

**Synthesis of Molecularly Defined Conjugated Oligomers and  
Polymers through Dehydrative Coupling**

by

Sara Abuadas

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## **Author's Declaration**

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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# Abstract

The development of scalable methods for the synthesis of conjugated materials remains among the most important aspects for their integration into devices at a commercial level. Drawing inspiration from nature as well as polymers made on a scale of many millions of tons annually, one type of reaction often used is a dehydration reaction in which two monomers react together eliminating a small molecule such as water. Although dehydration reactions are widely used to synthesize non-conjugated polymers, advances in utilizing dehydration methods to prepare conjugated poly(hetero)arenes are lacking. Herein, we describe the development of a dehydration type reaction where two thiazole *N*-oxides are coupled to afford the corresponding dimer with simply an addition of a base. This dimer formation occurs in 10 minutes, at room temperature, forming an C(sp<sup>2</sup>)-C(sp<sup>2</sup>) bond without the need for transition metals. Various conjugated small molecules and polymers were synthesized using this simple method. Extending this reaction to synthesis of molecularly defined oligomers as well as other classes of poly(hetero)arenes could be a powerful tool allowing access to a wider variety of conjugated materials.

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## List of Abbreviations

<b>°C</b>	<b>degree(s) Celsius</b>
<b>CMD</b>	<b>concerted-metalation-deprotonation</b>
<b>DArP</b>	<b>direct arylation polymerization</b>
<b>DCE</b>	<b>1,2-dichloroethane</b>
<b>DCM</b>	<b>dichloromethane</b>
<b>DMA</b>	<b>N,N-dimethyl acetamide</b>
<b>DMDO</b>	<b>dimethyldioxirane</b>
<b>EDG</b>	<b>electron donating group</b>
<b>E<sub>g</sub></b>	<b>band gap</b>
<b>equiv</b>	<b>equivalent(s)</b>
<b>eV</b>	<b>electron volt(s)</b>
<b>EWG</b>	<b>electron withdrawing group</b>
<b>g</b>	<b>gram(s)</b>
<b>GPC</b>	<b>gel permeation chromatography</b>
<b>h</b>	<b>hour(s)</b>
<b>HOMO</b>	<b>highest occupied molecular orbital</b>
<b>HRMS</b>	<b>high resolution mass spectrometry</b>
<b>IDC</b>	<b>iterative divergent/convergent</b>
<b>kDa</b>	<b>kilo dalton(s)</b>
<b>LUMO</b>	<b>lowest unoccupied molecular orbital</b>



<b>M</b>	<b>molar</b>
<b><i>m</i>CPBA</b>	<b>meta-chloroperbenzoic acid</b>
<b>MDO</b>	<b>molecularly defined oligomer(s)</b>
<b>M<sub>n</sub></b>	<b>number average molecular weight</b>
<b>MMPP</b>	<b>magnesium monoperoxyphthalate</b>
<b>M<sub>w</sub></b>	<b>weight average molecular weight</b>
<b>NaDMSO</b>	<b>sodium methylsulfinylmethyllide</b>
<b>NMR</b>	<b>nuclear magnetic resonance</b>
<b>OPVs</b>	<b>organic photovoltaics</b>
<b>OLEDs</b>	<b>organic light emitting diodes</b>
<b>OTEs</b>	<b>oligo(thiophene ethynylene)s</b>
<b>OTFTs</b>	<b>organic thin-film transistors</b>
<b>PET</b>	<b>polyethylene terephthalate</b>
<b>PCE</b>	<b>power conversion efficiency</b>
<b>PivOH</b>	<b>pivalic acid</b>
<b>R<sub>f</sub></b>	<b>retention factor</b>
<b>RT</b>	<b>room temperature</b>
<b>SEC</b>	<b>size exclusion chromatography</b>
<b>THF</b>	<b>tetrahydrofuran</b>
<b>TLC</b>	<b>thin layer chromatography</b>
<b>TMS</b>	<b>trimethylsilyl</b>
<b>VS</b>	<b>versus</b>

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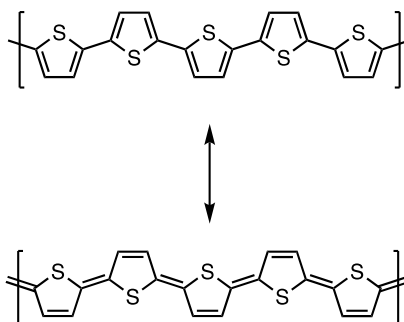
# Chapter 1

## 1.1 Conjugated Organic Materials

Organic semiconductors are an attractive alternative to inorganic semiconductors due to the characteristics they possess such as flexibility, easy processability, high amount of tunability, as well as having the potential to be less expensive than traditional inorganic semiconductors.<sup>1</sup> These organic semiconductors have found the most potential for use in applications such as organic light emitting diodes (OLEDs), organic field effect transistors (OFETs) and organic photovoltaics (OPVs), among others. Two classes of organic conjugated compounds are mainly used for their optoelectronic properties: conjugated polymers and conjugated small molecules. Interest in synthesizing organic conjugated molecules has grown widely since the discovery of their application as semiconductors.<sup>1,2</sup>

Typically, conjugated polymers consist of alternating single and double bonds, in which overlap of the p-orbitals allows for electron delocalization along the polymer backbone giving them their unique electronic and optical properties (Figure 1). The semiconducting properties of conjugated materials in electronic devices are a characteristic of their band gap. This is directly related to the HOMO–LUMO gap of the molecule, which is the amount of energy (eV) required to excite an electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) of a conjugated molecule. Due to the variety of synthetic transformations possible, the band gap can be tuned towards desired applications.<sup>2</sup> Therefore,

discovering new synthetic routes to novel conjugated molecules may allow us to access unique sets of properties that were previously unknown or inaccessible.

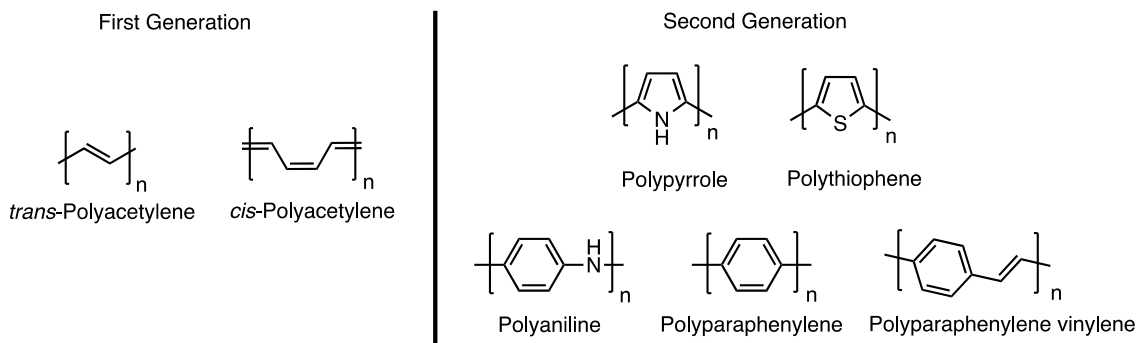


**Figure 1: Electron Delocalization Across Polythiophene.**

### 1.1.1 Discovery of Conjugated Polymers

Interest in conjugated polymers increased once their electrical conductivity was accidentally discovered. Their discovery occurred when a student in Shirakawa's laboratory accidentally added more catalyst than required while synthesizing polyacetylene through the Zeigler-Natta polymerization. Instead of the usual dark powder of polyacetylene produced by the reaction, an unusual silvery film was isolated. Prof. MacDiarmid was intrigued and further studied the silvery film with the collaboration of physics professor Alan Heeger. It was then concluded that the silvery film was doped polyacetylene in which doping had increased its conductivity significantly earning Heeger, MacDiarmid and Shirakawa the Nobel Prize in Chemistry in the year 2000.<sup>1,3</sup> While polyacetylene does possess conducting properties, due to its lack of stability in oxygen and its poor processability, other classes of conjugated polymers have since been synthesized and became the mainstay for these types of materials. Conjugated polymers such as polyaniline (PANI), polypyrrole (PPy), polythiophene (PT), poly(p-phenylene) (PP) and polyphenylene vinylene (PPV) are examples of what are known as second generation conjugated polymers (Figure 2). While these conjugated polymers provided a significant improvement in their

electronic properties compared to polyacetylene, processability remained an issue mainly due to their poor solubility.

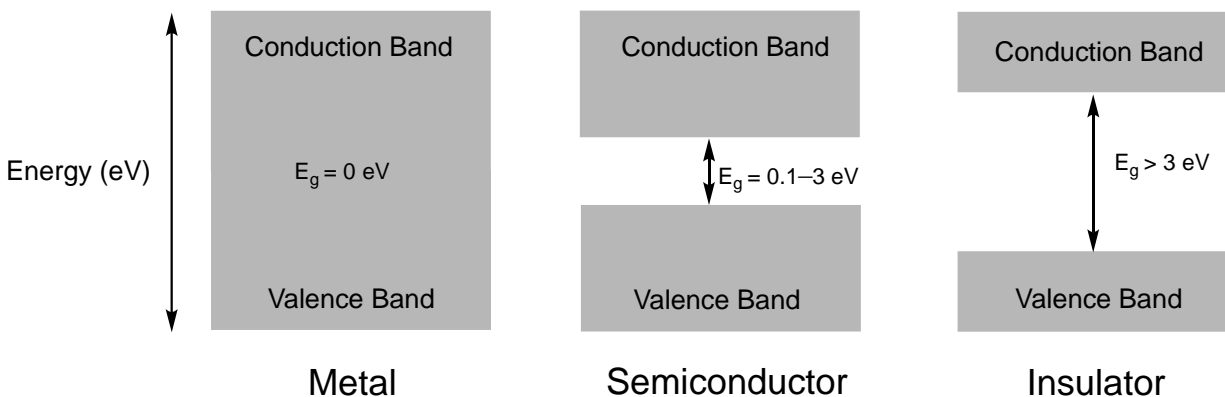


**Figure 2: a) First Generation Polyacetylene, b) Second Generation Conjugated Polymers.**

### 1.1.2 Band Gap/ HOMO–LUMO Gap Engineering

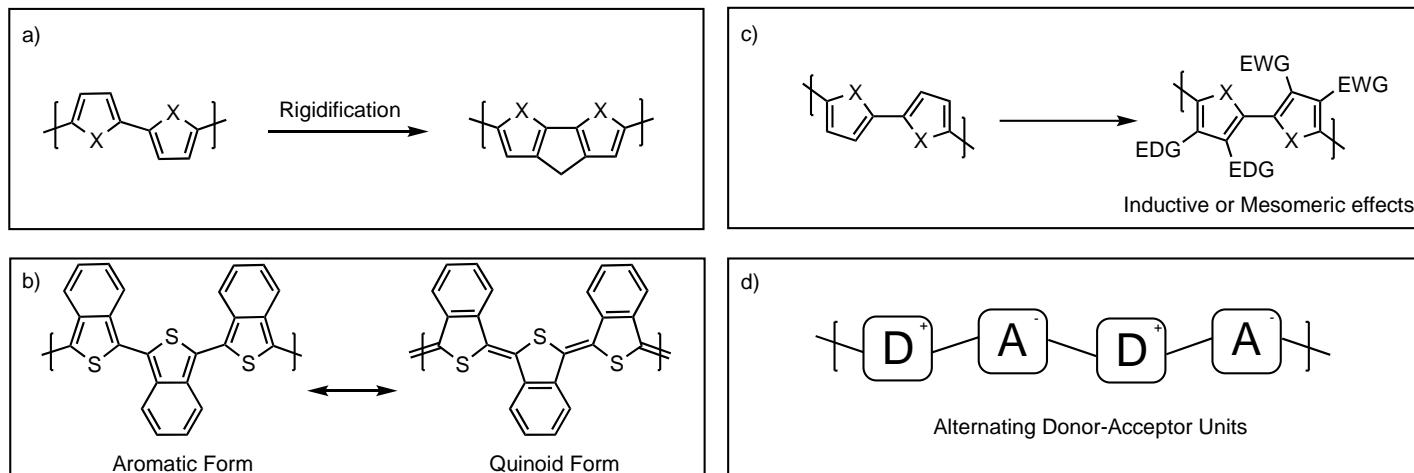
The semiconducting properties of conjugated polymers stem from the alternating single and double bond structure which allows for electron delocalization throughout the polymer backbone. The band gap is one of many properties of conjugated materials, however it is the most important since it allows the material to be semiconducting. Typically, conjugated small molecules and polymers in materials are considered semiconducting if they possess a band gap between 0.1 eV – 3 eV whereas insulating materials are considered to have a band gap of greater than 3 eV (Figure 3) and a conducting material less than 0.1 eV.<sup>4</sup> This HOMO–LUMO gap is mainly dependent on the extent of conjugation of the molecule. Typically increasing conjugation results in a decrease to the HOMO–LUMO gap until a point at which the further increase results in no further decrease.<sup>2</sup>





**Figure 3: Band Gaps of Metals, Semiconductors and Insulators.**

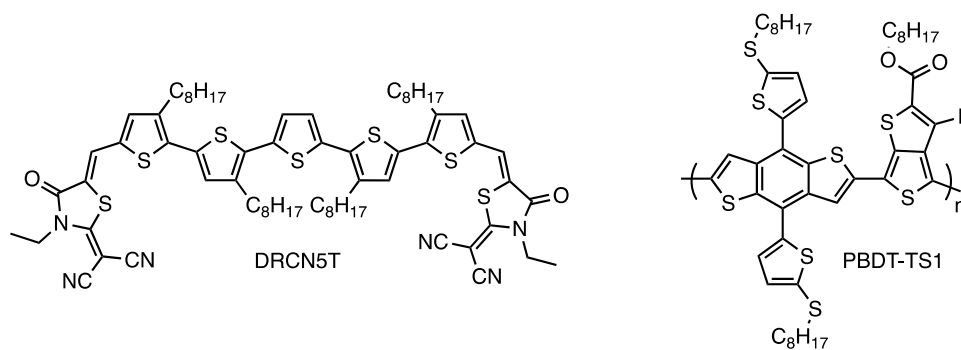
The HOMO–LUMO gap can be tuned in other various ways such as rigidification of the polymer backbone by introducing covalent bonds between two adjacent aromatic units. Stabilization of the quinoid resonance structure also decreases the HOMO–LUMO gap. The band gap of poly(thiophene) (2 eV) is higher than the bandgap of poly(isothianaphthene) (1 eV) due to the stabilization of the latter quinoid resonance form through incorporation of benzene (Figure 4).<sup>5</sup> In addition to these methods, introducing electron-donating groups (EDG) and electron withdrawing group (EWG) onto the polymer backbone is another way to alter the HOMO–LUMO gap through inductive or mesomeric effects.<sup>5</sup> The most utilized method for lowering the HOMO–LUMO gap is to incorporate a push-pull motif, in which an electron rich unit and an electron poor unit are both incorporated into the same polymer backbone. The hybridization of the molecular orbitals of the electron rich system and the electron poor system leads to a significant decrease in the HOMO–LUMO gap through the raising of the HOMO and lowering of the LUMO. The ideal HOMO–LUMO gap of a material is targeted based on the desired application of the material, but typically materials with lower band gaps have a wider range of use.<sup>2</sup>



**Figure 4: Traditional Methods to Tune the HOMO-LUMO Gap.**

### 1.1.3 Conjugated Small Molecules

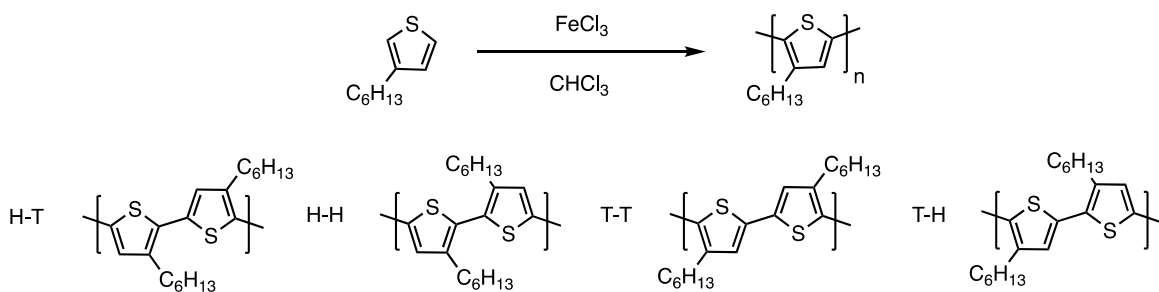
Conjugated organic small molecules have shown to be competitive with conjugated polymers for use in a number of material applications.<sup>6,7</sup> Extensive research during the past decade has currently enabled a maximum power conversion efficiency (PCE) of over 10% to be achieved in polymer-based OPV's (P-OPV's) with bulk heterojunction architectures.<sup>8</sup> Solution processed small molecule OPV's have recently reached competing power conversion efficiencies of near 10% for single-junction, which displays their potential for use in applications where polymers have been traditionally used (Figure 5).<sup>8</sup> Conjugated small molecules can, in fact, possess a number of advantages when compared to their polymeric counterparts. These advantages stem from the well-defined structures that conjugated small molecules possess, including: the elimination of batch-to-batch variation and end group contaminants, as well as easier control of the HOMO-LUMO gap.<sup>2,8,9</sup> Similar to conjugated polymers, the HOMO-LUMO gaps of small molecules can also be tuned through similar methods such as stabilization of the quinoid resonance structure and introduction of strong donor-acceptor motifs.<sup>10</sup> These small molecules have in fact played a very significant role in the development of organic electronic materials.<sup>2,6,8,9</sup>



**Figure 5: a) Small Molecule OPV with PCE = 10.01%<sup>8</sup>, b) Polymer OPV with PCE = 9.48%.<sup>11</sup>**

## 1.2 Synthesis of Conjugated Materials

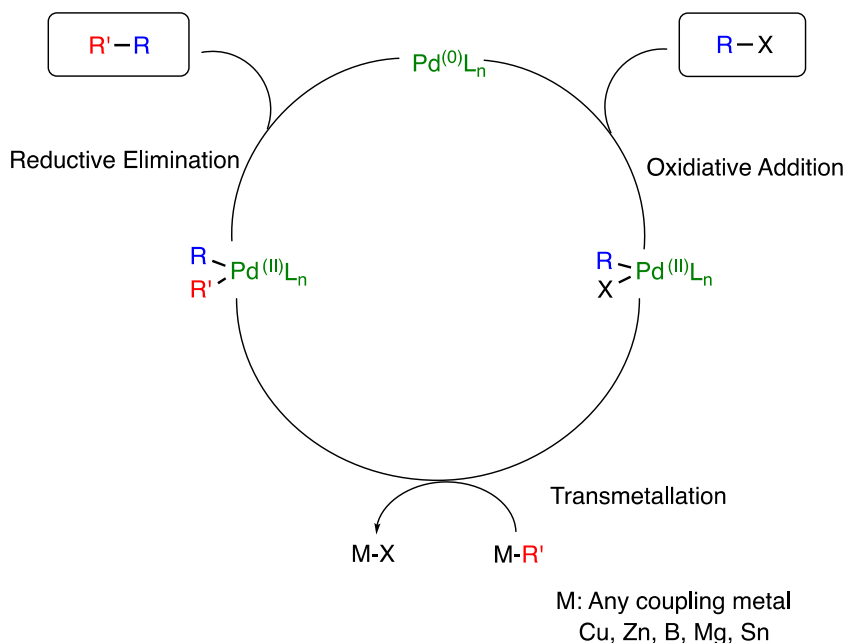
The synthesis of conjugated small molecules and polymers requires efficient formation of  $C(sp^2)-C(sp^2)$  bonds. An early method for the synthesis of conjugated polymers is oxidative polymerization, in which an aryl monomer is oxidized via chemical (an oxidizing agent) or electrochemical (applying a potential) means to create cation or cation radical sites, ultimately causing polymer growth. One advantage of this simple approach is that monomer prefunctionalization is not required.<sup>12</sup> An example of oxidative coupling is the formation of poly-3-hexylthiophene from 3-hexylthiophene, in which ferric chloride (III) is used as an oxidizing agent in chloroform (Scheme 1). While technically simple, these reactions are typically not ideal due to a major drawback in the fact that the degree of cross-linking and branching of the polymer chains cannot be controlled.<sup>13</sup> In addition, they tend to make regiorandom polymers consisting of head-to-tail, head-to-head, tail-to-tail and tail-to-head linkages (H-T, H-H, T-T, T-H) which can bestow negative effects on the properties of the polymer such as unfavourable steric interactions that disrupt planarity.<sup>12</sup>



**Scheme 1: Oxidative Coupling of 3-Hexylthiophene Using Ferric Chloride.**

### 1.2.1 Palladium-Catalyzed Cross-Coupling

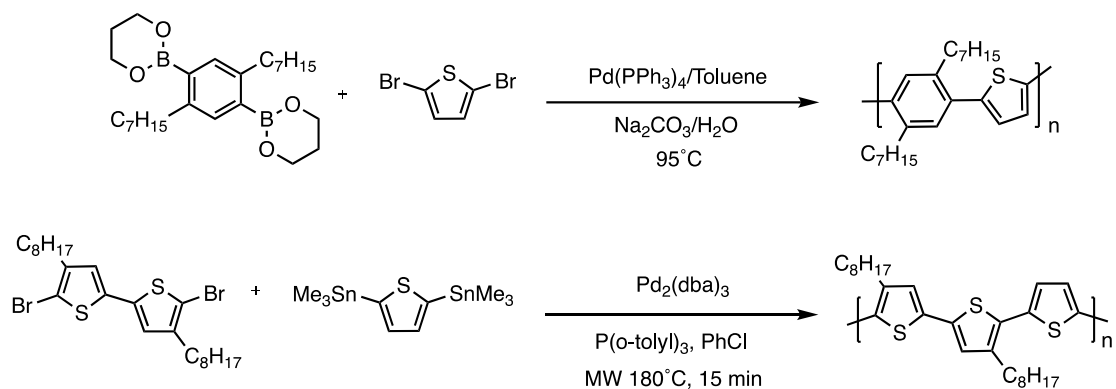
The emergence of palladium-catalyzed cross-coupling reactions has played an enormous role on the development of new organic methods. These advances have provided new opportunities for functionalization of sensitive substrates and have opened the door to many pharmaceutical and material developments. Generally, palladium-catalyzed cross-coupling reactions begin with oxidative addition of the palladium (0) catalyst across a  $\text{C}(\text{sp}^2)\text{-X}$  bond. Next, transmetalation occurs with the organometallic nucleophile, and finally reductive elimination of the coupled product occurs as the active palladium catalyst is regenerated (Scheme 2). Common types of palladium catalyzed cross-couplings include Sonogashira, Stille, Suzuki-Miyaura, Heck, and Negishi where each type adopts a different organometallic nucleophile.<sup>14</sup> These reactions are widely used for conjugated polymer synthesis as they provide a high level of regioregularity and therefore uniform properties and low batch-to-batch variation. These reactions are also known for their ability to tolerate a wide variety of functional groups, which is an attractive feature for the synthesis of conjugated polymers.



### Scheme 2: General Mechanism for Traditional Cross-Coupling Reactions.

The most popular synthetic methods for conjugated polymer synthesis are Stille couplings, mainly used for thiophene-containing polymers, and Suzuki-Miyaura couplings for benzene-containing polymers.<sup>5</sup> Stille couplings are attractive for the synthesis of conjugated polymers due to the high yields generally obtained, as well as the relatively low moisture and air sensitivity of organotin compounds relative to other classes of organometallic reagents (Grignard, organolithium).<sup>15</sup> Furthermore, organotin and organohalide compounds required for Stille coupling can be synthesized with relative ease and good functional group tolerance, eliminating the requirement for any protecting groups. The main disadvantage of using the Stille coupling is the stoichiometric amounts of organotin waste that is generated with each reaction. These organotin by-products are harmful to the environment as well as difficult to remove from the final products.<sup>16</sup> Although Suzuki couplings are also widely used, some drawbacks do exist, such as the basic conditions required which not all functional groups can tolerate making it a less widely

applicable cross-coupling reaction. Additionally, two phase solvent systems are also required which is a problem for some conjugated polymers since their solubility decreases with increasing molecular weights resulting in the isolation of low molecular weight polymers under these conditions.<sup>15</sup> However, both cross-coupling reactions are powerful synthetic tools and have been used extensively to enable access to a wide variety of synthetically complex conjugated polymers and small molecules (Scheme 3).<sup>17,18</sup>



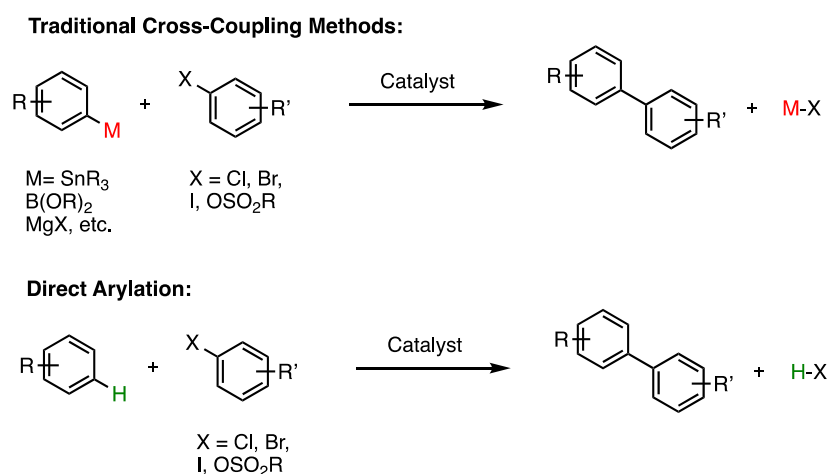
**Scheme 3: Example of Suzuki and Stille Polymerization of Thiophene Containing Based Monomers.**

Although palladium-catalyzed cross-coupling reactions are efficient in creating C(sp<sup>2</sup>)–C(sp<sup>2</sup>) bonds, there are drawbacks that prevent scaling of these syntheses to wide-scale use. These disadvantages include the stoichiometric amount of organometallic waste generated in reactions such as the Stille coupling (organotin). Moreover, palladium-catalyzed cross-couplings require pre-functionalization of both coupling substrates in order to generate the precursors required for cross-coupling reactions, ultimately adding further synthetic complexity to the synthesis.

### 1.2.2 Direct Arylation

In order to combat the inherent disadvantages found in traditional palladium-catalyzed cross-coupling, alternate methods for the formation of C(sp<sup>2</sup>)–C(sp<sup>2</sup>) bonds have been of high interest. Of these alternate methods, the most developed is the direct arylation reaction wherein an

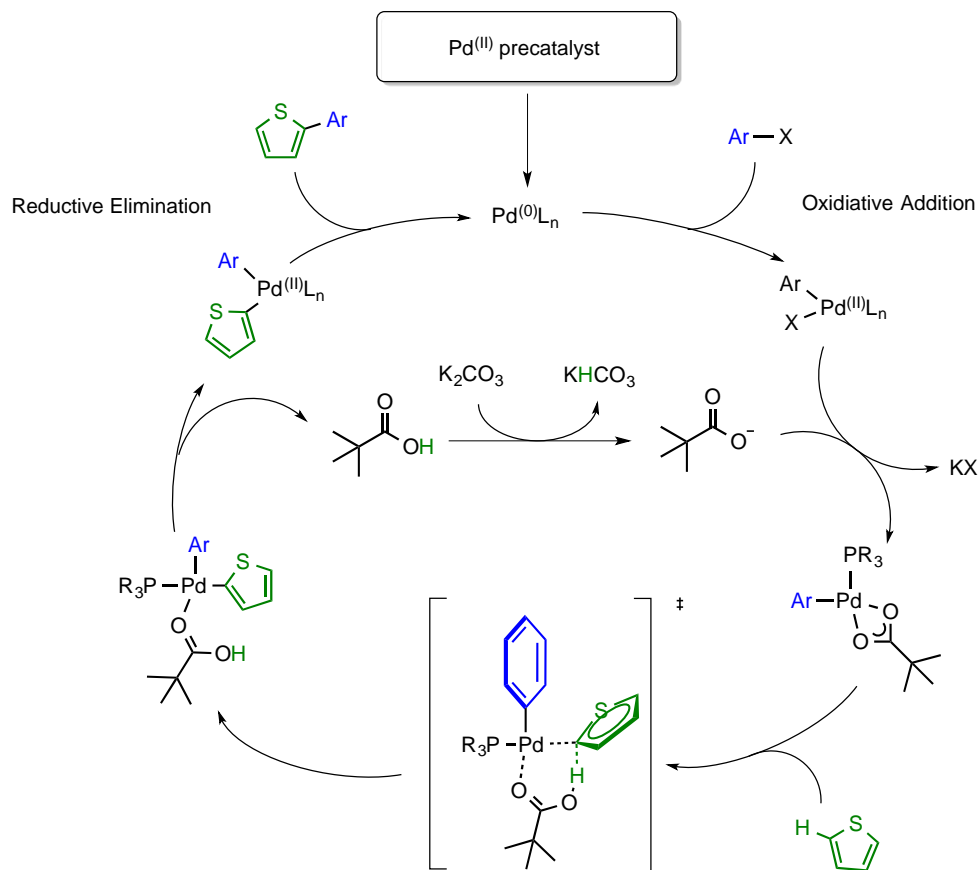
aryl halide is coupled to a non-functionalized arene through palladium-catalyzed C-H activation (Scheme 4).<sup>19</sup> This method eliminates the need for prefunctionalization of one of the arene species to an organometallic (such as a borate or stannane), and therefore eliminates the stoichiometric amount of metal waste produced as well as reduces the number of synthetic steps required to achieve the cross-coupled product. Direct arylation has proven to allow access to a number of cross-coupled products, typically synthesized using traditional cross-coupling methods, in higher yields and fewer synthetic steps.<sup>20</sup>



**Scheme 4: General Scheme for Direct Arylation Reactions.**

Direct arylation is proposed to proceed through a catalytic cycle similar to traditional cross-couplings, beginning with oxidative addition of palladium (0) into the aryl halide substrate. Following this, the mechanism does not involve a transmetalation step, but rather proceeds through a C-H activation step in which the palladium is inserted into the most active C(sp<sup>2</sup>)-H bond through a concerted-metalation-deprotonation (CMD).<sup>21</sup> This CMD step proceeds due to the addition of a carboxylate ligand co-catalyst to the palladium which is able to subsequently act as a proton shuttle from the unactivated arene as the new palladium-carbon bond is being formed. Reductive elimination of the cross-coupled product regenerates palladium (0) and deprotonation

of the resulting carboxylic acid by stoichiometric base regenerates the carboxylate co-catalyst (Scheme 5). The arene reactivity and selectivity is dependent on both the C-H bond acidity and nucleophilicity of the arene, since both electron rich and electron deficient systems can participate in direct arylation reactions.



**Scheme 5: Proposed Direct Arylation Mechanism.**

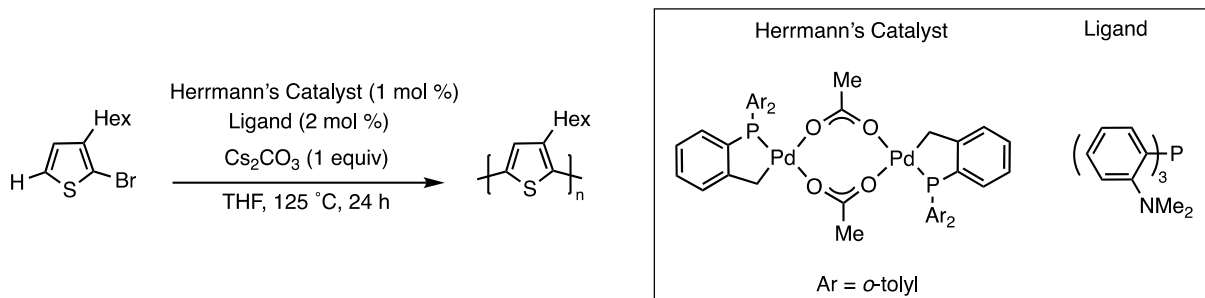
### 1.2.3 Direct Arylation Polymerization

The need to develop economical methods for the synthesis of conjugated polymers is important to be able to develop these materials on a large-scale. The concept of utilizing C-H activation through direct arylation for synthesis of carbon-carbon bonds was therefore extended to

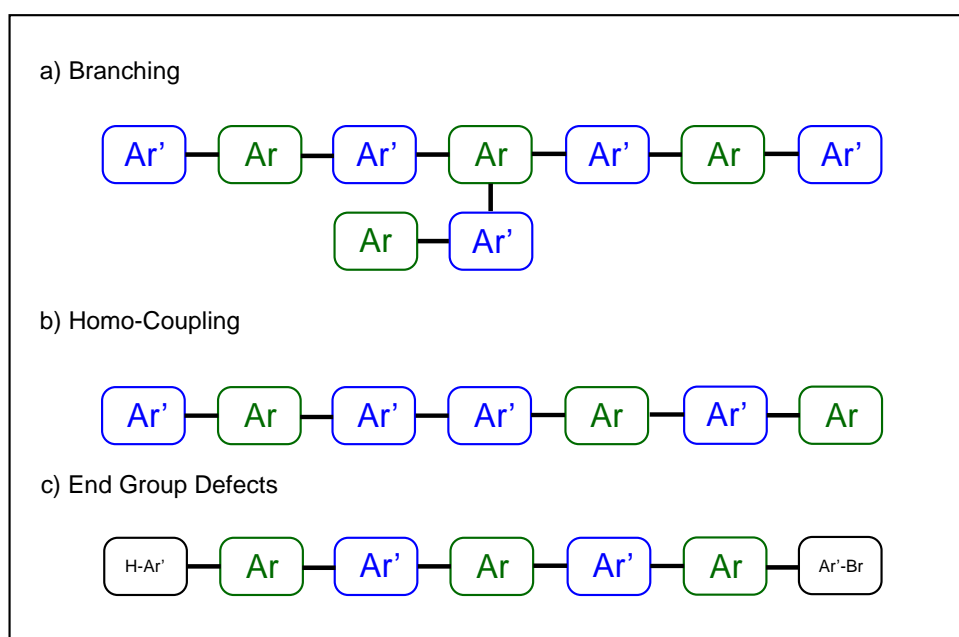


the synthesis of conjugated polymers.<sup>22</sup> Direct arylation polymerization (DArP) was first reported by Lemaire et al. in 1999, wherein commercially important poly(3-alkylthiophene)s were synthesized via direct arylation conditions through the homopolymerization of bromothiophene and a palladium source.<sup>23</sup> While this was an important first step into the use of DArP, only molecular weights of around 3 kDa were achieved which is speculated to be due to the decomposition of the catalyst. In 2010, Ozawa et al. were able to access high molecular weight and regioregularity of poly(3-hexylthiophene) via DArP by employing a Herrmann-Beller catalyst as the palladium source which has high thermal stability (Scheme 6).<sup>24</sup> Since then, DArP has been used extensively for polymer synthesis based on small molecule reaction conditions developed by Fagnou in which high molecular weights and yields can easily be obtained.<sup>25</sup> Both reactions conditions developed by Ozawa and Fagnou have since then been utilized for synthesis of a wide variety of conjugated polymers by many research groups.<sup>26-29</sup>

Interest in DArP has grown widely due to the many advantages it offers, such as eliminating the need for prefunctionalization of the monomers of interest with organometallic activating groups. This reduces the overall number of synthetic steps, and eliminates the stoichiometric amounts of organometallic waste generated making DArP an attractive alternative to traditional cross-coupling methods for the synthesis of conjugated polymers as it is one step closer to a streamlined synthesis that could be performed commercially. While the molecular weights as well as regioregularity are comparable to conjugated polymers achieved through traditional methods, conjugated polymers synthesized through the DArP route can still contain defects that result from both homo-coupling and branching of the polymer chain as well as end group defects (Figure 6).<sup>30</sup>



