

BORONATE MACROCYCLE FORMATION USING BORON-LEWIS BASE DATIVE
BONDS AND BORONIC ACID-DIOL CONDENSATION REACTIONS

A thesis presented to the faculty of the Graduate School of
Western Carolina University in partial fulfillment of the
requirements for the degree of Masters of Science in Chemistry

By

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ABSTRACT

BORONATE MACROCYCLE FORMATION USING BORON-LEWIS BASE DATIVE BONDS AND BORONIC ACID-DIOL CONDENSATION REACTIONS

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Western Carolina University (July 2013)

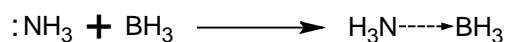
Director: Dr. William R. Kwochka

Synthesis of boronate ester compounds via condensation reactions using either an amine or an amine *N*-oxide coupled with a boronic acid. Synthesis of boronate ester compounds using quinoline isomers coupled with 2, 3-dihydroxynaphthalene was also attempted. These compounds form B-N dative bonds, and potentially form macrocycles capable of trapping a guest molecule in the cavity. The exact sizes of the complexes are unknown at this time. Characterization of these compounds was performed by ^1H NMR, FT-IR, mass spectroscopy, and ^{13}C NMR.

CHAPTER ONE: INTRODUCTION

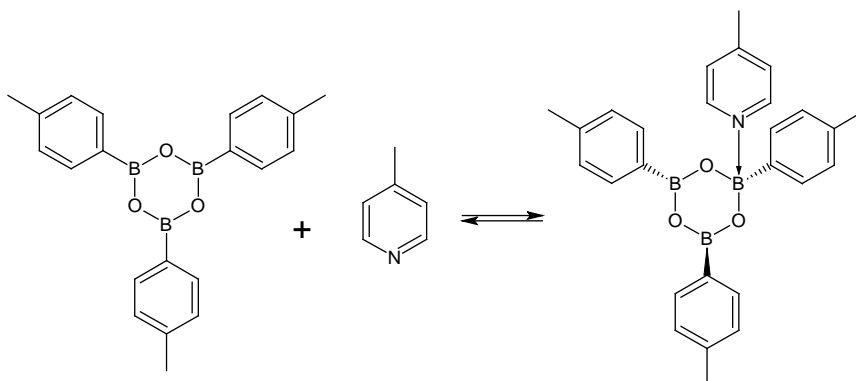
1.1 The B-N Dative Bond

In a dative (or coordinate) covalent bond, one atom acts as a Lewis base and contributes both electrons to the bond it forms with a Lewis acid, or electron acceptor. In the case of boron and nitrogen, the nitrogen atom acts as the Lewis base and the boron atom is the Lewis acid (scheme 1). This type of bond develops between boron and nitrogen, because when boron is in its neutral state in a molecule, it has an unoccupied p-orbital. When nitrogen is in its neutral state in a molecule, its lone pair orbital has p character.



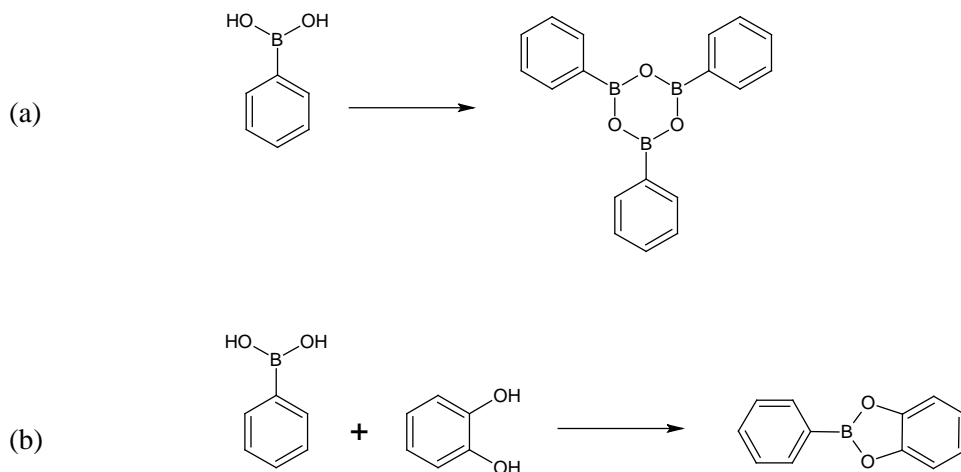
Scheme 1. Ammonia and borane form a dative covalent bond in which nitrogen is the electron donor.

The resulting dative bond between nitrogen and boron in a boroxine is dynamic, allowing the two atoms to rapidly associate and dissociate (Scheme 2).



Scheme 2. Methylphenylboroxine and picoline combine to form a complex in which the nitrogen atom can shift from one boron atom to another.¹

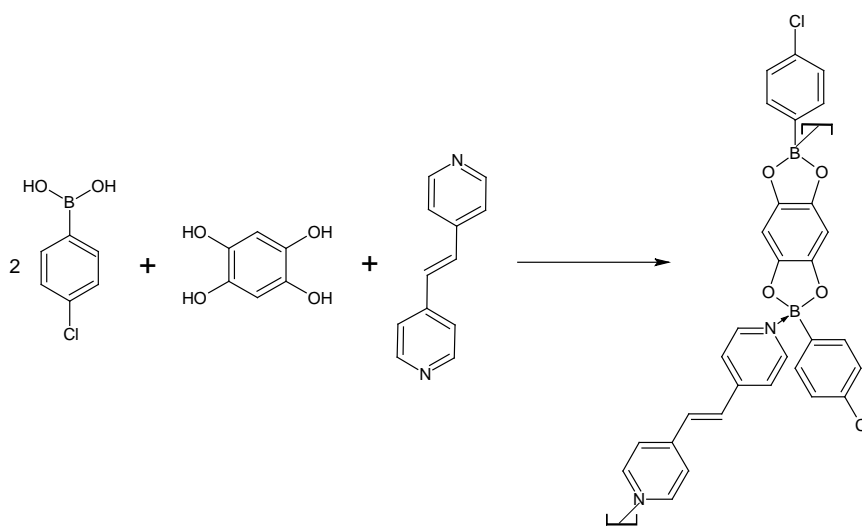
Both boroxines and boronates (scheme 3) can be produced through condensation reactions. A boroxine is produced by reacting a boronic acid with itself (scheme 3a), while a boronate is produced by reacting a boronic acid with a vicinal diol (scheme 3b), which results in the loss of H₂O.¹



Scheme 3. Boroxines (a) and boronates (b) can be produced by condensation reactions.¹

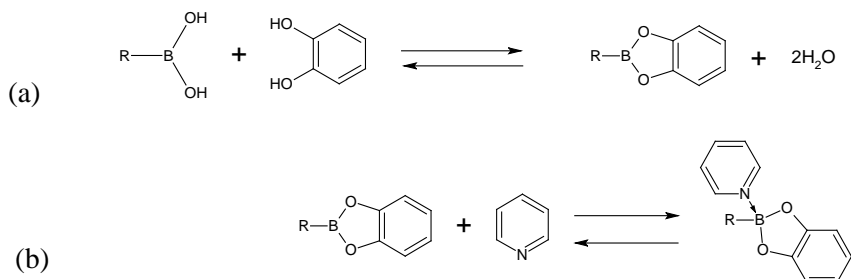
1.2 Polymers

By combining boronic acid-diol condensations (scheme 5a) and the formation of boron-nitrogen dative bonded complexes (scheme 5b), polymers may be produced in a single step (scheme 4)². Through his work, Severin has shown that not only is this type of reaction possible, but also reversible when dissolved in hot chloroform. In addition to this, when the solution is cooled to room temperature, the polymer spontaneously reassembles.



Scheme 4. Severin's polymer produced via boronic acid-diol condensation and boron-nitrogen dative bonds.²

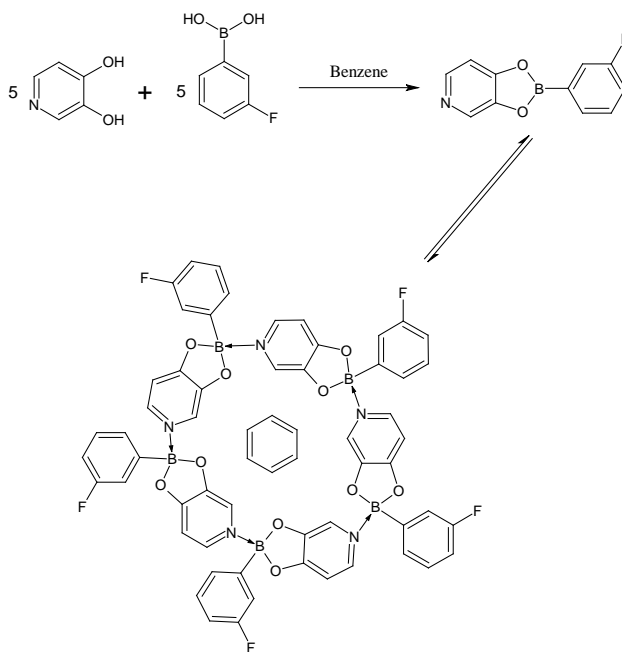
Such structures can be described as not only self-assembling, but significantly structurally flexible as well². The flexibility of these polymers can be attributed to the use of two chemically distinct building blocks: a condensation product and an amine.³



Scheme 5. Boronic acid-diol condensation reaction (a), and complexation of boronate ester and N-donor ligand (b)³.

1.3 Boronate Macrocycles

Using boronic acid-diol condensations and B-N dative bonding, Severin also found that macrocycles can be produced in one step reactions. Like polymers, macrocycles consist of repeating units; however, these structures close in on themselves to form rings. In addition to this, Severin was also able to produce a macrocycle with a guest molecule housed in its cavity (scheme 6).⁴



Scheme 6. Combining a boronic acid-diol condensation reaction and the complexation of a boronate ester and N-donor ligand in a simultaneous one step reaction with benzene as the solvent produces a boronate macrocycle with a benzene guest molecule lodged in its macrocyclic cavity.⁴

1.4 Rotaxanes

A rotaxane is a host macrocycle in which a guest molecule is housed. It consists of two interlocking molecules: a linear “thread” and a circular “loop”. “Stoppers” are also present at either end of the thread component to prevent the loop and thread from dissociating from one another. The “thread” and “stoppers” together form the dumbbell-shaped component of the rotaxane seen in figure 1.⁵ A long-term goal of our research lab is to produce boronate macrocycle-based rotaxanes using this work as the foundation. Hopefully, this can eventually be achieved by adding onto the guest molecule in the macrocyclic cavity, thus extending it outward to form the linear component of a rotaxane.

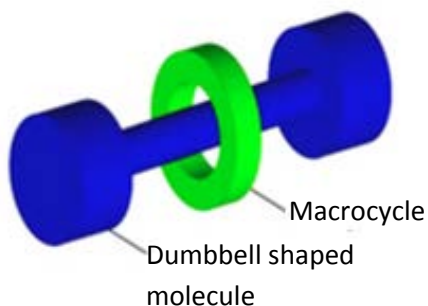


Figure 1. A rotaxane consists of three components: a cyclic “ring”, a linear “thread” and stoppers, which are attached to either end of the thread. Together the “thread” and stoppers make the dumbbell shaped molecule pictured.⁵

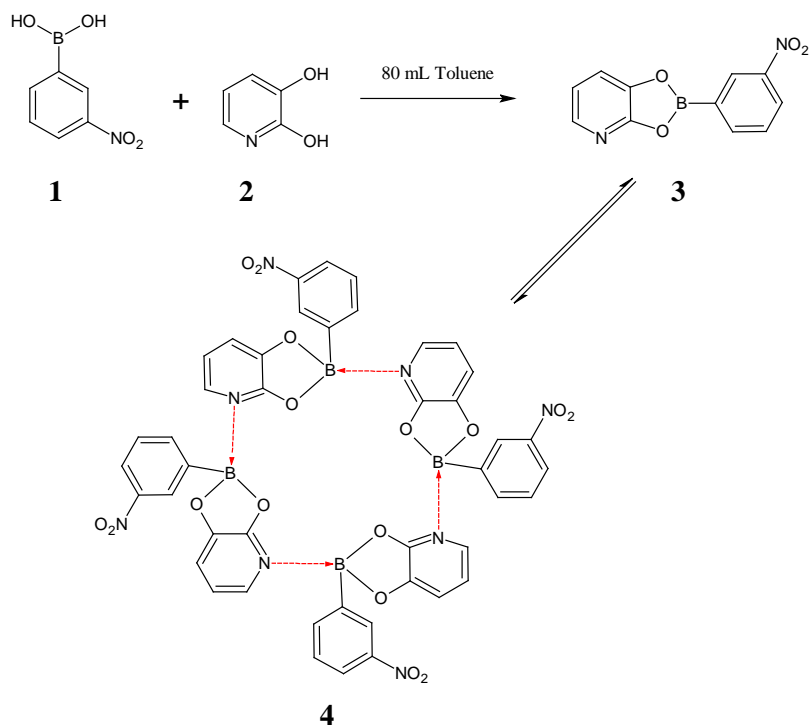
CHAPTER TWO: RESULTS AND DISCUSSION

2.0 General

This project was centered on the creation of boronate macrocycles via condensation reactions and dative bonding. The goal was not only to synthesize these unique structures, but also to explore whether a guest molecule would readily become trapped in the macrocyclic cavity if the reactions were run in toluene. In most of the complexes that were made, we tried to form the dative bond using nitrogen and boron. We also tried to use oxygen and boron to form dative bonds in one of the complexes produced, which necessitated the synthesis of an *N*-oxide prior to complex formation. Additionally, we also made some complexes using quinoline compounds, in which both the boron and nitrogen atoms originate from the same molecule.

2.1 Boronate Macrocycles

This series of reactions was designed to explore the potential of synthesizing boronate macrocycles in which the dative bond was made through the interaction of the nitrogen atom of a pyridine derivative and the boron atom of a boronate ester. The objective of these reactions was firstly, to explore whether these macrocycles could be made using various nitrogen-containing compounds, and secondly, to attempt to incorporate a toluene guest molecule within the macrocyclic cavity.



Scheme 7. 3-nitrophenylboronic acid **1** and 2, 3-dihydroxypyridine **2** are condensed to produce a compound **3**. The expected product is macrocycle **4**.

The first step in the synthesis of these boronate macrocycles was to perform a reaction that originally appeared in a paper published by Severin to determine what conditions were needed for subsequent reactions.⁴ The difference between this reaction and the one from the paper we referenced was that Severin's was a 15 hour reaction, whereas we were able to complete this reaction in 30 minutes using a microwave synthesizer.

In order to synthesize complex **4**, starting materials **1** and **2** were added to a round bottom flask along with toluene. The reaction mixture was heated and stirred at reflux for 30 minutes using a microwave synthesizer and a Dean-Stark trap with molecular sieves to remove water from the reaction mixture.⁴ Upon removal of the solvent, the resulting product was a white powder with a 34% yield, which was confirmed by ¹H NMR, FT-IR and mass spectroscopy to be the desired complex **4** (figures 2 and 3).

A comparison of the ^1H NMR spectra of starting materials **1** and **2** with the complex **4** (figure 2) shows the following chemical shift changes: proton **g'** shifts from 7.16 ppm to 8.61 ppm, **f'** shifts from 8.17 ppm to 8.31 ppm, proton **d'** shifts from 7.81 ppm to 8.08 ppm, proton **e'** shifts from 7.53 ppm to 7.59 ppm, proton **a'** shifts from 7.32 ppm to 6.87 ppm, proton **c'** shifts from 6.53 ppm to 6.80 ppm, and proton **b'** shifts from 6.85 ppm to 6.19 ppm. Protons **g**, **f**, **d**, and **e** in complex **4** have shifted upfield compared to protons **g'**, **f'**, **d'**, and **e'** in **1** because when **1** and **2** are condensed to form compound **3**, electron density is added to them. Conversely, electron density is taken away from protons **a** and **b** in compound **3**, which is why they have shifted downfield compared to protons **a'** and **b'** in **2** (figure 2).

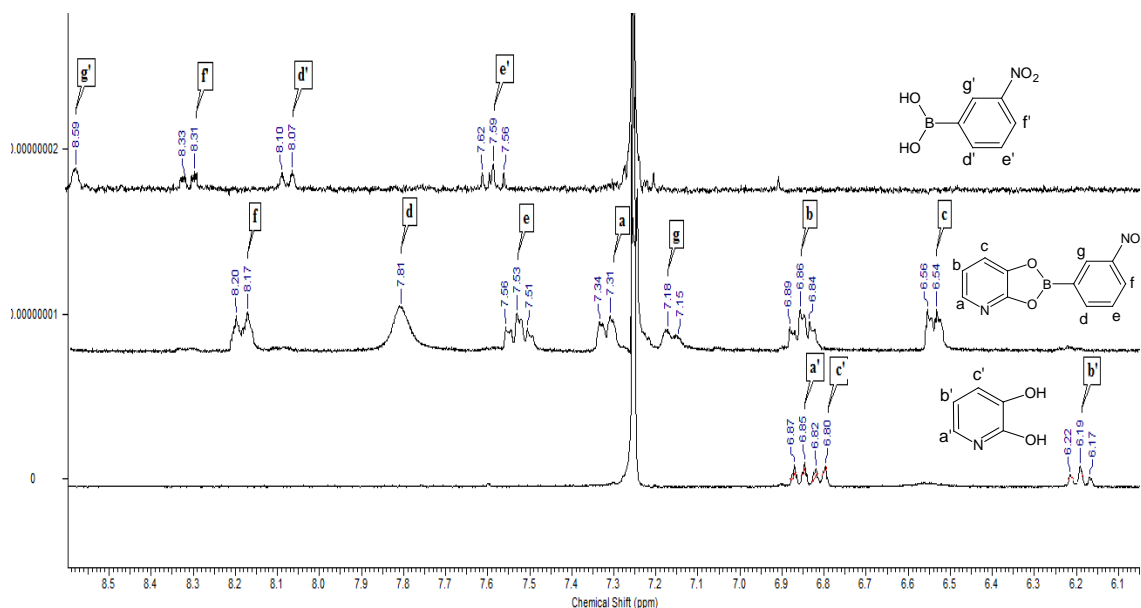


Figure 2. ^1H NMR spectrum of 2, 3-dihydroxypyridine **2**, 3-nitrophenylboronic acid **1** and complex **4** in CDCl_3 .

In the FT-IR spectrum of complex **4** (figure 3) the following signals were observed: aromatic C-H stretch at 3077.16 cm^{-1} , aromatic C=C bend at 1644.97 cm^{-1} , and B-N stretch at

563.06 cm^{-1} . According to a paper published by Dana N. Reinmann, et al the B-N stretching mode for a boronate ester shows up between 560 and 650 cm^{-1} .⁶ The B-N stretch observed at 563.06 cm^{-1} is of particular importance because it provides evidence that a macrocyclic structure is present.

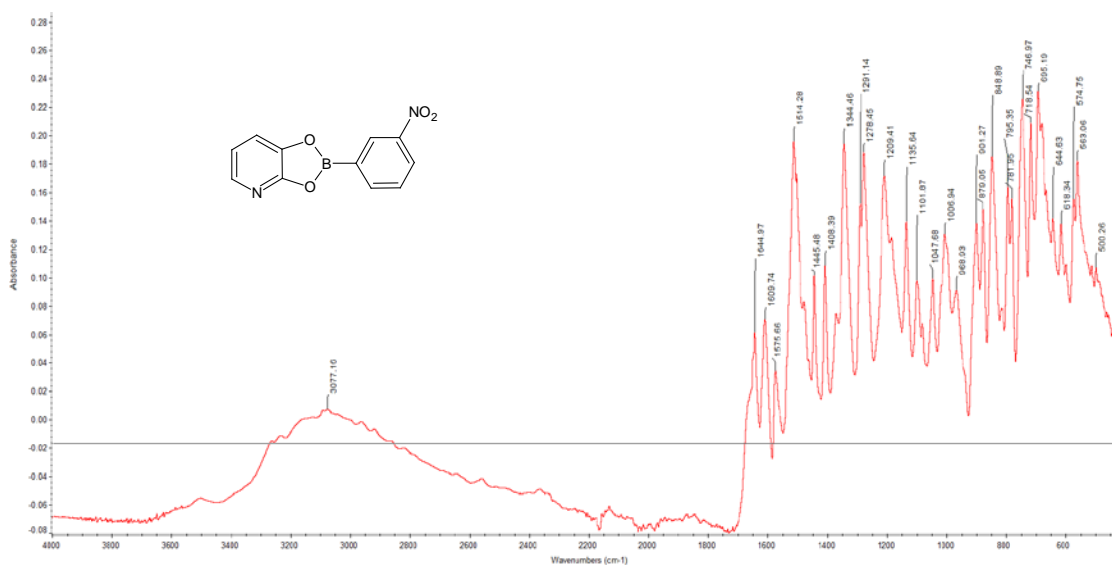


Figure 3. FT-IR spectrum of complex **4**.

A mass spectrum of complex **4** dissolved in methanol was taken in order to confirm its formation from **1** and **2** (figure 4). The following peak was detected: 241.0 m/z representing $[M]-1$. The molecular mass of compound **3** is 242.00 g/mol , so the $[M]-1$ peak at 241.0 m/z is significant because it provides evidence that the desired compound was formed.

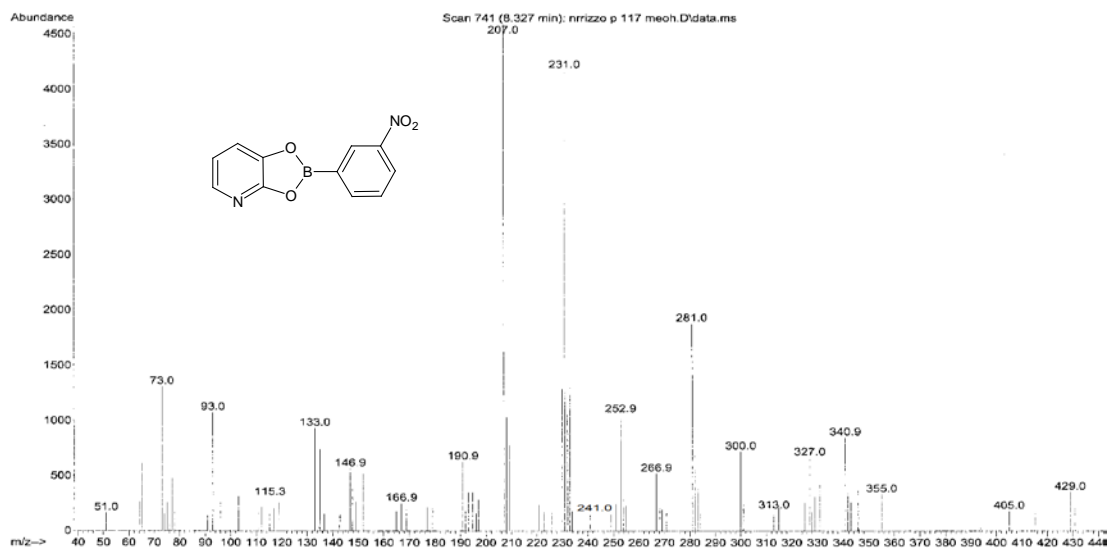
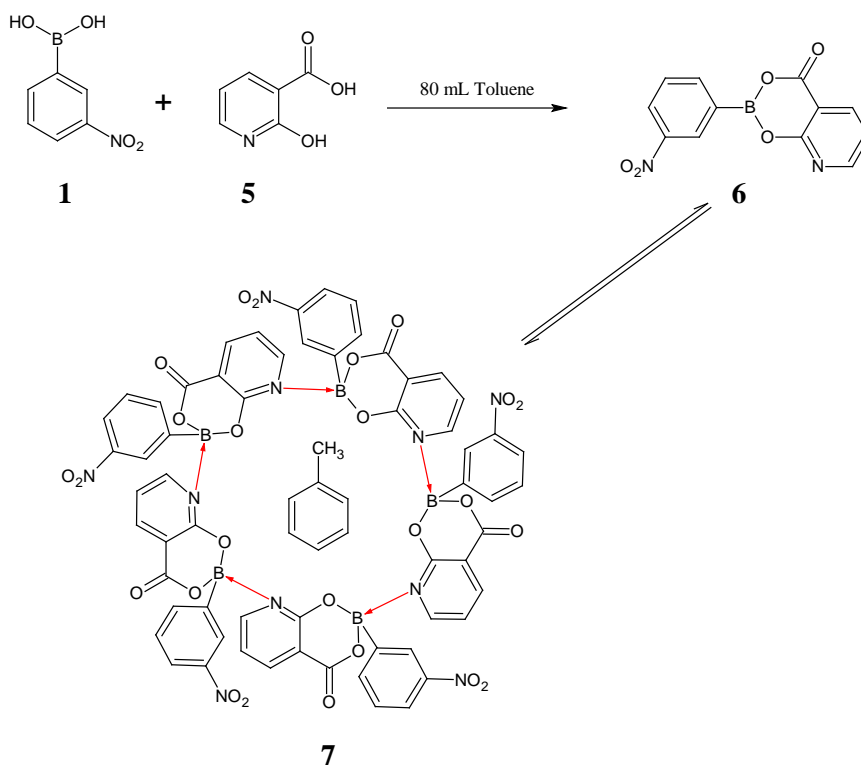


Figure 4. Mass spectrum of complex **4** dissolved in methanol.



Scheme 8. 3-nitrophenylboronic acid **1** and 2-hydroxynicotinic acid **5** are condensed to produce compound **6**. The expected product is macrocycle **7**.

After successfully synthesizing macrocycle **4** (scheme 7), as our proof-of-concept reaction, we were then ready to synthesize a macrocycle with a potentially larger ring cavity. The increased size of the macrocyclic cavity would hopefully facilitate the incorporation of a guest molecule into the ring quite easily. We chose to use starting materials **1** and **5** to produce compound **6** with a different overall shape than that of the previous compound **3**. This would hopefully allow the dative bonds to form at larger angles relative to each other, thus creating a pentameric structure with a larger macrocyclic cavity than the previous tetramer **4** (scheme 7).

This compound **6** was synthesized from **1** and **5** using the same method outlined for the synthesis of the previous compound **3**.⁴ The resulting product was a white powder with a 66% yield, which was confirmed by ¹H NMR, FT-IR and mass spectroscopy to be the desired product **6** (figures 5, 6, 7, 8 and 9).

A comparison of the ¹H NMR spectra of starting materials **1** and **5** to product **6** (figure 5) shows the following chemical shift changes: proton **g'** shifts from 9.02 ppm to 8.59 ppm, proton **c'** shifts from 8.09 ppm to 7.56 ppm, and proton **b'** shifts from 6.61 ppm to 6.58 ppm. Protons **b** and **c** have shifted downfield compared to protons **b'** and **c'** because the formation of compound **6** removes electron density. These chemical shift changes provide evidence that compound **6** was produced, though there is an impurity present at 8.47 ppm, the identity of which we are unsure of at this time. Signals from protons **i**, **j**, and **k** corresponding to the toluene molecule can also be seen at 7.59 ppm overlapping the signal from proton **e**. This provides evidence that a guest molecule may be present in the macrocyclic cavity (figure 5).

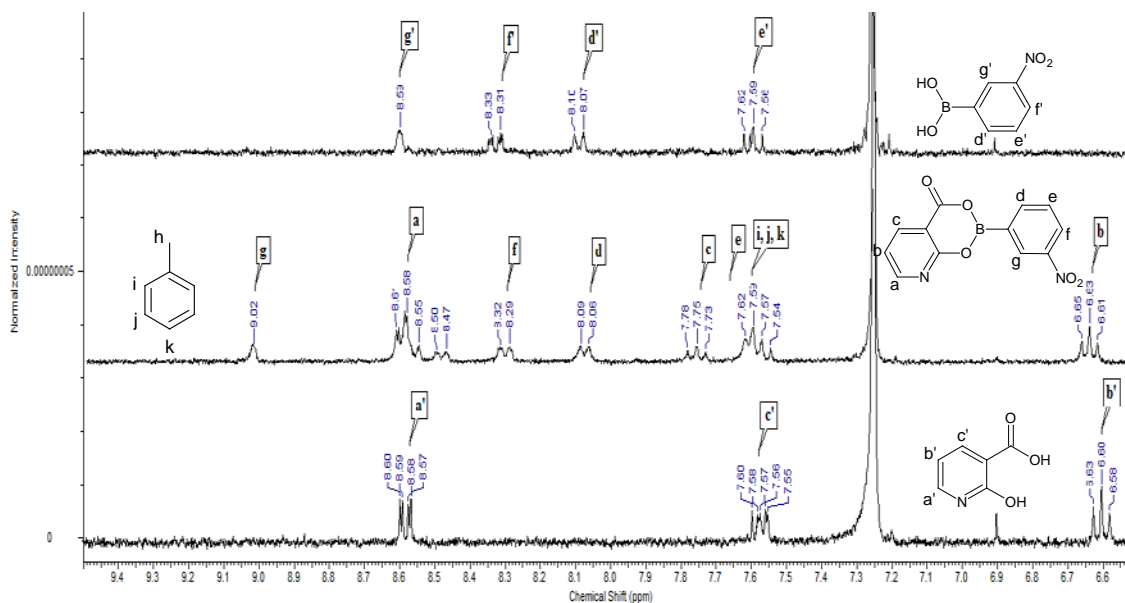


Figure 5. ^1H NMR spectrum of 2-hydroxynicotinic acid **5**, 3-nitrophenylboronic acid **1**, and product **6** in CDCl_3 .

Evidence that toluene is present as a guest molecule can be seen by looking at the ^1H NMR spectrum of the product **6** in DMSO-d_6 (figure 6). The relative integrations of the product's protons **6** to those of the methyl group on the toluene molecule are roughly 5:3, which indicates not only the presence of the guest molecule in the macrocyclic cavity, but also that the macrocycle is likely a pentamer (figure 6). There does, however, seem to be an impurity present in the product, as is indicated by the signal present at δ 8.51, which suggests that an OH peak from excess **1** may be present in the product. This could indicate that some amount of **1** did not complex with **5**, likely due to a slight excess of **1** in the reaction mixture or the reaction time being too short for all of **1** and **5** to complex.

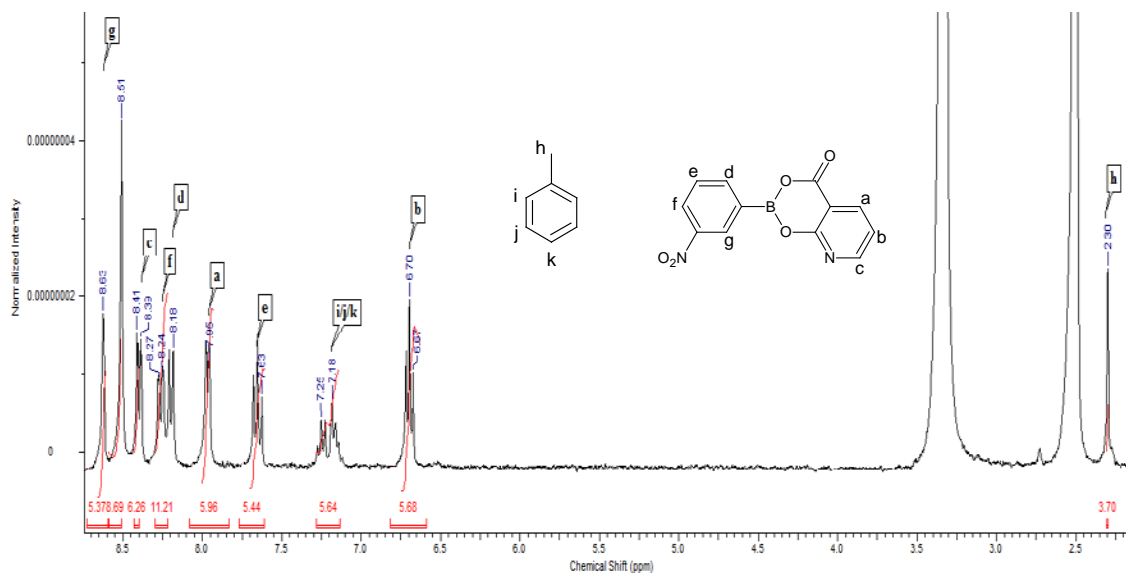


Figure 6. ¹H NMR spectrum of product **6** in DMSO-d₆.

