

Synthesis of Organic Building Blocks Featuring the Ene-Imine Motif

by

Brandon Fillmore

Bachelor of Science. Medicinal Chemistry, Honors. 2016

A Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of

Master of Science

in the Graduate Academic Unit of Chemistry

Supervisor: Sara Eisler, PhD, Chemistry

Examining Board: Adam Dyker, PhD, Chemistry
Igor Mastikhin, PhD, Physics

This thesis is accepted by the
Dean of Graduate Studies

THE UNIVERSITY OF NEW BRUNSWICK

December, 2018

©Brandon Fillmore, 2019

ABSTRACT

Nitrogen-containing heterocycles, or building blocks, have been shown to possess outstanding properties, in small molecules and polymers, for applications in organic solar cells (OSCs), organic light-emitting diodes (OLEDs), and organic thin-film transistors (OTFTs). To further advance our understanding of structure-activity relationships in organic semiconductors, and to improve their performance, new organic building blocks that can be fine-tuned to have desired properties are required.

The ene-imine conjugation pathway is of interest for various reasons. For example, boron-dipyrromethenes (BODIPYS) are planar, π -conjugated small molecules that can be tuned to absorb light in the red to near-infrared region, which is beneficial for applications such as organic electronics and bioimaging. However, available synthetic strategies toward BODIPY systems limits the scope of derivatives that can be achieved. Several ene-imine derivatives were prepared according to the developed synthetic procedure described herein in yields of 23-52% over two steps. The optical properties were determined by UV-vis, and the solid-state packing properties by X-ray crystallography.

DEDICATION

This thesis is dedicated to my parents, Chris and Deanna Fillmore, for their continuous support and love throughout my life and university career.

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Dr. Sara Eisler, for teaching me skills necessary to further my abilities as an organic chemist. Being a part of her group the past three years has been a valuable learning experience, and I am extremely grateful to have worked under her guidance. Her enthusiasm for chemistry has had a strong influence on my appreciation for the field.

I would also like to thank past and present Eisler group members for their helpful suggestions. I would especially like to thank Genesis Infante for teaching me laboratory techniques necessary for completing my research in Dr. Eisler's lab. I thank my summer student, Amy Brown, for her contributions to my project. I greatly appreciated having her work with me for over a year to get as many new compounds synthesized as possible.

A sincere thank you to all my professors throughout my time at UNB, including Dr. Dyker for frequent visits to his ammonia tank and glove box, Dr. James Tait and Dr. Larry Calhoun for their helpful advice with my experimental data, Dr. Val Reeves for encouraging me to study chemistry over biology, and Dr. Andreas Decken for X-ray crystallographic analysis.

I would like to thank my boyfriend, Brandon Poole, for his attention when I showed him neat chemistry ideas, even if he did not understand what was going on. I have certainly appreciated his love and support throughout the entirety of my degree.

Lastly, I would like to thank my family and friends for their support, especially Andrée-Anne Marks, Cassandra Parsons, and Corey Renouf.

Table of Contents

ABSTRACT.....	ii
DEDICATION.....	iii
ACKNOWLEDGEMENTS.....	iv
Table of Contents.....	v
List of Tables	vi
List of Figures and Schemes.....	vii
List of Symbols, Nomenclature or Abbreviations	xiii
Chapter 1: Introduction.....	1
1.1 The Building Block Approach: Accessing π -Conjugated Organic Materials.....	1
1.2 Synthetic Strategies for Extending the Ene-Imine Motif.....	5
1.3 Project Goals.....	9
Chapter 2: Synthesis	10
2.1 Synthetic Strategy for Obtaining Triflate 23b	10
2.2 Synthesis of Triflate 23b	11
2.3 Synthesis of Ene-Imine Derivatives from Triflate 23b	18
2.4 Synthesis of an Ene-Imine Derivative Featuring a Push-Pull System.....	20
2.5 Synthesis of Ene-Imine Oligomers	23
2.6 Synthetic Strategy for Obtaining Triflate 49	29
2.7 Synthesis of Triflate 49	32
2.8 Synthesis of Ene-Imine Derivatives from Lactam 51	35
2.9: Synthesis of Triflate 50	36
2.10 Synthesis of Ene-Imine Derivatives from Lactam 68	38

2.10 Synthesis of Thienopyridine Derivatives 73 and 74	38
2.12 Conclusion	41
2.13 Future work.....	42
Chapter 3: Optical and Crystallographic Analysis.....	43
3.1 Optical Properties.....	43
3.2 Crystallographic Analysis.....	48
3.2.1 Crystal Analysis for Thienopyrrole 51	48
3.2.2 Crystal Analysis for Isoindoles 34 & 36	50
3.2.3 Crystal Analysis for Dimer 75	53
Chapter 4: Experimental	56
4.1 General Information.....	56
4.2 Experimental Procedures	57
References.....	79
Appendix A: ¹ H and ¹³ C NMR for all new compounds.....	88
Appendix B: Crystal Data for Thienopyrrole 51	142
Appendix C: Crystal data for Isoindole 34	156
Appendix D: Crystal data for Isoindole 36	168
Appendix E: Crystal data for Isoindole Dimer 75	187
Curriculum Vitae	

List of Tables

Table 2.1. Optimization of the Conversion of Lactam 24 to Triflate 25	15
Table 2.2. Product Distribution when the R Group in 55a is Altered.....	30

List of Figures and Schemes

Figure 1.1. Properties that can be controlled by modifying the structure of organic compounds.....	1
Scheme 1.1 Synthesis of polymers 1-2 from isoindigo building blocks 3-4	2
Scheme 1.2. Synthesis of DPP derivatives 5-9 from building blocks 10 and 11	3
Figure 1.2. General structure of the BODIPY scaffold, with the ene-imine motif highlighted in red.....	3
Scheme 1.3. Synthetic route for BODIPY derivatives 16a-f	5
Scheme 1.4. Synthesis of asymmetric isoindole BODIPY derivatives using POCl ₃ condensation.....	6
Scheme 1.5. Synthesis of BODIPY 22 from BODIPY 20 using Knoevenagel condensation.....	7
Figure 1.3. Structure of the BODIPY core with various attachment points for Substituents.....	7
Figure 1.4. Ene-imine derivatives accessible from triflate precursors via palladium cross-coupling reactions.....	9
Figure 2.1. Structure of the isoindole trifluoromethanesulfonate building blocks 23a, b	10
Scheme 2.1. Retrosynthetic pathway for triflate 23b	10
Scheme 2.2. Synthesis of amide 26 from carboxylic acid 27	11
Scheme 2.3. Synthesis of alkyne 25 from iodo amide 26	12
Scheme 2.4. Synthesis of lactam 24 from alkyne 25	12
Scheme 2.5. Synthesis of triflates 29a-c from lactams 30a-c	13

Scheme 2.6. Synthesis of triflate 31 from lactam 32	13
Scheme 2.7. Synthesis of triflate 23b from lactam 24	13
Figure 2.2. The proposed mechanism for sulfonyl ester cleavage by hydroxide anion....	15
Figure 2.3. The proposed mechanism for sulfonyl ester cleavage by triflate anion.....	16
Scheme 2.8. Synthesis of isoindole 33 from lactam 24	18
Scheme 2.9. Synthesis of isoindoles 34-36 from lactam 24	19
Figure 2.4. An example of a push-pull system. Changing the donor (D) substituent has a significant influence on the electronic properties.....	20
Figure 2.5. The ene-imine-yne fragment end-capped with electron donating and withdrawing moieties.....	21
Scheme 2.10. Synthetic routes toward push-pull systems bridged by the ene-imine-yne fragment.....	22
Figure 2.6. Oligomer structure consisting of four building blocks.....	23
Scheme 2.11. Ene-imine oligomers accessible from a triflate building block.....	24
Scheme 2.12. Retrosynthesis for accessing lactam 45	24
Scheme 2.13. Synthesis of alkyne 46 from lactam 24	25
Scheme 2.14. The three possible products from the Sonogashira reaction, with arrows pointing to protons that could be responsible for two singlets in the vinyl region of the ¹ H NMR.....	26
Figure 2.7. HSQC 2D spectrum used to rule out alkyne 47	26
Figure 2.8. Two possible compounds, lactams 23 and 25 , showing potential intramolecular hydrogen bonding interactions.....	27

Figure 2.9. Similar pyrrole structure from literature, showing two hydrogen bonding interactions similar to those in lactam 46 and 47	28
Figure 2.10. The suggested isomer synthesized.....	28
Figure 2.11. Structures for isoindole and thienopyrrole scaffolds.....	29
Figure 2.12. Structures of the benzyldiene thienopyrrole trifluoromethanesulfonate (triflate 49 & 50) building blocks.....	29
Scheme 2.15. Retrosynthetic pathway to triflate 49	30
Scheme 2.16. Substituents on the alkyne can shift selectivity to the 5- <i>exo-dig</i> or 6- <i>endo-dig</i> products.....	30
Scheme 2.17. Anion development after nucleophilic attack at the alpha or beta carbon of the alkyne.....	31
Scheme 2.18. Synthetic approach for obtaining triflate.....	31
Scheme 2.19. Cyclization of alkyne 52 , obtaining lactam 58 as the major product.....	32
Scheme 2.20. Rationale for cyclizing alkyne 59 to obtain thienopyrrole 60	32
Scheme 2.21. Cyclization of alkyne 59 to thienopyrrolone E-60 using TBAF.....	33
Scheme 2.22. Synthesis of lactam E-51 from thienopyrrolone E-60	34
Scheme 2.23. Synthesis of triflate 49 from lactam 51	34
Scheme 2.24. Synthesis of thienopyrrole 38 from lactam 28	35
Scheme 2.25. Attempted synthesis of thienopyrroles 63-65 from lactam 51	35
Scheme 2.26. Synthesis of triflate 50 from amide 66 in three steps.....	36
Scheme 2.27. Synthesis of lactams 67 and 68 from alkyne 66	36
Scheme 2.28. Synthesis of thienopyrrolone 71 from alkyne 70	37
Scheme 2.29. Synthesis of lactam 69 from thienopyrrolone 71	37

Scheme 2.30. Synthesis of thienopyrrole 72 from lactam 68	38
Scheme 2.31. Synthesis of thienopyridine 73 from lactam 58	38
Scheme 2.32. Synthesis of thienopyridine 74 from lactam 69	39
Scheme 2.33. Synthesis of dimer 75 from lactam 24	40
Figure 2.13: Ene-imine derivatives that were synthesized & isolated for this project.	41
Figure 2.14: Possible ene-imine derivatives that could be accessed using the developed synthetic approach.....	42
Scheme 2.34. Approach to functionalized BODIPY derivatives using my synthetic approach.....	42
Figure 3.1: UV-vis spectra for isoindoles 33-36 , 44	44
Figure 3.2: Structure for 1H-benzo[c]thio- and 1H-benzo[c]selenophen-2-ium tetrafluoroborates.....	45
Figure 3.3. UV-vis spectra for isoindole 33 , thienopyrrole 62 , 72 and thienopyridines 73 , 74	46
Figure 3.4. Normalized fluorescence spectra for thienopyridines 73 and 74	47
Figure 3.5. Crystal structure for thienopyrrole 51	48
Figure 3.6. Hydrogen bonding interaction between the lactam moieties in thienopyrrole 51	49
Figure 3.7. Crystal structure for isoindole 34	50
Figure 3.8. Crystal structure for isoindole 34 showing weak C-H...pi interactions.....	51
Figure 3.9. Crystal structure for isoindole 36	52
Figure 3.10. Stacking motif of isoindole 36 in the solid state.....	52
Figure 3.11. Crystal structure for isoindole dimer 75	53

Figure 3.12. Crystal structure of isoindole dimer 75 stacks.....	54
Figure 3.13. Adjacent stacks are stabilized by aggregation of the propyl Groups.....	54
Figure 3.14. The stacks isoindole dimer 75 are oriented in a herringbone packing arrangement.....	55

List of Symbols, Nomenclature or Abbreviations

OEs: Organic electronics

OSCs: Organic semiconductors

HOMO: Highest occupied molecular orbital

LUMO: Lowest unoccupied molecular orbital

DPP: Diketopyrrolopyrrole

BODIPY: Boron dipyrromethene

DCM: dichloromethane

THF: tetrahydrofuran

DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

POCl₃: phosphoryl chloride

OTf: trifluoromethanesulfonate group

TBAF: tetrabutylammonium fluoride

TLC: thin-layer chromatography

NaH: sodium hydride

M: molarity (mol/L)

NMR: nuclear magnetic resonance

SOCl₂: thionyl chloride

NH₃: Ammonia

Et₂O: diethyl ether

Tf₂NPh: *N*-phenyl(bis)trifluoromethanesulfonate

NaHCO₃: sodium bicarbonate

DMF: dimethylformamide

NaOH: sodium hydroxide

Tf₂O: trifluoromethanesulfonic anhydride

Et₃N: triethylamine

NaCl: sodium chloride

EDG: electron-donating group

EWG: electron-withdrawing group

HSQC: heteronuclear single quantum coherence spectroscopy

TFA: trifluoroacetic acid

NOESY: nuclear overhauser effect spectroscopy

UV-vis: ultraviolet-visible

Mp: melting point

IR: infrared

HRMS: High-resolution mass spectrometry

Chapter 1: Introduction

1.1 The Building Block Approach: Accessing π -Conjugated Organic Materials

Organic molecules possessing discrete π -conjugation pathways are crucial targets due to their importance in the field of organic electronics (OEs).¹⁻⁴ One methodology toward advancing the understanding of OEs is through the synthesis of π -conjugated organic molecules, investigation of their electronic and physical properties, then evaluation of their performance in organic semiconductors (OSCs). Small π -conjugated organic molecules, known as molecular building blocks, are a critical element of the “bottom up” approach for accessing materials that could be utilized in OEs.⁵

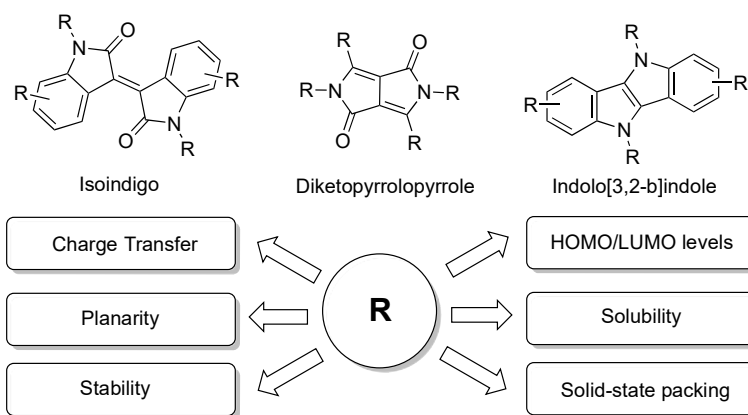
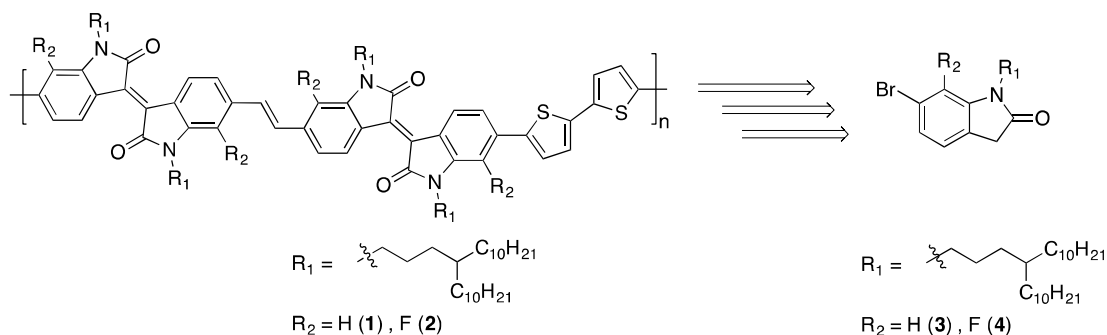


Figure 1.1 Properties that can be controlled by modifying the structure of organic compounds

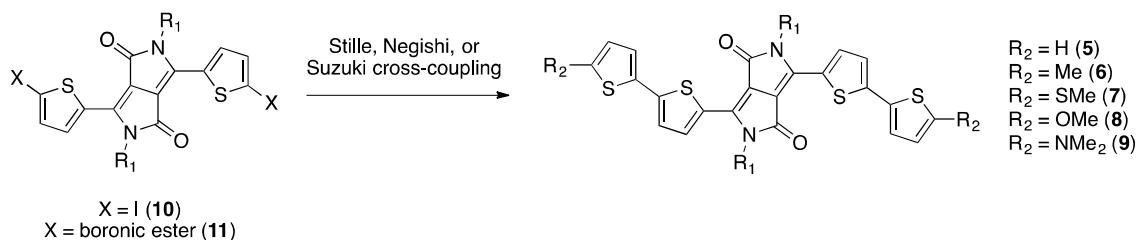
Various substituents (R) can be incorporated onto molecular building blocks such as isoindigo, diketopyrrolopyrrole, and indolo[3,2-b]indole frameworks (Figure 1.1).⁶⁻¹² This approach enables properties such as charge transfer, planarity, stability, HOMO/LUMO levels, solubility and solid-state packing to be controlled at the molecular

level, which has led to considerable progress with regard to advancing the practicality of OSCs.⁶⁻¹²



Scheme 1.1 Synthesis of polymers 1-2 from isoindigo building blocks 3-4

For example, *Lui et al.* synthesized isoindigo polymers **1** and **2** from isoindigo building blocks **3** and **4**, respectively (Scheme 1.1).¹³ To facilitate solubility in organic solvents, alkyl chains were put in place for R_1 . Substitution of a proton at R_2 with a fluorine atom had a significant influence on the properties of the polymer targets. For example, polymer **2** had a lower LUMO energy level compared to polymer **1**, indicating increased stability toward oxidation.¹⁴⁻¹⁵ Polymer **2** was also found to possess a hole mobility of $1.03 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ compared to $0.43 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ for polymer **1**, which suggests better performance in OSCs. This difference in hole mobility was ascribed to the intramolecular $\text{H}\cdots\text{F}$ interaction between vinyl and thienyl protons with the fluorine substituents in polymer **2**. This interaction “locks” the rotatable bonds in polymer **2**, increasing its planarity, which is typically correlated with increased hole-mobility.¹⁶⁻¹⁹



Scheme 1.2: Synthesis of DPP derivatives 5-9 from building blocks 10 and 11

In another example, *Wurthner et al.* synthesized a series of diketopyrrolopyrrole (DPP) derivatives **5-9** from building blocks **10** and **11** (Scheme 1.2).²⁰ Solubilizing alkyl groups were incorporated via the nitrogen atoms. Iodide atoms and boronic ester groups were employed in DPP **10** and **11**, respectively, as synthetic handles for systematic elaboration of the DPP scaffold via Negishi, Suzuki and Stille cross-coupling reactions. Substitution of the substituent at R_2 allowed the optical properties to be systematically fine-tuned, where an absorption maximum of 613, 621, 627, 631 and 684 nm was observed for DPP **5**, **6**, **7**, **8** and **9**, respectively.²⁰ This data determined that the systematic increase in electron-donor strength of R_2 from DPP **5-9** could decrease the HOMO-LUMO gap, which is the energy required to promote an electron from the molecule's HOMO to its LUMO.²¹⁻²² Since an organic molecule's efficiency in OSCs generally increases as their HOMO-LUMO gap is minimized,²³⁻²⁵ the ability to fine-tune this gap through incorporation of substituents onto an organic scaffold, such as DPP **10** and **11**, is an important feature the building block approach provides.²⁶⁻²⁸

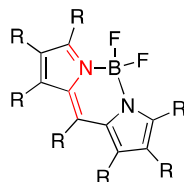
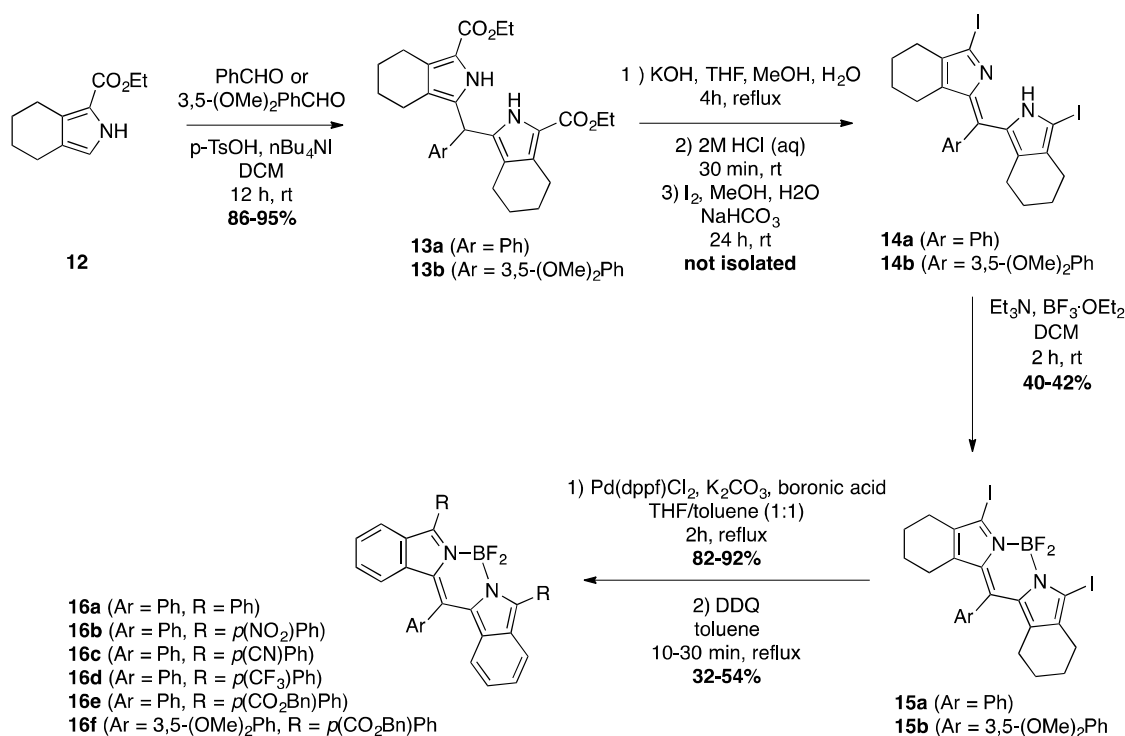


Figure 1.2: General structure of the BODIPY scaffold, with the ene-imine motif highlighted in red

Boron dipyrromethene (BODIPY, Figure 1.2) derivatives are small molecules featuring two pyrrole rings connected by a methine bridge. The pyrrole nitrogen atoms are coordinated to a boron difluoride ligand, forming a rigid, planar core. With respect to OEs, the electronic and physical properties of this core can be fine-tuned via addition of substituents at the R positions. Derivatives containing the BODIPY core often have low energy HOMO-LUMO gaps, which enables its employment in a wide variety of applications, including photovoltaic devices,²⁹⁻³⁰ laser dyes,³¹⁻³³ fluorescence labeling agents,³⁴⁻³⁷ sensors,³⁸⁻⁴² fluorescent switches,⁴³⁻⁴⁵ and photosensitizers.⁴⁶⁻⁵⁰ Despite their success in these fields, organic molecules containing the BODIPY core are often limited in terms of the variety of substituents that can be incorporated at the R positions.⁵¹⁻⁵³ Synthetic approaches that have successfully extended the integral component of BODIPY cores, the ene-imine motif (shown in red, Figure 1.4), will be discussed in the following section.

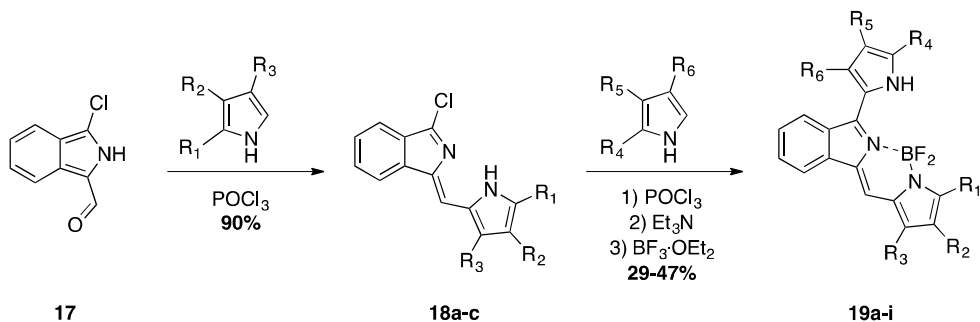
1.2 Synthetic Strategies for Extending the Ene-Imine Motif



Scheme 1.3: Synthetic route for BODIPY derivatives 16a-f

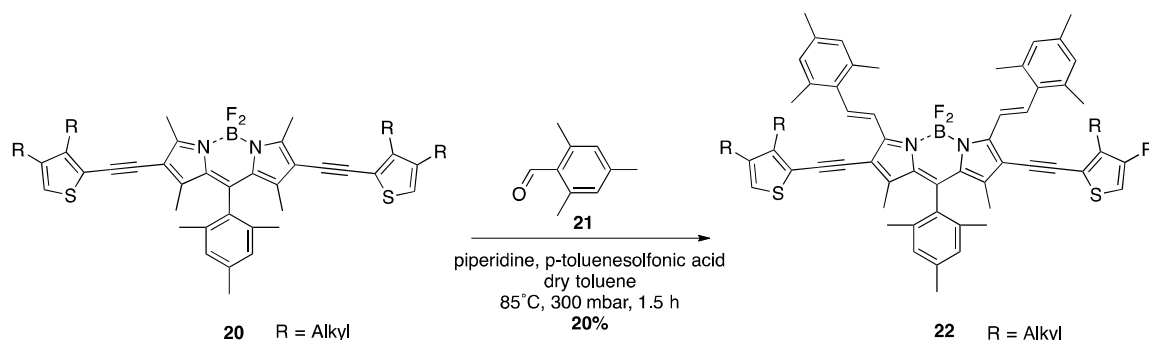
If the ene-imine motif is end-capped with a leaving group (such as a halogen), its extension can be achieved by employing palladium cross-coupling reactions.^{51, 54-56} For example, Vicente *et al.* converted tetrahydroisoindole **12** to dipyrromethanes **13a-b** in the presence of benzaldehyde or 3,5-dimethoxybenzaldehyde using an acid catalyzed condensation reaction (Scheme 1.3).⁵¹ Carboxylate groups in **13a-b** were then converted to carboxylic acid groups, which were then decarboxylated and subsequently iodinated in one step to afford diiodo **14a,b**. Subsequent coordination to boron difluoride in the presence of triethylamine successfully converted diiodo **14a,b** to BODIPY diiodo **15a,b** in moderate yields over 4 steps. Elaboration of the ene-imine fragment could then be achieved by employing the iodo groups as synthetic handles for Suzuki cross-coupling

reactions using a variety of boronic acids, followed by aromatization using DDQ, effectively synthesizing BODIPY derivatives **16a-f** in moderate yields over 2 steps from diiodo **15a,b**.⁵¹



Scheme 1.4: Synthesis of asymmetric isoindole BODIPY derivatives using POCl₃ condensation

In the presence of phosphoryl chloride, 3-chloro-1-formylpyrroles will undergo a condensation reaction with substituted pyrroles to afford ene-imine derivatives end-capped with a chlorine atom, which can be substituted by nucleophilic substitution (Scheme 1.4).^{52, 57-58} For example, *Jiao et al.* synthesized α -chlorodipyrromethenes **18a-c** in high yields by combining isoindole **17** with alkyl substituted pyrrole rings in the presence of POCl₃.⁵² The ene-imine motif was then further extended by substitution of the chloro group in α -chlorodipyrromethenes **18a-c** with alkyl substituted pyrrole rings, followed by coordination to boron difluoride in the presence of triethylamine, to afford a variety of unsymmetrical alkyl substituted BODIPY derivatives **19a-i** in low-moderate yields.⁵² Although various BODIPY derivatives can be synthesized using this method, the substituents that can be added onto the ene-imine motif are typically limited to pyrrole and indole groups.^{52,57,58}



Scheme 1.5: Synthesis of BODIPY 22 from BODIPY 20 using Knoevenagel condensation

Ene-imine motifs can also be extended by their terminal alkyl substituents by employing a Knoevenagel condensation reaction.^{52,53,59} For example, *Harvey et al.* employed a Knoevenagel condensation reaction to successfully convert BODIPY **20** to BODIPY **22** in low yield using mesitaldehyde, piperidine and *p*-toluenesulfonic acid in dry toluene (Scheme 1.5).⁵³ Given that saturated alkyl groups such as those in BODIPY **20** are usually inert to chemical reactions, the Knoevenagel condensation reaction is a convenient method for extending the ene-imine fragment. However, the necessity for an aldehyde precursor (mesitaldehyde **21**), low yields, and harsh conditions limit the versatility of substituents that can be incorporated onto the ene-imine fragment by using this condensation reaction.^{52,53,59}

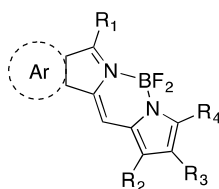


Figure 1.3: Structure of the BODIPY core with various attachment points for substituents

To further broaden the scope of BODIPY derivatives that can be accessed, a new synthetic approach that enables the attachment of various R groups to the ene-imine fragment is desired (Figure 1.3). Herein, we developed a concise synthetic pathway toward a highly tuneable building block that features the ene-imine motif.

1.3 Project Goals

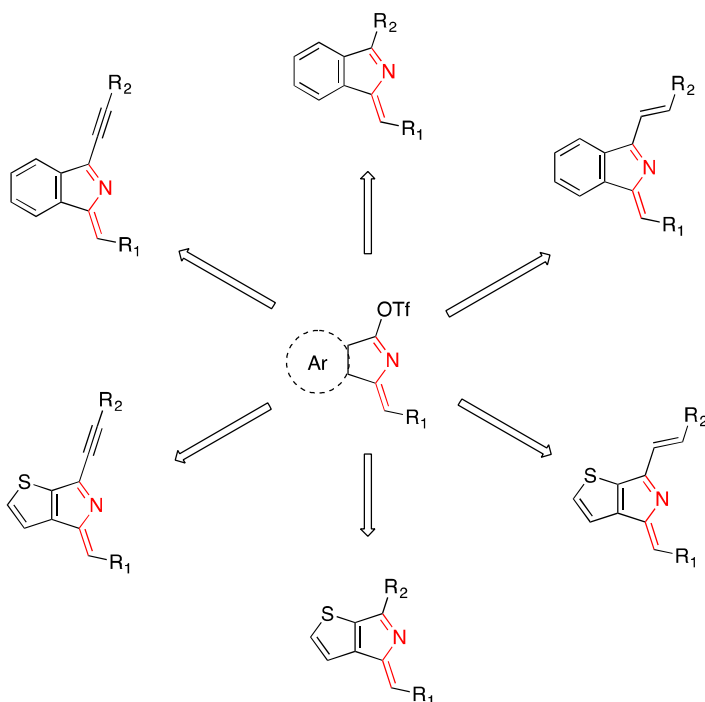


Figure 1.4: Ene-imine derivatives accessible from triflate precursors via palladium cross-coupling reactions

Using the building block approach, a variety of ene-imine derivatives will be synthesized from a triflate (OTf) precursor (Figure 1.4). The OTf group was chosen as it can be easily substituted with aryl, alkenyl and alkynyl substituents by employing palladium cross-coupling reactions.⁶⁰⁻⁶³ Further, modulation of the fused aryl group, such as a benzyl or thienyl, will provide an additional handle for broadening the scope of ene-imine derivatives that can be accessed using this synthetic approach. A short, concise synthetic pathway toward a number of triflate building blocks was therefore developed, and will be discussed in the next chapter.

Chapter 2: Synthesis

2.1 Synthetic Strategy for Obtaining Triflate **23b**

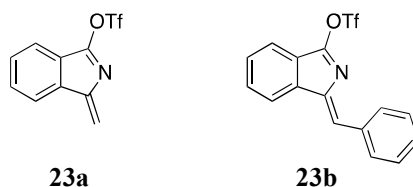
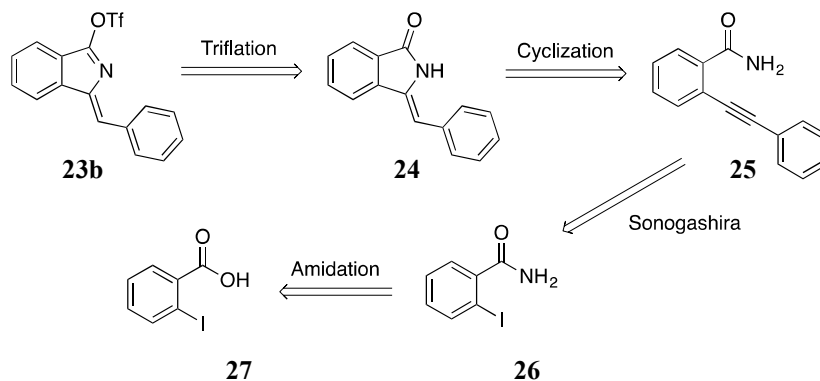


Figure 2.1: Structure of the isoindole trifluoromethanesulfonate building blocks **23a, b**.

The initial target building blocks **23a-b** feature an ene-imine moiety end-capped with a triflate group (Figure 2.1). Triflates are excellent leaving groups that are employed in cross-coupling reactions such as Sonogashira, Heck, Suzuki, and Stille to form carbon-carbon bonds,⁶⁰⁻⁶³ suggesting this target building block would facilitate access to a variety of ene-imine derivatives.



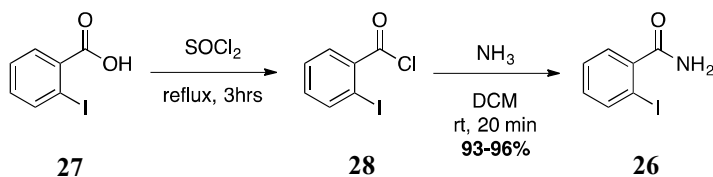
Scheme 2.1: Retrosynthetic pathway for triflate **23b**

Attempts to cross-couple **23a** were not successful. I proposed the triflyl group was attached to the nitrogen as opposed to the oxygen in **23a**, preventing substitution. **23b** was therefore targeted with the rational that the exocyclic phenyl group would provide steric bulk, facilitating O-triflation. Illustrated in Scheme 2.1, triflate **23b** can be made

from lactam **24** by employing a triflation reaction, which is typically high-yielding with few by-products.⁶⁴⁻⁶⁵ Lactam **24** is accessible from alkyne **25** by an intramolecular cyclization reaction using tetrabutylammonium fluoride (TBAF).⁶⁶⁻⁶⁷ The alkyne in **25** can be put in place using a Sonogashira-Hagihara cross-coupling reaction,⁶⁸ and amide **26** can be synthesized from commercially available carboxylic acid **27** via standard methodology.⁶⁹ High-yielding literature procedures are available for compounds **24-26**, suggesting this is a viable synthetic route for accessing triflate **23b**.

The optimization of the synthetic pathway toward triflate building block **23b**, as well its use for the synthesis of a range of ene-imine derivatives, will be discussed in the following sections.

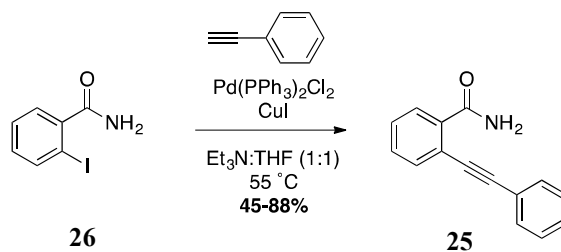
2.2 Synthesis of Triflate 23b



Scheme 2.2: Synthesis of amide 26 from carboxylic acid 27

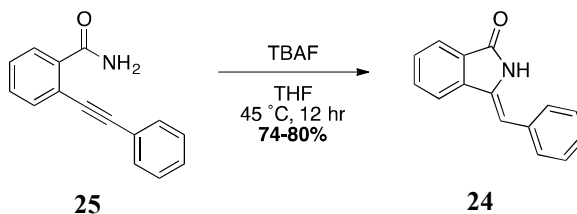
Carboxylic acid **27** was converted to amide **26** through the formation of aryl chloride **28** followed by amidation using gaseous ammonia (Scheme 2.2).⁶⁹ To facilitate efficient access to amide **26**, the synthesis of amide **26** was scaled up, although the extraction process was found to be tedious due to low solubility of amide **26**. A more efficient purification process was therefore developed: after ammonia was added, the reaction mixture was concentrated under reduced pressure, followed by addition of

distilled water, then vacuum filtration provides amide **26** in yields of 93-96% without the need for further purification.



Scheme 2.3: Synthesis of alkyne 25 from iodo amide 26

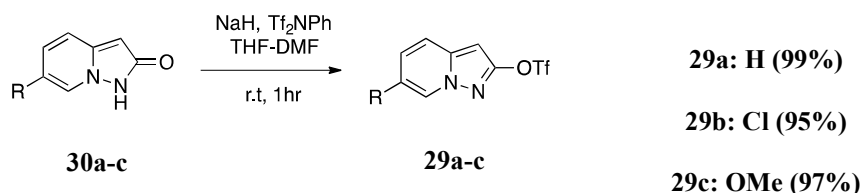
Amide **26** was converted to alkyne **25** using standard Sonogashira-Hagihara cross-coupling conditions (Scheme 2.3).⁶⁸ Small scale reactions were purified by column chromatography. However, when the reaction was performed on a larger scale, purification by column chromatography resulted in yields as low as 45% due to the low solubility of alkyne **25** in the eluent system. Instead, alkyne **25** was purified by precipitation from cold Et₂O, followed by vacuum filtration with a yield of 88%.



Scheme 2.4: Synthesis of lactam 24 from alkyne 25

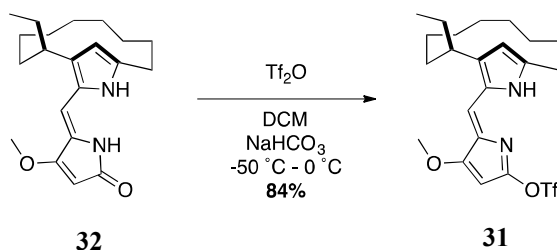
Using fluoride as a base, lactam **24** was formed via cyclization of alkyne **25** (Scheme 2.4).⁶⁶⁻⁶⁷ At room temperature this reaction can require over two days to complete as monitored by TLC. Heating the reaction to 45 °C was found to significantly reduce the reaction time to 12 hours. No purification was necessary as the Z isomer of

lactam **24** is the sole product of the reaction. With lactam **25** in hand, a triflation reaction could then be performed to synthesize the target building block **23b**.



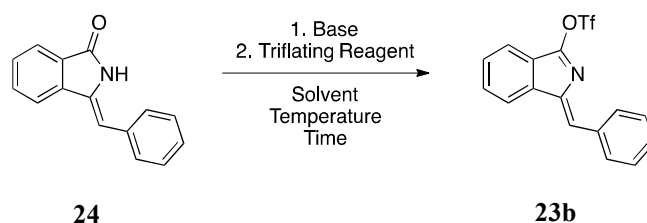
Scheme 2.5: Synthesis of triflates **29a-c from lactams **30a-c****

In the literature, lactams can typically be converted to heteroaryl triflates in high yields using a base and triflating reagent. For example, Kentaro *et al.* employed NaH and Tf₂NPh to synthesize heteroaryl triflates **29a-c** from lactams **30a-c** in near-quantitative yields (Scheme 2.5).⁶⁴ Triflates **29a-c** could then be further elaborated to the 2-arylpyrazolo[1,5-a]pyridine moiety, which is an important pharmacophore for drug discovery.⁷⁰⁻⁷²



Scheme 2.6: Synthesis of triflate **31 from lactam **32****

Thomson *et al.* employed Tf₂O and NaHCO₃ to synthesize heteroaryl triflate **31** from lactam **32** in high yield (Scheme 2.6).⁶⁵ Triflate **31** served as the precursor for assessing prodigiosin derivatives, which have antimalarial, antifungal, and antibiotic properties.⁷³⁻⁷⁵



Scheme 2.7: Synthesis of triflate **23b from lactam **24****

Given that the aforementioned triflation conditions enable access to heteroaryl triflates from lactam precursors, it was reasonable to believe that lactam **24** could be converted to triflate **23b** in high yield fairly easily (Scheme 2.7). However, this transformation proved to be difficult, and much experimentation was required to obtain triflate **23b** in reasonable amounts. Table 2.1 summarizes the optimization for the synthesis of triflate **23b**. Reaction progress was monitored by ^1H NMR. Trials 1-7 involved the use of NaH as the base and Tf_2NPh as the triflating reagent. No conversion to triflate **23b** was observed until the solvent was changed to DMF, where 30% product conversion was observed. Increasing the temperature in trials 6-7 resulted in only a slightly higher conversion (40-41%) to triflate **23b**, which was increased to 43% when the triflating reagent was changed to Comin's reagent in trial 8. A significant change was observed in trial 9 when the triflating reagent was changed to a to Tf_2O . Changing the solvent from DCM to Et_2O resulted between trials 10 and 11 had a slightly better conversion, and heating the reaction to reflux in Et_2O resulted in the highest conversion observed. This is likely due to increased nucleophilicity of the oxyanion in non-polar aprotic solvent such as Et_2O .⁷⁶

Table 2.1: Triflation results for synthesis of triflate 23b from lactam 24

Trial	Base (eq.)	Triflating reagent (eq.)	Solvent	Temperature (°C)	Time (hr)	Highest completion by ¹ H NMR (%)
1	NaH (1.1)	Tf ₂ NPh (1.1)	THF	24	3	0
2	NaH (1.1)	Tf ₂ NPh (1.1)	Et ₂ O	24	3	0
3	NaH (2)	Tf ₂ NPh (1.5)	Et ₂ O	24	3	0
4	NaH (2)	Tf ₂ NPh (1.5)	MeCN	24	3	0
5	NaH (2)	Tf ₂ NPh (1.5)	DMF	24	3	30
6	NaH (2)	Tf ₂ NPh (1.5)	DMF	50	3	40
7	NaH (2)	Tf ₂ NPh (1.5)	DMF	70	3	41
8	NaH (2)	Comin's (1.5)	DMF	70	3	43
9	NaH (2)	Tf ₂ O (1.5)	THF	24	1	76-80
10	NaH (2)	Tf ₂ O (1.5)	DCM	24	1	80-84
11	NaH (2)	Tf ₂ O (1.5)	Et ₂ O	24	1	84-89
12	NaH (2)	Tf ₂ O (1.5)	Et ₂ O	reflux	1	86-100

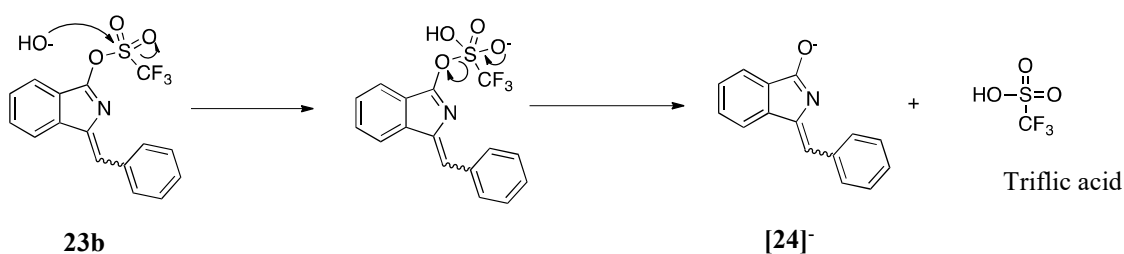


Figure 2.2: The proposed mechanism for sulfonyl ester cleavage by hydroxide anion

In all trials, if the reaction was left to stir for over an hour, any of the triflate **23b** that was produced converted back to lactam **24** either partially or completely. This observation could be attributed to trace amounts of water present in the reaction. Excess NaH could deprotonate H₂O to form NaOH, which is known to cleave sulfonyl esters such as organo triflates to produce alcohols.⁷⁷⁻⁸¹ The proposed mechanism for this process is illustrated in Figure 2.2. The nucleophilic hydroxide anion forms a bond with the electrophilic sulphur atom, forming triflic acid and anionic **24**.

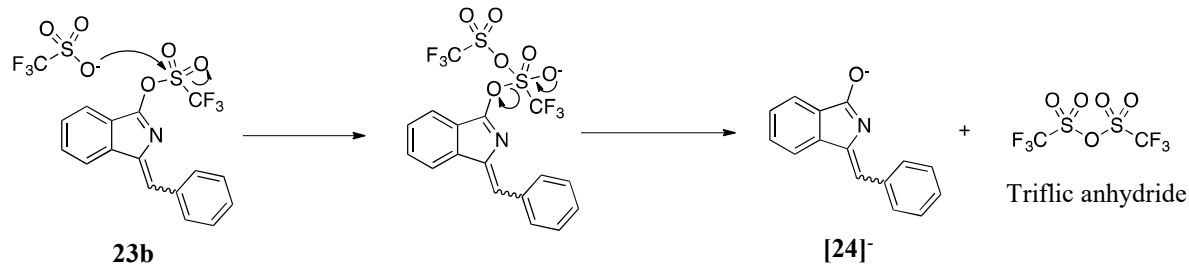


Figure 2.3: The proposed mechanism for sulfonyl ester cleavage by triflate anion

To ensure anhydrous conditions, lactam **24** was dried under vacuum overnight, and trial 9 was attempted once more with THF that had been exhaustively dried using CaH₂. Unfortunately, the same conversion process back to lactam **24** occurred over a short time frame. Anhydrous conditions producing the same result suggested the triflate anion could also be acting as a nucleophile toward triflate **23b**.⁸² The proposed mechanism for this process is illustrated in Figure 2.3. In this case, the triflate anion

forms a bond with the electrophilic sulphur atom, forming triflic anhydride and anionic **24**.

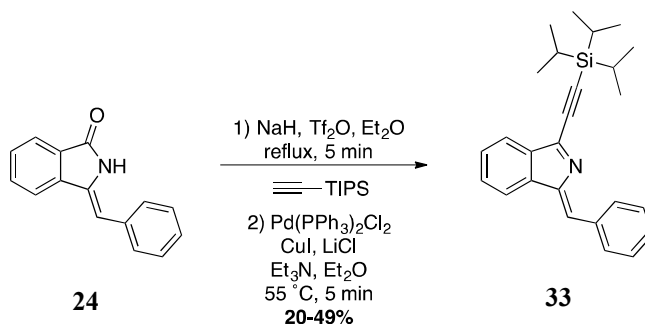
It is likely that triflate **23b** forms first rapidly then steadily converts back to anionic **24**, where a upon meeting a proton source produces lactam **24**. My strategy to circumvent this problem was to stop the triflation once conversion to triflate **23b** was the highest as monitored by TLC, which is typically reached 1-2 minutes after NaH and Tf₂O are added. The reaction was halted at this point by adding saturated NaCl_(aq), followed by extraction using a separatory funnel with Et₂O, which does not appear to hydrolyse triflate **23b** to lactam **24** based on TLC and integrations in the crude ¹H NMR.

Purification of triflate **23b** was unsurprisingly difficult. Initially, silica gel was used as the stationary phase, eluting only lactam **24**. Because water would be present in the column, the slightly acidic conditions introduced by silica gel could catalyzed the hydrolysis of triflate **23b** back to lactam **24**. Silica gel was deactivated by addition of Et₃N (3% by volume) to the eluent system on a separate purification, again resulting in elution of solely lactam **24**. The stationary phase was changed to neutral alumina, which resulted in elution of trace amounts of product that resembled triflate **23b** based on ¹H NMR. Despite these promising results, leaving this pure sample of what we assigned to be triflate **23b** under vacuum resulted in complete conversion to lactam **24** in under 2 hours. Based on these observations, we concluded that triflate **23b** is not stable to ambient conditions and readily converts back to lactam **24**.

A new synthetic procedure was therefore developed to synthesize derivatives that feature the ene-imine conjugation pathway, which will be discussed in the next section.

2.3 Synthesis of Ene-Imine Derivatives from Triflate **23b**

My initial approach to synthesizing ene-imine derivatives was to first synthesize the triflate **23b** building block using my optimized conditions, and then immediately expose it to cross-coupling conditions. In comparison to other types of cross-coupling, Sonogashira reactions can be accomplished under mild conditions with air-stable catalysts and less toxic reagents.⁸³⁻⁸⁴ Using this rationale, I decided to test the versatility of the triflate **23b** building block by synthesizing a number of ene-imine-yne derivatives using functionalized acetylenes.

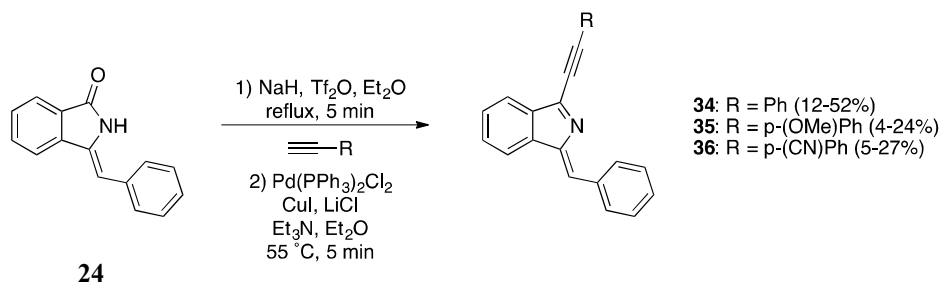


Scheme 2.8: Synthesis of isoindole **33** from lactam **24**

The first ene-imine-yne derivative to be targeted was isoindole **33** (Scheme 2.8). Lactam **24** was converted to **23b** as followed by TLC, followed by addition of the reaction mixture to an extraction funnel containing Et₂O and saturated NaCl_(aq). After drying the solution of crude triflate in Et₂O over MgSO₄, it was filtered directly into a reaction flask containing Et₃N, followed by addition of lithium chloride, bis(triphenylphosphine)palladium chloride, and copper iodide. Once the reaction mixture had been purged of oxygen and heated to 55 °C, a TLC was taken to ensure the presence of **23b**, indicating no decomposition at that point. Next, (triisopropylsilyl)acetylene was added, and the reaction mixture quickly changed color from yellow to red. TLC analysis

indicated not only the consumption of **23b** in under 5 minutes, but also the presence of a new spot. From there, the reaction was worked-up and purified by column chromatography, providing pure isoindole **33** in a 20% yield.

Because the cross-coupling appears to go to completion, the low yield of isoindole **33** could be attributed to protonation of the imine moiety under mildly acidic conditions introduced by silica gel during purification by column chromatography, preventing complete elution of isoindole **33**. To alleviate this, silica gel was neutralized using Et₃N⁸⁵ (3% by volume) to the eluent, and the pure yield for isoindole **33** was increased to 49%.



Scheme 2.9: Synthesis of isoindoles 34-36 from lactam 24

Electronic and physical properties of π -conjugated organic systems can be fine-tuned by substituent effects.^{20, 23-25} For example, introduction of phenyl groups into π -conjugated backbones often increases the degree of conjugation.⁸⁶ Further, the electronic properties can be modulated by the introduction of electron donating and withdrawing substituents.^{20, 87} My next approach was to therefore expand the scope of ene-imine-yne derivatives that could be accessible from triflate **23b**, and to probe their electronic and physical properties, by employing a variety of appropriately substituted acetylenes (R, Scheme 2.9).

The synthetic methodology used to obtain isoindole **33** was employed to access isoindoles **34**, **35**, and **36** using phenylacetylene, 1-ethynyl-4-methoxybenzene, and 4-ethynylbenzonitrile, respectively. Similar reaction times were observed for the conversion of triflate **23b** to isoindoles **34-36**, each achieving completion in under 5 minutes.

Purification of isoindoles **34-36** was accomplished by column chromatography. Similar to isoindole **33**, yields for isoindoles **34-36** could be increased by using deactivated silica gel as the stationary phase. Despite isolation, the pure yield for isoindoles **35** and **36** remained below 30%. Neutral alumina was employed as the stationary phase in an effort to increase the yield of these compounds, however separation of oxidatively coupled impurities was not possible with this method.

In contrast to the low stability of triflate **23b**, isoindoles **33-36** are stable under ambient conditions for months at a time. We can conclude that although triflate **23b** is sensitive to back conversion to lactam **24**, it was successfully converted to a variety of stable ene-imine-yne derivatives using the synthetic approach developed.

2.4 Synthesis of an Ene-Imine Derivative Featuring a Push-Pull System

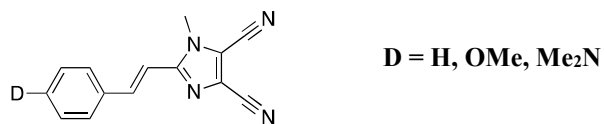


Figure 2.4: An example of a push-pull system. Changing the donor (**D**) substituent has a significant influence on the electronic properties.

When end-capped with electron donor and acceptor moieties, organic π -systems can be fine-tuned electronically via modulation of their frontier molecular orbital energy

levels.⁸⁷ An example of a push-pull structure is illustrated in Figure 2.4. Increasing the strength of the donating groups (D) with a dicyanoimidazole acceptor increased the HOMO energy levels significantly, while the LUMO energy levels were relatively unaffected. The net result was a decrease in energy needed to promote an electron from the HOMO to the LUMO, which provides an overall increase in π -conjugation due to increased communication between the π -orbitals.

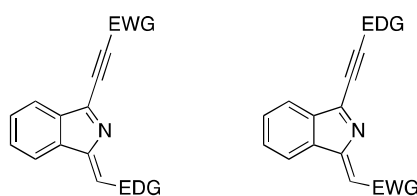
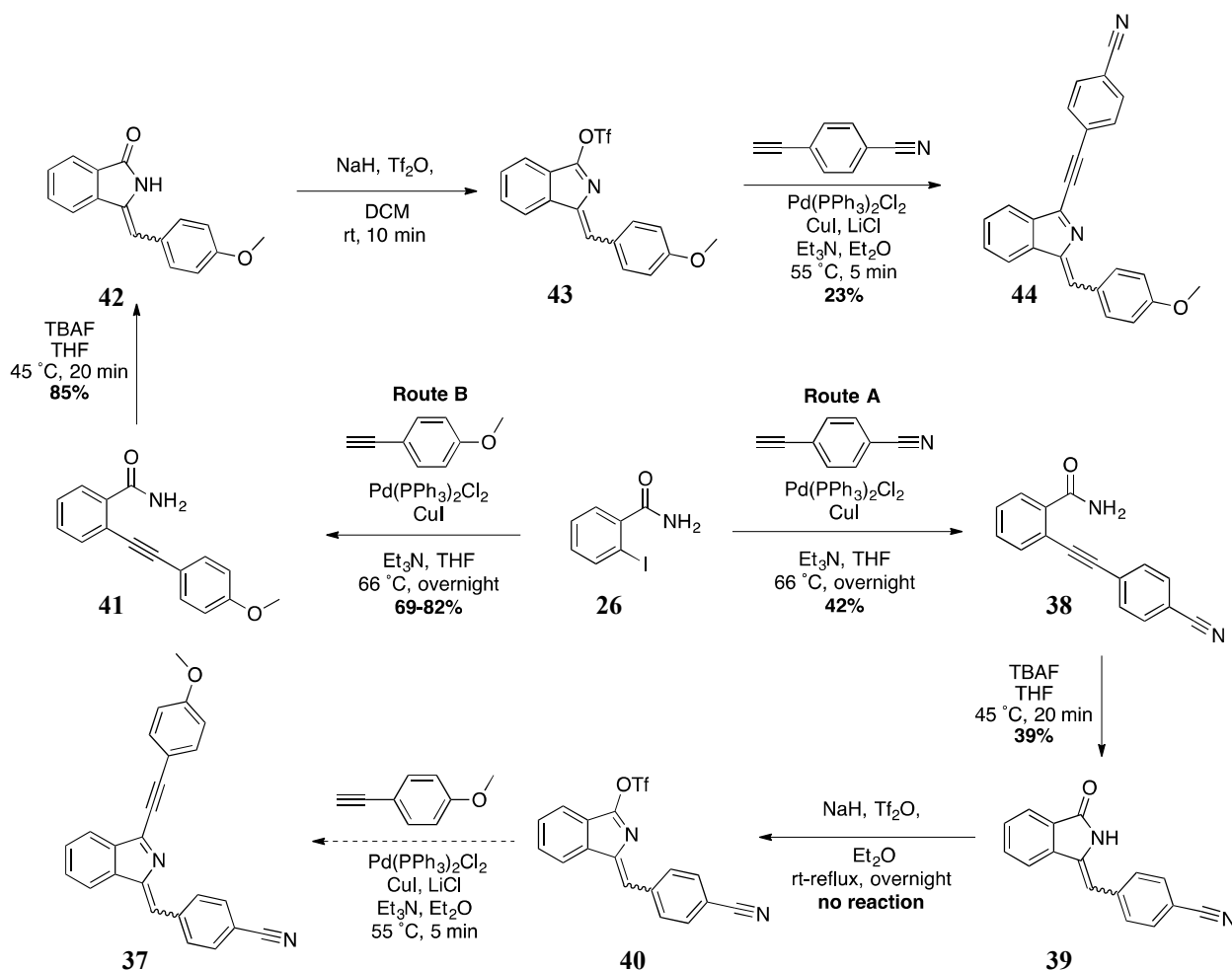


Figure 2.5: The ene-imine-yne fragment end-capped with electron donating and withdrawing moities

As illustrated in Figure 2.5, it was proposed that attaching an electron withdrawing group (EWG) or electron donating group (EDG) at the alkenyl and alkynyl positions would enable access to a push-pull system bridged by the ene-imine-yne fragment, providing another handle for tuning the electronic properties.