**Scheme 6: Synthesis of Poly(3-hexylthiophene)s Using DAoP.**

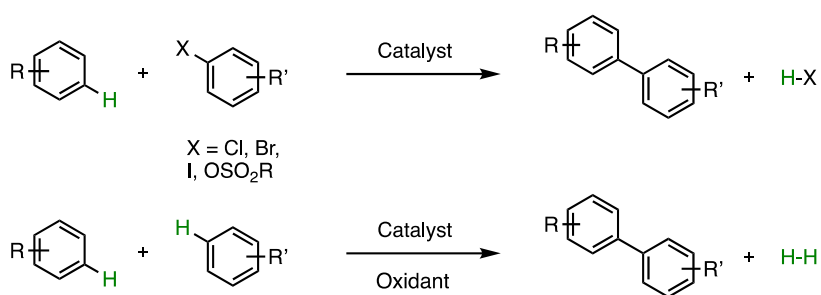


**Figure 6: Defects Associated with Direct Arylation Polymerization Reactions.**

### 1.2.4 Oxidative Cross-Coupling

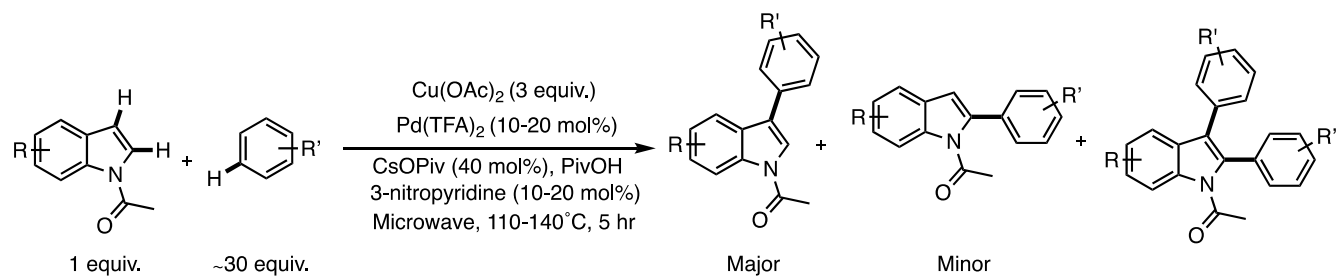
Although the development of direct arylation reactions helped streamline the synthesis of conjugated materials as mentioned previously, prefunctionalization of one arene species is still necessary for the cross-coupling reaction. Efforts have also been directed towards the development of cross-coupling methods to couple two unfunctionalized arenes (Scheme 7).<sup>31</sup> However, that is a challenging task due to the general lack of reactivity of C–H bonds relative to C–X and C–M

bonds. In addition, the presence of multiple C–H bonds introduces regioselectivity problems.<sup>32</sup> The selectivity issue could be addressed through various methods such as introducing directing groups as well as steric interactions forcing the coupling to occur at a certain position on the molecule. Catalyst design is also very important since this oxidative coupling would require a catalyst that would selectively react with the first unactivated arene, causing a change in the reactivity of the catalyst, then consequentially reacting solely with the second unactivated arene eventually generating the coupled product.<sup>31</sup>



**Scheme 7: General Scheme for Oxidative Cross-Coupling.**

In 2007, Fagnou and co-workers reported the oxidative coupling of *N*-acetylindoles with benzene using a palladium catalyst and copper acetate as the oxidant.<sup>33</sup> Great regioselectivity and conversion were obtained with no spectroscopic detection of any homo-coupled by-products. Various *N*-acetylindole derivatives were subjected to the optimal conditions and obtained great regioselectivity (C3:C2) and respectable yields for 9 examples (42%–84% isolated yields) (Scheme 8). The oxidative coupling was able to occur at the C3 position of the indole with zero to minimal amounts of di-coupled product formed. A mechanism was not reported by the Fagnou group since insufficient information was collected to provide a plausible mechanism, however, since this development, various examples of homo/cross oxidative coupling of arenes/heteroarenes have made their way into the literature.<sup>31</sup>

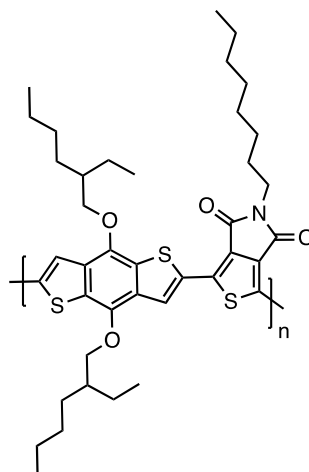


**Scheme 8: Oxidative Cross-Coupling of Indole Derivatives with Benzene Derivatives.**

# Chapter 2

## 2.1 Dehydration Polymerization

Although advances in homo/cross-coupling methods to create conjugated heteroaromatic small molecules and polymers have come a long way since interest in organic semiconductors began, development of newer, more practical methods is always of importance. These new methods can give us the tools to access conjugated organic materials with properties different to those that were previously accessible. Moreover, development of more economical methods that reduce the number of synthetic steps and eliminate the use of transition metals help reduce the costs of total synthesis of these conjugated materials. This allows for a higher potential for use at the commercial scale where millions of tonnes of a material may need to be produced. For example, a polymer PBDTTPD, used in organic photovoltaics, is synthesized through 10 reactions and has an calculated cost of over USD\$400/g, which is not feasible for large scale synthesis (Figure 7).<sup>34,35</sup> Conversely, commercial polymers such as polyethylene terephthalate (PET) and polyamides (nylon-6 and nylon-6,6) have an estimated cost of less than USD\$0.03/g and USD\$0.12/g respectively, which is largely reflective of the ease of synthesis.<sup>36,37</sup>

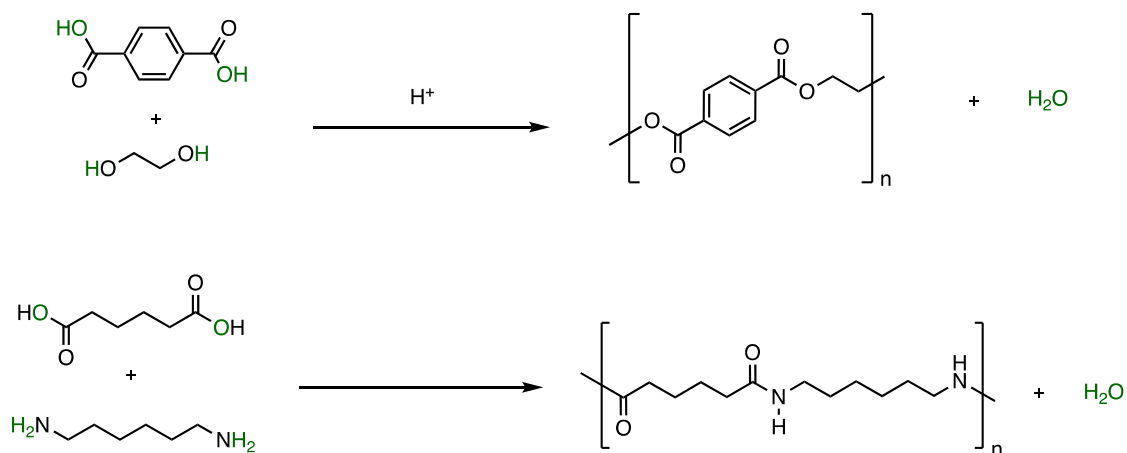


Steps	Reagents (\$ per g)	Solvent (\$ per g)	Workup (\$ per g)	Total (\$ per g)
10	70.97	14.95	361.92	447.83

**Figure 7: Calculated Cost of Synthesis of Polymer PBDTTPD.**

### 2.1.1 Industrial Dehydration Polymerization of Non-Conjugated Polymers

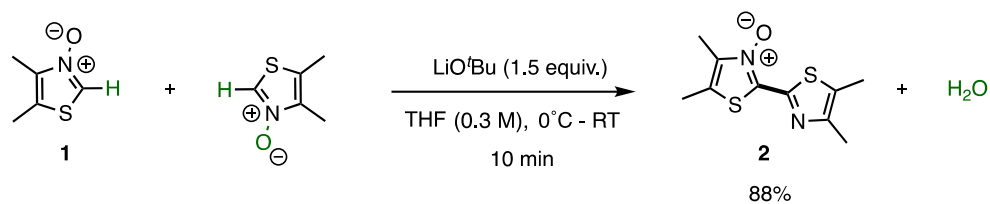
Many industrial polymers produced on a multi-ton scale annually are synthesized via dehydration polymerization in which two monomers react together with formal loss of water. With water as the only by-product of this reaction, it is more feasible to produce these polymers on a large-scale synthesis. The water produced as the by-product is significantly easier to dispose of, and not environmentally harsh relative to the organometallic waste generated from organometallic polymerization reactions used to synthesize conjugated materials. In 2017, 30 million metric tons of PET were produced from the dehydration reaction of ethylene glycol and terephthalic acid.<sup>36</sup> Similarly, nylon-6,6 was produced in 3.4 million metric tons in 2016 from the dehydration reaction of adipic acid and hexamethylenediamine (Scheme 9).<sup>37</sup>



**Scheme 9: Dehydration Polymerization Reaction of PET and Nylon-6,6.**

### 2.1.2 Dehydration Coupling of Thiazole *N*-Oxides and Previous Work

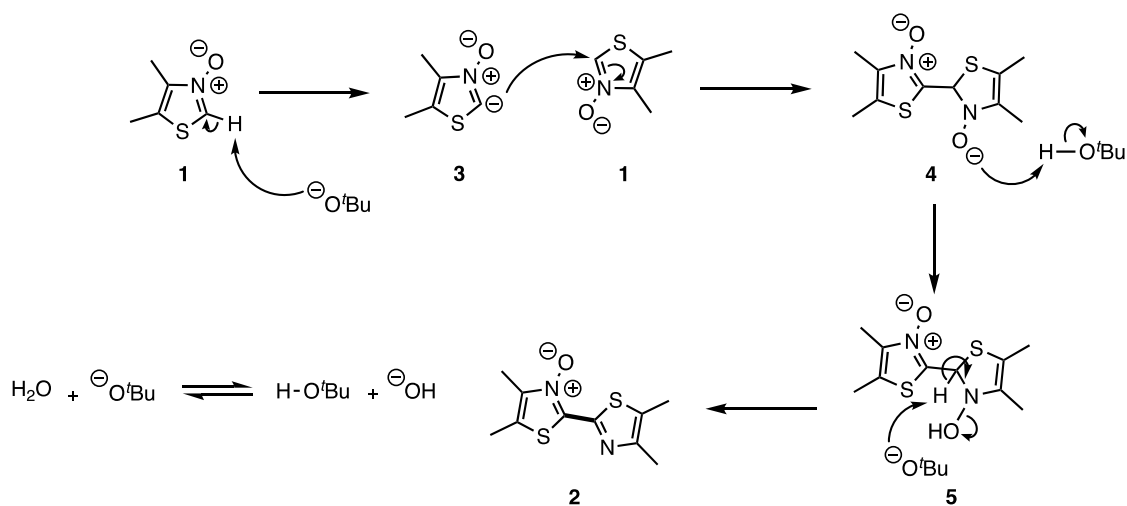
Drawing inspiration from the synthesis of industrial scale polymers made via dehydration reactions, it was envisioned that the development of a reaction that could allow for the dehydration of (hetero)arenes would be of extreme value towards the synthesis of conjugated materials. This could potentially mitigate some of the costs by reducing the number of synthetic steps and potentially eliminating the use of transition metals. While the development of new methods for the synthesis of conjugated polymers are highly studied, there has not been extensive research towards the development of such a dehydration method. Recently, the Schipper group reported a dehydration polymerization of poly(hetero)arenes using thiazole di-*N*-oxide monomers. The initial discovery occurred when an equivalent of thiazole *N*-oxide (**1**) dimerized upon the addition of a base to yield a conjugated bithiazole system (**2**) containing a single *N*-oxide moiety (Scheme 10).<sup>38</sup> The dehydration reaction was able to occur in 10 minutes, coupling two thiazole *N*-oxide molecules by forming a new bi-aryl carbon-carbon bond with the stoichiometric loss of water and without the use of transition metals.



**Scheme 10: Dehydration Reaction of 4,5-Dimethylthiazole 3-oxide.**

Upon initial reaction discovery, the reaction conditions were optimized with a variety of bases, temperatures and reaction times being screened. Optimization of the reaction conditions afforded the addition of 1.5 equiv. of lithium *tert*-butoxide at 0°C to a 0.3 M solution of the *N*-oxide in THF. The reaction was then allowed to warm up to room temperature and further stirred for an additional 10 minutes.

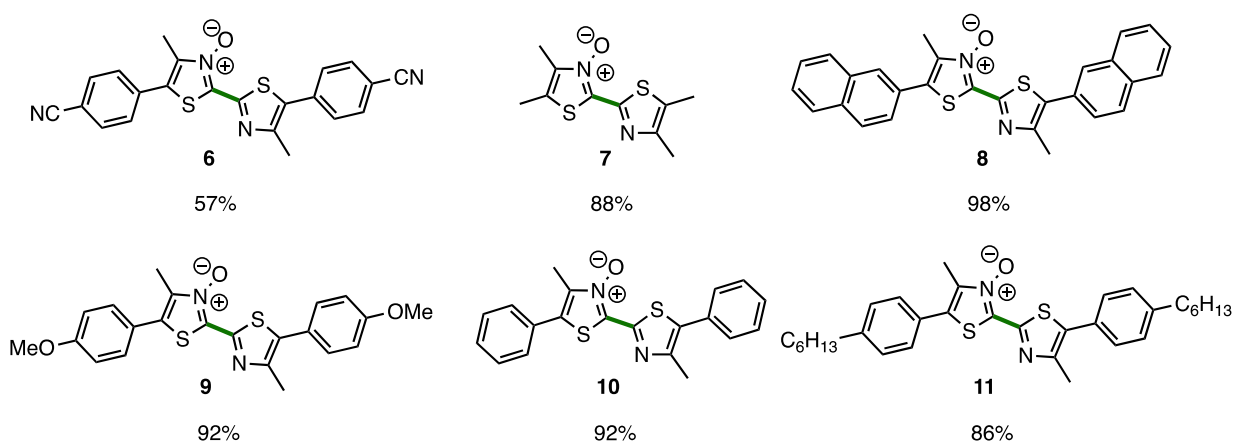
Based on the known reactivity of the starting materials and reagents, a proposed mechanism has been developed (Scheme 11). It begins with deprotonation of the most acidic proton (C-2) of a thiazole *N*-oxide (**1**) forming a carbanion (**3**). The carbanion (**3**) can then act as a nucleophile attacking the C-2 position of another equivalent of thiazole *N*-oxide (**1**) resulting in loss of aromaticity (**4**). Upon proton transfer, hydroxide can then be eliminated from **5** in order to restore aromaticity and afford the thiazole dimer (**2**).



**Scheme 11: Proposed Dehydration Reaction Mechanism.**

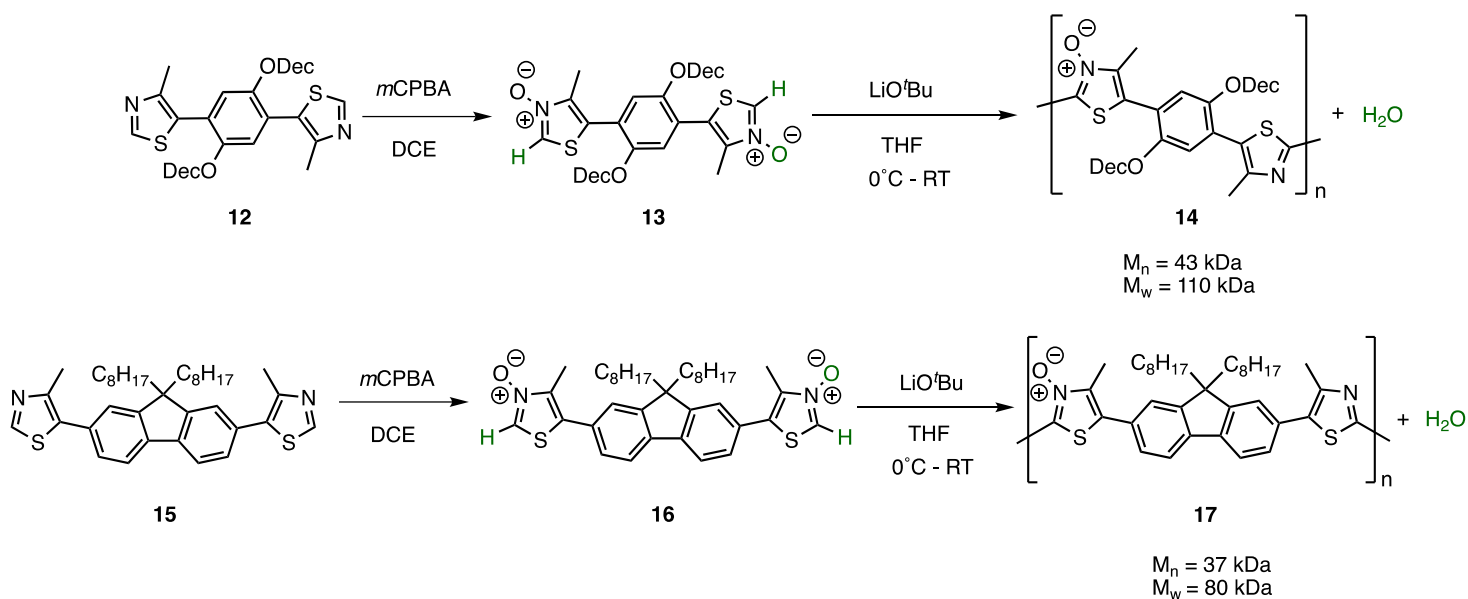


In order to test the functional group tolerance of the developed reaction, a previous member of the Schipper group successfully synthesized various small molecules examples (**6–11**) with yields ranging from (57%–92%) (Figure 8). The reaction proceeded well with various thiazole *N*-oxide derivatives containing alkyl groups (**7**), aryl groups with electron-donating (**9**), electron-withdrawing (**6**) and electron-neutral substituents (**8,10**). The dimers synthesized were purified through extraction from the reaction mixture using dichloromethane (DCM), with no need for purification using silica-gel column chromatography.



**Figure 8: Small Molecule Scope of Various Thiazole *N*-Oxide Dimers.**

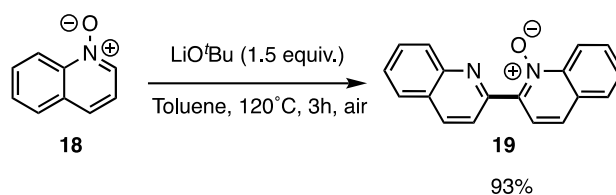
This chemistry was then extended to the synthesis of conjugated polymers using the dehydration reaction. In order to accomplish this, di-*N*-oxide thiazole derivatives were accessed through the direct arylation reaction of two equivalents of thiazole with a conjugated  $\pi$ -spacer (**12**, **15**) (Scheme 12), followed by subsequent oxidation of both thiazole moieties. With the di-*N*-oxides **13** and **16** synthesized, the addition of base allowed for the synthesis of two conjugated polymers (by a previous member of the Schipper group) possessing two distinct  $\pi$ -spacers (benzene **14**, fluorene **17**) in quantitative yields and molecular weights between 80 – 110 kDa (Scheme 12).



**Scheme 12: Dehydration Polymerization of Thiazole Di-*N*-Oxides.**

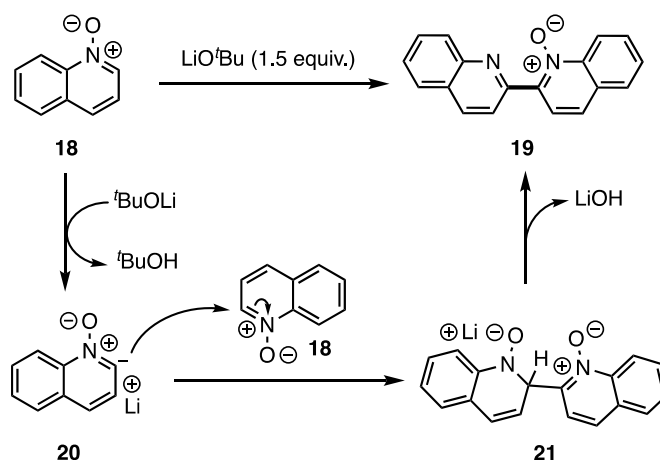
### 2.1.3 Prior Metal-Free Coupling Reactions

The development of transition metal-free coupling methods is attractive since the removal of residual metal contaminants from the final product is often necessary.<sup>39,40</sup> In addition, transition metals are expensive and not environmentally friendly for utilization in large-scale synthesis. In 2014, Wang et al. reported a metal-free coupling of quinoline *N*-Oxide (**18**), using lithium *tert*-butoxide as the base (Scheme 13).<sup>41</sup> Various reaction conditions were screened and it was determined that 1.5 equiv. of lithium *tert*-butoxide, in toluene at 120°C for three hours yielded the highest amount of dimer product **19**.



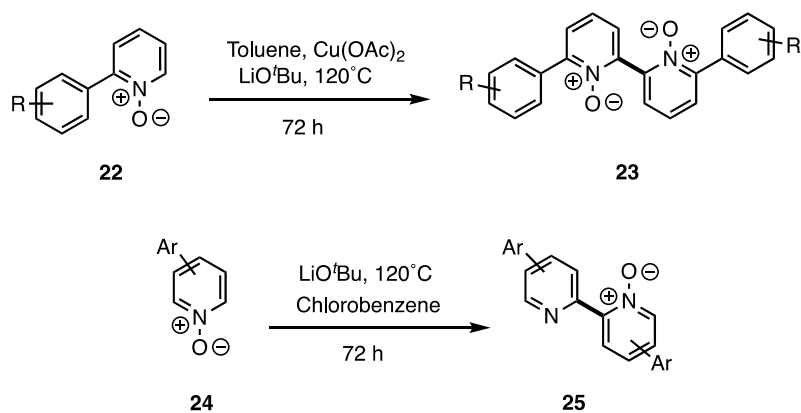
**Scheme 13: Metal-Free Coupling of Quinoline *N*-Oxide Using Base.**

Various quinoline *N*-oxides were subjected to the optimal conditions and their respective dimers were isolated in respectable yields for 11 examples (28%–93%). When quinoline *N*-oxide derivatives containing electron-withdrawing substituents were reacted (including Br, Cl), the yields remained fairly high (75%–87%); however, when electron-donating substituents were employed on the quinoline, lower yields were observed (53%–65%). In addition, when the pyridine ring was functionalized with electron-donating substituents, even lower yields were obtained (28%–49%). Lastly, switching the substrate to quinoxaline *N*-oxide, also afforded the dimer in a good yield (72%). The mechanism was proposed to begin with deprotonation of the most acidic proton of the quinoline *N*-oxide (**18**) generating an anion (**20**) and *tert*-butanol. The anion then is able to attack a second equivalent of the *N*-oxide (**18**), generating a non-aromatic intermediate (**21**). Lastly, through elimination of lithium hydroxide, the dimer **19** is generated (Scheme 14).



**Scheme 14: Proposed Metal-Free Coupling Mechanism of Quinoline *N*-Oxide.**

Jain and Jha, also developed a homo dimerization reaction of pyridine *N*-oxide derivatives generating both the di-*N*-oxide (**23**) and the mono *N*-oxide (**25**) dimer products depending on the addition of copper acetate (Scheme 15).<sup>42</sup> The mechanism for the di-*N*-oxide dimer was proposed to proceed through oxidative coupling in air while the mechanism for the mono *N*-oxide dimer was proposed to be very similar to that proposed by the Wang group. While these reports have described methods for the dehydration reaction of similar classes of heteroarenes to that reported by the Schipper group, none of these methods were employed towards conjugated polymer synthesis.

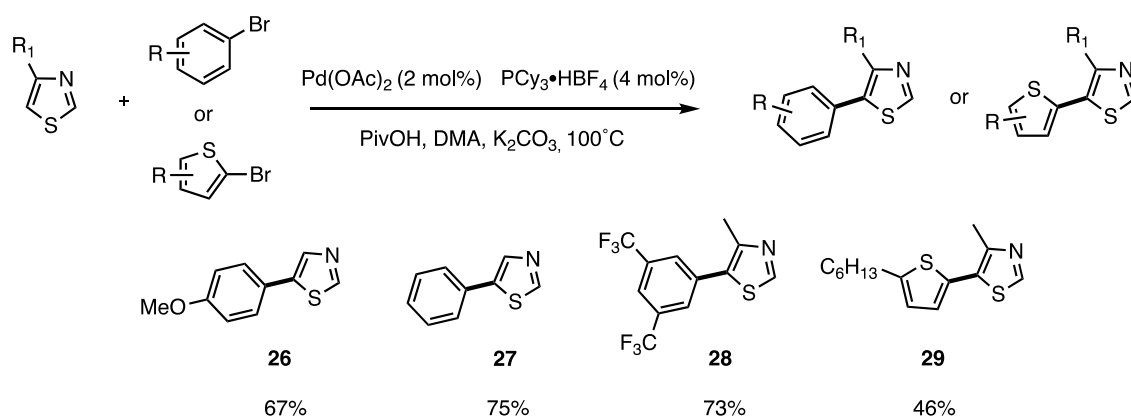


**Scheme 15: Coupling of Pyridine *N*-Oxide Derivatives.**

## 2.2 Dehydration of Novel Heteroaromatic *N*-oxides Results and Discussion

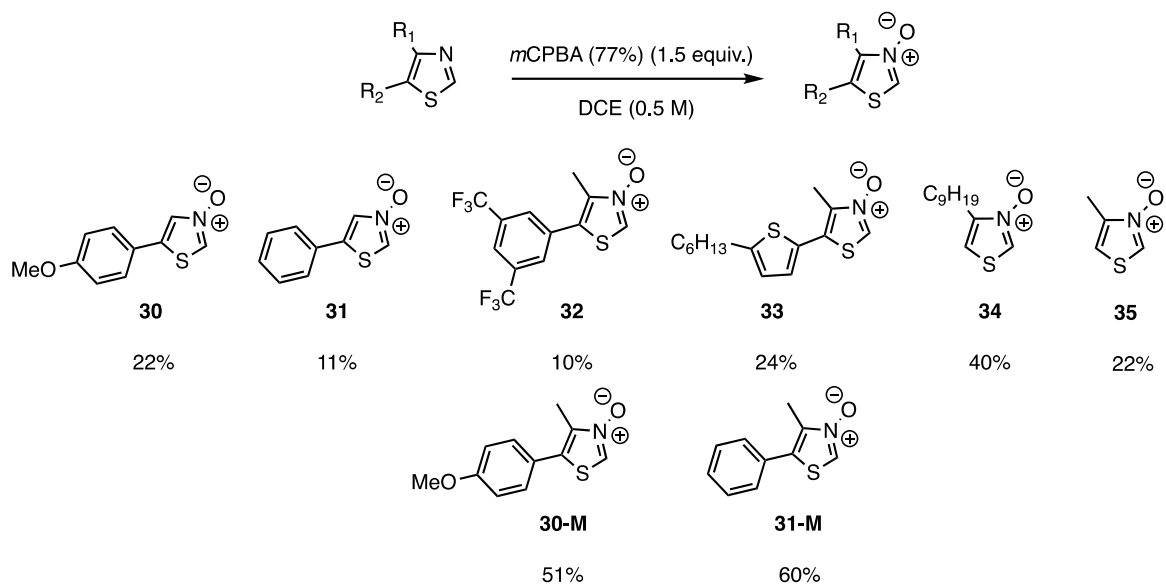
To further expand upon the scope of the dehydration reaction developed in our lab, additional small molecules were synthesized. The thiazole moiety on the previously synthesized small molecules (Figure 8) contained a methyl substituent at the 4- position; however, this disrupts the planarity of the molecule, which consequently affects the properties. Therefore, unsubstituted thiazole was used instead to access relatively more planar small molecules through the dehydration reaction route (**26**, **27**) (Scheme 16). An aryl group with electron-withdrawing substituents (**28**) was chosen due to their scarcity in previous work done in this research group. In addition, a hexyl

substituted thiophene (**29**) was chosen to allow access to extended conjugated systems. The hexyl substituent is important for solubility of the substrate since it introduces steric interactions to disrupt the strong intermolecular  $\pi$ - $\pi$  stacking.<sup>5</sup> Introduction of aliphatic chains therefore increases the solubility of organic conjugated materials. Starting substrates were prepared by first coupling thiazole or 4-methylthiazole to various substituted aryl or heteroaryl bromides via direct arylation cross-coupling reaction. These direct arylation reactions proceeded in one pot with overall yields ranging from 46%–75%.<sup>43</sup>



**Scheme 16: Direct Arylation to Synthesize 5-Substituted Thiazole Derivatives.**

Once the coupled compounds were isolated, they were oxidized to their respective thiazole *N*-oxides using *m*CPBA (77% pure, 1.5 equiv.) as the oxygen transfer agent in dichloroethane (DCE) (0.5 M) at room temperature for 4 hours. These optimal oxidation conditions were previously determined by the Schipper group where various alternate oxidants as well as conditions were screened, including: hydrogen peroxide, magnesium monoperoxyphthalate (MMPP), chlorine dioxide and dimethyldioxirane (DMDO). Although *m*CPBA provided the most optimal yields; fairly low yields are almost always obtained. The yields for the oxidation reactions were fairly low ranging from 10%–60% (Scheme 17).

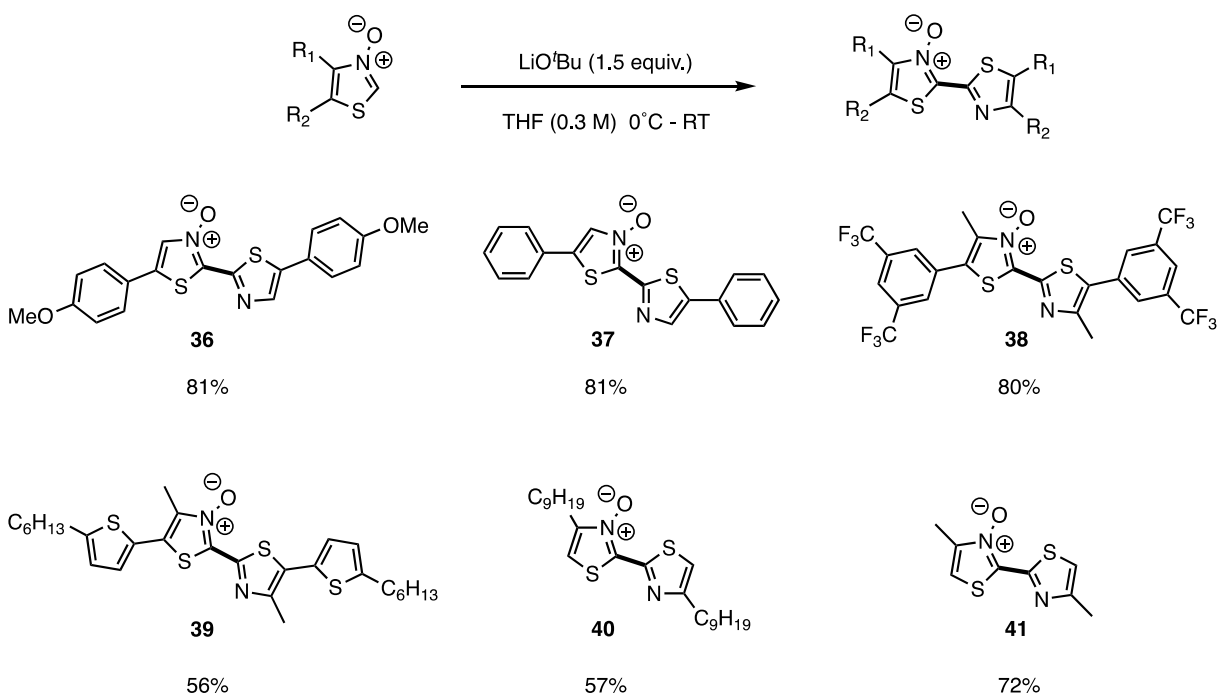


**Scheme 17: Oxidation of Various Thiazole Derivatives to their Corresponding *N*-oxides.**

It was observed that compounds possessing no methyl substituent at the 4- position on the thiazole ring afforded a significantly decreased amount of oxidized product compared to those possessing a 4-methyl substituent. When compounds **30** and **31** were oxidized where the thiazole possessed a methyl substituent (**30-M**, **31-M**), the oxidation yields obtained were 51% and 60% respectively. A plausible explanation for this increase in yield could be attributed to the inductive donating effect the methyl substituent was introducing through hyperconjugation possibly enhancing the thiazoles nucleophilicity. The *N*-oxide of 4,5-dimethylthiazole was previously obtained in a 90% yield, however, when 4-methylthiazole was oxidized, 22% of **35** was isolated. When the methyl group was switched to a nonyl group, the oxidation yield increased to 40% (**34**).

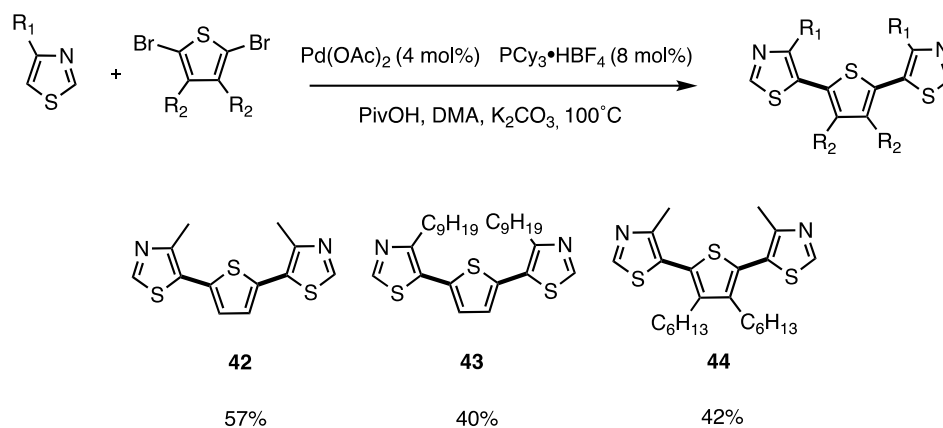
Once the *N*-oxides were purified and isolated, they were reacted with lithium *tert*-butoxide (1.5 equiv.) forming the respective dimers. The desired products were obtained in moderate to good yields ranging from 56% to 81% (Scheme 18). The dehydration dimer yields obtained for the compounds lacking a methyl substituent on the thiazole (**36**, **37**) (81%) were slightly lower than when the thiazole possessed a methyl substituent (**9**, **10**) (92%). When the aryl group

possessed an electron-withdrawing substituent, a yield of 80% was obtained for the corresponding dimer (**38**). Accessing an extended conjugated system through the incorporation of another (hetero)arene resulted in a low dehydration yield of 56% for dimer **39**. Dehydration reaction of 4-methylthiazole resulted in isolation of dimer **41** in a 72% yield, however, substituting the methyl group with a nonyl group (**40**), resulted in a reduction of the yield to 57%. The yields obtained from the dehydration of 4-substituted thiazoles (**40, 41**) were moderate. This is of importance since alkyl chains are required for solubility when synthesizing conjugated polymers. There was no significant change in yield when the aryl group on the thiazole consisted of electron-withdrawing, electron-donating or electron-neutral substituents (**36–38**).



**Scheme 18: Dehydration of Various Thiazole *N*-Oxide Derivatives.**

The next main goal was to synthesize the di-*N*-oxide monomers necessary to facilitate the formation of our desired conjugated polymers through the dehydration reaction route. The monomers chosen contained two thiazole molecules with a conjugated  $\pi$ -spacer in between to further extend conjugation. To create these, aliphatic substituted thiazoles were coupled to 2,5-dibromothiophene derivatives through a direct arylation reaction to access the precursors needed to synthesize the di-*N*-oxides. The yields obtained were lower (40%–57%) since the mono-arylated compound was always isolated as well (Scheme 19).

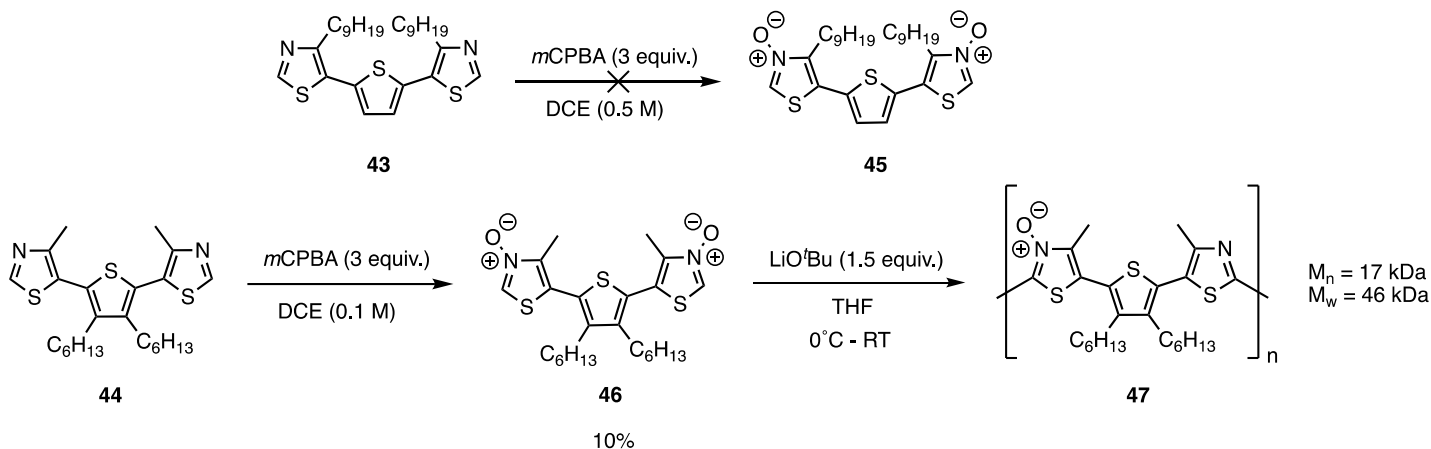


**Scheme 19: Direct Arylation to Synthesize Dehydration Polymerization Monomer Precursors.**

The next objective was to synthesize di-*N*-oxides in order to access thiophene-containing conjugated polymers through the dehydrative coupling reaction. In the absence of solubilizing chains, strong  $\pi$ - $\pi$  interactions cause oligomers to crash out of solution before long chain lengths can be reached. Compound **42** lacks aliphatic solubilizing chains and therefore, polymerization of this compound would result in formation of undesirable oligomers. As such, the synthesis of the di-*N*-oxide of compound **42** was not attempted and solubilizing chains were incorporated in compound **43**. Previously, the di-*N*-oxides were accessed through allowing 3 equiv. of *m*CPBA to react with the monomers of interest. Adopting those conditions to synthesize the di-*N*-oxide of



compound **43** was attempted, however, the di-*N*-oxide was not formed nor observed on thin-layer chromatography (TLC). This was thought to possibly be due to the steric effects of the nonyl groups present on the thiazoles. After various attempts, efforts were directed to synthesis of the di-*N*-oxide of compound **44** where the solubilizing chains were present on the thiophene instead of the thiazole. The di-*N*-oxide was first successfully isolated in a 10% yield using 1.5 equiv. of *m*CPBA while trying to isolate the mono oxidized product. In another attempt to force the reaction towards the di-*N*-oxide product, the equivalents of *m*CPBA was increased to 3, however, the excess amount of oxidant caused oxidation of the thiophene sulfur to the S,S-dioxide, in addition to oxidation of the nitrogen. With the di-*N*-oxide **46** in hand, it was subjected to the dehydration polymerization reaction in order to form **47** (Scheme 20). The polymerization reaction proceeded rapidly, and the conjugated polymer isolated had  $M_n$  and  $M_w$  values of 17 kDa and 46 kDa respectively as determined by gel permeation chromatography (GPC) in THF at room temperature relative to polystyrene standard.



