpha\)-boryl aldehyde 3.2d only afforded the boryl alcohol product 3.10b with poor diastereoselectivity (\(\text{syn:anti} = 60:40\)) (Scheme 3.6B). The mechanism for the diastereoselective outcome is still elusive. A tentative explanation using Felkin-Ahn Model is conceivable. Considering both its possible steric and electronic effect, the MIDA boryl group might be gauche to the carbonyl, whereas the phenyl group is perpendicular to the carbonyl and anti to the incoming nucleophile (Scheme 3.6C).

Scheme 3.6 Synthesis and transformations of \(\beta\)-boryl alcohols
It is also intriguing that allylated boryl alcohol 3.10 can be directly converted to 1,2-diol 3.11 through the oxidative cleavage of the carbon-boron bond with basic hydrogen peroxide solution (H₂O₂/NaOH). In contrast, treatment of compound 3.10 using 1.0 M aq. NaOH in the absence of hydrogen peroxide alternatively resulted in the stereospecific formation of 1,4-diene 3.12, a type of “skipped diene” which is not easily prepared from other methodologies. It was likely that the reaction proceeded via a Wittig-type syn-elimination process (boro-Wittig elimination) promoted by the base.

### 3.3.3 Enolization and α-functionalization

We were curious about the enolization property of these α-boryl aldehydes. These novel α-borylcarbonyl compounds were thus treated with a variety of electrophiles in the presence of bases. Gratifyingly, a series of β-functionalized vinyl boronates, which are hard or impossible to obtain from other established methods, were smoothly synthesized with high chemo- and stereoselectivity (Scheme 3.7). For example, heating α-boryl aldehyde 3.2a with tert-butyldimethylsilyl chloride (TBDMSCl) in the presence of triethylamine in THF at 80 °C furnished silyl enol ether 3.13a in 55% yield with Z-isomer as the major product. Alternatively, treatment of the alkyl substituted substrate 3.2d with triisopropylsilyl trifluoromethanesulfonate (TIPSOTf) at room temperature using DBU as the base in THF afforded the corresponding (Z)-TIPS enol ether 3.13c exclusively in 80% yield. Reactions between pyrrolidin-2-one and α-boryl aldehydes 3.2a and 3.2d under reflux condition in toluene were found generating amidovinyl MIDA boronates 3.14a and 3.14b, respectively, in moderate yields. Comparatively, a mild condition using 4 Å molecular sieves as the dehydration agent in DCM at room temperature easily afforded enamine 3.15 from α-boryl aldehyde 3.2a. Finally, β-borylated triflate enol ether 3.16 can also be achieved by treating the α-boryl aldehyde starting material carefully with KHMDS in the presence of triflating reagent N-phenylbis(trifluoromethanesulfonimide) (PhNTf₂) at low temperature.
These results prompted us to further explore transformations that could functionalize the \( \alpha \)-position of \( \alpha \)-boryl aldehydes with retaining of the boryl group. At the outset, we opted to expose compound 3.2a with \( \text{Br}_2 \) in dioxane/DCM mixed solvent. To our delight, the reaction easily furnished a highly functionalized \( \alpha \)-bromo-\( \alpha \)-borylaldehyde 3.17 in good yield through the \( \alpha \)-bromination (Scheme 3.7). The MIDA boryl group was intact during the course of this transformation. The structure of the product was confirmed by X-ray crystallography.
Scheme 3.8 α-Bromination of α-boryl aldehyde 3.2a

Encouraged by the bromination result, we decided to employ palladium-catalyzed α-allylation\(^9\) to our α-boryl aldehydes. Compound 3.2a was mixed with allyl alcohol and catalytical amount of Pd(PPh\(_3\))\(_4\) in the presence of triethylamine and additives, such as triethylborane and 4 Å molecular sieves (Equation 3.6). After heated at 50 °C for 12 to 24 hours, gratifyingly, the reaction afforded the expected α-allylated boryl aldehydes 3.18 in good yield.

Equation 3.6

Triethylborane used in this reaction behaves as a Lewis acid promoter to activate the O-H free allyl alcohol leading to the formation of \(\pi\)-allylpalladium species (Scheme 3.9). In addition, interactions of starting α-boryl aldehyde together with acidic triethylborane and basic triethylamine facilitate the formation of the enolate intermediates, which will subsequently react with the \(\pi\)-allylpalladium electrophile to form the allylated products.
3.3.4 Oxidation to α-borylcarboxylic acids

We believed that the chemoselective transformation from aldehydes to carboxylic acids with the α-boryl group intact could potentially generate another class of α-borylcarbonyl compounds – α-borylcarboxylic acids. As a testing run, α-boryl aldehyde 3.2a was subjected to the mild Pinnick (Lindgren-Kraus) oxidation condition\(^1\) using sodium chlorite and sodium dihydrogen phosphate in the presence of cyclohexene in a mixture of tert-butanol and water. Encouragingly, the desired α-borylcarboxylic acid 3.19a was isolated as a white powder in 73% yield. This result prompted us to evaluate the generality of this transformation. In the same manner, a range of α-borylcarboxylic acids with different substituents were successfully prepared (Table 3.2). As their aldehyde precursors, all the acid products are also bench-stable and can be purified by silica gel chromatography or crystallization.

Table 3.2 Preparation of α-borylcarboxylic acids from α-boryl aldehydes\(^a\)
<table>
<thead>
<tr>
<th>Entry</th>
<th>α-Boryl aldehyde</th>
<th>Product</th>
<th>Yield$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="3.2a" /></td>
<td><img src="image" alt="3.19a" /></td>
<td>73%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="3.2b" /></td>
<td><img src="image" alt="3.19b" /></td>
<td>86%</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="3.2c" /></td>
<td><img src="image" alt="3.19c" /></td>
<td>74%</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="3.2d" /></td>
<td><img src="image" alt="3.19d" /></td>
<td>83%</td>
</tr>
</tbody>
</table>
Reactions were carried out using 1.0 equiv of α-boryl aldehyde, 1.2 equiv of NaClO₂, 1.2 equiv of NaH₂PO₄, and 3.0 equiv of cyclohexene in t-BuOH/H₂O (1:1) at 25 °C for 1-2 hr. Isolated yields after silica gel chromatography.
In order to evaluate the racemization possibility of the starting aldehydes or acid products during the course of the reaction, we have subjected α-boryl aldehyde 3.2a to the same oxidation condition, but using D\textsubscript{2}O instead of water (Equation 3.7). Surprisingly, \textsuperscript{1}H NMR analysis of the crude mixture indicated no deuterium incorporation at the α-position of the corresponding acid product 3.19a'. This result attests to the configurational stability of both the α-boryl aldehyde and the acid under this oxidation condition.

\[
\begin{align*}
\text{MeN} & \quad \text{Ph} \\
\text{B} & \quad \text{H} \\
3.2a & \quad \text{NaClO}_2, \text{NaH}_2\text{PO}_4 \\
& \quad \text{cyclohexene} \\
& \quad \text{t-BuOH/D}_2\text{O, r.t.} \\
\text{MeN} & \quad \text{Ph} \\
\text{B} & \quad \text{H} \\
\text{O} & \quad \text{COOD} \\
3.19a' &
\end{align*}
\]

(3.7)

### 3.3.5 Transformations of nucleophilic carbon-boron bonds

The transformations discussed above mainly involve the reactivity of electrophilic aldehyde functions in α-boryl aldehydes. In order to fully utilize the amphoteric property of α-boryl aldehydes in synthetic application, we are also interested in exploring transformations that can take advantage of the nucleophilic carbon-boron bonds.

β-Functionalized vinyl boronates presented in Scheme 3.7 (Section 3.3.3) formally maintained the amphoteric reactivity of the original α-boryl aldehyde precursors. For instance, triflate enol ether 3.16 has the nucleophilic carbon possessing the MIDA boryl group, whereas the carbon center originated from the carbonyl group, now connecting with triflate functionality, is still electrophilic. Hence, the amphoteric reactivity pattern can be realized by subjecting compound 3.16 to an iterative Suzuki-Miyaura coupling reaction sequence\textsuperscript{11} leading to a trisubstituted
olefin **3.21** (Scheme 3.10). By using phenylboronic acid as a nucleophile, the first step involving an anhydrous condition furnished compound **3.20** selectively by coupling with the reaction site possessing the triflate group. The MIDA boryl group was intact in this process. Subsequently, an aqueous basic cross-coupling condition was employed. In this step, the MIDA protecting group was hydrolyzed in-situ and released the active $sp^2$-boron species, leading to the formation of the final trisubstituted olefin product **3.21**.

![Scheme 3.10](image-url)

Scheme 3.10 Iterative Suzuki-Miyaura cross-coupling of triflate enol ether **3.16**

Further careful inspection of those functionalized vinyl boronate molecules, such as silyloxyvinyl boronates **3.13** and amidovinyl boronates **3.14**, revealed that these species actually possess ambident nucleophilicity at their carbon center equipped with the boryl group. These molecules can react as either enolate nucleophiles or vinyl boronate nucleophiles (Figure 3.3). Bis-nucleophilic character of these building blocks aroused our curiosity to investigate the possibility for chemoselective transformations of their nucleophilic carbon-boron bonds. Since reactive iminium ion species in Petasis borono-Mannich reaction (Figure 3.4)$^{12}$ are potentially reactive towards these ambident nucleophiles in both fashions, we opted to use Petasis reaction as a testing ground in the hope of selectively transforming the vinyl boronate to $\alpha$-amino acids.
We thus chose TIPS enol ethers 3.13b-c and enamides 3.14a-b as the testing substrates. They were first transformed to the corresponding pinacolyl boronates 19a-b and 20a-b, respectively (Scheme 3.12), by treating the original MIDA boronates with pinacol in the presence of \( \text{NaHCO}_3 \) in methanol. These pinacol boronic esters, expected to be reactive in Petasis conditions,\(^\text{13}\) were subsequently subjected to the Petasis reaction with glyoxylic acid in the presence of different secondary or primary amines in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as the solvent. To our delight, several novel unnatural amino acids 3.24a-k with intact silyl enol ether or enamide functionalities were successfully obtained (Table 3.3). Importantly, no regular Mannich-type products, generated in the fashion of enolate attack, were detected in the course of these reactions.
The reactions were carried out using 1.0 equiv of MIDA boronate, 1.5 equiv of pinacol, and 5.0 equiv of NaHCO$_3$ in MeOH at 45 °C. $^b$ Isolated yield after silica gel chromatography. $^c$ E/Z ratios were determined by analysis of purified product mixtures with $^1$H NMR.

Scheme 3.11 Preparation of functionalized pinacolyl boronates$^a$

Table 3.3 Preparation of unnatural amino acids with functionalized boronates$^a$
<table>
<thead>
<tr>
<th>Entry</th>
<th>Pinacolyl boronate</th>
<th>Amine</th>
<th>Product</th>
<th>Yield&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
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<td><img src="image2" alt="Structure" /></td>
<td><img src="image3" alt="Structure" /></td>
<td>84%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td><img src="image4" alt="Structure" /></td>
<td><img src="image5" alt="Structure" /></td>
<td><img src="image6" alt="Structure" /></td>
<td>(E/Z 60:40)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td><img src="image7" alt="Structure" /></td>
<td><img src="image8" alt="Structure" /></td>
<td><img src="image9" alt="Structure" /></td>
<td>74%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td><img src="image10" alt="Structure" /></td>
<td><img src="image11" alt="Structure" /></td>
<td><img src="image12" alt="Structure" /></td>
<td>(E/Z 60:40)</td>
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<tr>
<td>3</td>
<td><img src="image13" alt="Structure" /></td>
<td><img src="image14" alt="Structure" /></td>
<td><img src="image15" alt="Structure" /></td>
<td>50%&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td><img src="image16" alt="Structure" /></td>
<td><img src="image17" alt="Structure" /></td>
<td><img src="image18" alt="Structure" /></td>
<td>(E/Z 80:20)</td>
</tr>
<tr>
<td>4</td>
<td><img src="image19" alt="Structure" /></td>
<td><img src="image20" alt="Structure" /></td>
<td><img src="image21" alt="Structure" /></td>
<td>55%&lt;sup&gt;c&lt;/sup&gt;</td>
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<td></td>
<td><img src="image22" alt="Structure" /></td>
<td><img src="image23" alt="Structure" /></td>
<td><img src="image24" alt="Structure" /></td>
<td>(E/Z 75:25)</td>
</tr>
</tbody>
</table>
5. **3.22b**

67%

(d.r.>95:5)

6. **3.22b**

67%

7. **3.23a**

70%

8. **3.23a**

97%
9. \[ \begin{align*} &\text{3.23a} \\ &\text{85\%} \\ &\text{(d.r.}>95:5) \end{align*} \]

10. \[ \begin{align*} &\text{3.23a} \\ &\text{51\%} \\ &\text{(d.r.}=75:25) \end{align*} \]

11. \[ \begin{align*} &\text{3.23b} \\ &\text{92\%} \end{align*} \]

12. \[ \begin{align*} &\text{3.23a} \\ &\text{No reaction} \\ &\text{N/A} \end{align*} \]
Generally, the alkyl-substituted boronates 3.22b and 3.23b were found to be more reactive than their aryl-substituted counterparts 3.22a and 3.23a. On the other hand, electron-rich substrates 3.22a and 3.22b possessing silyl enol ether groups showed much higher reactivity than their corresponding enamide counterparts 3.22a and 3.23b. Thus, silyloxy vinyl boronates reacted not only faster than amido ones with secondary amines, but also worked very well with primary amines, with which the amido vinyl boronates 3.23a and 3.23b showed no reactivity (Table 3.3, entry 12 and 13).

In addition, we were able to gain insight into the diastereoselectivity of the Petasis reaction of these functionalized vinyl boronates. While (S)-N-methyl-1-phenylethylamine14 gave inferior results (Table 3.3, entry 10, d.r. = 75:25), the reaction between 2-methylpyrrolidine,15 glyoxylic acid, and pinacolyl boronate 2.32b or 2.33a afforded the alkenylglycine 3.24e (entry 5) or 3.24i (entry 9) with excellent diastereoselectivity (d.r. > 95:5).

It is worth pointing out that the original amino acid products resulted from the reaction between TIPS enol ethers primary amines were found unstable during prolonged storage, probably due to

---

3.23b

Reactions were carried out using 1.0 equiv of pinacolyl boronic esters, 1.2 equiv of glyoxylic acid, and 1.2 equiv of amines (1st or 2nd) in HFIP at 23 °C or 50 °C for 5 to 72 hours. \(^b\) Isolated yield after silica gel chromatography. \(^c\) \(E/Z\) ratios were determined by analysis of purified product mixtures with \(^1\)H NMR. \(^d\) Diastereoisomeric ratios (d.r.) were determined by analysis of crude reaction mixtures with \(^1\)H NMR. \(^e\) Stable methyl esters were generated by one-pot esterification using TMSCHN₂.
the sensitivity of TIPS group to acids. Thus, a one-port esterification of the amino acid products using TMSCHN$_2$ was conducted to remove the acidity of the molecule, affording the final isolated products as more stable methyl ester derivatives (Table 3.3, entry 3 and 4).

### 3.4 Summary

We discovered a class of bench-stable amphoteric $\alpha$-boryl aldehydes equipped with MIDA boryl group, attesting the pivotal role of tetracoordinate boron center in the stability of $\alpha$-borylcarbonyl compounds. These novel boryl aldehydes can be prepared from oxiranyl MIDA boronates via a 1,2-boryl migration in the BF$_3$-promoted epoxide rearrangement. A range of boryl imines, alkenes, alcohols, enol ethers, enamides, carboxylic acids and other functionalized boronic acid derivatives that are difficult or impossible to prepare using established methods can be accessed from $\alpha$-boryl aldehydes. These molecules have enabled facile and highly selective construction of densely functionalized molecules such as 1,2-diols, 1,4-dienes, multisubstituted olefins and unnatural amino acids, attesting the potential of $\alpha$-boryl aldehydes in chemical synthesis.

### 3.5 Experimental details

#### 3.5.1 General information

**General:** Anhydrous methylene chloride (DCM) and chloroform (CHCl$_3$) were purchased and used as received. Anhydrous tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. All other solvents were of reagent grade quality.

**Chromatography:** Flash column chromatography was carried out using Silicycle 230-400 mesh silica gel. Thin-layer chromatography (TLC) was performed on Macherey Nagel pre-coated glass backed TLC plates (SIL G/UV254, 0.25 mm) and visualized using a UV lamp (254 nm) or KMnO$_4$ stain in case of no UV activity.
Nuclear Magnetic Resonance Spectroscopy: $^1$H NMR and $^{13}$C NMR spectra were recorded on Varian Mercury 400 MHz spectrometer. $^1$H NMR spectra chemical shifts (δ) are reported in parts per million (ppm) referenced to TMS (0 ppm) or residual protium in the NMR solvent (DMSO-d$_6$, δ = 2.49, center line). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doubles, dt = doublet of triplets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, m = multiplet, br = broad), coupling constant (J) in Hertz (Hz), and integration. $^{13}$C NMR spectra chemical shifts (δ) are reported in parts per million (ppm) were referenced to carbon resonances in the NMR solvent (CDCl$_3$, δ = 77.0; DMSO-d$_6$, δ = 39.5, center line). Carbons exhibiting significant line broadening brought about by boron substituents were not reported (quadrupolar relaxation). $^{11}$B NMR was recorded using Varian VnmrS 400 MHz spectrometer and referenced to an external standard of BF$_3$·Et$_2$O.

Infrared Spectroscopy: IR spectra were recorded on a Perkin-Elmer Spectrum 100 instrument equipped with a single-reflection diamond/ZnSe ATR accessory.

Mass Spectroscopy: High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities.

3.5.2 General procedure for synthesis of oxiranyl MIDA boronates

Oxiranyl MIDA boronates were prepared according to literature method,$^{2d}$ in which the preparation and characterization of unsubstituted substrate 3.1j was reported. Other new oxiranyl MIDA boronates 3.1a-i and 3.5 were prepared in the same manner:

To a solution of the vinyl MIDA boronate (5.0 mmol) in 30 mL DCM was added mCPBA (5.5 mmol) at 0 ºC. The mixture was warmed to room temperature and stirred for 1~3 hours until the
reaction was complete as indicated by TLC or crude $^1$H NMR. The reaction solution was then washed with saturated aqueous NaHCO$_3$ (30 mL). The organic layer was then separated and concentrated to dryness. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford pure products.

**MIDA (trans-3-phenyloxiran-2-yl)boronate (3.1a)**

White solid; 94% yield; TLC (EtOAc) $R_f$ = 0.50; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.37-7.25 (m, 5H), 4.35 (d, $J = 17.2$ Hz, 1H), 4.26 (d, $J = 17.1$ Hz, 1H), 4.10 (d, $J = 17.2$ Hz, 1H), 4.01 (d, $J = 17.1$ Hz, 1H), 3.72 (d, $J = 2.9$ Hz, 1H), 3.07 (s, 3H), 2.44 (d, $J = 2.9$ Hz, 1H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.3, 168.6, 138.8, 128.4, 127.8, 125.6, 62.0, 61.9, 54.8, 46.4 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.5 ppm; IR (thin film, cm$^{-1}$) 2965, 1753, 1459, 1416, 1341, 1281, 1249, 1197, 1154, 1111, 1033, 958, 899, 882, 856, 830, 762, 720, 698.

**MIDA (trans-3-(p-tolyl)oxiran-2-yl)boronate (3.1b)**

White solid; 85% yield; TLC (EtOAc) $R_f$ = 0.40; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.18 (d, $J = 8.2$ Hz, 2H), 7.13 (d, $J = 8.2$ Hz, 2H), 4.34 (d, $J = 17.2$ Hz, 1H), 4.24 (d, $J = 17.1$ Hz, 1H), 4.10 (d, $J = 17.2$ Hz, 1H), 4.00 (d, $J = 17.1$ Hz, 1H), 3.66 (d, $J = 3.0$ Hz, 1H), 3.06 (s, 3H), 2.42 (d, $J = 3.0$ Hz, 1H), 2.28 (s, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.3, 168.6, 137.0, 135.7, 128.9, 125.6, 62.0, 61.9, 54.8, 46.4, 20.7 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 10.2 ppm; IR (thin film, cm$^{-1}$) 2957, 2997, 1758, 1517, 1453, 1398, 1342, 1302, 1281, 1242, 1196, 1164, 1111, 1086, 1025, 962, 898, 861, 847, 817, 726.

**MIDA (trans-3-(4-fluorophenyl)oxiran-2-yl)boronate (3.1c)**

White solid; 80% yield; TLC (EtOAc) $R_f$ = 0.35; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.38-7.34 (m, 2H), 7.19-7.14 (m, 2H), 4.35 (d, $J = 17.2$ Hz, 1H), 4.25 (d, $J = 17.1$ Hz, 1H), 4.10 (d, $J = 17.2$ Hz, 1H), 4.02 (d, $J = 17.1$ Hz, 1H), 3.75 (d, $J = 2.7$ Hz, 1H), 3.06 (s, 3H), 2.43 (d, $J = 2.7$ Hz, 1H)
ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.2, 168.6, 161.8 (d, $^1J_{CF} = 243.4$ Hz), 135.0 (d, $^4J_{CF} = 2.8$ Hz), 127.6 (d, $^3J_{CF} = 8.3$ Hz), 115.2 (d, $^2J_{CF} = 21.6$ Hz), 62.0, 61.9, 54.2, 46.4 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.5 ppm; IR (thin film, cm$^{-1}$) 1756, 1609, 1513, 1461, 1438, 1398, 1332, 1277, 1237, 1221, 1196, 1157, 1113, 1072, 1038, 994, 958, 896, 850, 825, 769, 726.

MIDA (trans-3-phenethyloxiran-2-yl)boronate (3.1d)

White solid; 94% yield; TLC (EtOAc) $R_f = 0.30$; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.29-7.25 (m, 2H), 7.22-7.15 (m, 3H), 4.30 (d, $J = 17.2$ Hz, 1H), 4.17 (d, $J = 17.0$ Hz, 1H), 4.05 (d, $J = 17.2$ Hz, 1H), 3.91 (d, $J = 17.0$ Hz, 1H), 2.99 (s, 3H), 2.81-2.74 (m, 1H), 2.72-2.66 (m, 2H), 2.07 (d, $J = 3.0$ Hz, 1H), 1.90-1.81 (m, 1H), 1.77-1.68 (m, 1H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.3, 168.5, 141.4, 128.3, 128.2, 125.8, 61.9, 61.7, 54.9, 46.2, 34.7, 32.1 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.9 ppm; IR (thin film, cm$^{-1}$) 2949, 1756, 1496, 1453, 1336, 1280, 1194, 1159, 1123, 1036, 990, 952, 896, 858, 788, 751, 699.

MIDA (trans-3-cyclohexyloxiran-2-yl)boronate (3.1e)

White solid; 96% yield; TLC (EtOAc) $R_f = 0.32$; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 4.30 (d, $J = 17.3$ Hz, 1H), 4.16 (d, $J = 17.0$ Hz, 1H), 4.04 (d, $J = 17.3$ Hz, 1H), 3.90 (d, $J = 17.0$ Hz, 1H), 2.99 (s, 3H), 2.51 (dd, $J = 5.9$, 3.1 Hz, 1H), 2.07 (d, $J = 3.1$ Hz, 1H), 1.76-1.59 (m, 5H), 1.22-1.03 (m, 6H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.4, 168.4, 61.8, 61.7, 59.5, 46.2, 40.6, 29.6, 28.7, 25.9, 25.3, 25.1 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.8 ppm; IR (thin film, cm$^{-1}$) 2925, 2851, 1748, 1451, 1337, 1283, 1217, 1204, 1162, 1121, 1087, 1030, 966, 952, 925, 898, 876, 856, 791, 723

MIDA (trans-3-(tert-butyl)oxiran-2-yl)boronate (3.1i)

White solid; 93% yield; TLC (EtOAc) $R_f = 0.33$; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 4.30 (d, $J = 17.2$ Hz, 1H), 4.17 (d, $J = 17.0$ Hz, 1H), 4.05 (d, $J = 17.2$ Hz, 1H), 3.92 (d, $J = 17.0$ Hz, 1H), 3.00 (s, 3H), 2.56 (d, $J = 3.2$ Hz, 1H), 1.90-1.81 (m, 1H), 1.76-1.59 (m, 5H), 1.22-1.03 (m, 6H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.3, 168.5, 141.4, 128.3, 128.2, 125.8, 61.9, 61.7, 54.9, 46.2, 34.7, 32.1 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.9 ppm; IR (thin film, cm$^{-1}$) 2925, 2851, 1748, 1451, 1337, 1283, 1217, 1204, 1162, 1121, 1087, 1030, 966, 952, 925, 898, 876, 856, 791, 723
121 Hz, 1H), 2.16 (d, J = 3.2 Hz, 1H), 0.86 (s, 9H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 169.4, 168.4, 63.0, 61.8, 46.2, 30.6, 25.6 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 10.0 ppm; IR (thin film, cm$^{-1}$) 2960, 1740, 1464, 1448, 1433, 1362, 1327, 1340, 1297, 1259, 1234, 1196, 1164, 1139, 1126, 1089, 1069, 1040, 992, 960, 900, 889, 852, 794, 720.

MIDA (2-phenyloxiran-2-yl)boronate (3.5)

White solid; 86% yield; TLC (EtOAc) $R_f$ = 0.60; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.40-7.38 (m, 2H), 7.33-7.29 (m, 2H), 7.23-7.19 (m, 1H), 4.34 (d, $J = 17.5$ Hz, 1H), 4.18 (d, $J = 16.9$ Hz, 1H), 3.97 (d, $J = 16.9$ Hz, 1H), 2.99 (d, $J = 6.5$ Hz, 1H), 2.68 (s, 3H), 2.39 (d, $J = 6.5$ Hz, 1H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 169.2, 168.1, 141.5, 128.2, 126.5, 125.2, 62.3, 62.0, 54.6, 47.0 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 9.3 ppm; IR (thin film, cm$^{-1}$) 2963, 1765, 1496, 1459, 1445, 1335, 1323, 1289, 1273, 1244, 1194, 1173, 1146, 1114, 1100, 1089, 1061, 1044, 1028, 992, 963, 933, 911, 895, 864, 826, 758, 713, 668.

3.5.3 General procedure for synthesis of $\alpha$-boryl aldehydes

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added oxiranyl MIDA boroante 3.1 (1.0 mmol) in 50 mL anhydrous DCM. The solution was cooled to −30 °C. BF$_3$·Et$_2$O (0.14 g, 0.123 mL, 1.0 mmol) was added dropwise with stirring. The mixture was then stirred at −30 to 0 °C over 30 min. The reaction was quenched by adding 30 mL saturated aqueous NaHCO$_3$. The organic layer was then separated; the aqueous layer was extracted with EtOAc (10 mL × 2). The combined organic layer was dried over anhydrous
Na₂SO₄ and concentrated to dryness. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford pure products.

2-(MIDA boryl)-2-phenylacetaldehyde (3.2a)

White solid; 98% yield; TLC (EtOAc) Rᵢ = 0.45; ¹H NMR (400 MHz, DMSO-d₆) δ 9.73 (d, J = 2.5 Hz, 1H), 7.34-7.30 (m, 2H), 7.27-7.20 (m, 3H), 4.28 (d, J = 17.0 Hz, 1H), 4.27 (d, J = 17.2 Hz, 1H), 4.05 (d, J = 17.0 Hz, 1H), 3.76 (d, J = 2.5 Hz, 1H), 3.69 (d, J = 17.2 Hz, 1H), 2.88 (s, 3H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 203.6, 168.4, 168.3, 136.2, 129.6, 128.4, 126.0, 62.4, 62.2, 46.5 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 10.7 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₁₃H₁₅BNO₂ 276.1037, found 276.1031; IR (thin film, cm⁻¹) 3004, 1760, 1701, 1600, 1493, 1452, 1338, 1282, 1194, 1154, 1028, 955, 895, 833, 766, 705.

2-(MIDA boryl)-2-(p-tolyl)acetaldehyde (3.2b)

White solid; 97% yield; TLC (EtOAc) Rᵢ = 0.35; ¹H NMR (400 MHz, DMSO-d₆) δ 9.70 (d, J = 2.5 Hz, 1H), 7.13 (ap. s, 5H), 4.27 (d, J = 17.0 Hz, 1H), 4.25 (d, J = 17.2 Hz, 1H), 4.04 (d, J = 17.0 Hz, 1H), 3.69 (d, J = 2.5 Hz, 1H), 3.65 (d, J = 17.2 Hz, 1H), 2.86 (s, 3H), 2.27 (s, 3H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 203.5, 168.3, 135.0, 133.0, 129.4, 129.0, 62.4, 62.1, 20.6 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 10.7 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₁₄H₁₇BNO₂ 290.1194, found 290.1189; IR (thin film, cm⁻¹) 3021, 2735, 1774, 1697, 1514, 1455, 1421, 1327, 1264, 1241, 1188, 1158, 1114, 1097, 1039, 1008, 997, 942, 891, 848, 820, 732, 702.
2-(4-fluorophenyl)-2-(MIDA boryl)acetaldehyde (3.2c)

White solid; quantitative yield; TLC (EtOAc) Rf = 0.30; 1H NMR (400 MHz, DMSO-d6) δ 9.72 (d, J = 2.2 Hz, 1H), 7.29-7.24 (m, 2H), 7.18-7.13 (m, 2H), 4.28 (d, J = 17.0 Hz, 1H), 4.27 (d, J = 17.3 Hz, 1H), 4.06 (d, J = 17.0 Hz, 1H), 3.83 (d, J = 2.2 Hz, 1H), 3.73 (d, J = 17.3 Hz, 1H), 2.88 (s, 3H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 203.3, 168.3, 168.2, 160.8 (d, JCF = 241.7 Hz), 132.3 (d, JCF = 3.1 Hz), 131.3 (d, JCF = 7.9 Hz), 115.0 (d, JCF = 21.0 Hz), 62.4, 62.2, 46.6 ppm; 11B NMR (128 MHz, DMSO-d6) δ 10.6 ppm; HRMS (ESI) [M+H]+ calcd. For C13H14BFNO5 294.0943, found 294.0952; IR (thin film, cm⁻¹) 2962, 1760, 1702, 1603, 1507, 1452, 1338, 1284, 1222, 1195, 1161, 1097, 1031, 946, 895, 832, 796, 728.

2-(MIDA boryl)-4-phenylbutanal (3.2d)

White solid; 76% yield; TLC (EtOAc) Rf = 0.35; 1H NMR (400 MHz, DMSO-d6) δ 9.67 (d, J = 3.0 Hz, 1H), 7.28-7.24 (m, 2H), 7.19-7.16 (m, 3H), 4.26 (d, J = 17.2 Hz, 1H), 4.25 (d, J = 17.2 Hz, 1H), 4.09 (d, J = 17.2 Hz, 1H), 3.96 (d, J = 17.2 Hz, 1H), 2.90 (s, 3H), 2.61-2.49 (m, 1H), 2.46-2.39 (m, 1H), 2.32 (ddd, J = 10.5, 3.0, 2.0 Hz, 1H), 2.14-2.04 (m, 1H), 1.68-1.60 (m, 1H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 206.3, 168.4, 168.3, 141.8, 128.3, 128.2, 125.8, 62.3, 62.2, 46.1, 35.2, 26.3 ppm; 11B NMR (128 MHz, DMSO-d6) δ 11.1 ppm; HRMS (ESI) [M+NH4]+ calcd. For C15H22BN2O5 321.1616, found 321.1617; IR (thin film, cm⁻¹) 3024, 2953, 2853, 1758, 1697, 1602, 1496, 1454, 133.8, 1287, 1246, 1191, 1163, 1028, 988, 892, 853, 751, 729, 700.

2-(MIDA boryl)-3-phenylpropanal (3.2e)

White solid; 69% yield; TLC (EtOAc) Rf = 0.38; 1H NMR (400 MHz, DMSO-d6) δ 9.66 (d, J = 3.3 Hz, 1H), 7.27 – 7.12 (m, 5H), 4.33 (d, J = 17.2 Hz, 1H), 4.32 (d, J = 17.2 Hz, 1H), 4.17 (d, J = 17.2 Hz, 1H), 4.03 (d, J = 17.2 Hz, 1H), 3.14 (dd, J = 15.0, 11.6 Hz, 1H), 3.05 (s, 3H), 2.80-2.77 (m, 1H), 2.76-2.4 (m, 1H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 206.0, 168.4, 168.3, 141.8, 128.3, 128.2, 125.7, 62.3,
62.2, 46.2, 29.9 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 11.0 ppm; HRMS (DART-TOF) [M+NH$_4^+$] calcd. For C$_{14}$H$_{20}$BN$_2$O$_5$ 307.14653, found 307.14700; IR (thin film, cm$^{-1}$) 1741, 1702, 1496, 1447, 1343, 1292, 1254, 1195, 1165, 1102, 1046, 1010, 961, 947, 895, 856, 817, 746, 698.

4-methyl-2-(MIDA boryl)pentanal (3.2f)

White solid; 66% yield; TLC (EtOAc) R$_f$ = 0.28; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.62 (d, $J$ = 3.6 Hz, 1H), 4.26 (d, $J$ = 17.2 Hz, 1H), 4.25 (d, $J$ = 17.2 Hz, 1H), 4.10 (d, $J$ = 17.2 Hz, 1H), 3.97 (d, $J$ = 17.2 Hz, 1H), 2.95 (s, 3H), 2.38 (ddd, $J$ = 11.0, 4.8, 3.6 Hz, 1H), 1.85 (ddd, $J$ = 14.0, 11.0, 4.8 Hz, 1H), 1.48-1.38 (m, 1H), 1.15 (ddd, $J$ = 14.0, 9.0, 1.9 Hz, 1H), 0.85 (d, $J$ = 6.6 Hz, 3H), 0.81 (d, $J$ = 6.6 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 207.2, 169.1, 169.0, 63.0, 62.9, 46.8, 33.6, 28.3, 24.0, 21.9 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 11.1 ppm; HRMS (DART-TOF) [M+NH$_4^+$] calcd. For C$_{11}$H$_{22}$BN$_2$O$_5$ 273.16218, found 273.16286; IR (thin film, cm$^{-1}$) 3009, 2957, 2928, 2870, 2734, 1757, 1700, 1465, 1455, 1397, 1385, 1367, 1338, 1294, 1246, 1181, 1165, 1138, 1127, 1093, 1028, 1010, 985, 958, 984, 848, 762, 703.

2-(MIDA boryl)hexanal (3.2g)

White solid; 80% yield; TLC (EtOAc) R$_f$ = 0.50; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.62 (d, $J$ = 3.4 Hz, 1H), 4.26 (d, $J$ = 17.2 Hz, 2H), 4.09 (d, $J$ = 17.2 Hz, 1H), 3.96 (d, $J$ = 17.2 Hz, 1H), 2.94 (s, 3H), 2.24 (ddd, $J$ = 10.7, 3.3, 2.5 Hz, 1H), 1.87-1.77 (m, 1H), 1.42-1.33 (m, 1H), 1.32-1.11 (m, 4H), 0.85 (t, $J$ = 7.1 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 206.7, 168.4, 168.4, 62.2, 62.1, 46.1, 31.7, 23.9, 22.1, 13.8 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 11.1 ppm; HRMS (DART-TOF) [M+NH$_4^+$] calcd. For C$_{11}$H$_{22}$BN$_2$O$_5$ 273.16218, found 273.16286; IR (thin film, cm$^{-1}$) 2932, 2957, 2861, 1746, 1698, 1456, 1338, 1289, 1247, 1192, 1096, 1024, 989, 960, 893, 852, 706.
MIDA (1-cyclohexyl-2-oxoethyl)boronate (3.2h)

White solid; 94% yield; TLC (EtOAc) R<sub>f</sub> = 0.35; <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 9.74 (d, J = 3.9 Hz, 1H), 4.26 (d, J = 17.2 Hz, 1H), 4.17 (d, J = 17.1 Hz, 1H), 4.04 (d, J = 17.2 Hz, 1H), 3.80 (d, J = 17.1 Hz, 1H), 2.89 (s, 3H), 2.04 (ap. t, J = 3.9 Hz, 1H), 1.86-1.60 (m, 6H), 1.41-1.32 (m, 1H), 1.25-1.09 (m, 4H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 209.2, 168.6, 168.4, 62.1, 61.9, 46.4, 36.9, 33.1, 30.1, 26.6, 25.7 ppm; <sup>11</sup>B NMR (128 MHz, DMSO-d<sub>6</sub>) δ 11.1 ppm; HRMS (ESI) [M+H]<sup>+</sup> calcd. For C<sub>13</sub>H<sub>21</sub>BNO<sub>5</sub> 282.1507, found 282.1500; IR (thin film, cm<sup>-1</sup>) 2922, 2851, 1747, 1695, 1449, 1339, 1292, 1196, 1156, 1099, 1034, 1004, 893, 852, 729.

