The Use of a Nitrone to form substituted Isoquinolines via Boron-mediated Transfer

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by

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List of Abbreviation

NMR	Nuclear Magnetic Resonance
BNMR	Boron Nuclear Magnetic Resonance
HNMR	Proton Nuclear Magnetic Resonance
TLC	Thin Layer Chromatography
THIQ	Tetrahydroisoquinoline
THIQ-nitrone	Tetrahydroisoquinoline-nitrone
C-C	Carbon – Carbon
THF	Tetrahydrofuran
KHF_2	Potassium bifluoride
BH_3THF	Borane-tetrahydrofuran complex
K_2CO_3	Potassium Carbonate
BH_3	Borane, Borhydride
TMSCl	Trimethylsilyl chloride
B_2H_6	Diborane
MTBE	Methyl-tert-butyl ether
TMANO	Trimethylamine N-oxide
TMSF	Trimethylsilyl fluoride
UV	Ultraviolet

Introduction

C-C bond formation is still the most attention-grabbing and important strategy in synthetic organic chemistry, especially in the synthesis of organic compounds. The bonding properties of carbon atoms are important, mostly in those living organisms. In addition, Nitrogen is an essential element for all living organisms and plays a crucial part in various biological and physiological processes. The production of nitrogenous bases, which are essential for the formation of life-sustaining molecules, starting from its role in nitrogen cycle, to keep the ecosystem running to its chemical involvement in protein synthesis. One interesting nitrogen derivative is nitrone. They are a functional group and have been used in various synthesis, starting from spin traps to stabilize free radical intermediates to forming 5-membered rings in 1,3-dipolar cycloaddition reactions. However, have they ever been used to make new C-C single bonds? This goal is tried to achieve through combining them with organoboranes. The catalytic approach in this work, the formation of a carbon-carbon bond via boron-mediated transfer, will bring new pathways to the organic chemistry field. It allows to find new diverse products and offers versatility for further modification.

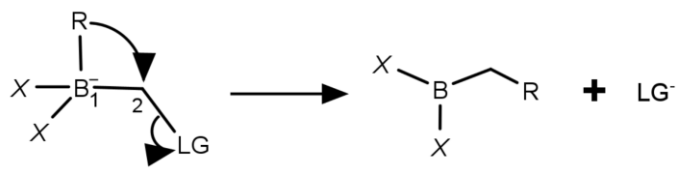
Boron mediated transfer

Boron transfers are really useful in organic chemistry, when making or changing organic molecules. They help create new bonds between carbon atoms, and that's what we are focusing on, in our work. We know, boron-enolate chemistry and Suzuki based coupling result in C-C bonds, but it doesn't lead to boron being directly involved in the formation of these bonds.[1]

Boron transfers occur when a carbon-containing nucleophilic moiety is migrating from boron to a nearby electrophilic carbon. There hasn't been a review and classification on the carbon-carbon bond formation through boron mediated transfer. The intention is to have a layout for in future to categorize various boron-mediated reactions. The classification of boron-mediated transfer is sorted by numbering from boron to the carbon center where the new bond is to be formed. These are examples to show boron mediated transfers being directly involved in the formation of a new carbon-carbon bond.[1]

1,2- boron-mediated transfer

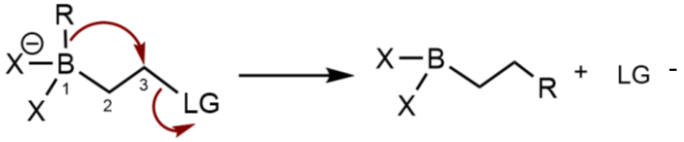
If the carbon is immediately next to the boron, it is called a 1,2-boron-mediated transfer, starting at the α,β-unsaturated boron, and ending at the electrophilic α-positioned carbon, where a new bond is formed adjacent to the boron. The X represents any non-participating group, and the R represents a carbon-containing group (Scheme 1).[1]



Scheme 1: 1,2-boron-mediated transfer

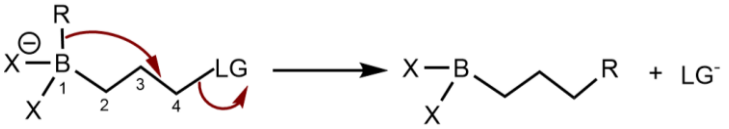
This pattern will be visible in many common reactions with boron. For instance, hydroboration-oxidation, the oxidation is categorized as carbon-oxygen bond formation through a boron mediated 1,2-transfer. Shown through these cases, the arrangement would continue in the same pattern up to 1,6 boron-mediated transfer.[1]

1,3- boron-mediated transfer



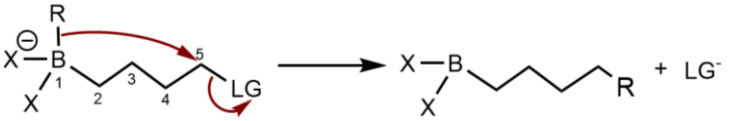
Scheme 2: 1,3-boron-mediated transfer

1,4- boron-mediated transfer



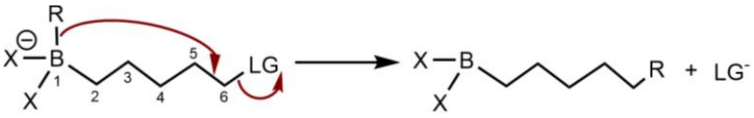
Scheme 3: 1,4-boron-mediated transfer

1,5- boron-mediated transfer



Scheme 4: 1,5-boron-mediated transfer

1,6- boron-mediated transfer



Scheme 5: 1,6-boron-mediated transfer

Over time, there have been significant developments in organoboron chemistry, leading to big changes in general methodology of synthetic organic chemistry. The utility of boron has been illustrated in many reactions.[1]

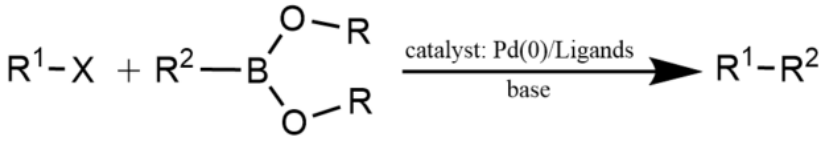
Organoboranes

Organoboranes are organic compounds, which contain a boron-carbon bond. They are synthesized through various different techniques, including borylation of organic halides, hydroboration, and metal-catalyzed cross-coupling reactions. Organoboranes are also used in the production of medicines, agrochemicals, and functional substances. Their distinguishing characteristics, such as Lewis acidity and steric effects, make them useful tools in synthetic chemistry.

Typical outcomes of these synthesis are trialkyl boranes, BR_3. The C-B σ-single bond has a low polarity but are bench stable and easy to oxidize. Another example is boronic acid, $B(OH)_3$. They act as Lewis acids. They have been used in Suzuki coupling reactions or oxidations.[2,3]

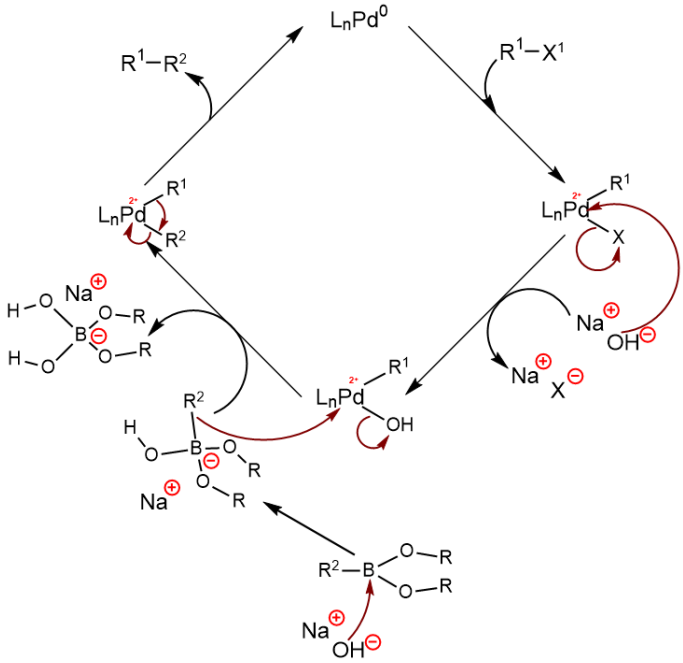
Suzuki cross coupling

Since the 1970s, transition-metal-catalyzed cross-coupling reactions were of curiosity. This reaction involves oxidative addition step, following with transmetallation and a reductive elimination steps. The majority of these cross-coupling reactions are catalyzed by Nickel(0), Palladium(0), and Iron(I).[2,3] (Scheme 6)



Scheme 6: Suzuki cross-coupling reaction

In the oxidative addition step, to a palladium complex, 1-alkenyl, 1-alkynyl, allyl, benzyl and aryl halides are added to form a stable trans-σ-palladium(II)-complex. reacts with an aryl halide to form a cis complex which then isomerizes to its trans isomer. The transmetallation step involves the transfer from the organoborane to the palladium center. The reaction is stereo- and regiospecific, providing a convenient method for the synthesis of various organic compounds (Scheme 7).[2–4]



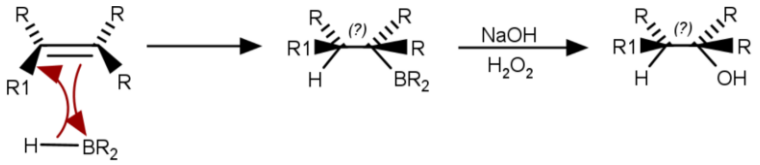
Scheme 7: Mechanism of Suzuki cross-coupling reaction[4]

Suzuki cross-coupling is a metal-mediated reaction. This project doesn't include any type of metallic elements. On the contrary, the goal of this project is to find bench stable and easy to handle, health and environmentally friendly compounds in reactions to execute.

