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Synthesis and Characterization of Peri-Naphthalene Derivatives

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Last but not least, for all my friends that were in Nottingham and my family for the support in all the moments.

CONTENTS

1 Abstract

The Peri-naphthalenes was proved that is a molecular skeleton which is extremely useful for studying the interaction between electrophile and nucleophile groups, and in this form has the chance to study the behaviours of those, in close proximity.

So in this project, it was tried to focus the attention on the possible interactions between a boron group with different substituents in a close proximity in the peri-positions such as a double or triple bond carbon-carbon. It was tried also to look at the interactions between a double bond with a carbonyl group.

None has studied until this moment this type of interaction at boron or carbonyl with double or triple bonds in relative peri-positions.

Successful results to obtain the target molecules have not been reached yet and try to analyse with X-Ray crystallography has not been possible to do. Nevertheless, a lot of chemistry has been done, various routes for prepare the target molecules have been investigated.

The research carried in this project is important for the next studies in this area, to try to obtain the target molecules and observe the behaviour between this two groups.

2 Introduction

2.1 Scope of work

This project has been done in the department of Chemistry and Forensic Science in Nottingham Trent University in the group of Intermolecular Interactions. In this group they are studying the reactions between functional groups by measuring the molecular structures with X-Ray crystallography. This group works following the chemistry of naphthalene and looking for these interactions starting with cheapest compounds and doing in these form expensive products only for scientific interest. The aim of this group is to search the behaviour of the different compounds of the functional groups in naphthalene and try to develop new methods to obtain these different structures. [1]

2.2 Peri-naphthalene

In the chemistry of naphthalene, the molecules which are substituted at the positions 1 and 8 are called to be peri to each other. In the case of naphthalene peri-substitution is to be substituted in relative positions 1 and 8 in the naphthalene ring. These compounds have been used extensively for investigating the interactions between the groups in peri-positions. [2]

Peri-substituted naphthalene seems like a rigid molecule, this stems from the nature of the compounds. The naphthalene molecule is planar, and all the angles are close to 120°. In the simple naphthalene there are only sets of two peri-atoms, if it is not substituted with other groups these positions are occupied by hydrogen atoms, which are placed comfortably. The distance between these atoms placed in peri-positions is the “ideal” 2.5Å. [3]

Through the space between these groups positioned in peri-positions are involved different interactions like Van der Waals forces and dipole-dipole. All of them play an important role in the packing to form crystals, making attractive interactions in supramolecular processes.

These chemical process is more important when the interactions are taking between two chemical groups, in which one of them is electron-rich and the other electron-poor, in this way they can interact more or less like in an early stage of a chemical reaction. When the interaction has done it seems that it is forming a semi-bond between the two groups. [4]

This behaviour of naphthalene focusing more in peri-naphthalene has attracted a great deal of attention. A large number of studies it have been done, focusing on the formation of the semi-bond. Until now, only some groups are studied in the chemistry of peri-naphthalene as Group 15 and 16 from the periodic table , also using a nitrogen group with different substituents and the “proton sponges” [3].

All the chemistry about coordination in peri-substituted naphthalene were focused in the study bis(phosphines) and bis(thiolates); also mixed donor as NapPN, NapPO, NapPS, NapPF, NapPC and $NapAs_2$ had been studied too. [2] [3]

Nevertheless there had never been done a study with boron groups peri-positioned with alkene or alkyne. The other works which were done in this area, studied naphthalene with one of the groups is a tertiary amines this acts like a nucleophiles in front of the double or triple bond.

This project was focused in the role that boron can play in front of the double and triple bond in peri-position and try to study this interaction with X-Ray crystallography.

2.3 Antecedents

In the field of peri-naphthalenes disubstitution was done a lot of studies to observe the interaction between two groups. The different studies, which were done until this moment are reflected below in this section.

One of the studies was done using different tertiary amino groups as nucleophile and using on the other peri-position a carbonyl group as electrophile**.** The first studies in this type of peri-naphthalene groups were carried by Leonard and co-workers in the 1950's. Others groups carried this studies because of the importance of it in the physiological activity of some biomolecules. Most of the synthesized molecules showed repulsion between the substituents. The exocyclic bonds are splayed outwards and the substituents are displaced to opposite sides as shown Figure 1 (a). But if one of the groups is a tertiary amino group (nucleophile) and the other the carbonyl (electrophile), it was observed that in the plane distortion, the substituents are displaced to the same sides, as shown Figure 1 (b). Recent studies done in NTU (Nottingham Trent University) by Professor John Wallis showed that if two peri-groups of this characteristics were to react to form a bond then the two groups would be displaced towards each other, as shown Figure 1 (c). [5]

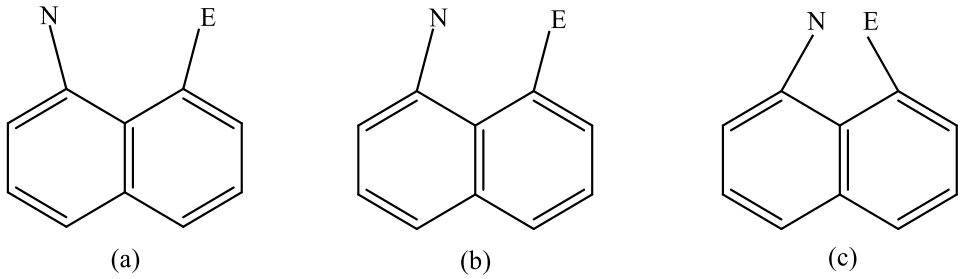


Figure 1: different behaviour in the groups peri-positioned in naphthalene

According to Professor John Wallis Figure 2 shown the bond formation with the help of a medium acid and a decrease of the distance between the two functional groups. [5]

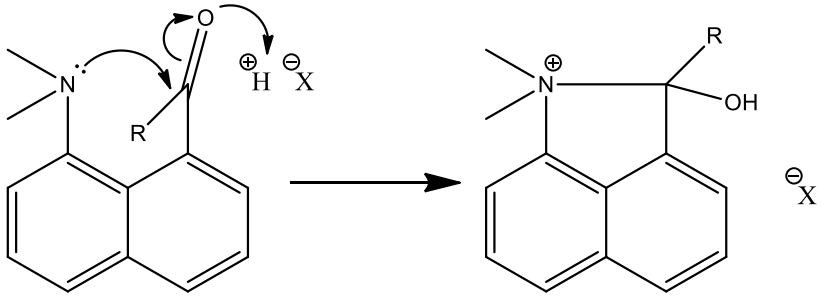


Figure 2: attack of the tertiary amine group to carbonyl activated in medium acid

It was tried to form a bond with other different reagents. One which was possible to do, was with benzoyl chloride. In this case the product of the reaction was very different compared with the others examples, the reaction is explained in Figure 3. [6]

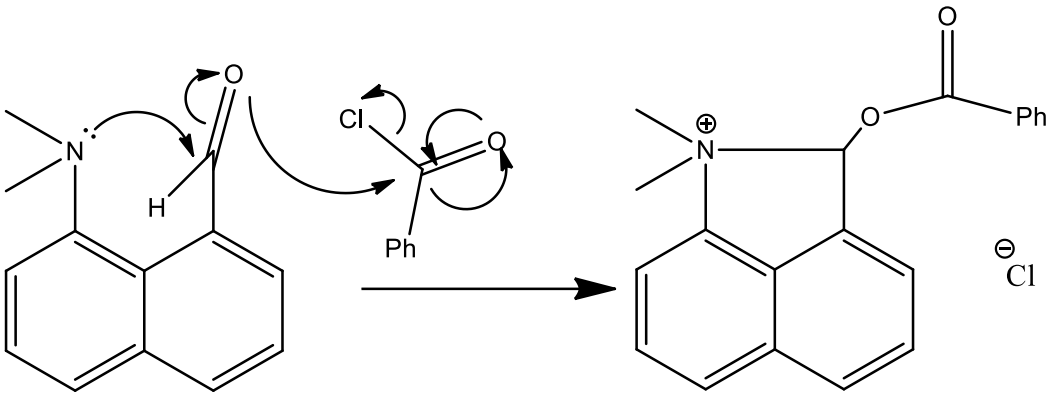


Figure 3: attack of the tertiary amine group to carbonyl activated with benzoyl chloride

Another similar idea was tried with disubstitued peri-naphthalene was groups with phosphorus and the other with boron. The role that they play in this compounds could be similar as expected in this project. Several studies have been done with this compound with different substituents. One of them is shown in the Figure 4. Without knowledge how can act the boron with the double bond or triple bond is expected a similar behaviour like in the case of phosphorus and boron. Therefore it has to be studied, to be sure it is the same behaviour like expected. In the case with boron and phosphorus groups the different compounds were studied and was theoretically calculated electron and pair densities to confirm the bonding between P and B atoms. [7]

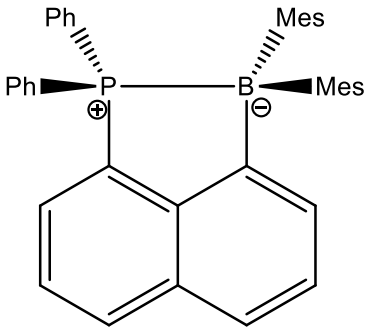


Figure 4: NapPB peri-positioned

3 Aims

This work is involved in the context of naphthalene chemistry. The main aim of the project, is the synthesis of compounds which have groups in the peri-positions. There are two types of interactions that need to be observed between this groups.

The first interactions using boron as electrophile group with different substituents and observe the interaction that are shown with an alkene or alkyne in the peri-positioned groups, as is shown in the Figure 5.

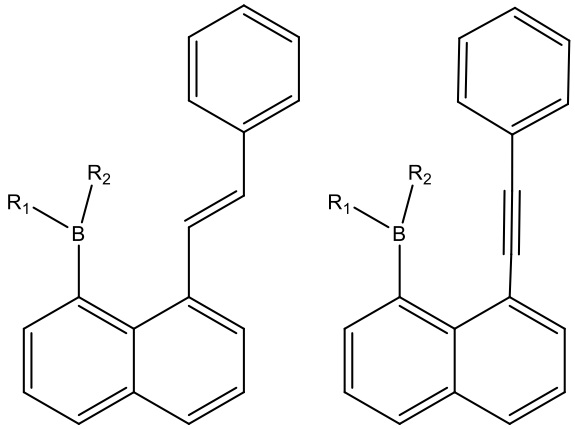


Figure 5: peri-naphthalene with boron and double or triple bond

The second type of compounds are the interactions between groups in peri-positions. In this case the interactions between alkenes or alkyne and carbonyl groups wants to be observed. The reaction has to be activated by the complexation with a Lewis acid as is shown in Figure 6.

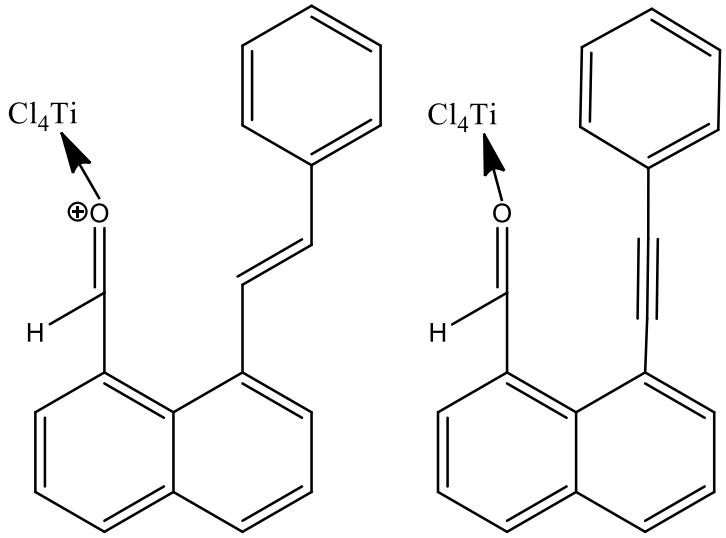


Figure 6: carbonyl activated with Lewis acid in naphthalene peri-positioned with a double or triple bond

4 Methods and techniques implemented in the laboratory

4.1 Methods [8]

In this section are described all the different methods used in the synthesis for the different compounds.

4.1.1 Distillation simple [9]

Many reagents were opened some time ago, is because of this that are impurities. Some reagents like trimethyl borate were boiled with sodium metallic and after that all the liquid were distillate at atmospheric pressure to obtain a reagent with high level of purity. The system used to distil the liquids was dry glassware that was left in the oven for a period of time and then joined and put it in the same form as shown Figure 7 heat it up to boiling point and collect the fraction that distil at the temperature predicted from the pure reagent.

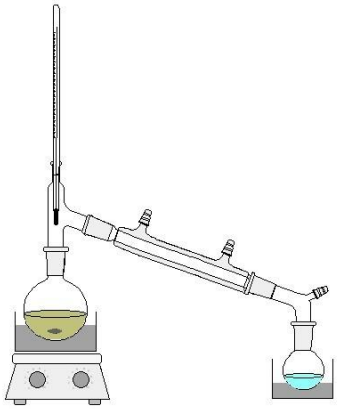


Figure 7: distillation simple system

4.1.2 Drying liquids [10]

There are many times when after do the work up of the reaction is necessary to remove traces of water from the solution or liquids. In all the reactions done it were used for dry the organic layer after the extraction Na_2SO_4 or $MgSO_4$ both anhydrous. After that both reagents are removed by gravity filtration.

Reactions (hidratation of drying reagents):

$$Na_2SO_4 + 10H_2O \rightarrow Na_2SO_4 * 10H_2O$$

$$MgSO_4 + 7H_2O \rightarrow MgSO_4 * 7H_2O$$

4.1.3 Filtration [8]

This methods is commonly used to separate to phases in a mixture reaction. One of them a solid and other a liquid. Depends which phase want to be collected it is done with two different type of filtration.

4.1.3.1 Gravity filtration

It is the simple kind of filtration. It is commonly used if the solid has to be discarded and not used for subsequent reactions. The solution with the solid is filtered through a filter paper in a filter funnel. For liquids that has to be recrystallized, the hot mixture is filtrated through a pre-heated funnel and fluted paper. Commonly this method is used to remove impurities and isolate solids as used for dry the organic layers, the commonly system used is ilustratd in the Figure 8.

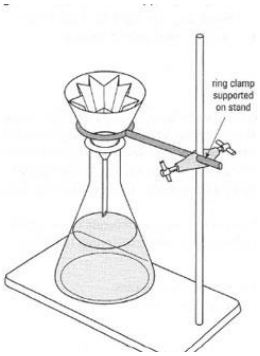


Figure 8: funnel with filter paper

4.1.3.2 Büchner filtration

If the solid needs to be insolated from the mixture reaction it is normally done in a special funnel called Büchner funnel and a conical Büchner under reduced pressure connected to a pump vacuum. To prevent the suck back of solvent into the vacuum pump it is essential to use like a trap. It has to be disconnected the vacuum before turn it off the vacuum pump. A simple Büchner filtration without the trap is illustrated in the Figure 9.

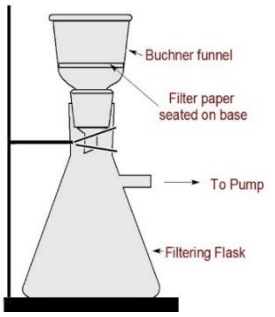


Figure 9: Büchner funnel with the different parts explained

4.1.4 Liquid-liquid extraction [8]

Liquid-liquid extraction is a method used in almost of the reactions during the work up. Is based on the relative solubility of the compounds in two different immiscible solvents both in liquid phase. In all this project it was used for extract the organic expected compounds from the water phase using an organic solvent immiscible in water.

For the application of this method has to be used a separating funnel (Figure 10) is a piece of laboratory glassware to separate the components of the mixture between two immiscible solvent phases of different densities. The funnel has to be shake gently and many times is inverted and then the tap carefully opened to release excess vapour pressure. After that the top and the bottom tap are opened and the two phases are released by gravitation.

