DISPLACEMENT REACTIONS AND FLUORESCENCE STUDIES OF BOROXINE AMINE COMPLEXES

A thesis presented to the faculty of the Graduate School of Western Carolina University in partial fulfillment of the requirements of the degree of Master of Science.

By

Terryol Wilson

Director: William R. Kwochka, Associate Professor

Department of Chemistry and Physics

April 2011

ACKNOWLEDGEMENTS

I would like to give special thanks to my wife and kids for the monumental efforts and sacrifices which they have made in support of my research and thesis. I would also like to thank Professor Kwochka for his patience and guidance in this project and life in general he has been an inspiration to me. I would also like to thank Professor Evanoff and Dinkelmeyer for their guidance on this project without which I would have been unable to progress as far as I have. Lastly, I would like to give thanks to Western Carolina University for providing me a studious environment in which to learn and especially the Graduate School for providing the opportunity to achieve a graduate level education.

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LIST OF ABREVIATIONS

DMAP:	4-Dimethyl amino pyridine
H-Bor-	Phenylboroxine-
F-Bor-	4-Fluorophenylboroxine-
Cl-Bor-	4-Chlorophenylboroxine-
Me-Bor-	4-methylphenylboroxine-
MeO-Bor-	4-Methoxyphenylboroxine-
-Un:	Uncomplexed
-Pyr:	Pyridine
-Pic:	Picoline
-DMAP:	4-Dimethyl amino pyridine

ABSTRACT

DISPLACEMENT REACTIONS AND FLUORESCENCE STUDIES OF BOROXINE AMINE COMPLEXES.

Terryol B. Wilson, M.S.

Western Carolina University (May 2011)

Director: Dr. William R. Kwochka

The Boron atom has seen an increase in usefulness over the last half century due in part to the unique properties of boron that allow for dative binding. Aspects of the boron-nitrogen bond were examined through both displacement reactions, which were monitored by NMR, and photoluminescence studies done with a Fluorometer. Through the NMR study it was discovered that the dative bond is affected by both the electronic configuration of the boroxine and the pK_a of the Lewis base being used for complexation. It appears that the displacement of pyridine from the original complex is dictated by the pK_a of the displacing base; a stronger base leading to more complete displacement of pyridine from the complex. Using fluorimetry, several Lewis base-boroxine complexes were studied in order to observe possible differences in the λ_{max} emission between the uncomplexed boroxine and the coupled base-boroxine pair, a behavior believed to be dependent on the shifting of electron density from the Lewis base towards the boroxine.

1.1 Dative Bonds

Nature has made use of dative bonding to form complex macromolecules. Dative, or coordinate covalent, bonds are formed when one atom which has a free pair of electrons, combines with another atom that either lacks a complete octet of electrons, or can accept electron density like a cation. Chemists have been investigating the elements responsible and their unique bonding for the last fifty years trying to understand the characteristics and uses of dative bonding.[1] For example, porphyrin relies upon dative bonding to host a cation (usually a metal) inside of its structure. Most commonly, these porphyrin complexes use the lone pair of electrons on nitrogen to bond with the metal cation. Without this unique bonding many molecules like chlorophyll (Fig 1) would not be able to function. Chlorophyll contains porphyrin molecules to enable vegetation to gather sunlight and convert it to energy.

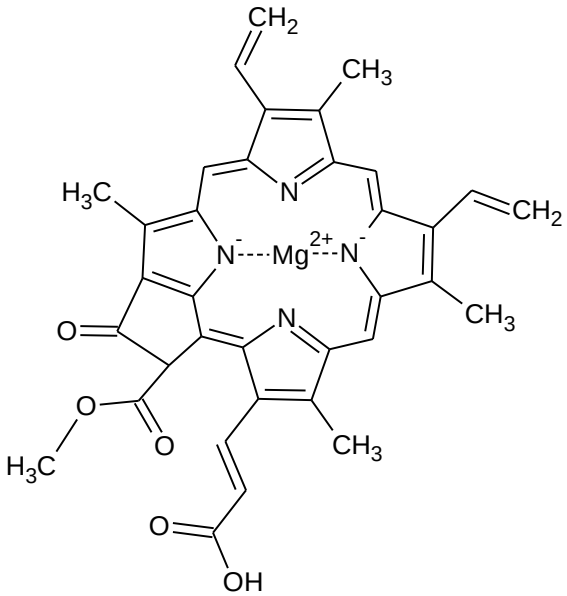


Figure 1 Chlorophyll c2.[2]

Some common examples of dative bonds are ammonium molecules and sublimating aluminum chloride (Fig. 2 & 3).

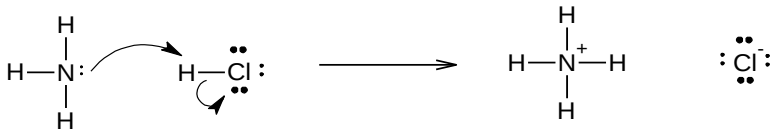


Figure 2 Dative bond between the nitrogen and hydrogen atoms in ammonium.

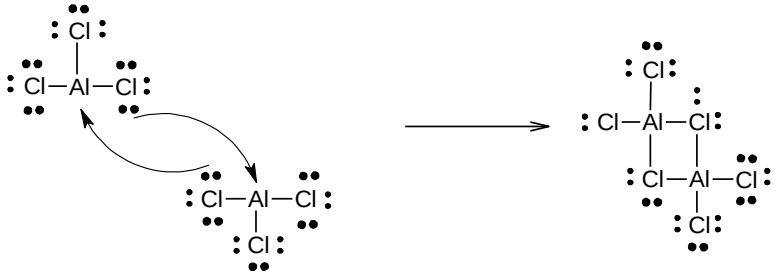


Figure 3 Sublimating aluminum chloride forming dative bonds.

Boron can also form a dative bond when it combines with a Lewis base; the boron atom has an empty p-orbital and is a Lewis acid (Fig.4) which can accept the pair of electrons from the Lewis base forming a bond.

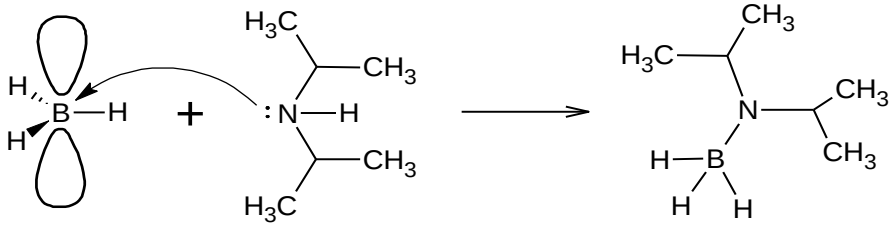


Figure 4 Borane forms a dative bond with diisoproplyamine.

A dative bonding site is useful because it is highly specific allowing construction of a macromolecule from a smaller Lewis base and boron containing pieces which bond in a known and predictable manner. Shown below (Fig.5) are two reactions which use dative bonding to complex with Lewis bases. The mechanisms for both reactions are the same; the empty p-orbital of 1 and 4 interact with the lone pair of electrons on the nitrogen of 2 and 5 to coordinate forming a new bond and thus new molecules 3 and 6.[3]

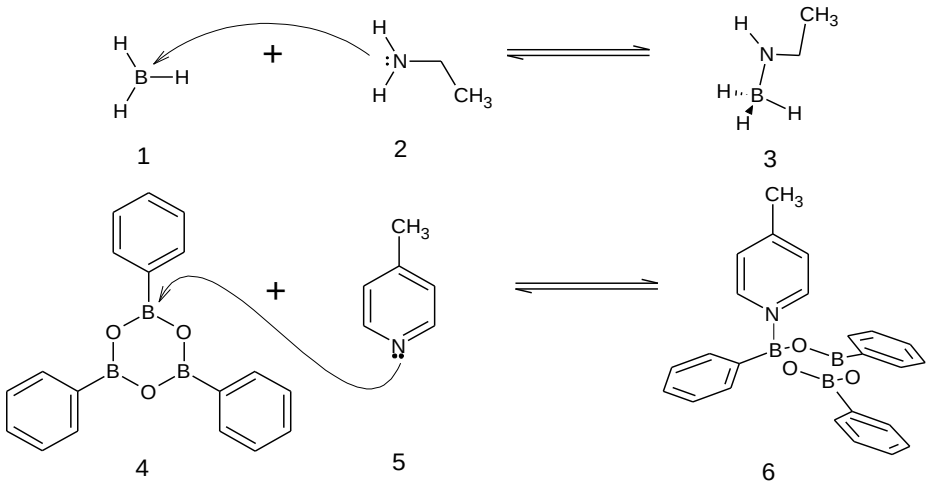


Figure 5 Two examples of dative bonding between nitrogen and boron atoms.

1.2 Boronic Acids

The boronic acid functional group is defined by an R group attached to a boron atom with two acidic diols (Fig 6). The R group can be any useful alkyl or aromatic group.

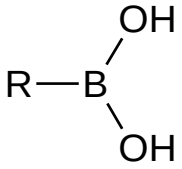


Figure 6 The boronic acid functional group.

Important characteristic of boronic acids include the trigonal planar geometry, the hydroxyl groups which are easily converted into esters, and the empty p-orbital perpendicular to the plane of the functional group. Specifically, phenylboronic acids have drawn increasing interest since 1979 when Suzuki[4] discovered a new coupling reaction which directly bonds two phenyl groups together through a carbon-carbon bond (Fig 7).

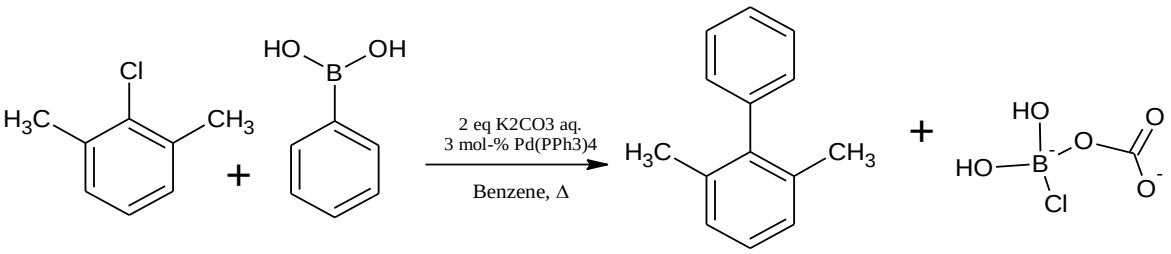


Figure 7 Example schematic of the Suzuki coupling reaction.

1.2.1 Boronates, Sensors, polymers and COFs

Recently research has focused on using the trigonal planar geometry and the boronic acids ability to easily form esters with diols. Phenylboronic acid's trigonal planar structure makes it ideal to react with 1,2-diols to form esters which are known as boronates. The esterification reaction to form boronates involves the removal of water from the reaction. This water removal is the driving force behind the high yields and purity of these boroxines and boronates. Using a Dean-Stark trap the water is removed by forming an azeotrope with toluene which separates again after cooling into the trap where it is unable to reenter the reaction vessel. This reaction mechanism causes this reaction to be extremely efficient with very high yields. (see fig 8).

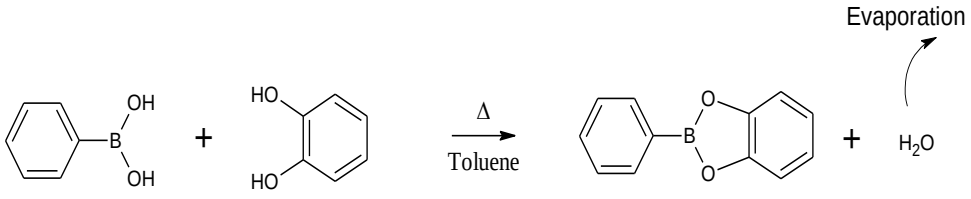


Figure 8 Example of a dehydration reaction used to construct boronates.

The planar geometry and dative bonding capacity of boron has led to its use as molecular sensors. For example sugars, amino acids and other non-fluorescent diols, which have potential to diagnose and treat many different diseases ranging from diabetes (Fig 9) to

pancreatic cancer, are being studied in conjunction with various boronic acids for fluorophore attachment and enzymatic inhibition.[5,6]

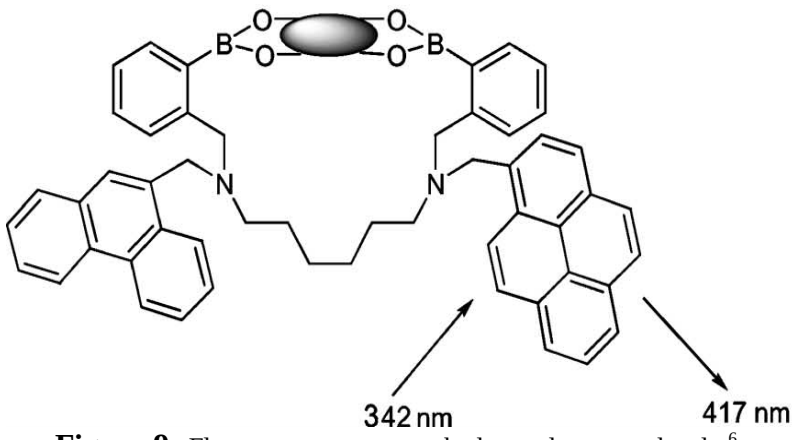


Figure 9: Fluorescent sensor attached to a glucose molecule.[6]

Figure 9 shows how a macromolecule with two boronic acids is used to bond with four of the alcohol groups on the glucose molecule. Once bonded, the boronic acid sensor acts as a fluorophore for the glucose which is detectable at very low concentrations. The sensor works by mechanically changing shape when it attaches to a glucose which then causes a detectable shift in the fluorescence spectra of the sensor. This sensor is designed specifically to bind with d-glucose and to eliminate the problems of enzyme-based detectors breaking down in harsh systems and screening effects from aqueous systems. The reversible covalent ester bonds that form have been used to attach fluorophores to other *in vivo* molecules which are difficult to detect and show the usefulness of these types of synthetic chemical sensors. [6]

Boronates are also being investigated as potential conductive polymers.[7] The boron and oxygen atoms possess aligned p-orbitals forming conjugation because of this it

has potential use in organic electronic devices as conductive or semi conductive material depending on molecular structure. Despite the complexity of some of these polymeric systems they are all synthesized using a simple dehydration reaction between boronic acid and diols (Fig 10).

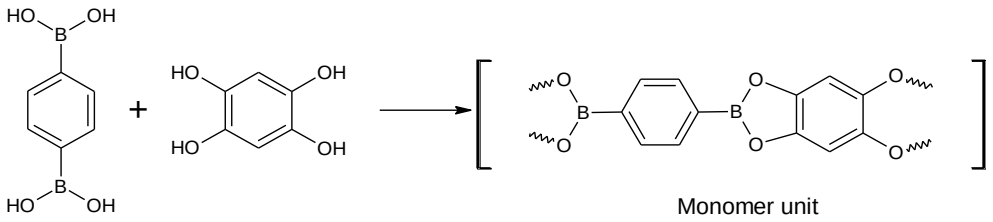


Figure 10: Polymer based upon the dehydration reaction between boronic acid and diol.[7]

Some of the more complex structures which have been built using these boronic acid building blocks are Covalent Organic Frameworks (COFs). COFs are large polymer-like molecules which form a rigid framework that is a highly organized and repetitive structure. One of the most important aspects of a COF is the large predictable cavities which can accommodate guest molecules.[8]

Below (Fig 11) shows how the COF's are able to have the size of their host site varied by changing the molecular building blocks used in its construction. In this way their functionality can be manipulated to fit a useful purpose.