In the FT-IR spectrum of the product **6** (figure 7), the following signals were observed: aromatic C-H stretch at 3098.76 cm⁻¹, carboxylic acid C=O stretch at 1713.53 cm⁻¹, aromatic C=C bend at 1613.51 cm⁻¹ and B-N stretch at 568.76 cm⁻¹. The B-N stretch at 568.76 cm⁻¹ is of particular interest because it, along with the ¹H NMR spectrum (figure 6), provides evidence suggesting that a macrocyclic ring is present. Whether or not the ring is a pentamer **7** is inconclusive at this time, although the ¹H NMR spectrum (figure 7) does suggest that it likely is.

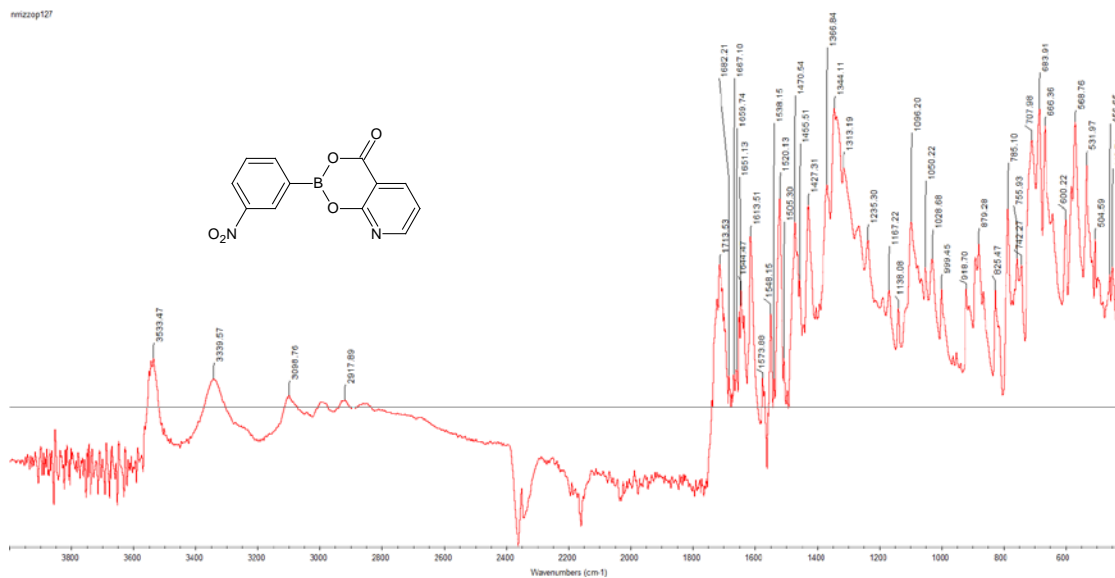


Figure 7. FT-IR spectrum of product **6**.

A mass spectrum of product **6** dissolved in methanol was taken in order to confirm its formation from **1** and **5** (figure 8). The following peaks were detected: 122.0 m/z representing $[M]-C_6H_4BNO_3$ and 271.0 m/z representing $[M]+1$. The molecular mass of compound **6** is 270.00 g/mol, so the $[M]+1$ peak at 271.0 m/z is of particular interest because it provides evidence that it was indeed formed.

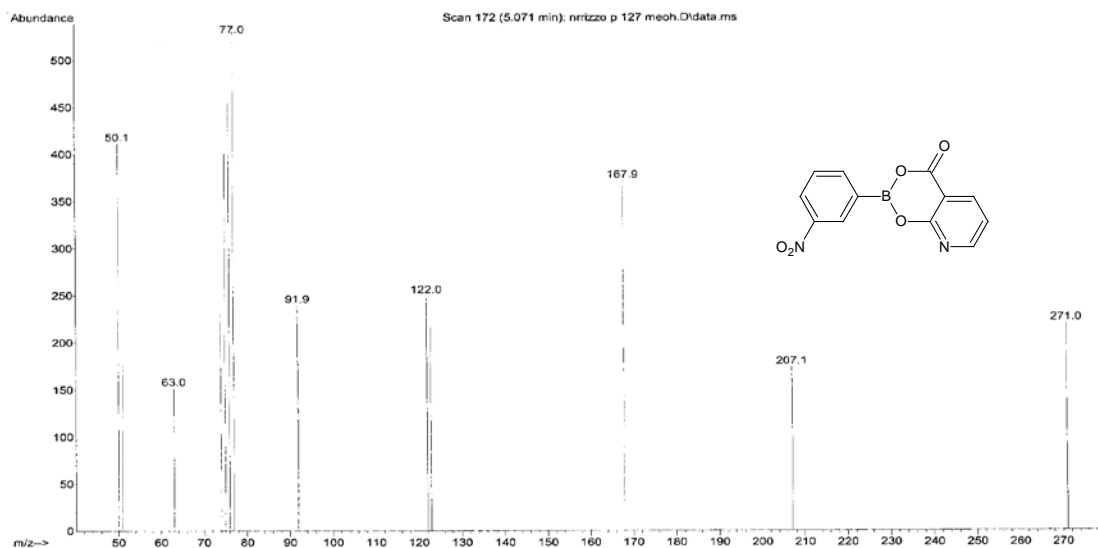
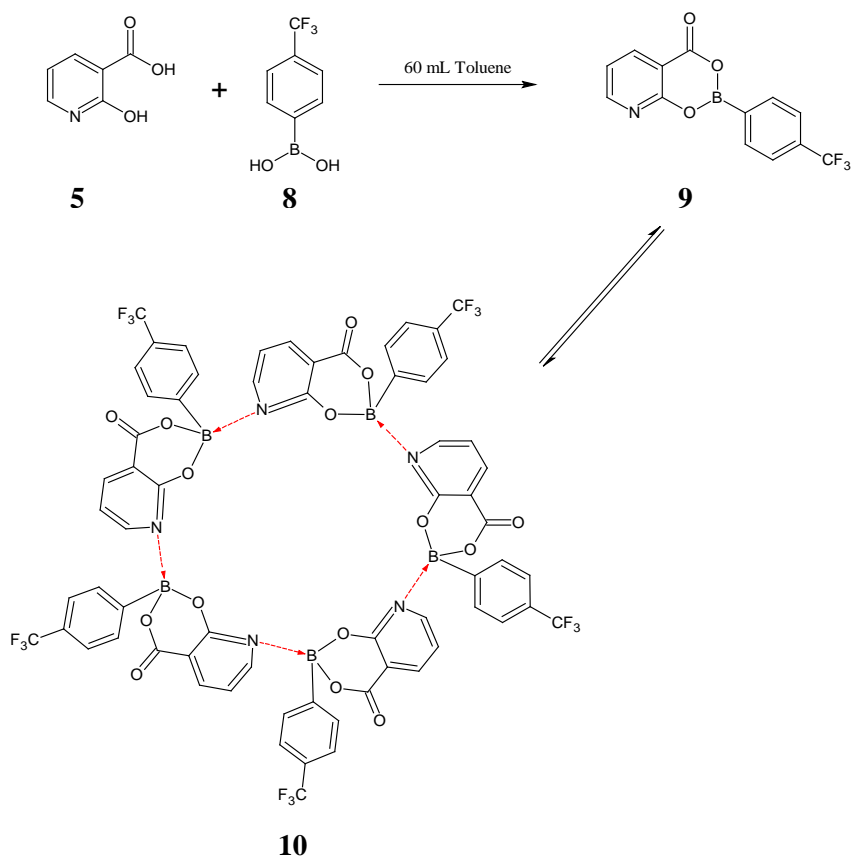


Figure 8. Mass spectrum of product **6** dissolved in methanol.



Scheme 9. 2-hydroxynicotinic acid **5** and 4-trifluoromethyl phenylboronic acid **8** are condensed to produce a compound **9**. The expected product is macrocycle **10**.

Over the course of this research project, it occurred to us that it may be beneficial to use a boronic acid other than **1** in order to minimize the number of proton signals present in the NMR spectra, thus making it less complicated and easier to interpret. This reaction was carried out using the same method employed to synthesize compound **6**, except boronic acid **8** was used instead of **1**.⁴ The resulting product was a white powder with a 66% yield, and was confirmed by ¹H NMR and FT-IR spectroscopy to be the desired compound **9** (figures 9, 10 and 11).

The ¹H NMR signal at 7.97 ppm is actually two overlapping signals from protons **e** and **c** (figure 9). The ¹H NMR signal seen at 8.38 ppm should be a doublet, but an impurity is present, which causes it to look like a triplet. Other than this impurity, the relative integrations and multiplicities are correct. However, a toluene guest molecule did not become incorporated into the compound's **9** macrocyclic cavity, if a macrocycle is even present (figure 9). This may be due to the CF₃ group on boronic acid **8** being less electron withdrawing than the NO₂ group on **1**.⁷ The CF₃ group on **8** may cause the product to form more quickly so that a toluene molecule cannot become trapped in the macrocyclic cavity of the product **10**, if indeed the product is a macrocycle. At this time there is no real evidence to indicate the formation of a macrocycle, but since the only difference between compounds **9** and **6** is the boronic acid used, it is likely that a macrocycle **10** formed if indeed compound **6** formed a macrocycle **7**, as we suspect.

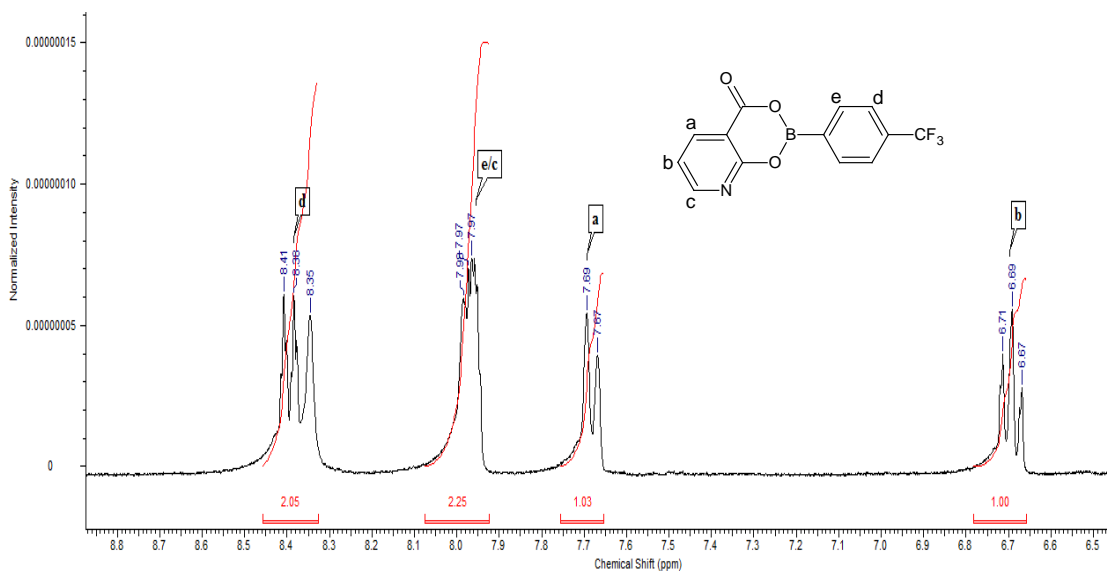


Figure 9. ^1H NMR spectrum of product **9** in DMSO-d_6 .

A comparison of the ^1H NMR spectrum of starting material **5** to product **9** in CDCl_3 (figure 10) shows the following chemical shift changes: proton **c'** shifts from 7.83 ppm to 8.57 ppm, **a'** shifts from 7.76 ppm to 7.55 ppm, and **b'** shifts from 7.62 ppm to 6.58 ppm. Protons **a** and **b** have shifted downfield compared to **a'** and **b'** because the formation of **9** takes electron density away from **5**. These chemical shift changes provide evidence that the desired compound **9** was formed.

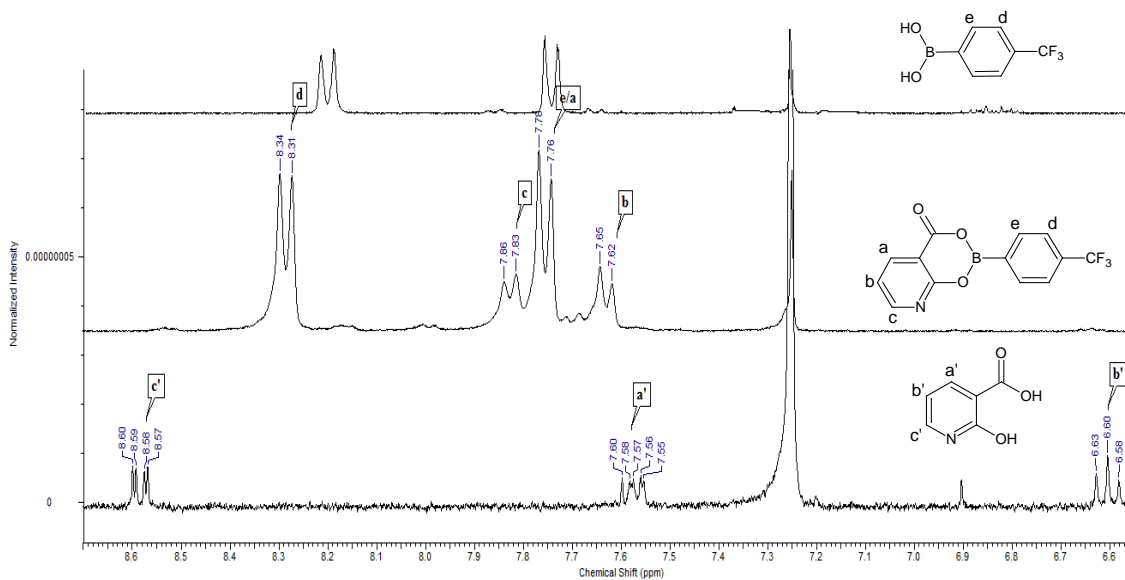


Figure 10. ¹H NMR spectrum of 2-hydroxynicotinic acid **5** 4-trifluoromethyl phenyl boronic acid **8** and the product **9** in CDCl₃.

In the FT-IR spectrum of product **9** (figure 11) the following signals were observed: carboxylic acid-OH stretch at 3231.05 cm⁻¹, aromatic C=C bend at 1605.73 cm⁻¹, aromatic C-H bend at 778.55 cm⁻¹ and B-N stretch at 639.67 cm⁻¹. The carboxylic acid-OH stretch at 3231.05 cm⁻¹ indicates that the impurity seen in the ¹H NMR spectrum of the product at 8.38 ppm (figure 9) could be from the presence of an OH peak from excess **5**.

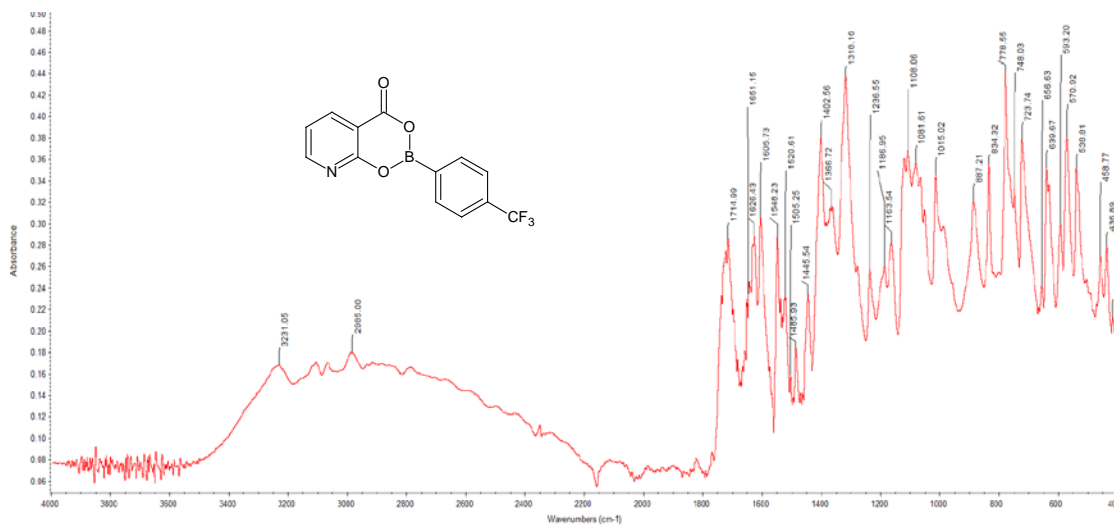
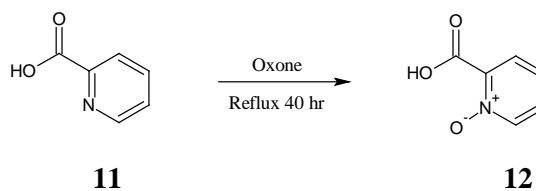


Figure 11. FT-IR spectrum of product **9**.

2.2 *N*-Oxides

These reactions were centered on the synthesis of *N*-oxides so that they could be used in subsequent reactions in an attempt to synthesize boronate macrocycles. The potential use of *N*-oxides in the assembly of macrocycles was explored for two reasons. Firstly, to see whether the dative bond could be made using oxygen, and secondly, to explore whether the larger ring opening could possibly facilitate the addition of a guest molecule more easily (or perhaps a larger guest molecule could be introduced).



Scheme 10. Picolinic acid is oxidized to yield picolinic acid *N*-oxide.

Before attempting to synthesize the unique *N*-oxides needed to produce our targeted macrocycles, **12** was synthesized and compared to a sample of commercially obtained picolinic acid *N*-oxide, so that the proper reaction conditions could be determined. In order to synthesize **12** from **11**, a solution of **11** in dichloromethane was added to a solution of oxone in water. The mixture was allowed to reflux at 45°C for 40 hours.⁸ The resulting product was a white powder with a 54% yield, which was confirmed by ¹H NMR and FT-IR to be compound **12** (figures 12 and 13).

The ¹H NMR spectra of the product **12** and a sample of commercially obtained picolinic acid *N*-oxide were compared to one another and found to be identical (figure 12). Signals from protons **b**, **c**, **a** and **d** can be seen at 7.63 ppm, 7.71 ppm, 8.36 ppm and 8.44 ppm, respectively. The identical ¹H NMR spectra confirms the formation of the desired compound **12**.

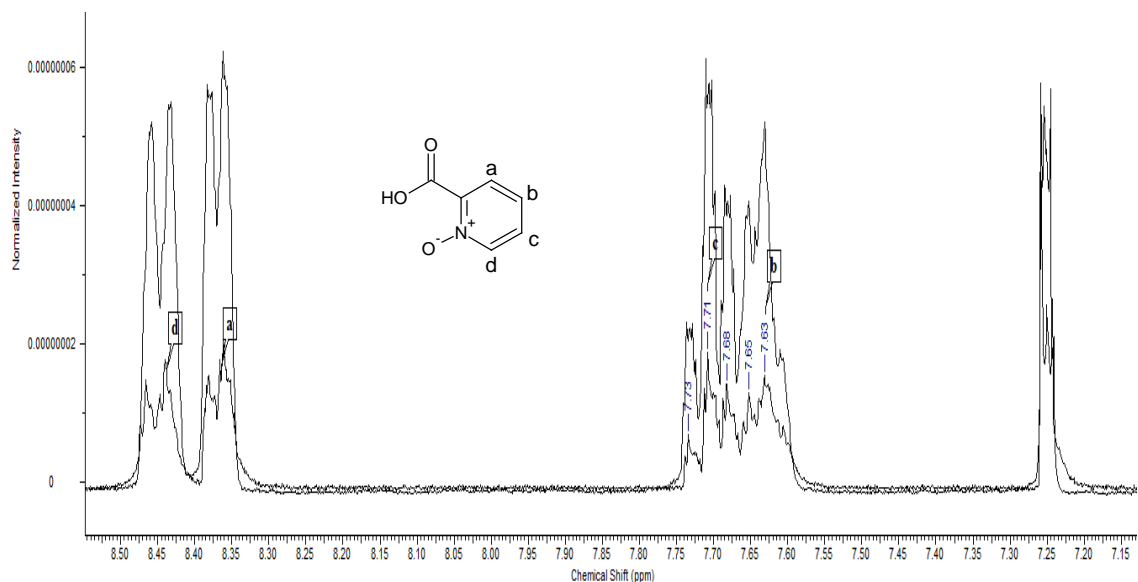


Figure 12. ¹H NMR spectra of picolinic acid *N*-oxide **12** and commercially obtained picolinic acid *N*-oxide in CDCl₃.

In the FT-IR spectrum of product **12** (figure 13) the following signals can be observed: aromatic C-H stretch at 3119.17 cm^{-1} , aromatic C=C bend at 1557.12 cm^{-1} , and N-O stretch at 1251.89 cm^{-1} . The N-O stretch provides more evidence that the desired compound **12** was indeed formed.

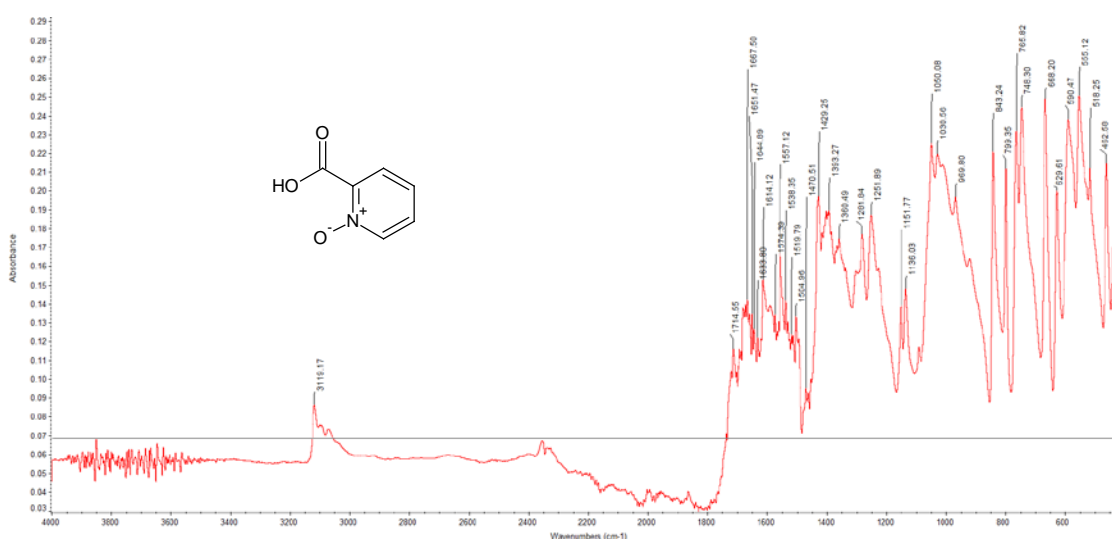
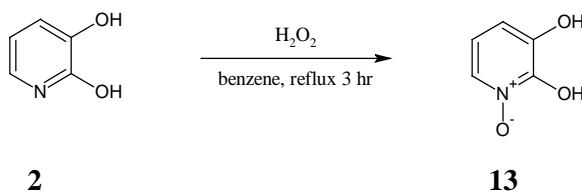


Figure 13. FT-IR spectrum of picolinic acid *N*-oxide **12**.



Scheme 11. 2, 3-dihydroxypyridine **2** is oxidized to yield 2, 3-dihydroxypyridine *N*-oxide **13**.

After successfully completing our proof-of-concept synthesis (scheme 10), the next step was to attempt the synthesis **13**. This *N*-oxide product was targeted because we wanted to see if adding oxygen atoms through which a dative bond could be made with boron (as opposed to

nitrogen) would allow us to build a macrocycle similar to the one seen in scheme 7, yet large enough to house a guest molecule in its cavity.

Two unsuccessful attempts at making **13** using the method previously employed for the synthesis of **12** necessitated the use of a different method for this, as well as subsequent reactions used to make *N*-oxides. In order to produce **13**, 30% H₂O₂ was added to a solution of **2** in water at room temperature. The mixture was allowed to warm to 70°C whilst stirring before being cooled to room temperature. Benzene was added and the mixture was allowed to reflux for three hours.⁹ The resulting product was a yellow-white solid with a 30% yield. In the ¹H NMR spectrum, no chemical shift changes can be seen between starting material **2** and the product **13**, which indicates that the desired product was not formed (figure 14). This reaction was attempted multiple times with the same end result.

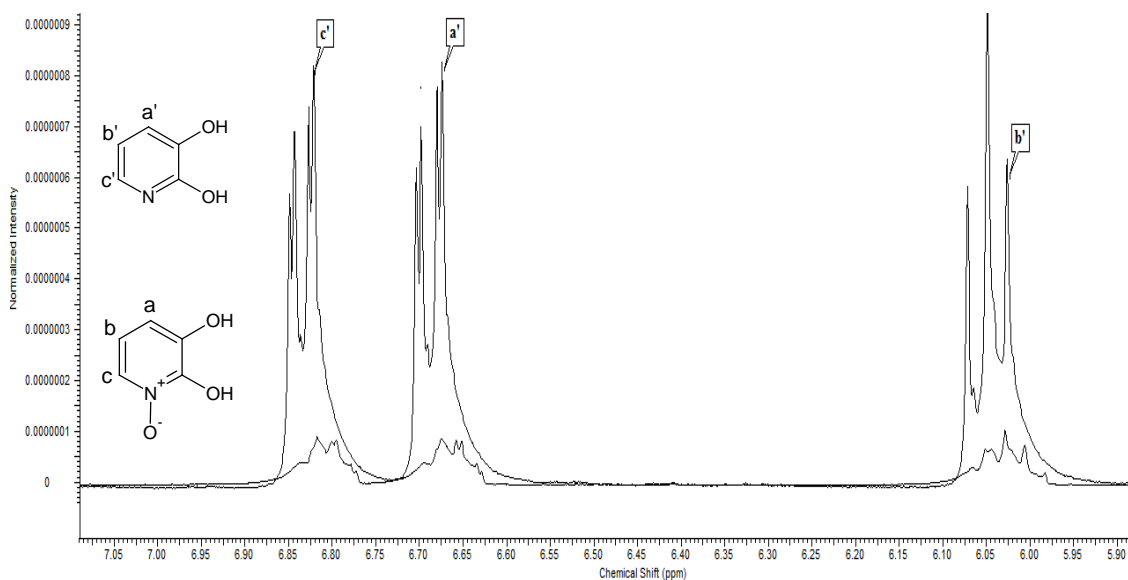
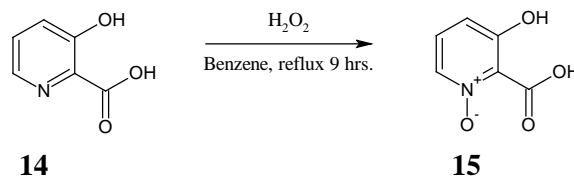


Figure 14. ¹H NMR spectra of 2, 3-dihydroxypyridine **2** and unsuccessful reaction product (scheme 11) in DMSO-d₆.



Scheme 12. 3-hydroxypyridine-2-carboxylic acid **14** is oxidized to yield 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**.

Using the same method that was employed for the synthesis of the previous *N*-oxide product **13**, **15** was produced from **14**.⁹ The product was a white solid with a 67% yield, and was confirmed by ^1H NMR and FT-IR spectroscopy to be the desired compound **15** (Figures 15 and 16).

In comparing the ^1H NMR spectra of starting material **14** and product **15** (figure 15) the following chemical shift changes can be seen: proton **c'** shifts from 7.95 ppm to 8.16 ppm, **a'** shifts from 7.32 ppm to 7.52 ppm, and **b'** shifts from 7.42 ppm to 7.52 ppm. The protons in the *N*-oxide product **15** have gained electron density from the addition of the oxygen atom to the molecule, so they have shifted upfield. The observed chemical shift changes provide evidence that the desired compound **15** has indeed been formed. However, there is a peak at 7.58 ppm that indicates that an impurity is present in the product **15** (figure 15), the identity of which we are unsure of at this time.

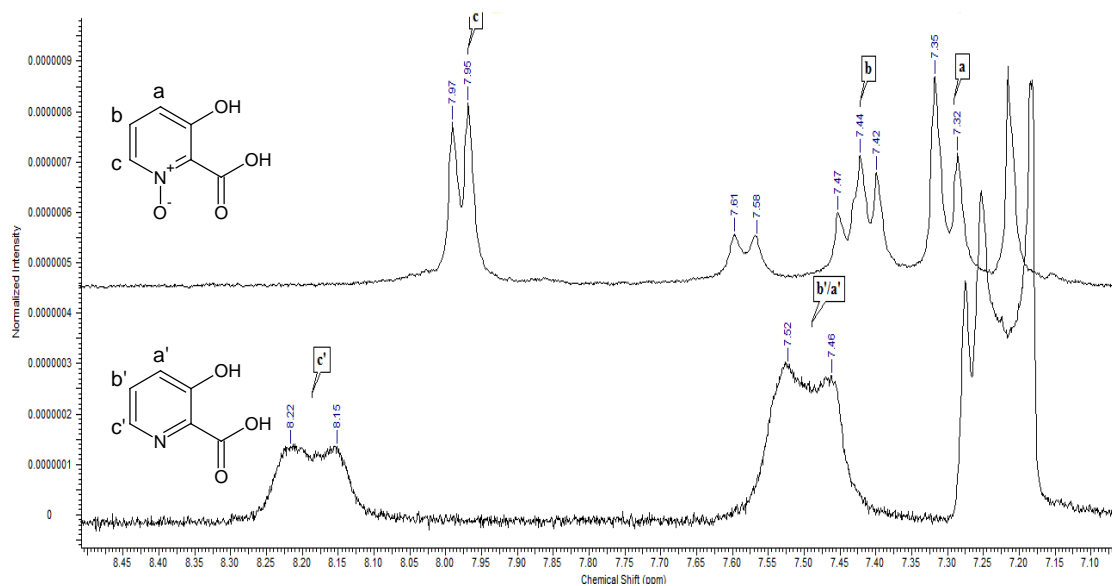


Figure 15. ¹H NMR spectra of 3-hydroxypyridine-2-carboxylic acid **14** and 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15** in CDCl₃.

In the FT-IR spectrum of the product **15** (figure 16), the following signals can be seen: aromatic C-H stretch at 3043.50 cm⁻¹, aromatic C=C bend at 1602.94 cm⁻¹, and N-O stretch at 1271.96 cm⁻¹. The N-O stretch seen provides additional evidence that the desired compound **15** was formed.