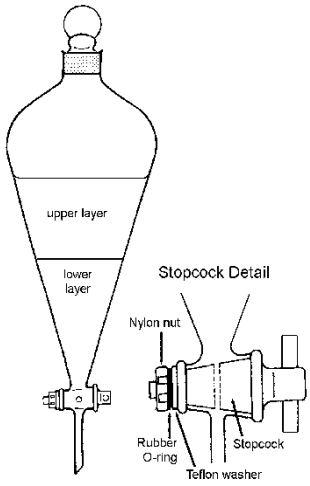


Figure 10: separating funnel for liquid-liquid extraction

4.1.5 Recrystallization [8] [11]

This method means try to obtain a solid crystal that has born only with molecules of same structure and in this form a high level of purity. All reactions done often several compounds were obtained, that were not the only one expected, is because of this, that has to be purified and one of the form to do that is by recrystallization. This method involves dissolving the product in the minimum amount of solvent chosen and the mixture has to be dissolved in this minimum amount of solvent but when the solvent is hot, after that hot filtration to remove any insoluble

impurities. The last step is allowing crystals of the purified product to form. The crystals are collected by Büchner filtration.

4.1.6 Reflux [8] [12]

Reflux is usually used for some reactions which ones has to be done at the boiling point of the solvent, for does not evaporate the solvent this method has the possibility to recondense back to the flask using a condenser illustrated in the Figure 11. Also this method has the possibility to maintain the mixture reaction at the same temperature. The advantage of using this system is that it can be left for a long period time without add more solvent. There are different types of condensers, commonly a simple condenser was used in the reactions of this project.

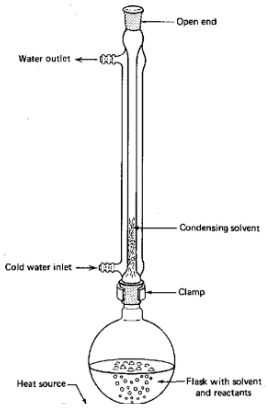


Figure 11: flask with a condenser

4.1.7 Rotary evaporator [8]

Rotary evaporation, illustrated in Figure 12 is an expensive apparatus that needs to be used with great care. Is commonly used in the laboratory to remove volatile solvents from a non-volatile sample. It works reducing the pressure in this form can be increase the rate evaporation of the solvent. Also a bath of water helps with the evaporation for give less work to the vacuum pump. Furthermore has the possibility to rotate the flask forming a thin film with a greatly increased surface area, helping to not form sudden boils and a progressive evaporation of the solvent.

Figure 12: rotary evaporator used during all the project

4.1.8 Schlenk line [13]

Schlenk line (Figure 13) has often been used in this project for some reactions. Some of the reactions in this project has been used pyrophoric reactants or in other cases reactants sensitive with oxygen, water or carbon dioxide. With this glassware system could be alternate vacuum with a gas stream. Commonly the gas stream uses is argon or nitrogen gas. As argon is more expensive the most used is nitrogen and the only one in this project. Also is equipped with a cold trap for the solvents evaporate does not pass to the vacuum pump and an oil bubbler to see the intensity of the nitrogen stream and further to avoid the contact with the atmosphere.

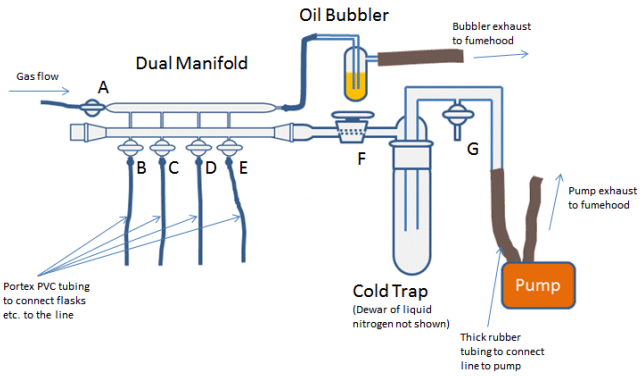


Figure 13: basic system of a Schlenk line

4.1.9 Chromatography column [8]

This is another method commonly used in organic chemistry, trying to purify in this form the mixture reactions. The method is very simple, only is used some silica as stationary phase, the elected solvent, different sizes of columns and sand to put on the top of the chromatography column. The size of the column depends of the quantity of product to purify, how near are the spots (similarity between the polarity) of the different compounds produced in the reaction. This method has the drawback that a lot of solvent is wasted for purify small amount of product, a simple chromatography columns is presented in the Figure 14.

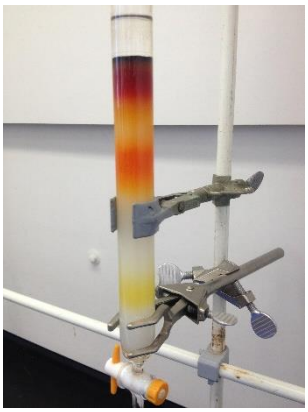


Figure 14: chromatography column used for purify some reactions

4.2 Characterization techniques

This has been the most used techniques for follow the reactions and check the structure for the compounds obtained.

4.2.1 Thin layer chromatography [14]

Thin layer chromatography is a generally technique used in chemistry to follow the reactions, see how many compounds has done the reaction and helps for chose the solvent in the purification by column chromatography. It is used like a preparation technique for the purification by column or for follow the reactions. The plates used has a stationary phase that is silica gel, is coated in glass plates. With a small amount from the mixture reaction, with the help from a capilar, is spotted on the silica plate and then the chosen solvent is allowed to run up the plate and separate the different compounds. The behaviour between the silica plate and the silica column use to be similar but not exactly equal. When the solvent reaches the top end of the plate, this has to be removed from the solvent and allowed to evaporate all the solvent.

Different methods are used to revelate the spots in the silica plate. In this project has been used a UV lamp. Observing under the UV light lamp has been recognized all the spots, commonly in short wavelength. Another factor that could be characterized in a TLC plate is the “Retention factor” expressed also as Rf. This factor is a measure of how far it has moved up the spot under certain conditions, is because of that the product can be quickly characterized if it is the expected compound.

The simple form to calculate this factor is:

$$Rf = \frac{distance\ moved\ by\ spot\ (compund)}{distance\ moved\ by\ solvent}$$

4.2.2 Nuclear magnetic resonance [15]

Is one of the most techniques used in chemistry. This one give physical, electronical, chemical and structural information about the compound studied. It is a non-destructive technique, but compared with other techniques needs a larger amounts of sample for determinate the structure and obtain a clear signals. With modern instruments can be obtained a good data with

less than a milligram. Isotopes which have spin I=1/2 shown particular interest in this technique, like ^{1}H, ^{13}C, ^{19}F and ^{31}P. Because of the spin, can be generated a magnetic moment (μ), in presence of an external magnetic field (Bo), generating two spin states. The difference between these states develop a small difference energy, which one is normally given in frequency units of MHz.

Studying the peaks produced for this difference energy, the chemist has the opportunity to determine the structure of the compound produced in the reaction done. It is consider a selective technique, distinguishing between among many atom with similar chemical environment. Also can be studied the spin-spin coupling that in most of the cases shown the stereochemical of the compound. This effect is commonly observed in ^{1}H or ^{13}C NMR.

5 Experimental part

All the reactions were done with dried glassware when the reaction conditions required it. Some solvents and reagents were dried or were bought in some cases dried. All the reagents contemplate below were ordered with high level of purity from Sigma-Aldrich, Fisher Scientific, and Acros Organics. Distillation processes were performed at room pressure. Solvent evaporation was done under Buchi Rotor Vap vacuum stills. All the reactions were followed by TLC plates (TLC Silica gel 60 F_{254} 2.5x7.5cm) from Merck Company. The analysis done by NMR technique were performed from a JEOL Delta2 Nuclear Magnetic Resonances spectrometer (400 MHz). Flash column chromatography was applied for the purification in most of the reactions done. The reactions that need to heat it up were warmed under a condenser. Many reactions were performed under nitrogen (anhydrous conditions). Almost the reactions done in this project were supervised by Professor John Wallis and COSHH's were taken according to HR regulations.

5.1 Reagents and solvents

In these list are collected all reagents (Table 1) and solvents (Table 2) used in the experimental part with his handling and dangerousness in the ANNEX.

Table 1: Reagents with his purity and company where were bought it.

Reagents		
NaOH 97% Fisher	n-BuLi 1.6M in hexanes	CuI 99.5% Sigma-Aldrich
KOH 85% Fisher	Diethyl Benzylphosphonate 95% Acros organics	Triphenylphosphine 99% Sigma-Aldrich
$Hg(OAc)_2$ 98% Sigma-Aldrich	K_3PO_4 97% Sigma-Aldrich	Phenylacetylene 98% Sigma-Aldrich
AcOH 99.7 w/w% Fisher	NH_4Cl 99.5% Fisher	Et_3N 99% Fisher
KI 99% Sigma-Aldrich	DMF 99% Sigma-Aldrich	$Pd(Cl_2(PPh_3)_2$ 98% Sigma-Aldrich
I_2 99.999% Sigma-Aldrich	H_2SO_4 98.0 w/w% Fisher	$Pd(PPh_3)_4$ 99% Sigma-Aldrich
$Na_2S_2O_3$*$5H_20$ 99% Fisher	$NaNO_2$ 97% Fisher	$MgSO_4$ 99% Fisher
CH_3I 99% Sigma-Aldrich	Triisopropyl borate 98% Sigma-Aldrich	Na_2SO_4 99% Fisher
MnO_2 99% Sigma-Aldrich	Trimety borate 99% Sigma-Aldrich	HCl 36.5% v/v 12M Fisher
DIBAL-H 1.0M in THF Sigma-Aldrich	9-BBN triflate 0.5M in hexanes	Styrene 99% Sigma-Aldrich

Table 2: Solvents with his purity and company where were bought it.

Solvents	
DMSO 99.7% Fisher	Cyclohexane 99% Fisher
Et_2O 99% Fisher	EtOAc 99.9% Fisher
THF 99.9% Sigma-Aldrich	$CHCl_3$ 99.8% Fisher
MeOH 99.8% Fisher	Propan-2-ol 99.5% Fisher
Hexane 95% Fisher	Acetone 99.5% Fisher

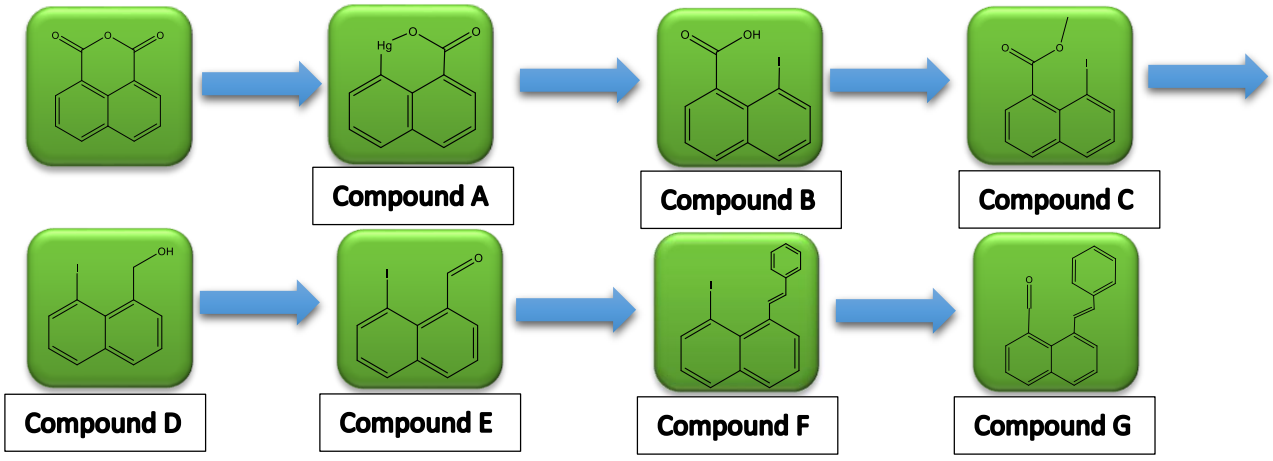
5.2 Synthesis

The target compounds for this project, has been tried to synthesize with two different starting reagents. The first one was 1,8-naphthalic anhydride and the other one was 1,8-diaminonaphthalene. Starting with the second route it is quicker to arrive to the target compounds or in the penultimate step from the target compound. In both routes are tried different reactions to obtain the expected compounds. Furthermore, some reactions were tried for intermediate compounds to find which one give the best yield and easy conditions. Only the reactions that shown best yield and conditions has been explained in this experimental procedure.

5.2.1 Route 1: starting with 1.8-naphthalic anhydride

The first route is exemplified in the Scheme 1.

Scheme 1: long route tried



5.2.1.1 Compound A: Preparation of 8-carboxynaphth-1-yl-mercury (II) [16]

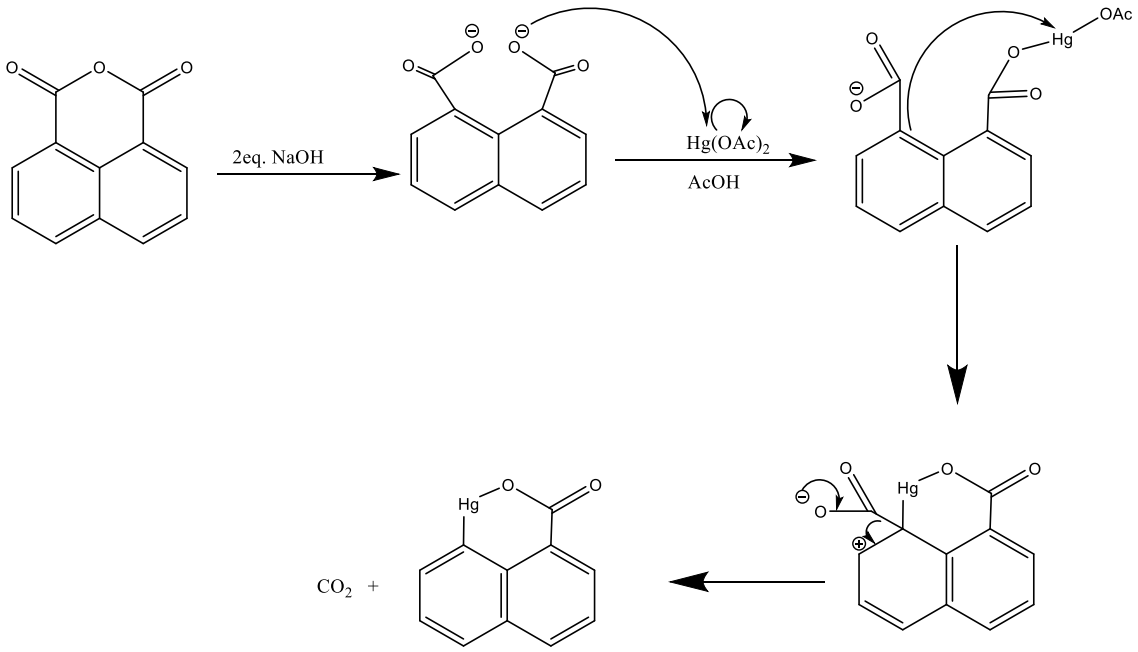


Figure 15: Preparation of 8-carboxynaphth-1-yl-mercury (II)

1.8-Naphthalic anhydride (10.0g, 0.05mol) was added to a round bottomed flask containing a solution of NaOH (7.0g, 0.18mol) in H_2O (350mL). The mixture formed was refluxed with stirring until the reagents dissolved. The excess NaOH was neutralized with AcOH (5mL), leading to the pH changing from 12 to 6-7. A solution of $Hg(OAc)_2$ (16.35g, 0.05mol), H_2O (50mL) and AcOH (3mL) was added to the reaction mixture all at once. The mixture was refluxed for 30 minutes and then AcOH (9mL) was added to ensure the evolution of CO_2. This mixture was refluxed for 48 hours at 150ºC, cooled to room temperature, filtered under vacuum (Büchner filtration). The

solid was washed with water, to obtain the product that is shown in the Figure 15. There was no need to dry the product because the following reaction uses water as solvent.