3.5.4 Deuterium labeling experiments for α-boryl aldehyde generation

Prepartion of 1-deuterated oxiranyl MIDA boronates 3.3a and 3.3b:

**Step 1.** To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added 10 mL anhydrous THF and terminal alkyne (10.0 mmol). The solution was cooled to −78 °C followed by adding n-BuLi (2.5M in hexanes, 4.8 mL, 12.0 mmol) dropwise. The reaction was stirred at −78 to −30 °C for an additional 30 min. D<sub>2</sub>O (10 mL) was added to quench the reaction. The mixture was then separated; the organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>.
and concentrated to dryness, affording the terminal deuterated alkyne product, which was subjected directly to the next step without further purification.

**Step 2.** A 25 mL flask was charged with the terminal deuterated alkyne, catecholborane (1.0M in THF, 15.0 mL, 15.0 mmol). The solution was stirred at 65 °C for 18 hr followed by cooling to room temperature, then transferred to a flask containing 60 mL water. The mixture was vigorously stirred for 3 hours at room temperature and then evaporated under reduced pressure to remove THF. The resulted boronic acid suspension was collected by vacuum filtration, washed with 10 mL water, and dried in desiccator. The crude 1-deuterated vinyl boronic acid product was subjected to the next step without further purification.

**Step 3.** A 100 mL flask was charged with the 1-deuterated vinyl boronic acid (5 mmol), N-methyliminodiacetic acid (5.5 mmol), 50 mL toluene and 5 mL DMSO. The flask was fitted with a Dean-Stark trap and a reflux condenser, and the mixture was refluxed (bath temperature 130 °C) with stirring for 2 h followed by concentration in vacuo. The resulting crude product was diluted with EtOAc (50 mL) and washed with saturated water (20 mL) and brine (20 mL). The EtOAc solution was then concentrated in vacuo. The residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford the pure 1-deuterated vinyl MIDA boronate as white solid.

**Step 4.** To a solution of the 1-deuterated vinyl MIDA boronate (5.0 mmol) in 30 mL DCM was added mCPBA (5.5 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 2 hours until the reaction was complete as indicated by TLC. The reaction solution was washed with saturated aqueous NaHCO₃ (30 mL). The organic layer was then separated and concentrated to dryness. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford pure product 3a or 3b as white solid.

White solid; 90% yield; TLC (EtOAc) Rₜ = 0.50; ¹H NMR (400 MHz, DMSO-d₆) δ 7.37-7.25 (m, 5H), 4.35 (d, J = 17.2 Hz, 1H), 4.26 (d, J = 17.1 Hz, 1H), 4.10 (d, J = 17.2 Hz, 1H), 4.01 (d, J = 17.1 Hz, 1H), 3.72 (s,
1H), 3.07 (s, 3H).

White solid; 96% yield; TLC (EtOAc) R_f = 0.30; ^1H NMR (400 MHz, DMSO-d_6) δ 7.29-7.25 (m, 2H), 7.22-7.15 (m, 3H), 4.30 (d, J = 17.2 Hz, 1H), 4.17 (d, J = 17.0 Hz, 1H), 4.05 (d, J = 17.2 Hz, 1H), 3.91 (d, J = 17.0 Hz, 1H), 2.99 (s, 3H), 2.77 (dd, J = 6.5, 4.7 Hz, 1H), 2.72-2.66 (m, 2H), 1.90-1.81 (m, 1H), 1.77-1.68 (m, 1H)

BF_3-Promoted Rearrangement of 3.3a and 3.3b:

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added oxiranyl MIDA boronate 3.3 (1.0 mmol) in 50 mL anhydrous DCM. The solution was cooled to –30 °C. BF_3·Et_2O (0.14 g, 0.123 mL, 1.0 mmol) was added dropwise with stirring. The mixture was then stirred at –30 to 0 °C over 30 min. The reaction was quenched by adding 30 mL saturated aqueous NaHCO_3. The organic layer was then separated; the aqueous layer was extracted with EtOAc (10 mL × 2). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to dryness. The ^1H NMR of the crude residue indicated the formation of α-boryl aldehyde 4 with exclusive deuterium-incorporation at the aldehyde carbon. The crude product was then further purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford pure product as white solid.

White solid; 98% yield; TLC (EtOAc) R_f = 0.45; ^1H NMR (400 MHz, DMSO-d_6) δ 7.34-7.30 (m, 2H), 7.27-7.20 (m, 3H), 4.28 (d, J = 17.0 Hz, 1H), 4.27 (d, J = 17.2 Hz, 1H), 4.05 (d, J = 17.0 Hz, 1H), 3.76 (s, 1H), 3.69 (d, J = 17.2 Hz, 1H), 2.88 (s, 3H)

White solid; 80% yield; TLC (EtOAc) R_f = 0.35; ^1H NMR (400 MHz, DMSO-d_6) δ 7.28-7.24 (m, 2H), 7.19-7.16 (m, 3H), 4.26 (d, J = 17.2 Hz, 1H), 4.25 (d, J = 17.2 Hz, 1H), 4.09 (d, J = 17.2 Hz, 1H), 3.96 (d, J = 17.2 Hz, 1H), 2.90 (s, 3H), 2.61-2.49 (m, 1H), 2.46-2.39 (m, 1H), 2.32 (dd, J = 10.5, 2.0 Hz, 1H), 2.14-2.04 (m, 1H), 1.68-1.60 (m, 1H).
3.5.5 Investigation for synthesis of α-boryl imines

The reactions between α-boryl aldehyde 3.2a and benzylamine or aniline:

![Chemical reaction image]

To a solution of the α-boryl aldehyde 3.2a (0.20 g, 0.727 mmol) in 10 mL anhydrous DCM was added anhydrous MgSO₄ (0.44 g, 3.64 mmol) and the corresponding primary amine (0.727 mmol) at 0 °C. The mixture was stirred at 23 °C for 24 hours. The reaction mixture was then filtered; the filtrate was concentrated to dryness. The solid residue was purified using flash column chromatography on silica gel (pre-deactivated with Et₃N, eluent gradient: Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford N-boryl enamines product 3.6a or 3.6b.

(E)-MIDA benzyl(styryl)boramide (3.6a)

Yellow solid; 54% yield; TLC (pre-deactivated with Et₃N, EtOAc) Rf = 0.27; ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.28 (m, 6H), 7.26-7.19 (m, 3H), 7.16-7.11 (m, 1H), 6.60 (d, J = 12.6 Hz, 1H), 4.41 (dt, J = 12.6, 6.1 Hz, 1H), 4.18 (d, J = 6.1 Hz, 2H), 3.65 (d, J = 16.2 Hz, 2H), 3.34 (d, J = 16.2 Hz, 2H), 2.70 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 143.3, 140.1, 140.0, 129.7, 129.2, 128.5, 127.1, 127.0, 125.6, 61.7, 51.4, 46.4 ppm; ¹¹B NMR (128 MHz, CDCl₃) δ 12.5 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₂₀H₂₂BN₂O₄ 365.1667, found 365.1677; IR (thin film, cm⁻¹) 3021, 1764, 1741, 1616, 1595, 1492, 1454, 1337, 1288, 1243, 1221, 1149, 1107, 1082, 1060, 1019, 1003, 957, 903, 864, 801, 774, 721, 695, 660.
(E)-MIDA phenyl(styryl)boramidate (3.6b)

White solid; 83% yield; TLC (pre-deactivated with Et₃N, EtOAc) Rᵣ = 0.50; ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.33 (m, 4H), 7.27-7.18 (m, 4H), 6.85 (t, J = 7.4, 0.9 Hz, 1H), 6.78 (d, J = 8.7 Hz, 2H), 6.24 (d, J = 12.9 Hz, 1H), 3.70 (d, J = 16.2 Hz, 2H), 3.39 (d, J = 16.2 Hz, 2H), 2.77 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 141.9, 138.9, 133.5, 129.7, 129.5(1), 129.4(7), 126.4, 120.3, 114.0, 61.9, 46.5 ppm; ¹¹B NMR (128 MHz, CDCl₃) δ 12.5 ppm; HRMS (EI) [M]+ calcd. For C₁₉H₁₉BN₂O₄ 350.1438, found 350.1442; IR (thin film, cm⁻¹) 3017, 1756, 1624, 1599, 1504, 1456, 1335, 1265, 1230, 1191, 1146, 1112, 1022, 990, 963, 893, 873, 845, 797, 774, 751, 717, 691, 660.

The reaction between α-boryl aldehyde 3.2a and tert-butanesulfinamide:

To a solution of the α-boryl aldehyde 3.2a (0.27 g, 1.0 mmol) in 10 mL anhydrous DCM was added anhydrous CuSO₄ (0.80 g, 5.0 mmol) and rac-2-methylpropane-2-sulfinamide (0.12 g, 1.0 mmol) at 0 °C. The mixture was stirred at 23 °C for 24 hours. The reaction mixture was then filtered; the filtrate was concentrated to dryness. The solid residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 8:2) to afford N-boryl enamines 3.6c (0.045 g) and α-boryl imines 3.7c (0.21 g, 1:1 mixture of diastereomers) as white solid. (0.054 g of starting 3.2a was recovered).

(E)-MIDA tert-butylsulfinyl(styryl)boramidate (3.6c)

White solid; 15% yield (based on converted 3.2a); TLC (EtOAc) Rᵣ = 0.20; ¹H NMR (400 MHz, DMSO-d₆) δ 7.36-7.31 (m, 2H), 7.21-7.15 (m, 3H), 6.85
(d, J = 11.8 Hz, 1H), 6.54 (d, J = 11.8 Hz, 1H), 4.15 (d, J = 17.2 Hz, 2H), 3.70 (d, J = 17.2 Hz, 1H), 3.69 (d, J = 17.2 Hz, 1H), 2.64 (s, 3H), 1.05 (s, 9H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 168.9, 168.8, 138.8, 132.7, 129.2, 128.7, 125.9, 61.5(99), 61.5(87), 56.7, 46.9, 22.1 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 10.9 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{24}$BN$_2$O$_5$S 379.1493, found 379.1498; IR (thin film, cm$^{-1}$) 3355, 2960, 1615, 1492, 1458, 1364, 1337, 1287, 1230, 1192, 1112, 1024, 967, 872, 842, 798, 771, 706.

$(E)$-MIDA (2-((tert-butylsulfinyl)imino)-1-phenylethyl)boronate (3.7c)

White solid; 70% yield (based on converted 3.2a); TLC (EtOAc) R$_f$ = 0.25; $^1$H NMR (400 MHz, DMSO-d$_6$) (1:1 mixture of diastereomers) δ 8.08 (d, J = 6.0 Hz, 0.5H), 7.99 (d, J = 5.8 Hz, 0.5H), 7.23-7.17 (m, 1H), 4.31 (d, J = 17.0 Hz, 0.5H), 4.29 (d, J = 17.3 Hz, 0.5H), 4.27 (d, J = 16.8 Hz, 0.5H), 4.22 (d, J = 17.1 Hz, 0.5H), 4.06 (d, J = 16.8 Hz, 0.5H), 4.02 (d, J = 17.0 Hz, 0.5H), 3.85 (d, J = 6.0 Hz, 0.5H), 3.77 (d, J = 5.8 Hz, 0.5H), 3.67 (d, J = 17.3 Hz, 0.5H), 3.60 (d, J = 17.1 Hz, 0.5H), 2.85 (s, 1.5H), 2.82 (s, 1.5H), 1.07 (s, 4.5H), 1.04 (s, 4.5H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) (1:1 mixture of diastereomers) δ 171.0, 170.9, 168.6, 168.5, 168.3, 168.2, 138.6, 138.5, 129.4, 129.3, 128.5, 128.3, 126.0, 125.9, 62.6, 62.5, 62.2(4), 62.2(2), 56.4, 56.3, 46.5, 46.4, 21.7(8), 21.7(5) ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) (1:1 mixture of diastereomers) δ 11.0 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{17}$H$_{24}$BN$_2$O$_5$S 379.1493, found 379.1495; IR (thin film, cm$^{-1}$) (1:1 mixture of diastereomers) 2965, 1760, 1611, 1595, 1452, 1337, 1284, 1193, 1032, 950, 895, 773, 728, 903.

The reaction between α-boryl aldehyde 3.2a and p-toluenesulfonamide:
To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added α-boryl aldehyde 3.2a (0.27 g, 1.0 mmol) in 10 mL anhydrous DCM. p-Toluenesulfonamide (0.26 g, 1.5 mmol) and E3N (0.41 g, 0.56 mL, 4.0 mmol) was added. The solution was cooled to 0 °C. A solution of TiCl4 (0.14 g, 0.123 mL, 1.0 mmol) in 1 mL anhydrous DCM was then added dropwise. The mixture was warmed to room temperature and stirred for 24 hours. The final dark red solution was concentrated to dryness and purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford pure product 3.6d (0.099 g) as white solid. (0.083 g of starting 3.2a was recovered).

(E)-MIDA styryl(tosyl)boramidate (3.6d)

White solid; 33% yield (based on converted 3.2a); TLC (EtOAc) Rf = 0.50; 1H NMR (400 MHz, CDCl3) δ 7.64 (d, J = 7.6 Hz, 2H), 7.34-7.26 (m, 4H), 7.25-7.20 (m, 1H), 7.06 (d, J = 7.6 Hz, 2H), 6.78 (d, J = 11.4 Hz, 1H), 6.60 (d, J = 11.4 Hz, 1H), 3.80 (d, J = 16.6 Hz, 2H), 3.38 (d, J = 16.6 Hz, 2H), 2.71 (s, 3H), 2.41 (s, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 169.4, 144.1, 136.7, 136.6, 129.9, 129.6(9), 129.6 (8), 128.8, 127.4, 126.6, 62.0, 46.5, 21.5 ppm; 11B NMR (128 MHz, CDCl3) δ 11.1 ppm; HRMS (ESI) [M+H]+ calcd. For C20H22BN2O6S 429.1286, found 429.1297; IR (thin film, cm⁻¹) 3006, 1762, 1621, 1493, 1448, 1330, 1288, 1228, 1161, 1113, 1086, 1024, 970, 884, 855, 813, 772, 717, 705, 692.

3.5.6 Preparation of γ-boryl α,β-unsaturated ester

To a solution of the α-boryl aldehyde 3.2a (0.200 g, 0.727 mmol) in 10 mL anhydrous DCM was added ethyl 2-(triphenylphosphoranylidene)propanoate (0.316 g, 0.873 mmol). The solution was heated at 60 °C in a sealed vial for 48 hours. The reaction mixture was then cooled to room
temperature and concentrated to dryness. \(^1\)H NMR of the crude residue indicated formation of the \(E\)-olefine as the major product \((E/Z > 95:5)\). The crude product was then further purified using flash column chromatography on silica gel (DCM \(\rightarrow\) DCM/MeCN 6:4) to afford the \((E)\)-\(\gamma\)-boryl-\(\alpha,\beta\)-unsaturated ester \(3.8\) (0.188 g) as white solid.

\((E)\)-MIDA (4-ethoxy-3-methyl-4-oxo-1-phenylbut-2-en-1-yl)boronate (3.8)

\[\text{White solid; 72\% yield; TLC (DCM/MeCN 8:2) } R_f = 0.40; \text{ } ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.33-7.26 (m, 4H), 7.19-7.15 (m, 1H), 7.13 (dd, } J = 11.1, 1.0 \text{ Hz, 1H}), 4.16 (q, } J = 7.1 \text{ Hz, 2H}), 3.81 (d, } J = 16.6 \text{ Hz, 1H}), 3.72 (d, } J = 16.3 \text{ Hz, 1H}), 3.58 (d, } J = 16.6 \text{ Hz, 1H}), 3.31 (d, } J = 11.6 \text{ Hz, 1H}), 3.13 (d, } J = 16.3 \text{ Hz, 1H}), 2.82 (s, 3H), 1.92 (d, } J = 1.0 \text{ Hz, 3H}), 1.27 (t, } J = 7.1 \text{ Hz, 3H}) \text{ ppm; } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 168.1, 167.8, 167.7, 142.1, 140.0, 128.9, 128.5, 127.5, 126.0, 62.5, 62.3, 60.6, 45.4, 24.2, 12.8 \text{ ppm; } ^{11}\text{B NMR (128 MHz, CDCl}_3\text{)} \delta 12.0 \text{ ppm; HRMS (ESI) [M+H]}^+ \text{ calcd. For C}_{18}\text{H}_{23}\text{BNO}_6 360.1612, \text{ found 360.1620; IR (thin film, cm}^{-1} \text{) 2978, 1758, 1697, 1637, 1598, 1494, 1451, 1367, 1336, 1275, 1225, 1067, 1022, 952, 894, 869, 808, 749, 728, 702.}\]

### 3.5.7 Preparation of \(\text{gem}\)-dibromoallyl boronates

\[\text{To a solution of the } \alpha\text{-boryl aldehyde 3.2a or 3.2d (1.82 mmol) and CBr}_4\text{ (0.905 g, 2.73 mmol) in 20 mL anhydrous DCM was added a solution of Ph}_3\text{P (1.43 g, 5.45 mmol) in anhydrous DCM (20 mL) dropwise at 0 }^\circ\text{C over 1 hour. The solution was warmed to room temperature and stirred for additional 2-4 hours. The reaction mixture was then concentrated to remove solvents. The crude residue was purified using flash column chromatography on silica gel (DCM } \rightarrow\]
DCM/MeCN 6:4) to afford the *gem*-dibromoallyl boronate 3.9a or 3.9b, respectively, as white solid.

**MIDA (3,3-dibromo-1-phenylallyl)boronate (3.9a)**

```
MeN
\(\text{Ph} \)\( \text{Br} \)\( \text{Br} \)\( \text{O} \)\( \text{O} \)
```

White solid; 60% yield; TLC (DCM/MeCN 6:4) \( R_f = 0.80 \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta 7.28-7.13\) (m, 5H), 6.79 (d, \( J = 10.8\) Hz, 1H), 4.29 (d, \( J = 17.3\) Hz, 1H), 4.20 (d, \( J = 17.0\) Hz, 1H), 4.02 (d, \( J = 17.3\) Hz, 1H), 3.85 (d, \( J = 17.0\) Hz, 1H), 3.23 (d, \( J = 10.8\) Hz, 1H), 2.84 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \( \delta 168.8, 168.3, 140.9, 140.3, 128.4(4), 128.4(1), 125.6, 88.2, 62.3(2), 62.3(0), 46.0\) ppm; \(^{11}\)B NMR (128 MHz, DMSO-\(d_6\)) \( \delta 11.1\) ppm; HRMS (ESI) [M+\(\text{NH}_4\)]\(^+\) calcd. For \(\text{C}_{14}\text{H}_{18}\text{BBr}_2\text{N}_2\text{O}_4\) 446.97264, found 446.97183; IR (thin film, cm\(^{-1}\)) 3021, 1748, 1598, 1492, 1452, 1348, 1322, 1198, 1099, 1022, 948, 907, 869, 831, 781, 765, 730, 715, 702.

**MIDA (1,1-dibromo-5-phenylpent-1-en-3-yl)boronate (3.9b)**

```
MeN
\(\text{Ph} \)\( \text{Br} \)\( \text{Br} \)\( \text{O} \)\( \text{O} \)
```

White solid; 65% yield; TLC (MeCN/DCM 4:6) \( R_f = 0.85 \); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 7.28-7.25\) (m, 2H), 7.19-7.15 (m, 3H), 6.38 (d, \( J = 10.9\) Hz, 1H), 3.92 (d, \( J = 16.6\) Hz, 2H), 3.67 (d, \( J = 16.6\) Hz, 1H), 3.57 (d, \( J = 16.6\) Hz, 1H), 2.87 (s, 3H), 2.76-2.69 (m, 1H), 2.57-2.49 (m, 1H), 2.00-1.94 (m, 2H), 1.80-1.70 (m, 1H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta 167.4, 167.1, 141.9, 140.5, 128.5, 128.3, 125.9, 88.5, 62.5, 62.170, 45.9, 34.6, 31.7\) ppm; \(^{11}\)B NMR (128 MHz, CDCl\(_3\)) \( \delta 11.9\) ppm; HRMS (ESI) [M+\(\text{NH}_4\)]\(^+\) calcd. For \(\text{C}_{16}\text{H}_{22}\text{BBr}_2\text{N}_2\text{O}_4\) 475.00394, found 475.00363; IR (thin film, cm\(^{-1}\)) 3027, 2930, 1758, 1602, 1496, 1454, 1336, 1288, 1243, 1205, 1153, 1104, 1070, 1022, 989, 951, 892, 855, 798, 749, 717, 699.

### 3.5.8 Preparation and transformation of β-boryl alcohol

**Preparation of β-boryl alcohol 3.10:**
In a vial equipped with stirring-bar and a screw-cap lid was dissolved α-boryl aldehyde 3.2a (0.100 g, 0.364 mmol) in 4 mL of a 1:1 (v/v) mixture of THF and H2O. Indium (0.050 g, 0.436 mmol) then allyl bromide (0.066 g, 0.046 mL, 0.546 mmol) was added and the reaction mixture was stirred at room temperature for 2 hours. Water, EtOAc and a few drops of 1N aq. HCl were then added to the reaction and the mixture was extracted with EtOAc (2mL×3). The combined organic layers were dried over Na2SO4, filtered, and then concentrated to remove solvents. The crude product was purified using flash column chromatography on silica gel (EtOAc → EtOAc/MeCN 6:4) to afford the β-boryl alcohol 3.10 (0.112 g, mixture of diastereoisomers, syn:anti = 93:7) as white solid.

**MIDA (2-hydroxy-1-phenylpent-4-en-1-yl)boronate (3.10)**

White solid; 97% yield; TLC (EtOAc/MeCN 6:4) Rf = 0.48; 1H NMR (400 MHz, CDCl3) (mixture of diastereoisomers, syn:anti = 93:7) δ 7.35-7.13 (m, 5H), 5.81 (m, 0.07H) (anti), 6.68 (m, 0.93H) (syn), 5.13 (d, J = 9.7 Hz, 1H), 5.07 (d, J = 17.1 Hz, 1H), 4.21 (d, J = 15.8 Hz, 1H), 4.00 (ttdd, J = 9.7, 1.9, 1.6 Hz, 1H), 3.74 (d, J = 16.9 Hz, 1H), 3.68 (d, J = 15.8 Hz, 1H), 3.59 (d, J = 16.9 Hz, 1H), 3.05 (s, 2.79H) (syn), 2.70 (s, 0.21H) (anti), 2.29 (d, J = 1.6 Hz, 1H), 2.22-2.15 (m, 2H), 1.82 (m, 1H) ppm; 13C NMR (100 MHz, CDCl3) (mixture of diastereoisomers, syn:anti = 93:7) syn-isomer: δ 169.2(5), 169.1(8), 142.4, 135.0, 129.2, 128.4, 125.4, 118.6, 72.7, 63.6, 62.7, 46.5, 41.2 ppm, anti-isomer: δ 168.9, 167.9, 139.4, 135.7, 130.7, 128.4, 126.1, 117.3, 72.1, 62.3, 61.9, 45.4, 40.5 ppm; 11B NMR (128 MHz, DMSO-d6) (mixture of diastereoisomers, syn:anti = 93:7) δ 12.8 ppm; HRMS (ESI) [M+NH4]⁺ calcd. For C16H24BN2O5 335.17783, found 335.17774; IR (thin film, cm⁻¹) (mixture of diastereoisomers, syn:anti = 93:7) 3489, 3023, 1739,
1639, 1600, 1492, 1450, 1340, 1304, 1254, 1195, 1157, 1103, 1071, 1018, 999, 962, 897, 871, 822, 702

**Preparation of 1,2-diol 3.11**

![Chemical Structure](image)

To the solution of boryl alcohol **3.10** (0.100 g, 0.315 mmol) in THF (5 mL) was added a premixed solution of 0.6 mL of 10% NaOH and 0.2 mL of 30% H2O2 dropwise at 0 °C. The reaction was then stirred at room temperature for 1 hour and diluted with 5 mL water. The reaction mixture was extracted with EtOAc (5 mL×3). The organic layers were combined, dried with anhydrous Na2SO4, filtered and concentrated. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 5:5) to afford the 1,2-diol **3.11** (0.051 g, mixture of diastereoisomers, syn:anti = 93:7) as colorless oil. Spectral data were identical to the known structure in literature reports.16 ^1^H NMR: δ 4.51 (dd, J = 6.8, 3.5 Hz, 1 H) and 3.77 (m, 1H) for syn; 4.79 (dd, J = 4.5, 3.3 Hz, 1 H) and 3.88 (m, 1H) for anti.

**Preparation of 1,4-Diene 3.12**

![Chemical Structure](image)

To the solution of boryl alcohol **3.10** (0.100 g, 0.315 mmol) in THF (5 mL) was added 1.0 M aq. NaOH (1 mL) dropwise at room temperature and stirred for 30 min. The reaction mixture was then diluted with 10 mL water and extracted with Et2O (5 mL×3). The organic layers were
combined, dried with anhydrous Na$_2$SO$_4$, filtered and concentrated. The crude residue was purified using flash column chromatography on silica gel (Hexanes/Et$_2$O 20:1) to afford the 1,4-diene **3.12** (0.034 g, mixture of trans:cis = 93:7) as colorless oil. Spectral data were identical to the known structure in literature reports.$^{17}$ $^1$H NMR: $\delta$ 6.41 (d, $J = 15.9$, 1 H) and 6.23 (dt, $J = 15.9$, 6.6 Hz, 1H) for *trans*; 6.52 (d, $J = 11.6$ Hz, 1 H) and 5.71 (dt, $J = 11.6$, 7.6 Hz, 1H) for *cis*.

### 3.5.9 Preparation of β-functionalized vinyl boronates

#### Preparation of silyl enol ether 3.13a

A 25 mL flask was charged with α-boryl aldehyde **3.2a** (0.250 g, 0.91 mmol), TBDMSCl (0.301 g, 2.00 mmol), Et$_3$N (0.253 g, 0.348 mL, 2.50 mmol), NaI (0.136 g, 0.91 mmol) and 10 mL anhydrous MeCN. The mixture was stirred at 80 °C for 24 hr followed by adding 10 mL water. The mixture was separated; aqueous layer was extracted with EtOAc (10 mL x 2). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated to dryness. $^1$H NMR of the resulted crude mixture showed the formation of mixture of isomers ($E/Z = 10:90$). The crude products were further purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 $\rightarrow$ EtOAc) to afford the silyl enol ether **3.13a** (0.197 g, mixture of isomers, $E/Z = 30:70$) as white solid.

**MIDA (2-((tert-butyldimethylsilyl)oxy)-1-phenylvinyl)boronate (3.13a)**

![MIDA structure](image)

White solid; 55% yield; TLC (EtOAc) $R_f = 0.75$; $^1$H NMR (400 MHz, CDCl$_3$) (mixture of isomers, $E/Z = 30:70$) $\delta$ 7.30-7.22 (m, 3H), 7.18-7.12(m, 2H), 6.82(s, 0.7H), 6.80 (s, 0.3H), 3.85 (d, $J = 16.4$ Hz, 0.6H), 3.77 (d, $J = 16.4$ Hz, 0.6H), 3.72 (d, $J = 16.4$ Hz, 1.4H), 3.32 (d, $J = 16.4$ Hz, 1.4H), 2.90
(s, 0.9H), 2.69 (s, 2.1H), 0.95 (s, 2.7H), 0.77 (s, 6.3H), 0.19 (s, 1.8H), 0.07 (s, 4.2H) ppm; \( ^{13} \)C NMR (100 MHz, CDCl\(_3\)) (mixture of isomers, E/Z = 30:70) \( \delta \) 167.8 (E), 167.5 (Z), 150.7 (E), 146.6 (Z), 141.1 (E), 138.0 (Z), 129.8 (Z), 129.3 (E), 128.1 (Z), 128.0 (E), 125.7(3) (Z), 125.7(1) (E), 63.1 (E), 61.8 (Z), 47.0 (E), 46.4 (Z), 25.8 (E), 25.3 (Z), 18.9 (E), 18.0 (Z), -5.3(2) (E), -5.3(5) (Z) ppm; \( ^{11} \)B NMR (128 MHz, CDCl\(_3\)) (mixture of isomers, E/Z = 30:70) \( \delta \) 12.0 ppm; HRMS (ESI) [M+H]\(^{+}\) calcd. For C\(_{10}\)H\(_{29}\)BNO\(_5\)Si 390.1902, found 390.1910; IR (thin film, cm\(^{-1}\)) (mixture of isomers, E/Z = 30:70) 2930, 2857, 1760, 1606, 1493, 1462, 1336, 1290, 1252, 1194, 1148, 1103, 1022, 968, 875, 836, 783, 701

**Preparation of silyl enol ether 3.13b and 3.13c**

A 100 mL flask was charged with \( \alpha \)-boryl aldehyde 3.2a or 3.2d (3.64 mmol), DBU (1.66 g, 1.63 mL, 10.92 mmol), DMAP (0.09 g, 0.73 mmol) and 50 mL anhydrous THF. The mixture was cooled to 0 \(^{\circ}\)C. TIPSOTf (1.45 g, 1.28 mL, 4.73 mmol) was added dropwise. The resulted reaction solution was then warmed to room temperature and stirred for 12 hours. The reaction was concentrated to remove solvents. \( ^{1} \)H NMR of the resulted crude mixture showed the formation of mixture of isomers (3.13b: E/Z = 20:80; 3.13c: E/Z < 5:95). The crude products were further purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 \( \rightarrow \) EtOAc) to afford the silyl enol ether 3.13b (E/Z = 40:60) or 3.13c (Z-isomer), respectively, as white solid.
MIDA (1-phenyl-2-((triisopropylsilyl)oxy)vinyl)boronate (3.13b)

White solid; 81% yield; TLC (EtOAc) R_f = 0.75; ^1H NMR (400 MHz, CDCl_3) (mixture of isomers, E/Z = 40:60) E-isomer: δ 7.32-7.22 (m, 3H), 7.17-7.11 (m, 2H), 6.84 (s, 1H), 3.81 (d, J = 16.4 Hz, 2H), 3.76 (d, J = 16.4 Hz, 2H), 2.92 (s, 3H), 1.21 (m, 3H), 1.10 (d, J = 7.0 Hz, 18H), Z-isomer: δ 7.32-7.22 (m, 3H), 7.17-7.11 (m, 2H), 6.90 (s, 1H), 3.70 (d, J = 16.4 Hz, 2H), 3.30 (d, J = 16.4 Hz, 2H), 2.69 (s, 2H), 1.10 (m, 3H), 0.97 (d, J = 7.0 Hz, 18H); ^13C NMR (100 MHz, CDCl_3) (mixture of isomers, E/Z = 40:60) E-isomer: δ 167.7, 161.4, 141.3, 129.4, 127.9(8), 125.7, 62.9, 46.9, 17.7, 11.9, Z-isomer: δ 167.5, 147.1, 138.1, 129.8, 128.0(3), 125.7, 61.7, 46.3, 17.6, 11.8 ppm; ^11B NMR (128 MHz, DMSO-d_6) (mixture of isomers, E/Z = 40:60) δ 11.9 ppm; HRMS (ESI) [M+H]^+ calcd. For C_{22}H_{35}BNO_5Si 432.23775, found 432.23926; IR (thin film, cm^{-1}) (mixture of isomers, E/Z = 40:60) 2942, 2866, 1760, 1622, 1496, 1455, 1336, 1291, 1249, 1159, 1030, 988, 881, 839, 778, 766, 703, 692, 656.

(Z)-MIDA (4-phenyl-1-((triisopropylsilyl)oxy)but-1-en-2-yl)boronate (3.13c)

White solid; 80% yield; TLC (EtOAc) R_f = 0.75; ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.20 (m, 4H), 7.18-7.13 (m, 1H), 6.64 (s, 1H), 3.83 (d, J = 16.4 Hz, 2H), 3.60 (d, J = 16.4 Hz, 2H), 2.79-2.73 (m, 2H), 2.71 (s, 3H), 2.23-2.19 (m, 2H), 1.25-1.16 (m, 3H), 1.10 (d, J = 6.8 Hz, 18H) ppm; ^13C NMR (100 MHz, CDCl_3) δ 168.0, 147.0, 143.2, 128.4, 128.3, 125.6, 61.6, 46.6, 35.7, 29.6, 17.7, 11.8 ppm; ^11B NMR (128 MHz, CDCl_3) δ 12.8 ppm; HRMS (ESI) [M+H]^+ calcd. For C_{24}H_{39}BNO_5Si 460.2685, found 460.2700; IR (thin film, cm^{-1}) 2944, 2867, 1760, 1622, 1496, 1455, 1336, 1291, 1249, 1159, 1030, 988, 881, 839, 748, 689

Preparation of enamides 3.14a and 3.14b
A 25 mL flask was charged with α-boryl aldehyde 3.2a or 3.2d (0.360 mmol), pyrrolidin-2-one (0.034 g, 0.400 mmol), p-toluenesulfonic acid (0.008 g, 0.040 mmol) and in 11 mL toluene/DMSO (10:1 v/v). The flask was fitted with a Dean-Stark trap and a reflux condenser, and the mixture was refluxed with stirring for 2 h followed by concentration in vacuo. The residue was diluted with EtOAc (20 mL) and washed subsequently with saturated aqueous NaHCO₃ (10 mL) and water (10 mL). The EtOAc solution was dried with anhydrous Na₂SO₄ and concentrated to dryness. ¹H NMR of the crude residue indicated exclusive formation of the Z-enamide. The crude product was then further purified using flash column chromatography on silica gel (EtOAc → EtOAc/MeCN 1:1) to afford the enamide 3.14a or 3.14b as white solid.

(Z)-MIDA (2-(2-oxypyrrolidin-1-yl)-1-phenylvinyl)boronate (3.14a)

White solid; 50% yield; TLC (EtOAc/MeCN 8:2) Rₓ = 0.20; ¹H NMR (400 MHz, DMSO-d₆) δ 7.29-7.25 (m, 2H), 7.22-7.18 (m, 1H), 7.15-7.13 (m, 2H), 7.05 (s, 1H), 4.16 (d, J = 17.1 Hz, 2H), 3.63 (d, J = 17.1 Hz, 2H), 2.78 (t, J = 7.0 Hz, 2H), 2.74 (s, 3H), 2.22 (t, J = 8.0 Hz, 2H), 1.70 (m, 2H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 174.8, 168.7, 139.7, 129.9, 129.0, 127.5, 126.1, 61.8, 47.5, 46.7, 29.7, 18.0 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 11.1 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₁₇H₂₀BN₂O₅ 343.1459, found 343.1457; IR (thin film, cm⁻¹) 2942, 1757, 1683, 1622, 1483, 1465, 1451, 1404, 1375, 1332, 1285, 1271, 1242, 1190, 1149, 1120, 1091, 1059, 1036, 1045, 1007, 988, 971, 888, 846, 780, 721.
(Z)-MIDA (1-(2-oxopyrrolidin-1-yl)-4-phenylbut-1-en-2-yl)boronate (3.14b)

White solid; 43% yield; TLC (MeOH/EtOAc 1:9) R_f = 0.20; ^1H NMR (400 MHz, DMSO-d_6) δ 7.28-7.24 (m, 2H), 7.18-7.14 (m, 3H), 6.55 (s, 1H), 4.23 (d, J = 17.2 Hz, 2H), 4.04 (d, J = 17.2 Hz, 2H), 3.73 (t, J = 7.0 Hz, 2H), 2.73 (s, 3H), 2.59-2.55 (m, 2H), 2.30-2.25 (m, 4H), 2.02-1.95 (m, 2H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 174.2, 169.3, 142.0, 128.8, 128.2, 128.2, 125.7, 61.8, 47.5, 46.9, 36.6, 30.7, 29.7, 18.2 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 11.9 ppm; HRMS (ESI) [M+H]^+ calcd. For C_{19}H_{24}BN_2O_5 371.1772, found 371.1787; IR (thin film, cm^{-1}) 2944, 1740, 1689, 1629, 1495, 1470, 1454, 1407, 1381, 1341, 1323, 1273, 1258, 1207, 1153, 1132, 1077, 1033, 990, 891, 858, 748, 701.