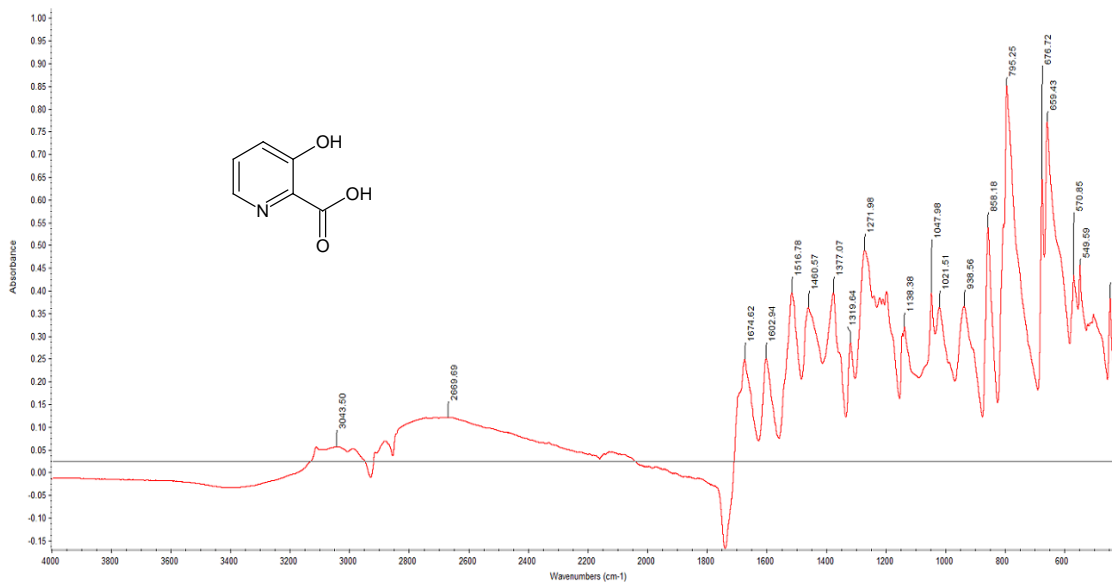
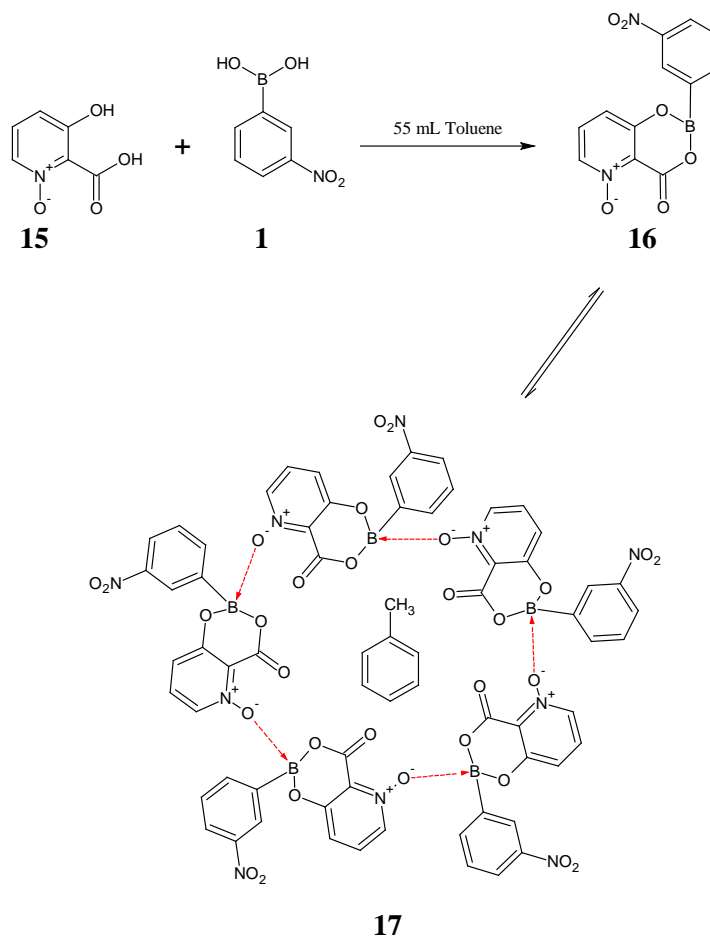


Figure 16. FT-IR spectrum of 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**.

2.3 Boronate Macrocycles Made From *N*-Oxides

Originally, we planned to produce three macrocycles in which the dative bond was formed through oxygen and nitrogen instead of boron and nitrogen. However, multiple attempts to synthesize 2, 3-dihydroxypyridine *N*-oxide **13** and 2-hydroxynicotinic acid *N*-oxide failed. The only *N*-oxide we were able to successfully synthesize was 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**. As a result, the only *N*-oxide complex we were able to attempt to produce was complex **17**.



Scheme 13. 3-nitrophenylboronic acid **1** and 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15** are condensed to produce a compound **16**. The expected product is macrocycle **17**.

This product **16** was synthesized from **1** and **15** by combining both starting materials with toluene, and refluxing the resulting reaction mixture for 10 hours using a heating mantle. A Dean-Stark trap and molecular sieves were used to remove water from the reaction mixture.⁴ The resulting product was a light tan solid, with a 77% yield, and was characterized by ¹H NMR, FT-IR and mass spectroscopy (figures 17, 18 and 19).

After we attempted to purify the product via sublimation, an ¹H NMR spectrum was taken, which revealed that although some impurities had been removed, many impurities were still present (figure 17). Although the mass spectroscopy data provides evidence that compound

16 may have been formed (figures 18 and 19), we were not able to obtain ^1H NMR data that supports this, and therefore our results for this reaction are inconclusive.

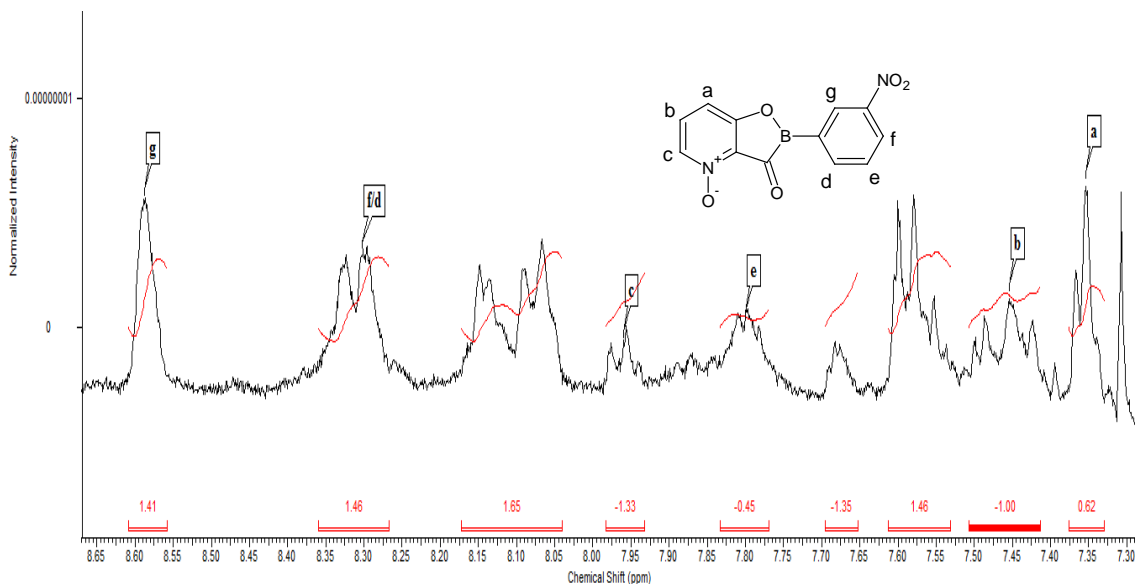


Figure 17. ^1H NMR spectrum of 3-nitrophenylboronic acid **1**, 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15** and the compound **16** in CDCl_3 .

In the FT-IR spectrum of product **16** the following signals were observed: aromatic C-H stretch at 3102.55 cm^{-1} , carboxylic acid-OH stretch at 2514.31 cm^{-1} , B-O stretch at 1726.88 , aromatic C=C bend at 1694.18 cm^{-1} , N-O stretch at 1283.38 cm^{-1} , a B-N stretch at 577.84 cm^{-1} . The carboxylic acid-OH stretch at 2514.31 cm^{-1} indicates that some unreacted starting material **15** is present. The presence of both a B-O stretch and a B-N stretch indicate that a mixture of two compounds is possibly present in the product.

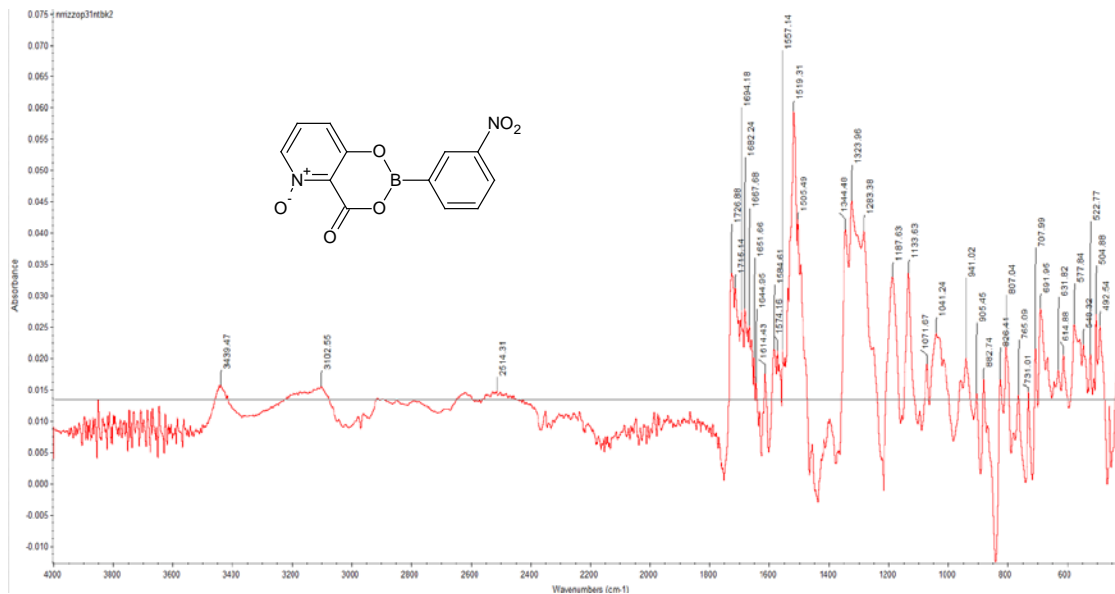


Figure 18. FT-IR spectrum of product **16**.

A mass spectrum of the product dissolved in methanol was taken in order to confirm that compound **16** was actually formed from starting materials **15** and **1** (figure 19). The molecular weight of compound **16** is 286.00 g/mol. A small peak at 269.8 m/z suggests an [M]-O loss, which could indicate that a small amount of the desired compound **16** was indeed formed, though our results are inconclusive.

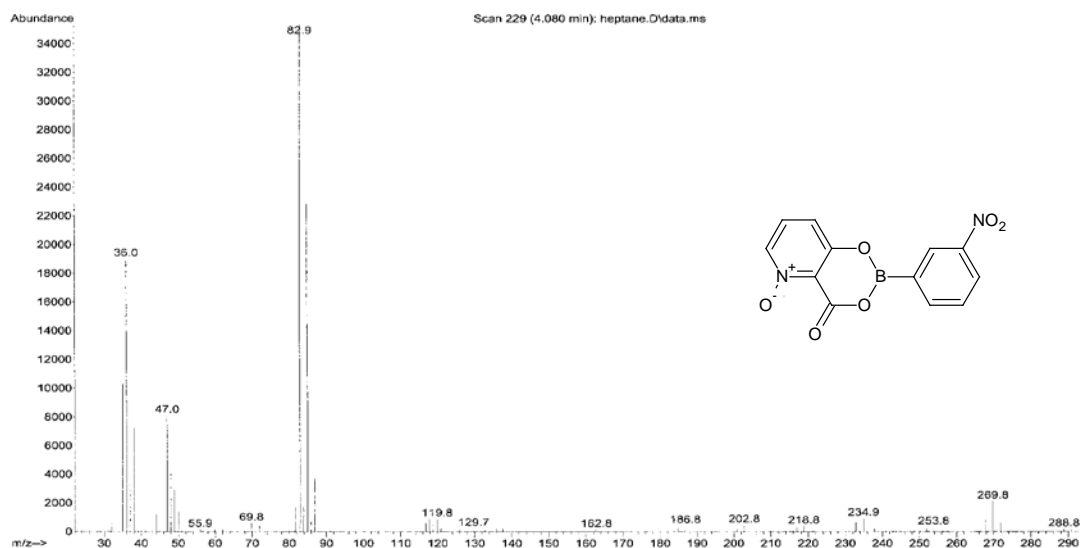
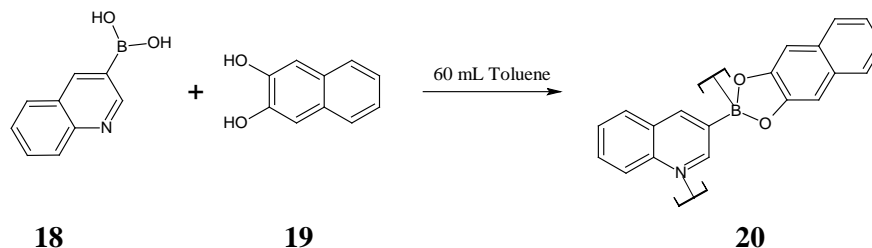


Figure 19. Mass spectrum of product **16** dissolved in methanol.

2.4 Boronate Macrocycles Made From Quinoline Boronic Acid Compounds

These reactions were centered on the synthesis of boronate macrocycles in which the dative bond could be made through nitrogen and boron atoms originating from the same molecule. The objective of these reactions was firstly, to explore whether these macrocycles could be made using 3-quinoline boronic acid and two of its isomers, and secondly, to attempt to incorporate a toluene guest molecule into the macrocyclic cavity.



Scheme 14. 3-quinoline boronic acid **18** and 2, 3-dihydroxynaphthalene **19** are condensed to yield compound **20**.

In order to synthesize this compound **20**, starting materials **18**, **19** and toluene were added to a round bottom flask and heated at reflux for 45 minutes using a microwave synthesizer, and a Dean-Stark trap with dry molecular sieves to remove water from the reaction mixture.⁴ We tried to purify the product via column chromatography using silica gel as the stationary phase and a 1% solution of methanol in dichloromethane as the mobile phase, but unfortunately the product clung to the silica even after we finally flushed the column with methanol in a final effort to recover the product. The resulting product was a yellow powder with a 70% yield, which was somewhat purified via sublimation, and confirmed by ¹H NMR, FT-IR, and mass spectroscopy to be the desired compound **20** (figures 20, 21 and 22).

In the ¹H NMR spectrum of product **20** (figure 20) the integrations are roughly a 2:2 ratio of starting material **18** protons to starting material **19** protons when there should be a 1:2 ratio. This indicates that excess **18** may be present, as does the OH signal at 8.50 ppm. An OH signal can also be seen at 9.49 ppm, which indicates that some uncomplexed **19** is also present. Typically, signals corresponding to protons on the toluene guest molecule show up at a range of approximately 7.20-7.30 ppm. Since no such signal can be seen in the ¹H NMR spectrum of product **20** (figure 20), no guest molecule seems to be present.

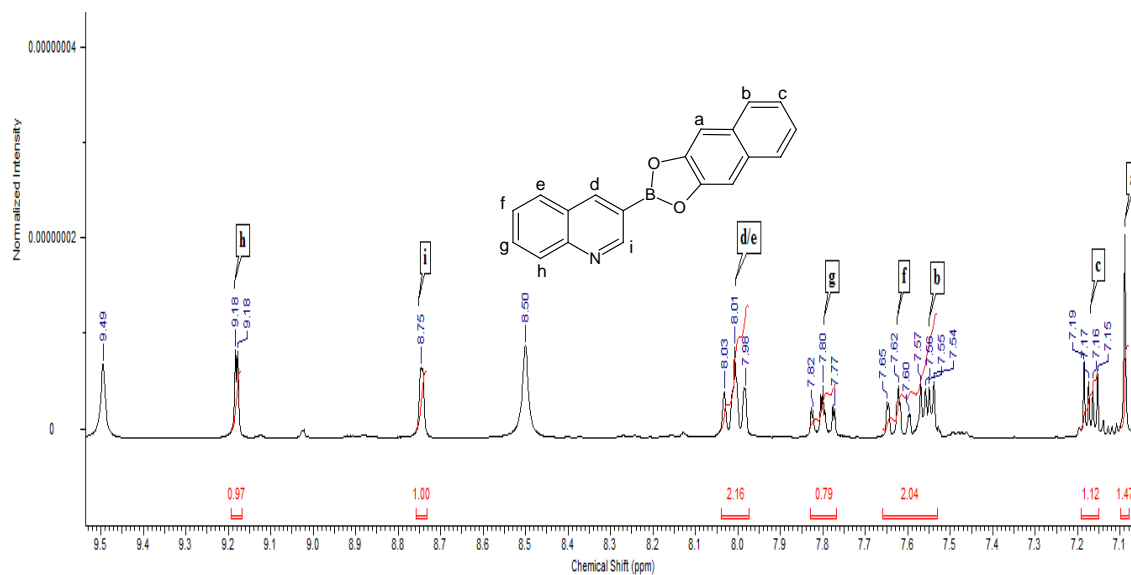


Figure 20. ^1H NMR spectrum of “purified” product **20** in DMSO-d_6 .

In the FT-IR spectrum of product **20** (figure 21) the following signals were observed: aromatic C-H stretch at 3030 cm^{-1} , aromatic C=C bend at 1644.03 cm^{-1} , and B-N stretch at 622.53 cm^{-1} . The B-N stretch seen provides evidence that a macrocycle may have been formed, though we are unsure as to its exact size at this time.

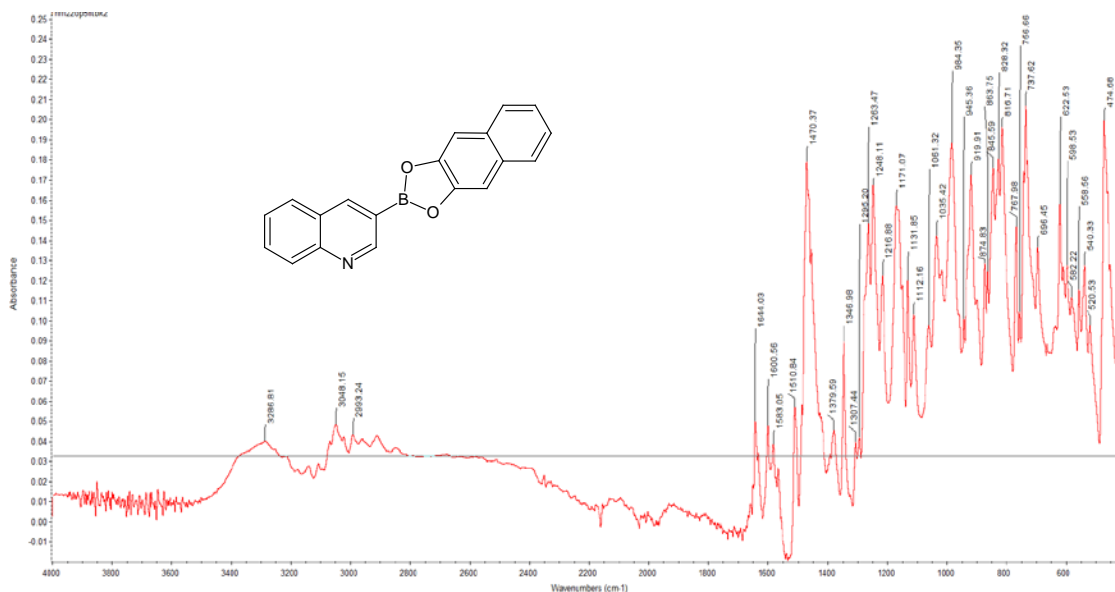


Figure 21. FT-IR spectrum of product **20**.

A mass spectrum of the product **20** dissolved in methanol was taken in order to confirm its formation from **18** and **19** (figure 22). An [M] peak was detected at 297.1 m/z. The molecular mass of compound **20** is 297.12 g/mol, so the presence of an [M] peak at 297.1 m/z provides evidence that the desired compound was indeed formed.

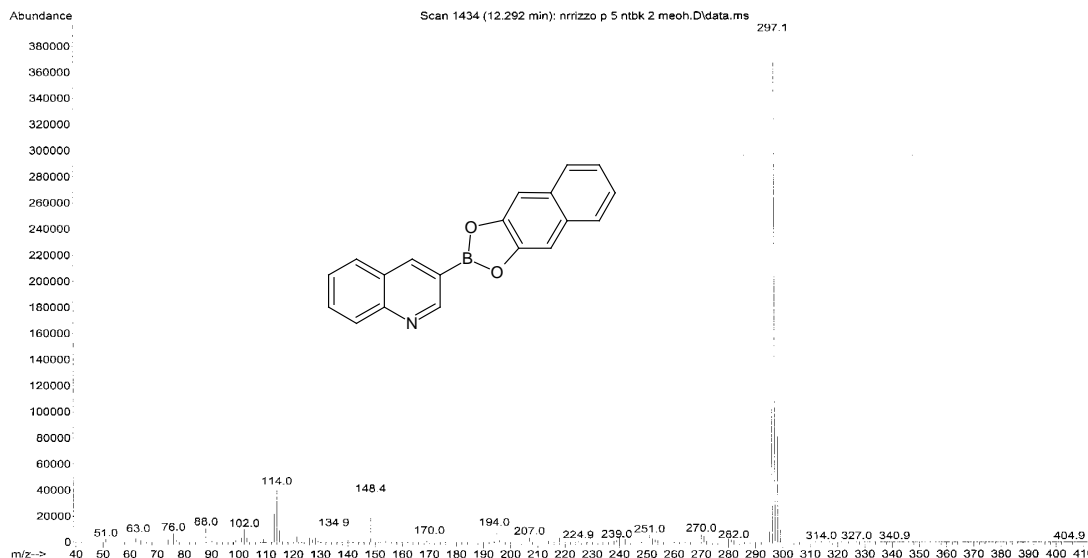
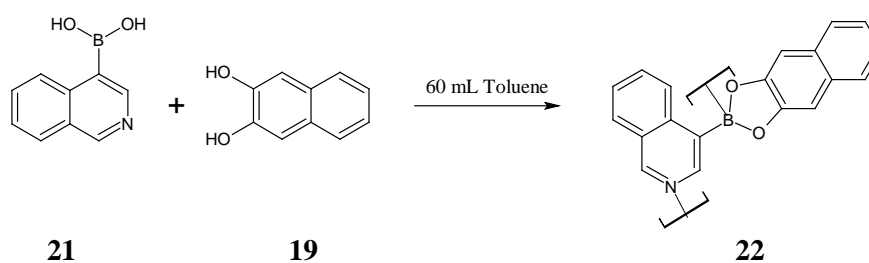


Figure 22. Mass spectrum of product **20** dissolved in methanol.



Scheme 15. 3-isoquinoline boronic acid and 2,3-dihydroxynaphthalene condense to form compound **22**.

Using the same method that was used to produce compound **20**, compound **22** was produced from **21** and **19**.⁴ The resulting product was a tan-colored powder with a 79% yield, which was somewhat purified via sublimation, and confirmed by ¹H NMR, FT-IR and mass spectroscopy to be the desired compound **22** (figures 23, 24 and 25).

In the ¹H NMR spectrum of the product **22**, both protons **h** and **i** appear to be doublets when in fact they should be singlets (figure 23). This indicates that although many impurities were removed via sublimation, there are still some impurities present. Impurities are also

indicated by the integrations of protons **a**, **b** and **c**, which are 5.14, 5.42 and 4.47, respectively when they should all be 2.0. This indicates the presence of uncomplexed **19**. Additionally, no guest molecule seems to be present in the ^1H NMR spectrum of the product **22**.

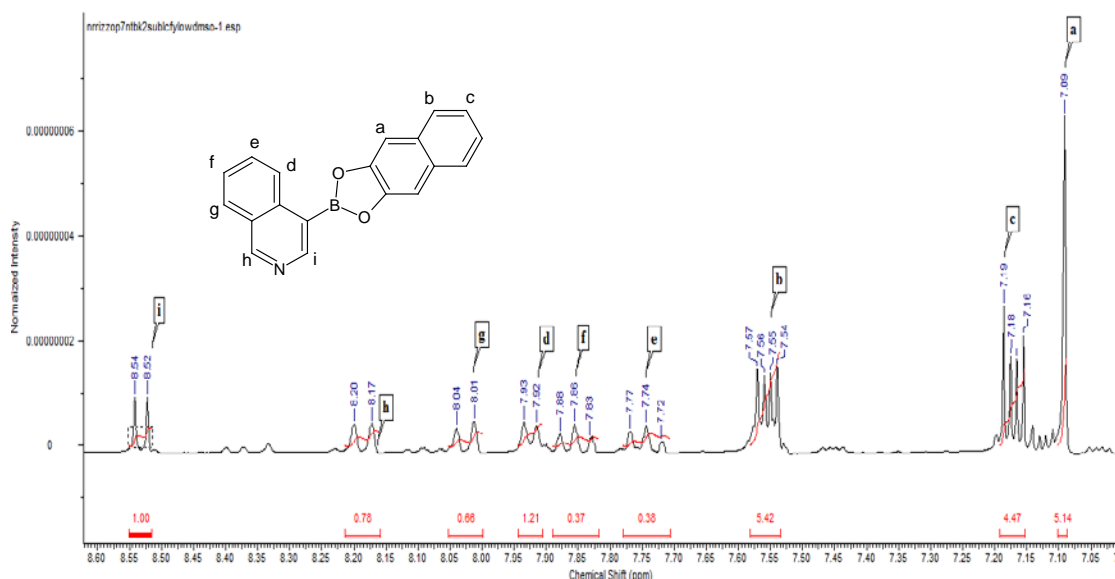


Figure 23. ^1H NMR spectrum of "purified" product **22** in DMSO-d_6 .

In the FT-IR spectrum of product **22** (figure 24) the following signals were observed: aromatic C-H stretch at 3051.27 cm^{-1} , aromatic C=C bend at 1626.22 cm^{-1} , and B-N stretch at 643.80 cm^{-1} . The presence of the B-N stretch suggests that a macrocycle may have been formed, though we are unsure as to its size at this time.

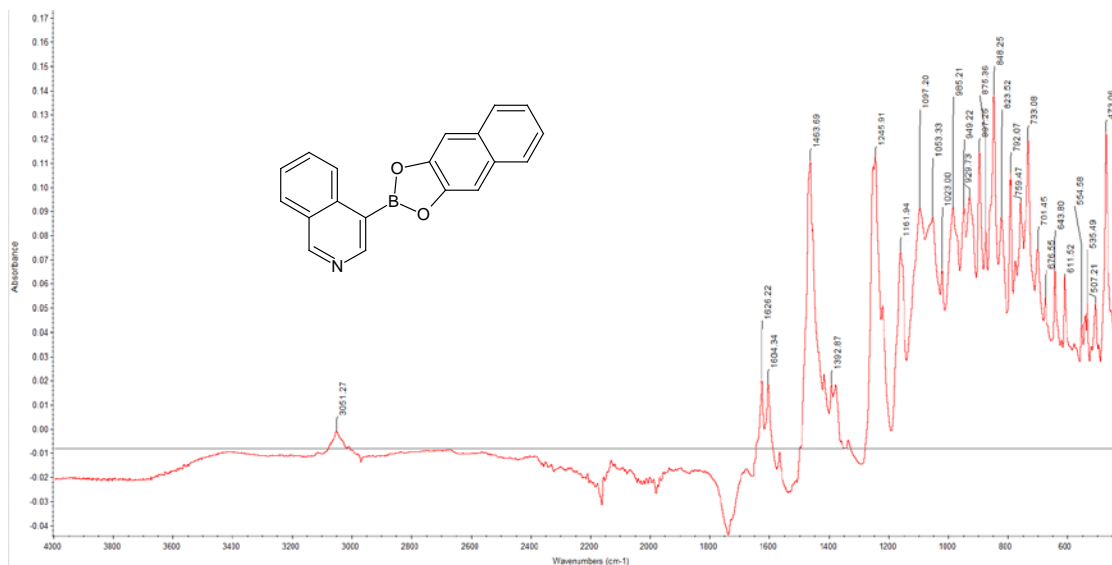


Figure 24. FT-IR spectrum of product **22**.

In the mass spectrum of the product (figure 25) dissolved in methanol, an [M] peak can be seen at 297.1 m/z. The molecular weight of compound **22** is 297.12 g/mol, so the presence of the [M] peak at 297.1 m/z provides evidence that it was actually formed.

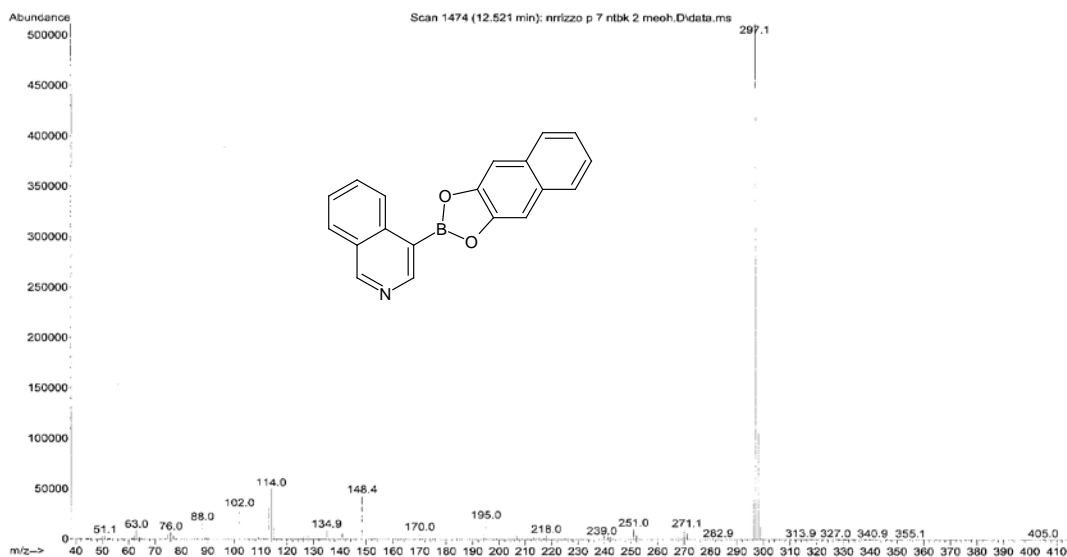
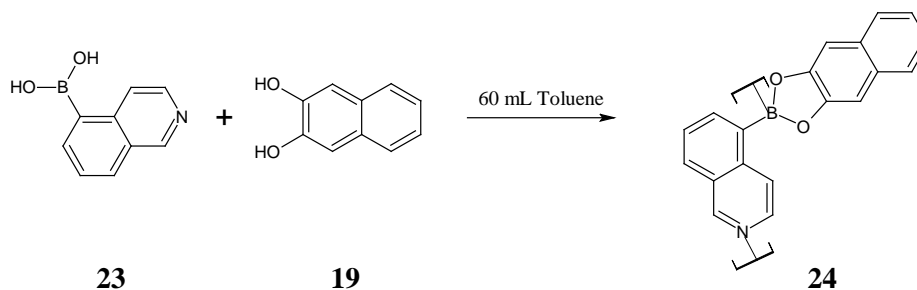


Figure 25. Mass spectrum of product **22** dissolved in methanol.



Scheme 16. 5-isoquinoline boronic acid and 2,3-dihydroxynaphthalene condense to form compound **24**.

Using the same method that was employed to produce compound **20**, **24** was produced from **23** and **19**.⁴ The resulting product was a tan-colored powder with a 79% yield, which was confirmed by ¹H NMR, FT-IR and mass spectroscopy to be the desired compound **24** (figures 26, 27 and 28).