Hydroboration-Oxidation

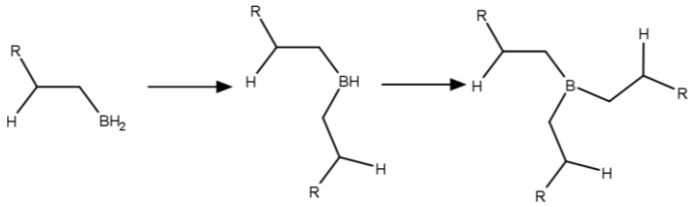
The hydroboration-oxidation reaction is a two-step process in which alkenes are converted into alcohols. In the hydroboration step, borane (B_2H_6), can also react as BH_3, is electron deficient and ready to react with π-bonds. This type of reaction is regioselective, the boron atom adds to the least substituted end of a double bond, and stereospecific, in syn-addition, thus the B and H atoms always face the same side of

the double bond during the addition. First step is focusing on the regioselective addition of the alkene π-bond to a B-H bond. After the hydroboration, hydrogen peroxide is added for the oxidative cleavage of C-B bonds. Through addition of water, the OH group adds to the least substituted end of the double bond (Scheme 8).[5]



Scheme 8: General reaction of Hydroboration-Oxidation

If BH_3 is used, the hydroboration takes place three times, which forms a trialkylborane (Scheme 9).[5]



Scheme 9: Hydroboration of BH_3 to generate trialkylboranes

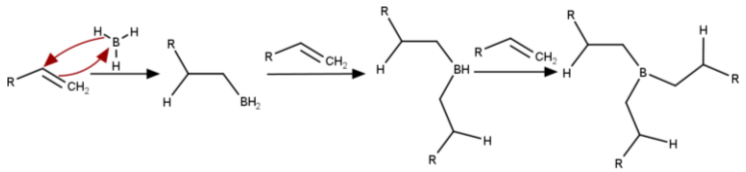
Both reactions reflect characteristics of the topic of this work and the aim for carbon-carbon bond formation via boron-mediated transfer. Boron was directly involved in both reactions.

Trialkylboranes

Trialkylboranes are compounds which have a boron atom bonded to three alkyl appendages. They can be synthesized through the reaction of amine-boranes with olefins or as mentioned, through hydroboration of BH_3. Based on the empty p-orbital on boron, trialkylboranes are electrophilic and Lewis acidic, and they readily coordinate with nucleophiles to synthesize boron ate-complexes. These complexes are essential in the main structure of trialkylborane transformations, which result in carbon-carbon and carbon-heteroatom bond formation steps. The trialkylboranes are monomeric, thermally stable, and can be isolated. However, they undergo isomerization at higher temperatures, with the boron atom migrating to the less hindered position. Some hindered trialkylboranes can undergo isomerization even at lower temperatures. They do not readily react with typical electrophiles and are not sensitive to protonating agents or hydrolysis. Their low nucleophilicity allows them to tolerate a variety of electrophilic functional groups, making them useful in C-C and carbon-heteroatom bond-forming reactions. They are relatively stable, not sensitive to air nor moisture. They can undergo olefin elimination to synthesize many different functional groups, like ketones, nitriles, and esters. Therefore, they are mostly stored in solvents to prevent any pre-reactions.[6]

Synthesis of Trialkylboranes

The synthesis of trialkylboranes through hydroboration-oxidation typically involves the reaction of an alkene with diboranes as well (B_2H_6). During the Hydroboration, an intermediate boron-carbon is formed. This reaction follows an anti-Markovnikov regioselectivity (Scheme 10).[7]

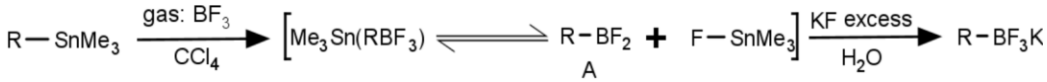


Scheme 10: Hydroboration-oxidation reaction mechanism of diboranes to generate trialkylboranes

Trifluoroborates

Organoboranes have become popular and important organometallic reagents, playing an important role in the formation of carbon-carbon bonds. One of them are trifluoroborates which contain an anion. Organotrifluoroborates are in general solids, which can be purified through precipitation. They are resistant to air, moisture and can be stored for very long on the bench without further precautions. They are strong nucleophiles and react with electrophiles in absence of transition-metal catalysts and possess a strong balance of stability to reactivity. One common way they are synthesized from, is trifluoroborane etherate reacting with potassium bifluoride in trimethyltin solution to form trifluoroborate salts. Many other counterions were used to stabilize trifluoroborate products, but the most stable was potassium trifluoroborate derivative.[8]

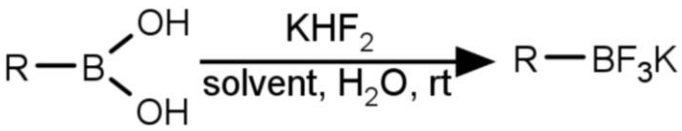
A R-group transfer led to the formation of the intermediate (**A**). Due to the boron atom having strong acceptor properties in the trivalent intermediate, it was not possible to isolate this compound. However, as a chemical valence of four ion, the compound was more stable and isolable as ionic pair (Scheme 11).[9]



Scheme 11: First published synthesis of potassium organotrifluoroborate

Potassium organotrifluoroborate

The first announced synthesis of potassium organotrifluoroborate, started by using trimethyltin derivatives. The wanted compounds were treated with the reagents trifluoroborane and an excess of potassium fluoride. Due to toxicity issues, other solutions were tried with the final result, the use of potassium hydrogen fluoride. Potassium organoborates can be directly obtained by converting boronic acid and its derivatives into the target compound by aqueous treatment with KHF_2 (Scheme 12).[9]



Scheme 12: Reaction of potassium organotrifluoroborate

Boron NMR spectroscopy

Nuclear Magnetic Resonance is a physical method used to observe Carbons and Hydrogens. It gives useful information on their structure and properties. NMR spectroscopy includes the interaction of atomic nuclei with a high magnetic field and radiofrequency radiation. When placed in a magnetic field, the nuclei align with the field and can absorb and emit energy at precise frequencies. NMR can determine the chemical environment and connectivity of the atoms in a compound. In the case of boron compounds, NMR can be used to examine the chemical shifts and number of

peaks in the spectra. One common tool that we are using to understand the reactions and results is Boron NMR. In this huge field of chemistry, Boron NMR spectroscopy is one most economical and fastest method to determine structures with a boron skeleton. There are two naturally occurring NMR active boron isotopes: ^{10}B and ^{11}B. ^{11}B is commonly seen as more suitable for NMR because of its higher sensitivity, broader resonance, and better resolution. In $^{11}BNMR$, certain peaks will be various times visible and will be highlighted in this research project (Figure 1).[10,11]

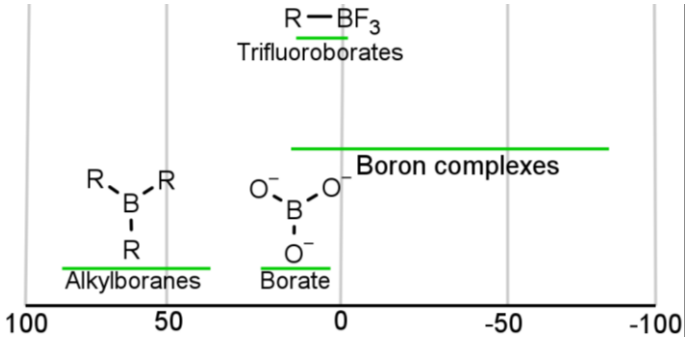
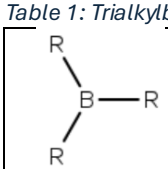
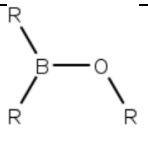
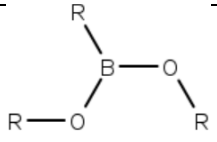
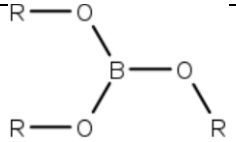
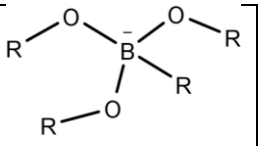


Figure 1: A general depiction of a boron spectrum

Further, the range of trialkylboranes are broken down, since we are working with them and analysing their behaviour after the reactions to confirm with the table, their appearance in the NMR analysis. Through the synthesis of trialkylboranes, the location of the peaks in the boron NMR can be explained. The starting material triisopropylborane reacts with lithium triethyl borohydride or ethyl Grignard. Each of the isopropyl groups are displaced with an ethyl anion. One displacement leads to a peak at 32ppm, after another displacement, it shows a peak at 52ppm up to all displaced parts showing a final peak at 82ppm. This explains the positions of the peaks visible at their distinct positions of the trialkylboranes. Therefore, three alkyl-appendages show a peak at 80ppm. One heteroatom and two alkyl-appendages show a peak at 50 ppm. Two heteroatoms and one alkyl-appendage show a peak at 30 ppm. All three heteroatoms show a peak at 18 ppm. At 0 ppm we have a boron ate-complex.

Table 1: Trialkylboranes with various heteroatoms

				
80 ppm	50 ppm	30 ppm	18 ppm	0ppm

Amines

Amines are weak organic bases that can hydrogen bond with each other. They are naturally found in proteins, vitamins, alkaloids, and are also manufactured for use in polymers and medicines. One way of making amines is alkylation of Ammonia with alkyl halide. It's a nucleophilic aliphatic substitution. Also usually formed from nitro compounds, amides, etc. They react with water to produce alkylammonium ions and hydroxide anions, and with acids to produce alkylammonium salts. The number of alkyl or aryl groups connected to the nitrogen atom determines whether an amine is primary, secondary, or tertiary. Amines are classified into primary amines, which include only

one alkyl or aryl group, secondary amines contain two, and tertiary amines containing three. The three types of amines have an unshared electron pair on the nitrogen which leads them to behave as Lewis bases. (Figure 2)[12]

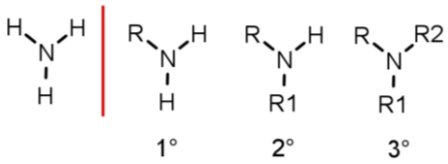
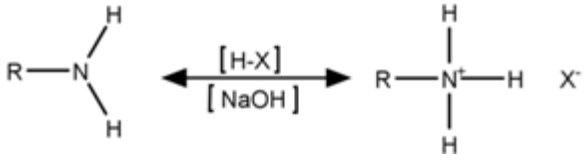