Preparation of Enamine 3.15

To a solution of the α-boryl aldehyde 3.2a (0.200 g, 0.727 mmol) in 10 mL anhydrous chloroform was added activated 4Å molecular seives (1.0 g) and dibenzylamine (0.172 g, 0.872 mmol) at 0 °C. The mixture was stirred at 23 °C for 12 hours. The reaction mixture was then filtered; the filtrate was concentrated to dryness. ^1H NMR of the crude residue indicated exclusive formation of the Z-enamine. The crude product was then further purified using flash column chromatography on silica gel (pre-deactivated with Et_3N, eluent gradient: Hexanes/EtOAc 1:1 → EtOAc → EtOAc/MeCN 9:1) to afford the enamine product 3.15 (0.28 g) as white solid.
(Z)-MIDA (2-(dibenzylamino)-1-phenylvinyl)boronate (3.15)

White solid; 85% yield; TLC (EtOAc) R_f = 0.25; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.30-7.21 (m, 7H), 7.13-7.08 (m, 7H), 7.05-7.00 (m, 1H), 6.74 (s, 1H), 3.96 (s, 4H), 3.58 (d, \(J = 16.1\) Hz, 2H), 3.20 (d, \(J = 16.1\) Hz, 2H), 2.75 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.9, 144.2, 140.8, 138.5, 130.4, 128.3, 128.0, 127.4, 126.9, 125.3, 61.9, 55.1, 45.9 ppm; \(^{11}\)B NMR (128 MHz, CDCl\(_3\)) \(\delta\) 12.9 ppm; HRMS (EI) [M]+ calcd. For C\(_{27}\)H\(_{27}\)BN\(_2\)O\(_4\) 454.2064, found 454.2069; IR (thin film, cm\(^{-1}\)) 3027, 1744, 1599, 1494, 1452, 1334, 1283, 1247, 1220, 1146, 1103, 1091, 1073, 1022, 1009, 984, 961, 888, 851, 796, 721, 696.

Preparation of enol triflate 3.16

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added anhydrous THF (50 mL) and KHMDS solution (0.5M in toluene, 8.72 mL, 4.34 mmol). The solution was cooled to -78 °C. A solution of \(\alpha\)-boryl aldehyde 3.2a (1.00 g, 3.64 mmol) in 5 mL anhydrous THF was added dropwise and stirred at -78 °C for 30 min. A solution of PhNTf\(_2\) (1.43 g, 4.00 mmol) in 5 mL anhydrous THF was then added dropwise and continue stirring for additional 1.5 hour. The reaction was quenched with saturated aqueous NH\(_4\)Cl (50 mL) at −78 °C and extracted with EtOAc (20 mL × 3). The combined organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated to dryness. \(^1^H\) NMR of the crude residue indicated exclusive formation of the E-triflate enol ether. The crude product was then further purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc) to afford pure product 3.16 (0.607 g) as white solid.
(E)-MIDA (1-phenyl-2-(((trifluoromethyl)sulfonyl)oxy)vinyl)boronate (3.16)

White solid; 41% yield; TLC (EtOAc) Rf = 0.60; 1H NMR (400 MHz, DMSO-d6) δ 7.37-7.31 (m, 3H), 7.25-7.24 (m, 2H), 7.03 (s, 1H), 4.35 (d, J = 17.3 Hz, 2H), 3.92 (d, J = 17.3 Hz, 2H), 2.84 (s, 3H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 168.3, 142.8, 136.8, 128.9, 128.3, 127.4, 119.6, 116.4, 118.0 (q, JCF = 321.2 Hz), 62.3, 47.3 ppm; 11B NMR (128 MHz, DMSO-d6) δ 9.6 ppm; HRMS (ESI) [M+H]+ calcd. For C14H14BF3NO2S 408.0530, found 408.0545; IR (thin film, cm⁻¹) 2964, 1745, 1612, 1492, 1418, 1341, 1296, 1245, 1223, 1202, 1158, 1136, 1108, 1092, 1075, 1043, 989, 948, 916, 900, 886, 869, 810, 764, 700

3.5.10 Preparation of α-bromo-α-boryl aldehyde

To a solution of the α-boryl aldehyde 3.2a (0.50 g, 1.82 mmol) in 20 mL DCM/Dioxane (1:1) was added a solution of Br₂ (0.29 g, 1.82 mmol) in 1 mL DCM at 0 °C. The mixture was stirred at 0 °C for 1 hour until the reaction was complete as indicated by TLC. The reaction mixture was diluted with 100 mL EtOAc and washed with water (50 mL) and brine (50 mL). The organic layer was dried with anhydrous Na₂SO₄ and concentrated to dryness. The resulted crude solid was purified using flash column chromatography on silica gel (EtOAc) to afford pure product 3.17 (0.49 g) as a white solid.

MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17)

White solid; 77% yield; TLC (EtOAc) Rf = 0.60; 1H NMR (400 MHz, DMSO-d6) δ 9.63 (s, 1H), 7.48-7.31 (m, 5H), 4.44 (d, J = 17.2 Hz, 1H), 4.36 (d, J = 17.2 Hz, 1H), 4.09 (d, J = 17.2 Hz, 1H), 4.05 (d, J = 17.2 Hz, 1H), 2.78 (s, 3H) ppm;
\(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) 194.7, 167.9(4), 167.8(8), 135.4, 128.9, 128.5, 128.0, 63.7, 63.5, 47.5 ppm; \(^{11}\)B NMR (128 MHz, DMSO-\(d_6\)) \(\delta\) 9.7 ppm; HRMS (ESI) [M+H]\(^+\) calcd. For C\(_{13}\)H\(_14\)BBrNO\(_5\) 354.0142, found 354.0142; IR (thin film, cm\(^{-1}\)) 3021, 2966, 2836, 1767, 1706, 1495, 1460, 1426, 1382, 1342, 1279, 1240, 1199, 1160, 1142, 1035, 989, 961, 900, 876, 840, 768, 727, 699, 665.

X-ray quality crystals were grown by layering pentane onto a dissolved solution of 3.17 in acetone. The layers slowly mixed, forming crystals.

3.5.11 Preparation of \(\alpha\)-allyl-\(\alpha\)-boryl aldehyde

To an oven dried vial was added activated powdered 4Å molecular sieves (100 mg). The reaction vessel was allowed to cool to room temperature under vacuum. \(\alpha\)-Boryl aldehyde 3.2a (50 mg, 0.182 mmol, 1.0 equiv.) and Pd(PPh\(_3\))\(_4\) (21 mg, 0.009 mmol, 0.05 equiv) were added
sequentially. The mixture was then evacuated for approximately 5 minutes under vacuum and then back filled with nitrogen. THF (2 mL) was added, followed by allyl alcohol (16 mg, 0.274 mmol, 1.5 equiv), Et₃N (28 mg, 0.274 mmol, 1.5 equiv.), and Et₃B (1.0 M in THF, 0.548 mmol, 3.0 equiv.). The vial was then sealed and then transferred to a preheated 50 °C oil bath (or reaction block). The reaction was stirred for 24 hours at which time the mixture was cooled to room temperature and added saturated NaHCO₃ solution. The mixture was extracted with EtOAc (2 mL ×3), the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. The resultant residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 5:5 → EtOAc) to afford pure product 3.18.

2-(MIDA boryl)-2-phenylpent-4-enal (3.18)

White solid; 78% yield; TLC (EtOAc) Rₚ = 0.72; ¹H NMR (400 MHz, CDCl₃) δ 9.94 (s, 1H), 7.38-7.30 (m, 4H), 7.24-7.20 (m, 1H), 5.64-5.53 (m, 1H), 5.13 (ddd, J = 17.0, 2.9, 1.4 Hz, 1H), 5.02 (d, J = 10.1 Hz, 1H), 4.05 (d, J = 16.0 Hz, 1H), 3.70 (d, J = 16.0 Hz, 1H), 3.69 (d, J = 16.7 Hz, 2H), 3.37 (d, J = 16.7 Hz, 1H), 3.19-3.08 (m, 2H), 2.57 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 211.3, 166.9, 166.8, 139.2, 133.8, 129.2, 127.6, 126.8, 118.7, 64.2, 64.1, 47.9, 39.4 ppm; ¹¹B NMR (125 MHz, CDCl₃) δ 11.2 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₁₆H₁₃BNO₃ 316.1350, found=316.1346.

3.5.12 General procedure for synthesis of α-borylcarboxylic acids

To a suspension of α-boryl aldehyde (5.0 mmol) in 30 mL t-BuOH, was added cyclohexene (15.0 mmol, 3.0 equiv). A solution of NaClO₂ (6.0 mmol, 1.2 equiv) and NaH₂PO₄ (6.0 mmol, 1.2 equiv) in 30 mL H₂O was added dropwise at room temperature. The mixture was vigorously
stirred at room temperature for 1–2 hours until the reaction was complete as indicated by TLC. The reaction solution was then diluted with 60 mL brine, and extracted EtOAc (20 mL×3). The combined organic layers were concentrated to remove solvents. The crude product was purified by washing with the combination of DCM/Et₂O or using flash column chromatography on silica gel (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeOH 90:10 → EtOAc/MeOH/AcOH 90:10:0.1) to afford the pure product.

2-(MIDA boryl)-2-phenylacetic acid (3.19a)

White solid; 73% yield; TLC (DCM/EtOAc/MeOH/AcOH 45:45:10:0.1) R_f = 0.47; ¹H NMR (400 MHz, DMSO-d₆) δ 12.13 (bs, 1H), 7.29-7.22 (m, 4H), 7.17-7.13 (m, 1H), 4.33 (d, J = 17.4 Hz, 1H), 4.19 (d, J = 16.7 Hz, 1H), 3.95 (d, J = 16.7 Hz, 1H), 3.86 (d, J = 17.4 Hz, 1H), 3.44 (s, 1H), 2.97 (s, 3H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 175.4, 168.8, 168.3, 138.6, 129.4, 127.7, 125.5, 62.8, 62.5, 46.3 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 11.3 ppm; HRMS (ESI) [M+NH₄⁺] calcd. For C₁₃H₁₈BN₂O₆ 309.12579, found 309.12647; IR (thin film, cm⁻¹) 3017, 1745, 1690, 1599, 1453, 1340, 1286, 1249, 1154, 1097, 1059, 1026, 990, 960, 894, 833, 705.

2-(MIDA boryl)-2-(p-tolyl)acetic acid (3.19b)

White solid; 86% yield; TLC (EtOAc) R_f = 0.10; ¹H NMR (400 MHz, DMSO-d₆) δ 12.06 (bs, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 4.32 (d, J = 17.3 Hz, 1H), 4.19 (d, J = 16.7 Hz, 1H), 3.95 (d, J = 16.7 Hz, 1H), 3.83 (d, J = 17.3 Hz, 1H), 3.39 (s, 1H), 2.96 (s, 3H), 2.26 (s, 3H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 175.5, 168.8, 168.3, 135.5, 134.3, 129.3, 128.3, 62.8, 62.5, 46.3, 20.6 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 11.7 ppm; HRMS (DART-TOF) [M+NH₄⁺] calcd. For C₁₄H₂₀BN₂O₆ 323.14144, found 323.14248; IR (thin film, cm⁻¹) 2965, 1749, 1704, 1513, 1451, 1340, 1282, 1153, 1096, 1059, 1028, 960, 897, 845, 815, 727, 685.

2-(MIDA boryl)-2-(4-fluorophenyl)acetic acid (3.19c)
White solid; 74% yield; TLC (EtOAc/MeOH 9:1) \( R_f = 0.10 \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 12.19 (bs, 1H), 7.31-7.28 (m, 2H), 7.10-7.06 (m, 2H), 4.36 (d, \( J = 17.5 \) Hz, 1H), 4.20 (d, \( J = 16.6 \) Hz, 1H), 3.97 (d, \( J = 16.6 \) Hz, 1H), 3.90 (d, \( J = 17.5 \) Hz, 1H), 3.49 (s, 1H), 3.00 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \( \delta \) 175.4, 168.8, 168.2, 160.5 (d, \( J_{CF} = 241.0 \) Hz), 134.9 (d, \( J_{CF} = 2.9 \) Hz), 131.1 (d, \( J_{CF} = 7.8 \) Hz), 114.4 (d, \( J_{CF} = 21.0 \) Hz), 62.9, 62.5, 46.4 ppm; \(^{11}\)B NMR (128 MHz, DMSO-\(d_6\)) \( \delta \) 11.7; HRMS (DART-TOF) [M+NH\(_4^+\)] calcd. For C\(_{13}\)H\(_{17}\)BFN\(_2\)O\(_6\) 327.11637, found 327.11727; IR (thin film, cm\(^{-1}\)) 2956, 1757, 1706, 1666, 1510, 1451, 1338, 1278, 1215, 1164, 1093, 1062, 1033, 959, 893, 850, 825, 793, 733, 678.

2-(MIDA boryl)-4-phenylbutanoic acid (3.19d)

White solid; 83% yield; TLC (EtOAc) \( R_f = 0.13 \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 7.29-7.25 (m, 2H), 7.18-7.15 (m, 3H), 4.30 (d, \( J = 17.3 \) Hz, 1H), 4.18 (d, \( J = 16.9 \) Hz, 1H), 4.00 (d, \( J = 17.3 \) Hz, 1H), 3.85 (d, \( J = 16.9 \) Hz, 1H), 2.97 (s, 3H), 2.69-2.62 (m, 1H), 2.52-2.44 (m, 1H), 2.03 (dd, \( J = 10.8, 2.4 \) Hz, 1H), 1.97-1.87 (m, 1H), 1.74-1.65 (m, 1H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\)) \( \delta \) 177.1, 168.8, 168.2, 142.2, 128.3, 125.7, 62.5, 62.2, 46.0, 39.5, 35.2, 29.4 ppm; \(^{11}\)B NMR (128 MHz, DMSO-\(d_6\)) \( \delta \) 11.6 ppm; HRMS (DART-TOF) (neg.) [M-H] calcd. For C\(_{15}\)H\(_{17}\)BNO\(_6\) 318.11489, found 318.11440; IR (thin film, cm\(^{-1}\)) 3027, 2951, 1745, 1695, 1451, 1339, 1292, 1246, 1192, 1152, 1099, 1062, 1026, 990, 962, 895, 855, 751, 700.

2-(MIDA boryl)-3-phenylpropanoic acid (3.19e)

White solid; 68% yield; TLC (EtOAc) \( R_f = 0.08 \); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 11.75 (s, 1H), 7.81 – 6.76 (m, 5H), 4.34 (d, \( J = 17.3 \) Hz, 1H), 4.22 (d, \( J = 17.0 \) Hz, 1H), 4.07 (d, \( J = 17.3 \) Hz, 1H), 3.90 (d, \( J = 17.0 \) Hz, 1H), 3.08 (s, 3H), 2.96-2.83 (m, 1H), 2.81-2.73 (m, 1H), 2.39 (dd, \( J = 11.8, 2.9 \) Hz, 1H) ppm; \(^{13}\)C NMR (100 MHz,
DMSO-d$_6$ δ 177.1, 169.5, 168.8, 143.0, 129.0, 128.7, 126.3, 63.1, 62.8, 46.7, 33.6 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 11.3 ppm; HRMS (DART-TOF) [M+NH$_4$]$^+$ calcd. For C$_{14}$H$_{20}$BN$_2$O$_6$ 323.1414; found 323.1405; IR (thin film, cm$^{-1}$) 3009, 2961, 1780, 1744, 1683, 1497, 1455, 1409, 1326, 1339, 1284, 1243, 1192, 1097, 1064, 1039, 1011, 991, 944, 898, 868, 842, 825, 790, 738, 696.

**4-methyl-2-(MIDA boryl)pentanoic acid (3.19f)**

White solid; 64% yield; TLC (EtOAc) R$_f$ = 0.10; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.73 (bs, 1H), 4.29 (d, $J$ = 17.3 Hz, 1H), 4.20 (d, $J$ = 16.9 Hz, 1H), 4.01 (d, $J$ = 17.3 Hz, 1H), 3.88 (d, $J$ = 16.9 Hz, 1H), 3.01 (s, 3H), 2.06 (dd, $J$ = 11.7, 2.7 Hz, 1H), 1.71 (ddd, $J$ = 13.7, 11.7, 4.5 Hz, 1H), 1.55-1.45 (m, 1H), 1.16 (ddd, $J$ = 13.7, 9.3, 2.7 Hz, 1H), 0.86 (d, $J$ = 6.7 Hz, 3H), 0.84 (d, $J$ = 6.7 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 178.1, 169.5, 168.9, 63.1, 62.8, 46.5, 36.9, 28.1, 24.2, 21.9 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 11.4 ppm; HRMS (DART-TOF) [M+NH$_4$]$^+$ calcd. For C$_{11}$H$_{22}$BN$_2$O$_6$ 289.15709, found 289.1578; IR (thin film, cm$^{-1}$) 3010, 2955, 2877, 1778, 1742, 1675, 1464, 1446, 1413, 1386, 1369, 1324, 1337, 1291, 1248, 1206, 1194, 1129, 1094, 1062, 1044, 1021, 994, 963, 896, 863, 804, 666.

**2-(MIDA boryl)hexanoic acid (3.19g)**

White solid; 70% yield; TLC (EtOAc) R$_f$ = 0.12; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 4.29 (d, $J$ = 17.3 Hz, 1H), 4.17 (d, $J$ = 16.9 Hz, 1H), 3.99 (d, $J$ = 17.3 Hz, 1H), 3.84 (d, $J$ = 16.9 Hz, 1H), 3.00 (s, 3H), 1.98-1.93 (m, 1H), 1.67-1.59 (m, 1H), 1.48-1.36 (m, 1H), 1.35-1.13 (m, 4H), 0.86 (t, $J$ = 6.0 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 177.3, 168.8, 168.2, 62.4, 62.1, 45.9, 31.6, 27.0, 22.2, 14.0 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 11.1 ppm; HRMS (DART-TOF) [M+NH$_4$]$^+$ calcd. For C$_{11}$H$_{22}$BN$_2$O$_6$ 289.15709, found 289.15764; IR (thin film, cm$^{-1}$) 2959, 2872, 1742, 1693, 1665, 1449, 1405, 1339, 1279, 1256, 1198, 1171, 1092, 1014, 991, 959, 892, 848, 730, 667.
2-cyclohexyl-2-(MIDA boryl)acetic acid (3.19h)

White solid; 69% yield; TLC (EtOAc) R_f = 0.20; \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 11.85 (bs, 1H), 4.31 (d, \(J = 17.4\) Hz, 1H), 4.10 (d, \(J = 16.6\) Hz, 1H), 3.97 (d, \(J = 16.6\) Hz, 1H), 3.72 (d, \(J = 17.4\) Hz, 1H), 2.97 (s, 3H), 1.85 (d, \(J = 5.2\) Hz, 1H), 1.74-1.63 (m, 5H), 1.63-1.55 (m, 1H), 1.31-1.03 (m, 5H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 177.2, 169.1, 168.2, 62.4, 62.2, 45.9, 37.7, 32.4, 30.9, 26.6, 26.5, 26.0 ppm; \(^{11}\)B NMR (128 MHz, DMSO-d\(_6\)) \(\delta\) 11.6 ppm; HRMS (DART-TOF) \([M+NH_4]^+\) calcd. For C\(_{13}\)H\(_{24}\)BN\(_2\)O\(_6\) 315.17274, found 315.17381; IR (thin film, cm\(^{-1}\)) 2922, 1780, 1743, 1686, 1446, 1339, 1300, 1279, 1198, 1159, 1095, 1030, 991, 975, 952, 895, 867, 852, 842.

3.5.13 General procedure for synthesis of functionalized unnatural amino acids

Preparation of functionalized pinacolyl boronate:

The transformation of MIDA boronate to pinacolyl boronate was carried out according to a literature method. To a 50 mL round-bottom flask equipped with a stir bar and charge with MIDA boronate (2 mmol) was added pinacol (3 mmol) and solid anhydrous NaHCO\(_3\) (10 mmol). MeOH (25 mL) was added and the suspension was stirred at 45 oC for 5-6 hours. The mixture was cooled to room temperature and concentrated to remove most of solvent under reduced pressure. The residue was diluted with EtOAc (50mL) and washed with 0.5M pH 7 phosphorous buffer (20 mL). The organic layer was separated, dried and concentrated. The crude product was
purified using flash column chromatography on silica gel to afford the desired pinacolyl boroante.

**Triisopropyl((2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)oxy)silane (3.22a)**

Colorless oil; 75% yield; TLC (Hexanes/EtOAc 95:5) \( R_f = 0.50 \); \(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) (mixture of isomers, \( E/Z = 40:60 \)) \( \delta \) 7.54-7.52 (m, 1.2H) (Z), 7.27-7.22 (m, 2.8H) \((E+Z)\), 7.18 (s, 0.6H) (Z), 7.15-7.08 (m, 1.4H) \((E+Z)\), 1.29 (s, 4.8H) \((E)\), 1.26 (s, 7.2H) (Z), 1.23-1.10 (m, 3H), 1.13 (d, \( J = 6.6 \text{ Hz} \), 7.2H) \((E)\), 1.06 (d, \( J = 7.1 \text{ Hz} \), 10.8H) (Z) ppm; \(^13\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)) (mixture of isomers, \( E/Z = 40:60 \)) \( E \)-isomer: \( \delta \) 154.2, 140.3, 128.1, 127.6, 125.3, 82.8, 24.9, 17.7, 11.9, \( Z \)-isomer: \( \delta \) 152.2, 137.3, 129.8, 127.2, 125.1, 82.7, 24.7, 17.6, 11.8 ppm; HRMS (ESI) \([\text{M+H}]^+ \) calcd. For C\(_{23}\)H\(_{40}\)BO\(_3\)Si 403.28398, found 403.28500.

**((Z)-triisopropyl((4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl)oxy)silane (3.22b)**

Colorless oil; 86% yield; TLC (EtOAc/hexanes 5:95) \( R_f = 0.40 \); \(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.25-7.19 (m, 4H), 7.15-7.10 (m, 1H), 6.94 (s, 1H), 2.69-2.65 (m, 2H), 2.46-2.42 (m, 2H), 1.20 (s, 12H), 1.19-1.14 (m, 3H), 1.08 (d, \( J = 6.8 \text{ Hz} \), 18H) ppm; \(^13\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 151.5, 143.3, 128.6, 127.9, 125.2, 82.4, 36.1, 27.00, 24.7, 17.7, 11.9 ppm; HRMS (ESI) \([\text{M+H}]^+ \) calcd. For C\(_{25}\)H\(_{44}\)BO\(_3\)Si 431.31528, found 431.31601.

**((Z)-1-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyrrolidin-2-one (3.23a)**

White solid; 70% yield; TLC (Hexanes/EtOAc 6:4) \( R_f = 0.65 \); \(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.60 (s, 1H), 7.29-7.19 (m, 3H), 7.12 (d, \( J = 6.9 \text{ Hz} \), 2H), 2.96 (t, \( J = 7.0 \text{ Hz} \), 2H), 2.36 (t, \( J = 8.0 \text{ Hz} \), 2H), 1.81 (m, 2H), 1.25 (s, 12H) ppm; \(^13\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 154.2, 140.3, 128.1, 127.6, 125.3, 82.8, 24.9, 17.7, 11.9, \( Z \)-isomer: \( \delta \) 152.2, 137.3, 129.8, 127.2, 125.1, 82.7, 24.7, 17.6, 11.8 ppm; HRMS (ESI) \([\text{M+H}]^+ \) calcd. For C\(_{23}\)H\(_{40}\)BO\(_3\)Si 403.28398, found 403.28500.
NMR (100 MHz, CDCl₃) δ 175.6, 139.1, 134.2, 129.7, 127.4, 126.1, 83.5, 48.0, 30.3, 24.7, 18.8 ppm; HRMS (ESI) [M+H]+ calcd. For C₁₈H₂₅BNO₃ 314.19275, found 314.19330.

(Z)-1-(4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl)pyrrolidin-2-one (3.23b)

White solid; 71% yield; TLC (MeOH/DCM 5:95) Rᵣ = 0.45; ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.24 (m, 3H), 7.18-7.14 (m, 3H), 3.62 (t, J = 7.1 Hz, 2H), 2.71-2.67 (m, 2H), 2.57-2.53 (m, 2H), 2.36 (t, J = 8.1 Hz, 2H), 2.01-1.93 (m, 2H), 1.25 (s, 12H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 174.9, 141.9, 133.4, 128.5, 128.1, 125.7, 83.2, 48.0, 37.2, 30.0, 29.8, 24.7, 18.6 ppm; HRMS (ESI) [M+H]+ calcd. For C₂₀H₂₉BNO₃ 342.22405, found 342.22368.

Petasis reaction for the synthesis of unnatural amino acids

In a vial equipped with stirring-bar and a screw-cap lid was dissolved pinacolyl boronate (0.30 mmol, 1.0 equiv) in 0.5 mL 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP). Glyoxylic acid (0.36 mmol, 1.2 equiv) then amine (0.36 mmol, 1.2 equiv) was added and the reaction mixture was stirred at the requisite temperature (25 or 50 °C) for 5-72 hours until the reaction was complete by TLC. The solution was concentrated to remove the solvent by reduced pressure. The crude residue was then either subjected to purification by flash column chromatography on silica gel to afford the desired amino acids (3.24a-b or 3.24c-k), or the subsequent one-pot esterification to afford the amino acid methyl esters (3.24c-d): the crude amino acid residue was directly dissolved in 3 mL of a 1:2 (v/v) mixture of MeOH and DCM. TMS-CHN₂ (0.60 mmol, 2M in hexane, 2 equiv) was added dropwise. The reaction mixture was stirred at room temperature for
1 hour and concentrated, then purified by flash column chromatography on silica gel to afford the amino acid methyl esters (3.24c-d).

Summary for the synthesis of functionalized unnatural amino acids:

<table>
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<th>Boronic ester</th>
<th>Amine</th>
<th>Temp.</th>
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<th>Final products</th>
<th>Isolated yield</th>
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<tr>
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<td>24hr</td>
<td>Ph[NHCOOH] OTIPS 3.24a</td>
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<tr>
<td></td>
<td>O[NH]</td>
<td>25°C</td>
<td>24hr</td>
<td>O[NHCOOH] OTIPS 3.24b</td>
<td>74%</td>
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<tr>
<td>3.22a</td>
<td>Ph[NH2]</td>
<td>25°C</td>
<td>48hr</td>
<td>Ph[NHCOOMe] OTIPS 3.24c</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Cl[NH2]</td>
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<td>48hr</td>
<td>Cl[NHCOOMe] OTIPS 3.24d</td>
<td>55%</td>
</tr>
<tr>
<td>3.22b</td>
<td>N[Me]</td>
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<td>5hr</td>
<td>N[MeCOOH] OTIPS 3.24e</td>
<td>67%</td>
</tr>
<tr>
<td>3.22b</td>
<td>Ph[NH2]</td>
<td>25°C</td>
<td>5hr</td>
<td>Ph[NHCOOH] OTIPS 3.24f</td>
<td>67%</td>
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### 2-(dibenzylamino)-3-phenyl-4-((triisopropylsilyl)oxy)but-3-enoic acid (3.24a)

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<th>Temperature</th>
<th>Time</th>
<th>TLC Rf</th>
<th>Yield</th>
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<td>3.23a</td>
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<td>24hr</td>
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<td>3.23b</td>
<td>25°C</td>
<td>24hr</td>
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</table>

White solid (foam); 84% yield; TLC (Hexanes/EtOAc 8:2) Rf = 0.48 (Z), 0.43 (E); ¹H NMR (400 MHz, CDCl₃) (mixture of isomers, E/Z = 60:40) E-isomer: δ 7.40-7.37 (m, 1H), 7.34-7.23 (m, 10H), 7.13-7.10 (m, 4H), 6.76 (d, J = 0.8 Hz,
1H), 3.81 (d, J = 13.6 Hz, 2H), 3.62 (d, J = 13.6 Hz, 2H), 1.14-1.07 (m, 3H), 1.00 (d, J = 6.7 Hz, 18H) ppm, Z-isomer: δ 7.40-7.37 (m, 1H), 7.34-7.23 (m, 10H), 7.13-7.10 (m, 4H), 6.81 (s, 1H), 4.04 (d, J = 13.5 Hz, 2H), 3.46 (d, J = 13.5 Hz, 2H), 1.26-1.16 (m, 3H), 1.09(7) (d, J = 7.2 Hz, 9H), 1.08(8) (d, J = 7.2 Hz, 9H) ppm; 13C NMR (100 MHz, CDCl3) (mixture of isomers, EI/Z = 60:40) E-isomer: δ 174.8, 143.1, 137.5, 136.6, 129.2, 129.0(3), 128.4, 127.7, 127.5, 126.5, 114.0, 65.0, 54.3, 17.5(7), 17.5(5), 11.7 ppm, Z-isomer: δ 174.9, 142.7, 140.0, 138.4, 129.0(3) 128.9(7), 128.4, 127.6, 127.3, 126.6, 115.3, 61.5, 54.8, 17.6(8), 17.6(5), 11.8 ppm; HRMS (ESI) [M+H]+ calcd. For C33H44NO3Si 530.30904, found 530.31025.

2-morpholino-3-phenyl-4-((triisopropylsilyl)oxy)but-3-enoic acid (3.24b)

White solid (foam); 74% yield; TLC (DCM/MeOH 9:1) Rf = 0.51 (Z), 0.46 (E); 1H NMR (400 MHz, CDCl3) (mixture of isomers, EI/Z = 60:40) E-isomer: δ 7.55 (d, J = 7.3 Hz, 2H), 7.29-7.25 (m, 2H), 7.18-7.14 (m, 1H), 6.85 (s, 1H), 4.07 (s, 1H), 3.75 (m, 4H), 2.89-2.82 (m, 4H), 1.16-1.08 (m, 3H), 1.00(3) (d, J = 7.2 Hz, 9H), 0.99(9) (d, J = 7.3 Hz, 9H) ppm, Z-isomer: δ 7.37-7.35 (m, 2H), 7.30-7.20 (m, 3H), 6.85 (s, 1H), 4.48 (s, 1H), 3.74 (t, J = 4.7 Hz, 4H), 2.84 (m, 4H), 1.29-1.20 (m, 3H), 1.12(4) (d, J = 7.2 Hz, 9H), 1.11(9) (d, J = 7.3 Hz, 9H) ppm; 13C NMR (100 MHz, CDCl3) (mixture of isomers, EI/Z = 60:40) E-isomer: δ 171.5, 145.4, 136.1, 129.0, 127.9, 126.9, 112.4, 73.5, 65.3, 51.2, 17.5(2), 17.5(1), 11.7 ppm, Z-isomer: δ 171.4, 144.7, 138.2, 128.5, 127.4, 126.8, 114.3, 67.9, 66.2, 51.6, 17.6(92), 17.6(86), 11.8 ppm; HRMS (ESI) [M+H]+ calcd. For C23H38NO4Si 420.2564, 420.2554.

Methyl 2-(benzylamino)-3-phenyl-4-((triisopropylsilyl)oxy)but-3-enoate (3.24c)

Thick oil; 50% yield; TLC (Hexanes/EtOAc 9:1) Rf = 0.30; 1H NMR (400 MHz, CDCl3) (mixture of isomers, EI/Z = 80:20) E-isomer: δ 7.49-7.46 (m, 2H), 7.30-7.25 (m, 6H), 7.23-7.16 (m, 2H), 6.60 (s, 1H), 4.03 (s, 1H), 3.81 (d, J = 13.2 Hz, 1H), 3.75 (d, J = 13.2 Hz, 1H), 3.67 (s, 3H), 1.18-1.08 (m, 3H), 1.02 (d, J = 6.8 Hz, 18H) ppm, Z-isomer: δ 7.30-7.25 (m, 8H), 7.25-7.18 (m, 2H), 6.76 (s, 1H), 4.77 (s, 1H), 3.80 (d, J = 13.0 Hz, 1H), 3.79 (d, J = 13.0 Hz, 1H), 3.67 (s, 3H), 1.24-1.14 (m, 3H), 1.09 (d, J = 6.6 Hz, 18H) ppm, Z-isomer: δ 7.40-7.37 (m, 1H), 7.34-7.23 (m, 10H), 7.13-7.10 (m, 4H), 6.81 (s, 1H), 4.04 (d, J = 13.5 Hz, 2H), 3.46 (d, J = 13.5 Hz, 2H), 1.26-1.16 (m, 3H), 1.09(7) (d, J = 7.2 Hz, 9H), 1.08(8) (d, J = 7.2 Hz, 9H) ppm; 13C NMR (100 MHz, CDCl3) (mixture of isomers, EI/Z = 60:40) E-isomer: δ 174.8, 143.1, 137.5, 136.6, 129.2, 129.0(3), 128.4, 127.7, 127.5, 126.5, 114.0, 65.0, 54.3, 17.5(7), 17.5(5), 11.7 ppm, Z-isomer: δ 174.9, 142.7, 140.0, 138.4, 129.0(3) 128.9(7), 128.4, 127.6, 127.3, 126.6, 115.3, 61.5, 54.8, 17.6(8), 17.6(5), 11.8 ppm; HRMS (ESI) [M+H]+ calcd. For C33H44NO3Si 530.30904, found 530.31025.
Hz, 18H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) (mixture of isomers, $E/Z = 80:20$) $E$-isomer: δ 174.0, 141.7, 139.7, 135.7, 128.7, 128.3, 128.2(9), 127.7, 127.0, 126.3, 117.1, 62.6, 51.9, 50.8, 17.5(7), 11.8(3) ppm, Z-isomer: δ 173.6, 141.9, 140.0, 138.0, 128.3(4), 128.3(2), 128.2, 127.2, 126.8, 126.5, 118.9, 57.9, 51.8, 51.1, 17.6(3), 17.6(1), 11.7(7) ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{27}$H$_{40}$NO$_3$Si 454.2771, found 454.2758.

**Methyl 2-((4-chlorophenethyl)amino)-3-phenyl-4-((triisopropylsilyl)oxy)but-3-enoate** (3.24d)

Thick oil; 55% yield; TLC (Hexanes/EtOAc 8:2) $R_f = 0.45$ ($Z$), 0.38 ($E$); $^1$H NMR (400 MHz, CDCl$_3$) (mixture of isomers, $E/Z = 75:25$) $E$-isomer: δ 7.38-7.35 (m, 2H), 7.27-7.18 (m, 5H), 7.07-7.04 (m, 2H), 6.61 (s, 1H), 4.03 (s, 1H), 3.66 (s, 3H), 2.83-2.79 (m, 2H), 2.75-2.71 (m, 2H), 1.16-1.07 (m, 3H), 1.00 (d, $J = 6.2$ Hz, 18H) ppm, Z-isomer: δ 7.26-7.17 (m, 7H), 7.06-7.03 (m, 2H), 6.71 (s, 1H), 4.73 (s, 1H), 3.66 (s, 3H), 2.87-2.73 (m, 4H), 1.21-1.14 (m, 3H), 1.09(3) (d, $J = 6.9$ Hz, 9H), 1.08(9) (d, $J = 7.1$ Hz, 9H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) (mixture of isomers, $E/Z = 75:25$) $E$-isomer: δ 173.8, 141.5, 138.3, 135.6, 131.8, 130.0, 128.6, 128.4, 127.7, 126.4, 117.3, 63.7, 51.9, 48.3, 35.6, 17.5(5), 11.7(6) ppm, Z-isomer: δ 173.4, 141.7, 138.5, 137.8, 131.7, 130.0, 128.4(3), 128.3(8), 127.1, 126.5, 118.9, 58.7, 51.8, 48.5, 35.7, 17.6(3), 17.6(1), 11.8(2) ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{28}$H$_{41}$ClNO$_3$Si 502.2538, found 502.2544.

**(E)-2-(2-methylpyrrolidin-1-yl)-5-phenyl-3-(((triisopropsilyoxy)methylene)pentanoic acid** (3.24e)

White solid; 67% yield; TLC (MeOH/DCM 1:9) $R_f = 0.48$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.24-7.17 (m, 4H), 7.12-7.09 (m, 1H), 6.52 (s, 1H), 3.90 (s, 1H), 3.40-3.34 (m, 1H), 3.32-3.25 (m, 1H), 2.96-2.84 (m, 3H), 2.52-2.44 (m, 1H), 2.22-1.99 (m, 3H), 1.94-1.86 (m, 1H), 1.80-1.71 (m, 1H), 1.39 (d, $J = 6.6$ Hz, 3H), 1.24-1.15 (m, 3H), 1.10 (d, $J = 7.1$ Hz, 9H), 1.09 (d, $J = 7.1$ Hz, 9H) ppm; $^{13}$C
NMR (100 MHz, CDCl$_3$) $\delta$ 168.4, 145.4, 142.8, 128.3, 128.0, 125.4, 112.3, 70.8, 62.7, 49.4, 33.8, 30.1, 29.1, 21.3, 17.6(4), 17.6(3), 16.8, 11.8 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{26}$H$_{44}$NO$_3$Si 446.30904, found 446.30971.