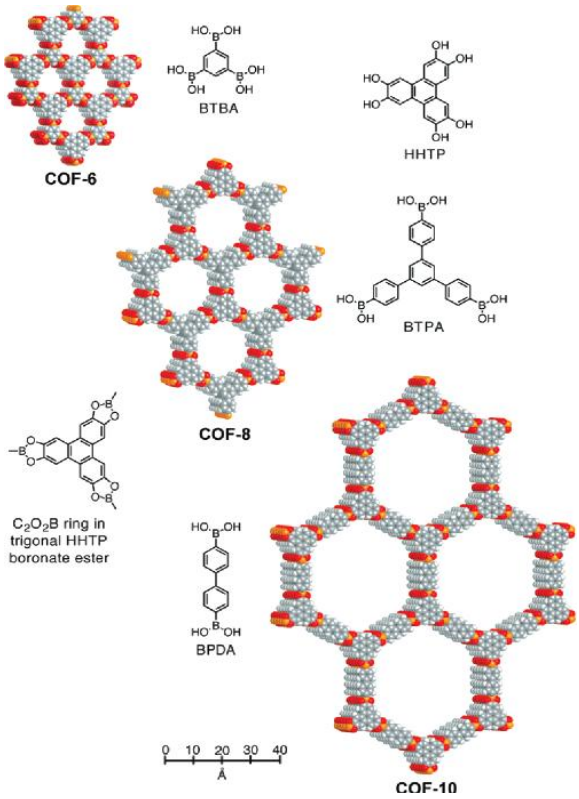


Figure 11: Various boronic acids used to construct surface covalent organic frameworks (SCOF) and covalent organic frameworks (COFs).[7]

The porous nature of the COF enables them to act as host to a guest molecule.[8] Certain COF's were also used to adsorb ammonia gas by having the nitrogen atom of ammonia and the empty p-orbital of the boron in each monomer of the COF to create a dative bond. This COF material absorbed ammonia better (15 mol kg(-1), 298 K, 1 bar) than microporous 13X zeolite (9 mol kg(-1)), Amberlyst 15 (11 mol kg(-1)) and mesoporous silica, MCM-41 (7.9 mol kg(-1). This high absorption makes COFs more successful than other chemical scrubbers currently used with ammonia.[9]

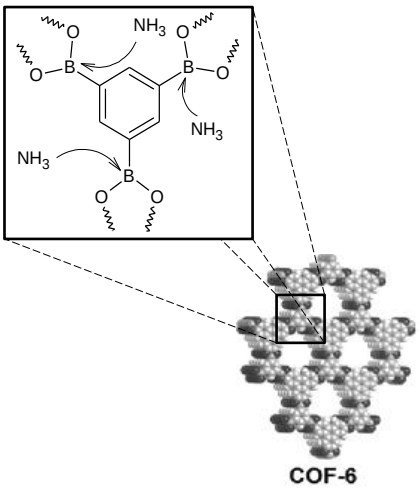


Figure 12 Ammonia absorption of a COF.

1.3 Literature Review

The following is a review of literature which led to the choice of a boroxine molecular system for this characterization study. We intended to investigate bonding character through an NMR study and applications as sensors through a fluorescence study. We wanted a system which had similar properties to the most popular boronic systems currently being investigated while remaining simple enough to make a study feasible. The resulting boroxine system was selected because it offered a simple NMR spectrum and contained the two functional groups of interest, namely a planar boron atom with an acidic p-orbital and a boron oxygen connecting system.

1.3.1 Suzuki-Miyaura Fluorescence Sensor – Buchwald Research Group

Recently, a method for the real-time monitoring of the Suzuki-Miyaura reaction using 6, 7-dihydroxy-4-methylcoumarin as a fluorescent agent was developed. The group reported an on/off mechanism for the sensor which is reactant dependant. The reaction vial fluoresces when boronic acid, coumarin, and a complexing base are present in the reaction mixture (Fig. 13). In the study the complexing base was varied to test for

flexibility of the sensor and variations in the intensity of the fluorescence were reported. Since the base dative bond is affecting the coumarin boronate fluorescence in the Buchwald study, we think these changes can be used to develop a sensing technique for dative bond complexation reactions.[10] We want to develop this sensor for application with

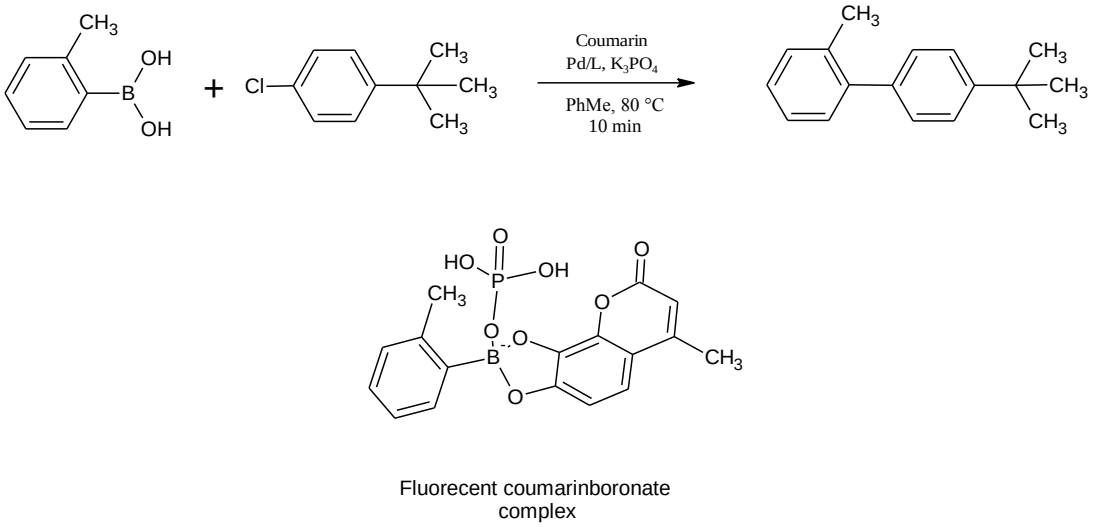


Figure 13: Coumarin-boronate fluorescent sensor.

real time monitoring of monolayer formation or attachment to a monolayer.

1.3.2 Displacement Reactions – Ritchey thesis 1968

A study of the characteristics and properties of triphenylboroxine-amine complexes was completed in the late 1960s which indicated the possibility of the dative bonded molecule being displaced through a competitive reaction in which the more basic amine will displace a less basic one. A Triphenylboroxine was complexed with pyridine and then exposed to cyclohexylamine (Fig 14). The reaction yielded a 100% displacement of the pyridine base. Base displacement was determined to be the result of the difference in pK_a between the two competitors with the cyclohexylamine being much more basic (pK_a 10.64) then the pyridine (pK_a 5.25).

Further research was done which showed a consistent trend that the displacement reactions were dominated by the pK_a of the complexing Lewis base.[3] The experimental

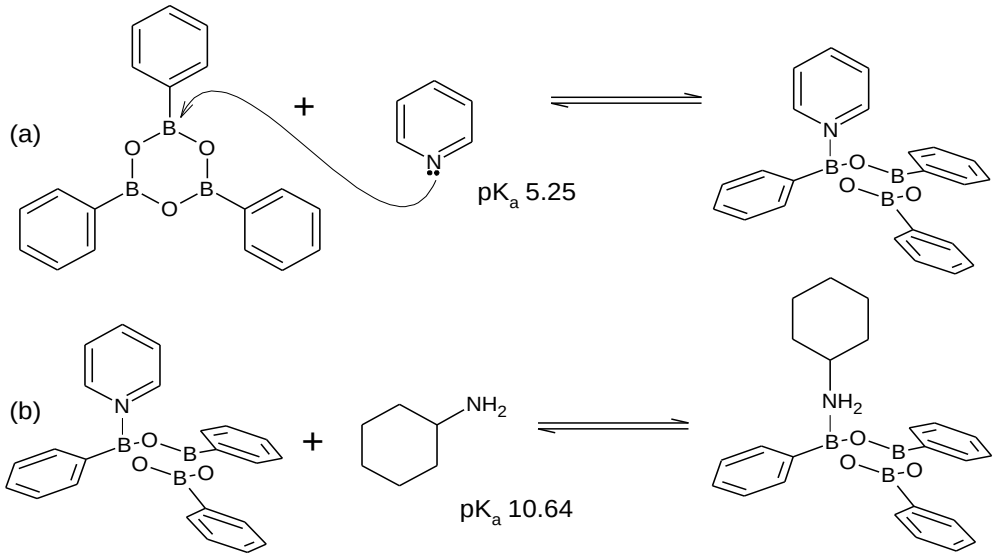
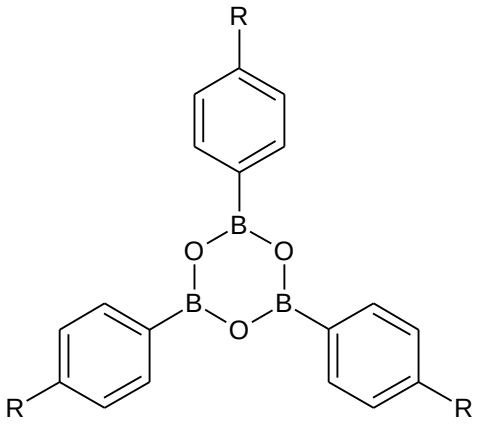


Figure 14 Complexation of triphenylborxine with pyridine (a) and displacement reaction between the product of (a) and cyclohexylamine (b).

design used a precipitation reactions which caused all bases to replace at one hundred percent efficiency by the higher pK_a base. These results were reported by infrared spectroscopy comparisons between both possible complexes and the sample.

1.4 Research Plan

The boroxines that were used in this study consisted of five phenylboroxines which have various R functional groups at the 4 position of the aryl group. The five phenylboroxines were varied by attaching two different inductively electron withdrawing groups (Cl and F), a different inductively electron donating group (CH_3), a pi donating group (CH_3O), and one phenyl boroxine (H) in place of the R group. (Fig 15).



R
H-
F-
Cl-
Me-
Methoxy-

Figure 15 The different boroxines studied and corresponding R groups for modification.

The boroxines were prepared using a microwave-assisted synthesis and chloroform as a solvent to eliminate impurities and expedite synthesis. Previously, toluene had been used in preparing the boroxines for the displacement reactions but chloroform was used to minimize solvent changes in preparation and remove toluene as a contaminant for the fluorescence study. Any interactions between the chloroform and boroxine are minimal especially in the presence of a Lewis base. The boroxine-amine complexes were made using the boroxines and commercially available amines which had been previously distilled. The uncomplexed boroxine was placed in a 50mL RBF and dissolved with chloroform before adding the amine. Once the amine was added one hour was allowed to complete complexation. All compounds were verified using ^{1}H NMR and ^{13}C NMR to insure that compounds were pure for testing.

1.4.1 Fluorescence Studies

We were interested in doing a general fluorescence study on the properties of boroxines and the effects of electron density on the emission spectra. We wanted to determine if it would be possible to develop a sensor that could detect differences in

electron density of the substituents on the boroxine and the different amines. The five boroxines were used in conjunction with three different complexing bases, pyridine, picoline, and 4-Dimethylaminopyridine (DMAP). These 20 boroxines were dissolved into chloroform and diluted to approximately 50 μM concentrations using 50 mL volumetric flasks. Once the solutions are prepared the samples were run in the Fluorometer using a quartz cuvette with the intent to collect lambda max data for each boroxines excitation and emission spectra. This data was verified by taking 5 scans of each spectra and averaging them together.

After the spectra are collected they will be processed using Spectra Solve and Origin graphing software. The spectra will then be analyzed with respect to differences and trends caused by the variation of the respective R groups and complexed bases.

1.4.2 Displacement Reactions

Previous work has determined that replacement of the amine of the boroxine-amine complex base is determined by the pK_a of both bases.[3] We tested to determine if the boroxine itself effects these displacement reactions by removal or addition of electron density to the phenylboroxine by variation of attached substituent groups. As such we will be using the five boroxines and the three bases which were used in the fluorescence study.

To minimize variability the same procedure was used to synthesize all the boroxines. They were then complexed to pyridine and identified using a ^1H NMR spectra. After preparing the materials for testing, the complexation reactions were carried out in chloroform with one equivalent of the selected base introduced into the solution. After

the solution equilibrated the complex was identified and analyzed using ^{1}H NMR to determine if the boroxine structure effected displacement of the pyridine base and if the base replaces completely in all instances by pK_a. We expected the electron deficient boroxines to be more readily available for bonding to the Lewis bases while the electron rich boroxines were less so. One equivalent of the Lewis base was chosen because of saturation over powering the displacement reactions which had been recorded previously by Tyler Jones an undergraduate researcher in unpublished results.

CHAPTER 2: RESULTS AND DISCUSSION

We prepared a series of boroxines and their Lewis base complexes for testing. Our strategy required the preparation and characterization of five different aromatic boroxines, the preparation and characterization of five pyridine-aromatic boroxine complexes, the subsequent displacement reactions of each of those pyridine-aromatic boroxine complexes with two Lewis bases, and the preparation and characterization of 10 additional Lewis base-aromatic boroxine reference complexes. The five boroxines which were prepared include are Phenylboroxine (H-Bor), 4-Fluorophenylboroxine (F-Bor), 4-Chlorophenylboroxine (Cl-Bor), 4-methylphenylboroxine (Me-Bor), and 4-Methoxyphenylboroxine (MeO-Bor). The bases used to complex the boroxines were pyridine, picoline, and 4-dimethylaminopyridine (DMAP).

2.1 Preparation of Boroxines and amine complexes

All the uncomplexed boroxines were prepared and then complexed to insure a uniform set of samples. The uncomplexed boroxines were prepared using microwave assisted synthesis and a dean stark trap to remove water from the reaction vessel. Once the reactions were completed the solvent was removed via Rotovap and vacuum pump. The boroxines were then verified using ^{1}H NMR. Figure 16 shows the reaction scheme for formation of a boroxine and isolated yields.

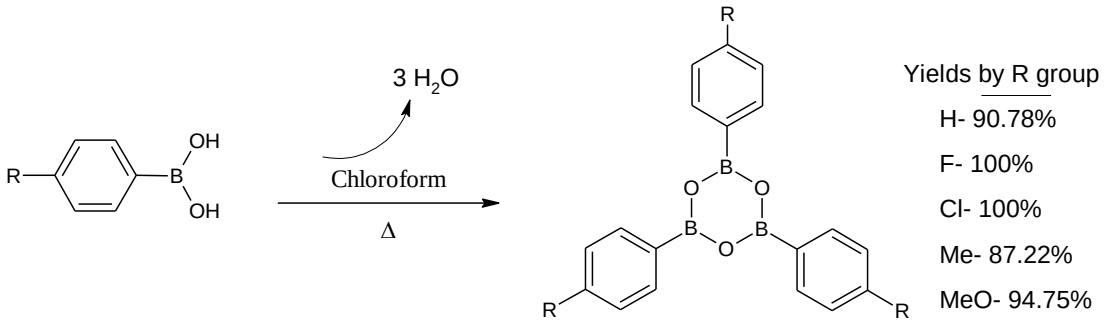


Figure 86 Synthesis reaction scheme for boroxines and yields by substituent R group.

Boroxines give a simple spectrum which is easy to interpret because of the symmetrical environment of the hydrogen atoms found on both sides of the 4 substituent on the phenyl ring. The boroxine's three-fold axis of symmetry simplifies the structures into two signals, **a** and **b.** (Fig. 17).

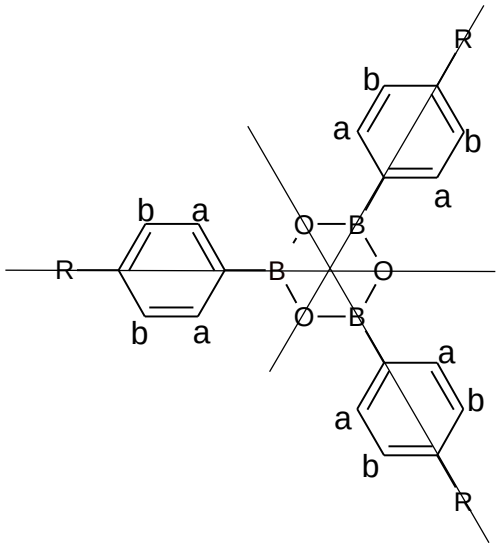


Figure 17 Boroxine molecule showing 3 of the 4 planes of symmetry which the molecule possesses. The fourth plane bisects the molecules "top" and "bottom".

In NMR spectroscopy the electronic environment of the hydrogen atom dictates the NMR signal's shape and position. Figure 18 shows a sample reference spectrum for Me-Bor with the characteristic aromatic doublets.