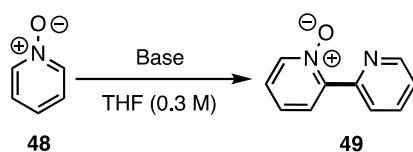
**Scheme 20: Dehydration Polymerization of the Di-*N*-Oxides Synthesized.**

### 2.2.1 Dehydration of Pyridine *N*-Oxides

Impressed with the success of the dehydration reaction of thiazole *N*-oxides, it was envisioned that the dehydration scope could be extended to other classes of *N*-oxide containing

heterocycles. First the reaction conditions would be optimized for the dimerization of small molecules, then the chemistry can be extended to the dehydration polymerization of different classes of *N*-oxide heterocycles. In the work by Wang et al., optimized reaction conditions for the dimerization of quinoline *N*-oxide using LiO<sup>t</sup>Bu had previously been reported, however, only a single example of the pyridine *N*-oxide dehydration had been shown in a 72% yield using LiO<sup>t</sup>Bu in toluene at 120 °C for 3 hours.<sup>41</sup>

Investigation of the dehydration of pyridine *N*-oxide (**48**), which was obtained from Sigma Aldrich, began with the addition of LiO<sup>t</sup>Bu (1.5 equiv.) at room temperature, which afforded dimer **49** in a 20% yield (Table 1, Entry 1). Upon increase of the reaction temperature to 60 °C, an increase in yield of the dehydration product to 65% was observed (Table 1, Entry 2). Changing the base to NaO<sup>t</sup>Bu resulted in no formation of the dehydration product and only starting material was recovered, indicating that simply changing the counterion affects the reaction outcome (Table 1, Entry 3). Interestingly, substituting the base with KO<sup>t</sup>Bu resulted in an isolated yield of 55% of the dehydration dimer (Table 1, Entry 4). The counterion clearly plays a role in these reactions as no reaction occurred when NaO<sup>t</sup>Bu was used. In the case of LiO<sup>t</sup>Bu, this was thought to be due to the ability of the lithium ion to coordinate to the *N*-oxide allowing for deprotonation. As for KO<sup>t</sup>Bu, the large size of the potassium ion creates a weaker ion base pair making it a stronger base relative to both NaO<sup>t</sup>Bu and LiO<sup>t</sup>Bu. As the development of the dehydration of pyridine *N*-oxides was previously reported by Jain and Jha, the focus was shifted to the dehydration of pyrazine *N*-oxide derivatives.<sup>42</sup>

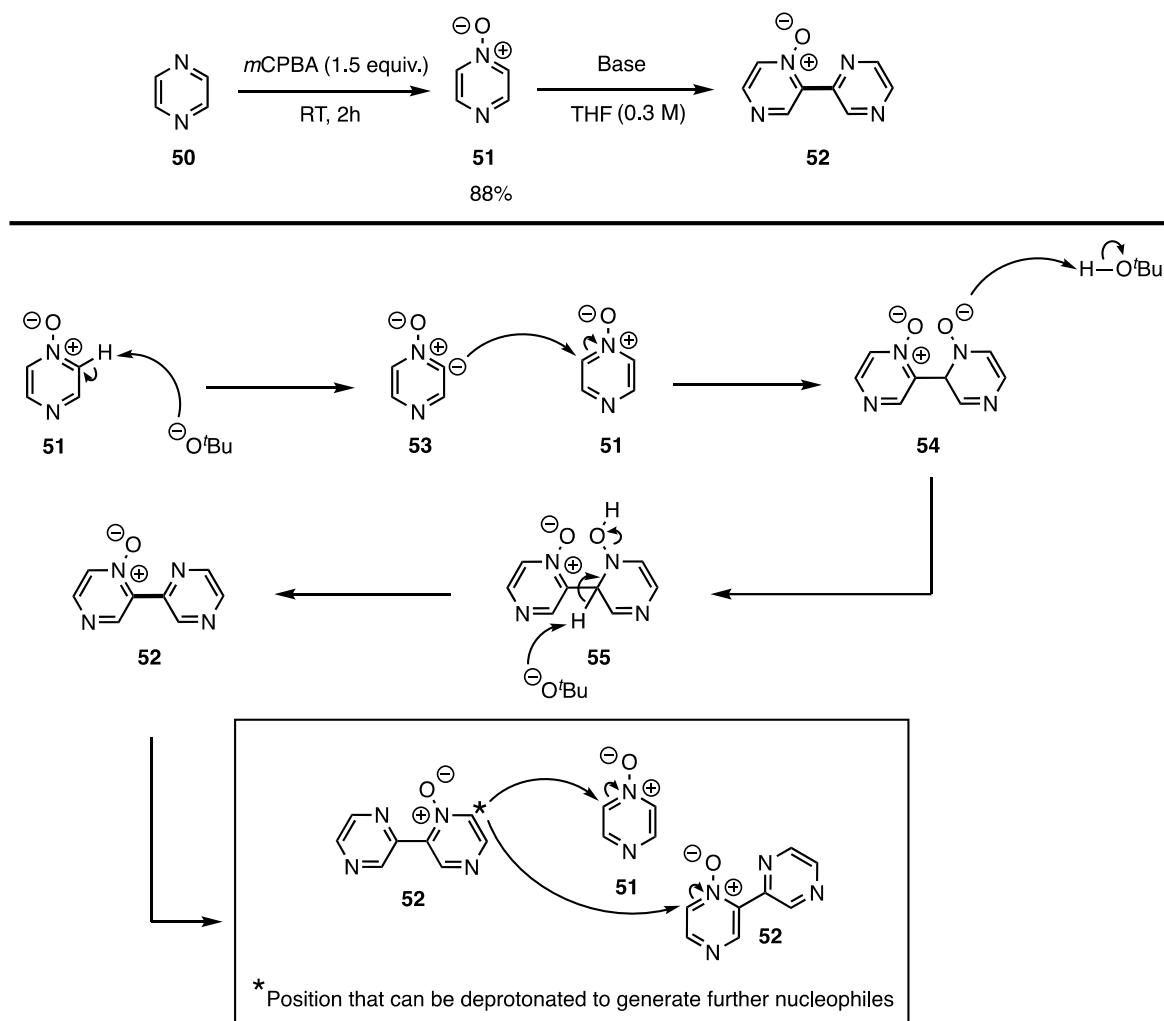
**Table 1: Optimization for Dehydration Reaction of Pyridine *N*-Oxide.**

Entry	Base	Temp (°C)	Dimer Yield
1	LiO <sup>t</sup> Bu	RT	20%
2	LiO <sup>t</sup> Bu	60	65%
3	NaO <sup>t</sup> Bu	60	0%
4	KO <sup>t</sup> Bu	60	55%

### 2.2.2 Dehydration of Pyrazine *N*-Oxides

The focus was next turned towards the dehydration of pyrazine *N*-oxides in the same manner. Firstly, oxidation of pyrazine (**50**) to the *N*-oxide (**51**) proceeded using 1.5 equiv. of *m*CPBA in DCM (0.5 M) for 2 hours affording the mono-oxidized compound in an 88% yield. Once the *N*-oxide was isolated, the dehydration was attempted using 1.5 equiv. of LiO<sup>t</sup>Bu as the base at room temperature in THF (0.3 M), however, formation of the dimerized product proved to be difficult. Instead of formation of the dimer, multiple compounds were isolated from the reaction which corresponded to pyrazine *N*-oxide trimer and tetramer in 6% and 38% yield respectively. This could be due to the ability for the reaction to continue to proceed at a carbon adjacent to the nitrogen once the dimer has been formed (Scheme 21). Both the 2-, and 6- positions of the pyrazine dimer can be deprotonated, once again generating a nucleophile, which can in turn attack another equivalent of pyrazine *N*-oxide, or an equivalent of the dimer, ultimately forming a trimer or tetramer. Once again, changing the base to NaO<sup>t</sup>Bu resulted in no reaction occurring and re-isolation of the starting *N*-oxide material. Using LiO<sup>t</sup>Bu, reducing the temperature of the reaction

to 0 °C and closely monitoring the reaction for 90 minutes allowed for the pyrazine *N*-oxide dimer (**52**) to be isolated in a 35% yield with 52% of the starting material recovered.

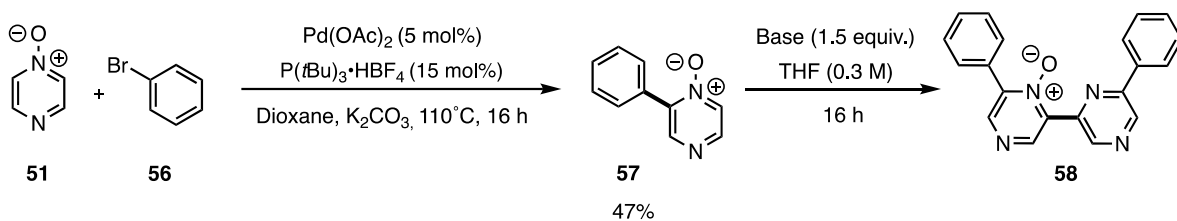


**Scheme 21: Proposed Reaction Mechanism for Trimer and Tetramer Formation.**

It was then envisioned that a substituent at the 2-position, such as a phenyl group, could be used as a blocking group to eliminate the formation of trimers and tetramers. Synthesis of 2-phenylpyrazine 1-oxide occurred through a direct arylation reaction of pyrazine *N*-oxide (**56**) with bromobenzene (**57**), and the desired compound (**58**) was isolated in a 47% yield.<sup>44</sup> This compound (**58**) was then subjected to 1.5 equiv. of LiO<sup>t</sup>Bu at room temperature for 16 h, however, no reaction

was observed (Table 2, Entry 1). Once again, the base was substituted with KO<sup>t</sup>Bu and the reactants were allowed to react for 16 h which resulted in the dimer formation in a 31% yield (Table 2, Entry 2). It was also found that increasing the temperature to 60 °C using LiO<sup>t</sup>Bu resulted in formation of the dimer (**58**) in a 54% yield with no signs of any by-products (Table 2, Entry 3).

**Table 2: Optimization for Dehydration Reaction of Pyrazine *N*-Oxide.**

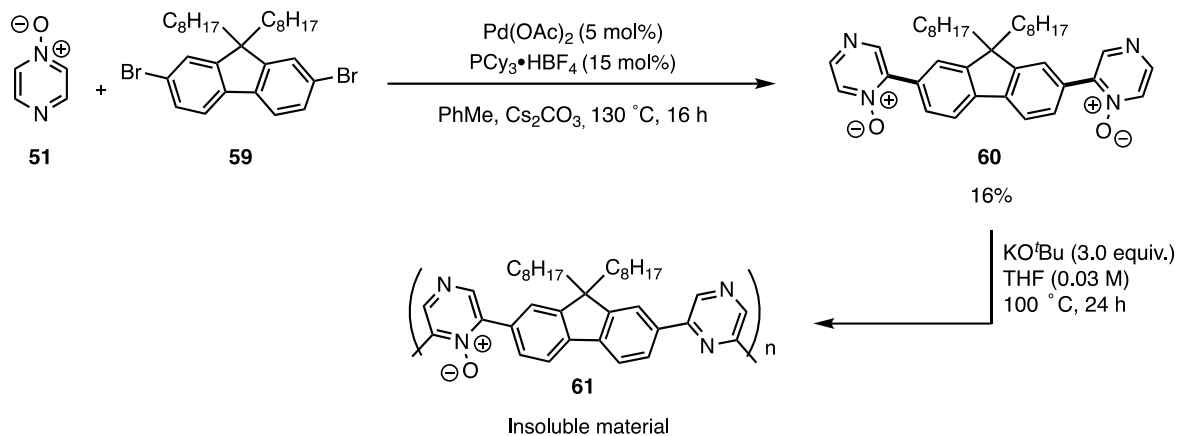


Entry	Base	Temp (°C)	Dimer Yield
1	LiO <sup>t</sup> Bu	RT	0%
2	KO <sup>t</sup> Bu	RT	31%
3	LiO <sup>t</sup> Bu	60	54%

### 2.2.3 Dehydration Polymerization of Alternate *N*-oxide Heterocycles

Having had some success in the formation of small molecules, the ultimate goal remained to extend the scope of the reaction to synthesize conjugated polymers containing different classes of *N*-oxide heterocycles. The investigation began towards the synthesis of pyrazine containing conjugated polymers. In order to synthesize the desired monomer containing a fluorene spacer, 4 equivalents of pyrazine *N*-oxide (**56**) were reacted with 2,7-dibromo-9,9-dioctyl-9*H*-fluorene (**60**) through a direct arylation reaction (Scheme 22). The desired direct arylated compound possessing two pyrazine *N*-oxide moieties (**61**) was obtained in a 16% yield while the mono-arylated was obtained in a 24% yield. The di-*N*-oxide monomer was then allowed to react with 3.0 equiv. of KO<sup>t</sup>Bu at room temperature, however, no reaction was observed. The temperature was then

increased to 70 °C and the reactants were allowed to react overnight, however, the polymer formed was not soluble in any solvent and could not be characterized.



**Scheme 22: Synthetic Route to Synthesize Pyrazine *N*-Oxide Containing Polymer.**

Extending the dehydration reaction to include the dehydration of various classes of nitrogen containing heterocycles remains an interesting prospect, however, extensive work is still required. Ultimately, complete conversion of the *N*-oxide starting materials was not obtained through the dehydrative coupling of pyrazine and pyridine *N*-oxides. Since complete monomer conversion is required to access high molecular weight polymers, this was not ideal, resulting in the lack of interest in further pursuing dehydrative coupling of these substrates.


# Chapter 3

## 3.1 Molecularly Defined Oligomers

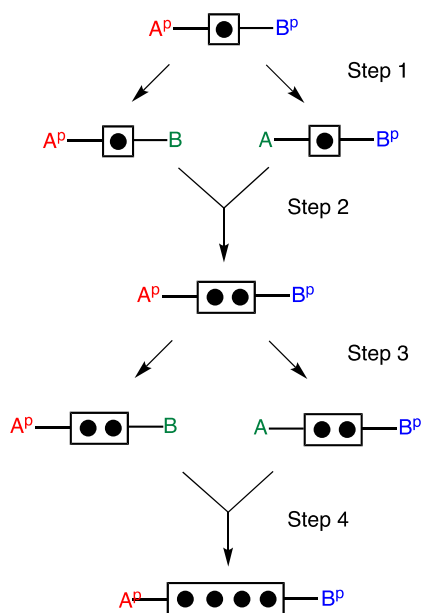
As previously discussed, conjugated polymers are of high interest for integration into various electronic applications since they allow the combination of polymeric mechanical properties with the semiconducting properties of conjugated molecules. While conjugated small molecules share the inherent electronic properties of conjugated polymers, integration into devices is rather more difficult as they do not possess similar mechanical properties such as tensile strength.<sup>46</sup> On the other hand, while conjugated polymers can possess good mechanical and electronic properties, their synthesis results in polymers with a distribution of molecular weights which introduces batch-to-batch variation. A study conducted on five batches of a conjugated polymer (PCDTBT) used in solar cells, shows that the solar cell PCE was reduced from 5.3% to 2.5% with an increasing amount of lower molecular weight components in the batch.<sup>47</sup> This fluctuation of PCE as a result of the batch-to-batch variation obtained is a major disadvantage as high efficiencies need to be achieved consistently. To combat this inherent defect, there has been a growing interest in synthesizing precisely defined “large” conjugated small molecules, or molecularly defined oligomers (MDOs). These oligomers would essentially help combine the advantages of both conjugated small molecules and polymers as they would possess a defined structure with a defined molecular weight eliminating the variations in conjugated molecule length.<sup>48</sup> In addition, they can still possess the desired mechanical properties for integration in electronic applications.<sup>49</sup> The syntheses of the molecules can, however, be challenging and complex due to the multiple steps required to couple the (hetero)arene functional groups required

to increase chain length. A step-wise approach was previously developed to minimize the number of synthetic steps required to achieve these defined molecules as well as to control the chain length sequence.

### 3.1.1 Iterative Divergent/Convergent Approaches

The iterative divergent/convergent (IDC) approach is a step-wise method used for the synthesis of molecularly defined oligomers. This involves repetitive deprotecting and cross-coupling of an orthogonally protected monomer of choice. A general IDC approach involves a monomer, () possessing functional groups **A** and **B**, that are protected to **A<sup>P</sup>** and **B<sup>P</sup>** (Figure 9). The reaction mixture is then divided into two portions and each portion is subsequently deprotected at opposite ends forming two reaction mixtures possessing either intermediates **A<sup>P</sup>B** and **AB<sup>P</sup>** (Figure 9, Step 1). The deprotected intermediates are then coupled using a coupling reaction forming the orthogonally protected dimer (Figure 9, Step 2). The dimer is again divided into two portions, deprotected at opposite ends of each half (Figure 9, Step 3) and then subjected to another round of coupling reactions in order to form the orthogonally protected tetramer (Figure 9, Step 4). With each successful deprotection/coupling cycle, the number of repeat units is doubled and therefore allows for the precise synthesis of MDOs (and potentially polymeric molecules) in minimal synthetic steps. In addition, utilizing this type of approach, chemists are able to control chain length, sequence order of monomers, as well as end group functionality.<sup>50</sup>



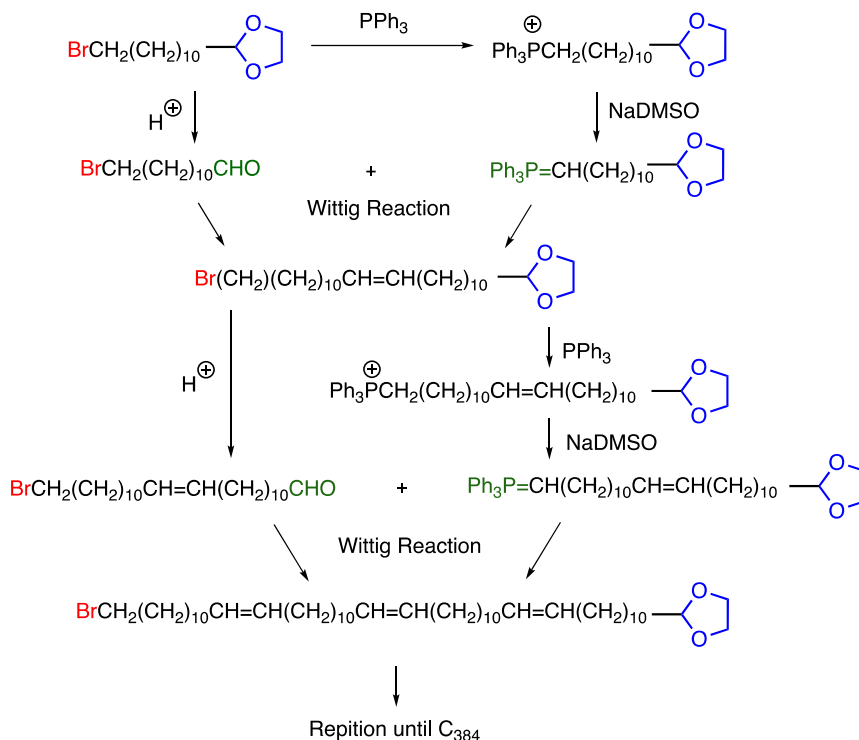


**Figure 9: IDC Approach Flowchart for the Synthesis of MDOs.**

### 3.1.2 Previous use of Iterative Divergent/Convergent Approach

The use of an iterative divergent convergent approach was first reported by Whiting et al. in 1982 in which oligo(ethylene)s were successfully synthesized with chain lengths containing up to 390 carbon atoms.<sup>51</sup> This approach began with the readily available building block cyclododecanone which was first allowed to react with permaleic acid to generate the lactone through a Baeyer-Villiger reaction. Hydrolysis of the lactone generated the long chain hydroxy acid, which was then converted to the orthogonally protected bromo-acetal monomer. The bromo-acetal monomer was divided into two portions, where one portion was allowed to react with triphenylphosphine to generate the phosphonium salt, while the remaining portion was deprotected in order to generate a free aldehyde (Scheme 23). The phosphonium ylide was generated upon addition of NaDMSO and the two portions were allowed to react through a Wittig reaction to produce the orthogonally protected C<sub>24</sub> bromo-acetal.<sup>52</sup> Repetition of these three reaction steps doubled the chain length of the molecule, generating the C<sub>48</sub> oligomer, and upon continued

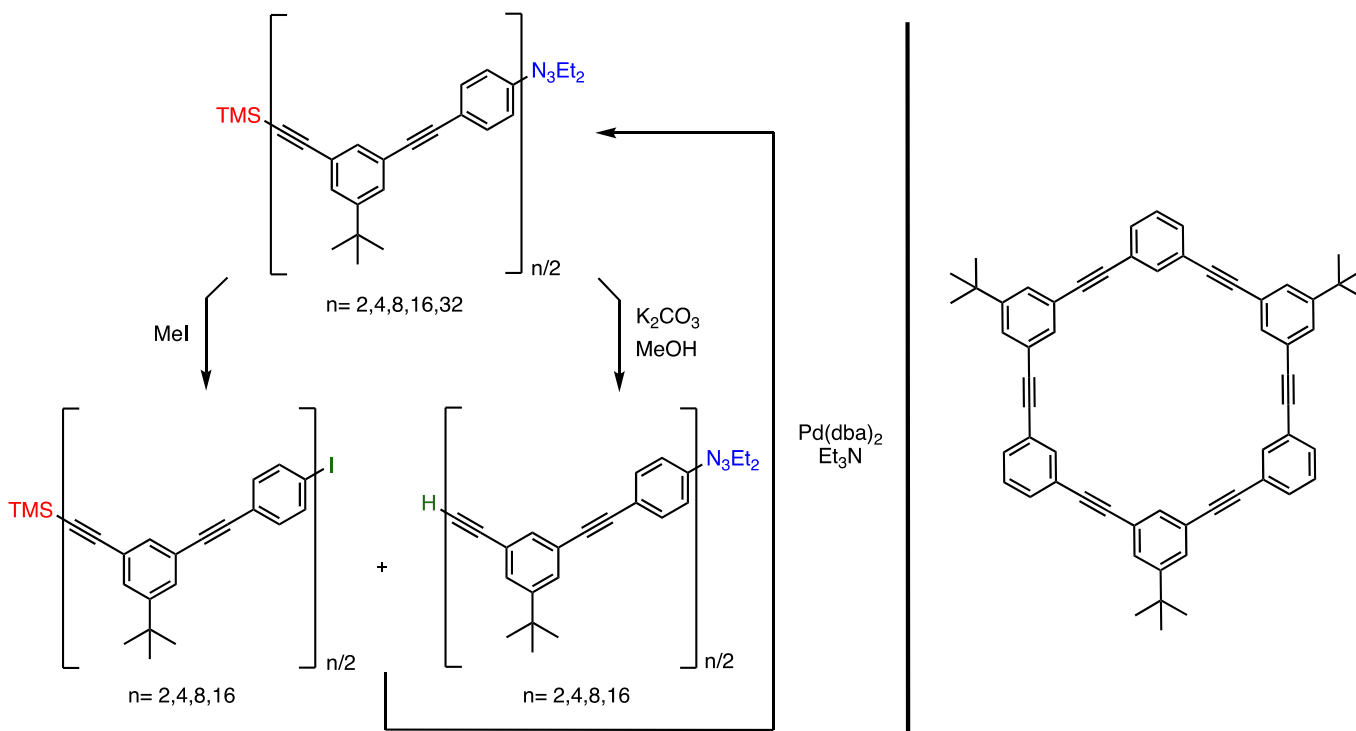
reactions, eventually the C<sub>96</sub>, C<sub>192</sub>, and C<sub>384</sub> analogues.<sup>53</sup> These compounds were then hydrogenated at high temperatures in order to generate high purity *n*-paraffins that would be used to serve as models for the understanding of phase transitions in polyethylene. At that time, these *n*-paraffins were the longest reported and were synthesized in a very efficient and controlled manner.



**Scheme 23: First Iterative Divergent/Convergent Approach of Dodecanal Monomer.**

In 1991, the IDC approach was employed by Moore et al. to synthesize oligo(phenylene ethynylene)s as precursors for the synthesis of structurally well-defined conjugated macrocycles.<sup>54</sup> The asymmetrically protected dimer used in this case was synthesized with a trimethylsilyl (TMS) protected alkyne and a 3,3-diethyltriazene substituent protecting the position of interest on the aryl group (Scheme 24). The protecting groups were chosen based on their ability to be easily removed in presence of the other protecting group, as well as their stability towards the desired cross-

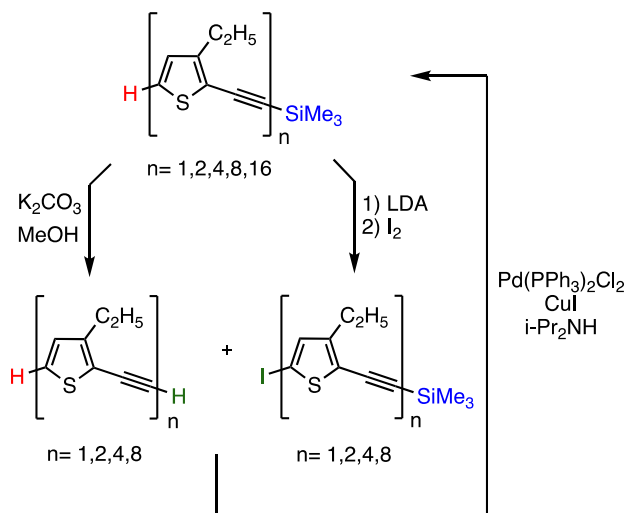
coupling conditions. In one portion, deprotection of the alkyne using potassium carbonate in methanol afforded the free acetylene group required for a Sonogashira cross-coupling reaction. On the other hand, methyl iodide was used to transform the aryl- $N_3Et_2$  group to an aryl iodide which would be the second prerequisite for the cross-coupling. The two deprotected precursors were allowed to react through a Sonogashira cross-coupling reaction and afforded the orthogonally protected dimer in an 84% yield over the three reactions. Repetition of the same reaction sequence allowed for the synthesis of phenylacetylene oligomers with respectable yields (67%–78%) reaching chain-lengths as high as the 16-mer. These oligomers were then used in an intramolecular cyclization reaction to afford structurally defined phenylacetylene macrocycles in respectable yields (70%–75%).<sup>55</sup> This method was further extended by Moore et al. to synthesize various macrocycles using a wide variety of building blocks bearing the same protecting groups.<sup>56</sup>



**Scheme 24: a) Synthesis of Oligo(phenylene ethynylene)s Through an IDC approach.**

**b) Example of Macrocycle Synthesized Using the Oligomers Synthesized.**

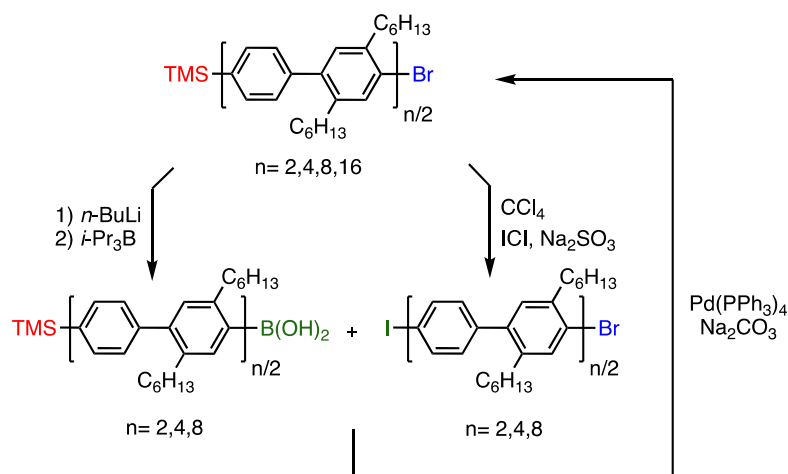
The IDC approach was further extended to the synthesis of other classes of conjugated materials including oligo(thiophene ethynylene)s (OTEs) by Tour et al. in 1994 (Scheme 25).<sup>57</sup> First the thiophene-containing monomer was synthesized through the Sonogashira cross-coupling reaction of 2-iodothiophene and a trimethylsilylacetylene which formed the orthogonally protected monomer. The monomer was then split into two portions, one in which the thiophene was iodinated at the 5-position, while in the other portion the alkyne TMS-group was deprotected to afford the unprotected terminal alkyne. The two were then coupled through a Sonogashira cross-coupling reaction affording the dimer in a 90% yield. Once again, through a series of deprotecting/coupling cycles, the length of the dimer was continued to double in order to form the tetramer, octamer and eventually the 16-mer in relatively high yields.



**Scheme 25: Synthesis of Oligo(thiophene ethynylene)s Through an IDC Approach.**

Furthermore, oligo(paraphenylene)s were synthesized using an IDC approach in 1996 by Schluter in attempt to synthesize monodispersed rods.<sup>58</sup> The orthogonally protected paraphenylene monomer was first synthesized through a Suzuki cross-coupling reaction of 4-trimethylsilylbenzene with 2,5-dihexyl-4-bromoiodo-benzene. Once isolated, the aryl bromide was converted to an aryl boronic acid in one portion, while the TMS-group was converted to an

iodine in the other. The aryl iodide and aryl boronic acid were then allowed to undergo a Suzuki cross-coupling reaction to form the orthogonally protected dimer (Scheme 26). Solubilizing chains were incorporated onto the aryl group to ensure solubility of the oligomers as their length doubles with each subsequent deprotection/coupling iteration. Repetition of the same three reaction steps afforded the tetramer and octamer all of which were characterized by nuclear magnetic resonance (NMR) spectroscopy and size exclusion chromatography (SEC). The octamer which contained 16 phenylene units was the longest mono-disperse oligophenylene reported at the time and was able to maintain solubility in most organic solvents. These oligo(phenylene)s were then used to synthesize hexagon macrocycles containing 12 and 24 phenylene units.<sup>59</sup>

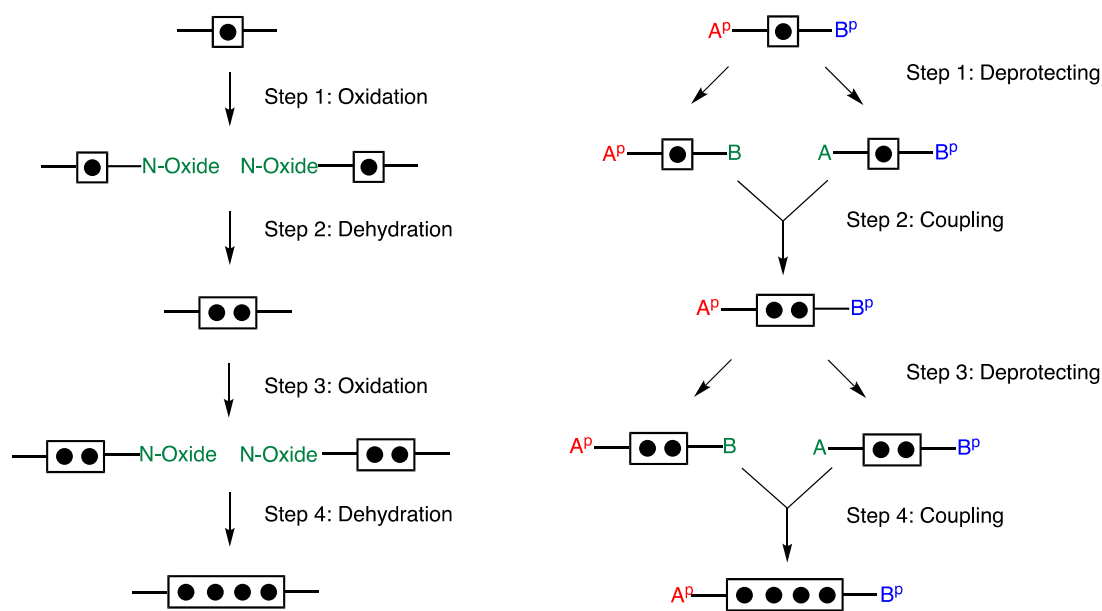


**Scheme 26: Synthesis of Oligo(*p*-phenylene)s Through an IDC approach.**

The concept of the IDC approach has proven to be an attractive method since it allows for the synthesis of mono-disperse conjugated compounds through repetitions of well-known reactions. Through the many examples previously discussed, sequences as high as 16-mers were synthesized in an efficient manner with minimal synthetic steps and moderate yields.

### 3.2 Dehydration Coupling towards Molecularly Defined Oligomers

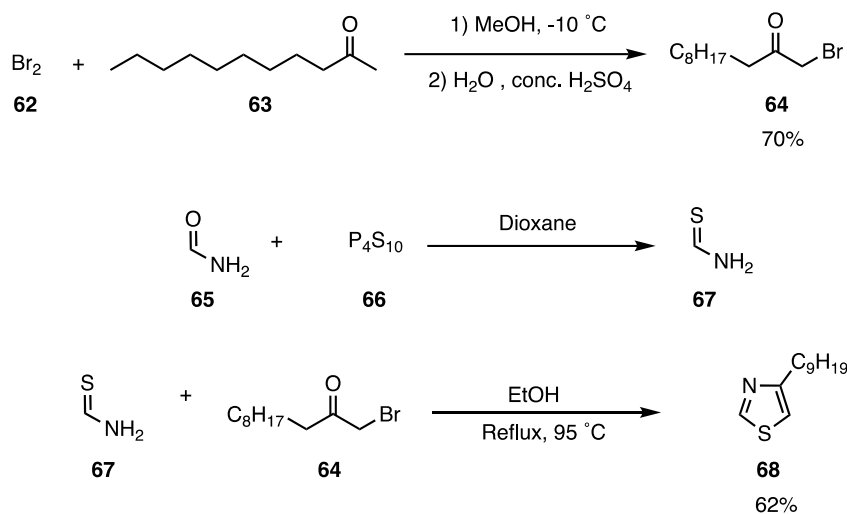
Since molecularly defined conjugated compounds are of high interest for electronic applications, accessing these compounds on a larger scale without the need for precious transition metals is also of great importance. The dehydration of thiazole *N*-oxides has allowed for rapid access to various conjugated small molecules and polymers and possesses many advantages including: short reaction time and minimal isolation required. Due to the nature of the reaction, it was envisioned that the thiazole *N*-oxide dehydration could provide a unique approach to this synthesis of molecularly defined conjugated oligomers by an iterative approach (Figure 10). It could be achieved by incorporating two thiazole moieties to each end of an electron-rich conjugated  $\pi$ -spacer. However, instead of oxidizing both terminal thiazoles to thiazole *N*-oxides as was previously done, one could oxidize only a single thiazole to the mono *N*-oxide (Figure 10, Step 1). The mono-oxidized monomer could then be subjected to dehydration conditions in order to form a dimer bearing two terminal non-oxidized thiazoles (Figure 10, Step 2). This molecule can then be subjected to further oxidation to yield the singly-oxidized terminal thiazole dimer (Figure 10, Step 3) and subjected to dehydration conditions again to afford the tetramer product (Figure 10, Step 4). Through each oxidation/dehydration cycle, the length of the molecule is doubled allowing access to MDOs in fewer synthetic steps relative to traditional methods as well as the typical IDC approach. The conjugated  $\pi$ -spacer can be further varied allowing access to a family of conjugated MDOs with varying properties.