Scheme 2.10: Synthetic routes toward push-pull systems bridged by the ene-imine-yne fragment

My summer student, Amy Brown, was initially tasked with synthesizing push-pull isoindole **37** using my procedure (Scheme 2.10, Route A). Sonogashira cross-coupling provided *p*-cyano **38** in a 42% yield from amide **26**, followed by cyclization using TBAF to obtain lactam **39** in a yield of 39%. Unfortunately, the conversion of lactam **39** to triflate **40** was unsuccessful, preventing access to isoindole **37**. It is likely the electron withdrawing cyano substituent in lactam **39** lowers the nucleophilicity of the oxygen atom, preventing triflation. We proposed that replacing this cyano group with an electron

donating methoxy group would increase nucleophilicity of the oxygen, facilitating triflation, and we therefore targeted isoindole **44**.

Our next approach (Route B, Scheme 2.10) was to put in place an electron donating group via Sonogahira cross-coupling of amide **26**, to obtain *p*-methoxy **41**. Cyclization of alkyne **41** provided access to lactam **42**, which was successfully converted to triflate **43** (up to 90% conversion by ^1H NMR). This result suggests electron donating alkenyl substituents in isoindolinone systems facilitate conversion to their respective triflates, while electron withdrawing alkenyl substituents inhibit the process.

Similar to triflate **23b**, methoxy triflate **43** was found to be sensitive to conversion back to lactam **42**. To solve this problem, the synthetic approach developed for isoindoles **23-26** was employed to access isoindole **44** in a 23% overall yield from lactam **42**.

Having successfully obtained monomeric isoindoles **23-26** and **44** using the synthetic approach developed, we proposed structures containing linked ene-imine motifs could be accessed, which will be discussed in the following section.

2.5 Synthesis of Ene-Imine Oligomers

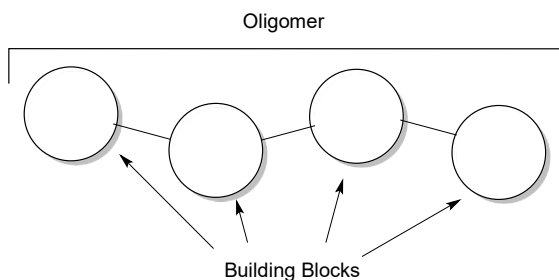
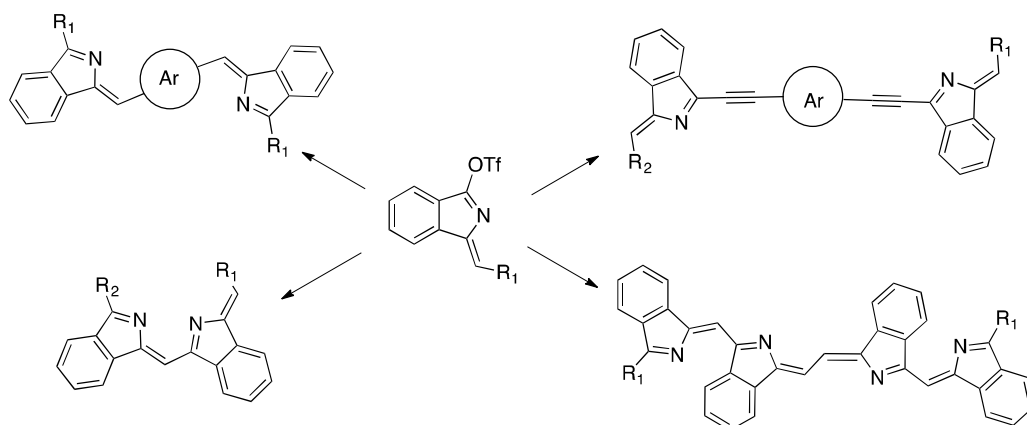


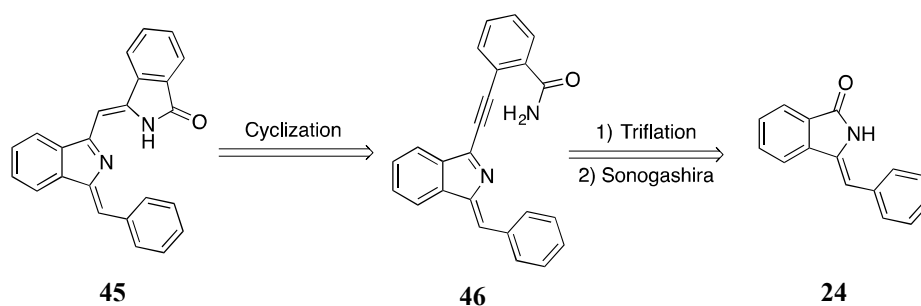
Figure 2.6: Oligomer structure consisting of four building blocks

The electronic and physical properties of organic building blocks can be fine-tuned by tethering them in sequence to form an oligomeric chain of repeating or of unique units, known as an oligomer (Figure 2.6).⁸⁸⁻⁸⁹ To broaden the scope of ene-imine derivatives we could access with the developed synthetic pathway, our next goal was to synthesize π -conjugated organic compounds which featured tethered ene-imine fragments.



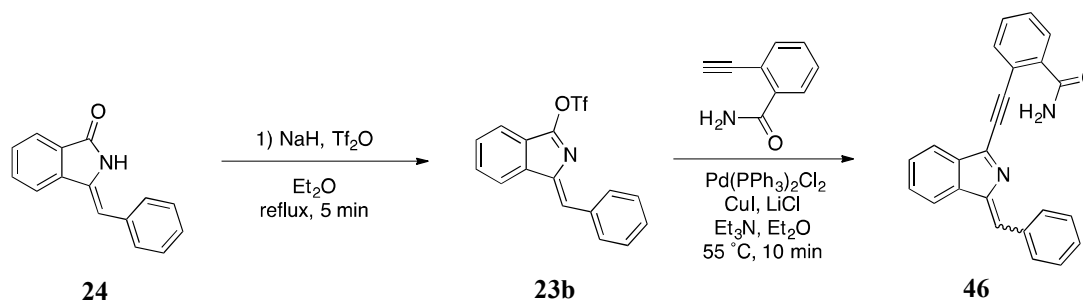
Scheme 2.11: Ene-imine oligomers accessible from a triflate building block

An isoindole unit featuring a triflate group is the key precursor building block for a variety of ene-imine oligomers that possess discrete conjugation pathways such as those illustrated in Scheme 2.11.



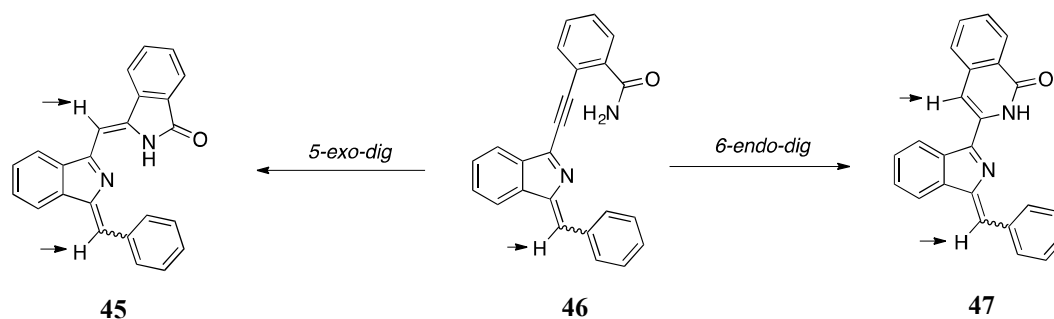
Scheme 2.12: Retrosynthesis for accessing pyrrolone 45

As illustrated in Scheme 2.12, pyrrolone **45** can be made from alkyne **46** by an intramolecular cyclization reaction using TBAF. Alkyne **46** is accessible from lactam **24** by first triflation followed by Sonogashira cross-coupling with 2-ethynylbenzamide.



Scheme 2.13: Synthesis of alkyne 46 from lactam 24

To access alkyne **46**, triflate **23b** was first synthesized *in-situ* from lactam **24**, followed by Sonogashira cross-coupling with excess 2-ethynylbenzamide (Scheme 2.13). TLC monitoring indicated the reaction was complete in under 10 minutes. The main product was separated from impurities using column chromatography, and ¹H NMR revealed two singlets of equal intensity at 6.56 and 6.69 ppm. These singlets appear in the vinyl region, and could be attributed to the vinyl proton from the Z and E isomers of alkyne **46**.



Scheme 2.14: The three possible products from the Sonogashira reaction, with arrows pointing to protons that could be responsible for two singlets in the vinyl region of the ^1H NMR

However, these two singlets of equal intensity also suggest that alkyne **46** could have cyclized to either pyrrolone **45** or pyridinone **47** during the Sonogashira reaction (Scheme 2.14). Based on this observation in the ^1H NMR, we can propose that we have one of the three products illustrated in Scheme 2.14.

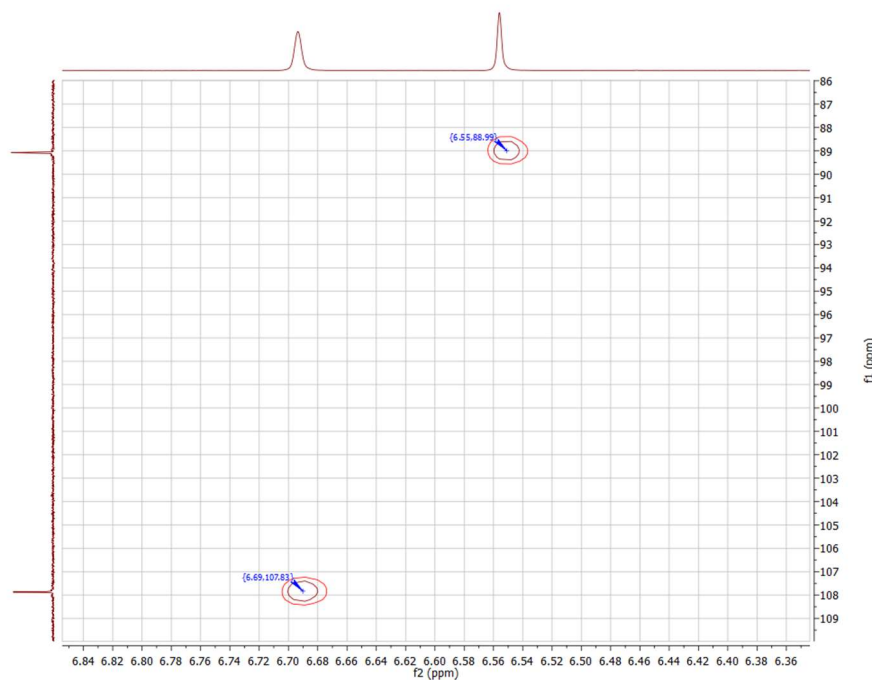


Figure 2.7: HSQC 2D spectrum used to rule out alkyne **46**

To rule out alkyne **46**, I conducted an HSQC experiment, which is a 2D NMR experiment that provides a correlation between directly bonded ^1H and ^{13}C nuclei.

Resonances at 108.0 and 89.2 ppm in the ^{13}C spectra are the only two that are within the alkynyl region. HSQC determined that these ^{13}C peaks are each correlated to a vinyl singlet in the ^1H NMR, proving these are not quaternary carbons, and subsequently proving this compound is not alkyne **46** (Figure 2.7).

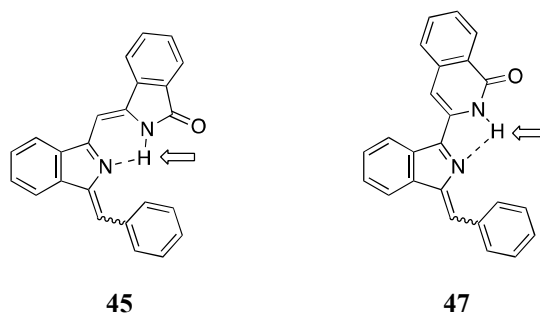
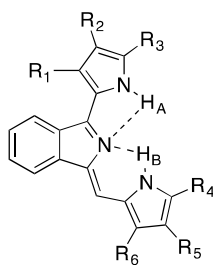


Figure 2.8: Two possible compounds, pyrrolone **45 and pyridinone **47**, showing potential intramolecular hydrogen bonding interactions**

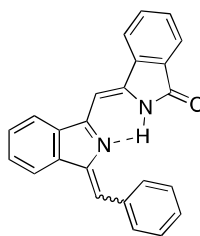
The next step was to determine if we had synthesized lactam **45** or **47**. Unfortunately, an X-ray crystal structure could not be obtained. However, in the ^1H NMR of this compound, we observe a broad singlet at 12.35 ppm, which can be attributed to the nitrogen proton (see Appendix A, page 138). It is likely that an intramolecular hydrogen bonding interaction between the imine and lactam moieties causes this downfield shift in the ^1H NMR spectrum (Figure 2.8). To determine which isomer we had synthesized, we compared this shift to similar molecules in the literature.



48a-g

Figure 2.9: Similar pyrrole derivatives synthesized by Jiao *et al.* from literature, showing two hydrogen bonding interactions similar to those in pyrrolone **46 and pyridinone **47****

Molecules similar to pyrrolone **45** and pyridinone **47** possess similar resonance in the ^1H NMR spectrum for their N-H protons. A series of pyrrolyldipyrromethenes **48a-g** were synthesized by Jiao *et al.* (Figure 2.9).⁵⁸ Among compounds **48a-g**, the resonance for H_B appears between 10.13-12.44 ppm in CHCl_3 , which is comparable to the broad singlet I observe for my compound at 12.35 ppm.



45

Figure 2.10: The suggested isomer synthesized

Based on ^1H NMR resonances of the N-H proton for H_B in Figure 2.9, it is proposed that lactam **45** is my isolated compound (Figure 2.10). Further, the position of the N-H proton in my ^1H NMR resembles shifts for N-H protons in similar hydrogen-bonding motifs.^{58, 90} However, due to the similarities between lactams **45** and **47**, further work will need to be conducted to confirm pyrrolone **45** is the product.

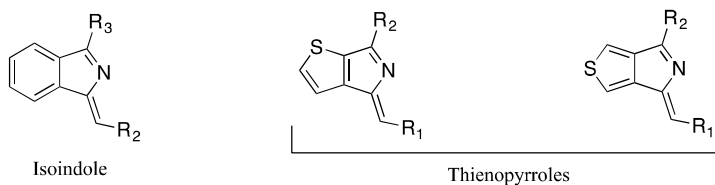


Figure 2.11: Structures for isoindole and thienopyrrole scaffolds

After demonstrating that our synthetic approach enabled access to ene-imine derivatives based on the isoindole scaffold, our next approach was to alter the benzo-fused backbone to a thienyl group (Figure 2.11). The synthesis of thienopyrrole building blocks featuring a triflate group will be discussed in the following sections. Alteration of the fused backbone would not only expand the scope of ene-imine derivatives that could be accessed, but would facilitate the synthesis of thienopyrrole scaffolds illustrated in Figure 2.11, which have not been synthesized in literature to date.

2.6 Synthetic Strategy for Obtaining Triflate **49**

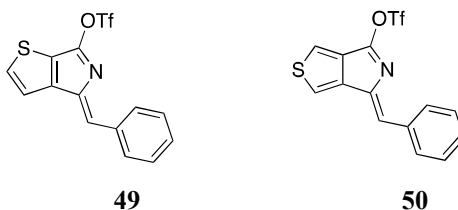
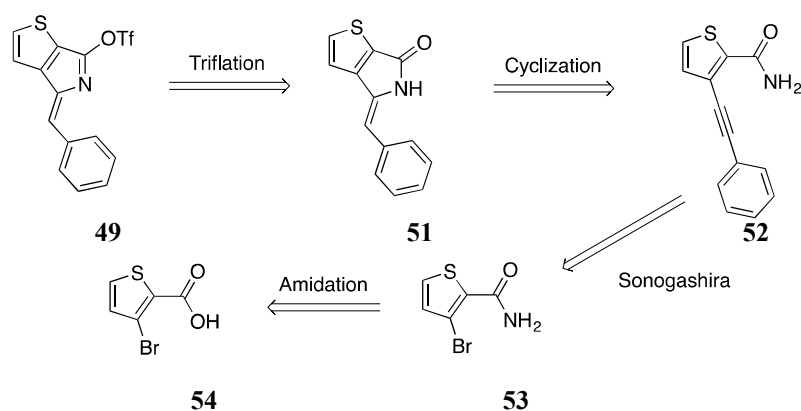


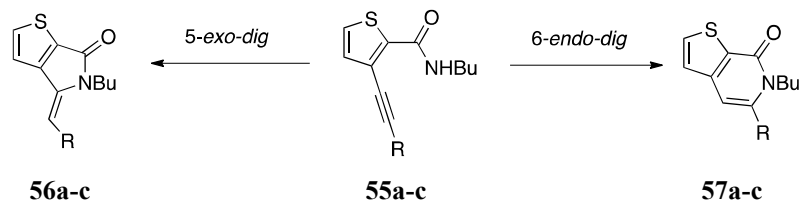
Figure 2.12: Structures of the thienopyrrole building blocks, **49 and **50****

To broaden the scope of our synthetic pathway toward ene-imine derivatives, and to incorporate another handle for fine-tuning their electronic and physical properties, thienopyrrole scaffolds **49** and **50** were the next targets of interest (Figure 2.12).



Scheme 2.15: Retrosynthetic pathway to triflate 49

My initial goal was to synthesize triflate **49**, a 2,3-fused thienopyrrole. Illustrated in Scheme 2.15, triflate **49** will be obtained from lactam **51** via a triflation.⁶⁴⁻⁶⁵ Lactam **51** can be synthesized from alkyne **52** by an intramolecular *5-exo-dig* cyclization using TBAF.⁶⁶⁻⁶⁷ The alkyne in **52** can be put in place using a Sonogashira-Hagihara reaction,⁶⁸ and amide **53** can be synthesized from commercially available carboxylic acid **54** using standard methodology.⁶⁹

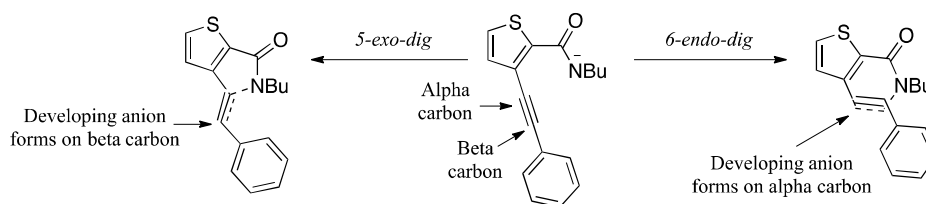


Scheme 2.16: Substituents on the alkyne can shift selectivity to the 5-*exo-dig* or 6-*endo-dig* products

Table 1.2 Product distribution when the R group in 55a is altered

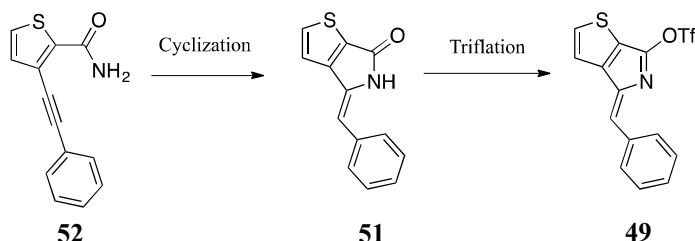
Alkyne	R	56a-c (5- <i>exo-dig</i>)	57a-c (6- <i>endo-dig</i>)
55a	H	10%	90%
55b	Pentyl	0%	100%
55c	Phenyl	93%	7%

However, unlike the benzo-fused derivatives **25**, **38** and **41**, thienyl alkynyl amides can cyclize via the *5-exo-dig*, or the *6-endo-dig* process, producing one or both cyclization products (Scheme 2.16).⁶⁷ Previous work in our group determined that the alkynyl substituent (R) has a significant influence on which product will form in the subsequent cyclization using TBAF,⁶⁷ Table 2.2. Cyclization of **55a-b** resulted in strong favorability toward the 6-endo-dig products, **57a-b**. However, changing the R group to a phenyl substituent drastically alters the product favorability, producing **56c** as the major product.



Scheme 2.17: Anion development after nucleophilic attack at the alpha or beta carbon of the alkyne

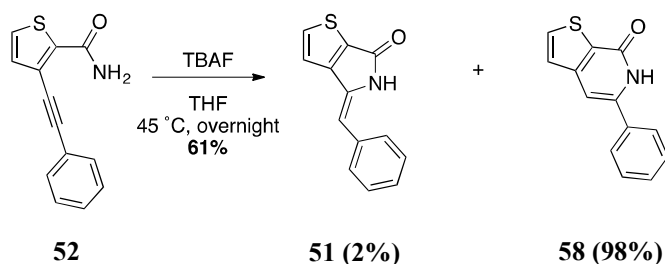
We hypothesize that an electron-withdrawing group on the beta carbon of the alkyne, such as a phenyl substituent, stabilizes the developing anion as the nitrogen attacks the alkyne. This stereoelectronic effect favors the transition state of the *5-exo-dig* pathway over the *6-endo-dig* pathway, resulting in the *5-exo-dig* product being the major isomer formed (Scheme 2.17).⁶⁷ Further, this stabilization is enough to compensate for the higher degree of strain the *5-exo-dig* product has with respect to the *6-endo-dig* product.⁶⁷



Scheme 2.18: Synthetic approach for obtaining triflate 49

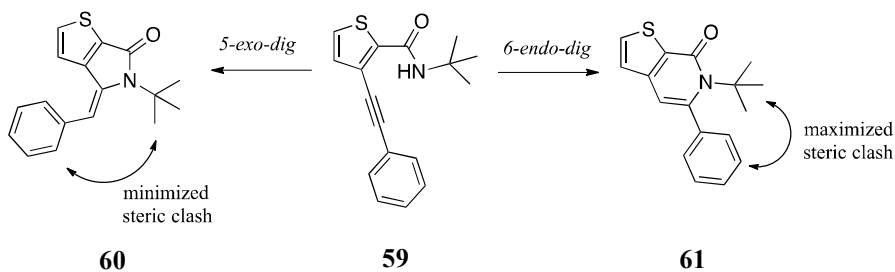
Based on this rationale, the cyclization of alkyne **52** should favour the *5-exo-dig* pathway, giving access to lactam **51**, and subsequently triflate **49** (Scheme 2.18). The optimization toward the synthesis of triflate **49** will be discussed in the following section.

2.7 Synthesis of Triflate **49**



Scheme 2.19: Cyclization of alkyne **52**, obtaining lactam **58** as the major product

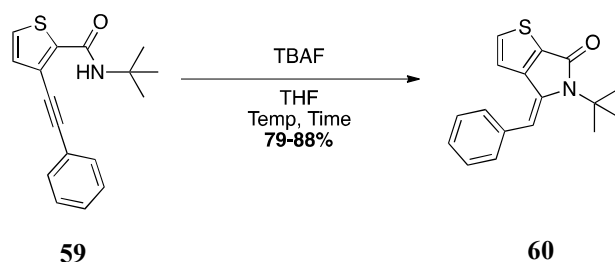
Alkyne **52** was synthesized in high yield from commercially available 3-bromothiophene-2-carboxylic acid using literature procedures (see Chapter 4: Experimental).⁶⁹ To our surprise, cyclization of alkyne **52** favored the *6-endo-dig* product, lactam **58**, in a 49:1 ratio with desired lactam **51** (Scheme 2.19). To circumvent this outcome, my next approach was to modify the amide substituent in alkyne **52**, so that the *5-exo-dig* pathway was favored.



Scheme 2.20: Rationale for cyclizing alkyne **59** to obtain thienopyrrole **60**

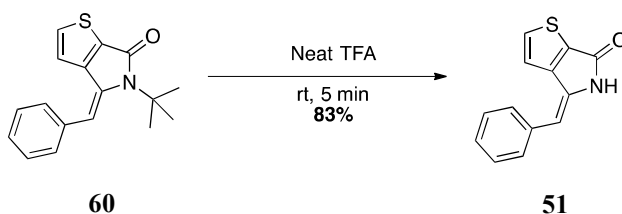
I hypothesized a bulky protecting group, such as a *tert*-butyl substituent, on the nitrogen would favour the *5-exo-dig* pathway. If alkyne **59** is cyclized, the *5-exo-dig*

product (**60**) could be favored as the phenyl group can rotate away from the *tert*-butyl group via *Z/E* isomerization, minimizing steric clash (Scheme 2.20). In the *6-endo-dig* product (**61**), the phenyl and *tert*-butyl groups are in close proximity, maximizing steric clash and disfavoring its formation. To test this hypothesis, I synthesized alkyne **59** over two steps from 3-bromothiophene-2-carboxylic acid by employing an amidation reaction with *tert*-butyl amine followed by a Sonogashira to put in place the alkyne (see chapter 4: Experimental).



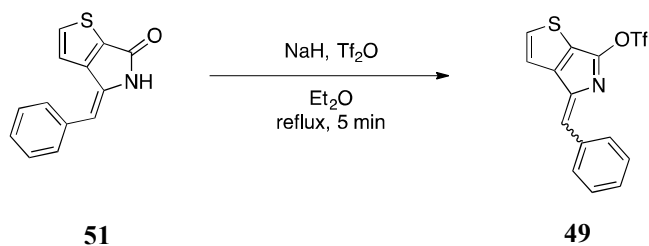
Scheme 2.21: Cyclization of alkyne 59 to thienopyrrolone 60 using TBAF

Initially, cyclization of alkyne **59** was conducted at room temperature with a 1.1 equiv. of TBAF (Scheme 2.21). At these conditions, the reaction was very slow with completion being reached in one week, when I obtained the desired thienopyrrolone **60** as the sole product in a 79% yield. A NOESY confirmed that I had obtained the *E* isomer of the reaction, suggesting the phenyl substituent had rotated away from the *tert*-butyl group to alleviate steric clash. In an effort to optimize the reaction, I heated it to reflux and added 3 equivalence of TBAF, reducing the reaction time from 1 week to 5 minutes. Further, these reaction conditions convert alkyne **59** to thienopyrrolone **60** in yields of 79-88% without the need for purification.



Scheme 2.22: Synthesis of lactam **51 from thienopyrrolone **60****

With thienopyrrolone **60** in hand, the next step was to remove the *tert*-butyl group, which can be accomplished by employing neat trifluoroacetic acid (TFA).⁹¹ By dissolving thienopyrrolone **60** in neat TFA at room temperature, complete conversion to lactam **51** was achieved in 5 minutes according to TLC analysis (Scheme 2.22). Excess acid was neutralized using sodium bicarbonate, followed by extraction of the organic phase with CHCl₃, which was then concentrated under reduced pressure to obtain lactam **51** in yields of 80-83% without the need for further purification.

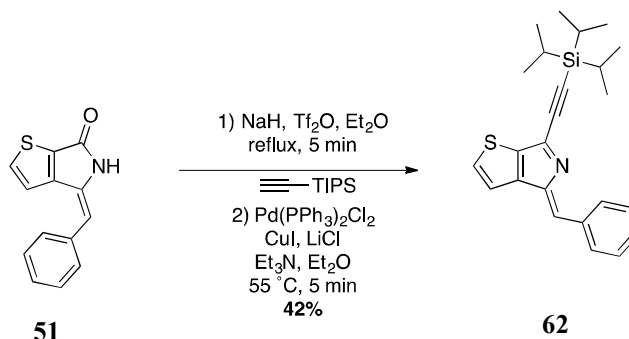


Scheme 2.23: Synthesis of triflate **49 from lactam **51****

The optimized triflation conditions developed in the earlier stages of this project were employed to convert lactam **51** to triflate **49**, with 90-100% conversion according to TLC analysis (Scheme 2.23). It was determined that much like the previously synthesized triflates, triflate **49** readily converted back to lactam **51** over a short time frame. Assuming purification and characterization of triflate **49** would not be possible, I decided to employ the triflation-coupling procedure that was developed for accessing isoindole

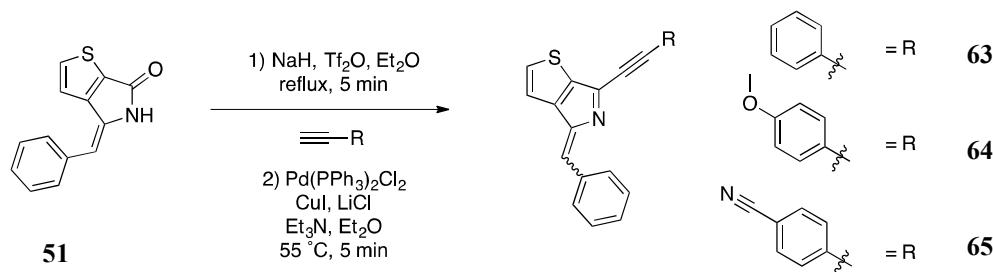
derivatives, and apply it here to access thienopyrrole derivatives. The following section will discuss the synthesis of thienopyrrole derivatives.

2.8 Synthesis of Ene-Imine Derivatives from Lactam **51**



Scheme 2.24: Synthesis of thienopyrrole **Z-62 from lactam **E-51****

Lactam **51** was treated to the optimized triflation conditions followed by Sonogashira cross-coupling consuming the triflate in under 5 minutes (Scheme 2.24). The crude reaction mixture was purified by column chromatography using deactivated silica gel and thienopyrrole **62** was obtained as a yellow oil in a yield of 42%.

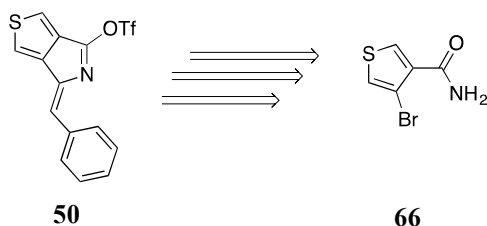


Scheme 2.25: Attempted synthesis of thienopyrroles **63-65 from lactam **51****

With the successful synthesis of thienopyrrole **51**, I decided to probe the electronic and physical properties further by employing a variety of acetylenes. Unfortunately, isolation of thienopyrroles **63-65** (Scheme 2.25) was not possible due to their susceptibility to decomposition upon concentration under vacuum. This result suggests that the use of bulky groups such as TIPS could stabilize thienopyrrole

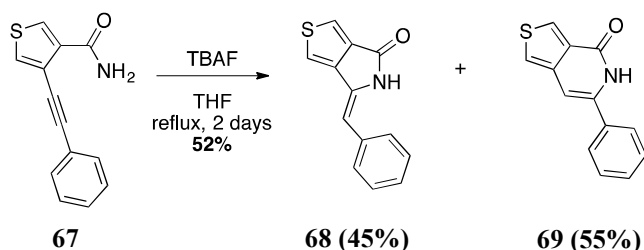
derivatives such as thienopyrrole **Z-62**. Further work will need to be conducted to access stable ene-imine derivatives with a thienopyrrole scaffold.

2.9: Synthesis of Triflate **50**



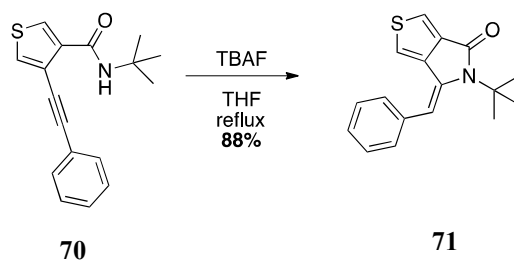
Scheme 2.26: Synthesis of triflate **50 from amide **66** in three steps**

The next thienopyrrole building block of interest was triflate **50**, which my summer student, Amy Brown, was tasked with synthesizing. Initially, we proposed that triflate **50** could be accessed in three steps from commercially available amide **66** (Scheme 2.26).



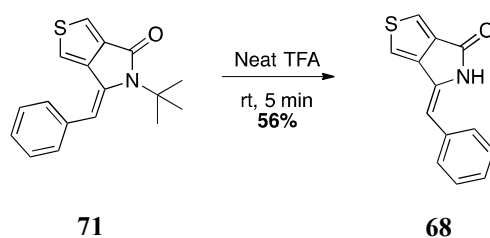
Scheme 2.27: Synthesis of lactams **67 and **68** from alkyne **66****

Alkyne **67** was accessed from commercially available 4-bromothiophene-3-carboxamide via a Sonogashira cross-coupling reaction. Cyclization of alkyne **67** was accomplished using TBAF (Scheme 2.27). The reaction took about 1 week to achieve completion at 45 °C. Increasing the temperature to reflux decreased the reaction time to 2 days. The cyclization of alkyne **67** resulted in both cyclization products, lactams **68** and **69**, in a 45:55 ratio.



Scheme 2.28: Synthesis of thienopyrrolone 71 from alkyne 70

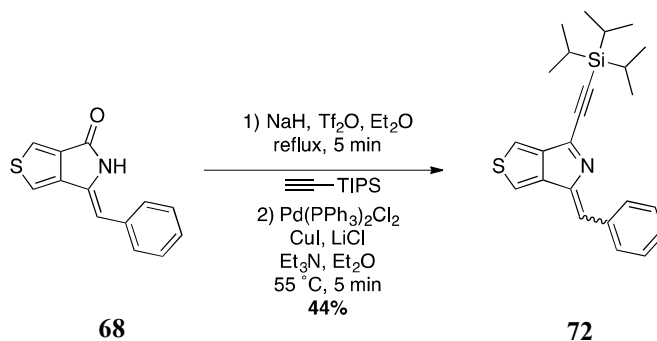
To optimize the synthesis of triflate **50**, I hypothesized we could again employ the *tert*-butyl protecting group on the nitrogen atom to encourage favourability for the 5-*exo*-*dig* product. Alkyne **70** was therefore synthesized in two steps from commercially available 4-bromothiophene-3-carboxylic acid (see Chapter 4: Experimental). Initially, the cyclization of alkyne **70** took 6 days to complete at reflux (Scheme 2.28). This reaction time was decreased to 5 minutes by increasing the equivalence of TBAF from 3 to 6. Fortunately, desired thienopyrrolone **71** was the sole product with a yield of 88%, requiring no further purification.



Scheme 2.29: Synthesis of lactam 68 from thienopyrrolone 71

With thienopyrrolone **71** in hand, the next step was to remove the *tert*-butyl group, which was accomplished by employing neat trifluoroacetic acid (TFA).⁹¹ Lactam **68** was obtained after work-up in a yield of 56% without the need for further purification.

2.10 Synthesis of Ene-Imine Derivatives from Lactam 68

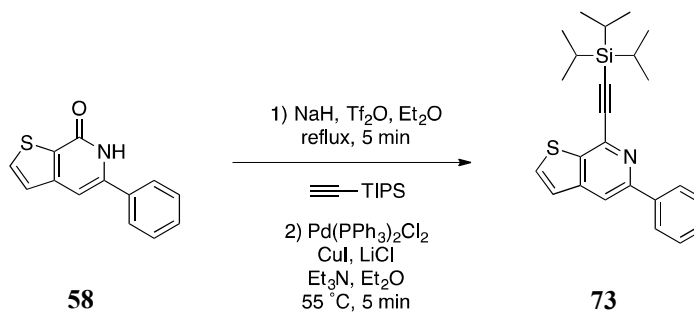


Scheme 2.30: Synthesis of thienopyrrole 72 from lactam 68

Triflate **50** was first synthesized from lactam **68** using the optimized triflation conditions, followed by Sonogashira cross-coupling, which consumed triflate **50** in under 5 minutes (Scheme 2.30). The crude reaction mixture was purified by column chromatography using deactivated silica gel, where thienopyrrole **72** was obtained as a mixture of isomers as a yellow oil in a yield of 44%.

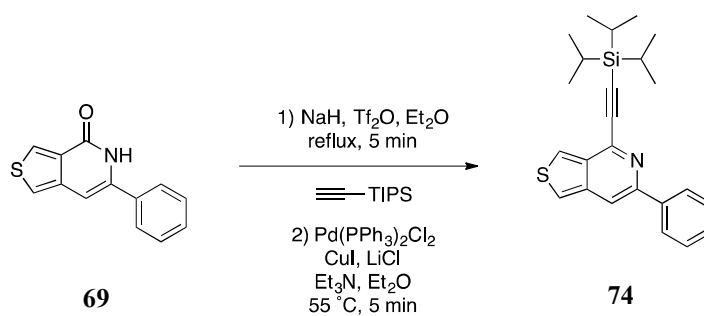
2.10 Synthesis of Thienopyridine Derivatives 73 and 74

Realizing the rarity of techniques to access thienopyridines, I wanted to attempt a coupling reaction on the 6-*endo-dig* products from the cyclization of thienyl alkynyl amides **52** and **67**.



Scheme 2.31: Synthesis of thienopyridine 73 from lactam 58

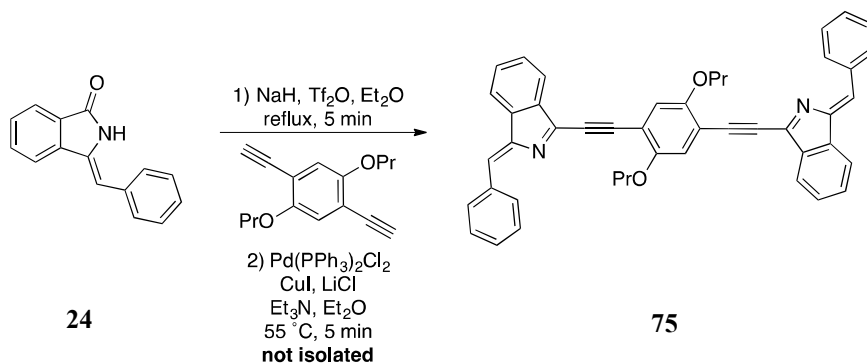
Thienopyridine derivatives, such as **73**, are studied for their pharmaceutical properties.⁹²⁻⁹³ With the interest in expanding the scope of my synthetic methodology, I decided to apply my triflation/cross coupling conditions to lactam **58** (Scheme 2.31). The triflation step proceeded smoothly, and the crude organic phase was then subjected to Sonogashira cross-coupling conditions to obtain thienopyridine **73** in a 53% yield.



Scheme 2.32: Synthesis of thienopyridine 74 from lactam 69

Further, lactam **69** was subjected to the same conditions to obtain thienopyridine **74** in a 58% yield (Scheme 2.32).

2.11 Synthesis of Isoindole Dimer 75



Scheme 2.33: Synthesis of dimer 75 from lactam 24

To further test the applicability of my building blocks in π -extended systems, I employed my synthetic approach to access isoindole dimer **75**. Despite unsuccessful isolation of dimer **75**, its structure was confirmed by X-ray crystallography (see Appendix E, page 187) and its chemical formula by HRMS. This result suggests that π -extended systems that feature the ene-imine motif could be accessed using this synthetic approach.

2.12 Conclusion

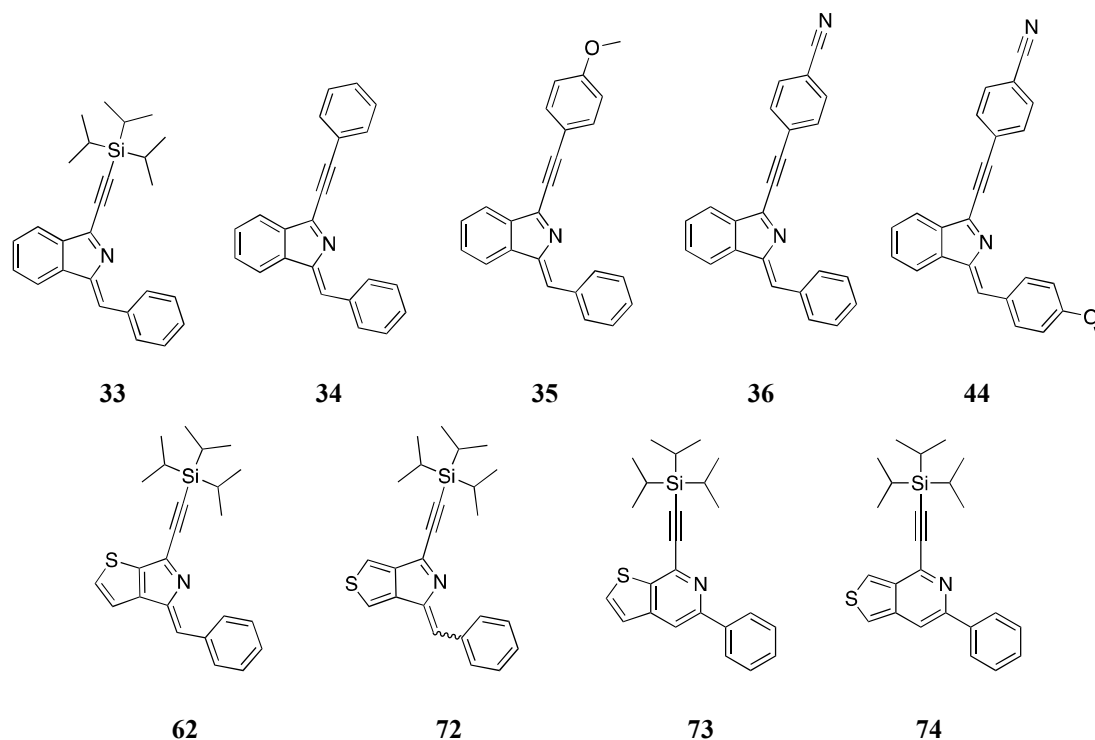


Figure 2.13: Ene-imine derivatives that were synthesized and isolated for this project

A synthetic pathway was developed that allowed access a variety of ene-imine derivatives. It was determined that although unstable, ene-imine triflates **32b**, **43**, **49** and **50** react quickly under Sonogashira conditions to enable the synthesis of ene-imine-yne derivatives **33-36**, **44**, **62** and **72** in yields of 21-49% over 2 steps (Figure 2.13).

Further, thienopyridines **73** and **74** were prepared using the developed synthetic approach in yields of 53 and 58%, respectively. This result is promising for accessing a variety of thienopyridine derivatives, which are important scaffolds in pharmaceuticals.⁹²⁻

2.13 Future work

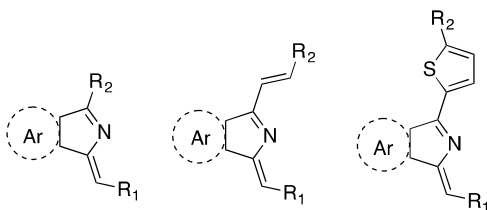
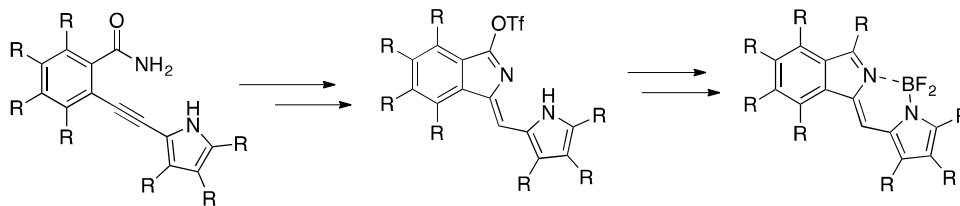


Figure 2.14: Possible ene-imine derivatives that could be accessed using the developed synthetic approach

The synthetic approach developed for this project can be applied to synthesize a broad arrangement of ene-imine derivatives, facilitating the incorporation of the ene-imine fragment into organic π -systems. Future work will involve the incorporation of different π -systems containing the ene-imine fragment using Heck, Stille and Suzuki reactions (Figure 2.14).



Scheme 2.34: Approach to functionalized BODIPY derivatives using my synthetic approach

With respect to BODIPY derivatives, the synthetic approach that I have developed could enable access to a wide variety of BODIPY derivatives using the synthetic pathway illustrated in Scheme 2.33, with the key advantage of incorporating a variety of alkynyl, alkenyl and aryl substituents via the triflate group.

Chapter 3: Optical and Crystallographic Analysis

3.1 Optical Properties

By employing the building block approach, the wavelengths at which a molecule absorbs light at can be systematically tuned by addition of substituents and extension of conjugation.²⁶⁻²⁷ This is a convenient method for investigating some of the structure-property relationships of organic molecules possessing discrete conjugation pathways. To evaluate the absorption properties of isoindoles **33-36**, **44**, thienopyrroles **62** and **72**, and thienopyridines **73** and **74**, UV-vis was employed. The UV-vis absorption spectra of all ene-imine derivatives were measured quantitatively in CHCl₃ solution.

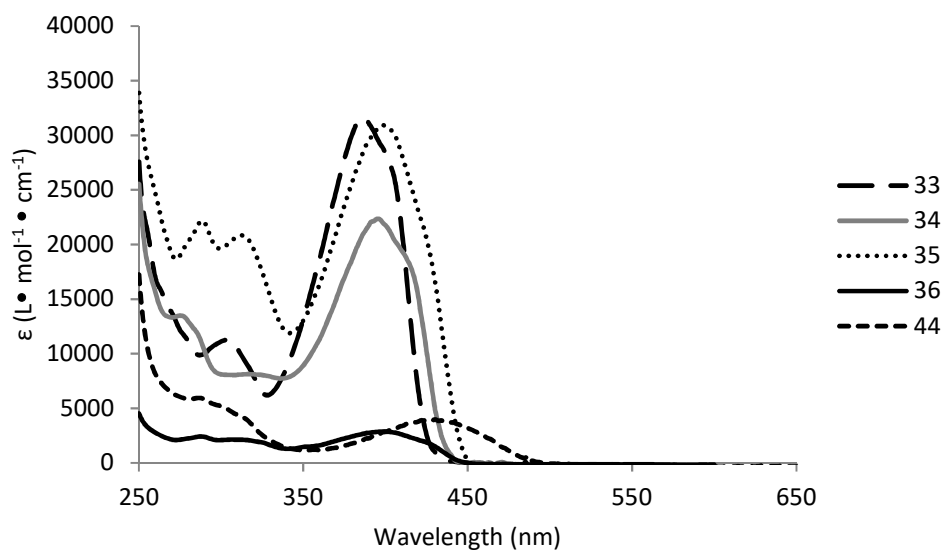
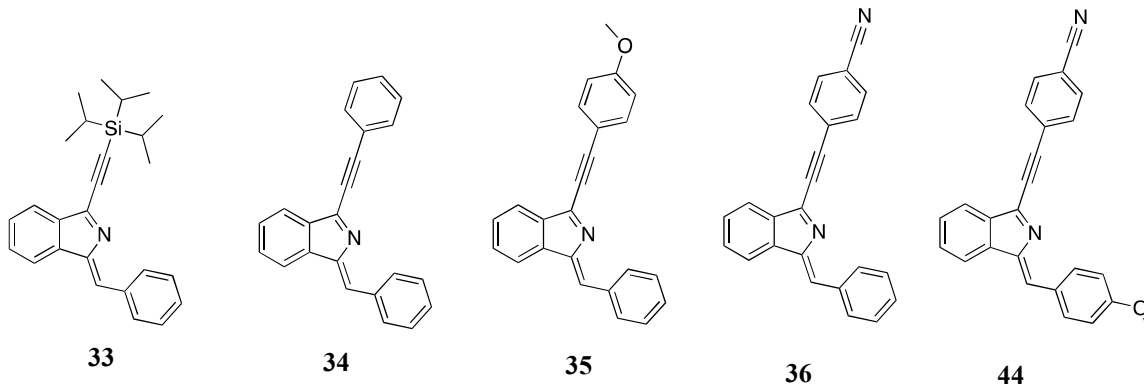


Figure 3.1: UV-vis spectra for isoindoles 33-36, 44



Isoindole **33** exhibited an absorbance maxima at approximately 387 nm (Figure 3.1). Replacing the TIPS group in isoindole **33** with a phenyl substituent resulted in a small bathochromic shift of 8 nm, with an absorbance maxima at approximately 395 nm for isoindole **34**. The addition of a methoxy group (isoindole **35**) and a cyano group (isoindole **36**) resulted in a bathochromic shift of 4 nm in comparison to isoindole **34**, with an absorption maxima of 399 nm for both isoindole **35** and **36**. Isoindole **44** has an absorbance maxima at 287 nm, with a slightly weaker absorbance at 430 nm, which is

bathochromically shifted by 31 nm when compared to isoindoles **35** and **36**. This significant bathochromic shift can be attributed to the push-pull system possessed by isoindoles **44**, which is consistent with literature.⁸⁷ We can conclude that the structural differences between isoindoles **33-36** resulted in small shifts in their UV-vis absorption profile, and the push-pull motif of isoindole **44** had a significant influence on the optical properties.

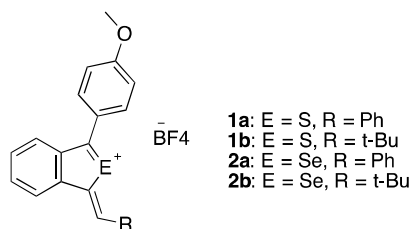


Figure 3.2: Structure for *1H*-benzo[c]thio- and *1H*-benzo[c]selenophen-2-ium tetrafluoroborates

These subtle shifts in the absorption maxima are consistent with data reported in literature for π -conjugated systems featuring motifs similar to the ene-imine pathway.³⁻⁴ For example, a series of *1H*-benzo[c]thio- and *1H*-benzo[c]selenophen-2-ium tetrafluoroborates were synthesized by Nagahora *et al.* (Figure 3.2).⁴ Substitution of the phenyl group for a *t*-Bu group resulted in a bathochromic shift of only 7 nm for sulfur derivatives **80-81**, and 17 nm for selenium derivatives **82-83**.

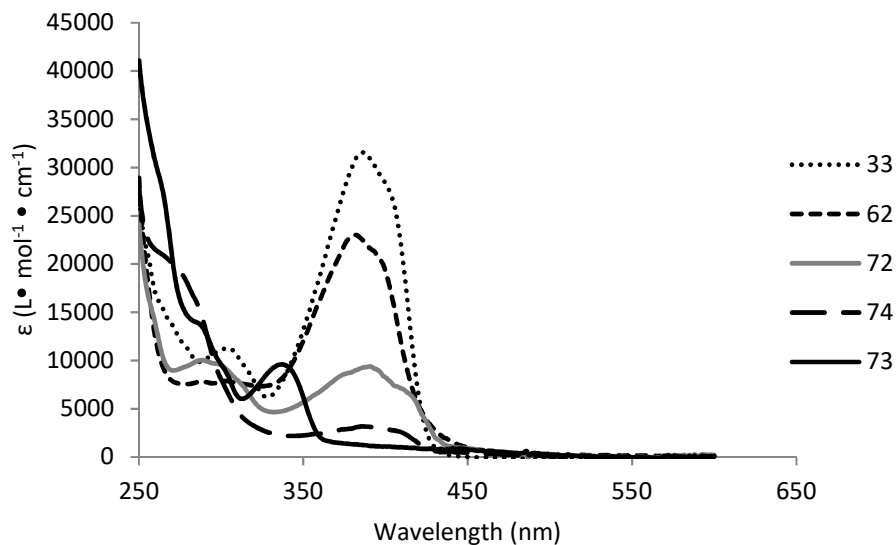
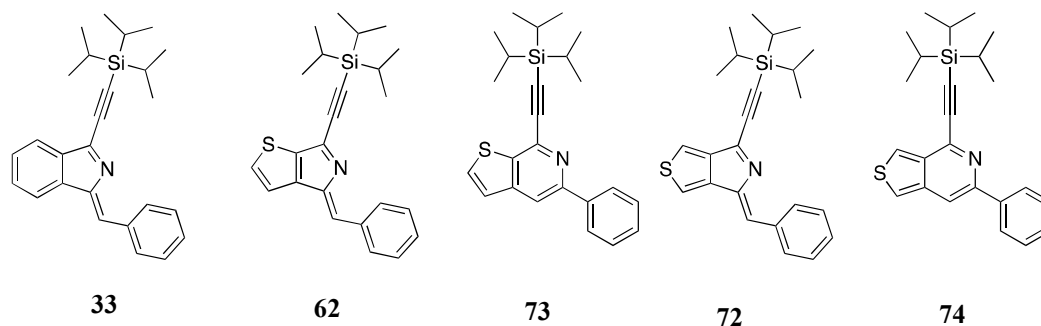


Figure 3.3 UV-vis spectra for isoindole **33**, thienopyrroles **62**, **72** and thienopyridines **73**, **74**.



To systematically investigate the influence of the fused backbone on the optical properties of these ene-imine derivatives, thienyl derivatives **62** and **72** were compared with TIPS substituted isoindole **33** (Figure 3.3). Replacing the phenyl group with a 2,3-substituted thienyl group resulted in a 5 nm hypsochromic shift, with an absorption maxima of 382 nm for thienopyrrole **62**. Thienopyrrole **72** has an absorbance maximum at 288 nm, with a weaker absorbance at 390 nm, which is a 3 nm red shift compared to isoindole **33**.

To compare the influence of ring size on the optical properties of these compounds, thienopyridine **73** can be compared with thienopyrrole **62**. Thienopyridine **73** has an absorbance maxima of 337 nm, which is a significant hypsochromic shift of 45 nm when compared to the maximum absorbance of thienopyrrole **62** (382 nm). Similarly, thienopyridine **74** can be compared with thienopyrrole **72**. Thienopyridine **74** has an absorbance maxima at 386 nm, which is a hypsochromic shift of 4 nm when compared to the weaker absorbance possessed by thienopyrrole **72** (390 nm). Based on this result, it is reasonable to conclude that the ene-imine motif offers a greater degree of π -conjugation when compared to the π -systems of thienopyridines **73** and **74**. The extinction coefficients for thienopyridines **73** and **74**, as well as thienopyrrole **72**, are significantly lower in intensity than isoindole **33** and thienopyrrole **62**.

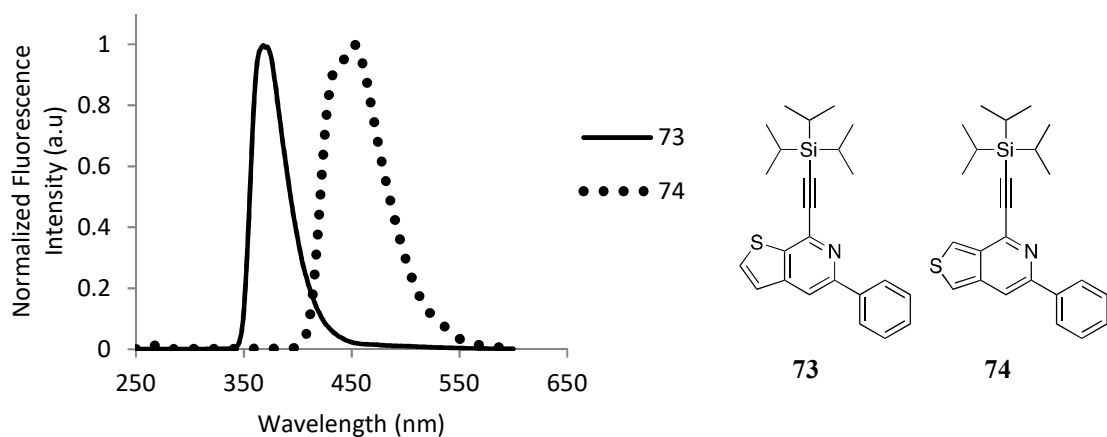


Figure 3.4: Fluorescence spectra for thienopyridines **73 and **74**.**

Among the compounds fully characterized and isolated, thienopyridines **73** and **74** were the only two that possessed fluorescent properties. Thienopyridine **73** has an emission maxima at 370 nm with a Stokes shift of 33 nm. Thienopyridine **74** has an emission maxima of 452 nm with a Stokes shift of 66 nm. This result demonstrates

changing the position of the sulfur heteroatom has a significant impact on the optical properties of these thienopyridine derivatives.

3.2 Crystallographic Analysis

To analyze the solid-state structure of the compounds synthesized for this project, single crystal growth was attempted. Crystals suitable for crystal structure analysis were successfully obtained for 3 classes of compounds: thienopyrrole **51**, isoindoles **34**, **36** and isoindole dimer **75**.

3.2.1 Crystal Analysis for Thienopyrrole **51**

Thienopyrrole **51** was grown via vapour diffusion (EtOAc/Hexanes) at room temperature to form yellow crystals. A summary of all the bond lengths and angles can be found in Appendix B.

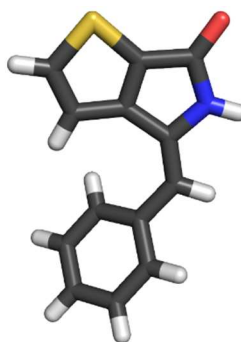


Figure 3.5: Crystal structure for thienopyrrole **51**

The fused thiophene and lactam rings are planar, although due to steric crowding the appended phenyl ring is twisted from the plane of the thienopyrrole core by a dihedral angle of 35° (Figure 3.5). The crystal structure confirms that thienopyrrole **51** is isolated as the E isomer, which is consistent with NMR analysis (see Chapter 4: Experimental).

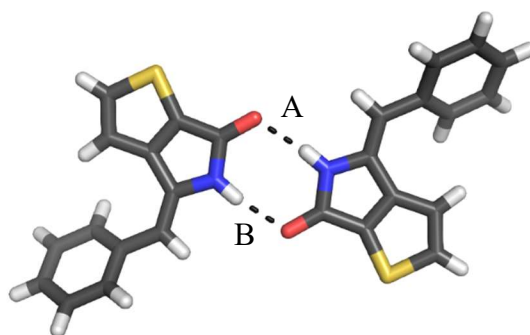


Figure 3.6: Hydrogen bonding interaction between the lactam moieties in thienopyrrole 51

Intermolecularly, the lactam moieties undergo a hydrogen bonding interaction, forming a thienopyrrole N-H $\cdots$ O=C dimer (Figure 3.6). With respect to the nitrogen and oxygen atom involved in these bonding interactions, the distances found between them was approximately 2.8 Å, which is less than the sum of the vdW radii (3.22 Å).⁹⁴ This hydrogen bonding interaction is observed in similar 5-membered lactam motifs, such as in diketopyrrolopyrrole systems,⁹⁵ and is an important feature in self-assembly in the solid state.

3.2.2 Crystal Analysis for Isoindoles 34 & 36

Isoindole **34** was grown via vapour diffusion (EtOAc/Hexanes) at room temperature to form black crystals. A summary of all the bond lengths and angles can be found in Appendix C.

