# Development of New Reaction Methodologies Using Palladium Catalysts

A Dissertation

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By

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# Abstract for Dissertation

Development of New Reaction Methodologies Using Palladium Catalysts

By

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Abstract for the thesis: The dissertation begins with the introduction of C–C sigma-bond activation chemistry. The challenges of C–C sigma-bond activation are discussed. C–CN sigma-bond activation is presented as a potential possible solution to overcome the challenges of C–C sigma-bond activation. Development of new reaction methodologies intramolecular cyanoesterification and intramolecular cyanoacylation using C–CN sigma-bond activation are described.

Chapter 1: This chapter provides a brief review of the chemistry of metal catalyzed C–C sigma-bond activation reactions. Literature examples for a variety of methods to activate C–C sigma-bonds and their limitations are discussed in detail. Introduction to C–CN sigma-bond reaction and its advantages over the

typical C–C sigma-bond activation reactions are discussed with literature examples. Motivation for the current work is also presented.

Chapter 2: Presented herein development of new reaction methodology, intramolecular cyanoesterification of alkynes to synthesize highly functionalized butenolides. The reaction proceeds with commonly used palladium catalyst ($Pd(PPh_3)_4$) under microwave conditions in five minutes. The reaction tolerates wide variety of substrates and corresponding results are presented. Plausible mechanistic hypothesis is also discussed.

Chapter 3: Presented herein new methodology for intramolecular cyanoacylation of alkenes to synthesize highly functionalized indanones . The major challenge of decarbonylation has been overcome using α-iminonitriles. The reaction proceeds in the presence of commonly used palladium catalyst ($Pd(PPh_3)_4$) and very common Lewis acid $ZnCl_2$. The reaction tolerates wide variety of substrates and corresponding results are presented. Results of mechanistic study of the reaction and plausible mechanism are also presented.

Chapter 4: Presented herein our attempt towards development of intramolecular azidocyanation of alkenes using carbamoyl azides. Interestingly instead of azidoacylation product, 2-quinazolinone was isolated by the loss of $CH_2$ and $N_2$. Future work on optimization and applications of this interesting reaction are discussed

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# List of Abbreviations

| | |
|---|---|
| Ac | acetyl |
| Ar | aryl |
| Bn | benzyl |
| Boc | *tert*-butyloxy carbonyl |
| bu | Butyl |
| $^{t}$Bu | *tert*-butyl |
| CDI | carbonyldiimidazole |
| cod | 1,5-cyclooctadiene |
| Cp* | petamethylcyclopentadienyl |
| Cy | cyclohexyl |
| DCE | 1,2-dichloroethane |
| DCM | dichloromethane |
| DIBAL-H | diisobutyl aluminium hydride |
| DMAP | 4-dimethylaminopyridine |
| DMF | *N,N*-dimethylformamide |
| dppb | 1,4-bis(diphenylphophino)butane |
| dppp | 1,3-bis(diphenylphosphino)propane |
| Et | ethyl |
| Hex | hexane |
| IBX | 2-iodoxybenzoicacid |
| LDA | lithium diisopropylamide |
| Me | methyl |

| | |
|---|---|
| nbd | norbornadiene |
| NBS | *N*-bromosuccinimide |
| PEPPSI | pyridine-enhanced precatalyst preparation stabilization and initiation |
| Ph | Phenyl |
| Py | pyridine |
| PTSA | *para*-toluenesulfonic acid |
| TBAB | tetrabutyl ammonium bromide |
| THF | tetrahydrofuran |
| Tf | trifluoromethanesulfonyl |
| TMS | trimethylsilyl |
| TPP | tetraphenyl porphyrin |
| Ts | *para*-toluenesulfonyl |

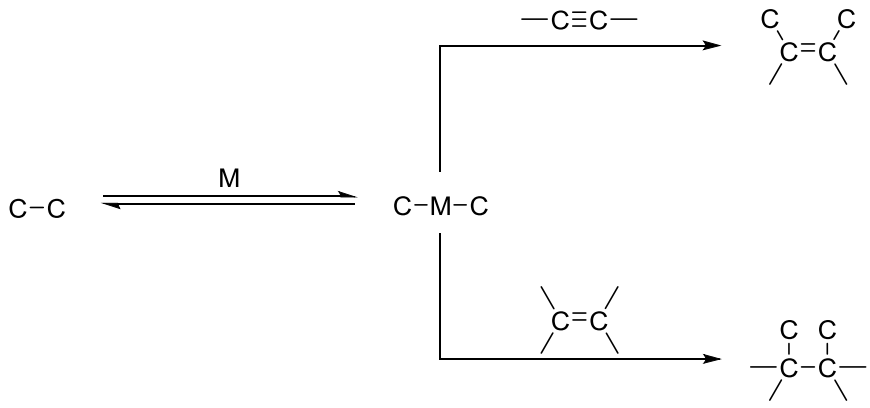
# Chapter 1

# Introduction

## 1.1 Introduction to C–C sigma-bond activation

Organic synthesis is the construction of complex molecules from simple and readily available molecules. The simple molecules are joined by forming new chemical bonds, most often using C–C bonds to build complex molecules. Various efficient methods have been developed to construct new C–C bonds over the last few decades. Examples of some of them are Aldol reaction,[1] Diels-Alder reaction,[2] metathesis reaction,[3] cross coupling reactions,[4] C–H activation.[5] These methods have been extensively developed and successfully used in the synthesis of new compounds that have broad applications in the pharmaceutical, material and agricultural industries.[6]

Though many methods have been developed for the construction of new C–C bonds, there is always potential importance for the atom economical and ingenious new methods for making new C–C bonds. Among these methods is transition metal catalyzed C–C sigma-bond activation. C–C sigma-bond activation and subsequent insertion across carbon–carbon π-bonds would make products with two new carbon–carbon bonds with high atom economy (Scheme 1.1). Also, the products formed by C–C sigma-bond activation may be difficult to synthesize by conventional organic synthesis.[7] A few examples are illustrated in the later part of the chapter.



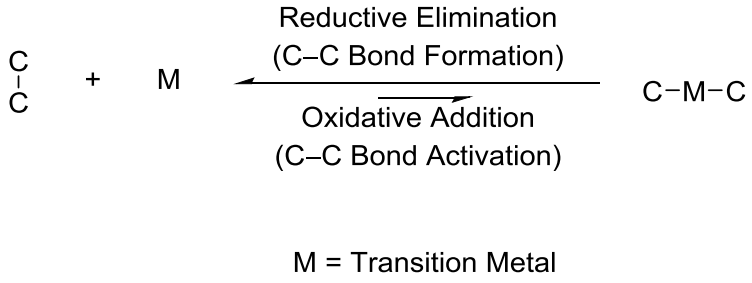

M = Transition Metal

**Scheme 1.1**: Importance of C–C sigma-bond Activation

In spite of the advantages, transition metal catalyzed C–C sigma-bond activation is underdeveloped compared to C–H activation. One reason for this is the higher activation barrier for C–C sigma-bond activation compared to C–H sigma-bond activation.[8] Theoretical calculations also suggest that the typical activation energy of C–C sigma-bond is generally higher than C–H sigma-bond. For instance activation energies of C–C sigma-bond and C–H sigma-bond of ethane for first row (3d) transition metals are 40-45 kcal/mol and 20-25 kcal/mol. For second row transition metals (4d) the activation energies for C–C sigma-bond and C–H sigma-bond of ethane are 13-27 kcal/mol$^{-1}$ and 0-9 kcal/mol.[9] The higher activation barrier for C–C sigma-bond activation and statistical abundance of C–H sigma-bonds over C–C sigma-bonds makes C–H activation more favorable than the C–C activation. Also, in general M–H (M = transition metal)

bonds are significantly stronger than M–C bonds in alkyl metal complexes, which makes C–H activation more thermodynamically favorable than C–C activation.[10]

Another barrier for the C–C sigma-bond activation by transition metal is the thermodynamic stability of C–C sigma-bond.[11] The typical strength of M–C bond is about 20-30 $kcalmol^{-1}$ and C–C bond is about 90 $kcalmol^{-1}$. Consequently a C–C sigma-bond is stronger than two M–C bonds by a minimum of 30 kcal/mol. Hence the activation of C–C bond by transition metal to form two M–C bonds (oxidative addition) is thermodynamically unfavorable compared to reverse process of forming C–C sigma-bond from two M–C bonds (reductive elimination) by a minimum of 30 kcal/mol. This makes the equilibrium of C–C sigma-bond activation lie significantly towards the formation of C–C sigma-bond in most cases (Scheme 1.2).




**Scheme 1.2**: Equilibrium of C–C Sigma-bond Activation

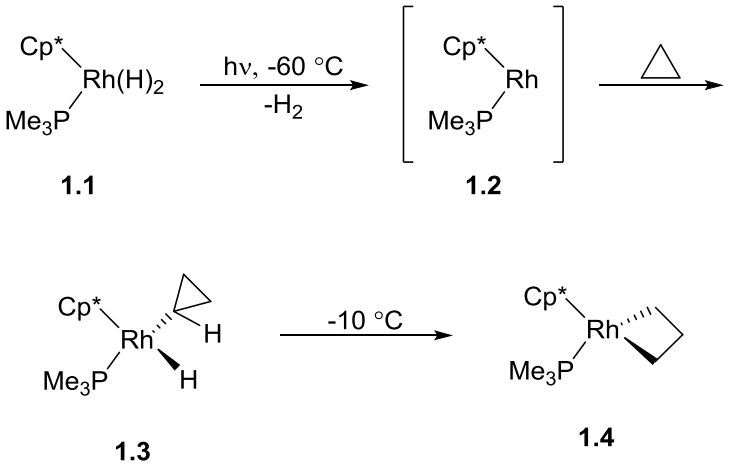
The challenges of C–C sigma-bond activation can be overcome by adopting two different strategies. One strategy is to increase the energy of the

C–C sigma-bond of the starting materials which would decrease the activation energy and facilitate C–C sigma-bond activation. This can be done using angle strain or using starting materials having a reactive C–C sigma-bond (which will be discussed in detail in the later part of the section). Another strategy is to form stabilized products after the C–C sigma-bond cleavage.

## 1.2 Precedence

### C–C sigma-bond activation using strained systems

The inherent stability of C–C sigma-bond makes it difficult to activate by transition metals. To overcome this challenge high energy starting materials like strained cyclopropane and cyclobutane systems have been used. Due to the high inherent strain energy in these systems it requires lower activation energy and also relief of ring-strain compensates for the thermodynamic disadvantage of C–C sigma-bond activation. Periana and Bergman reported C–C sigma-bond activation of cyclopropane using rhodium dihydride complex **1.1** (Scheme 1.3).[12] Upon ultraviolet irradiation at -60 $^{o}$C rhodium dihydride complex **1.1** liberates $H_2$ and forms coordinatively unsaturated complex **1.2**. Subsequently it reacts with cyclopropane to give complex **1.3** *via* C–H bond activation. Upon warming to -10 $^{o}$C, it undergoes C–C sigma-bond activation and leads to thermodynamically more stable four membered metalacycle complex **1.4**.



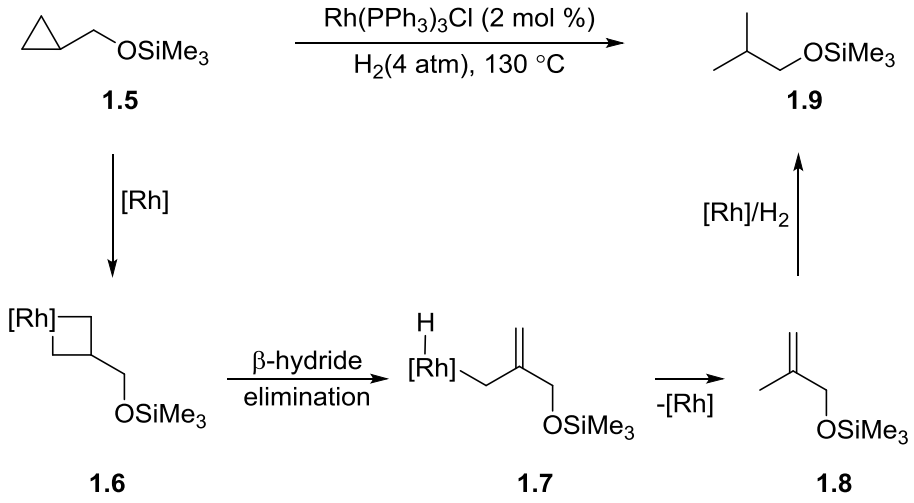

Cp* = $\eta^5$-$C_5Me_5$

**Scheme 1.3**: C–C Sigma-bond Activation of Cyclopropane

This strategy though successful in accomplishing C–C sigma bond activation, requires a stoichiometric amount of transition metal which is not economically viable. The high stability of intermediate transition metal complex (**1.4** in Scheme 1.3) possibly is the reason for the difficulty in converting the stoichiometric reaction to a catalytic reaction. The reaction can be made catalytic by having an energy releasing step subsequent to the formation of C–C sigma-bond activation (for instance after **1.4** Scheme 1.3). This would lead to the formation of thermodynamically more stable products and regeneration of the metal which can be further used in reaction cycles.[11b]

Bart and Chirik reported catalytic C–C sigma-bond activation of cyclopropane system using Wilkinson's catalyst.[13] The reaction begins with the

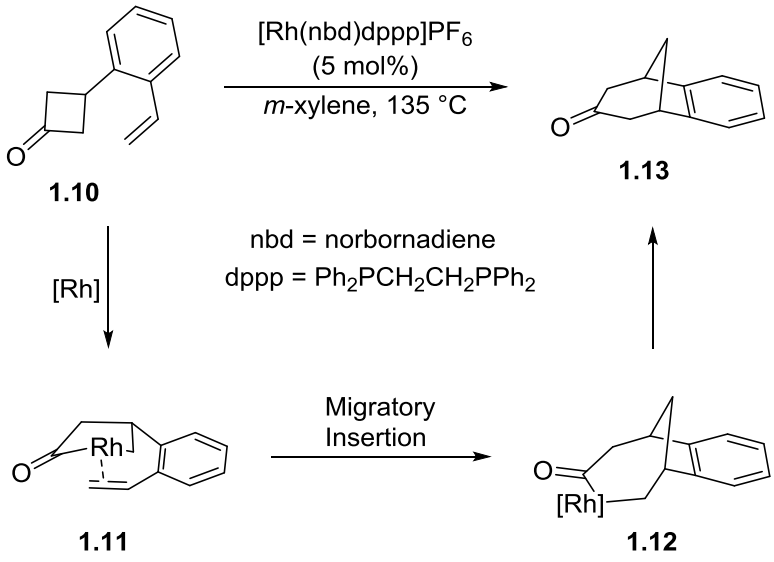
activation of less hindered C–C sigma-bond of cyclopropane ring of **1.5** to form four membered rhodium complex **1.6** (Scheme 1.4). β-hydride elimination of complex **1.6** leads to the rhodium hydride complex **1.7** and subsequent reductive elimination gives branched olefin **1.8** and regenerates the catalyst. The formation of thermodynamically stable olefin **1.8** drives the reaction forward. In the absence of hydrogen gas the reaction stops at olefin **1.8** and if the reaction is performed under hydrogen pressure, reduction of the double bond occurs to give compound **1.9**.




**Scheme 1.4**: Catalytic C–C Sigma-bond Activation

Murakami and coworkers used the C–C sigma-bond activation of strained systems to increase molecular complexity by inserting an olefin into the C–C sigma-bond (Scheme 1.5).[14] When the compound **1.10** was heated with rhodium

catalyst, it inserts into C–C sigma-bond (oxidative addition) of the strained cyclobutanone to form more stable five-membered rhodium complex **1.11**. Complex **1.12** undergoes migratory insertion onto tethered alkene to give seven membered complex **1.12** which upon reductive elimination gives bicyclic compound **1.13**.

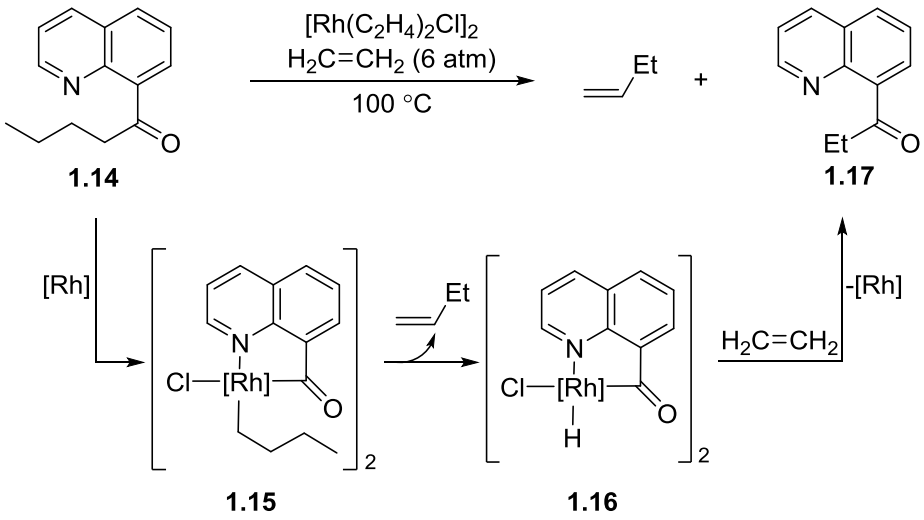



**Scheme 1.5**: Alkene Insertion into Activated C–C Sigma-bond

Another important point to be noted is that if compound **1.13** has to be synthesized by conventional organic synthesis cyclobutanone **1.10** may not be first choice. Thus C–C sigma-bond activation provides non-traditional routes to synthesize complex molecules.

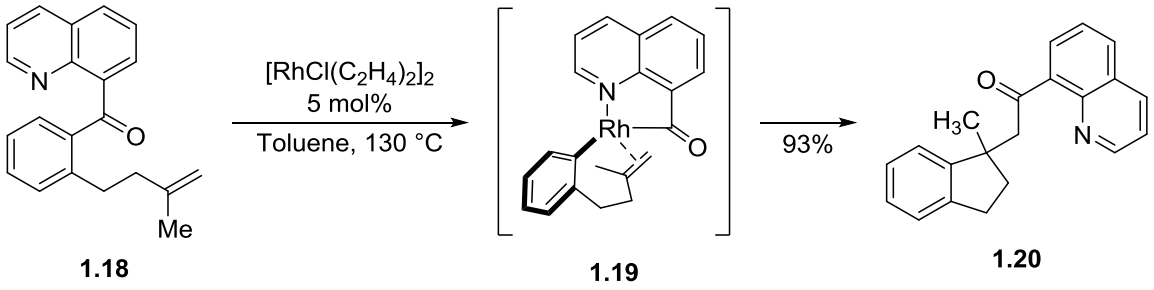
**Substrate Directed C–C Sigma-bond Activation**

The major limitation of the strategy discussed in the previous examples is that it is limited to strained systems. Another strategy that overcomes this challenge was developed by Suggs and Jun. They used 8-quinoline as directing group to activate a C–C sigma-bond of unstrained systems (Scheme 1.6).[15] The nitrogen of 8-acylquinoline in **1.14** coordinates to rhodium and brings it to close proximity to the C–C sigma-bond between the carbonyl and its alpha carbon. This facilitates the activation of the C–C sigma-bond and forms a five-membered metallacycle **1.15** by C–C sigma-bond activation. Rhodium complex **1.15** then undergoes β-hydride elimination to form rhodium hydride complex **1.16** and 1-butene. Intermediate **1.16** undergoes migratory insertion of an olefin onto ethylene and subsequent reductive elimination gives 8-quinolinyl ethyl ketone **1.17** as final product. However, the migratory insertion to form alkyl ketones after C–C activation (**1.16**→**1.17**) is limited to only ethylene. Use of other alkenes other than ethylene is inefficient possibly due to faster β-hydride elimination over reductive elimination.




**Scheme 1.6**: Chelation Assisted C–C Sigma-bond Activation

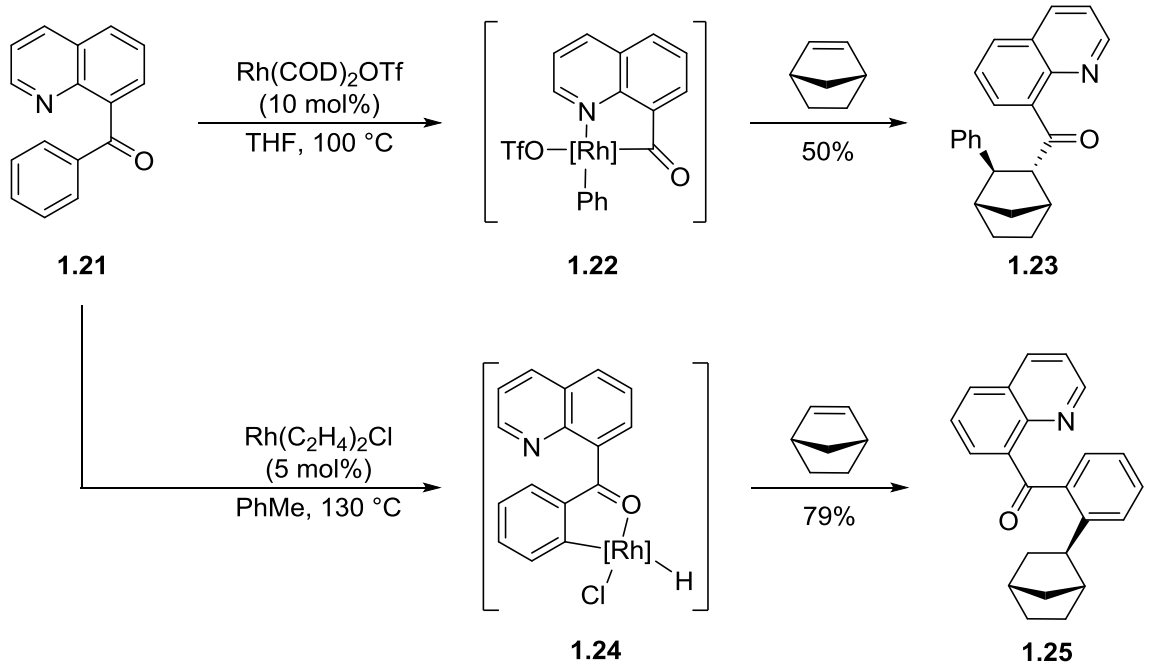
Though the work of Jun and Suggs is pioneering, the products formed are either equal or less complex than the staring material. Our group recently reported intramolecular carboacylation of alkenes *via* C–C sigma-bond activation using 8-quinoline as directing group (Scheme 1.7).[16] Nitrogen of the 8-quinoline ring in compound **1.18** coordinates to rhodium complex and facilitates C–C activation to form metallacyclic complex **1.19** where rhodium coordinates to the alkene. Intermediate **1.19** then undergoes migratory insertion onto the alkene and subsequent reductive elimination gives dihydroindene **1.20** in high yield. The products formed in this reaction are of higher complexity than the starting materials. This pathway is useful to synthesize dihydroindenes and similar heterocycles containing all-carbon quaternary center.




**1.18** **1.19** **1.20**

**Scheme 1.7**: Intramolecular Carboacylation Using 8-quinoline as Directing Group

Our group has also reported intermolecular carboacylation of alkenes using quinoline as the directing group (Scheme 1.8).[17] When 8-benzoyl quinoline **1.21** heated with $Rh(cod)_2OTf$ and norbonene at 100 $^oC$ in THF it undergoes C–C sigma-bond activation to form a five-membered rhodium complex **1.22**. Intermediate **1.22** undergoes migratory insertion onto norbornene and subsequent reductive elimination gave carboacylation product **1.23**. Initially *syn* product is formed upon reductive elimination which isomerizes under reaction condition to form *anti* product **1.23**. It is very interesting to note that the nature of counter ion (triflate) and solvent (THF) in very important for the formation of C–C activation product **1.23**. When the reaction is carried out in the presence different rhodium catalyst $[Rh(C_2H_4)_2Cl]_2$ (with counterion as chloride) in a non-polar solvent like toluene at 130 $^oC$ (conditions used for intramolecular carboacylation in Scheme 1.7) it undergoes C–H activation to form rhodium complex **1.24** which upon addition across norbonene gives hydroarylation product **1.25**.




**Scheme 1.8**: Intermolecular Carboacylation of Alkenes Using Directing Group

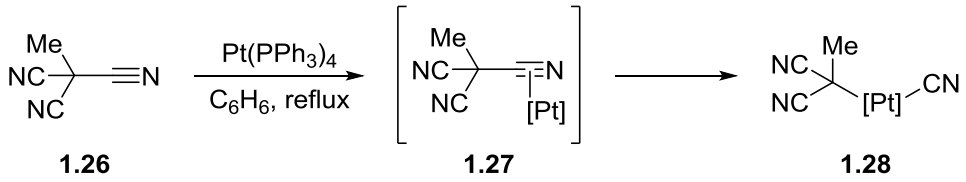
## 1.3 Introduction to C–CN Activation

C–C sigma-bond activation using directing groups though is very advantageous in constructing new C–C bonds, the major limitation of the strategy is the presence of the directing group in the starting material and product. The directing group may not be present in many target molecules. Implanting and removing of directing groups require additional steps which impact the yield and efficiency of the overall synthesis. Hence methods directed towards the activation of unstrained C–C sigma-bonds without the requirement of directing group in the starting material would be valuable.[18] Particularly methods aimed towards

activation of already functionalized C–C sigma-bonds would be very beneficial as the functionality retained in the final products could be further used to build molecular complexity. Among this class of C–C sigma-bond activation reactions is C–CN sigma-bond activation. The C–CN sigma-bond is polar making it more reactive than an unpolarized C–C bond. This effect makes its activation easier and selective over other unpolarized C–C sigma-bonds present in the molecule.[19] The activation is also facilitated by the ability of nitrile to coordinate to the metal center in $\eta^2$ fashion employing the π-bond of nitrile which makes oxidative addition kinetically favorable.[20] Also M–CN bond is believed to be stronger than typical M–C bond which makes the process thermodynamically favorable than normal C–C sigma bond activation.[21] In addition to the ease of activation, the resultant products of C–CN sigma-bond activation retain the nitrile functional group, which can be converted to variety of different functional groups like amines, aldehydes, carboxylic acids and amides.

## 1.4 Precedence

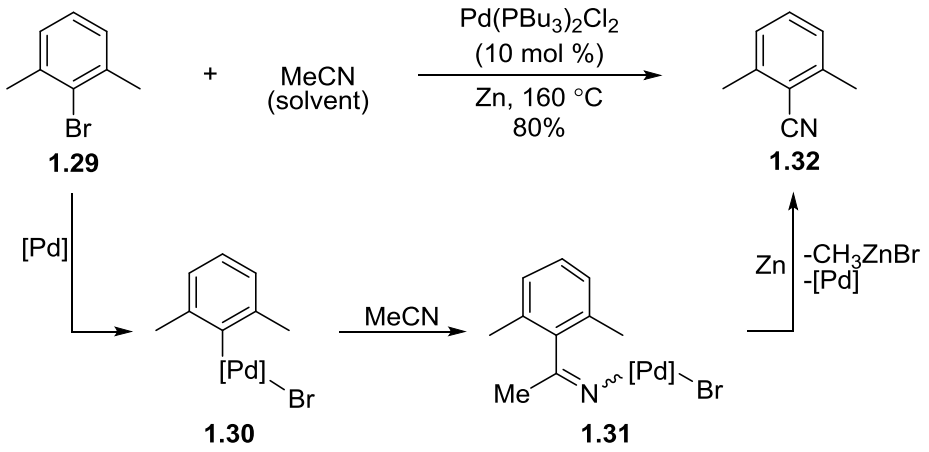
Transition metal cleavage of C–CN sigma-bond was reported as early as 1971 by Burmeister.[22] When 1,1,1,-tricyanoethane (**1.26**) is refluxed in benzene in the presence of stoichiometric amount of $Pt(PPh_3)_4$ it undergoes C–CN sigma-bond activation and forms platinum complex **1.28** (Scheme 1.9). The reaction possibly proceeds through the intermediate **1.27**, where platinum co-ordinates to the nitrile triple bond in $\eta^2$ fashion, leading to oxidative addition of the C–CN sigma-bond and formation of platinum complex **1.28**.




**1.26** **1.27** **1.28**

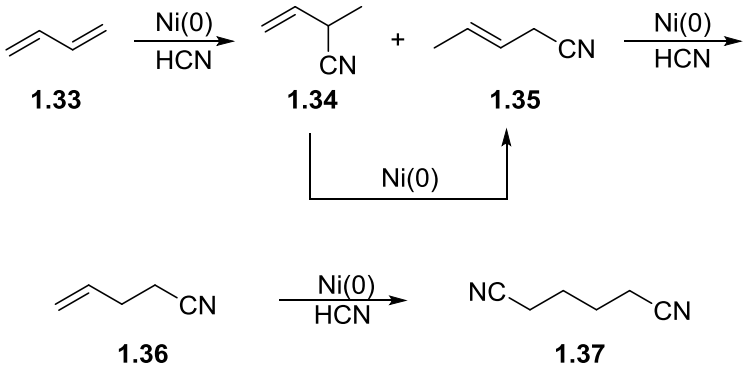
**Scheme 1.9**: Cleavage of C–CN Sigma-bond by Platinum

One of the earliest examples of catalytic C–CN sigma-bond activation was reported by Cheng.[23] When 2-bromo-1,3-dimethylbenzene (**1.29**) in acetonitrile was heated in an autoclave at 160 $^{o}$C in the presence of catalytic $Pd(PBu_3)_2Cl_2$ and Zn powder 2,6-dimethylbenzonitrile **1.32** is formed by the substitution of bromide with nitrile group (Scheme 1.10). The reaction proceeds with the oxidative addition of aryl bromide onto palladium to form aryl palladium complex **1.30**. Addition of palladium complex to acetonitrile leads to iminyl palladium complex **1.31** *via* insertion into π-bond of nitrile. Subsequent transmetalation with zinc and β-methyl elimination provides 2,6-dimethylbenzonitrile **1.32.** Mechanistic study was carried out using a different substrate and intermediate similar to **1.30** was isolated and characterized. When the above intermediate (similar to **1.30**) was heated in acetonitrile at 160 $^{o}$C in the absence of Zn, it undergoes insertion into acetonitrile, leading to imine similar to **1.31** (without Pd) which was also isolated. When the intermediate is heated in the presence of Zn and acetonitrile, it gives the corresponding nitrile. All these results support the mechanism shown in Scheme 1.10.



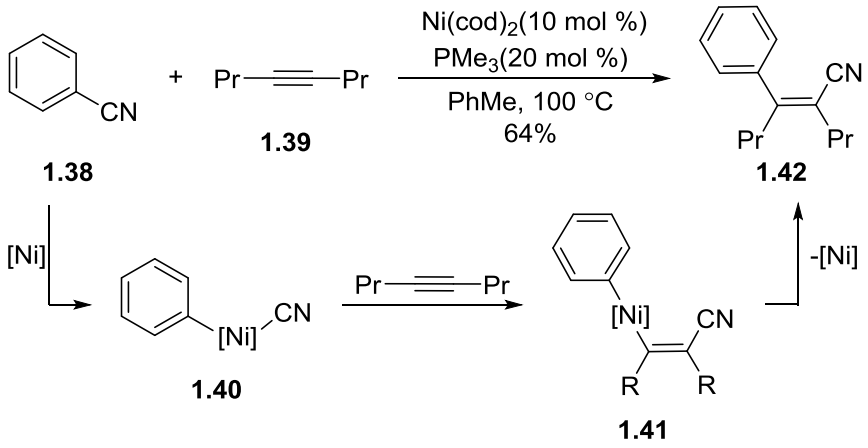

**Scheme 1.10**: Catalytic Cleavage of C–CN Sigma-bond Using Palladium

Another example of catalytic C–CN sigma-bond activation is seen in DuPont's production of adiponitrile.[24] Adiponitrile **1.37** is synthesized by double hydrocyanation of 1,3-butadiene **1.33** in the presence of Ni(0) catalyst (Scheme 1.11). During the first addition of HCN a kinetic mixture of undesired branched isomer **1.34** and desired linear isomer **1.35** are formed. The branched isomer **1.34** is isomerized *in situ* to the linear isomer **1.35** by reversible C–CN sigma bond activation in the presence of catalytic Ni(0). The isomerization of branched isomer to the linear isomer, proceeds through oxidative addition C–CN sigma-bond onto Ni(0).[25] Addition of a second molecule of HCN in the presence of catalytic Ni(0) provides adiponitrile **1.37.**



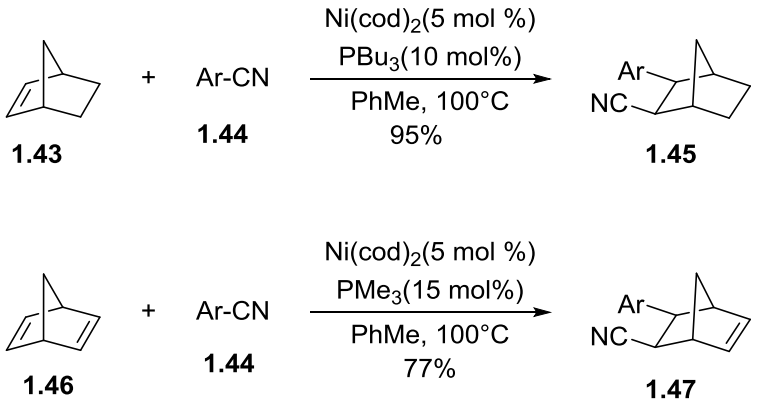

**Scheme 1.11**: DuPont's Synthesis of Adiponitrile

Nakao and Hiyama reported intramolecular arylcyanation of alkynes in the presence of $Ni(cod)_2$ and $PMe_3$ (Scheme 1.12).[26] The reaction begins with the insertion of nickel into C–CN bond (oxidative addition) of benzonitrile (**1.38**) to form a Ni(II) complex **1.40**. Migratory insertion onto 4-octyne (**1.39**) gives alkenylnickel complex **1.41**, which upon reductive elimination, gives α,β-unsaturated nitrile **1.42**. The usage of Ni(0) and less hindered, electron rich ligand ($PMe_3$) is critical for the reaction yield. Palladium-based catalysts, though very efficient for cross coupling reactions, are not very efficient for the arylcyanation.



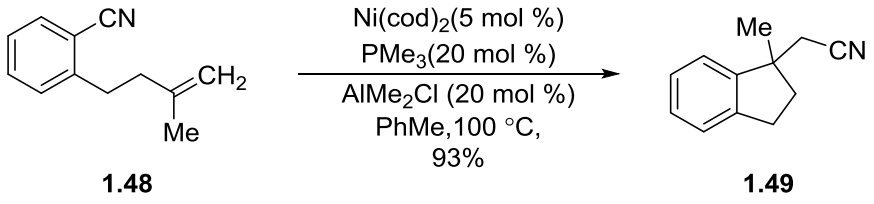

**Scheme 1.12**: Ni-catalysed Arylcyanation of Alkynes

Under similar conditions reported for arylcyanation of alkynes Nakao and Hiyama also reported arylcyanation of norbornene and norbornadiene (Scheme 1.13).[27] Treatment of norbornene **1.43** with arylcyanide **1.44** in the presence of $Ni(cod)_2$ and $PBu_3$ norbornene undergoes arylcyanation to give corresponding addition product **1.45**. For the arylcyanation of norbornadiene **1.46** combination of $Ni(cod)_2$ and $PMe_3$ was more efficient and corresponding arylcyanation product **1.47** was isolated in good yield.



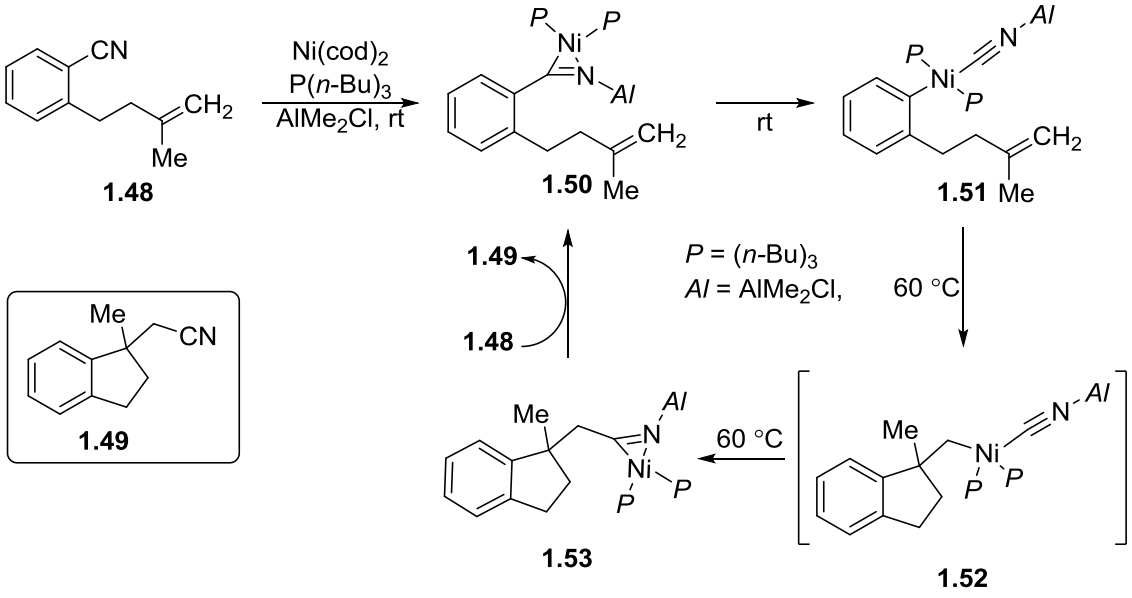

**Scheme 1.13**: Ni-catalysed Arylcyanation of Norbornene and Norbornadiene

Nakao and Hiyama also reported intramolecular arylcyanation of alkenes in the presence of Ni(0) catalyst and a Lewis acid as a co-catalyst (Scheme 1.14).[28] When arylcyanide **1.48** is heated in toluene in the presence of $Ni(cod)_2$ $PMe_3$ and $AlMe_2Cl$, it undergoes arylcyanation to give dihydryoindene **1.49** with benzylic quaternary center in high yield.



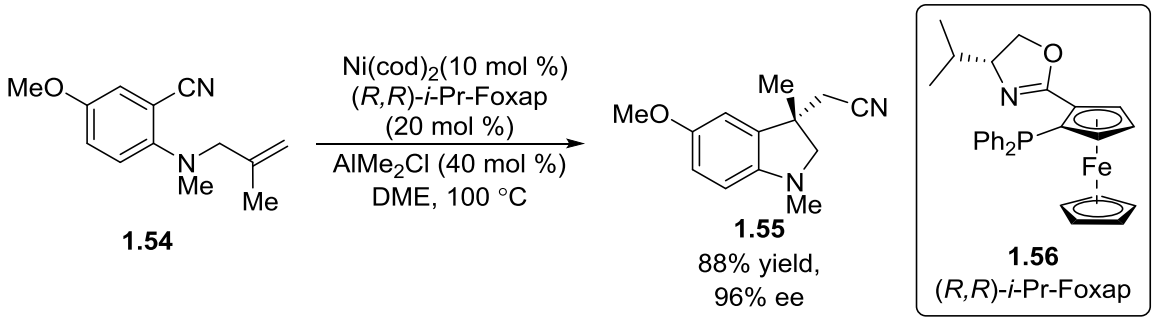

**Scheme 1.14**: Intramolecular Arylcyanation of Alkenes

Lewis acid plays an important role in the reaction. Only a trace amount of product was observed in the absence of $AlMe_2Cl$. This intriguing observation led them to the study of mechanism of the reaction. Mixing the stoichimetric amounts of arylcyanide **1.48**, $Ni(cod)_2$, $PMe_3$ and $AlMe_2Cl$ at room temperature immediately lead to formation of $\eta^2$-nitrile complex **1.50** (Scheme 1.15). In the absence of $AlMe_2Cl$ no $\eta^2$-nitrile complex is observed. Further stirring the complex **1.50** at room temperature provides Ni(II) complex **1.51**. Both the intermediates **1.50** and **1.51** are characterized by X-ray crystallography.[28] Heating the intermediate at 60 $^oC$ leads to formation of arylcyanation product **1.49** and $\eta^2$-nitrile complex **1.50.** Based on these observations the following mechanism is proposed (Scheme 1.15). $AlMe_2Cl$ binds to the nitrile and facilitates the coordination of the cyano group to nickel to form $\eta^2$-nitrile complex **1.50.** Complex **1.50** undergoes oxidative addition on Ar–CN to form complex aryl -Ni(II)-cyanide complex **1.51** which upon migratory insertion onto alkene gives $\eta^2$-nitrile complex **1.52.** Reductive elimination of **1.52** provides arylcyanation product **1.49** and regenerates the catalyst, which binds to another molecule of starting material **1.48.**



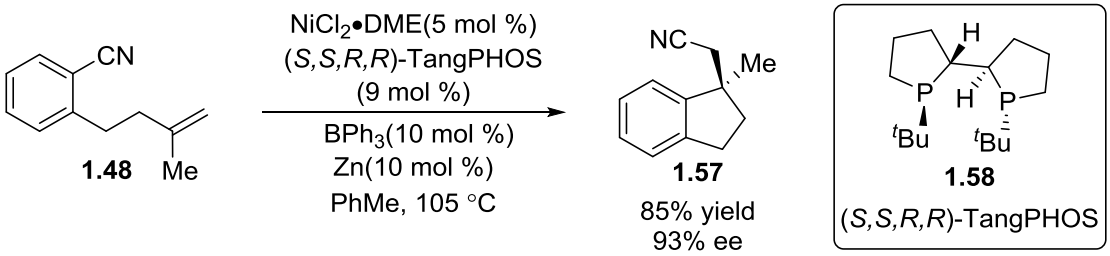

**Scheme 1.15**: Mechanism of Intramolecular Arylcyanation of Alkenes

In the same communication, Nakao and Hiyama also reported asymmetric variant of the reaction (Scheme 1.16). Among various chiral ligands tested chiral ferrocenyl phophine lignad (*R,R*)-*i*-Pr-Foxap (**1.56**)[29] gave best yield and ee. The reaction required further optimization. After increasing the catalyst loading (from 5 to 10 mol %), switching the solvent from toluene to DME and increasing the amount of Lewis acid (from 20 to 40 mol %), arylnitrile **1.54** underwent asymmetric arylcyanation to give indoline **1.55** in high yield and ee.



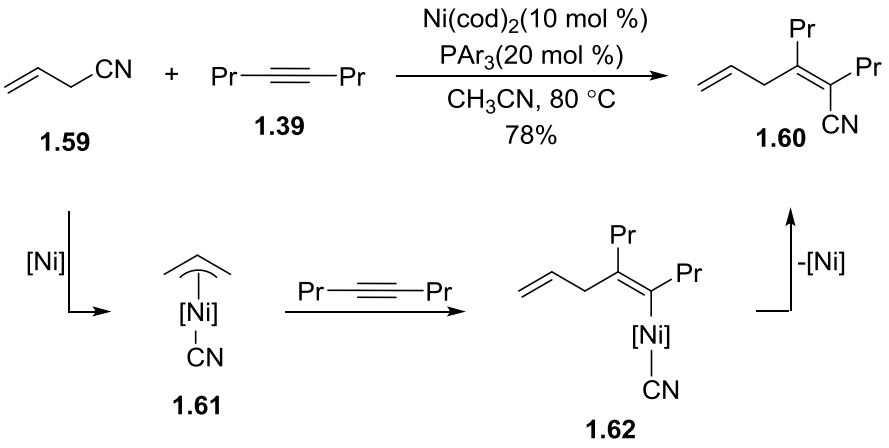

**Scheme 1.16**: Asymmetric Intramolecular Arylcyanation of Alkenes

In the same year Jacobsen and co-workers independently reported another enantioselective intramolecular arylcyanation using Ni(0) catalyst (Scheme 1.17).[30] Among various conditions screened chiral ligand (*S,S,R,R*)-TangPHOS **1.58**,[31] *in situ* generated Ni(0) catalyst (from $NiCl_2$•DME and Zn) and $BPh_3$ (as Lewis acid) gave the best yield and ee. Under optimized conditions arylcyanide **1.48** undergoes enantioselective arylcyanation and gives indane **1.57** in high yield and ee. The above two methods are very useful for the asymmetric synthesis of benzofused cyclic compounds possessing all-carbon quaternary centers, which are very challenging to construct.[32]




**Scheme 1.17**: Enantioselective Intramolecular Arylcyanation of Alkenes

Nakao and Hiyama also reported allylcyanation of alkynes using $Ni(cod)_2$ catalyst.[33] Unlike arylcyanation of alkynes and alkenes, the reaction is efficient in the presence of an electron deficient phosphine ligand and polar solvent ($CH_3CN$) (Scheme 1.18). The reaction begins with oxidative addition of allylcyanide **1.59** to form π-allylnickel intermediate **1.61**. It then undergoes migratory insertion onto 4-octyne (**1.39**) to form alkenyl-Ni(II)cyanide **1.62** which upon reductive elimination gives allylcyanation product **1.60**. Only the *Z*-isomer is observed indicating that migratory insertion occurs in *syn* fashion and reductive elimination takes place with retention of alkene stereochemistry.

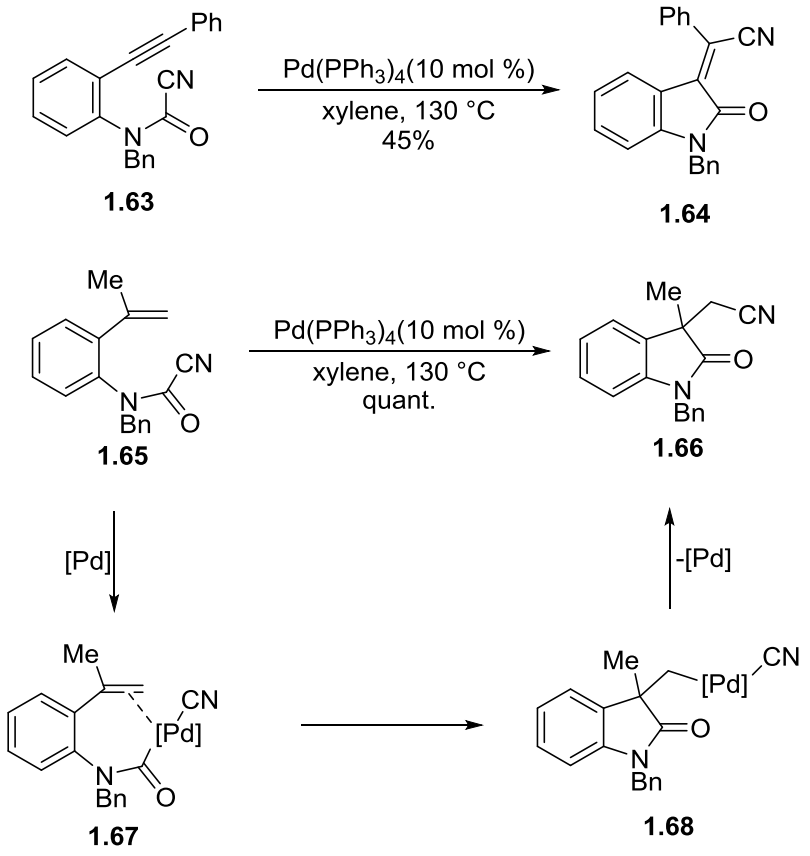



**Scheme 1.18**: Ni-catalysed Allylcyanation of Alkynes

It can be inferred from the previous examples that Ni(0) is very efficient in activating Ar–CN sigma-bond. Other transition metals like Pd(0) are not very efficient in activating Ar–CN sigma-bond because of its high strength (~130 kcal $mol^{-1}$) as compared to Ar–Br (~80 kcal $mol^{-1}$), Ar–Cl (~100 kcal $mol^{-1}$).[18] One possible reason for the special ability of Ni(0) to activate Ar–CN is the ability of Ni(0) to coordinate to π-bond of nitrile in $\eta^2$ fashion and thus facilitating oxidative addition.[21, 34] However if the C–CN sigma-bond is between carbonyl carbon and nitrile, it can be cleaved by other transition metals, due to the more polarized character of the acyl C–CN sigma-bond.[19, 35] The additional polarization of bond makes it weaker and makes the activation of C–CN sigma-bond relatively facile.

An example of such C–CN sigma-bond between carbonyl carbon and nitrile is reported by Takemoto (Scheme 1.19) using cyanoformamides in the presence of Pd(0). [36] When cyanoformamide **1.63** is heated in xylene in the

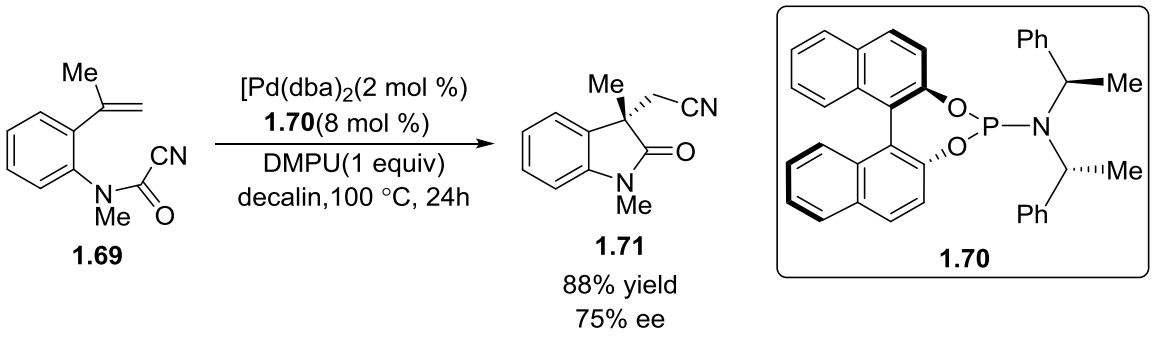
presence of $Pd(PPh_3)_4$, it undergoes intramolecular cyanoamidation and gives α-alkylidene lactam **1.64**. The reaction predominantly gives the *Z* isomer though a very small amount of *E* isomer is also observed. The reaction was also tested with 1,1-disubstituted alkenes. When cyanoformamide **1.65** is subjected to the cyanoamidation conditions, it smoothly undergoes oxidative addition on C–CN bond to give palladium(II) complex **1.67**. The palladium complex undergoes migratory insertion onto alkene to form complex **1.68**, which upon reductive elimination, gives oxindole **1.66** in quantitative yield. Another important advantage of the process is that both carbonyl and nitrile functional groups are retained in the product each can be further used to build molecular complexity.




**Scheme 1.19**: Pd-catalysed Intramolecular Cyanoamidation

Takemoto also reported an enantioselective variant of cyanoamidation of 1,1-disubstituted alkenes using chiral phosphoramidite ligand (Scheme 1.20).[37] When cyanoformamide **1.69** is heated in decalin at 100 $^{o}$C in the presence of $Pd(dba)_2$, phosphoramidite **1.70** as chiral ligand and DMPU as a polar additive, it undergoes enantioselective cyanoamidation and gives 3,3-disubstituted oxidindole **1.71** in high yield and good ee. The reaction results in the formation of chiral all-carbon quaternary center and also in 1,2-difunctionalization of alkenes

with amide and nitrile functional groups, which can be useful in subsequent transformations.




**Scheme 1.20**: Pd-catalysed Enantioselective Cyanoamidation

The above examples illustrate the potential of C–CN sigma-bond activation and particularly C–CN sigma-bond activation between a carbonyl and nitrile. In the following chapters our new methodological developments in organic synthesis using the activation of C–CN bond as the mechanistic basis is described. Chapter 2 describes cyanoesterification of alkynes using C–CN sigma-bond activation. Cyanoacylation of alkynes using C–CN sigma-bond activation is described in chapter 3. Chapter 4 introduces unprecedented reaction of carbamoyl azides. All the relevant literature precedence, motivation for the work, reaction schemes, and experimental details are presented in each chapter.

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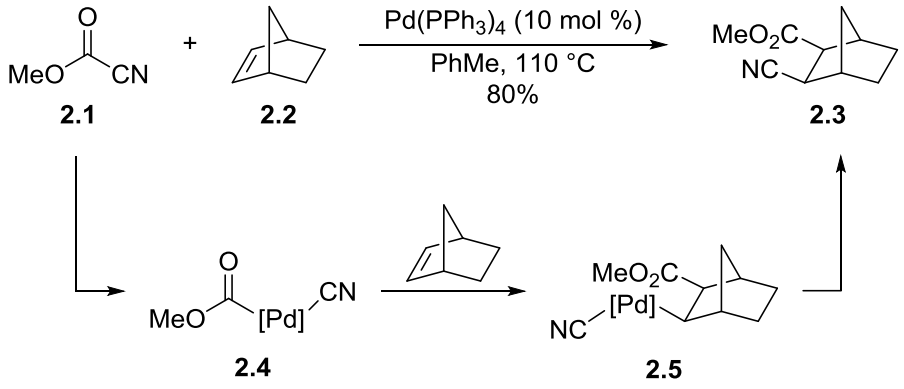
# Chapter 2

# Palladium Catalysed Intramolecular Cyanoesterification of Alkynes

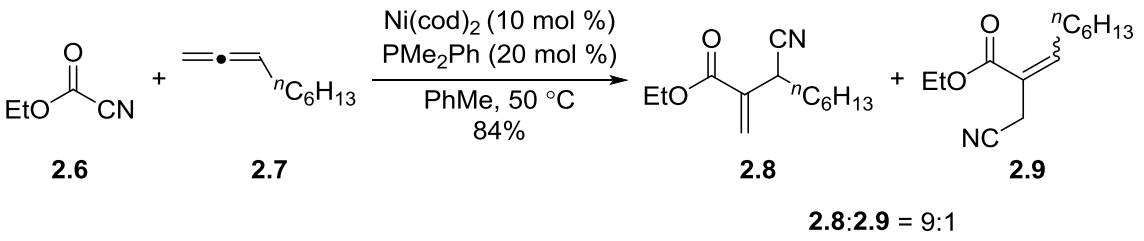
## 2.1 Introduction

In the previous chapter importance of transition metal catalyzed C–CN activation of carbonyl carbon and nitrile was introduced. Reports of cyanoamidation of alkynes and alkenes using C–CN activation of cyanoformamides also were presented. In this chapter, C–CN activation of cyanoformate esters will be discussed. The first example of cyanoesterification was reported by Nishihara using strained alkenes like norbornene (Scheme 2.1).[1] When methylcyanoformate (**2.1**) and norbornene (**2.2**) are heated in toluene in the presence of $Pd(PPh_3)_4$ the alkene undergoes cyanoesterification and gives vicinal di-functionalized norbornane **2.3**. The reaction begins with the oxidative addition of methylcyanoformate to give Pd(II) complex **2.4** which upon migratory insertion onto norbornene **2.2** gives palladium complex **2.5**. Subsequent reductive elimination of intermediate **2.5** provides norbornane **2.3**. Though the reaction can be used for di-functionalization of double bond, it is restricted to only strained systems such as norbornene and norbornadiene. When the reaction was tested with other unstrained alknes like 1-octene or styrene, no cyanoesterification was observed.[2]



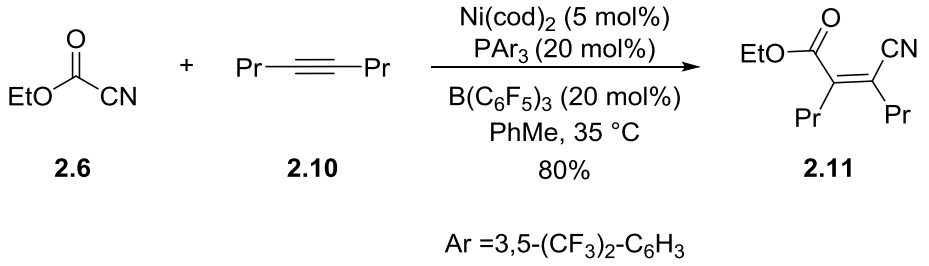

**Scheme 2.1**: Pd-catalysed Cyanoesterification of Norbornene

Another example of cyanoesterification was reported by Nakao and Hiyama using Ni(0) catalyst (Scheme 2.2).[3] When a solution of ethylcyanoformate (**2.6**) and allene **2.7** in toluene is heated in the presence of $Ni(cod)_2$ and $PMe_2Ph$, the allene undergoes cyanoesterification to give mixture of α,β-unsaturated esters **2.8** and **2.9**. Conjugated ester **2.8** is isolated as the major product at the reaction temperature (50 $^oC$) and ester **2.9** is formed as mixture of *E* and *Z* isomers with *Z* being the predominant isomer. However, when the reaction is performed at 110 $^oC$ ester, **2.9** (mixture of *E* and *Z* isomers) is observed as the major product.




**Scheme 2.2**: Ni-catalysed Cyanoesterification of 1,2-allenes

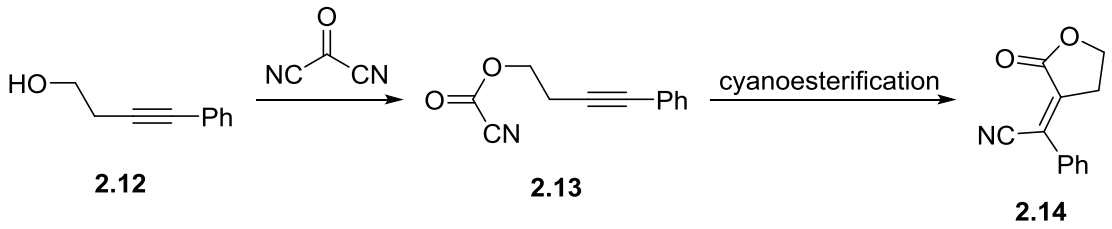
Nakao and Hiyama also reported cyanoesterification of alkynes using Ni(0) (Scheme 2.3).[4] When mixture of ethylcyanoformate (**2.6**) and 4-octyne (**2.10**) is treated with $Ni(cod)_2$ and an electron deficient phosphine ligand in the presence of the Lewis acid $B(C_6F_5)_3$ it undergoes stereospecific cyanoesterification to give β-cyano-α,β-unsaturated ester **2.11**. Both electron deficient phosphine ligand and the strong Lewis acid $B(C_6F_5)_3$ are very critical for the reaction.




**Scheme 2.3**: Ni-catalysed Cyanoesterification of Alkynes

## 2.2 Proposal

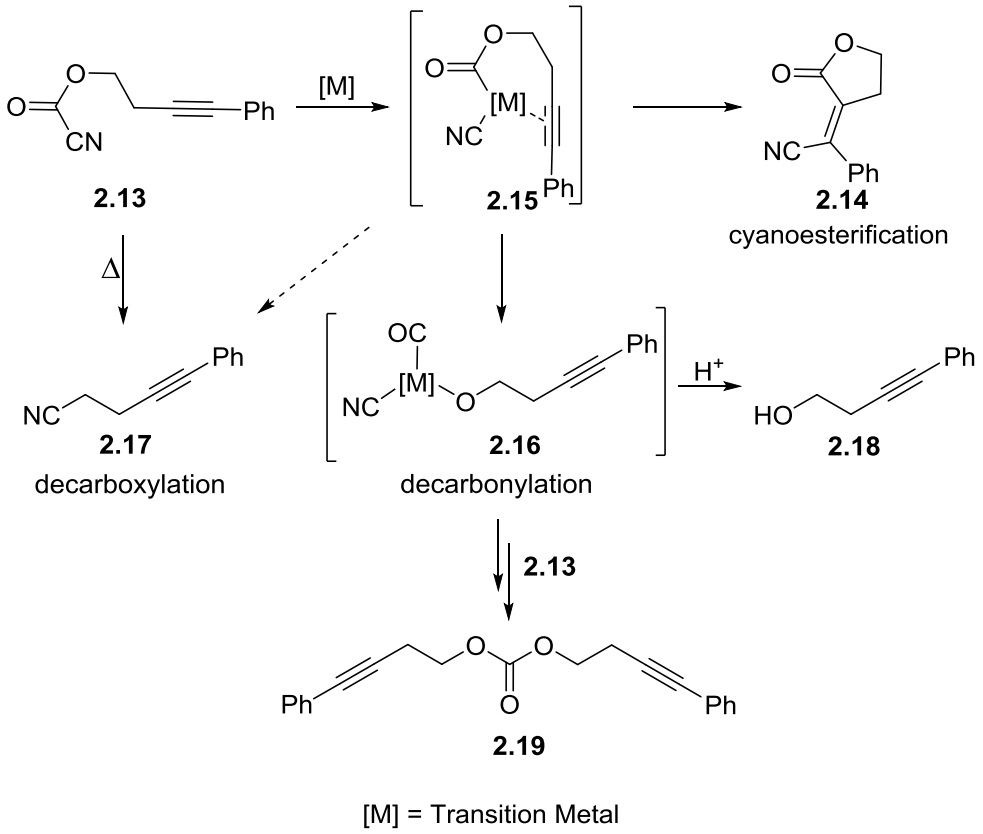
We wanted to develop simple and readily usable conditions for the intramolecular cyanoesterification of alkynes using cyanoformate esters such as **2.13** (Scheme 2.4). Cyanoformate ester **2.13** can be made in one step from the commercially available 4-phenyl-3-butyn-1-ol (**2.12**) by treatment with carbonyl cyanide.[5] Successful cyanoesterfication of **2.13** would provide highly funtionalized lactone **2.14** in just two steps from commercially available 3-butynol **2.12**.




**Scheme 2.4**: Proposal for Intramolecular Cyanoesterification of Alkynes

Cyanoestericaton of alkenes or alkynes is not as smooth as cyanoamidation or arylcyanation. The example of cyanoesterification reported by Nishihara is restricted to only strained alkenes and no cyanoesterification is observed with unstrained alkenes (Scheme 2.1).[1] Also the conditions reported for cyanoesterification of alkynes by Nakao and Hiyama (Scheme 2.3) require very the addition of a strong Lewis acid $B(C_6F_5)_3$ and highly electron deficient

phosphine ligand.[4] These observations might be attributed to the variety of side reactions cyanoformate esters undergo in the presence of transition metals (Scheme 2.5). Transition metal activation of the C–CN bond *via* oxidative addition forms intermediate metal complex **2.15**, which is susceptible to various reaction pathways. Cyanoesterification of the alkyne in intermediate **2.15** would lead to desired butenolide **2.14**. Intermediate **2.15** can also undergo decarbonylation to form metal complex **2.16**, which upon protonation provides alcohol **2.18** (vide infra). Intermediates such as **2.16** also undergo disproportionation in the presence of alcohol **2.13** to form carbonate **2.19**.[6] Intermediate **2.15** may also decarboxylate and form nitrile **2.17**. In addition to the above reactions, cyanoformate esters like **2.13** rapidly undergo nucleophilic addition elimination reactions[7] even in the presence of mild nucleophiles.[8] Cyanoformate esters like **2.13** may also decarboxylate to form nitriles **2.17** when heated to high temperatures.[9] Due to the multitude of potential side reactions, developing a simple reaction condition for cyanoesterfication of alkynes *via* C–CN bond activation can be very challenging.



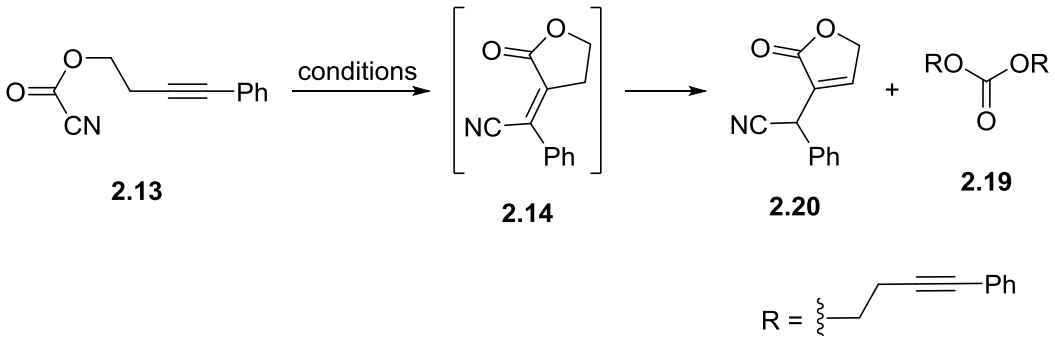

**Scheme 2.5**: Potential Reactions of Cyanoformate Esters

## 2.3 Reaction Optimization

We began testing cyanoesterfication of **2.13** with Nishihara's conditions,[1] but these resulted only in unconsumed starting material (Table 2.1, entry 1). When the reaction was diluted to 0.03 M in toluene (entry 2), carbonate **2.19** was formed as the major product, but a minor amount of another compound with a molecular weight corresponding to **2.14** was also observed. Closer inspection of the NMR spectra indicated that the product was a structural isomer of **2.14**, but

with an endocyclic alkene assigned in the structure **2.20**, likely resulting from isomerization of **2.14**. Trials to increase the ratio of **2.20:2.19** by varying temperature, catalyst loading, and concentration failed (not shown). Recalling previous successes with Lewis basic additives in somewhat similar cyanoamidation reactions,[10] stoichiometric amounts of *N,N*-dimethylpropylene urea (DMPU) and *N*-methylpyrollidinone (NMP) were added, with the hypothesis that the Lewis basic additives will coordinate to Pd and stabilize intermediate complexes. Although stoichiometric amounts of Lewis basic additives were not particularly fruitful (results not shown), a much higher ratio of **2.20:2.19** was observed when DMPU was used as a solvent. The subsequent removal of DMPU and isolation proved difficult (not shown). Our success with DMPU prompted us to employ a more convenient, relatively lower boiling, Lewis basic solvent, DMF, and higher ratio (2.8:1) of **2.20:2.19** was obtained (entry 4). As we monitored reaction progress and altered the reaction temperatures, we observed that shorter reaction times (entry 5) and higher temperatures (entry 6) provided better yields of **2.20**. Under similar conditions of higher temperature and lower reaction time, cyanoesterification in toluene provided a poor ratio of **2.20:2.19** (entry 7). Finally, when we switched to using a microwave reactor (5 minutes, 200 °C), an excellent ratio of **2.20:2.19** was observed (16:1, entry 8), with butenolide **2.20** isolated in 80% yield. A control experiment subjecting **2.13** to the same microwave irradiation conditions as described in entry 8 but without any $Pd(PPh_3)_4$ catalyst resulted in no product formation (entry 9).

**Table 2.1**: Optimization of Intramolecular Cyanoesterification




| Entry | $Pd(PPh_3)_4$ (mol %) | Solvent | Temp (°C) | concn (M) | time | 2.20:2.19[a] | Yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | 10 | PhMe | 110 | 0.1 | 24 h | - | 0 |
| 2 | 10 | PhMe | 115 | 0.03 | 48 h | 1:1.5 | 17[d] |
| 3 | 25 | PhMe | 115 | 0.03 | 24 h | 1:1.5 | 16[c] |
| 4 | 25 | DMF | 115 | 0.03 | 24 h | 2.8:1 | 45 |
| 5 | 25 | DMF | 115 | 0.03 | 1.5 h | 4:1 | 50[b] |
| 6 | 10 | DMF | 130 | 0.1 | 1.5 h | 3.9:1 | 73 |
| 7 | 10 | PhMe | 130 | 0.1 | 1.5 h | 1:1.3 | 21 |
| **8**[d] | **10** | **DMF** | **200** | **0.1** | **5 min** | **16:1** | **80**[e] |
| 9[d] | 0 | DMF | 200 | 0.1 | 5 min | - | 0 |

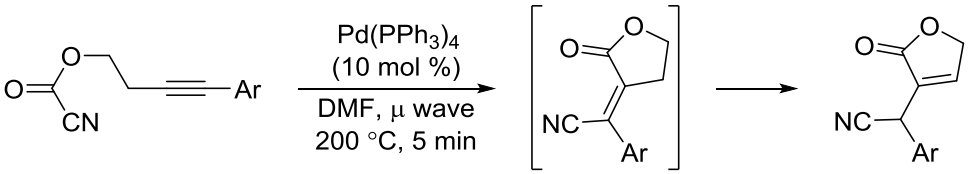
[a] ratio determined by $^1$H NMR spectroscopy of the crude reaction mixture. [b] yields determined by $^1$H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. [c] A significant amount of starting material was observed. [d] Reaction performed in microwave reactor. [e] Isolated yield. Carbonate **2.19** (5%) was also isolated. **Bold** conditions (entry 8) indicate those used for exploring the reaction scope.

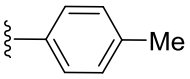
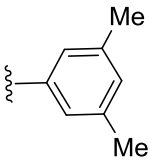
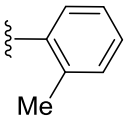
## 2.4 Substrate Scope

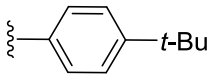
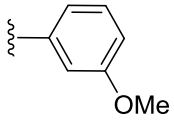
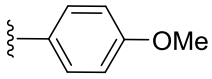
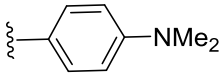
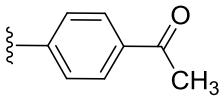
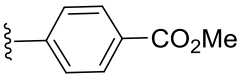
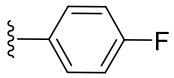
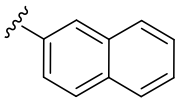
Using the microwave reactor conditions described in Table 2.1, entry 8, we explored the steric and stereoelectronic effects of various aryl substituents upon cyanoesterification (Table 2.2). Results using cyanoformate ester **2.13** are included as a reference (entry 1). Cyanoesterification tolerates alkyl substitution at various positions of the aromatic ring (entries 2–5), with *p*-Me providing the highest yield of **2.22** (96%, entry 2), while *o*-Me provided the lowest, but still acceptable yield of **2.26** (53%, entry 4). 3.5-dimethyl phenyl substrate **2.23** also provided good yield of the corresponding butenolide **2.24** (73%, entry 3). Electron-donating substituents like OMe and $NMe_2$ gave good yields of the corresponding butenolides **2.30** and **2.32** respectively (entries 6–8). When electron withdrawing substituents C(O)Me (**2.35**) and $CO_2Me$ (**2.37**) were incorporated at the *para* position lower yields of the butenolies (**2.36** and **2.38**) were observed (entries 9–10). With these substrates, minor amounts of the corresponding alcohols analogous to **2.18** were isolated. It is interesting to note that the catalyst selectively activated the cyanoformate ester in the presence of another ester (entry 10). The reaction tolerates fluorine substitution on the aromatic ring and cyanoesterification of 4-F-$C_6H_4$- substituted alkyne **2.39** provided the butenolide **2.40** in good yield (82%, entry 11). Other aromatic substituents like 2-naphthyl **2.41** also provided corresponding butenolide **2.42** in good yield (70%, entry 12). When substrates with very strong electron withdrawing substituents were incorporated at *ortho* ($NO_2$, **2.43**) or *para* ($CF_3$,

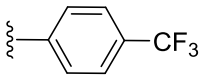
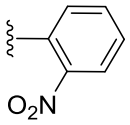
**2.45**) positions, a complex reaction mixture was formed and no desired product was detected by crude $^{1}$H NMR.[11]

**Table 2.2**: Substrate Scope of Intramolecuar Cyanoesterifcation




| Entry | Substrate | Ar | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 | **2.13** | Ph | **2.20** | 80 |
| 2 | **2.21** |  | **2.22** | 96 |
| 3 | **2.23** |  | **2.24** | 73 |
| 4 | **2.25** |  | **2.26** | 53[b] |

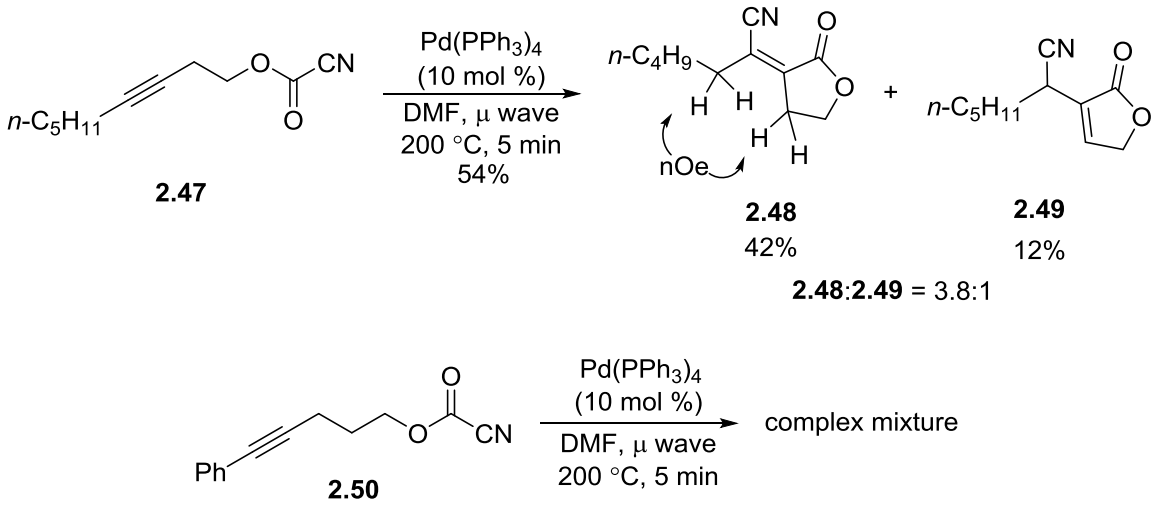
| | | | | |
|---|---|---|---|---|
| 5 | **2.27** |   | **2.28** | 70 |
| 6 | **2.29** |   | **2.30** | 83 |
| 7 | **2.31** |   | **2.32** | 75 |
| 8 | **2.33** |   | **2.34** | 68 |
| 9 | **2.35** |   | **2.36** | 50[c] |
| 10 | **2.37** |   | **2.38** | 54[d] |
| 11 | **2.39** |   | **2.40** | 82 |
| 12 | **2.41** |  | **2.42** | 70 |

| | | | | |
|---|---|---|---|---|
| 13 | **2.43** |  | **2.44** | --[e] |
| 14 | **2.45** |  | **2.46** | --[e] |

[a] Isolated yield after column chromatography on silica. [b] Yields of **2.26** determined by $^1$H NMR spectroscopy of the product mixture. We could not separate butenolide **2.26** from the carbonate by-product. [c] 22% of the corresponding alcohol of **2.35** analogous to **2.18** was isolated. [d] 19% of the corresponding alcohol of **2.37** analogous to **2.18**. [e] No cyanoesterification product was detected in the crude $^1$H NMR.

Replacing the aryl substituent with an alkyl group, and extending the alkyne tether length drastically altered the product distribution (Scheme 2.6). When alkyl-substituted cyanoformate ester **2.47** was subjected to the optimized cyanoesterification conditions, mixture of lactones **2.48** with an exocyclic alkene and **2.49** with endocyclic alkene in the ratio 3.8:1 (as determined $^1$H NMR of the crude reaction mixture) was observed. Both the isomers were separated by chromatography and lactone **2.48** and butenolide **2.49** were isolated in 42% and 12% yields respectively. The *Z*-geometry of the lactone **2.48** was assigned by nOe. The result indicates that when an alkyl group is present, the exocyclic double bond is less likely to undergo olefin isomerization compared to when an aryl group is present. This example also supports the idea that in the case of aryl substrate, a butenolide with exocyclic double bond (**2.14**) is formed first (Table

2.1) and subsequent isomerization to a butenolide with an endocylic double bond (**2.15**) occurs under reaction conditions. Unfortunately, when we attempted to synthesize δ-lactones via the cyanoesterification with cyanoformate ester **2.50**, no desired product was detected. Instead, a complex mixture was formed that could not be characterized.



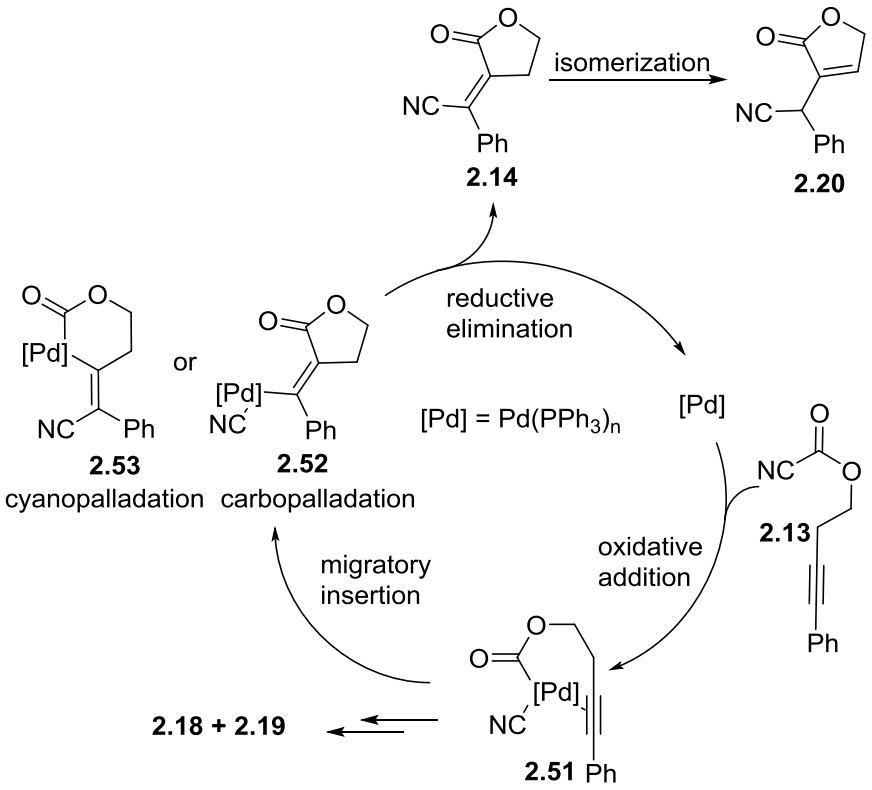

**Scheme 2.6**: Additional Substrate Scope

## 2.5 Mechanistic Considerations

We propose the following mechanism based on these results and prior work on C–CN activation (Scheme 2.7).[1, 6] Cyanoesterification likely begins with the oxidative addition of Pd(0) into the C–CN bond of the cyanoformate ester **2.13** to form a Pd(II) complex **2.51** in which an alkyne pi-bond is coordinated to

Pd.[12] The DMF solvent likely coordinates to the Pd, stabilizing the resulting intermediate and decreasing competitive decarbonylation. Migratory insertion of the alkyne into the Pd-acyl bond in a 5-*exo*-dig, *syn* fashion leads to provide the *Z* isomer **2.52**. Reductive elimination regenerates the Pd(0) catalyst while providing lactone **2.14** with an exocyclic olefin. When an aryl group is present, the tetrasubstituted olefin readily isomerizes to the trisubstituted butenolide **2.20**. Decarbonylation of **2.51** allows the subsequent formation of alcohol **2.18** and carbonate **2.19**, as detailed in Scheme 2.5. It is unclear to us why higher temperatures would favor cyanoesterification over decarbonylation pathways.

Alternatively, intermediate **2.51** might undergo cyanopalladation, rather than carbopalladation to provide intermediate **2.53** which upon reductive elimination would also result in lactone **2.14**. Takemoto's mechanistic experiments in cyanoamidation (rather than cyanoesterification) suggest that cyanoamidation proceeds *via* carbopalladation rather than cyanopalladation.[13] In analogy to Takemoto's work, cyanoesterification might also proceed via carbopalladation, though cyanopalladation cannot be ruled out.




**Scheme 2.7**: Plausible Reaction Mechansim

The presence of moderately electron deficient $CO_2Me$ and C(O)Me(Table 2.2, entries 9, 10) subtituents and sterically congested substituents (entry 4) upon the alkyne decreases the chemoselectivity for cyanoesterification and the yields of corresponding butenolides. The presence of strong electron withdrawing groups $CF_3$ and $NO_2$ (Table 2.2 entries 13, 14) completely shuts down the formation of the respective butenolides **2.44** and **2.46**. The electron withdrawing substituents lower the electron density on the alkyne, which could weaken Pd(II) coordination to the alkyne. Aryl groups possessing *ortho* substituents increase

steric congestion, which might also weaken alkyne coordination. Poorer alkyne coordination might slow migratory insertion, thereby reducing the yield of butenolides. Due to slowed migratory insertion, alternative decomposition pathways, such as decarbonylation to provide corresponding alcohols (similar to **2.18**) and carbonates (similar to **2.19**), might compete. Moreover, extending the tether length may also slow coordination or migratory insertion allowing alternative decomposition pathways to take place, with no cyanoesterification products observed. Based on these results, we propose that migratory insertion could be the product-determining step.

## 2.6 Conclusion

In conclusion, we discovered conditions for C–CN activation and intramolecular cyanoesterification of alkynes in the presence of a relatively inexpensive and common palladium source, $Pd(PPh_3)_4$, to provide butenolides in good to excellent yields. Formation of carbonate byproducts can be minimized by employing high temperatures and shorter reaction times (microwave irradiation) in Lewis basic solvents. Sterically less encumbered, electron-rich alkynes underwent cyanoesterification with greater ease compared to sterically encumbered, electron-deficient alkynes. Our results led us to hypothesize that migratory insertion of the alkyne, rather than C–CN activation, is the product determining step.

## 2.7 Experimental

### Section A: General Details

All reactions were carried out using flame-dried glassware under nitrogen. DMF (*N,N*-dimethylformamide) and toluene were dried according to published procedures,[14] purged with $N_2$ and stored in an $N_2$ atmosphere glove box. Carbonyl cyanide was prepared from tetracyanoethylene oxide according to established procedures. Carbonyl cyanide was stored as a solution in $Et_2O$ under $N_2$ in a –15°C freezer and remained effective for several weeks. $Pd(PPh_3)_4$ was purchased from Pressure Chemical Co. All other chemicals were purchased from AK Scientific, Acros Organics or Sigma-Aldrich and used as received. All Microwave reactions were prepared in sealed reactor tubes and conducted in a Biotage Initiator 8 microwave reactor.

Analytical thin layer chromatography (TLC) was carried out using 0.25 mm silica plates from E. Merck. Eluted plates were visualized first with UV light and then by staining with ceric sulfate/molybdic acid or potassium permanganate/potassium carbonate. Flash chromatography was performed using 230–400 mesh (particle size 0.04–0.063 mm) silica gel purchased from Merck. $^1$H NMR (300 and 400 MHz) and $^{13}$C NMR (75 MHz) spectra were obtained on Varian FT NMR instruments. NMR spectra were reported as $\delta$ values in ppm relative to benzene, chloroform or tetramethylsilane. $^1$H NMR coupling constants are reported in Hz; multiplicity was indicated as follows; s (singlet); d (doublet); t (triplet); q (quartet); quint (quintet); m (multiplet); dd

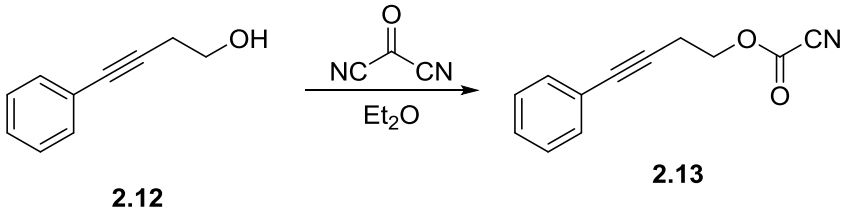
(doublet of doublets); ddd (doublet of doublet of doublets); dddd (doublet of doublet of doublet of doublets); dt (doublet of triplets); td (triplet of doublets); ddt (doublet of doublet of triplets); app (apparent); br (broad). Infrared (IR) spectra were obtained as films from $CH_2Cl_2$ or $CDCl_3$. Low-resolution mass spectra (LRMS) in EI or CI experiments were performed on a Varian Saturn 2200 GC-MS system, and LRMS and high-resolution mass spectra (HRMS) in electrospray (ESI) were performed on a Bruker BioTOF II and in chemical ionization (CI) were performed on a Finnigan MAT95 instrument.

**Section B: Experimental**

**Preparation of carbonyl cyanide:** (~1 M in $Et_2O$): To a suspension of tetracyanoethyleneoxide (TCEO) (21.8 g, 151 mmol) in $Et_2O$ (100 mL), $Me_2S$ (13.4 ml, 182 mmol) was added at 0 °C. After stirring for 1 h at 0 °C the precipitate was removed through syringe filter (0.2 μm) and the filtrate was diluted with $Et_2O$ (50 mL) to give the carbonyl cyanide solution (~1.0 M) in $Et_2O$ which was used for the following reactions without further purification.

Note: Based on our experience, the solution was stable for few months in freezer (~ –15 °C).

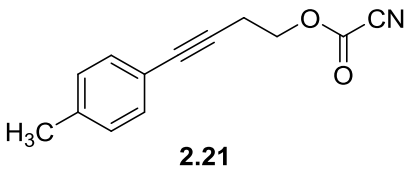
**General Procedure for Cyanoformate Ester Synthesis:**




**2.12** **2.13**

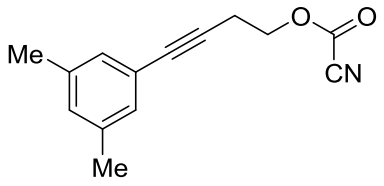
**Scheme 2.8**: Synthesis of Cyanoformate Esters

Carbonyl cyanide solution (22 ml, 1M in $Et_2O$) was added to the 4-phenylbut-3-yn-1-ol (1.07 g, 7.33 mmol) and the reaction was stirred for 12 h at room temperature. The reaction mixture was filtered through celite was concentrated *in vacuo* to remove $Et_2O$. The crude mixture was dissolved in warm hexanes and decanted. Dissolving and decanting procedure was repeated 3 times and combined hexanes extracts were concentrated to provide cyanoformate ester **2.13** as brown oil which solidified to brown crystals on cooling (1.06 g, 5.33 mmol, 73%). $R_f$ = 0.68 (1:4 EtOAc:Hex); $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 7.43-7.41 (m, 2H), 7.34-7.32 (m, 3H), 4.52 (t, *J* = 6.9 Hz, 2H), 2.88 (t, *J* = 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.1, 131.8, 128.5, 128.2, 122.8, 109.3, 83.4, 83.2, 66.5, 19.7; IR (thin film) 3060, 2965, 2245, 1750, 1598, 1490, 1248, 1069, 978, 758 cm$^{-1}$; HRMS (CI) calcd for $[C_{12}H_9NO_2 + NH_4]^+$, *m/z* 217.0972, found 217.0980.



**2.21**

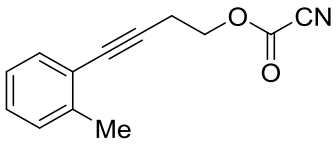
**Cyanoformate 2.21:** Prepared using the general procedure of cyanoformate ester synthesis from (4-Methyl)-4-phenylbutynol (87 mg, 0.54 mmol) and carbonyl cyanide (3.4 ml, 0.27 mmol 0.8 M solution). The cyanoformate **2.21** was obtained as light pink oil. (109 mg, 0.50 mmol, 93%) $R_f$ = 0.69 (1:4 EtOAc:Hex) $^1$H NMR (400 MHz, CDCl3) $\delta$ 7.30 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.4 Hz 2H), 4.51 (t, J = 6.8 Hz, 2H), 2.86 (t, J = 6.8 Hz, 2H), 2.35 (s, 3H); 13C NMR (75 MHz, $CDCl_3$) $\delta$ 144.1 138.6, 131.7, 129.2, 119.7, 109.3, 83.3, 82.6, 66.6, 21.6, 19.7; IR (thin film) 3026, 2921, 2246, 1752, 1509, 1459, 1247, 980, 818 cm-1; HRMS (CI) calcd for $[C_{13}H_{11}NO_2 + NH_4]$+, m/z 231.1128, found 231.1139.



**2.23**

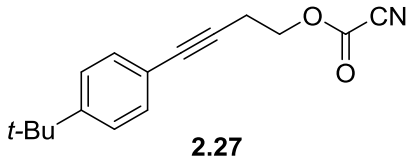
**Cyanoformate 2.23:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(3,5-Dimethylphenyl)-butynol (120 mg, 0.69 mmol) and carbonyl cyanide (2.75 ml of 1M solution, 2.75 mmol). The cyanoformate **2.23** was obtained as yellow oil (131 mg, 0.58 mmol, 84%). $R_f$ = 0.65 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.04 (brs, 2H), 6.96 (brs, 1H), 4.50 (t, *J* = 6.9 Hz, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 2.29 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.2,

138.1, 130.4, 129.5, 122.4, 109.3, 83.5, 82.5, 66.6, 21.2, 19.7; IR (thin film) 3033, 2962, 2249, 1756, 1598, 1461, 1379, 1246, 852 $cm^{-1}$; HRMS (CI) calcd for $[C_{14}H_{13}NO_2 + NH_4]^+$, *m/z* 245.1285, found 245.1300.




**2.25**

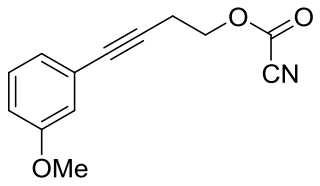
**Cyanoformate 2.25:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(2-Methylphenyl)-butynol (135 mg, 0.84 mmol) and carbonyl cyanide (1.7 ml of 1M solution, 1.7 mmol). The cyanoformate **2.25** was obtained as light yellow oil (150 mg, 0.70 mmol, 83%). $R_f$ = 0.62 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.37 (d, *J* = 7.5 Hz, 1H), 7.25-7.10 (m, 3H), 4.53 (t, *J* = 6.9 Hz, 2H), 2.92 (t, *J* = 6.6 Hz, 2H), 2.41 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.7, 140.9, 132.7 130.2, 129.1, 126.3, 123.2, 109.9, 87.9, 82.7, 66.6, 21.3, 20.4; IR (thin film) 3018, 2964, 2919, 2245, 1747, 1485, 1456, 1248, 979, 759 $cm^{-1}$. HRMS (CI) calcd for $[C_{13}H_{11}NO_2 + NH_4]^+$, *m/z* 231.1128, found 231.1146.




**2.27**

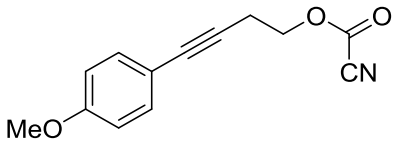
**Cyanoformate 2.27:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-Methoxyphenyl)-butynol (150 mg, 0.91 mmol) and

carbonyl cyanide (2.7 ml of 1M solution, 2.7 mmol). The cyanoformate **2.27** was obtained as light red oil (170 mg, 0.78 mmol, 85%). $R_f$ = 0.70 (3:7 EtOAc:Hex) $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (s, 4H), 4.51 (t, *J* = 6.8 Hz, 2H), 2.86 (t, *J* = 6.8 Hz, 2H), 1.31 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 151.7, 144.1, 131.5, 125.5, 119.8, 109.3, 83.3, 82.6, 66.6, 34.9, 31.3, 19.7; IR (thin film) 3038, 2964, 2906, 2245, 1752, 1505, 1461, 1247, 1109, 836 cm$^{-1}$; HRMS (CI) calcd for $[C_{16}H_{17}NO_2 + NH_4]^+$, *m/z* 273.1598, found 273.1599.



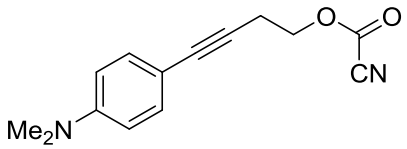

**2.29**

**Cyanoformate 2.29:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(3-methoxyphenyl)-butynol (160 mg, 0.91 mmol) and carbonyl cyanide (2.5 ml of 1M solution, 2.5 mmol). The cyanoformate **2.29** was obtained as light yellow oil (150 mg, 0.65 mmol, 72%). $R_f$ = 0.60 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.23 (dd, *J* = 8.1, 8.1 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.95 (brs, 1H), 6.89 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.50 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 2.86 (t, *J* = 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 159.4, 144.1, 129.5, 124.2, 123.7, 116.6, 114.9, 109.2, 83.3, 83.0, 66.4, 55.3, 19.6; IR (thin film) 3003, 2964, 2837, 2246, 1752, 1600, 1576, 1483, 1247, 1045, 784 cm$^{-1}$. HRMS (CI) calcd for $[C_{13}H_{11}NO_3 + NH_4]^+$, *m/z* 247.1077, found 247.1097.




**2.31**

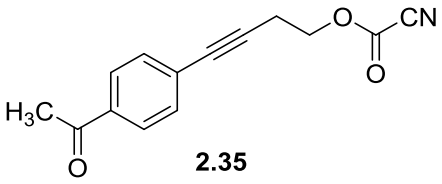
**Cyanoformate 1.31:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-Methoxyphenyl)-butynol (100 mg, 0.57 mmol) and carbonyl cyanide (4.2 ml of 0.27M solution, 1.2 mmol). The cyanoformate **2.31** was obtained as light red oil (120 mg, 0.45 mmol, 91%). $R_f$ = 0.71 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.35 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 4.49 (t, *J* = 6.9 Hz, 2H), 3.81 (s, 3H), 2.84 (t, *J* = 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 159.7, 144.1, 133.2, 114.8 114.0, 109.3, 83.0, 81.8, 66.6, 55.4, 19.6; IR (thin film) 3009, 2962, 2840, 2244, 1749, 1605, 1508, 1456, 1246, 1029, 833 cm$^{-1}$; HRMS (CI) calcd for $[C_{13}H_{11}NO_3 + NH_4]^+$, *m/z* 247.1077, found 247.1063.




**2.33**

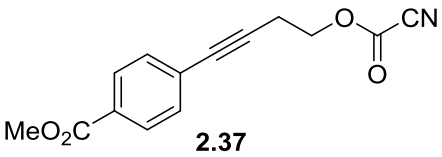
**Cyanoformate 2.33**: Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-N,N-dimethylphenyl)-butynol (100 mg, 0.53mmol) and carbonyl cyanide (1.1 ml of 1M solution, 1.1 mmol). The cyanoformate **2.33** was obtained as light red oil (110 mg, 0.45 mmol, 86%). $R_f$ = 0.48 (1:4 EtOAc:Hex) 1H NMR (300 MHz, CDCl3) $\delta$ 7.27 (d, J = 6.9 Hz, 2H), 6.62 (d, J = 6.9 Hz, 2H),

4.49 (t, J = 6.9 Hz, 2H), 2.97 (s, 6H), 2.85 (t, J = 6.9 Hz, 2H); 13C NMR (75 MHz, CDCl3) δ 150.2, 144.2, 132.8, 111.9, 109.5, 109.3, 83.9, 80.7, 66.8, 40.3, 19.8; IR (thin film) 2902, 2816, 2247, 1747, 1608, 1523, 1451, 1240, 908, 819 $cm^{-1}$; HRMS (CI) calcd for $[C_{14}H_{14}N_2O_2+ H]+$, *m/z* 243.1128, found 243.1124.



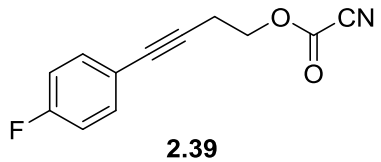

**2.35**

**Cyanoformate 2.35:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-Acetylphenyl)-butynol (104 mg, 0.55 mmol) and carbonyl cyanide (2.0 ml of 0.56 M solution, 1.1 mmol). Cyanoformate **2.35** was obtained as yellow oil and solidified upon cooling (103 mg, 0.43 mmol, 78%) $R_f$ = 0.63 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 4.53 (t, *J* = 6.6 Hz, 2H), 2.90 (t, *J* = 6.9 Hz, 2H), 2.58 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 198.1, 144.7, 136.9, 132.5, 128.9, 128.2, 109.8, 87.7, 83.1, 66.8, 27.3, 20.3; IR (thin film) 3051, 2956, 2245, 1754, 1686, 1601, 1403, 1359, 1261, 1180, 958 $cm^{-1}$; HRMS (CI) calcd for $[C_{14}H_{11}NO_3 H]^+$, *m/z* 242.0812, found 242.0802.




**2.37**

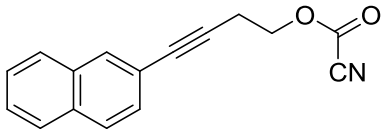
**Cyanoformate 2.37:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-Methoxycarbonylphenyl)-butynol (120 mg, 0.59 mmol) and carbonyl cyanide (2.36 ml of 1M solution, 2.36 mmol). The cyanoformate **2.37** was obtained as a white solid (128 mg, 0.50 mmol, 85%). $R_f$ = 0.60 (3:7 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.98 (d, *J* = 9 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 4.53 (t, *J* = 6.9 Hz, 2H), 3.92 (s, 3H), 2.90 (t, *J* = 6.6 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.6, 144.1, 131.7, 129.7, 129.6, 127.5, 109.2, 86.6, 82.5, 66.2, 52.4, 19.7; IR (thin film) 2999, 2954, 2246, 1752, 1720, 1606, 1437, 1277, 1110, 860 cm$^{-1}$; HRMS (CI) calcd for $[C_{14}H_{11}NO_4 + H]^+$, *m/z* 258.0755, found 258.0767.




**2.39**

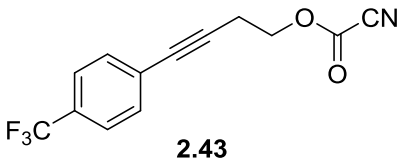
**Cyanoformate 2.39:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-fluorophenyl)-butynol (150 mg, 0.91 mmol) and carbonyl cyanide (2.7 ml of 1M solution, 2.7 mmol). The cyanoformate **2.39** was obtained as light red oil (170 mg, 0.78 mmol, 85%). $R_f$ = 0.70 (3:7 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.39 (dd, *J* = 5.1, 8.7 Hz, 2H), 7.01 (dd, *J* = 8.7, 8.7 Hz, 2H), 4.51 (t, *J* = 6.6 Hz, 2H), 2.86 (t, *J* = 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 162.6 (*J* = 247.7 Hz), 144.1, 134.3 (*J* = 247.7 Hz), 119.6, 115.8 (*J* = 21 Hz), 109.2, 83.1, 82.1, 66.4, 19.7; IR (thin film) 2970, 2911, 2244, 1752, 1601, 1505,

1247, 836 $cm^{-1}$; HRMS (CI) calcd for $[C_{12}H_8FNO_2 + NH_4]^+$, *m/z* 235.0877, found 235.0890.



**2.41**

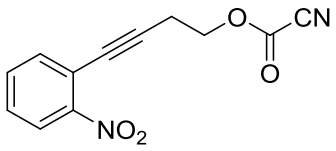
**Cyanoformate 2.41:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(2-Napthyl)-butynol (120 mg, 0.61 mmol) and carbonyldicyanide (1.83 ml of 1M solution, 1.83 mmol). The cyanoformate **2.41** was obtained as a brown solid (110 mg, 0.56 mmol, 91%). $R_f$ = 0.52 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.97 (s, 1H), 7.84-7.79 (m, 3H), 7.54-7.45 (m, 3H), 4.53 (t, *J* = 6.9 Hz, 2H), 2.91 (t, *J* = 6.9 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.8, 133.6, 133.5, 132.3, 129.1, 128.8, 128.5, 128.4, 127.5, 127.3 120.8, 109.9, 84.5, 84.1, 67.1, 20.4; IR (thin film) 3058, 2967, 2246, 1749, 1597, 1501, 1459, 1247, 979, 819 $cm^{-1}$; HRMS (CI) calcd for $[C_{16}H_{11}NO_2 + NH_4]^+$, *m/z* 267.1128, found 267.1158.



**2.43**

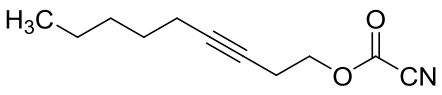
**Cyanoformate 2.43:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(4-trifluoromethylphenyl)-butynol $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.58 - 7.49 (m, 4H), 4.52 (t, *J* = 6.6 Hz, 2H), 2.89 (t, *J* = 6.6 Hz, 2H);

$^{13}C$ NMR (75MHz , $CDCl_3$) $\delta$ 143.9, 132.1, 131.9, 130.2, 128.1 (q, *J* = 250 Hz), 125.2 (q, *J* = 3.5Hz), 122.0, 109.0, 86.0, 81.8, 66.0, 19.5; GC-MS (CI) calcd for $[C_{13}H_8F_3NO_3 + H]^+$, *m/z* 268, found 268.




**2.45**

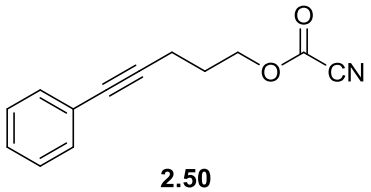
**Cyanoformate 2.45:** Prepared using the general procedure of cyanoformate ester synthesis from 4-(2-nitrophenyl)-but-3-yn-1-ol (101 mg, 0.53 mmol) and carbonyldicyanide (3.2 ml of 0.33 M solution, 1.06 mmol). The cyanoformate **2.45** was obtained as a brown solid (82 mg, 0.34 mmol, 64%). $R_f$ = 0.60 (1:4 EtOAc:Hex) $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.03 (dd, *J* = 0.8, 7.8 Hz, 1H), 7.61 - 7.54 (m, 2 H), 7.50 - 7.44 (m, 1H), 4.56 (t, *J* = 6.6 Hz, 2H), 2.95 (t, *J* = 6.6 Hz, 2H); $^{13}C$ NMR (75MHz , $CDCl_3$) $\delta$ 149.9, 143.9, 134.7, 132.8, 128.8, 124.5, 117.9, 109.0, 91.8, 78.3, 65.8, 19.8; GC-MS (CI) calcd for $[C_{12}H_8N_2O_4 + H]^+$, *m/z* 245, found 245.




**2.47**

**Cyanoformate 2.47:** Prepared using the general procedure of cyanoformate ester synthesis from 3-nonyne-1-ol (75 mg, 0.54 mmol) and carbonyldicyanide (1.6 ml of 1M solution, 1.6 mmol). The cyanoformate **2.47** was obtained as

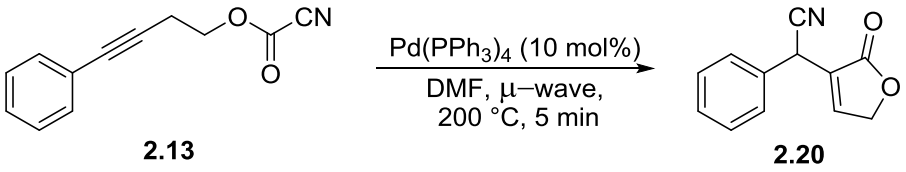
colorless oil (91 mg, 0.47 mmol, 88%). $R_f$ = 0.78 (1:4 EtOAc:Hex) $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.39 (t, *J* = 6.8 Hz, 2H), 2.63-2.58 (m, 2H), 2.17-2.12 (m, 2H), 1.49 (quint, *J* = 6.8 Hz, 2H), 1.36-1.31 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.2, 109.3, 83.6, 73.6, 67.0, 31.1, 28.5, 22.3, 19.1, 18.7, 14.1; IR (thin film) 2959, 2932, 2860, 2244, 1753, 1458, 1379, 1249, 985, 959, $cm^{-1}$; HRMS (CI) calcd for $[C_{11}H_{15}NO_2 + NH_4]^+$, *m/z* 211.1441, found 211.1430.




**2.50**

**Cyanoformate 2.50:** Prepared using the general procedure of cyanoformate ester synthesis from 5-phenylpent-4-yn-1-ol (100 mg, 0.625 mmol) and carbonyldicyanide (4.7 ml of 0.26 M solution, 1.27 mmol). The cyanoformate **2.50** was obtained as brown oil (120 mg, 0.60 mmol, 96%). $R_f$ = 0.55 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.41 - 7.38 (m, 2H), 7.32 - 7.28 (m, 3H), 4.53 (t, *J* = 6.3 Hz, 2H), 2.58 (t, *J* = 6.8 Hz, 2H), 2.02 (q, *J* = 6.6 Hz, 2H); $^{13}$C NMR (75 MHz , $CDCl_3$) $\delta$ 144.1, 131.5, 128.2, 127.9, 123.1, 109.2, 87.2, 81.9, 67.5, 26.8, 15.7; IR (thin film) 3048, 2924, 2241, 1749, 1589, 1448, 1248 $cm^{-1}$; GC-MS (CI) calcd for $[C_{13}H_{11}NO_2 + H]^+$, *m/z* 214, found 214.

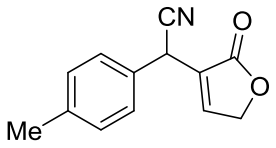
**General Procedure for Cyanoesterfication**




**2.13** **2.20**

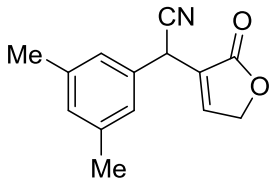
**Scheme 2.9**: Intramolecular Cyanoesterification of Alkynes

Cyanoformate **2.13** (100 mg, 0.5 mmol), $Pd(PPh_3)_4$ (60 mg, 0.051mmol) and dry DMF (5 ml, 0.1 M) were added to a microwave vial inside a $N_2$ filled glove box. The vial was sealed, removed from glove box and irradiated with microwaves at 200 $^oC$ for five minutes. The mixture was allowed to cool to RT and solvent was removed *in vacuo*. Traces of DMF were removed by co-evaporation with toluene (10 to 15 ml). The crude reaction mixture was purified by silica gel flash column chromatography (30 to 35% v/v EtOAc in hexanes) to provide butenolide **2.20** as yellow oil (80 mg, 0.40 mmol, 80%). $R_f$ = 0.52 (1:1 EtOAc:Hex); $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 7.23 (dd, *J* = 1.5, 8.1 Hz, 2H), 7.06-6.95 (m, 3H), 6.34 (ddd, *J* = 1.5 ,1.5, 1.5 Hz, 1H), 4.41(d, *J* = 1.2 Hz, 1H), 3.74-3.54 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.9, 148.3, 132.2, 130.2, 129.5, 129.0, 127.7, 117.7, 70.5, 34.1; IR (thin film) 3089, 2929, 2249, 1770, 1652, 1494, 1455, 1196, 1046, 701 $cm^{-1}$; HRMS (ESI) calcd for $[C_{12}H_9NO_2 + Na]^+$, *m/z* 222.0525, found 222.0527.




**2.22**

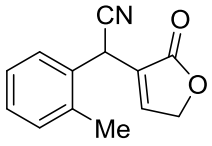
**Butenolide 2.22:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.21**(60 mg, 0.28 mmol), $Pd(PPh_3)_4$ (34 mg, 0.029mmol) and DMF (2.8 ml). The crude product was purified by silica gel flash column chromatography (25% EtOAc in hexanes) to provide butenolide **2.22** as a yellow oil (57.8 mg, 0.27 mmol, 96%) $R_f$ = 0.60 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.15 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 7.8 Hz, 2H), 6.27 (ddd, *J* = 1.5, 1.5, 1.5 Hz, 1H), 4.32 (d, *J* = 1.2 Hz, 1H), 3.60-3.40 (m, 2H), 1.98 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 147.9, 139.1, 131.3, 130.2, 129.2, 127.6, 117.9, 70.5, 33.8, 21.2; IR (thin film) 3089, 2925, 2248, 1758, 1651, 1513, 1445, 1193, 1080, 819 cm$^{-1}$; HRMS (ESI) calcd for $[C_{13}H_{11}NO_2 + Na]^+$, *m/z* 236.0682, found 236.0683.




**2.24**

**Butenolide 2.24**: Prepared using the general procedure for cyanoesterification from cyanoformate **2.23** (45 mg, 0.2 mmol), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and DMF (2.0 ml). The crude product was purified by silica gel flash column

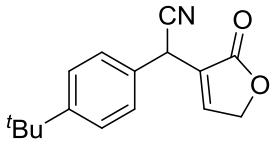
chromatography (25% EtOAc in hexanes) to provide butenolide **2.24** as yellow oil (33 mg, 0.14 mmol, 73%) $R_f$ = 0.51 (1:1EtOAc: Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 6.94 (s, 2H), 6.64 (s, 1H), 6.29 (s, 1H), 4.36 (s, 1H), 3.58-3.39 (m, 2H), 2.01(s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.7, 148.6, 139.9, 132.7, 131.3, 126.1, 126.0, 118.6, 71.1, 34.6, 21.9; IR (thin film) 3094, 2921, 2246, 1756, 1603, 1445, 1072, 1045, 824 cm$^{-1}$; HRMS (ESI) calcd for $[C_{14}H_{14}NO_2 + Na]^+$, *m/z* 250.0838, found 250.0842.




**2.26**

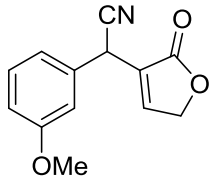
**Butenolide 2.26:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.25** (60 mg, 0.28 mmol), $Pd(PPh_3)_4$ (34 mg, 0.02mmol) and DMF (2.9 ml). The crude product was purified by silica gel flash column chromatography (25% EtOAc in hexanes) to provide butenolide **2.26** as yellow oil (36 mg, 0.14 mmol, 60 %). $R_f$ = 0.53 (1:1EtOAc: Hex); (The product contained small amount of carbonate which could not be separated. Corrected yield from $^1$H NMR after adjusting the carbonate was 53%).$^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.23-7.20 (m, 1H), 6.96-6.93 (m, 2H), 6.85-6.82 (m, 1H), 6.19 (ddd, *J* = 1.5, 1.5, 1.5, Hz, 1H), 4.57 (d, *J* = 1.5 Hz, 1H), 3.62-3.46 (m, 2H), 1.99 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.9, 148.8, 136.1, 131.6 130.4, 129.3, 127.9, 127.2, 126.9, 117.7, 65.1, 31.1, 19.5; IR (thin film) 3092, 2963, 2249, 1760, 1652, 1463, 1195,

1078, 1046 $cm^{-1}$; HRMS (ESI) calcd for $[C_{13}H_{11}NO_2 + Na]^+$, *m/z* 236.0682, found 236.0669.



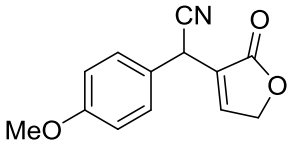

**2.28**

**Butenolide 2.28:** Prepared using the general procedure for cyanoesterification with cyanoformate **2.27** (50 mg, 0.20 mmol), $Pd(PPh_3)_4$ (22.5 mg, 0.02mmol) and DMF (2.0 ml). The crude product was purified by silica gel flash column chromatography (25% EtOAc in hexanes) to provide butenolide **2.28** as a yellow oil (35 mg, 0.14 mmol, 70%). $R_f$ = 0.49 (1:1 EtOAc:Hex);$^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.26 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1,Hz, 2H), 6.25 (s, 1H), 4.36 (s, 1H), 3.55-3.35 (m, 2H), 1.12 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 152.3, 147.8, 130.8, 129.2, 127.5, 126.5, 118.0, 70.5, 34.8, 33.8, 31.4; IR (thin film) 3092, 2963, 2249, 1760, 1652, 1463, 1195, 1078, 1046 $cm^{-1}$; HRMS (ESI) calcd for $[C_{16}H_{17}NO_2 + Na]^+$, *m/z* 278.1151, found 278.1143.




**2.30**

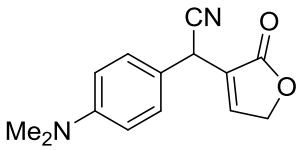
**Butenolide 2.30:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.29** (65 mg, 0.28 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028mmol) and DMF (2.8 ml). The crude product was purified by silica gel flash column chromatography (25 to 30% EtOAc in hexanes) to provide butenolide **2.30** as a yellow oil (53 mg, 0.14 mmol, 83%). $R_f$ = 0.50 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.00-6.95 (m, 2H), 6.89 (ddd, *J* = 1.2, 1.2, 7.5 Hz, 1H), 6.61 (ddd, J = 0.9, 2.7, 8.1 Hz, 1H), 6.29 (ddd, *J* = 1.5 ,1.5, 1.5 Hz, 1H), 4.36 (s, 1H), 3.64-3.45 (m, 2H), 3.27 (s, 3H);$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 160.3, 148.4, 133.6, 130.6, 130.3, 119.8, 117.7, 114.4, 113.6, 70.5, 55.5, 34.1 IR (thin film) 3086, 2939, 2247, 1758, 1601, 1491, 1078, 1046, 786; HRMS (ESI) calcd for $[C_{13}H_{11}NO_3 + Na]^+$, *m/z* 252.0631, found 252.0627.




**2.32**

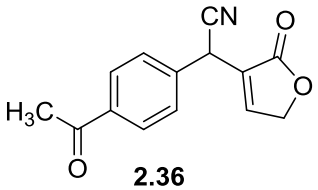
**Butenolide 2.32:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.31** (65 mg, 0.28 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028 mmol) and DMF (2.8 ml). The crude product was purified by silica gel flash column chromatography (25 to 30% EtOAc in hexanes) to provide butenolide **2.32** as yellow oil (53 mg, 0.14 mmol, 75%). $R_f$ = 0.50 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.16 (d, *J* = 8.4 Hz, 2H), 6.65 (d, *J* = 8.7 Hz, 2H), 6.34 (ddd, *J* =

1.2, 1.2, 1.2 Hz, 1H), 4.35 (d, *J* = 0.9 Hz, 1H), 3.69-3.51 (m, 2H), 3.23 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 160.1, 147.7, 130.9 129.1, 124.1, 118.0, 114.9, 70.5, 55.5, 33.6; IR (thin film) 3082, 2932, 2247, 1757, 1609, 1512, 1443, 1081, 1044, 828 cm$^{-1}$; HRMS (ESI) calcd for $[C_{13}H_{11}NO_3 + Na]^+$, *m/z* 252.0631, found 252.0615.



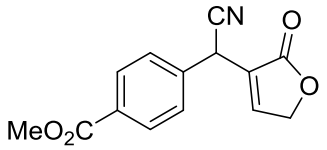

**2.34**

**Butenolide 2.34:** Prepared using the general procedure for cyanoesterification with cyanoformate **2.33** (50 mg, 0.21 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol) and DMF (2.0 ml). The crude product was purified by silica gel flash column chromatography (25 to 30% EtOAc in hexanes) to provide butenolide **2.34** as a red solid (34.1 mg, 0.14 mmol, 68%). $R_f$ = 0.48 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.22 (d, *J* = 8.7 Hz, 2H), 6.43 (d, *J* = 9 Hz, 2H), 6.36 (d, *J* = 1.2 Hz, 1H), 4.39 (d, *J* = 1.5 Hz, 1H), 3.64-3.46 (m, 2H), 2.41 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.2, 150.7, 147.3, 131.1 128.6, 119.0, 118.4, 112.7, 70.4, 40.4, 33.4; IR (thin film) 2893, 2806, 2245, 1755, 1610, 1522, 1350, 1075, 1045, 814 cm$^{-1}$; HRMS (ESI) calcd for $[C_{14}H_{14}N_2O_2 + Na]^+$, *m/z* 265.0947, found 265.0954.




**2.36**

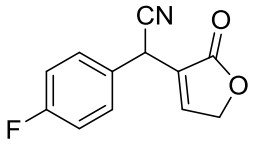
**Butenolide 2.36:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.35** (41 mg, 0.17 mmol), $Pd(PPh_3)_4$ (20 mg, 0.017mmol) and DMF (1.7 ml). The crude product was purified by silica gel flash column chromatography (35% EtOAc in hexanes) to provide lactone **2.36** as a yellow oil (20.5 mg, 0.085 mmol, 50%). $R_f$ = 0.40 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.62 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 7.8, Hz, 2H), 6.23 (ddd, *J* = 1.5, 1.5, 1.5 Hz, 1H), 4.25 (d, *J* = 1.2 Hz, 1H), 3.61-3.44 (m, 2H) 2.03 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.2, 170.8, 148.5, 137.7, 136.9, 130.0, 139.5, 128.2, 117.2, 70.6, 34.2, 26.8; IR (thin film) 3092, 2925, 2250, 1757, 1684, 1439, 1358, 1194, 1080, 1046 cm$^{-1}$; HRMS (ESI) calcd for $[C_{14}H_{11}NO_3 + Na]^+$, *m/z* 264.0631, found 264.0639.