**(E)-2-(benzylamino)-5-phenyl-3-(((triisopropylsilyl)oxy)methylene)pentanoic acid (3.24f)**

White solid; 67% yield; TLC (MeOH/DCM 1:9) $R_f$ = 0.52; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37-7.34 (m, 2H), 7.21-7.06 (m, 8H), 6.44 (s, 1H), 4.01-3.88 (m, 3H), 2.83-2.76 (m, 2H), 2.51-2.43 (m, 1H), 2.35-2.26 (m, 1H), 1.20-1.10 (m, 3H), 1.08 (d, $J$ = 6.4 Hz, 18H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.6, 144.3, 142.7, 132.6, 129.4, 128.8, 128.5, 128.4, 128.1, 125.4, 112.1, 63.5, 47.4, 34.3, 27.3, 17.7, 11.8 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{28}$H$_{42}$NO$_3$Si 468.29339, found 468.29220.

**(E)-2-(dibenzylamino)-4-(2-oxopyrrolidin-1-yl)-3-phenylbut-3-enoic acid (3.24g)**

White solid (foam); 70% yield; TLC (DCM/MeOH 95:5) $R_f$ = 0.47; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37-7.26 (m, 3H), 7.26-7.18 (m, 8H), 7.08-7.05 (m, 5H), 4.42 (d, $J$ = 1.1 Hz, 1H), 3.79 (s, 4H), 3.00 (dt, $J$ = 10.7, 7.3 Hz, 1H), 2.81 (dt, $J$ = 10.7, 6.8 Hz, 1H), 2.37 (t, $J$ = 8.1 Hz, 2H), 1.82 (m, 2H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 176.0, 173.8, 138.5, 137.8, 130.0, 128.8, 128.2, 127.8, 127.7, 127.0, 125.5, 121.1, 67.4, 54.2, 48.4, 30.3, 18.8 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{28}$H$_{29}$N$_2$O$_3$ 441.21782, found 441.21785.

**(E)-2-morpholino-4-(2-oxopyrrolidin-1-yl)-3-phenylbut-3-enoic acid (3.24h)**

White solid; 97% yield; TLC (EtOAc/MeCN/MeOH/H$_2$O 60:20:20:10) $R_f$ = 0.50; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36-7.30 (m, 6H), 4.09 (s, 1H), 3.87 (m, 4H), 3.05 (m, 4H), 2.96 (m, 1H), 2.81 (m, 1H), 2.33 (m, 2H), 1.82 (m, 2H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 175.4, 170.0, 137.4, 129.9, 128.0, 127.9, 127.8, 115.7, 76.1, 64.8, 51.3, 47.9, 30.1, 18.5 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{18}$H$_{23}$N$_2$O$_4$ 331.1652, found 331.1651
(E)-2-(2-methylpyrrolidin-1-yl)-4-(2-oxopyrrolidin-1-yl)-3-phenylbut-3-enolic acid (3.24i)

Thick oil; 85% yield; TLC (EtOAc/MeCN/MeOH/H₂O 60:20:20:15) Rf = 0.40; 1H NMR (400 MHz, CDCl₃) δ 7.44-7.42 (m, 2H), 7.34-7.32 (m, 3H), 7.22 (s, 1H), 5.16 (s, 1H), 3.56 (dt, J = 11.3, 7.0 Hz, 1H), 3.50-3.42 (m, 1H), 3.08-3.01 (m, 1H), 2.91 (dt, J = 10.3, 6.8 Hz, 1H), 2.77 (dt, J = 10.5, 7.6 Hz, 1H), 2.32 (t, J = 8.1 Hz, 2H), 2.15-2.05 (m, 1H), 2.03-1.95 (m, 1H), 1.92-1.65 (m, 4H), 1.43 (d, J = 6.6 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl₃) δ 175.3, 168.1, 136.7, 130.4, 129.7, 128.0, 128.0, 115.7, 73.5, 63.5, 50.4, 47.6, 30.5, 30.0, 21.8, 18.5, 16.8 ppm; HRMS (ESI) [M+H]^+ calcd. For C₁₉H₂₅N₂O₃ 329.1859, found 329.1866

(S)-2-(methyl(1-phenylethyl)amino)-4-(2-oxopyrrolidin-1-yl)-3-phenylbut-3-enolic acid (3.24j)

Thick oil; 51% yield; TLC (EtOAc/MeCN/MeOH/H₂O 60:20:20:7) Rf = 0.40; 1H NMR (400 MHz, CDCl₃) (mixture of diastereoisomers, d.r. = 75:25) major-isomer: δ 7.51-7.49 (m, 1H), 7.42-7.24 (m, 10H), 4.72 (t, J = 6.9 Hz, 1H), 4.22 (s, 1H), 2.94-2.85 (m, 2H), 2.52 (s, 3H), 2.35-2.27 (m, 2H), 1.85-1.74 (m, 2H), 1.65 (d, J = 6.9 Hz, 3H) ppm, minor-isomer: δ 7.51-7.49 (m, 1H), 7.42-7.24 (m, 10H), 4.45 (s, 1H), 4.20 (t, J = 6.9 Hz, 1H), 2.78-2.73 (m, 2H), 2.38 (s, 3H), 2.35-2.27 (m, 2H), 1.85-1.74 (m, 2H), 1.53 (d, J = 6.9 Hz, 3H) 13C NMR (100 MHz, CDCl₃) (mixture of diastereoisomers, d.r. = 75:25) ppm; major-isomer: δ 175.5, 170.1, 136.6, 130.1, 129.5, 129.1, 128.8(7), 128.3, 128.0, 127.9, 127.7, 116.5, 73.3, 63.2, 47.9, 33.3, 30.1, 18.6, 16.9 ppm, minor-isomer: δ 175.6, 169.8, 137.4, 130.2, 129.3, 129.0, 128.9(3), 128.6, 128.1, 127.8, 127.3, 116.2, 72.3, 63.5, 47.8, 34.7, 30.6, 19.8, 16.5 ppm; HRMS (ESI) [M+H]^+ calcd. For C₂₃H₂₇N₂O₃ 379.2016, found 379.2028
(E)-2-morpholino-3-((2-oxopyrrolidin-1-yl)methylene)-5-phenylpentanoic acid (3.24k)

White solid; 92% yield; TLC (MeOH/DCM 2:8) $R_f = 0.55$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.27-7.24 (m, 2H), 7.19-7.15 (m, 3H), 6.58 (s, 1H), 3.84-3.81 (m, 4H), 3.70 (s, 1H), 3.54-3.41 (m, 2H), 2.93-2.71 (m, 6H), 2.55-2.46 (m, 2H), 2.34 (t, $J = 8.1$ Hz, 2H), 2.02-1.95 (m, 2H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) δ 174.6, 170.5, 141.2, 128.4, 128.3, 127.7, 126.0, 120.6, 75.2, 65.0, 51.3, 48.1, 34.7, 31.1, 30.2, 18.4 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{20}$H$_{27}$N$_2$O$_4$ 359.19708, found 359.19708.

3.6 References


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4 Stable α-boryl imines are even rarer than α-borylcarbonyl compounds; an example of α-boryl ketazines was isolated and characterized: Groh, T.; Elter, G.; Noltemeyer, M.; Schmidt, H.-G.; Meller, A. Main Group Met. Chem. 2000, 23, 709–718.

5 For examples of bond energy: 536 kJ/mol (B-OR); 446 kJ/mol (B₃N₃H₃Cl₃).


Chapter Four

*Synthetic applications of α-borylcarboxylic acids*
4. Synthetic applications of $\alpha$-borylcarboxylic acids

4.1 Introduction

Organometallic compounds are widely used in modern synthesis, but their efficient preparation remains a long-term challenge. Since the labile carbon-metal bonds usually have poor functional group compatibility and chemical transformation tolerance, the vast majority of established synthetic routes to organometallic species involve late-stage installation of the carbon-metal bond via metathesis, insertion, or other ionic reactions using appropriate precursors. In the case of organoboron reagents, their synthesis usually utilizes boron electrophiles to install a carbon-boron bond. This approach, however, suffers from significant limitations including use of expensive transition-metal catalysts, dangerous strong bases, anhydrous or cryogenic conditions, thereby presents regio- or chemoselectivity challenges. With the aim of accessing functionalized organoboron reagents in complex molecule synthesis, it would be advantageous to have an early-stage installation of boron moieties followed by a sequence of late-stage functionality manipulation. Thus, we have been interested in developing mild reactions that can functionalize early-installed boron-containing scaffolds to access organoboron compounds difficult or impossible to obtain via established methods.

Encouraged by our recent development in facile synthesis of $\alpha$-borylcarboxylic acids from the MIDA boronate-derived $\alpha$-boryl aldehydes, we anticipated that the versatility of the carboxylic acid function in decarboxylative transformations could supply us opportunities to functionalize the $\alpha$-borylated carbon and ultimately afford us useful boron-containing molecules. In this chapter, we will discuss two classes of decarboxylative manipulation, namely, Curtius rearrangement and Barton radical decarboxylation, of $\alpha$-borylcarboxylic acids to synthesize novel bench-stable borylated reagents, $\alpha$-boryl isocyanates and acylboronates, respectively. The downstream applications of these functionalized boron-containing building blocks for the synthesis of $\alpha$-aminoboronic acid derivatives and borylated heterocyclic compounds will also be discussed.
4.2 Stable α-boryl isocyanates and their applications

4.2.1 Synthesis of α-boryl isocyanates via Curtius rearrangement

At the outset, in order to test the feasibility of Curtius rearrangement with α-borylcarboxylic acid, we first prepared α-borylacyl azide 4.1 by treating acid 3.19a with oxalyl chloride and sodium azide. Encouragingly, leaving compound 4.1 in methanol overnight at room temperature afforded α-boryl carbamate 4.2 as a white solid in moderate yield (Scheme 4.1A). This preliminary result suggested that the Curtius rearrangement indeed occurred. A migration of the α-boroalkyl group from carbon to nitrogen was involved in this transformation (Scheme 4.1B), leading to the generation of a α-boryl isocyanate intermediate that was attacked by methanol to form the observed final carbamate product. To the best of our knowledge, reactions accompanied by migration of boron-substituted carbon are presently unknown.

![Scheme 4.1](image)

Scheme 4.1 Curtius rearrangement via α-boroalkyl migration

In the hope of trapping the intermediate α-boryl isocyanate species, we subjected the α-borylcarboxylic acid 3.19a to a one-pot diphenylphosphoryl azide (DPPA)/Et3N mediated Curtius rearrangement procedure in anhydrous acetonitrile in the absence of alcohol.
nucleophiles.\textsuperscript{3,4} After a one-hour reaction at 50 °C, we detected a clean conversion of the starting material to α-boryl isocyanate 4.3a, which exhibited an IR stretch of 2244 cm\(^{-1}\) and a \(^{13}\)C NMR chemical shift of 122.9 ppm, consistent with the presence of isocyanate functionality. The α-boryl isocyanate 4.3a can be isolated with silica gel chromatography in good yield and was found to be a stable white solid at ambient conditions. It should be noted that stable α-metallo isocyanate compounds are very rare: only a single example of α-silyl isocyanates has been reported.\textsuperscript{5} To the best of our knowledge, this is the first time to obtain isocyanates equipped with a α-boryl group. These results prompted us to test the generality of the preparation of stable α-boryl isocyanates. A range of mono-substituted α-boryl carboxylic acids were thus subjected to the one-pot Curtius rearrangement condition (Table 4.1). The reaction worked well with aryl substrates (3.19a-c). Primary and secondary alkyl-substituted α-boryl carboxylic acids (3.19d-h) also afforded the desired isocyanates in good to excellent yields. All of these α-boryl isocyanates can be isolated using silica gel chromatography and stored on the bench in sealed vials.

Table 4.1 Preparation of α-boryl isocyanates via Curtius rearrangement\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>α-Borylcarboxylic acid</th>
<th>Product</th>
<th>Yield\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.19a</td>
<td>4.3a</td>
<td>71%</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: DPPA, \(\text{Et}_3\text{N}\), MeCN, 50 °C.
2. $\text{MeN}_3\text{BO}_3\text{COOH}$

3. $\text{MeN}_3\text{BO}_3\text{COOH}$

4. $\text{PhMeN}_3\text{BO}_3\text{COOH}$

5. $\text{PhMeN}_3\text{BO}_3\text{COOH}$
Although the Curtius rearrangement is known to undergo migration with retention of the configuration of migrating groups, in view of the novelty of this α-boroalkyl migratory process, we were still interested in obtaining its stereochemical information. In order to achieve this goal, α-boryl carboxylic acids 4.4a and 4.4b, equipped with the chiral pinene-derived iminodiacetic acid (PIDA) boryl group, were prepared as single diastereomers (d.r. > 95:5) using diastereoselective epoxidation of the corresponding vinyl boronates developed by Burke and co-workers, followed by stereospecific rearrangement and oxidation (Scheme 4.2). Compounds 4.4a and 4.4b were then subjected to the same one-pot DPPA/Et₃N mediated Curtius rearrangement. Indeed, ¹H NMR analysis of the crude reaction mixture revealed that α-boryl
isocyanate 4.5b was produced from alkyl-substituted acid 4.4b with complete retention of stereochemistry (d.r. > 95:5), which is expected for a Curtius rearrangement process. However, the rearrangement of phenyl-substituted acid 4.4a resulted in the isocyanate product 4.5a with a slightly eroded diastereoisomeric ratio (d.r. = 85:15). This could be attributed to the vulnerability of the acidic α-proton (benzylic proton) in either the acid starting material or the isocyanate product to the basic reaction condition.

Scheme 4.2 Stereochemistry investigation for the α-boroalkyl migration

4.2.2 Synthesis of α-aminoboronic acid derivatives from α-boryl isocyanates

Over the past decade, the significance of α-aminoboronic acids and their derivatives, such as boropeptides, has come into the limelight both in academia and in the pharmaceutical industry. A number of studies have documented the utility of aminoboronic acid derivatives as biochemical probes of protein function. These studies hinge on reversible covalent interactions that are possible between boron and nucleophilic protein residues. The realization of α-aminoboronic acids as promising drug candidates culminated in the recent success of Bortezomib (Velcade), an FDA approved boropeptide used for the treatment of multiple myeloma. Such studies have resulted in increased interest in the design of boron-containing peptides. The emergence of biotechnology companies that are focused on the boropeptide platform further underscores the growing interest in this area.
Despite the significance of the α-aminoboron functionality, the application of these molecules in chemical biology and drug discovery programs is made difficult by the lack of methods adaptable to synthesis using mild reaction conditions.\(^\text{10}\) For instance, the most popular method is based on Matteson’s protocol. It involves the conversion of α-chloroboronic esters to α-aminoboronic esters by a substitution with nitrogen nucleophiles.\(^\text{10a}\) Borylation of α-lithiated protected secondary amines, particularly cyclic amines such as pyrrolidines, affords the corresponding α-aminoboronic esters.\(^\text{10b}\) Ellman and coworkers recently reported the preparation of α-aminoboronic acids by a copper-catalyzed addition of bis(pinacolato)diboron to N-sulfinylimines.\(^\text{10c}\) While these reactions are effective towards the synthesis of mono-substituted α-aminoboronic acids, they are still suffer from significant limitations, such as use of strong base, cryogenic condition, or expensive borylating reagents. In addition, none of these methods can provide access to α,α-disubstituted α-aminoboronic acid derivatives, which would potentially supply more opportunities for SAR investigations in drug discovery. Therefore, new synthetic methods that can provide versatile entries into α-aminoboronic acid derivatives under mild conditions are highly demanded.

The “boron-carbon-nitrogen” connectivity in α-boryl isocyanates makes them potential precursors for α-aminoboronic acid derivatives. At the outset, we were aiming at chemoselective generation of the free amino group from α-boryl isocyanates with the MIDA boryl group intact. To realize this goal, we first treated α-boryl isocyanate \(\text{4.3d}\) with mild aqueous bases (e.g. 5% \(\text{NaHCO}_3\), sat. \(\text{NaHCO}_3\), 5% \(\text{Na}_2\text{CO}_3\)) in polar solvents (e.g. MeCN, THF) for various period of time. Unfortunately, these reactions only resulted in decomposition of the starting material to intractable mixtures, which could be attributed to the instability of the MIDA boryl group. We thus switched to utilize acid hydrolysis. Surprisingly, treatment of α-boryl isocyanate \(\text{4.3d}\) with 3.0 M HCl aqueous solutions in MeCN afforded α-aminoboronic acid \(\text{4.6}\) as a hydrogen chloride salt (Equation 4.1). The acidic hydrolysis not only resulted in decomposition of the starting material to intractable mixtures, which could be attributed to the instability of the MIDA boryl group. We thus switched to utilize acid hydrolysis. Surprisingly, treatment of α-boryl isocyanate \(\text{4.3d}\) with 3.0 M HCl aqueous solutions in MeCN afforded α-aminoboronic acid \(\text{4.6}\) as a hydrogen chloride salt (Equation 4.1). The acidic hydrolysis not only resulted in the formation of the free amine from the isocyanate functional group, but also converted the MIDA boronate to the free boronic acid. Compound \(\text{4.6}\) from this unselective hydrolysis was found difficult to be separated from the by-product \(N\)-methyliminodiacetic acid (MIDA). In addition, attempts at further functionalization of \(\text{4.6}\), such as peptide coupling reactions, to prepare more complex derivatives
only resulted in decomposition of the starting material. The difficulty in derivatization of \( \alpha \)-aminoboronic acid 4.6 prompted us to look for alternative ways to achieve complex \( \alpha \)-amino boronic acid derivatives.

![Image](image.png)

We thus explored the reactivity of boryl isocyanates toward amines and alcohols with the goal of preparing \( \alpha \)-boryl ureas and carbamates respectively, which we envisioned as precursors to \( \alpha \)-amino boronic acid derivatives. We had initially suspected that conditions required for nucleophilic attack at the isocyanate would be incompatible with the adjacent boronate functionality. Interestingly, reactions between \( \alpha \)-boryl isocyanates and different types of amines were found to occur smoothly at room temperature in THF with retention of the boronate groups. A series of \( \alpha \)-boryl urea products 4.7 (\( \alpha \)-ureido MIDA boronates) were obtained in good to excellent yields (Table 4.2). All aliphatic amines afforded the desired products in full conversion within 1–5 hours, although reactions with aromatic amines, such as aniline, reached only 50% completion after 12 hours (Table 4.2, entry 5). In contrast to the facile reactions between amines and \( \alpha \)-boryl isocyanates, alcohols were found to be reactive only in the presence of CuCl in DMF. By choosing different alkoxy nucleophiles, a series of \( \alpha \)-boryl carbamates 4.8 with representative amino-protecting groups were obtained (Table 4.3). Most alcohols afforded the desired products in good yields at ambient temperature, whereas in the case of bulky alcohols – tert-butanol, elevated temperature and prolonged reaction time were needed. In view of the wide use of ureas and carbamates in medicinal chemistry and material science, these borylated analogues are expected to find utility in solid phase peptide synthesis. The orthogonality of
protecting groups in these building blocks will be useful in the synthesis of complex \(\alpha\)-amino boronic acid derivatives.

**Table 4.2** Preparation of \(\alpha\)-boryl ureas\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>(\alpha)-Boryl isocyanate</th>
<th>Amine</th>
<th>Product</th>
<th>Yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[\text{MeN} \begin{array}{c} \text{B} \ \text{R} \end{array} \text{N} = \text{O} ] (4.3)</td>
<td>(-\text{NH}_2)</td>
<td>[\text{MeN} \begin{array}{c} \text{B} \ \text{R} \end{array} \text{N} = \text{C} \begin{array}{c} \text{H} \ \text{R}^* \end{array} \text{N} \begin{array}{c} \text{H} \ \text{R}^* \end{array} ] (4.7)</td>
<td>93%</td>
</tr>
<tr>
<td>2</td>
<td>[\text{MeN} \begin{array}{c} \text{B} \ \text{R} \end{array} \text{N} = \text{O} ] (4.3)</td>
<td>(-\text{NH}_2)</td>
<td>[\text{MeN} \begin{array}{c} \text{B} \ \text{R} \end{array} \text{N} = \text{C} \begin{array}{c} \text{H} \ \text{R}^* \end{array} \text{N} \begin{array}{c} \text{H} \ \text{R}^* \end{array} ] (4.7)</td>
<td>95%</td>
</tr>
</tbody>
</table>
Reactions were carried out using 1.0 equiv of α-boryl isocyanate and 1.5 equiv of amine in anhydrous THF at 23 °C for 1–12 hours. \(^a\) Isolated yields after silica gel chromatography. \(^b\) 50% conversion after 12 hours reaction at room temperature.

**Table 4.3 Preparation of α-boryl carbamates**

\(^a\) Aromatic substituent.
<table>
<thead>
<tr>
<th>Entry</th>
<th>α-Boryl isocyanate</th>
<th>Alcohol</th>
<th>Product</th>
<th>Yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td><img src="image3" alt="Chemical Structure" /></td>
<td>75%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image4" alt="Chemical Structure" /></td>
<td><img src="image5" alt="Chemical Structure" /></td>
<td><img src="image6" alt="Chemical Structure" /></td>
<td>80%</td>
</tr>
<tr>
<td>3(^c)</td>
<td><img src="image7" alt="Chemical Structure" /></td>
<td><img src="image8" alt="Chemical Structure" /></td>
<td><img src="image9" alt="Chemical Structure" /></td>
<td>60%</td>
</tr>
<tr>
<td>4</td>
<td><img src="image10" alt="Chemical Structure" /></td>
<td><img src="image11" alt="Chemical Structure" /></td>
<td><img src="image12" alt="Chemical Structure" /></td>
<td>77%</td>
</tr>
</tbody>
</table>
Unless specified otherwise, reactions were carried out using 1.0 equiv of α-boryl isocyanate, 3.0 equiv of alcohol and 1.0 equiv of CuCl in anhydrous DMF at 23 °C for 3 hr. 

Isolated yields after silica gel chromatography.

The reaction was carried out using 10.0 equiv of tert-BuOH at 70 °C for 24 hr.

A range of deprotection procedures/conditions was tested in an attempt to achieve chemoselective release of the free boronic acids or amino groups. For instance, treating α-boryl urea 4.7c with 1.0 M aqueous NaOH in THF at room temperature selectively removed the MIDA protecting group and resulted in the α-ureido boronic acid 4.9 (Equation 4.2). Given the possibility of reversible molecular interaction, the combination of boronic acid and urea functionality in this type of multi-functionalized molecules could have potential for applications in organocatalysis and molecular recognition.12,13,14,15

\[(\text{4.2})\]

\[(\text{4.3})\]
In contrast, Pd(PPh$_3$)$_4$-catalyzed dealylation of carbamate **4.8d** gave stable α-amino boronate **4.10** with the MIDA boryl group intact (Equation 4.3). To the best of our knowledge, stable α-aminoboronic acid derivatives of this type, containing an unsubstituted primary α-amino group are presently unknown. Usually, α-aminoboronic acid derivatives containing free primary or secondary α-amino groups are unstable due to a fast 1,2-migration of boron groups from carbon to nitrogen (Scheme 4.3). It is likely that the tetracoordinate MIDA boron center inhibits the initial intramolecular attacks from the α-amino groups, thereby preventing the decomposition of compound **4.10**.

![Scheme 4.3 A mechanism for the decomposition of α-aminoboronic acid derivatives](image)

In order to demonstrate the potential of α-amino boronate **4.10** in boropeptide synthesis, a subsequent coupling of **4.10** with amino acid, such as $N$-Cbz-$L$-leucine, was carried out (Equation 4.4). The reaction successfully afforded the MIDA-protected boro-dipeptide **4.11** as a mixture of two diastereomers which can be easily separated by flash chromatography in good yields.

![Equation 4.3](image)
The successful preparation of mono-substituted $\alpha$-aminoboronic acids via $\alpha$-boryl isocyanates encouraged us to further pursue the synthesis of $\alpha,\alpha$-disubstituted derivatives. This type of $\alpha$-aminoboronic acid analogue is not easy to obtain using known methodologies due to the difficulty in installing a quaternary $\alpha$-carbon center. A single report in preparation of $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic acids from $\alpha,\alpha$-disubstituted isocyanides was found (Scheme 4.4). A series of $\alpha$-boryl isocyanide was obtained by treating the $\alpha$-deprotonated disubstituted isocyanides with boron electrophiles, however, in extremely low yields. Although the next step involving acidic hydrolysis of isocyanide group resulted in excellent yields, the whole procedure targeting the $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic esters was still inefficient.

Scheme 4.4 Synthesis of $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic ester from isocyanides

It is conceivable that the low-yielding of the above methodology is attributed to the intrinsic difficulties of intermolecular reactions at sterically hindered reaction centers. We had thought that the Curtius rearrangement should not have this problem due to the “intramolecular” fashion of the process. In order to evaluate the feasibility of $\alpha$-boroalkyl migration for the synthesis of bulky $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic acids, we chose $\alpha$-borylcarboxylic acid 4.12 as a testing ground (Scheme 4.5). Compound 4.12 was first prepared from the corresponding $\alpha$-allylated $\alpha$-boryl aldehyde 3.18 (Chapter 3, section 3.3.3) via Pinnick oxidation. Gratifyingly, the Curtius rearrangement of carboxylic acid 4.12 occurred smoothly at 50 °C in MeCN. Although a longer reaction time was required for full conversion, $\alpha$-boryl isocyanate product 4.13 was afforded in good isolated yield. Further transformations of 4.13, such as acidic hydrolysis and nucleophilic
attack, were also conducted. The final $\alpha,\alpha$-disubstituted aminoboronic acid products 4.14 and 4.15 were thus successfully obtained. These transformations clearly demonstrated the potential of Curtius rearrangement in the preparation of $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic acid derivatives, which are difficult or impossible to access via established methodologies.

Scheme 4.5 Preparation of $\alpha,\alpha$-disubstituted $\alpha$-aminoboronic acid derivatives
4.3 Stable acylboronates and their applications

The successful installation of amino moiety geminal to boryl groups by taking advantages of the decarboxylative transformation of α-borylcarboxylic acids encouraged us to evaluate possibilities of constructing oxygen-based functions at the same carbon. In this section, we will describe the decarboxylative conversion of α-borylcarboxylic acids to α-hydroxyboronates, which supplied subsequent access to a new class of stable acylboronates via oxidation of the hydroxyl group. Acyl boronates were also found to be capable of preparing a range of borylated heterocycles, which are difficult or impossible to obtain via established methods.

4.3.1 Synthesis of α-hydroxyboronates via Barton radical decarboxylation

We opted to utilize Barton radical decarboxylation, a well-established method for replacing carboxylic acid with other functional groups, as a testing ground to evaluate the feasibility of α-hydroxyboronate preparation. At the outset, α-borylcarboxylic acid 3.19d was first converted to its corresponding thiohydroxamate ester by reacting with N-hydroxypyridine-2-thione under a standard DCC coupling condition. The resulted bright-yellow ester solution was subsequently exposed to tungsten light with the bubbling of O₂ gas in the presence of tert-butylthiol. Upon irradiation, a α-boryl radical species was expected to generate from the photo-induced decomposition of the thiohydroxamate ester. It was immediately trapped by molecular oxygen and converted to the α-boryl hydroperoxyl radical that was in turn quenched by tert-butylthiol as a hydrogen donor. This reaction occurred by a free radical chain mechanism in which the tert-butylthiol not only acted as an efficient trap for α-boryl hydroperoxyl radicals, but also provided the tert-butylthiyl radical necessary for efficient chain propagation (Scheme 4.6). The final reductive treatment of the reaction mixture with trimethylphosphite smoothly converted the α-boryl hydroperoxide intermediate to the desired product α-hydroxyl MIDA boronate 4.16d in 73% isolated yield (see Table 4.4, entry 4). It is worth pointing out that, although compounds
containing a gem-hydroxyboron motif have been reported, this is the first time to obtain the analogous molecule equipped with a tetrahedral boron center.

Scheme 4.6 Mechanism of Barton radical decarboxylation

This preliminary result prompted us to expand the scope of preparation (Table 4.4). It was found that alkyl-substituted substrates generally afforded the desired α-hydroxyboronate products in good yields (entries 4−8). However, the starting α-borylcarboxylic acids with aryl substituents only resulted in the isolation of products with 30-40% yields (entries 1−3). This is likely attributable to the delocalization of the α-boryl radical by the aromatic ring, thereby leading to generation of intractable by-products. It is also worth pointing out that, although the carbon-centered radicals with ordinary trivalent α-boronic ester substituents are known intermediates in a range of reactions, this is the first report of chemical transformations involving α-boryl radicals containing a $sp^3$-boron group, which does not supply moderate delocalizing stabilization to the radical center.
Table 4.4 Preparation of $\alpha$-hydroxyboronates via Barton radical decarboxylation

![Chemical Structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>$\alpha$-Borylcarboxylic acid</th>
<th>Product</th>
<th>Yield $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="3.19a" /></td>
<td><img src="image" alt="4.16a" /></td>
<td>32%</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="3.19b" /></td>
<td><img src="image" alt="4.16b" /></td>
<td>32%</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="3.19c" /></td>
<td><img src="image" alt="4.16c" /></td>
<td>35%</td>
</tr>
</tbody>
</table>
4

3.19d  4.16d

5

3.19e  4.16e

6

3.19f  4.16f

7

3.19g  4.16g
Reactions were carried out using: Step 1: 1.0 equiv of α-borylcarboxylic acid, 1.2 equiv of DCC and 0.1 equiv of DMAP in anhydrous DCM at 23 °C for 12 hr; Step 2: slow O₂ bubbling, 9.0 equiv of t-BuSH, irradiation with 250 W tungsten light at 23 °C for 2–8 hr; Step 3: 2.0 equiv of (MeO)₃P at 23 °C for 2 hr. b Isolated yields after silica gel chromatography.

4.3.2 Synthesis of acylboronates via Dess-Martin oxidation

With these α-hydroxyboronates in hand, we questioned the possibility of alcohol oxidation as a general means of accessing acylboronates, an emerging class of highly valuable synthetic building blocks. Tetracoordinate boryl groups were proved to be stable under a variety of oxidative conditions converting the distal alcohol function to aldehydes, ketones or carboxylic acids. However, no oxidation at the same carbon of the boryl group was investigated. In order to examine the feasibility of this novel transformation, α-hydroxyboronate 4.16d was first subject to the Ley oxidation (TPAP/NMO). Encouragingly, the desired acylboronate 3a was isolated from the reaction, however, by using a large amount of toxic catalyst tetrabutylammonium perruthenate (TPAP) (0.5 equiv). Lower TPAP loading (e.g. 5 mol%) failed to afford the desired product, even with prolonged reaction times, and only resulted in significant decomposition. The inefficiency of this reaction prompted us to examine other mild oxidants. To our delight, the reaction between 4.16d and stoichiometric amount of Dess-Martin periodinane in DCM smoothly afforded the acylboronate 4.17d as a white solid in 70% yield after silica gel chromatography. To evaluate the generality, a variety of other α-hydroxyboronates was also tested in Dess-Martin oxidation (Scheme 1). Alkyl- and aryl-substituted substrates were all tolerated and afforded the corresponding acylboronates in good isolated yields.
Table 4.5 Preparation of acylboronates via Dess-Martin oxidation$^a$

![Dess-Martin oxidation](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>$\alpha$-Borylcarboxylic acid</th>
<th>Product</th>
<th>Yield$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[\text{MeN}_2\text{BCOOH} ]</td>
<td>[\text{MeN}_2\text{B} ]</td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td>4.16a</td>
<td>4.17a</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>[\text{MeN}_2\text{BCOOH} ]</td>
<td>[\text{MeN}_2\text{B} ]</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>4.16b</td>
<td>4.17b</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>[\text{MeN}_2\text{BCOOH} ]</td>
<td>[\text{MeN}_2\text{B} ]</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td>4.16c</td>
<td>4.17c</td>
<td></td>
</tr>
</tbody>
</table>
4.16d

4.17d

70%

4.16e

4.17e

66%

4.16f

4.17f

70%

4.16g

4.17g

85%
4.3.3 Reactivity of acylboronates and their applications in the synthesis of borylated heterocycles

We next turned our attention to the stability and reactivity of acylboronates. In order to test the tolerance of their carbon-boron bond towards chemical transformations, acylboronates were subject to a range of reactions. Treatment of compounds 4.17a and 4.17d with mCPBA, somewhat to our surprise, afforded quantitative yields of acyloxyborane products 4.18a and 4.18b respectively (Equation 4.4). Unlike ordinary acyloxyboranes, which are a class of unstable strong Lewis acids, compounds 4.18a and 4.18b are bench-stable and can be purified with silica gel chromatography. Formation of acyloxyboranes from acylboronates unambiguously indicated the occurrence of a Baeyer-Villager transformation accompanied by the migration of the boryl group, revealing a stronger migratory aptitude of the tetracoordinate MIDA boron center than alkyl or aryl groups. Considering the fact that an analogous 1,2-boryl migration also takes place in the BF$_3$-promoted rearrangement of oxiranyl MIDA boronates (Chapter 3, section 3.3), we believe the potential of MIDA boryl group in migratory transformation will find wide applications in organic synthesis.
It was found that exposure of acylboronates 4.17d and 4.17e to Br₂ in dioxane/DCM smoothly generated the α-bromination products 4.19a and 4.19b in good yields (Equation 4.5). The ease of α-bromination of acylboronates with α-proton clearly shows their capability of enolization. For the further validation, 1-(silyloxy)vinylboronates 4.20a and 4.20b were successfully synthesized in moderate yields by treating the starting acylboronates 4.17e and 4.17f with trimethylsilyl trifluoromethanesulfonate (TMSOTf) in the presence of DBU (Equation 4.6).

With these α-bromoacylboronates 4.19a and 4.19b in hand, we examined their potentials in downstream transformations leading to heterocycles with retention of the MIDA boryl moiety. We were pleased to find that reacting 4.19a or 4.19b with thioamide in DMF at 65 °C afforded a range of 4-borylated thiazoles in good yields (Table 4.6, entries 1–4). Replacement of thioamides
with thioureas in the reaction also resulted in the smooth generation of the expected thiazol-2-
amine products (Table 4.6, entries 5–6). No cleavage of the boryl group was observed. These
stable borylated thiazol compounds, difficult or impossible to obtain via established borylation
methodologies, are valuable building blocks for cross-coupling reaction in the synthesis of
active pharmaceutical ingredients.

Table 4.6 Preparation of thiazol-4-ylboronates

<table>
<thead>
<tr>
<th>Entry</th>
<th>α-Bromoacylboronate</th>
<th>Thioamide</th>
<th>Product</th>
<th>Yield(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="4.19a" alt="Image" /></td>
<td><img src="4.21a" alt="Image" /></td>
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</tr>
<tr>
<td>2</td>
<td><img src="4.19a" alt="Image" /></td>
<td><img src="4.21b" alt="Image" /></td>
<td><img src="4.21b" alt="Image" /></td>
<td>66%</td>
</tr>
</tbody>
</table>
4.19b

4.21c

4.19b

4.21d

4.19a

4.21e
Successful access to thiazolylboronates aroused our curiosity to further explore new possibilities toward borylated heterocyclic compounds from acylboronates and their derivatives. We first proposed a conversion of 1-(silyloxy)vinylboronates to α-hydroxyacylboronates. To our surprise, upon treatment of compounds 4.20a and 4.20b in the Rubottom oxidation with mCPBA and TBAF continuously, α-hydroxy-α-boryl ketones 4.22a and 4.22b were isolated respectively (Scheme 4.7). It was likely that the initially formed α-hydroxyacylboronates 4.21a/b isomerized to the more stable 4.22a/b via the proton transfer process. Indeed, in the case of vinylboronate 4.20b, a 1:1 mixture of the corresponding α-hydroxyacylboronate 4.21b and the rearranged α-boryl ketone 4.22b was first isolated after the TBAF desilylation. Upon standing in solvents (e.g. DMSO, MeCN, CHCl₃), the mixture spontaneously converted to pure compound 4.22b completely within hours.