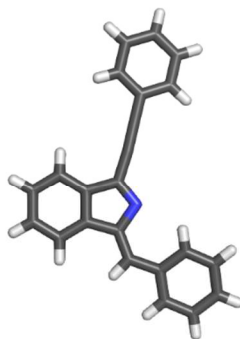


Figure 3.7: Crystal structure for isoindole **34**

The crystal structure of isoindole **34** shows near planarity through the entire structure from the phenyl-pyrrole backbone to the attached phenyl moieties, which are twisted with respect to the isoindole backbone by only 6.4°-7.4°, indicating that there is communication across the entire molecule (Figure 3.7). The crystal structure also confirms that isoindole **34** is isolated as the Z isomer, which is consistent with NMR experiments (see Chapter 4: Experimental).

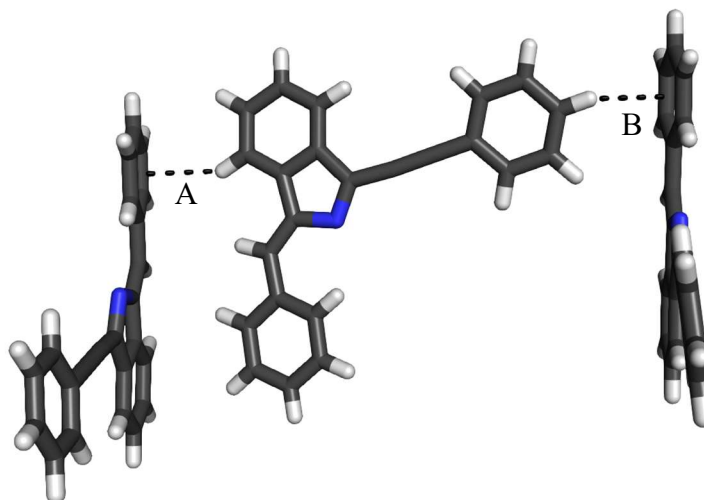


Figure 3.8: Crystal structure for isoindole 34 showing weak C-H $\cdots$ π interactions

As illustrated in Figure 3.8, isoindole **34** units are organized in a perpendicular fashion with respect to one another. The phenyl groups attached to the exocyclic alkenes act as hydrogen bond acceptors with respect to the aryl proton donors indicated by interactions A and B (Figure 3.8). The C-H $\cdots$ π interactions A and B have angles of 147° and 160° , respectively. The bond lengths for interactions A and B are both approximately $2.80 \text{ \AA}$, which is less than the sum of the vdW radii.⁹⁴ According to literature,⁸ these interactions can be classified as weak C-H $\cdots$ π hydrogen bonds. The perpendicular stacking motif of isoindole **34** prevents sufficient space required for π - π stacking to occur.⁹⁶

Isoindole **36** was grown via vapour diffusion (EtOAc/Hexanes) at room temperature to form yellow crystals. A summary of all the bond lengths and angles can be found in Appendix D.

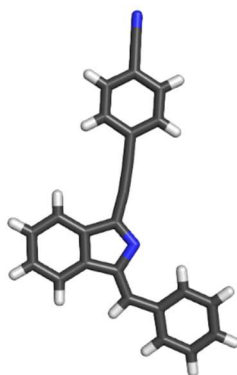


Figure 3.9: Crystal structure for isoindole 36

The crystal structure of isoindole **36** again shows planarity throughout the phenyl-pyrrole backbone (Figure 3.9). Similar to isoindole **34**, the alkynyl and alkenyl phenyl substituents are twisted out of planarity by only 4.2° and 6.0° , respectively, indicating that there is communication across the entire molecule in the solid state. The crystal structure also indicates that isoindole **36** is the Z isomer in the solid state.



Figure 3.10: Stacking motif of isoindole 36 in the solid state

In contrast to isoindole **34**, the units of cyano-substituted isoindole **36** are stacked parallel to one another. Illustrated in Figure 3.10, the molecules are arranged in a slip-

stacked arrangement, with no pi-pi stacking observed. The distances indicated by the dotted lines between layers range from 3.326 – 3.394 Å between the carbon atoms.

3.2.3 Crystal Analysis for Dimer 75

Isoindole dimer **75** was synthesized to access π -conjugated molecules containing more than one ene-imine motif. Despite unsuccessful isolation, a crystal structure for isoindole dimer **75** was grown via vapour diffusion (EtOAc/Hexanes) at room temperature, forming red crystals. A summary of all the bond lengths and angles can be found in Appendix E.

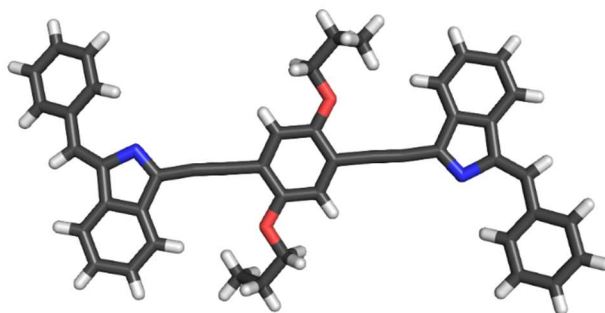


Figure 3.11: Crystal structure for isoindole dimer 75

The crystal structure for isoindole dimer **75** shows the extended planarity of the structure, indicating electronic communication between the two terminal isoindole units via the central phenyl group (Figure 3.11). The dipropoxyphenyl bridge between the two isoindole units is twisted by only 10° - 12°. Further, the alkenyl phenyl substituents are twisted by 10° - 12° with respect to the isoindole units. The crystal structure also confirms that both exocyclic alkenes are in their Z form.

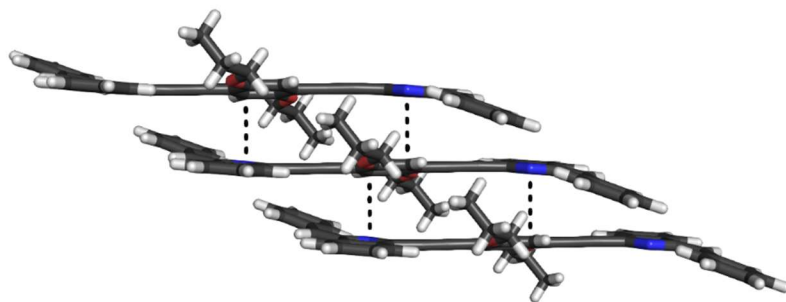


Figure 3.12: Crystal structure of isoindole dimer 75 showing stacking interactions

Illustrated in Figure 3.12, the molecules are closely packed to one another, with an intermolecular distance of 3.229 - 3.245 Å. The molecules are arranged in a slip-stacked pattern, with no π - π stacking observed (Figure 3.12).

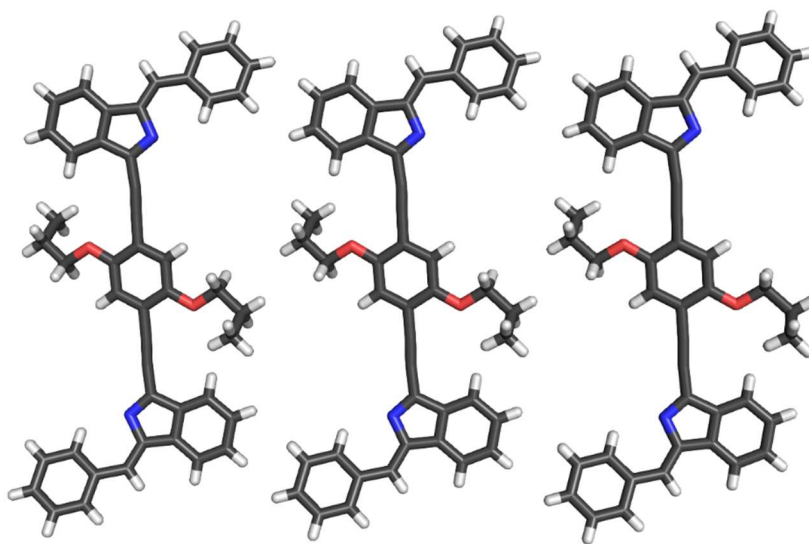


Figure 3.13: Adjacent stacks are stabilized by aggregation of the propyl groups

Illustrated in Figure 3.13, there are no significant interactions between the stacks illustrated in Figure 3.13. However, a hydrophobic effect is observed between the stacks from the propyl groups of the propoxy substituents.

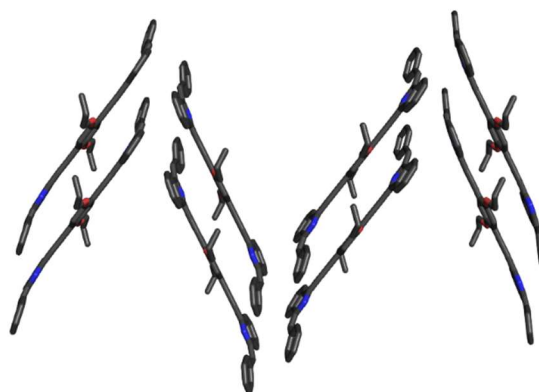


Figure 3.14: The stacks of isoindole dimer 75 are oriented in a herringbone packing arrangement

Illustrated in Figure 3.14 are rows of stacks represented in Figure 3.12. The hydrogens have been omitted for clarity. These rows of stacks are oriented in a herringbone pattern, which is a common packing motif adopted by π -conjugated organic materials.⁹⁷

In summary, four crystal structures featuring different packing motifs were obtained. The hydrogen bonding interaction between the lactam moieties in thienopyrrole **51** enabled the formation of dimers in the solid state, which can assist in self-assembly in related structures.⁹⁵ The small structural difference between isoindole **34** and **36**, the cyano substituent, influenced the packing pattern of the two molecules. Dimer **75** was found to pack in a herringbone arrangement. However, none of these compounds seem to exhibit any π -stacking interactions in the solid state, due to the slip-stacked nature of their packing motifs.

Chapter 4: Experimental

4.1 General Information

All commercially available reagents were purchased and used as received. All solvents were dried using a Grubbs apparatus prior to use. Tetrabutylammonium fluoride (TBAF) was used at a 1.0 mol/L concentration in tetrahydrofuran (THF). Sodium hydride (NaH) was used at a 60% dispersion in mineral oil. Trifluoromethanesulfonic anhydride (Tf₂O) was used at a 1.0 mol/L concentration in dichloromethane (DCM). Sonogashira-Hagihara and triflation reactions were performed under N₂. All other reactions were performed in air. TLC analysis was performed on glass-backed plates (60Å) and flash chromatography was performed on ultra-pure flash silica (230-400 mesh size). When appropriate, silica was deactivated by adding triethylamine (3% by volume) to the appropriate eluent and stirring with silica at rt for 30 minutes prior to being used for column chromatography. NMR spectra were recorded using a Varian Inova 300 MHz (¹H: 299.838 MHz, ¹³C: 75.402 MHz) or Varian Unity 400 MHz spectrometer (¹H: 399.945 MHz, ¹³C: 100.577 MHz) with CDCl₃ referenced at 7.26 ppm (¹H) or 77.16 ppm (¹³C). X-ray diffraction data sets for compounds **51**, **34**, **36**, and **75** were collected on a Bruker AXS P4/SMART 1000 diffractometer. IR spectra were recorded using KBr discs on a Nicolet Nexus 470 FTIR spectrometer. UV-Visible spectra were recorded on an Agilent 8453 spectrophotometer in CHCl₃. Fluorescence measurements were carried out using an Agilent Cary Eclipse Fluorescence Spectrophotometer in CHCl₃. High-resolution mass spectra were recorded on a Bruker Daltonics spectrometer using Electrospray Ionization (ESI). Isomer determination was conducted by NOESY.

4.2 Experimental Procedures

General procedure for Sonogashira-Hagihara reactions for iodo substrates (A).

Used to access compounds **78**, **25**, and **41**. One equiv. of aryl iodide was dissolved in a 3:1 mixture of anhydrous THF:Et₃N. Pd(PPh₃)₂Cl₂ (6-8 mol%) and CuI (6-8 mol%) were then added, and the solution was simultaneously degassed with nitrogen and heated to 55°C. The terminal acetylene (2.5 equiv.) was then added to the solution, and the reaction was allowed to stir at 55 °C until TLC or ¹H NMR analysis indicated reaction completion. Saturated NH₄Cl_(aq) was added to the solution, and the organic phase was extracted with EtOAc, dried over MgSO₄, filtered and solvent was removed under reduced pressure. The crude product was purified by column chromatography.

General procedure for Sonogashira-Hagihara reactions for bromo substrates (B)

Used to access compounds **52**, **59**, **67**, and **70**. One equiv. of aryl bromide was dissolved in a 1:1 mixture of anhydrous DMF:diisopropylamine. Pd(PPh₃)₂Cl₂ (8 mol%) and CuI (8 mol%) were then added, and the solution was degassed with nitrogen and heated to 90°C. The terminal acetylene (2.5 equiv.) was then added to the solution, and the reaction was allowed to stir at 90 °C until TLC or ¹HNMR analysis indicated reaction completion (5-12 hrs). Saturated NH₄Cl_(aq) was added to the solution, and the organic phase was extracted with EtOAc, dried over MgSO₄, filtered, and solvent was removed under reduced pressure. The crude product was purified by column chromatography.

General procedure for cyclization reactions (C)

Used to access compounds **24**, **42**, **58**, **60**, **69** and **71**. One equiv. of alkynyl amide was dissolved in anhydrous THF at rt. The solution was heated to the desired temperature. Tetrabutylammonium fluoride (1.1-3 equiv) was added and the reaction was allowed to stir at the corresponding temperature until TLC analysis indicated reaction completion (5 min- 12 hrs). Saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ was added to the solution, and the organic phase was extracted with Et_2O , dried over MgSO_4 , and filtered. The solvent was removed under reduced pressure. No further purification was necessary.

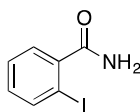
General procedure for removal of tert-butyl groups (D)

Used to access compounds **51** and **68**. One equiv. of *tert*-butyl protected thienopyrrolone was dissolved in neat TFA at rt. The solution was stirred until TLC analysis indicated reaction completion. CHCl_3 was added to the solution, where saturated NaHCO_3 was added until the evolution of CO_2 gas subsided. The organic phase was dried over MgSO_4 , filtered, and solvent removed under reduced pressure. No further purification was necessary.

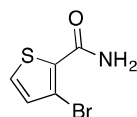
General procedure for triflation-Sonogashira-Hagihara coupling sequence (E)

Used to access compounds **33-36**, **44**, **62**, **72-75**. Anhydrous Et_2O was brought to reflux, followed by addition of one equiv. of lactam. NaH (2 equiv.) was added, followed by immediate addition of Tf_2O (1.5 equiv.). The reaction was monitored by TLC until no further conversion to triflate was observed (about 3 minutes). The reaction mixture was then extracted with Et_2O , washed with saturated $\text{NaCl}_{(\text{aq})}$, dried over MgSO_4 , and filtered directly into a two-neck flask containing Et_3N . $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.06 equiv.), CuI (0.06 equiv.), and LiCl (3 equiv.) were then added. The solution was degassed with N_2 and

heated to 55 °C. The appropriate acetylene (2.5 equiv.) was then added and the reaction was monitored by TLC analysis until all aryl triflate was consumed. Saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ was added to the solution, and the organic phase was extracted with EtOAc, dried over MgSO_4 , filtered, and solvent removed under reduced pressure. The crude product was purified by column chromatography.

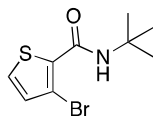


2-iodobenzamide 26 2-iodobenzoic acid (1.00 g, 4.03 mmol) was added to excess SOCl_2 (10.0 mL) at rt. The solution was heated to reflux and the reaction was stirred for 3 hours. Excess SOCl_2 was removed and solid residue was dissolved with anhydrous DCM (180 mL). Ammonia gas was then bubbled through the solution at rt for 20 minutes. The contents of the reaction flask were then concentrated under reduced pressure, followed by vacuum filtration using distilled H_2O to obtain a white solid (0.936 g, 94%). The ^1H and ^{13}C NMR spectra agreed with literature reports.⁹⁸

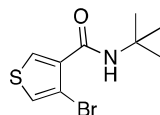


3-bromothiophene-2-carboxamide 53 3-bromothiophene-2-carboxylic acid (1.00 g, 4.83 mmol) was added to excess SOCl_2 (10 mL) at rt. The solution was heated to reflux and the reaction was stirred for 3 hours. Excess SOCl_2 was removed and the solid residue was dissolved with anhydrous DCM (180 mL). Ammonia gas was then bubbled through

the solution at rt for 20 minutes. Saturated NH_4Cl was added to the solution, and the organic phase was extracted with DCM, dried over MgSO_4 , filtered, and concentrated under reduced pressure to obtain a white solid (0.955 g, 97%). The ^1H and ^{13}C NMR spectra agreed with literature reports.⁹⁹

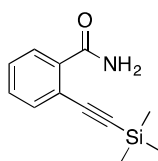


3-bromo-*N*-(*tert*-butyl)thiophene-2-carboxamide 76 3-bromothiophene-2-carboxylic acid (1.00 g, 4.83 mmol) was added to excess SOCl_2 (10 mL) at rt. The solution was heated to reflux and the reaction was stirred for 3 hours. Excess SOCl_2 was evaporated using N_2 gas. The solid residue was dissolved with anhydrous DCM (180 mL). *tert*-Butylamine (1.52 mL, 14.5 mmol) was added to the reaction at rt and the reaction was stirred overnight at rt. Saturated NH_4Cl was added to the reaction, and the organic phase was extracted with DCM, dried over MgSO_4 , filtered, and concentrated under reduced pressure to obtain an off white solid (1.19 g, 94%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰⁰

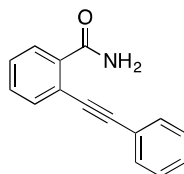


4-bromo-*N*-(*tert*-butyl)thiophene-3-carboxamide 77 4-bromothiophene-3-carboxylic acid (1.00 g, 4.83 mmol) was added to excess SOCl_2 (10 mL) at rt. The solution was heated to reflux and the reaction was stirred for 3 hours. Excess SOCl_2 was evaporated using N_2 gas. The solid residue was dissolved with anhydrous DCM (180 mL). *Tert*-butyl

amine (3.04 mL, 28.9 mmol) was added to the reaction at room temperature and the reaction was stirred overnight at room temperature. Saturated NH_4Cl was added to the reaction, and the organic phase was extracted with DCM, dried over MgSO_4 , filtered, and concentrated under reduced pressure to obtain an off white solid (1.24 g, 98%). Mp: 71 - 73 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.99 (d, J = 3.6 Hz, 1H), 7.30 (d, J = 3.6 Hz), 6.52 (b, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 161.0, 137.1, 131.5, 125.4, 107.2, 52.1, 29.0; IR (film, KBr) 3295, 3104, 2967, 2926, 1648, 1540 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_9\text{H}_{12}\text{NBrNaOS}$ $[\text{M} + \text{Na}]^+$: 283.9715, found 283.9705.

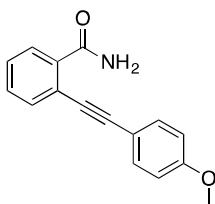


2-((trimethylsilyl)ethynyl)benzamide 78 Prepared according to general procedure A using amide **26** (0.200 g, 0.810 mmol), THF (10.0 mL), Et_3N (2.5 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.0341 g, 0.0486 mmol), CuI (0.0092 g, 0.0485 mmol) and trimethylsilylacetylene (0.29 mL, 2.03 mmol). The crude product was purified by column chromatography (2:3 EtOAc:Hexanes, v/v) on silica gel to obtain a beige solid (0.132 g, 75%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰¹

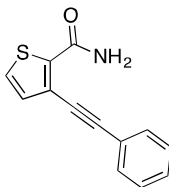


2-(phenylethynyl)benzamide 25 Prepared according to general procedure A using amide **26** (0.200mg, 0.810 mmol), THF (10 mL), Et_3N (2.50 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.0341 g,

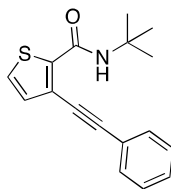
0.0485 mmol), CuI (0.0092 g, 0.0486 mmol) and phenylacetylene (0.22 mL, 2.025 mmol). The crude product was purified by column chromatography (1:1 EtOAc:Hexanes, v/v) on silica gel to obtain a white solid (0.157 g, 88%). The ^1H and ^{13}C NMR spectra agreed with literature reports.⁶⁸



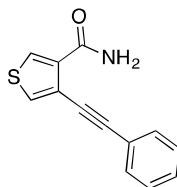
2-((4-methoxy)ethynyl)benzamide 41 Prepared according to general procedure A using amide **26** (0.140 g, 0.567 mmol), THF (30 mL), Et₃N (10 mL), Pd(PPh₃)₂Cl₂ (0.0456 g, 0.0340 mmol), CuI (0.0086 g, 0.0456 mmol) and 1-ethynyl-4-methoxybenzene (0.187 g, 1.42 mmol). The crude product was purified by column chromatography (3:2 EtOAc:Hexanes, v/v) on silica gel to obtain a light yellow solid (0.098 g, 69%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰²



3-(phenylethynyl)thiophene-2-carboxamide 52 Prepared according to general procedure B using **53** (0.750 g, 3.64 mmol), DMF (20 mL), diisopropylamine (20 mL), Pd(PPh₃)₂Cl₂ (0.204 g, 0.291 mmol), CuI (0.0554 g, 0.291 mmol) and phenylacetylene (1.00 mL, 9.11 mmol). The crude product was purified by column chromatography (2:3 EtOAc:Hexanes, v/v) on silica gel to obtain a yellow solid (0.570 g, 76%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰³

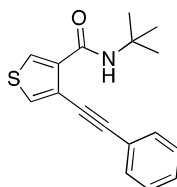


N*-(*tert*-butyl)-3-(phenylethynyl)thiophene-2-carboxamide **59* Prepared according to general procedure B using **75** (1.00 g, 3.81 mmol), DMF (20 mL), diisopropylamine (20 mL), Pd(PPh₃)₂Cl₂ (0.214 g, 0.305 mmol), CuI (0.0580 g, 0.305 mmol) and phenylacetylene (1 mL, 9.56 mmol). The crude product was purified by column chromatography (1:5 EtOAc:Hexanes, v/v) to obtain an orange solid (0.822 g, 76%). Mp: 96-97 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.55-7.52 (m, 2H), 7.47 (b, 1H), 7.42-7.38 (m, 3H), 7.40 (d, *J* = 5.2 Hz, 1H), 7.17 (d, *J* = 5.2 Hz, 1H), 1.45 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 160.5, 143.5, 131.7, 131.7, 129.5, 128.8, 128.8, 121.9, 119.2, 96.0, 83.6, 51.9, 29.1; IR (film, KBr) 3386, 2964, 2928, 2205, 1652, 1534 cm⁻¹; HRMS (ESI⁺): *m/z* calculated for C₁₇H₁₇NNaOS [M + Na]⁺: 306.0923, found 306.0914.

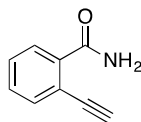


4-(phenylethynyl)thiophene-3-carboxamide **67** Prepared according to general procedure B using **66** (0.750 g, 3.64 mmol), DMF (20 mL), diisopropylamine (20 mL), Pd(PPh₃)₂Cl₂ (0.204 g, 0.291 mmol), CuI (0.0553 g, 0.291 mmol) and phenylacetylene (1 mL, 9.10 mmol). The crude product was purified by column chromatography (2:3 EtOAc:Hexanes, v/v) to obtain an off-white solid (0.500 g, 60%). Mp: 143-144 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.24 (d, *J* = 3.56 Hz, 1H), 7.61 (d, *J* = 3.52 Hz, 1H), 7.53-7.50 (m, 2H), 7.43-7.36 (m, 4H), 5.95 (b, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 163.5,

136.1, 133.3, 131.7, 131.6, 129.4, 128.8, 121.9, 119.4, 93.7, 83.4; IR (film, KBr) 3431, 3106, 1665, 1605 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_{13}\text{H}_9\text{NNaOS}$ [$\text{M} + \text{Na}$]⁺: 250.0297, found 250.0294.

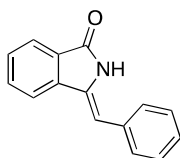


N-(tert-butyl)-4-(phenylethynyl)thiophene-3-carboxamide 70 Prepared according to general procedure B using **76** (1.50 g, 5.72 mmol), DMF (20 mL), diisopropylamine (20 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.321 g, 0.458 mmol), CuI (0.0870 g, 0.457 mmol) and phenylacetylene (1.58 mL, 14.3 mmol). The crude product was purified by column chromatography (1:5 EtOAc:Hexanes, v/v) on silica gel to obtain an orange oil (1.18 g, 73%). ^1H NMR (400 MHz, CDCl_3): δ 8.15 (d, $J = 3.6$ Hz, 1H), 7.58 (d, $J = 3.6$ Hz, 1H), 7.54-7.52 (m, 2H), 7.41-7.37 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 161.1, 137.9, 131.8, 131.7, 131.6, 129.3, 128.8, 122.0, 118.7, 93.7, 83.5, 51.6, 29.1; IR (film, KBr) 3389, 3107, 2965, 1660, 1538 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_{17}\text{H}_{17}\text{NNaOS}$ [$\text{M} + \text{Na}$]⁺: 306.0923, found 306.0919.

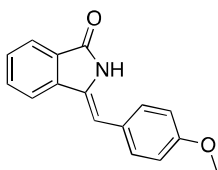


2-ethynylbenzamide 79 2-((trimethylsilyl)ethynyl)benzamide (0.150 g, 0.690 mmol) was dissolved in 20:1 THF/ H_2O and cooled to 0 °C. TBAF (0.829 mL, 0.829 mmol) was added to the solution. The reaction mixture was stirred at 0°C until TLC analysis

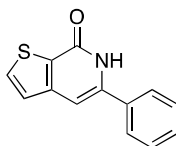
indicated reaction completion (2-5 minutes). Saturated NH_4Cl was added to the solution, and the organic phase was extracted with Et_2O , dried over MgSO_4 , and filtered. Solvent was removed under reduced pressure to obtain a yellow solid (0.0802 g, 80%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰¹



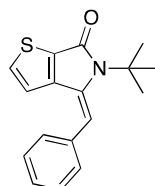
(Z)-3-benzylideneisoindolin-1-one 24 Prepared according to general procedure C using **25** (0.100 g, 0.452 mmol), TBAF (0.5 mL, 0.500 mmol), and anhydrous THF (10 mL). Obtained as a yellow solid (0.080 g, 80%). The ^1H and ^{13}C NMR spectra agreed with literature reports.⁶⁸



(Z)-3-(4-methoxybenzylidene)isoindolin-1-one 42 Prepared according to general procedure C using **41** (0.140 g, 0.567 mmol), THF (30 mL), Et_3N (10 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.0456 g, 0.0340 mmol), CuI (0.0086 g, 0.0456 mmol) and 1-ethynyl-4-methoxybenzene (0.187 g, 1.42 mmol). The crude product was purified by column chromatography (3:2 $\text{EtOAc}:\text{Hexanes}$, v/v) on silica gel to obtain a light yellow solid (0.098 g, 69%). The ^1H and ^{13}C NMR spectra agreed with literature reports¹⁰²

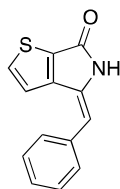


5-phenylthieno[2,3-c]pyridin-7(6H)-one 58 Prepared according to general procedure C using **52** (0.500 g, 2.20 mmol), TBAF (2.63 mL, 2.63 mmol), and anhydrous THF (50 mL). Obtained as a yellow solid (0.299 g, 60%). The ^1H and ^{13}C NMR spectra agreed with literature reports.¹⁰³

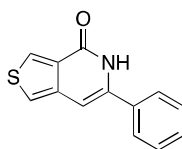


(E)-4-benzylidene-5-(tert-butyl)-4,5-dihydro-6H-thieno[2,3-c]pyrrol-6-one 60

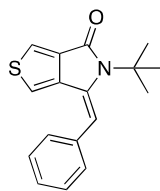
Prepared according to general procedure C using **59** (0.500 g, 1.76 mmol), TBAF (5.30 mL, 5.30 mmol), THF (105 mL). Obtained as a yellow solid (0.440 g, 88%). Mp: 135-137 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.43-7.34 (m, 5H), 7.26 (d, $J = 4.8$ Hz, 1H), 6.90 (s, 1H), 6.32 (d, $J = 4.8$ Hz, 1H), 1.82 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 163.7, 146.0, 136.4, 136.1, 135.7, 133.0, 129.9, 128.6, 127.9, 122.3, 114.2, 58.4, 30.9; IR (film, KBr) 3095, 3080, 2982, 2936, 1693, 1626, 1443, 1397 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_{17}\text{H}_{17}\text{NNaOS}$ [$\text{M} + \text{Na}$]⁺: 306.0923, found 306.0911.



(E)-4-benzylidene-4H-thieno[2,3-c]pyrrol-6(5H)-one 51 Prepared according to general procedure D using **60** (0.250 g, 0.882 mmol) and neat TFA (2 mL). Obtained as a yellow solid (0.166 g, 83%). Mp: 119-121 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.78 (b, 1H), 7.53 (dd, $J = 4.92$ Hz, 1 Hz, 1H), 7.48-7.33 (m, 5H), 7.06 (d, $J = 4.92$ Hz, 1H), 6.48 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 163.7, 146.4, 136.0, 135.1, 135.0, 132.5, 129.4, 128.7, 128.2, 122.0, 111.9; IR (film, KBr) 3211, 1686, 1447 cm^{-1} ; HRMS (ESI $^{+}$): m/z calculated for $\text{C}_{13}\text{H}_9\text{NNaOS}$ $[\text{M} + \text{Na}]^{+}$: 250.0297, found 250.0302.

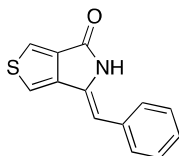


6-phenylthieno[3,4-c]pyridin-4(5H)-one 69 Prepared according to literature procedure C using **67** (0.300 g, 1.32 mmol), TBAF (1.5 mL, 1.50 mmol), THF (30 mL). Obtained as an off-white solid (0.086 g, 29%). Mp: 150-151 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.39 (dd, $J = 3.2$ Hz, 0.84 Hz, 1H), 8.32 (b, 1H), 7.60-7.57 (m, 2H), 7.51-7.43 (m, 3H), 7.41 (d, $J = 3.2$ Hz, 1H), 6.66 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 160.0, 139.2, 137.6, 134.9, 130.7, 129.5, 129.4, 129.0, 125.9, 118.1, 99.8; IR (film, KBr) 3173, 1654, 1648 cm^{-1} ; HRMS (ESI $^{+}$): m/z calculated for $\text{C}_{13}\text{H}_9\text{NNaOS}$ $[\text{M} + \text{Na}]^{+}$: 250.0297, found 250.0298.



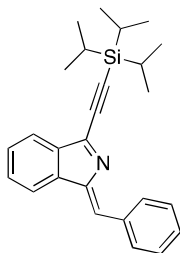
(E)-6-benzylidene-5-(tert-butyl)-5,6-dihydro-4H-thieno[3,4-c]pyrrol-4-one 71

Prepared according to general procedure C using **70** (0.525 g, 1.85 mmol), TBAF (11.1 mL, 11.1 mmol), and THF (200 mL). Obtained as a yellow solid (0.389 g, 75%). Mp: 135-137 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.58 (d, $J = 2.4$ Hz, 1H), 7.42-7.35 (m, 5H), 6.69 (s, 1H), 6.49 (d, $J = 2.4$ Hz, 1H), 1.81 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.9, 138.3, 137.7, 136.9, 134.7, 129.5, 128.9, 127.7, 121.3, 118.2, 112.0, 58.3, 30.4; Additional ^{13}C shifts from trace amounts of Z isomer: 145.9, 138.8, 128.7, 127.4, 122.0, 112.7, 110.5, 60.4, 29.3; IR (film, KBr) 2974, 1705, 1630, 1496 cm^{-1} ; HRMS (ESI $^{+}$): m/z calculated for $\text{C}_{17}\text{H}_{18}\text{NOS}$ $[\text{M} + \text{H}]^{+}$: 284.1104, found 284.1109.

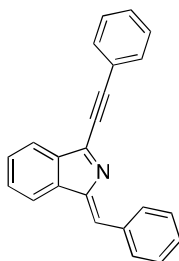


(Z)-6-benzylidene-5,6-dihydro-4H-thieno[3,4-c]pyrrol-4-one 68 Prepared according to general procedure D using **71** (0.200 g, 0.706 mmol) and neat TFA (1.50 mL). Obtained as a yellow solid (0.089 g, 56%). Mp: 153-155 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.92 (b, 1H), 7.82 (d, $J = 2.28$ Hz, 1H), 7.44 (d, $J = 2.28$ Hz, 1H), 7.42-7.39 (m, 2H), 7.37-7.34 (m, 2H), 7.31-7.27 (m, 1H), 6.28 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.9, 142.0, 135.4, 135.2, 129.6, 129.4, 128.2, 127.5, 123.6, 115.8, 104.8; IR (film, KBr) 3218,

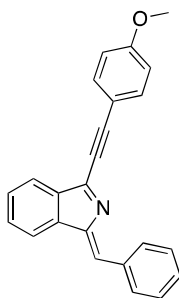
2923, 1700 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_{13}\text{H}_9\text{NOSNa}$ $[\text{M} + \text{Na}]^+$: 250.0297, found 250.0299.



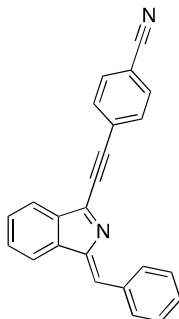
(Z)-1-benzylidene-3-((triisopropylsilyl)ethynyl)-1H-isoindole 33 Prepared according to general procedure E using **24** (0.0500 g, 0.226 mmol), NaH (0.0181 g, 0.452 mmol), TiF_2O (0.34 mL, 0.340 mmol), Et_2O (15 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.0096 g, 0.0140 mmol), CuI (0.0026 g, 0.0140 mmol), LiCl (0.0285 g, 0.672 mmol), triisopropylsilyl acetylene (0.13 mL, 0.566 mmol), and Et_3N (5 mL). The crude product was purified by column chromatography (Hexanes) on deactivated silica gel to obtain a yellow oil (0.0427 g, 49%). ^1H NMR (400 MHz, CDCl_3): δ 8.31-8.29 (m, 2H), 7.84-7.82 (m, 1H), 7.68-7.66 (m, 1H), 7.49-7.35 (m, 5H), 7.31 (s, 1H), 1.22 (s, 21H); ^{13}C NMR (100 MHz, CDCl_3): δ 155.0, 149.9, 141.2, 138.8, 135.5, 132.9, 129.9, 128.9, 128.9, 128.6, 128.0, 121.1, 119.6, 104.6, 101.1, 18.9, 11.4; IR (film, KBr) 2943, 2890, 2865, 1626, 1571, 1478, 1463 cm^{-1} ; HRMS (ESI⁺): m/z calculated for $\text{C}_{26}\text{H}_{32}\text{NSi}$ $[\text{M} + \text{H}]^+$: 386.2299, found 386.2297.



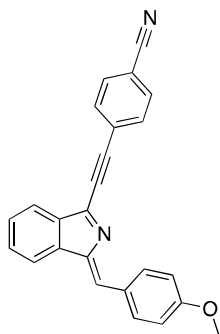
(Z)-1-benzylidene-3-(phenylethynyl)-1H-isoindole 34 Prepared according to general procedure E using **24** (0.0539 g, 0.244 mmol), NaH (0.0195 g, 0.487 mmol), Tf₂O (0.37 mL, 0.370 mmol), Et₂O (15 mL), Pd(PPh₃)₂Cl₂ (0.0103 g, 0.0147 mmol), CuI (0.0028 g, 0.0147 mmol), LiCl (0.0307 g, 0.724 mmol), phenylacetylene (0.1 mL, 0.912 mmol), and Et₃N (5 mL). The crude product was purified by column chromatography (1:8 EtOAc:Hexanes, v/v) on deactivated silica gel to obtain a yellow solid (0.0387 g, 52%). Mp: 124-126 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.34-8.31 (m, 2H), 7.87-7.85 (m, 1H), 7.80-7.77 (m, 1H), 7.74-7.72 (m, 2H), 7.52-7.36 (m, 8H), 7.34 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 155.1, 150.0, 141.3, 138.4, 135.5, 132.8, 132.7, 129.9, 129.9, 129.0, 128.9, 128.7, 128.3, 127.9, 122.0, 121.2, 119.6, 100.0, 84.6; IR (film, KBr) 2203, 1625, 1497 cm⁻¹; HRMS (ESI⁺): m/z calculated for C₂₃H₁₆N [M + H]⁺: 306.1277, found 306.1291.



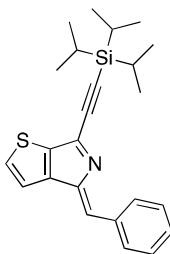
(Z)-1-benzylidene-3-((4-methoxyphenyl)ethynyl)-1H-isoindole 35 Prepared according to general procedure E using **24** (0.0250 g, 0.113 mmol), NaH (0.0091 g, 0.226 mmol), Tf₂O (0.17 mL, 0.17 mmol), Et₂O (10 mL), Pd(PPh₃)₂Cl₂ (0.0048 g, 0.0068 mmol), CuI (0.0013 g, 0.068 mmol), LiCl (0.0143 g, 0.337 mmol), 1-ethynyl-4-methoxybenzene (0.0374 g, 0.283 mmol), and Et₃N (5 mL). The crude product was purified by column chromatography (1:9 EtOAc:Hexanes, v/v) on deactivated silica gel to obtain a yellow solid (0.0091 g, 24%). Mp: 106-107 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.33-8.30 (m, 2H), 7.86-7.84 (m, 1H), 7.79-7.76 (m, 1H), 7.67 (d, *J* = 9.2 Hz, 2H), 7.51-7.43 (m, 4H), 7.39-7.35 (m, 1H), 7.31 (s, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 161.1, 155.3, 150.1, 141.3, 138.4, 135.6, 134.4, 132.7, 129.8, 128.9, 128.9, 127.9, 127.7, 121.2, 119.6, 114.4, 114.0, 100.8, 83.9, 55.6; IR (film, KBr) 2197, 1625, 1603, 1514 cm⁻¹; HRMS (ESI⁺): *m/z* calculated for C₂₄H₁₈NO [M + H]⁺: 336.1383, found 336.1392.



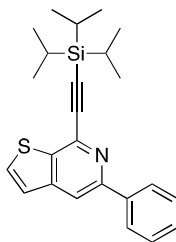
(Z)-4-((1-benzylidene-1H-isoindol-3-yl)ethynyl)benzonitrile 36 Prepared according to general procedure E using **24** (0.0250 g, 0.113 mmol), NaH (0.0091 g, 0.226 mmol), TiF_2O (0.17 mL, 0.170 mmol), Et_2O (10 mL), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.0048 g, 0.00678 mmol), CuI (0.0013 g, 0.0678 mmol), LiCl (0.0143 g, 0.339 mmol), 4-ethynylbenzonitrile (0.0360 g, 0.283 mmol), Et_3N (5 mL). The crude product was purified by column chromatography (1:7 THF:Hexanes, v/v) on deactivated silica gel to obtain a yellow solid (0.0101 g, 27%). Mp: 181-183 °C; ^1H NMR (400 MHz, CDCl_3): δ 8.33-8.30 (m, 2H), 7.89-7.87 (m, 1H), 7.80 (d, $J = 8$ Hz, 2H), 7.76-7.74 (m, 1H), 7.72 (d, 8.4 Hz, 2H), 7.54-7.39 (m, 5H), 7.40 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 154.1, 149.9, 141.3, 138.1, 135.3, 133.0, 133.0, 132.4, 130.3, 129.7, 129.2, 129.0, 128.1, 126.8, 121.0, 119.8, 118.3, 113.2, 96.8, 88.1; IR (film, KBr) 3064, 2228, 1625, 1603, 1505 cm^{-1} ; HRMS (ESI $^{+}$): m/z calculated for $\text{C}_{24}\text{H}_{15}\text{N}_2$ $[\text{M} + \text{H}]^{+}$: 331.1230, found 331.1237.



(Z)-4-((1-(4-methoxybenzylidene)-1H-indol-3-yl)ethynyl)benzonitrile 44 Prepared according to general procedure E using **42** (0.0250 g, 0.0995 mmol), NaH (0.0160 g, 0.200 mmol), Tf₂O (0.150 mL, 0.150 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0120 g, 0.006 mmol), CuI (0.0030 g, 0.006 mmol), LiCl (0.0260 g, 0.613 mmol), 4-ethynylbenzonitrile (0.0316 g, 0.249 mmol), Et₃N (5 mL). The crude product was purified by column chromatography (1:9 EtOAc:Hexanes, v/v) on deactivated silica gel to obtain an orange solid (0.0082 g, 23%). Mp: 181-183 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.32 (d, *J* = 8.8 Hz, 2H), 7.87-7.84 (m, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.76-7.74 (m, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.49 (td, *J* = 7.6, 1.2 Hz, 1H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H), 7.36 (s, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 161.7, 152.5, 148.1, 141.4, 137.8, 135.0, 133.0, 132.4, 129.7, 128.9, 128.5, 127.5, 127.0, 120.9, 119.5, 118.4, 114.7, 113.0, 96.4, 88.5, 55.6; IR (KBr, film) 2962, 2919, 2850, 2228, 1627, 1599, 1509 cm⁻¹; HRMS (ESI⁺): *m/z* calculated for C₂₅H₁₇N₂O [M + H]⁺: 361.1335, found 361.1328.

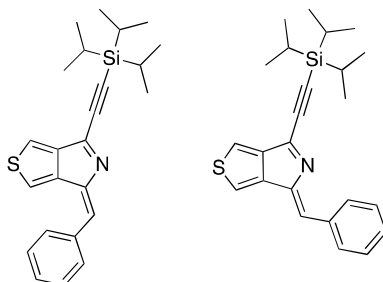


(Z)-4-benzylidene-6-((triisopropylsilyl)ethynyl)-4H-thieno[2,3-c]pyrrole 62 Prepared according to general procedure E using **51** (0.0500 g, 0.220 mmol), NaH (0.0176 g, 0.440 mmol), Tf₂O (0.33 mL, 0.33 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0093 g, 0.0133 mmol), CuI (0.0025 g, 0.0132 mmol), LiCl (0.0278 g, 0.656 mmol), (triisopropylsilyl)acetylene (0.12 mL, 0.548 mmol), and Et₃N (5 mL). The crude product was purified by column chromatography (1:9 EtOAc:Hexanes, *v/v*) on deactivated silica gel to obtain a yellow oil (0.0362 g, 42%). ¹H NMR (400 MHz, CDCl₃): δ 8.26-8.24 (m, 2H), 7.47 (d, *J* = 4.8Hz, 1H), 7.46-7.36 (m, 3H), 7.25 (d, *J* = 4.8Hz, 1H), 7.16 (s, 1H), 1.19 (s, 21H); ¹³C NMR (100 MHz, CDCl₃): δ 153.3, 148.4, 146.3, 143.6, 135.3, 133.2, 132.8, 132.1, 130.4, 128.9, 118.6, 103.9, 101.3, 18.8, 11.4; IR (film, KBr) 2942, 2865, 2136, 1623, 1461, 1329 cm⁻¹; HRMS (ESI⁺): *m/z* calculated for C₂₄H₃₀NSSi [M + H]⁺: 392.1863, found 392.1852.



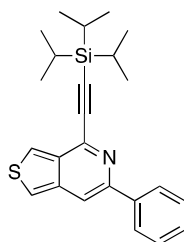
5-phenyl-7-((triisopropylsilyl)ethynyl)thieno[2,3-c]pyridine 73 Prepared according to general procedure E using **58** (0.0300 g, 0.132 mmol), NaH (0.0106 g, 0.266 mmol), Tf₂O (0.200 mL, 0.199 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0056 g, 0.0080 mmol),

CuI (0.0015 g, 0.0079 mmol), LiCl (0.0167 g, 0.394 mmol), (triisopropylsilyl)acetylene (0.1 mL, 0.450 mmol), and Et₃N (3 mL). The crude product was purified by column chromatography (1:19 EtOAc:Hexanes, v/v) on silica gel to obtain a yellow oil (0.0274 g, 53%). ¹H NMR (400 MHz, CDCl₃): δ 8.08-8.06 (m, 2H), 8.06 (s, 1H), 7.72 (d, *J* = 5.4 Hz, 1H), 7.51-7.47 (m, 2H), 7.42 (d, *J* = 5.4 Hz, 1H), 7.42-7.39 (m, 1H), 1.22 (s, 21H); ¹³C NMR (100 MHz, CDCl₃): δ 152.7, 145.9, 139.6, 139.2, 138.0, 132.9, 128.9, 128.7, 127.4, 123.9, 114.4, 104.1, 96.7, 18.9, 11.4; IR (film, KBr) 2961, 2923, 2865, 1574, 1461, 1384 cm⁻¹; HRMS (ESI⁺): *m/z* calculated for C₂₄H₃₀NSSi [M + H]⁺: 392.1863, found 392.1875

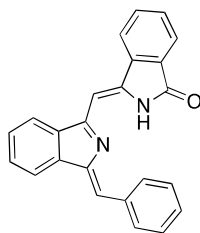


4-benzylidene-6-((triisopropylsilyl)ethynyl)-4*H*-thieno[3,4-*c*]pyrrole 72 Prepared according to general procedure E using **68** (0.0400 g, 0.176 mmol), NaH (0.0141 g, 0.354 mmol), Tf₂O (0.27 mL, 0.270 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0075 g, 0.0107 mmol), CuI (0.0020 g, 0.0105 mmol), LiCl (0.0222 g, 0.524 mmol), (triisopropylsilyl)acetylene (0.10 mL, 0.446 mmol), and Et₃N (3 mL). The crude product was purified by column chromatography (1:9 EtOAc:Hexanes, v/v) on deactivated silica gel to obtain a yellow oil (0.0303 g, 44%). Z:E ratio approximately 3.5:1. ¹H NMR (400

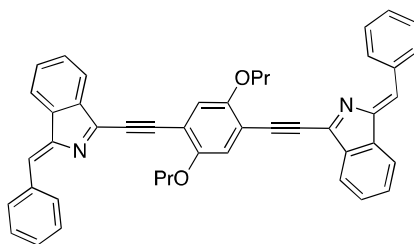
MHz, CDCl₃) δ Z isomer: 8.15-8.13 (m, 2H), 7.43-7.39 (m, 2H), 7.34-7.29 (m, 1H), 7.28 (d, J = 2 Hz, 1H), 7.25 (d, J = 2 Hz, 1H), 6.93 (s, 1H), 1.19 (s, 21H); E isomer: 7.70-7.68 (m, 2H), 7.50 (d, J = 2.4 Hz, 1H), 7.48-7.42 (m, 2H), 7.35 (s, 1H), missing peaks due to overlap; ¹³C NMR (100 MHz, CDCl₃): δ **Z-21a**: 147.0, 135.6, 132.0, 128.7, 125.9, 115.1, 113.4, 103.7, 101.1, 18.8, 11.4; **E-21a**: 129.1; Additional ¹³C peaks: 148.3, 147.5, 143.6, 129.4, 128.8; IR (film, KBr) 2921, 2865, 2247, 1459 cm⁻¹; HRMS (ESI⁺): m/z calculated for C₂₄H₃₀NSSi [M + H]⁺: 392.1863, found 392.1862.



6-phenyl-4-((triisopropylsilyl)ethynyl)thieno[3,4-c]pyridine 74 Prepared according to general procedure E using **69** (0.0300 g, 0.132 mmol), NaH (0.0106 g, 0.264 mmol), Tf₂O (0.20 mL, 0.200 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0056 g, 0.0079 mmol), CuI (0.0015 g, 0.079 mmol), LiCl (0.0167 g, 0.396 mmol), (triisopropylsilyl)acetylene (0.1 mL, 0.445 mmol), and Et₃N (3.00 mL). The crude product was purified by column chromatography (1:9 EtOAc:Hexanes) on silica gel to obtain a yellow oil (0.030 g, 58%). ¹H NMR (400 MHz, CDCl₃): δ 8.20 (dd, J = 3.28, 1.12 Hz, 1H), 8.08-8.05 (m, 2H), 7.82 (d, J = 1.12 Hz, 1H), 7.75 (d, J = 3.32 Hz, 1H), 7.49-7.44 (m, 2H), 7.39-7.35 (m, 1H), 1.23 (s, 21H); ¹³C NMR (100 MHz, CDCl₃): δ 148.1, 140.5, 139.5, 139.2, 135.3, 128.8, 128.3, 127.1, 122.4, 117.9, 110.8, 104.3, 96.5, 18.9, 11.5; IR (film, KBr) 2961, 2923, 2865, 1588, 1577, 1474, 1384 cm⁻¹; HRMS (ESI⁺): m/z calculated for C₂₄H₃₀NSSi [M + H]⁺: 392.1863, found 392.1865.



3-((1-benzylidene-1H-isoindol-3-yl)methylene)isoindolin-1-one 45 Prepared according to general procedure E using lactam **24** (0.50 g, 0.226 mmol), NaH (0.0181 g, 0.452 mmol), Tf₂O (0.34 mL, 0.340 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0095 g, 0.0136 mmol), CuI (0.0026 g, 0.0137 mmol), LiCl (0.0286 g, 0.678 mmol), 2-ethynylbenzamide (0.0820 g, 0.565 mmol), and Et₃N (10 mL). ¹H NMR (400 MHz, CDCl₃): δ 12.35 (b, 1H), 7.95-7.93 (m, 1H), 7.87-7.79 (m, 3H), 7.70-7.50 (m, 8H), 7.36-7.32 (m, 1H), 6.69 (s, 1H), 6.56 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 187.6, 156.4, 144.4, 136.9, 136.3, 135.3, 134.5, 133.1, 132.6, 131.6, 130.6, 129.7, 129.0, 128.8, 128.6, 128.1, 122.0, 120.5, 118.7, 110.6, 108.0, 89.2. HRMS (ESI⁺): m/z calculated for C₂₄H₁₆N₂NaO [M + Na]⁺: 371.1155, found 371.1148.



3,3'-((2,5-dipropoxy-1,4-phenylene)bis(ethyne-2,1-diyl))bis(1-benzylidene-1H-isoindole) 75 Prepared according to general procedure E using lactam **24** (0.100 g, 0.452 mmol), NaH (0.0361 g, 0.903 mmol), Tf₂O (0.68 mL, 0.680 mmol), Et₂O (30 mL), Pd(PPh₃)₂Cl₂ (0.0190 g, 0.0271 mmol), CuI (0.0051 g, 0.0271 mmol), LiCl (0.0571 g,

1.36 mmol), 1,4-diethynyl-2,5-dipropoxybenzene (0.0439 g, 0.181 mmol), and Et₃N (10 mL). The crude product could not be purified. Red-orange solid. ¹H NMR (400 MHz, CDCl₃): δ 8.35-8.33 (m, 4H), 7.88-7.85 (m, 4H), 7.52-7.43 (m, 8H), 7.41-7.37 (m, 2H), 7.34 (s, 2H), 7.25 (s, 2H), 4.11 (t, J = 6.44 Hz, 6.48 Hz, 4H), 2.01 (m, 4H), 1.19 (t, J = 7.36 Hz, 9.88 Hz, 6H). HRMS (ESI⁺): m/z calculated for C₄₆H₃₇N₂O₂ [M + H]⁺: 649.2850, found 649.2869.

References

- (1) Stalder, R.; Mei, J.; Graham, K. R.; Estrada, L. A.; Reynolds, J. R. *Chem. Mater.* **2014**, *26*, 664–678.
- (2) Hendbee, A. D.; Sun, J. P.; Rutledge, L. R.; Hill, I. G.; Welch, G. C. *J. Mater. Chem. A*, **2014**, *2*, 4198-4207.
- (3) Cho, I.; Park, S. K.; Kang, B.; Chung, J. W.; Kim, J. H.; Cho, K.; Park, S. Y. *Adv. Funct. Mater.* **2016**, *26*, 2966-2973.
- (4) Nagahora, N.; Takemoto, I.; Fujii, M.; Shioji, K.; Okuma, K. *Org. Lett.* **2017**, *19*, 2110-2113.
- (5) Acharya, S.; Das, B.; Thupakula, U.; Ariga, K.; Sarma, D. D.; Israelachvili, J.; Golan, Y. *Nano. Lett.* **2013**, *13*, 409-415.
- (6) Dhar, J.; Mukhopadhyay, T.; Yaacobi-Gross, N.; Anthopoulos, T. D.; Salzner, U.; Swaraj, S.; Patil, S. *J. Phys. Chem. B*, **2015**, *119*, 11307-11316
- (7) Ying, W.; Guo, F.; Li, J.; Zhang, Q.; Wu, W.; Tian, H.; Hua, J. *ACS Appl. Mater. Interfaces.* **2012**, *4*, 4215-4224.
- (8) Owczarczyk, Z. R.; Braunecker, W. A.; Gracia, A.; Larsen, R.; Nardes, A. M.; Kopidakis, N.; Ginley, D. S.; Olson, D. C. *Macromolecules*, **2013**, *46*, 1350-1360.
- (9) Hwang, J.; Park, J.; Kim, Y. J.; Ha, Y. H.; Park, C. E.; Chung, D. S.; Kwon, S-K.; Kim, Y-H. *Chem. Mater.* **2017**, *29*, 2135-2140.
- (10) Dincalp, H.; Saltan, G. M.; Zafer, C.; Mutlu, A. *Molecular and Biomolecular Spectroscopy*, **2018**, *202*, 196-206.

- (11) Pruissen, G. W. P. V.; Gholamrezaie, F.; Wienk, M. M.; Janssen, R. A. J. *J. Mater. Chem.*, **2012**, 22, 20387-20393.
- (12) Tang, A.; Zhan, C.; Yao, J.; Zhou, E. *Adv. Mater.* **2017**, 29, 1600013-1600052.
- (13) Xu, L.; Zhao, Z.; Xiao, M.; Yang, J.; Xiao, J.; Yi, Z.; Wang, S.; Liu, Y. *ACS Appl. Mater. Interfaces* **2017**, 9, 40549-40555.
- (14) Quinn, J. T. E.; Zhu, J.; Li, Xu.; Wang, J.; Li, Y. *J. Mater. Chem. C*, **2017**, 5, 8654-8681.
- (15) Qiao, Y.; Guo, Y.; Yu, C.; Zhang, F.; Xu, W.; Liu, Y.; Zhu, D. *J. Am. Chem. Soc.* **2012**, 134, 4084-4087.
- (16) Huang, H.; Chen, Z.; Ortix, R. P.; Newman, C.; Usta, H.; Lou, S.; Youn, J.; Noh, Y.; Baeg, K. J.; Chen, L. X.; Facchetti, A.; Marks, T. *J. Am. Chem. Soc.* **2012**, 134, 10966-10973.
- (17) Lei, T.; Dou, J. H.; Cao, X. Y.; Wang, J. Y.; Pei, J. *J. Am. Chem. Soc.* **2013**, 135, 12168-12171.
- (18) Guo, X.; Quinn, J.; Chen, Z.; Usta, H.; Zheng, Y.; Xia, Y.; Hennek, J. W.; Ortiz, R. P.; Marks, T. J.; Facchetti, A. *J. Am. Chem. Soc.* **2013**, 135, 1986-1996.
- (19) Lui, Y.; Zhang, Z.; Feng, S.; Li, M.; Wu, L.; Hou, R.; Xu, X.; Chen, X.; Bo, Z. *J. Am. Chem. Soc.* **2017**, 139, 3356-3359.
- (20) Burckstummer, H.; Weissenstein, A.; Bialas, D.; Wurthner, F. *J. Org. Chem.* **2011**, 76, 2426-2432.
- (21) Wen, L.; Nietfeld, J. P.; Amb, C. M.; Rasmussen, S. C. *J. Org. Chem.* **2008**, 73, 8529-8536.

- (22) Wang, H.; Shi, Q.; Lin, Y.; Fan, H.; Cheng, P.; Zhan, X.; Li, Y.; Zhu, D. *Macromolecules*, **2011**, *44*, 4213-4221.
- (23) Shi, X.; Zuo, L.; Jo, S. B.; Gao, K.; Lin, F.; Liu, F.; Jen, A. K. Y. *Chem. Mater.* **2017**, *29*, 8369-8376.
- (24) Miller, S. A.; Stuart, A. C.; Womick, J. M.; Zhou, H.; You, W.; Moran, A. M. *J. Phys. Chem. C*. **2011**, *115*, 2371-2380.
- (25) Kleinhenz, N.; Yang, L.; Zhou, H.; Price, S. M.; You, W. *Macromolecules*, **2011**, *44*, 872-877.
- (26) Henson, Z. B.; Welch, G. C.; Poll, T.; Bazan, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 3766-3779.
- (27) Liu, X.; Sun, Y.; Hsu, B. B. Y.; Lorbach, A.; Qi, L.; Heeger, A. J.; Bazan, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 5697-5708.
- (28) Aeschi, Y.; Li, H.; Cao, Z.; Chen, S.; Amacher, A.; Bieri, N.; Ozen, B.; Hauser, J.; Decurtins, S.; Tan, S.; Liu, S.X. *Org. Lett.*, **2013**, *15*, 5586-5589.
- (29) Bura, T.; Leclerc, N.; Fall, S.; Levéque, P.; Heiser, T.; Retailleau, P.; Rihn, S.; Mirloup, A.; Ziessel, R. *J. Am. Chem. Soc.* **2012**, *134*, 17404– 17407
- (30) Chen, J. J.; Conron, S. M.; Erwin, P.; Dimitriou, M.; McAlahney, K.; Thompson, M. E. *ACS Appl. Mater. Interfaces* **2015**, *7*, 662–669.
- (31) Thorat, K. G.; Kamble, P.; Mallah, R.; Ray, A. K.; Sekar, N. *J. Org. Chem.* **2015**, *80*, 6152–6164.
- (32) Gutierrez-Ramos, B. D.; Banuelos, J.; Arbeloa, T.; Arbeloa, I. L.; Gonzalez-Navarro, P. E.; Wrobel, K.; Cerdan, L.; Garcia-Moreno, I.; Costela, A.; Peña-Cabrera, E. *Chem. Eur. J.* **2015**, *21*, 1755–1764.

