Decarboxylative Cross-Coupling as An Efficient Synthetic Tool for Thiophene-Based Materials

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ABSTRACT

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Conjugated thiophene-based material are highly desired materials in various fields of organic electronic materials. Poly/oligothiophene are among the most common substrate used in many different organic electronic materials. The general synthesis involves cross-coupling reactions such as Migita-Stille, Corriu-Kumada, Negishi, and Suzuki-Miyaura. These reactions are robust methodologies, but often involves organometallic reagents and produce metallic waste. Direct (hetero)arylation has been proposed as a greener approach for constructing conjugate-polymeric materials. However, for the many thiophene-based materials they suffer from regioselectivity issues and unwanted side-reactions. Alternatively, decarboxylative cross-coupling provides excellent regioselectivity through the carboxylic acid functional group, that has been demonstrated as an excellent synthetic tool for bi-aryl and/or tri-aryl targets. We envisioned utilizing this method as an efficient strategy for constructing a library of oligothiophenes, where it would be complementary to existing methodologies, and provides a greener approach for green energy applications. Herein, we developed improved reaction conditions without the need of base to prepare a library of poly/oligothiophene. The modularity of our new approach is demonstrated with a scope of 25 different type of symmetric oligothiophenes with highlights in synthesizing symmetrical oligothiophenes with up to 10 thiophene units. Furthermore, this method was also applied towards the synthesis of regioregular oligothiophene and polythiophene. Decarboxylative cross-coupling has demonstrated complete chemoselectivity for thiophene-based oligomers through this work and proven as a comprehensive greener approach compared to the existing synthetic methodologies.

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List of abbreviations

Ar - aryl group
μw - microwave heating
Δ - conventional heating (silicon oil bath with hot plate)
*i*Pr - *iso*-propyl group
*t*Bu - *tert*-butyl group
OMe - methoxy group
OTs - tosylate
o - ortho
p - para
m - meta
J - coupling constant in Hz
δ - chemical shift in ppm
s - singlet
d - doublet
t - triplet
q - quartet
p - pentet
m - mutiplet
equiv. - equivalents
NBS - *N*-Bromosuccinimide
NCS - *N*-Chlorosuccinimide
TBAB - *tetra*-butyl ammonium bromide
TBAC - *tetra*-butyl ammonium chloride
DMA - *N,N*-dimethylacetamide
DMF - *N,N*-dimethylformamide
NMP - *N*-methyl-2-pyrrolidone
EtOAc - ethyl acetate
DCM - dichloromethane
$CHCl_3$ - chloroform
THF - tetrahydrofuran
PPh_3 - triphenylphosphine
P(*o*-Tolyl)$_3$ -Tris(o-tolyl)phosphine
dba - dibenzylideneacetone
JohnPhos - (2-biphenyl)di-*tert*-butylphosphine
MePhos - 2-dicyclohexylphosphino-2′-methylbiphenyl
Dppf -1,1'-bis(diphenylphosphino)ferrocene
*t*BuP -tri-*tert*-butylphosphine
GC-MS - gas chromatography with mass spectrometry
NMR - nuclear magnetic resonance

Chapter 1. Introduction

1.1. Importance of Thiophene-based Materials

Thiophene based-materials (Figure 1) have attracted a tremendous amount of attention in recent decades.[1] π-conjugated poly/oligothiophenes (**1**) have been the center of focus due to their applicability as organic electronic materials in organic photovoltaic cells (OPVCs),[2] organic light emitting diodes (OLEDs),[1,3] organic field-effect transistors (OFETs),[4] liquid crystal,[5] and fluorescent biomarkers.[6] The popularity of thiophene-based materials is largely credited to the ground breaking research initiated in the late 1970s by Alan MacDiarmid, Alan J. Heeger, and Hideki Shirakawa. In 2000, the Nobel prize in chemistry was awarded "for the discovery and development of conductive polymers".[7] Their ground-breaking advancements lead today's growing demands of thiophene-based materials as next-generation electronic materials. Compared to other common five-membered heteroaromatic rings, thiophene possessed the highest electron density with good chemical stability.[1,8]

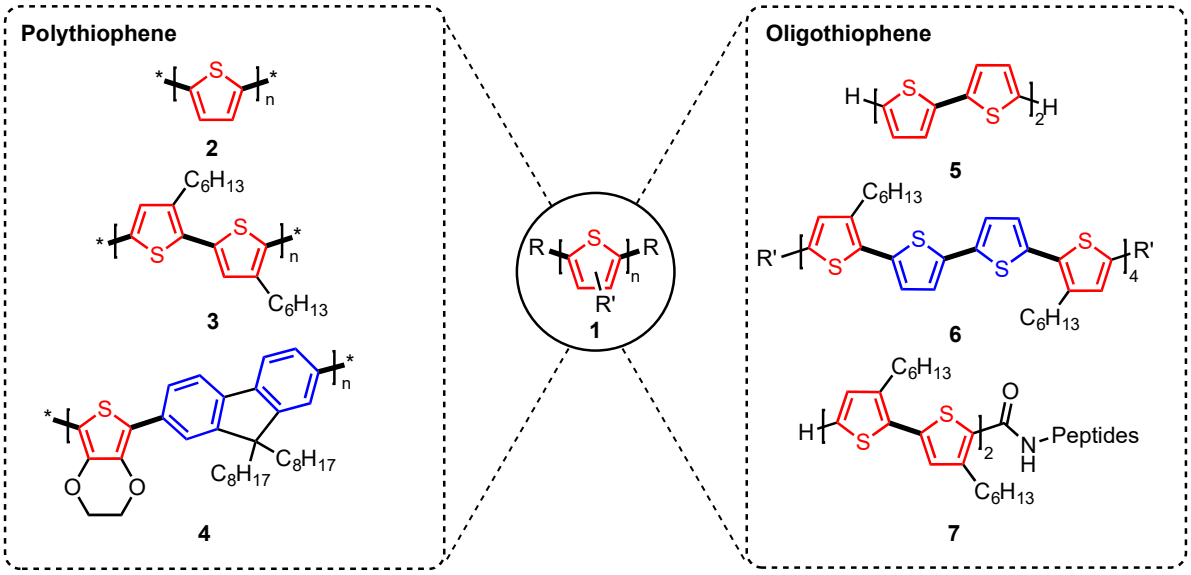


Figure 1. Example of Thiophene-based Materials

Through the decades, unsubstituted polythiophene (**2**) was the first of the thiophene based functional-materials to be synthesized.[8] Unfortunately, the insoluble nature of the resulting polymers severely limited the processability and subsequent studies on these molecules.[8] Soon after this report, solubility problem was addressed by incorporating alkyl substituents on the

thiophene backbone, where any alkyl chain with more than four carbons would allow the resulting polymer such as 3-hexylthiophene (**3**) to be more soluble and can be processed for various applications.[9] Over the years, many different functional thiophene-base materials have been developed. The incorporation of a variety of substituents and conjugated system allows for tunable physical properties,[10] for example, the fluorene-ethylenedioxythiophene copolymer (**4**) was developed as a substrate for OPVC.[11] Oligothiophene unlike their macromolecule counterpart has uniform chain length, which make them an excellent model substrate for understanding the properties related to thiophene-based materials.[3] For example, unsubstituted quaterthiophene (**5**) or the alkyl-substituted analogue (**6**) are also commonly used as model substrates in organic electronic application in place of polymeric form.[12] Many of the recent studies aim toward synthesizing water-soluble thiophene-based materials, which can be utilized for various bio-imaging applications.[6] One of the recent examples show a quaterthiophene that was subsequently conjugated to a peptide (**7**) that designed for use as a bio-imaging markers.[13]

1.1.1. Polythiophene Vs. Oligothiophene

Arguably, polythiophenes are the most popular choice and promising candidate for future electronic applications.[8] This is mainly due to the ease of access to a long, conjugated system *via* a single pot of reaction.[3] However, all the existing polythiophene synthesis generated a mixture of polymers with different chain lengths, and commonly exhibited a batch to batch differences. This reproducibility issue, along with the nature of disperse polymer length complicates the ongoing research of the thiophene-based materials.[3] The most affordable path is synthesizing discrete oligomers through an extensive multi-step synthesis. One of the recent studies highlight this impact by comparing an artificial blend of oligomers with different chain length against discrete oligomers.[14] As shown in Figure 2, the solution only contains sexithiophene (**8**) which emits a green light under UV light excitation. The dispersed mixture consisting of four-, five-, and six-unit oligomers (**9**) affords yellow fluorescence under same conditions. This is attributed to the mixture of three different oligomers gave three different fluorescent wavelengths.[3,14]

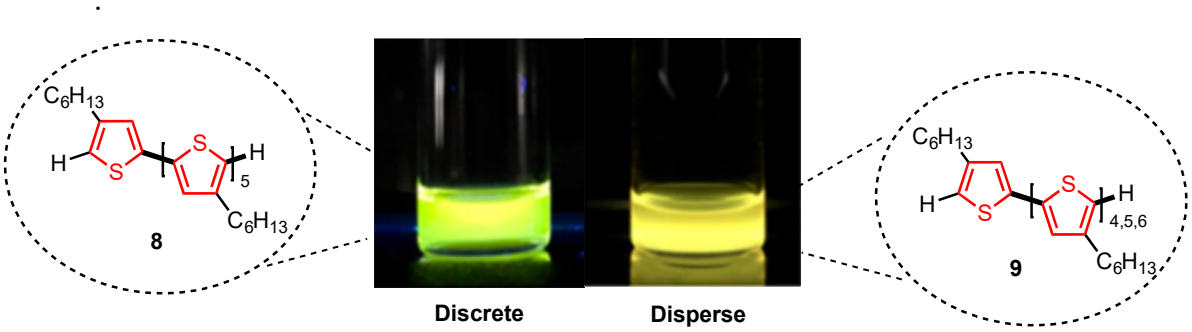


Figure 2. Example of Discrete and Disperse Oligothiophene [14]

1.1.2. Structural Defects for Poly/oligothiophene

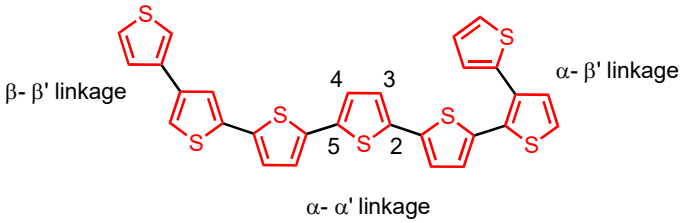


Figure 3. Backbone Linkage of Thiophene-based Materials

In addition to the dispersity of polymer chain lengths, one of the biggest impacts on the physical properties of poly/oligothiophene is the backbone connectivity.[8] As shown in Figure 3, there are three possible backbone linkages for a polythiophene molecule. The most desirable linkage is between positions 2 and 5 on the thiophene ring, commonly referred to as the α-α' linkage.[8,9] This linkage allows for a conjugated system extended with the same co-planar conformation.[3] Alternatively, connection between other positions are referred as α-β' and β-β' linkages, both types of linkages break co-planarity of the polythiophene molecule, which negatively affect the physical properties.[3]

Another factor associated with connectivity is the orientation of the substituents. This term is referred as regioregularity.[8,15] The effective conjugation and desired co-planar conformation of a polythiophene backbone is affected by position of their substituents even if they are all α-α' connected, which is especially common in 3-substitued polythiophene.[15] Polythiophene are referred to as regioregular (Figure 4) when the substituents of the repeating units are on the same position throughout polymer chain.[8] In this case, the thiophene backbone has the lowest angle torsion from the substituent, allowing for an optimal alignment of π-

conjugation.[3] polythiophene is considered as regioirregular when the substituents are facing toward or away from each other on the polymer chain.[8] As a result, the thiophene backbone would adopt a non-co-planar formation to release the torsion strain created by steric hinderance generated from the substituents, thereby affecting the electronic properties of the material.[16] To avoid these structural defects, a highly selective synthetic pathway for poly/oligothiophene has become an obvious solution for the rapid development of thiophene-based materials.

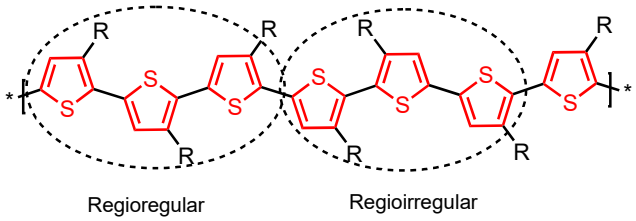


Figure 4. Regioregularity of Thiophene-based Materials

1.2. Synthesis of Thiophene-based Materials

1.2.1. Oxidative Radical Coupling for Polythiophene

The most convenient synthetic route to producing polythiophenes is the oxidative radical coupling reaction.[3,17] The method directly utilizes thiophene molecules (**Figure 5, 10**) without the need of pre-functionalization. The polymerization is initiated in the presence of an oxidant, where reports have shown that $FeCl_3$, $CuCl_2$, and Ag salt can be used.[8,18] Later reports also demonstrated simple functional electrodes with electrolyte solution was able to produce polythiophene **(11)**.[17] The mechanism is postulated to start with the formation of a radical cationic intermediate **12** from thiophene monomers **10** under oxidative conditions.[19] The radical cationic intermediate would further react with another radical intermediate **12** to form a di-cationic intermediate **13**. A subsequent elimination reaction forms the desired dimer **14**, and elongation continues through the same sequence.[19] The selectivity of the reaction is reliant on the difference of electron density on the thiophene-ring, where the α-α' linkage is preferred.[18] However, rapid radical formation and resonance structures often lead to a mixed linkage.[19] Most of the literature involving this method reports a regioirregular random polymer with possible branching of the polymer chains.[17] Consequentially, this method became increasingly less common due to the lack of control and selectivity for the desired α-α' linkage, and unpredictable results from each batch.[15]

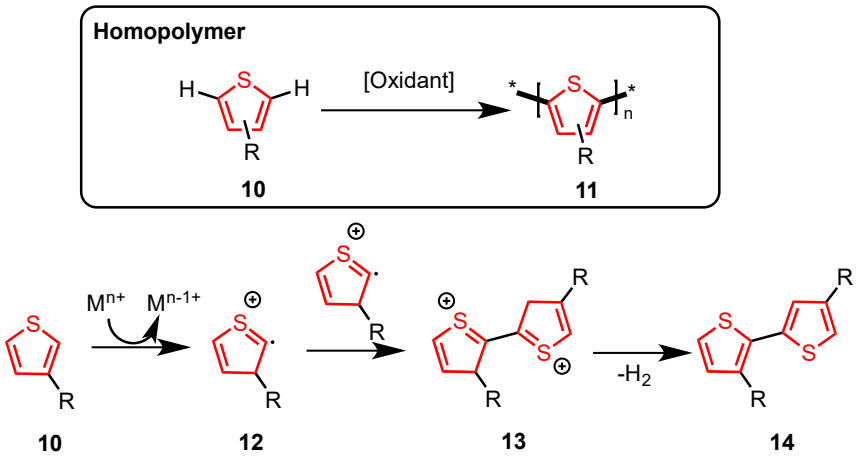


Figure 5. Electrochemical Poly/Oligomerization of Thiophene-based Materials

1.2.2. Palladium Catalyzed Cross-coupling for Poly/oligothiophene

Around the same time period with the development of conductive polymers, palladium catalyzed cross-coupling has emerged as a powerful tool for constructing thiophene-based materials.[20] In 1980, the first example of polythiophene prepared through palladium-catalyzed Kumada cross-coupling was reported.[21] Soon after this report, along with the rapid development of various palladium catalyzed cross-coupling reactions, these reactions have prevailed as the first choice for synthesizing thiophene-based materials.[22] The popularity of cross-coupling as a synthetic tool is derived from their superior regioselectivity through different pre-installed functional groups.[22] Common structural defects such as α-β'and β-β' linkages can be easily eliminated as the reaction would only occur at pre-installed functional groups. The general cross-coupling mechanism (Figure 6) is initiated through oxidative addition of a palladium (0) catalyst to halogenated thiophene derivative **15** that are commonly referred to as the electrophilic coupling partner.[20] The resulting palladium (II) intermediate **16** undergoes transmetallation with another thiophene bearing organometallic functional group (**17**) that is referred as the nucleophilic coupling partner.[20] This step leads to a bi-aryl palladium (II) intermediate **18** and an organometallic salt as a by-product. Final reductive elimination generates the desired bithiophene product **19** and re-generation of the palladium (0) catalyst.

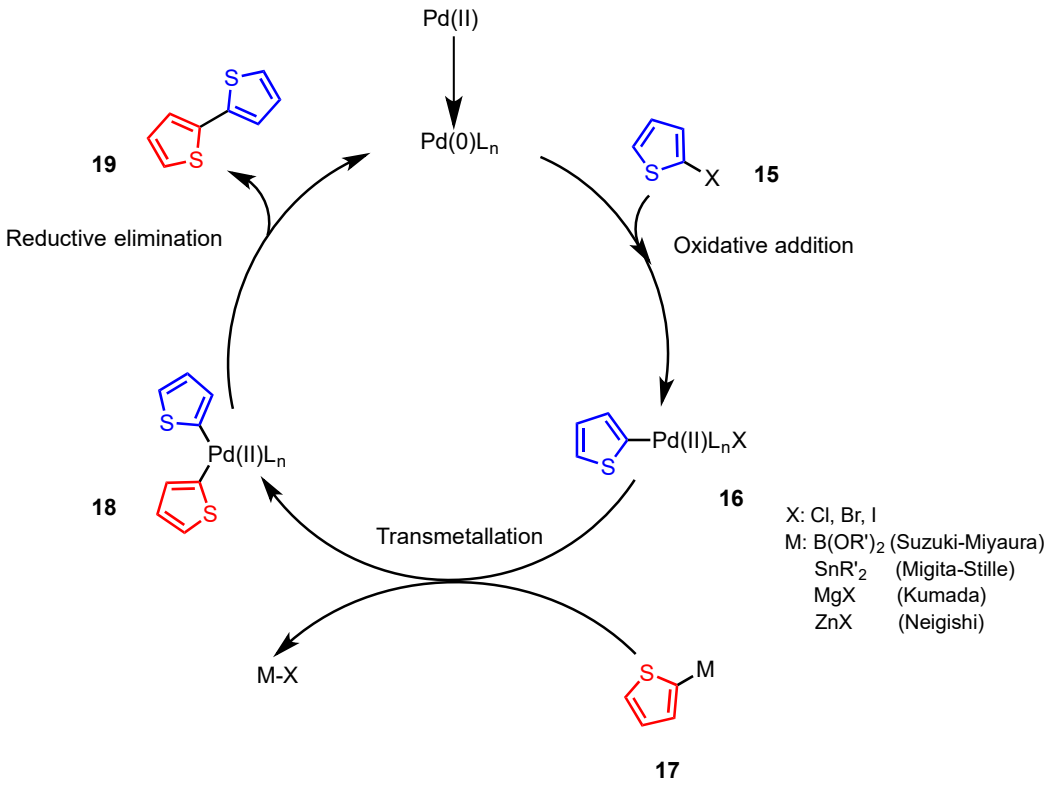


Figure 6. General Mechanism for Transition Metal Mediated Cross-coupling Reaction

Over the decades, cross-coupling has expanded to the synthesis of almost all poly/oligothiophene derivatives.[22] The general synthetic strategy for polythiophene can be expressed in scheme 3 for two different types of polymers. Generally, homopolymers (Figure 7**,** **21**) are obtained through reaction of di-functional monomers (**20**) containing both halide and organometallic functional groups.[23] Alternatively, thiophene monomers could bear the same functional group with either the organometallic (**22**) or halide (**23**), and cross-coupling would afford co-polymers (**24**).[23] Bi-functional monomers allow the incorporation of different aromatic system, but the composition of repeating units could be affected by the reactivity of the propagating polymer chain.[15] Nevertheless, both strategies have been utilized to prepare a variety of conjugated polymers.

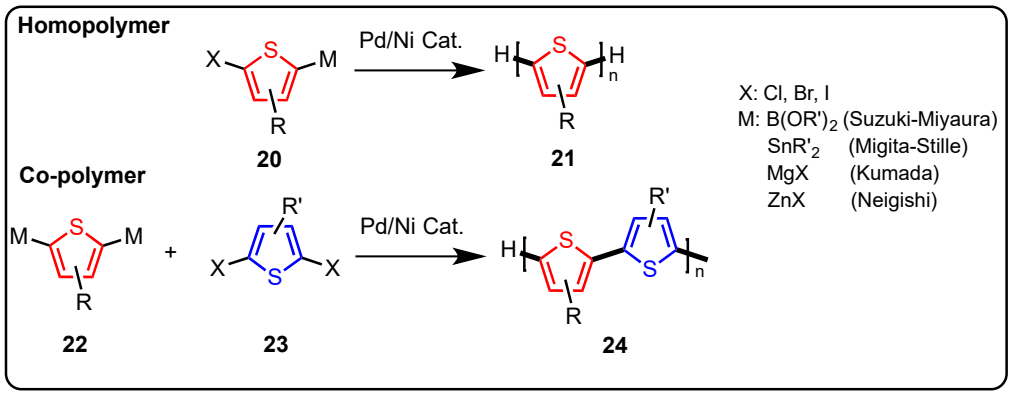


Figure 7. General Synthetic Strategies for Polythiophene

Oligothiophene on the other hand requires a step-wise synthesis, the synthetic strategies usually involve an iterative process consisting of the addition of repeating units and functionalization.[14,24] This method allows much more diversification and a guaranteed mono-dispersity. Generally, there are two different approaches for oligothiophene synthesis (Figure 8). A seven-unit oligothiophene (Figure 8, **33**) can be obtained through either a divergent or convergent pathway. Divergent pathways construct oligomers through the core molecules, which generally is the electrophilic cross-coupling partner (**25**). It proceeds through an iterative addition of units through the nucleophilic cross-coupling partner and functionalization of the resulting oligomer. This pathway starts with formation of terthiophene (**27**) from the cross-coupling between a bi-functional dihalide thiophene (**25**) and two nucleophilic thiophene partners (**26**). The following steps repeats the same iteration for elongating the electrophilic thiophene partners for pentathiophene (**28)** to obtain the desired product **33**. Alternatively, the convergent approach focuses on the nucleophilic thiophene partner **26** and is initiated with the elongation of the nucleophilic partner through a step-wise addition of repeating units. The iterative process extended through the cross-coupling with mono-functional electrophilic thiophene partner **29** and subsequent functionalization to obtain intermediate **30**. The desired oligothiophene **33** is obtained by a single cross-coupling between elongated thiophene derivative **31** and core thiophene derivative **25**. The preferences for each synthetic approach are highly dependent on the type of cross-coupling reaction employed for the target molecules, such as the difficulty for installing the functional groups and reaction yields.[9]

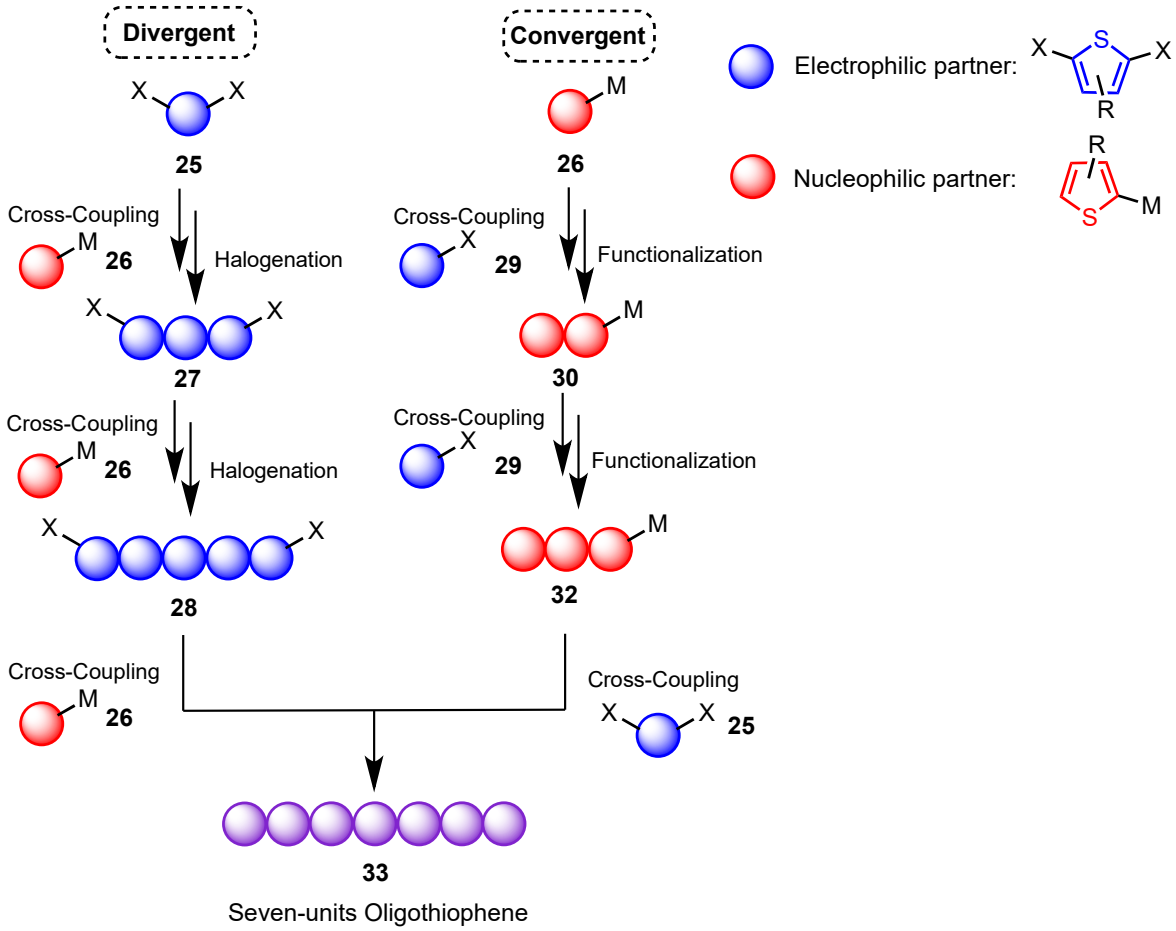


Figure 8. General Synthetic Strategies for Oligohiophene

1.2.2.1. Corriu-Kumada Cross-coupling Method

In 1972, Robert Corriu and Makota Kumada independently reported a novel synthetic method that utilized a catalytic amount of nickel metal to form a carbon-carbon bond between sp^2 carbons by Grignard reagent (Figure 9, **34**) and aryl halide (**35**).[25,26] Shortly after, they also reported the use of palladium as a catalyst to improve the selectivity and reaction yield.[27,28] This method has quickly transformed into the preferred synthesis of poly/oligothiophene (Figure 10). One of the earliest reports of regioregular polythiophene synthesis was achieved using the Kumada coupling.[29] Polythiophenes are prepared thorough di-functional monomers (**37**) bearing both cross-coupling partners with the addition of a nickel(II) catalyst to afford a regioregular 3-alkylpolythiophene (**38**).[29] Similarly, the first oligothiophene example (**41**) was also prepared by Kumada cross-coupling.[30] The report used a divergent approach to prepare oligothiophene by mono-functional thiophene **39** with di-functional thiophenes **40** contain the electrophilic cross-

coupling partners.[30] One of the limitations for this method is that the Grignard reagents are generally unstable and needed to be prepared *in-situ*. In terms of polymerization, monomers need to be activated by Grignard reagent formation, where often impacts the resulting polymers by the rate of monomer activation.[8]

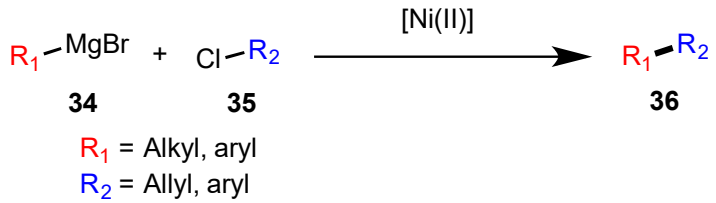


Figure 9. General Scheme for Kumada Cross-coupling

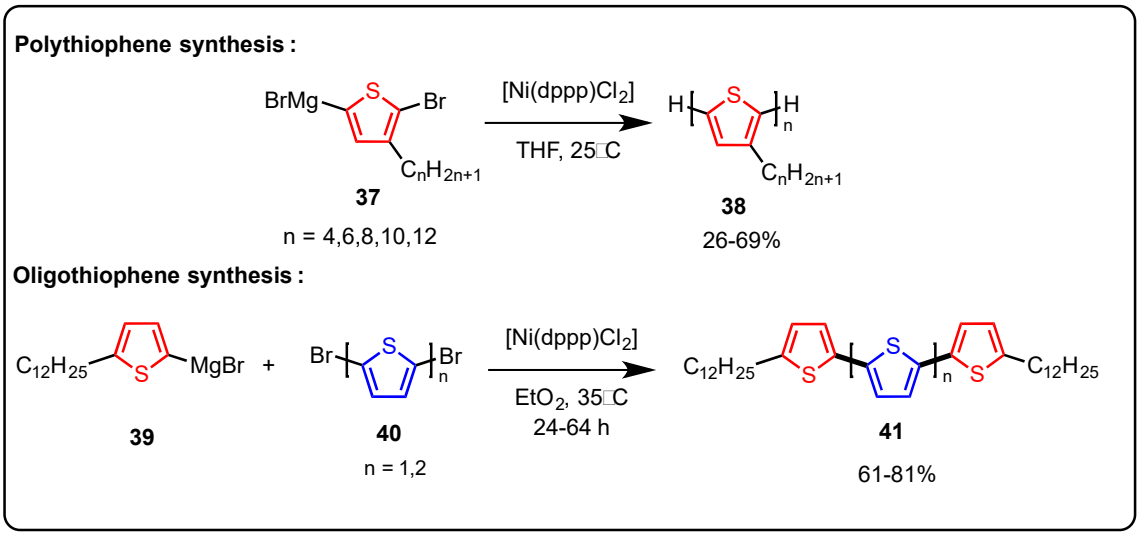


Figure 10. First Examples of Kumada Cross-Coupling for Thiophene-based Materials.

1.2.2.2. Neighshi Cross-coupling Method

Soon after, organozinc reagent (Figure 11, **42**) had also been established as another robust cross-coupling partner with aryl halide (**43**) by Negishi in 1977.[31,32] This method also explored the use of nickel and palladium catalyst, and later the palladium catalyst was determined to offer better yield and selectivity.[33] In 1992, first reported Negishi cross-coupling synthesis of regioregular 3-alkylpolythiophene (Figure 12, **46**) was obtained with di-functional monomer prepared *in-situ* (**45**), which was designed in similar fashion like Kumada cross-coupling.[34] Three years later, oligothiophene was prepared by similar method. This method also demonstrated diverse functional group tolerance with zinc chloride thiophene derivative (**47**)

with various iodothiophene derivative (**48**).[35] Notably, in the same report some bithiophene derivatives (**49**) synthesis show the formation of an inseparable by-product from the homo-coupling reaction.[35]

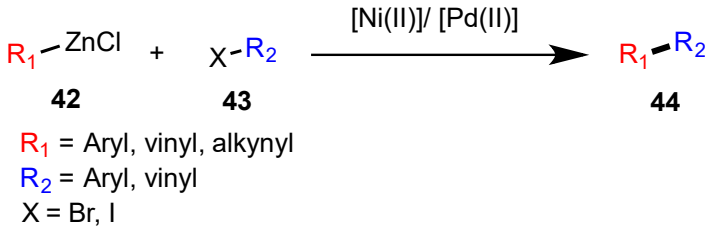


Figure 11. General Scheme for Negishi Cross-Coupling

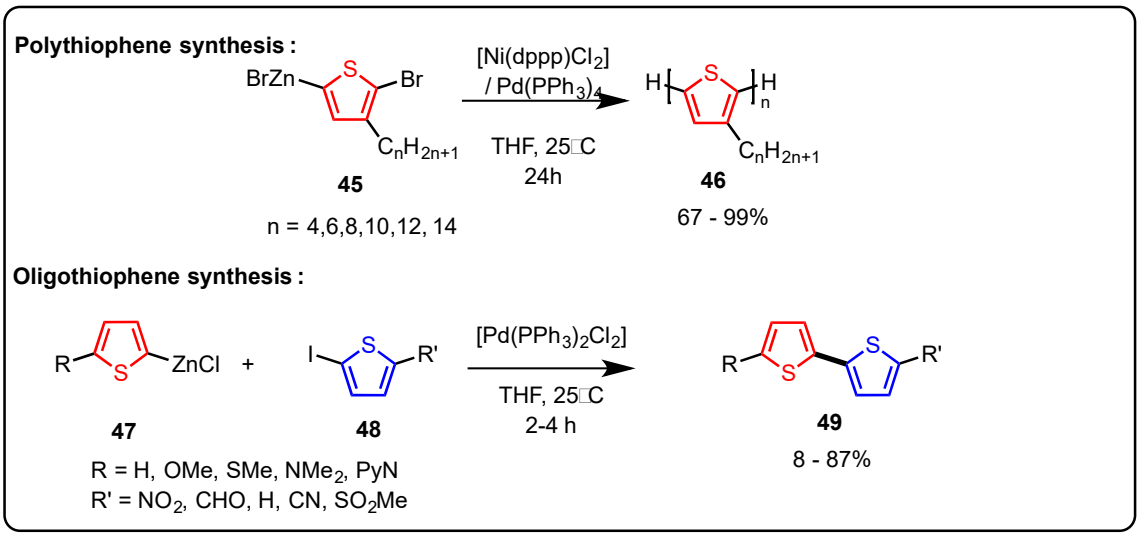


Figure 12. First Examples of Negishi Cross-Coupling for Thiophene-based Materials

1.2.2.3. Stille Cross-coupling Methods

In 1978, organotin reagent (**50**) also emerged as a potential cross-coupling partner with aryl halides (**51**) by Stille and co-workers (Figure 13).[36] The reaction was first reported to use palladium catalyzed alkylation with aryl halide, but shortly after cross-coupling between two aromatic systems was also reported.[37] The first example of Stille cross-coupling demonstrated the synthesis of a copolymer (Figure 14, **55**).[38] This report used diiodobenzene derivative **53** and di-tributyltin thiophene **54** to co-polymerize with palladium catallyst.[38] One year later, a library of oligothiophene derivatives (**58**) were also prepared through this method.[39] A similar strategy was employed with di-tributyltin thiophene (**56**) with various lengths of dibromo thiophene

derivative **57** with relatively higher yields compared to other cross-coupling reaction.[39] Organotin reagents are relatively more stable than Grignard or organozinc reagent and are not required to be formed *in-situ*, which allows it to be stored for a period of time.

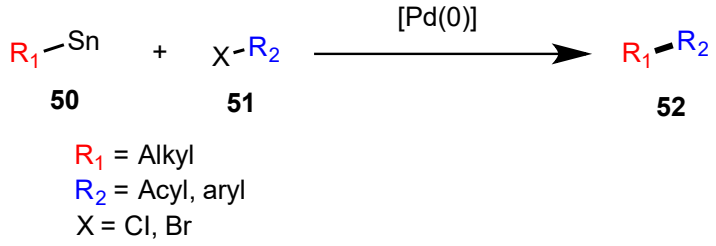


Figure 13. General Scheme for Stille Cross-coupling

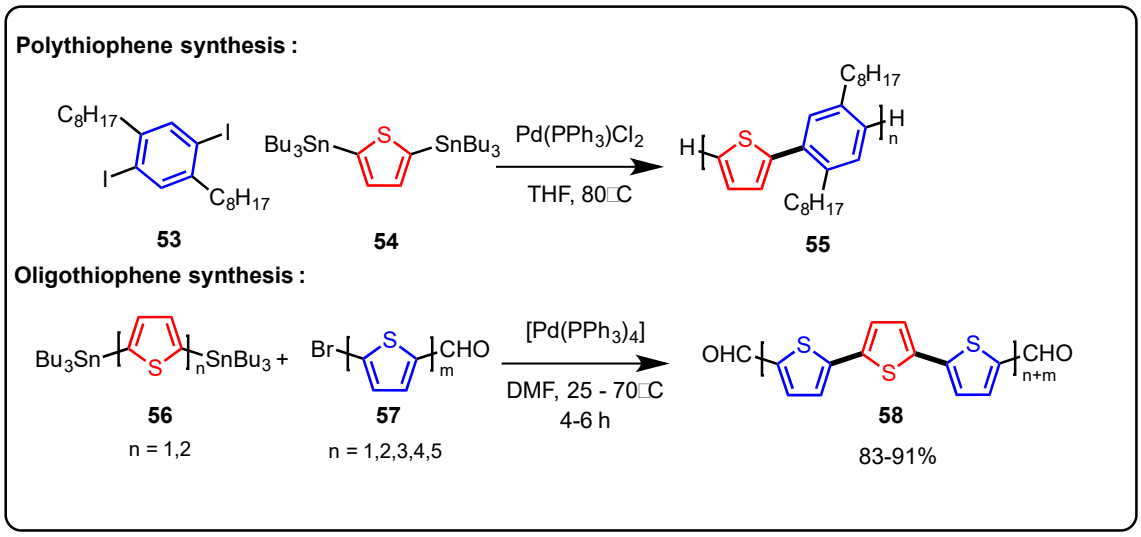


Figure 14. First Example of Stille Cross-coupling for Thiophene-based Materials

1.2.2.4. Suzuki-Miyaura Cross-coupling Methods

In the same period of time, boronic acids was also discovered as a potential cross-coupling partner. Suzuki and Miyaura first reported this method in 1979, where they utilized palladium catalysts to form carbon-carbon bonds between boronic esters (Figure 15, **59**) and various brominated substrates **60**.[40] Due to the further improved stability and lower toxicity of the boronic ester, this method has soon became immensely popular for various thiophene-based materials.[41] Similarly, it has been realized for constructing more elaborate terthiophene-benzyl copolymer **64** with two bi-functional monomers (**62, 63**).[42] The first example of this method for the synthesis of oligothiophene was limited to bithiophene (**67**).[43] This report used thiophene

with boronic methyl ester **65** and iodothiophene **66**. Nevertheless, more elaborate syntheses also emerged in the following years. [22] This method generally demands high reaction temperature and long reaction time, and also often require the use of aqueous base.

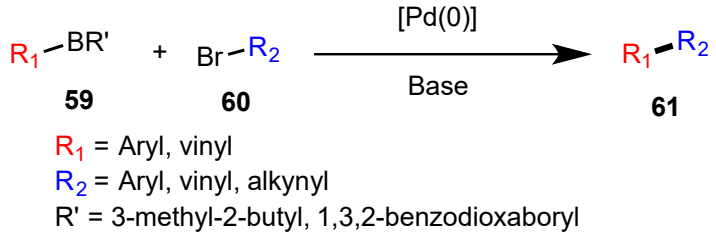


Figure 15. General Scheme for Suzuki Cross-coupling

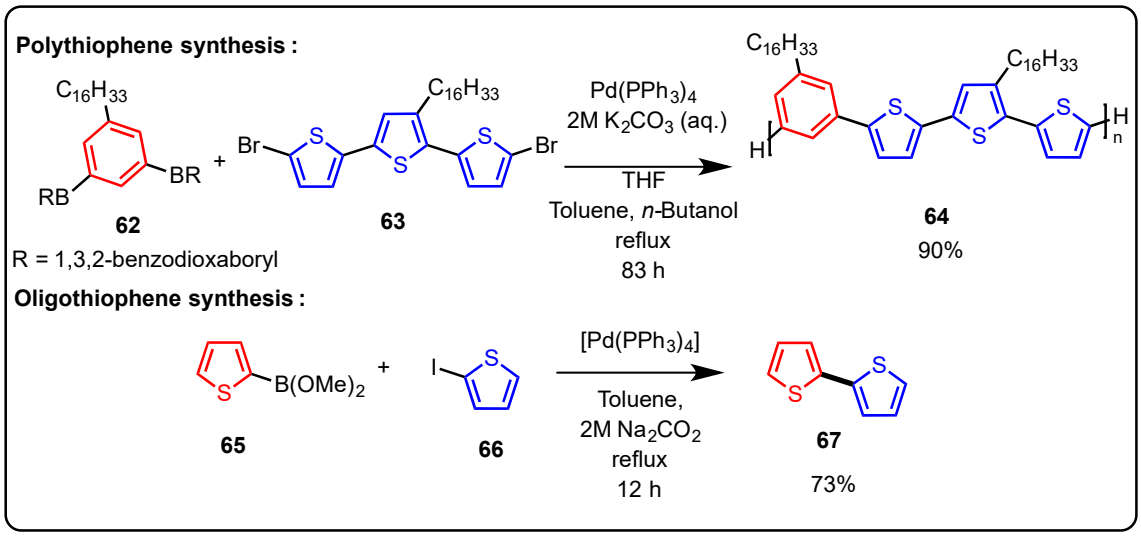


Figure 16. First Examples of Suzuki Cross-coupling for Thiophene-based M aterials.

1.3. Recent Developments of Cross-coupling Reaction

1.3.1. Green Chemistry

Over the years, these traditional cross-coupling reactions have been proven to be a robust reaction process and demonstrated excellent diversity that allowed a steady supply of different thiophene-based materials. However, several underling problems associated with these methods are the production of stoichiometric amount of by-product, and requirement for the pre-installation of the organometallic functional groups. In 1991, Barry Trost first introduced the concept of atom economy, which is based on improving the atom efficiency for a synthesis of

product should be a focus, alongside the development of the synthetic methodology.[44] Atom economy represents the first ever measurement of green chemistry, which defined the percentage of atoms from starting material that are incorporated into the final product.[44] Years later, a group of scientists published a set of principles for defining comprehensive green chemistry measurement, which has been named as the "12 principles of Green Chemistry".[45]

The 12 principles of Green Chemistry are:

1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.
8. Reduce derivatives – Unnecessary derivatization (blocking group, protection/deprotection, and temporary modification) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. Substances and the form of a substance used in a chemical process should be chosen to minimize potential for chemical accidents, including releases, explosions, and fires.

These principles served as a guideline for the development of green chemistry. For the traditional cross-coupling reaction, the major drawback is the production of metallic waste during the reaction. These metallic contaminants could cause a huge impact for the application of thiophene-based material.[46] One recent report demonstrated that metal residues from the synthesis of polythiophene by Kumada cross-coupling lower the performance of photovoltaic cell.[47] Furthermore, as shown in Figure 17, a terthiophene derivatives (**70**) synthesized by Stille cross-coupling was achieved with excellent 83% yield from tributyltin thiophene **68** and bromothiophene **69**.[39] However, upon closer examination, it also revealed that the reaction also generated two equivalents of tributyltin bromide (**71**) for each equivalent of the desired product **70**. The tributyltin bromide also has a higher molecule weight than the terthiophene product **70**. As a result, this method generally produces more waste than product. Not to mention the high toxicity of organotin reagent toward the environment and living organisms. Consequently, ongoing research on the thiophene-based material should always aim toward a versatile synthesis with less waste production.

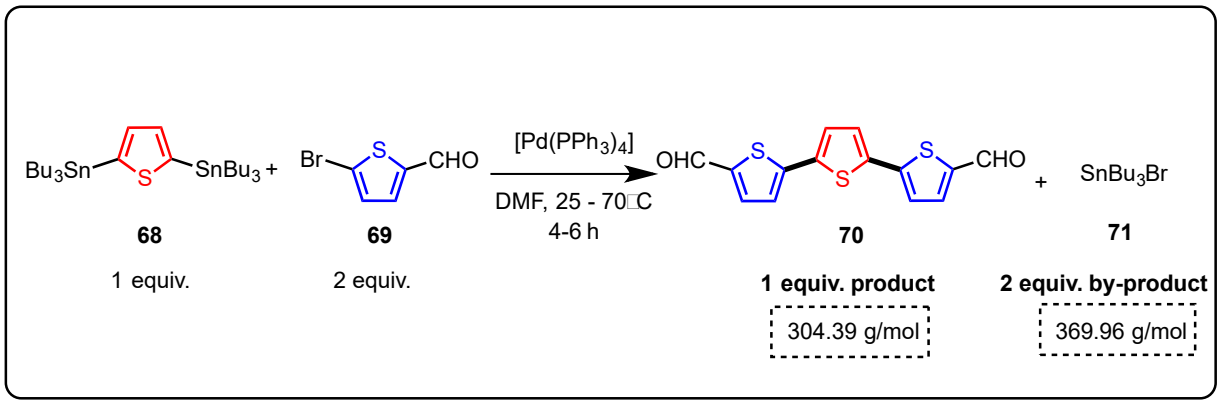


Figure 17. Example of Waste Production from Stille Cross-Coupling

1.3.2. Palladium Catalysed Direct (Hetero)arylation

Direct (hetero)arylation has been consequently developed years after, aiming for improving the efficiency and lowering the waste production of the traditional methods.[48] This method is always considered as a first choice for greener synthesis of (hetero)aromatic molecules. This method utilizes the protons on the nucleophilic aromatic substrate (Figure 18,

71), which undergoes cross-coupling with another aryl halide (**72**) in the presence of a palladium catalyst and a base to produce corresponding product **73**.[49] Avoiding the use of an organometallic functional group improved the atom economy dramatically and consequently lowered the waste production.[48,49]

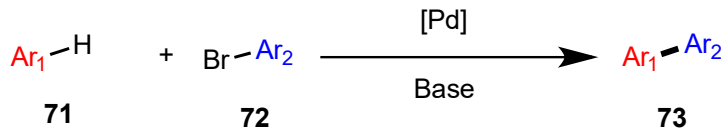


Figure 18. General Scheme for Direct (Hetero)arylation

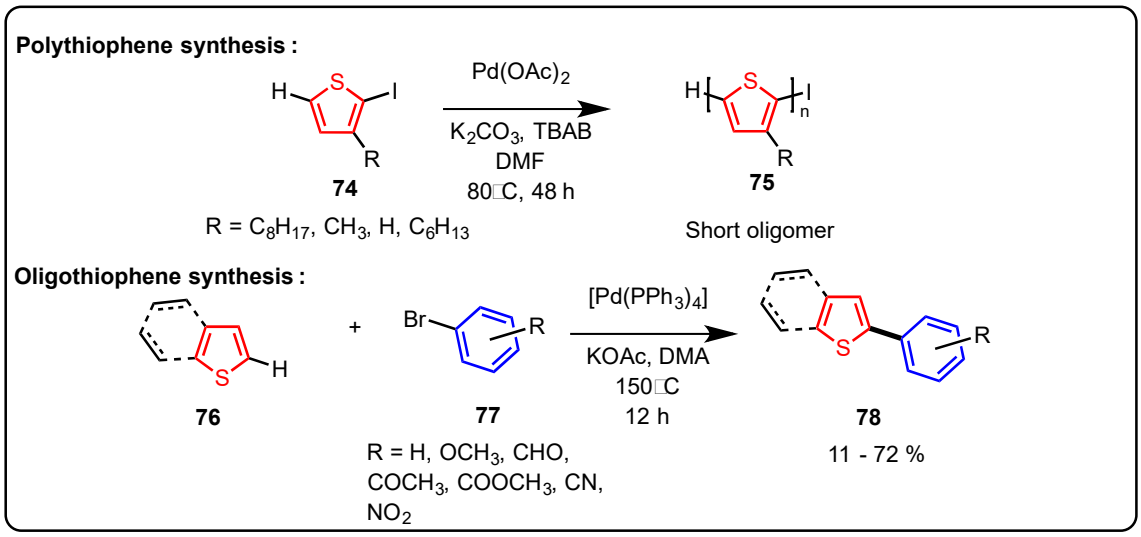


Figure 19. Example of Direct Arylation for Thiophene-based Material.

Subsequently, the 3-alkylpolythiophene (Figure 19, **75**) can be prepared directly from 2-iodo-3-alkylthiophene (**74**) with a palladium catalyst.[50] However, the first reported synthesis of the polythiophene only yield a short oligomer.[50] The earliest report of oligothiophene synthesis could be traced back to 1990, where a report demonstrates a series of simple thiophene derivatives (**78**) was prepared from thiophene molecule (**76**) and aryl bromide (**77**).[51] In the same report, the selectivity issue for mono- and di-arylation was observed and result in difficult separation for desired product.

In addition to these reactivity issues, this method also demonstrated limited selectivity on the C2 position (Figure 20, **80**) and C5 position (**81**) for direct arylation of thiophene.[52] As shown in Figure 11, the palladium catalyst with a phosphine ligand in non-polar solvents leads to

more selective for arylation at the C2 position (**80**) on the thiophene derivative (**79**).[52] In the absence of ligand and with a polar solvent lead to a less selective arylation on the C2 position of the thiophene derivative (**80**).[52] The resulting isomers often are inseparable mixtures, which decreases the advantages of this method.

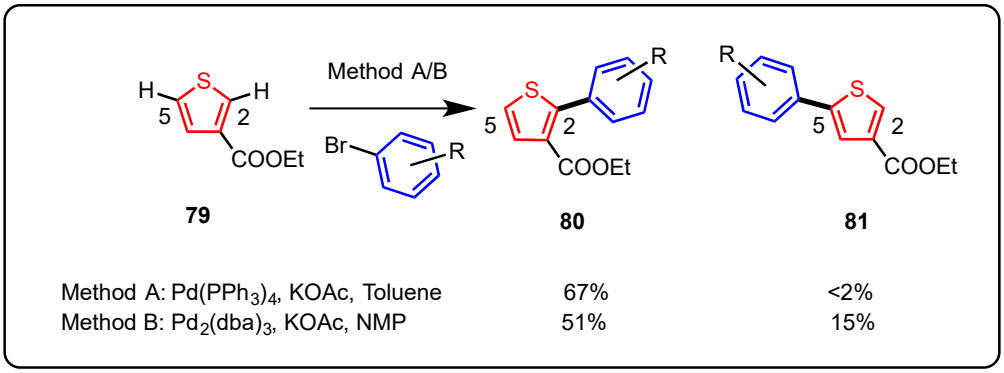


Figure 20. Early Example for Selectivity Issue with Direct Arylation

In the following decade after the initial reports, this regioselectivity issues has been addressed by numerous research groups, and many postulated mechanisms such as oxidative C-H insertion, electrophilic aromatic substitution, and concerted-metallation deprotonation mechanisms have been proposed.[49,53] With the pioneering work has been shown by the late professor Keith Fagnou, a general protocol for more selective direct arylation for aromatic molecules has been developed with better efficiency.[54] As shown in Figure 21, this method introduced an additional carboxylic acid additive, where excellent yields were achieved for a series bi-aryl moiety (**84**) with C5 position functionalized thiophene (**82**) and various aryl bromide (**83**).[54] Later reports also demonstrated good selectivity with unsubstituted thiophene as well.[55] However, selective mono-arylation (**87**) on the unsubstituted thiophene (**85**) requires higher molar equivalents (5 equiv. vs. 2 equiv.) to bromobenzene (**86**).[55] Similarly, diarylation (**89**) also requires higher molar equivalent of thiophene (**85**) to dibromobenzene (**88**).[55] The report states that the higher equivalent was required to supressed side-reactions.[55] A more recent report also reported similar challenge, where 20 equivalents of 3-hexylthiophene (**90**) were used with 4,7-dibromo-2,1,3-benzothiadiazole (**91**) to prepare a trimer molecule **91**.[56] The report stated the lowering the thiophene ratio would result in polymerization instead of di-arylation, as the resulting trimer also bearing reactive protons.[56]

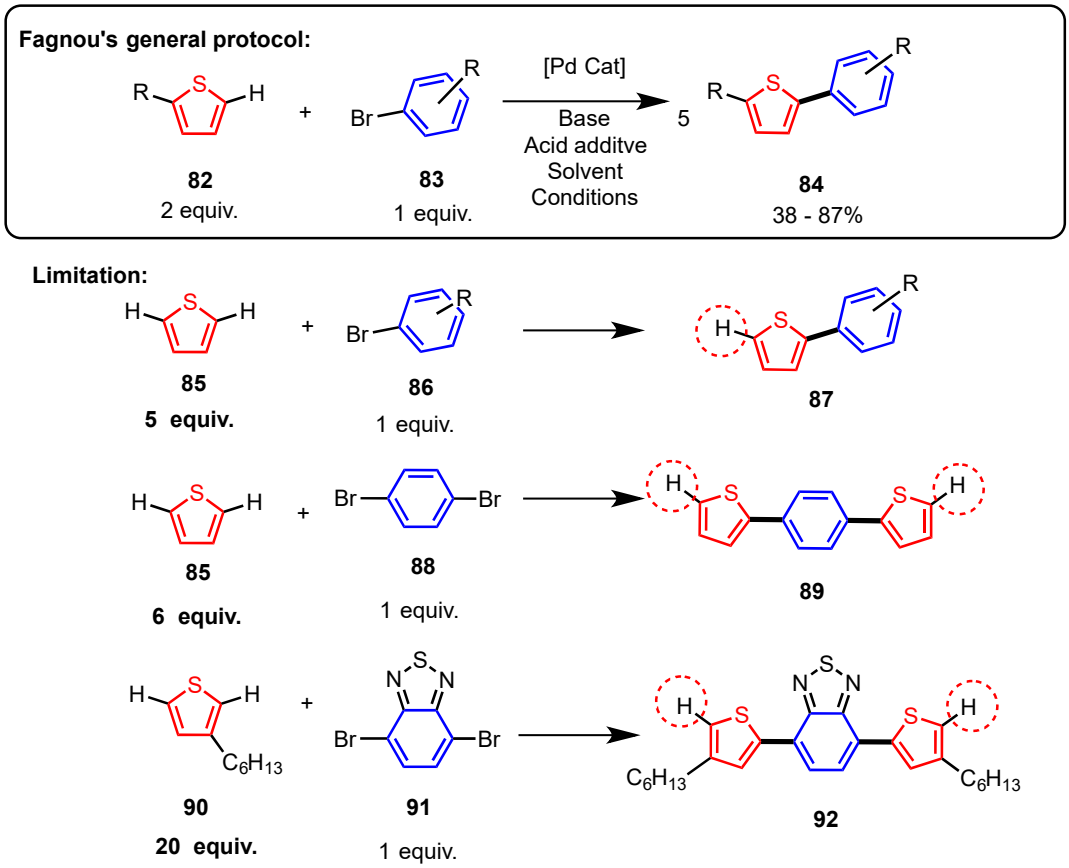


Figure 21. General Scheme of Fagnou Protocol for Various Oligothiophenes

Consequently, most of oligothiophenes prepared with direction arylation often requires protecting group and/or deprotection reactions.[57] However, this unwanted polymerization was advantageous for polymerization reaction. Many complex conjugated polymers were synthesized over the years.[58] Nonetheless, another limitation occurred as branching of polymer was observed for some examples.[59] The exact nature of these β-defects are still ongoing research.[60]

1.3.3. Decarboxylative Cross-Coupling Reaction

Decarboxylative cross-coupling has emerged as an alternative synthetic strategy for regioselective catalysis. This method utilizes carboxylic acids or carboxylate salts as a cross-coupling partner instead of organometallic reagents with aryl halides. Regioselectivity issues that occurred during the direct arylation can be easily eliminated. Carboxylic acid is a stable and easy to install functional group. For aromatic compound synthesis, the carboxylic acid was first reported as a potential cross-coupling partner with quantitative amount of a palladium reagent for

an intramolecular cross-coupling for natural product.[61] In the following years, decarboxylation has been further explored for cross-coupling reactions with two distinct approaches.