In the ¹H NMR spectrum of product **24** (figure 26) there seem to be no OH peaks present. However, the integrations of the protons of starting materials **19** to **23** is not a 2:1 ratio as it should be. For example, the signal at 7.09 ppm that corresponds to proton **a** has an integration of

4.2 when it should be 2.0. Also, protons **c** at 7.15 ppm and **b** at 7.52 ppm have integrations of 2.89 and 2.99 respectively, when they should both have integrations of 2.0. This indicates that uncomplexed **19** may be present in the product. Additionally, the integration of proton **g** at 8.52 ppm is 2.02 when it should be 1.00. Since the integrations of all the other protons from **23** are roughly 1.0 it is likely that an OH signal from **19** is present at 8.52 ppm and is overlapping with the signal from proton **g**, as opposed to uncomplexed **23** being present. Additionally, no signals indicating the presence of a guest molecule can be seen in the ^1H NMR spectrum of the product **24**.

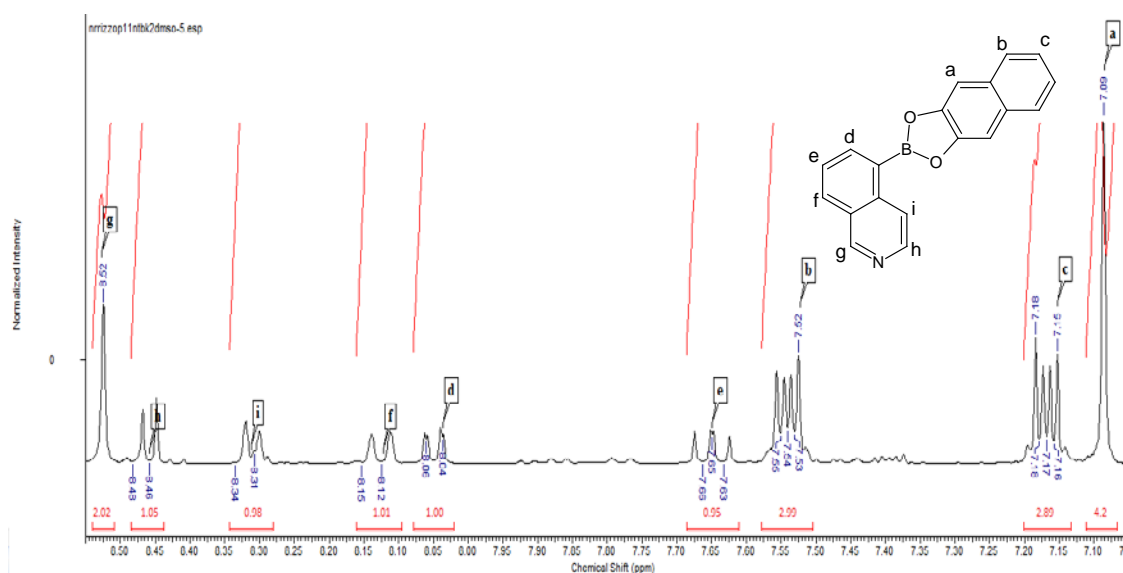


Figure 26. ^1H NMR spectrum of product **24** in DMSO-d_6 .

In the FT-IR spectrum of product **24** (figure 27) the following signals can be seen: phenol-OH stretch at 3362.88 cm^{-1} , aromatic C-H stretch at 3046.27 cm^{-1} , aromatic C=C bend at 1633.30 cm^{-1} , and B-N stretch at 670.58 cm^{-1} . The OH stretch at 3362.88 cm^{-1} indicates that

uncomplexed **19** may be present. The B-N stretch at 670.58 cm^{-1} suggests that a macrocycle may have been formed.

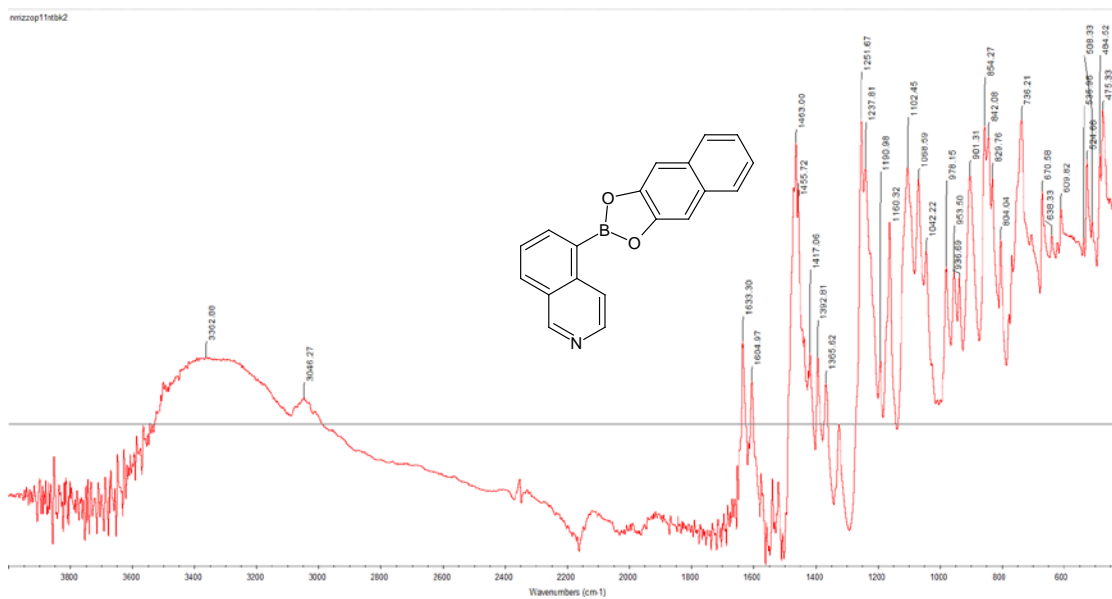


Figure 27. FT-IR spectrum of product **24**.

A mass spectrum of product **24** dissolved in methanol was taken, and an [M] peak at 297.1 m/z was observed (figure 28). Since the molecular weight of compound **24** is 297.12 g/mol, this [M] peak at 297.1 m/z indicates its formation.

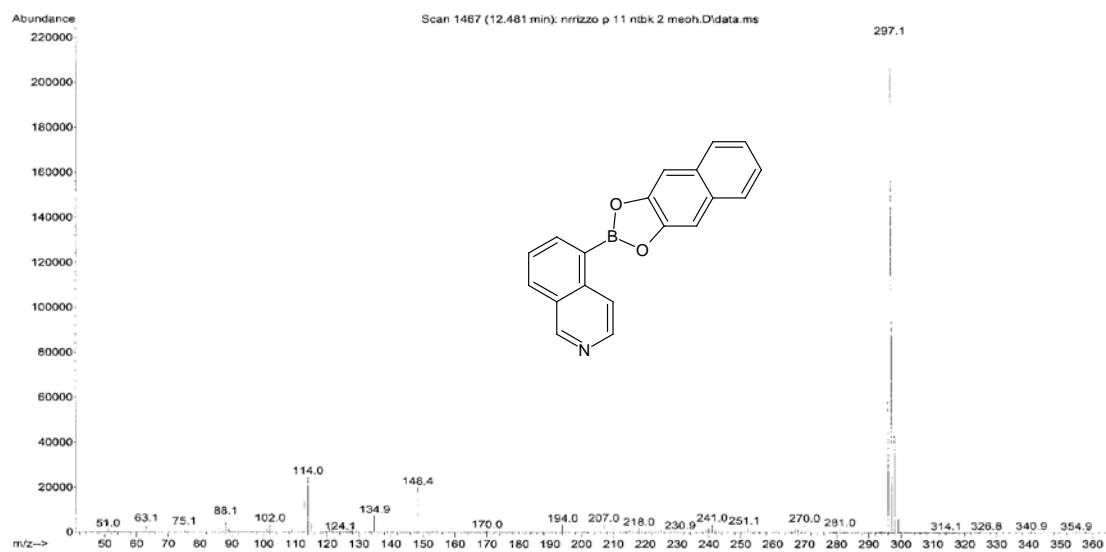


Figure 28. Mass spectrum of product **24** dissolved in methanol.

CHAPTER THREE: CONCLUSIONS

This thesis describes the synthesis and characterization of unique boronate macrocycles using condensation reactions and dative bonding. In most of the complexes that were made, we attempted to form dative bonds using nitrogen and boron. However, we did attempt to make pyridine *N*-oxides that could then be combined with 3-nitrophenylboronic acid **1** in an attempt to produce macrocycles in which the dative bond could form through boron and oxygen instead of boron and nitrogen. Additionally, we explored whether these structures would readily trap a guest molecule within the macrocyclic cavity if toluene was used as the solvent. Our hope was that using this work as the foundation, eventually rotaxanes could be produced from these macrocyclic structures by building onto the guest molecule, thus extending it outward. If this could be achieved, it would prove to be a unique method for the synthesis of rotaxanes.

Three of the boronate macrocycles we attempted to produce were made from condensing a pyridine with a boronic acid, in which we attempted to make the dative bond through nitrogen and boron. The “monomer units” of these structures were successfully produced, as is indicated by the ^1H NMR and mass spectroscopy data. The FT-IR data provides evidence that dative bonds are present in all of these complexes, though more evidence is needed to confirm specific ring sizes. From this work we discovered that the choice of functional group on the boronic acid can either facilitate or hinder the addition of a guest molecule to the macrocyclic cavity. For example, 3-nitrophenyl boronic acid **1** was used to synthesize complex **7**, and a toluene signal is clearly present in the ^1H NMR spectrum of the product. In contrast, complex **10** was synthesized using 4-trifluoromethyl phenylboronic acid **8**, yet a guest molecule was not observed in the ^1H NMR spectrum of the product. Since the only difference between complexes **7** and **10** is the functional

group on the boronic acid, this must be why complex **7** can house a guest molecule in its cavity and complex **10** cannot.

We also tried to produce pyridine *N*-oxides, so that they could then be combined with 3-nitrophenyl boronic acid **1** to produce compounds that would hopefully form a dative bond through oxygen and nitrogen to form unique macrocycles. Aside from picolinic acid *N*-oxide **12**, which was our proof-of-concept reaction, the only *N*-oxide we were able to successfully produce was 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**. Unfortunately, reacting **15** with 3-nitrophenylboronic acid **1** yielded inconclusive results. Although there is some evidence from the FT-IR and mass spectra that suggests that complex **17** was formed, there are also so many impurities present (even after some impurities were removed by sublimation) in both the ^1H NMR and IR data that we are unsure as to whether this complex was actually formed.

Additionally, we attempted to produce three macrocycles from the condensation of quinoline isomers with 2, 3-dihydroxynaphthalene **20**. The ^1H NMR and mass spectroscopy data confirms the formation of all of these monomer units, while the IR data suggests the presence of B-N dative bonds, although we are unsure as to the exact ring sizes of these structures at this time. Unfortunately, none of the complexes produced seem to be capable of trapping a guest molecule in the macrocyclic cavity, if indeed macrocycles were formed.

In our work with boronate macrocycles, we have successfully synthesized the “monomer units” of six structures, as is indicated by the ^1H NMR and mass spectroscopy data. The FT-IR data also confirms the presence of a B-N dative bond, which provides evidence that macrocycles have likely been formed, although the exact sizes of the rings are inconclusive at this time. The main problem we encountered was trying to characterize the sizes of these macrocyclic rings. The B-N dative bond was too weak for the rings to be characterized by methods such as mass spectroscopy, and although a macrocycle is a mini polymer of sorts, the rings were too small to

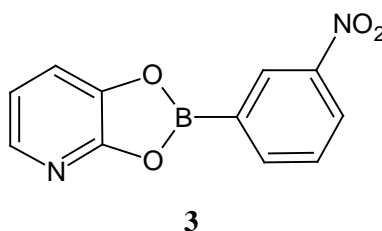
be characterized by methods typical for the characterization of polymers, such as viscosity experiments. In addition to mass spectroscopy, we did also attempt to characterize the sizes of the rings by recrystallization and Thermogravimetric Analysis (which was used on complex **7**). The problem with Thermogravimetric Analysis was that after two mass losses complex **7** would degrade, so we were unable to determine the ring size using that method. Although we were able to recrystallize some of the complexes produced, we were never able to produce x-ray quality crystals.

Future work with such compounds could involve the attempted synthesis of more macrocyclic structures in which the boronic acid is varied instead of the pyridine. It would be interesting to see which of these compounds are capable of trapping a guest molecule and which are not, and then to explore why. Future work could also include trying to insert a di-substituted guest molecule into the ring cavity of complex **7**, and then trying to construct a rotaxane by extending it outward.

CHAPTER FOUR: EXPERIMENTAL

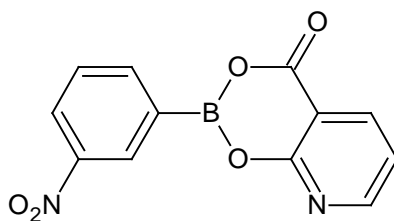
4.0 General

All of the reagents used were purchased from commercial suppliers (Alfa Aesar, Acros, or Frontier Scientific) and used as is unless otherwise stated. The boronic acids that were purchased from Frontier Scientific and used directly from the bottle without prior purification. Toluene was purchased from Acros and used without any further purification. All reactions were performed using oven-dried glassware and a Teflon stir bar. The microwave syntheses were performed open to the atmosphere in a CEM Discover Microwave Synthesizer. All ^1H NMR, ^{13}C NMR experiments were conducted on a JEOL Eclipse 300 FT 300 MHz NMR Spectrometer. The rotavap used was BUCHI Rotavapor R-205. IR spectra were collected on a Smiths IdentifyIR. The mass spectra were collected on an Agilent Technologies 7890 A GC Sampler.

4.1 Boronate Macrocycles**Compound 3**

To a 250 mL round bottom flask, 2, 3-dihydroxypyridine (0.170 g, 1.53 mmol), 3-nitrophenylboronic acid (0.218 g, 1.31 mmol), and toluene (80.0 mL) were added. The mixture

was heated at reflux for 30 minutes using a microwave synthesizer and a Dean-Stark trap. The solvent was removed under reduced pressure to obtain the final product, which was a white solid (yield: 34%, 0.93 g). ^1H NMR (300 MHz, CDCl_3): δ 6.56 (d, $J=6.6$ Hz, 1 H), 6.86 (t, $J=1$ Hz, 1 H), 7.16 (d, $J=7.4$ Hz, 1 H), 7.31 (d, $J=7.4$ Hz, 1 H), 7.53 (t, $J=1$ Hz, 1 H), 7.81 (br. s 1 H), and 8.20 (d, $J=1$ Hz, 1 H). ^{13}C NMR (300 MHz, DMSO-d_6): δ 104.73, 115.88, 117.63, 123.42, 126.19, 127.49, 128.97, 132.74, 138.27, 148.25, and 150.93. FT-IR spectrum: aromatic C-H stretch at 3077.16 cm^{-1} , aromatic C=C bend at 1644.97 cm^{-1} , and B-N stretch at 563.06 cm^{-1} . Mass spectrum: $[\text{M}]-1$ peak at 241.0 m/z .

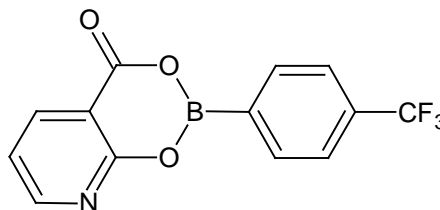


6

Compound 6

To a 125 mL round bottom flask, 2-hydroxynicotinic acid (0.245 g, 1.80 mmol), 3-nitrophenylboronic acid (0.311 g, 1.86 mmol), and toluene (60.0 mL) were added. The reaction mixture was heated at reflux using a microwave synthesizer and a Dean-Stark trap. After 30 minutes, the solvent was removed under reduced pressure to obtain the final product, which was a white solid. (yield: 66%, 0.32 g). ^1H NMR (300 MHz, DMSO-d_6): δ 2.30 (s, 3 H), 6.67 (t, $J=1$ Hz, 5 H), 7.18-7.25 (m, 5 H), 7.63 (t, $J=1$ Hz, 5 H), 7.95 (d, $J=1$ Hz, 5 H), 8.18-8.27 (m, 10 H), 8.39 (d, $J=7.2$ Hz, 6 H), 8.51 (s, 16 H), and 8.63 (s, 5 H). ^1H NMR (300 MHz, CDCl_3): δ 1.26 (s, 1 H), 6.61 (t, $J=6.7$ Hz, 1 H), 7.54-7.61 (m, 2 H), 7.73 (t, $J=7.7$ Hz, 1 H), 8.06 (d, $J=8$ Hz, 1 H), 8.28 (d, $J=10.2$ Hz, 1 H), 8.47 (d, $J=6.9$ Hz, 1 H), 8.59 (m, 9 H), and 9.02 (s, 1 H). ^{13}C NMR (300 MHz, DMSO-d_6): δ 109.28, 125.36, 128.82, 129.65, 141.17, 142.09, 146.82, 147.99, 165.18, and 165.60. FT-IR spectrum: aromatic C-H stretch at 3098.76 cm^{-1} , carboxylic acid C=O stretch at

1713.53 cm^{-1} , aromatic C=C bend at 1613.51 cm^{-1} , and B-N stretch at 568.76 cm^{-1} . Mass spectrum: $[\text{M}] - \text{C}_6\text{H}_4\text{BNO}_3$ and $[\text{M}] + 1$. at 271.0 m/z.

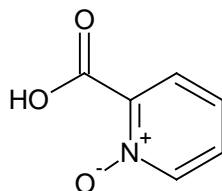


9

Compound 9

To a 125 mL round bottom flask, 2-hydroxypyridine-3-carboxylic acid (0.349 g, 2.51 mmol), 4-trifluoromethyl phenylboronic acid (0.442 g, 2.33 mmol) and toluene (60.0 mL) were added. The reaction mixture was heated at reflux and stirred using a microwave synthesizer and a dean stark trap with dry molecular sieves. After 45 minutes, the solvent was removed under reduced pressure to obtain the final product, which was a white solid. (yield: 70%, 0.91 g). ^1H NMR (300 MHz, DMSO-d_6): δ 6.69 (t, $J=1$ Hz, 1 H), 7.67 (d, $J=7.7$ Hz, 1 H), 7.97 (m, 2 H), and 8.38 (t, $J=1$ Hz, 2 H). ^1H NMR (300 MHz, CDCl_3): δ 7.62 (d, $J=7.7$ Hz, 1 H), 7.69-7.91 (m, 3 H), 7.83 (d, $J=7.7$ Hz, 1 H), and 8.31 (d, $J=7.7$ Hz, 2 H). ^{13}C NMR (300 MHz, DMSO-d_6): δ 109.31, 117.20, 135.21, 142.10, 146.82, 165.18, and 165.64. FT-IR spectrum: carboxylic acid-OH stretch at 3231.05 cm^{-1} , aromatic C=C bend at 1605.73 cm^{-1} , aromatic C-H bend at 778.55 cm^{-1} , and B-N stretch at 639.67 cm^{-1} .

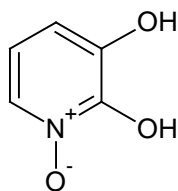
4.2 N-Oxides



12

N-Oxide 12

To a solution of picolinic acid (1.66 g, 13.5 mmol) in dichloromethane (14.0 mL) a saturated solution of oxone (10.2 g, 67.1 mmol) in water (42.0 mL) was added. The mixture was refluxed at 45°C for 40 hours in an oil bath before being cooled to room temperature and extracted with dichloromethane (10 x 50 mL). The organic phases were combined and dried over anhydrous MgSO₄. The product was filtered and the solvent was removed under reduced pressure to obtain a white solid product. (yield: 54%, 1.00 g). ¹H NMR (300 MHz, DMSO-d₆): δ 7.88-7.96 (m, 2 H), 8.31 (d, J=1 Hz, 1 H), and 8.74 (d, J=1 Hz, 1 H). FT-IR spectrum: aromatic C-H stretch at 3119.17 cm⁻¹, aromatic C=C bend at 1557.12 cm⁻¹, and N-O stretch at 1251.89 cm⁻¹.

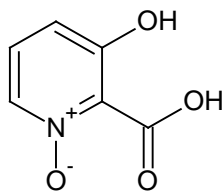


13

N-Oxide 13

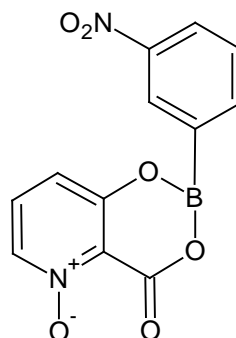
A solution of 2, 3-dihydroxypyridine (0.297 g, 2.68 mmol) and water (1.50 mL) in a 100 mL round bottom flask was allowed to stir at room temperature for several minutes before 30% hydrogen peroxide (1.40 mL, 36.8 mmol) was added. The mixture was slowly heated to 70°C, and then allowed to cool down to room temperature before benzene (68.0 mL) and 30% hydrogen

peroxide (0.500 mL, 10.4 mmol) were added to the reaction mixture. Using a Dean-Stark trap with dry molecular sieves, the solution was allowed to reflux for approximately 3 hours before the solvent was removed under reduced pressure to obtain the final product, which was a yellow-white solid. (yield: 30%, 0.10 g). $^1\text{H NMR}$ (300 MHz, DMSO-d_6): δ 6.01 (t, $J=6.9$ Hz, 1 H), 6.65 (d, $J=6.9$ Hz, 1 H), 6.80 (d, $J=6.6$ Hz, 1 H). FT-IR spectrum: aromatic C=C bend at 1670.69 cm^{-1} , N-O stretch at 1294.16 cm^{-1} , and aromatic C-H bend at 748.32 cm^{-1} .

**15*****N*-Oxide 15**

A solution of 3-hydroxypyridine-2-carboxylic acid (0.605 g, 4.35 mmol) and water (1.50 mL) in a 100 mL round bottom flask was allowed to stir at room temperature for several minutes before 30% hydrogen peroxide (6.00 mL, 155 mmol) was added. The mixture was slowly heated to 70°C , and then allowed to cool down to room temperature before benzene (60.0 mL) and 30% hydrogen peroxide (2.00 mL, 51.8 mmol) were added to the reaction mixture. Using a Dean-Stark trap with dry molecular sieves, the solution was allowed to reflux for approximately 9 hours before the solvent was removed under reduced pressure to obtain the final product, which was a white solid. (yield: 67%, 0.40 g). $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.32 (d, $J=1$ Hz, 1 H), 7.42 (t, $J=1$ Hz, 1 H), and 7.95 (d, $J=6.1$ Hz, 1 H). FT-IR spectrum: aromatic C-H stretch at 3043.50 cm^{-1} , aromatic C=C bend at 1602.94 cm^{-1} , and N-O stretch at 1271.96 cm^{-1} .

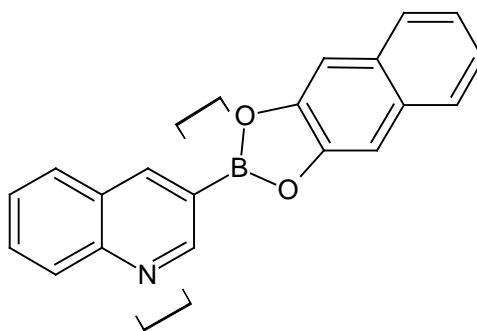
4.3 Boronate Macrocycles Made From *N*-Oxides

**16**

Compound 16

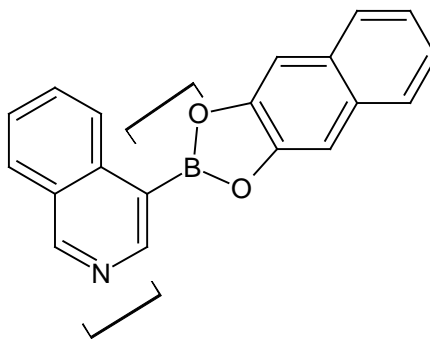
To a 100 mL round bottom flask, 3-hydroxypyridine-2-carboxylic acid *N*-oxide (0.287 g, 1.84 mmol), 3-nitrophenylboronic acid (0.301 g, 1.81 mmol) and toluene (60.0 mL) were added. The reaction mixture was heated at reflux and stirred using a microwave synthesizer and a Dean-Stark trap with dry molecular sieves. After 45 minutes, the solvent was removed under reduced pressure to obtain the final product, which was a light-tan solid. (yield: 77%, 0.43 g). ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.35 (d, *J*=1, 1 H), 7.45 (t, *J*=1, 1 H), 7.58 (m, *J*=1, 1 H), 7.68 (br. s, 1 H), 7.80 (d, *J*=1, 1 H), 7.96 (m, 1 H), 8.07-8.15 (m, 1 H), 8.30 (d, *J*=6.9, 1 H), and 8.58 (s, 1 H). FT-IR spectrum: aromatic C-H stretch at 3102.55 cm⁻¹, carboxylic acid-OH stretch at 2514.31 cm⁻¹, aromatic C=C bend at 1694.18 cm⁻¹, N-O stretch at 1283.38 cm⁻¹, and B-N stretch at 577.84 cm⁻¹. Mass spectrum: [M]-O loss at 269.8 m/z.

4.4 Boronate Macrocycles Made From Quinoline Boronic Acid Compounds

**20**

Compound 20

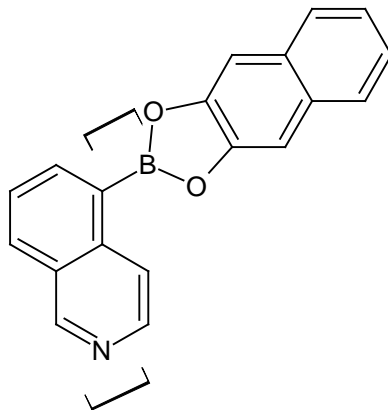
To a 100 mL round bottom flask, 3-quinoline boronic acid (0.301 g, 1.74 mmol), 2, 3-dihydroxynaphthalene (0.285 g, 1.78 mmol) and toluene (60.0 mL) were added. The reaction mixture was heated at reflux and stirred using a microwave synthesizer and a Dean-Stark trap with dry molecular sieves. After 45 min, the solvent was removed under reduced pressure to obtain the final product, which was a yellow solid. (yield: 70%, 0.51 g). ^1H NMR (300 MHz, DMSO d_6): δ 7.15-7.19 (m, 1 H), 7.54-7.65 (m, 2 H), 7.77 (t, $J=7.7$ Hz, 1 H), 7.98 (t, $J=7.4$ Hz, 2 H), 8.50 (s, 2 H), 8.75 (s, 1 H), 9.18 (d, $J=1.7$ Hz, 1 H), and 9.49 (s, 1 H). ^{13}C NMR (300 MHz, DMSO- d_6): δ 110.08, 123.43, 126.09, 129.33, 130.35, and 141.87. FT-IR spectrum: aromatic C-H stretch at 3030 cm^{-1} , aromatic C=C bend at 1644.03 cm^{-1} , and B-N stretch at 622.53 cm^{-1} . Mass spectrum: 297.1 m/z ($[\text{M}]$).



22

Compound 22

To a 100 mL round bottom flask, 4-isoquinoline boronic acid (0.315 g, 1.82 mmol), 2, 3-dihydroxynaphthalene (0.300 g, 1.87 mmol) and toluene (60.0 mL) were added. The reaction mixture was heated at reflux and stirred using a heating mantle. After 10 hours dry molecular sieves were added to the Dean-Stark trap, and the reaction mixture was allowed to reflux for 5 more hours. The solvent was removed under reduced pressure to obtain the final product, which was a tan-colored solid. (yield: 79%, 0.41 g). ^1H NMR (300 MHz, DMSO-d_6): δ 7.09 (s, 5 H), 7.16-7.19 (dd, $J=1$, 5 Hz, H), 7.54-7.57 (dd, $J=1$ Hz, 6 H), 7.74 (t, $J=1$ Hz, 1 H), 7.86 (t, $J=1$ Hz, 1 H), 7.92 (d, $J=5.8$ Hz, 1 H), 8.01 (d, $J=8.3$ Hz, 1 H), 8.17 (d, $J=8.3$ Hz, 1 H), and 8.52 (d, $J=5.8$ Hz, 1 H). ^{13}C NMR (300 MHz, DMSO-d_6): δ 110.07, 119.59, 123.42, 126.07, 129.33, and 147.40. FT-IR spectrum: aromatic C-H stretch at 3051.27 cm^{-1} , aromatic C=C bend at 1626.22 cm^{-1} , and B-N stretch at 643.80 cm^{-1} . Mass spectrum: 297.1 m/z ([M]).



24

Complex 24

To a 100 mL round bottom flask, 5-isoquinoline boronic acid (0.312 g, 1.80 mmol), 2, 3-dihydroxynaphthalene (0.302 g, 1.89 mmol) and toluene (60.0 mL) were added. The reaction mixture was heated at reflux and stirred using a heating mantle. After 10 hours, dry molecular sieves were added to the dean stark trap, and the reaction mixture was allowed to reflux for 5 more hours. The solvent was removed under reduced pressure to obtain the final product, which was a tan-colored solid. (yield: 79%, 0.41 g). ^1H NMR (300 MHz, DMSO- d_6): δ 7.16 (d, $J=3.3$ Hz, 1 H), 7.54 (d, $J=3.3$ Hz, 12 H), 7.64 (t, $J=1$ Hz, 7 H), 8.07 (d, $J=1$ Hz, 1 H), 8.13 (d, $J=8.5$ Hz, 2 H), 8.35 (d, $J=4.1$ Hz, 1 H), 8.48 (d, $J=1$ Hz, 5 H), 9.30 (s, 1 H), and 9.50 (br. s, 4 H). ^{13}C NMR (300 MHz, DMSO- d_6): δ 123.54, 126.07, 129.30, 147.30, 166.00, and 169.80. FT-IR spectrum: phenol-OH stretch at 3362.88 cm^{-1} , aromatic C-H stretch at 3046.27 cm^{-1} , aromatic C=C bend at 1633.30 cm^{-1} , and B-N stretch at 670.58 cm^{-1} . Mass spectrum: 297.1 m/z ([M]).

REFERENCES

- ¹Varma, Sukumar K, et al. *Synthesis and Characterization of Amine Adducts of Tri(4-bromophenyl)boroxine, Tri(3-nitrophenyl)boroxine, and Tri(3-aminophenyl)boroxine; Molecular Structure of 3-Picoline-tri(4-bromophenyl)boroxine*. *Main Group Chem.* 1997, 2, 251-258.
- ²Christinat, Nicolas; Croisier, Emmanuel; Scopelliti, Rosario; Cascella, Michele; Rothlisberger, Ursula; and Severin, Kay. *Formation of Boronate Ester Polymers with Efficient Intrastrand Charge-Transfer Transitions by Three-Component Reactions*. *Eur. J. Inorg. Chem.* **2007**, 5177-5181.
- ³Christinat, Nicolas; Scopelliti, Rosario; and Severin, Kay. *Multicomponent Assembly of Boron-Based Dendritic Nanostructures*. *J. Org. Chem.* **2006**, 72, 2192-2200.
- ⁴Christinat, Nicolas; Scopelliti, Rosario, and Severin, Kay. *A new method for the synthesis of boronate macrocycles*. *Chem. Commun.* **2004**, 1158-1159.
- ⁵Wikipedia.org. <http://en.wikipedia.org/wiki/Rotaxane> (image accessed March 18, 2013). **2013**.
- ⁶Reinemann, Dana N; Wright, Ashley M; Wolfe, Jonathan D; Tschumper, Gregory S; and Hammer, Nathan I. *Vibrational spectroscopy of N-methyliminodiacetic acid (MIDA)-protected Boronate Ester: Examination of the B-N Dative Bond*. *J. Phys. Chem. A.* **2011**, 6426-6431.
- ⁷Hunt, Ian; and Spinney, Rick. Chem.ucalgary.ca. <http://chem.ucalgary.ca/courses/350/Carey5th/Carey.html> (accessed June 26, 2013). McGraw-Hill, web version **2006**
- ⁸Kucharski, Timothy J.; Oxsher, Jerry R.; and Blackstock, Silas C. *Pyrazine-N, N'-dioxide/tetracyanoethylene electron donor-acceptor bonding and the effect of donor steric demand and symmetry on the cocrystal assembly*. *Tetrahedron Letters.* **2006**, 4569-4572.
- ⁹Farkas, Adalbert; Mascioli, RL; Miller, Frank; and Strohm, PF. *Some Derivatives of 1, 4-Diazabicyclo(2.2.2)octane(Triethylenediamine)*. *J. Chemical and Engineering Data.* **1968**, 2078-2083.
- ¹⁰Rao, Chintamani Nagesa Ramachandra. *Chemical Applications of Infrared Spectroscopy*. New York and London: Academic Press. 1963.