- (33) Gomez-Dura[´]n, C. FA; Esnal, I.;[´] Valois-Escamilla, I.; Urías-Benavides, A.; Ba[˜]uelos, J.; Arbeloa, I. L.; Garcí a-Moreno, I.; Pe[˜]ñ a-Cabrera, E. *Chem. Eur. J.* **2016**, *22*, 1048–1061.
- (34) Zhang, X.; Xiao, Y.; Qi, J.; Qu, J.; Kim, B.; Yue, X.; Belfield, K. D. *J. Org. Chem.* **2013**, *78*, 9153–9160.
- (35) Wang, D.; Fan, J.; Gao, X.; Wang, B.; Sun, S.; Peng, X. *J. Org. Chem.* **2009**, *74*, 7675–7683.
- (36) Ehrenschwender, T.; Wagenknecht, H.-A. *J. Org. Chem.* **2011**, *76*, 2301–2304.
- (37) Kim, J.-Y.; Sahu, S.; Yau, Y.-H.; Wang, X.; Shochat, S. G.; Nielsen; Per, H.; Ducholm, M. S.; Otzen, D. E.; Lee, J.; Santos, M. M. S. D.; Yam, J. K. H.; Kang, N.-Y.; Park, S.-J.; Kwon, H.; Seviour, T.; Yang, L.; Givskov, M.; Chang, Y.-T. *J. Am. Chem. Soc.* **2016**, *138*, 402–407.
- (38) Yuan, L.; Lin, W.; Zheng, K.; He, L.; Huang, W. *Chem. Soc. Rev.* **2013**, *42*, 622–661.
- (39) Ekmekci, Z.; Yilmaz, M. D.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 461–464.
- (40) Atilgan, S.; Ozdemir, T.; Akkaya, E. U. *Org. Lett.* **2008**, *10*, 4065–4067.
- (41) Chen, Y.; Wang, H.; Wan, L.; Bian, Y.; Jiang, J. *J. Org. Chem.* **2011**, *76*, 3774–3781.
- (42) Wang, F.; Zhu, Y.; Zhou, L.; Pan, L.; Cui, Z.; Fei, Q.; Luo, S.; Pan, D.; Huang, Q.; Wang, R.; Zhao, C.; Tian, H.; Fan, C. *Angew. Chem., Int. Ed.* **2015**, *54*, 7349–7353.
- (43) Golovkova, T. A.; Kozlov, D. V.; Neckers, D. C. *J. Org. Chem.* **2005**, *70*, 5545–5549.

- (44) Tomasulo, M.; Deniz, E.; Alvarado, R. J.; Raymo, F. M. *J. Phys. Chem. C* **2008**, *112*, 8038–8045.
- (45) Moreno, J.; Schweighöfer, F.; Wachtveitl, J.; Hecht, S. *Chem. Eur. J.* **2016**, *22*, 1070–1075.
- (46) Zhao, J.; Wu, W.; Sun, J.; Guo, S. *Chem. Soc. Rev.* **2013**, *42*, 5323–5351.
- (47) Huang, L.; Yang, W.; Zhao, J. *J. Org. Chem.* **2014**, *79*, 10240–10255.
- (48) Ji, S.; Ge, J.; Escudero, D.; Wang, Z.; Zhao, J.; Jacquemin, D. *J. Org. Chem.* **2015**, *80*, 5958–5963.
- (49) Turan, I. S.; Yildiz, D.; Turksoy, A.; Gunaydin, G.; Akkaya, E. U. *Angew. Chem., Int. Ed.* **2016**, *55*, 2875–2878.
- (50) Awuah, S. G.; You, Y. *RSC Adv.* **2012**, *2*, 11169–111
- (51) Meng, Q.; Fronczok, F. R.; Vicente, G. H. *New J. Chem.* **2016**, *40*, 5740–5751.
- (52) Yu, C.; Wu, Q.; Wang, J.; Wei, Y.; Hao, E.; Jiao, L. *J. Org. Chem.*, **2016**, *81*, 3761–3770.
- (53) Bucher, L.; Aly, S.; Desbois, N.; Karsenti, P. L.; Gros, C. P.; Harvey, P. D. *J. Phys. Chem. C*, **2017**, *121*, 6478–6491.
- (54) Lui, P.; Gao, F.; Zhou, L.; Chen, Y.; Chen, Z. *Org. Biomol. Chem.*, **2017**, *15*, 1393–1400.
- (55) Debnath, S.; Singh, S.; Bedi, A.; Krishnamoorthy, K.; Zade, S. S. *Polymer Chemistry* **2016**, *54*, 1978–1986.
- (56) Taguchi, D.; Nakamura, T.; Horiuchi, H.; Saikawa, M.; Nabeshima, T. *J. Org. Chem.* **2018**, *83*, 5331–5337.

- (57) Miao, W.; Dai, En.; Sheng, W.; Yu, C.; Hao, E.; Liu, W.; Wei, Y.; Jiao, L. *Org. Lett.* **2017**, *19*, 6244-6247.
- (58) Yu, C.; Jiao, L.; Tan, X.; Wang, J.; Xu, Y.; Wu, Y.; Yang, G.; Wang, Z.; Hao, E. *Angew. Chem. Int. Ed.* **2012**, *51*, 7688-7691.
- (59) Zhang, L. Y.; Tu, F. Q.; Guo, X. F.; Wang, H.; Wang, P.; Zhang, H. S. *Anal. Bioanal. Chem.* **2014**, *406*, 6723-6733.
- (60) Ansari, N.; Cummings, M. M.; Soderberg, B. C. G. *Tetrahedron*, **2018**, *74*, 2547-2560.
- (61) Zheng, X.; Kerr, M. A. *Org. Lett.*, **2006**, *17*, 3777-3779.
- (62) O'Connell, D. P.; LeBlanc, D. F.; Cromley, D.; Billheimer, J.; Rader, D. J.; Bachovchin, W. W. *Bioorganic & Medicinal Chemistry Letters*, **2012**, *22*, 1397-1401.
- (63) Satoh, M.; Shibata, Yu.; Tanaka, K. *Chem. Eur. J.* **2018**, *24*, 5434-5438.
- (64) Umei, K.; Nishigaya, Y.; Kamiya, M.; Kohno, Y.; Seto, S. *Synthesis*, **2015**, *47*, 3221-3230.
- (65) Clift, M. D.; Thomson, R. J. *J. Am. Chem. Soc.* **2009**, *131*, 14579-14583.
- (66) Bubar, A.; Estey, P.; Lawson, M.; Eisler, S. *J. Org. Chem.*, **2012**, *77*, 1572-1578.
- (67) Infante, G.; Eisler, S. *Canadian Journal of Chemistry*, **2017**, *95*, 415-423.
- (68) Mehta, S.; Yao, T.; Larock, R. C. *J. Org. Chem.*, **2012**, *77*, 10938-10944.
- (69) Chary, R. G.; Dhananjaya, G.; Prasad, K. V.; Vaishaly, S.; Ganesh, Y. S. S.; Dulla, B.; Kumar, K. S.; Pal, M. *Chem. Commun.*, **2014**, *50*, 6797-6800.
- (70) Jones, P.; Altamura, S.; Boueres, J.; Ferrigno, F.; Fonsi, M.; Giomini, C.; Lamartina, S.; Monteagudo, E.; Ontoria, J. M.; Orsale, M. V.; Palumbi, M. C.; Pesci, S.; Roscilli, G.;

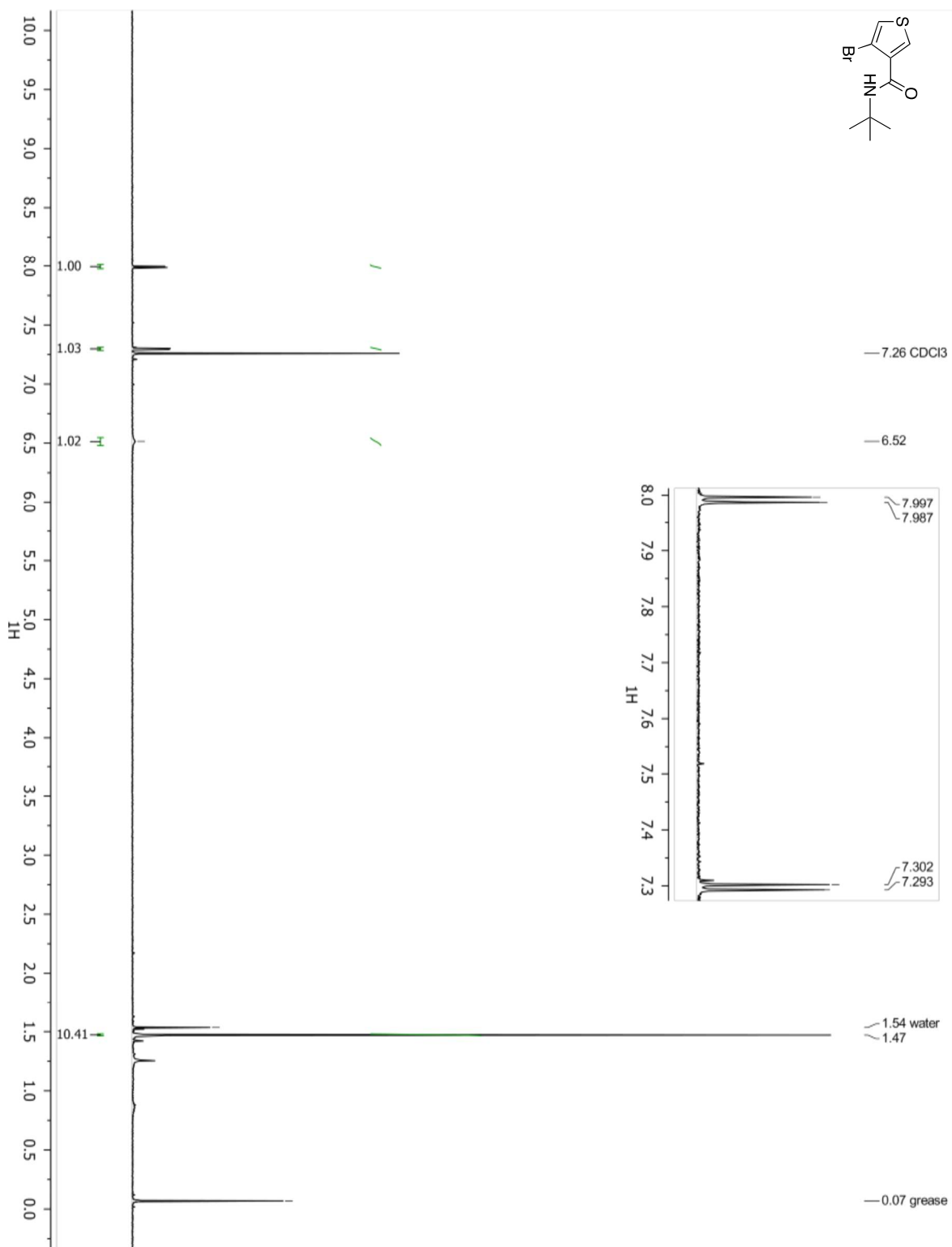
- Scarpelli, R.; Shultz-Fademrecht, C.; Toniatti, C.; Rowley, M. *J. Med. Chem.* **2009**, *52*, 7170.
- (71) Kettle, J. G.; Brown, S.; Crafter, C.; Davies, B. R.; Dudley, P.; Fairley, G.; Faulder, P.; Fillery, S.; Greenwood, H.; Hawkins, J.; James, M.; Johnson, K.; Lane, C. D.; Pass, M.; Pink, J. H.; Plant, H.; Cosulich, S. C. *J. Med. Chem.* **2012**, *55*, 1261.
- (72) Satake, N.; Zhou, Q.; Sato, N.; Matsuo, M.; Sawada, T.; Shibata, S. *Pharmacology* **1992**, *44*, 206.
- (73) Castro, A. J. *Nature*, 1967, 213, 903-904.
- (74) Berg, G. *J. Appl. Microbiol.*, **2000**, *88*, 952-960.
- (75) Kataoka, T. et al. *FEBS Lett.*, **1995**, *359*, 53-59.
- (76) Chen, X.; Brauman, J. I.; *J. Am. Chem. Soc.*, **2008**, *130*, 15038-15046.
- (77) Loewenthal, H. J. E. *Tetrahedron*, **1959**, *5*, 269-303.
- (78) Shibuya, K.; Takahashi, Y.; Shigyo, H.; Ohta, T. *Heterocycles*, **1989**, *29*, 2199-2207.
- (79) Kerrigan, N. J.; Dunne, E. C.; Cunningham, D.; McArdle, P.; Gilligan, K.; Gilheany, D. G. *Tetrahedron Lett.* **2003**, *44*, 8461-8465.
- (80) Uozumi, Y.; Kawatsura, M.; Hayashi, T. *Org. Syn.* **2002**, *78*, 1-13.
- (81) Ohgiya, T.; Nishiyama, S. *Tetrahedron Lett.* **2004**, *45*, 6317-6320.
- (82) Dhakal, B.; Bohe, L.; Crich, D. *J. Org. Chem.* **2017**, *82*, 9263-9269.
- (83) Hoashi, Y.; Takai, T.; Kotani, E.; Koike, T. *Tetrahedron Letters*, **2013**, *54*, 2199-2202.
- (84) Sonawane, M. R.; Vavra, J.; Saman, D.; Cisarova, I.; Teply, F. *Synthesis*, **2015**, *47*, 3479-3488.
- (85) Patil, M.; Kapdi, A. R.; Kumar, A. V. *RSC Adv.* **2015**, *5*, 54505.

- (86) Geramita, K.; McBee, J.; Tilley, T. D. *J. Org. Chem.* **2009**, *74*, 820-829.
- (87) Bures, F. *RSC. Adv.*, **2014**, *4*, 58826-58851.
- (88) Kumarasamy, E.; Sanders, S. N.; Pun, A. B.; Vaselabadi, S. A.; Low, J. Z.; Sfeir, M. Y.; Steigerwald, M. L.; Stein, G. E.; Campos, L. M. *Macromolecules* **2016**, *49*, 1279-1285.
- (89) Lin, Y.; Zhan, X. *Acc. Chem. Res.* **2016**, *49*, 175-183.
- (90) Groves, B. R.; Crawford, S. M.; Lundrigan, T.; Matta, C. F.; Sowlati-Hashjin, S.; Thompson, A. *Chem. Commun.*, 2013, *49*, 816-818.
- (91) Lopez-Valdez, G.; Olguin-Urbe, S.; Millan-Ortiz, A.; Gamez-Montano, R.; Miranda, L.D. *Tetrahedron* **2011**, *67*, 2693-2701.
- (92) Elansary, A. K.; Moneer, A. A.; Kadry, H. H.; Gedawy, E. M. *Arch Pharm Res* **2012**, *35*, 1909-1917.
- (93) Yang, D.; Burugupalli, S.; Daniel, D.; Chen, Y. *J. Org. Chem.* **2012**, *77*, 4466-4472.
- (94) Rowland, R. S.; Taylor, R. *J. Phys. Chem.* **1996**, *100*, 7384-7391.
- (95) Fu, C.; Beldon, P. J.; Perepichka, D. F. *Chem. Mater.* **2017**, *29*, 2979-2987.
- (96) Karle, I. L.; Butcher, R. J.; Wolak, M. A.; Filho, D. A.; Uchida, M.; Bredas, J. L.; Kafafi, Z. H. *J. Phys. Chem. C* 2007, *111*, 9543-9547.
- (97) Ke, Z.; Huanli, D.; Hao-Li, Z.; Wenping, H.
- (98) Suginome, M.; Collet, S.; Ito, Y. *Org. Lett.* **2002**, *4*, 3, 351-354.
- (99) Huddleston, P. R. et al. *Journal of Chemical Research, Synopses*, **1993**, *2*, 72.
- (100) Christophersen, C.; Begtrup, M.; Ebdrup, S.; Petersen, H.; Vedso, P. *J. Org. Chem.* **2003**, *68*, 9513-9516.
- (101) Long, Y.; She, Z.; Liu, X.; Chen, Y. *J. Org. Chem.* **2013**, *78*, *6*, 2579-2588.

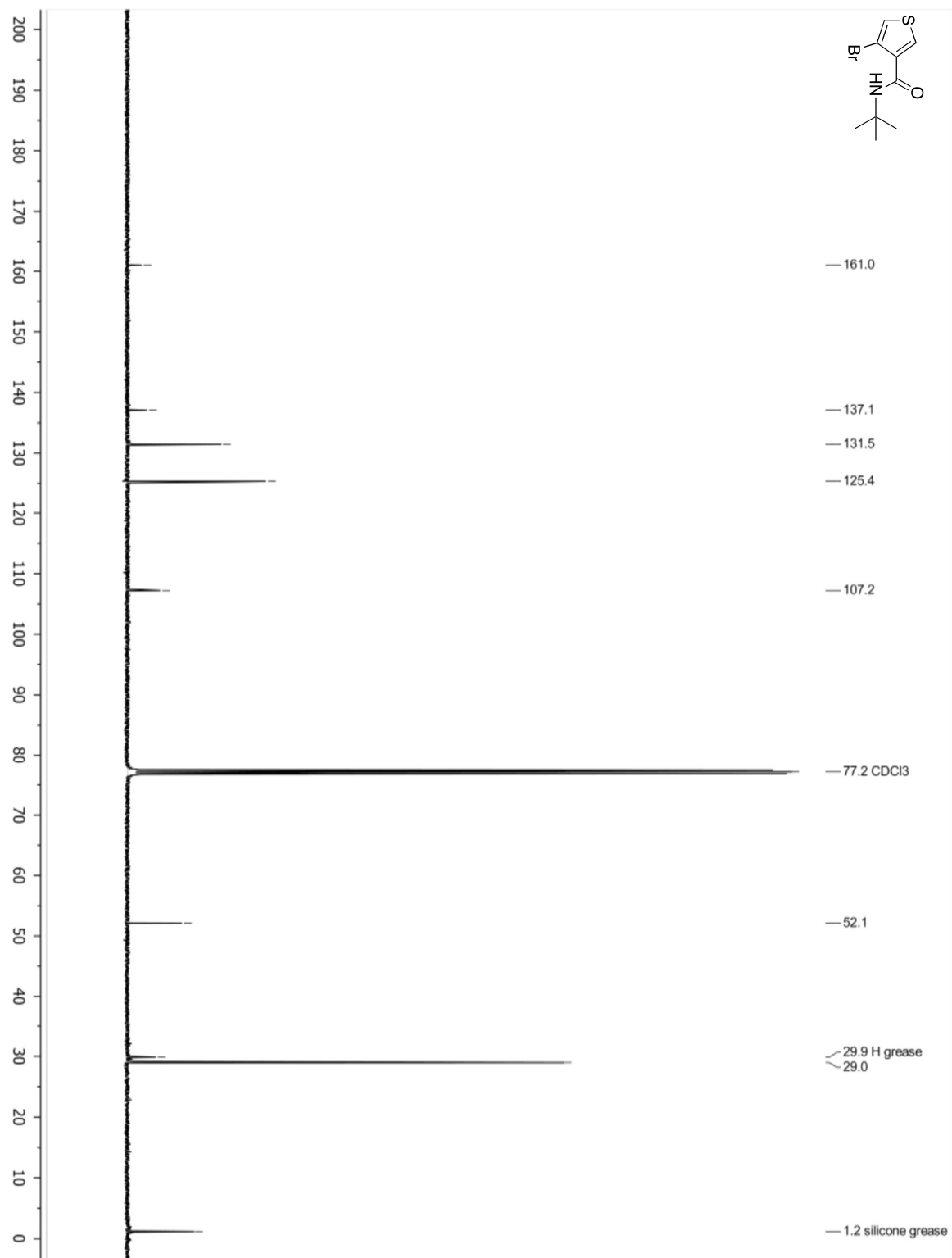
- (102) Kundu, N. G.; Khan, M. W. *Tetrahedron* **2000**, *56*, 4777-4792.
- (103) Iaroshenko, V. O.; Ali, S.; Babar, T. M.; Abbasi, M. S. A.; Sosnovskikh, V. Y.; Villinger, A.; Tolmachev, A.; Langer, P. *Tetrahedron* **2013**, *69*, 3167-3181.

Appendix A: ^1H and ^{13}C NMR for all new compounds

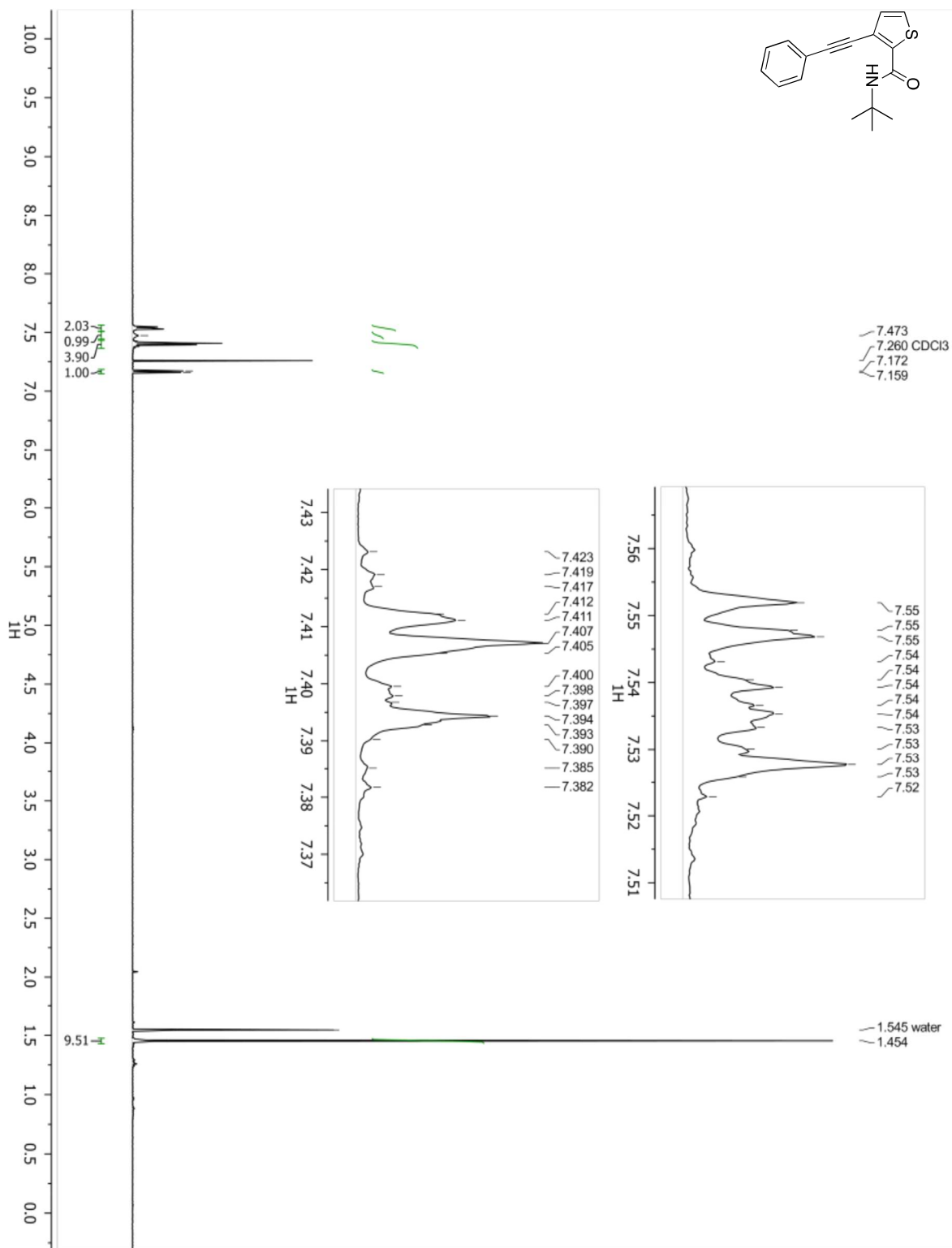
77: ^1H NMR



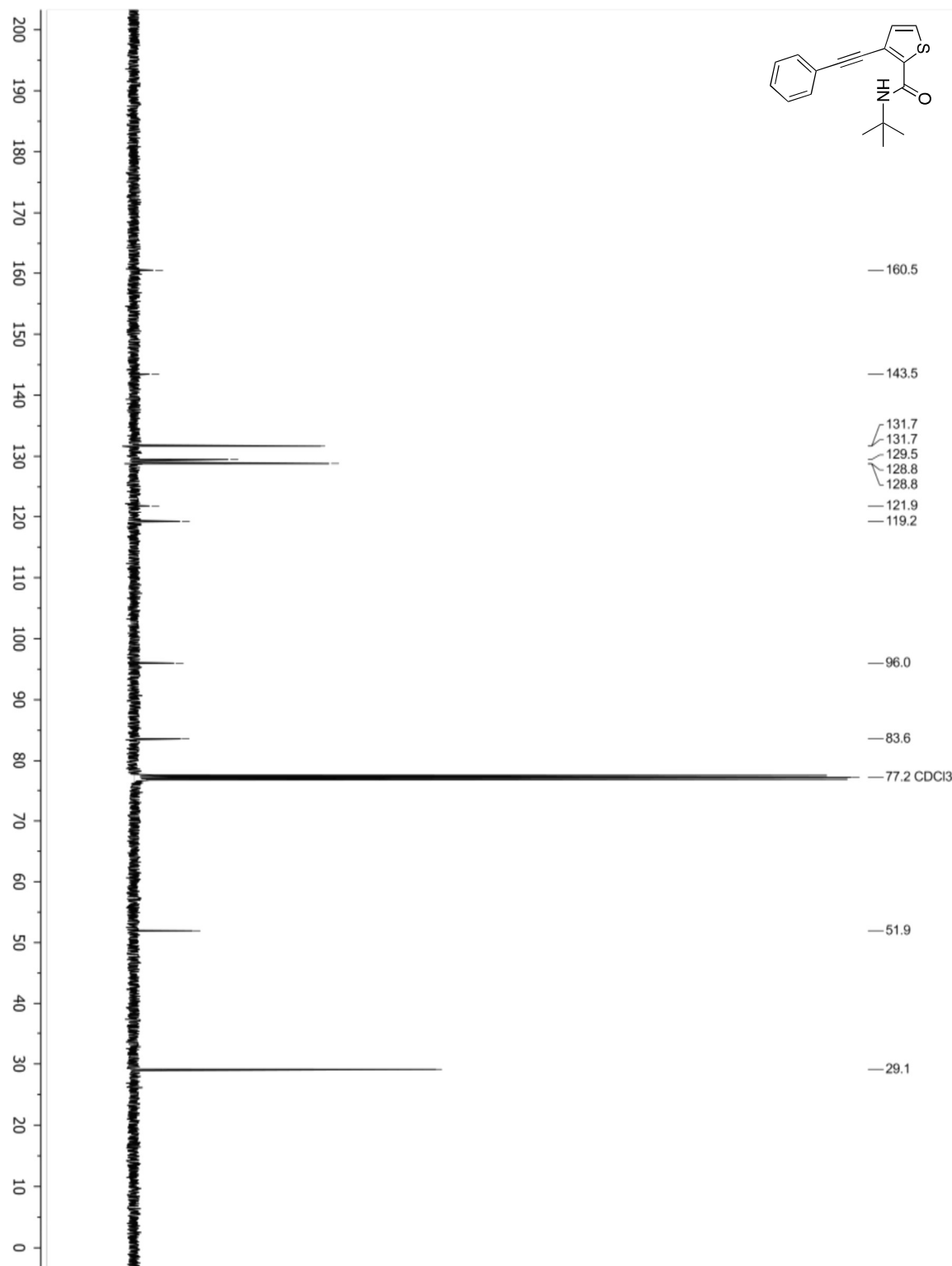
77: ^{13}C NMR



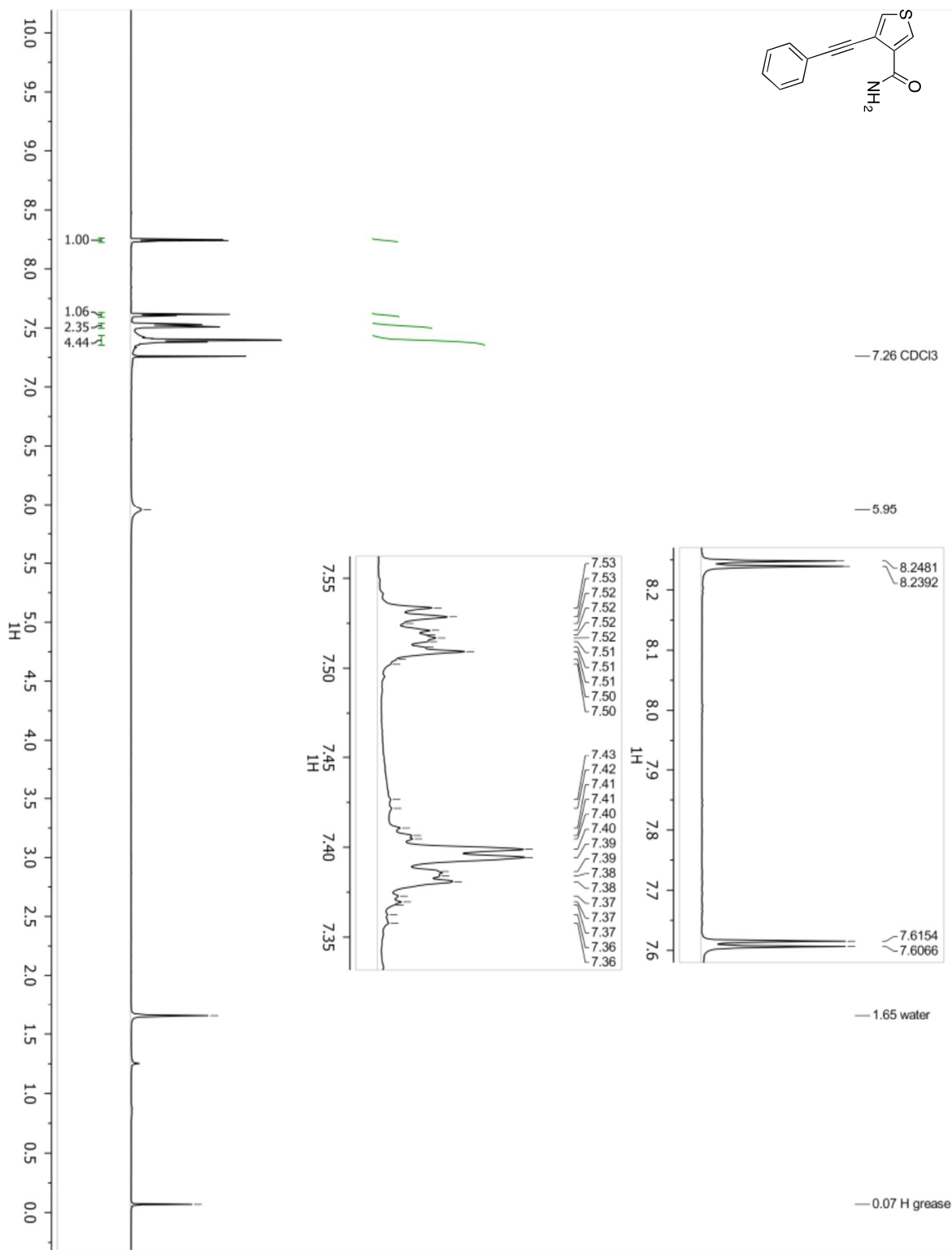
59: ^1H NMR



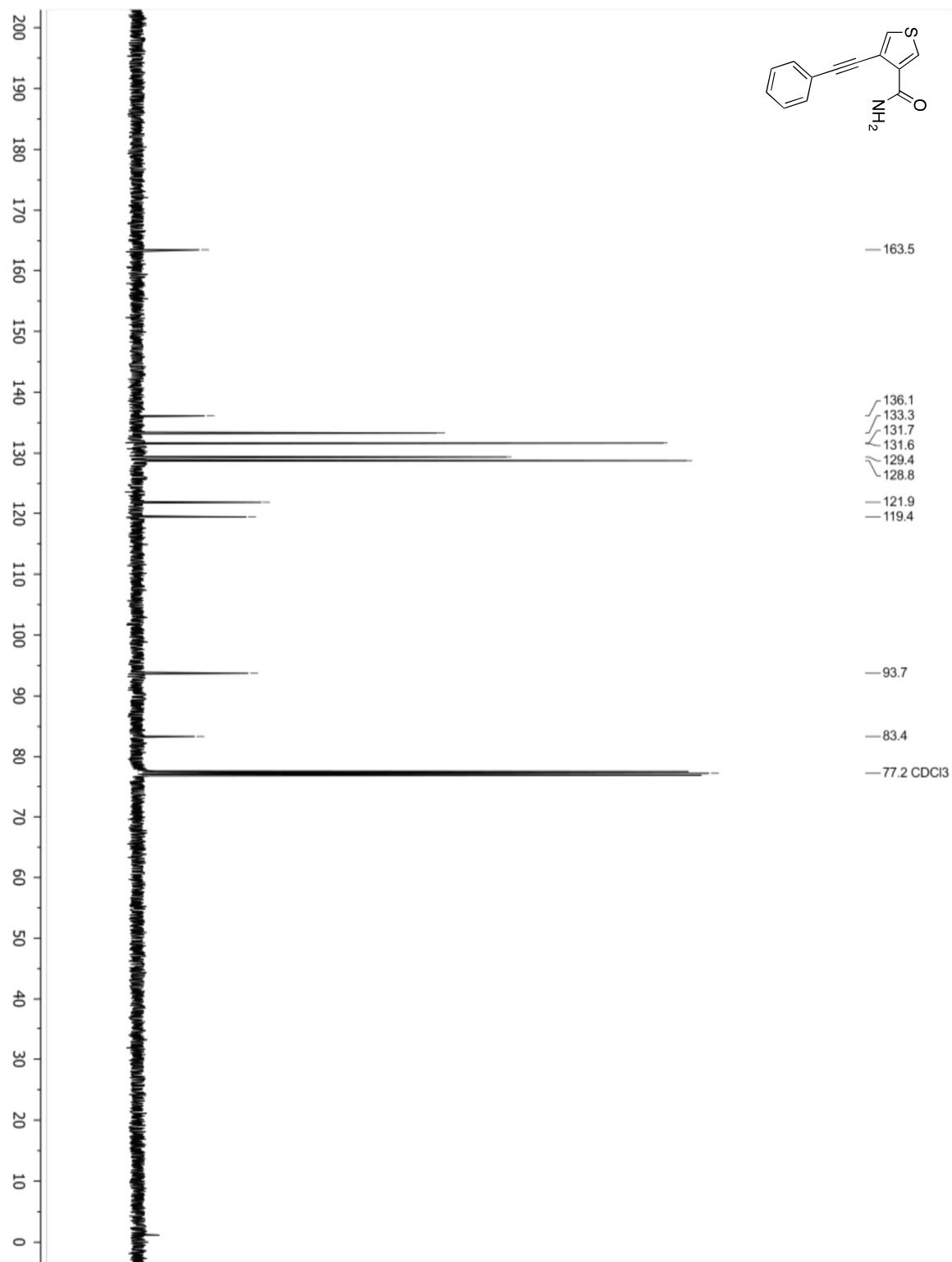
59: ^{13}C NMR



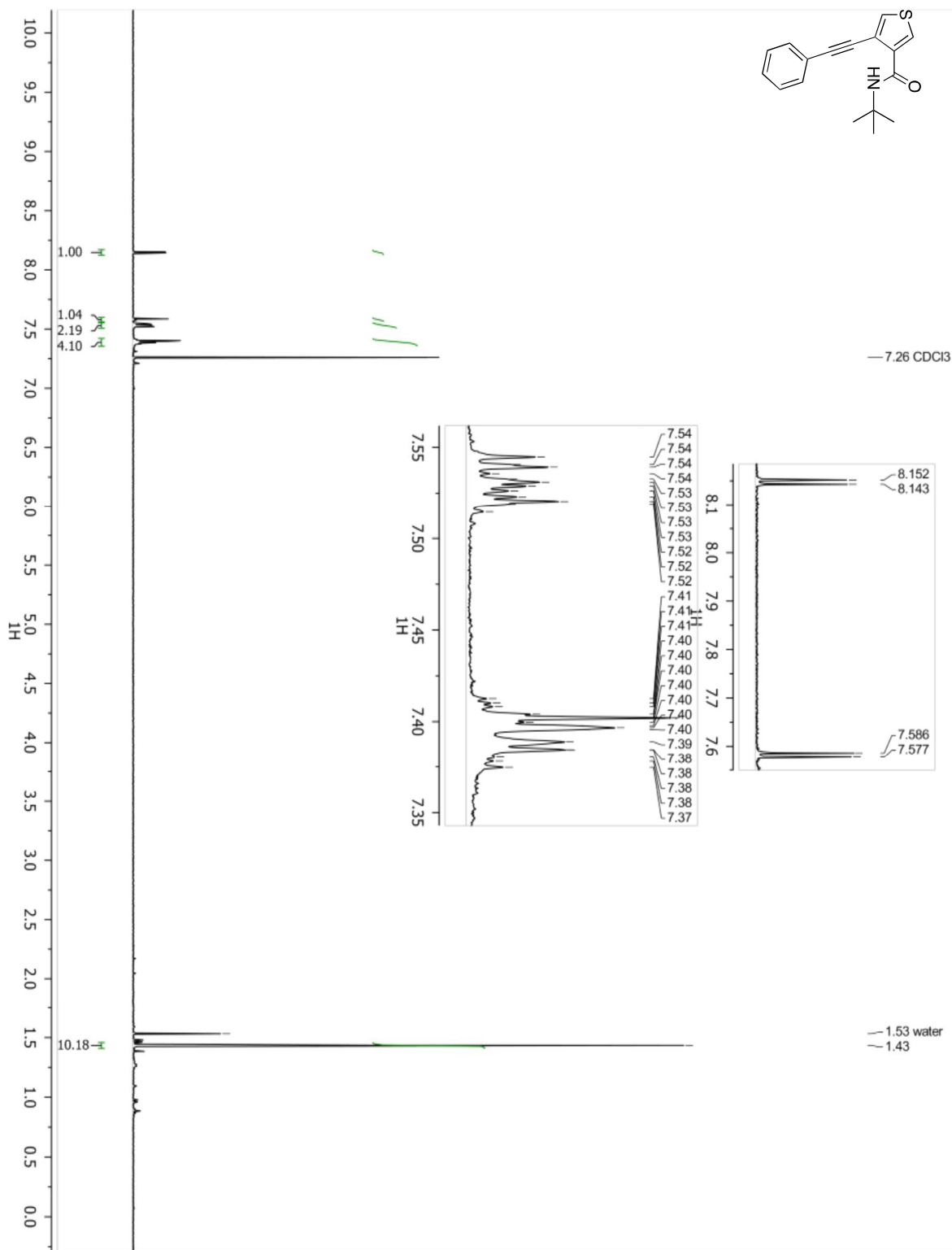
67: ^1H NMR



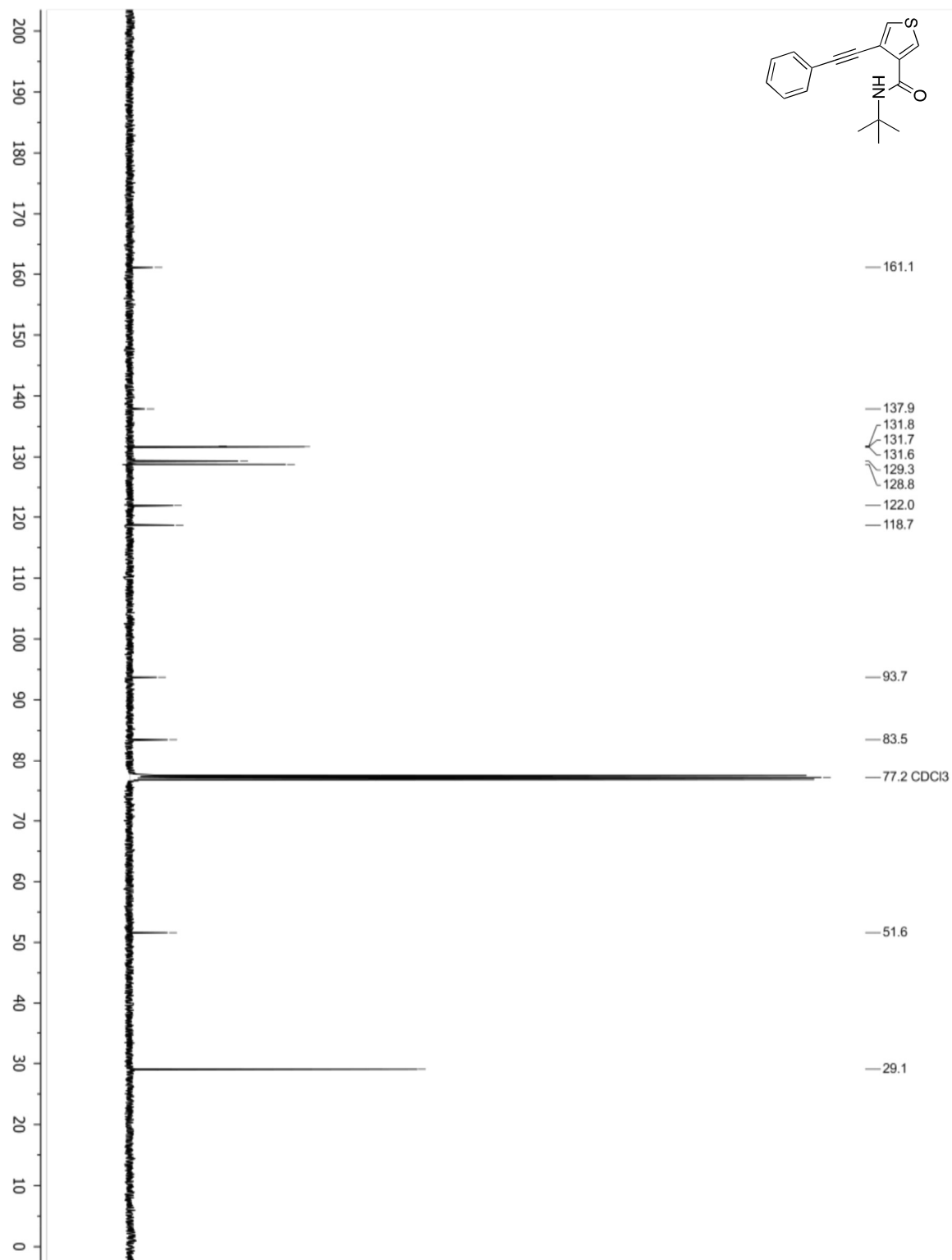
67: ^{13}C NMR



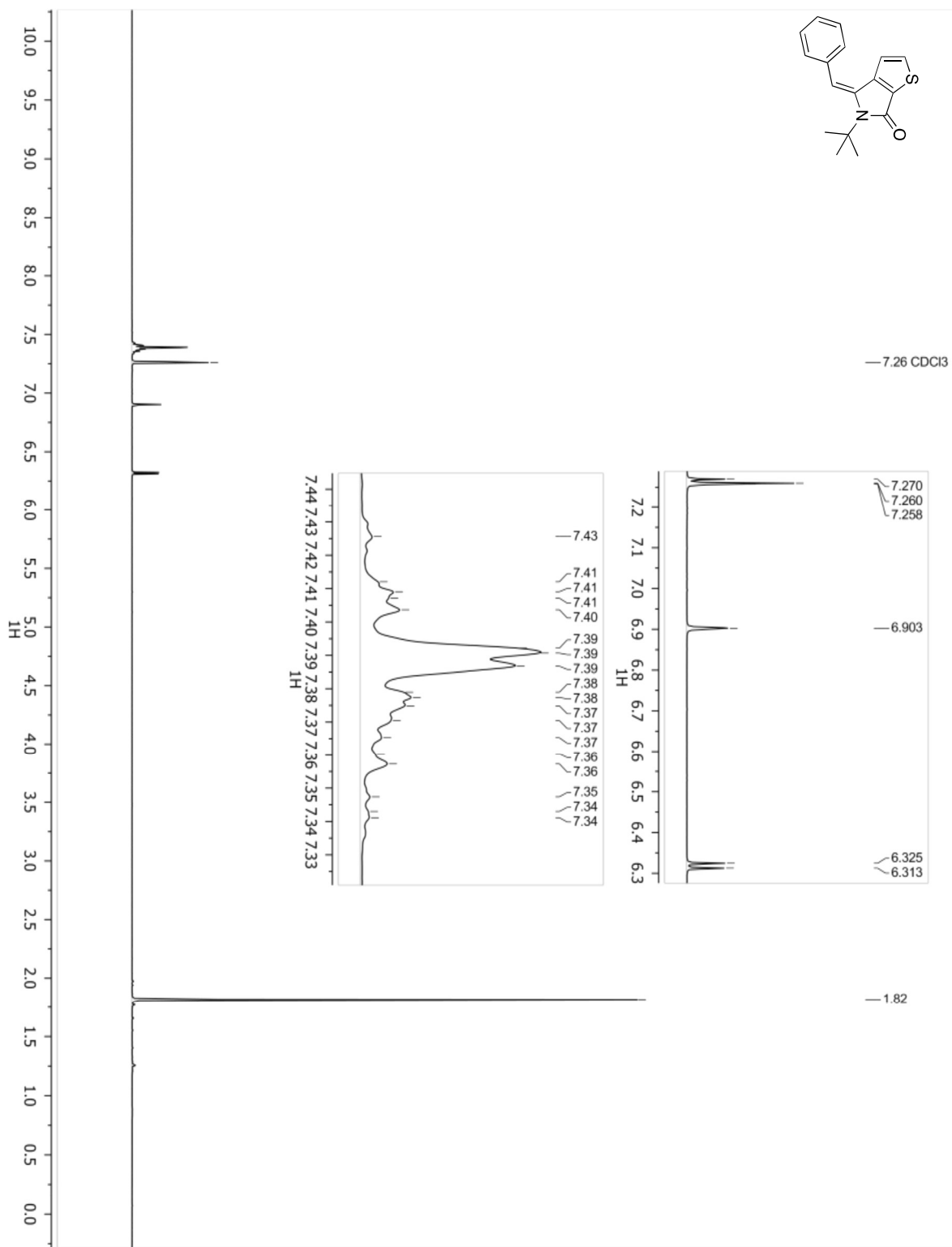
70: ^1H NMR



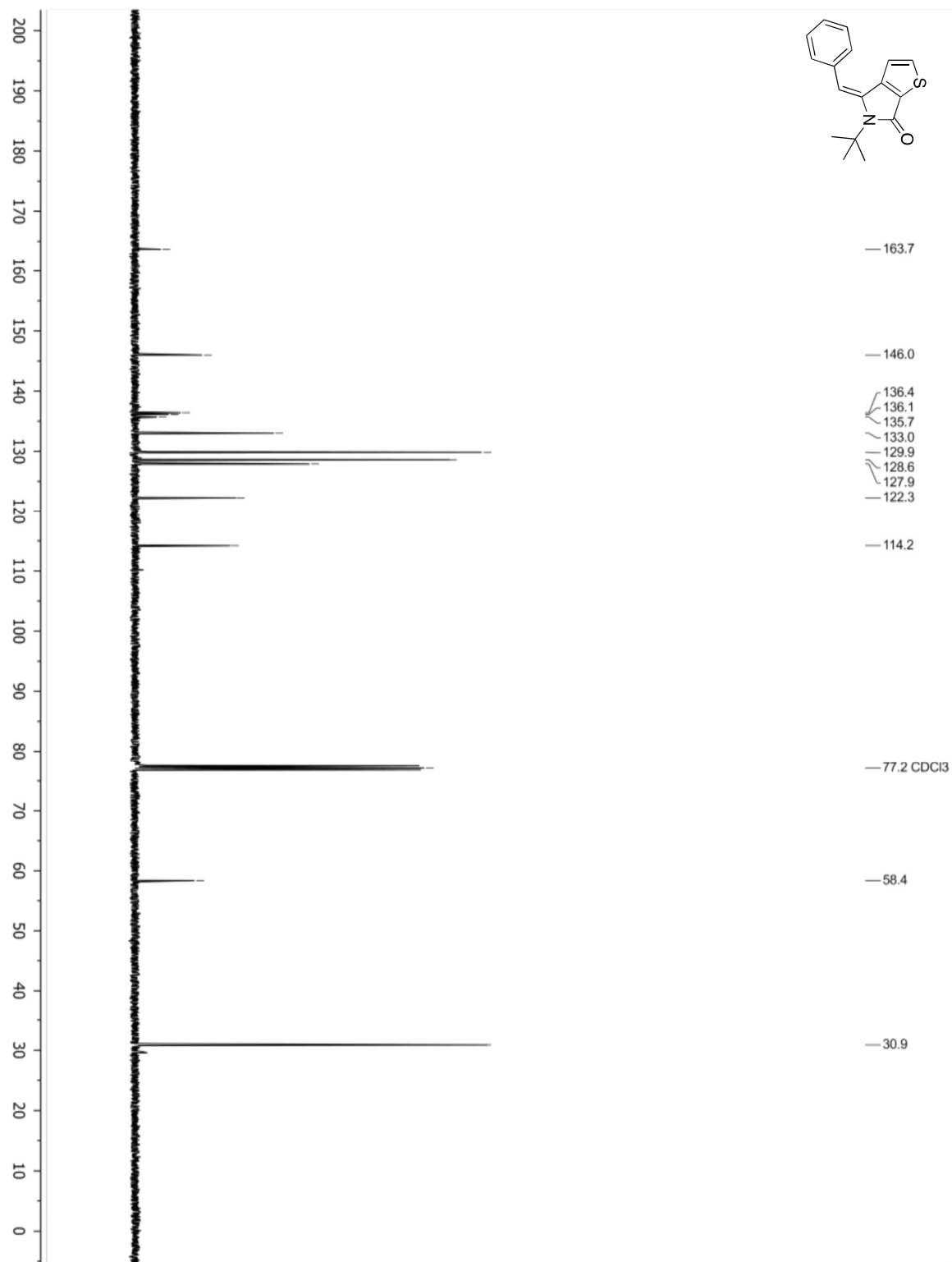
70: ^{13}C NMR



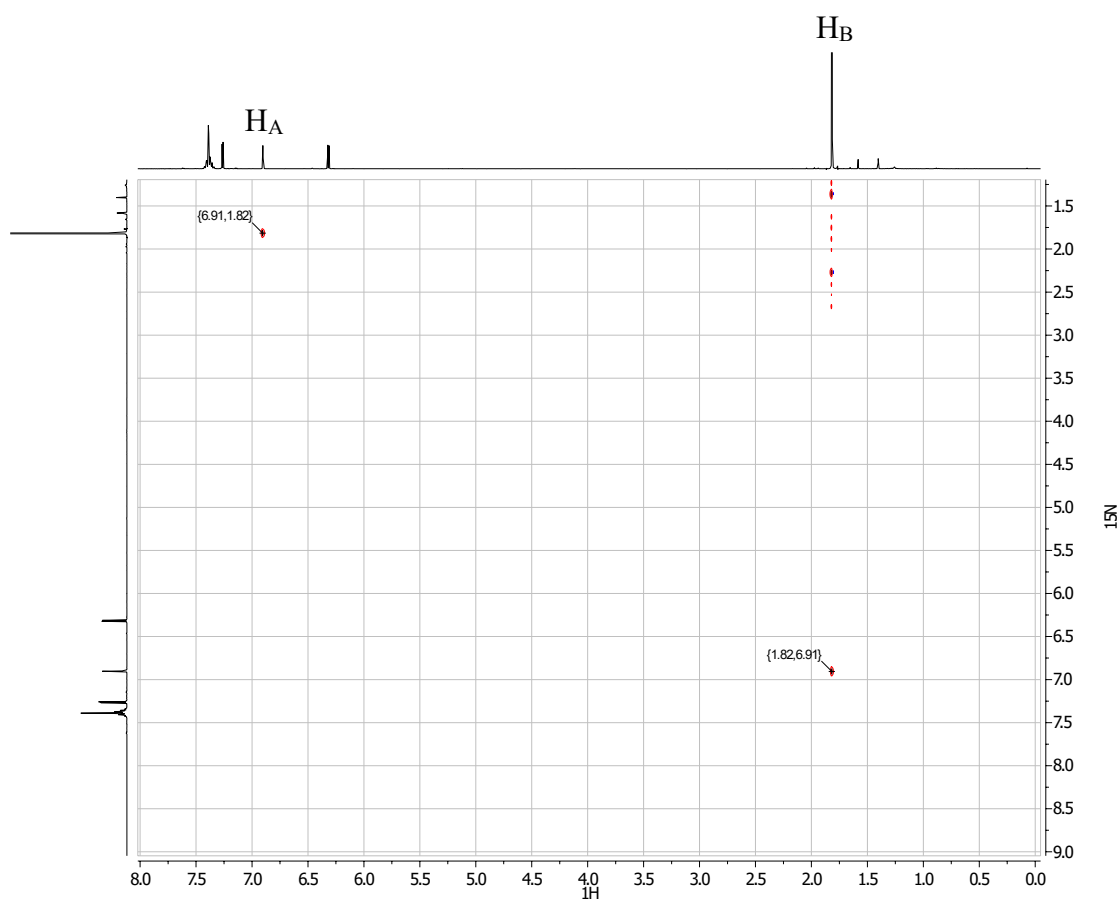
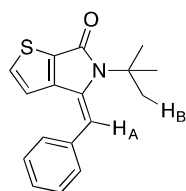
60: ^1H NMR