**Figure 10: Proposed Iterative Approach to Access MDO's.**

### 3.2.1 Synthesis of Thiazole-Containing Molecularly Defined Oligomers

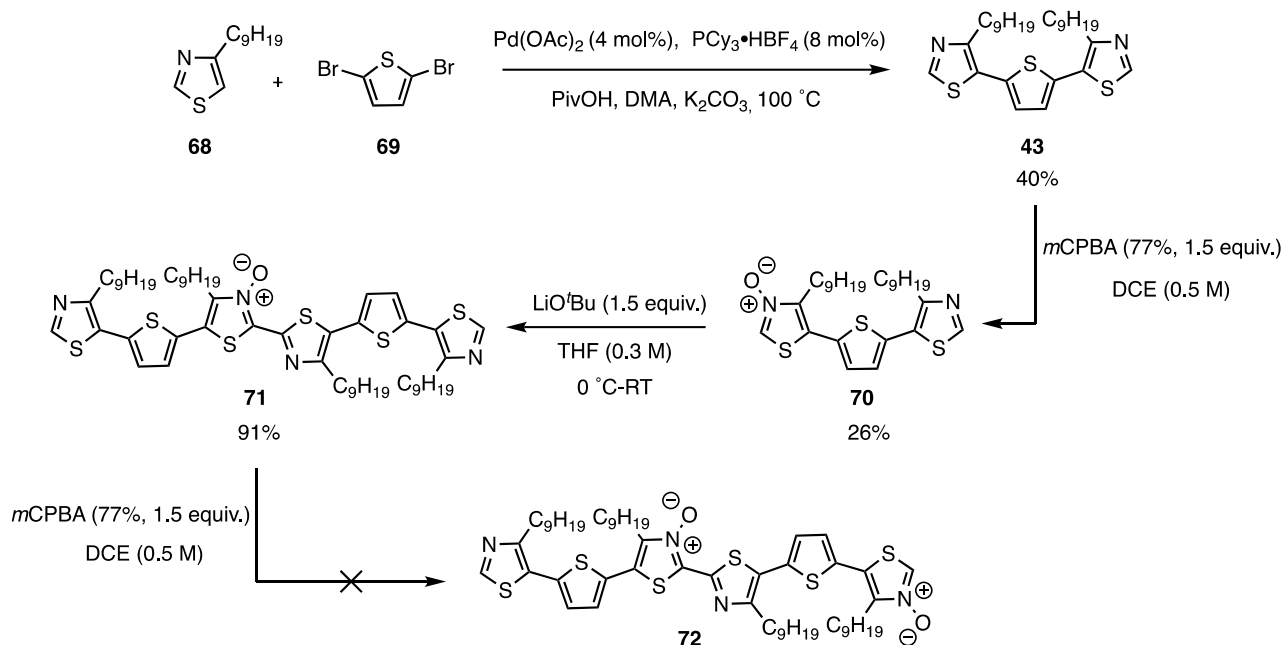
The first step of this project was to synthesize the starting material of interest from two equivalents of a thiazole and a conjugated aryl halide spacer. In this case, 4-nonylthiazole was chosen due to its long alkane chain substituent in the 4-position since the solubility of the molecule will decrease as the number of repeat units doubles after every iteration. 4-Nonylthiazole was synthesized in three steps from 1-bromoundecanone and formamide. First, the synthesis of 1-bromoundecanone occurred by allowing bromine (**62**) and undecanone (**63**) to react through an  $\alpha$ -substitution reaction which generated compound **64** in a 70% yield (Scheme 27). Next, thioamide (**67**) was synthesized through the reaction of formamide (**65**) with a thionating reagent (**66**). Compound **67** was not isolated but directly refluxed with 1-bromoundecanone (**64**) in ethanol to afford 4-nonylthiazole (**68**) in a 62% yield through the Hantzsch thiazole synthesis.



**Scheme 27: Synthesis of 4-Nonylthiazole.**

With 4-nonylthiazole in hand, two equivalents were coupled to the conjugated  $\pi$ -spacer (in this case 2,5-dibromothiophene) through a direct arylation reaction affording the di-substituted compound **43** in a 40% yield (Scheme 28). Conjugated species **43** was then dissolved in DCE to form a 0.5 M solution, then oxidized using 1.5 equiv. of *m*CPBA to afford the mono *N*-oxide (**70**) in a 26% yield. Upon purification, the mono *N*-oxide was subjected to the optimal dehydration conditions: addition of 1.5 equiv. of LiO<sup>t</sup>Bu to a 0.3 M solution of the *N*-oxide **70** in THF in order to afford dimer **71** in a 91% yield. The dimer **71**, bearing a thiazole molecule on each end with the ability to be oxidized, was then reacted with *m*CPBA. The oxidation reaction was monitored by TLC for the first few hours then left to continue reacting overnight (16 h), however, no new compounds were observed, and mainly peaks corresponding to *m*CPBA and *m*-chlorobenzoic acid were observed through crude <sup>1</sup>H NMR.



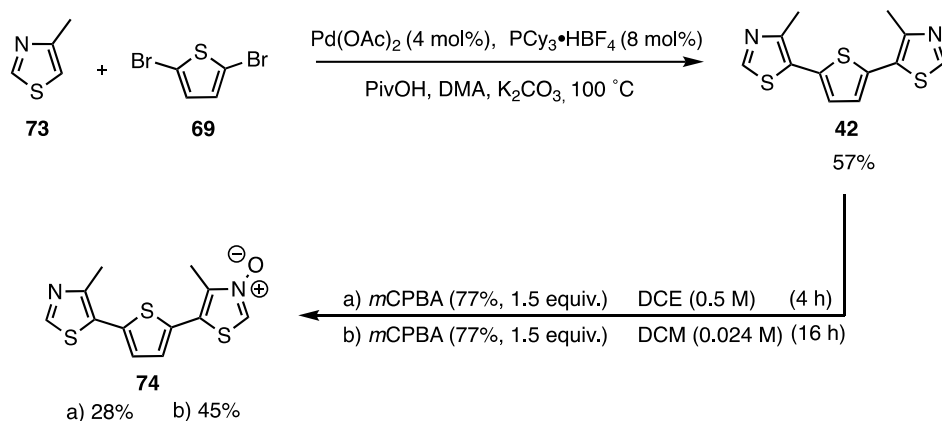


**Scheme 28: Synthetic Route to 4-Nonylthiazole Containing Dimer.**

In order to simplify the multi-step synthesis, 4-nonylthiazole was replaced with 4-methylthiazole due to its commercial availability and previous success with these compounds. Simplification of the synthetic route was important to allow for understanding and optimization of this synthetic approach towards molecularly defined conjugated oligomers. 4-Methylthiazole (**73**) (2.0 equiv.) was coupled to 2,5-dibromothiophene (**69**) through a direct arylation reaction to yield compound **42** in a 57% yield (Scheme 29). Compound **42** was then oxidized using *m*CPBA (77%, 1.5 equiv.) in DCE (0.5 M) and afford the mono-*N*-oxide **74** in a 28% yield.

Although oxidation reaction conditions have been previously optimized, slight variations in the oxidation conditions were attempted by varying solvent and solvent concentration in an effort to increase the *N*-oxide yields. Based on a literature procedure for the oxidation of imines to the oxaziridine/nitrone derivatives, 1.5 equiv. of *m*CPBA in a 0.024 M solution of DCM was added dropwise to a 0.02 M solution of DCM containing the imine was reported as their optimal oxidation

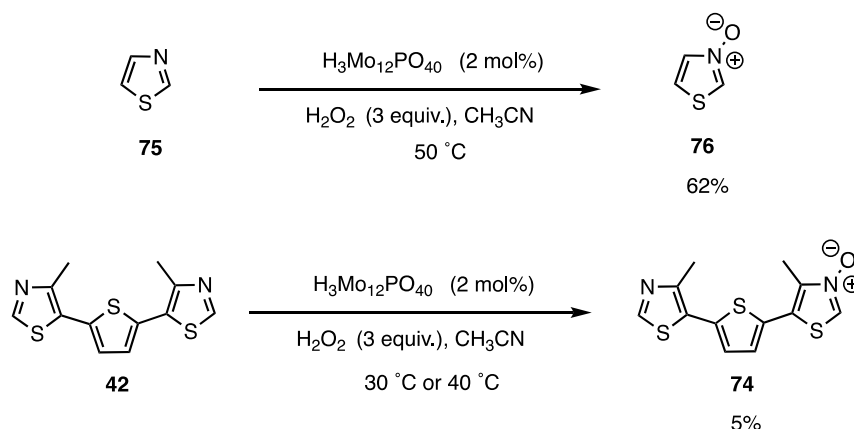
conditions.<sup>60</sup> Adopting these reaction conditions to the oxidation of thiazoles actually afforded a higher yield than observed under our previously optimized conditions (45% VS 28% yield) (Scheme 29). These conditions were then extended to the oxidation of previously synthesized 5-aryl thiazoles, however, the results were inconclusive as to whether the dilute reaction conditions resulted in an increase in yield.



### Scheme 29: Synthesis of 4-Methylthiazole *N*-Oxide Derivative.

Inspired by the slight increase in yield the dilute *m*CPBA conditions provided, a few more attempts at reaction optimization were carried out keeping in mind the oxygen transfer agents previously screened. Oxidation using hydrogen peroxide, and catalytic amounts of transition metal catalysts such as rhenium have been widely utilized throughout the literature.<sup>61,62</sup> Similarly, the Larionov group reported the oxidation of *N*-heterocycles to their respective *N*-oxides using catalytic amounts of phosphomolybdic acid with hydrogen peroxide in acetonitrile. The scope of this reaction was excellent obtaining relatively high oxidation yields for a wide variety of *N*-heterocycles.<sup>63</sup> Thiazole (**75**) was also shown to be oxidized using these reaction conditions to the corresponding *N*-oxide (**76**) in a 62% yield without the oxidation of the thiazole sulfur (Scheme 30). Due to this success, these conditions were adopted to potentially further increase the general

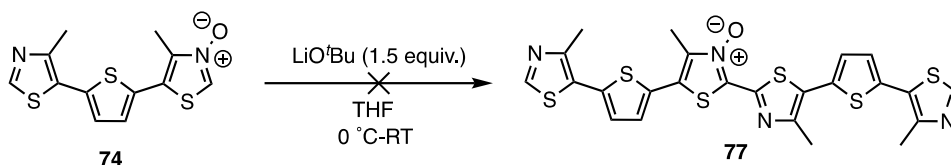
oxidation yields obtained for the di-arylated compounds (**43**, **42**) synthesized. If successful, these conditions would ultimately be used to oxidize the dimers synthesized in order to access tetrameric molecules through the dehydration homo-coupling method. Due to the known temperature sensitivity of 2-unsubstituted thiazole *N*-oxides above 30°C, reactions were carried out at both 30°C and 40°C instead of 50°C.<sup>64</sup> The observed reaction yields were low as only trace amounts (5%) of product **74** was isolated, and this approach was not further explored (Scheme 30). Next, since silica-gel supported oxidation using MMPP has been shown to oxidize sulfur to sulfones, an attempt to extend this chemistry to the oxidation of the thiazole nitrogen was attempted.<sup>65</sup> No reaction was observed and *m*CPBA in dilute conditions remained the best yielding oxygen transfer agent.



**Scheme 30: Oxidations Using Phosphomolybdic Acid and Hydrogen Peroxide.**

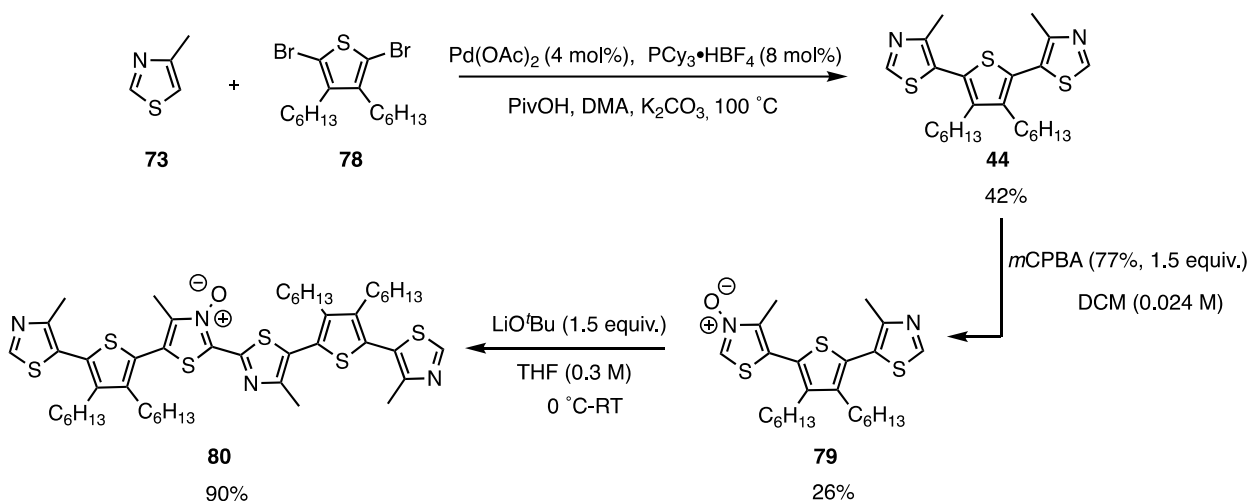
With substantial amounts of oxidized thiazole **74** in hand, the dehydration reaction was attempted, however, dimer **77** was not isolated (Scheme 31). It was suspected that this was likely due to the lack of solubilizing chains present on the molecule as when the thiazole possessed nonyl chain substituents, the dehydration product **71** was isolated in a 91% yield (Scheme 28). <sup>1</sup>H NMR analysis of the isolated product indicated that starting material may still be present, and full

conversion was likely not achieved. Repeated attempts at this dehydration did not yield any isolable product and therefore the second round of oxidation/dehydration conditions could not be attempted with the dehydration compound **77** as previously planned.



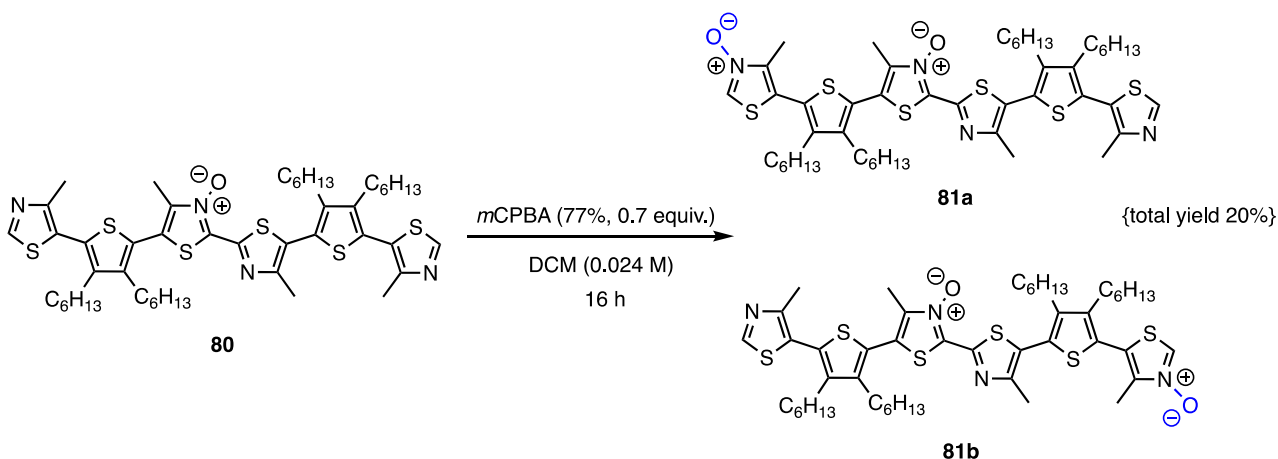
**Scheme 31: Dehydration of 4-Methylthiazole *N*-Oxide Derivative.**

Since optimization of the iterative oxidation/dehydration approach using thiazole bearing no solubilizing chains did not yield a usable product, a thiophene  $\pi$ -spacer was modified to one that possesses solubilizing chains. Standard direct arylation conditions were used to couple 3,4-dihexyl-2,5-dibromothiophene (**78**) to 4-methylthiazole (**73**). While the reaction proceeded well, separation of the mono- and the di-arylated products (**44**) was challenging due to their very similar  $R_f$  values. Nevertheless, the di-arylated product was isolated in a 42% and the mono-product was subjected to further direct arylation conditions to synthesize the desired compound (**44**). The compound was then oxidized using *m*CPBA, and the mono-*N*-oxide (**79**) was isolated in a 26% yield. Finally, the compound was reacted with lithium *tert*-butoxide (1.5 equiv.) to form the 6-ring dimer **80** in a 90% yield (Scheme 32). Due to the presence of solubilizing hexyl chains on the thiophene moiety, there was no difficulty in isolation of the dimer (**80**).



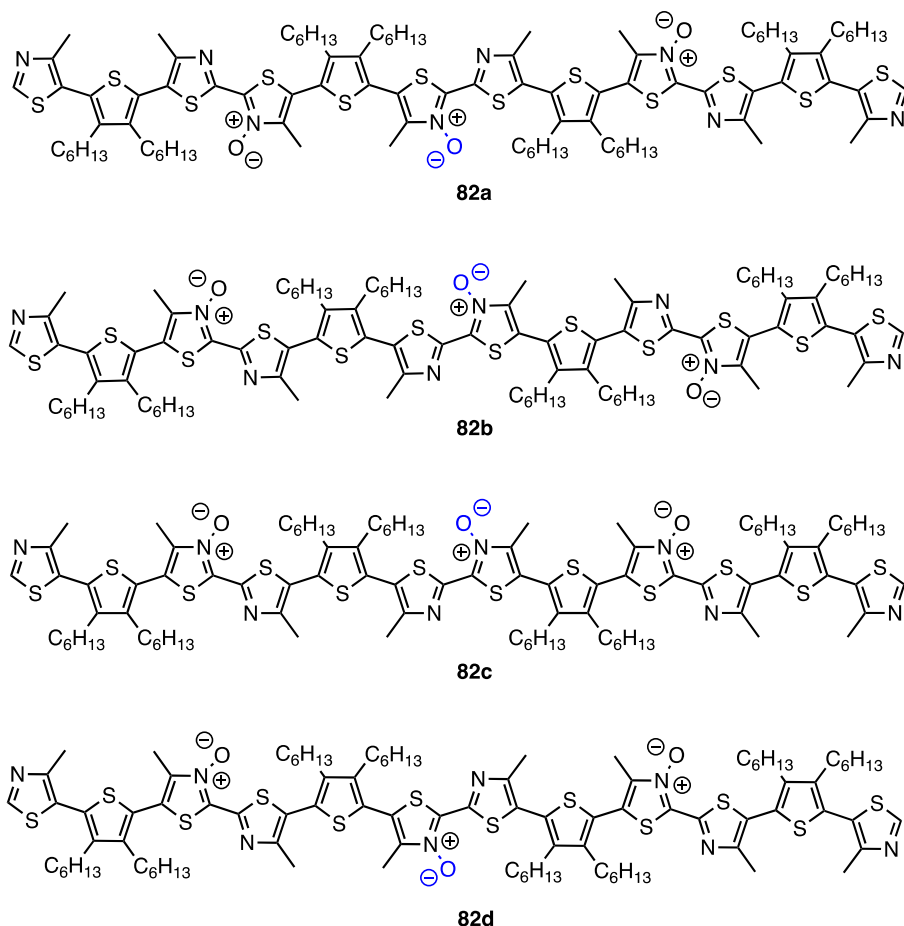
### Scheme 32: Synthesis of Di-hexylthiophene Containing Dimer.

With dimer **80** isolated, it could then be oxidized once again with *m*CPBA in attempt to oxidize a single terminal thiazole moiety. One must consider now that due to the dehydration compound being non-symmetrical, depending on which terminal thiazole is oxidized, two different isomers could be formed, **81a** and **81b** (Scheme 33). Dehydration of the mixture of *N*-oxides **81** would also lead to four different isomers where separation and isolation of each isomer would be difficult. This structural irregularity would be removed by reducing all thiazole *N*-oxides to the deoxygenated compound in a final synthetic step. After allowing compound **80** to react with 0.7 equiv. of *m*CPBA, a new product was observed on TLC with a similar  $R_f$  to the previously synthesized *N*-oxide **79**. Since the reaction would produce a mixture of isomers, separation and isolation of each isomer would be difficult therefore, the mixture of both compounds was isolated and purified in a 20% yield.



**Scheme 33: Oxidation of the Di-hexylthiophene Dehydration Dimer.**

Subjecting this mixture to the dehydration reaction conditions would yield 4 isomers depending on whether the *N*-oxide reacted with another equivalent of the same *N*-oxide or the other *N*-oxide isomer (Figure 11). Carrying out the dehydration reaction by addition of 1.5 equiv. of LiO<sup>t</sup>Bu on the mixture of **81a** and **81b** dissolved in THF, resulted in rapid color change to wine red as typically produced through the dehydration reaction. Characterization of the compound isolated through this dehydration reaction was difficult. Disappearance of the thiazole proton peak closest to the terminal *N*-oxide moiety (as determined by <sup>1</sup>H NMR) was a significant indication that a reaction did occur. Although the peaks on the <sup>1</sup>H NMR spectrum could correspond to the formation of tetramers, <sup>13</sup>C NMR spectrum was not obtained as only peaks corresponding to the aliphatic hexyl chain carbons were observed even after significantly prolonged scans. In addition, the mixture of compounds was not able to be characterized through mass-spectrometry, as neither electrospray ionization (ESI) mass spectrometry nor matrix-assisted laser desorption/ionization mass spectrometry produced any results that could correspond to the tetramers formed. Reduction of the mixture to the deoxygenated compound was not attempted. That could provide some insight as to whether the dehydration reaction was successful.

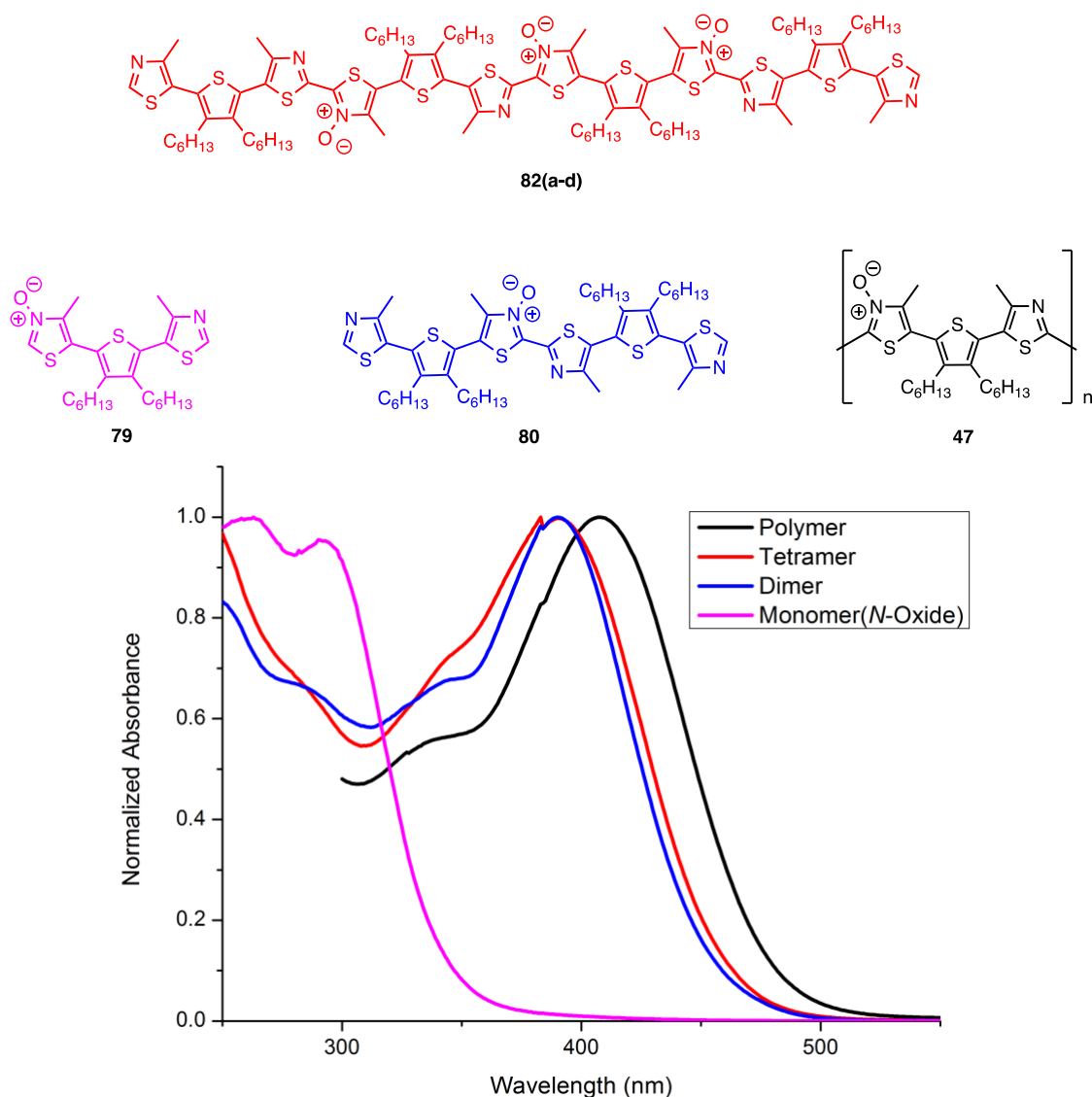


**Figure 11: Isomers Produced Through the Dehydration Reaction of the Mono Oxidized Dimer.**

### 3.2.2 Properties of Thiazole-Containing Molecularly Defined Oligomers

Having synthesized the dimer (**81**) and a mixture of tetramers (**82**) through our approach, there remained an interest in studying the photophysical properties of these new compounds. As the size doubles with each successive oxidation/dehydration cycle, it would be of interest to see how the band gaps of these molecules compare to both the monomer (**79**) and the polymer (**47**) previously synthesized. UV-Vis spectroscopy was carried out on the monomer (**79**), dimer (**80**), tetramer (**82**) and polymer (**47**) where absorbance VS wavelength was plotted for each compound (Figure 12). The mono *N*-oxide (**79**) had a maximum absorbance peak at 230 nm and a secondary peak at 300 nm. Once the length of the molecules was doubled to the dimer (**80**), there was a

significant red shift of the absorbance maximum to around 390 nm which is a direct result of the increase in conjugation length causing a decrease in the HOMO–LUMO gap. Although further doubling of the length of the dimer would expectedly cause a further red shift of the absorbance maximum, this was not observed as there was no significant difference between the absorbance maximum of the dimer (**80**) and tetramer (**82**). However, there was a slight red shift to an absorbance maximum of 410 nm when the length of the molecule reached polymeric molecular weights (**47**).

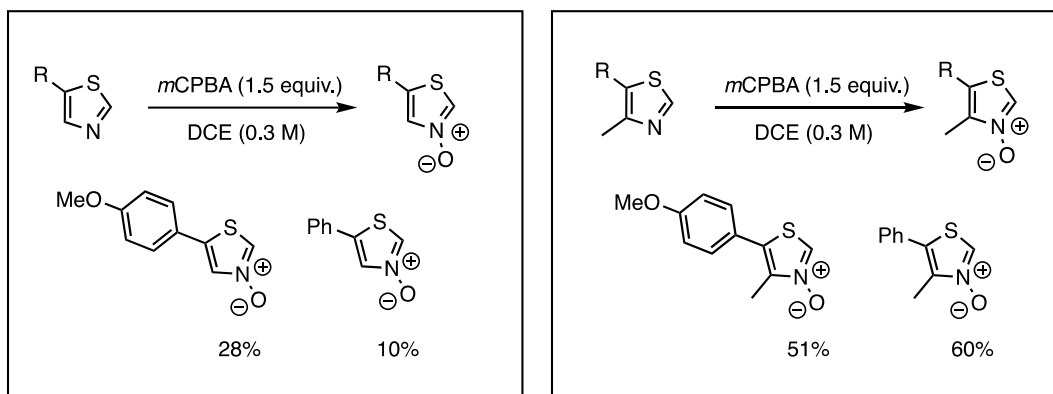


**Figure 12: UV-Vis Spectrum of the Monomer, Dimer, Tetramer and Polymer Synthesized.**



## Future work

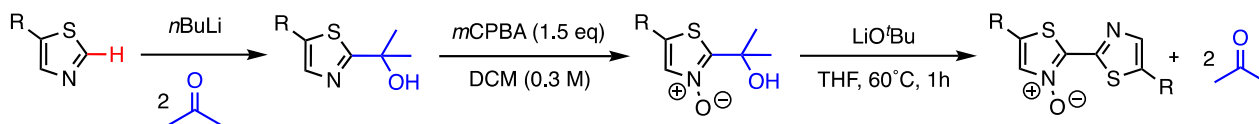
Synthesis of conjugated small molecules and polymers through the dehydrative coupling method remains the main focus of this project, however, a few drawbacks need to be addressed. Firstly, the *N*-oxide precursors required for dehydrative coupling that are typically accessed through oxidation reactions using *m*CPBA are typically low yielding. Although the oxidation yields have been shown to increase when a methyl substituent occupies the 4- position of the thiazole molecule (Scheme 34), presence of the methyl substituent disrupts the planarity of the molecule, which is detrimental to the properties of these conjugated compounds. In addition, when the 2-position of the thiazole molecule is unoccupied, the corresponding *N*-oxide derivative is unstable at temperatures above 30°C.<sup>64</sup>



**Scheme 34: Oxidation Yields of Thiazole Derivatives Possessing/Lacking a Methyl Substituent.**

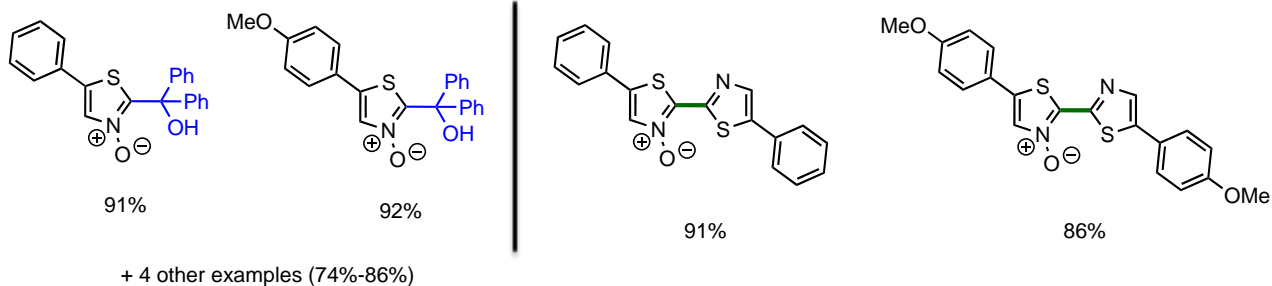
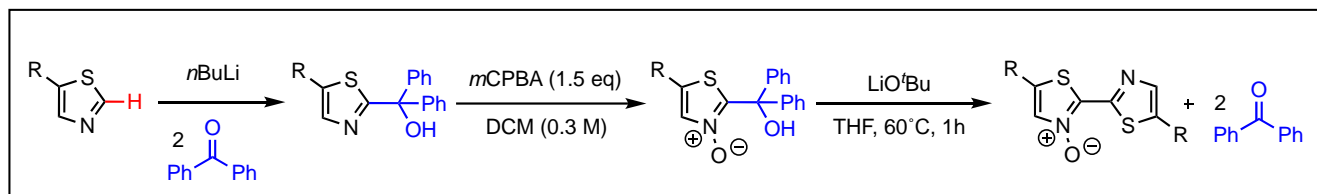
In order to combat these inherent problems, installation of a protecting/directing group was explored by members of the Schipper group. The proposed idea was to install an acetone protecting group at the 2-position to aid in stability of the molecule, as well as to direct *m*CPBA to potentially

increase oxidation yields (Scheme 35). Furthermore, since the protecting group is base labile, no additional reaction step is required for removal of the group as the subsequent dehydration reaction is carried out under basic conditions.



**Scheme 35: Installation of Acetone Protecting Group.**

Initial results were promising as there was a significant increase in oxidation yields after employing the acetone protecting group. Moreover, substrates that were previously non-oxidizable have been successfully oxidized using this new oxidation method. After optimization of the oxidation reaction, dehydration reaction conditions of the acetone protected small molecules were also optimized however, benzophenone protecting group provided better results, therefore the protecting group was switched to benzophenone where promising results have been recently achieved (Scheme 36).



**Scheme 36: Current Promising Results Using the Oxidation/Dehydration Method.**

Future work involves utilizing this newly developed oxidation method to synthesize a wide variety of conjugated molecularly defined oligomers containing various aryl/heteroaryl building blocks and studying their electronic and optical properties. Although this approach would essentially add an additional step prior to each oxidation/dehydration cycle, the significant increase in yield and overall stability of the molecule is worth the extra step. In addition, this allows access to relatively more planar conjugated molecularly defined oligomers relative to the molecules previously accessed. Studying the effect of the *N*-oxide functional group on the properties of these materials is also of interest to the Schipper group with hopes of potentially integrating these compounds in future electronic applications.

## Conclusion

Conjugated small molecules and polymers have integrated their way into various applications such as OLEDs, OFETs, and OSCs due to their optical and electronic properties. Traditional synthesis of these materials include metal catalyzed cross-coupling reactions which have many drawbacks such as harsh conditions, requiring prefunctionalization of substrates with organometallic reagents as well as producing toxic organometallic waste. The lack of scalable methods for the synthesis of conjugated materials inspired the development of dehydrative coupling reaction of *N*-oxide containing heteroarenes.

This dehydration reaction developed by the Schipper lab allows the homo-coupling of thiazole *N*-oxide derivatives upon addition of a base (LiO<sup>t</sup>Bu) with water as the by-product. It involves the rapid synthesis of a C(sp<sup>2</sup>)–C(sp<sup>2</sup>) bond without the utilization of transition metals, or the installation of organometallic activating groups, at room temperature with minimal work up. After optimization of the reaction conditions, a wide variety of conjugated small molecules were synthesized through the homo dimerization of various thiazole *N*-oxide derivatives with yields ranging from 57%–98%. The reaction was further extended to the synthesis of conjugated polymers through accessing di-*N*-oxide moieties by installation of two thiazoles on each end of a conjugated  $\pi$ -spacer. Respectable molecular weights (46–110 kDa) were obtained with incorporation of three different conjugated  $\pi$ -spacers (thiophene, fluorene, aryl).

Extending the dehydration reaction to the dimerization of other *N*-oxide containing heterocycles such as pyridine and pyrazine was a difficult affair due to the symmetry of the molecules, which allowed further deprotonation of the C-H bonds on the dimers formed and

resulted in further undesirable reactivity. In addition, full starting material conversion was not obtained under the optimized reaction conditions which would be a major drawback in the synthesis of conjugated polymers as high monomer conversion is needed.

Although conjugated small molecules and polymers are widely used, synthesis of molecularly defined oligomers has been of interest as that combines the advantages of both. The main advantage is the elimination of batch to batch variation that occurs since the MDOs possess a defined structure. One method of accessing these MDOs is through an IDC approach which involves the repetitive deprotecting and coupling of an orthogonally protected monomer. With each deprotecting/coupling cycle, the molecule length is doubled allowing rapid synthesis of these defined conjugated molecules. Our approach, inspired by the IDC approach, involved utilizing the oxidation/dehydration reactions to double the molecule length to access MDOs using thiophene and thiazole building blocks.

When further extending the dehydrative coupling reaction to synthesis of MDO's through a stepwise approach, the reactions did not work as predicted. Oxidation of the 4-nonylthiazole containing dimer proved relatively difficult relative to oxidation of the di-hexylthiophene containing dimer. Although some success was obtained with oxidation of the di-hexylthiophene dimer, two structural isomers were generated since the dehydration compound is not fully symmetrical. An attempt to further push the reaction forward to synthesize the tetramer resulted in the isolation of a new compound, however, complete characterization of this new compound proved to be difficult.

To this end, development of a novel method to access conjugated small molecules and polymers has been optimized in the Schipper lab. Although success was obtained in the synthesis of conjugated small molecules, the low yielding oxidation reaction needs to be improved for

greater impact on the synthesis of conjugated polymers. Significant work is currently underway for the improvement of the oxidation reaction through protection of the thiazole 2-position using benzophenone. This work will hopefully lead to an optimized method for accessing novel conjugated materials.

# Supplementary

## Information

### General Methods:

Unless otherwise specified all reactions were run without regard to exclusion of ambient air or moisture. All starting materials were purchased from Sigma-Aldrich. The *m*CPBA used was <77% purity and obtained through Sigma-Aldrich. Dry THF, DCM, were obtained from a JC Meyer solvent purification system when needed. DMA and DCE were not distilled, but dried by storing over 4Å molecular sieves. Reactions were monitored using commercial thin-layer chromatography (TLC) plates. Developed TLC plates were examined under a UV lamp (254 nm). Flash chromatography was performed using 230–400 mesh silica gel.

<sup>1</sup>H-NMR spectra were recorded on a Brüker AVANCE300 (300 MHz) δ or Brüker AC300 (300 MHz) δ NMR spectrometers. <sup>13</sup>C-NMR spectra were broad band decoupled and recorded on a Brüker AVANCE300 (75.5 MHz) δ or Brüker AC300 (75.5 MHz) δ NMR spectrometers using the carbon signal of the deuterated solvent as the internal standard. Number-average ( $M_n$ ) and weight-average ( $M_w$ ) molecular weights are relative to polystyrene standards and were determined by size exclusion chromatography using a Viscotek GPC MAX VE 2001 at 35 °C in THF equipped with a VE 3580 RI detector and two PAS-104 Styrene-Divinylbenzene gel columns. The following abbreviations are used for NMR peak multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet; br, broad. Chemical shifts are reported in parts per million (ppm) relative to chloroform (δ 7.26) for <sup>1</sup>H-NMR, and chloroform (δ 77.0) for <sup>13</sup>C-NMR. Missing spectra are reported in the literature by our research group.<sup>38</sup> <sup>1</sup>H and <sup>13</sup>C NMR

peaks are reported as observed. High resolution mass spectra (HRMS) were obtained via electrospray ionization (ESI) which were measured on a Thermo Scientific Q Exactive™ Plus Hybrid Quadrupole-Orbitrap™ the University of Waterloo Mass Spectrometry Facility.

#### **General Direct Arylation Procedure:**

5-Aryl thiazoles were synthesized following literature procedure.<sup>43</sup> K<sub>2</sub>CO<sub>3</sub> (3.00 mmol, 1.5 equiv.), Pd(OAc)<sub>2</sub> (0.04 mmol, 0.02 equiv.), PCy<sub>3</sub>·HBF<sub>4</sub> (0.08 mmol, 0.04 equiv.), and PivOH (0.60 mmol, 0.3 equiv.) were weighed and placed in a screw-cap vial equipped with a magnetic stir bar. The thiazole (3.00 mmol, 1.5 equiv.) and the aryl halide (2.00 mmol, 1.0 equiv.) were added at this point if solids. The vial was purged with argon, and DMA was added to produce a reaction concentration of 0.3 M relative to the aryl halide. The thiazole (3.00 mmol, 1.5 equiv.) and the aromatic halide (2.00 mmol, 1.0 equiv.) were added at this point if liquids. The reaction mixture was then vigorously stirred at 100 °C for 16 hours. The solution was then cooled to RT, diluted with EtOAc, washed with H<sub>2</sub>O (3 times), dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The mixtures were then purified via silica gel column chromatography to afford the corresponding product in 40%–75% yield.

#### **General Oxidation Procedure:**

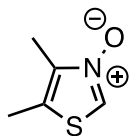
The thiazole (0.80 mmol, 1.0 equiv.) was dissolved in reagent grade dichloroethane to make a solution of 0.5 M. To this solution *m*CPBA (1.20 mmol, 1.5 equiv.) was added portion-wise. Once all of the *m*CPBA has been added, the reaction was stirred for 2–4 h. The *N*-oxides were then purified via silica gel column chromatography using a gradient of 0–15% MeOH/EtOAc as the eluent to afford the corresponding products in 10%–40% yield.



### General Dehydration Procedure:

The *N*-oxide (0.16 mmol, 1.0 equiv.) was dissolved in reagent grade THF to make a solution of 0.3 M and the solution was cooled in an ice bath. To this cold solution was added 1.0 M LiO<sup>t</sup>Bu in THF (0.24 mmol, 1.5 equiv.), which usually resulted in a significant color change. After consumption of starting material (5–15 minutes), the mixture was poured into an extraction funnel containing CH<sub>2</sub>Cl<sub>2</sub> and saturated NH<sub>4</sub>Cl. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 15 mL) and the organics were combined, dried with MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The products were generally analytically pure after work up and did not need further purification in 56%–91% yield.

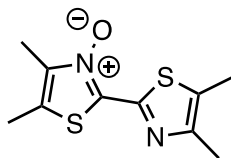
### 4,5-Dimethylthiazole 3-oxide (1)



This compound was synthesized according to the general oxidation procedure in 90% yield and exhibited identical <sup>1</sup>H NMR data to previously reported.<sup>66</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** δ 8.06 (s, 1H), 2.39 (s, 3H), 2.30 (s, 3H).

### 4,4',5,5'-Tetramethyl-[2,2'-bithiazole] 3-oxide (2)



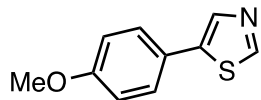
This compound was synthesized according to the general dehydration procedure in 88% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 2.43–2.40 (m, 6H), 2.35 (s, 3H), 2.30 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.1, 148.4, 140.9, 137.8, 128.1, 123.5, 14.7, 13.0, 11.2, 10.4;

**HRMS** calculated for C<sub>10</sub>H<sub>13</sub>N<sub>2</sub>OS<sub>2</sub> (M+H)<sup>+</sup> 241.0464; found: 241.0463.

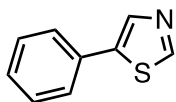
### 5-(4-Methoxyphenyl)-thiazole (26)



This compound was synthesized in 67% yield according to the general direct arylation procedure and exhibited identical <sup>1</sup>H NMR data to previously reported literature.<sup>67</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.70 (s, 1H), 7.98 (s, 1H), 7.51 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H).

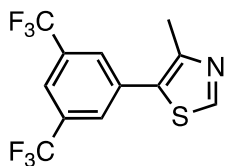
### 5-Phenylthiazole (27)



This compound was synthesized in 75% yield according to the general direct arylation procedure and exhibited identical <sup>1</sup>H NMR data to previously reported literature.<sup>67</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.76 (s, 1H), 8.09 (s, 1H), 7.59 (dd, *J* = 6.9, 1.5 Hz, 2H), 7.44–7.30 (m, 3H).

### 5-(3,5-Bis(trifluoromethyl)phenyl)-4-methylthiazole (28)



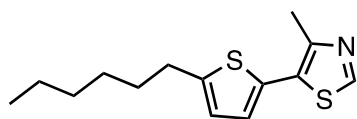
This compound was synthesized in 73% yield according to the general direct arylation procedure.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.32 (s, 1H), 7.96 (s, 1H), 7.89 (s, 2H), 2.56 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 151.8, 150.6, 134.5, 132.4 (q, *J* = 33 Hz), 129.3, 128.9, 123.1 (q, *J* = 273 Hz), 121.6 (sept, *J* = 3.7 Hz), 16.00;

**HRMS** calculated for C<sub>12</sub>H<sub>8</sub>F<sub>6</sub>NS (M+H)<sup>+</sup> 312.0276; found: 312.0275.

### 5-(5-Hexylthiophen-2-yl)-4-methylthiazole (29)



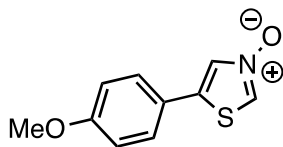
This compound was synthesized in 46% yield according to the general direct arylation procedure.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.47 (s, 1H), 6.86 (d, *J* = 3.6 Hz, 1H), 6.65 (d, *J* = 3.5 Hz, 1H), 2.77 (t, *J* = 7.6 Hz, 2H), 2.56 (s, 3H), 1.62 (tt, *J* = 7.6, 7.2 Hz, 2H), 1.36–1.20 (m, 6H), 0.84 (t, *J* = 6.6 Hz, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.2, 148.2, 147.0, 130.4, 126.7, 126.0, 124.5, 31.4, 30.0, 28.9, 23.6, 22.5, 16.4, 14.0;

**HRMS** calculated for C<sub>14</sub>H<sub>20</sub>NS<sub>2</sub> (M+H)<sup>+</sup> 266.1032; found: 266.1033.

### 5-(4-Methoxyphenyl)thiazole 3-oxide (30)



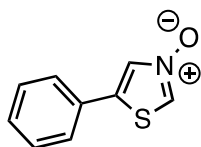
This compound was synthesized according to the general oxidation procedure in 22% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.05 (s, 1H), 7.78 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 161.0, 137.6, 131.4, 129.2, 127.4, 121.2, 114.7, 55.3;

**HRMS** calculated for C<sub>10</sub>H<sub>10</sub>NO<sub>2</sub>S (M+H)<sup>+</sup> 208.0427; found: 208.0427.

### 5-Phenylthiazole 3-oxide (31)



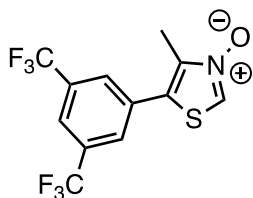
This compound was synthesized according to the general oxidation procedure in 11% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.22 (s, 1H), 7.89 (s, 1H), 7.46–7.40 (m, 5H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 139.2, 134.1, 131.6, 130.8, 129.8, 128.3, 126.4;

**HRMS** calculated for C<sub>9</sub>H<sub>8</sub>NOS (M+H)<sup>+</sup> 178.0321; found: 178.0321.

### 5-(3,5-Bis(trifluoromethyl)phenyl)-4-methylthiazole 3-oxide (32)



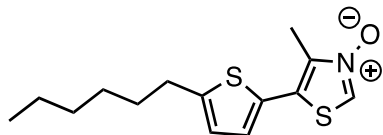
This compound was synthesized according to the general oxidation procedure in 18% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.34 (s, 1H), 7.98 (s, 1H), 7.88 (s, 2H), 2.48 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 143.7, 133.0, 133.2 (q, *J* = 34 Hz), 129.6, 128.9, 127.6, 123.4 (sept, *J* = 3.6), 122.9 (q, *J* = 273 Hz), 12.00;

**HRMS** calculated for C<sub>12</sub>H<sub>8</sub>F<sub>6</sub>NOS (M+H)<sup>+</sup> 328.0225; found: 328.0226.

### 5-(5-Hexylthiophen-2-yl)-4-methylthiazole 3-oxide (33)



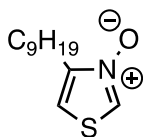
This compound was synthesized according to the general oxidation procedure in 29% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.21 (s, 1H), 7.04 (d, *J* = 3.6 Hz, 1H), 6.78 (d, *J* = 3.6 Hz, 1H), 2.82 (t, *J* = 7.6 Hz, 2H), 2.51 (s, 3H), 1.68 (tt, *J* = 7.6, 7.2 Hz, 2H), 1.42–1.24 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.0, 140.4, 128.8, 127.9, 127.3, 125.3, 124.9, 31.4, 30.0, 28.6, 22.4, 13.9, 11.9;

**HRMS** calculated for C<sub>14</sub>H<sub>20</sub>NOS<sub>2</sub> (M+H)<sup>+</sup> 282.0981; found: 282.0981.

#### 4-Nonylthiazole 3-oxide (34)



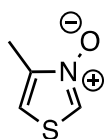
This compound was synthesized according to the general oxidation procedure in 40% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.24 (d, *J* = 3.1 Hz, 1H), 6.96 (d, *J* = 3.1 Hz, 1H), 2.70 (t, *J* = 7.7 Hz, 2H), 1.64 (tt, *J* = 7.7, 7.3 Hz, 2H), 1.25–1.00 (m, 12H), 0.81 (t, *J* = 6.9 Hz, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.8, 130.2, 112.5, 31.7, 29.3, 29.2, 29.1, 29.0, 26.5, 22.5, 14.0;

**HRMS** calculated for C<sub>12</sub>H<sub>22</sub>NOS (M+H)<sup>+</sup> 228.1422; found: 228.1417.

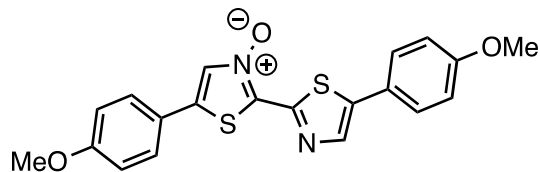
#### 4-Methylthiazole 3-oxide (35)



This compound was synthesized according to the general oxidation procedure in a 22% yield and exhibited identical  $^1\text{H}$  NMR data to previously reported.<sup>64</sup>

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 8.20 (d,  $J = 3.1$  Hz, 1H), 7.05 (d,  $J = 2.1$  Hz, 1H), 2.38 (s, 3H).

### 5,5'-Bis(4-methoxyphenyl)-[2,2'-bithiazole] 3-oxide (36)



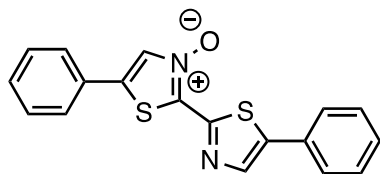
This compound was synthesized according to the general dehydration procedure in 81% yield.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 8.08 (s, 1H), 7.91 (s, 1H), 7.62 (d,  $J = 7.5$  Hz, 2H), 7.52 (d,  $J = 7.5$  Hz, 2H), 7.01 (d,  $J = 7.0$  Hz, 2H), 6.97 (d,  $J = 7.0$  Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H);

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 161.4, 160.1, 140.7, 139.2, 138.2, 132.2, 130.9, 128.3, 127.5, 123.7, 121.3, 115.0, 114.8, 113.6, 55.5, 55.4;

HRMS calculated for  $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}_3\text{S}_2$  ( $\text{M}+\text{H}$ )<sup>+</sup> 397.0675; found: 397.0676.

### 5,5'-Diphenyl-[2,2'-bithiazole] 3-oxide (37)



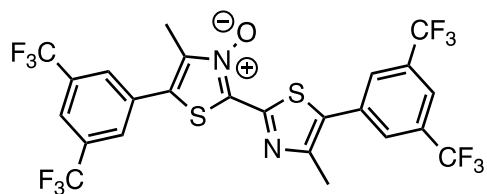
This compound was synthesized according to the general dehydration procedure but required flash column chromatography on silica gel to purify using 40% EtOAc/hexanes to afford the product in 81% yield.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 8.19 (s, 1H), 8.01 (s, 1H), 7.71–7.35 (m, 10H);

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 151.1, 140.6, 139.6, 139.2, 135.7, 131.9, 131.0, 130.4, 129.5, 129.2, 128.7, 128.7, 126.9, 126.0;

HRMS calculated for  $\text{C}_{18}\text{H}_{13}\text{N}_2\text{OS}_2$  ( $\text{M}+\text{H}$ ) $^+$  337.0464; found: 337.0463.

**5,5'-Bis(3,5-bis(trifluoromethyl)phenyl)-4,4'-dimethyl-[2,2'-bithiazole] 3-oxide (38)**



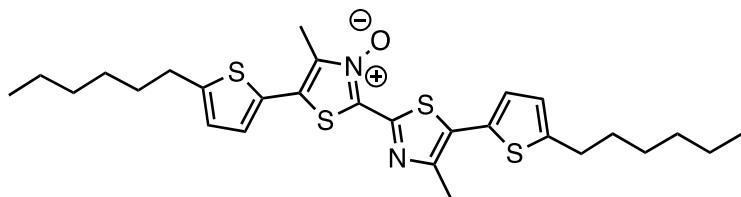
This compound was synthesized according to the general dehydration procedure in 80% yield.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ): 8.01 (s, 1H), 7.98 (s, 4H), 7.90 (s, 1H), 2.63 (s, 3H), 2.61 (s, 3H);

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 151.0, 151.0, 143.2, 139.9, 134.4, 133.3 (q,  $J = 34$  Hz), 132.6 (q,  $J = 34$  Hz), 132.8, 130.9, 129.3 (m), 128.8 (m), 126.5, 123.5 (sept,  $J = 3.7$ ), 121.9 (sept,  $J = 3.7$  Hz) 123.2 (q,  $J = 273$  Hz), 122.9 (q,  $J = 273$  Hz), 16.5, 12.1;

HRMS calculated for  $\text{C}_{24}\text{H}_{13}\text{F}_{12}\text{N}_2\text{OS}_2$  ( $\text{M}+\text{H}$ ) $^+$  637.0272; found: 637.0256.

**5,5'-Bis(5-hexylthiophen-2-yl)-4,4'-dimethyl-[2,2'-bithiazole] 3-oxide (39)**



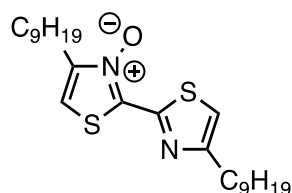
This compound was synthesized according to the general dehydration procedure in 56% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 7.13 (d, *J* = 3.5 Hz, 1H), 7.07 (d, *J* = 3.5 Hz, 1H), 6.82 (d, *J* = 3.5 Hz, 1H), 6.76 (d, *J* = 3.5 Hz, 1H), 2.88–2.81 (m, 4H), 2.66 (s, 3H), 2.62 (s, 3H), 1.73–1.66 (m, 4H), 1.40–1.20 (m, 12H), 0.90–0.83 (m, 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.4, 148.5, 148.5, 147.7, 139.7, 137.8, 130.9, 129.2, 128.3, 127.4, 126.9, 125.2, 125.0, 123.8, 31.6, 31.5, 30.2, 30.2, 29.7, 28.8, 28.8, 22.7, 22.6, 22.6, 17.0, 14.2, 14.1, 12.1;

**HRMS** calculated for C<sub>28</sub>H<sub>37</sub>N<sub>2</sub>OS<sub>4</sub> (M+H)<sup>+</sup> 545.1783; found: 545.1782.

#### 4,4'-Dinonyl-[2,2'-bithiazole] 3-oxide (40)



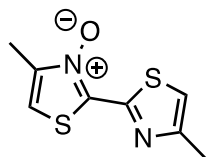
This compound was synthesized according to the general dehydration procedure in 57% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 7.08 (s, 1H), 7.01 (s, 1H), 2.83 (t, *J* = 7.6 Hz, 4H), 1.78–1.68 (m, 4H), 1.47–1.20 (m, 24H), 0.87 (t, *J* = 6.7 Hz 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 158.6, 152.5, 149.7, 140.5, 115.0, 111.0, 31.9, 31.9, 31.5, 29.6, 29.5, 29.5, 29.3, 29.3, 29.3, 26.8, 26.6, 22.7, 22.7, 14.1;

**HRMS** calculated for C<sub>24</sub>H<sub>40</sub>N<sub>2</sub>OS<sub>2</sub> (M+H)<sup>+</sup> 437.2655; found: 437.2655.

#### 4,4'-Dimethyl-[2,2'-bithiazole] 3-oxide (41)



This compound was synthesized according to the general dehydration procedure in 72% yield.

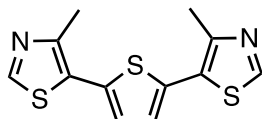


**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 7.07 (s, 1H), 7.06 (s, 1H), 2.50 (s, 3H), 2.42 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 153.6, 152.7, 145.4, 140.1, 115.8, 111.7, 17.2, 12.7;

**HRMS** calculated for C<sub>8</sub>H<sub>9</sub>N<sub>2</sub>OS<sub>2</sub> (M+H)<sup>+</sup> 213.0151; found: 213.0142.

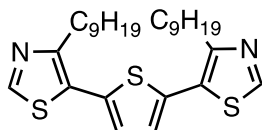
### 2,5-Bis(4-methylthiazol-5-yl)thiophene (42)



This compound was synthesized according to the general direct arylation procedure with the exception of employing 0.6 equivalents of the aryl bromide to give the product in 57% yield and exhibited identical <sup>1</sup>H NMR data to previously reported.<sup>68</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.64 (s, 2H), 7.11 (s, 2H), 2.65 (s, 6H).

### 2,5-Bis(4-nonylthiazol-5-yl)thiophene (43)



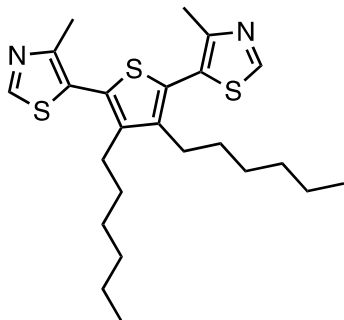
This compound was synthesized according to the general direct arylation procedure with the exception of employing 0.6 equivalents of the aryl bromide to give the product in 40% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.72 (s, 2H), 7.08 (s, 2H), 2.94 (t, *J* = 7.7 Hz, 4H), 1.81–1.71 (m, 4H), 1.39–1.23 (m, 24H), 0.85 (t, *J* = 6.4 Hz, 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 154.2, 151.1, 133.8, 127.9, 124.8, 32.0, 30.2, 29.6, 29.6, 29.5, 29.4, 27.2, 22.8, 14.2;

**HRMS** calculated for C<sub>28</sub>H<sub>43</sub>N<sub>2</sub>S<sub>3</sub> (M+H)<sup>+</sup> 503.2583; found: 503.2591.

**5,5'-(3,4-Dihexylthiophene-2,5-diyl)bis(4-methylthiazole) (44)**



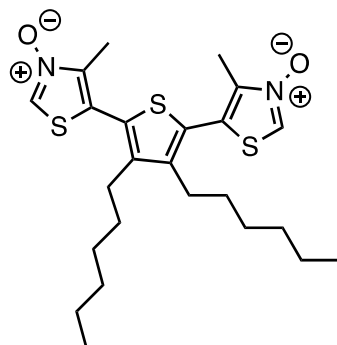
This compound was synthesized according to the general direct arylation procedure with the exception of employing 0.6 equivalents of the aryl bromide to give the product in 42% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.78 (s, 2H), 2.50–2.40 (m, 10H), 1.70–1.20 (m, 16H), 0.85 (t, *J* = 6.8 Hz, 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 152.3, 152.2, 143.1, 127.1, 123.5, 31.5, 30.6, 29.5, 28.1, 22.6, 16.1, 14.1;

**HRMS** calculated for C<sub>24</sub>H<sub>35</sub>N<sub>2</sub>S<sub>3</sub> (M+H)<sup>+</sup> 447.1957; found: 447.1956.

**5,5'-(3,4-Dihexylthiophene-2,5-diyl)bis(4-methylthiazole 3-oxide) (46)**



This compound was synthesized according to the general oxidation procedure, with the exception of employing 3.0 equiv. of *m*CPBA. The product was obtained in 10% yield and separated from the mono-*N*-oxide that was also produced.

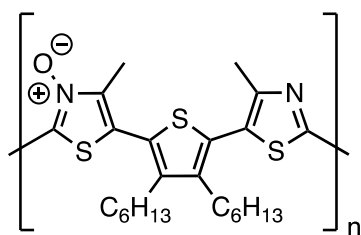
**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.37 (s, 2H), 2.51 (t, *J* = 7.4 Hz, 4H), 2.33 (s, 6H), 1.50–1.10 (m, 16H), 0.84 (t, *J* = 6.7 Hz, 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 144.6, 144.5, 130.1, 126.4, 122.3, 31.3, 30.6, 29.3, 27.9, 22.4, 13.9, 12.0;

**HRMS** calculated for C<sub>24</sub>H<sub>35</sub>N<sub>2</sub>O<sub>2</sub>S<sub>3</sub> (M+H)<sup>+</sup> 479.1855; found: 479.1855.

**Poly[5-(3,4-dihexanoyl-5-(4-methylthiazol-5-yl)thiophen-2-yl)-4-methylthiazole 3-oxide]**

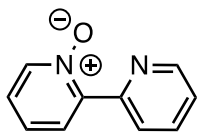
(47)



The di-*N*-oxide (0.200 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.03 M) and the solution was placed in an ice bath. To this cold solution was added 1.0 M LiO<sup>t</sup>Bu in THF (0.300 mmol, 1.5 equiv.) which resulted in a significant color change from yellow to wine red. The mixture was allowed to warm to RT and was stirred for 3 hours. The solution was then concentrated, precipitated in methanol and isolated through filtration in quantitative yield, *M<sub>n</sub>* = 17 kDa, *M<sub>w</sub>* = 46 kDa.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 2.65–2.40 (br, 10H), 2.35 (s, 3H), 1.50–1.10 (m, 16H), 0.85 (br, 6H).

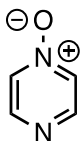
### [2,2'-Bipyridine] 1-oxide (49)



The pyridine *N*-oxide (1.10 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.3 M) and LiO<sup>t</sup>Bu (1.65 mmol, 1.5 equiv.) was added. The reaction mixture was left to stir for 16 h at 60°C. The volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography using EtOAc/methanol (0–10%) to afford the product in 65% yield. The compound exhibited identical <sup>1</sup>H NMR characterization data as previously reported in the literature.<sup>41</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.87 (d, *J* = 8.1 Hz, 1H), 8.71 (d, *J* = 4.3 Hz, 1H), 8.30 (d, *J* = 6.4 Hz, 1H), 8.16 (d, *J* = 7.8, 1H), 7.81 (t, *J* = 7.8, 1H), 7.38–7.23 (m, 3H).

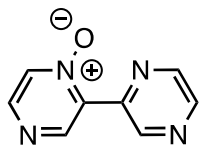
### Pyrazine 1-oxide (51)



To a solution of pyrazine (12.0 mmol, 1.0 equiv.) in DCM (0.3 M) was slowly added *m*CPBA (18.0 mmol, 1.5 equiv.) and continued stirring for 2 h at RT. The crude reaction mixture was concentrated under reduced pressure then purified by a silica-gel column chromatography using EtOAc/MeOH (0–10%), affording the product in an 88% yield. The compound exhibited identical <sup>1</sup>H NMR characterization data as previously reported in the literature.<sup>44</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.45 (d, *J* = 3.6 Hz, 2H), 8.09 (d, *J* = 3.6 Hz, 2H).

### [2,2'-Bipyrazine] 1-oxide (52)



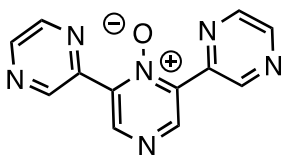
The pyrazine *N*-oxide (1.10 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.3 M) and LiO<sup>t</sup>Bu (1.65 mmol, 1.5 equiv.) was added. The reaction mixture was left to stir for 1 h at room temp. The volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography using EtOAc/MeOH (0–15%) to afford the product in 35% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 10.06 (s, 1H), 9.39 (s, 1H), 8.77–8.69 (m, 2H), 8.48 (d, *J* = 4.0 Hz, 1H), 8.21 (d, *J* = 4.0 Hz, 1H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 150.0, 146.8, 146.5, 145.7, 144.4, 143.8, 134.7;

**HRMS** calculated for C<sub>8</sub>H<sub>7</sub>N<sub>4</sub>O (M+H)<sup>+</sup> 175.0625; found: 175.0614.

### [2,2':6',2''-Terpyrazine] 1'-oxide



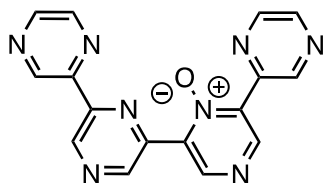
Compound **51** (0.300 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.3 M) and LiO<sup>t</sup>Bu (0.450 mmol, 1.5 equiv.) was added. The reaction mixture was left to stir for 16 h at RT. The volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography using EtOAc/MeOH (0–10%) to afford the product in 6% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 9.77 (s, 2H), 9.70 (s, 2H), 8.72 (s, 4H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.1, 148.1, 145.5, 143.9, 143.7, 143.6;

**HRMS** calculated for C<sub>12</sub>H<sub>9</sub>N<sub>6</sub>O (M+H)<sup>+</sup> 253.0832; found: 253.0832.

### [2,2':6',2'':6'',2''':2''''-Quaterpyrazine] 1'-oxide



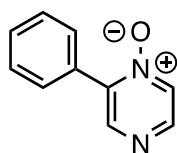
Compound **51** (0.300 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.3 M) and LiO<sup>t</sup>Bu (0.450 mmol, 1.5 equiv.) was added. The reaction mixture was left to stir for 16 h at RT. The volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography using EtOAc/MeOH (0–10%) to afford the product in 38% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 10.05 (s, 1H), 9.99 (s, 1H), 9.39 (s, 1H), 9.33 (s, 1H), 8.77–8.69 (m, 4H), 8.47 (d, *J* = 4.1 Hz, 1H), 8.21 (d, *J* = 4.1 Hz, 1H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 149.8, 149.2, 146.7, 146.6, 146.3, 145.5, 145.5, 144.3, 144.2, 143.9, 143.7, 140.7, 140.5, 134.5;

**HRMS** calculated for C<sub>16</sub>H<sub>11</sub>N<sub>8</sub>O (M+H)<sup>+</sup> 331.1050; found: 331.1050.

### 2-Phenylpyrazine 1-oxide (**57**)

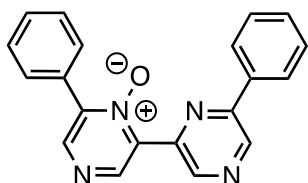


To a dried flask was added pyrazine *N*-oxide (**51**) (10.0 mmol, 1.0 equiv.), K<sub>2</sub>CO<sub>3</sub> (2.0 equiv.), Pd(OAc)<sub>2</sub> (5 mol %), and P(*t*Bu)<sub>3</sub>·HBF<sub>4</sub> (15 mol %). The flask and its contents were then purged under argon for 10 min after which bromobenzene (6.60 mmol, 0.6 equiv.) was added by syringe. Degassed dioxane was then added to produce a reaction concentration of 0.3 M relative to pyrazine *N*-oxide. The reaction mixture was heated at 110 °C for 16 h, after which the volatiles were

removed under reduced pressure and the residue was purified by silica gel column chromatography using hexanes/EtOAc (40–80%). The compound was isolated in 47% yield and exhibited identical  $^1\text{H}$  NMR characterization data as previously reported in the literature.<sup>69</sup>

**$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):** 8.62 (s, 1H), 8.39 (br s, 1H), 8.21 (br s, 1H), 7.81 (br s, 2H), 7.52 (br s, 3H).

### 6,6'-Diphenyl-[2,2'-bipyrazine] 1-oxide (58)



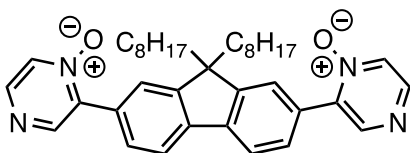
Compound **58** (0.300 mmol, 1.0 equiv.) was dissolved in reagent grade THF (0.3 M) and LiO<sup>t</sup>Bu (0.450 mmol, 1.5 equiv.) was added. The reaction mixture was left to stir for 16 h at 60°C. The volatiles were removed under reduced pressure and the residue was purified via silica gel column chromatography using Hexanes/EtOAc (30–35%) to afford the product in 55% yield.

**$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):** 9.99 (s, 1H), 9.46 (s, 1H), 9.13 (s, 1H), 8.65 (s, 1H), 8.15–8.12 (m, 2H), 7.84–7.81 (m, 2H), 7.60–7.53 (m, 6H);

**$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):** 151.9, 148.4, 147.4, 145.1, 144.5, 143.3, 142.4, 141.0, 135.8, 130.6, 130.5, 129.6, 129.3, 129.2, 128.8, 127.1;

**HRMS** calculated for  $\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}$  ( $\text{M}+\text{H}$ )<sup>+</sup> 327.1240; found: 327.1239.

### 2,2'-(9,9-dioctyl-9H-fluorene-2,7-diyl)bis(1-( $\lambda^1$ -oxidaneyl)-1 $\lambda^4$ -pyrazine) (60)



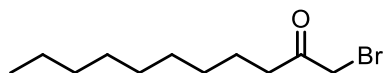
To a dried flask was added pyrazine *N*-oxide (**51**) (7.28 mmol, 4.0 equiv.), 2,7-dibromo-9,9-dioctyl-9*H*-fluorene (1.82 mmol, 1.0 equiv.), Cs<sub>2</sub>CO<sub>3</sub> (3.0 equiv.), Pd(OAc)<sub>2</sub> (5 mol %), and PCy<sub>3</sub>·HBF<sub>4</sub> (15 mol %). The flask and its contents were then purged under argon for 10 min followed by the addition of toluene to produce a reaction concentration of 0.23 M relative to the fluorene. The reaction mixture was heated at 130 °C for 16 h after which the volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography using hexanes/EtOAc (80–100%) to afford the compound in 16% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.73 (s, 2H), 8.40 (d, *J* = 4.1 Hz, 2H), 8.23 (d, *J* = 4.0 Hz, 2H), 7.89 (s, 6H), 2.06–1.99 (m, 4H), 1.20–1.07 (m, 20H), 0.80 (t, *J* = 6.8 Hz, 6H), 0.75–0.71 (m, 4H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 151.6, 148.5, 145.3, 144.8, 142.2, 134.6, 128.3, 128.2, 123.9, 120.4, 55.7, 40.0, 31.7, 30.0, 29.2, 24.0, 22.6, 14.0;

**HRMS** calculated for C<sub>37</sub>H<sub>47</sub>N<sub>4</sub>O<sub>2</sub> (M+H)<sup>+</sup> 579.3693; found: 579.3691

### 1-Bromoundecan-2-one (**64**)

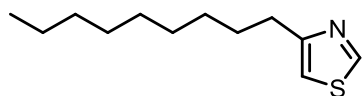


This compound was prepared according to a previously reported procedure to give the product in 32% yield. The compound exhibited identical <sup>1</sup>H NMR characterization data as previously reported.<sup>70</sup>

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 3.87 (s, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 1.62 (tt, *J* = 7.1, 7.1 Hz, 2H), 1.30–1.20 (m, 12H), 0.86 (t, *J* = 6.9 Hz, 3H).

### 4-Nonyl thiazole (**68**)

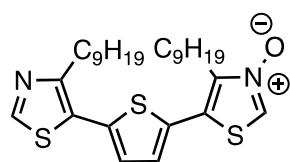




This compound was synthesized according to a previously reported procedure to give the product in 62% yield. The compound exhibited identical  $^1\text{H}$  NMR characterization data as previously reported.<sup>71</sup>

**$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):** 8.60 (s, 1H), 6.78 (s, 1H), 2.70 (t,  $J = 7.7$  Hz, 2H), 1.61 (tt,  $J = 7.6$ , 7.6 Hz, 2H), 1.30–1.10 (m, 12H), 0.76 (t,  $J = 6.6$  Hz, 3H).

#### 4-Nonyl-5-(5-(4-nonylthiazol-5-yl)thiophen-2-yl)thiazole 3-oxide (70)



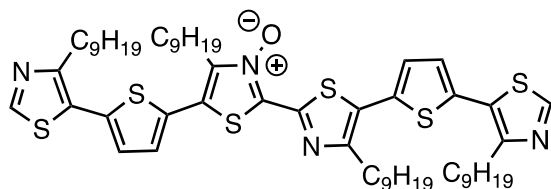
This compound was synthesized according to the general oxidation procedure in 26% yield.

**$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):** 8.70 (s, 1H), 8.37 (s, 1H), 7.18 (d,  $J = 3.8$ , 1H), 7.11 (d,  $J = 3.8$ , 1H), 3.01–2.91 (m, 4H), 1.82–1.67 (m, 4H), 1.40–1.23 (m, 24H), 0.86–0.82 (m, 6H);

**$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):** 155.0, 151.2, 145.8, 135.7, 132.1, 129.3, 128.1, 128.0, 124.3, 124.1, 32.0, 30.4, 29.7, 29.6, 29.6, 29.4, 27.5, 26.2, 22.8, 14.2;

**HRMS** calculated for  $\text{C}_{28}\text{H}_{43}\text{N}_2\text{OS}_3$  ( $\text{M}+\text{H}$ )<sup>+</sup> 519.2532; found: 519.2525.

#### 4,4'-Dinonyl-5,5'-bis(5-(4-nonylthiazol-5-yl)thiophen-2-yl)-[2,2'-bithiazole] 3-oxide (71)



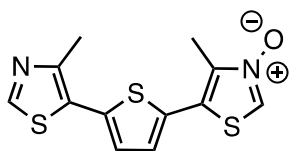
This compound was synthesized according to the general dehydration procedure in 91% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.72 (s, 1H), 8.69 (s, 1H), 7.29 (d, *J* = 3.8 Hz, 1H), 7.21 (d, *J* = 3.8 Hz, 1H), 7.17 (d, *J* = 3.8 Hz, 1H), 7.13 (d, *J* = 3.8 Hz, 1H), 3.13–2.89 (m, 8H), 1.88–1.70 (m, 8H), 1.43–1.21 (m, 48H), 0.86 (t, *J* = 6.3 Hz, 12H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 154.9, 154.4, 154.3, 151.2, 150.7, 149.3, 145.1, 144.1, 138.4, 135.7, 134.1, 134.0, 132.2, 128.1, 127.9, 127.6, 126.7, 124.7, 124.1, 122.7, 31.9, 31.9, 30.6, 30.3, 30.3, 30.2, 29.8, 29.7, 29.6, 29.6, 29.5, 29.5, 29.5, 29.3, 29.3, 29.2, 27.3, 27.3, 26.4, 22.7, 14.1;

**HRMS** calculated for C<sub>56</sub>H<sub>83</sub>N<sub>4</sub>OS<sub>6</sub> (M+H)<sup>+</sup> 1019.4886; found: 1019.4964.

#### 4-Methyl-5-(5-(4-methylthiazol-5-yl)thiophen-2-yl)thiazole 3-oxide (74)



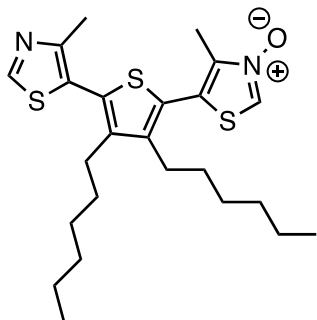
This compound was synthesized according to the general oxidation procedure in 28% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.69 (s, 1H), 8.20 (s, 1H), 7.23 (d, *J* = 7.1, 1H), 7.17 (d, *J* = 7.1, 1H), 2.66 (s, 3H), 2.58 (s, 3H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 150.7, 150.0, 141.6, 135.8, 132.1, 128.1, 128.0, 127.6, 124.4, 124.1, 16.75, 12.16;

**HRMS** calculated for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>OS<sub>3</sub> (M+H)<sup>+</sup> 295.0028; found: 295.0028.

**5-(3,4-Dihexyl-5-(4-methylthiazol-5-yl)thiophen-2-yl)-4-methylthiazole 3-oxide (79)**



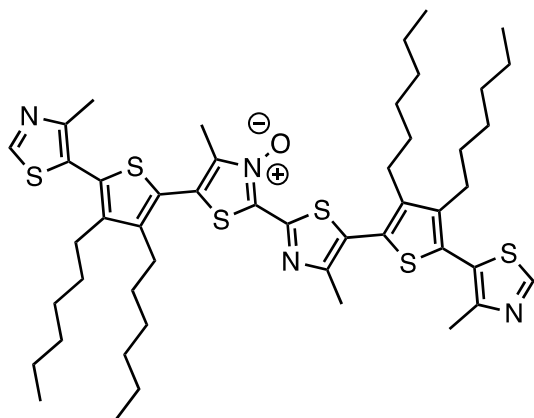
This compound was synthesized according to the general oxidation procedure and was obtained in 26% yield and separated from the di-*N*-oxide that was also produced.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.80 (s, 1H), 8.41 (s, 1H), 2.52–2.45 (m, 4H), 2.42 (s, 3H), 2.36 (s, 3H), 1.44–1.34 (m, 4H), 1.23–1.21 (m, 12H), 0.85 (t, *J* = 5.5 Hz, 6H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 152.5, 152.2, 144.1, 143.3, 130.9, 128.7, 127.8, 124.7, 123.1, 122.5, 31.3, 30.6, 30.2, 29.3, 29.2, 28.0, 27.8, 22.4, 15.8, 13.9, 12.0;

**HRMS** calculated for C<sub>24</sub>H<sub>35</sub>N<sub>2</sub>OS<sub>3</sub> (M+H)<sup>+</sup> 463.1906; found: 463.1906.

**5,5'-Bis(3,4-dihexyl-5-(4-methylthiazol-5-yl)thiophen-2-yl)-4,4'-dimethyl-[2,2'-bithiazole] 3-oxide (80)**



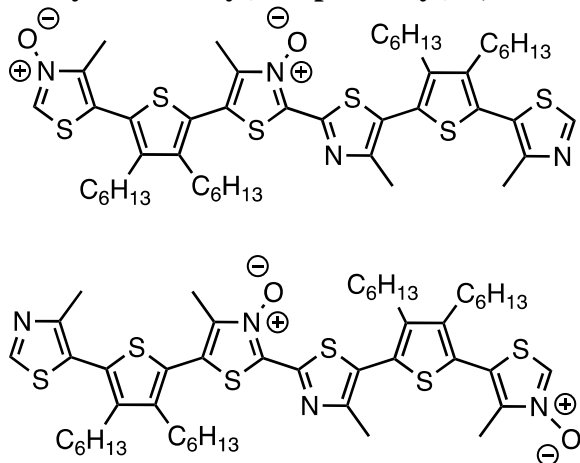
This compound was synthesized according to the general dehydration procedure in 90% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.81–8.75 (m, 2H), 2.62–2.40 (m, 20H), 1.48–1.37 (m, 8H), 1.23–1.18 (m, 24H), 0.87–0.80 (m, 12H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 152.5, 152.1, 151.3, 144.2, 143.6, 143.5, 143.1, 143.0, 140.1, 128.9, 127.3, 127.0, 125.8, 124.7, 121.6, 31.4, 31.3, 31.3, 30.7, 30.4, 30.3, 30.3, 29.3, 29.2, 29.2, 27.9, 27.9, 22.4, 22.4, 16.1, 15.9, 13.9, 12.0;

**HRMS** calculated for C<sub>48</sub>H<sub>67</sub>N<sub>4</sub>OS<sub>6</sub> (M+H)<sup>+</sup> 907.3634; found: 907.3623.

**5-(3,4-dihexyl-5-(4-methyl-3-oxidothiazol-5-yl)thiophen-2-yl)-5'-(3,4-dihexyl-5-(4-methylthiazol-5-yl)thiophen-2-yl)-4,4'-dimethyl-[2,2'-bithiazole] 3-oxide (81a/82b)**



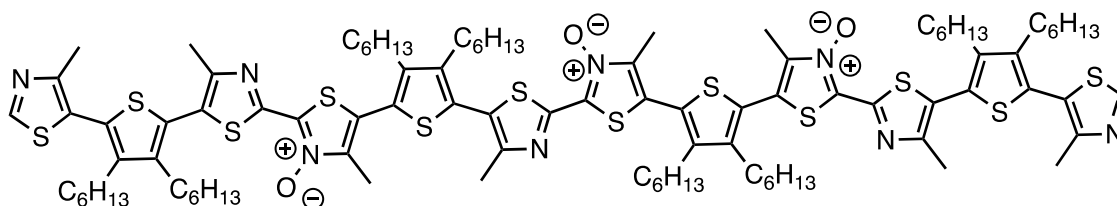
This compound was synthesized according to the general oxidation procedure with the exception of employing 0.7 equiv. of *m*CPBA and a mixture of compounds was isolated in a 20% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.82 (m, 1H), 8.69 (s, 1H), 2.60–2.39 (m, 20H), 1.52–1.35 (m, 8H), 1.23–1.18 (m, 24H), 0.85–0.79 (m, 12H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** 152.8, 152.6, 152.5, 151.9, 151.3, 145.0, 144.9, 144.6, 144.5, 144.3, 143.9, 143.8, 143.6, 143.4, 143.3, 140.7, 140.3, 132.7, 129.7, 129.2, 129.1, 127.6, 127.1, 126.6, 125.1, 125.1, 124.9, 123.5, 122.7, 122.1, 120.9, 31.6, 31.6, 31.5, 30.9, 30.9, 30.7, 30.6, 30.6, 30.5, 29.6, 29.5, 29.5, 28.3, 28.3, 28.2, 28.2, 28.1, 22.5, 22.7, 16.4, 16.1, 14.1, 12.3, 12.3;

**HRMS** calculated for C<sub>48</sub>H<sub>67</sub>N<sub>4</sub>O<sub>2</sub>S<sub>6</sub> (M+H)<sup>+</sup> 923.3590; found: 923.3583.

**5,5''-((4,4'-dimethyl-3-oxido-[2,2'-bithiazole]-5,5'-diyl)bis(3,4-dihexylthiophene-5,2-diyl))bis(5'-(3,4-dihexyl-5-(4-methylthiazol-5-yl)thiophen-2-yl)-4,4'-dimethyl-[2,2'-bithiazole] 3-oxide) (mixture of four structural isomers 82a-d)**



This compound was synthesized according to the general dehydration procedure in a 27% yield.

**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** 8.82–8.79 (m, 2H), 2.59–2.46 (m, 40H), 1.55–1.41 (m, 16H), 1.33–1.20 (br s, 48H), 0.88–0.82 (m, 24H);

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** Not obtained.

**HRMS** calculated for C<sub>96</sub>H<sub>130</sub>N<sub>8</sub>O<sub>3</sub>S<sub>12</sub> (M+H)<sup>+</sup> 1827.6987; found: Not obtained.

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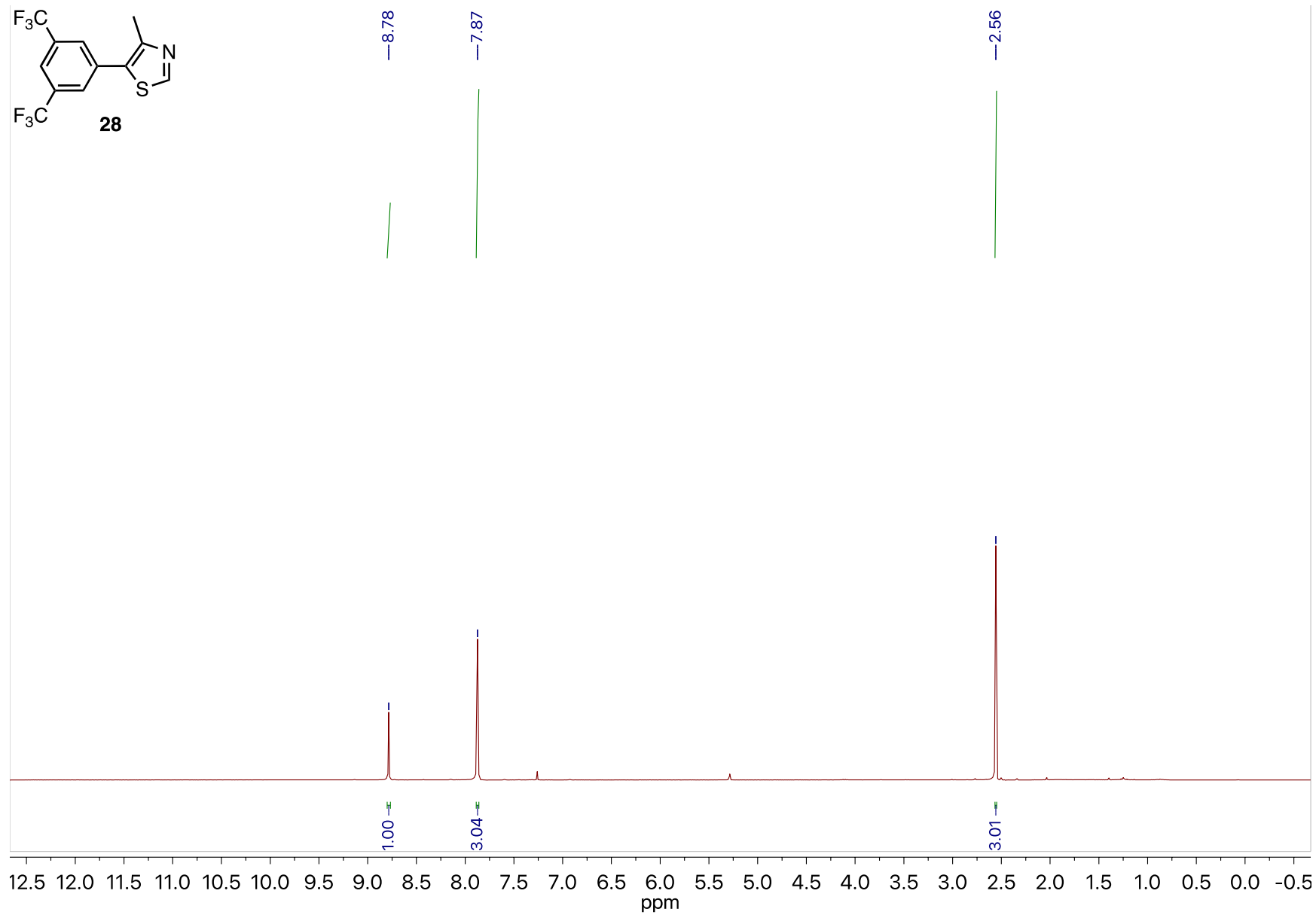
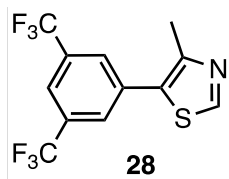
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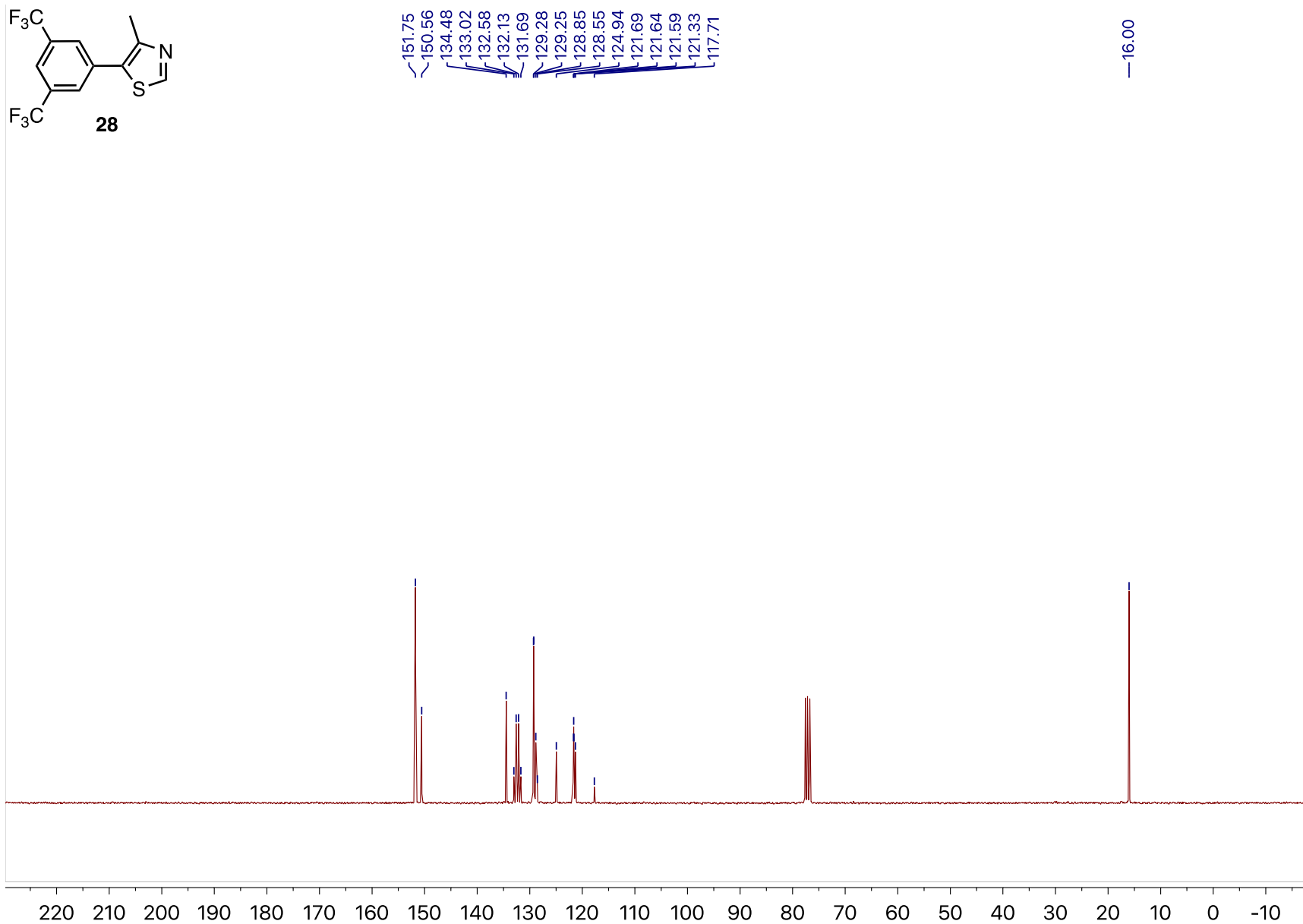
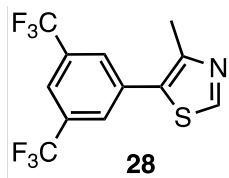
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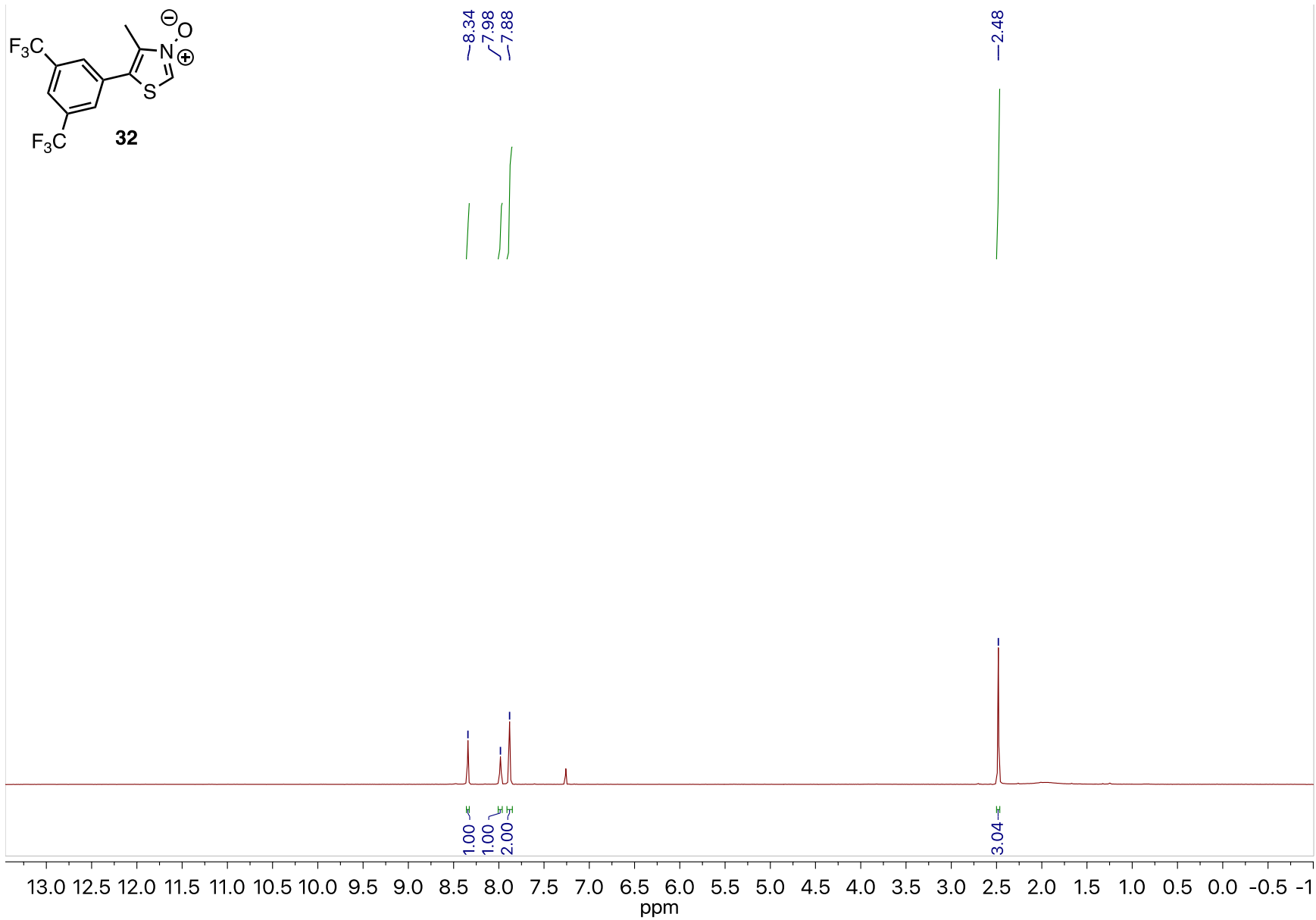
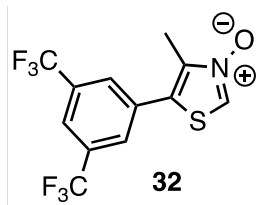
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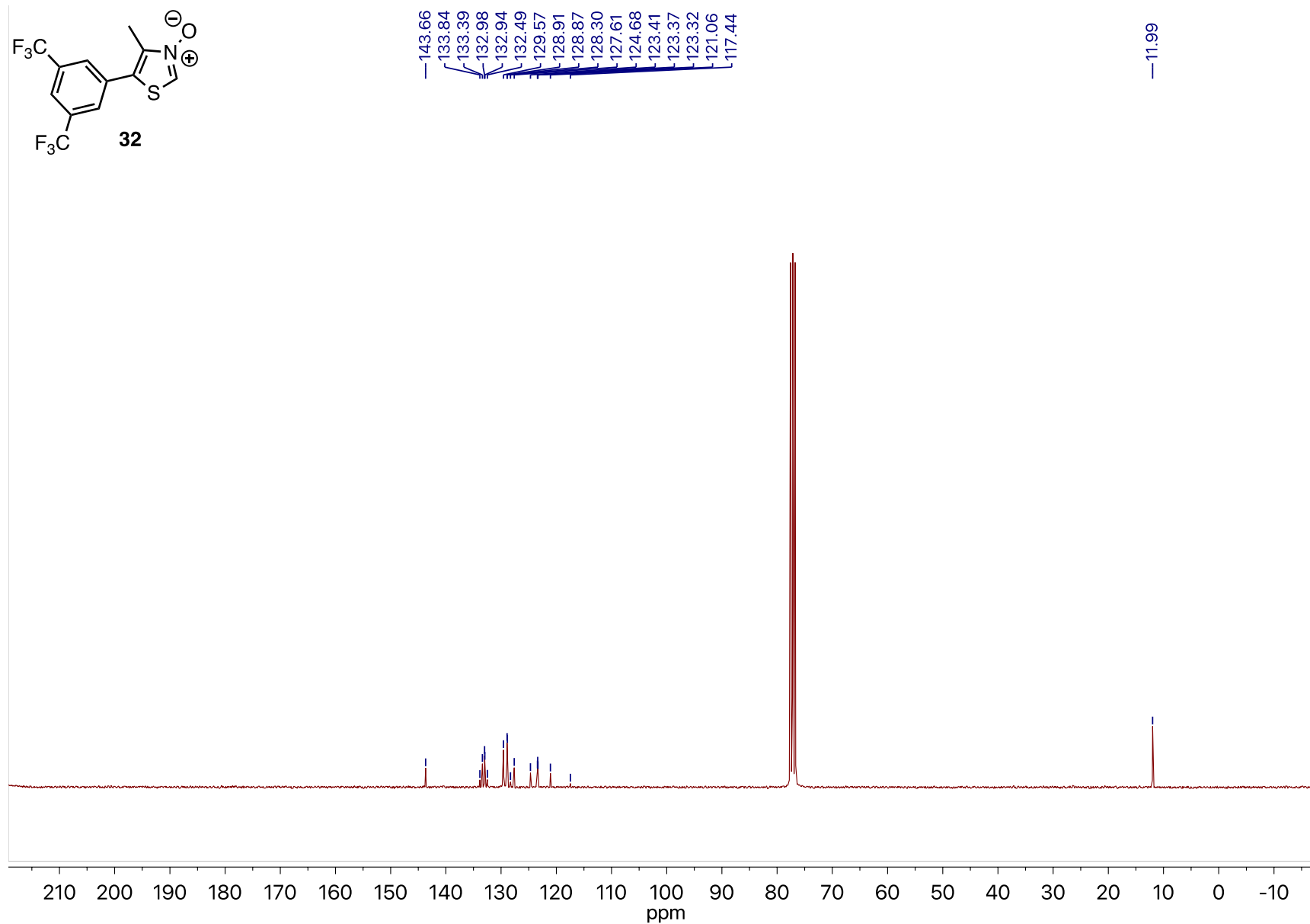
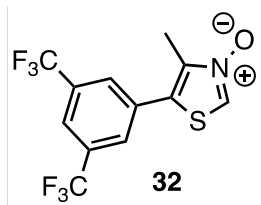
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## **Spectral Data**

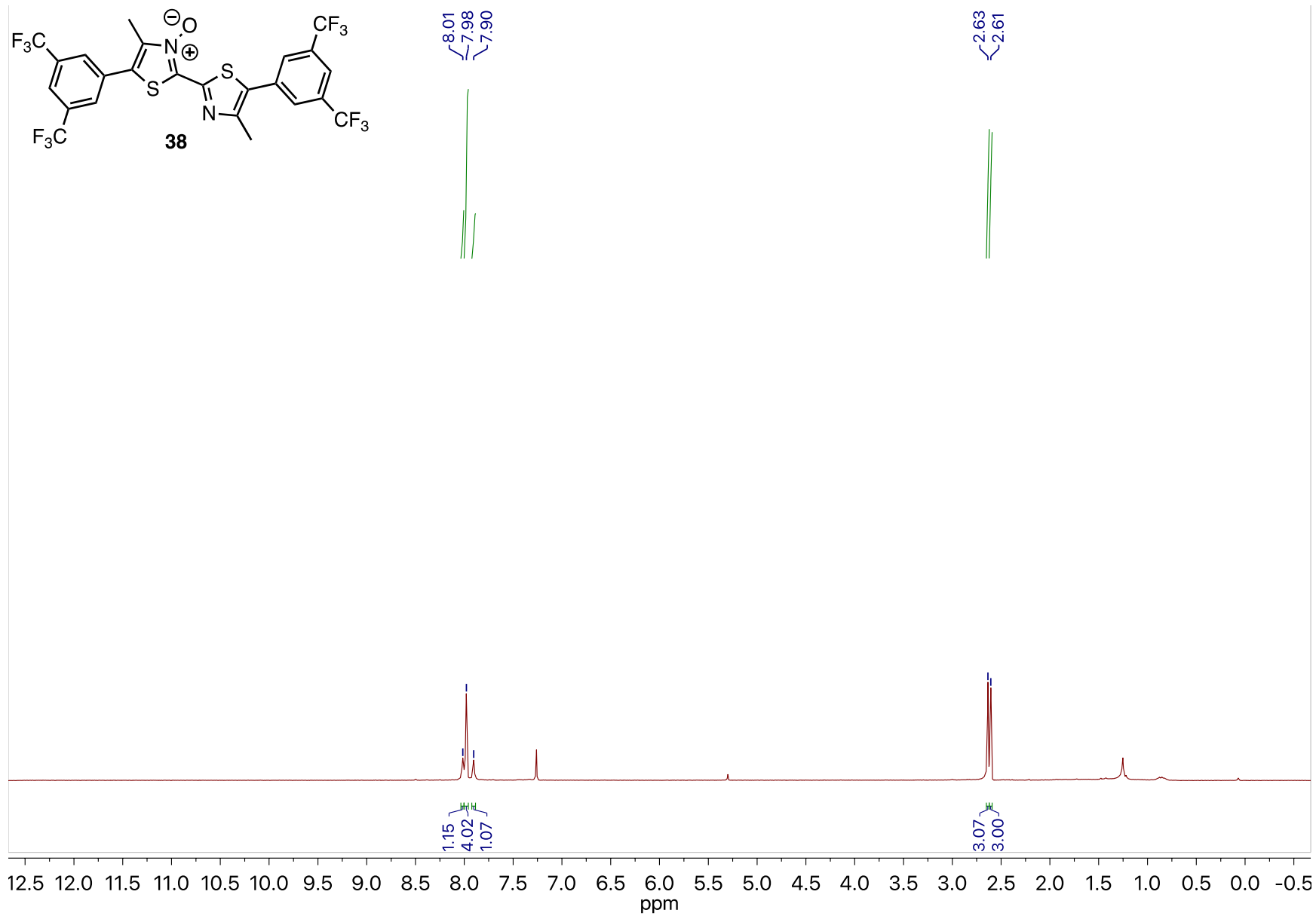


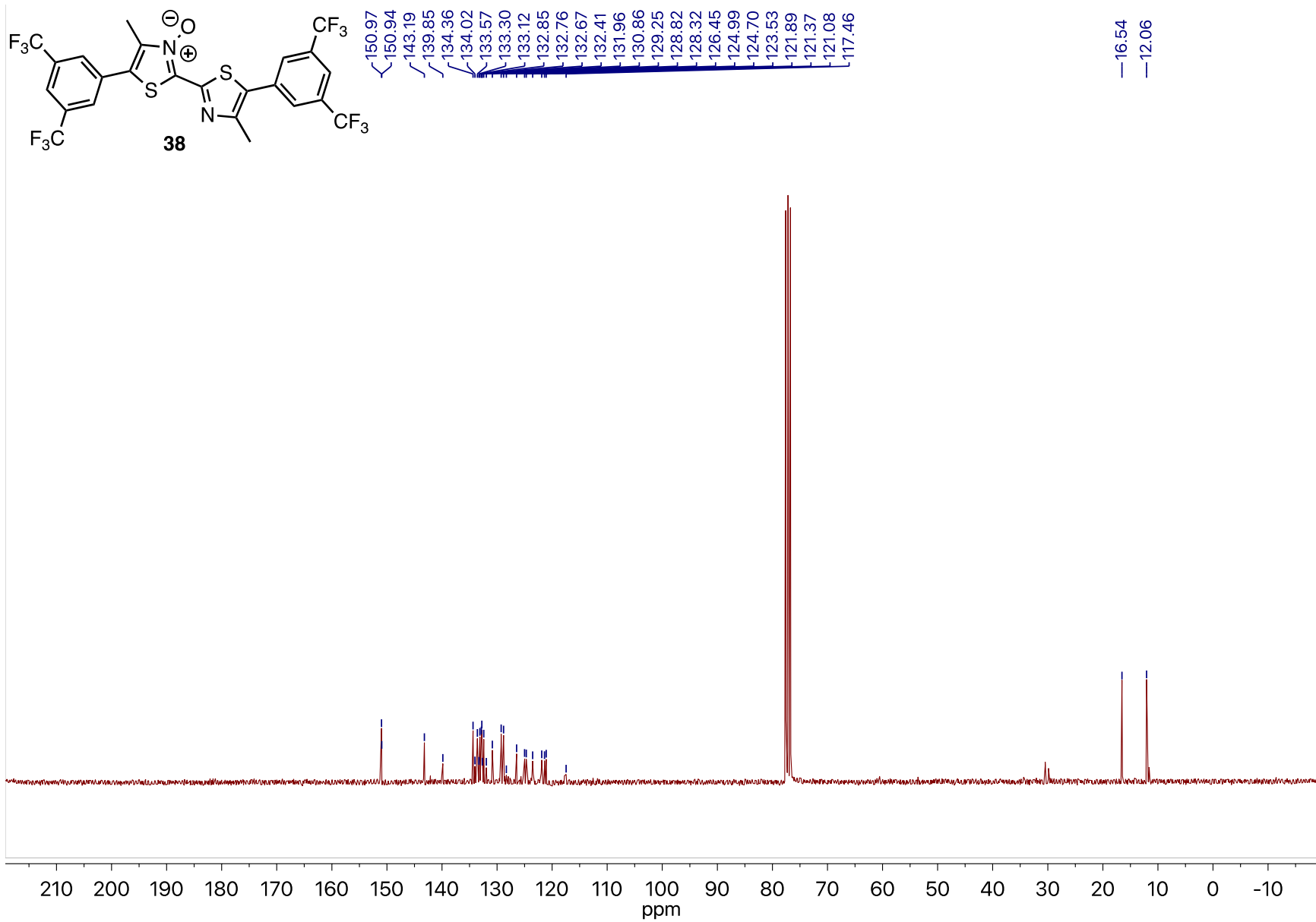


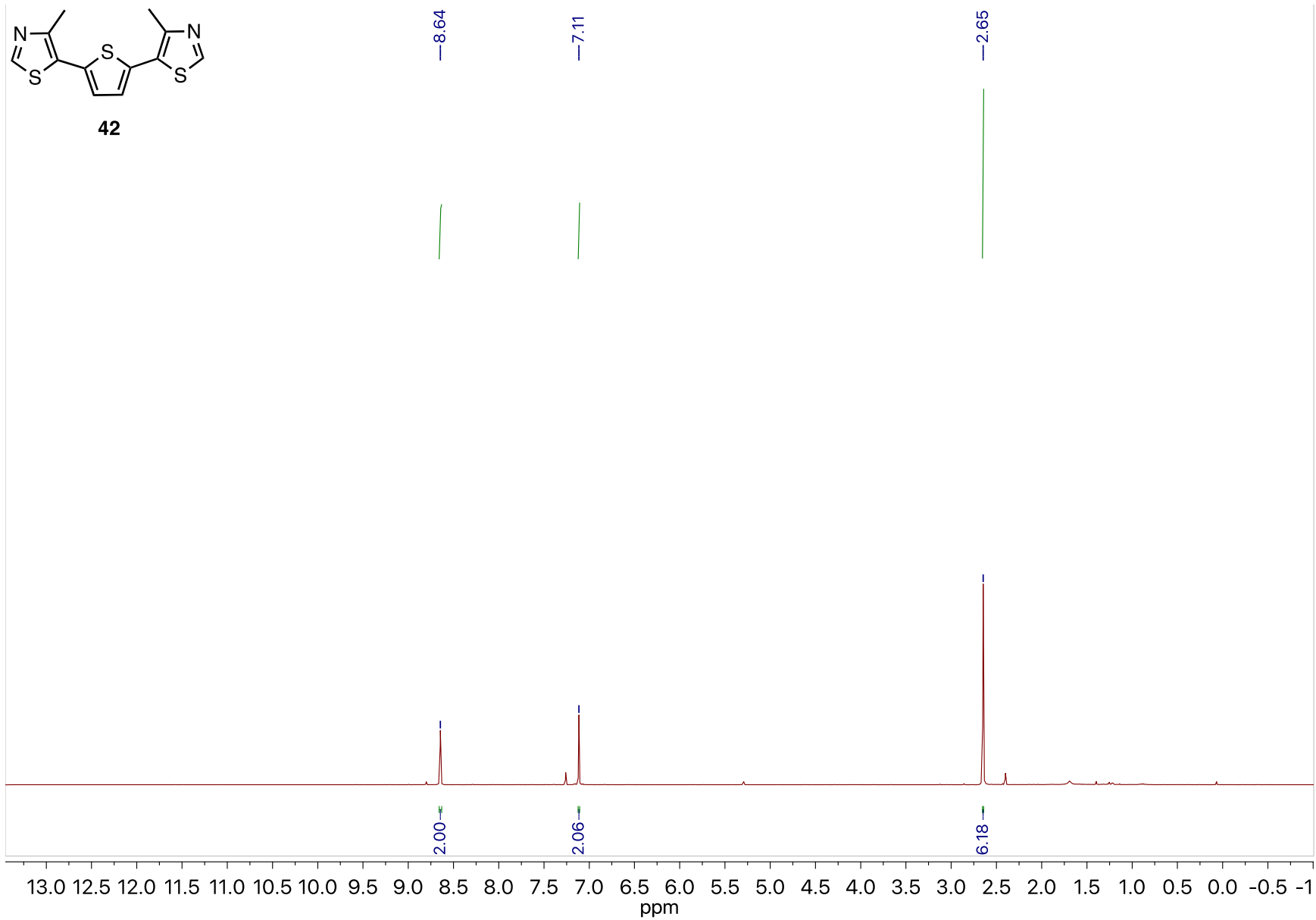
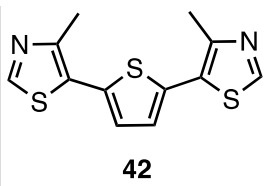


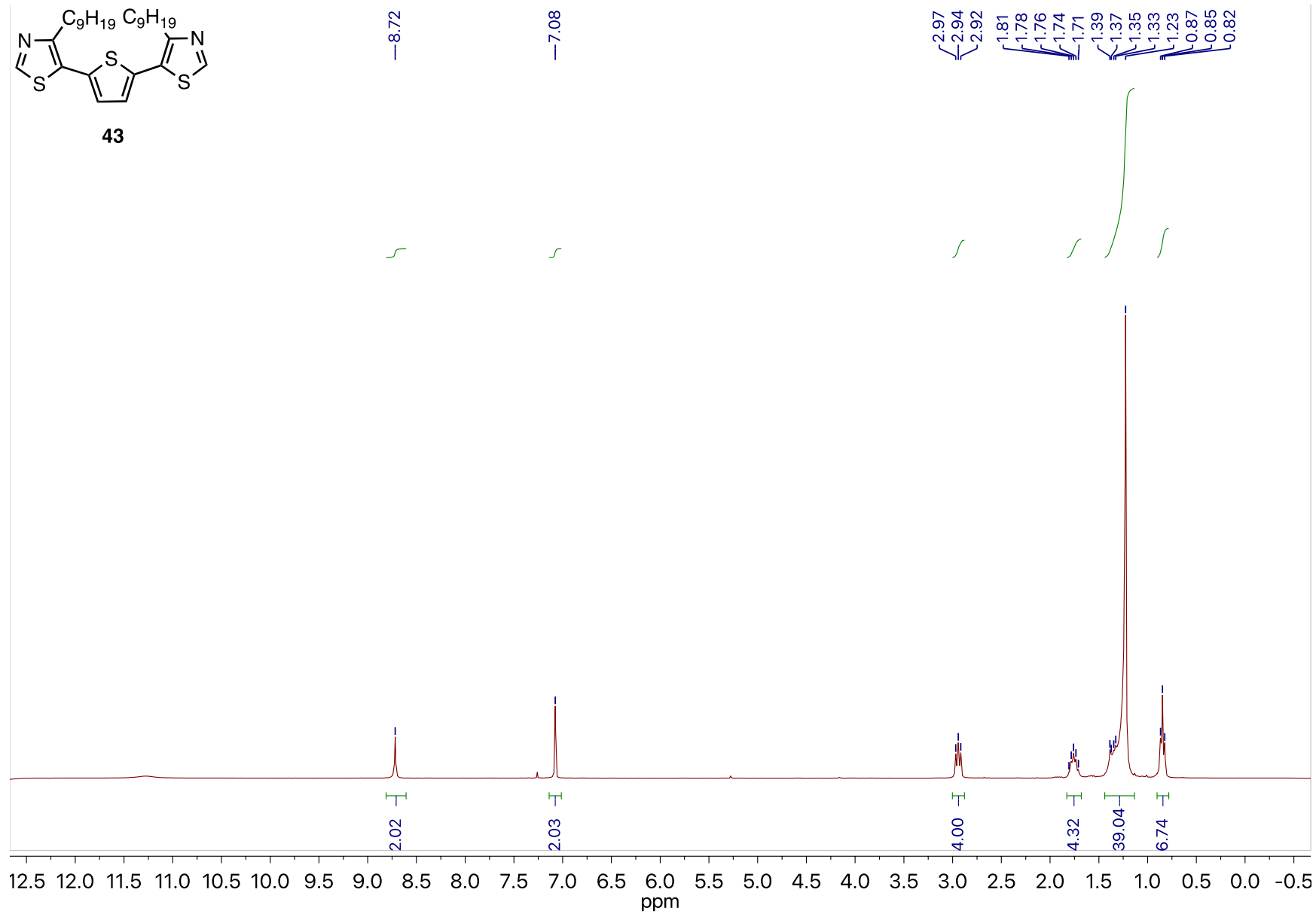
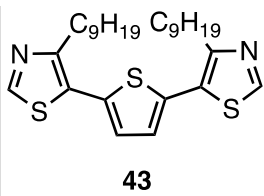