5.2.1.2 Compound B: Preparation of 8-Iodo-1-naphthoic acid [16]

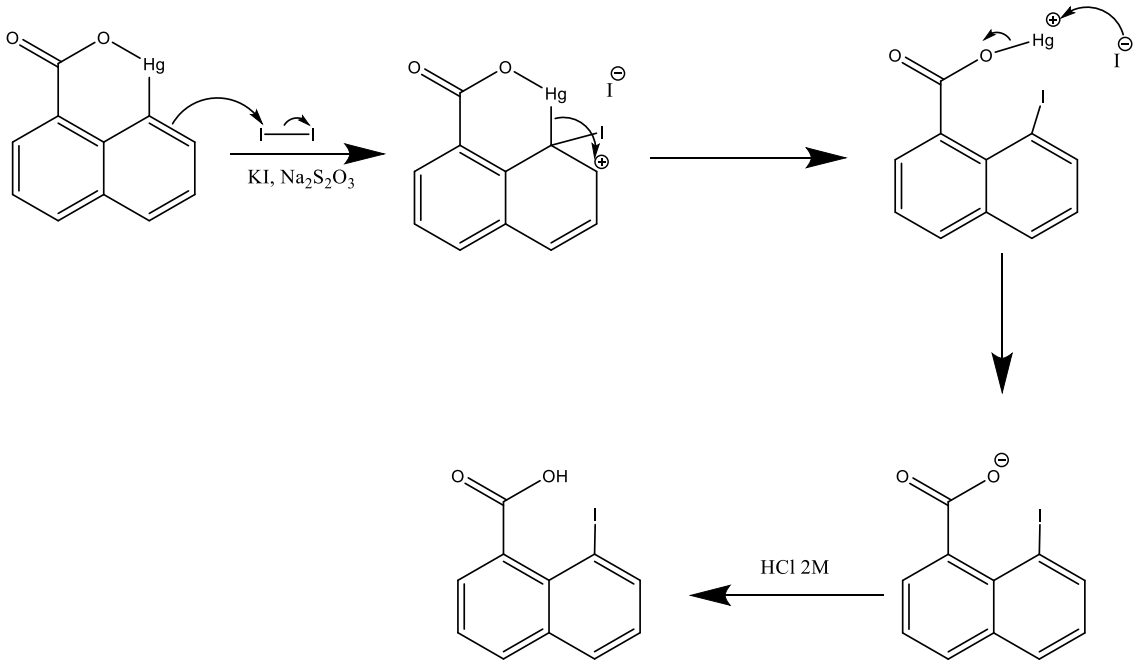


Figure 16: Preparation of 8-Iodo-1-naphthoic acid

In a round bottomed flask 8-carboxynaphth-1-yl-mercury (II) (17.2g, 46.41mmol), was stirred with KI (31.4g, 0.18mol) in H_2O (170mL). After dissolution of this mixture at room temperature, I_2 (12.1g, 47.6mmol) was added and the mixture was refluxed overnight. The next day the solution was cooled to room temperature, then the brown precipitate was filtered off with a Büchner flask under vacuum and washed with water. To this filtrate was added a solution of $Na_2S_2O_3$ (8.6g, 55mmol) in H_2O (35mL) to destroy the excess of iodine. The solution was acidified to pH 3 by addition of 2M HCl prepared by a dilution from 12M HCl, to form a precipitate. This precipitate was filtered under vacuum with a Büchner flask. This solid obtained was purified with hot acetone under reflux and treated with activated charcoal. Much acetone it could be add to dissolve the crude acid, with some stirring and heat to 60ºC. The mixture was filtered to eliminate the activated charcoal and the acetone was evaporated in the rotary evaporator, then dried under vacuum overnight. Purification with acetone gave 8-iodo-1-naphthoic acid 6.5g (45%) as a white-brown solid. Ilustrated the effect from each reagent in the Figure 16 . ^{1}H NMR (400 MHz, DMSO-d_6) δ:8.24 (1 H, d, J= 8.56 Hz), 8.00 (2 H,m), 7.72 (1 H, d, J= 8.24 Hz), 7.55 (1 H, m) .26 (1 H, t, J=15.56); ^{13}C NMR (400 MHz, DMSO-d_6) δ: 170.2 (COOH), 141.34, 135.8, 134.8, 131.2, 129.4, 128.2, 127.5, 125.4, 93.7 (Ar-C one peak is doubly degenerate).

5.2.1.3 Compound C: Preparation of methyl 8-iodo-1-naphtoate [17]

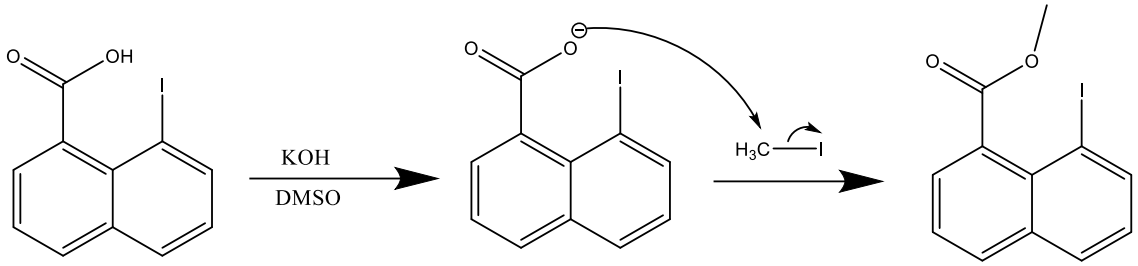


Figure 17: Preparation of methyl 8-iodo-1-naphtoate

In a round bottomed flask 8-iodo-1-naphthoic acid (6.5g, 21.7mmol) was dissolved in DMSO (65mL). To the stirred solution was added KOH (5.2g, 0.09mmol) which has been previously crushed in a mortar with a pestle, finally at the mixture CH_3I (13.1g, 0.09mmol) was added and the mixture was allowed to stir at room temperature overnight.

To extract the product, an excess of H_2O (500mL) was added, to continue extract with EtOAc (3x100mL). The combined extracts were dried with 3 spatulas of anhydrous $MgSO_4$. The mixture was filtered and then evaporate in the rotary evaporator to eliminate the ethyl acetate to obtain an oil, to eliminate de DMSO was washed with a brine solution (3x20mL) and extract with more ethyl acetate added previously, then collected the organic phase, dried with 3 spatulas of anhydrous $MgSO_4$. The mixture was filtered to obtain the organic phase and the solvent evaporated in the rotary evaporator and dried under vacuum overnight to obtain 4.0g (58%). Reaction explained in the Figure 17. ^{1}H NMR (400 MHz, $CDCl_3$) δ:8.23 (1H, d, J= 7.32 Hz), 7.88 (2H,m), 7.71 (1H, d, J= 8.24 Hz), 7.49 (1H, m), 7.19 (1H, t, J=7.32), 3.04 (3H,s); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 169.9 (COOR), 141.4, 135.2, 134.1, 131.8, 129.5, 129, 127.2, 125.1, 92.5 (Ar-C one peak is doubly degenerate), 52.9 (Me from COOMe).

5.2.1.4 Compound D: Preparation of (8-iodo-1-naphthyl) methanol [16]

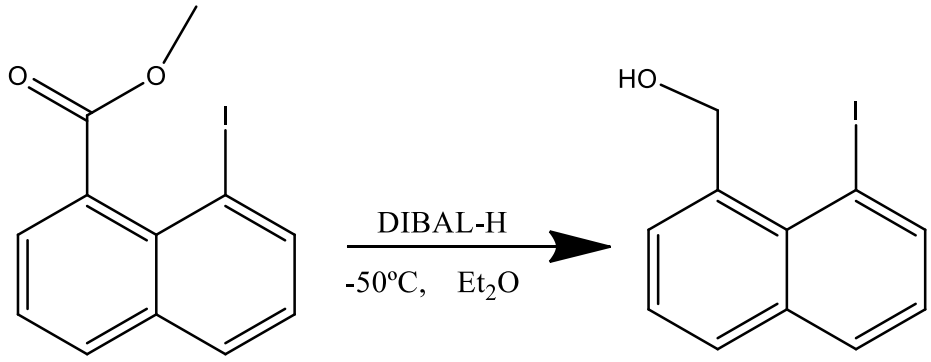


Figure 18: Preparation of (8-iodo-1-naphthyl) methanol

To a round bottom flask of 50mL with three necks, was added methyl 8-iodo-1-naphthoate (1.53g,4.91mmol) and was left under N_2 atmosphere around 15 minutes, after this dry diethyl ether (30mL) was added and the mixture was stirred during 30 minutes to arrive at -50ºC (dry ice + acetone) and then DIBAL-H (10mL) under N_2 (carefully DIBAL-H in contact with water or air form flammable gas) and was added dropwise and then stirred during 30 min. Then at this mixture was added MeOH/H_2O 1:1 (2mL) dropwise and was warmed to room temperature. When this happened, a precipitated salt was formed and the solution turn more viscous like a

solid solution. To dissolve the salt was added 3M HCl (8ml) or more if the salt is not dissolved. Then the mixture was placed in an extraction funnel to separate more quickly the organic layer and extract with more diethyl ether (20mL), after this the organic layer was dried with 3 spatulas anhydrous $MgSO_4$. The organic solvent was evaporated in the rotary evaporator to obtain 0.856g of product (60%).Reduction with DIBAL-H is explained in Figure 18. ^{1}H NMR (400 MHz, $CDCl_3$) δ:4.01 (1H, -OH), 5.53 (2H,d,-CH_2-OH J=6.88), 8.43 (1H, d, J= 7.76Hz) 7.82(1H,d,J= Hz), 7.71(1H, d, J= Hz), 7.63 (1H, d, J= Hz), 7.43 (1H, t, J= Hz), 7,1 (1H, t, J= Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ: 142.41 (-CH_2-OH), 136.77,135.60, 131.52, 130.58, 130.38, 126.37, 125.83 (Ar-C_{10} two peak are doubly degenerate), 89.97 (C-I).

5.2.1.5 Compound E: Preparation of 8-iodo-1-naphtyhaldehyde [18]

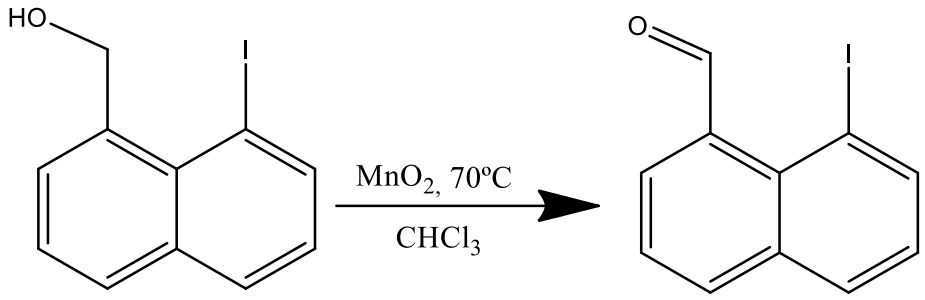


Figure 19: Preparation of 8-iodo-1-naphtyhaldehyde

To a round bottom flask of 50 ml was added (8-iodo-1-naphthyl) methanol (0.856g, 2.9 mmol), $CHCl_3$ (15mL) as solvent and MnO_2 (0.52g, 6mmol). This reagent was mixed together and was heated with a reflux connected to 70ºC with continuous stirring overnight. The next day the mixture was filtered through a celite (SiO_2), and was washed with $CHCl_3$ many times. After this in an extraction funnel the organic layer was washed with H_2O (60mL) and collected, dried with anhydrous sodium sulphate, filtered and purified by column (Φ 3.0cm , 400 mL of silica gel) and eluted with ethyl acetate/cyclohexane 3:1. The portions that contains the compound were collected and evaporates the organic solvent in the rotary evaporator to obtain an oil. The oil was dried under vacuum to obtain brown crystals 0.78g (92%) during 2 hours. Oxidation illustrate in Figure 19. ^{1}H NMR (400 MHz, $CDCl_3$) δ:11.68 (1H, -CHO), 8.25 (1H, d, J= 7.32Hz) 7.87(1H,d,J=7.36 Hz), 7.86(1H, d, J=7.36 Hz), 7.85(1H, d, J=7.36 Hz), 7.52 (1H, t, J= 8.24Hz), 7,21 (1H, t, J= 8.24Hz) ; ^{13}C NMR (400 MHz, $CDCl_3$) δ: 191.58 (-CHO), 141.17, 136.41, 135.52, 134.10, 130.07, 129.63, 127.59, 125.85(Ar-C one peak is doubly degenerate), 89.75 (C-I).

5.2.1.6 Compound F: Preparation of 1-iodo-8-styrylnaphthalene [19]

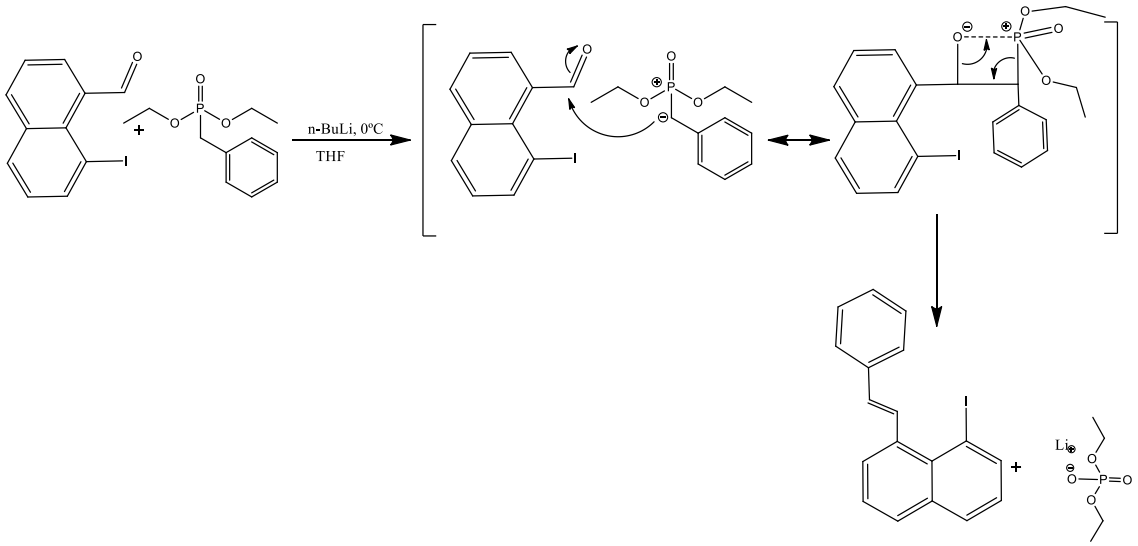


Figure 20: Preparation of 1-iodo-8-styrylnaphthalene

To a round bottom flask of 50 mL was added diethyl benzylphosphonate (0.35mL) and mixed with THF (5mL) in a cool bath at 0ºC, under N_2 stream with continuous stirring. After that was added n-BuLi (2.5mL) carefully dropwise (intense yellow was observed). The mixture were left during 2 hours under N_2 stream at 0ºC. After that 8-iodo-1-naphtyhaldehyde (3.5g, 1.17mmol) previously dissolved in THF (3mL) and leave it overnight. The next day in the reaction was added EtOAc (25mL), then washed with water (3x30mL). The aqueous layer was extracted with more EtOAc (3x20mL), the two organic layers were mixed and dried with anhydrous $MgSO_4$ and evaporate the solvent under vacuum. Purification has done with a chromatography column (Φ 2.5cm, 400 mL of silica gel) with pure hexane to obtain a yellow oil 3.0g (67%) (Rf= 0.24 in pure hexane). Wadsworth Emmons reaction is illustrated, in Figure 20.^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.78 (1 H, d, J=16.01 Hz) 7.06 - 7.11 (1 H, m) 7.28 - 7.34 (1 H, m) 7.42 (2 H, s) 7.47 (1 H, d, J=7.78 Hz) 7.63 (2 H, d, J=7.78 Hz) 7.79 (1 H, d, J=8.23 Hz) 7.85 (1 H, d, J=7.32 Hz) 8.29 (1 H, s) 8.43 (1 H, d, J=16.01 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 91.33 (1 C-I, s), 126.10 (1 C double bond alkene, s), 132.26 (1 C double bond alkene, s), 126.74, 127.60, 128.72, 128.84, 128.89, 129.92, 131.01, 135.55, 137.61, 137.91 (Ar-C two peaks are doubly degenerate).