**2.38**

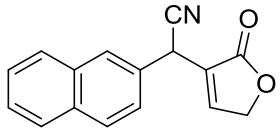
**Butenolide 2.38:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.37** (45 mg, 0.175 mmol), $Pd(PPh_3)_4$ (20 mg, 0.017mmol) and DMF (1.8 ml). The crude product was purified by silica gel flash column chromatography (35% EtOAc in hexanes) to provide butenolide **2.38** as a yellow oil which was solidified on cooling (24.5 mg, 0.095 mmol, 54%). $R_f$ = 0.40 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.97 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 8.7, Hz, 2H), 6.17 (d, *J* = 1.5 Hz, 1H), 4.23 (s, 1H), 3.57-3.39 (m, 5H); $^{13}$C NMR

(75 MHz, $CDCl_3$) $\delta$ 170.8, 166.2, 148.5, 136.9, 131.0, 130.8, 130.6, 127.9, 117.2, 70.6, 52.2, 34.2; IR (thin film2950, 2916, 2245, 1761, 1722, 1613, 1437, 1285, 1189, 1111, 1079, 1045 $cm^{-1}$; HRMS (ESI) calcd $[C_{14}H_{11}NO_4 + Na]^+$, *m/z* 280.0580, found 280.0585.



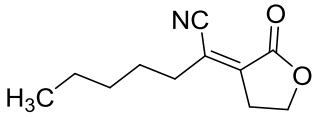

**2.40**

**Butenolide 2.40:** Prepared using the general procedure for cyanoesterification with cyanoformate **2.39** (45 mg, 0.28 mmol), $Pd(PPh_3)_4$ (33 mg, 0.028mmol) and DMF (2.8 ml). The crude product was purified by silica gel flash column chromatography (25 to 30% EtOAc in hexanes) to provide butenolide **2.40** as a yellow oil (53 mg, 0.14 mmol, 82%). $R_f$ = 0.47 (1:1 EtOAc:Hex); $^1H$ NMR (300MHz, $C_6D_6$) $\delta$ 6.97 (dd, *J* = 5.7, 8.7 Hz, 2H), 6.63 (dd, *J* = 8.4, 8.4 Hz, 2H), 6.18 (d, *J* = 1.2 Hz, 1H), 4.17 (s, 1H), 3.59-3.41 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 163.0 (d, *J* = 247.6 Hz), 148.1, 130.4 (d, *J* = 8.5 Hz), 129.6, 128.0, 117.6, 116.6 (d, *J* = 21.6 Hz), 70.6, 33.6; IR (thin film) 3083, 2920, 2249, 1757, 1604, 1509, 1443, 1081, 1046, 834 $cm^{-1}$; HRMS (ESI) calcd for $[C_{12}H_8FNO_2 + Na]^+$, *m/z* 240.0431, found 240.0421.

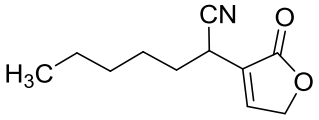



**2.42**

**Butenolide 2.42:** Prepared using the general procedure for cyanoesterification from cyanoformate **2.41** (60 mg, 0.24 mmol), $Pd(PPh_3)_4$ (28 mg, 0.024 mmol) and DMF (2.4 ml). The crude product was purified by silica gel flash column chromatography (25% EtOAc in hexanes) to provide butenolide **2.42** as a white solid (42 mg, 0.17 mmol, 70%). $R_f$ = 0.52 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.75 (s, 1H), 7.51-7.49 (m, 3H), 7.29-7.20 (m, 3H), 6.26 (s, 1H), 4.52 (d, *J* = 1.2 Hz, 1H), 3.64-3.46 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 148.4, 133.3, 133.2, 130.6, 129.6, 129.5, 128.2, 127.9, 127.2, 127.2, 127.1, 124.8, 117.8, 70.6, 34.3; IR (thin film) 3062, 2092, 2253, 1753, 1651, 1439, 1085, 1046, 824 cm$^{-1}$; HRMS (ESI) calcd $[C_{16}H_{11}NO_2 + Na]^+$, *m/z* 272.0682, found 272.0689.




**2.48**




**2.49**

**Lactone (2.48) and Butenolide (2.49):** Prepared using the general procedure for cyanoesterification from cyanoformate **2.47** (39 mg, 0.20 mmol), $Pd(PPh_3)_4$ (24 mg, 0.021 mmol) and DMF (2.0 ml). The crude product was purified by silica gel flash column chromatography (30 to 40% EtOAc in hexanes) to provide butenolide **2.48** as a colorless oil (16.2 mg, 0.08 mmol, 42%). The sample had

small amount of lactone **2.49** which could not be completely separated. $R_f$ = 0.48 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.43 (t, *J* = 6.9 Hz, 2H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.68 (quint, *J* = 7.2 Hz, 2H) 1.36-1.31 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.7, 138.4, 121.3, 115.2, 64.8, 33.8, 31.2, 27.5, 26.8, 22.4, 13.9; IR (thin film) 2957, 2930, 2861, 2217, 1761, 1653, 1458, 1376, 1257, 1175, 1025, 959, cm$^{-1}$; HRMS (ESI) calcd $[C_{11}H_{15}NO_2 + Na]^+$, *m/z* 216.0995, found 216.1009. Only *Z* isomer was observed. The *Z* alkene geomentry was ass geometry was assigned nOe (**Figure 2.1**).

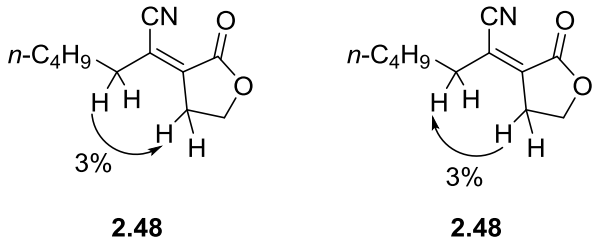



**Figure 2.1**: Geometry Confirmation of **2.48**

Lactone **2.49** was purified by silica gel flash column chromatography (40% EtOAc in hexanes) and **2.49** was isolated as a colorless oil (4.6 mg, 0.02 mmol, 12%). $R_f$ = 0.40 (1:1 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.56 (ddd, *J* = 1.5, 1.5, 1.5 Hz, 1H), 4.91 (s, 2H), 3.65 (ddd, *J* = 1.8, 4.8, 9.0 Hz, 1H), 2.02-1.90 (m, 1H), 1.82-1.70 (m, 1H), 1.53-1.49 (m, 2H), 1.39-1.32 (m, 4H), 0.90 (t, *J* = 6.9, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.3, 147.8, 130.0, 118.9, 70.5, 31.4, 31.0,

29.3, 26.7, 22.5, 14.1; IR (thin film) 2960, 2932, 2860, 2244, 1750, 1459, 1375, 1250, 985, $cm^{-1}$; HRMS (ESI) calcd $[C_{11}H_{15}NO_2 + Na]^+$, *m/z* 216.0995, found 216.0994.

## 2.8 References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# Chapter 3

# Intramolecular Cyanoacylation of Alkenes Using α-iminonitriles

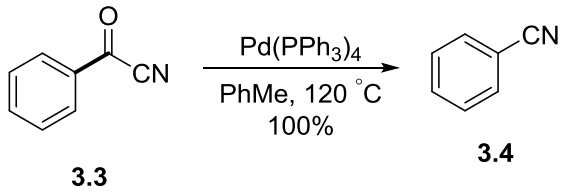
## 3.1 Introduction

In the first chapter, C–CN sigma-bond activation of cyanoformamides was introduced and the corresponding literature reports were presented. In the previous chapter challenges associated with C–CN sigma-bond activation of cyanoformate esters have been summarized which is caused by their propensity to undergo decarbonylation when heated in the presence of transition metals. One of the possible reasons for this observation is the greater donation ability of nitrogen lone pair (like in compound **3.1**) compared to its oxygen counterpart (like in compound **3.2**) (Figure 3.1). The availability of nitrogen lone pair strengthens the bond between nitrogen and carbonyl, decreasing the propensity for decarbonylation. As oxygen is not as good donor as nitrogen, it exhibits tendency to decarbonylate, leading to other by products.


**3.1** **3.2**

**Figure 3.1**: Decarbonylation of Cyanoformamides vs Cyanoformate esters

Considering the above logic, C–CN sigma-bond activation of acylnitriles like **3.3** (Scheme 3.1) can be extremely challenging as such compounds have no donating groups to strengthen bond between phenyl group and carbonyl group. When such compounds are heated in the presence of late transition metals they immediately decarbonylate to give the corresponding nitriles. Murahashi reported that heating benzoyl nitrile (**3.3**) in toluene in the presence of $Pd(PPh_{3)4}$ (commonly used catalyst for C–CN sigma-bond activation of cyanoformamides and cyanoformate esters), resulted in decarbonylation to give benzonitrile (**3.4**) in quantitative yield.[1]

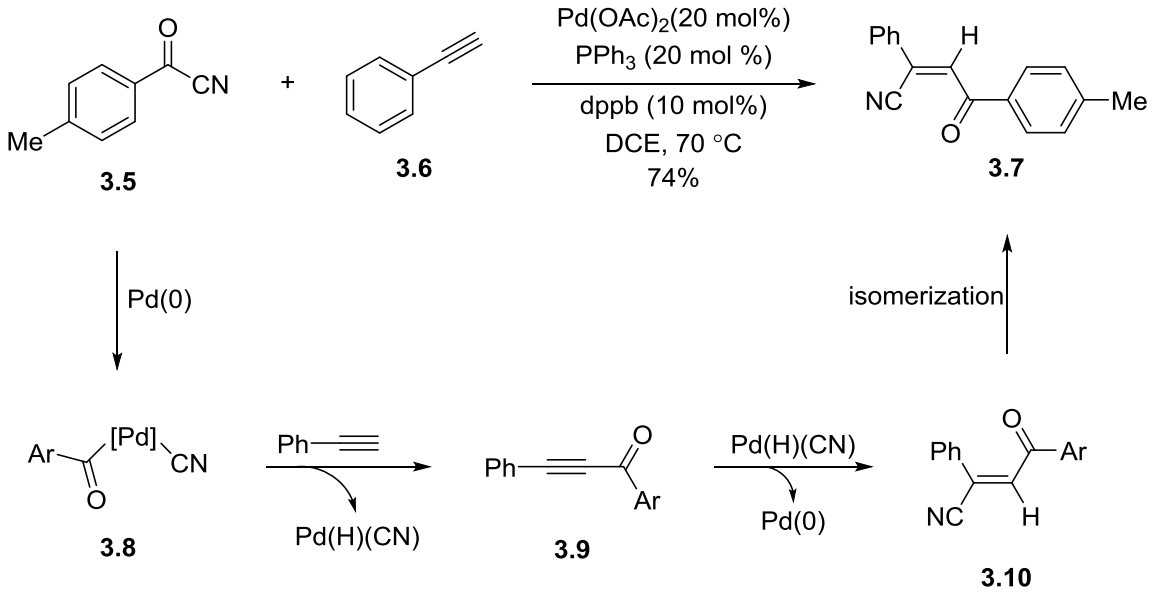



**3.3** **3.4**

**Scheme 3.1**: Decarbonylation of Acylnitriles in the Presence of Pd

The first example of acylcyanation of alkynes using transition metal was reported by Takaya (Scheme 3.2).[2] When solution of benzoyl cyanide **3.5** and phenyl acetylene (**3.6**) in 1,2-dichloroethane are heated in the presence of $Pd(OAc)_2$ and $PPh_3$ it gives acylcyanation product **3.7** is obtained in good yield. At first glance, it appears that the reaction proceeds *via* a typical C–CN sigma-

bond activation pathway, further study of the reaction mechanism provided evidence for different mechanism.[3] The reaction begins with the C–CN sigma-bond activation of benzoyl cyanide **3.5** by Pd(0) (generated *in situ)* to form Pd(II) complex **3.8** which upon ligand exchange with phenyl acetylene gives acetylenic ketone **3.9** and Pd(H)(CN). Subsequent hydrocyantion gives *E* olefin **3.10** which upon isomerization gives *Z* olefin and overall acylcyanation product **3.7**. This pathway limits the scope of reaction to terminal alkynes and also product ratio is determined by the thermodynamic stability of the *E* and *Z* isomers.

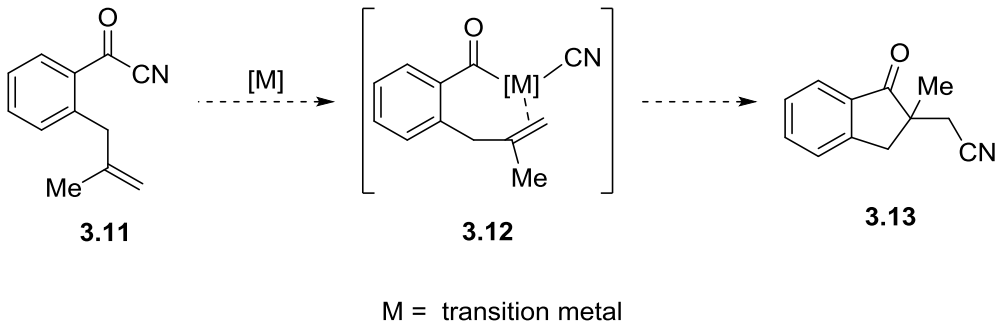



**Scheme 3.2**: Pd-catalyzed Acylcyanation of Terminal Alkynes

To the best of our knowledge no other example of acylcyantion *via* transition metal catalyzed C–CN sigma-bond activation not been reported. However oxycyanation *via* O–CN sigma-bond activation[4] and β-cyanation of styrenes *via* N–CN sigma-bond activation[5] have also been reported.

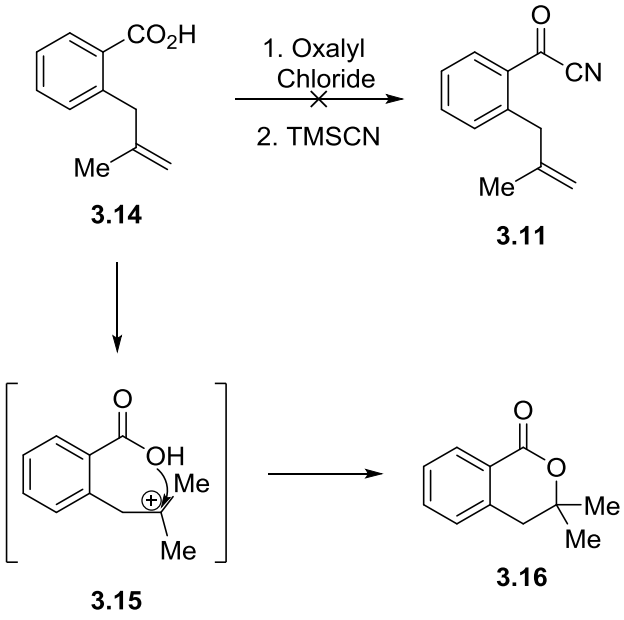
## 3.2 Initial Proposal

We hypothesized that acylcyanation of benzoyl cyanide **3.11** can be feasible by attaching a methallyl group ortho to the benzoyl cyanide (Scheme 3.3). When benzoyl cyanide **3.11** is treated with transition metal, it undergoes oxidative addition to form intermediate metal complex **3.12**. Presence of an alkene (or possibly triple bond) might cause coordination to metal center and inhibit by chelating the propensity to decarbonylate. Subsequent migratory insertion and reductive elimination would give indanone **3.13** completing acylcyanation process.



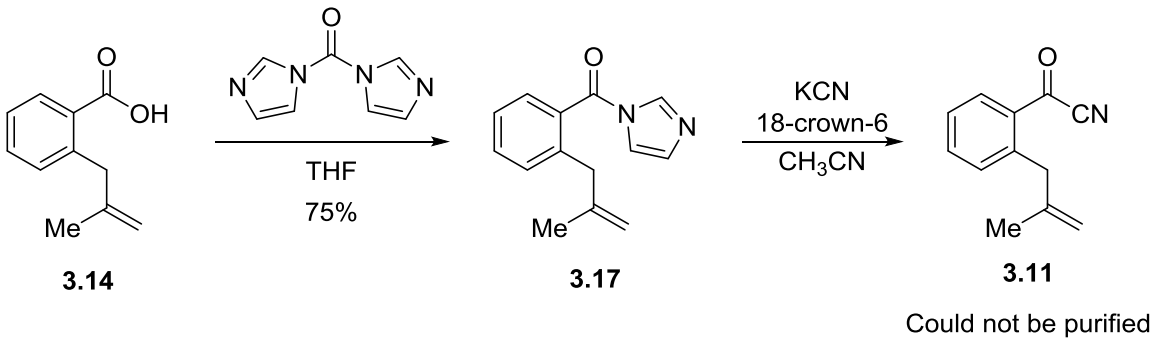

**Scheme 3.3**: Initial Proposal for Acylcyanation

Intrigued by this idea, we decided to synthesize benzoyl cyanide **3.11** and test the hypothesis. Generally benzoyl cyanides are synthesized from corresponding acid chlorides, which in turn are made from the corresponding carboxylic acids.[1] Benzoic acid **3.14** was synthesized following a reported procedure.[6] An attempt to convert benzoic acid **3.14** to benzoyl cyanide **3.11** *via* acid chloride and subsequent treatment with TMSCN was unsuccessful (Scheme 3.4). Instead isochromanone **3.16** was detected by $^1$H NMR. Possible reason for this reactivity is due to the byproduct HCl formed during the formation of acid chloride. HCl might have protonated double bond to form teritiary carbocation **3.15** and subsequent cyclization of carboxylic acid onto carbocation would lead to isochromanone **3.16** after the loss of proton.




**Scheme 3.4**: Attempt to Synthesize Benzoyl Cyanide **3.13**

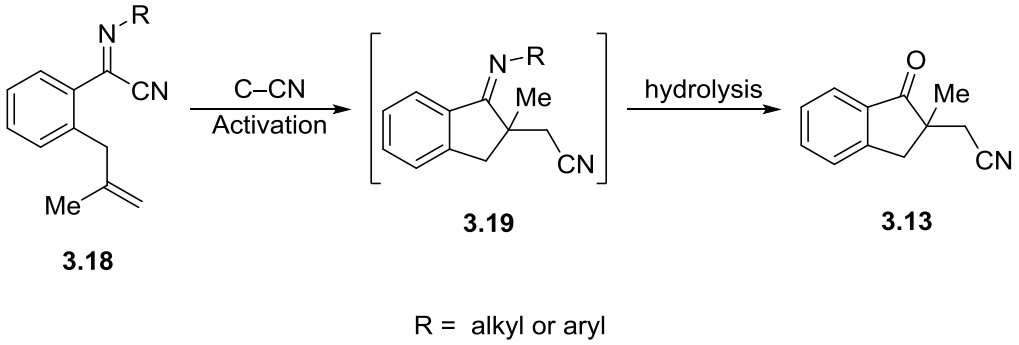
We then considered that benzoyl cyanide **3.11** could be made by activating carboxylic acid **3.14** using carbonyl dimidazole (CDI)[7] and subsequent displacement of imidazole by cyanide ion. Imidazole amide **3.17** was prepared from benzoic acid **3.14** using carbonyl dimidazole (CDI) in 75% yield (Scheme 3.5).[8] Amide **3.17** was treated with KCN in the presence of 18-crown-6 and the reaction was monitored by $^1$H NMR. Monitoring the reaction by spectroscopy indicated complete consumption of the starting material **3.17** and the formation of new product with $^1$H NMR signals consistent with the benzoyl cyanide **3.11** in addition to the formation of imidazole byproduct. However, benzoyl cyanide **3.11** was very reactive and reacted with water upon aqueous work up and gave benzoic acid **3.14**. All attempts to purify benzoyl cyanide **3.11** from byproduct (imidazole) and catalyst (18-crown-6) were unsuccessful and resulted in isolation of benzoic acid **3.14**.




**Scheme 3.5**: Attempt to Synthesize Benzoyl Cyanide 3.13 using CDI

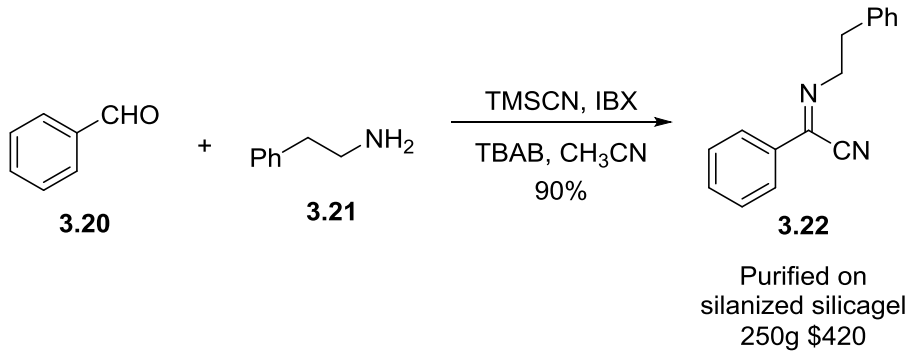
## 3.3 Alternate Strategy

We hypothesized that challenges of substrate synthesis could be overcome by using alternate substrate like α-iminonitrile **3.18** (Scheme 3.6). C–CN sigma-bond activation of **3.18** and subsequent addition across olefin gives imine **3.19**, which further could undergo hydrolysis to ketone **3.13** thus accomplishing overall acylcyantion process. This strategy can also reduce the possibility of decarbonylation which is a very competitive side reaction in the case of benzoyl cyanides. Similar strategy has been employed by our group to accomplish intramolecular hydracylation of benzaldehyes. *In situ* conversion of aldehydes to imines *via* cooperative catalysis significantly reduces the competitive decarbonylation giving corresponding hydroacylated products in high yields.[9]




**Scheme 3.6**: Alternate Strategy for Acylcyanation using α-iminonitrile

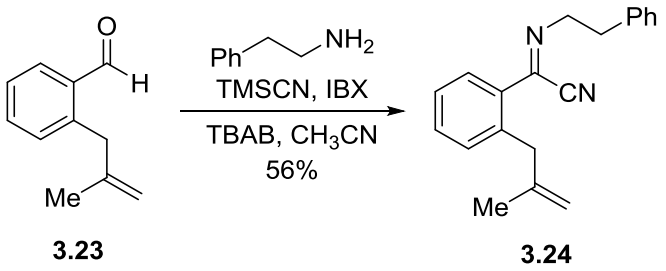
One challenge anticipated for the above strategy was the synthesis and purification of α-iminonitrile **3.18**. Zhu's report of the synthesis of α-iminonitrile **3.22** (Scheme 3.7) using benzaldehyde (**3.20**) and phethylamine (**3.21**) in the presence of TMSCN using IBX as oxidant was attractive.[10] A drawback of the reaction was that expensive silanized silica gel was used for purification. However repeating Zhu's reaction, but using neutral alumina for purification, we were able to isolate α-iminonitrile **3.22** in 70% yield. The yield though is slightly lower than the reported yield, but employing commonly used and less expensive alumina would be more economical for the development of α-iminonitriles in synthesis.[9]




**Scheme 3.7**: Literature Precedent for the Synthesis of α-iminonitrile[10]

Encouraged by the above result aldehyde **3.23** was synthesized following a reported procedure.[9] By slightly modifying the reaction conditions developed by Zhu (see experimental for more details) and using neutral alumina for purification

we were able to isolate α-iminonitrile **3.24** using aldehyde **3.23** in 56% yield (Scheme 3.8).



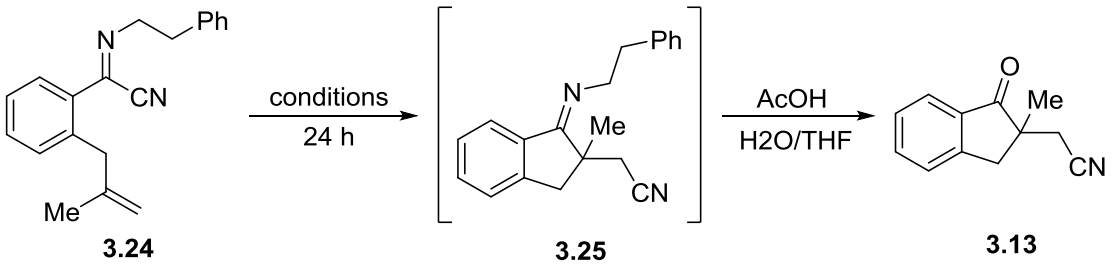

**3.23** **3.24**

**Scheme 3.8**: Synthesis of α-iminonitrile **3.24**

With substrate α-iminonitrile **3.24** in hand the possibility of C–CN sigma bond activation was explored (Table 3.1). Using standard catalyst $Pd(PPh_3)_4$ in *m*-xylene at 140 $^oC$ (entry 1) but no desired product was detected. Lewis acid additives were investigated based on earlier reports that these additives significantly improved the yields of alkene arylcyanation via C–CN activation of aryl nitriles.[11] When $BPh_3$ (20 mol %) was added (entry 2), signals anticipated for the desired product were detected in the $^1H$ NMR of the crude reaction mixture and a subsequent attempt to isolate imine **3.25** by chromatography was unsuccessful. Instead indanone **3.13** was isolated in 55% yield along with a double bond isomer of the starting material (23%). Various attempts were made to improve the yield of the desired product and reduce the formation of double

bond isomer of the starting material. Increasing the amount of $BPh_3$ (50 mol %) (entry 3) did not have any positive effect on the yield and desired product was isolated in slightly lower yield of 51%. Usage of stronger Lewis acid $B(C_6F_5)_3$ resulted in complete decomposition of the starting material and no product was detected (entry 4). When we tested the reaction with another source of palladium $Pd_2(dba)_3$ by adding external ligand $PPh_3$(20 mol %) and using $BPh_3$ (20 mol %) as Lewis acid, only 23% (NMR yield calculated using *p*-methoxyacetophenone as internal standard) of the intermediate imine **3.25** was detected (entry 5). We then switched back to the initial catalyst $Pd(PPh_3)_4$ and tested the reaction with other Lewis acids. Addition of $ZnCl_2$ (20 mol %) improved the yield of the product to 65% (entry 6). But moving to stronger zinc Lewis acid $Zn(OTf)_2$ was ineffective and no product was detected (entry 7). Changing to polar solvent 1,4-dioxane from *m*-xylene lead to incomplete conversion of the starting material and only 26% of the product observed by $^1H$ NMR of the crude reaction mixture (entry 8). Polar solvents seemed to have negative effect on the reaction yield. Gratifyingly lowering the temperature to 130 $^oC$ slightly improved the yield of the reaction (entry 9). Further decrease in the temperature in *m*-xylene did not improve the yield (not shown in the table). However lowering the temperature to 120 $^oC$ in toluene and increasing the catalyst loading to 15 mol % significantly enhanced the yield of the reaction and indanone **3.13** was isolated in 82% yield (entry 10) after hydrolysis in the presence of AcOH. Control reaction was run

**Table 3.1**: Optimization of Acylcyanation




**3.24** **3.25** **3.13**

| Entry | Catalyst (mol %) | Lewis Acid (mol %) | Solvent (0.2 M) | Temp (°C) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | $Pd(PPh_3)_4$(10) | - | *m*-xylene | 140 | 0 |
| 2 | $Pd(PPh_3)_4$(10) | $BPh_3$(20) | *m*-xylene | 140 | 55 |
| 3 | $Pd(PPh_3)_4$(10) | $BPh_3$(50) | *m*-xylene | 140 | 51 |
| 4 | $Pd(PPh_3)_4$(10) | $B(C_6F_5)_3$(20) | *m*-xylene | 140 | 0 |
| 5 | $Pd_2(dba)_3$(5)[b] | $BPh_3$(20) | *m*-xylene | 140 | 23[c] |
| 6 | $Pd(PPh_3)_4$(10) | $ZnCl_2$(20) | *m*-xylene | 140 | 65 |
| 7 | $Pd(PPh_3)_4$(10) | $Zn(OTf)_2$(20) | *m*-xylene | 140 | 0 |
| 8 | $Pd(PPh_3)_4$(10) | $ZnCl_2$(20) | 1,4-dioxane | 120 | 26[c],[d] |
| 9 | $Pd(PPh_3)_4$(10) | $ZnCl_2$(20) | *m*-xylene | 130 | 68 |
| 10 | **$Pd(PPh_3)_4$(15)** | **$ZnCl_2$(20)** | **PhMe** | **120** | **82** |
| 11 | -- | - | PhMe | 120 | 0 |
| 12 | -- | $ZnCl_2$(20) | PhMe | 120 | 0 |

[a] Isolated Yield of Indanone **3.13**. [b] $PPh_3$ (20 mol %) was added as ligand. [c] NMR yield of the intermediate imine calculated using *p*-methoxy acetophenone as internal standard. [d] 65% of the starting material detected.

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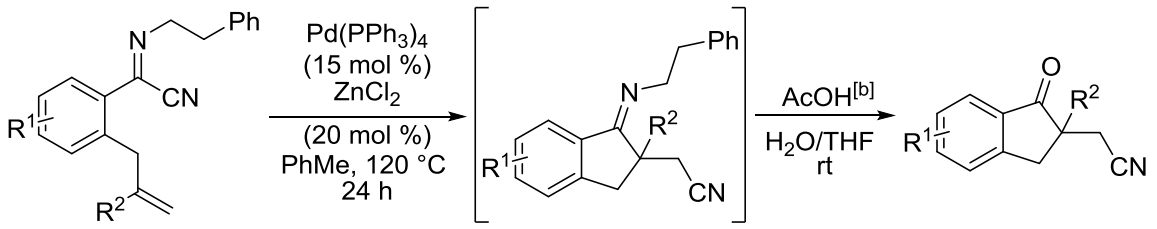
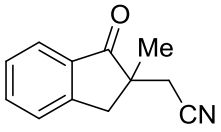
without any palladium and/or Lewis acid, and no product was detected (entries 11 and 12).

With optimized conditions in hand we studied the scope of the reaction by changing the substitution at various positions of the aromatic ring and double bond (Table 3.2). A very minor amount of product **3.26** was detected for *o*-fluorosubsrate at optimized conditions but upon increasing the temperature to 130 $^{o}$C, reaction proceeded smoothly corresponding indanone **3.26** was isolated in 73% yield. The reaction tolerates substitution at *meta* positions and the reaction with 3,5 difluoro substrate gave corresponding indanone **3.27** in 64% yield. Substitution at *para* position is also tolerated with *p*-methyl and *p*-fluoro substrates gave corresponding indanones **3.28** and **3.29** in high yields of 81% and 85% respectively. The reaction thus tolerates substitution at various positions of the phenyl ring. Interestingly reaction also tolerates *p*-chloro substitution on phenyl ring and the corresponding indanone **3.30** was isolated in 79% yield. A 3,5 difluoro, 4-trimethyl silyl substrate gave corresponding indanone **3.31** in 75% yield indicating that the reaction also tolerates tri-substitution on the aromatic ring. The reaction was tested by changing the substitution on the double bond from methyl to an ethyl group. Very little product was detected by $^{1}$H NMR

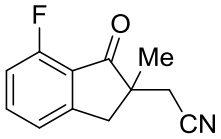
analysis of the crude reaction mixture with some un-consumed starting material when the α-iminonitrile was subjected to optimized conditions. Increasing the reaction temperature from 120 $^{o}$C to 130 $^{o}$C, lead to cleaner reaction and complete consumption of starting material. The corresponding indanone **3.32** was isolated after hydrolysis in 76% yield. No desired product **3.33** was detected when unsubstituted allyl substrate ($R^1$ = $R^2$ = H) was subjected to reaction conditions, possibly due to β–hydride elimination. Also no desired product **3.34** was detected by introducing benzyloxy methyl group instead of methyl. Instead complex reaction mixture was observed by $^1$H NMR analysis of crude reaction mixture. Possible reason for the observation is decrease in the electron density on the double bond due to inductively electron withdrawing nature of benzyloxy methyl group, which might have lowered the ability of the double bond to coordinate to Pd and therefore inhibited migratory insertion. Reaction was also studied by changing electron density on the aromatic ring. Presence of strong electron withdrawing group ($CF_3$) significantly improved the yield of the reaction and corresponding indanone **3.35** was isolated 90% yield. When the reaction was also tested with electron donating groups (*p*-$^t$Bu and *p*-OMe) on the aromatic ring, very small amount of corresponding intermediate imines were detected when subjected to optimized conditions. Increasing the catalyst loading to 20 mol % and raising the reaction temperature to 130 $^{o}$C led to cleaner reactions and the corresponding indanones **3.36** and **3.37** were isolated in 77% and 60% yields respectively, after hydrolysis.

**Table 3.2**: Substrate Scope of Acylcyanation[a,b]

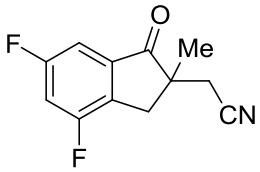


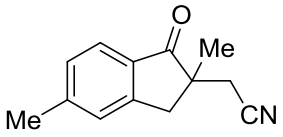

**3.13**, 82%



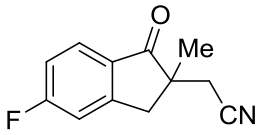

**3.26**, 73%[c]



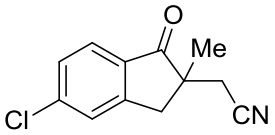

**3.27**, 64%



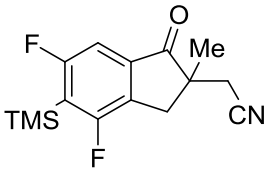

**3.28**, 81%



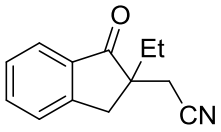

**3.29**, 85%



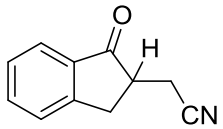

**3.30**, 79%



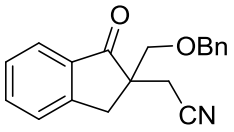

**3.31**, 75%



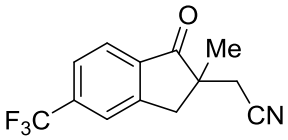

**3.32**, 76%[c]



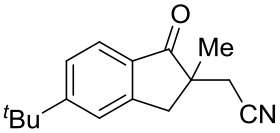

**3.33**, NR[d]



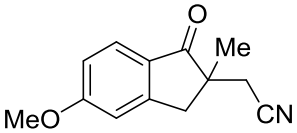

**3.34**, NR[d]




**3.35**, 90%



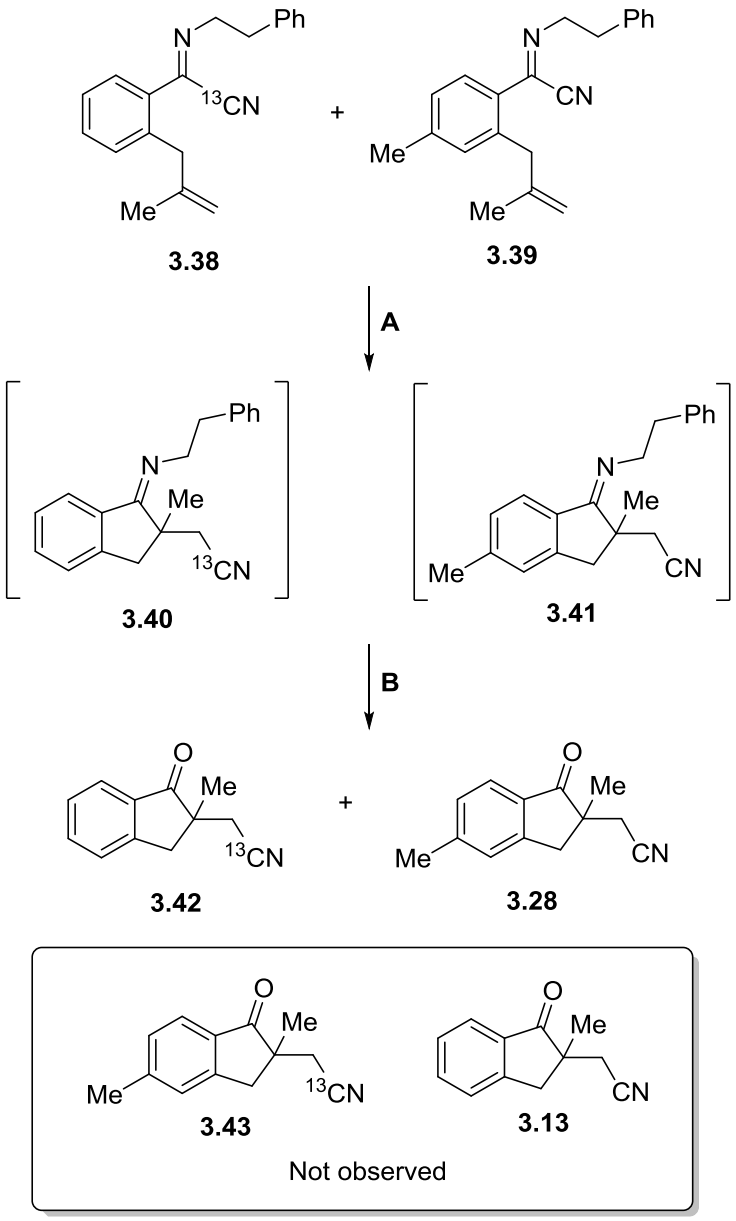

**3.36**, 77%[e]




**3.37**, 60%[e]

[a] Isolated yield of indanones after column chromatography on silica gel. [b] Please refer to experimental for exact time of hydrolysis for each substrate. [c] C–CN activation reaction was run at 130 °C. [d] No product was detected by $^1$H NMR analysis of crude reaction mixture. [e] C–CN activation reaction was run at 130 °C using 20 mol % $Pd(PPh_3)_4$.

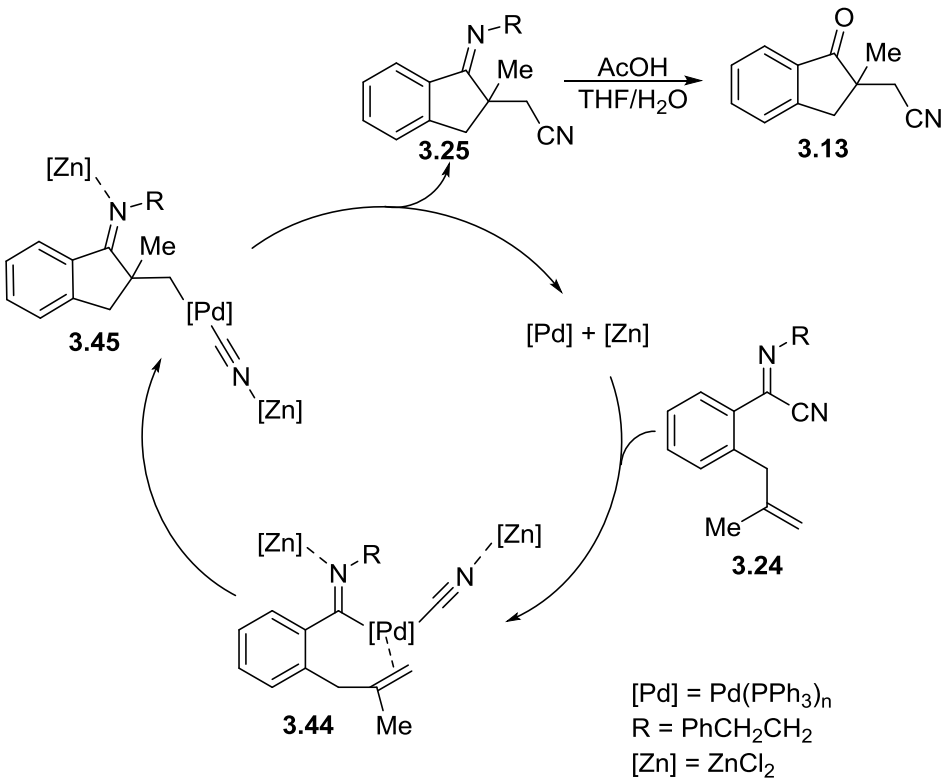
The presence of Lewis acid being critical to the reaction, we wanted to test if the binding of $ZnCl_2$ leads to cleavage of [Pd]–CN bond during the catalytic cycle. We subjected mixture of a $^{13}C$ labeled α-iminonitrile **3.38** and unlabelled α-iminonitrile **3.39** to the optimized reaction conditions (Scheme 3.9). If binding of $ZnCl_2$ leads to cleavage of [Pd]–CN bond during catalytic cycle, crossover products would be observed. On the other hand if binding of $ZnCl_2$ leads to simple activation of the bond without cleavage, no crossover products would be observed. We observed only the indanones **3.42** and **3.28** after hydrolysis and no crossover products (**3.43** and **3.13**) were observed. This indicates that $ZnCl_2$ simply promotes the reaction by binding to nitrogen and does not completely cleave the bond during catalytic cycle.




**A**: $Pd(PPh_3)_4$ (15 mol %), $ZnCl_2$ (20 mol %), PhMe, 120°C, 24 h
**B**: AcOH, AcOH, rt, 12 h

**Scheme 3.9**: Crossover Experiment

Based on the above observation, and previous studies[12] we believe that the reaction proceeds with the mechanism shown in Scheme 3.10. The reaction probably begins with oxidative addition of the C–CN sigma bond of the α-iminonitrile **3.24** on to Pd(0) catalyst. The reaction is very likely facilitated by binding of $ZnCl_2$ to the nitrogen of nitrile, imine or both leading to Pd(II) complex **3.44** where the olefin also coordinates to the complex. The complex **3.44** would then undergo migratory insertion onto olefin leading to complex **3.45**. Subsequent reductive elimination of complex **3.45** would lead to imine **3.25** and regeneration of active Pd(0) catalyst. Hydrolysis of imine **3.25** would provide indanone **3.13**.




**Scheme 3.10**: Plausible Mechansim

## 3.4 Conclusion and Future Work

In summary we reported the first metal catalyzed acylcyanation of alkenes by overcoming the challenge of decarbonylation. The reaction proceeds in good to excellent yields using a common palladium source ($Pd(PPh_3)_4$) and Lewis acid ($ZnCl_2$), without use of any designer ligands. A crossover experiment proved that the reaction proceeds in an intramolecular fashion with nitrile bound to the metal during catalytic cycle. In future work we would like to develop conditions for an asymmetric version of the reaction and intermolecular variant of the reaction.

## 3.5 Experimental

### Section A: General Details

General Details: All reactions were carried out using flame-dried glassware under nitrogen. Acetonitrile, toluene, dichloromethane and THF (tetrahydrofuran) were dried according to published procedures.[13] After drying toluene and dichloromethane were further deoxygenated by bubbling a stream of argon through the liquid for 30 min in a Strauss flask and then stored in a nitrogen filled glove box. $Pd(PPh_3)_4$ was purchased from Strem Chemicals. All palladium-catalyzed reactions were carried out in a Vacuum Atmospheres nitrogen filled glove box in 1 or 4 dram vials sealed with PTFE lined caps. Heating was applied by aluminum block heaters. All other chemicals were purchased from commercial vendors and used as received.

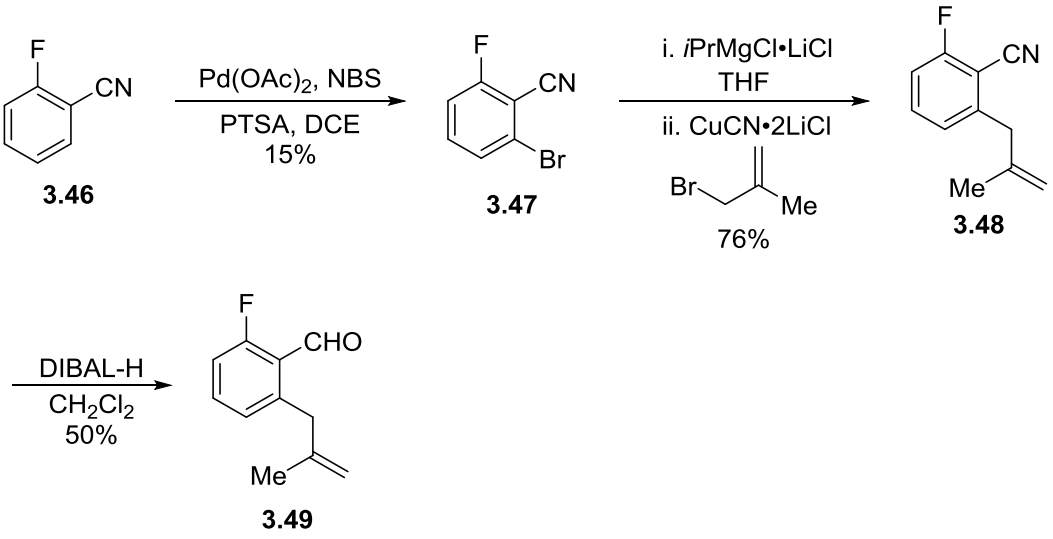
Analytical thin layer chromatography (TLC) was carried out using 0.25 mm silica plates from Silacycle and 200 μm alumina plates from Sorbent Technologies. Eluted plates are visualized first with UV light and then by staining with potassium permanganate/potassium carbonate. Flash chromatography was performed using 230–400 mesh (particle size 0.04–0.063 mm) silica gel purchased from Silacycle or neutral alumina (particle size 50 to 200 μm) purchased from Sorbent Technologies. $^{1}$H NMR (300 and 500 MHz) and $^{13}$C NMR (75 and 126 MHz) spectra were obtained on Varian and Bruker FT NMR instruments. NMR spectra were reported as $\delta$ values in ppm relative to, chloroform, dichloromethane, hexafluorobenzene, tetramethylsilane or using instrument standard. $^{1}$H NMR coupling constants are reported in Hz; multiplicity was indicated as follows; s (singlet); d (doublet); t (triplet); q (quartet); quint (quintet); m (multiplet); dd (doublet of doublets); ddd (doublet of doublet of doublets); dddd (doublet of doublet of doublet of doublets); dt (doublet of triplets); td (triplet of doublets); ddt (doublet of doublet of triplets); app (apparent); br (broad). Infrared (IR) spectra were obtained on films from $CH_2Cl_2$ or $CDCl_3$. Low-resolution mass spectra (LRMS) in EI or CI experiments were performed on a Varian Saturn 2200 GC-MS system or on Bruker BioTOF II using electrospray ionization (ESI) method. The column used in GC-MS was a capillary column of 30 meters in length and 0.4 mm in diameter. The method begins with initial temperature of 100 °C maintained for two min and increased with ramp of 5 °C per min until 250 °C which was maintained for 5 min. High-resolution mass

spectra (HRMS) with electrospray ionization (ESI) were performed on a Bruker BioTOF II and in chemical ionization (CI) were performed on a Finnigan MAT95 instrument.

## Section B

## Synthesis of Aldehydes:

### 2-(2-methylallyl)benzaldehyde (3.49):




2-bromo-6-fluorobenzonitrile **3.47** was prepared by slightly modifying the procedure reported by Sun.[14] To the mixture of 2-fluorobenzonitrile **3.46** (1.06 g, 8.8 mmol), NBS (3.2 g, 18 mmol) and *p*-toluenesulfonic acid (1.35 g, 7.0 mmol) in 1,2-dichloroethane (30 mL), $Pd(OAc)_2$ (200 mg, 0.9 mmol) was added and the reaction mixture was heated at 80 °C under air for 14 hours. After allowing to

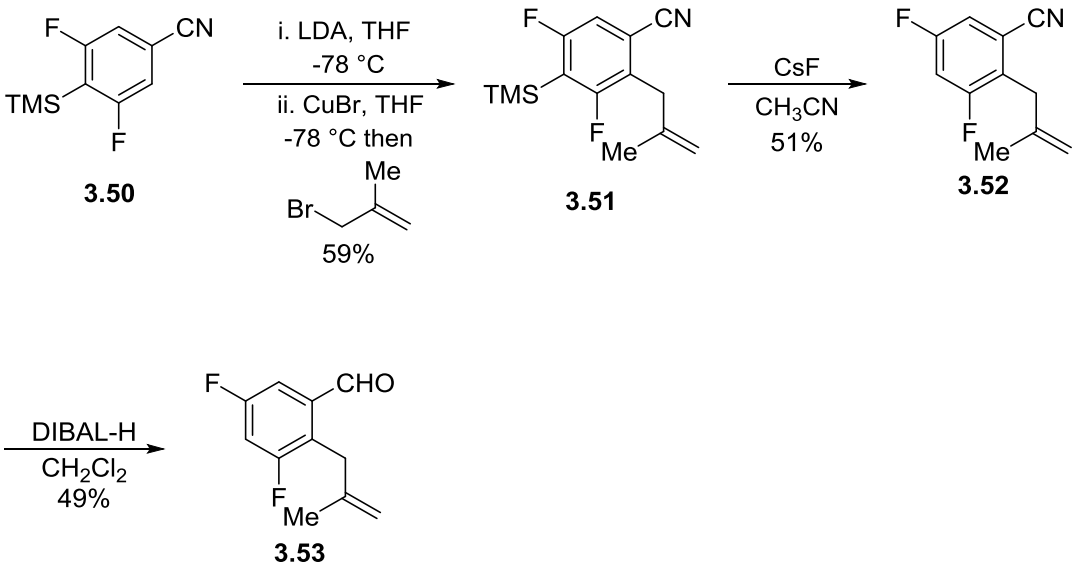
cool to room temperature, the reaction mixture was concentrated to remove solvent and other volatiles. The crude material was purified by flash column chromatography on silica (20 to 30% EtOAc in hexanes) to give slightly impure 2-bromo-6-fluorobenzonitrile **3.47** (0.25 g, 1.32 mmol, 15%). $R_f$ = 0.72 (3:7 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.54−7.44 (m, 2H), 7.20 (dt, *J* = 8.2, 1.4 Hz, 1H); $^{13}$C NMR (126MHz, $CDCl_3$) $\delta$ 163.8 (d, *J* = 263 Hz), 135.2 (app d, *J* = 10 Hz), 128.9, 125.8, 115.1 (d, *J* = 20 Hz), 112.4, 105.6; LRMS (GC-MS, CI, MeOH) *m*/*z* 201 (M + 2 + H) and 199 $(M + H)^+$, $t_R$ = 24.6 min. The material was of suitable purity to undergo next step.

2-bromo-6-fluorobenzonitrile, **3.47** (250 mg, 1.26 mmol) was dissolved in THF (0.2 mL) and cooled to 0 °C. *i*PrMgCl•LiCl.[15] (1.2 mL of a 1.3 M solution in THF, 1.6 mmol) was added and the reaction mixture was stirred for one hour at 0 °C. CuCN•2LiCl (0.13 mL of 1M solution in THF, 0.13 mmol) and 3-bromo-2-methyl-1-propene (0.2 mL, 2 mmol) were added at 0 °C and the solution was allowed to warm to room temperature and stirred for 14 hours at room temp. The reaction was quenched by addition of aqueous saturated $NH_4Cl$ solution (10 mL) and extracted with diethyl ether (2 x 30 mL). The organic layer was washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (15 g) and concentrated. The crude material was purified by flash column chromatography on silica (10% EtOAc in hexanes) to give 2-fluoro-6-(2-methylallyl)benzonitrile, **3.48** (167 mg, 1.6 mmol, 76%) $R_f$ = 0.50 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.52 (ddd, *J* = 8.1, 8.1, 5.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.07 (dt, *J* = 8.6, 1.0 Hz, 1H),

4.92−4.91 (m, 1H), 4.71 (d, *J* = 0.6 Hz, 1H), 3.54 (s, 2H), 1.74 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 177 $(M + H)^+$, $t_R$ = 12.9 min.

DIBAL-H (1.4 mL of 1 M solution in toluene, 1.4 mmol) was added to a solution of 2-fluoro-6-(2-methylallyl)benzonitrile, **3.48** (165 mg, 0.93 mmol) in methylene chloride (5 mL) maintained at 0 °C under nitrogen. The reaction was allowed to warm to room temperature and stirred for 14 hours. The reaction mixture was diluted with diethyl ether (7 mL) and cooled to 0 °C. HCl (5 mL of 3N solution) was added. The reaction mixture was heated to reflux for thirty minutes. Diethyl ether (30 mL) was added to the reaction mixture and layers were separated. The aqueous layer was extracted with diethyl ether (30 mL) and the combined organic extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated. The crude material was purified by flash column chromatography on silica (5% EtOAc in hexanes) to give **2-(2-methylallyl)benzaldehyde 3.49** (84 mg, 1.26 mmol 50%) $R_f$ = 0.70 (1:4 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 10.48 (s, 1H), 7.49 (ddd, *J* = 8.0, 8.0, 5.8 Hz, 1H), 7.08−7.03 (m, 2H), 4.81−4.79 (m, 1H), 4.43−4.42 (m, 1H), 3.73 (s, 2H), 1.78 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 179 $(M + H)^+$, $t_R$ = 12.7 min.

**3,5-difluoro-2-(2-methylallyl)benzaldehyde (3.53)**:



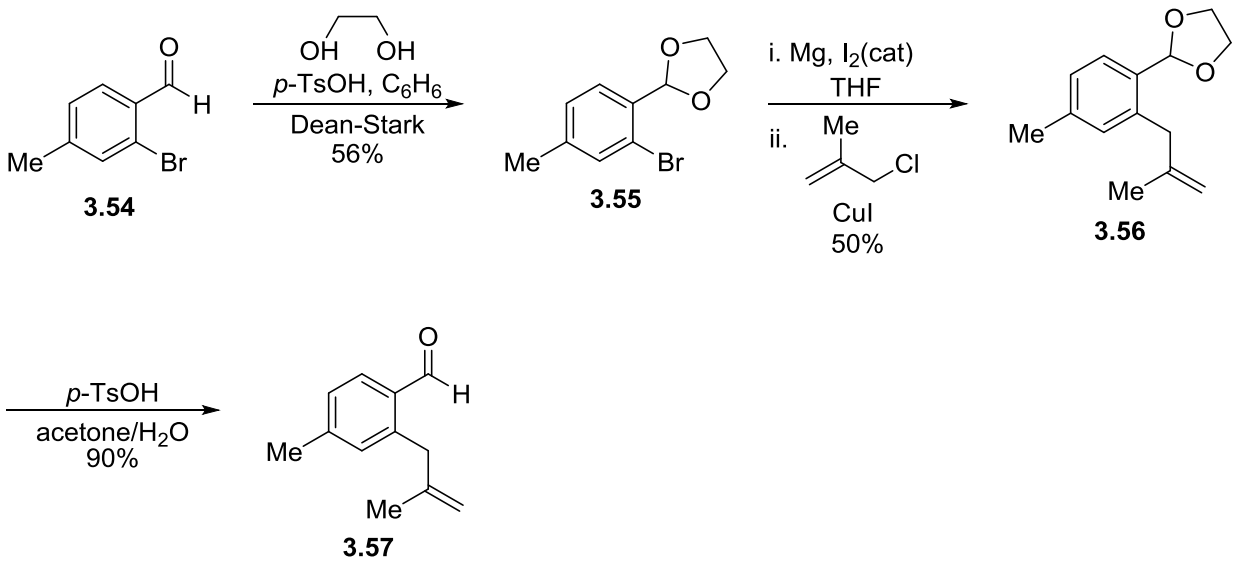

3,5-difluoro-4-(trimethylsilyl)benzonitrile **3.50** is prepared using the reported procedure.[16] A solution of diisopropyl amine (1.59 mL, 11.37 mmol) in THF (26 mL) was cooled to –78 °C under nitrogen. A solution of *n*-BuLi in hexanes (1.6 M hexanes, 4.55 mL, 11.37 mmol) was added dropwise and this solution was allowed to stir for 30 minutes. A solution of 3,5-difluoro-4-(trimethylsilyl)benzonitrile **3.50** (2.23 g, 10.53 mmol) in THF (4 mL) was added dropwise to the LDA solution and this was allowed to stir at –78 °C for 2 hours. The solution was then transferred *via* cannula cold to a stirred suspension of CuBr (1.5 g, 10.42 mmol) in THF (20 mL) that was cooled at –78 °C. The resulting dark blue solution was allowed to stir for 30 minutes, at which point methallyl bromide (1.06 mL, 10.53 mmol) was added dropwise. The solution was then allowed to warm to room temperature and was stirred for 15 hours. The

reaction was quenched with saturated aqueous $NH_4Cl$ (50 mL) and the aqueous layer was washed with $Et_2O$ (2 X 40 mL). The organics were then washed with brine (80 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The product was purified by column chromatography (2% EtOAc in hexanes) to yield 3,5-difluoro-2-(2-methylallyl)-4-(trimethylsilyl)benzonitrile **3.51** (1.66 g, 6.25 mmol, 59% yield). $R_f$ = 0.72 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.09 (dd, *J* = 7.7, 1.2 Hz, 1H), 4.84 – 4.83 (m, 1H), 4.57 (app s, 1H), 3.49 (s, 2H), 1.79 (s, 3H), 0.39 (t, *J* = 1.5 Hz, 9H); LRMS (GC-MS, CI, MeOH) *m*/*z* 266 $(C_{14}H_{17}F_2NSi + H)^+$, $t_R$ = 15.1 min.

To a stirred solution of 3,5-difluoro-2-(2-methylallyl)-4-(trimethylsilyl)benzonitrile **3.51** (1.6 g, 6.0 mmol) in distilled acetonitrile (22 mL) at room temperature was added anhydrous CsF (1.098 g, 7.2 mmol). This reaction was allowed to stir at room temperature until no starting material was observed by TLC (~12 hours). The reaction was then diluted with water and the layers were separated. The aqueous layer was extracted with $Et_2O$ (2 X 20 mL) and then the combined organics were washed with brine (40 mL), dried over $Na_2SO_4$, were filtered and concentrated *in vacuo*. The product was purified by column chromatography (2% EtOAc in hexanes) to yield 3,5-difluoro-2-(2-methylallyl)benzonitrile **3.52** (0.60 g, 3.11 mmol, 51% yield). $R_f$ = 0.50 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.25 – 7.20 (m, 1H), 7.10 (td, *J* = 9.2, 2.4 Hz, 1H), 4.85 (m, 1H), 4.59 (m, 1H), 3.53 (s, 2H), 1.79 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 194 $(C_{11}H_9F_2N + H)^+$, $t_R$ = 8.6 min.

A flame-dried flask under $N_2$ was charged with 3,5-difluoro-2-(2-methylallyl)benzonitrile **3.52** (0.5985 g, 3.1 mmol) and dichloromethane (21 mL). The solution was cooled to 0 °C and a solution of DIBAL-H in toluene (1M, 3.7 mL, 3.7 mmol) was added dropwise. The reaction was allowed to warm to room temperature over 15 h. The reaction mixture was then diluted with $Et_2O$ (18 mL) and HCl (3N, 18 mL) was added. The reaction was headed to reflux for 1 h, after which it was cooled to room temperature and was diluted with more $Et_2O$ (18 mL). The organics were separated and washed with $H_2O$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL), brine (50 mL) and were then dried over $Na_2SO_4$, filtered and concentrated. The product was purified by column chromatography (2% EtOAc in Hexanes) to yield **3,5-difluoro-2-(2-methylallyl)benzaldehyde 3.53** (0.2969 g, 1.51 mmol, 49% yield) as a yellow oil. $R_f$ = 0.5 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 10.17 (d, *J* = 2.6 Hz, 1H), 7.43 (ddd, *J* = 8.4, 2.6, 1.3 Hz, 1H), 7.07 (ddd, *J* = 9.3, 8.2, 2.7 Hz, 1H), 4.83 (dt, *J* = 2.5, 1.2 Hz, 1H), 4.38 (app s, 1H), 3.70 (s, 2H), 1.83 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 197 $(C_{11}H_{10}F_2O + H)^+$, $t_R$ = 9.5 min.

**2-(2-methylallyl)benzaldehyde (3.57):**



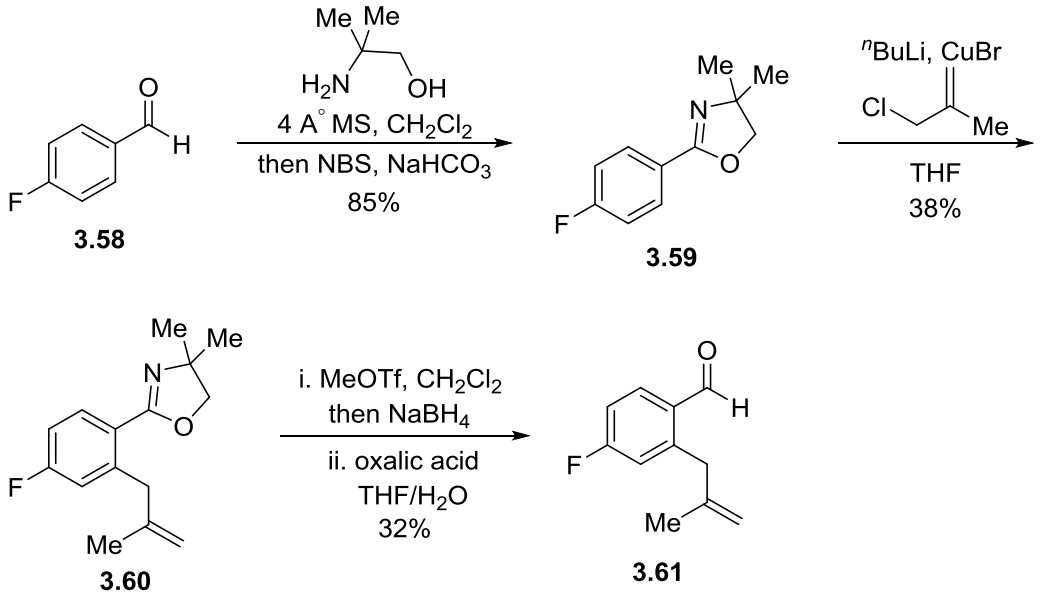

A solution of 2-bromo-4-methylbenzaldehyde, **3.54** (1.51 g, 7.6 mmol), ethylene glycol (0.86 mL, 15.2 mmol) benzene (4.2 mL) and *p*-TsOH (29 mg, 0.15 mmol) was heated to reflux with Dean-Stark trap and maintained for 14 hours. The reaction was neutralized with saturated aqueous $NaHCO_3$ solution (20 mL) and extracted twice with diethyl ether (2 x 50 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ (25 g) and concentrated. The crude material was purified by flash column chromatography on silica (gradient 5-10% EtOAc in hexanes) to give 2-(2-bromo-4-methylphenyl)-1,3-dioxolane **3.55** (1.05 g, 4.32 mmol, 56%) $R_f$ = 0.72 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 7.47 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 0.8 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.07 (s, 1H), 4.18−4.03 (m, 4H), 2.33 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 245 $(M+2+H)^+$ and 243 $(M+H)^+$, $t_R$ = 10.0 min.

A round-bottom flask equipped with a reflux condenser and magnetic stir bar under nitrogen was charged with Mg (121 mg, 5.04 mmol) and a small crystal of $I_2$. The flask was flame-dried under vacuum. Solution of THF (2.5 mL) and 2-(2-bromo-4-methylphenyl)-1,3-dioxolane **3.55** (1.02 g, 4.2 mmol) was slowly added. After complete addition the mixture was maintained at reflux for two hours. The resulting solution was allowed to cool to room temperature then added dropwise to a stirred suspension of isobutenyl chloride (0.62 mL, 6.3 mmol) and CuI (80 mg, 0.42 mmol) in THF (3 mL) maintained at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, allowed to warm to room temperature and stirred overnight. $CH_2Cl_2$ (15 mL) was added and the mixture was washed with a saturated aqueous $NH_4Cl$ (10 mL) solution. The organic phase was washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated in vacuo. The crude material was purified by flash column chromatography on silica (4% EtOAc in hexanes) to give 2-(4-methyl-2-(2-methylallyl) phenyl)-1,3-dioxolane, **3.56** (453 mg, 2.12 mmol, 50%) as colorless oil. $R_f$ = 0.51 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.47 (d, $J$ = 7.9 Hz, 1H), 7.06 (d, $J$ = 8.0 Hz, 1H), 6.99 (s, 1H), 5.95 (s, 1H), 4.83 (app s, 1H), 4.56 (app s, 1H), 4.16−3.98 (m, 4H), 3.44 (s, 2H), 2.32 (s, 3H), 1.74 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 219 $(M+1)^+$, $t_R$ = 13.5 min.

A solution of 2-(4-methyl-2-(2-methylallyl) phenyl)-1,3-dioxolane **3.56** (450 mg, 2.10 mmol) in water (8 mL), acetone (8 mL) and *p*-TsOH (22 mg, 0.11 mmol) was heated to reflux and maintained for 45 minutes. The reaction mixture was

allowed to cool to room temperature and extracted with $CH_2Cl_2$ (40 mL). The organic phase was separated, dried over $Na_2SO_4$ (10 g) and concentrated in vacuo. The crude reaction mixture was purified by flash column chromatography on silica (4% EtOAc in hexanes) to give compound **2-(2-methylallyl)benzaldehyde, 3.57** (322 mg, 1.85 mmol, 90%) as a colorless oil $R_f$ = 0.54 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 10.18 (s, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.08 (s, 1H), 4.84−4.83 (m, 1H), 4.46 (app s, 1H), 3.70 (s, 2H), 2.40 (s, 3H), 1.78 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 175 $(M+H)^+$, $t_R$ = 9.9 min.

**4-fluoro-2-(2-methylallyl)benzaldehyde (3.61)**:



In analogy to the procedure reported by Glorius et al.[17] 2-amino-2-methyl-1-propanol (1.6 mL, 16.6) and 4-fluorobenzaldehyde, **3.58** (2.04 g, 16.4 mmol) were dissolved in $CH_2Cl_2$ (110 mL) and stirred over 4 Å Molecular Sieves (MS) (24 g) for 14 h. NBS (2.93 g, 16.6 mmol) was added and the solution was stirred for an additional 30 min. The mixture was filtered through celite and washed with saturated aqueous $NaHCO_3$ (100 mL) and $H_2O$ (50 mL). The organic layer was dried over anhydrous $Na_2SO_4$ (30 g) and concentrated in vacuo. The resulting residue was purified by flash column chromatography (gradient 10 to 15% EtOAc in hexanes) to give 4,4-dimethyl-2-(4-fluoro)phenyl-2-oxazoline, **3.59** (2.79 g, 14.5 mmol, 85%) $R_f$ = 0.50 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 7.96−7.91 (m, 2H), 7.08 (app t, $J$ = 8.6 Hz, 2H), 4.11 (s, 2H), 1.38 (s, 6H); LRMS (ESI) $m/z$ 193 $(M)^+$.

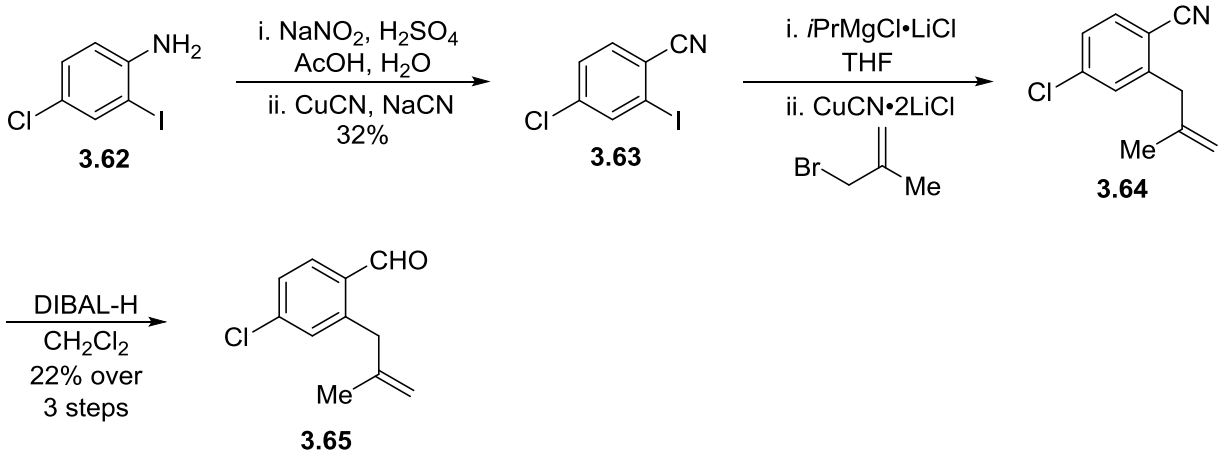
In analogy to the reported procedure[6] *n*-BuLi (2.5 M in hexanes, 3.8 mL, 9.5 mmol, 1.4 equiv) was added dropwise to a solution of 4,4-dimethyl-2-(4-fluoro)phenyl-2-oxazoline **3.59** (1.3 g, 6.74 mmol, 1.0 equiv) in THF (19 mL) maintained at 0 °C. The mixture was stirred at 0°C for 3.5 hours and was transferred to a suspension of CuBr (960 mg, 6.1 mmol, 1.1 equiv) in THF (7 mL) via cannula. The resulting green mixture was stirred at 0 °C for 1.5 hours and isobutenyl chloride (0.76 mL, 6.1 mmol, 0.9 equiv) was added. The reaction mixture was stirred at room temperature overnight. The reaction was quenched with saturated aqueous $NH_4Cl$ (20 mL) solution. The aqueous layer was

extracted with diethyl ether (3 x 20 mL) and the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ (15 g) and concentrated in vacuo. The crude material was purified by flash column chromatography on silica (gradient 5 to 10% EtOAc in hexanes) to give 4,4-dimethyl-2-(4-fluoro-(2-(2-methylallyl))phenyl)-4,5-oxazoline, **3.60** (660 g, 2.66 mmol, 38%) as dark green oil $R_f$ = 0.75 (1:4 EtOAc:Hex); $^1$H NMR (300MHz , $CDCl_3$) $\delta$ 7.74 (dd, *J* = 8.3, 5.9 Hz, 1H), 6.98−6.90 (m, 2H), 4.81 (app s, 1H), 4.55 (app s, 1H), 4.04 (s, 2H), 3.73 (s, 2H), 1.69 (s, 3H), 1.36 (s, 6H); LRMS (ESI) *m*/*z* 248 $(M+1)^+$.

To a solution of 4,4-dimethyl-2-(4-fluoro-(2-(2-methylallyl))phenyl)-4,5-oxazoline, **3.60** (660 g, 2.66 mmol) (320 mg, 1.29 mmol) in 2.6 mL of $CH_2Cl_2$ was added methyl trifluoromethanesulfonate (0.31 mL, 2.7 mmol) in nitrogen filled glove box and the solution was stirred for 2 h at ambient temperature inside nitrogen filled glove box . The solution was taken out of glove box and cooled to 0 °C. A solution of $NaBH_4$ (1.56 g, 4.12 mmol) in THF/MeOH (4:1, 37.5 mL) was added to the mixture. After stirring for 1 h at 0 °C, saturated aqueous $NH_4Cl$ (10 mL) was added and the mixture was extracted with diethyl ether (2 x 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (10 mL), brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated in vacuo. The resulting residue was dissolved in a solution of THF/$H_2O$ (4:1, 5 mL) and treated with oxalic acid dihydrate (1.05 g, 8.3 mmol). The solution was stirred at room temperature for 18 hours. Diethyl ether (30 mL) was added and the mixture was

washed with saturated aqueous $NaHCO_3$ (10 mL) solution, brine (10 mL), dried over anhydrous $Na_2SO_4$ (15 g) and concentrated in vacuo. The resulting residue was purified by flash column chromatography on silica (5-10% EtOAc in hexanes) to give **4-fluoro-2-(2-methylallyl)benzaldehyde**, **3.61** (76 mg, 0.43 mmol, 32%) = 0.85 (1:4 EtOAc:Hex); $^1$H NMR (300MHz , $CDCl_3$) $\delta$ 10.17 (s, 1 H), 7.90 (dd, *J* = 8.6, 6.0 Hz, 1H), 7.07 (dt, *J* = 8.2, 2.5 Hz, 1H), 6.99 (dd, *J* = 9.5, 2.5 Hz, 1H), 4.89−4.88 (m, 1H), 4.50 (app s, 1H), 3.73 (s, 2H), 1.78 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 178 $(M+H)^+$, $t_R$ = 13.4 min.

**4-chloro-2-(2-methylallyl)benzaldehyde (3.65):**




A solution of $NaNO_2$ (330 mg, 5 mmol) in water (1.2 mL) was added dropwise to a solution of 4-chloro-2-iodoaniline, **3.62** (1.02 g, 4.1 mmol) in concentrated $H_2SO_4$ (1 mL), AcOH (4 mL) and water (2 mL) that was maintained at 0 °C. The mixture was stirred for 30 min at 0 °C. The resulting cold diazonium salt mixture

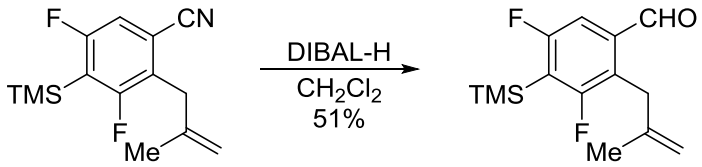
was added to the solution of CuCN (390 mg, 4.5 mmol), NaCN (420 mg, 8.3 mmol) and $NaHCO_3$ (2.0 g) in water (4.3 mL) maintained at 0 °C in a very large round bottomed flask (1 L) to keep the foam formed during the reaction from spilling. The reaction mixture was allowed to warm to room temperature and stirred for one hour. The brown precipitate that was formed was dissolved in dichloromethane (30 mL) and layers were separated. The aqueous layer was extracted again with dichloromethane (20 mL). The combined organic extracts were washed with water (20 mL), saturated $NaHCO_3$ (15 mL), brine (15 mL), dried over anhydrous $Na_2SO_4$ (20 g) and concentrated in vacuo. The resulting crude material was purified by flash column chromatography on silica (10%EtOAc in hexanes) to give 4-chloro-2-iodobenzonitrile, **3.63** (340 mg, 1.29 mmol, 32%) $R_f$ = 0.75 (1:4 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.95 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 1H); LRMS (GC-MS, CI, MeOH) *m*/*z* 264 $(M+H)^+$, $t_R$ = 15.5 min.

4-chloro-2-iodobenzonitrile, **3.63** (316 mg, 1.20 mmol) was dissolved in THF (0.3 mL) and cooled to −10 °C. *i*PrMgCl•LiCl[15] (2 mL of a 0.77 M solution in THF, 1.45 mmol) was added and the reaction mixture was stirred for 30 min at −10 °C. Then CuCN•2LiCl (0.1 mL of 1M solution in THF, 0.2 mmol) and 3-bromo-2-methyl-1-propene (0.18 mL, 1.8 mmol) were added to the reaction at −10 °C. The resulting mixture was slowly allowed to warm to room temperature and stirred for 14 hours. The reaction was quenched with saturated aqueous $NH_4Cl$ solution (15

mL) and extracted using diethyl ether (2 x 30 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated. Attempted purification of the crude product provided mixture of 4-chloro-2-iodobenzonitrile (**3.64)** and *p*-chlorobenzonitrile (~15%) which was taken to the next step.

DIBAL-H (1.0 mL of 1 M solution in toluene, 1.5 mmol) was added to a solution of 4-chloro-2-(2-methylallyl)benzonitrile, **3.64** (134 mg with ~15 mol % *p*-chlorobenzonitrile) in methylene chloride (2.8 mL) maintained at 0 °C under nitrogen. The reaction was slowly allowed to warm to room temperature and stirred for 14 hours. The reaction mixture was diluted with diethyl ether (5 mL) and cooled to 0 °C. HCl (4 mL of 3N solution) was slowly added at 0 °C and the mixture was refluxed for thirty minutes. Diethyl ether (30 mL) was added to the reaction mixture and layers were separated. The aqueous layer was extracted with diethyl ether (30 mL) and the combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The crude material was purified by flash column chromatography (8% $Et_2O$ in hexanes) on silica to give **4-chloro-2-(2-methylallyl)benzaldehyde, 3.65** (50 mg, 0.26 mmol 22%) $R_f$ = 0.80 (1:4 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 10.19 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.37 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 4.89−4.88 (m, 1H), 4.48 - 4.47 (m, 1H), 3.70 (s, 2H), 1.79 (d, *J* = 0.5 Hz, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 195 $(M+H)^+$, $t_R$ = 14.8 min.

**3,5-difluoro-2-(2-methylallyl)-4-(trimethylsilyl)benzaldehyde (3.66):**

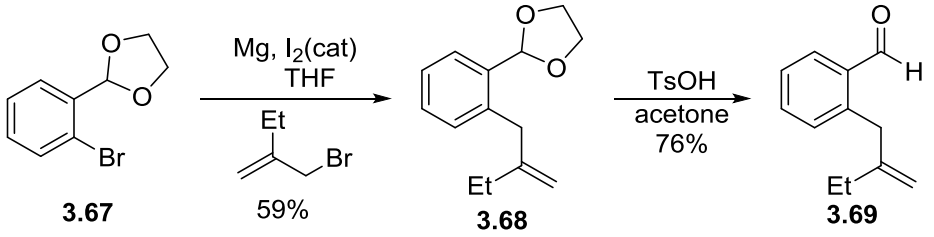



**3.51** **3.66**

A flame-dried flask under $N_2$ was charged with 3,5-difluoro-2-(2-methylallyl)-4-(trimethylsilyl)benzonitrile **3.51** (1.028 g, 3.87 mmol) and dichloromethane (22 mL). The solution was cooled to 0 °C and a solution of DIBAL-H in toluene (1M, 4.65 mL, 4.65 mmol) was added dropwise. The reaction was allowed to warm slowly to room temperature and was stirred for 15 h. The reaction mixture was then diluted with $Et_2O$ (20 mL) and HCl (3N, 20 mL) was added. The reaction was headed to reflux for 1 h at which time it was cooled back down to room temperature and was diluted with more $Et_2O$ (20 mL). The organics were separated and washed sequentially with $H_2O$ (60 mL), saturated aqueous $NaHCO_3$ (60 mL), brine (60 mL) followed by drying over $Na_2SO_4$, filtration and concentration. The crude product was purified by column chromatography (2% EtOAc in Hexanes) to yield **3,5-difluoro-2-(2-methylallyl)-4-(trimethylsilyl)benzaldehyde 3.66** (0.5325 g, 1.98 mmol, 51% yield) as a yellow oil (Note: The product contains a minor, inseparable impurity observable in the $^1H$ NMR that we believe is the di-TMS protected product. As this impurity will also undergo the desired key reaction, we have deemed the purity level appropriate to carry on to the key step). $R_f$ = 0.6 (1:9 EtOAc:Hex); $^1H$ NMR (500 MHz , $CDCl_3$) $\delta$

10.12 (d, *J* = 2.5 Hz, 1H), 7.30 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.80 – 4.79 (m, 1H), 4.35 (app s, 1H), 3.64 (s, 2H), 1.80 (s, 3H), 0.37 (t, *J* = 1.5 Hz, 9H); LRMS (GC-MS, CI, MeOH) *m/z* 269 $(C_{14}H_{18}F_2OSi + H)^+$, $t_R$ = 15.4 min.

**2-(2-methylenebutyl)benzaldehyde (3.69):**



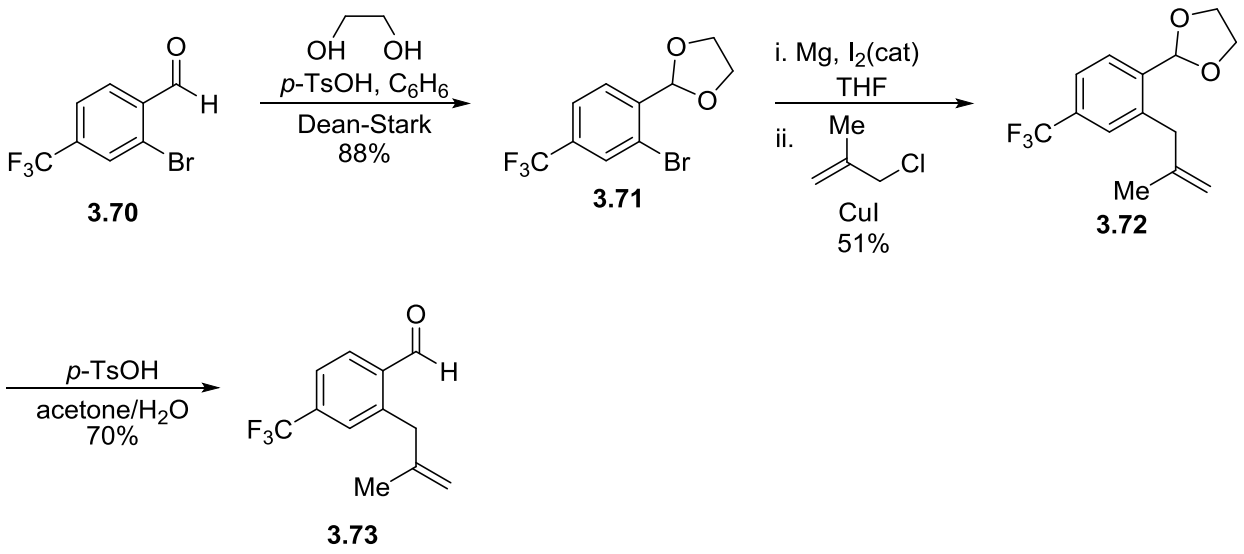

**3.67** **3.68** **3.69**

A round-bottom flask equipped with a reflux condenser and magnetic stir bar under nitrogen was charged with Mg (72 mg, 3.0 mmol) and a small crystal of $I_2$. The flask was flame-dried under high vacuum. Solution of 2-(2-bromophenyl)-1,3-dioxolane, **3.67** (570 mg, 2.5 mmol)[18] and THF was slowly added to Mg at room temperature and the mixture was maintained at reflux for two hours. The resulting solution was allowed to cool to room temperature then added dropwise to a stirring suspension of 2-(bromomethyl) but-1-ene[19](420 mg, 2.82 mmol) and CuI (50 mg, 0.26 mmol) in THF (3 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then allowed to warm to room temperature and stirred overnight. Diethyl ether (30 mL) was added, and the mixture was washed with a saturated aqueous $NH_4Cl$ solution (10 mL). The organic phase was separated, washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and

concentrated in vacuo. The crude material was purified by flash column chromatography on silica (4% EtOAc in hexanes) to give 2-(2-(2-methylenebutyl) phenyl)-1,3-dioxolane, **3.68** (320 mg, 1.47 mmol, 59%) as colorless oil. $R_f$ = 0.75 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) *d* 7.59 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.30−7.25 (m, 2H), 7.17 (dd, *J* = 7.2, 1.9 Hz, 1H), 5.96 (s, 1H), 4.85−4.84 (m, 1H), 4.52−4.51 (m, 1H), 4.16−4.00 (m, 4H), 3.50 (s, 2H), 2.05 (q, *J* = 7.3 Hz, 2H), 1.06 (t, *J* = 7.4 Hz, 3H) LRMS (GC-MS, CI, MeOH) *m*/*z* 219 $(M + H)^+$, $t_R$ = 16.5 min.

A solution of 2-(2-(2-methylenebutyl)phenyl)-1,3-dioxolane, **3.68** (320 mg, 1.47 mmol) in water (5 mL), acetone (5 mL) and *p*-TsOH (10 mg, 0.05 mmol) was heated to reflux for 50 min. The reaction mixture was allowed to cool to room temperature and extracted with $CH_2Cl_2$ (30 mL). The organic phase was separated, washed with brine (10 mL), dried over $Na_2SO_4$ (10 g) and concentrated in vacuo. The resulting crude material was purified by flash column chromatography (4% EtOAc in hexanes) on silica to give **2-(2-methylenebutyl)benzaldehyde, 3.69** (193 mg, 1.11 mmol, 76%) as a colorless oil $R_f$ = 0.80 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 10.24 (s, 1H), 7.88 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.53 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.39 (dt, *J* = 7.5, 0.9 Hz, 1H), 7.29 (d, *J* = 0.5 Hz, 1H), 4.86−4.85 (m, 1H), 4.42−4.41 (m, 1H), 3.75 (s, 2H), 2.10 (q, *J* = 7.5 Hz, 2H), 1.08 (t, *J* = 7.4 Hz, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 175 $(M + H)^+$, $t_R$ = 13.5 min.

**2-(2-methylallyl)-4-(trifluoromethyl)benzaldehyde (3.73):**



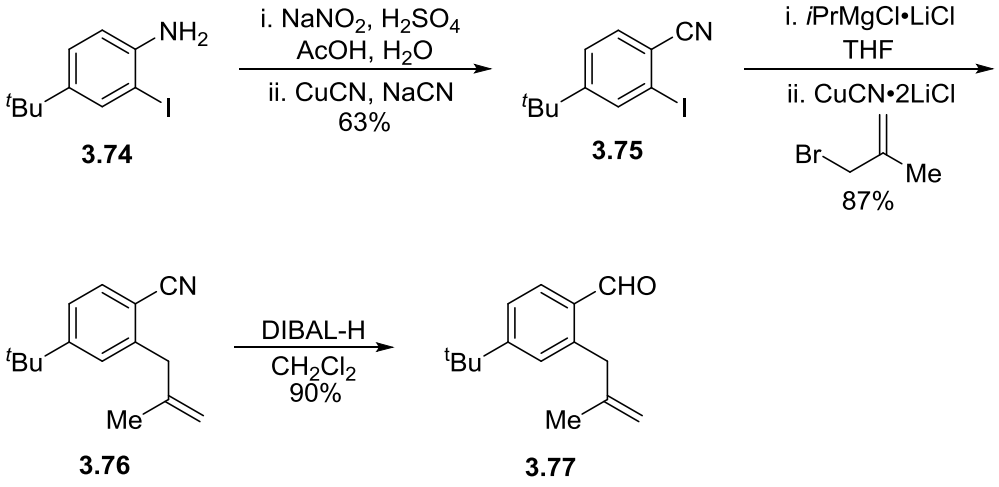

A solution of 2-bromo-4-(trifluoromethyl)benzaldehyde, **3.70** (498 mg, 1.97 mmol), ethylene glycol (0.23 mL, 4.0 mmol), *p*-TsOH (8 mg, 0.04 mmol) in benzene (1.3 mL), was heated to reflux with Dean-Stark trap for 14 hours. The reaction was neutralized with saturated aqueous $NaHCO_3$ solution and extracted with diethyl ether (2 x 30 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated. The resulting crude material was purified by flash column chromatography on silica (10% EtOAc in hexanes) to give 2-(2-bromo-4-(trifluoromethyl)phenyl)-1,3-dioxolane, **3.71** (496 mg, 1.67 mmol, 88%) as colorless oil $R_f$ = 0.70 (1:4 EtOAc:Hex); $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 7.84 (d, *J* = 0.7 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 6.10 (s, 1 H), 4.17−4.09 (m, 4H); LRMS (GC-MS, CI, MeOH) *m/z* 297 $(M + H)^+$ and 299 $(M + H)^+$, $t_R$ = 10.5 min.

A round-bottom flask equipped with a reflux condenser and magnetic stir bar under nitrogen was charged with Mg (40 mg, 1.7 mmol) and a small crystal of $I_2$. The flask was flame-dried under high vacuum. A solution of THF (2 mL) and 2-(2-bromo-4-(trifluoromethyl)phenyl)-1,3-dioxolane **3.71** (390 mg, 1.30 mmol) was slowly added to Mg at room temperature and the mixture was maintained at reflux for two hours. The resulting solution was allowed to cool to room temperature then added dropwise to a suspension of isobutenyl chloride (0.2 mL, 2.1 mmol) and CuI (27 mg, 0.14 mmol) in THF (3 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then allowed to warm to room temperature overnight. Diethyl ether (30 mL) was added, and the mixture was washed with a saturated aqueous $NH_4Cl$ solution (10 mL). The organic phase was separated, washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated in vacuo. The crude material was purified by flash column chromatography on silica (4% EtOAc in hexanes) to give (2-(2-methylallyl)-4-(trifluoromethyl)phenyl)-1,3-dioxolane, **3.72**(140 mg, 0.51 mmol, 40%) as colorless oil. $R_f$ = 0.70 (1:9 EtOAc:Hex);$^1$H NMR (300MHz , $CDCl_3$) $\delta$ 7.71 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.44 (s, 1H), 6.00 (s, 1H), 4.88 (app s, 1H), 4.54 (app s, 1H), 4.15−4.03 (m, 4H), 3.53 (s, 2H), 1.75 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 273 $(M + H)^+$, $t_R$ = 9.2 min..

A solution of (2-(2-methylallyl)-4-(trifluoromethyl)phenyl)-1,3-dioxolane, **3.72** (140 mg, 0.51 mmol), *p*-TsOH, water (2.5 mL) and acetone (2.5 mL) (6 mg, 0.03 mmol) was heated to refluxed for 50 min. The reaction mixture was allowed to

cool to room temperature and extracted with $CH_2Cl_2$ (25 mL). The organic phase was separated, washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ (10 g) and concentrated in vacuo. The crude material was purified by flash column chromatograph on silica (4% EtOAc in hexanes) to give **2-(2-methylallyl)-4-(trifluoromethyl)benzaldehyde, 3.73** (82 mg, 0.36 mmol, 70%) as a colorless oil $R_f$ = 0.80 (1:9 EtOAc:Hex); $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 10.29 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 4.91−4.90 (m, 1H), 4.44 (app s, 1H), 3.77 (s, 2H), 1.81 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 229 (M + H)$^+$, $t_R$ = 9.5 min.

**4-(tert-butyl)-2-(2-methylallyl)benzaldehyde (3.77):**




4-(*tert*-butyl)-2-iodoaniline **3.74** was prepared using previously reported procedure.[20] To a solution of 4-(*tert*-butyl)-2-iodoaniline **3.74** (2.391g, 8.7 mmol), ice (10g), acetic acid (3.98 mL, 69.6 mmol) and $H_2SO_4$ (0.97 mL, 17.4 mmol) at 0

°C under $N_2$ was added a solution of $NaNO_2$ (0.659 g, 9.6 mmol) in $H_2O$ (4 mL). This solution was stirred for 45 minutes at 0 °C. The resulting diazonium salt was then added at 0 °C to a stirred solution of CuCN (0.822 g, 9.14 mmol), NaCN (0.895 g, 18.3 mmol) and $NaHCO_3$ (21.93 g, 261 mmol) in $H_2O$ (15 mL) in a 500 mL Erlenmeyer flask. Slow addition was necessary to control gas evolution and foaming. Deionized water (~50 mL total) was also added to control foaming and ensure the solid remained suspended in solution and not stuck to the side of the flask. After the addition was finished, the flask was allowed to warm to room temperature and was stirred for 1 hr.

Dichloromethane (50 mL) was added to dissolve the resulting brown precipitate and the layers were separated. The aqueous layer was washed again with dichloromethane (50 mL). The organic layers were combined, washed with brine (100 mL), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The product was purified by column chromatography (5% EtOAc in Hexanes) to yield 4-(*tert*-butyl)-2-iodobenzonitrile **3.75** (1.5644 g, 5.49 mmol, 63% yield) as a yellow oil. $R_f$ = 0.40 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.92 (d, *J* = 1.7 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.48 (dd, *J* = 8.2, 1.7 Hz, 1H), 1.32 (s, 9H); ); LRMS (GC-MS, CI, MeOH) *m*/*z* 286 $(C_{11}H_{12}IN + H)^+$, $t_R$ = 16.3 min.

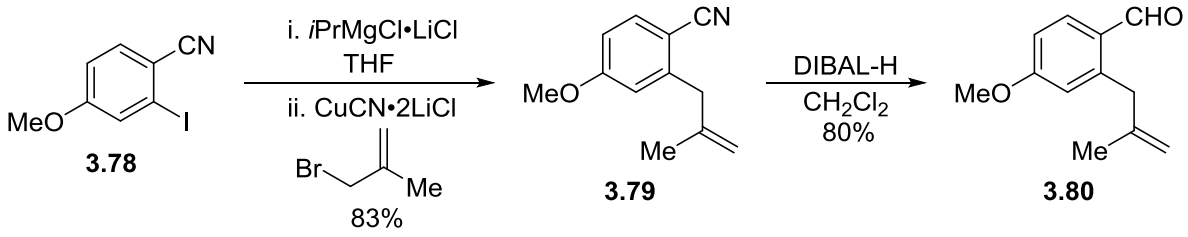
A flame-dried flask containing a stir bar under $N_2$ was charged with 4-(*tert*-butyl)-2-iodobenzonitrile **3.75** (1.3504 g, 4.47 mmol) and dry THF (2 mL). The solution was cooled to –10 °C. A solution of *i*PrMgCl•LiCl in THF (2.52 mL, 0.76M, 2.3 mmol) was added dropwise and the reaction was allowed to stir for 2 h at –10 °C.

CuCN•2LiCl (0.34 mL, 1.12M in THF, 0.038 mmol) and 3-bromo-2-methyl-1-propene (0.29 mL, 2.9 mmol) were added and stirred at –10 °C for 1 h then the reaction was allowed to warm to room temperature and stirred for 15 hours. The reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (20 mL) and extracted with diethyl ether (2 X 20 mL). The organic layer was washed with brine (50 mL), dried over anhydrous $Na_2SO_4$, filtered and concentrated. The crude material was purified by flash column chromatography on silica (2% EtOAc in hexanes) to give 4-(*tert*-butyl)-2-(2-methylallyl)benzonitrile **3.76** (0.874 g, 4.1 mmol, 87%) as a yellow oil. $R_f$ = 0.46 (9:1 Hex:EtOAc); $^1H$ NMR (500 MHz , $CDCl_3$) $\delta$ 7.54 (d, $J$ = 8.1 Hz, 1H), 7.36 – 7.32 (m, 2H), 4.87 (app s, 1H), 4.69 (app s, 1H), 3.53 (s, 2H), 1.74 (s, 3H), 1.32 (s, 9H); LRMS (GC-MS, CI, MeOH) $m/z$ 214 $(C_{15}H_{19}N + H)^+$, $t_R$ = 15.6 min.

A flame-dried flask under $N_2$ was charged with 4-(*tert*-butyl)-2-(2-methylallyl)benzonitrile, **3.76** (0.86 g, 4.03 mmol) and dichloromethane (23 mL). The solution was cooled to 0 °C and a solution of DIBAL-H in toluene (1M, 4.84 mL, 4.84 mmol) was added dropwise. The reaction was allowed to warm to room temperature and was stirred for 15 h. The reaction mixture was then diluted with $Et_2O$ (20 mL) and HCl (3N, 20 mL) was added. The reaction was headed at reflux for 1 h at and was allowed to cool to room temperature. The mixture was diluted with more $Et_2O$ (10 mL). The organic portion was separated and washed with $H_2O$ (50 mL), saturated aqueous $NaHCO_3$ (50 mL), brine (50 mL) and were dried over $Na_2SO_4$, filtered and concentrated. The product was purified by column

chromatography (2% EtOAc in Hexanes) to yield **4-(*tert*-butyl)-2-(2-methylallyl)benzaldehyde 3.77** (0.7878 g, 3.64 mmol, 90% yield) as a yellow oil. $R_f$ = 0.45 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 10.19 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.41 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.28 (d, *J* = 1.9 Hz, 1H), 4.83 (app s, 1H), 4.46 (app s, 1H), 3.73 (s, 2H), 1.79 (s, 3H), 1.34 (s, 9H); LRMS (GC-MS, CI, MeOH) *m*/*z* 217 $(C_{15}H_{20}O + H)^+$, $t_R$ = 15.7 min.

**4-methoxy-2-(2-methylallyl)benzaldehyde (3.80):**



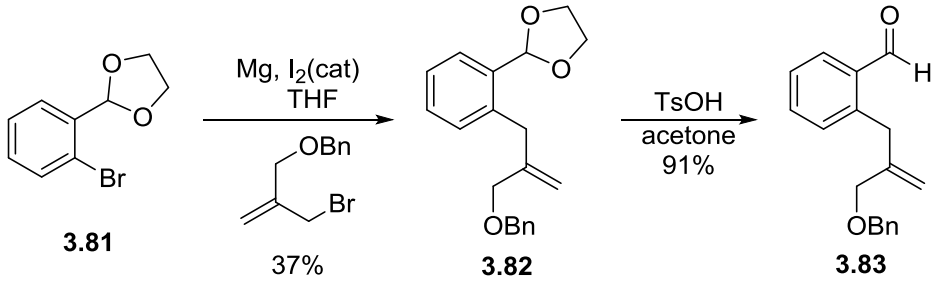

2-iodo-4-methoxybenzonitrile, **3.78** (prepared using the procedure reported by Larock et al.[21]) (501 mg, 1.93 mmol) was dissolved in 0.5 mL dry THF and cooled to −10 °C. *i*PrMgCl•LiCl (3 mL of 0.77 M solution in THF, 2.3 mmol) was added and the reaction mixture was stirred for one hour at −10 °C. CuCN•2LiCl (0.2 mL of 1M solution in THF, 0.2 mmol) and 3-bromo-2-methyl-1-propene (0.3 mL, 2.9 mmol) were added at −10 °C and the reaction mixture was allowed to warm to room temperature and stirred for 14 hours. The reaction was quenched with saturated $NH_4Cl$ solution (15 mL) and extracted with diethyl ether (2 x 30 mL). The organic layer was washed with brine (10 mL), dried over anhydrous $Na_2SO_4$

(15 g) and concentrated. The resulting crude material was purified by flash column chromatography on silica (6% EtOAc in hexanes) to give 4-methoxy-2-(2-methylallyl)benzonitrile, **3.79** (300 mg, 1.6 mmol, 83%) as colorless oil. $R_f$ = 0.75 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.56 (d, $J$ = 9.3 Hz, 1H), 6.84−6.80 (m, 2H), 4.89 (app s, 1H), 4.72 (app s, 1H), 3.85 (s, 3H), 3.51 (s, 2H), 1.74 (s, 3H); LRMS (GC-MS, CI, MeOH) $m/z$ 188 $(M+H)^+$, $t_R$ = 14.1 min.

DIBAL-H (2.4 mL of 1 M solution in toluene, 2.4 mmol) was added to the solution of 4-methoxy-2-(2-methylallyl)benzonitrile, **3.79** (300 mg, 1.6 mmol) in methylene chloride (6.5 mL) maintained at 0 °C under nitrogen. The reaction was allowed to warm to room temperature and stirred for 14 hours. The reaction mixture was diluted with diethyl ether (11 mL) and cooled to 0 °C followed by the addition of HCl (8.5 mL of 3N solution). The reaction mixture was heated to reflux for thirty minutes. The reaction was allowed to cool to room temperature and diethyl ether (30 mL) was added to the reaction mixture and layers were separated. The aqueous layer was extracted again with diethyl ether (30 mL) and the combined organic extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ and concentrated. The crude material was purified by flash column chromatography on silica (5% EtOAc in hexanes) to give **4-methoxy-2-(2-methylallyl)benzaldehyde, 3.80** (240 mg, 1.26 mmol 80%) $R_f$ = 0.77 (1:4 EtOAc:Hex); $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 10.10 (s, 1H), 7.84 (d, $J$ = 8.6 Hz, 1H), 6.88 (dd, $J$ = 8.6, 2.5 Hz, 1H), 6.77 (d, $J$ = 2.6 Hz, 1H), 4.85−4.84 (m, 1H), 4.50

(app s, 1H), 3.88 (s, 3H), 3.71 (s, 2H), 1.78 (s, 3H); LRMS (GC-MS, CI, MeOH) *m*/*z* 191 $(M+H)^+$, $t_R$ = 14.3 min.

**2-(2-((benzyloxy)methyl)allyl)benzaldehyde (3.83):**

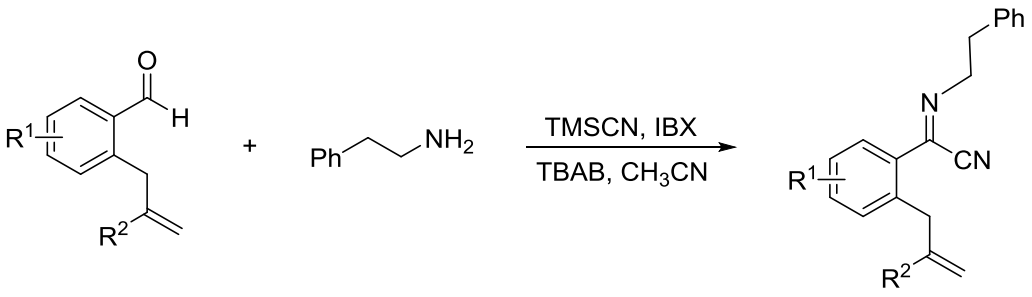



2-(2-(2-((benzyloxy)methyl)allyl)phenyl)-1,3-dioxolane (**3.82**) was prepared using procedure similar to the synthesis of **3.68** using 2-(2-bromophenyl)-1,3-dioxolane 5h (400 mg, 1.75 mmol), Mg(50 mg, 2.1 mmol) CuI (33 mg, 0.175 mmol), (((2-(bromomethyl)allyl)oxy)methyl)benzene (**3.81**) (460 mg, 1.9 mmol) in THF (4 ml) and 2-(2-(2-((benzyloxy)methyl)allyl)phenyl)-1,3-dioxolane (**3.82**) was isolated as colorless oil ( 202 mg, 0.66 mmol, 37%) $R_f$ = 0.80 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.60 (dd, *J* = 6.8, 1.6 Hz 1H), 7.39 - 7.18 (m, 8H), 5.97 (s, 1H), 5.15 (s, 1H), 4.76 - 4.75 (m, 1H), 4.50 (s, 2H), 4.13 - 3.93 (m, 6H), 3.58 (s, 2H); LRMS (GC-MS, CI, MeOH) *m*/*z* 311 (M+H).

2-(2-((benzyloxy)methyl)allyl)benzaldehyde (**3.83**) was prepared using procedure similar to the synthesis of **3.69** from -((benzyloxy)methyl)allyl)phenyl)-1,3-dioxolane (**3.82**) PTSA (6 mg, 0.03 mmol), acetone (4 ml) and water (4 ml). **2-(2-**

**((benzyloxy)methyl)allyl)benzaldehyde (3.83)** was isolated as colorless oil (158 mg, 0.59 mmol, 91%) $R_f$ = 0.85 (1:9 EtOAc:Hex); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 10.24 (s, 1H), 7.88 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.53 (dt, 7.6, 1.5 Hz 1H), 7.43 - 7.26 (m, 7H), 5.14 (s, 1H), 4.66 (d, *J* = 0.8 Hz, 1H), 4.51 (s, 2 H), 4.01 (s, 2H), 3.83 (s, 2H); LRMS (GC-MS, CI, MeOH) *m*/*z* 267 (M+H).

## Synthesis of α-iminonitriles:

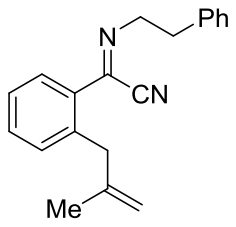



### General Procedure

α-Iminonitriles were synthesized by slight modification of procedure reported by Zhu.[10] To the stirred solution of aldehyde (0.5 mmol), phenethylamine (0.5 mmol, 1.0 eq) in acetonitrile (0.5 mL, [RCHO] = 1.0 M) at room temperature, TMSCN (0.55 mmol, 1.1 eq) was added and stirred for 15 minutes. Then finely powdered IBX[22](0.75 mmol, 1.5 eq) and tetrabutylammonium bromide (0.33 mmol, 1.1 eq) were added. The heterogeneous reaction was stirred at room temperature for two hours. After ensuring complete consumption of starting material by TLC (on

alumina plates) the mixture was filtered through celite and concentrated. The crude product was purified by flash chromatography on neutral alumina (2% EtOAc in hexanes) to afford pure α-iminonitrile. The product appeared to decompose on column and was flushed as quickly as possible.

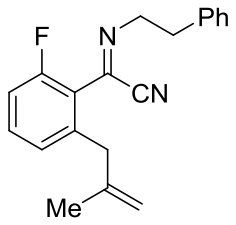
**α-iminonitrile 3.24:**




**3.24**

α-iminonitrile **3.24**: Prepared using general procedure for α-iminonitrile synthesis from 2-(2-methylallyl)benzaldehyde **3.23**[9] (302 mg, 1.88 mmol), phenethylamine (229 mg, 1.90 mmol), acetonitrile (2.0 mL), TMSCN (260 µl 2.09 mmol) IBX (800 mg, 2.85 mmol) tetrabutylammonium bromide (673 mg, 2.09 mmol). iminonitrile **3.24** was isolated was yellow oil (338 mg, 1.17 mmol 62%) $R_f$ = 0.85 (1:9 EtOAc:Hex on alumina TLC). $\delta$ 7.60 (dd, $J$ = 7.6, 1.3 Hz, 1H), 7.43−7.23 (m, 8H), 4.78 (app s, 1H), 4.43 (app s, 1H), 4.22 (t, $J$ = 7.2 Hz, 2H), 3.58 (s, 2H), 3.11 (t, $J$ = 7.2 Hz, 2H), 1.64 (d, $J$ = 0.4 Hz, 3H); $^{13}$C NMR (75 MHz , $CDCl_3$) $\delta$ 144.4, 142.5, 138.9, 138.7, 133.2, 131.5, 130.8, 130.0, 129.0, 128.5, 126.7, 126.5, 112.2, 110.1, 60.4, 41.1, 36.5, 22.6; IR (thin film) 3064, 3027, 2928, 2213, 1604, 1446 cm$^{-1}$; HRMS (CI, $NH_3$) calcd for $[C_{20}H_{20}N_2 + H]^+$, *m/z* 289.1700, found 289.1703.

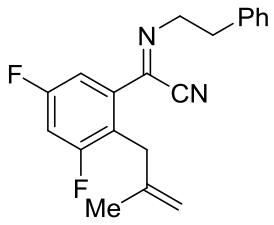
**α-iminonitrile 3.84**:




**3.84**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.49** (80 mg, 0.45 mmol), phenethylamine (55 mg, 0.45 mmol), acetonitrile (0.5 mL), TMSCN (85 µl, 0.68 mmol,) IBX (190 mg, 0.68 mmol) tetrabutylammonium bromide (160 mg, 0.49 mmol). Iminonitrile **3.84** was isolated as yellow oil (80 mg, 0.26 mmol 55%) $R_f$ = 0.75 (1:9 EtOAc:Hex on alumina TLC); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.38−7.22 (m, 6H), 7.06−7.00 (m, 2H), 4.83 (app s, 1H), 4.48 (app s, 1H), 4.24 (t, *J* = 7.2 Hz, 2H), 3.31 (s, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 1.58 (s, 3H); $^{13}$C NMR (126MHz , $CDCl_3$) $\delta$ 160.5 (d, *J* = 250 Hz), 143.2, 140.8, 138.4, 137.2, 131.7 (d, *J* = 9 Hz), 128.9, 128.6, 126.6, 126.3 (d, *J* = 3 Hz), 122.6, (d, *J* = 14 Hz), 114.0, (d, *J* = 21 Hz) 113.2, 109.7, 60.4, 40.4, 36.3, 22.3; $^{19}$F NMR (471 MHz, $CDCl_3$) $\delta$-115.5; IR (thin film) 3079, 3029, 2927, 2215, 1623, 1460 $cm^{-1}$; HRMS (ESI) calcd for $[C_{20}H_{19}FN_2+Na]^+$, *m/z* 329.1424, found 329.1425.

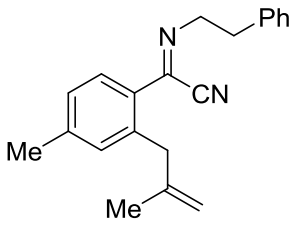
**α-iminonitrile 3.85:**




**3.85**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.53** (100 mg, 0.51 mmol), phenethylamine (0.064 mL, 0.51 mmol), acetonitrile (0.51 mL), TMSCN (0.07 mL, 0.56 mmol), IBX (0.214 g, 0.76 mmol), and tetrabutylammonium bromide (0.181 g, 0.56 mmol). Iminonitrile **3.85** was isolated (0.043 g, 0.133 mmol, 26% yield) as yellow oil. $R_f$ = 0.6 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.37–7.32 (m, 2H), 7.30–7.25 (m, 3H), 7.18 (d, *J* = 8.6 Hz, 1H), 7.01–6.95 (m, 1H), 4.75 (s, 1H), 4.29 (s, 1H), 4.25 (t, *J* = 7.1 Hz, 2H), 3.60 (s, 2H), 3.13 (t, *J* = 7.1 Hz, 2H), 1.72 (s, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 162.5 (dd, *J* = 82.0, 12.5 Hz), 160.5 (dd, *J* = 82.4, 12.5 Hz), 143.2, 140.7 (d, *J* = 3.5 Hz), 138.6, 136.0 (dd, *J* = 8.6, 6.2 Hz), 129.2, 128.8, 126.9, 122.8 (dd, *J* = 17.9, 4.2 Hz), 113.1 (*J* = 23.2, 3.6 Hz), 111.3, 109.6, 106.5 (dd, *J* = 28.0, 24.7 Hz), 60.7, 36.6, 32.1 (*J* = 4.4 Hz), 23.0; $^{19}$F NMR (471 MHz, $CDCl_3$) $\delta$ -110.5 (app t, *J* = 8.6 Hz), -111.2 (app q, *J* = 8.3 Hz); IR (thin film) 3085, 3029, 2928, 2216, 1616,1331 $cm^{-1}$; HRMS (ESI) calcd for $[C_{20}H_{18}F_2N_2+Na]^+$, *m/z* 137.1330, found 347.1320.

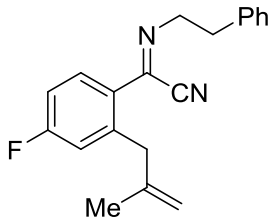
**α-iminonitrile 3.39:**




**3.39**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.57** (101 mg, 0.58 mmol), phenethylamine (70 mg, 0.58 mmol, 1.0 eq), acetonitrile (0.6 mL), TMSCN (80 µl, 0.64 mmol,) IBX (244 mg, 0.87 mmol) and tetrabutylammonium bromide (206 mg, 0.64 mmol), iminonitrile **3.39** was isolated as yellow oil (66 mg, 0.22 mmol 38%) $R_f$ = 0.15 (1:9 EtOAc:Hex on alumina TLC); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.52 (d, *J* = 7.9 Hz, 1H), 7.34−7.23 (m, 5H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.07 (s, 1H), 4.76 (app s, 1H), 4.41 (app s, 1H), 4.19 (t, *J* = 7.3 Hz, 2H), 3.57 (s, 2H), 3.09 (t, *J* = 7.2 Hz, 2H), 2.37 (s, 3H), 1.64 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 144.7, 142.4, 141.2, 138.9, 138.8, 132.4, 130.4, 130.2, 128.9, 128.4, 127.4, 126.4, 111.9, 110.1, 60.3, 41.1, 36.6, 22.7, 21.3; IR (thin film) 3064, 3027, 2923, 2213, 1649, 1453 cm$^{-1}$; HRMS (ESI) calcd for $[C_{21}H_{22}N_2Na]^+$, *m/z* 325.1675, found 325.1670.

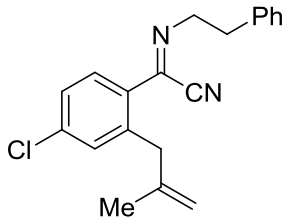
**α-iminonitrile 3.86:**




**3.86**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.61** (76 mg, 0.43 mmol), phenethylamine (52 mg, 0.43 mmol), acetonitrile (0.5 mL), TMSCN (60 µl, 0.47 mmol), IBX (181 mg, 0.65 mmol) and tetrabutylammonium bromide (152 mg, 0.47 mmol), iminonitrile **3.86** was isolated as yellow oil (58 mg, 0.19 mmol 44%) $R_f$ = 0.82 (1:9 EtOAc:Hex on alumina TLC); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.61 (dd, *J* = 8.6, 5.7 Hz, 1H), 7.32−7.30 (m, 2H), 7.26−7.22 (m, 3H), 7.03−6.98 (m, 2H), 4.82 (app s, 1H), 4.48 (app s, 1H), 4.21 (t, *J* = 7.1 Hz, 2H), 3.56 (s, 2H), 3.10 (t, *J* = 7.1 Hz, 2H), 1.64 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 163.8 (d, *J* = 250 Hz), 143.6, 142.3 (d, *J* = 7 Hz), 141.5, 138.6, 132.3 (d, *J* = 10 Hz), 128.9, 128.5, 126.5, 118.2 (d, *J* = 21 Hz), 113.7 (d, *J* = 22 Hz), 112.9, 109.9, 60.4, 41.1, 36.5, 22.5; $^{19}$F NMR (282 MHz, $CDCl_3$) $\delta$ -105.0; IR IR (thin film) 3064, 3028, 2928, 2215, 1608, 1495, 1100 cm$^{-1}$; HRMS (CI, $NH_3$) calcd for $[C_{20}H_{19}FN_2 + H]^+$, *m/z* 307.1606, found 307.1601.

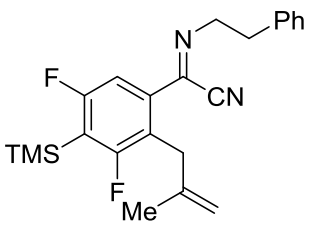
**α-iminonitrile 3.87:**




**3.87**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.65** (49 mg, 0.26 mmol), phenethylamine (32 mg, 0.26 mmol), acetonitrile (0.3 mL), TMSCN (36 µl, 0.29 mmol,) IBX (109 mg, 0.39 mmol), tetrabutylammonium bromide (92 mg, 0.29 mmol), iminonitrile **3.87** was isolated as yellow oil (44 mg, 0.14 mmol, 54%) $R_f$ = 0.85 (1:10 EtOAc:Hex on alumina TLC).$^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.54 (d, *J* = 8.3 Hz, 1H), 7.33−7.24 (m, 3H), 7.27−7.24 (m, overlapped with $CHCl_3$, 4H), 4.82 (app s, 1H), 4.46 (app s, 1H), 4.21 (t, *J* = 7.2 Hz, 2H), 3.55 (s, 2H), 3.10 (t, *J* = 7.1 Hz, 2H), 1.64 (s, 3H); $^{13}$C NMR (126 MHz, $CD_2Cl_2$) $\delta$ 144.6, 141.9, 141.8, 139.5, 137.3, 132.4, 132.0, 131.9, 129.5, 129.0, 127.3, 127.0, 113.0, 110.4, 61.1, 41.4, 37.0, 22.9; IR (thin film) 3080, 3028, 2930, 2214, 1604, 1495, 1098 cm$^{-1}$; HRMS (ESI) calcd for $[C_{20}H_{19}ClN_2Na]^+$, *m/z* 345.1129, found 345.1123.

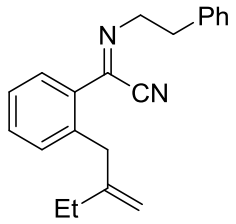
**α-iminonitrile 3.88:**




**3.88**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.66** (0.2213 g, 0.82 mmol), phenethylamine (0.1 mL, 0.82 mmol), acetonitrile (0.82 mL), TMSCN (0.07 mL, 0.56 mmol), IBX (0.214 g, 0.76 mmol), and tetrabutylammonium bromide (0.181 g, 0.56 mmol). Iminonitrile **3.88** (0.1254 g, 0.316 mmol, 38%) was isolated as a yellow oil. $R_f$ = 0.6 (1:9 EtOAc:Hex); $^1$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.33 – 7.28 (m, 2H), 7.25 – 7.21 (m, 3H), 7.07 (d, *J* = 8.8 Hz, 1H), 4.70 (s, 1H), 4.26 (s, 1H), 4.20 (t, *J* = 7.1 Hz, 2H), 3.55 (s, 2H), 3.09 (t, *J* = 7.1 Hz, 2H), 1.68 (s, 3H), 0.38 (s, 9H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 166.4 (dd, *J* = 49.9, 16.6 Hz), 164.4 (dd, *J* = 50.0, 16.7 Hz), 143.5, 140.8 (d, *J* = 3.8 Hz), 138.7, 136.8 (d, *J* = 9.5, 6.8 Hz), 129.2, 128.8, 126.8, 121.9 (dd, *J* = 22.7, 4.2 Hz), 117.1 (dd, *J* = 37.9, 33.7 Hz), 112.6 (*J* = 29.3, 3.5 Hz), 110.8, 109.7, 60.7, 36.6, 32.2 (*J* = 5.1 Hz), 23.1, 0.2 (d, *J* = 2.9 Hz); $^{19}$F NMR (471 MHz, $CDCl_3$) $\delta$ -98.2, -98.87; IR (thin film) 3083, 3029, 2956, 2215, 1612, 1386, 486 $cm^{-1}$; HRMS (ESI) calcd for $[C_{23}H_{26}F_2N_2Si+Na]^+$, *m/z* 419.1726, found 419.1735.