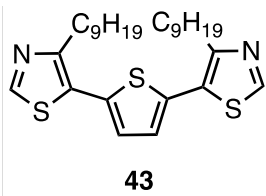








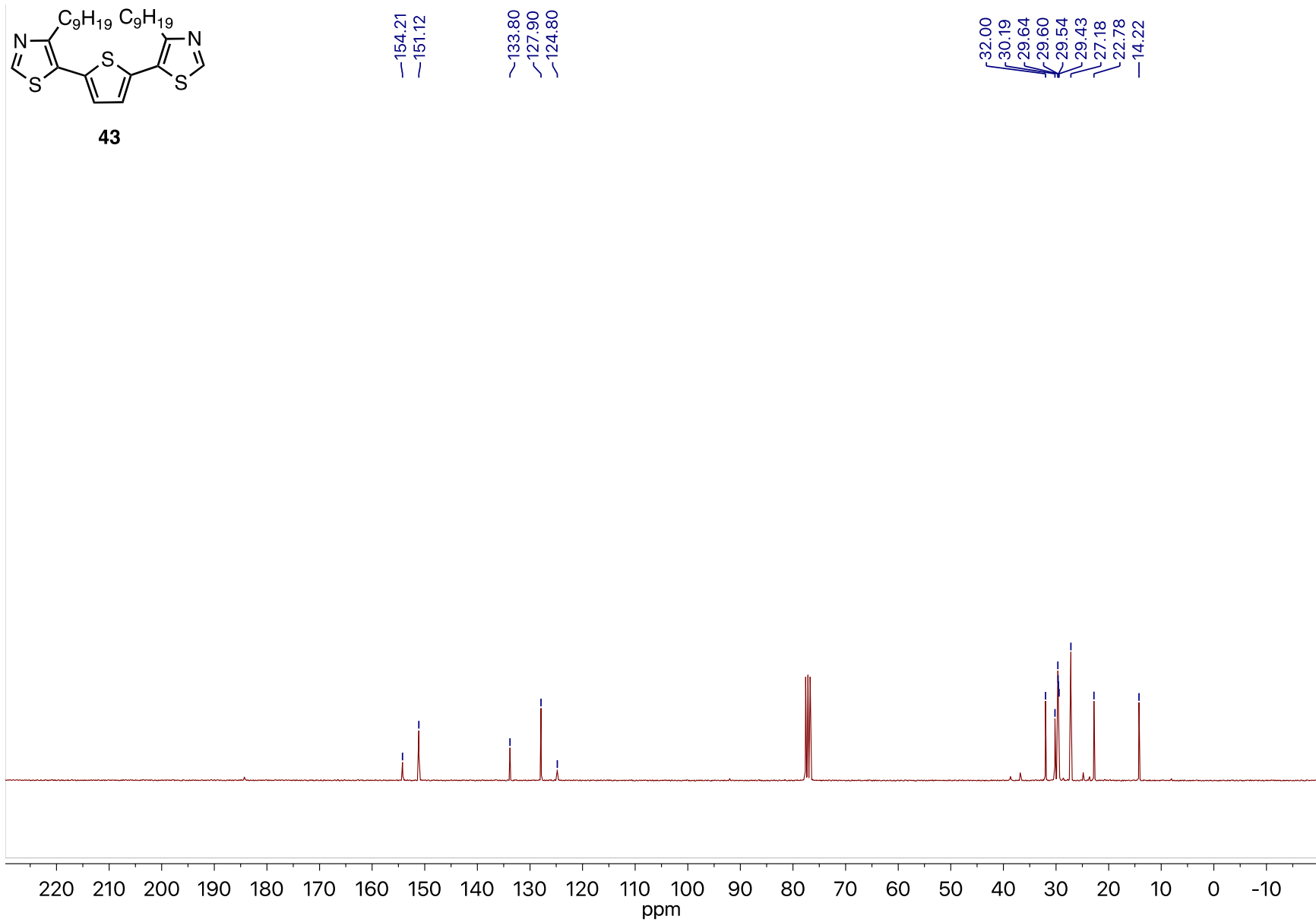


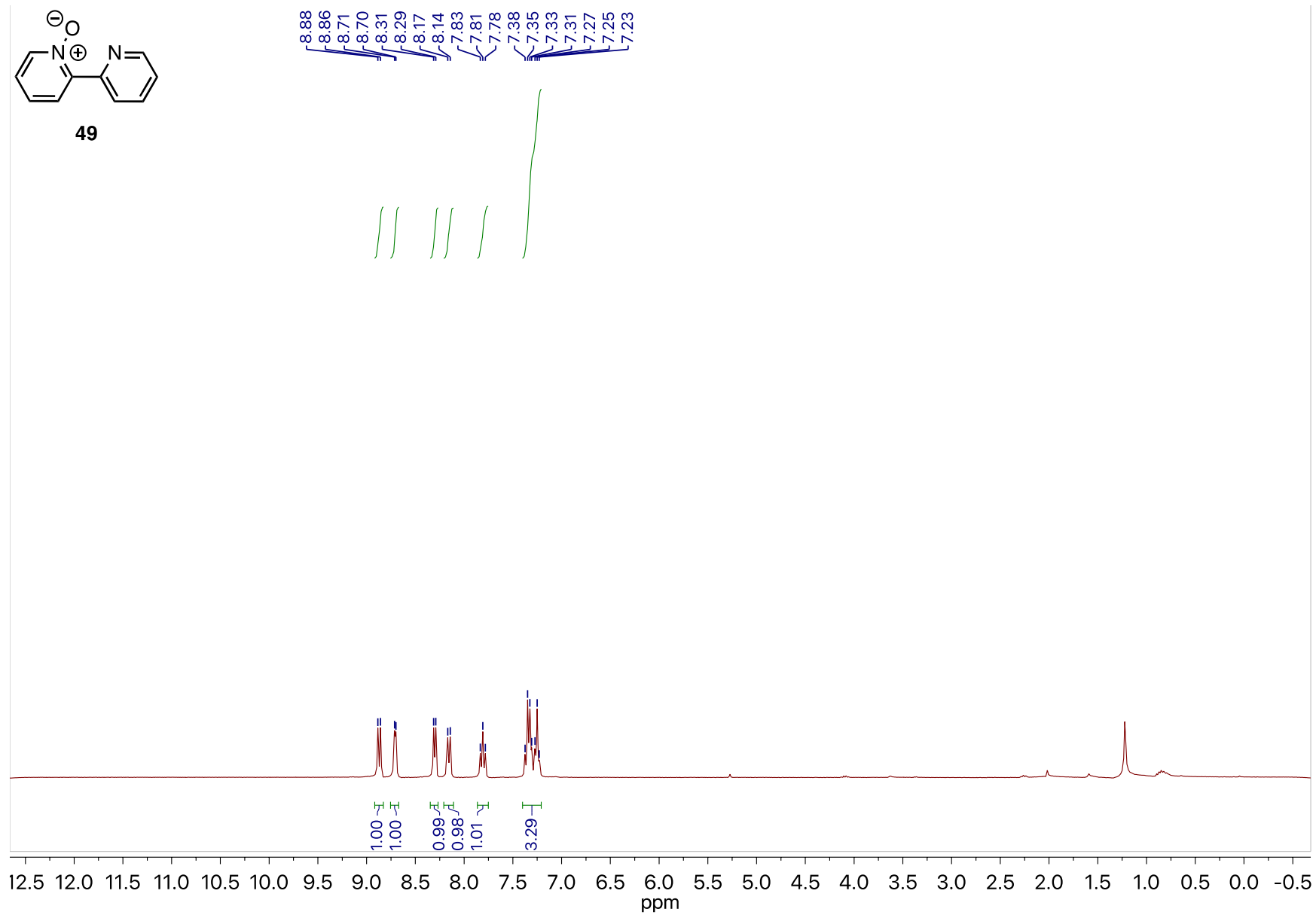
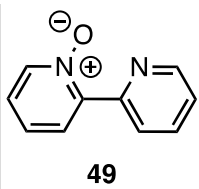


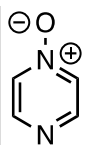
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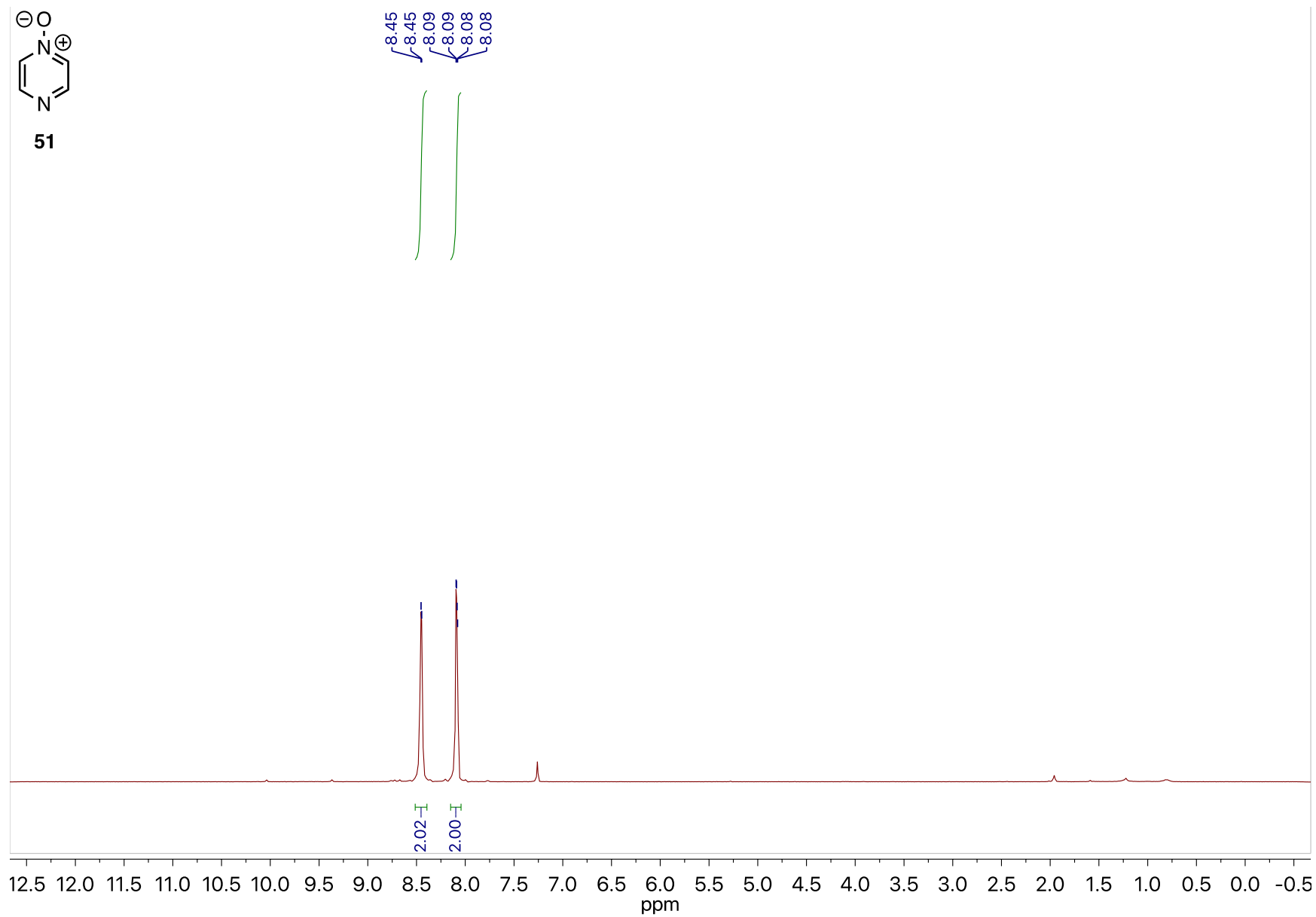
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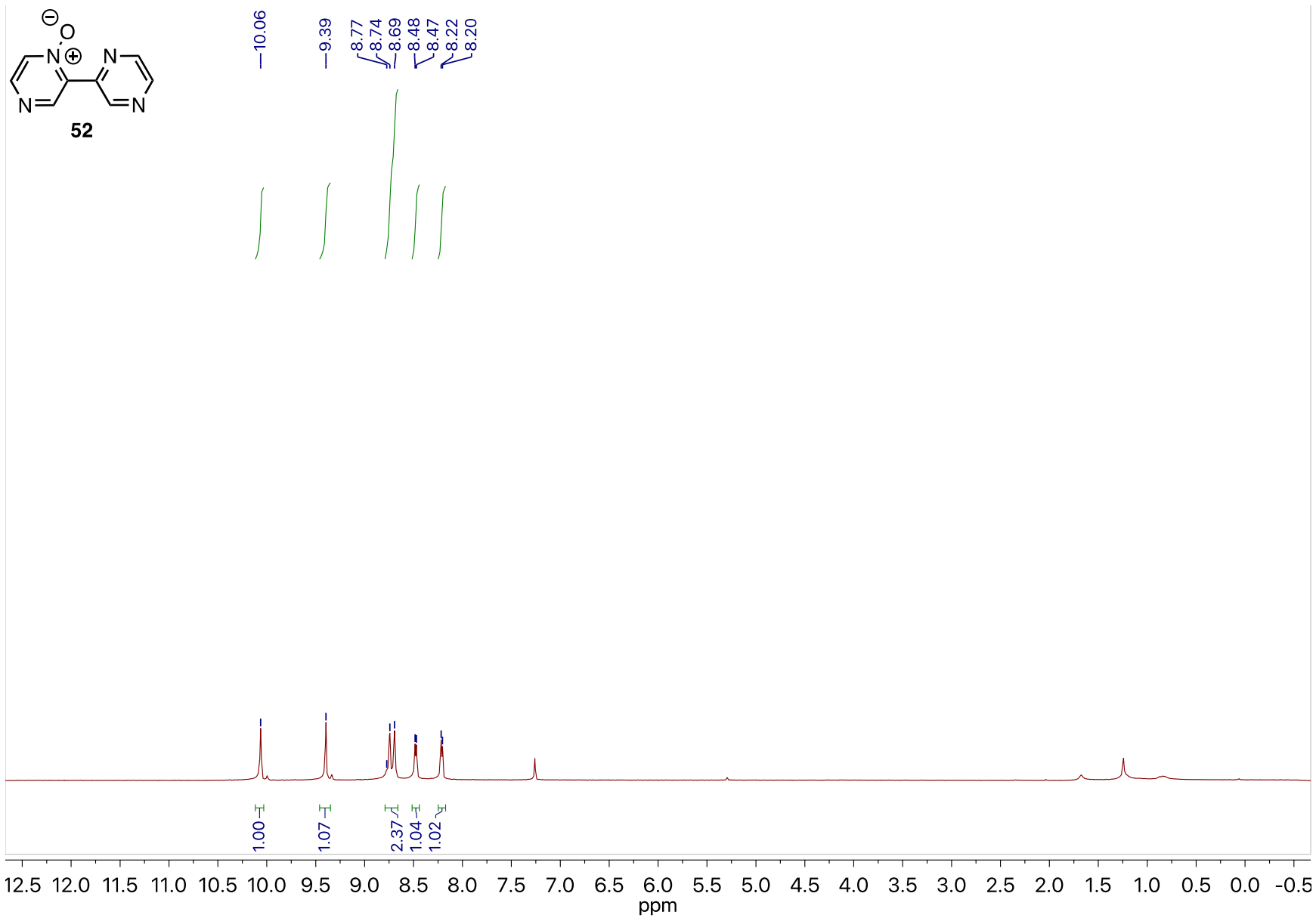




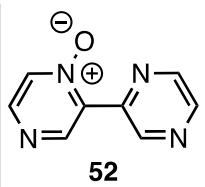


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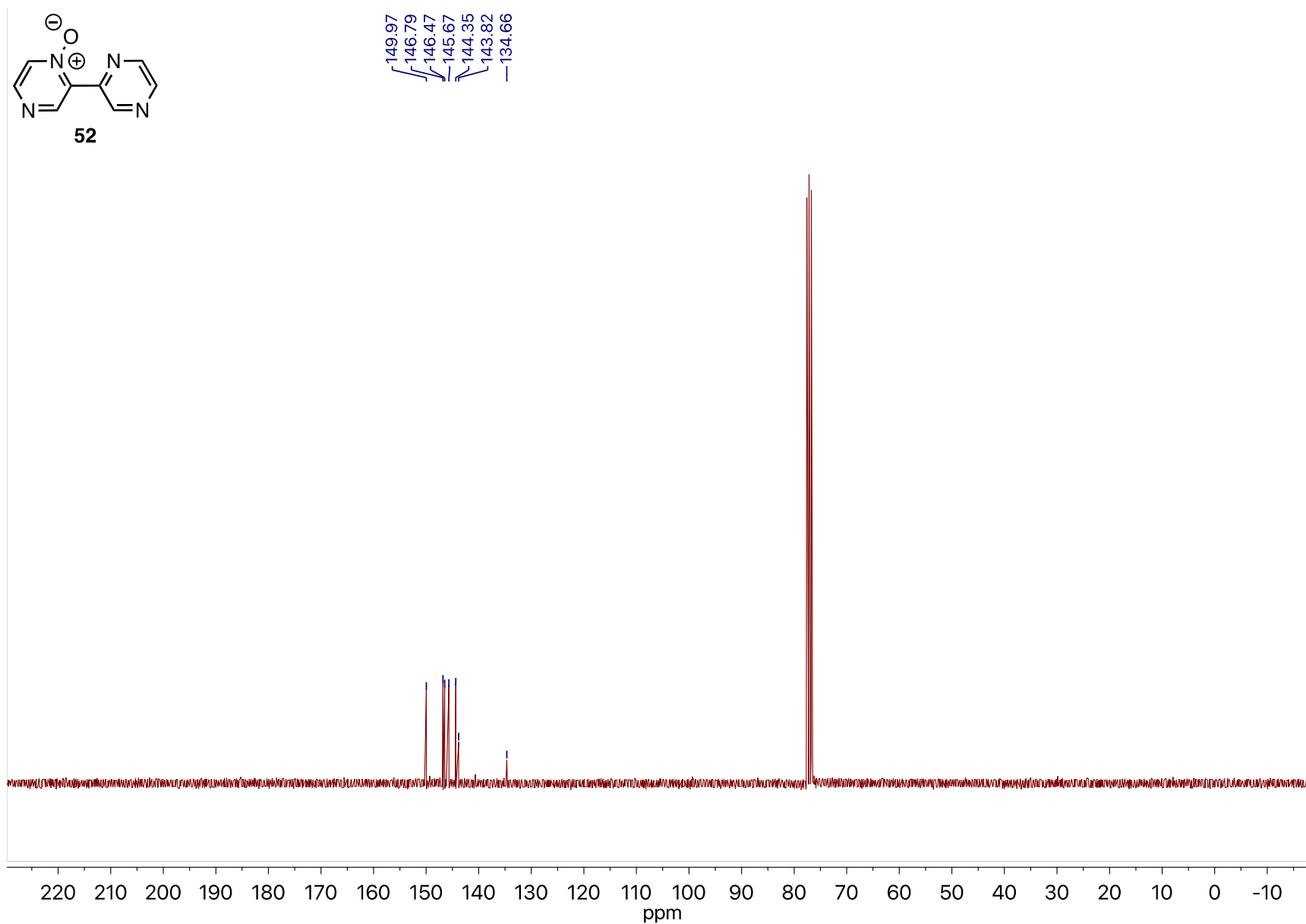


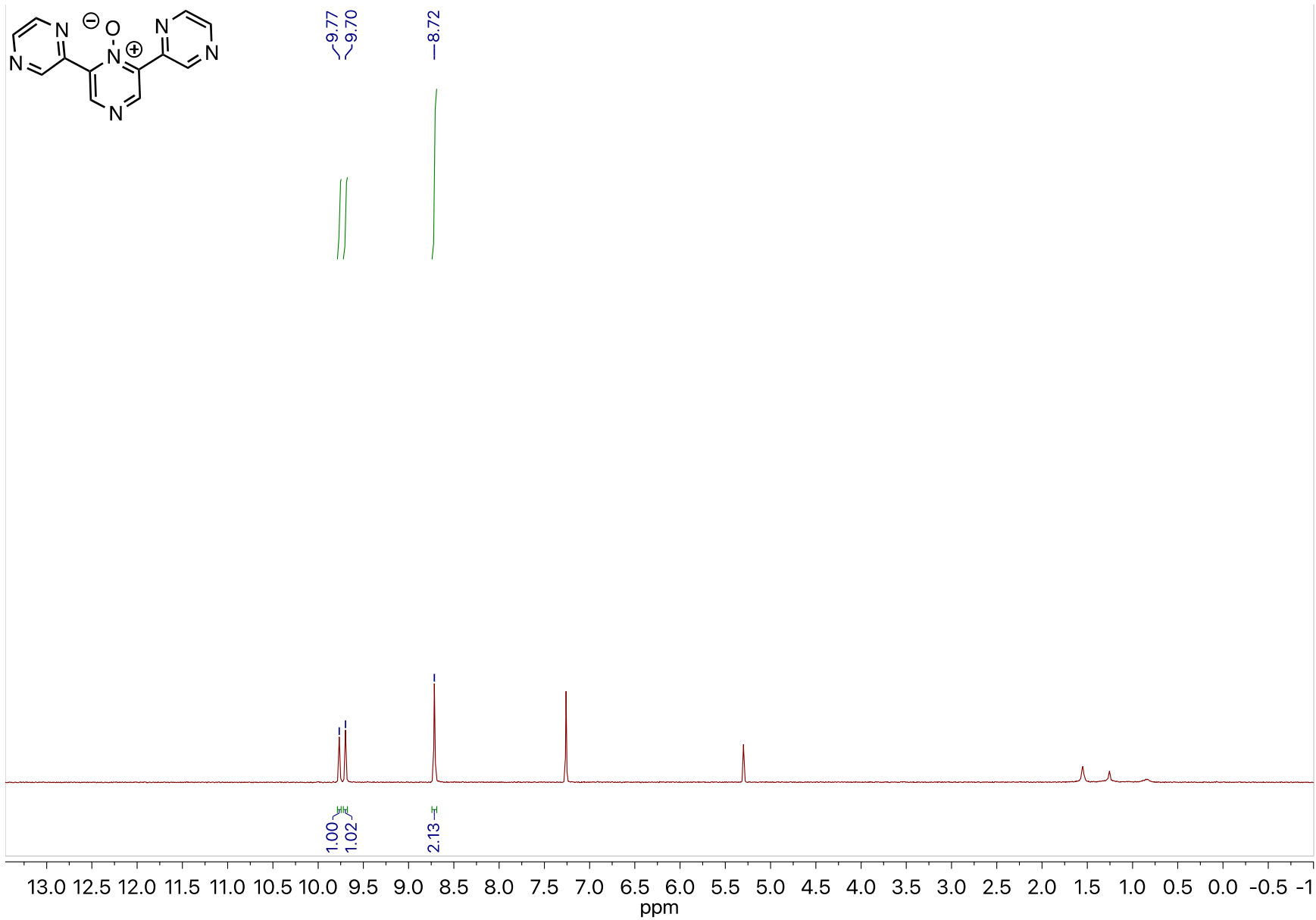


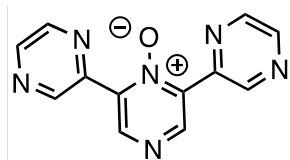




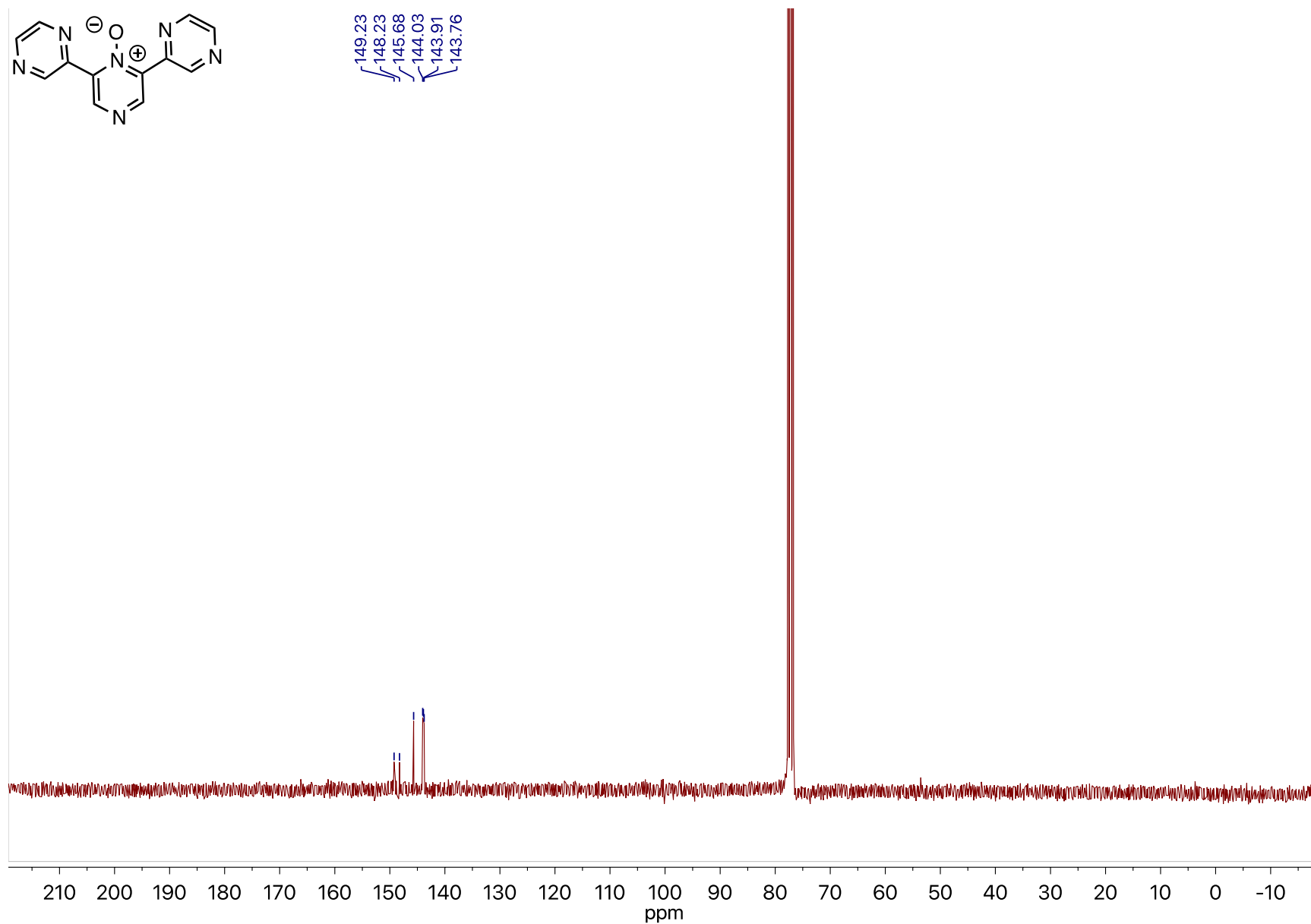
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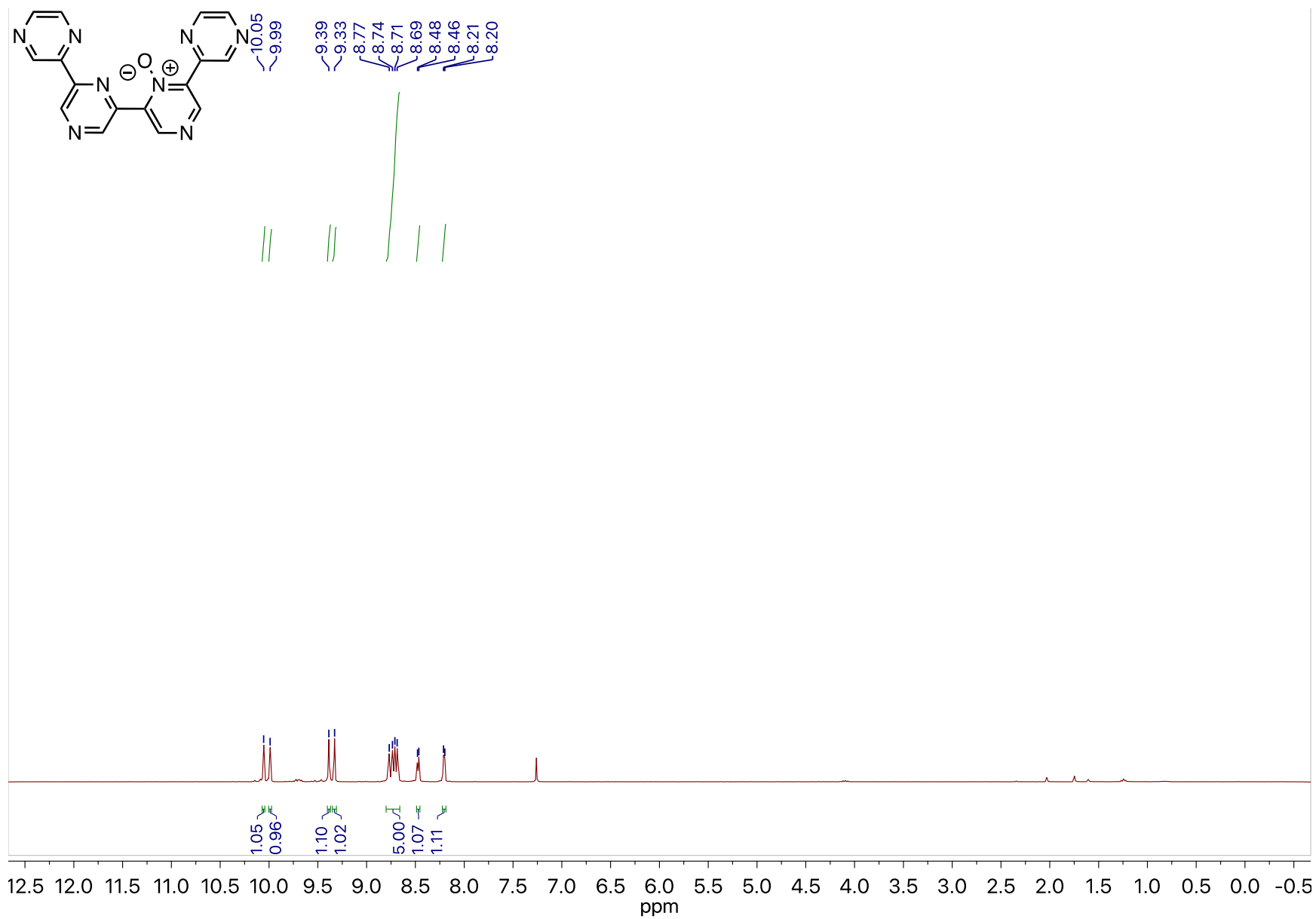


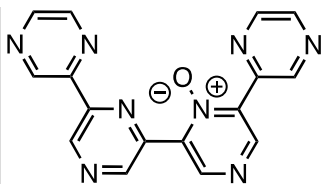




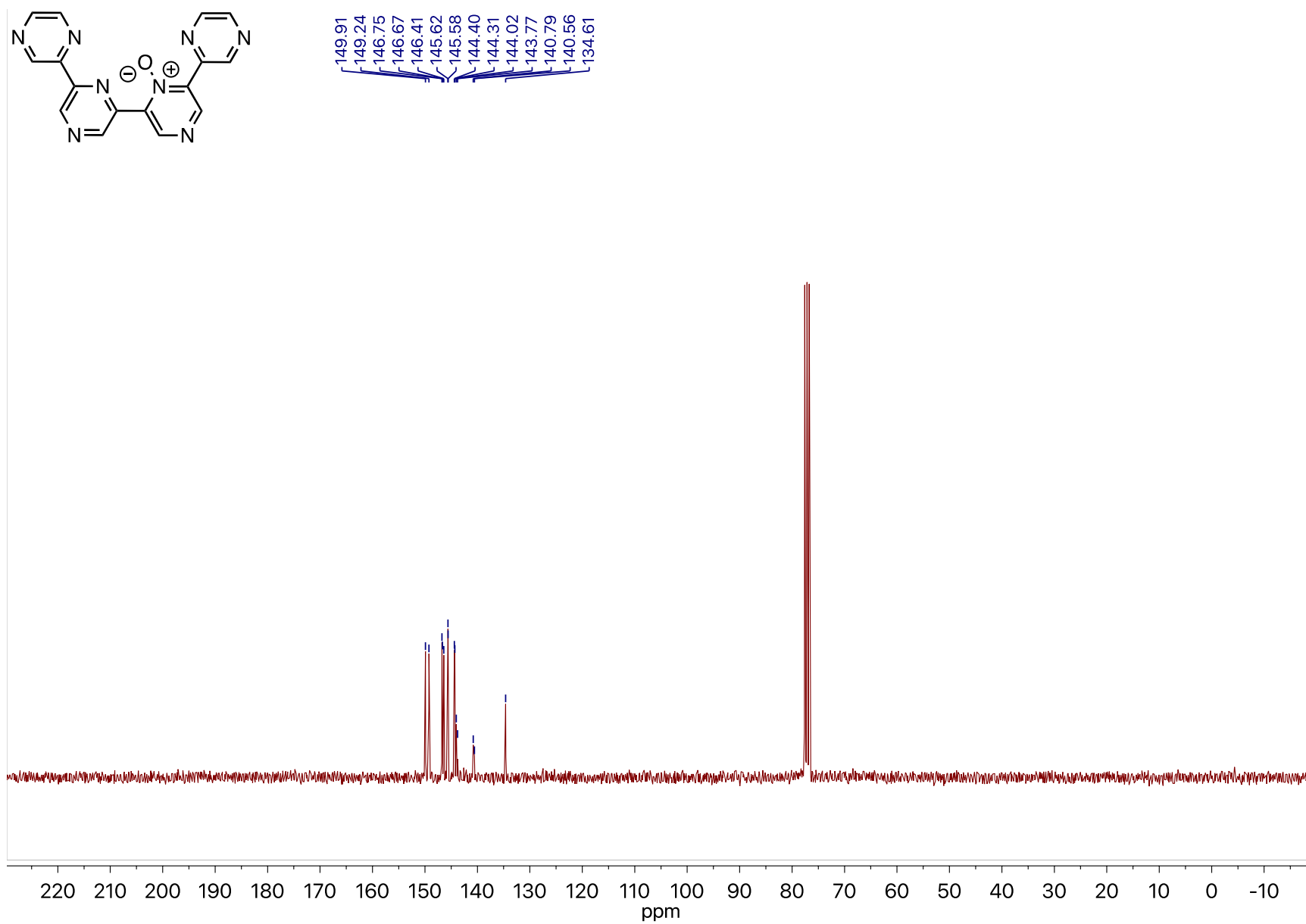
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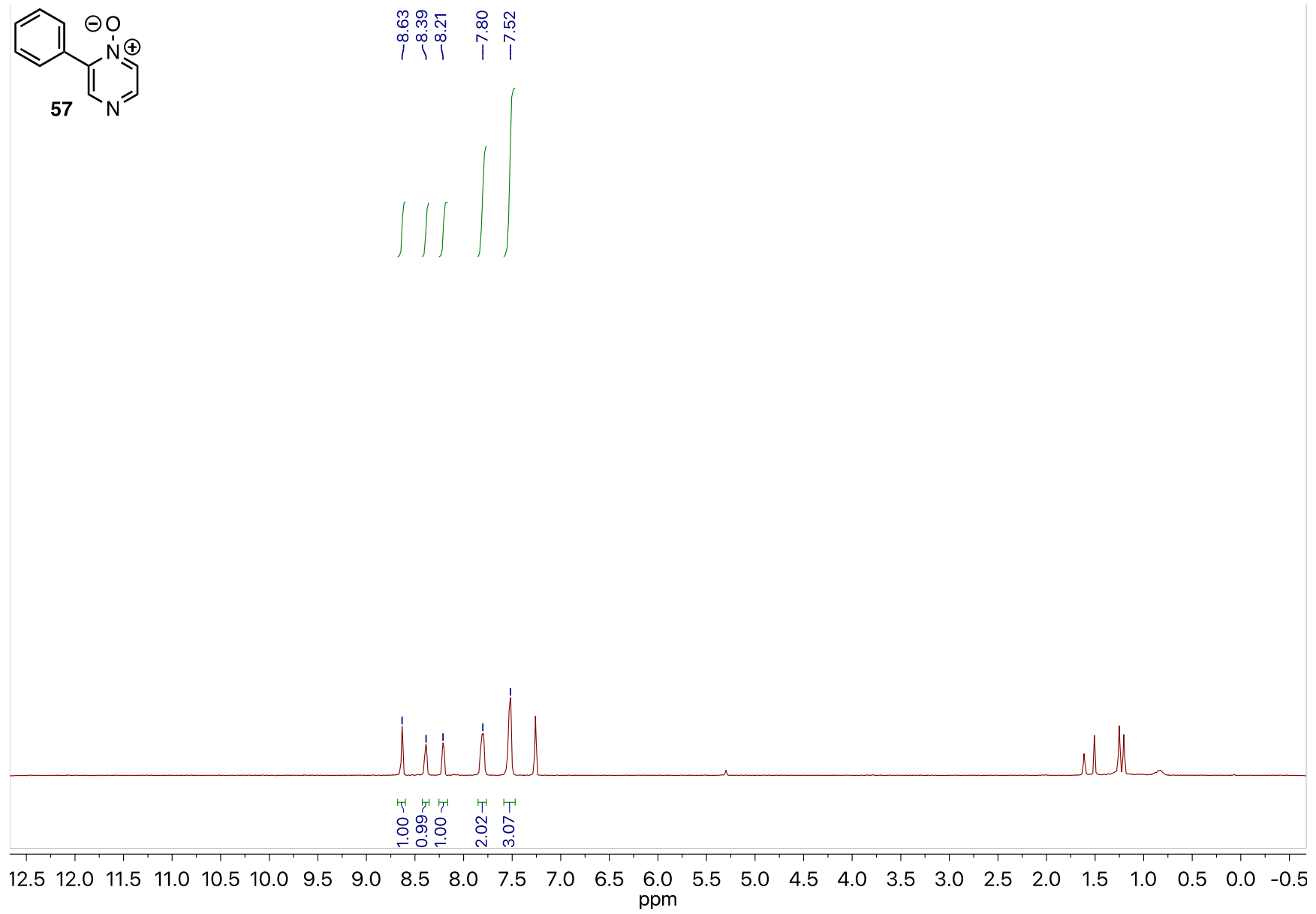
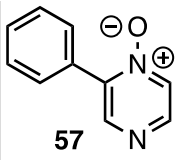