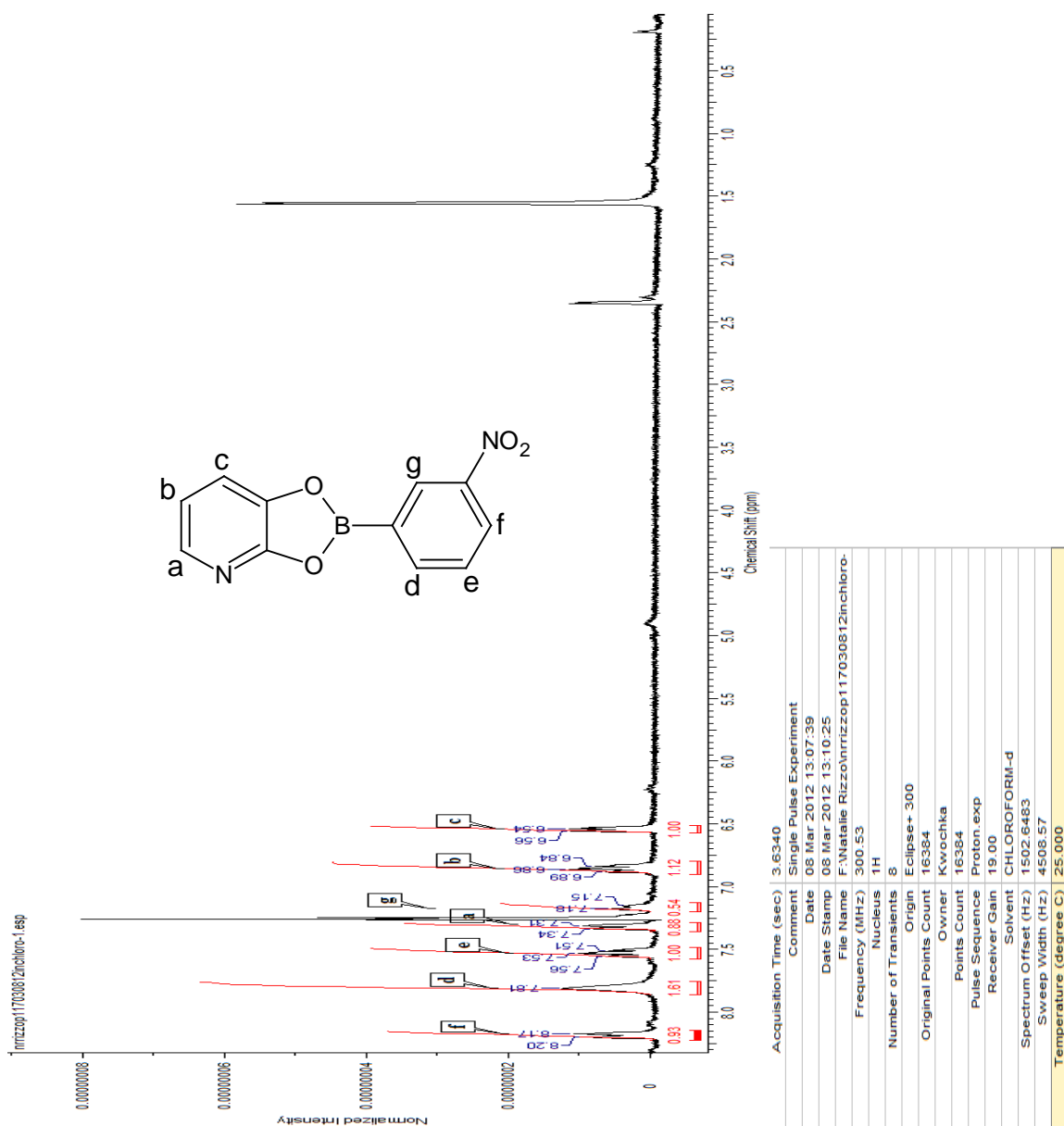
APPENDIX A: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND 3

Figure 29. ^1H NMR spectrum of compound 3 formed from 2, 3-dihydroxypyridine and 3-nitrophenylboronic acid in CDCl_3 .

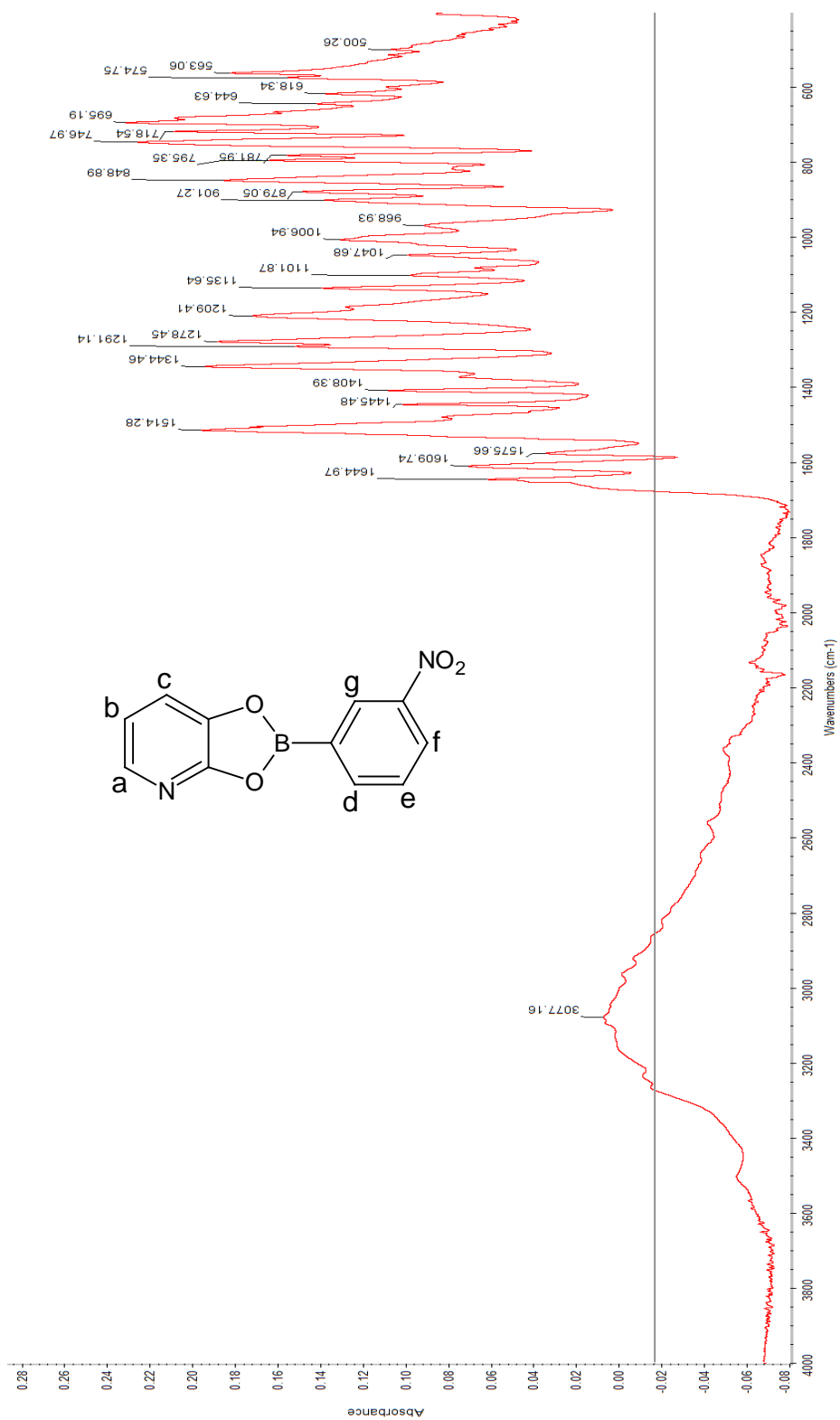


Figure 30. FT-IR spectrum of compound **3** formed from 2, 3-dihydroxypyridine and 3-nitrophenylboronic acid.



Figure 31. Mass spectrum of compound **3** formed from 2, 3-dihydroxy-pyridine and 3-nitrophenylboronic acid dissolved in methanol.

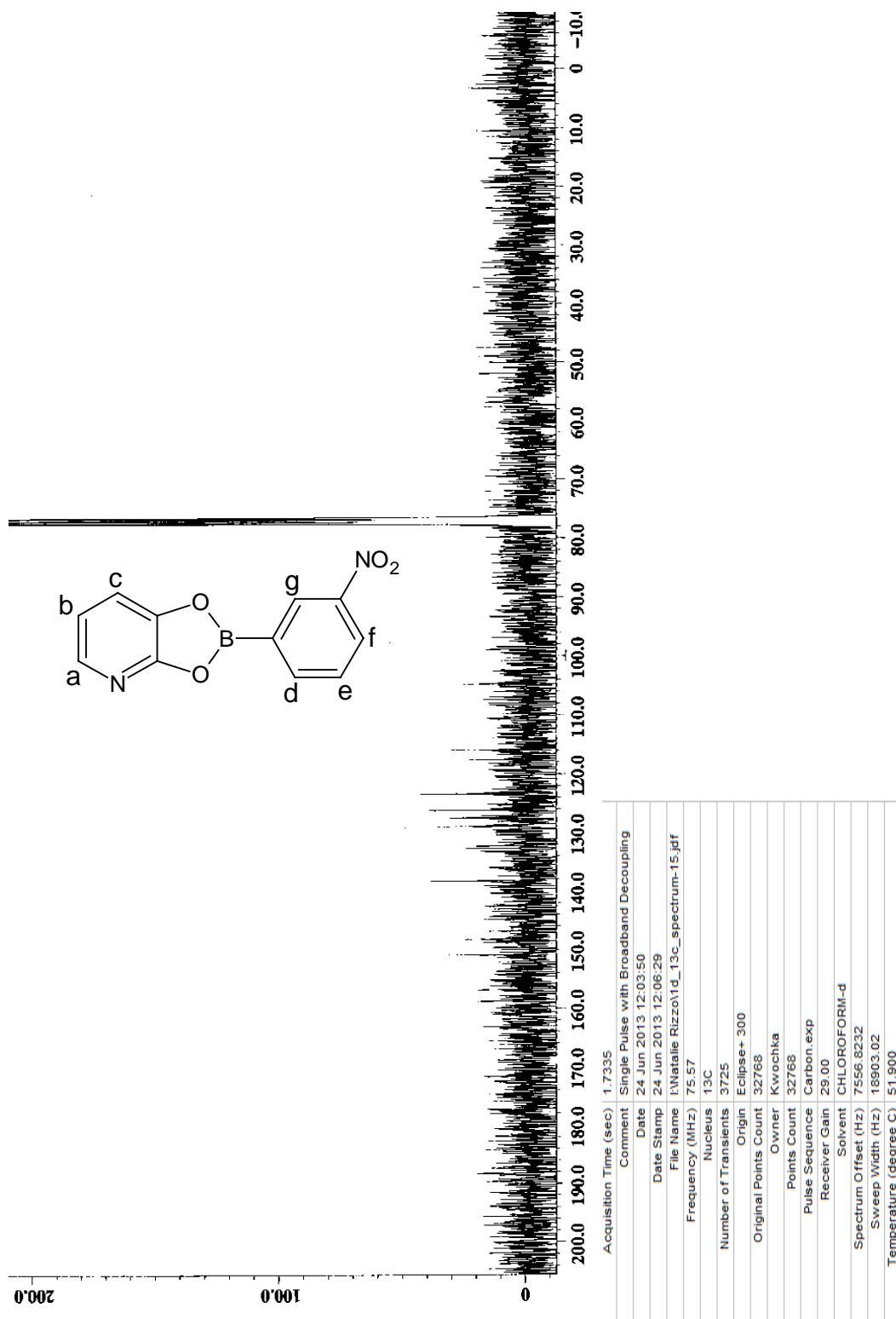


Figure 32. ¹³C NMR spectrum of compound 3 in DMSO-d₆.

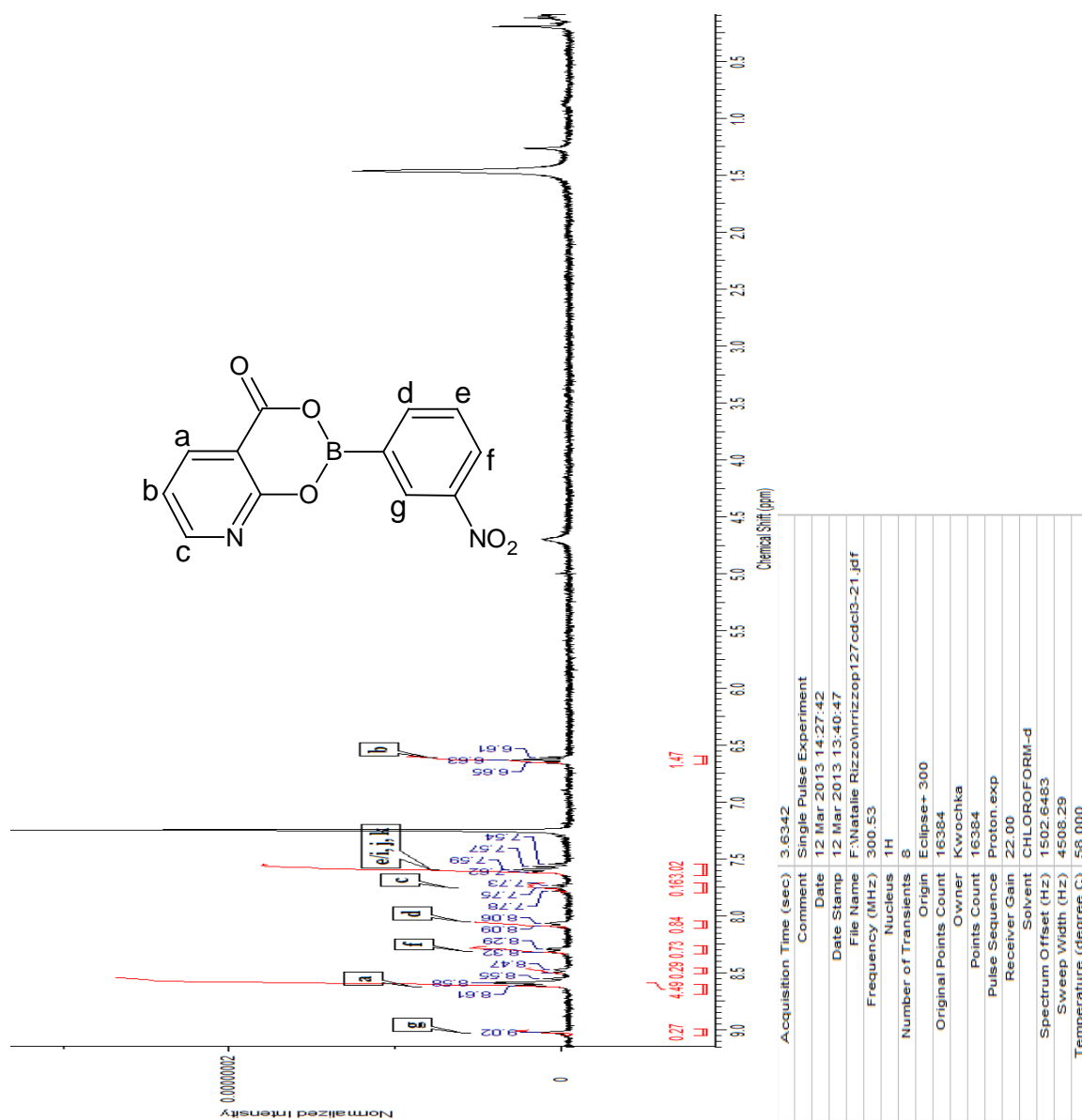
APPENDIX B: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND 6

Figure 33. ^1H NMR spectrum of compound 6 formed from 2-hydroxynicotinic acid and 3-nitrophenylboronic acid in CDCl_3 .

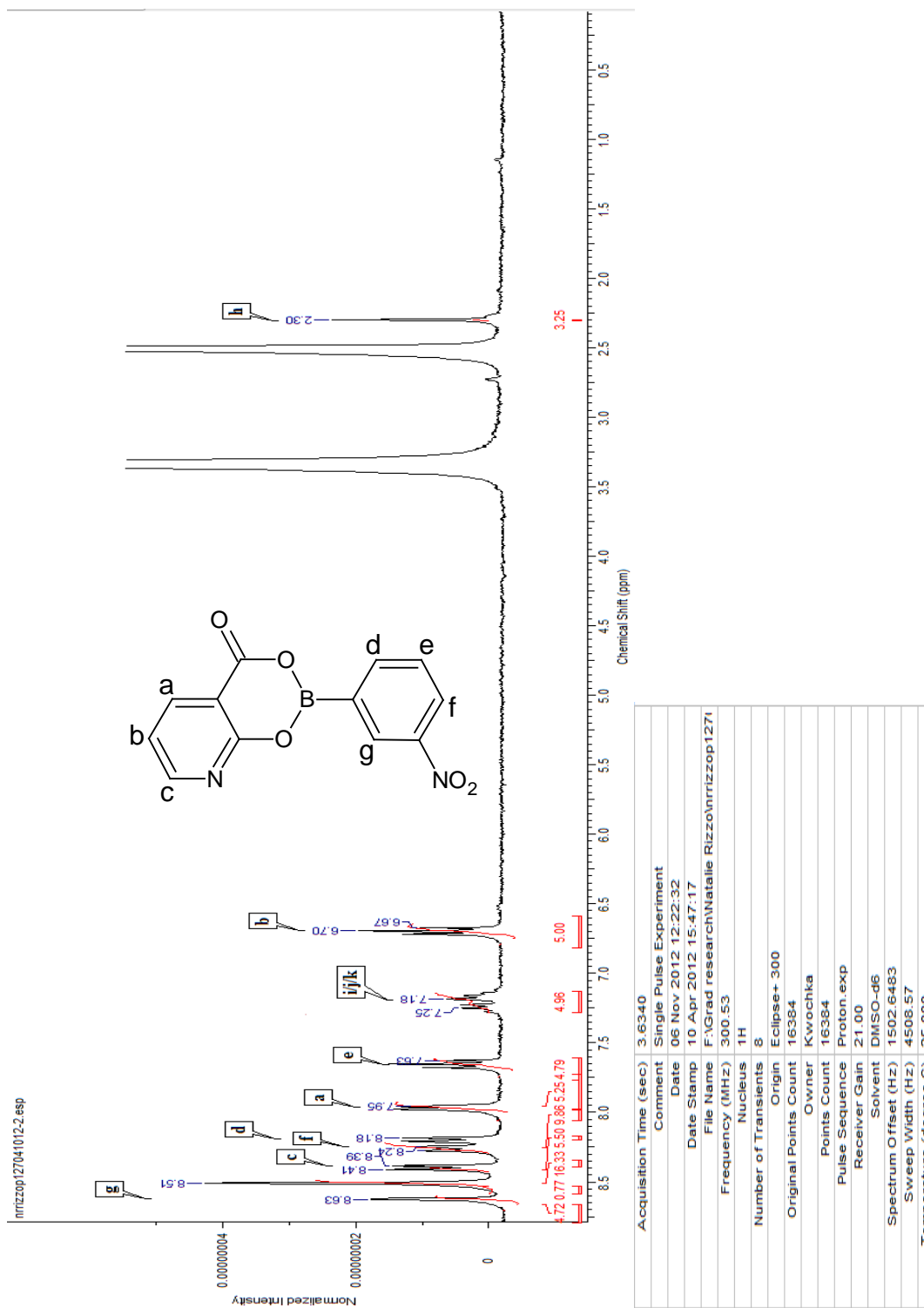


Figure 34. ¹H NMR spectrum of compound 6 formed from 2-hydroxynicotinic acid and 3-nitrophenylboronic acid in DMSO-d₆.

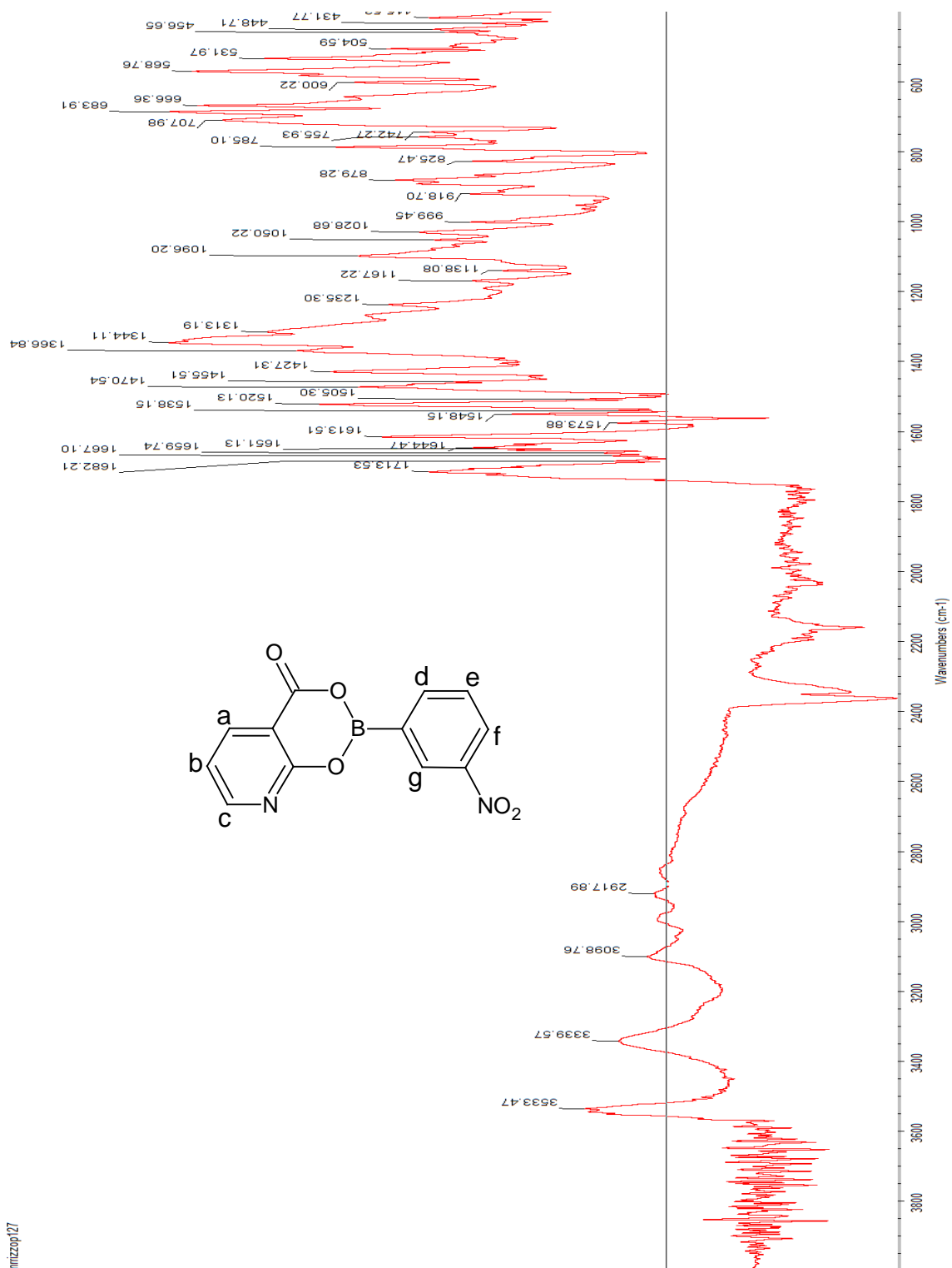


Figure 35. FT-IR spectrum of compound **6** formed from 2-hydroxynicotinic acid and 3-nitrophenylboronic acid.

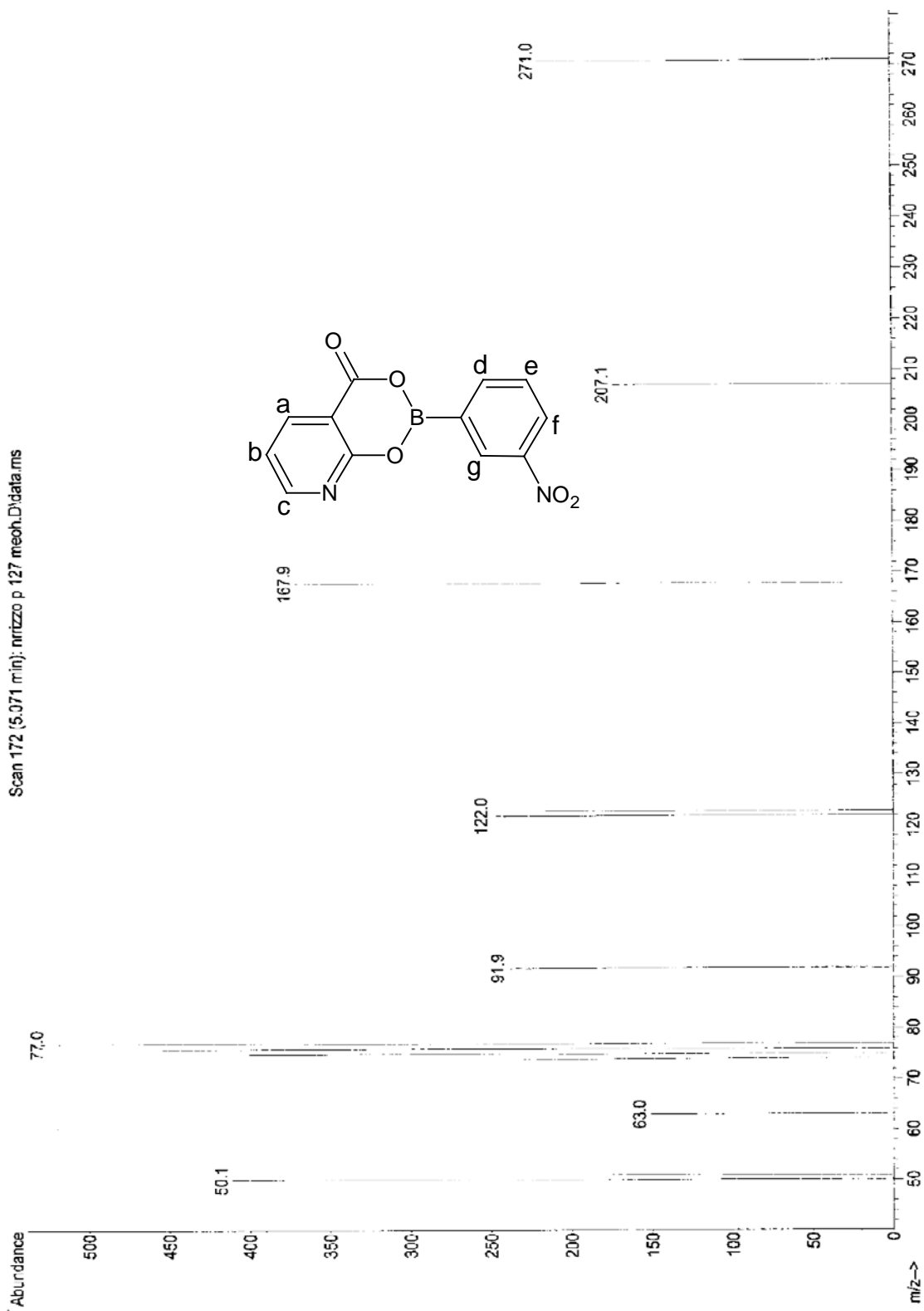


Figure 36. Mass spectrum of compound **6** formed from 2-hydroxynicotinic acid and 3-nitrophenylboronic acid dissolved in methanol.

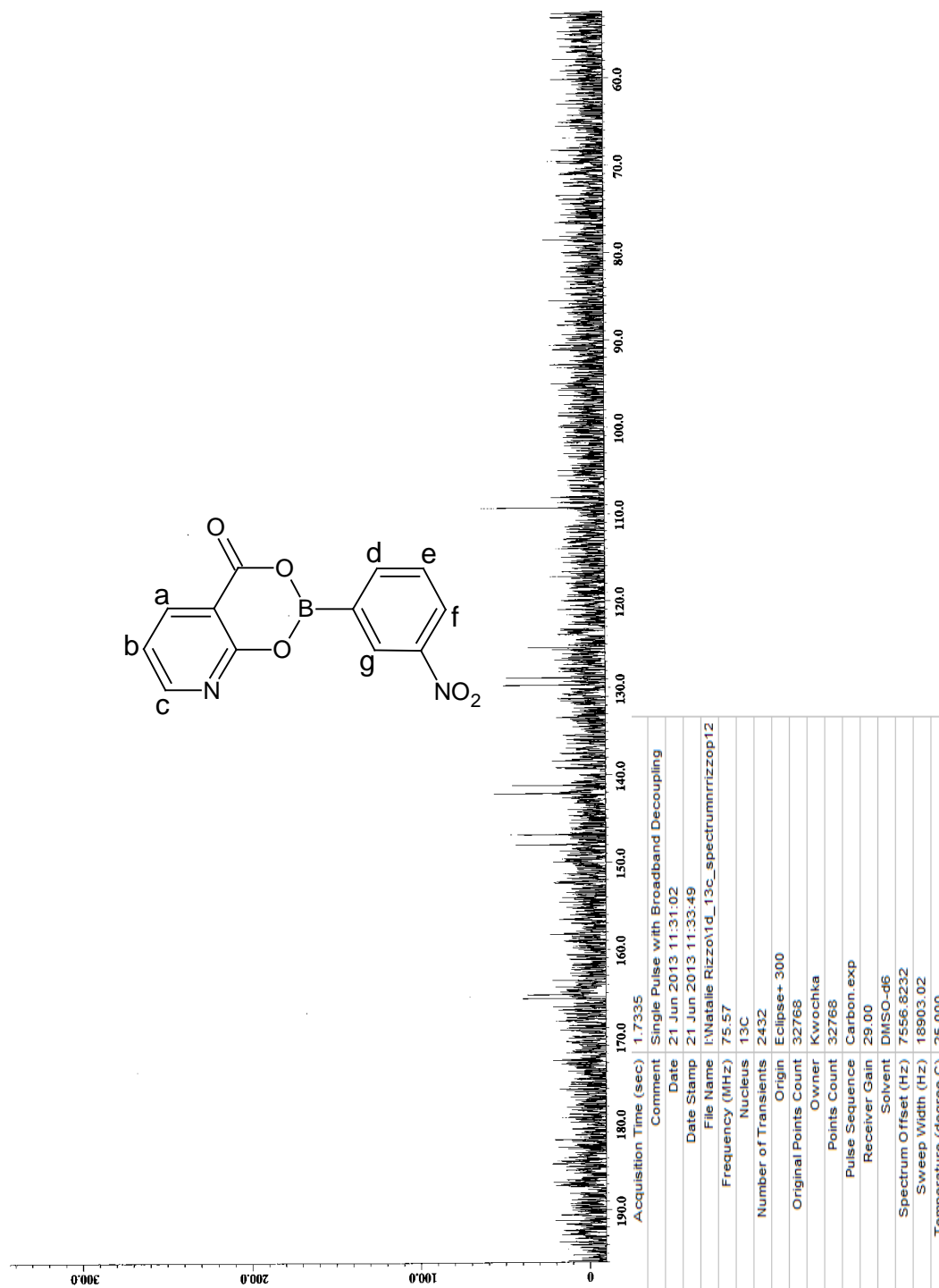


Figure 37. ¹³C NMR spectrum of compound 6 in DMSO-d₆.