**α-iminonitrile 3.89:**

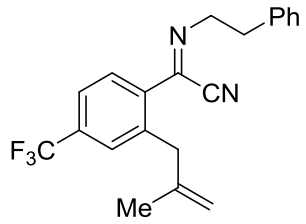



**3.89**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.69** (80 mg, 0.46 mmol), phenethylamine (56 mg, 0.46 mmol), acetonitrile (0.5

mL), TMSCN (63 µl, 0.51 mmol), IBX (193 mg, 0.69 mmol), tetrabutylammonium bromide (164 mg, 0.51 mmol), iminonitrile **3.89** was isolated as yellow oil (61 mg, 0.14 mmol 44%) $R_f$ = 0.85 (1:10 EtOAc:Hex on alumina TLC). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.58 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.43−7.20 (m, overlaped with $CHCl_3$, 8H), 4.80−4.79 (m, 1H), 4.42−4.41 (m, 1H), 4.21 (t, *J* = 7.3 Hz, 2H), 3.62 (s, 2H), 3.09 (t, *J* = 7.2 Hz, 2H), 1.94 (q, *J* = 7.7 Hz, 2H), 1.00 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 150.0, 142.6, 139.1, 138.7, 133.4, 131.7, 130.8, 130.0, 129.0, 128.6, 126.7, 126.5, 110.1, 110.0, 60.4, 39.9, 36.5, 28.9, 12.2; IR (thin film) 3063, 3027, 2964, 2932, 2213, 1604, 1453, 1360 cm$^{-1}$; HRMS (CI, $NH_3$) calcd for $[C_{21}H_{22}N_2 + H]^+$, *m/z* 303.1856, found 303.1878.

**α-iminonitrile 3.90:**

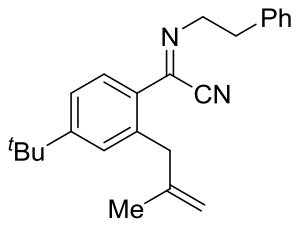



**3.90**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.73** (72 mg, 0.31 mmol), phenethylamine (39 mg, 0.32 mmol), acetonitrile (0.5 mL), TMSCN (43 µl, 0.34 mmol), IBX (132 mg, 0.47 mmol), tetrabutylammonium bromide (110 mg, 0.34 mmol), iminonitrile **3.90** was isolated as yellow oil (66 mg, 0.19 mmol 59%) $R_f$ = 0.80 (1:10 EtOAc:Hex on alumina TLC). $R_f$ = 0.80; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.68 (d, *J* = 8.3 Hz, 1H), 7.58 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.53

(s, 1H), 7.34−7.22 (m, 5H), 4.84−4.83 (m, 1H), 4.44−4.43 (m, 1H), 4.25 (t, *J* = 7.1 Hz, 2H), 3.59 (s, 2H), 3.12 (t, *J* = 7.1 Hz, 2H), 1.64 (s, 3H); $^{13}$C NMR (126 MHz , $CDCl_3$) $\delta$ 143.4, 141.4, 140.0, 138.4, 136.4 (app d, *J* = 3 Hz), 132.5 (q, *J* = 33 Hz), 130.4, 129.0, 128.6, 128.2 (q, *J* = 4 Hz), 126.7, 123.6 (q, *J* = 273 Hz), 123.6 (q, *J* = 4 Hz), 113.1, 109.7, 60.6, 41.0, 36.4, 22.5; $^{19}$F NMR (282 MHz , $CDCl_3$) $\delta$ -64.2; IR (thin film) 3084, 2931, 2929, 2215, 1612, 1454, 1333, 1169, 1086, 837 cm$^{-1}$; HRMS (CI, $NH_3$) calcd for $[C_{21}H_{19}F_3N_2 + H]^+$, *m/z* 357.1574, found 357.1559.

**α-iminonitrile 3.91:**

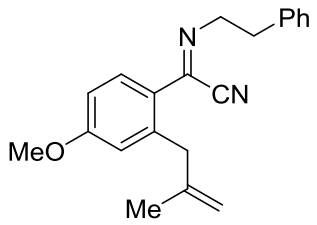



**3.91**

Aldehyde **3.77** (98 mg, 0.045 mmol) and phenethylamine (55 mg,0.46 mmol) are stirred for one hour at room temperature. A small aliquot was taken and analyzed by $^1$H NMR to ensure complete formation of imine. Acetonitrile (0.5 mL), TMSCN (85 µl, 0.68 mmol) were added and stirred for another 20 min at room temp. IBX (190 mg, 0.60 mmol) and tetrabutylammonium bromide (160 mg, 0.49 mmol) were added and stirred for one hour at room temperature. The reaction mixture was diluted with EtOAc (10 mL), filtered through celite and concentrated. The crude product was purified by flash chromatography on alumina (0 to 2% EtOAc in hexanes) to afford α-iminonitrile **3.91** as yellow oil (92 mg, 0.27 mmol 59%) $R_f$

= 0.90 (1:9 EtOAc:Hex on alumina TLC).$^{1}$H NMR (500 MHz , $CDCl_3$) $\delta$ 7.57 (d, *J* = 8.2 Hz, 1H), 7.35 - 7.29 (m, 3H), 7.27 - 7.21 (m, 5H), 4.76 (s, 1H), 4.40 (s, 1H), 4.20 (t, *J* = 7.2 Hz, 2H), 3.60 (s, 2H), 3.09 (t, *J* = 7.2 Hz, 2H), 1.65 (s, 3H), 1.32 (s, 9H); $^{13}$C NMR (126MHz , $CDCl_3$) $\delta$ 154.2, 144.7, 142.4, 138.8, 138.6, 130.4, 130.1, 128.9, 128.8, 128.5, 126.4, 123.6, 111.9, 110.1, 60.3, 41.5, 36.6, 34.8, 31.0, 22.7; IR (thin film) 3064, 3028, 2964, 2867, 2214, 1604, 1454, 1112, 699 cm$^{-1}$;HRMS (ESI) calcd for $[C_{24}H_{28}N_2Na]^+$, *m/z* 367.2145, found 367.2144.

**α-iminonitrile 3.92:**

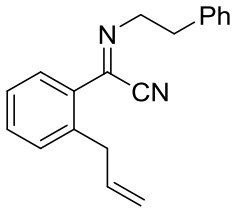



**3.92**

Aldehyde **3.80** (76 mg, 0.40 mmol) and phenethylamine (60 mg,0.50 mmol) are stirred for one hour at room temperature. A small aliquot was taken and analyzed by NMR to ensure complete formation of imine. Acetonitrile (0.4 mL), TMSCN (60 µl, 0.50 mmol,) were added and stirred for another 15 min at room temp. IBX (169 mg, 0.60 mmol) and tetrabutylammonium bromide (144 mg, 0.44 mmol) were added and stirred for additional two hours at room temperature. The reaction mixture was diluted with EtOAc (10 mL), filtered through celite and concentrated. The crude product was purified by flash chromatograph alumina (20 to 30% $CH_2Cl_2$ in hexanes) to afford pure α-iminonitrile **3.92** as yellow oil (55

mg, 0.17 mmol 43%) $R_f$ = 0.80 (1:9 EtOAc:Hex on alumina TLC). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.63 (d, *J* = 8.7 Hz, 1H), 7.33 - 7.21 (m, 5H), 6.84 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 4.78 (s, 1H), 4.44 (s, 1H), 4.18 (t, *J* = 7.3 Hz, 2H), 3.84 (s, 3H), 3.60 (s, 2H), 3.08 (t, *J* = 7.2 Hz, 2H), 1.65 (s, 3H); $^{13}$C NMR (75 MHz , $CDCl_3$) $\delta$ 161.3, 144.4, 141.9, 141.4, 138.9, 132.3, 128.9, 128.4, 126.4, 125.7, 117.3, 112.0, 111.5, 110.1, 60.2, 55.3, 41.4, 36.7, 22.6; ; IR (thin film) IR (thin film) 3064, 3028, 2936, 2214, 1604, 1497, 1117, 699 $cm^{-1}$; HRMS (ESI) calcd for $[C_{21}H_{22}N_2NaO]^+$, *m/z* 341.1624, found 341.1621.

**α-iminonitrile 3.93:**

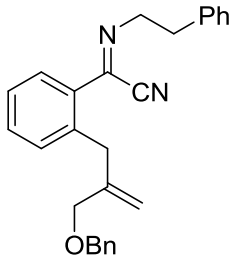



**3.93**

Prepared using general procedure for α-iminonitrile synthesis using 2-allylbenzaldehyde (195 mg, 1.34 mmol), phenethylamine (162 mg, 1.34 mmol), acetonitrile (1.34 ml), TMSCN (190 µl, 1.47 mmol,) IBX (563 mg, 2.01 mmol) and tetrabutylammonium bromide (473 mg, 1.47 mmol) and α-iminonitrile **3.93** was isolated was yellow oil (140 mg, 0.51 mmol 44%) $R_f$ = 0.90 (1:9 EtOAc:Hex on alumina TLC).$^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.62 (dd, *J* = 1.3, 7.7 Hz, 1H), 7.42 (dt, *J* = 1.4, 7.5 Hz 1H), 7.34 - 7.22 (m, 7H), 5.88 (tdd, *J* = 6.4, 10.3, 17.0 Hz, 2

H), 5.03(qd, *J* = 1.5, 10.1 Hz, 1H), 4.97 (qd, *J* = 1.7, 17.1 Hz, 1H), 4.25 (t, *J* = 7.1 Hz, 2H), 3.61 (d, *J* = 6.4 Hz, 2H), 3.13 (t, *J* = 7.1 Hz, 2H); $^{13}$C NMR (126MHz , $CDCl_3$) $\delta$ 142.4, 139.5, 138.7, 136.8, 132.6, 131.1, 130.9, 130.1, 129.0, 128.5, 126.6, 126.5, 116.1, 110.1, 60.4, 37.5, 36.5; IR (thin film) IR (thin film) 3064, 3027, 2925, 2214, 1636, 1454, 952, 762 $cm^{-1}$; HRMS (ESI) calcd for $[C_{19}H_{18}N_2Na]^+$, *m/z* 297.1362, found 341. 297.1367.

**α-iminonitrile 3.94:**

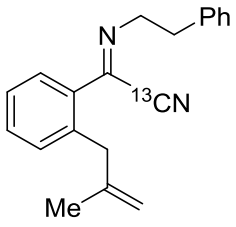



**3.94**

Prepared using general procedure for α-iminonitrile synthesis using 2-(2-((benzyloxy)methyl)allyl)benzaldehyde **3.83** (100 mg, 0.38 mmol), phenethylamine (46 mg, 0.38 mmol), acetonitrile (0.5 ml), TMSCN (53 µl, 0.42 mmol,) IBX (160 mg, 0.57 mmol) and tetrabutylammonium bromide (135 mg, 0.42 mmol) and **α-iminonitrile 3.94** was isolated was yellow oil (60 mg, 0.15 mmol 40%) $R_f$ = 0.90 (1:9 EtOAc:Hex on alumina TLC). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.62 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.41 - 7.19 (m, 13H), 5.10-5.09 (m, 1H), 4.62 (s, 1H), 4.46 (s, 2H), 4.16 (t, *J* = 7.2 Hz, 2H), 3.86 (s, 2H), 3.69 (s, 2H), 3.04 (t, *J* = 7.2 Hz, 2H); $^{13}$C NMR (75MHz , $CDCl_3$) $\delta$ 144.9, 142.4, 138.7, 138.4,

138.2, 133.1, 131.9, 130.8, 130.2, 129.0, 128.5, 128.4, 127.6, 127.6, 126.8, 126.5, 113.4, 110.0, 72.8, 72.0, 60.4, 36.9, 36.5; LRMS (GC-MS, CI, MeOH) *m*/*z* 395 (M+H).

**α-iminonitrile 3.38:**

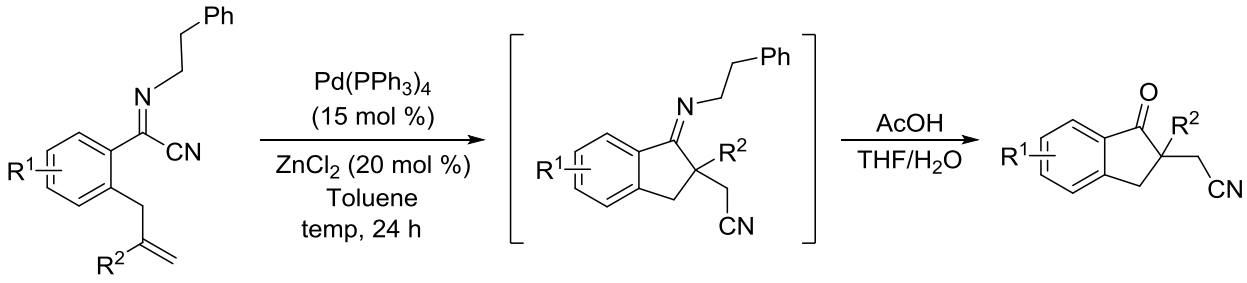



**3.38**

Prepared using general procedure for α-iminonitrile synthesis using aldehyde **3.23** (101 mg, 0.63 mmol), phenethylamine (76 mg, 0.63 mmol), acetonitrile (0.7 mL), TMS$^{13}$CN (88 µl 0.69 mmol), IBX (264 mg, 0.95 mmol) tetrabutylammonium bromide (222 mg, 0.69 mmol). α-iminonitrile **3.38** was isolated was yellow oil (114 mg, 0.39 mmol 64%) $R_f$ = 0.85 (1:9 EtOAc:Hex on alumina TLC).$^1$H NMR (500 MHz , $CDCl_3$) $\delta$7.59 (dd, *J* = 1.2, 7.7 Hz, 1H), 7.41 (dt, *J* = 7.5, 1.4 Hz, 1H), 7.35−7.30 (m, 3H), 7.28−7.20 (m, 4H), 4.78 (s, 1H), 4.43 (d, *J* = 0.8 Hz, 1H), 4.22 (dt, *J* = 1.2, 7.2 Hz, 2H), 3.58 (s, 2H), 3.11 (t, *J* = 7.2 Hz, 2H), 1.64 (s, 3H); $^{13}$C

NMR[1] (126 MHz, $CDCl_3$) $\delta$ 144.4, 142.5 ($J$ = 65 Hz), 138.9 ($J$ = 2.5 Hz), 138.7, 133.2 ($J$ = 11 Hz), 131.5, 130.8, 130.0, 129.0, 128.5, 126.7, 126.5, 112.2, 110.1, 60.4, 41.1, 36.5, 22.6; IR (thin film) 3064, 3028, 2931, 2163, 1604, 1453, 1030 $cm^{-1}$; HRMS (CI, $NH_3$) calcd for $[C_{19}{}^{13}CH_{20}N_2Na]^+$, *m/z* 312.1552, found 312.1551.

## Cyanoacylation Reaction:



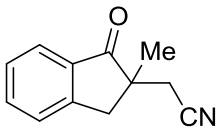

### General Procedure:

In a nitrogen filled glove box, a 1 or 4 dram reaction vial (Chemglass, polytetrafluoroethylene cap) was charged with iminonitrile (0.34 mmol 1equiv), $Pd(PPh_3)_4$ (0.05 mmol, 0.15 equiv), $ZnCl_2$ (0.07 mmol, 0.20 equiv) and toluene (1.6 mL). The mixture was heated at 120 or 130 °C for 24 hr inside nitrogen filled glove box. The mixture was then taken out of glove box, filtered through celite and concentrated. The crude product was dissolved in THF and 30% (v/v)

[1] $^{13}C–^{13}C$ coupling constants are assigned by comparison to $^{13}C$ NMR of **3.24**.

aqueous acetic acid was added dropwise. The reaction was stirred at room temperature for 1.5 to 18 hr. After ensuring complete hydrolysis of imine by TLC, the reaction mixture was diluted with diethyl ether (20 mL). The layers were separated and aqueous layer was again extracted with diethyl ether (20 mL). The combined organic extracts were washed with water, saturated aqueous $NaHCO_3$ solution, brine and dried over anhydrous $Na_2SO_4$ and concentrated. The crude product was purified by flash column chromatography on silica gel (gradient, EtOAc: Hex) to afford the indanone (acylcyanation product).

**Indanone 3.13:**

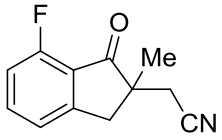



**3.13**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.24** (97 mg, 0.34 mmol), $Pd(PPh_3)_4$ (59 mg, 0.05 mmol), $ZnCl_2$ (9.2 mg, 0.67 mmol) and toluene (1.6 ml) at 120 °C. Hydrolysis of imine was accomplished with THF (2 ml) and 20% (v/v) aqueous AcOH (3 mL). The crude product was purified by flash column chromatography (10 to 15% EtOAc in hexanes) and indanone **3.13** was obtained as yellow oil (51 mg, 0.28 mmol, 82%) $R_f$ = 0.45 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.80 (d, *J* = 7.7 Hz, 1H), 7.67 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.54−7.39 (m, 2H), 3.31 (d, *J* = 17.3 Hz, 1H), 3.12 (d, *J* = 17.3 Hz, 1H), 2.71 (d, *J* = 16.7 Hz, 1H), 2.53 (d, *J* = 16.7 Hz, 1H), 1.38 (s, 3H); $^{13}$C NMR (75 MHz ,

$CDCl_3$) $\delta$ 206.6, 151.3, 135.8, 134.1, 128.1, 126.7, 124.8, 117.4, 46.6, 40.0, 25.9, 23.7; IR (thin film) 2967, 2929, 2249, 1714, 1615, 1459, 1394, 1251, $cm^{-1}$; HRMS (ESI) calcd for $[C_{12}H_{11}NNaO]^+$, *m/z* 208.0738, found 208.0735.

**Indanone 3.26:**



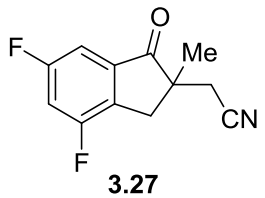

**3.26**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.84** (31 mg, 0.10 mmol), $Pd(PPh_3)_4$ (18 mg, 0.015 mmol), $ZnCl_2$ (3 mg, 0.02 mmol) and toluene (0.45 mL) at 130 °C. Hydrolysis of imine was accomplished using THF (0.4 mL) and 30% (v/v) aqueous AcOH (9 mL) for two hours. The crude product was purified by flash column chromatography (20% EtOAc in hexanes) and indanone **3.26** was isolated as yellow oil (15.0 mg, 0.076 mmol, 73%) $R_f$ = 0.40 (1:3 EtOAc:Hex) (The sample could not be separated from 1% triphenylphosphine oxide and the yield was corrected accordingly); $^1$H NMR[2] (500 MHz, $CDCl_3$) $\delta$ 7.65 (dt, *J* = 7.9, 5.0 Hz, 1H), 7.28−7.27 (m, 1H), 7.05 (app t, *J* = 8.6 Hz, 1H), 3.32 (d, *J* = 17.5 Hz, 1H), 3.13 (d, *J* = 17.5 Hz, 1H), 2.71 (d, *J* = 16.8 Hz, 1H), 2.56 (d, *J* = 16.8 Hz, 1H), 1.39 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 202.8, 159.5 (d, *J* = 265 Hz), 153.1, 137.8 (d, *J* = 10 Hz), 122.6, 122.2, 117.3, 115.0 (d, *J* = 19 Hz), 47.3, 39.9, 25.9, 23.8; $^{19}$F NMR (471 MHz , $CDCl_3$) $\delta$ -

[2] No attempt was made to distinguish $^{19}$F−$^1$H coupling from $^{19}$F−$^1$H coupling.

113.9; IR (thin film) 3082, 2968, 2929, 2248, 1714, 1615, 1475, 1198 $cm^{-1}$; HRMS (ESI) calcd for $[C_{12}H_{10}FNNaO]^+$, *m/z* 226.0639, found 226.0633.

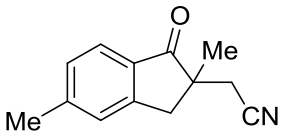
**Indanone 3.27:**




**3.27**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.85** (36 mg, 0.116 mmol), $Pd(PPh_3)_4$ (12.7 mg, 0.011 mmol), $ZnCl_2$ (3 mg, 0.022 mmol) and toluene (0.53 mL) at 120 °C. Hydrolysis of imine was accomplished with (0.5 mL), water (1.11 mL) and AcOH (0.184 mL) for one hour. The crude product was purified by flash column chromatography (15% v/v DCM in hexanes) and indanone **3.27** was isolated as orange oil. (15.6 mg, 0.071 mmol, 64%) $R_f$ = 0.6 (1:4 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.29 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.13 (dt, *J* = 8.5, 2.1 Hz, 1H), 3.25 (d, *J* = 17.4 Hz, 1H), 3.11 (d, *J* = 17.4 Hz, 1H), 2.70 (d, *J* = 16.8 Hz, 1H), 2.58 (d, *J* = 16.8 Hz, 1 H), 1.39 (s, 3H);$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 204.7, 163.3 (*J* = 252.4, 9.2 Hz), 160.1 (*J* = 254.9, 11.5 Hz), 137.8 (*J* = 8.6, 5.9 Hz), 133.4 (*J* = 19.9, 2.7 Hz), 129.2 (*J* = 167.2 Hz), 117.1, 111.0 (*J* = 27.3, 23.7 Hz), 107.2 (*J* = 22.2, 4.4 Hz), 47.5, 35.6, 26.1, 24.0; $^{19}$F NMR (471 MHz, $CDCl_3$) $\delta$ -108.3 (app q, *J* = 8.2, 1.7 Hz), -113.3 (app t, *J* = 7.9 Hz); IR (thin film) 3061, 2972, 2917, 2251, 1724, 1490, 1327 $cm^{-1}$; HRMS (ESI) calcd for $[C_{12}H_9F_2N_2+Na]^+$, *m/z* 244.0539.

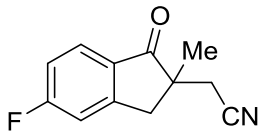
**Indanone 3.28:**




**3.28**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.39** (30 mg, 0.10 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), $ZnCl_2$ (2.7 mg, 0.02 mmol) and toluene (0.5 mL) at 120 °C. Hydrolysis of imine was accomplished with THF (0.4 mL) and 20% (v/v) aqueous AcOH (0.8 mL) for six hours. The crude product was purified by flash column chromatography (10 to 15% EtOAc in hexanes) and indanone **3.28** was isolated as yellow oil (16.1 mg, 0.081 mmol, 81%) $R_f$ = 0.45 (1:4 EtOAc:Hex). $^1$H NMR (300 MHz ,$CDCl_3$) $\delta$ 7.68 (d, $J$ = 7.8 Hz, 1H), 7.28−7.22 (m, 2H), 3.24 (d, $J$ = 17.4 Hz, 1H), 3.06 (d, $J$ = 17.3 Hz, 1H), 2.69 (d, $J$ = 16.7 Hz, 1H), 2.54−2.46 (m, 4H), 1.36 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 206.1, 151.9, 147.3, 131.9, 129.4, 127.1, 124.7, 117.6, 46.8, 39.9, 26.1, 23.7, 22.2; IR (thin film) 2966, 2927, 2248, 1709, 1709, 1609, 1456, 1331, 1282, 987 $cm^{-1}$; HRMS (ESI) calcd for $[C_{13}H_{13}NNaO]^+$, *m/z* 222.0895, found 222.0883.

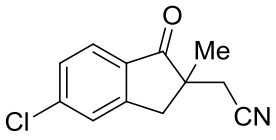
**Indanone 3.29:**




**3.29**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.86** (53 mg, 0.174 mmol), $Pd(PPh_3)_4$ (30 mg, 0.026 mmol), $ZnCl_2$ (4.8 mg, 0.035 mmol) and toluene (0.8 mL) at 120 °C. Hydrolysis of imine was accomplished using THF (0.7 mL) and 30% aqueous AcOH (0.8 mL) for 1.5 hours. The crude product was purified by flash column chromatography (10 to 15% EtOAc in hexanes) and indanone **3.29** was isolated as yellow oil (30.0 mg, 0.148 mmol, 85%) $R_f$ = 0.40 (1:4 EtOAc:Hex). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.80 (dd, *J* = 8.4, 5.3 Hz, 1H), 7.17−7.12 (m, 2H), 3.29 (d, *J* = 17.5 Hz, 1H), 3.11 (d, *J* = 17.5 Hz, 1H), 2.69 (d, *J* = 16.8 Hz, 1H), 2.54 (d, *J* = 16.8 Hz, 1H), 1.38 (s, 3H); $^{13}$C NMR (126 MHz ,$CDCl_3$) $\delta$ 204.7, 167.8 (d, *J* = 258 Hz), 154.3 (d, *J* = 10 Hz), 130.6, 127.3 (*J* = 10 Hz), 117.3, 116.6 (d, *J* = 24 Hz), 113.5 (d, *J* = 23 Hz), 47.0, 39.9, 26.0, 23.8; $^{19}$F NMR (282 MHz , $CDCl_3$) $\delta$ -101.7; IR (thin film) 2968, 2930, 2250, 1715, 1615, 1594, 1456, 1251, 1086, 988, $cm^{-1}$. HRMS (ESI) calcd for $[C_{12}H_{10}FNNaO]^+$, *m/z* 226.0639, found 226.0644.

**Indanone 3.30**:

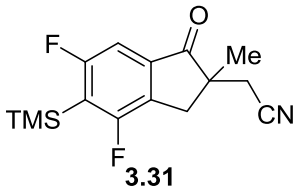



**3.30**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.87** (30 mg, 0.09 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol), $ZnCl_2$ (2.5 mg, 0.02 mmol) and toluene (0.4 mL) at 120 °C. Hydrolysis of imine was run using THF (0.4 mL)

and 30% (v/v) aqueous AcOH (0.7 mL) for 2 hours. The crude product was purified by flash column chromatography (15% EtOAc in hexanes) and indanone **3.30** was isolated as yellow oil (16.1 mg, 0.073 mmol, 79%) $R_f$ = 0.40 (1:4 EtOAc:Hex). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.72 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 0.9 Hz, 1H), 7.42 (dd, *J* = 8.2, 0.8 Hz, 1H), 3.28 (d, *J* = 17.5 Hz, 1H), 3.10 (d, *J* = 17.5 Hz, 1H), 2.70 (d, *J* = 16.8 Hz, 1H), 2.54 (d, *J* = 16.8 Hz, 1H), 1.38 (s, 3H) $^{13}$C NMR (126 MHz , $CDCl_3$) $\delta$ 205.2, 152.8, 142.5, 132.6, 129.1, 127.0, 126.0, 117.2, 47.0, 39.7, 25.9, 23.8; IR (thin film) 3061, 2968, 2930, 2248, 1715, 1600, 1578, 1327, 1310, 1071, 897, cm$^{-1}$. HRMS (ESI) calcd for $[C_{12}H_{10}ClNNaO]^+$, *m/z* 242.0343, found 242.0347.

**Indanone 3.31**:

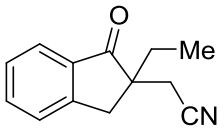



**3.31**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.88** (56.6 mg, 0.142 mmol), $Pd(PPh_3)_4$ (16.5 mg, 0.014 mmol), $ZnCl_2$ (3.9 mg, 0.029 mmol) and toluene (0.68 mL) at 120 °C. Hydrolysis of imine was accomplished with THF (0.59 mL), water (1.43 mL) and AcOH (0.24 mL) for one hour. The crude product was purified by column chromatography (gradient running from pure hexanes to 15% v/v DCM in hexanes with steps of a column volume of hexanes, 2 column volumes of 5% DCM, 1 column volume of 10% DCM and 1

column volume of 15% DCM) and indanone **3.31** was isolated as an orange oil (0.0263 g, 63%). $R_f$ = 0.6 (1:4 EtOAc:Hex); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.19 (d, *J* = 6.9 Hz, 1H), 3.21 (d, *J* = 17.5 Hz, 1H), 3.06 (d, *J* = 17.4 Hz, 1H), 2.68 (d, *J* = 16.8 Hz, 1H), 2.56 (d, *J* = 16.8 Hz, 1H), 1.38 (s, 3H), 0.42 (s, 9H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 205.0 (t, *J* = 3.2 Hz), 167.2 (app dd, *J* = 246.6, 13.1 Hz), 163.9 (app dd, *J* = 248.8, 15.4 Hz), 138.6 (dd, *J* = 9.6, 6.7 Hz), 132.8 (dd, *J* = 25.2, 2.8 Hz), 129.0 (d, *J* = 18.2 Hz), 122.90 (app dd, *J* = 36.5, 32.6 Hz), 117.28, 106.8 (dd, *J* = 28.3, 4.5 Hz), 47.6, 35.8, 26.2, 24.0, 0.17 (t, *J* = 3.0 Hz); $^{19}$F NMR (471 MHz, $CDCl_3$) $\delta$ -96.1, -101.3; IR (thin film) 2962, 2930, 2359, 2250, 1723, 1411, 1012, 848 cm$^{-1}$; HRMS (ESI) calcd for $[C_{15}H_{17}F_2NO+Na]^+$, *m/z* 316.0940, found 316.0934.

**Indanone 3.32:**

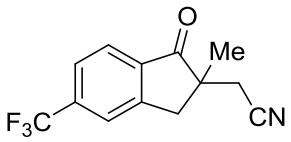



**3.32**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.89** (21 mg, 0.070 mmol), $Pd(PPh_3)_4$ (12 mg, 0.010 mmol), $ZnCl_2$ (2.0 mg, 0.014 mmol) and toluene (0.35 mL) at 130 °C. Hydrolysis of imine was accomplished using THF (0.5 mL) and 30% (v/v) aqueous AcOH (0.7 mL) for 12 hours. The crude product was purified by flash column chromatography (10% EtOAc in hexanes) and indanone **3.32** was isolated as yellow oil (10.5 mg, 0.079 mmol,

76%) $R_f$ = 0.45 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz , $CDCl_3$) $\delta$ 7.78 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 3.21 (s, 2H), 2.71 (d, *J* = 16.7 Hz, 1H), 2.55 (d, *J* = 16.7 Hz, 1H), 1.92 - 1.70 (m, 2H), 0.80 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 206.7, 152.0, 135.7, 135.5, 128.1, 126.6, 124.5, 117.4, 50.3, 37.4, 30.2, 24.9, 8.5; IR (thin film) 2967, 2924, 2880, 2248, 1711, 1608, 1465, 1298, 1187, 927, cm$^{-1}$. HRMS (ESI) calcd for $[C_{13}H_{13}NNaO]^+$, *m/z* 222.0895, found 222.0900.

**Indanone 3.35:**

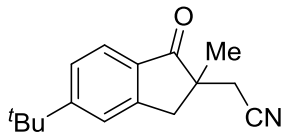



**3.35**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.90** (31 mg, 0.087 mmol), $Pd(PPh_3)_4$ (15 mg, 0.013 mmol), $ZnCl_2$ (2.5 mg, 0.018 mmol) and toluene (0.4 mL) at 120 °C. Hydrolysis of imine was run using THF (0.4 mL) and 30% aqueous AcOH (0.8 mL) for 1.5 hours. The crude product was purified by flash column chromatography (15% EtOAc in hexanes) and indanone **3.35** was isolated as yellow oil (20 mg, 0.079 mmol, 90%) $R_f$ = 0.38 (1:4 EtOAc:Hex) $^1$H NMR (300 MHz ,$CDCl_3$) $\delta$ 7.91 (d, *J* = 8.0 Hz, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 3.37 (d, *J* = 17.5 Hz, 1H), 3.19 (d, *J* = 17.6 Hz, 1H), 2.73 (d, *J* = 16.8 Hz, 1H), 2.58 (d, *J* = 17.5 Hz, 1H), 1.40 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 205.7, 151.5, 137.1 (q, *J* = 26 Hz), 136.9, 125.5, 125.3, 124.1, 123.4 (q,

$J$ = 274 Hz), 117.0, 47.2, 39.9, 25.8, 23.8; $^{19}$F NMR (282 MHz , $CDCl_3$) $\delta$ -64.2; IR (thin film) 2971, 2932, 2248, 1723, 1622, 1456, 1206, 1170, 930, cm$^{-1}$. HRMS (ESI) calcd for $[C_{13}H_{10}F_3NNaO]^+$, *m/z* 276.0607, found 276.0612.

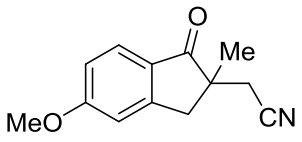
**Indanone 3.36:**




**3.36**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.91** (37 mg, 0.11 mmol), $Pd(PPh_3)_4$ (25 mg, 0.021 mmol), $ZnCl_2$ (2.9 mg, 0.02 mmol) and toluene (0.5 mL) at 130 °C. Hydrolysis of imine was run using THF (0.4 mL) and 30% aqueous AcOH (0.9 mL) for 18 hours. The crude product was purified by flash column chromatography (10-15% EtOAc in hexanes) and indanone **3.36** was isolated as light yellow oil (20.2 mg, 0.084 mmol, 77%) $R_f$ = 0.40 (1:4 EtOAc:Hex).$^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.72 (dd, $J$ = 7.2, 1.5 Hz, 1H), 7.49 - 7.46 (m, 2H), 3.27 (d, $J$ = 17.2 Hz, 1H), 3.09 (d, $J$ = 17.2 Hz, 1H), 2.69 (d, $J$ = 16.8 Hz, 1H), 2.51 (d, $J$ = 16.8 Hz, 1H), 1.42 - 1.37 (m, 12H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 206.2, 160.3, 151.7, 131.8, 126.0, 124.5, 123.3, 117.6, 46.8, 40.1, 35.6, 31.1, 26.0, 23.7; IR (thin film) 2965, 2870, 2248, 1711, 1608, 1438, 1225, 987, cm$^{-1}$; HRMS (ESI) calcd for $[C_{16}H_{19}NNaO]^+$; *m/z* 264.1359, found 264.1364.

**Indanone 3.37:**

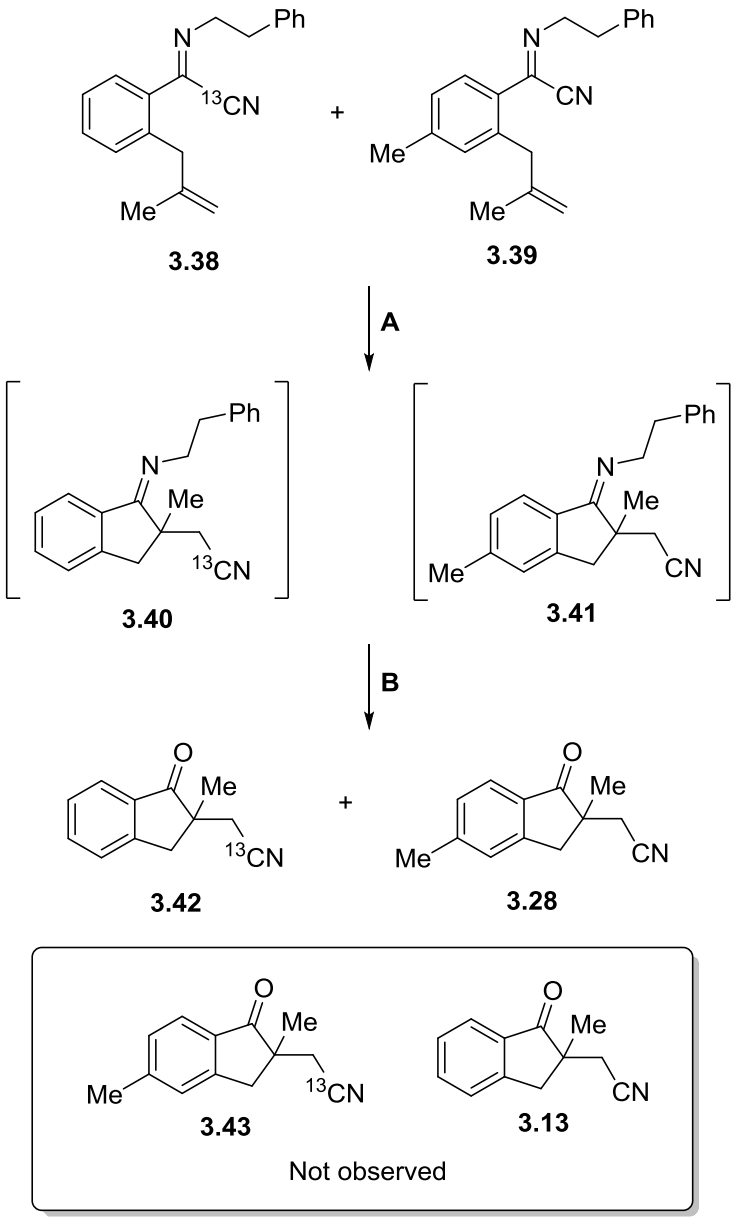



**3.37**

Prepared using the general procedure for cyanoacylation from iminonitrile **3.92** (51 mg, 0.16 mmol), $Pd(PPh_3)_4$ (37 mg, 0.032 mmol), $ZnCl_2$ (4.4 mg, 0.032 mmol) and toluene (0.7 mL) at 130 °C. Hydrolysis of imine was run using THF (0.5 mL) and 30% (v/v) aqueous AcOH (0.7 mL) for 14 hours. The crude product was purified by flash column chromatography (20% EtOAc in hexanes) and indanone **3.37** was isolated as colorless oil (21 mg, 0.097 mmol, 60%) $R_f$ = 0.40 (3:7 EtOAc:Hex). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.72 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.90 (d, *J* = 1.9 Hz, 1H), 3.91 (s, 3H), 3.24 (d, *J* = 17.3 Hz, 1H), 3.06 (d, *J* = 17.3 Hz, 1H), 2.69 (d, *J* = 16.8 Hz, 1H), 2.50 (d, *J* = 16.8 Hz, 1H), 1.37 (s, 3H) $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 204.6, 166.2, 154.4, 127.2, 126.6, 117.7, 116.3, 109.7, 55.8, 46.8, 40.1, 26.2, 23.8; IR (thin film) 2967, 2930, 2248, 1702, 1599, 1490, 1340, 1295, 1104, 986, $cm^{-1}$; HRMS (ESI) calcd for $[C_{13}H_{13}NNaO_2]^+$; *m/z* 238.0844, found 238.0843.

**Crossover Experiment**: In a nitrogen filled glove box, a 1 dram reaction vial was charged with α-iminonitrile **3.39** (38 mg 0.125 mmol), and α-iminonitrile **3.38** (36 mg 0.125 mmol) $Pd(PPh_3)_4$ (43 mg, 0.038 mmol), $ZnCl_2$ (7.0 mg, 0.05 mmol) and toluene (1.0 mL). The mixture was heated at 120 °C for 24 hr inside nitrogen filled glove box. The mixture was then taken out of glove box, filtered through celite and concentrated. The crude product was dissolved in THF (1.5 mL) and

then 30% aqueous acetic acid (2.5 mL) was added. The reaction was stirred at room temperature for 12 hr. After ensuring complete hydrolysis of imine by TLC, the reaction was diluted with diethyl ether (20 mL). The layers were separated and aqueous layer was again extracted with diethyl ether (20 mL). The combined organic layers were washed with water, sat $NaHCO_3$, brine and dried over anhydrous $Na_2SO_4$ and concentrated. The crude purified by flash column chromatography on silica gel (15% EtOAc in Hex) to afford the mixture of indanones **3.42** and **3.28** (39 mg). No crossover products **3.43** and **3.13** were observed by $^{13}C$ NMR.




**A**: $Pd(PPh_3)_4$ (15 mol %), $ZnCl_2$ (20 mol %), PhMe, 120°C, 24 h
**B**: AcOH, AcOH, rt, 12 h

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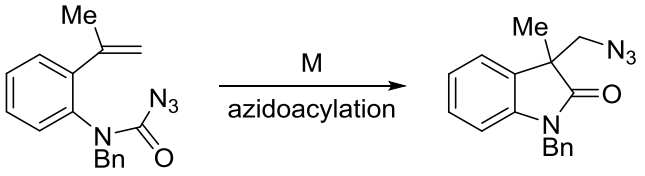
# Chapter 4

# Unprecedented Reactions Carbamoyl Azides

## 4.1 Introduction

Introduction to C–CN sigma-bond activation of cyanoformamides was discussed in the first chapter. Our contribution to the development of C–CN sigma-bond activation of cyanoformate esters and α-iminonitriles was discussed in the second and third chapters. The highly functionalized products formed in these reactions can be used as building blocks to synthesise more complex products. Having developed C–CN sigma-bond activation reactions, attention was drawn on the possibility of azidoacylation of alkenes using C–N bond activation of carbamoyl azides like **4.1**(Scheme 4.1). Successful azidoacylation will be a very useful strategy as the products (like **4.2**) are formed with new C–C and C–N bonds and also with the retention of azide and amide functional groups.



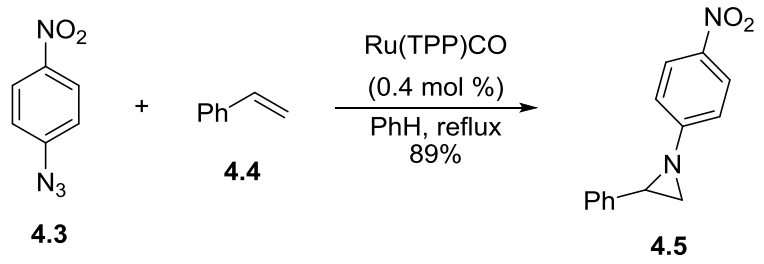

**4.1** **4.2**

M = transition metal

**Scheme 4.1**: Initial proposal for Intramolecular Azidoacylation

Azides are prominent functional groups in organic chemistry participating in variety of reactions.[1] Azides can be converted to primary amines using the Staudinger reaction.[2] Acyl azides also undergo Curtius rearrangement to form isocyanates. These isocyanates can be used to synthesize carbamic acids and protected primary amines.[3] Azides are also extensively be used in cycloaddition reactions, particularly to make triazoles. Azides are very efficient starting materials for click chemistry particularly the azide-alkyne Huigsen cycloaddition which is referred as “the cream of the crop” of click chemistry.[4]

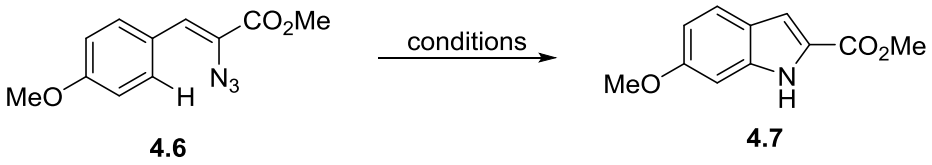
However development of C–N activation of azides can be challenging as azides are unstable when heated at high temperatures and have propensity to form nitrenes with the liberation of nitrogen gas. These nitrenes, like carbenes are very reactive intermediates, which undergo a variety of reactions. Nitrenes, like carbenes, react with double bonds in [2+1] fashion forming aziridine rings. One such example is shown in Scheme 4.2. When *p*-nitrophenyl azide **4.3** is heated in the presence of catalytic amount of Ru(TPP)CO it forms the corresponding nitrene by the evolution of nitrogen gas. The nitrene subsequently reacts with styrene **4.4** to form aziridine **4.5**.[5] The presence of the Ru catalyst is critical for the yield of the reaction and in the absence of the catalyst very little product was detected.




TPP = tetraphenylphorphyrin

**Scheme 4.2**: Ruthenium Catalyzed Aziridine Formation from Aryl Azides

Nitrenes, similar to carbenes, have the ability to undergo insertion into a C–H bond leading to the formation of C–N and N–H bonds.[6] This strategy was utilized by Moddy to form 2-carboxylate-substituted indoles from vinyl azides (Scheme 4.3).[7] When vinylazide **4.6** is heated at 150 $^{o}$C, it forms the corresponding nitrene by the liberation of nitrogen. Subsequent insertion into an aromatic C–H bond gives indole **4.7** in 80% yield. Driver reported that the rate of the reaction can be accelerated such that the reaction can be performed at ambient temperature by using rhodium(II) perfluorobutyrate (shown in the box) as a catalyst and the corresponding 2-carboxylate-substituted indole was isolated in greater than 95% yield (Scheme 4.3).[8]

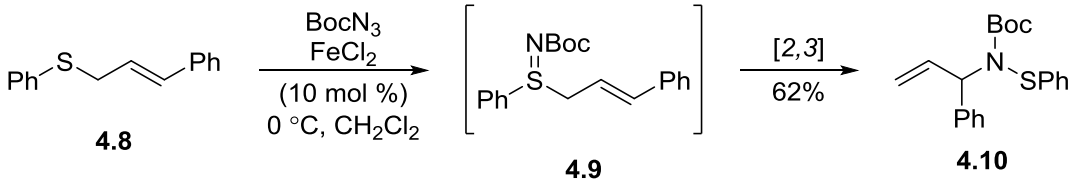



**4.6** **4.7**

| conditions | yield (%) |
|---|---|
| 150 °C | 80 |
| $Rh_2(O_2CC_3F_7)_4$ (5 mol %), rt | >95 |

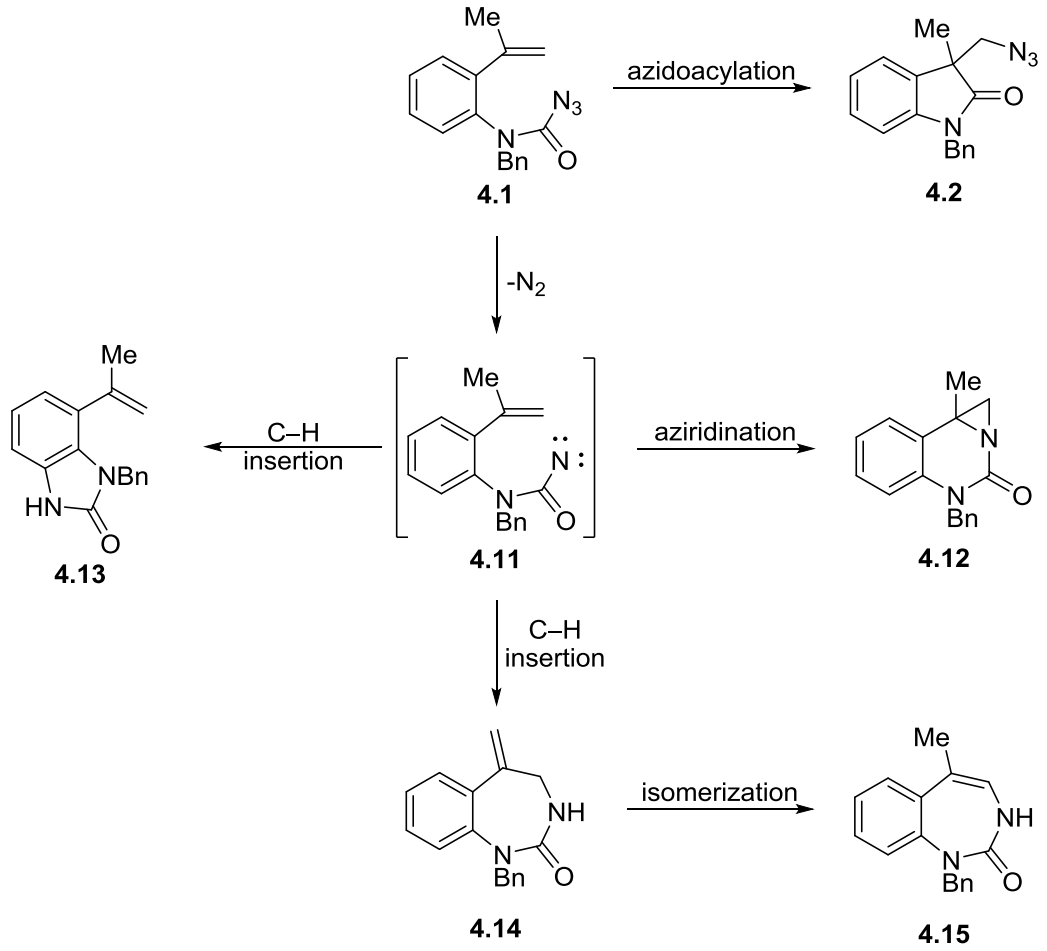
**Scheme 4.3**: C–H Insertion Reactions of Azides

Nitrenes also undergo *N*-atom transfer reactions to the sulfur-atom of sulfides and sulfoxides.[9] Bach reported *N*-atom transfer reaction to sulfur in allyl sulphide using *tert*-butoxycarbonyl azide (Boc-$N_3$).[10] When allyl sufide **4.8** is treated with with $BocN_3$ in the presence of catalytic $FeCl_2$, it undergoes *N*-atom transfer to form iminosulfide **4.9** and subsequent *in situ* [2,3] sigmatropic rearrangement gives allyl amine **4.10** (Scheme 4.4). The presence of $FeCl_2$ is critical for the reaction efficiency. In the absence of $FeCl_2$ the reaction requires higher temperature and also results in a lower yield of the product.




**Scheme 4.4**: Fe(II)-catalyzed Imidation of Allylsulfides using $BocN_3$

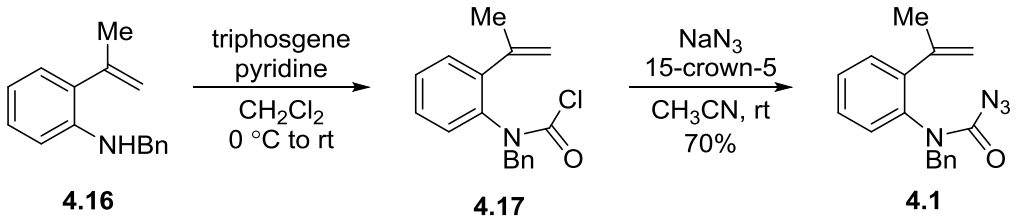
Considering the potential reactions of azides, intramolecular azidoacylation of carbamoyl azide **4.1** to provide azide **4.2** is challenging (Scheme 4.5). Treatment of carbomoyl azide **4.1** with transition metals at high temperature could lead to the formation of nitrene **4.11** which can undergo a variety of undesired side reactions. Reaction of nitrene **4.11** with the olefin can lead to aziridination giving bicyclic compound **4.12**. Nitrene **4.11** could also undergo C–H insertion into the aromatic C–H bond to form benzimidazolinone **4.13**. Nitrene **4.11** can also undergo C–H insertion into allylic C–H bond to form 1,3 benzodiazopine **4.14** with exocylic double bond, which could isomerise to the more conjugated 1,3 benzodiazopine **4.15**, with an endocyclic double bond. Due to the multitude of potential side reactions that could happen and the possibility of formation of number of by-products, developing reaction conditions for azidoacylation of alkenes *via* C–N bond activation may be an uphill task.




**Scheme 4.5**: Potential Reactions of Carbamoyl Azides

## 4.2 Substrate Synthesis and Initial Trails

Carbamoyl azide **4.1** was prepared in two steps from known aniline **4.16**[11] (Scheme 4.6). Aniline **4.16** was converted to carbamoyl chloride **4.17** using a by adopting procedure.[12] Treatment of carbamoyl chloride **4.17** with $NaN_3$ in the presence of 15-crown-5 gave desired carbamoyl azide **4.1** in 70% yield.




**4.16** **4.17** **4.1**

**Scheme 4.6**: Synthesis of Carbamoyl Azide

Having synthesized carbamoyl azide, the reaction was tested for azidoacylation using $Pd(PPh_3)_4$ in *m*-xylene at 130 $^oC$. $^1H$ NMR analysis of the crude reaction mixture indicated complete consumption of the starting material and a mixture of products were observed. Careful analysis of TLC and crude $^1H$ NMR indicated the presence of two major products along with traces of other by products. Attempts to isolate any of the major products by chromatography were unsuccessful. It was hypothesized that in addition to metal catalyzed reactions, a Staudinger reaction between azide and $PPh_3$ (generated from $Pd(Ph_3)_4$) might have led to complex reaction mixture. Then it was decided to test the reaction with palladium metal without phosphine ligands. The reaction was tested with PEPPSI-IPr®[13] under similar conditions used previously in *m*-xylene at 130 $^oC$. $^1H$ NMR analysis revealed the formation of one major product, whose signals were consistent with one of the major products observed in the reaction in the presence of $Pd(PPh_3)_4$. Gratifyingly enough pure product was successfully isolated and subjected to analysis.

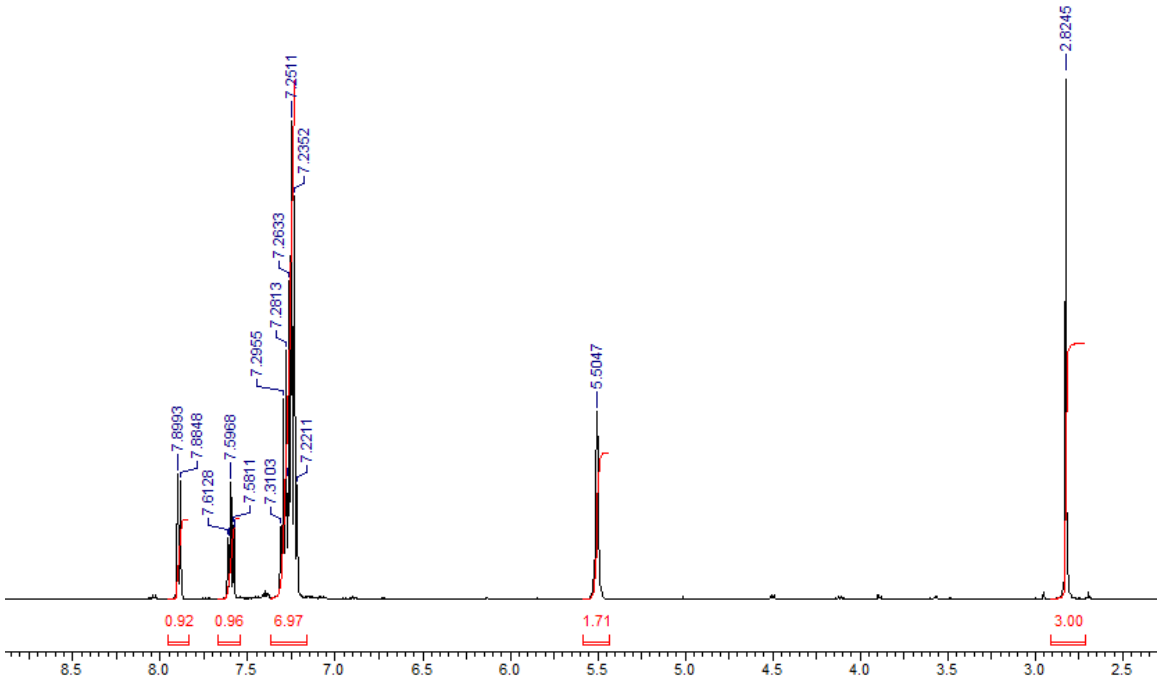
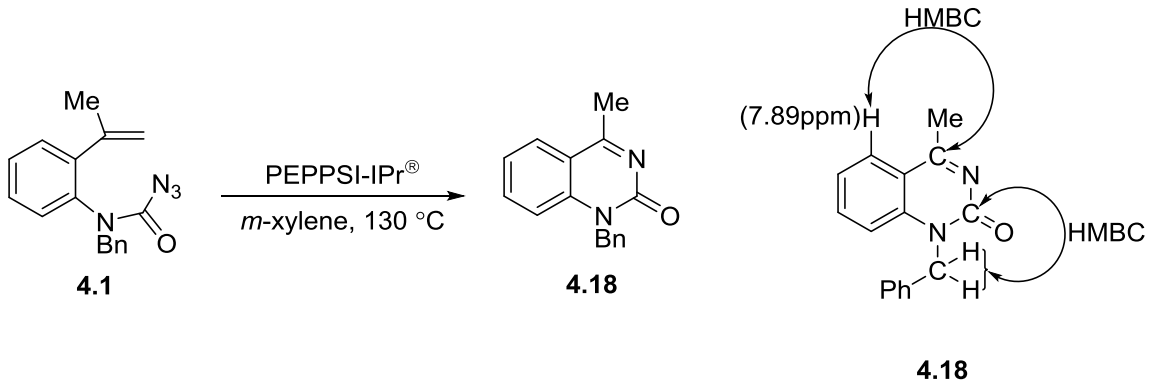



**Figure 4.1**: $^{1}$H NMR of the Product Isolated with PEPPSI-IPr® Reaction

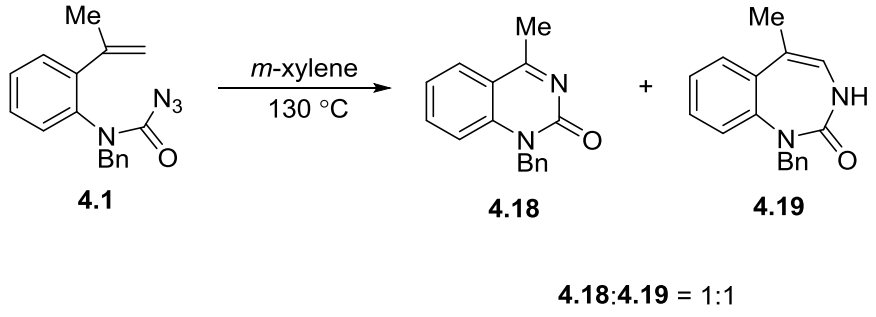
Analysis of $^{1}$H NMR data provided interesting observations (Figure 4.1). A singlet at was seen at 2.83 ppm with integration of three protons which is rather down field for a methyl group attached to normal double bond. The appearance of a singlet at 5.51 ppm with an integration of 2H suggested that the benzyl group was intact. Examination of the aromatic region showed a deshielded proton at 7.89 ppm suggesting the presence of an electron withdrawing group on the aromatic ring. Also, the total proton count, calculated by the integration of all the $^{1}$H NMR peaks was found to be two less than the starting material assuming no oligomerization. Inspection of the $^{13}$C NMR data revealed that the product has one less carbon compared to the starting material carbamoyl azide **4.1**. The

molecular weight of the product was found to be 42 less than the staring material indicating loss $CH_2$ and $N_2$ fragment consistent with the $^1H$ NMR and $^{13}C$ NMR data. Based on the above observations, the isolated product was assigned to be 2-quinazolinone **4.18** (Scheme 4.7). Further support of this structure was indicated by two important HMBC correlations. One was the correlation between the imine carbon and most deshielded proton of the aromatic proton at 7.89 ppm. The other was the correlation between carbonyl carbon and benzylic hydrogens. Other 2D NMR data, COSY and HMQC were also consistent with the structure. Formation of 2-quinazolinone from carbamoyl azides is an interesting reaction and has not been reported before to the best of our knowledge. The product formed has 1,3-dinitrogen functionality that can be converted to 1,3-diamines, which have significant importance in organic synthesis.




**Scheme 4.7**: Formation of 2-quinazolinone from Carbamoyl Azide

Interestingly when carbamoyl azide **4.1** was heated in *m*-xylene at 130 $^{o}$C in the absence of Pd catalyst a mixture of 2-quinazolinone **4.18** and 1,3-benzodiazepinone **4.19** were observed in equal ratio (Scheme 4.8). 1,3-benzodiazepinone **4.19** could possibly be formed by the insertion of nitrene into allylic C–H bond and subsequent isomerization as shown in Scheme 4.5. Hence PEPPSI-IPr® plays a critical role in dictating the chemoselectivity of the reaction.




**Scheme 4.8**: Thermolysis of Carbamoyl Azide

## 4.3 Conclusion and Future work

Formation of 2-quinazolinone **4.18** from carbamoyl azide **4.1** in the presence of PEPPSI-IPr® appears to be an interesting transformation. The 2-quinazolinone (**4.18**) can be used as precursor to make 1,3-diamines which have enormous applications in organic chemistry. They act as ligands[14] and can also be used for the synthesis of *N*-heterocyclic carbenes[15] which in turn have myriad of utility in catalysis. The reaction requires further optimization to improve the

yield of 2-quinazolinone (**4.18**)**.** The reaction could be tested with other Pd catalysts, in the presence of various ligands. Temperature dependence and consequences of additives like Lewis acids[16] and Lewis bases[17] which had improved yields in transition metal catalyzed reactions can also be explored. We suspect that during the formation of 2-quinazolinone (**4.18**) diazomethane ($CH_2N_2$) is being formed as the by product. Experiments to trap diazomethane could to be performed to ascertain its formation and experiments could be designed to study this intriguing reaction. As PEPPSI-IPr® plays important role avoiding the formation of 1,3-benzodiazepinone **4.19**, studying its role in the reaction should prove advantageous.

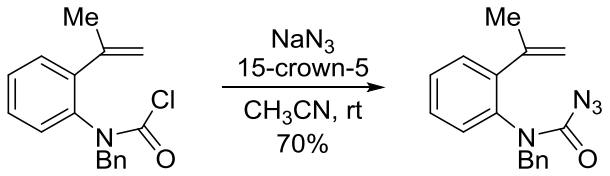
## 4.4 Experimental

**General Details:** All air and water sensitive reactions were carried out using flame-dried glassware under $N_2$ inert atmosphere. Reaction vials purchased from Chemglass Inc. were used for all transition metal catalyzed reactions. Reactions using air sensitive catalysts were prepared and sealed in reaction vial in glove box. $Pd(PPh_3)_4$ was purchased from Pressure Chemical Co. All other chemicals were purchased from AK Scientific, Acros Organics, or Sigma-Aldrich and used as received.

Analytical thin layer chromatography (TLC) was performed using 0.25 mm silica plates from E. Merck. TLC plates were visualized with UV light and

standard stains if necessary. Flash chromatography was performed using 230-400 mesh (particle size (0.04-0.063 mm) silica gel from Merck. $^{1}H$ NMR (300 MHz) were obtained using Varian FT NMR instruments. $^{13}C$ NMR and 2D NMR were carried out on Varian FT (300 or 500 MHz) or Bruker (500 MHz) instruments. NMR spectra were reported as $\delta$ values in ppm relative to TMS or $CHCl_3$. $^{1}H$ NMR are reported in Hz. Coupling information was indicated in the manner that follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); ddd (doublet of doublet of doublets); dq (doublet of quartets); br (broad). Infrared (IR) spectra were obtained as films from $CH_2Cl_2$ with a Thermo Scientific FTIR instrument. Low-resolution mass spectra (LRMS) CI experiments were performed on a Varian Saturn 2200 GC-MS system and ESI experiments were performed on a Bruker BioTOF II.

**Synthesis of Carbamoyl Azide**:



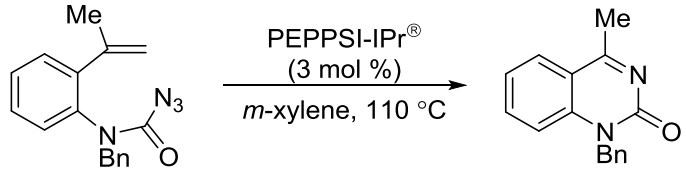

**4.17** **4.1**

**Scheme 4.9**: Synthesis of Carbamoyl Azide **4.1**

Carbamoyl chloride **4.17** (1.59g, 5.60 mmol) was dissolved in anhydrous acetonitrile (32 mL) from still in round bottom flask. $NaN_3$ (0.54g, 8.30 mmol) was

added to the solution. 15-crown-5 (2.45 g, 11.1 mmol) was then added to the reaction mixture. The reaction was stirred at room temperature overnight. The solution was concentrated *in vacuo*. EtOAc (25 ml) and $H_2O$ (25 ml) were added. The aqueous layer was extracted two times with EtOAc (25 ml) and the organic layers were then combined at concentrated *in vacuo*. The crude mixture was purified by flash silica gel column chromatography (gradient 0-5% EtOAc:hexanes) and a viscous oil was obtained (1.14 g, 3.92 mmol, 70%). The oil was stored at -20 °C and after one week solidified to beige solid. The solid was then recrystallized from MeOH/$H_2O$. $R_f$ = 0.71 (1:9 EtOAc:hexanes) $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 7.09-7.31 (m, 8H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.39 (d, 14.5 Hz, 1H), 5.27(dq, *J* = 1.5, 1.5 Hz, 1H), 5.04 (dq, *J* = 1.5,0.7 Hz, 1H), 4.05 (d, *J* = 14.5 Hz, 1H), 2.10 (dd, *J* = 1.5, 0.7 Hz, 3H) $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 157.0, 142.9, 141.2 137.2, 136.4, 130.1, 129.7, 129.0, 128.5, 127.8, 127.6, 116.8, 53.7, 23.3; IR (thin film) 3064, 2974, 2155, 1686, 1598, 1490, 1447, 1383, 1229, 1080, 998, 906, 741, 700 cm$^{-1}$ LRMS (CI) calculated for $[C_{17}H_{16}N_2O + H]^+$, m/z 265, found 265; calculated for $[C_{16}H_{16}N + H]^+$, m/z 223, found 223.

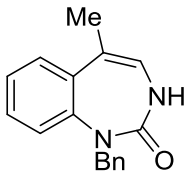
**Synthesis of 2-quinazolinone:**




**4.1** **4.18**

**Scheme 4.10**: Synthesis of 2-quinazolinone

PEPPSI$^{TM}$-IPr (0.0018g, 0.0027 mmol) was added to a reaction vial. Carbamoyl azide **2** (0.025 g, 0.086 mmol) was massed in the vial. Toluene (0.85 ml) was added to the reaction vial and the vial was then sealed. The vial was place in a preheated heating block at 110 ˚C. The reaction mixture stirred overnight. The solution was then cooled to room temperature. A Celite® plug was prepared in a Pasteur pipette and the reaction mixture was eluted through it with use of excess toluene. The solution was then concentrated *in vacuo*. The crude mixture was purified by flash silica gel column chromatography (gradient 0-70 % EtOAc:hexanes) to reveal a red solid. (isolated yield not yet obtained currently). $R_f$ = 0.32 (7:3 EtOAc:hexanes) $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 7.89 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.60 (ddd, *J* = 8.5, 1.4, 0.6 Hz, 1H), 7.21-7.33 (m, 7H), 5.51 (s, 2H), 2.83 (s, 3H) $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 175.0, 155.5, 142.0, 135.5, 134.9, 128.6, 127.3, 127.1, 126.5, 122.2, 116.8, 114.7, 47.1, 22.8; IR (thin film) 3032, 1659, 1611, 1556, 1495,1453, 1317, 754, 716 cm$^{-1}$; LRMS (ESI) BioTOF II calcd for $[C_{16}H_{14}N_2O + Na]^+$, m/z 273, found 273.




**4.19**

The reaction mixtures from several thermolysis reactions of carbamoyl azide **4.1** were combined. This mixture of reactions was known by $^1$H NMR data to contain a high concentration of 1,3-benzodiazepinone **4.19**. The mixture was condensed

on to silica gel and was purified by flash silica gel column chromatography. (Eluted 3:7 EtOAc:hexanes) $R_f$ = 0.34 (3:7 EtOAc:hexanes) $^1$H NMR (300MHz, $CDCl_3$) $\delta$ 6.93-7.26 (m, 9H), 5.93 (b, 1H), 5.84 (s, 1H), 4.98 (s, 1H), 1.97 (d, 3H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 164.3,140.2, 138.0, 137.7, 132.4, 128.3, 127.8, 127.2, 127.1, 126.8, 124.7, 122.1, 110.7, 52.7, 23.0; IR (thin film) 3055, 2984, 1696, 1660, 1579, 1496, 1438, 1161, 701 cm$^{-1}$, LRMS (ESI) BioTOF II calculated for $[C_{17}H_{116}N_2O + H]^+$, m/z 265, found 265.

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# Chapter 5

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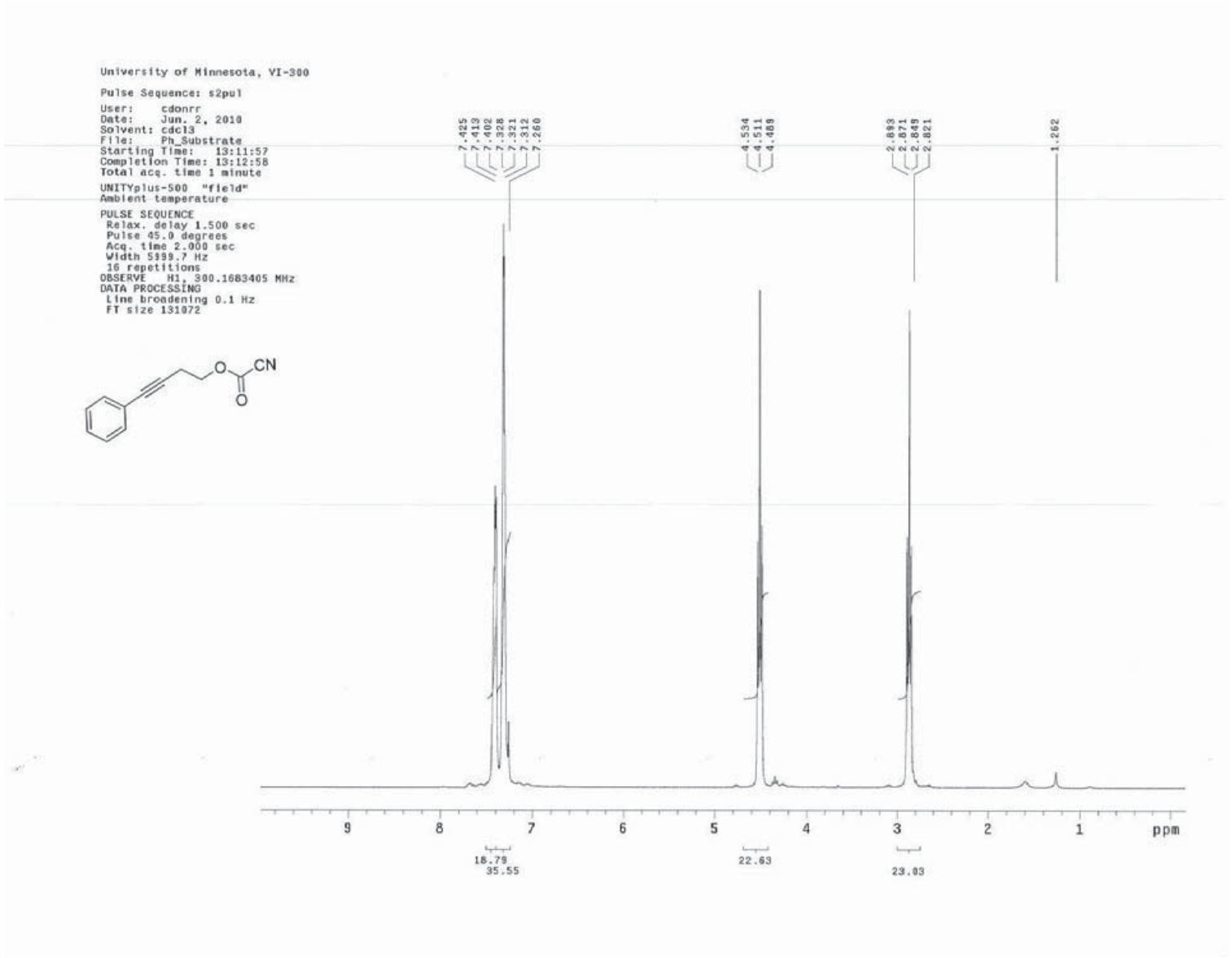
# Appendix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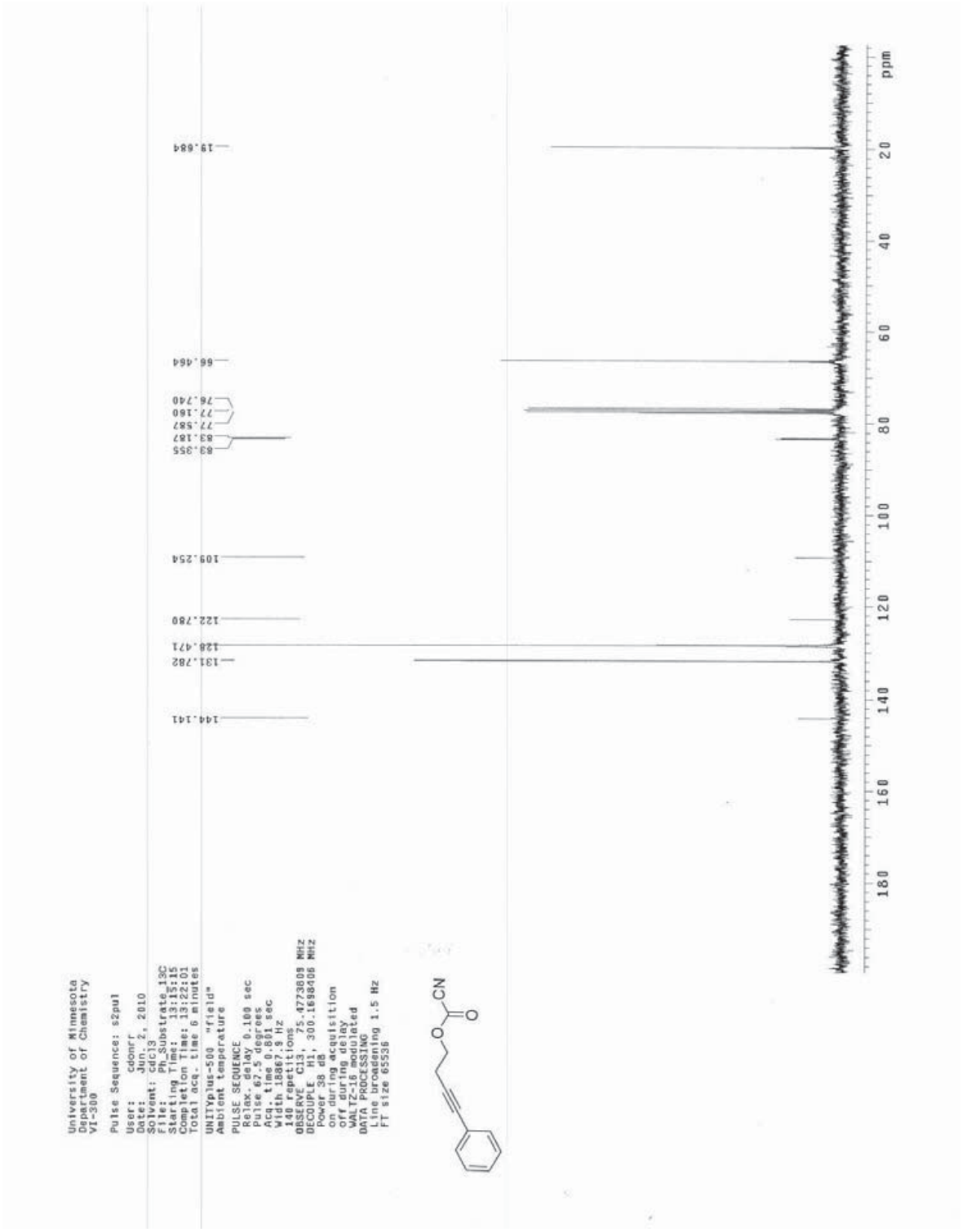
University of Minnesota
Department of Chemistry
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off during delay
WALTZ-16 modulated
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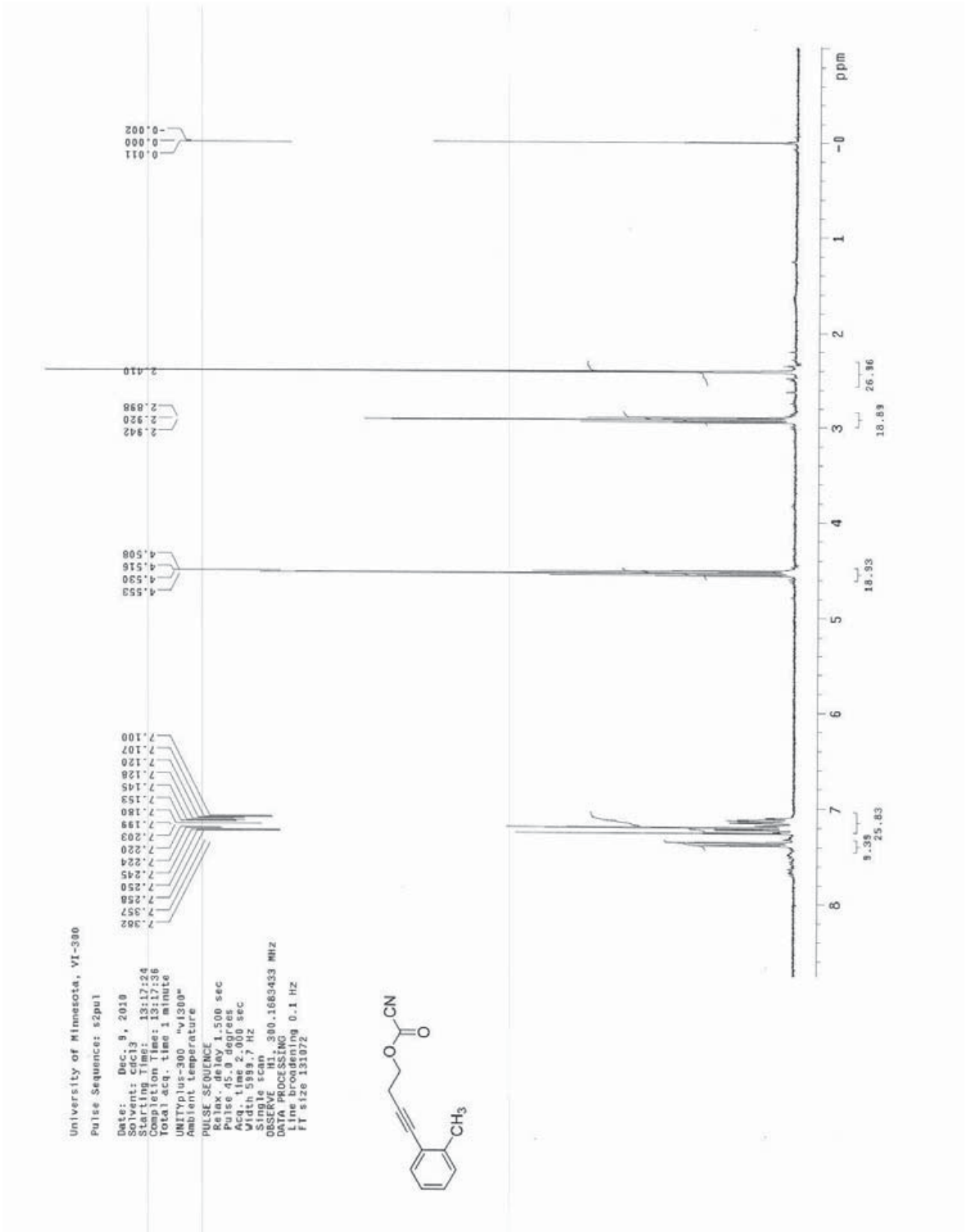
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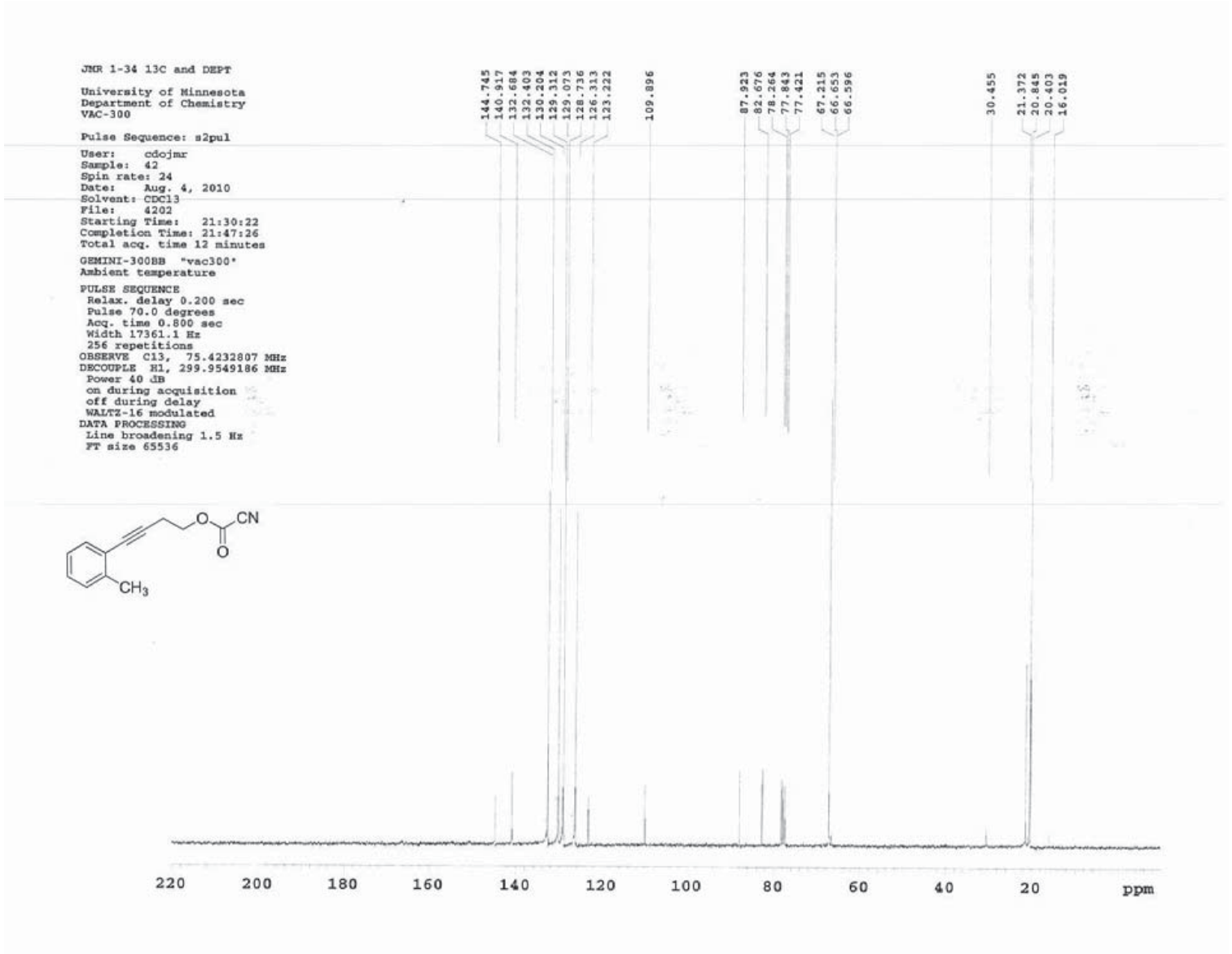
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Department of Chemistry
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DECOUPLE H1, 299.9549186 MHz
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on during acquisition
off during delay
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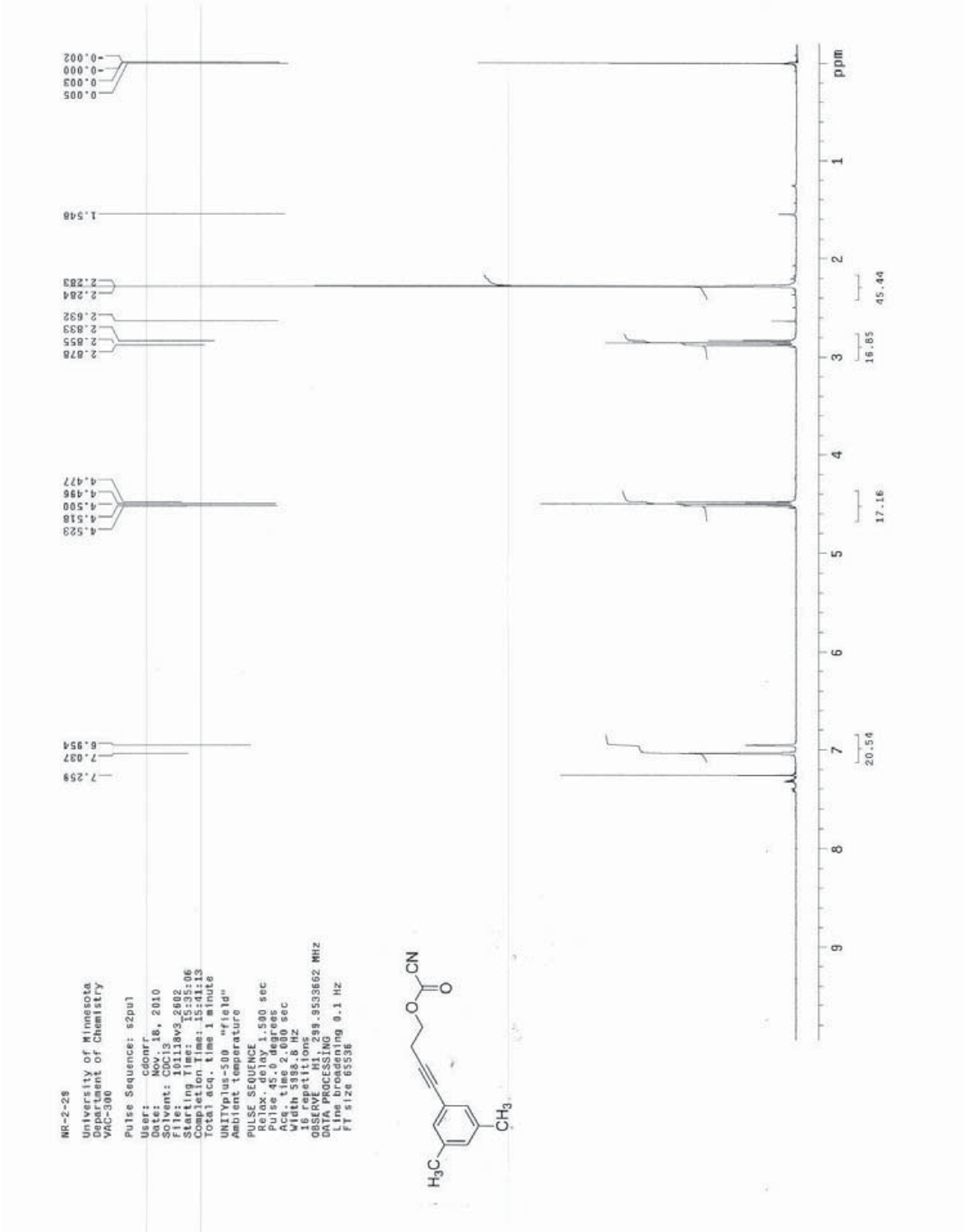
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University of Minnesota
Department of Chemistry
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University of Minnesota
Department of Chemistry
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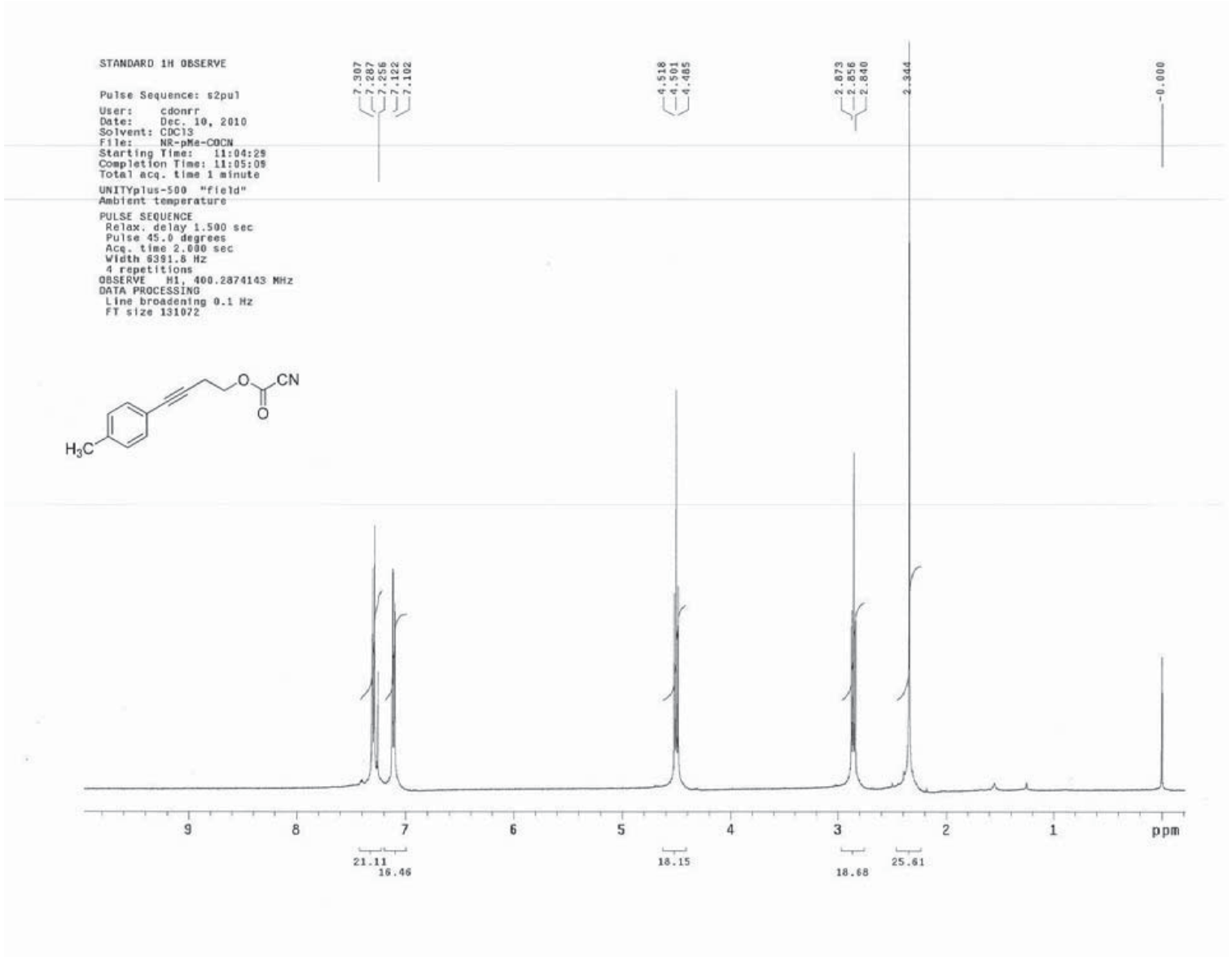
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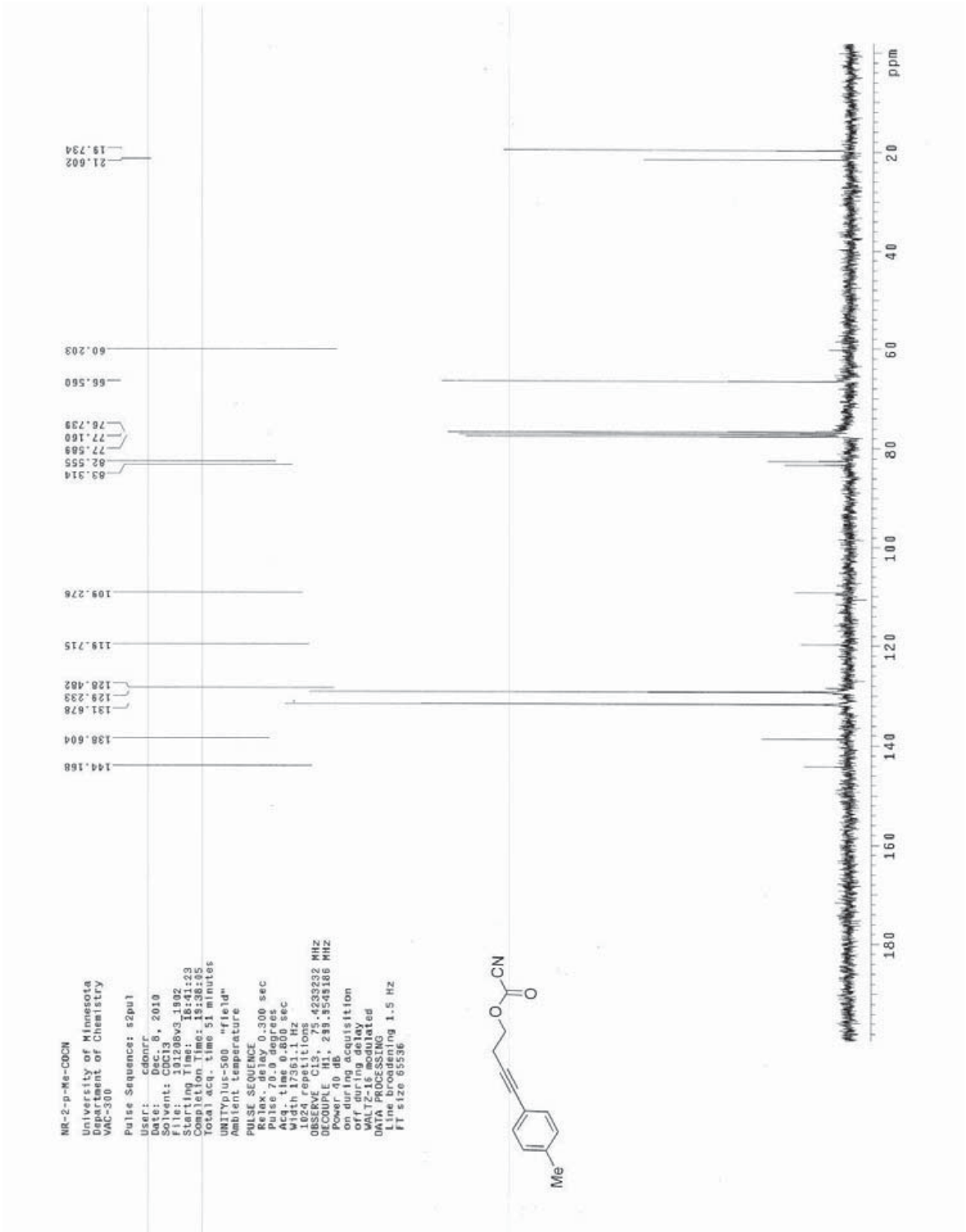
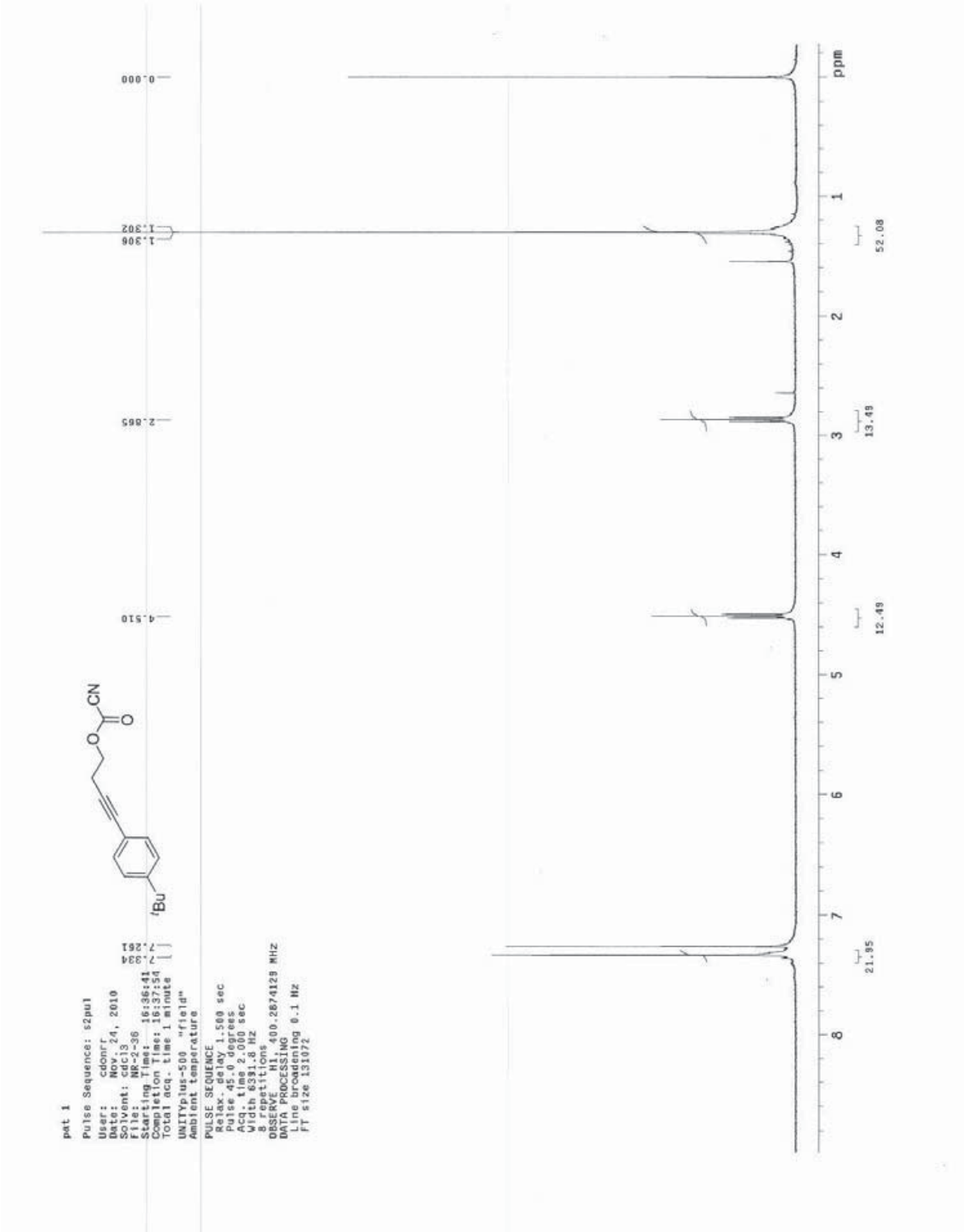
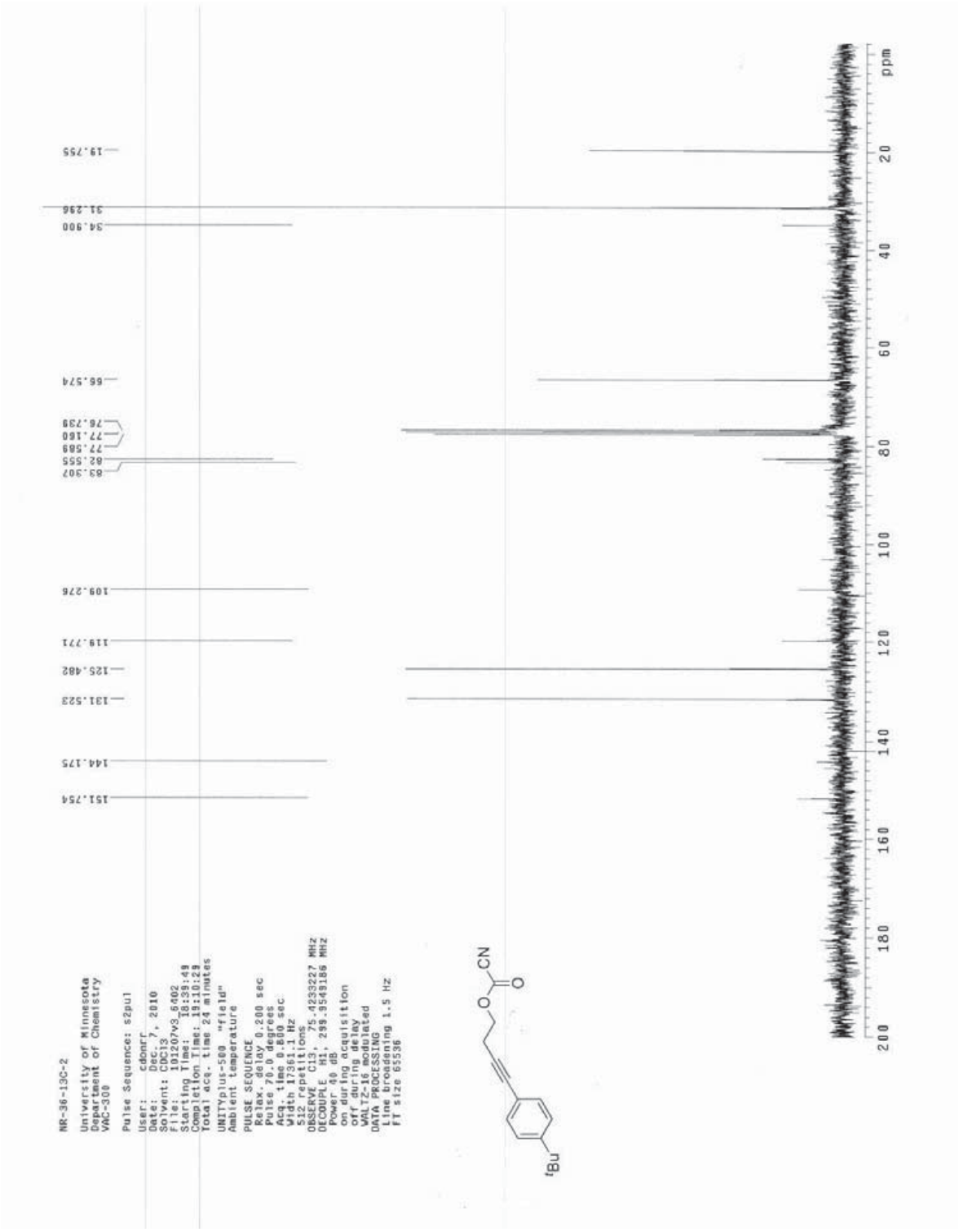
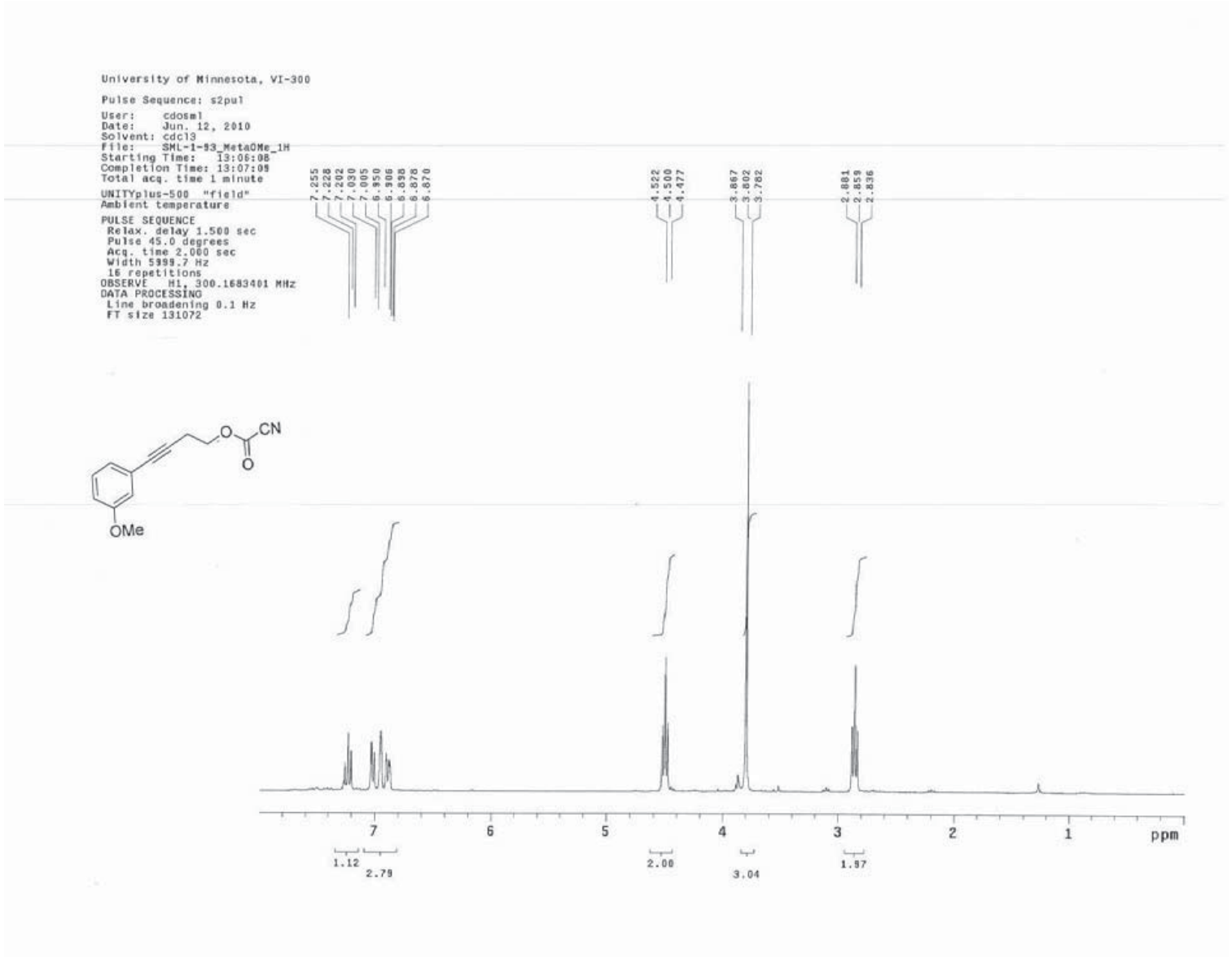
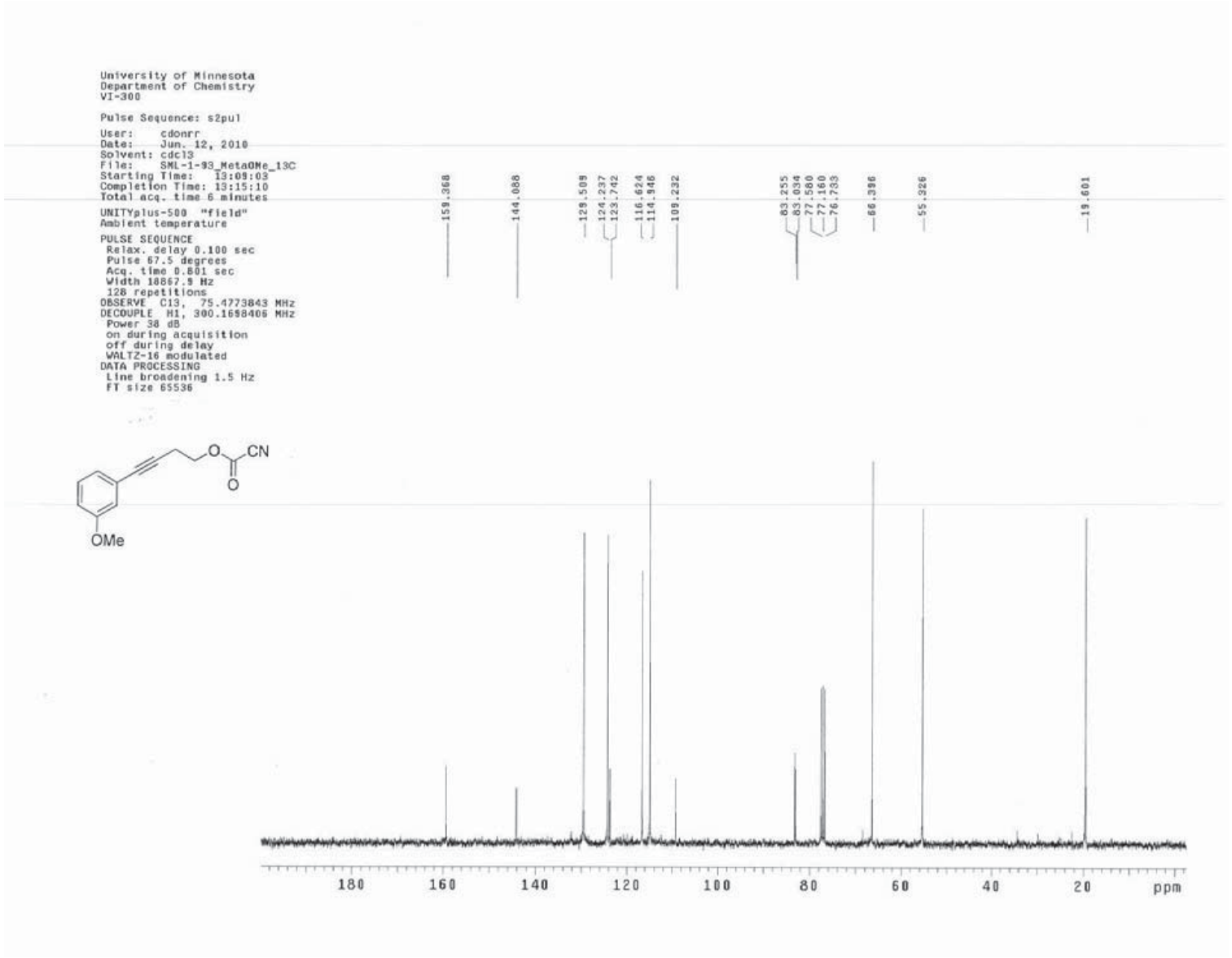
Solvent: CDCl3
File: NR-pMe-COCN
Starting Time: 11:04:29
Completion Time: 11:05:05
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 6391.8 Hz
4 repetitions
OBSERVE H1, 400.2874143 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.307
7.287
7.256
7.122
7.102
4.518
4.501
4.485
2.873
2.856
2.840
2.344
-0.000
O
CN
O
H3C
9
8
7
6
5
4
3
2
1
ppm
21.11
16.46
18.15
18.68
25.61

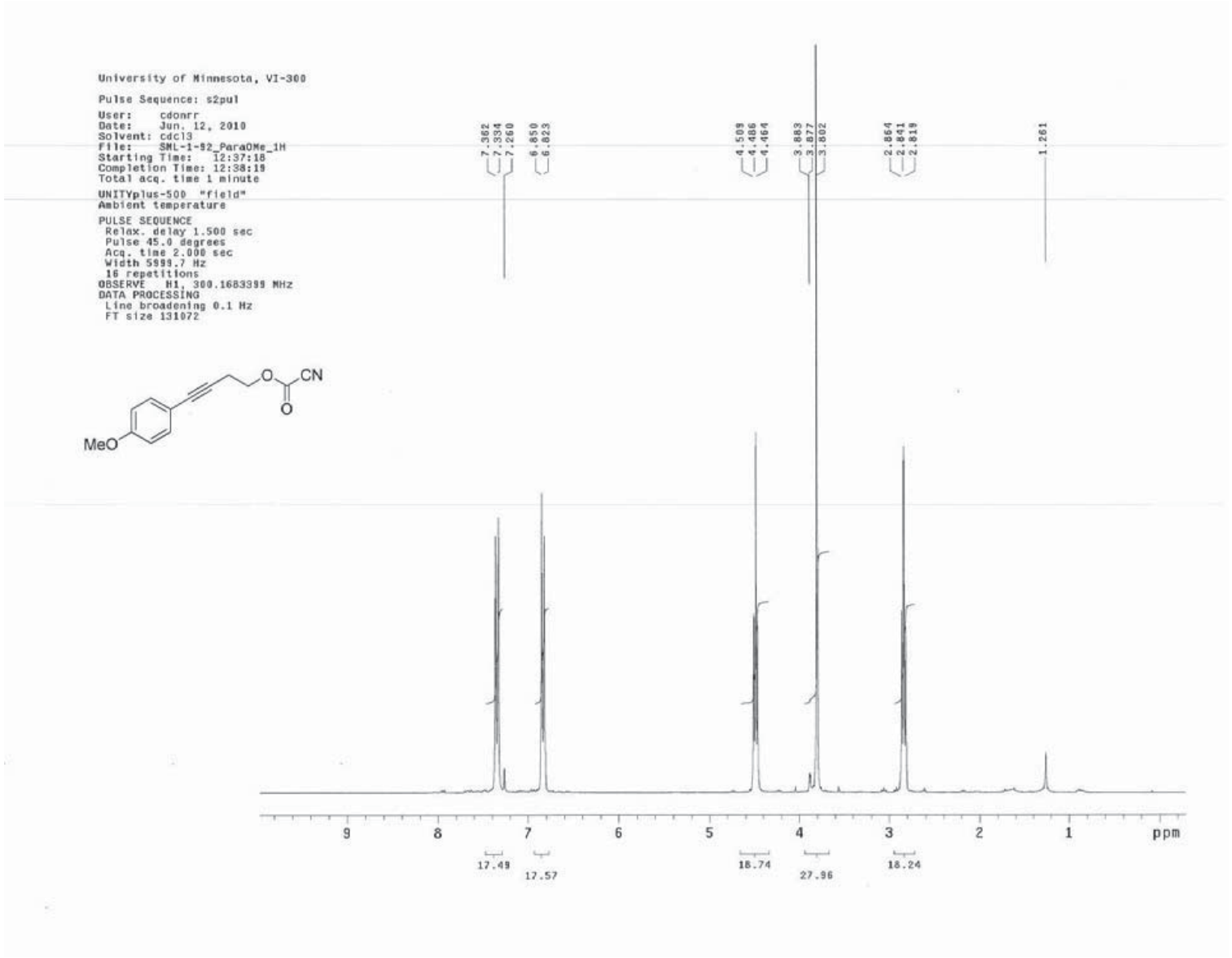

NR-2-p-Me-CDCN
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 8, 2010
Solvent: CDCl3
File: 101208v3_1802
Starting Time: 18:41:23
Completion Time: 19:36:05
Total acq. time 51 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
1024 repetitions
OBSERVE C13, 75.4233232 MHz
DECOUPLE H1, 299.9548186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
144.168
138.604
131.678
129.233
128.462
119.715
109.276
83.314
82.555
77.589
77.160
76.739
66.560
60.203
21.602
19.734
O
CN
O
Me
ppm

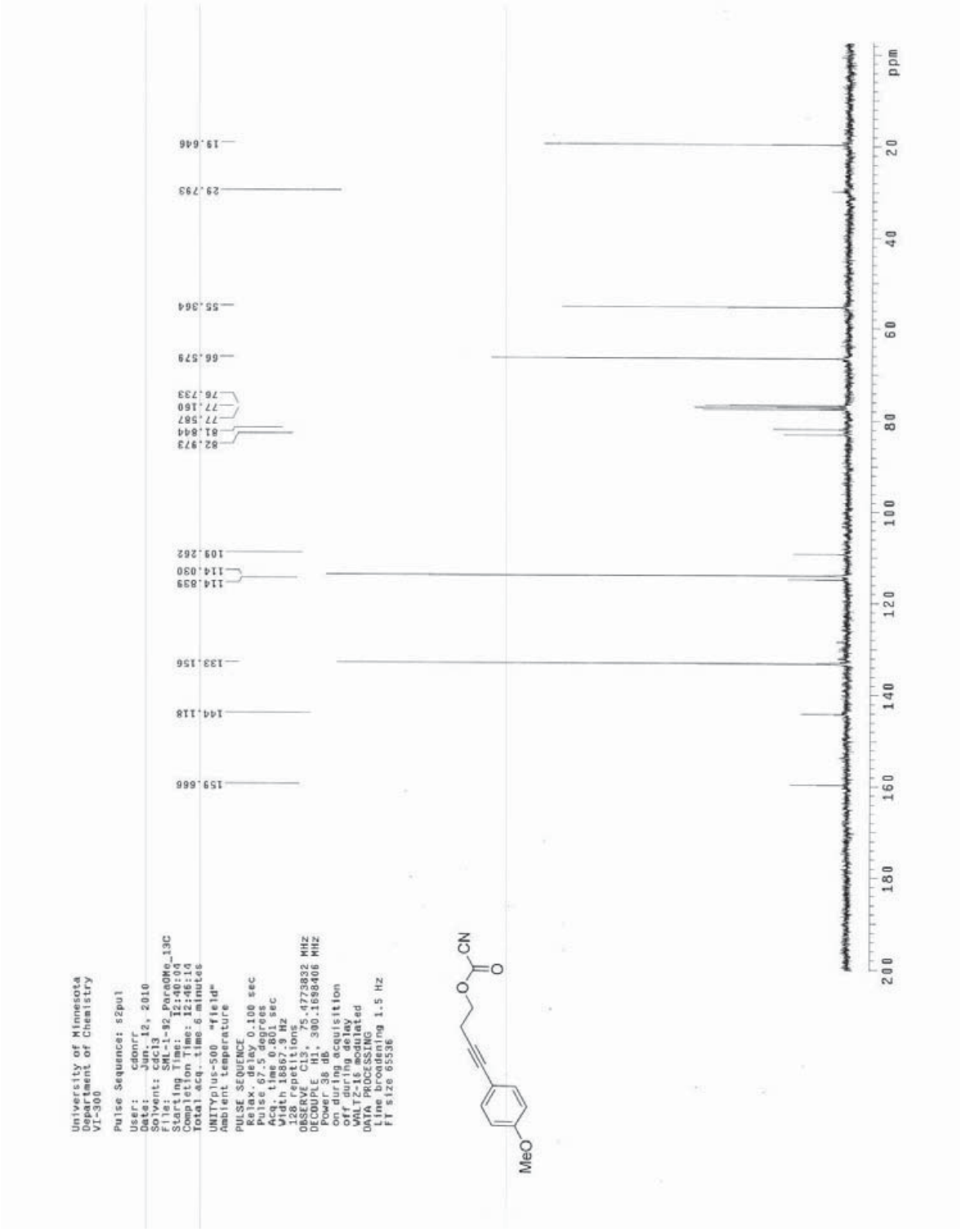

pat 1
Pulse Sequence: s2pul
User: cdonfr
Date: Nov. 24, 2010
Solvent: cdcl3
File: MA-2-36
Starting Time: 16:36:41
Completion Time: 16:37:54
Total acq. time 1 minute
UNITYplus-500 "rlela"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 6331.8 Hz
8 repetitions
OBSERVE H1, 400.2874129 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.384
7.261
4.510
2.865
1.306
1.302
0.000
tBu
O
CN
ppm
21.95
12.49
13.49
52.08