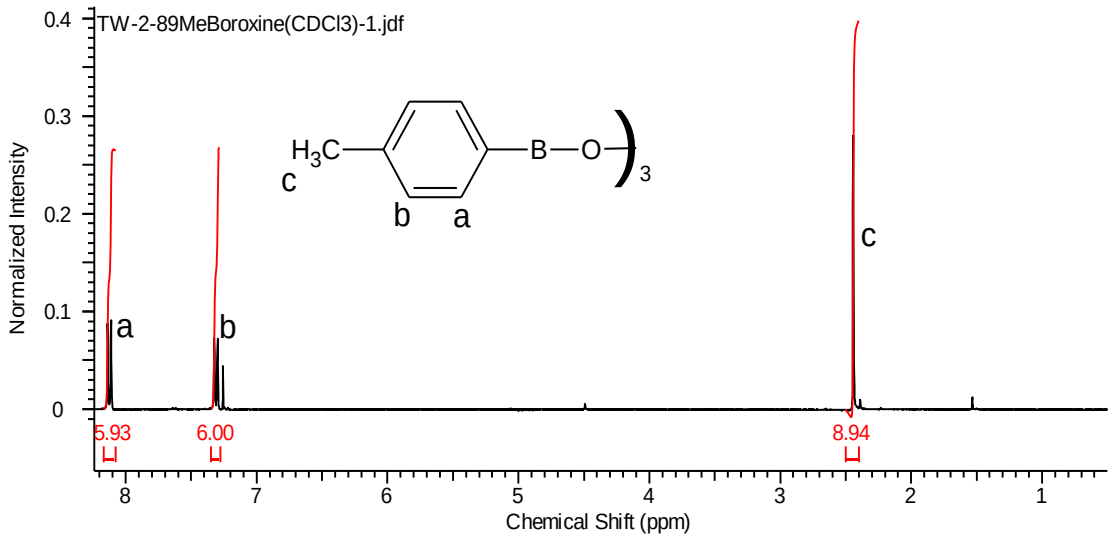


Figure 18 ^{1}H NMR spectra for Me-Bor with hydrogens labeled.

When symmetry of the molecule is disrupted, the environment changes and the signals representing the different hydrogens in the molecule become more complicated. After complexation of boroxines with a Lewis base such as pyridine, the symmetry of the system remains intact because the base dissociates and reattaches much faster than the NMR detection timescale. When the Lewis base association/dissociation approaches the time scale of the NMR spectrometer the hydrogen atoms start to separate into different environments which cause a broadening of the signals.

To complex the boroxines a 50 mL flask was used in which the uncomplexed boroxine was dissolved in chloroform. Once the boroxine was dissolved, the complexing base was added in a 1:1 ratio. The solvent was removed by Rotovap and vacuum pump before ^{1}H NMR was taken of each compound as reference spectra for the displacement reactions.

The displacement reactions were prepared using the boroxine-pyridine complexes and a 100 ml flask with ether as the reaction solvent so that it could be quickly removed.

The displacing base was added to the RBF at a 1:1 ratio and allowed to stir at ambient temperature and pressure for one hour. One hour was chosen as the reaction time based on observation of complex formation which appears to take between 4-6 minutes so a factor of 10 should allow for the reaction to reach equilibrium. The reaction solvent was removed and the product was dissolved in chloroform and extracted with water two times to remove excess base. The chloroform was used because ether and water are miscible. The reaction was then dried and solvent removed via rotovap and vacuum pump. Product yielded a white solid powder (Fig. 19).

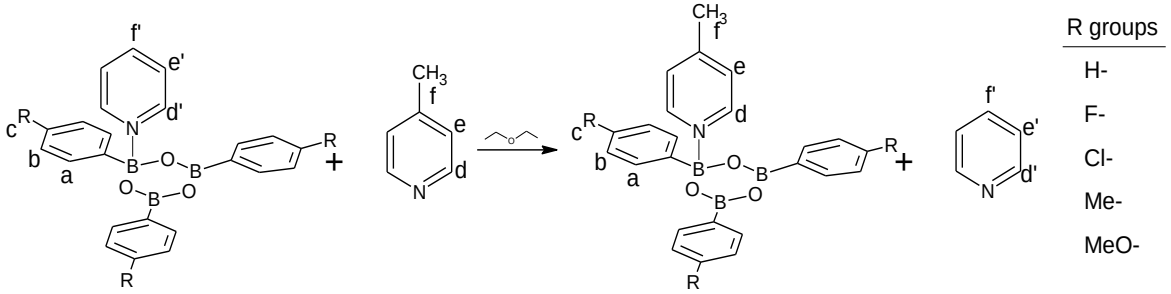


Figure 19 Displacement reactions between Bor-Pyr and Picoline.

2.2 Displacement reactions of pyridine – boroxine complexes

We hypothesized that the higher pK_a Lewis (stronger) base will dominate the displacement reaction removing the lower pK_a (weaker) base from the complex. Likewise, the substituent group attached to the aromatic ring of the boroxine should affect this process by making it more or less favorable depending on the electron withdrawing/donating properties of the substituent.

In the first series of experiments, the pyridine (pK_a=5.25) of the pyridine-boroxine complex was displaced by a picoline (pK_a=5.96) molecule and the progress of the displacement was followed by ^{1}H NMR.[11] In the case of the one equivalence of picoline

base the replacement was not complete and a mixture of boroxine/pyridine and boroxine/picoline complexes were both present in the NMR tube during sample scans. It is unclear why only partial completion of the reaction took place and the picoline did not completely remove the pyridine and must be theorized that it was due to the relatively close pK_as, and thus preference for binding with the Lewis acid, which picoline shares with pyridine.

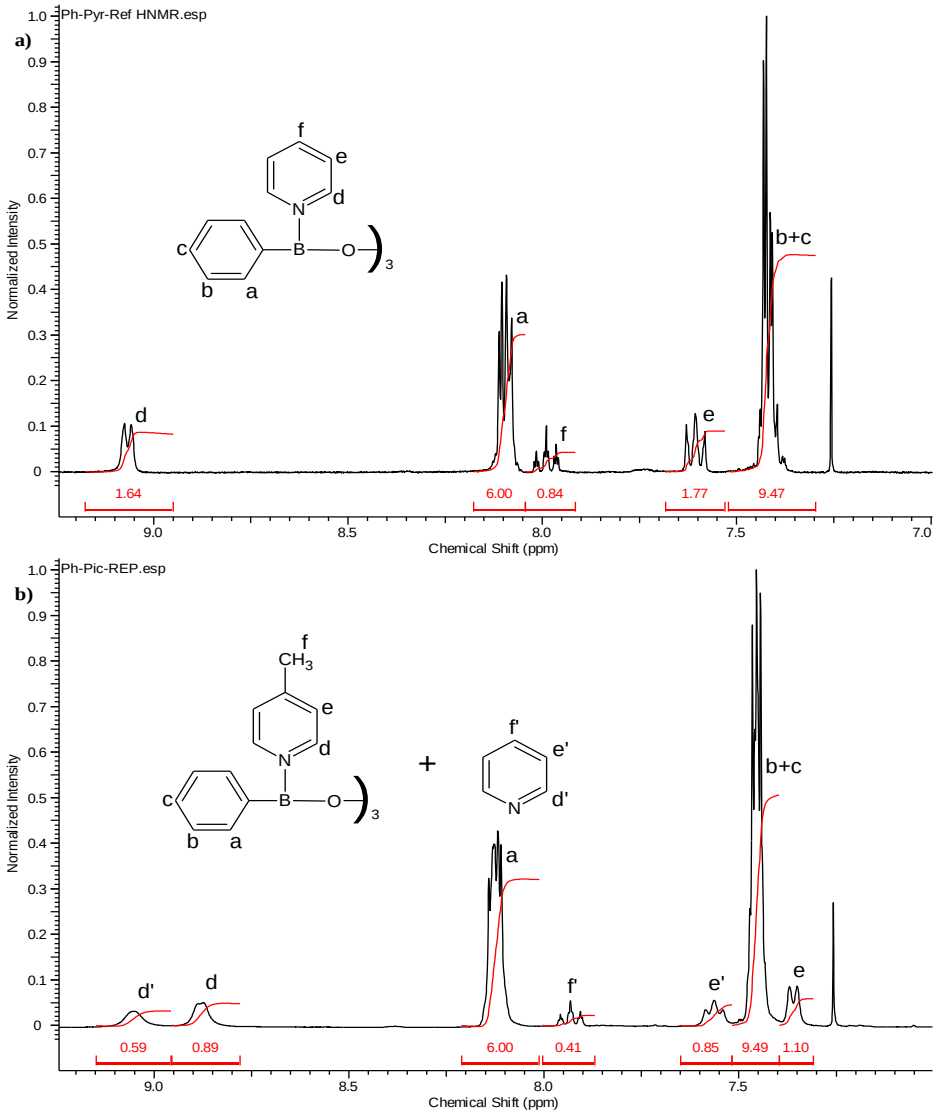


Figure 20 Phenylboroxine pyridine ^{1}H NMR reference spectra (a) and phenylboroxines pyridine/picoline displacement reaction (b) showing the partial displacement of the pyridine group by the picoline base.

H-Bor-Pyr ^{1}H NMR displacement spectra (fig 20) show the **d** & **d^{1}** hydrogen peaks for both pyridine and picoline at 9.05 ppm and 8.88ppm, respectively. It is clear from the reference spectra that the pyridine base has been partially replaced because one can see the **d'** peak in both spectra. In the reference spectra (fig 20-a) a doublet at 9.075 ppm 1.64 H signal compares favorably with the broad peak at 9.05 ppm in the displacement reaction spectrum while a new peak at 8.88 ppm forms representing the picoline which has displaced the pyridine.

The pKa of the base has a significant effect on the displacement reaction; the pyridine was not completely removed by picoline but instead led to a mixture of pyridine and picoline complexes as evidenced by ^{1}H NMR. On the other hand later testing using DMAP completely displaced the pyridine to any detectable level. There is however no identifiable correlation that links the substituent group of the boroxine with an effect on the displacement of pyridine by DMAP.

An interesting phenomenon is observed involving the two hydrogens ortho to the nitrogen in the aromatic ring of the bases. The **d** and **d'** signals broaden and this is possibly due to the equilibrium shifting towards the bonded form of the complex. The dative bond between the base and boroxine is permanent enough that the dissociation and attachment of the base with the boroxine is beginning to approach the NMRs detectable timescale. To further support this is the peak at 8.2 ppm which corresponds to the **a** hydrogen (fig 20-b) which has lost some resolution through broadening of the original signal. It is hypothesized that the picoline has a different equilibrium shifted more towards the bonded complex. This means that the picoline is staying attached longer to

the boroxine and the change in electronic environment is becoming detectable to the NMR.

When one compares the spectrum from the H-Bor-Pic displacement reaction with the Cl-Bor-Pic displacement you can see a difference in the amount of displaced pyridine (fig 21). The Cl-Bor-Pic displacement reaction clearly indicated little to none of the initial pyridine Lewis base still present. This may be due to the withdrawal of electron density by the chloro group increasing boroxine preference to the picoline because the picoline has more electron density to donate. Unfortunately, a clear correlation is not possible because in the Fl-Bor-Pic spectra you do not see a similar trend of picoline completely displacing the pyridine base (fig 22).

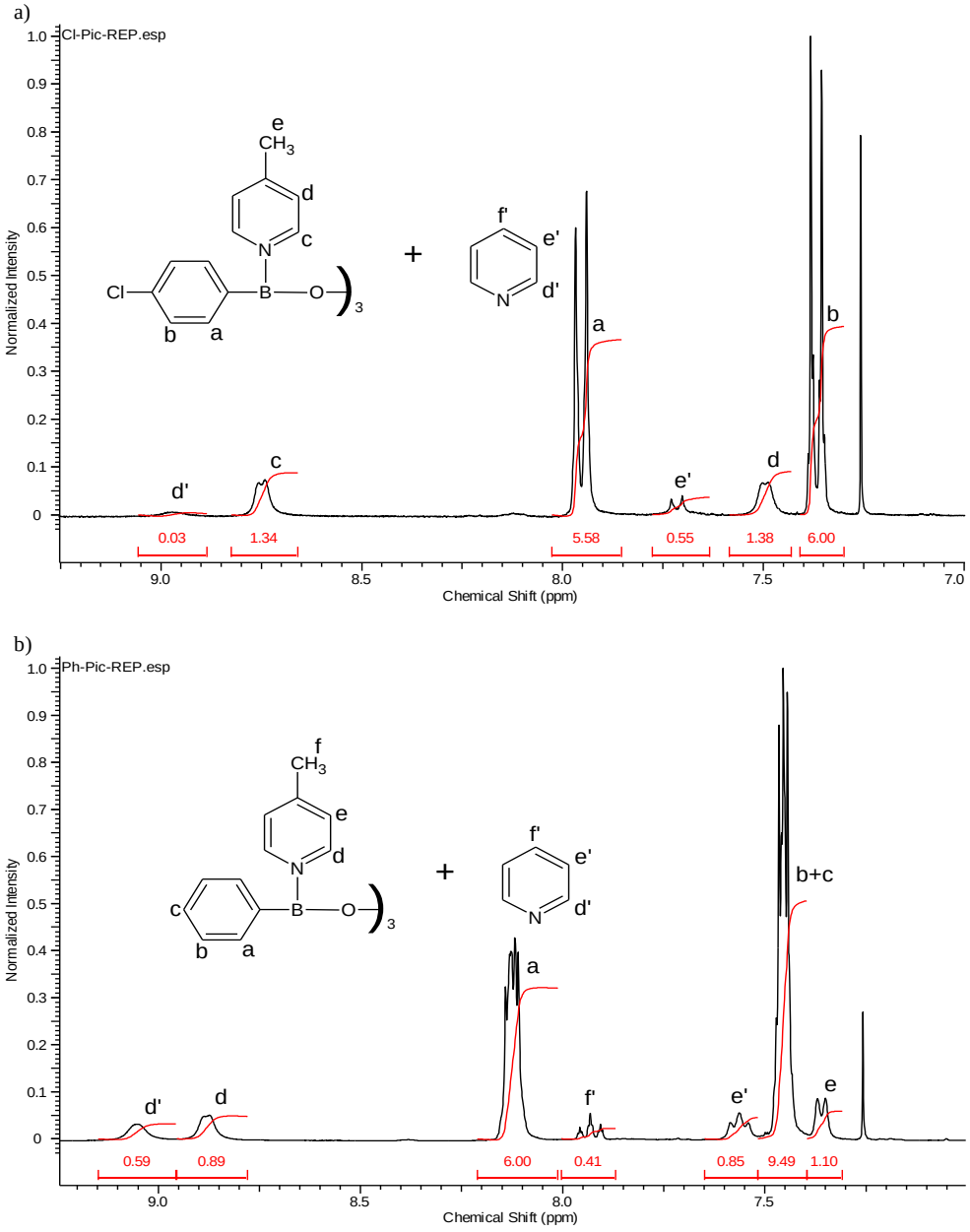


Figure 21 Comparison between Cl-Bor-Pic displacement reaction (a) and H-Bor-Pic displacement reaction (b) showing the difference in the amount of residual pyridine still bonded to the two boroxines.

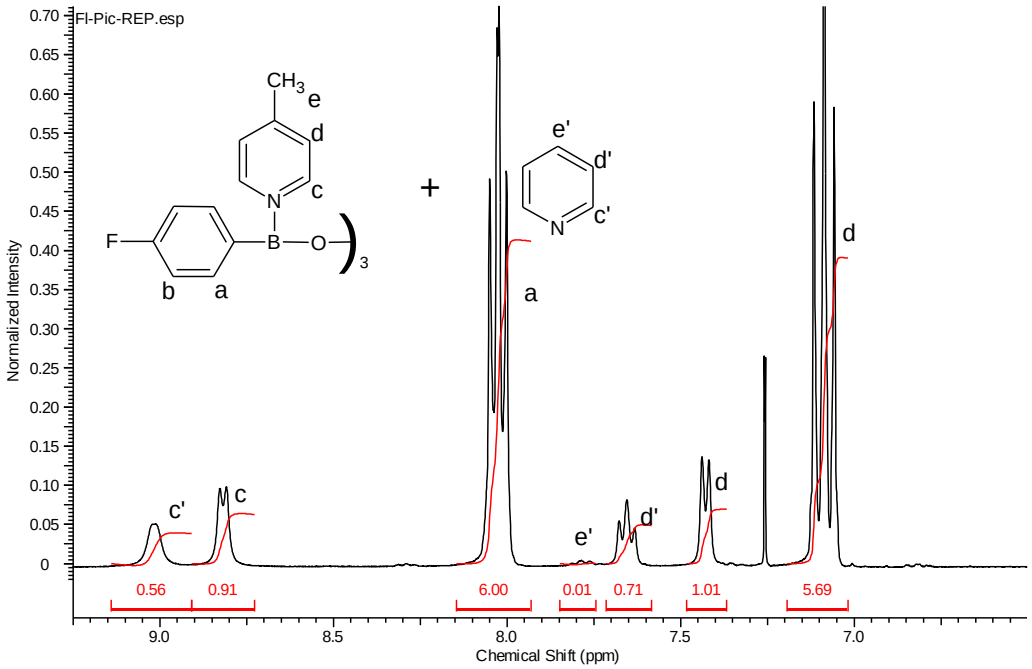


Figure 22 The ^{1}H NMR spectrum for the F-Bor-pyridine/picoline displacement reaction.