5.2.1.7 Compound G: Preparation of (E)-8-styryl-1-naphthaldehyde [20]

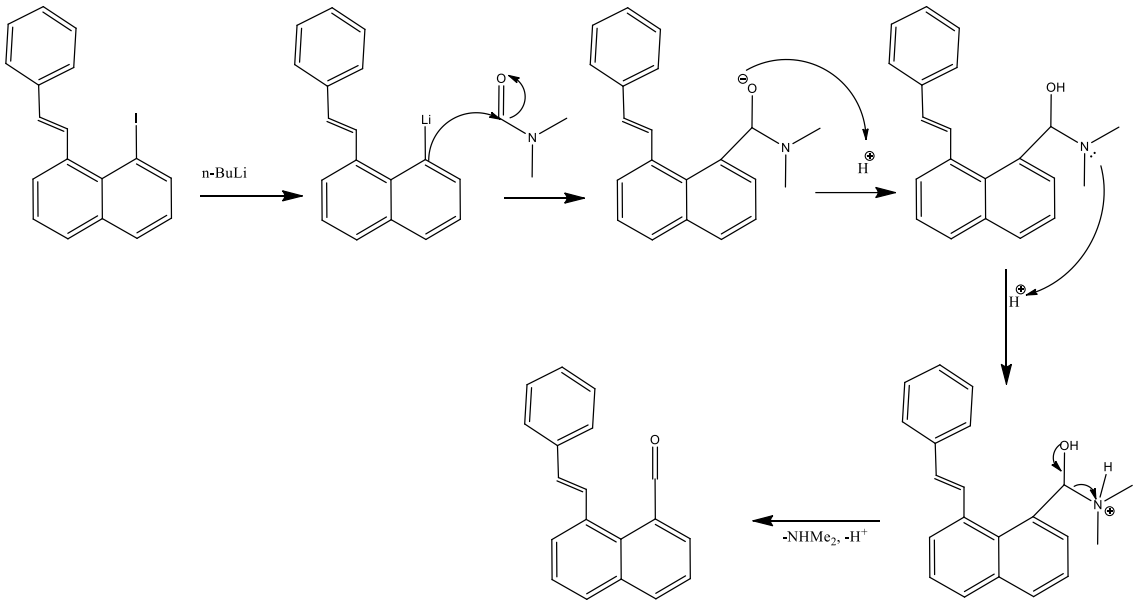


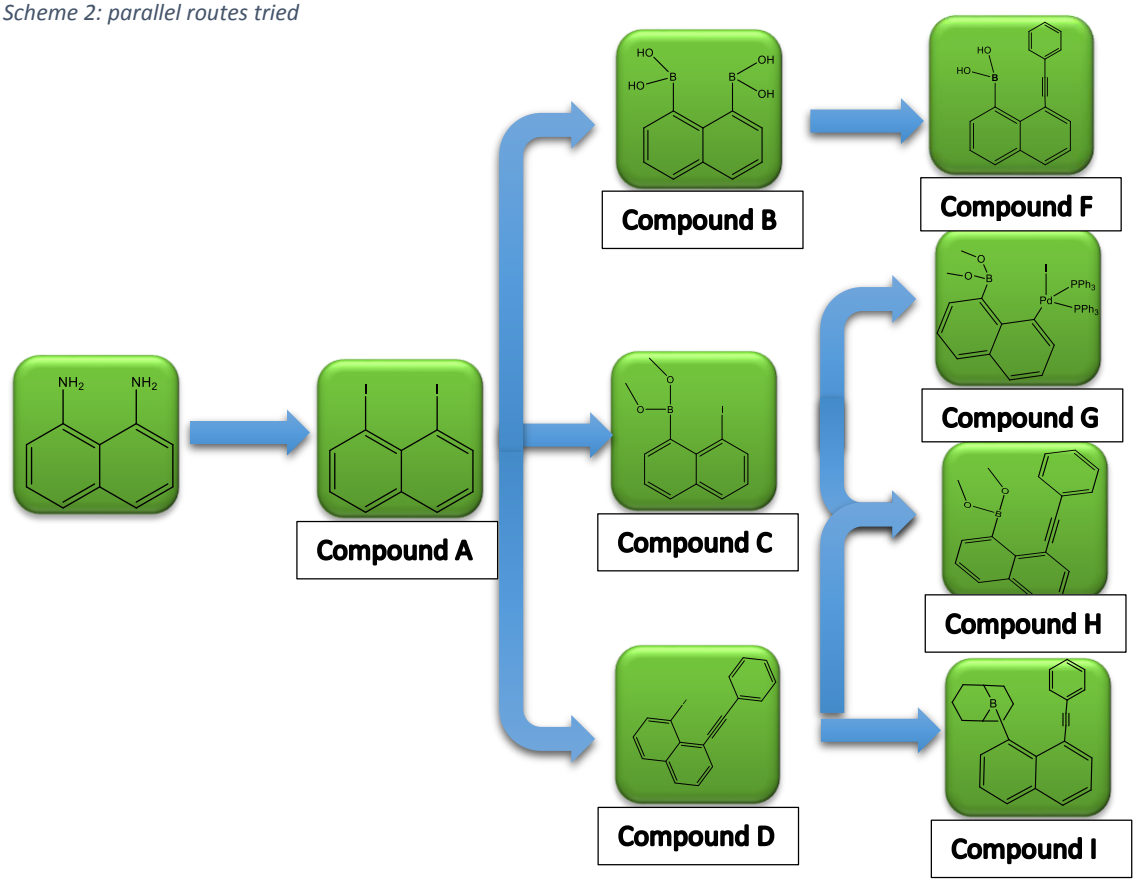
Figure 21: Preparation of (E)-8-styryl-1-naphthaldehyde

To a round bottom flask with three necks of 150 mL were added (E)-1-iodo-8-styrylnaphthalene (0.150g, 0.42mmol) in dry Et_2O (5mL). The mixture solution was cooled to -78ºC and stirring during 20 minutes. After that n-BuLi (0.3mL, 0.46mmol) was added dropwise to the mixture solution. The mixture solution was left warming during 2 hours. The last reagent to add is DMF (0.16 mL, 2.18mmol) and was left under a N_2 stream overnight. A solution of NH_4Cl (20mL; 10%w/v) was added and was left stirring during 5 minutes. The next step was to extract with EtOAc (3x25 mL) as a solvent. The organic layers were collected and mixed together and washed with brine (3x10 mL). The organic layer was dried with anhydrous $MgSO_4$. Many products were observed in the TLC plate. It was tried to purify the compound with column chromatography (Φ 4.5cm, 400 mL of silica gel) using pure cyclohexane as solvent. The theoretical reaction illustrate in Figure 21.

5.2.2 Route 2: starting with 1,8-diaminonaphthalene

The second route with the different ways tried is exemplified in Scheme 2.

Scheme 2: parallel routes tried



5.2.2.1 Compound A: Preparation of 1, 8-diiodonaphthalene [20]

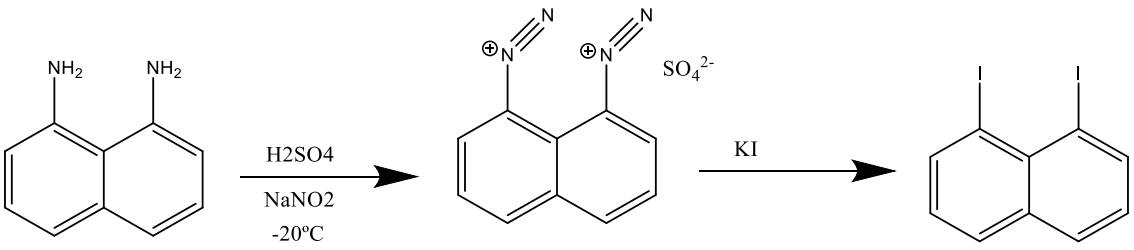


Figure 22: Preparation of 1, 8-diiodonaphthalene

This is a complicated reaction, since the intermediate is a very reactive diazonium salt and there are two diazonium groups in the same structure. To a three neck round-bottom flask containing 1, 8-diaminonaphthalene (3.0g, 18.9mmol) and H_2O (21mL). Was added a solution of sulphuric acid (H_2SO_4 14mL/ H_2O 21mL). This solution was added dropwise slowly with compensated pressure funnel since it is an exothermic reaction. This mixture was stirred for 30 minutes and

then placed in a cooling bath at -20ºC (Dewar vassar with acetone and dry ice CO_2). The next step was to add a solution of $NaNO_2$ (3.8g, 55.85mmol) in H_2O (14mL). This solution was added dropwise with stirring for 10 minutes. The next step was to add a solution of KI (19.2g, 115mmol) in H_2O (16mL) to destroy the double diazonium salt. This solution was added portionwise with occasional shaking to be sure that it was an homogeneous reaction, this addition was carried out for 15 minutes. When the addition was finished, the mixture was heated to room temperature and then heated slowly to 40ºC, during 15 minutes. It is formed a black rock solid. This was washed two times with water and the brown water was decanted, then the solid was dissolved in toluene (200mL) and heated to boiling point. In this form the rock solid was dissolved. The hot solution was filtered through silica gel pad, and the silica was washed with fresh hot toluene. The organic solution was washed with H_2O (63mL), then with an aqueous solution of $Na_2S_2O_3$ (30 mL every time; 25% w/v), brine solution (63mL), and then dried with anhydrous $MgSO_4$. The solution was filtered and the solvent removed in the rotary evaporator. Then was added to the product silica and dissolved in toluene (the silica absorbed the product) and evaporated another time the solvent to obtain a dry silica with our compound adherent to silica. This silica was placed on a top of chromatographic column (Φ 4.5cm, 400 mL of silica gel) and eluted with cyclohexane. 5 Portions of 150 mL were collected and then a TLC prepared to see where the product was. The fractions of interest were evaporated to obtain 1,8-diiodonaphthalene 2.6g (36%) as yellowish crystal(Rf= 0.34 in pure hexane). Scheme of the reaction in Figure 22. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42 (2 H, d, J= 7.32 Hz), 7.85 (2 H,d, J=8.24), 7.09 (2 H, t, J= 7.76Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 144.01, 135.77, 132.08, 131.00, 126.92 (Ar-C), 95.97 (C-I).

5.2.2.2 Compound B: Preparation of 1,8-naphthalenediboronic acid [21]

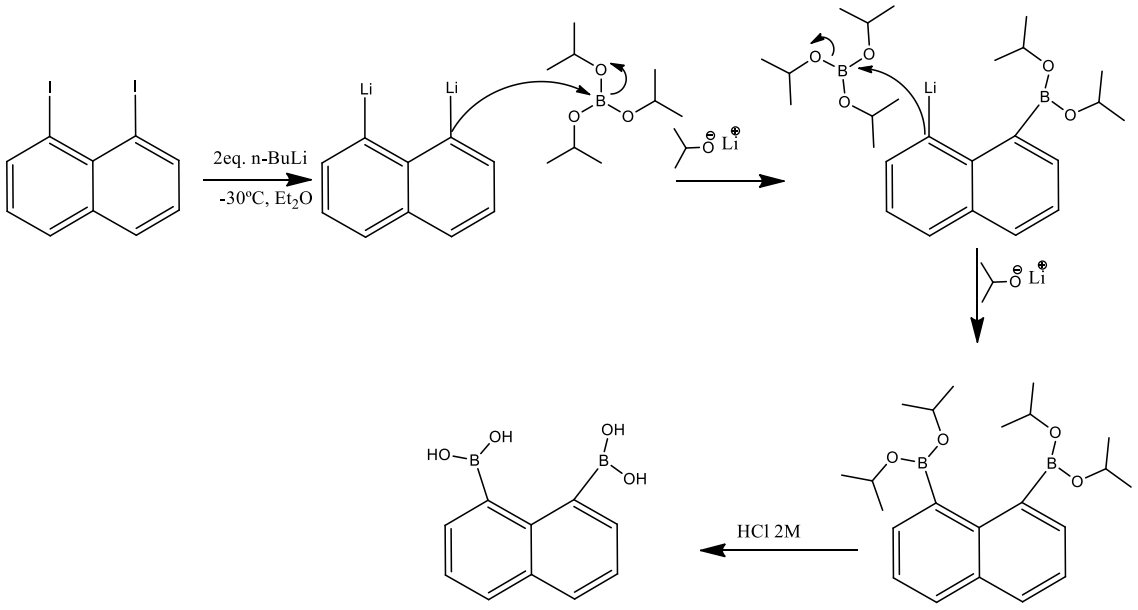


Figure 23: Preparation of 1,8-naphthalenediboronic acid

To a round bottom flask of 250 mL with 2 necks were added 1,8-diiodonaphthalene (1.0g, 2.63mmol) and a N_2 stream passed through alternated with vacuum, three times. In the round bottom flask was added dry Et_2O (40mL). The mixture solution was cooled down to -30ºC with continuous stirring. Once the target temperature was reached n-BuLi was added (3.8mL, 6.08mmol) dropwise (change of colour has to be observed) and was left at -30ºC during 20

minutes with continuous stirring under N_2 stream. The mixture reaction was cooled down to -78ºC and the electrophilic reagent was added in this case triisopropyl borate (18 mL; 98% redistilled) and was left warming up slowly to room temperature overnight. The next day in the mixture solution was a white precipitate. This could be an indicator that the reaction has been successful (the white precipitate is the salt of lithium propan-2-olate). To the mixture was added 2M HCl (20mL), the precipitate disappeared and it is formed a small amount again. The organic layer is decanted and the precipitate filtered off. The organic layers were combined to be treated with more 2M HCl (20 mL). The organic layer was collected and treated with 1M NaOH (washed 3x10 mL), and the aqueous solution combine. The aqueous solution was acidificated with more 2M HCl (40 mL) to obtain a white yellow solid and filtered off with a Büchner funnel. Dried under vacuum to obtain 0.250g (44% yield). According to the Figure 23. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.76 (4 H, s) 7.55 - 7.64 (2 H, m) 8.05 (2 H, d, J=9.15 Hz) 8.19 (2 H, d, J=7.78 Hz). No available ^{13}C NMR.

5.2.2.3 Compound C: Preparation of dimethyl (8-iodonaphthalen-1-yl) boronate [22]

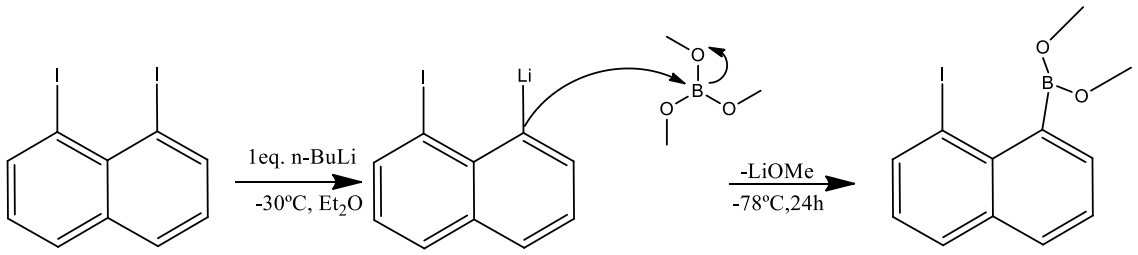


Figure 24: Preparation of dimethyl (8-iodonaphthalen-1-yl) boronate

To a round bottom flask of 100 mL with 3 necks, was added 1,8-diiodonaphthalene (0.5g, 1.31mmol) and dissolved with dry Et_2O (19mL) and cooled down to -25ºC under N_2 stream all the reaction. When the mixture reaction it was at -25ºC n-BuLi (0.8mL, 1.31mmol) was added dropwise with continuous stirring and was left during 20 minutes. Finally the mixture was cooled down to -78ºC and distilled and dried $(MeO)_3B$ (0.3mL, 2.63mmol) added and left warming up slowly overnight to room temperature. The next day the TLC eluted with pure hexane only showed two spots, the starting reagent and the product (dimethyl (8-iodonaphthalen-1-yl) boronate). The mixture was washed with H_2O (3x20 mL), The aqueous solution was washed with more Et_2O and the combined organic layers dried with anhydrous Na_2SO_3, the solid filtered off and the solvent evaporated under vacuum to obtain 0.075g (17% of yield)(Rf= 0.45 in pure hexane), as is explained the reaction in the Figure 24. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.58 (6 H, s), 7.45 - 7.51 (1 H, m), 7.52 - 7.55 (1 H, m), 7.79 (1 H, d, J=7.78 Hz), 7.86 (1 H, d, J=8.23 Hz), 8.08 (1 H, d, J=8.23 Hz), 8.14 (1 H, d, J=7.32 Hz). ^{13}C NMR (400 MHz, $CDCl_3$) δ: 52.87 (2 O-CH3, s), 99.30 (1 C-I, s), 132.22 (1 C-B, s), 126.00, 126.73, 129.90, 131.74, 134.96, 137.15, 137.52, 138.68 (Ar-C).

5.2.2.4 Compound D: Preparation of 1-iodo-8-(phenylethynyl)naphthalene [23]

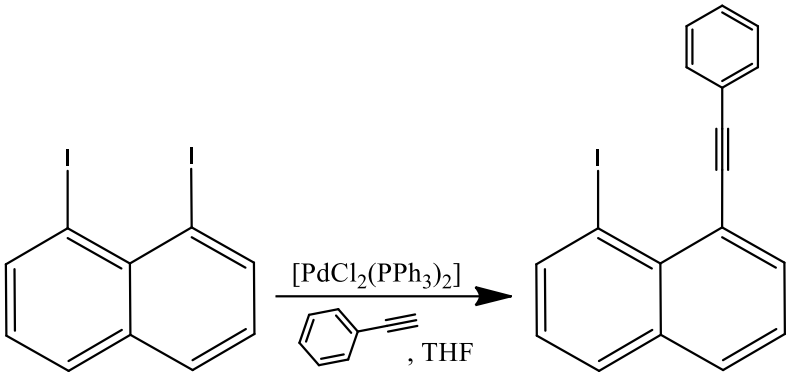


Figure 25: Preparation of 1-iodo-8-(phenylethynyl)naphthalene

To a round bottom flask of 100 mL with three necks were added all the reagents: 1,8-diiodonaphthalene (1.0g, 2.63mmol), bis(triphenylphosphine)palladium(II) dichloride [$PdCl_2(PPh_3)_2$] (66.2mg), copper (I) iodide (62.0mg, 0.32mmol), recrystallized triphenylphosphine (85.0mg), phenylacetylene (0.18mL, 1.89mmol) and add a solution previously prepared (1:1) Et_3N (16.2mL) and THF (16.2 mL). The reaction was left under N_2 stream with continuous stirring heating with reflux overnight about 18-20 hours. After this the solvent was evaporated under vacuum. The obtained solid were dissolved in $CHCl_3$ and washed with water (3x25mL), then with a brine solution (3x15mL) and dried with anhydrous Na_2SO_4.The purification has done with a chromatography column (Φ2.5cm , 400mL of silica gel) using as eluent pure hexane, and evaporated the right fraction to obtain an oil 0.82g (89%)(Rf= 0.22 in pure hexane).Reaction done is explain in the Figure 25. ^{1}H NMR (400 MHz,$CDCl_3$) δ:7.10 (1 H, s), 7.25 (1 H, s), 7.37 - 7.40 (1 H, m), 7.40 - 7.43 (2 H, m), 7.45 (2 H, d, J=7.32 Hz), 7.65 - 7.70 (1 H, m), 7.77 - 7.87 (1 H, m), 7.94 (1 H, d, J=5.83 Hz), 8.31 (1 H, d, J=7.32 Hz). 13C NMR (400 MHz, CDCl3) δ: 89.35 (1 C triple bond, s), 93.06 (1 C triple bond, s), 100.89 (1 C-I, s), 122.88,124.09, 125.58, 127.22, 128.51, 128.54, 128.60, 130.27, 130.53, 130.93, 131.96, 134.99, 136.08, 142.78. (Ar-C one peak is double degenerate).

5.2.2.5 Compound F: Preparation of (8-(phenylethynyl)naphthalen-1-yl)boronic acid [24]

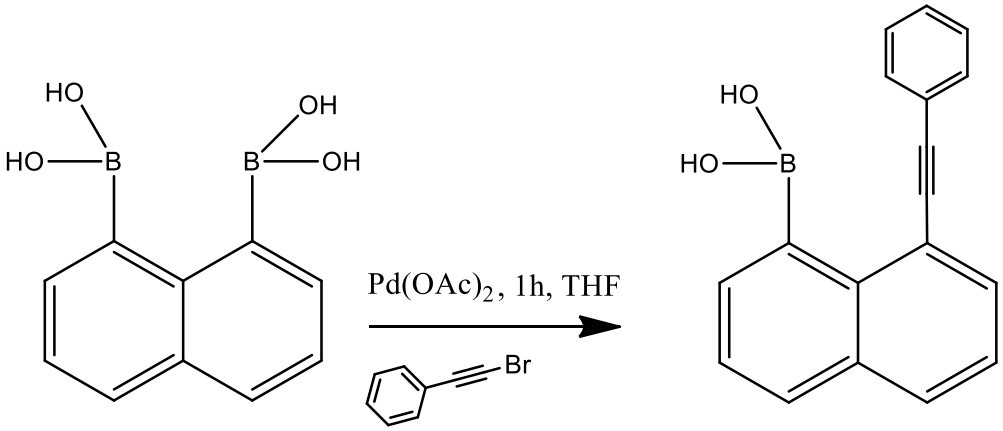


Figure 26: Preparation of (8-(phenylethynyl)naphthalen-1-yl)boronic acid

To a round bottom flack with two necks of 25mL were added: 1,8-naphthalenediboronic acid (0.087mg, 0.40mmol) , with (bromoethynyl)benzene (0.109g, 0.60mmol) and using as a solvent

n-propanol (4mL). To the mixture reaction was passed a N_2 stream alternate with vacuum. After doing this process three times, the Pd catalyst was added, in this case $Pd(OAc)_2$ (2.5mg;0.0046mmol) and PPh_3 (2.5mg, 0.0095mmol) and heated up with reflux during 1 hour. The reaction was followed by TLC using as eluent (4:1 hexane: ethyl acetate). The mixture reaction was evaporated mixed with silica and putted on the top of a chromatography column (Φ 1.0cm, 80 mL of silica gel) to purify. Theoretical reaction is illustrate in Figure 26.

5.2.2.6 Compound G: Preparation of a pre-catalyst for following reactions [25]

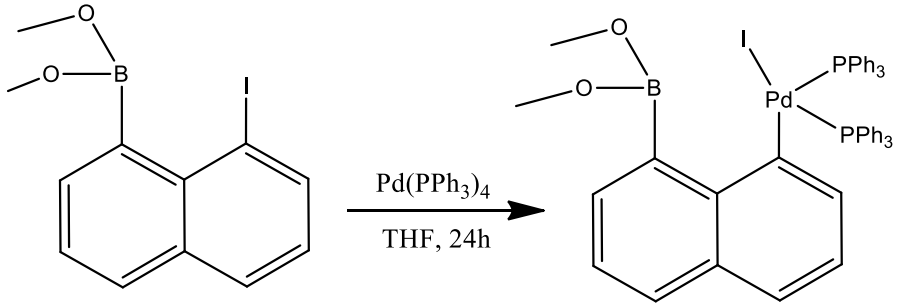


Figure 27: Preparation of a pre-catalyst for following reactions

To a round bottom flask of 25 mL with 3 necks were added dimethyl (8-iodonaphthalen-1-yl)boronate (0.184g, 0.56mmol), a complex Pd catalyst in this case $Pd(PPh_3)_4$ (0.5g, 0.56mmol) dissolved in dry THF (3mL) at room temperature, under N_2 stream overnight. The next day the reaction was checked by TLC plate with pure hexane (Rf=0.21 in pure hexane). The product was forced to precipitate adding pure hexane (30 mL). The precipitate was filtered off with a Büchner funnel and dried to obtain an orange solid 0.244g (37% yield). Pre-catalyst formed is illustrate in Figure 27. ^{1}H NMR (400 MHz, $CDCl_3$-d) δ:3.58 (6 H, s), 7.11 - 7.18 (2H, m), 7.42 - 7.49 (12 H, m), 7.51 - 7.57 (6 H, m), 7.68 (12 H, d, J=7.32 Hz), 7.70 - 7.70 (1 H, m), 7.78 (1 H, d, J=7.78 Hz), 7.85 (1 H, d, J=8.23 Hz), 8.06 - 8.10 (1 H, m), 8.13 (1 H, d, J=6.86 Hz). No available ^{13}C NMR.

5.2.2.7 Compound H: Preparation of dimethyl (8-(phenylethynyl)naphthalene-1-yl)boronate [23] [22]

It was tried to synthesize compound G with different ways. Neither of them were successful. The conditions applied for adding any of the two groups, has been done in the same way if is started with the 1,8-diiodonaphtalene and add one group. The procedure used was the same that for do compound C or D.

5.2.2.8 Compound I: Preparation of 9-(8-(phenylethynyl)naphthalene-1-yl)-9-borabicyclo[3.3.1]nonane [22]

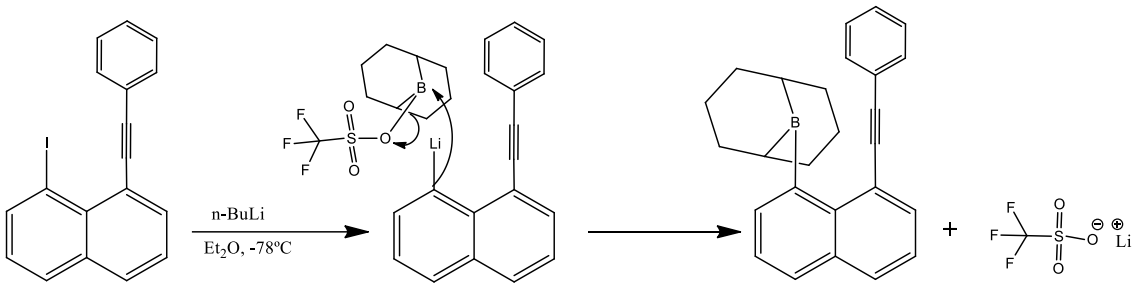


Figure 28: Preparation of 9-(8-(phenylethynyl)naphthalene-1-yl)-9-borabicyclo[3.3.1]nonane

To a round bottom flask of 250mL with 2 necks were added dry Et_2O (20mL) with 1-iodo-8-(phenylethynyl)naphthalene (0.668g, 1.69mmol) under N_2 stream, and the mixture was cooled down to -78ºC with continuous stirring during 20 minutes. To the mixture reaction was added n-BuLi (1.33mL, 2.08mmol) dropwise. The mixture reaction was left during 1 hour with continuous stirring under N_2 stream at -78ºC. After 1 hour was added the electrophile group 9-BBN triflate (4.16mL, 2.08mmol; 0.5M in hexanes) and was left overnight under N_2 stream warming up to room temperature. The next day to the mixture solution was added hexane to precipitate the salt and filtered off to collect the organic layer. The mixture was mixed with silica and the solvent evaporated and put on the top of the chromatography column (Φ 4.0cm, 400 mL of silica gel) eluted with pure hexane. Reaction with 9-BBN triflate is illustrated in Figure 28.

6 Results and discussion

The experimentation done in this project has mainly consisted in the synthesis of some molecules of interest trying to arrive to the expected molecule proposed in the aim of this project. All of them has been tried to characterize with NMR technique to ensure that has been obtained the expected compounds. Below is a discussion of the methods and results obtained in the molecules that was in the previous steps to be the right molecule and the reactions did not work successfully.

As is explained in the experimental procedure two routes were tried. The first one is a long route to arrive a small amount of compound that is the direct intermediate to form the target molecule.

The second route has the possibility to work in parallel form starting different ways with 1,8-diiodonaphthalene to the target compounds.

6.1 Discussion of the preparation of (E)-8-styryl-1-naphthaldehyde

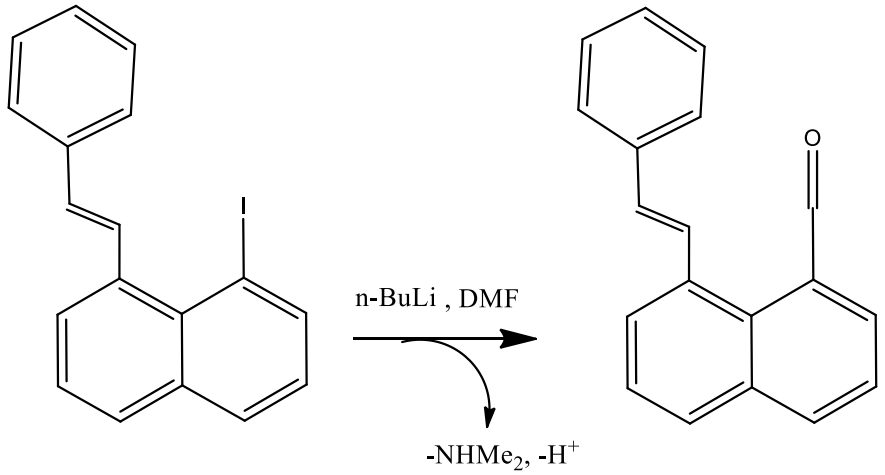


Figure 29: Reaction for the formation of (E)-8-styryl-1-naphthaldehyde

In most of the reactions has done this method of the lithiation and to add afterwards an electrophile reagent. This reaction was done at low temperature -78ºC and under N_2 conditions. Only 1,1eq of n-BuLi was used, should lithiate only one of the positions (because of there is only one position possible to lithiate). And after 2 hours was added the electrophile, as is shown in Figure 29. The NMR did not looks like the expected compound. No signal of aldehyde proton or carbon was there. With the NMR was not possible to predict the right structure. It is not observed any signal in the carbon NMR of iodo in the position 8, that should appear arround 98ppm We can consider in that point that the step of the lithiaton of our compound has done. The reaction was left warming up during 2 hours, maybe one of the problems is that the lithiation has done and the molecule becomes more reactive when the temperature is less lower, in that point could react the double bond forming a cycle of three atoms carbons. The NMR (Figure 30) present a little bit of impurities and has not been possible to predict which structure it is.

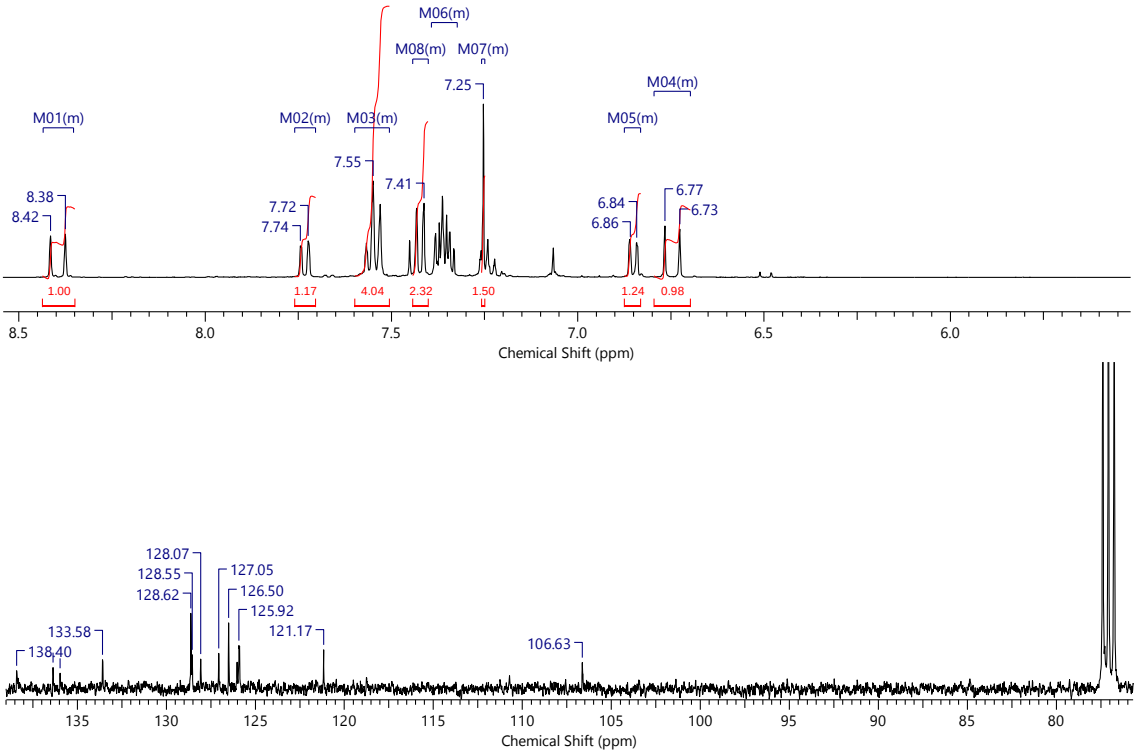


Figure 30 upper it is ^{1}H NMR and the other ^{13}C NMR

6.2 Discussion of preparation of dimethyl (8-(phenylethynyl)naphthalene-1-yl)boronate

Two routes were tried for produce this compound. None of them had a successful result. The first one was starting with the 1-iodo-8-(phenylethynyl) naphthalene and added the trimethyl borate. Previously it was lithiated with n-BuLi, as is shown in Figure 31.

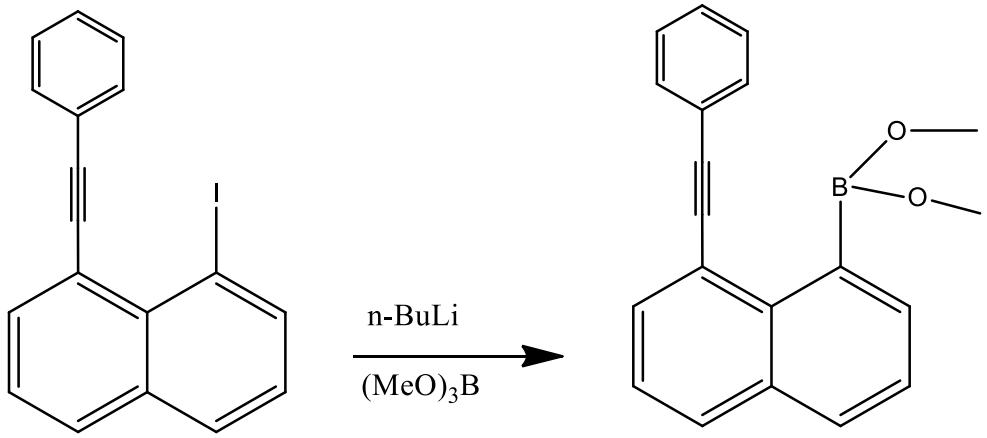


Figure 31: Reaction for the formation of dimethyl (8-(phenylethynyl)naphthalene-1-yl)boronate

Multiple spots appeared in the TLC plate, the only thing that was obtained was two spots together with other two spots more. Any of the two fractions looks like is the expected compound. Iodo has disappeared in the NMR, in this point is considered that the lithiation has been done but none of the NMR looks like containing the methoxy groups joined to boron. It

was thought that the triple bond could be attacked by the product of lithiation formed as in the previous case, one of the products formed was the protonation in the position occupied previously by the iodo atom. The other compound thought was that one time the trimethyl borate is added to the 1-iodo-8-(phenylethynyl)naphthalene the boron group becomes more reactive than trimethyl borate and the next molecule of 1-iodo-8-(phenylethynyl)naphthalene react with this one forming like a big molecule. It could not say certainly that this is what was formed because NMR (Figure 32) contain some impurities and it is difficult to predict. The complex thought was illustrated in the Figure 33.

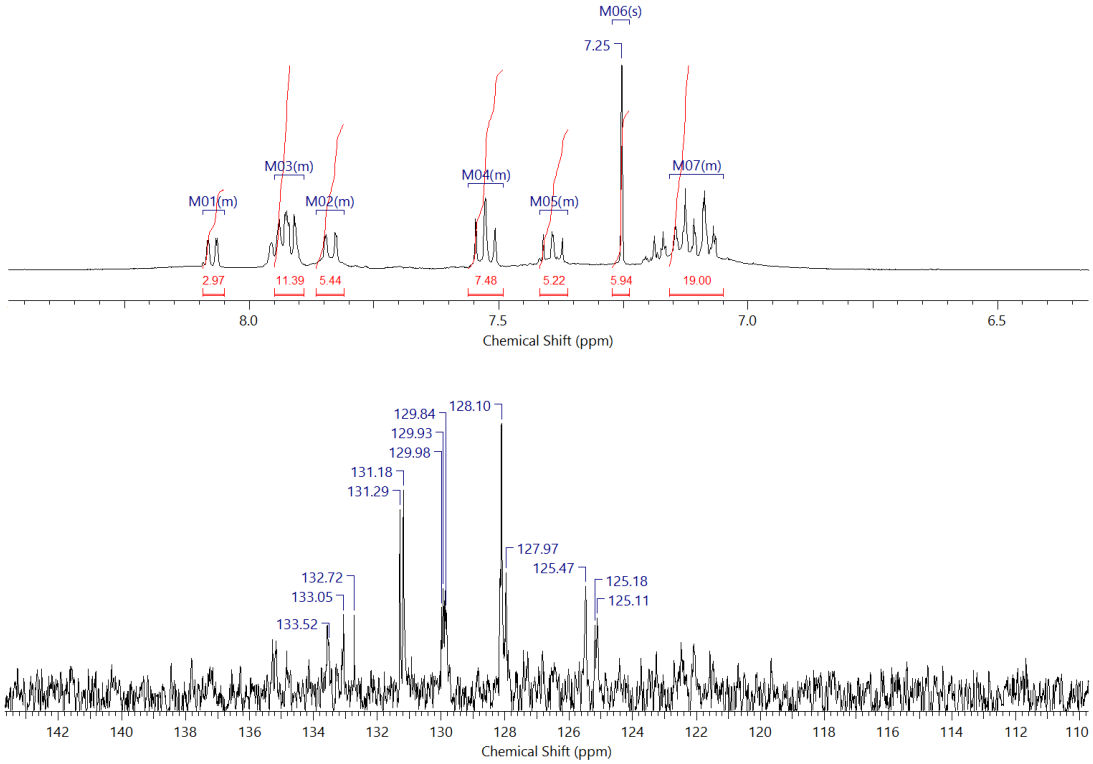


Figure 32 upper it is ^{1}H NMR and the other ^{13}C NMR

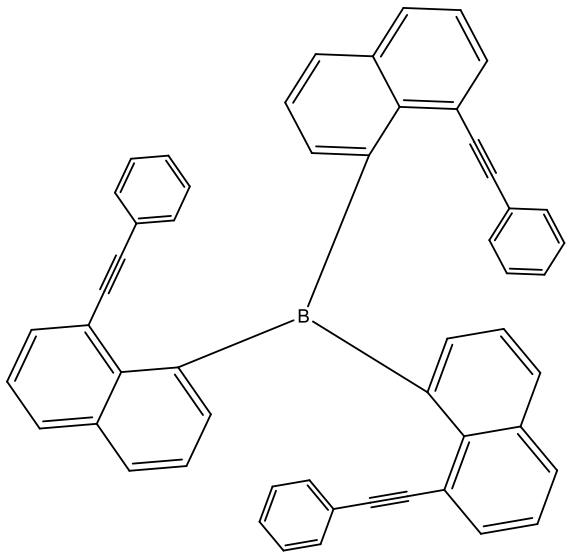


Figure 33: possible compound predicted in the NMR

At this moment it was decided to try another way, in this case starting with the compound with boron group.

The second route tried to form this compound was starting with dimethyl (8-(phenylethynyl)naphthalen-1-yl)boronate, as is illustrated in the Figure 34.

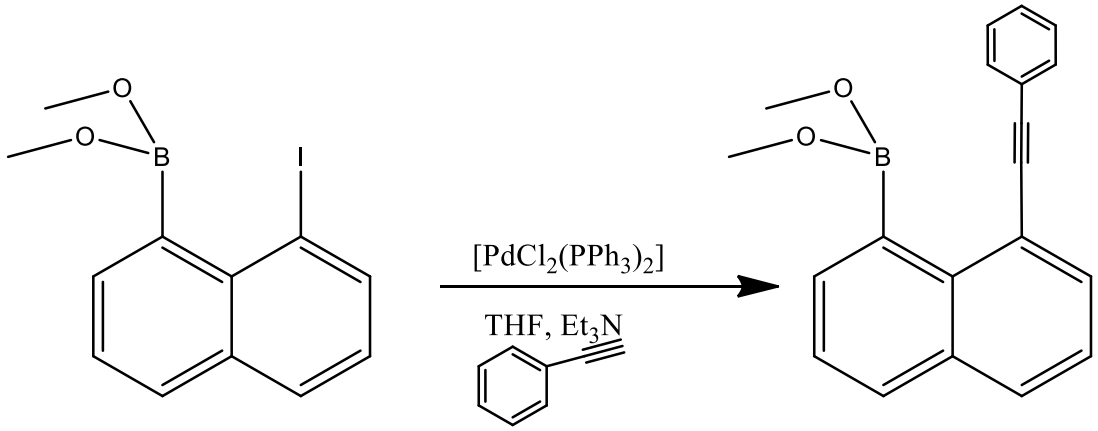


Figure 34: Reaction for the formation of dimethyl (8-(phenylethynyl)naphthalene-1-yl)boronate

This reaction was left overnight at room temperature under N_2 stream. In the morning the TLC plate was checked and four spots were there, one of them presented the same Rf as the starting material. After purifying by column chromatography the four fractions were checked in the NMR, only the NMR from the fraction that could be a compound that is not the reagent or some salts and impurities are illustrated in the Figure 35.

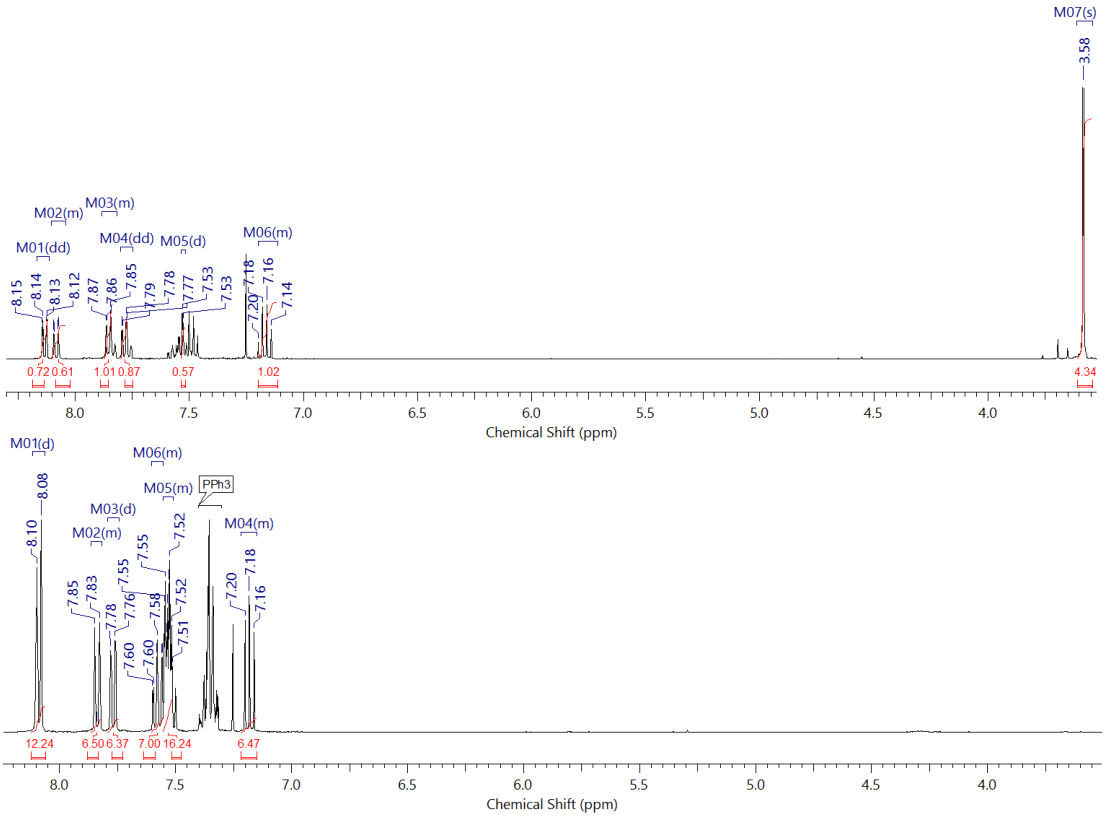


Figure 35: ^1H NMR the upper NMR is the starting reagent and the other is the product

After the reaction it is observed that there are not any signal of the protons (Figure 35) from the methoxy group joined to the boron. At this point we could consider that the Pd catalyst has more affinity to react with the boron than iodo group.

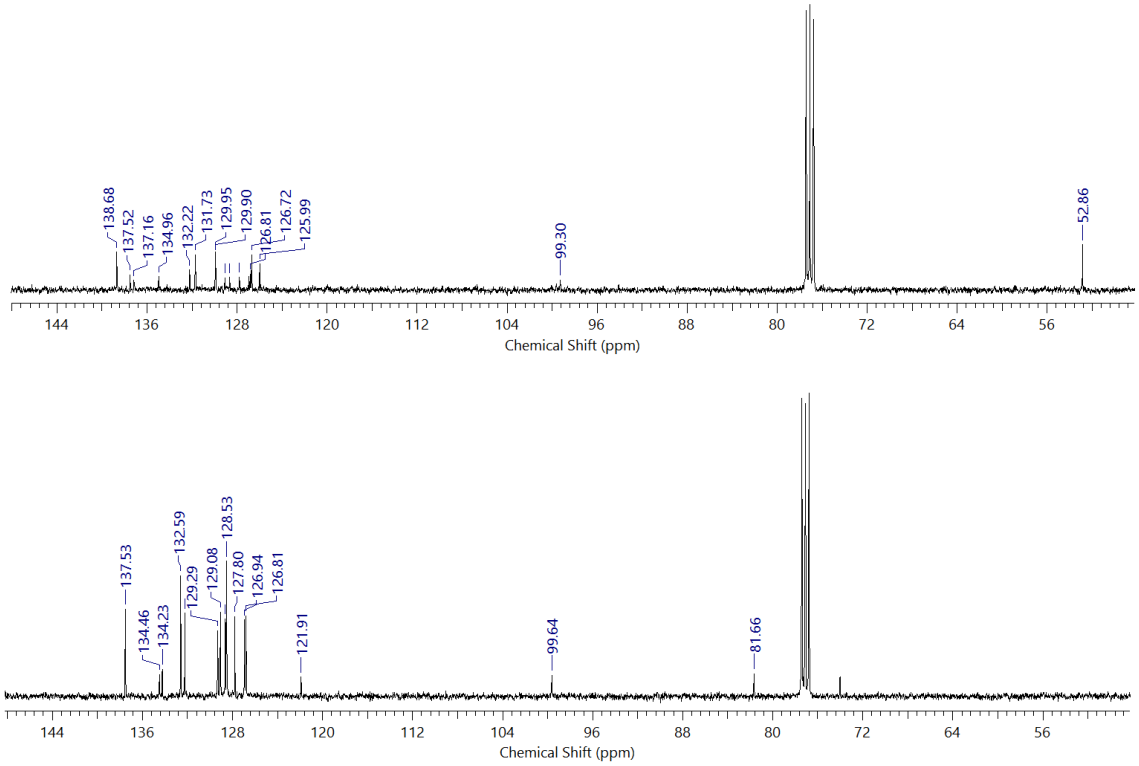


Figure 36: ^{13}C NMR the upper NMR is the starting reagent and the other is the product

As could be observed in the Figure 36, after the reaction the peak observed at 52.86 ppm which one is the carbon from the methoxy group joined to the boron has disappeared, is because of that at this moment it is consider that Pd has more affinity for the boron group and the signal from de carbon joined to the iodo is still there, is the peak that appear in 99.30-99.64 ppm.

After that, conclusions were drawn and was the moment to try to think in other ways to synthetize compound that was tried to do during all the project.

6.3 Discusion of preparation of dimethyl (8-(phenylethynyl)naphthalen-1-yl)boronic acid

With the experience from the other reactions, and all that was learned was thought to try this way, illustrated in the Figure 37.

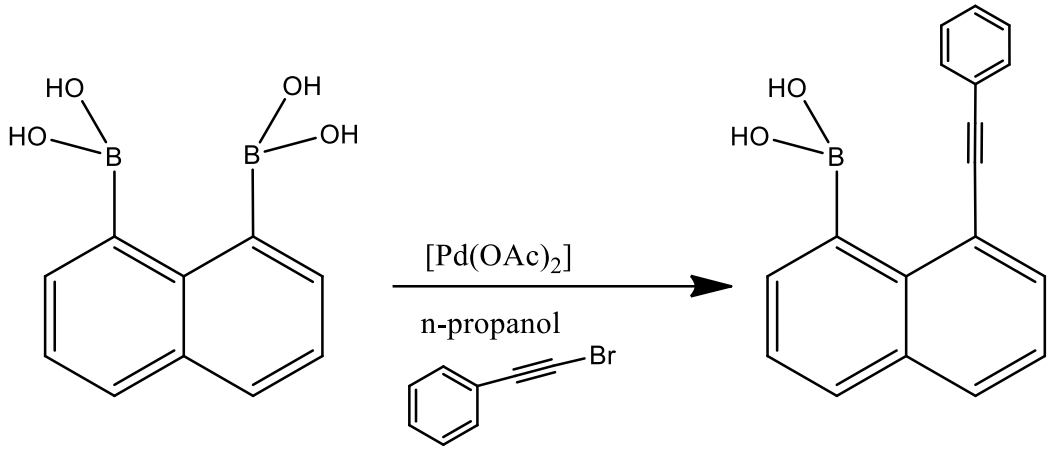


Figure 37: Reaction for the formation of dimethyl (8-(phenylethynyl)naphthalen-1-yl)boronic acid

The Suzuki reaction tried was only done one time and with small amount following a general procedure. As shown ^{1}H NMR in the Figure 38, because of the small amount of reagent and the low selectivity from the catalyst different compounds were formed in only 1 hour of reaction. After that was tried to purify but it was not possible to obtain separately the spots and small amount of each compound was obtained. The NMR from the product looks with a lot of impurities but something that could be observed is that the proton from the diboronic acid has disappeared. The effect is that both groups has reacted with Pd catalyst. Taking control from the reaction conditions could be obtained the expected product. One of the thinks to try is do it at room temperature in this form is less active the catalyst and follow the reaction by TLC.

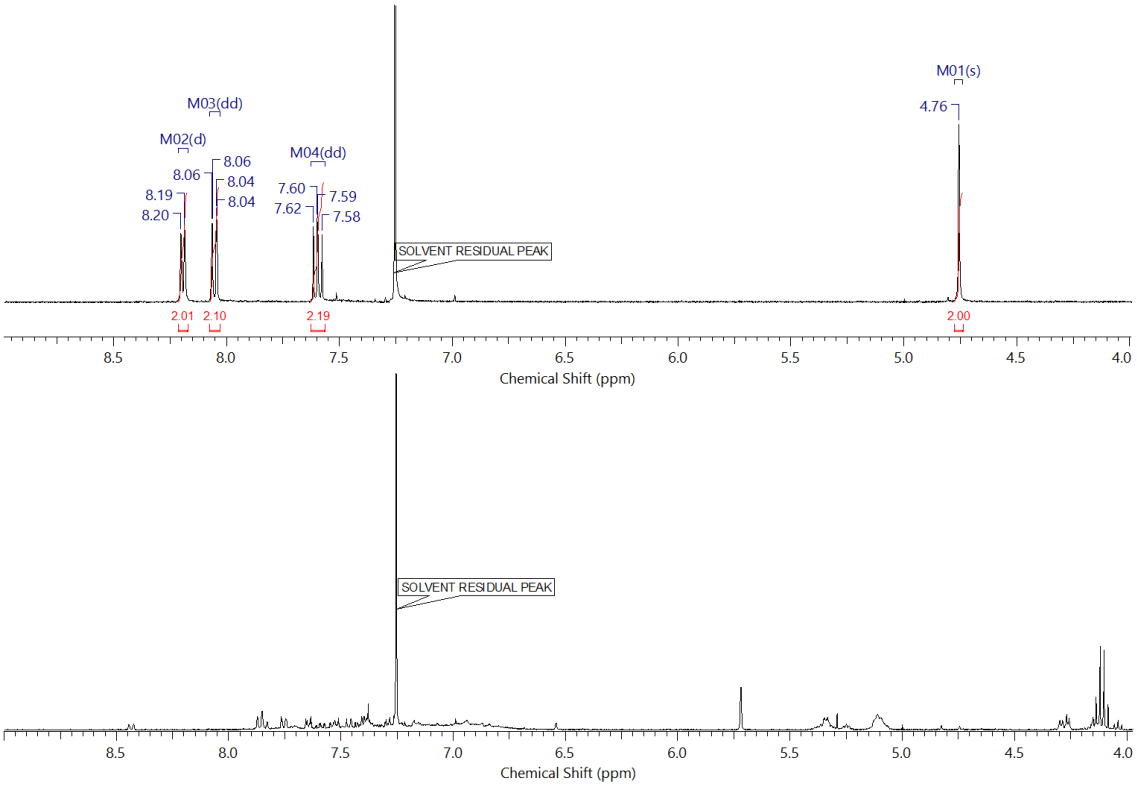


Figure 38 NMR ^{1}H the upper NMR is the starting reagent and the other is the product

6.4 Discusion of the preparation of the pre-catalyst

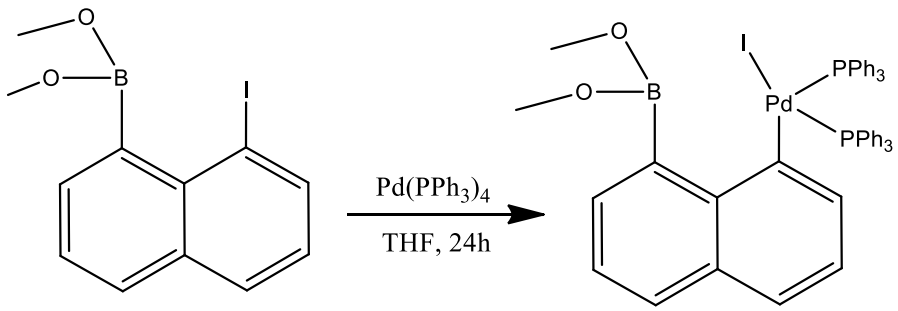


Figure 39: Reaction for the formation of a Pd (II) pre-catalyst

After do all the reactions and try different routes and having experiences learning all that was done, the last reaction to try to obtain the right compound was preparing the catalyst with our ligand. As is shown in the Figure 39. In this case was started with a catalyst of Pd (0) and leave it overnight. After adding some hexane a salt was precipitated and filtered off. The compound was checked by NMR technique and looks like the product that is expected, as shown Figure 40. The upper ^{1}H NMR is the starting material and the peak that appear at 3.58 ppm are the protons from the methoxy group and the other peaks are the aromatic protons from the naphthalene. The ^{1}H NMR below is the product, the signal from the methoxy groups joined to boron are still there is a signal that Pd (0) has not reacted with the boron group and appear as well an intensive signals in the aromatic zone that are from the protons of PPh_3.

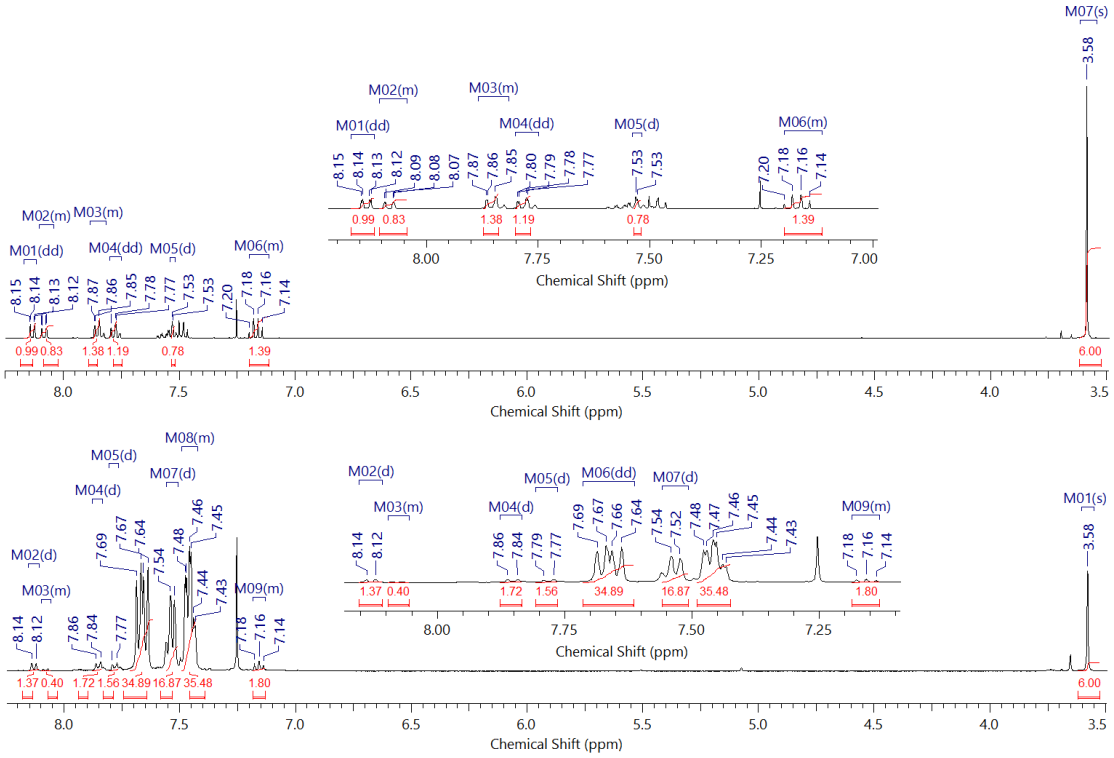


Figure 40: ^{1}H NMR upper is the starting material and the other is the product

The next step to do is use this catalyst and mix with phenyl acetylene as the other times, it has to choose the ideal conditions and could be the right way to obtain the compound that it has been trying during all this period in the project. Probably this will be the right direction to obtain similar compounds. In this form there are the possibility to take control in the intermediate comparing with the other reactions done.

The use of this catalyst with the ligand interest for future reactions has not been possible to uses because of there was not enough time, but is considerate as a possible route to obtain this type of compounds and try to analyse the interactions between different boron groups and double or triple bonds.

6.5 Discussion of the preparation of 9-(8-(phenylethynyl)naphthalene-1-yl)-9-borabicyclo[3.3.1]nonane

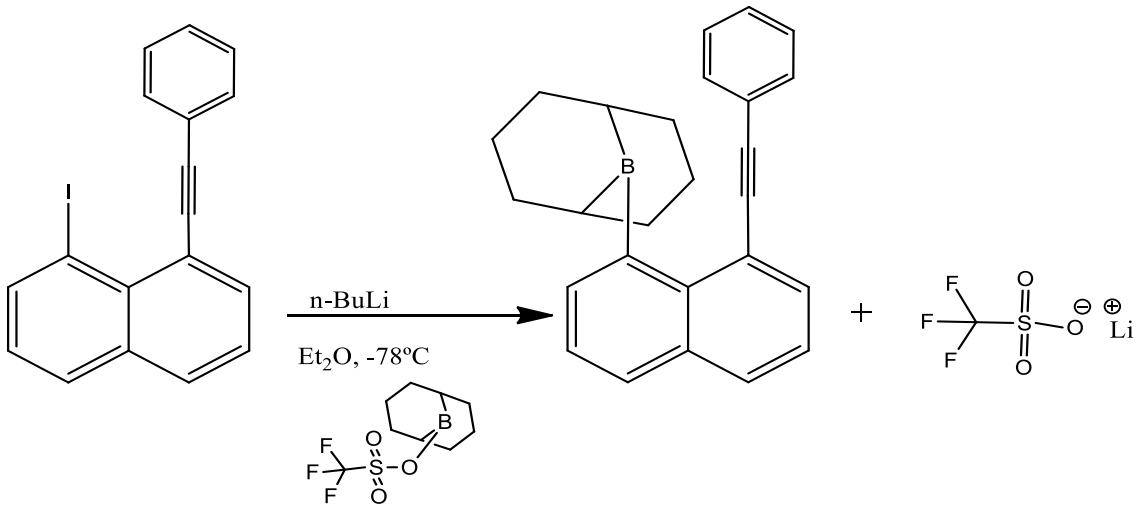


Figure 41: Reaction for the formation of 9-(8-(phenylethynyl)naphthalene-1-yl)-9-borabicyclo[3.3.1]nonane

Another reaction starting with 1-iodo-8-(phenylethynyl)naphthalene was done, as is shown in the Figure 41. In this case was tried to use another boron reagent, and have a look, if in this case one of the groups comes out. After do the reaction and try to purify via chromatography column, three different spots completely separated were obtained in the TLC plates eluted with pure hexane. One of them was the starting material, the other one was the product from hydrogenation as in the other reactions (similar behaviour, at least it is an indicator that n-BuLi is working) and the last spot, that was down in the TLC plate (Rf=0.072 eluted with pure hexane) it is a product without a clear identification. As is shown in Figure 42 the ^{1}H NMR from starting material and product looks different, a strange singlet appeared at 8,94ppm suggests that the position that was occupied by the iodo atom was protonated and some group is added in the adjacent position but not 9-BBN. The fraction was sent to a company for obtain a MS-spectrum, are awaited to this MS-spectrum and also the aim is try to crystallize the oil for do an X-Ray crystallography.