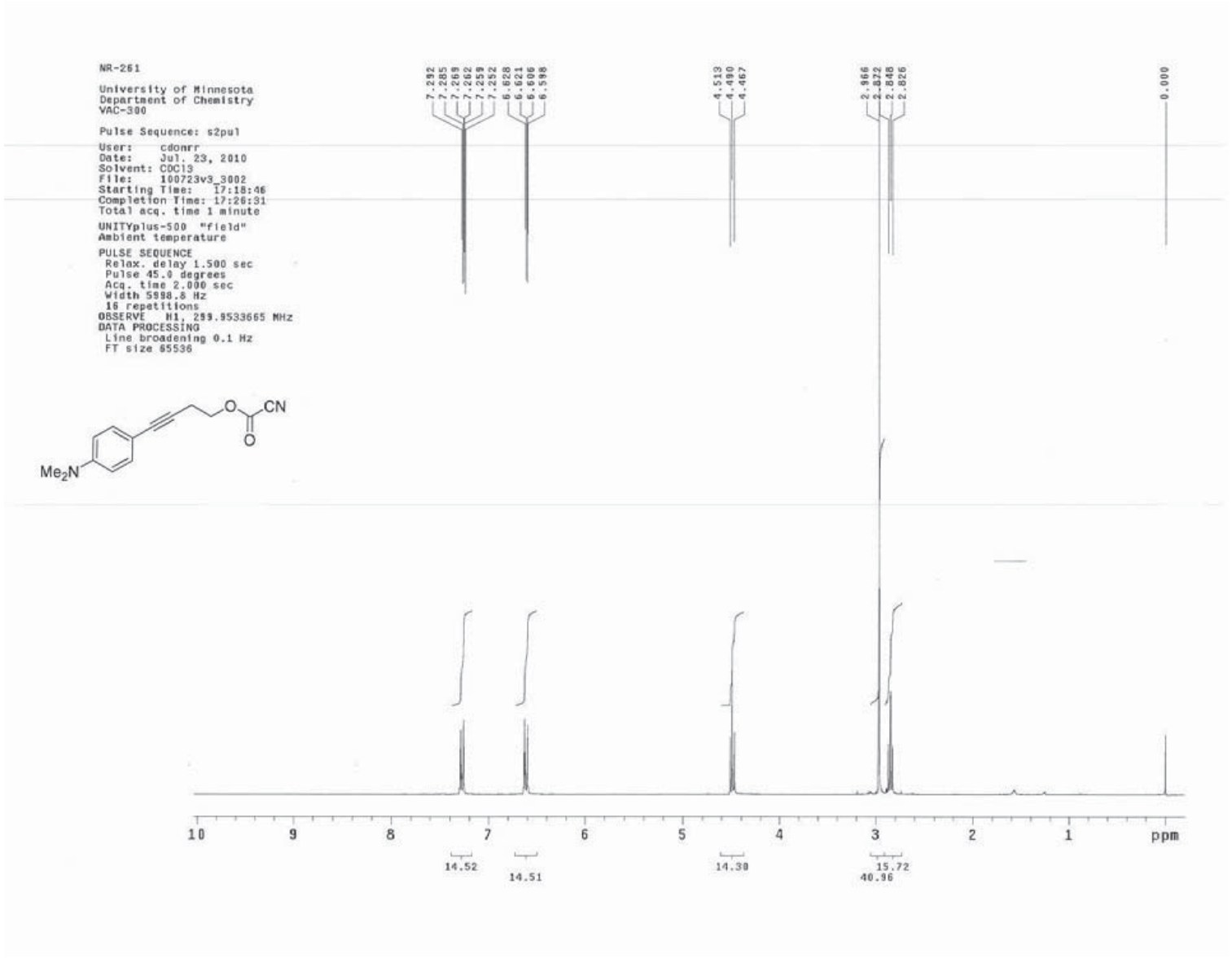

NR-36-13C-2
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 7, 2010
Solvent: CDCl3
File: 101207v3_6402
Starting Time: 18:39:49
Completion Time: 19:10:28
Total acq. time 24 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233227 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
19.755
31.296
34.900
66.574
76.738
77.160
77.589
82.555
83.307
109.276
119.771
125.482
131.523
144.175
151.754
CN
O
O
tBu
200
180
160
140
120
100
80
60
40
20
ppm

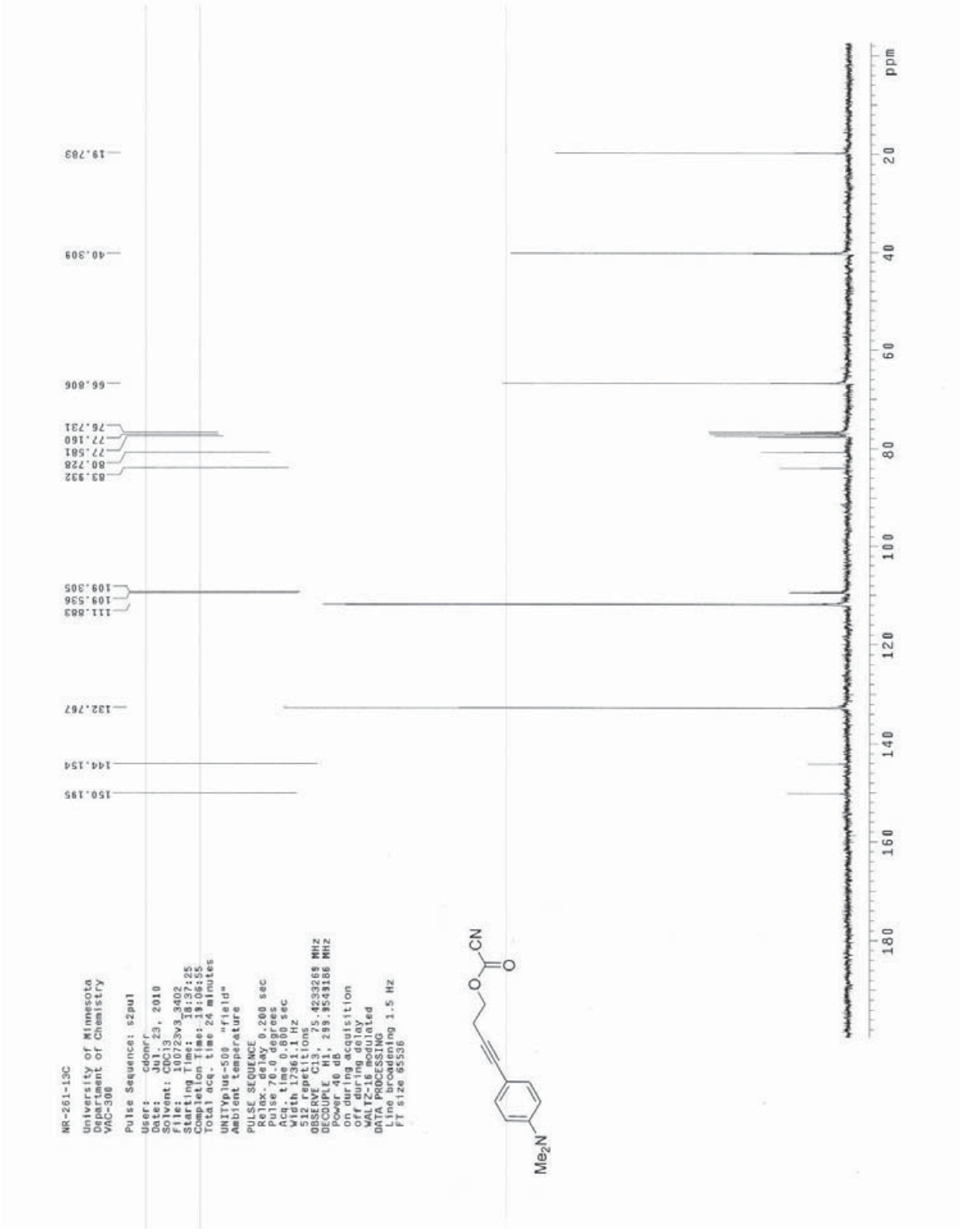

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdosml
Date: Jun. 12, 2010
Solvent: cdcl3
File: SML-1-93_MetaOMe_1H
Starting Time: 13:06:08
Completion Time: 13:07:09
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5999.7 Hz
16 repetitions
OBSERVE H1, 300.1683401 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.255
7.228
7.202
7.030
7.005
6.950
6.906
6.898
6.878
6.870
4.522
4.500
4.477
3.867
3.802
3.782
2.881
2.859
2.836
O
CN
O
OMe
7
6
5
4
3
2
1
ppm
1.12
2.79
2.00
3.04
1.97

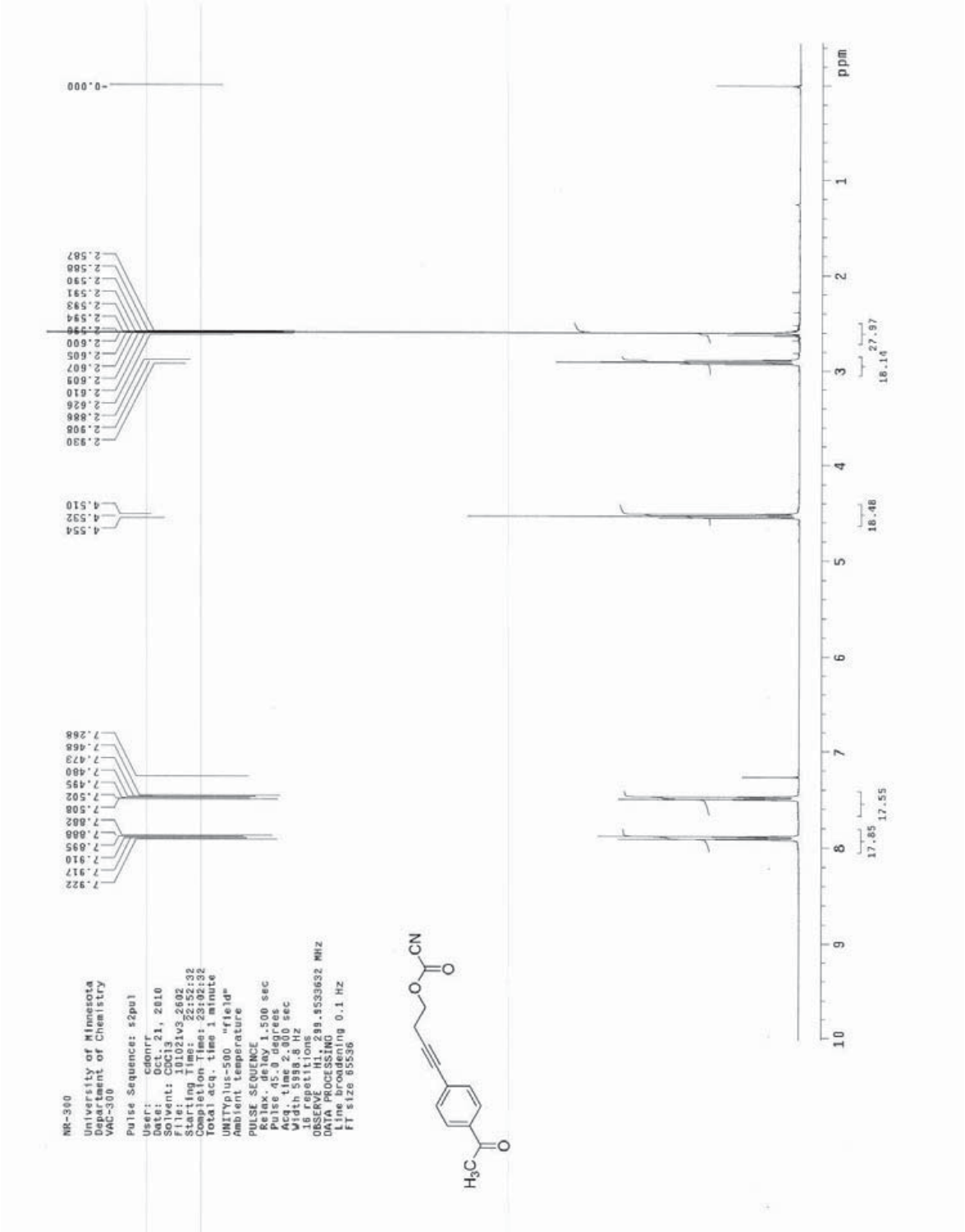

University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jun. 12, 2010
Solvent: cdcl3
File: SML-1-93_MetaOMe_13C
Starting Time: 13:09:03
Completion Time: 13:15:10
Total acq. time 6 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.801 sec
Width 18867.9 Hz
128 repetitions
OBSERVE C13, 75.4773843 MHz
DECOUPLE H1, 300.1658406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
159.368
144.088
129.509
124.237
123.742
116.624
114.946
109.232
83.255
83.034
77.580
77.160
76.733
66.396
55.326
19.601
O
CN
O
OMe
180
160
140
120
100
80
60
40
20
ppm

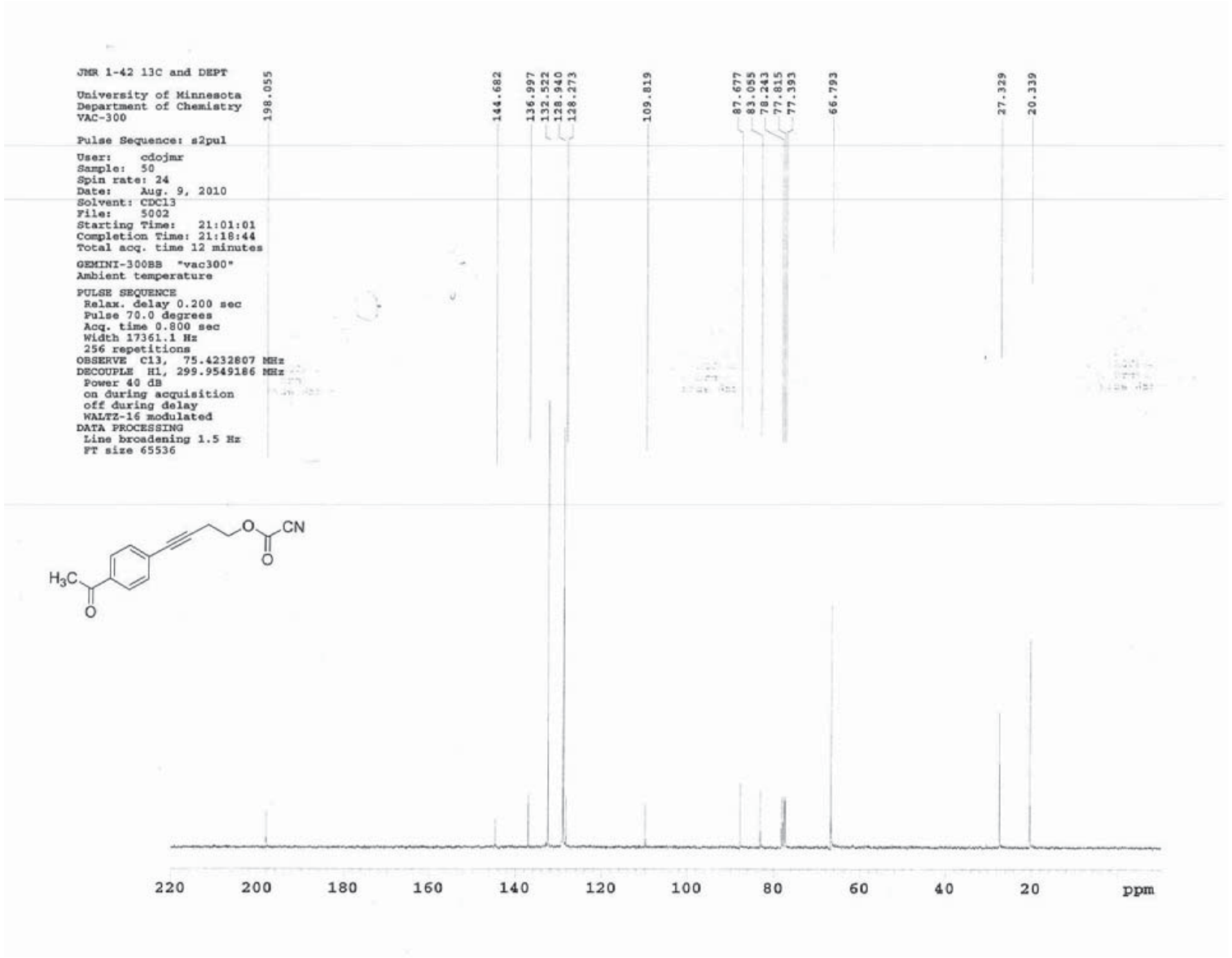

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jun. 12, 2010
Solvent: cdcl3
File: SML-1-92_ParaOMe_1H
Starting Time: 12:37:18
Completion Time: 12:38:19
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5999.7 Hz
16 repetitions
OBSERVE H1, 300.1683999 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.362
7.334
7.260
6.850
6.823
4.509
4.486
4.464
3.883
3.877
3.802
2.864
2.841
2.819
1.261
MeO
O
O
CN
9
8
7
6
5
4
3
2
1
ppm
17.49
12.57
18.74
27.96
18.24

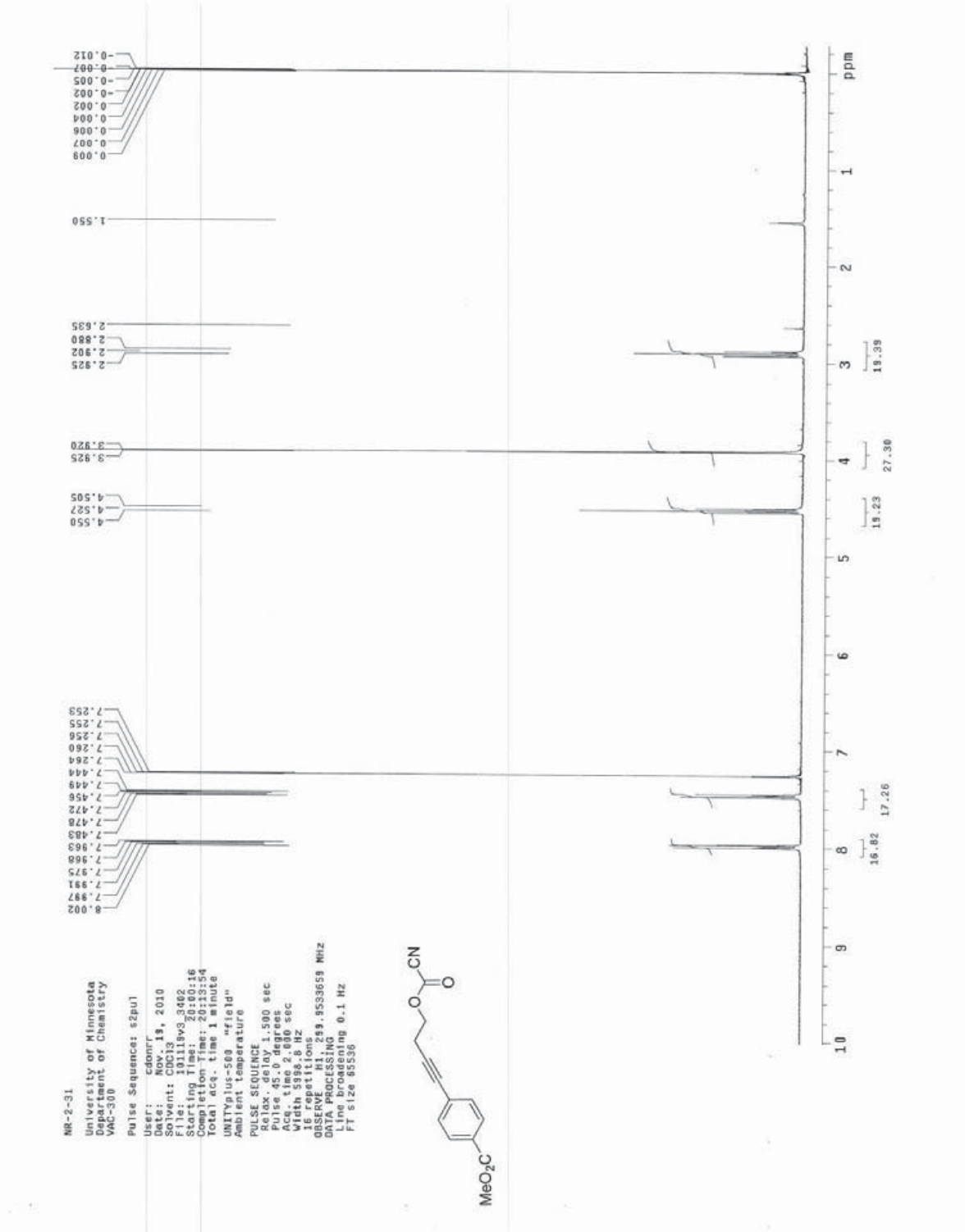

University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: June 12, 2010
Solvent: cdcl3
File: SML-1-92_ParaOMe_13C
Starting Time: 12:40:05
Completion Time: 12:46:14
Total acq. time 6 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.801 sec
Width 18871.3 Hz
128 repetitions
OBSERVE C13, 75.4773832 MHz
DECOUPLE H1, 300.1698406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
159.666
144.118
133.156
114.839
114.030
109.262
82.973
81.844
77.587
77.160
76.733
66.579
55.364
29.793
19.646
MeO
O
O
CN
200
180
160
140
120
100
80
60
40
20
ppm

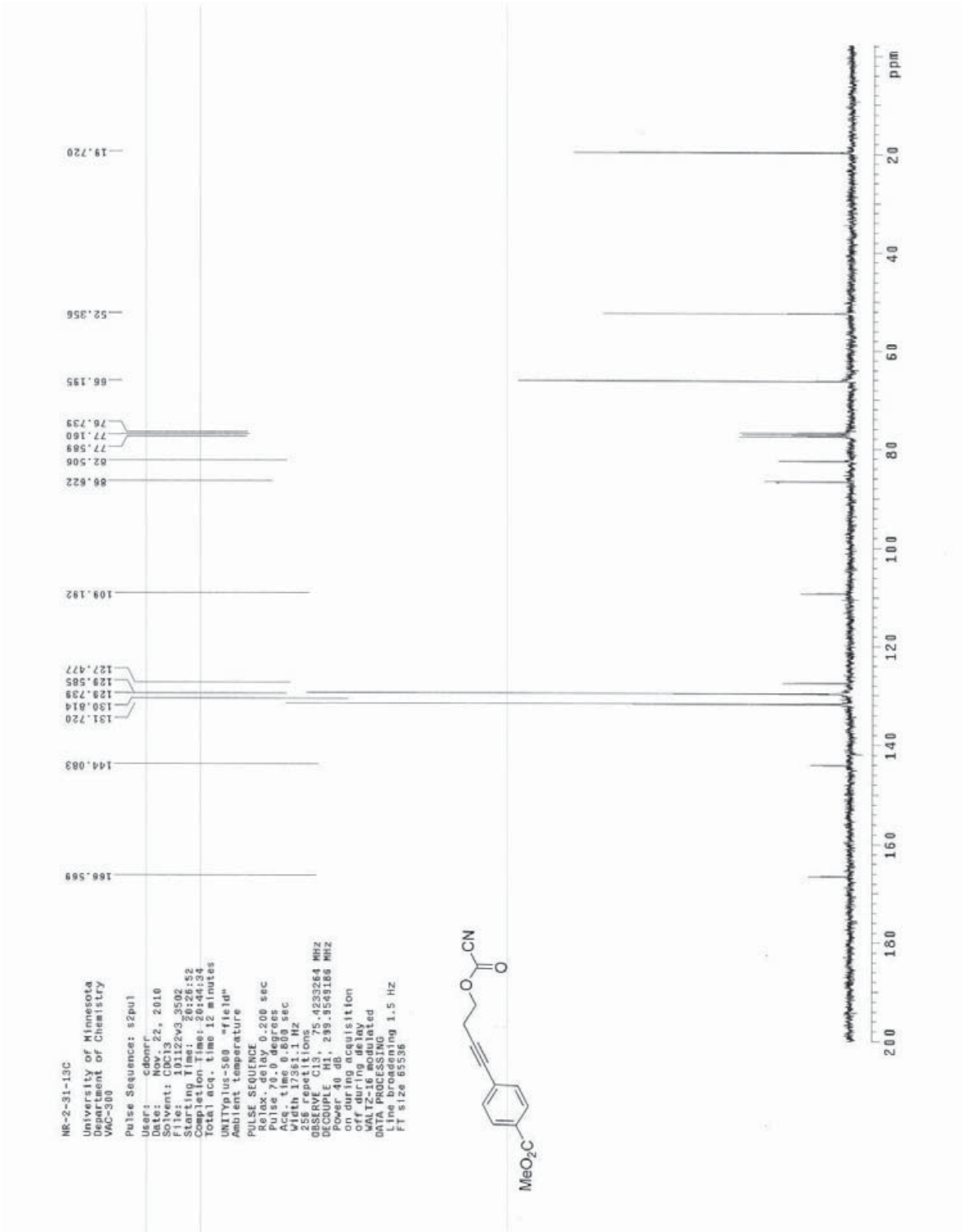

NR-261
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jul. 23, 2010
Solvent: CDCl3
File: 100723v3_3002
Starting Time: 17:18:46
Completion Time: 17:26:31
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533665 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.292
7.285
7.269
7.262
7.259
7.252
6.628
6.621
6.606
6.598
4.513
4.490
4.467
2.966
2.872
2.848
2.826
0.000
Me2N
O
CN
O
10
9
8
7
6
5
4
3
2
1
ppm
14.52
14.51
14.30
15.72
40.96

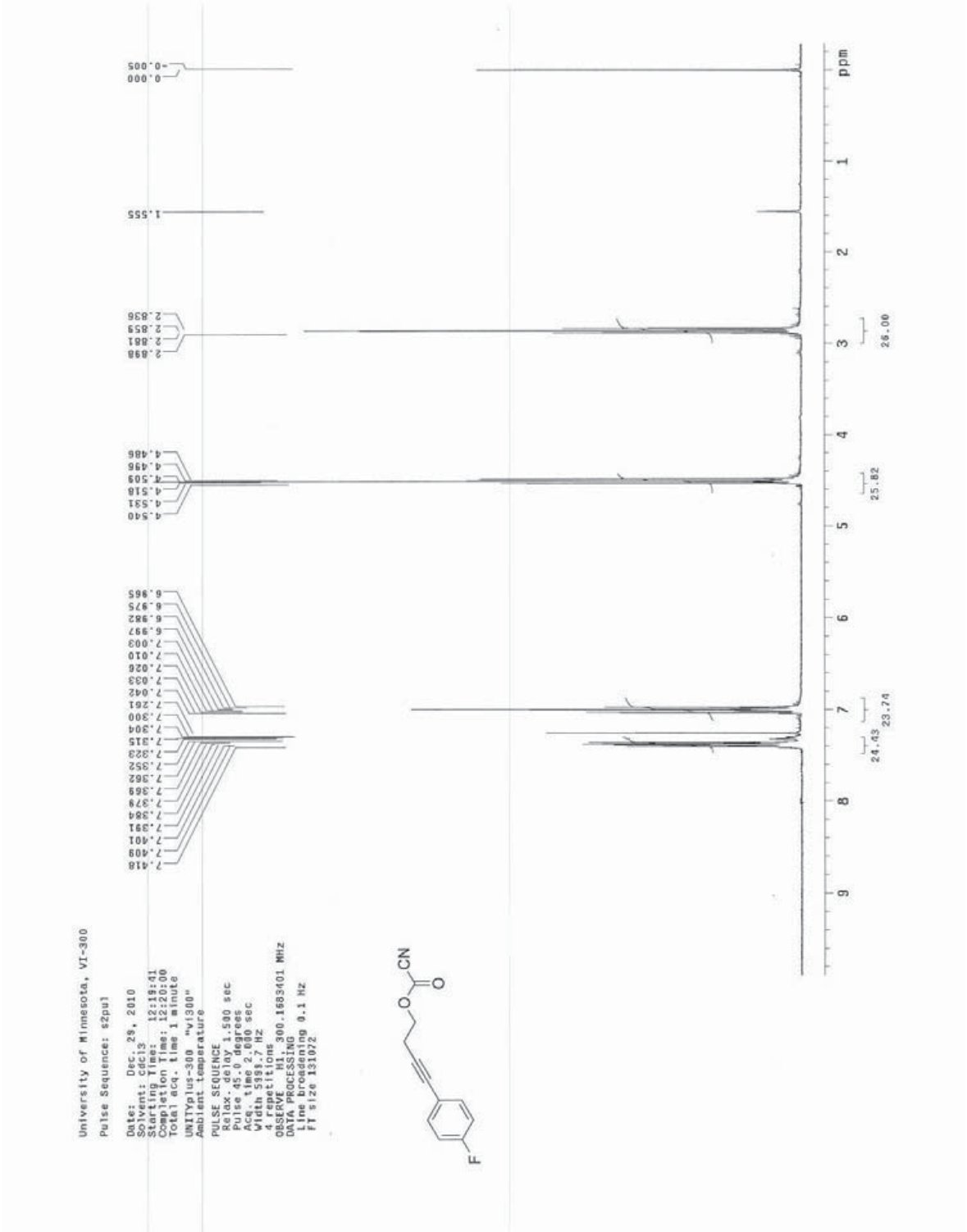

NR-261-13C
University of Minnesota
Department of Chemistry
VNC-300
Pulse Sequence: s2pul
User: cdonr
Date: Jul 23, 2010
Solvent: CDCl3
File: 100723v3_3402
Starting Time: 18:37:25
Completion Time: 19:06:55
Total acq. time 24 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 29411.1 Hz
512 repetitions
OBSERVE C13, 75.4233265 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
19.783
40.309
66.806
76.731
77.160
77.581
80.728
83.932
109.305
109.596
111.883
132.767
144.154
150.195
O
CN
O
Me2N
180
160
140
120
100
80
60
40
20
ppm

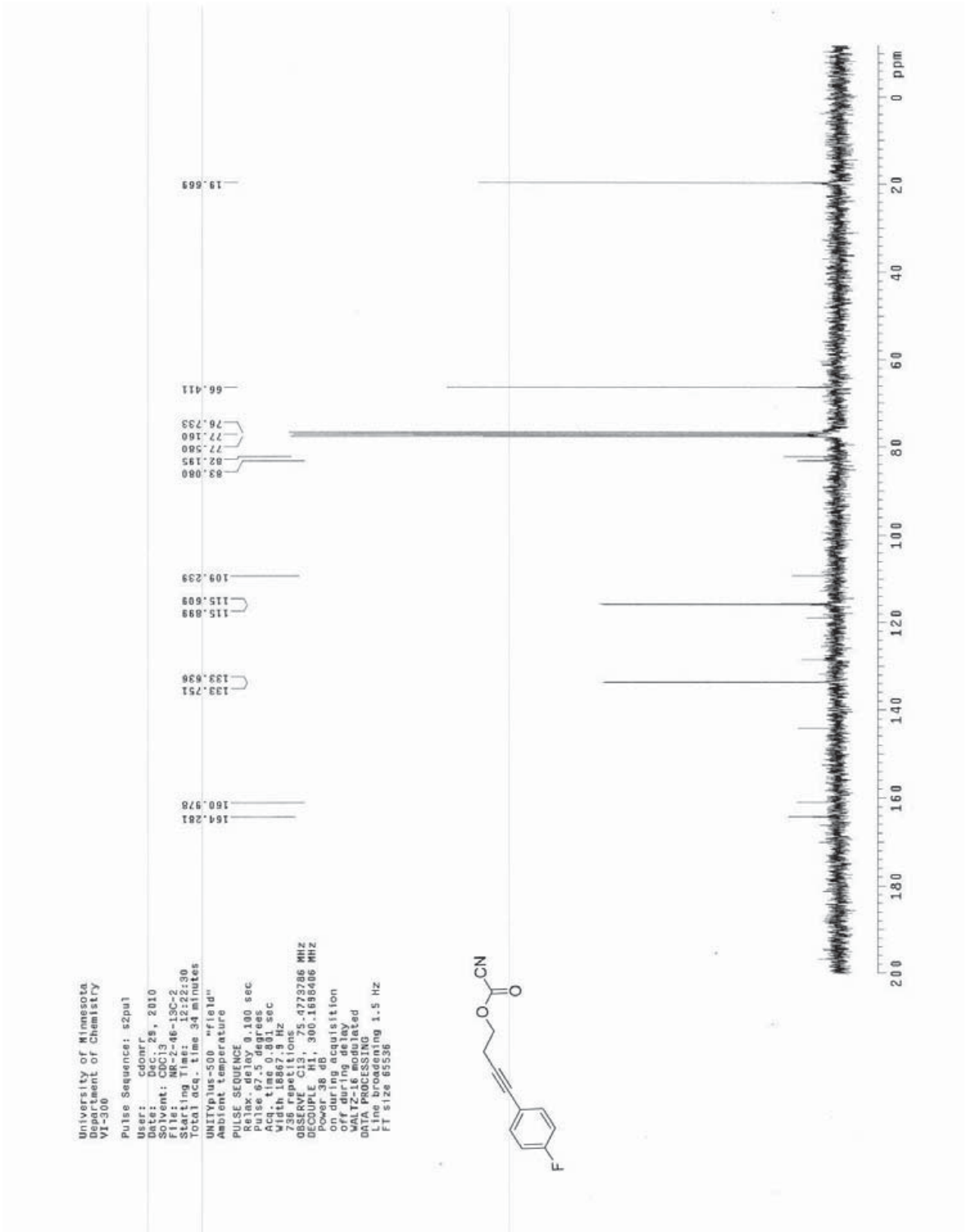

NR-300
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Oct 21, 2010
Solvent: CDCl3
File: 10102lv3.2602
Starting Time: 22:52:32
Completion Time: 23:02:32
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
1 repetitions
OBSERVE H1, 299.8533632 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.922
7.917
7.910
7.695
7.686
7.682
7.508
7.502
7.495
7.480
7.473
7.468
7.288
4.554
4.532
4.510
2.930
2.908
2.886
2.626
2.610
2.609
2.607
2.605
2.600
2.598
2.594
2.593
2.591
2.590
2.588
2.587
0.000
17.85
17.55
18.48
18.14
27.97
ppm
O
O
CN
O
H3C
O

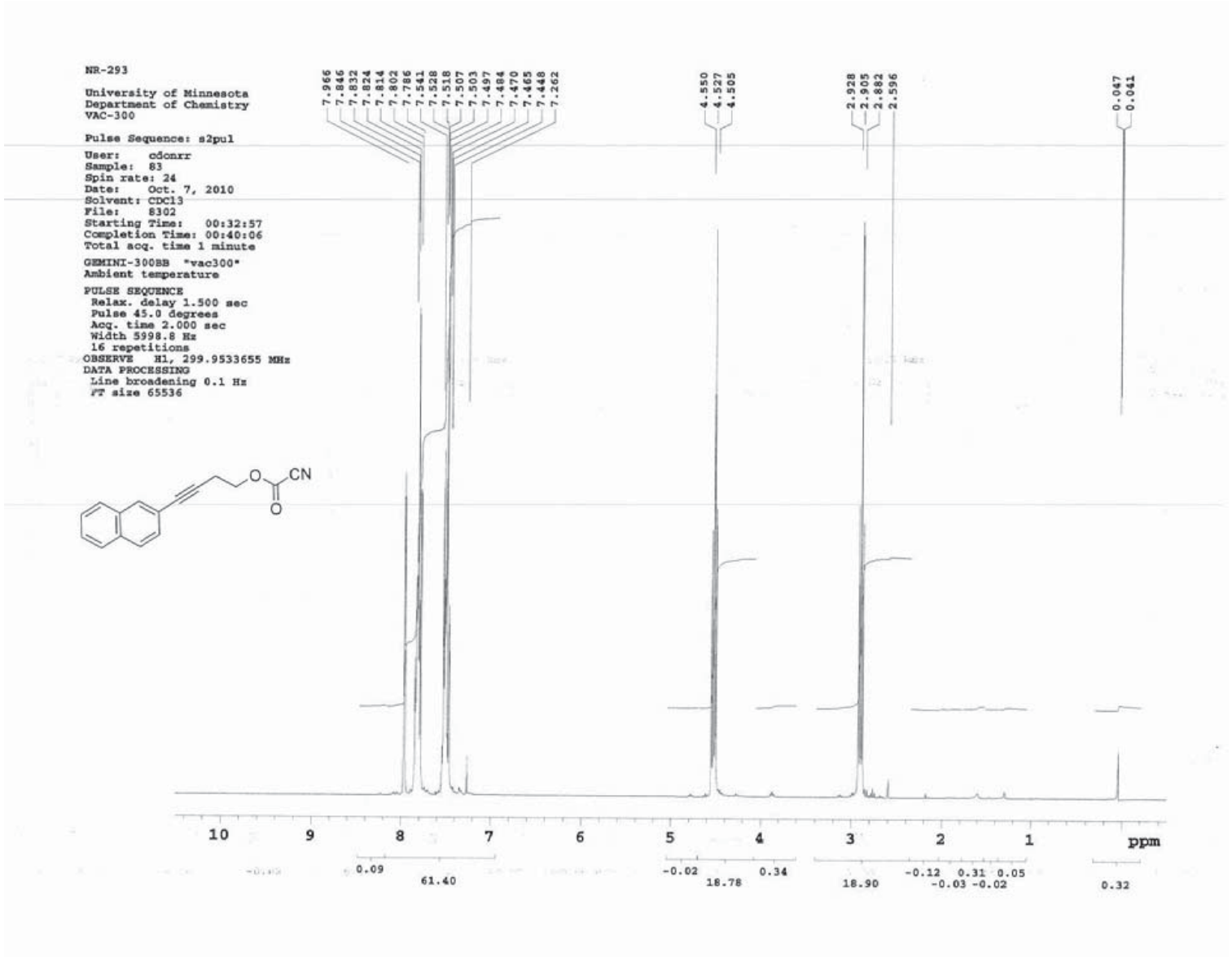

JMR 1-42 13C and DEPT
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdojmr
Sample: 50
Spin rate: 24
Date: Aug. 9, 2010
Solvent: CDCl3
File: 5002
Starting Time: 21:01:01
Completion Time: 21:18:44
Total acq. time 12 minutes
GEMINI-300BB "vac300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
256 repetitions
OBSERVE C13, 75.4232807 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
198.055
144.682
136.997
132.522
128.940
128.273
109.819
87.677
83.055
78.243
77.815
77.393
66.793
27.329
20.339
H3C
O
O
O
CN
220
200
180
160
140
120
100
80
60
40
20
ppm

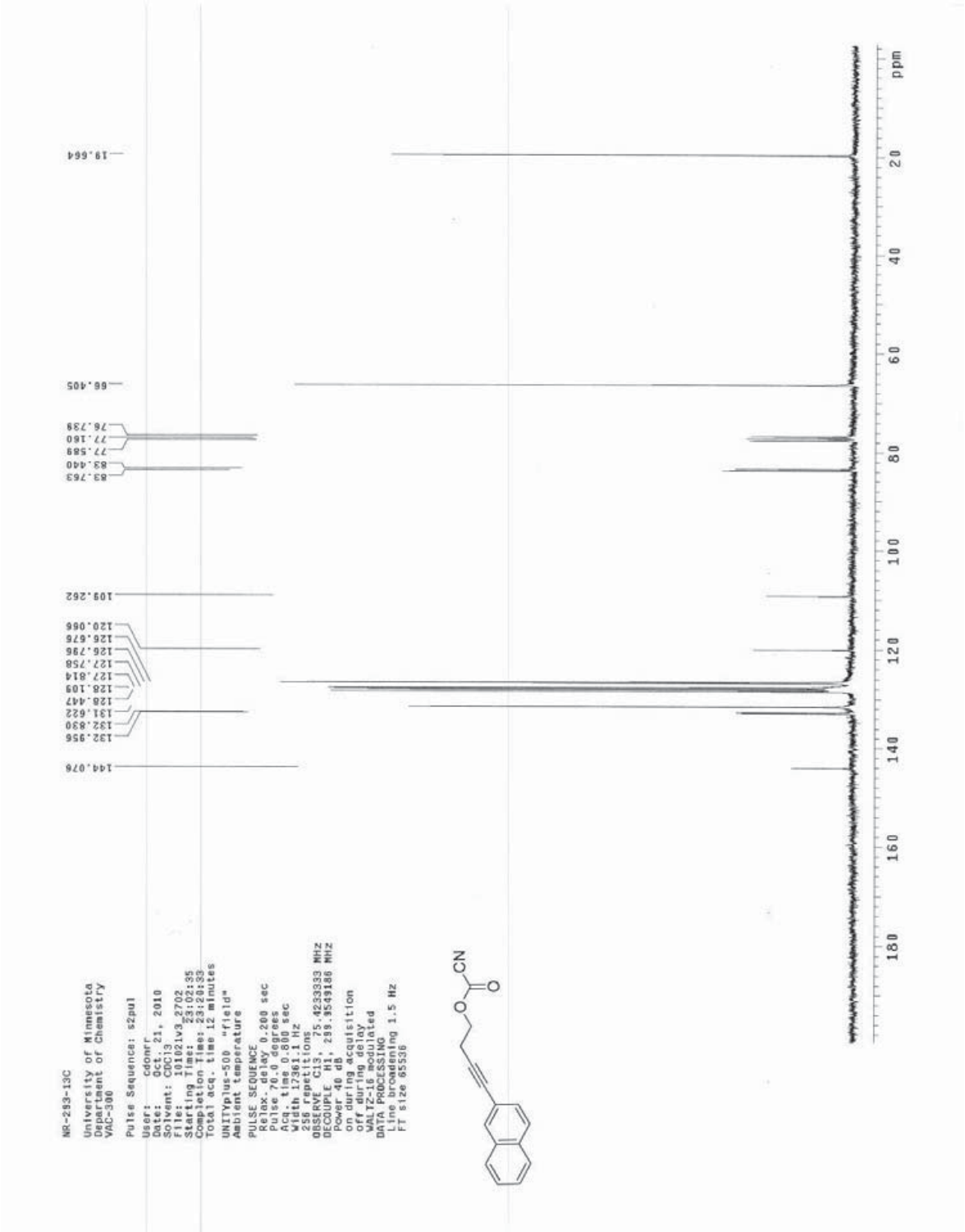

NR-2-31
University of Minnesota
Department of Chemistry
VNC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 19, 2010
Solvent: CDCl3
File: nr-2-19v3.3402
Starting Time: 20:16:16
Completion Time: 20:19:54
Total acq. time 1 minute
UNITYplus-500 "#field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533659 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
8.002
7.987
7.981
7.975
7.968
7.963
7.483
7.478
7.472
7.456
7.449
7.444
7.264
7.260
7.256
7.255
7.253
4.550
4.527
4.505
3.925
3.920
2.925
2.902
2.880
2.635
1.550
0.009
0.007
0.006
0.004
0.002
0.002
-0.002
-0.005
-0.007
-0.012
16.82
17.26
19.23
27.30
19.39
ppm
MeO2C
O
O
CN

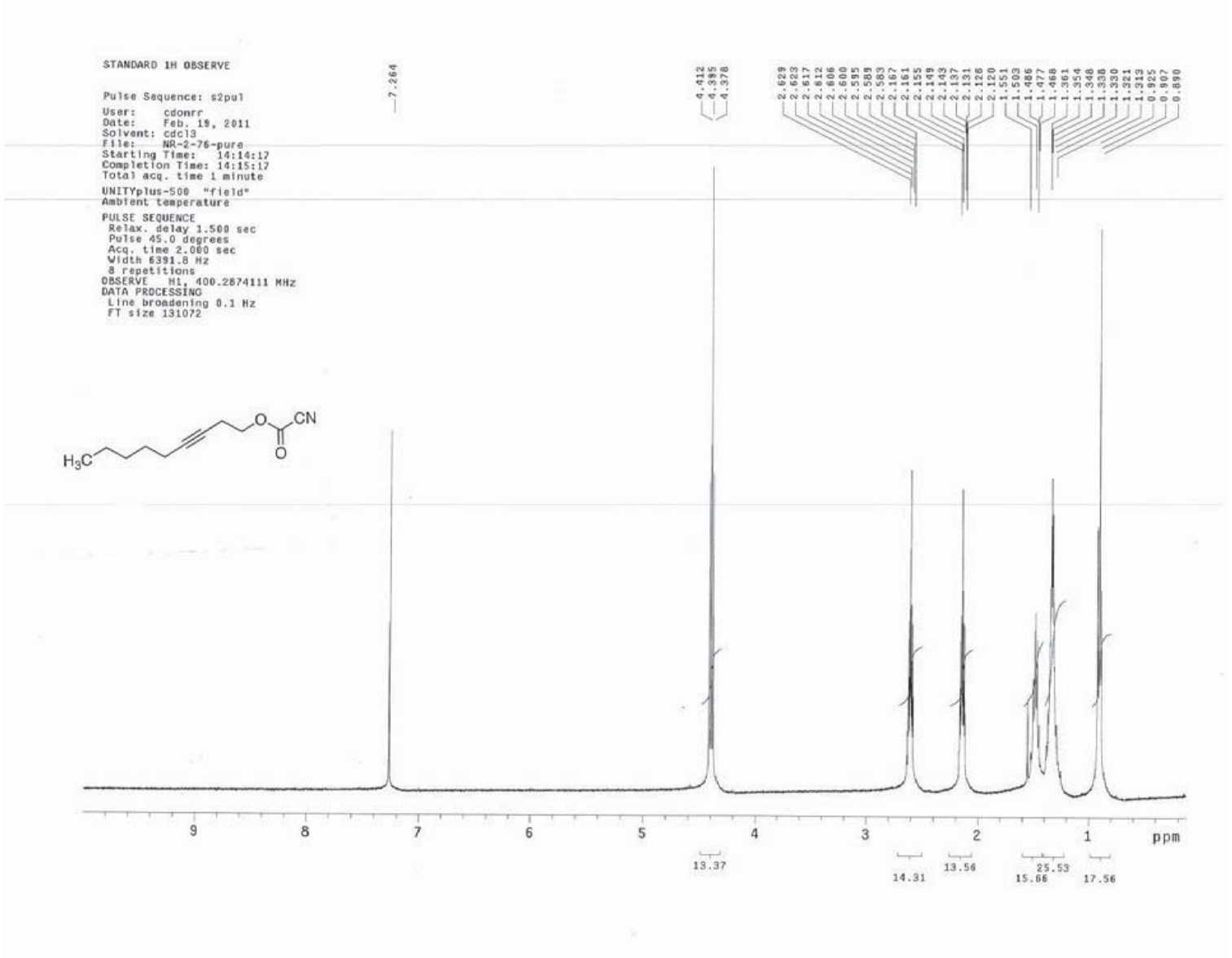

NR-2-31-13C
University of Minnesota
Department of Chemistry
VNC-300
Pulse Sequence: s2pul
User: cdonr
Date: Nov 22, 2010
Solvent: CDCl3
File: 101122v3_3502
Starting Time: 20:26:52
Completion Time: 20:44:34
Total acq. time 12 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.600 sec
Width 31311.1 Hz
256 repetitions
OBSERVE C13, 75.4233264 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
166.569
144.083
131.720
130.614
129.799
129.585
127.477
109.192
86.622
82.506
77.589
77.160
76.739
66.195
52.356
19.720
200
180
160
140
120
100
80
60
40
20
ppm
CN
O
O
O
MeO2C

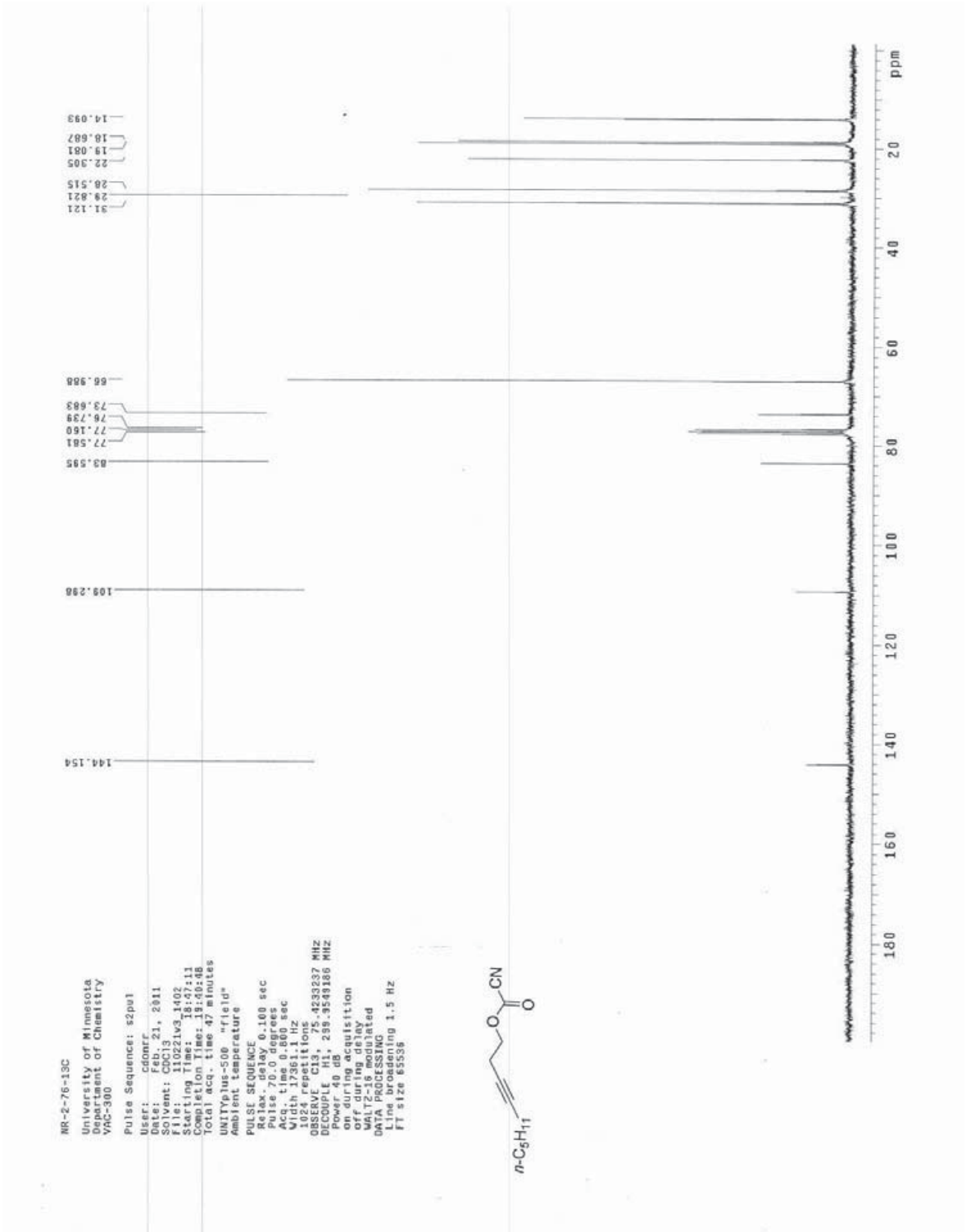

University of Minnesota, VI-300
Pulse Sequence: s2pul
Date: Dec. 29, 2010
Solvent: cdcl3
Starting Time: 12:19:41
Completion Time: 12:20:00
Total acq. time 1 minute
UNITYplus-300 "vi300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.600 sec
Width 5998.7 Hz
4 repetitions
OBSERVE H1, 300.1683401 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.418
7.409
7.401
7.391
7.384
7.379
7.369
7.362
7.352
7.323
7.315
7.304
7.300
7.261
7.042
7.033
7.026
7.010
7.003
6.997
6.982
6.975
6.965
4.540
4.531
4.518
4.509
4.496
4.486
2.898
2.881
2.859
2.836
1.555
0.000
0.005
O
CN
O
F
ppm
24.43
23.74
25.82
26.00


University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 28, 2010
Solvent: CDCl3
File: NR-2-46-13C-2
Starting Time: 12:22:30
Total acq. time 34 minutes
UNITYplus-500 "vfield"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.881 sec
Width 18867.9 Hz
736 repetitions
OBSERVE C13, 75.4773786 MHz
DECOUPLE H1, 300.1698406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
164.281
160.978
133.751
133.636
115.899
115.609
109.239
83.080
82.195
77.560
77.160
76.735
66.411
19.669
CN
O
O
F
200
180
160
140
120
100
80
60
40
20
0 ppm


NR-293
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Sample: 83
Spin rate: 24
Date: Oct. 7, 2010
Solvent: CDCl3
File: 8302
Starting Time: 00:32:57
Completion Time: 00:40:06
Total acq. time 1 minute
GEMINI-300BB "vac300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533655 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.966
7.846
7.832
7.824
7.814
7.802
7.786
7.541
7.528
7.518
7.507
7.503
7.497
7.484
7.470
7.465
7.448
7.262
4.550
4.527
4.505
2.928
2.905
2.882
2.596
0.047
0.041
O
CN
O
10
9
8
7
6
5
4
3
2
1
ppm
0.09
61.40
-0.02
18.78
0.34
18.90
-0.12
0.31
0.05
-0.03
-0.02
0.32

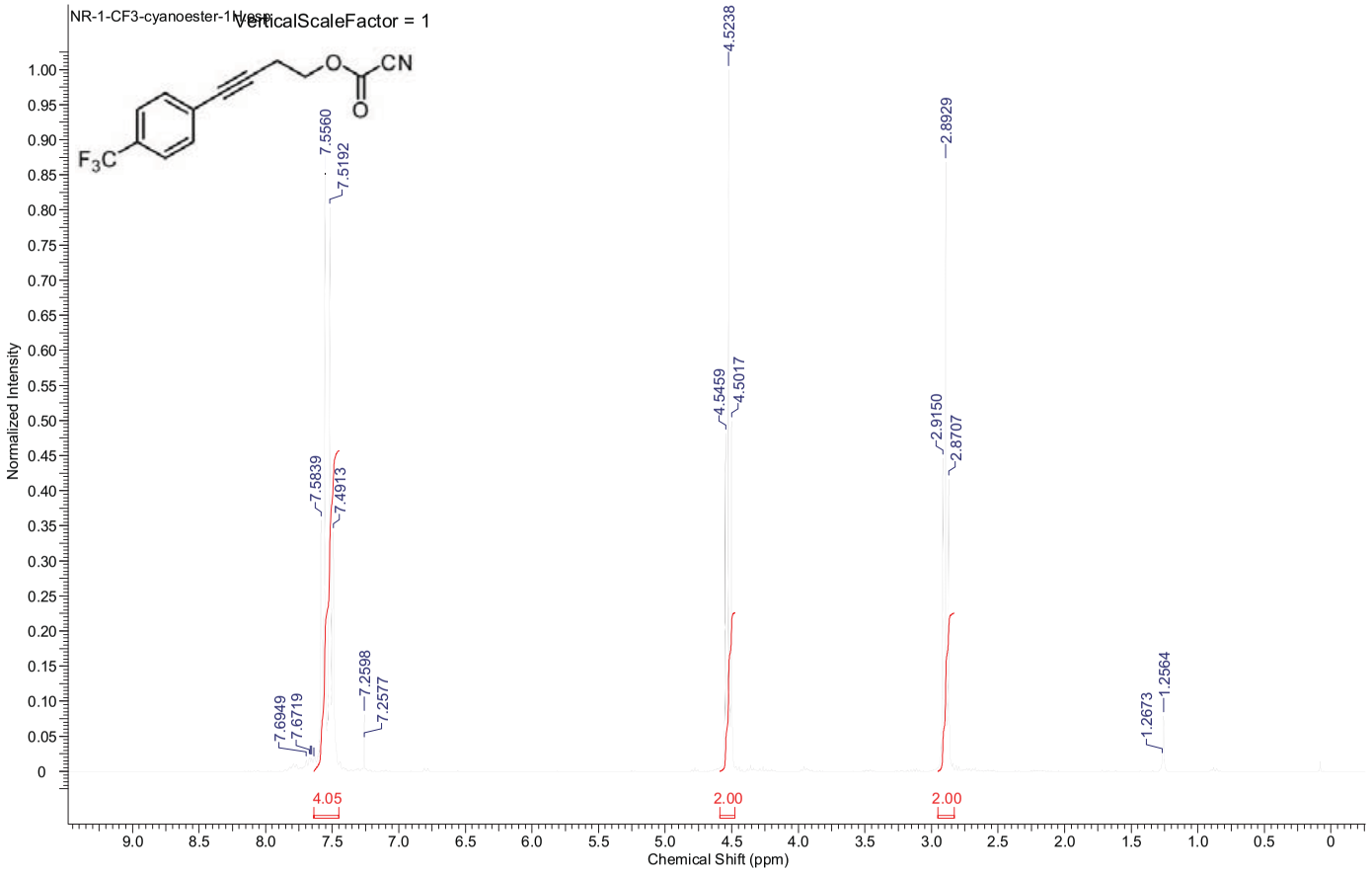

NR-293-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonr
Date: Oct 21, 2010
Solvent: CDCl3
File: 101021v3.2702
Starting Time: 23:02:35
Completion Time: 23:20:33
Total acq. time 12 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 23041.1 Hz
256 repetitions
OBSERVE C13, 75.4233333 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
144.076
132.956
132.830
131.622
128.447
128.109
127.814
127.758
126.796
126.676
120.066
109.262
83.763
83.440
77.589
77.160
76.739
66.405
19.664
O
O
CN
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
User: cdonrr
Date: Feb. 19, 2011
Solvent: cdcl3
File: NR-2-76-pure
Starting Time: 14:14:17
Completion Time: 14:15:17
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 6391.8 Hz
8 repetitions
OBSERVE H1, 400.2874111 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.264
4.412
4.385
4.378
2.628
2.623
2.617
2.612
2.606
2.600
2.595
2.589
2.583
2.167
2.161
2.155
2.149
2.143
2.137
2.131
2.126
2.120
1.551
1.503
1.486
1.477
1.468
1.361
1.354
1.348
1.338
1.330
1.321
1.313
0.925
0.907
0.890
O
CN
O
H3C
9
8
7
6
5
4
3
2
1
ppm
13.37
14.31
13.56
25.53
15.66
17.56


NR-2-76-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Feb. 21, 2011
Solvent: CDCl3
File: 110221v3_1402
Starting Time: 18:47:11
Completion Time: 19:40:48
Total acq. time 47 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
1024 repetitions
OBSERVE C13, 75.4233237 MHz
DECOUPLE H1, 299.3549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
144.154
109.298
83.595
77.581
77.160
76.739
73.683
66.988
31.121
29.821
28.515
22.305
19.081
18.687
14.093
O
O
CN
n-C5H11
ppm

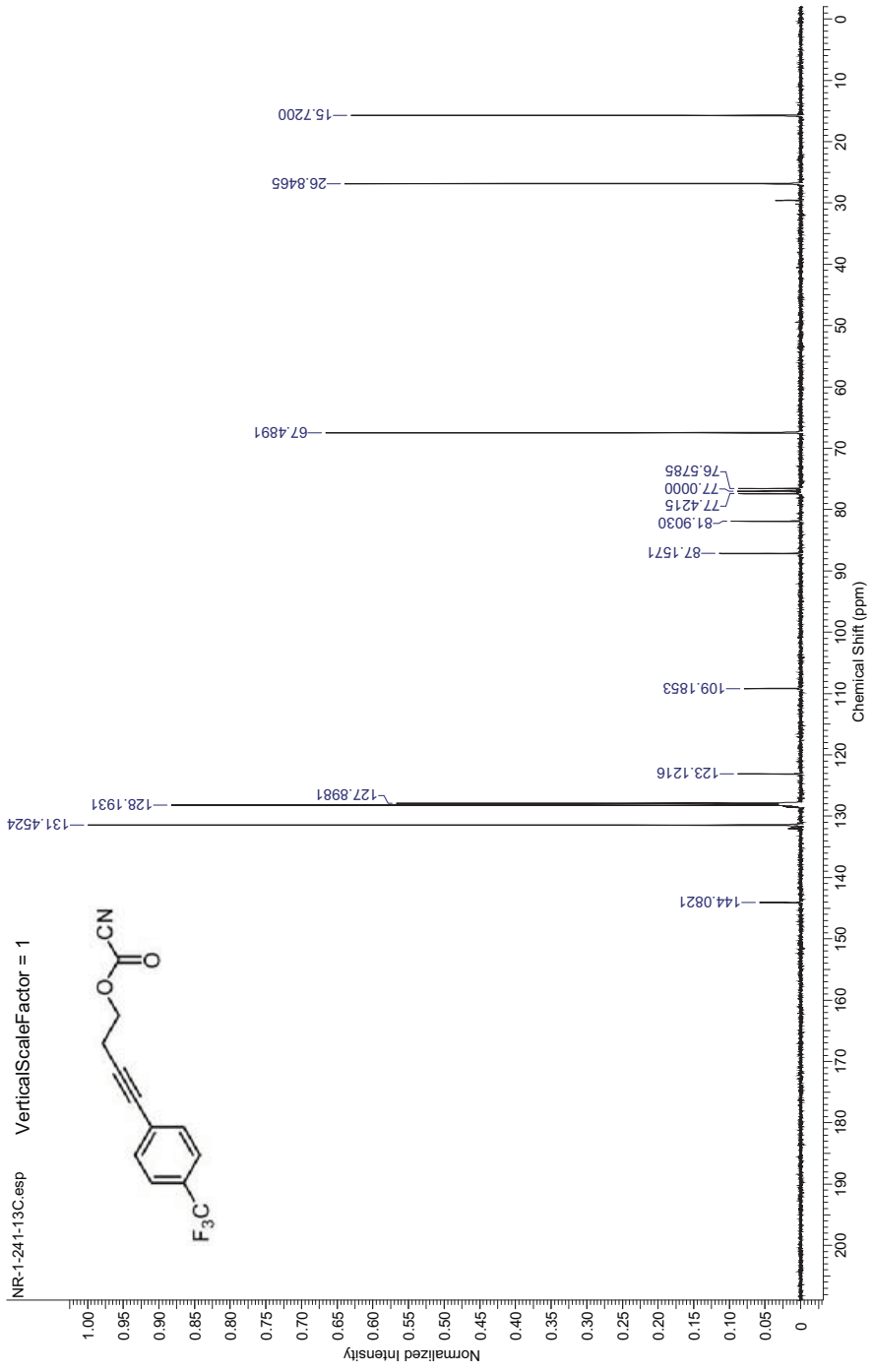
9/23/2013 12:13:23 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 2.0001 | ***Comment*** | University of Minnesota, VI-300 | | | ***Date*** | Jun 12 2010 |
| ***Date Stamp*** | Jun 12 2010 | ***File Name*** | C:\Users\Naveen\Desktop\NR-1-CF3-cyanoester-1H.fid\fid | | | ***Frequency (MHz)*** | 300.17 |
| ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 12000 | ***Points Count*** | 131072 |
| ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 38.00 | ***Solvent*** | CHLOROFORM-d | | |
| ***Spectrum Offset (Hz)*** | 2407.1277 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5999.70 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



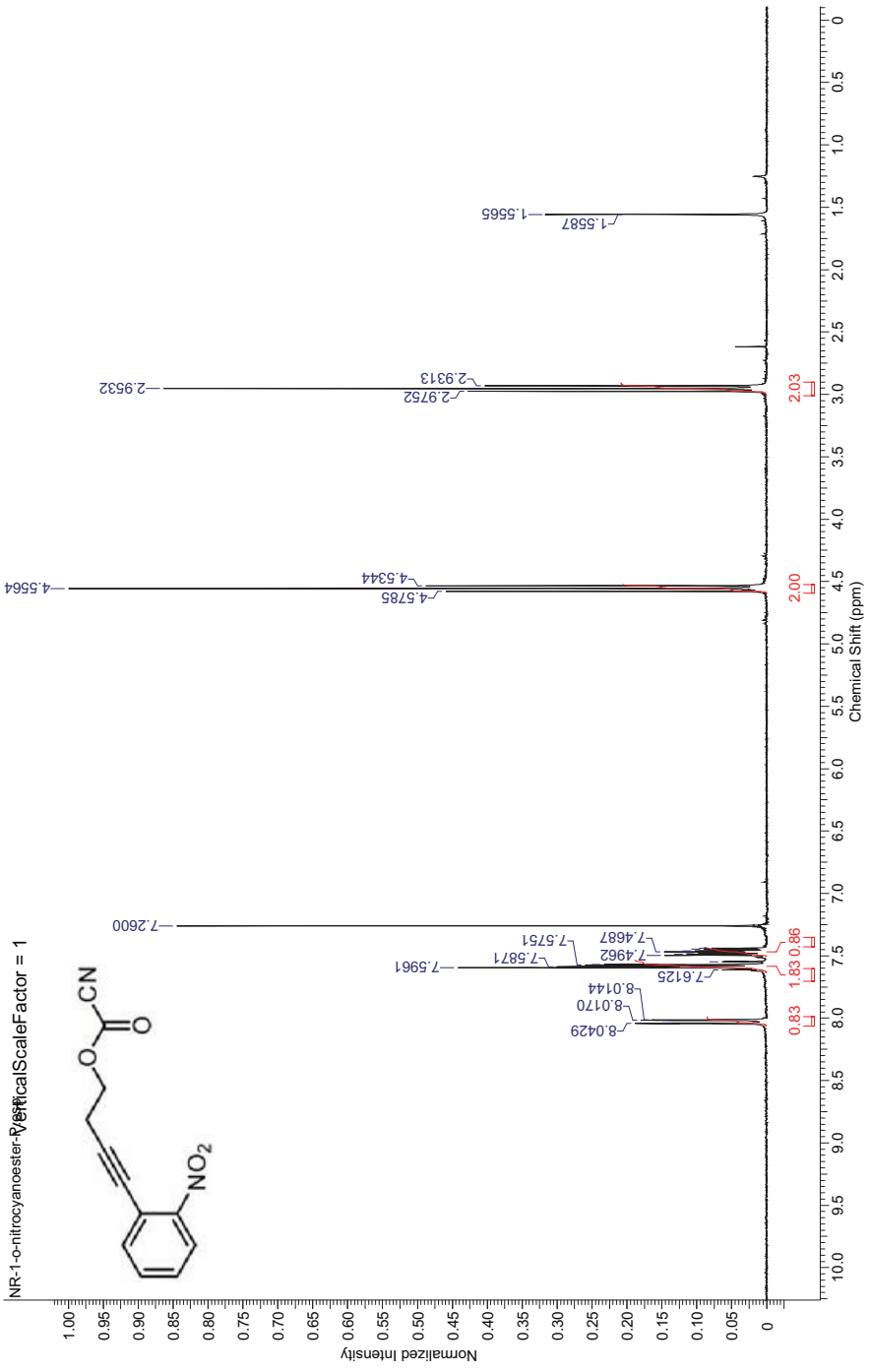
9/21/2013 4:48:58 PM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 0.8000 | *Comment* | NR-241-Dept University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Jul 6 2010 | *Date Stamp* | Jul 6 2010 *File Name* C:\Users\Naveen\Desktop\100706\3 5602.fid\fid |
| *Frequency (MHz)* | 75.43 | *Nucleus* | 13C *Number of Transients* 256 *Original Points Count* 13889 |
| *Points Count* | 16384 | *Pulse Sequence* | s2pul *Receiver Gain* 30.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 7855.0186 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 17361.11 *Temperature (degree C)* AMBIENT TEMPERATURE |



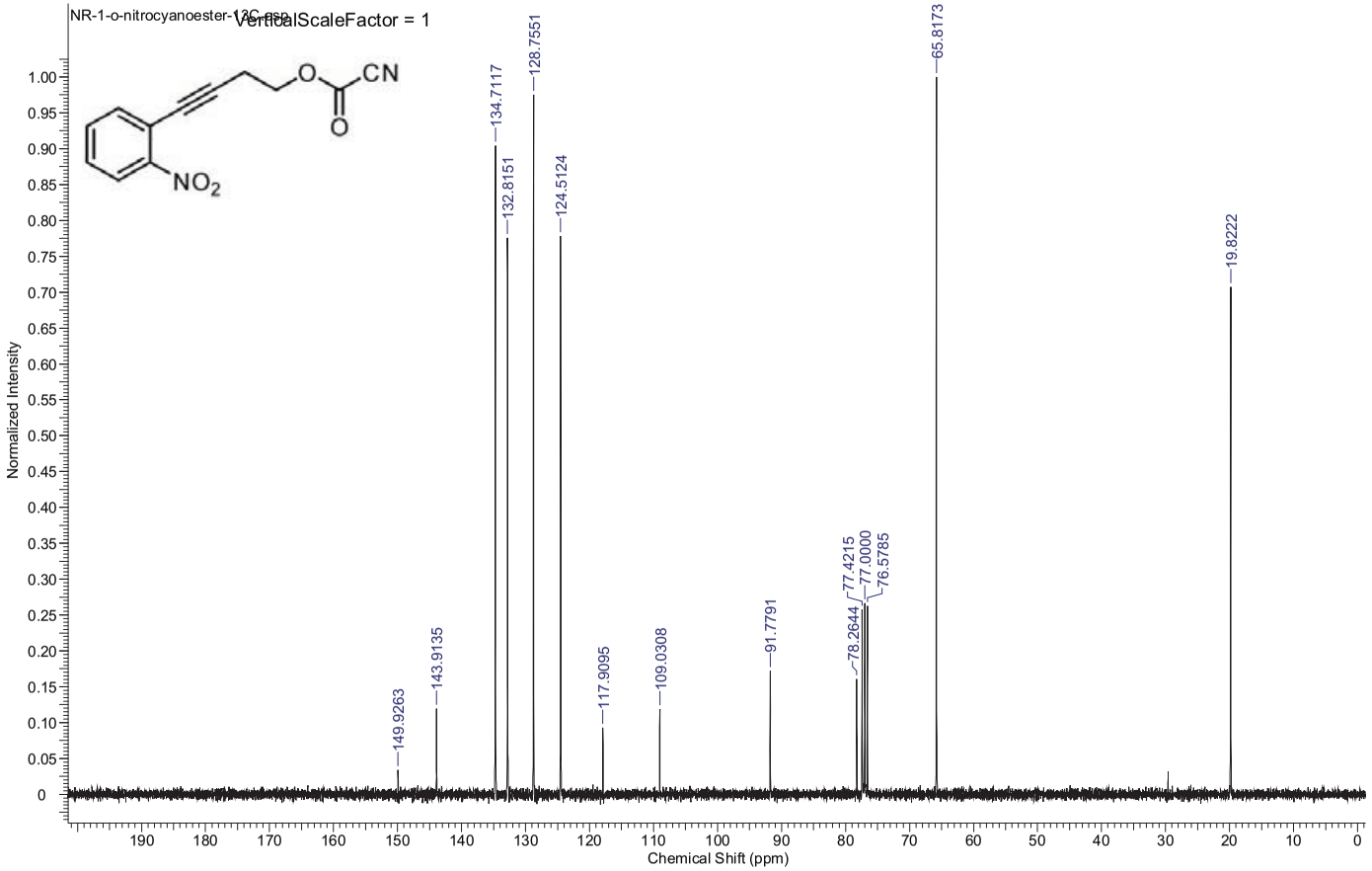
9/21/2013 5:09:26 PM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | JMR 1-14 University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Jun 17 2010 | *Date Stamp* | Jun 17 2010 *File Name* C:\Users\Naveen\Desktop\100617v3_2702.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.0337 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



9/21/2013 5:24:08 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 0.8000 | ***Comment*** | NR-John-Nitrocyanoester University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | Jun 17 2010 | ***Date Stamp*** | Jun 17 2010 | ***File Name*** | C:\Users\Naveen\Desktop\100617v3_4102.fid\fid | | |
| ***Frequency (MHz)*** | 75.43 | ***Nucleus*** | 13C | ***Number of Transients*** | 256 | ***Original Points Count*** | 13889 |
| ***Points Count*** | 16384 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 30.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 7860.3169 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 17361.11 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



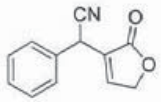
University of Minnesota, VI-300

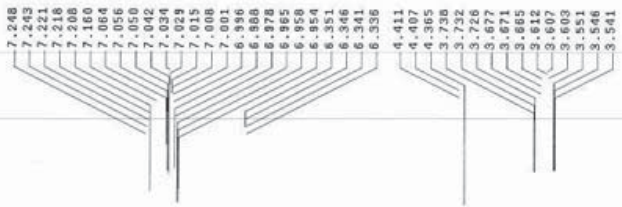
Pulse Sequence: s2pul

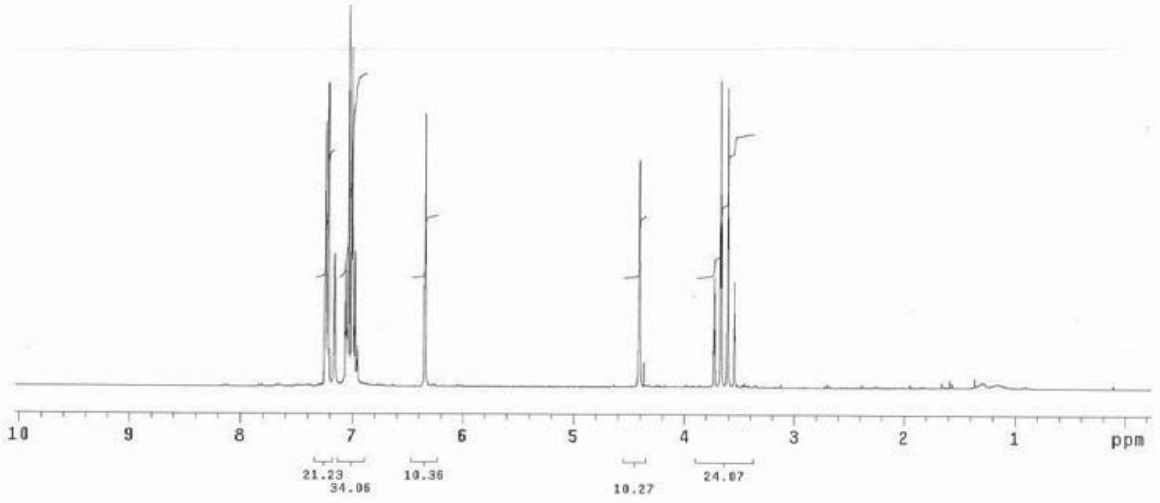
User: cdonrr
Date: Jun. 8, 2010
Solvent: c6d6
File: SML-1-91_Pure1H
Starting Time: 19:46:13
Completion Time: 19:47:14
Total acq. time 1 minute

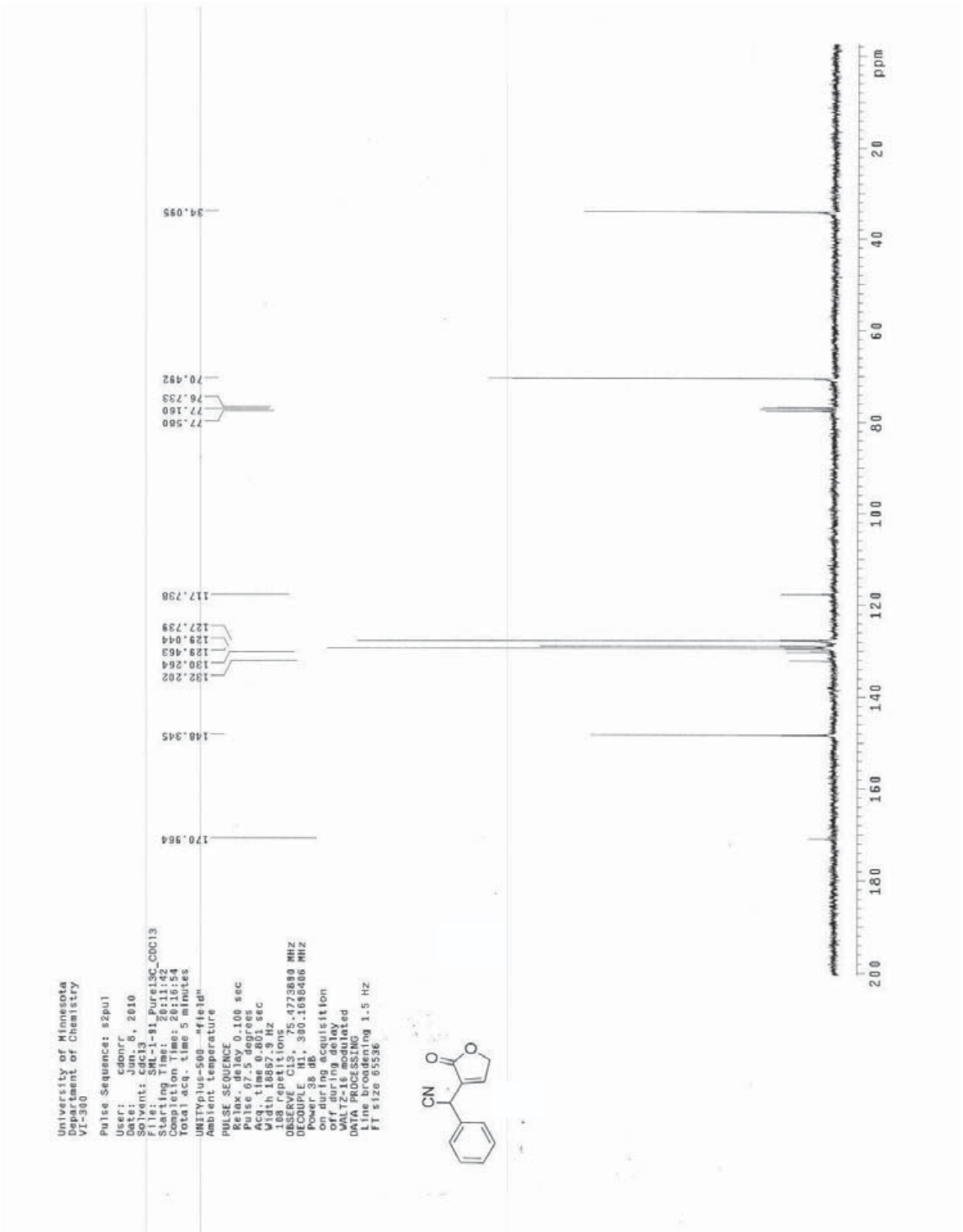
UNITYplus-500 "field"
Ambient temperature

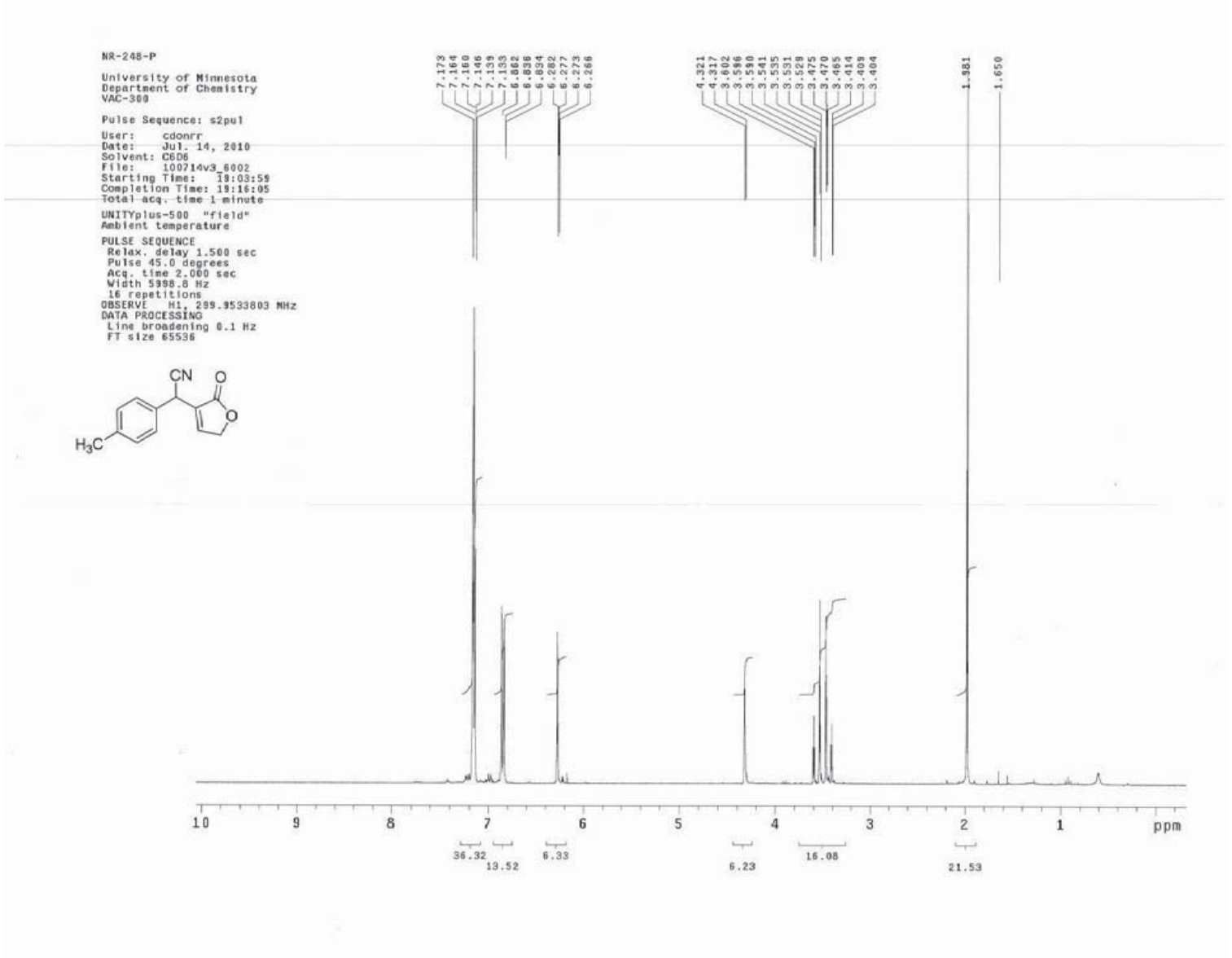
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5995.7 Hz
16 repetitions
OBSERVE H1, 300.1683545 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072

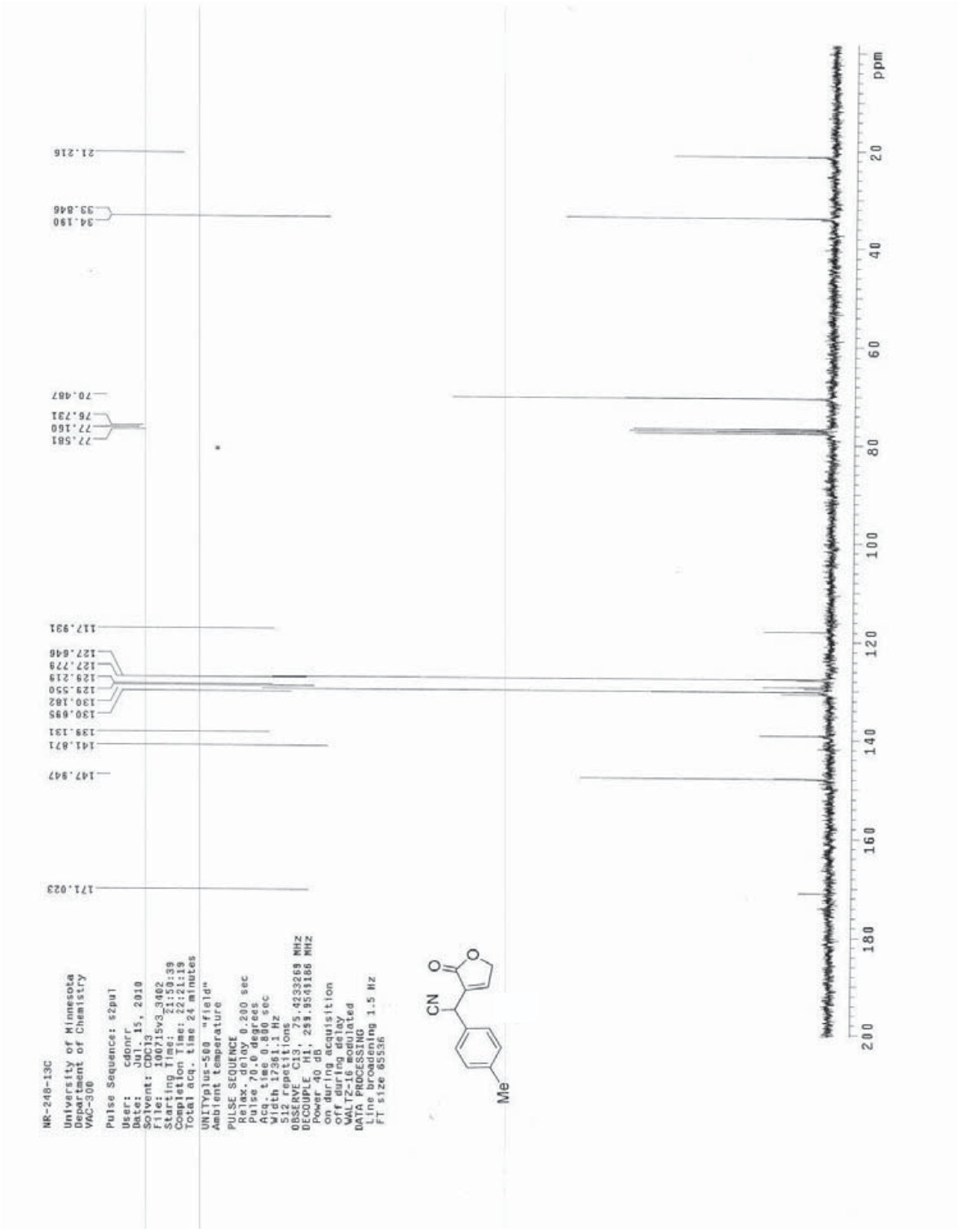


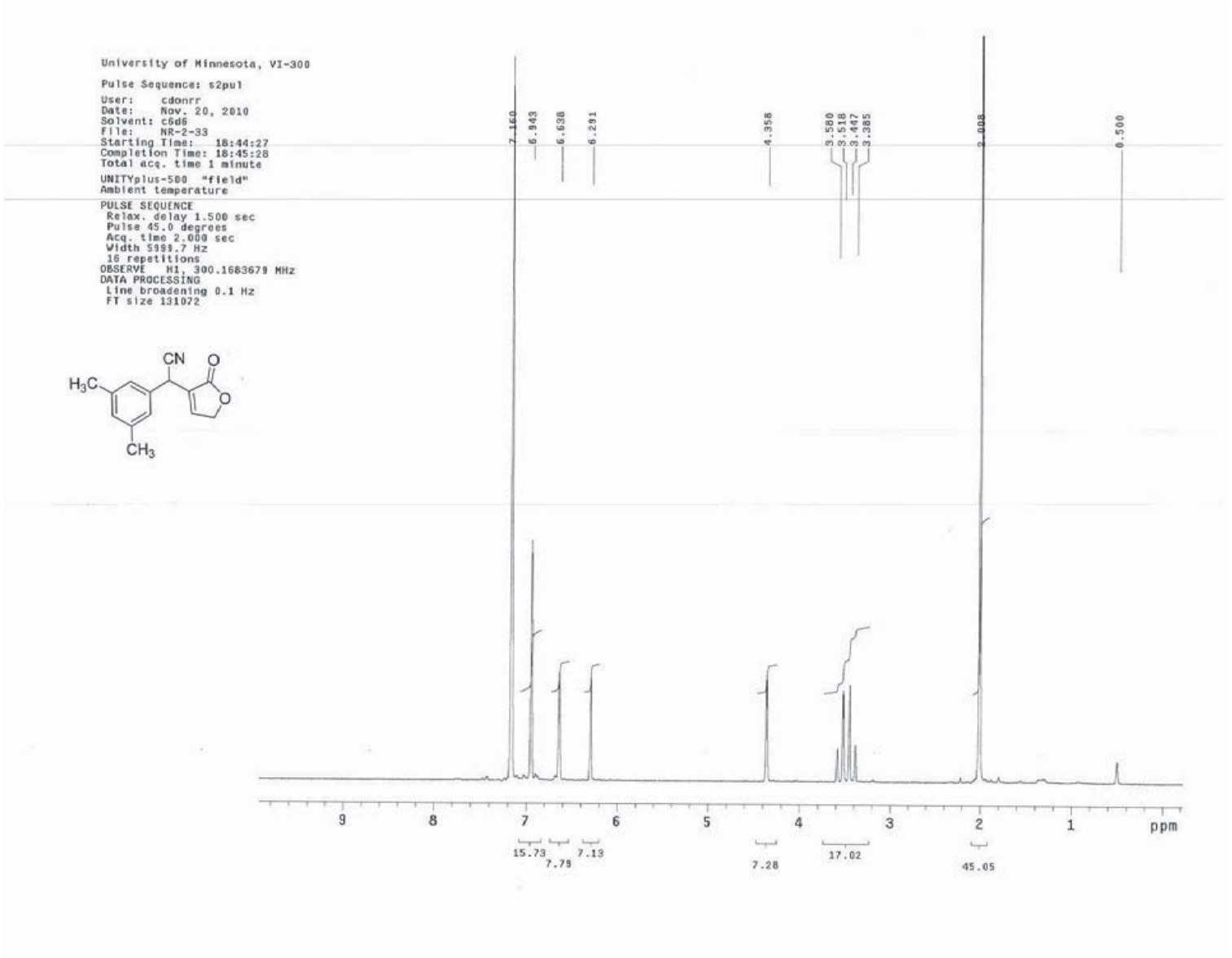



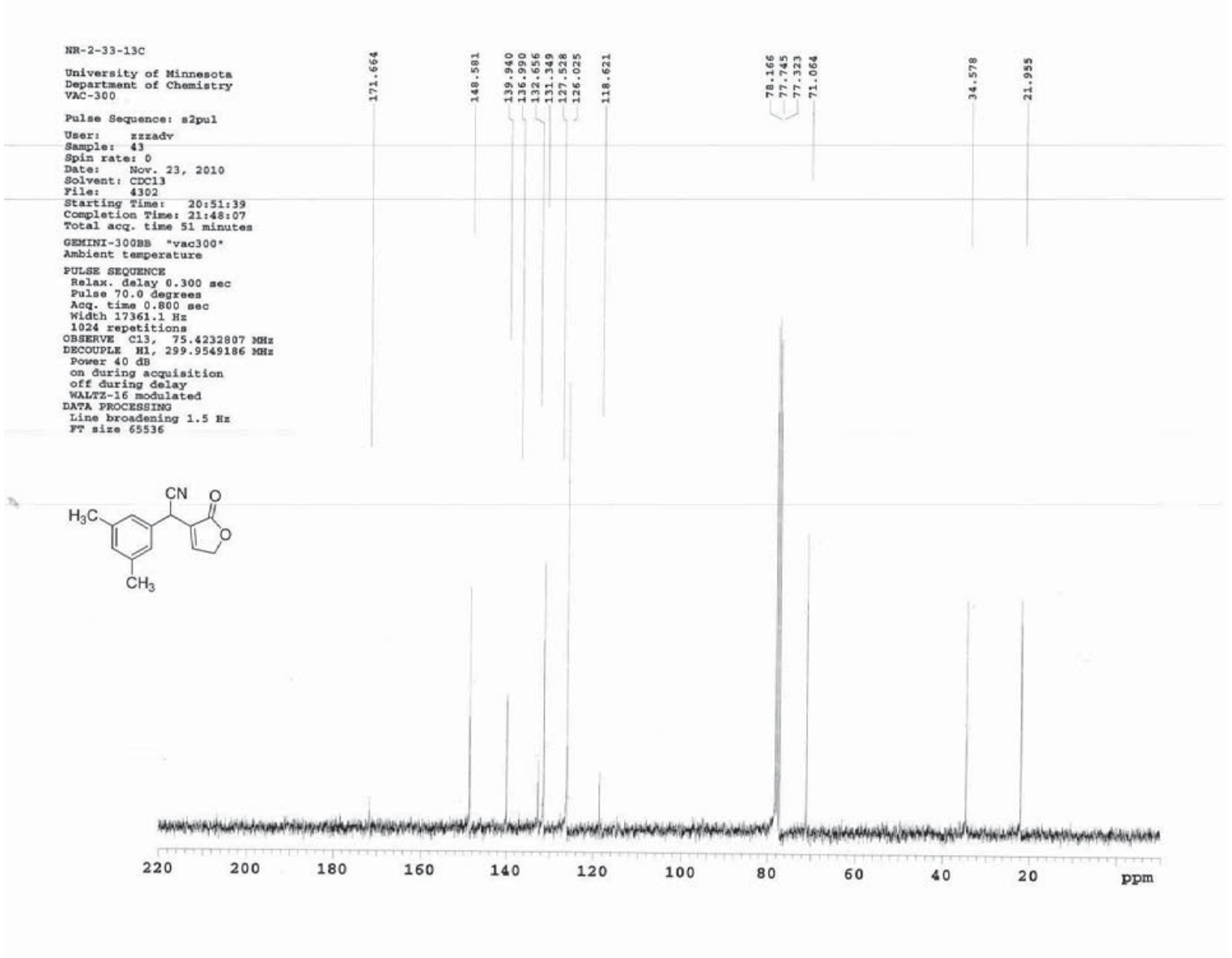



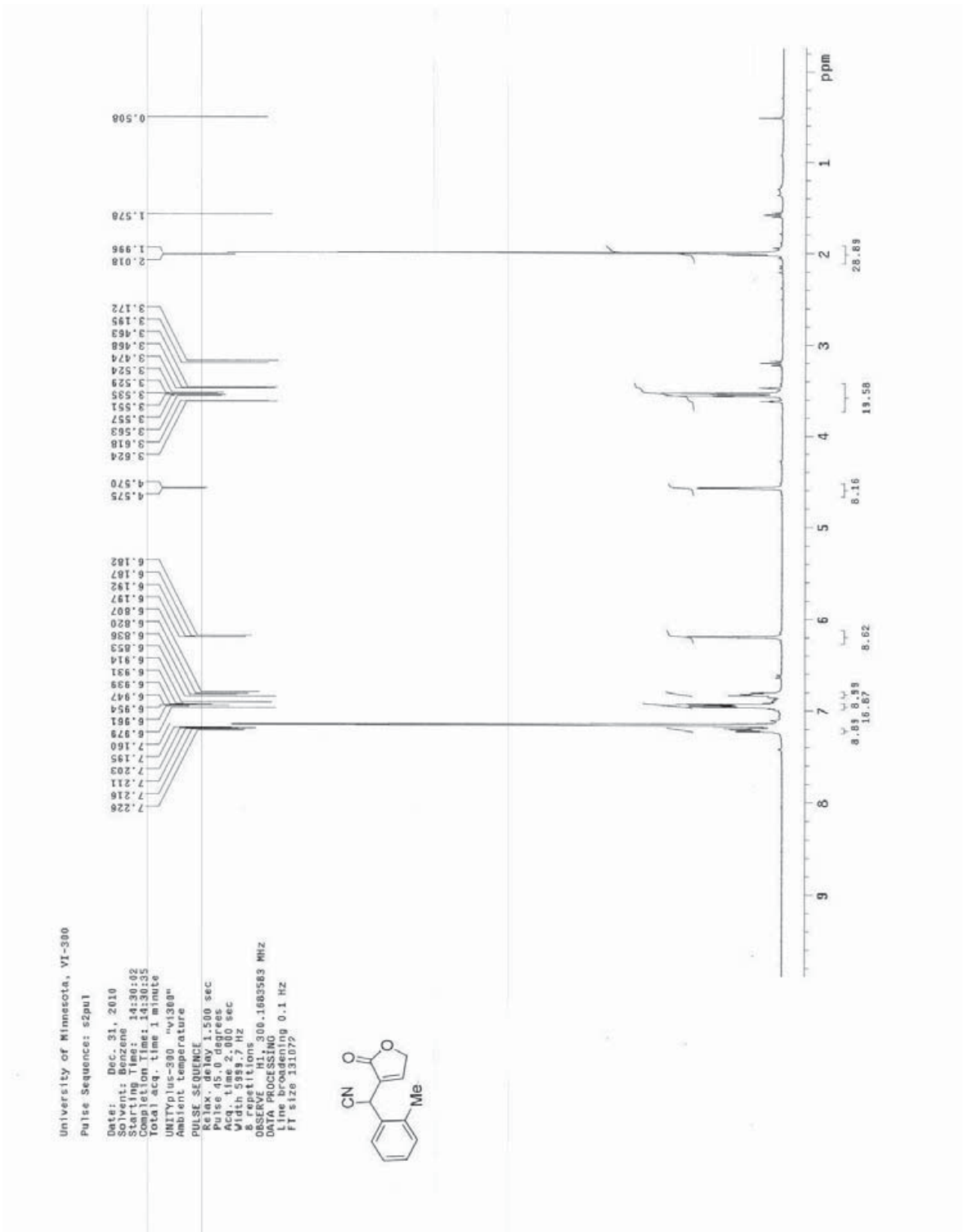

University of Minnesota
Departament of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jun. 8, 2010
Solvent: cdcl3
File: SML-1-91_Pure13C_CDCl3
Starting Time: 20:11:42
Completion Time: 20:16:54
Total acq. time 5 minutes
UNITYplus-500 "ifield"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.801 sec
Width 18867.9 Hz
108 repetitions
OBSERVE C13, 75.4773890 MHz
DECOUPLE H1, 300.1688406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
170.964
140.345
132.202
130.264
129.463
129.044
127.739
117.738
77.580
77.160
76.733
70.492
34.095
CN
O
O
200
180
160
140
120
100
80
60
40
20
ppm

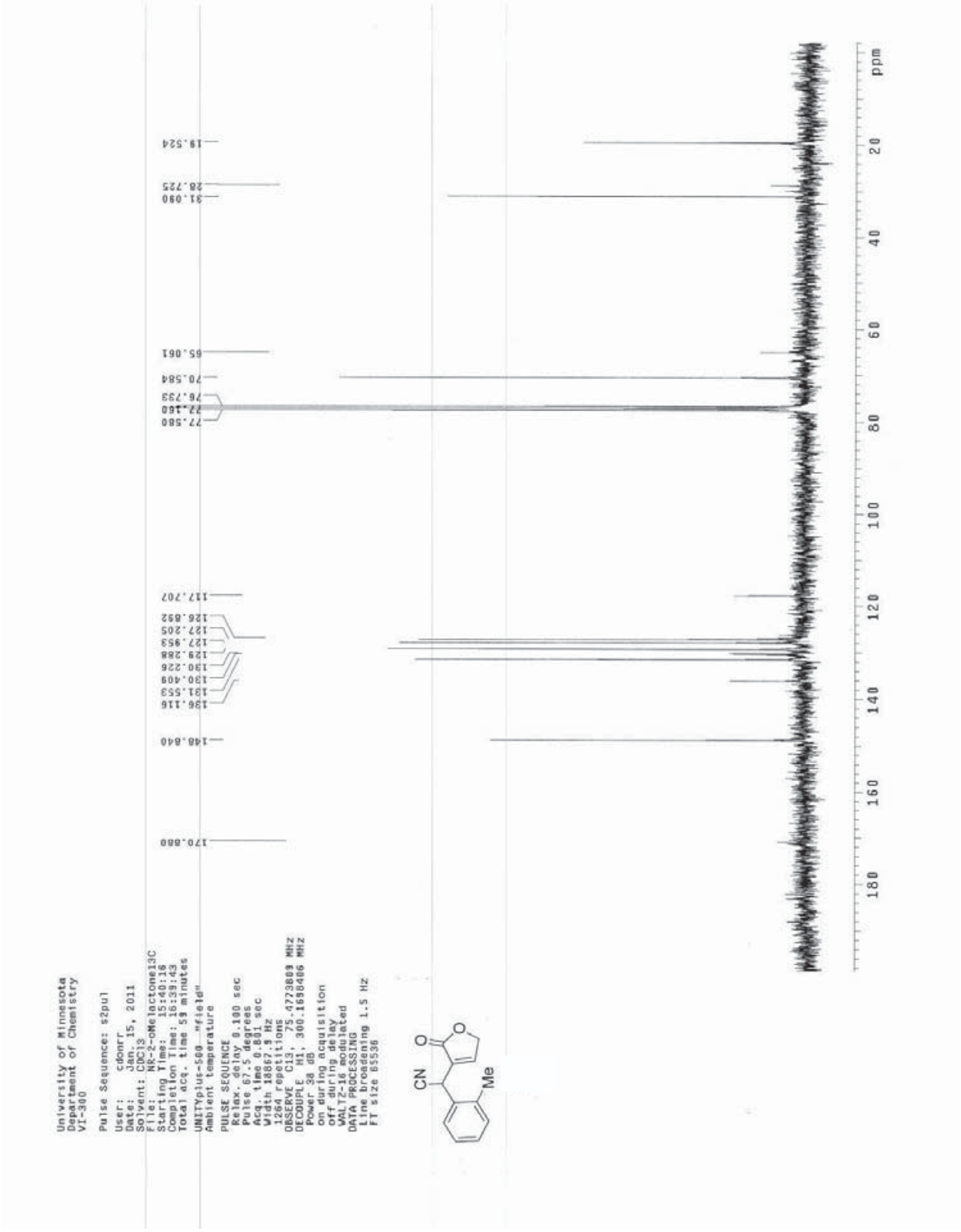

NR-248-P
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jul. 14, 2010
Solvent: C6D6
File: 100714v3_6002
Starting Time: 19:03:55
Completion Time: 19:16:05
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533803 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
CN
O
O
H3C
7.173
7.164
7.160
7.146
7.139
7.133
6.862
6.838
6.834
6.282
6.277
6.273
6.266
4.321
4.317
3.602
3.596
3.590
3.541
3.535
3.531
3.529
3.475
3.470
3.465
3.414
3.409
3.404
1.981
1.650
10
9
8
7
6
5
4
3
2
1
ppm
36.32
13.52
6.33
6.23
16.08
21.53

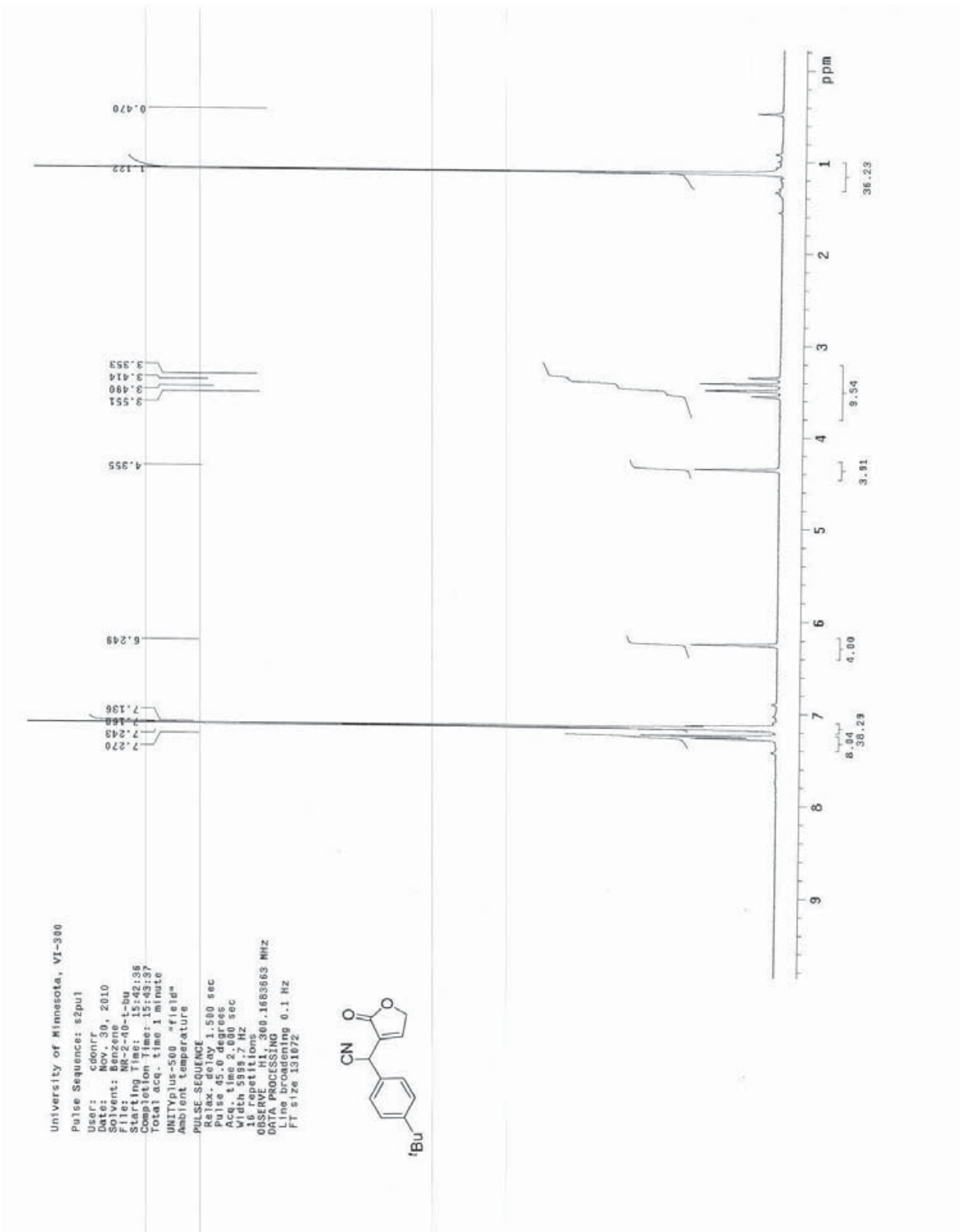

NR-248-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jul 15, 2010
Solvent: CDCl3
File: 100715v3_3402
Starting Time: 21:50:39
Completion Time: 22:12:19
Total acq. time 24 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.880 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233269 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.023
147.947
141.871
139.131
130.095
130.182
129.550
129.219
127.779
127.646
117.931
77.581
77.160
76.731
70.487
34.190
33.846
21.216
CN
O
O
Me
200
180
160
140
120
100
80
60
40
20
ppm

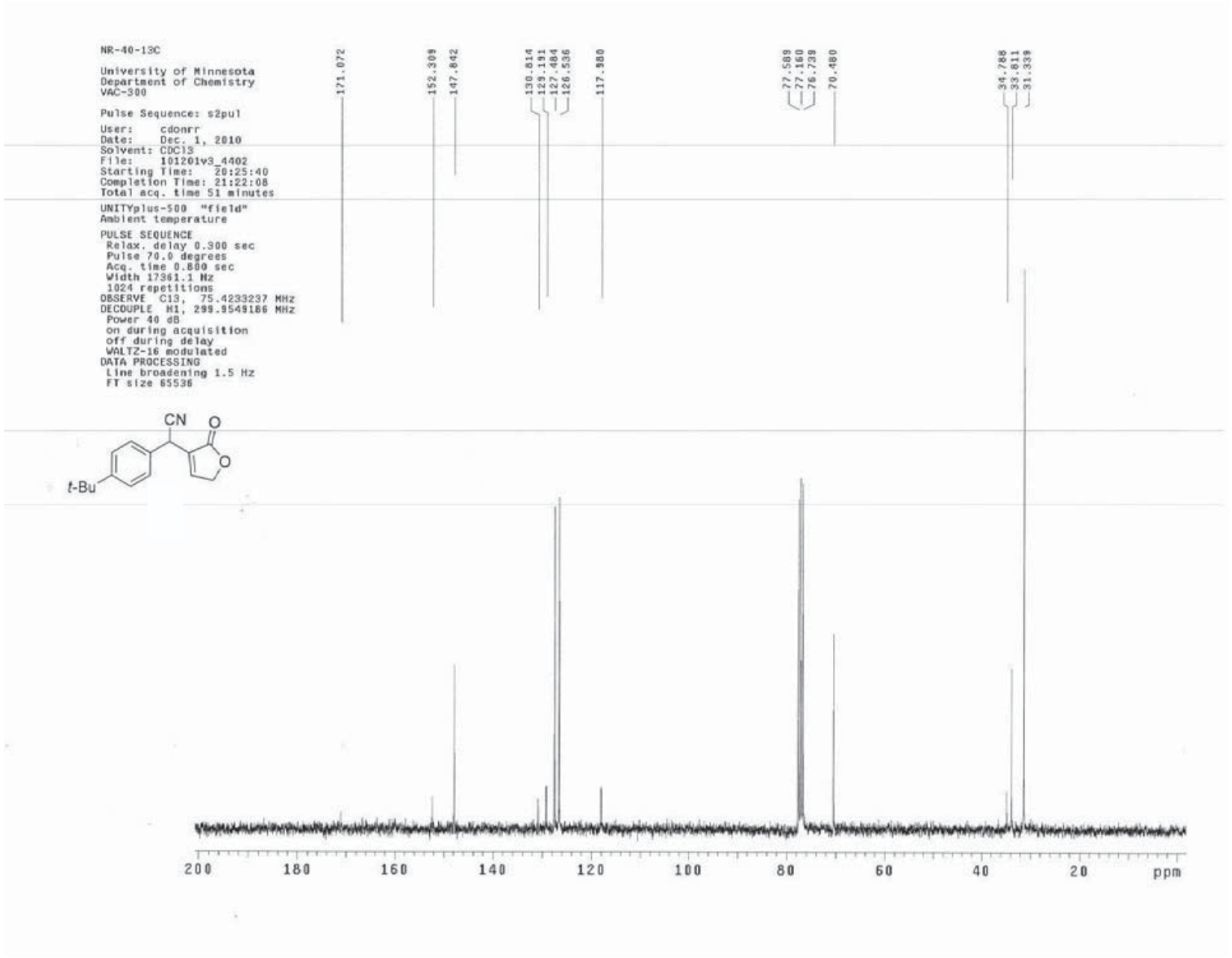

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 20, 2010
Solvent: c6d6
File: NR-2-33
Starting Time: 18:44:27
Completion Time: 18:45:28
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5989.7 Hz
16 repetitions
OBSERVE H1, 300.1683679 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
CN
O
H3C
O
CH3
7.160
6.943
6.638
6.291
4.358
3.580
3.518
3.447
3.385
2.008
0.500
9
8
7
6
5
4
3
2
1
ppm
15.73
7.79
7.13
7.28
17.02
45.05

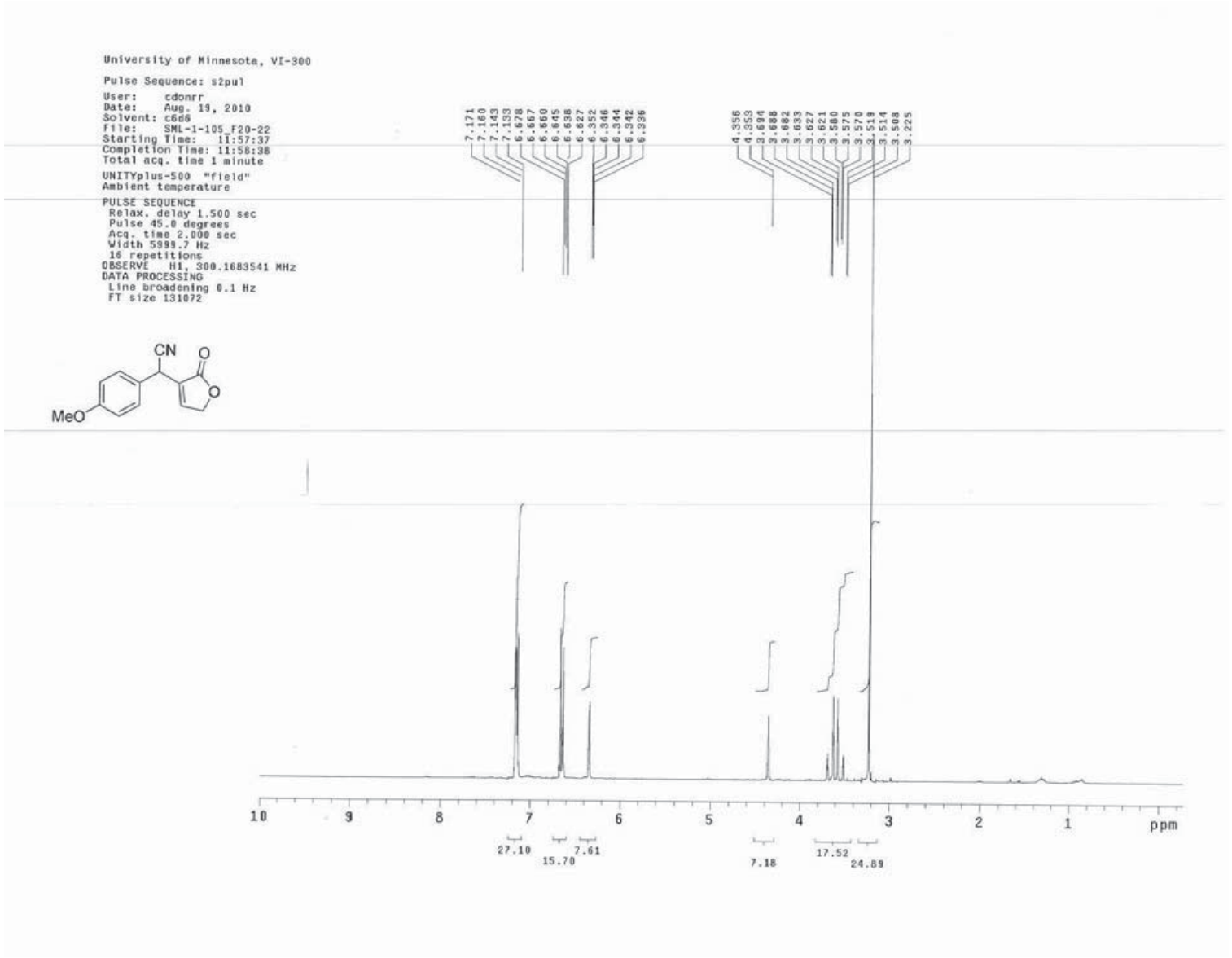

NR-2-33-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: zzzadv
Sample: 43
Spin rate: 0
Date: Nov. 23, 2010
Solvent: CDCl3
File: 4302
Starting Time: 20:51:39
Completion Time: 21:48:07
Total acq. time 51 minutes
GEMINI-300BB "vac300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
1024 repetitions
OBSERVE C13, 75.4232807 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.664
148.581
139.940
136.990
132.656
131.349
127.528
126.025
118.621
78.166
77.745
77.323
71.064
34.578
21.955
CN
O
H3C
O
CH3
220
200
180
160
140
120
100
80
60
40
20
ppm