1.3.3.1. Co-Catalytical Systems

The first approach of decarboxylative cross-coupling involves the usage of co-catalyst, as to facilitate the decarboxylation process. Most of the early reports focused on benzoic acid derivatives with various non-aromatic cross-coupling partners with palladium and silver carbonate as co-catalysts.[62,63] In 2006, Goossen and coworkers first described the cross-coupling of 2-nitro benzoic acid that underwent a cross-coupling with aryl halides with copper acting as the decarboxylation reagent.[64] Soon after, this method had expanded to various aromatic compounds with lower temperature, less co-catalyst loading, and usage of silver as a co-catalyst.[65,66] At the same time, Becht and coworkers also report the usage of silver.[67] Overall, this method could be summarized in Figure 22, the generic bi-aryl product **95** generally uses a palladium catalyst with silver or copper co-catalyst for cross-coupling between arene carboxylic acids or carboxylate salts (**93**) react and aryl halides (**94**).

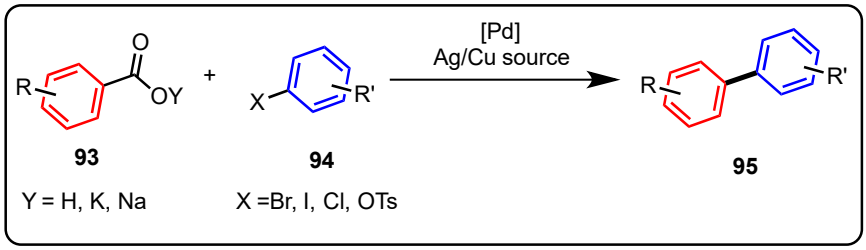


Figure 22. General Scheme for Decarboxylative Cross-Coupling with Co-catalyst

The proposed mechanism involves a bi-catalytical system.[62] The reaction starts with oxidative addition of palladium into the aryl halide (**94**) to form a arylpalladium(II) intermediate (**94a**). The resulting intermediate then undergoes transmetallation with metallated aryl cross-coupling partners (**93b**) to form biarylpalladium(II) intermediates (**94b**). The bi-aryl product (**95**) is formed from subsequent reductive elimination and regeneration of the palladium(0) specie to re-enter the catalytic cycle. Concurrently, the co-catalytic cycle initiates with the anion exchange of deprotonated carboxylate intermediate **93** to form metal carboxylate intermediate **93a**, then followed by extrusion of CO_2 to form metallated nucleophilic cross-coupling partner **93b**.

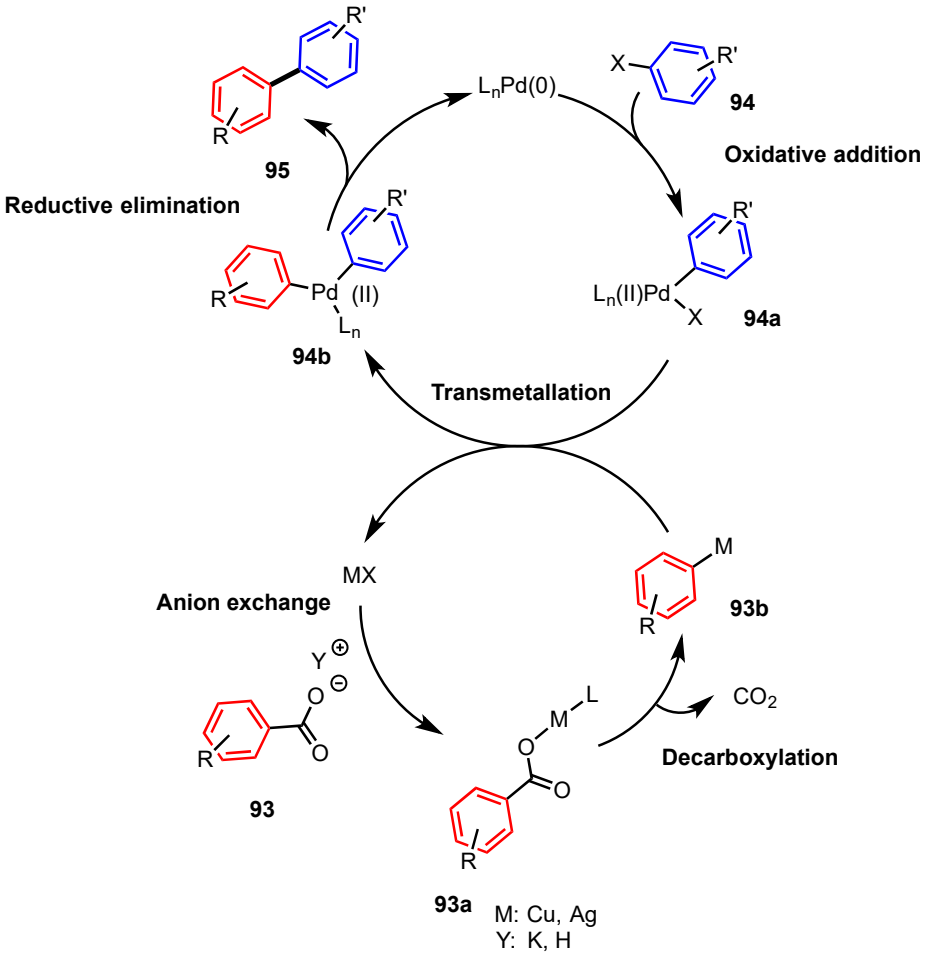


Figure 23. Postulated Mechanism for Co-catalytic System

1.3.3.2. Monometallic System

In 2006, Forgione and co-workers reported an unexpected decarboxylative cross-coupling of aryl bromide with heteroaromatic carboxylic acid, where the original attempt was to obtain a C5 direct arylation.[68] This method differs from other decarboxylative cross-couplings for the absence of a co-catalyst during the cross-coupling reaction (Figure 24). The method generally requires a heteroaromatic-2-carboxylic acid (**96**) with a carbonate base and an aryl halide (**97**) to produce a hetero-biaryl product (**98**) with a palladium catalyst.[68]

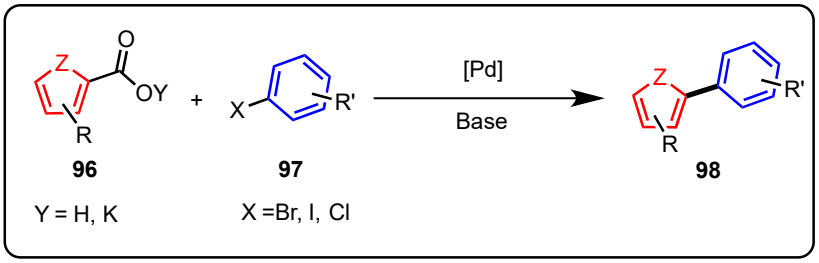


Figure 24. General Scheme for Decarboxylative Cross-Coupling without Co-catalyst

Following the reported study from Forgione and co-workers, a different plausible reaction mechanism was proposed for this monometallic condition.[69] The catalytic cycle initiates with oxidative addition of the palladium catalyst into aryl halide (Figure 25, **97**) to formed palladium (II) intermediate **97a**, which then undergoes ligand exchange with heteroaromatic carboxylate (**96**) to form a coordinated complex **99**. At this point, it diverges into two possible pathways. First is C2 palladation pathway, where the electrophilic palladation is driven by the electron rich heteroaromatic compound to form intermediate **99a**. Restoring aromaticity on the heteroaromatic ring result from CO_2 extrusion to forms the biarylated palladium (II) intermediate **100**, and desired bi-aryl product **98a** is obtained from subsequent reductive elimination. Furthermore, in the same report, C3 arylated product is also observed as minor product. This observation was explained by a C3 palladation pathway, starting with the electrophilic palladation on the C3 position of the heteroaromatic ring. The resulting intermediate **99b** could first go through C2-C3 palladium migration to form relatively stable intermediate **99a**, which would result in same product (**98a**). If the C3 position is unsubstituted with any functional group, deprotonation could occur that lead to a different biarylated intermediate **101** and resulting reductive elimination would result in a C3 arylated product **102**.[69]

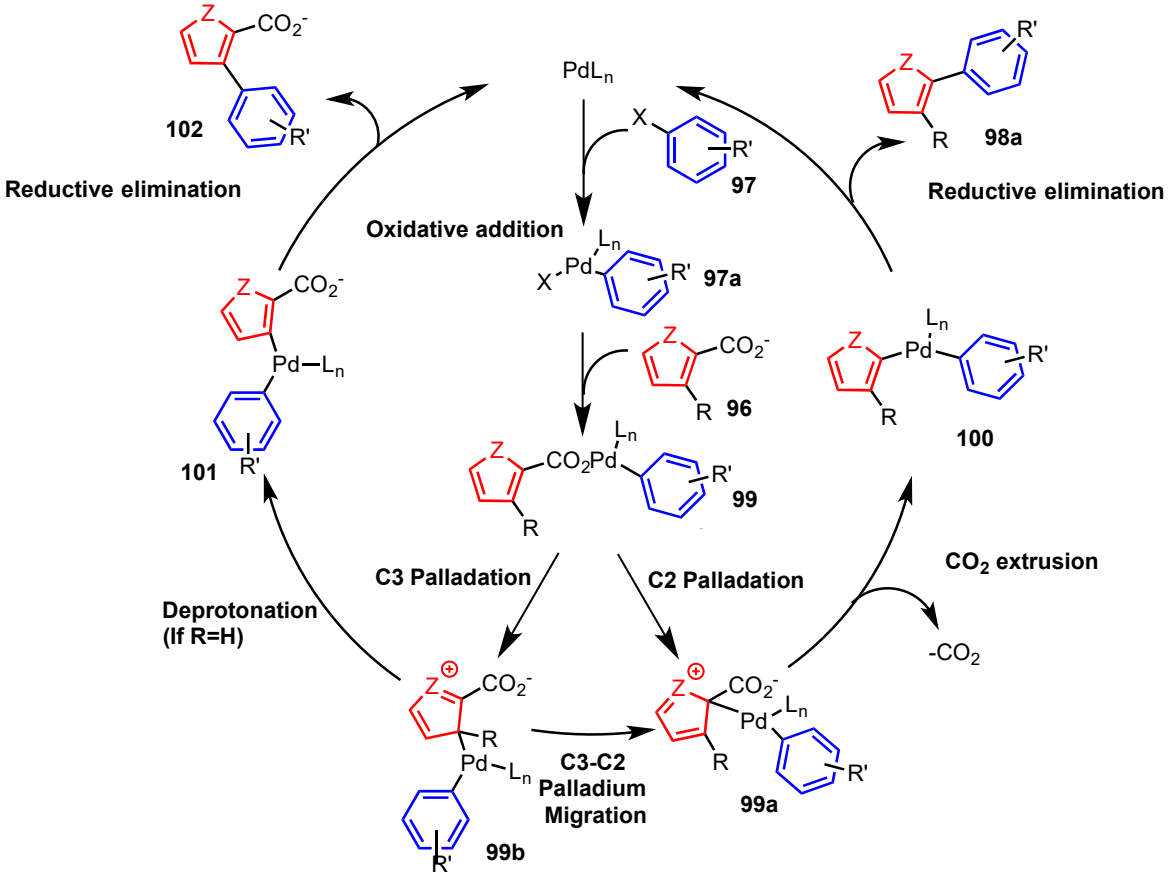


Figure 25. Postulated Mechanism for Monometallic System

Over the years, this heteroaromatic decarboxylative cross-coupling has been demonstrated to be a versatile synthetic tool. Numerous research groups have reported its utility in lead compound synthesis in medicinal chemistry and bio-mass derived small molecule synthesis.[70–74] To our knowledge, there is only one related report of utilizing this method for organic electronic materials with a pyrrole derivative.[75]

1.4. Research Objective and Thesis Organization

The main objective in this thesis is to develop a versatile synthetic strategy for thiophene based material utilizing decarboxylative cross-coupling. Chapter 1 of this thesis introduce the synthesis of the thiophene-based material and the established synthetic pathways and highlight the underlying waste production that could influence the ongoing research applications.

Furthermore, it introduced the ongoing research of greener synthesis of aromatic compounds and potential use for thiophene-based materials.

Chapter 2 includes the synthesis of a diverse library of symmetrical oligothiophene. The reaction was optimized with thiophene carboxylate salt as a versatile functional group. Part of this chapter was adapted into a manuscript and submitted for publication.

Chapter 3 presents the synthesis of regioregular poly/oligothiophene with decarboxylative cross-coupling. Regioregular oligothiophene was successfully prepared through an iterative process involving decarboxylative cross-coupling and saponification. Part of the work was done in collaboration with Sarah Taylor as part of her honour CHEM 450 project. Further research demonstrates the synthesis of polythiophene through decarboxylative polymerization with di-functional monomers. Part of this chapter was adapted into a manuscript prepared to be submitted.

Chapter 4 discusses the conclusion of this research and perspective of the future research related to decarboxylative cross-coupling for thiophene-based materials.

Chapter 2. Decarboxylative Cross-Coupling as an Efficient Tool for Synthesis of Symmetric Oligothiophene

2.1. Synthesis of Symmetrical Oligothiophene

The initial goal of this project was to develop an efficient strategy for the preparation of thiophene-based materials, which are more environmentally benign compared to the common synthetic methods. As demonstrated in Figure 26, we aim towards using decarboxylative cross-coupling between thiophene carboxylic acid (**103**) with dibromothiophene derivative (**104**) to obtain a scaffold of symmetrical oligothiophenes (**105**), and further extend the oligomer chain with an iterative process of halogenation of this scaffold (**105**) and cross-coupling reaction to obtain a library of symmetrical oligothiophenes. Towards this end, we pursued a modified strategy based on previously reported decarboxylative cross-couplings of thiophene derivatives that preclude the use of co-catalysts and avoids the generation of metallic waste that can interfere with electronic applications of oligothiophenes.[47,69] However, among the many decarboxylative cross-coupling methods reported, none have been utilized for the construction of oligothiophenes. Furthermore, many developed methodologies require the use of silver or copper as co-catalyst that generate more metallic waste.[62] This monometallic approach has been developed for the construction of bi-(hetero) aryls through various heteroaromatic carboxylic acid as cross-coupling partners.

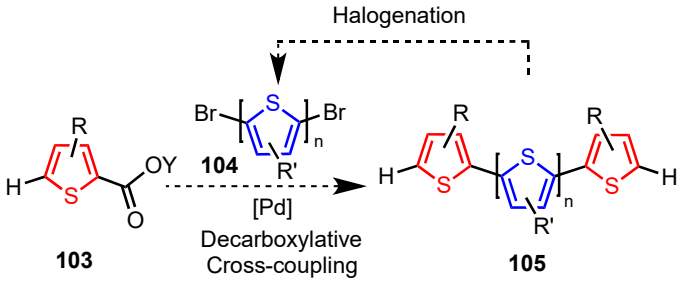


Figure 26. Proposed Iterative Synthesis of Symmetric Oligothiophene

2.2. Optimization of Reaction Condition

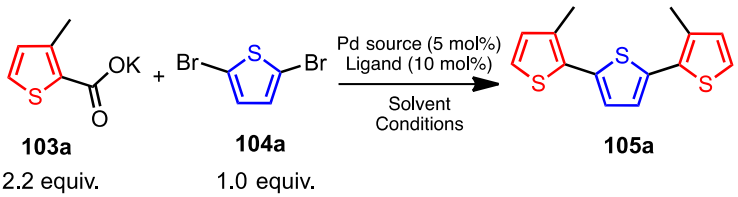


Figure 27. Model Terthiophene Synthesis for Optimization of Reaction Condition

Table 1. Optimization of Reaction Condition

Entry	Pd Sources/Ligand	Solvent	Conditions	Yield (%)
1	Pd(*t*-Bu_3P)$_2$	DMF	170 °C, μw, 8 min	31[a]
2	Pd(*t*-Bu_3P)$_2$	DMF	170 °C, μw, 8 min	51[b], [c]
3	Pd(*t*-Bu_3P)$_2$	DMA	190 °C, μw, 8 min	49[c]
4	$PdCl_2$/P(*t*-Bu_3)$_2$	DMA	190 °C, μw, 8 min	54[c]
5	$PdCl_2$/dppf			43[c]
6	$PdCl_2$/JohnPhos			81
7	$PdCl_2$/PPh_3			72
8	$PdCl_2$/P(*o*-Tolyl)$_2$			85

[a] 4 equiv. of carboxylic acid, 1 equiv. of TBAC, 1.5 equiv. of Cs_2CO_3. [b] 4 equiv. of carboxylic acid, 1.5 equiv. of Cs_2CO_3 [c] Yield determined by ^{1}H-NMR with 1,3,5-Trimethoxybenzene as internal standard

Initial effort was focused on exploring and optimizing reaction conditions for the synthesis of symmetrical terthiophene **105a**, starting from two commercially available thiophene derivatives **103a** and **104a** (Figure 27). Our first attempt was focused using conditions previously disclosed that provided the corresponding product **105a** with a limited yield of 31% (Entry 1, Table 1).[69] This low yield was expected as this condition only applied to electron-deficient aryl halides and was not demonstrated for electron-rich arenes like dibromothiophene.[69] Interestingly, removing tetra-butyl ammonium chloride improved the yield to 51% (Entry 2), which is in contrast to previous reports that indicated this additive was essential to obtain high yields.[69,74] Further optimization allowed us to determine that using the potassium salt of **1** with higher temperature and dimethyl acetamide (DMA) as solvent yielded a comparable yield of 49% (Entry 3). Subsequent atom efficiency could be achieved by eliminating the need for Cs_2CO_3 as the base since we were no longer employing the carboxylic acid but rather the corresponding salt and reducing the carboxylate loading from 2 to 1.1 equivalent (Entries 3-8). Further optimization focused on the palladium and ligand sources. Using palladium chloride with tri-*tert*butyl-phosphine ligand provided the product with a similar yield of 54% (Entry 4). Employing a

bidentate ligand such as 1,1'Bis(diphenylphosphino)ferrocene (dppf) did not further improved the yield (Entry 5). The more sterically hindered monodentate ligand JohnPhos improved the yield to 81% (Entry 6) and with the less sterically hindered triphenylphosphine (PPh_3) had a reduced yield of 72% (Entry 7). Lastly, employing a moderately steric hindered tris(*o*-tolyl) phosphine offered the best isolated yield of 85% (Entry 8). This new set of conditions offered a high yielding route that avoids both the use of cesium carbonate as base and tetrabutylammonium chloride as additive. Importantly for materials-based applications, the only by-products are water-soluble potassium bromide and CO_2 gas, which can be easily removed

2.3. Scope of Substrate

This condition was subsequently used to explore other thiophene-based substrates for applications in materials chemistry. A series of thiophene carboxylate derivatives is prepared (Figure 28). The potassium 3-hexylthiophene-2-carboxylate (**103b**) and potassium 3,4-ethylenedioxylthiophene-5-carboxylate salts (**103c**) were prepared from 3-hexyl thiophene and 3,4-ethylenedioxylthiophene (EDOT), respectively, from a modified procedure previously reported.[75] The synthesis involved the formylation of commercially available thiophene derivatives, and then followed by Pinnick oxidation to obtain the desired 3-hexylthiophene carboxylic acid (**92a)** with 65% yield overall, and 3,4-ethylenedioxylthiophene carboxylic acid (**92b**) with limited yield of 15% overall.[76] Thiophene-2-carboxylate (**103c**) and 5-methylthiophene-2-carboxylate (**103d**) were prepared directly from the commercially available carboxylic acids.

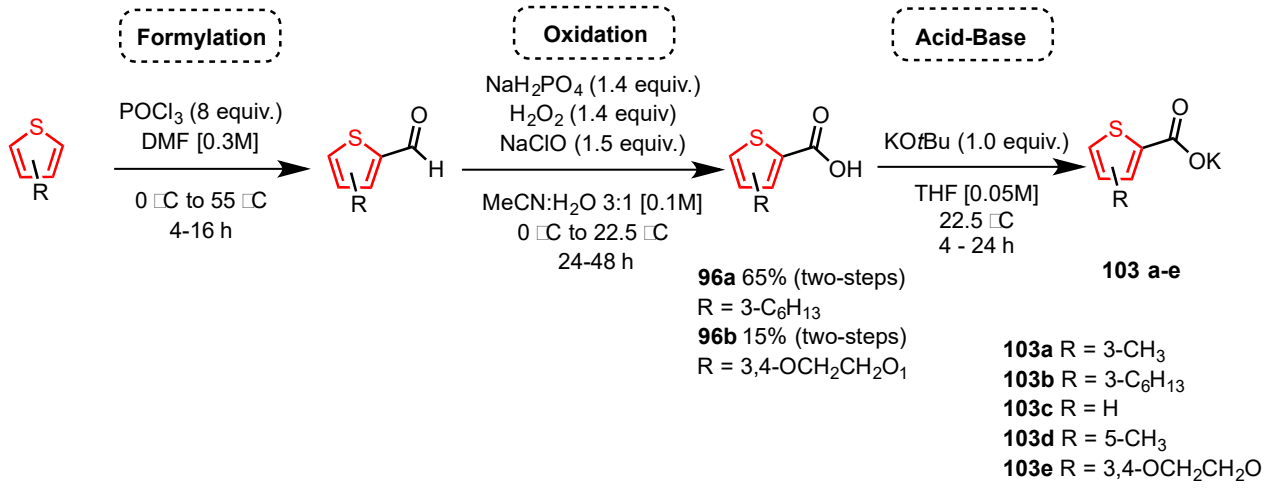


Figure 28. General Protocol for Preparation of Carboxylate Substrates

The 3,3-hexyl substituted terthiophene **105b** is a common moiety featured in OPVCs or serve as building block for conjugate polymers.[10] Employing the decarboxylative cross-coupling provide the corresponding product (**105b**) in excellent yield (83%) from 3-hexylthiophene carboxylate (**103b**). Similarly, unsubstituted terthiophene product **105c** is commonly found as a fundamental building block in material chemistry.[10] However, this route only affords a limited yield of 22% from potassium 2-thiophene carboxylate (**103c**). Terminal substituted oligothiophenes are also valuable in various material applications.[1] We utilize potassium 5-methylthiophene carboxylate (**103d**) to synthesize product **105d** as an example, for this class of molecules, yet it only offers a moderate 44% yield for terthiophene product **105d**. Nevertheless, the lower yields of compound **105c** and **105d** likely due to the fact that both thiophene carboxylate salts lack a substituent at the C3-position as previously observed.[69]

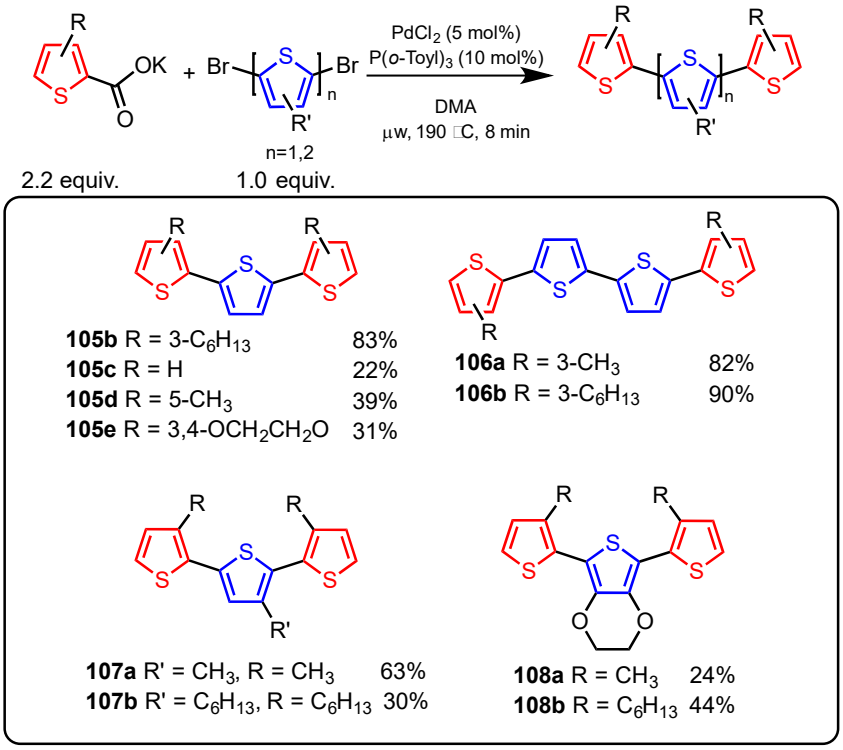


Figure 29. Scope of thiophene-based substrates

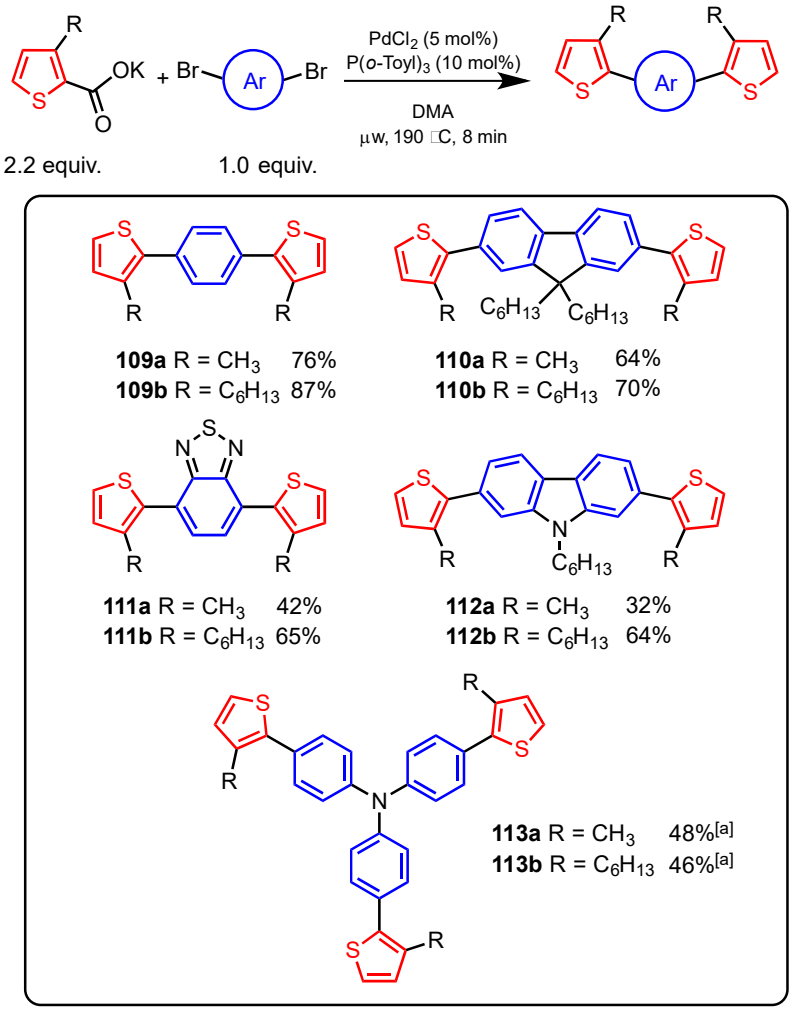
Furthermore, electron rich thiophene substrates such 3,4-ethylenedioxylthiophene (EDOT) is also a key structural feature for tuning the electronic properties of material for different applications.[10] The decarboxylative cross-coupling demonstrated the ability to incorporate

EDOT units into the corresponding product (**105e**), albeit in a moderate yield of 31% from potassium 3,4-ethylenedioxylthiophene-5-carboxylate salts. Subsequently, two quaterthiophene derivatives with similar feature are obtained through cross-coupling with 5,5'-dibromo-2,2'-bithiophene. 3-substituted quaterthiophene product **106a** and **106b** are commonly used building blocks for poly/oligothiophene.[1,23] This method affords an excellent yield of 82% for 3-methyl substituted product **106a** with 3-methyl thiophene carboxylate salt **103a** while 3-hexyl substituted product **106b** gave the highest yield of 90% from 3-hexyl thiophene carboxylate salt **103b**. Further efforts focused on examining this approach with different electrophilic coupling-partners, along with the most compatible 3-substituted carboxylate thiophene substrate (**103a** and **103b**). Sterically hindered 2,5-dibromo 3-methylthiophene with 3-methyl thiophene carboxylate salt (**103a**) afford product **107a** with 63% yield, which is also a preliminary example for ability to synthesize regioirregular oligothiophenes. The increasingly sterically hindered 2,5-dibromo 3-hethylthiophene with 3-hexylthiophene carboxylate salt (**103b**) provided the corresponding regioirregular terthiophene product **107b** in moderate yield (30%), which further supports that the preparation of regioirregular oligothiophenes is not favored employing this method. Moreover, mono-arylation is not observed on either substrate. EDOT was also revisited as the electrophilic cross-coupling partner. 2,5-dibromo-3,4-ethylenedioxythiophene only offered a limited yield of 24% with 3-methyl carboxylate salt (**103a**) for product **108a**, and a slight increased yield of 44% is obtained from 3-hexylthiophene carboxylate salt (**103b**) for product **108b**.

2.3.1. Scope of Arene Based Cross-Coupling Partners

Further effort focused on demonstrating to apply this method on more electron deficient aromatic system as electrophilic cross-coupling partners. As shown in Figure 30, a series of commonly featured aromatic derivatives were attempted. The first substrate was 1,4-dibromobenzene that is simplest electron-poor system that exist in many organic electronic applications.[10] This substrate, when combined with 3-methyl thiophene carboxylate salt (**103a**), formed the corresponding methyl substituted trimer product **109a** in 76% yield . A Higher yield of 87% is obtained for hexyl substituted trimer product **109b** with 3-hexyl thiophene carboxylate salt (**103b**). 9,9-dihexylfluorene is a common moiety exist in many organic electronic materials.[22] This approach affords a 64% yield for the corresponding trimer product **110a** with 3-

methylthiophene carboxylate salt (**103a**). Similarly, 3-hexylthiophene carboxylate salt (**103b**) and 9,9-dihexyl-2,7-dibromofluorene offered with a slight increase yield of 70% for corresponding trimer product **110b**. Furthermore, a more complex substrates like 4,7-dibromobenzo[*c*]-1,2,5-thiadiazole group were also examined with two thiophene carboxylate salt (**103a**, **103b**). 3-methylthiophene arylated trimer product **111a** is obtained with 42% yield, and 3-hexylthiophene arylated trimer product **111b** with an increased yield of 65%. Further attempts tested 3,6-dibromo-9-hexyl-9H-carbazole molecule, where the 3-methylthiophene carboxylate salt (**103a**) gave a limited yield of 43% for desired trimer product **112a**, and again, an increased yield of 65% for trimer product **112b** with 3-hexylthiophene carboxylate salt. Triphenyl amine moiety is also commonly existed in different advance functional materials.[10] We further apply this method with tris(4-bromophenyl) amine with 3.3 equivalent of 3-alkythiophene carboxylate salts (**103a**, **103b**). 3-methylthiophene tri-arylated product **113a** is obtained with 48% yield, and 3-hexylthiophene carboxylate salt on afford slight lower yield of 46% for tri-arylated product **113b**, where unlike the previous result that hexyl substituted thiophene carboxylate salt generally offered a higher yield to methyl substituted.



[a] 3.3 equiv. of thiophene carboxylate salt

Figure 30. Scope of Different Arene-based Substrates

2.4. Iterative Synthesis of Symmetric Oligothiophene

This approach was subsequently applied to construct long, discreet oligothiophenes by extension of terthiophene product (**105a**) and phenylthiophene product (**109a**) as shown in Figure 31. We initiated the synthesis by bromination of **105a** and **109a** following previously reported conditions.[77] The subsequent cross-coupling followed the same conditions employed for tri- and tertrameric products. Pentathiophene derivatives from 3-methyl thiophene carboxylate salt **103a** provided the product **114a** in a 69% yield for 3-methyl pentathiophene, and 75% yield for pentathiophene product **114b** from 3-hexyl thiophene carboxylate salt (**103b**). 3-methyl substituted phenylthiophene pentamer **115a** afford a 55% yield with 3-methyl thiophene carboxylate salt (**103a**), and 3-hexylthiophene carboxylate salt (**103b**) offered pentameric

product **115b** with 67% yield. All of these pentamers followed a similar trend observed on previous syntheses of tri- and tetrameric derivatives as hexyl substituted thiophene offered a higher yield than methyl substituted. Solubility issue for methyl substituted pentameric derivatives has prevent further extension of **114a** and **115a**. This limitation underlies a major drawback to this approach, where some thiophene substrates may not be soluble in DMA but are compatible with toluene or THF as reported in other synthetic protocols.[3,77]

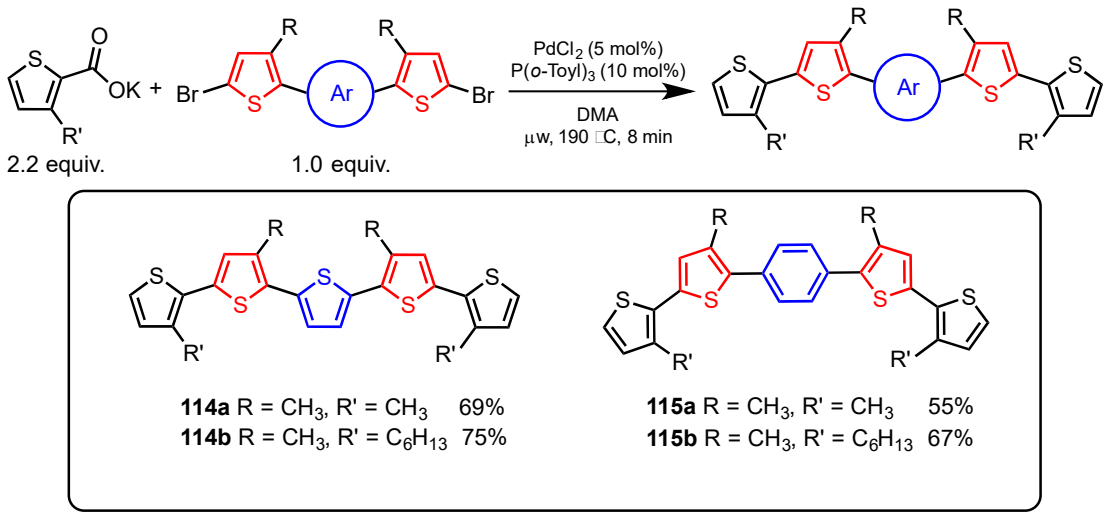


Figure 31. Synthesis of Pentathiophene Derivatives

We further aimed to extended quaterthiophene derivatives to obtain even long symmetrical oligothiophene that more suitable for physical property study, and further pave the way toward polythiophene.[78] An iterative sequence (Figure 32) with 3-hexyl substituted quaterthiophene product **106b** was undertaken. The synthesis starts with the bromination of the core oligothiophene (**106b)** and followed by cross-coupling with 2.2 equivalent of 3-hexylthiophene carboxylate salt (**103b**). The bromination reaction afforded the corresponding product with yield 91%, and subsequent cross-coupling provided the sexithiophene **116** in 61% yield. The octithiophene derivative (**117**) was obtained from the same iterative reaction sequent, where product **116** is brominated in 89% yield, then underwent cross-coupling with the same carboxylate salt (**103b**) to afford product **117** in 81% yield. Further iteration of octithiophene derivative **117** afforded decithiophene derivative (**118**) with excellent yields of 89% for the bromination of **117** and 81% yield for subsequent decarboxylative cross-coupling reaction of brominated **117**. Interestingly, we did not observe any homo-coupling product from the carboxylate coupling partner throughout all of our synthesis, where similar reports using a Stille

reaction sequence often afforded a homo-coupling by-product (5-15%) from the organotin functionalized thiophene substrates.[78] The absence of homo-coupling by-product provides a more efficient purification as the homo-coupling impurities often have similar properties to the target molecules.

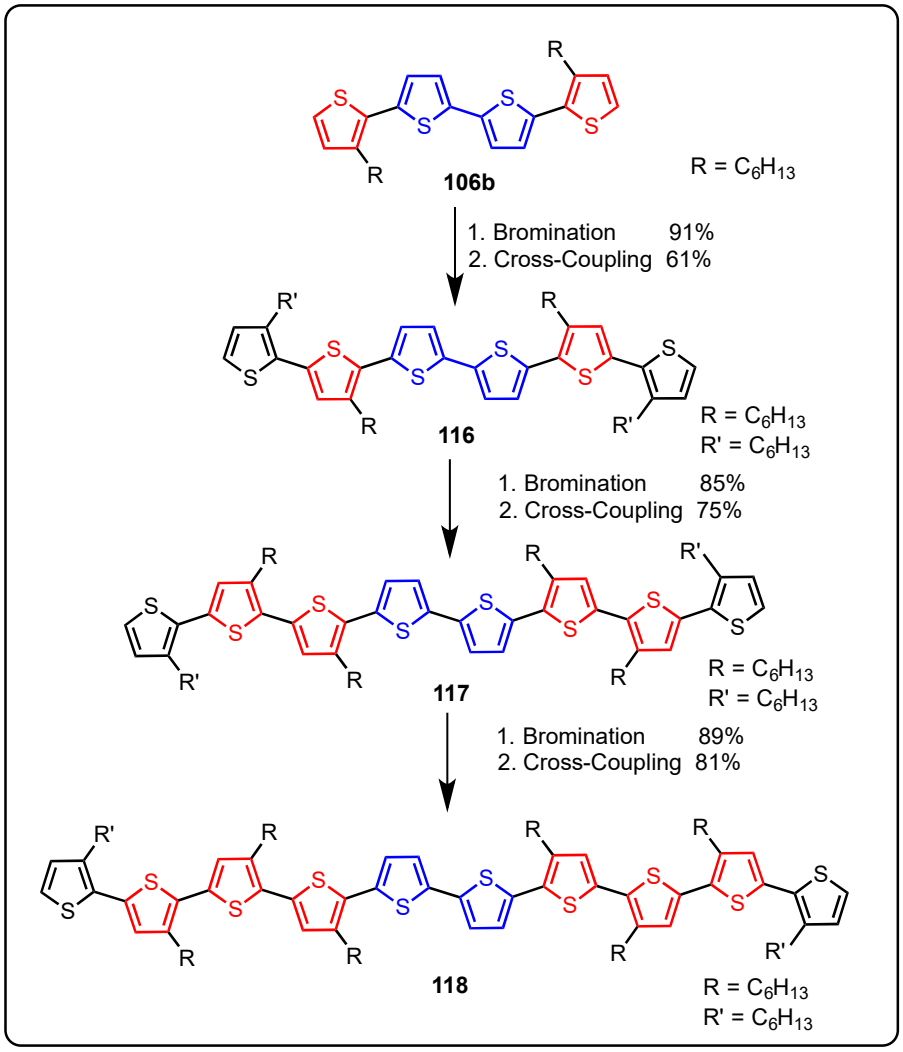


Figure 32. Iterative Synthesis of Oligothiophenes

2.5. E-factors of Methodologies

As shown in Figure 33, we compared our conditions with related synthetic methods utilizing palladium catalysts through the environmental-factor (E-factor) and atom economy metrics to evaluate the sustainability of this decarboxylative cross-coupling method.[79] Similar synthesis use Suzuki cross-coupling to obtained product **106b** with 78% yield, where they

utilized 2-(3-hexylthiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**119**) as nucleophilic cross-coupling partner with 2,5-dibromothiophene(**104a**).[80] Another report uses Still cross-coupling with **2**-bromo-3-hexylthiophene (**120**) and 2,5-bis(trimethylstannyl)thiophene (**121**) to obtained product **106b** with a 70% yield.[81] The E-factor is a measurement of the waste produced over the product obtained for each reaction. The reaction with low E-factor value translate to a lower waste production process compare to others. In this scenario of producing terthiophene **106b**, our method only has E-factor of 4.1 compared to 9.0 for the Suzuki reaction, and 5.1 from the Stille cross-coupling for model product **106b**. Atom economy reflects the conversion efficiency for a synthesis. It depicts how efficiently the atoms of the starting material are incorporated into the desired product.[79] In this case, the decarboxylative coupling method demonstrated a higher efficiency (55%) compared to both the corresponding Suzuki (49%) and Stille (44%) cross-couplings.[80,81] Additionally, our method also provides further improvements based on the short reaction time (8 min) compared to the Suzuki (48h)[80] and Stille (16h)[81] alternatives.

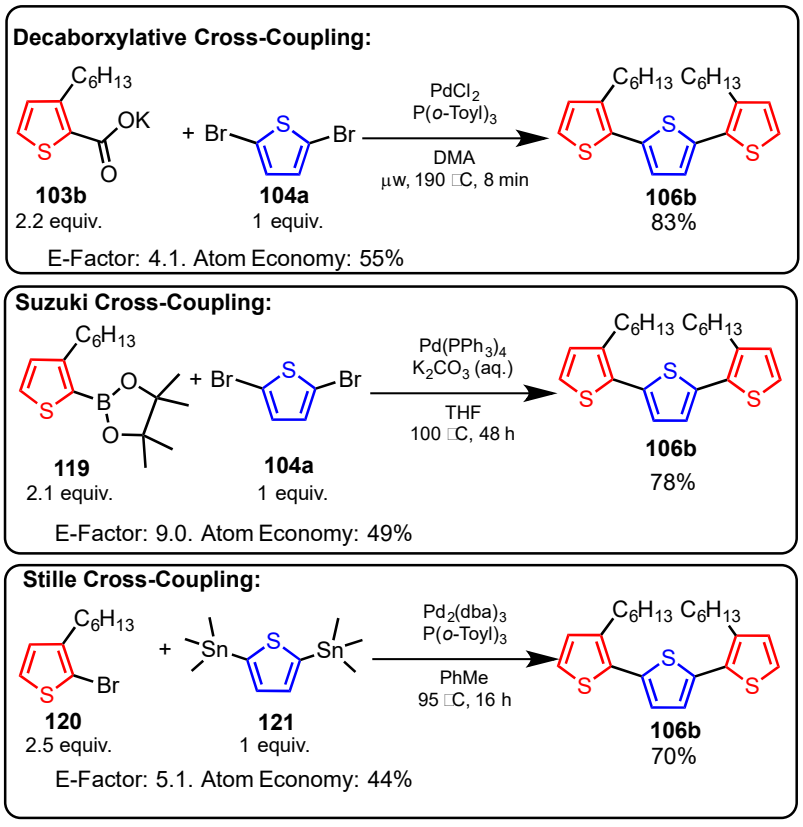


Figure 33. Comparison of Green Chemistry Index with Different Synthetic Methods

Chapter 3. Synthesis of Regioregular Poly/oligothiophene by Decarboxylative Cross-Coupling

3.1. Decarboxylative Cross-coupling for Regioregular Poly- and Oligo-thiophene

Regioregularity of the poly/oligothiophene previously have been shown to play an important role for the performance organic electronic application.[15] The exact nature of the structure-property relationship is still under debate.[1] A well-established synthetic method to readily access a library of regioregular oligothiophene would facilitate the study of this relationship. Previous reported synthesis of discrete oligothiophene often followed an iterative process with protection-deprotection reactions and/or installation of functional groups for extending the oligomer chain.[13,24] The introduction of protecting groups and metallic by-product from the traditional cross-couplings undermined the prospect of oligothiophenes as promising candidate for green energy application, as a result, there is need for a greener synthetic approach. The synthesis of polythiophene with traditional cross-coupling reactions faces the same dilemma from their stoichiometric metallic by-product.[14,78] A chemical compromise could be made by using carboxylic acid as a relative benign cross-coupling partner to lower the metallic by-product. The aim of the research described in this chapter is first to apply decarboxylate cross-coupling for the synthesis of regioregular oligothiophenes and then further extending this method to polythiophene synthesis. The utilization of potassium 3-allkylthiophene carboxylate salts (**103**) has been examined in chapter two and proven to be a robust synthetic approach for symmetrical oligothiophene. We proposed to synthesize regioregular oligothiophene through an iterative sequence (Figure 34). The iterative process initiates with cross-coupling between of alkyl 2-bromo-3-alkylthiophene carboxylate ester (**122**) with thiophene carboxylate salts (**103**), then followed by the hydrolysis of the resulting bithiophene carboxylate ester (**123**) to generate carboxylate salt that could re-enter the sequence for further elongation of the oligomer chain. Furthermore, the di-functional monomer (Figure 35, **124**) that bears both cross-coupling partners will be tested toward the synthesis of poly 3-alkylthiophene (**125**).

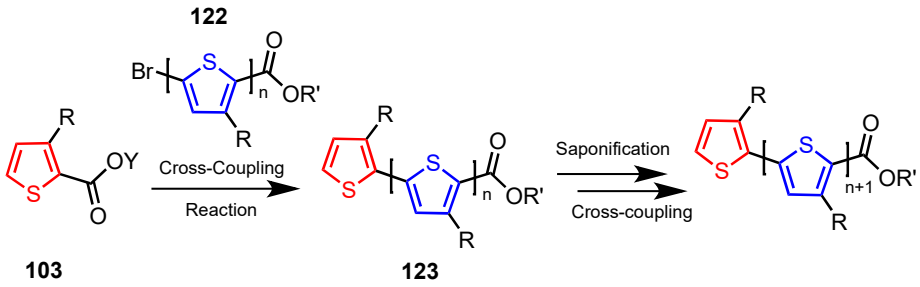


Figure 34. Proposed Iterative Synthesis of Regioregular Oligothiophenes

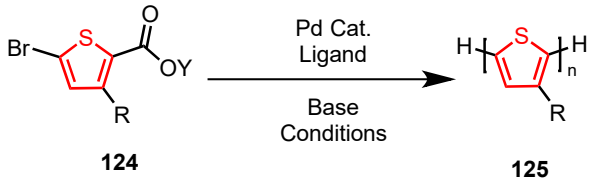


Figure 35. Proposed Synthesis of Regioregular Polythiophene

3.2. Synthesis of di-Functional Building Blocks

The first goal of this project is to synthesize the di-functional thiophene derivative (**124b**) since it can be easily converted to carboxylate ester (**122**). There are few reports related to 5-bromo-3-methylthiophene-2-carboxylic acid and its corresponding ester.[76,82] Without a published procedure, we devised two possible synthetic pathways (Figure 36) that diverge from the commercially available 3-hexylthiophene (**82**). In path A, the formylation of 3-hexylthiophene (**82**) is followed by the bromination of the resulting product **126**. Oxidation of the brominated product **127** subsequently affords the desired di-functional monomer **128.** Alternatively, path B begins with the bromination of 3-hexylthiophene (**82**) to afford 5-bromo 3-hexylthiophene (**126a**). Subsequent formylation of the brominated derivative yields the common intermediate product **127**. The efficiency of the two synthetic pathways was evaluated based on the yield of di-functional monomers **128**.

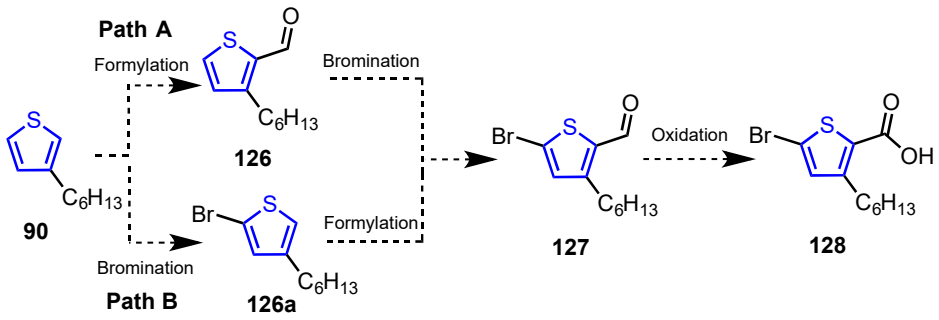


Figure 36. Proposed Synthetic Pathways for Target di-Functional Building Block (128).

The formylation of 3-hexylthiophene (**82**) proceeds in 90% conversion to produce 3-hexylthiophene carbaldehyde intermediates (Figure 37). The selectivity for desired 3-hexylthiophene-2-carbaldehyde (**126)** is 80%, while the other 20% is the 3-hexylthiophene-5-carbaldehyde. The crude mixture was used directly in the bromination step without further purification. The 5-bromo-3-hexylthiophene-2-carbaldehyde (**127**) is obtained in a 96% conversion from the aldehyde intermediate **126** as a mixture of the two isomers. Subsequent oxidation results in essentially complete conversion from the brominated aldehyde product **127**, and the isomer mixture is separated by column chromatography with 62% isolated yield for the desired di-functional thiophene derivative (**128**).

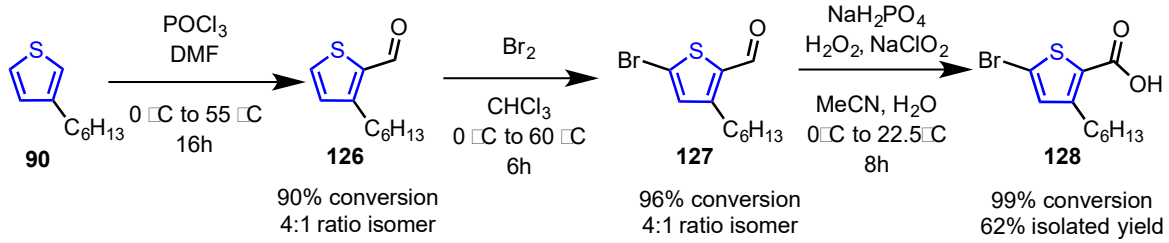


Figure 37. Synthetic Pathway of di-Functional Building Block (128) by Path A.

In Path B (Figure 38), the initial bromination of **82** was achieved with a moderate yield of 66% for 5-bromo-3hexylthiophene (**126a**). The formylation step results in a mixture of the bromo- and chloro- substituted derivatives. The side-product 5-chloro-3-hexylthiophene-2-carbaldehyde (**127a**) is difficult to separate from the desired intermediate **127**, which is only observed in 10% yield based on ^{1}H NMR spectroscopy.

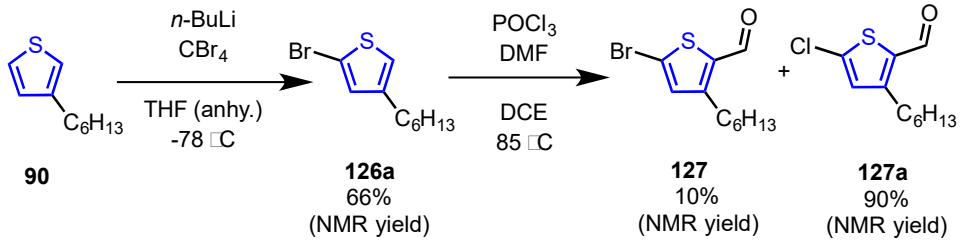


Figure 38. Synthetic Pathway of di-Functional Building Block (128) by Path B.