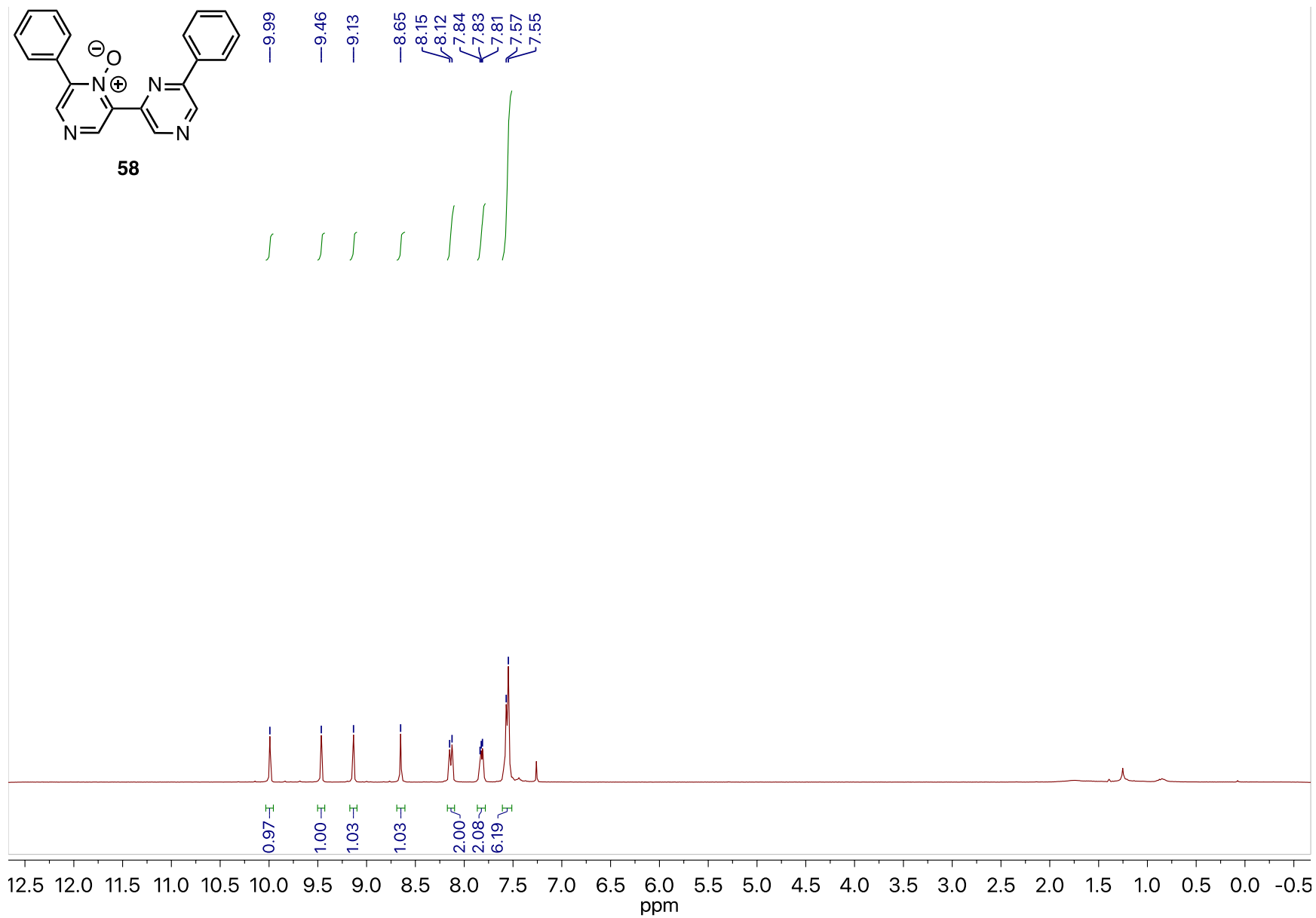


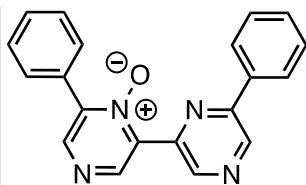


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134.61



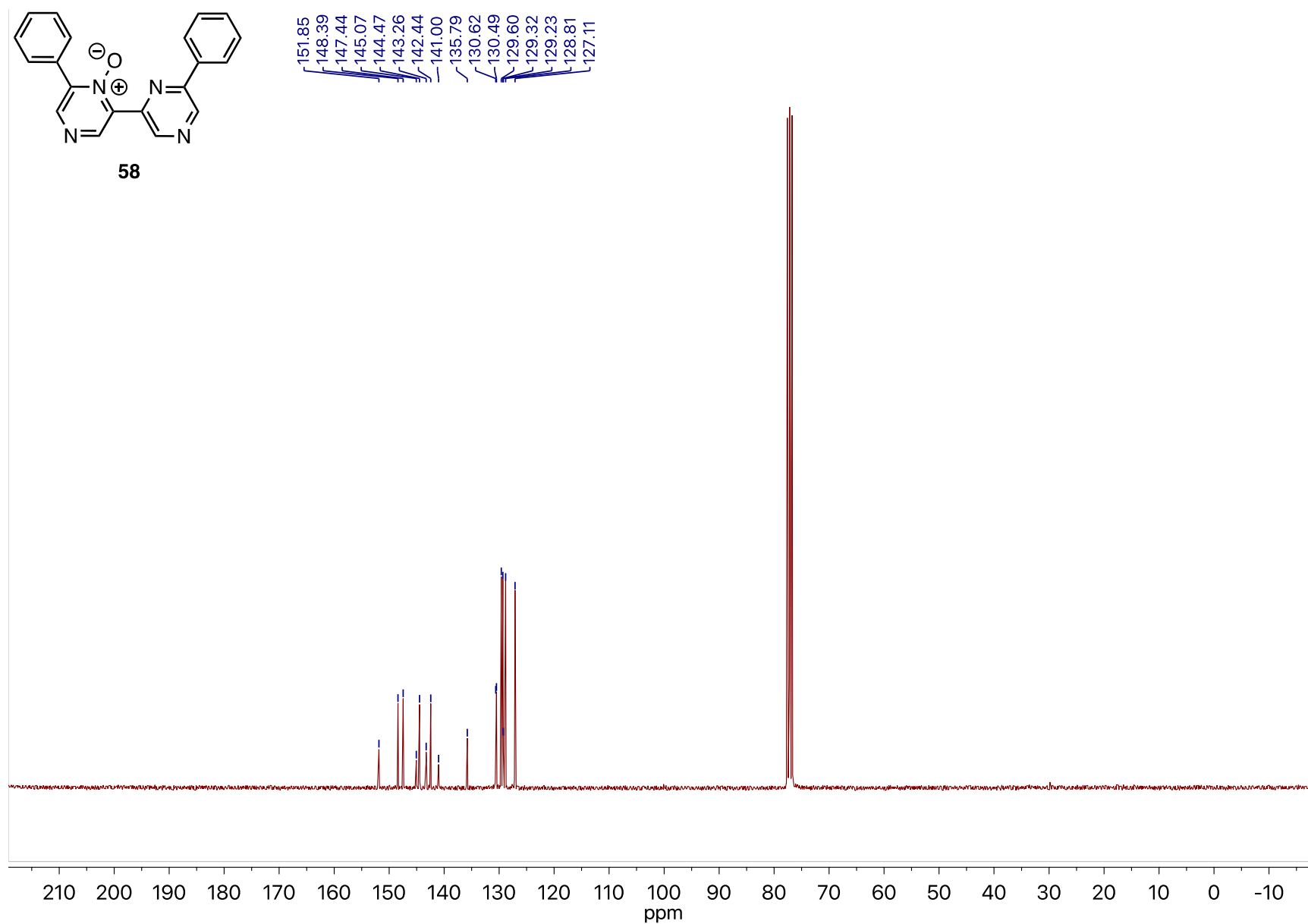




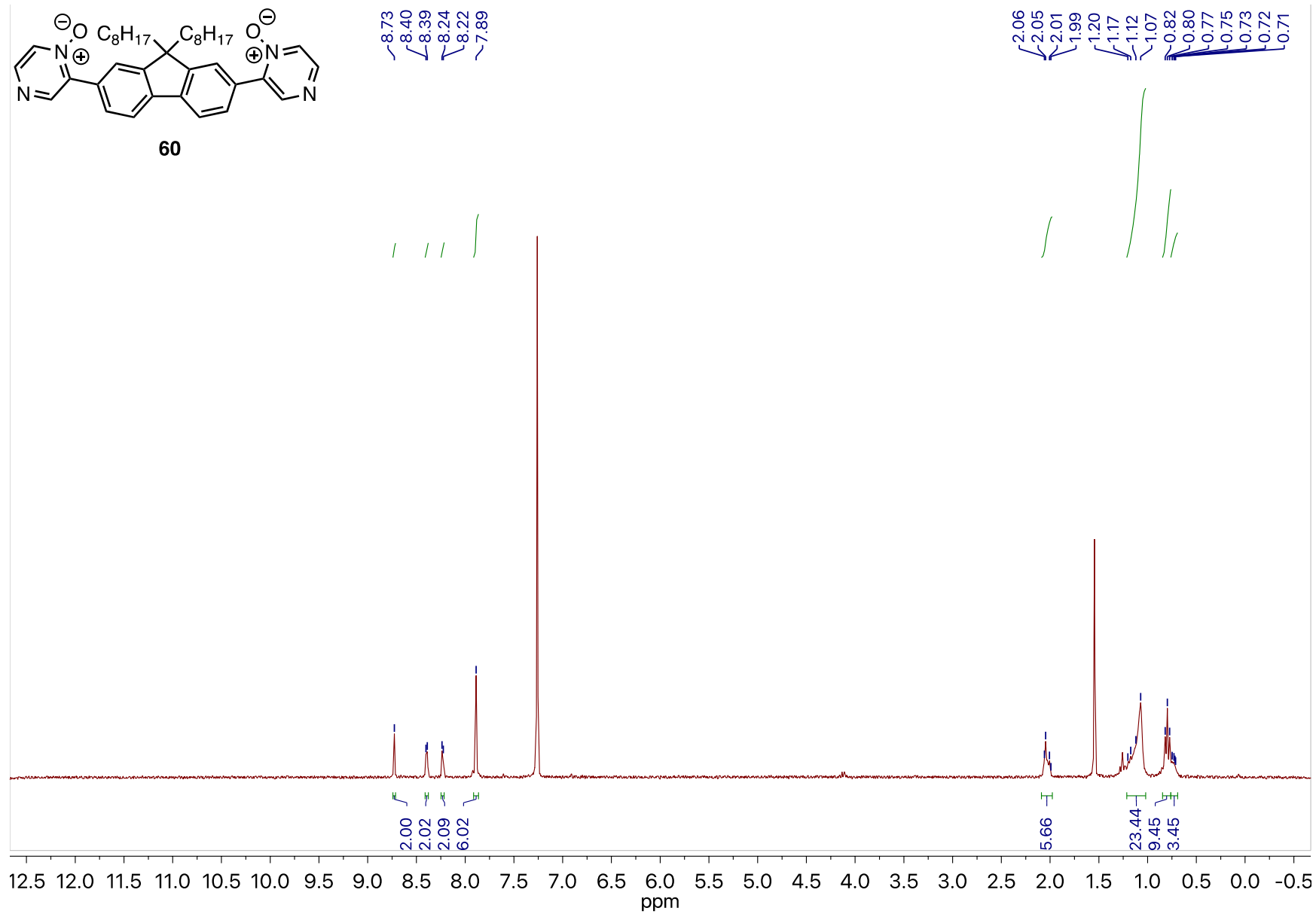
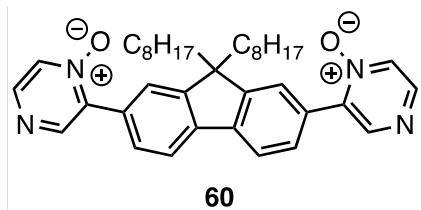


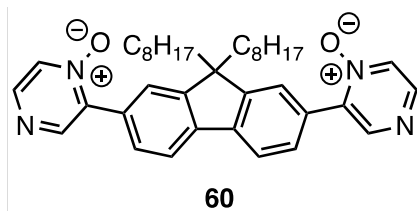
58

151.85  
148.39  
147.44  
145.07  
144.47  
143.26  
142.44  
141.00  
135.79  
130.62  
130.49  
129.60  
129.32  
129.23  
128.81  
127.11





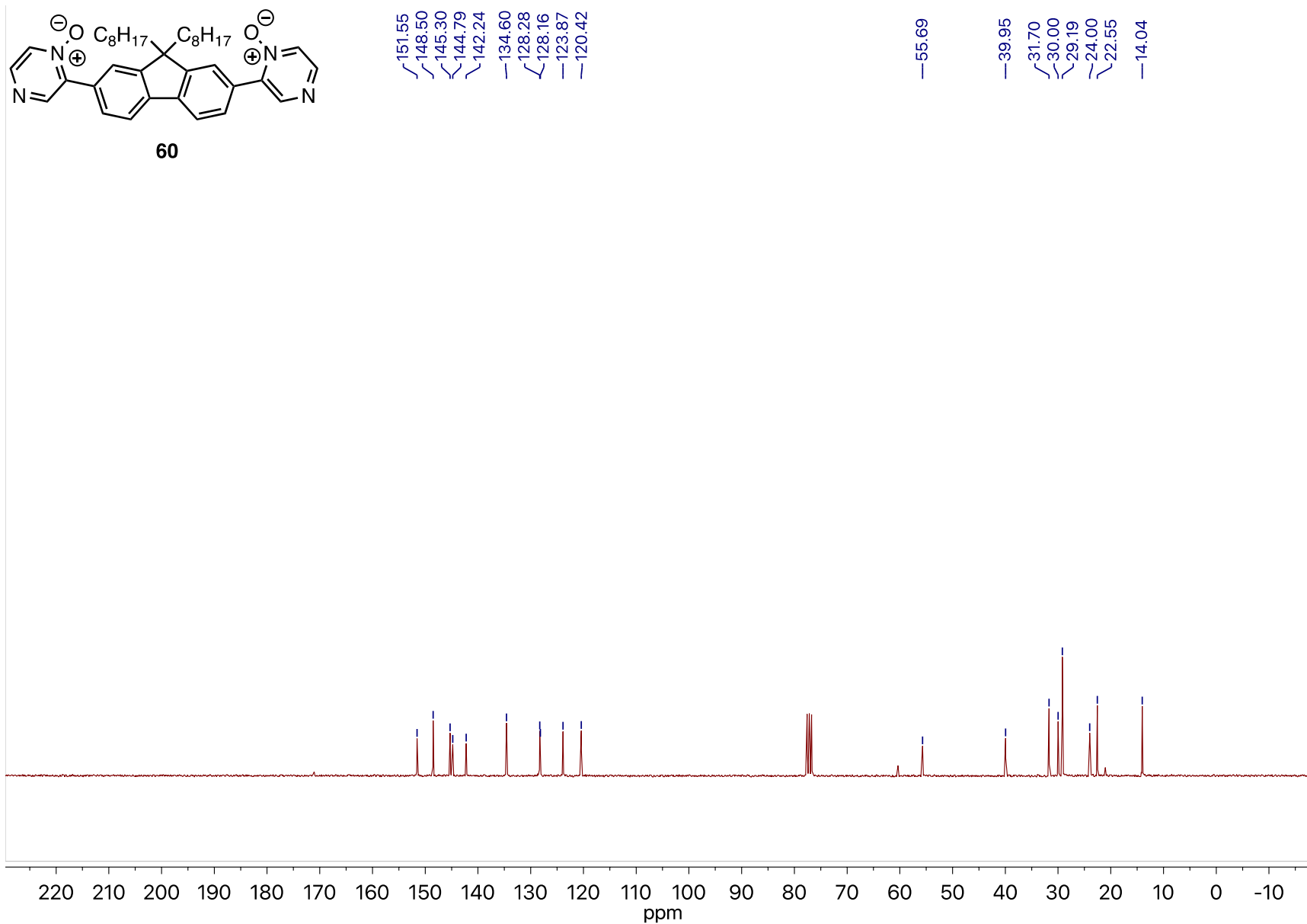


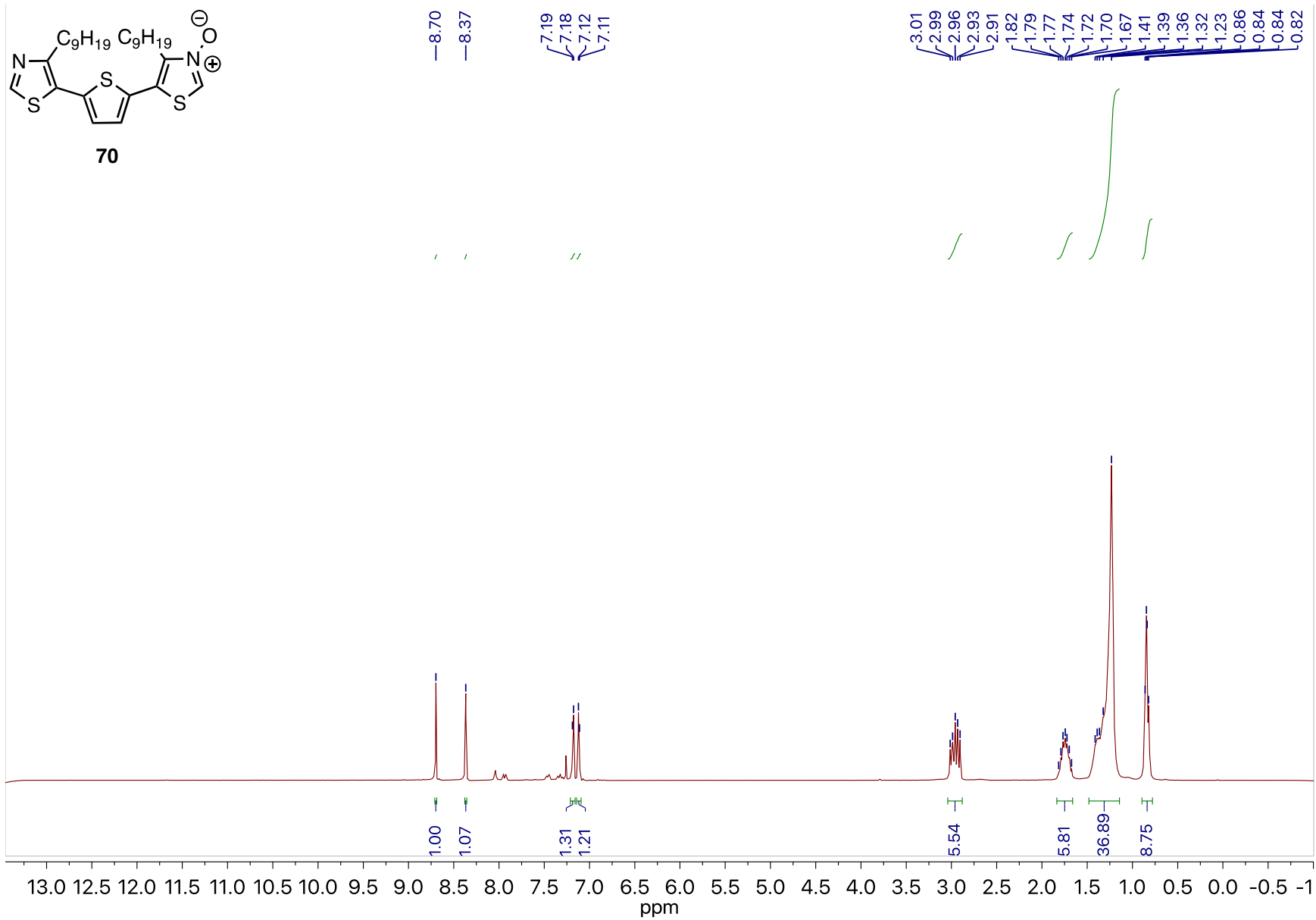


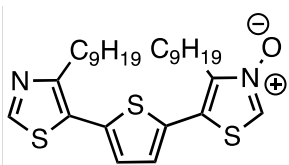
151.55  
148.50  
145.30  
144.79  
142.24  
134.60  
128.28  
128.16  
123.87  
120.42

55.69

39.95  
31.70  
30.00  
29.19  
24.00  
22.55  
14.04



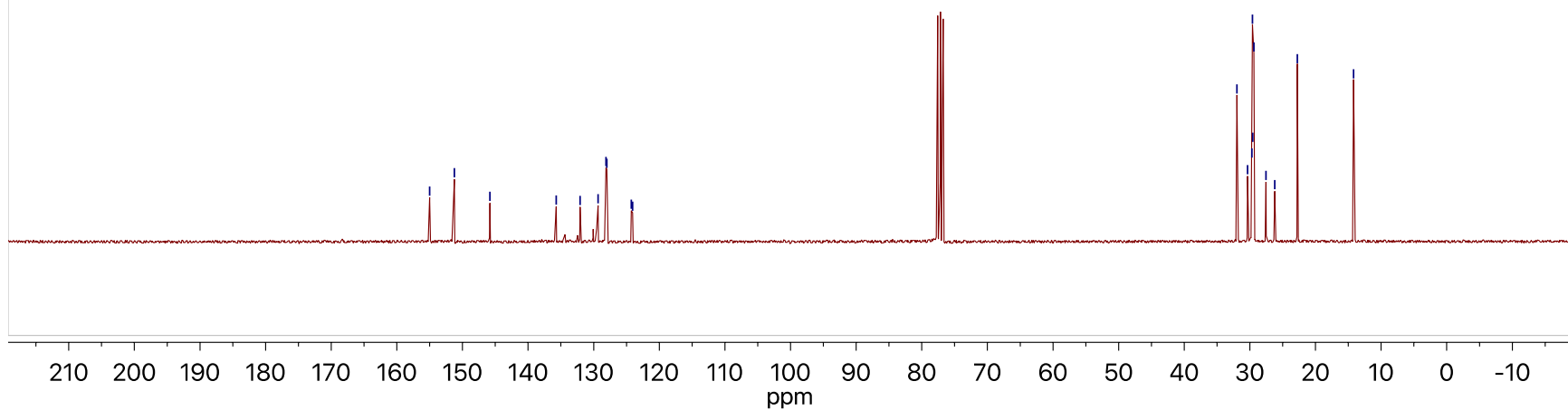


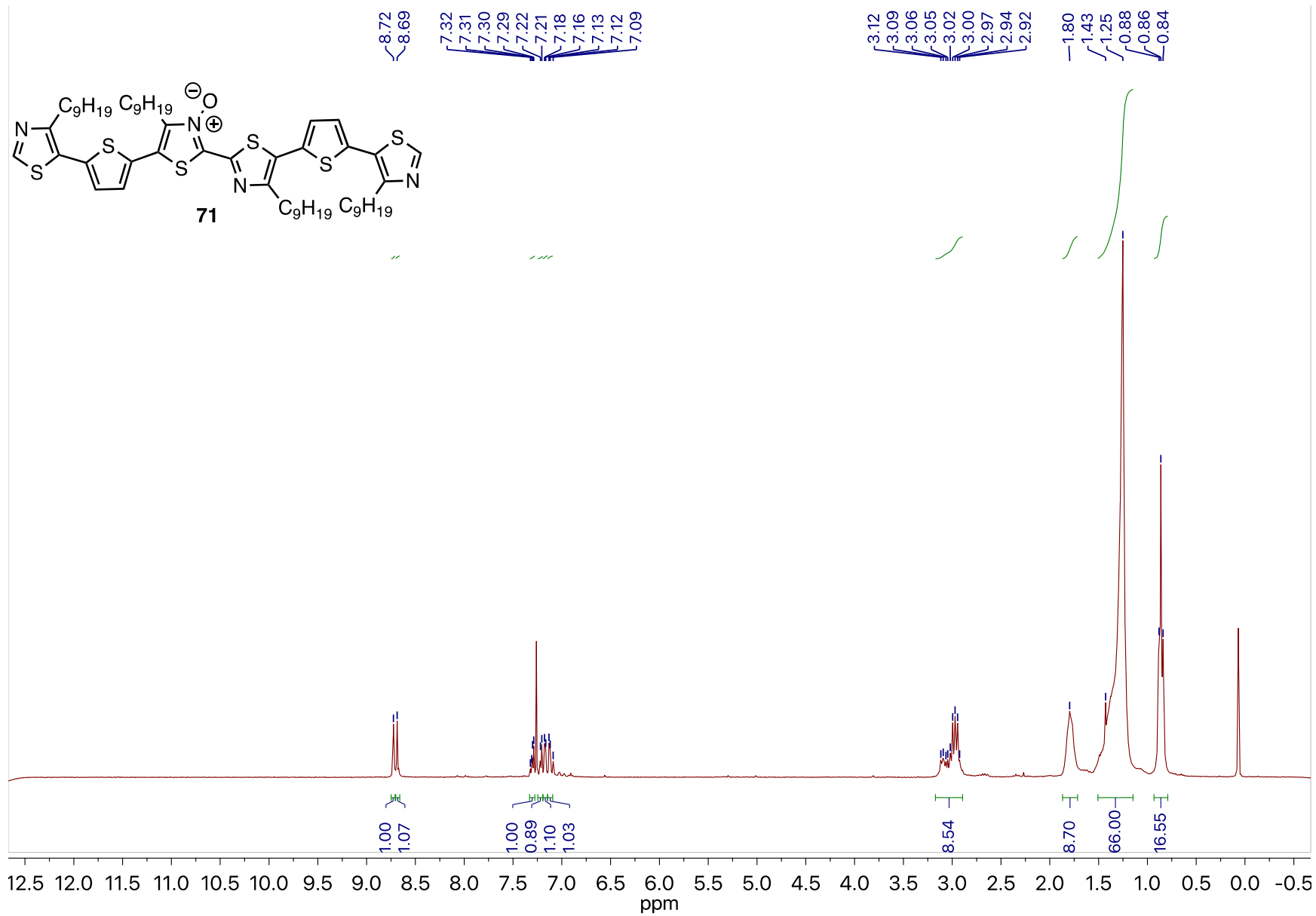


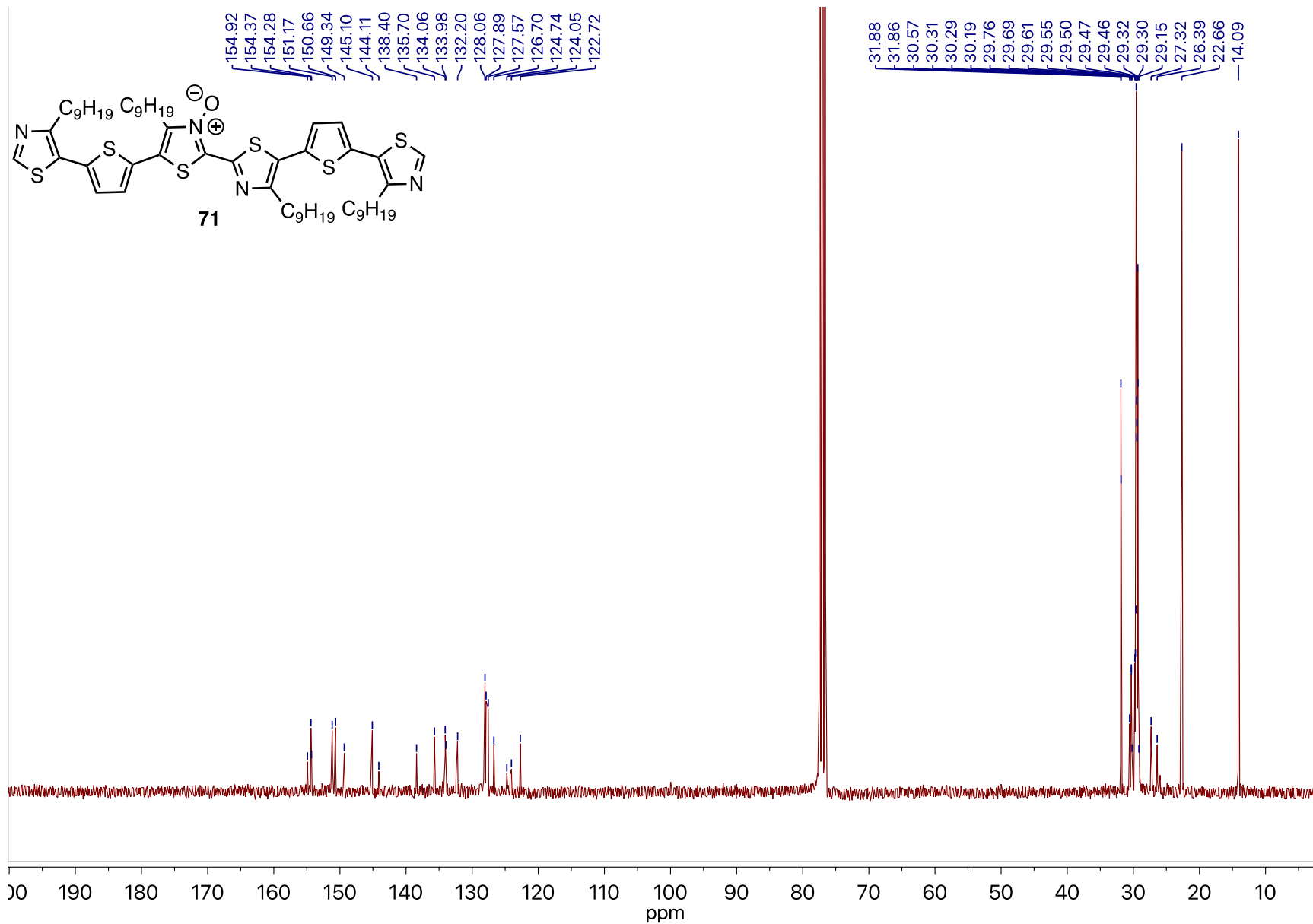
70

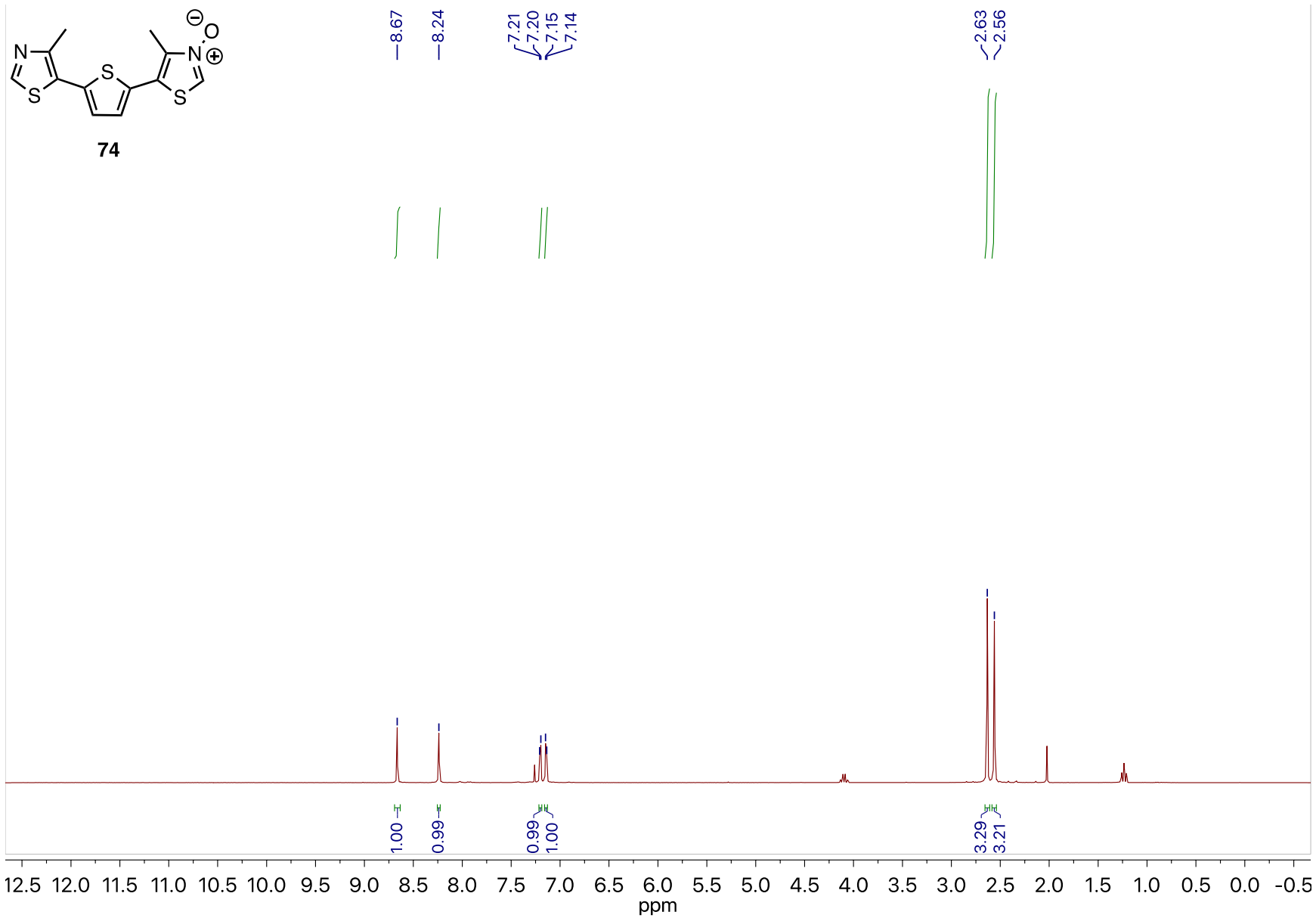
154.99  
151.23  
145.82  
135.71  
132.07  
129.34  
128.13  
127.99  
124.26  
124.06

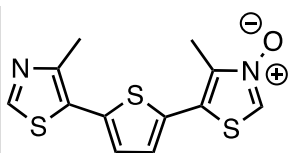
31.97  
30.36  
29.70  
29.62  
29.55  
29.40  
27.54  
26.21  
22.76  
14.20











74

150.78  
150.10  
141.64  
135.85  
132.17  
128.21  
128.07  
127.67  
124.51  
124.20

16.82  
12.23