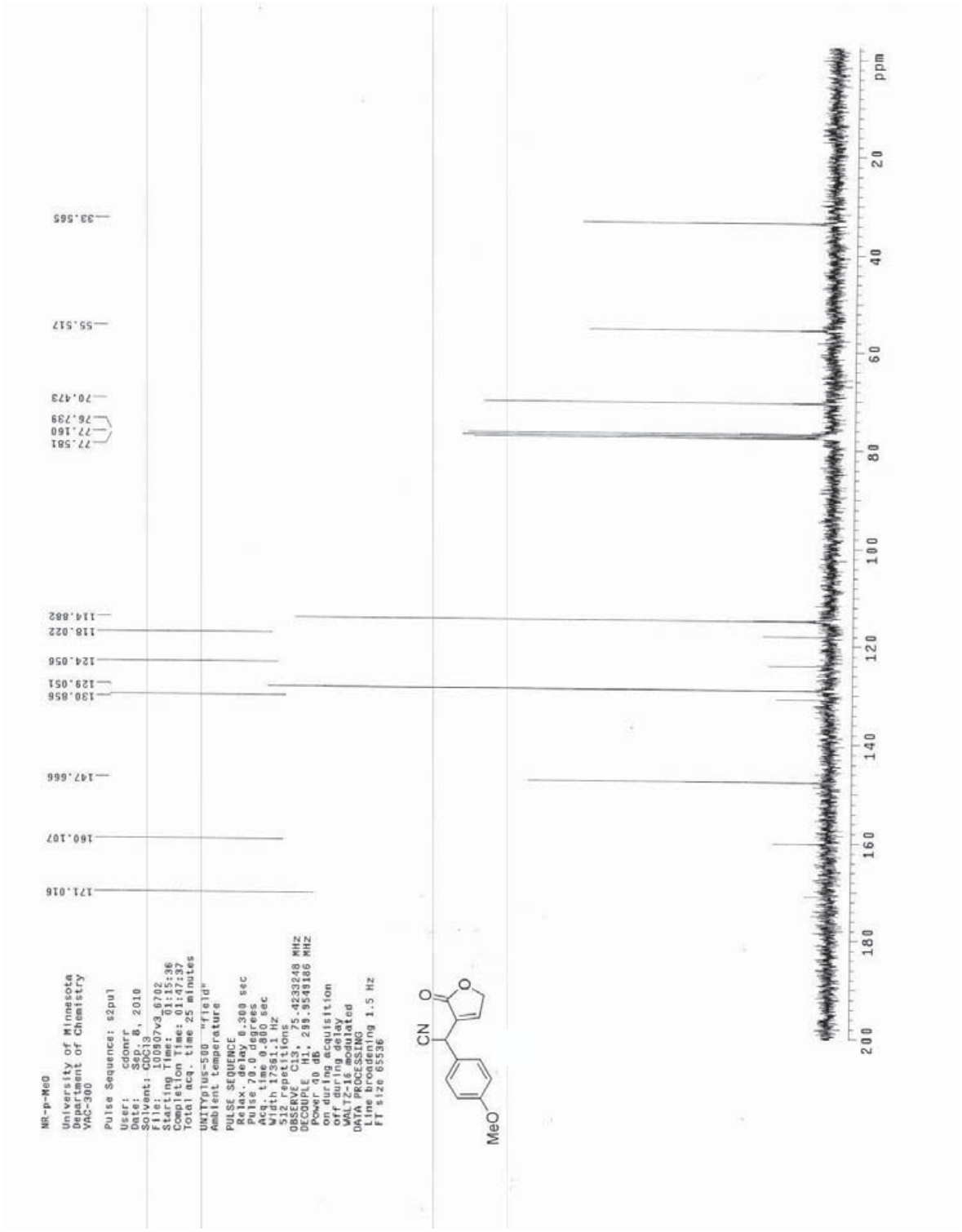

University of Minnesota, VI-300
Pulse Sequence: s2pul
Date: Dec. 31, 2010
Solvent: Benzene
Starting Time: 14:30:02
Completion Time: 14:30:35
Total acq. time 1 minute
UNITYplus-300 "wv130a"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5319.7 Hz
8 repetitions
OBSERVE H1, 300.1683583 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
0.508
1.578
1.996
2.018
3.172
3.195
3.463
3.468
3.474
3.524
3.529
3.535
3.551
3.557
3.563
3.618
3.624
4.570
4.575
6.182
6.187
6.192
6.197
6.807
6.820
6.836
6.853
6.914
6.931
6.939
6.947
6.954
6.961
6.979
7.160
7.195
7.203
7.211
7.216
7.226
8.89 8.89
16.87
8.62
8.16
19.58
28.89
ppm
CN
O
O
Me

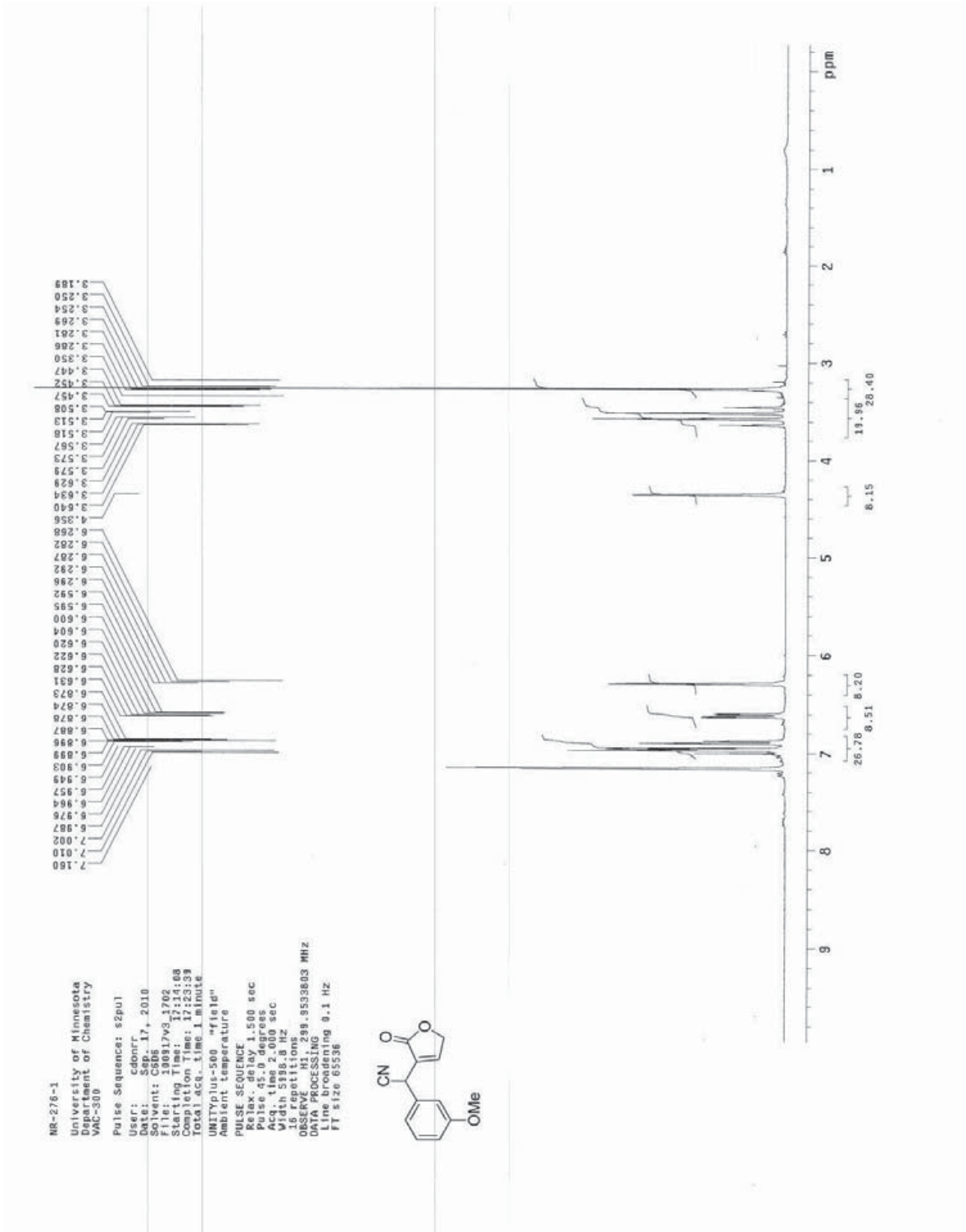

University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jan. 15, 2011
Solvent: CDCl3
File: NR-2-oMelactone13C
Starting Time: 15:40:16
Completion Time: 16:39:43
Total acq. time 59 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.881 sec
Width 18867.9 Hz
1264 repetitions
OBSERVE C13, 75.4723809 MHz
DECOUPLE H1, 300.1688406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
170.880
148.840
136.116
131.553
130.409
130.226
129.288
127.953
127.205
126.892
117.707
77.580
77.160
76.733
70.584
65.061
31.090
28.725
19.524
CN
O
O
Me
ppm

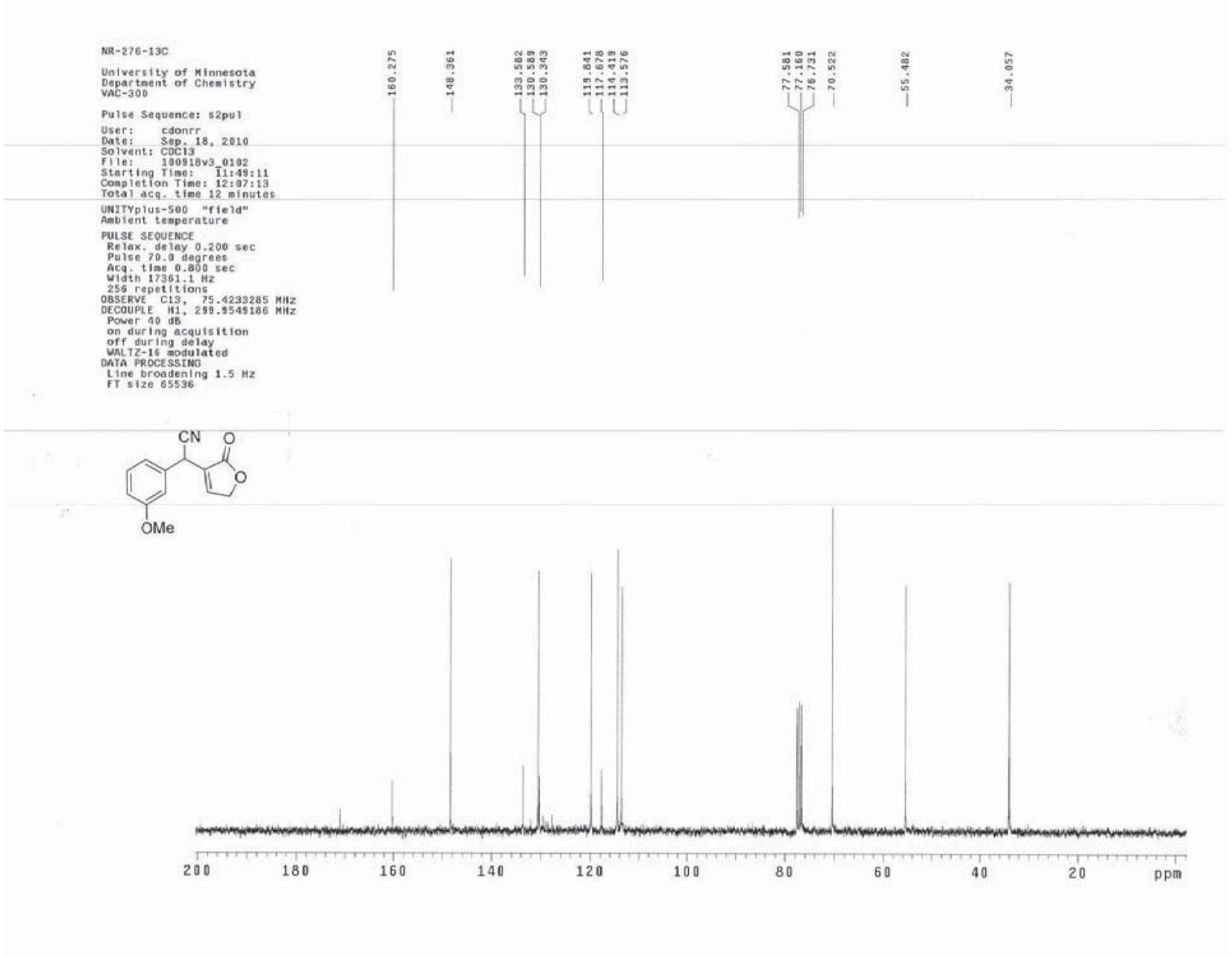

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 30, 2010
Solvent: Benzene
File: NR-2-40-t-bu
Starting Time: 15:42:36
Completion Time: 15:43:37
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5999.7 Hz
16 repetitions
OBSERVE H1, 300.1683663 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
0.470
1.122
3.353
3.414
3.490
3.551
4.355
6.249
7.136
7.160
7.243
7.270
8.04
38.23
4.00
3.91
9.54
36.23
ppm
CN
O
O
tBu

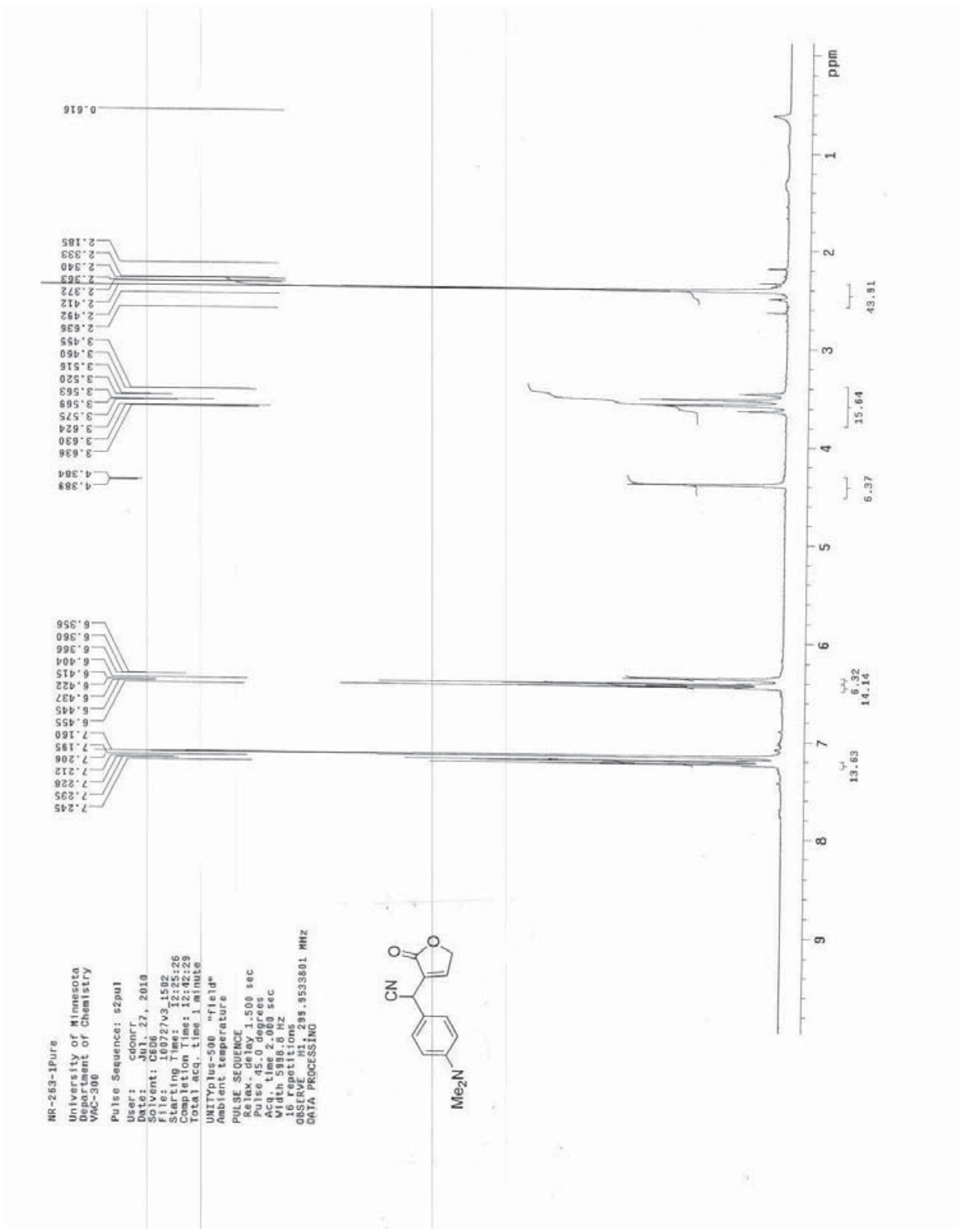

NR-40-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 1, 2010
Solvent: CDCl3
File: 101201v3_4402
Starting Time: 20:25:40
Completion Time: 21:22:08
Total acq. time 51 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
1024 repetitions
OBSERVE C13, 75.4233237 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.072
152.309
147.642
130.814
129.191
127.484
126.536
117.980
77.589
77.160
76.739
70.480
34.788
33.611
31.339
CN
O
O
t-Bu
200
180
160
140
120
100
80
60
40
20
ppm

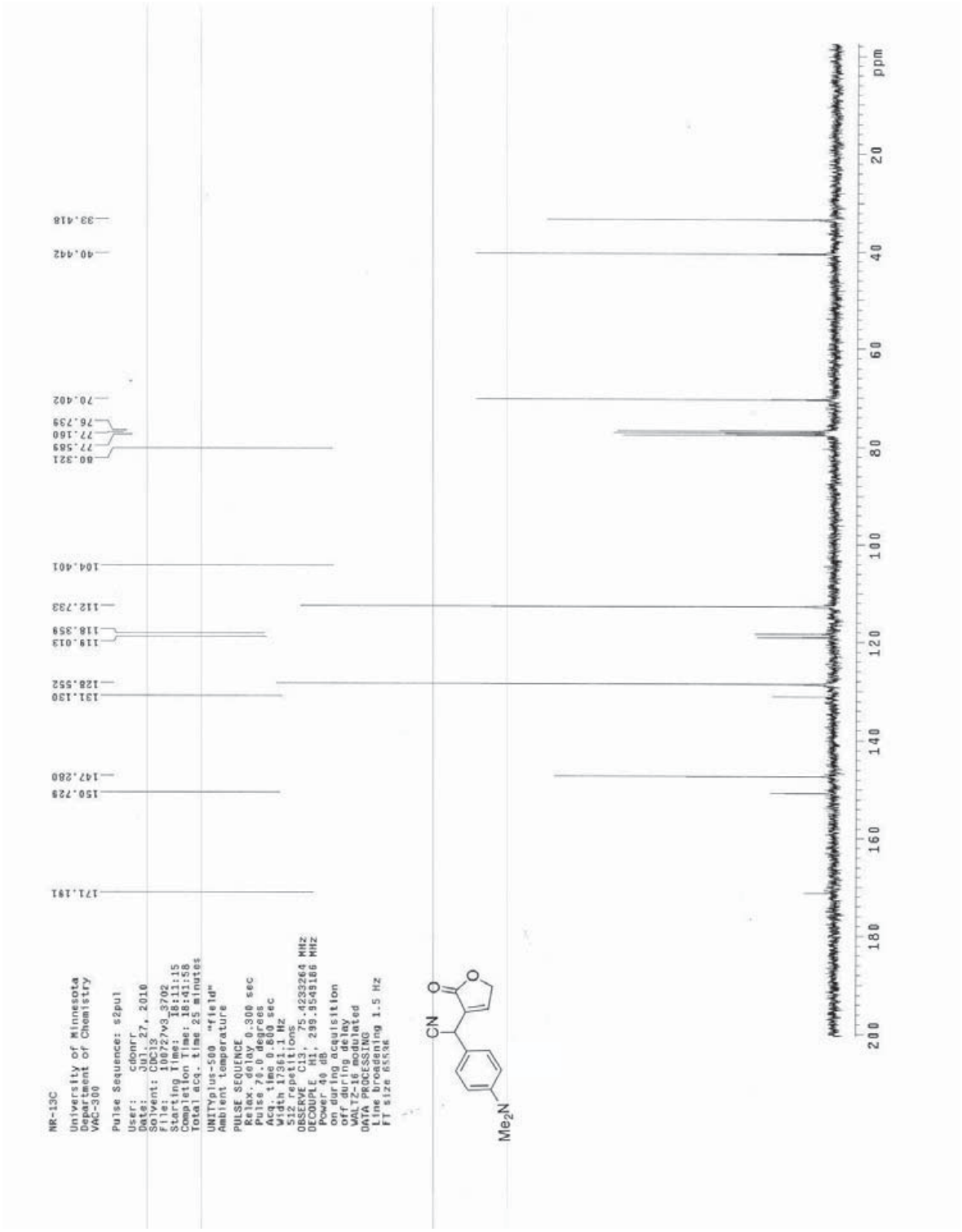

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Aug. 19, 2010
Solvent: c6d6
File: SML-1-105_F20-22
Starting Time: 11:57:37
Completion Time: 11:58:38
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5999.7 Hz
16 repetitions
OBSERVE H1, 300.1683541 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
CN
O
O
MeO
7.171
7.160
7.143
7.133
6.678
6.667
6.660
6.645
6.638
6.627
6.352
6.346
6.344
6.342
6.336
4.356
4.353
3.694
3.688
3.682
3.633
3.627
3.621
3.580
3.575
3.570
3.519
3.514
3.508
3.225
10
9
8
7
6
5
4
3
2
1
ppm
27.10
15.70
7.61
7.18
17.52
24.89

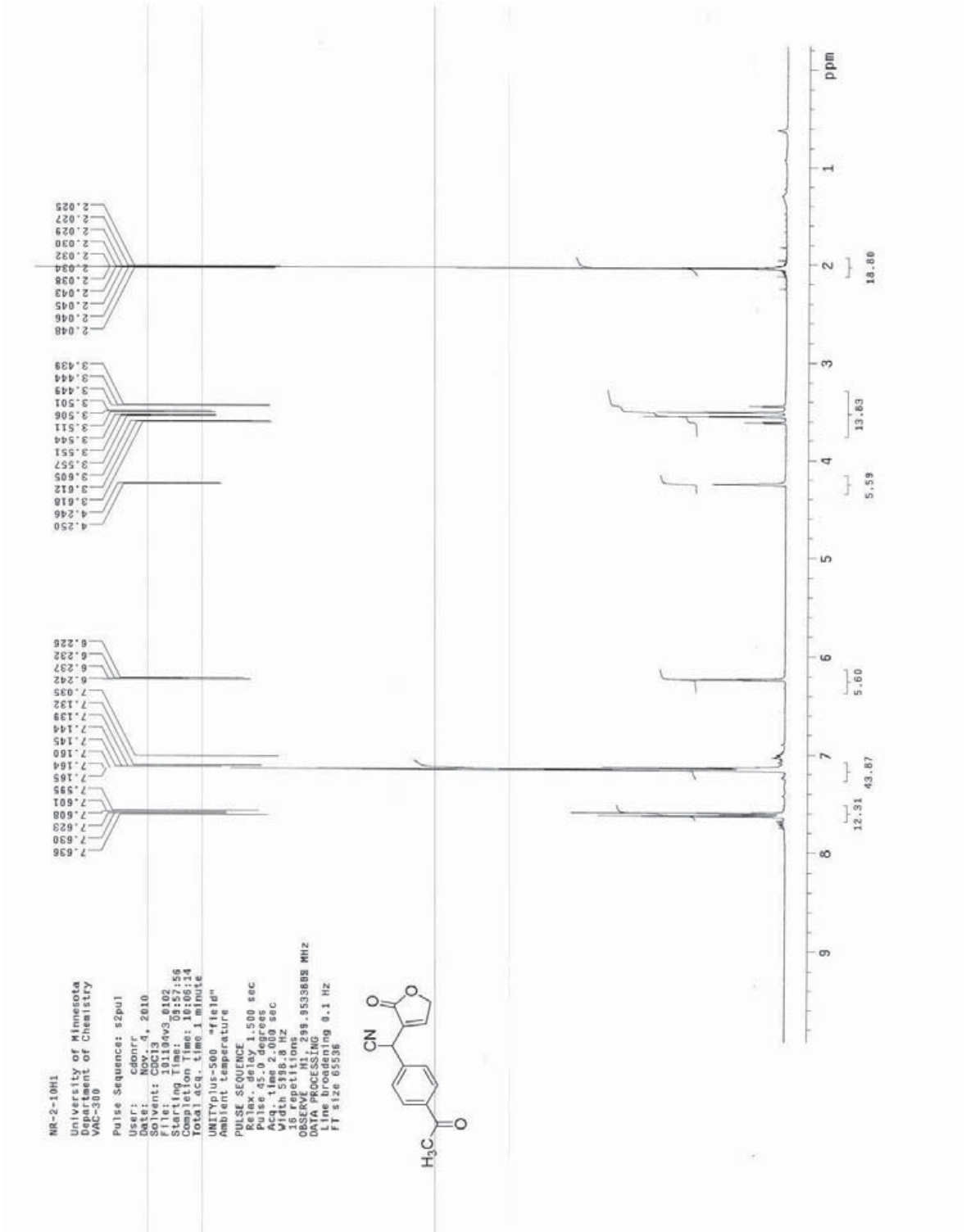

NR-p-MeO
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: sdonrr
Date: Sep 8, 2010
Solvent: CDCl3
File: I0907v3_6702
Starting Time: 01:15:36
Completion Time: 01:47:37
Total acq. time 25 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233248 MHz
DECOUPLE H1, 299.9549166 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.016
160.107
147.666
130.856
129.051
124.056
118.022
114.882
77.581
77.160
76.739
70.473
55.517
33.565
CN
O
O
MeO
200
180
160
140
120
100
80
60
40
20
ppm

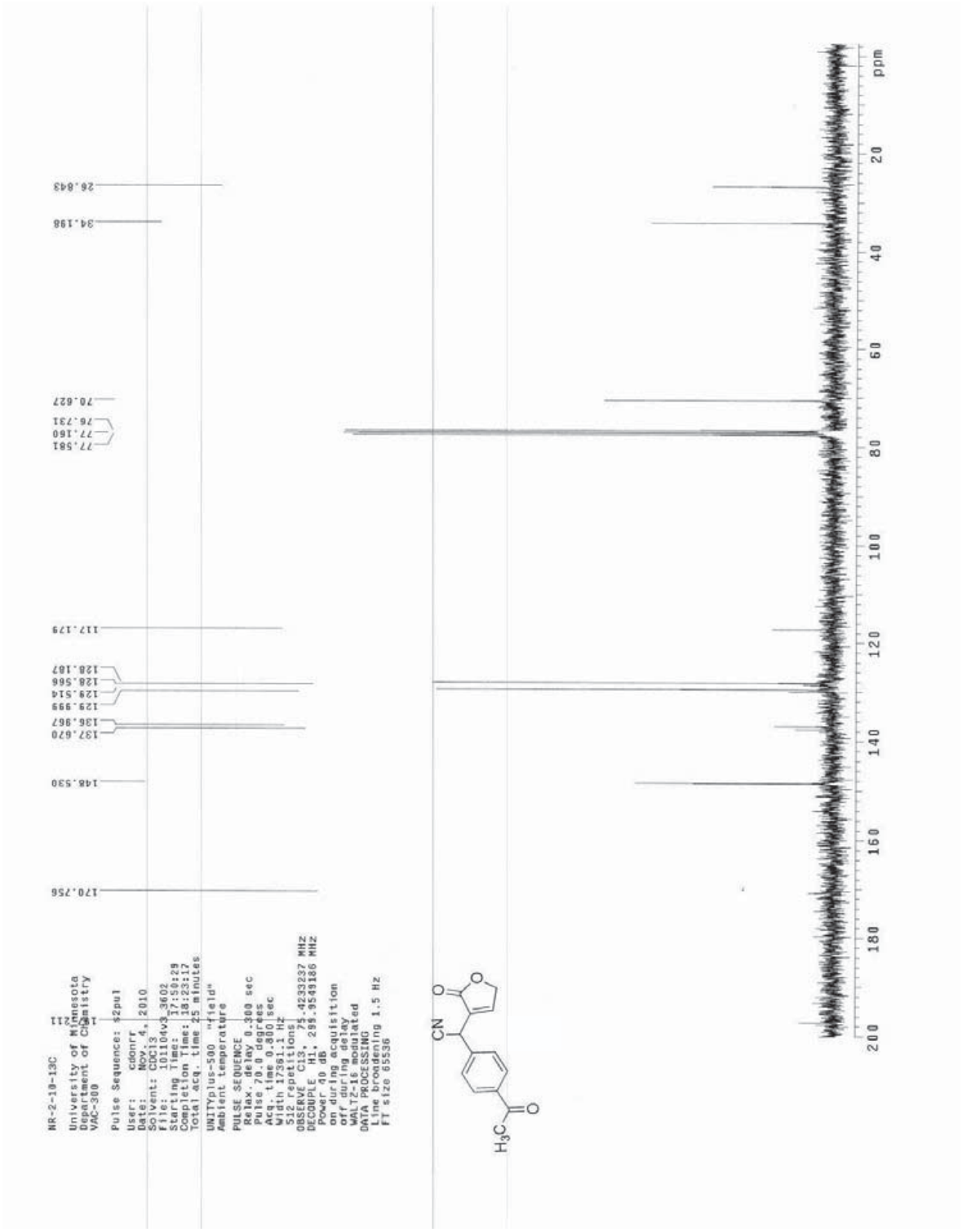

NR-276-1
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Sep. 17, 2010
Solvent: CDCl3
File: 100917v3_1702
Starting Time: 17:14:08
Completion Time: 17:23:39
Total Acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5198.8 Hz
16 repetitions
OBSERVE H1, 299.9533803 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
CN
O
O
OMe
ppm
26.78
8.51
8.20
8.15
19.96
28.40

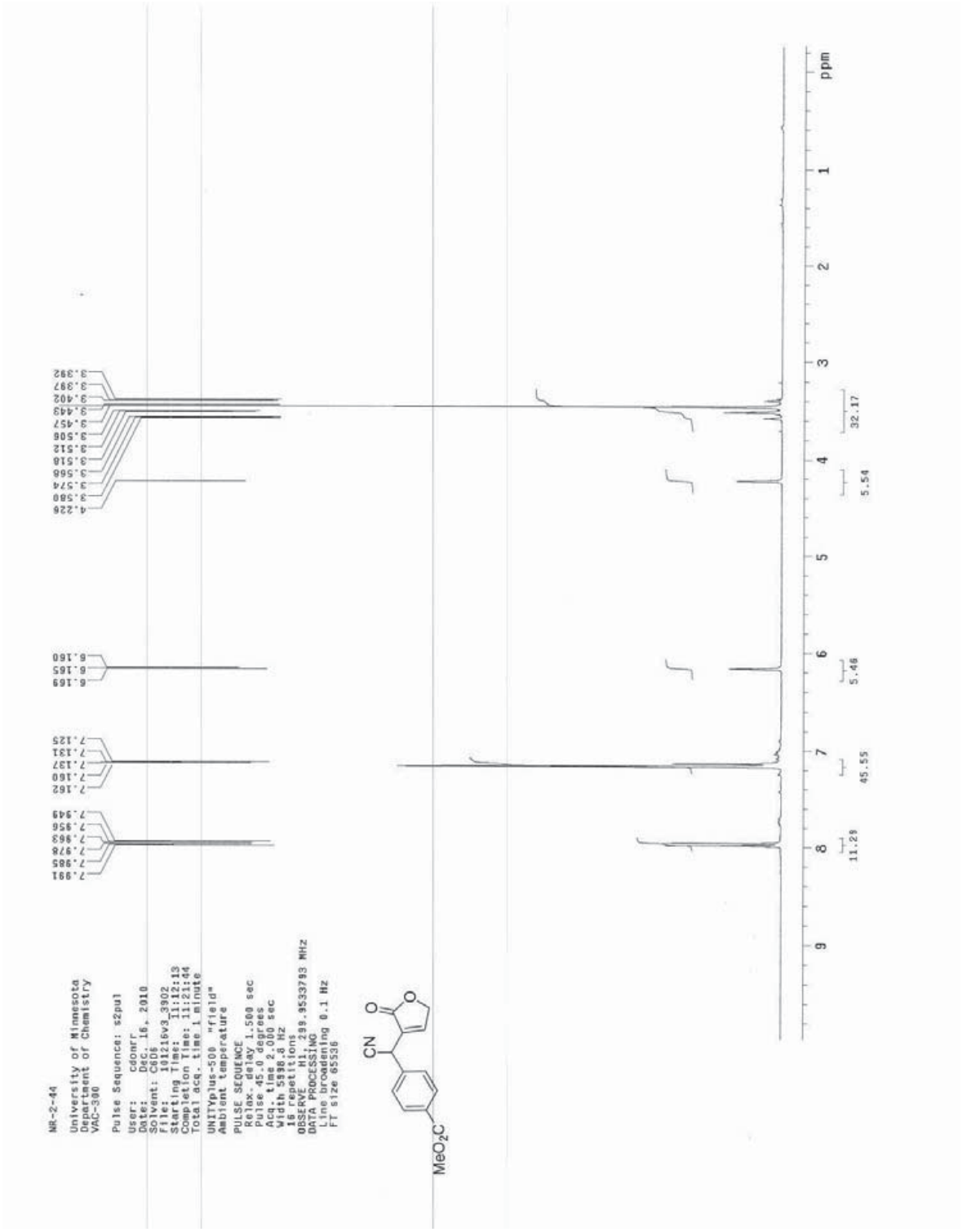

NR-276-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Sep. 18, 2010
Solvent: CDCl3
File: 100918v3_0102
Starting Time: 11:49:11
Completion Time: 12:07:13
Total acq. time 12 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
256 repetitions
OBSERVE C13, 75.4233285 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
160.275
148.361
133.582
130.589
130.343
118.841
117.678
114.418
113.576
77.581
77.160
76.731
70.522
55.482
34.057
CN
O
O
OMe
200
180
160
140
120
100
80
60
40
20
ppm

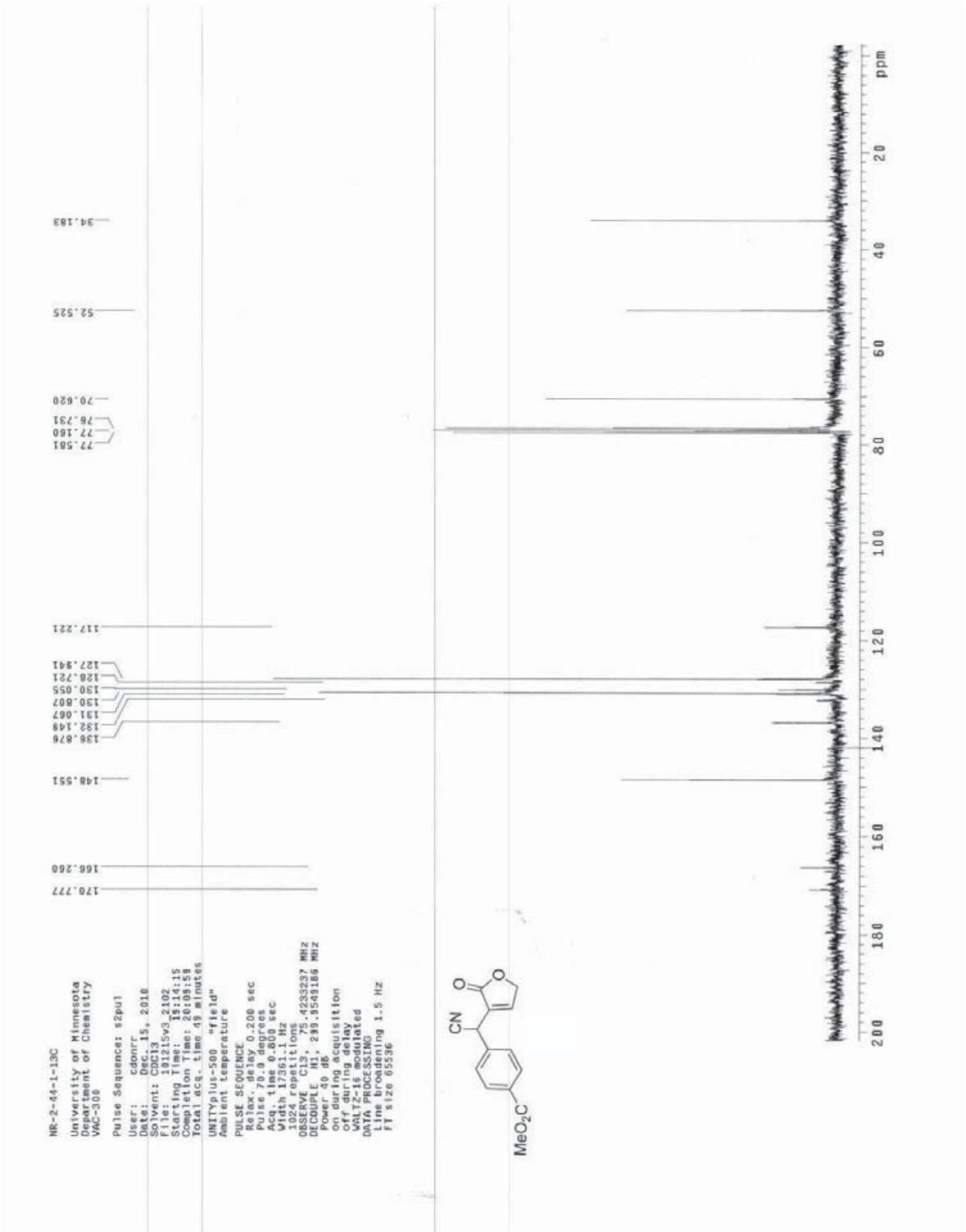

NR-263-1Pure
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jul. 27, 2010
Solvent: C6D6
File: 10727v3_1502
Starting Time: 12:25:26
Completion Time: 12:42:29
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
delay 1.500 sec
Pulse d5.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533801 MHz
DATA PROCESSING
7.245
7.235
7.228
7.212
7.206
7.195
7.160
6.455
6.445
6.437
6.422
6.415
6.404
6.366
6.360
6.356
4.389
4.384
3.636
3.630
3.624
3.575
3.569
3.563
3.520
3.516
3.460
3.455
2.636
2.492
2.412
2.372
2.363
2.340
2.333
2.185
0.616
13.63
6.32
14.14
6.37
15.64
43.91
ppm
CN
O
O
Me2N

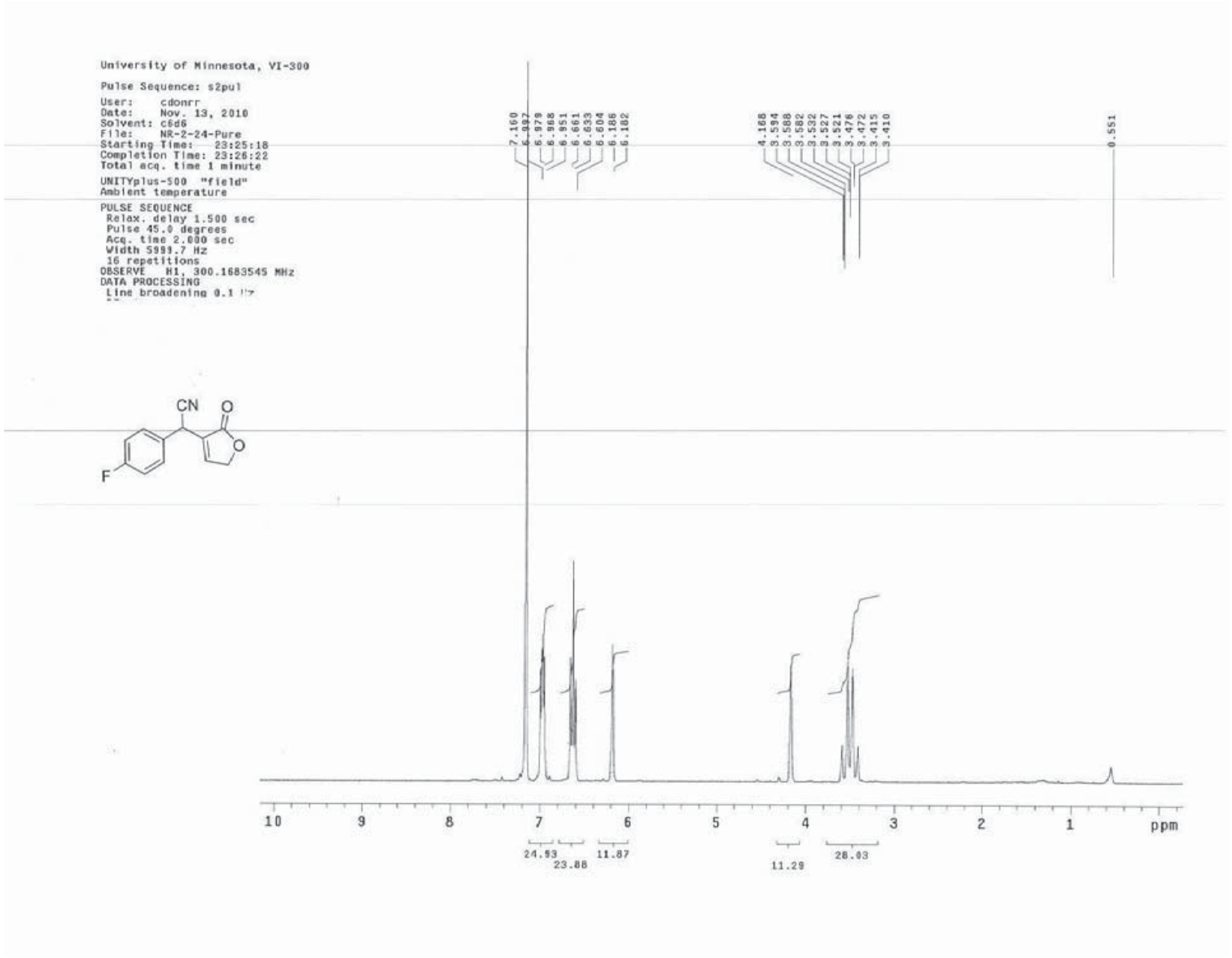

NR-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Jul. 27, 2010
Solvent: CDCl3
File: 10727v3_3702
Starting Time: 18:11:15
Completion Time: 18:41:58
Total acq. time 25 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233264 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.191
150.729
147.280
131.130
128.552
119.013
118.359
112.733
104.401
80.321
77.589
77.160
76.739
70.402
40.942
33.418
CN
O
O
Me2N
200
180
160
140
120
100
80
60
40
20
ppm

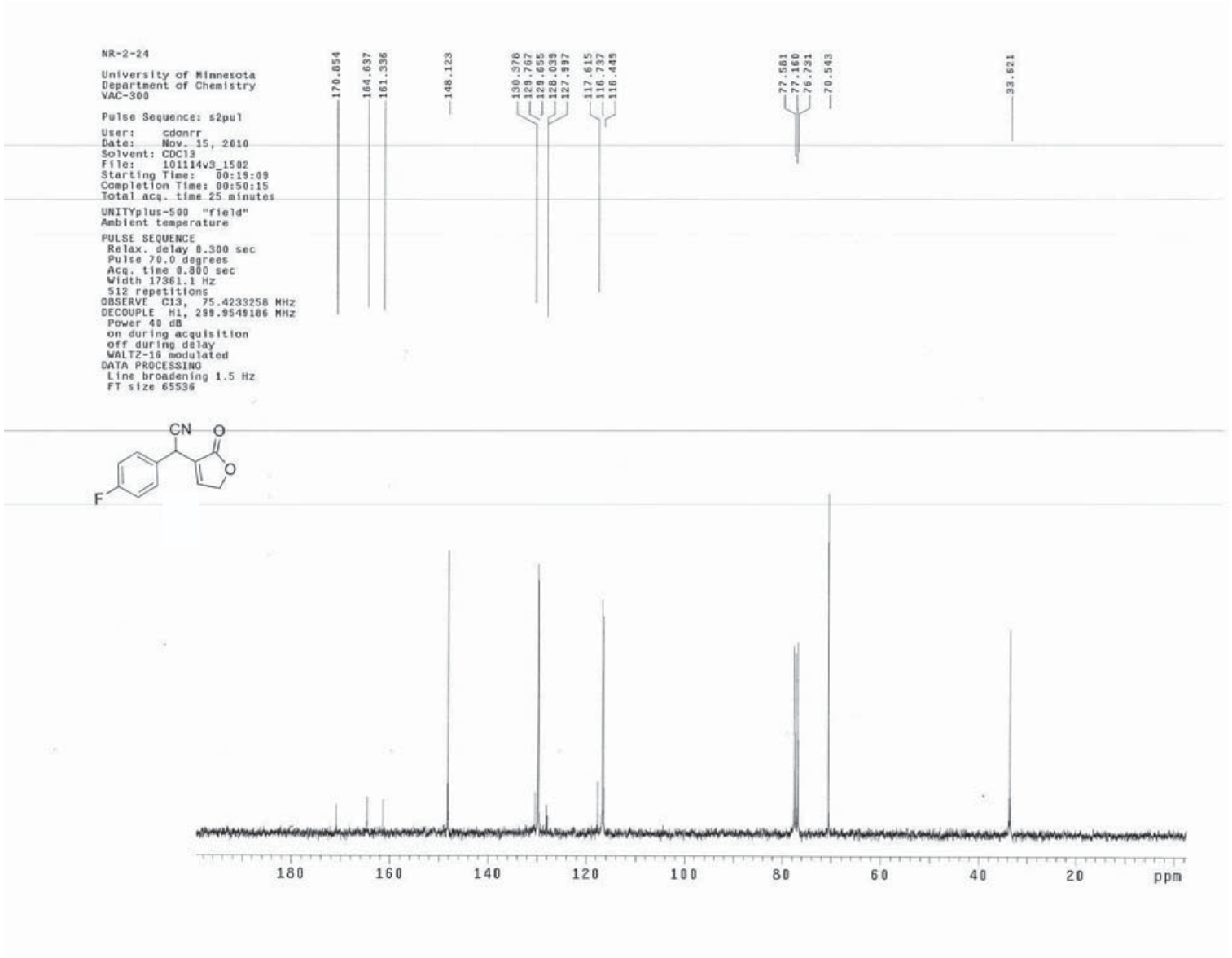

NR-2-10H1
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 4, 2010
Solvent: CDCl3
File: 101104v3_0102
Starting Time: 03:57:56
Completion Time: 10:05:14
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9538898 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.636
7.630
7.629
7.608
7.601
7.595
7.165
7.164
7.160
7.145
7.144
7.139
7.132
7.035
6.242
6.237
6.232
6.226
4.250
4.246
3.618
3.612
3.605
3.557
3.551
3.544
3.511
3.506
3.501
3.449
3.444
3.439
2.048
2.046
2.045
2.043
2.038
2.034
2.032
2.030
2.029
2.027
2.025
12.31
43.87
5.60
5.59
13.63
18.80
ppm
CN
O
O
O
H3C

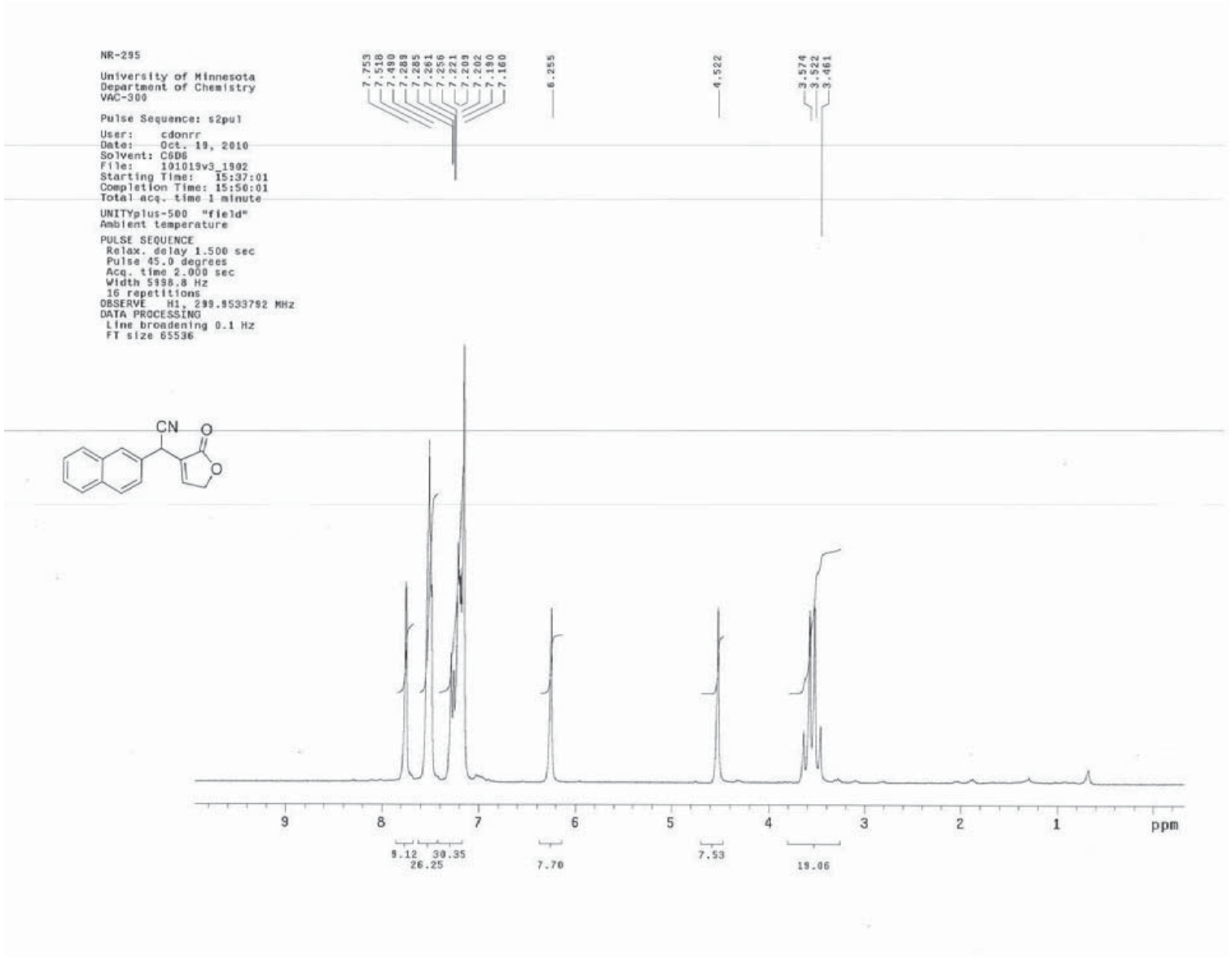

NR-2-10-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 4, 2010
Solvent: CDCl3
File: 101104v3_3602
Starting Time: 17:50:29
Completion Time: 18:23:17
Total acq. time 25 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233237 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
170.756
148.530
137.670
136.867
129.999
129.514
128.566
128.187
117.179
77.581
77.160
76.731
76.627
34.198
26.843
CN
O
O
O
H3C
200
180
160
140
120
100
80
60
40
20
ppm

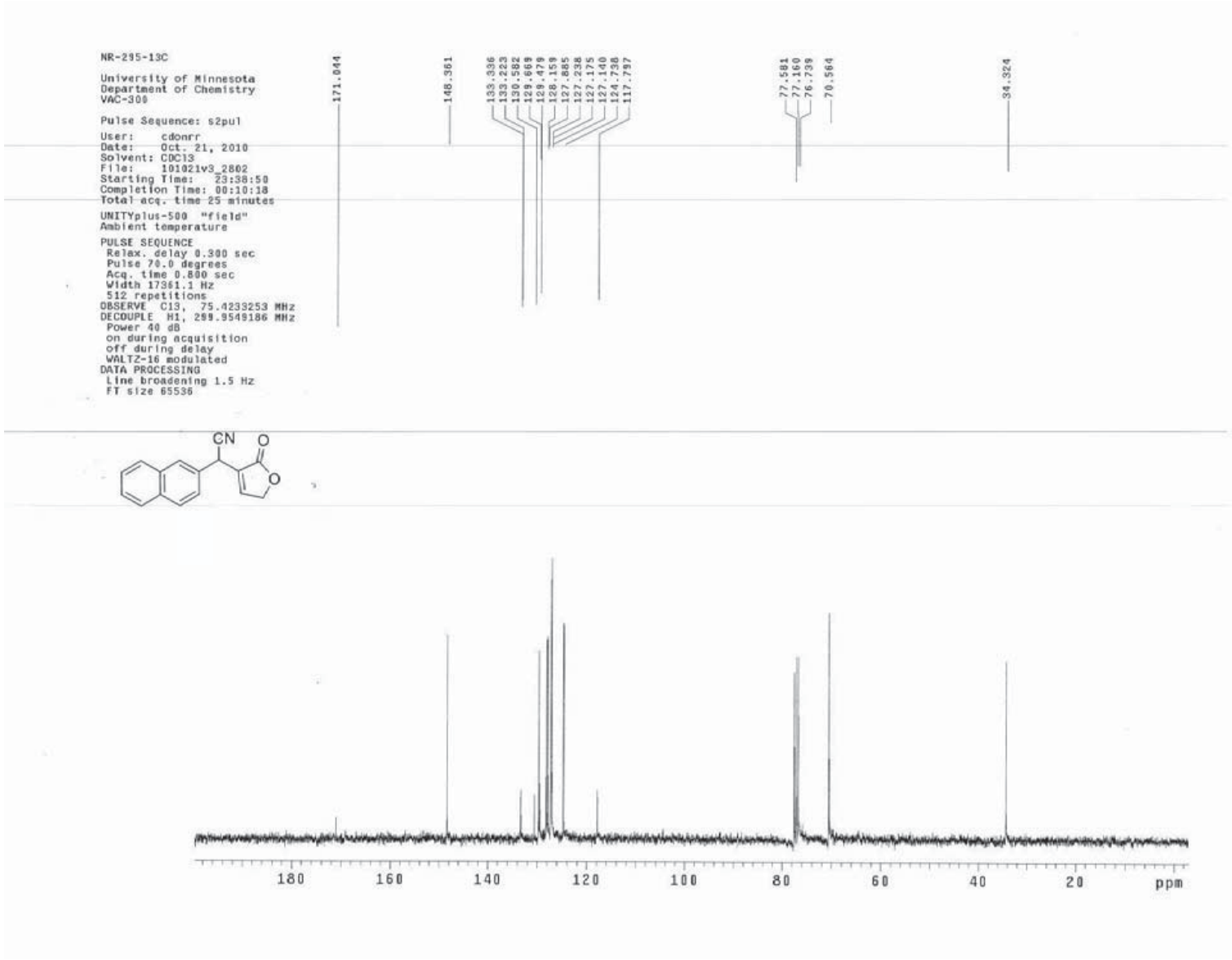

NR-2-44
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 16, 2010
Solvent: C6D6
File: 101216v3_3902
Starting Time: 11:12:13
Completion Time: 11:21:44
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533793 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.991
7.985
7.978
7.963
7.956
7.949
7.162
7.160
7.137
7.131
7.125
6.169
6.165
6.160
4.226
3.580
3.574
3.560
3.518
3.512
3.506
3.457
3.449
3.402
3.397
3.392
CN
O
O
MeO2C
11.28
45.55
5.46
5.54
32.17
ppm

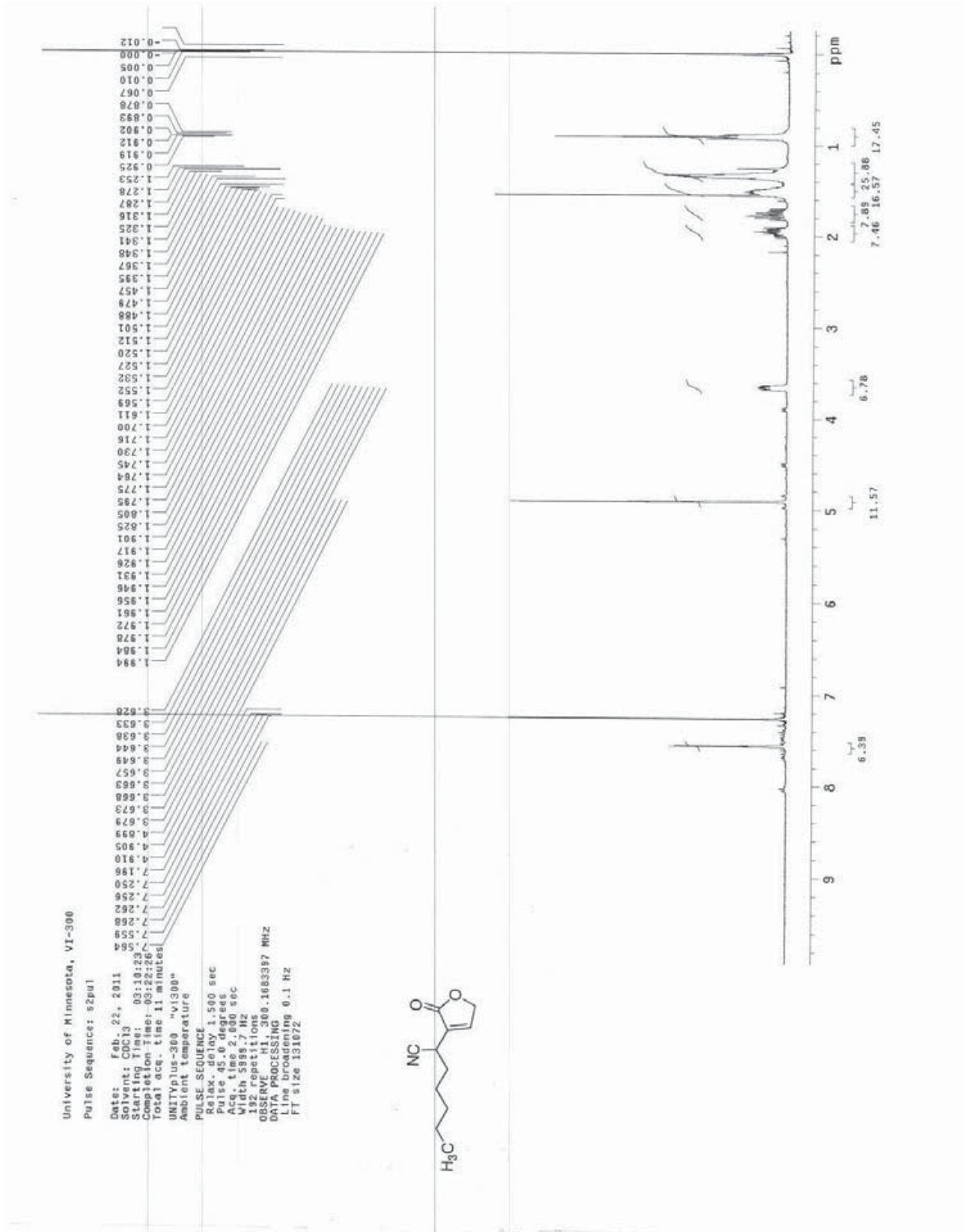

NR-2-44-1-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Dec. 15, 2010
Solvent: CDCl3
File: 101215v3_2102
Starting Time: 13:14:15
Completion Time: 20:05:59
Total acq. time 49 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.200 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
1024 repetitions
OBSERVE C13, 75.4233237 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
170.777
166.260
148.551
136.876
132.149
131.067
130.807
130.055
128.721
127.941
117.221
77.581
77.160
76.731
70.620
52.525
34.183
CN
O
O
MeO2C
200
180
160
140
120
100
80
60
40
20
ppm

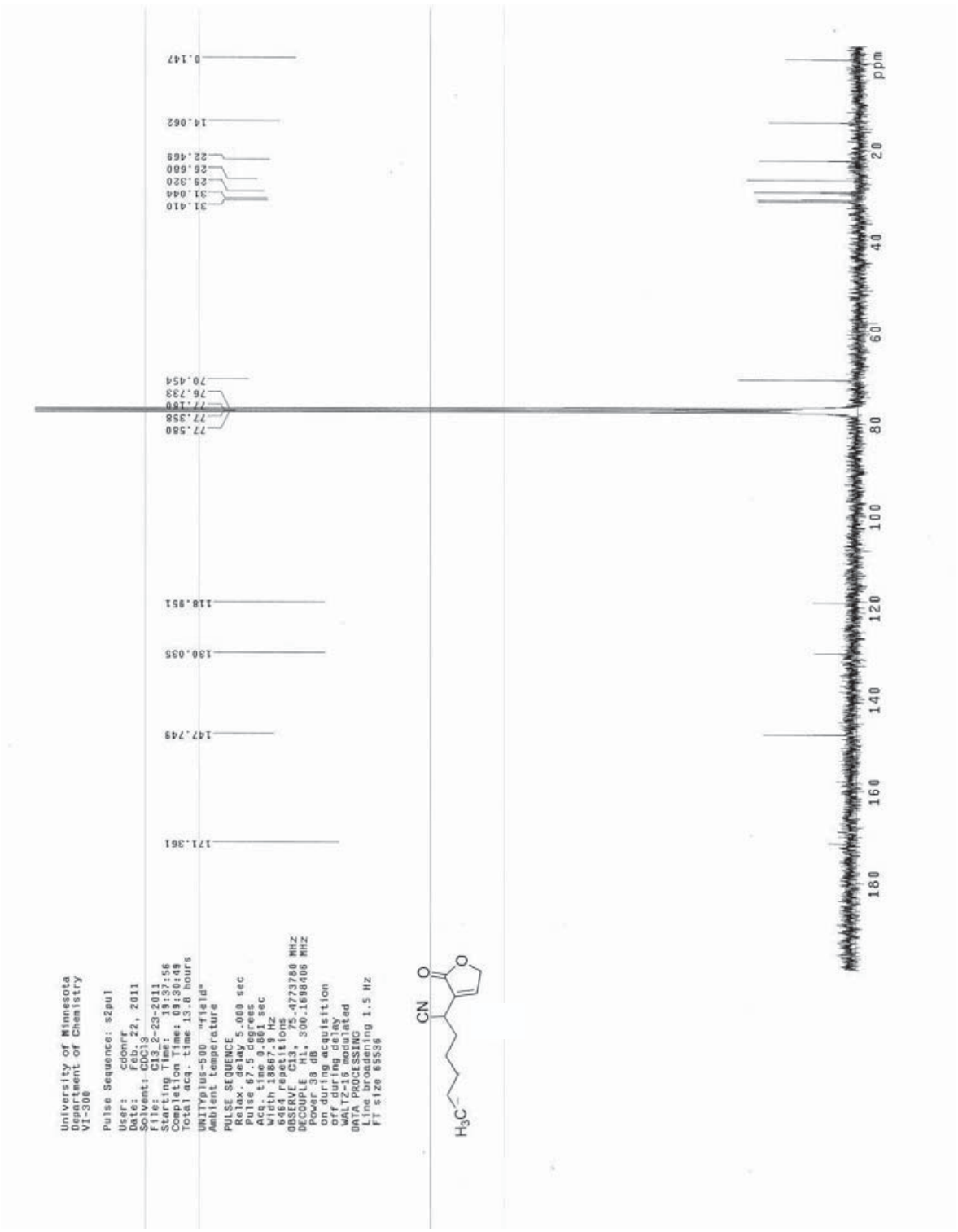

University of Minnesota, VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 13, 2010
Solvent: c6d6
File: NR-2-24-Pure
Starting Time: 23:25:18
Completion Time: 23:26:22
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5993.7 Hz
16 repetitions
OBSERVE H1, 300.1683545 MHz
DATA PROCESSING
Line broadening 0.1 Hz
7.160
6.997
6.979
6.968
6.951
6.661
6.653
6.604
6.186
6.182
4.168
3.594
3.588
3.582
3.532
3.527
3.521
3.476
3.472
3.415
3.410
0.551
CN
O
O
F
10
9
8
7
6
5
4
3
2
1
ppm
24.93
23.88
11.87
11.29
28.03

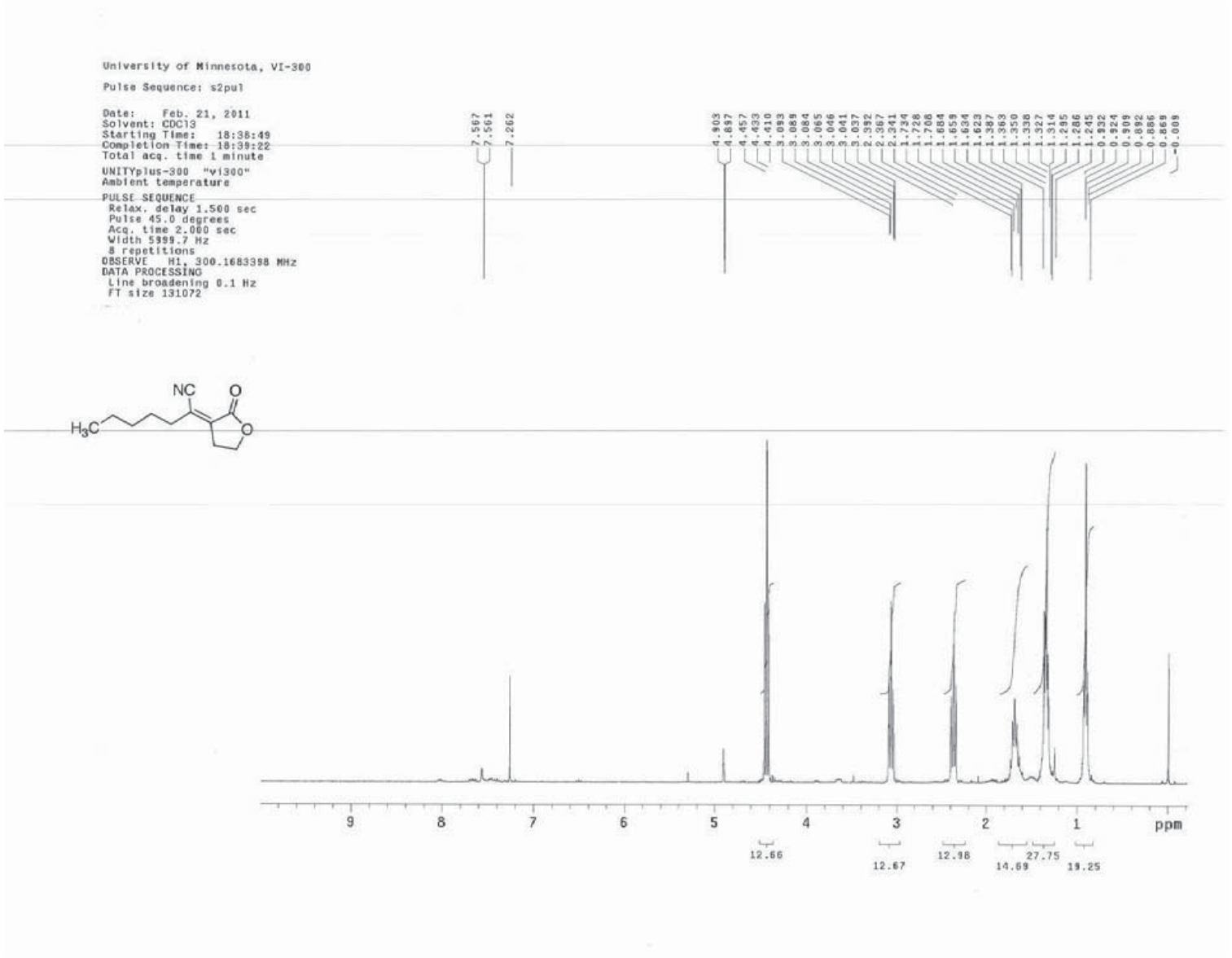

NR-2-24
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Nov. 15, 2010
Solvent: CDCl3
File: 101114v3_1502
Starting Time: 00:19:09
Completion Time: 00:50:15
Total acq. time 25 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17961.1 Hz
512 repetitions
OBSERVE C13, 75.4233258 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
170.854
164.637
161.336
148.123
130.376
129.767
129.655
128.039
127.997
117.615
116.737
116.449
77.581
77.160
76.731
70.543
33.621
CN
O
O
F
180
160
140
120
100
80
60
40
20
ppm

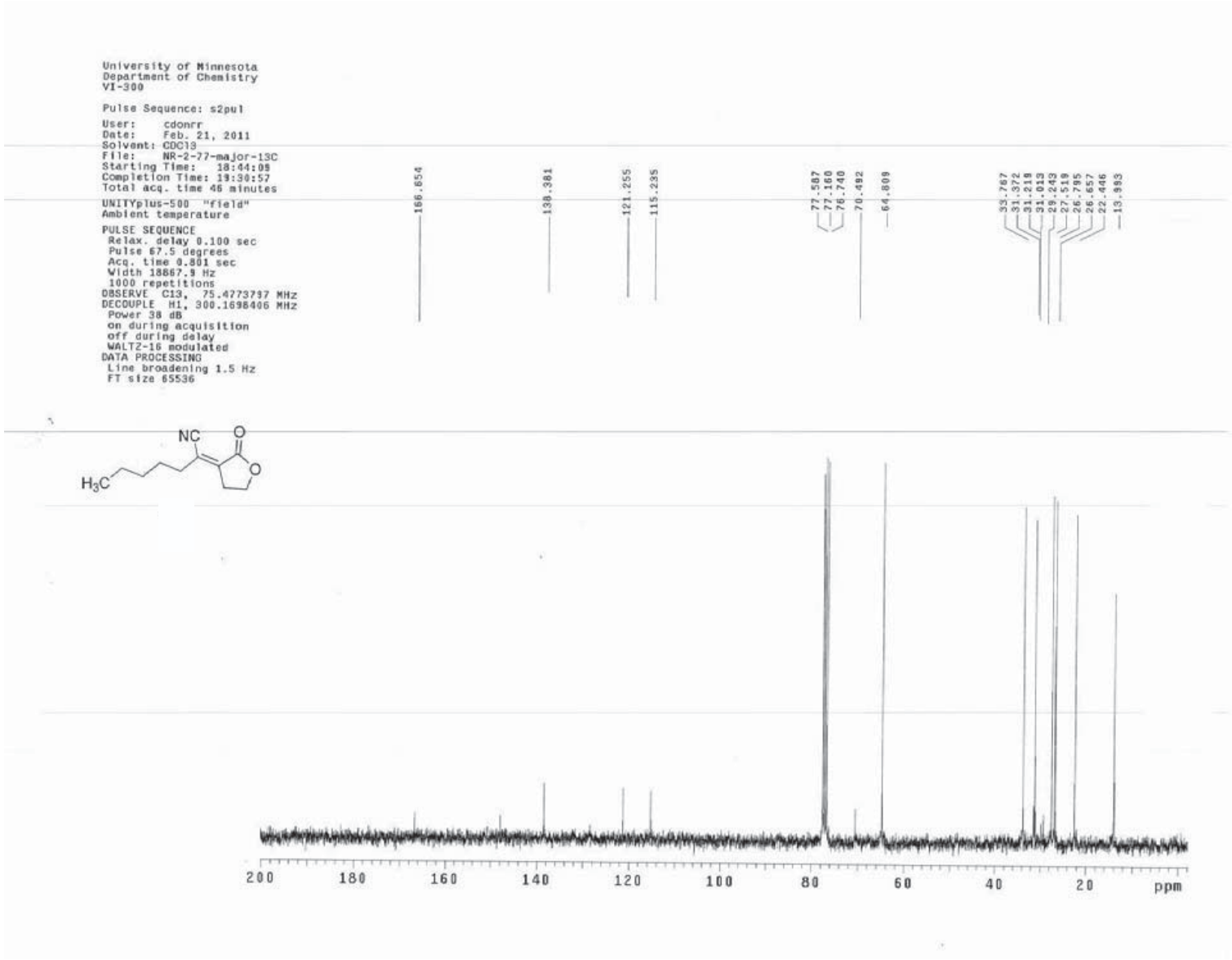

NR-295
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Oct. 19, 2010
Solvent: C6D6
File: 101019v3_1902
Starting Time: 15:37:01
Completion Time: 15:50:01
Total acq. time 1 minute
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9533792 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
7.753
7.518
7.490
7.288
7.285
7.261
7.256
7.221
7.209
7.202
7.190
7.160
6.255
4.522
3.574
3.522
3.461
CN
O
O
9
8
7
6
5
4
3
2
1
ppm
5.12
30.35
26.25
7.70
7.53
19.06

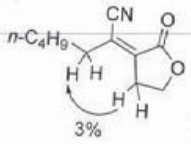

NR-295-13C
University of Minnesota
Department of Chemistry
VAC-300
Pulse Sequence: s2pul
User: cdonrr
Date: Oct. 21, 2010
Solvent: CDCl3
File: 101021v3_2802
Starting Time: 23:38:50
Completion Time: 00:10:18
Total acq. time 25 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.300 sec
Pulse 70.0 degrees
Acq. time 0.800 sec
Width 17361.1 Hz
512 repetitions
OBSERVE C13, 75.4233253 MHz
DECOUPLE H1, 299.9549186 MHz
Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
171.044
148.361
133.336
133.223
130.582
129.669
129.479
128.159
127.885
127.238
127.175
127.140
124.738
117.797
77.581
77.160
76.739
70.564
34.324
CN
O
O
180
160
140
120
100
80
60
40
20
ppm

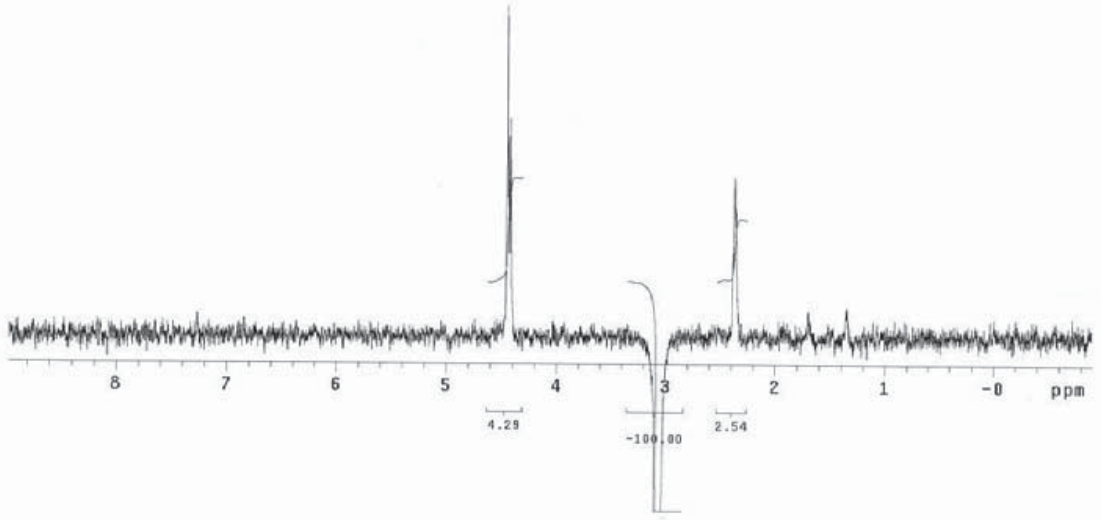

University of Minnesota, VI-300
Pulse Sequence: s2pul
Date: Feb 22, 2011
Solvent: CDCl3
Starting Time: 03:10:23
Completion Time: 03:22:26
Total acq. time 11 minutes
UNITYplus-300 "vi300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5995.7 Hz
192 repetitions
OBSERVE H1, 300.1683387 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
NC
O
O
H3C
ppm

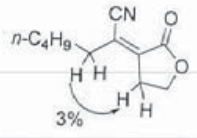

University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonr
Date: Feb. 22, 2011
Solvent: CDCl3
File: C13_2-23-2011
Starting Time: 13:37:56
Completion Time: 09:30:49
Total acq. time 13.8 hours
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 5.000 sec
Pulse 67.5 degrees
Acq. time 9.861 sec
Width 1866.9 Hz
4 repetitions
OBSERVE C13, 75.4733780 MHz
DECOUPLE H1, 300.1698400 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
0.147
14.062
22.468
26.680
29.320
31.044
31.410
70.454
76.733
77.160
77.358
77.580
118.951
130.035
147.749
171.361
CN
O
O
H3C
ppm
20
40
60
80
100
120
140
160
180

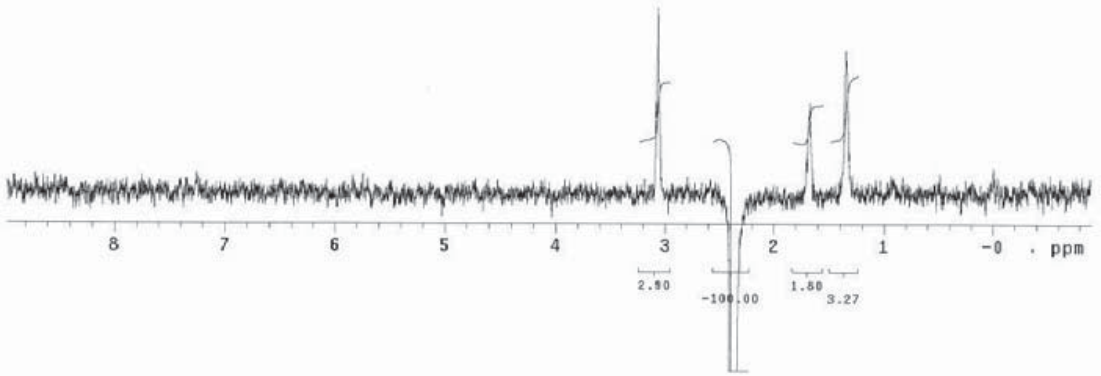

University of Minnesota, VI-300
Pulse Sequence: s2pul
Date: Feb. 21, 2011
Solvent: CDCl3
Starting Time: 18:38:49
Completion Time: 18:39:22
Total acq. time 1 minute
UNITYplus-300 "vi300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 5999.7 Hz
8 repetitions
OBSERVE H1, 300.1683398 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
7.567
7.561
7.262
4.903
4.897
4.457
4.433
4.410
3.093
3.089
3.084
3.065
3.046
3.041
3.037
2.392
2.387
2.341
1.734
1.728
1.708
1.684
1.659
1.654
1.623
1.387
1.363
1.350
1.338
1.327
1.314
1.295
1.286
1.245
0.932
0.924
0.909
0.892
0.886
0.869
-0.009
NC
O
O
H3C
9
8
7
6
5
4
3
2
1
ppm
12.66
12.67
12.98
14.69
27.75
19.25


University of Minnesota
Department of Chemistry
VI-300
Pulse Sequence: s2pul
User: cdonrr
Date: Feb. 21, 2011
Solvent: CDCl3
File: NR-2-77-major-13C
Starting Time: 18:44:08
Completion Time: 19:30:57
Total acq. time 46 minutes
UNITYplus-500 "field"
Ambient temperature
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 67.5 degrees
Acq. time 0.801 sec
Width 18867.9 Hz
1000 repetitions
OBSERVE C13, 75.4773787 MHz
DECOUPLE H1, 300.1698406 MHz
Power 38 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.5 Hz
FT size 65536
166.654
138.381
121.255
115.235
77.587
77.160
76.740
70.492
64.809
33.767
31.372
31.219
31.013
29.243
27.519
26.795
26.657
22.446
13.993
NC
O
O
H3C
200
180
160
140
120
100
80
60
40
20
ppm


CN
O
n-C4H9
H H
O
H
H
3%

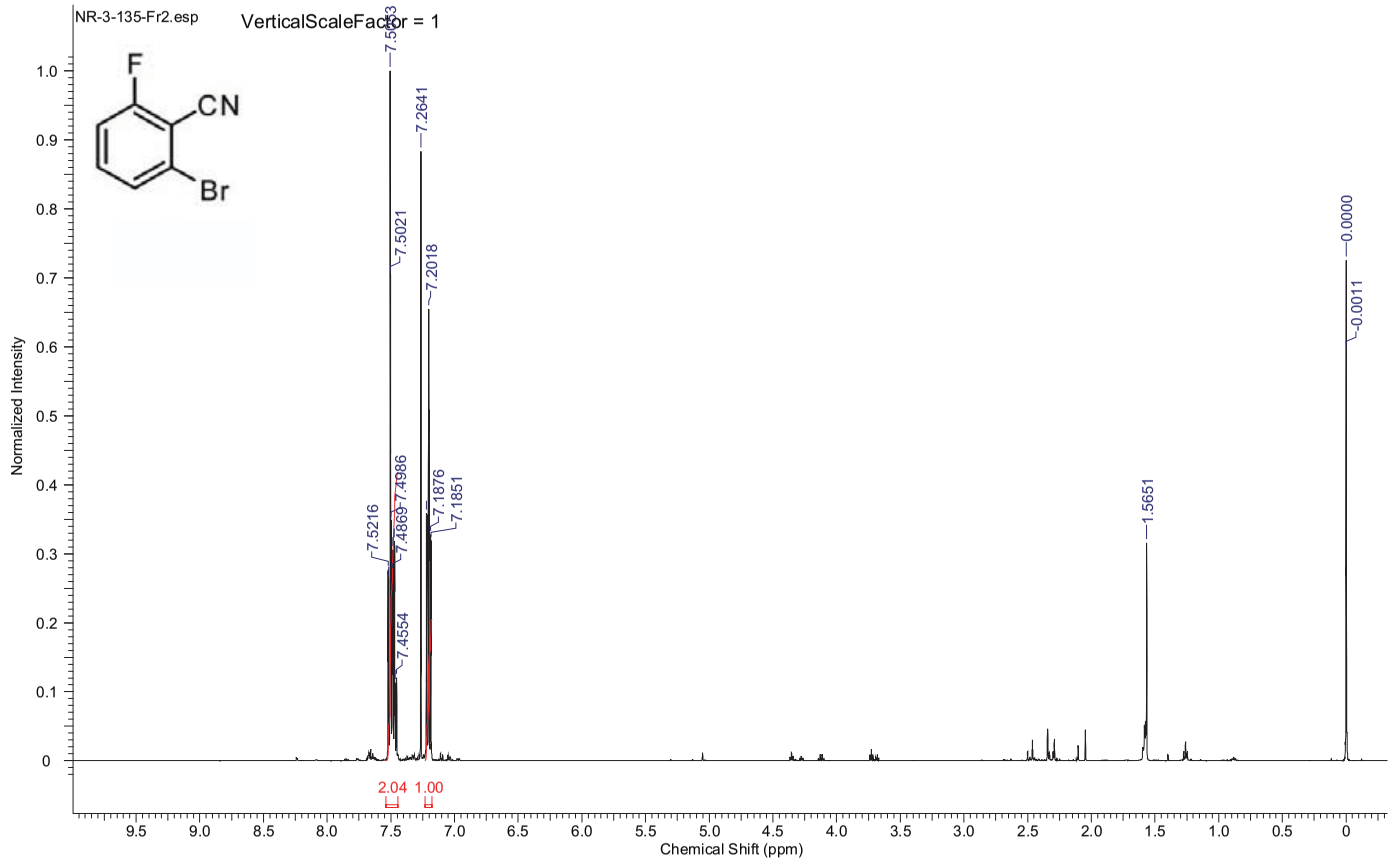

8
7
6
5
4
3
2
1
-0
ppm
4.29
-100.00
2.54


CN
O
n-C4H9
H H
O
H H
3%


8
7
6
5
4
3
2
1
-0
. ppm
2.50
-100.00
1.80
3.27

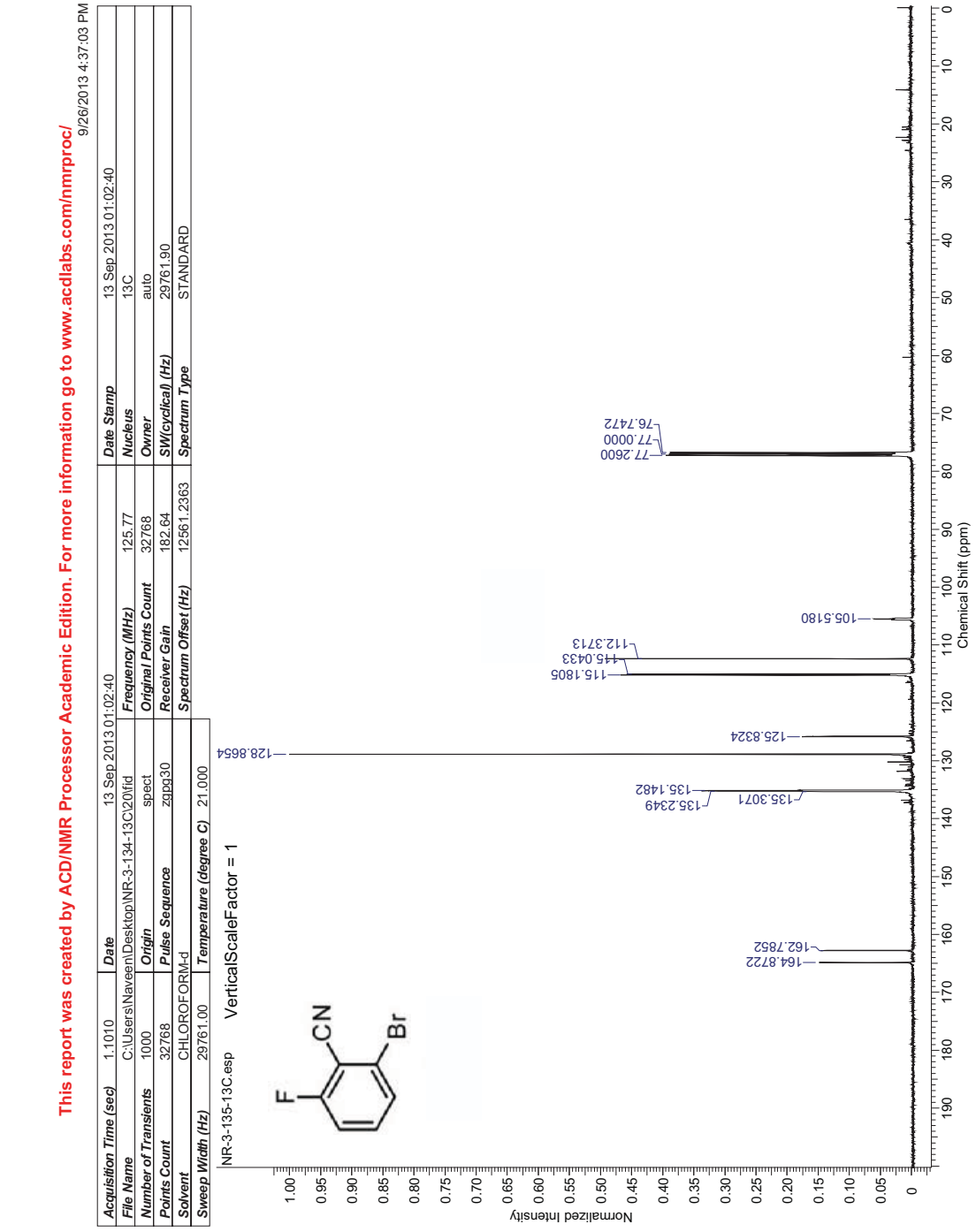
9/26/2013 4:33:18 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 3.2768 | ***Date*** | 12 Sep 2013 16:49:52 | | | ***Date Stamp*** | 12 Sep 2013 16:49:52 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-135-Fr2\10\fid | | | ***Frequency (MHz)*** | 500.13 | ***Nucleus*** | 1H |
| ***Number of Transients*** | 16 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | zg30 | ***Receiver Gain*** | 105.23 | ***SW(cyclical) (Hz)*** | 10000.00 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 3077.8884 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 9999.92 | ***Temperature (degree C)*** | 20.998 | | | | |



9/26/2013 4:37:03 PM

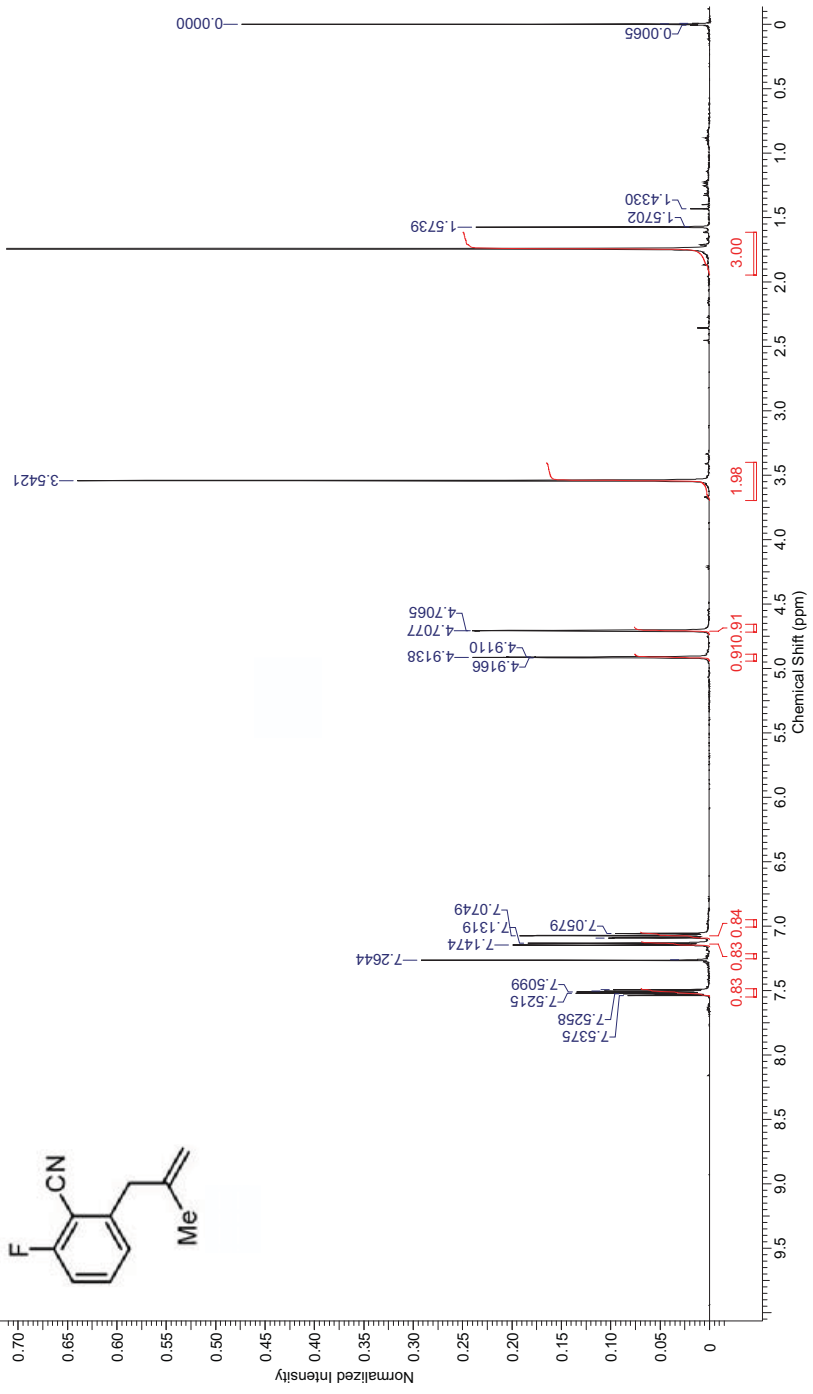
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 13 Sep 2013 01:02:40 | | | ***Date Stamp*** | 13 Sep 2013 01:02:40 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-134-13C\20\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 1000 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12561.2363 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 21.000 | | | | |



9/26/2013 4:39:22 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Sep 17 2013 |
| *Date Stamp* | Sep 17 2013 | *File Name* | C:\Users\Naveen\Desktop\NR-3-136-P.fid\fid | *Frequency (MHz)* | 499.87 |
| *Nucleus* | 1H | *Number of Transients* | 8 | *Original Points Count* | 15136 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul | *Receiver Gain* | 60.00 |
| *Solvent* | CHLOROFORM-d | *Spectrum Offset (Hz)* | 2498.4626 | *Spectrum Type* | STANDARD |
| *Sweep Width (Hz)* | 8000.00 | *Temperature (degree C)* | AMBIENT TEMPERATURE | | |

NR-3-136-P.esp VerticalScaleFactor = 1



9/26/2013 4:53:01 PM

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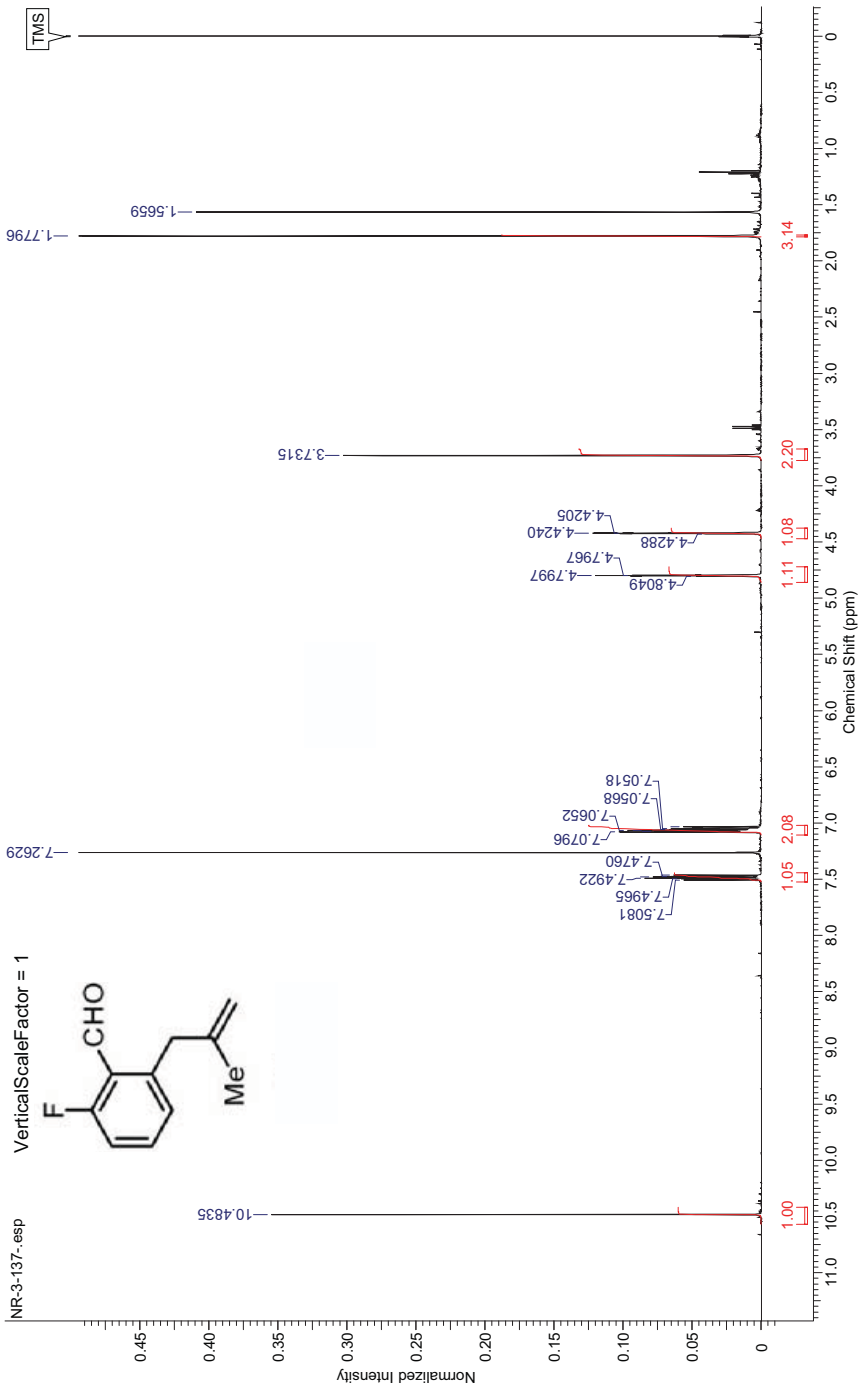
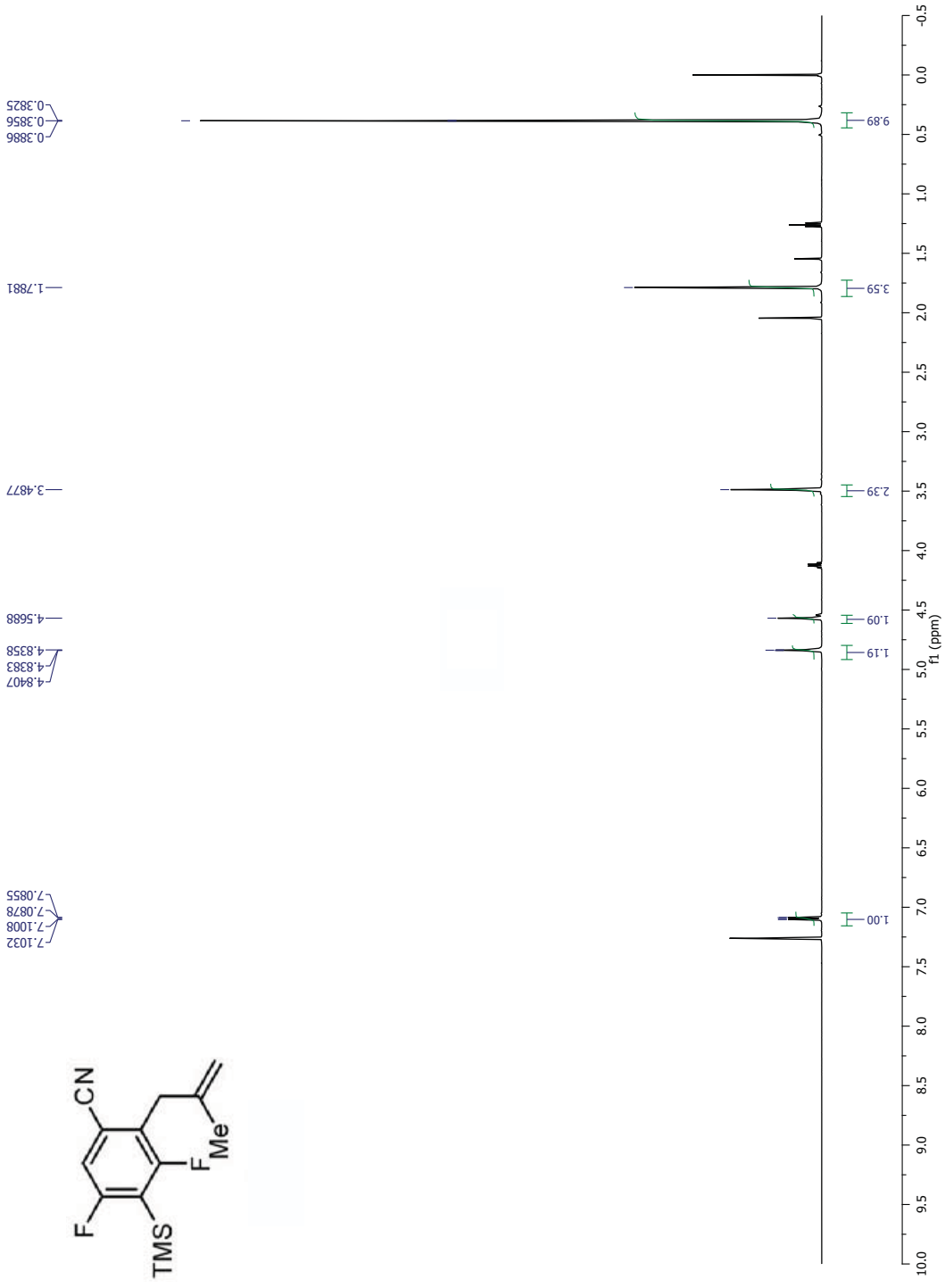
| File Name | C:\Users\Naveen\Desktop\NR-3-137-P\10\fid | Frequency (MHz) | 500.13 | Nucleus | 1H |
| Number of Transients | 16 | Origin | spect | Original Points Count | 32768 | Owner | auto |
| Points Count | 131072 | Pulse Sequence | zg30 | Receiver Gain | 105.23 | SW(cyclical) (Hz) | 10000.00 |
| Solvent | CHLOROFORM-d | | | Spectrum Offset (Hz) | 3077.2781 | Spectrum Type | STANDARD |
| Sweep Width (Hz) | 9999.92 | Temperature (degree C) | 21.000 | | | | |

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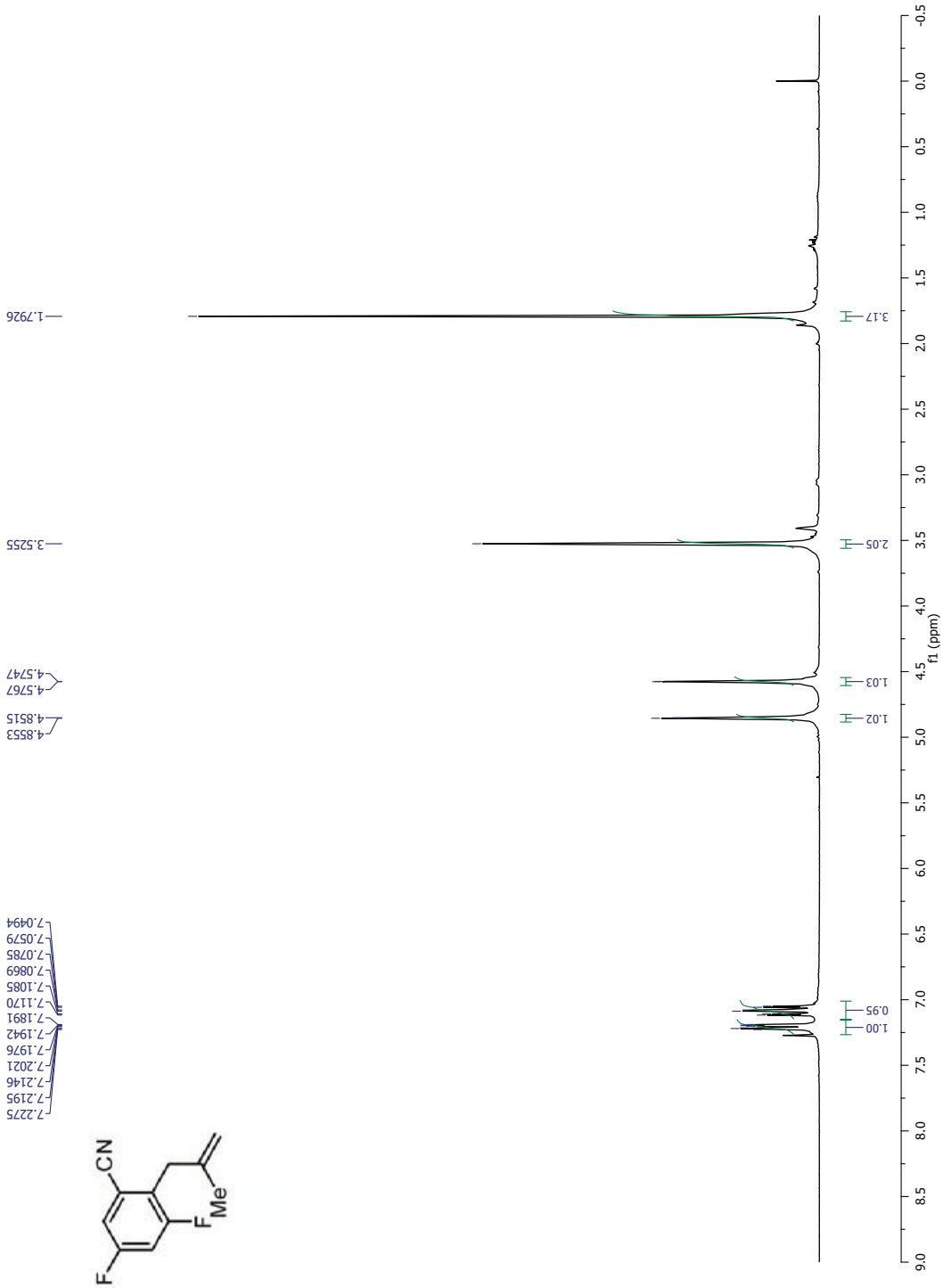
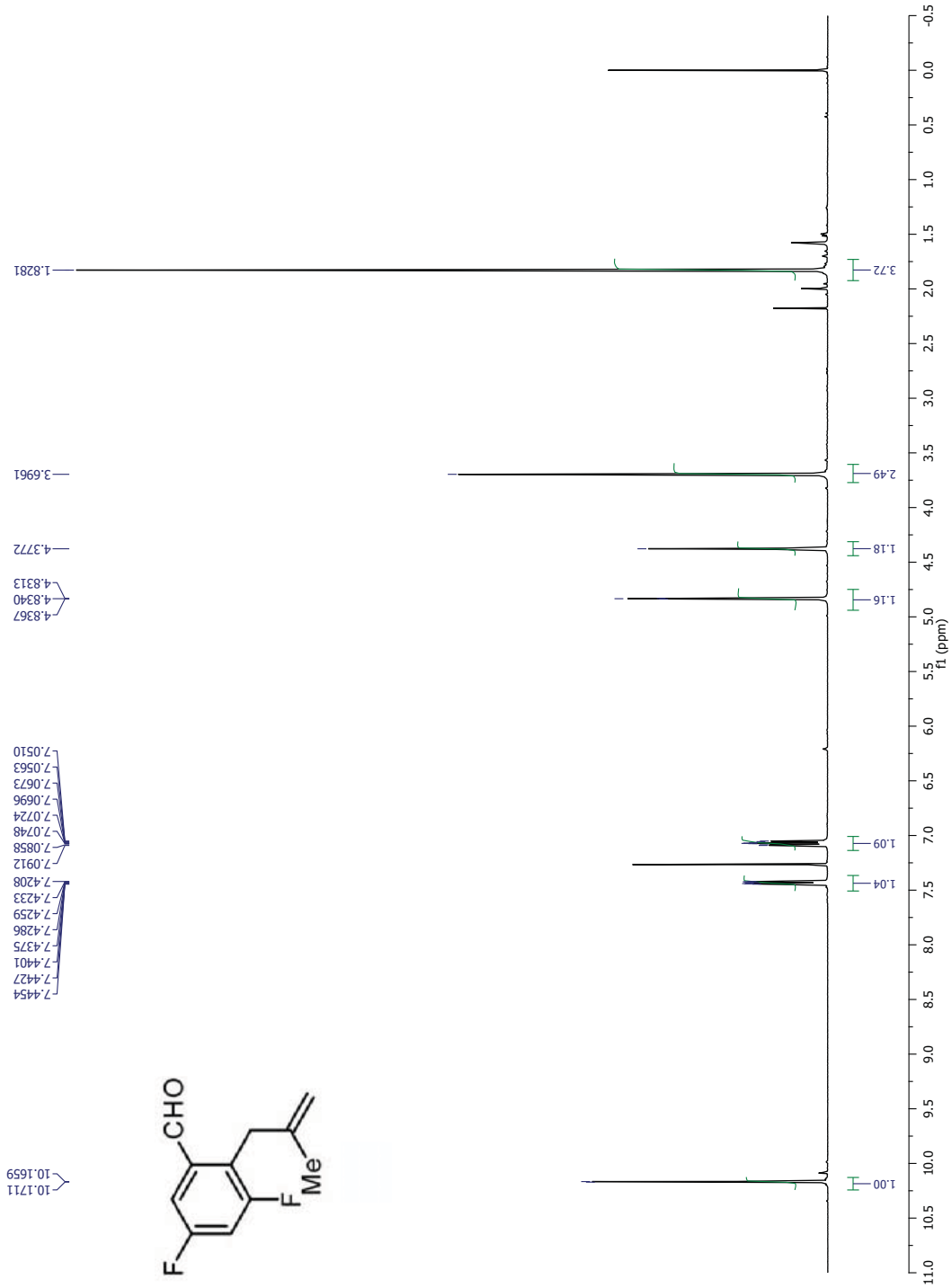
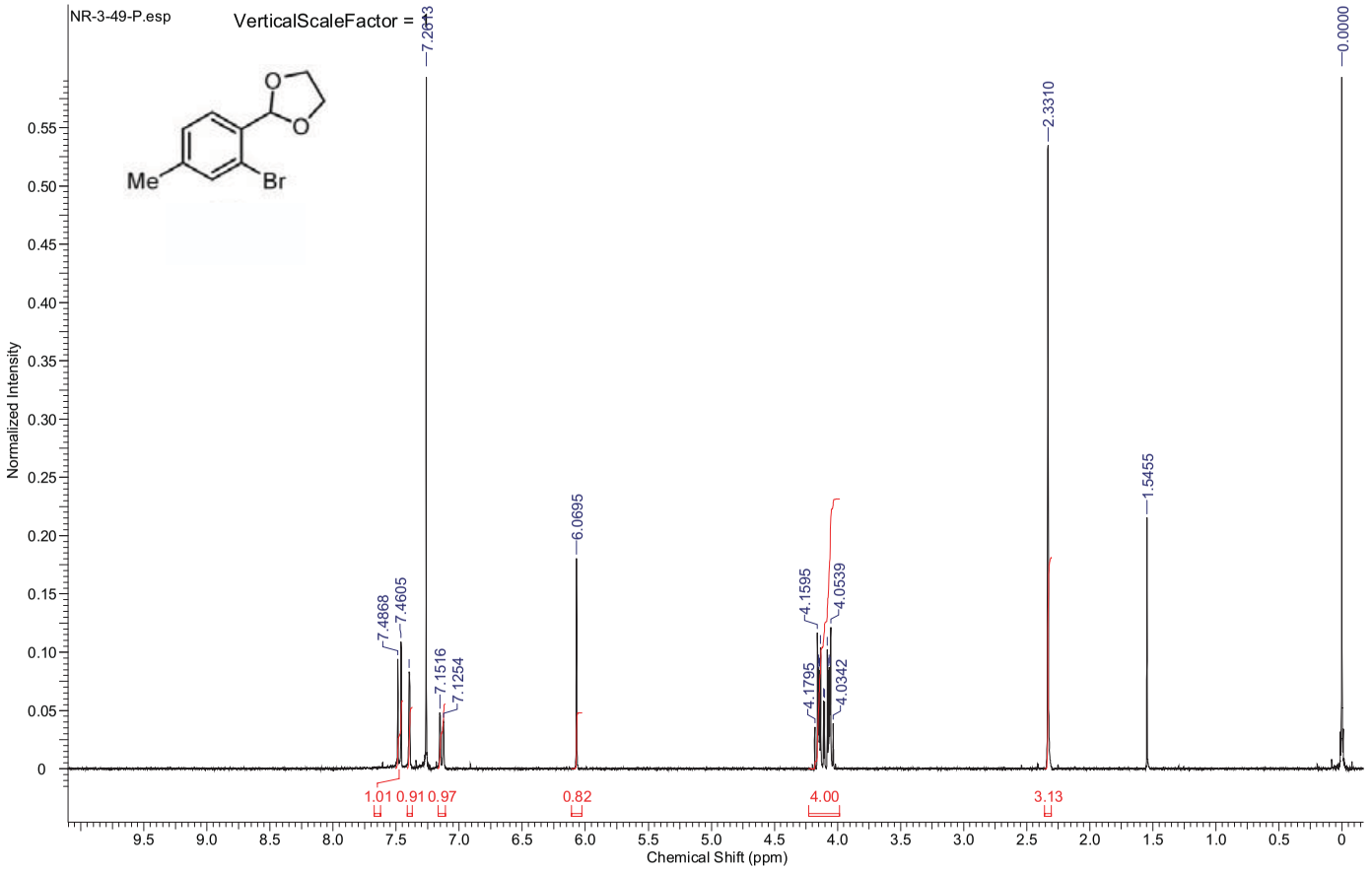
7.1008
7.0878
7.0855
4.8407
4.8383
4.8358
4.5688
3.4877
1.7881
0.3886
0.3856
0.3825
1.00
1.09
1.19
2.39
3.59
9.89
f1 (ppm)
CN
F
TMS
F
Me


7.2275
7.2195
7.2146
7.2021
7.1976
7.1942
7.1891
7.1170
7.1085
7.0869
7.0785
7.0579
7.0494
4.8553
4.8515
4.5767
4.5747
3.5255
1.7926
0.95
1.00
1.02
1.03
2.05
3.17
f1 (ppm)
CN
F
Me
F


10.1711
10.1659
7.4454
7.4427
7.4401
7.4375
7.4286
7.4259
7.4233
7.4208
7.0912
7.0858
7.0748
7.0724
7.0696
7.0673
7.0563
7.0510
4.8367
4.8340
4.8313
4.3772
3.6961
1.8281
1.00
1.04
1.09
1.16
1.18
2.49
3.72
CHO
F
Me
F
f1 (ppm)

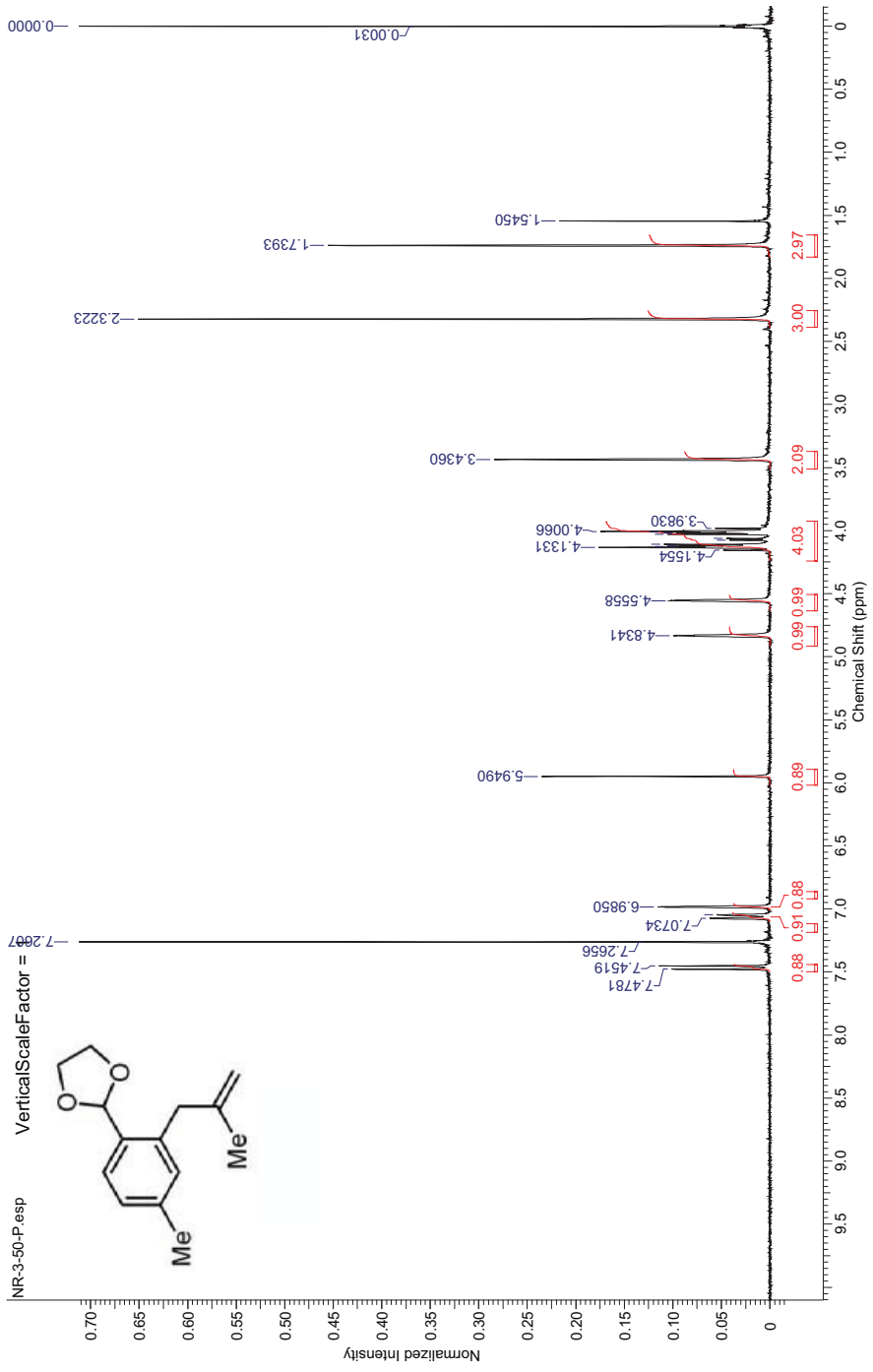
9/26/2013 5:00:03 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 2.0001 | ***Comment*** | NR-3-49-P University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | May 1 2013 | ***Date Stamp*** | May 1 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130501v3_4102.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 38.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2399.4790 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



9/26/2013 5:07:44 PM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-50-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | May 3 2013 | *Date Stamp* | May 3 2013 *File Name* C:\Users\Naveen\Desktop\130503v3 0802.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.4331 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