Figure 2: types of amines: primary, secondary, tertiary amines

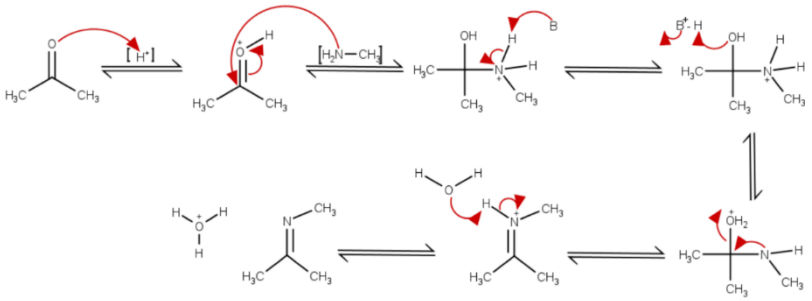
Use of amines

They have been used in reactions as proton base. A protonation of amines with acids is completely converted to Aminium salts. These salts are formed from primary, secondary, and tertiary amines and aminium ion with one Hydrogen. This reaction is also reversible, which is also called deprotonation (Scheme 13).[13]



Scheme 13: Reversible reaction from primary amine to ammonia

Imines are made by combining an aldehyde or ketone with a primary amine. Because an amine is introduced and water is eliminated during this process, the reaction is known as a nucleophilic addition-elimination reaction. Protonation activates a carbonyl, which makes it easier for a primary amine to attack the electrophilic C. Removing a proton, neutralizes and forms an intermediate carbinolamine. Deprotonation of the iminium N releases the imine product (Scheme 14).[13]



Scheme 14: Mechanism with ketone to synthesize imine

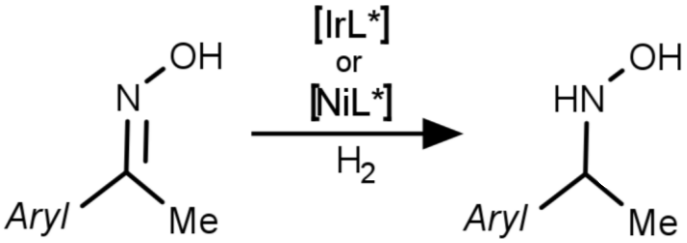
Hydroxylamines

Their unique chemical structure and flexible synthetic intermediates, makes hydroxylamines more and more a commonly used asset in pharmaceutical and agrochemicals. Due to competing chemo selectivity, metal catalyst deactivation, and ease of overoxidation, direct oxidation of amines to hydroxylamines in a catalytic asymmetric manner is challenging.

Synthesis

Utilizing a catalytic asymmetric approach, enantioselective oxidation of amines can be used to create hydroxylamines. A suitable metal complex with oxygen transfer reactivity and reversible coordination ability is required for this process to be used for

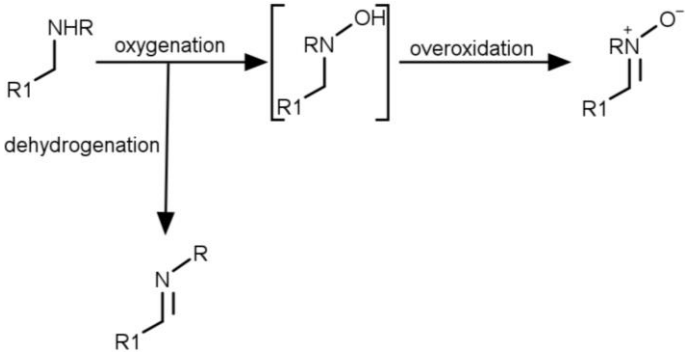
an amine oxidation to hydroxylamines. Titanium-catalyzed asymmetric oxidation of racemic amines has been developed. This technique uses simple titanium complexes as the catalyst and hydrogen peroxide as the oxidant. Hydroxylamines, including ester-alkyl, amide-alkyl, aryl-alkyl, and alkynyl-alkyl, are well tolerated and have good functional group compatibility. The chiral titanium complex coordinates with the amine substrate. The oxidant reacts with the titanium complex, forming an intermediate, titanium-peroxo. A nucleophilic attack occurs on the amine substrate, which leads to the formation of an imine. The last step is a hydrolysis which finally results in a hydroxylamine product (Scheme 15).[14]



Scheme 15: Reaction of N-OH oxime to synthesize hydroxylamine

The first big challenge in the oxidation of amines to hydroxylamines is the formation of another compound due to dehydrogenation. While oxygenation introduces an oxygen atom to the amine substrate to form the hydroxylamine product, an undesirable dehydrogenation side reaction can occur, caused by high reaction temperatures, extended reaction time, catalyst not selective towards the substrate and impurities which lead to the formation of imines or imine oxides.[14]

The second big challenge in the oxidation of amines to hydroxylamines is the formation of another compound, a nitrone, due to overoxidation. This unwanted side reaction can occur due to high reactive intermediate formation, excessive oxidant and a non-selective catalyst or overly active catalyst, which remains active after the desired oxidation state (Scheme 16).[14,15]

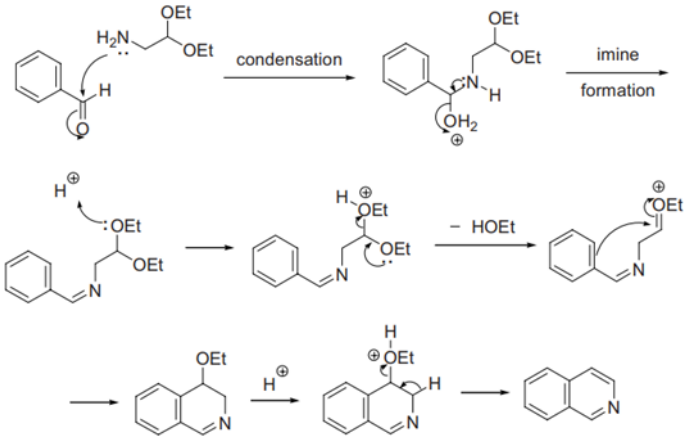


Scheme 16: Depiction of the challenges of dehydrogenation and overoxidation

Isoquinoline Alkaloids

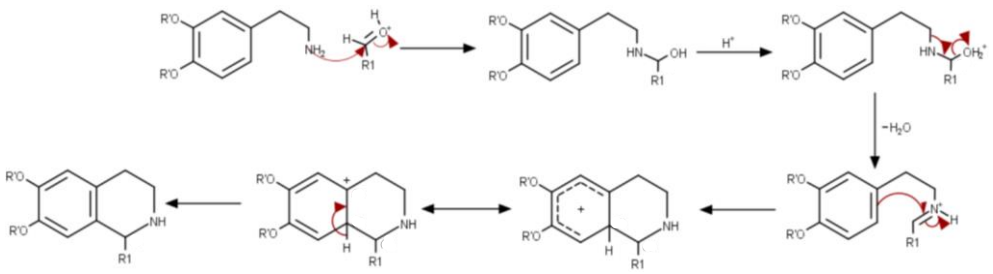
Isoquinoline, a heterocyclic aromatic organic compound, was first isolated in 1885 from coal tar by Hoogewerf and van Drop. Coal tar is derived from coal and is a byproduct of coke, a solid that contains carbon and coal gas. Isoquinoline has one of many biological activities which are anti-HIV, antitumor, antimicrobial, antibacterial, Parkinsons disease, etc. They also come from Cactaceae, Fabaceae cacti families. [15]

In correlation with pyridine, isoquinoline is a weak base. It protonates to form salts with strong acids. It also forms attachments with Lewis acids. There are many methods on how to synthesize isoquinolines, yet no direct methods lead to substituted isoquinoline. One efficient method is the Pomeranz-Fritsch reaction. Isoquinoline is synthesized through an acid-mediated cyclization of an amino acetal intermediate. The amino acetal intermediate is protonated by an acid, which forms a carbocation. The carbocation undergoes an intramolecular cyclization, which results in a cyclic intermediate, which then rearranges to an iminium ion. Final step is a reduction to get the isoquinoline product (Scheme 17).[15]



Scheme 17: Pomeranz-Fritsch reaction for tetrahydroisoquinoline

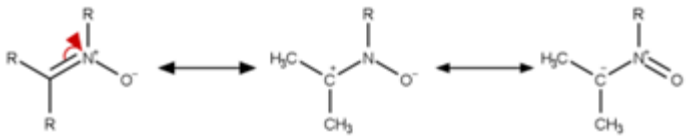
One of the derivatives are tetrahydroisoquinoline, which is a natural product class that belongs to the isoquinoline alkaloids family. THIQ-based compounds have demonstrated a wide range of biological activity against infections and neurological diseases. They have been utilized as anti-inflammatory, anti-bacterial, anti-viral, anti-fungal, anti-leishmanial, anti-cancer, and anti-malarial agents. One way of synthesizing THIQ is the Pinctet-Spengler reaction. It's a two-step chemical cyclization reaction discovered by Amé Pinctet and Theodor Spengler in 1911. They heated b-phenylethylamine and formaldehyde dimethyl acetal in the presence of HCl. It formed an alkaloid 1,2,3,4-tetrahydroisoquinoline. A protonation of carbonyl oxygen is occurring by the acid, which is attacked by the amine reagent. An iminium intermediate is formed which releases a water molecule. That undergoes a 6-endo-tri cyclization reaction. Final step is a deprotonation step that restores the aromaticity and gives the product THIQ. They have a stereo genic center at the C1-carbon and various oxidation patterns on the arene ring (Scheme 18).[16]



Scheme 18: Pictet-Spengler mechanism for Tetrahydroisoquinoline

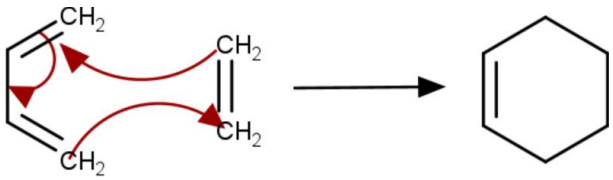
Nitrones

Nitrones are a functional group. It is an Imine containing an N-oxide. It is capable to resonance, but the first structure contributes most to different type of reactions. This resonance stabilization allows nitrones to act as radical traps, reacting with short-lived free radicals and forming stable nitroxide radicals (Scheme 19).[17]