Overall, Path A is the more practical approach for the synthesis of 5-bromo-3-hexylthiophene-2-carboxylic acid (**128**) (Scheme 20). The esterification of the carboxylic acid in **128** under acidic condition affords the alkyl esters **129a**, **129b**, and **129c.** The reaction with ethanol results in an

80% yield of the ethyl ester **129a**, while the methyl ester **129b** is obtained with 35% yield from methanol, and the *iso*-propyl ester **129c** was obtained with 51% from isopropanol.

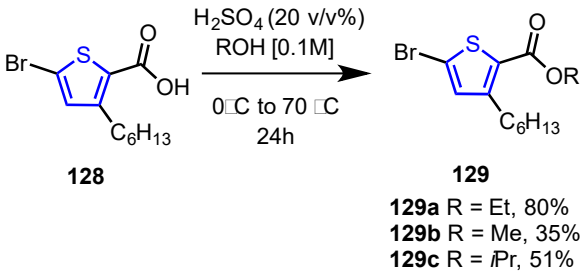


Figure 39. Esterification for di-functional building block 128

3.3. Optimization of Cross-Coupling Reaction Condition

The first step of oligothiophene synthesis is to optimize the cross-coupling reaction for elongating the oligomer chain. Bithiophene derivative **130a** is used as a model substrate for exploring reaction conditions (Figure 40). The bithiophene derivative **130a** is prepared from potassium 3-hexylthiophene carboxylate salt **103b** with the ethyl ester substrate **129a**. The bithiophene product **130a** was synthesized using a previously reported procedure (Table 2, Entry 1) which offer a limited yield of 55%. The yield was only partially improved to 59% by increasing the reaction time from 8 mins to 16 mins (Entry 2). To further optimize the reaction, different palladium sources and ligands evaluate for the decarboxylative cross-coupling. The bidentate ligand 1,1'-bis(diphenylphosphino)ferrocene (dppf) with palladium chloride ($PdCl_2$) did not improve the yield (Entry 3). While the sterically-hindered ligand Johnphos with $PdCl_2$ offered an improved yield of 71% (Entry 4), changing the palladium source to Pd_2dba_3 reduced the yield to 61% (Entry 5). Because the moderately bulky ligand tris(*o*-tolyl) phosphine provided the greatest improvement in yield (76%, Entry 6), it was used in the final optimization. By substituting of the solvent from dimethyl formamide (DMF) to dimethyl acetamide (DMA), the yield was improved to 84% (Entry 7). During the course of optimization, we did not observe any homo-coupling product of the unreacted starting material **129a**.

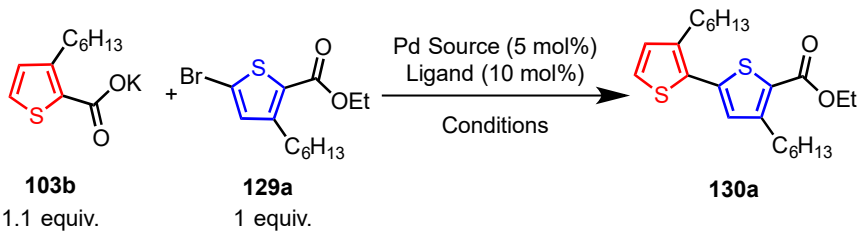


Figure 40. Mode Synthesis of Bihiophene for Optimization of Reaction Condition

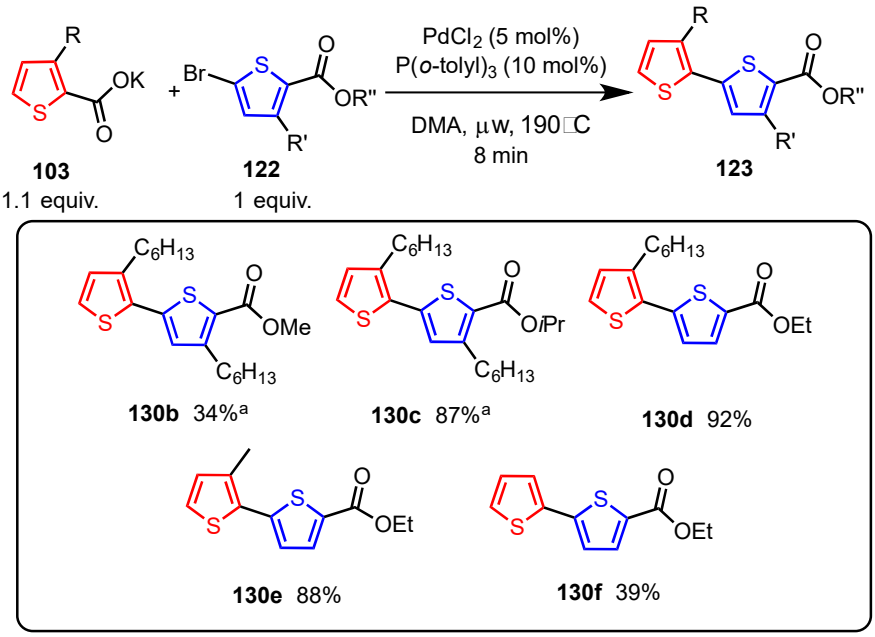
Table 2. Optimization of Bithiophene Synthesis

Entry	Pd source, ligands	Condition	Yield (%)
1	Pd(*t*-Bu$_3$P)$_2$	DMF, µw, 190 ℃, 8 min	55
2	Pd(*t*-Bu$_3$P)$_2$	DMF, µw, 190 ℃, 16 min	59[a]
3	PdCl$_2$/dppf	DMF, µw, 190 ℃, 8 min	55[a]
4	PdCl$_2$/JohnPhos		71
5	Pd$_2$dba$_3$/JohnPhos		61[a]
6	PdCl$_2$/P(*o*-Tolyl)$_3$		76
7	PdCl$_2$/P(*o*-Tolyl)$_3$	DMA, µw, 190 ℃, 8 min	84

[a] Yield determined by ^{1}H-NMR with 1,3,5-Trimethoxybenzene as internal standard

Next, we explored the substrate scope by using different thiophene carboxylate salts **103** and the brominated thiophene carboxylate ester **122** (Figure 24). This condition is further applied to 3-hexylthiophene carboxylate methyl ester **129b** but only affords a 34% yield for the corresponding bithiophene product **130b** with the methyl 3-hexylthiophene-2-carboxylate ester as the major by-product. The more sterically hindered isopropyl ester derivative **129c** with the 3-hexylthiophene carboxylate salt **103b** gave an excellent yield of 87% for bithiophene product **130c**. Commercially available ethyl 2-bromo-thiophene carboxylate was also tested with 3-methyl thiophene carboxylate salt **103a** to produce the bithiophene derivative **130d** with an excellent yield of 92%. This showed that the alkyl substituent at the 3-position of electrophilic cross-coupling partner does not affect the reaction yield. 3-methyl thiophene carboxylate salt (**103a**) was also tested with ethyl 2-bromo-thiophene carboxylate to afford 88% yield of the

corresponding bithiophene product **130e**. Unsubstituted potassium thiophene carboxylate salt (**103c**) only resulted in a limited yield of 39% for the bithiophene product **130f**.



[a]. Yield determined by ^{1}H-NMR with 1,3,5-Trimethoxybenzene as internal standard

Figure 41. Substrate Scope for Bithiophene Moieties

3.4. Optimization of Saponification

Subsequently, conditions for the hydrolysis of bithiophene ethyl ester **130a** were investigated (Figure 42). The initial experiments were conducted with NaOH (Table 3, Entry 1) and KOH (Entry 2) in a 1:1 mixture of THF:water heated at reflux for 72 hours. NaOH affords the carboxylate acid product **131** with 68% isolated yield, and KOH resulted in a similar yield of 69%. Despite the acceptable yields, these conditions did not achieve a full conversion of the ethyl ester **130a** and required a lengthy three-day heating process. The reaction was further optimized by introducing additives to generate the *tetra*-butyl ammonium hydroxide (*n*Bu4NOH) *in-situ* as it has been used to hydrolyze a similar hydrophobic thiophene carboxylate ester.[13] When *tetra*-butyl ammonium chloride (TBAC) and *tetra*-butyl ammonium bromide (TBAB) were added with KOH at two equivalents, only trace amount of product **131** were observed even after 16 hours heating at reflux (Entry 3,4). In subsequent reactions, the molar equivalent of KOH and TBAC were increased to determine the effect on yield. At 4 equivalents to ethyl ester **130a** (Entry 5), an improved yield of 58% for product **131** was observed. Further increasing the

KOH and TBAC to 8 equivalents (Entry 6) afforded an excellent yield of 80% for carboxylic acid **131**. Full conversion of carboxylate ester **130a** is obtained when KOH and TBAC were increased to 10 equivalents (Entry 7).

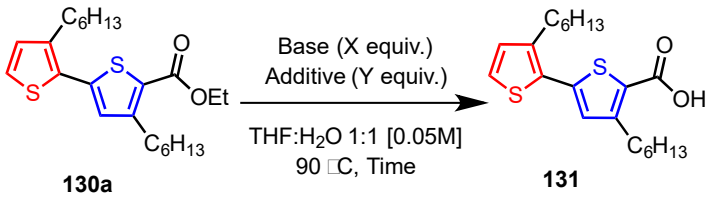


Figure 42. Hydrolysis of Bithiophene Ethyl Ester 130a

Table 3. Optimization of Saponification

Entry	Base (X equiv.)	Additive (Y equiv.)	Time	Isolated Yield (%)
1	NaOH (5 equiv.)	None	72 h	68
2	KOH (5 equiv.)	None	72 h	69
3	KOH (2 equiv.)	TBAC (2 equiv.)	16 h	Trace[a]
4	KOH (2 equiv.)	TBAB (2 equiv.)	16 h	Trace[a]
5	KOH (4 equiv.)	TBAC (4 equiv.)	16 h	58[a]
6	KOH (8 equiv.)	TBAC (8 equiv.)	16 h	80[a]
7	KOH (10 equiv.)	TBAC (10 equiv.)	16 h	81[a, b]

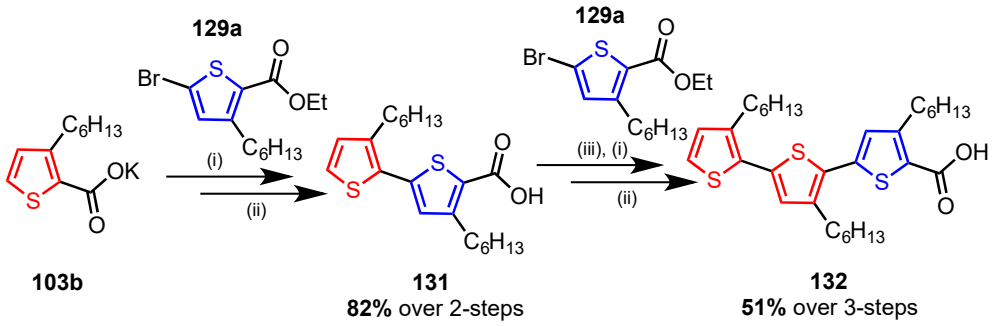
[a] Data is provided by Sarah Taylor. [b] Full conversion is achieved, only 81% isolated.

3.5. Synthesis of Regioregular Poly/Oligothiophene

3.5.1. Iterative Synthesis of Regioregular Oligothiophene

Following the cross-coupling and saponification reactions, oligomerization was explored *via* the iterative synthesis of regioregular oligothiophenes. This iterative approach consists of a cross-coupling reaction between the 3-hexylthiophene carboxylate salt **103b** and bromo thiophene carboxylate ester **129a** (Figure 43). The resulting crude mixture was subsequently saponified without purification and the corresponding bithiophene carboxylic acid is obtained in 82% yield over the two steps. The subsequent iteration, initiated with salt formation using

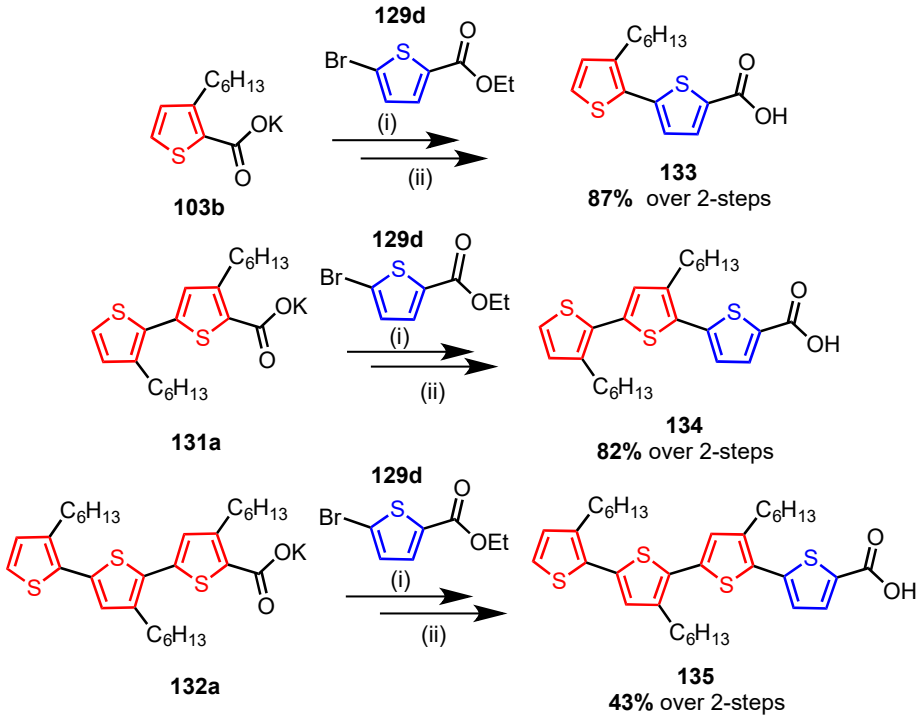
potassium *tert*-butoxide in THF, resulted in the carboxylate salt. This salt is directly used for the cross-coupling with carboxylate ester **129a**. The desired terthiophene carboxylic acid **132** was obtained from bithiophene starting material **131** in three steps and with 51% overall yield.



(i) $PdCl_2$/P(*o*-Tolyl)$_3$, DMA, 190°C, μw, 8 min. (ii) KOH, TBAC, THF:H_2O, 90 °C, 16 h
(iii) KO*t*Bu, THF, 22.5 °C, 16 h

Figure 43. Iterative Synthesis of Terthiophene and Quaterthiophene

We have demonstrated the possibility of constructing regioregular oligothiophenes. However, we have also observed a decrease of 30% in yield from bithiophene product (**131**) to terthiophene product (**132**), as well as a mixture of side products that are difficult to separate. One variable that may influence reactivity and subsequently cause decreases in yield is the length of the oligothiophene carboxylate salt. Using 3-hexylthiophene carboxylate salt **103b**, **131a**, and **132a**, we investigated the effect of the oligothiophene length (Figure 44). An excellent yield of 87% for bithiophene product **133** is obtained with monomeric thiophene carboxylate salt (**103b**) cross-coupled with ethyl-2-bromo-5-thiophene carboxylate ester (**129d**). A slight decreased is observed with bithiophene carboxylate salt (**131a**) for the corresponding product **134** (82% yield). A large decrease in yield is observed when the terthiophene carboxylate salt (**132a**) is employed, where only 43% yield of quaterthiophene product **135** was observed.



(i) $PdCl_2/P(o\text{-Tolyl})_3$, DMA, 190 °C, μw, 8 min. (ii) KOH, TBAC, $THF:H_2O$, 90 °C, 2 – 4 h

Figure 44. Reactivity of Oligothiophene Carboxylate Salt.

3.5.2. Synthesis of Polythiophene

Concurrently, the decarboxylative cross-coupling polymerization was also explored with 5-bromo-3-hexylthiophene-2-carboxylic acid (**128**) and potassium 5-bromo-3-hexylthiophene-2-carboxylate (**128a**) (Figure 45). First attempts use previously reported condition, where the carboxylic acid monomer **128** was polymerized with $Pd(t\text{-}Bu_3P)_2$ and an excess amount of cesium carbonate based at 190℃ for 8 minute (Table 4, Entry 1). The resulting polymerization offer a 90% conversion of monomer into polythiophene **136**, and the corresponding polymer has a weight average molecule weight of 6499 Da with moderate dispersity ($Đ_M$) of 1.93. Increasing the reaction time to 16 min (Entry 2) decreased the molecular weight to 5258 Da and resulted in a more dispersed polymer with a $Đ_M$ of 4.32. Further extending reaction time to 32 min (Entry 3) slightly increased the molecular weight to 6925 Da with a similar $Đ_M$ of 4.41. Overall, increasing the reaction time only lowered the conversion of monomer to 71% (16 min) and 66% (32 min).

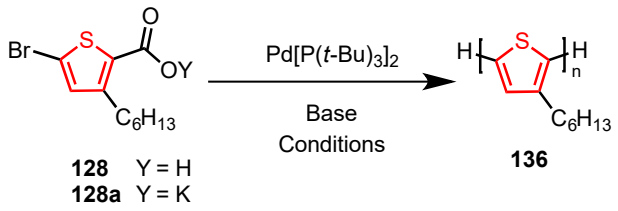


Figure 45. Polythiophene Synthesis from di-Functional Monomer

Table 4. Decarboxylative Cross-Couplng Polymerization under Microwave Condition

Entry	Condition	Base	Mw (Da)[a]	$Đ_M$[a]	Conversion (%)
1	μw, 190 ℃, 8 min	Cs_2CO_3 (1.5 equiv.)	6499	1.93	90
2	μw, 190 ℃, 16 min	Cs_2CO_3 (1.5 equiv.)	5258	4.32	71
3	μw, 190 ℃, 32 min	Cs_2CO_3 (1.5 equiv.)	6925	4.41	66

a. Data is measured by GPC with THF as eluent.

Notably, despite the low conversion for polymerization, none of the entries in Table 4 showed residual monomer **128**. The thermal stability of monomer **128** was then determined with thermogravimetric analysis to examine the possible degradation. As shown in Figure 27, initial decomposition of the 5-bromo 3-hexylthiophene-2-carboxylic acid (**128**, red line) begins at 140 ℃, with approximately 50 percent decomposation at the reaction temperature of 190 ℃. Additionally, the 5-chloro 3-hexylthiophene-2-carboxylic acid (**128b**, blue line) has slightly lower decomposition temperature as compared to the bromo substituted monomer. As a result, subsequent polymerizations were subsequently adapted to proceed at lower reaction temperatures. The result of this low temperature approach is shown in Table 5. The polymerization of carboxylate salt **128a** was conducted at 120 ℃, for 24h with Pd(t-Bu_3P)$_2$ (table 5, Entry 1). The resulting polymer has a higher molecular weight of 8483 Da compare to the results described in Table 4. However, it only affords 22% conversion of the monomer **128a** with increasing $Đ_M$ of 6.15 for the corresponding polymer. The molecular weight of the polythiophene further increased to 10650 Da when the reaction time was extended to 48h (Entry 2). Conversion of monomer **128a** was improved to 44%, however with an extremely high dispersity of 9.44. Interestingly, further increasing the reaction time to 72h reaction time only produced lower

molecule weight of corresponding polythiophene **136** to 5605 Da (Entry 3,), but with similar conversion of 45% and lower $Đ_M$ of 6.44.

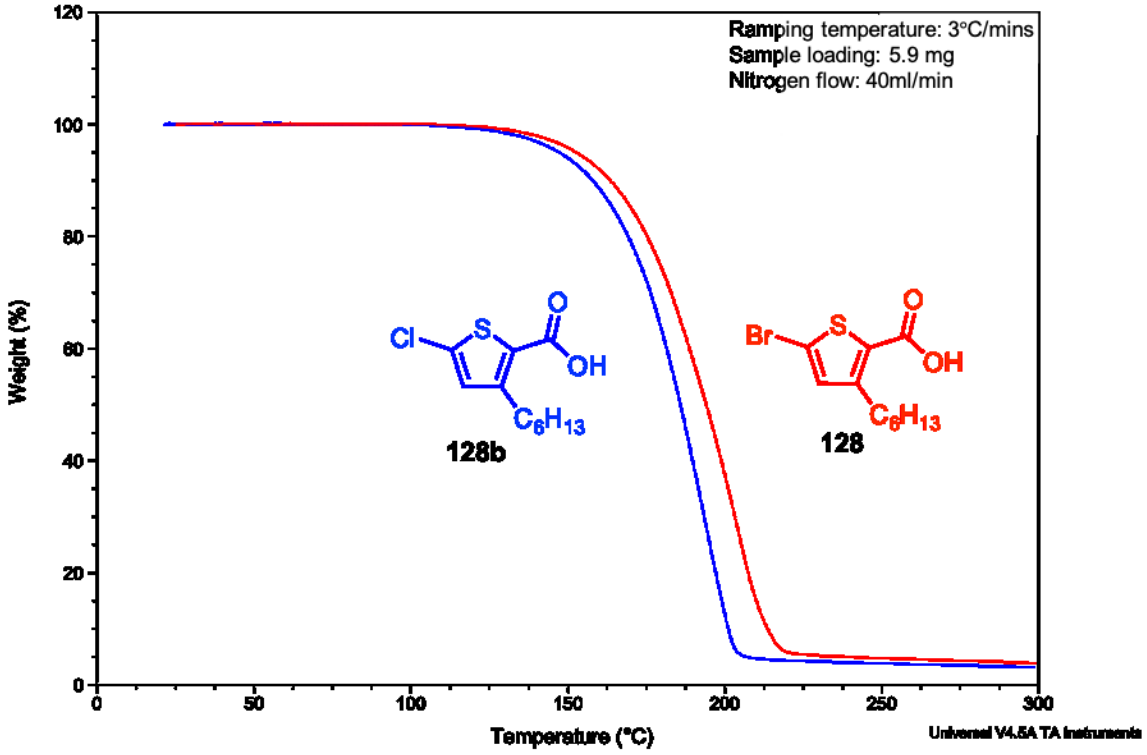


Figure 46. Thermal Grametric Analysis (TGA) of Monomers.

Table 5. Polymerization Under Thermal Conditions

Entry	Condition	Base	Mw (Da)[a]	$Đ_M$[a]	Conversion
1	Δ, 120 ℃, 24 h	None, Y = K	8483	6.15	22
2	Δ, 120 ℃, 48 h	None, Y = K	10650	9.44	40
3	Δ, 120 ℃, 72 h	None, Y = K	5605	6.44	45

a. Data is measured by GPC with THF as eluent.

Chapter 4. General Conclusions

The overall objective of this thesis was to explore decarboxylative cross-coupling as an efficient synthetic tool for thiophene-based materials as there have been only a few reports of decarboxylative cross-coupling related to these materials. In summary, we have developed a new method for the iterative synthesis of symmetrical oligothiophenes. This methodology has higher efficiency with improved E-factor and higher atom economy compared to related routes. The scope of this method has been extended to a library of thiophene-based materials. We further demonstrated a modular route to construct a discrete library of symmetric oligothiophenes with various chain lengths. Based thereon, we have synthesized linear oligothiophenes up to a length of ten thiophene units. Furthermore, we also demonstrated the step-wise synthesis of regioregular oligothiophene with an iterative process by decarboxylative cross-coupling and hydrolysis of carboxylate ester on di-functional monomer. Similarly, poly 3-hexylthiophene was prepared utilizing the same synthetic condition. Overall, our works highlights the utility of decarboxylative cross-coupling methodologies and its applications in the ongoing development of organic electronic materials.

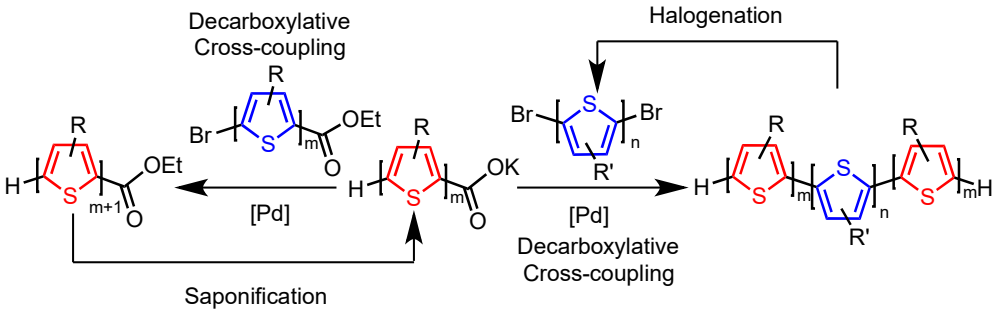


Figure 47. Decarboxylative Cross-Coupling as Versatile Tool for Thiophene-based Materials.

Chapter 5. Future Work

Future research will continue on constructing long regioregular oligothiophene, as well as polythiophene. Amphiphilic oligothiophenes have been attracting more attention in the recent years, where it been proposed and tested as biomarker for amyloid aggregates.[83] Recent report demonstrated oligothiophenes could be the potential lead compound for Alzheimer's and prion diseases.[84] The hydrophobic nature of the alkyl substituents prevents the usage of traditional oligothiophene derivatives in biological application, and generally form aggregates in aqueous media. Previous research from our group explored the usage of tri-arylated thiophene with 3-sulfonamide substituents for modulating amyloid aggregates formation.[73] Herein, we propose the synthesis of sulfonamide-substituted oligothiophenes as potential biomarker for amyloid related diseases. The established synthesis should be further tested with thiophene carboxylic acid with hydrophilic substituents at the C3-position.

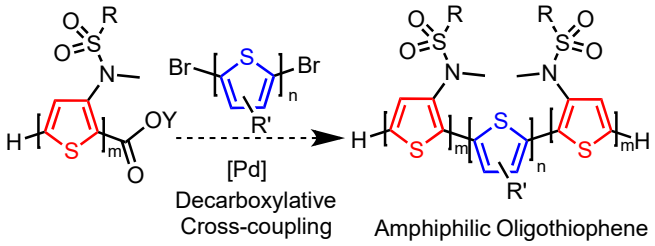


Figure 48. Proposed Synthesis of Amphiphilic Poly/Oligothiophene

Chapter 6. Experimental

6.1. General procedure

General procedure for decarboxylative cross-coupling (diarylation) (Procedure 1)

The procedure employed by Forgione and co-workers was used with modifications.[69] In a 2-5 mL oven dried microwave vial that is open to air, potassium thiophene carboxylate salt (2.2 equiv), aryl di-bromide (1 equiv), palladium (II) chloride (0.05 equiv), Tri(*o*-tolyl)phosphine (0.1 equiv.) and anhydrous DMA (0.1 M of the aryl di-bromide solution). The vial was capped with a septum and the mixture was pre-stirred for 45 seconds at 23 °C and submitted to microwave heating at 190 °C for 8 min with stirring and the very high absorption setting. The crude mixture was cooled to 23 °C. The solution was then diluted with EtOAc or Chloroform and the organic layer was washed with saturated NaCl aqueous solution (3x), saturated $NaHCO_3$ aqueous solution (1x), distill water (3x), and saturated NaCl aqueous solution (1x). The aqueous phases were combined and extracted with EtOAc. The combined organic phases were dried over sodium sulfate, and after filtration the solvent was evaporated to provide the crude compound. The crude compound is purified by column chromatography.

General procedure for bromination with NBS under sonication (Procedure 2)

The procedure was adapted from previous report with some modifications.[77] Oligothiophene (1 equiv.) and NBS (2.2 equiv.) was dissolved in 0.05 M EtOAc in an oven-dried round bottom flask covered with aluminum foil. The mixture was immersed in ultrasonic bath for 1 hour at room temperature. The solution was diluted with EtOAc and washed with distilled water (3x), and saturated NaCl aqueous solution (2x). The aqueous phase was extracted with additional EtOAc. Combined organic phases were dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure. The compound was purified with column chromatography.

General procedure for decarboxylative cross-coupling (monoarylation) (Procedure 3)

The procedure employed by Forgione and co-workers was used with modifications.[69,73] In a 2-5 mL oven dried microwave vial that is open to air, potassium thiophene carboxylate salt (1.1 equiv), thiophene bromide (1 equiv), palladium (II) chloride (0.05 equiv), Tri(*o*-tolyl)phosphine

(0.1 equiv.) and anhydrous DMA (0.1 M of the thiophene bromide solution). The vial was capped with a septum and the mixture was pre-stirred for 45 seconds at 23 °C and submitted to microwave heating at 190 °C for 8 min with stirring and the very high absorption setting. The crude mixture was cooled to 23 °C. The solution was then diluted with EtOAc or Chloroform and the organic layer was washed with saturated NaCl aqueous solution (3x), saturated $NaHCO_3$ aqueous solution (1x), distill water (3x), and saturated NaCl aqueous solution (1x). The aqueous phases were combined and extracted with EtOAc. The combined organic phases were dried over sodium sulfate, and after filtration the solvent was evaporated to provide the crude compound. The crude compound is purified by column chromatography or directly used for saponification.

General procedure for saponification (Procedure 4)

The reported procedure was adopted with modifications.[13] Ethyl thiophene ester was dissolved in an THF:water mixture (1:1, 0.1M). Potassium hydroxide (10 equiv.) and TBAC (10 equiv.) was added into the stirred solution. The reaction mixture was heated to 90 °C under reflux for 16 hours. The reaction mixture was extracted with EtOAc (3x). The combined organic phases were washed with distilled water (5x) and NaCl aqueous solution (3x), then dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture is separated by column chromatography.

General procedure for formylation of thiophene (Procedure 5)

The reported procedure was adopted with modifications.[85] Thiophene substrate was dissolved in anhydrous DMF (0.7 M). Phosphoryl chloride (8 equiv.) was added drop-wise into the stirred solution in an ice-water bath. The reaction mixture was slowly warmed to 22.5 °C, and was heated in an oil bath for 16 hours at 55°C. The reaction mixture was then quenched with ice-cold saturated sodium acetate solution until solution is pH neutral. The mixture was extracted with diethyl ether (3x). The combined organic phases were washed with distilled water (5x) and NaCl aqueous solution (3x), then dried over anhydrous sodium sulfate, filtered through a short silica column, and evaporated under reduced pressure. The reaction mixture is used directly for the next step.

General procedure for oxidation of thiophene carbaldehyde (Procedure 6)

The reported procedure was adopted with modifications.[76] Thiophene carbaldehyde was dissolved in an acetonitrile:water mixture (1:1, 0.1M). Sodium Phosphate monobasic (1.3 equiv.) and H_2O_2 (1.3 equiv. 10% v/v) was added into the stirred solution in an ice-water bath. After 30 mins, sodium chlorite (1.5 equiv.) was added in one portion. The reaction mixture was slowly warmed to 22.5 °C and left for 24 hours. The reaction mixture was extracted with EtOAc (3x). The combined organic phases were washed with distilled water (5x) and NaCl aqueous solution (3x), then dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture is separated by column chromatography.

General procedure for salt preparation (Procedure 7)

Thiophene-2-carboxylic acid and potassium *tert*-butoxide (1.0 equiv.) were placed in oven-dried, argon purged round bottom flask. Anhydrous degassed THF was added into reaction flask under argon flow. The reaction mixture was stirred under 22.5 °C for 4-24 hours. The solvent was evaporated under reduced pressure, and dried under high-vacuum line overnight. The product yield is quantitative and used without purification and stored under argon.

General procedure for esterification (Procedure 8)

Thiophene-2-carboxylic acid (1.0 equiv.) was dissolved in desired alcohol (0.1M) and were placed ice-bath, concentrate sulfuric acid was added into cold solution drop-wise (20% V/V to total alcohol solvent). The mixture was slowly heated to 70 °C and stirred for 16 hours. The reaction mixture was neutralized with $NaHCO_3$ solution, and then extracted with EtOAc (2x), then the combined organic phases were washed with distilled water (3x), NaCl aqueous solution (1x), and then dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture is separated by column chromatography.

General procedure for bromination of starting materials (Procedure 9)

The reported procedure was adopted with modification.[86] Thiophene derivative, NBS (2.2 equiv.) were mixed in DMF solution (0.1 M) in an amber vial. The mixture was stirred in ice bath and slowly warmed to 22.5°C for 16 hours. The reaction mixture was extracted with EtOAc or diethyl ether (2x), then the combined organic phases were washed with distilled water (3x), NaCl aqueous solution (1x), and then dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture is separated by column chromatography.

6.2. E-Factor & Atom economy calculation

Simple E factor values are based on reference literatures,[79] where only the mass of reagents, product, 10% of reaction solvent, and by-product generated in reaction are considered.

The equation used for calculation depicted as following:

$$EF = \frac{\sum m(\textit{starting materials}) + \sum m(0.1 * \textit{solvent}) - \sum m(\textit{product})}{\sum m(\textit{product})}$$

Atom economy values are based on reference literature, the calculation only consider the molecular weight of all the reagent and product. 90% of solvent, catalyst, additives are omitted in this calculation

The equation used for calculation depicted as following:

For a reaction 2A+B→C

$$\text{Atom economy} = \left(\frac{M.W\ of\ product(C)}{2*(MW\ of\ A)+(MW\ of\ B)}\right) * 100\%$$

Decarboxylative reaction:

Density of DMA= 0.940 g/ml[3]

$$EF = \frac{[(0.0362+0.0826)+\left(0.1*1.5ml*0.94\frac{g}{ml3}\right)]-(0.052g)}{0.052g} = 4.1$$

$$\text{Atom economy} = \left(\frac{416.7}{2*(250.4)+(241.9)}\right) * 100\% = 55\%$$

Suzuki reaction[80]:

Density of THF = 0.889 g/ml[3], Density of water = 1.00 g/ml[3]

$$EF = \frac{[(1.0g+2.55g)+\left(0.1*30ml*0.889\frac{g}{ml3}\right)+\left(0.1*16.5ml*1.0\frac{g}{ml3}\right)]-(0.78g)}{0.78g} = 9.0$$

$$\text{Atom economy} = \left(\frac{416.7}{2*(294.3)+(241.9)}\right) * 100\% = 49\%$$

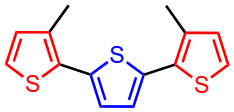
Stille reaction[81]:

Density of toluene = 0.867 g/ml[3]

EF= $\frac{[(1.86g+2.80g)+(0.1*40ml*0.867)]-(1.33g)}{1.33g}$ = 5.1

Atom economy = $\left(\frac{416.7}{(409.75)+2*(247.2)}\right) * 100\%$ = 44%

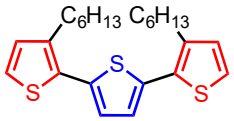
6.3. Characterization of Compounds



3,3''-dimethyl-2,2':5',2''-terthiophene (105a)

General procedure 1 was followed using 2,5-dibromothiophene (36.2 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a yellow oil (36 mg, 85%).

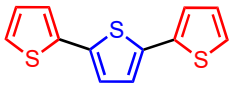
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 5.1 Hz, 1H), 7.08 (s, 1H), 6.89 (d, *J* = 5.1 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.21, 134.01, 131.41, 130.83, 125.69, 123.29, 15.44. HRMS (EI): calculated for $C_{14}H_{12}S_3$ $[M]^+$: 276.00956, found: 276.00934.



3,3''-dihexyl-2,2':5',2''-terthiophene (105b)

General procedure 1 was followed using 2,5-dibromothiophene (36.2 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a light yellow solid (52 mg, 83%).

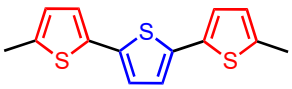
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 5.2 Hz, 2H), 7.06 (s, 2H), 6.94 (d, *J* = 5.2 Hz, 2H), 2.81 – 2.77 (m, 4H), 1.65 (p, *J* = 7.5 Hz, 4H), 1.39 (dt, *J* = 14.6, 6.8 Hz, 4H), 1.33 – 1.29 (m, 8H), 0.89 (t, *J* = 7.0 Hz, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.69, 136.04, 130.38, 130.02, 126.04, 123.71, 31.68, 30.71, 29.23, 22.62, 14.07. HRMS (EI): calculated for $C_{24}H_{32}S_3$ $[M]^+$: 417.17384, found: 417.17443.



2,2':5',2''-terthiophene (105c)

General procedure 1 was followed using 2,5-dibromothiophene (36.2 mg, 0.15 mmol) and potassium thiophene-2-carboxylate (54.8 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a light yellow solid (8 mg, 22%).

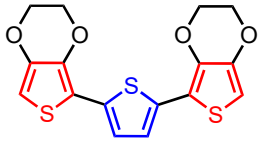
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.22 (dd, *J* = 3.6, 1.1 Hz, 2H), 7.18 (dd, *J* = 3.6, 1.1 Hz, 2H), 7.08 (s, 2H) 7.02 (dd, *J* = 5.1, 3.6 Hz, 2H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.10 (2C), 136.18 (2C), 127.85(2C), 124.45(2C), 124.28(2C), 123.67(2C). HRMS (EI): calculated for $C_{12}H_8S_3$ $[M]^+$: 247.97826, found: 247.97819.



5,5''-dimethyl-2,2':5',2''-terthiophene (105d)

General procedure 1 was followed using 2,5-dibromothiophene (36.2 mg, 0.35 mmol) and potassium 5-methylthiophene-2-carboxylate (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a yellow solid. (16 mg, 39%).

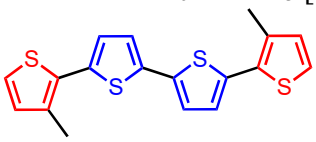
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.95 (d, *J* = 0.8 Hz, 2H), 6.94 (d, *J* = 3.6 Hz, 2H), 6.65 (d, *J* = 4.3 Hz, 2H), 2.48 (d, *J* = 1.0 Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.14, 136.02, 134.89,126.00, 125.93, 123.59, 123.47, 123.38, 15.35. HRMS (EI): calculated for $C_{14}H_{12}S_3$ $[M]^+$: 276.00956, found: 276.00926.



2,5-bis(2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)thiophene (105e)

General procedure 1 was followed using 2,5-dibromothiophene (36.2 mg, 0.15 mmol) and **103c** (74 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as orange solid (17 mg, 31%).

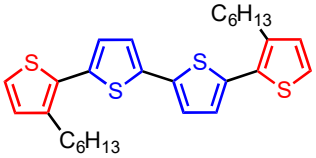
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.12 (s, 2H), 6.21 (s, 2H), 4.42 – 4.29 (m, 11H), 4.27 – 4.18 (m, 8H) ^{13}C NMR (125 MHz, Chloroform-*d*) δ 141.85, 137.37, 133.17, 122.88, 112.34, 96.73, 65.00, 64.59. HRMS (EI): calculated for $C_{16}H_{12}O_4S_3$ $[M]^+$: 363.98977, found: 363.98922.



3,3'''-dimethyl-2,2':5',2'':5'',2'''-quaterthiophene (106a)

General procedure 1 was followed using 5,5'-dibromo-2,2'-bithiophene (46.8 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a yellow solid (44 mg, 82%).

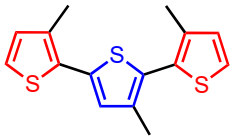
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 5.1 Hz, 2H), 7.13 (d, *J* = 3.8 Hz, 2H), 7.05 (d, *J* = 3.8 Hz, 2H), 6.89 (d, *J* = 5.1 Hz, 2H), 2.43 (s, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.55, 135.65, 134.13, 131.48, 130.84, 126.05, 123.82, 123.37, 15.49. HRMS (EI): calculated for $C_{18}H_{14}S_4$ $[M]^+$: 357.99737, found: 357.99783.



3,3'''-dihexyl-2,2':5',2'':5'',2'''-quaterthiophene (106b)

General procedure 1 was followed using compound 5,5'-dibromo-2,2'-bithiophene (46.8 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a yellow oil (68 mg, 90%).

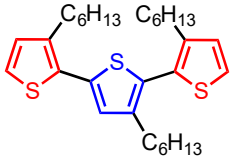
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.20 (s, 0H), 7.19 (d, *J* = 5.2 Hz, 1H), 7.14 (d, *J* = 3.7 Hz, 1H), 7.04 (d, *J* = 3.7 Hz, 1H), 6.95 (d, *J* = 5.2 Hz, 1H), 2.82 – 2.78 (m, 2H), 1.72 – 1.61 (m, 2H), 1.46 – 1.26 (m, 5H), 0.97 – 0.85 (m, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.86, 136.77, 135.30, 130.28, 130.05, 127.82, 126.51, 123.83, 31.65, 30.63, 29.69, 29.27, 22.60, 14.07. HRMS (EI): calculated for $C_{28}H_{34}S_4$ $[M + H]^+$: 498.15335, found: 498.15433.



3,3',3''-trimethyl-2,2':5',2''-terthiophene (107a)

General procedure 1 was followed using 2,5-dibromo-3-methylthiophene (38.4 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a light yellow solid (28 mg, 63%).

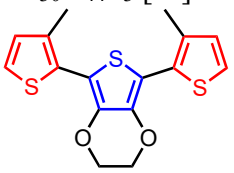
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 5.2 Hz, 1H), 7.13 (d, *J* = 5.1 Hz, 1H), 6.97 (s, 1H), 6.93 (d, *J* = 5.1 Hz, 1H), 6.88 (d, *J* = 5.1 Hz, 1H), 2.41 (s, 3H), 2.23 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.74, 136.59, 135.90, 133.81, 131.43, 130.99, 130.12, 129.11, 129.09, 128.22, 125.08, 123.09, 29.70, 15.45, 14.80. HRMS (EI): calculated for $C_{15}H_{14}S_3$ $[M]^+$: 290.02521, found: 290.02514.



3,3',3''-trihexyl-2,2':5',2''-terthiophene (107b)

General procedure 1 was followed using 2,5-dibromo-3-hexylthiophene (48.9 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as light-yellow oil (22.5 mg, 30%).

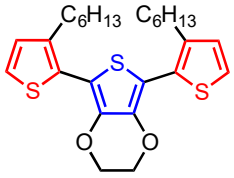
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 5.2 Hz, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 6.97 (d, *J* = 4.0 Hz, 2H), 6.92 (d, *J* = 5.2 Hz, 1H), 2.80 – 2.75 (m, 2H), 2.57 – 2.53 (m, 2H), 2.51 – 2.47 (m, 2H), 1.64 (p, *J* = 7.7 Hz, 2H), 1.57 (d, *J* = 7.1 Hz, 2H), 1.37 (dt, *J* = 14.3, 7.5 Hz, 2H), 1.33 – 1.19 (m, 18H), 0.89 – 0.82 (m, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.74, 136.59, 135.90, 133.81, 131.43, 130.99, 130.12, 129.11, 129.09, 128.22, 125.08, 123.09, 29.70, 15.45, 14.82, 14.80. HRMS (EI): calculated for $C_{30}H_{44}S_3$ $[M]^+$: 500.25996, found: 500.25973.



5,7-bis(3-methylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108a)

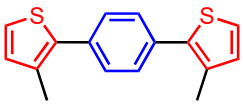
General procedure 1 was followed using 5,7-dibromo-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (40 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a light yellow solid (12 mg, 24%).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 5.1 Hz, 2H), 6.89 (d, *J* = 5.1 Hz, 2H), 4.33 (s, 4H), 2.37 (s, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.60, 135.09, 130.61, 127.42, 124.41, 109.89, 64.69, 15.49. HRMS (EI): calculated for $C_{16}H_{14}O_2S_3$ $[M]^+$: 334.01504, found: 334.01509.

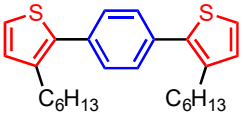


5,7-bis(3-hexylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108b)

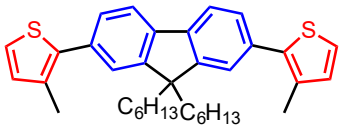
General procedure 1 was followed using 5,7-dibromo-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (40 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as light yellow oil (31 mg, 44%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 5.1 Hz, 2H), 6.97 (d, *J* = 5.0 Hz, 2H), 6.12 (s, 4H), 3.04 – 2.97 (m, 4H), 1.60 (p, *J* = 7.5 Hz, 4H), 1.37 – 1.29 (m, 4H), 1.30 – 1.23 (m, 8H), 0.89 – 0.83 (m, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.92, 153.15, 131.40, 130.80, 125.03, 79.24, 31.64, 30.40, 29.82, 29.19, 22.57, 14.05. HRMS (EI): calculated for $C_{26}H_{34}O_2S_3$ $[M]^+$: 474.17209, found: 474.17099.



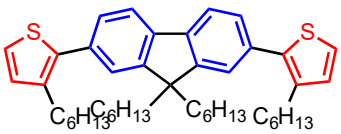
1,4-bis(3-methylthiophen-2-yl)benzene (109a)
General procedure 1 was followed using 1,4-dibromobenzene (35.4 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a colorless solid (31 mg, 76%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.52 (s, 4H), 7.23 (d, *J* = 5.2 Hz, 2H), 6.95 (d, *J* = 5.2 Hz, 2H), 2.39 (s, 6H) ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.40, 133.58, 133.36, 131.25, 131.24, 129.16, 128.96, 128.95, 123.51, 77.21, 29.71, 15.08, 15.06. HRMS (EI): calculated for $C_{16}H_{14}S_2$ $[M]^+$: 270.05369, found: 270.05304.



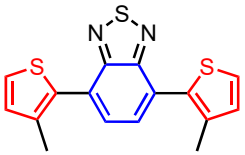
1,4-bis(3-hexylthiophen-2-yl)benzene (109b)
General procedure 1 was followed using 1,4-dibromobenzene (35.4 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a colorless oil (54 mg, 87%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 (s, 4H), 7.24 (d, *J* = 5.2 Hz, 2H), 7.00 (d, *J* = 5.2 Hz, 2H), 2.72 – 2.67 (m, 2H), 1.63 (p, *J* = 7.5 Hz, 2H), 1.36 – 1.26 (m, 6H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 138.84, 137.32, 133.72, 129.60, 129.29, 123.73, 31.61, 30.97, 29.15, 28.71, 22.58, 14.06. HRMS (EI): calculated for $C_{26}H_{34}S_2$ $[M]^+$: 410.20964, found: 410.20980.



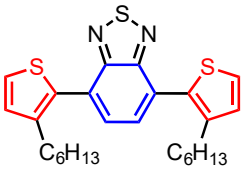
2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-methylthiophene) (110a)
General procedure 1 was followed using 9,9-Dihexyl-2,7-dibromofluorene (73.8 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a colorless oil (51 mg, 64%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 7.7 Hz, 2H), 7.46 – 7.42 (m, 4H), 7.23 (d, *J* = 5.1 Hz, 2H), 6.96 (d, *J* = 5.1 Hz, 2H), 2.38 (s, 6H), 2.02 – 1.98 (m, 4H), 1.09 (dd, *J* = 21.1, 6.4 Hz, 13H), 0.76 (t, *J* = 7.1 Hz, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 151.20, 139.75, 138.60, 133.45, 133.02, 131.18, 127.88, 123.45, 123.14, 119.69, 55.18, 40.29, 31.45, 29.63, 23.79, 22.51, 15.08, 13.96. HRMS (EI): calculated for $C_{35}H_{42}S_2$ $[M]^+$: 526.27224, found: 526.27197.



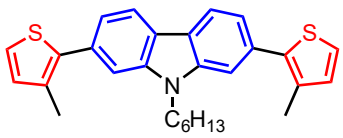
2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-hexylthiophene) (110b)
General procedure 1 was followed using 9,9-Dihexyl-2,7-dibromofluorene (73.8 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a colorless oil (70 mg, 70%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 7.7 Hz, 2H), 7.42 – 7.38 (m, 4H), 7.24 (d, *J* = 5.2 Hz, 2H), 7.00 (d, *J* = 5.2 Hz, 2H), 2.71 – 2.67 (m, 4H), 2.01 – 1.96 (m, 4H), 1.62 (q, *J* = 7.7 Hz, 4H), 1.34 – 1.24 (m, 12H), 1.15 – 1.01 (m, 12H), 0.86 (t, *J* = 6.8 Hz, 6H), 0.74 (dt, *J* = 24.5, 7.7 Hz, 10H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 151.08, 139.88, 138.58, 138.49, 133.50, 129.63, 128.26, 123.72, 123.36, 119.67, 55.12, 40.44, 31.68, 31.52, 31.09, 29.75, 29.27, 28.92, 23.85, 22.59, 22.57, 14.03, 13.95. HRMS (EI): calculated for $C_{45}H_{62}S_2$ $[M]^+$: 666.42875, found: 666.42878.



4,7-bis(3-methylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111a)
General procedure 1 was followed using 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (44 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a yellow solid (21 mg, 42%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (s, 2H), 7.42 (d, *J* = 5.1 Hz, 2H), 7.05 (d, *J* = 5.1 Hz, 2H), 2.36 (s, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 154.01, 136.37, 132.47, 130.79, 129.60, 127.23, 125.75, 15.65. HRMS (EI): calculated for $C_{16}H_{12}N_2S_3$ $[M+H]^+$: 329.02408, found: 329.02336.

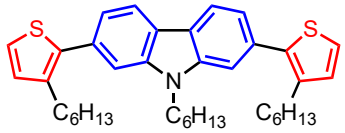


4,7-bis(3-hexylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111b)
General procedure 1 was followed using 4,7-dibromobenzo[*c*][1,2,5]thiadiazole (44 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as orange oil (46 mg, 65%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 (s, 2H), 7.43 (d, *J* = 5.2 Hz, 2H), 7.10 (d, *J* = 5.2 Hz, 2H), 2.68 – 2.64 (m, 4H), 1.62 (p, *J* = 7.6 Hz, 4H), 1.25 – 1.16 (m, 12H), 0.81 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 154.26, 141.68, 132.15, 129.88, 129.20, 127.45, 125.83, 31.54, 30.65, 29.33, 29.08, 22.51, 14.01. HRMS (EI): calculated for $C_{26}H_{32}N_2S_3$ $[M + H]^+$: 469.18058, found: 469.17979.



9-hexyl-2,7-bis(3-methylthiophen-2-yl)-9*H*-carbazole (112a)
General procedure 1 was followed using 2,7-dibromo-9-hexyl-9*H*-carbazole (61 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a colorless oil (28 mg, 43%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17 (s, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 5.1 Hz, 2H), 6.97 (d, *J* = 5.1 Hz, 2H), 4.33 (t, *J* = 7.3 Hz, 2H), 2.38 (s, 6H),

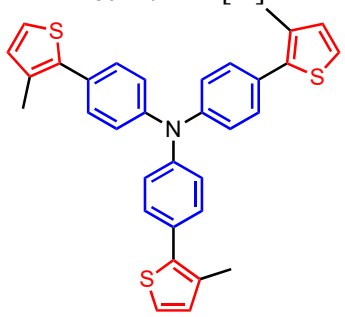
1.91 (q, J = 7.5 Hz, 2H), 1.46 – 1.41 (m, 2H), 1.37 – 1.29 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.05, 138.89, 132.49, 130.87, 127.34, 125.58, 122.87, 122.74, 121.06, 108.71, 43.36, 31.58, 29.03, 26.99, 22.55, 14.88, 14.01. HRMS (EI): calculated for $C_{28}H_{29}NS_2$ $[M]^+$: 443.17359, found: 443.17345.



9-hexyl-2,7-bis(3-hexylthiophen-2-yl)-9*H*-carbazole (112b)

General procedure 1 was followed using 2,7-dibromo-9-hexyl-9*H*-carbazole (61 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as colorless oil (57 mg, 65%).

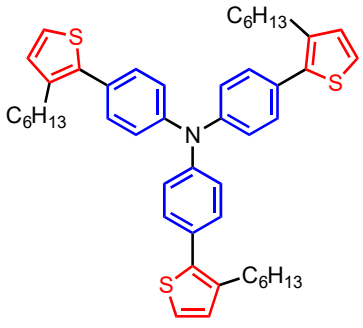
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.13 (d, J = 1.3 Hz, 2H), 7.55 (dd, J = 8.4, 1.7 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 5.2 Hz, 2H), 7.02 (d, J = 5.2 Hz, 2H), 4.33 (t, J = 7.3 Hz, 2H), 2.73 – 2.69 (m, 4H), 1.92 (p, J = 7.5 Hz, 2H), 1.64 (p, J = 7.5 Hz, 4H), 1.48 – 1.42 (m, 2H), 1.40 – 1.21 (m, 18H), 0.89 (t, J = 7.1 Hz, 3H), 0.85 – 0.80 (m, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.12, 138.80, 138.79, 138.13, 129.30, 127.62, 125.55, 123.02, 122.83, 121.37, 108.64, 43.38, 31.64, 31.58, 31.09, 31.05, 29.18, 29.04, 28.67, 27.01, 22.59, 22.56, 14.02, 14.01. HRMS (EI): calculated for $C_{38}H_{49}NS_2$ $[H]^+$: 583.33009, found: 583.33020.



Tris(4-(3-methylthiophen-2-yl)phenyl)amine (113a)

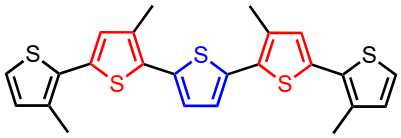
General procedure 1 was followed using tris(4-bromophenyl)amine (72.3 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as a light yellow solid (38 mg, 48%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.37 (m, 6H), 7.22 – 7.17 (m, 9H), 6.93 (d, J = 5.1 Hz, 3H), 2.36 (s, 9H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 146.30, 137.59, 132.78, 131.15, 129.80, 129.40, 124.05, 122.90, 15.05. HRMS (EI): calculated for $C_{33}H_{27}NS_3$ $[M]^+$: 533.13001, found: 533.12972.

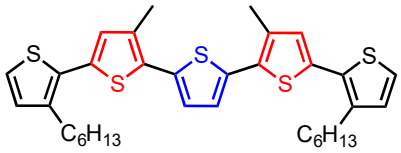


Tris(4-(3-hexylthiophen-2-yl)phenyl)amine (113b)

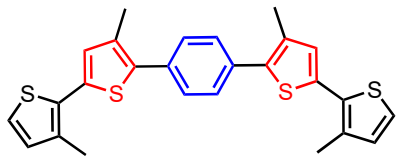
General procedure 1 was followed using tris(4-bromophenyl)amine (72.3 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as light-yellow oil (51 mg, 46%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.5 Hz, 6H), 7.21 – 7.16 (m, 9H), 6.97 (d, *J* = 5.2 Hz, 3H), 2.70 – 2.65 (m, 6H), 1.62 (p, *J* = 7.5 Hz, 7H), 1.36 – 1.23 (m, 20H), 0.87 (t, *J* = 6.7 Hz, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 146.42, 138.34, 137.50, 130.14, 129.54, 129.39, 124.01, 123.18, 31.63, 30.98, 29.15, 28.70, 22.58, 14.08. HRMS (EI): calculated for $C_{48}H_{57}NS_3$ $[M]^+$: 743.36476, found: 743.36433.



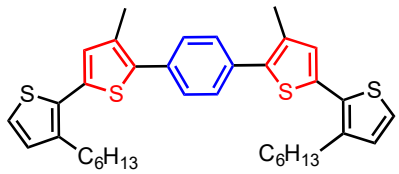
3,3''',3'''',4'-tetramethyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''-quinquethiophene (114a)
General procedure 1 was followed using compound **105f** (65.1 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as orange solid 48.5 mg, 69%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.13 (d, *J* = 5.1 Hz, 2H), 7.11 (s, 2H), 6.94 (s, 2H), 6.88 (d, *J* = 5.1 Hz, 2H), 2.44 (s, 6H), 2.43 (s, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 135.93, 134.27, 134.21, 134.02, 131.48, 130.81, 130.51, 129.62, 125.56, 123.22, 15.64, 15.49. HRMS (EI): calculated for $C_{24}H_{20}S_5$ $[M]^+$: 468.01601, found: 468.01685.



3,3''''-dihexyl-3''',4'-dimethyl-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (114b)
General procedure 1 was followed using compound **105f** (65.1 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as orange oil (68.5 mg, 75%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 5.2 Hz, 2H), 7.11 (s, 2H), 6.93 (d, *J* = 5.2 Hz, 2H), 6.91 (s, 2H), 2.80 – 2.77 (m, 4H), 2.44 (s, 6H), 1.65 (q, *J* = 7.8 Hz, 4H), 1.42 – 1.36 (m, 4H), 1.32 (m, 8H), 0.89 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.70, 135.95, 134.19, 133.88, 130.68, 130.30, 130.08, 130.07, 125.58, 123.66, 31.66, 30.62, 29.26, 29.19, 22.60, 15.63, 14.08. HRMS (EI): calculated for $C_{34}H_{40}S_5$ $[M]^+$: 608.17254, found: 608.17335.

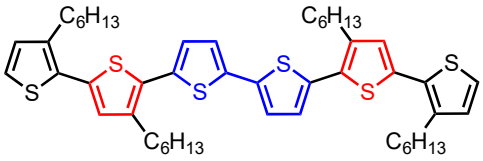


1,4-bis(3',4-dimethyl-[2,2'-bithiophen]-5-yl)benzene (115a)
General procedure 1 was followed using compound **109c** (64.2 mg, 0.15 mmol) and **103a** (56.5 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as yellow solid (38 mg, 55%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.54 (s, 4H), 7.26 (s, 2H), 7.14 (d, *J* = 5.1 Hz, 2H), 6.89 (d, *J* = 5.1 Hz, 2H), 2.44 (s, 6H), 2.39 (s, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.02, 134.58, 133.82, 133.77, 133.27, 131.43, 131.07, 129.61, 128.78, 123.07, 29.69, 15.20. HRMS (EI): calculated for $C_{26}H_{22}S_4$ $[M]^+$: 462.05988, found: 462.06012.



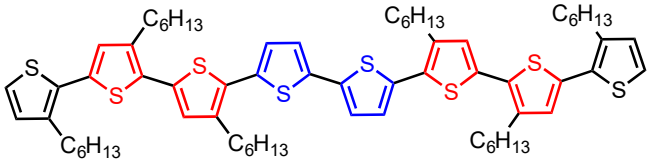
1,4-bis(3'-hexyl-4-methyl-[2,2'-bithiophen]-5-yl)benzene (115b)

General procedure 1 was followed using compound **109c** (64.2 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as yellow oil (61 mg, 67%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 (s, 4H), 7.17 (d, *J* = 5.2 Hz, 2H), 6.97 (s, 2H), 6.94 (d, *J* = 5.2 Hz, 2H), 2.83 – 2.78 (m, 4H), 2.39 (s, 6H), 1.66 (p, *J* = 7.5 Hz, 4H), 1.43 – 1.37 (m, 4H), 1.32 (dd, *J* = 7.3, 3.5 Hz, 8H), 0.93 – 0.86 (m, 6H).^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.50, 137.20, 134.25, 133.67, 133.29, 131.26, 130.60, 130.03, 128.99, 128.79, 123.50, 31.68, 30.68, 29.22, 22.61, 15.20, 14.09. HRMS (EI): calculated for $C_{36}H_{42}S_4$ $[M]^+$: 602.21638, found: 602.21611.



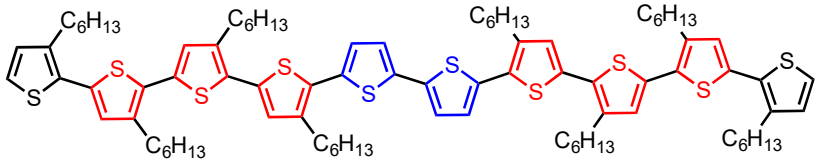
3,3'''',3''''',4'-tetrahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''-sexithiophene (116)

General procedure 1 was followed using compound **106c** (98.5 mg, 0.15 mmol) and compound **103b** (82.6 mg, 0.33 mmol, 2.2 equiv.) to yield the title compound as orange oil (76 mg, 61%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 5.2 Hz, 2H), 7.14 (d, *J* = 3.8 Hz, 2H), 7.05 (d, *J* = 3.8 Hz, 2H), 6.95 (s, 2H), 6.93 (d, *J* = 5.2 Hz, 2H), 2.82 – 2.75 (m, 8H), 1.73 – 1.61 (m, 8H), 1.40 (tt, *J* = 14.2, 6.7 Hz, 8H), 1.32 (tdd, *J* = 8.6, 6.1, 2.7 Hz, 16H), 0.93 – 0.86 (m, 12H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.99, 139.70, 136.70, 135.02, 134.35, 130.39, 130.14, 130.09, 128.73, 126.31, 123.87, 123.65, 31.67, 30.64, 30.49, 29.69, 29.42, 29.29, 29.22, 22.62, 14.09. HRMS (EI): calculated for $C_{48}H_{62}S_6$ $[M]^+$: 830.31757, found: 830.31757.



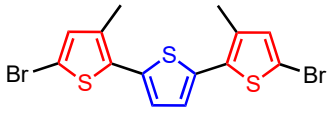
3,3'''',3''''',3''''''',4',4''-hexahexyl-
2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''':5'''''',2''''''-octithiophene (117)

General procedure 1 was followed using compound **116b** (98.9 mg, 0.1 mmol) and compound **103b** (55.1 mg, 0.22 mmol, 2.2 equiv.) to yield the title compound as orange oil (88 mg, 75%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.18 – 7.14 (m, 4H), 7.06 (d, *J* = 3.8 Hz, 2H), 6.97 (s, 2H), 6.95 – 6.92 (m, 4H), 2.79 (td, *J* = 7.9, 5.0 Hz, 12H), 1.73 – 1.62 (m, 12H), 1.45 – 1.36 (m, 12H), 1.37 – 1.30 (m, 24H), 0.93 – 0.87 (m, 18H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.06, 139.87, 139.64, 136.72, 135.02, 134.16, 134.03, 130.47, 130.24, 130.18, 130.09, 128.76, 128.54, 126.32, 123.90, 123.60, 31.68, 31.67, 30.64, 30.51, 30.49, 29.44, 29.29, 29.24, 29.21, 22.64, 22.62, 14.10. HRMS (EI): calculated for $C_{68}H_{90}S_8$ $[M]^+$: 1162.48081, found: 1162.47945.



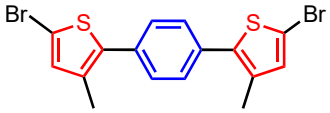
3,3''''',3''''''',3'''''''',3''''''''',4',4'',4'''-octahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''':5'''''',2''''''':5''''''',2'''''''':5'''''''-decithiophene (118)

General procedure 1 was followed using compound **117bf** (132 mg, 0.1 mmol) and compound **103b** (55.1 mg, 0.22 mmol, 2.2 equiv.) to yield the title compound as red oil (121 mg, 81%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.17 – 7.14 (m, 4H), 7.07 – 7.04 (m, 2H), 6.98 – 6.92 (m, 8H), 2.82 – 2.74 (m, 16H), 1.72 – 1.61 (m, 16H), 1.37 (m, 48H), 0.90 (q, *J* = 6.9, 6.2 Hz, 24H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.08, 139.93, 139.80, 139.61, 136.73, 135.02, 134.17, 134.10, 134.00, 133.84, 130.50, 130.32, 130.29, 130.22, 130.08, 128.76, 128.56, 128.54, 126.31, 123.91, 123.57, 31.67, 30.64, 30.49, 29.70, 29.46, 29.24, 29.22, 22.63, 14.10. HRMS (EI): calculated for $C_{88}H_{118}S_{10}$ [M]$^{+}$: 1494.64406, found: 1494.64264.



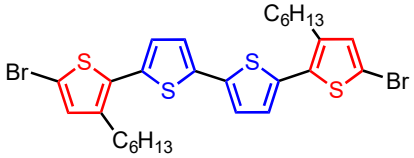
5,5''-dibromo-3,3''-dimethyl-2,2':5',2''-terthiophene (105f)

General procedure 2 was followed using compound **103a** (124 mg, 0.45 mmol) to yield the title compound as a yellow solid (166 mg, 85%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.00 (s, 2H), 6.86 (s, 2H), 2.35 (s, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 135.36, 134.68, 133.98, 132.07, 126.07, 110.25, 15.32. HRMS (EI): calculated for $C_{14}H_{10}Br_2S_3$ [M]$^{+}$: 432.83825, found: 432.83896.



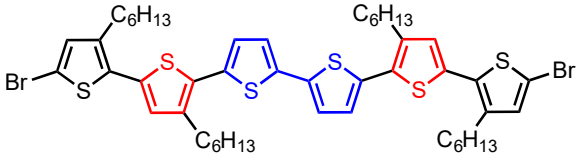
1,4-bis(5-bromo-3-methylthiophen-2-yl)benzene (109c)

General procedure 2 was followed using compound **109a** (108 mg, 0.45 mmol) to yield the title compound as a light yellow solid (174 mg, 90%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 (s, 4H), 6.90 (s, 2H), 2.30 (s, 6H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 138.76, 134.06, 133.79, 132.93, 128.92, 110.35, 14.91. HRMS (EI): calculated for $C_{16}H_{12}Br_2S_2$ [M]$^{+}$: 425.87471, found: 425.87405.



5,5'''-dibromo-3,3'''-dihexyl-2,2':5',2'':5'',2'''-quaterthiophene (106c)

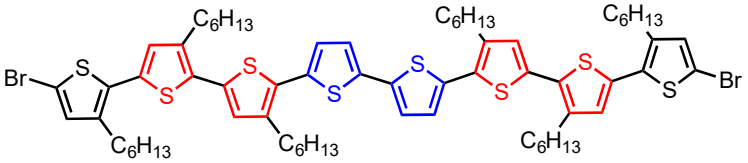
General procedure 2 was followed using compound **106b** (150 mg, 0.3 mmol) to yield the title compound as a yellow solid (180 mg, 91%).
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.11 (s, 2H), 6.97 (s, 2H), 6.90 (s, 2H), 2.74 – 2.68 (m, 4H), 1.61 (p, *J* = 7.5 Hz, 4H), 1.36 (p, *J* = 6.7, 6.3 Hz, 4H), 1.30 (m, 8H), 0.91 – 0.86 (m, 6H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 140.52, 137.02, 134.05, 132.69, 131.66, 126.96, 123.99, 110.64, 31.59, 30.49, 29.20, 29.08, 22.57, 14.07. HRMS (EI): calculated for $C_{28}H_{32}Br_2S_4$ [M]$^{+}$: 653.97450, found 653.97536.



5,5''''-dibromo-3,3'''',3''''',4'-tetrahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2'''''-sexithiophene (116b)

General procedure 2 was followed using compound **116** (166 mg, 0.2 mmol) to yield the title compound as a dark orange oil (168mg, 85%).

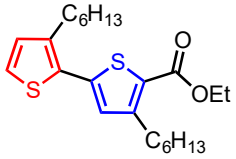
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.11 (d, *J* = 3.8 Hz, 2H), 7.02 (d, *J* = 3.8 Hz, 2H), 6.88 (s, 2H), 6.87 (s, 2H), 2.73 (dt, *J* = 16.1, 7.8 Hz, 8H), 1.72 – 1.58 (m, 8H), 1.42 – 1.28 (m, 24H), 0.94 – 0.83 (m, 12H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.96, 140.32, 132.71, 131.58, 129.77, 129.15, 129.06, 126.83, 125.87, 110.41, 107.81, 102.98, 31.59, 30.49, 29.68, 29.22, 29.08, 22.57, 14.07. HRMS (EI): calculated for $C_{48}H_{60}Br_2S_6$ $[M]^+$: 986.13860, found: 986.13796.



5,5''''''-dibromo-3,3'''',3''''',3''''''',4',4''-hexahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''':5'''''',2''''''-octithiophene (117b)

General procedure 2 was followed using compound **117** (116 mg, 0.1 mmol) to yield the title compound as a red oil (118 mg, 89%).

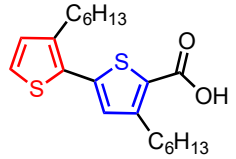
^{1}H NMR (500 MHz, Chloroform-*d*) δ δ 7.15 (d, *J* = 3.7 Hz, 2H), 7.06 (d, *J* = 3.8 Hz, 2H), 6.97 (s, 2H), 6.89 (s, 2H), 6.88 (s, 2H), 2.85 – 2.68 (m, 12H), 1.73 – 1.52 (m, 12H), 1.46 – 1.27 (m, 42H), 0.94 – 0.80 (m, 12H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 140.20, 140.10, 139.90, 136.76, 134.94, 133.71, 132.74, 131.99, 130.80, 130.41, 129.12, 128.71, 126.38, 125.54, 123.93, 110.29, 31.66, 31.61, 30.48, 29.69, 29.43, 29.38, 29.22, 29.09, 22.62, 14.09. HRMS (EI): calculated for $C_{68}H_{88}Br_2S_8$ $[M]^+$: 1318.30184, found: 1318.29999.



Ethyl 3',4-dihexyl-[2,2'-bithiophene]-5-carboxylate (130a)

General procedure 3 was followed using compound **129a** (64 mg, 0.15 mmol) and compound **103b** (41 mg, 0.165 mmol, 1.1 equiv.) to yield the title compound as yellow oil (53 mg, 84%).

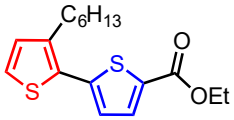
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.20 (d, *J* = 5.2 Hz, 1H), 6.97 – 6.92 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.00 – 2.96 (m, 2H), 2.81 – 2.75 (m, 2H), 1.67 – 1.60 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 6H), 1.34 – 1.28 (m, 8H), 0.88 (td, *J* = 7.1, 2.6 Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 162.58, 151.55, 140.86, 140.62, 130.27, 129.97, 128.95, 125.58, 124.59, 60.64, 31.68, 31.60, 30.46, 30.41, 29.76, 29.32, 29.24, 29.13, 22.61, 22.57, 14.37, 14.07, 14.03. HRMS (EI): calculated for $C_{23}H_{34}O_2S_2$ $[M + H]^+$: 407.20693, found: 407.20784



3',4-dihexyl-[2,2'-bithiophene]-5-carboxylic acid (131)

General procedure 3 and 4 were followed using **129a** (64 mg, 0.2 mmol) and compound **103b** (55.1 mg, 0.22 mmol, 1.1 equiv.), then reflux with KOH (112mg, 2 mmol, 10 equiv.to yield the title compound as a yellow oil (51 mg, 87%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 5.2 Hz, 1H), 7.00 (s, 1H), 6.95 (d, *J* = 5.2 Hz, 1H), 3.03 – 2.99 (m, 2H), 2.82 – 2.78 (m, 2H), 1.66 (h, *J* = 8.5 Hz, 4H), 1.42 – 1.35 (m, 4H), 1.32 (dd, *J* = 10.9, 5.2 Hz, 9H), 0.89 (q, *J* = 6.8 Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.15, 153.48, 142.51, 141.30, 130.40, 129.80, 129.13, 124.93, 124.56, 77.24, 77.19, 76.99, 76.73, 31.65, 31.63, 30.45, 30.34, 29.83, 29.68, 29.42, 29.17, 22.59, 14.07, 14.04. HRMS (EI): calculated for $C_{21}H_{30}O_2S_2$ [M - H]$^-$: 377.16091, found: 377.16089

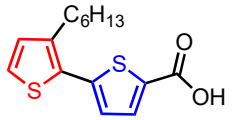


ethyl 3'-hexyl-[2,2'-bithiophene]-5-carboxylate (130d)

General procedure 3 was followed using compound ethyl 5-bromothiophene-2-carboxylate **(**35 mg, 0.15 mmol) and compound **103b** (41.3mg, 0.165 mmol, 1.1 equiv.) to yield the title compound as yellow oil (44 mg, 92%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 3.9 Hz, 1H), 7.24 (d, *J* = 5.2 Hz, 1H), 7.10 (d, *J* = 3.9 Hz, 1H), 6.97 (d, *J* = 5.2 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.81 – 2.77 (m, 2H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.39 (m, 5H), 1.31 (m, , 4H), 0.89 (t, *J* = 6.9 Hz, 3H).

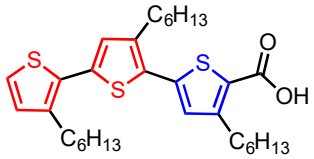
^{13}C NMR (126 MHz, cdcl$_3$) δ 162.22, 143.31, 141.05, 133.54, 132.67, 130.29, 129.77, 126.01, 124.89, 61.16, 31.62, 30.47, 29.33, 22.58, 14.37, 14.05. HRMS (EI): calculated for $C_{17}H_{22}O_2S_2$ [M + H]$^+$: 323.11348, found: 323.11339



3'-hexyl-[2,2'-bithiophene]-5-carboxylic acid (133)

General procedure 3 and 4 were followed using ethyl 5-bromothiophene-2-carboxylate (47 mg, 0.2 mmol) and compound **103b** (55.1 mg, 0.22 mmol, 1.1 equiv.), then reflux with KOH (112mg, 2 mmol, 10 equiv.to yield the title compound as a yellow oil (51 mg, 87%).

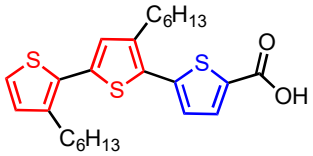
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 3.9 Hz, 1H), 7.24 (s, 1H), 7.13 (d, *J* = 3.9 Hz, 1H), 6.96 (d, *J* = 5.2 Hz, 1H), 2.82 – 2.77 (m, 2H), 1.68 – 1.61 (m, 2H), 1.39 (d, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 4H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.65, 145.25, 141.45, 135.31, 131.27, 130.40, 129.59, 126.21, 125.24, 31.62, 30.44, 29.41, 29.16, 22.58, 14.05. HRMS (EI): calculated for $C_{21}H_{30}O_2S_2$ [M - H]$^-$: 293.06699, found: 293.06755



3',3'',4-trihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (132)

General procedure 3 and 4 were followed using **129a** (64 mg, 0.15 mmol) and compound **131a** (69 mg, 0.165 mmol, 1.1 equiv.), then reflux with KOH (112mg, 2 mmol, 10 equiv.to yield the title compound as a yellow oil (41 mg, 51%).

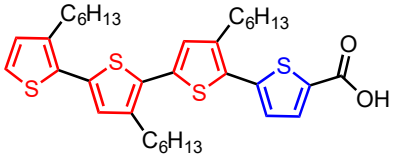
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 5.2 Hz, 1H), 7.02 (s, 1H), 6.96 (s, 1H), 6.94 (d, *J* = 5.2 Hz, 1H), 3.04 – 3.00 (m, 2H), 2.83 – 2.76 (m, 4H), 1.71 – 1.63 (m, 7H), 1.46 – 1.37 (m, 6H), 1.32 (tt, *J* = 7.3, 3.3 Hz, 12H), 0.90 (m, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.66, 153.51, 142.11, 141.60, 140.09, 135.63, 130.17, 130.06, 129.50, 128.95, 128.79, 124.33, 124.00, 31.65, 30.59, 30.36, 30.30, 29.84, 29.59, 29.30, 29.19, 22.60, 14.08, 14.06. HRMS (EI): calculated for $C_{31}H_{44}O_2S_3$ [M - H]$^-$: 543.24306, found: 543.24296.



3',3''-dihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (134)

General procedure 3 and 4 were followed using compound **131a** (69 mg, 0.165 mmol, 1.1 equiv.) and ethyl 5-bromothiophene-2-carboxylate **(**35 mg, 0.15 mmol), then reflux with KOH (112mg, 2 mmol, 10 equiv.to yield the title compound as a yellow oil (62 mg, 82%).

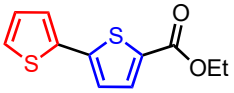
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 3.9 Hz, 1H), 7.19 (d, *J* = 5.2 Hz, 1H), 7.15 (d, *J* = 3.9 Hz, 1H), 6.97 (s, 1H), 6.94 (d, *J* = 5.2 Hz, 1H), 2.83 – 2.76 (m, 5H), 1.67 (dp, *J* = 23.5, 7.6 Hz, 5H), 1.41 (dq, *J* = 15.3, 8.4, 7.8 Hz, 5H), 1.32 (dq, *J* = 7.2, 4.5, 3.7 Hz, 9H), 0.89 (td, *J* = 7.0, 4.5 Hz, 6H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 167.29, 144.85, 141.72, 140.18, 135.96, 135.33, 131.06, 130.18, 129.95, 129.29, 128.93, 125.88, 124.08, 31.65, 31.63, 30.61, 30.29, 29.59, 29.32, 29.20, 22.61, 22.59, 14.07, 14.06. HRMS (EI): calculated for $C_{25}H_{32}O_2S_3$ [M - H]$^-$: 459.14862, found: 459.14877



3',3'',3'''-trihexyl-[2,2':5',2'':5'',2'''-quaterthiophene]-5-carboxylic acid (135)

General procedure 3 and 4 were followed using compound **134a** (82 mg, 0.165 mmol, 1.1 equiv.) and ethyl 5-bromothiophene-2-carboxylate **(**35 mg, 0.15 mmol), then reflux with KOH (112mg, 2 mmol, 10 equiv.to yield the title compound as a yellow oil (44 mg, 43%).

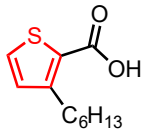
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.83 (s, 1H), 7.17 (d, *J* = 5.1 Hz, 2H), 6.99 (s, 1H), 6.95 – 6.92 (m, 2H), 2.80 (dt, *J* = 15.4, 7.9 Hz, 6H), 1.67 (m, 6H), 1.44 – 1.38 (m, 6H), 1.35 – 1.30 (m, 12H), 0.92 – 0.87 (m, 9H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.47, 141.77, 140.37, 139.79, 135.61, 134.64, 130.30, 130.11, 129.74, 128.80, 128.70, 125.87, 123.74, 31.65, 30.61, 30.46, 30.29, 29.59, 29.46, 29.28, 29.20, 22.61, 14.08. HRMS (EI): calculated for $C_{35}H_{46}O_2S_4$ [M - H]$^-$: 625.2302, found: 625.2305



Ethyl [2,2'-bithiophene]-5-carboxylate (130f)

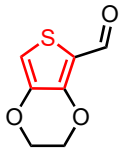
General procedure 3 was followed using compound ethyl 5-bromothiophene-2-carboxylate **(**35 mg, 0.15 mmol) and potassium thiophene-2-carboxylate (28 mg, 0.165 mmol, 1.1 equiv.) to yield the title compound as yellow oil (14 mg, 39%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 3.8 Hz, 1H), 7.28 (dd, *J* = 8.9, 4.2 Hz, 2H), 7.14 (d, *J* = 3.8 Hz, 1H), 7.06 – 7.03 (m, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 162.08, 144.00, 136.39, 134.03, 131.79, 128.09, 125.99, 125.14, 123.86, 61.20, 14.34.



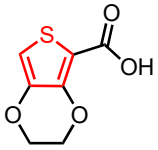
3-hexylthiophene-2-carboxylic acid (96b)

General procedure 6 was followed. The isomer is separated by column chromatography (Hexanes:EtOAc gradient increase from 0% to 10%, R_f=0.1 to 0.15) to yield an clear light yellow oil that slowly solidify over time. (Yield: 62%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 5.0 Hz, 1H), 6.99 (d, *J* = 5.0 Hz, 1H), 3.05 – 3.00 (m, 2H), 1.64 (p, *J* = 7.5 Hz, 2H), 1.39 – 1.29 (m, 6H), 0.91 – 0.86 (m, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.43, 153.20, 131.77, 130.96, 125.87, 31.63, 30.38, 29.71, 29.14, 22.57, 14.06. HRMS (EI): calculated for $C_{11}H_{15}O_2S$ [M + H]$^+$: 213.09448, found: 213.09444



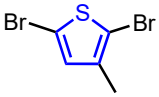
2,3-dihydrothieno[3,4-*b*][1,4]dioxine-5-carbaldehyde

The synthesis follows general procedure 5 and reaction temperature was lowered to 22.5 °C. The compound is purified by re-crystallization with chloroform and methanol. Afford a light-yellow color solid. (Yield: 70%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.90 (s, 1H), 6.79 (s, 1H), 4.38 – 4.25 (m, 4H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 180.12, 148.45, 141.76, 118.50, 110.76, 65.28, 64.36.



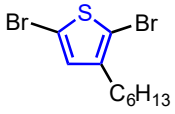
2,3-dihydrothieno[3,4-*b*][1,4]dioxine-5-carboxylic acid (96b)

General procedure 6 was followed. The isomer is separated by column chromatography (20% EtOAc : 80% Hexanes) to yield an white solid that is sensitive to light. (Yield: 20%)
^{1}H NMR (500 MHz, DMSO-d_6) δ 6.92 (s, 1H), 4.30 – 4.17 (m, 4H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.50, 145.92, 142.00, 107.40, 106.73, 65.19, 64.24. HRMS (EI): calculated for $C_7H_6O_4S$ [M - H]$^-$: 184.991403, found: 184.99151



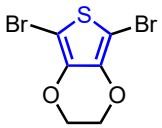
2,5-dibromo-3-methylthiophene (107c)

General procedure 9 was followed. 3-methylthiophene (0.196 g, 2.00 mmol), NBS (0.78 g, 4.4 mmol, 2.2 equiv.) were mixed in DMF solution (20 ml). The compound is purified by column chromatography to afford a colorless that is light sensitive. (yield= 65%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.76 (s, 1H), 2.15 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 138.04, 131.86, 110.13, 108.37, 15.14.



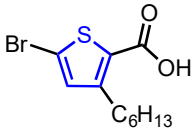
2,5-dibromo-3-hexylthiophene (107d)

General procedure 9 was followed. 3-hexylthiophene (0.5g, 2.97 mmol), NBS (1.163 g, 6.53 mmol, 2.2 equiv.) were mixed in DMF solution (30 ml) in an amber vial. The compound is purified by column chromatography to afford a colorless oil that is light sensitive. (Yield= 80%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.78 (s, 1H), 2.54 – 2.47 (m, 2H), 1.58 – 1.49 (m, 2H), 1.37 – 1.25 (m, 6H), 0.93 – 0.86 (m, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 142.97, 130.93, 110.29, 107.91, 31.56, 29.54, 29.48, 28.78, 22.57, 14.07.



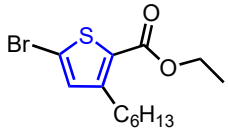
5,7-dibromo-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108c)

General procedure 9 was followed. 3,4-Ethylenedioxylthiophene (0.71g, 5 mmol), NBS (19 g, 11 mmol, 2.2 equiv.) were mixed in DMF solution (50 ml) The compound is purified by column chromatography to afford a white solid that is light sensitive. (Yield=60%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.27 (s, 4H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 157.29, 139.67, 85.52, 77.20, 64.95, 19.33.

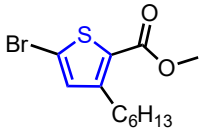


5-bromo-3-hexylthiophene-2-carboxylic acid (128)

General procedure 5,6 was followed. The isomer is separated by column chromatography (Hexane:EtOAc gradient increase from 0% to 15%, R_f=0.15 to 0.2) to yield an clear light yellow oil that slowly solidify over time. (Yield: 51%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.98 (s, 1H), 3.01 – 2.94 (m, 2H), 1.65 – 1.56 (m, 2H), 1.42 – 1.34 (m, 1H), 1.37 – 1.27 (m, 4H), 0.94 – 0.86 (m, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.03, 153.97, 133.96, 127.13, 120.48, 31.57, 30.22, 29.62, 29.06, 22.54, 14.06. HRMS (EI): calculated for $C_{11}H_{15}BrO_2S$ [M - H]$^-$: 291.00543, found: 291.00494.

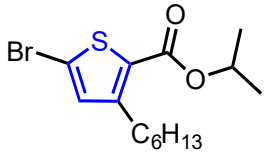


Ethyl 5-bromo-3-hexylthiophene-2-carboxylate (129a)
General procedure 8 was followed with Ethanol. The product is isolated by column chromatography. (Yield: 80%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.91 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.96 – 2.91 (m, 2H), 1.57 (p, *J* = 7.5 Hz, 2H), 1.37 – 1.26 (m, 9H), 0.91 – 0.84 (m, 3H).
^{13}C NMR (125 MHz, Chloroform-*d*) δ 161.49, 151.88, 133.51, 133.50, 128.04, 118.29, 60.85, 31.60, 30.28, 29.50, 29.11, 22.56, 14.26, 14.04. HRMS (EI): calculated for $C_{13}H_{19}BrO_2S$ [M + H]$^+$: 319.03615, found: 319.03673.



Methyl 5-bromo-3-hexylthiophene-2-carboxylate (129b)

General procedure 8 was followed with Methanol. The product is isolated by column chromatography. (Yield: 35%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.93 (s, 1H), 3.83 (s, 3H), 2.97 – 2.93 (m, 2H), 1.58 (p, *J* = 7.4 Hz, 2H), 1.37 – 1.28 (m, 6H), 0.91 – 0.86 (m, 3H).^{13}C NMR (125 MHz, Chloroform-*d*) δ 161.87, 152.26, 133.52, 127.46, 118.48, 51.82, 31.59, 30.24, 29.47, 29.09, 22.55, 14.05.

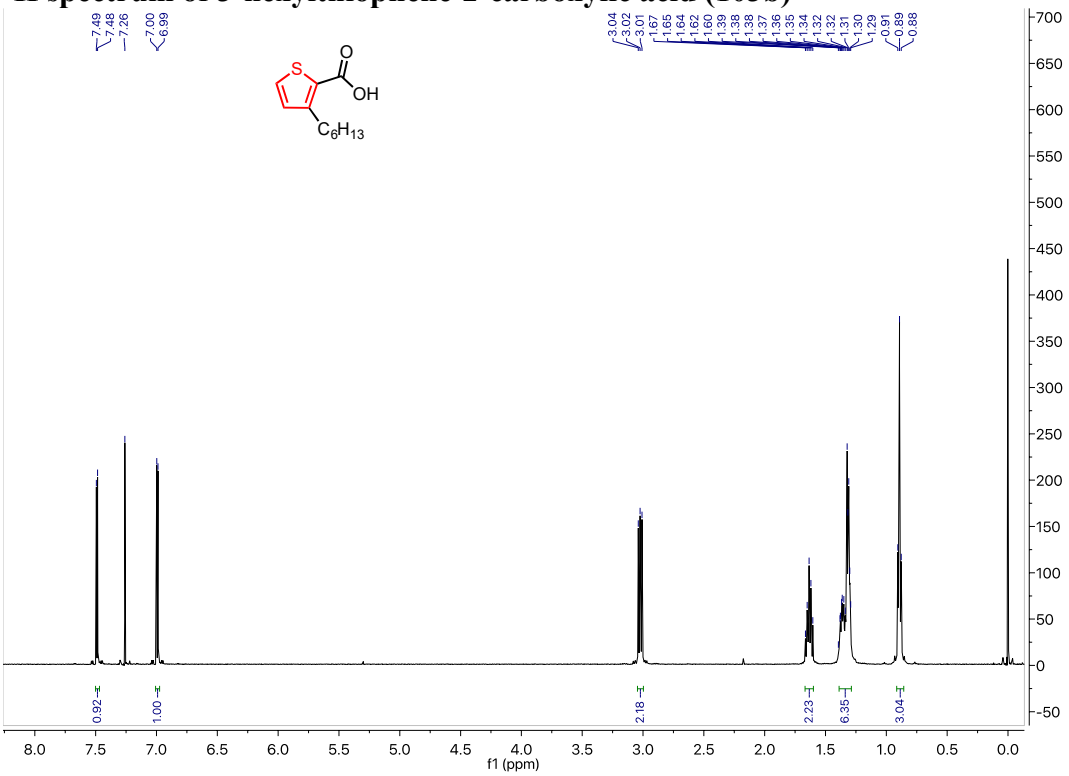


Isopropyl 5-bromo-3-hexylthiophene-2-carboxylate (129c)

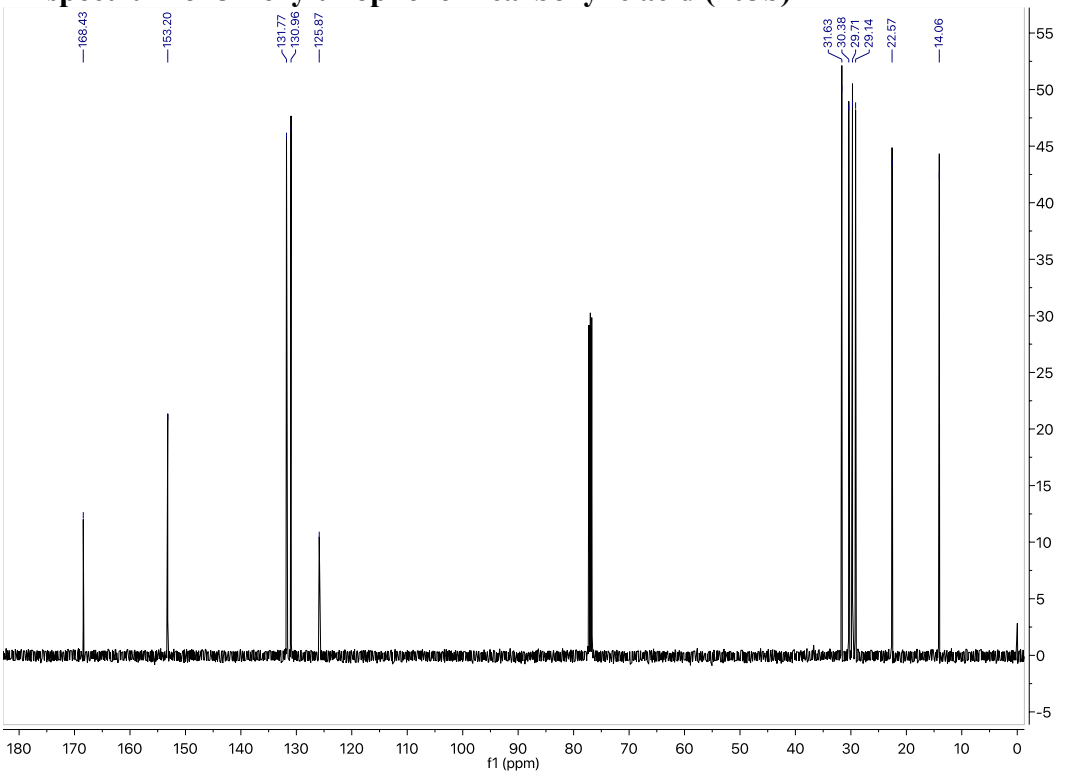
General procedure 8 was followed with Isopropanol. The product is isolated by column chromatography. (Yield: 51%)
^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.91 (s, 1H), 5.16 (hept, *J* = 6.3 Hz, 1H), 2.96 – 2.91 (m, 2H), 1.58 (p, *J* = 7.5 Hz, 2H), 1.38 – 1.28 (m, 12H), 0.90 – 0.85 (m, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 161.10, 151.53, 133.51, 128.68, 118.14, 68.56, 31.67, 31.63, 30.35, 29.55, 29.15, 29.14, 29.11, 22.57, 21.90, 14.04.

6.4. ^{1}H NMR, ^{13}C NMR, and Mass Spectra

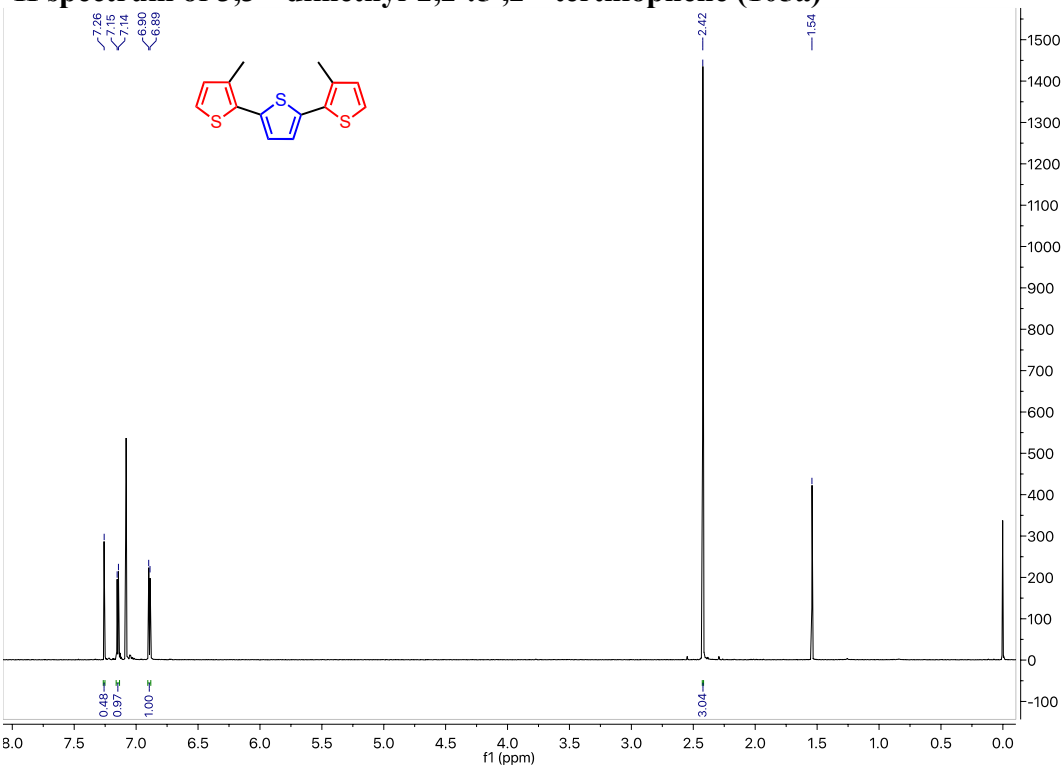
^{1}H spectrum of 3-hexylthiophene-2-carboxylic acid (103b)



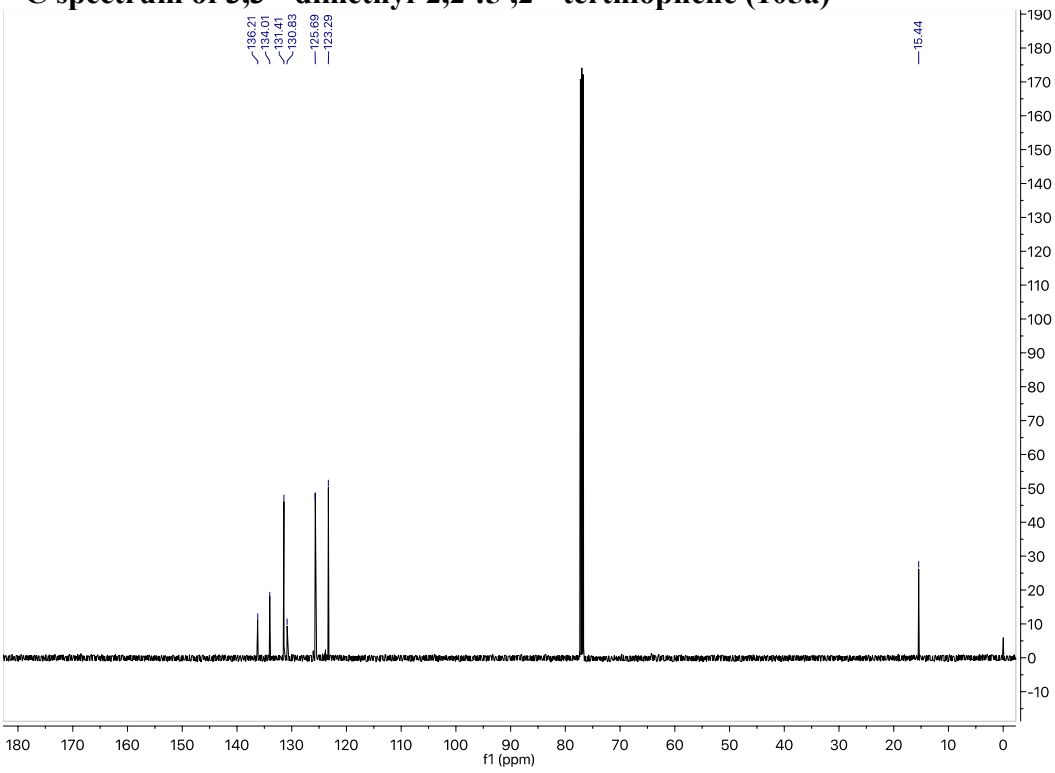
^{1}H spectrum of 3-hexylthiophene-2-carboxylic acid (103b)



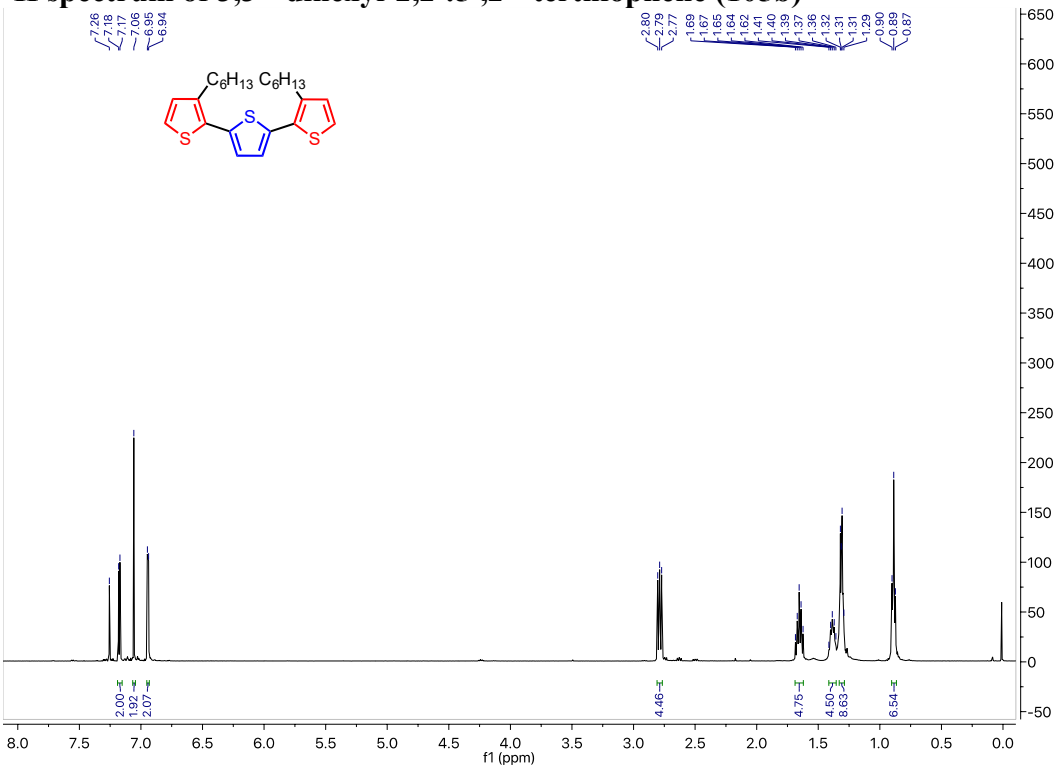
^{1}H spectrum of 3,3''-dimethyl-2,2':5',2''-terthiophene (105a)



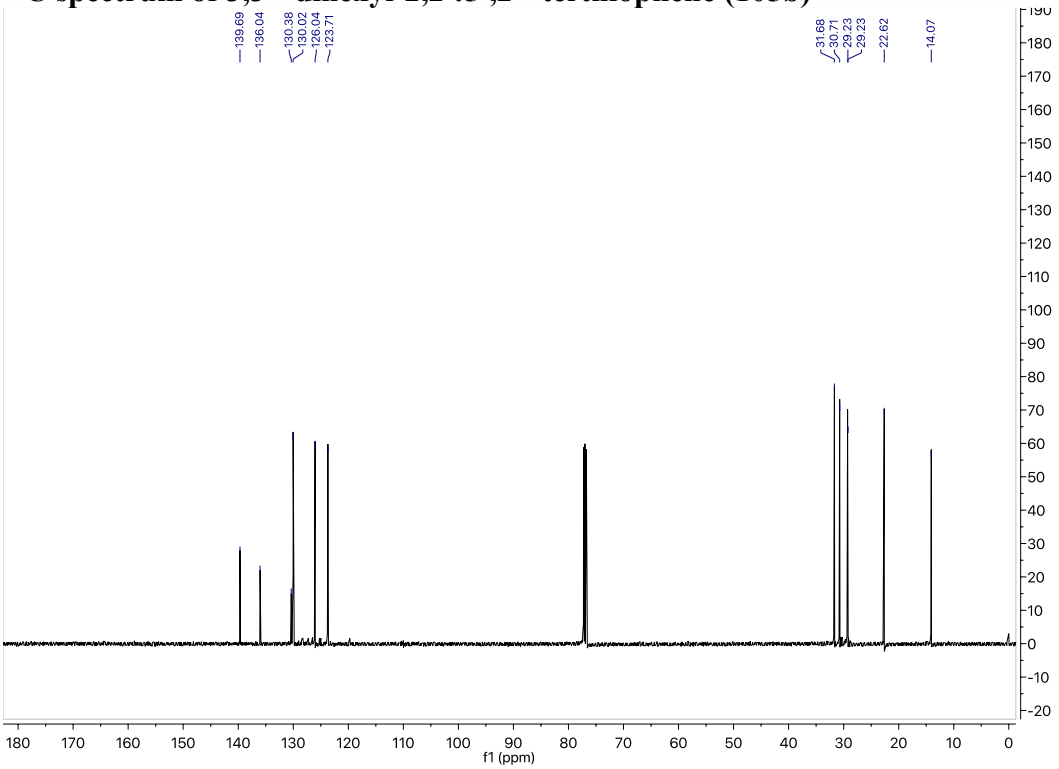
^{13}C spectrum of 3,3''-dimethyl-2,2':5',2''-terthiophene (105a)



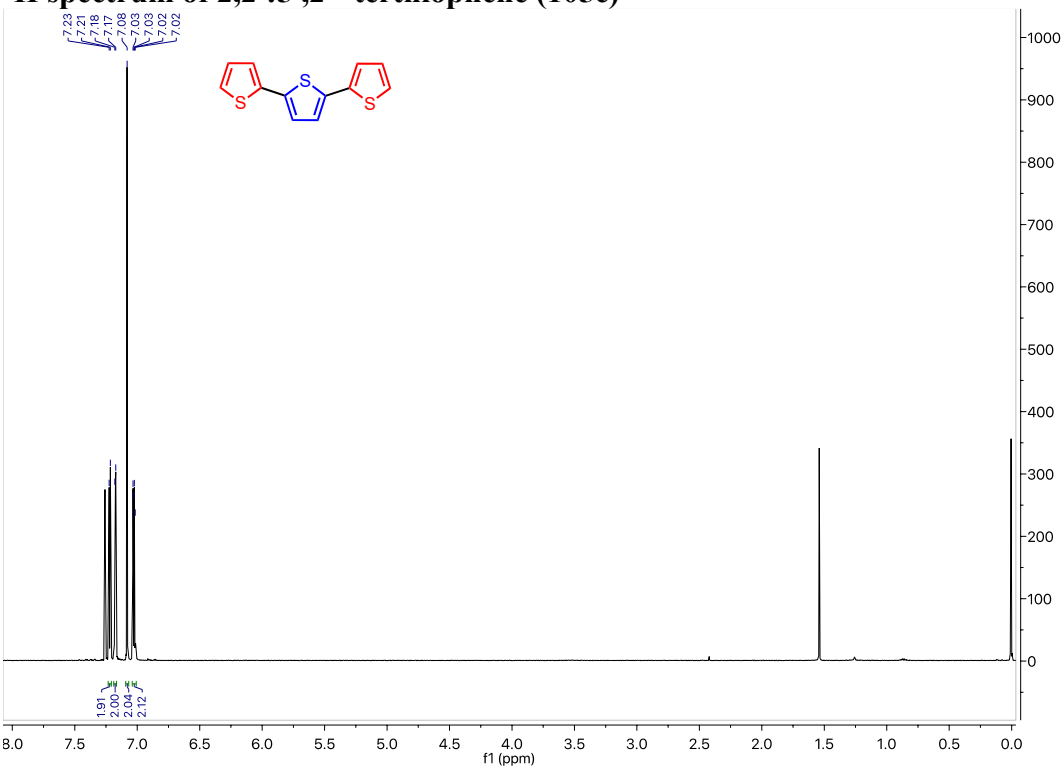
^{1}H spectrum of 3,3''-dihexyl-2,2':5',2''-terthiophene (105b)



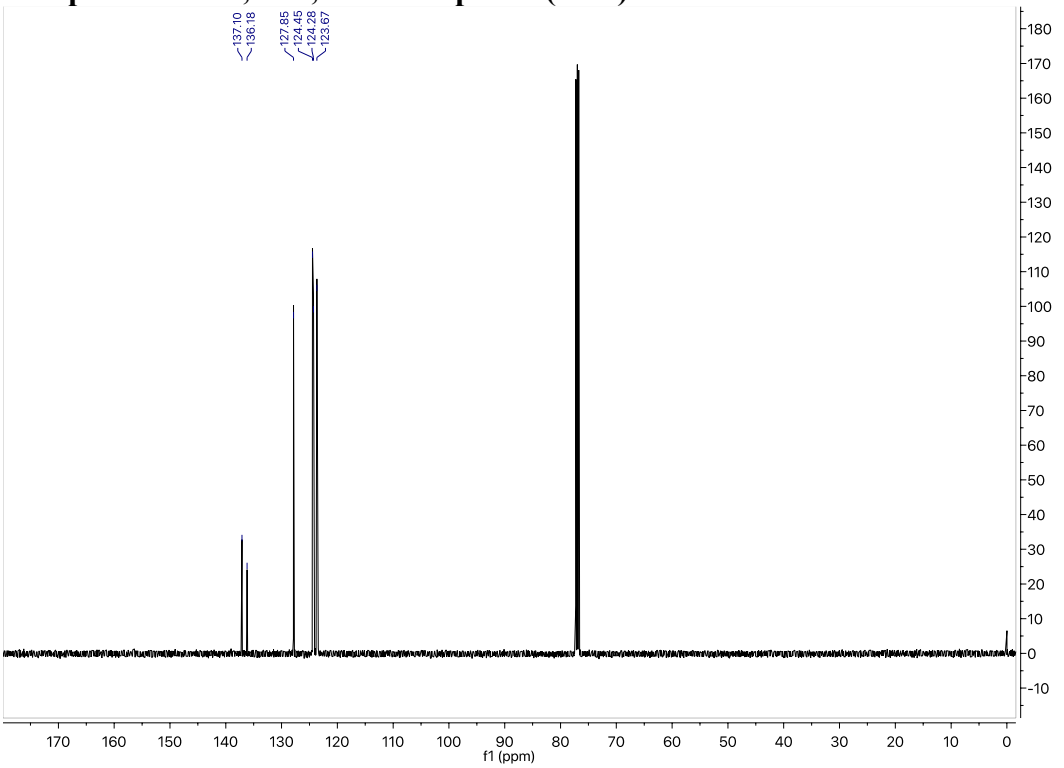
^{13}C spectrum of 3,3''-dihexyl-2,2':5',2''-terthiophene (105b)



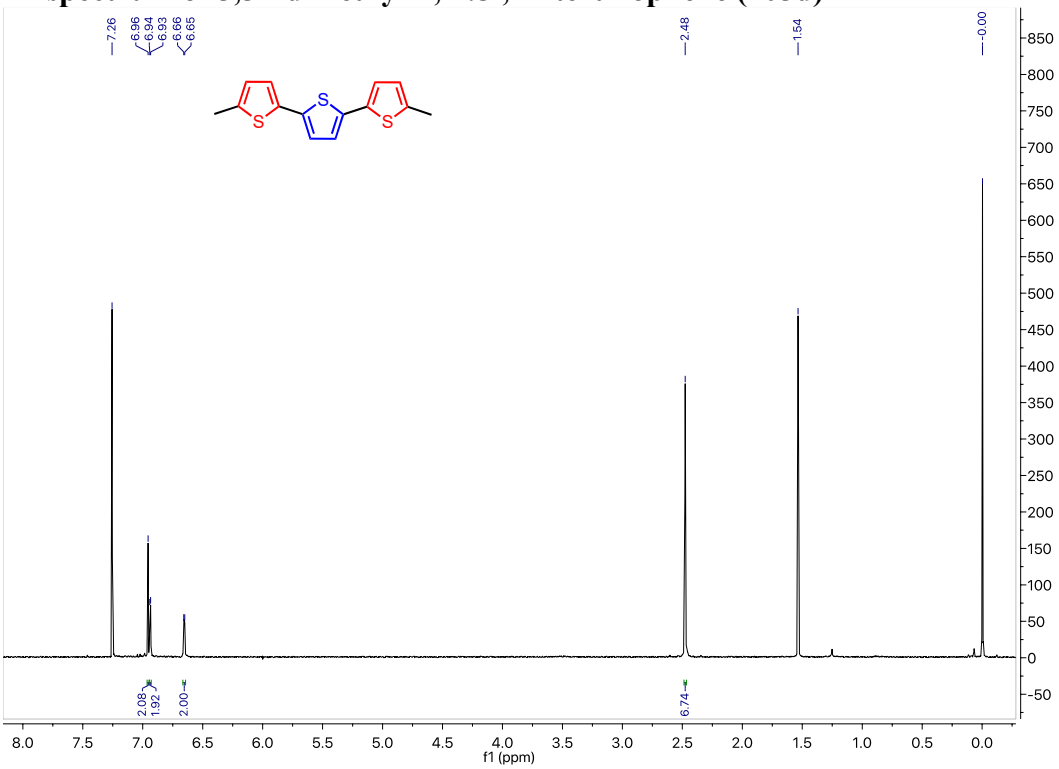
^{1}H spectrum of 2,2':5',2''-terthiophene (105c)



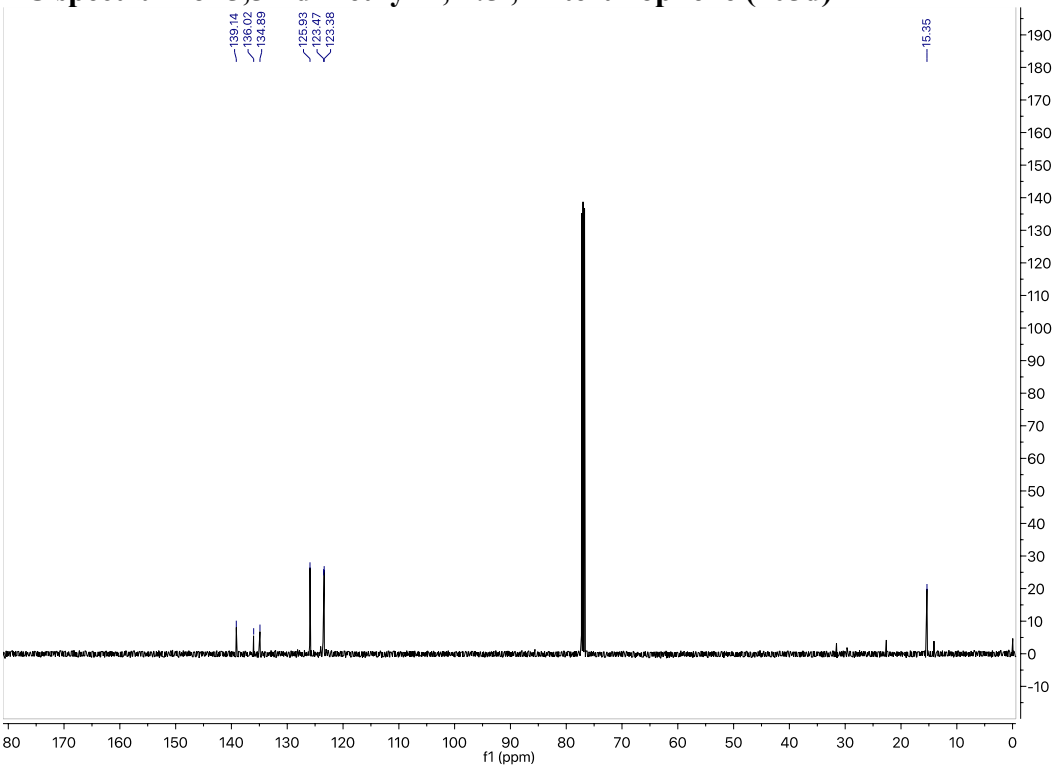
^{13}C spectrum of 2,2':5',2''-terthiophene (105c)



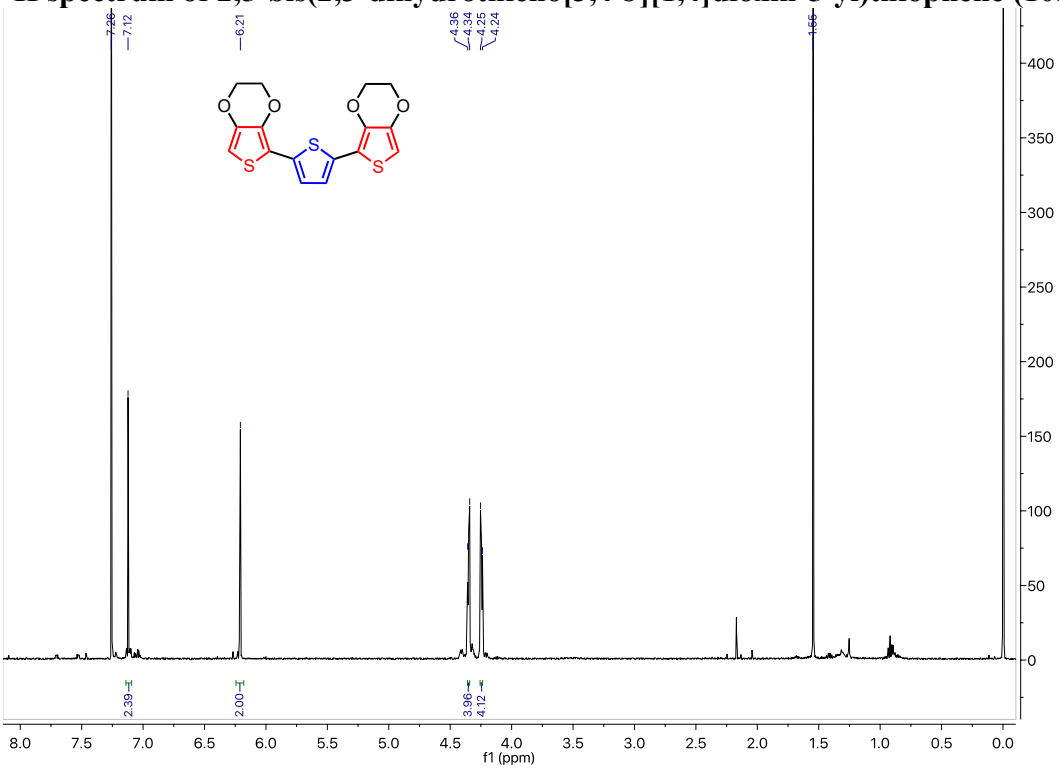
^{1}H spectrum of 5,5''-dimethyl-2,2':5',2''-terthiophene (105d)



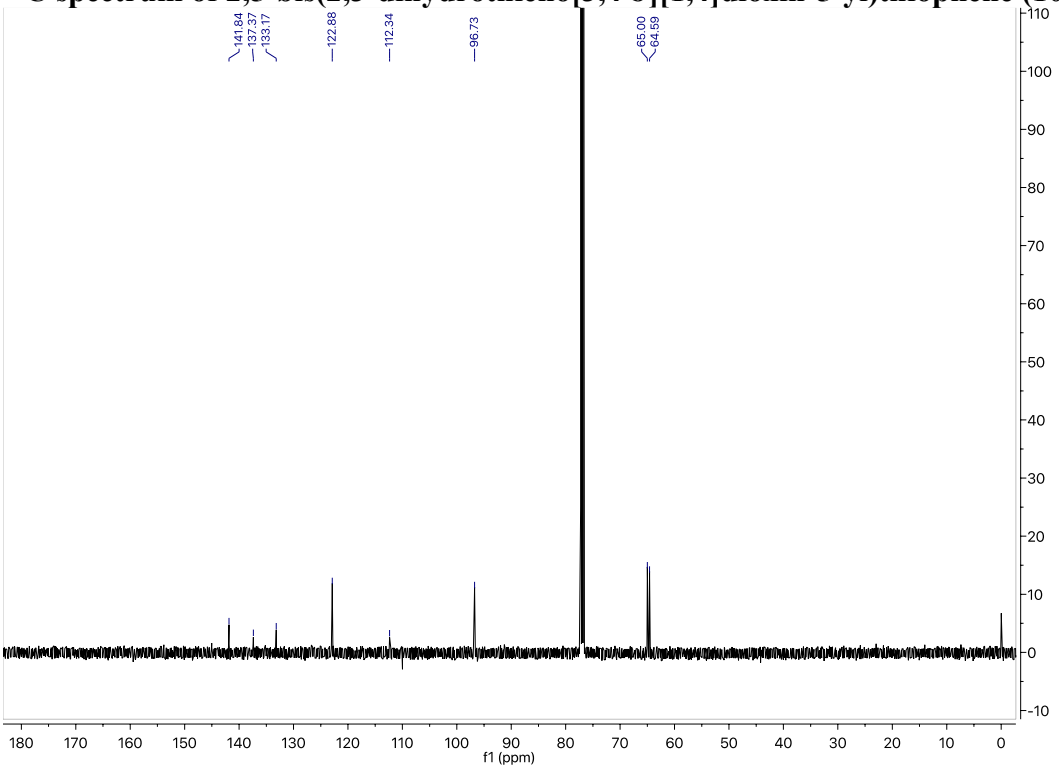
^{13}C spectrum of 5,5''-dimethyl-2,2':5',2''-terthiophene (105d)



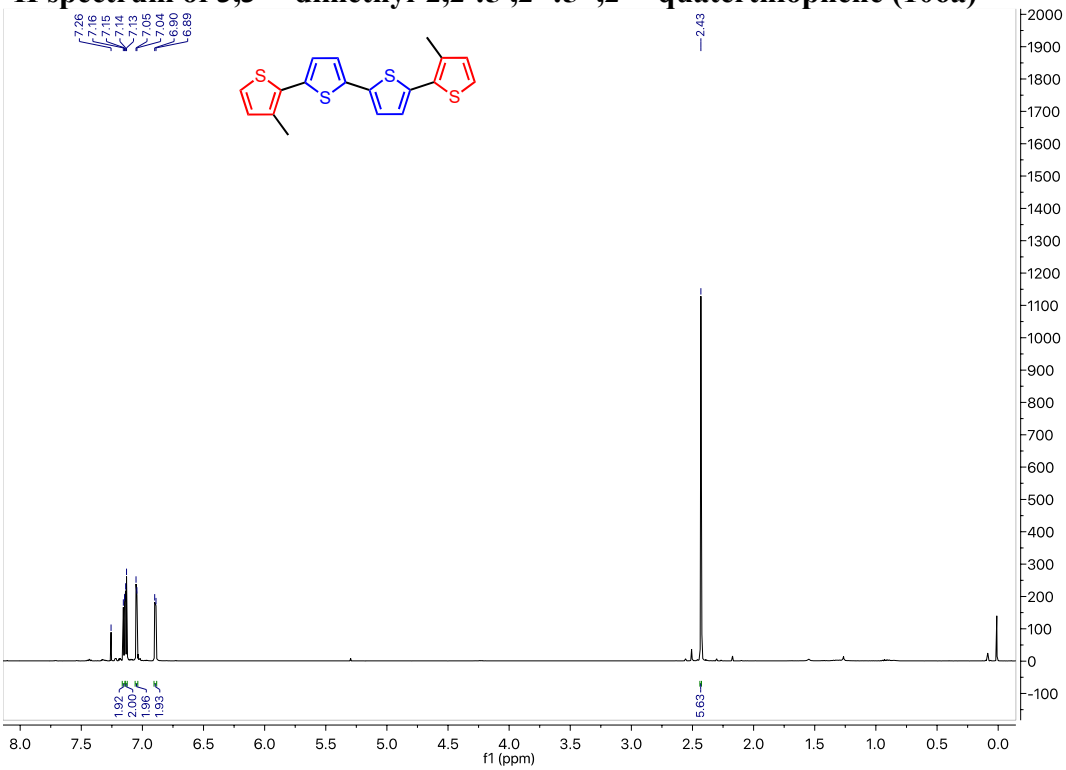
^{1}H spectrum of 2,5-bis(2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)thiophene (105e)



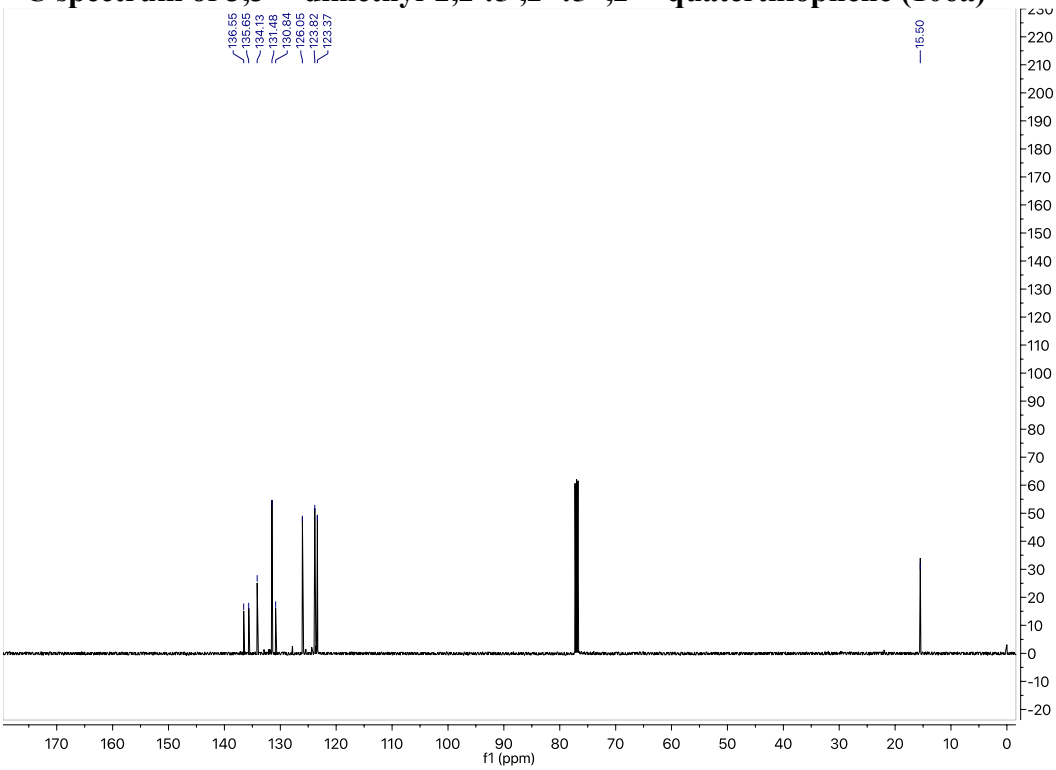
^{13}C spectrum of 2,5-bis(2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)thiophene (105e)



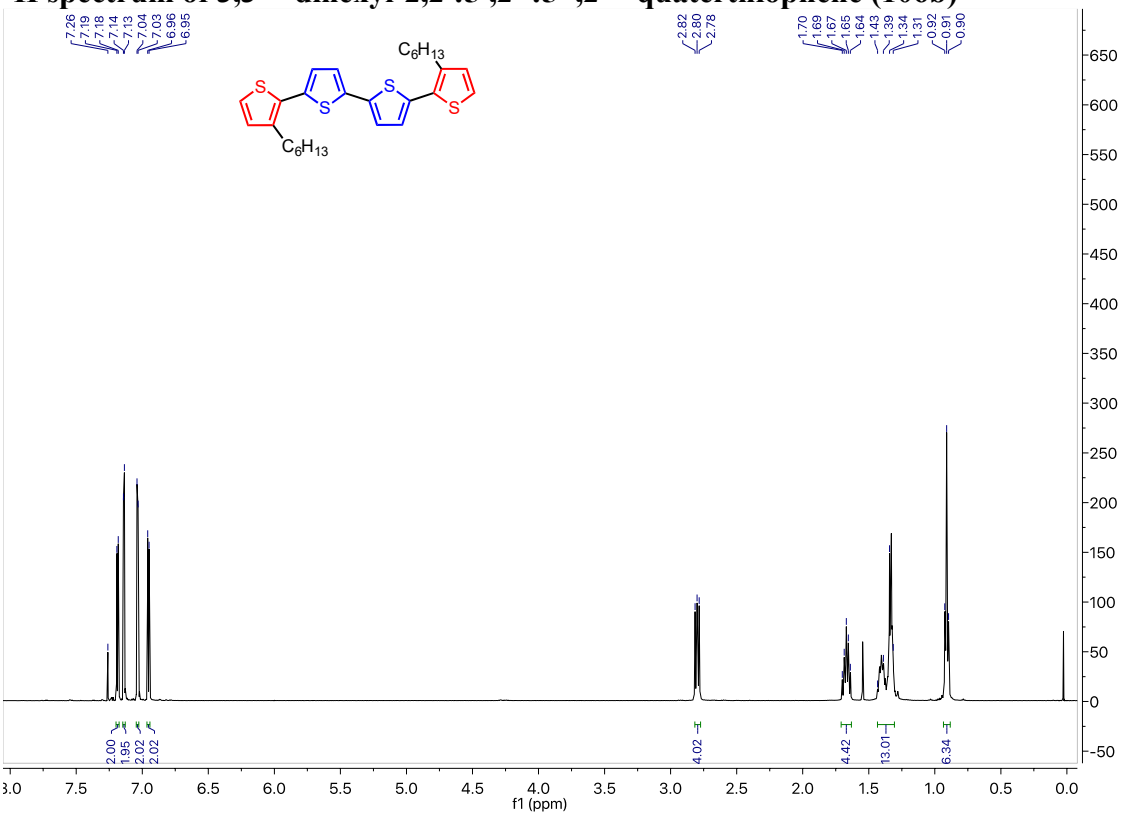
^{1}H spectrum of 3,3'''-dimethyl-2,2':5',2'':5'',2'''-quaterthiophene (106a)



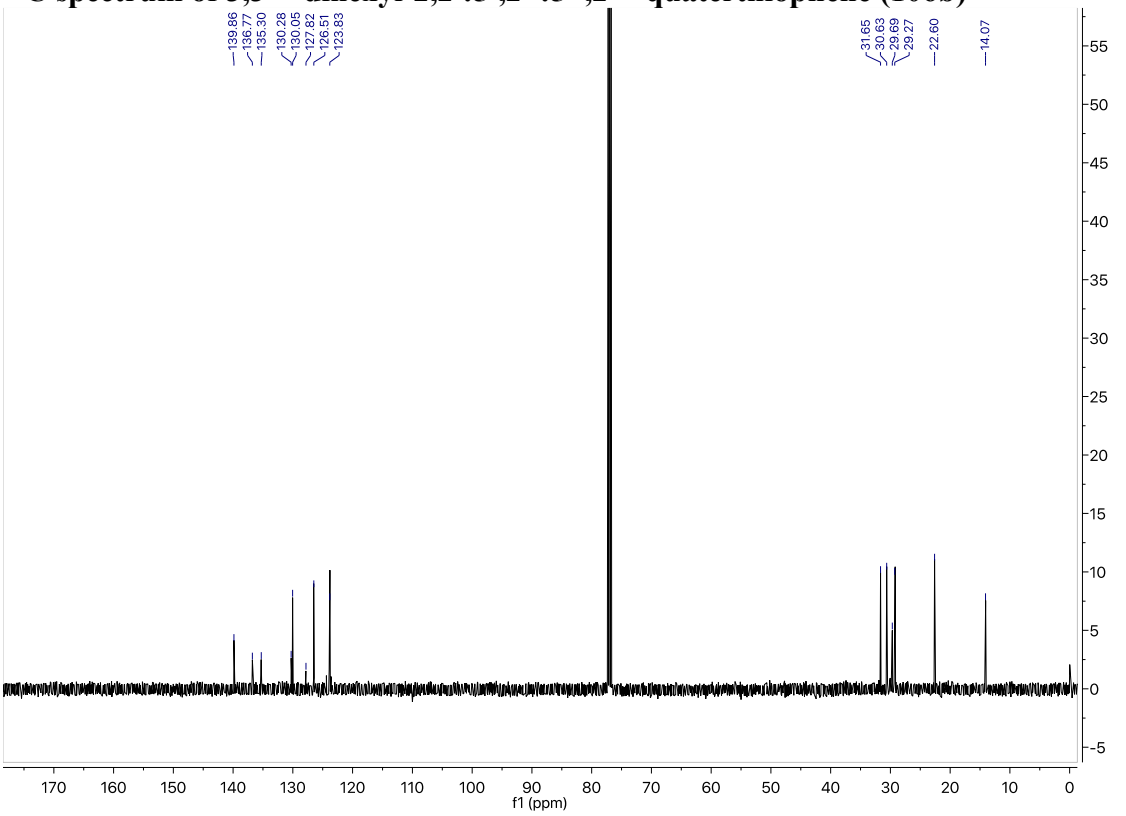
^{13}C spectrum of 3,3'''-dimethyl-2,2':5',2'':5'',2'''-quaterthiophene (106a)



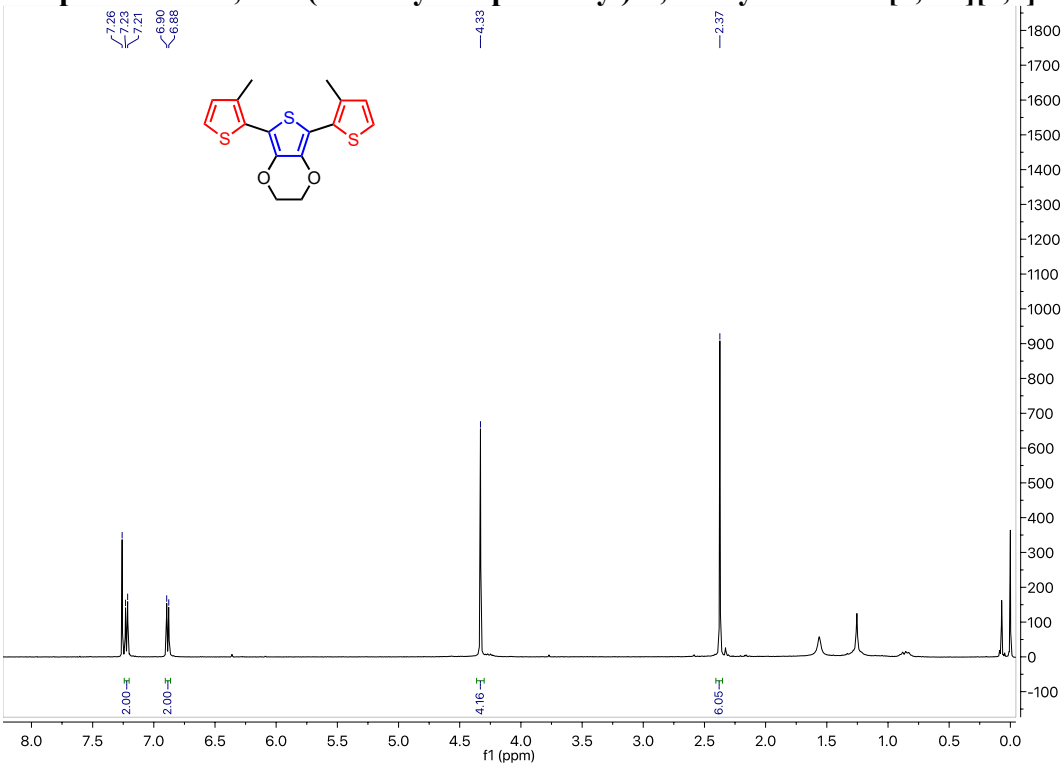
^{1}H spectrum of 3,3'''-dihexyl-2,2':5',2'':5'',2'''-quaterthiophene (106b)



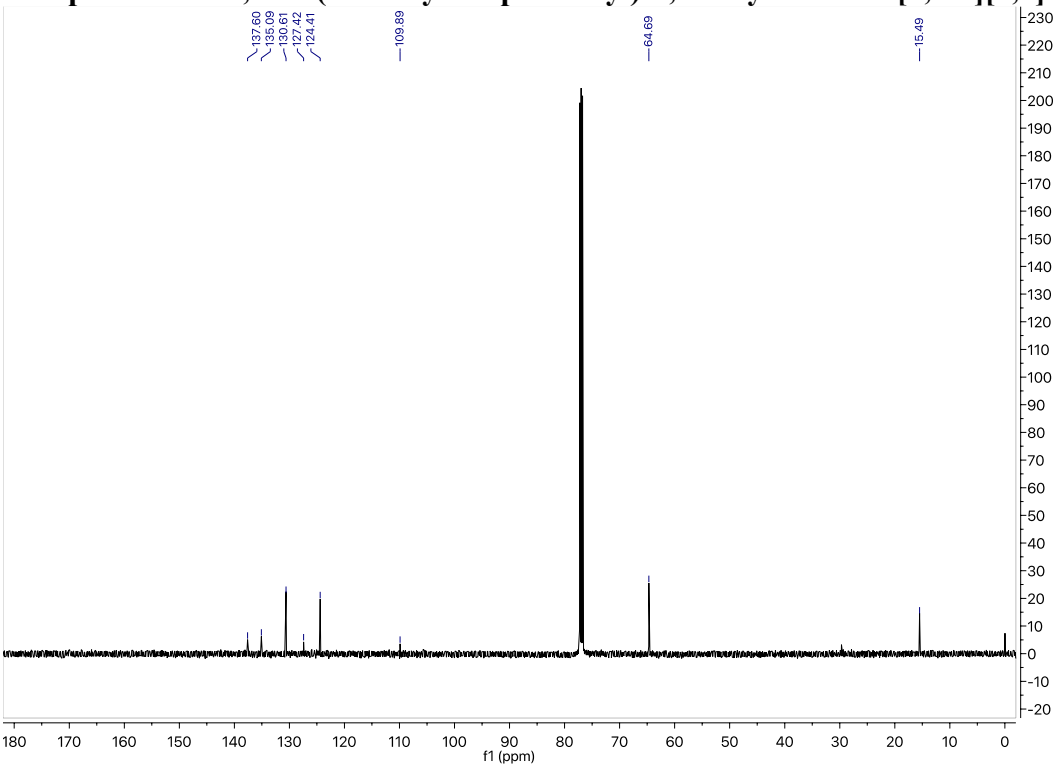
^{13}C spectrum of 3,3'''-dihexyl-2,2':5',2'':5'',2'''-quaterthiophene (106b)



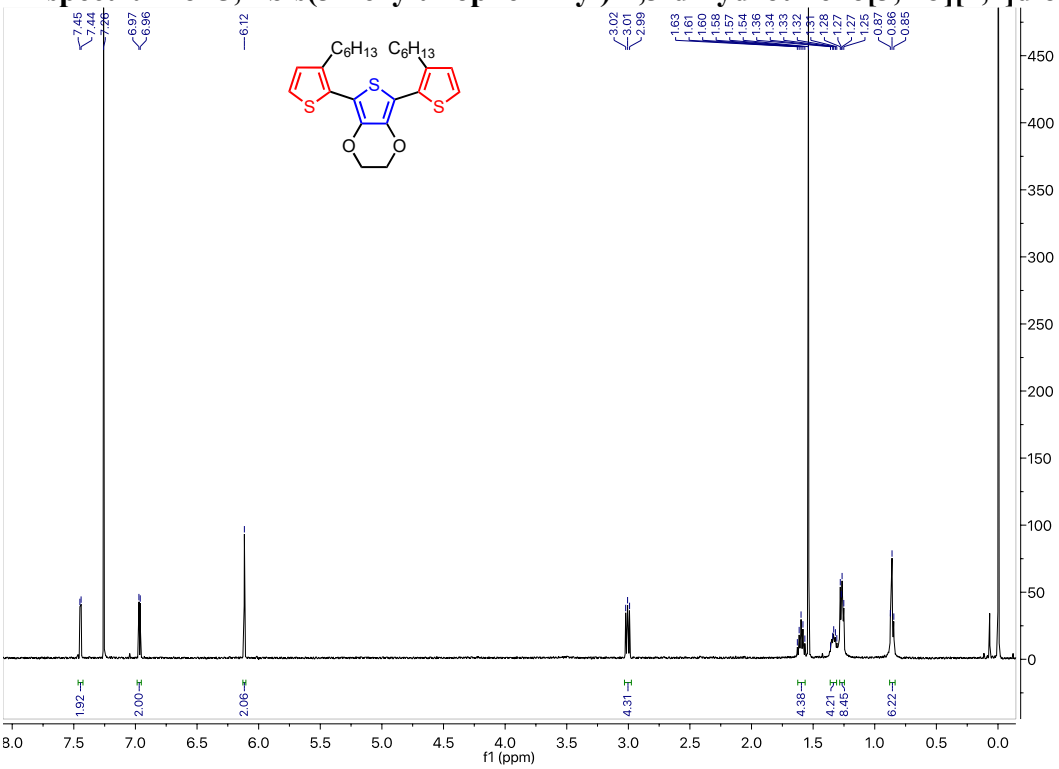
^{1}H spectrum of 5,7-bis(3-methylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108a)



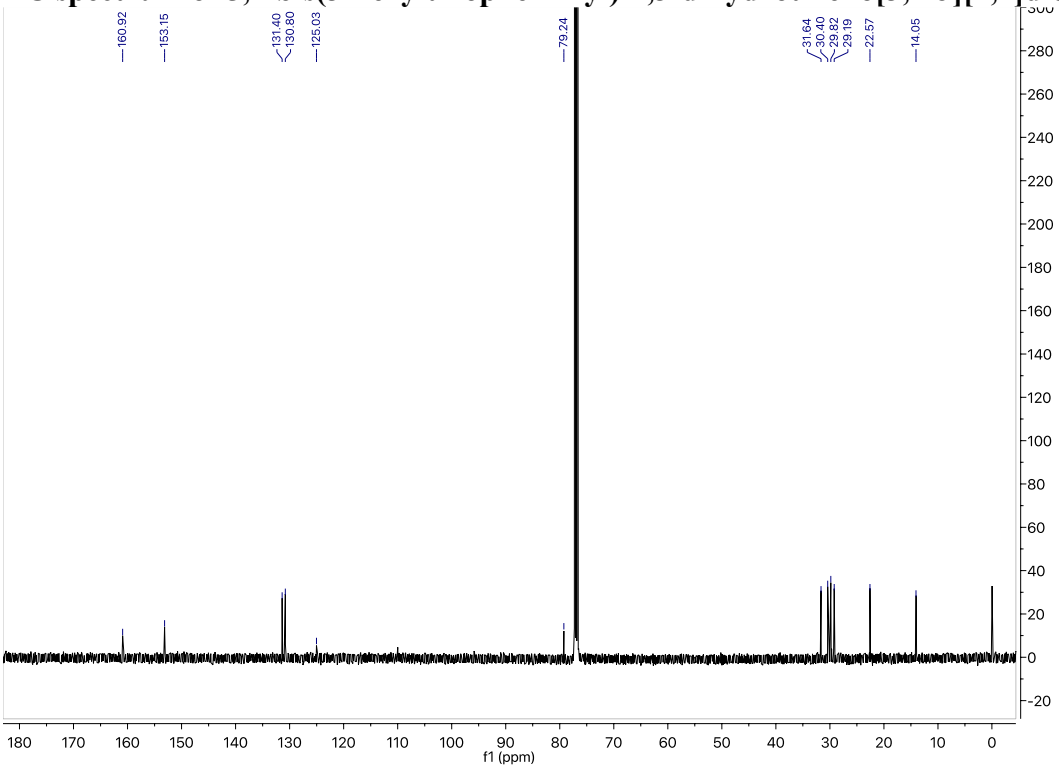
^{13}C spectrum of 5,7-bis(3-methylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108a)



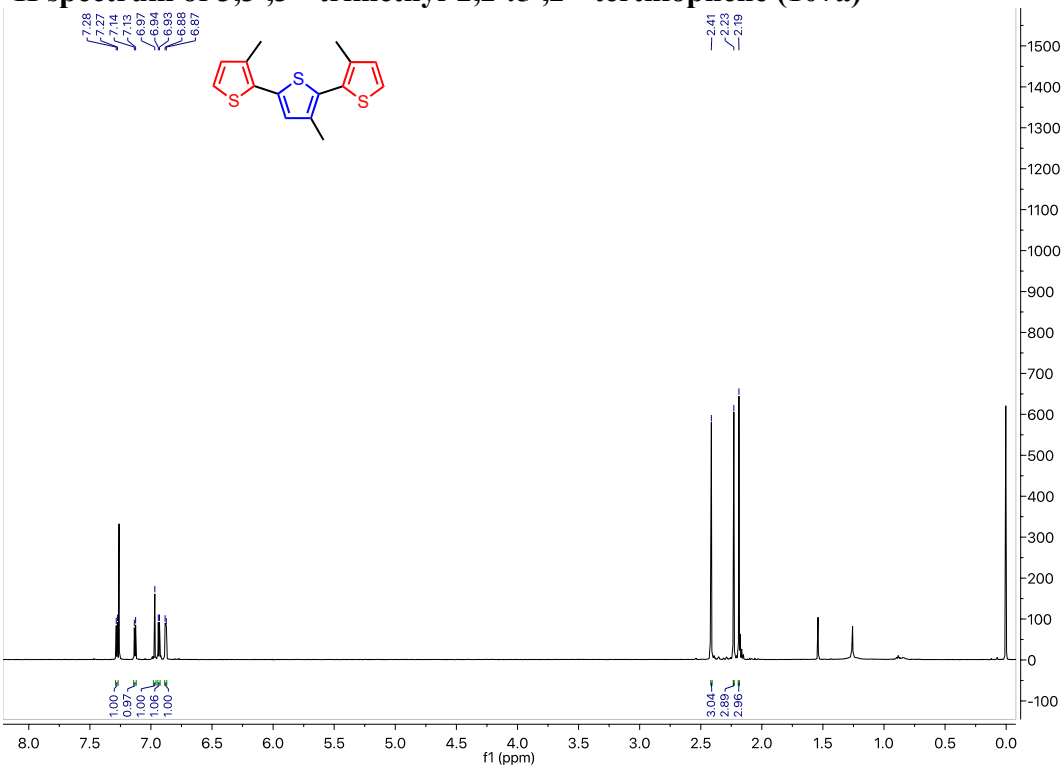
^{1}H spectrum of 5,7-bis(3-hexylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108b)



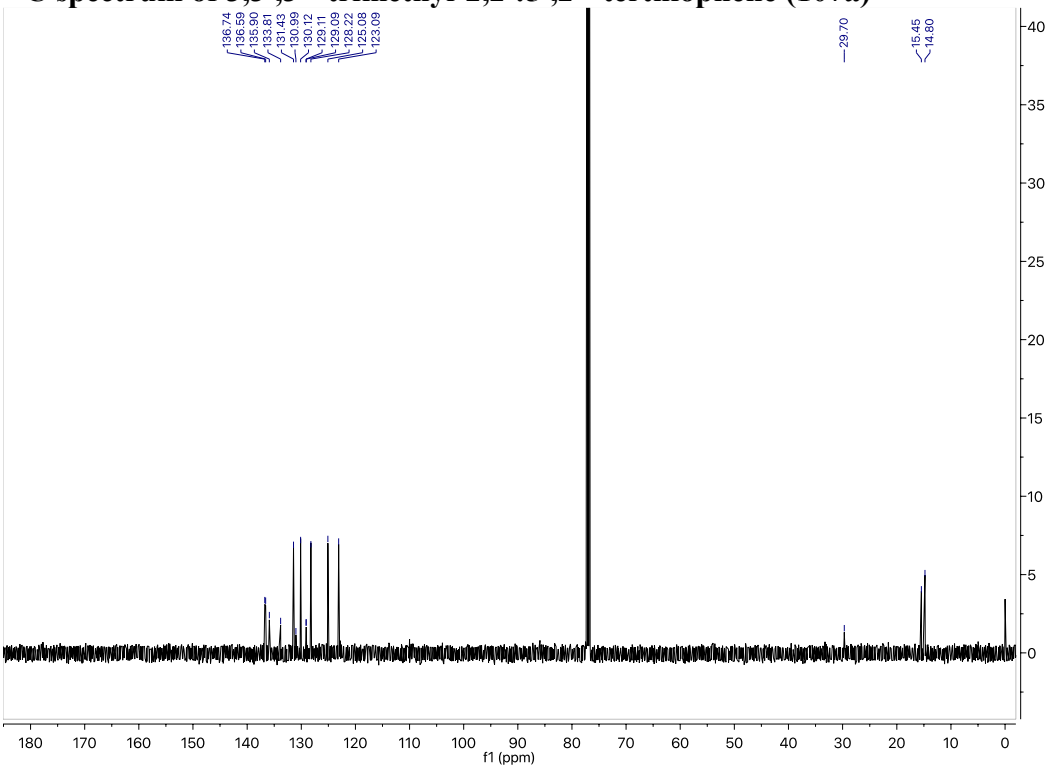
^{13}C spectrum of 5,7-bis(3-hexylthiophen-2-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (108b)



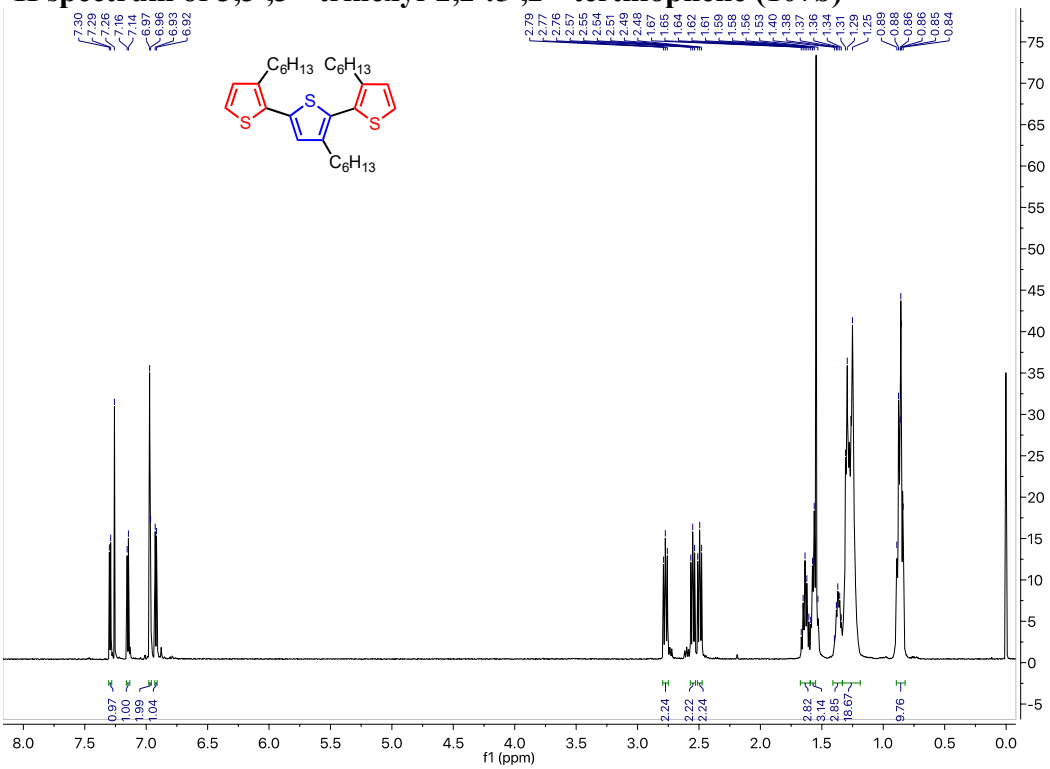
^{1}H spectrum of 3,3',3''-trimethyl-2,2':5',2''-terthiophene (107a)



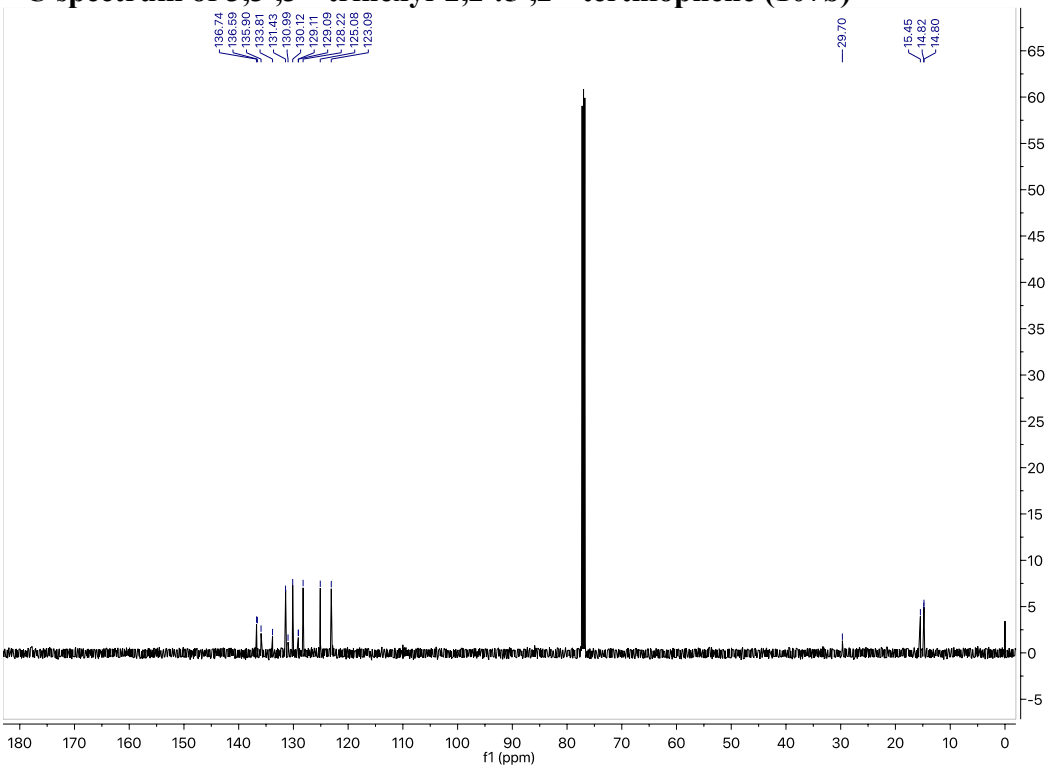
^{13}C spectrum of 3,3',3''-trimethyl-2,2':5',2''-terthiophene (107a)



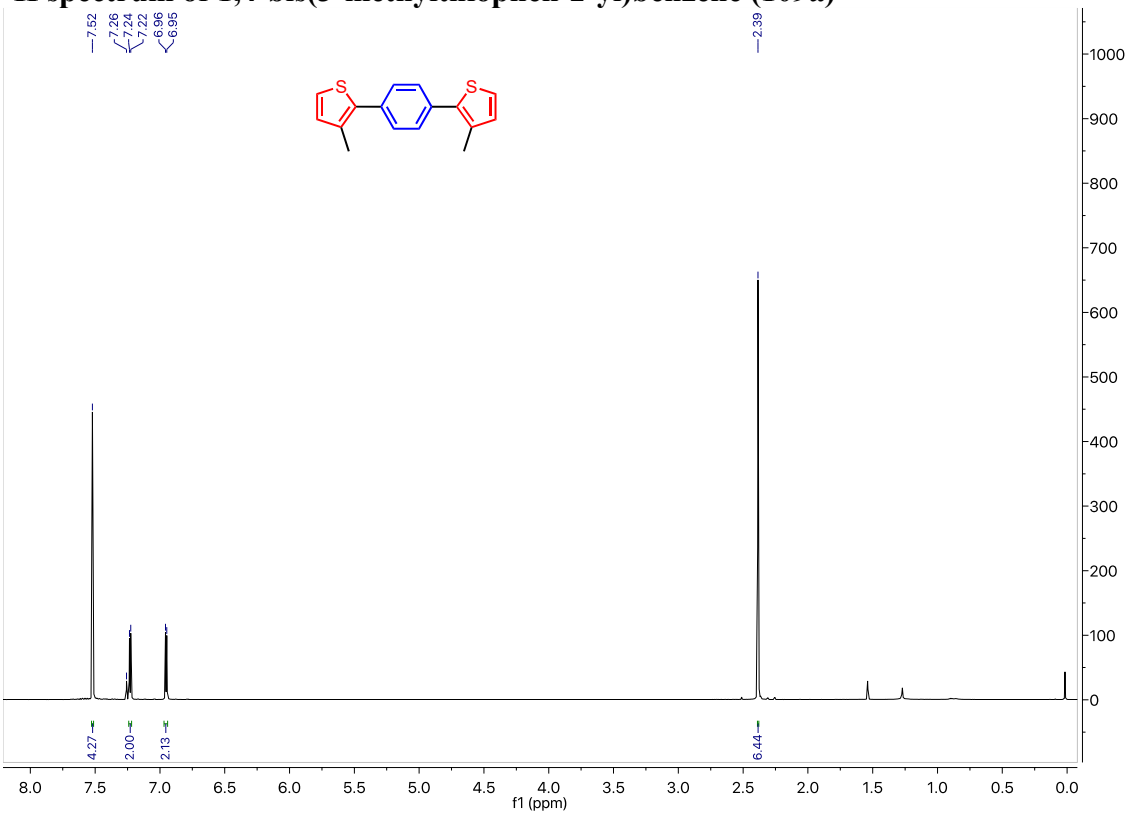
^{1}H spectrum of 3,3',3''-trihexyl-2,2':5',2''-terthiophene (107b)



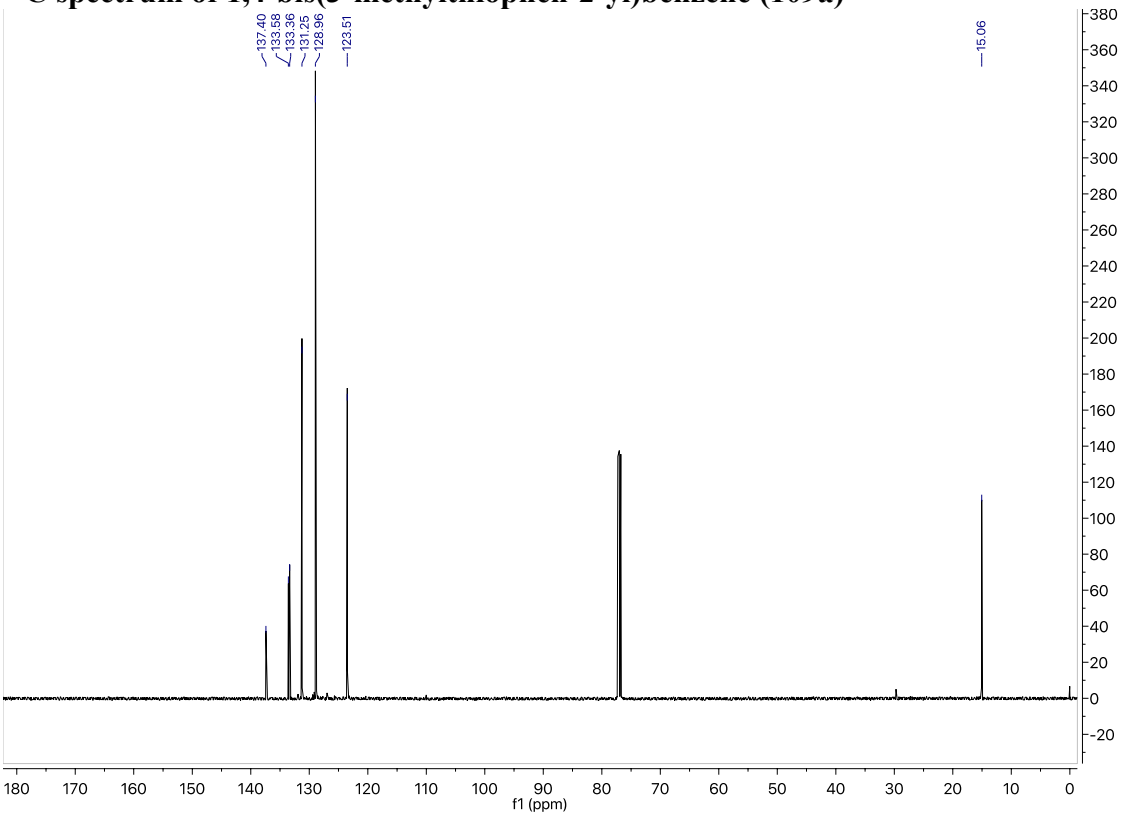
^{13}C spectrum of 3,3',3''-trihexyl-2,2':5',2''-terthiophene (107b)



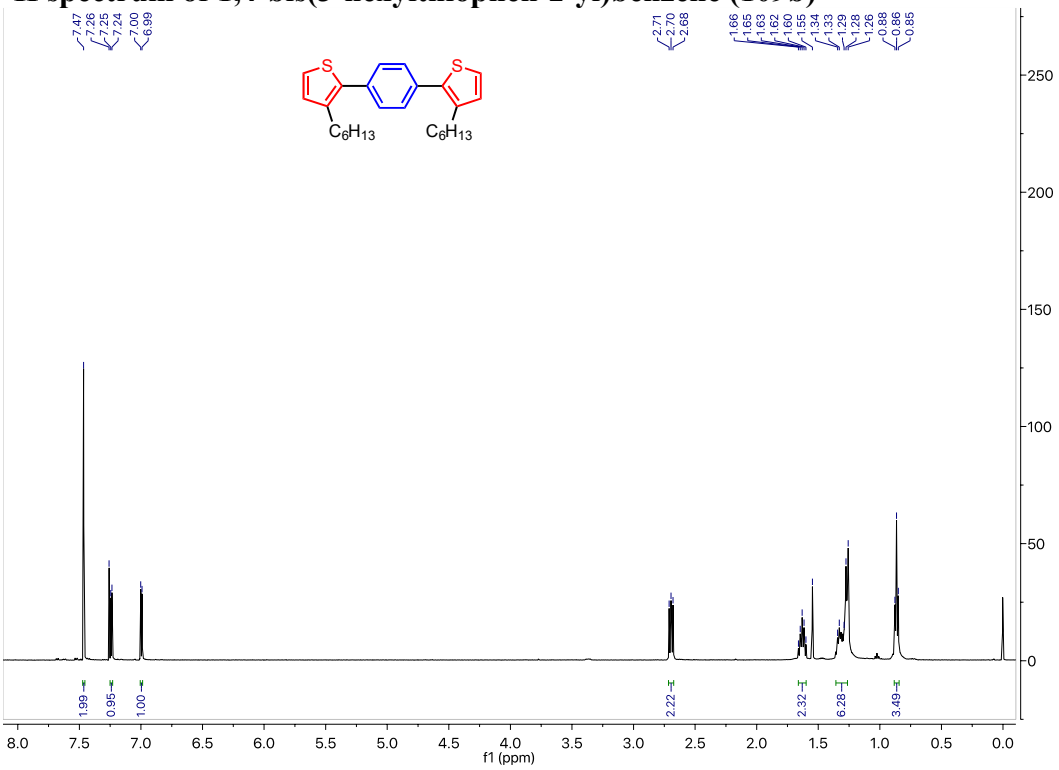
^{1}H spectrum of 1,4-bis(3-methylthiophen-2-yl)benzene (109a)



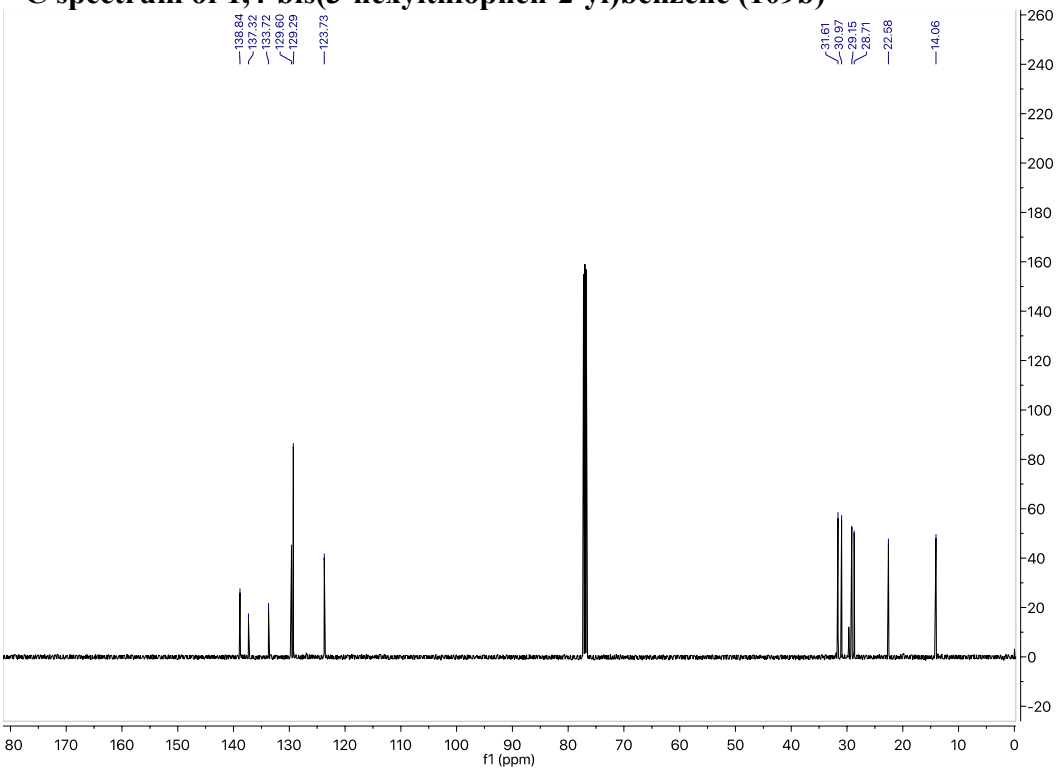
^{13}C spectrum of 1,4-bis(3-methylthiophen-2-yl)benzene (109a)



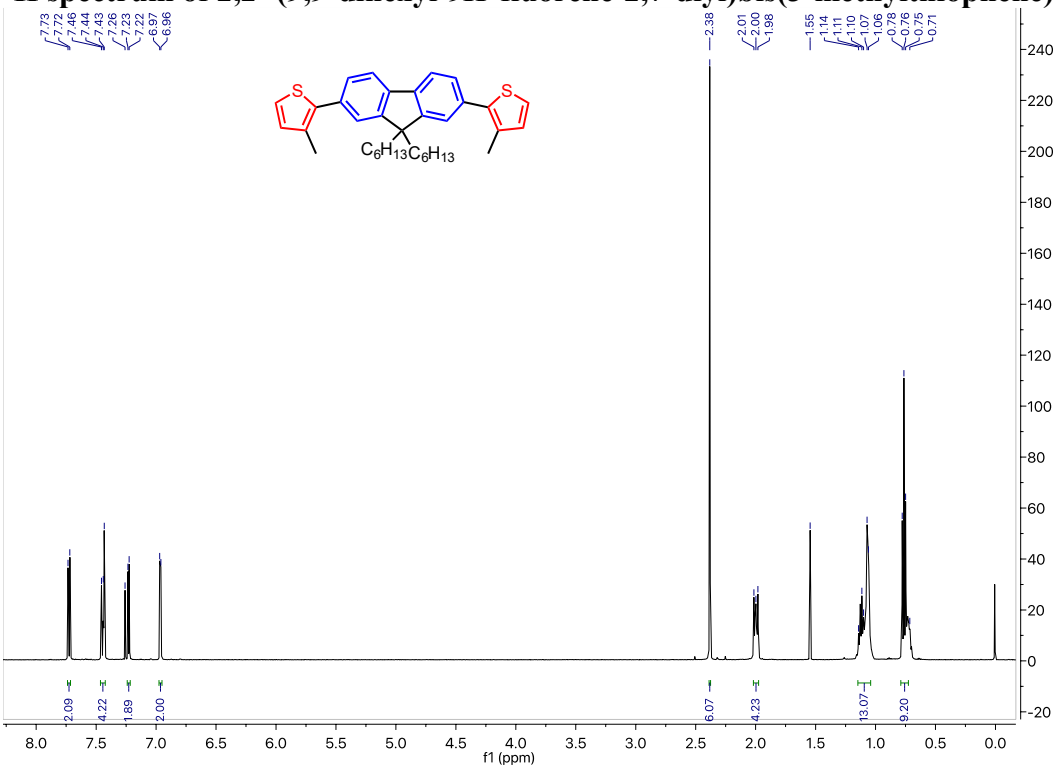
^{1}H spectrum of 1,4-bis(3-hexylthiophen-2-yl)benzene (109b)



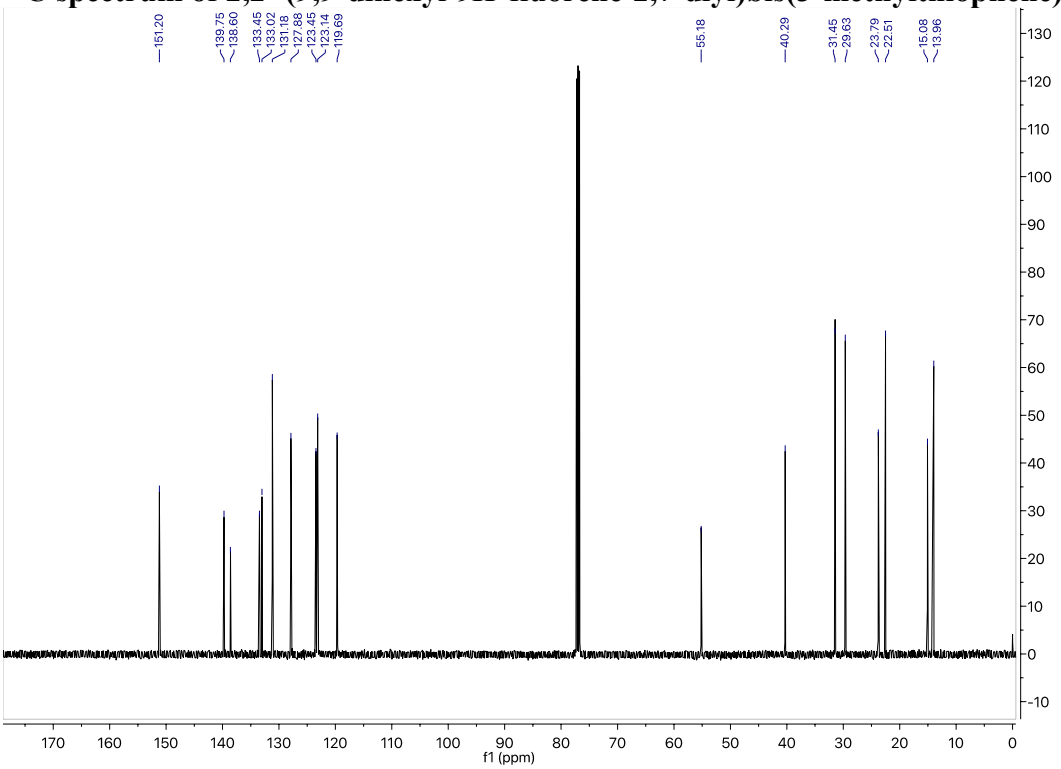
^{13}C spectrum of 1,4-bis(3-hexylthiophen-2-yl)benzene (109b)



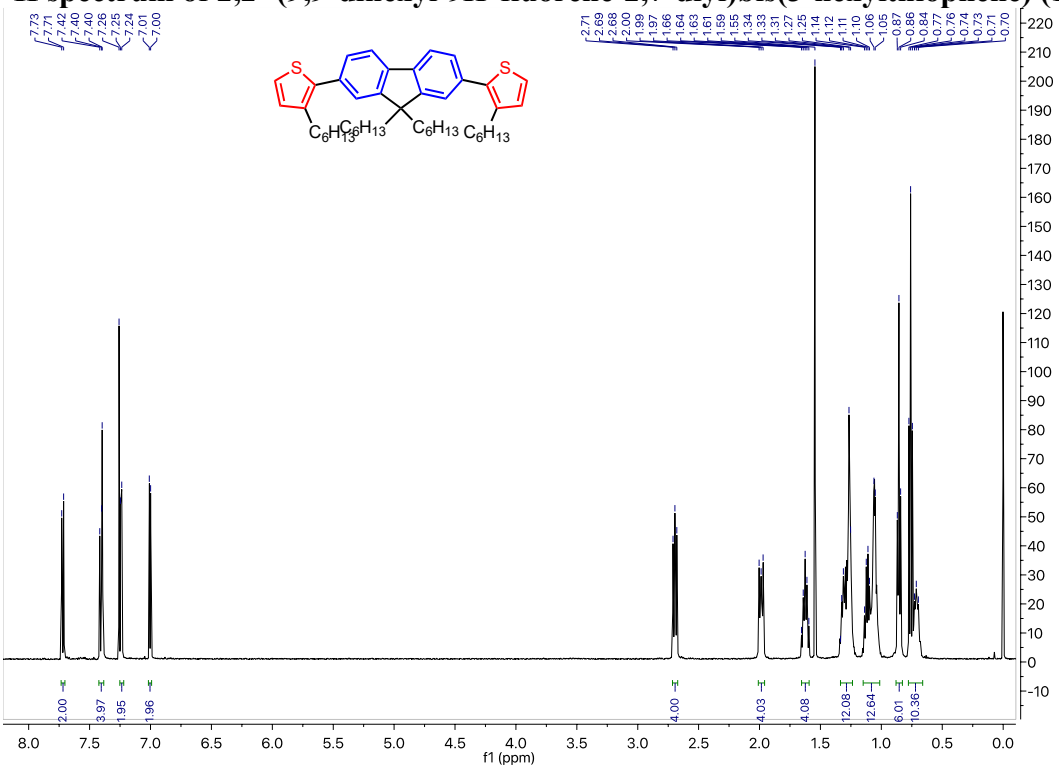
^{1}H spectrum of 2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-methylthiophene) (110a)



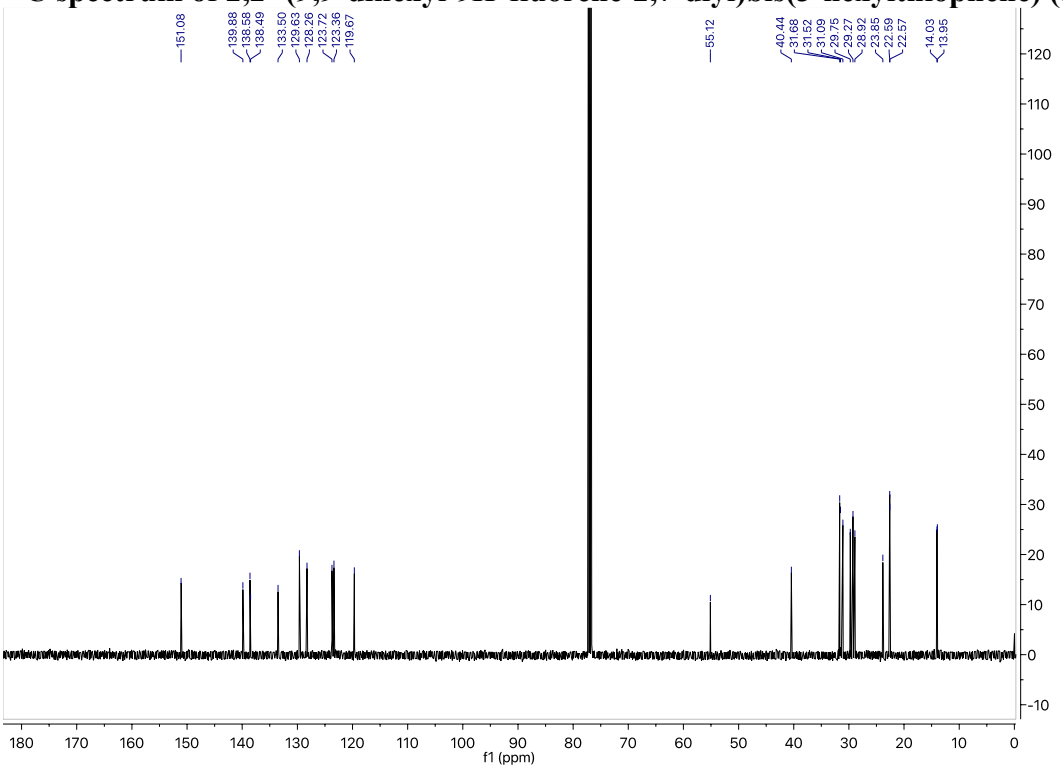
^{13}C spectrum of 2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-methylthiophene) (110a)



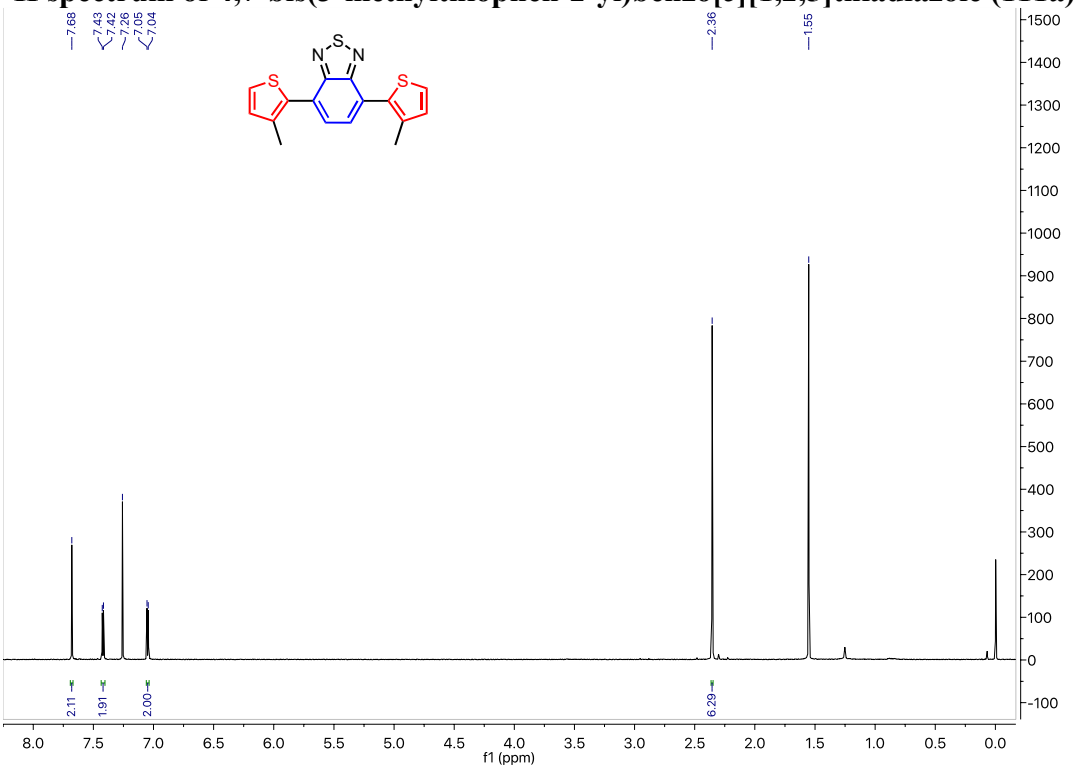
^{1}H spectrum of 2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-hexylthiophene) (110b)



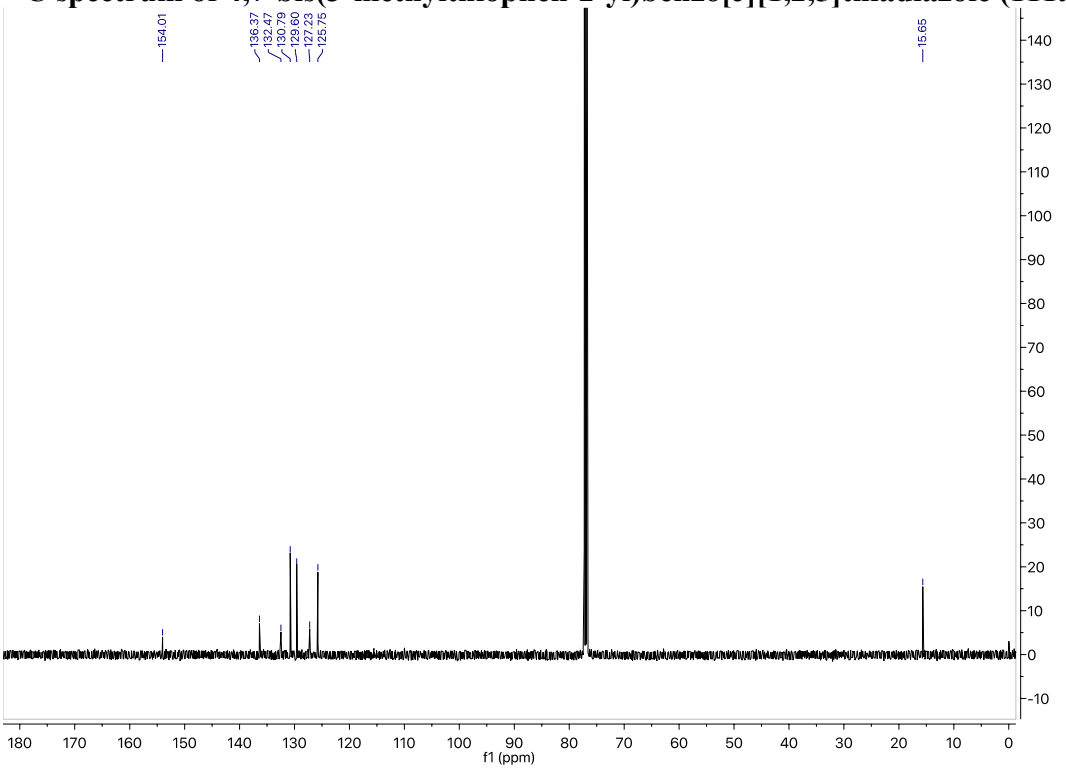
^{13}C spectrum of 2,2'-(9,9-dihexyl-9*H*-fluorene-2,7-diyl)bis(3-hexylthiophene) (110b)



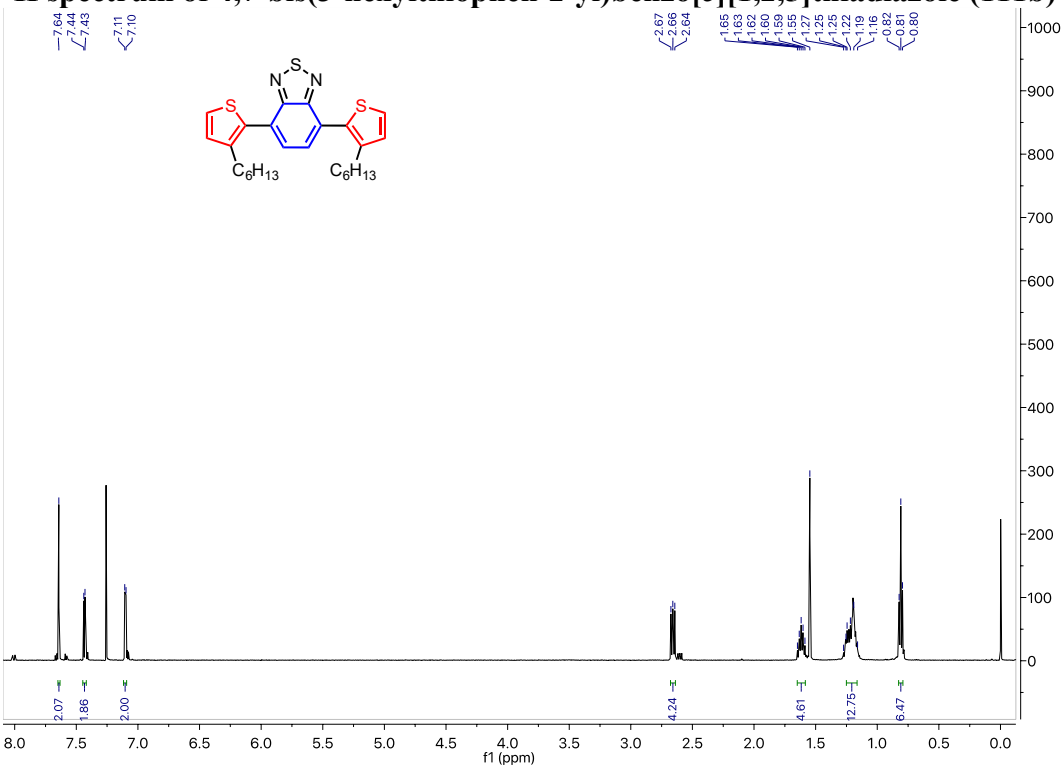
^{1}H spectrum of 4,7-bis(3-methylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111a)



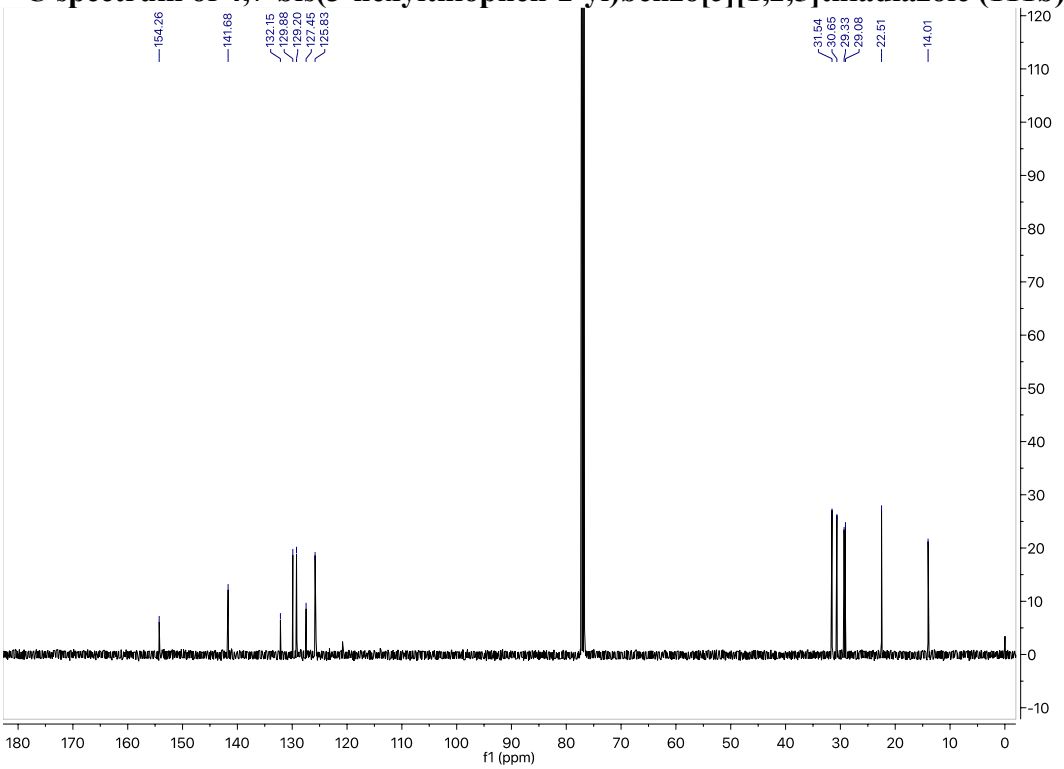
^{13}C spectrum of 4,7-bis(3-methylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111a)



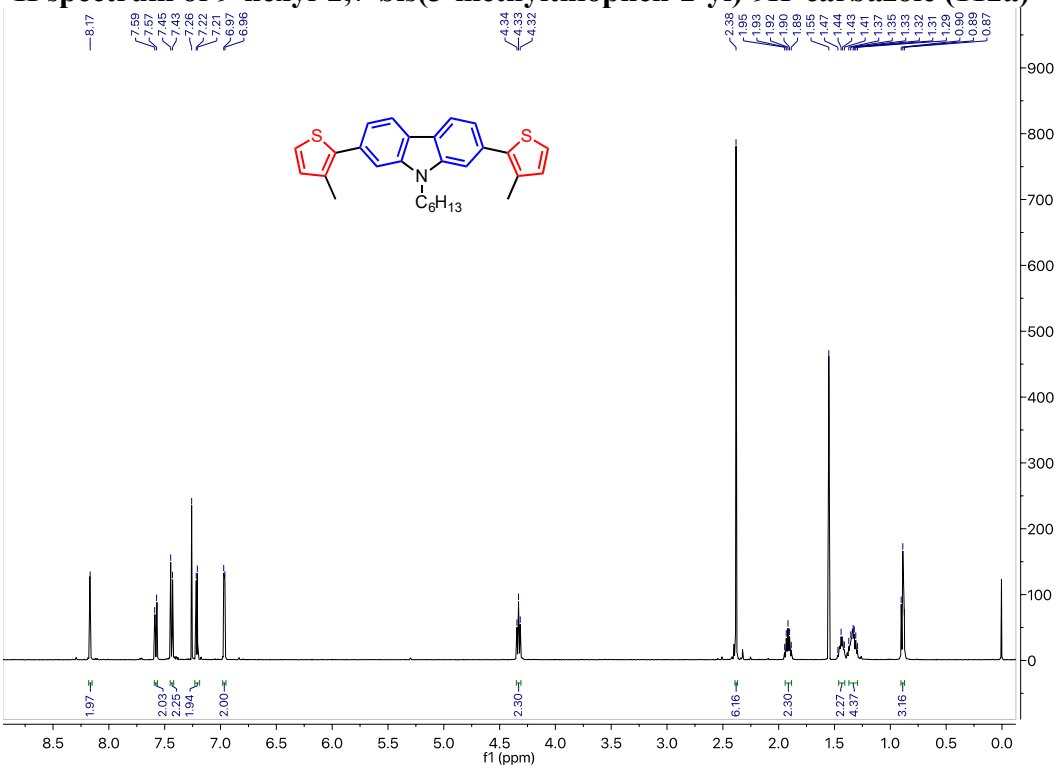
^{1}H spectrum of 4,7-bis(3-hexylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111b)



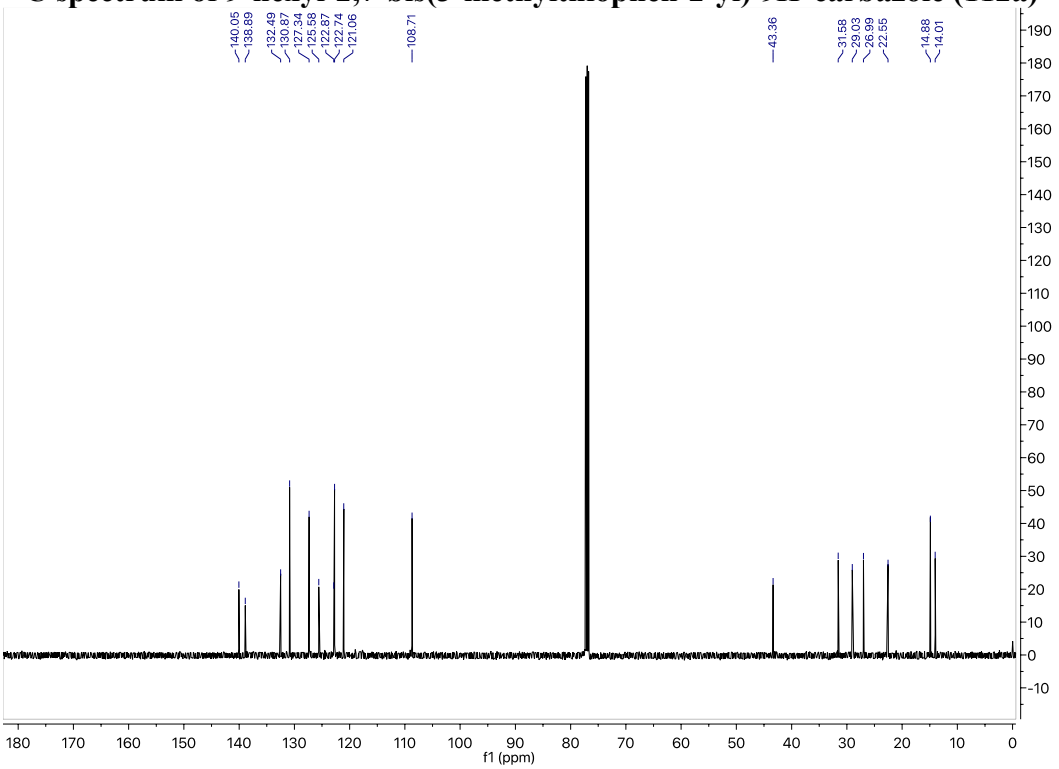
^{13}C spectrum of 4,7-bis(3-hexylthiophen-2-yl)benzo[*c*][1,2,5]thiadiazole (111b)



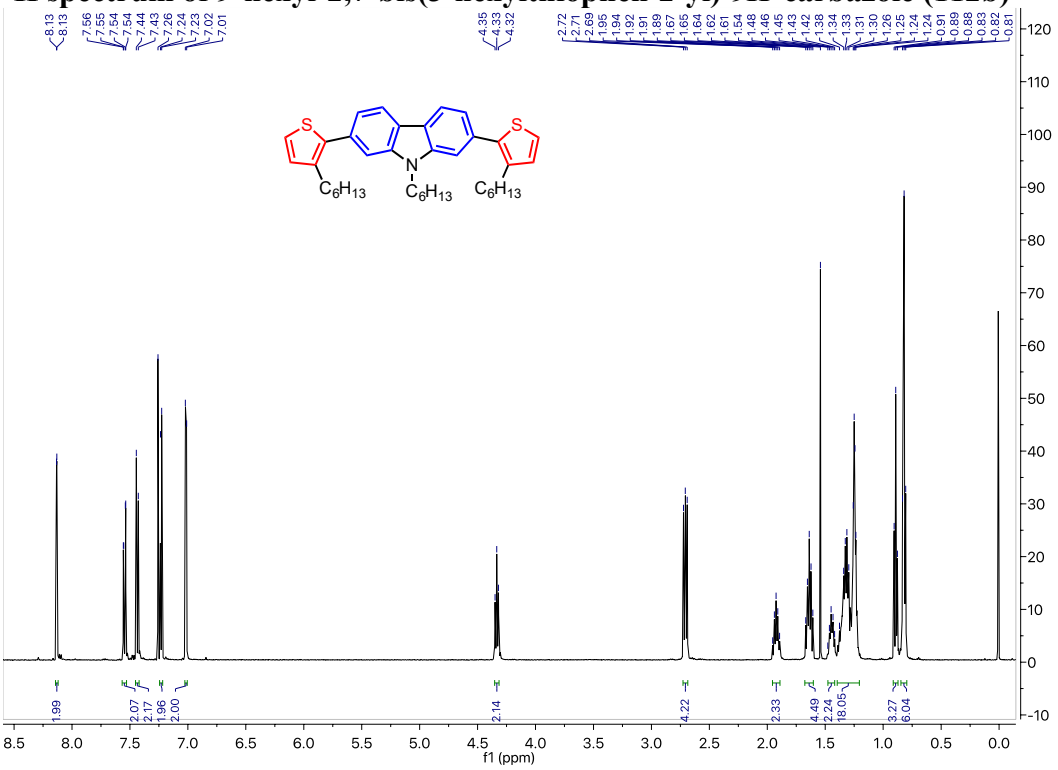
^{1}H spectrum of 9-hexyl-2,7-bis(3-methylthiophen-2-yl)-9*H*-carbazole (112a)



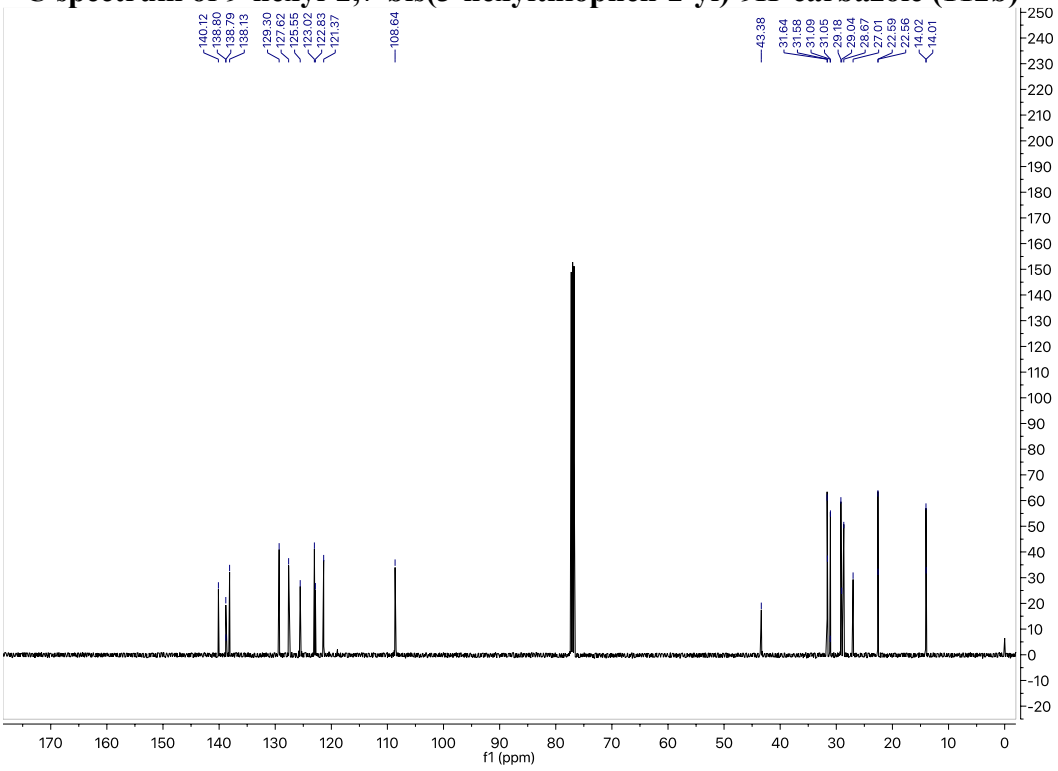
^{13}C spectrum of 9-hexyl-2,7-bis(3-methylthiophen-2-yl)-9*H*-carbazole (112a)



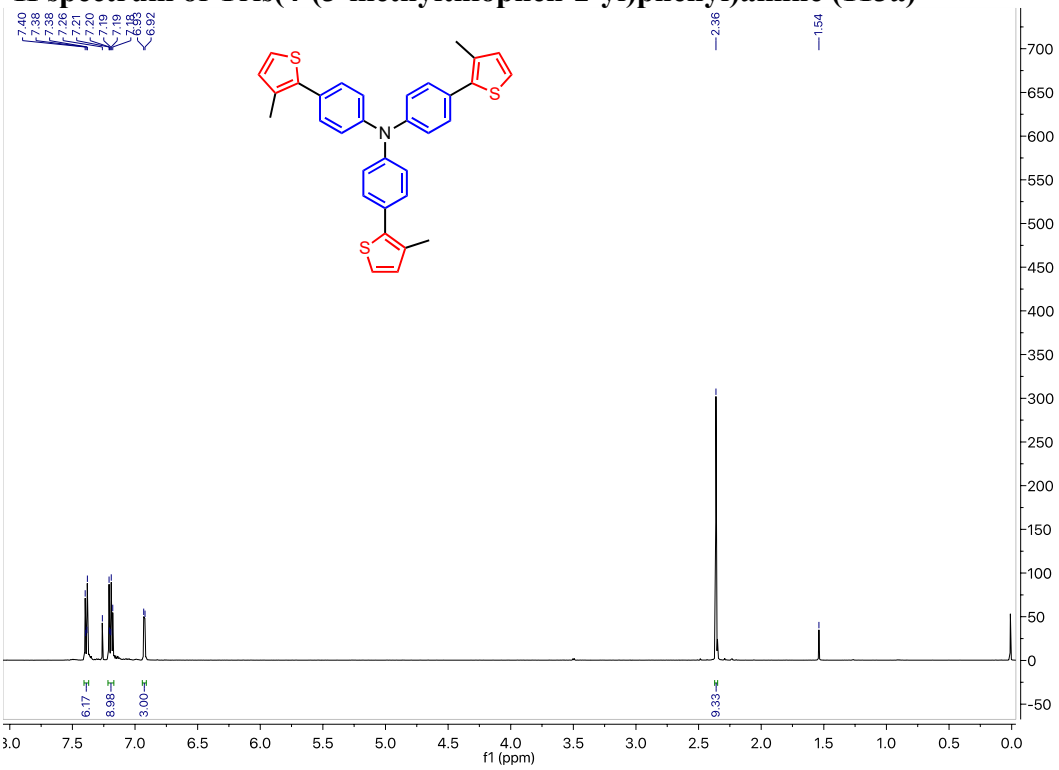
^{1}H spectrum of 9-hexyl-2,7-bis(3-hexylthiophen-2-yl)-9*H*-carbazole (112b)



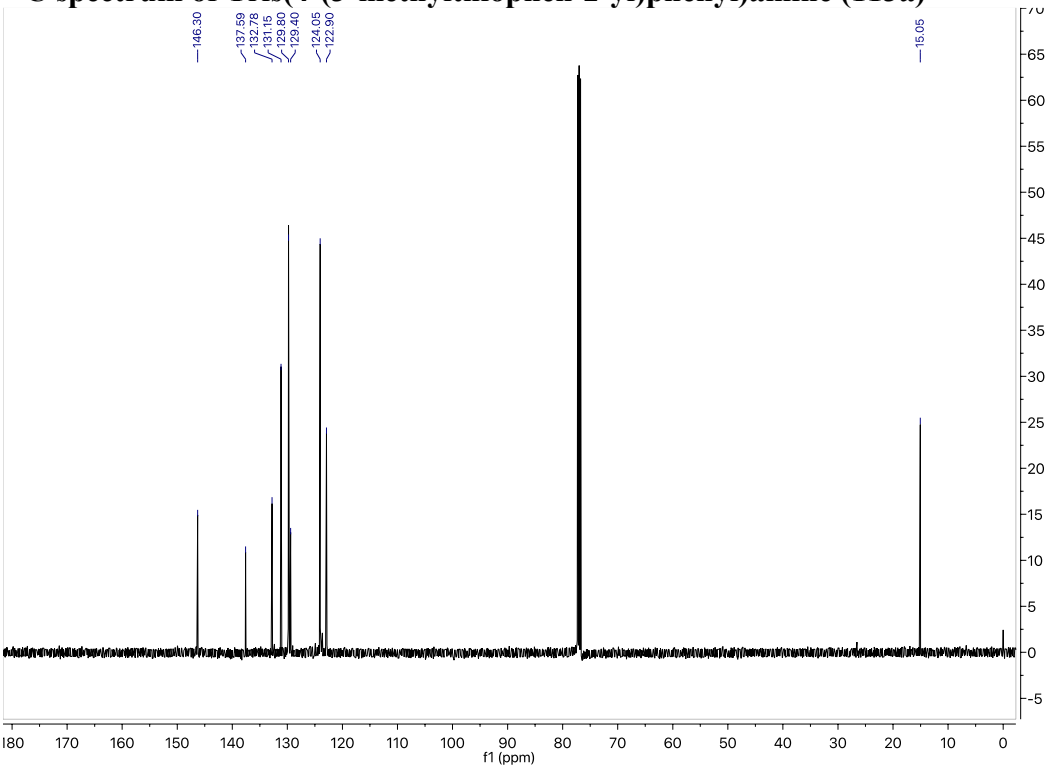
^{13}C spectrum of 9-hexyl-2,7-bis(3-hexylthiophen-2-yl)-9*H*-carbazole (112b)



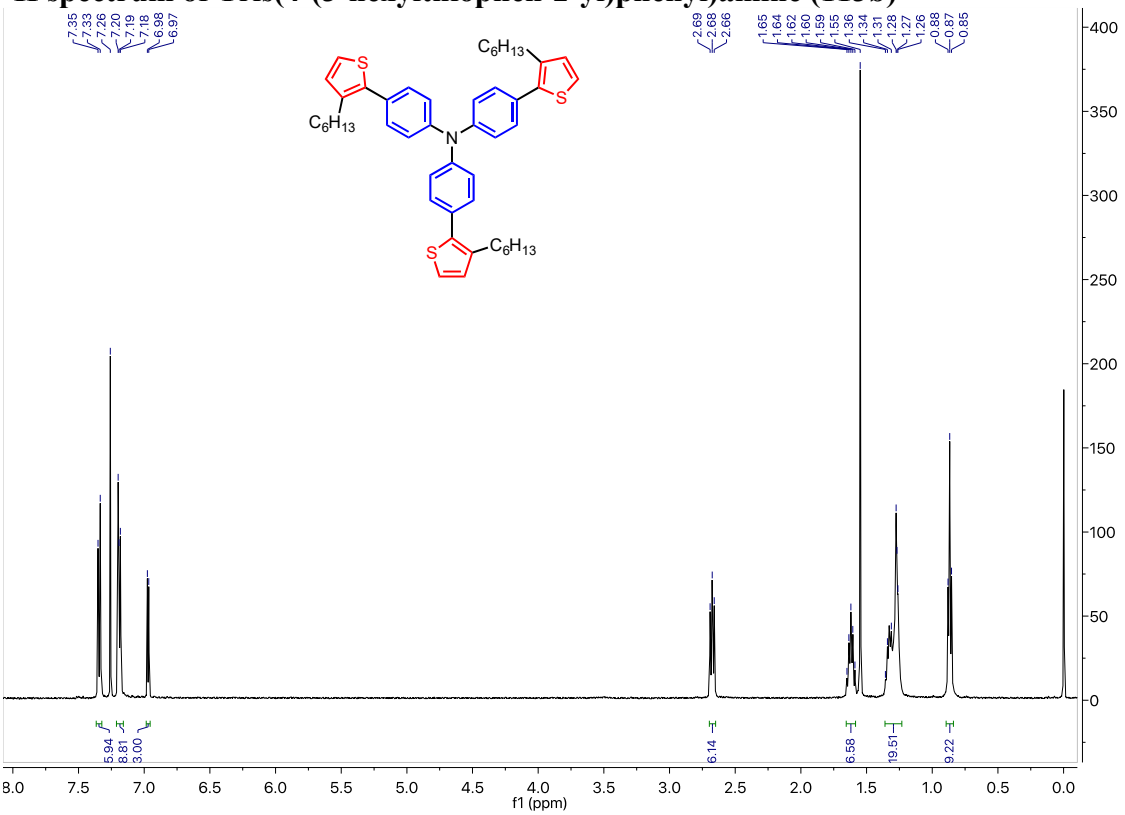
^{1}H spectrum of Tris(4-(3-methylthiophen-2-yl)phenyl)amine (113a)



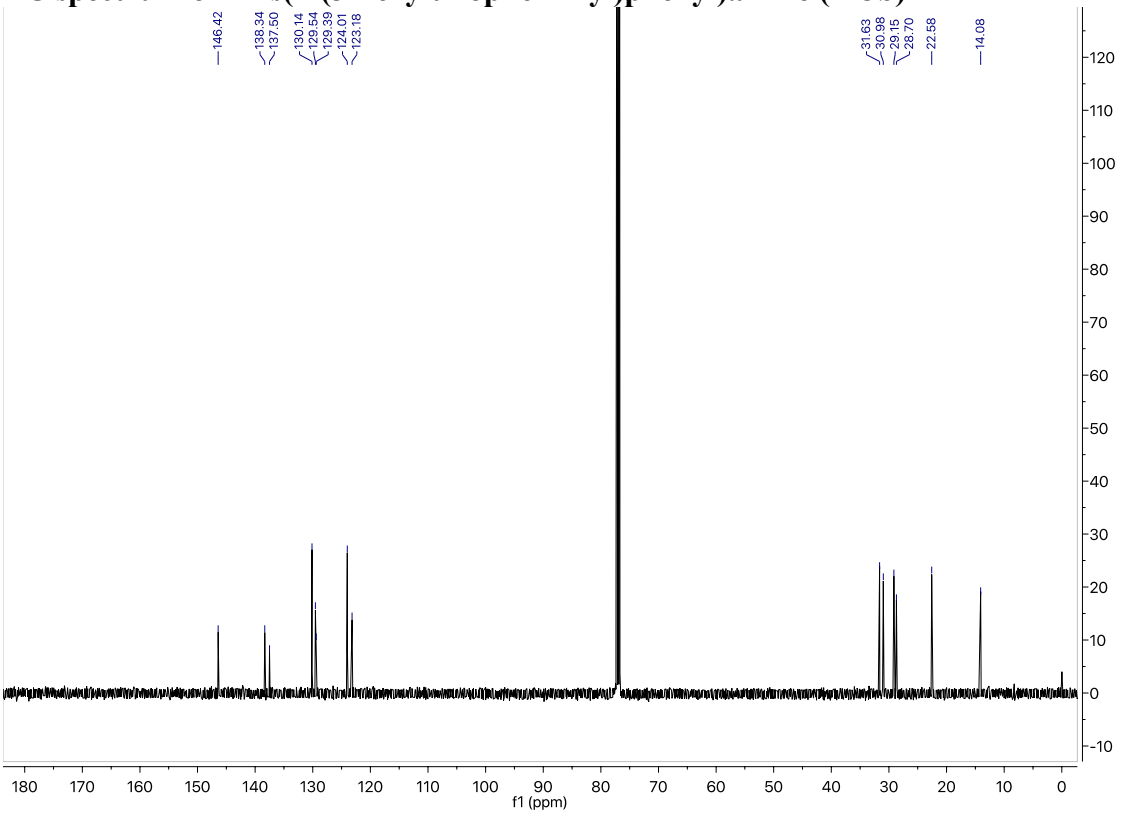
^{13}C spectrum of Tris(4-(3-methylthiophen-2-yl)phenyl)amine (113a)



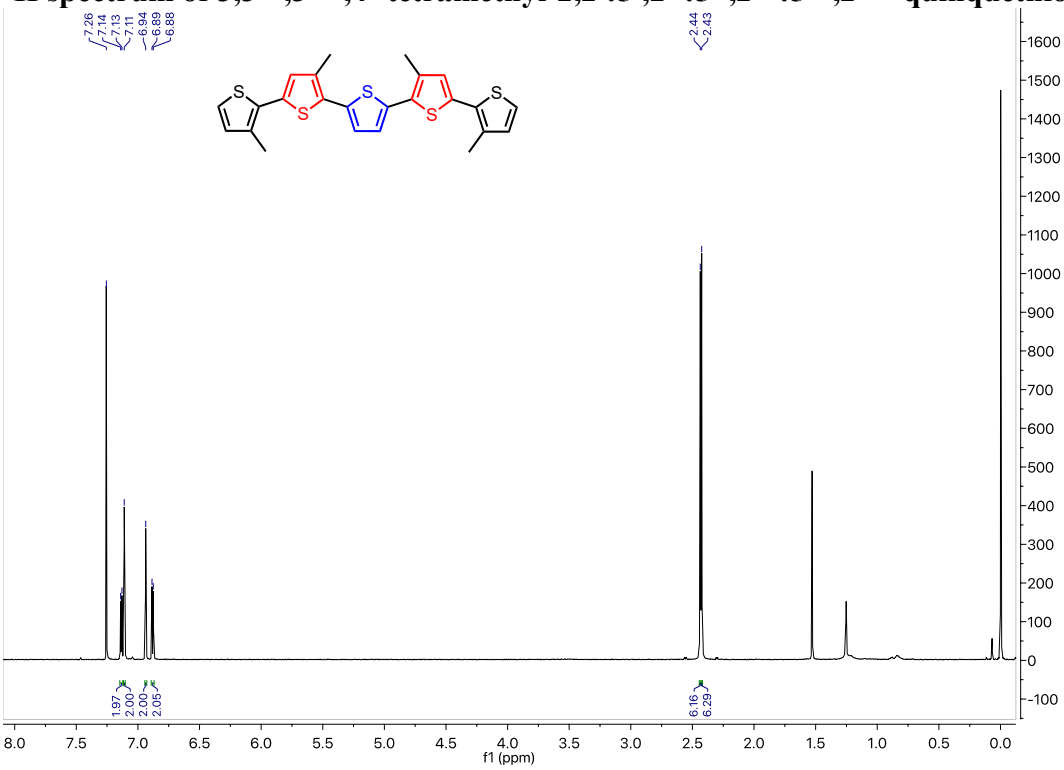
^{1}H spectrum of Tris(4-(3-hexylthiophen-2-yl)phenyl)amine (113b)



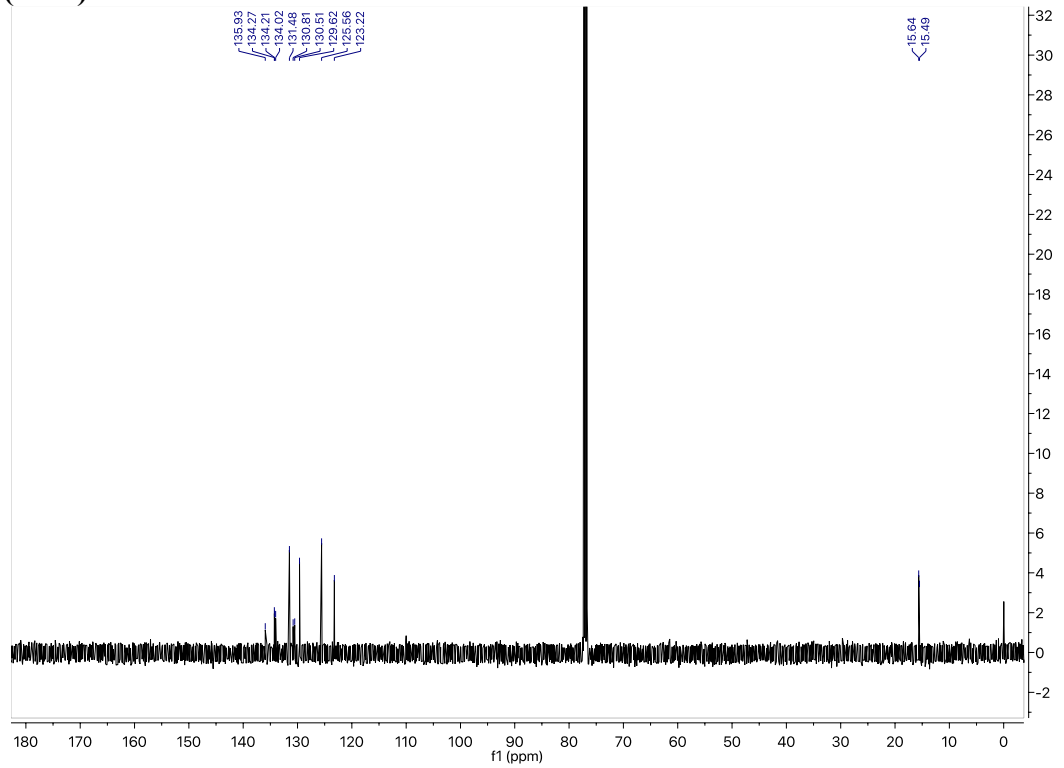
^{13}C spectrum of Tris(4-(3-hexylthiophen-2-yl)phenyl)amine (113b)



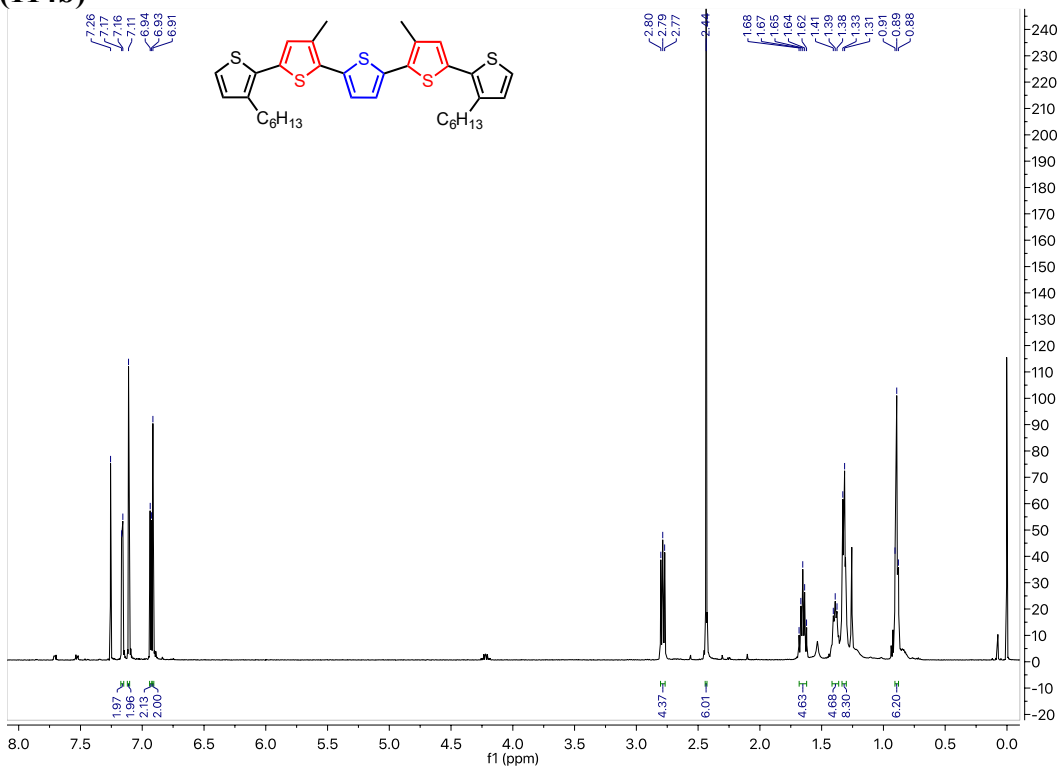
^{1}H spectrum of 3,3''',3'''',4'-tetramethyl-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (114a)



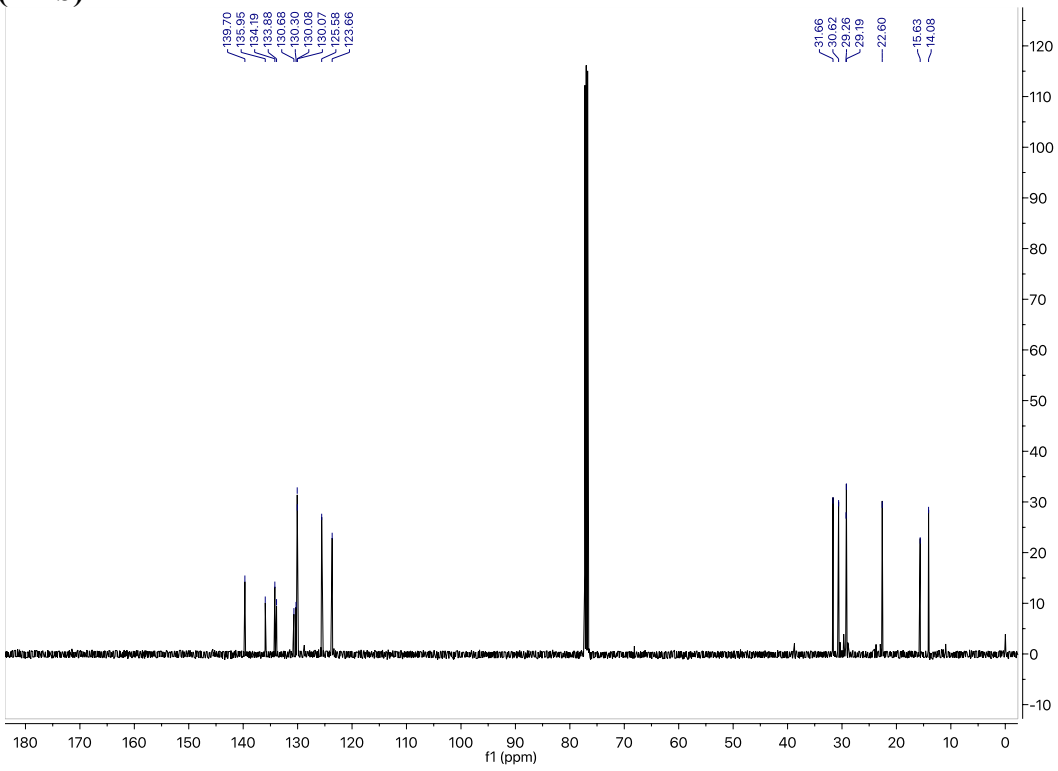
^{13}C spectrum of 3,3''',3'''',4'-tetramethyl-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (114a)



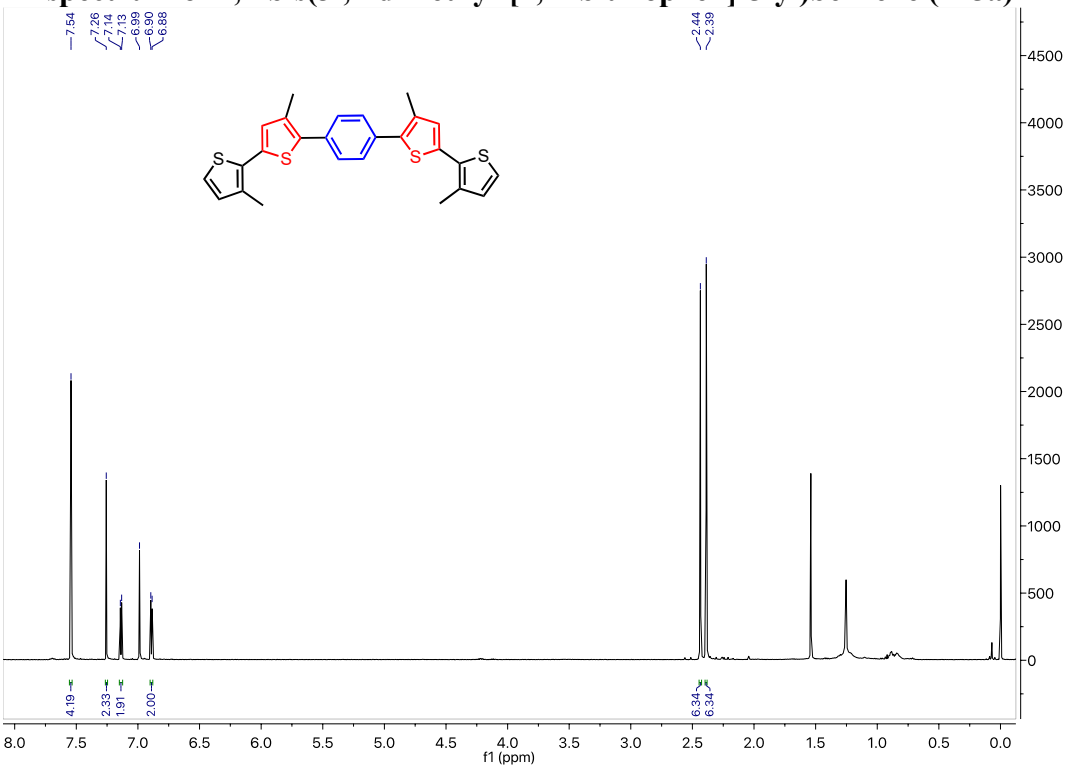
^{1}H spectrum of 3,3''''-dihexyl-3''',4'-dimethyl-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (114b)



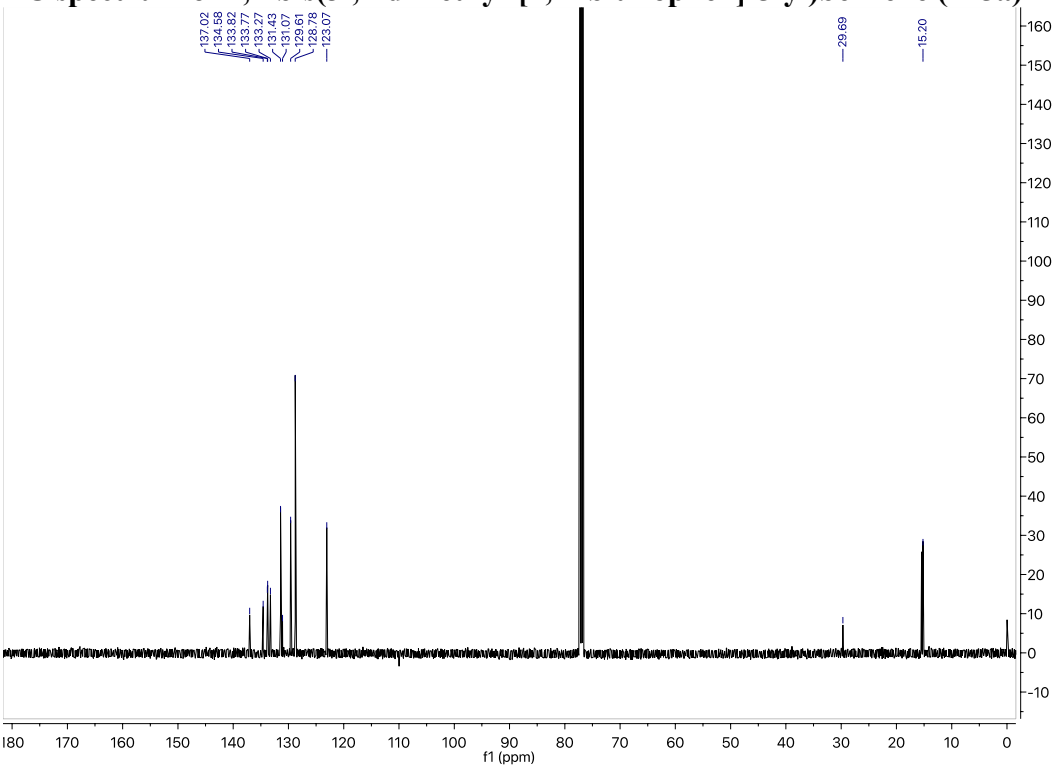
^{13}C spectrum of 3,3''''-dihexyl-3''',4'-dimethyl-2,2':5',2'':5'',2''':5''',2''''-quinquethiophene (114b)



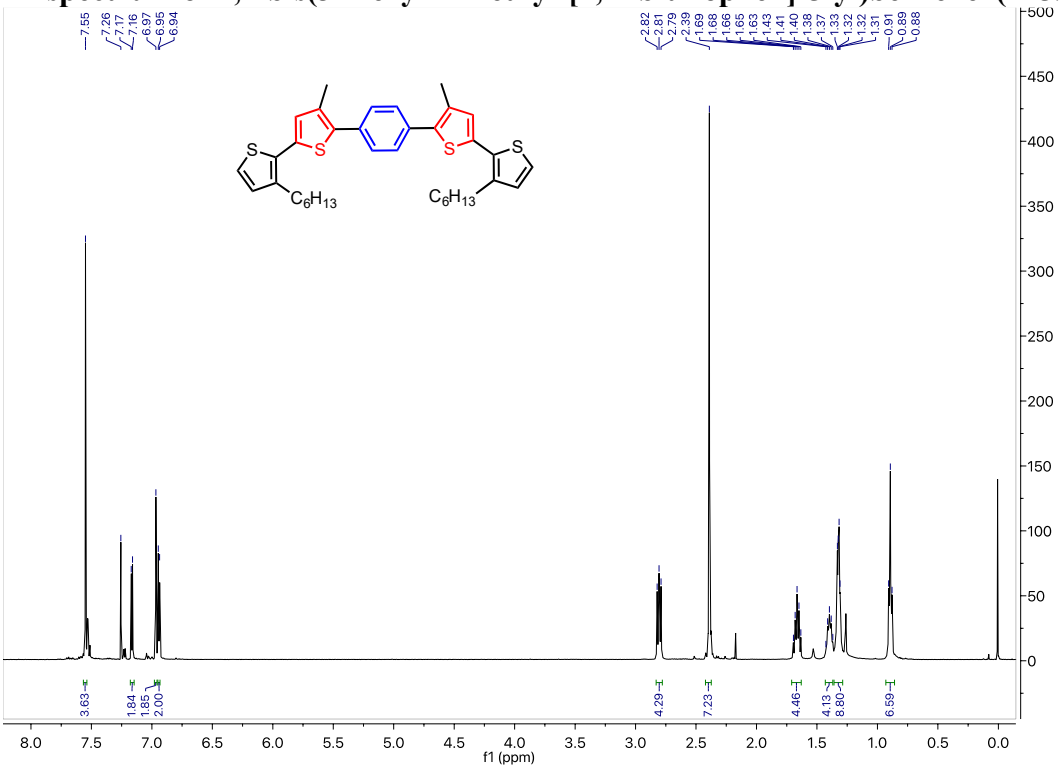
^{1}H spectrum of 1,4-bis(3',4-dimethyl-[2,2'-bithiophen]-5-yl)benzene (115a)



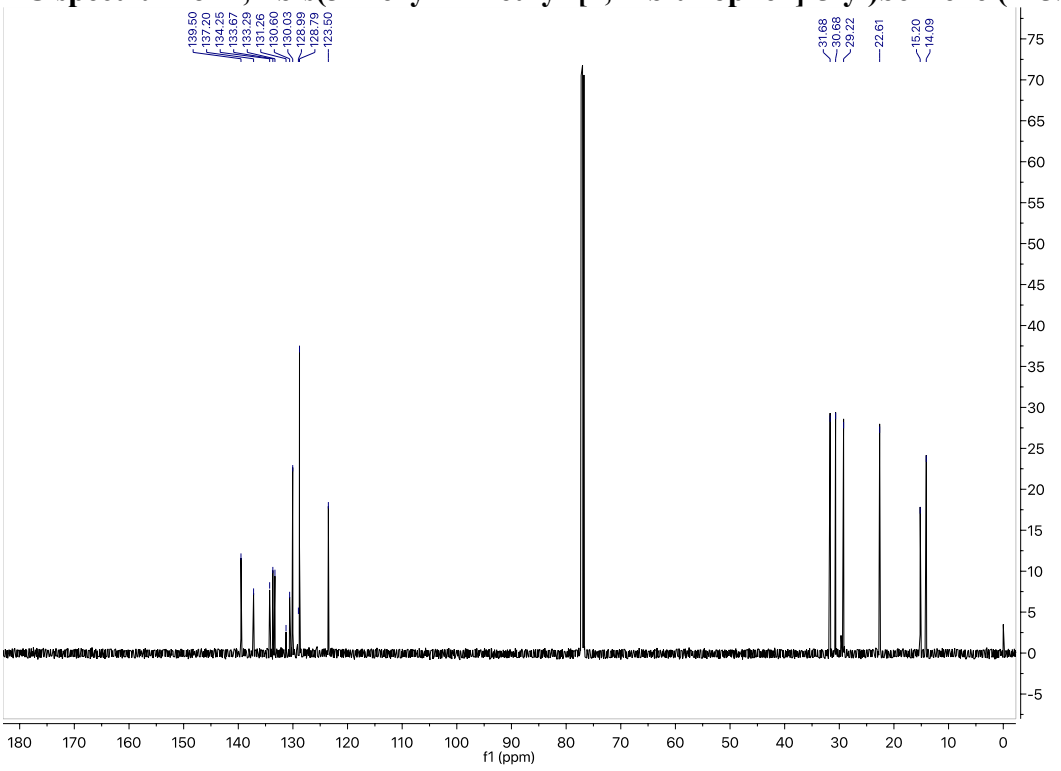
^{13}C spectrum of 1,4-bis(3',4-dimethyl-[2,2'-bithiophen]-5-yl)benzene (115a)



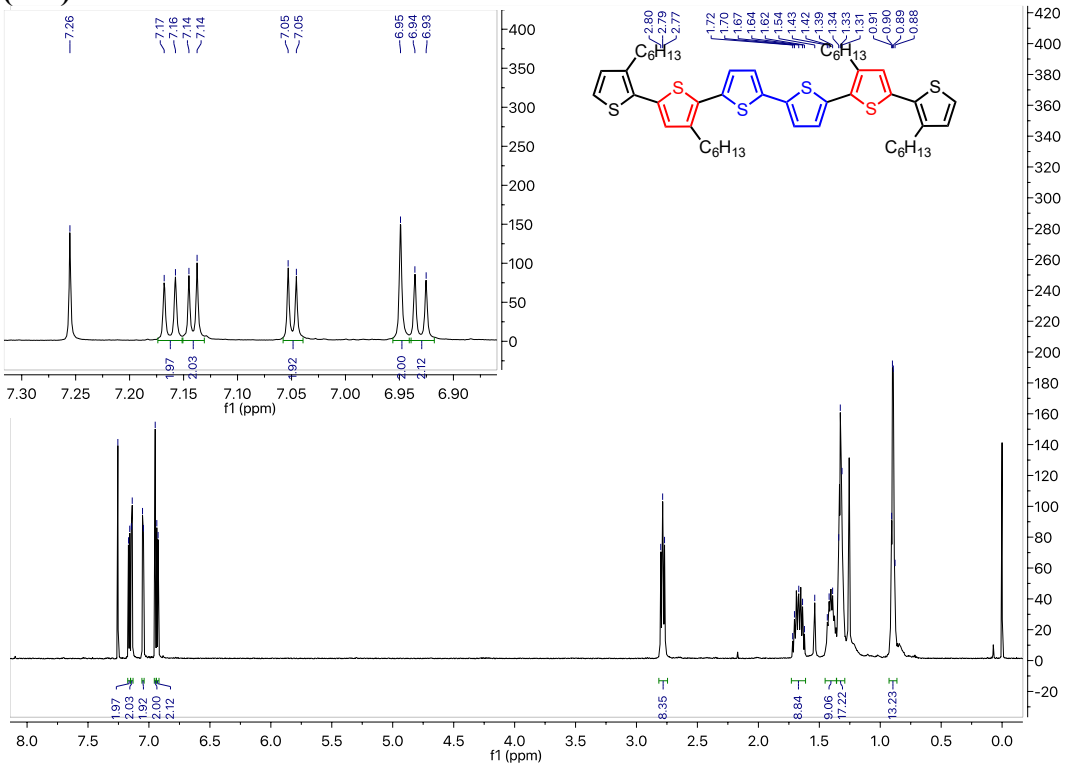
^{1}H spectrum of 1,4-bis(3'-hexyl-4-methyl-[2,2'-bithiophen]-5-yl)benzene (115b)



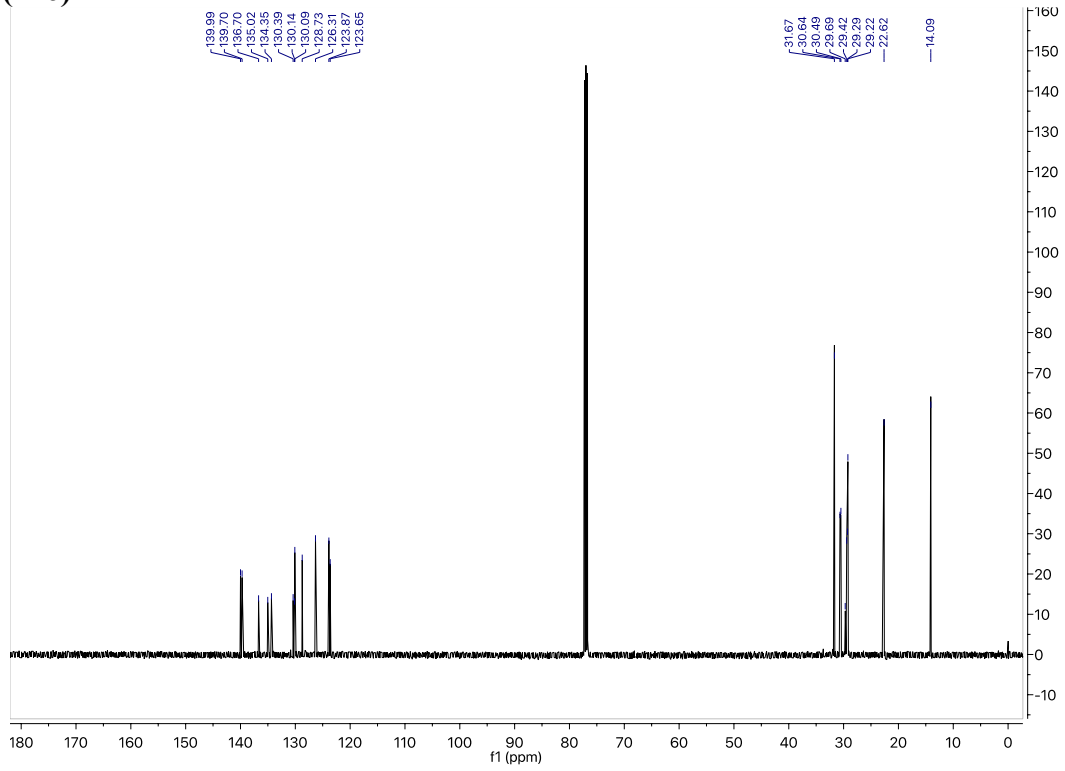
^{13}C spectrum of 1,4-bis(3'-hexyl-4-methyl-[2,2'-bithiophen]-5-yl)benzene (115b)



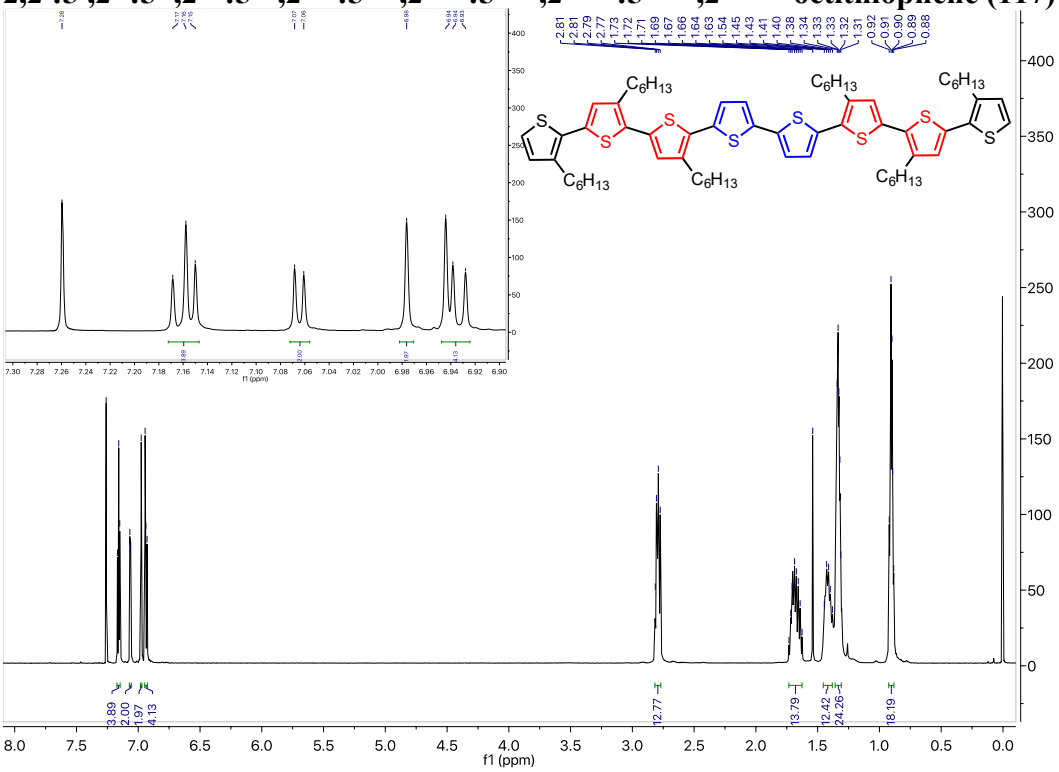
^{1}H spectrum of 3,3'''',3''''',4'-tetrahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2'''''-sexithiophene (116)



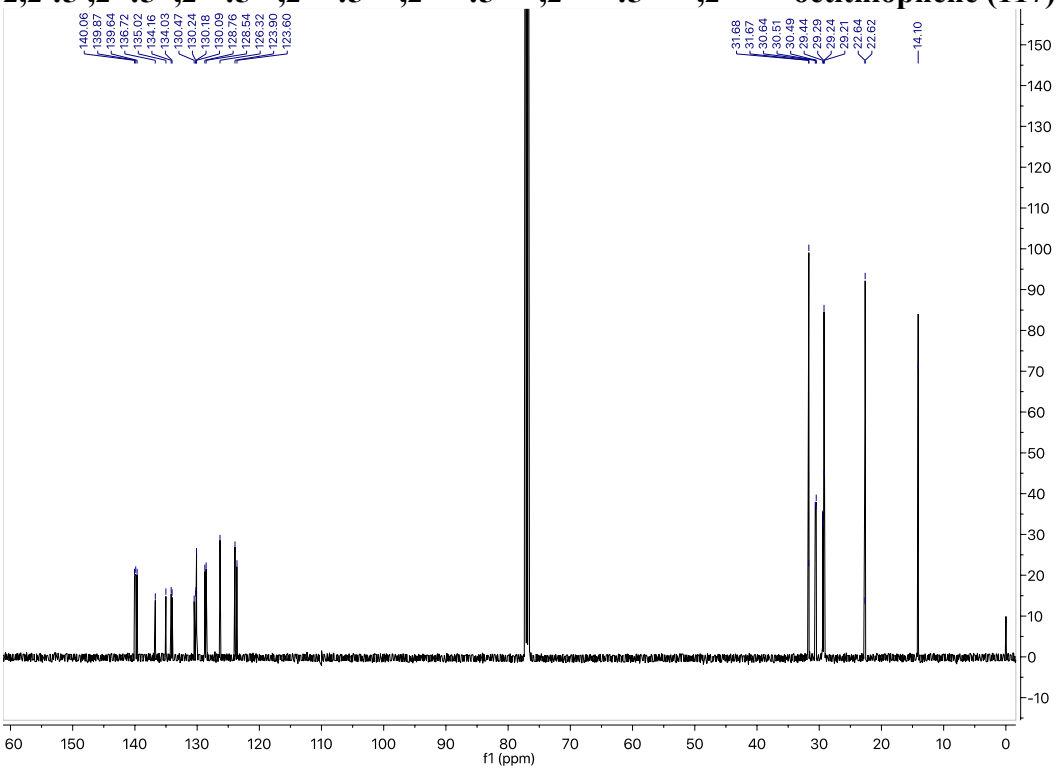
^{13}C spectrum of 3,3'''',3''''',4'-tetrahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2'''''-sexithiophene (116)



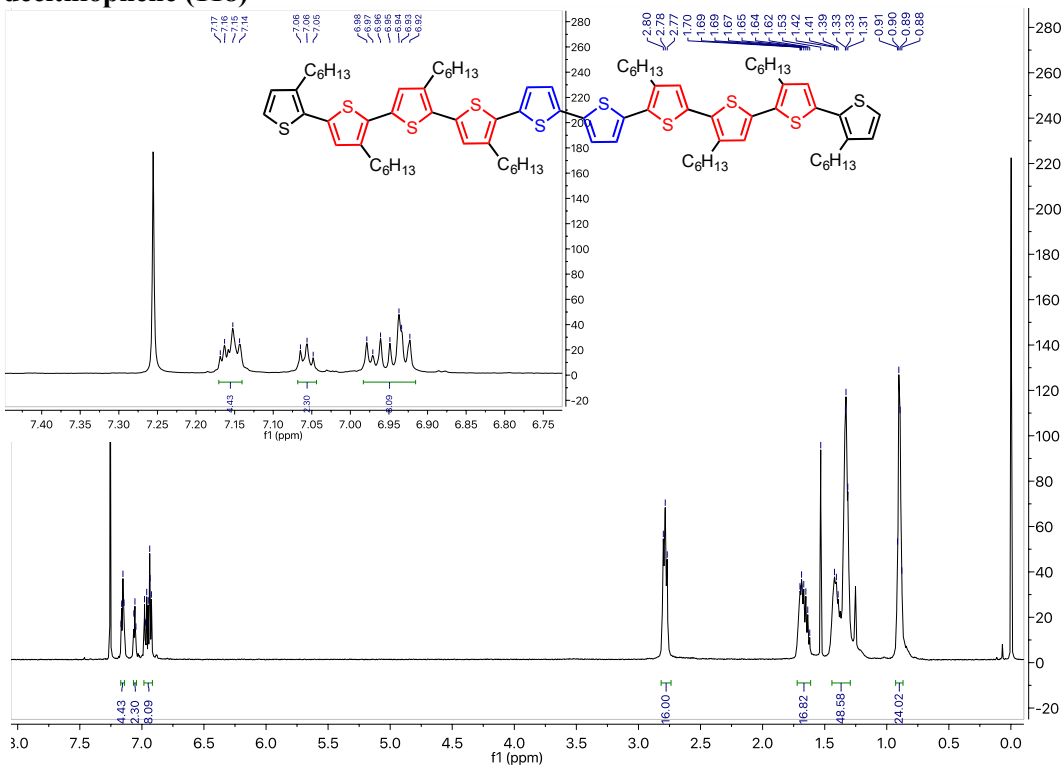
^{1}H spectrum of 3,3''''',3''''',3''''''',4',4''-hexahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''':5'''''',2''''''-octithiophene (117)



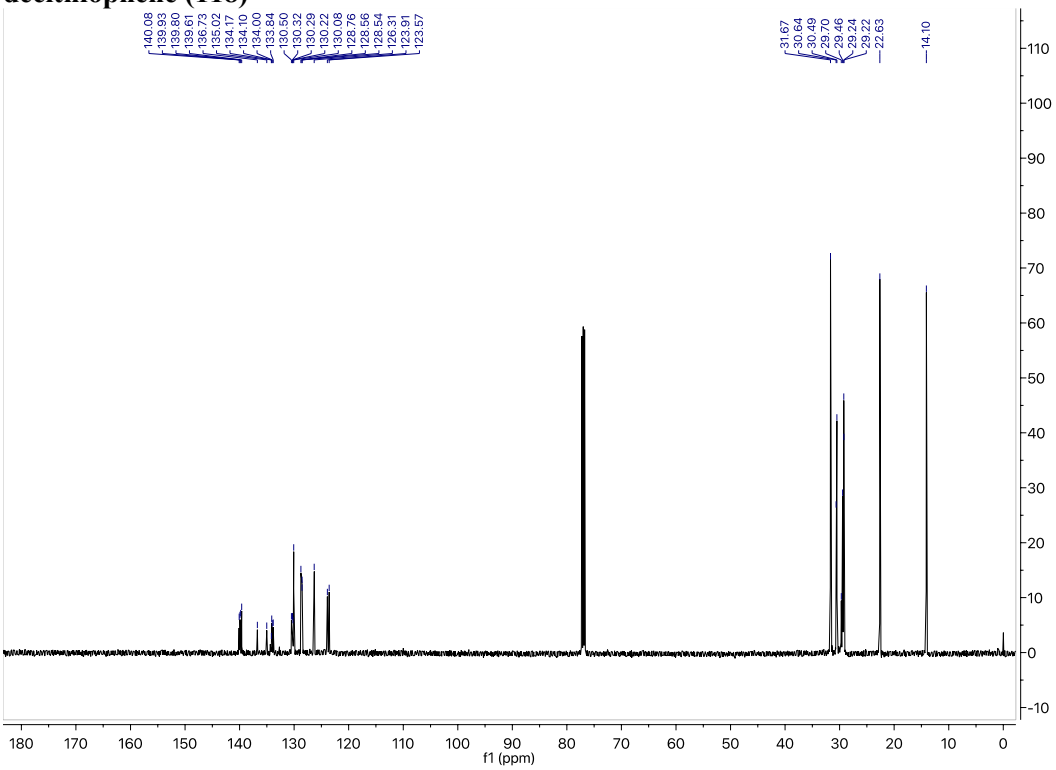
^{13}C spectrum of 3,3'''',3''''',3''''''',4',4''-hexahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2''''''':5''''''-octithiophene (117)



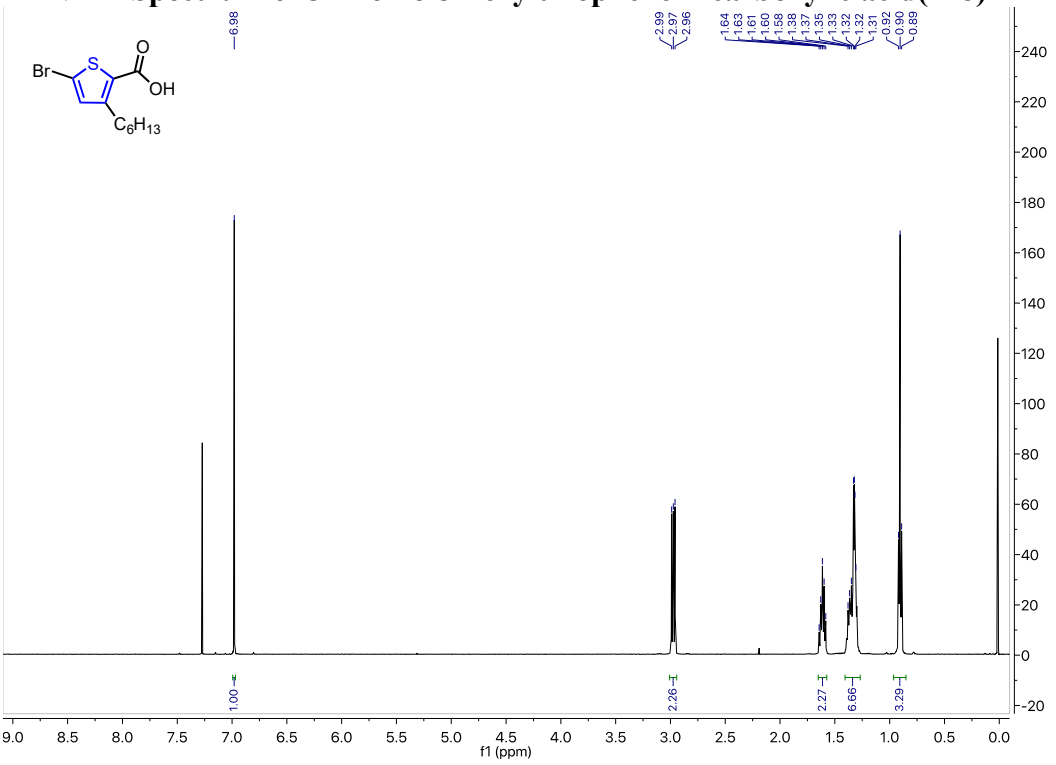
^{1}H spectrum of 3,3''''',3''''''',3''''''',3''''''''',4',4'',4'''-octahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2''''''':5''''''',2''''''':5''''''',2''''''''-decithiophene (118)



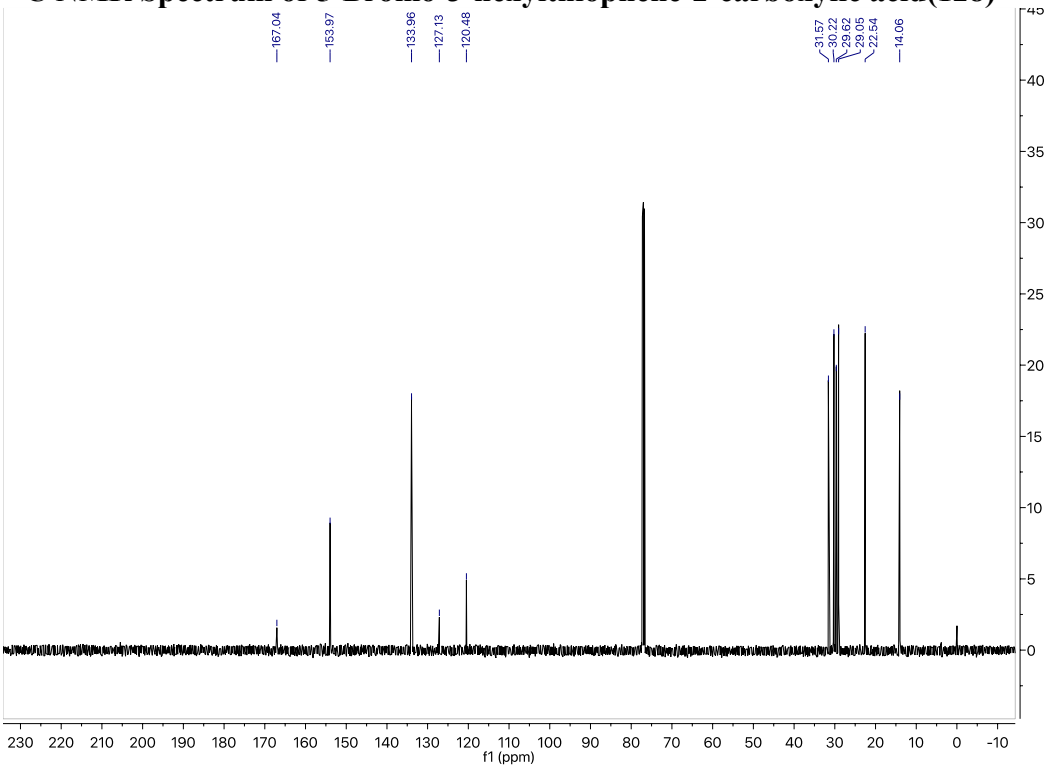
^{13}C spectrum of 3,3''''',3''''''',3'''''''',3''''''''',4',4'',4'''-octahexyl-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':5''''',2'''''':5'''''',2''''''':5''''''',2'''''''':5'''''''-decithiophene (118)



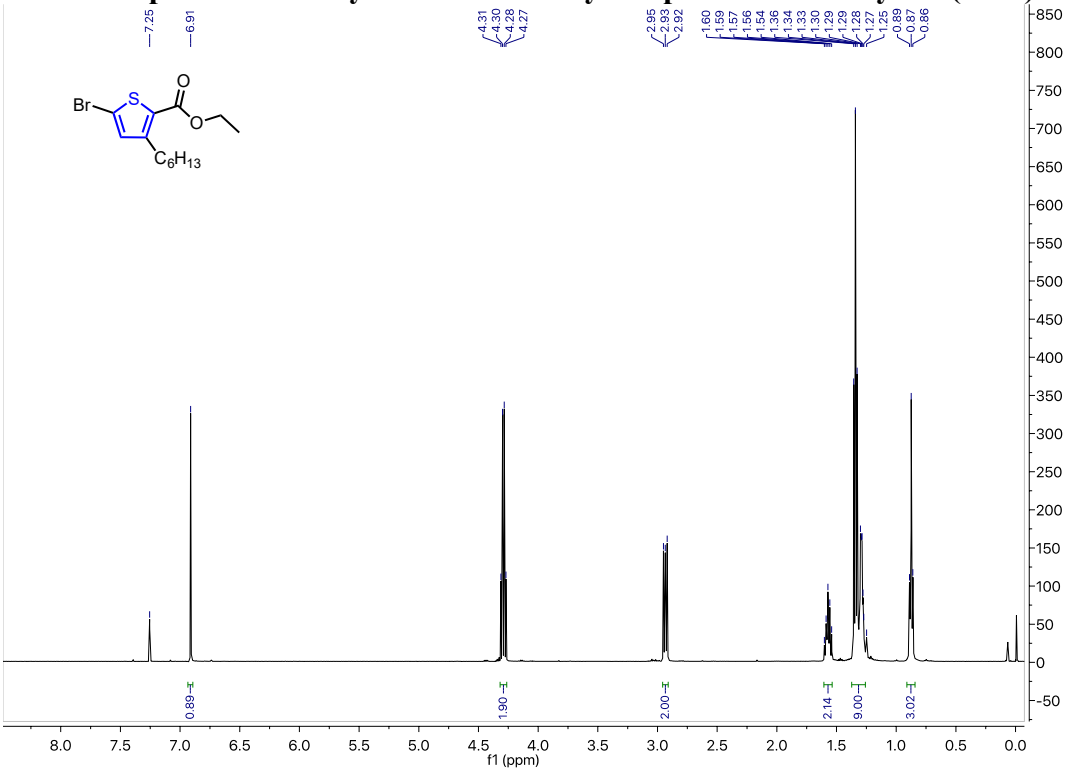
^{1}H NMR Spectrum of 5-Bromo-3-hexylthiophene-2-carboxylic acid(128)



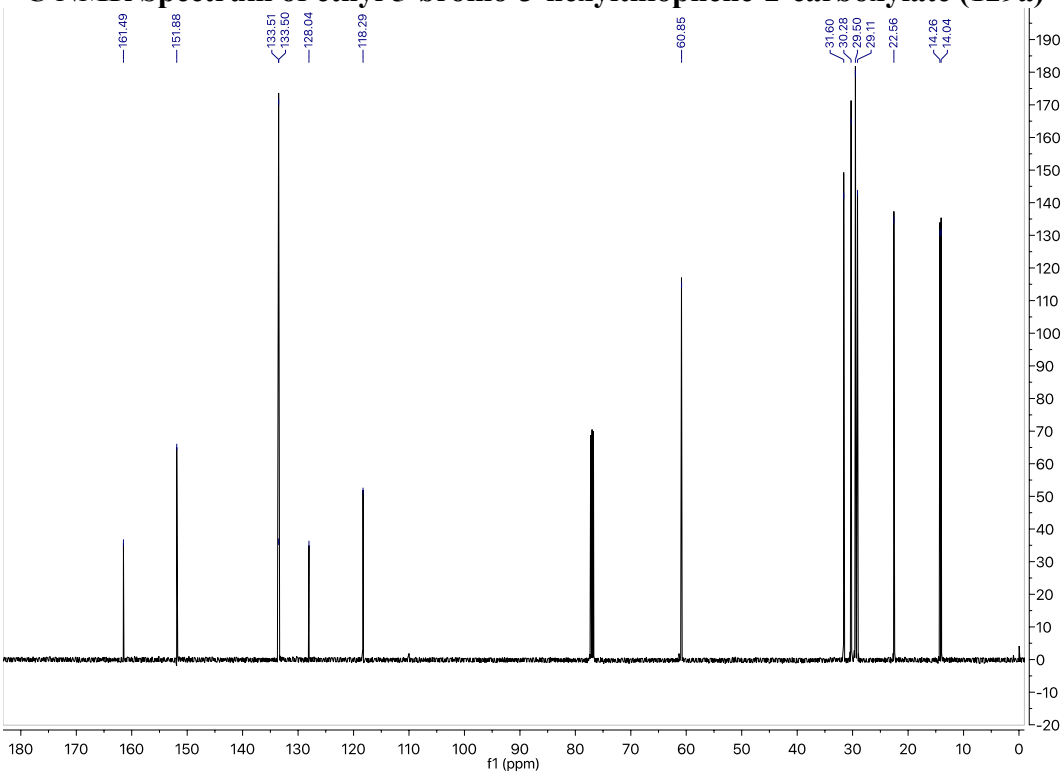
^{13}C NMR Spectrum of 5-Bromo-3-hexylthiophene-2-carboxylic acid(128)



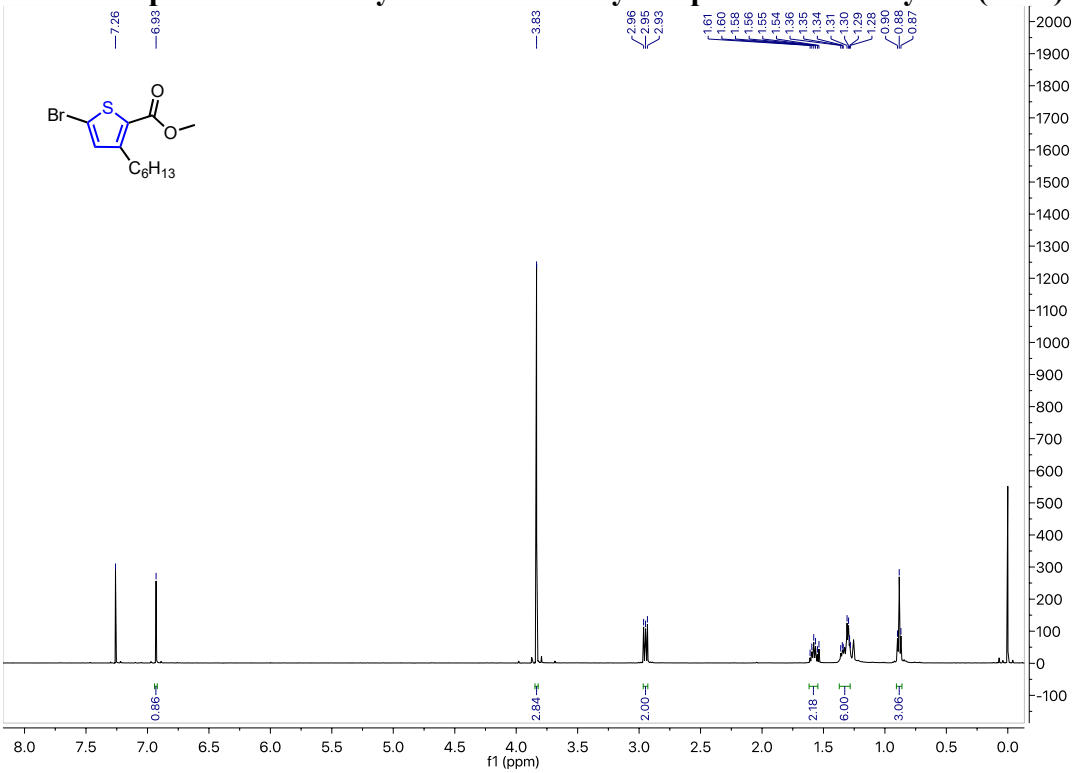
^{1}H NMR Spectrum of ethyl 5-bromo-3-hexylthiophene-2-carboxylate (129a)



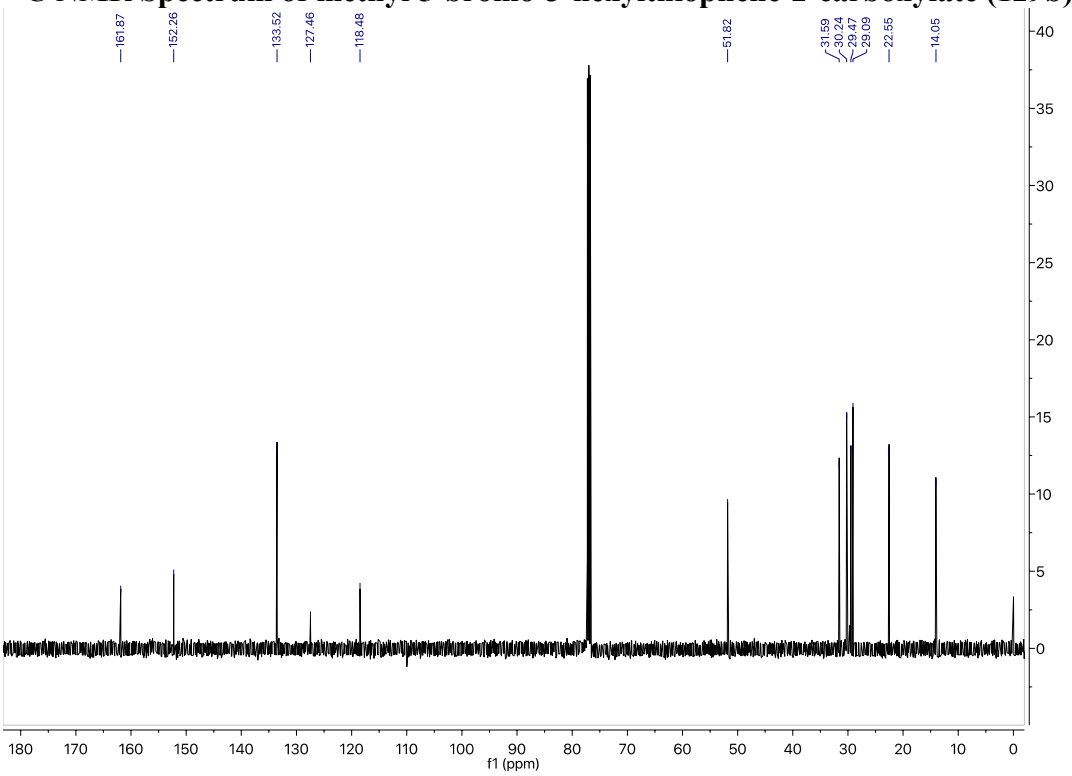
^{13}C NMR Spectrum of ethyl 5-bromo-3-hexylthiophene-2-carboxylate (129a)



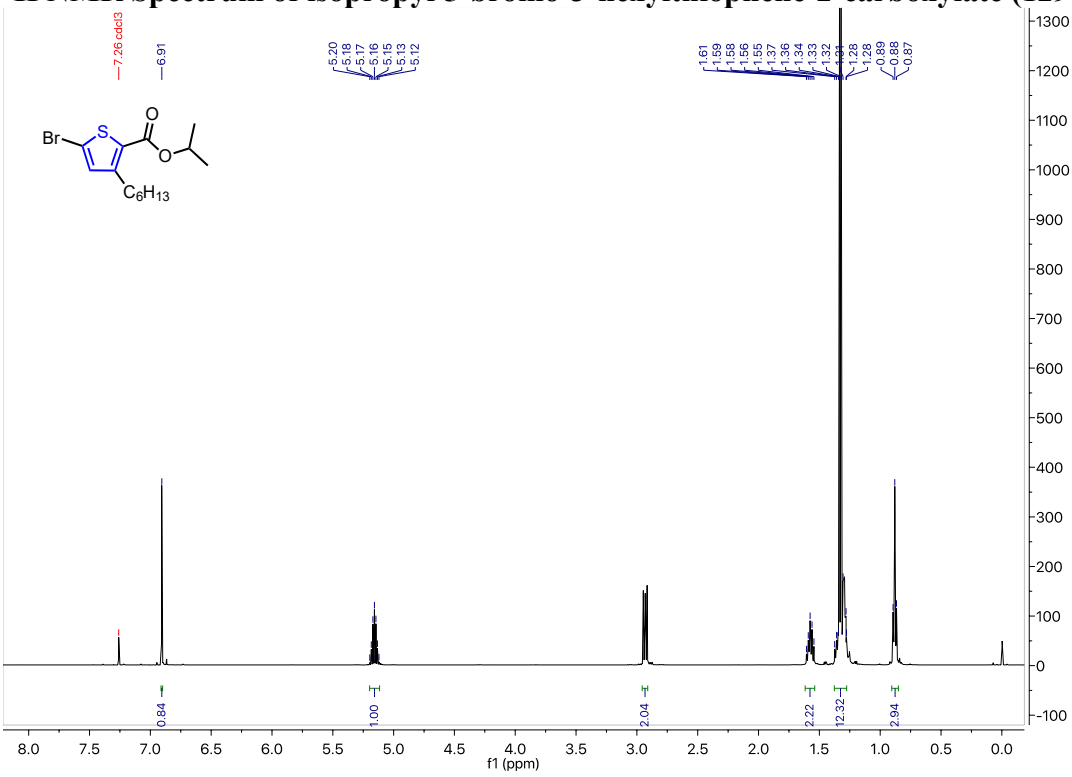
^{1}H NMR Spectrum of methyl 5-bromo-3-hexylthiophene-2-carboxylate (129b)



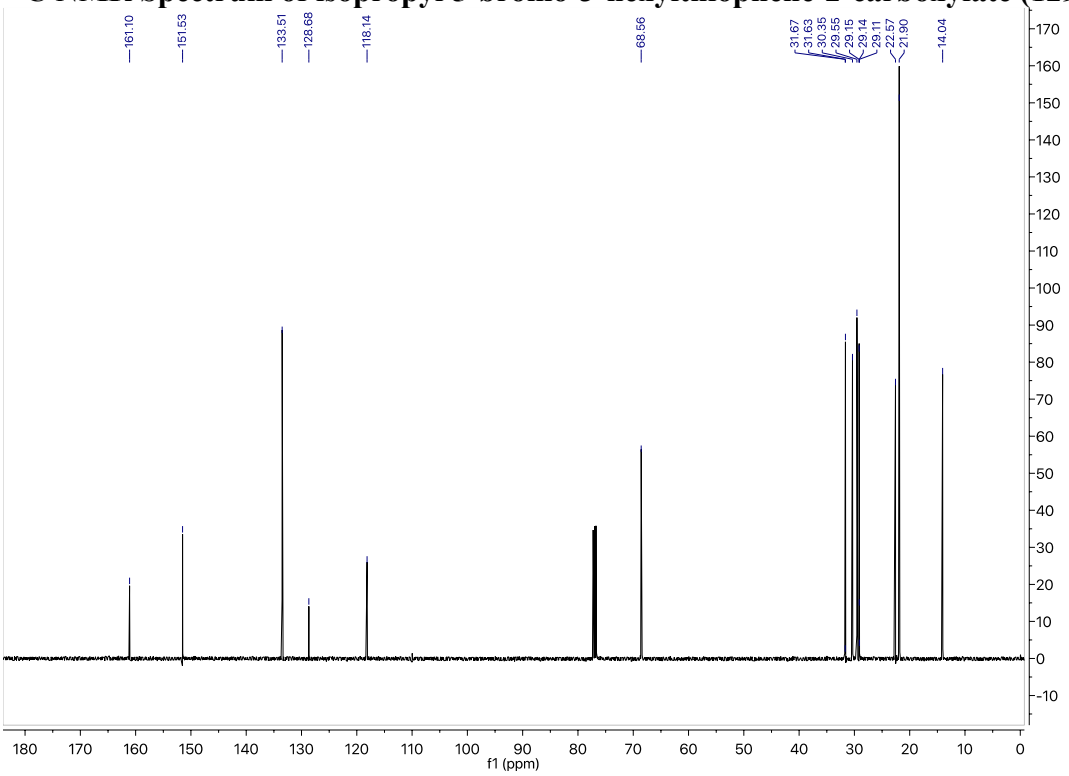
^{13}C NMR Spectrum of methyl 5-bromo-3-hexylthiophene-2-carboxylate (129b)



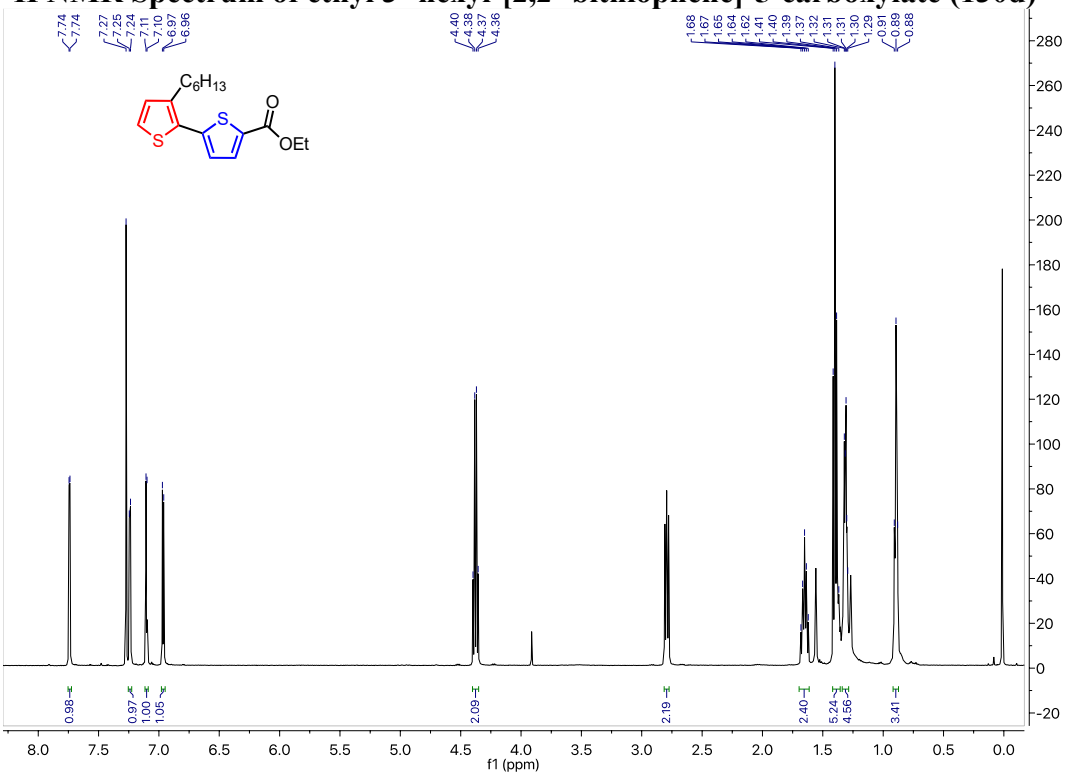
^{1}H NMR Spectrum of isopropyl 5-bromo-3-hexylthiophene-2-carboxylate (129c)



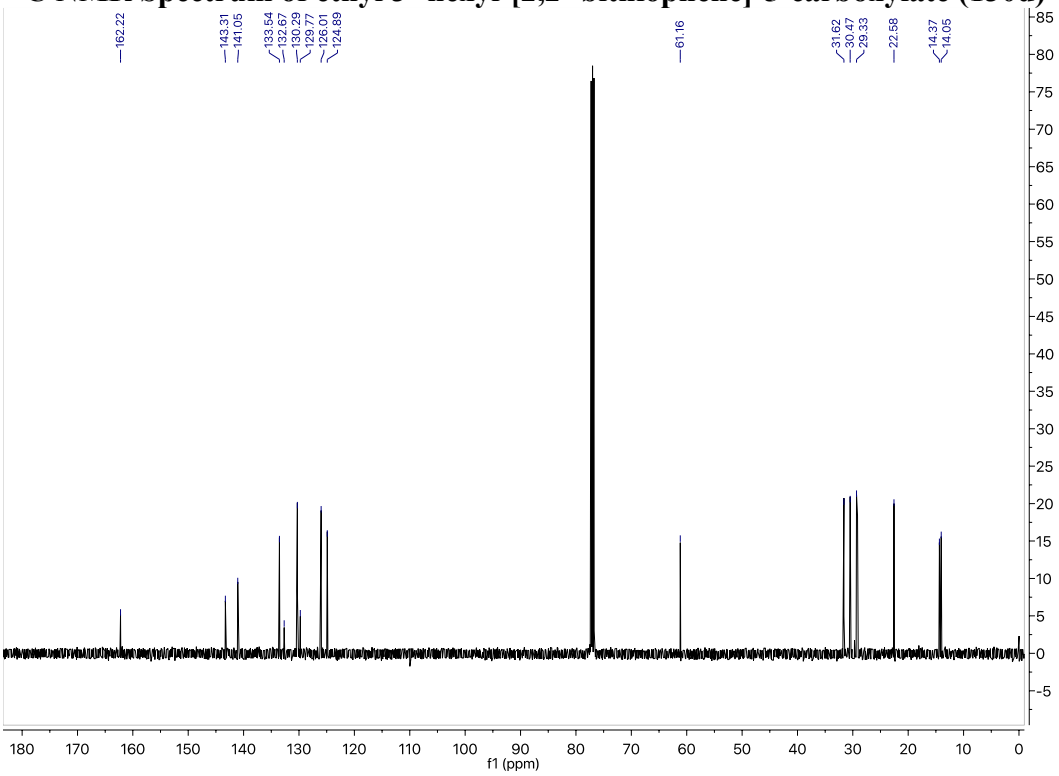
^{13}C NMR Spectrum of isopropyl 5-bromo-3-hexylthiophene-2-carboxylate (129c)



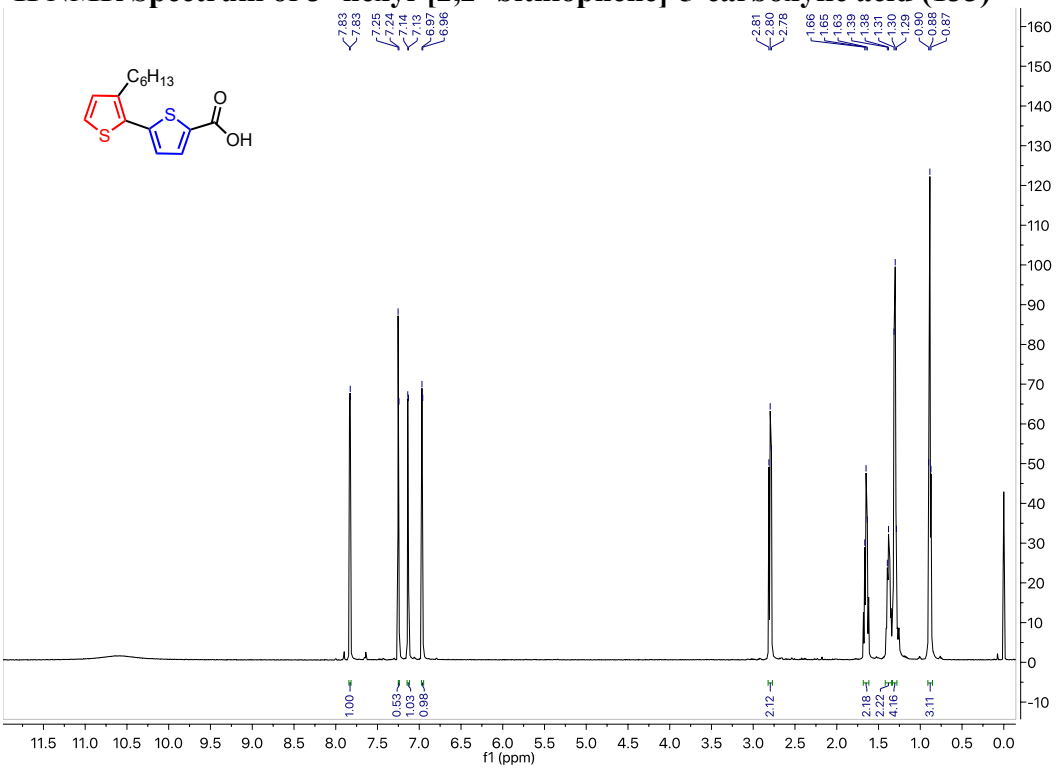
^{1}H NMR Spectrum of ethyl 3'-hexyl-[2,2'-bithiophene]-5-carboxylate (130d)



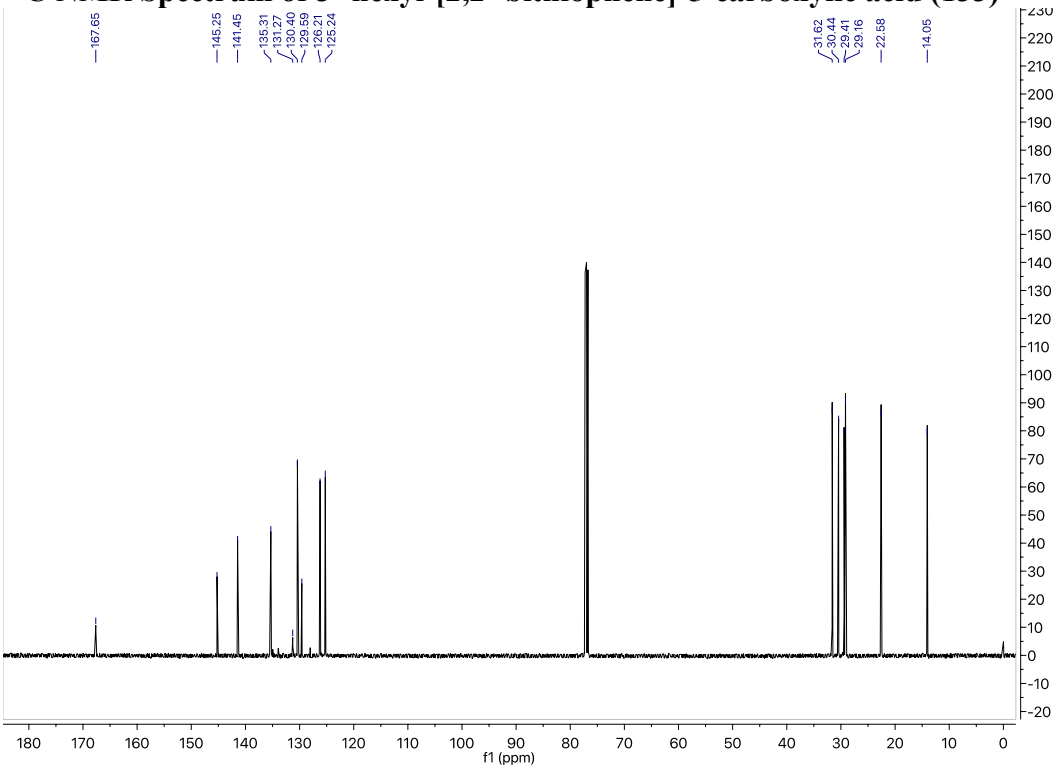
^{13}C NMR Spectrum of ethyl 3'-hexyl-[2,2'-bithiophene]-5-carboxylate (130d)



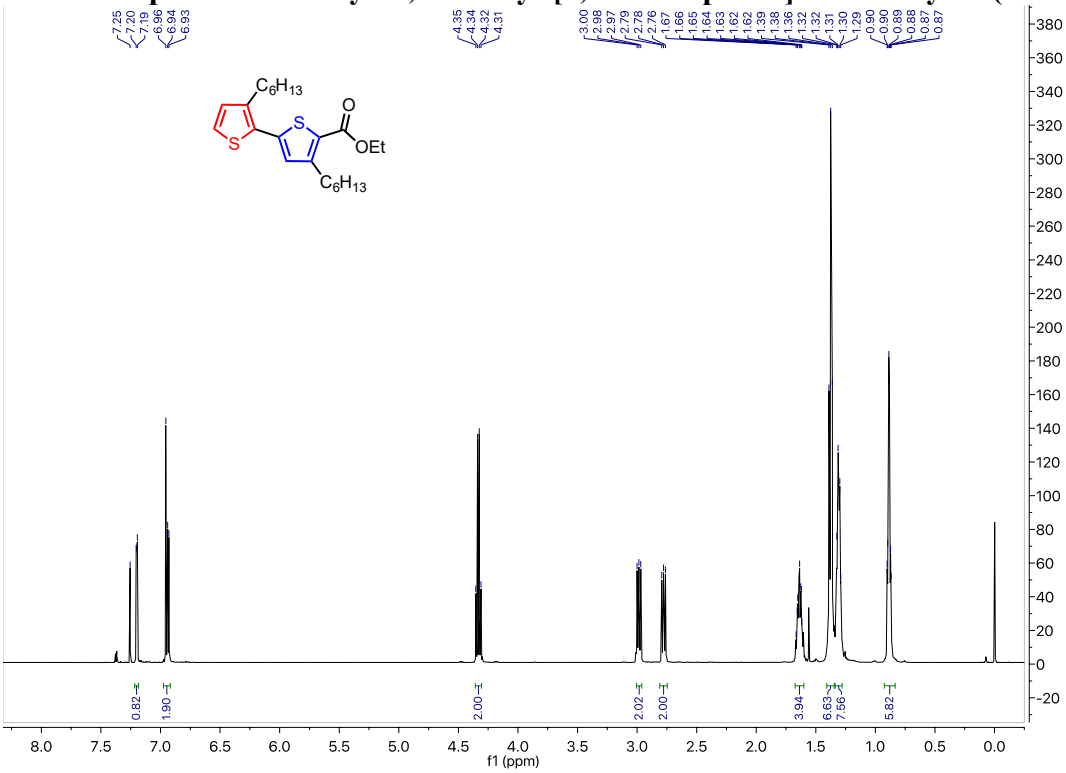
^{1}H NMR Spectrum of 3'-hexyl-[2,2'-bithiophene]-5-carboxylic acid (133)



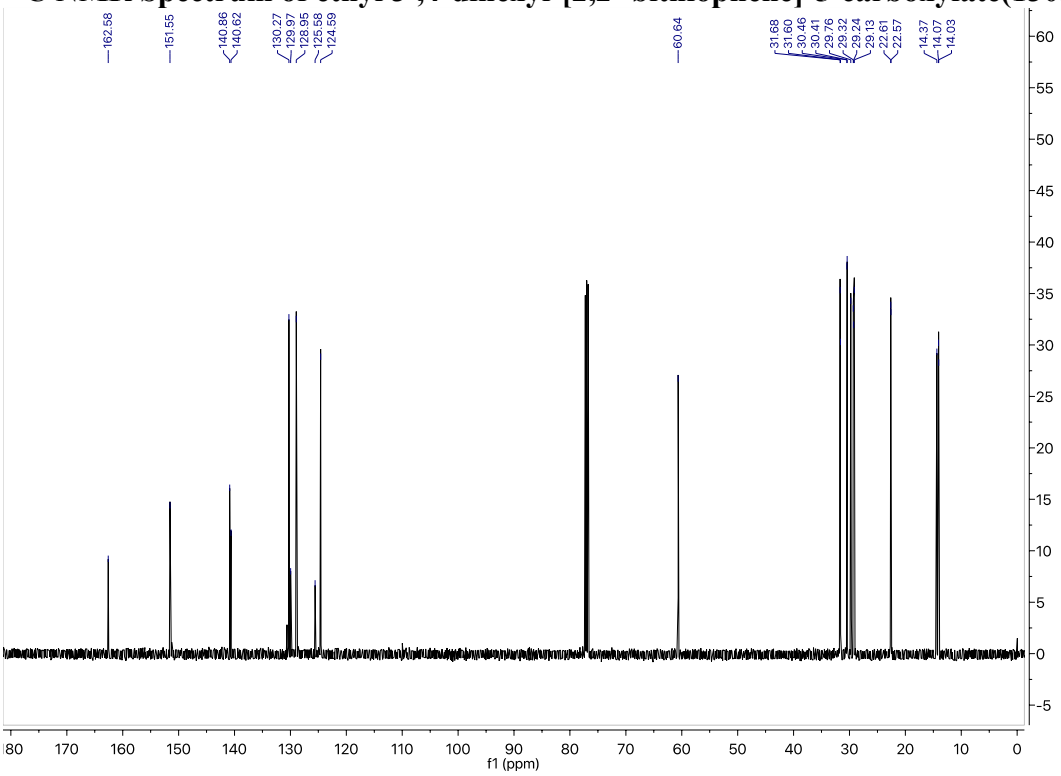
^{13}C NMR Spectrum of 3'-hexyl-[2,2'-bithiophene]-5-carboxylic acid (133)



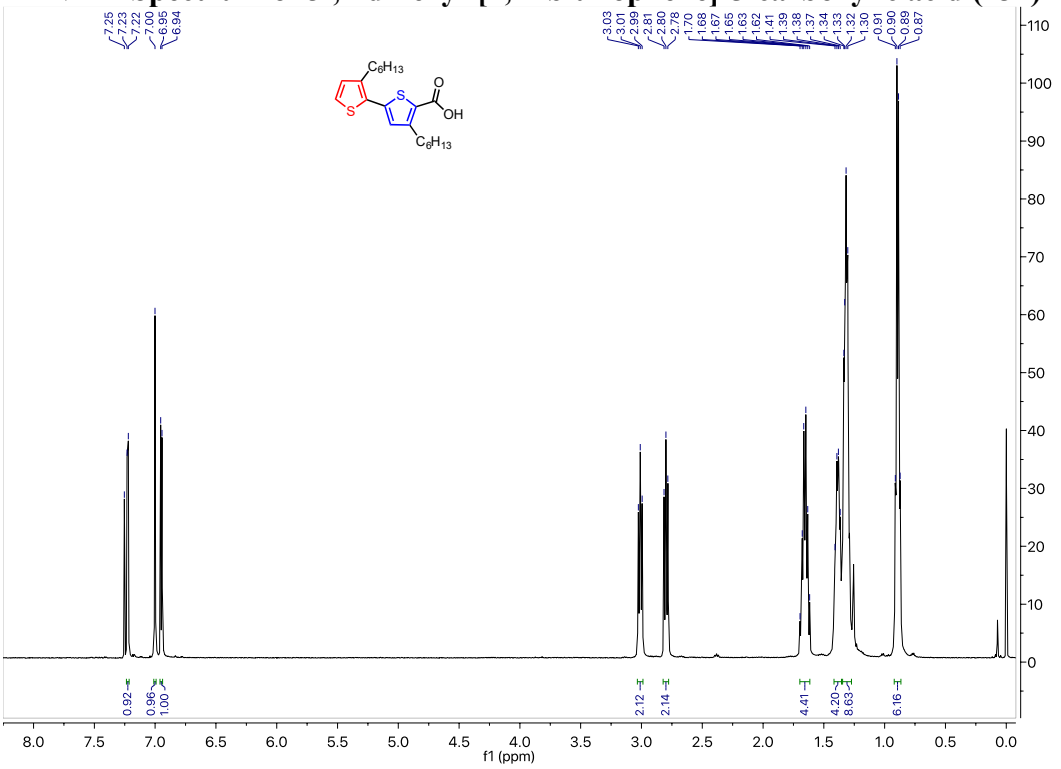
^{1}H NMR Spectrum of ethyl 3',4-dihexyl-[2,2'-bithiophene]-5-carboxylate(130a)



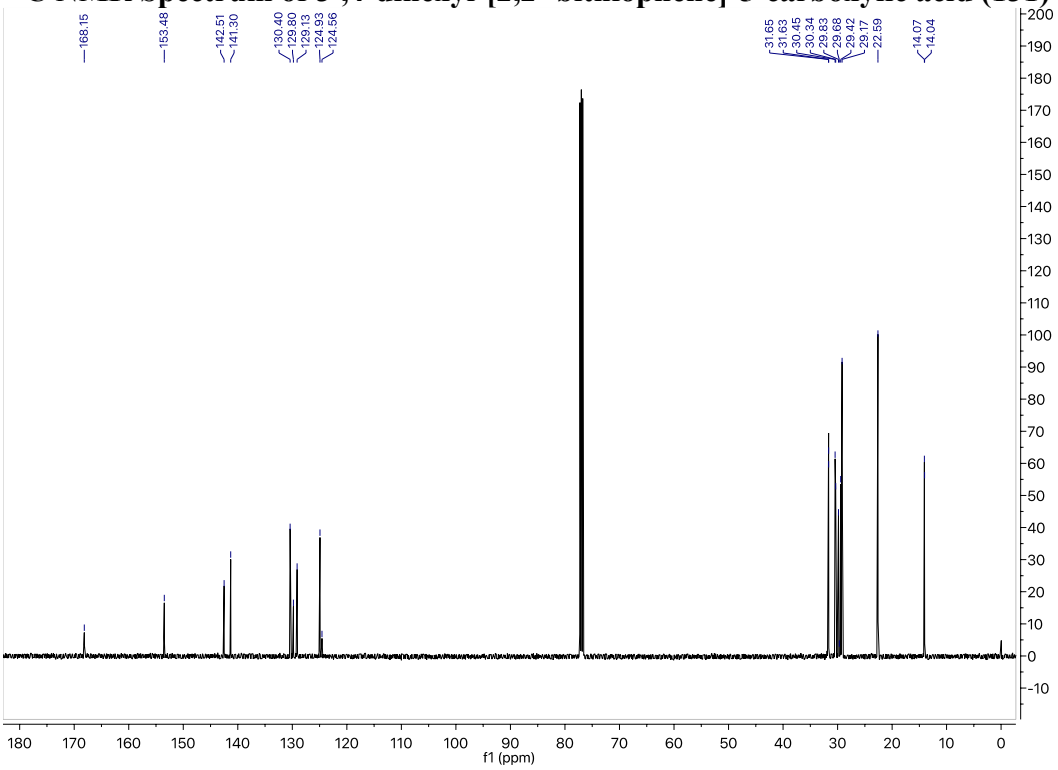
^{13}C NMR Spectrum of ethyl 3',4-dihexyl-[2,2'-bithiophene]-5-carboxylate(130a)



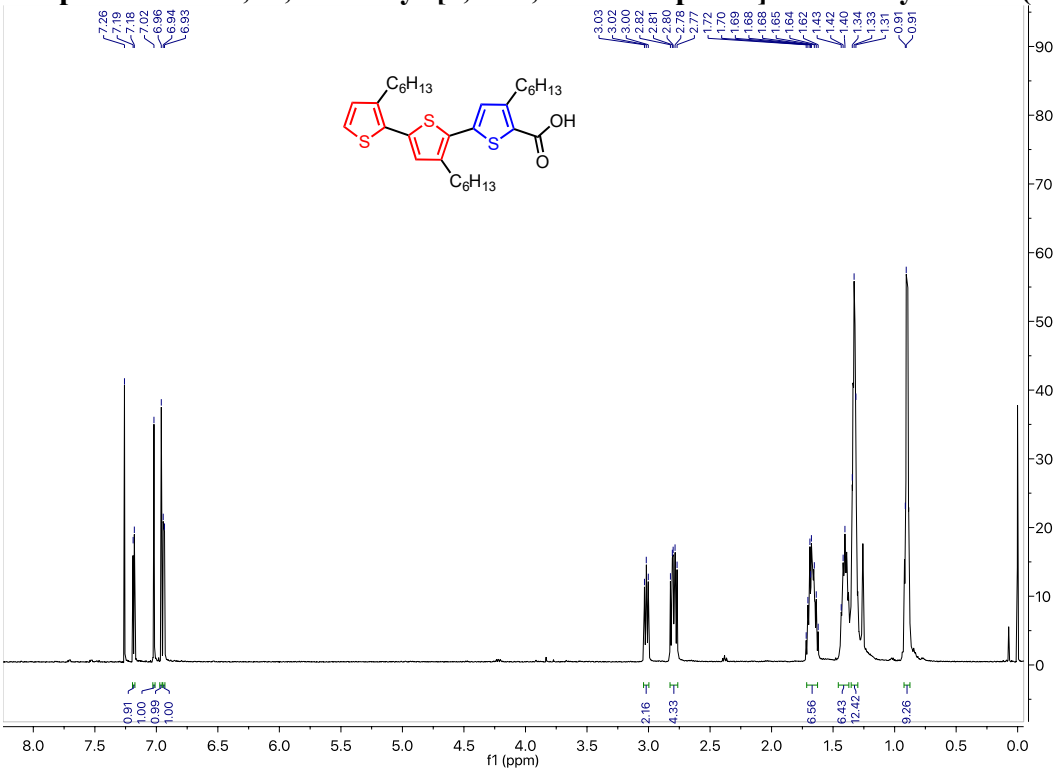
^{1}H NMR Spectrum of 3',4-dihexyl-[2,2'-bithiophene]-5-carboxylic acid (131)



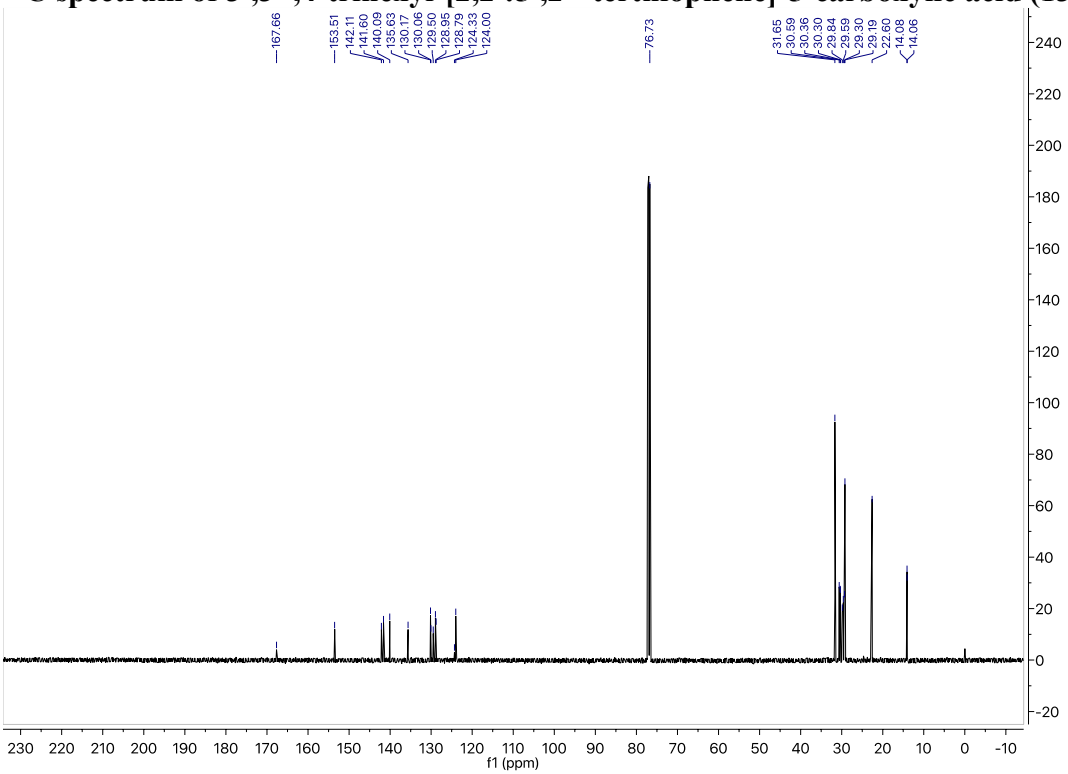
^{13}C NMR Spectrum of 3',4-dihexyl-[2,2'-bithiophene]-5-carboxylic acid (131)



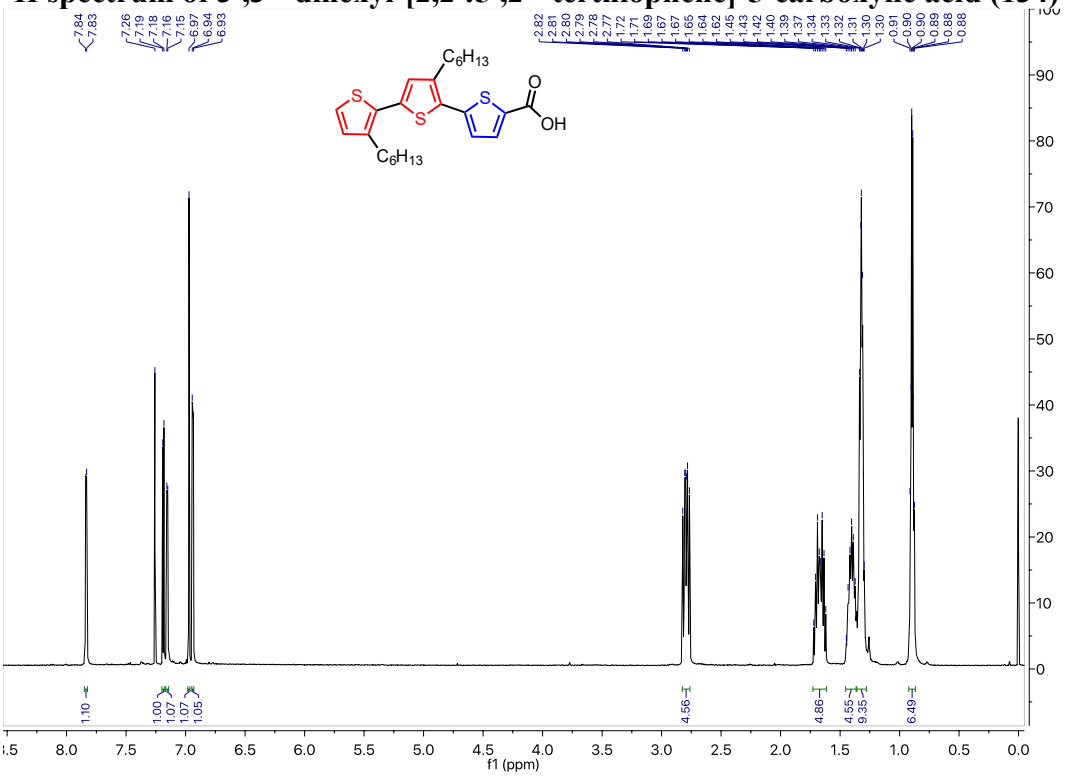
^{1}H spectrum of 3',3'',4-trihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (132)



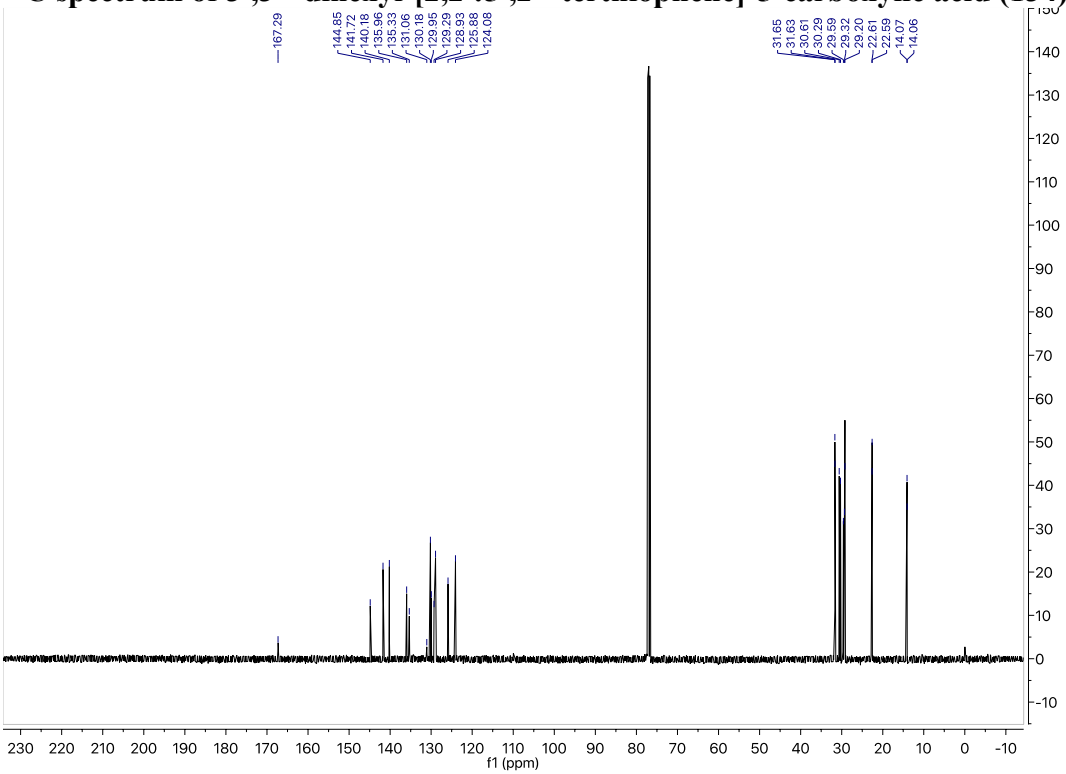
^{13}C spectrum of 3',3'',4-trihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (132)



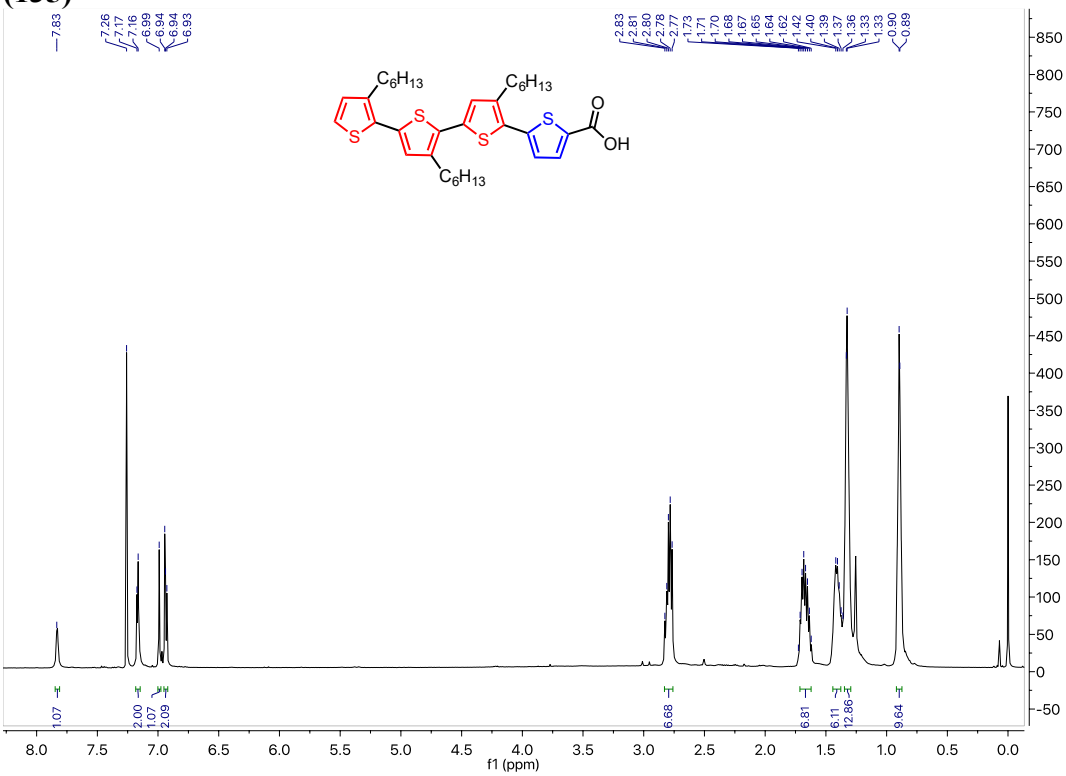
^{1}H spectrum of 3',3''-dihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (134)



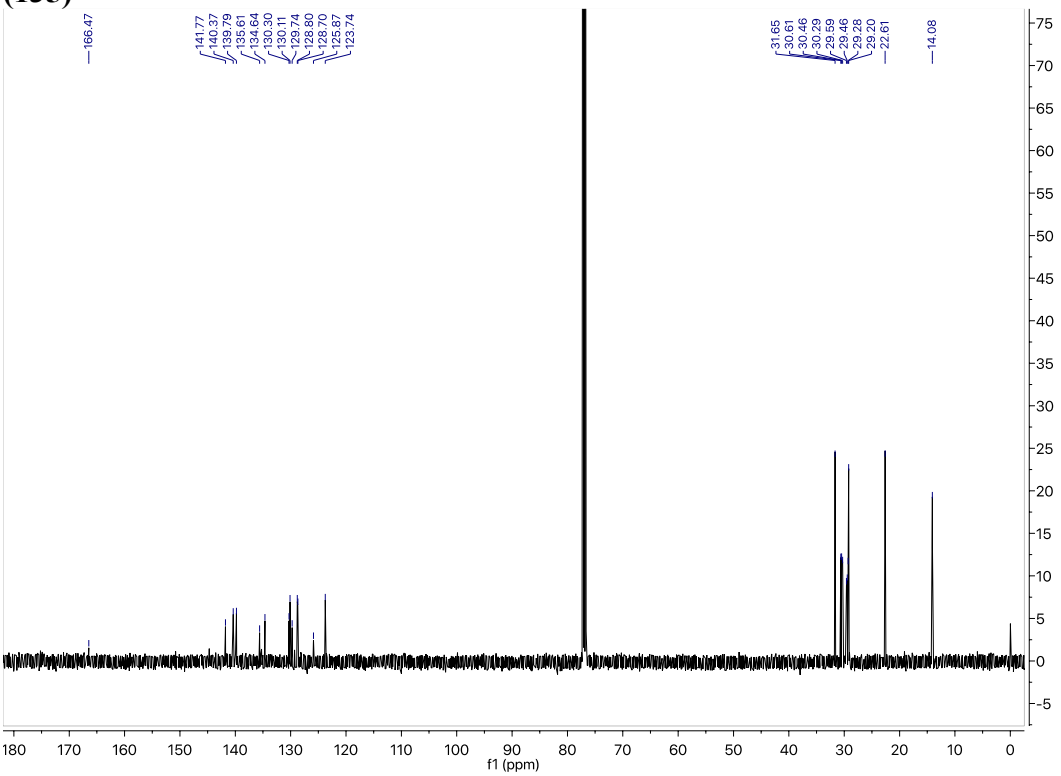
^{13}C spectrum of 3',3''-dihexyl-[2,2':5',2''-terthiophene]-5-carboxylic acid (134)



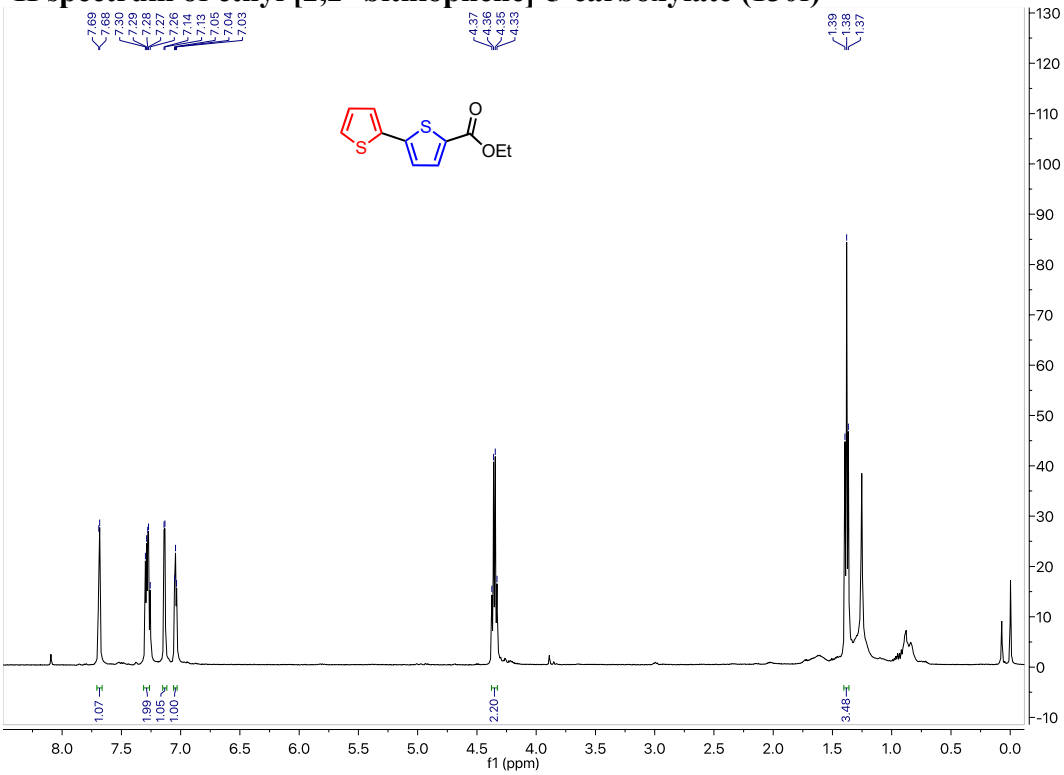
^{1}H spectrum of 3',3'',3'''-trihexyl-[2,2':5',2'':5'',2'''-quaterthiophene]-5-carboxylic acid (135)



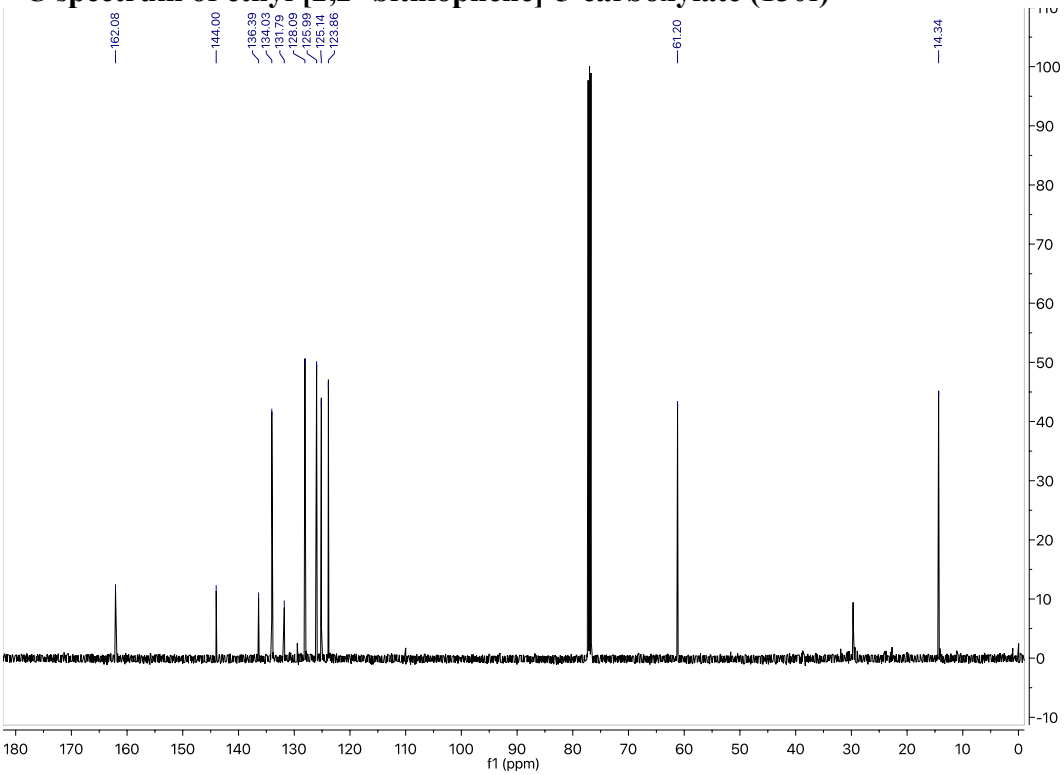
^{13}C spectrum of 3',3'',3'''-trihexyl-[2,2':5',2'':5'',2'''-quaterthiophene]-5-carboxylic acid (135)



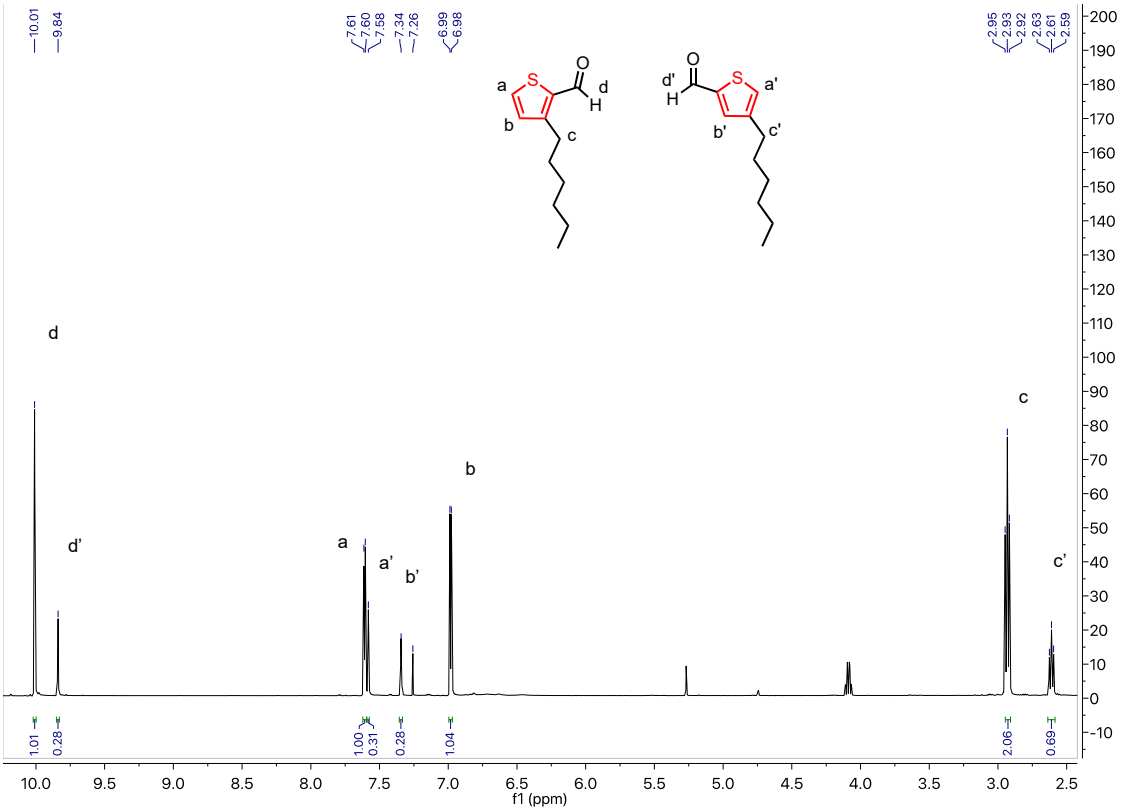
^{1}H spectrum of ethyl [2,2'-bithiophene]-5-carboxylate (130f)



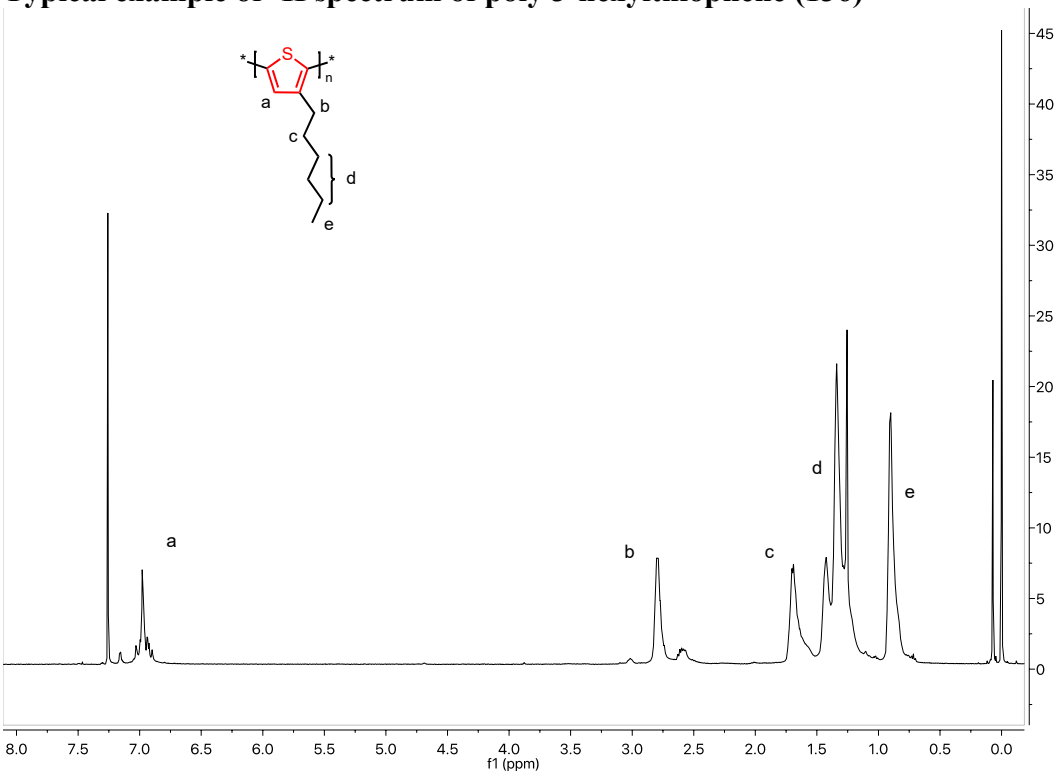
^{13}C spectrum of ethyl [2,2'-bithiophene]-5-carboxylate (130f)



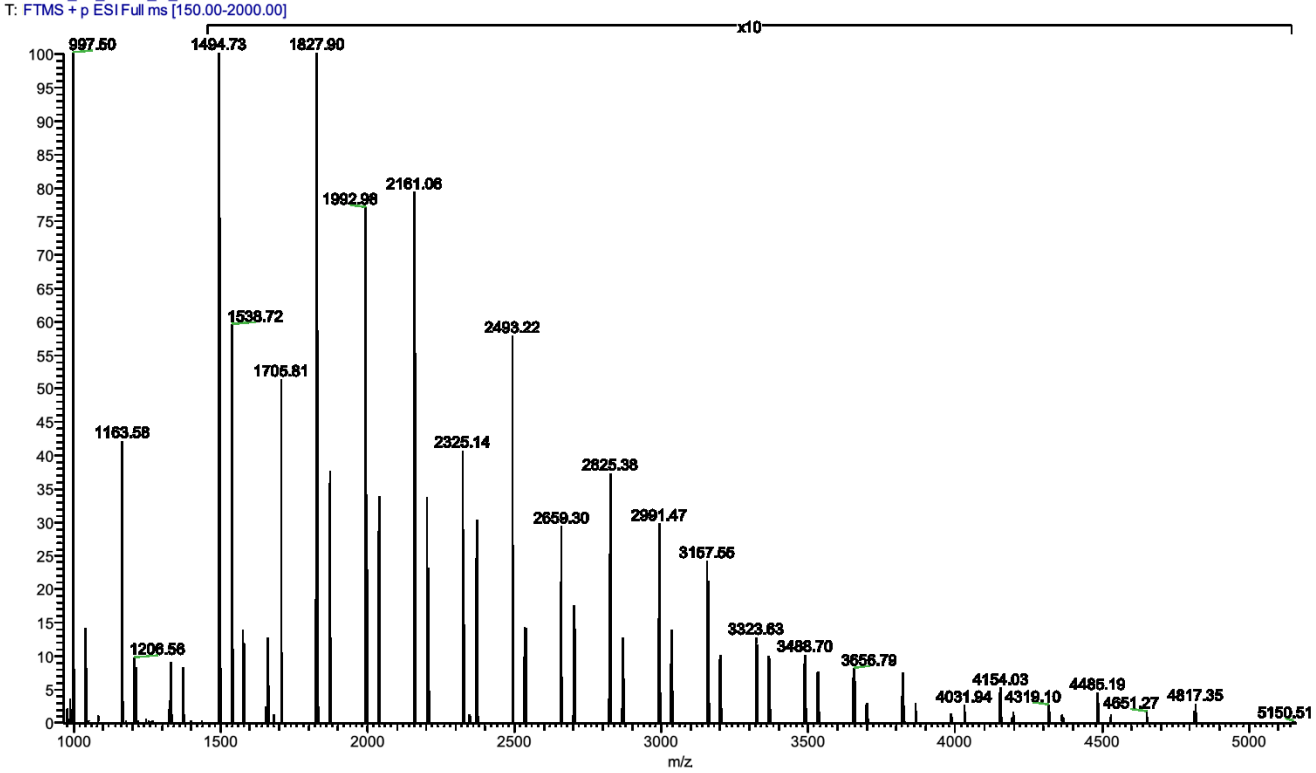
^{1}H spectrum of 3-hexylthiophene-2-carbaldehyde and 3-hexylthiophene-5-carbaldehyde isomers.



Typical example of ^{1}H spectrum of poly 3-hexylthiophene (136)



Typical Example of ESI-MS of poly 3-hexylthiophene (136)



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