9/26/2013 5:14:56 PM

| | | | |
|---|---|---|---|
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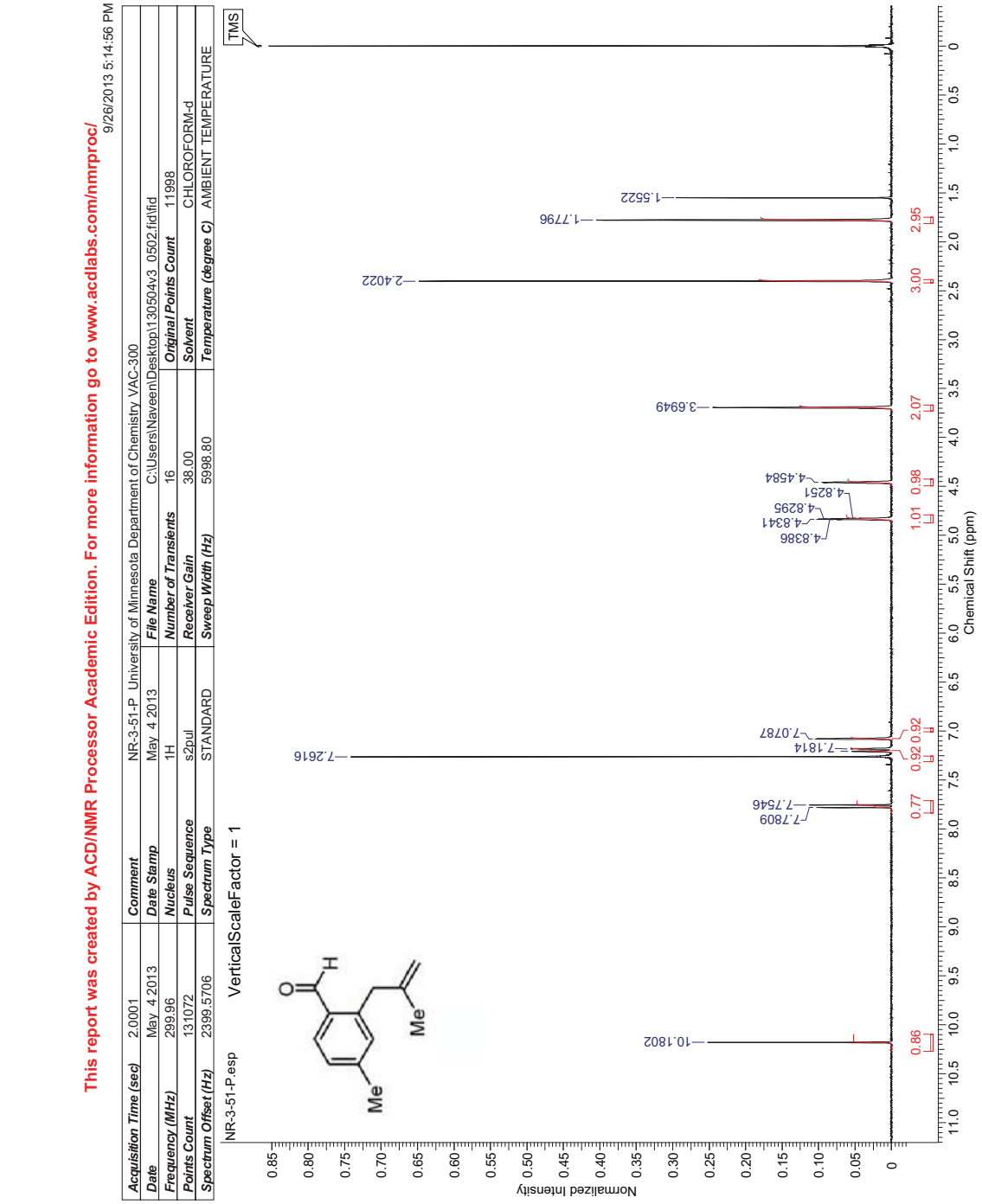
| ***Date*** | May 4 2013 | ***Date Stamp*** | May 4 2013 |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul |
| ***Spectrum Offset (Hz)*** | 2399.5706 | ***Spectrum Type*** | STANDARD |
| | | ***File Name*** | C:\Users\Naveen\Desktop\130504v3 0502.fid\fid |
| | | ***Number of Transients*** | 16 |
| | | ***Original Points Count*** | 11998 |
| | | ***Receiver Gain*** | 38.00 |
| | | ***Solvent*** | CHLOROFORM-d |
| | | ***Sweep Width (Hz)*** | 5998.80 |
| | | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |

NR-3-51-P.esp VerticalScaleFactor = 1



9/27/2013 10:23:38 AM

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|---|---|---|---|---|---|---|---|
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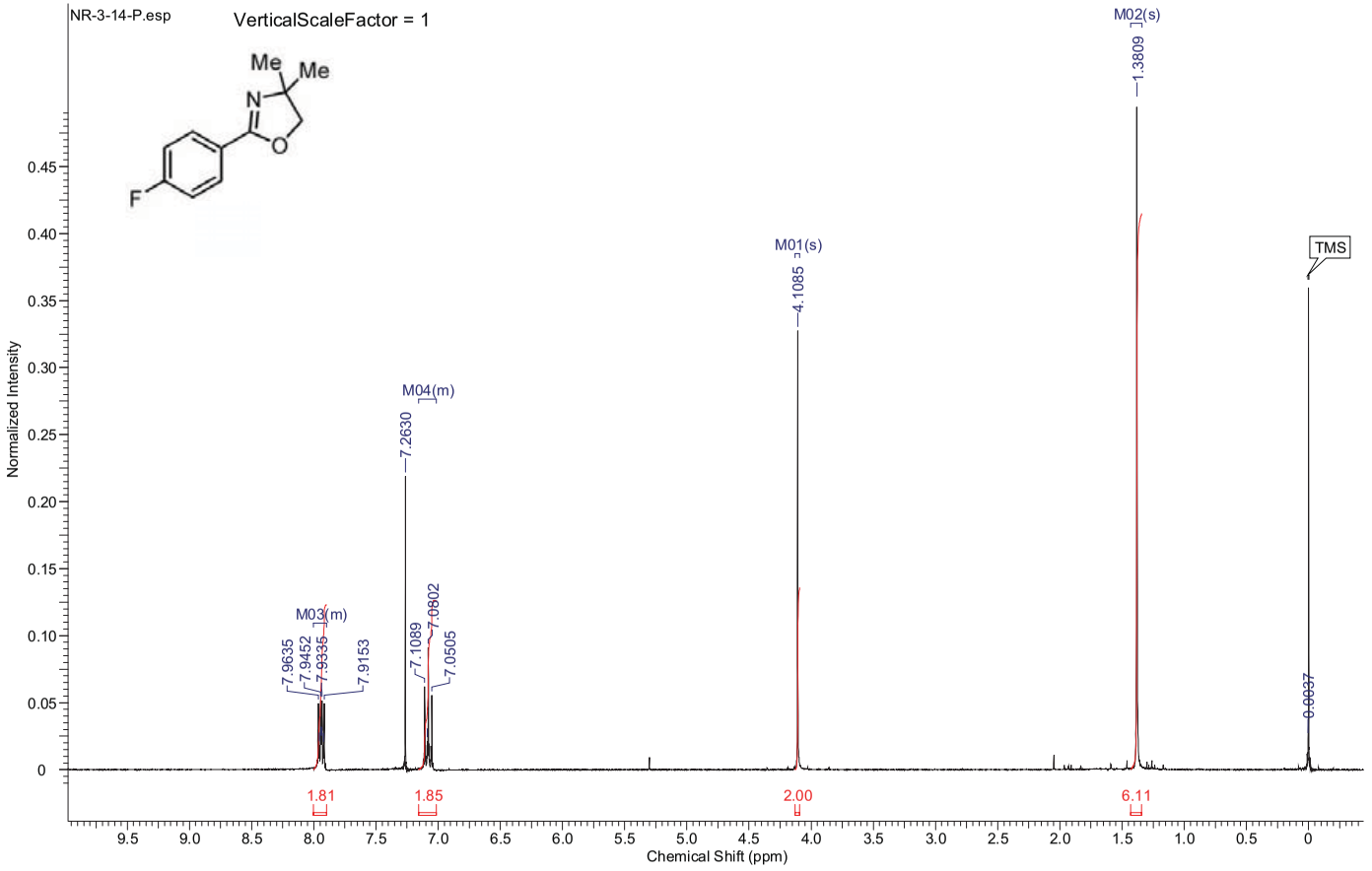
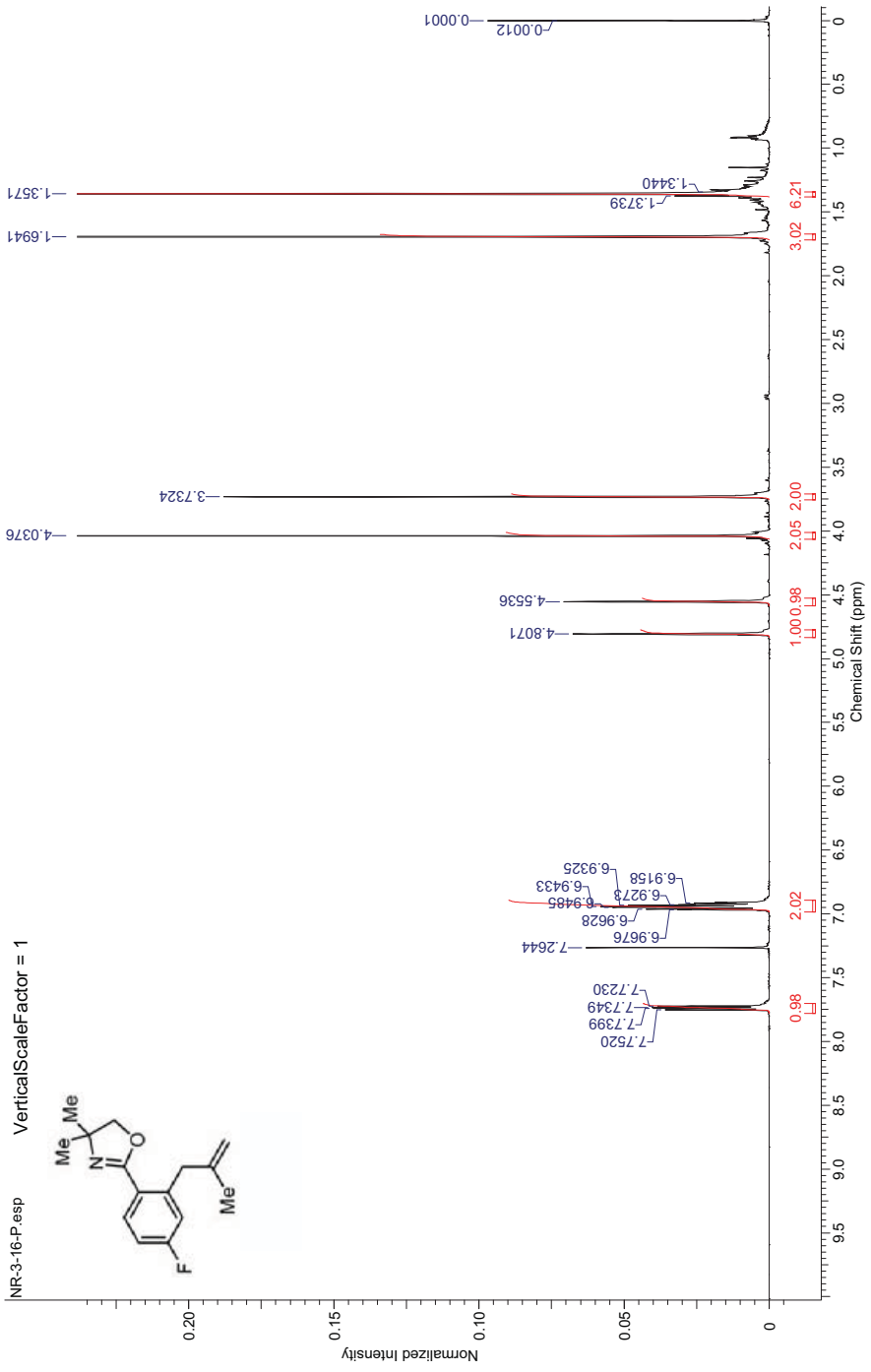
| ***Date*** | Jan 3 2013 | ***Date Stamp*** | Jan 3 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130103v3_2402.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 38.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2399.9365 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



9/27/2013 10:31:34 AM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Jan 8 2013 |
| *Date Stamp* | Jan 8 2013 | *File Name* | C:\Users\Naveen\Desktop\NR-3-16-P.fid\fid | *Frequency (MHz)* | 499.87 |
| *Nucleus* | 1H | *Number of Transients* | 8 | *Original Points Count* | 15136 |
| *Pulse Sequence* | s2pul | *Receiver Gain* | 54.00 | *Solvent* | CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2498.9509 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 8000.00 |
| | | | | *Temperature (degree C)* | AMBIENT TEMPERATURE |



9/27/2013 10:41:21 AM

| | | | |
|---|---|---|---|
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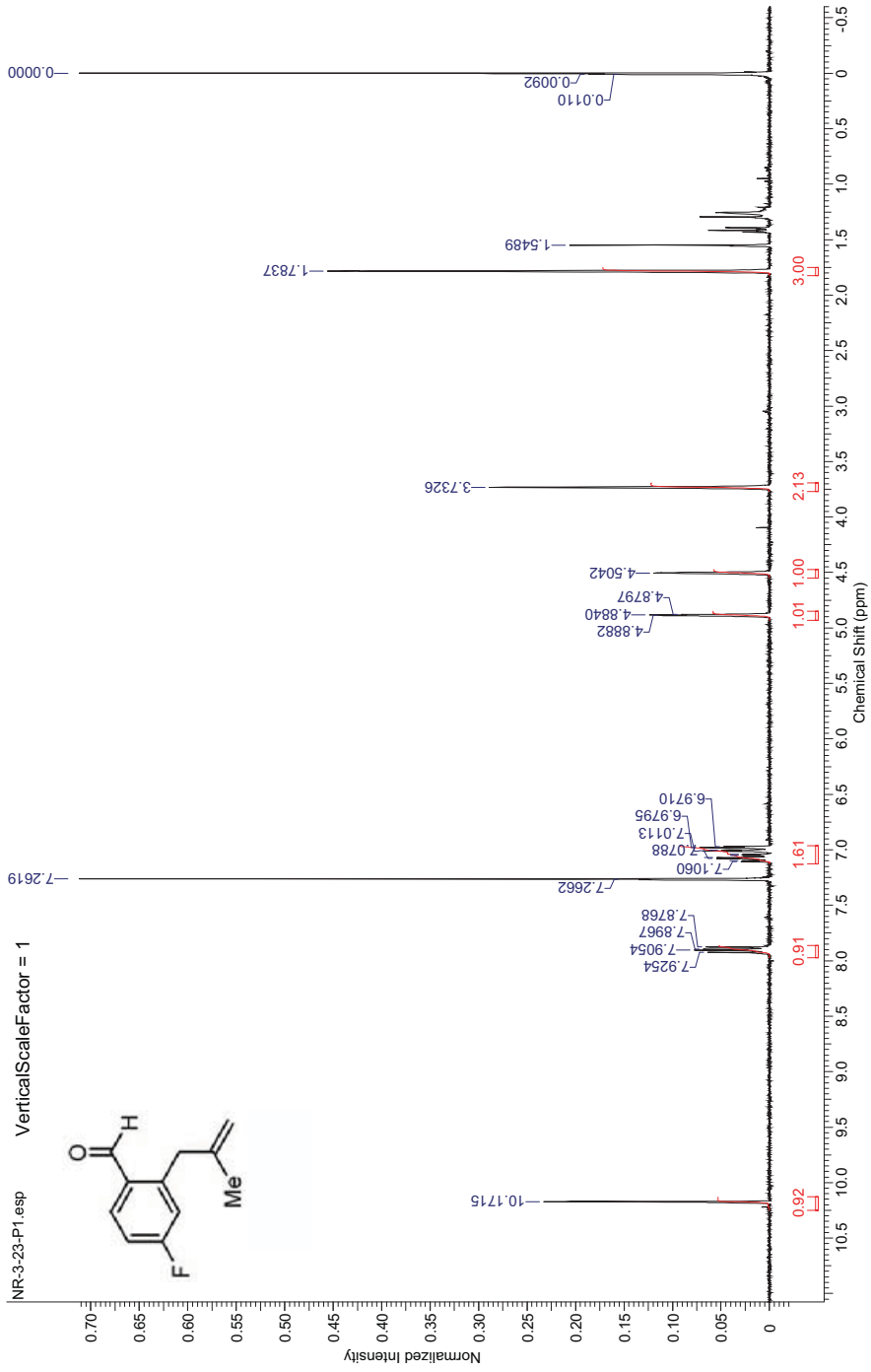
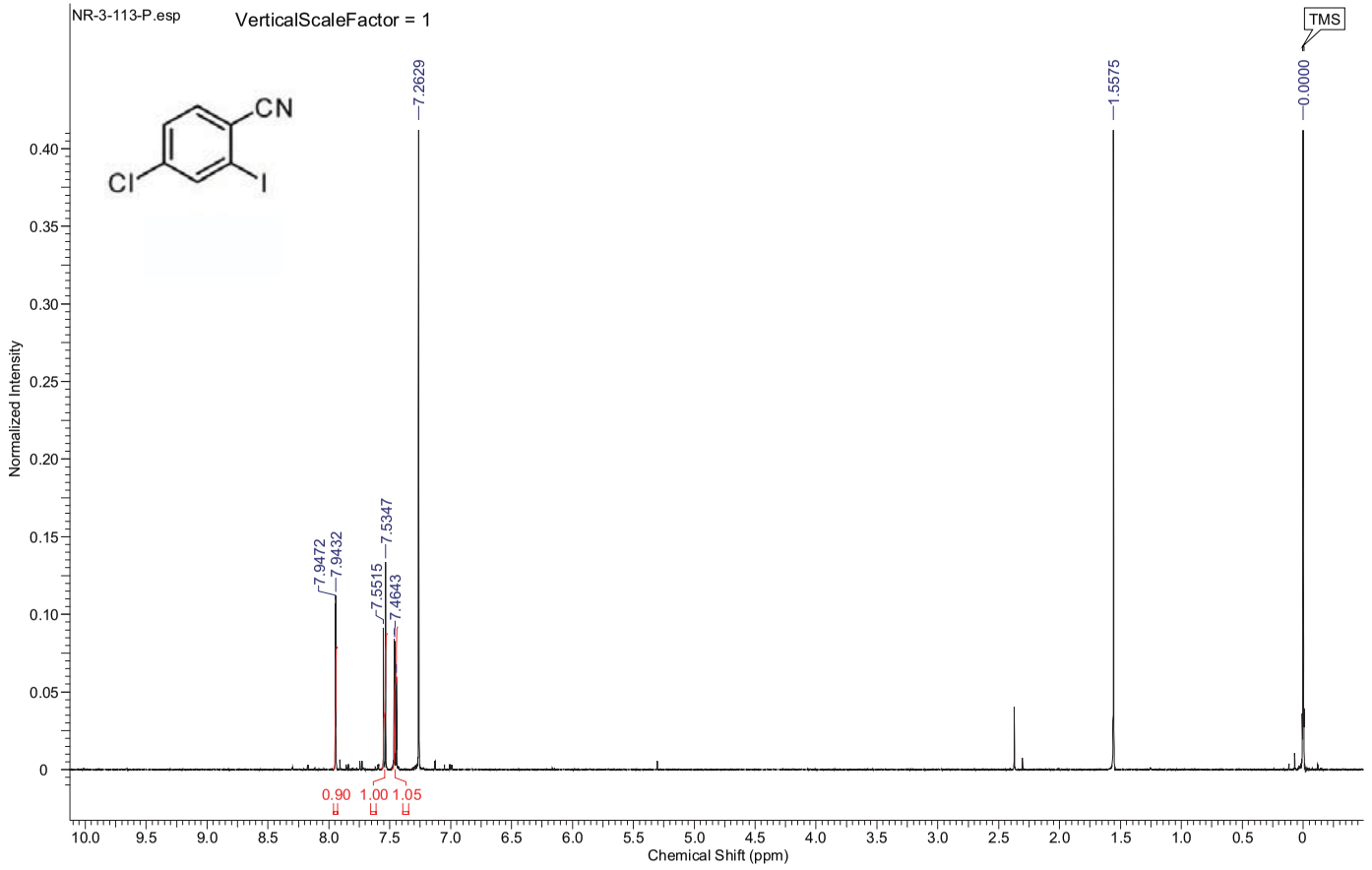
| *Date* | Mar 15 2013 | *Date Stamp* | Mar 15 2013 |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul |
| *Spectrum Offset (Hz)* | 2399.7993 | *Spectrum Type* | STANDARD |
| | | *File Name* | C:\Users\Naveen\Desktop\130315v3 1402.fid\fid |
| | | *Number of Transients* | 16 |
| | | *Receiver Gain* | 38.00 |
| | | *Sweep Width (Hz)* | 5998.80 |
| | | *Original Points Count* | 11998 |
| | | *Solvent* | CHLOROFORM-d |
| | | *Temperature (degree C)* | AMBIENT TEMPERATURE |



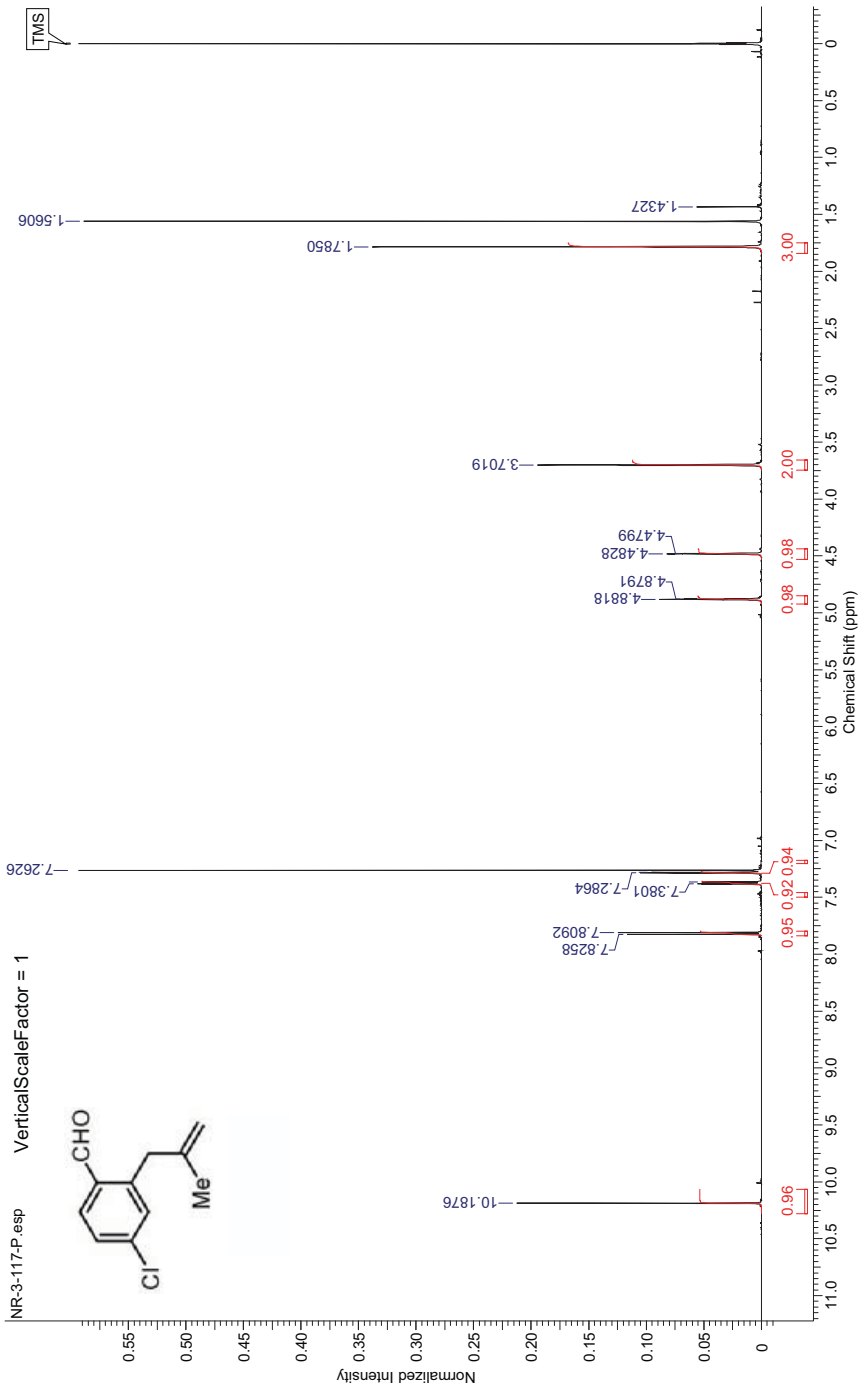
9/27/2013 11:37:13 AM

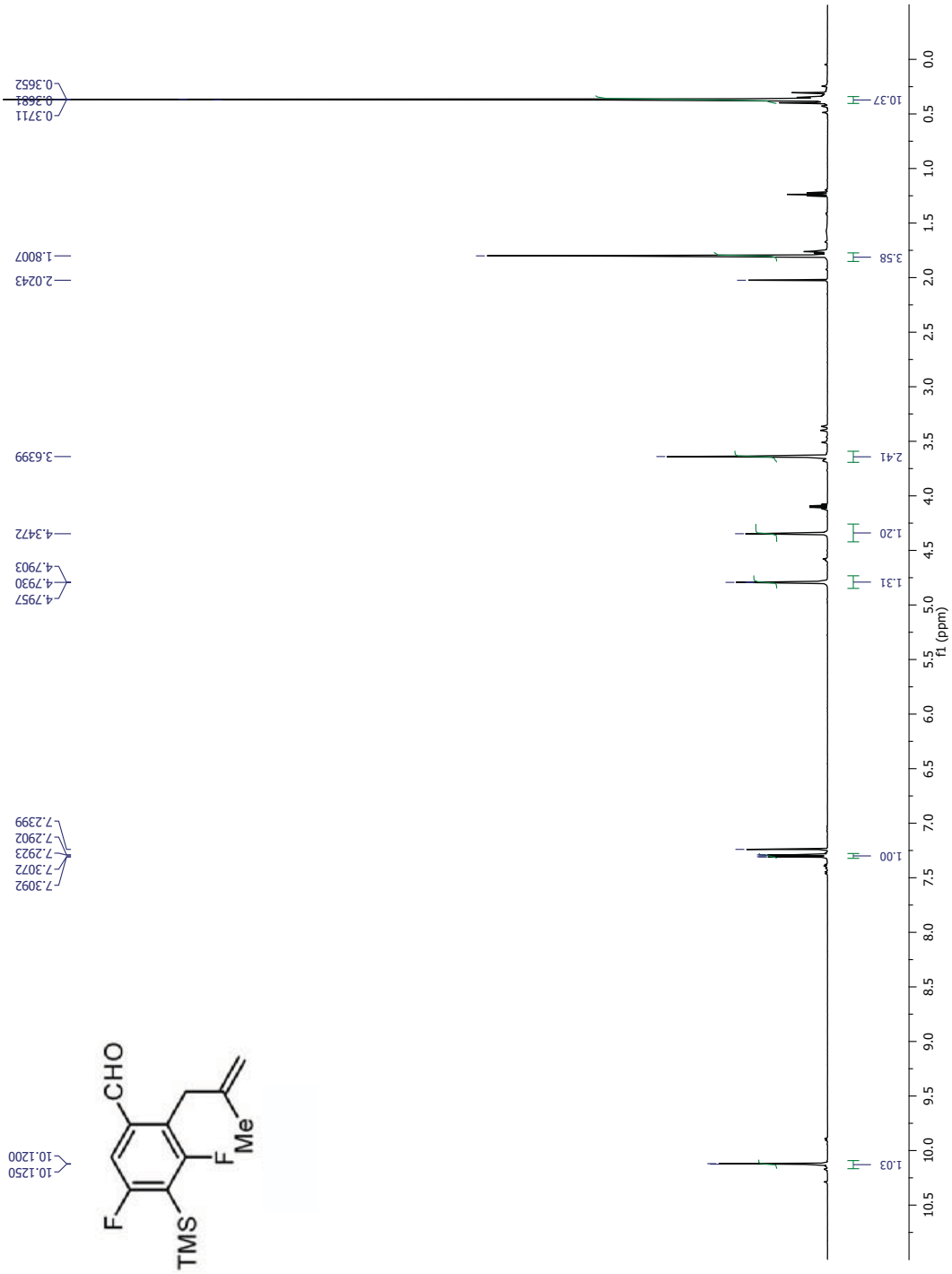
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.8920 | ***Comment*** | Univ of Minnesota, VI-500 | | | ***Date*** | Jul 18 2013 |
| ***Date Stamp*** | Jul 18 2013 | ***File Name*** | C:\Users\Naveen\Desktop\Cyanoacylation NMRs\NR-3-112-P.fid\fid | | | | |
| ***Frequency (MHz)*** | 499.87 | ***Nucleus*** | 1H | ***Number of Transients*** | 8 | ***Original Points Count*** | 15136 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 60.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2497.6692 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 8000.00 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



9/27/2013 11:43:42 AM

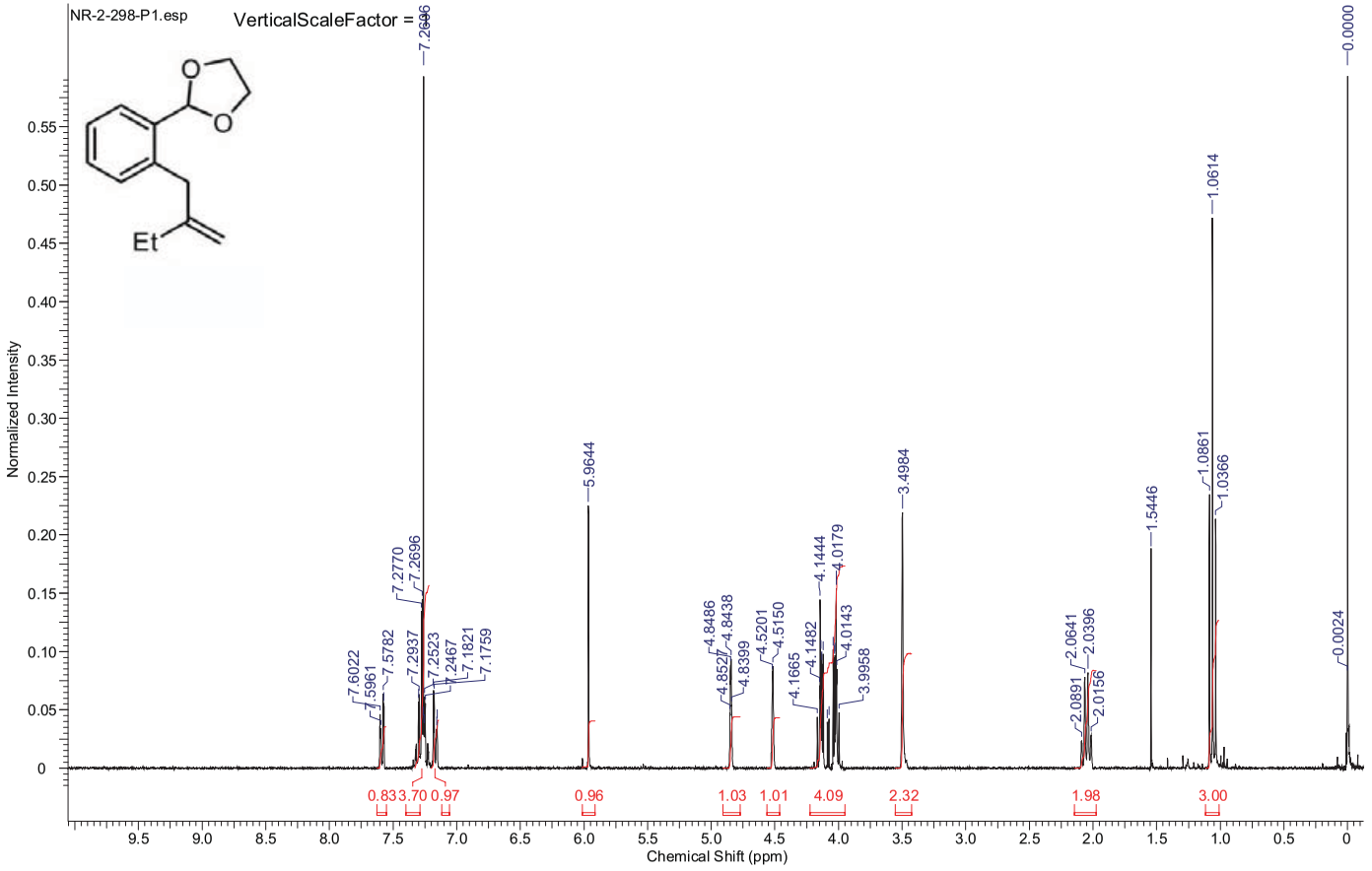
| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 3.2768 | *Date* | 20 Jul 2013 16:56:16 | *Date Stamp* | 20 Jul 2013 16:56:16 |
| *File Name* | C:\Users\Naveen\Desktop\NR-3-117-P\10\fid | *Frequency (MHz)* | 500.13 | *Nucleus* | 1H |
| *Number of Transients* | 16 *Origin* spect | *Original Points Count* | 32768 | *Owner* | auto |
| *Points Count* | 131072 *Pulse Sequence* zg30 | *Receiver Gain* | 127.25 | *SW(cyclical) (Hz)* | 10000.00 |
| *Solvent* | CHLOROFORM-d | *Spectrum Offset (Hz)* | 3077.3545 | *Spectrum Type* | STANDARD |
| *Sweep Width (Hz)* | 9999.92 *Temperature (degree C)* 20.998 | | | | |




10.1250
10.1200
7.3092
7.3072
7.2923
7.2902
7.2399
4.7957
4.7930
4.7903
4.3472
3.6399
2.0243
1.8007
0.3711
0.3681
0.3652
CHO
F
TMS
F
Me
10.37
3.58
2.41
1.20
1.31
1.00
1.03
f1 (ppm)

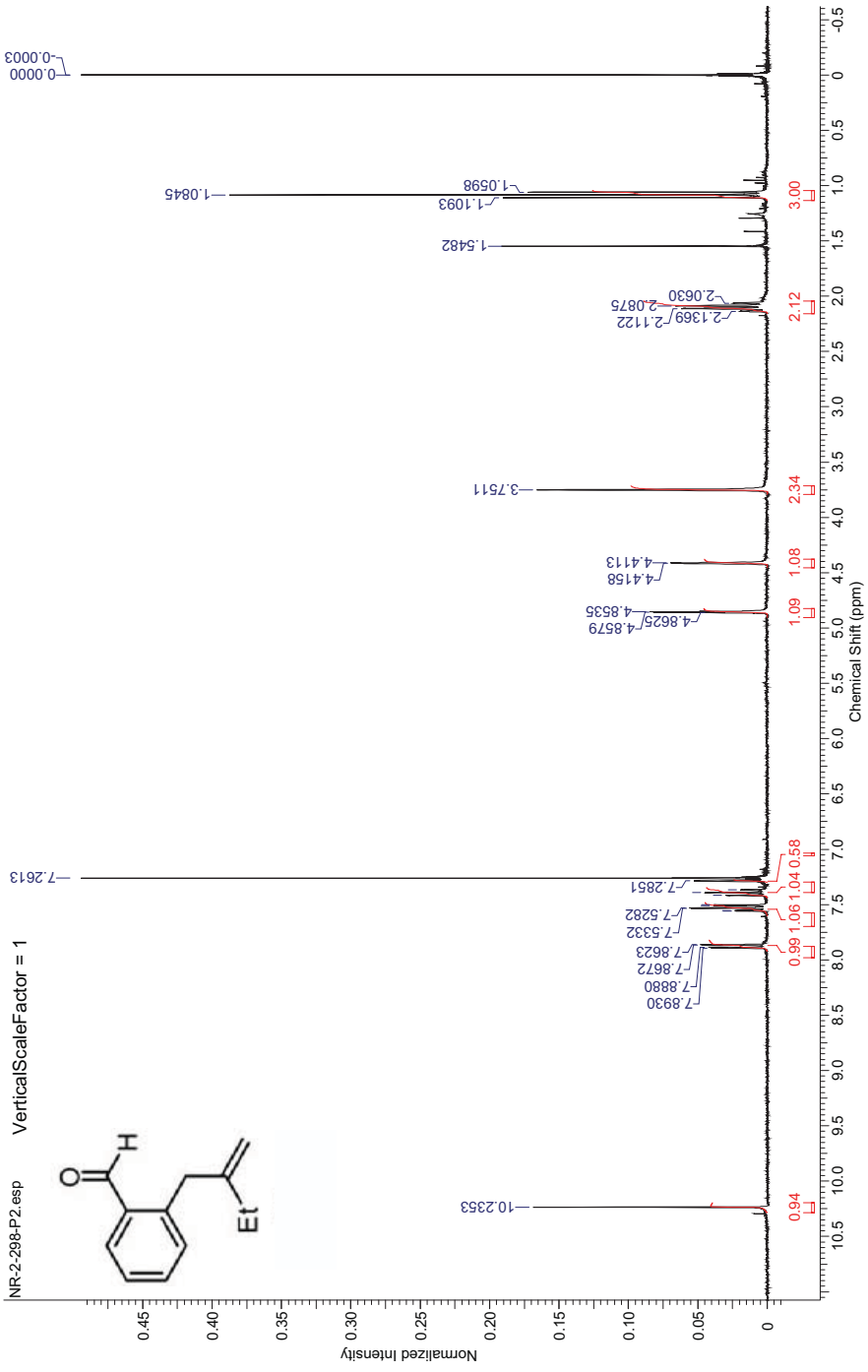
9/27/2013 11:54:24 AM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 2.0001 | ***Comment*** | NR-2-298-P1 University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | Dec 13 2012 | ***Date Stamp*** | Dec 13 2012 | ***File Name*** | C:\Users\Naveen\Desktop\121213v3 2302.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 38.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2399.1584 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



9/27/2013 11:57:30 AM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-2-298-P2 University of Minnesota Department of Chemistry VAC-300 | | |
| *Date* | Dec 14 2012 | *Date Stamp* | Dec 14 2012 | *File Name* | C:\Users\Naveen\Desktop\121214v3 1302.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H | *Number of Transients* | 16 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul | *Receiver Gain* | 38.00 |
| *Spectrum Offset (Hz)* | 2399.5706 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 5998.80 |
| *Original Points Count* | 11998 | *Solvent* | CHLOROFORM-d | | |
| *Temperature (degree C)* | AMBIENT TEMPERATURE | | | | |



9/27/2013 12:06:27 PM

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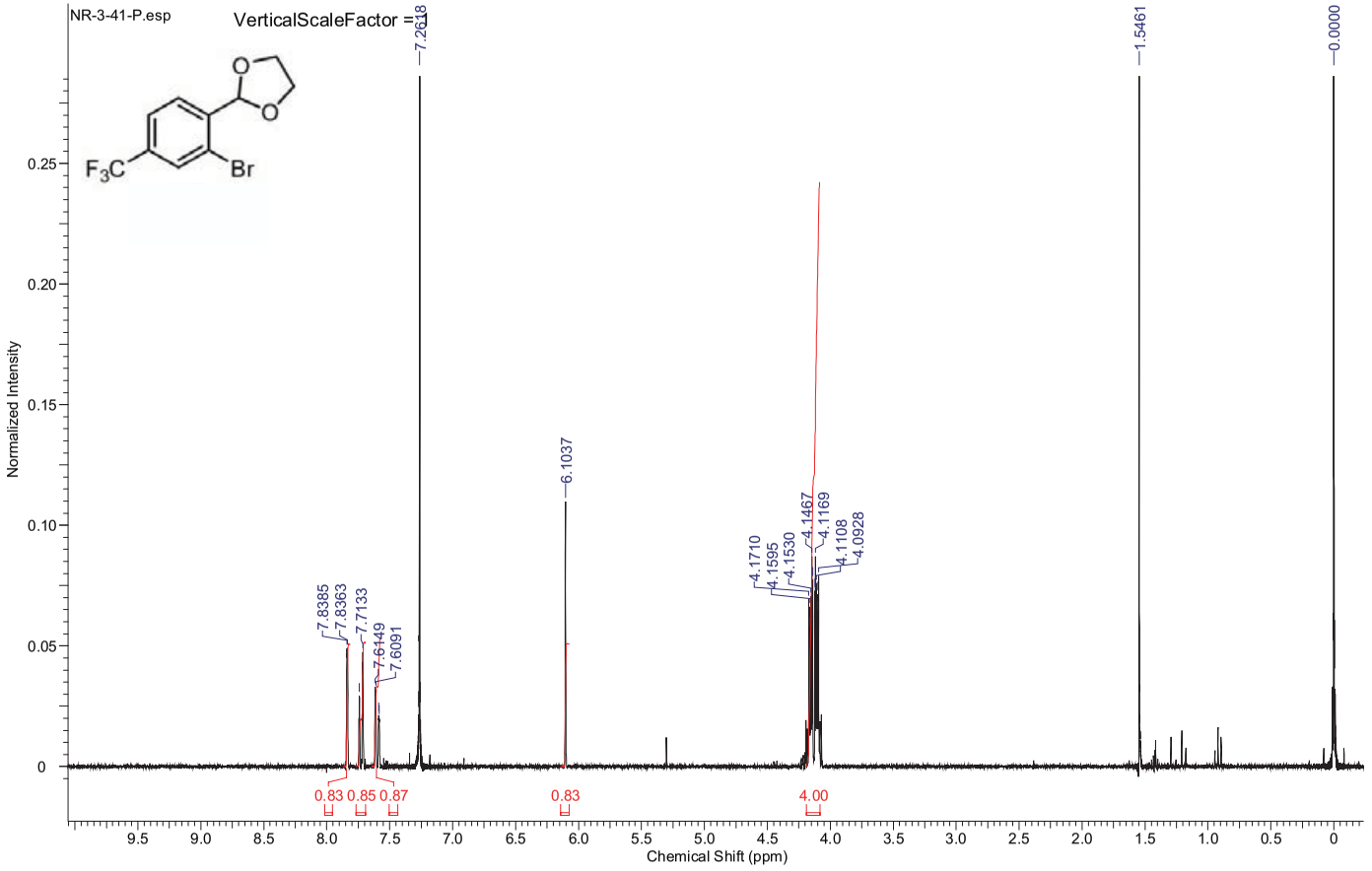
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 2.0001 | ***Comment*** | NR-3-41-P University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | Apr 18 2013 | ***Date Stamp*** | Apr 18 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130418v3_4302.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 38.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2399.5706 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



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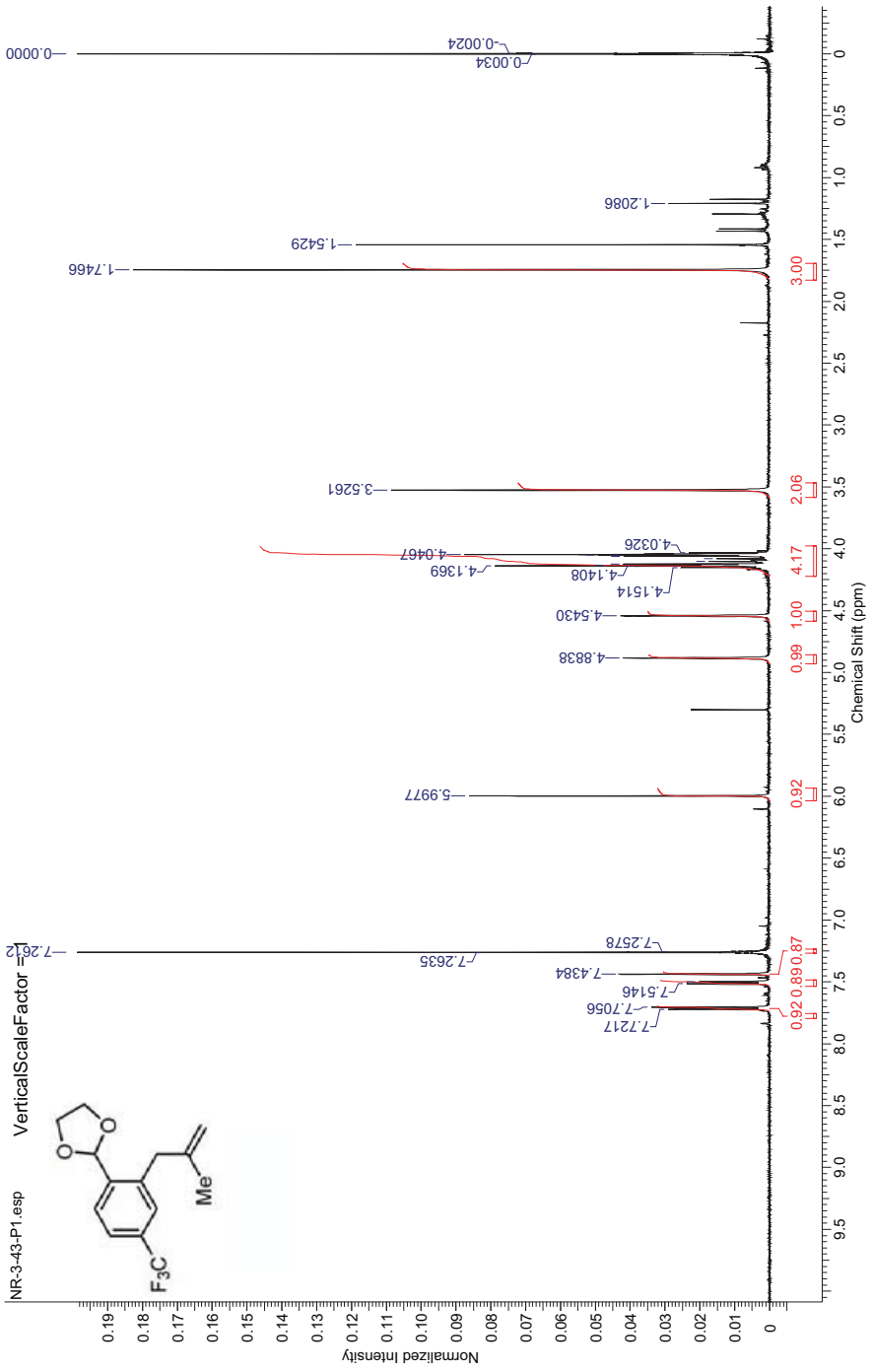
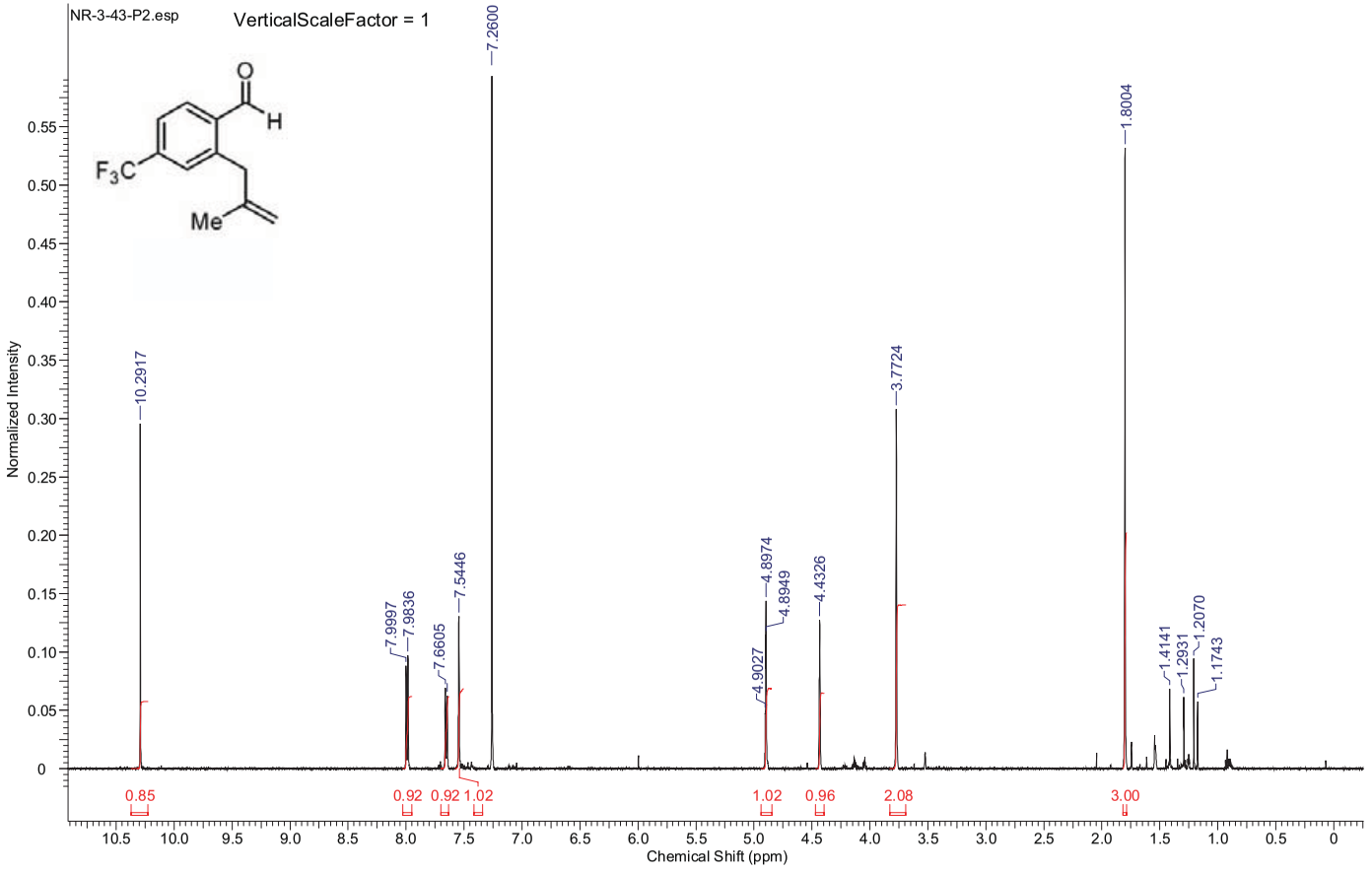
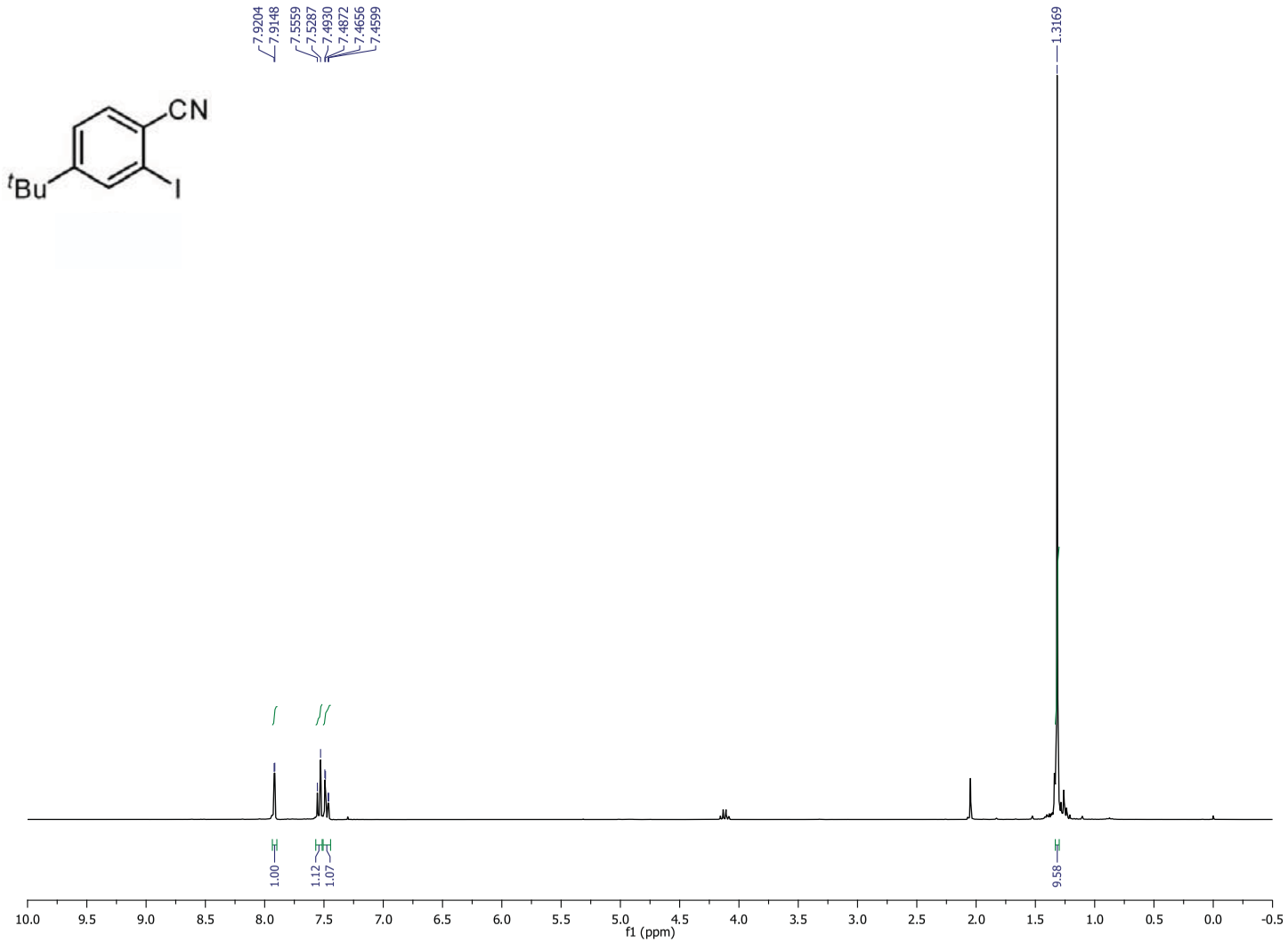
| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Apr 25 2013 |
| *Date Stamp* | Apr 25 2013 | *File Name* | C:\Users\Naveen\Desktop\NR-3-43-P1.fid\fid | *Frequency (MHz)* | 499.87 |
| *Nucleus* | 1H | *Number of Transients* | 8 | *Original Points Count* | 15136 |
| *Pulse Sequence* | s2pul | *Receiver Gain* | 60.00 | *Solvent* | CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2497.0588 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 8000.00 |
| | | | | *Temperature (degree C)* | AMBIENT TEMPERATURE |

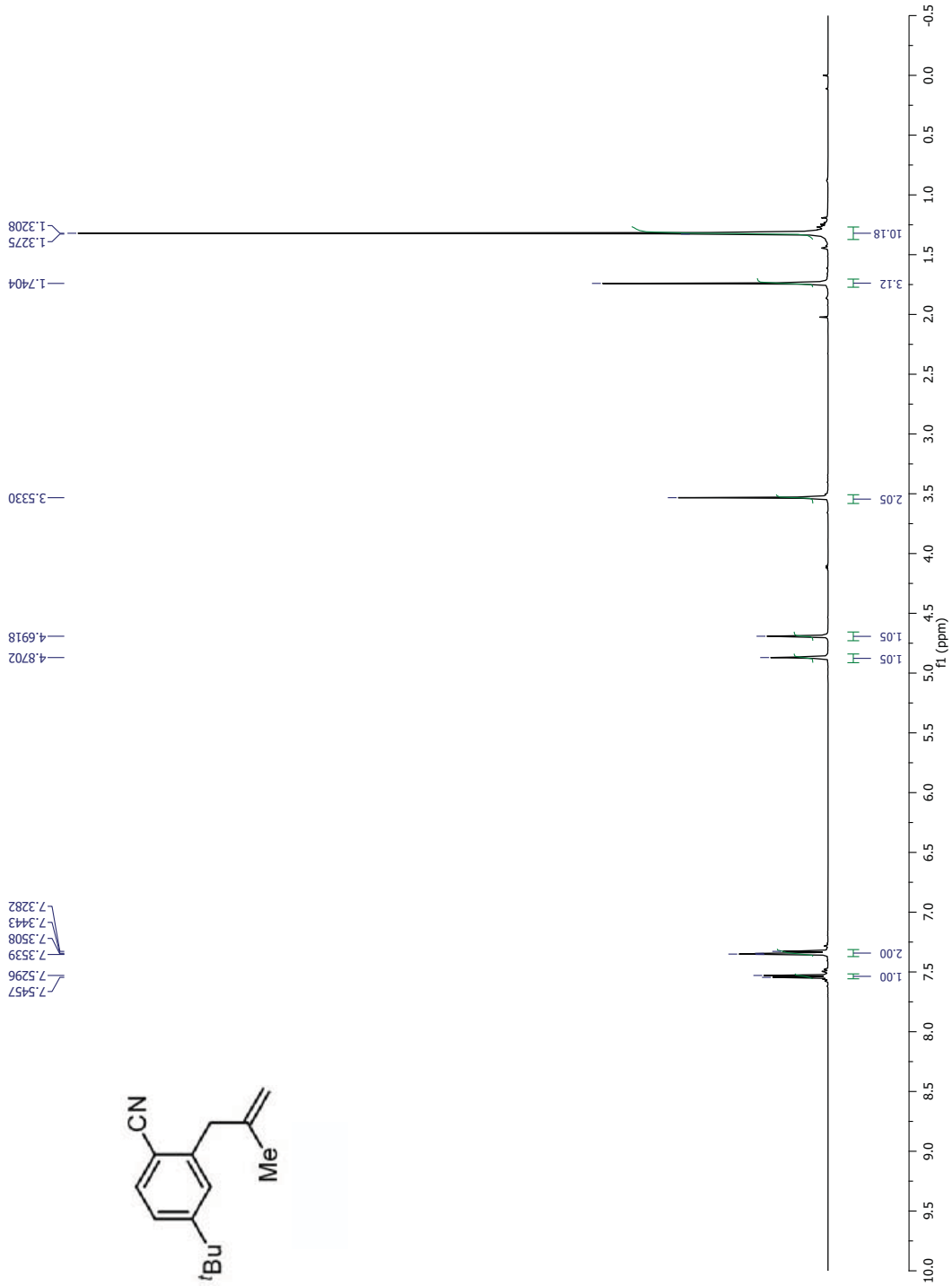


9/27/2013 12:16:07 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.8920 | ***Comment*** | Univ of Minnesota, VI-500 | | | ***Date*** | Apr 25 2013 |
| ***Date Stamp*** | Apr 25 2013 | ***File Name*** | C:\Users\Naveen\Desktop\NR-3-43-P2.fid\fid | | | ***Frequency (MHz)*** | 499.87 |
| ***Nucleus*** | 1H | ***Number of Transients*** | 8 | ***Original Points Count*** | 15136 | ***Points Count*** | 131072 |
| ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 60.00 | ***Solvent*** | CHLOROFORM-d | | |
| ***Spectrum Offset (Hz)*** | 2496.1409 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 8000.00 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |




7.9204
7.9148
7.5559
7.5287
7.4930
7.4872
7.4656
7.4599
1.3169
CN
tBu
I
1.00
1.12
1.07
9.58
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


CN
Me
tBu
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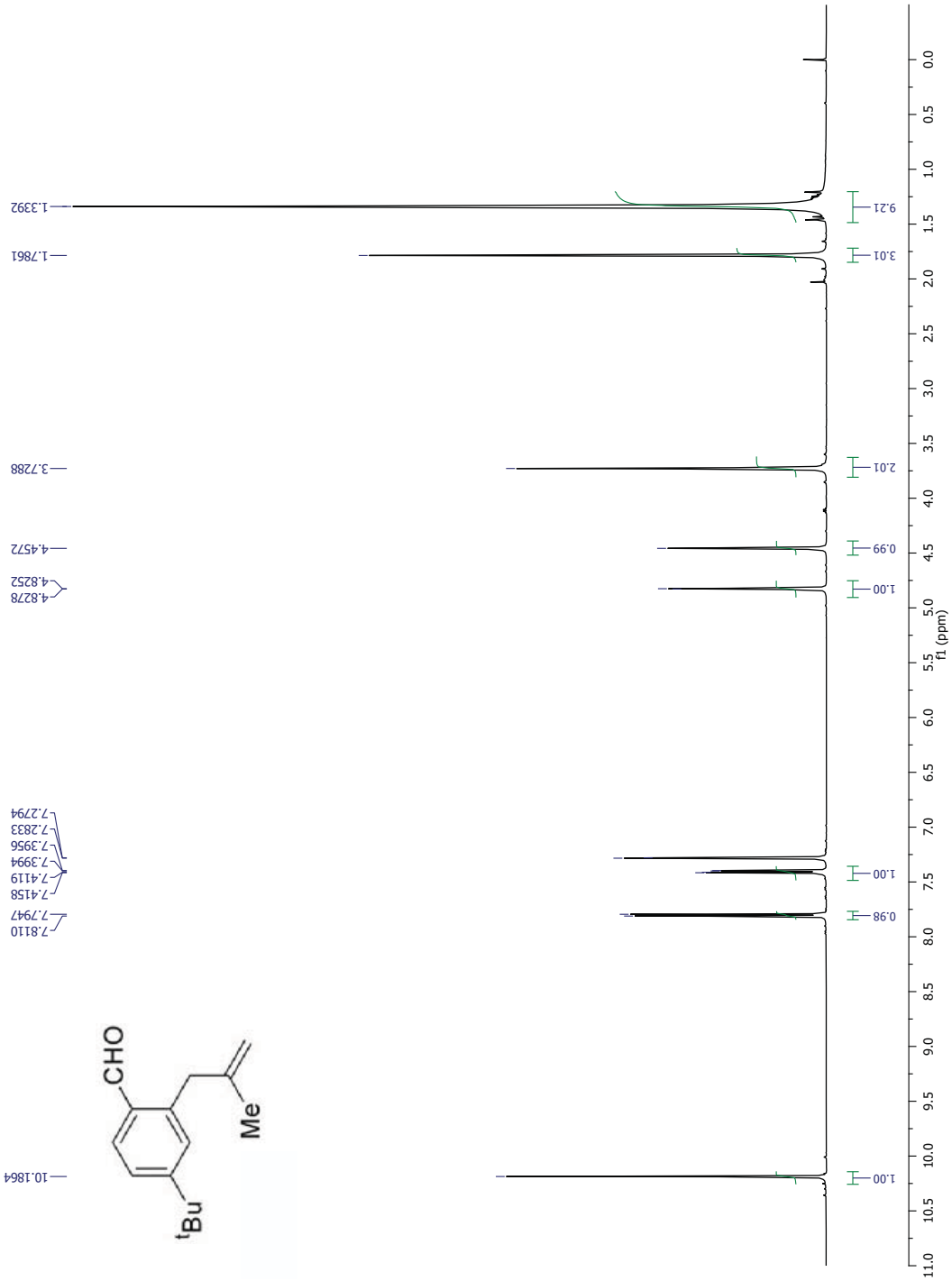
7.5296
7.3539
7.3508
7.3443
7.3282
4.8702
4.6918
3.5330
1.7404
1.3275
1.3208
1.00
2.00
1.05
1.05
2.05
3.12
10.18
f1 (ppm)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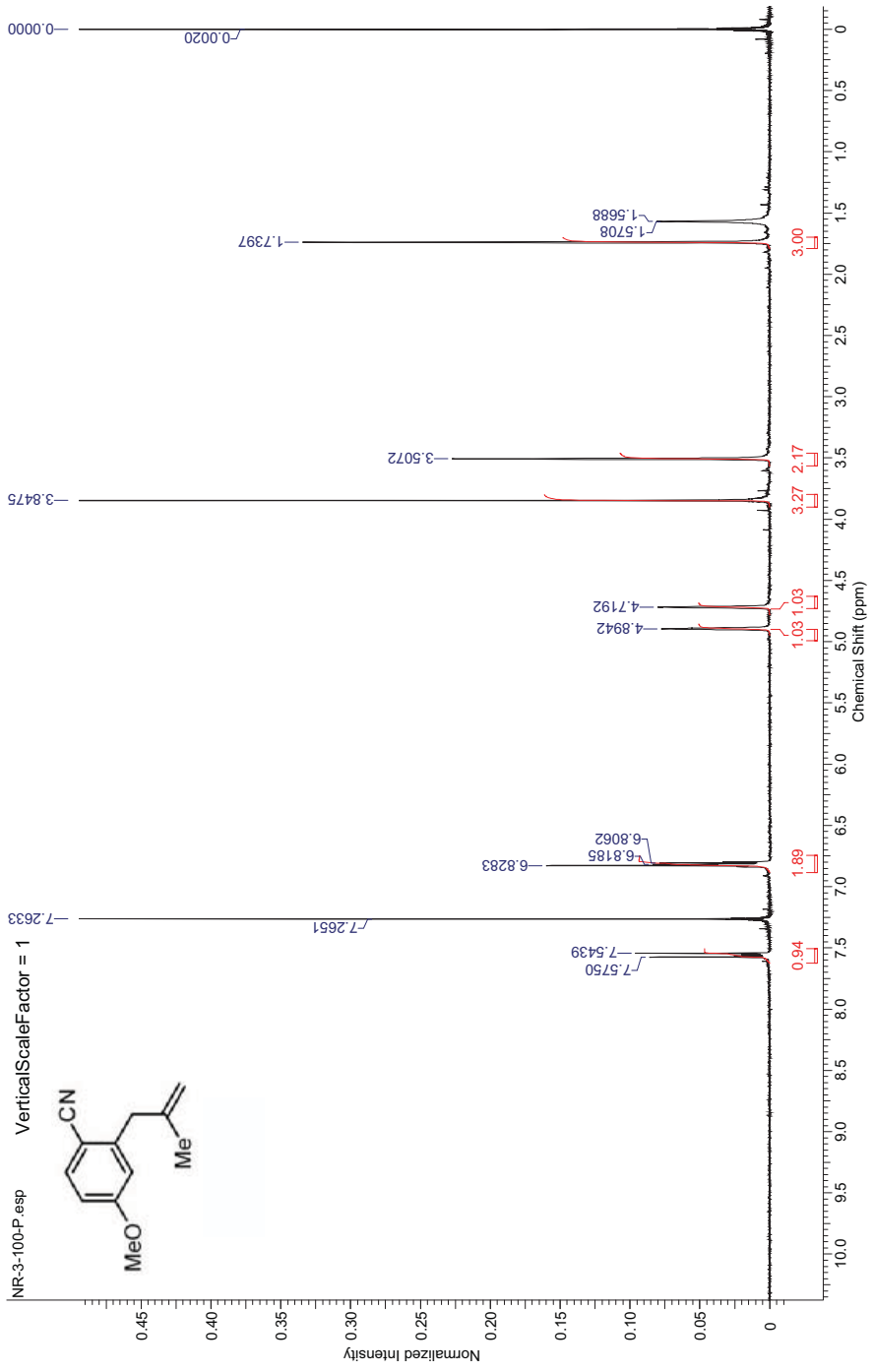
7.8110
7.7947
7.4158
7.4119
7.3994
7.3956
7.2833
7.2794
4.8278
4.8252
4.4572
3.7288
1.7861
1.3392
CHO
Me
tBu
1.00
0.98
1.00
2.01
0.99
1.00
3.01
9.21
f1 (ppm)

9/27/2013 12:27:10 PM

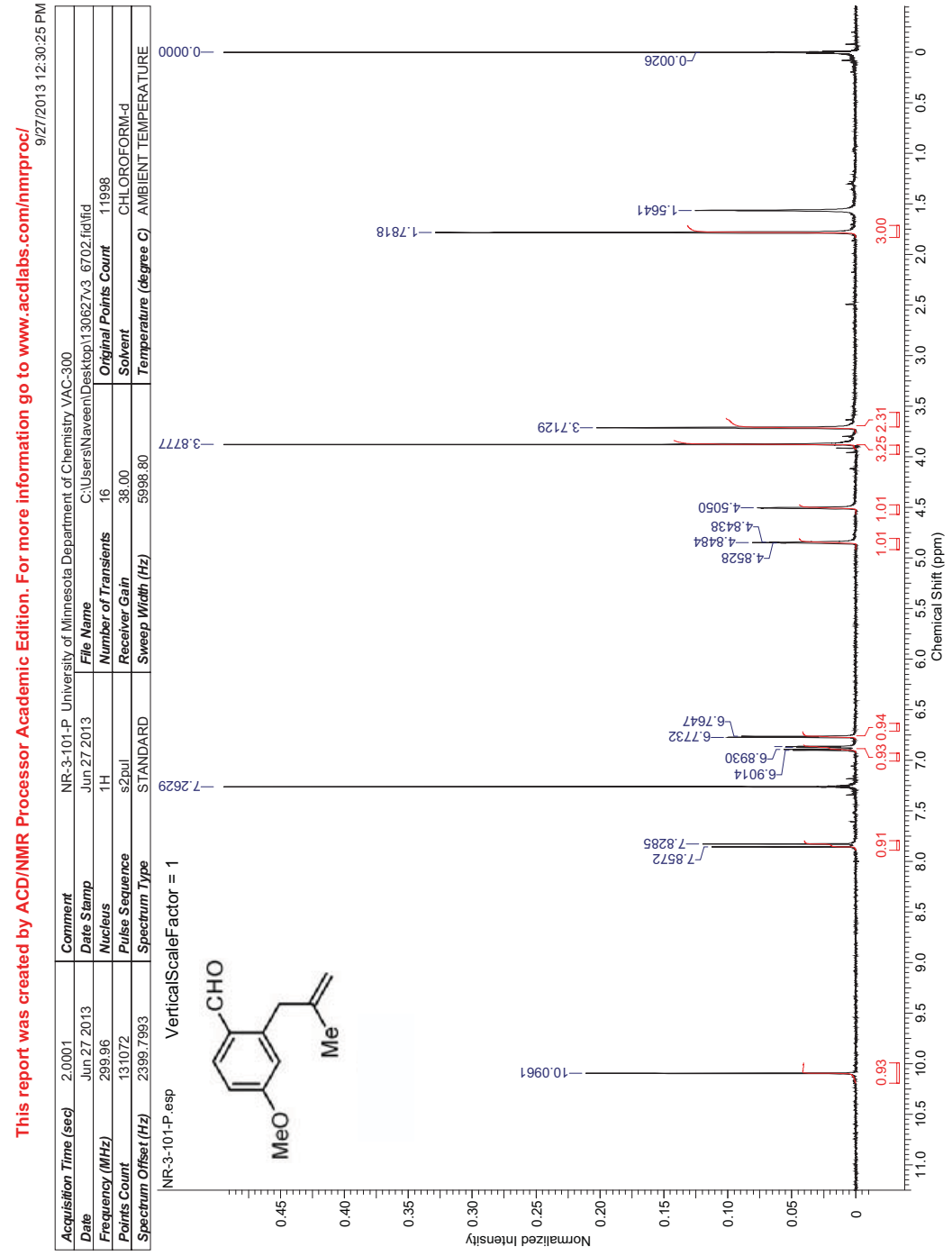
| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-100-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Jun 26 2013 | *Date Stamp* | Jun 26 2013 *File Name* C:\Users\Naveen\Desktop\130626v3 2402.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2400.0740 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



9/27/2013 12:30:25 PM

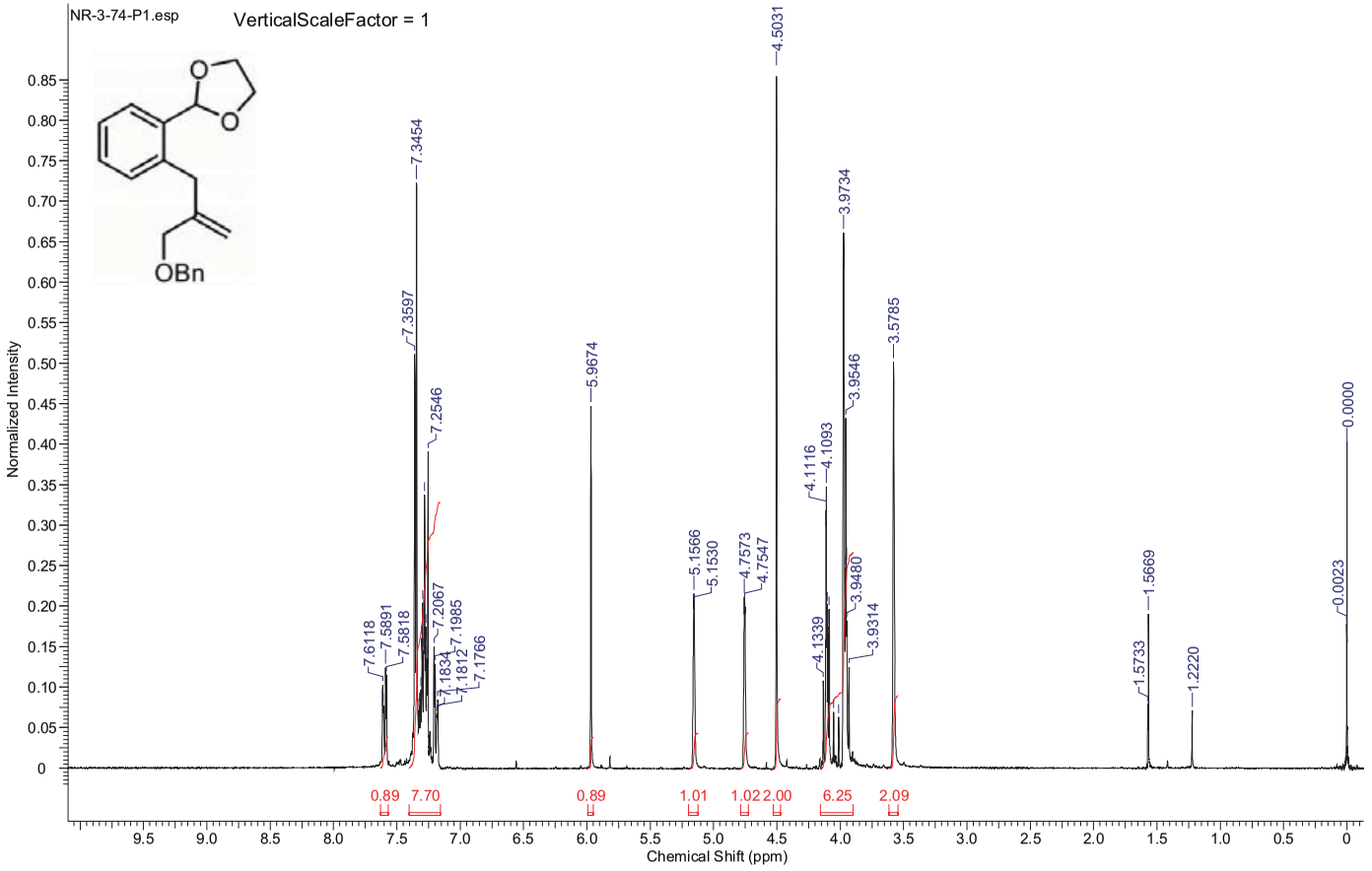
| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-101-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Jun 27 2013 | *Date Stamp* | Jun 27 2013 |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul |
| *Spectrum Offset (Hz)* | 2399.7993 | *Spectrum Type* | STANDARD |

| | |
|---|---|
| *File Name* | C:\Users\Naveen\Desktop\130627v3_6702.fid\fid |
| *Number of Transients* | 16 |
| *Receiver Gain* | 38.00 |
| *Sweep Width (Hz)* | 5998.80 |
| *Original Points Count* | 11998 |
| *Solvent* | CHLOROFORM-d |
| *Temperature (degree C)* | AMBIENT TEMPERATURE |



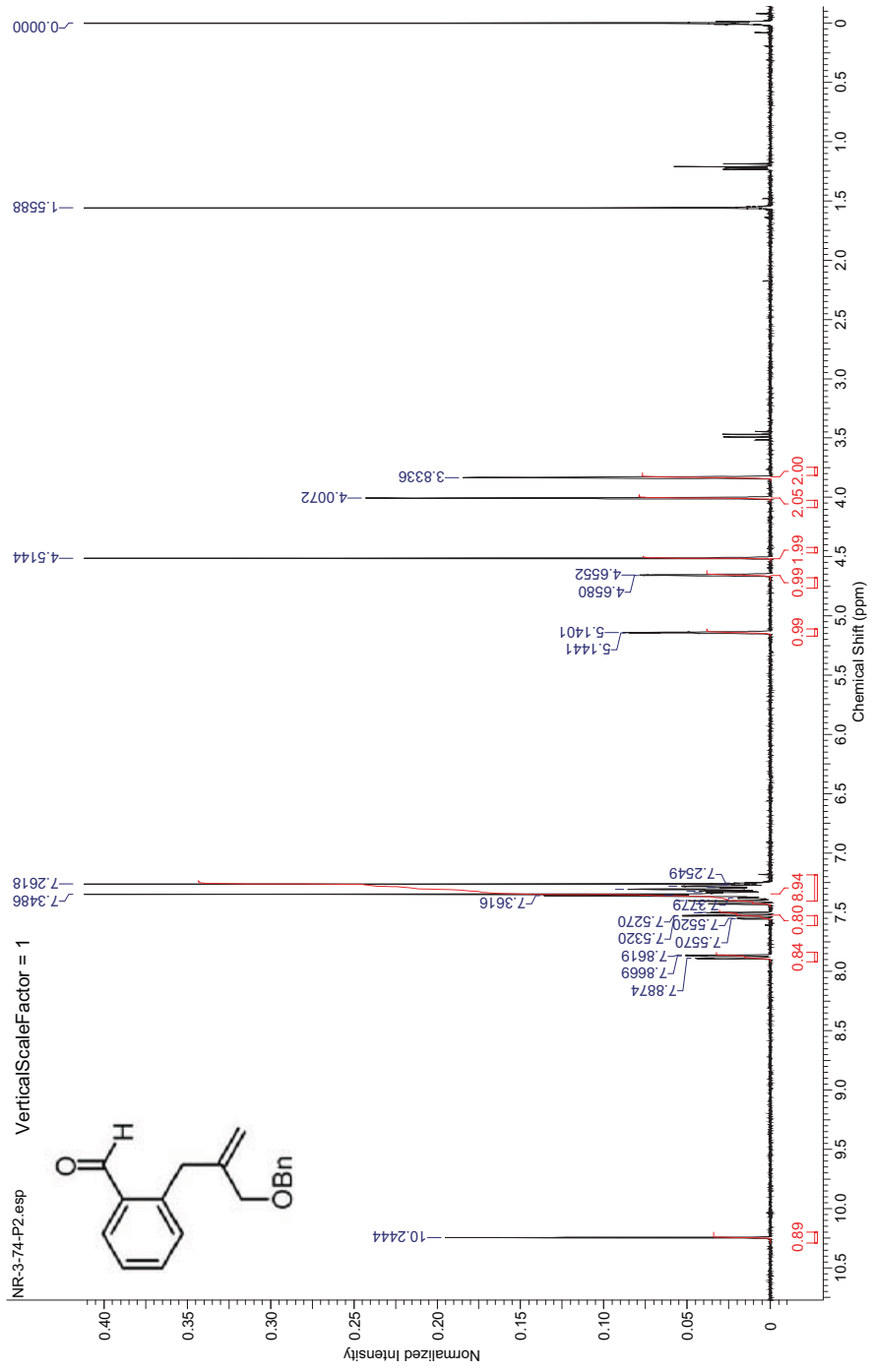
10/8/2013 5:20:19 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 2.0001 | ***Comment*** | NR-3-74-P1 University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | May 29 2013 | ***Date Stamp*** | May 29 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130529v3_1502.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 34.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2397.5566 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



10/8/2013 5:19:15 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-74-P2 University of Minnesota Department of Chemistry VAC-300 | | |
| *Date* | May 29 2013 | *Date Stamp* | May 29 2013 | *File Name* | C:\Users\Naveen\Desktop\130529v3_3702.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H | *Number of Transients* | 16 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul | *Receiver Gain* | 38.00 |
| *Spectrum Offset (Hz)* | 2399.4331 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 5998.80 |
| *Original Points Count* | 11998 | | | | |
| *Solvent* | CHLOROFORM-d | | | | |
| *Temperature (degree C)* | AMBIENT TEMPERATURE | | | | |



8/22/2013 5:37:35 PM

| | | | |
|---|---|---|---|
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| *Date* | Aug 20 2012 | *Date Stamp* | Aug 20 2012 |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul |
| *Spectrum Offset (Hz)* | 2396.8245 | *Spectrum Type* | STANDARD |
| | | *File Name* | C:\Users\Naveen\Desktop\120820v3_2202.fid\fid |
| | | *Number of Transients* | 16 |
| | | *Receiver Gain* | 30.00 |
| | | *Sweep Width (Hz)* | 5998.80 |
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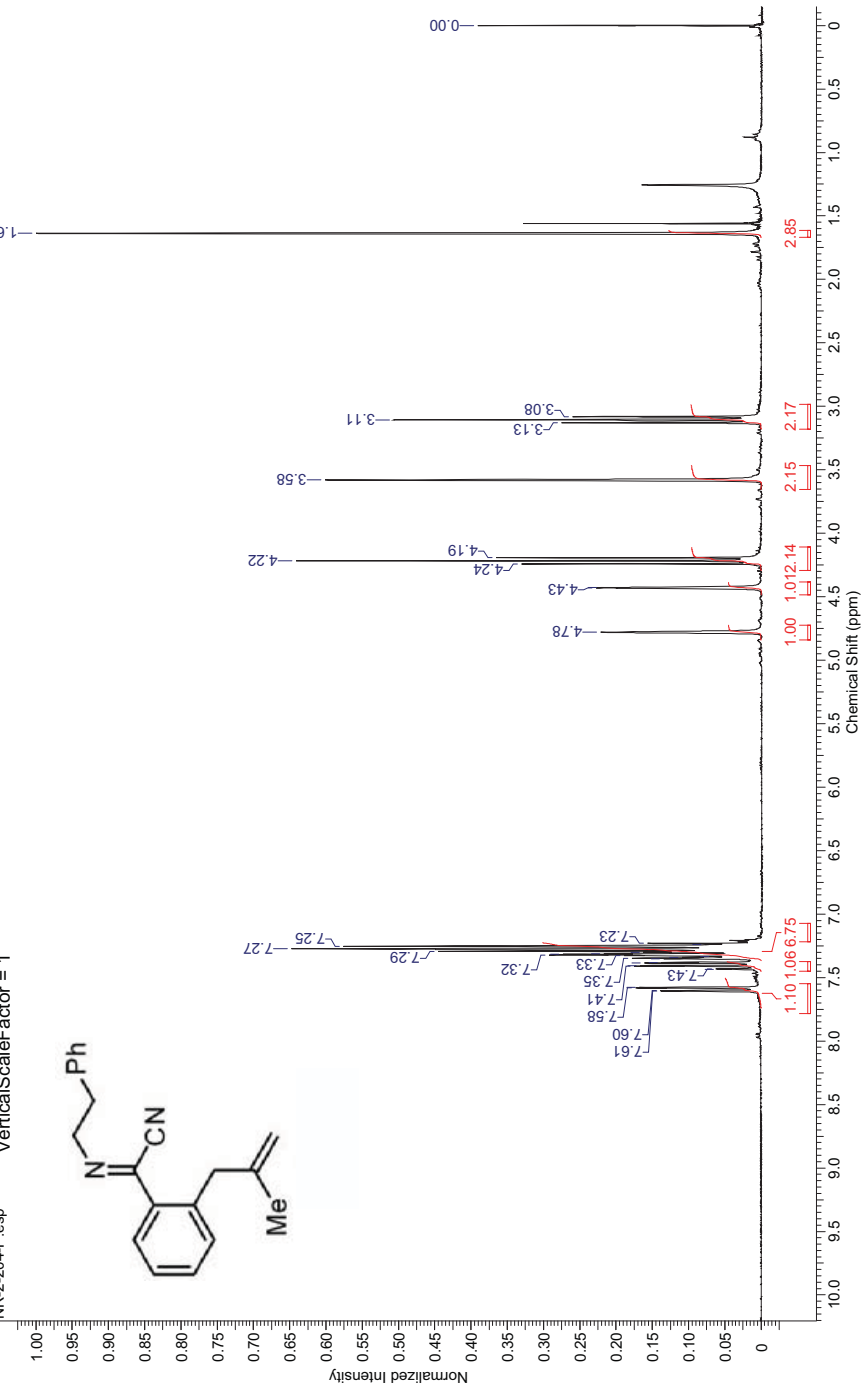
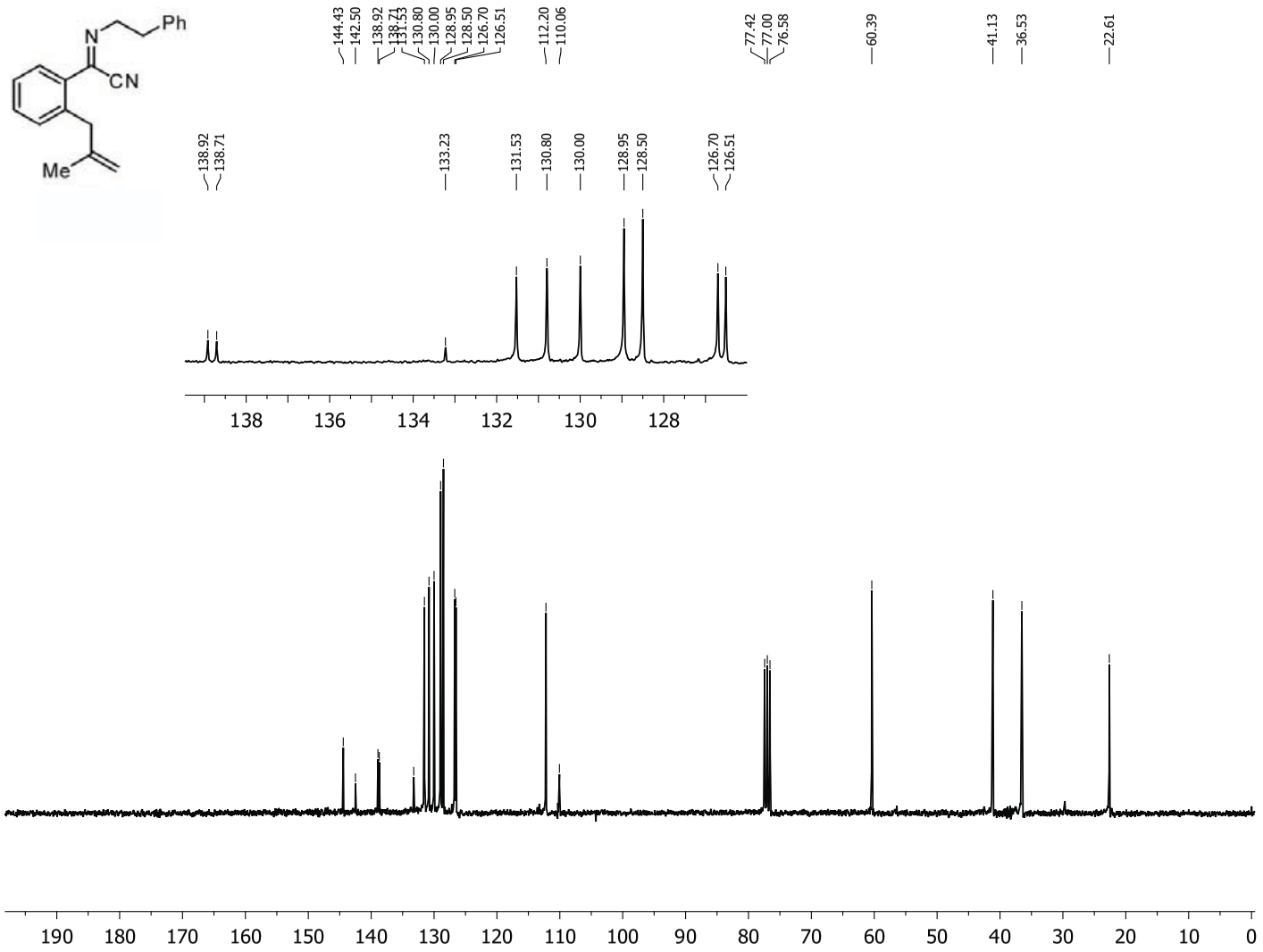
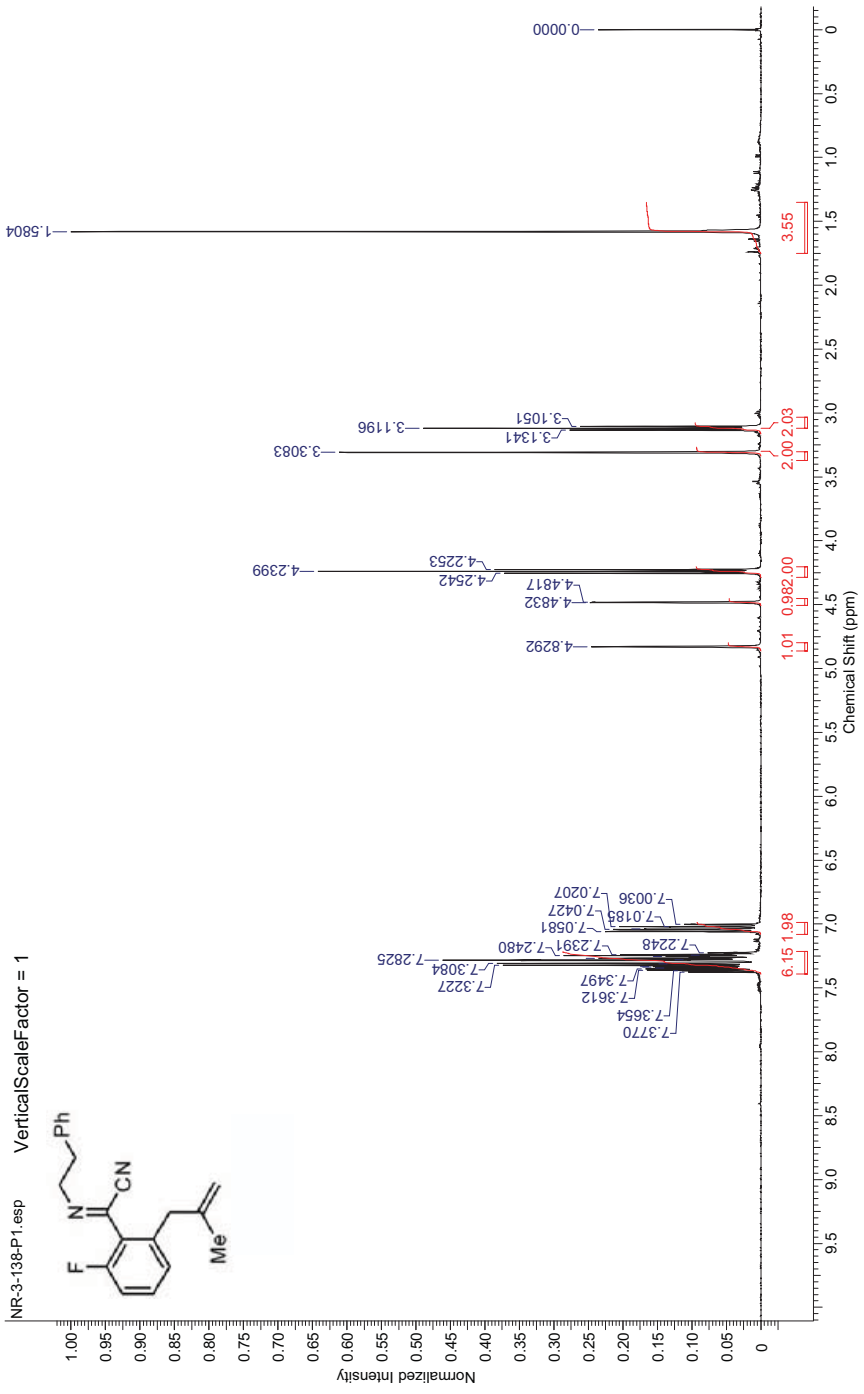
| | | *Solvent* | CHLOROFORM-d |
| | | *Temperature (degree C)* | AMBIENT TEMPERATURE |




N
Ph
CN
Me
144.43
142.50
138.92
138.71
131.53
130.80
130.00
128.95
128.50
126.70
126.51
112.20
110.06
77.42
77.00
76.58
60.39
41.13
36.53
22.61
138.92
138.71
133.23
131.53
130.80
130.00
128.95
128.50
126.70
126.51
138
136
134
132
130
128
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

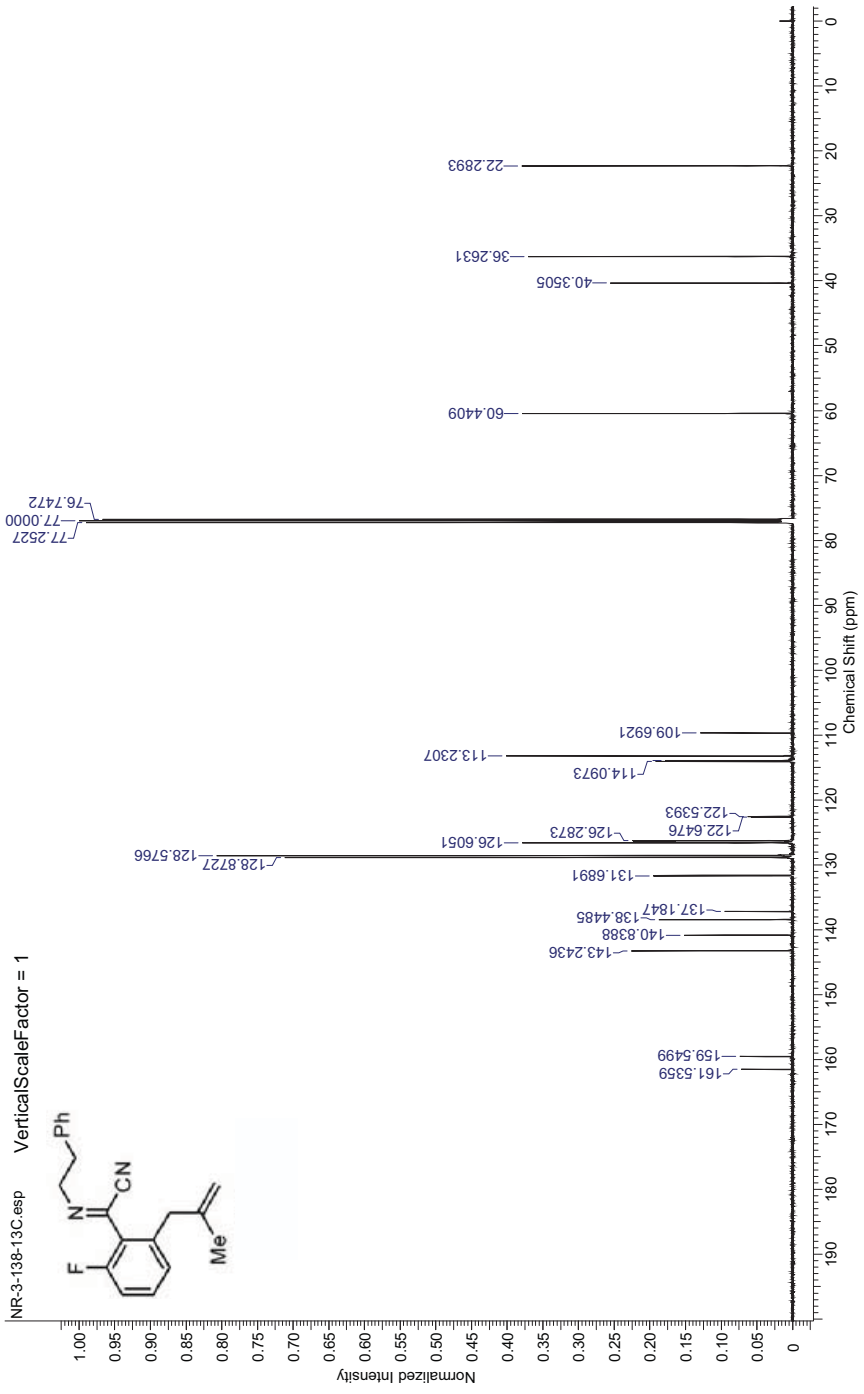
9/24/2013 1:31:52 PM

| | | | | | |
|---|---|---|---|---|---|
| **Acquisition Time (sec)** | 3.2768 | **Date** | 21 Sep 2013 17:02:40 | **Date Stamp** | 21 Sep 2013 17:02:40 |
| **File Name** | C:\Users\Naveen\Desktop\NR-3-138-P1\10\fid | **Frequency (MHz)** | 500.13 | **Nucleus** | 1H |
| **Number of Transients** | 16 | **Origin** | spect | **Original Points Count** | 32768 | **Owner** | auto |
| **Points Count** | 131072 | **Pulse Sequence** | zg30 | **Receiver Gain** | 29.25 | **SW(cyclical) (Hz)** | 10000.00 |
| **Solvent** | CHLOROFORM-d | | | **Spectrum Offset (Hz)** | 3069.8013 | **Spectrum Type** | STANDARD |
| **Sweep Width (Hz)** | 9999.92 | **Temperature (degree C)** | 21.000 | | | | |



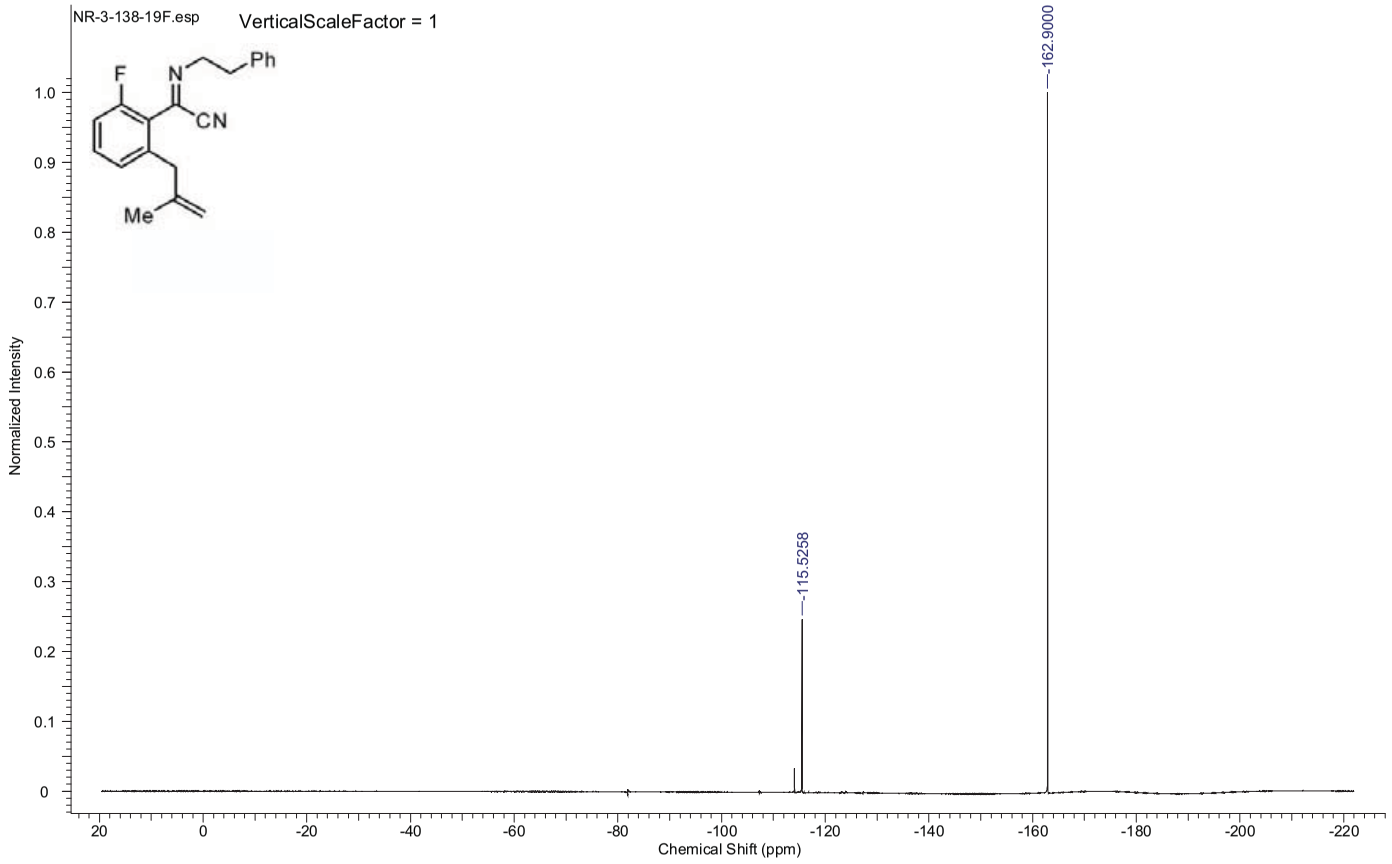
9/24/2013 1:55:31 PM

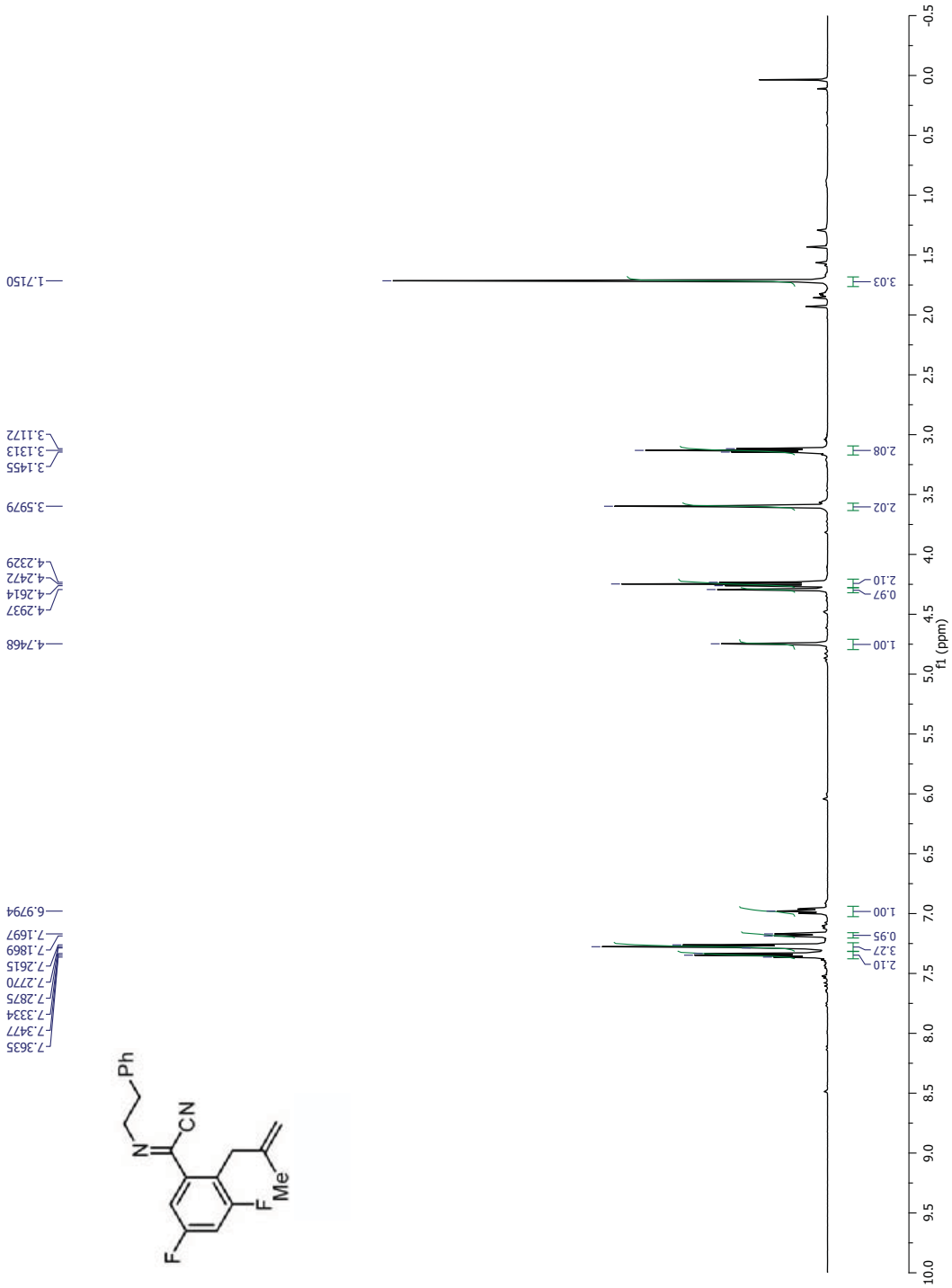
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 21 Sep 2013 17:58:08 | | | ***Date Stamp*** | 21 Sep 2013 17:58:08 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-138-13C\1\10\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 1000 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12566.6855 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 20.999 | | | | |



9/27/2013 1:28:56 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 0.5767 | ***Date*** | 24 Sep 2013 10:36:32 | | | ***Date Stamp*** | 24 Sep 2013 10:36:32 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-138-19F\10\fid | | | ***Frequency (MHz)*** | 470.55 | ***Nucleus*** | 19F |
| ***Number of Transients*** | 16 | ***Origin*** | spect | ***Original Points Count*** | 65536 | ***Owner*** | auto |
| ***Points Count*** | 65536 | ***Pulse Sequence*** | zg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 113636.37 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | -47628.0508 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 113634.63 | ***Temperature (degree C)*** | 21.000 | | | | |

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7.3334
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7.2770
7.2615
7.1869
7.1697
6.9794
4.7468
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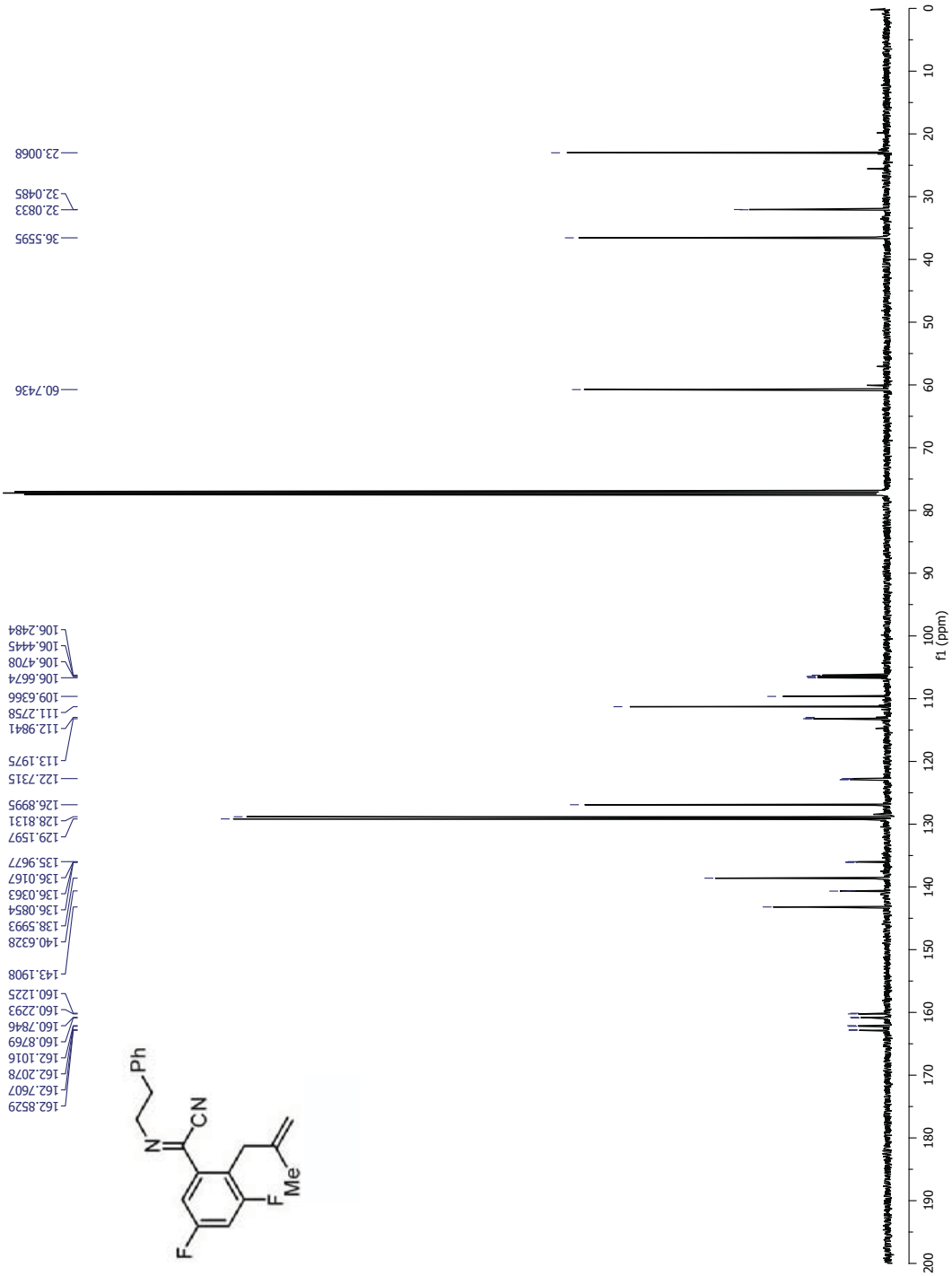
4.2614
4.2472
4.2329
3.5979
3.1455
3.1313
3.1172
1.7150
2.10
3.27
0.95
2.10
1.00
0.97
2.10
2.02
2.08
3.03
f1 (ppm)
Ph
N
CN
F
Me
F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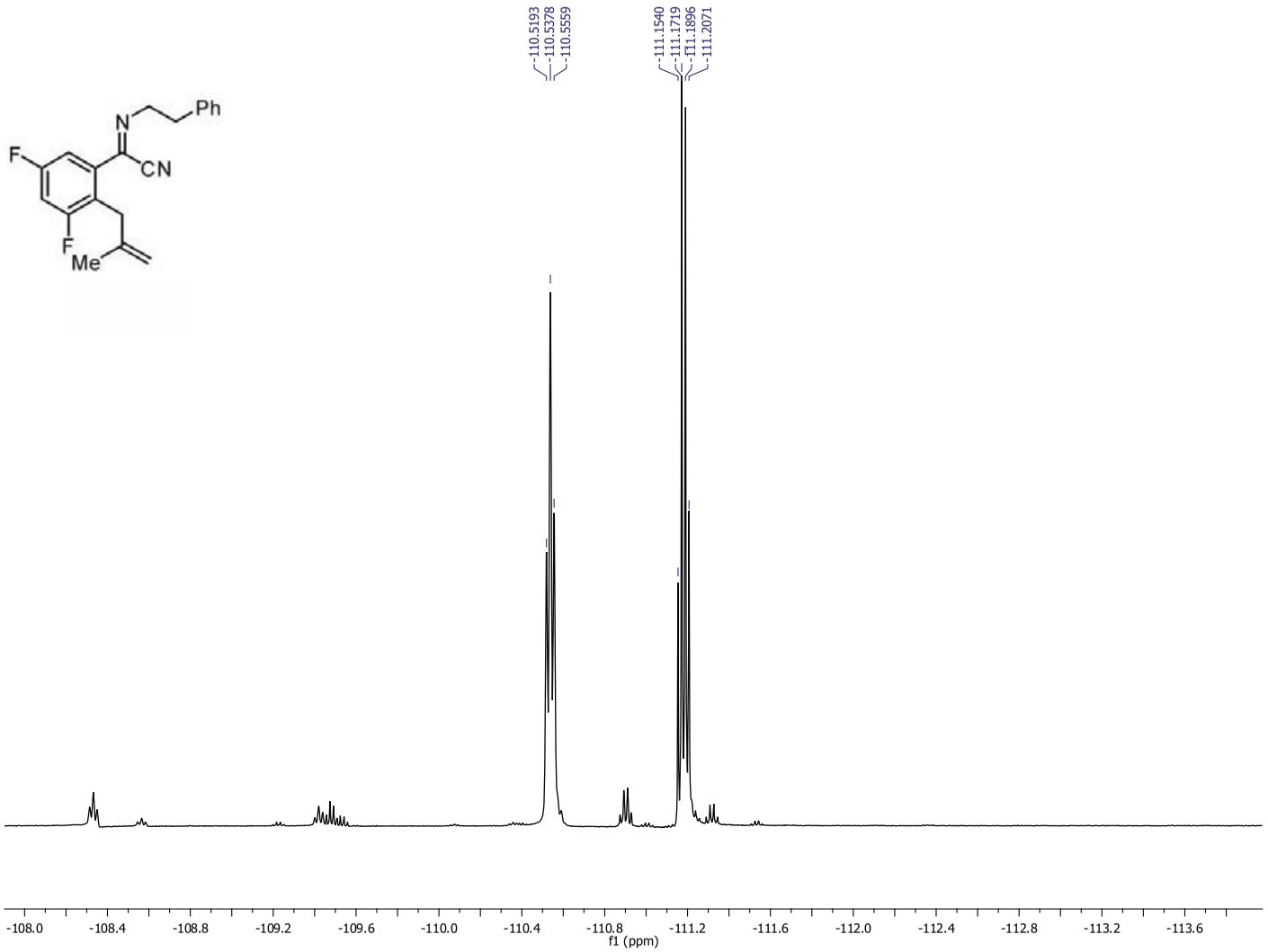
32.0485
32.0833
36.5595
60.7436
106.2484
106.4445
106.4708
106.6674
109.6366
111.2758
112.9841
113.1975
122.7315
126.8995
128.8131
129.1597
135.9677
136.0167
136.0363
136.0854
138.5993
140.6328
143.1908
160.1225
160.2293
160.7846
160.8769
162.1016
162.2078
162.7607
162.8529
Ph
N
CN
F
Me
F
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
f1 (ppm)