After the Rubottom procedure, a subsequent Dess-Martin oxidation of 4.22a and 4.22b was performed. Gratifyingly, the oxidation afforded the desired 2-oxo-acylboronate products 4.23a and 4.23b without difficulties (Scheme 4.7). To the best of our knowledge, diketo compounds equipped with boryl groups are presently unknown. X-ray structure of 4.23a revealed the bond length of its two C=O was about 1.22–1.23 Å, indicating a set of ordinary diketone carbonyl groups. The smooth transition of 4.23b to the presently unknown air-stable 2-borylated quinoxaline derivative 4.24 upon treatment of o-phenylenediamine corroborated the potential of
this type of molecules in heterocycle synthesis. Given the existence of quinoxaline subunits in many bioactive compounds, direct access of boronic acid building blocks of this type via 2-oxo-acyl boronates is of particular importance for medicinal chemistry research.

Scheme 4.7 Synthesis of 2-oxo-acylboronates and 2-borylated quinoxalines

4.4 Summary

Late-stage functionality manipulation of organoboron compounds with retention of the boron moieties supplies efficient access to novel functionalized boron-containing molecules that are difficult or impossible to obtain through established methodologies. This strategy was exemplified by a series of successful installations of nitrogen or oxygen-based functions geminal to boron groups by taking advantages of the decarboxylative transformation of MIDA-derived α-borylcarboxylic acids.
We have realized the first synthesis of α-boryl isocyanates via the Curtius rearrangement of the MIDA-derived α-borylcarboxylic acids. This new type of bench-stable molecules has enabled mild and convenient access to a wide range of mono- or di-substituted α-aminoboronic acid derivatives, including carbamates, ureas and peptides.

A facile installation of hydroxyl group geminal to boryl moiety via Barton radical decarboxylation from α-borylcarboxylic acids was also demonstrated. The resulting α-hydroxyboronates were subsequently transformed to a class of bench-stable acylboronates. These new carbonyl-based building blocks are capable of generating a range of novel functionalized boron derivatives, including acyloxyboranes, α-bromoacylboronates, 1-(silyloxy)vinylboronates, α-hydroxy-α-boryl ketones, and 2-oxo-acyl boronates. These densely functionalized boron-containing molecules further enabled straightforward preparation of borylated thiazoles and quinoxalines, which are difficult to obtain via other established methods.

In view of the robust functional group compatibility and chemical transformation tolerance of MIDA boryl groups, downstream functionalization of these bench-stable organoboron compounds provides opportunities to achieve novel synthetic entities. Given the recent development in boronic acid chemistry, we expect that our new discovery will find a wide range of applications in organic synthesis.

4.5 Experimental details

4.5.1 General information

**General:** Anhydrous dichloromethane (DCM), acetonitrile (MeCN), and chloroform (CHCl₃) were purchased and used as received. Anhydrous tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. All other solvents were of reagent grade quality.

**Chromatography:** Flash column chromatography was carried out using Silicycle 230-400 mesh silica gel. Thin-layer chromatography (TLC) was performed on Macherey Nagel pre-
coated glass backed TLC plates (SIL G/UV254, 0.25 mm) and visualized using a UV lamp (254 nm) or KMnO₄ stain in case of no UV activity.

**Nuclear Magnetic Resonance Spectroscopy:** ¹H NMR and ¹³C NMR spectra were recorded on Varian Mercury 400 MHz spectrometer. ¹H NMR spectra chemical shifts (δ) are reported in parts per million (ppm) referenced to TMS (0 ppm) or residual protium in the NMR solvent (DMSO-d₆, δ = 2.50 ppm; MeCN-d₃, δ = 1.94 ppm; acetone-d₆, δ = 2.05 ppm; MeOD-d₄, δ = 3.31 ppm; center line). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, m = multiplet, br = broad), coupling constant (J) in Hertz (Hz), and integration. ¹³C NMR spectra chemical shifts (δ) are reported in parts per million (ppm) were referenced to carbon resonances in the NMR solvent (CDCl₃, δ = 77.23 ppm; DMSO-d₆, δ = 39.51 ppm; MeCN-d₃, δ = 1.39 ppm; acetone-d₆, δ = 29.92 ppm; MeOD-d₄, δ = 49.15 ppm center line). **Carbon exhibiting significant line broadening brought about by boron substituents were not reported (quadrupolar relaxation).** ¹¹B NMR was recorded using Varian VnmrS 400 MHz spectrometer or Bruker Avance III 400 MHz spectrometer and referenced to an external standard of BF₃·Et₂O.

**Infrared Spectroscopy:** IR spectra were recorded on a Perkin-Elmer Spectrum 100 instrument equipped with a single-reflection diamond/ZnSe ATR accessory.

**Mass Spectroscopy:** High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities or on JEOL AccuTOF-DART instrument.
4.5.2 General procedure for synthesis of α-boryl isocyanates

To a solution (or suspension) of α-boryl carboxylic acid (5.0 mmol) in 30 mL anhydrous MeCN was added Et₃N (6.0 mmol, 1.2 equiv) and DPPA (6.0 mmol, 1.2 equiv) subsequently. The resulting solution was stirred at room temperature under N₂ for 15 min, and then heated at 50 °C for 1 hr until the reaction was complete as indicated by crude ¹H NMR. The reaction mixture was cooled to room temperature, evaporated under reduced pressure to remove the solvent. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 80:20 → Hexanes/EtOAc 50:50 → EtOAc) to afford pure products.

(MIDA boryl)(phenyl)methyl isocyanate (4.3a)

White solid; 71% yield; TLC (EtOAc) Rₜ = 0.55; ¹H NMR (400 MHz, DMSO-d₆) δ 7.39-7.24 (m, 5H), 4.39 (d, J = 17.2 Hz, 1H), 4.31 (d, J = 17.2 Hz, 1H), 4.31 (s, 1H), 4.16 (d, J = 17.2 Hz, 1H), 4.07 (d, J = 17.2 Hz, 1H), 3.09 (s, 3H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 168.4, 168.4, 140.7, 128.3, 126.8, 126.7, 122.9, 62.6, 62.3, 46.1 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 10.5 ppm; HRMS (DART-TOF) [M+NH₄]⁺ calcd. For C₁₃H₁₇BN₃O₅ 306.12613, found 306.12679. IR (thin film, cm⁻¹) 2244, 1752, 1453, 1341, 1297, 1252, 1100, 1039, 948, 904, 868, 770, 718, 701.
(MIDA boryl)(p-tolyl)methyl isocyanate (4.3b)

White solid; 57% yield; TLC (EtOAc) R_f = 0.72; ^1H NMR (400 MHz, DMSO-d_6) δ 7.18 (ap. bs, 4H), 4.37 (d, J = 17.2 Hz, 1H), 4.30 (d, J = 17.2 Hz, 1H), 4.24 (s, 1H), 4.15 (d, J = 17.2 Hz, 1H), 4.05 (d, J = 17.2 Hz, 1H), 3.06 (s, 3H), 2.29 (s, 3H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 168.4, 168.4, 137.6, 135.9, 128.9, 126.7, 123.0, 62.6, 62.3, 46.1, 20.6 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 10.3 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{14}H_{19}BN_3O_5 320.14178, found 320.14169; IR (thin film, cm^{-1}) 2242, 1756, 1513, 1455, 1336, 1292, 1102, 1071, 1038, 949, 902, 886, 868, 810, 761, 736.

(MIDA boryl)(4-fluorophenyl)methyl isocyanate (4.3c)

White solid; 62% yield; TLC (EtOAc) R_f = 0.75; ^1H NMR (400 MHz, DMSO-d_6) δ 7.34-7.29 (m, 2H), 7.24-7.18 (m, 2H), 4.39 (d, J = 17.2 Hz, 1H), 4.35 (s, 1H), 4.32 (d, J = 17.2 Hz, 1H), 4.18 (d, J = 17.2 Hz, 1H), 4.08 (d, J = 17.2 Hz, 1H), 3.08 (s, 3H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 168.3(8), 168.3(6), 161.1 (d, ^1J_{CF} = 242.6 Hz), 136.8 (d, ^4J_{CF} = 3.0 Hz), 128.6 (d, ^3J_{CF} = 8.2 Hz), 122.9, 115.1 (d, ^2J_{CF} = 21.4 Hz), 62.7, 62.3, 46.2 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 10.2 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{13}H_{16}BFN_3O_5 324.11670, found 324.11736; IR (thin film, cm^{-1}) 2246, 1756, 1603, 1508, 1465, 1336, 1279, 1218, 1158, 1100, 1071, 1035, 954, 897, 824, 739.

1-(MIDA boryl)-3-phenylpropyl isocyanate (4.3d)

White solid; 92% yield; TLC (EtOAc) R_f = 0.80; ^1H NMR (400 MHz, DMSO-d_6) δ 7.32-7.28 (m, 2H), 7.23-7.17 (m, 3H), 4.34 (d, J = 17.2 Hz, 1H), 4.27 (d, J = 17.2 Hz, 1H), 4.11 (d, J = 17.2 Hz, 1H), 4.04 (d, J = 17.2 Hz, 1H), 3.04 (dd, J = 10.5, 3.2 Hz, 1H), 2.97 (s, 3H), 2.87-2.80 (m, 1H), 2.67-2.56 (m, 1H), 1.94-1.85 (m, 1H), 1.83-1.73 (m, 1H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 168.6, 168.4, 141.2, 128.4, 128.3, 125.8, 121.5, 62.5, 62.3, 45.9, 34.3, 32.8 ppm; ^11B NMR
(128 MHz, DMSO-d$_6$) δ 10.7 ppm; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{15}$H$_{18}$BN$_2$O$_5$ 317.13088, found 317.13060; IR (thin film, cm$^{-1}$) 2254, 1752, 1497, 1454, 1337, 1284, 1245, 1193, 1111, 1032, 990, 952, 897, 861, 820, 725, 700.

1-(MIDA boryl)-2-phenylethyl isocyanate (4.3e)

![Structural formula]

White solid; 84% yield; TLC (EtOAc) R$_f$ = 0.56; $^1$H NMR (400 MHz, MeCN-d$_3$) δ 7.38-7.32 (m, 4H), 7.29-7.25 (m, 1H), 4.06 (d, $J$ = 17.2 Hz, 1H), 4.05 (d, $J$ = 17.0 Hz, 1H), 3.95 (d, $J$ = 17.0 Hz, 1H), 3.91 (d, $J$ = 17.2 Hz, 1H), 3.37 (dd, $J$ = 12.0, 2.8 Hz, 1H), 3.11 (dd, $J$ = 14.2, 2.8 Hz, 1H), 3.02 (s, 3H), 2.77 (dd, $J$ = 14.2, 12.0 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, MeCN-d$_3$) δ 169.1, 168.7, 140.6, 130.2, 129.5, 127.7, 118.4, 63.7, 63.4, 47.0, 39.4 ppm; $^{11}$B NMR (128 MHz, MeCN-d$_3$) δ 10.6 ppm; HRMS (DART-TOF) [M+NH$_4^+$]$^+$ calcd. For C$_{14}$H$_{19}$BN$_3$O$_5$ 320.14178, found 320.14186; IR (thin film, cm$^{-1}$) 3065, 3027, 2953, 2904, 2257, 2170, 1773, 1741, 1709, 1590, 1511, 1489, 1455, 1448, 1426, 1343, 1327, 1294, 1252, 1237, 1200, 1183, 1161, 1117, 1072, 1041, 1010, 991, 960, 944, 904, 873, 822, 781, 754, 739, 724, 695.

3-methyl-1-(MIDA boryl)butyl isocyanate (4.3f)

![Structural formula]

White solid; 71% yield; TLC (EtOAc) R$_f$ = 0.55; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 4.34 (d, $J$ = 17.2 Hz, 1H), 4.25 (d, $J$ = 17.2 Hz, 1H), 4.09 (d, $J$ = 17.2 Hz, 1H), 4.04 (d, $J$ = 17.2 Hz, 1H), 3.09 (dd, $J$ = 11.8, 2.9 Hz, 1H), 2.99 (s, 3H), 1.79-1.69 (m, 1H), 1.53 (ddd, $J$ = 14.0, 11.8, 3.8 Hz, 1H), 1.28 (ddd, $J$ = 14.0, 10.3, 2.9 Hz, 1H), 0.95 (d, $J$ = 6.6 Hz, 3H), 0.90 (d, $J$ = 6.6 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 168.7, 168.4, 121.4, 62.5, 62.3, 45.9, 41.0, 24.8, 23.4, 20.6 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 10.7 ppm; HRMS (DART-TOF) [M+NH$_4^+$]$^+$ calcd. For C$_{11}$H$_{21}$BN$_3$O$_5$ 286.15743, found 286.15807; IR (thin film, cm$^{-1}$) 3016, 2961, 2873, 2266, 2139,
1-(MIDA boryl)pentyl isocyanate (4.3g)

White solid; 86% yield; TLC (EtOAc) Rf = 0.60; \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 4.34 (d, \(J = 17.2\) Hz, 1H), 4.26 (d, \(J = 17.2\) Hz, 1H), 4.09 (d, \(J = 17.2\) Hz, 1H), 4.04 (d, \(J = 17.2\) Hz, 1H), 3.03 (dd, \(J = 10.0, 3.2\) Hz, 1H), 2.98 (s, 3H), 1.68-1.56 (m, 1H), 1.56-1.42 (m, 2H), 1.40-1.25 (m, 3H), 0.90 (t, \(J = 6.9\) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 168.7, 168.5, 121.5, 62.4, 62.2, 45.9, 31.8, 28.8, 21.7, 13.9 ppm; \(^{11}\)B NMR (128 MHz, DMSO-d\(_6\)) \(\delta\) 10.6 ppm; HRMS (DART-TOF) [M+NH\(_4\)]\(^{+}\) calcd. For C\(_{11}\)H\(_{21}\)BN\(_3\)O\(_5\) 285.15743, found 286.15789; IR (thin film, cm\(^{-1}\)) 2959, 2261, 1742, 1465, 1339, 1294, 1230, 1160, 1141, 1099, 1069, 1045, 1026, 990, 954, 900, 861, 726.

Cyclohexyl(MIDA boryl)methyl isocyanate (4.3h)

White solid; 69% yield; TLC (EtOAc) Rf = 0.39; \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 4.29 (d, \(J = 17.2\) Hz, 1H), 4.25 (d, \(J = 17.1\) Hz, 1H), 4.05 (d, \(J = 17.2\) Hz, 1H), 4.03 (d, \(J = 17.1\) Hz, 1H), 2.96 (s, 3H), 1.76-1.73 (m, 3H), 1.64-1.56 (m, 4H), 1.30-1.17 (m, 3H), 1.29-1.00 (m, 2H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 168.6(3), 168.6(0), 121.0, 62.0, 61.8, 45.9, 39.9, 31.4, 27.8, 26.1, 25.7(5), 25.7(2) ppm; \(^{11}\)B NMR (128 MHz, DMSO-d\(_6\)) \(\delta\) 10.6 ppm; HRMS (DART-TOF) [M+NH\(_4\)]\(^{+}\) calcd. For C\(_{13}\)H\(_{23}\)BN\(_3\)O\(_5\) 312.17308, found 312.17444; IR (thin film, cm\(^{-1}\)) 2925, 2852, 2261, 1749, 1449, 1338, 1292, 1233, 1109, 1030, 969, 894, 862, 818, 729.
4.5.3 Stereochemical investigation for α-boroalkyl migration

Preparation of PIDA-derived α-boryl aldehydes

The phenyl-substituted α-(PIDA)boryl aldehyde A is known compound and was prepared according to literature procedures via diastereoselective epoxidation of the vinyl PIDA boronate followed by a Mg(ClO₄)₂-promoted stereospecific rearrangement of the epoxide.

The phenylethyl-substituted α-(PIDA)boryl aldehyde B was prepared using the same sequence of transformations: epoxidation and rearrangement. However, BF₃·Et₂O was used as the Lewis acid promoter for the epoxide rearrangement step.

Although Mg(ClO₄)₂ worked well in the rearrangement of phenyl-substituted oxiranyl boronate to the corresponding aldehyde A, it did not work for the preparation of alkyl-substituted substrate B. Only trace of conversion was observed when the alkyl-substituted epoxide was treated with 1 equiv of Mg(ClO₄)₂ at room temperature for 24 hr. Therefore, stronger Lewis acid BF₃·Et₂O has to be applied.

Experimental procedures for the synthesis of α-(PIDA)boryl aldehyde B:

To a solution of (E)-(4-phenylbut-1-en-1-yl)boronic acid (1.52g, 8.635 mmol, 1.0 equiv) in toluene/DMSO (50 ml/5 mL) was added PIDA (2.33g, 8.635 mmol, 1.0 equiv). The flask was fitted with a Dean-Stark trap and an air-cooled condenser vented to ambient atmosphere. The stirred solution was refluxed with azeotropic removal of water for 2 h. After cooling to room temperature, the reaction solution was diluted with EtOAc (50 mL), and then washed with water.
(20 mL×2) and brine (20 mL). The organic phase was concentrated to dryness, obtained the crude vinyl PIDA boronate intermediate, which was directly subjected to the next step.

To a solution of the above crude vinyl PIDA boronate in 100 mL DCM was added mCPBA (4.4 g, 20 mmol, 2.5 equiv) at 0 °C. The mixture was warmed to room temperature and stirred for 24 hours until the reaction was complete as indicated by TLC. The reaction solution was then washed with saturated aqueous NaHCO$_3$ (30 mL) and brine (30 mL). The organic layer was then separated and concentrated to dryness. The residue was washed with 150 mL Et$_2$O and filtered. The solid crude product further purified using flash column chromatography on silica gel (Hexanes/EtOAc 8:2 → Hexanes/EtOAc 1:1 → EtOAc) to afford pure oxiranyl PIDA boronate intermediate as a white solid (1.47 g).

To a flame dried flask equipped with a magnetic stirring bar and a rubber septum was added the above oxiranyl PIDA boronate (1.35 g, 3.17 mmol, 1.0 equiv) in 40 mL anhydrous DCM. The solution was cooled to –30 °C. BF$_3$·Et$_2$O (0.39 mL, 3.17 mmol) was added dropwise with stirring. The mixture was then stirred at –30 to 5 °C over 1 hour. The reaction was quenched by adding 20 mL saturated aqueous NaHCO$_3$. The organic layer was then separated; the aqueous layer was extracted with EtOAc (5 mL × 2). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated to dryness. $^1$H NMR analysis of the crude residue indicated exclusive formation of one diastereoisomer of the desired α-boryl aldehyde product (d.r. > 95:5). The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 8:2 → Hexanes/EtOAc 1:1 → EtOAc) to afford pure product B as a white solid (0.64 g).

2-(PIDA boryl)-4-phenylbutanal (B)

White solid; 50% yield; TLC (EtOAc/Hexanes 1:1) R$_f$ = 0.48; $^1$H NMR (400 MHz, acetone-$d_6$) δ 9.77 (d, $J$ = 3.7 Hz, 1H), 7.31-7.23 (m, 4H), 7.20-7.16 (m, 1H), 4.35 (dt, $J$ = 10.4, 6.3 Hz, 1H), 4.27 (d, $J$ = 18.1 Hz, 1H), 4.12 (d, $J$ = 15.5 Hz, 1H), 4.03 (d, $J$ = 18.1 Hz, 1H), 3.89 (d, $J$ = 15.5 Hz, 1H), 2.86-2.79 (m, 1H), 2.69-2.62 (m, 1H), 2.52-2.31 (m, 4H), 2.30-2.21 (m, 1H), 2.17-2.08 (m, 1H), 1.98-
1.91 (m, 2H), 1.54 (ddd, \( J = 14.6, 6.2, 2.4 \text{ Hz}, 1H \)), 1.36 (d, \( J = 6.9 \text{ Hz}, 3H \)), 1.26 (s, 3H), 1.06 (d, \( J = 10.9 \text{ Hz}, 1H \)), 1.00 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 211.1, 169.7, 166.8, 142.5, 129.5, 129.2, 126.7, 67.8, 61.7, 56.3, 50.1, 41.6, 39.6, 39.0, 36.4, 32.0, 30.8, 28.7, 27.4, 23.6 ppm; \(^{11}\)B NMR (128 MHz, CDCl\(_3\)) \( \delta \) 11.5 ppm; HRMS (DART-TOF) [M+NH\(_4\)]\(^+\) calcd. For C\(_{24}\)H\(_{36}\)BN\(_2\)O\(_5\) 443.27173, found 443.27237; IR (thin film, cm\(^{-1}\)) 2931, 1760, 1743, 1696, 1454, 1439, 1334, 1290, 1242, 1224, 1093, 1075, 1022, 1001, 968, 955, 926, 905, 860, 743, 697.

**Preparation of PIDA-derived \( \alpha \)-borylcarboxylic acids:**

![Chemical reaction diagram](image)

Compound 4.4a and 4.4b were prepared using the same general procedure for \( \alpha \)-borylcarboxylic acid (chapter 3).

However, it was found that the PIDA \( \alpha \)-borylcarboxylic acids 4.4a and 4.4b were not stable under the NaClO\(_2\)/NaH\(_2\)PO\(_4\) oxidation condition. Prolonged reaction time (> 1 hr) resulted in significant decomposition of the acid products. It is necessary to ground the solid starting aldehydes to fine powder to make the reaction more efficient and thus shorten the reaction time (within 30 min for full conversion) to decrease the product decomposition.

Experimental procedure for the synthesis of 4.4a and 4.4b:

To a suspension of fine powder \( \alpha \)-boryl aldehyde A or B (0.8 mmol, 1.0 equiv) in 6 mL \( t \)-BuOH, was added cyclohexene (2.4 mmol, 3.0 equiv). A solution of NaClO\(_2\) (0.96 mmol, 1.2 equiv) and NaH\(_2\)PO\(_4\) (0.96 mmol, 1.2 equiv) in 6 mL H\(_2\)O was added dropwise at room temperature. The mixture was vigorously stirred at room temperature for 30 min hours until the reaction was complete as indicated by TLC. The reaction solution was then diluted with 10 mL brine, and...
extracted EtOAc (5 mL×3). The combined organic layers were concentrated to remove solvents, obtained the crude products as white solid. **Crude $^1$H NMR analysis indicated the maintenance of the stereochemical purity of the α-boryl acid products 3a or 3b (d.r. > 95:5).** The crude products were subjected to silica gel flash column chromatography purification (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeCN 90:10). However, the isolated α-boryl acid products were still contaminated with unidentified impurities and only low isolated yields were obtained, probably due to decomposition on silica gel chromatography. Although the desired compounds are difficult to obtain analytically pure, the $^1$H NMR spectra data are consistent with the assigned structures. The isolated materials were directly subjected to the next step transformation without further purification.

**2-(PIDA boryl)-2-phenylacetic acid (4.4a)**

White solid (foam); 21% yield; TLC (EtOAc/Hexanes 1:1) $R_f = 0.08$; $^1$H NMR (400 MHz, acetone-d$_6$) $\delta$ 7.62-7.60 (m, 2H), 7.37-7.32 (m, 2H), 7.31-7.26 (m, 1H), 4.26 (d, $J = 17.9$ Hz, 1H), 4.00 (d, $J = 17.9$ Hz, 1H), 3.96 (d, $J = 15.3$ Hz, 1H), 3.79 (dt, $J = 10.5$, 6.1 Hz, 1H), 3.71 (s, 1H), 2.99 (d, $J = 15.3$ Hz, 1H), 2.70 (dddd, $J = 14.4$, 10.4, 3.1, 2.2 Hz, 1H), 2.44 (dt, $J = 11.1$, 6.1, 2.3 Hz, 1H), 2.36 (qddd, $J = 6.9$, 6.7, 2.3 Hz, 1H), 1.88 (td, $J = 6.1$, 2.3 Hz, 1H), 1.77 (ddd, $J = 14.9$, 6.1, 2.8 Hz, 1H), 1.26 (s, 3H), 1.07 (d, $J = 11.1$ Hz, 1H), 1.02 (s, 3H), 1.01 (d, $J = 6.9$ Hz, 3H)
2-(PIDA boryl)-4-phenylbutanoic acid (4.4b)

White solid (foam); 22% yield; TLC (EtOAc/Hexanes 8:2) \( R_f = 0.25; \) \(^1\)H NMR (400 MHz, MeCN-d\(_3\)) \( \delta \) 7.31-7.24 (m, 2H), 7.23-7.17 (m, 3H), 4.23 (dt, \( J = 10.4, 6.4 \) Hz, 1H), 4.12 (d, \( J = 18.0 \) Hz, 1H), 3.93 (d, \( J = 15.5 \) Hz, 1H), 3.88 (d, \( J = 15.5 \) Hz, 1H), 3.77 (d, \( J = 18.0 \) Hz, 1H), 2.82-2.75 (m, 1H), 2.65-2.56 (m, 1H), 2.40-2.34 (m, 1H), 2.30-2.07 (m, 4H), 1.88-1.84 (m, 3H), 1.41 (ddd, \( J = 13.8, 6.3, 2.0 \) Hz, 1H), 1.23 (d, \( J = 6.9 \) Hz, 3H), 1.22 (s, 3H), 0.91 (d, \( J = 10.9 \) Hz, 1H), 0.90 (s, 3H)

Curtius rearrangement of PIDA-derived \( \alpha \)-borylcarboxylic acids 4.4a and 4.4b: 

4.4a: \( R = \text{Ph} \) (d.r. > 95:5)  
4.4b: \( R = \text{CH}_2\text{CH}_2\text{Ph} \) (d.r. > 95:5)  
4.5a: \( R = \text{Ph} \) (d.r. = 85:15)  
4.5b: \( R = \text{CH}_2\text{CH}_2\text{Ph} \) (d.r. > 95:5)
The α-(PIDA)borylcarboxylic acid 4.4a and 4.4b were subjected to the same general Curtius rearrangement conditions for α-borylcarboxylic acids 4.3. The stereochemical outcomes were monitored by $^1$H NMR analysis of the crude reaction mixture.

Experimental procedures:

To a solution of a-boryl carboxylic acid 4.4a or 4.4b (0.1 mmol) in 1 mL anhydrous MeCN was added Et$_3$N (0.12 mmol, 1.2 equiv) and DPPA (0.12 mmol, 1,2 equiv) subsequently. The resulting solution was stirred at room temperature under N$_2$ for 15 min, and then heated at 50 °C for 1.5 hours. The reaction mixture was cooled to room temperature, evaporated under reduced pressure to remove the solvent. $^1$H NMR analysis of the crude residue indicated that isocyanate 4.5a was generated with erosion of stereochemical purity (d.r. = 85:15), whereas 4.5b was produced with complete retention of stereo-chemistry (d.r. > 95:5). The crude residue could be further purified using flash column chromatography on silica gel (Hexanes/EtOAc 80:20 → Hexanes/EtOAc 50:50 → EtOAc). However, the isolated α-boryl acid products were still contaminated with unidentified impurities and only low isolated yields were obtained, probably due to decomposition on silica gel chromatography. Although the desired compounds are difficult to obtain analytically pure, the $^1$H NMR spectra data are consistent with the assigned structures.

(PIDA boryl)(phenyl)methyl isocyanate (4.5a)

Yellowish solid (foam); 47% yield; TLC (EtOAc/Hexanes 1:1) $R_f$ = 0.40 (major diastereomer); $^1$H NMR (400 MHz, MeCN-d$_3$) $\delta$ 7.42-7.40 (m, 4H), 7.37-7.35 (m, 1H), 4.41 (s, 1H), 4.19 (d, $J$ = 17.7 Hz, 1H), 3.85 (d, $J$ = 17.7 Hz, 1H), 3.83 (d, $J$ = 15.9 Hz, 1H), 3.69 (dt, $J$ = 10.5, 6.3 Hz, 1H), 3.17 (d, $J$ = 15.9 Hz, 1H), 2.54 (dddd, $J$ = 14.6, 10.4, 3.3, 2.3 Hz, 1H), 2.40 (dt, $J$ = 11.2, 6.1, 2.2 Hz, 1H), 2.15 (qdd, $J$ = 7.0, 6.7, 2.3 Hz, 1H), 2.02-1.97 (m, 1H), 1.84 (td, $J$ = 6.1, 2.3 Hz,
1H), 1.69 (ddd, \( J = 14.8, 6.2, 2.7 \) Hz, 1H), 1.23 (s, 3H), 1.02 (d, \( J = 7.0 \) Hz, 3H), 0.95 (s, 3H), 0.94 (d, \( J = 10.5 \) Hz, 1H)

1-\((\text{PIDA boryl})\)-3-phenylpropyl isocyanate (4.5b)

Thick oil; 18% yield; TLC (EtOAc/Hexanes 1:1) \( R_f = 0.40 \); \(^1\)H NMR (400 MHz, MeCN-\( d_3 \)) \( \delta 7.33-7.18 \) (m, 5H), 4.15 (d, \( J = 18.0 \) Hz, 1H), 4.10 (d, \( J = 15.7 \) Hz, 1H), 4.02-3.98 (m, 1H), 3.99 (d, \( J = 18.0 \) Hz, 1H), 3.82 (d, \( J = 15.7 \) Hz, 1H), 3.13 (dd, \( J = 9.9, 3.9 \) Hz, 1H), 2.95-2.88 (m, 1H), 2.77-2.69 (m, 1H), 2.38 (dt, \( J = 11.1, 6.1, 2.2 \) Hz, 1H), 2.31-2.26 (m, 2H), 2.01-1.93 (m, 2H), 1.91-1.88 (m, 2H), 1.48 (ddd, \( J = 14.5, 6.0, 2.0 \) Hz, 1H), 1.29 (d, \( J = 6.9 \) Hz, 3H), 1.23 (s, 3H), 0.95 (s, 3H), 0.93 (d, \( J = 10.6 \) Hz, 1H)
4.5.4 General procedure for synthesis of α-boryl ureas

In a vial equipped with stirring-bar and a screw-cap lid was dissolved α-boryl isocyanate (0.30 mmol, 1.0 equiv) in 2 mL THF. Amine (0.36 mmol, 1.2 equiv) was added and the reaction mixture was stirred at the room temperature for 1-5 hours until the reaction was complete by TLC. The resulting cloudy mixture was concentrated to remove the solvent by reduced pressure, obtained desired product as a white solid. The crude product was subjected to purification by flash column chromatography on silica gel to obtain pure product.
1-ethyl-3-((MIDA boryl)(phenyl)methyl)urea (4.7a)

White solid; 93% yield; TLC (EtOAc) $R_f = 0.20$; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.25-7.09 (m, 5H), 6.05 (d, $J = 9.7$ Hz, 1H), 6.02 (t, $J = 5.5$ Hz, 1H), 4.34 (d, $J = 9.7$ Hz, 1H), 4.26 (d, $J = 17.1$ Hz, 1H), 4.25 (d, $J = 16.9$ Hz, 1H), 4.15 (d, $J = 17.1$ Hz, 1H), 3.89 (d, $J = 16.9$ Hz, 1H), 2.98 (s, 3H), 2.97-2.91 (m, 2H), 0.94 (t, $J = 7.2$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 168.8, 168.5, 158.0, 144.6, 127.4, 126.9, 125.0, 62.3, 62.3, 45.7, 34.1, 15.5 ppm; $^{11}$B NMR (128 MHz, DMSO-$d_6$) δ 11.5 ppm; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{15}$H$_{21}$BN$_3$O$_5$ 334.15743, found 334.15849; IR (thin film, cm$^{-1}$) 3374, 2967, 1748, 1634, 1547, 1494, 1451, 1338, 1282, 1244, 1107, 1075, 1028, 991, 950, 895, 878, 802, 703

1-isopropyl-3-((MIDA boryl)(phenyl)methyl)urea (4.7b)

White solid; 95% yield; TLC (EtOAc) $R_f = 0.22$; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.25-7.21 (m, 2H), 7.17-7.08 (m, 3H), 6.00 (d, $J = 9.6$ Hz, 1H), 5.95 (d, $J = 7.6$ Hz, 1H), 4.33 (d, $J = 9.6$ Hz, 1H), 4.26 (d, $J = 17.0$ Hz, 1H), 4.25 (d, $J = 17.1$ Hz, 1H), 4.16 (d, $J = 17.1$ Hz, 1H), 3.88 (d, $J = 17.0$ Hz, 1H), 3.60-3.52 (m, 1H), 2.98 (s, 3H), 0.99 (d, $J = 6.5$ Hz, 3H), 0.96 (d, $J = 6.5$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 168.8, 168.4, 157.5, 144.6, 127.4, 126.9, 125.0, 62.4, 62.3, 45.6, 40.9, 23.3, 23.2 ppm; $^{11}$B NMR (128 MHz, DMSO-$d_6$) δ 11.7 ppm; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{16}$H$_{23}$BN$_3$O$_5$ 348.17308, found 348.17306; IR (thin film, cm$^{-1}$) 3405, 2965, 1747, 1639, 1539, 1495, 1451, 1338, 1282, 1239, 1152, 1099, 1028, 950, 896, 817, 704

1-(tert-butyl)-3-(1-(MIDA boryl)-3-phenylpropyl)urea (4.7c)

White solid; 87% yield; TLC (EtOAc) $R_f = 0.25$; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.28-7.23 (m, 2H), 7.18-7.13 (m, 3H), 5.32 (bs, 1H), 4.24 (d, $J = 17.1$ Hz, 1H), 4.20 (d, $J = 16.7$ Hz, 1H), 4.04 (d, $J = 17.1$ Hz, 1H), 3.75 (d, $J = 16.7$ Hz, 1H), 3.26 (ap, d, $J = 6.3$ Hz, 1H), 2.89 (s, 3H), 2.64-2.55 (m, 1H), 2.52-2.45 (m, 1H), 1.76-1.67 (m, 1H), 1.51-1.41 (m, 1H), 1.22 (s, 9H)
ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 168.8, 168.7, 158.3, 143.1, 128.2, 128.2, 125.4, 62.2, 62.1, 49.1, 45.4, 35.1, 32.5, 29.3 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 11.5 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{19}$H$_{29}$BN$_3$O$_5$ 390.2200, found 390.2202; IR (thin film, cm$^{-1}$) 3381, 2963, 1762, 1747, 1644, 1549, 1497, 1453, 1337, 1285, 1216, 1110, 993, 952, 896, 862, 749, 699 ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.7, 167.6, 157.6, 142.6, 128.6, 128.5, 125.9, 62.8, 62.2, 46.0, 41.6, 34.3, 33.4, 14.2 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 12.3 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{19}$H$_{29}$BN$_3$O$_5$ 390.2200, found 390.2181; IR (thin film, cm$^{-1}$) 3382, 2979, 2933, 1770, 1740, 1617, 1521, 1521, 1496, 1455, 1401, 1334, 1293, 1247, 1198, 1122, 1080, 1061, 1017, 1000, 955, 897, 856, 757, 702

$^{1,1}$diethyl-3-(1-(MIDA boryl)-3-phenylpropyl)urea (4.7d)

![Image of 1,1-diethyl-3-(1-(MIDA boryl)-3-phenylpropyl)urea (4.7d)](image)

White solid; 77% yield; TLC (EtOAc/MeOH 9:1) R$_f$ = 0.40; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.27-7.23 (m, 2H), 7.19-7.12 (m, 3H), 5.07 (d, $J$ = 9.1 Hz, 1H), 4.24 (d, $J$ = 17.2 Hz, 1H), 4.17 (d, $J$ = 16.8 Hz, 1H), 4.01 (d, $J$ = 17.2 Hz, 1H), 3.70 (d, $J$ = 16.8 Hz, 1H), 3.50-3.44 (m, 1H), 3.30-3.23 (m, 2H), 3.20-3.11 (m, 2H), 2.92 (s, 3H), 2.64-2.56 (m, 1H), 2.46-2.38 (m, 1H), 1.74-1.68 (m, 2H), 1.01 (t, $J$ = 7.0 Hz, 6H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 167.7, 167.6, 157.6, 142.6, 128.6, 128.5, 125.9, 62.8, 62.2, 46.0, 41.6, 34.3, 33.4, 14.2 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 12.3 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{19}$H$_{29}$BN$_3$O$_5$ 390.2200, found 390.2181; IR (thin film, cm$^{-1}$) 3382, 2979, 2933, 1770, 1740, 1617, 1521, 1496, 1455, 1401, 1334, 1293, 1247, 1198, 1122, 1080, 1061, 1017, 1000, 955, 897, 856, 757, 702

$^{1,1}$diethyl-3-(1-(MIDA boryl)-3-phenylpropyl)urea (4.7d)

![Image of 1,1-diethyl-3-(1-(MIDA boryl)-3-phenylpropyl)urea (4.7d)](image)

White solid; 30% yield; TLC (EtOAc) R$_f$ = 0.45; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 8.55 (s, 1H), 7.38 (d, $J$ = 7.7 Hz, 2H), 7.31-7.13 (m, 7H), 6.87 (ap. t, $J$ = 7.2 Hz, 1H), 5.83 (d, $J$ = 9.6 Hz, 1H), 4.26 (d, $J$ = 17.1 Hz, 1H), 4.24 (d, $J$ = 17.1 Hz, 1H), 4.10 (d, $J$ = 17.1 Hz, 1H), 3.90 (d, $J$ = 17.1 Hz, 1H), 3.46-3.40 (m, 1H), 2.91 (s, 3H), 2.69-2.60 (m, 1H), 2.60-2.51 (m, 1H), 1.85-1.75 (m, 1H), 1.61-1.51 (m, 1H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 168.9, 168.7, 155.6, 142.8, 140.7, 128.6, 128.2, 128.1, 125.5, 120.7, 117.2, 62.1(8), 62.1(7), 45.6, 34.9, 32.5 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 11.4 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{21}$H$_{25}$BN$_3$O$_5$ 410.1881, found 410.1880; IR (thin film, cm$^{-1}$) 3382, 2943, 1762, 1745, 1646, 1597, 1540, 1497, 1440, 1292, 1230, 1119, 1075, 1046, 1029, 991, 952, 895, 861, 749, 694. 
4.5.5 General procedure for synthesis of α-boryl carbamates

In a vial equipped with stirring-bar and a screw-cap lid was dissolved α-boryl isocyanate (0.30 mmol, 1.0 equiv) in 2 mL anhydrous DMF. Alcohol (0.90 mmol, 3.0 equiv) and CuCl (0.30 mmol, 1.0 equiv.) were added subsequently and the reaction mixture was stirred at the room temperature for 3 hours until the reaction was complete by TLC or crude $^1$H NMR. The resulting green mixture was diluted with 10 mL EtOAc, filtered off the CuCl suspension. The filtrate was washed with water (3 mL×2) and brine (3 mL). The organic layers were concentrated to remove solvents. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeCN 90:10) to afford the pure product.