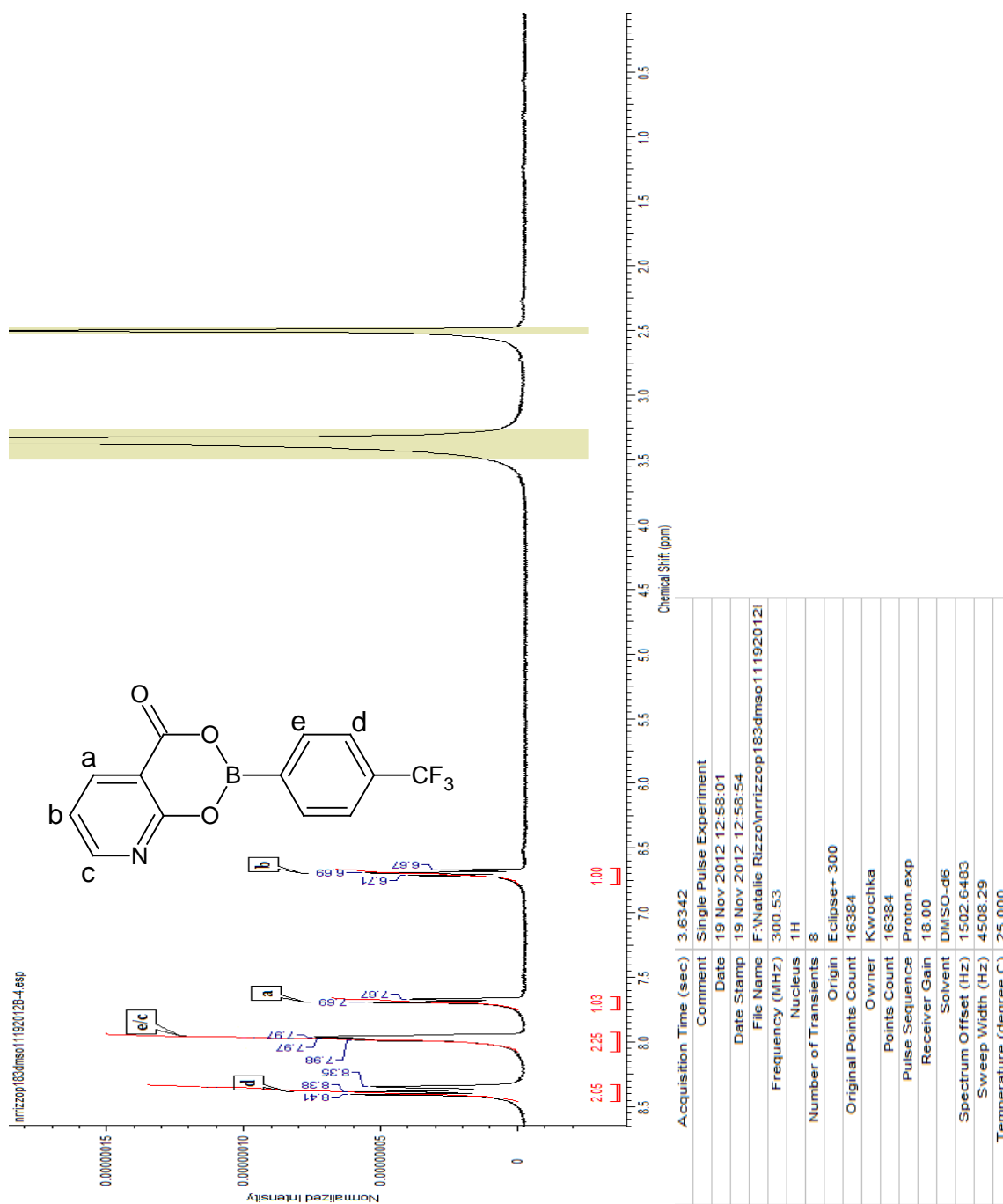
APPENDIX C: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND **9**

Figure 38. ^1H NMR spectrum of compound **9** formed from 4-trifluoromethyl phenylboronic acid and 2-hydroxynicotinic acid in DMSO-d_6 .

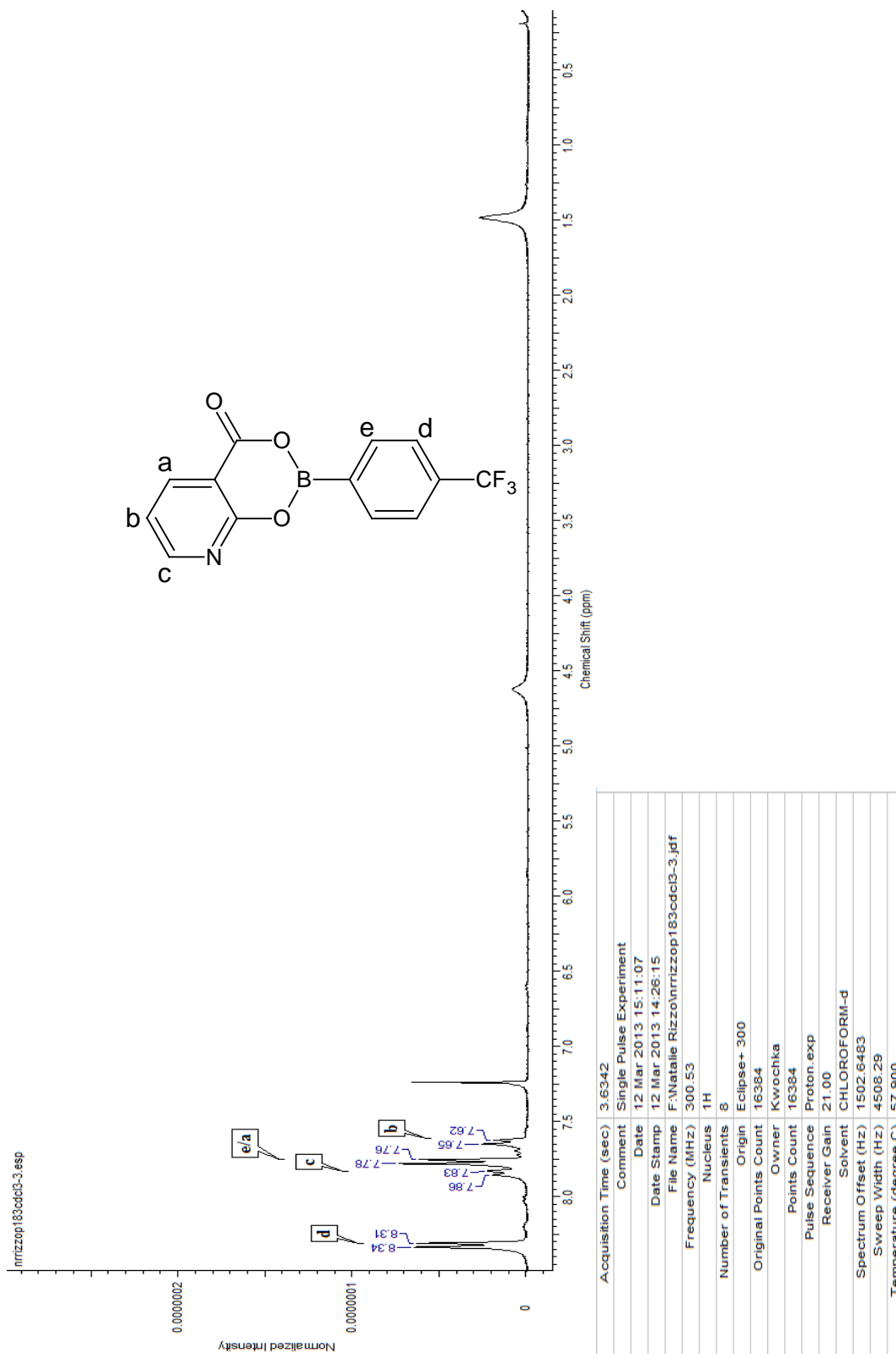


Figure 39. ¹H NMR spectrum of compound **9** formed from 4-trifluoromethyl phenylboronic acid and 2-hydroxynicotinic acid CDCl₃.

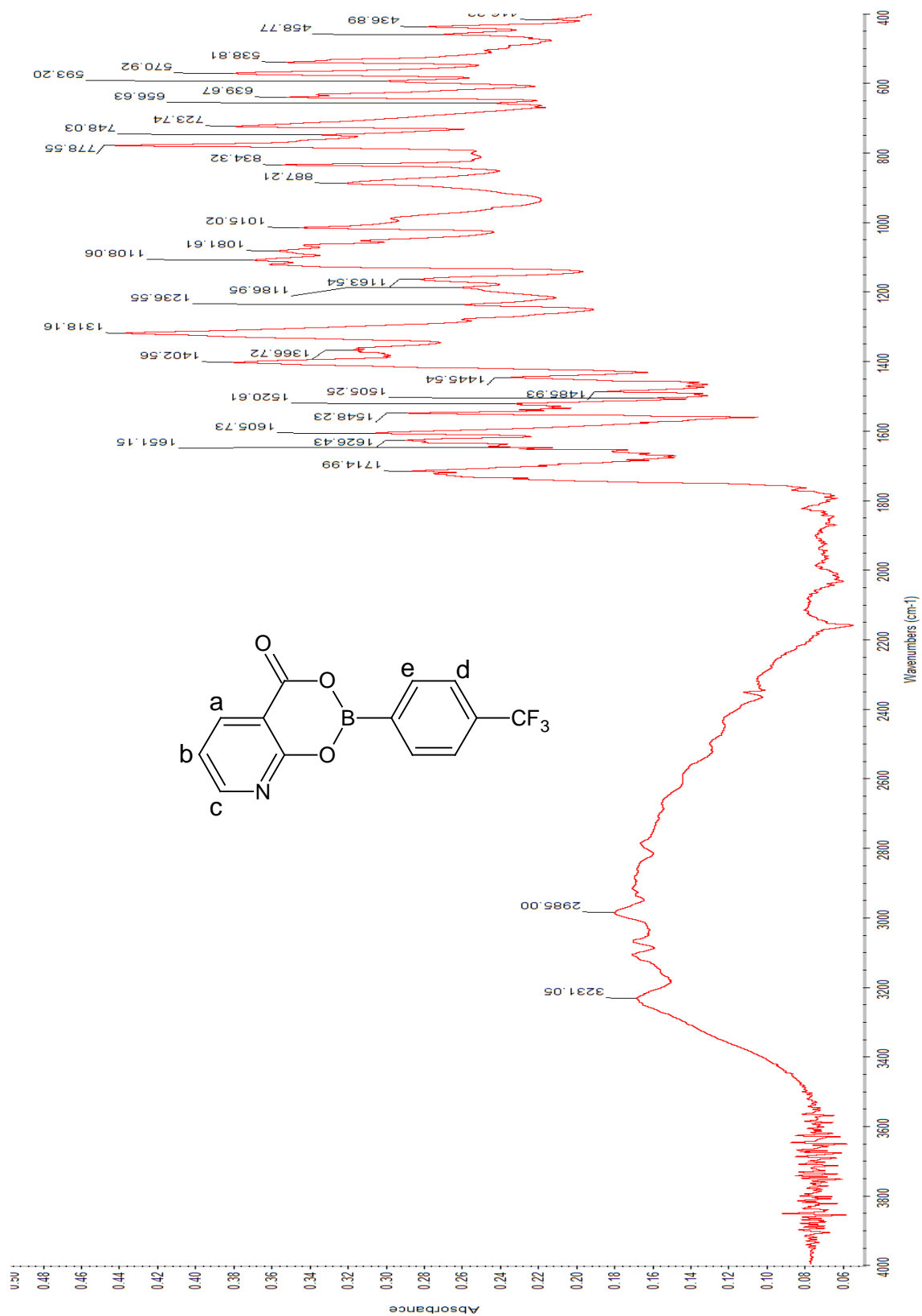


Figure 40. FT-IR spectrum of compound **9** formed from 4-trifluoromethyl phenylboronic acid and 2-hydroxynicotinic acid.

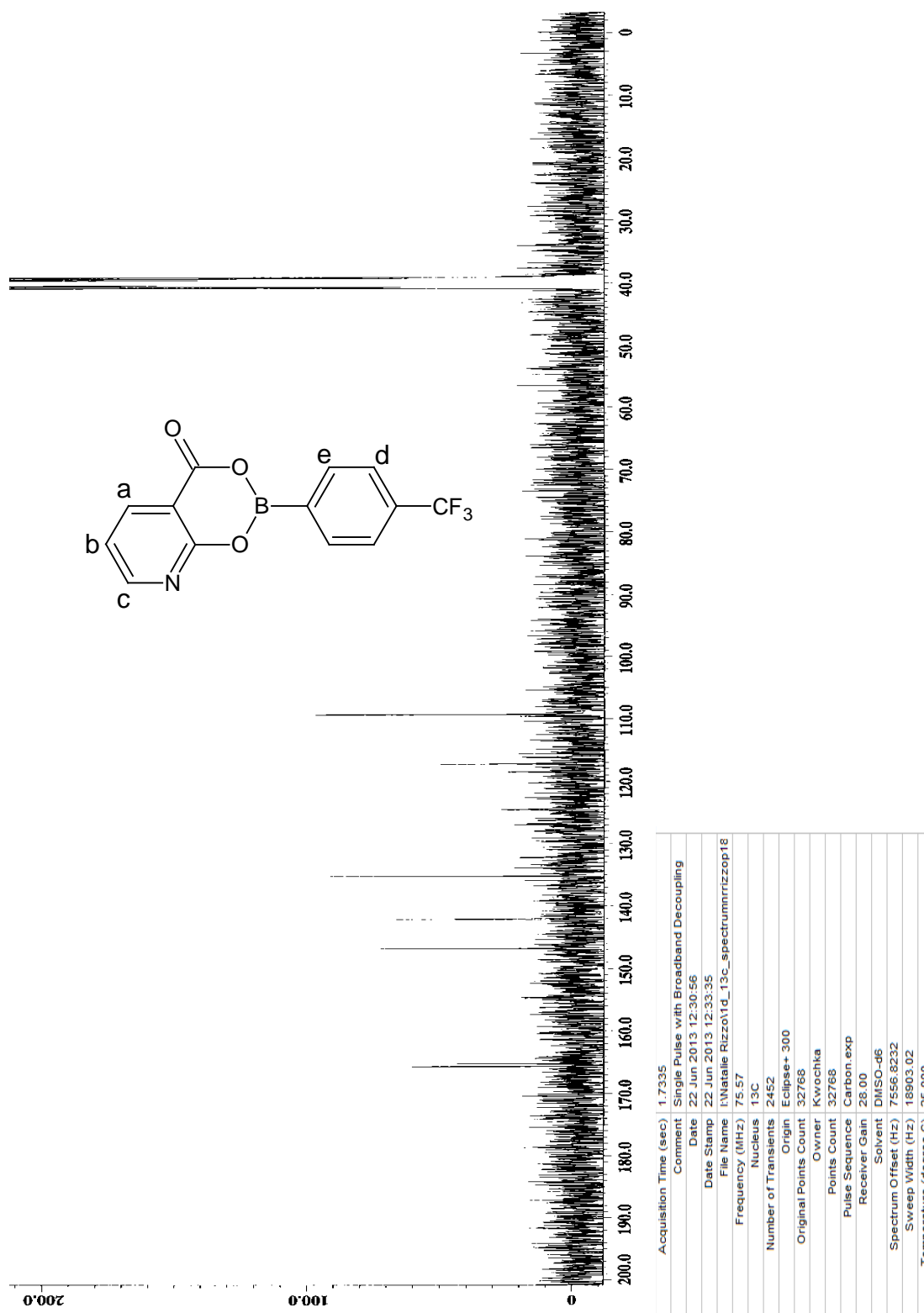


Figure 41. ^{13}C NMR spectrum of compound **9** in DMSO-d_6 .

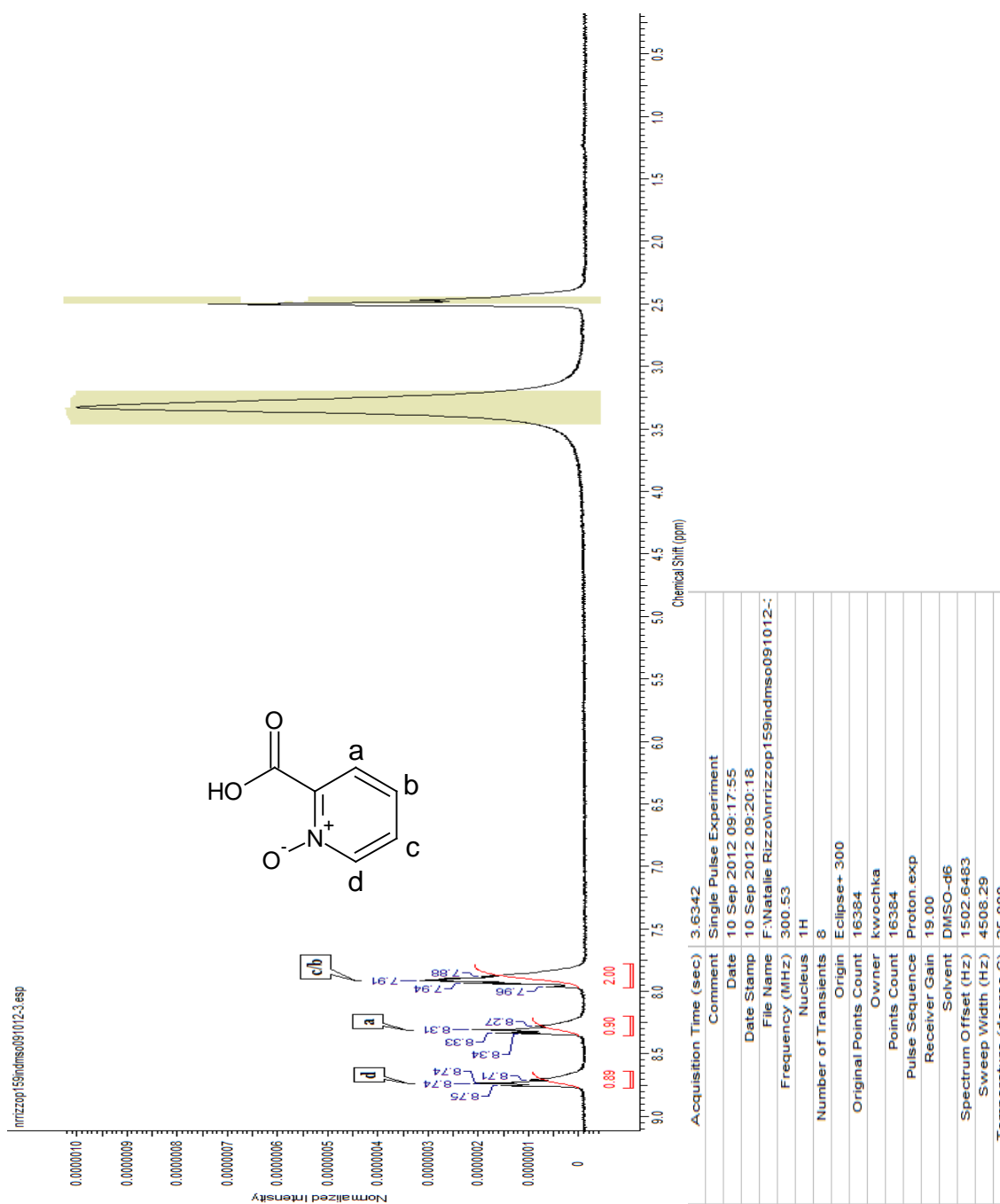
APPENDIX D: ^1H NMR AND FT-IR SPECTRA OF COMPOUND 12

Figure 42. ^1H NMR spectrum of picolinic acid *N*-oxide 12 in CDCl_3 .

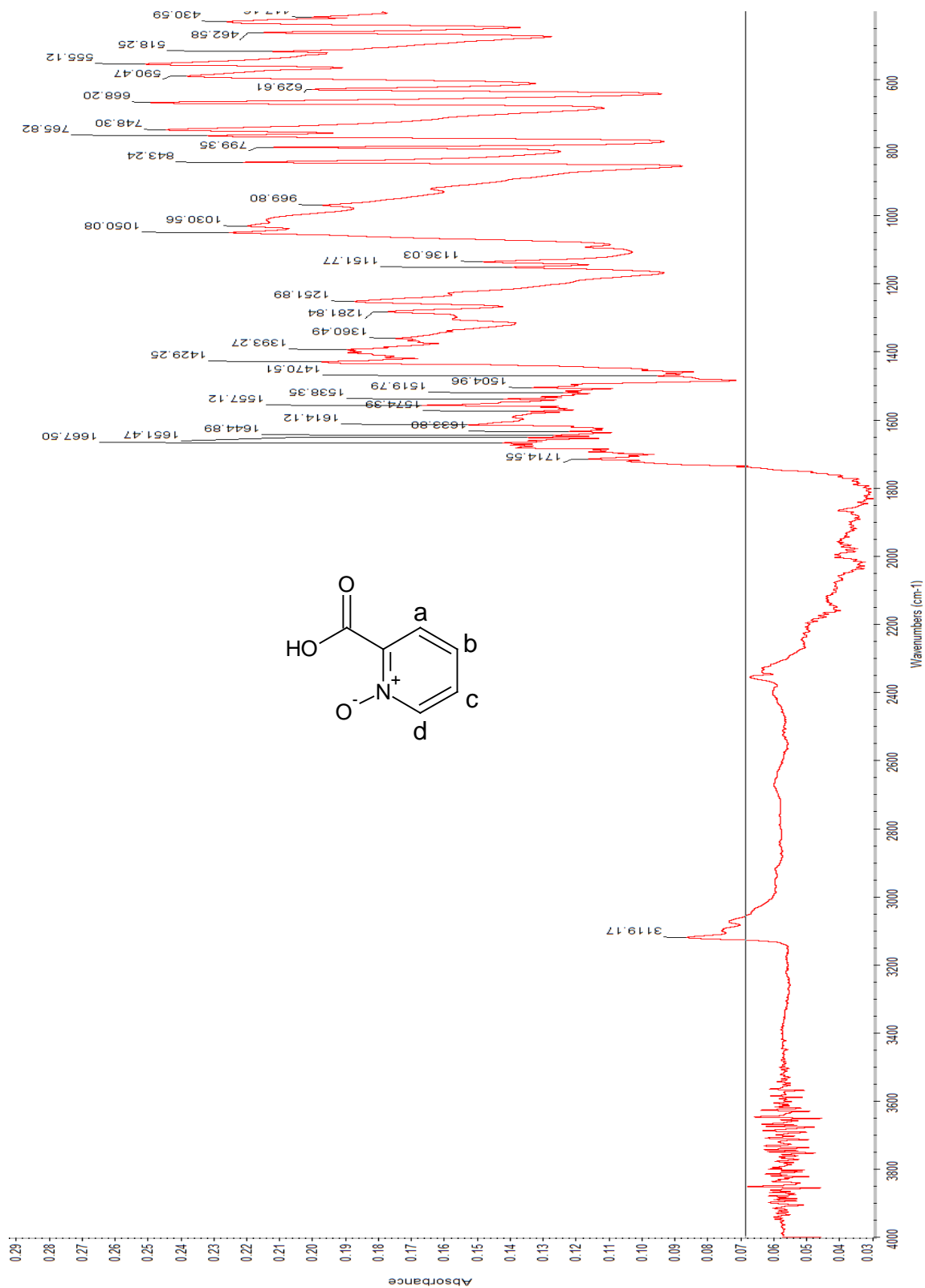
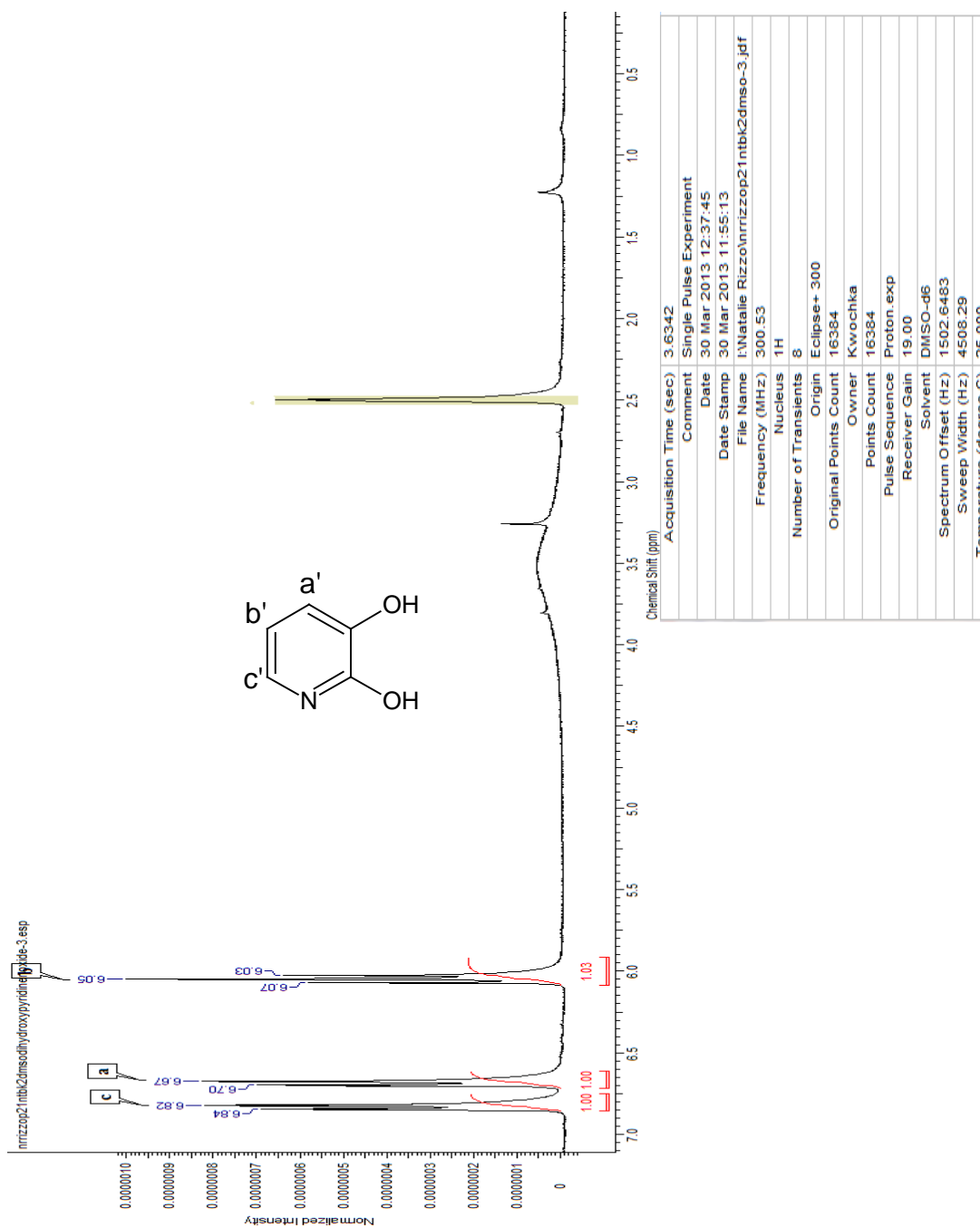


Figure 43. FT-IR spectrum of picolinic acid *N*-oxide **12**.

APPENDIX E: ^1H NMR SPECTRUM OF COMPOUND 13

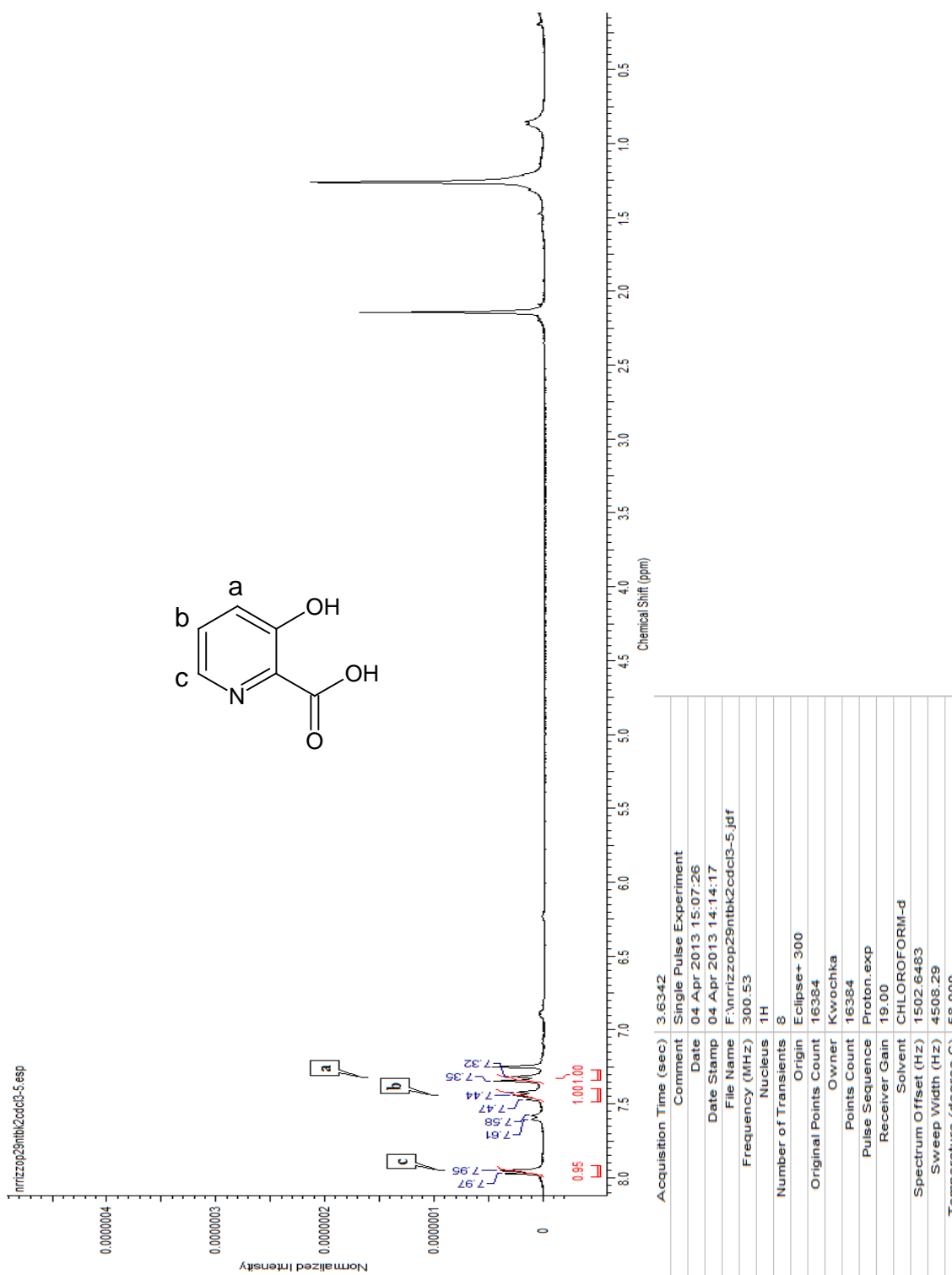
APPENDIX F: ^1H NMR AND FT-IR SPECTRA OF COMPOUND **15**

Figure 45. ^1H NMR spectrum of 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15** in CDCl_3 .