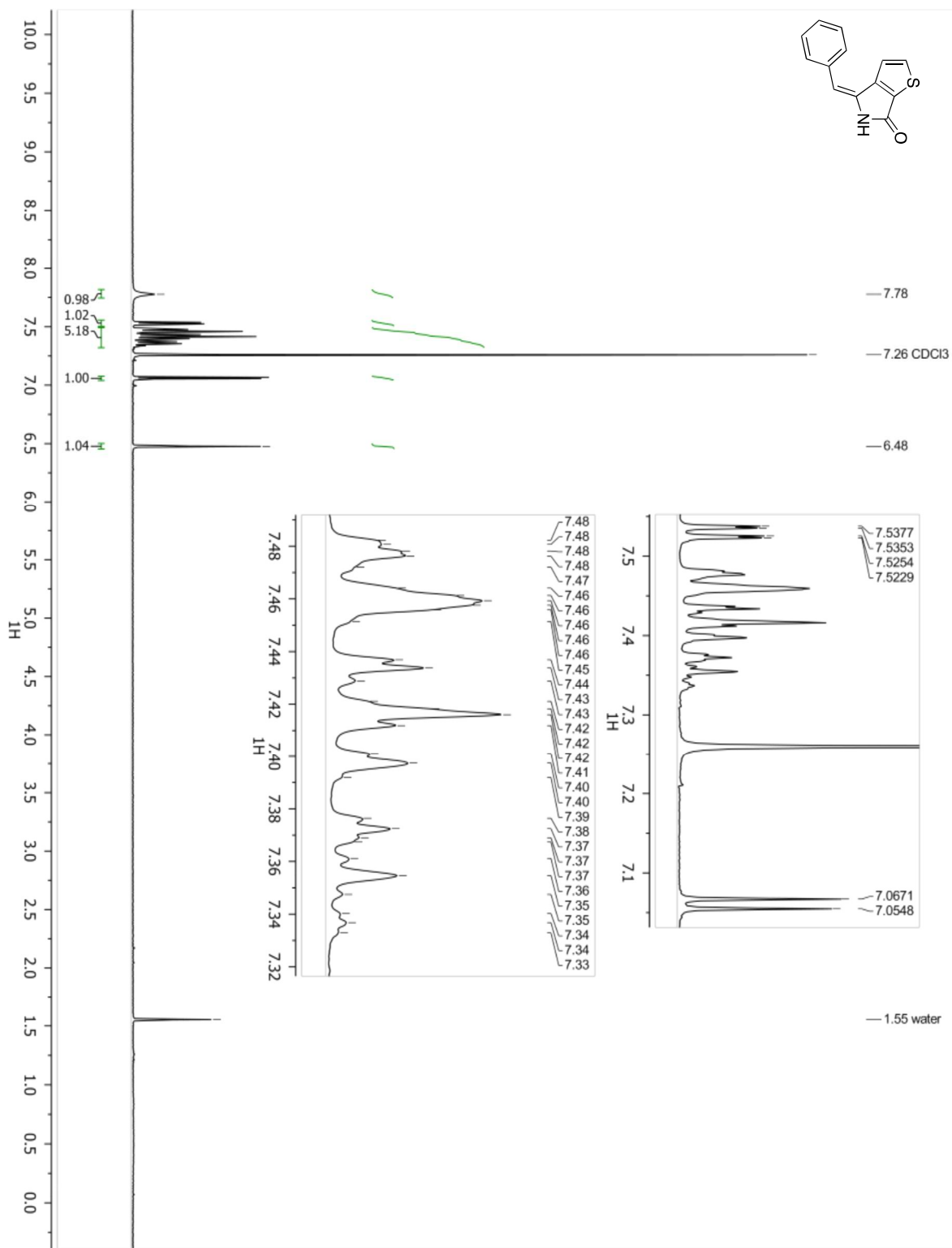
60: ^{13}C NMR



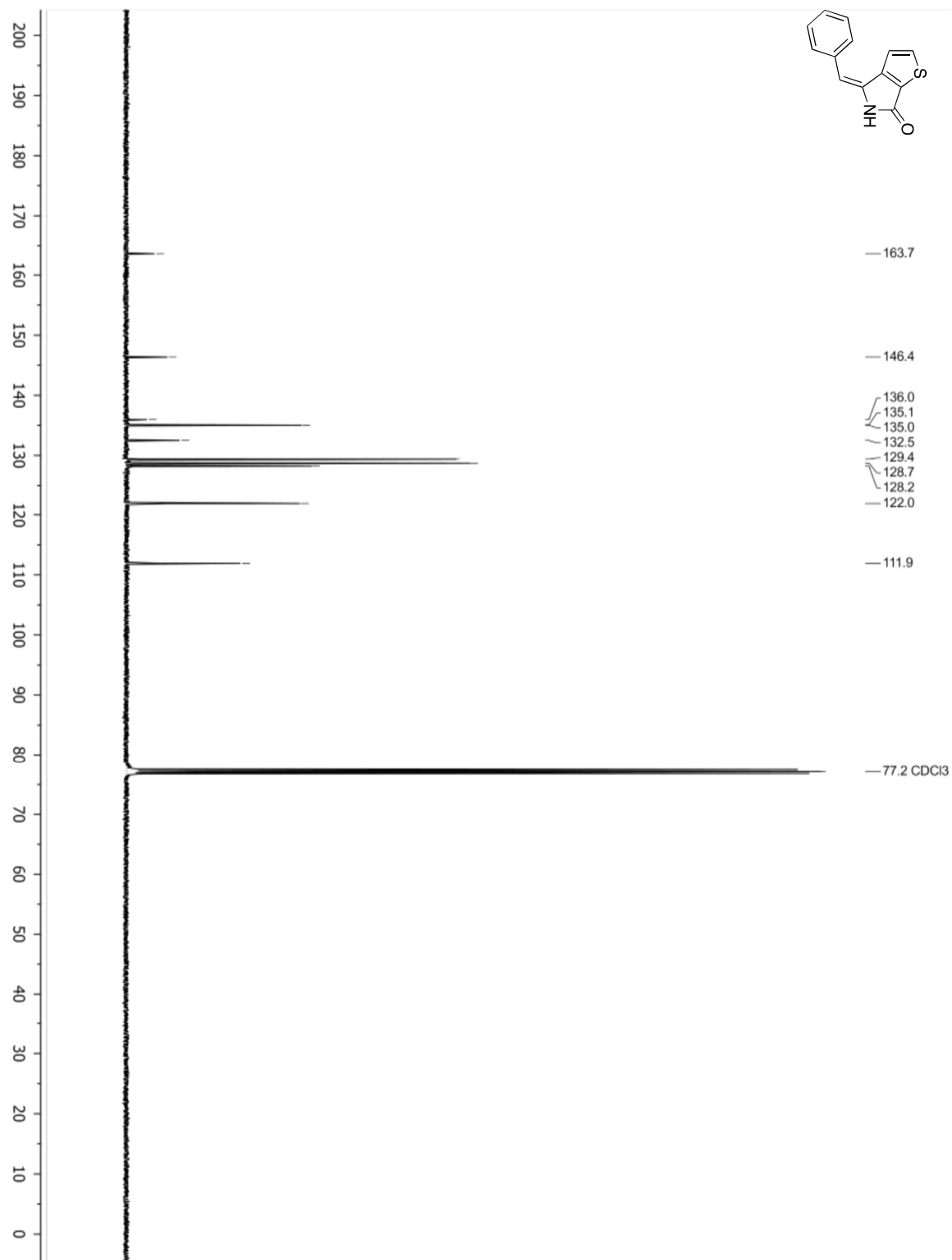
60: NOESY



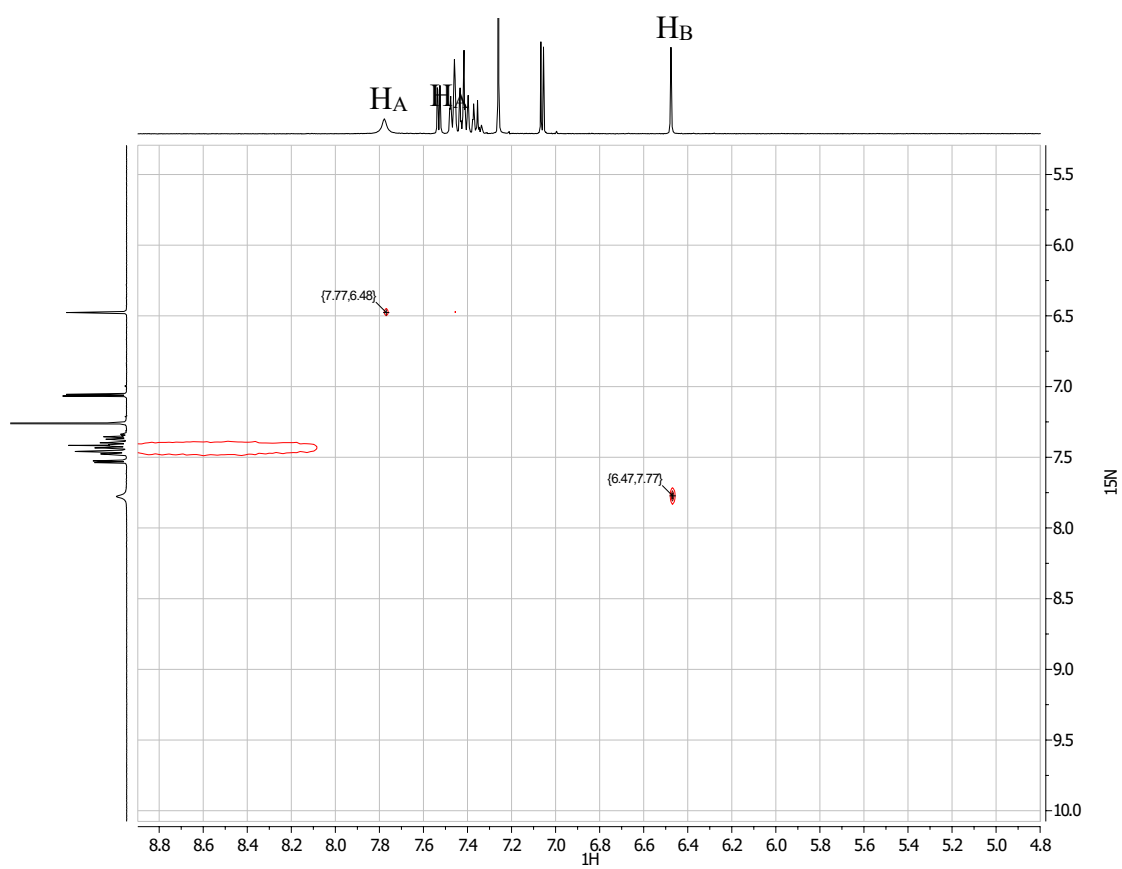
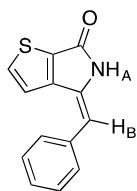
51: ^1H NMR



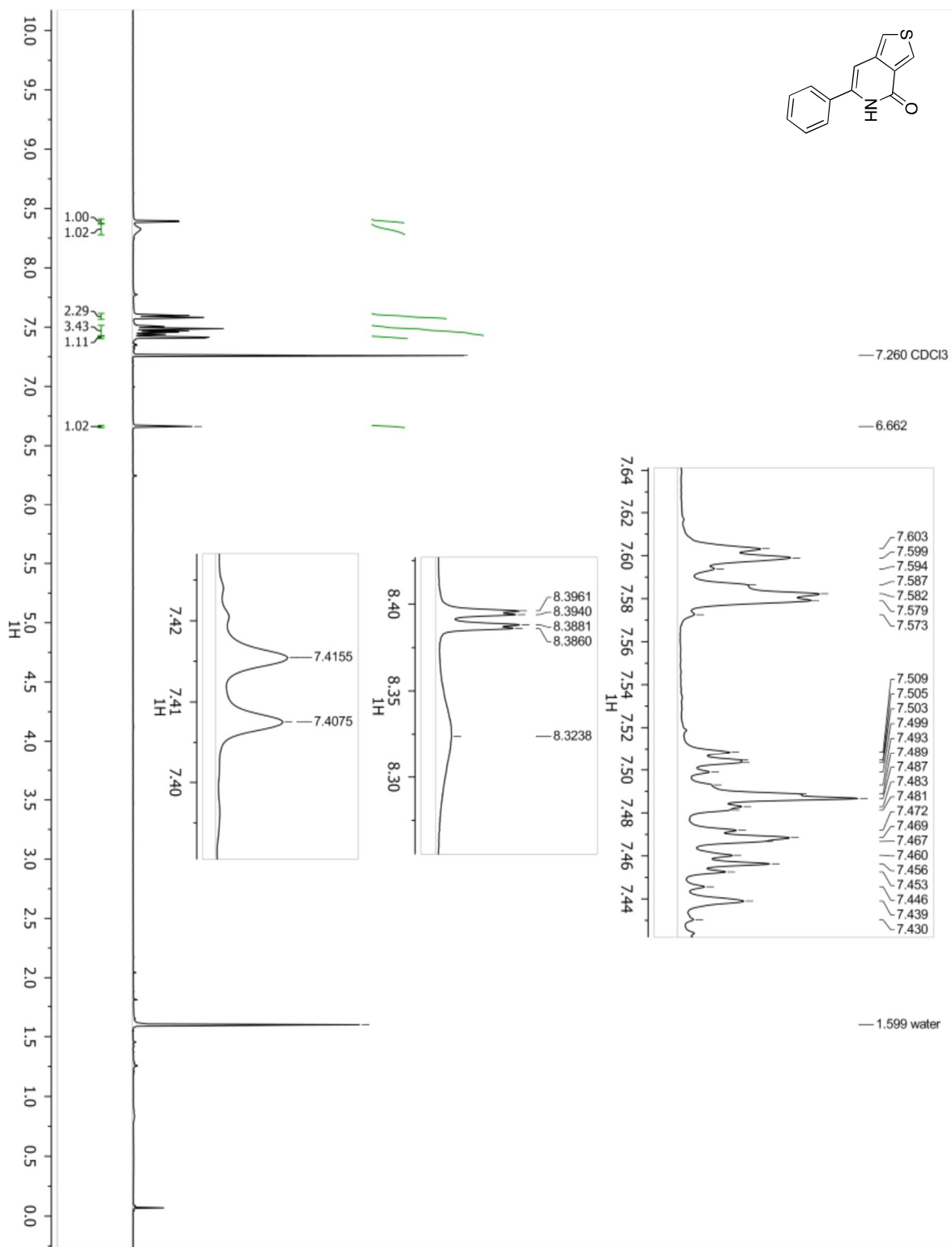
51: ^{13}C NMR



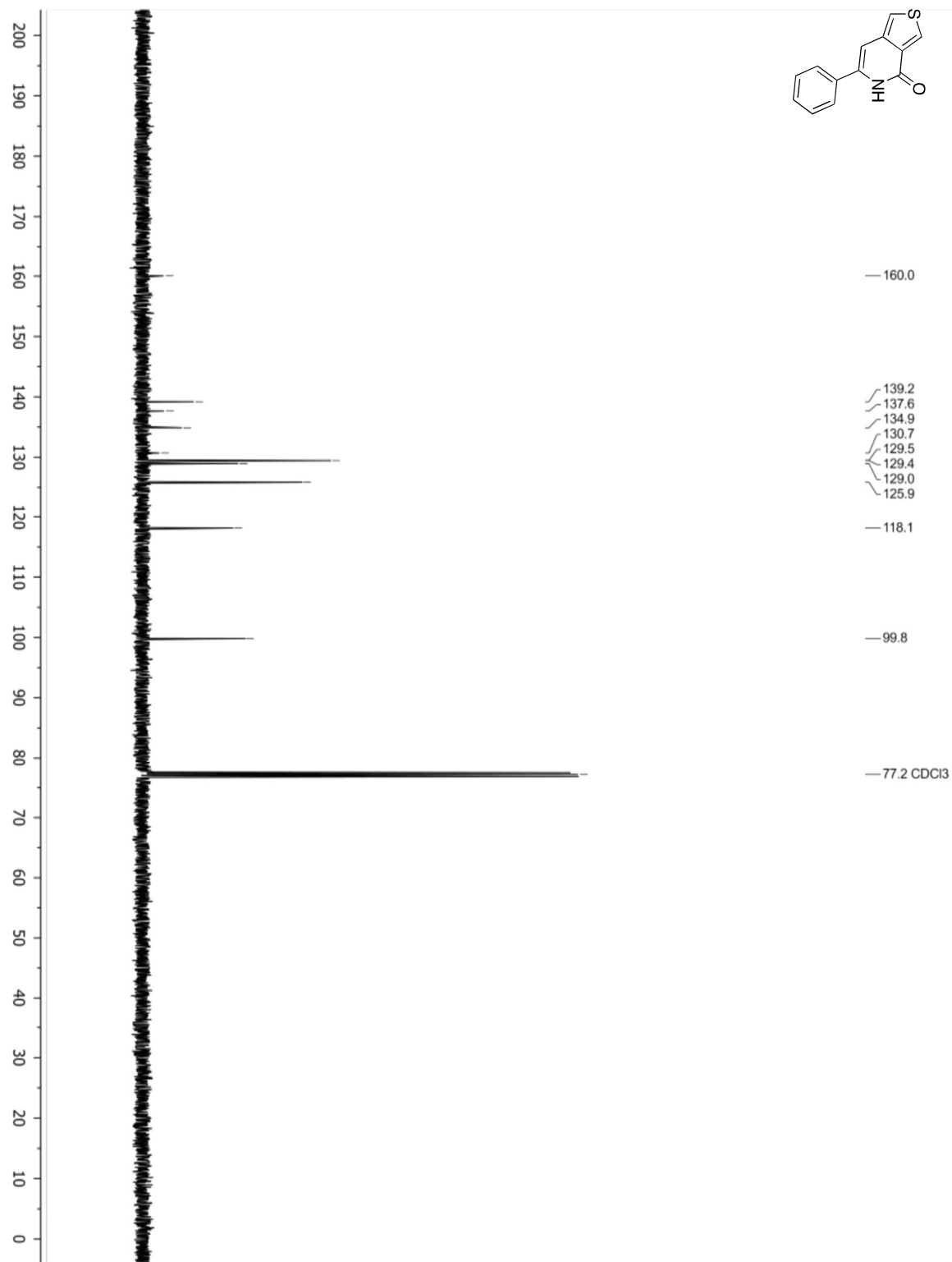
51: NOESY



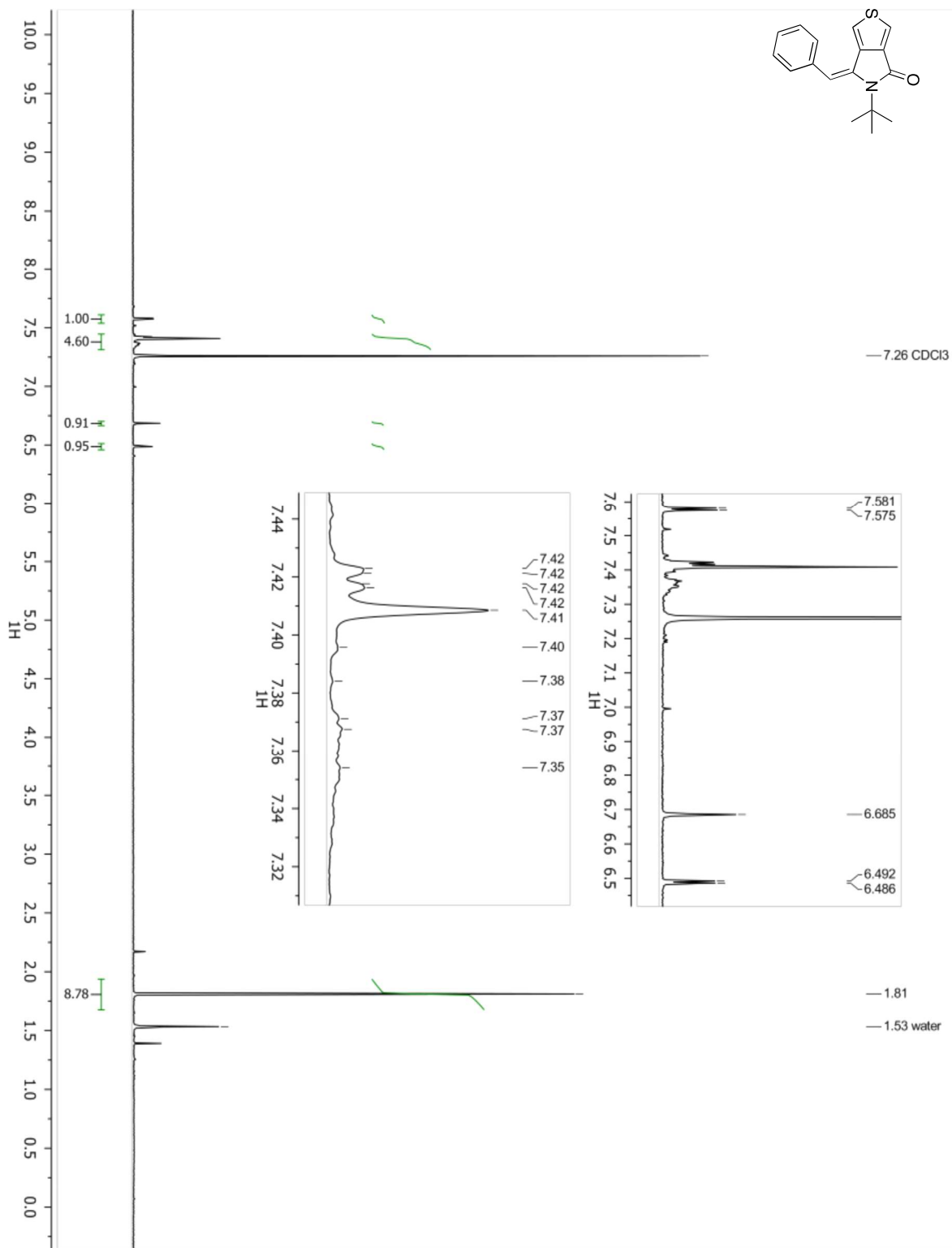
69: ^1H NMR



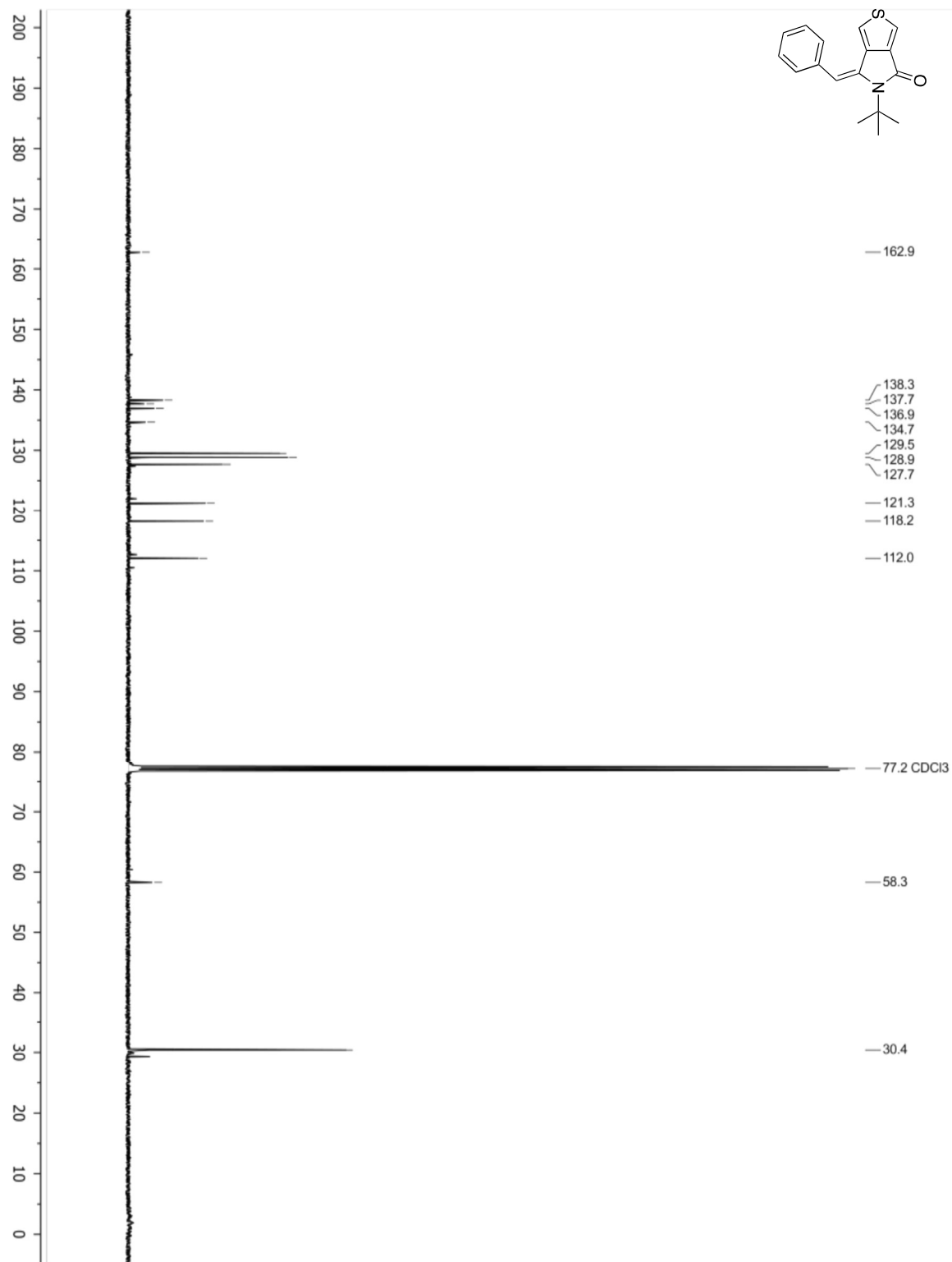
69: ^{13}C NMR



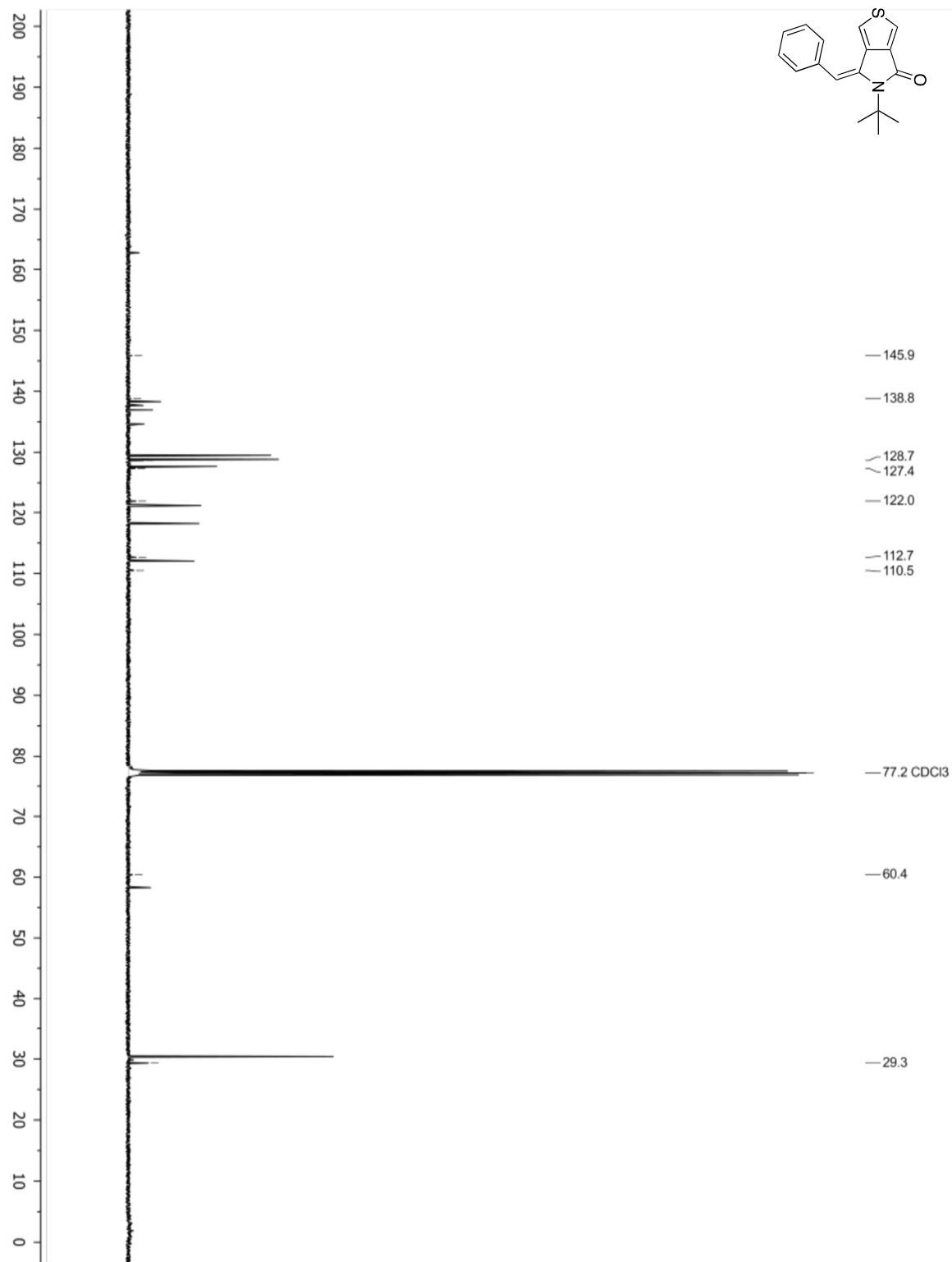
71: ^1H NMR



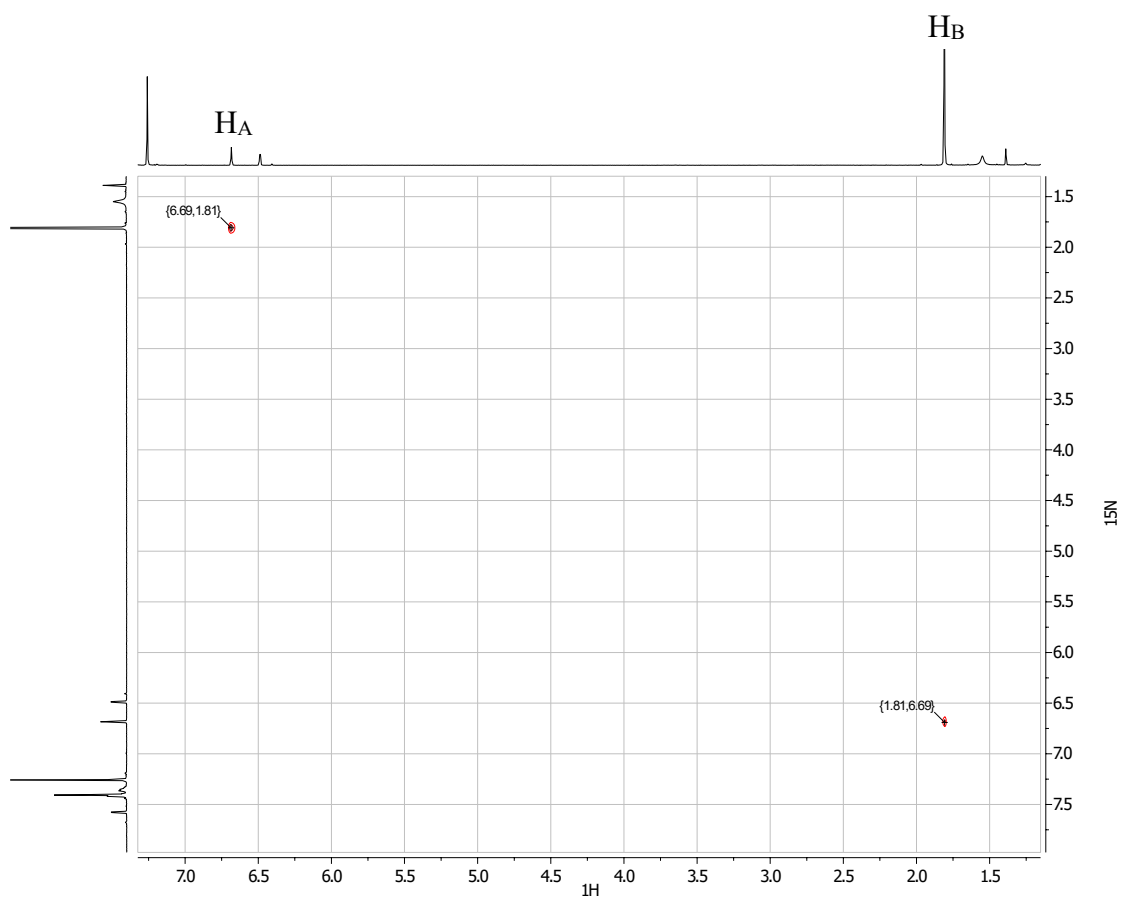
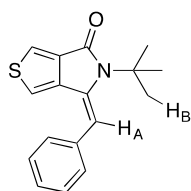
71: ^{13}C NMR (E isomer)



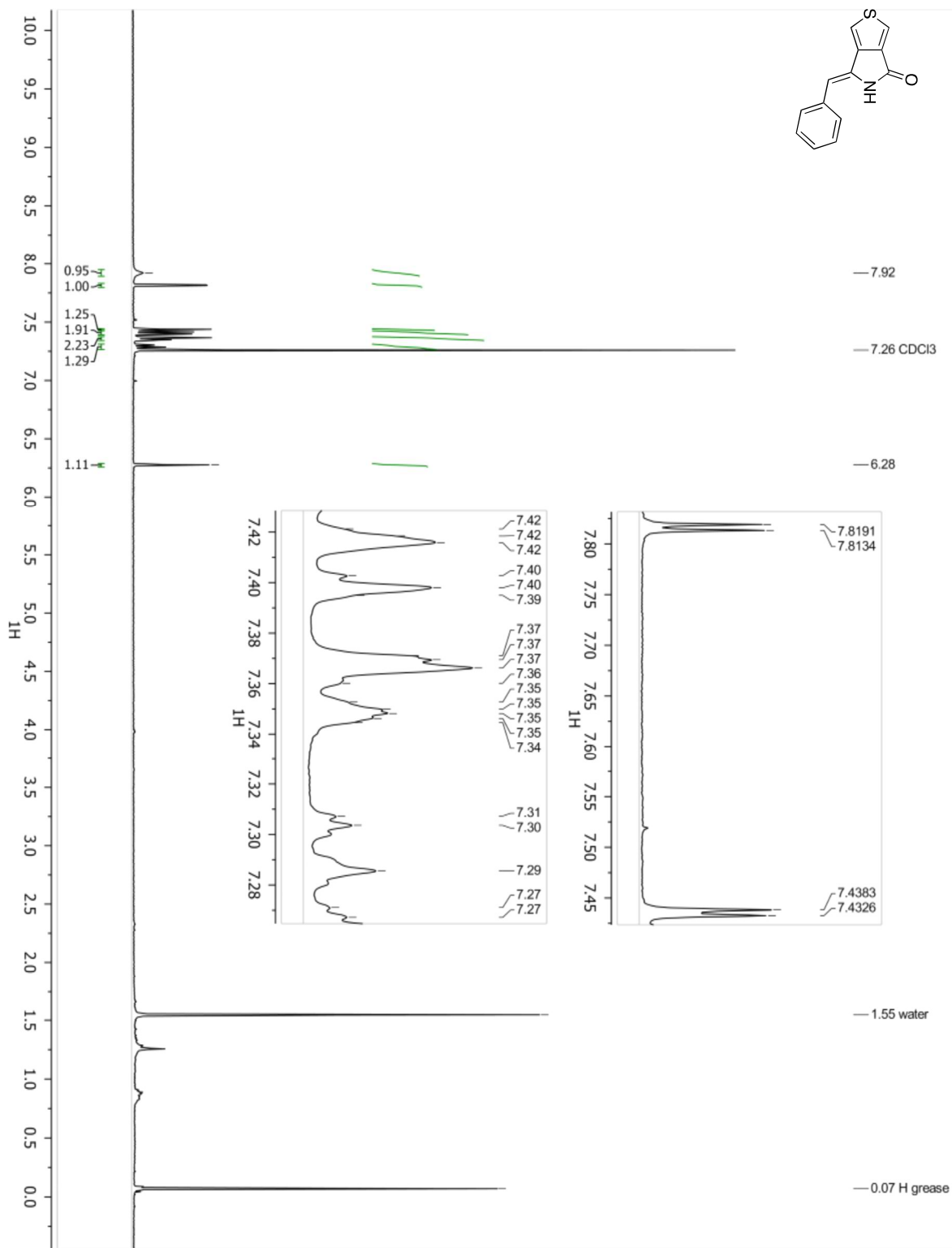
71: ^{13}C NMR (additional peaks from Z isomer)



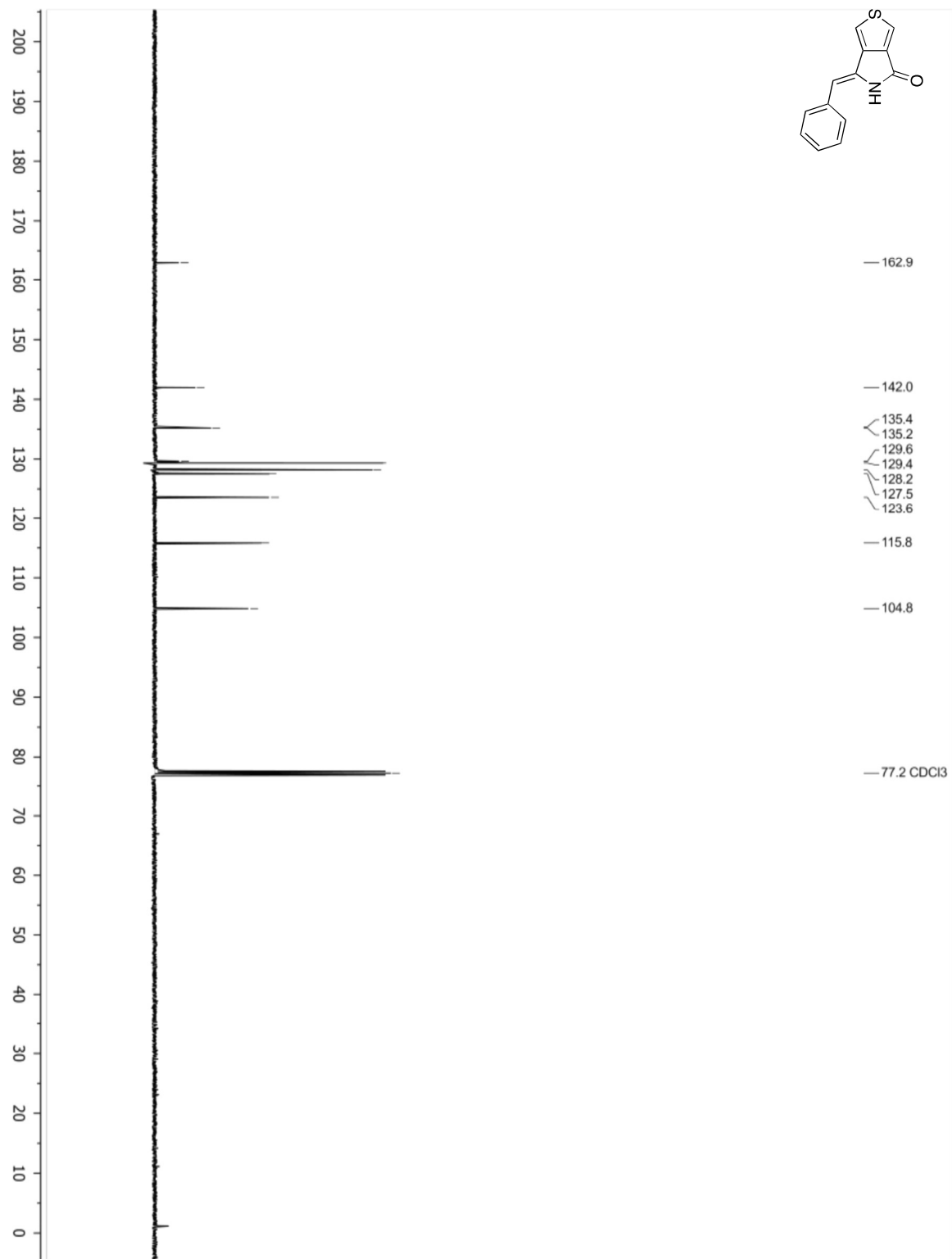
71: NOESY



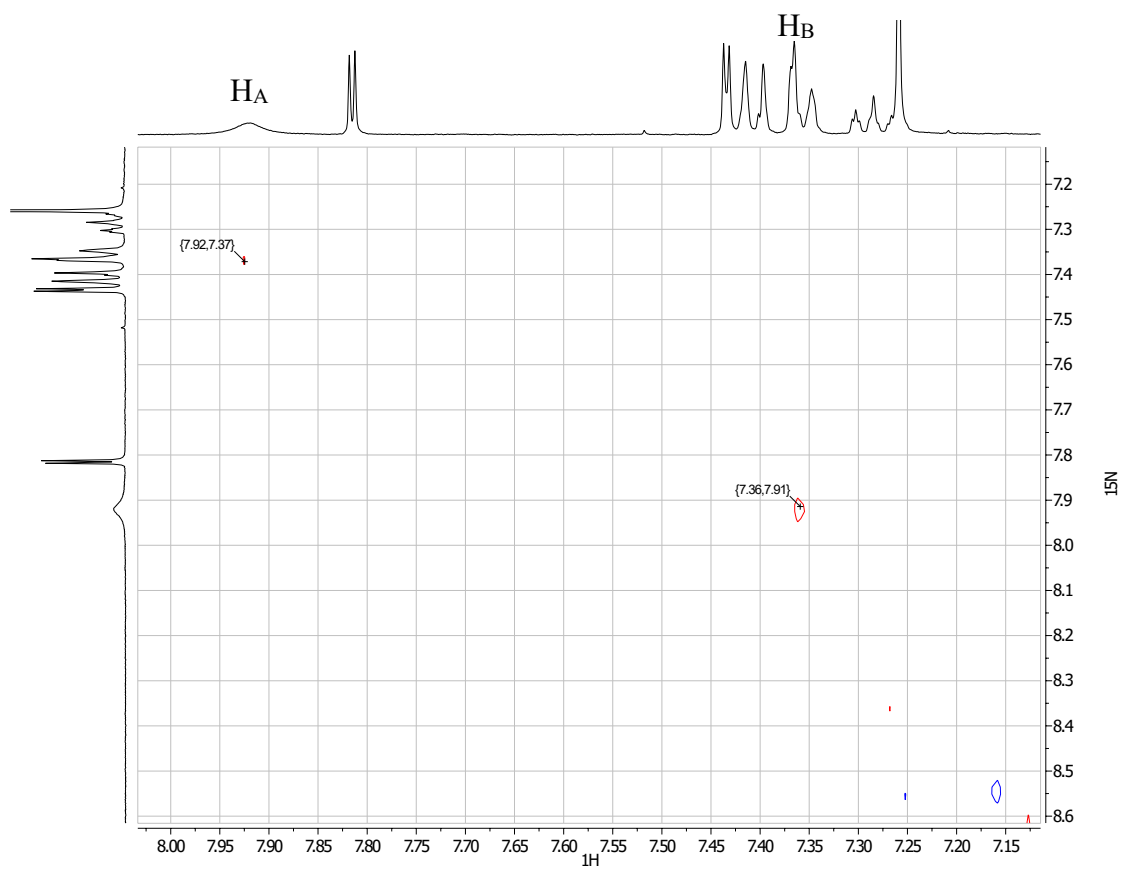
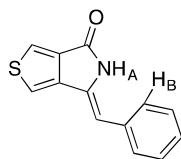
68: ^1H NMR



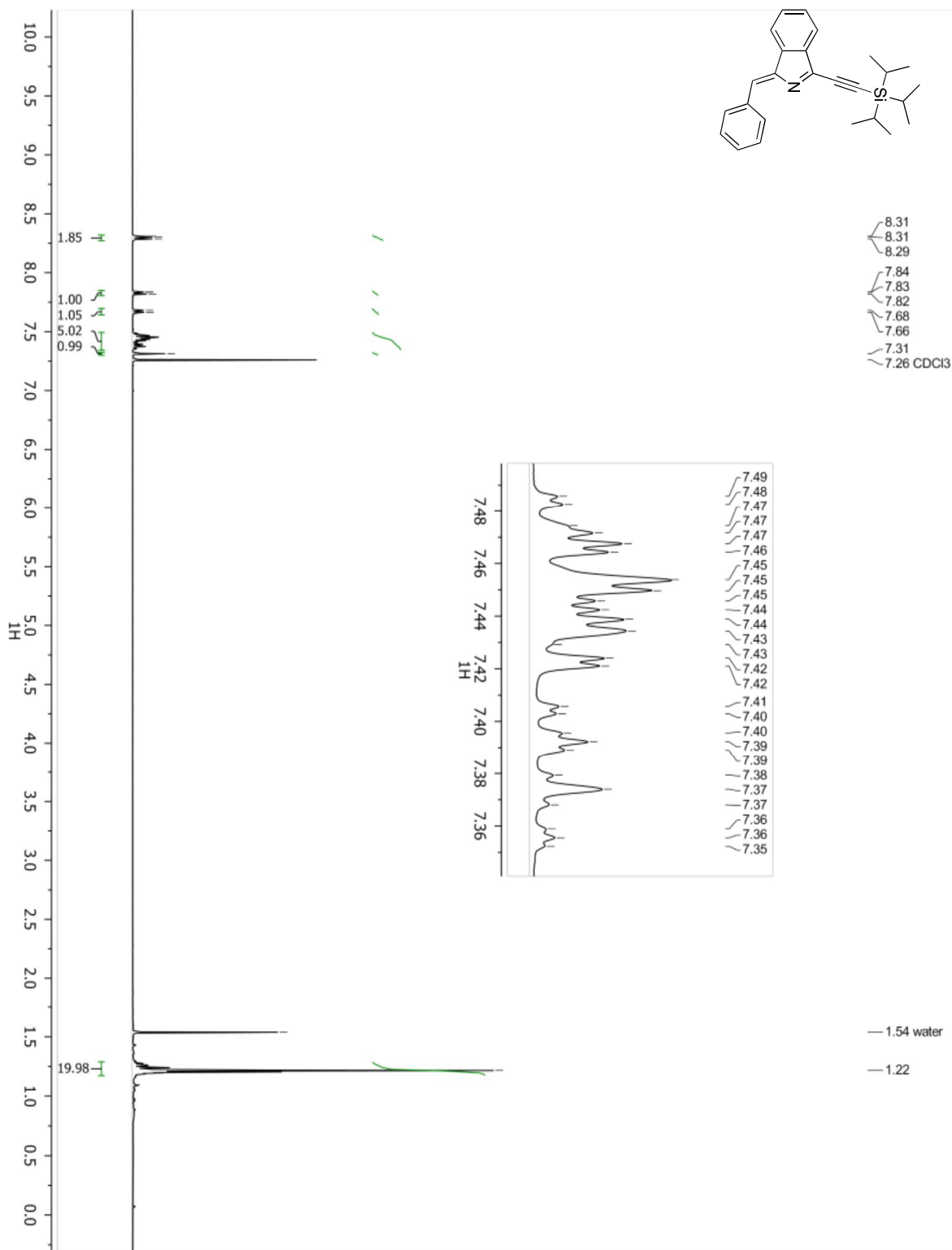
68: ^{13}C NMR



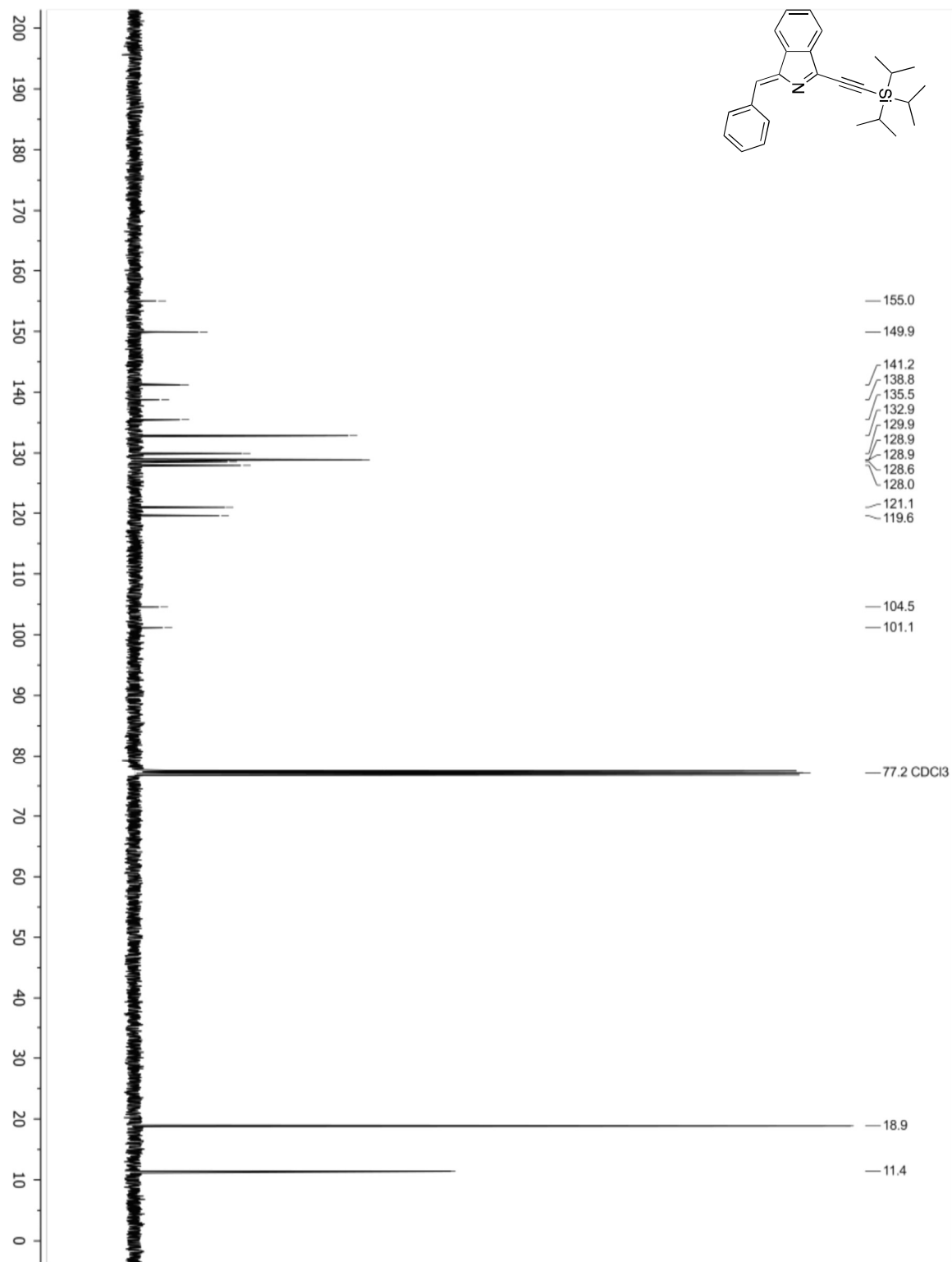
68: NOESY



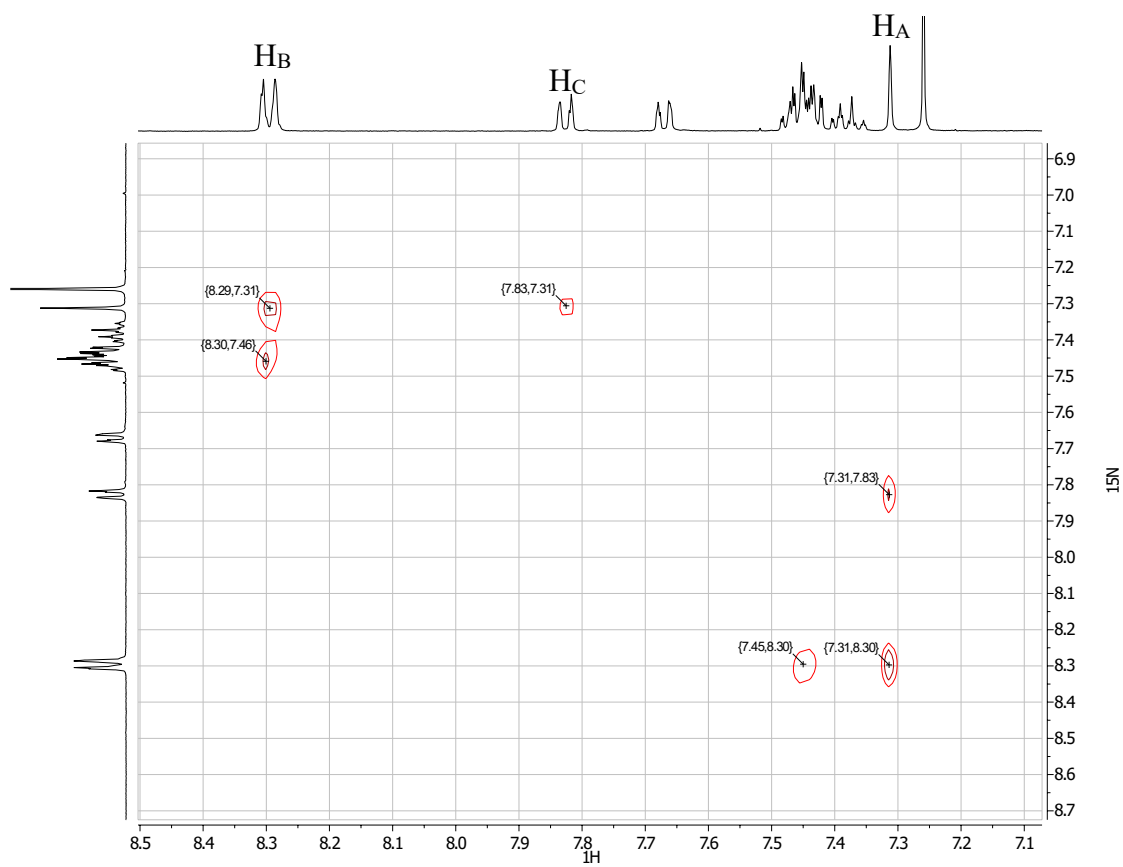
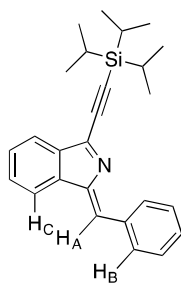
33: ^1H NMR



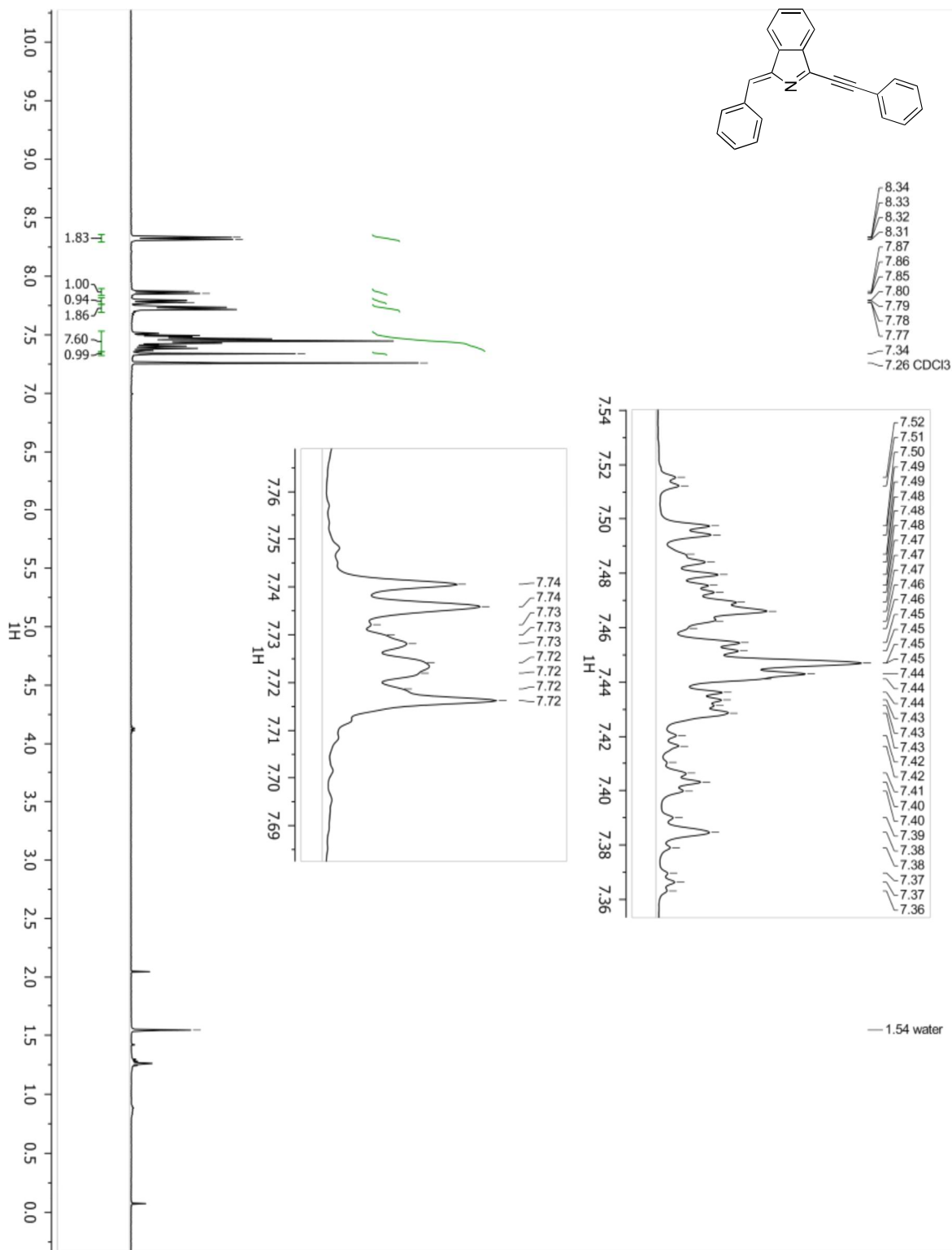
33: ^{13}C NMR



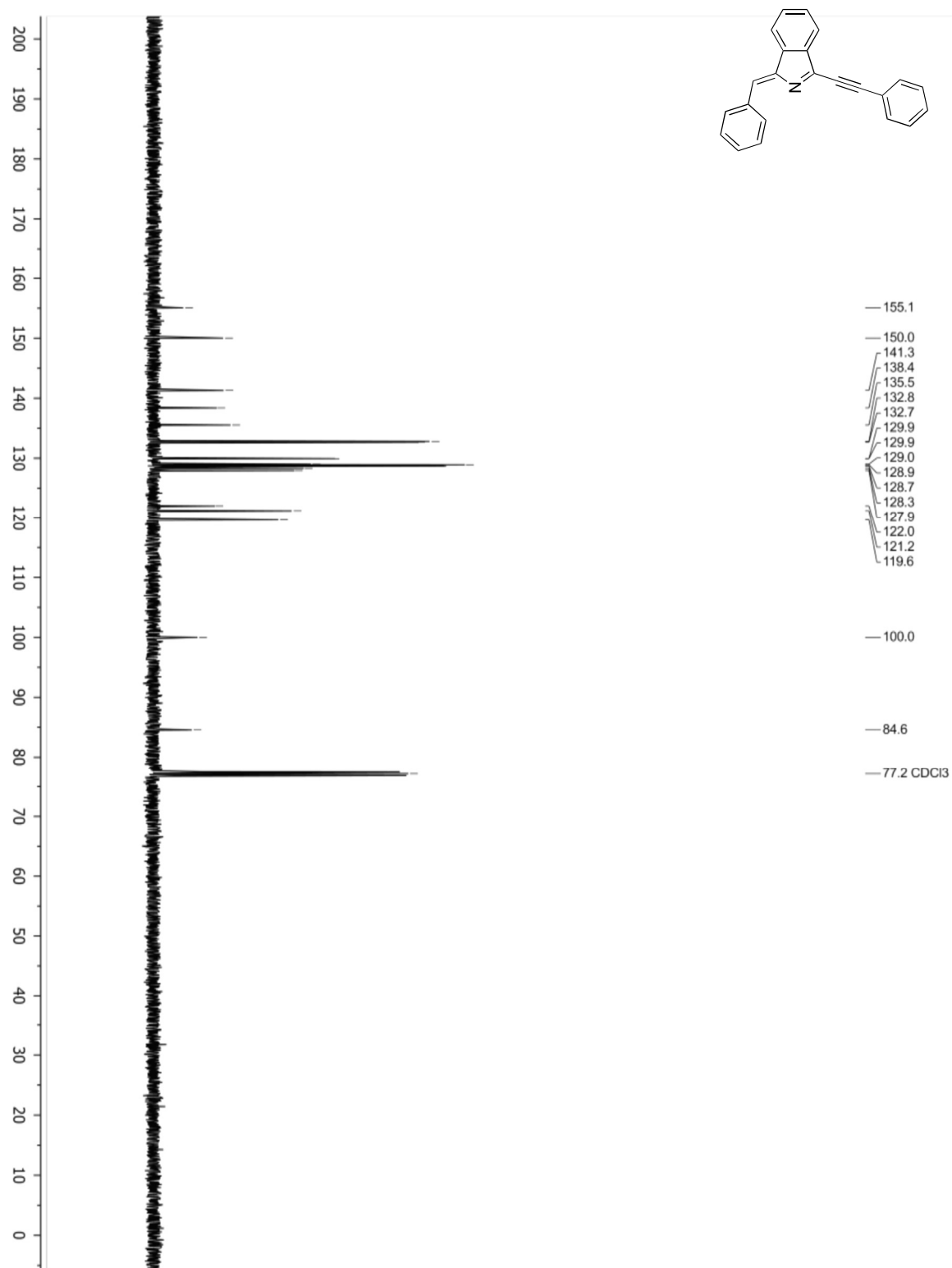
33: NOESY



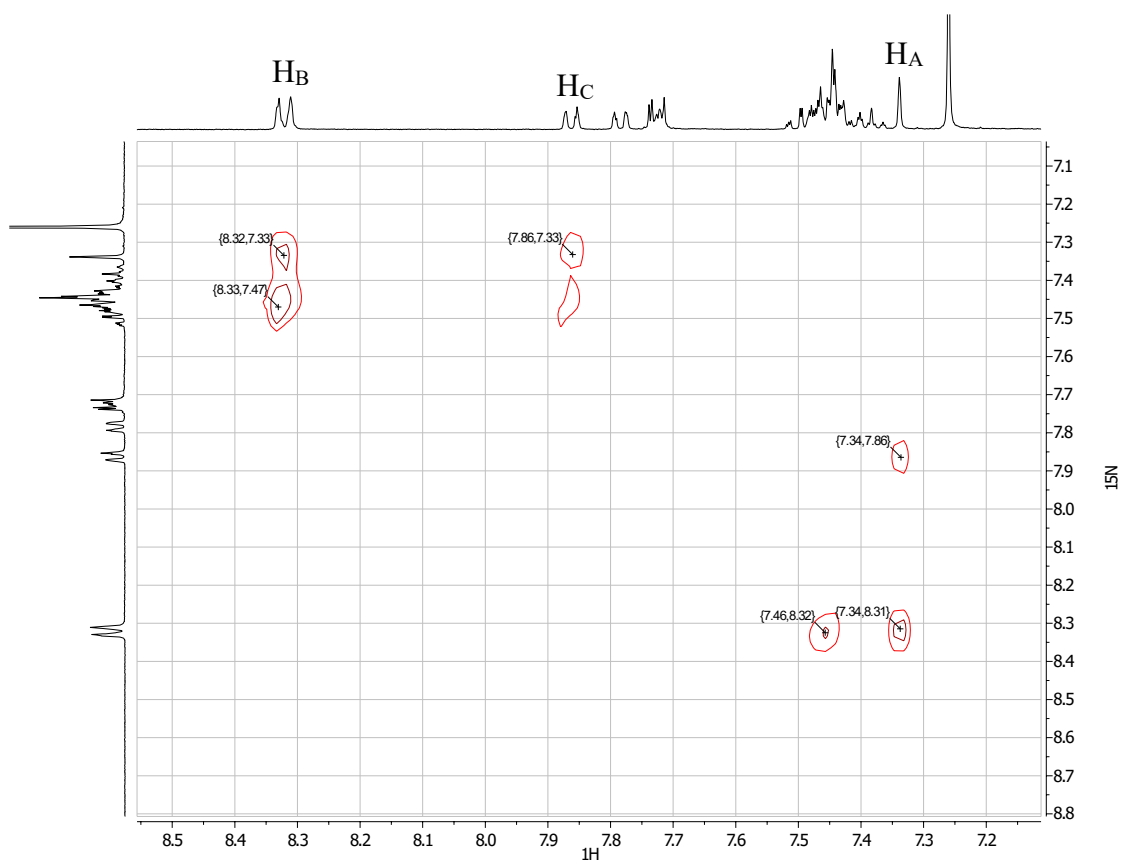
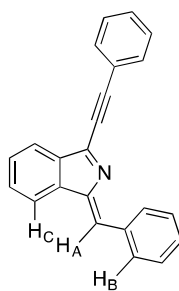
34: ^1H NMR