Note: For the preparation of compound 7c, 10.0 equiv of tert-BuOH was used. The reaction was carried out at 70 °C for 24 hours.

2-(trimethylsilyl)ethyl ((MIDA boryl)(phenyl)methyl)carbamate (4.8a)

White solid; 75% yield; TLC (EtOAc) $R_f = 0.55$; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.25-7.19 (m, 5H), 7.13-7.09 (m, 1H), 4.24 (d, $J = 17.1$ Hz, 1H), 4.22 (d, $J = 17.1$ Hz, 2H), 4.19 (s, 1H), 3.97 (t, $J = 7.3$ Hz, 2H), 3.85 (d, $J = 17.1$ Hz, 1H), 2.99 (s, 3H), 0.88 (t, $J = 7.3$ Hz, 2H), -0.01 (s, 9H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 168.9, 168.2, 156.6, 143.8, 127.4, 127.1, 125.2, 62.6, 62.5, 61.5, 45.9, 17.4, -1.5 ppm; $^{11}$B NMR (128 MHz, DMSO-$d_6$) δ 10.2 ppm; HRMS (DART-TOF) [M+NH$_4^+$] calcd. For C$_{18}$H$_{31}$BN$_3$O$_6$Si 424.20752, found 424.20952; IR (thin film, cm$^{-1}$) 2958, 1760, 1696, 1496, 1337, 1284, 1246, 1136, 1102, 1074, 1031, 1003, 952, 896, 858, 834, 702.
(9H-fluoren-9-yl)methyl (1-(MIDA boryl)pentyl)carbamate (4.8b)

White solid; 80% yield; TLC (EtOAc) Rf = 0.70; 1H NMR (400 MHz, DMSO-d6) δ 7.88 (d, J = 7.4 Hz, 2H), 7.72 (dd, J = 7.1, 3.9 Hz, 2H), 7.41 (dd, J = 7.4, 7.1 Hz, 2H), 7.31 (dd, J = 11.1, 7.1 Hz, 2H), 6.73 (d, J = 9.4 Hz, 1H), 4.29-4.15 (m, 5H), 4.04 (d, J = 17.3 Hz, 1H), 3.67 (d, J = 16.8 Hz, 1H), 3.09 (ddd, J = 11.3, 9.4, 2.5 Hz, 1H), 2.85 (s, 3H), 1.54-1.41 (m, 1H), 1.40-1.18 (m, 5H), 0.83 (t, J = 5.8 Hz, 3H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 168.7, 168.6, 156.8, 143.9(5), 143.9(1), 140.7(0), 140.6(8), 127.6, 127.0, 125.3, 125.2, 120.0(3), 120.0(1), 65.1, 62.2, 46.9, 45.5, 30.9, 28.4, 22.2, 14.0. 11B NMR (128 MHz, DMSO-d6) δ 11.6 ppm; HRMS (DART-TOF) [M+H]+ calcd. For C25H30BN2O6 465.21969, found 465.22061; IR (thin film, cm⁻¹) 2955, 1761, 1695, 1515, 1450, 1335, 1293, 1234, 1161, 1101, 1080, 1023, 990, 896, 856, 759, 739.

tert-butyl (1-(MIDA boryl)pentyl)carbamate (4.8c)

White solid; 60% yield; TLC (EtOAc) Rf = 0.50; 1H NMR (400 MHz, acetone-d6) δ 5.20 (d, J = 10.5 Hz, 1H), 4.22 (d, J = 17.0 Hz, 1H), 4.20 (d, J = 16.7 Hz, 1H), 4.12 (d, J = 17.0 Hz, 1H), 3.89 (d, J = 16.7 Hz, 1H), 3.24 (ddd, J = 10.5, 9.8, 3.5 Hz, 1H), 3.15 (s, 3H), 1.65-1.56 (m, 1H), 1.39 (s, 9H), 1.47-1.23 (m, 5H), 0.89 (t, J = 6.9 Hz, 3H) ppm; 13C NMR (100 MHz, acetone-d6) δ 168.8, 168.7, 157.5, 78.5, 63.3, 63.2, 46.3, 32.6, 29.6, 28.7, 23.4, 14.6 ppm; 11B NMR (128 MHz, DMSO-d6) δ 11.5 ppm; HRMS (DART-TOF) [M+H]+ calcd. For C15H30BN2O6 343.20404, found 343.20510; IR (thin film, cm⁻¹) 2959, 1763, 1688, 1503, 1457, 1365, 1336, 1296, 1243, 1165, 1101, 1079, 1023, 991, 947, 896, 863, 731.
allyl ((MIDA boryl)(phenyl)methyl)carbamate (4.8d)

White solid; 67% yield; TLC (EtOAc) Rf = 0.45; 1H NMR (400 MHz, DMSO-d6) δ 7.46 (d, J = 8.6 Hz, 1H), 7.27-7.20 (m, 4H), 7.14-7.10 (m, 1H), 5.92-5.82 (m, 1H), 5.26 (dd, J = 17.3, 1.5 Hz, 1H), 5.13 (dd, J = 10.6, 1.5 Hz, 1H), 4.46-4.37 (m, 2H), 4.25 (d, J = 17.1 Hz, 1H), 4.23 (d, J = 17.1 Hz, 2H), 4.20 (s, 1H), 3.87 (d, J = 17.1, 1H), 3.00 ppm; 13C NMR (100 MHz, DMSO-d6) δ 168.9, 168.2, 156.2, 143.6, 133.8, 127.5, 127.1, 125.3, 116.6, 64.2, 62.7, 62.5, 45.9 ppm; 11B NMR (128 MHz, DMSO-d6) δ 11.1 ppm; HRMS (ESI) [M+H]+ calcd. For C16H20BN2O6 347.1414, found 347.1418; IR (thin film, cm⁻¹) 3423, 3372, 1753, 1700, 1524, 1496, 1452, 1342, 1299, 1239, 1146, 1101, 1072, 1046, 1022, 992, 945, 882, 817, 804, 746, 710

benzyl (1-(MIDA boryl)-3-phenylpropyl)carbamate (4.8e)

White solid; 90% yield; TLC (EtOAc) Rf = 0.55; 1H NMR (400 MHz, CDCl3) δ 7.36-7.31 (m, 5H), 7.27-7.23 (m, 2H), 7.17-7.14 (m, 3H), 5.10 (d, J = 12.2 Hz, 1H), 5.06 (d, J = 12.2 Hz, 1H), 4.68 (d, J = 10.3 Hz, 1H), 3.76 (d, J = 16.5 Hz, 1H), 3.72 (d, J = 16.1 Hz, 1H), 3.67 (d, J = 16.5 Hz, 1H), 3.52 (d, J = 16.1 Hz, 1H), 3.33 (ddd, J = 10.3, 10.1, 3.3 Hz, 1H), 2.91 (s, 3H), 2.77-2.69 (m, 1H), 2.62-2.54 (m, 1H), 2.07-1.99 (m, 1H), 1.80-1.70 (m, 1H) ppm; 13C NMR (100 MHz, CDCl3) δ 167.9, 167.7, 157.3, 142.2, 136.9, 128.7, 128.6, 128.5, 128.4, 128.2, 126.0, 67.0, 62.7, 62.3, 46.0, 33.9, 32.9 ppm; 11B NMR (128 MHz, DMSO-d6) δ 12.6 ppm; HRMS (ESI) [M+H]+ calcd. For C22H36BN2O6 425.1884, found 425.1894; IR (thin film, cm⁻¹) 3328, 3030, 2947, 1761, 1694, 1517, 1497, 1454, 1335, 1291, 1234, 1124, 1076, 1017, 954, 896, 859, 741, 697.
4.5.6 Chemoselective release of free boronic acids or amino groups from α-boryl urea and α-boryl carbamate

Synthesis of α-ureido boronic acid 4.9

In a vial equipped with stirring-bar and a screw-cap lid was dissolved α-boryl ureas 4.7c (87 mg, 0.225 mmol, 1.0 equiv) in 3 mL THF. 1.0 M NaOH (0.676 mL, 3.0 equiv) was added dropwise and the reaction mixture was stirred at the room temperature for 15 min. The reaction was then quenched with saturated NH₄Cl solution (3 mL). 3 mL Et₂O was added, extracted and separated. The aqueous layer was further extracted with mixed solvent E₂O/THF (1:1) (3 mL×2). The organic phase was combined and concentrated to dryness under reduced pressure, obtained the desired free boronic acid product 55.8 mg as a white solid powder.

(1-(3-(tert-butyl)ureido)-3-phenylpropyl)boronic acid (4.9)

White solid; 90% yield; ¹H NMR (400 MHz, DMSO-d₆) δ 7.19-7.15 (m, 2H), 7.10-7.06 (m, 3H), 6.49 (bs, 1H), 6.16 (bs, 1H), 2.57-2.50 (m, 2H), 2.45-2.39 (m, 1H), 1.80-1.69 (m, 1H), 1.63-1.53 (m, 1H), 1.21 (s, 9H) ppm; ¹³C NMR (100 MHz, DMSO-d₆) δ 160.7, 143.4, 128.1, 127.9, 125.1, 50.0, 33.3, 30.4, 29.2 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 16.7 ppm; HRMS (DART-TOF) [(M+H)-H₂O]⁺ calcd. For C₁₄H₂₃BN₂O₂ 261.17743, found 261.17655; IR (thin film, cm⁻¹) 3369, 2964, 2931, 1627, 1595, 1526, 1496, 1453, 1387, 1365, 1316, 1192, 1098, 811, 747, 697.
Preparation of α-amino boronate 4.10

To a solution of carbamate 4.8d (0.664 g, 1.92 mmol, 1.0 equiv) in DCM/MeOH (2:1) (60 mL, pre-degassed with N₂) was added 1,3-dimethylbarbituric acid (0.599 g, 3.84 mmol, 2.0 equiv) and Pd(PPh₃)₄ (44 mg, 0.0384 mmol, 0.02 equiv) subsequently. The reaction was stirred at room temperature under N₂ for 1 hour until the reaction was complete by TLC. The reaction mixture was concentrated to remove solvent. The residue was diluted with EtOAc (100 mL) and quickly washed with sat. Na₂CO₃ (25 mL ×2) and brine (25 mL). The organic phase was concentrated to dryness, obtained the crude product as a yellowish solid. The crude product was purified using a short pad of silica gel (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeCN/MeOH 70:10:10 → EtOAc/MeCN/MeOH/H₂O 70:10:10:5) to afford the pure product 4.10 as a beige solid.

2-amino(phenyl)methyl MIDA boronate (4.10)

Yellowish solid; 50% yield; TLC (EtOAc/MeCN/MeOH/H₂O 70:10:10:5) Rₜ = 0.15; ¹H NMR (400 MHz, MeCN-d₃) δ 7.34-7.27 (m, 4H), 7.20-7.15 (m, 1H), 4.02 (d, J = 16.3 Hz, 1H), 3.95 (d, J = 16.3 Hz, 1H), 3.94 (d, J = 17.3 Hz, 1H), 3.84 (d, J = 17.3 Hz, 1H), 3.41 (s, 1H), 3.19 (s, 3H) ppm; ¹³C NMR (100 MHz, MeCN-d₃) δ 169.6, 169.1, 148.1, 129.0, 127.9, 126.6, 63.7, 63.5, 46.7 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 11.5 ppm; HRMS (ESI) [M+H]⁺ calcd. For C₁₂H₁₆BN₂O₄ 263.1203, found 263.1192; IR (thin film, cm⁻¹) 1762, 1747, 1599, 1448, 1339, 1290, 1246, 1194, 1155, 1106, 1073, 1046, 1004, 949, 898, 862, 773, 703.


4.5.7 Preparation of boro-dipeptide

To the solution of Cbz-Leu-OH (69 mg, 0.261 mmol, 1.2 equiv) and α-amino MIDA boronate 4.10 (57 mg, 0.217 mmol, 1.0 equiv) in anhydrous CHCl₃ (5 mL) was added PyBop (147 mg, 0.283 mmol, 1.3 equiv) and DIPEA (75 µL, 0.434 mmol, 2 equiv) subsequently. The reaction was stirred at room temperature under N2 for 5 hours. The reaction solution was washed with 10% citric acid (2 mL) and sat. NaHCO₃ (2 mL). The organic layer was concentrated and was purified using flash column chromatography on silica gel (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeCN 90:10) to afford the two diastereoisomers of the desired coupling products.

**benzyl (2S)-4-methyl-1-(((MIDA boryl)(phenyl)methyl)amino)-1-oxopentan-2-yl)carbamate (4.11)**

**Diastereomer 1:** White solid; 40% yield; TLC (EtOAc) Rₜ = 0.60; ¹H NMR (400 MHz, MeCN-d₃) δ 7.41-7.33 (m, 5H), 7.30-7.24 (m, 4H), 7.20-7.16 (m, 1H), 7.10 (d, J = 10.0 Hz, 1H), 5.89 (d, J = 6.5 Hz, 1H), 5.10 (d, J = 12.6 Hz, 1H), 5.02 (d, J = 12.6 Hz, 1H), 4.68 (d, J = 10.0 Hz, 1H), 4.06 (d, J = 16.0 Hz, 1H), 4.08-4.00 (m, 1H), 3.96 (d, J = 17.1 Hz, 1H), 3.93 (d, J = 16.0 Hz, 1H), 3.89 (d, J = 17.1 Hz, 1H), 2.86 (s, 3H), 1.58-1.48 (m, 1H), 1.46-1.30 (m, 2H), 0.86 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.6 Hz, 3H) ppm; ¹³C NMR (100 MHz, MeCN-d₃) δ 173.5, 169.1, 168.7, 157.5, 143.7, 138.3, 129.6, 129.0, 128.7, 128.4, 127.0, 67.2, 63.86, 63.3, 54.8, 46.7, 41.1, 25.4, 23.324, 22.0 ppm; ¹¹B NMR (128 MHz, DMSO-d₆) δ 11.1 ppm; HRMS (ESI) [M+H]^+ calcd. For C₃₈H₅₃BN₅O₇ 510.2412, found 510.2404; IR (thin film, cm⁻¹) 3303, 2956, 1758, 1705, 1656, 1532, 1453, 1338, 1290,
1236, 1114, 1036, 950, 896, 736, 699. **Diastereomer 2:** White solid; 40% yield; TLC (EtOAc) R<sub>f</sub> = 0.37; <sup>1</sup>H NMR (400 MHz, MeCN-d<sub>3</sub>) δ 7.39-7.32 (m, 5H), 7.30-7.24 (m, 4H), 7.21-7.17 (m, 1H), 6.97 (d, \( J = 9.9 \) Hz, 1H), 5.91 (d, \( J = 5.4 \) Hz, 1H), 5.10 (d, \( J = 12.2 \) Hz, 1H), 5.03 (d, \( J = 12.2 \) Hz, 1H), 4.65 (d, \( J = 9.9 \) Hz, 1H), 4.07-4.00 (m, 1H), 4.00 (d, \( J = 17.0 \) Hz, 1H), 3.99 (d, \( J = 17.1 \) Hz, 1H), 3.93 (d, \( J = 17.0 \) Hz, 1H), 3.83 (d, \( J = 17.1 \) Hz, 1H), 2.97 (s, 3H), 1.66-1.54 (m, 1H), 1.46-1.42 (m, 2H), 0.88 (d, \( J = 7.1 \) Hz, 3H), 0.86 (d, \( J = 6.9 \) Hz, 3H) ppm; <sup>13</sup>C NMR (100 MHz, MeCN-d<sub>3</sub>) δ 173.2, 169.1, 168.5, 157.6, 143.6, 137.9, 129.6, 129.0(9), 129.0(6), 128.4, 127.17, 67.6, 63.7, 63.5, 55.3, 47.0, 41.1, 25.6, 23.3, 21.8 ppm; <sup>11</sup>B NMR (128 MHz, DMSO-d<sub>6</sub>) δ 11.1 ppm; HRMS (ESI) [M+H]<sup>+</sup> calcd. For C<sub>26</sub>H<sub>33</sub>N<sub>3</sub>O<sub>7</sub> 510.2412, found 510.2404; IR (thin film, cm<sup>-1</sup>) 3328, 2959, 1760, 1706, 1668, 1518, 1454, 1337, 1287, 1251, 1111, 1038, 950, 895, 843, 739, 698

### 4.5.8 Preparation of α,α-disubstituted α-aminoboronic acid derivatives

![Diagram](image)

To a suspension of α,α-disubstituted α-boryl aldehyde 3.18 (250 mg, 0.79 mmol, 1 equiv) in 5 mL t-BuOH, was added cyclohexene (2.38 mmol, 0.24 mL, 3.0 equiv). A solution of NaClO<sub>2</sub> (0.107 g (80% purity), 0.95 mmol, 1.2 equiv) and NaH<sub>2</sub>PO<sub>4</sub> (0.131 g, 0.95 mmol, 1.2 equiv) in 5 mL H<sub>2</sub>O was added dropwise at room temperature. The mixture was vigorously stirred at room temperature for 12 hours. The reaction solution was then diluted with 10 mL brine, and extracted EtOAc (5 mL×3). The combined organic layers were concentrated to remove solvents. The crude product was purified using flash column chromatography on silica gel (Hexanes/EtOAc 50:50 → EtOAc → EtOAc/MeCN 90:10) to afford the pure product as a white solid (162 mg, 65% yield).
2-(MIDA boryl)-2-phenylpent-4-enoic acid (4.12)

White solid (foam); 65% yield; TLC (EtOAc) Rf = 0.37; 1H NMR (400 MHz, acetone-d6) δ 7.43 – 7.33 (m, 2H), 7.33 – 7.23 (m, 2H), 7.22 – 7.11 (m, 1H), 5.88 (dddd, J = 17.1, 10.2, 8.0, 5.8 Hz, 1H), 4.86 (ddt, J = 17.1, 2.6, 1.5 Hz, 1H), 4.75 (ddt, J = 10.2, 2.6, 1.2 Hz, 1H), 4.30 (d, J = 17.5 Hz, 1H), 4.13 (d, J = 16.3 Hz, 1H), 4.06 (d, J = 16.3 Hz, 1H), 3.92 (d, J = 17.5 Hz, 1H), 3.01 (ddt, J = 14.4, 5.8, 1.5 Hz, 1H), 2.78 (dd, J = 14.4, 8.0 Hz, 1H), 2.62 (s, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 180.7, 168.9, 168.3, 140.4, 135.8, 129.0, 127.6, 126.7, 117.7, 65.1, 64.5, 48.6, 41.3 ppm; 11B NMR (128 MHz, CDCl3) δ 11.5 ppm; HRMS (ESI) [M+H]+ calcd. For C16H19BNO6 332.1306, found 332.1304; IR (thin film, cm⁻¹) 2926, 1765, 1743, 1467, 1447, 1344, 1291, 1243, 1195, 1162, 1096, 1066, 1022, 992, 962, 899, 874, 827, 734, 703.

To a solution of α-borylcarboxylic acid 4.12 (75 mg, 0.227 mmol) in 1 mL anhydrous MeCN was added Et3N (38 μL, 0.273 mmol, 1.2 equiv) and DPPA (59 μL, 0.273 mmol, 1.2 equiv) subsequently. The resulting solution was stirred at room temperature under N2 for 15 min, and then heated at 50 °C for 2 hr until the reaction was complete as indicated by crude 1H NMR. The reaction mixture was cooled to room temperature, evaporated under reduced pressure to remove the solvent. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 80:20 → Hexanes/EtOAc 50:50 → EtOAc) to afford pure product.
1-(MIDA boryl)-1-phenylbut-3-en-1-yl isocyanate (4.13)

White solid; 70% yield; TLC (EtOAc) \( R_f = 0.70 \); \(^1\)H NMR (400 MHz, CDCl\(_3\)) 7.52-7.48 (m, 2H), 7.38-7.34 (m, 2H), 7.29-7.23 (m, 1H), 5.43-5.33 (m, 1H), 5.22 (d, \( J = 17.1 \) Hz, 1H), 5.12 (d, \( J = 9.9 \) Hz, 1H), 3.85 (d, \( J = 16.3 \) Hz, 1H), 3.77 (d, \( J = 16.3 \) Hz, 1H), 3.62 (d, \( J = 16.2 \) Hz, 1H), 2.97 (d, \( J = 16.2 \) Hz, 1H), 3.02 (ddt, \( J = 14.3, 5.2, 1.3 \) Hz, 1H), 2.95 (dd, \( J = 14.3, 8.8 \) Hz, 1H), 2.68 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta = 167.2, 166.8, 140.7, 131.9, 129.1, 127.1, 126.0, 124.9, 121.0, 63.8, 63.3, 46.9, 45.8 \) ppm; \(^{11}\)B NMR (128 MHz, CDCl\(_3\)) \( \delta = 10.8 \) ppm; HRMS (DART-TOF) [M+H]\(^+\) calcd. For C\(_{16}\)H\(_{18}\)BN\(_2\)O\(_5\) 329.13088, found 329.12999; IR (thin film, cm\(^{-1}\)) 3009, 2964, 2250, 1773, 1746, 1494, 1448, 1347, 1303, 1253, 1197, 1162, 1127, 1082, 1061, 1033, 993, 976, 963, 926, 901, 874, 803, 759, 712.

In a vial equipped with stirring-bar and a screw-cap lid was dissolved \( \alpha \)-boryl isocyanate 4.13 (25 mg, 0.0762 mmol, 1.0 equiv) in 2 mL MeCN. 6.0 M HCl (0.127 mL, 10 equiv) was added dropwise and the reaction mixture was stirred at the room temperature for 48 hours until the reaction was complete by TLC. The resulting solution was evaporated to remove the solvent under reduced pressure; the residue was azeotroped with MeCN three times to obtained desired product as a white powder.
(1-amino-1-phenylbut-3-en-1-yl)boronic acid (4.15)

White solid (1:1 mixture with MIDA); quantitative yield; $^1$H NMR (400 MHz, Methanol-\textit{d}$_4$) $\delta$ 7.48-7.43 (m, 4H), 7.41-7.32 (m, 1H), 5.88-5.76 (m, 1H), 5.34 (d, $J = 17.1$ Hz, 1H), 5.27 (d, $J = 9.8$ Hz, 1H), 4.11 (s, 4H) (MIDA $\alpha$-CH$_2$), 3.05 (s, 3H) (MIDA CH$_3$), 3.00-2.90 (m, 2H) ppm; $^{13}$C NMR (100 MHz, Methanol-\textit{d}$_4$) $\delta$ 168.7 (MIDA C=O), 140.0, 133.1, 130.4, 129.6, 127.7, 121.6, 57.4 (MIDA $\alpha$-CH$_2$), 43.4 (MIDA CH$_3$), 22.2 ppm; $^{11}$B NMR (128 MHz, Methanol-\textit{d}$_4$) $\delta$ 28.5 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{10}$H$_{15}$BNO$_2$ 192.1196, found 192.1191.

In a vial equipped with stirring-bar and a screw-cap lid was dissolved $\alpha$-boryl isocyanate 4.13 (13.1 mg, 0.0399 mmol, 1.0 equiv) in 1 mL anhydrous THF. Ethylamine (2.0M in THF, 0.0479 mmol, 1.2 equiv) was added and the reaction mixture was stirred at the room temperature for 5 hours until the reaction was complete by TLC. The resulting solution was concentrated to remove the solvent under reduced pressure. The crude product was subjected to purification by flash column chromatography on silica gel to obtain pure product.

1-ethyl-3-(1-(MIDA boryl)-1-phenylbut-3-en-1-yl)urea (4.15)

White solid; 85% yield; TLC (EtOAc) $R_f = 0.33$; $^1$H NMR (400 MHz, DMSO-\textit{d}$_6$) $\delta$ 7.26-7.19 (m, 4H), 7.15-7.11 (m, 1H), 6.21 (t, $J = 3.5$ Hz, 1H), 5.82-5.71 (m, 1H), 5.57 (bs, 1H), 5.01 (dd, $J = 18.4, 2.3$ Hz, 1H), 4.97 (dd, $J = 10.1, 2.3$ Hz, 1H), 4.11 (d, $J = 17.0$ Hz, 1H), 4.02 (d, $J = 17.1$ Hz, 1H), 3.97 (d, $J = 17.1$ Hz, 1H), 2.79 (d, $J = 17.0$ Hz, 1H), 2.99 (qd, $J = 7.1, 3.5$ Hz, 2H), 2.94 (dd, $J = 13.9, 7.5$ Hz, 1H), 2.72 (dd, $J = 13.9, 6.8$ Hz, 1H), 2.64 (s, 3H), 1.00 (t, $J =$
7.1 Hz, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 169.2, 168.2, 157.9, 145.1, 135.6, 127.5, 126.2, 125.1, 117.1, 63.1, 62.9, 46.0, 43.2, 33.9, 15.7 ppm; $^{11}$B NMR (128 MHz, DMSO-$d_6$) δ 11.6 ppm; HRMS (ESI) [M+H]$^+$ calcd. For C$_{13}$H$_{23}$BN$_3$O$_5$ 374.1887, found 374.1882; IR (thin film, cm$^{-1}$) 3389, 2973, 1762, 1740, 1667, 1542, 1493, 1444, 1347, 1303, 1271, 1193, 1111, 1024, 1003, 953, 906, 864, 824, 766, 724, 704.

4.5.9 General procedure for synthesis of α-hydroxyboronates

![Chemical structure](attachment:structure.png)

To a mixture of α-borylcarboxylic acid 3.19 (5 mmol, 1.0 equiv) and N-hydroxypyridine-2-thione (6 mmol, 1.2 equiv) in anhydrous DCM (150 mL) was added DCC (6 mmol, 1.2 equiv) and DMAP (0.25 mmol, 0.05 equiv). After the reaction was stirred at room temperature under N$_2$ in the dark for 12 hours, a gentle stream of O$_2$ gas was introduced and the mixture was kept in the dark for an additional 30 min with the O$_2$ bubbling. The reaction mixture was then added t-BuSH (45 mmol, 9.0 equiv) and irradiated with a 250 W tungsten lamp until the bright-yellow solution faded out in the course of 2-8 hours, during which the gentle stream of O$_2$ was maintained. Subsequently, (MeO)$_3$P (10 mmol, 2.0 equiv) was added to the reaction and stirred for an additional 2 hours. The reaction mixture was then filtered; the white solid filter cake was washed with DCM (25 mL x2); The organic filtrate was combined and concentrated under reduced pressure to remove solvents. The crude residue was then purified using flash column chromatography on silica gel (DCM/MeOH 10:0 → 9:1; or Hexanes/EtOAc 5:5 → EtOAc → EtOAc/MeCN 9:1 → 8:2) to afford the α-hydroxyboronate products 4.16.
MIDA (hydroxy(phenyl)methyl)boronate (4.16a)

White solid; 32% yield; TLC (EtOAc) R_f = 0.40; ^1H NMR (400 MHz, DMSO-d_6) δ 7.29-7.26 (m, 4H), 7.16-7.11 (m, 1H), 5.03 (broad s, 1H), 4.36-4.31 (m, 2H), 4.10 (d, J = 16.3 Hz, 1H), 3.99 (d, J = 17.3 Hz, 1H), 3.89 (d, J = 16.3 Hz, 1H), 3.10 (s, 3H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 169.4, 168.3, 145.2, 127.2, 126.1, 125.2, 62.1, 62.0, 45.2 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 11.1 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{12}H_{18}BN_2O_5 281.13088, found 281.13052; IR (thin film, cm^{-1}) 3545, 2952, 1760, 1471, 1443, 1339, 1279, 1246, 1200, 1152, 1109, 1053, 1029, 1007, 951, 896, 876, 807, 775, 719, 704.

MIDA (hydroxy(p-tolyl)methyl)boronate (4.16b)

White solid; 32% yield; TLC (EtOAc) R_f = 0.41; ^1H NMR (400 MHz, CD_3CN) δ 7.21 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 4.41 (d, J = 3.2 Hz, 1H), 3.95 (d, J = 16.2 Hz, 1H), 3.94 (d, J = 17.2 Hz, 1H), 3.89 (d, J = 16.3 Hz, 1H), 3.84 (d, J = 17.2 Hz, 1H), 3.12 (s, 3H), 3.01 (d, J = 3.4 Hz, 1H), 2.31 (s, 3H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 169.6, 168.8, 142.2, 136.4, 129.3, 136.4, 63.2, 63.1, 46.2, 21.0 ppm; ^11B NMR (128 MHz, CD_3CN) δ 10.7 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{13}H_{20}BN_2O_5 295.14653, found 295.14746; IR (thin film, cm^{-1}) 3422, 2976, 1743, 1510, 1449, 1340, 1293, 1248, 1196, 1156, 1106, 1083, 1061, 1033, 989, 952, 899, 880, 820, 760, 736, 713.

MIDA ((4-fluorophenyl)(hydroxy)methyl)boronate (4.16c)

White solid; 35% yield; TLC (EtOAc) R_f = 0.38; ^1H NMR (400 MHz, DMSO-d_6) δ 7.30-7.26 (m, 4H), 7.11-7.07 (m, 2H), 5.08 (d, J = 3.6 Hz, 1H), 4.37-4.32 (m, 2H), 4.10 (d, J = 16.3 Hz, 1H), 3.99 (d, J = 17.3 Hz, 1H), 3.89 (d, J = 16.3 Hz, 1H), 3.09 (s, 3H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 169.5, 168.8, 162.3 (d, ^1JC_F = 241.0 Hz), 141.4 (d, ^4JC_F = 2.9 Hz), 128.7 (d, ^3JC_F = 7.9 Hz), 115.2 (d, ^2JC_F = 21.3 Hz), 83.2, 83.2, 46.3 ppm; ^11B NMR (128 MHz, CD_3CN) δ 10.6 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{12}H_{17}BFN_2O_5 299.12146, found
299.12183; IR (thin film, cm\(^{-1}\)) 2971, 1750, 1602, 1466, 1449, 1341, 1294, 1251, 1217, 1155, 1111, 1084, 1033, 990, 951, 899, 883, 833, 743, 713.

**MIDA (1-hydroxy-3-phenylpropyl)boronate (4.16d)**

White solid; 73% yield; TLC (EtOAc) \( R_f = 0.30 \); \(^1\)H NMR (400 MHz, CD\(_3\)CN) \( \delta 7.31-7.24 \) (m, 4H), 7.20-7.15 (m, 1H), 3.93 (d, \( J = 17.2 \) Hz, 1H), 3.91 (d, \( J = 16.2 \) Hz, 1H), 3.82 (d, \( J = 16.2 \) Hz, 1H), 3.78 (d, \( J = 17.2 \) Hz, 1H), 3.29 (dd, \( J = 9.2, 4.3 \) Hz, 1H), 3.01 (s, 3H), 2.83 (ddd, \( J = 13.7, 10.0, 5.6 \) Hz, 1H), 2.63 (ddd, \( J = 13.6, 9.7, 6.8 \) Hz, 1H), 2.44 (bs, 1H), 1.87-1.71 (m, 2H) ppm; \(^{13}\)C NMR (100 MHz, CD\(_3\)CN) \( \delta 169.8, 168.9, 143.9, 129.4, 129.2, 126.5, 63.2, 62.9, 46.1, 36.4, 33.2 \) ppm; \(^{11}\)B NMR (128 MHz, CD\(_3\)CN) \( \delta 11.1 \) ppm; HRMS (DART-TOF) [M+NH\(_4\)]\(^+\) calcd. For C\(_{14}\)H\(_{22}\)BN\(_2\)O\(_5\) 309.16218, found 309.16334; IR (thin film, cm\(^{-1}\)) 3588, 2961, 2856, 1744, 1601, 1465, 1449, 1340, 1283, 1247, 1188, 1116, 1019, 988, 952, 897, 852, 752, 720, 697.

**MIDA (1-hydroxy-2-phenylethyl)boronate (4.16e)**

White solid; 70% yield; TLC (EtOAc) \( R_f = 0.38 \); \(^1\)H NMR (400 MHz, CD\(_3\)CN) \( \delta 7.32-7.25 \) (m, 4H), 7.23-7.18 (m, 1H), 3.96 (d, \( J = 17.2 \) Hz, 1H), 3.93 (d, \( J = 16.3 \) Hz, 1H), 3.83 (d, \( J = 17.2 \) Hz, 1H), 3.82 (d, \( J = 16.2 \) Hz, 1H), 3.52-3.49 (m, 1H), 3.02 (s, 3H), 2.89 (dd, \( J = 14.0, 2.9 \) Hz, 1H), 2.66 (dd, \( J = 14.0, 11.1 \) Hz, 1H), 2.15 (d, \( J = 17.4 \) Hz, 1H) ppm; \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)) \( \delta 169.5, 168.4, 141.3, 129.1, 127.8, 125.3, 62.2, 61.9, 45.2 \) ppm; \(^{11}\)B NMR (128 MHz, DMSO-d\(_6\)) \( \delta 11.0 \) ppm; HRMS (DART-TOF) [M+NH\(_4\)]\(^+\) calcd. For C\(_{13}\)H\(_{20}\)BN\(_2\)O\(_5\) 295.14653, found 295.14691; IR (thin film, cm\(^{-1}\)) 3023, 2976, 2847, 1765, 1740, 1495, 1467, 1444, 1380, 1343, 1328, 1301, 1272, 1251, 1195, 1165, 1121, 1061, 1030, 988, 947, 902, 868, 749, 723, 702.
MIDA (1-hydroxy-3-methylbutyl)boronate (4.16f)

White solid; 50% yield; TLC (EtOAc) R_f = 0.30; ^1H NMR (400 MHz, DMSO-d_6) δ 4.27 (d, J = 17.3 Hz, 1H), 4.05 (d, J = 16.3 Hz, 1H), 3.96 (d, J = 4.0 Hz, 1H), 3.90 (d, J = 17.3 Hz, 1H), 3.77 (d, J = 16.3 Hz, 1H), 3.20-3.16 (m, 1H), 3.00 (s, 3H), 1.85-1.75 (m, 1H), 1.41 (dd, J = 14.8, 10.7, 4.3 Hz, 1H), 1.10 (ddd, J = 14.8, 10.7, 4.3 Hz, 1H), 0.88 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 169.6, 168.4, 62.1, 61.8, 45.1, 42.3, 23.9, 23.3, 21.5 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 11.2 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{10}H_{22}BN_2O_5 261.16218, found 261.16260; IR (thin film, cm^-1) 2957, 2872, 1750, 1471, 1449, 1338, 1292, 1159, 1105, 1085, 1025, 1007, 965, 900, 864, 821, 720.