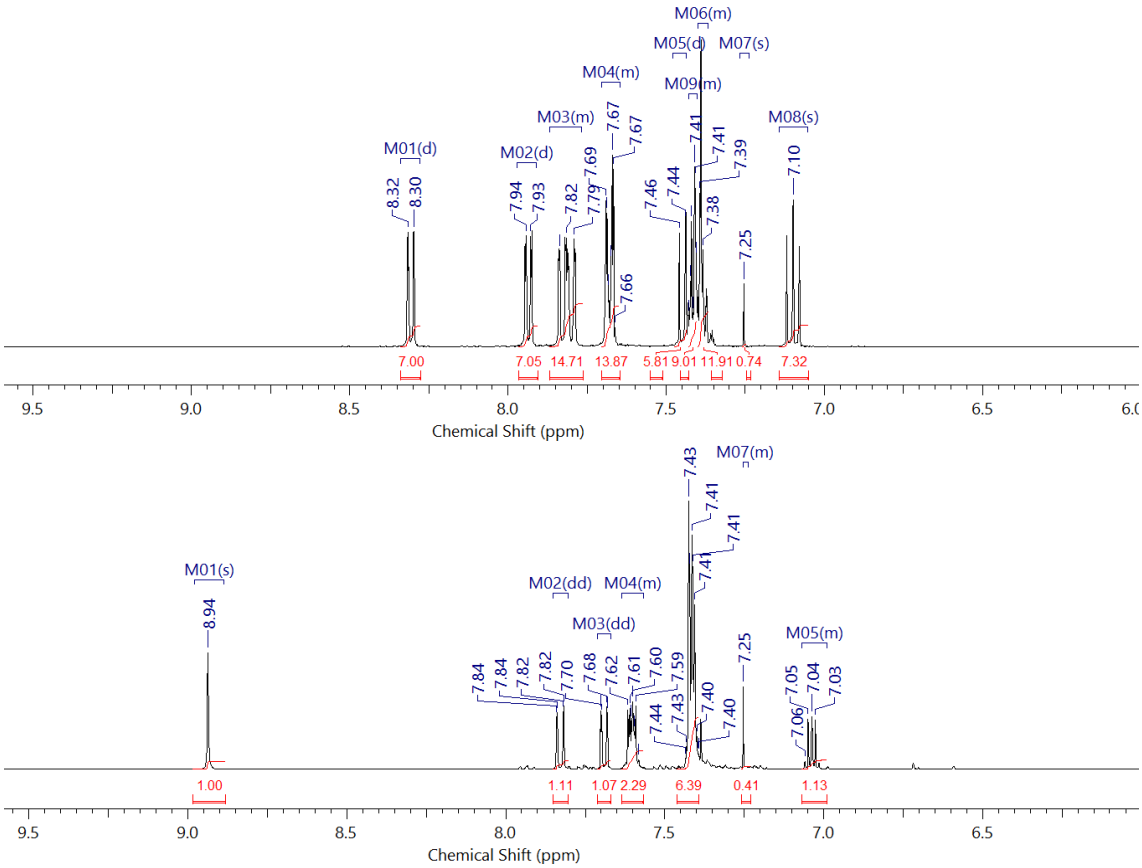


Figure 42: ^{1}H NMR: upper is starting material (1-iodo-8-(phenylethynyl)naphthalene) and the other is from portion 3

7 Conclusions

The two aims of this project was the study of two families of new compounds and look the interactions that could happen between the groups in peri-position. None of these molecules were possible to be synthetized. Nevertheless some interesting routes has been tried and possible ways were discarded. For next investigations there are the possibility to start at that point and have a look which reactions are not possible to do. In this form new conclusions can be extracted and new routes to try. At first was thought that was convenient that the last group to add would be the boron, because was thought that can react with Pd catalyst and is one of the the things that happened, but in the other way if it is added a Pd (0) as observed that has more affinity to react with the iodo group and be oxidized the Pd (0) to Pd (II). Some reactions were performed following the best solvent and conditions. Therefore these reactions tried until that moment open a way to the next investigations, trying other routes to obtain the desired compound. This project is near to find the right way for the target molecule.

8 References

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9 ANNEX

All the reagents and solvents in Table 1 and 2 are in this annex with his dangerousness and handling.

Reagents

NaOH 97% Fisher:

Dangerousness: Corrosive. Causes eye and skin burns. Hygroscopic. May cause severe respiratory tract irritation with possible burns. May cause severe digestive tract irritation with possible burns.

Handling: Wash thoroughly after handling. Do not allow water to get into the container because of violent reaction. Minimize dust generation and accumulation. Do not get in eyes, on skin, or on clothing. Keep container tightly closed. Avoid ingestion and inhalation. Discard contaminated shoes. Use only with adequate ventilation.

KOH 85% Fisher:

Dangerousness: Corrosive. Water-Reactive. Harmful if swallowed. Causes severe eye and skin burns. Causes severe digestive and respiratory tract burns

Handling: Basic protections laboratory, as gloves, glasses and lab coat. Work in a fume hood and ventilated place.

$Hg(OAc)_2$ 98%; Sigma-Aldrich:

Dangerousness: Hazardous in contact with skin, inhalation or ingestions. Accumulative effects. High toxicity for aquatics animals.

Handling: Avoid the contact with eyes and skin, avoid the formation of dust and aerosols as well.

AcOH 99.7 w/w%; Fisher:

Dangerousness: it is classified as a weak acid, acetic acid is highly dangerous to skin.

Handling: Use nitrile rubber gloves. Double-gloving is a good precaution. You should wear full protection in addition to non-latex gloves: lab coat, googles or face mask, covered lower extremities. Good ventilation is very important when working with this chemical.

KI 99% Sigma-Aldrich:

Dangerousness: Slightly hazardous, irritant in case of skin contact, eye contact, ingestion or inhalation.

Handling: Do not breathe dust. Wear suitable protective clothing as glasses, lab coat and gloves. Keep away from incompatibles such as oxidizing agents, reducing agents, metals, acids, moisture.

I_2 99.999% Sigma-Aldrich:

Dangerousness: Irritant and corrosive in case of skin contact, eye contact, ingestion, inhalation. Permeator in case of skin contact.

Handling: Keep container dry. Do not ingest. Do not breathe dust. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, reducing agents, metals.

$Na_2S_2O_3$*5H_20 99% Fisher:

Dangerousness: May cause eye and skin irritation. Hygroscopic. May cause respiratory and digestive tract irritation.

Handling: Wash thoroughly after handling. Use with adequate ventilation. Minimize dust generation and accumulation. Avoid prolonged or repeated contact with skin. Avoid contact with eyes, skin, and clothing. Keep container tightly closed. Avoid ingestion and inhalation.

CH_3I 99% Sigma-Aldrich:

Dangerousness: This material is toxic with acts on the central nervous system, targeted organs being the liver and kidneys. It is also a suspected carcinogen. May be fatal if swallowed, inhaled or absorbed through skin. Prolonged and repeated contact with this chemical may be harmful. Prolonged exposure to iodides may produce iodism in sensitive individuals.

Handling: Do not store in direct sunlight. Store in a tightly closed container. Store in a cool, dry, well-ventilated area away from incompatible substances. Wash thoroughly after handling. Do not breathe dust, vapor, mist, or gas. Use only in a chemical fume hood.

MnO_2 99% Sigma-Aldrich:

Dangerousness: They can cause central nervous and pulmonary system damage by inhalation of fumes and dust. Very few poisonings have occurred from ingestion. Chronic manganese poisoning is a clearly characterized disease which results from inhalation of fumes or dusts of manganese.

Handling: Keep container tightly sealed. Store in cool, dry place in tightly closed containers. Minimize dust generation and accumulation. Ensure good ventilation at the workplace.

DIBAL-H 1.0M in THF Sigma-Aldrich:

Dangerousness: is a reagent highly flammable in contact with the air, water or ethers.

Handling: must be handled under dry, inert atmosphere, like nitrogen or argon. Water must be scrupulously removed from process equipment prior to putting it into metal alkyls service. Failure to do so may result in an explosion.

n-BuLi 1.6M in hexane:

Dangerousness: is highly moisture sensitive and react violently with air and/or water. Upon reaction with water, they can ignite and/or liberate highly toxic gases.

Handling: Wear a laboratory coat made of flame-retardant material or cotton. Wear flame-resistant gloves over the top of chemically resistant gloves, and safety glasses.

Diethyl Benzylphosphonate 95% Acros organics:

Dangerousness: May cause irritation. The toxicological properties of this material have not been fully investigated.

Handling: Wash thoroughly after handling. Use only in a well-ventilated area. Avoid contact with eyes, skin, and clothing. Keep container tightly closed. Avoid ingestion and inhalation.

K_3PO_4 97% Sigma-Aldrich:

Dangerousness: irritant and corrosive in case of skin contact, eye contact. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Handling: Keep container dry. Do not breathe dust. Never add water to this product In case of insufficient ventilation, wear suitable respiratory equipment, if you feel unwell, seek medical attention and show the label when possible. Avoid contact with skin and eyes.

NH_4Cl 99.5% Fisher:

Dangerousness: May cause respiratory and digestive tract irritation. May be harmful if swallowed. Causes eye irritation. May cause skin irritation.

Handling: Wash thoroughly after handling. Use with adequate ventilation. Minimize dust generation and accumulation. Do not get in eyes, on skin, or on clothing. Keep container tightly closed. Avoid ingestion and inhalation.

DMF 99% Sigma-Aldrich:

Dangerousness: The acute toxicity of DMF is low by inhalation, ingestion, and skin contact. Contact with liquid DMF may cause eye and skin irritation. DMF is an excellent solvent for many toxic materials that are not ordinarily absorbed and can increase the hazard of these substances by skin contact.

Handling: Wash thoroughly after handling. Use spark-proof tools and explosion proof equipment. Avoid contact with eyes, skin, and clothing. Do not breathe dust, vapor, mist, or gas.

H_2SO_4 98.0 w/w% Fisher:

Dangerousness: Corrosive. Causes eye and skin burns. May cause severe respiratory tract irritation with possible burns. May cause severe digestive tract irritation with possible burns. Cancer hazard. May cause severe eye, skin and respiratory tract irritation with possible burns.

Handling: Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Do not get in eyes, on skin, or on clothing. Keep container tightly closed. Do not ingest or inhale. Do not allow contact with water. Use only in a chemical fume.

$NaNO_2$ 97% Fisher:

Dangerousness: May be fatal if inhaled. Strong oxidizer. Contact with other material may cause a fire. Harmful if swallowed. Causes eye, skin, and respiratory tract irritation. May cause methemoglobinemia.

Handling: Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Minimize dust generation and accumulation. Avoid contact with eyes, skin, and clothing. Keep container tightly closed. Avoid contact with clothing and other combustible materials. Do not ingest or inhale.

Triisopropylborate 98% Sigma-Aldrich:

Dangerousness: Highly flammable liquid and vapour. May be harmful if swallowed. Causes eye irritation.

Handling: Keep away from heat, sparks, open flames, hot surfaces. No smoking.

Trimethyl borate 99% Sigma-Aldrich:

Dangerousness: Contact with eyes and skin can cause irritation. Breathing can irritate nose, throat and lungs. High exposure to this reagent can cause headache, nausea, vomiting, diarrhea, loss of appetite and convulsions.

Handling: Change clothes if they are contaminated. Eye wash fountains should be provided in the immediate work area and emergency shower if the skin could be expose to this reagent. Do not smoke, drink where the reagent is handled, processed, stored. Wash hands carefully after use.

9-BBN Triflate 0.5M in hexanes:

Dangerousness: Highly flammable. Contact with water liberates extremely flammable gases. Causes burns. Possible risk of impaired fertility. Harmful: may cause lung damage if swallowed. Vapors may cause drowsiness and dizziness. Harmful danger of serious damage to health by prolonged exposure through inhalation. Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Handling: Wear eye protection or face protection.If swallowed rinse mouth, do not induce vomiting.If in eyes rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Avoid breathing dust, fume, gas, mist, vapors, spray. Avoid release to the environment.

CuI 99.5% Sigma-Aldrich:

Dangerousness: Very hazardous in case of ingestion. Hazardous in case of skin contact cause irritation and as well in eye contact or inhalation.

Handling: Do not breathe dust. Wear suitable protective clothing In case of insufficient ventilation, wear suitable respiratory equipment If you feel unwell, seek medical attention and show the label when possible. Avoid contact with skin and eyes.

Triphenylphosphine 99% Sigma-Aldrich:

Dangerousness: Harmful if swallowed. May cause eye, skin, and respiratory tract irritation.

Handling: Minimize dust generation and accumulation. Avoid contact with eyes, skin, and clothing. Do not ingest or inhale. Use with adequate ventilation.

Phenylacetylene 98% Sigma-Aldrich:

Dangerousness: Flammable liquid and vapour. May be fatal if swallowed and enters airways. Causes skin irritation. Causes serious eye irritation.

Handling: Wear personal protective equipment. Ensure adequate ventilation. Do not get in eyes, on skin, or on clothing. Avoid ingestion and inhalation. Keep away from open flames, hot surfaces and sources of ignition. Use only non-sparking tools. Take precautionary measures against static discharges.

Et_3N 99% Fisher:

Dangerousness: Flammable, colorless liquid with an ammonia-like odor. Causes skin, eye and respiratory tract irritation. May cause chemical burns.

Handling: Keep away from heat, sparks, open flames and sources of ignition. Use with adequate ventilation. Avoid contact with skin, eyes and clothing.

$Pd(Cl_2(PPh_3)_2$ 98% Sigma-Aldrich:

Dangerousness: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

Handling: Provide appropriate exhaust ventilation at places where dust is formed. . Keep container tightly closed in a dry and well-ventilated place. hygroscopic Handle under nitrogen, protect from moisture. Store under nitrogen.

$Pd(PPh_3)_4$ 99% Sigma-Aldrich:

Dangerousness: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic, or very persistent and very bioaccumulative at levels of 0.1% or higher.

Handling: Provide appropriate exhaust ventilation at places where dust is formed. Store in cool place. Store under argon. Handle under argon. Store in cool place. Keep container tightly closed in a dry and well-ventilated place.

$MgSO_4$ 99% Fisher:

Dangerousness: Hazardous in case of ingestion. Slightly irritant in case of skin contact, of eye contact, of inhalation.

Handling: No specific safety phrase has been found applicable for this product

Na_2SO_4 99% Fisher:

Dangerousness: Irritant in case of eye contact. Slightly irritant in case of skin contact, of ingestion, of inhalation.

Handling: Do not ingest. Do not breathe dust. Avoid contact with eyes. Wear suitable protective clothing. If ingested, seek medical advice immediately and show the container or the label. Keep away from incompatibles such as oxidizing agents, metals.

HCl 36.5% v/v 12M Fisher:

Dangerousness: Causes severe skin burns and eye damage. Causes serious eye damage.

Handling: Do not breathe dust, fume, gas, mist, vapors, spray. Wash thoroughly after handling. Wear protective gloves, protective clothing, eye protection, face protection.

Solvents

DMSO 99.7% Fisher:

Dangerousness: Slightly irritant effect in case of inhalation (lung irritant). Slightly irritant and permeator in case of skin contact,irritant if there are eye contact or ingestion.

Handling: Keep away from heat. Keep away from sources of ignition. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

Et_2O 99% Fisher:

Dangerousness: Irritant in case of skin contact, of eye contact, of ingestion, of inhalation. Slightly permeator in case of skin contact with hazardous effects.

Handling: Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

THF 99.9% Sigma-Aldrich:

Dangerousness: Irritant in case of skin contact, of eye contact. Slightly hazardous in case of skin contact with permeator effect.

Handling: Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

MeOH 99.8% Fisher:

Dangerousness: Flammable liquid! May cause skin irritation. May cause central nervous system depression. May be absorbed through the skin. May cause kidney damage. May cause respiratory and digestive tract irritation.

Handling: Protect self against physical damage. Avoid contact with skin, eyes and clothing. Do not breathe vapor. Use only in well ventilated areas.

Hexane 95% Fisher:

Dangerousness: Hazardous in case of skin contact permeator effect, of ingestion, of inhalation. Slightly irritant in case of skin contact, of eye contact.

Handling: Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

Cyclohexane 99% Fisher:

Dangerousness: Slightly hazardous in case of skin contact irritant and permeator effect, of eye contact irritant effect, of ingestion, of inhalation.

Handling: Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

EtOAc 99.9% Fisher:

Dangerousness: Hazardous in case of ingestion, of inhalation. Slightly hazardous in case of skin contact irritant and permeator effect, of eye contact irritant effect.

Handling: Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

$CHCl_3$ 99.8% Fisher:

Dangerousness: Irritant in case of skin contact, of eye contact, of ingestion, of inhalation. Permeator in case of skin contact with slightly hazardous effects.

Handling: Do not breathe gas, fumes, vapour or spray. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment.

Propan-2-ol 99.5% Fisher:

Dangerousness: May cause central nervous system depression. May form explosive peroxides. Flammable liquid and vapor. Hygroscopic. Causes respiratory tract irritation.

Handling: Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Ground and bond containers when transferring material. Use spark-proof tools and explosion proof equipment. Avoid contact with eyes, skin, and clothing.

Acetone 99.5% Fisher:

Dangerousness: Highly flammable. Irritating to eyes. Repeated exposure may cause skin dryness or cracking. Vapours may cause drowsiness and dizziness.

Handling: Product should be used in accordance with good industrial principles for handling and storing of hazardous chemicals. Avoid vapour inhalation, skin and eye contact. Do not use contact lenses. Avoid vapour formation and ignition sources.