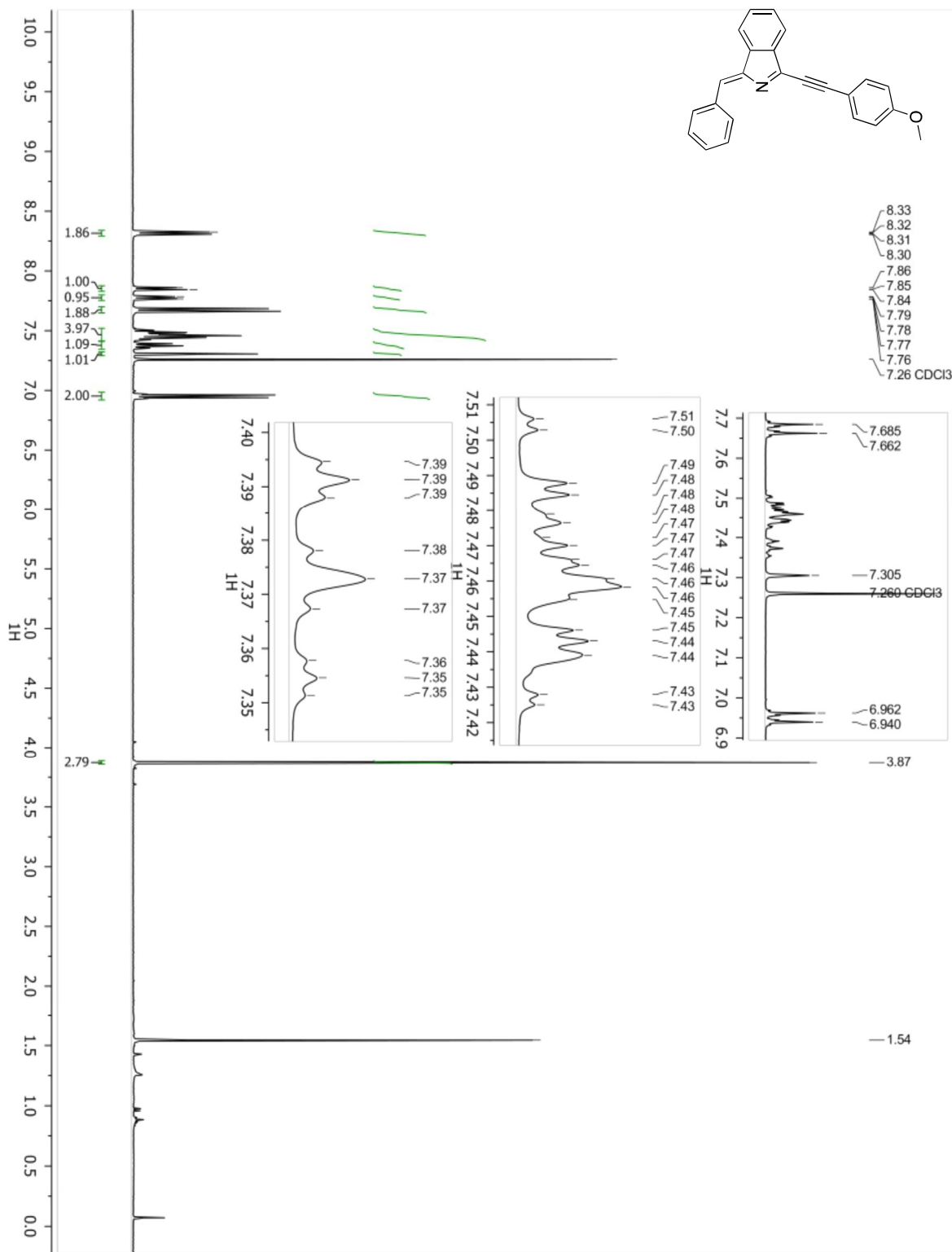
34: ^{13}C NMR



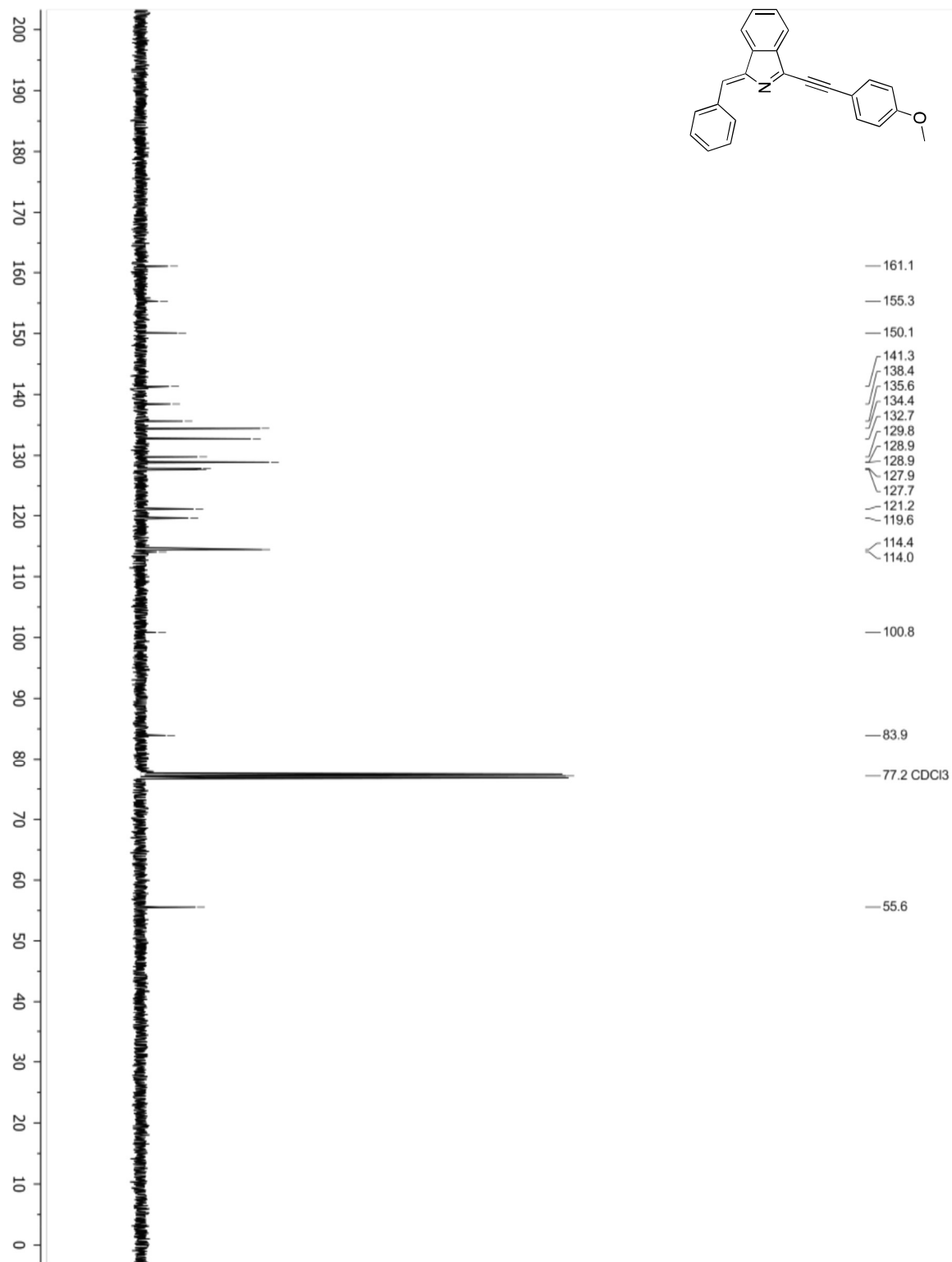
34: NOESY



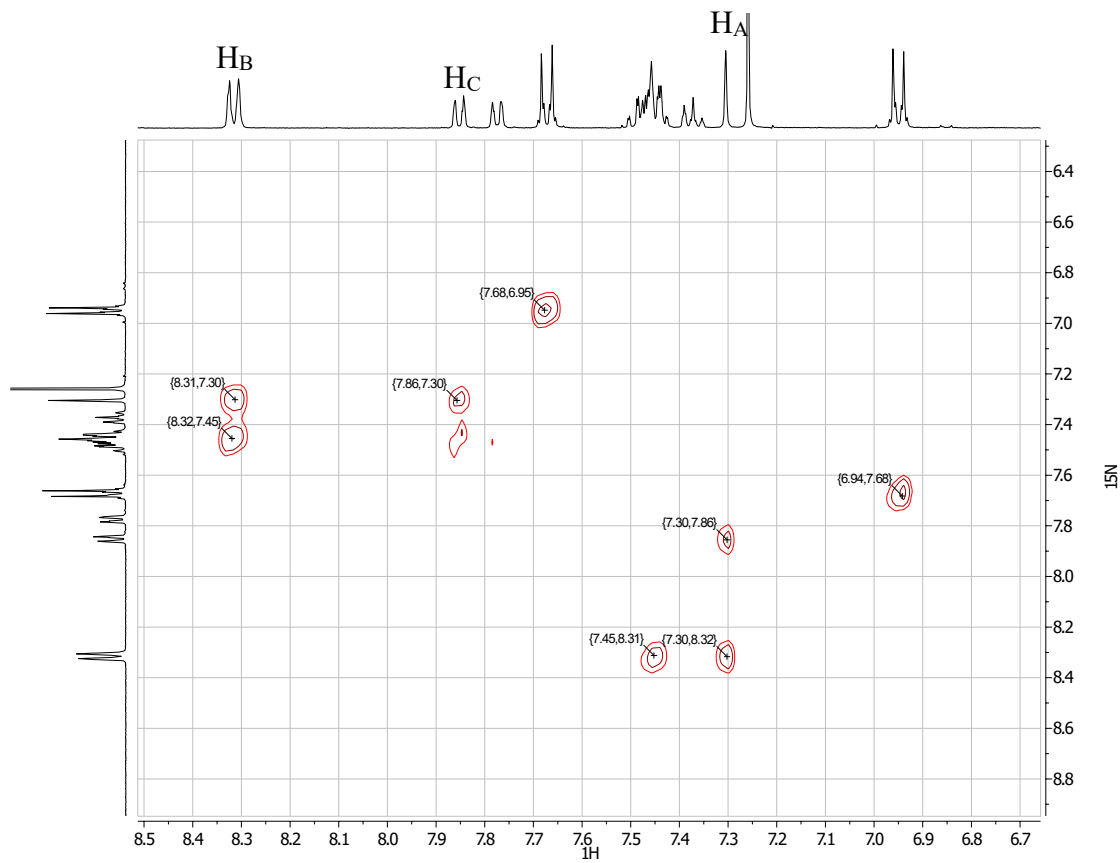
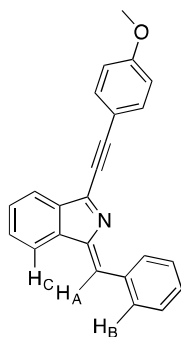
35: ^1H NMR



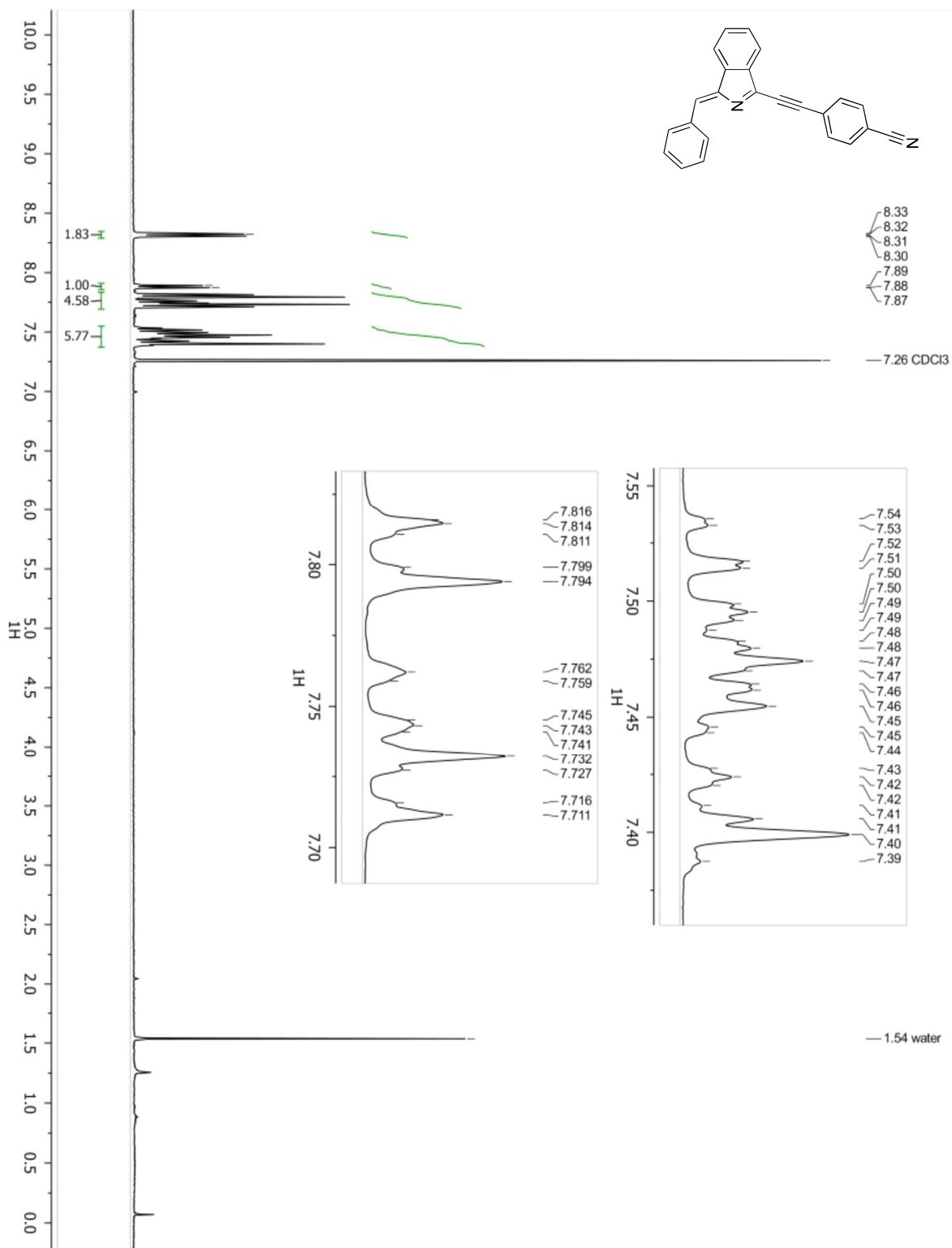
35: ^{13}C NMR



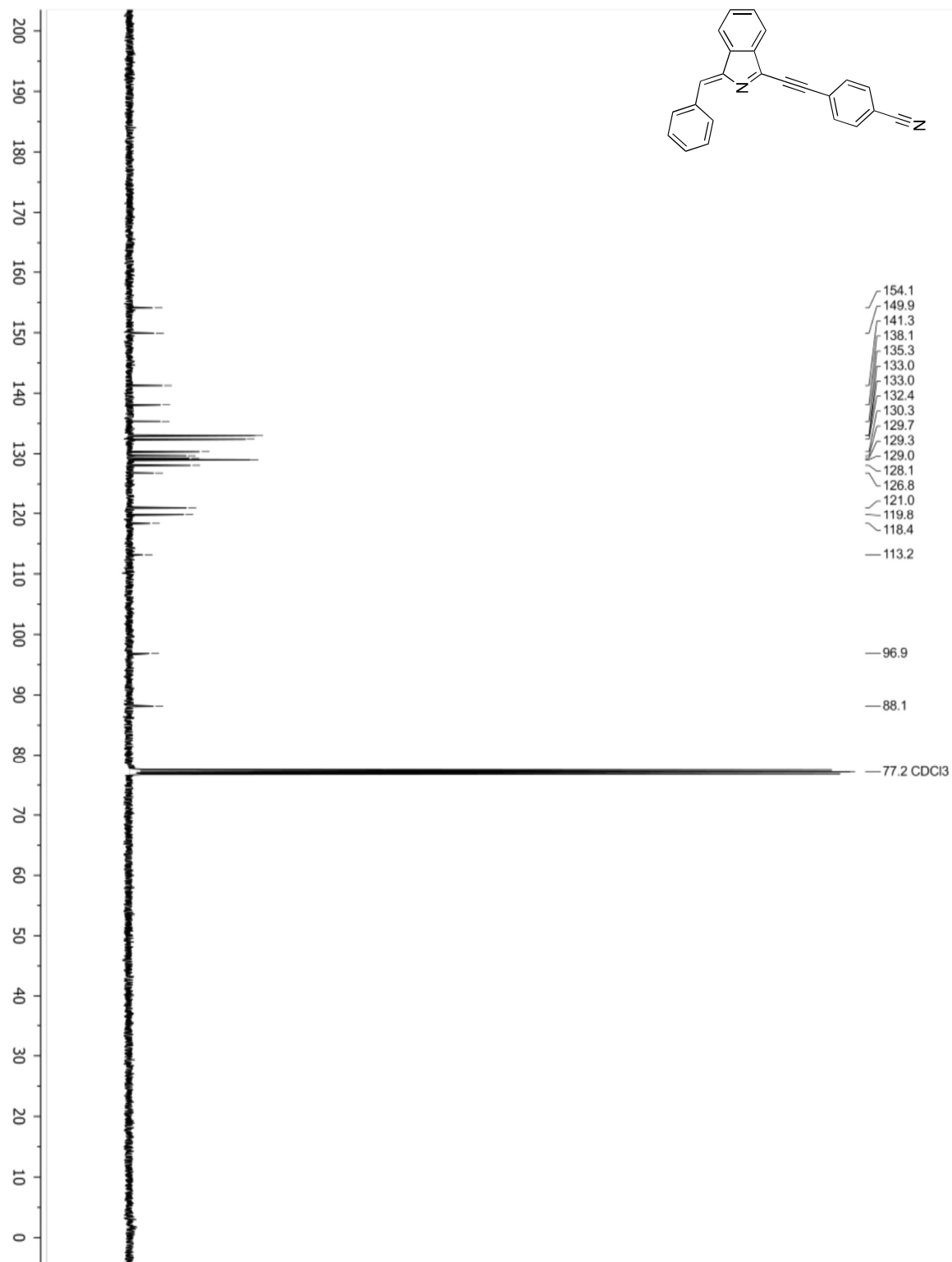
35: NOESY



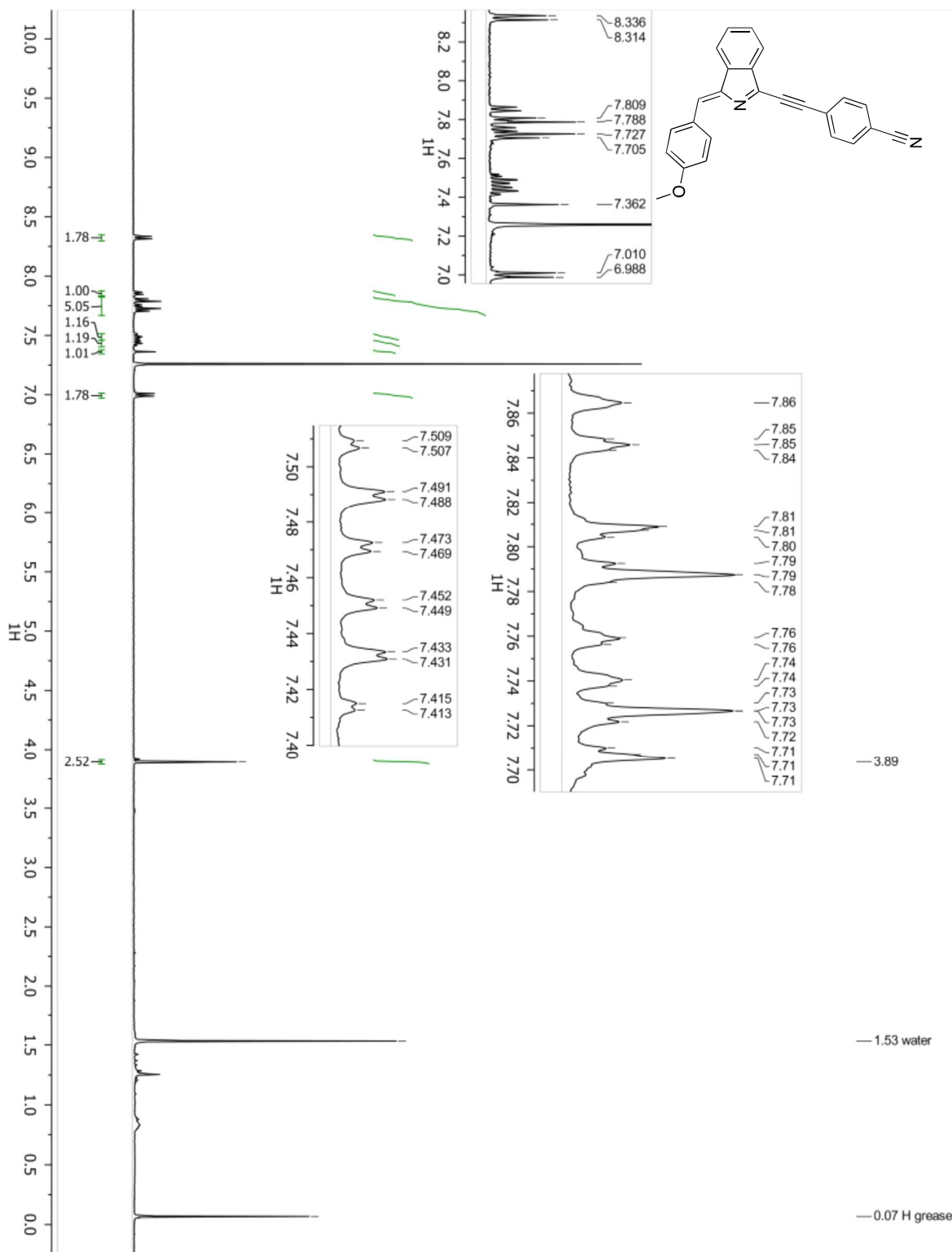
36: ^1H NMR



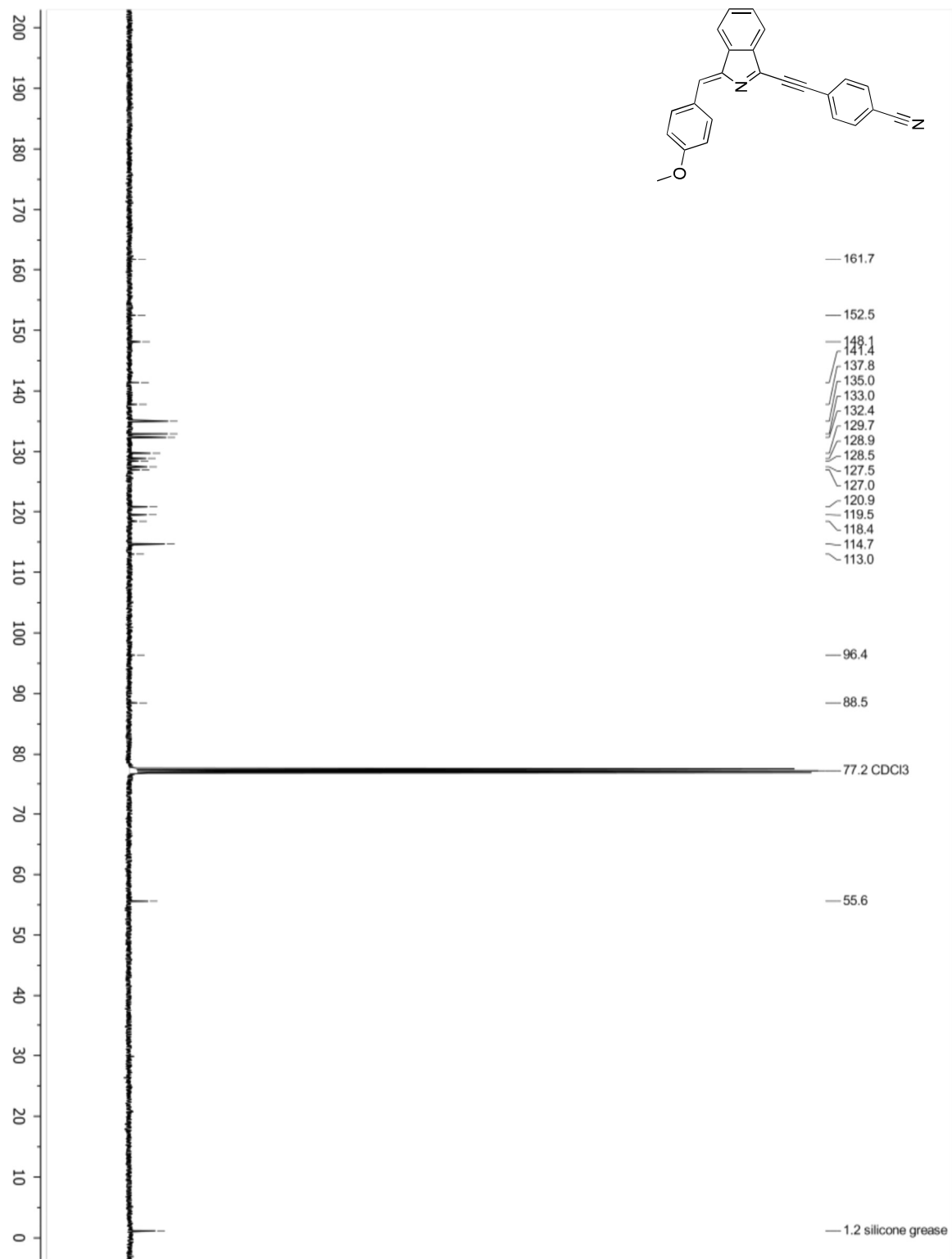
36: ^{13}C NMR



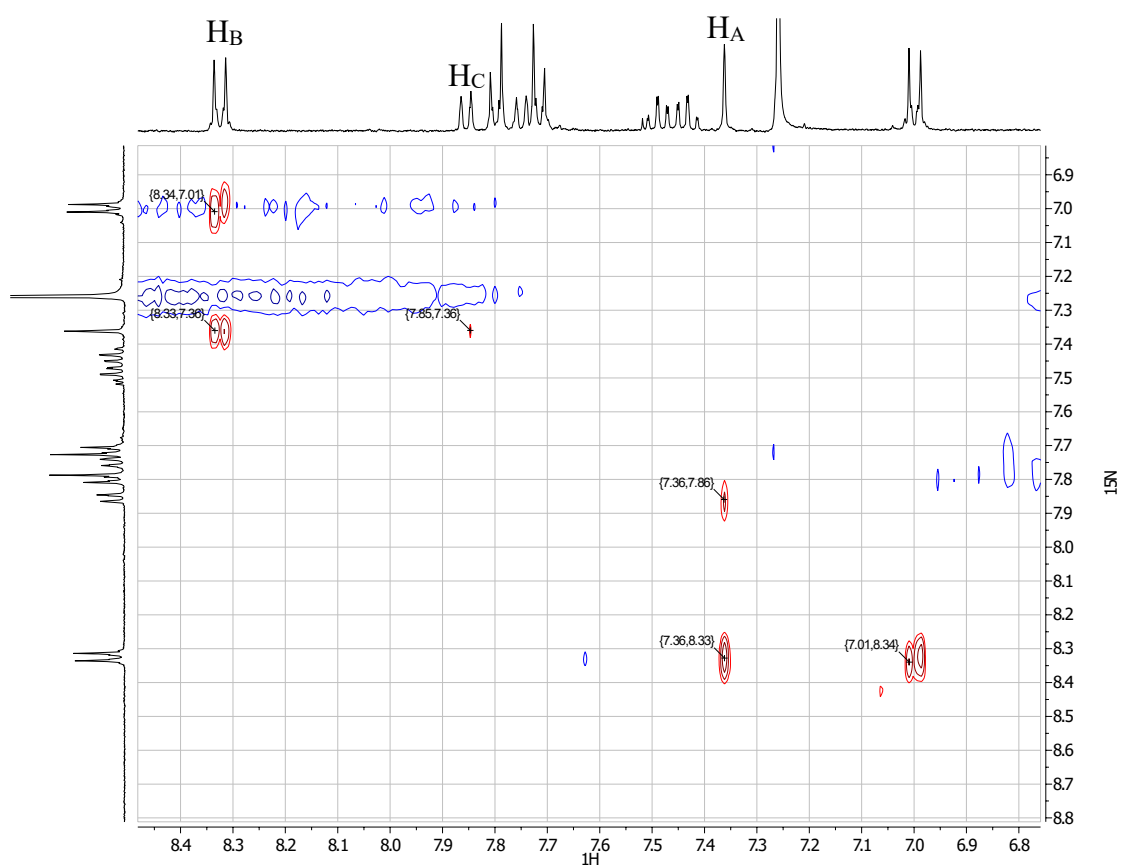
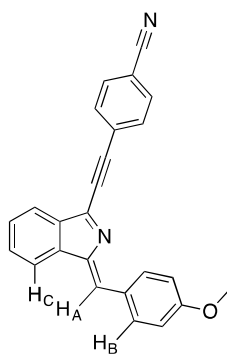
44: ^1H NMR



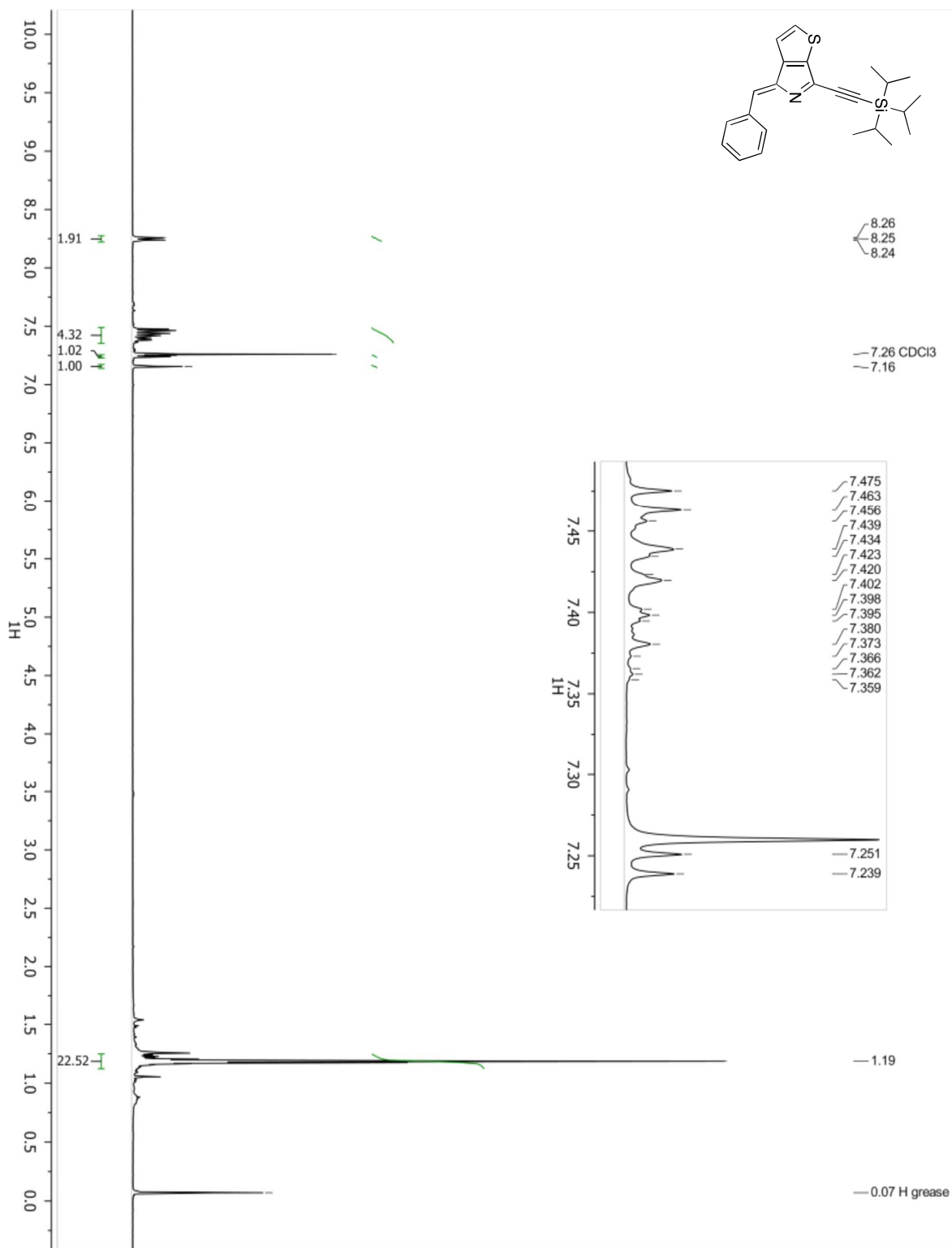
44: ^{13}C NMR



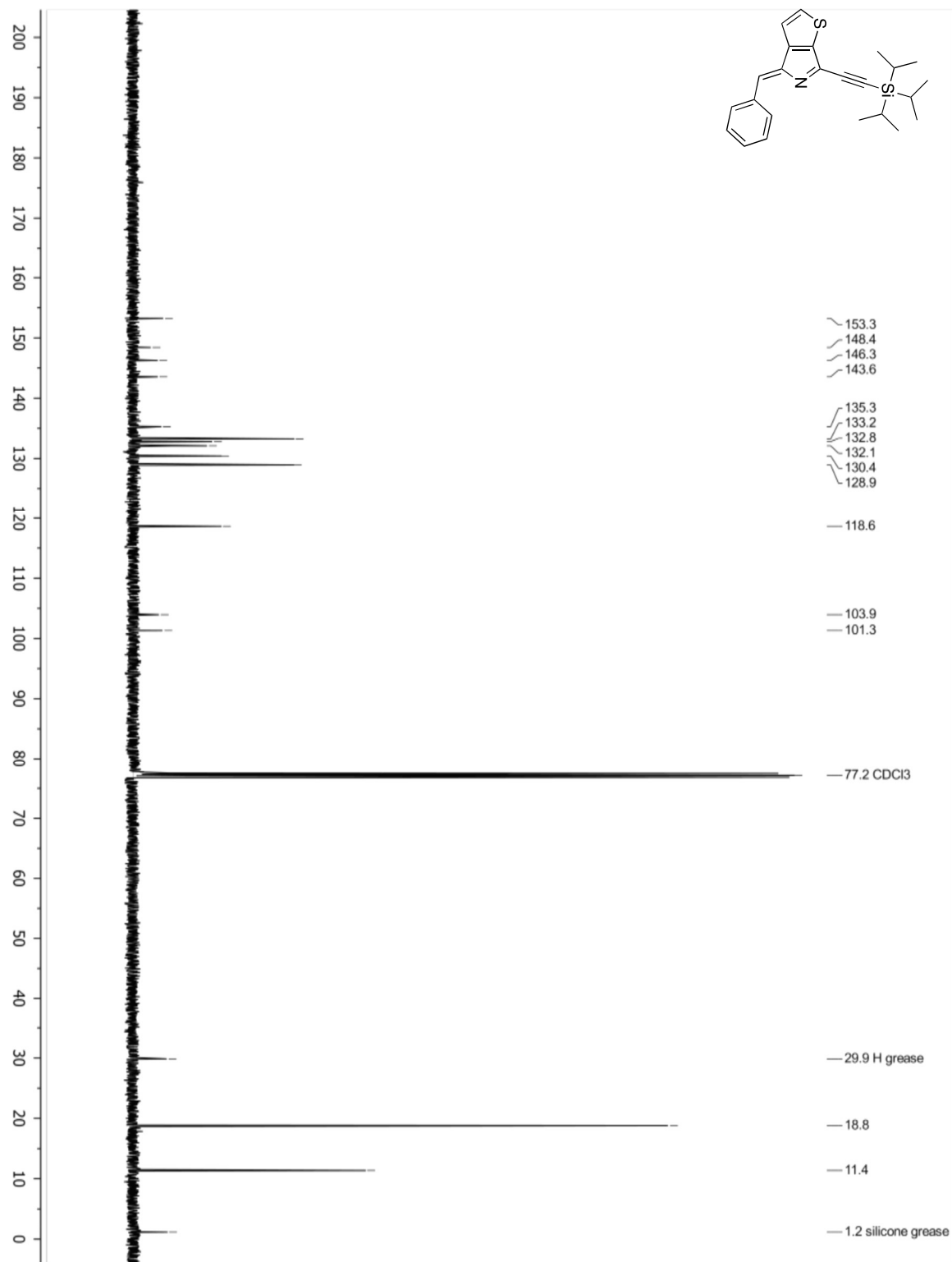
44: NOESY



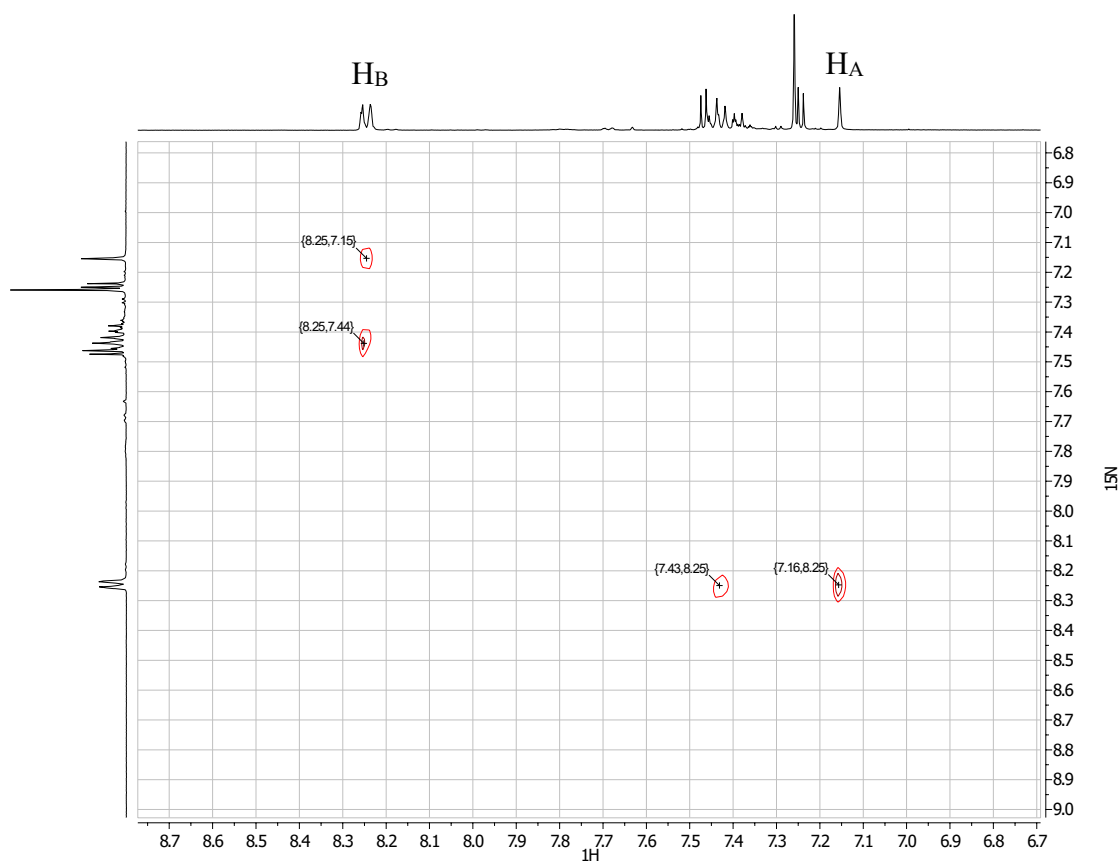
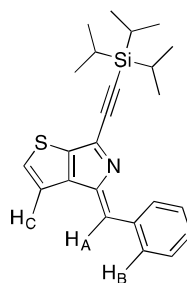
62: ^1H NMR



62: ^{13}C NMR

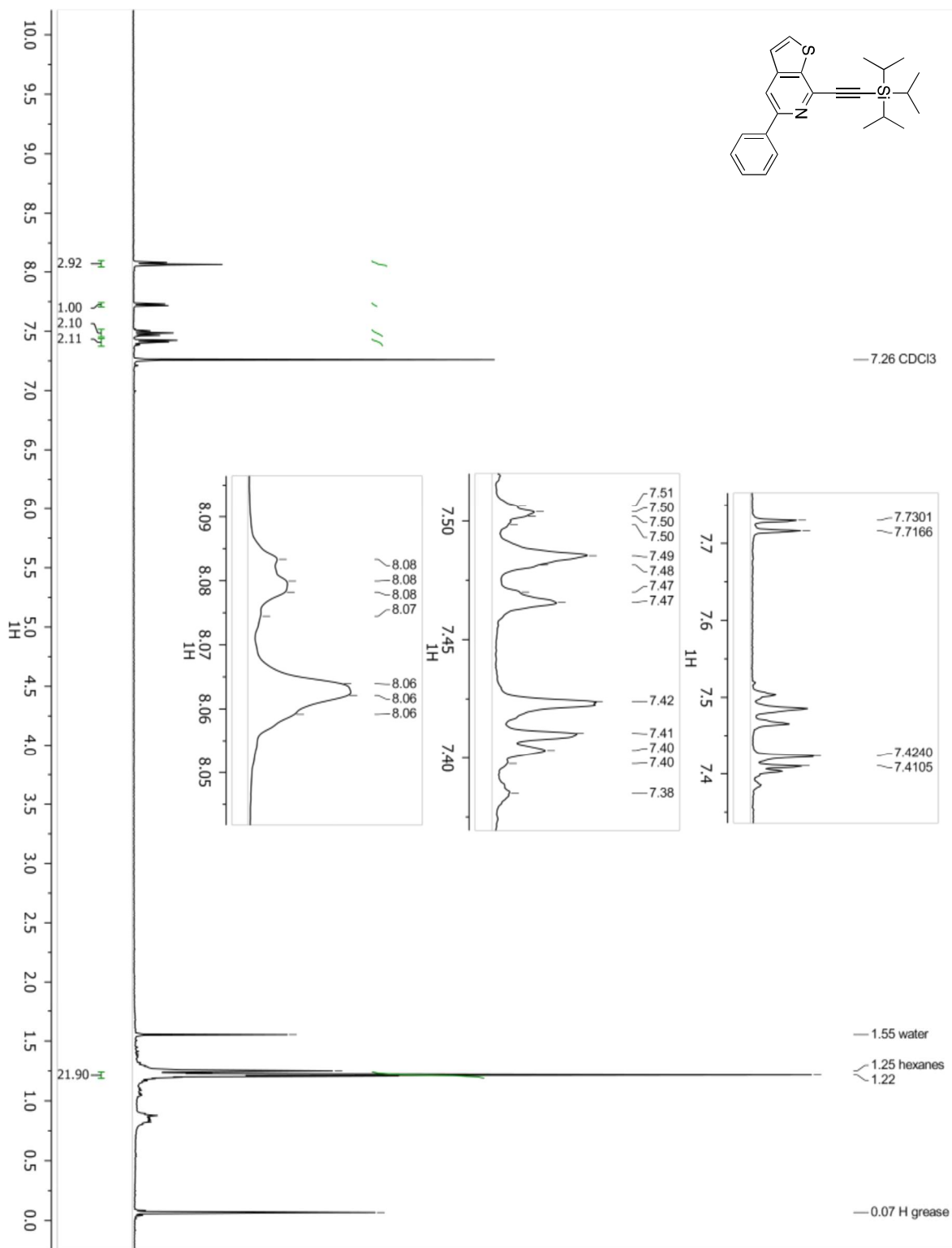


62: NOESY

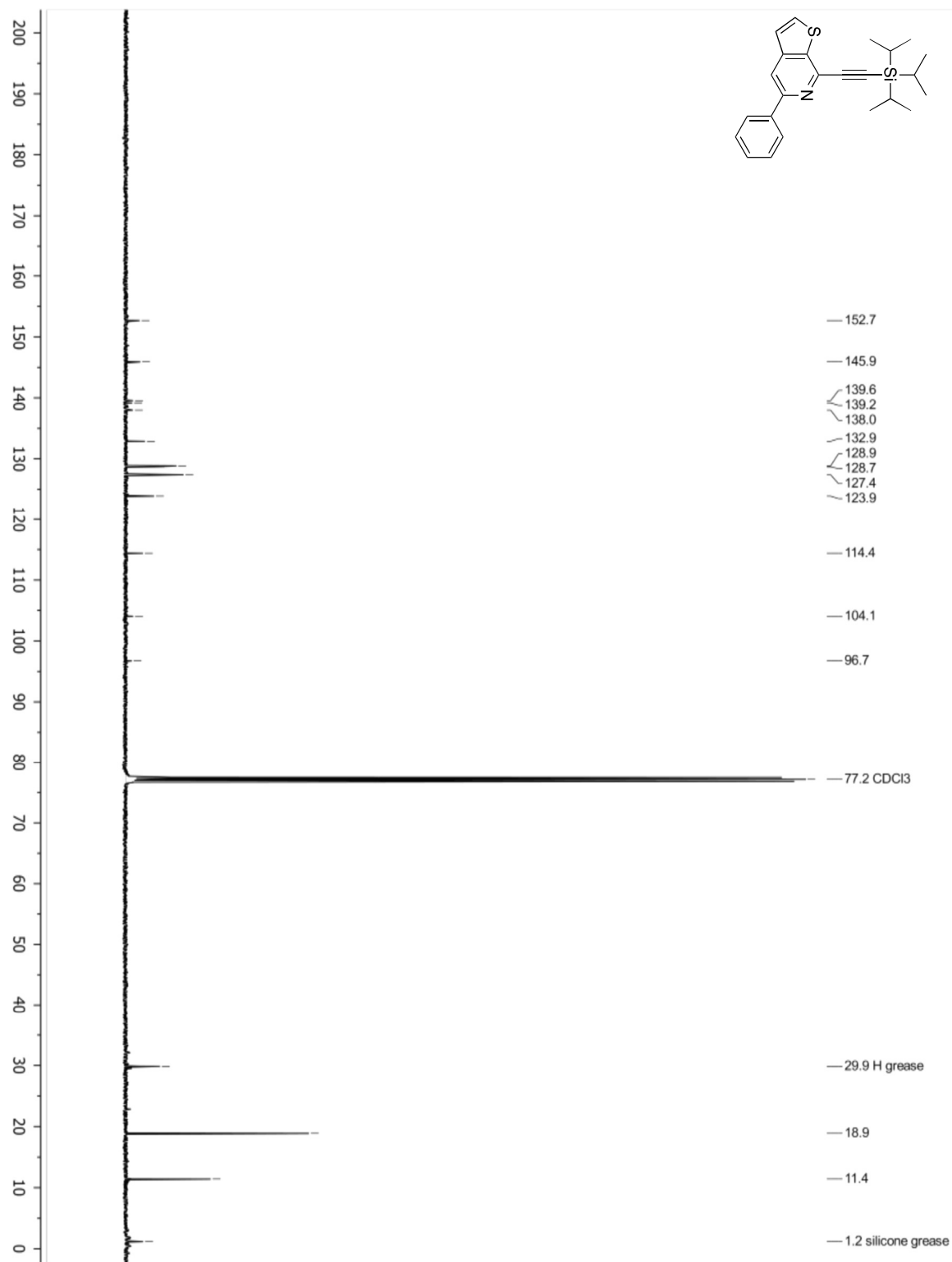


The absence of a correlation between H_B and a thiophene doublet (H_C) confirms the Z isomer

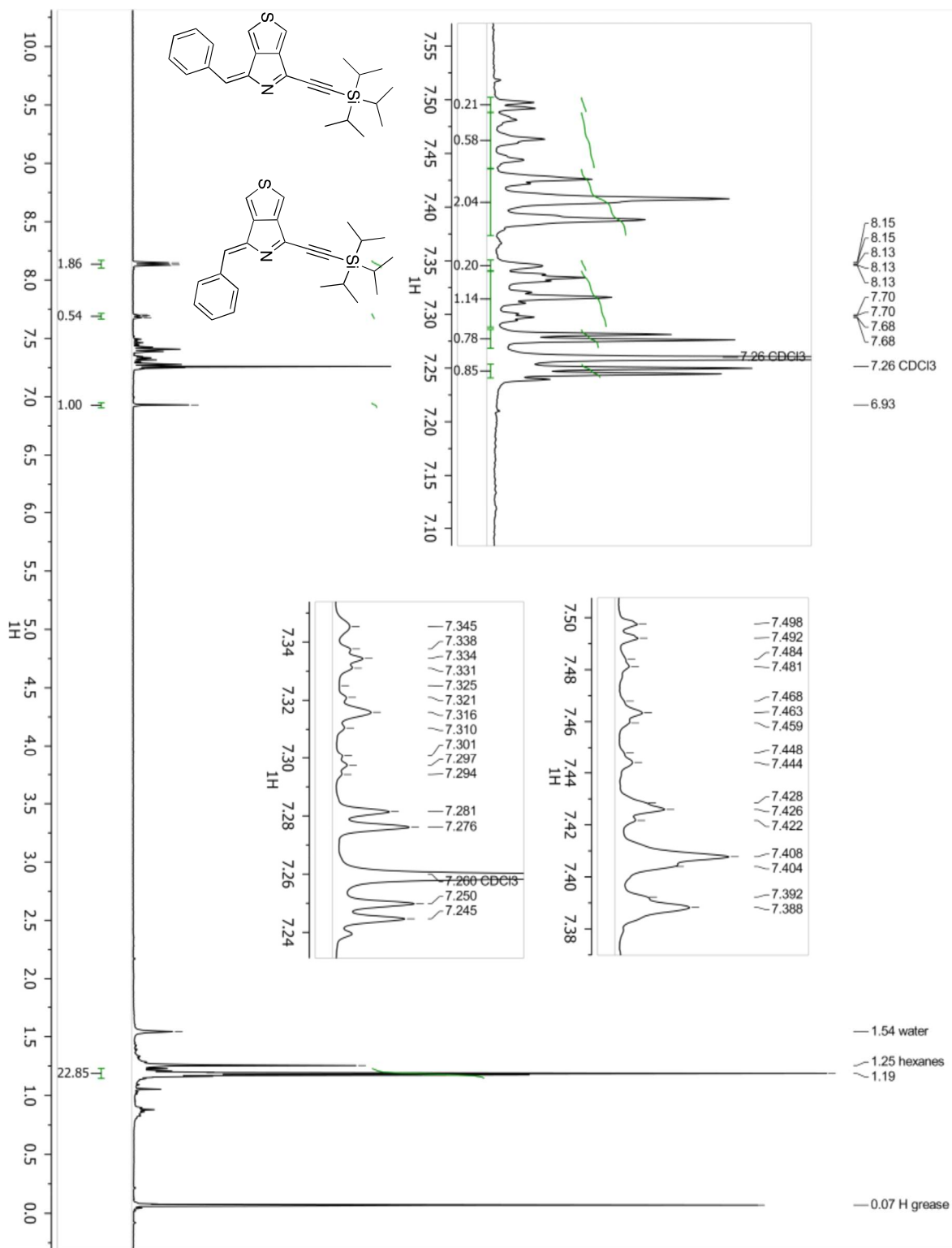
73: ^1H NMR



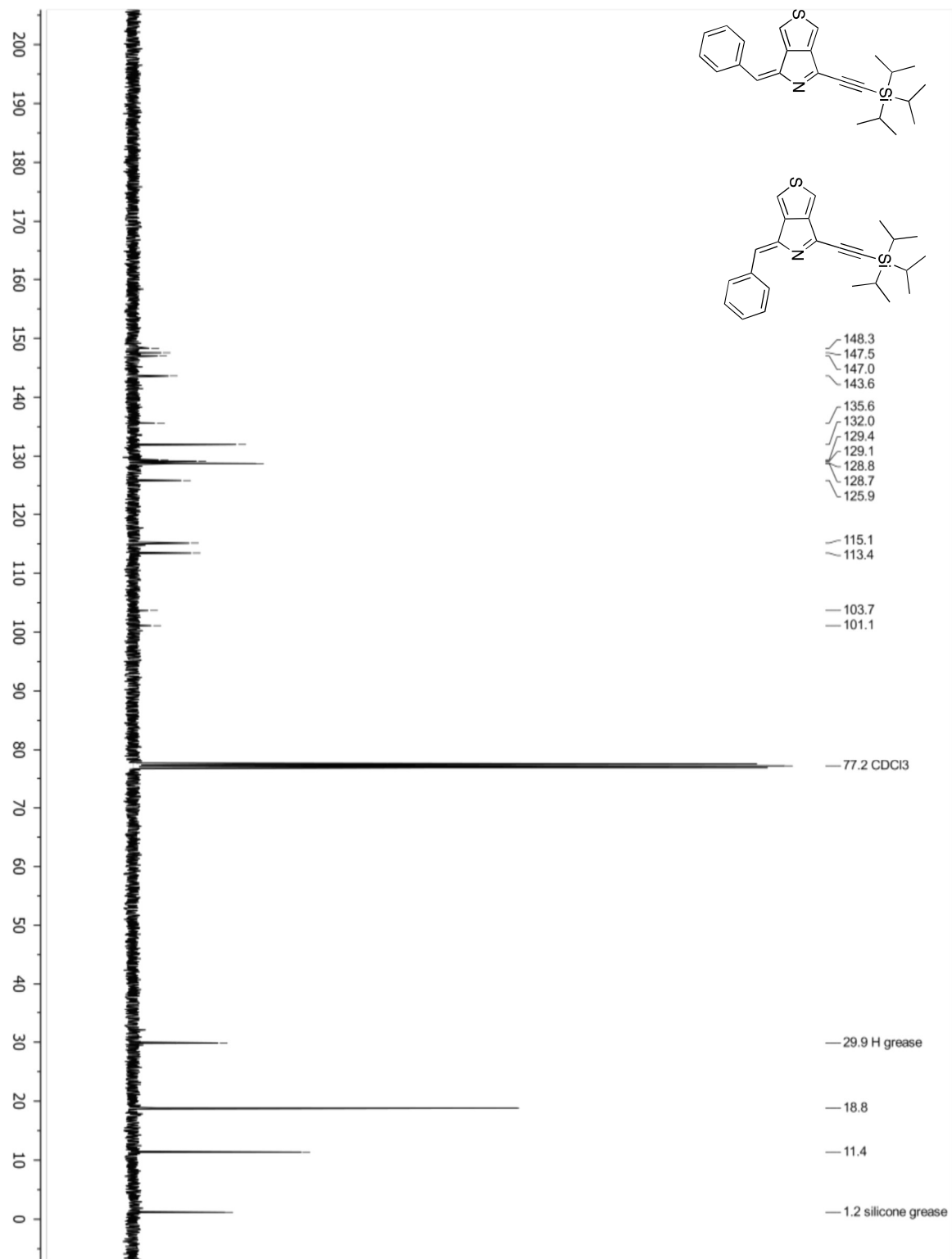
73: ^{13}C NMR



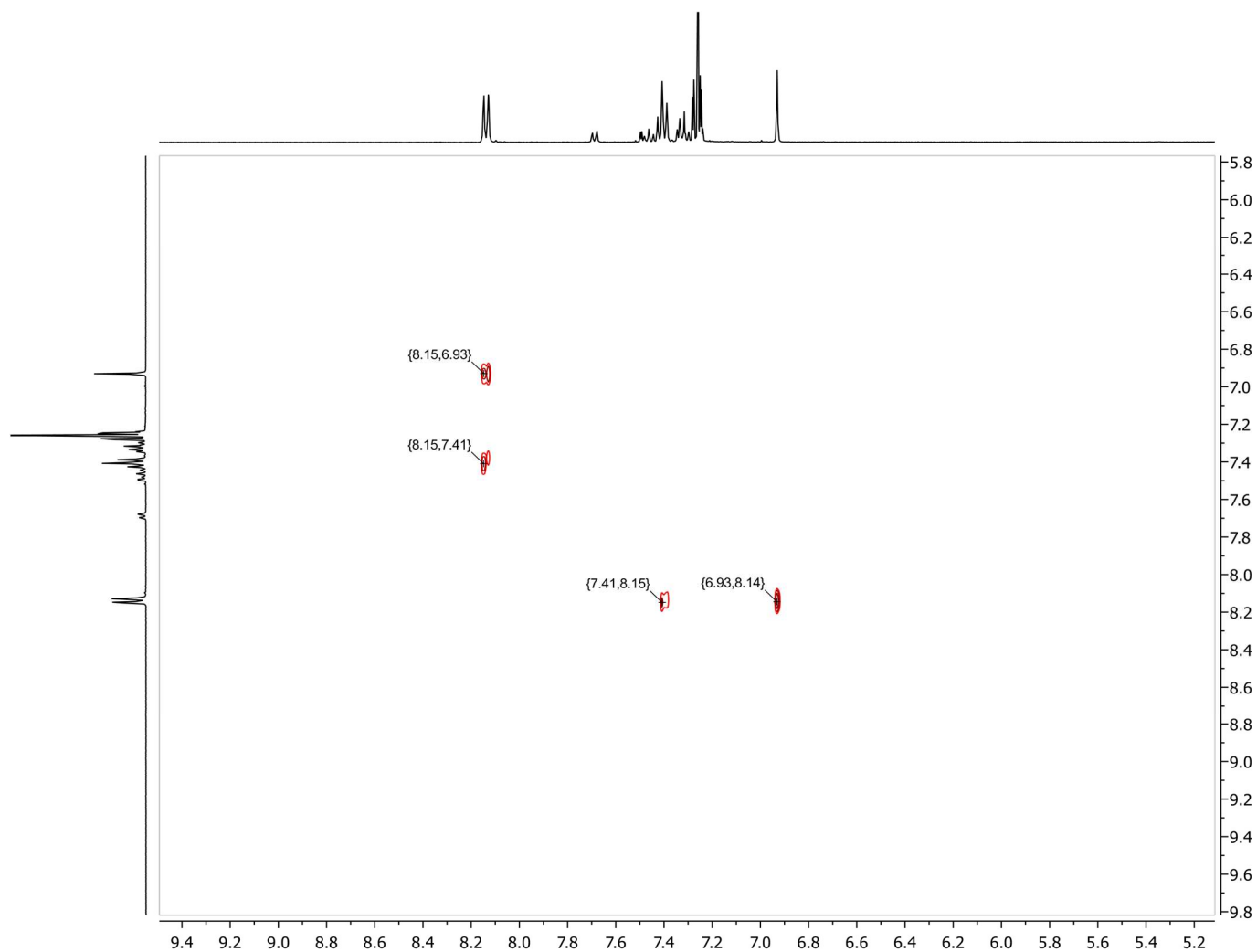
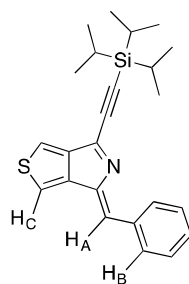
72: ^1H NMR



72: ^{13}C NMR

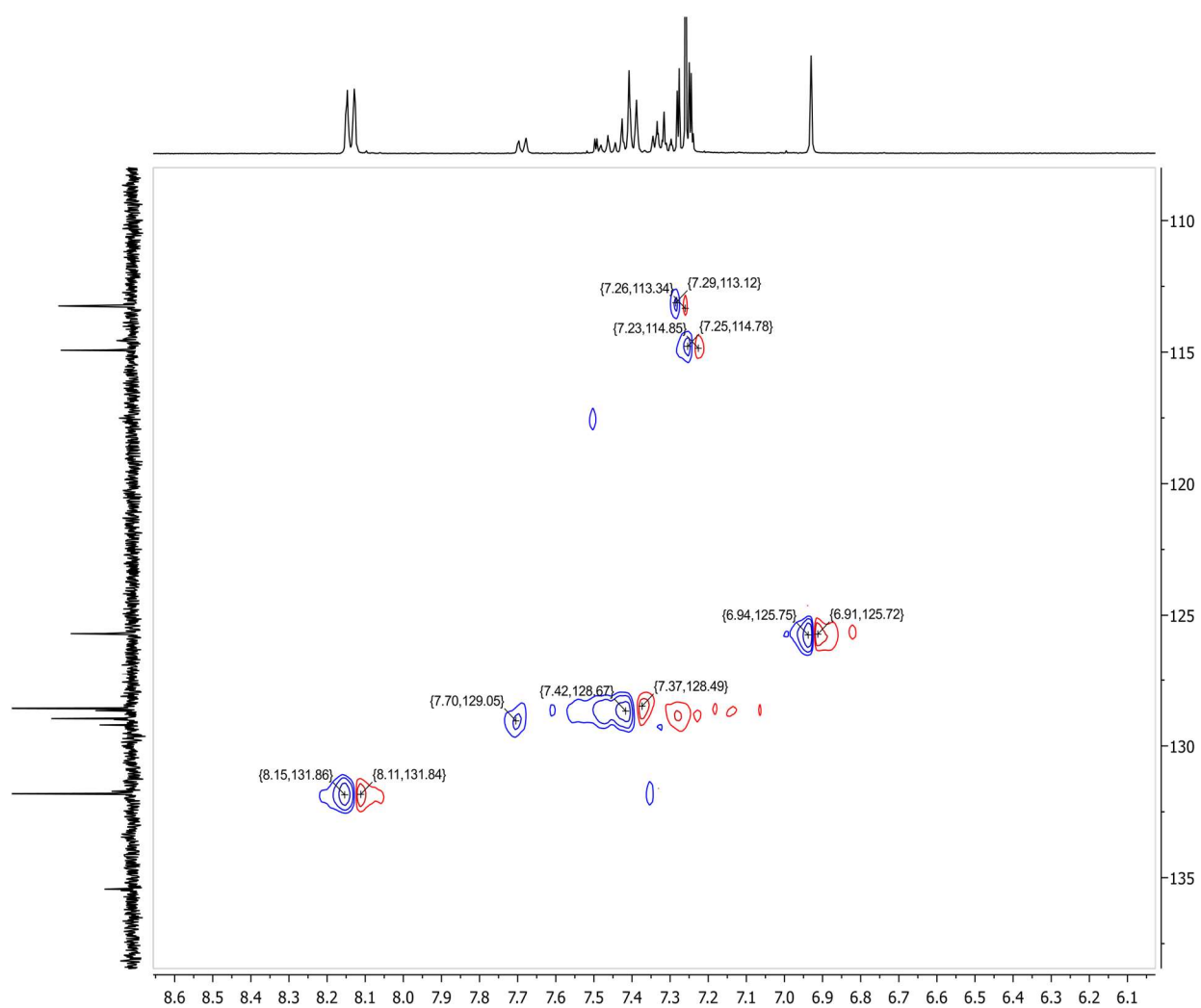
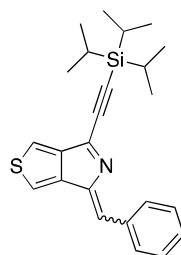


72: NOESY

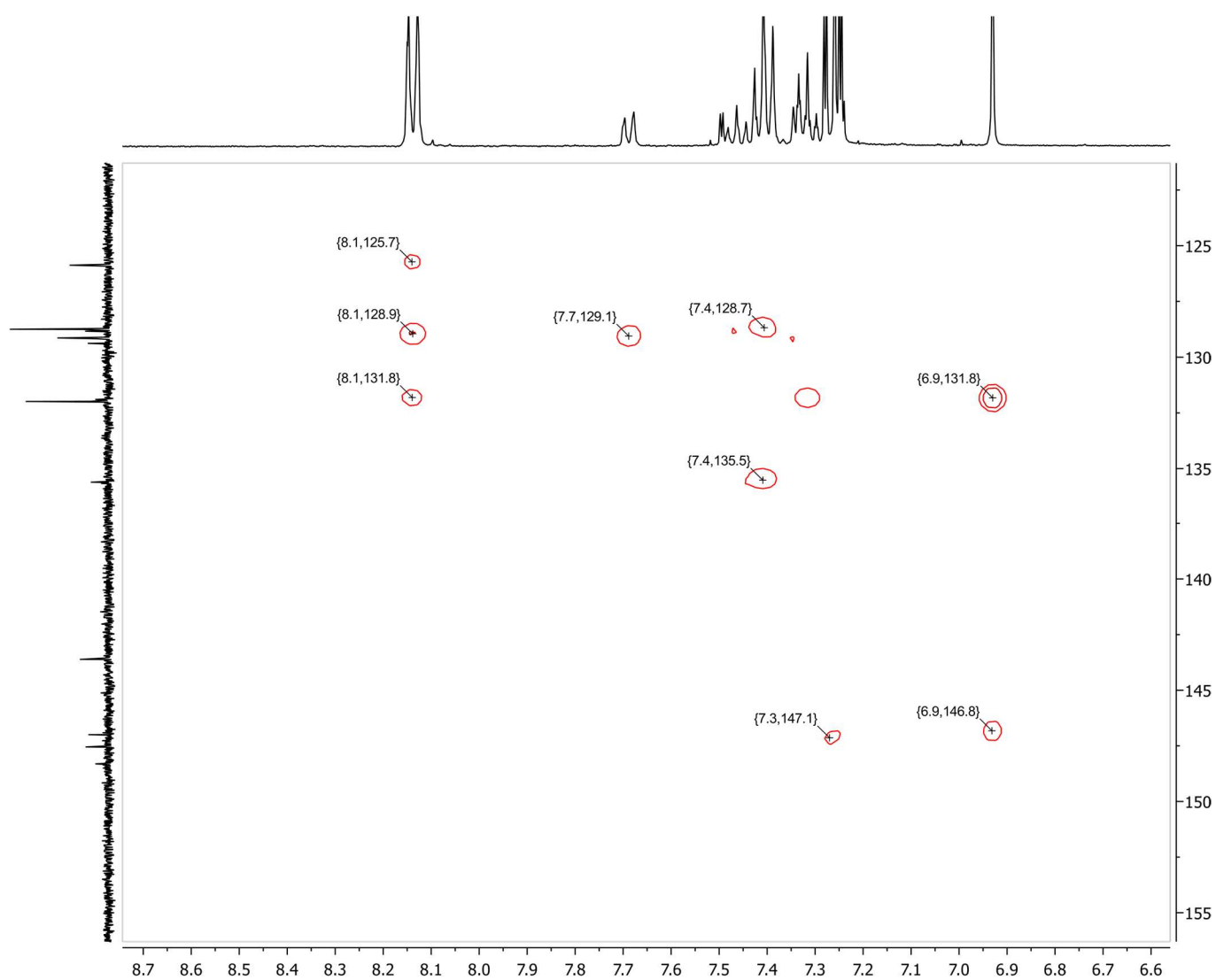
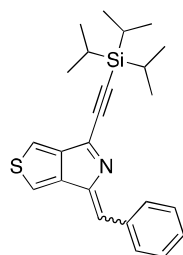


The absence of a correlation between H_B and a thiophene doublet (H_C) confirms the Z isomer

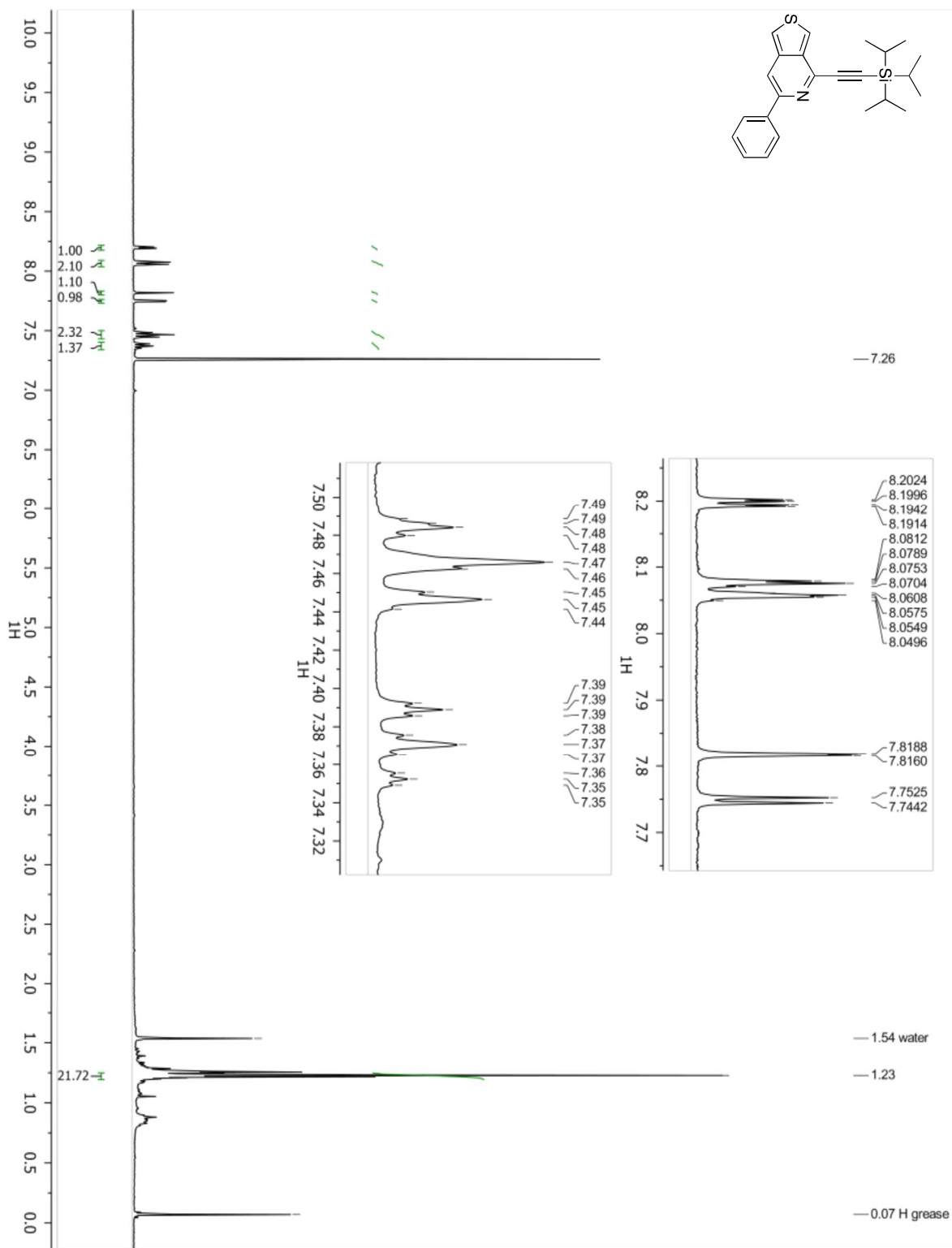
72: HSQC



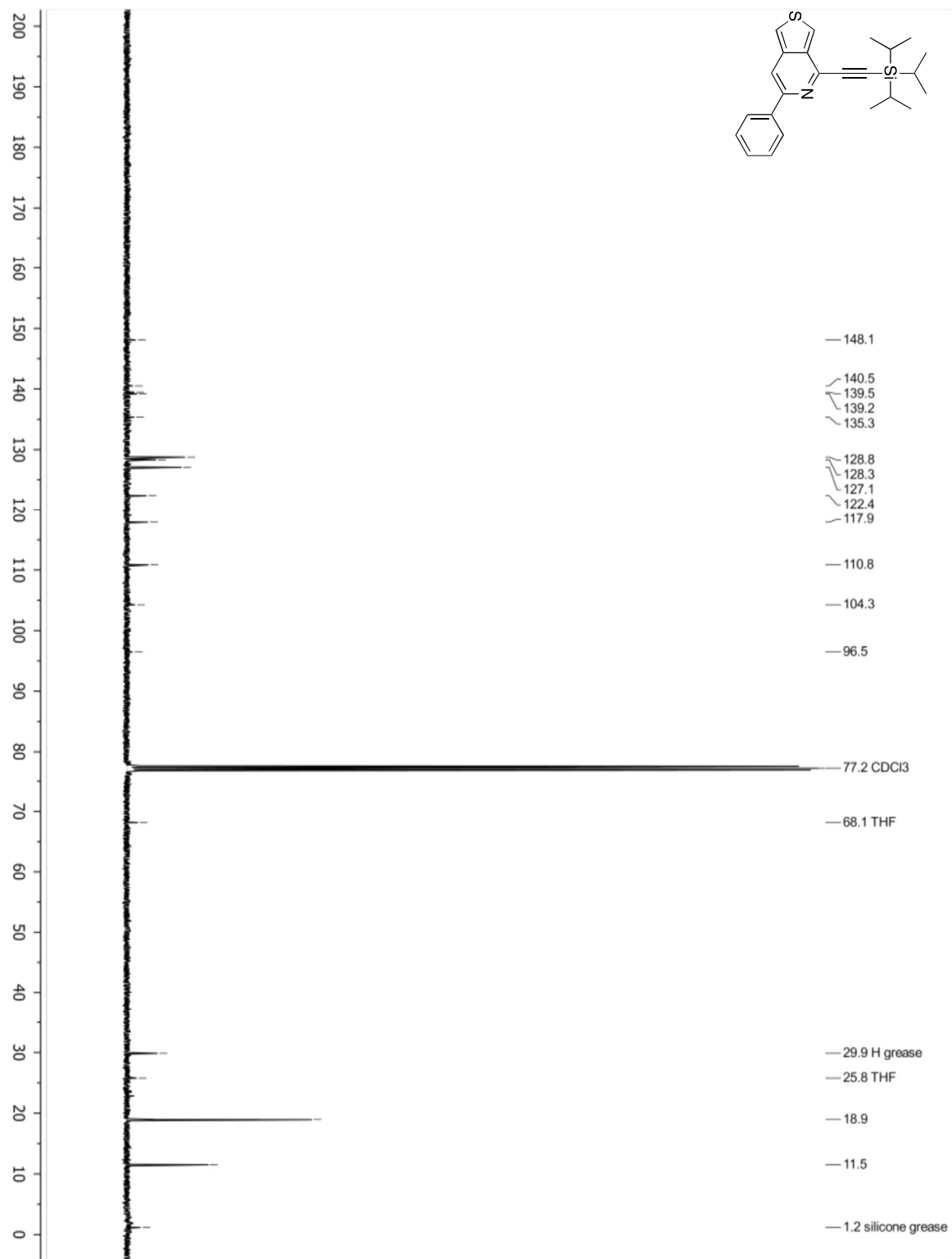
72: HMBC



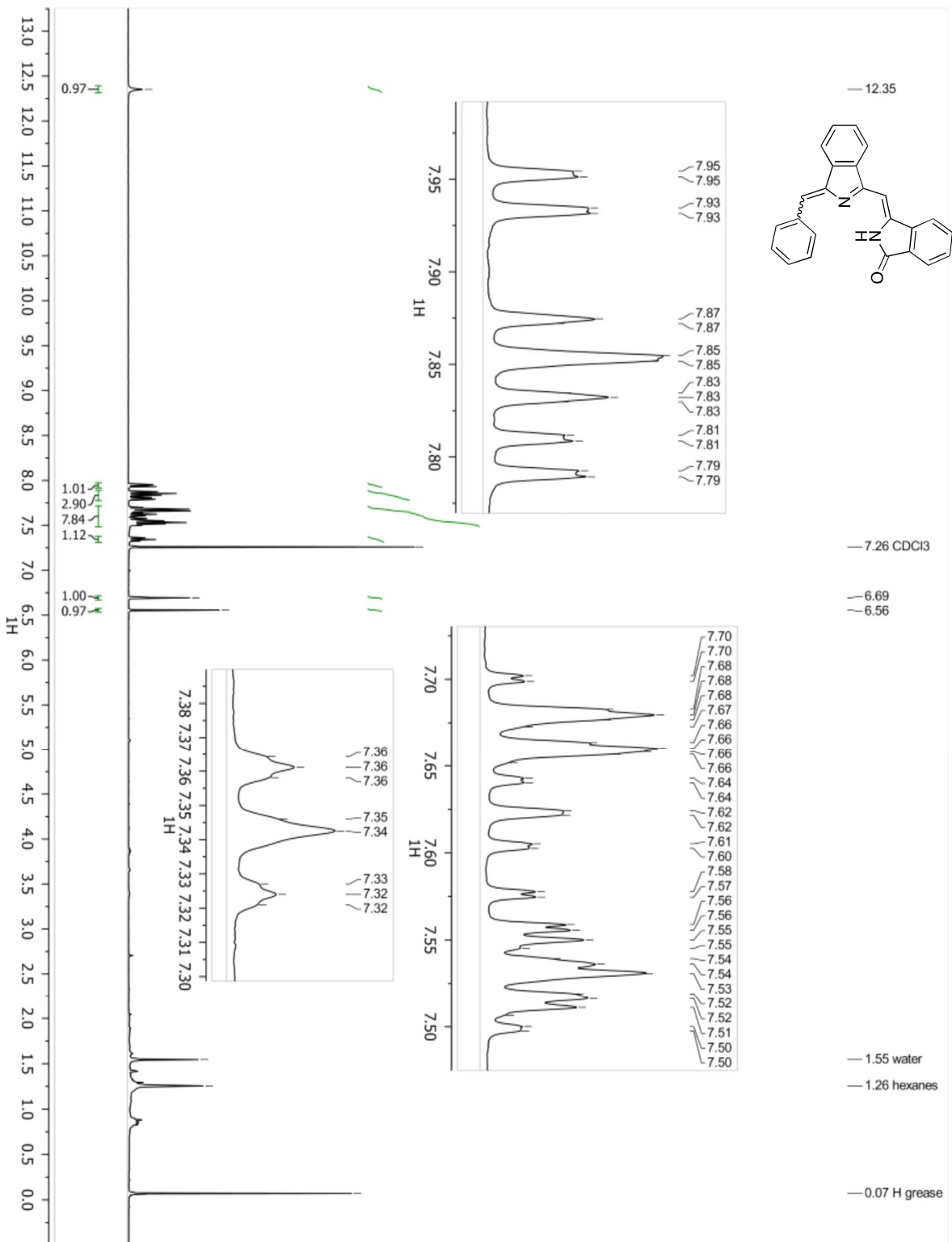
74: ^1H NMR



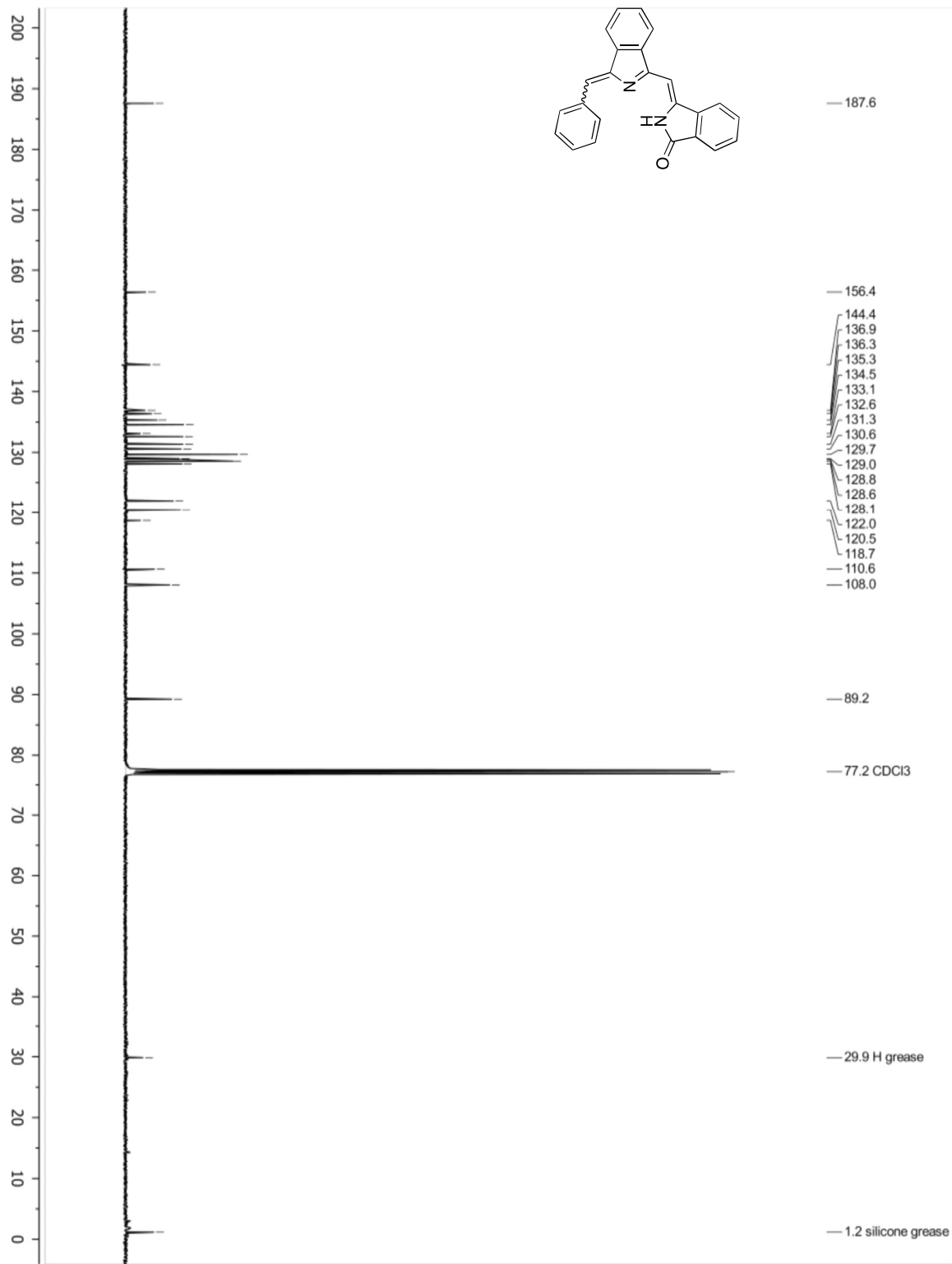
74: ^{13}C NMR



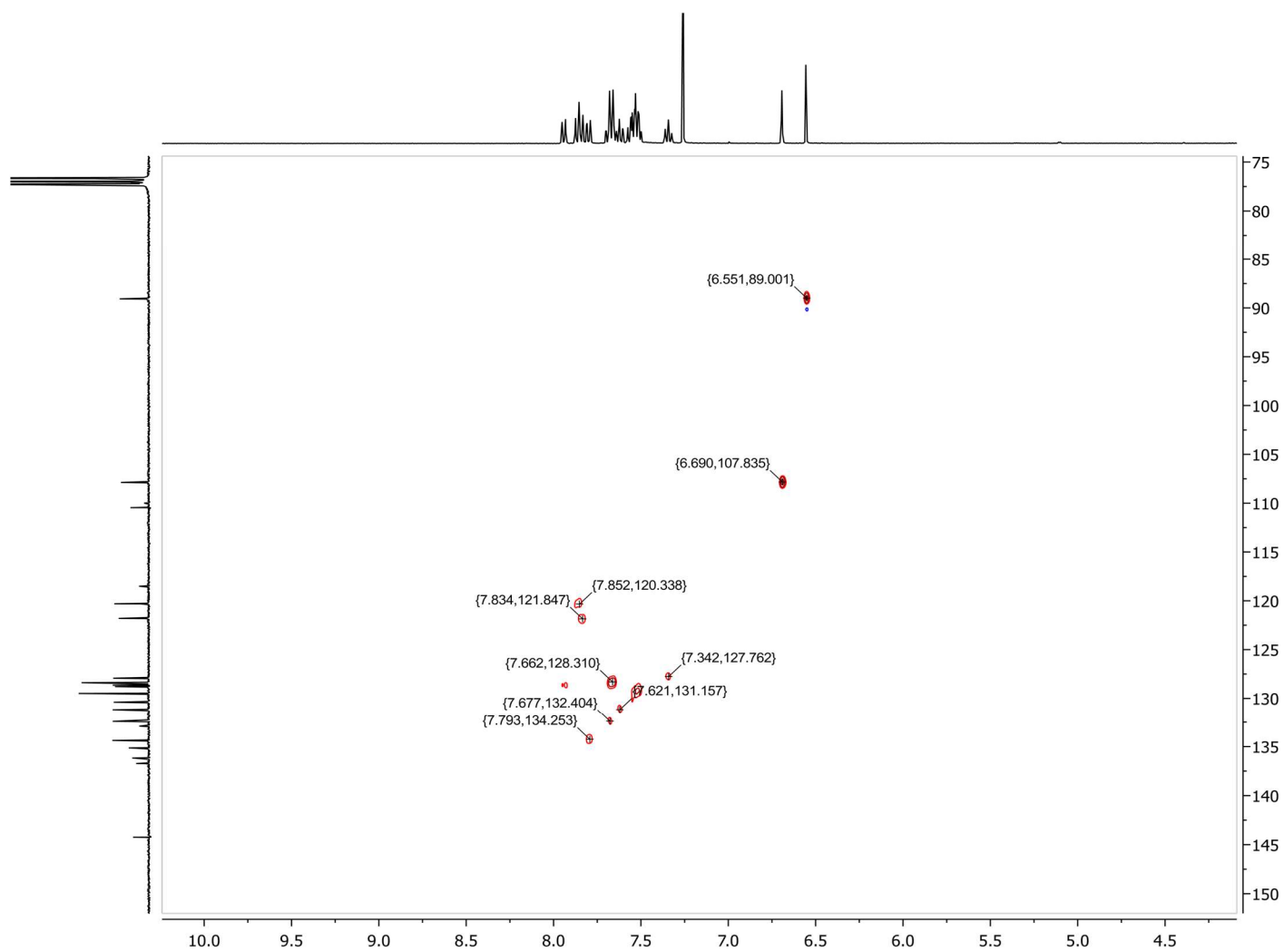
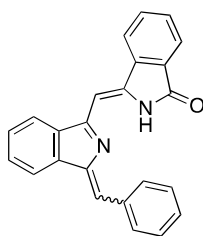
45: ^1H NMR



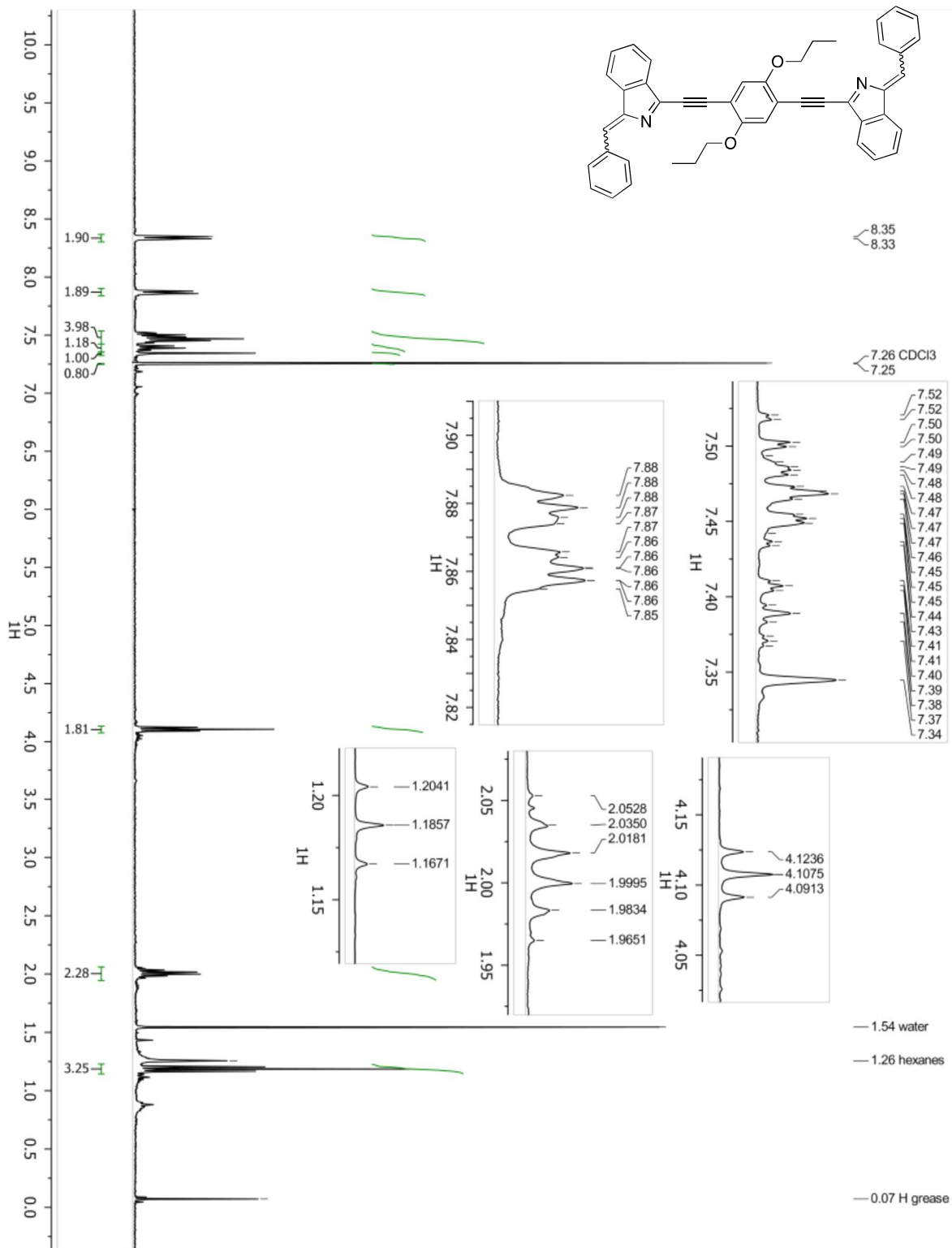
45: ^{13}C NMR



45: HSQC



75: ^1H NMR (Crude)



Appendix B: Crystal Data for Thienopyrrole 51

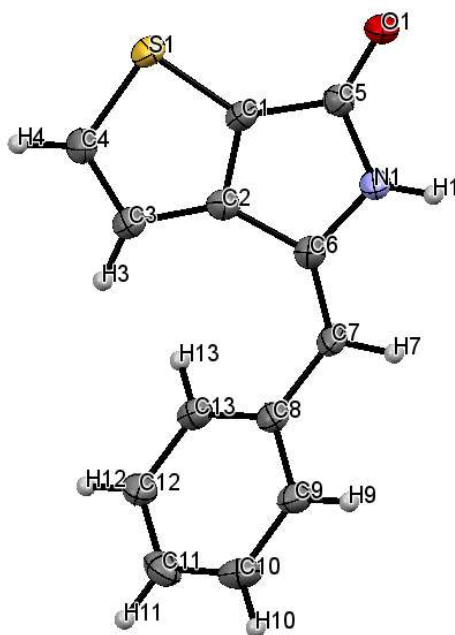


Figure 1. Molecular structure of (E)-4-benzylidene-4H-thieno[2,3-c]pyrrol-6(5H)-one **51** showing the atom labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius.

Table 1. Crystal data and structure refinement for BF-Thienopyrrole.

Identification code	SE171185
Empirical formula	C ₁₃ H ₉ N O S
Formula weight	227.27
Temperature	173(1) K
Wavelength	0.71073 Å
Diffractometer used	Bruker AXS P4/SMART 1000
Detector distance	5 cm 142

Monochromator used	Graphite	
Crystal size	0.60 x 0.20 x 0.05 mm ³	
Colour and habit	Colourless, rod	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 11.430(4) Å	$\alpha = 90^\circ$
	b = 10.602(4) Å	$\beta = 99.691(6)^\circ$
	c = 18.074(7) Å	$\gamma = 90^\circ$
Volume	2159.2(13) Å ³	
Z	8	
Density (calculated)	1.398 Mg/m ³	
Absorption coefficient	0.274 mm ⁻¹	
F(000)	944	
Theta range for data collection	1.97 to 27.50°	
Completeness to theta = 25.00°	95.8 %	
Scan type	ω and ϕ	
Scan range	0.3°	
Exposure time	10s	

Index ranges	-14 ≤ h ≤ 14, 0 ≤ k ≤ 13, 0 ≤ l ≤ 23
Standard reflections collection	50 frames at beginning and end of data
Crystal stability	no decay
Reflections collected	4615
Independent reflections	4615
Solution	Direct methods
Hydrogen atoms	Calculated positions, riding model
Absorption correction	SADABS
Max. and min. transmission	0.9864 and 0.8529
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4615 / 0 / 290
Goodness-of-fit on F ²	1.082
Final R indices [I>2sigma(I)]	R1 = 0.0618, wR2 = 0.1624
R indices (all data)	R1 = 0.0856, wR2 = 0.1947
Largest/mean shift/esd	0.000/0.000
Largest diff. peak and hole	0.382 and -0.485 e.Å ⁻³

$$wR2 = (\sum[w(F_o^2 - F_c^2)^2] / \sum[wF_o^4])^{1/2}$$

$$R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$$

$$\text{Weight} = 1 / [\sigma^2(F_o^2) + (0.0738 * P)^2 + (5.5891 * P)]$$

$$\text{where } P = (\max(F_o^2, 0) + 2 * F_c^2) / 3$$

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-Thienopyrrole. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
S(1)	590(1)	8633(1)	294(1)	35(1)
S(2)	3362(1)	4885(1)	2816(1)	33(1)
N(1)	2125(3)	5418(3)	953(2)	30(1)
N(2)	4893(3)	8066(3)	3564(2)	32(1)
O(1)	75(2)	5552(3)	838(2)	33(1)
O(2)	2851(3)	7873(3)	3516(2)	36(1)
C(1)	1359(4)	7310(4)	605(2)	27(1)
C(2)	2561(3)	7448(4)	670(2)	24(1)
C(3)	2889(4)	8677(4)	459(3)	30(1)
C(4)	1907(4)	9402(4)	245(3)	36(1)
C(5)	1055(4)	6023(4)	797(2)	25(1)
C(6)	3100(4)	6212(4)	895(2)	26(1)
C(7)	4226(4)	5784(4)	999(2)	29(1)
C(8)	5313(4)	6492(4)	981(2)	26(1)
C(9)	6240(4)	5900(4)	698(3)	30(1)
C(10)	7290(4)	6532(5)	642(3)	34(1)
C(11)	7430(4)	7769(5)	887(3)	34(1)
C(12)	6534(4)	8373(4)	1186(3)	34(1)
C(13)	5487(4)	7731(4)	1240(3)	29(1)
C(21)	4114(4)	6226(4)	3110(3)	28(1)
C(22)	5311(3)	6146(4)	3100(2)	24(1)

C(23)	5644(4)	4947(4)	2850(3)	29(1)
C(24)	4668(4)	4183(4)	2680(3)	36(1)
C(25)	3817(4)	7451(4)	3410(3)	28(1)
C(26)	5857(4)	7351(4)	3406(2)	26(1)
C(27)	6983(4)	7764(4)	3562(3)	31(1)
C(28)	8060(3)	7145(4)	3400(3)	28(1)
C(29)	9116(4)	7238(4)	3929(3)	32(1)
C(30)	10153(4)	6665(5)	3794(3)	38(1)
C(31)	10166(4)	6014(5)	3124(3)	41(1)
C(32)	9138(4)	5950(4)	2593(3)	39(1)
C(33)	8093(4)	6513(4)	2726(3)	31(1)

Table 3. Bond lengths [Å] and angles [°] for BF-Thienopyrrole.

S(1)-C(1)	1.700(4)
S(1)-C(4)	1.727(5)
S(2)-C(21)	1.699(4)
S(2)-C(24)	1.722(5)
N(1)-C(5)	1.368(5)
N(1)-C(6)	1.414(5)
N(1)-H(1)	0.8800
N(2)-C(25)	1.379(5)
N(2)-C(26)	1.406(5)
N(2)-H(2)	0.8800
O(1)-C(5)	1.241(5)
O(2)-C(25)	1.236(5)
C(1)-C(2)	1.367(6)
C(1)-C(5)	1.464(6)
C(2)-C(3)	1.426(6)
C(2)-C(6)	1.476(5)
C(3)-C(4)	1.362(6)
C(3)-H(3)	0.9500
C(4)-H(4)	0.9500
C(6)-C(7)	1.348(6)
C(7)-C(8)	1.456(6)
C(7)-H(7)	0.9500
C(8)-C(13)	1.397(6)
C(8)-C(9)	1.401(6)
C(9)-C(10)	1.393(6)
C(9)-H(9)	0.9500
C(10)-C(11)	1.384(7)
C(10)-H(10)	0.9500

C(11)-C(12)	1.392(7)
C(11)-H(11)	0.9500
C(12)-C(13)	1.394(6)
C(12)-H(12)	0.9500
C(13)-H(13)	0.9500
C(21)-C(22)	1.374(6)
C(21)-C(25)	1.469(6)
C(22)-C(23)	1.423(6)
C(22)-C(26)	1.487(6)
C(23)-C(24)	1.370(6)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(26)-C(27)	1.344(6)
C(27)-C(28)	1.468(6)
C(27)-H(27)	0.9500
C(28)-C(33)	1.396(6)
C(28)-C(29)	1.412(6)
C(29)-C(30)	1.390(6)
C(29)-H(29)	0.9500
C(30)-C(31)	1.396(8)
C(30)-H(30)	0.9500
C(31)-C(32)	1.388(7)
C(31)-H(31)	0.9500
C(32)-C(33)	1.392(6)
C(32)-H(32)	0.9500
C(33)-H(33)	0.9500
C(1)-S(1)-C(4)	90.0(2)
C(21)-S(2)-C(24)	90.1(2)
C(5)-N(1)-C(6)	113.2(3)

C(5)-N(1)-H(1)	123.4
C(6)-N(1)-H(1)	123.4
C(25)-N(2)-C(26)	114.0(3)
C(25)-N(2)-H(2)	123.0
C(26)-N(2)-H(2)	123.0
C(2)-C(1)-C(5)	110.8(4)
C(2)-C(1)-S(1)	113.4(3)
C(5)-C(1)-S(1)	135.8(3)
C(1)-C(2)-C(3)	112.4(4)
C(1)-C(2)-C(6)	107.2(4)
C(3)-C(2)-C(6)	140.3(4)
C(4)-C(3)-C(2)	110.5(4)
C(4)-C(3)-H(3)	124.7
C(2)-C(3)-H(3)	124.7
C(3)-C(4)-S(1)	113.8(3)
C(3)-C(4)-H(4)	123.1
S(1)-C(4)-H(4)	123.1
O(1)-C(5)-N(1)	125.7(4)
O(1)-C(5)-C(1)	130.0(4)
N(1)-C(5)-C(1)	104.2(3)
C(7)-C(6)-N(1)	122.4(4)
C(7)-C(6)-C(2)	133.0(4)
N(1)-C(6)-C(2)	104.5(3)
C(6)-C(7)-C(8)	128.4(4)
C(6)-C(7)-H(7)	115.8
C(8)-C(7)-H(7)	115.8
C(13)-C(8)-C(9)	118.0(4)
C(13)-C(8)-C(7)	123.5(4)
C(9)-C(8)-C(7)	118.5(4)
C(10)-C(9)-C(8)	121.7(4)

C(10)-C(9)-H(9)	119.2
C(8)-C(9)-H(9)	119.2
C(11)-C(10)-C(9)	119.1(4)
C(11)-C(10)-H(10)	120.4
C(9)-C(10)-H(10)	120.4
C(10)-C(11)-C(12)	120.4(4)
C(10)-C(11)-H(11)	119.8
C(12)-C(11)-H(11)	119.8
C(11)-C(12)-C(13)	120.0(4)
C(11)-C(12)-H(12)	120.0
C(13)-C(12)-H(12)	120.0
C(12)-C(13)-C(8)	120.7(4)
C(12)-C(13)-H(13)	119.6
C(8)-C(13)-H(13)	119.6
C(22)-C(21)-C(25)	110.6(4)
C(22)-C(21)-S(2)	113.4(3)
C(25)-C(21)-S(2)	136.0(3)
C(21)-C(22)-C(23)	112.3(4)
C(21)-C(22)-C(26)	107.4(4)
C(23)-C(22)-C(26)	140.1(4)
C(24)-C(23)-C(22)	110.4(4)
C(24)-C(23)-H(23)	124.8
C(22)-C(23)-H(23)	124.8
C(23)-C(24)-S(2)	113.9(3)
C(23)-C(24)-H(24)	123.1
S(2)-C(24)-H(24)	123.1
O(2)-C(25)-N(2)	126.0(4)
O(2)-C(25)-C(21)	130.2(4)
N(2)-C(25)-C(21)	103.8(3)
C(27)-C(26)-N(2)	122.5(4)

C(27)-C(26)-C(22)	133.3(4)
N(2)-C(26)-C(22)	104.1(3)
C(26)-C(27)-C(28)	128.1(4)
C(26)-C(27)-H(27)	115.9
C(28)-C(27)-H(27)	115.9
C(33)-C(28)-C(29)	118.6(4)
C(33)-C(28)-C(27)	122.4(4)
C(29)-C(28)-C(27)	118.9(4)
C(30)-C(29)-C(28)	120.5(5)
C(30)-C(29)-H(29)	119.8
C(28)-C(29)-H(29)	119.8
C(29)-C(30)-C(31)	120.1(4)
C(29)-C(30)-H(30)	119.9
C(31)-C(30)-H(30)	119.9
C(32)-C(31)-C(30)	119.6(4)
C(32)-C(31)-H(31)	120.2
C(30)-C(31)-H(31)	120.2
C(31)-C(32)-C(33)	120.7(5)
C(31)-C(32)-H(32)	119.7
C(33)-C(32)-H(32)	119.7
C(32)-C(33)-C(28)	120.4(4)
C(32)-C(33)-H(33)	119.8
C(28)-C(33)-H(33)	119.8

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-Thienopyrrole. The anisotropic

displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
S(1)	22(1)	31(1)	52(1)	13(1)	5(1)	7(1)
S(2)	27(1)	27(1)	43(1)	-6(1)	4(1)	-4(1)
N(1)	21(2)	24(2)	43(2)	7(2)	-1(2)	-1(1)
N(2)	21(2)	22(2)	55(2)	-5(2)	4(2)	2(1)
O(1)	19(1)	29(2)	50(2)	8(1)	2(1)	-1(1)
O(2)	25(2)	30(2)	54(2)	-5(2)	8(1)	1(1)
C(1)	22(2)	23(2)	36(2)	1(2)	4(2)	5(2)
C(2)	21(2)	26(2)	25(2)	0(2)	5(2)	0(2)
C(3)	23(2)	25(2)	42(3)	4(2)	2(2)	2(2)
C(4)	28(2)	28(2)	51(3)	13(2)	6(2)	0(2)
C(5)	23(2)	26(2)	26(2)	3(2)	5(2)	1(2)
C(6)	24(2)	22(2)	33(2)	2(2)	6(2)	0(2)
C(7)	23(2)	21(2)	39(2)	5(2)	-3(2)	3(2)
C(8)	22(2)	25(2)	28(2)	4(2)	0(2)	2(2)
C(9)	21(2)	28(2)	40(3)	-2(2)	1(2)	4(2)
C(10)	22(2)	44(3)	37(3)	-1(2)	6(2)	6(2)
C(11)	25(2)	40(3)	36(3)	8(2)	0(2)	-9(2)
C(12)	23(2)	29(2)	45(3)	2(2)	-1(2)	-2(2)
C(13)	23(2)	29(2)	36(2)	0(2)	6(2)	4(2)
C(21)	21(2)	21(2)	39(2)	2(2)	0(2)	0(2)
C(22)	19(2)	22(2)	29(2)	2(2)	1(2)	3(2)
C(23)	26(2)	26(2)	36(2)	0(2)	5(2)	4(2)

C(24)	34(2)	27(2)	46(3)	-11(2)	6(2)	2(2)
C(25)	21(2)	25(2)	36(2)	0(2)	0(2)	4(2)
C(26)	23(2)	22(2)	34(2)	-1(2)	4(2)	4(2)
C(27)	28(2)	23(2)	41(3)	-3(2)	0(2)	0(2)
C(28)	19(2)	21(2)	43(3)	3(2)	2(2)	-1(2)
C(29)	26(2)	29(2)	38(3)	4(2)	1(2)	-3(2)
C(30)	20(2)	41(3)	54(3)	12(2)	2(2)	-3(2)
C(31)	26(2)	35(3)	65(4)	9(2)	20(2)	5(2)
C(32)	37(3)	29(2)	52(3)	0(2)	15(2)	2(2)
C(33)	26(2)	29(2)	35(2)	4(2)	0(2)	-3(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-Thienopyrrole.

	x	y	z	U(eq)
H(1)	2200	4616	1077	36
H(2)	4970	8838	3745	39
H(3)	3682	8953	467	37
H(4)	1942	10252	83	43
H(7)	4324	4906	1096	34
H(9)	6151	5046	541	36
H(10)	7902	6120	438	41
H(11)	8142	8208	851	41
H(12)	6636	9221	1353	40
H(13)	4885	8141	1455	35
H(23)	6431	4709	2808	35
H(24)	4709	3344	2502	43
H(27)	7096	8557	3809	37
H(29)	9118	7696	4381	38
H(30)	10855	6716	4158	46
H(31)	10873	5618	3032	49
H(32)	9148	5517	2134	46
H(33)	7398	6468	2356	37

Table 6. Hydrogen bonds for BF-Thienopyrrole [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
N(1)-H(1)...O(2)#1	0.88	1.99	2.863(5)	169.2
N(2)-H(2)...O(1)#2	0.88	1.97	2.846(5)	172.7

Symmetry transformations used to generate equivalent atoms:

#1 $-x+1/2, y-1/2, -z+1/2$ #2 $-x+1/2, y+1/2, -z+1/2$

Appendix C: Crystal data for Isoindole 34

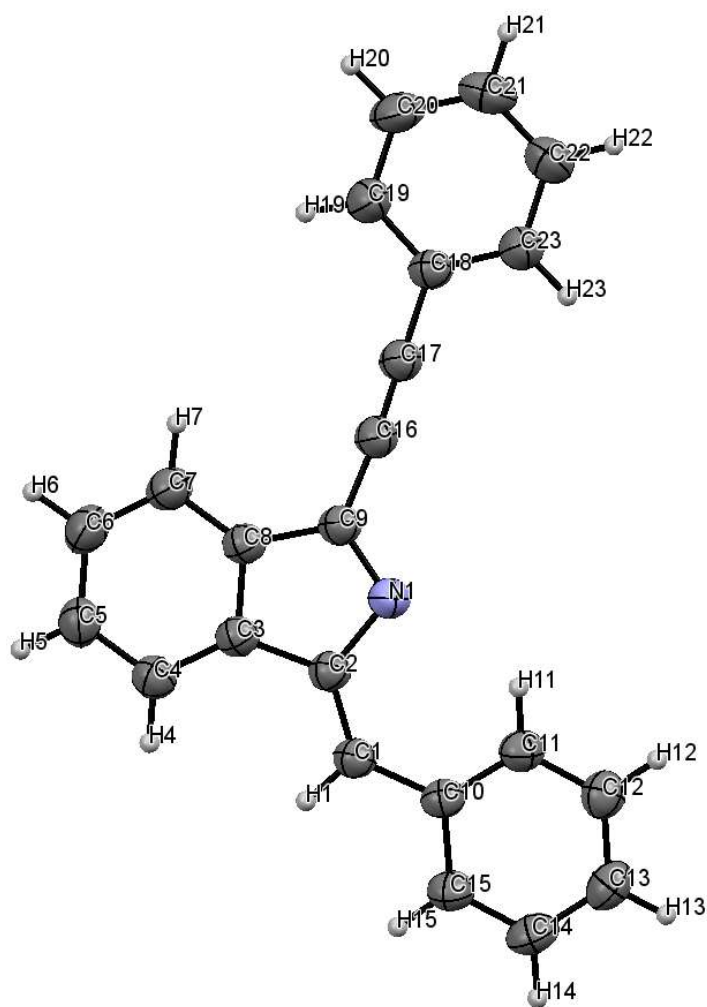


Figure 1. Molecular structure of (Z)-1-benzylidene-3-(phenylethynyl)-1H-isoindole **34** showing the atom labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius.

Table 1. Crystal data and structure refinement for BF-Isoindole-Phenyl.

Identification code	SE180616
Empirical formula	C ₂₃ H ₁₅ N
Formula weight	305.36
	156

Temperature	173(1) K	
Wavelength	0.71073 Å	
Diffractometer used	Bruker AXS P4/SMART 1000	
Detector distance	5 cm	
Monochromator used	Graphite	
Crystal size	0.60 x 0.40 x 0.30 mm ³	
Colour and habit	Brown, irregular	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 12.953(3) Å	$\alpha = 90^\circ$
	b = 5.4174(11) Å	$\beta = 97.490(3)^\circ$
	c = 23.656(5) Å	$\gamma = 90^\circ$
Volume	1645.8(6) Å ³	
Z	4	
Density (calculated)	1.232 Mg/m ³	
Absorption coefficient	0.071 mm ⁻¹	
F(000)	640	
Theta range for data collection	1.59 to 27.48°	
Completeness to theta = 25.00°	100.0 %	
Scan type	ω and ϕ	
Scan range	0.3°	
Exposure time	10s	

Index ranges	-16 ≤ h ≤ 16, -7 ≤ k ≤ 6, -30 ≤ l ≤ 28
Standard reflections collection	50 frames at beginning and end of data
Crystal stability	no decay
Reflections collected	10839
Independent reflections	3673 [R(int) = 0.0500]
Solution	Direct methods
Hydrogen atoms	Found, refined isotropically
Absorption correction	SADABS
Max. and min. transmission	0.9789 and 0.9585
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3673 / 0 / 277
Goodness-of-fit on F ²	1.023
Final R indices [I>2sigma(I)]	R1 = 0.0444, wR2 = 0.1103
R indices (all data)	R1 = 0.0660, wR2 = 0.1269
Largest/mean shift/esd	0.000/0.000
Largest diff. peak and hole	0.214 and -0.124 e.Å ⁻³

$$wR2 = (\sum[w(F_o^2 - F_c^2)^2] / \sum[wF_o^4])^{1/2}$$

$$R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$$

$$\text{Weight} = 1 / [\sigma^2(F_o^2) + (0.0610 * P)^2 + (0.1088 * P)]$$

$$\text{where } P = (\max(F_o^2, 0) + 2 * F_c^2) / 3$$

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-Isoindole-Phenyl. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
N(1)	2523(1)	5427(2)	2764(1)	45(1)
C(1)	1253(1)	8653(2)	2454(1)	42(1)
C(2)	1885(1)	7463(2)	2862(1)	40(1)
C(3)	2040(1)	8054(2)	3474(1)	40(1)
C(4)	1629(1)	9840(3)	3802(1)	47(1)
C(5)	1960(1)	9854(3)	4380(1)	54(1)
C(6)	2677(1)	8148(3)	4631(1)	58(1)
C(7)	3092(1)	6373(3)	4306(1)	51(1)
C(8)	2762(1)	6353(2)	3727(1)	41(1)
C(9)	3029(1)	4811(2)	3260(1)	42(1)
C(10)	1049(1)	8199(2)	1845(1)	40(1)
C(11)	1435(1)	6165(3)	1569(1)	46(1)
C(12)	1209(1)	5899(3)	988(1)	50(1)
C(13)	601(1)	7608(3)	666(1)	53(1)
C(14)	203(1)	9600(3)	929(1)	54(1)
C(15)	427(1)	9891(3)	1510(1)	47(1)
C(16)	3776(1)	2872(3)	3335(1)	46(1)
C(17)	4427(1)	1309(3)	3437(1)	45(1)
C(18)	5198(1)	-572(2)	3556(1)	42(1)
C(19)	5576(1)	-1145(3)	4113(1)	57(1)
C(20)	6317(1)	-2973(4)	4229(1)	67(1)

C(21)	6681(1)	-4227(3)	3792(1)	63(1)
C(22)	6322(1)	-3659(3)	3240(1)	61(1)
C(23)	5584(1)	-1837(3)	3119(1)	52(1)

Table 3. Bond lengths [Å] and angles [°] for BF-Isoindole-Phenyl.

N(1)-C(9)	1.3094(17)
N(1)-C(2)	1.4157(16)
C(1)-C(2)	1.3467(19)
C(1)-C(10)	1.452(2)
C(1)-H(1)	0.981(13)
C(2)-C(3)	1.4691(19)
C(3)-C(4)	1.3893(18)
C(3)-C(8)	1.3924(18)
C(4)-C(5)	1.378(2)
C(4)-H(4)	0.987(16)
C(5)-C(6)	1.388(2)
C(5)-H(5)	0.984(15)
C(6)-C(7)	1.384(2)
C(6)-H(6)	0.983(18)
C(7)-C(8)	1.379(2)
C(7)-H(7)	0.980(16)
C(8)-C(9)	1.4625(19)
C(9)-C(16)	1.4239(18)
C(10)-C(15)	1.3971(19)
C(10)-C(11)	1.4049(19)
C(11)-C(12)	1.375(2)
C(11)-H(11)	0.955(17)
C(12)-C(13)	1.379(2)
C(12)-H(12)	0.975(16)
C(13)-C(14)	1.379(2)
C(13)-H(13)	0.952(16)
C(14)-C(15)	1.375(2)
C(14)-H(14)	0.972(19)

C(15)-H(15)	0.977(16)
C(16)-C(17)	1.1966(18)
C(17)-C(18)	1.4296(18)
C(18)-C(19)	1.380(2)
C(18)-C(23)	1.387(2)
C(19)-C(20)	1.382(2)
C(19)-H(19)	0.965(17)
C(20)-C(21)	1.371(3)
C(20)-H(20)	1.00(2)
C(21)-C(22)	1.364(2)
C(21)-H(21)	0.955(18)
C(22)-C(23)	1.378(2)
C(22)-H(22)	0.985(18)
C(23)-H(23)	0.989(17)

C(9)-N(1)-C(2)	106.64(11)
C(2)-C(1)-C(10)	130.27(12)
C(2)-C(1)-H(1)	115.1(8)
C(10)-C(1)-H(1)	114.6(8)
C(1)-C(2)-N(1)	124.64(13)
C(1)-C(2)-C(3)	126.47(12)
N(1)-C(2)-C(3)	108.89(11)
C(4)-C(3)-C(8)	120.33(13)
C(4)-C(3)-C(2)	133.56(13)
C(8)-C(3)-C(2)	106.10(11)
C(5)-C(4)-C(3)	117.77(14)
C(5)-C(4)-H(4)	121.6(9)
C(3)-C(4)-H(4)	120.7(9)
C(4)-C(5)-C(6)	121.71(14)
C(4)-C(5)-H(5)	119.0(9)

C(6)-C(5)-H(5)	119.3(9)
C(7)-C(6)-C(5)	120.77(15)
C(7)-C(6)-H(6)	119.1(9)
C(5)-C(6)-H(6)	120.2(9)
C(8)-C(7)-C(6)	117.66(14)
C(8)-C(7)-H(7)	119.6(9)
C(6)-C(7)-H(7)	122.8(9)
C(7)-C(8)-C(3)	121.76(13)
C(7)-C(8)-C(9)	132.91(13)
C(3)-C(8)-C(9)	105.32(12)
N(1)-C(9)-C(16)	123.50(13)
N(1)-C(9)-C(8)	113.05(12)
C(16)-C(9)-C(8)	123.44(12)
C(15)-C(10)-C(11)	117.74(13)
C(15)-C(10)-C(1)	117.93(12)
C(11)-C(10)-C(1)	124.33(12)
C(12)-C(11)-C(10)	120.28(14)
C(12)-C(11)-H(11)	120.7(10)
C(10)-C(11)-H(11)	119.0(10)
C(11)-C(12)-C(13)	120.84(14)
C(11)-C(12)-H(12)	118.6(10)
C(13)-C(12)-H(12)	120.5(10)
C(12)-C(13)-C(14)	119.81(15)
C(12)-C(13)-H(13)	119.7(9)
C(14)-C(13)-H(13)	120.5(9)
C(15)-C(14)-C(13)	119.87(15)
C(15)-C(14)-H(14)	121.1(10)
C(13)-C(14)-H(14)	119.1(10)
C(14)-C(15)-C(10)	121.45(14)
C(14)-C(15)-H(15)	118.2(10)

C(10)-C(15)-H(15)	120.3(10)
C(17)-C(16)-C(9)	175.17(16)
C(16)-C(17)-C(18)	179.49(18)
C(19)-C(18)-C(23)	118.94(13)
C(19)-C(18)-C(17)	120.01(13)
C(23)-C(18)-C(17)	121.05(13)
C(18)-C(19)-C(20)	120.06(15)
C(18)-C(19)-H(19)	121.4(10)
C(20)-C(19)-H(19)	118.5(10)
C(21)-C(20)-C(19)	120.30(16)
C(21)-C(20)-H(20)	122.2(10)
C(19)-C(20)-H(20)	117.5(11)
C(22)-C(21)-C(20)	120.15(15)
C(22)-C(21)-H(21)	119.6(11)
C(20)-C(21)-H(21)	120.2(11)
C(21)-C(22)-C(23)	120.09(15)
C(21)-C(22)-H(22)	119.8(11)
C(23)-C(22)-H(22)	120.1(11)
C(22)-C(23)-C(18)	120.45(15)
C(22)-C(23)-H(23)	118.6(9)
C(18)-C(23)-H(23)	120.9(9)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-Isoindole-Phenyl.

The anisotropic

displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
N(1)	45(1)	49(1)	42(1)	3(1)	5(1)	9(1)
C(1)	39(1)	42(1)	44(1)	3(1)	6(1)	4(1)
C(2)	38(1)	43(1)	41(1)	3(1)	6(1)	2(1)
C(3)	35(1)	44(1)	42(1)	3(1)	5(1)	-2(1)
C(4)	43(1)	49(1)	49(1)	-1(1)	7(1)	3(1)
C(5)	56(1)	60(1)	47(1)	-9(1)	9(1)	3(1)
C(6)	60(1)	73(1)	40(1)	-3(1)	1(1)	1(1)
C(7)	48(1)	60(1)	44(1)	6(1)	2(1)	3(1)
C(8)	36(1)	46(1)	41(1)	4(1)	5(1)	0(1)
C(9)	38(1)	47(1)	42(1)	5(1)	5(1)	4(1)
C(10)	36(1)	40(1)	42(1)	6(1)	4(1)	-2(1)
C(11)	46(1)	43(1)	48(1)	3(1)	2(1)	3(1)
C(12)	53(1)	49(1)	47(1)	-2(1)	7(1)	-4(1)
C(13)	58(1)	60(1)	40(1)	5(1)	4(1)	-9(1)
C(14)	57(1)	56(1)	47(1)	16(1)	-1(1)	3(1)
C(15)	48(1)	43(1)	48(1)	8(1)	4(1)	4(1)
C(16)	44(1)	52(1)	43(1)	4(1)	7(1)	6(1)
C(17)	41(1)	50(1)	42(1)	4(1)	5(1)	4(1)
C(18)	36(1)	45(1)	44(1)	5(1)	4(1)	2(1)
C(19)	57(1)	69(1)	45(1)	5(1)	6(1)	14(1)
C(20)	63(1)	82(1)	55(1)	20(1)	-2(1)	20(1)
C(21)	49(1)	58(1)	82(1)	10(1)	6(1)	16(1)

C(22)	53(1)	64(1)	65(1)	-5(1)	10(1)	14(1)
C(23)	50(1)	61(1)	45(1)	0(1)	4(1)	10(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$)
for BF-Isoindole-Phenyl.

	x	y	z	U(eq)
H(1)	887(10)	10080(20)	2586(5)	43(4)
H(4)	1132(12)	11080(30)	3623(6)	55(4)
H(5)	1695(11)	11140(30)	4618(7)	56(4)
H(6)	2896(12)	8180(30)	5045(8)	66(5)
H(7)	3602(12)	5150(30)	4470(6)	57(4)
H(11)	1873(13)	5000(30)	1790(7)	64(5)
H(12)	1502(12)	4490(30)	806(7)	60(4)
H(13)	456(11)	7400(30)	264(7)	56(4)
H(14)	-232(14)	10780(30)	699(8)	75(5)
H(15)	116(12)	11290(30)	1687(7)	63(5)
H(19)	5341(13)	-280(30)	4429(7)	69(5)
H(20)	6567(14)	-3330(30)	4638(9)	83(6)
H(21)	7169(14)	-5540(30)	3873(8)	79(5)
H(22)	6603(14)	-4530(40)	2928(8)	81(5)
H(23)	5328(12)	-1470(30)	2716(7)	60(4)

Appendix D: Crystal data for Isoindole 36

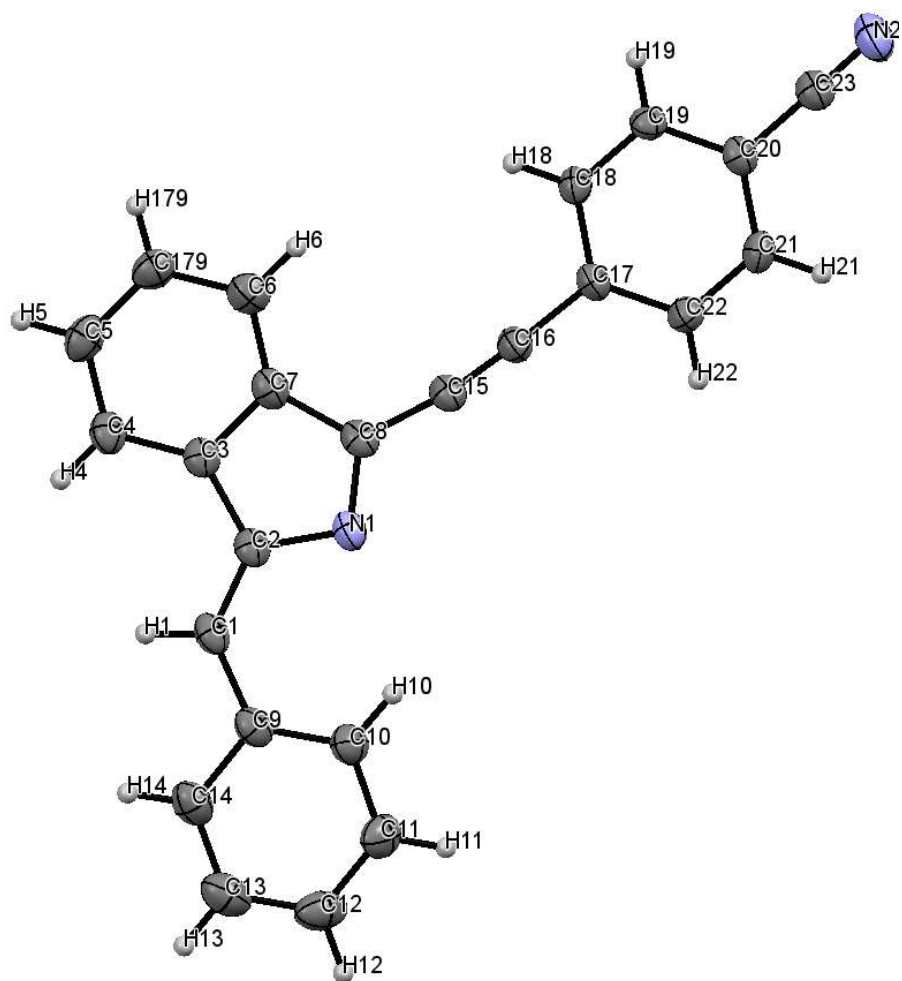


Figure 1. Molecular structure of (Z)-4-((1-benzylidene-1H-isoindol-3-yl)ethynyl)benzonitrile **36** showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius.

Table 1. Crystal data and structure refinement for BF-IsoindoleNitrile.

Identification code	SE180510	
Empirical formula	C ₂₄ H ₁₄ N ₂	
Formula weight	330.37	
Temperature	173(1) K	
Wavelength	0.71073 Å	
Diffractometer used	Bruker AXS P4/SMART 1000	
Detector distance	5 cm	
Monochromator used	Graphite	
Crystal size	0.60 x 0.40 x 0.40 mm ³	
Colour and habit	Orange, irregular	
Crystal system	Orthorhombic	
Space group	Pca2(1)	
Unit cell dimensions	a = 16.054(3) Å	$\alpha = 90^\circ$
	b = 8.6112(18) Å	$\beta = 90^\circ$
	c = 24.649(5) Å	$\gamma = 90^\circ$
Volume	3407.6(12) Å ³	
Z	8	
Density (calculated)	1.288 Mg/m ³	
Absorption coefficient	0.076 mm ⁻¹	
F(000)	1376	
Theta range for data collection	1.65 to 27.49°	
Completeness to theta = 25.00°	99.9 %	
Scan type	ω and ϕ	
Scan range	0.3°	
Exposure time	10s	

Index ranges	-20 ≤ h ≤ 19, -10 ≤ k ≤ 11, -31 ≤ l ≤ 31
Standard reflections collection	50 frames at beginning and end of data
Crystal stability	no decay
Reflections collected	21987
Independent reflections	7595 [R(int) = 0.0521]
Solution	Direct methods
Hydrogen atoms	Calculated positions, riding model
Absorption correction	SADABS
Max. and min. transmission	0.9702 and 0.9558
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7595 / 1 / 469
Goodness-of-fit on F ²	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0756, wR2 = 0.1738
R indices (all data)	R1 = 0.0900, wR2 = 0.1917
Largest/mean shift/esd	0.000/0.000
Largest diff. peak and hole	0.783 and -0.225 e.Å ⁻³

$$wR2 = (\sum[w(F_o^2 - F_c^2)^2] / \sum[wF_o^4])^{1/2}$$

$$R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$$

$$\text{Weight} = 1 / [\sigma^2(F_o^2) + (0.1373 * P)^2]$$

$$\text{where } P = (\max(F_o^2, 0) + 2 * F_c^2) / 3$$

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-IsoindoleNitrile. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	37(2)	2991(3)	3737(1)	30(1)
C(2)	606(2)	2066(3)	3484(1)	28(1)
C(3)	1325(2)	1309(3)	3744(1)	28(1)
C(4)	1645(2)	1314(3)	4268(1)	34(1)
C(5)	2335(2)	391(4)	4379(1)	39(1)
C(6)	2394(2)	-522(4)	3445(1)	36(1)
C(7)	1702(2)	420(3)	3341(1)	30(1)
C(8)	1207(2)	674(3)	2851(1)	27(1)
C(9)	-680(2)	3830(3)	3522(1)	31(1)
C(10)	-874(2)	3949(3)	2968(1)	35(1)
C(11)	-1529(2)	4903(4)	2801(2)	41(1)
C(12)	-2004(2)	5704(4)	3170(2)	47(1)
C(13)	-1832(2)	5561(4)	3721(2)	45(1)
C(14)	-1174(2)	4637(4)	3897(1)	38(1)
C(15)	1376(2)	-68(3)	2348(1)	28(1)
C(16)	1594(2)	-789(3)	1962(1)	29(1)
C(17)	1900(2)	-1677(3)	1510(1)	26(1)
C(18)	2583(2)	-2667(3)	1593(1)	28(1)
C(19)	2897(2)	-3533(3)	1171(1)	28(1)
C(20)	2535(2)	-3420(3)	659(1)	27(1)
C(21)	1861(2)	-2413(3)	567(1)	30(1)

C(22)	1541(2)	-1561(3)	992(1)	30(1)
C(23)	2847(2)	-4374(3)	228(1)	32(1)
C(31)	2578(2)	2015(3)	1056(1)	31(1)
C(32)	2004(2)	2939(3)	1301(1)	30(1)
C(33)	1288(2)	3679(3)	1028(1)	30(1)
C(34)	978(2)	3672(4)	502(1)	36(1)
C(35)	282(2)	4579(4)	392(1)	42(1)
C(36)	-97(2)	5477(4)	791(1)	40(1)
C(37)	201(2)	5484(4)	1316(1)	36(1)
C(38)	892(2)	4578(4)	1428(1)	29(1)
C(39)	1386(2)	4310(3)	1925(1)	29(1)
C(40)	3280(2)	1153(3)	1282(1)	31(1)
C(41)	3453(2)	1020(3)	1838(1)	36(1)
C(42)	4084(2)	55(3)	2021(2)	40(1)
C(43)	4571(2)	-772(4)	1646(2)	45(1)
C(44)	4420(2)	-635(4)	1103(2)	44(1)
C(45)	3781(2)	306(4)	922(2)	38(1)
C(46)	1190(2)	5067(3)	2414(1)	30(1)
C(47)	969(2)	5803(3)	2812(1)	30(1)
C(48)	666(2)	6676(3)	3261(1)	28(1)
C(49)	-20(2)	7668(3)	3178(1)	30(1)
C(50)	-330(2)	8545(3)	3591(1)	31(1)
C(51)	45(2)	8453(3)	4106(1)	29(1)
C(52)	719(2)	7484(3)	4194(1)	30(1)
C(53)	1026(2)	6584(3)	3770(1)	31(1)
C(54)	-262(2)	9451(4)	4537(1)	37(1)
C(179)	2702(2)	-525(4)	3976(1)	39(1)
N(1)	575(1)	1633(3)	2930(1)	29(1)
N(2)	3100(2)	-5141(4)	-109(1)	47(1)
N(3)	2017(1)	3371(3)	1854(1)	30(1)

N(4)	-504(2)	10211(4)	4877(1)	52(1)
------	---------	----------	---------	-------

Table 3. Bond lengths [Å] and angles [°] for BF-IsoindoleNitrile.

C(1)-C(2)	1.363(4)
C(1)-C(9)	1.459(4)
C(1)-H(1)	0.9500
C(2)-N(1)	1.416(4)
C(2)-C(3)	1.473(4)
C(3)-C(4)	1.389(4)
C(3)-C(7)	1.393(4)
C(4)-C(5)	1.390(4)
C(4)-H(4)	0.9500
C(5)-C(179)	1.399(5)
C(5)-H(5)	0.9500
C(6)-C(179)	1.398(4)
C(6)-C(7)	1.399(4)
C(6)-H(6)	0.9500
C(7)-C(8)	1.462(4)
C(8)-N(1)	1.323(3)
C(8)-C(15)	1.422(4)
C(9)-C(14)	1.402(4)
C(9)-C(10)	1.404(4)
C(10)-C(11)	1.397(4)
C(10)-H(10)	0.9500
C(11)-C(12)	1.372(5)
C(11)-H(11)	0.9500
C(12)-C(13)	1.390(5)
C(12)-H(12)	0.9500
C(13)-C(14)	1.393(5)
C(13)-H(13)	0.9500
C(14)-H(14)	0.9500

C(15)-C(16)	1.189(4)
C(16)-C(17)	1.438(4)
C(17)-C(22)	1.404(4)
C(17)-C(18)	1.405(4)
C(18)-C(19)	1.376(4)
C(18)-H(18)	0.9500
C(19)-C(20)	1.393(4)
C(19)-H(19)	0.9500
C(20)-C(21)	1.405(4)
C(20)-C(23)	1.433(4)
C(21)-C(22)	1.376(4)
C(21)-H(21)	0.9500
C(22)-H(22)	0.9500
C(23)-N(2)	1.137(4)
C(31)-C(32)	1.358(4)
C(31)-C(40)	1.460(4)
C(31)-H(31)	0.9500
C(32)-N(3)	1.413(4)
C(32)-C(33)	1.476(4)
C(33)-C(34)	1.389(4)
C(33)-C(38)	1.406(4)
C(34)-C(35)	1.390(5)
C(34)-H(34)	0.9500
C(35)-C(36)	1.390(5)
C(35)-H(35)	0.9500
C(36)-C(37)	1.379(4)
C(36)-H(36)	0.9500
C(37)-C(38)	1.385(4)
C(37)-H(37)	0.9500
C(38)-C(39)	1.476(4)

C(39)-N(3)	1.307(3)
C(39)-C(46)	1.407(4)
C(40)-C(45)	1.402(4)
C(40)-C(41)	1.404(4)
C(41)-C(42)	1.386(4)
C(41)-H(41)	0.9500
C(42)-C(43)	1.403(5)
C(42)-H(42)	0.9500
C(43)-C(44)	1.366(5)
C(43)-H(43)	0.9500
C(44)-C(45)	1.381(5)
C(44)-H(44)	0.9500
C(45)-H(45)	0.9500
C(46)-C(47)	1.221(4)
C(47)-C(48)	1.422(4)
C(48)-C(53)	1.385(4)
C(48)-C(49)	1.409(4)
C(49)-C(50)	1.362(4)
C(49)-H(49)	0.9500
C(50)-C(51)	1.406(4)
C(50)-H(50)	0.9500
C(51)-C(52)	1.384(4)
C(51)-C(54)	1.453(4)
C(52)-C(53)	1.391(4)
C(52)-H(52)	0.9500
C(53)-H(53)	0.9500
C(54)-N(4)	1.132(4)
C(179)-H(179)	0.9500
C(2)-C(1)-C(9)	130.7(3)

C(2)-C(1)-H(1)	114.7
C(9)-C(1)-H(1)	114.7
C(1)-C(2)-N(1)	124.8(3)
C(1)-C(2)-C(3)	125.8(3)
N(1)-C(2)-C(3)	109.4(2)
C(4)-C(3)-C(7)	120.3(3)
C(4)-C(3)-C(2)	133.9(3)
C(7)-C(3)-C(2)	105.8(2)
C(3)-C(4)-C(5)	118.4(3)
C(3)-C(4)-H(4)	120.8
C(5)-C(4)-H(4)	120.8
C(4)-C(5)-C(179)	121.2(3)
C(4)-C(5)-H(5)	119.4
C(179)-C(5)-H(5)	119.4
C(179)-C(6)-C(7)	117.0(3)
C(179)-C(6)-H(6)	121.5
C(7)-C(6)-H(6)	121.5
C(3)-C(7)-C(6)	122.2(3)
C(3)-C(7)-C(8)	105.7(2)
C(6)-C(7)-C(8)	132.1(3)
N(1)-C(8)-C(15)	123.7(3)
N(1)-C(8)-C(7)	112.9(2)
C(15)-C(8)-C(7)	123.3(2)
C(14)-C(9)-C(10)	118.6(3)
C(14)-C(9)-C(1)	116.8(3)
C(10)-C(9)-C(1)	124.4(3)
C(11)-C(10)-C(9)	119.7(3)
C(11)-C(10)-H(10)	120.1
C(9)-C(10)-H(10)	120.1
C(12)-C(11)-C(10)	121.3(4)

C(12)-C(11)-H(11)	119.4
C(10)-C(11)-H(11)	119.4
C(11)-C(12)-C(13)	119.5(3)
C(11)-C(12)-H(12)	120.3
C(13)-C(12)-H(12)	120.3
C(12)-C(13)-C(14)	120.3(3)
C(12)-C(13)-H(13)	119.8
C(14)-C(13)-H(13)	119.8
C(13)-C(14)-C(9)	120.5(3)
C(13)-C(14)-H(14)	119.8
C(9)-C(14)-H(14)	119.8
C(16)-C(15)-C(8)	171.7(3)
C(15)-C(16)-C(17)	176.9(3)
C(22)-C(17)-C(18)	119.8(2)
C(22)-C(17)-C(16)	121.8(2)
C(18)-C(17)-C(16)	118.4(3)
C(19)-C(18)-C(17)	120.2(3)
C(19)-C(18)-H(18)	119.9
C(17)-C(18)-H(18)	119.9
C(18)-C(19)-C(20)	119.7(2)
C(18)-C(19)-H(19)	120.2
C(20)-C(19)-H(19)	120.2
C(19)-C(20)-C(21)	120.7(2)
C(19)-C(20)-C(23)	119.0(2)
C(21)-C(20)-C(23)	120.3(3)
C(22)-C(21)-C(20)	119.6(3)
C(22)-C(21)-H(21)	120.2
C(20)-C(21)-H(21)	120.2
C(21)-C(22)-C(17)	120.0(2)
C(21)-C(22)-H(22)	120.0

C(17)-C(22)-H(22)	120.0
N(2)-C(23)-C(20)	179.2(4)
C(32)-C(31)-C(40)	130.7(3)
C(32)-C(31)-H(31)	114.7
C(40)-C(31)-H(31)	114.7
C(31)-C(32)-N(3)	125.0(3)
C(31)-C(32)-C(33)	125.4(3)
N(3)-C(32)-C(33)	109.7(2)
C(34)-C(33)-C(38)	119.6(3)
C(34)-C(33)-C(32)	134.6(3)
C(38)-C(33)-C(32)	105.7(2)
C(33)-C(34)-C(35)	117.9(3)
C(33)-C(34)-H(34)	121.0
C(35)-C(34)-H(34)	121.0
C(34)-C(35)-C(36)	121.7(3)
C(34)-C(35)-H(35)	119.1
C(36)-C(35)-H(35)	119.1
C(37)-C(36)-C(35)	121.0(3)
C(37)-C(36)-H(36)	119.5
C(35)-C(36)-H(36)	119.5
C(36)-C(37)-C(38)	117.6(3)
C(36)-C(37)-H(37)	121.2
C(38)-C(37)-H(37)	121.2
C(37)-C(38)-C(33)	122.2(3)
C(37)-C(38)-C(39)	133.2(3)
C(33)-C(38)-C(39)	104.6(2)
N(3)-C(39)-C(46)	125.1(3)
N(3)-C(39)-C(38)	113.7(3)
C(46)-C(39)-C(38)	121.2(2)
C(45)-C(40)-C(41)	117.5(3)

C(45)-C(40)-C(31)	117.8(3)
C(41)-C(40)-C(31)	124.5(3)
C(42)-C(41)-C(40)	120.8(3)
C(42)-C(41)-H(41)	119.6
C(40)-C(41)-H(41)	119.6
C(41)-C(42)-C(43)	119.8(4)
C(41)-C(42)-H(42)	120.1
C(43)-C(42)-H(42)	120.1
C(44)-C(43)-C(42)	120.2(3)
C(44)-C(43)-H(43)	119.9
C(42)-C(43)-H(43)	119.9
C(43)-C(44)-C(45)	120.0(3)
C(43)-C(44)-H(44)	120.0
C(45)-C(44)-H(44)	120.0
C(44)-C(45)-C(40)	121.8(3)
C(44)-C(45)-H(45)	119.1
C(40)-C(45)-H(45)	119.1
C(47)-C(46)-C(39)	174.1(3)
C(46)-C(47)-C(48)	176.6(3)
C(53)-C(48)-C(49)	119.5(2)
C(53)-C(48)-C(47)	122.1(2)
C(49)-C(48)-C(47)	118.4(3)
C(50)-C(49)-C(48)	120.8(3)
C(50)-C(49)-H(49)	119.6
C(48)-C(49)-H(49)	119.6
C(49)-C(50)-C(51)	119.2(3)
C(49)-C(50)-H(50)	120.4
C(51)-C(50)-H(50)	120.4
C(52)-C(51)-C(50)	120.7(3)
C(52)-C(51)-C(54)	120.5(3)

C(50)-C(51)-C(54)	118.8(3)
C(51)-C(52)-C(53)	119.7(3)
C(51)-C(52)-H(52)	120.2
C(53)-C(52)-H(52)	120.2
C(48)-C(53)-C(52)	120.1(3)
C(48)-C(53)-H(53)	120.0
C(52)-C(53)-H(53)	120.0
N(4)-C(54)-C(51)	179.1(4)
C(6)-C(179)-C(5)	121.0(3)
C(6)-C(179)-H(179)	119.5
C(5)-C(179)-H(179)	119.5
C(8)-N(1)-C(2)	106.2(2)
C(39)-N(3)-C(32)	106.3(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-IsoindoleNitrile. The anisotropic

displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
C(1)	40(1)	23(1)	27(1)	-3(1)	5(1)	-4(1)
C(2)	35(1)	20(1)	28(1)	-1(1)	1(1)	-4(1)
C(3)	33(1)	21(1)	29(1)	0(1)	1(1)	-5(1)
C(4)	42(1)	28(1)	31(2)	-4(1)	-2(1)	-3(1)
C(5)	38(2)	40(2)	40(2)	0(2)	-11(1)	-9(1)
C(6)	31(1)	37(2)	40(2)	-1(2)	2(1)	-5(1)
C(7)	30(1)	28(1)	31(2)	-3(1)	3(1)	-7(1)
C(8)	33(1)	20(1)	30(1)	0(1)	5(1)	-3(1)
C(9)	34(1)	27(1)	34(2)	-6(1)	4(1)	-4(1)
C(10)	36(1)	32(1)	36(2)	-8(1)	-4(1)	-1(1)
C(11)	40(2)	36(2)	46(2)	-12(1)	-15(1)	-2(1)
C(12)	34(1)	39(2)	67(2)	-8(2)	-10(2)	3(1)
C(13)	38(2)	40(2)	57(2)	-10(2)	9(2)	-3(1)
C(14)	34(1)	43(2)	37(2)	-4(2)	10(1)	-6(1)
C(15)	33(1)	22(2)	28(2)	1(1)	3(1)	-1(1)
C(16)	32(1)	28(1)	27(1)	-1(1)	1(1)	2(1)
C(17)	29(1)	25(1)	24(1)	-3(1)	3(1)	-2(1)
C(18)	34(1)	27(1)	24(1)	-2(1)	-1(1)	-1(1)
C(19)	29(1)	23(1)	30(1)	-1(1)	0(1)	2(1)
C(20)	30(1)	24(1)	27(1)	-2(1)	2(1)	-5(1)
C(21)	35(1)	32(2)	22(1)	2(1)	-4(1)	-4(1)
C(22)	31(1)	29(2)	29(1)	2(1)	-2(1)	2(1)

C(23)	37(1)	27(2)	32(2)	1(1)	2(1)	-2(1)
C(31)	37(1)	29(1)	27(1)	0(1)	4(1)	-5(1)
C(32)	43(2)	24(1)	25(1)	-3(1)	1(1)	-4(1)
C(33)	36(1)	26(1)	28(2)	-1(1)	4(1)	-8(1)
C(34)	40(2)	38(2)	30(2)	-4(1)	0(1)	-11(1)
C(35)	43(2)	50(2)	33(2)	6(2)	-9(1)	-15(1)
C(36)	32(1)	43(2)	46(2)	8(2)	-4(1)	-7(1)
C(37)	32(1)	35(2)	39(2)	0(1)	2(1)	-4(1)
C(38)	28(1)	33(1)	25(1)	0(1)	1(1)	-10(1)
C(39)	33(1)	25(1)	29(1)	1(1)	1(1)	-4(1)
C(40)	34(1)	23(1)	36(2)	-3(1)	4(1)	-4(1)
C(41)	39(1)	32(2)	38(2)	-9(1)	0(1)	-1(1)
C(42)	41(2)	36(2)	43(2)	-8(1)	-9(1)	2(1)
C(43)	32(1)	38(2)	64(2)	-12(2)	-6(2)	-1(1)
C(44)	38(2)	40(2)	53(2)	-9(2)	14(1)	0(1)
C(45)	42(2)	40(2)	34(2)	-6(2)	9(1)	-2(1)
C(46)	33(1)	28(2)	30(2)	0(1)	0(1)	1(1)
C(47)	34(1)	27(1)	30(2)	1(1)	0(1)	-2(1)
C(48)	32(1)	21(1)	30(2)	1(1)	3(1)	-3(1)
C(49)	32(1)	29(1)	28(1)	1(1)	-4(1)	-2(1)
C(50)	28(1)	33(2)	32(2)	0(1)	0(1)	1(1)
C(51)	32(1)	30(1)	26(1)	-1(1)	7(1)	-3(1)
C(52)	33(1)	31(2)	25(1)	1(1)	-2(1)	-3(1)
C(53)	30(1)	29(1)	34(2)	0(1)	0(1)	1(1)
C(54)	36(1)	48(2)	28(2)	-2(1)	4(1)	3(1)
C(179)	28(1)	43(2)	45(2)	1(2)	-6(1)	-2(1)
N(1)	36(1)	26(1)	25(1)	-2(1)	3(1)	-1(1)
N(2)	61(2)	44(2)	35(2)	-8(1)	6(1)	2(1)
N(3)	38(1)	26(1)	28(1)	-1(1)	4(1)	0(1)
N(4)	53(2)	68(2)	35(2)	-14(2)	4(1)	18(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BF-IsoindoleNitrile.

	x	y	z	U(eq)
H(1)	122	3110	4116	36
H(4)	1399	1934	4543	41
H(5)	2561	382	4735	47
H(6)	2642	-1133	3168	43
H(10)	-562	3381	2708	42
H(11)	-1648	5001	2425	49
H(12)	-2447	6350	3050	56
H(13)	-2166	6097	3978	54
H(14)	-1058	4552	4273	46
H(18)	2830	-2739	1943	34
H(19)	3358	-4204	1228	33
H(21)	1627	-2320	215	36
H(22)	1078	-895	934	36
H(31)	2511	1913	675	37
H(34)	1233	3067	227	43
H(35)	59	4586	35	50
H(36)	-567	6094	701	48
H(37)	-59	6090	1590	43
H(41)	3134	1598	2092	44
H(42)	4188	-46	2399	48
H(43)	5007	-1428	1771	54

H(44)		4754	-1187	850	52
H(45)		3678	381	543	46
H(49)		-270	7727	2829	36
H(50)		-793	9210	3533	37
H(52)		971	7433	4542	36
H(53)		1484	5907	3830	37
H(179)	3167	-1158	4064	47	

Appendix E: Crystal data for Isoindole Dimer 75

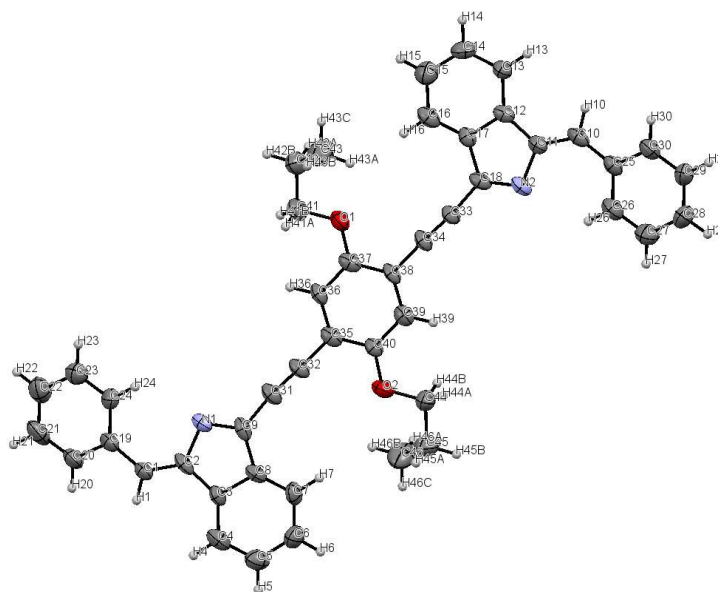


Figure 1. Molecular structure of dimer X showing the atom labelling scheme.

Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radius.

Table 1. Crystal data and structure refinement for BFdimerOPr.

Identification code	SE180595
Empirical formula	C ₄₆ H ₃₆ N ₂ O ₂
Formula weight	648.77
Temperature	173(1) K
Wavelength	0.71073 Å
Diffractometer used	Bruker AXS P4/SMART 1000
Detector distance	5 cm
Monochromator used	Graphite
Crystal size	0.60 x 0.20 x 0.10 mm ³

Colour and habit	Orange, irregular	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 6.564(3) Å	$\alpha = 90^\circ$
	b = 22.161(9) Å	$\beta = 97.261(6)^\circ$
	c = 12.016(5) Å	$\gamma = 90^\circ$
Volume	1733.8(12) Å ³	
Z	2	
Density (calculated)	1.243 Mg/m ³	
Absorption coefficient	0.076 mm ⁻¹	
F(000)	684	
Theta range for data collection	1.71 to 27.48°	
Completeness to theta = 25.00°	100.0 %	
Scan type	ω and ϕ	
Scan range	0.3°	
Exposure time	10s	

Index ranges	-8 ≤ h ≤ 8, -26 ≤ k ≤ 28, -15 ≤ l ≤ 15
Standard reflections collection	50 frames at beginning and end of data
Crystal stability	no decay
Reflections collected	11674
Independent reflections	6017 [R(int) = 0.0488]
Solution	Direct methods
Hydrogen atoms	Calculated positions, riding model
Absorption correction	SADABS
Max. and min. transmission	0.9925 and 0.9560
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6017 / 1 / 453
Goodness-of-fit on F ²	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0575, wR2 = 0.1191
R indices (all data)	R1 = 0.1107, wR2 = 0.1418
Largest/mean shift/esd	0.000/0.000
Absolute structure parameter	1(3)
Largest diff. peak and hole	0.268 and -0.182 e.Å ⁻³

$$wR2 = (\sum[w(F_o^2 - F_c^2)^2] / \sum[wF_o^4])^{1/2}$$

$$R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$$

$$\text{Weight} = 1 / [\sigma^2(F_o^2) + (0.0487 * P)^2 + (0.5850 * P)]$$

$$\text{where } P = (\max(F_o^2, 0) + 2 * F_c^2) / 3$$

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$)

for BFdimerOPr. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	-4157(6)	11780(2)	3823(4)	36(1)
C(2)	-2445(6)	11636(2)	4512(4)	38(1)
C(3)	-2174(6)	11665(2)	5737(4)	34(1)
C(4)	-3362(8)	11893(2)	6521(4)	48(1)
C(5)	-2620(8)	11837(2)	7648(4)	59(1)
C(6)	-750(8)	11552(2)	7993(4)	59(1)
C(7)	439(7)	11323(2)	7228(4)	47(1)
C(8)	-289(7)	11385(2)	6122(4)	37(1)
C(9)	519(6)	11206(2)	5078(4)	36(1)
C(10)	19356(7)	8035(2)	6698(4)	41(1)
C(11)	17630(6)	8188(2)	6010(3)	34(1)
C(12)	17323(7)	8157(2)	4795(4)	34(1)
C(13)	18528(7)	7945(2)	3993(4)	41(1)
C(14)	17797(8)	8013(2)	2879(4)	54(1)
C(15)	15897(8)	8290(2)	2536(4)	58(1)
C(16)	14722(8)	8503(2)	3344(5)	48(1)
C(17)	15445(6)	8434(2)	4467(4)	35(1)
C(18)	14671(7)	8610(2)	5494(4)	38(1)
C(19)	-4681(7)	11704(2)	2630(4)	39(1)
C(20)	-6708(7)	11806(2)	2174(4)	51(1)
C(21)	-7326(9)	11751(3)	1016(5)	69(2)

C(22)	-5947(9)	11575(2)	310(5)	67(2)
C(23)	-3922(9)	11469(2)	771(4)	57(1)
C(24)	-3313(7)	11528(2)	1892(4)	44(1)
C(25)	19906(7)	8100(2)	7894(4)	39(1)
C(26)	18489(8)	8255(2)	8636(4)	50(1)
C(27)	19109(8)	8305(2)	9773(4)	57(1)
C(28)	21141(8)	8186(2)	10205(4)	59(1)
C(29)	22528(8)	8037(3)	9487(4)	61(1)
C(30)	21944(8)	7999(2)	8358(4)	50(1)
C(31)	2391(6)	10876(2)	5044(4)	41(1)
C(32)	3940(6)	10586(2)	5145(3)	39(1)
C(33)	12815(6)	8939(2)	5496(3)	37(1)
C(34)	11266(6)	9230(2)	5395(3)	38(1)
C(35)	5804(6)	10243(2)	5236(4)	39(1)
C(36)	6681(6)	10121(2)	4251(4)	37(1)
C(37)	8506(7)	9786(2)	4314(4)	40(1)
C(38)	9395(6)	9579(2)	5344(4)	34(1)
C(39)	8506(6)	9694(2)	6311(4)	38(1)
C(40)	6705(6)	10027(2)	6266(4)	34(1)
C(41)	8671(7)	9918(3)	2352(4)	57(1)
C(42)	10157(7)	9767(3)	1532(4)	69(2)
C(43)	12270(8)	10009(3)	1868(4)	82(2)
C(44)	6458(7)	9884(3)	8213(4)	58(1)
C(45)	4995(8)	10016(3)	9013(4)	75(2)
C(46)	2879(8)	9779(3)	8652(5)	85(2)
N(1)	-677(5)	11353(2)	4154(3)	37(1)
N(2)	15905(5)	8462(2)	6399(3)	40(1)
O(1)	9436(4)	9653(1)	3390(3)	46(1)
O(2)	5733(5)	10160(1)	7167(3)	49(1)

Table 3. Bond lengths [Å] and angles [°] for BFdimerOPr.

C(1)-C(2)	1.348(6)
C(1)-C(19)	1.441(6)
C(1)-H(1)	0.9500
C(2)-N(1)	1.432(5)
C(2)-C(3)	1.462(6)
C(3)-C(4)	1.392(6)
C(3)-C(8)	1.408(6)
C(4)-C(5)	1.386(6)
C(4)-H(4)	0.9500
C(5)-C(6)	1.396(7)
C(5)-H(5)	0.9500
C(6)-C(7)	1.376(6)
C(6)-H(6)	0.9500
C(7)-C(8)	1.362(5)
C(7)-H(7)	0.9500
C(8)-C(9)	1.476(6)
C(9)-N(1)	1.317(5)
C(9)-C(31)	1.435(6)
C(10)-C(11)	1.358(6)
C(10)-C(25)	1.443(6)
C(10)-H(10)	0.9500
C(11)-N(2)	1.416(5)
C(11)-C(12)	1.450(6)
C(12)-C(17)	1.389(6)
C(12)-C(13)	1.403(6)
C(13)-C(14)	1.372(6)
C(13)-H(13)	0.9500

C(14)-C(15)	1.405(7)
C(14)-H(14)	0.9500
C(15)-C(16)	1.397(7)
C(15)-H(15)	0.9500
C(16)-C(17)	1.380(6)
C(16)-H(16)	0.9500
C(17)-C(18)	1.445(6)
C(18)-N(2)	1.313(5)
C(18)-C(33)	1.421(6)
C(19)-C(20)	1.392(7)
C(19)-C(24)	1.395(6)
C(20)-C(21)	1.404(7)
C(20)-H(20)	0.9500
C(21)-C(22)	1.373(8)
C(21)-H(21)	0.9500
C(22)-C(23)	1.394(7)
C(22)-H(22)	0.9500
C(23)-C(24)	1.362(6)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(25)-C(30)	1.400(6)
C(25)-C(26)	1.410(7)
C(26)-C(27)	1.380(6)
C(26)-H(26)	0.9500
C(27)-C(28)	1.394(6)
C(27)-H(27)	0.9500
C(28)-C(29)	1.371(7)
C(28)-H(28)	0.9500
C(29)-C(30)	1.365(6)
C(29)-H(29)	0.9500

C(30)-H(30)	0.9500
C(31)-C(32)	1.196(5)
C(32)-C(35)	1.433(6)
C(33)-C(34)	1.197(5)
C(34)-C(38)	1.446(6)
C(35)-C(40)	1.388(6)
C(35)-C(36)	1.407(6)
C(36)-C(37)	1.403(6)
C(36)-H(36)	0.9500
C(37)-O(1)	1.365(5)
C(37)-C(38)	1.378(6)
C(38)-C(39)	1.388(6)
C(39)-C(40)	1.389(6)
C(39)-H(39)	0.9500
C(40)-O(2)	1.357(5)
C(41)-O(1)	1.412(5)
C(41)-C(42)	1.509(7)
C(41)-H(41A)	0.9900
C(41)-H(41B)	0.9900
C(42)-C(43)	1.494(7)
C(42)-H(42A)	0.9900
C(42)-H(42B)	0.9900
C(43)-H(43A)	0.9800
C(43)-H(43B)	0.9800
C(43)-H(43C)	0.9800
C(44)-O(2)	1.424(5)
C(44)-C(45)	1.471(6)
C(44)-H(44A)	0.9900
C(44)-H(44B)	0.9900
C(45)-C(46)	1.496(7)

C(45)-H(45A)	0.9900
C(45)-H(45B)	0.9900
C(46)-H(46A)	0.9800
C(46)-H(46B)	0.9800
C(46)-H(46C)	0.9800

C(2)-C(1)-C(19)	131.2(4)
C(2)-C(1)-H(1)	114.4
C(19)-C(1)-H(1)	114.4
C(1)-C(2)-N(1)	124.3(5)
C(1)-C(2)-C(3)	126.5(4)
N(1)-C(2)-C(3)	108.7(3)
C(4)-C(3)-C(8)	118.8(4)
C(4)-C(3)-C(2)	133.6(4)
C(8)-C(3)-C(2)	107.5(4)
C(5)-C(4)-C(3)	118.1(5)
C(5)-C(4)-H(4)	121.0
C(3)-C(4)-H(4)	121.0
C(4)-C(5)-C(6)	121.3(5)
C(4)-C(5)-H(5)	119.4
C(6)-C(5)-H(5)	119.4
C(7)-C(6)-C(5)	121.3(4)
C(7)-C(6)-H(6)	119.4
C(5)-C(6)-H(6)	119.4
C(8)-C(7)-C(6)	117.1(4)
C(8)-C(7)-H(7)	121.4
C(6)-C(7)-H(7)	121.4
C(7)-C(8)-C(3)	123.4(4)
C(7)-C(8)-C(9)	133.0(4)
C(3)-C(8)-C(9)	103.6(4)

N(1)-C(9)-C(31)	121.5(4)
N(1)-C(9)-C(8)	114.2(4)
C(31)-C(9)-C(8)	124.3(4)
C(11)-C(10)-C(25)	131.7(4)
C(11)-C(10)-H(10)	114.1
C(25)-C(10)-H(10)	114.1
C(10)-C(11)-N(2)	123.1(4)
C(10)-C(11)-C(12)	126.9(4)
N(2)-C(11)-C(12)	109.7(3)
C(17)-C(12)-C(13)	120.7(4)
C(17)-C(12)-C(11)	105.7(4)
C(13)-C(12)-C(11)	133.5(4)
C(14)-C(13)-C(12)	118.4(4)
C(14)-C(13)-H(13)	120.8
C(12)-C(13)-H(13)	120.8
C(13)-C(14)-C(15)	121.5(4)
C(13)-C(14)-H(14)	119.3
C(15)-C(14)-H(14)	119.3
C(16)-C(15)-C(14)	119.5(5)
C(16)-C(15)-H(15)	120.3
C(14)-C(15)-H(15)	120.3
C(17)-C(16)-C(15)	119.4(5)
C(17)-C(16)-H(16)	120.3
C(15)-C(16)-H(16)	120.3
C(16)-C(17)-C(12)	120.6(4)
C(16)-C(17)-C(18)	133.6(4)
C(12)-C(17)-C(18)	105.8(4)
N(2)-C(18)-C(33)	124.4(4)
N(2)-C(18)-C(17)	113.2(4)
C(33)-C(18)-C(17)	122.2(4)

C(20)-C(19)-C(24)	117.1(4)
C(20)-C(19)-C(1)	117.9(4)
C(24)-C(19)-C(1)	125.0(4)
C(19)-C(20)-C(21)	121.2(5)
C(19)-C(20)-H(20)	119.4
C(21)-C(20)-H(20)	119.4
C(22)-C(21)-C(20)	120.4(5)
C(22)-C(21)-H(21)	119.8
C(20)-C(21)-H(21)	119.8
C(21)-C(22)-C(23)	118.2(5)
C(21)-C(22)-H(22)	120.9
C(23)-C(22)-H(22)	120.9
C(24)-C(23)-C(22)	121.5(5)
C(24)-C(23)-H(23)	119.3
C(22)-C(23)-H(23)	119.3
C(23)-C(24)-C(19)	121.6(4)
C(23)-C(24)-H(24)	119.2
C(19)-C(24)-H(24)	119.2
C(30)-C(25)-C(26)	117.4(4)
C(30)-C(25)-C(10)	119.1(4)
C(26)-C(25)-C(10)	123.5(4)
C(27)-C(26)-C(25)	120.7(5)
C(27)-C(26)-H(26)	119.7
C(25)-C(26)-H(26)	119.7
C(26)-C(27)-C(28)	120.1(4)
C(26)-C(27)-H(27)	119.9
C(28)-C(27)-H(27)	119.9
C(29)-C(28)-C(27)	119.4(5)
C(29)-C(28)-H(28)	120.3
C(27)-C(28)-H(28)	120.3

C(30)-C(29)-C(28)	121.0(5)
C(30)-C(29)-H(29)	119.5
C(28)-C(29)-H(29)	119.5
C(29)-C(30)-C(25)	121.3(5)
C(29)-C(30)-H(30)	119.3
C(25)-C(30)-H(30)	119.3
C(32)-C(31)-C(9)	172.3(5)
C(31)-C(32)-C(35)	178.4(5)
C(34)-C(33)-C(18)	173.8(4)
C(33)-C(34)-C(38)	176.6(4)
C(40)-C(35)-C(36)	120.7(4)
C(40)-C(35)-C(32)	121.0(4)
C(36)-C(35)-C(32)	118.3(4)
C(37)-C(36)-C(35)	119.6(4)
C(37)-C(36)-H(36)	120.2
C(35)-C(36)-H(36)	120.2
O(1)-C(37)-C(38)	118.4(4)
O(1)-C(37)-C(36)	122.5(4)
C(38)-C(37)-C(36)	119.1(4)
C(37)-C(38)-C(39)	121.0(4)
C(37)-C(38)-C(34)	118.5(4)
C(39)-C(38)-C(34)	120.5(4)
C(38)-C(39)-C(40)	120.7(4)
C(38)-C(39)-H(39)	119.7
C(40)-C(39)-H(39)	119.7
O(2)-C(40)-C(35)	116.5(4)
O(2)-C(40)-C(39)	124.6(4)
C(35)-C(40)-C(39)	118.9(4)
O(1)-C(41)-C(42)	107.4(4)
O(1)-C(41)-H(41A)	110.2

C(42)-C(41)-H(41A)	110.2
O(1)-C(41)-H(41B)	110.2
C(42)-C(41)-H(41B)	110.2
H(41A)-C(41)-H(41B)	108.5
C(43)-C(42)-C(41)	113.5(4)
C(43)-C(42)-H(42A)	108.9
C(41)-C(42)-H(42A)	108.9
C(43)-C(42)-H(42B)	108.9
C(41)-C(42)-H(42B)	108.9
H(42A)-C(42)-H(42B)	107.7
C(42)-C(43)-H(43A)	109.5
C(42)-C(43)-H(43B)	109.5
H(43A)-C(43)-H(43B)	109.5
C(42)-C(43)-H(43C)	109.5
H(43A)-C(43)-H(43C)	109.5
H(43B)-C(43)-H(43C)	109.5
O(2)-C(44)-C(45)	108.6(4)
O(2)-C(44)-H(44A)	110.0
C(45)-C(44)-H(44A)	110.0
O(2)-C(44)-H(44B)	110.0
C(45)-C(44)-H(44B)	110.0
H(44A)-C(44)-H(44B)	108.4
C(44)-C(45)-C(46)	113.6(4)
C(44)-C(45)-H(45A)	108.9
C(46)-C(45)-H(45A)	108.9
C(44)-C(45)-H(45B)	108.9
C(46)-C(45)-H(45B)	108.9
H(45A)-C(45)-H(45B)	107.7
C(45)-C(46)-H(46A)	109.5
C(45)-C(46)-H(46B)	109.5

H(46A)-C(46)-H(46B)	109.5
C(45)-C(46)-H(46C)	109.5
H(46A)-C(46)-H(46C)	109.5
H(46B)-C(46)-H(46C)	109.5
C(9)-N(1)-C(2)	105.9(4)
C(18)-N(2)-C(11)	105.6(4)
C(37)-O(1)-C(41)	118.9(4)
C(40)-O(2)-C(44)	118.2(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BFdimerOPr. The anisotropic

displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
C(1)	32(3)	32(2)	46(3)	4(2)	7(2)	7(2)
C(2)	20(3)	26(2)	68(3)	7(2)	5(2)	1(2)
C(3)	24(2)	31(2)	46(3)	0(2)	-2(2)	0(2)
C(4)	32(3)	37(3)	76(4)	-8(2)	7(3)	2(2)
C(5)	44(3)	72(3)	60(4)	-16(3)	8(3)	1(3)
C(6)	54(3)	81(4)	40(3)	-7(3)	-3(2)	4(3)
C(7)	37(3)	55(3)	46(3)	-2(2)	-13(2)	3(2)
C(8)	26(3)	29(2)	57(3)	-5(2)	9(2)	0(2)
C(9)	23(2)	25(2)	58(3)	8(2)	-5(2)	-4(2)
C(10)	33(3)	26(2)	65(4)	6(2)	16(2)	4(2)
C(11)	32(3)	25(2)	44(3)	2(2)	9(2)	-1(2)
C(12)	28(3)	26(2)	51(3)	-3(2)	12(2)	-4(2)
C(13)	34(3)	47(3)	43(3)	-1(2)	8(2)	4(2)
C(14)	54(3)	61(3)	51(3)	-8(3)	23(3)	-1(3)
C(15)	55(4)	62(3)	57(4)	3(3)	8(3)	-4(3)
C(16)	31(3)	40(3)	72(4)	-1(2)	10(2)	-1(2)
C(17)	27(2)	33(2)	45(3)	5(2)	3(2)	-2(2)
C(18)	26(2)	31(2)	58(3)	-4(2)	14(2)	-3(2)
C(19)	34(3)	33(3)	50(3)	4(2)	7(2)	8(2)
C(20)	40(3)	54(3)	59(3)	-6(2)	1(2)	17(2)
C(21)	47(4)	64(4)	92(5)	-19(3)	-12(3)	22(3)
C(22)	63(4)	62(3)	70(4)	-8(3)	-9(3)	9(3)

C(23)	57(4)	56(3)	59(4)	-4(3)	9(3)	6(3)
C(24)	45(3)	48(3)	38(3)	6(2)	1(2)	6(2)
C(25)	33(3)	28(2)	55(3)	2(2)	5(2)	2(2)
C(26)	37(3)	47(3)	66(4)	3(2)	9(2)	4(2)
C(27)	51(3)	61(3)	61(4)	-1(3)	16(3)	3(3)
C(28)	64(4)	73(4)	38(3)	-7(2)	-3(2)	5(3)
C(29)	57(3)	80(4)	42(3)	-6(3)	-7(2)	19(3)
C(30)	41(3)	47(3)	61(4)	-3(2)	6(2)	11(3)
C(31)	27(3)	33(2)	64(3)	2(2)	5(2)	0(2)
C(32)	25(2)	34(2)	60(3)	0(2)	8(2)	-1(2)
C(33)	25(2)	39(2)	47(3)	4(2)	7(2)	-1(2)
C(34)	22(2)	35(2)	55(3)	6(2)	3(2)	0(2)
C(35)	27(2)	29(2)	61(3)	-3(2)	8(2)	-5(2)
C(36)	21(2)	35(2)	54(3)	6(2)	0(2)	2(2)
C(37)	30(3)	30(2)	61(4)	-5(2)	12(2)	-5(2)
C(38)	18(2)	29(2)	56(3)	7(2)	4(2)	-1(2)
C(39)	33(3)	32(2)	51(3)	2(2)	5(2)	-4(2)
C(40)	24(2)	32(2)	46(3)	0(2)	4(2)	-3(2)
C(41)	36(3)	75(4)	58(4)	-4(3)	0(2)	11(3)
C(42)	45(3)	104(5)	57(4)	-12(3)	-2(2)	11(3)
C(43)	70(4)	116(5)	63(4)	9(3)	21(3)	-12(4)
C(44)	48(3)	83(4)	40(3)	-4(3)	1(2)	14(3)
C(45)	55(4)	117(5)	54(4)	-11(3)	13(3)	16(3)
C(46)	48(4)	136(6)	74(4)	9(4)	19(3)	-11(4)
N(1)	30(2)	30(2)	54(2)	4(2)	14(2)	4(2)
N(2)	26(2)	36(2)	57(3)	-2(2)	6(2)	3(2)
O(1)	34(2)	50(2)	55(2)	7(2)	8(2)	10(2)
O(2)	41(2)	51(2)	58(2)	-3(2)	17(2)	12(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for BFdimerOPr.

	x	y	z	U(eq)
H(1)	-5200	11965	4186	44
H(4)	-4645	12082	6290	58
H(5)	-3399	11995	8195	70
H(6)	-288	11516	8772	71
H(7)	1712	11129	7462	57
H(10)	20390	7853	6325	49
H(13)	19818	7758	4216	49
H(14)	18594	7869	2327	64
H(15)	15415	8332	1760	69
H(16)	13437	8693	3124	57
H(20)	-7692	11915	2654	61
H(21)	-8707	11836	719	83
H(22)	-6361	11527	-471	80
H(23)	-2945	11352	293	69
H(24)	-1923	11449	2178	53
H(26)	17093	8326	8350	60
H(27)	18150	8422	10263	68
H(28)	21562	8207	10990	71
H(29)	23917	7960	9780	73
H(30)	22939	7902	7877	60
H(36)	6041	10264	3547	45

H(39)	9136	9543	7011	46
H(41A)	8561	10361	2435	68
H(41B)	7292	9755	2083	68
H(42A)	10236	9323	1458	83
H(42B)	9620	9933	787	83
H(43A)	12776	9871	2627	123
H(43B)	12232	10451	1853	123
H(43C)	13188	9864	1343	123
H(44A)	7831	10045	8501	69
H(44B)	6577	9443	8115	69
H(45A)	4920	10458	9114	90
H(45B)	5518	9837	9749	90
H(46A)	2924	9338	8599	128
H(46B)	2357	9948	7917	128
H(46C)	1971	9896	9202	128

Curriculum Vitae

Candidate's full name: Brandon Christopher Fillmore

Universities attended:

- University of New Brunswick, Department of Chemistry, Masters of Science, in Organic Chemistry (2016-2018)
- University of New Brunswick, Department of Chemistry, Bachelor of Science (Honors), in Medicinal Chemistry (2012-2016)

Conference Presentations:

- Presentation: B. C. Fillmore, S. Eisler, "Synthesis and electronic properties of benzo- and thieno-pyrrole derivatives", 43rd Science Atlantic/ CIC Student Chemistry Conference 2018
- Poster: B. C. Fillmore, S. Eisler, "Highly functionalized building blocks for the synthesis of new π -conjugated oligomers" 100th Canadian Chemistry Conference and Exhibition (CSC) 2017
- Attendee: 99th Canadian Chemistry Conference and Exhibition (CSC) 2015