MIDA (1-hydroxypentyl)boronate (4.16g)

White solid; 70% yield; TLC (EtOAc) R_f = 0.25; ^1H NMR (400 MHz, DMSO-d_6) δ 4.27 (d, J = 17.3 Hz, 1H), 4.06-4.02 (m, 2H), 3.90 (d, J = 17.3 Hz, 1H), 3.77 (d, J = 16.3 Hz, 1H), 3.09-3.11 (m, 1H), 2.98 (s, 3H), 1.47-1.34 (m, 3H), 1.33-1.23 (m, 3H), 0.88 (t, J = 7.0 Hz, 3H) ppm; ^13C NMR (100 MHz, CDCl_3) δ 168.9, 168.3, 62.4, 62.3, 45.5, 32.8, 28.3, 22.6, 14.0 ppm; ^11B NMR (128 MHz, CDCl_3) δ 12.3 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{10}H_{22}BN_2O_5 261.16218, found 261.16260; IR (thin film, cm^-1) 3501, 2956, 2932, 2860, 2118, 1739, 1466, 1339, 1294, 1248, 1196, 1160, 1100, 1083, 1022, 991, 966, 943, 897, 853, 723.

MIDA (cyclohexyl(hydroxy)methyl)boronate (4.16h)

White solid; 71% yield; TLC (EtOAc) R_f = 0.28; ^1H NMR (400 MHz, DMSO-d_6) δ 4.23 (d, J = 17.4 Hz, 1H), 4.00 (d, J = 16.1 Hz, 1H), 3.92 (d, J = 5.3 Hz, 1H), 3.88 (d, J = 17.4 Hz, 1H), 3.75 (d, J = 16.1 Hz, 1H), 2.97 (s, 3H), 2.90 (t, J = 5.6 Hz, 1H), 1.84-1.80 (m, 1H), 1.70-1.59 (m, 4H), 1.42-1.33 (m, 1H), 1.24-0.94 (m, 5H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 170.0, 169.0, 63.0, 62.5, 46.0, 42.4, 31.0, 29.8, 27.3, 27.3, 27.2 ppm; ^11B NMR (128 MHz, CD_3CN) δ 11.1 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{12}H_{24}BN_2O_5 287.17783, found 287.17844; IR (thin film, cm^-1)
2922, 2851, 1760, 1742, 1449, 1341, 1302, 1245, 1195, 1160, 1114, 1079, 1022, 1007, 990, 961, 911, 893, 857, 723.

4.5.10 General procedure for synthesis of acylboronates

To a solution of α-hydroxyboronate 4.16 (2 mmol, 1.0 equiv) in 40 mL DCM was added Dess-Martin periodinane (2 mmol, 1.0 equiv). The solution was then added few drops of wet DCM (H₂O saturated) and stirred for 30 min. The clear solution grew cloudy. The mixture was washed with 10 mL of 1:1 10% Na₂S₂O₃/saturated aqueous NaHCO₃, followed by 10 mL of H₂O and 10 mL of brine. The organic phase was dried with Na₂SO₄ and concentrated. The crude solid product contains trace of Dess-Martin periodinane by-product. Further purification using flash column chromatography with a short pad of silica gel (Hexanes/EtOAc 5:5) afforded analytically pure product 4.17.

MIDA (oxo(phenyl)methyl)boronate (4.17a)

White solid; 72% yield; TLC (EtOAc) Rₜ = 0.67; ¹H NMR (400 MHz, CD₃CN) δ 8.07-8.04 (m, 2H), 7.64-7.59 (m, 1H), 7.55-7.51 (m, 2H), 4.08 (d, J = 16.8 Hz, 2H), 3.99 (d, J = 16.8 Hz, 2H), 2.94 (s, 3H) ppm; ¹³C NMR (100 MHz, CD₃CN) δ 168.8, 134.1, 129.5, 129.0, 118.2, 62.9, 47.4 ppm; ¹¹B NMR (128 MHz, CD₃CN) δ 5.4 ppm; HRMS (DART-TOF) [M+NH₄]⁺ calcd. For C₁₂H₁₆B₉O₅ 279.11523, found 279.11570; IR (thin film, cm⁻¹) 3326, 2928, 2850, 1752, 1647, 1628, 1594, 1577, 1465, 1448, 1328, 1310, 1269, 1224, 1194, 1099, 1086, 1029, 972, 895, 880, 835, 812, 786, 773, 707, 691, 666.
MIDA (oxo(p-tolyl)methyl)boronate (4.17b)

White solid; 76% yield; TLC (EtOAc) R_f = 0.67; ^1H NMR (400 MHz, CD_3CN) δ 7.97 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.08 (d, J = 16.8 Hz, 2H), 3.98 (d, J = 16.8 Hz, 2H), 2.92 (s, 3H), 2.40 (s, 3H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 168.9, 145.1, 130.1, 129.2, 62.9, 47.3, 21.6 ppm; ^11B NMR (128 MHz, CD_3CN) δ 5.4 ppm; HRMS (DART-TOF) [M+H]^+ calcld. For C_{13}H_{15}BNO_5 276.10378, found 295.10413; IR (thin film, cm^{-1}) 3017, 2958, 1759, 1639, 1628, 1600, 1465, 1327, 1273, 1237, 1221, 1196, 1161, 1098, 1085, 1042, 1024, 997, 970, 894, 844, 827, 819, 773, 741, 731, 709, 697.

MIDA ((4-fluorophenyl)oxomethyl)boronate (4.17c)

White solid; 70% yield; TLC (EtOAc) R_f = 0.67; ^1H NMR (400 MHz, CD_3CN) δ 8.16-8.12 (m, 2H), 7.27-7.22 (m, 2H), 4.10 (d, J = 16.8 Hz, 2H), 3.99 (d, J = 16.8 Hz, 2H), 2.94 (s, 3H) ppm; ^13C NMR (100 MHz, DMSO-d_6) δ 168.6, 164.8 (d, ^1J_\text{CF} = 251.8 Hz), 137.2 (d, ^4J_\text{CF} = 2.6 Hz), 130.8 (d, ^3J_\text{CF} = 9.5 Hz), 115.5 (d, ^2J_\text{CF} = 21.8 Hz), 61.9, 46.5 ppm; ^11B NMR (128 MHz, DMSO-d_6) δ 5.4 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcld. For C_{12}H_{15}BFN_O_5 297.10581, found 297.10575; IR (thin film, cm^{-1}) 3004, 1802, 1745, 1624, 1598, 1585, 1506, 1472, 1450, 1410, 1337, 1259, 1232, 1196, 1154, 1128, 1104, 1088, 1031, 994, 964, 897, 878, 850, 835, 791, 740, 709, 696.

MIDA (1-oxo-3-phenylpropyl)boronate (4.17d)

White solid; 70% yield; TLC (EtOAc) R_f = 0.61; ^1H NMR (400 MHz, CD_3CN) δ 7.28-7.25 (m, 2H), 7.22-7.20 (m, 2H), 7.18-7.14 (m, 1H), 4.02 (d, J = 16.9 Hz, 2H), 3.87 (d, J = 16.9 Hz, 2H), 2.98 (t, J = 7.7 Hz, 2H), 2.82 (t, J = 7.4 Hz, 2H), 2.77 (s, 3H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 169.0, 142.9, 129.2, 129.2, 126.6, 62.9, 48.7, 47.2, 28.5 ppm; ^11B NMR (128 MHz, CD_3CN) δ 4.3 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcld. For C_{14}H_{20}BN_2O_5 307.14653, found 307.14751; IR (thin film,
MIDA (1-oxo-2-phenylethyl)boronate (4.17e)

White solid; 66% yield; TLC (EtOAc) R<sub>f</sub> = 0.73; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN) δ 7.33-7.29 (m, 2H), 7.26-7.21 (m, 1H), 7.16-7.13 (m, 2H), 4.02 (d, J = 16.9 Hz, 2H), 3.97 (s, 2H), 3.84 (d, J = 16.9 Hz, 2H), 2.75 (s, 3H) ppm; <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>CN) δ 168.9, 135.0, 130.9, 129.2, 127.4, 63.0, 53.9, 47.4 ppm; <sup>11</sup>B NMR (128 MHz, CD<sub>3</sub>CN) δ 4.4 ppm; HRMS (DART-TOF) [M+NH<sub>4</sub>]<sup>+</sup> calcd. For C<sub>13</sub>H<sub>18</sub>BN<sub>2</sub>O<sub>5</sub> 293.13088, found 293.13248; IR (thin film, cm<sup>-1</sup>) 3033, 2952, 1760, 1660, 1498, 1471, 1451, 1418, 1339, 1278, 1256, 1197, 1171, 1150, 1088, 1057, 1007, 987, 962, 901, 885, 832, 763, 709, 692, 663.

MIDA (3-methyl-1-oxobutyl)boronate (4.17)

White solid; 70% yield; TLC (EtOAc) R<sub>f</sub> = 0.61; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN) δ 4.02 (d, J = 16.9 Hz, 2H), 3.88 (d, J = 16.9 Hz, 2H), 2.81 (s, 3H), 2.52 (d, J = 6.7 Hz, 2H), 2.22-2.08 (m, 1H), 0.87 (d, J = 6.7 Hz, 6H) ppm; <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 168.9, 62.0, 56.7, 55.1, 46.4, 22.5 ppm; <sup>11</sup>B NMR (128 MHz, DMSO-d<sub>6</sub>) δ 4.3 ppm; HRMS (DART-TOF) [M+NH<sub>4</sub>]<sup>+</sup> calcd. For C<sub>10</sub>H<sub>20</sub>BN<sub>2</sub>O<sub>5</sub> 259.14653, found 259.14612; IR (thin film, cm<sup>-1</sup>) 3200, 3018, 2963, 2873, 1747, 1657, 1465, 1449, 1396, 1363, 1338, 1279, 1257, 1188, 1153, 1117, 1092, 1064, 989, 962, 888, 876, 820, 730, 705, 660.

MIDA (1-oxopentyl)boronate (4.17g)

White solid; 85% yield; TLC (EtOAc) R<sub>f</sub> = 0.60; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN) δ 4.02 (d, J = 16.9 Hz, 2H), 3.88 (d, J = 16.9 Hz, 2H), 2.80 (s, 3H), 2.63 (t, J = 7.2 Hz, 2H), 1.52-1.44 (m, 2H), 1.33-1.24 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H) ppm; <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>CN) δ 169.0, 62.9, 47.3, 47.1, 24.8, 23.0, 14.2 ppm; <sup>11</sup>B NMR (128 MHz, CD<sub>3</sub>CN) δ 4.3 ppm; HRMS (DART-TOF) [M+NH<sub>4</sub>]<sup>+</sup> calcd. For C<sub>10</sub>H<sub>20</sub>BN<sub>2</sub>O<sub>5</sub> 259.14653, found 259.14583; IR (thin film, cm<sup>-1</sup>) 3017, 2961, 2872,

**MIDA (cyclohexyloxomethyl)boronate (4.17h)**

![MIDA (cyclohexyloxomethyl)boronate (4.17h) structure](image)

White solid; 60% yield; TLC (EtOAc) R\(_f\) = 0.60; \(^1\)H NMR (400 MHz, CD\(_3\)CN) \(\delta\) 4.01 (d, \(J = 16.9\) Hz, 2H), 3.89 (d, \(J = 16.9\) Hz, 2H), 2.79 (s, 3H), 2.77 (dt, \(J = 11.3, 3.2\) Hz, 1H), 1.83-1.73 (m, 4H), 1.70-1.63 (m, 1H), 1.38-1.27 (m, 2H), 1.23-1.11 (m, 3H) ppm; \(^{13}\)C NMR (100 MHz, CD\(_3\)CN) \(\delta\) 169.0, 62.9, 63.7, 47.3, 26.8, 27.3, 26.3 ppm; \(^{11}\)B NMR (128 MHz, CD\(_3\)CN) \(\delta\) 4.5 ppm; HRMS (DART-TOF) [M+NH\(_4^+\)]\(^+\) calcld. For C\(_{12}\)H\(_{22}\)BN\(_2\)O\(_5\) 285.16218, found 285.16130; IR (thin film, cm\(^{-1}\)) 2926, 2854, 1756, 1649, 1467, 1449, 1339, 1295, 1280, 1242, 1189, 1150, 1119, 1057, 1025, 981, 964, 895, 867, 843, 757, 746, 736, 709.

### 4.5.11 General procedure for synthesis of acyloxyboranes

![General procedure for synthesis of acyloxyboranes](image)

To a solution of acylboronate (2 mmol, 1.0 equiv) in 5 mL DCM was added \(m\)CPBA (2 mmol, 1.0 equiv) and anhydrous NaHCO\(_3\) (2 mmol, 1.0 equiv). The suspension was stirred at room temperature for 1 hour. The reaction mixture was washed with saturated aqueous NaHCO\(_3\) (2 mL), followed by 2 mL of brine. The organic phase was dried with Na\(_2\)SO\(_4\) and concentrated. The crude product was purified by flash column chromatography on silica gel (Hexanes/EtOAc 5:5) to afford pure acyloxyborane product.
MIDA boryl benzoate (4.18a)

White solid; 65% yield; TLC (EtOAc) R_f = 0.68; ^1H NMR (400 MHz, CD_3CN) δ 8.09-8.06 (m, 2H), 7.66-7.64 (m, 1H), 7.54-7.50 (m, 2H), 4.17 (d, J = 17.1 Hz, 2H), 4.11 (d, J = 17.1 Hz, 2H), 2.98 (s, 3H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 168.1, 167.9, 134.5, 130.9, 129.5, 64.6, 46.9 ppm; HRMS (DART-TOF) [M+H]^+ calcd. For C_{12}H_{13}BNO_6 278.08359, found 278.08398

MIDA boryl 3-methylbutanoate (4.18b)

White solid; 75% yield; TLC (EtOAc) R_f = 0.70; ^1H NMR (400 MHz, CD_3CN) δ 4.09 (d, J = 17.1 Hz, 2H), 4.01 (d, J = 17.1 Hz, 2H), 2.90 (s, 3H), 2.27 (d, J = 7.1 Hz, 2H), 2.11-2.00 (m, 1H), 0.95 (d, J = 6.7 Hz, 6H) ppm; ^13C NMR (100 MHz, CD_3CN) δ 175.2, 168.1, 64.5, 46.7, 45.1, 26.2, 22.4 ppm; ^11B NMR (128 MHz, CD_3CN) δ 8.4 ppm; HRMS (DART-TOF) [M+NH_4]^+ calcd. For C_{10}H_{20}BNO_6 275.14144, found 275.14105

4.5.12 General procedure for synthesis of α-bromoacylboronates

To a solution of the acylboroante (2.0 mmol, 1.0 equiv) in 20 mL DCM/Dioxane (1:1) was added a solution of Br_2 (2.0 mmol, 1.0 equiv) in 1 mL DCM at 0 °C. The mixture was stirred at 0 °C for 1 hour until the reaction was complete as indicated by TLC. The reaction mixture was diluted with 50 mL EtOAc and washed with water (20 mL) and brine (20 mL). The organic layer was dried with anhydrous Na_2SO_4 and concentrated to dryness. The resulted crude solid was purified using flash column chromatography on silica gel (EtOAc) to afford pure product.
MIDA (2-bromo-3-phenylpropanoyl)boronate (4.19a)

White solid; 96% yield; TLC (EtAc) \( R_f = 0.70 \); \(^1\)H NMR (400 MHz, CD\(_3\)CN) \( \delta \) 7.42–7.21 (m, 5H), 5.03 (dd, \( J = 8.3, 6.6 \) Hz, 1H), 4.06 (d, \( J = 17.0 \) Hz, 1H), 4.05 (d, \( J = 17.1 \) Hz, 1H), 3.94 (d, \( J = 17.0 \) Hz, 1H), 3.92 (d, \( J = 17.1 \) Hz, 1H), 3.43 (dd, \( J = 14.5, 6.6 \) Hz, 1H), 3.09 (dd, \( J = 14.5, 8.3 \) Hz, 1H), 2.75 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CD\(_3\)CN) \( \delta \) 168.8, 168.6, 132.4, 130.3, 129.3, 127.7, 63.4, 63.3, 63.2, 47.9, 37.6 ppm; \(^{11}\)B NMR (128 MHz, CD\(_3\)CN) \( \delta \) 4.7 ppm; HRMS (DART-TOF) \([\text{M+NH}_4]^+\) calcd. For C\(_{14}\)H\(_{19}\)BBrN\(_2\)O\(_5\) 385.05704, found 385.05589; IR (thin film, cm\(^{-1}\)) 3024, 2962, 1666, 1604, 1497, 1453, 1423, 1337, 1277, 1192, 1163, 1124, 1047, 986, 958, 932, 898, 879, 845, 832, 750, 732, 696.

MIDA (2-bromo-2-phenylacetyl)boronate (4.19b)

White solid; 70% yield; TLC (EtOAc) \( R_f = 0.60 \); \(^1\)H NMR (400 MHz, CD\(_3\)CN) \( \delta \) 7.44–7.36 (m, 5H), 6.11 (1H, s), 4.40–3.90 (m, 3H), 3.78 (d, \( J = 16.8 \) Hz, 1H), 2.77 (s, 3H) ppm; \(^{13}\)C NMR (100 MHz, CD\(_3\)CN) \( \delta \) 169.1, 168.9, 135.8, 131.3, 130.2, 128.7, 63.6, 63.5, 48.4 ppm; \(^{11}\)B NMR (128 MHz, CD\(_3\)CN) \( \delta \) 4.69 ppm; HRMS (DART-TOF) \([\text{M+NH}_4]^+\) calcd. For C\(_{13}\)H\(_{17}\)BBrN\(_2\)O\(_5\) 371.0414, found 371.0424.

4.5.13 General procedure for synthesis of 1-(silyloxy)vinylboronates

\[
\begin{align*}
\text{TMSOTf, DBU} &\quad \text{DCM} \\
4.17e \text{ or } 4.17f &\quad \text{MeN} \\
\rightarrow &\quad \text{OTMS} \\
4.20a \text{ or } 4.20b
\end{align*}
\]
To a solution of acylboronate (5 mmol, 1 equiv) in anhydrous DCM (50 mL) was added DBU (15 mmol, 3 equiv), DMAP (0.5 mmol, 0.1 equiv) and TMSOTf (10 mmol, 2 equiv). The resulted reaction solution was stirred at room temperature for 12 hours under N₂. The reaction was concentrated to remove solvents. The crude residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 → EtOAc) to afford the silyl enol ether product.

(Z)-MIDA (2-phenyl-1-((trimethylsilyl)oxy)vinyl)boronate (4.20a)

White solid; 50% yield; TLC (EtAc) Rf = 0.79; ¹H NMR (400 MHz, CD₃CN) δ 7.55-7.53 (m, 2H), 7.32-7.28 (m, 2H), 7.21-7.17 (m, 1H), 6.12 (s, 1H), 3.99 (d, J = 17.0 Hz, 2H), 3.86 (d, J = 16.9 Hz, 2H), 2.95 (s, 3H), 0.02 (s, 9H) ppm; ¹³C NMR (100 MHz, CD₃CN) δ 169.3, 137.3, 130.1, 128.9, 127.4, 121.8, 62.7, 47.8, 0.9 ppm; ¹¹B NMR (128 MHz, CD₃CN) δ 8.9 ppm; HRMS (DART-TOF) [M+NH₄]⁺ calcd. For C₁₆H₂₆BN₂O₅Si 365.17040, found 365.17323; IR (thin film, cm⁻¹) 2998, 2955, 1767, 1743, 1630, 1463, 1446, 1345, 1332, 1306, 1260, 1247, 1214, 1198, 1076, 1049, 1007, 990, 954, 879, 852, 838, 754, 698, 669.

MIDA (2-isopropyl-1-((trimethylsilyl)oxy)vinyl)boronate

White solid; 52% yield; TLC (EtAc) Rf = 0.77; ¹H NMR (400 MHz, CD₃CN) δ 4.99 (d, J = 9.5 Hz, 1H), 3.93 (d, J = 16.9 Hz, 2H), 3.75 (d, J = 16.9 Hz, 2H), 2.82 (s, 3H), 2.80-2.71 (m, 1H), 0.95 (d, J = 6.7 Hz, 6H), 0.15 (s, 9H) ppm; ¹³C NMR (100 MHz, CD₃CN) δ 169.3, 131.3, 62.6, 47.6, 25.4, 23.0, 0.7 ppm; ¹¹B NMR (128 MHz, CD₃CN) δ 8.9 ppm; HRMS (DART-TOF) [M+NH₄]⁺ calcd. For C₁₃H₂₈BN₂O₅Si 331.18605, found 331.18869; IR (thin film, cm⁻¹) 2954, 2865, 1762, 1644, 1463, 1378, 1330, 1284, 1248, 1230, 1169, 1128, 1029, 958, 938, 876, 835, 754, 712, 682, 663.
4.5.14 General procedure for synthesis of thiazol-4-ylboronates

A solution of α-bromoacetylboronates 4.19 (0.283 mmol, 1.0 equiv) and thioamide or thio urea (0.339 mmol, 1.2 equiv) in 2.5 mL of DMF was heated at 65 °C for 6 h. The reaction mixture was diluted with 10 mL EtOAc, then washed with 5% NaHCO₃ (2 mL) and H₂O (2 mL). The organic extracts were concentrated. The residue was purified using flash column chromatography on silica gel to afford the corresponding thiazole product 4.21.

5-benzyl-4-(MIDA boryl)-2-methylthiazole (4.21a)

White solid; 50% yield; TLC (EtOAc) Rₖ = 0.20; ¹H NMR (400 MHz, CD₃CN) δ 7.32–7.19 (m, 5H), 4.30 (s, 2H), 4.05 (d, J = 16.8 Hz, 2H), 3.95 (d, J = 16.4 Hz, 2H), 2.56 (s, 3H), 2.55 (s, 3H) ppm; ¹³C NMR (100 MHz, CD₃CN) δ 169.8, 166.1, 146.3, 142.7, 129.9, 129.8, 127.8, 63.0, 47.5, 33.6, 19.4 ppm; ¹¹B NMR (128 MHz, CD₃CN) δ 9.8 ppm; HRMS (DART-TOF) [M+H]+ calcd. For C₁₆H₁₈BN₂O₄S 345.1080, found 345.1085.

5-benzyl-4-(MIDA boryl)-2-phenylthiazole (4.21b)

White solid; 66% yield; TLC (EtOAc) Rₖ = 0.70; ¹H NMR (400 MHz, CD₃CN) δ 7.90–7.86 (m, 2H), 7.43–7.41 (m, 3H), 7.34–7.31 (m, 4H), 7.27–7.21 (m, 1H), 4.41 (s, 2H), 4.11 (d, J = 16.8 Hz, 2H), 4.04 (d, J = 16.8 Hz, 2H), 2.63 (s, 3H) ppm; ¹³C NMR (100 MHz, CD₃CN) δ 169.8, 167.9, 147.0, 142.4, 134.9, 131.2, 130.3, 130.0, 129.8, 127.9, 127.7, 63.1, 47.7, 33.7 ppm; ¹¹B NMR (128...
MHz, CD$_3$CN) δ 9.9; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{21}$H$_{20}$BN$_2$O$_4$S 407.1231, found 407.1236.

4-(MIDA boryl)-2-methyl-5-phenylthiazole (4.21c)

White solid; 33% yield; TLC (EtOAc) R$_f$ = 0.20; $^1$H NMR (400 MHz, CD$_3$CN) δ 7.45–7.37 (m, 5H), 4.00 (d, 2H, $J = 16.4$ Hz), 3.93 (d, 2H, $J = 16.8$ Hz), 2.68 (s, 3H), 2.66 (s, 3H) ppm; $^{13}$C NMR (100 MHz, CD$_3$CN) δ 169.6, 166.9, 146.0, 133.6, 131.5, 129.5, 129.3, 63.0, 47.7, 19.4 ppm; $^{11}$B NMR (128 MHz, CD$_3$CN) δ 9.7 ppm; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{15}$H$_{16}$BN$_2$O$_4$S 331.0924, found 331.0923.

4-(MIDA boryl)-2,5-diphenylthiazole (4.21d)

White solid; 66% yield; TLC (EtOAc) R$_f$ = 0.50; $^1$H NMR (400 MHz, CD$_3$CN) δ 7.99–7.97 (m, 2H), 7.54–7.42 (m, 8H), 4.04 (s, 4H), 2.76 (s, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 168.9, 166.2, 144.3, 132.9, 131.4, 130.2, 130.0, 129.2, 128.4, 128.1, 126.4, 61.8, 46.8 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 9.7 ppm; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{20}$H$_{18}$BN$_2$O$_4$S 393.1080, found 393.1085.

5-benzyl-4-(MIDA boryl)thiazol-2-amine (4.21e)

Yellow solid; 88% yield; TLC (CH$_3$CN/EtOAc 2:8) R$_f$ = 0.20; $^1$H NMR (400 MHz, CD$_3$CN) δ 7.31–7.20 (m, 5H), 5.25 (br s, 2H), 4.16 (s, 2H), 3.99 (d, $J = 16.4$ Hz, 2H), 3.92 (d, $J = 16.8$ Hz, 2H), 2.64 (s, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 169.1, 166.9, 141.5, 131.8, 128.3, 128.1, 126.0, 61.3, 46.2, 32.1 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) δ 9.9; HRMS (DART-TOF) [M+H]$^+$ calcd. For C$_{15}$H$_{17}$BN$_3$O$_4$S 346.1033, found 346.1028.
4-(MIDA boryl)-5-phenythiazol-2-amine (4.21f)

Yellow solid; 61% yield; TLC (CH$_3$CN/EtOAc 20%) $R_f$ = 0.30; $^1$H NMR (400 MHz, CD$_3$CN) $\delta$ 7.42–7.31 (m, 5H), 5.50 (br s, 2H), 3.96 (d, 2H, $J = 16.8$ Hz), 3.91 (d, 2H, $J = 16.8$ Hz), 2.75 (s, 3H) ppm; $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 168.8, 167.3, 132.9, 131.6, 129.8, 127.7, 127.0, 61.6, 46.4 ppm; $^{11}$B NMR (128 MHz, DMSO-d$_6$) $\delta$ 9.56 ppm; HRMS (DART-TOF) [M+H]$^+$ calcld. For C$_{14}$H$_{15}$BN$_3$O$_4$S 332.0876, found 332.0885

4.5.15 Synthesis of 2-oxo-acylboronates and 2-borylated quinoxalines

To a solution of 1-(silyloxy)vinylboronates 4.20 (5.0 mmol, 1.0 equiv) in DCM (10 mL) was added mCPBA (7.5 mmol, 1.5 equiv) and stirred at room temperature for 2 hours. The solvent DCM was then removed under reduced pressure and replaced with THF (10 mL). The resulted THF solution was added TBAF (1.0 M in THF, 7.5 mmol, 1.5 equiv) and stirred at room temperature for an additional hour. The reaction mixture was diluted with EtOAc (20 mL) and washed with sat. NH$_4$Cl (20 mL). The organic layer was dried with anhydrous Na$_2$SO$_4$ and filtered. The filtrate was left on bench at room temperature for additional 24 hours, and then evaporated to dryness under reduced pressure. The residue was purified using flash column chromatography on silica gel (Hexanes/EtOAc 1:1 $\rightarrow$ EtOAc) to afford the final product $\alpha$-hydroxy-$\alpha$-boryl ketones 4.22.
MIDA (1-hydroxy-2-oxo-2-phenylethyl)boronate (4.22a)

White solid; 70% yield; TLC (EtOAc) Rf = 0.47; 1H NMR (400 MHz, DMSO-d6) δ 7.98-7.95 (m, 2H), 7.65-7.58 (m, 1H), 7.51-7.45 (m, 2H), 5.11 (d, J = 4.1 Hz, 1H), 4.71 (d, J = 4.2 Hz, 1H), 4.33 (d, J = 17.3 Hz, 1H), 4.13 (d, J = 16.5 Hz, 1H), 4.02 (d, J = 17.3 Hz, 1H), 3.89 (d, J = 16.4 Hz, 1H), 3.16 (s, 3H) ppm; 13C NMR (100 MHz, DMSO-d6) δ 202.1, 168.9, 168.1, 135.7, 132.8, 128.6, 128.0, 62.2, 61.9, 45.7 ppm; 11B NMR (128 MHz, DMSO-d6) δ 10.2 ppm; HRMS (DART-TOF) [M+NH4]+ calcd. For C13H18BN2O6 309.12579, found 309.12621; IR (thin film, cm⁻¹) 3017, 2962, 1747, 1641, 1599, 1578, 1471, 1449, 1337, 1287, 1242, 1196, 1167, 1101, 1042, 1056, 1012, 977, 900, 822, 801, 745, 703, 691, 669.

MIDA (1-hydroxy-3-methyl-2-oxobutyl)boronate (4.22b)

White solid; 60% yield; TLC (EtAc) Rf = 0.47; 1H NMR (400 MHz, CD3CN) δ 4.34 (s, 1H), 3.99 (d, J = 17.3 Hz, 1H), 3.96 (d, J = 16.3 Hz, 1H), 3.90 (d, J = 17.2 Hz, 1H), 3.88 (d, J = 16.3 Hz, 1H), 3.51 (broad s, 1H), 3.10 (s, 3H), 3.02-2.92 (m, 1H), 1.09 (d, J = 7.0 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H) ppm; 13C NMR (100 MHz, CD3CN) δ 217.0, 169.4, 168.4, 63.1, 62.9, 46.6, 36.8, 20.0, 18.0 ppm; 11B NMR (128 MHz, CD3CN) δ 9.6 ppm; HRMS (DART-TOF) [M+NH4]+ calcd. For C10H20BN2O6 275.14144, found 275.14205; IR (thin film, cm⁻¹) 3476, 2966, 2877, 1755, 1694, 1664, 1466, 1385, 1338, 1275, 1175, 1130, 1035, 988, 955, 897, 872, 824, 783, 732, 707.

To a solution of α-hydroxy-α-boryl ketones 4.22 (2 mmol, 1.0 equiv) in 40 mL DCM was added Dess-Martin periodinane (2 mmol, 1.0 equiv). The solution was then added few drops of wet
DCM (H$_2$O saturated) and stirred for 30 min. The clear solution grew cloudy. The mixture was then washed with 10 mL of 1:1 10% Na$_2$S$_2$O$_3$/saturated aqueous NaHCO$_3$, followed by 10 mL of H$_2$O and 10 mL of brine. The organic phase was dried with anhydrous Na$_2$SO$_4$ and concentrated. The crude solid product contains trace of Dess-Martin periodinane by-product. Further purification using flash column chromatography with a short pad of silica gel (Hexanes/EtOAc 5:5) afforded analytically pure product 4.23.

**MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a)**

Yellow solid; 87% yield; TLC (EtAc) $R_f = 0.67$; $^1$H NMR (400 MHz, acetone-$d_6$) $d$ 7.96-7.93 (m, 2H), 7.78-7.74 (m, 1H), 7.63-7.59 (m, 2H), 4.51 (d, $J = 17.0$ Hz, 2H), 4.32 (d, $J = 17.0$ Hz, 2H), 3.21 (s, 3H) ppm; $^{13}$C NMR (100 MHz, acetone-$d_6$) $\delta$ 169.7, 138.0, 136.8, 131.7, 131.0, 64.6, 49.6 ppm; $^{11}$B NMR (128 MHz, acetone-$d_6$) $\delta$ 5.3 ppm; HRMS (DART-TOF) [M+NH$_4$]$^+$ calcd. For C$_{13}$H$_{16}$BN$_2$O$_6$ 307.11014, found 307.11077.

X-ray quality crystals were grown by layering hexanes onto a dissolved solution of 4.23a in acetone. The layers slowly mixed, forming crystals.
MIDA (3-methyl-1,2-dioxobutyl)boronate (4.23b)

Yellow solid; 76% yield; TLC (EtAc) Rf = 0.65; 1H NMR (400 MHz, acetone-d6) δ 4.45 (d, J = 16.9 Hz, 2H), 4.26 (d, J = 16.9 Hz, 2H), 3.16 (sept, J = 7.0 Hz, 1H), 3.08 (s, 3H), 1.07 (d, J = 7.0 Hz, 6H) ppm; 13C NMR (100 MHz, acetone-d6) δ 64.6, 49.2, 35.3, 18.0 ppm; 11B NMR (128 MHz, acetone-d6) δ 5.4 ppm; HRMS (DART-TOF) [M+NH4]+ calcd. For C10H18BN2O6 273.12579, found 273.12608.

To a solution of 2-oxo-acyl boronate 4.23 (30.8 mg, 0.121 mmol, 1.0 equiv) in 2 mL anhydrous DCM was added benzene-1,2-diamine (14.4 mg, 0.133 mmol, 1.1 equiv) and 100 mg anhydrous MgSO4. The mixture was stirred at room temperature for 1 hour and then diluted with 5 mL EtOAc. The solution was then washed with 2 mL of 1:1 1N HCl/brine. The organic layer was dried with anhydrous Na2SO4 and concentrated. The residue was purified with flash column chromatography on silica gel (Hexanes/EtOAc 5:5) to pure product 4.24.

MIDA (3-isopropylquinoxalin-2-yl)boronate (4.24)

Yellow solid; 80% yield; TLC (EtAc) Rf = 0.50; 1H NMR (400 MHz, CDCl3) δ 8.04 (ddd, J = 8.2, 1.5, 0.5 Hz, 1H), 7.91 (ddd, J = 8.1, 1.6, 0.6 Hz, 1H), 7.71 (ddd, J = 8.4, 6.9, 1.6 Hz, 1H), 7.65 (ddd, J = 8.3, 6.9, 1.5 Hz, 1H), 4.29 (d, J = 15.8 Hz, 2H), 4.00-3.91 (m, 3H), 3.06 (s, 6H), 1.39 (d, J = 6.7 Hz, 6H) ppm; 13C NMR (100 MHz, CD3CN) δ 169.4, 166.0, 130.9, 129.9, 129.5, 129.5, 63.2, 47.3, 33.2, 22.7 ppm; 11B NMR (128 MHz, CD3CN) δ 9.5 ppm; HRMS (DART-TOF) [M+H]+ calcd. For C16H19BN5O4 328.14631, found 328.14631.

4.6 References


5 A single example of α-metallo isocyanate was reported (α-silyl isocyanates): Roy, S.; Spino, C. Org. Lett. 2006, 8, 939-942.


19


20


21


23 For oxidation of hydroxyl-substituted organo(MIDA)boronates under Swern and Jones oxidations, see: Gillis, E. P.; Burke, M. D. J. Am. Chem. Soc. 2008, 130, 14084–14085.


Appendix I

Selected Chapter 2 NMR Spectra and X-ray crystal data
**NH₂**

**2.1h**

**2.1h**
Sample: 255040601
Sample ID: a_255040601_33

Pulse Sequence: Xypll

Source: ohiol3

Temp: 29.0°C / 299.1 K
Sample ESL, Operator: ire1

VNMRS-600 "parker nr'

NMR: Delay 0.2 sec
Pulse at 1 degree
Acq. time 1.396 sec
Width 6398.5 Hz
14 acquisitions

GcLobes ML: 399.218920 MHz

DATA PROCESSING
Line broadening 0.2 Hz
PT slice ext 24
Total time 1 min, 12 sec

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Sample: 255040601
Sample ID: a_255040601_33

Pulse Sequence: Xypll

Source: ohiol3

Temp: 29.0°C / 299.1 K
Sample ESL, Operator: ire1

VNMRS-600 "parker nr'

NMR: Delay 0.2 sec
Pulse at 1 degree
Acq. time 1.396 sec
Width 6398.5 Hz
14 acquisitions

GcLobes ML: 399.218920 MHz

DATA PROCESSING
Line broadening 0.2 Hz
PT slice ext 24
Total time 1 min, 12 sec
NH₂

MeO

2.5b

NH₂

MeO

2.5b
**Page 266**

**Image Description:**
- Two images of chemical spectra graphs are shown, each with a molecule and a spectrum line.
- The molecule structure is similar in both images, indicating a comparison or analysis.
- The spectra appear to be from NMR (Nuclear Magnetic Resonance) experiments.
- The spectra are labeled with a chemical formula and a reference code, suggesting a scientific context.

**Textual Content:**
- The text is not visible in the image, but the presence of spectra and chemical structures indicates a chemistry-related report or study.

**Analysis:**
- The images likely represent NMR spectra of the same or similar compounds, possibly used to analyze the purity, structure, or concentration of the substances.
- The similar formulas across both images suggest a focus on the same chemical compound or a comparison of similar compounds.