Since the F-Bor and Cl-Bor behave differently with Cl-Bor indicating the expected affect due to electron withdrawal while F-Bor other does not; it becomes difficult to conclude if the electron withdrawal or donation had a clear effect on the displacement of an attached base. It was consistently observed that the base with the higher pK_a replaced the base with the lower pK_a. It seems that the difference in pK_a plays a much more dominant role in displacement than any electron density differences in the boroxines. This phenomenon is shown in figure 23 which compares ^{1}H NMR spectra for both Fl-Bor replacement reactions. Even though the F-Bor is electronically similar to the Cl-Bor, it is apparent that the F-Bor-Pic displacement reaction (b) is not a complete displacement. Again, the higher pK_a of DMAP pushes the displacement to almost complete removal of the pyridine as seen in the F-Bor-DMAP (b).

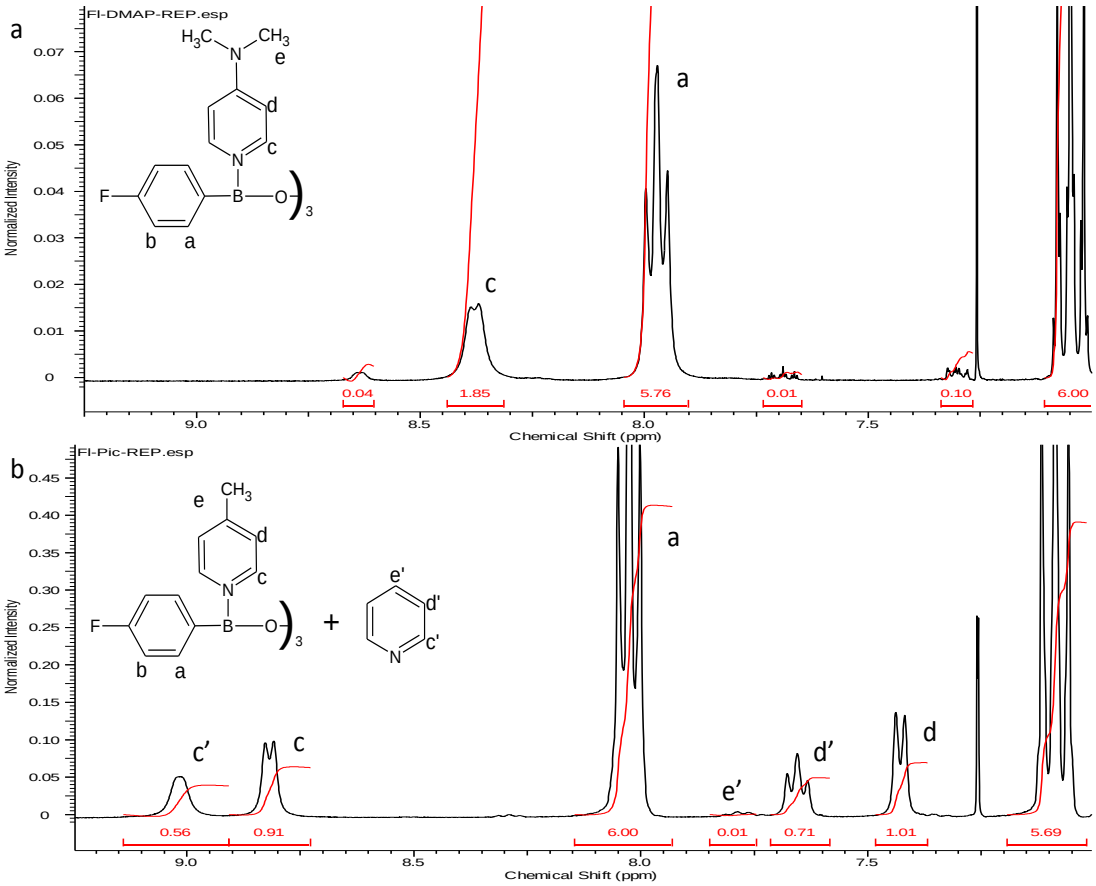


Figure 23 Comparison between F-Bor-DMAP displacement (a) and F-Bor-Pic displacement (b).

The base DMAP, which has a much higher pK_a (9.2) than picoline (5.96) and pyridine (5.25), dominates the displacement reactions almost completely displacing the pyridine the majority of the time. DMAP also exhibits the largest broadening of the ^1H NMR spectra peaks.[11] Comparing the Cl-Bor-Pic displacement reaction with the Cl-Bor-DMAP displacement reaction (fig 24) it becomes easy to see the broadening which is amplified by the stronger DMAP-boroxine bond.

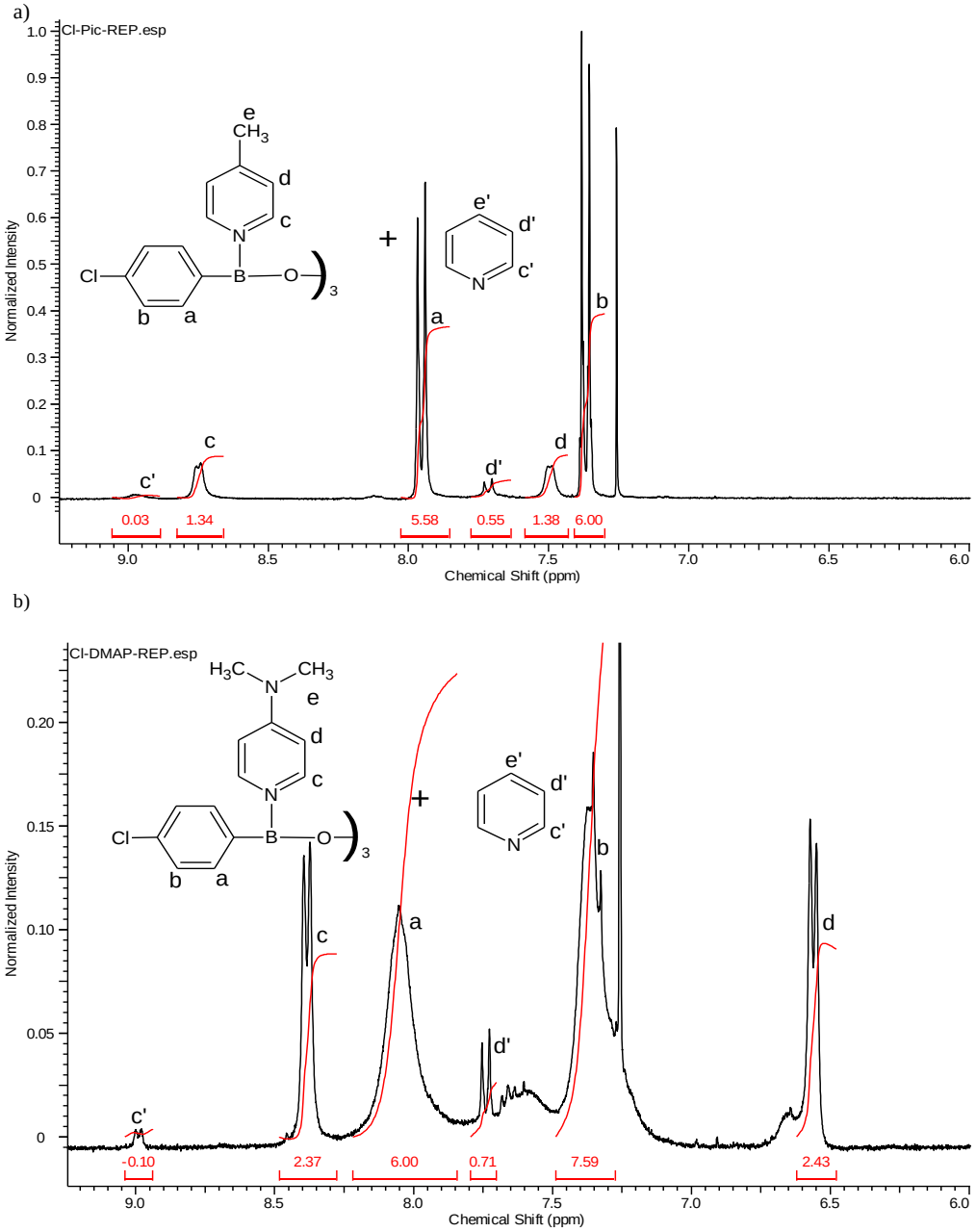


Figure 24 Comparison between Cl-Bor-Pic displacement reaction ^{1}H NMR spectra and Cl-Bor-DMAP displacement reaction spectra showing the large broadening which is occurring in the DMAP bonded boroxine.

The broadening of the boroxine peaks in the Cl-Bor-DMAP spectra suggests that the DMAP/boroxine is thought to be a much more tightly bound complex than either the picoline or pyridine complexes. The high pK_a of DMAP and the strong electron withdrawing effect of the chloro substituent is the suspected cause. The spectrum further

suggests that the bonded DMAP/boroxine complex is more prevalent in solution than the uncomplexed reactants. The **c** hydrogen signal appears as expected, but begins to resolve into a defined doublet instead of being a weak, broad, unresolved peak, as is normally seen in DMAP boroxine complexes. In contrast, the Cl-Bor **a** and **b** hydrogen signals both experience very large broadening due to the possibility of a dissociation rate approaching the time scale for NMR spectra scans, leading to a dative bond dissociation equilibrium in favor of the bonded species. The trend in the broadening seems to be effected by the electron substituent which is attached to the boroxine. When the Cl-Bor-DMAP is compared to the Me-Bor-DMAP it becomes possible to see the differences which can be attributed to the substituents and effecting the reaction equilibrium. In figure 25 blue arrows below the peaks show how the peak resolution is affected when compared against each other. The arrows pointing together indicate a peak which is resolving while arrows pointing away from each other indicate a broadening in the peak. As reported previously the changes in the spectra peaks is possibly linked to changes in equilibrium and reaction rates.

It appears that the broadening is much more a cooperative effect between pK_a and the boroxine phenyl substituent. It is hypothesized that a trend exists between the rate of reaction and electron withdrawal of the boroxine substituent. This is demonstrated in figure 25 a comparison between Cl-Bor-DMAP (a) and Me-Bor-DMAP (b). The Cl-Bor-DMAP shows broadening in both boroxine peaks suggesting that the NMR is beginning to see a breakup of the symmetry commonly observed with boroxine complexes. It appears as if the resolution of these peaks can be linked to the equilibrium of the reactions becoming very distinct with the higher pK_a DMAP.

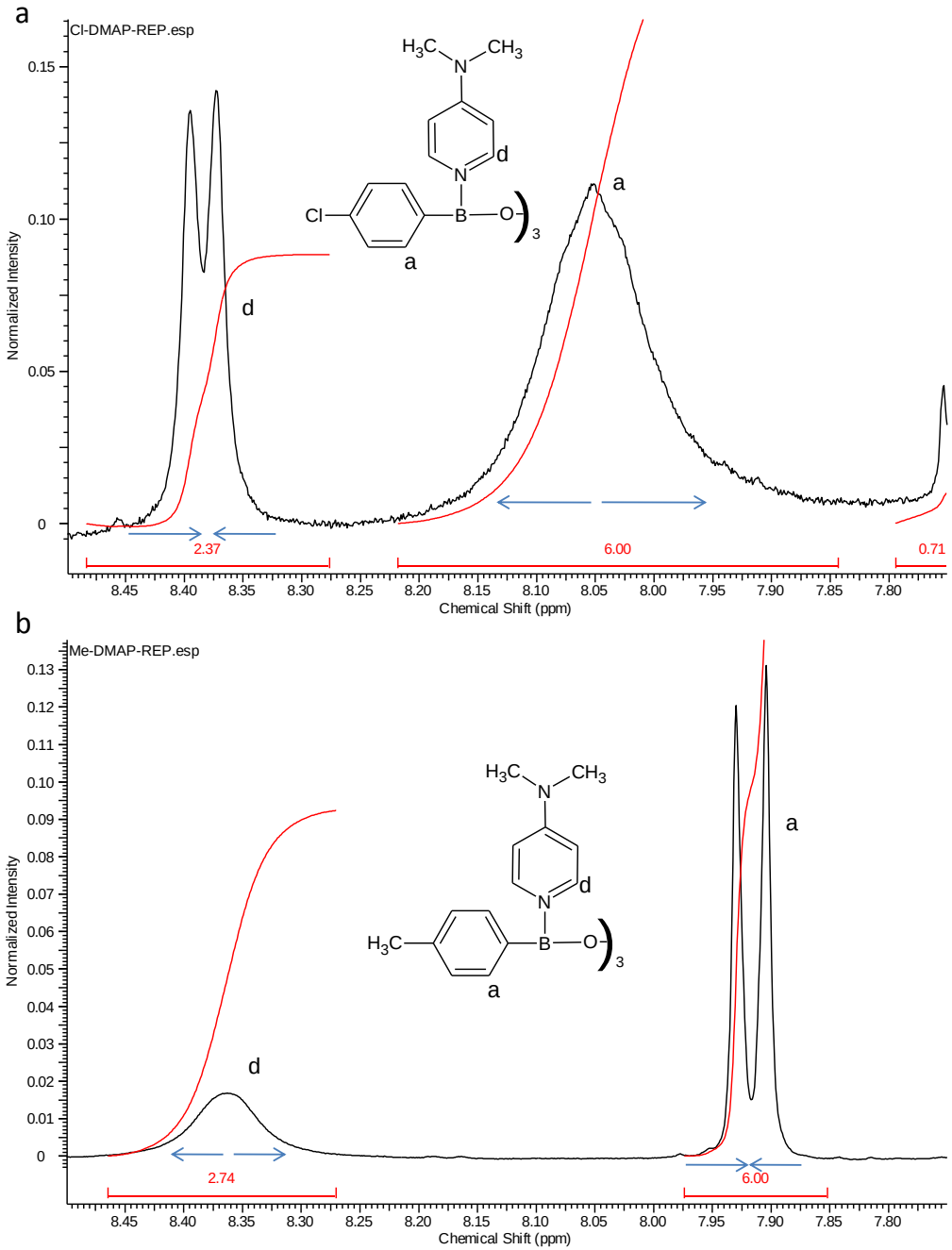


Figure 25 Comparisons between Cl-Bor-DMAP (a) and Me-Bor-DMAP (b).

The **a** and **b** hydrogen signals are separating into two or more signals because the DMAP is breaking the symmetry by complexing and causing the molecule to pucker similar to crystal structures that have been previously found in laboratory (fig 26). In

contrast to the broadening of the Cl-Bor-DMAP, the Me-Bor-DMAP broadens with a reverse trend to the Cl-Bor-DMAP. The **c** DMAP signal broadens and the boroxine **a** signal resolving into a distinct doublet (fig 25-b). It is assumed that the solution state complex begins to resemble the solid state confirmation as the dative bond becomes more permanent because a crystal boroxine is the only model thus far for a permanent dative bond.

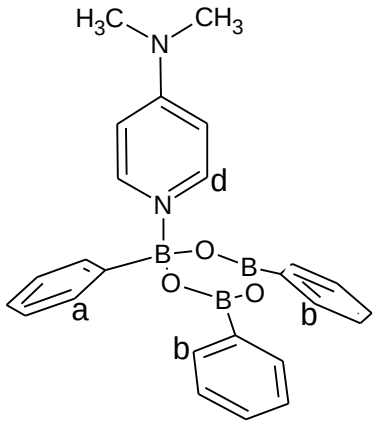


Figure 26 Solid state conformation of a boroxine and DMAP complex.

2.2.2 Displacement Reaction Summary

Of the two variables that were explored in these displacement reactions, varying the pKa of the base and varying the electronic properties of the substituents, it appears that the strength of the base has a greater impact on the extent of the displacement reaction. Table 1 shows the different compounds and the ratio of the ortho hydrogens to the nitrogen hydrogens for the pyridine/picoline and pyridine/DMAP complexes.

Table 1 Integration ratios for each of the ten replacement reactions.