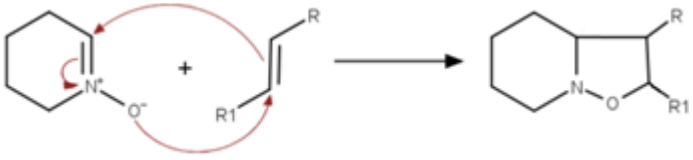
Scheme 19: Resonance structure

Nitrones are neutral, although they have a nitrogen positively and oxygen negatively charged. Nitrogen has a lone pair of electrons, the number of positive and negative charge is equal, which leads to a net charge of zero. They are used in various fields. Nitrones are used in the medical field as radical spin trapping agents and act as antioxidants against diseases with oxidative stress. Radical traps are compounds designed to intercept and stabilize reactive radicals in chemical reactions. Due to nitrones active carbon nitrogen double bond, it traps reactive oxygen and nitrogen. They have already been used against hearing loss, stroke, neurodegenerative disorder, and cancer. They also have anti-inflammatory, anti-apoptotic and NO-releasing properties.[18,19] A common and known reaction is the [4+2] Diels-Alder reaction. A conjugated diene group and alkene, also dienophile, form a cyclohexene. Good dienophiles, which are electron withdrawing groups, are conjugated carbonyls, like aldehydes and ketones. Dienes are the electron donating groups (Scheme 20).[20]



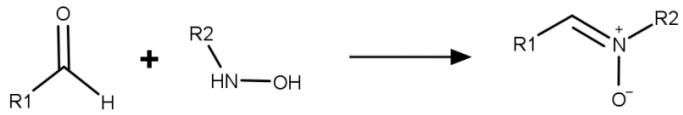
Scheme 20: General reaction scheme of Diels-Alder reaction

Nitrones are 1,3-dipolar species which undergo a similar method, the [3+2] cycloaddition reaction, also known as Huisgen 1,3-Dipolar Cycloaddition, with alkenes, also called dipolarphile, and results in isoxazolidines (Scheme 21). The formation of a C-C bond and a nitrogen and oxygen atom are introduced. These can be further converted into amine and alcohol functionalities. [21]



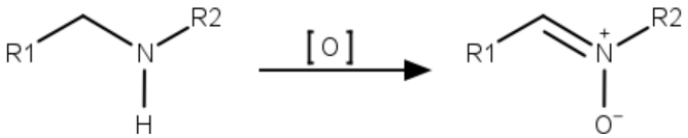
Scheme 21: Reaction of [3+2] cycloaddition

They are synthesized through condensation of aldehydes with N-monosubstituted hydroxylamines. Through a nucleophilic addition-elimination reaction, aldehyde reacts with the N-monosubstituted hydroxylamines and form an intermediate imine. This oxidizes to a nitrone (Scheme 22).[22]



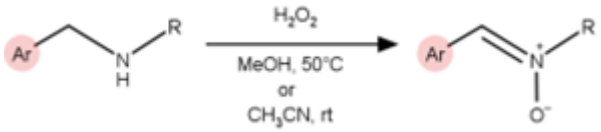
Scheme 22: Reaction of the synthesis of a nitrone

Typically, nitrones are from oxidized secondary amines. However, due to the conflict between C-N bond formation and N-O bond formation, it can be challenging to form N-O bonds. This is a two-step process. First, the secondary amine will be oxidized to form an imine intermediate. Various oxidizing reagents can be used, among them mercury(II) oxide. In the second step, the imine intermediate is further oxidized to form the target compound nitrone. This step can be catalyzed diversely, among them palladium black catalyst (Scheme 23).[23]



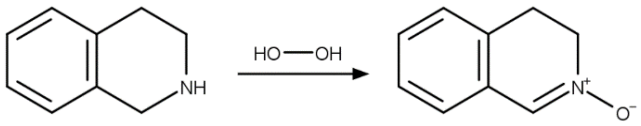
Scheme 23: Oxidation reaction of secondary amine to nitrone

The use of toxic heavy metal, as mercury oxide, has a negative impact on the ecosystem and human health. If not carefully handled can lead to kidney damage. Mercury is persistent in the environment and can be stored in organisms, which leads to long-term contamination and harm to wildlife. The shortcomings in these methods are inaccessibility of precursors and problem of finding regioselectivity in the oxidation reaction. Our focus relied on these matters. To reduce these issues, a well-developed approach was established in the laboratory of Granato et. al. (Scheme 24).[24]



Scheme 24: Oxidation reaction of nitrone in laboratory of Granato et. al.

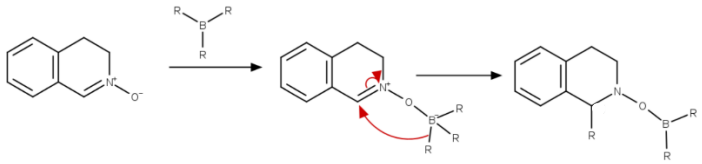
We are using 1,2,3,4-Tetrahydroisoquinoline and hydrogen peroxide 30%, both very versatile, health and environmentally friendly compounds to synthesize 1,2,3,4-THIQ-nitrone. The benzylic secondary amine reacts with hydrogen peroxide in the presence of a solvent, such as Methanol. We used acetonitrile. The hydrogen peroxide undergoes a cleavage which forms a hydroxyl radical. The amine then oxidizes by the radical to form a N-oxide intermediate. It undergoes more oxidation or a rearrangement to form the N-O double bond characteristic, also leads to a loss of water molecule. Then the target compound, nitrone, is extracted and purified. (Scheme 25)



Scheme 25: Oxidation reaction of nitrone

All the steps were performed as in the work of Granato et. al.[24] starting from a smaller to a bigger mmol scale. Additionally, the solvent acetonitrile was used, and a little more Hydrogen peroxide was added then the minimum requirement for more purified crude product development.

The center of this work is a small part of this huge topic. The focus lies on reacting 1,2,3,4-tetrahydroisoquinoline-nitrone with all possible trialkylboranes and organotrifluoroborates, provided in the laboratory space (Scheme 26).



Scheme 26: General reaction of nitrone reacting with boron compound to form new carbon-carbon bond

Objectives

The current goal for this project is to form a new carbon-carbon bond via boron-mediated transfer to open more pathways for organic methodologies. Our main starting material involves the nitrogen containing functional group referred to as a nitrone, which will be prepared based literature procedure. The method which was selected is an efficient and environmentally friendly method producing nitrones routinely high yields. Our method revolved around the use of Tetrahydroisoquinoline with hydrogen peroxide 30% being used as the oxidant.

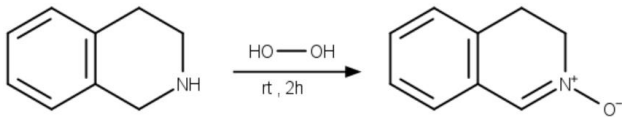
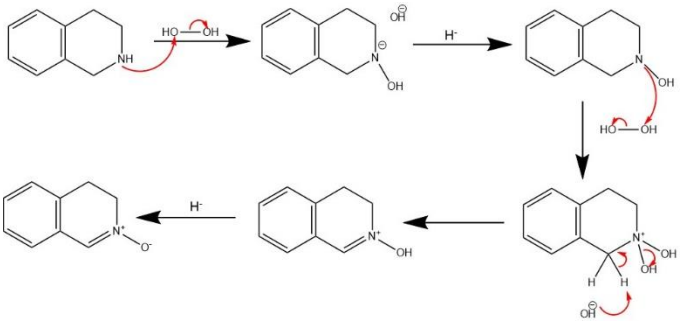
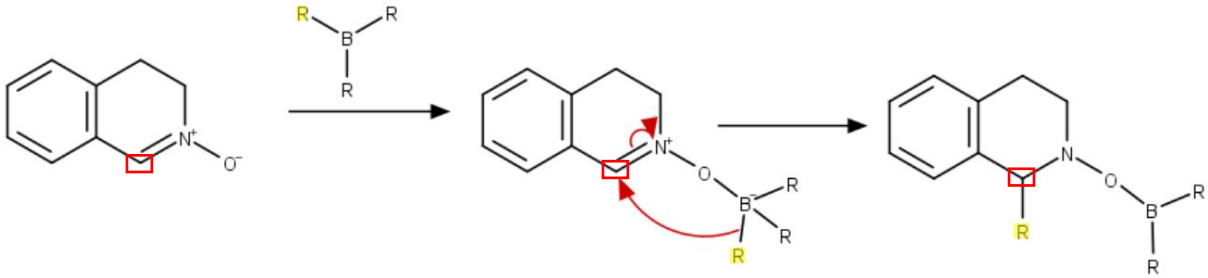


Figure 3: Oxidation reaction of nitrone



Scheme 27: Mechanism of Oxidation reaction of nitrone

The nitrone of tetrahydroisoquinoline was chosen to study a new method that would result in functionalising the α- or 1-C of isoquinoline natural structures. This method involved the use of a boron-containing reactive counterpart. They contain a boron atom center and bound to alkyl groups.



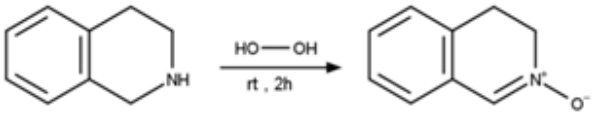
Scheme 28: Nitrone reacting with boron compound

The reactive nitrone has a negatively charged oxygen which attacks the boron center of the trialkylborane or trifluoroborate. This immediately forms a Lewis acid-base complex. Boron is now negatively charged and gives readily one appendage away to the active carbon on the C=N of the nitrone and breaks the double bond. The product is a neutral compound with a new carbon bond formation. Starting from this interaction, further changes in the reaction will be evaluated by ^{11}BNMR and ^{1}HNMR spectroscopy.

Results and Discussion

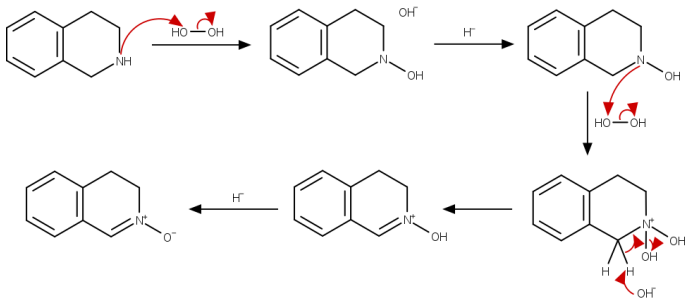
Nitrone Synthesis

The nitrones were introduced in our laboratory. This work is based on the procedure of Granato et al. The required nitrones are formed using the starting materials 1,2,3,4-tetrahydroisoquinoline and hydrogen peroxide 30% in the solvent acetonitrile. Molecular sieves were added to the solvent to prevent the reaction shifting due to hydrolysis. This reaction is executed under room temperature. Covering the reaction was not of a necessity due to the stability of the mixture.



Scheme 29: Oxidation reaction of nitrones

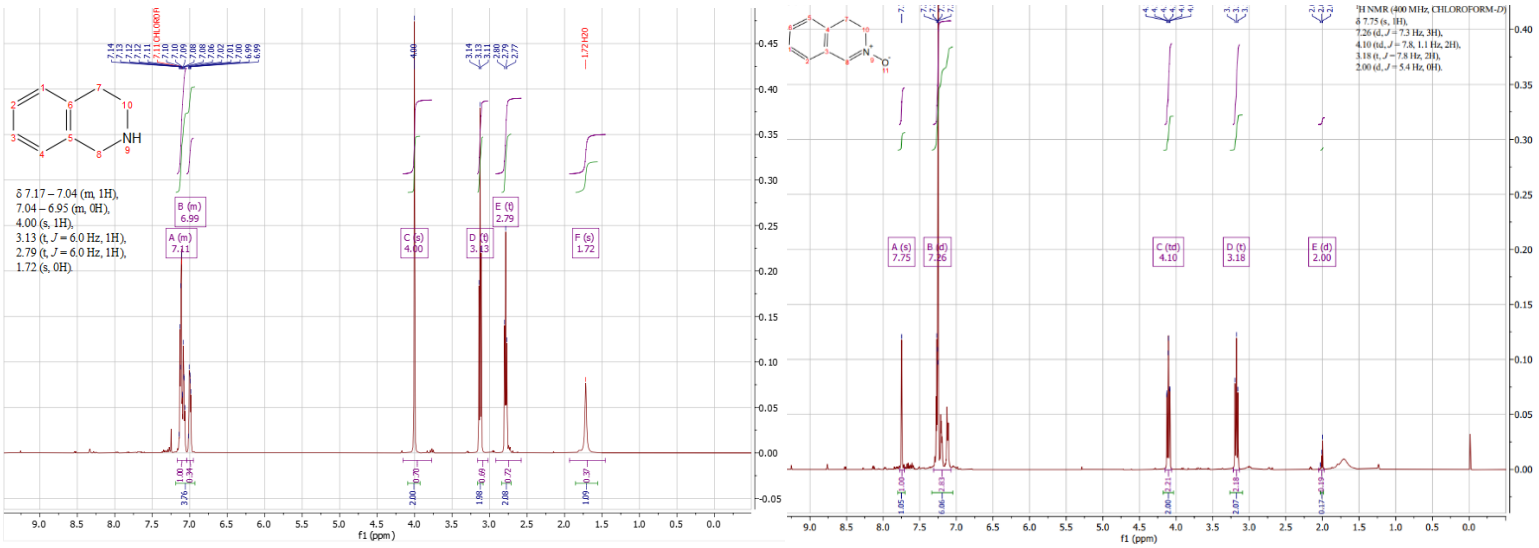
The Nitrogen of the tetrahydroisoquinoline attacks the oxygen of hydrogen peroxide, forming a N-OH bond and breaks the bond to the OH^-. A deprotonation takes place. Because this experiment is in an aqueous environment, with excess of hydrogen peroxide, the first step reaction is repeated again. Due to OH^- in the environment, it takes a proton of the C-N, forms a double bond, and cleaves off an OH^- from the nitrogen, thus being positive. Last step is another deprotonation, forming the negatively charged O^- (Scheme 30).



Scheme 30: Mechanism of Nitrone synthesis

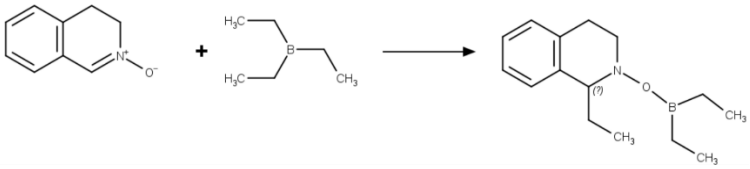
^{1}HNMR spectra were taken and analysed. For the aromate, there should be no change applied, therefore it shows peaks between ~7-7.5 ppm. The two triplets around ~3ppm and ~4ppm have shifted, which represent the H's on C-7 and C-10. One change that strongly indicates that nitrones have been formed, is the singlet between ~7.5ppm and ~8ppm. It represents the methyne group on the C-8=N bond. All the expected peaks of the crude product were visible as in the reference peaks and can be compared (Scheme 32).[24]

As mentioned, these nitrones are now used to react with available trialkylboranes and organotrifluoroborate.



Scheme 31: [1]HNMR of tetrahydroisoquinoline and nitrone

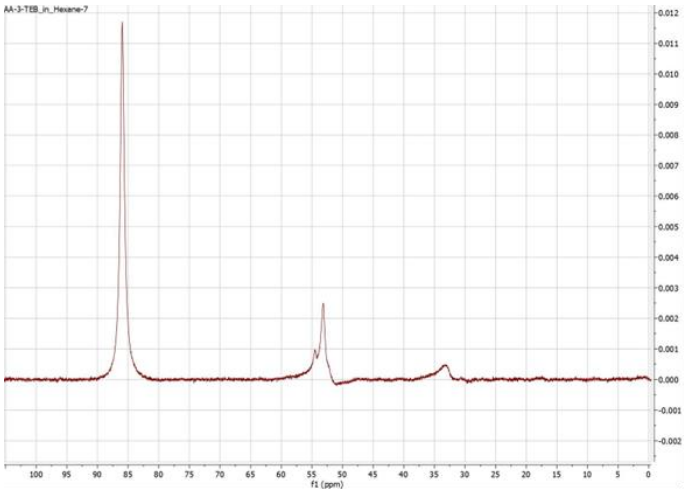
Reaction between nitrone and triethylborane



Scheme 32: Nitrone reacting with triethylborane

The THIQ-nitrone product was reacted with triethylborane which was stored in a container in the solvent, hexane. An unweighted NMR test was done and dissolved in D-Chloroform. The NMR tube was analyzed after an hour, 24 hours, and 48 hours. The NMR results showed some changes which led us to the experiment in a bigger mmol scale.

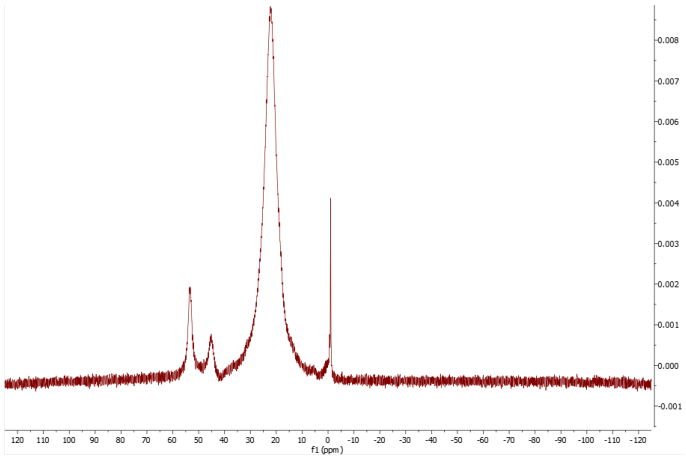
The reaction between THIQ-nitrone and triethylborane was conducted in the solvent acetonitrile. It was set under nitrogen atmosphere. After one hour, 24 hours and 48 hours, the 1HNMR and 11BNMR were observed. Triethylboranes have peaks around ~80ppm, ~50ppm and ~20ppm. (Scheme 33)



Scheme 33: [11]Boron NMR of starting material of triethylborane

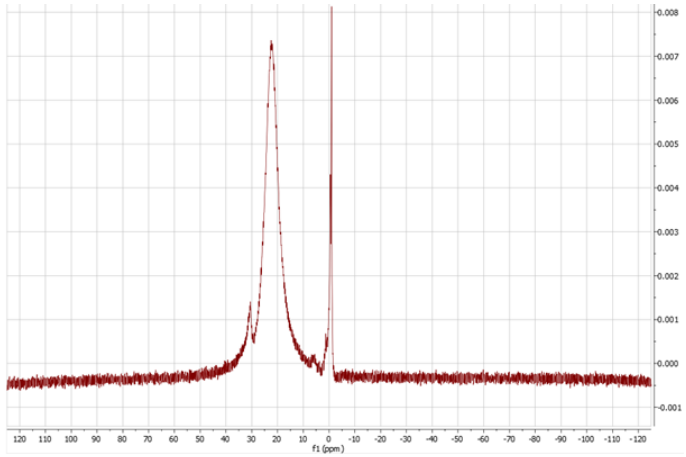
In one hour, the first peak around 80ppm was already gone, indicating that the starting material has reacted and altered during the reaction. ~50ppm, represents one heteroatom and two ethyl appendages and ~25ppm, represents two heteroatoms and

one ethyl appendage and a peak at 0ppm, which represents a boron ate-complex, were visible. (Scheme 34)



Scheme 34: [11]Boron NMR of starting material of triethylborane after one hour reaction with nitrone

After 24 hours, only one large peak was visible ~25ppm and a peak at 0ppm for the boron ate-complex. After 48 hours, there was a stable 25ppm peak (Scheme 35). That disapproved our initial proposal.



Scheme 35: [11]Boron NMR of starting material of triethylborane after 48 hours reaction with nitrone

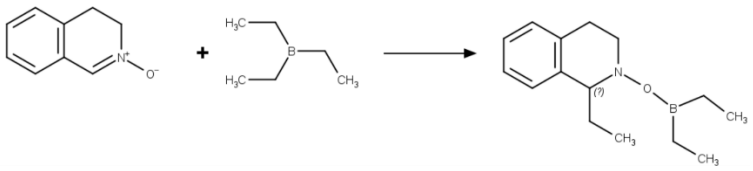
After the [1]HNMR and [11]BNMR analysis, the product was not as expected. As we can see in the previous established mechanism, the product would show a signal at ~50ppm, due to one heteroatom attached to it. Our NMR results are one strong peak at 25ppm, which implies two heteroatom and one ethyl appendages.

This experiment was repeated and put into a monowave for faster reaction results. The solvent was changed too for better reaction, MTBE and acetonitrile were used. Nitrone didn't dissolve in MTBE. Using MTBE and acetonitrile was making the solution cloudy, and nothing went properly into solution. We held onto the use of acetonitrile as a solvent and added molecular sieves to it. The purpose of the use of molecular sieves is the removal of water to avoid any side reactions and maintain the purity. Molecular sieves are porous solids to adsorb certain molecules, in our case our impurity was water. Furthermore, this experiment was also carried out with all provided triethylboranes in different solutions as in hexane and in diethyl ether, to compare differences and in which solution it has a faster and a more precise reaction. The triethylborane in THF solution was expired and therefore unreactive, which was visible

in the NMR spectra; they didn't match the other evaluations and were therefore taken out from any further analysis.

After the NMR data, we tried to separate the compound through TLC's. TLC, also called Thin Layer Chromatography, which is a method that analyses mixtures by separating the compounds in there. Many TLC testing was approached because it's a short time analysis method. The product was tested against hexane and ethyl acetate to 1:2 ratio. The product was streaking with an Rf value of 0.4. After these results, we separated it furthermore using a one column volume chromatography. It's a type of chromatography, where one eluent is used. 10% deactivated silica gel was used. First it was washed with hexane, the product was put on top of the layer and flushed through with ethyl acetate for separation. Out of the six separations which were collected, three were further analysed. Their 11BNMR spectrum was all the same, one peak near 0ppm indicating a boron ate-complex.

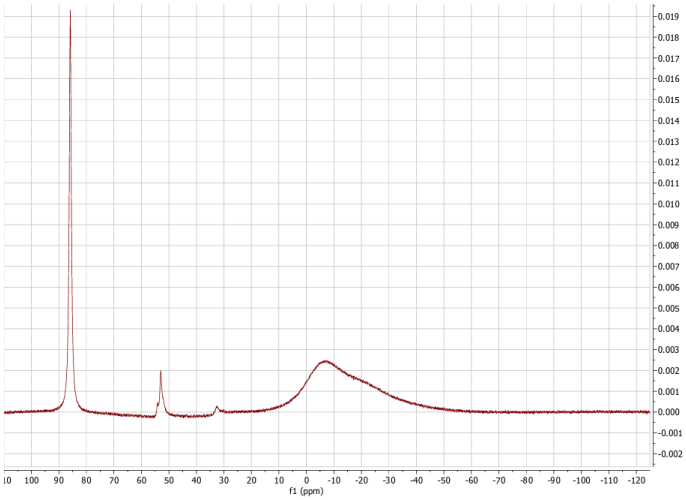
Reaction between nitrone and triethylborane



Scheme 36: Nitrone reacting with triethylborane

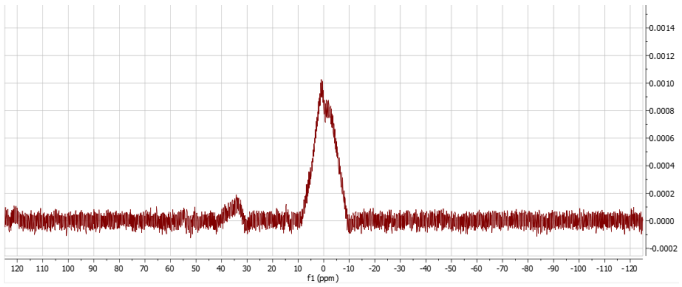
The THIQ-nitrone product was reacted with triethylborane which was sealed in a container with the solvent diethyl ether. An unweighted NMR test was done and dissolved in D-Chloroform. The NMR tube was analysed after an hour, 24 hours, and 48 hours. The NMR results showed some changes which led us to the experiment in a bigger mmol scale.

The reaction between THIQ-nitrone and triethylborane was conducted in the solvent acetonitrile. It was set under nitrogen atmosphere. After one hour, 24 hours and 48 hours, the ^{1}HNMR and ^{11}BNMR were observed. Triethylboranes have peaks around ~80ppm, ~50ppm and ~20ppm. (Scheme 37) In this BNMR there is a 'peak' between ~0ppm and ~30ppm. This is a software issue, after the transfer of the data from the spectroscopy desktop.



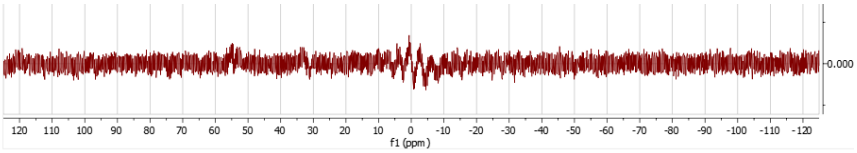
Scheme 37: ^{11}Boron NMR of starting material of triethylborane

After 24 hours, only one smaller peak was visible between ~40ppm and ~30ppm and a larger peak at ~0ppm for the boron ate-complex (Scheme 38).



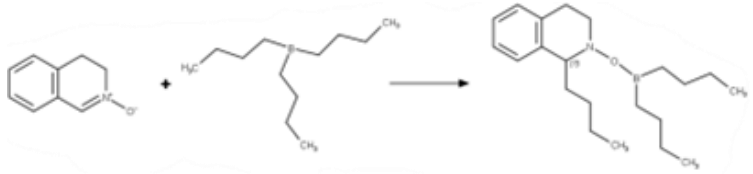
Scheme 38: [11]Boron NMR of starting material of triethylborane after 24 hours reaction with nitrone

After 48 hours, there was a stable ~0ppm peak. Minor peaks at ~30ppm (Scheme 39). That disapproved our first proposal. Due to technical issues, transferring the document from the NMR spectroscopy computer to the software MestReNova on my laptop, editing was not as ideally conducted as aimed for.



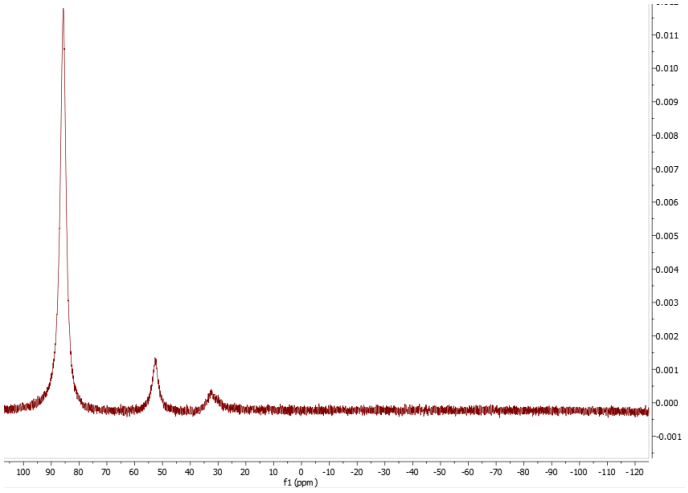
Scheme 39: [11]Boron NMR of starting material of triethylborane after 48 hours reaction with nitrone

Reaction between nitrone and tributylborane



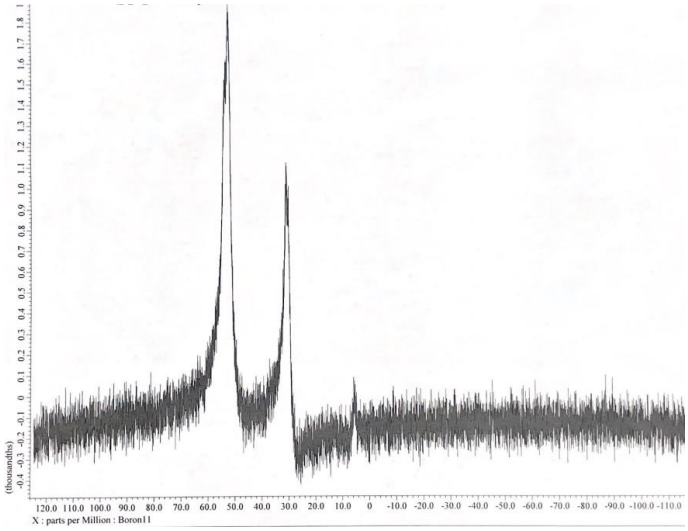
Scheme 40: Nitrone reacting with tributylborane

An unweighted NMR test was done, tributylborane (Scheme 41) which was sealed in a container with the solvent diethyl ether was added and dissolved in D-Chloroform. The NMR tube was analysed after an hour, 24 hours, and 48 hours. The NMR results showed some positive changes which led us repeating the experiment in a bigger mmol scale with appropriate equivalent.



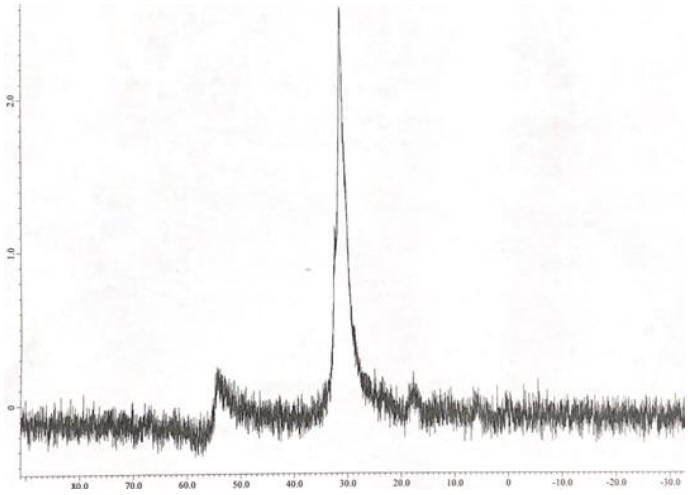
Scheme 41: [11]Boron NMR of starting material of tributylborane

The reaction between THIQ-nitrone and tributylborane was conducted in the solvent acetonitrile. It was set under nitrogen atmosphere. After one hour, 24 hours and 48 hours, the ^{1}HNMR and ^{11}BNMR were observed. The ^{11}BNMR of tributylborane in diethyl ether solution, has peaks at ~80ppm, ~50ppm and ~20ppm. After one hour, the peak at ~80ppm disappeared, ~60ppm, which represents one heteroatom and two butyl appendages, ~30ppm, which represents two heteroatoms and one butyl appendage and ~0ppm, which represents a boron-ate-complex, were visible (Scheme 42).



Scheme 42: ^{11}Boron NMR of starting material of tributylborane after one hour reaction with nitrone

After 24 hours we still didn't see much change in the ^{11}BNMR. Finally, after 48 hours, we also had one large peak around ~25ppm (Scheme 43). That disapproved our first proposal.

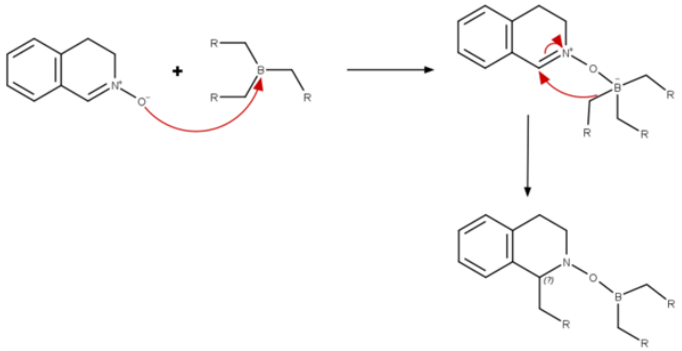


Scheme 43: ^{11}Boron NMR of starting material of tributylborane after 48 hours reaction with nitrone

Like the triethylboranes, the ^{1}HNMR and ^{11}BNMR analysis wasn't as expected. A peak at ~25ppm appeared, which indicates two heteroatom and one butyl appendage. This experiment was repeated and put into a monowave for faster reaction results.

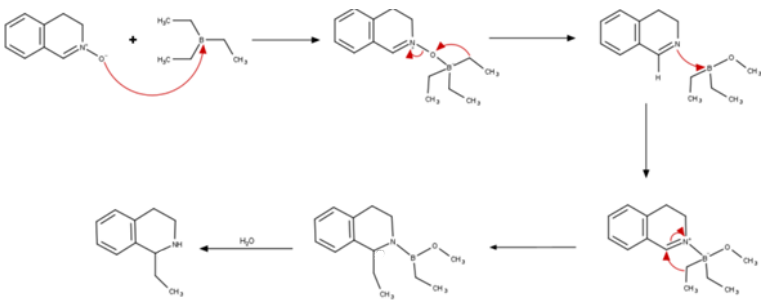
After analysing the NMR spectra of all the above-mentioned experiments, we realised that the behaviour is different than the theory we have developed. Our initial proposal was nitrone reacting with the trialkylborane and forming a boron-ate-complex. We

could follow this process through the ^{11}BNMR. From the unreacted trialkylborane, peaks around ~80ppm, ~50ppm and ~20ppm should be visible. After the boron-ate complex is formed, a peak at 0ppm is expected. The alkyl appendage is transferred to the active C=N and the double bond would be broken. From the general table we would see a peak at ~50ppm, which represents two heteroatoms and one alkyl appendage and it's likely to see for the ^{1}HNMR, the peak around ~8ppm, should according to the theory, disappear, confirming a new carbon-carbon bond formation on the active C=N bond (Scheme 44).



Scheme 44: Mechanism of proposed carbon-carbon bond formation via boron mediated transfer

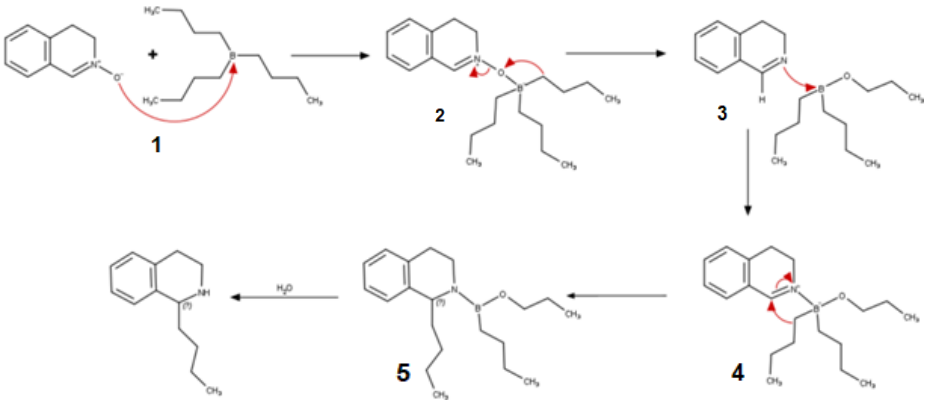
From the evaluations, a strong peak around ~25ppm was visible in all the experiments after the 48 hours waiting period. Not seeing the theoretical match with the spectra, directed us to find another literature reference by Soderquist's et al. work. He describes the selective oxidation of organoboranes with anhydrous TMANO to give isolable borinate and borate esters. Although this paper analyses the method of estimating the position of the primary band in the ultraviolet absorption spectra, its mechanism of the oxidation reaction of organoboranes by N-oxides, helped us understand our reaction halfway. The mechanism for THIQ-nitrone and triethylborane after analysing the NMR spectrum, was straightforwardly explainable according to Soderquist et. al. The nucleophilic O^- attacks the electrophilic boron to form a boron-ate-complex and is cleaved off, after the oxygen is attached to the trialkylboranes. The N attacks the boron, forming another boron-ate-complex. The carbon on the C=N is very active, therefore the boron cliffs off one appendage and the double bond breaks. Through hydrolysing the trialkylborane and we get the secondary amine with a new C-C bond formed. In the oxidation step, relies on the essential boron-mediated carbon oxygen bond forming reaction, referred to as a 1,2 boron-mediated transfer (Scheme 45).



Scheme 45: New proposed mechanism with triethylborane and nitrone for new carbon-carbon bond formation

Same with the mechanism for THIQ-nitrone and tributylborane, after analysing the NMR spectra results. The nucleophilic O^- attacks the electrophilic boron to form a

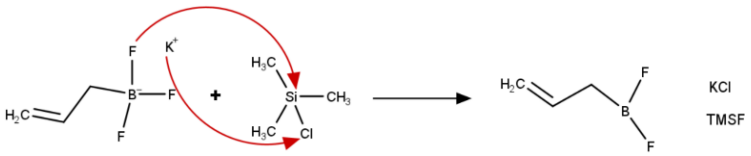
boron-ate-complex. After the oxygen is attached to the tributylborane, the N attacks the boron, forming another boron-ate-complex. The carbon on the C=N is very active, therefore the boron cliffs off one appendage and the double bond breaks. Hydrolysing the tributylborane and we get the secondary amine with a new c-c bond formed. In the oxidation step, relies on the essential boron-mediated carbon oxygen bond forming reaction, referred to as a 1,2 boron-mediated transfer.



Scheme 46: New proposed mechanism with tributylborane and nitrone for new carbon-carbon bond formation

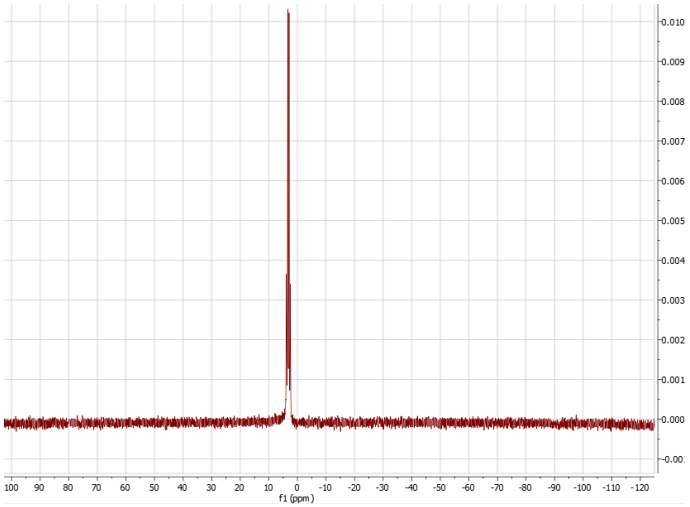
In both cases the NMR spectra have a large peak at ~25ppm after minimum of 48 hours. Which confirms that there is the trialkylboranes with two heteroatom, and one ethyl appendage forming as depicted in the last step, before the product of the mechanism. We can also see a peak at 0ppm, referring to the 4th step, showing us a boron ate-complex (Scheme 46).

Reaction between THIQ-nitrone and potassium allyltrifluoroborate



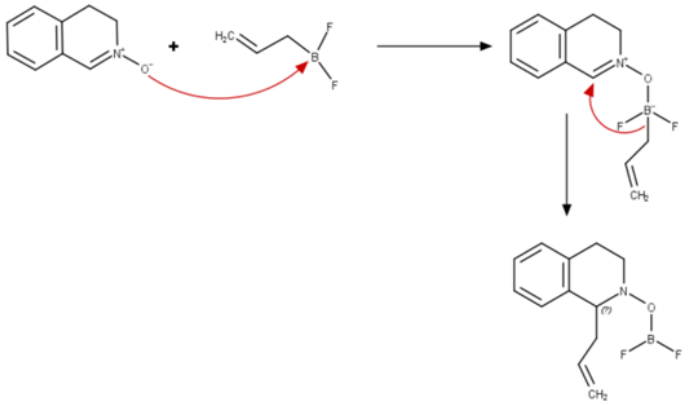
Scheme 47: Reaction of allyltrifluoroborate with TMSCl to generate allyldifluoroborate

To react potassium allyltrifluoroborate (Scheme 48) with THIQ-nitrone, we first have to activate the allyltrifluoroborate. After adding TMSCl, the potassium will obtain the chloride and one fluorine attach to the TMS forming allyldifluoroborate, KCl and TMSF. Now the allyldifluoroborate is activated (Scheme 47).



Scheme 48: [11]Boron NMR of starting material of potassium allyltrifluoroborate

The allyldifluoroborate cannot be analysed through NMR. After the synthesis, if the nitrogen environment is interrupted, it immediately evaporates, being very volatile. Therefore, the THIQ-nitrone is added directly. The boron on the allyldifluoroborate attacked by the nucleophilic O^- forming a boron-ate-complex. The carbon on the C=N is very active, therefore the boron cliffs off the allyl appendage and breaks the double bond (Scheme 49).



Scheme 49: Mechanism of nitrone with allyldifluoroborate

This experiment was carried out in solvent acetonitrile. An aliquot was taken and analysed after an hour and 24 hours. The mechanism for this experiment wasn't changed due to the results. The [11]BNMR showed a peak between ~60-50ppm, which indicates one heteroatom and two appendages. One peak at 0ppm is visible, which stands for boron-ate-complex. TLC chromatographies were taken of this product. Interesting notice was, there was no visibility under the UV-light, but after we submerged it into iodine, the spots were stained, and the migration with the solvent stood out. We then continued with a one column volume chromatography against hexane and ethyl acetate to 1:4 ratio. Twelve fractions were collected, three of them were further analysed. Although the [11]BNMR was frequently changing, the [1]HNMR didn't show any changes in the nitrone. There are different interpretations for this reaction, one conclusion which was made, is that the boron didn't interact with the nitrone compound rather was degrading due to many outside factors, like exposure to air and manual handling error. This experiment was also put into monowave for one

hour at 100°C, this led to a burned solution in the monowave tube. This reaction will be tried again with a different approach.

Experimental

General and instrumental details

Reactions were performed under nitrogen. The chemicals were purchased from Sigma Aldrich and used without further purification. Any water added is assumed to be deionized water.