-110.5193
-110.5378
-110.5559
-111.1540
-111.1719
-111.1896
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F
N
Ph
CN
F
Me
-108.0
-108.4
-108.8
-109.2
-109.6
-110.0
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-112.8
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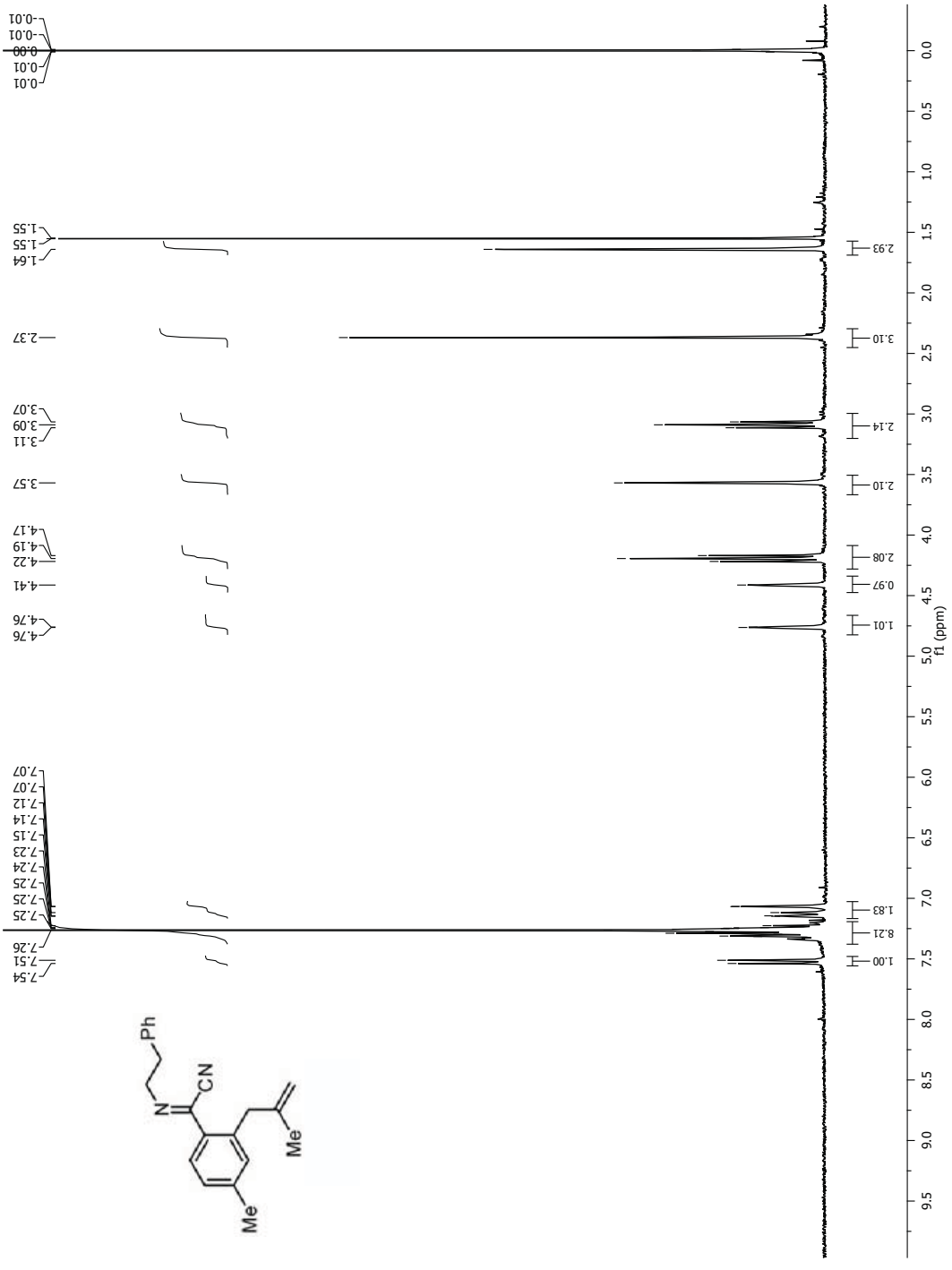
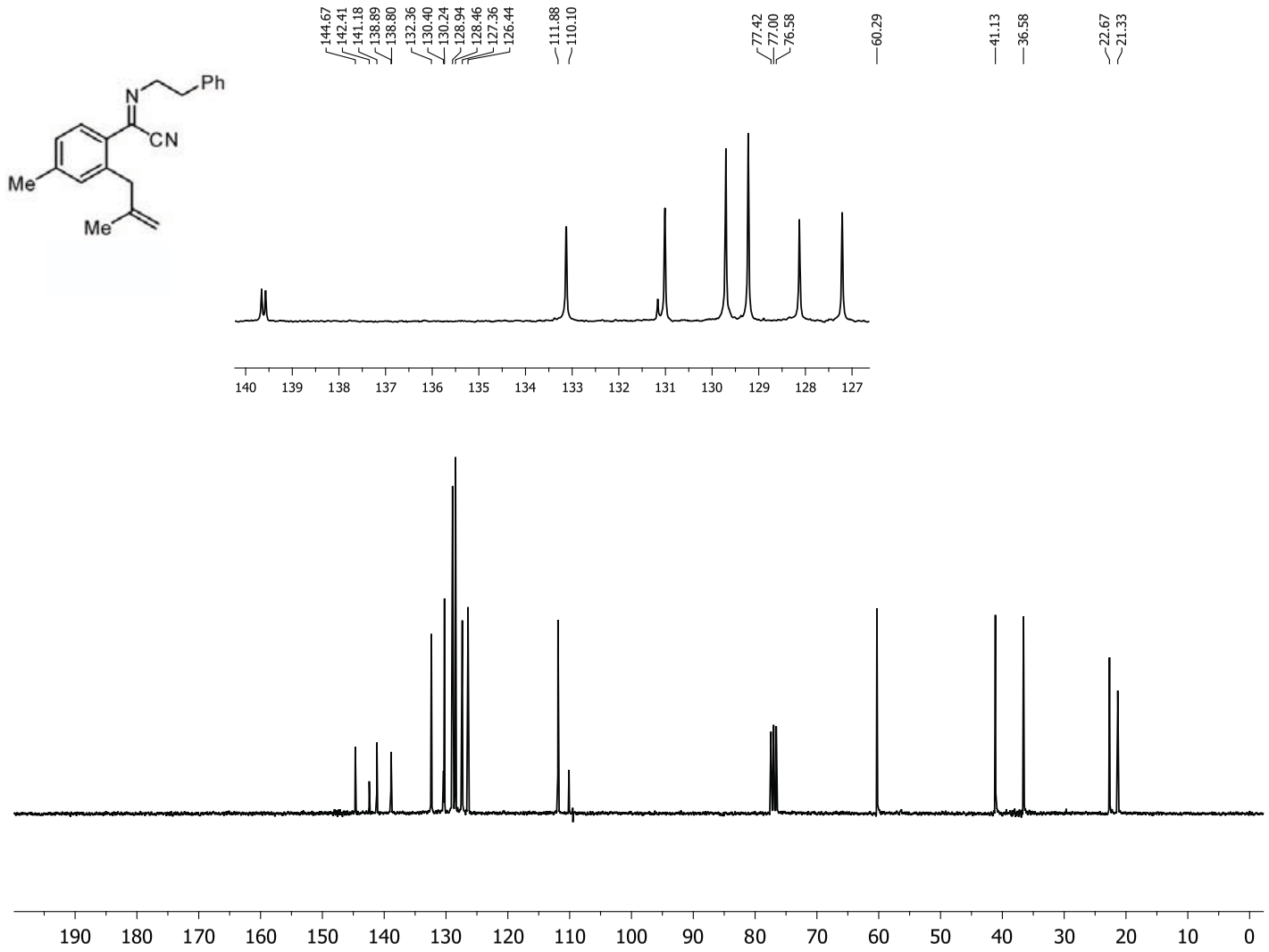
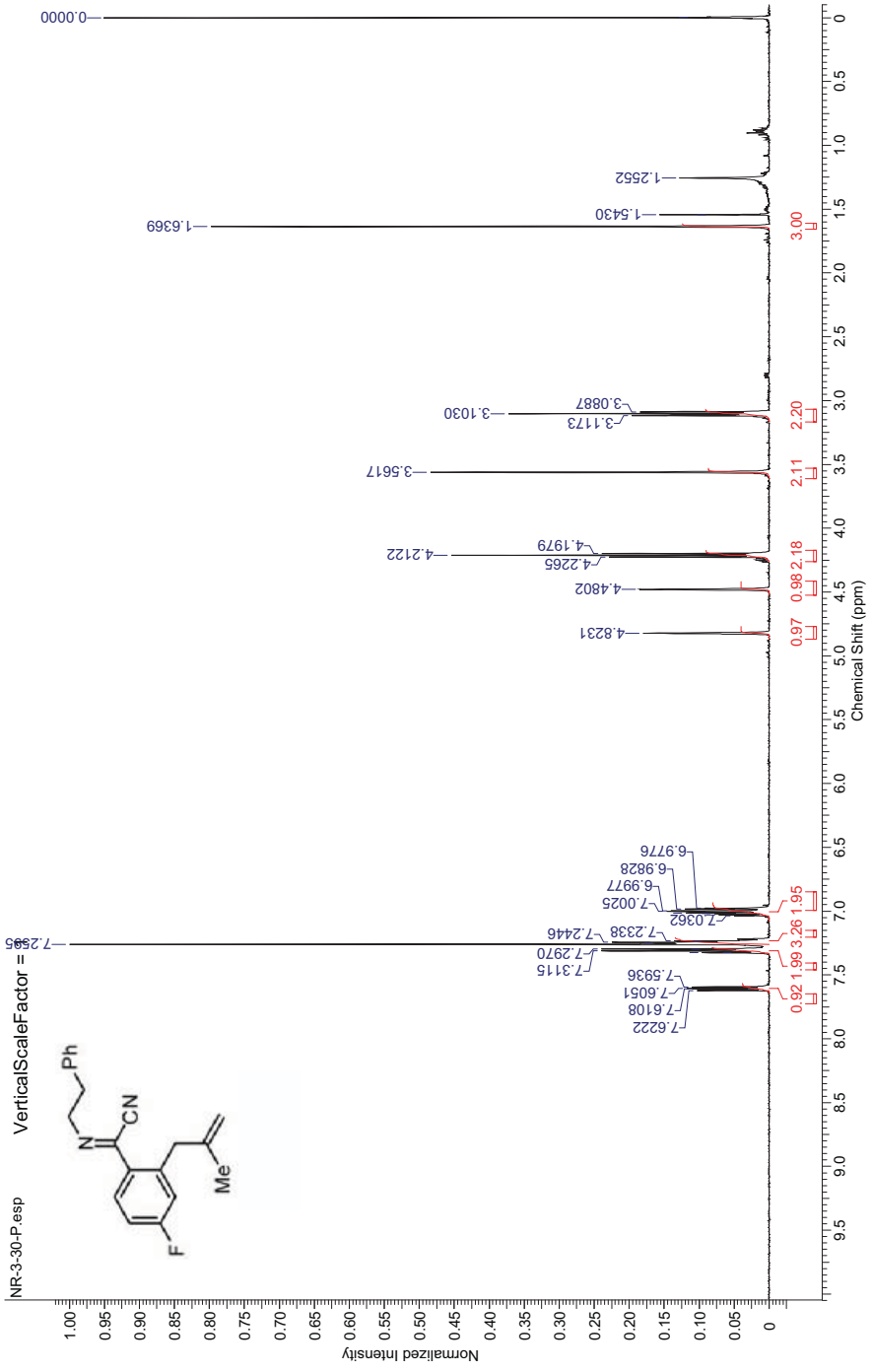
-113.6
f1 (ppm)

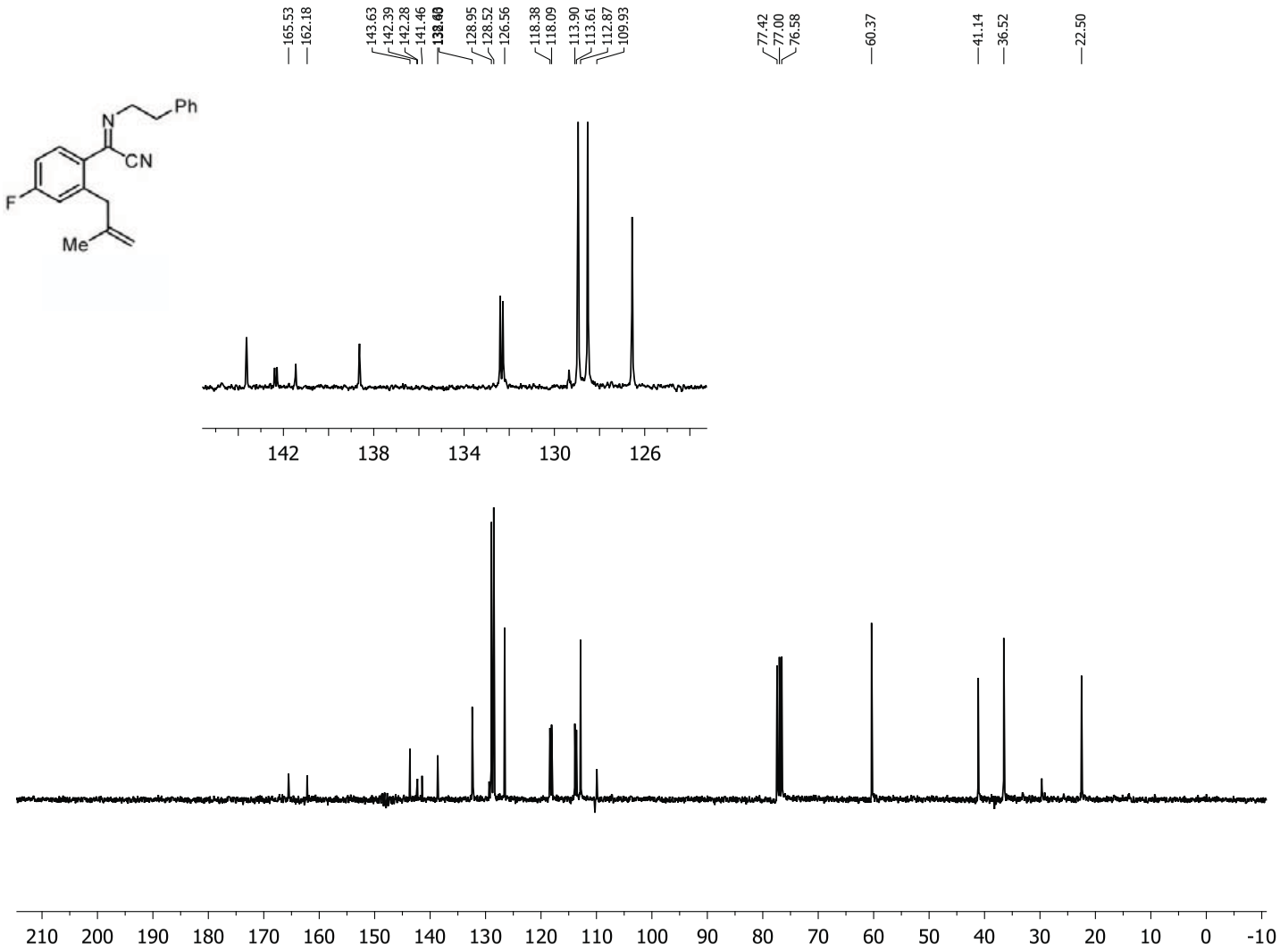

Ph
N
CN
Me
Me
f1 (ppm)


144.67
142.41
141.18
138.89
138.80
132.36
130.40
130.24
128.94
128.46
127.36
126.44
111.88
110.10
77.42
77.00
76.58
60.29
41.13
36.58
22.67
21.33
N
Ph
CN
Me
Me
140 139 138 137 136 135 134 133 132 131 130 129 128 127
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

8/22/2013 6:11:14 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Mar 27 2013 |
| *Date Stamp* | Mar 27 2013 | *File Name* | C:\Users\Naveen\Desktop\NR-3-30-P.fid\fid | *Frequency (MHz)* | 499.87 |
| *Nucleus* | 1H | *Number of Transients* | 8 | *Original Points Count* | 15136 | *Points Count* | 131072 |
| *Pulse Sequence* | s2pul | *Receiver Gain* | 60.00 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 2496.1433 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 8000.00 | *Temperature (degree C)* | AMBIENT TEMPERATURE |




165.53
162.18
143.63
142.39
142.28
141.46
128.95
128.52
126.56
118.38
118.09
113.90
113.61
112.87
109.93
77.42
77.00
76.58
60.37
41.14
36.52
22.50
Ph
N
CN
F
Me
142
138
134
130
126
210
200
190
180
170
160
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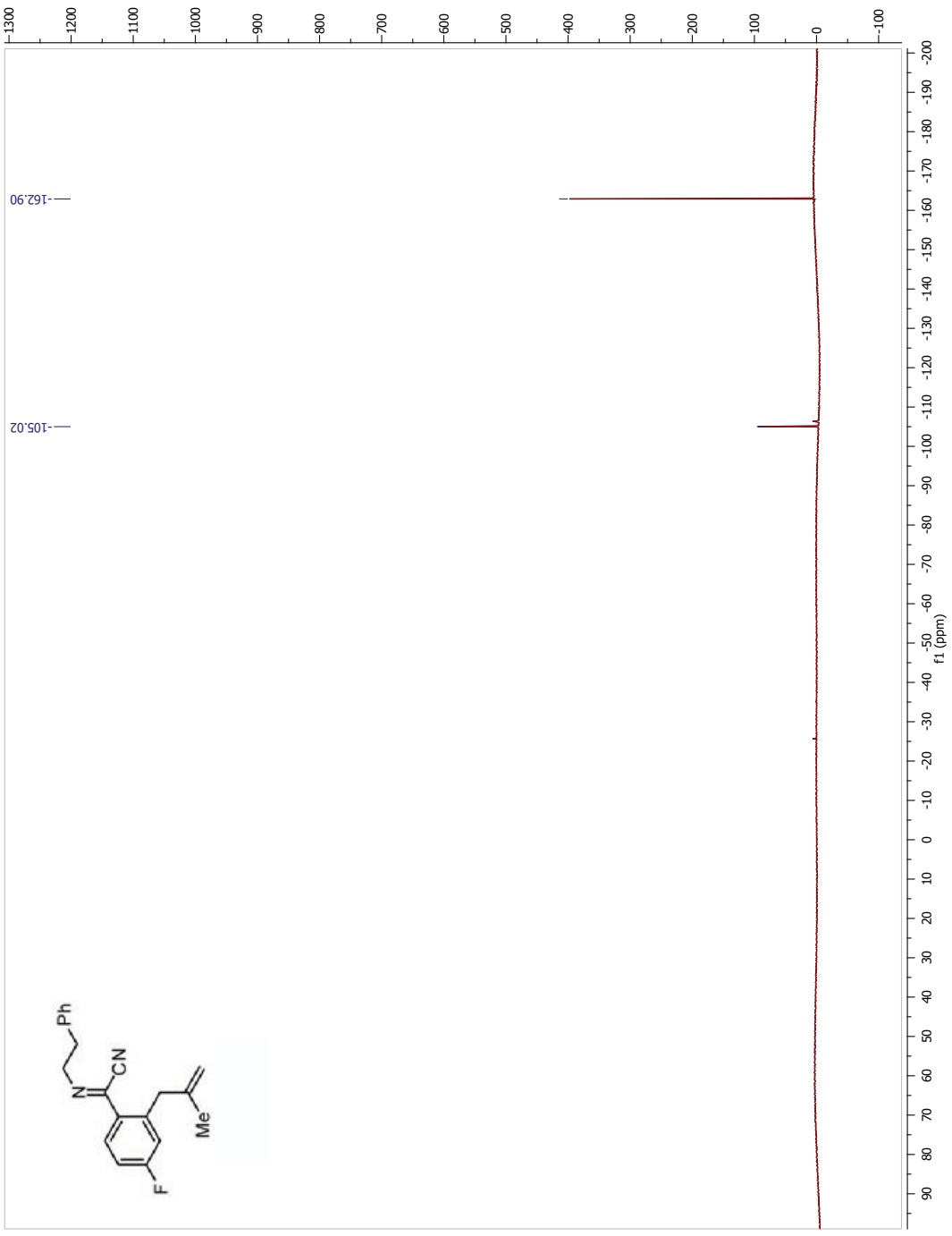
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


-162.90
-105.02
f1 (ppm)
Ph
N
CN
Me
F

| | | | | | |
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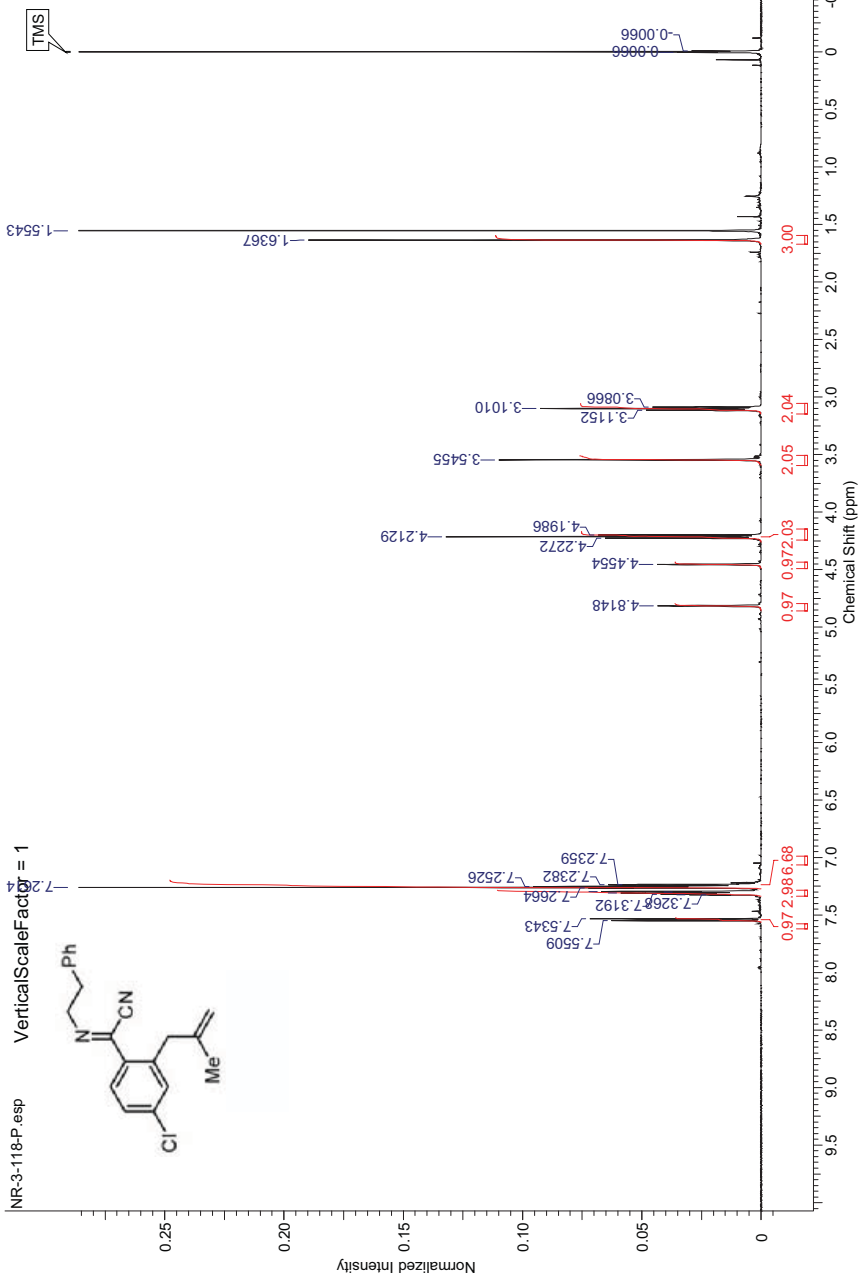
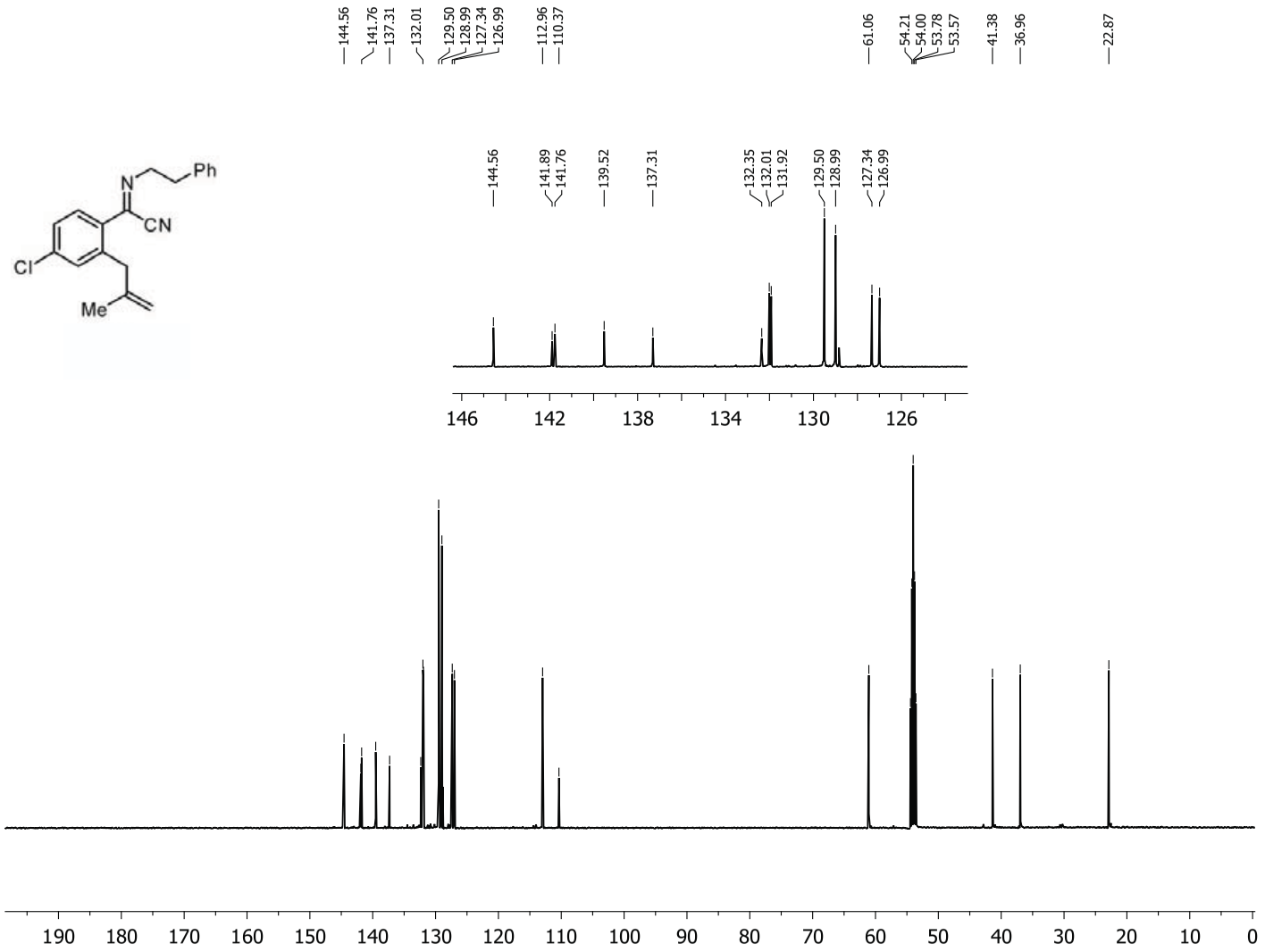
| Acquisition Time (sec) | 3.2768 | Date | 23 Jul 2013 15:35:12 | Date Stamp | 23 Jul 2013 15:35:12 |
| File Name | C:\Users\Naveen\Desktop\NR-3-118-P\10\fid | Frequency (MHz) | 500.13 | Nucleus | 1H |
| Number of Transients | 16 | Origin | spect | Original Points Count | 32768 | Owner | auto |
| Points Count | 131072 | Pulse Sequence | zg30 | Receiver Gain | 134.85 | SW(cyclical) (Hz) | 10000.00 |
| Solvent | CHLOROFORM-d | | | Spectrum Offset (Hz) | 3076.5151 | Spectrum Type | STANDARD |
| Sweep Width (Hz) | 9999.92 | Temperature (degree C) | 21.003 | | | | |

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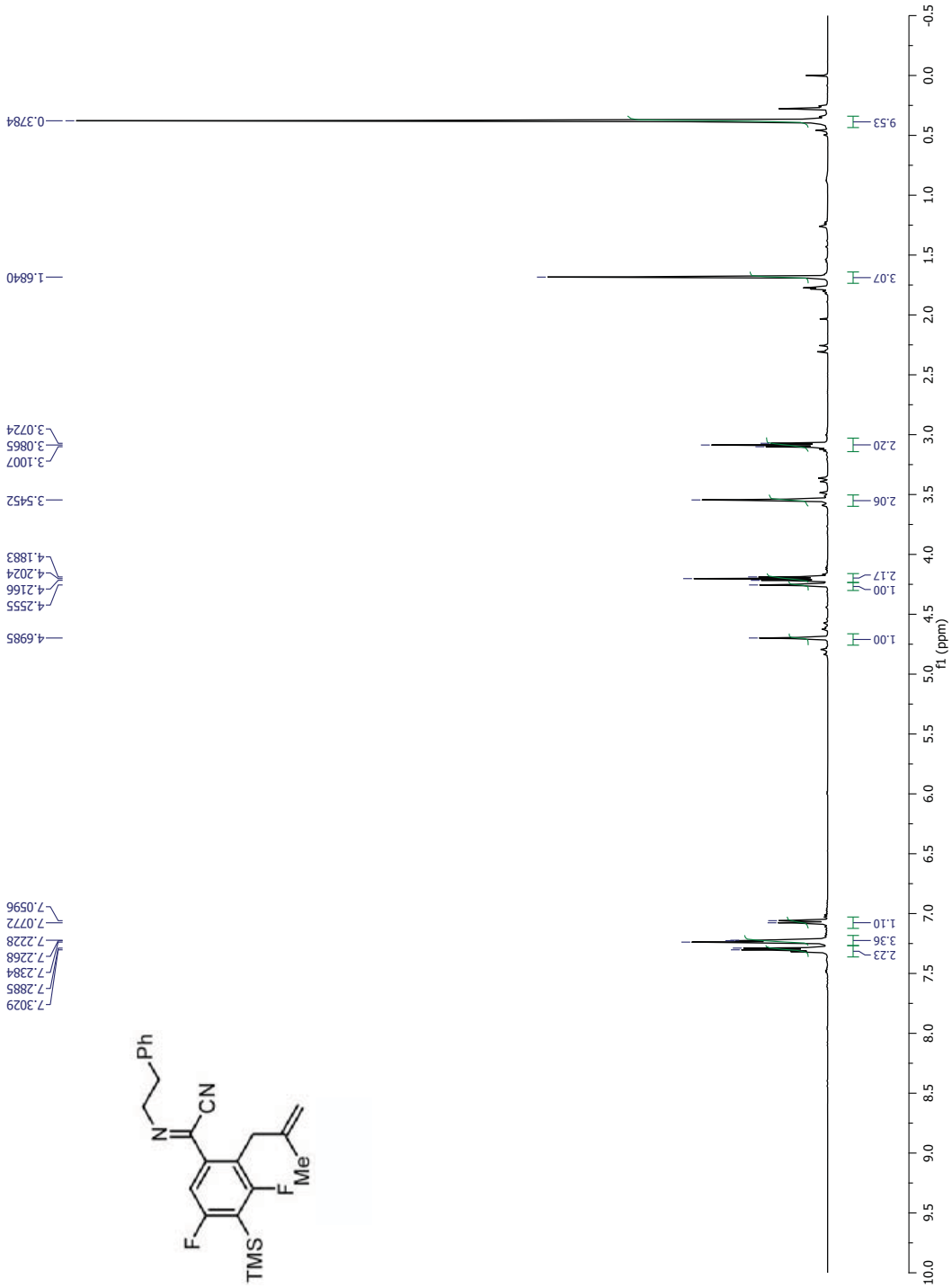
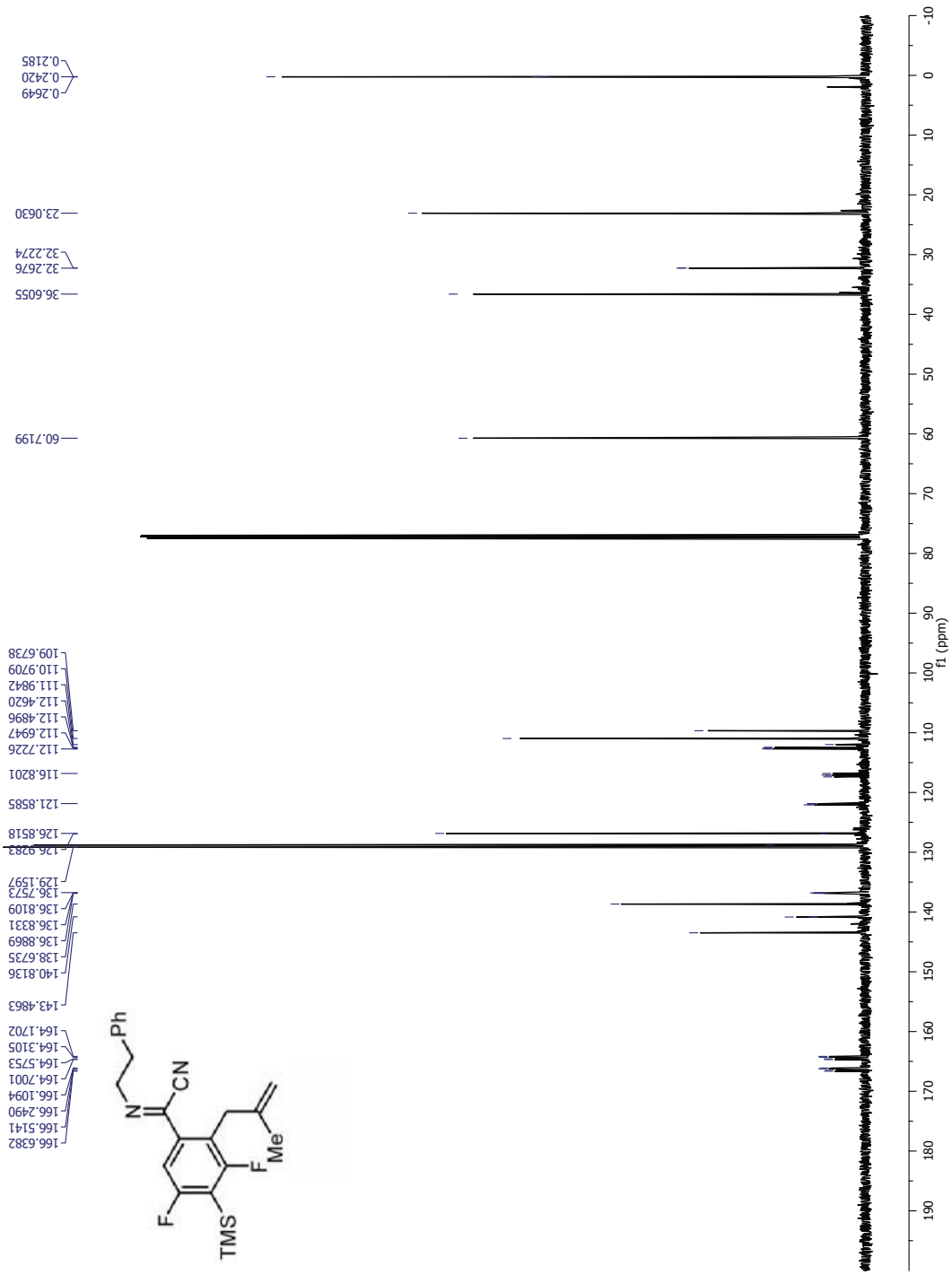
141.76
137.31
132.01
129.50
128.99
127.34
126.99
112.96
110.37
61.06
54.21
54.00
53.78
53.57
41.38
36.96
22.87
Ph
N
CN
Cl
Me
144.56
141.89
141.76
139.52
137.31
132.35
132.01
131.92
129.50
128.99
127.34
126.99
146
142
138
134
130
126
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Ph
N
CN
F
Me
F
TMS
0.3784
1.6840
3.0724
3.0865
3.1007
3.5452
4.1883
4.2024
4.2166
4.2555
4.6985
7.0596
7.0772
7.2228
7.2268
7.2384
7.2885
7.3029
9.53
3.07
2.20
2.06
2.17
1.00
1.00
1.10
3.36
2.23
f1 (ppm)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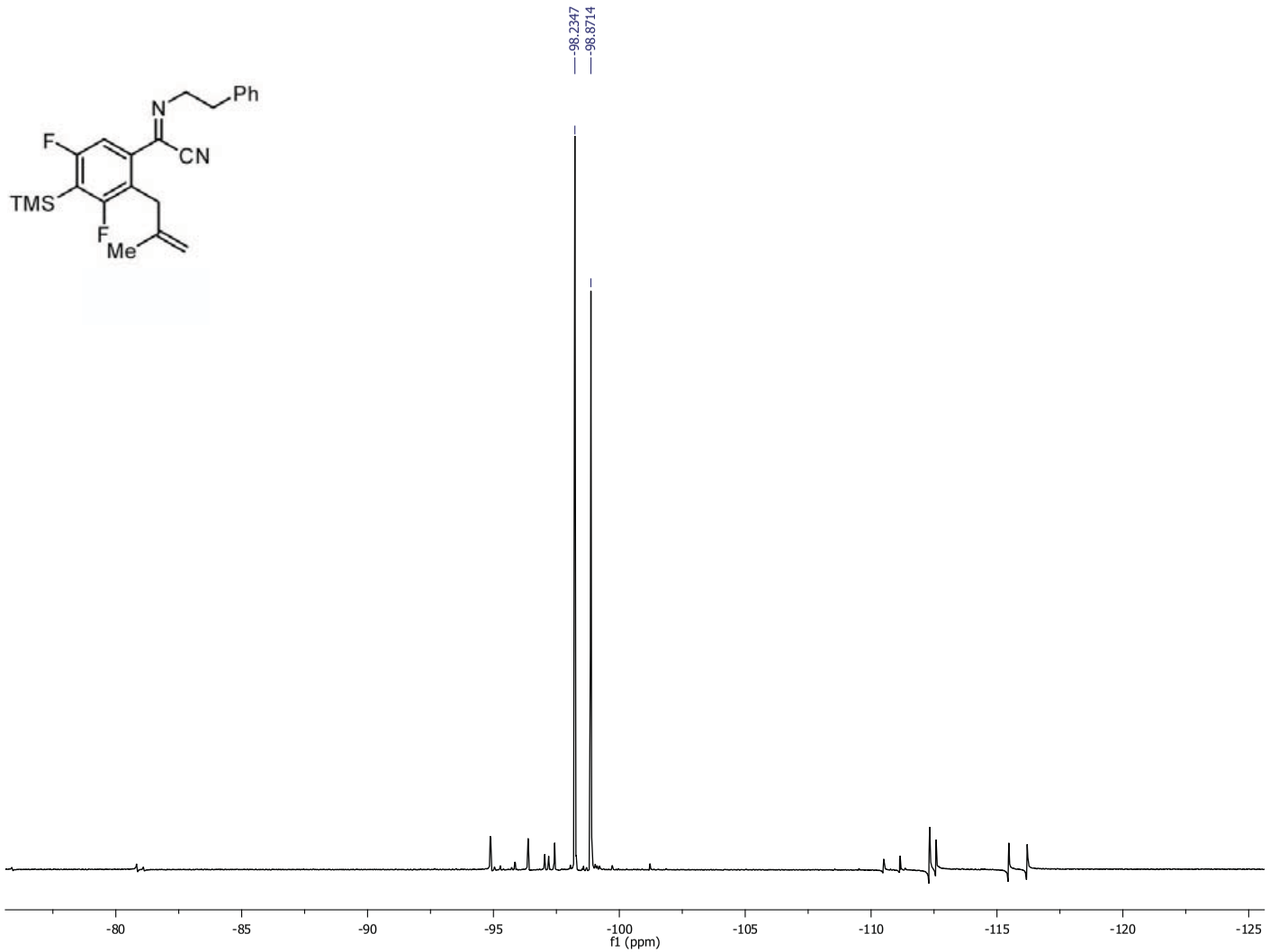
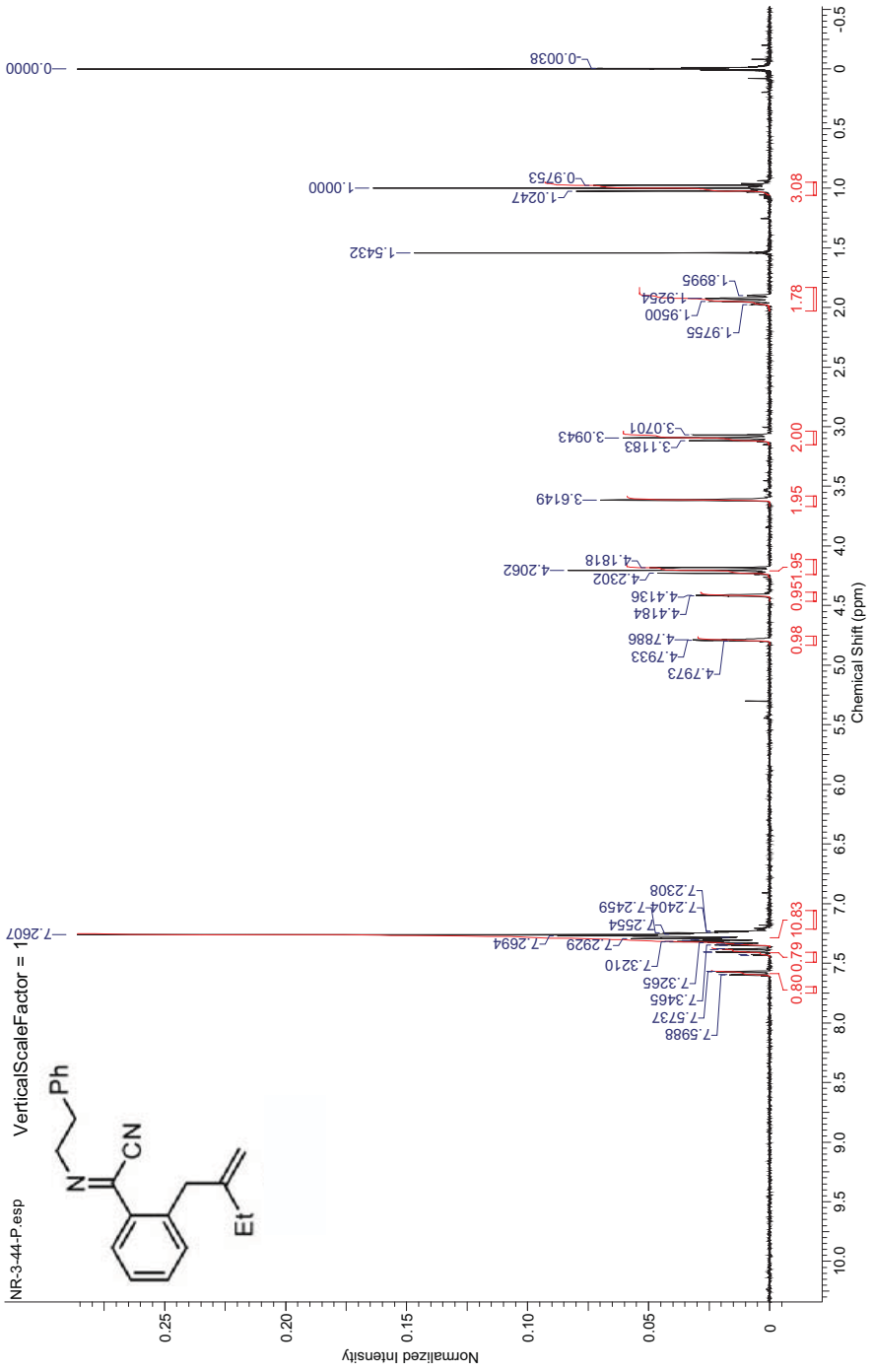
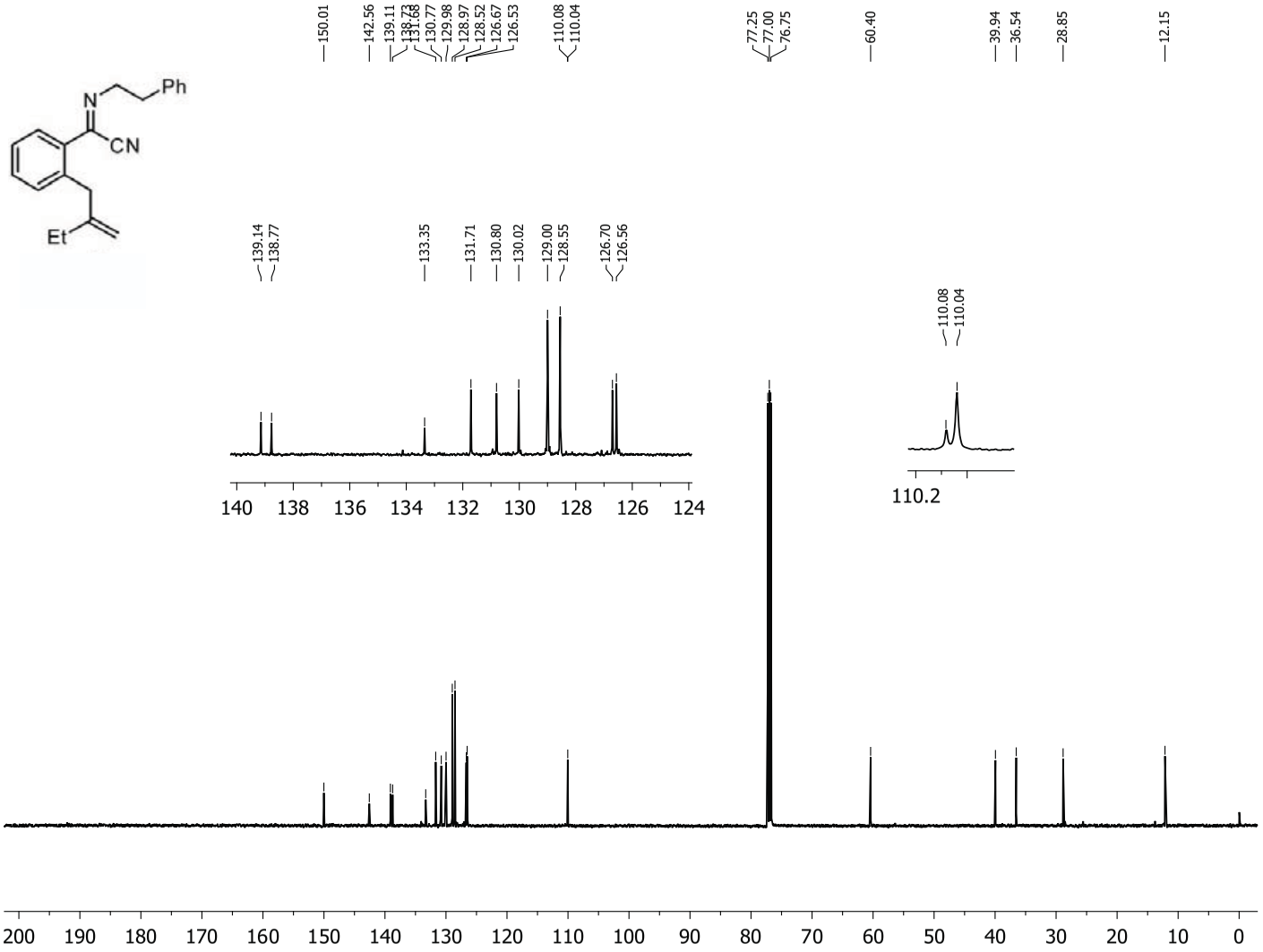
0.2420
0.2649
23.0630
32.2274
32.2676
36.6055
60.7199
109.6738
110.9709
111.9842
112.4620
112.4896
112.6947
112.7226
116.8201
121.8585
126.8518
126.9283
129.1597
136.7573
136.8109
136.8331
136.8869
138.6735
140.8136
143.4863
164.1702
164.3105
164.5753
164.7001
166.1094
166.2490
166.5141
166.6382
Ph
N
CN
F
Me
F
TMS
f1 (ppm)


-98.2347
-98.8714
N
Ph
CN
F
TMS
F
Me
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
f1 (ppm)

9/26/2013 2:52:47 PM

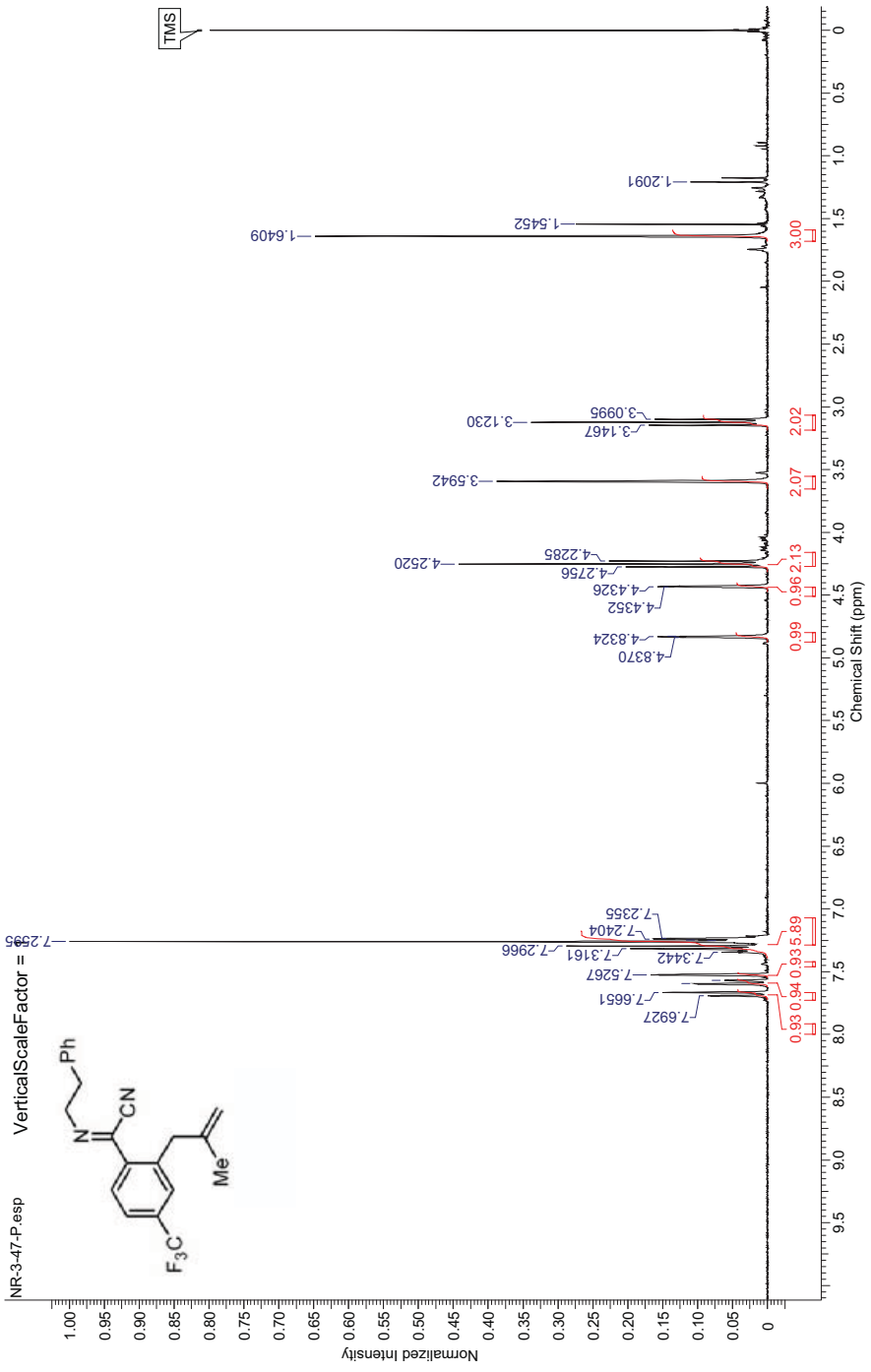
| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-44-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Apr 23 2013 | *Date Stamp* | Apr 23 2013 *File Name* C:\Users\Naveen\Desktop\130423v3_3702.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.2959 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |

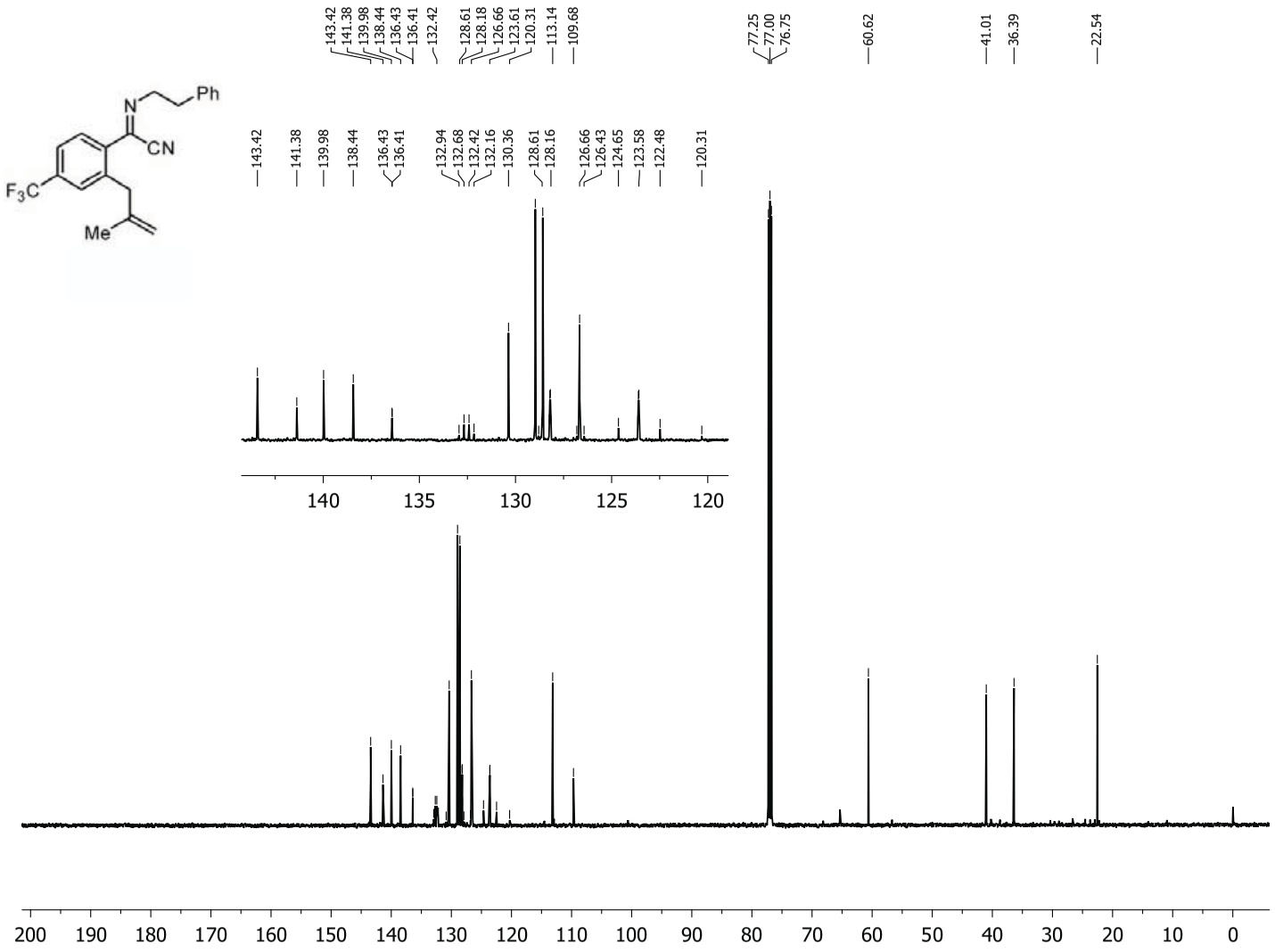



150.01
142.56
139.11
138.73
131.68
130.77
129.98
128.97
128.52
126.67
126.53
110.08
110.04
77.25
77.00
76.75
60.40
39.94
36.54
28.85
12.15
Ph
N
CN
Et
139.14
138.77
133.35
131.71
130.80
130.02
129.00
128.55
126.70
126.56
110.08
110.04
110.2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
140 138 136 134 132 130 128 126 124

9/26/2013 2:55:32 PM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-47-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Apr 27 2013 | *Date Stamp* | Apr 27 2013 *File Name* C:\Users\Naveen\Desktop\130427v3_0102.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.0212 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |




143.42
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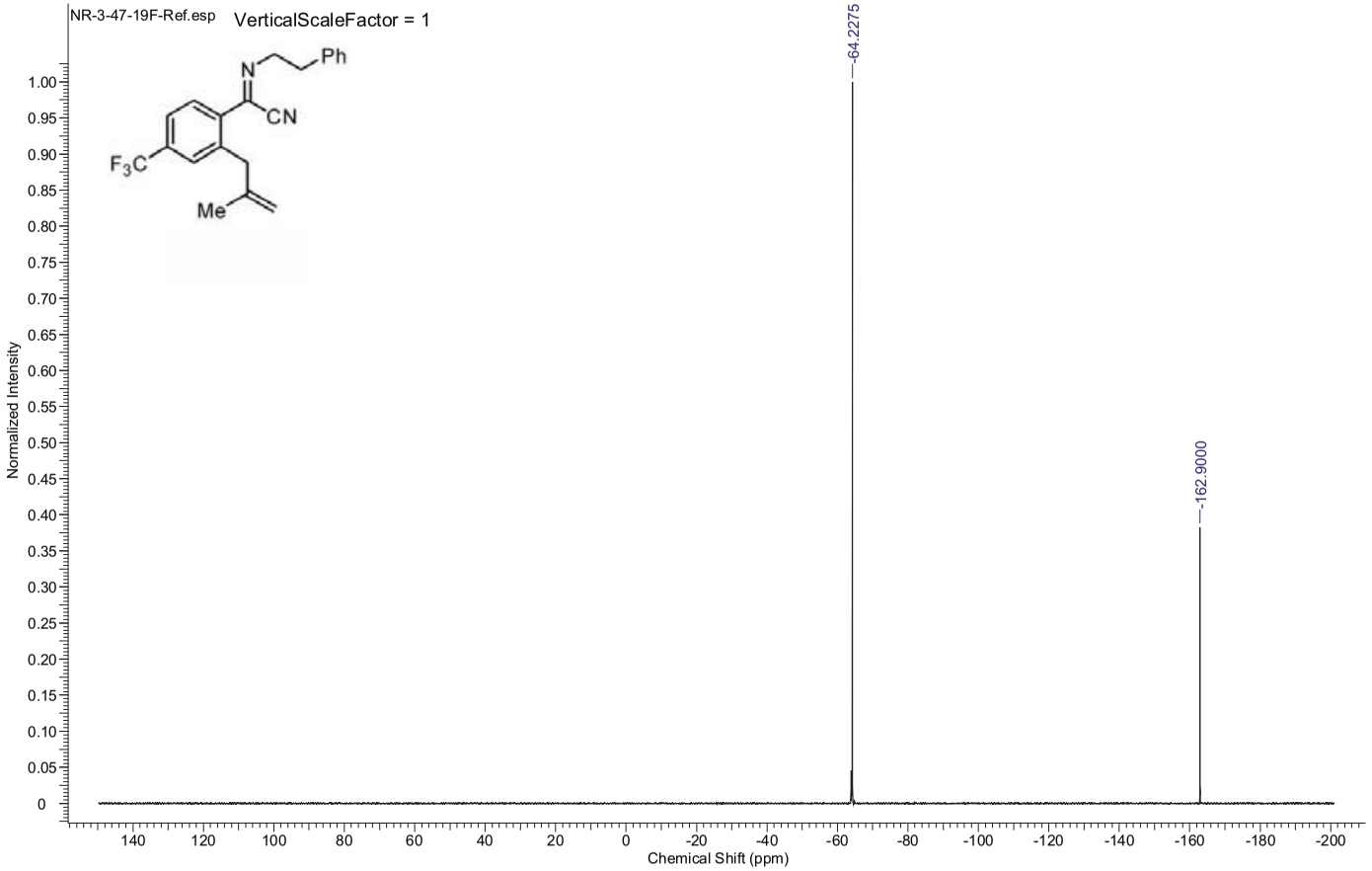
136.41
132.42
128.61
128.18
126.66
123.61
120.31
113.14
109.68
77.25
77.00
76.75
60.62
41.01
36.39
22.54
N
Ph
CN
F3C
Me
132.94
132.68
132.42
132.16
130.36
128.16
126.43
124.65
123.58
122.48
140
135
130
125
120
200
190
180
170
160
150
110
100
90
80
70
50
40
30
20
10
0

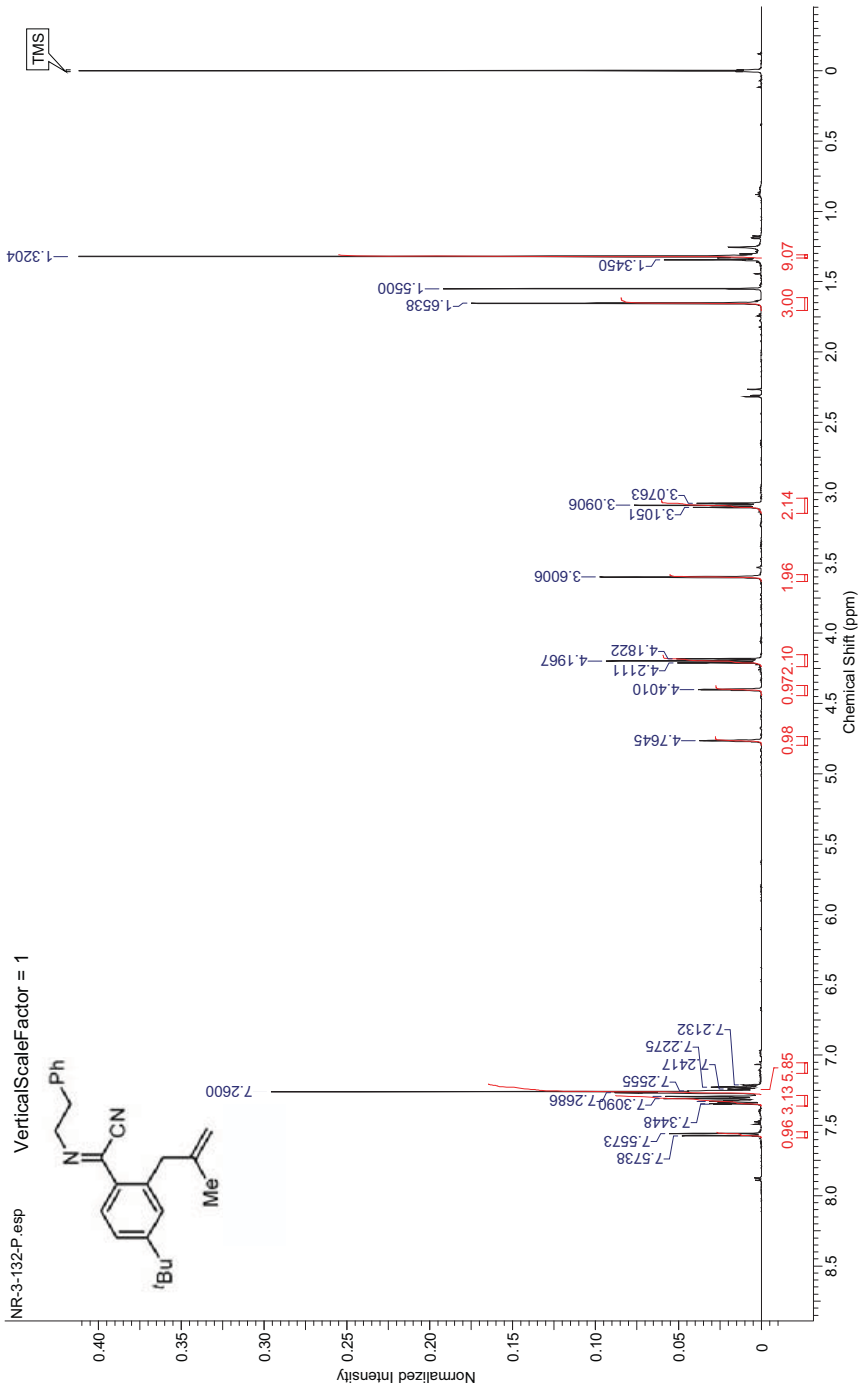
9/26/2013 3:12:04 PM

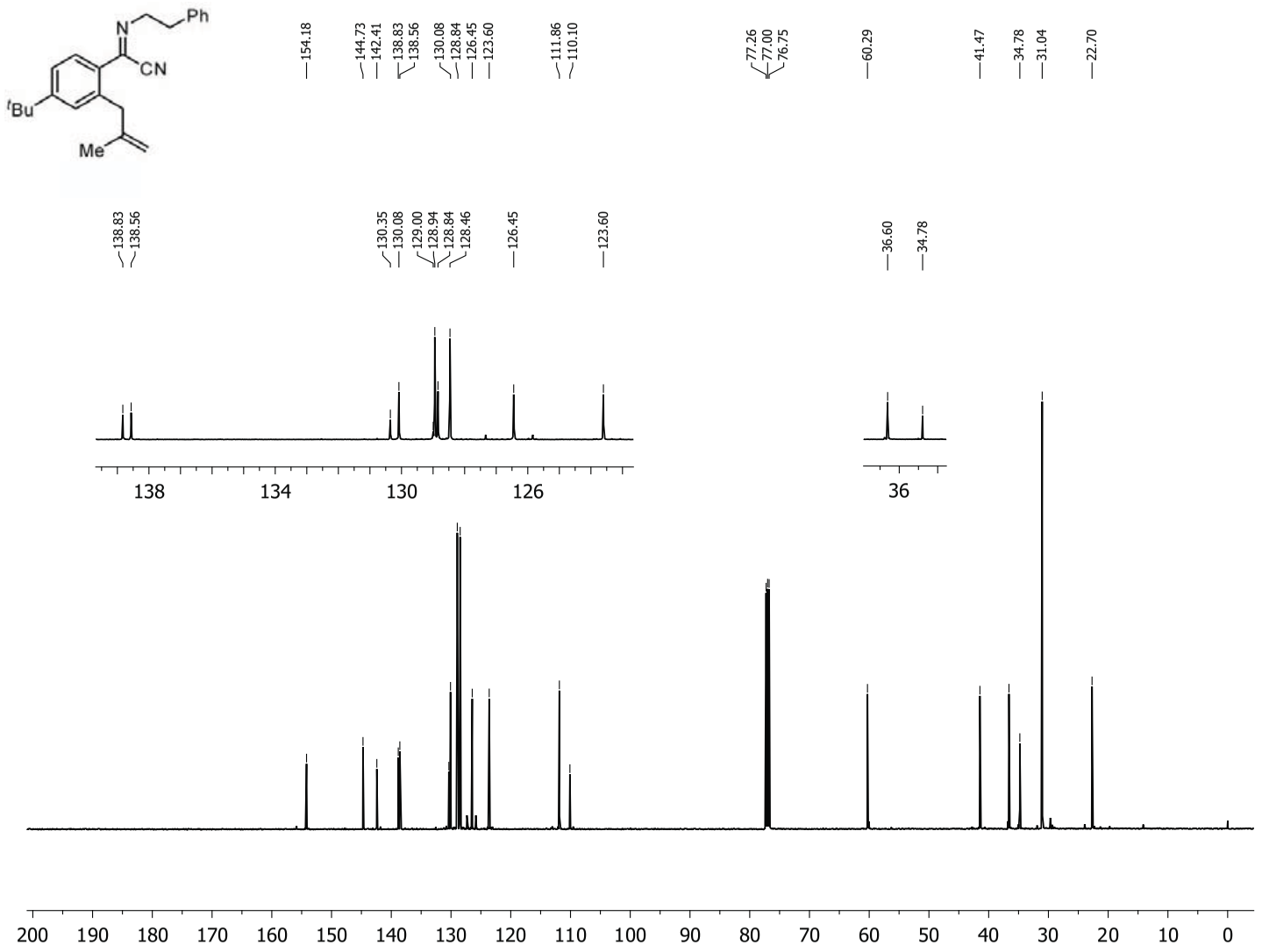
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 0.6464 | ***Comment*** | NR-3-47-19F-Ref University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | May 9 2013 | ***Date Stamp*** | May 9 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130509v3_1102.fid\fid | | |
| ***Frequency (MHz)*** | 282.23 | ***Nucleus*** | 19F | ***Number of Transients*** | 32 | ***Original Points Count*** | 64000 |
| ***Points Count*** | 65536 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 12.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | -7242.4761 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 99009.90 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



8/28/2013 6:37:07 PM

| | | | | | |
|---|---|---|---|---|---|
| **Acquisition Time (sec)** | 3.2768 | **Date** | 26 Aug 2013 15:48:00 | **Date Stamp** | 26 Aug 2013 15:48:00 |
| **File Name** | C:\Users\Naveen\Desktop\NR-3-132-P\10\fid | **Frequency (MHz)** | 500.13 | **Nucleus** | 1H |
| **Number of Transients** | 16 | **Origin** | spect | **Original Points Count** | 32768 | **Owner** | auto |
| **Points Count** | 131072 | **Pulse Sequence** | zg30 | **Receiver Gain** | 92.58 | **SW(cyclical) (Hz)** | 10000.00 |
| **Solvent** | CHLOROFORM-d | | | **Spectrum Offset (Hz)** | 3075.7522 | **Spectrum Type** | STANDARD |
| **Sweep Width (Hz)** | 9999.92 | **Temperature (degree C)** | 21.000 | | | | |




Ph
N
CN
tBu
Me
154.18
144.73
142.41
138.83
138.56
130.08
128.84
126.45
123.60
111.86
110.10
77.26
77.00
76.75
60.29
41.47
34.78
31.04
22.70
138.83
138.56
130.35
130.08
129.00
128.94
128.84
128.46
126.45
123.60
36.60
34.78
138
134
130
126
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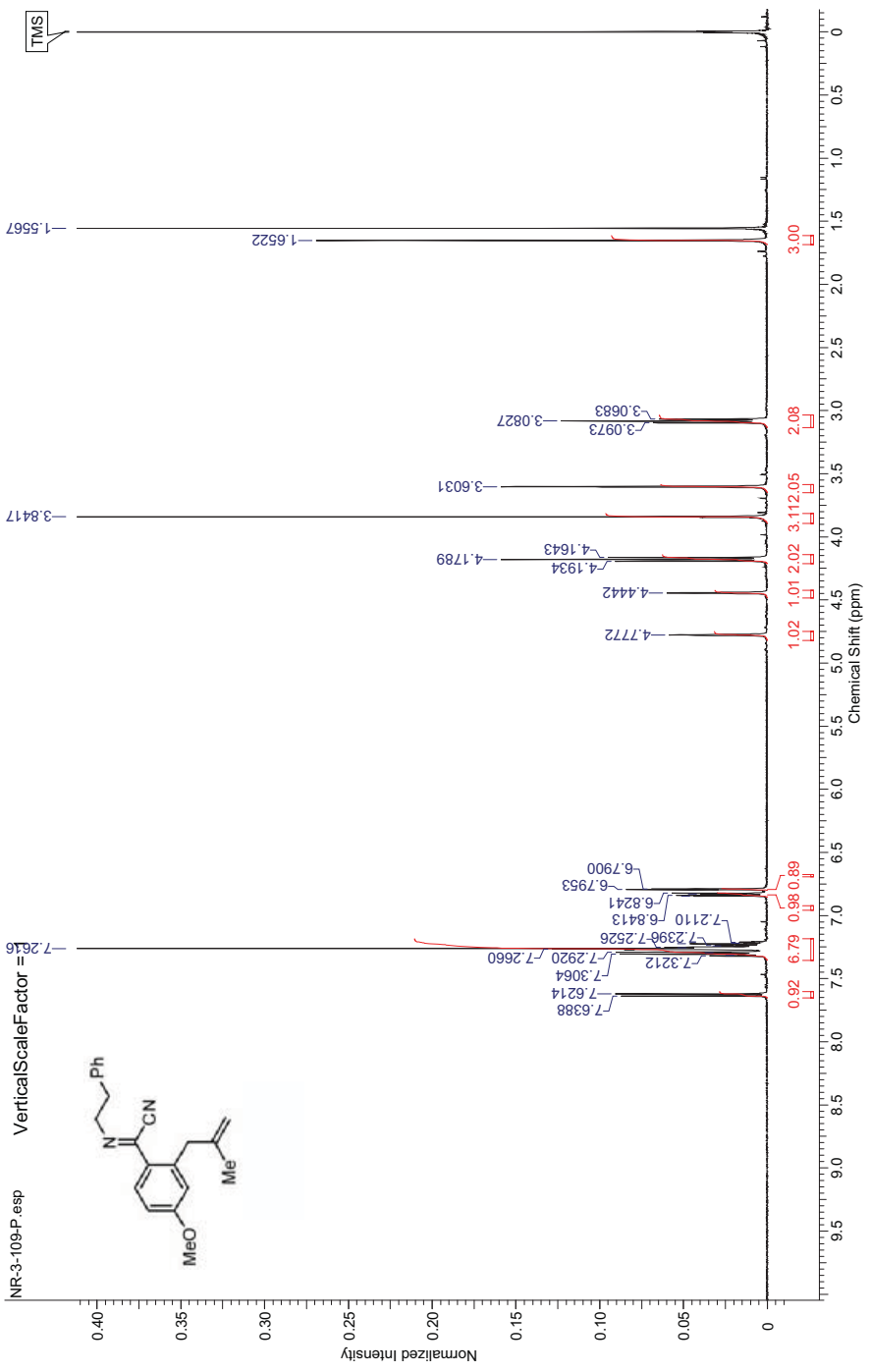
130
120
110
100
90
80
70
60
50
40
30
20
10
0

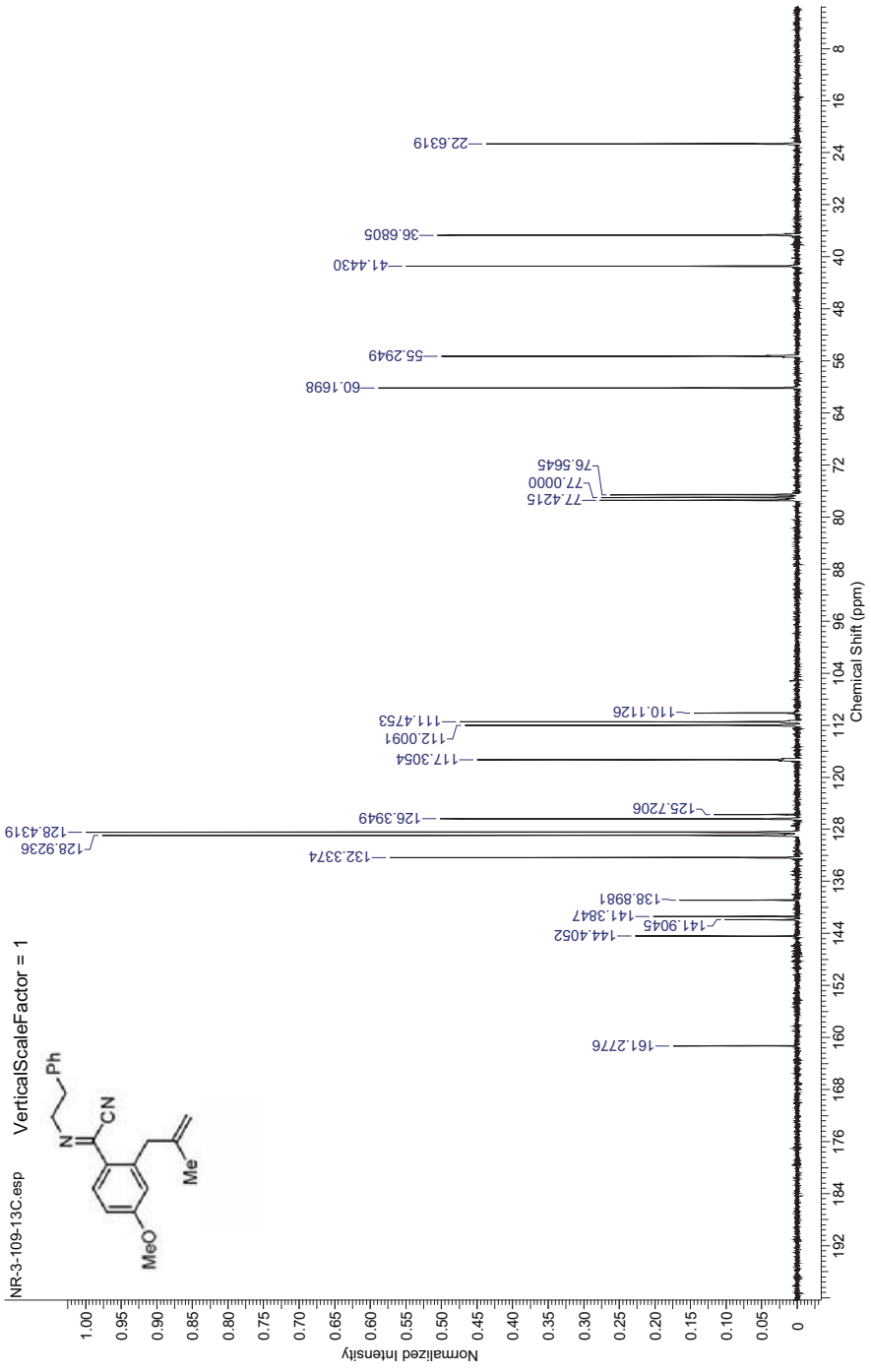
9/26/2013 3:08:16 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Jul 6 2013 |
| *Date Stamp* | Jul 6 2013 | *File Name* | C:\Users\Naveen\Desktop\NR-3-109-Fr3.fid\fid | *Frequency (MHz)* | 499.87 |
| *Nucleus* | 1H | *Number of Transients* | 16 | *Original Points Count* | 15136 |
| *Pulse Sequence* | s2pul | *Receiver Gain* | 60.00 | *Solvent* | CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2496.9368 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 8000.00 |
| | | | | *Temperature (degree C)* | AMBIENT TEMPERATURE |



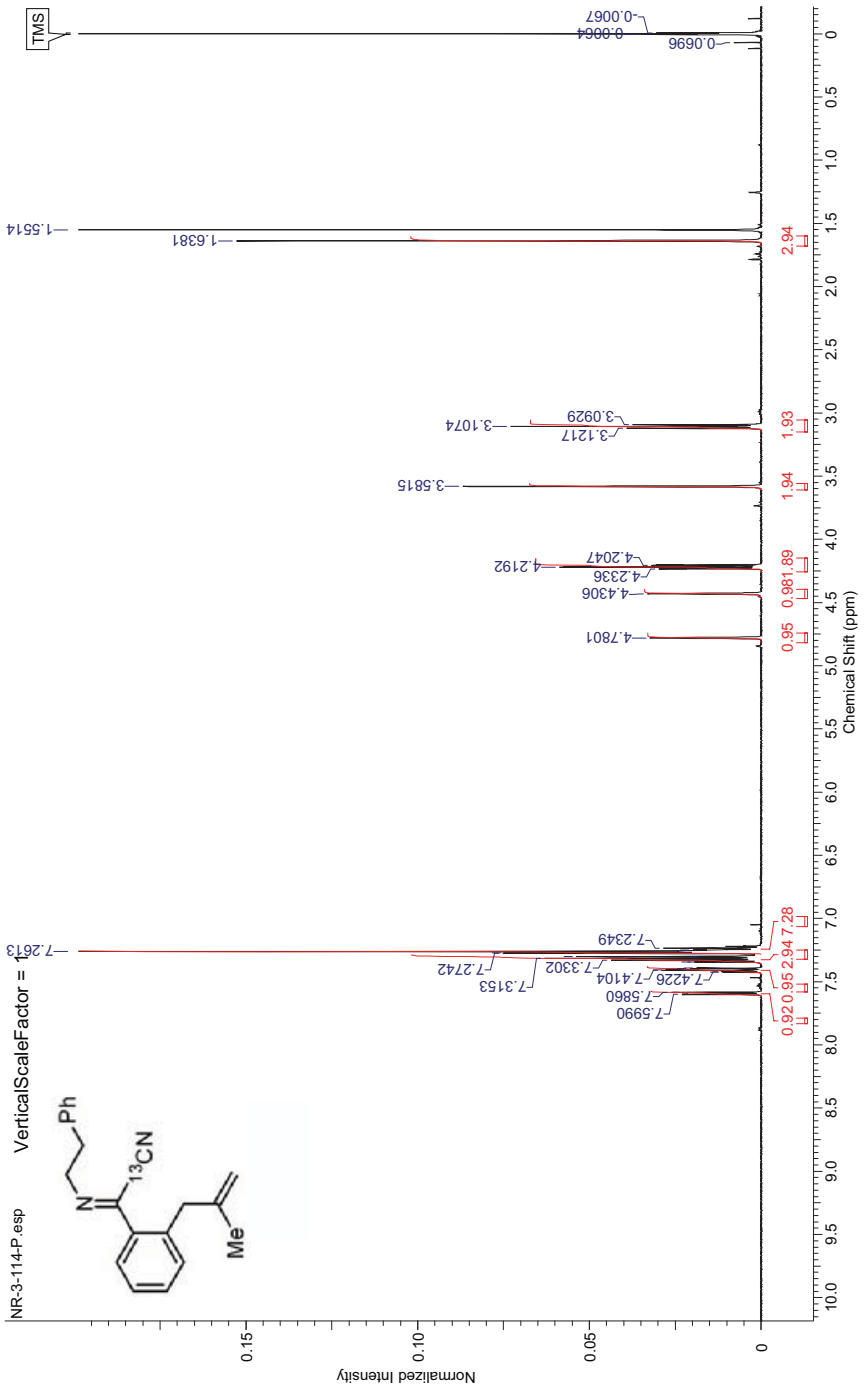
9/26/2013 3:10:36 PM

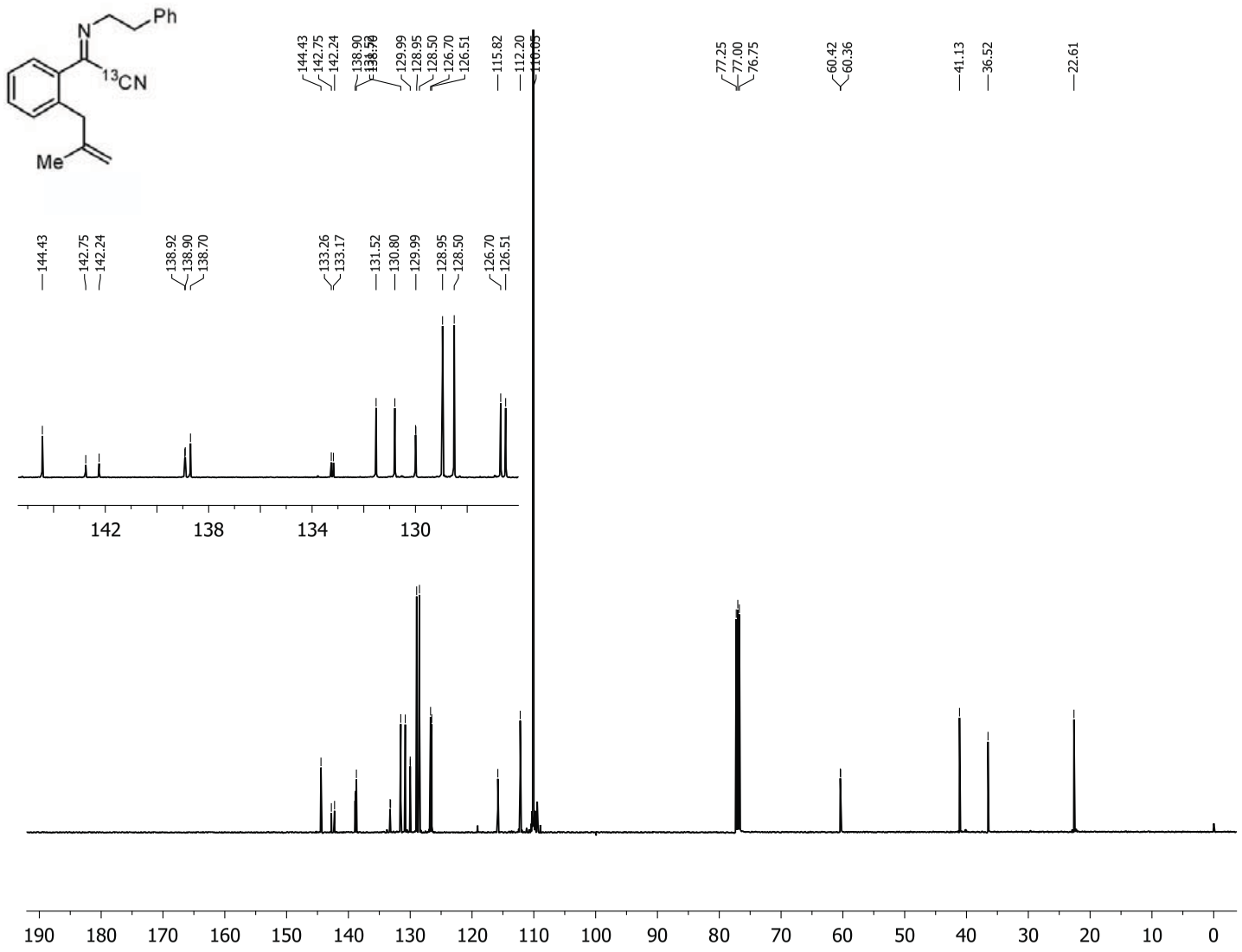
| | | | |
|---|---|---|---|
| **Acquisition Time (sec)** | 0.8000 | **Comment** | NR-3-109-13C University of Minnesota Department of Chemistry VAC-300 |
| **Date** | Jul 8 2013 | **Date Stamp** | Jul 8 2013 **File Name** C:\Users\Naveen\Desktop\130708v3 3203.fid\fid |
| **Frequency (MHz)** | 75.43 | **Nucleus** | 13C **Number of Transients** 1024 **Original Points Count** 13889 |
| **Points Count** | 16384 | **Pulse Sequence** | s2pul **Receiver Gain** 30.00 **Solvent** CHLOROFORM-d |
| **Spectrum Offset (Hz)** | 7860.3169 | **Spectrum Type** | STANDARD **Sweep Width (Hz)** 17361.11 **Temperature (degree C)** AMBIENT TEMPERATURE |



8/20/2013 4:00:28 PM

| | | | | | |
|---|---|---|---|---|---|
| **Acquisition Time (sec)** | 3.2768 | **Date** | 15 Jul 2013 15:24:32 | **Date Stamp** | 15 Jul 2013 15:24:32 |
| **File Name** | C:\Users\Naveen\Desktop\NR-3-114-P\10\fid | **Frequency (MHz)** | 500.13 | **Nucleus** | 1H |
| **Number of Transients** | 16 **Origin** spect | **Original Points Count** | 32768 | **Owner** | auto |
| **Points Count** | 131072 **Pulse Sequence** zg30 | **Receiver Gain** | 127.25 | **SW(cyclical) (Hz)** | 10000.00 |
| **Solvent** | CHLOROFORM-d | **Spectrum Offset (Hz)** | 3076.6677 | **Spectrum Type** | STANDARD |
| **Sweep Width (Hz)** | 9999.92 **Temperature (degree C)** 20.999 | | | | |




Ph
N
13CN
Me
144.43
142.75
142.24
138.90
138.70
133.26
133.17
131.52
130.80
129.99
128.95
128.50
126.70
126.51
115.82
112.20
77.25
77.00
76.75
60.42
60.36
41.13
36.52
22.61
142
138
134
130
190
180
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130
120
110
100
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70
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50
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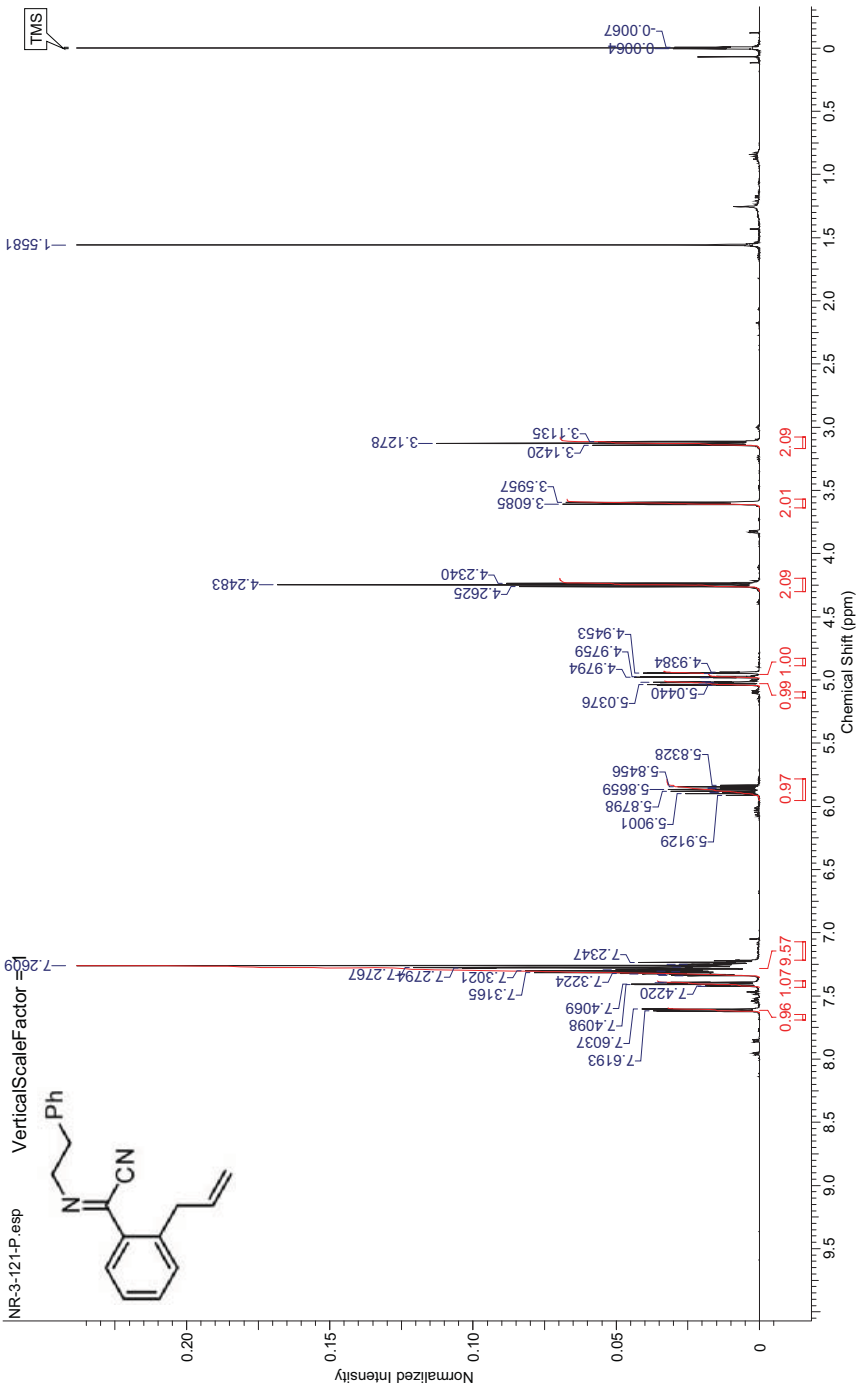
30
20
10
0

10/7/2013 6:13:32 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 3.2768 | *Date* | 29 Jul 2013 15:09:36 | *Date Stamp* | 29 Jul 2013 15:09:36 |
| *File Name* | C:\Users\Naveen\Desktop\NR-3-121-P\10\fid | *Frequency (MHz)* | 500.13 | *Nucleus* | 1H |
| *Number of Transients* | 16 *Origin* spect | *Original Points Count* | 32768 | *Owner* | auto |
| *Points Count* | 131072 *Pulse Sequence* zg30 | *Receiver Gain* | 134.85 | *SW(cyclical) (Hz)* | 10000.00 |
| *Solvent* | CHLOROFORM-d | *Spectrum Offset (Hz)* | 3076.2864 | *Spectrum Type* | STANDARD |
| *Sweep Width (Hz)* | 9999.92 *Temperature (degree C)* 21.000 | | | | |



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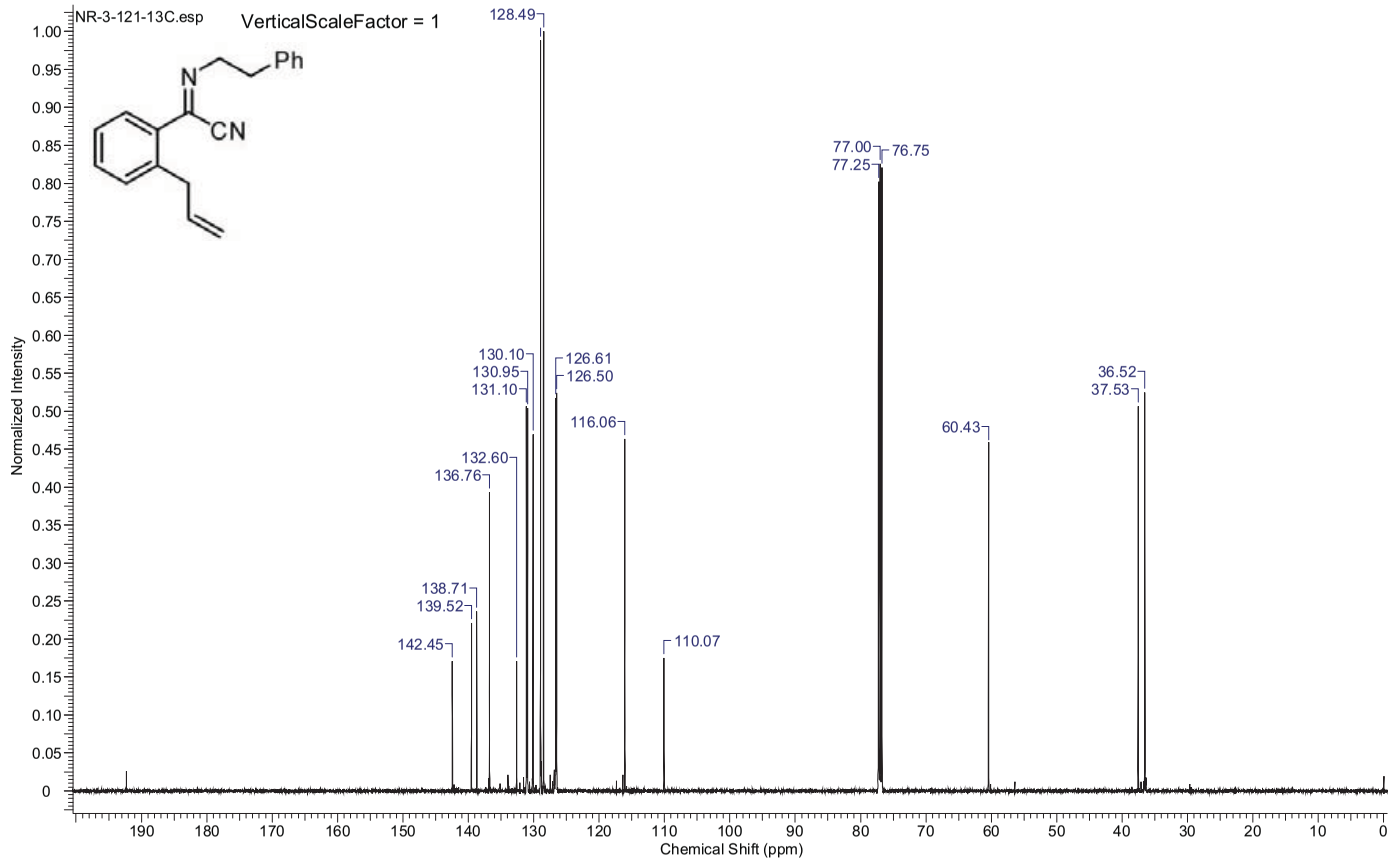
| ***Number of Transients*** | 512 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12563.9600 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 20.999 | | | | |



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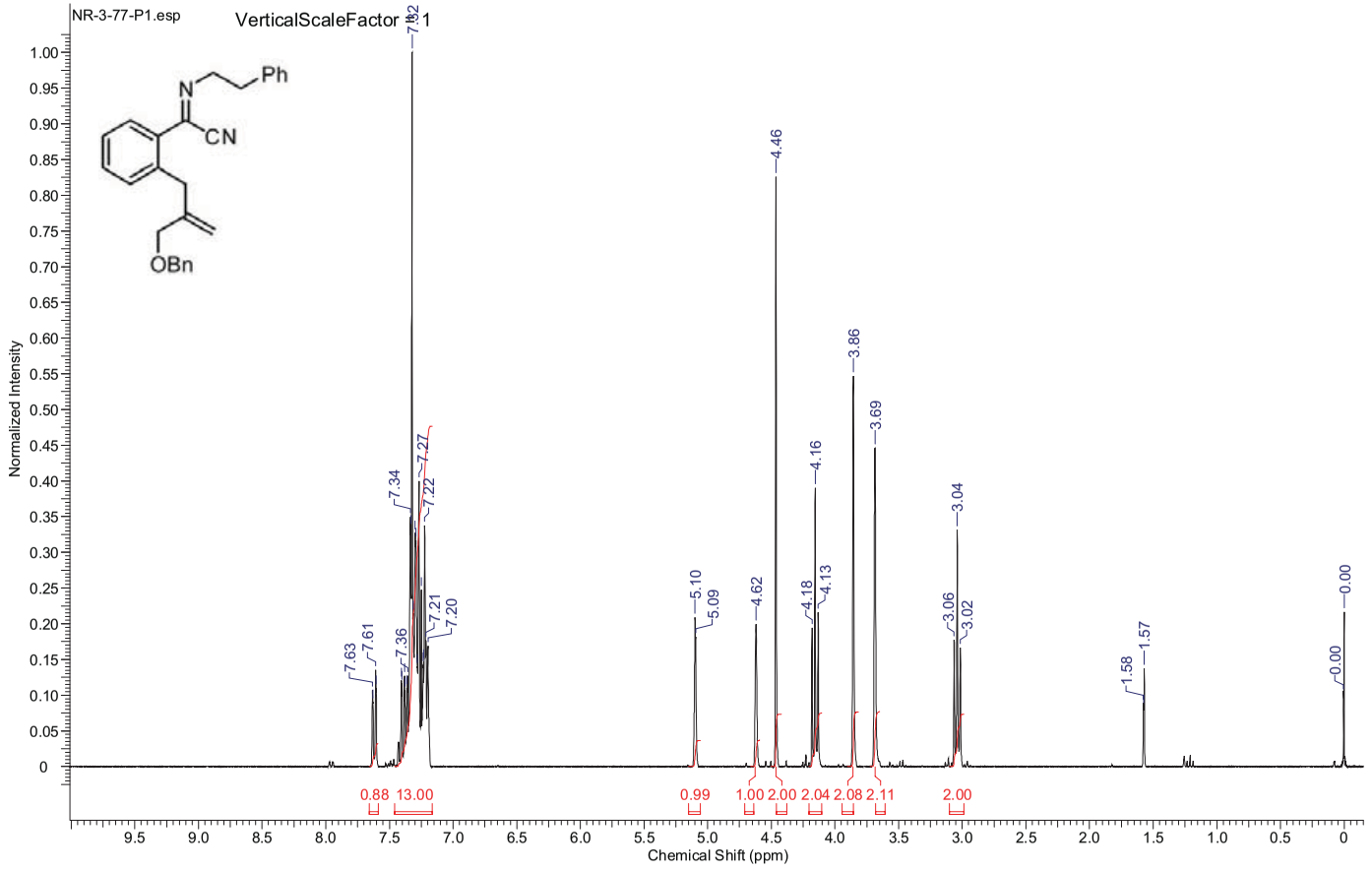
| ***Date*** | May 30 2013 | ***Date Stamp*** | May 30 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130530v3_3002.fid\fid | | |
| ***Frequency (MHz)*** | 299.96 | ***Nucleus*** | 1H | ***Number of Transients*** | 16 | ***Original Points Count*** | 11998 |
| ***Points Count*** | 131072 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 30.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 2395.7717 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 5998.80 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



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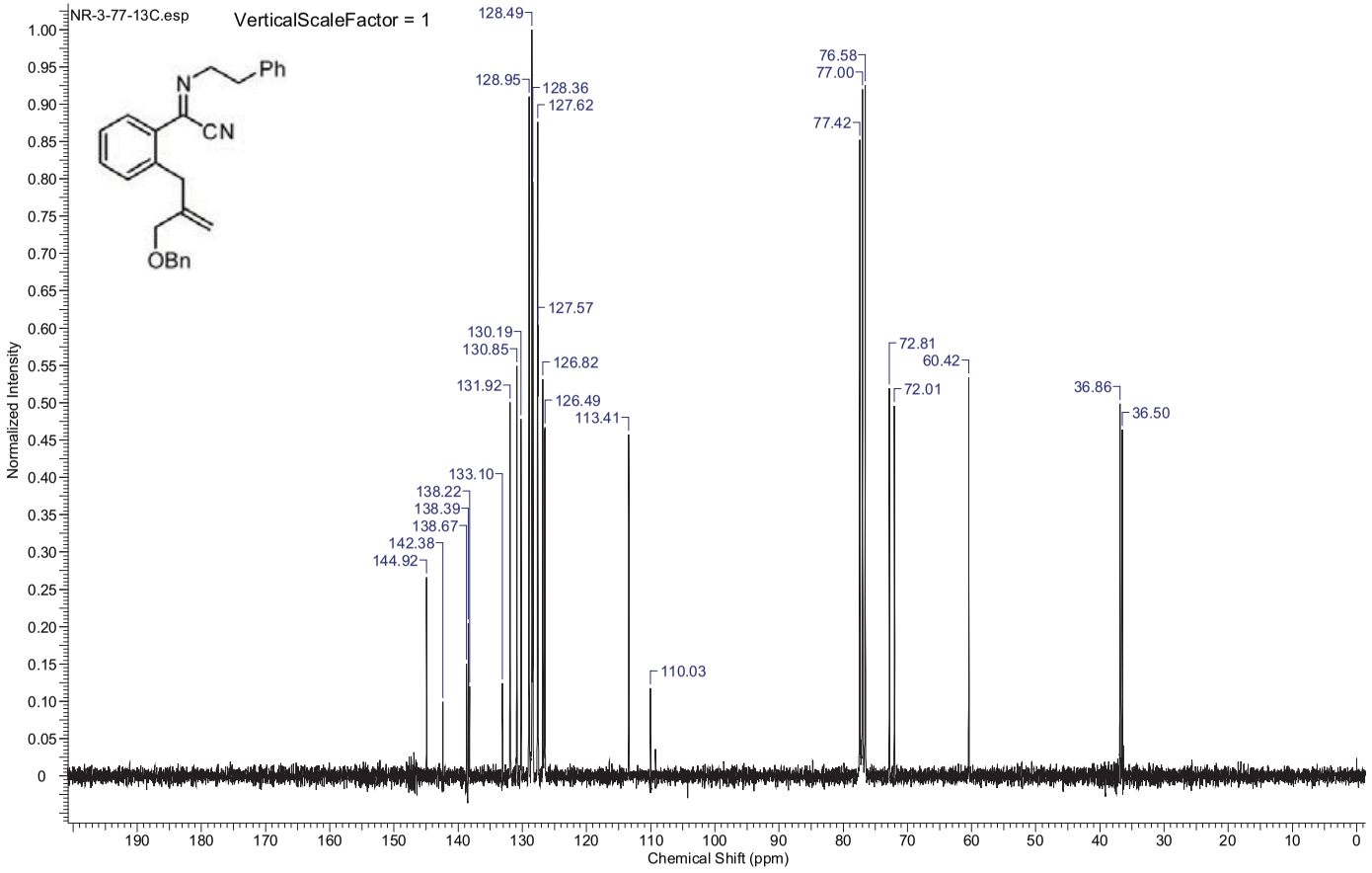
| ***Date*** | May 30 2013 | ***Date Stamp*** | May 30 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130530v3_3003.fid\fid | | |
| ***Frequency (MHz)*** | 75.43 | ***Nucleus*** | 13C | ***Number of Transients*** | 1024 | ***Original Points Count*** | 13889 |
| ***Points Count*** | 16384 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 30.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | 7863.4961 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 17361.11 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |



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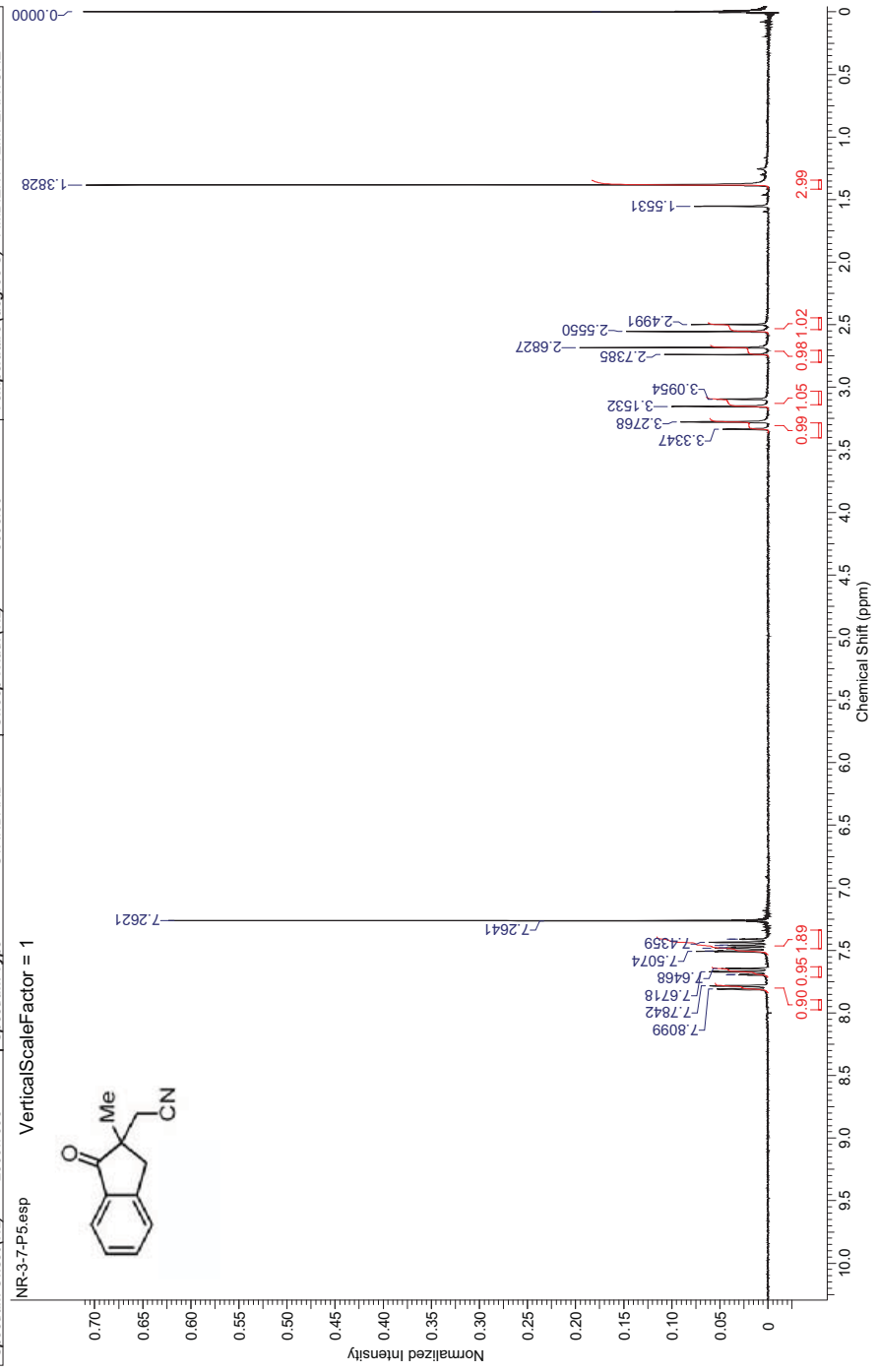
| *Date* | Dec 20 2012 | *Date Stamp* | Dec 20 2012 *File Name* C:\Users\Naveen\Desktop\121220v3 1302.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.7993 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



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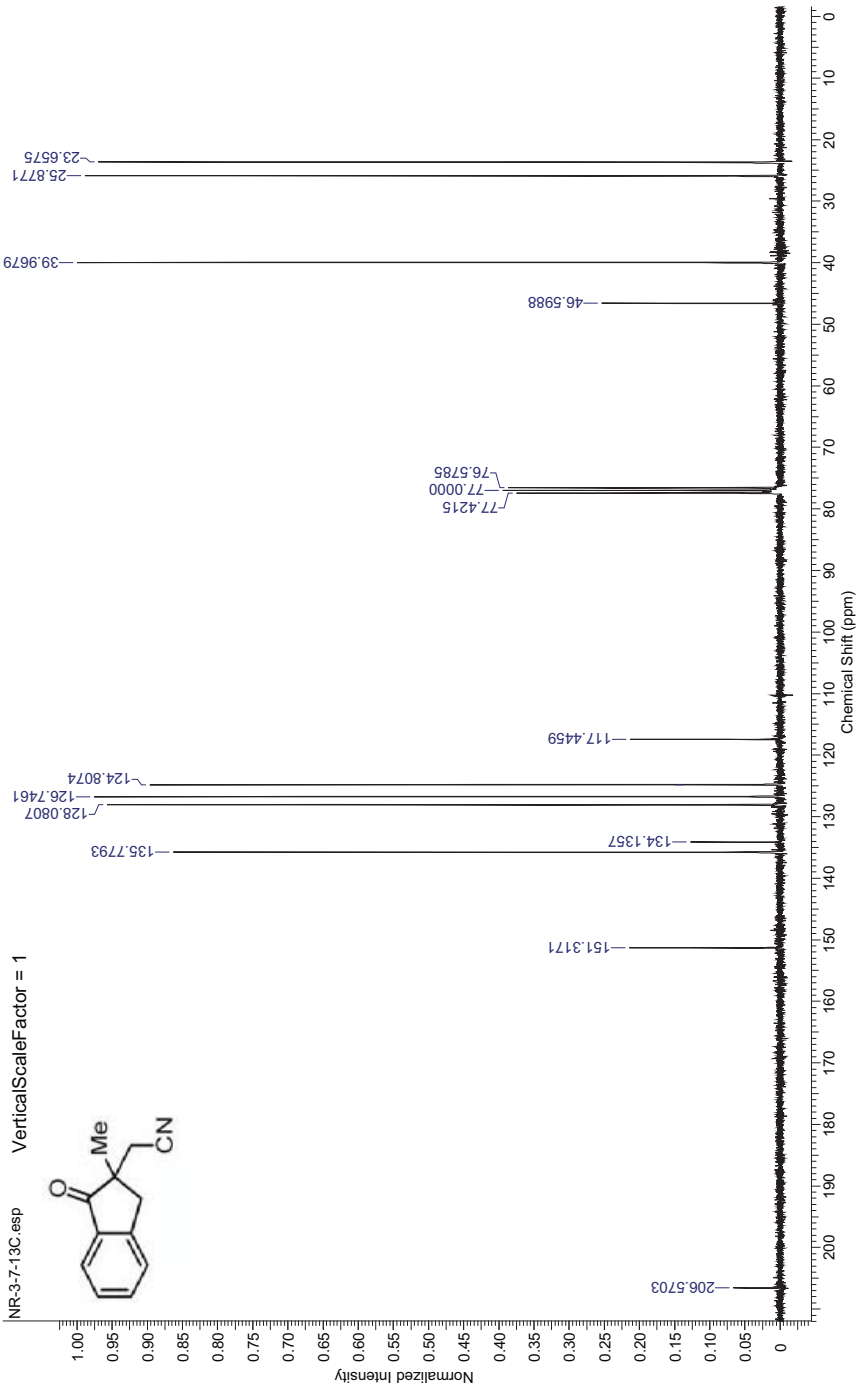
| **Date** | Dec 21 2012 | **Date Stamp** | Dec 21 2012 |
| **File Name** | C:\Data\Study\Chris\Cyanoacylation\NMRs Cyanoacylation\121221v3 2403.fid\fid | | |
| **Nucleus** | 13C | **Number of Transients** | 1024 |
| **Pulse Sequence** | s2pul | **Receiver Gain** | 30.00 |
| **Spectrum Type** | STANDARD | **Sweep Width (Hz)** | 17361.11 |
| **Frequency (MHz)** | 75.43 | | |
| **Points Count** | 16384 | | |
| **Original Points Count** | 13889 | | |
| **Solvent** | CHLOROFORM-d | | |
| **Spectrum Offset (Hz)** | 7860.3169 | | |
| **Temperature (degree C)** | AMBIENT TEMPERATURE | | |



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|---|---|---|---|---|---|
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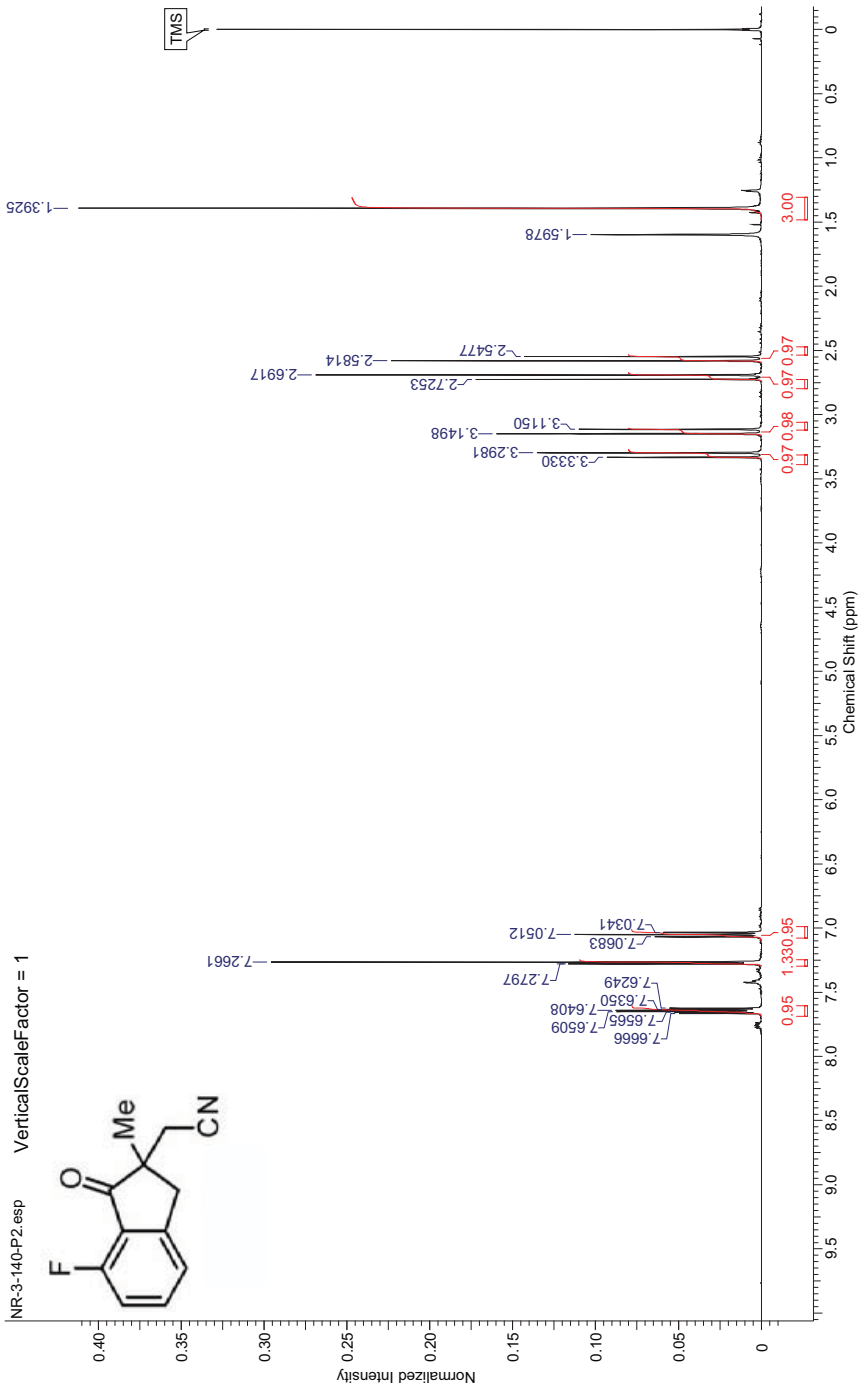
| **File Name** | C:\Users\Naveen\Desktop\NR-3-140-P2\10\fid | **Frequency (MHz)** | 500.13 | **Nucleus** | 1H |
| **Number of Transients** | 16 | **Origin** | spect | **Original Points Count** | 32768 | **Owner** | auto |
| **Points Count** | 131072 | **Pulse Sequence** | zg30 | **Receiver Gain** | 73.82 | **SW(cyclical) (Hz)** | 10000.00 |
| **Solvent** | CHLOROFORM-d | | | **Spectrum Offset (Hz)** | 3078.9565 | **Spectrum Type** | STANDARD |
| **Sweep Width (Hz)** | 9999.92 | **Temperature (degree C)** | 21.000 | | | | |



9/26/2013 12:09:49 PM

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|---|---|---|---|---|---|---|---|
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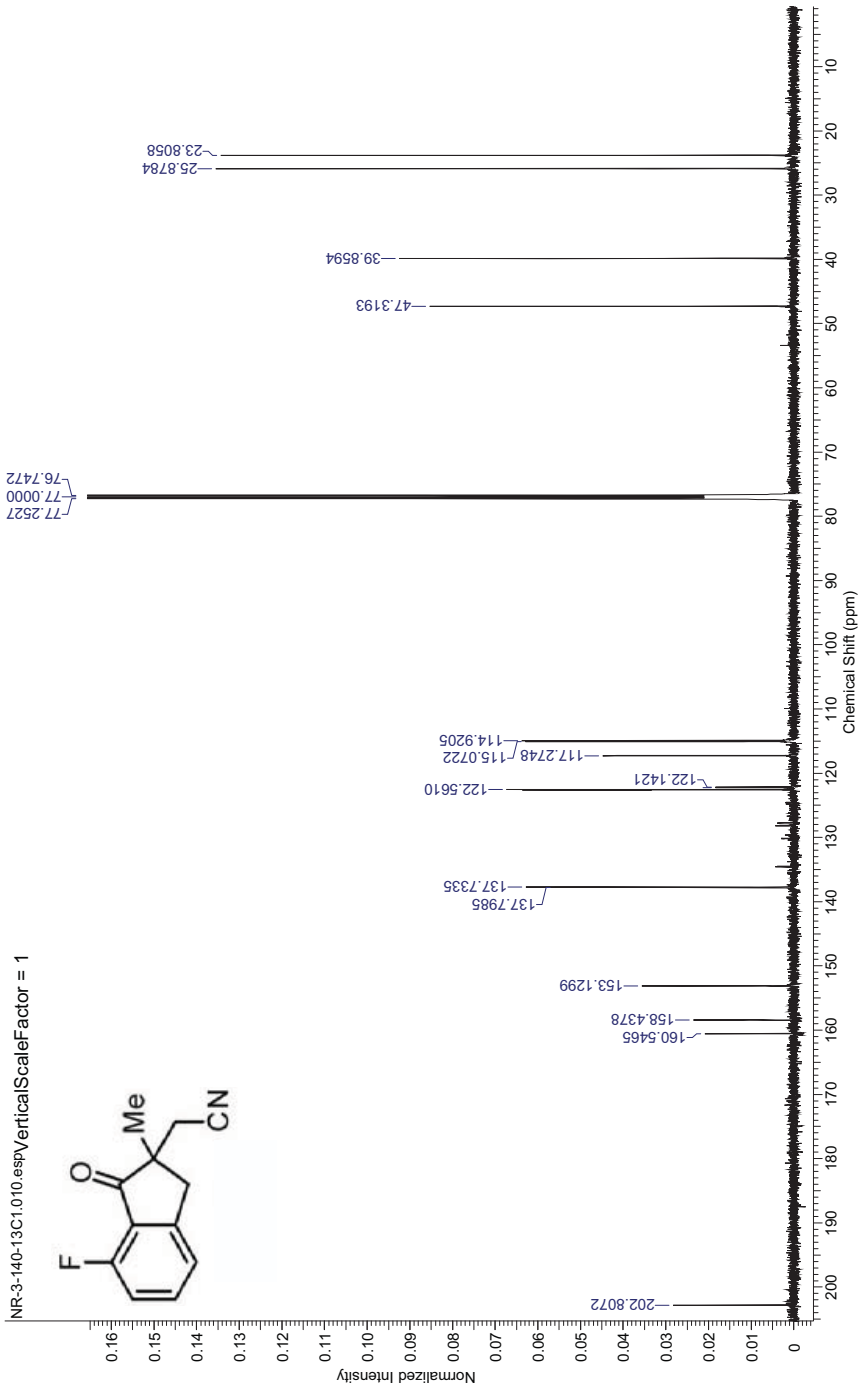
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-140-13C1\10\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 1000 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12569.4092 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 21.000 | | | | |