Boroxine	Pyr/Pic	Pyr/DMAP
H-Bor	1/1.508	0/1.68
F-Bor	1/1.625	.04/1.85
Cl-Bor	1/44.67	0/2.37
ME-Bor	0/1.64	0/2.74
MO-Bor	1/18	0/1.72

It is of interest to note that the substituent group appears to affect the bond strength/rate of the boroxine/Lewis base complex but doesn't seem to have as much effect on whether the pyridine base will be displaced. The Lewis bases themselves dictate to what extent the displacement reaction will take place. The probability for the electron withdrawing groups affecting the reaction rate is very strong and may be a source for potential control or at least manipulation of displacement reactions. Further study into the displacement reactions kinetics is strongly suggested using temperature controlled NMR studies since evidence shows that the equilibrium seems to vary based on the structure and bases of each displacement reaction studied.

2.3 Fluorescence Studies of Various Amine–Boroxine Complexes

In 2007, the Buchwald group reported that the Suzuki Coupling Reaction could be monitored in real time using a bench top detection method using a qualitative fluorescence technique.[9] At the heart of this method was the observation that the intermediate boronate- base complex was fluorescent using long wave UV light. In addition, through work done by Heather Hawkins an undergraduate in our research

laboratory in unpublished results, it was observed that several fluoro substituted boronates and boroxines showed photoluminescence when uncomplexed but when complexed, these same boronates and boroxines lost most of their photo luminescent activity. It has been determined that this is due to excimer formation and the complexation breaks up the excimer. It was then hypothesized that the electron donation of a base and the structure of the boroxine to which it complexed would alter the fluorescence emission in a quantitative and predictable manner which would allow identification of boroxine through a simple fluorescence test.

The first boroxine (H-Bor) data suggested that the section of the boroxine responsible for fluorescence is independent from affect of a Lewis base bonding (fig 27).

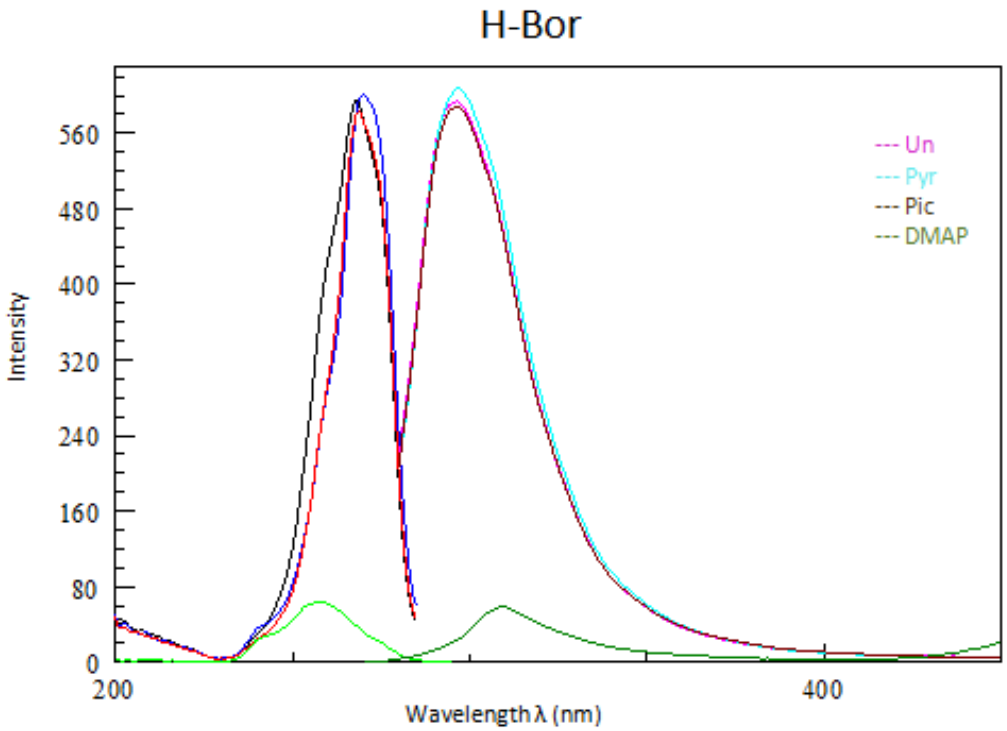


Figure 27 Fluorescence excitation/emission spectra of uncomplexed Bor-1 and pyridine, picoline, and DMAP H-Bor complexes.

Figure 27 shows no identifiable changes in the emission spectra. The only change is when there is a decrease in intensity for the Ph-Bor-DMAP complex. Currently this change cannot be explained. The Cl-Bor spectra, on the other hand, had a significant shift in the λ_{max} of the pyridine complexed species (fig 28). The uncomplexed and picoline complexed Cl-Bor aligns approximately at the 300nm mark while the pyridine complexed Cl-Bor lambda max is at approximately 355nm. It is unknown what this shift indicates at this time.

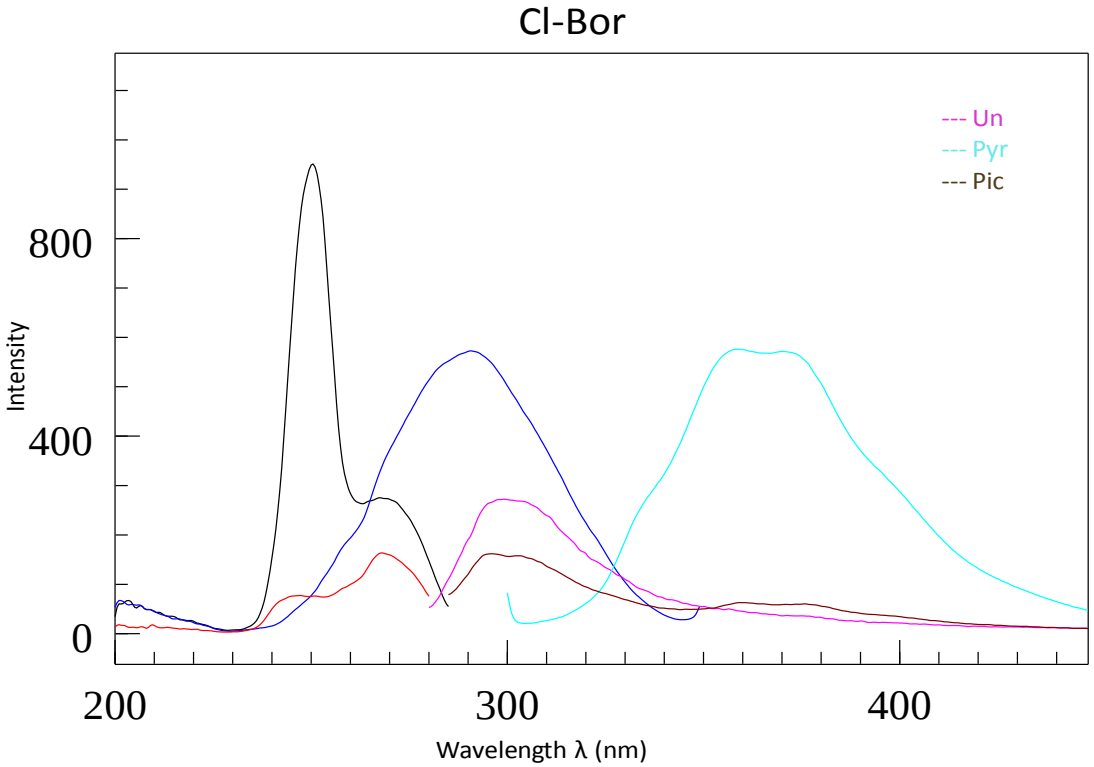


Figure 28 The excitation and emission spectra of Cl-Bor The represented species graphed being uncomplexed, pyridine, and picoline complexed.

The peak shift in the pyridine curve λ_{max} is the desired observed effect because it allows detection of a change in fluorescence as the molecule structure changes. It is unfortunate that the other peaks in this spectrum line up because it is possible that the pyridine shift is an isolated change possibly due to a concentration problem. These

compounds seemed to be highly concentration dependant with what appears to be excimer formation in Cl-Bor-uncomplexed samples run at different concentrations (fig 29). An excimer is a dimer made of two molecules which combine through intermolecular forces. One molecule is in a ground state and the other dimer member is excited. The excited molecule is stabilized by the ground state molecule which causes a shift in the emission to a less energetic λ_{max}.

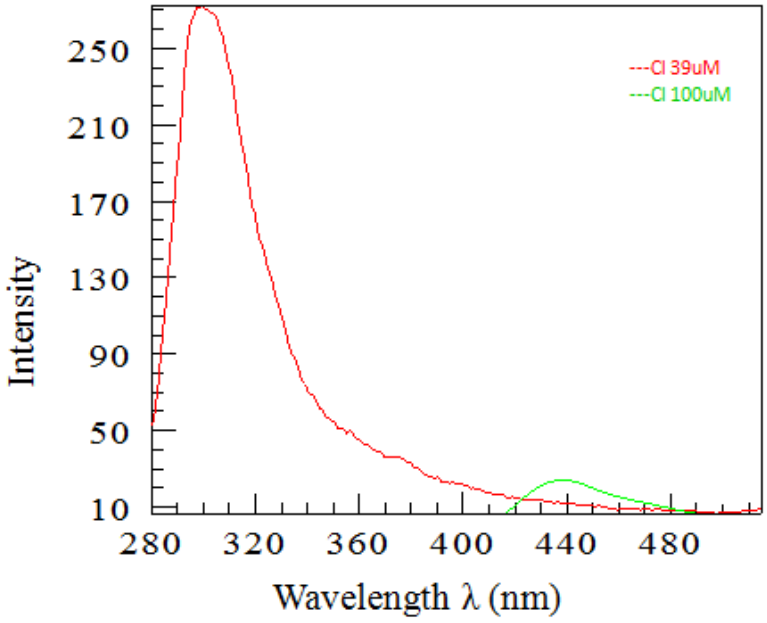


Figure 29 Graph of Cl-Bor at 100µM and 39µM concentrations showing large red shift which could indicate formation of an excimer at higher concentrations.

The only easily identifiable characteristic was when all the pyridine complexed boroxines were plotted together (fig 30). Figure 30 shows how the electron withdrawing curves fluoro and chloro overlap near 375nm while the electron donating groups overlap near 300nm. This could mean that the electron withdrawing groups share an electronic configuration that allows a less energetic fluorescence emission.

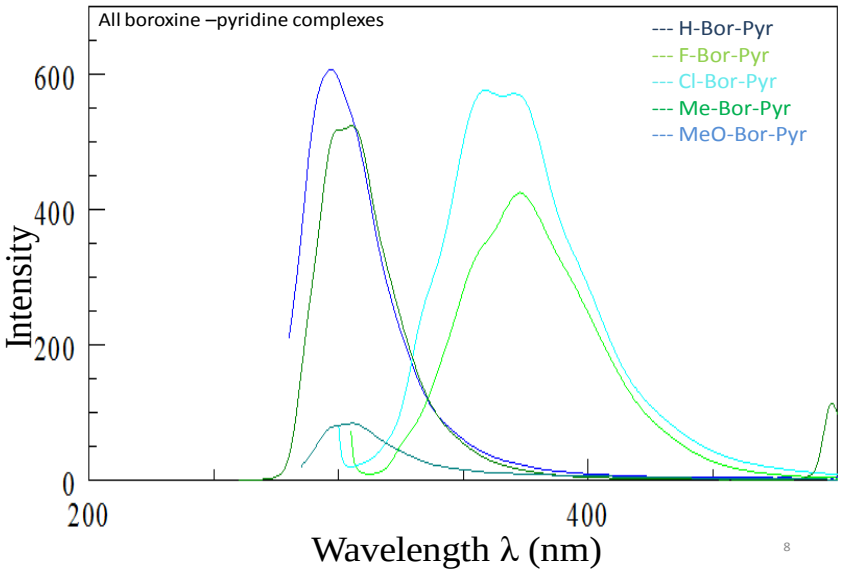


Figure 30 Emission spectra for each of the pyridine complexed boroxines.

Both the picoline and DMAP complexed fluorescence spectra showed no clear trends (fig 31 and 32). Consistently F-Bor was seen to emit at higher wavelengths then the other complexed boroxines. Again it is unclear what if any significance this shift holds in regards to fluorescence sensor development.

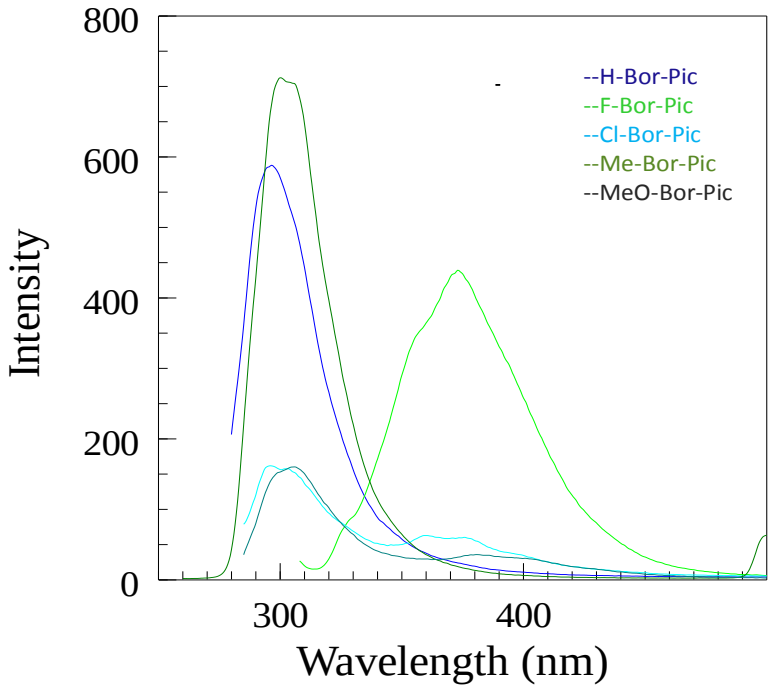


Figure 31 Overlaid spectra from each of the boroxine-picoline fluorescence tests.

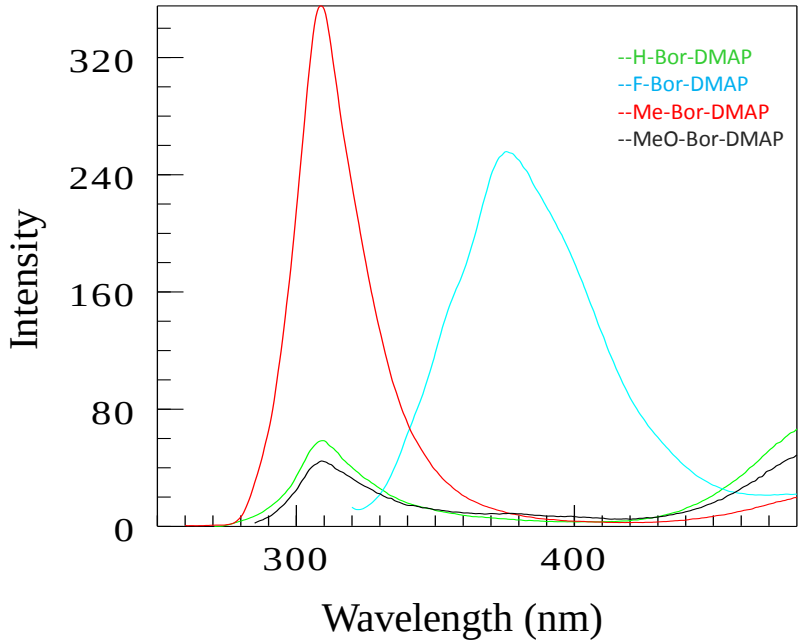


Figure 92 Overlaid spectra of Bor-DMAP complexed boroxines except for Cl-Bor-DMAP because it was discarded as an outlier due to concentration variation.

2.4 Conclusions

In the NMR studies it is apparent that the pKa of the Lewis base dominates the displacement between the bases. That is, a stronger base (picoline) will displace a weaker base (pyridine) of a complex; the greater the differences in pK_a, the more complete the displacement. It did not appear that the substituent group on the aromatic ring had an effect on the bases in regards to their displacement. It did appear that the substituents on the aromatic ring affect the binding equilibrium of the different bases. It is recommended that a temperature dependant NMR study be done of the compounds to confirm this possible trend.

The boroxines examined in this research project all show visible fluorescence (in solids and in solution) under long-wave UV light. When the fluorescence emission spectra of these boroxines are measured all show emission at 300 nm. Likewise, when the

emission spectra of the Lewis base complexes of these boroxines are measured, it shows emission spectra at the same wavelength. It appears as though complexation of the boroxine with a Lewis base has no effect on the emission spectra of the boroxine.

The identifiable trends are the possible excimer formation and fluorine red shifting. It is unclear what is causing the 80 nm red shift in the fluorine substituted boroxine's fluorescence, but it is consistent throughout all of the other complexes. To understand these phenomena, more tests are required with other boroxines to see if the fluorine red shift is an identifiable difference in emission pathways or an isolated exception to the otherwise consistent spectra.

CHAPTER 3: EXPERIMENTAL

General

All solvents and reagents were purchased from Sigma Aldrich, Acros, or Fisher chemical manufacturers. Solvents and reagents were used at purities specified by the manufacturer. Amines were distilled from calcium hydride. A CEM discover microwave unit was used as an alternative heat source. ^{1}H and ^{13}C NMR were taken using a JEOL Eclipse 300 FT 300 MHz NMR spectrometer. Melting point data was acquired using a Melt Temp II Laboratory Devices, USA. UV-Vis and Fluorometer used were a Hewlett Packard 8453 UV-Vis and Perkin Elmer model LS 55 respectively. Rotovap and vacuum pumping was accomplished using a BUCHI Rotavapor R-205 and Edwards model E2M2 High Vacuum Pump. All solutions were made using volumetric flasks and a Mettler Toledo AB104-S/Fact analytical scale.

Boroxine preparation

All boroxines were synthesized using a Discover microwave as a heat source. The specified boronic acid was weighted out then placed into a 100mL round bottom flask (RBF). 50mL of chloroform was then used as a solvent. The RBF was stirred with heat for 30 minutes using the microwave. The RBF was then placed on the Rotovap and then vacuum pumped to remove solvent and dry product. ^{1}H NMR was taken to quickly confirm successful synthesis. Once synthesis was completed and confirmed yields, melting points, and ^{13}C NMR were taken.

Solution preparation

All solutions were prepared using 50mL volumetric flasks and Metter Toledo AB104-S/FACT scale. The boroxine/complex powder was weighted out onto weighing

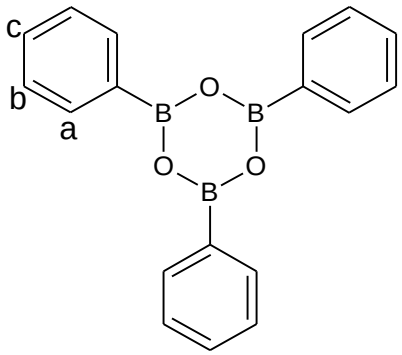
paper then deposited into the volumetric flask. The flask was then filled. A second dilution was required for all solutions to bring them into the correct μM concentration range. The dilution was made using a mechanical pipette (info) and small 10mL beaker. The Pipette tip was too large to fit down the neck of the volumetric flasks so a small amount of stock solution was poured out into the beaker and 2 mL of solution was drawn into the mechanical pipette and deposited into a new 50mL volumetric flask. The remaining contents of the 10mL beaker were returned to the stock solution and the beaker was cleaned using alconox and acetone before being used with the next solution.

Fluorescence Procedure

50 μM Solutions were placed into a crystal cuvette. A UV-Vis measurement was taken of each solution to verify contaminants were not present and get an initial excitation lambda max for the Fluorometer. Samples were then placed into the Fluorometer and initial scans were made using the predetermined lambda max. Determination of the emission lambda max was completed by the initial scan and used to scan the sample for the actual excitation lambda max. Once both the excitation and emission lambda max were determined 5 scans were run and averaged together. The resulting data was graphed using spectra solve software.

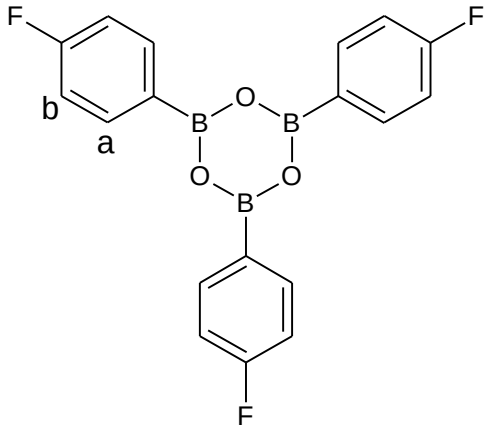
3.1 Boroxine Synthesis

Phenyl boroxine Uncomplexed (H-Bor-UN)



Phenyl boroxine was synthesized using the general procedure. Place phenyl Boronic acid (.5866g, 4.811mmol) in Chloroform (50ml). Yield .4539g (90.78%), m.p. 201˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.26 (dd, 2H, a), 7.61 (m, .96H c), 7.54 (d, 1.99H, b); ^{13}C NMR (300MHz, $CDCl_3$): δ = 135.77, 133.57, 132.81, 131.38, 128.11.

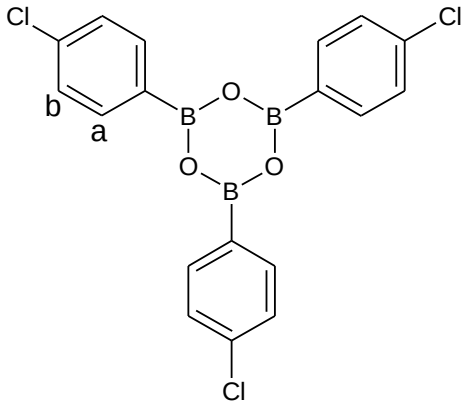
Fluorophenyl boroxine Uncomplexed (F-Bor-UN)



4-Fluorophenyl boroxine was synthesized using the general procedure. Place 4-Fluorophenyl Boronic acid (.5739g, 4.102mmol) in Chloroform (50ml). Yield .5007g

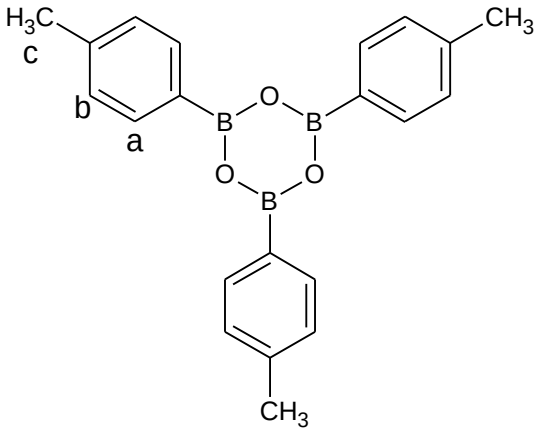
(100.14%), m.p. 270˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.22 (td, 2H, a), 7.19 (td, 1.81H, b); ^{13}C NMR (300MHz, $CDCl_3$): δ = 138.19, 138.07, 135.9, 115.54, 115.27.

Chlorophenyl boroxine Uncomplexed (ClBor-Un)



4-Chlorophenyl boroxine was synthesized using the general procedure. Place 4-Chlorophenyl Boronic acid (3.00 g, 18.82 mmol) in Chloroform (50 ml). Yield 2.604 g (102 %), m.p. 289˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.13 (td, 6H, a), 7.48 (td, 5.96H, b); ^{13}C NMR (300MHz, $CDCl_3$): δ = 139.40, 137.07, 134.50, 128.55. (CB-19)

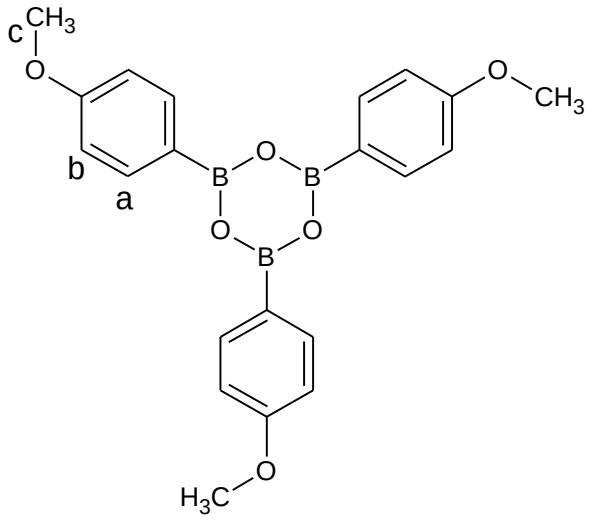
Methylphenyl boroxine Uncomplexed (Me-Bor-Un)



4-Methylphenyl boroxine was synthesized using the general procedure. Place 4-Methylphenyl Boronic acid (.5764 g, 4.239 mmol) in Chloroform (50ml). Yield .4361 g

(87.22 %), m.p. 258˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.12 (d, 6.11H, a), 7.31 (d, 6H, b), 2.43 (s, 9.04H, c); ^{13}C NMR (300MHz, $CDCl_3$): δ = 143.02, 137.17, 129.01, 21.22. (CB-1)

Methoxyphenyl boroxine Uncomplexed (MeO-Bor-Un)



4-Methoxyphenyl boroxine was synthesized using the general procedure. Place 4-Methoxyphenyl Boronic acid (1.139g, 7.495mmol) in Chloroform (50ml). Yield .9512g (94.75%), m.p. 206˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.16 (d, 2.0H, a), 7.01(d, 2.0H, b), 3.89(s, 3.0H, c); ^{13}C NMR (300MHz, $CDCl_3$): δ = 163.279, 137.590, 113.711, 113.596, 55.272.

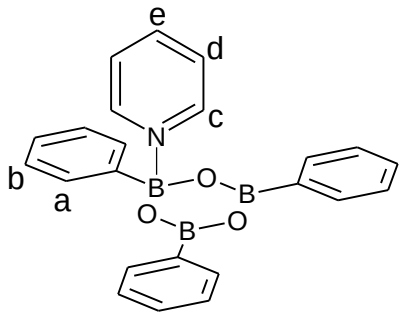
3.2 Complexation

All boroxine complexes were synthesized in the same manner and all pyridine/picoline/DMAP will be referred to as a Lewis base for purposes of this procedure. The boroxine was placed into a 25mL RBF and filled to half with chloroform as a solvent. Then using a glass syringe or scale one equivalent of the Lewis base was

measured out and placed into the RBF as it was stirring. The mixture was allowed to stir for one hour to insure equilibrium was reached. The RBF was placed on the rotovap and vacuum pump to remove solvent and dry the product. Once complexation was completed molecules identity was confirmed by ^{1}H NMR. Yields, melting point, and ^{13}C NMR data was also taken.

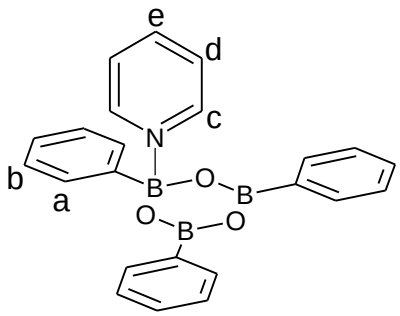
3.2.1 Pyridine Complexation

Phenyl boroxine Pyridine complex (H-Bor-Pyr)



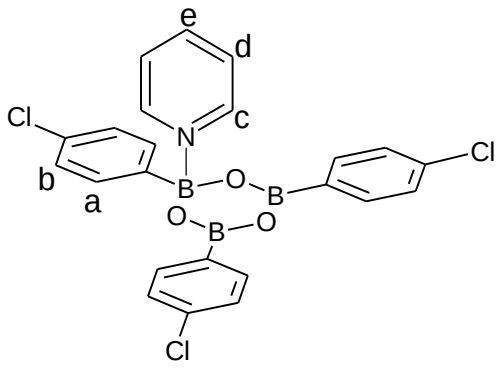
Phenyl boroxine pyridine complex was synthesized using the complexation procedure. Phenyl boroxine (.1g, .321mmol) and pyridine (25.9µL, .321mmol) were placed in a RBF with chloroform (25mL). Yield .1153g (91.87%), m.p. 150˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 9.02(d, 2.0H, d), 8.09(m, 7.23H, a & f), 7.65(t, 2.8H, e), 7.42(m, 9.69H c & b); ^{13}C NMR (300MHz, $CDCl_3$): δ = 143.476, 141.583, 133.934, 129.987, 127.673, 125.887.

Fluorophenyl boroxine pyridine complex (F-Bor-Pyr)



4-Fluorophenyl boroxine pyridine complex was synthesized with the complexation procedure. 4-Fluorophenyl boroxine (.1g, .273mmol) and pyridine (21.99µL, .273mmol) were placed into 50mL RBF with chloroform (25mL). Yield .0763g (62.85%), m.p. 252˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.98(d, 2.0H, c), 8.03(m, 6.9H, a & e), 7.68(t, 1.99H, d), 7.08(t, 6.04H b); ^{13}C NMR (300MHz, $CDCl_3$): δ =166.149, 162.866, 143.369, 141.766, 135.872, 135.773, 126.009, 114.787, 114.528.

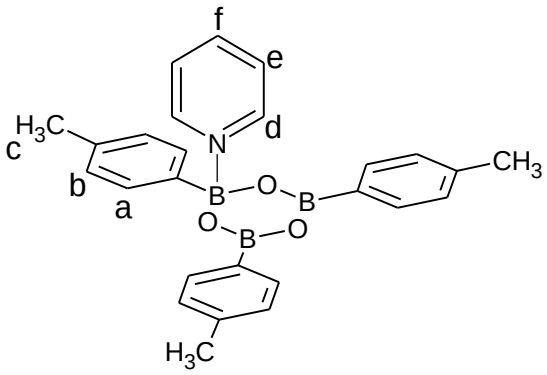
Chlorophenyl boroxine Pyridine Complex (Cl-Bor-Pyr)



4-Chlorophenyl boroxine pyridine complex was synthesized using the complexation procedure. 4-Chlorophenyl boroxine (.752 g, 1.806 mmol) and pyridine (146 µL, 1.806 mmol) were placed into a 50mL RBF with chloroform (25mL). Yield .893 g (97.4 %), m.p. 187˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.98(td, 2H, c), 8.05(tt,

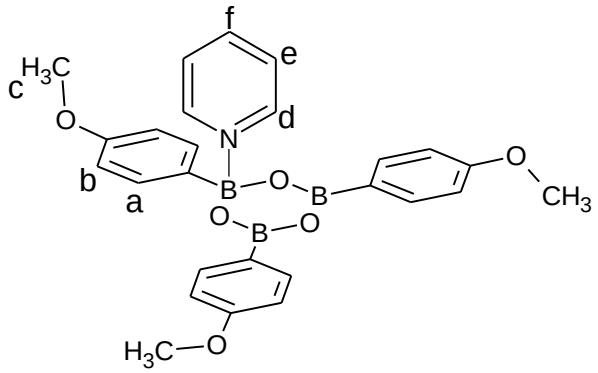
.99H, e), 7.93 (d, 5.84H, a), 7.65(t, 2.09H d) 7.35(dd, 6.05H, b); ^{13}C NMR (300MHz, $CDCl_3$): δ =143.44, 141.64, 136.02, 135.12, 127.94, 126.01.

Methylphenyl boroxine Pyridine Complex (Me-Bor-Pyr)



4-Methylphenyl boroxine pyridine complex was synthesized using the complexation procedure. 4-Methylphenyl boroxine (.1 g, .283 mmol) and pyridine (22.8 µL, .283 mmol) were placed in a 50mL RBF with chloroform (25mL). Yield .1026 g (83.76 %), m.p. 146/261˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 9.04(ds, 1.14H, d), 8.02(m, 6.13H, a & f), 7.57(t, 1.36H, e), 7.24(d, 6.82H, b), 2.39(s, 9H, c); ^{13}C NMR (300MHz, $CDCl_3$): δ =144.29, 140.67, 139.57, 133.92, 128.44, 125.54, 21.73.

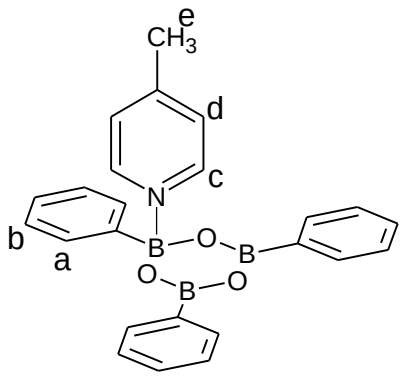
Methoxyphenyl boroxine Pyridine Complex (MeO-Bor-Pyr)



4-Methoxyphenyl boroxine pyridine complex was synthesized using the complexation procedure. 4-Methoxyphenyl boroxine (.750g, 1.866mmol) and pyridine (15.1µL, 1.866mmol) were placed in a 50mL RBF with chloroform (25mL). Yield .6616g (73.7%), m.p. 120/187˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.92(d, 1.87H, d), 8.03(d, 5.46H, a), 7.98(t, .53H, f), 7.58(t, 1.96H e), 6.95(d, 6.08, b) 3.85(s, 9.0H, c; ^{13}C NMR (300MHz, $CDCl_3$): δ = 161.477,144.232, 140.781, 135.758, 125.589, 113.260, 55.196.

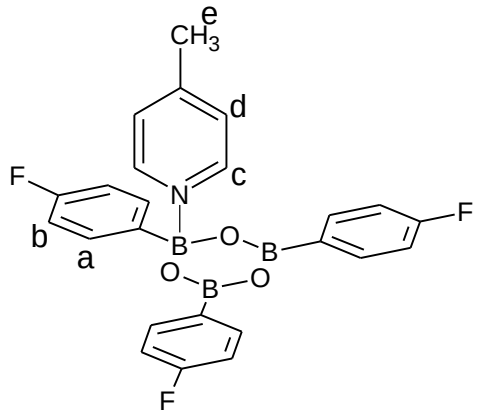
3.2.2 Picoline Complexation

Phenyl boroxine Picoline Complex (H-Bor-Pic)



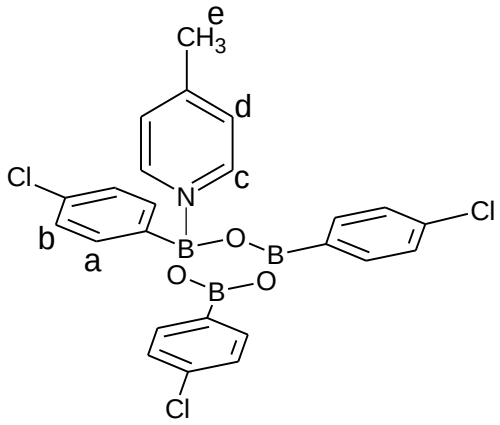
Phenyl boroxine picoline complex was synthesized using the complexation procedure. Phenyl boroxine (.1g .321mmol) and picoline (31.2µL, .321mmol) were placed in a 50mL RBF with chloroform (25mL). Yield .1220g (94.48%), m.p. 127˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.88(d, 1.92H, d), 8.07(m, 6.0H, a), 7.40(m, 11.32H, b & c & e), 7.25(m, 7.35H b & $CDCl_3$), 2.46(s, 2.87H, f); ^{13}C NMR (300MHz, $CDCl_3$): δ =153.77, 143.11, 133.90, 129.86, 127.63, 126.34, 21.58.

Fluorophenyl boroxine Picoline (F-Bor-Pic)



4-Fluorophenyl boroxine picoline complex was synthesized using the complexation procedure. 4-Fluorophenyl boroxine (.1g, .273mmol) and picoline (26.57µL, .273mmol) were placed in a 50mL RBF with chloroform (25mL). Yield .0288g (22.99%), m.p. 151˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.82(d, 1.72H, c), 8.03(t, 6.0H, a), 7.41(d, 1.72H, d), 7.09(t, 6.0H b), 2.49(s, 2.35H, e); ^{13}C NMR (300MHz, $CDCl_3$): δ = 166.15, 162.88, 142.43, 135.82, 126.71, 114.50, 21.80.

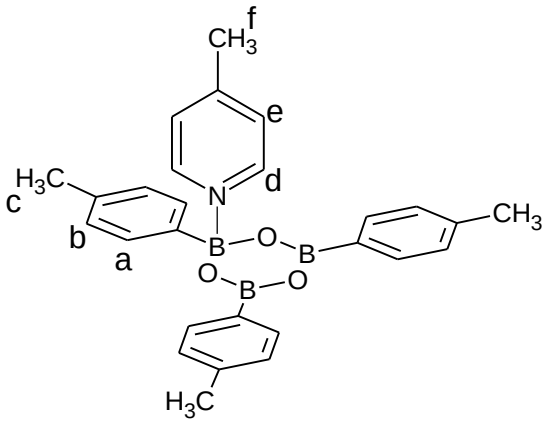
Chlorophenyl boroxine Picoline complex (Me-Bor-Pic)



4-Chlorophenyl boroxine picoline complex was synthesized using the complexation procedure. 4-Chlorophenyl boroxine (.1g, .241mmol) and picoline (23.4µL,

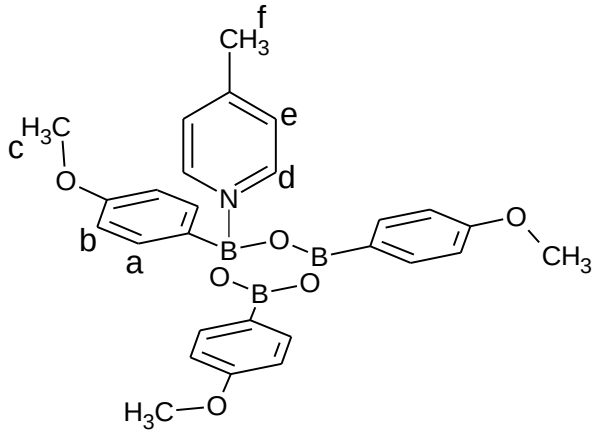
.241mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .0655g (53.47%), m.p. 186 ˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.79(d, 2.0H, c), 7.92(d, 6.0H, a), 7.41(d, 2.0H, d), 7.34(d, 6.07H, b), 2.49(s, 2.9H, e); ^{13}C NMR (300MHz, $CDCl_3$): δ = 148.91, 147.94, 135.81, 135.03, 127.85, 125.19, 21.22.

Methylphenyl boroxine Picoline Complex (Cl-Bor-Pic)



4-Methylphenyl boroxine picoline complex was synthesized using the complexation procedure. 4-Methylphenyl boroxine (.1g, .283mmol) and picoline (27.5 µL, .283mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .1050g (83.14%), m.p. 172/255˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.86(d, 1.43H, d), 7.99(d, 5.98H, a), 7.34(d, 1.38H, e), 7.25(m, 7.35H b & $CDCl_3$), 2.45(s, 2.07H, f) 2.38(s, 9.0H, c); ^{13}C NMR (300MHz, $CDCl_3$): δ = 153.44, 143.21, 140.32, 134.36, 128.50, 126.24, 21.78, 21.54.

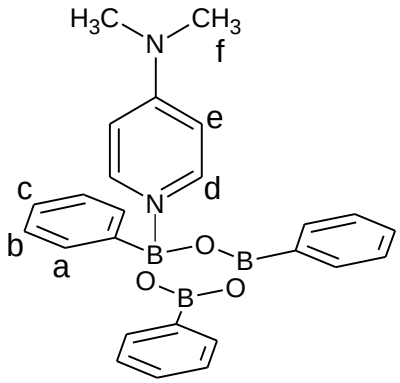
Methoxyphenyl boroxine Picoline Complex (MeO-Bor-Pic)



4-Methoxyphenyl boroxine picoline complex was synthesized using the complexation procedure. 4-Methoxyphenyl boroxine (.109g, .219mmol) and picoline (21.3µL, .219mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .959g (86.7%), m.p. 158˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 1.93(d, 1.93H, d), 8.00(d, 6.0H, a), 7.31(d, 1.86H, e), 6.92(d, 6.05H, b), 3.81(s, 8.91H, c) 2.45(s, 2.83H, f); ^{13}C NMR (300MHz, $CDCl_3$): δ = 161.49, 144.65, 135.81, 125.91, 113.23, 55.18, 21.45.

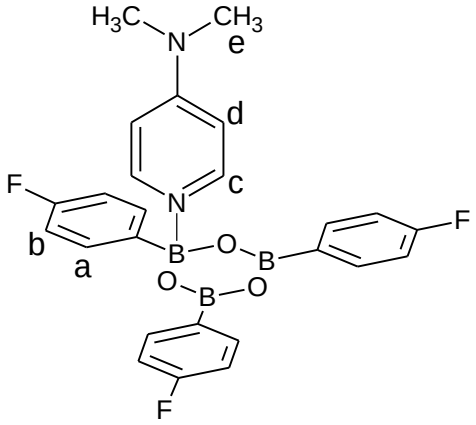
3.2.3 DMAP complexation

Phenyl boroxine DMAP Complex (H-Bor-DMAP)



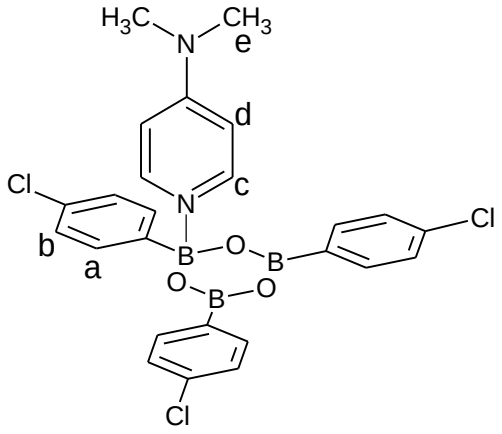
The phenyl boroxine DMAP complex was synthesized using the complexation procedure. Phenyl boroxine (.1g, .321mmol) and DMAP (.0392g, .321mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .1090g (78.25%), m.p. 164˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.48(d, 2.0H, d), 8.02(m, 5.15H, a), 7.37(m, 8.52H, b & c), 6.52(d, 2.09H, e), 3.05(s, 6.24, f); ^{13}C NMR (300MHz, $CDCl_3$): δ = 155.90, 142.49, 133.93, 127.91, 127.51, 106.41, 39.58.

Fluorophenyl boroxine DMAP Complex (F-Bor-DMAP)



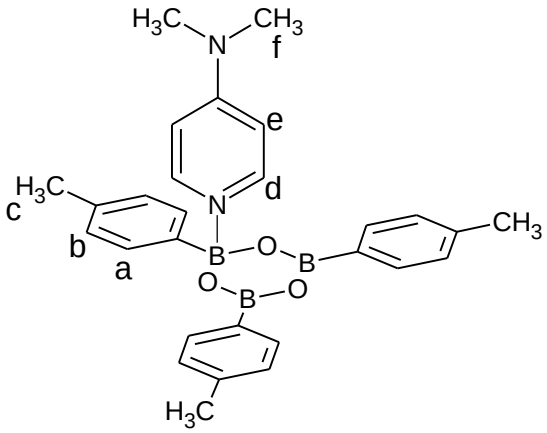
The 4-Fluorophenyl boroxine DMAP complex was synthesized using the complexation procedure. 4-Fluorophenyl boroxine (.1g, .273mmol) and DMAP (.0334g, .273mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .1029g (77.25%), m.p. 104˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.41(td, 2.1H, c), 7.97(m, 5.55H, a), 7.04(t, 6.0H, b), 6.57(td, 2.1H, d), 3.09(s, 6.1, e); ^{13}C NMR (300MHz, $CDCl_3$): δ =142.41, 114.57, 114.29, 106.50, 36.64.

Chlorophenyl boroxine DMAP Complex (Cl-Bor-DMAP)



The 4-Chlorophenyl boroxine DMAP complex was synthesized using the complexation procedure. 4-Chlorophenyl boroxine (.1g, .241mmol) and DMAP (.0294g, .214mmol) were placed in a 50mL RBF with chloroform (25µL). Yield .0867g (66.95%), m.p. 118/152˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.39(d, 1.95H, c), 8.05(m, 3.16H, a), 7.37(m, 4.7H, b), 6.56(d, 2.0H, d), 3.10(s, 5.77H, e); ^{13}C NMR (300MHz, $CDCl_3$): δ =142.35, 136.20, 136.04, 128.14, 127.76, 106.54, 39.65.

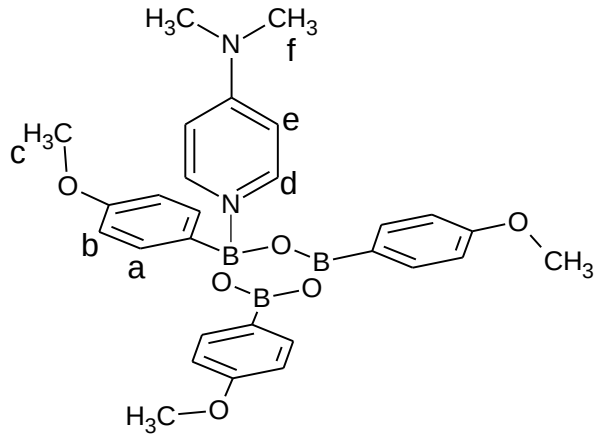
Methylphenyl boroxine DMAP Complex (Me-Bor-DMAP)



The 4-methylphenyl boroxine DMAP complex was synthesized using the complexation procedure. 4-methylphenyl boroxine (.1g, .283mmol) and DMAP (.0346g,

.283mmol) were placed in 50mL RBF with chloroform (25µL). Yield .1215g (90.2%), m.p. 105/189˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.46(d, 2.0H, d), 7.92(m, 5.06H, a), 7.18(d, 5.44H, b), 6.51(d, 2.02H, e), 3.03(s, 5.97H, f) 2.35(s, 8.93H, c); ^{13}C NMR (300MHz, $CDCl_3$): δ = 155.35, 144.80, 138.83, 133.80, 128.26, 106.51, 39.42, 21.70.

Methoxy boroxine DMAP Complex (MeO-Bor-DMAP)



The 4-methoxyphenyl boroxine DMAP complex was synthesized using the procedure outlined in journal tdj-148. 4-methoxyphenyl boroxine (.1103g, .2294mmol) and DMAP (.1240 .2294mmol) were placed in a 25mL RBF with chloroform (25µL). Yield .1046g (87.0%), m.p. 241˚C; ^{1}H NMR (300MHz, $CDCl_3$): δ = 8.44(d, 2.05H, d), 7.94(d, 5.33H, a), 6.90(d, 6.0H, b), 6.52(d, 1.99H, e), 3.81(s, 8.9H, c), 3.08(s, 6.17H, f); ^{13}C NMR (300MHz, $CDCl_3$): δ = 135.63, 113.17, 106.45, 55.19, 39.79.

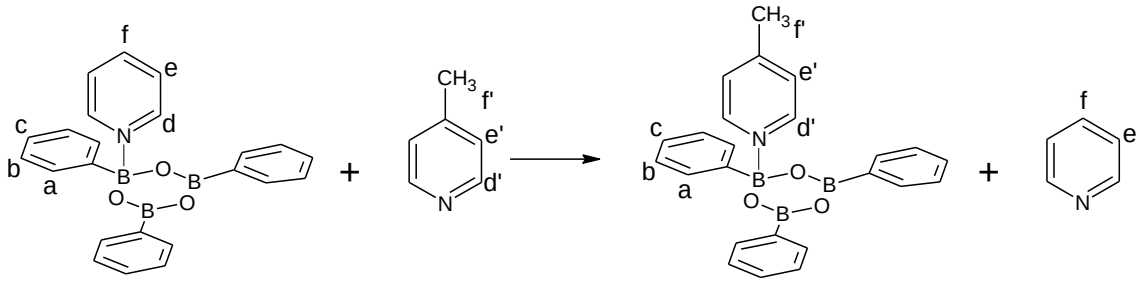
3.3 Displacement Reactions (Picoline/DMAP)

A boroxine which had been previously complexed with pyridine was placed into a 100mL RBF with 50mL of ether and dissolved. 1 equivalent of picoline or DMAP was measured out using a 50µL glass syringe or analytical scale and placed into the RBF. The mixture was allowed to stir at STP for one hour. The RBF was then placed on the

rotovap and vacuum pumped to remove solvent. Chloroform (25mL) was then added to the RBF. Two extractions were made using water (2mL) to remove any excess pyridal compounds. $MgSO_4$ was used to dry the mixture and then was filtered out with gravimetric techniques. Chloroform was removed via Rotovap and vacuum pump. ^1H NMR and Yields were taken to characterize the percentage of pyridine which had been replaced by picoline or DMAP.