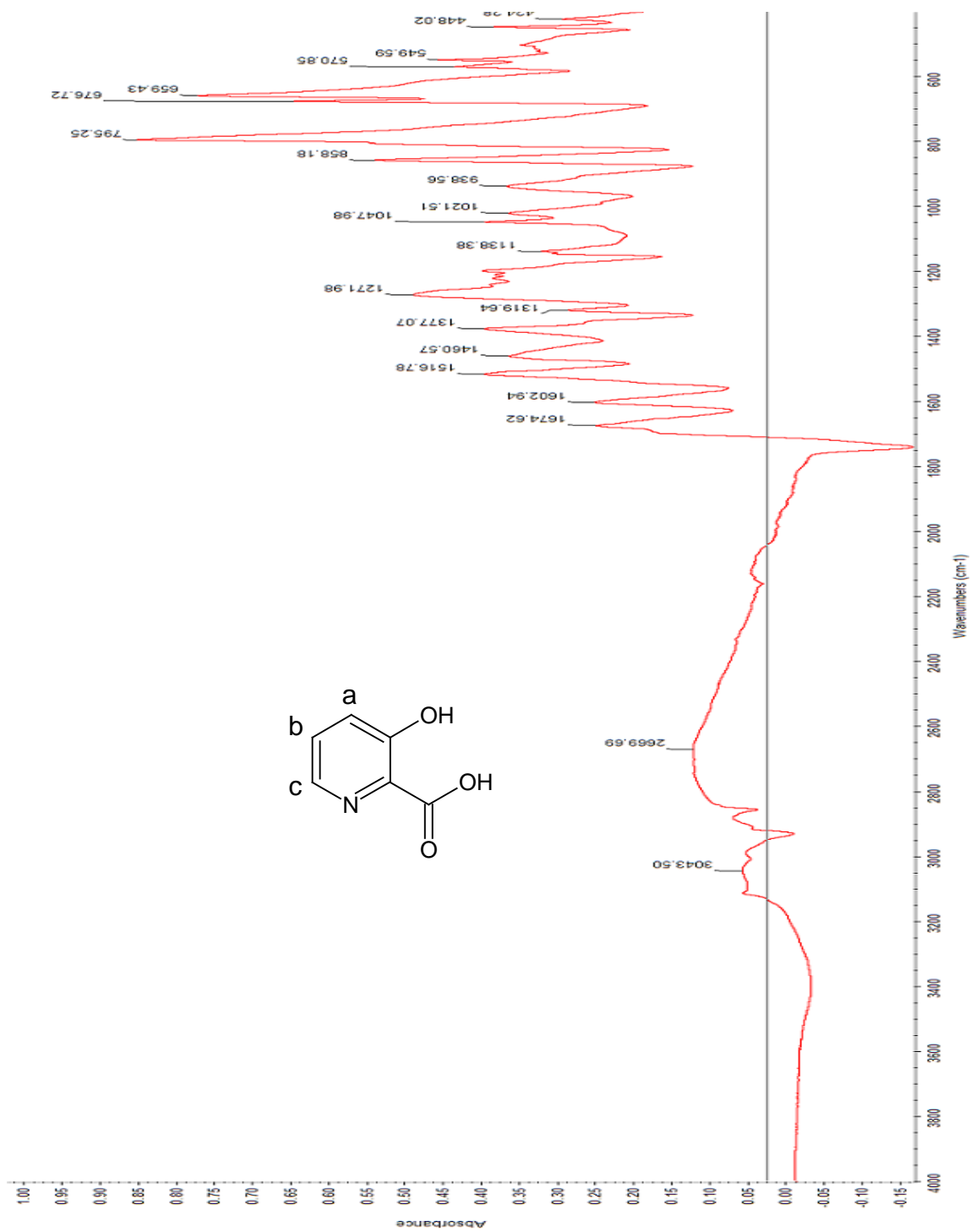


Figure 46. FT-IR spectrum of 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**.

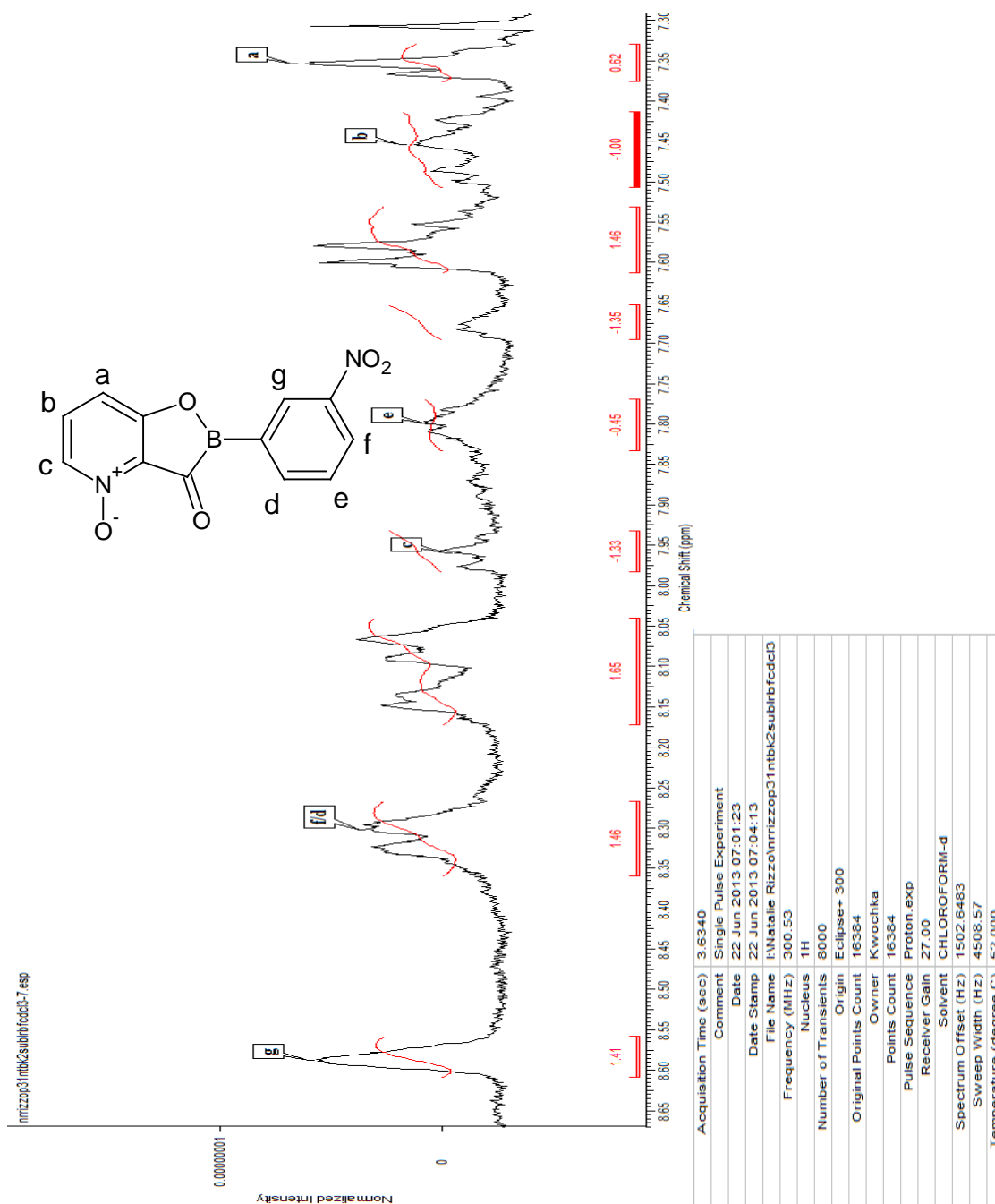
APPENDIX G: ^1H NMR, FT-IR AND GCMS SPECTRA OF COMPOUND **16**

Figure 47. ^1H NMR spectrum of compound **16** formed from 3-nitrophenylboronic acid and 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**.

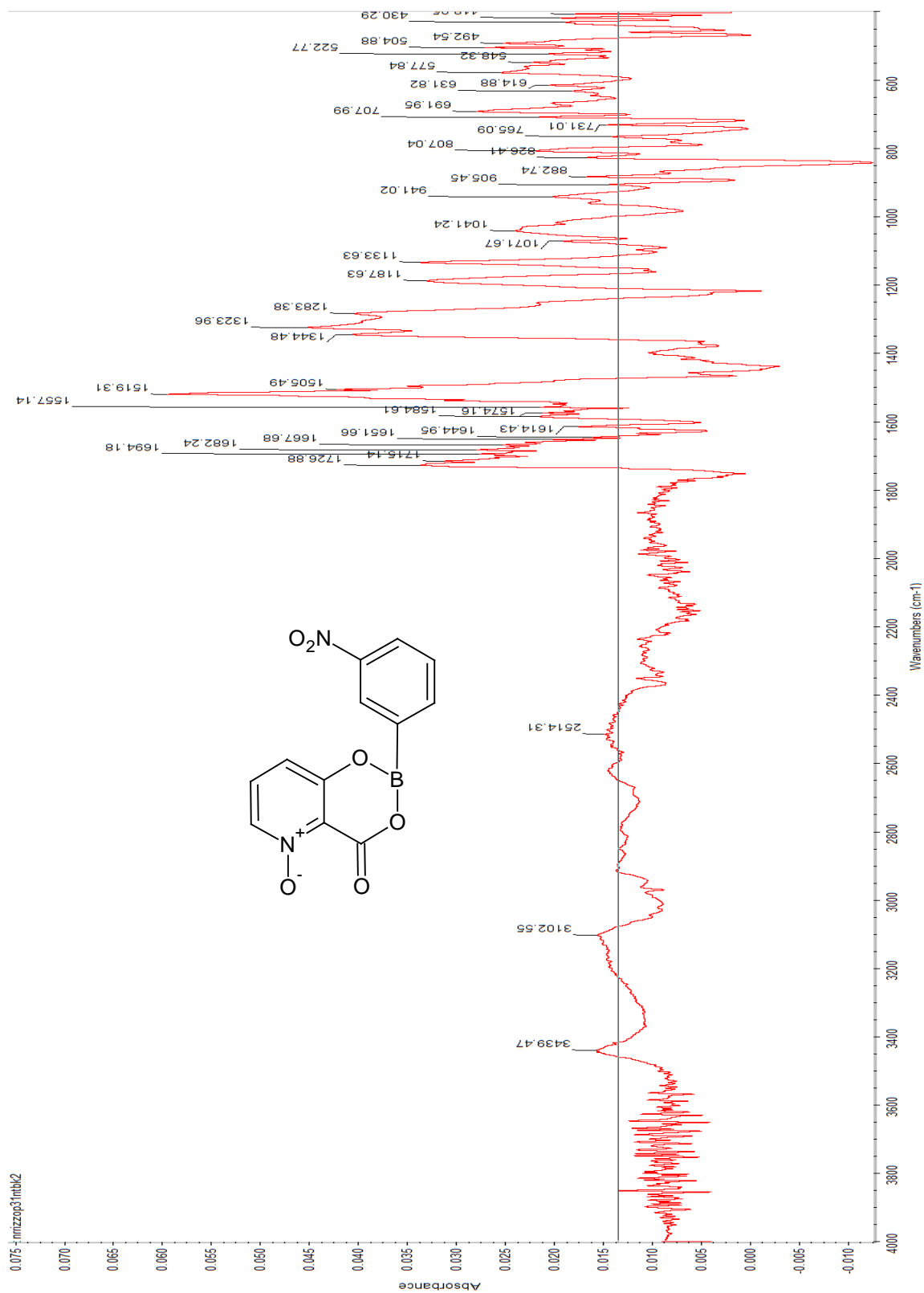


Figure 48. FT-IR spectrum of compound **16** formed from 3-nitrophenylboronic acid and 3-hydroxypyridine-2-carboxylic acid *N*-oxide **15**.

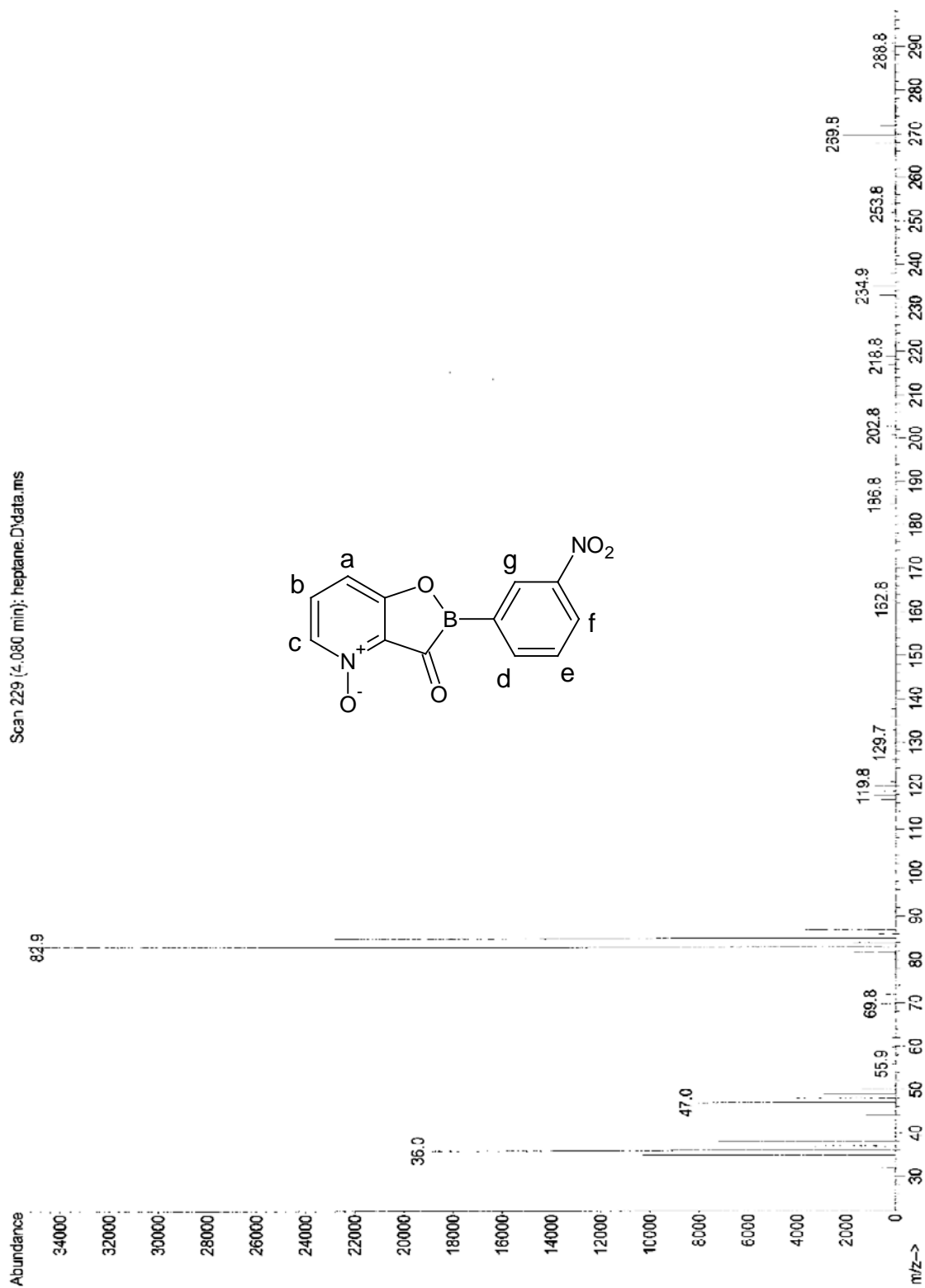


Figure 49. Mass spectrum of compound **16** formed from 3-nitrophenylboronic acid and 3-hydroxypyridine-2-carboxylic acid *N*-oxide dissolved in methanol.

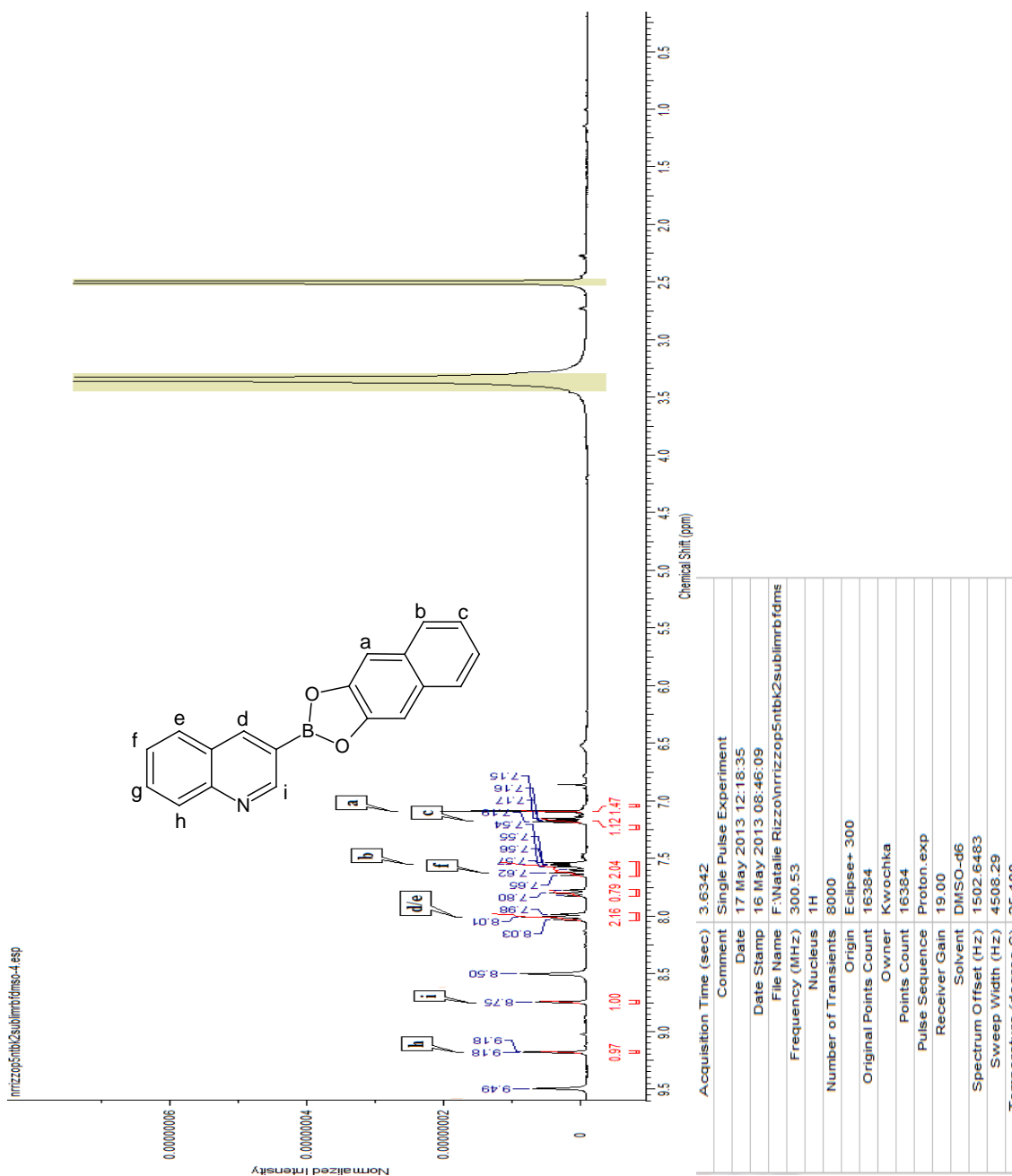
APPENDIX H: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND **20**

Figure 50. ^1H NMR spectrum of “purified” compound **20** formed from 2, 3-dihydroxynaphthalene and 3-quinoline boronic acid in DMSO- d_6 .

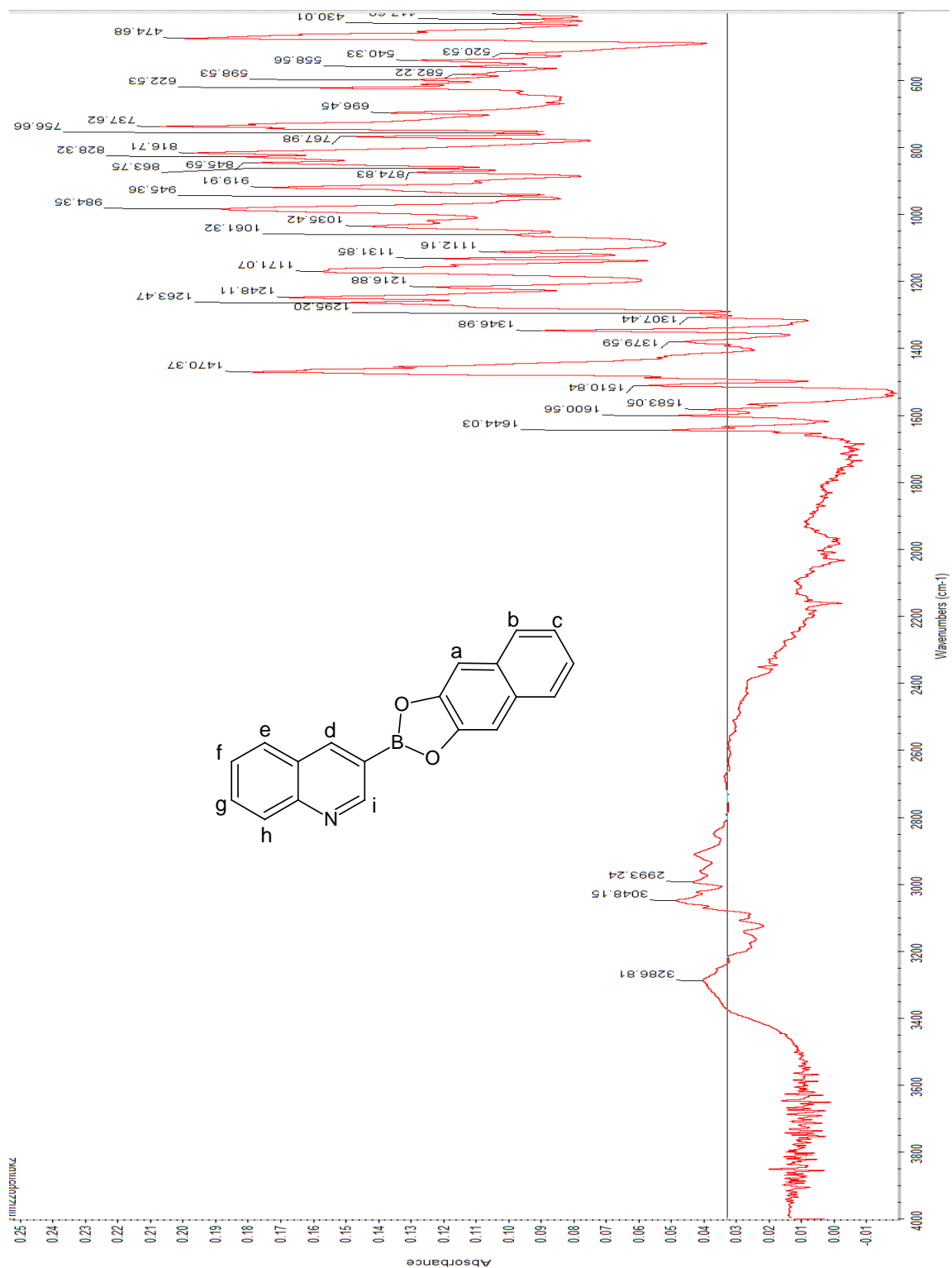


Figure 51. FT-IR spectrum of compound **20** formed from 2, 3-dihydroxynaphthalene and 3-quinoline boronic acid.

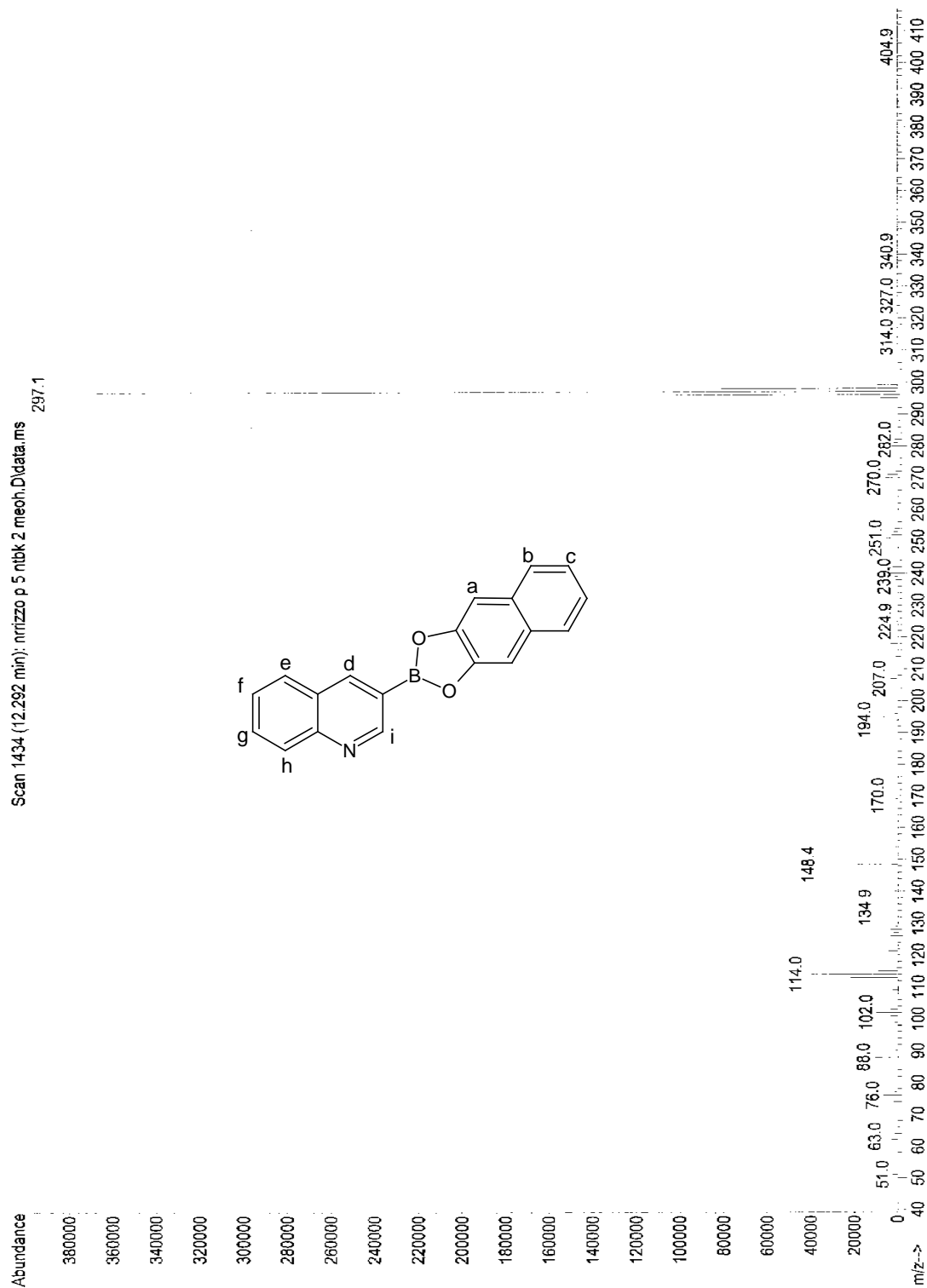


Figure 52. Mass spectrum of compound **20** formed from 2, 3-dihydroxynaphthalene and 3-quinoline boronic acid dissolved in methanol.

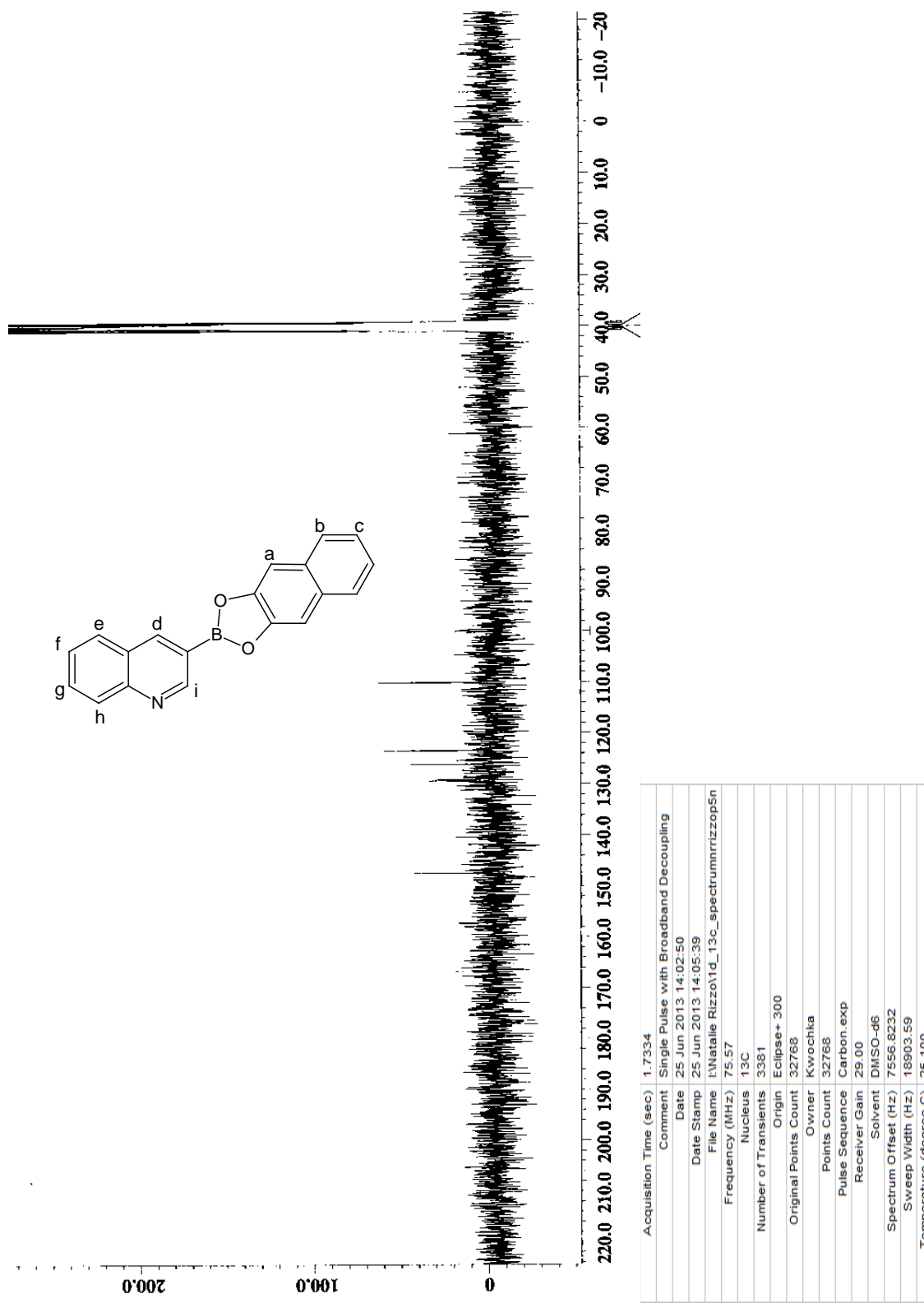


Figure 53. ¹³C NMR spectrum of compound 20 in DMSO-d₆.