NMR: A JEOL JNM-ECP 400 FT-NMR spectrometer was used, which provided H-NMR (400 MHz), C-NMR (101 MHz), B-NMR (128 MHz) and F-NMR (376 MHz)

Monowave: Anton Paar, Monowave 50+P, P/N: 168600, S/N: 81991198

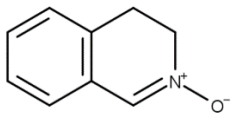
Monowave 400, P/N: 163523, S/N: 83937941

TLC: Thin Layer Chromatography was glass plated with a pre-coated silica and developed using standard visualising equipment: UV light and iodine

One column Volume Chromatography: the setup was a fritted funnel and an Erlenmeyer flask with a side arm which was connected to a vacuum. 10% deactivated silica was used. Solvents which were used against, are hexane and ethyl acetate

Mastrenova: This program has been used to analyse NMR results. Unfortunately, this program cannot process boron NMR spectra.

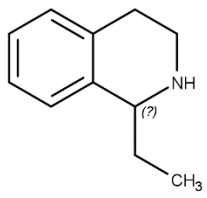
1,2,3,4-Tetrahydroisoquinoline-nitrone



The round bottom flask was charged with 1,2,3,4-tetrahydroisoquinoline (3 mmol, 0.39 mL) and acetonitrile (9 mL) and stirred. To the stirred solution, H2O2 30% (6 mmol, ~0.68 mL) was added. The resulting solution was stirred for 2h at room temperature. Then CH2Cl2 (30mL) and water (30mL) were added. The organic layer was separated from aqueous layer, which was again, extracted with CH2Cl2 (45mL) and added to the organic layer. The organic layer was washed with brine and dried over MgSO4. It was concentrated down on the rotary evaporator and vacuum pump. A 1H NMR was taken. Final product is a yellow viscous solid (70% yield). 1HNMR (400 MHz, CHLOROFORM-D) δ 7.75 (s, 1H), 7.33 – 6.91 (m, 4H), 4.14 – 3.99 (m, 2H), 3.22 – 3.11 (m, 2H).

This experiment was carried out with different mole amounts and then stocked.

1,2,3,4-Tetrahydroisoquinoline-nitrone with triethylborane



The clean round bottom flask was filled with Tetrahydroisoquinoline-nitrone (2 mmol, 0.29g), acetonitrile (2 mL), a magnetic stirrer and stirred. A septa was put on. The

reaction was put under nitrogen and triethylborane (2 mmol, 2mL) was added via syringe. It was stirred for one hour, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. Final product was a clear orange liquid, white solid at the bottom of the flask. Interestingly, after few minutes there was just half of the solution there, although the reaction was closed, and no leakage was discovered. Turned into brown viscous liquid. Same results every time this reaction was repeated. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.75 (s, 1H), 7.31 – 7.04 (m, 4H), 4.15 – 4.02 (m, 2H), 3.17 (dd, J = 8.8, 6.9 Hz, 2H).

Used:
1M Triethylborane in hexane solution

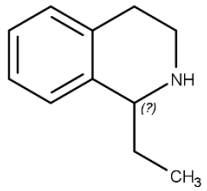
First an unweight NMR tube test was carried out

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

1,2,3,4-Tetrahydroisoquinoline-nitrone with triethylborane



The monowave tube was charged with tetrahydroisoquinoline-nitrone (2 mmol, 0.29g), dry acetonitrile (2 mL) and a magnetic stirrer. A septa was put on and set under nitrogen. The triethylborane (2 mmol, 2mL) was added with a syringe. The monowave tube was put into the monowave for one hour, 100°C. An aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. The final product was a clear orange liquid, white solid at the bottom of the flask. Interestingly, after few minutes there was just half of the solution there, although the reaction was closed, and no leakage was discovered. Same results every time this reaction was repeated. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.34 – 6.95 (m, 4H), 4.09 – 3.87 (m, 1H), 3.03 (tdd, J = 16.5, 7.3, 4.5 Hz, 1H)

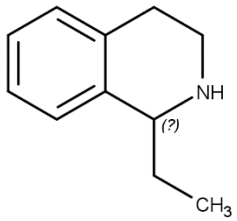
Used:
1M Triethylborane in hexane solution

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A ^{1}HNMR and ^{11}BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A ^{1}HNMR and ^{11}BNMR was taken.

1,2,3,4-Tetrahydroisoquinoline-nitrone with triethylborane



The clean round bottom flask was filled with Tetrahydroisoquinoline-nitrone (1 mmol, 0.15g), acetonitrile (3mL), a magnetic stirrer and stirred. A septa was put on. The reaction was put under nitrogen and tributylborane (1 mmol, 1mL) was added via syringe. It was stirred for one hour, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. The final product was a clear orange liquid, white solid at the bottom of the tube. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.36 – 6.87 (m, 4H), 4.05 (dd, J = 7.9, 5.2 Hz, 1H), 3.15 – 2.78 (m, 3H).

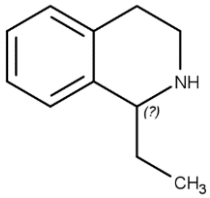
Used:
1M Triethylborane in diethyl ether solution

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

1,2,3,4-Tetrahydroisoquinoline-nitrone with triethylborane



The monowave tube was charged with tetrahydroisoquinoline-nitrone (2 mmol, 0.29g), dry acetonitrile (2 mL) and a magnetic stirrer. A septa was put on and set under nitrogen. The triethylborane (2 mmol, 2mL) was added with a syringe. The monowave tube was put into the monowave for one hour, 100°C. An aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. The final product is a cloudy orange liquid, white solid at the bottom. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.36 – 6.87 (m, 4H), 4.05 (dd, J = 7.9, 5.2 Hz, 1H), 3.15 – 2.78 (m, 3H)

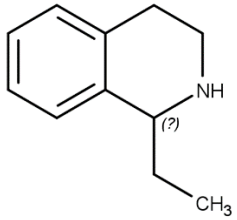
Used:
1M Triethylborane in diethyl ether solution

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken

1,2,3,4-Tetrahydroisoquinoline-nitrone with triethylborane



The clean round bottom flask was filled with Tetrahydroisoquinoline-nitrone (2 mmol, 0.15g), acetonitrile (3mL), a magnetic stirrer and stirred. A septa was put on. The reaction was put under nitrogen and tributylborane (1 mmol, 1mL) was added via syringe. It was stirred for one hour, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. The final product was a cloudy orange liquid, white solid at the bottom of the flask. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.74 (s, 1H), 7.41 – 6.96 (m, 4H), 4.12 – 4.01 (m, 2H), 3.13 (t, J = 7.8 Hz, 2H).

Used:
1M Triethylborane in THF solution

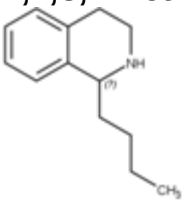
This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

This experiment is invalid due to the already opened 1M triethylborane in THF solution being expired and therefore unreactive.

1,2,3,4-Tetrahydroisoquinoline-nitrone with tributylborane



The monowave tube was charged with tetrahydroisoquinoline-nitrone (2 mmol, 0.29g), t-butyl-methyl-ether (3 mL) and a magnetic stirrer. A cap was put on and set under nitrogen. The tributylborane (2 mmol, 2mL) was added with a syringe. The monowave tube was put into the monowave for one hour, 100°C. An aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. The final product was a clear orange liquid, white solid at the bottom of the tube. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.38 – 6.89 (m, 4H), 3.88 (t, J = 6.6 Hz, 0H), 3.24 (dddt, J = 25.8, 17.0, 12.4, 8.0 Hz, 1H).

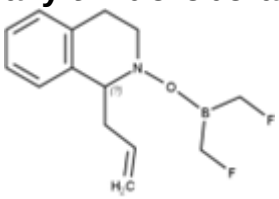
First an unweight NMR tube test was carried out

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

1,2,3,4-Tetrahydroisoquinoline-nitrone with potassium allyltrifluoroborate



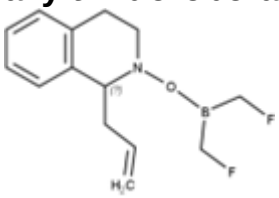
The clean round bottom flask was charged with potassium carbonate (9 mmol, 1.24g), potassium allyltrifluoroborate (3 mmol, 0.44g), TMSCl (9 mmol, 1.14mL) and a magnetic stirrer and stirred. Tetrahydroisoquinoline-nitrone (3 mmol, 0.44g), and acetonitrile (10mL) was added. The reaction was put under nitrogen and tributylborane (1 mmol, 1mL) was added via syringe. It was stirred for two hour, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken. 1HNMR (400 MHz, CHLOROFORM-D) δ 7.74 (s, 1H), 7.39 – 6.91 (m, 4H), 4.16 – 4.00 (m, 2H), 3.17 (t, J = 7.8 Hz, 1H).

This reaction has been monitored:

After 24 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

After 48 hours, an aliquot was taken, concentrated down on the rotavap and vacuum pump. A 1HNMR and 11BNMR was taken.

1,2,3,4-Tetrahydroisoquinoline-nitrone with potassium allyltrifluoroborate



The monowave tube was charged with tetrahydroisoquinoline-nitrone (1 mmol, 0.15g), acetonitrile (5 mL), potassium allyltrifluoroborate (1 mmol, 0.15g), K2CO3 (3 mmol, 0.41g) and a magnetic stirrer. A cap was put on and set under nitrogen. The TMSCl (3 mmol, 0.38mL) was added with a syringe. The monowave tube was put into the monowave for one hour, 100°C.

This experiment failed. The conditions will be changed and further modified for a better result.

Conclusion

As mentioned, nitrones play a crucial role in life, such as in amino acids and is a fundamental component of the building block in proteins. In the field of medicine, they have been investigated for neuroprotective properties which helped to find a key closer to the cure of atherosclerosis, stroke, and Alzheimer's. Additionally, it is used in fertilizers, aiding crop growth. If we take a look at organic chemistry, nitrones also have

been recognized as being capable of forming complex molecular structures and one of the most reactions nitrone compounds are involved in, are 1,3-Dipolar Cycloaddition reactions, sometimes called Huisgen Cycloaddition. Our interest relies in the active C=N bond and the high reactivity of the negatively charged oxygen. Reacting them with trialkylboranes and organotrifluoroborates to successfully initiate a boron mediated transfer would be a huge achievement. This opens more pathways for organic methodologies.

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