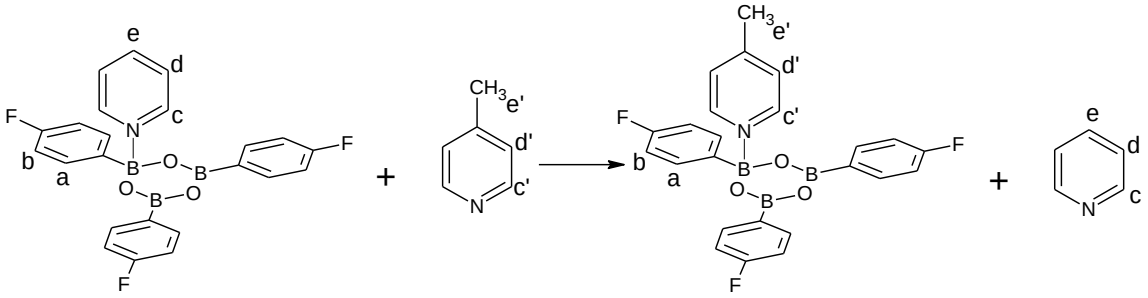
3.3.1 pyridine/picoline displacement reactions

Phenyl boroxine pyridine/picoline displacement reaction



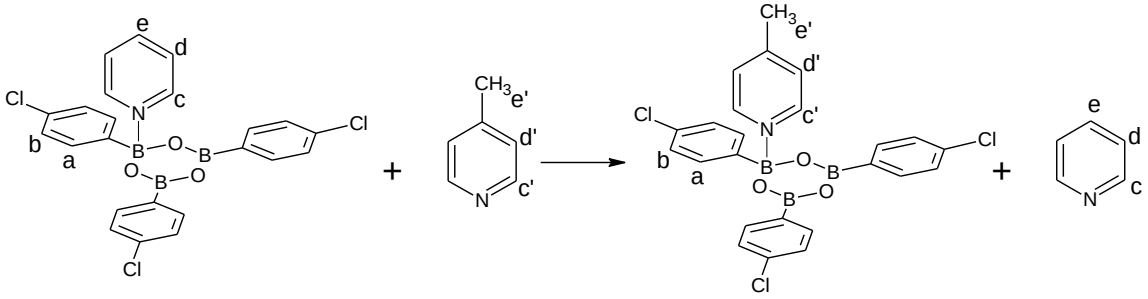
Phenyl boroxine pyridine complex (.100g, .256mmol) and Picoline (24.9µL, .256mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0887g (85.6%); ^1H NMR (300 MHz, $CDCl_3$): δ = 9.06 (m, .79H, d), 8.88(d, 1.05H, d'), 8.13(m, 6.6H, a), 7.93(t, .48H, f), 7.56(t, .75H, e), 7.45(m, 9.7H, b & c), 7.36(d, .979H, e'), 2.44(s, 1.78H, f').

Fluorophenyl boroxine pyridine/picoline displacement reaction



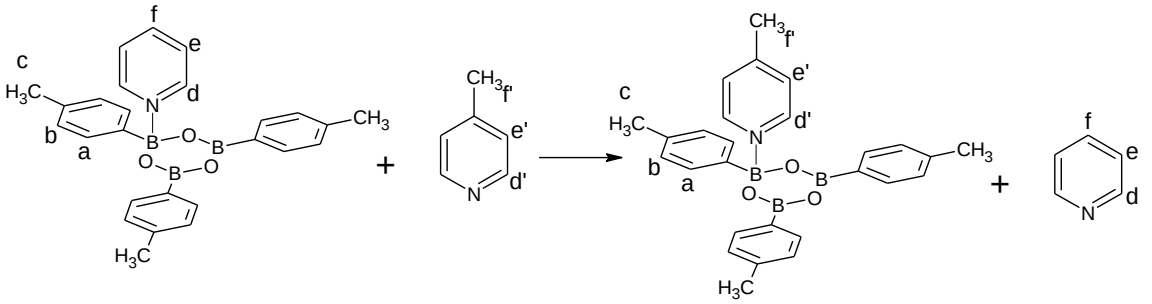
4-fluorophenyl boroxine pyridine complex (.1015g, .228mmol) and Picoline (22.2µL, .228mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .089g (85.0%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.02(d, .68H, d), 8.82(d, .98H, d'), 8.02(t, 6H, a), 7.67(t, .73H, e), 7.43(d, 1.06H, d'), 7.09(t, 5.67H, b), 2.49(s, 1.61H, e').

Chlorophenyl boroxine pyridine/picoline displacement reaction



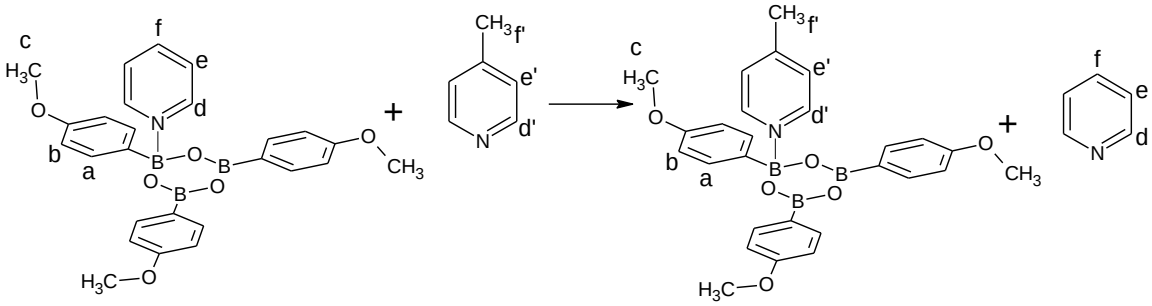
4-chlorophenyl boroxine pyridine complex (.1017g, .206mmol) and Picoline (20µL, .228mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .098g (93.7%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.99 (d, .21H, c), 8.74(d, 1.51H, c'), 7.95(d, 6H, a), 7.71(d, .43H, d), 7.49(d, 1.4H, d'), 7.37(d, 6.22H, b & e), 2.53(s, 2.5H, e').

Methylphenyl boroxine pyridine/picoline displacement reaction



4-methylphenyl boroxine pyridine complex (.1043g, .241mmol) and Picoline (23.5µL, .241mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0759g (70.5%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = .9.03 (m, .064H, d), 8.83(d, 1.8H, d'), 7.97(d, 6.0H, a), 7.68(t, .3H, e), 7.39(d, 1.84H, e'), 7.22(m, 6.74H, b & f), 2.48(s, 2.79H, f'), 2.39(s, 9.14H, c).

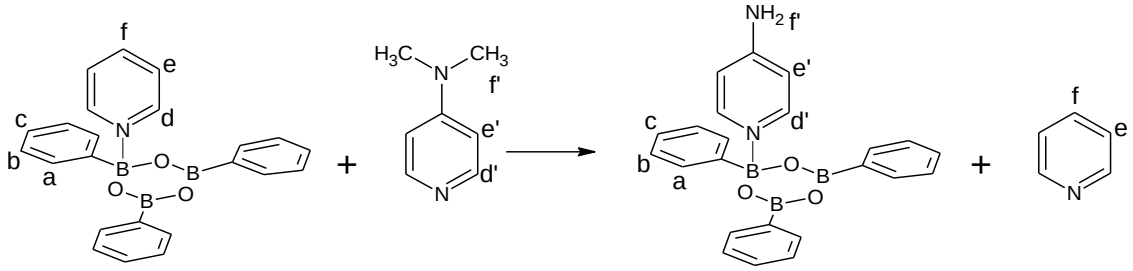
Methoxyphenyl boroxine pyridine/picoline displacement reaction



4-methoxyphenyl boroxine pyridine complex (.1092g, .227mmol) and Picoline (22µL, .227mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0986g (87.7%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.96(d, .24H, d), 8.82(d, 1.51H, d'), 8.01(d, 6.0H, a), 7.91(t, .2H, f), 7.53(t, .33H, e), 7.34(d, 1.68H, e'), 6.95(d, 6.19H, b), 3.83(s, 9.43H, c), 2.42(s, 2.7H, f').

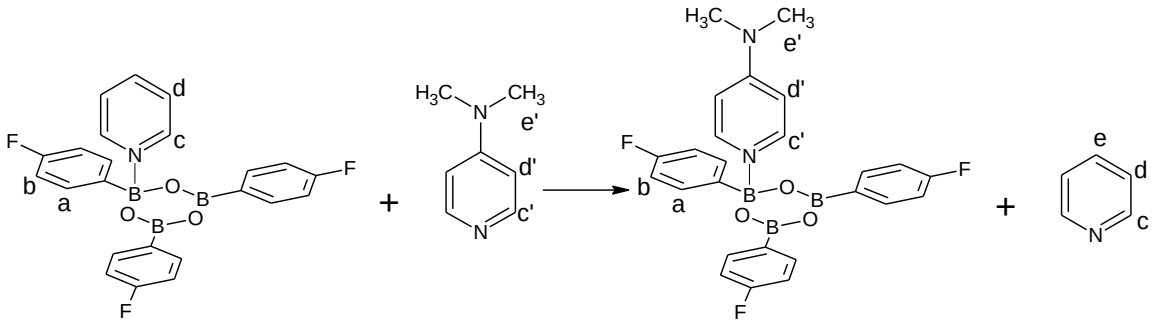
3.3.2 Pyridine/DMAP displacement reactions

Phenyl boroxine pyridine/DMAP displacement reaction



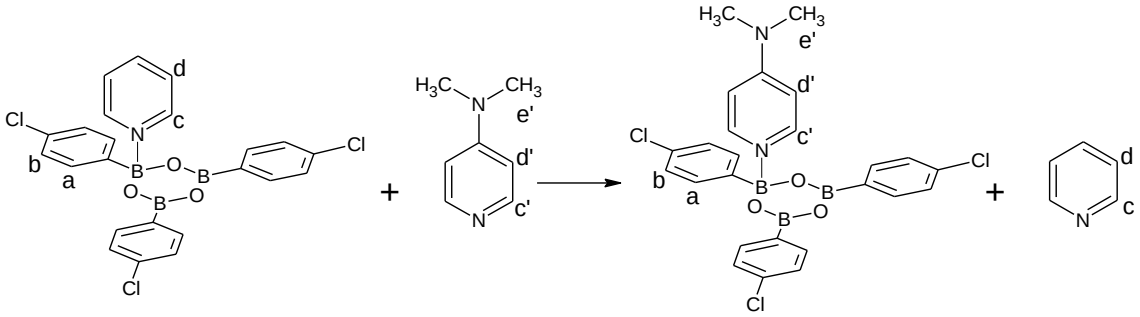
Phenyl boroxine pyridine complex (.1007g, .258mmol) and DMAP (.0308g, .258mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0988g (89%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.45(br, 1.39H, d'), 8.07(br, 3.61H, a), 7.4(br, 7.84H, b & c), 6.49(d, 1.93H, e'), 3.0(s, 6H, f').

Fluorophenyl boroxine pyridine/DMAP displacement reaction



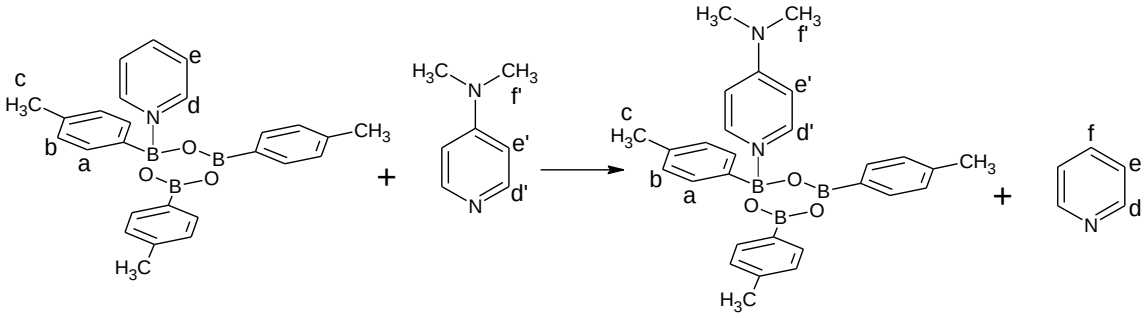
4-fluorophenyl boroxine pyridine complex (.1069g, .240mmol) and DMAP (.0294g, .240mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .1158g (98.7%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38(d, 1.88H, c'), 7.97(t, 6H, a), 7.04(tt, 6.26, b), 6.56(d, 2.25H, d'), 3.08(s, 6.74H, e').

Chlorophenyl boroxine pyridine/DMAP displacement reaction



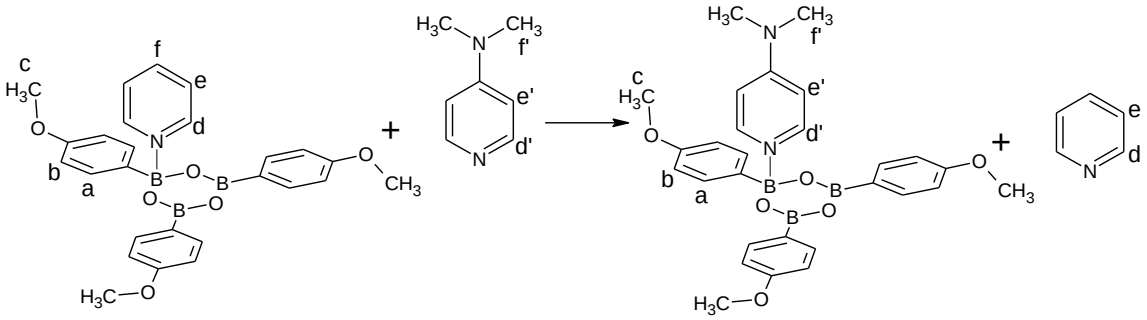
4-chlorophenyl boroxine pyridine complex (.1004g, .203mmol) and DMAP (.0248g, .203mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .1057g (96.9%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38(d, 2.02H, c'), 7.9(d, 5.81H, a), 7.33(d, 5.83H, b), 6.55(d, 2H, d'), 3.06(s, 6.27H, e').

Methylphenyl boroxine pyridine/DMAP displacement reaction



4-methylphenyl boroxine pyridine complex (.1061g, .245mmol) and DMAP (.0299g, .245mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0729g (62.5%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36(br, 2.48H, d'), 7.91(d, 6.01H, a), 7.19(d, 6.0H, b), 6.50(d, 3.12H, e'), 3.01(s, 10.3H, f'), 2.36(s, 9.09H, c).

Methoxyphenyl boroxine pyridine/DMAP displacement reaction



4-methoxyphenyl boroxine pyridine complex (.0996g, .207mmol) and DMAP (.0253g, .207mmol) were placed in ether (50mL). The replacement reaction method was followed for 1 hour. Yield .0930g (85.7%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33(br, 1.47H, d'), 7.97(d, 4.25H, a), 7.74(d, .38H, e), 6.91(d, 5.04H, b), 6.55(d, 1.93H, e'), 3.81(s, 7.62H, c), 3.09(s, 6.0H, f').

REFERENCES

[1] Snyder, H.R.; Konnecky, M.S.; Lennarz, W.J. Aryl Boronic Anhydrides and Amine Complexes. *J. Am. Chem. Soc*., **1958**, *80*, 3611-3615.

[2] Unv. of Bristol. School of Chemistry. Prof. Paul May. http://www.chm.bris.ac.uk/motm/chlorophyll/chlorophyll_h.htm (accessed **May 2010).**

[3] Ritchey, J. M. Synthesis and Properties of Addition Complexes of Boroxines and Other Selected Boron-Containing Systems. PhD Thesis Univ. Colorado, **July 1968**.

[4] Miyaura, N.; Yamada, K.; Suzuki, A. New Stereospecific Cross-Coupling by the Palladium-Catalyzed Reaction of 1-Alkenylboranes with 1-Alkenyl or 1-Alkynyl Halides. *Tetrahedron Lett.* **1979**, *23*, 36,3437-3440.

[5] Eckhert, C.; Henderson, K.; Stella, S.; Kobylewski, S. Receptor Activated Ca^{2+} Release Is Inhibited by Boric Acid in Prostate Cancer Cells. *Plos One*. [Online] **2009**, *4*, 6.

[6]Phillips, M.; James, T. Boronic Acid Based Modular Fluorescent Sensors for Glucose. *R. Chem. Soc.* **2000**, 963-970.

[7]Severin, K. Boronic Acids as Building Blocks for Molecular Nanostructures and Polymeric Materials. *Dalton Trans.* **2009**, *27*, 5254-5264.

[8] Cõté, A.; El-Kaderi, H.; Furukawa, H.; Hunt, J.; Yaghi, O. Reticular Synthesis of Microporous and Mesoporous @D Covalent Organic Frameworks. *J. Amer. Chem. Soc*. **2007**, 12914-12915.

[9] Doonan, C.; Tranchemontagne, D.; Glover, T.; Hunt, J.; Yaghi, O. Exceptional Ammonia Uptake by a Covalent Organic Framework. *Nature*. **2010**, *2*, 3, 235-238

[10] Buchwald, S.; Barder, T. Benchtop Monitoring of Reaction Progress via Visual Recognition with a Handheld UV Lamp: In Situ Monitoring of Boronic Acids in the Suzuki-Miyaura Reaction. *Org Ltr.s* **2007**, *9*, 1, 137-139.

[11] The Evans Group, Harvard University. http://evans.harvard.edu/pdf/evans_pKa_table.pdf (accessed March 2011).