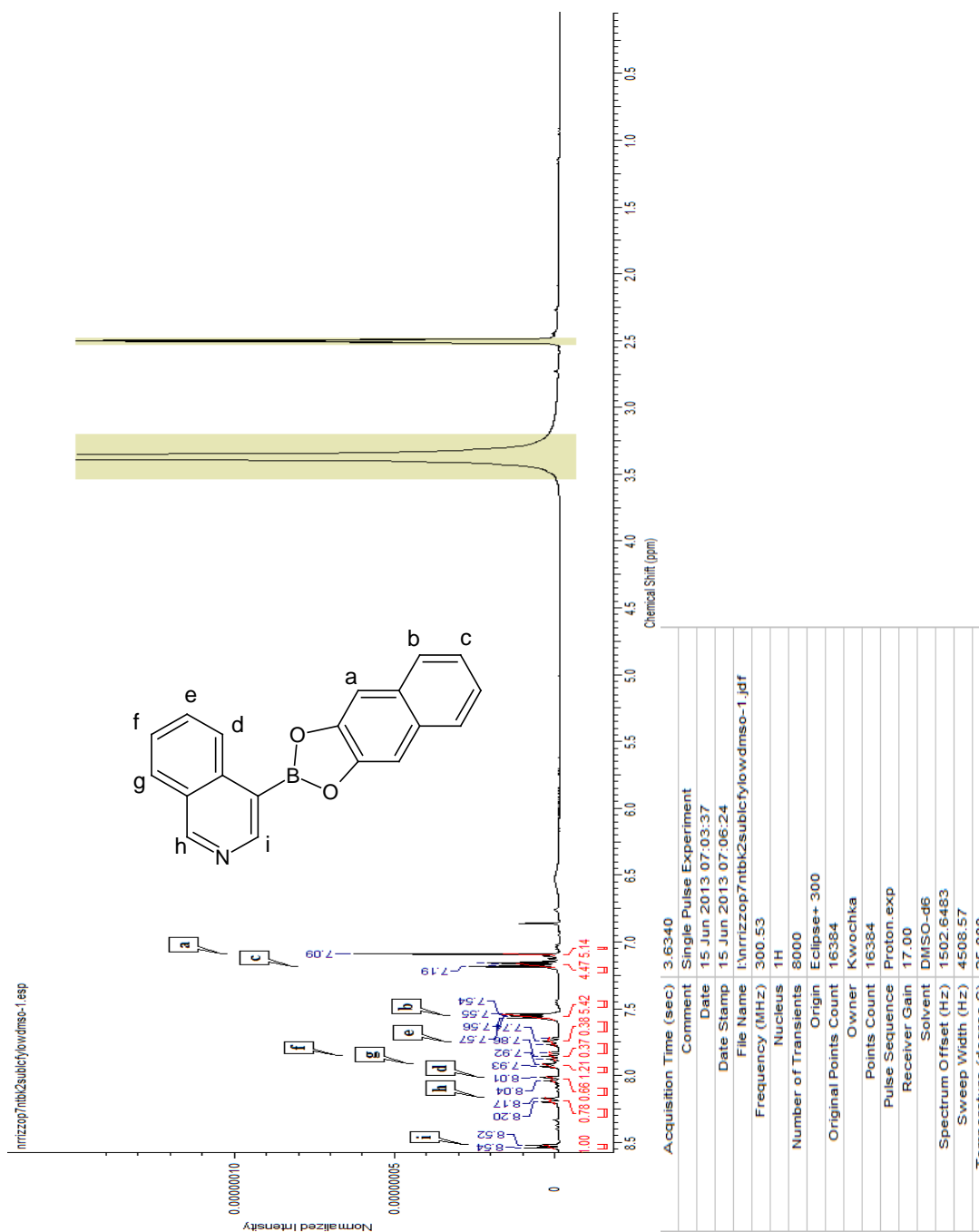
APPENDIX I: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND 22

Figure 54. ^1H NMR spectrum of “purified” compound 22 formed from 2, 3-dihydroxynaphthalene and 3-isoquinoline boronic acid in DMSO- d_6 .

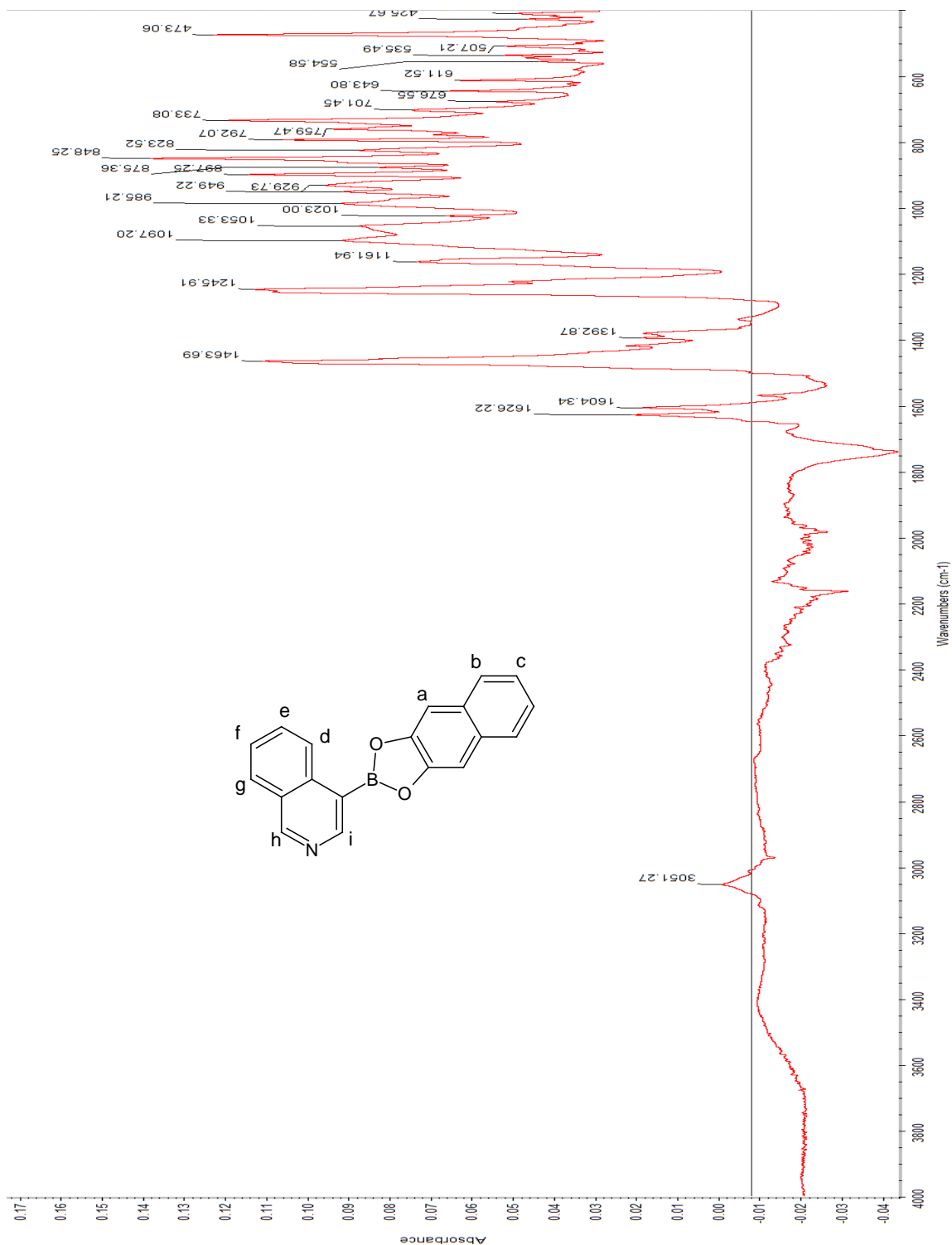


Figure 55. FT-IR spectrum of compound **22** formed from 2, 3-dihydroxynaphthalene and 3-isoquinoline boronic acid.

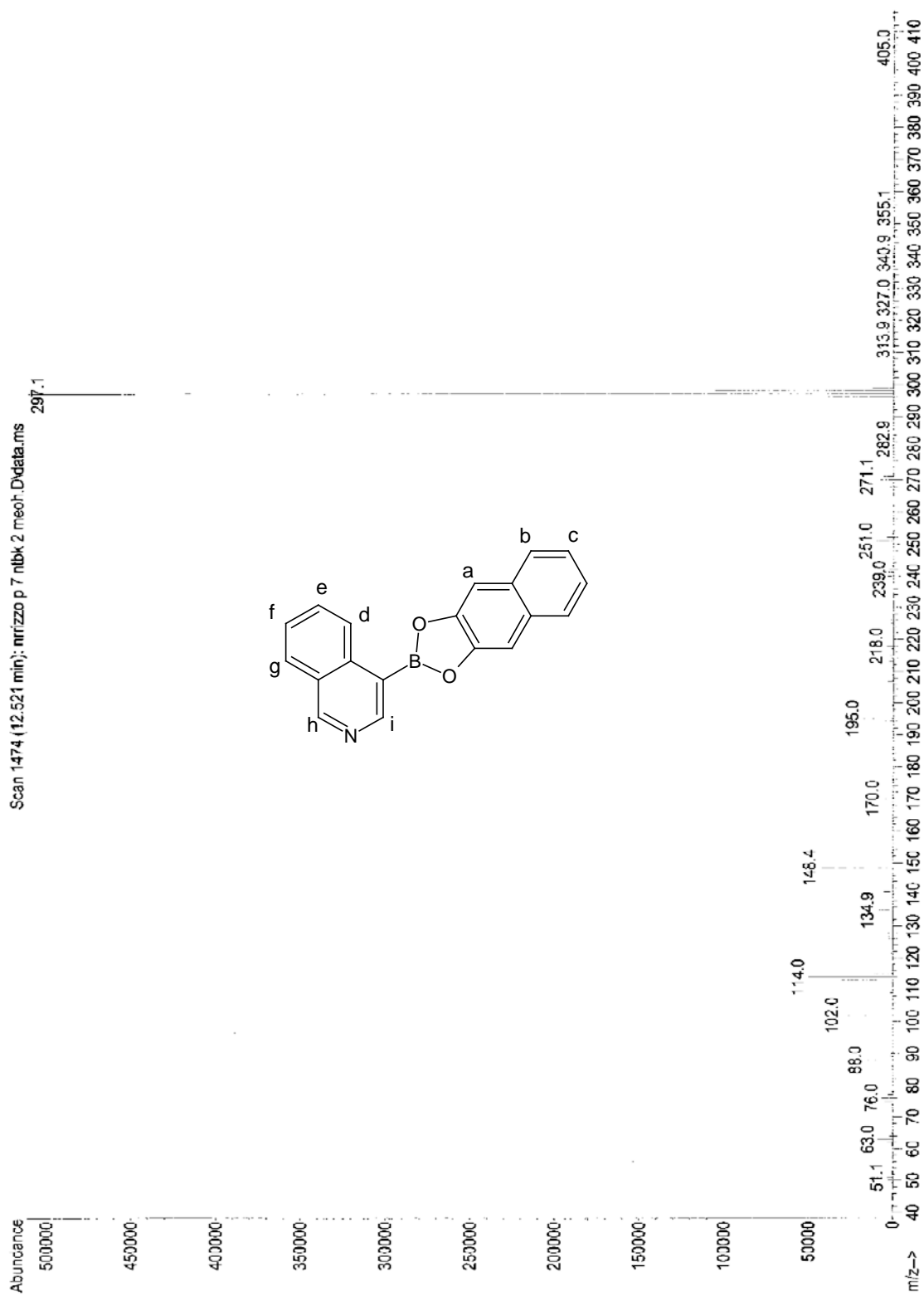


Figure 56. Mass spectrum of compound **22** formed from 2, 3-dihydroxynaphthalene and 3-isoquinoline boronic acid dissolved in methanol.

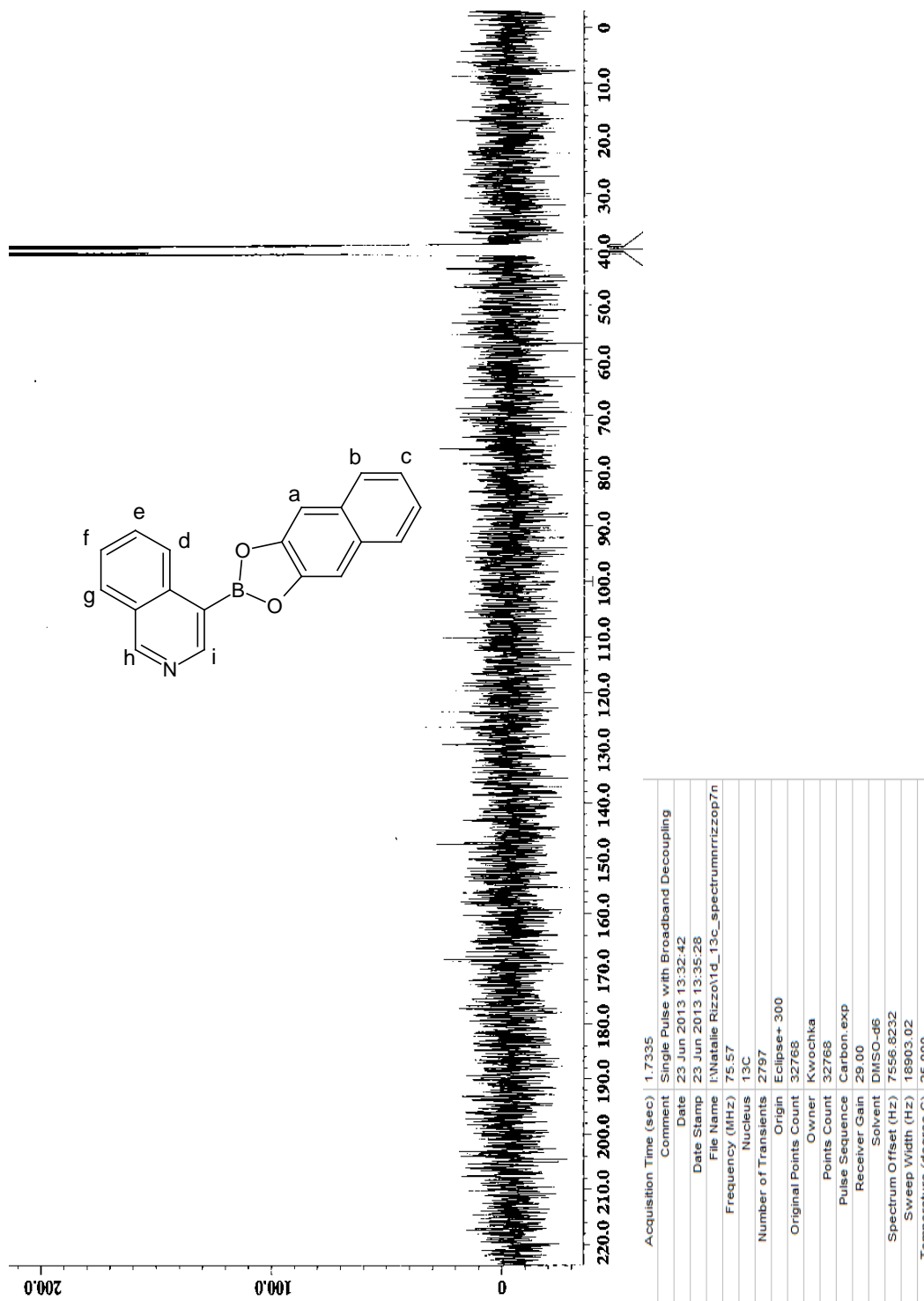


Figure 57. ¹³C NMR spectrum of compound 22 in DMSO-d₆.

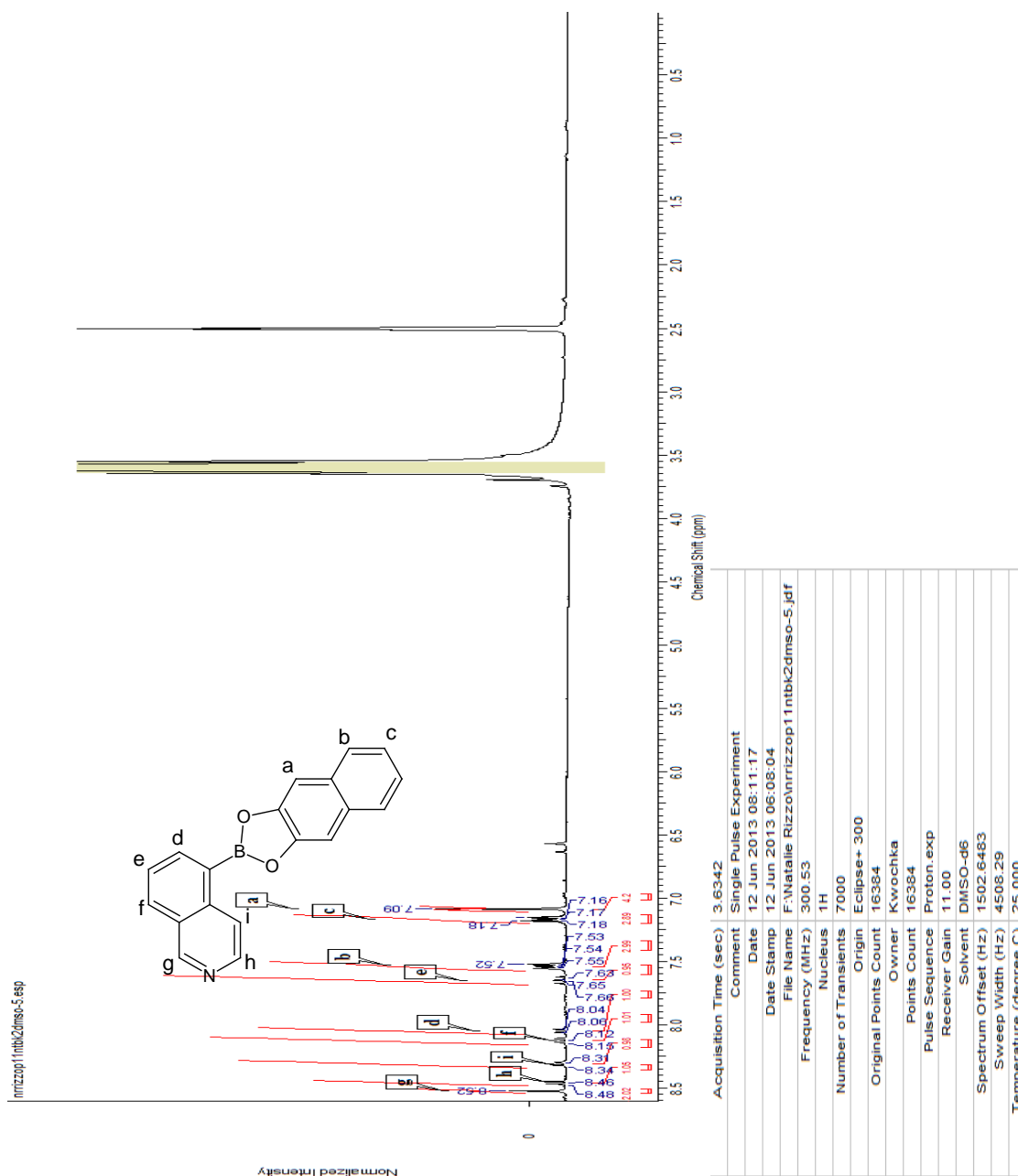
APPENDIX J: ^1H NMR, FT-IR, GCMS, AND ^{13}C NMR SPECTRA OF COMPOUND **24**

Figure 58. ^1H NMR spectrum of “purified” compound **24** formed from 2, 3-dihydroxynaphthalene and 5-isoquinoline boronic acid in DMSO- d_6 .

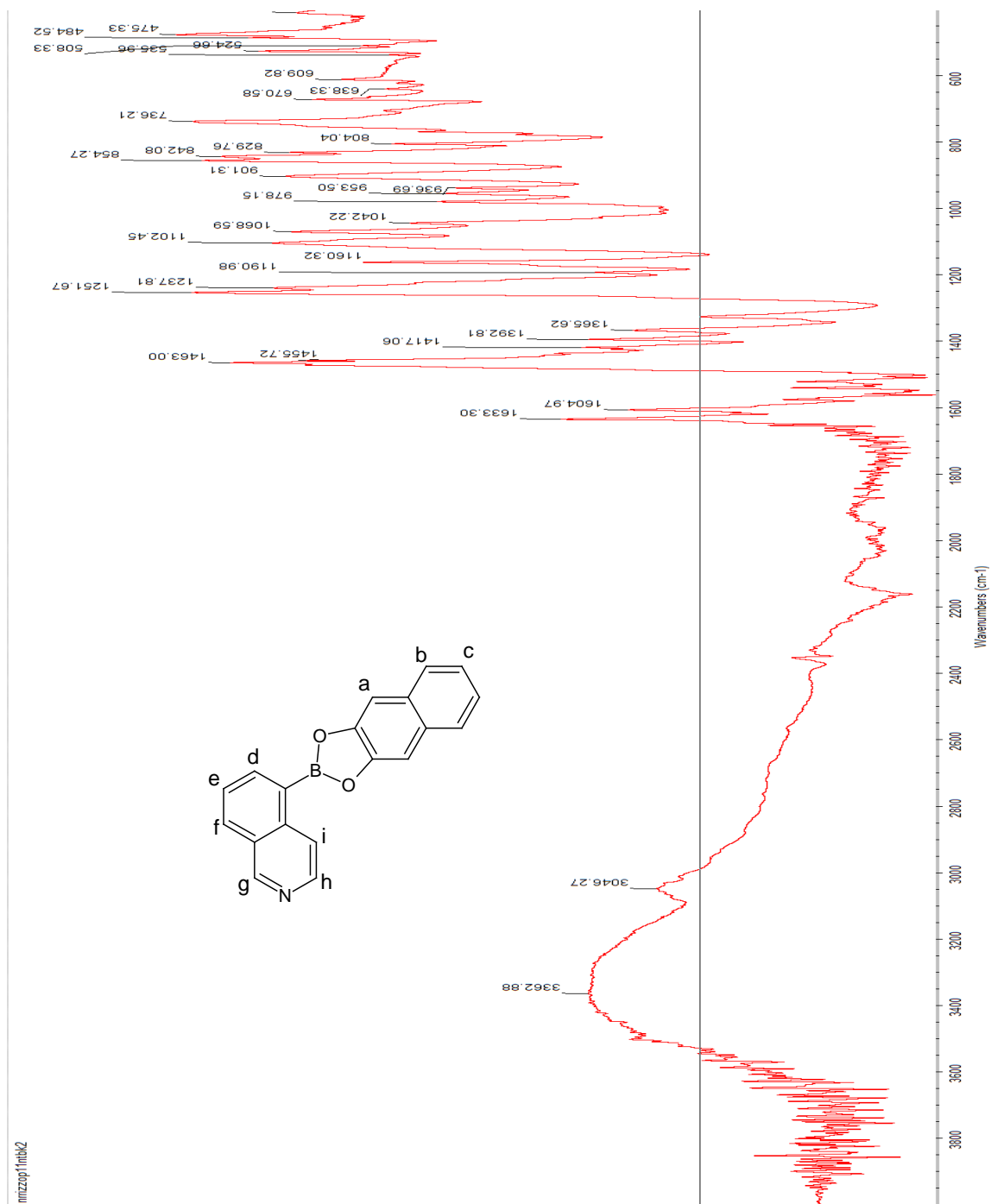


Figure 59. FT-IR spectrum of compound **24** formed from 2, 3-dihydroxynaphthalene and 5-isoquinoline boronic acid.

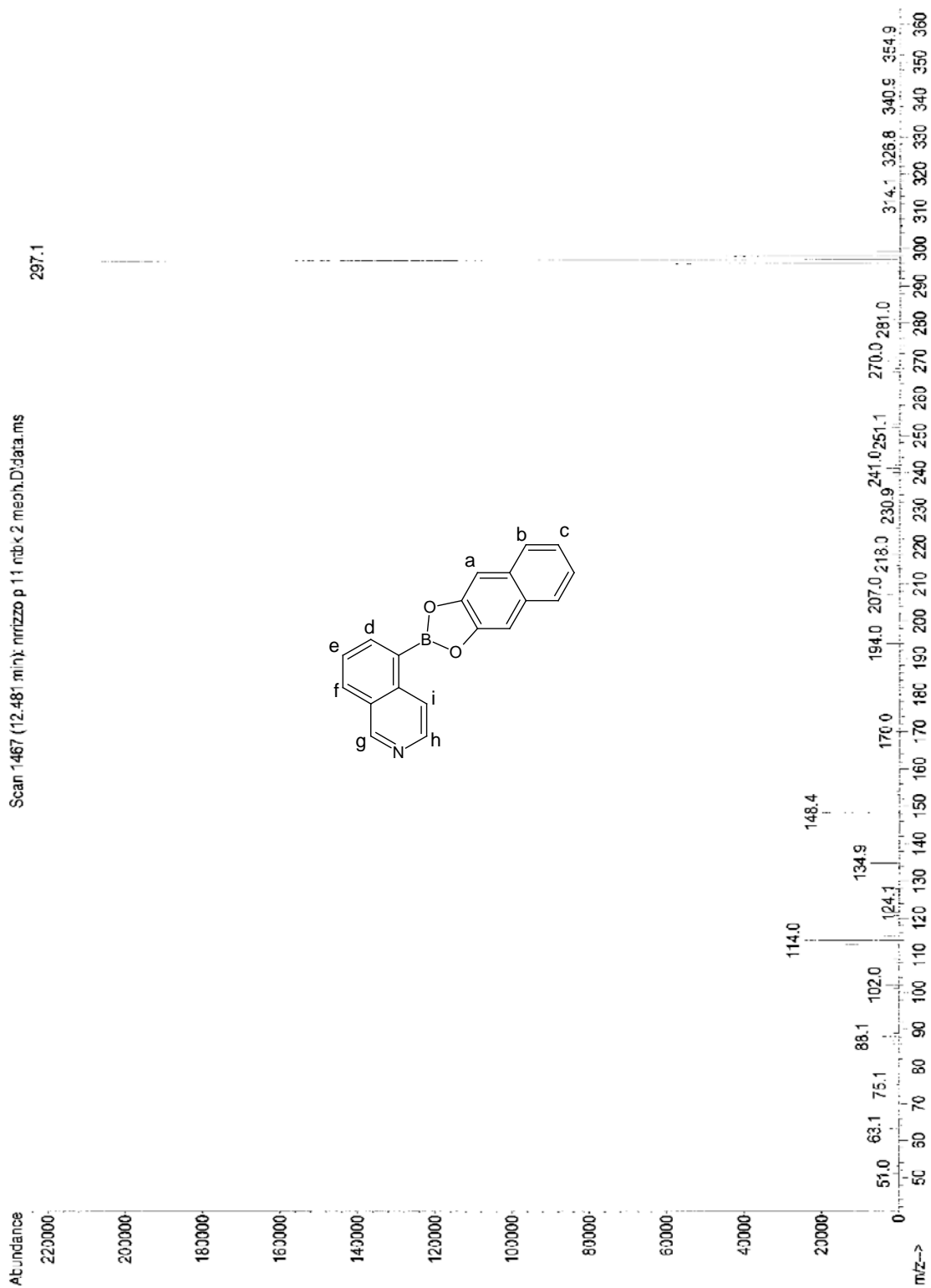


Figure 60. Mass spectrum of compound **24** formed from 2, 3-dihydroxynaphthalene and 5-isoquinoline boronic acid dissolved in methanol.

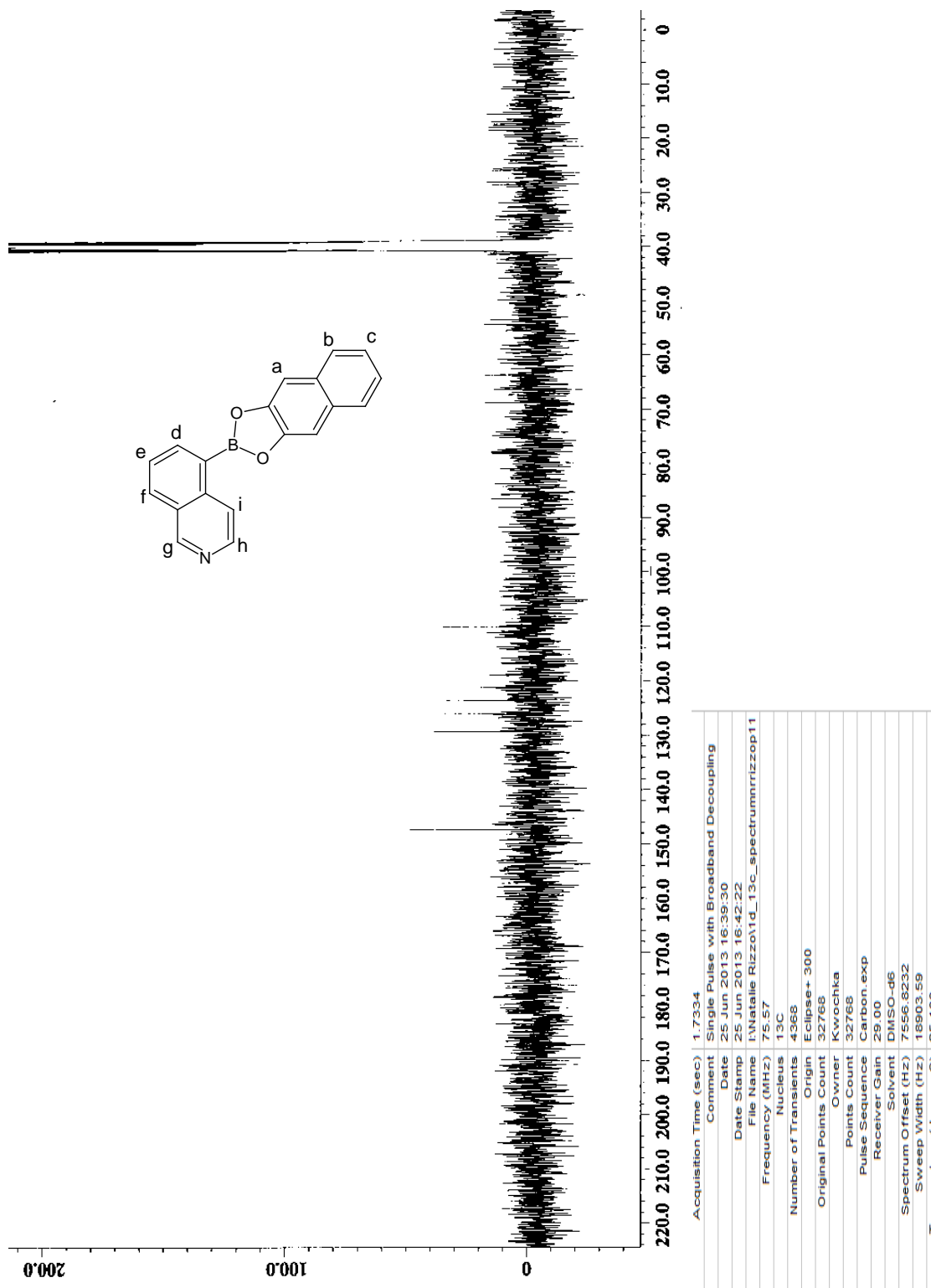


Figure 61. ¹³C NMR spectrum of compound 24 in DMSO-d₆.