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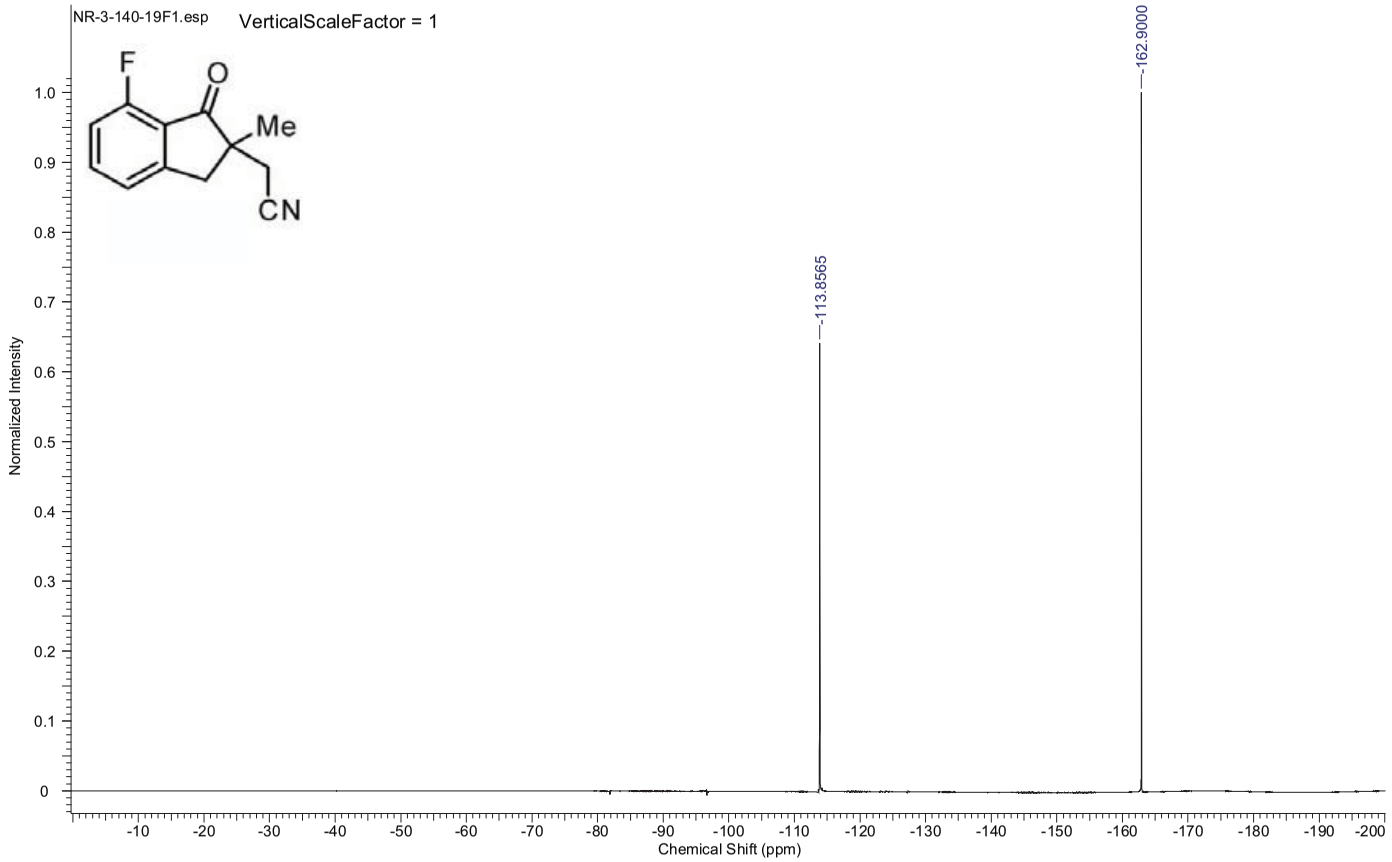
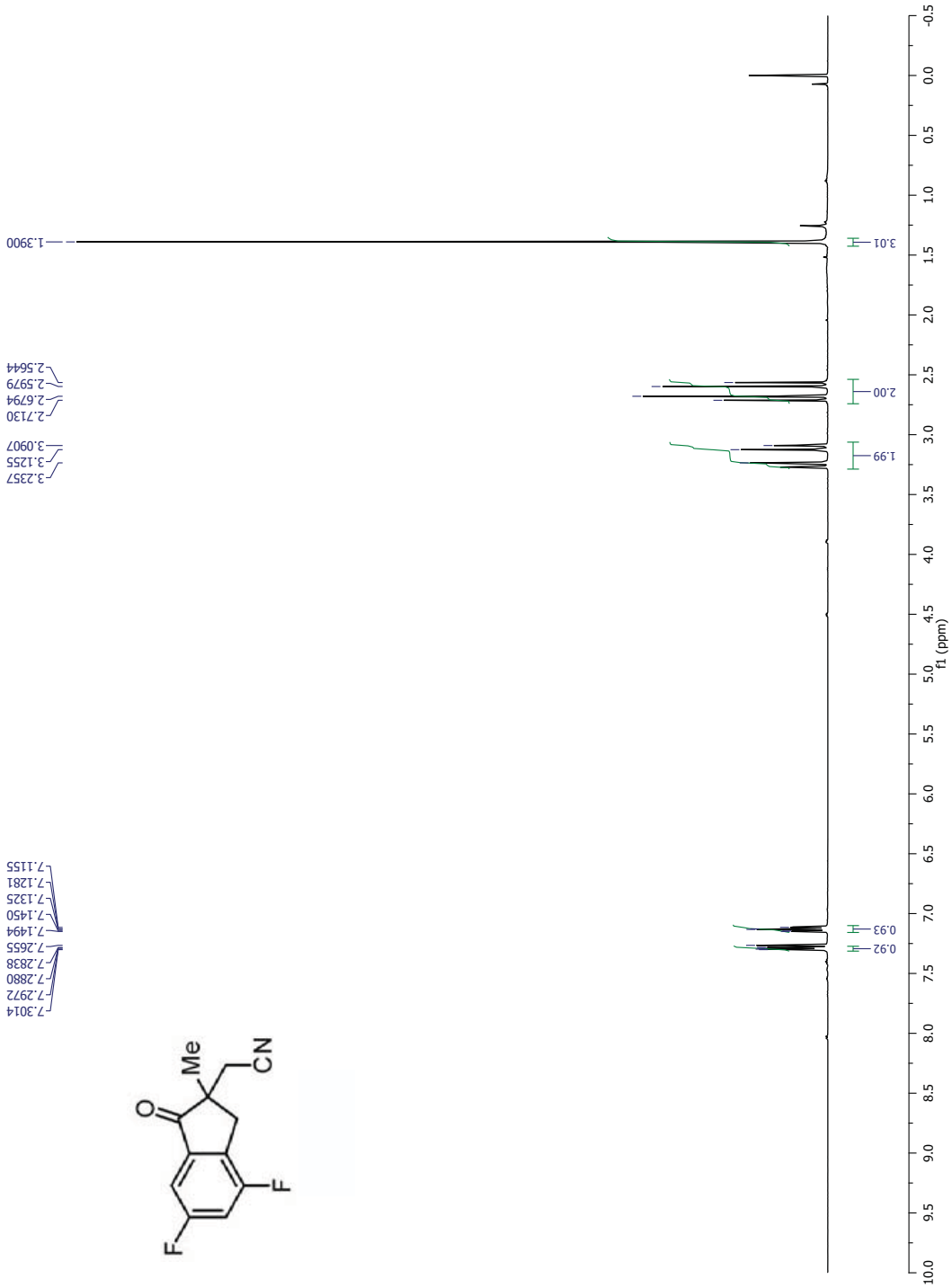
| ***Acquisition Time (sec)*** | 0.5767 | ***Date*** | 26 Sep 2013 12:44:32 | | | ***Date Stamp*** | 26 Sep 2013 12:44:32 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-140-19F1\10\fid | | | ***Frequency (MHz)*** | 470.55 | ***Nucleus*** | 19F |
| ***Number of Transients*** | 16 | ***Origin*** | spect | ***Original Points Count*** | 65536 | ***Owner*** | auto |
| ***Points Count*** | 65536 | ***Pulse Sequence*** | zg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 113636.37 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | -47624.5820 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 113634.63 | ***Temperature (degree C)*** | 21.000 | | | | |

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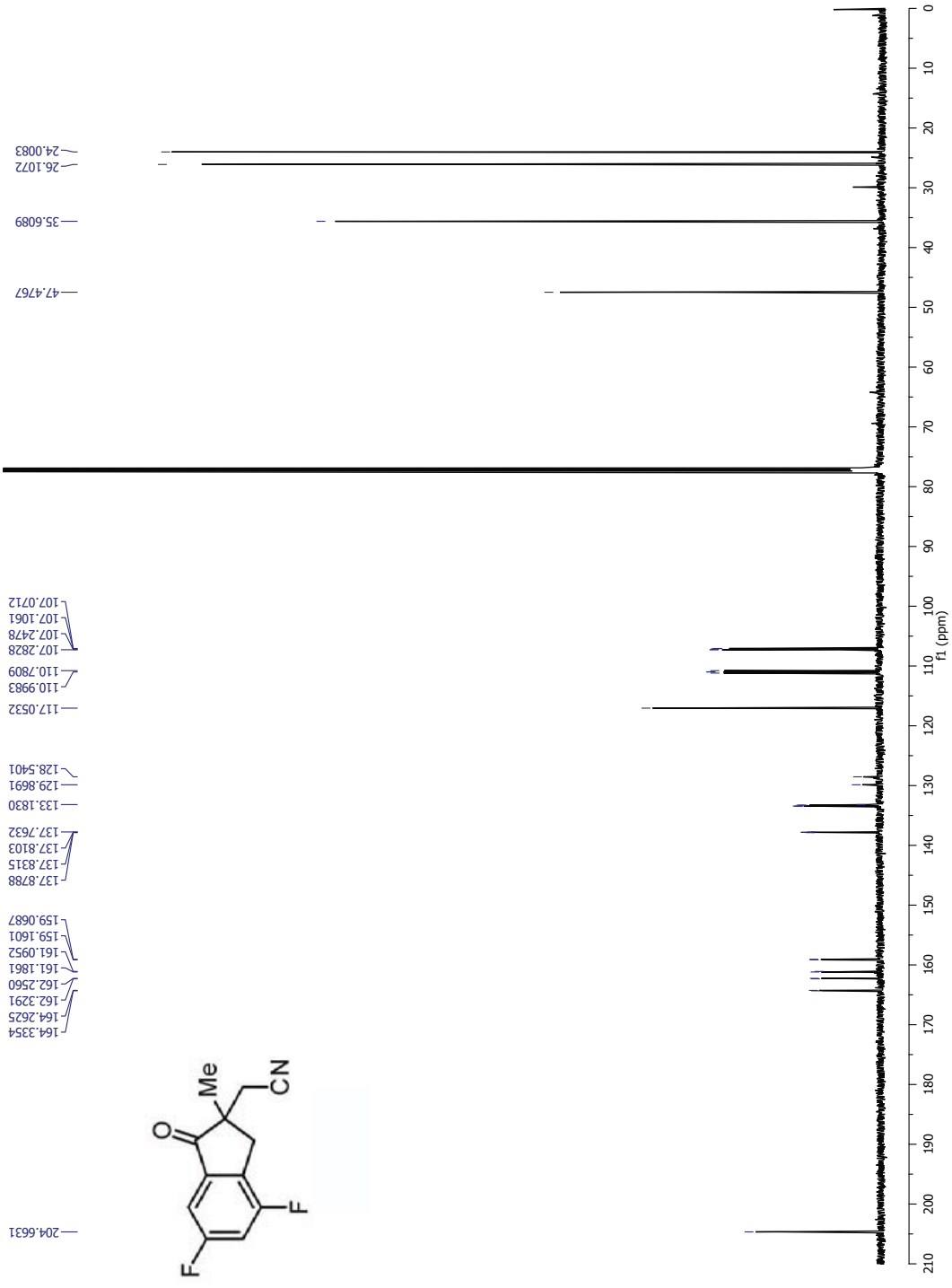
3.01
2.5644
2.5979
2.6794
2.7130
2.00
3.0907
3.1255
3.2357
1.99
7.1155
7.1281
7.1325
7.1450
7.1494
0.93
7.2655
7.2838
7.2880
7.2972
7.3014
0.92
Me
CN
O
F
F
f1 (ppm)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47.4767
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107.1061
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110.7809
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128.5401
129.8691
133.1830
137.7632
137.8103
137.8315
137.8788
159.0687
159.1601
161.0952
161.1861
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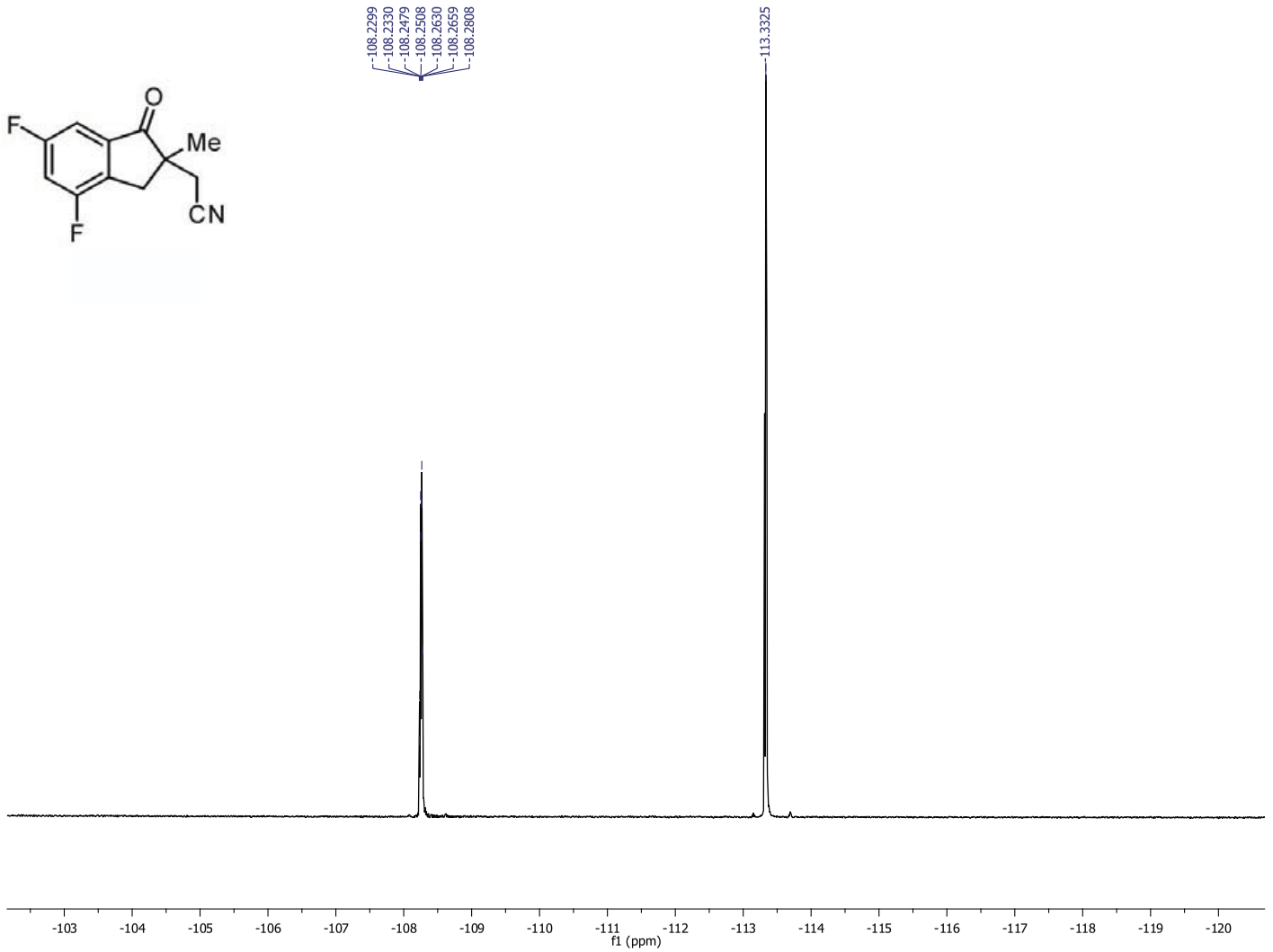
162.3291
164.2625
164.3354
204.6631
Me
CN
O
F
F
f1 (ppm)

300


O
F
Me
CN
F
108.2299
108.2330
108.2479
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108.2659
108.2808
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-103
-104
-105
-106
-107
-108
-109
-110
-111
-112
-113
-114
-115
-116
-117
-118
-119
-120
f1 (ppm)

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|---|---|---|---|
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| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
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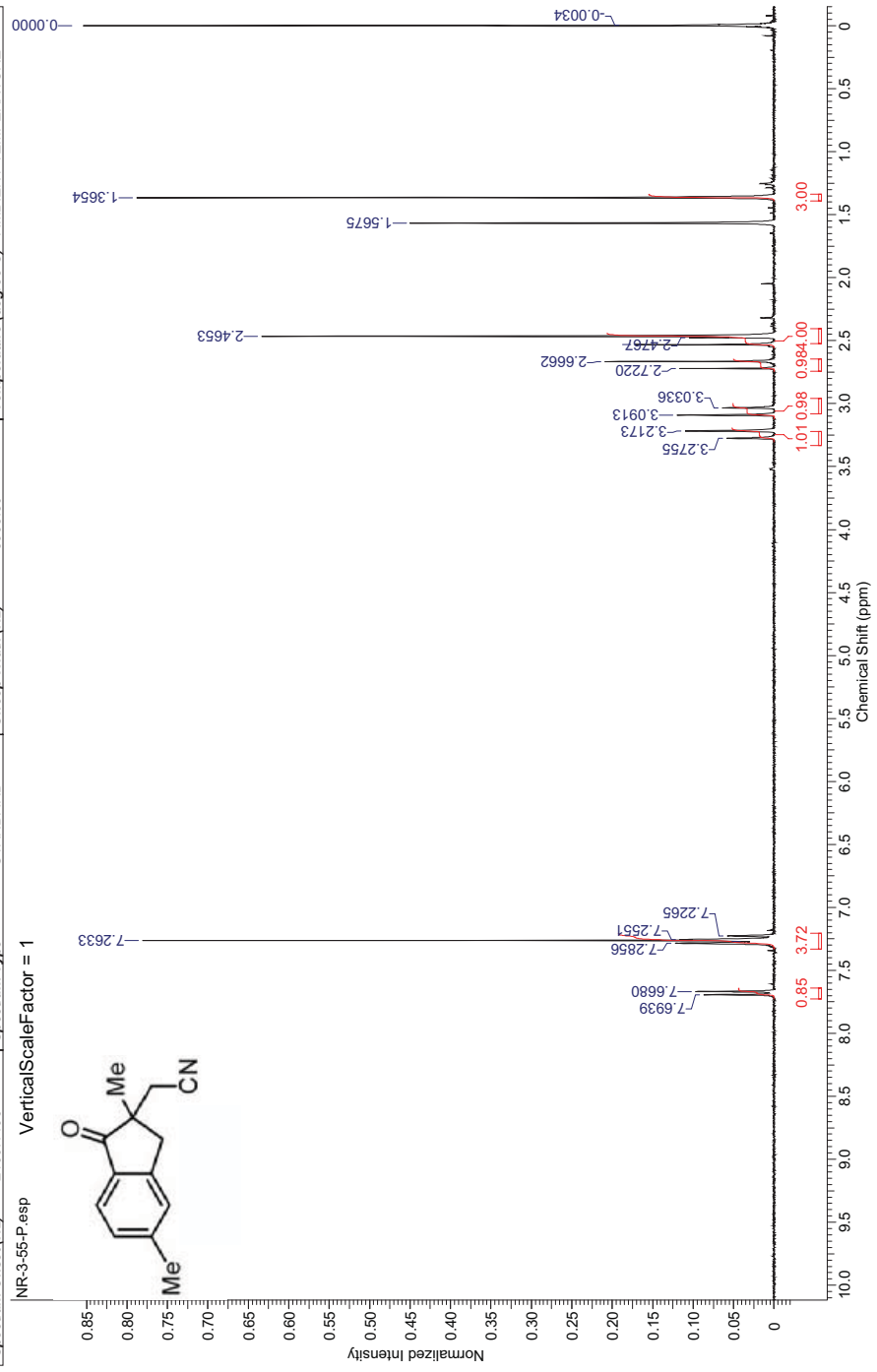

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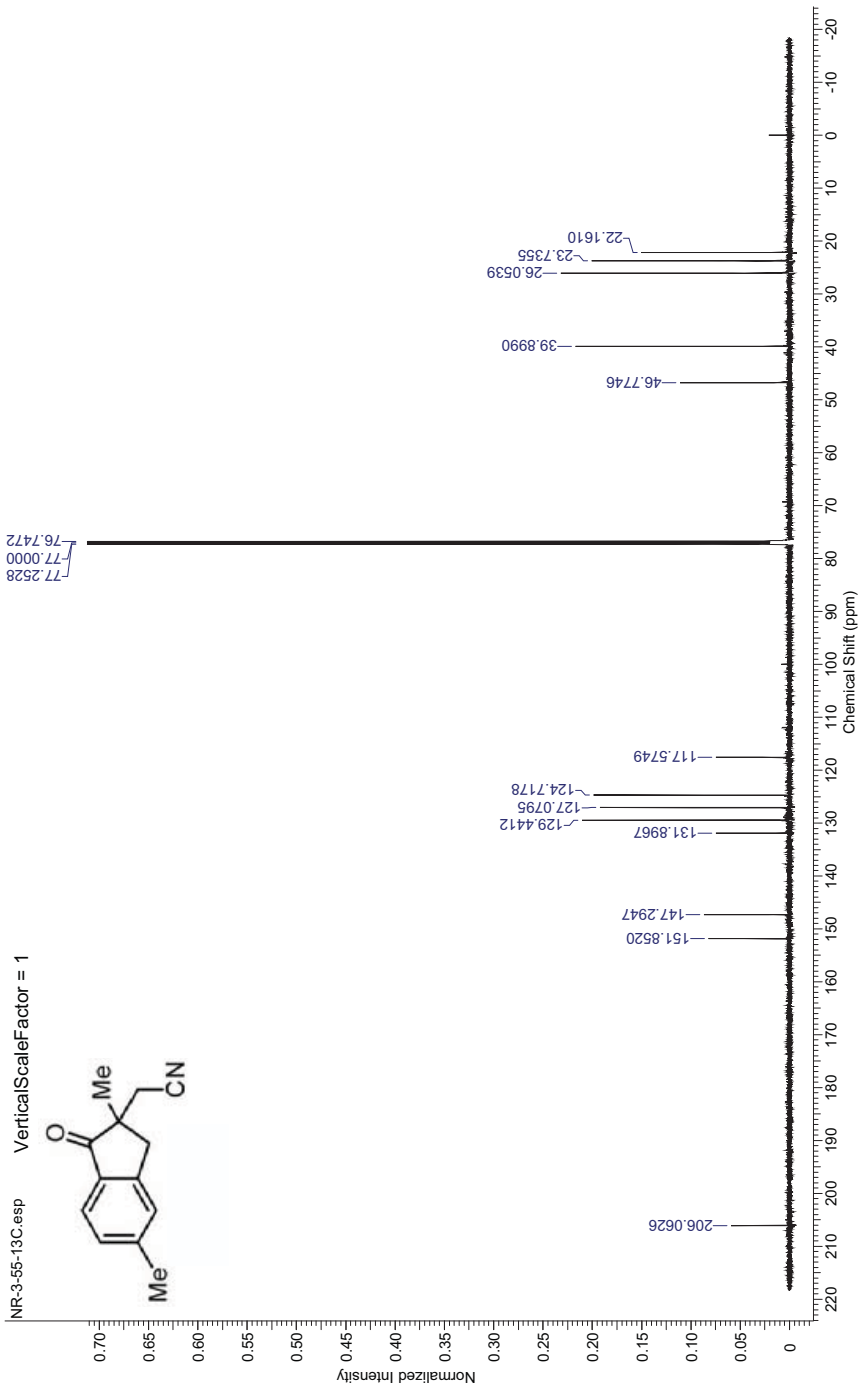
| *Date Stamp* | 09 May 2013 18:13:04 | *File Name* | C:\Users\Naveen\Desktop\NR-3-55-13C\1\fid | | |
| *Frequency (MHz)* | 125.76 | *Nucleus* | 13C | *Number of Transients* | 868 | *Origin* | spect |
| *Original Points Count* | 32768 | *Owner* | cdonrr | *Points Count* | 32768 | *Pulse Sequence* | zgpg30 |
| *Receiver Gain* | 194.68 | *SW(cyclical) (Hz)* | 29761.90 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 12569.3496 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 29761.00 | *Temperature (degree C)* | 25.025 |



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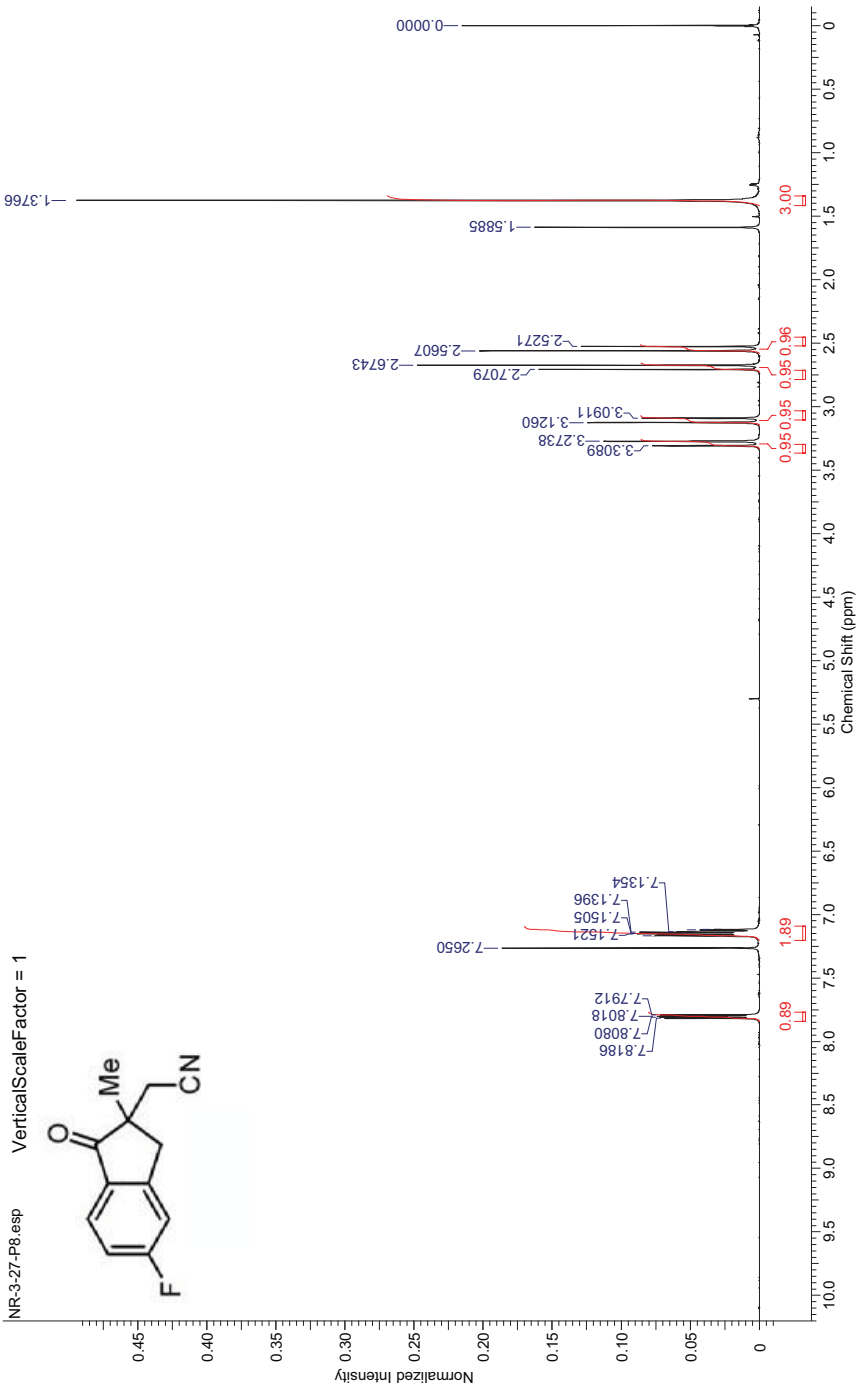
| *Acquisition Time (sec)* | 3.2768 | *Comment* | 5 mm PABBO BB/19F-1H/D Z-GRD Z119470/0030 | *Date* | 15 May 2013 20:16:48 |
| *Date Stamp* | 15 May 2013 20:16:48 | *File Name* | C:\Users\Naveen\Desktop\NR-3-27-P8\1\fid | | |
| *Frequency (MHz)* | 500.13 | *Nucleus* | 1H | *Number of Transients* | 16 | *Origin* | spect |
| *Original Points Count* | 32768 | *Owner* | cdonrr | *Points Count* | 131072 | *Pulse Sequence* | zg30 |
| *Receiver Gain* | 127.25 | *SW(cyclical) (Hz)* | 10000.00 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 3077.2781 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 9999.92 | *Temperature (degree C)* | 25.001 |



8/20/2013 6:35:17 PM

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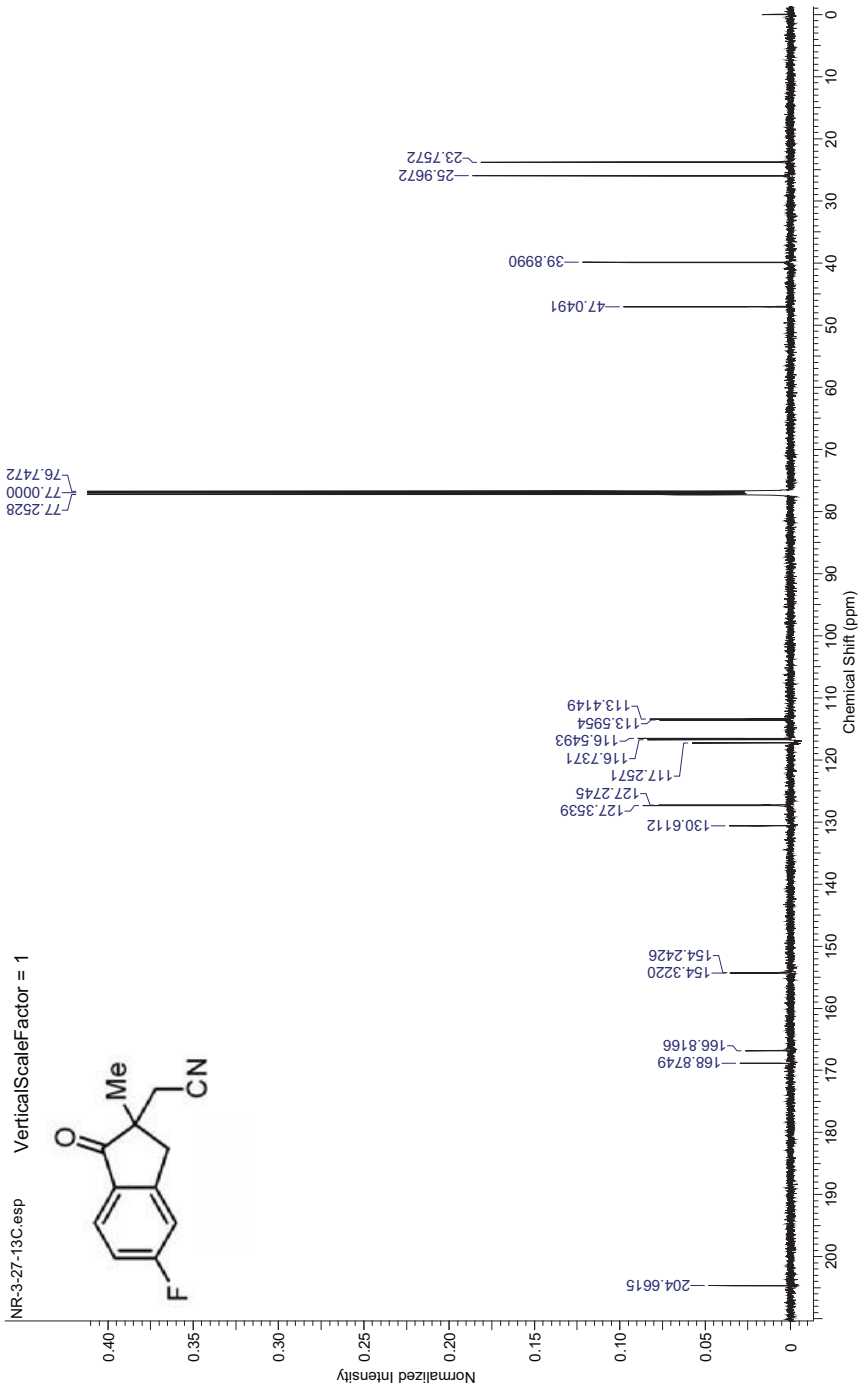
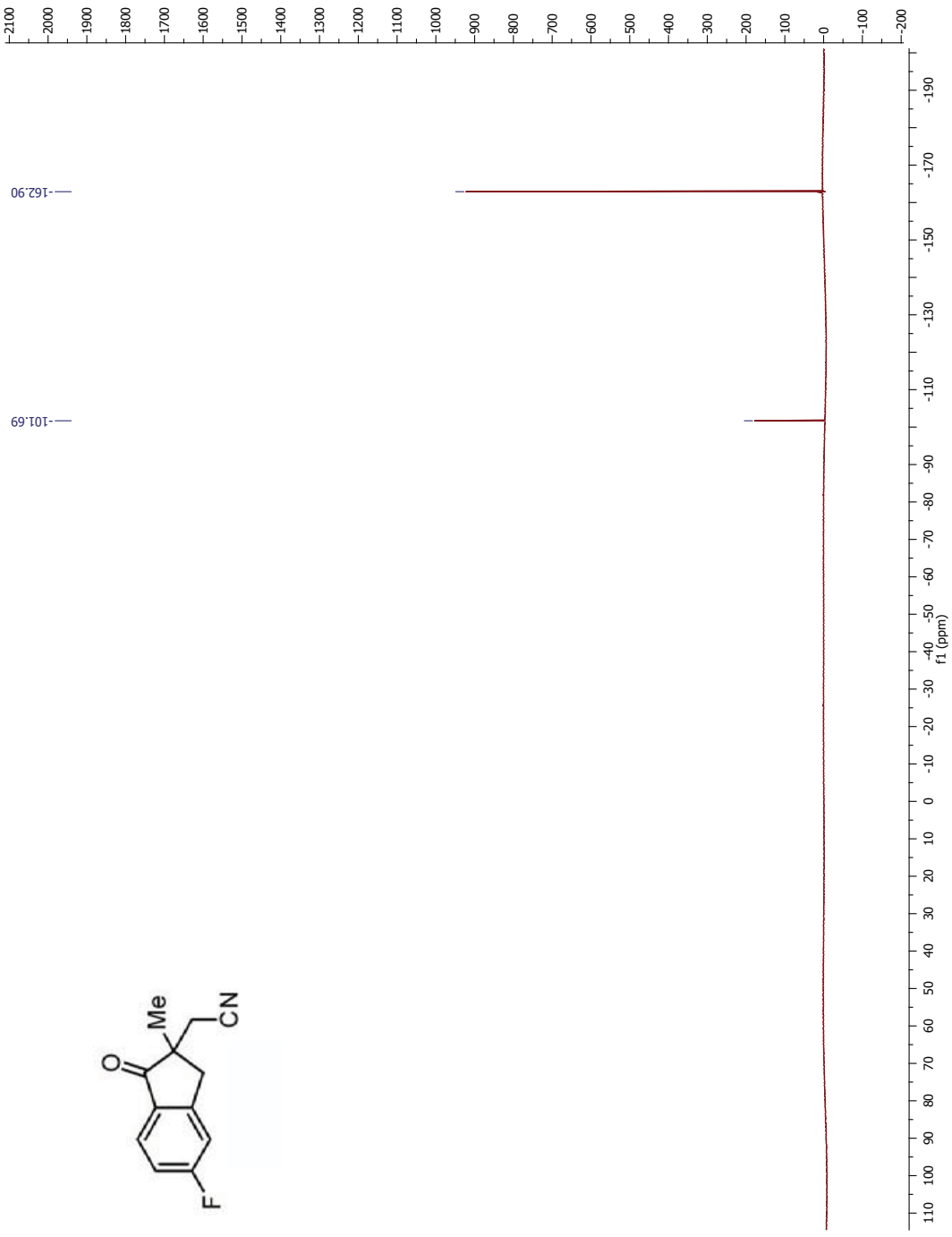
| *Date Stamp* | 15 May 2013 19:19:12 | *File Name* | C:\Users\Naveen\Desktop\NR-3-27-13C\1\fid | | |
| *Frequency (MHz)* | 125.76 | *Nucleus* | 13C | *Number of Transients* | 981 | *Origin* | spect |
| *Original Points Count* | 32768 | *Owner* | cdonrr | *Points Count* | 32768 | *Pulse Sequence* | zgpg30 |
| *Receiver Gain* | 194.68 | *SW(cyclical) (Hz)* | 29761.90 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 12570.2578 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 29761.00 | *Temperature (degree C)* | 25.036 |




-162.90
-101.69
f1 (ppm)
Me
CN
O
F

9/26/2013 3:42:22 AM

| | | | | | |
|---|---|---|---|---|---|
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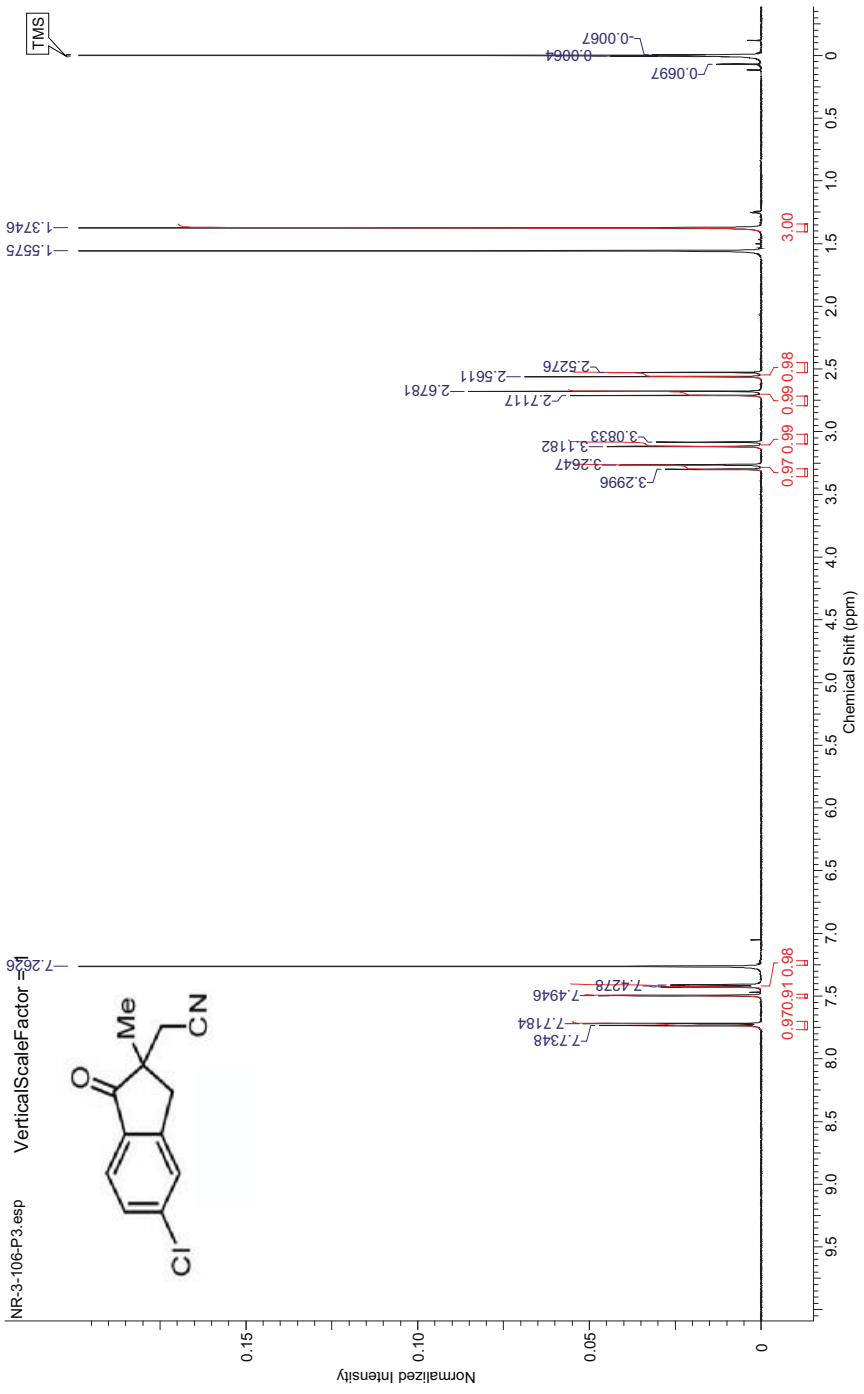
| **Number of Transients** | 16 | **Origin** | spect | **Original Points Count** | 32768 | **Owner** | auto |
| **Points Count** | 131072 | **Pulse Sequence** | zg30 | **Receiver Gain** | 141.70 | **SW(cyclical) (Hz)** | 10000.00 |
| **Solvent** | CHLOROFORM-d | | | **Spectrum Offset (Hz)** | 3077.4307 | **Spectrum Type** | STANDARD |
| **Sweep Width (Hz)** | 9999.92 | **Temperature (degree C)** | 20.999 | | | | |



10/1/2013 9:37:08 PM

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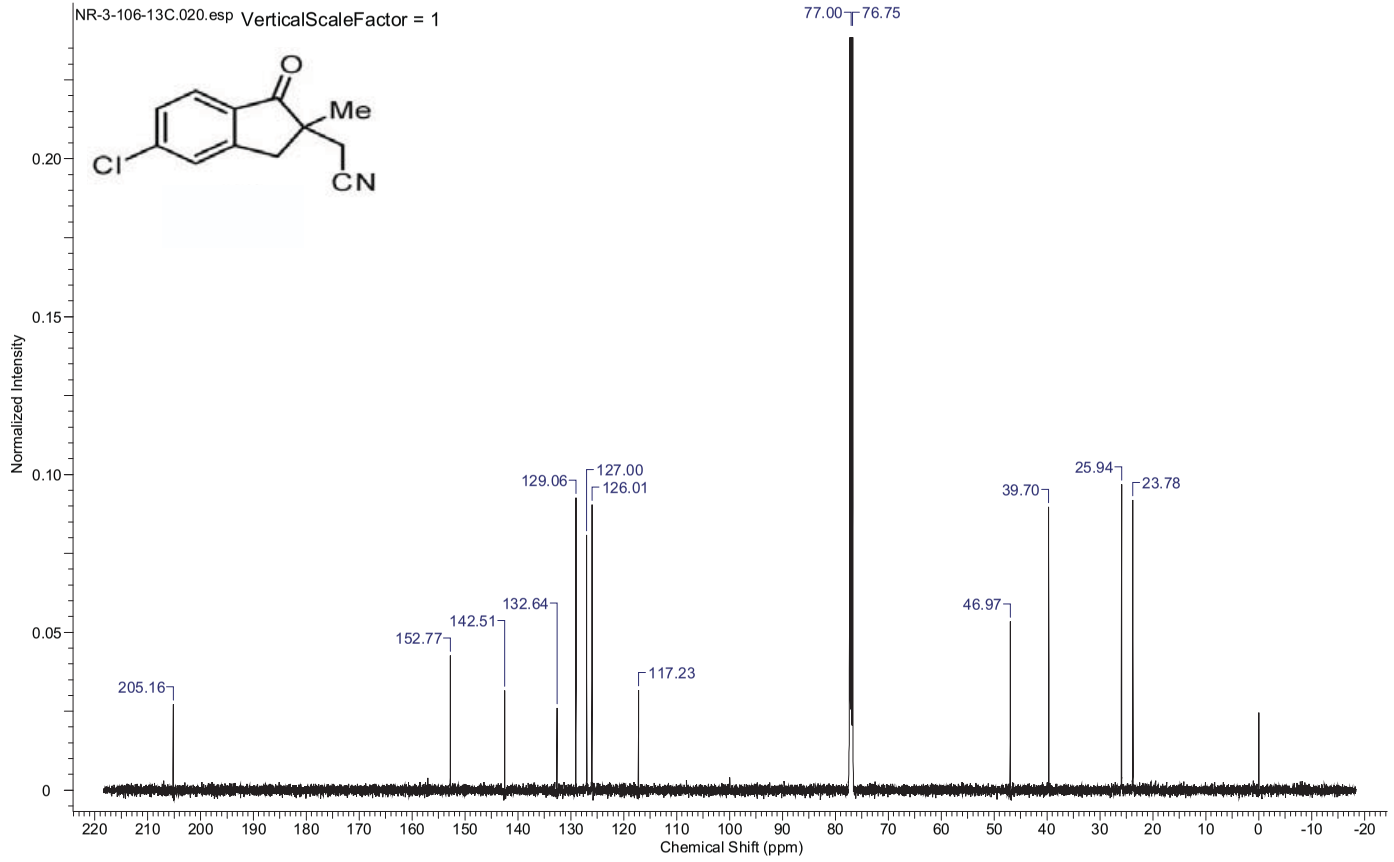
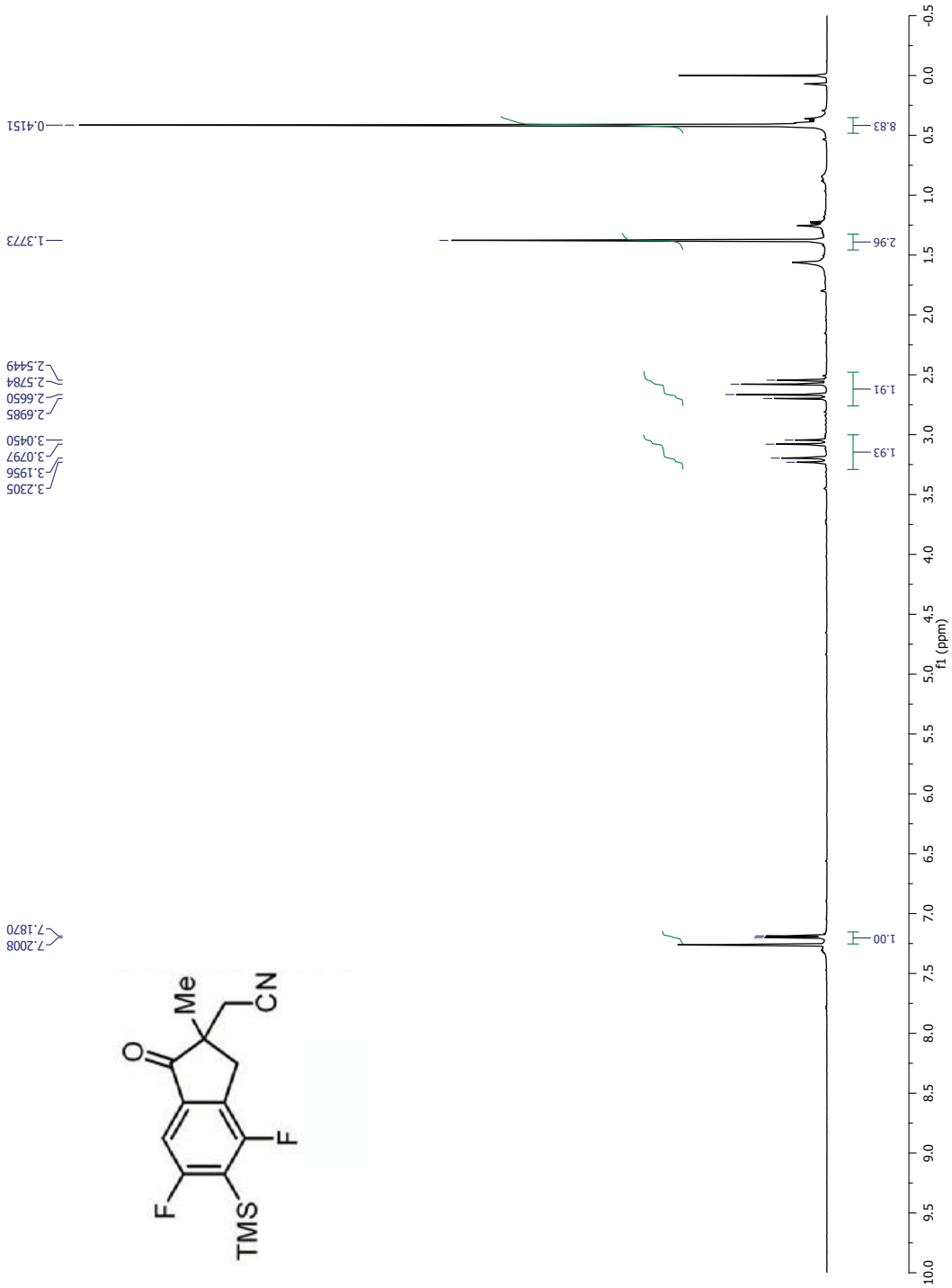
| ***File Name*** | C:\Users\Naveen\Desktop\Cyanoacylation NMRs\NR-3-106-13C\20\fid | | | | | ***Frequency (MHz)*** | 125.77 |
| ***Nucleus*** | 13C | ***Number of Transients*** | 1024 | ***Origin*** | spect | ***Original Points Count*** | 32768 |
| ***Owner*** | auto | ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 194.68 |
| ***SW(cyclical) (Hz)*** | 29761.90 | ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12570.3184 |
| ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 20.999 | | |

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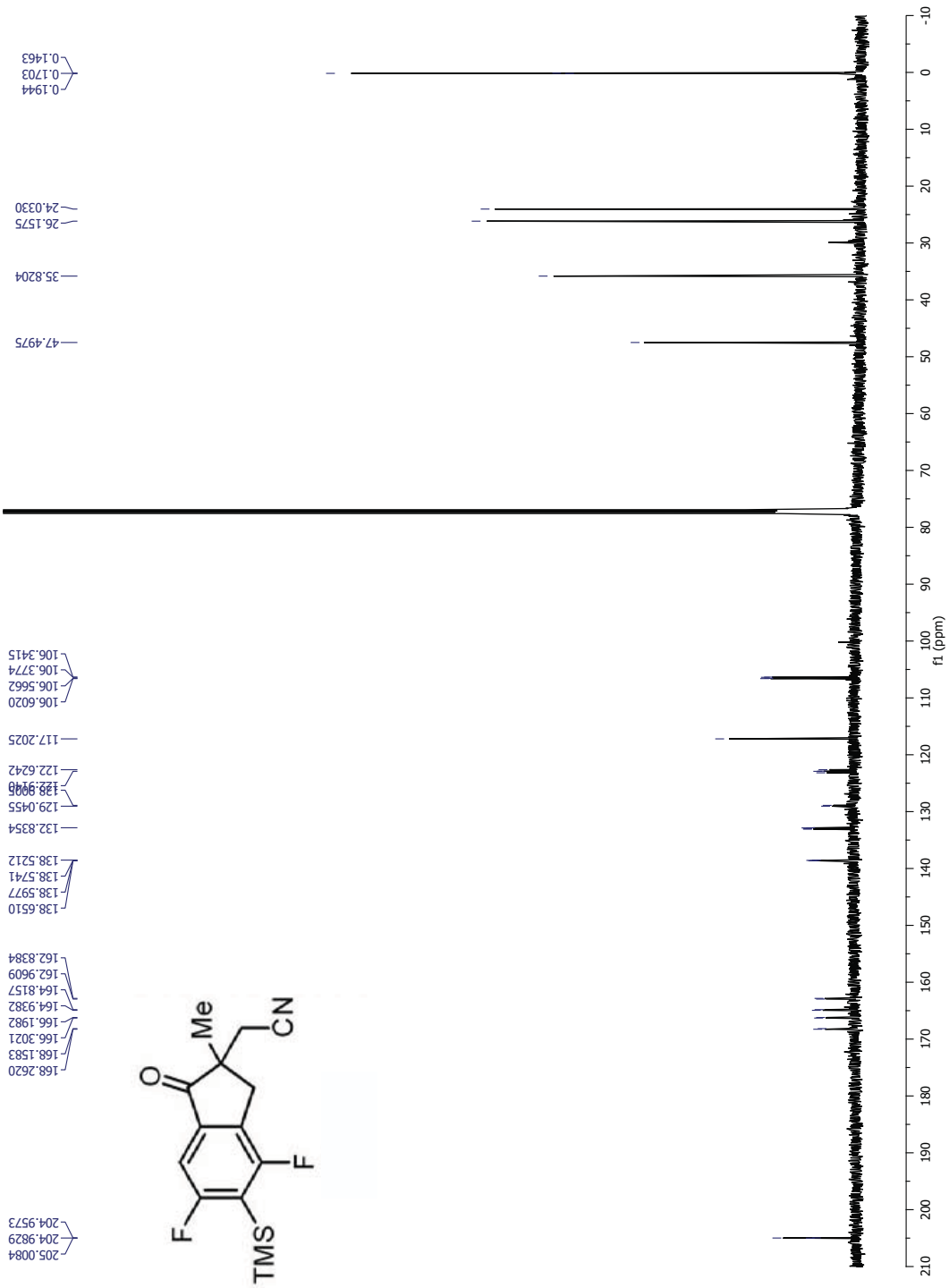
3.2305
3.1956
3.0797
3.0450
2.6985
2.6650
2.5784
2.5449
1.3773
0.4151
1.00
1.93
1.91
2.96
8.83
f1 (ppm)
Me
CN
O
F
F
TMS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117.2025
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132.8354
138.5212
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162.8384
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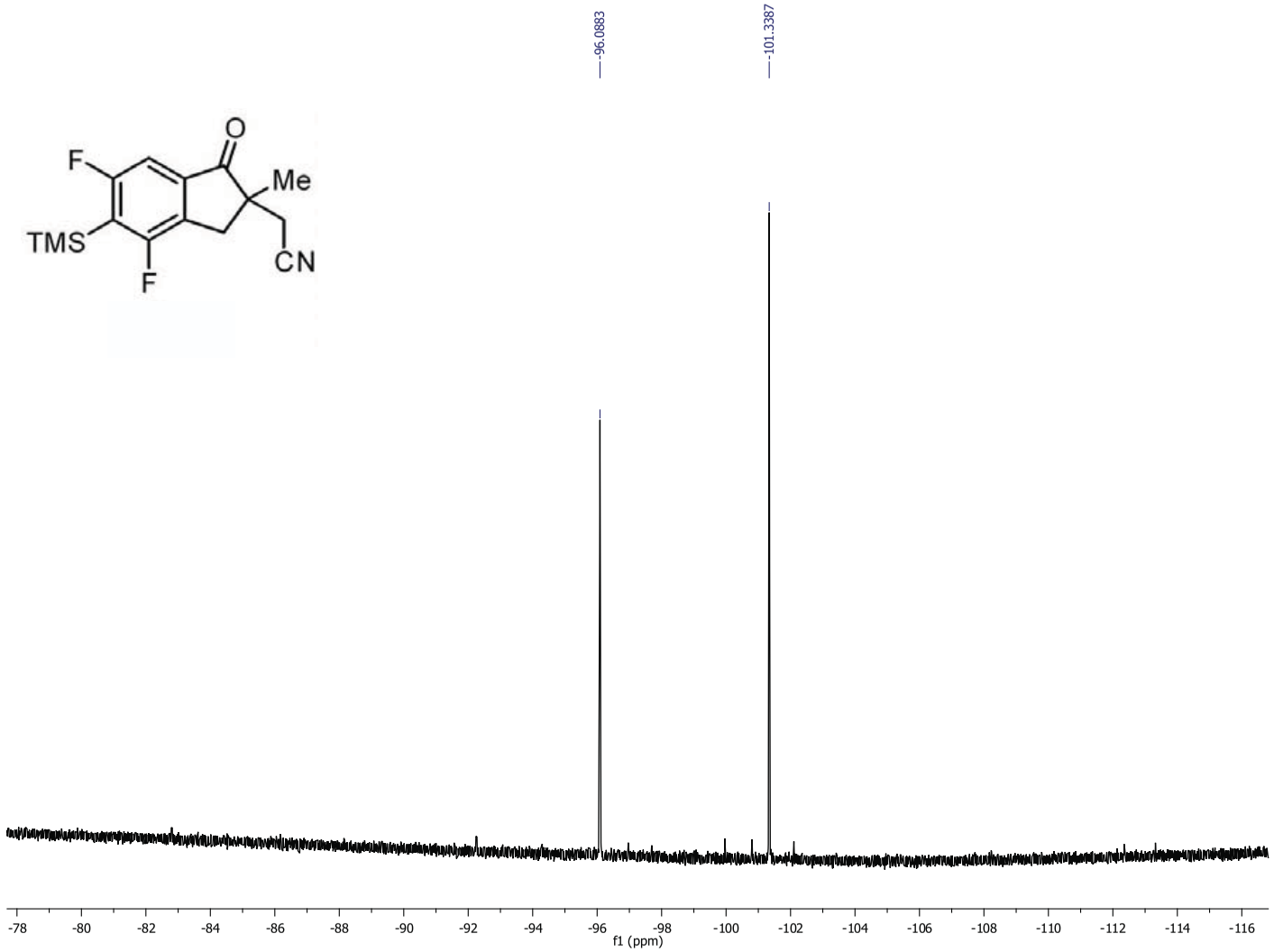
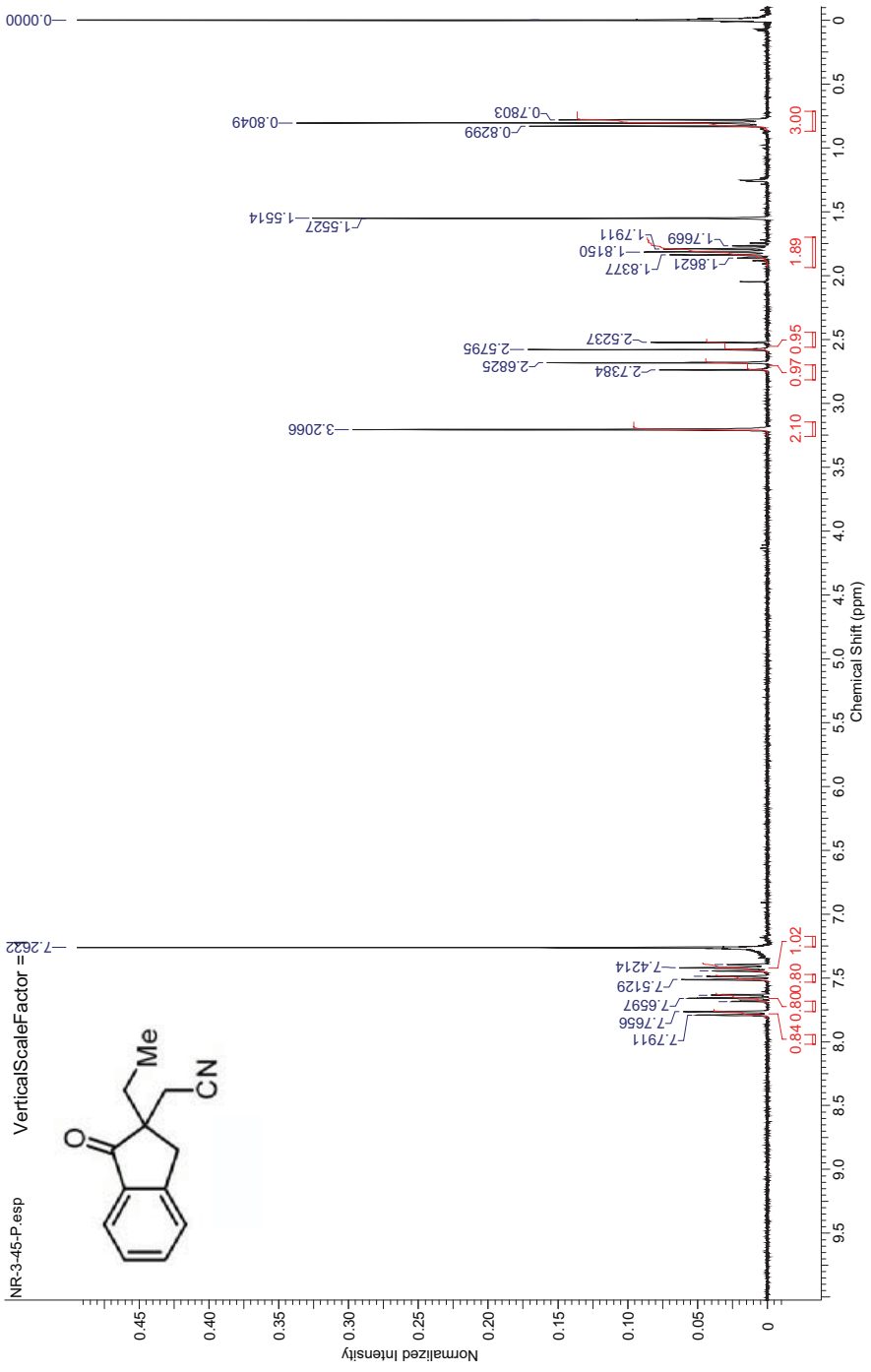
164.8157
164.9382
166.1982
166.3021
168.1583
168.2620
204.9573
204.9829
205.0084
Me
CN
O
F
F
TMS
f1 (ppm)


-96.0883
-101.3387
F
O
Me
TMS
CN
F
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
-98
-100
-102
-104
-106
-108
-110
-112
-114
-116
f1 (ppm)

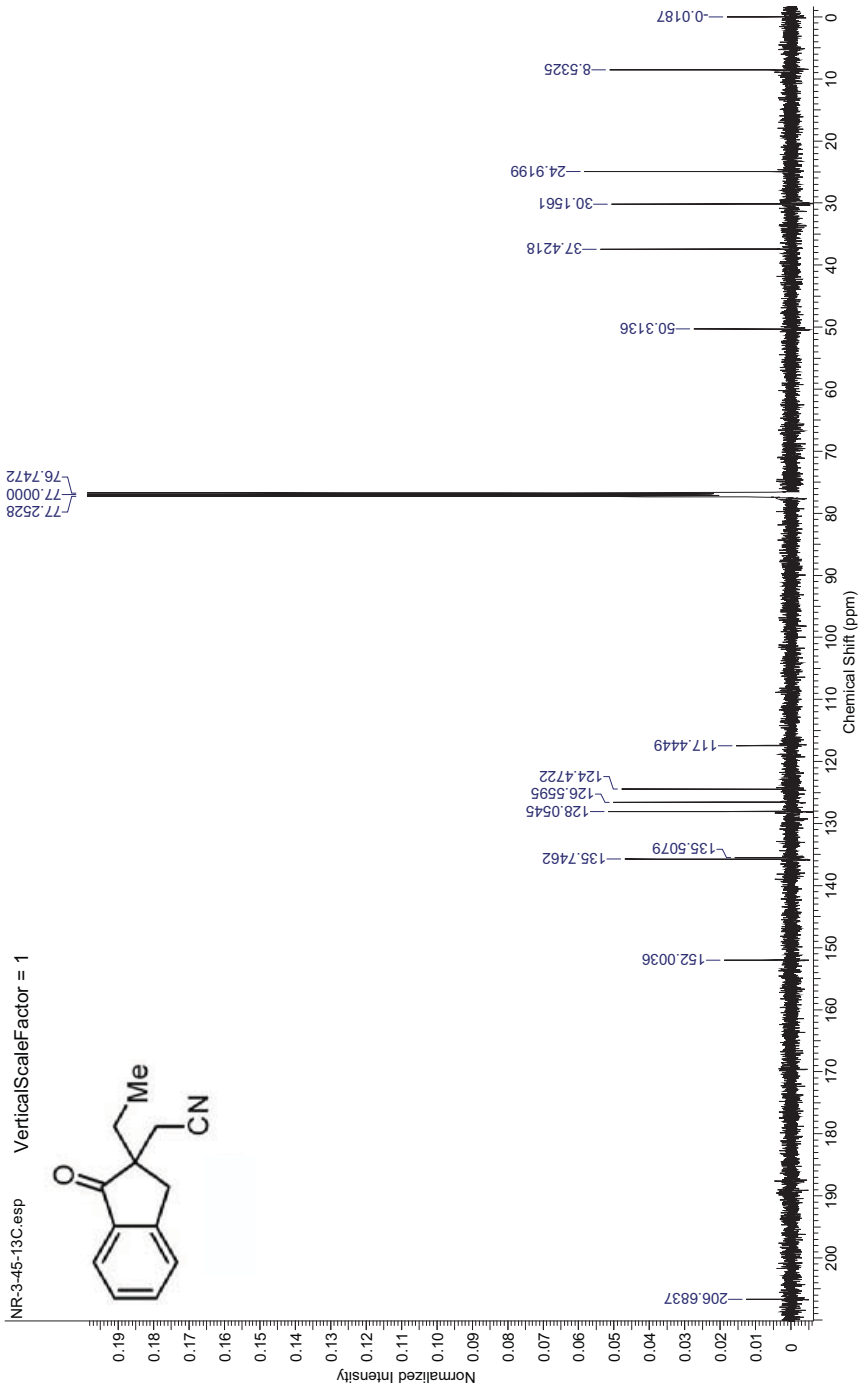
8/20/2013 5:35:40 PM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-45-P University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Apr 26 2013 | *Date Stamp* | Apr 26 2013 *File Name* C:\Users\Naveen\Desktop\130426v3 2302.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.7534 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



8/20/2013 6:15:29 PM

| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.1010 | *Comment* | 5 mm PABBO BB/19F-1H/D Z-GRD Z119470/0030 | *Date* | 27 Apr 2013 12:44:32 |
| *Date Stamp* | 27 Apr 2013 12:44:32 | *File Name* | C:\Users\Naveen\Desktop\NR-3-45-13C\1\fid | | |
| *Frequency (MHz)* | 125.76 | *Nucleus* | 13C | *Number of Transients* | 1024 | *Origin* | spect |
| *Original Points Count* | 32768 | *Owner* | cdonnr | *Points Count* | 32768 | *Pulse Sequence* | zgpg30 |
| *Receiver Gain* | 194.68 | *SW(cyclical) (Hz)* | 29761.90 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 12571.1660 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 29761.00 | *Temperature (degree C)* | 24.999 |



8/20/2013 6:43:15 PM

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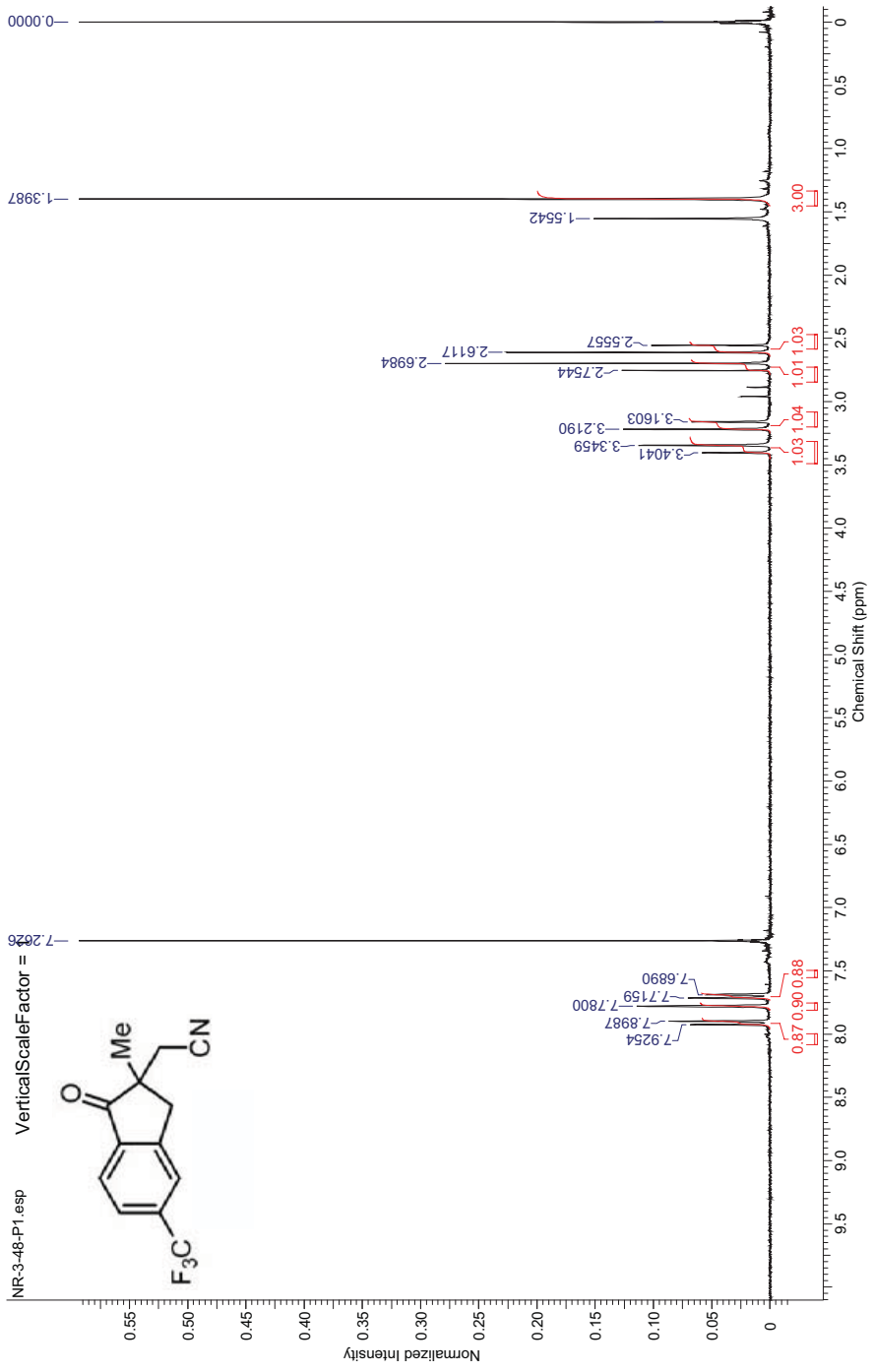
| *Acquisition Time (sec)* | 2.0001 | *Comment* | NR-3-48-P1 University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Apr 30 2013 | *Date Stamp* | Apr 30 2013 *File Name* C:\Users\Naveen\Desktop\130430v3 6902.fid\fid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 38.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2399.7534 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



8/20/2013 6:45:54 PM

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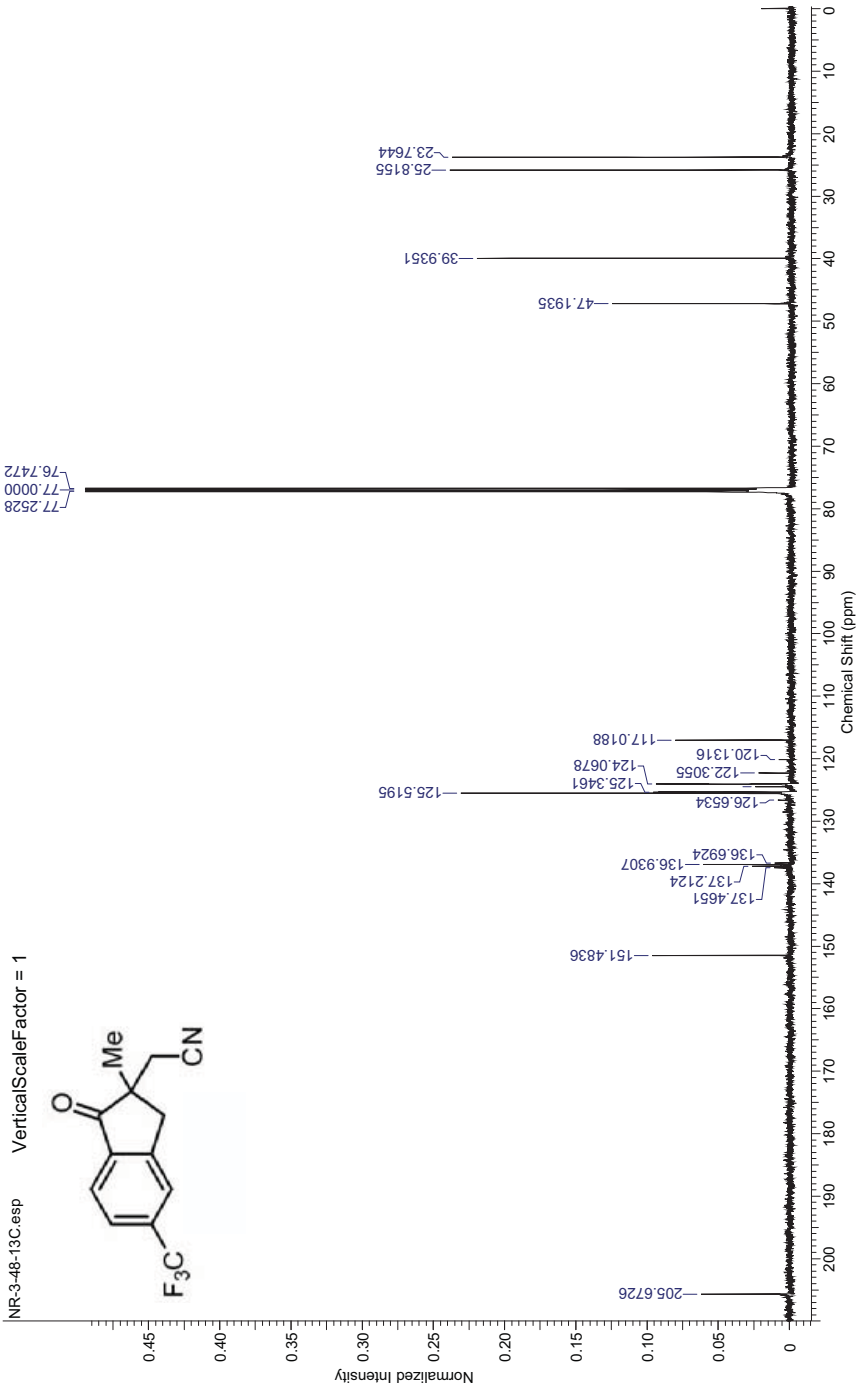
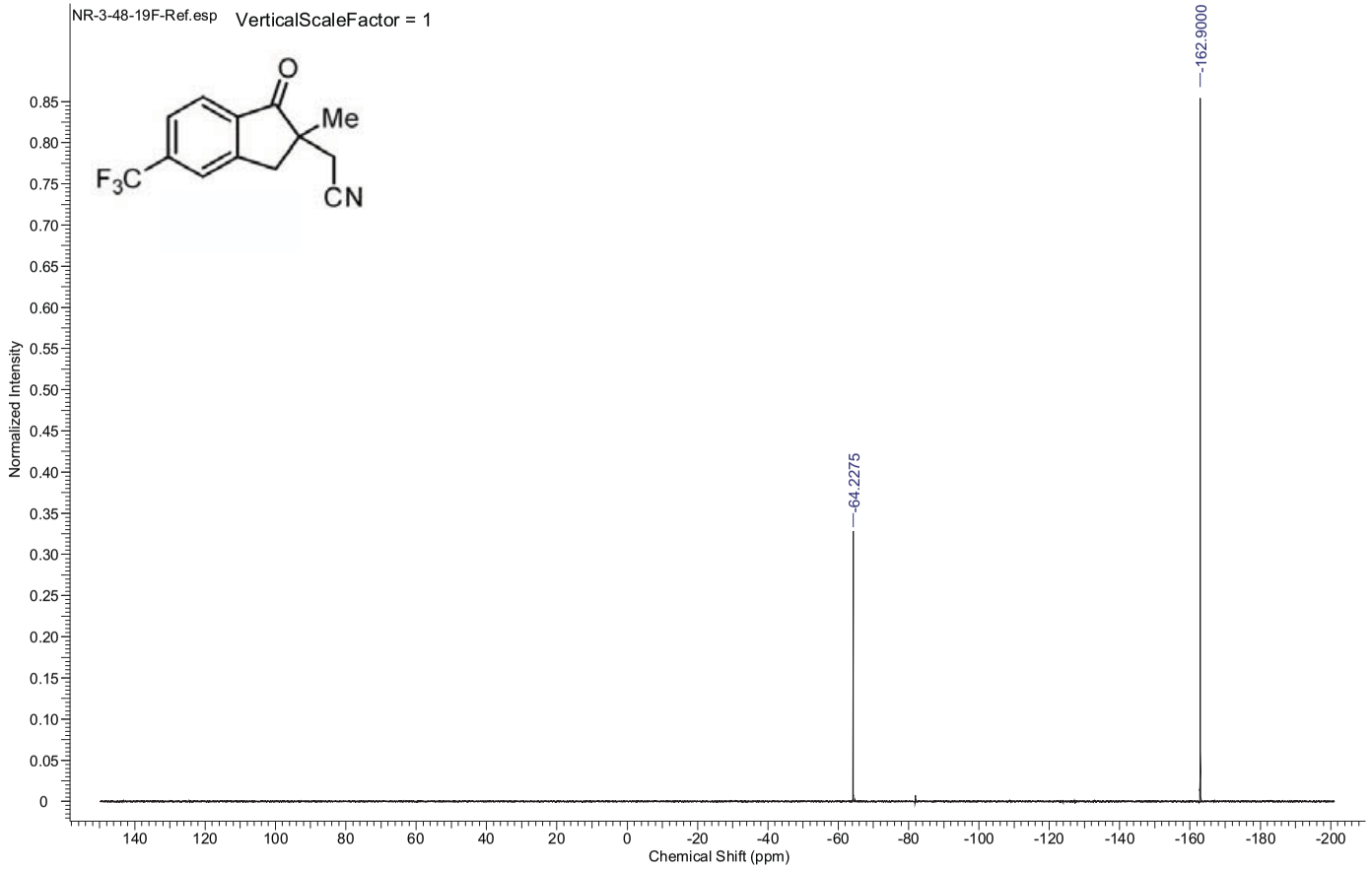
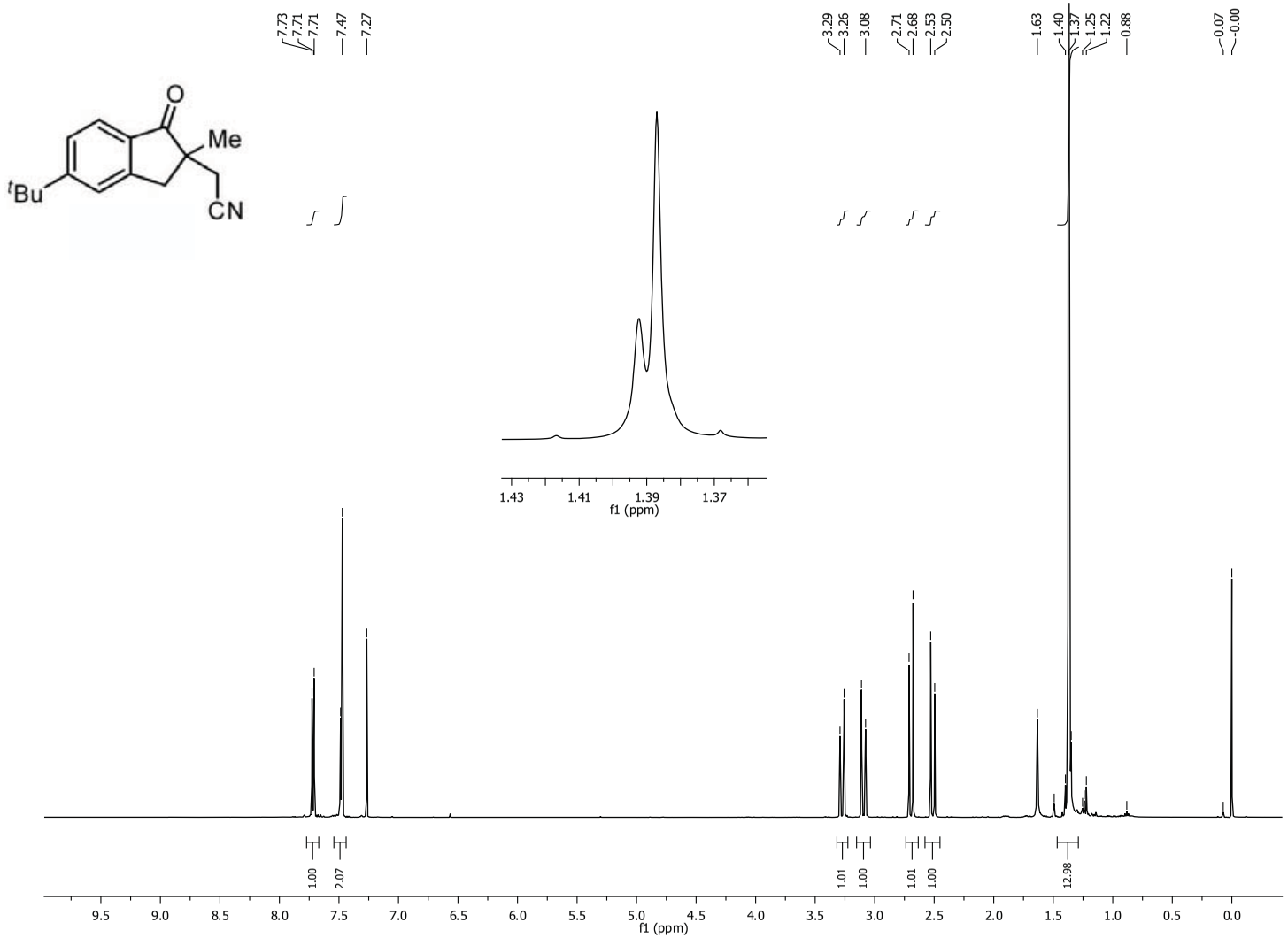
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.1010 | *Comment* | 5 mm PABBO BB/19F-1H/D Z-GRD Z119470/0030 | *Date* | 01 May 2013 17:04:48 |
| *Date Stamp* | 01 May 2013 17:04:48 | *File Name* | C:\Users\Naveen\Desktop\NR-3-48-13C\1\fid | | |
| *Frequency (MHz)* | 125.76 | *Nucleus* | 13C | *Number of Transients* | 1024 | *Origin* | spect |
| *Original Points Count* | 32768 | *Owner* | cdonnr | *Points Count* | 32768 | *Pulse Sequence* | zgpg30 |
| *Receiver Gain* | 194.68 | *SW(cyclical) (Hz)* | 29761.90 | *Solvent* | CHLOROFORM-d | | |
| *Spectrum Offset (Hz)* | 12570.2578 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 29761.00 | *Temperature (degree C)* | 25.159 |



9/26/2013 12:21:26 PM

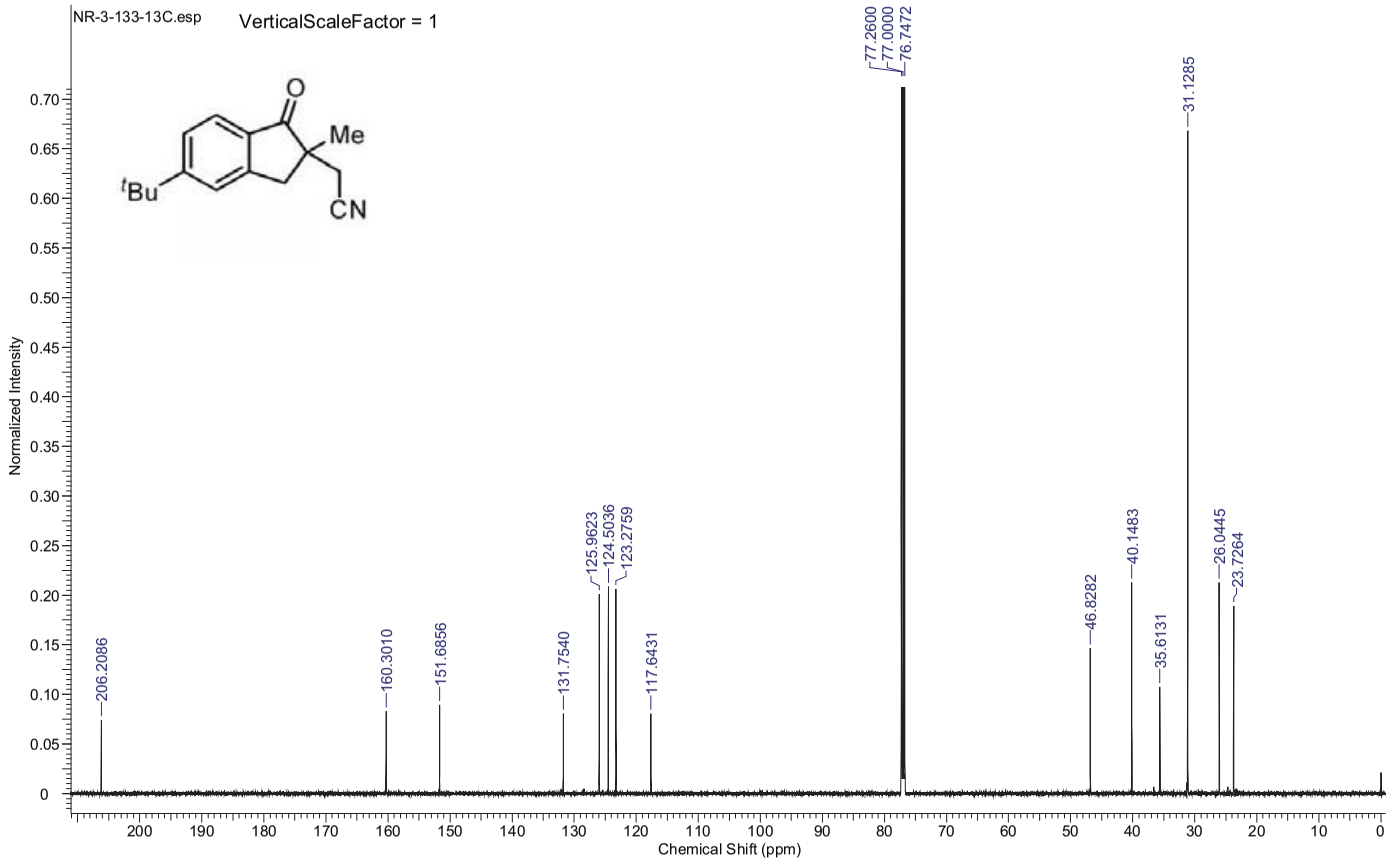
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 0.6464 | ***Comment*** | NR-3-48-19F University of Minnesota Department of Chemistry VAC-300 | | | | |
| ***Date*** | May 7 2013 | ***Date Stamp*** | May 7 2013 | ***File Name*** | C:\Users\Naveen\Desktop\130507v3 6902.fid\fid | | |
| ***Frequency (MHz)*** | 282.23 | ***Nucleus*** | 19F | ***Number of Transients*** | 32 | ***Original Points Count*** | 64000 |
| ***Points Count*** | 65536 | ***Pulse Sequence*** | s2pul | ***Receiver Gain*** | 12.00 | ***Solvent*** | CHLOROFORM-d |
| ***Spectrum Offset (Hz)*** | -7240.9688 | ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 99009.90 | ***Temperature (degree C)*** | AMBIENT TEMPERATURE |




O
Me
tBu
CN
7.73
7.71
7.71
7.47
7.27
3.29
3.26
3.08
2.71
2.68
2.53
2.50
1.63
1.40
1.37
1.25
1.22
0.88
0.07
0.00
1.43
1.41
1.39
1.37
f1 (ppm)
1.00
2.07
1.01
1.00
1.01
1.00
12.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

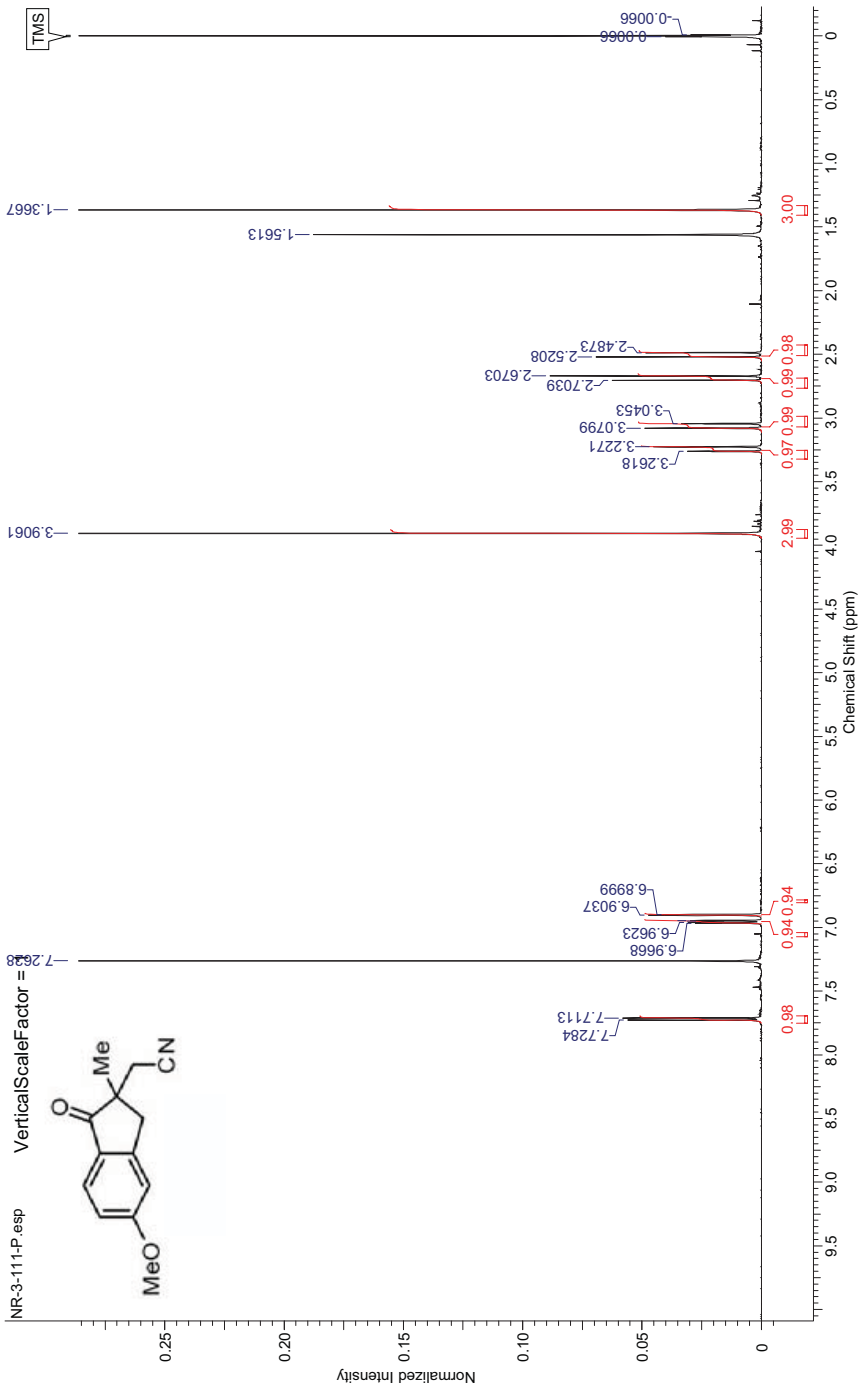
8/29/2013 11:39:11 AM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 28 Aug 2013 19:10:40 | | | ***Date Stamp*** | 28 Aug 2013 19:10:40 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-133-13C\10\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 1024 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 182.64 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12569.4092 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 21.000 | | | | |



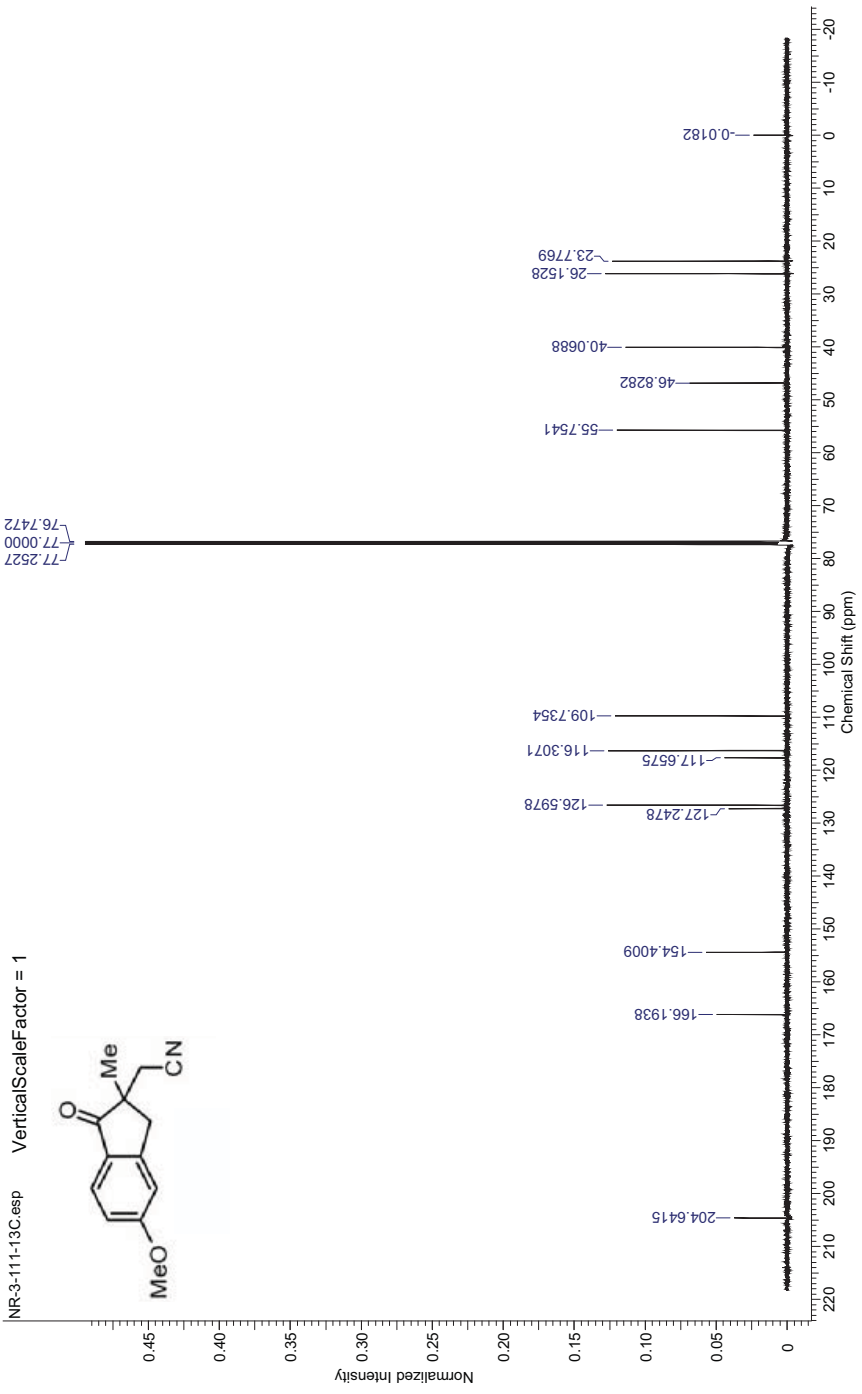
9/26/2013 3:59:25 AM

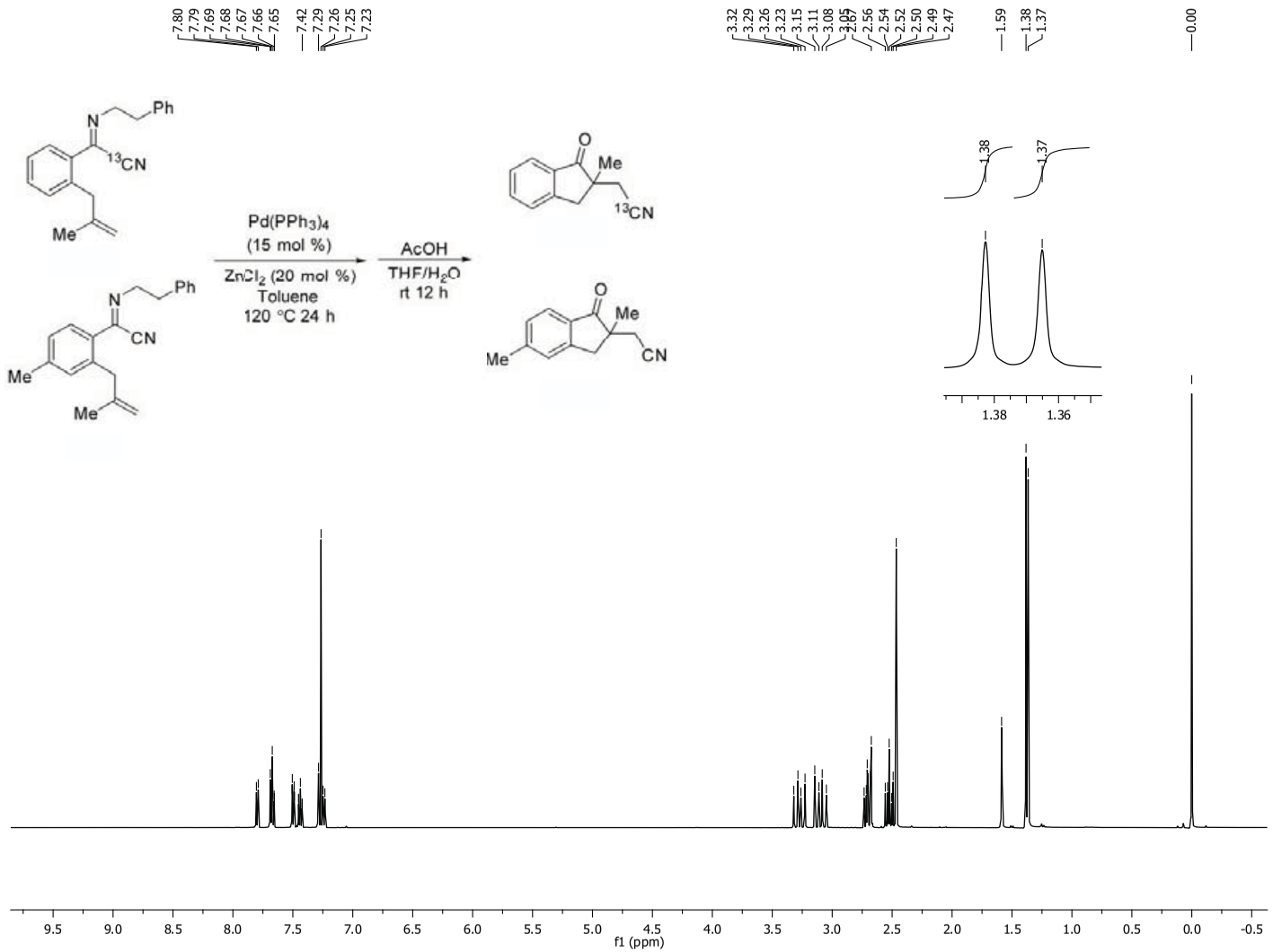
| | | | | | |
|---|---|---|---|---|---|
| Acquisition Time (sec) | 3.2768 | Date | 11 Jul 2013 15:33:04 | Date Stamp | 11 Jul 2013 15:33:04 |
| File Name | C:\Users\Naveen\Desktop\NR-3-111-P\10\fid | Frequency (MHz) | 500.13 | Nucleus | 1H |
| Number of Transients | 16 | Origin | spect | Original Points Count | 32768 | Owner | auto |
| Points Count | 131072 | Pulse Sequence | zg30 | Receiver Gain | 127.25 | SW(cyclical) (Hz) | 10000.00 |
| Solvent | CHLOROFORM-d | | | Spectrum Offset (Hz) | 3077.3545 | Spectrum Type | STANDARD |
| Sweep Width (Hz) | 9999.92 | Temperature (degree C) | 21.001 | | | | |



8/20/2013 5:31:02 PM

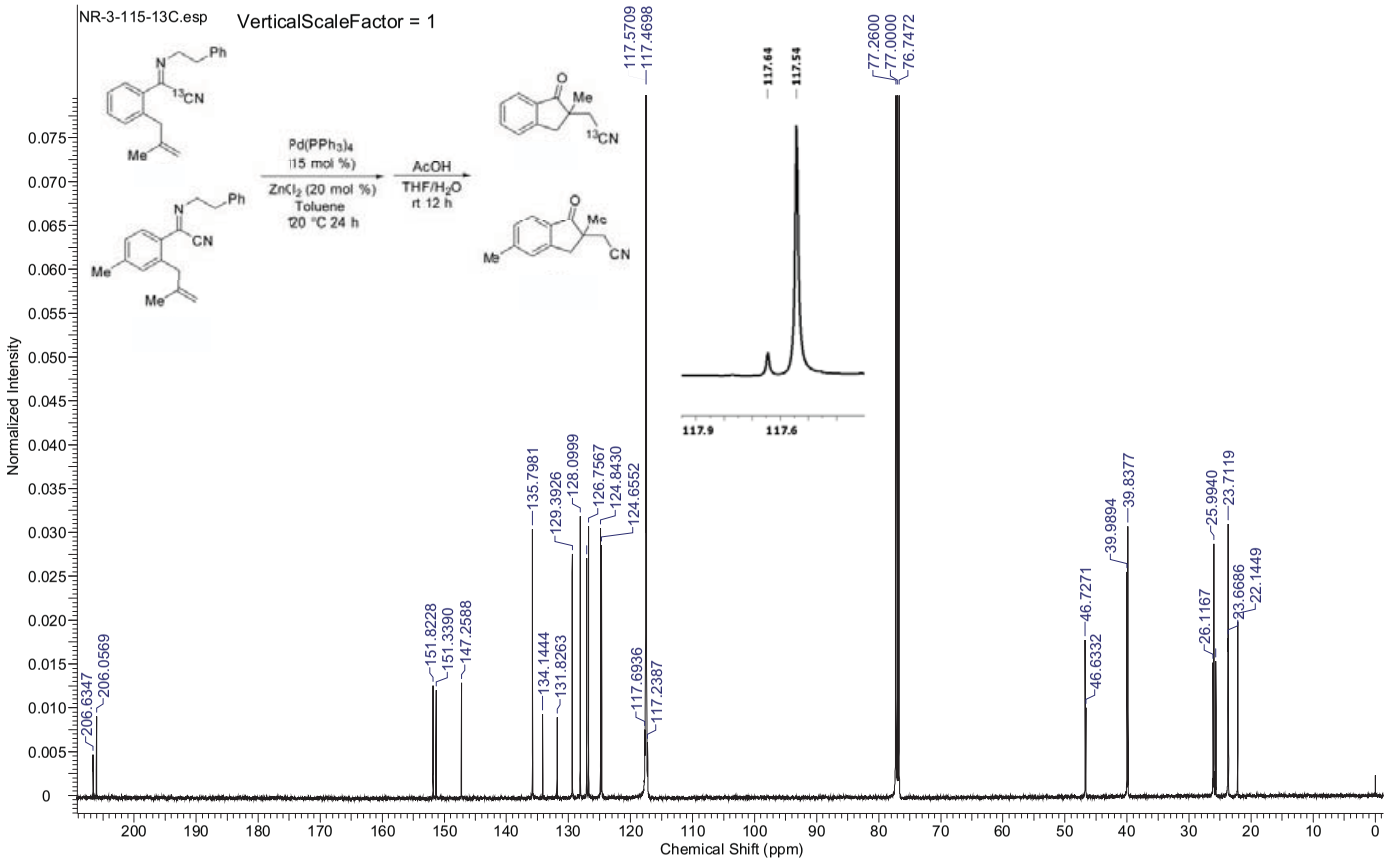
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 11 Jul 2013 19:06:24 | | | ***Date Stamp*** | 11 Jul 2013 19:06:24 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-111-13C\10\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 1024 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 194.68 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12569.4092 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 21.001 | | | | |




7.80
7.79
7.69
7.68
7.67
7.66
7.65
7.42
7.29
7.26
7.25
7.23
3.32
3.29
3.26
3.23
3.15
3.11
3.08
2.56
2.54
2.52
2.50
2.49
2.47
1.59
1.38
1.37
0.00
Ph
N
13CN
Me
Pd(PPh3)4
(15 mol %)
ZnCl2 (20 mol %)
Toluene
120 °C 24 h
AcOH
THF/H2O
rt 12 h
O
Me
13CN
CN
1.38
1.36
f1 (ppm)

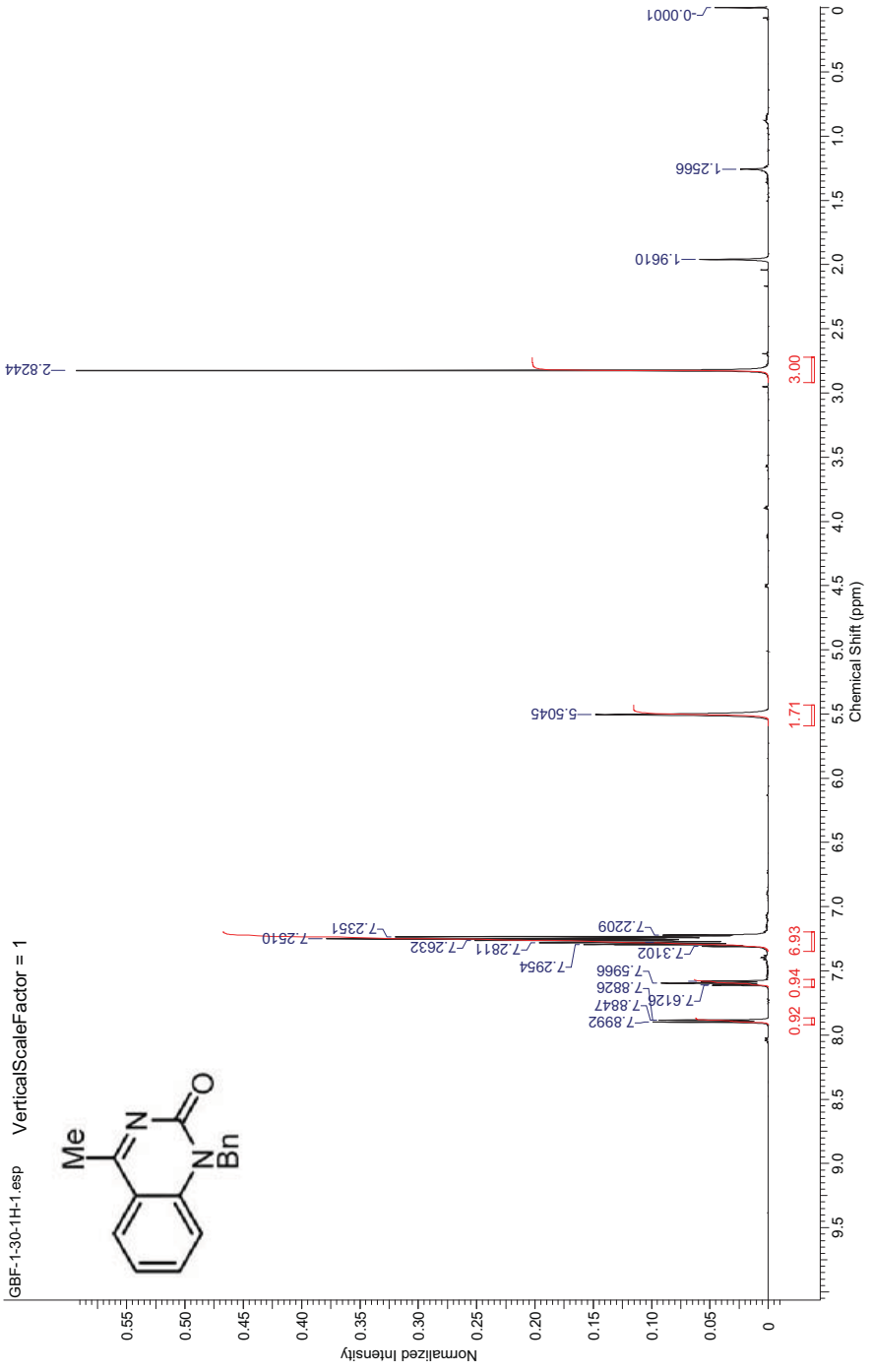
9/28/2013 6:34:11 PM

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 17 Jul 2013 15:56:32 | | | ***Date Stamp*** | 17 Jul 2013 15:56:32 |
| ***File Name*** | C:\Users\Naveen\Desktop\NR-3-115-13C\10\fid | | | ***Frequency (MHz)*** | 125.77 | ***Nucleus*** | 13C |
| ***Number of Transients*** | 800 | ***Origin*** | spect | ***Original Points Count*** | 32768 | ***Owner*** | auto |
| ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 | ***Receiver Gain*** | 194.68 | ***SW(cyclical) (Hz)*** | 29761.90 |
| ***Solvent*** | CHLOROFORM-d | | | ***Spectrum Offset (Hz)*** | 12564.8691 | ***Spectrum Type*** | STANDARD |
| ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 21.001 | | | | |



10/28/2013 9:11:50 AM

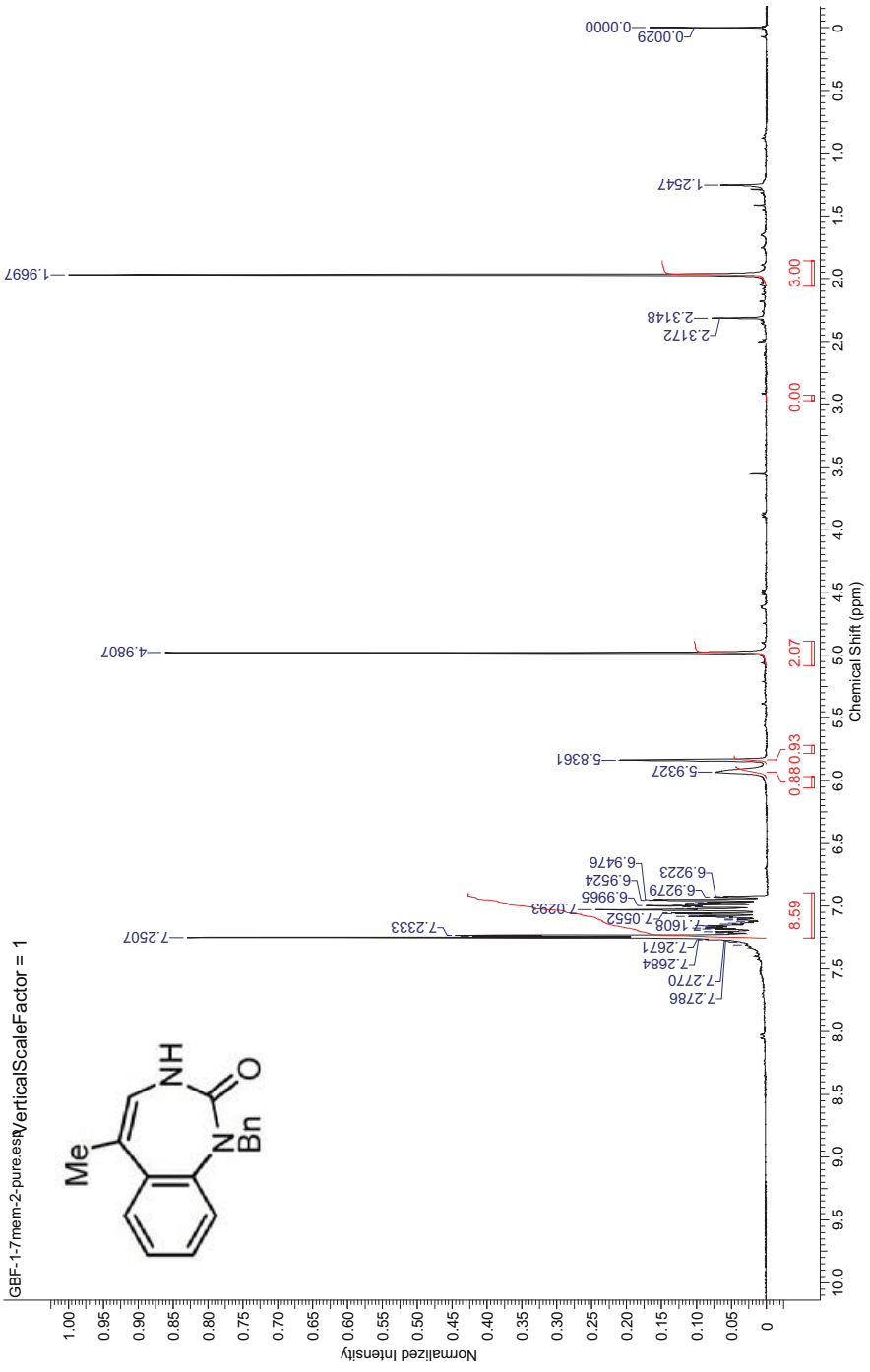
| | | | | | |
|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 1.8920 | *Comment* | Univ of Minnesota, VI-500 | *Date* | Aug 6 2012 |
| *Date Stamp* | Aug 6 2012 | *File Name* | C:\Data\Study\Research\Thesis\Chapter 4\NMRs FIDs\GBF-1-30-1H.fid\fid | | |
| *Frequency (MHz)* | 499.87 | *Nucleus* | 1H | *Number of Transients* | 1 | *Original Points Count* | 15136 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul | *Receiver Gain* | 50.00 | *Solvent* | CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2504.6272 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 8000.00 | *Temperature (degree C)* | AMBIENT TEMPERATURE |



Me
N
O
N
Bn
135.62
135.05
128.77
127.44
127.26
126.65
122.34
175.14
155.64
142.11
135.05
126.65
122.34
116.90
114.80
77.42
77.00
76.57
47.26
22.98

10/31/2013 10:23:16 AM

| | | | |
|---|---|---|---|
| *Acquisition Time (sec)* | 2.0001 | *Comment* | gbf-1-product 2-pure University of Minnesota Department of Chemistry VAC-300 |
| *Date* | Mar 25 2013 | *Date Stamp* | Mar 25 2013 *File Name* C:\Users\Naveen\Desktop\GBF-1-Product 2-purelfid |
| *Frequency (MHz)* | 299.96 | *Nucleus* | 1H *Number of Transients* 16 *Original Points Count* 11998 |
| *Points Count* | 131072 | *Pulse Sequence* | s2pul *Receiver Gain* 28.00 *Solvent* CHLOROFORM-d |
| *Spectrum Offset (Hz)* | 2396.0005 | *Spectrum Type* | STANDARD *Sweep Width (Hz)* 5998.80 *Temperature (degree C)* AMBIENT TEMPERATURE |



10/28/2013 9:08:14 AM

| | | | | | |
|---|---|---|---|---|---|
| ***Acquisition Time (sec)*** | 1.1010 | ***Date*** | 07 Oct 2013 12:18:56 | ***Date Stamp*** | 07 Oct 2013 12:18:56 |
| ***File Name*** | C:\Data\Study\Research\Thesis\Chapter 4\NMRs FIDs\GBF-carbazide\10\fid | | | ***Frequency (MHz)*** | 125.77 |
| ***Nucleus*** | 13C | ***Number of Transients*** | 800 | ***Origin*** | spect |
| ***Owner*** | auto | ***Points Count*** | 32768 | ***Pulse Sequence*** | zgpg30 |
| ***SW(cyclical) (Hz)*** | 29761.90 | ***Solvent*** | CHLOROFORM-d | ***Spectrum Offset (Hz)*** | 12561.2363 |
| ***Spectrum Type*** | STANDARD | ***Sweep Width (Hz)*** | 29761.00 | ***Temperature (degree C)*** | 20.999 |

GBF-carbazide.010.esp VerticalScaleFactor = 1