**Conclusion:**
- The document appears to be a scientific report or analysis involving chemical spectroscopy, specifically NMR, which is a common technique in chemistry for identifying and quantifying substances.
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Archive directory: 
Sample directory: 
Pulse Sequence: Carbon (x2pol)
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Temp: 293 K
Sample Ht.: Operator: GD00494
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1000 repetitions
SOMAVEC 20.0, 100.0, 400.0 Hz
DETECT 1, 394.181595 Wpp
Power 20 W
continuously on
WALTZ-16modulated
DATA PROCESSING
Line Broadening 0.5 Hz
FT size 1024 points
Total time 0 min 24 sec

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Archive directory: 
Sample directory: 
Pulse Sequence: PHOTON ( x2pol)
Solvent: chcl3
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ORIGINX K: 210.147532 mess
DATA PROCESSING
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FT size 12744
Total time 1 min 20 sec

Ph N Ph
Ph
2.15a

Ph N Ph
Ph
2.15a

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220 200 180 160 140 120 100 80 60 40 20 0 ppm
Sample Name: EN005989
ARCHIVE DIRECTORY:
Sample directory:
File Name: 20110703-EN005989_Carbon-000
Pulse Sequence: Carbon (1H pulse)
Data collected on: Jul 3 2011

Temp: 25.0 C / 298.3 K
Sample Size: Operator: SAB
VNMRS-400 "GEMINI"

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DECOUPL. RL 399.367188 MHz
Power 39 dB
Resulting on WATER-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
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Total time 0 min 24 sec
Detailed X-ray Crystallographic Information of \textit{trans}-2-ethynyl-3-(4-fluorophenyl)aziridine (2.2c):

**Crystallization Conditions:** In a 0.5 mL vial, 10 mg of purified compound \textit{2.2c} was dissolved at saturation in CCl\textsubscript{4}. The vial was placed in a 5 mL vial containing a small amount of hexanes, capped tight and placed in the dark. After 48 hours, crystal formation was observed, and a suitable crystal was selected for X-ray crystallographic analysis.

**Table I-1.** Crystal data and structure refinement for \textit{trans}-2-ethynyl-3-(4-fluorophenyl) aziridine \textit{2.2c}.

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Table I-2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for trans-2-ethynyl-3-(4-fluorophenyl) aziridine 2.2c. U(eq) is defined as one third of the trace of the orthogonalized U_ij tensor.
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**Table I-3.** Bond lengths [Å] and angles [°] for *trans*-2-ethynyl-3-(4-fluorophenyl) aziridine 2.2c.

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</tr>
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<td>C(4B)-C(5B)</td>
<td>1.482(4)</td>
</tr>
<tr>
<td>C(5B)-C(6B)</td>
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<td>C(5B)-C(10B)</td>
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<td>C(1A)-C(2A)</td>
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<td>C(2A)-C(3A)</td>
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C(5A)-C(6A)  1.387(4)
C(5A)-C(10A)  1.405(5)
C(6A)-C(7A)  1.392(5)
C(7A)-C(8A)  1.367(5)
C(8A)-C(9A)  1.382(5)
C(9A)-C(10A)  1.374(5)

C(4B)-N(1B)-C(3B)  60.8(2)
C(1B)-C(2B)-C(3B)  177.4(4)
C(2B)-C(3B)-N(1B)  119.6(3)
C(2B)-C(3B)-C(4B)  121.3(3)
N(1B)-C(3B)-C(4B)  59.47(19)
C(5B)-C(4B)-N(1B)  118.0(3)
C(5B)-C(4B)-C(3B)  122.5(3)
N(1B)-C(4B)-C(3B)  59.71(19)
C(6B)-C(5B)-C(10B)  118.8(3)
C(6B)-C(5B)-C(4B)  119.0(3)
C(10B)-C(5B)-C(4B)  122.1(3)
C(5B)-C(6B)-C(7B)  120.6(3)
C(8B)-C(7B)-C(6B)  118.9(3)
F(1B)-C(8B)-C(7B)  119.3(3)
F(1B)-C(8B)-C(9B)  118.4(3)
C(7B)-C(8B)-C(9B)  122.3(4)
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<td>118.4(3)</td>
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**Table I-4.** Anisotropic displacement parameters (Å² x 10³) for *trans*-2-ethynyl-3-(4-fluorophenyl) aziridine 2.2c. The anisotropic displacement factor exponent takes the form: 

\[-2\pi^2 [ h^2 a^* \times 2 U_{11} + \ldots + 2hk a^* b^* \times U_{12} ]\]
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<th>U^{22}</th>
<th>U^{33}</th>
<th>U^{23}</th>
<th>U^{13}</th>
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<td>1(1)</td>
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### Table I-5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for trans-2-ethynyl-3-(4-fluorophenyl) aziridine 2.2c.

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<th>U(eq)</th>
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<td>55</td>
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<td>7930(80)</td>
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<tr>
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<td>d(D...A)</td>
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<td>---------------</td>
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<td>-----------</td>
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Symmetry transformations used to generate equivalent atoms:

#1 x+1, y+1, z  #2 x-1, y, z
Detailed X-ray Crystallographic Information of 2-ethynyl-3-phenyl-2H-azirine (2.20)

Crystallization Conditions: The crystal of the titled compound was obtained by slowly evaporating the solvent of its DCM solution. The colorless large flakes of crystals were obtained. A suitable crystal was selected for X-ray crystallographic analysis.

Table I-7. Crystal data and structure refinement for 2-ethynyl-3-phenyl-2H-azirine 2.20.

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</tr>
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<tr>
<td>Wavelength</td>
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<tr>
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<tr>
<td></td>
<td>b = 7.2448(6) Å</td>
</tr>
<tr>
<td></td>
<td>b= 90°.</td>
</tr>
<tr>
<td></td>
<td>c = 19.3703(17) Å</td>
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<tr>
<td></td>
<td>g = 90°.</td>
</tr>
<tr>
<td>Property</td>
<td>Value</td>
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<tr>
<td>----------------------------------------------</td>
<td>------------------------</td>
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<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.997 and 0.445</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<tr>
<td>Data / restraints / parameters</td>
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<tr>
<td>Goodness-of-fit on F²</td>
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</tr>
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<td>R indices (all data)</td>
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<tr>
<td>Largest diff. peak and hole</td>
<td>0.146 and -0.220 e.Å⁻³</td>
</tr>
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</table>

**Table I-8.** Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³) for 2-ethyl-3-phenyl-2H-azirine 2.20. U(eq) is defined as one third of the trace of the orthogonalized Uᵢⱼ tensor.
<table>
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<th>y</th>
<th>z</th>
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</thead>
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<td>1649(3)</td>
<td>2391(1)</td>
<td>44(1)</td>
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**Table I-9.** Bond lengths [Å] and angles [°] for 2-ethynyl-3-phenyl-2H-azirine 2.20.
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<td>C(6)-H(6A)</td>
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<td>C(1)-N(1)-C(2)</td>
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<td>N(1)-C(1)-C(5)</td>
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<tr>
<td>C(1)-C(2)-H(2)</td>
<td>118.0(12)</td>
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<td>N(1)-C(2)-H(2)</td>
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<td>179.5(3)</td>
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<td>C(3)-C(4)-H(4)</td>
<td>176(2)</td>
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C(6)-C(5)-C(10)  119.9(2)
C(6)-C(5)-C(1)  120.15(19)
C(10)-C(5)-C(1)  119.94(19)
C(7)-C(6)-C(5)  119.8(2)
C(7)-C(6)-H(6A)  120.1
C(5)-C(6)-H(6A)  120.1
C(8)-C(7)-C(6)  120.0(2)
C(8)-C(7)-H(7A)  120.0
C(6)-C(7)-H(7A)  120.0
C(7)-C(8)-C(9)  120.4(2)
C(7)-C(8)-H(8A)  119.8
C(9)-C(8)-H(8A)  119.8
C(10)-C(9)-C(8)  120.0(2)
C(10)-C(9)-H(9A)  120.0
C(8)-C(9)-H(9A)  120.0
C(9)-C(10)-C(5)  119.8(2)
C(9)-C(10)-H(10A)  120.1
C(5)-C(10)-H(10A)  120.1

Symmetry transformations used to generate equivalent atoms:

Table I-10. Anisotropic displacement parameters (Å² x 10³) for 2-ethynyl-3-phenyl-2H-azirine 2.20. The anisotropic displacement factor exponent takes the form: -2π² [ h² a*² U₁₁ + ... + 2 ℎ k a* b* U₁₂ ]
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<th></th>
<th>U₁₁</th>
<th>U₂₂</th>
<th>U₃₃</th>
<th>U₂₃</th>
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**Table I-11.** Hydrogen coordinates (x 10⁴) and isotropic displacement parameters (Å² x 10³) for 2-ethynyl-3-phenyl-2H-azirine 2.20.

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<th>z</th>
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<td>3807</td>
<td>2689</td>
<td>51</td>
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<td>1500(40)</td>
<td>5017(16)</td>
<td>93(10)</td>
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</table>
Appendix II

Selected Chapter 3 NMR Spectra and X-ray crystal data
(1:1 mixture of diastereomers)
3.10 (syn:anti 93:7 mixture)
3.13a (E/Z = 3.7 mixture)
3.13b (E/Z = 40:60 mixture)
3.15

B
O
MeN
O
O
Ph
NBn₂

B
O
MeN
O
O
Ph
NBn₂

3.15
Sample Name:
AS_1_30_concentrated
Sample Directory:
3011.09.10_AS_1_30_concentrated_Carbon-001
Pulse Sequence: Carbon-1
SOLVENT: CD3OD
Data collected on: Sep 22, 2011
Temp. 298.0 °C / 39.1 °C
Sample H, Operator: shad
VNMRS-450 "Sarepta"
Relax delay 0.100 sec
Pulse 90.0 degree
Acq. time 1.100 sec
Width 316.7 Hz
6000 repetitions
OFFSIFT CS1, 100.615853 MHz
DECOUPLING H, 399.174624 MHz
Power 60 W
Continuously on: NLSRS-16 modulated
DATA PROCESSING
Line broaden 0.5 Hz
FT size 131072
Total time 8 min 24 sec

Sample Name:
E6708401
ARCHIVE DIRECTORY:
/usr/tmp/home/ruanzy/data
Sample directory:
3011.09.10-E6708401_Protom-001
Pulse Sequence: Proton-6
SOLVENT: CD3OD
Data collected on: Mar 19, 2003
Temp. 298.0 °C / 39.1 °C
Sample H, Operator: shad
VNMRS-450 "Sarepta"
Relax delay 0.100 sec
Pulse 90.0 degree
Acq. time 1.100 sec
Width 316.7 Hz
16 repetitions
OFFSIFT CS1, 100.615853 MHz
Data processing:
Line broaden 0.5 Hz
FT size 131072
Total time 8 min 24 sec
Sample Name: 3.22a (E/Z 4:6 mixture)

Sample directory: /report/chem/chem/chemsys/data

350

(various technical details and data collection parameters)
351

Sample Name: 186601111
Archive directory: /scott/home/marti/mercury/data
Sample directory: 
FileID: 20111520-186601111_Proton-000

Pulse sequence: Proton (spectrum)
Solvent: CDCl3
Date collected: Jun 20, 2014

Temp: 298.0 C / 298.1 K
Sample ID: Operator: main
VARNA-457 "Nanusqct"

 relax: delay 1.000 sec
 Pulse 60.0 degrees
 Acq. time 2.882 sec
 Rep. time 90.0 sec
 Mode: FID, saturated
 Path: 5.0 Hz
 Line broadening 0.3 Hz
 Total time 8 min 26 sec

3.22b

Sample Name: 186601111
Archive directory: /scott/home/marti/mercury/data
Sample directory:  
FileID: 20111520-186601111_Carbon-004

Pulse sequence: Carbon (spectrum)
Solvent: CDCl3
Date collected: Jun 20, 2014

Temp: 298.0 C / 298.1 K
Sample ID: Operator: main
VARNA-457 "Nanusqct"

 relax: delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.140 sec
 Rep. time 90.0 sec
 Mode: FID, saturated
 Path: 3 Hz
 Line broadening 0.3 Hz
 Total time 8 min 26 sec

220 200 180 160 140 120 100 80 60 40 20 0 -20 ppm

2.22b

OTIPS
$\text{Ph} \quad \text{OTIPS} \quad \text{Bn} \quad \text{2N} \quad \text{COOH}$

3.24a (E/Z 6:4 mixture)
Sample Name: 3202105023
Archive directory: /samples/3202105023
Sample directory: /samples/3202105023

Pulse Sequence: Proton (appr)
Detector: GSNI
Data collected on: Apr 19 2011

Temp: 298.0 C / 298.1 K
Sample 1.0, Operator: clean
Number: 001

Spectrometer: Varian
Line broadening: 0.5 Hz
PPM scale: 6000
Total time 10 min 28 sec

Pulse Delay: 10000 usec
Pulse 90 degrees
Avg. time 2.44 sec
Width 4250.7 Hz

Spectrometer: Varian
Line broadening: 0.5 Hz
PPM scale: 6000
Total time 10 min 28 sec
3.24d (E-isomer)

3.24d (Z-isomer)
3.24e

OTIPS

Ph

3.24e

OTIPS
Sample Name: 362
Archive directory: /var/tmp/cheml/mnla/memdir/data
Sample directory:

Identification: 10111120140609083017

Pulse Sequence: FID

Spectrum: 

Data collected on: 3/11/11

Temp. 25.0°C / 298.1 K
Sample size: 1.0 g

OTIPS Ph COOH H N Ph

3.24f OTIPS Ph COOH H N Ph

3.24f

VARIAN

Sample Name: 362
Archive directory: /var/tmp/cheml/mnla/memdir/data
Sample directory:

Identification: 10111120140609083017

Pulse Sequence: FID

Spectrum: 

Data collected on: 3/11/11

Temp. 25.0°C / 298.1 K
Sample size: 1.0 g

OTIPS Ph COOH H N Ph

3.24f OTIPS Ph COOH H N Ph

3.24f

VARIAN
3.24j (d.r. 75:25 mixture)
Detailed X-ray Crystallographic Information of MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17)

Crystallization Conditions: X-ray quality crystals were grown by layering pentane onto a dissolved solution of 3.17 in acetone. The layers slowly mixed, forming crystals.

Table II-1. Crystal data and structure refinement for MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17).

<table>
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<td>C13 H13 B Br N O5</td>
</tr>
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<td>Formula weight</td>
<td>353.96</td>
</tr>
<tr>
<td>Temperature</td>
<td>150(1) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P c a 21</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 13.550(3) Å  a= 90°.</td>
</tr>
<tr>
<td></td>
<td>b = 6.4558(13) Å  b= 90°.</td>
</tr>
<tr>
<td></td>
<td>c = 32.423(7) Å  g = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>2836.2(10) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
</tbody>
</table>
Density (calculated)  
1.658 Mg/m³

Absorption coefficient  
2.918 mm⁻¹

F(000)  
1424

Crystal size  
0.28 x 0.20 x 0.02 mm³

Theta range for data collection  
3.01 to 27.49°.

Index ranges  
-17≤h≤17, -8≤k≤8, -20≤l≤22

Reflections collected  
13204

Independent reflections  
4673 [R(int) = 0.0852]

Completeness to theta = 27.49°  
99.3 %

Absorption correction  
Semi-empirical from equivalents

Max. and min. transmission  
0.952 and 0.787

Refinement method  
Full-matrix least-squares on F²

Data / restraints / parameters  
4673 / 13 / 390

Goodness-of-fit on F²  
1.003

Final R indices [I>2sigma(I)]  
R1 = 0.0829, wR2 = 0.1961

R indices (all data)  
R1 = 0.1518, wR2 = 0.2369

Absolute structure parameter  
0.36(3)

Largest diff. peak and hole  
1.374 and -0.543 e.Å⁻³
Table II-2. Atomic coordinates \( (x \times 10^4) \) and equivalent isotropic displacement parameters \( (\text{Å}^2 \times 10^3) \) for MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17). \( U(\text{eq}) \) is defined as one third of the trace of the orthogonalized \( U_{ij} \) tensor.

<table>
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<th>( y )</th>
<th>( z )</th>
<th>( U(\text{eq}) )</th>
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**Table II-3.** Bond lengths [Å] and angles [°] for MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17).
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B(1A)-N(1A)-C(4A) 101.2(8)
O(4A)-C(1A)-O(2A) 123.9(13)
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O(2A)-C(1A)-C(2A) 111.8(11)
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O(2A)-B(1A)-N(1A) 101.7(9)
O(3A)-B(1A)-N(1A) 103.6(8)
O(2A)-B(1A)-C(6A) 112.8(8)
O(3A)-B(1A)-C(6A)  109.6(8)
N(1A)-B(1A)-C(6A)  117.4(9)
C(13B)-C(6B)-C(7B)  114.4(16)
C(13B)-C(6B)-B(1B)  110.0(16)
C(7B)-C(6B)-B(1B)  115.1(8)
C(13B)-C(6B)-Br(1B)  95.4(14)
C(7B)-C(6B)-Br(1B)  113.6(8)
B(1B)-C(6B)-Br(1B)  106.4(8)
O(1B)-C(13B)-C(6B)  126(2)
C(1B)-O(2B)-B(1B)  113.7(8)
C(4B)-O(3B)-B(1B)  111.9(8)
C(3B)-N(1B)-C(2B)  114.9(10)
C(3B)-N(1B)-C(5B)  110.9(9)
C(2B)-N(1B)-C(5B)  110.8(8)
C(3B)-N(1B)-B(1B)  103.3(7)
C(2B)-N(1B)-B(1B)  103.6(8)
C(5B)-N(1B)-B(1B)  113.0(9)
O(4B)-C(1B)-O(2B)  123.6(12)
O(4B)-C(1B)-C(2B)  126.2(13)
O(2B)-C(1B)-C(2B)  110.0(10)
N(1B)-C(2B)-C(1B)  104.3(9)
N(1B)-C(3B)-C(4B)  108.5(9)
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Symmetry transformations used to generate equivalent atoms:

Table II-4. Anisotropic displacement parameters (Å² x 10³) for MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17). The anisotropic displacement factor exponent takes the form: -2π²[ h² a*² U₁₁ + ... + 2 h k a* b* U₁₂ ]
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<tr>
<td>Br(1D)</td>
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<td>19</td>
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<td>-10</td>
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</table>
Table II-5. Hydrogen coordinates \((\times 10^4)\) and isotropic displacement parameters \((\AA^2 \times 10^3)\) for MIDA (1-bromo-2-oxo-1-phenylethyl)boronate (3.17).
<p>| | | | | |</p>
<table>
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<tr>
<th></th>
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<td>H(13A)</td>
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<td>5216</td>
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<td>H(2AA)</td>
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<td>H(2AB)</td>
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<td>H(5AC)</td>
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<td>H(9AA)</td>
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<td>H(10A)</td>
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<td>H(11A)</td>
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<td>-----</td>
<td>-------</td>
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<td>-------</td>
<td>-----</td>
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<td>H(9BA)</td>
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<td>H(10B)</td>
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<td>6619</td>
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<td>H(12B)</td>
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<td>11122</td>
<td>7103</td>
<td>48</td>
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</tbody>
</table>
Appendix III

Selected Chapter 4 NMR Spectra and X-ray crystal data
Sample Name: 3MB70441BCH_D3_concentrated
Sample directory:

PFS date: 20120411-3MB70441BCH_D3_concentrated

Data collected on: April 11, 2012

Sample: 387°C / 200.2 K
Sample size: 0.5 g
Operator: n/a

Pulse Sequence: Protons (All)

Temperature: 25.0°C / 298.1 K
Sample size: n/a
Operator: n/a

NMR: 600 MHz 60 MHz 60 MHz
60 repetitions

Data Processing
Line broadening: 6.0 Hz
FT size: 32k
Total time: 6 min 26 sec
Sample Name: AX_1_10A
Acq. Directory: /export/home/nxim/sumsys/data samp4 directory:

Pulse Lines: Proton
Pulse sequence: Proton (equl)
Duration: 60 s
Data collected on: Oct 27 2011

Temp: 25.4 C / 77.8 F
Sample HT: Operator: axaj25211
CH600-000 "axaj25211"

Delay: 12700 usec
Pulse: 45.0 degrees
Acq. time: 2.424 sec
VOXEL: 256.7 Hz
1D repetition
S/N ratio: 210.280217 MHz
Data Processing
Line broadening: 5.1 Hz
PT size: extra
Total time 0 min 26 sec
Sample Name:
AE_1.2C
Archive directory:
/sample/home/valeri/valmery/Data
Sample directory:

PROFILES: 20111201-AE_1.2C_ProtOx_Profiles.txt

Pulse Sequence: Proton [alp_ml]
Solvent: DMSO
Data collected on: Oct. 9 2011

Temp: 30.0 C / 84.8 F
Sample 87.484, Operator: sham
Vnmr2: 400 'Spectriq'

Spectrum Delay 1.000 sec
Pulse 45.0 degrees
Acq. Time 2.092 sec
Vnmr 126.7 HZ
16 repetitions

Observe 31, 399.946596 MHz
Data PROCESSING
Gaussian 0.2 Hz
FFT size 4096
Total time 7 min 24 sec

Sample Name:
AE_1.2C_concentrated
Archive directory:

Sample directory:

PROFILES: 20111201-AE_1.2C_concentrated_Carbon-001

Pulse Sequence: Carbon [alp_ml]
Solvent: DMSO
Data collected on: Oct. 9 2011

Temp: 30.0 C / 84.8 F
Sample 88.484, Operator: sham
Vnmr2: 400 'Spectriq'

Spectrum Delay 0.200 sec
Pulse 35.0 degrees
Acq. time 0.300 sec
Vnmr 24.091 HZ
3200 repetitions

Observe 31, 100.000232 MHz
DECouple 31, 399.946294 MHz
Power 40 db
CONTINUOUS on
Data PROCESSING
LINE Broadening 0.5 Hz
FFT size 3201
Total time 8 min 24 sec
Sample Name: 394
Sample Directory:
Profile: 20111117-394052890_DMSO_e6
Pulse Sequence: Proton (2D) 90-180-90
Setting: mass
Data collected on: 2011-11-17

Temp: 25.0 °C / 298.1 K
Sample Size: mass

Delay: 0.00 sec
Pulse 55.0 degrees
Acq. time 1.500 sec

Experiments:
OBSERVE E1, 299.510695 MHz
Data Processing:
Line Broading: 0.5 Hz

Total time: 8 min 24 sec

Sample Name: 394
Sample Directory:
Profile: 20111118-394052890_concentrated_Carbon-001
Pulse Sequence: Carbon (13C) 90-180-90
Setting: mass
Data collected on: 2011-11-18

Temp: 25.0 °C / 298.1 K
Sample Size: mass

Delay: 0.00 sec
Pulse 55.0 degrees
Acq. time 1.500 sec

Experiments:
OBSERVE E1, 299.510695 MHz
Data Processing:
Line Broading: 0.5 Hz

Total time: 8 min 24 sec
Sample Name: JNC-414 PC again
Sample directory: 
Sample directory: 
File: Carbon
Sample Name: JNC-414 PC again
Sample directory: 
Sample directory: 
File: Carbon
Proton
Pulse Sequence: Proton [2pul]
Solvent: Chloroform-d
Data collected on: Feb 9 2012
Temp. 25.0 °C / 198.1 K
Sample 9%, Operator: jpmendic
Varian 400 MHz, 400 MHz
Relax. delay 1.000 sec
Pulse width 8.0 deg/sec
Acq. time 1.500 sec
Spectra 360.0 sec
16 repetitions
OBSERVE (H) 399.34681 MHz
Data Processing
Line Broadening 9.2 MHz
FID time 600 sec
Total time 6 min 24 sec

Sample Name: JNC-414 PC again
Sample directory: 
Sample directory: 
File: Carbon
Sample Name: JNC-414 PC again
Sample directory: 
Sample directory: 
File: Carbon
Proton
Pulse Sequence: Proton [2pul]
Solvent: Chloroform-d
Data collected on: Feb 9 2012
Temp. 25.0 °C / 198.1 K
Sample 9%, Operator: jpmendic
Varian 400 MHz, 400 MHz
Relax. delay 1.000 sec
Pulse width 8.0 deg/sec
Acq. time 1.500 sec
Spectra 360.0 sec
16 repetitions
OBSERVE (H) 399.34681 MHz
Data Processing
Line Broadening 9.2 MHz
FID time 600 sec
Total time 6 min 24 sec
Sample Name: PTO4.a
Data Collected on: multiple-accuracy400
Archive directory:
/home/palmon/tungay/data
Sample directory:
PT04.a
PT04.a
409
Pulse Sequence: PROTON (49.29)
Solvent: dmso
Data collected on: Apr 30 2012
Temp: 25.0 °C / 298.1 K
Sample $15$, Operator: zhao
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.923 sec
WDRS 5000.0 Hz
16 repetitions
OBSESSION 359.274668 MHz
default processing
Line broadening 0.1 Hz
$27$ cycle $27$60
Total time 1 min 3 sec

PTO4.a_concentrated
Sample Name: PTO4.a_concentrated
Data Collected on: multiple-accuracy400
archive directory:
/home/palmon/tungay/data
Sample directory:
PT04.a_concentrated
PT04.a_concentrated
409
Pulse Sequence: CARBON (49.29)
Solvent: dmso
Data collected on: Apr 30 2012
Temp: 25.0 °C / 298.1 K
operator: zhao
Relax. delay 0.000 sec
Pulse 45.0 degrees
Acq. time 1.142 sec
WDRS 34590.5 Hz
1696 repetitions
OBSESSION 115.39987177 MHz
EXCELLE 115.39987177 MHz
PUSHER 11 DB
continuously on
WALTZ-16 modulated
default processing
Line broadening 0.5 Hz
$27$ cycle $27$60
Total time 1 hr. 44 min
Sample Name: E8760862
Data Collected on: 4/6/2012
Archive directory: /home/xilinx/xmry/data
Sample directory: E8760862_01
File date: 20120606 mercury_400 E8760862_PROTON_61-M405579-201206060815
Pulse Sequence: FROTON (H0G1)
Solvent: ocmn
Data collected on: May 4, 2012

Temp: 25.0 C / 298.1 K
Sample #43, Operator: xbe0
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.044 sec
Width 438.8 Hz
16 repetitions

Spectra:
410 MHz, 395.368794 MHz
DATA PROCESSING
Line broadening 0.1 Hz
DT ratio 1/16
Total time 1 min 13 sec
<table>
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<th>ppm</th>
<th>13</th>
<th>12</th>
<th>11</th>
<th>10</th>
<th>9</th>
<th>8</th>
<th>7</th>
<th>6</th>
<th>5</th>
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<th>3</th>
<th>2</th>
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<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

**Sample Name:**

`PTCB_02`

**Acquire Directory:**

`/Users/student/varian/vnmrj/data`

**Sample Directory:**

`/Users/student/varian/vnmrj/data`

**Pulse Sequence:**

`Proton (zgsp)`

**Solvent:**

`d8-DMSO`

**Data collected on:** Apr 22 2012

**Temp:** 298.1 K

**Sample Size:** 1.0 g

**Operator:** shao

**Vnmrj 400:**

`Eurospin`

**Delay:** 1.000 sec

**Delay setting:** 1.0000 deg/sec

**Arg. time:** 2.000 sec

**Width:** 1.677 Hz

**N rep.:** 10 repetitions

**Gershon:** 399.346965 MHz

**Data Processing:**

`Line Broadening: 9.2 Hz`

**FT atten:** 67500

**Total time:** 0 min 28 sec

---

**Sample Name:**

`PTCB_02_concentrated`

**Acquire Directory:**

`/Users/student/varian/vnmrj/data`

**Sample Directory:**

`/Users/student/varian/vnmrj/data`

**Pulse Sequence:**

`Carbon (zgsp)`

**Solvent:**

`d8-DMSO`

**Data collected on:** Apr 22 2012

**Temp:** 298.1 K

**Operator:** shao

**Delay:** 1.000 sec

**Delay setting:** 1.0000 deg/sec

**Arg. time:** 2.000 sec

**Width:** 2.613 Hz

**N rep.:** 10 repetitions

**Gershon:** 399.752500 MHz

**Data Processing:**

`Line Broadening: 9.2 Hz`

**FT atten:** 67500

**Total time:** 0 min 28 sec
Sample Name: 

Data Collected On: 

Archive Directory: 

Sample Directory: 

Pulse sequence: PROTON (29.10)

Solvent: dca

Data collected on: May 7, 2012

Temp: 20.0°C / 298.1 K

Sample 1

MeN

Ph

Br

4.19b

MeN

Ph

Br

4.19b

4.19b
Sample Name: 5AE102952
Data Collected on: 2012-02-03
Archive Directory: C:\\data
Sample Directory: 5AE102951_01
File Name: 5AE102951

Pulse Sequence: CARBON (500 MHz)
Solvent: CDCl3
Data collected on: May 09 2012

Temp. 29.0 °C / 298.1 K
Sample %: 1.000 mmol
Pulser 80.0 degrees
Acq. time 2.250 sec
MHzG 25626.8 Hz
5000 repetitions
ORDER C125, 129.4421676 MHz
DECOMPLEX ML 399.9302168 MHz
Power 41 dB continuous on
MULTI-JR EQUIVALENT

DATA PROCESSING
Line broadening 3.5 Hz
FT size 65536
Total time 3 hr. 14 min
Detailed X-ray Crystallographic Information of MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a)

Crystallization Conditions: X-ray quality crystals were grown by layering hexanes onto a dissolved solution of 4.23a in acetone. The layers slowly mixed, forming crystals.

Table III-1. Crystal data and structure refinement for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a).

<table>
<thead>
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<th>Property</th>
<th>Value</th>
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<td>Identification code</td>
<td>d12187</td>
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<tr>
<td>Empirical formula</td>
<td>C13 H12 B N O6</td>
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<tr>
<td>Formula weight</td>
<td>289.05</td>
</tr>
<tr>
<td>Temperature</td>
<td>147(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54178 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Tetragonal</td>
</tr>
<tr>
<td>Space group</td>
<td>I 41/a</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 29.1725(13) Å</td>
</tr>
<tr>
<td></td>
<td>a= 90°.</td>
</tr>
<tr>
<td></td>
<td>b = 29.1725(13) Å</td>
</tr>
<tr>
<td></td>
<td>b= 90°.</td>
</tr>
<tr>
<td></td>
<td>c = 6.4246(3) Å</td>
</tr>
<tr>
<td></td>
<td>g = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>5467.6(4) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>16</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.405 Mg/m³</td>
</tr>
</tbody>
</table>
Absorption coefficient 0.941 mm\(^{-1}\)

F(000) 2400

Crystal size 0.12 x 0.12 x 0.08 mm\(^3\)

Theta range for data collection 3.03 to 66.51\(^\circ\).

Index ranges -34\(\leq\)h\(\leq\)34, -26\(\leq\)k\(\leq\)33, -7\(\leq\)l\(\leq\)7

Reflections collected 17078

Independent reflections 2379 [R(int) = 0.0383]

Completeness to theta = 66.51\(^\circ\) 98.8 %

Absorption correction Semi-empirical from equivalents

Max. and min. transmission 0.7528 and 0.6918

Refinement method Full-matrix least-squares on F\(^2\)

Data / restraints / parameters 2379 / 0 / 191

Goodness-of-fit on F\(^2\) 1.062

Final R indices [I>2\(\sigma\)(I)] R1 = 0.0443, wR2 = 0.1147

R indices (all data) R1 = 0.0505, wR2 = 0.1202

Largest diff. peak and hole 0.360 and -0.306 e.Å\(^{-3}\)

Table 2. Atomic coordinates (x 10\(^4\)) and equivalent isotropic displacement parameters (Å\(^2\)x 10\(^3\)) for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a). U(eq) is defined as one third of the trace of the orthogonalized U\(^{ij}\) tensor.

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U(eq)</th>
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<tbody>
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<td>O(1)</td>
<td>9784(1)</td>
<td>3580(1)</td>
<td>132(2)</td>
</tr>
<tr>
<td>Element</td>
<td>x</td>
<td>y</td>
<td>z</td>
</tr>
<tr>
<td>---------</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>O(2)</td>
<td>10278(1)</td>
<td>3024(1)</td>
<td>-581(2)</td>
</tr>
<tr>
<td>O(3)</td>
<td>9254(1)</td>
<td>3816(1)</td>
<td>2832(2)</td>
</tr>
<tr>
<td>O(4)</td>
<td>9017(1)</td>
<td>3606(1)</td>
<td>5984(2)</td>
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<tr>
<td>O(5)</td>
<td>9892(1)</td>
<td>4522(1)</td>
<td>-876(2)</td>
</tr>
<tr>
<td>O(6)</td>
<td>9373(1)</td>
<td>4851(1)</td>
<td>3403(2)</td>
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<tr>
<td>N(1)</td>
<td>10077(1)</td>
<td>3844(1)</td>
<td>3449(2)</td>
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<tr>
<td>C(1)</td>
<td>10350(1)</td>
<td>3454(1)</td>
<td>2608(4)</td>
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<td>C(2)</td>
<td>10143(1)</td>
<td>3323(1)</td>
<td>551(3)</td>
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<tr>
<td>C(3)</td>
<td>9818(1)</td>
<td>3709(1)</td>
<td>5339(3)</td>
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<tr>
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<td>9320(1)</td>
<td>3699(1)</td>
<td>4808(3)</td>
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<td>3883(4)</td>
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<td>9653(1)</td>
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<td>C(7)</td>
<td>9334(1)</td>
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<td>1538(3)</td>
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<td>C(8)</td>
<td>8999(1)</td>
<td>5022(1)</td>
<td>189(3)</td>
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<td>C(9)</td>
<td>8767(1)</td>
<td>5402(1)</td>
<td>978(4)</td>
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<td>C(10)</td>
<td>8442(1)</td>
<td>5619(1)</td>
<td>-232(5)</td>
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<td>C(11)</td>
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<td>-2193(5)</td>
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<td>C(12)</td>
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<td>5081(1)</td>
<td>-2981(4)</td>
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<td>C(13)</td>
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<td>B(1)</td>
<td>9676(1)</td>
<td>3919(1)</td>
<td>1717(3)</td>
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Table III-3. Bond lengths [Å] and angles [°] for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a).

<table>
<thead>
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<th>Bond</th>
<th>Length</th>
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<td>O(1)-C(2)</td>
<td>1.315(2)</td>
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<tr>
<td>O(1)-B(1)</td>
<td>1.454(2)</td>
</tr>
<tr>
<td>O(2)-C(2)</td>
<td>1.201(2)</td>
</tr>
<tr>
<td>O(3)-C(4)</td>
<td>1.329(2)</td>
</tr>
<tr>
<td>O(3)-B(1)</td>
<td>1.454(2)</td>
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<tr>
<td>O(4)-C(4)</td>
<td>1.194(2)</td>
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C(8)-C(13)  1.386(3)
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C(11)-H(11A)  0.9500
C(12)-C(13)  1.382(3)
C(12)-H(12A)  0.9500
C(13)-H(13A)  0.9500

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C(4)-O(3)-B(1)  113.62(14)
C(5)-N(1)-C(3)  110.50(17)
C(5)-N(1)-C(1)  111.59(19)
C(3)-N(1)-C(1)  111.51(19)
C(5)-N(1)-B(1)  115.78(15)
C(3)-N(1)-B(1)  103.24(13)
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N(1)-C(1)-C(2)  107.28(16)
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O(3)-B(1)-C(6) 111.20(15)
O(1)-B(1)-N(1) 103.33(14)
O(3)-B(1)-N(1) 104.11(13)
C(6)-B(1)-N(1) 116.34(14)

Symmetry transformations used to generate equivalent atoms:

Table III-4. Anisotropic displacement parameters (Å²x 10³) for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a). The anisotropic displacement factor exponent takes the form: -2p²[ h² a*² U₁₁  + ... + 2 h k a* b* U₁₂ ]

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**Table III-5.** Hydrogen coordinates (x \(10^4\)) and isotropic displacement parameters (Å\(^2\)x \(10^3\)) for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a).
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Table 6. Torsion angles [°] for MIDA (1,2-dioxo-2-phenylethyl)boronate (4.23a).
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C(3)-N(1)-B(1)-O(1) -118.46(16)
C(1)-N(1)-B(1)-O(1) -2.0(2)
C(5)-N(1)-B(1)-O(3) -121.07(19)
C(3)-N(1)-B(1)-O(3) -0.20(19)
C(1)-N(1)-B(1)-O(3) 116.27(19)
C(5)-N(1)-B(1)-C(6) 1.6(2)
C(3)-N(1)-B(1)-C(6) 122.52(17)
C(1)-N(1)-B(1)-C(6) -121.0(2)

Symmetry transformations used to generate equivalent atoms: