Synthesis of redox-responsive tetrathiafulvalene derivatives with amphiphilic properties to be used in soft materials

A thesis submitted to the Faculty of Natural and Agricultural Sciences,
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In fulfilment of the requirements for the degree of

Master of Science

In

Nanoscience

by

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Supervisor:

Prof. VA Azov

2024

Bloemfontein

Declaration

I hereby declare that the work reported in this thesis titled, “Synthesis of redox-responsive tetrathiafulvalene derivatives with amphiphilic properties to be used in soft materials” is my own. Independently studied with the help and aid of my supervisor, and has never been submitted to another institution for examination or grading. It is therefore submitted for the degree, Master of Science in Nanoscience with specialisation in Nanochemistry. To the School of Chemistry, in the Faculty of Natural and Agricultural Sciences at the University of the Free State, Bloemfontein campus.

Signature:

June 2024

Katlego Paulos Tshehla

Dedications

This thesis is intensely dedicated to my late mom and dad (*L.S Mngomezulu Ngwenya-Tshehla & A.K Tshehla*). My beloved guardian angels, who have meant and continue to mean so much to me. Although they are no longer of this world, their memories and teachings continue to regulate my life. There isn't a single day passing by without pondering of the possibilities that I may have been subjected to, only if they were still alive. Amid thoughts of giving up as a result of turmoils during the conduction of this study, was the great words of my late parents, "*You start and you finish*"; "*the world is your oyster, you can be anything you want to be*". I've been through so much but I continue to feel their presence and aid in all circumstances. Their transition to a realm remains a heavy heartache I've learnt to live with. However, I believe they're proud wherever they are. *Tau! Go fedile, Go phethegile, TSHEHLA!! MALATŠANE!! MMINA TAU!!*.

Most importantly, I dedicate this thesis to my brothers. More particularly my beloved young hero, my baby brother (*Thapelo aka Tshabi*), his existence is the drive behind my resilience. My undying urge to fight and hope for a better tomorrow, would've been in vein without his existence. To everyone who has always rooted and prayed for me, this is for you (*Re Tsene! Re Within*).

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Furthermore, the completion of this study is a combined effort from a variety of people, who all in one way or the other made it to be a success.

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- To my **family**, both the late and the alive, as well as my **friends**. Your emotional support throughout my studies, kept me standing. I can't think of any other way I would've survived this journey without constantly having people to vent to. Much appreciated.
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Presentations

A portion of the work in this thesis was presented at the 8th international conference of Nanoscience and Nanotechnology in Africa (NanoAfrica), held from October 26th to 28th, 2022.

"Katlego Paulos Tshehla, Vladimir Azov. *Synthesis of redox-responsive tetrathiafulvalene derivatives with amphiphilic properties to be used in soft materials*."

Poster presentation, 8th international conference of Nanoscience and Nanotechnology in Africa.

Abstract

The well-known electron-rich donor system, Tetrathiafulvalene (TTF) has gained excessive interest in the field of supramolecular chemistry and complex ligand research. Continuous advancements in synthesis has allowed TTF along with its derivatives to be integrated into various intricate molecular systems. Such that, these systems have been investigated for their potential applications as sensors, models for electron transfer, molecular machines and many other applications. The study displayed in this piece of writing will examine the incorporation of TTF moieties through preparation by synthesis, as well as their characterisation. With the motive to add to the recent and existing synthetic advances, for utilization in constructing versatile systems of broad applications.

A series of functionalised bis- and tetra-tetrathiafulvalene derivatives has been prepared. A result stemming from a series of synthesis producing TTF intermediates, later used as key precursors for the successful synthesis of TTF derivatives. Amongst those, is the TTF thiolate anion used as a key intermediate which has shown to be quite a versatile reagent for this purpose. Shelf-stable precursors of the TTF thiolate anion have been prepared, making the preparation of novel, highly functionalised, amphiphilic cationic / anionic TTF derivatives **4** and **5** feasible. The series of steps include various reactions: cyclization, cross coupling and self-coupling, de-protection, re-alkylation, and nucleophilic substitution reactions. This synthetic pathway allows the tailoring of the properties of the TTF entity by the variation of the substitution pattern. For feasibility of the amphiphilic character, the analogues prepared constitute of long alkyl chains at different positions. This character adds in rendering these entities as versatile electron donor systems, well suited for use in construction of novel redox assemblies.

Through careful adjustments and development of methodologies, a range of symmetrical and unsymmetrical TTF derivatives of different substituents was covered. From alkyl-halides bearing TTF derivatives to the 1-methyl-imidazole units fused to the TTF frameworks. Certain compounds were obtained in significantly high yields. Such as the 1-methyl-imidazole bearing TTF derivative, 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene **4a** at a yield of 94%. With its identity qualitatively confirmed by high-resolution mass spectroscopy and NMR analysis.

In the study, several purification techniques were implemented with the hopes of producing highly pure and well isolated compounds. Some of the reactions produced several products which were difficult to separate. An attempt to conduct electrochemical studies on the new multi-TTF derivatives, was deemed unsuccessful for various reasons covered in the discussion.

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List of Abbreviations

Å – Angstrom

Ag/AgCl – Silver-Silver Chloride Electrode

BEDTTF – Bis(ethylenedithio)tetrathiafulvalene

BEDT-TTF – Bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF)

CNTs – Carbon nanotubes

CP – Coordination polymers

CT – Charge transport

DCM – Dichloromethane

DMF – Dimethylformamide

DMIT – 1,3-Dithiole-2-thione-4,5-dithiolate (2-thioxo-1,3-dithiole-4,5-dithiolate)

$E_{1/2}$ – Half-cell potential

ESI – Electrospray ionisation

HOMO – Highest occupied molecular orbital

HR-MS – High resolution mass spectroscopy

MeCN – Acetonitrile

MIM – Mechanically interlocked molecule

MOF – Metal–organic framework

MS – Mass Spectroscopy

NMR – Nuclear Magnetic Resonance

OFET – Organic field-effect transistor

Ppm – Parts per million

PRXD – Powder X-ray diffraction

PV – Photovoltaic

R_f – Retention factor

SCE – Saturated Calomel Electrode

SEM – Scanning electron microscopy

SMP3 – Stuart Melting Point 3

SN_2 – Bimolecular nucleophilic substitution

SWNTs – Single-walled carbon nanotubes

TCNQ – Tetracyano-p-quinodimethane

TLC – Thin layer chromatography

TMS – Tetramethylsilane

TTF – Tetrathiafulvalene

UV – ultraviolet

CHAPTER 1: Introduction

1.1 Background

Tetrathiafulvalene [2,2'-Bi(1,3-dithiolylidene)] **1**, commonly abbreviated as "TTF", is a highly versatile organosulfur compound, well known for its strong electron-donating properties. TTF is defined to be a heterocyclic compound composed of two planar, five-membered ring comprising sulphur and carbon atoms [1]. With the presence of the conjugated π-system allowing the tetrathiafulvalene entity to exhibit exceptional electron-donating and redox properties [2]. Their planar geometry make TTF-based systems susceptible to stacking, an essential quality in the formation of nanostructures [1].

Because of its unique electronic and redox properties, its derivatives have been extensively studied and researched. The first synthesis and interest in these sulphur-containing molecules commenced in the early 1970s, following a seminal paper, which was published by Wudl in 1970, giving rise to the raw, unsubstituted tetrathiafulvalene as an electron donor with exceptional redox properties [3]. From that point onwards, tetrathiafulvalene along with its derivatives have become and counted amongst the most well-known electron donor molecules. Numerous scientific papers have been published focusing on their synthesis, properties as well as applications.

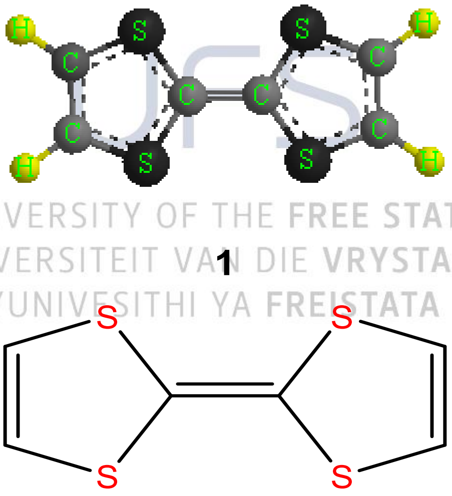

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Figure 1.1. Tetrathiafulvalene structure.

Furthermore, TTF is identified as a non-aromatic 14-π-electron system, which can be subjected to oxidation and reduction. Such that, consecutive oxidation of the neutral TTF moiety resulting in the radical cation and di-cation states, takes place sequentially and reversibly at relatively reduced and low oxidation potential values of $E^1_{1/2} = 0.37$ V and $E^2_{1/2} = 0.67$ V vs saturated calomel electrode (SCE) in dichloromethane [4] and with the oxidation potential values of $E^1_{1/2}$ = 0.34 V vs and $E^2_{1/2}$ = 0.78 V vs Ag/AgCl in acetonitrile [4]. These relatively low oxidation potentials permit the easy oxidation of the neutral TTF as well as its derivatives by either chemical or electrochemical means.

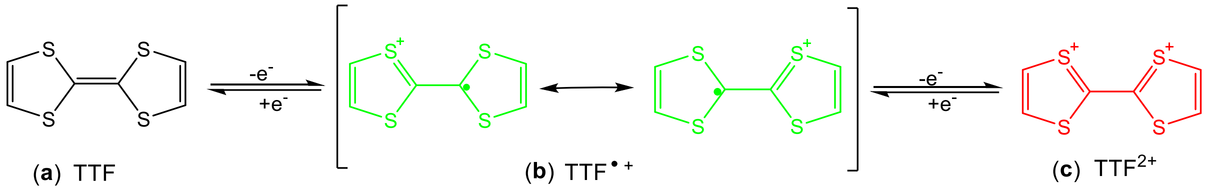

Figure 1.2. The reversible oxidation states of TTF, radical cation (TTF^+) and di-cation (TTF^{2+}).

Although the neutral TTF molecule constitutes of 14-π-electrons, the resulting radical cation (**b**) and di-cation (**c**) species upon oxidation constitute of either one (TTF^+) or two (TTF^{2+}) 6π-electron 1,3-dithiolium cations inside the framework. As of effect it displays aromatic character based on Hückel's rule, by having its cyclic fragments constitute of 6π electrons. Oxidation processes are depicted in Figure 1.2. The cation (TTF^+) shows a planar D_{2h} symmetry, meanwhile the di-cation (TTF^{2+}) is not planar and can freely rotate around the central bond. The neutral TTF constitutes of a slightly distorted boat-like structure while exhibiting a C_{2v} symmetry [5,6]. In the neutral and initial state, tetrathiafulvalene constitute of two pro-aromatic 1,3-dithiolylidene rings connected by a C=C double bond [7]. Oxidation results in conversion of one ring into an aromatic 6π-electron system, stabilized by persistence of two resonance structures. Meanwhile the second oxidation step results in two aromatic 1,3-dithiolium cations, each with 6π electrons and are connected by a C-C single bond [7]. In addition to the aromatic stabilization resulting from cationic forms as an effect of oxidation, TTF contains four polarizable sulphur atoms.

Aromatization effects reduce the energy of the oxidized species, making the oxidized species thermodynamically stable, with the two one-electron oxidation reactions being fully reversible. This oxidation reversibility feature permits modulation of interactions between molecules in instances where TTF is incorporated as a building block i.e., in supramolecular complexes. These modulations can further either increase or decrease the effect of repulsion and attraction of subunits, as well as induce global conformational changes throughout the entire complex's system [8]. This motivates and pushes the research that leads to the incorporation of TTF moieties as building-blocks for switchable processes [8].

Therefore, TTF and its derivatives sparked a lot of interest in the field of organic chemical sciences, leading to the applications of TTFs in various fields, such as organic electronics, materials science, and supramolecular chemistry. TTF derivatives are modified through altering potential functional groups attached to the TTF entity or core structure. These altered structural modifications can result and lead to enhanced unique electronic, optical, and physical properties, in turn raising beyond limit the potential applications of the TTF-based materials. Although expressed in depth in the next chapter, some of the common modifications include introducing different substituents or by means of changing the nature of the linkers connecting functional groups to the TTF core structure. Overall, as an effect of the fascinating properties, TTF derivatives have been extensively explored in the development of organic conductors and semiconductors, where their excellent charge transport properties make them suitable for possible applications in the fields. Such as organic field-effect transistors (OFETs), organic solar cells, as well as for the construction of advanced functional devices, such as molecular wires, switches, and sensors [9].

The character and behavior of TTF derivatives in macromolecular systems can be influenced by external stimuli, enabling these TTF-containing entities to operate and function as redox-responsive ligands. The systems incorporating TTF as a building block can be modulated by controlling the TTF moieties' oxidation states, thus allowing the moiety's electron donating effect make it feasible to tune the entire system. An example of an external stimuli effect is amongst others photo-induced electron transfer processes which includes modulation through oxidizing and reducing of the TTF subunits in the system [10]. Nonetheless, as stipulated before this explains the use of TTF and its derivatives in complex systems, such as redox-fluorescent switches, electrochemically driven conformational controls, molecular clips as well as molecular tweezers [10].

One of the most studied TTF derivatives is the easily accessible bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF) **2** [11]. Due to its symmetric almost planar structure, it has been reported to have produced and given rise to more superconducting salts than any other TTF derivative [11,12]. In the hope of finding new conducting systems with improved and more efficient properties, more TTF derivatives have been brought forth, leading to the climbing interest in preparation of new thio-substituted TTF analogs with the C_6S_8 core [13].

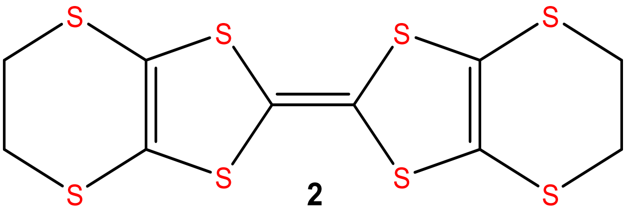

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Figure 1.3. Structural representation of simple BEDT-TTF moiety.

Due to the unique properties possessed by TTF derivatives, there has been a constant drive to prepare the new TTF-containing compounds to improve their properties, such as solubility in polar media, stability, and charge transport [13]. Therefore, the design and synthesis of novel TTF derivatives with enhanced physical and electronic properties continues to be a critical research objective. With the goal to make them compatible candidates for their application in organic electronics, including organic solar cells, organic field-effect transistors, and electrochemical sensors.

1.2 Purpose of the study

Overall, this proposed project aims to address the challenges stipulated in the previous sub-section by focusing on the design, synthesis, and characterization of new TTF derivatives. The primary goal is to develop TTF derivatives with improved solubility and charge transport properties, thereby enhancing their performance in organic electronic devices. The study is set to involve a combination of organic synthesis and characterization techniques, such as electrochemical activity testing. Furthermore, various strategies, such as functional group modifications, and structural variations, will be explored to tailor the properties of the TTF derivatives. The attachment of polar groups to TTFs render them an amphiphilic character, allowing them to be used for preparation of soft nanostructured materials, such as micelles, vesicles, gels, and other possible colloid phases, through self-assembly in aqueous solution (Figure 1.4) [10]. Self-organization serves as an alternative of top-down & bottom-up nano-fabrications methods in molecular nanotechnology. Following the self-assembly of ordered and interconnected molecular systems, in avoidance of the use of dull fabrication as well as manipulation series of steps [14]. Formation of soft materials is an example of such a self-assembly process [14].

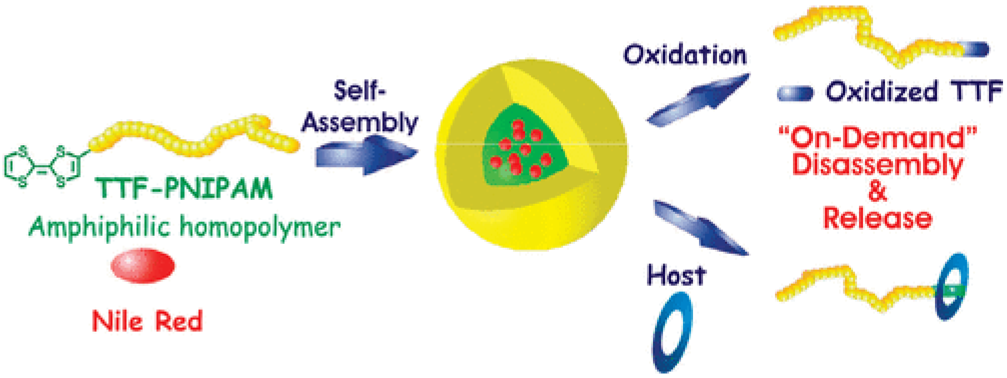


Figure 1.4. Schematic representation of the creation of Multi-stimuli Responsive Micelles composed of TTF [10].

In the proposed project, the key synthetic intermediate is bis-cyanoethyl protected TTF derivative **3**, obtained by cross-coupling reactions between 4.5-bis(alkylthiol)-1.3-dithiole-2-thione and 4.5-bis(2-cyanoethylthio)-1.3-dithiole-2-one with triethyl phosphite. Compound **3** is alkylated after the removal of cyanoethyl groups under basic conditions. The ultimate goal of the project is to synthesize amphiphilic cationic / anionic TTF derivatives **4** and **5**, and investigate their self-assembling properties in aqueous solution and the possibility to influence them by redox stimuli. In that way, this study seeks to potentially contribute to the existing knowledge databank on TTF derivatives, their synthesis, characterization, and applications.

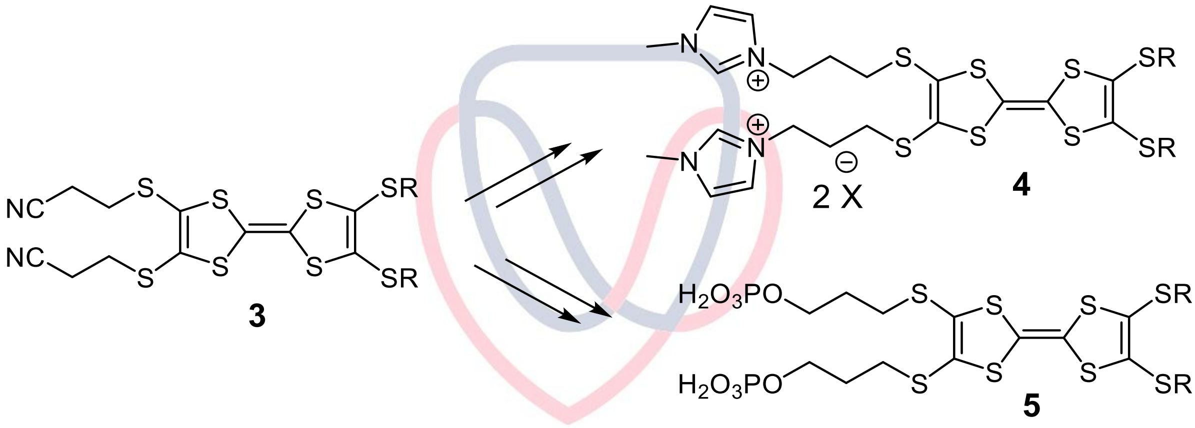


Figure 1.5. Overview reaction scheme of core compounds.

The outcomes of this research are expected to contribute to the development of advanced TTF derivatives with improved solubility properties, providing new opportunities for the design and optimization of new organic soft materials that may be used in the construction of electronic devices. The findings may not only expand the fundamental understanding of TTF-based materials but also pave the way for their integration into commercial applications. The synthesized TTF derivatives will later be investigated for their spectroscopic and electronic properties, including their redox behavior, charge carrier mobility, and photo-physical characteristics.

1.3 Mini-dissertation outline

The following outline gives a brief overview of the content through which this mini-dissertation is made up.

Chapter 2

The chapter embodies deeper and intense literature review on the history of tetrathiafulvalene and its analogs through exploring the possible series of synthetic approaches found in literature. Studies on their structural properties will be covered, along with how those render them suitable for supramolecular chemistry, material science and nanotechnology. Adding to literature studies on the examples of entities embodying TTF analogs as building blocks, and thereof the effect they have on such entities. In that way this chapter introduces the scope of the study by covering these entities' background, preparation and application.

Chapter 3

In Chapter 3, a series of synthetic procedures are explored with significant tailoring and adjustments. It commences with a brief introduction of the materials, methods and techniques used for the wet-chemistry preparation of TTF intermediates and derivatives. This is followed by the synthesis procedures used, inclusive of quantitative and qualitative results.

Chapter 4

This chapter covers the results as reported in the previous chapter in a form of a discussion, inclusive of both successful and unsuccessful synthesis of intermediates and derivatives. It further embodies the interpretation of some of the characterisation techniques used to confirm and characterise prepared compounds.

Chapter 5

In Chapter 5, an outline and summary is given, presenting the findings drawn from interpretation of the attained results from synthesis and characterization. By so doing, linking the project's aims and objectives with the outcomes of the study. Recommendations and future works are also presented.

CHAPTER 2: Literature review

2.1 Introduction

This chapter comprises an overview of tetrathiafulvalenes, their structure, properties and history. Aspects such as their linkage to supramolecular chemistry, material science and nanoscience are reviewed; in particular, their derivatives serving as versatile building blocks in various fields of chemistry, as well as properties making them eligible and qualified for material sciences are discussed. The scope of the review is further composed of the application and examples of colloid and nanostructured materials.

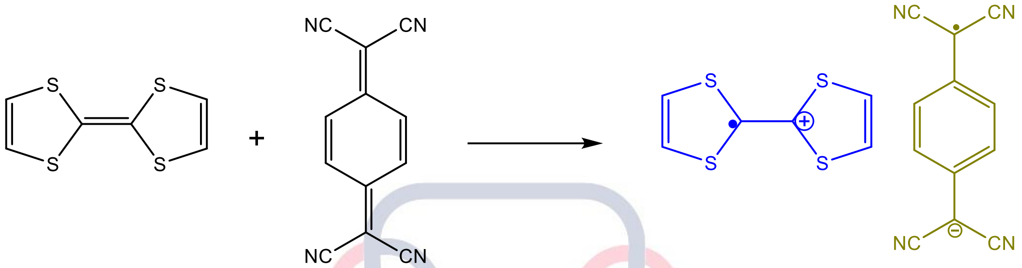
2.2 Tetrathiafulvalenes

2.2.1 Structure and properties of TTFs

Tetrathiafulvalene (TTF) and its derivatives in organic chemistry are known for their exquisite properties as far as the operation and functioning of molecular systems at molecular level is concerned. They are best defined as redox-switchable organosulfur compounds following the manner in which they evince electrochemical properties [7]. These properties allow TTF and derivatives to play a crucial role of being a switching unit in controlling molecular motions of rotaxanes and catenanes as mechanically interlocked molecules (MIMs). As well as in other macro or supramolecular systems i.e., receptor molecules and molecular cages [7].

TTF as a redox system exists in three different stable reversible oxidation states as depicted in Figure 1.2 in the previous chapter. It demonstrates TTF as a stable two electron donor that can undergo two reversible, easily accessible oxidation processes [15]. Due to the electron-rich property in its native state, it is a good electron donor qualifying it as an exquisite candidate to be incorporated into macrocyclic systems. Furthermore, tetrathiafulvalene moieties can form π–-π stacked columns with proportional short S---S interactions, which can facilitate systematic pathways for charge transport [7]. The π–-π and S---S interactions along with the CH–-π interactions have an effect on the packing pattern of the TTF molecules in crystals. Such crystals may possess intrinsic properties of organic semiconductors, thus permitting the implantation of ways through which crucial factors for enhanced performance devices and study of fundamental concepts in organic semiconductors were demonstrated. In turn, it guides TTF molecular design as well as its synthesis [16].

TTF's π-donating effect decreases as it goes through oxidation, as a result TTF^{2+} di-cation can be said to be a π-electron-poor molecule [17]. The π-donating tetrathiafulvalene reacts with π-electron-poor aromatic compounds to form donor–acceptor complexes. In 1973, *Ferraris et* *al*., reported the development of an extremely conducting complex between TTF as the electron-donor and tetracyano-p-quinodimethane (TCNQ) as the electron-acceptor, the complex exhibited a very high maximum electrical conductivity [18]. The electron-donor (TTF), and electron-acceptor (TCNQ) complex demonstrates interesting electron properties (Figure 2.1). Reason being that TTF as the electron-donor constitutes of sulfur atoms, making it highly a polarizable compound [19]. This further results in reduced coulomb repulsion (the force between charged entities) between electrons on neighbouring TCNQ sites [18,19].



TTF
1

TCNQ
6

TTF-TCNQ
7

Figure 2.1. TTF-TCNQ charge transfer complex formation.

The end product of these complexes with TTF-based electron-donors are crystals, in which the moieties form π–-π stacked columns with short S---S interactions, which attributes to charge-carrier mobilities. The molecules' packing structure motif can also be controlled by van der Waals interactions between attached alkyl substituents [9,20]. The π-π- stacking is known to be the highly effective packing for transporting charge carriers. That comes as a result of the ability of the large π–π overlap in stabilizing the +1 or -1 charged state [16]. The π-conjugated system plays a major role in the semi-conducting property of TTFs. The orbitals bridge adjacent single bonds, allowing delocalization of electrons over every π-orbital in the molecule, as a result of the p_z-orbitals forming π-bonds composed of small energy gaps [21]. However, in these semiconducting molecules, the packing of the molecules serves as a determining factor concerning charge transport (CT) efficiency. In Figure 2.2, is a demonstration of the schematic representation of simple molecular packing motifs in crystals of planar aromatic molecules, some of which demonstrate semiconductor properties [9,22]. The structures in the Figure represent crystal structures of enhanced charge-carrier mobilities. Denoted (a) and (b) is a herringbone-like structure, meanwhile (c) is 1D-π- stacking (lamellar) and lastly in (d) is the 2D-π-staking (brickwork) structure [9].

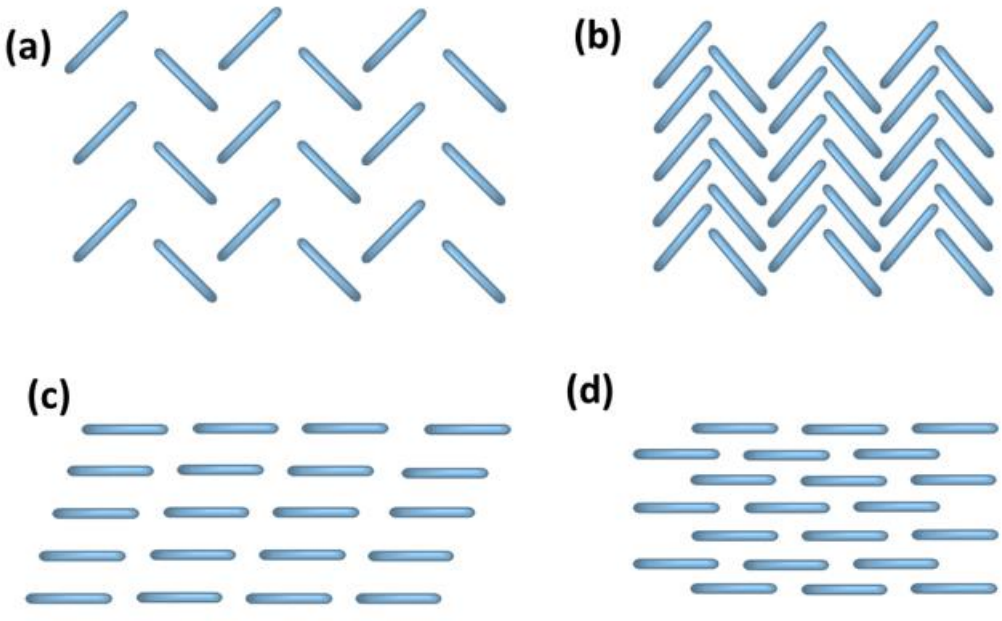


Figure 2.2. Schematic representation of molecular packing motifs in organic semi-conductor crystals [9]

Amongst the advantageous properties of TTF and its derivatives as organic semiconductors, is the ability of the radical cations to reversibly form co-facial dimers [17]. In an article published in 2018*, H. V. Schröder & C. A. Schalley* [7], reported that two monomers self-assemble into a mixed-valence dimer denoted $(1_2)^{\bullet+}$, which can be identified by a change in the redox conduction and low-energy absorption band [7]. However, both monomers are said to be paramagnetic radicals and their assembling resulting in a dimer with diamagnetic properties as a result of radical pairing [7,23]. Tetrathiafulvalene dimerization is acknowledged as one of the ways through which redox switchable mechanically interlocked molecules can evolve, where TTFs are used as key building blocks.

To conclude, tetrathiafulvalene in its neutral state appears to be a very strong π-donor molecule, which is an attribute making it a useful building block in material sciences or supramolecular chemistry. Therefore, TTFs are used to form donor–acceptor complexes with the π-electron poor species. However, upon oxidation the π-electron donating effect of TTF disappears, due to the fact that TTF^{2+} di-cation has electron deficiency nature [7].

The TTF backbone can be derivatized through introduction of a variety of substituents at its 4- and 5- positions symmetrically or unsymmetrically. Figure 2.3 serves as a depiction of how TTF moiety can be substituted at four identical possible attachment sites [24]. Attachment of only 1, 2, or 3 substituents leads to the de-symmetrization of the TTF backbone. As a result, the substituents can instigate change of properties on a TTF derivative.

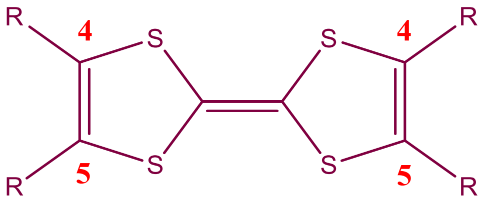


Figure 2.3. Positions 4- and 5- of TTF skeleton that can be symmetrically or unsymmetrically substituted.

Consider for instance, Figure 2.4, a N-donor ligand containing pyridyl functionality. Such entities have been shown to coordinate with metallic centres, resulting in interesting multifunctional materials demonstrating conducting and magnetic properties [25]. This is all enabled by the pyridyl functionality attached to the TTF entity. *Jia et al* reported the synthesis and study on one-dimensional μ-chloromanganese(II)-tetrathiafulvalene (TTF) coordination compound, resulting from the TTF derivative (organic donor) in Figure 2.4 [26]. The introduction of the functionalised redox-active TTF derivative affords complexes with interesting magnetic properties [27]. It renders them promising candidates for the construction of new hybrid inorganic-organic materials.

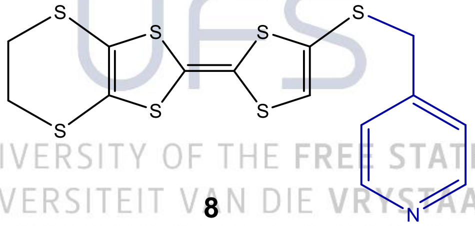


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Figure 2.4. Pyridyl-containing TTF derivative.

The resultant complex is made up of two N-donor ligands (Figure 2.4) bonded to Mn(II) via the two nitrogen atoms in *trans* positions, as well as two Cl^- anions on the axial direction linking the Mn(II) ions to a limitless chain [26]. The Mn(II) ion was found to be adopting a distorted octahedral coordination geometry. The calculations revealed how the complex exhibited moderate antiferromagnetic coupling amongst the Mn(II) centres [25].

Properties of TTF derivatives are further attested by their use as building blocks of charge-transfer salts used as organic conductors and superconductors [9]. For example, *Wang et al*. reported that incorporation of redox-active TTF unit with magnetic properties into cyanidebridged complexes presents another level of complexity to the design parameters for multifunctional materials [28]. Furthermore, the material's electrochemical properties showed that the TTF component's redox activity was maintained in these materials [25]. In this latter study, following their optoelectronic and conductive properties, TTF derivatives are used as organic ligands to produce TTF-based coordination polymers (CPs) prepared from different transition metals.

2.2.2 Synthetic approaches in preparation of tetrathiafulvalenes

There are several synthetic approaches for the preparation of the tetrathiafulvalene skeleton. The synthesis of tetrathiafulvalene derivatives has been reported in several scientific journals and reviews [16,24]. It generally commences with the preparation of a zincate salt, bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiol)zincate, which can be prepared in high yield from 1,3-dithiole-2-thione-4,5-dithiolate (2-thioxo-1,3-dithiole-4,5-dithiolate, DMIT). The reaction commences with carbon disulfide reacted with alkaline metal in dimethylformamide, producing 1,3-dithiole-2-thione-4.,5-dithiolate. Which stands to be isolated as zinc complex through the addition of zinc chloride ($ZnCl_2$) and tetraethyl ammonium bromide [29], as depicted in Figure 2.5.

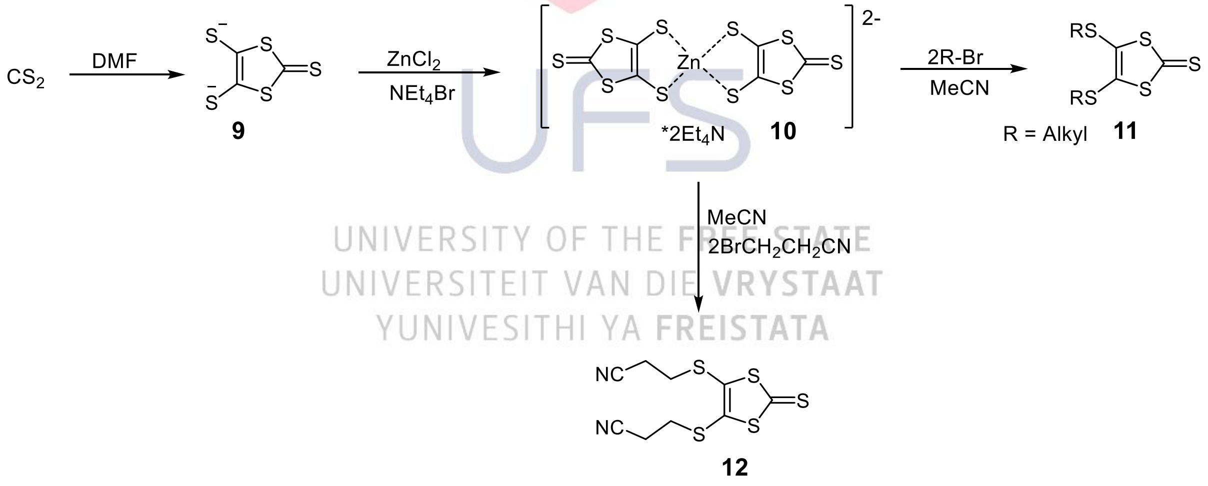
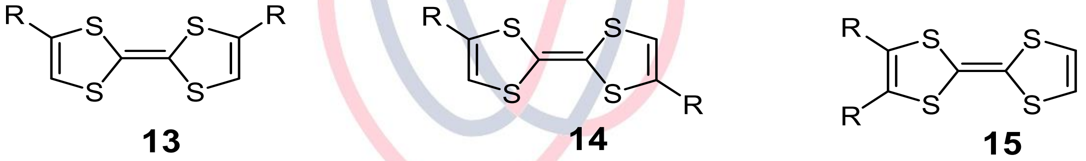


Figure 2.5. Formation of 2, bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiol)zincate salt from 1,3-Dithiole-2-thione-4,5-dithiolate (2-thioxo-1,3-dithiole-4,5-dithiolate, DMIT) 1.

The resulting zinc complex permits the preparation of a bis(cyanoethylthio) protected compound, such as the 4,5-bis(cyanoethylthio)-1.3-dithiole-2-thione **12**, by treatment with bromopropionitrile or compound **11** resulting from alkylation with an alkyl halide. The route of using the zinc chelate has appeared to be far better in comparison to other possible methods composed of sodium, potassium or lithium DMIT salts. This is due to its extensively high yields and stability at room temperature [29]. Literature reported several synthetic procedures for the preparation of the zincate salt with slight modifications [29,30]. The optimized amount of sodium leads to an increase in of the zincate complex as a pure product.

Di-functionalisation of TTF leads to three different substitution patterns of TTF derivatives (Fig 2.6) [24]. Compounds **13** and **14** may be subjected to cis/trans isomerization process of the central double bond, which may have an effect on the overall behaviour of the TTF derivative. In contrast, for compound **15** isomerization of the central double bond does not make any effect [24]. In our project, the goal was to prepare derivatives of the type **15**, where two functional substituents are located on one side of the TTF backbone. Type **15** is asymmetrical di-substituted tetrathiafulvalene, these type of TTF moieties serve as an approach to eradicate factors that inhibit the preparation of exceptional TTF derivatives. Factors such as pseudo-symmetrical di-substituted TTF (**13** & **14**), wherein facile isomerisation around the double bond often results in cis/trans problems [24].



13 **14** **15**

Figure 2.6. Different types of substitution patterns for double-substituted TTF derivatives.

The cyano-ethyl group has been reported as the TTF-compatible base labile protecting group, used to protect and shield the thiolate group. The cyano-ethylated thiolates are able to survive dithiolethiones' trialkyl/ triaryl phosphite mediated coupling. They can be effortlessly eliminated as acrylonitrile using a strong base to give the thiolate [31]. Alkylation of the zincate salt with 3-bromopropionitrile in refluxing acetonitrile yields **12** as 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione in about 87% yield. In the same way, alkylation of the zincate salt with an alkyl halide in acetonitrile yields 4,5-bis(alkylthio)-1,3-dithiole-2-thione **11** (Figure 2.5). Compound 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione **12** is then converted to 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-one **16**, an oxo derivative through mercuric acetate trans-chalcolgenation. It permits both cross-coupling (**11+16**) and homo-coupling (**16+16)**, as depicted in Figure 2.7.

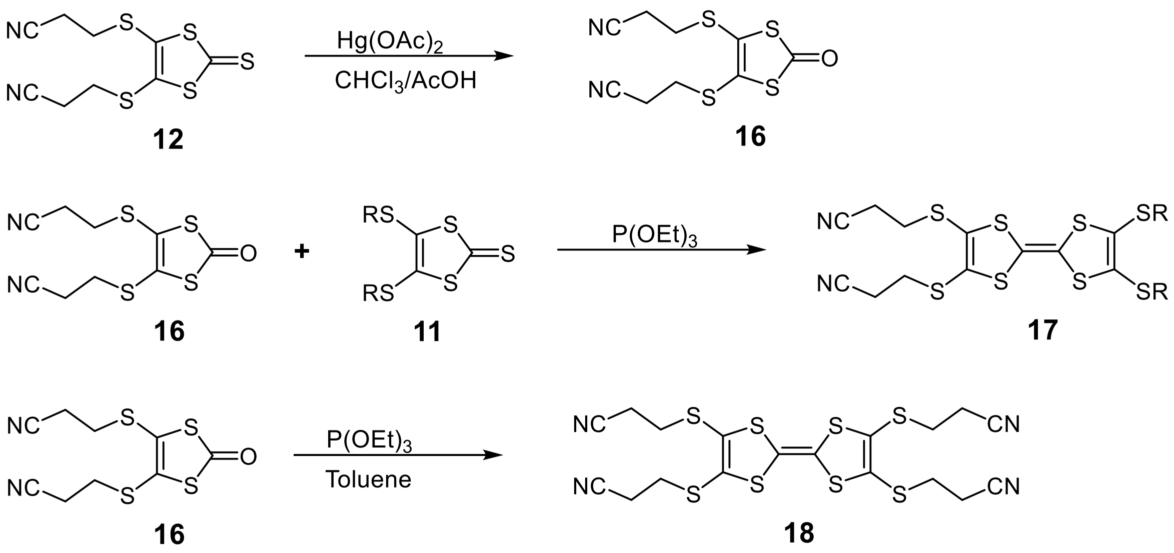


Figure 2.7. Synthetic approach to prepare cyanoethyl-protected TTF derivatives.

In a triethyl phosphite mediated cross-coupling the ketone **16** is coupled with the excess of appropriate 1,3-dithiole-2-thione **11** to prepare the un-symmetric TTF derivative **17** . The self-coupling of **16** yielding **18** usually takes place as a side reaction during the cross-coupling, but it can be also carried out as a separate reaction affording the good yield of TTF **18**. Coupling between two thiones (of the type **11+11**) is usually not favoured, due to the presence of the two bulky and relatively large sulphur atoms resulting in steric hindrance, making the coupling reaction less favourable. Another reason rendering the reaction unfavourable, is reduced electrophilicity of the thione carbon, as the sulphur atom is less electronegative than oxygen. Thus, making the thione carbon less reactive towards nucleophilic attack, which is a requirement for coupling reactions. This cross-coupling giving rise to un-symmetric TTF derivatives has been reported to be the efficient and preferred coupling mode [32].

The readily prepared intermediate **17** can undergo mono-deprotection or bis-deprotection under mild basic conditions depending on the number of equivalents of the base used for deprotection (1 or 2, respectively). The thiolates formed in the reaction can be re-alkylated with any appropriate electrophile (Figure 2.8). Use of methanolic solution of caesium hydroxide in dimethylformamide is the most widely used reaction procedure [13,33]. It can be reliably used for mono- and bis-deprotection of **17**. Other examples of strong bases that can be used for deprotection include potassium *tert*-butoxide in dimethylformamide, tetrabutylammonium hydroxide in acetonitrile, or sodium ethoxide in ethanol, and lastly sodium hydride in dimethylformamide [13,19]. The deprotected intermediate then subsequently undergoes alkylation as part of functionalisation with any appropriate electrophile with good yields. As alkylation agents, alkyl halogenides or tosylates can be used [13].

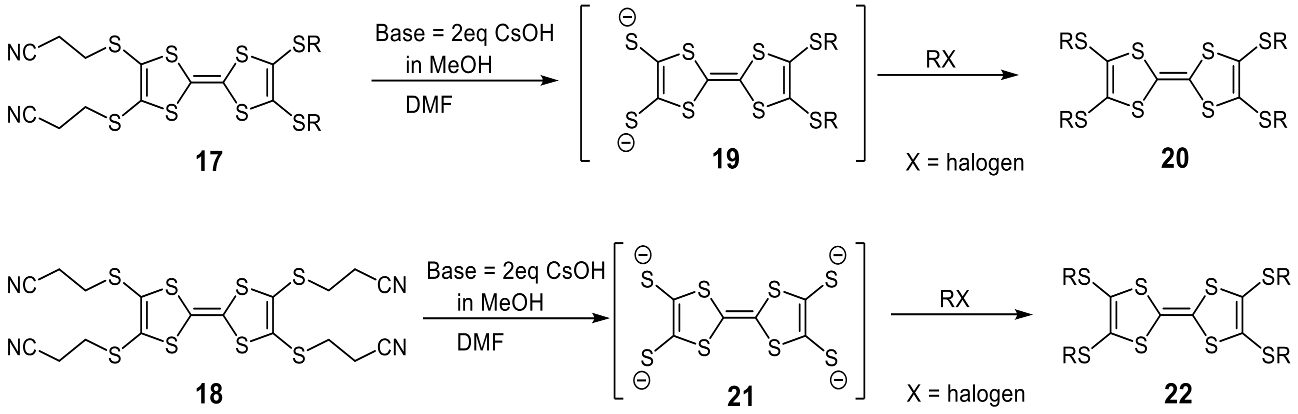


Figure 2.8. Deprotection and re-alkylation of Tetrathiafulvalene derivative intermediate.

2.2.3. Conductive and redox active TTF derivatives as building blocks in supramolecular chemistry, material science and nanoscience

According to *Lehn*, self-organization serves as an alternative of top-down nano-fabrications methods in molecular nanotechnology, following the managed assembly of ordered, fully integrated and connected operational systems by hierarchical growth [14]. However, the priority objective is to prepare complex organized analogues of collective operation instead of just small size and individual addressing materials (Figure 2.9) [34].

The redox-active properties of TTF enabled their use in material sciences as building blocks. This includes their incorporation into material systems such as macrocycles, rotaxanes, cyclophanes, catenanes, cage molecules, dendrimers, polymers, etc [35]. TTF derivatives can be controlling motions of molecular machines (receptors), thus referred to as molecular redox switches generating and controlling molecular motions. Their properties make them good candidates to be incorporated as building blocks of soft nanostructured materials. Such as gels, vesicles, peptide nanostructures and micelles, though this research area remains poorly explored.

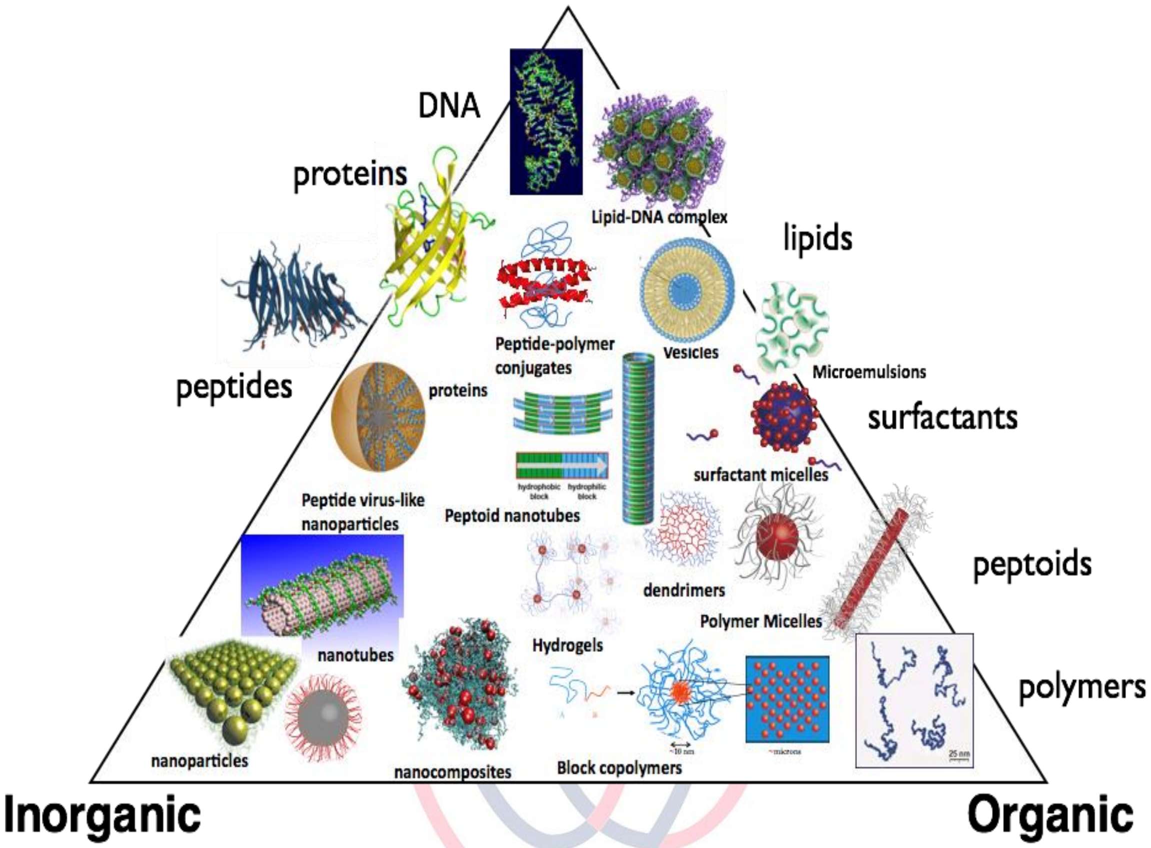


Figure 2.9. Schematic representation of soft nanostructured materials in which TTF can serve as a building block.

TTF readily acts as an electron donor: it forms a donor-acceptor complexes as it is mixed with an electron acceptor, such as tetracyanoquinodimethane (TCNQ) forming a crystalline charge-transfer (CT) complex. Which demonstrates an electrical conductance of higher magnitude than usual for organic solids [36]. Macrocyclic TTF-based systems are studied with the aim of making molecular devices, shuttles, switches and sensors. Such systems may consist of a central TTF moiety that is situated between two macrocycles serving as terminals. Figure 2.10 illustrates an example of a macrocyclic compound comprising a TTF moiety as a building block [36].

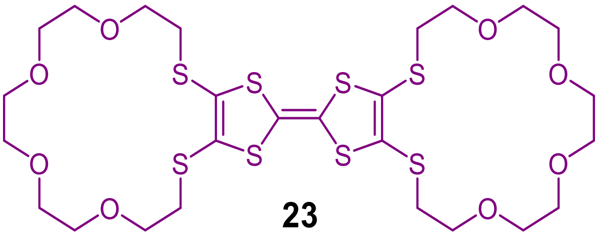


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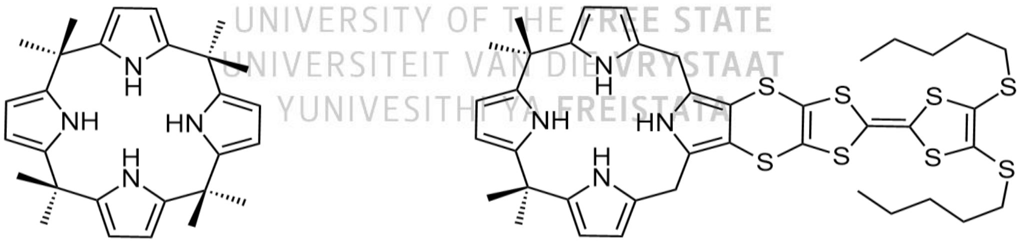
Figure 2.10. TTF containing macrocyclic system.

TTF macrocyclic systems may serve as potential receptors for electron-deficient guests. TTF can be incorporated into classic existing macrocyclic motifs with the aim of producing hybrid systems [37]. For example, by their grafting onto the periphery of crown ethers, they can give rise to calixpyrroles, as well as cryptands [37,38]. This allows operating them as transducers responding to external stimulus, producing change in the electronic features of the system, which can be detected by electrochemical means [37,38]. These systems when acting as receptor systems, were shown to be exhibiting enhanced sensing properties. In this context, it can be expected that when TTF is used as a transducer and is oxidised to its cation or di-cation state, a positive charge is created, which can reduce / decrease the binding ability of the attached host-unit towards cations [36].

It has been reported that TTF incorporation permitted the preparation of numerous molecular systems based on host–guest interactions with the ability to act either as sensors, molecular switches or mediators for certain reactions [39]. For example, TTF-pyrroles derivatives can act as anion sensors. They are composed of TTFs annulated onto a pyrrole subunit, which is said to be a useful building block presenting rigidity and electron-donating effect to different types of oligo-pyrrolic macrocycles such as calixpyrroles [38]. Through which a higher binding affinity towards anions is observed [38,40]. The enhanced binding affinity for anions is an effect of the NH-anion hydrogen-bonding interactions. Figure 2.11 illustrates chemical structures of a calix[n]pyrrole (n = 4) framework as well as the chemical structure of TTF-based calix[4]pyrrole receptor as examples [40].



24 **25**

Figure 2.11. Chemical structures of a calix[n]pyrrole (n = 4) framework **24**, and TTF-based calix[4]pyrrole receptor **25**.

As a result of the electrochemical analysis for compound **25**, an electrochemical response toward various anions was observed using cyclic voltammetry in MeCN. It was demonstrated that the redox-active tetrathiafulvalene unit of receptor **25** shows electrochemical response upon complexation with anions such as Br⁻ in MeCN. The results showed cathodic shift of the first oxidation potential upon the gradual addition of Br⁻ ions, as well as an increase in the intensity of the current linked to the second TTF oxidation potential [40].

Another class of supramolecular or material sciences systems that makes use of TTF as a well-established and successful building block include catenanes. They are defined to be classic molecular systems composed of at least two or more mechanically interlocked rings/ intertwined macrocylces [7,41]. Which is a structure that cannot be opened or separated without breaking at least one covalent bond [7]. TTF-based catenanes have been prepared with the aim of establishing molecular switches and molecular machines. TTF-containing catenanes as well as other related mechanically interlocked molecules (MIMs) allow controlling of molecular movement and, thus, making of devices able to function at molecular level [37,42]. Figure 2.12 shows an example of classic TTF-containing catenane **26** [43]. It has been reported to be the first TTF-based catenane by *Becher's* as well as *Sauvage's* group, stemming from a phenanthroline TTF-bearing macrocycle. A copper(I)-template was used to prepare this TTF-based catenane [43].

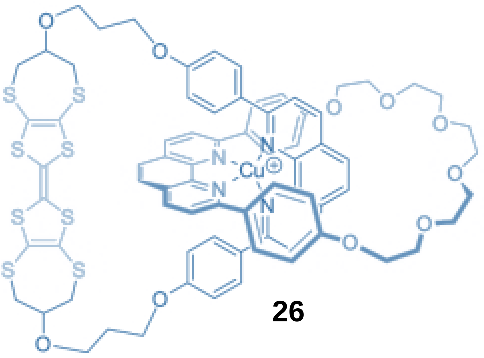


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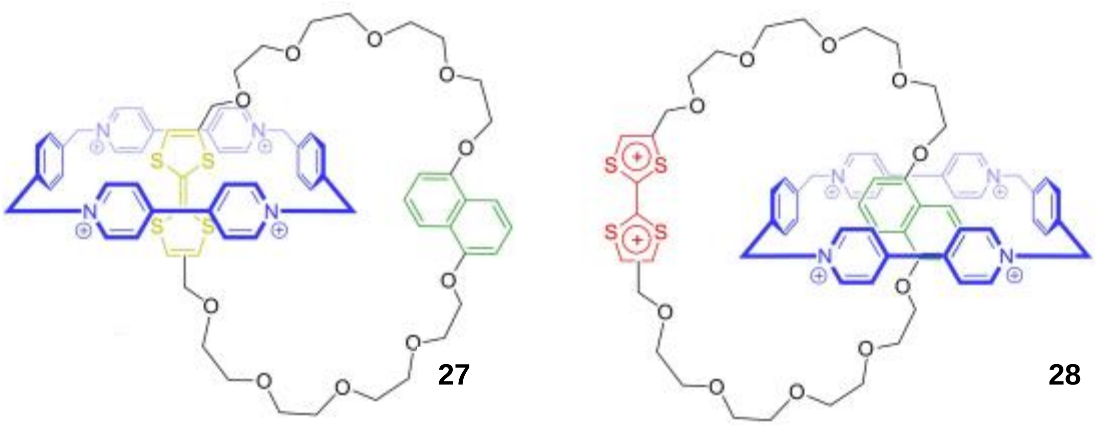
Figure 2.12. Cu(I)-templated TTF-containing catenate.

A TTF-based catenane **27** (Figure 2.13) has shown a high level of ability in behaving as a molecular switch taking advantage of TTF's reversible redox chemistry properties [44], by switching between two translational isomers **27** and **28** [44]. In the initial state **27**, the electron-deficient macrocycle appears to be encircling the TTF unit. Upon oxidation of the TTF unit either by chemical or electrochemical effect, the cyclic acceptor or macrocycle is translated from the TTF unit to the 1,5-dioxynaphthalene donor unit [45], which is also electron rich, but less than non-oxidized TTF, giving rise to compound **28** [45]. Therefore, chemical oxidation of the TTF activates an expulsion of the former state and the macrocycle translates to the alternative dihydroxynaphthalene site. Subsequent chemical reduction of the compound regenerates the original isomer, restoring the initial spectroscopic properties as well as the initial co-conformation of the TTF-based catenane [7].



27 **28**

Figure 2.13. Redox switching 4PF$_6^-$ (cis/ trans) TTF-based catenane. Left: Cis-isomer, Right: Trans-Isomer.

In the crystal structure of **27**, the TTF moiety appears to be positioned inside the tetracationic cyclophane and the 1,5-dioxynaphthalene ring system appears to be alongside it [45]. Of the two possible TTF isomers, only the *trans* isomer is perceived in the solid state [44]. According to reports by *Asakawa's group*, this TTF-catenane complex appears to be stabilized by normal combination of π-π stacking interactions as well as [C-H - - -O] hydrogen bonds from the alpha bipyridinium hydrogen atoms [44].

According to literature reports, *Stoddart and Becher* groups were the first group to carry out the synthesis of the first TTF based rotaxane [46]. Rotaxanes in general are composed of a dumbbell-shaped axle molecule, composed of bulky stopper groups at the ends of the axle both sides preventing de-slipping of the wheel [47]. The axle is encircled and enclosed by a macrocycle. The use of such mechanically interlocked molecules is effect induced by translational motion of the wheel along the axle [47,48]. Incorporation of TTF as a building block into mechanically interlocked molecules (MIMs) allows for the redox-controlled translational motion, through which the wheel position on the axle is susceptibly controlled by external stimuli thus producing switchable molecular shuttles. Rotaxanes like any other interlocked molecular structures can be prepared via template-directed synthesis strategies. That is reported to be namely: "(a) threading of a half-dumbbell-shaped component into the cavity of a preformed ring based on their mutual recognition, and then subsequently stoppering of the open end of the pseudorotaxane" [49]. Then, "(b) clipping of a ring around a recognition site on a preformed dumbbell component [49]. Then lastly, “(c) slippage of a preformed ring over one of the terminal stoppers onto a preformed dumbbell at elevated temperatures” [49].

Figure 2.14 below depicts a bi-stable switchable rotaxane in two of its possible states [7,50]. In the ground state, the supposed wheel encircles or encloses the TTF unit, and it is located on TTF binding site. Upon induction of external stimuli by oxidation, resulting in TTF oxidation (TTF^{2+} state), affinity is reduced between the TTF and the wheel [50]. Thus, the wheel is translated towards the new energetically preferred binding site, green dihydroxybenzene station [7]. Following the effect of the reversibility of TTF redox reactions property, TTF containing rotaxane molecular shuttle can be reversibly switched over many cycles.

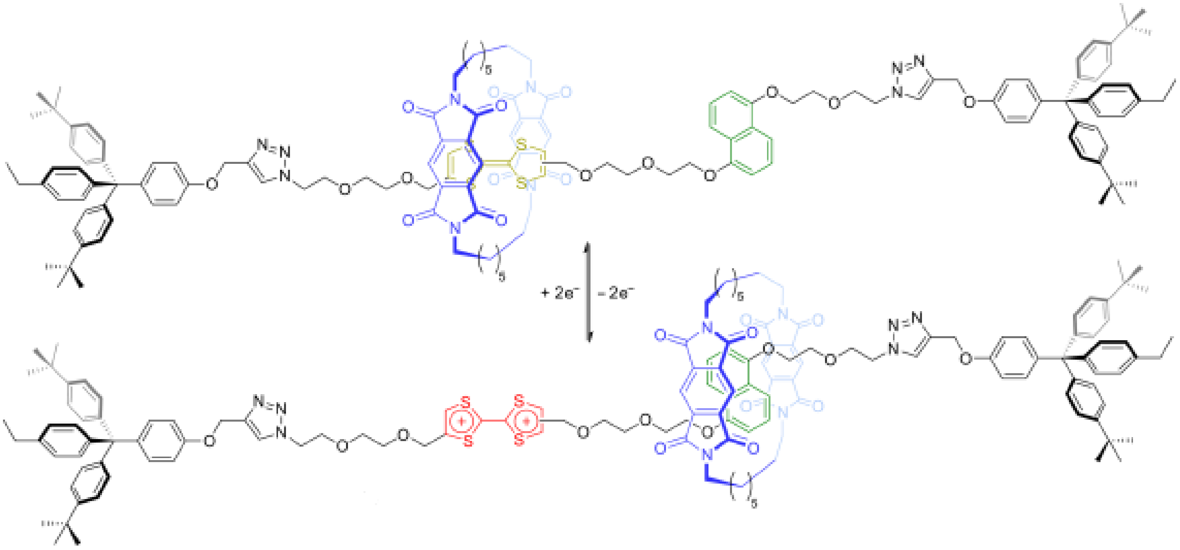


Figure 2.14. TTF-based rotaxane.

Mechanically interlocked molecules serve as one of the major scaffolds in the construction of molecular devices and machines and may serve as nanoscale switches for molecular electronics as well as nano-electro-mechanical systems. These artificial molecular machines will allow for the miniaturization through the bottom-up system construction approach in macroscale manufacturing. These TTF-containing MIMs are suitable for the nano-electronic devices’ construction, following the controlled switching in between different translational isomers enabled by several possible oxidation states of the TTF unit [51]

2.2.4. Nanostructured materials using TTFs

TTF-based metal–organic frameworks (MOFs) are amongst other TTF-based nanostructured materials. MOFs are defined as crystalline porous materials arising from metallic nodes and organic linkers [52]. Incorporation of redox-active moieties to MOFs gives rise to a class of functional porous systems with additional electronic features affording novel electrically conductive and redox-active MOFs [53]. Such structures with infinite channels within the three dimensions network demonstrate potential interest for a wide range of applications [54]. The structure of a tetratopic TTF tetracarboxylate ligand used as a common precursor for making MOFs [37] is depicted in Figure 2.15.

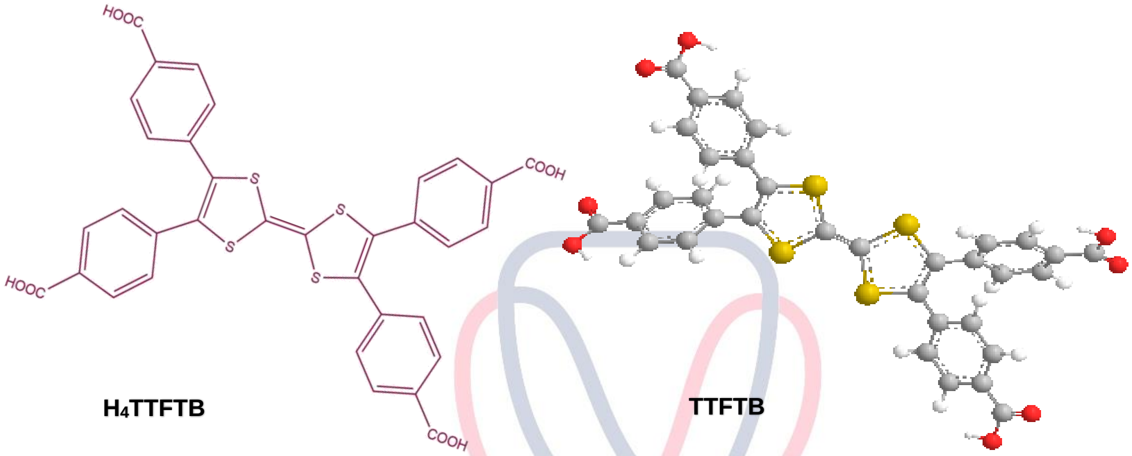


Figure 2.15. Chemical structure and ball-and-stick representation of a tetratopic ligand H_4TTFTB used in MOF construction.

MOFs based on H_4TTFTB are commonly denoted $M_2(TTFTB)$ wherein, M = Zn^{2+}, Co^{2+}, Mn^{2+} and Cd^{2+}. The π–π stacking is reported to support orbital overlap of neighbouring TTF moieties and gives an extended charge transport pathway within the MOF structure. Oxidation of these MOFs leads to production of TTF^{+} sites and results in increased conductivity, making them promising organic conductors [55]. *Su et al* reported the study of the breathing behaviour on TTF based MOFs induced by guest molecules in a single framework, arising from $[In(COO)_4]^{-}$ metal nodes and the tetratopic tetrathiafulvalene-based linkers (TTFTB- tetrathiafulvalene tetrabenzoate) [56]. Breathing behaviour refers to a reversible unit-cell dimensional change experienced by the framework due to guest adsorption or desorption, these MOFs respond to external stimuli such as redox conditions, guest molecules or temperature. In this context, redox-switchable properties were coupled with breathing behaviour induced by guest molecules in a single framework. Two flexible isomeric compounds were constructed using a combination of $[In(COO)_4]^{-}$ metal nodes and tetratopic tetrathiafulvalene-based linkers (TTFTB) [56]. These two isomeric compounds were reported to exhibit different breathing behaviours following introduction of N_2. The breathing mechanism of one compound involves the bending of metal–ligand bonds (bending of linkers) as well as sliding of interpenetrated frameworks [56]. Meanwhile, the other compound undergoes simple distortion of linkers [56]. However, reversible oxidation and reduction reactions of the TTF units induce changes in the linker's flexibility. Therefore, the TTF moiety in the MOF's linker serves the role of a redox switch used to control the framework's flexibility [56]. The TTF component permits reversible oxidation by I_2 as well as reduction by N,N-dimethylformamide (DMF), thus switching the linker flexibility and breathing conductivity. Furthermore, oxidation of the TTF results in the transformation of the S-heterocycles into an aromatic 6π-electron configuration, in turn transforming the central double bond to a single bond, forming a conjugated aromatic system rigidifying the TTF moiety [56]. It was further reported that upon doping with I_2, oxidation took place, meanwhile the product of the iodine reduction, I_3^-, was observed in the channel simultaneously with a small conformational change of the linkers: the central C-C distance of the TTF units went up from 1.343(9) to 1.387(6) Å. Subsequently, the initially flexible TTFTB entity became more rigid, and a rigid linker results in the loss of breathing behaviour. It was demonstrated that the behaviour of flexible MOFs is a reversible process and one that can be switched on and off by implementation of redox chemistry.

Zuo et al. reported similar Fe(II)-based MOFs made up of redox-active tetrakis(4-pyridyl) TTF precursor, which exhibit multifunctional electronic, optical, and magnetic properties, making them suitable candidates for the development of electronic devices [57]. Bistable catenanes can be incorporated into the rigid scaffold of MOFs, as reported for a Zr-based MOF denoted NU-1000 [58]. Rotaxanes can undergo the same effect wherein a bistable MIM is incorporated into a metal-based MOF, demonstrating that bistable MIMs are able to exhibit robust dynamics inside the nanopores of a MOF.

Fullerene–tetrathiafulvalene complexes represent a range of applications in varying fields, from molecular electronics to nanotechnology as well as biomedical applications. Fullerene C_{60} plays the role of an electron-acceptor that is able to accept up to six electrons in solution [59]. Understanding its charge transfer processes with electron-donor molecules is crucial as that would permit easy optimisation of photovoltaics and development of solar cells [60]. A number of charge-transfer complexes of fullerenes with planar TTF donors has been reported.

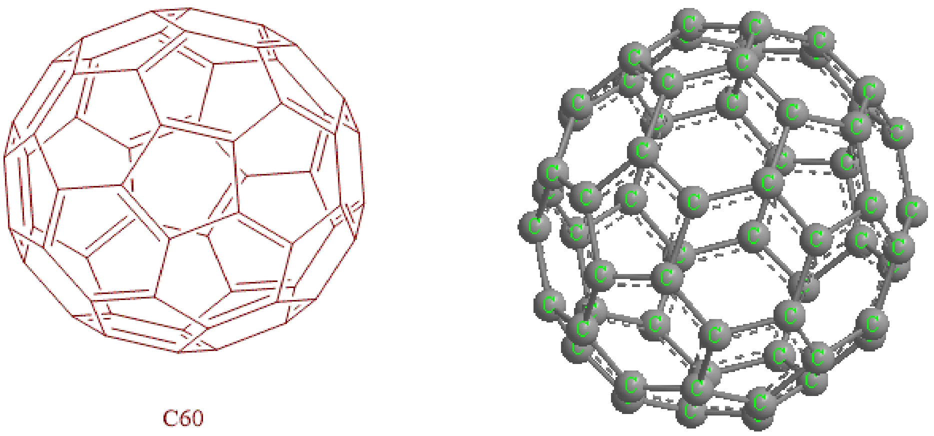


Figure 2.16. Molecular and ball-and-stick representations of fullerene C_{60}.

Sugawara's group reported crystals of a charge transfer complex composed of C_{60} and bis(ethylenedithio)tetrathiafulvalene (BEDTTTF). The X-Ray crystal analysis revealed that the C_{60} was sandwiched between largely concave BEDT-TTF molecules and its rotational motion was entirely quenched [61]. Majority of the crystal structures in literature for complexes between C_{60} and TTF derivatives show stoichiometry ratios of 2+1 between TTF and C_{60}. However, other ratios such as 1+1 have also been observed [45]. The ability of TTFs-C60 phases to form charge transfer complexes with tetrafluorotetracyano-p-quinodimethane as an electron acceptor has been studied by *Martín* and his group. These kinds of complexes were reported to exhibit semiconducting properties and, as a result, are useful in the development of molecular materials for use in molecular electronics [45].

The encapsulation of C_{60} in MOFs is an engrossing strategy for the incorporation of additional functionalities within the MOF as well as of fullerenes [53]. It can be used to enhance electrical conductivity because of the donor–acceptor interactions between the TTF-based ligand (donor) and the fullerene (acceptor), without reducing or decreasing the porosity. Gas sorption measurements show that sorption capacity is maintained after encapsulation of fullerenes [53]. Meanwhile the electrical conductivity undergoes an increase by at least two orders of magnitude as an effect of the charge transfer interactions between the C_{60} and TTF-based framework [62]. Figure 2.17 below demonstrates the encapsulation of C_{60} in the electron-donor TTF-based MUV-2 resulting in C60@MUV-2 complex. The grey, yellow, orange and red spheres stand to represent C, S, Fe and O atoms, respectively [53]. The encapsulation of C_{60} was carried out through immersing the microcrystalline powder of MUV-2 in a solution of C_{60} in o-dichlorobenzene for at least three days at elevated temperatures, followed by subsequent washing with o-dichlorobenzene and methanol and drying. Powder X-ray diffraction (PXRD) revealed that the C_{60}@MUV-2 crystallinity was maintained upon encapsulation and removal of the solvent. Scanning electron microscopy (SEM) also confirmed that the needle-like morphology of C_{60}@MUV-2 remained the same as for MUV-2 [53].

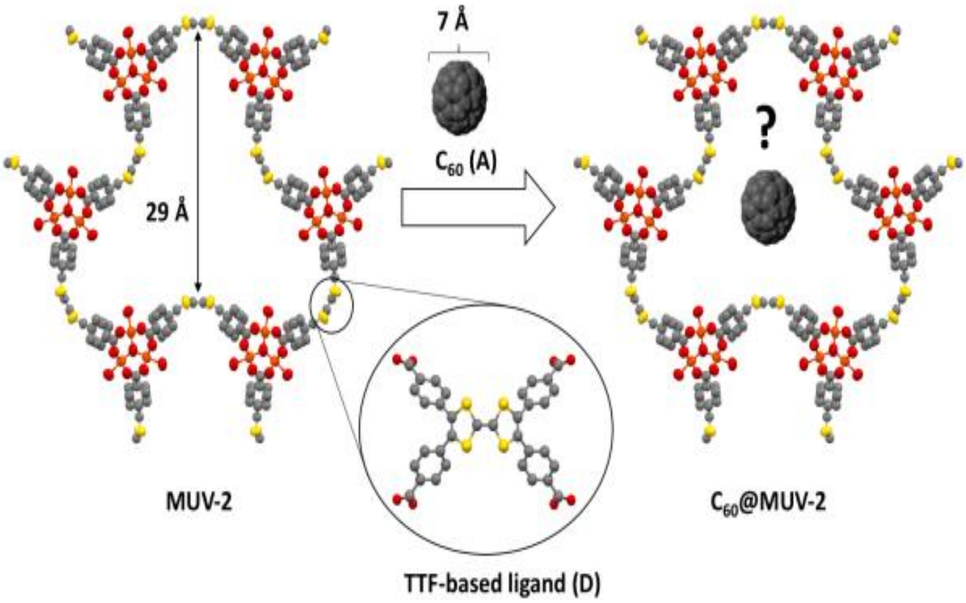


Figure 2.17. Schematic demonstration of the encapsulation of C_{60} in the electron-donor TTF-based MUV-2 denoted “D” resulting in C60@MUV-2.

Dendritic macromolecules comprise a polyfunctional core that is surrounded by covalently linked layers of monomer units, forming branches stemming at each monomer unit [45], Figure 2.18. Redox-dendrimer incorporating TTFs have been reported to be used as catalysts, sensors and in the design of solid-state devices. The electron-transfer processes between dendrimers and other molecules hold high potential in broad areas ranging from bio-engineering to sensing, catalysis as well as energy storage materials [63].

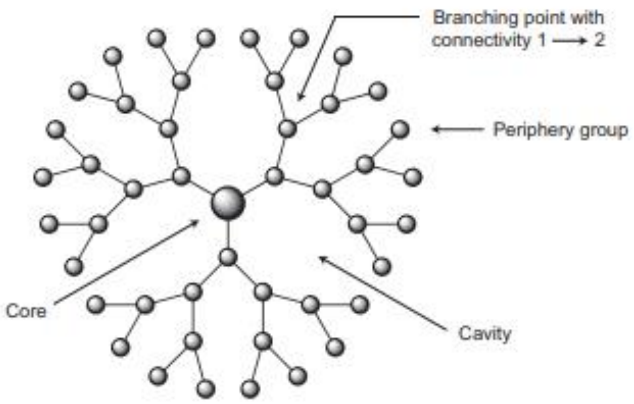


Figure 2.18. General schematic demonstration of a typical dendrimer.

In TTF-based dendrimers, the TTF units may be situated at the core or periphery of the dendrimer. Due to the presence of multiple redox units, TTF based dendrimers exhibit multi-electron transfer properties. Which may be useful in nanoscience applications, such as surface patterning, sensing, nanobatteries and electrocatalysis [63]. *Bryce et al* reported preparation and synthesis of different TTF based dendrimers. The central point of their reporting was the evaluation of the macromolecules' redox properties using a variety of electrochemical techniques [64]. It was found that all the prepared compounds exhibited two redox waves, which is typical of the TTF entity through formation of radical cation and di-cation. Attachment of an ester substituent to the TTF entity resulting in the TTF-CO_2R type derivatives was reported to have raised the two oxidation reactions potentials. The same predicament was observed with the attachment of thioalkyl substituents, demonstrating the increase of the consistent anodic shift values E_1 and E_2 for compounds having the TTF unit composed of four alkylsulfanyl groups [64]. For higher oligomers, increased peak separations at higher scan rates were reported [64]. A general trend for the aryl ester TTF macromolecules, reported by *Bryce* and co-workers, was an increase in the number of TTF units resulted in the broadening of the first redox wave simultaneously with the sharpening of the second wave [64].

Substitution of the TTF system with thio-alkyl chains led to an increase in the oxidation potential and also enhanced their stability to acids, yielding novel macromolecular architectures with beneficial properties [65]. Figure 2.19 illustrates an example of a dendrimer containing 21 thiolated TTF units. It was isolated as an air-stable, orange toffee-like solid and demonstrated good solubility in a range of organic solvents. The close spatial contact between the tetrathiafulvalene units in the dendrimer resulted in the intramolecular interactions of the radical cations generated during electrochemical oxidation, thus broadening oxidation waves in cyclic voltammograms [66].

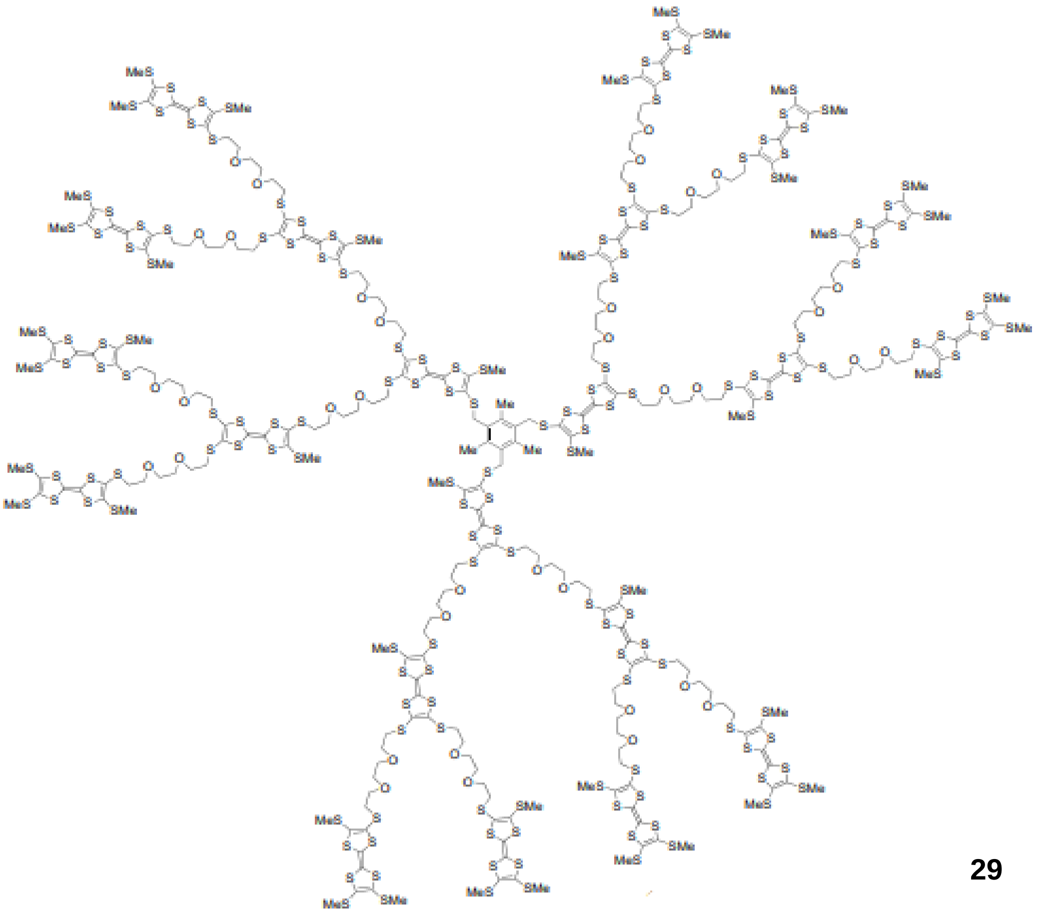


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Figure 2.19. Dendrimer containing 21 TTF units.

Recent examples of incorporation of TTF entities in nanoscience include assembly of donor–acceptor nano-sized materials for photo-induced electron-transfer, and carbon nanotubes (CNTs) decorated with TTF units as electron-donor moieties [67,68]. Such TTF-modified single-walled carbon nanotubes (SWNT) were reported to be prepared through the use of esterification reactions [69]. According to *Martin et al* it was possible to control the rate of electron transfer and charge separation for such nano-assemblies through systematically alteration of the donor–acceptor linkages or integration of different electron donors [69]. Such TTF-modified carbon nanotubes (CNTs) stand a chance to be used as materials for photovoltaic (PV) applications [68].

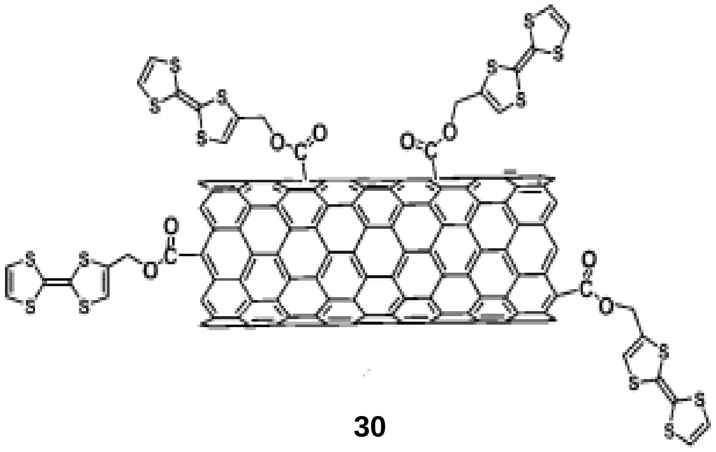

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Figure 2.20. Examples of a covalently linked SWNT/TTF.

Tetrathiafulvalene derivatives have been tested in manufacturing organic field-effect transistors (OFET). Such derivatives can be classified into three categories, namely:

(i) TTF derivatives used for single-crystal OFETs,

(ii) TTF derivatives used for vacuum-deposited thin-film OFETs,

(iii) TTF derivatives used for solution-processed thin-film OFETs.

In the context of this review, the focus will be on TTF-OFETs in general and TTF derivatives for thin-film OFETs [70]. *Bourgoin et al* reported the first OFET constituting of TTF in which Langmuir–Blodgett layers of TTF derivatives served as the active semiconducting channel [71]. The device was reported to be behaving as a p-type transistor in the depletion mode [71]. Furthermore, *Tanaka et al* also reported the successful preparation of OFETs using a certain donor compound, through which its stacked layers with the acceptor tetracyanoquinodimethane (TCNQ) served as the semiconducting channel [72]. A high-mobility OFET with value of 1.4 cm^2/Vs using single crystals of dithiophene-TTF as the active layer was reported, as well as a thin-film transistor using dichloroquinoxalino-pyrazino-TTF with a mobility of about 0.64 cm^2/Vs [70]. Gao and co-workers reported the design and synthesis of new TTF derivatives for high-performance OFETs, such as the single-crystal devices based on TTF derivatives fabricated by simple solution drop-casting method. However, they were reported to have drawbacks, such as the growth of large-area-coverage single crystals of organic materials resulting in crystals that appeared very brittle, which made it difficult to form electrical contact without causing damage.

Therefore, thin-film TTF-based OFETs appeared to be more promising for industrial applications due to the robustness and ease of manufacturing [70]. Vacuum sublimation was used in fabricating TTF-based thin-film OFET devices. *Yamashita et al* is the first group to report DB-TTF-based thin-film OFET devices exhibiting mobility of 0.06 cm^2/Vs [73]. In the instances where FETs exhibited poor performance in terms of low mobility, small on/off ratio, large off-current, and the lack of saturation current, these were reported to may have been a result of high HOMO levels making their thin films labile to oxygen [73,74]. To counteract this effect of poor TTF air stability the following modifications have been undertaken:

(i) introduction of fused aromatic rings,

(ii) further attachment of electron-withdrawing halogen groups to the fused TTF unit [73].

Gao and co-workers reported dinaptho-TTF-based devices constituting of a herringbone-type crystal structure, which showed high mobility of 0.42 cm^2/Vs due to the π-expanded structure benefiting the intermolecular π–π interactions [70]. According to reports by *Gao*, TTF based single-crystal OFETs fabricated by the drop-casting method showed high performance with mobility of up to 1.4 cm^2/Vs [70]. Vacuum deposited TTF-based thin films OFETs were well prepared, with some of them even demonstrating high performance in comparison to that of amorphous silicon, as well as good air-stability.

CHAPTER 3: Experimental Methodology

3.1. Introduction

This chapter comprises the characterisation and purification procedures, as well as techniques employed during the synthesis of tetrathiafulvalene intermediates and derivatives. The relevancy of these specific synthetic approaches shall be further elaborated in the results and discussion chapter.

3.2. Instruments and techniques

3.2.1. Melting point apparatus

Determination of solid samples' melting points was carried out through the use and aid of a Stuart Melting Point 3 (SMP3) apparatus in sealed capillary tubes, wherein the sample was viewed through a magnifying lens. This specialized scientific instrument was designed for precise use in measuring the temperature at which transformation of a sample from a solid state to a liquid state occur. Its operating principle lies in the cautious heating of a pure compound, wherein it changes from a solid to liquid state over a narrow controlled temperature range, and the transition temperature is then recorded as the melting point of that compound.

The analysis commenced with sample preparation, wherein a relatively small amount of the solid sample (crystalline or fine powder) was placed in a small capillary tube. The capillary tube was then inserted, and heat applied as the apparatus constitutes of a heating element (electrical coil), with controllable heating rate permitting accurate melting point determination. Since the apparatus constitutes of a magnifying lens, the transition of the sample in the tube was visually observed throughout, such as a change in the physical appearance either from solid to liquid phase, or a change in colour, or disappearance of crystalline structure. Subsequently, the narrow temperature range at which the sample compound completely transformed was noted as the substance's melting point. Lastly, the apparatus was left to cool down, and capillary tube removed, disposed or cleaned for next analysis.

3.2.2. Thin layer chromatography

TLC (thin layer chromatography) plates from Merck were composed of silica gel embedded on a thin layer of aluminium, with parameters 60 F254, 20 x 20 cm, layer thickness 0.2 mm were cut into approximately 2.5 x 5 cm stripes. The plotted spots and bands were observed under ultraviolet (UV) light of wavelength 254 nm. TLC analysis of most of the intermediates was carried-out using dichloromethane/hexane as an eluent at varying solvent ratios.

Furthermore, retention factor (R_f) values associated with TLC analysis were determined through careful visual analysis and observation of the TLC plates under ultraviolet light of wavelength 254 nm. The used UV light permitted clear visibility of the spots which appeared as darker spots under the light due to the stationary TLC phase constituting of a substance that fluoresces with exposure to ultraviolet light [75].

The silica gel served as the stationary phase, consisting of material that fluoresces under ultraviolet light, and the solvent system as the mobile phase. To give an overview of the analysis, upon having carefully cut plates of certain margins, a pencil line was drawn close to the bottom of the plate. Plots or small drops of a solution with the compound to be analysed were placed on the plate where the line is, using capillary spotters. Upon drying of the spotted mixture of intermediates or compounds, the TLC plate was stood upright in a layer of the appropriate solvent in a covered beaker, ensuring that solvent quantity is below the line with spots [76]. The solvent was visually observed traveling up the plate, wherein the spotted components travelled along at different rates and in that way the mixture was separated into different coloured spots according to varying polarity [76]. Figure 3,1, serves as a schematic overview of the thin layer chromatography analysis as briefly explained [75].

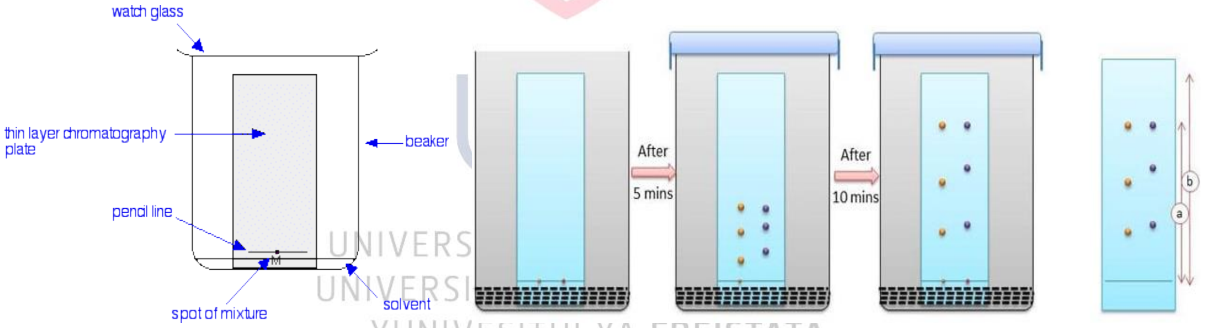


Figure 3.1. Thin layer chromatography analysis schematic illustration.

The retention factor (R_f) was then determined for each of the compounds using the formula:

$$R_f = \frac{distance\ travelled\ by\ compound}{distance\ travelled\ by\ solvent}$$

3.2.3. Column chromatography

The purification principle of column chromatography is similar to that of thin layer chromatography, such that it constitutes of silica as the stationary phase resulting in the adsorption and separation of compounds dissolved in the liquid mobile phase (eluent) [77]. The separation is based on the compound's chemical properties, such that they get adsorbed and eluted based on differential adsorption by the silica as an effect of polarity and forces amongst other factors. Figure 3.2 shows a schematic representation of column chromatography [78].

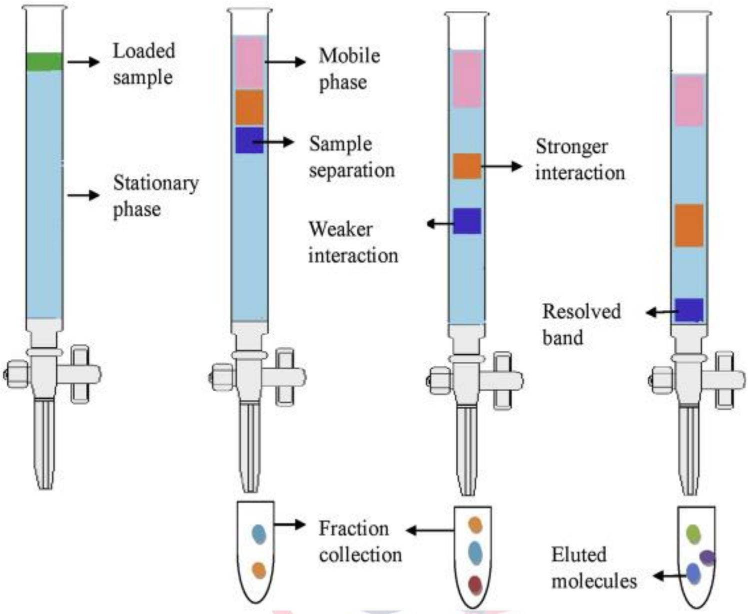


Figure 3.2. Column chromatography schematic representation.

Column chromatography was carried out using silica gel 60 (0.063-0.2 mm). The samples/ compounds to be purified or separated were introduced at the top of the column packed with silica and appropriate eluent. The compounds were allowed to move with the eluent, separating based on different polarities as they move through the column at different rates resulting in their separation. and desorbed with the appropriate solvent polarity. Wherein, the compound(s) partition themselves between the mobile and stationary phase based on their relative solubilities and interactions. Such that, those with higher affinity for the stationary phase interact with the phase resulting in them moving through the column slowly. Meanwhile those with lower affinity move through the column faster as they do not have prolonged interaction with the stationary phase. Upon separation of the components, the appropriate pure compound was then collected in fractions and concentrated on a rotary evaporator under low pressure and temperature of approximately 40°C.

3.2.4. Nuclear Magnetic Resonance (NMR) spectroscopy

Simple proton (^{1}H) NMR was used to confirm the availability and purity of the respective compounds, followed by carbon (^{13}C) NMR [79]. The analysis was carried-out on a Bruker NMR spectrometers at 300 MH, and 400 MHz for ^{1}H and at 75 MHz / 100 MHz for ^{13}C, respectively, operating at a 25°C with deuterated chloroform ($CDCl_3$) as the solvent. Tetramethylsilane (TMS) was used as an internal standard. Spectral analysis of the results constituted of the proton and carbon chemical shifts expressed in parts per million (ppm), with the residual signal/peak of deuterated chloroform at chemical shifts: δ = 7.26 ppm for ^1H NMR and 77.16 ppm for ^{13}C NMR, respectively, the internal standard TMS peak was set at δ = 0 ppm. A water signal was observed at chemical shift δ = 1.56 ppm in the proton spectra. Coupling constants (J) for multiplets peaks were reported in Hz, and the abbreviations s, d t, q as well as m represent singlet, doublet, triplet, and multiplet, respectively. Some trace impurities were observed at about δH 1.27 ppm, belonging to the long chain alkane derivatives (grease).

3.2.5. Mass spectroscopy (MS)

Mass spectrometry measurements were carried out using Waters MICROMASS® Q-Tof micro™ and ThermoFisher Orbitrap Exploris 480 mass-spectrometers in the ESI-(+) mode. Only previously unreported final products were characterized using HR-MS [80].

3.2.6 Cyclic voltammetry (CV)

The cyclic voltammetry was performed using computer-controlled BAS model 100 B/G potentiostat. The workstation was interfaced with the usual three-electrode cell setup consisting of the reference, working, and auxiliary electrodes [81]. The reference electrode was constructed from a silver wire (Ag/AgCl) inserted into a MeCN solution of 0.01 M silver nitrate. The BAS glassy carbon working electrode with surface area 7 mm^2 was pre-treated by polishing on a Buehler microcloth first with 1 μm and then 1/4 μm diamond paste. The auxiliary electrode consisted of a platinum wire. All the measurements were obtained using spectrochemical grade DCM with the presence of $[n\text{-}Bu_4N]\,[(PF_6)_4]$ *ca*. 0.1 M electrolyte solution. The system was purged with nitrogen before proceeding with any measurement. The concentrations of the analytes were *ca*. 1 mM. Ferrocene was used as the internal reference substance.

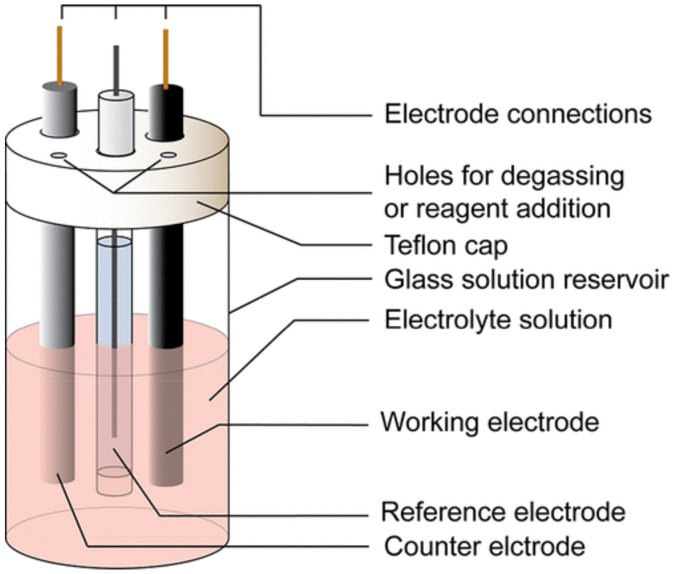


Figure 3.3. Schematic illustration of a 3-electrode electrochemical cell for cyclic voltammetry measurements.

3.2.6. Other purification techniques

Amongst other used techniques was suction filtration, for the separation of a solid component of a sample from a liquid component as suction or vacuum is applied. Extraction is another technique that has been extensively used during the study, also referred to as solvent or liquid-liquid extraction as it has both an aqueous and organic phase. Inorganic substances are dissolved in the aqueous phase, whereas organic substances or product are dissolved in the organic phase comprised of an organic solvent. The difference in densities is what results in two separate phases. The collected organic phases were put together and dried over a drying agent like anhydrous $MgSO_4$ or Na_2SO_4 to remove residual water prior to concentrating using a rotary evaporator. Another liquid separation method for a mixture of liquid components used was distillation. Essentially for purification, to ensure a certain standard of purity in the solvents for reaction syntheses. Its operating principle was a subject of differences in the boiling points of each species or component, such that the two liquid components were separated by raising the temperature to a point where one of the liquids would boil while the other remained a liquid. Resulting in the collection of the boiled liquid through condensing the resulting vapour.

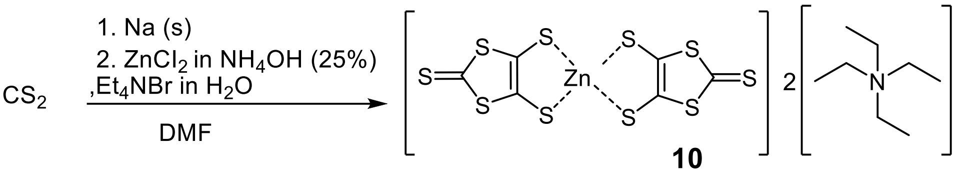
The concept of distillation is similar to concentration by rotary evaporator, whereby solvents were rapidly removed at reduced pressures. With the rotary evaporator, the distillation flask was rotated to increase the rate at which the solvent evaporates by spreading the contents around the flask’s walls. It has a vapour duct allowing the solvent vapour from the flask to run through a vacuum seal onto the spiral condenser, condensing the solvent into a separate receiving flask, resulting in the separation and concentration of a solvent-free compound and pure solvent collected in a separate flask. Recrystallization was also used constantly, as one of the most efficient methods for purifying solids embodying impurities. With the most crucial part being an appropriate solvent in which the impurities will be soluble, one that dissolve the compound of interest along with its impurities when it is hot. As it cools down, the impurities remain soluble in contrast to the compound of interest precipitating. After successfully dissolving the compound, cooling was done by leaving the flask to cool to room temperature and submerging the flask into an ice bath for roughly 10 minutes. The resultant crystals were then filtered and washed with the cold solvent.

3.2.7. Materials, Reagents and Solvents

The majority of the chemicals used in this project were of reagent grade and used as purchased from Merck and Sigma-Aldrich. Most of the reactions were carried out under inert gas using dry solvents. TTF intermediates and derivatives were prepared using the published procedures, with significant adjustments. Other chemical suppliers include Glassworld, CC Imelmann, or Promark Chemicals. Solvents were also purified through distillation, and reagents for dry reactions were stored in the vacuum gloves-box.

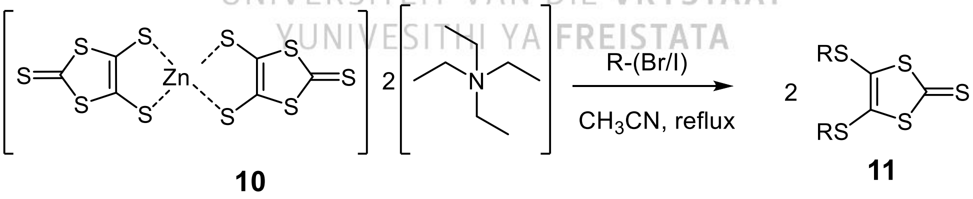
3.3. Experimental procedures

3.3.1. The synthesis of bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiol)zincate (Et4N)2[Zn(DMIT)2], 10 [30].



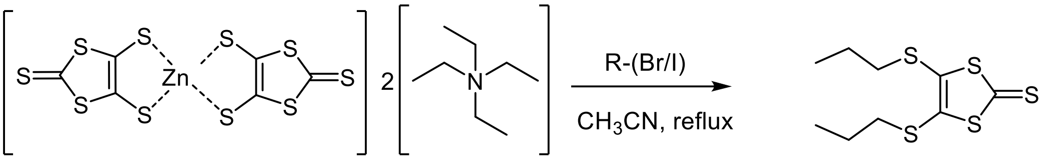
Dry DMF (48 mL) was degassed by bubbling argon for about 20 minutes, and carbon disulphide (24 mL, 0.399 mol, 30.4 g.) was added meanwhile the reaction mixture was kept under argon with cooling to 0℃. Sodium metal (1.45 g, 0.0631 mol, 4 eq.) was weighed in finely cut pieces under hexane and added gradually into the reaction mixture while continuously stirring at approximately 0℃. The resulting intense blood red mixture was then allowed to stir overnight. A solution of zinc chloride (2.13 g, 0.0156 mol, 2 eq.) in concentrated NH_4OH (46 mL) was slowly added while destroying small residues of unreacted sodium, and after 15 min, a solution of tetraethylammonium bromide (6.62 g, 0.0205 mol, 2 eq.) in H_2O (50 mL) was added. The reaction mixture was then again allowed to stir overnight, with the resultant precipitate collected by suction filtration upon that, and washed with isopropanol and ether (1:1), affording bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiol) zincate salt $(Et_4N)_2[Zn(DMIT)_2]$ **10** (8.76 g, 0.01219 mol, 76%) in the form of a pure red powder with a melting point of 205–209℃.

3.3.2. The synthesis of 1,3-dithiole-2-thiones, general procedure, 11 [82].



The zincate salt $(Et_4N)_2[Zn(DMIT)_2]$ (~1 eq.) and alkyl halide (~5 eq.) were suspended in acetonitrile and refluxed. The mixture was then cooled to room temperature and solvent was removed to dryness. If non-volatile alkyl bromides where used, the residue was left under high vacuum to remove the unreacted alkyl bromide. The residue was dissolved in DCM, precipitate was filtered off through celite and filtrate was concentrated to approximately 30 mL and treated with activated charcoal overnight. The solution was filtered once more through a plug of silica and concentrated under vacuum using a rotary evaporator.

3.3.2.1. The synthesis of 4,5-bis(proplythio)-1,3-dithiole-2-thione. (R = Propyl).



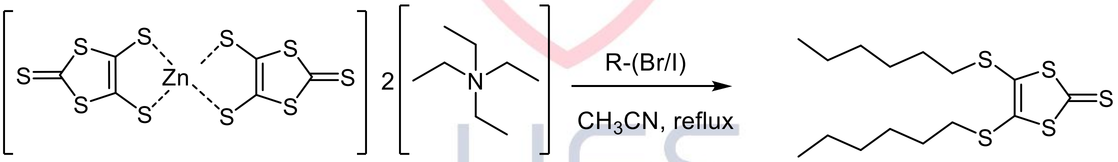
10 R = Propyl **11a**

$(Et_4N)_2[Zn(DMIT)_2]$ (4.02 g, 5.60 mmol, 1 eq.) was suspended in CH_3CN (45 mL) along with bromo-propane (2.92 mL, 3.95 g, 0.03208 mol, 6 eq.) and the reaction mixture was refluxed for 3 hours. Purification was carried out by means of filtration through silica, and concentration under vacuum, resulting in a dark green plus yellow oil of 4,5-bis(proplythio)-1,3-dithiole-2-thione **11a** (3.76 g, 0.01333 mol, 83 %). R_f (DCM) = 0.7.

^{1}H NMR (δ) (300. MHz, chloroform-d): 2.90 (t, *J* = 7.6 Hz, 4H, -SCH_2-), 1.77-1.68 (m, 4H, -CH_2-), 1.08 (t, *J* = 7.3 Hz, 6H, -CH_3);

^{13}C NMR (δ) (75 MHz, Chloroform-d): 136.4, 77.1, 38.7, 23.1, 13.1.

3.3.2.2. The synthesis of 4,5-bis(hexlythio)-1,3-dithiole-2-thione. (R= Hexyl).

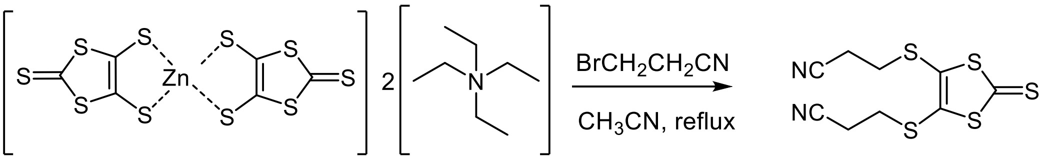


10 R = Hexyl **11b**

$(Et_4N)_2[Zn(DMIT)_2]$ (11.6 g, 15.8 mmol, 1 eq.) was suspended in CH_3CN (45 mL) along with hexyl bromide (11.14 mL, 13.1 g, 79.4 mmol, 5 eq.) and the reaction mixture was refluxed for 3 hours. Purification was carried out by means of filtration through silica, and concentration under vacuum resulted in a dark yellow oil of 4,5-bis(hexlythio)-1,3-dithiole-2-thione **11b** (9.05 g, 24.7 mmol, 78 %). R_f (DCM) = 0.81.

^{1}HNMR (δ) (300 MHz, Chloroform-d): 2.88 (t, *J* = 7.0 Hz, 4H, -SCH_2-), 1.67 (p, *J* = 8.2 Hz, 4H, -CH_2-), 1.49-1.38 (m, 4H, -CH_2-), 1.34-1.27 (m, 8H, -CH_2-), 0.91 (t, *J* =7.0 Hz, 6H, -CH_3).

3.3.3. The synthesis of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-thione, 12 [24].



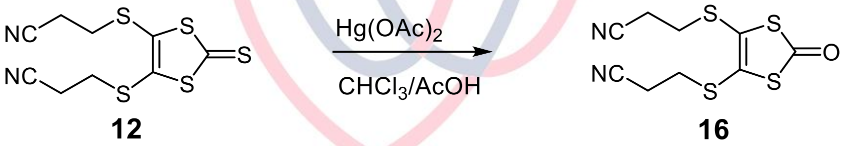
10 **12**

To a solution of $(Et_4N)_2[Zn(DMIT)_2]$ (7.413 g, 0.01032 mol, 1 eq.) suspended in CH_3CN (130 mL) was added 3-bromopropionitrile (4.3 mL, 6.95 g, 0.05184 mol, 5 eq.) and the reaction mixture was refluxed for 1 hour. The resulting solution was cooled to room temperature, and concentrated using rotary evaporator. The resultant brown-yellow solution was re-dissolved in dichloromethane (130 mL), and washed with water (4x 100 mL), dried using $MgSO_4$ as drying agent. The solvent was then removed in vacuo. Purification was carried-out through recrystallization of the product from toluene (bp 110.6℃) resulting in long, well-defined yellow, needle-like crystals of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-thione **12** (4.74 g, 0.01577 mol, 77%). Mp 86 ℃; R_f (DCM) = 0.82.

^{1}HNMR (δ) (400 MHz, Chloroform-d): 3.19 (t, *J* = 6.9 Hz, 4H, $-CH_2-$), 2.83 (t, *J* = 6.9 Hz, 4H, $-SCH_2-$);

^{13}C NMR (δ) (100 MHz, Chloroform-d): 209.1, 135.8, 117.1, 31.8, 19.1.

3.3.4. The synthesis of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-one, 16 [13,83].



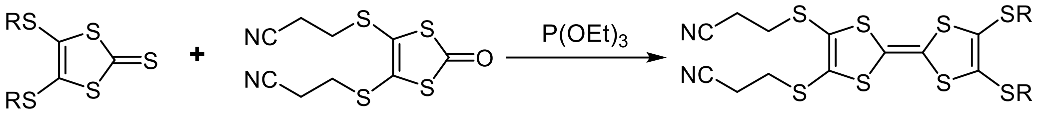
Under anaerobic conditions, a mixture of 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione **12** (4.55 g, 0.01515 mol) and mercuric acetate (18.87 g, 0.03634 mol) in a solution made up of chloroform and acetic acid (3:1) (150 mL), was stirred overnight under nitrogen. The resulting solution constituting of a whitish precipitate was filtered through celite, and washed with a fraction of water and $NaHCO_3$ solution. Upon washing, the organic phase was dried with $MgSO_4$ for about 20 minutes, and thereafter, the solvent was evaporated, resulting in light orange ore-like crystals of4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16** (4.406 g, 0.01528 mol, 99%). Mp 86 ℃; R_f (DCM) = 0.82.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.16 (t, *J* = 6.9 Hz, 4H, $-CH_2-$), 2.82 (t, *J* = 6.9 Hz, 4H, $-SCH_2-$);

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 187.7, 127.4, 117.3, 31.7, 19.0.

3.3.5 Cross coupling of intermediates

3.3.5.1 The synthesis of 2,3-bis(cyanoethylthio)-6,7-bis(propylthio)tetrathiafulvalene 17 [13,32,84].



11 **16** **17**

11a : R = Propyl
11b : R = Hexyl

17a : R = Propyl
17b : R = Hexyl

4,5-bis(2’-cyanoethylthio)-1,3-dithiole-2-one **16** (2.063 g, 7.15 mmol) and 4,5-bis(proplythio)-1,3-dithiole-2-thione **11a** (2.045 g, 6.81 mmol) were suspended in freshly distilled triethyl phosphite [$P(OEt)_3$] (21 mL) under nitrogen and heated with stirring at ~110℃. A dark orange precipitate started to from after 10 minutes, and stirring was continued for about 90 minutes. Thereafter, the mixture was allowed to cool to room temperature, and precipitate filtered. The resulting precipitate was dissolved and washed with methanol (3 x 30 mL) and dried using rotary evaporator. The solid was dissolved in DCM (dichloromethane) and purified by column chromatography constituting of silica gel with DCM and hexane (6:4) as elution solvent system. Isolation and elution of the middle fraction resulted in the cross-coupled product, which was dried in vacuo whilst evaporating the elution solvent, thus resulting in the pure product, in the form of an orange powder, of 2,3-bis(cyanoethylthio)-6,7-bis(propylthio)tetrathiafulvalene **17a** (2.25 g, 4.30 mmol, 60%). Mp ~119 ℃; R_f (DCM: Hexane, 6:4) = 0.5.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.11 (t, *J* = 7.1 Hz, 4H, NC-CH_2-), 2.84 (t, *J* = 7.2 Hz, 4H, -SCH_2-), 2.77 (t, *J* = 7.1 Hz, 4H, -SCH_2-), 1.76 – 1.64 (m, 4H, -CH_2-), 1.05 (t, *J* = 7.3 Hz, 6H, -CH_3).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 141.9, 129.5, 118.5, 38.3, 31.3, 23.1, 18.9, 13.2.

3.3.5.2 The synthesis of 2,3-bis(cyanoethylthio)-6,7-bis(hexyllthio)tetrathiafulvalene, 17b.

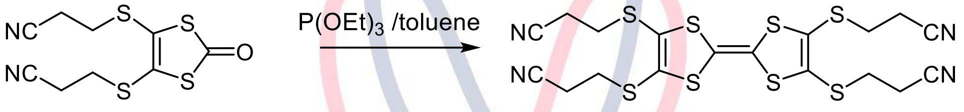
4,5-bis(2’-cyanoethylthio)-1,3-dithiole-2-one **16** (R = hexyl) (2.063 g, 7.15 mmol) and 4,5-bis(hexylthio)-1,3-dithiole-2-thione **11b** (2.045 g, 5.58 mmol) were suspended in freshly distilled triethyl phosphite [$P(OEt)_3$] (21 mL) under nitrogen and heated with stirring at ~120℃. A dark orange precipitate started to from after 10 minutes, and stirring was continued for about 90 minutes. Thereafter, the mixture was allowed to cool to room temperature, and precipitate was filtered. The resulting precipitate was dissolved and washed with methanol (3 x 30 mL) and dried using rotary evaporator. The solid was dissolved in DCM and purified by column chromatography constituting of silica gel with DCM and hexane (7:3) as elution solvent system. Isolation and elution of the appropriate fraction, which was dried in vacuo resulted in the pure product, in the form of a rich-orange powder, of 2,3-bis(cyanoethylthio)-6,7-bis(hexylthio)tetrathiafulvalene **17b** (2.03 g, 3.34 mmol, 46%). Mp ~119 ℃; R_f (DCM: Hexane, 7:3) = 0.63

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.11 (t, *J* = 7.1 Hz, 4H, NC-CH_2-), 2.85 (t, *J* = 7.1, 4H, -SCH_2-), 2.77 (t, *J* = 7.1 Hz, 4H, -SCH_2-), 1.72 – 1.60 (m, 4H, -CH_2-), 1.50 – 1.40 (m, 4H, -CH_2-), 1.38 – 1.21 (m, 8H, -CH_2-CH_2-), 0.92 (t, *J* = 3.8, 6H, -CH_3).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 128.1, 127.9, 117.4, 114.8, 36.4, 31.3, 30.9, 29.7, 28.2, 22.6, 18.9, 14.1.

3.3.6 Self coupling of intermediates

3.3.6.1 The synthesis of 2,3,6,7-Tetrakis(2’-cyanoethylthio)tetrathiafulvalene, 18 [13].



16 **18**

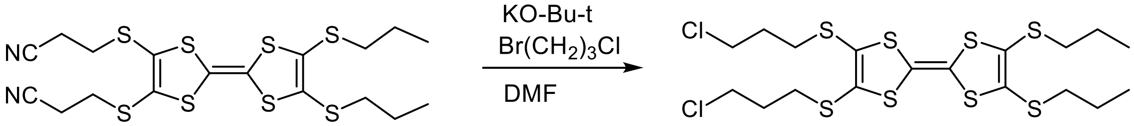
4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16** (1.00 g, 3.47 mmol) was suspended in toluene (34.61 mL) and refluxed with stirring, as freshly distilled triethyl phosphite [$P(OEt)_3$] (3.46 mL) was added along. After approximately 15 minutes, a dark red-orange precipitate started to form, and the red solution was allowed to stir in reflux for an extra 30 minutes. Upon that, the precipitate containing solution was allowed to cool to room temperature, and the solution was filtered by suction filtration, resulting in pure compound **18** as intense red-orange well-defined crystals; (0.52 g, 0.99 mmol, 55%). Mp ~212-214 ℃; R_f (DCM: Hexane, 6:4) = 0.91.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.13 (t, *J* = 7.0 Hz, 8H, NC-CH_2-), 2.78 (t, *J* = 7.0 Hz, 8H, -SCH_2-).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 187.7, 127.4, 117.3, 31.7, 19.1.

3.3.7. Deprotection and realkylation of TTF derivatives/ intermediates

3.3.7.1 The synthesis of 4,5-bis(3’-chloropropylthio)-6,7-bis(propylthio)-tetrathiafulvalene, 20a [31,32].



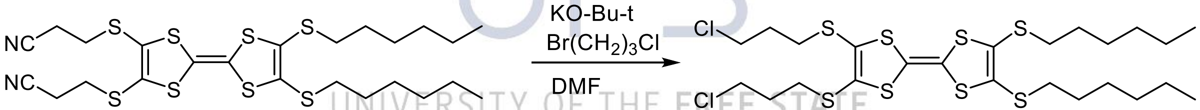
17a **20a**

To a solution of **17a** (1 g, 1.92 mmol) in anhydrous degassed DMF (33 mL) was quickly added in excess of potassium *tert*-butoxide (0.8 g, 7.13 mmol) in one portion. Upon starring for roughly 20 minutes in an ice bath under inert atmosphere, 1-bromo-3-chloropropane (0.90 mL, 1.43 g, 9.10 mmol) was added quickly in one portion. The reaction mixture was then stirred at room temperature for 1 hour, upon that the solvent was removed in vacuo using a rotary evaporator. The resultant dark brown residue was re-dissolved in DCM (~25 mL) and filtered through a plug of celite. Extraction / washing was then done using brine (3 x 25 mL), and organic phase was dried over $MgSO_4$. The compound dissolved in DCM was concentrated by evaporating the solvent in vacuo. Thereafter, the resulting compound was purified by column chromatography on silica gel with DCM and hexane in the ratio 6:4 as the solvent system, giving the product 4,5-bis(3’-chloropropylthio)-6,7-bis(propylthio)tetrathiafulvalene **20a** as brown sticky syrup (0.50 g, 0.88 mmol, 49%). R_f (DCM: Hexane, 6:4) = 0.63.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.71 (t, *J* = 6.2 Hz, 4H, Cl-CH$_2$-), 3.01 (t, *J* = 6.9 Hz, 4H, -SCH$_2$-), 2.82 (t, *J* = 7.6, 6.9 Hz, 4H, -SCH$_2$-), 2.17 – 2.06 (m, 4H, -CH$_2$-), 1.76 – 1.63 (m, 4H, -CH$_2$-), 1.04 (t, *J* = 7.3 Hz, 6H, -CH$_3$).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 144.5, 128.0, 42.9, 38.3, 33.2, 32.1, 23.2, 13.2.

3.3.7.2 The synthesis of 4,5-bis(3’-chloropropylthio)-6,7-bis(hexylthio)tetrathiafulvalene, 20b [31,32].



17b **20b**

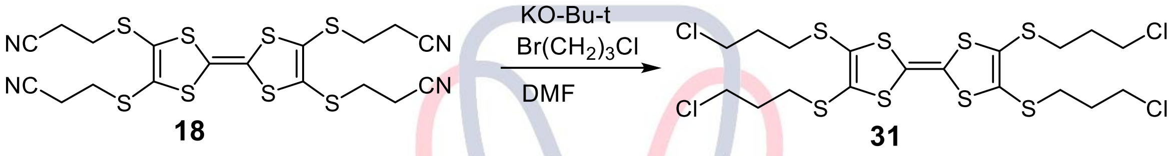
To a solution of **17b** (0.9 g, 1.48 mmol) in anhydrous degassed DMF (30 mL) was quickly added in slight excess potassium tert-butoxide (0.72 g, 6.42 mmol) in one portion. Upon stirring for roughly 20 minutes in an ice bath under inert atmosphere, 1-bromo-3-chloropropane (0.81 mL, 1.29 g, 8.19 mmol) was added quickly in one portion. The reaction mixture was then stirred at room temperature for 1 hour, upon that the solvent was removed in vacuo using a rotary evaporator. The resultant dark brown residue was re-dissolved in DCM (~25 mL) and filtered through a plug of celite. Extraction / washing was then done using brine water (3x 25 mL), and organic phase was dried over $MgSO_4$. The compound dissolved in DCM was concentrated by evaporating the solvent in vacuo. Thereafter, the resulting compound was purified by column chromatography on silica gel with DCM and hexane in the ratio 6:4 as the solvent system, giving the product 4,5-bis(3’-chloropropylthio)-6,7-

bis(hexylthio)tetrathiafulvalene **20b** as brown sticky syrup; (0.62 g, 0.95 mmol, 59%). R_f (DCM: Hexane, 6:4) = 0.73.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.70 (t, *J* = 6.2 Hz, 4H, Cl-CH$_2$-), 3.01 (t, *J* = 6.9 Hz, 4H, -SCH$_2$-), 2.84 (t, *J* = 6.8 Hz, 4H, -SCH$_2$-), 2.20 – 1.99 (m, 4H, -CH$_2$-), 1.73 – 1.59 (m, 4H, -CH2-), 1.49 – 1.21 (m, 12H, -CH$_2$-CH$_2$-CH$_2$-), 0.92 (t, *J* = 6.7 Hz, 6H,-CH$_3$).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 128.0, 127.8, 36.7, 36.3, 32.8, 31.3, 29.7, 28.2, 22.6, 14.1

3.3.7.3 The synthesis of 2,3,6,7-Tetrakis(3-Chloropropylthio)tetrathiafulvalene, 31 [31,32].



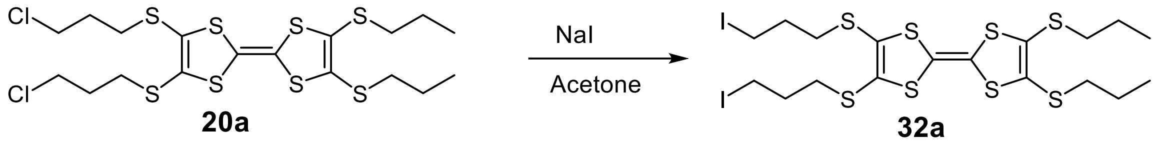
To a solution of **18** (0.18 g, 0.33 mmol) in anhydrous degassed DMF (7.46 mL) was quickly added in slight excess potassium tert-butoxide (0.19 g, 1.69 mmol) in one portion. Upon starring for roughly 20 minutes in an ice bath under inert atmosphere, 1-bromo-3-chloropropane (0.8 mL, 1.27 g, 8.09 mmol) was added quickly in one portion. The reaction mixture was then stirred at room temperature for 1 hour, upon that the solvent was removed in vacuo using a rotary evaporator. The resultant dark brown residue was re-dissolved in DCM (~25 mL) and filtered through a plug of celite. Extraction / washing was then done using brine water (3x 25 mL), and organic phase was dried over MgSO$_4$. The compound dissolved in DCM was concentrated by evaporating the solvent in vacuo. Thereafter, the resulting compound was purified by column chromatography on silica gel with DCM and hexane in the ratio 6:4 as the solvent system, giving the product 2,3,6,7-tetrakis(3-chloropropylthio)tetrathiafulvalene **31** as brown sticky syrup (0.12 g, 0.19 mmol, 65%). R_f (DCM: Hexane, 6:4) = 0.77.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.73 (t, *J* = 6.1 Hz, 8H, Cl-CH$_2$-), 3.59 (t, *J* = 6.2 Hz, 8H, -SCH$_2$-), 2.38 – 2.25 (m, 8H, -CH$_2$-).

^{13}C NMR (δ) (150.95 MHz, Chloroform-*d*) 128.0, 110.5, 42.9, 33.2, 32.1.

3.3.8 Halogen substitution

3.3.8.1. The synthesis of 4,5-bis(3’-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene, 32a [31,32].



4,5-bis(3’-chloropropylthio)-6,7-bis(propylthio)tetrathiafulvalene **20a** (0.078 g, 0.14 mmol) and sodium iodide (0.37 g, 2.45 mmol) were dissolved in degassed anhydrous acetone (3 mL) and refluxed at ~60°C for 4 days. The solvent was left to evaporate as the reaction mixture was cooled down, and the residue was redissolved in DCM (25 mL). Water (25 mL) was then used to wash the residue, followed by subsequent drying over $MgSO_4$, and concentration in vacuo. The resulting brown oil was purified by column chromatography on silica gel with DCM and hexane (6:4) as the solvent system, resulting in 4,5-bis(3’-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene **32a** as brown oil; (0.09 g, 0.19 mmol, 88%). R_f (DCM: Hexane, 6:4) = 0.57.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.34 (t, *J* = 6.7 Hz, 4H, I-CH_2-), 2.95 (t, *J* = 6.8 Hz, 4H, SCH_2-), 2.82 (t, *J*= 6.7, 4H, -SCH_2-), 2.25 – 2.05 (m, 4H, -CH_2-), 1.76 – 1.60 (m, 4H, -CH_2-), 1.04 (t, *J* = 7.3 Hz, 6H, -CH_3).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 128.0, 127.8, 111.9, 108.8, 38.3, 36.7, 32.8, 23.2, 13.2.

3.3.8.2. The synthesis of 4,5-bis(3’-iodopropylthio)-6,7-bis(hexylthio)tetrathiafulvalene, 32b [31,32].

4,5-bis(3’-chloropropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **20b** (0.05 g, 0.077 mmol) and sodium iodide (0.47 g, 3.14 mmol) were dissolved in degassed anhydrous acetone (2.45 mL) and refluxed at ~60°C for 4 days. The solvent was left to evaporate as the reaction mixture was cooled down, and the residue was redissolved in DCM (25 mL). Water (25 mL) was then used to wash the residue, followed by subsequent drying over $MgSO_4$, and concentration in vacuo. The resulting brown oil was purified by column chromatography on silica gel with DCM (CH_2Cl_2) and hexane (6:4) as the solvent system, resulting in 4,5-bis(3’-iodopropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **32b** as brown oil; (0.1 g, 0.12 mmol, 76%). R_f (DCM: Hexane, 6:4) = 0.75.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.70 (t, *J* = 10.0, 6.2 Hz, 4H, $-I-CH_2-$), 3.01 (t, *J* = 6.9 Hz, 4H, $-SCH_2-$), 2.84 (t, *J* = 6.8 Hz, 4H, $-SCH_2-$), 2.17 – 2.03 (m, 4H, $-CH_2-$), 1.71 – 1.61 (m, 4H, $-CH_2-$), 1.49 – 1.23 (m, 6H, $-CH_2-CH_2-CH_2-$), 0.92 (t, *J* = 6.7 Hz, 6H, $-CH_3$).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 128.0, 127.8, 36.7, 36.3, 32.8, 31.3, 29.7, 28.2, 22.6, 14.1.

3.3.8.3 The synthesis of 2,3,6,7-Tetrakis(3-Iodopropylthio)tetrathiafulvalene, 33 [31,32].

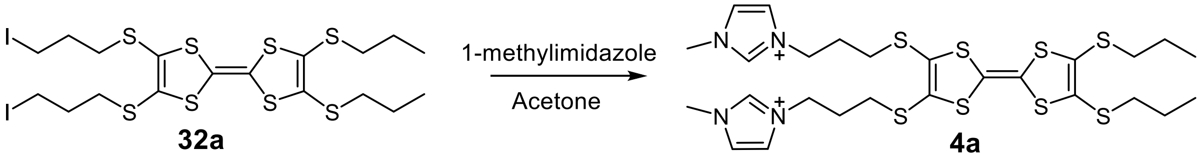
2,3,6,7-Tetrakis(3-chloropropylthio)tetrathiafulvalene **31** (0.1 g**,** 0.16 mmol) and sodium iodide (NaI) (0.95 g, 6.3 mmol) were dissolved in degassed anhydrous acetone (4.926 mL) and refluxed at ~60°C for 4 days. The solvent was left to evaporate as the reaction mixture was cooled down, and the residue was redissolved in DCM (25 mL). Water (25 mL) was then used to wash the residue, followed by subsequent drying over $MgSO_4$, and concentration in vacuo. The resulting brown oil was purified by column chromatography on silica gel with DCM (CH_2Cl_2) and hexane (6:4) as the solvent system, resulting in 2,3,6,7-tetrakis(3-iodopropylthio)tetrathiafulvalene **33** as a brown oil; (0.15 g, 0.15 mmol, 90%). R_f (DCM: Hexane, 6:4) = 0.75.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 3.71 (t, *J* = 6.2 Hz, 8H, $I-CH_2-$), 3.01 (t, *J* = 6.8 Hz, 8H, $-SCH_2-$), 2.17 – 2.02 (m, 8H, $-CH_2-$).

^{13}C NMR (δ) (100 MHz, Chloroform-*d*) 128.0, 110.5, 42.9, 33.2, 32.1.

3.3.9 Functionalisation by 1-methyl-imidazole

3.3.9.1 The synthesis of 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene, 4a.

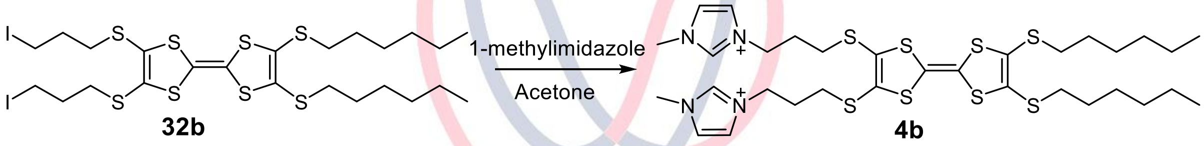


To a solution of 1-methyl-imidazole (0.45 mL, 0.47 g, 5.68 mmol) in anhydrous degassed acetone (5 mL) was added 4,5-bis(3’-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene **32a** (0.0937 g, 0.13 mmol). The reaction was then left to stir overnight under nitrogen at room temperature. Upon evaporation of the solvent, the brown residue was recrystallized from DCM and stored in a desiccator connected to a pump for further drying and removal of residual solvents, giving rise to 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene **4a** as brown slow crystallizing oil (0.39 g, 0.59 mmol, 94%). R_f (DCM: EtOAc, 8:2) = 0.47.

^{1}H NMR (δ) (400 MHz, Chloroform-*d*): 7.58 (s, 2H, N-CH-N), 7.09 (s, 2H, N-CH), 6.91 (s, 2H, N-CH), 4.73 (t, *J* = 7.2 Hz, 4H, N-CH_2-), 4.03 (s, 6H, N-CH_3), 3.02 (t, *J* = 6.7 Hz, 4H, -CH_2-), 2.84 (t, *J* = 7.3 Hz, 4H, -CH_2-), 2.31 – 2.39 (m, 4H, -CH_2-), 1.60 – 1.75 (m, 4H, -CH_2-), 1.04 (t, *J* = 7.3 Hz, 6H, -CH_3-).

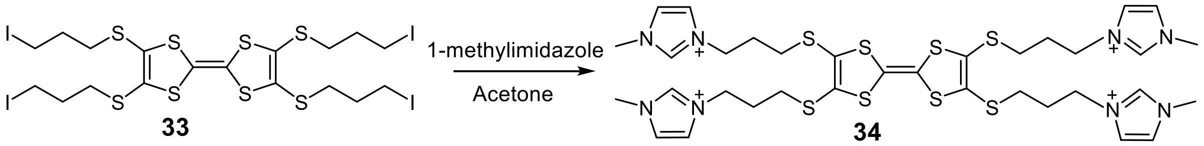
FT-MS (ESI): *m/z* = 335.0424 (M+); calcd for $C_{26}H_{38}N_4S_8^{2+}$, 331.0431 (M+).

3.3.9.2 The synthesis of 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(hexylthio)tetrathiafulvalene, 4b.



To a solution of 1-methyl-imidazole (2 mL, 2.06 g, 0.012 mol) in anhydrous degassed acetone (14 mL) was added 4,5-bis(3’-iodopropylthio)-6,7-bis(hexyllthio)tetrathiafulvalene **32b** (0.05 g, 0.060 mmol). The reaction was then left to stir overnight under nitrogen at room temperature. Upon evaporation of the solvent, the residue in the form of brown oil was stored in a desiccator connected to a pump for further drying and removal of solvent residues, giving rise to 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(hexyllthio)tetrathiafulvalene **4b** as brown oil (0.062 g, 0.083 mmol, 70%). R_f (DCM: EtOAc, 8:2) = 0.48.

3.3.9.3. The synthesis of 2,3,6,7-Tetrakis[3-(1-methylimidazole)propylthio]tetrathiafulvalene, 34.



To a solution of 1-methyl-imidazole (0.13 mL, 0.13 g, 1.58 mmol) in anhydrous degassed acetone (10 mL) was added 2,3,6,7-tetrakis[3-iodopropylthio]tetrathiafulvalene **33** (0.05 g, 0.050 mmol). The reaction was then left to stir overnight under nitrogen at room temperature. Upon evaporation of the solvent, the residue in the form of brown oil was stored in a desiccator connected to a pump for further drying and removal of solvent residues, giving rise to brown oily 2,3,6,7-tetrakis[3-(1-methylimidazole)propylthio]tetrathiafulvalene **34** (0.0261 g, 0.083 mmol, 70%). R_f (DCM: EtOAc, 8:2) = 0.51.

CHAPTER 4: Results and Discussion

4.1 Introduction

As noted throughout the contents of this mini-dissertation, my contribution to this project was limited to the responsibility of solely proving the ability to successfully prepare tetrathiafulvalene derivatives following various series of synthetic methods, which required and involved a couple of minor, significant adjustments resulting in successful synthesis. Initially, the scope of the project involved the preparation and characterisation of only components **4** and **5**, resulting from the cyano-ethyl protected intermediate **3**. In this chapter, results following the successful and unsuccessful preparation of these components, along with their intermediates are discussed. Supported by characterisation results as stipulated in aforementioned chapter, all attainable and significant spectra attached in the appendices.

Therefore, an insight into the outcomes of our research on these TTF compounds, modified to exhibit amphiphilic properties shall be given. Our investigation is aimed at understanding their properties, structural features, as well as potential utility, as they hold promise for applications in soft materials. By so doing, we at least hoping to address and tackle challenges encountered during TTF synthesis and characterization process. In the same breath, we hoping to propose avenues for further research, such that additional derivatives can be explored.

4.2 Synthesis and Characterization of the Compounds

4.2.1. Preparation of the key TTF intermediates.

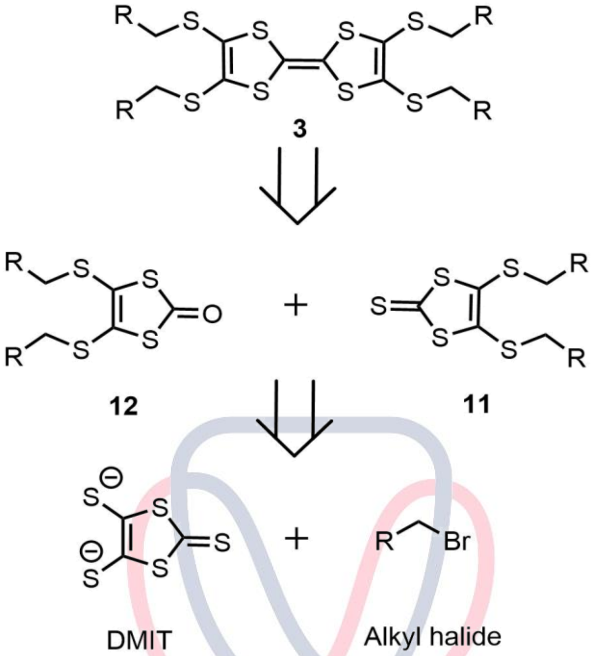
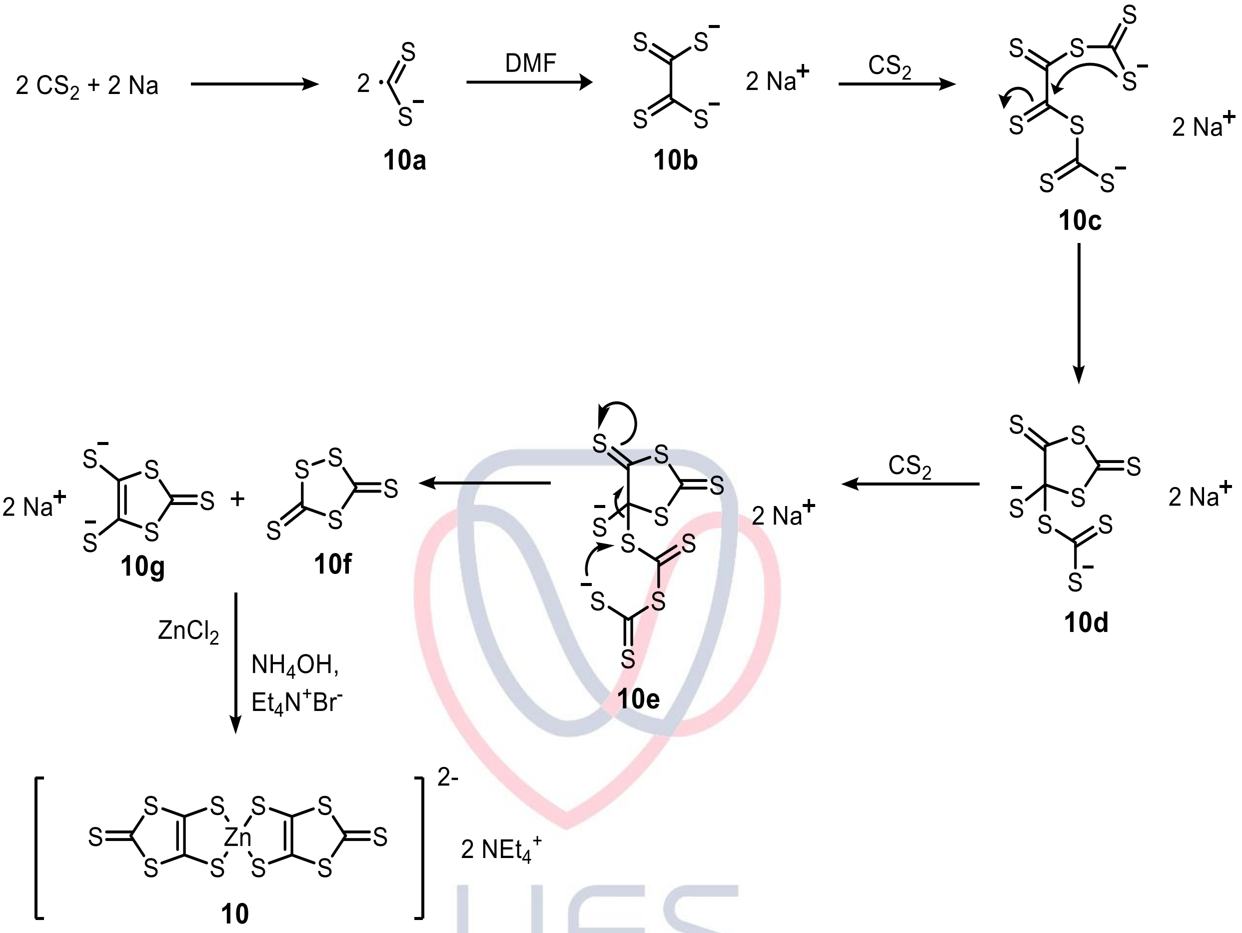


Figure 4.1. Retrosynthetic of TTF derivative **3**.

The key synthetic intermediate is the bis-cyanoethyl protected TTF derivative **3**, resulting from cross-coupling reactions between 4.5-bis(alkylthiol)-1.3-dithiole-2-thione and 4.5-bis(2-cyanoethylthio)-1.3-dithiole-2-one with triethyl phosphite (Figure 4.1). The synthesis of the intermediate compound **3** was carried out via a series of steps involving firstly the preparation of the nucleophilic zincate salt **10**. This is because the key TTF synthesis intermediate, 1.3-dithiole-2-thione (DMIT)'s inability to be isolated in its protonated neutral form, as well as it being unstable in acidic media [82,85].

Figure 4.2. Structure of 1,3-dithiole-2-thione-4,5-dithiolate (DMIT).

Scheme 4.1 shows the mechanism for the formation of the zincate complex, a shelf-stable synthon of dithiolate (DMIT) **10g**.



Scheme 4.1. Mechanism for the formation of **10**.

Carbon disulphide is reduced with alkaline metal in dimethylformamide (DMF) [86], producing 1.3-dithiole-2-thione4.5-dithiolate (DMIT), which stands to be isolated as zinc complex through the addition of zinc chloride ($ZnCl_2$) and tetraethyl ammonium bromide (Et_4NBr) [26]. The dithiolate intermediate **10b** reacts with one equivalent of carbon disulphide and the resultant product undergoes intramolecular cyclisation, resulting in dithiolate **10c**, which upon intramolecular cyclisation could yield isomer **10d**. A reaction between the latter **10d** and one equivalent of carbon disulphide then results in dithiolate intermediate **10e**. Fragmentation of **10e** then gives rise to the target 1,3-dithiole-2-thione-4,5-dithiolate **10g**, as well as the neutral C_2S_5 fragment **10f**. Regeneration of CS_2 and sulphur can occur, as a result of the decomposition of the neutral C_2S_5 [27,85,87]. Lastly, the zinc complex **10**, arising from a reaction of dithiolate (DMIT) **10g** and $ZnCl_2$ and Et_4NBr is produced.

The reaction was carried out readily under conditions of inert atmosphere, low temperatures, and carefully dried DMF and CS_2. The bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiol) zincate salt $(Et_4N)_2[Zn(DMIT)_2]$ **10** was isolated as a pure, intensely red powder, with a significantly high yield and the melting point matching reports in literature [27]. The DMIT's zinc complex precipitates from the reaction mixture as the main product, meanwhile the side or by-product, the neutral C_2S_5 fragment **10f** may further decompose into a trithiocarbonate intermediate and a CS_2. Upon collection of the precipitate by filtration, a residue filtrate of an unpleasant odour was collected and disposed of, the odour lessens one's interest in isolating any of the by-products. Nonetheless, an important standout observation as reported by literature was noted and confirmed that is how stable the zinc complex is, with literally zero degradation over a very long period at room temperature. Additionally, the DMIT chelates made up of other metals such as sodium, potassium and lithium [26,87].

Another observation was how exothermic the reaction was, particularly as the metal (sodium) was added, requiring it to be added in fine portions cautiously to the mixture of CS_2 and dried DMF. Amid the alkali metal added in portions, the flask was submerged in ice cold water bath with stirring, aiming to safely control the reaction with extreme caution and keep the temperature within a certain range. Otherwise, as reported, the reaction can proceed violently, such that it can result to an explosion [88].

The alkylation of $C_3S_5^{2-}$ gives rise to alkylthio-l,3-dithiol-2-thiones. Therefore, the prepared DMIT and its resultant alkylation products enable and give rise to a collection of substituted 1,3-dithiole-2-thiones. The highly nucleophilic DMIT was successfully alkylated in a reaction with the electrophilic bromo-alkane (alkane= R= propane or hexane) in MeCN, resulting in a combination of dark green plus yellow oil, as 4,5-bis(proplythio)-1,3-dithiole-2-thione **11**, and as well as the 4,5-bis(hexlythio)-1,3-dithiole-2-thione **11** in the form of a dark yellow oil, upon purification through a plug of silica. These compounds appear to be quite stable, though oxidizable on air. Therefore, it required tight sealing and packaging and storage in a cool environment [85]. Comparison of the ^1H spectra of the alkylated products shows definite similarities, with the two (S-CH_2-) groups appearing as a triplet peak at about ~2.90 ppm.

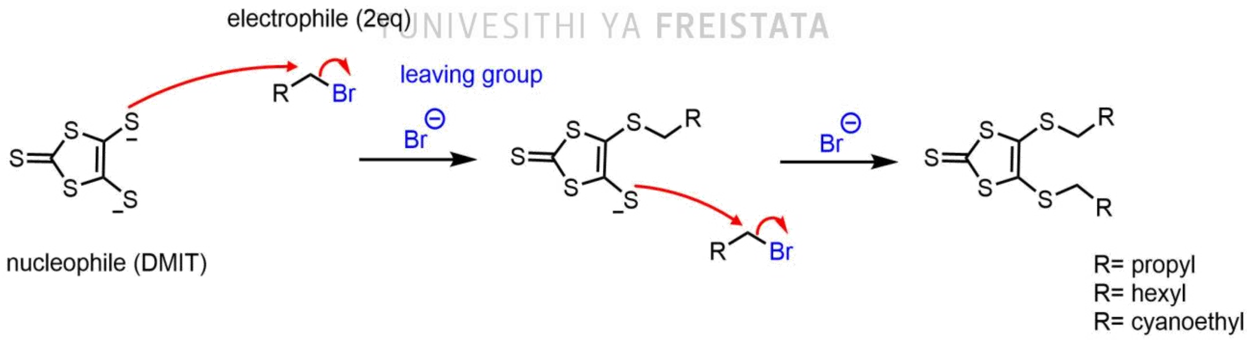
Alkylation was also carried-out using 3-bromopropinitrile as the electrophilic species. Purification was carried-out by recrystallization using toluene, resulting in long, well-defined yellow, needle-like crystals; as 4,5-bis(cyanoethylthio)-1,3-dithiole-2-thione **12**. These crystals appeared to be far more stable at any condition, even with exposure to air and solution. A shift to higher chemical shift of 3.19 ppm is observed in the proton NMR of the product.

The reaction contents were refluxed in a solvent, acetonitrile just as in alkylation with an alkyl halide. Generally, in most synthesis procedures, alkylation of DMIT is carried-out in acetonitrile, and as a result give rise to clean products in good yields, in contrast to the reactions carried out in acetone [26]. Thus, the alkylated thiones were successfully prepared and in high expected yields. Both ^{1}H and ^{13}C NMR analysis results complement the ones found in literature as per reference in the previous methodology chapter. As observed in the attached spectra (appendices), the compounds appear to be clean. Table shows summarised results as per different substituent upon alkylation of the DMIT.

Table 4.1. Bis(alkylthio)-1.3-dithiol-2-thione.

R	^{1}H (CDCl)/ppm	R_f (DCM)	Yield (%)
$-CH_2-CH_2-CH_3$	2.90 t (SCH_2-), 1.77-1.68 m (-CH_2-), 1.08 t (-CH_3).	0.70	83%
$-CH_2-CH_2-CN$	3.19 t (-CH_2-CN), 2.83 t (-SCH_2-).	0.82	77%
$-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3$	2.88 t (SCH_2-), 1.67 p (-CH_2-), 1.49-1.38 m (-CH_2-), 1.34-1.27 m (-CH_2-), 0.91 t (-CH_3).	0.81	78%

DMIT synthons salts are extremely powerful nucleophiles, with the ability to react with practically any primary or secondary alkyl halide in a suitable solvent of choice at very mild conditions (Scheme 4.2). It is a typical S_N2 substitution reaction. The efficiency of the reaction depends on the electrophile's nature, such as its electrophilicity and steric hindrance [26].



Scheme 4.2. Mechanism of the formation of 4,5-bis(alkylthio)-1,3-dithiole-2-thione.

Conversion of the thiocarbonyl group in 4,5-bis(alkylthio)-1,3-dithiole-2-thione into a carbonyl group, 4,5-bis(alkylthio)-1,3-dithiole-2-one was done by a reaction with mercury(II) acetate.

This reaction proceeds with very good yields because of the affinity of mercury to sulphur and extremely low solubility of mercury disulphide, HgS, thus replacing the carbonyl group with a thiocarbonyl group [89,90]. The reaction proceeds through the formation of an intermediate mercurinium ion. The desulfurization of the thioester was carried out on the cyanoethyl protected intermediate, 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione **12** in a mixture of chloroform/ acetic acid (3:1), and mercury(II) acetate at room temperature, giving rise to the corresponding ketone, 4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16** in the form of light yellow ore-like crystals, of a very high yield of 99%, mp 86 ℃. The NMR spectra (see experimental chapter, & appendices) is in accord with the proposed structure, with the ^{1}H NMR corresponding to that of 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione **12**. The same is observed in ^{13}C NMR, however the thiocarbonyl carbon peak appears to be at a higher chemical shift than the carbonyl peak.

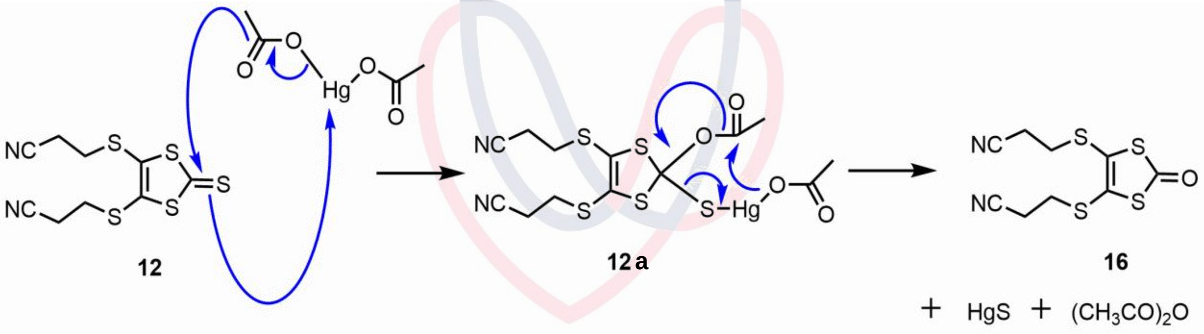


Figure 4.3. Desulfurization 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-thione **12** to 4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16** by mercury(II) acetate.

Both the 1,3-dithiole-2-ones and 1,3-dithiole-2-thiones are essential intermediates for the preparation of the TTF derivatives using the phosphite-mediated coupling reaction.

4.2.2 Synthesis of 2,3-bis(cyanoethylthio)-6,7-bis(R-thio)tetrathiafulvalene 3 intermediates by coupling.

As stipulated, cyanoethyl protected TTF derivatives **17**, a product of the cross-coupling reaction between 4.5-bis(alkylthiol)-1.3-dithiole-2-thione **11** and 4.5-bis(2-cyanoethylthio)-1.3-dithiole-2-one **16**, is the common TTF intermediate used for the synthesis of other TTF derivatives, along with 2,3,6,7-tetrakis(2'-cyanoethylthio)tetrathiafulvalene **18**, resulting from the homo-coupling of 4.5-bis(2-cyanoethylthio)-1.3-dithiole-2-one **16**. These compounds serve as the backbone of the synthesis of TTF derivatives in our study.

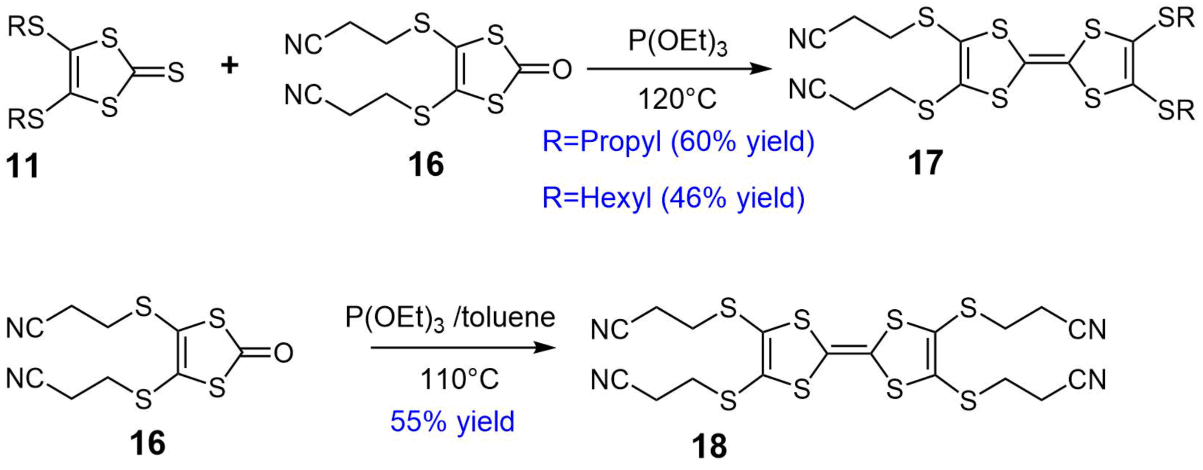


Figure 4.4. Homo and hetero-coupling using triethylphosphite.

As observed in Figure 4.4, the products arising from coupling are cyanoethyl-protected derivatives, on either positions 2- and 3-, or at all four positions possible for substitution. It permits TTF to have two (compound **17**) or four (compound **18**) available thiolate groups for alkylation later on, thus, serving as building blocks for the incorporation of TTF into large molecules. Making the synthesis of various TTF derivatives feasible. On the other end of the TTF intermediate **17**, are two alkyl chain (R= propyl, or R=hexyl group). Based on the amount of base equivalents added to remove the cyanoethyl protective groups, either one, two or four (in the case of compound **18**) groups can be substituted simultaneously. The strategy allows one to have control over selective stepwise incorporation of different alkylthio substituents in the two positions, making the resultant compound even more diverse [91,92]. Therefore, triethyl phosphite mediated homo and cross-coupling is a strategy employed to prepare both symmetric and asymmetric tetrathiafulvalene derivatives with substituents of different natures.

Two asymmetric compounds, **17a** and **17b** with R = propyl and R = hexyl substituents on 6- and 7- positions of the TTF backbone were respectively prepared, the variety in substituents permit unique modification of TTF moieties. These intermediates were prepared under the same conditions from compounds **11** and **16** in neat, freshly distilled triethyl phosphite. TTF products were separated and purified as stipulated in the methodology chapter by column chromatography. The polarity of the cyano-ethyl groups has an effect on the successful purification of the compounds by interaction and affinity with the phases making up the column. As of effect, the cross-coupling between thione **11** and dithiolone **16** led to a reasonable yields of the target compounds (60%, R= propyl) and (46%, R-hexyl), which complements reports in literature [21,93]. Furthermore, self-coupling of intermediate **16** in neat triethyl phophite and refluxing toluene gave rise to 2,3,6,7-tetrakis(2’-cyanoethylthio)tetrathiafulvalene **18** in 55%

yield [13]. This compound did not require chromatographic purification, as it precipitated well-defined, analytically pure and richly orange crystals.

Figure 4.5 shows the proposed mechanism for cross coupling TTF-forming reaction [94]. The reaction commences with the thiophilic addition of triethyl phosphite onto compound **11**'s atom, localized on the second position. Wherein, the triethyl phosphite acts as a nucleophile and attacks the thiocarbonyl carbon centre and forms a bond with the sulphur atom [95]. The then electron rich carbon centre attacks the carbonyl or ketone carbon centre, at the same time, a lone pair on the ketone's oxygen attacks the electro-deficient triethyl phosphite, followed by the subsequent elimination of a chalcogeno phosphite. Another equivalent amount of the nucleophilic triethyl phosphite reacts with the latter TTF intermediate resulting in the elimination of another chalcogeno phosphite, thus, leading to the expected TTF as a final product **17**. The nature of the substituents located in the 4- and 5-positions of the final TTF unit influence the efficiency of the reaction, with electron-withdrawing groups, such as cyanoethyl, facilitating the reaction [93] [96].

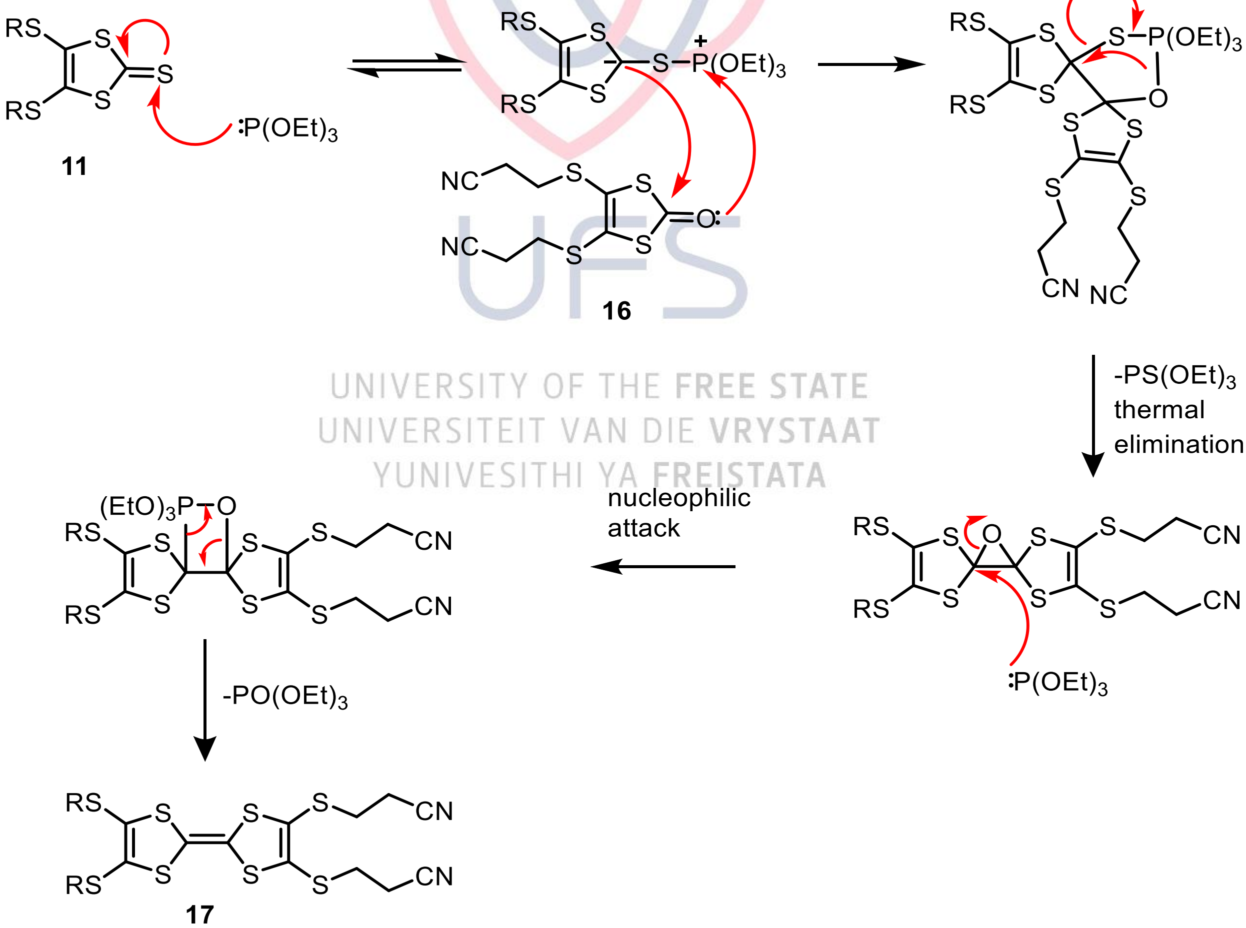


Figure 4.5. Proposed mechanism of the $P(OEt)_3$-mediated cross-coupling.

Therefore, coupling of oxo intermediate compound **16** with either thione **11**, or its self-coupling leads to reasonable yields of the corresponding TTFs **17** and **18**, respectively. Both ^{1}H and ^{13}C NMR spectra, melting point and R_f values were in accord with the characterization details reported in literature.

4.2.3 Deprotection and re-alkylation of tetrathiafulvalene intermediates.

The intermediates **17** and **18** can be deprotected under basic conditions and then re-alkylated with different alkylating agents containing functional groups. These functional groups can be further converted into the polar groups rendering the desired amphiphilic TTF derivatives. Figure 4.6 sums up and give an overview of the successful and unsuccessful TTF preparation series giving rise to functionalised TTF derivatives.

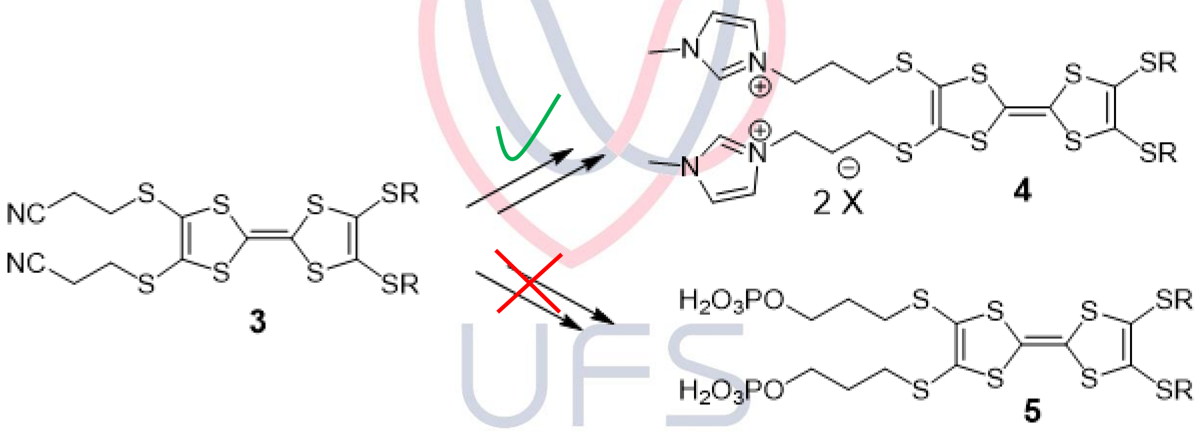


Figure 4.6. Overview of the successful and unsuccessful syntheses of amphiphilic TTF derivatives.

4.2.3.1 Deprotection of TTF intermediates 17 and 18.

TTF derivatives **17** and **18** can be fully deprotected under the basic conditions using slightly more than 2 and 4 equivalents of CsOH in MeOH, respectively. However, after several attempts this deprotection appeared to be unsuccessful. Though CsOH in MeOH is a recommended base, it didn’t work in our case [13]. A different base, also discovered from literature: potassium tert-butoxide (KOt-Bu) was used in excess and yielded positive results and successful deprotection [29].

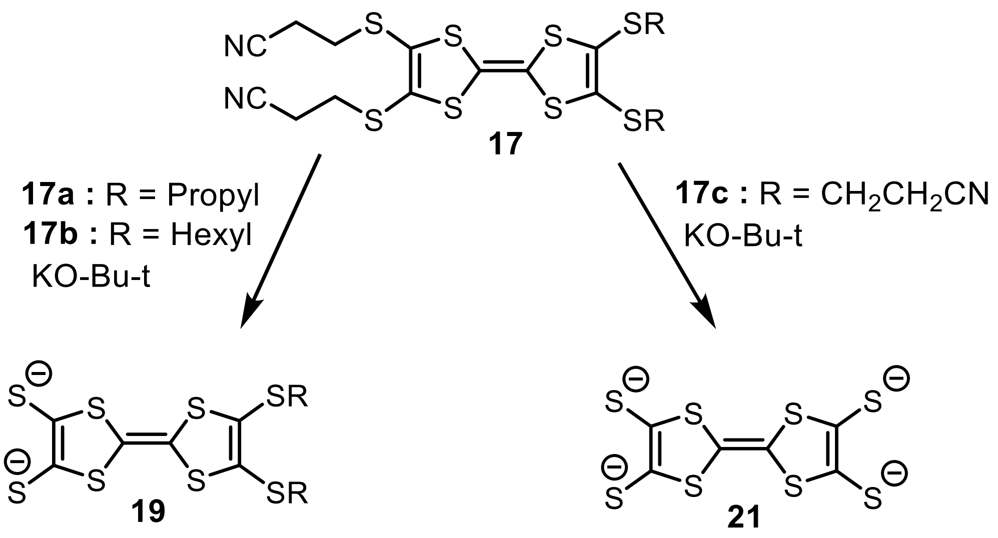


Figure 4.7. Potassium tert-butoxide mediated deprotection of cyanoethyl protected intermediates.

Potassium tert-butoxide (KOt-Bu) and caesium hydroxide (CsOH) are both strong bases, but have different properties and reactivity. The choice between KOt-Bu and CsOH depended on the specific requirements of the reaction, its conditions, solvent as well as the overall synthetic strategy. Since it was essentially about cleaving off the protecting group, steric hindrance and nucleophilicity weren't critical factors [97]. However, it is important that KOt-Bu is more basic, in particular because it is added without protic MeOH, and, thus, the enhanced reactivity [98]. This explains its ability to remove the cyanoethyl group successfully. Despite being a poor nucleophile, the bulky structure of KOt-Bu makes it perform exceptionally well in cleaving and elimination reactions [99]. Successful deprotection with the formation of thiolates is crucial for successful alkylation that follows. Figure 4.8 embodies the proposed deprotection mechanism by the strong base, potassium tert-butoxide.

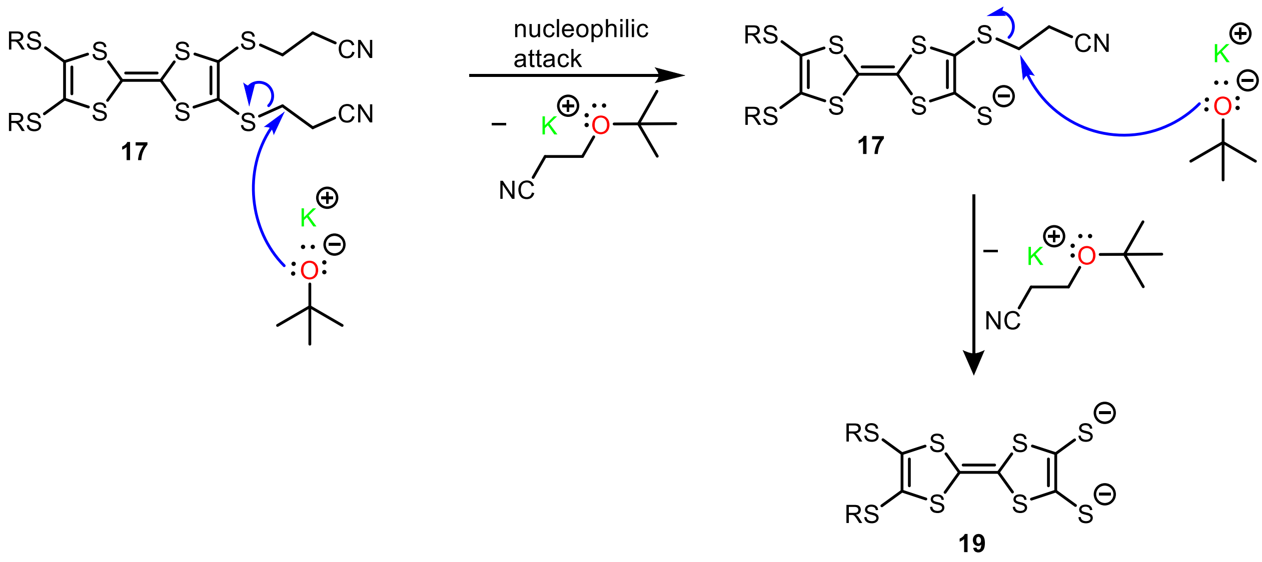


Figure 4.8. Deprotection of cyanoethyl protected compound mechanism by potassium tert-butoxide.

4.2.3.2 Re-alkylation of TTF intermediates 17 and 18.

The subsequent re-alkylation of the thiolates allows the synthesis of new functionalised TTF systems of diverse structures [100]. Re-alkylation as a method of functionalisation of the DMIT unit in the 4- and 5- positions, follows nucleophilic substitution reaction using an alkyl halide [101]. Wherein, alkyl groups are introduced onto the TTF intermediates' thiol group. The sulphur atom of the TTF intermediate acts as the nucleophile, attacking the alkyl halide's electrophilic centre by bimolecular nucleophilic substitution S_N2 reaction, see Figure 4.9.

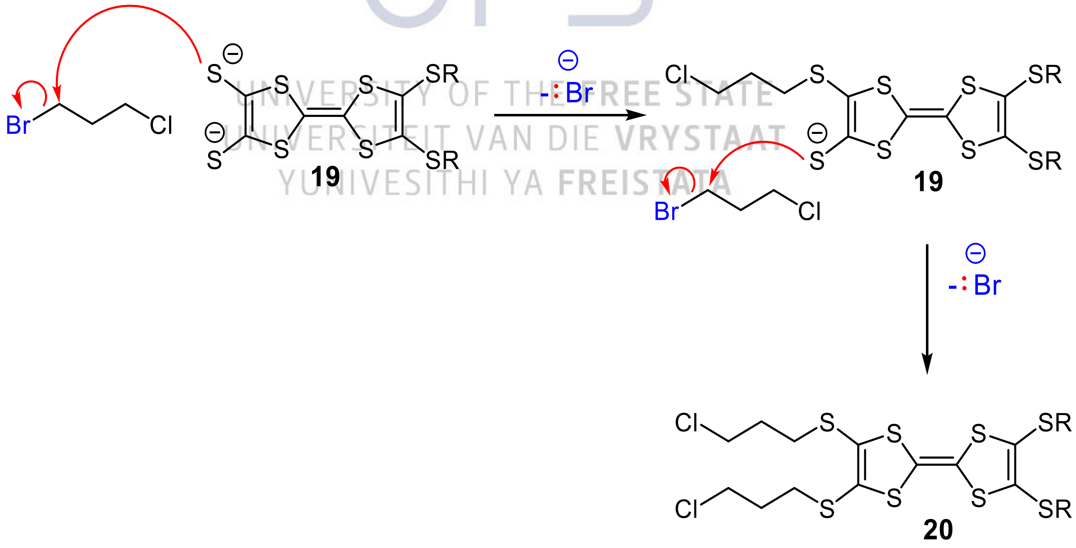
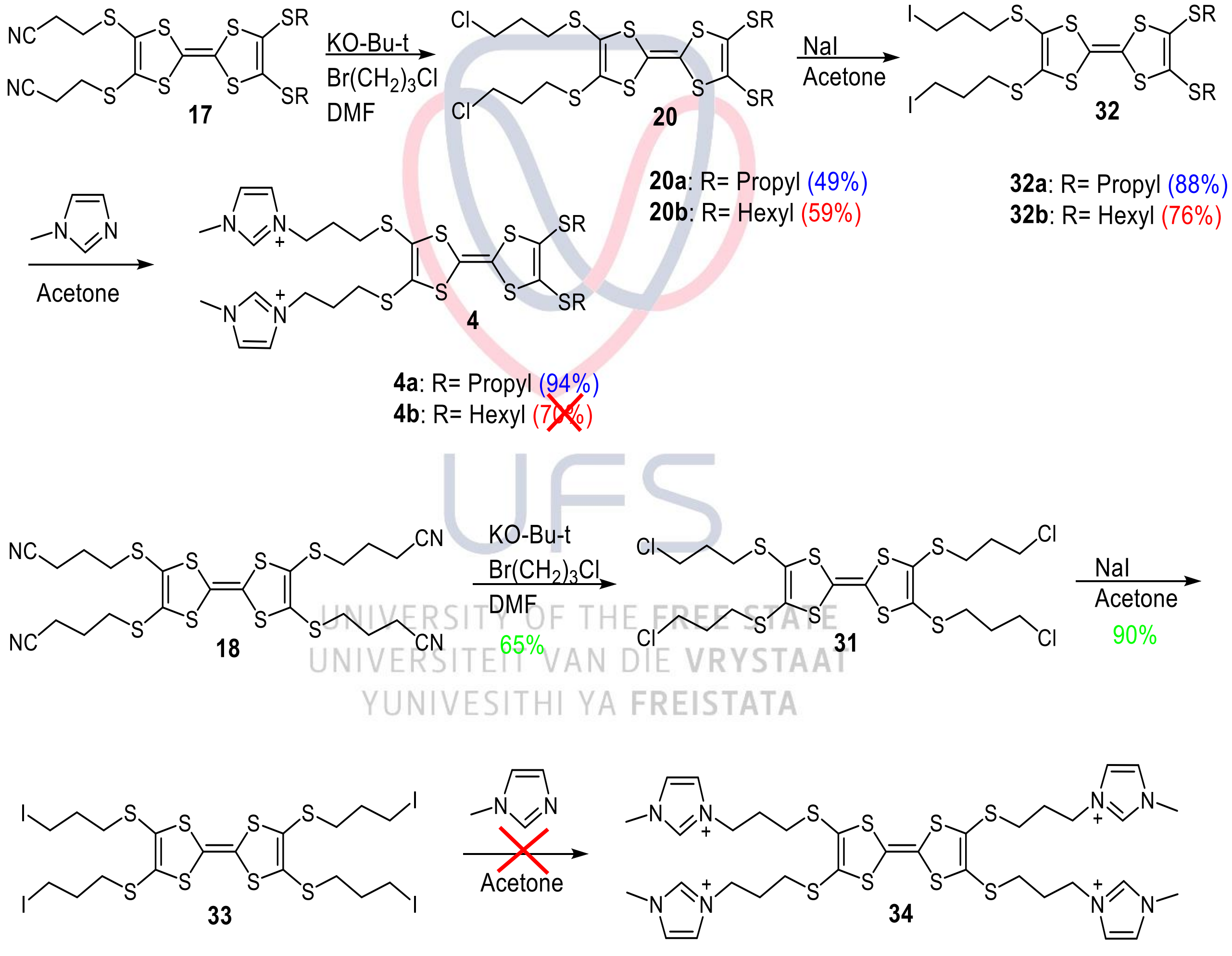


Figure 4.9. Nucleophilic substitution mechanism between TTF and alkyl halide.

The extent of the nucleophilic substitution depends on the amount of the alkyl halide. In our case it was always best to use an excess of most of the alkyl halide. As we used bis-alkyl halides with bromo- and chloro-substituents and, thus, two electrophilic centres. An excess of a reagent serves as a method of controlling the region-selectivity of the alkylation [102]. Since the TTF unit contains multiple nucleophilic sites (thiolates), an excess ensures that all the thiolates react with the more electrophilic bromide side of the electrophile. Therefore, circumvents formation of cyclic products, which could rise due to a reaction with the second thiolate group with a chloride substituent. Several other factors determining the outcome of nucleophilic substitution include reaction conditions; such as the base used during de-protection, choice of solvent and temperature [103].



Scheme 4.3. Synthesis route by de-protection and re-alkylation of TTF intermediates of different functionalities.

The thiolate generated in situ was re-alkylated with an excess of the appropriate alkyl halide, 1-bromo-3-chloropropane (Scheme 4.3), giving rise to a variety of TTF derivatives based on different substituents or functionalities, in quite reasonable yields of 49-65 %. The inability to achieve exceptionally high yields could presumably be due to the competing cyclization reaction as a subject of selectivity and region-selectivity amongst other factors. As of effect, these compounds had to be purified upon alkylation by column chromatography to isolate the desired product. These resultant products **20a**, **b** and **31** were in the form of highly viscous oils upon concentration.

In the next step, the alkyl substituted intermediates (**20a**, **b** and **31**) were reacted with an excess of sodium iodide for halogen exchange [29,104]. This substitution reaction was carried out with the aim of obtaining a more reactive iodo analogue [105]. The starting material was refluxed in acetone with an excess of the reagent sodium iodide for approximately 4 days under inert atmosphere [29]. The reaction was monitored by TLC, along with the formation of a white precipitate, NaCl serving as an indicator of successful substitution and completion. The reaction gave rise to iodinated intermediates **32a**, **b** and **33** in relatively high yields 88%, 76% and 90%, respectively, upon purification by column chromatography. These TTF products were all viscous brown oils. Nonetheless, the compounds were characterised by ^{1}H and ^{13}C NMR, with data consistent with assigned structures. The identity of compound **32a** was also proved by mass spectrometry, with *m/z* (%) = 751.8065 (M+), calculated for $C_{18}H_{26}I_2S_8$, 751.7890, and the isotopic pattern similar to the modelled one.

4.2.3.3. Substitution of TTF intermediates resulting in final product 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(alkylthio)tetrathiafulvalene 4.

1-Methyl-imidazole is a five-membered nitrogen-containing heterocyclic compound. It is known for its wide range of chemical and biological properties, amongst those, it is an important synthon in the development of new drugs [106]. Due to its amphoteric nature, the 1,3-diazole ring is susceptible to both electrophilic and nucleophilic attacks [107]. The non-substituted nitrogen atom has unshared pairs of electrons and, therefore, demonstrates nucleophilic nature [108]. 1-Methyl-imidazole is often used in the preparation of imiddazolium-based ionic liquids.

1-Methyl-imidazole was reacted with 4,5-bis(3'-iodopropylthio)-6,7-bis(alkylthio)tetrathiafulvalene **32** or 2,3,6,7-tetrakis(3-iodopropylthio)tetrathiafulvalene **33** in anhydrous, degassed acetone. The reaction was left to stir overnight under nitrogen at room temperature. In the first successful attempt, the product was purified by column chromatography, but decomposed or remained stuck on silica. This effect could be due to the extreme polarity of the compounds, such that they may bind too strongly to the silica, and decompose or just not elute [109,110].

After several attempts, compound **4a** was successfully synthesized and characterized, meanwhile the synthesis of compounds **4b** and **34** could not be finalized due to the lack of time. Final purification of **4a** was a challenge, different solvent recrystallization methods were attempted with little to no success. The compounds were in the form of viscous brown oil which formed crystals very slowly as the solvent evaporated with time, but the crystals were of purity not sufficient for X-ray analysis. However, successful preparation of the highly polar derivative, 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene **4a** is confirmed by MS results as both NMR and MS results concur. The mass spectrum of the compound is attached in the appendix, which definitely demonstrates its double charge (peaks with fractional x.5 masses), permanent charge (ionized without protonation.), and its isotope pattern well corresponds to the expected structure.

As shown in Figure 4.6, the scope was also inclusive of the unsuccessful preparation of compound **5**, a phosphate group containing TTF derivatives. Compounds **4** and **5** were the main objectives of the study, however, due to the limited time and size of the study, only one of the proposed was successfully prepared.

4.3. Characterisation of TTF intermediates and derivatives

Characterisation, as observed throughout the study, was carried-out using a variety of analysis tools. Notations for the successfully prepared compounds are included in the experimental chapter, and the NMR spectra in the appendices.

An interest and part of the study's aim was to carry-out electrochemical studies by cyclic voltammetry to observe how the charged TTF derivatives may behave. However, the amphiphilic nature of the compound posed challenges from the side of solvent selection and solubility, in particular the oxidized species, with net charges of 3+ and 4+. Electrochemical studies were carried out following the literature procedures for the similar TTF derivatives [98,99]. Using the standard three electrode cell setup with two Pt electrodes (working and auxiliary) and non-aqueous (MeCN) Ag+ reference electrode at 25℃ with 0.1 M Bu_4NBF_4 electrolyte in MeCN under inert atmosphere. However, poorly defined product oxidation waves were observed. An expected possible outcome was a cyclic voltammogram showing possibly two single-electron, reversible redox processes [111]. At potentials slightly more positive (i.e., $E_1^{Oxidation}$= ~0.6V & $E_2^{Oxidation}$= ~1.00V) than those of the parent TTF unit [112,113]. The potentials are usually said to be raised by the attached alkyl-thio substituents, due to destabilisation of the di-cation and radical di-cation entities, caused by the electron-withdrawing effect of the sulphur atoms [101]. The potentials are expected to be higher than in the parent TTF unit, due to the presence of the four thio-alkyl substituents attached to the TTF unit frame [114].

It was concluded by assumption that the material either quickly and irreversibly degrades upon oxidation or as it was deposited on the electrodes. Another factor to the unsuccessful electrochemical studies could be the level of purity or impurity surrounding the compound. As well as choice of the most compatible solvent. Unfortunately, multiple experiments in different solvents were not possible due to the reduced quantity of the remaining material. Therefore, the studies revealed that the TTF derivative does not interact to any significant extent [112].

CHAPTER 5: Conclusions and future-work

The preparation of several redox-active tetrathiafulvalene derivatives has been explored, with some of the intermediates and derivatives being susceptible to diverse use in modern materials science and supramolecular chemistry. Our study has managed to cover a range of potential functionalised symmetrical and unsymmetrical TTF derivatives with different substituents, from alkyl-halides bearing TTF derivatives to the 1-methyl-imidazolium units bound to the TTF frameworks. For feasibility of the amphiphilic character, it was crucial to prepare entities with long alkyl chains on one side and polar groups on another side of the TTF backbone, enabling these compounds to act as building blocks for incorporation into diverse and new classes of redox-active materials.

In summary, upon successful synthesis of cyanoethyl-protected TTFs, their deprotection in basic conditions was followed by re-alkylation. The subsequent re-alkylation involved the use of different alkyl halides and was a subject of carefully designing reaction conditions, with consideration of selectivity. The reactions produced products, separated and purified by column chromatography coupled with analysis by NMR and mass spectrometry. Thus, we obtained several new target amphiphilic functionalised TTF derivatives. Analysis mostly by NMR revealed qualitatively that some of the desired compounds were produced successfully. The study has therefore clearly demonstrated that the key intermediates can be used to prepare symmetric and un-symmetric TTFs. The ultimate goal of the project was to evaluate the possibility of synthesis of amphiphilic cationic / anionic TTF derivatives **4** and **5**, and the pathway for the preparation of the cationic derivatives was investigated with certain success.

For future-work would be an attempt to fully characterise the TTF material with the aims of observing any degradation from what was observed in the study. That is, in particular electrochemical studies, along with the addition of more characterisation techniques to comprehend the nature of these TTF derivatives. Lastly, application studies on the resultant TTF products should follow.

REFERENCES

(1) Cooper, W. F.; Kenny, N. C.; Edmonds, J. W.; Nagel, A.; Wudl, F.; Coppens, P. Crystal and Molecular Structure of the Aromatic Sulphur Compound 2,2′-Bi-1,3-Dithiole. Evidence for d-Orbital Participation in Bonding. *J. Chem. Soc. D* **1971**, (16), 889–890. https://doi.org/10.1039/C29710000889.

(2) Bendikov, M.; Wudl, F.; Perepichka, D. F. Tetrathiafulvalenes, Oligoacenenes, and Their Buckminsterfullerene Derivatives: The Brick and Mortar of Organic Electronics. *Chem Rev* **2004**, *104* (11), 4891–4946. https://doi.org/10.1021/cr030666m.

(3) Wudl, F.; Smith, G. M.; Hufnagel, E. J. Bis-1,3-Dithiolium Chloride: An Unusually Stable Organic Radical Cation. *J. Chem. Soc. D* **1970**, No. 21, 1453. https://doi.org/10.1039/c29700001453.

(4) Martín, N. Tetrathiafulvalene: The Advent of Organic Metals. *Chem Comm* **2013**, *49* (63), 7025. https://doi.org/10.1039/c3cc00240c.

(5) Katan, C. First-Principles Study of the Structures and Vibrational Frequencies for Tetrathiafulvalene TTF and TTF-d_4 in Different Oxidation States. *J Phys Chem A* **1999**, *103* (10), 1407–1413. https://doi.org/10.1021/jp983941v.

(6) Hargittai, I.; Brunvoll, J.; Kolonits, M.; Khodorkovsky, V. Tetrathiafulvalene: Gas-Phase Molecular Structure from Electron Diffraction. *J Mol Struct* **1994**, *317* (3), 273–277. https://doi.org/10.1016/0022-2860(93)07873-U.

(7) Schröder, H. V; Schalley, C. A. Tetrathiafulvalene – a Redox-Switchable Building Block to Control Motion in Mechanically Interlocked Molecules. *Beilstein J. Org Chem* **2018**, *14*, 2163–2185. https://doi.org/10.3762/bjoc.14.190.

(8) Canevet, D.; Sallé, M.; Zhang, G.; Zhang, D.; Zhu, D. Tetrathiafulvalene (TTF) Derivatives: Key Building-Blocks for Switchable Processes. *Chem Comm* **2009**, No. 17, 2245. https://doi.org/10.1039/b818607n.

(9) Yamada, H.; Yamashita, M.; Hayashi, H.; Suzuki, M.; Aratani, N. Semiconducting Π-Extended Tetrathiafulvalene Derivatives. *Chem. Eur. J* **2018**, *24* (70), 18601–18612. https://doi.org/10.1002/chem.201802744.

(10) Bigot, J.; Charleux, B.; Cooke, G.; Delattre, F.; Fournier, D.; Lyskawa, J.; Sambe, L.; Stoffelbach, F.; Woisel, P. Tetrathiafulvalene End-Functionalized Poly(*N* -Isopropylacrylamide): A New Class of Amphiphilic Polymer for the Creation of

Multistimuli Responsive Micelles. *J Am Chem Soc* **2010**, *132* (31), 10796–10801. https://doi.org/10.1021/ja1027452.

(11) Parkin, S. S. P.; Engler, E. M.; Schumaker, R. R.; Lagier, R.; Lee, V. Y.; Scott, J. C.; Greene, R. L. Superconductivity in a New Family of Organic Conductors. *Phys Rev Lett* **1983**, *50* (4), 270–273. https://doi.org/10.1103/PhysRevLett.50.270.

(12) Ishiguro, T.; Yamaji, K. DMET and MDT-TTF Salts: Conductors with Hybrid Molecules. *Organic superconductors* **1990**; pp 148–157. https://doi.org/10.1007/978-3-642-97190-7_6.

(13) Svenstrup, N.; Rasmussen, K. M.; Hansen, T. K.; Becher, J. The Chemistry of TTFTT; 1: New Efficient Synthesis and Reactions of Tetrathiafulvalene-2,3,6,7-Tetrathiolate (TTFTT): An Important Building Block in TTF-Syntheses. *Synthesis* **1994**, 809–812. https://doi.org/10.1055/s-1994-25580.

(14) Lehn, J.-M. Toward Self-Organization and Complex Matter. *Science* **2002**, *295* (5564), 2400–2403. https://doi.org/10.1126/science.1071063.

(15) Nielsen, M. B.; Becher, J. Two- and Three-Dimensional Tetrathiafulvalene Macrocycles. *Liebigs Annalen* **1997**, *1997* (11), 2177–2187. https://doi.org/10.1002/jlac.199719971103.

(16) Wang, C.; Dong, H.; Jiang, L.; Hu, W. Organic Semiconductor Crystals. *Chem Soc Rev* **2018**, *47* (2), 422–500. https://doi.org/10.1039/C7CS00490G.

(17) Bryce, M. R. Tetrathiafulvalenes as π-Electron Donors for Intramolecular Charge-Transfer Materials. *Advanced Materials* **1999**, *11* (1), 11–23. https://doi.org/10.1002/(SICI)1521-4095(199901)11:1<11::AID-ADMA11>3.0.CO;2-3.

(18) Ferraris, J.; Cowan, D. O.; Walatka, V.; Perlstein, J. H. Electron Transfer in a New Highly Conducting Donor-Acceptor Complex. *J Am Chem Soc* **1973**, *95* (3), 948–949. https://doi.org/10.1021/ja00784a066.

(19) John, D. E. New π-Electron Donor Systems Based on Multi-Tetrathiafulvalene Derivatives. Durham E-Theses. Durham University. **1999**. http://etheses.dur.ac.uk.

(20) Pfattner, R.; Bromley, S. T.; Rovira, C.; Mas-Torrent, M. Tuning Crystal Ordering, Electronic Structure, and Morphology in Organic Semiconductors: Tetrathiafulvalenes as a Model Case. *Adv Funct Mater* **2016**, *26* (14), 2256–2275. https://doi.org/10.1002/adfm.201502446.

(21) Wang, C.; Dong, H.; Hu, W.; Liu, Y.; Zhu, D. Semiconducting π-Conjugated Systems in Field-Effect Transistors: A Material Odyssey of Organic Electronics. *Chem Rev* **2012**, *112* (4), 2208–2267. https://doi.org/10.1021/cr100380z.

(22) Wang, J.; Li, Z. Significant Influence of Molecular Packing in Aggregates on Optoelectronic Properties. *Acta Chimi Sin* **2021**, *79* (5), 575. https://doi.org/10.6023/A21010029.

(23) Torrance, J. B.; Scott, B. A.; Welber, B.; Kaufman, F. B.; Seiden, P. E. Optical Properties of the Radical Cation Tetrathiafulvalenium in Its Mixed-Valence and Monovalence Halide Salts. *Phys Rev B* **1979**, *19* (2), 730–741. https://doi.org/10.1103/PhysRevB.19.730.

(24) Simonsen, K. B.; Svenstrup, N.; Lau, J.; Simonsen, O.; Mørk, P.; Kristensen, G. J.; Becher, J. Sequential Functionalisation of Bis-Protected Tetrathiafulvalene-Dithiolates. *Synthesis* **1996**, (03), 407–418. https://doi.org/10.1055/s-1996-4216.

(25) Wang, H.-Y.; Cui, L.; Xie, J.-Z.; Leong, C. F.; D'Alessandro, D. M.; Zuo, J.-L. Functional Coordination Polymers Based on Redox-Active Tetrathiafulvalene and Its Derivatives. *Coord Chem Rev* **2017**, *345*, 342–361. https://doi.org/10.1016/j.ccr.2016.10.011.

(26) Jia, C.; Liu, S.-X.; Ambrus, C.; Neels, A.; Labat, G.; Decurtins, S. One-Dimensional *μ*-Chloromanganese(II)−Tetrathiafulvalene (TTF) Coordination Compound. *Inorg Chem* **2006**, *45* (8), 3152–3154. https://doi.org/10.1021/ic060056f.

(27) Benbellat, N.; Gavrilenko, K. S.; Le Gal, Y.; Cador, O.; Golhen, S.; Gouasmia, A.; Fabre, J.-M.; Ouahab, L. Co(II)−Co(II) Paddlewheel Complex with a Redox-Active Ligand Derived from TTF. *Inorg Chem* **2006**, *45* (26), 10440–10442. https://doi.org/10.1021/ic061680v.

(28) ACHA, R., Ligand design for molecule-based magnetic and/or conducting materials. E-Theses. Brock University St. Catharines Ontario, Canada. **2013**. https://dr.library.brocku.ca/bitstream/10464/4406/1/Brock_Acha_Roland_2013.

(29) Svenstrup, N.; Becher, J. The Organic Chemistry of 1,3-Dithiole-2-Thione-4,5-Dithiolate (DMIT). *Synthesis* **1995**, 215–235. https://doi.org/10.1055/s-1995-3910.

(30) Wang, C.; Batsanov, A. S.; Bryce, M. R.; Howard, J. A. K. An Improved Large-Scale (90 g) Synthesis of Bis(Tetraethylammonium)Bis(1,3-Dithiole-2-Thione-4,5-Dithiol)Zincate: Synthesis and X-Ray Crystal Structures of Bicyclic and Tricyclic 1,4-Dithiocines Derived from 1,3-Dithiole-2-Thione-4,5-Dithiolate (DMIT). *Synthesis* **1998**, 1615–1618. https://doi.org/10.1055/s-1998-2197.

(31) Lau, J.; Simonsen, O.; Becher, J. Oligomeric Tetrathiafulvalenes: Stable Caesium Tetrathiafulvalene- and 1,3-Dithiole-2-Thionethiolates as Intermediates in the Synthesis of Pentakis(Tetrathiafulvalenes). *Synthesis* **1995**, 521–526. https://doi.org/10.1055/s-1995-3941.

(32) Simonsen, K.; Becher, J. Tetrathiafulvalene Thiolates: Important Synthetic Building Blocks for Macrocyclic and Supramolecular Chemistry. *Synlett* **1997**, 1211–1220. https://doi.org/10.1055/s-1997-1001.

(33) Becher, J. Tetrathiafulvalenes: Versatile Building Blocks in Macrocyclic and Supramolecular Chemistry. *Phosphorus Sulfur Silicon Relat Elem* **1999**, *153* (1), 99–117. https://doi.org/10.1080/10426509908546429.

(34) Mendes, P. M. Cellular Nanotechnology: Making Biological Interfaces Smarter. *Chem Soc Rev* **2013**, pp 9207–9218. https://doi.org/10.1039/c3cs60198f.

(35) Jeppesen, J. O.; Nielsen, M. B.; Becher, J. Tetrathiafulvalene Cyclophanes and Cage Molecules. *Chem Rev* **2004**, *104* (11), 5115–5132. https://doi.org/10.1021/cr030630u.

(36) Jørgensen, T.; Hansen, T. K.; Becher, J. Tetrathiafulvalenes as Building-Blocks in Supramolecular Chemistry. *Chem. Soc. Rev.* **1994**, *23* (1), 41–51. https://doi.org/10.1039/CS9942300041.

(37) Jana, A.; Bähring, S.; Ishida, M.; Goeb, S.; Canevet, D.; Sallé, M.; Jeppesen, J. O.; Sessler, J. L. Functionalised Tetrathiafulvalene- (TTF-) Macrocycles: Recent Trends in Applied Supramolecular Chemistry. *Chem Soc Rev* **2018**, *47* (15), 5614–5645. https://doi.org/10.1039/C8CS00035B.

(38) Nielsen, K. A.; Jeppesen, J. O.; Levillain, E.; Becher, J. Mono-Tetrathiafulvalene Calix[4]Pyrrole in the Electrochemical Sensing of Anions. *Angew. Chem. Int. Ed* **2003**, *42* (2), 187–191. https://doi.org/10.1002/anie.200390074.

(39) Herranz, M. Á.; Sánchez, L.; Martín, N. Tetrathiafulvalene: A Paradigmatic Electron Donor Molecule. *Phosphorus Sulfur Silicon Relat Elem* **2005**, *180* (5–6), 1133–1148. https://doi.org/10.1080/10426500590910666.

(40) Jana, A.; Ishida, M.; Park, J. S.; Bähring, S.; Jeppesen, J. O.; Sessler, J. L. Tetrathiafulvalene- (TTF-) Derived Oligopyrrolic Macrocycles. *Chem Rev* **2017**, *117* (4), 2641–2710. https://doi.org/10.1021/acs.chemrev.6b00375.

(41) Amabilino, D. B.; Ashton, P. R.; Bravo, J. A.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. Template-Directed Synthesis of a Rotacatenane. *Eur J Org Chem*

1999, *1999* (6), 1295–1302. https://doi.org/10.1002/(SICI)1099-0690(199906)1999:6<1295::AID-EJOC1295>3.0.CO;2-Z.

(42) Barin, G.; Coskun, A.; Friedman, D. C.; Olson, M. A.; Colvin, M. T.; Carmielli, R.; Dey, S. K.; Bozdemir, O. A.; Wasielewski, M. R.; Stoddart, J. F. A Multistate Switchable [3]Rotacatenane. *Chem. Eur. J* **2011**, *17* (1), 213–222. https://doi.org/10.1002/chem.201002152.

(43) Jørgensen, T.; Becher, J.; Chambron, J.-C.; Sauvage, J.-P. A Copper(I) [2]-Catenate Incorporating a Tetrathiafulvalene Unit. *Tetrahedron Lett* **1994**, *35* (25), 4339–4342. https://doi.org/10.1016/S0040-4039(00)73348-X.

(44) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. A Chemically and Electrochemically Switchable [2]Catenane Incorporating a Tetrathiafulvalene Unit. *Angewandte Chemie International Edition* **1998**, *37* (3), 333–337. https://doi.org/10.1002/(SICI)1521-3773(19980216)37:3<333::AID-ANIE333>3.0.CO;2-P.

(45) Nielsen, M. B.; Lomholt, C.; Becher, J. Tetrathiafulvalenes as Building Blocks in Supramolecular Chemistry II. *Chem Soc Rev* **2000**, *29* (3), 153–164. https://doi.org/10.1039/a803992e.

(46) Li, Z.; Stein, P. C.; Becher, J.; Jensen, D.; Mørk, P.; Svenstrup, N. Self-assembling Tetrathiafulvalene-based Rotaxanes and Catenanes. *Chem. Eur. J* **1996**, *2* (6), 624–633. https://doi.org/10.1002/chem.19960020605.

(47) Tan, S. Y.; Ang, C. Y.; Zhao, Y. Smart Therapeutics Achieved via Host–Guest Assemblies. In *Comprehensive Supramolecular Chemistry II*; Elsevier, **2017**; pp 391–420. https://doi.org/10.1016/B978-0-12-409547-2.12575-2.

(48) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. Towards Controllable Molecular Shuttles - 3. *Synlett* **1992**, *1992* (11), 923–926. https://doi.org/10.1055/s-1992-21542.

(49) Rescifina, A.; Zagni, C.; Iannazzo, D.; Merino, P. Recent Developments on Rotaxane-Based Shuttles. *Curr Org Chem* **2009**, *13* (5), 448–481. https://doi.org/10.2174/138527209787582222.

(50) Schröder, H. V.; Schalley, C. A. Electrochemically Switchable Rotaxanes: Recent Strides in New Directions. *Chem Sci* **2019**, *10* (42), 9626–9639. https://doi.org/10.1039/C9SC04118D.

(51) Tseng, H.; Vignon, S. A.; Stoddart, J. F. Toward Chemically Controlled Nanoscale Molecular Machinery. *Angew. Chem. Int. Ed* **2003**, *42* (13), 1491–1495. https://doi.org/10.1002/anie.200250453.

(52) Zhang, X.; Chen, Z.; Liu, X.; Hanna, S. L.; Wang, X.; Taheri-Ledari, R.; Maleki, A.; Li, P.; Farha, O. K. A Historical Overview of the Activation and Porosity of Metal–Organic Frameworks. *Chem Soc Rev* **2020**, *49* (20), 7406–7427. https://doi.org/10.1039/D0CS00997K.

(53) Souto, M.; Calbo, J.; Mañas-Valero, S.; Walsh, A.; Mínguez Espallargas, G. Charge-Transfer Interactions between Fullerenes and a Mesoporous Tetrathiafulvalene-Based Metal–Organic Framework. *Beilstein. J. Nanotechnol* **2019**, *10*, 1883–1893. https://doi.org/10.3762/bjnano.10.183.

(54) Rowsell, J. L. C.; Yaghi, O. M. Metal–Organic Frameworks: A New Class of Porous Materials. *Microp. M. M* **2004**, *73* (1–2), 3–14. https://doi.org/10.1016/j.micromeso.2004.03.034.

(55) Skorupskii, G.; Chanteux, G.; Le, K. N.; Stassen, I.; Hendon, C. H.; Dincă, M. Electrical Conductivity through π–π Stacking in a Two-dimensional Porous Gallium Catecholate Metal–Organic Framework. *Ann N Y Acad Sci* **2022**, *1518* (1), 226–230. https://doi.org/10.1111/nyas.14906.

(56) Su, J.; Yuan, S.; Wang, H.-Y.; Huang, L.; Ge, J.-Y.; Joseph, E.; Qin, J.; Cagin, T.; Zuo, J.-L.; Zhou, H.-C. Redox-Switchable Breathing Behavior in Tetrathiafulvalene-Based Metal–Organic Frameworks. *Nat Commun* **2017**, *8* (1), 2008. https://doi.org/10.1038/s41467-017-02256-y.

(57) Wang, H.; Ge, J.; Hua, C.; Jiao, C.; Wu, Y.; Leong, C. F.; D'Alessandro, D. M.; Liu, T.; Zuo, J. Photo- and Electronically Switchable Spin-Crossover Iron(II) Metal–Organic Frameworks Based on a Tetrathiafulvalene Ligand. *Angew. Chem. Int. Ed* **2017**, *56* (20), 5465–5470. https://doi.org/10.1002/anie.201611824.

(58) Chen, Q.; Sun, J.; Li, P.; Hod, I.; Moghadam, P. Z.; Kean, Z. S.; Snurr, R. Q.; Hupp, J. T.; Farha, O. K.; Stoddart, J. F. A Redox-Active Bistable Molecular Switch Mounted inside a Metal–Organic Framework. *J Am Chem Soc* **2016**, *138* (43), 14242–14245. https://doi.org/10.1021/jacs.6b09880.

(59) Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. C60: Buckminsterfullerene. *Nature* **1985**, *318* (6042), 162–163. https://doi.org/10.1038/318162a0.

(60) Hou, Y.; Zhang, X.; Chen, K.; Liu, D.; Wang, Z.; Liu, Q.; Zhao, J.; Barbon, A. Charge Separation, Charge Recombination, Long-Lived Charge Transfer State Formation and Intersystem Crossing in Organic Electron Donor/Acceptor Dyads. *J Mater Chem C Mater* **2019**, *7* (39), 12048–12074. https://doi.org/10.1039/C9TC04285G.

(61) Izuoka, A.; Tachikawa, T.; Sugawara, T.; Suzuki, Y.; Konno, M.; Saito, Y.; Shinohara, H. An X-Ray Crystallographic Analysis of a (BEDT-TTF)$_2$C$_{60}$ Charge-Transfer Complex. *J Chem Soc Chem Commun* **1992**, No. 19, 1472. https://doi.org/10.1039/c39920001472.

(62) Goswami, S.; Ray, D.; Otake, K.; Kung, C.-W.; Garibay, S. J.; Islamoglu, T.; Atilgan, A.; Cui, Y.; Cramer, C. J.; Farha, O. K.; Hupp, J. T. A Porous, Electrically Conductive Hexa-Zirconium Metal–Organic Framework. *Chem Sci* **2018**, *9* (19), 4477–4482. https://doi.org/10.1039/C8SC00961A.

(63) Astruc, D. Electron-Transfer Processes in Dendrimers and Their Implication in Biology, Catalysis, Sensing and Nanotechnology. *Nat Chem* **2012**, *4* (4), 255–267. https://doi.org/10.1038/nchem.1304.

(64) Bryce, M. R.; Devonport, W.; Goldenberg, L. M.; Wang, C. Macromolecular Tetrathiafulvalene Chemistry. *Chem Comm* **1998**, (9), 945–952. https://doi.org/10.1039/a800536b.

(65) Beeby, A.; Bryce, M. R.; Christensen, C. A.; Cooke, G.; Duclairoir, F. M. A.; Rotello, V. M. Electrochemically Controlled Interactions between TTF-Based Dendrimers and an Electron-Rich OligomerElectronic Supplementary Information (ESI) Available: CV Data for Dendrimers 1 and 2. *Chem Comm* **2002**, No. 24, 2950–2951. https://doi.org/10.1039/b209765f.

(66) Christensen, C. A.; Becher, J.; Christensen, C. A.; Goldenberg, L. M.; Bryce, M. R. Synthesis and Electrochemistry of a Tetrathiafulvalene (TTF)21–Glycol Dendrimer: Intradendrimer Aggregation of TTF Cation Radicals. *Chem Comm* **1998**, No. 4, 509–510. https://doi.org/10.1039/a707504i.

(67) Haddon, R. C. Carbon Nanotubes. *Acc Chem Res* **2002**, *35* (12), 997–997. https://doi.org/10.1021/ar020259h.

(68) Martín, N.; Sánchez, L.; Herranz, M. Á.; Illescas, B.; Guldi, D. M. Electronic Communication in Tetrathiafulvalene (TTF)/C $_{60}$ Systems: Toward Molecular Solar Energy Conversion Materials? *Acc Chem Res* **2007**, *40* (10), 1015–1024. https://doi.org/10.1021/ar700026t.

(69) Herranz, M. Á.; Martín, N.; Campidelli, S.; Prato, M.; Brehm, G.; Guldi, D. M. Control over Electron Transfer in Tetrathiafulvalene-Modified Single-Walled Carbon Nanotubes. *Angew. Chem. Int. Ed* **2006**, *45* (27), 4478–4482. https://doi.org/10.1002/anie.200504354.

(70) Gao, X.; Qiu, W.; Liu, Y.; Yu, G.; Zhu, D. Organic Field-Effect Transistors Based on Tetrathiafulvalene Derivatives. *Pure Appl. Chem* **2008**, *80* (11), 2405–2423. https://doi.org/10.1351/pac200880112405.

(71) Bourgoin, J. P.; Vandevyver, M.; Barraud, A.; Tremblay, G.; Hesto, P. Field-Effect Transistor Based on Conducting Langmuir-Blodgett Films of EDTTTF Derivatives. *Molecular Engineering* **1993**, *2* (4), 309–314. https://doi.org/10.1007/BF00999819.

(72) Iizuka, M.; Shiratori, Y.; Kuniyoshi, S.; Kudo, K.; Tanaka, K. Fabrication and Characterization of Field Effect Transistors Using Donor and Acceptor Stacked Layers. *Appl Surf Sci* **1998**, *130–132*, 914–918. https://doi.org/10.1016/S0169-4332(98)00176-7.

(73) Naraso; Nishida, J.; Ando, S.; Yamaguchi, J.; Itaka, K.; Koinuma, H.; Tada, H.; Tokito, S.; Yamashita, Y. High-Performance Organic Field-Effect Transistors Based on π-Extended Tetrathiafulvalene Derivatives. *J Am Chem Soc* **2005**, *127* (29), 10142–10143. https://doi.org/10.1021/ja051755e.

(74) Noda, B.; Wada, H.; Shibata, K.; Yoshino, T.; Katsuhara, M.; Aoyagi, I.; Mori, T.; Taguchi, T.; Kambayashi, T.; Ishikawa, K.; Takezoe, H. Crystal Structures and Transistor Properties of Phenyl-Substituted Tetrathiafulvalene Derivatives. *Nanotechnology* **2007**, *18* (42), 424009. https://doi.org/10.1088/0957-4484/18/42/424009.

(75) Sagar, A. Thin Layer Chromatography: Principle, Parts, Steps, Uses. Microbe notes. **2013**.

(76) Alsante, K. M.; Friedmann, R. C.; Hatajik, T. D.; Lohr, L. L.; Sharp, T. R.; Snyder, K. D.; Szczesny, E. J. Degradation and Impurity Analysis for Pharmaceutical Drug Candidates. *Handbook of modern pharmaceutical analysis* **2001**; pp 85–172. https://doi.org/10.1016/S0149-6395(01)80006-4.

(77) Singh, M.; Patra, S.; Singh, R. K. Common Techniques and Methods for Screening of Natural Products for Developing of Anticancer Drugs. In *Evolutionary Diversity as a Source for Anticancer Molecules*; Elsevier, **2021**; pp 323–353. https://doi.org/10.1016/B978-0-12-821710-8.00015-1.

(78) Srivastava, N.; Singh, A.; Kumari, P.; Nishad, J. H.; Gautam, V. S.; Yadav, M.; Bharti, R.; Kumar, D.; Kharwar, R. N. Advances in Extraction Technologies: Isolation and Purification of Bioactive Compounds from Biological Materials. In *Natural Bioactive Compounds*; Elsevier, **2021**; pp 409–433. https://doi.org/10.1016/B978-0-12-820655-3.00021-5.

(79) Kellner, R., Mermet, J.M., Otto, M., Valcarcel, M. and Widmer, H.M., 2004. Analytical chemistry: a modern approach to analytical science. Germany: Wiley-VCH; ISBN 3-527-30590-4. **2004**.

(80) McLafferty, F. W.; Stauffer, D. A.; Loh, S. Y.; Wesdemiotis, C. Unknown Identification Using Reference Mass Spectra. Quality Evaluation of Databases. *J Am Soc Mass Spectrom* **1999**, *10* (12), 1229–1240. https://doi.org/10.1016/S1044-0305(99)00104-X.

(81) Elgrishi, N.; Rountree, K. J.; McCarthy, B. D.; Rountree, E. S.; Eisenhart, T. T.; Dempsey, J. L. A Practical Beginner's Guide to Cyclic Voltammetry. *J Chem Educ* **2018**, *95* (2), 197–206. https://doi.org/10.1021/acs.jchemed.7b00361.

(82) Petersen, B. M.; Bjernemose, J. K.; Jeppesen, J. O. Characterization of a Byproduct in the Alkylation of DMIT: Alkylation on the Least Nucleophilic Sulfur Atom. *Eur J Inorg Chem* **2006**, *2006* (15), 3099–3104. https://doi.org/10.1002/ejic.200600213.

(83) Rabaça, S.; Oliveira, S.; Cerdeira, A. C.; Simão, D.; Santos, I. C.; Almeida, M. CyanobenzeneTTF-Type Donors; Synthesis and Characterization. *Tetrahedron Lett* **2014**, *55* (51), 6992–6997. https://doi.org/10.1016/j.tetlet.2014.10.111.

(84) Blanchard, Ph.; Sallé, M.; Duguay, G.; Jubault, M.; Gorgues, A. 2-Mono or 2,3-Bis(Hydroxymethyl)-6,7-Ethylenedithio-Tetrathiafulvalenes: New Potential Precursors of Organic Metals Endowed with Hydrogen Bonds. *Tetrahedron Lett* **1992**, *33* (19), 2685–2688. https://doi.org/10.1016/S0040-4039(00)79057-5.

(85) Steimecke, G.; Sieler, H.-J.; Kirmse, R.; Hoyer, E. 1.3-DITHIOL-2-THION-4.5-DITHIOLAT AUS SCHWEFELKOHLENSTOFF UND ALKALIMETALL. *Phosphorus. Sulfur. Relat. Elem.* **1979**, *7* (1), 49–55. https://doi.org/10.1080/03086647808069922.

(86) Lodmell, J. C.; Anderson, W. C.; Hurley, M. F.; Chambers, J. Q. High-Performance Liquid Chromatography of Electrolysis Solutions: A Study of the Reduction of Carbon Disulfide in n,n-Dimethylformamide. *Anal Chim Acta* **1981**, *129*, 49–56. https://doi.org/10.1016/S0003-2670(01)84118-0.

(87) Olk, R.-M.; Olk, B.; Dietzsch, W.; Kirmse, R.; Hoyer, E. The Chemistry of 1,3-Dithiole-2-Thione-4,5-Dithiolate (DMIT). *Coord Chem Rev* **1992**, *117*, 99–131. https://doi.org/10.1016/0010-8545(92)80021-I.

(88) Garin, D. L.; Henderson, K.; Bretherick, L. *Handbook of Reactive Chemical Hazards*; UTC, **1941**; Vol. 35. https://pubs.acs.org/sharingguidelines.

(89) Corsaro, A.; Pistarà, V. Conversion of the Thiocarbonyl Group into the Carbonyl Group. *Tetrahedron* **1998**, *54* (50), 15027–15062. https://doi.org/10.1016/S0040-4020(98)00880-1.

(90) Liu, G.; Yu, W.; Xue, G.; Liu, Z.; Fang, Q. 4,5-Bis(2-Cyanoethylthio)-1,3-Dithiol-2-One. *Acta Crystallogr Sect E Struct Rep Online* **2002**, *58* (5), o514–o516. https://doi.org/10.1107/S1600536802005445.

(91) Krief, A. Syntheses of Tetraheterofulvalenes and of Vinylene Triheterocarbonates-Strategy and Practice. *Tetrahedron* **1986**, *42* (5), 1204–1252. https://doi.org/10.1016/S0040-4020(01)87343-9.

(92) Hansen, T. K.; Lakshmikantham, M. V.; Cava, M. P.; Metzger, R. M.; Becher, J. Synthesis and Properties of New .PI.-Donor Sulfur Heterocycles. *J Org Chem* **1991**, *56* (8), 2720–2722. https://doi.org/10.1021/jo00008a027.

(93) Binet, L.; Fabre, J. M.; Montginoul, C.; Simonsen, K. B.; Becher, J. Preparation and Chemistry of New Unsymmetrically Substituted Tetrachalcogenofulvalenes Bearing CN(CH2)2X and HO(CH2)2X Groups (X = S or Se). *J Chem Soc Perkin 1* **1996**, No. 8, 783. https://doi.org/10.1039/p19960000783.

(94) Narita, M.; Pittman, Jr. , C. U. Preparation of Tetrathiafulvalenes (TTF) and Their Selenium Analogs -Tetraselenafulvalenes (TSeF). *Synthesis* **1976**, 489–514. https://doi.org/10.1055/s-1976-24099.

(95) Corey, E. J.; Märkl, G. Generation of Phosphite Ylides from Trithiocarbonates and Trimethyl Phosphite and Their Application to the Extension of Carbon Chains. *Tetrahedron Lett* **1967**, *8* (33), 3201–3204. https://doi.org/10.1016/S0040-4039(01)89899-3.

(96) Miles, M. G.; Wager, J. S.; Wilson, J. D.; Siedle, A. R. Reactions of 4,5-Dicyano-1,3-Dithiole-2-Thione and -1,3-Dithiol-2-One with Tervalent Phosphorus Compounds. *J Org Chem* **1975**, *40* (18), 2577–2582. https://doi.org/10.1021/jo00906a001.

(97) Saneyoshi, H.; Seio, K.; Sekine, M. A General Method for the Synthesis of 2‘-O-Cyanoethylated Oligoribonucleotides Having Promising Hybridization Affinity for DNA and RNA and Enhanced Nuclease Resistance. *J Org Chem* **2005**, *70* (25), 10453–10460. https://doi.org/10.1021/jo051741r.

(98) Horváth, A. Hofmann-Type Elimination in the Efficient *N* -Alkylation of Azoles: Imidazole and Benzimidazole. *Synthesis* **1994**, 102–106. https://doi.org/10.1055/s-1994-25414.

(99) De Los Santos Lagao, B.-J. LAB 1: ELIMINATION REACTION 1 An Investigative Analysis of Products of Elimination Reactions Using Gas Chromatography.

(100) Becher, J.; Li, Z.-T.; Blanchard, P.; Svenstrup, N.; Lau, J.; Nielsen, M. B.; Leriche, P. Tetrathiafulvalenes in Macrocyclic and Supramolecular Chemistry. *Pure. Appl. Chem* **1997**, *69* (3), 465–470. https://doi.org/10.1351/pac199769030465.

(101) Bryce, M. R. Recent Progress on Conducting Organic Charge-Transfer Salts. *Chem Soc Rev* **1991**, *20* (3), 355. https://doi.org/10.1039/cs9912000355.

(102) Yu, L.-J.; Coote, M. L. Electrostatic Switching between S_N1 and S_N2 Pathways. *J Phys Chem A* **2019**, *123* (2), 582–589. https://doi.org/10.1021/acs.jpca.8b11579.

(103) Adero, P. O.; Amarasekara, H.; Wen, P.; Bohé, L.; Crich, D. The Experimental Evidence in Support of Glycosylation Mechanisms at the S_N1–S_N2 Interface. *Chem Rev* **2018**, *118* (17), 8242–8284. https://doi.org/10.1021/acs.chemrev.8b00083.

(104) Batsanov, A. S.; Bryce, M. R.; Chesney, A.; Howard, J. A. K.; John, D. E.; Moore, A. J.; Wood, C. L.; Gershtenman, H.; Becker, J. Y.; Khodorkovsky, V. Y.; Ellern, A.; Bernstein, J.; Perepichka, I. F.; Rotello, V.; Gray, M.; Cuello, A. O. Synthesis and Crystal Engineering of New Halogenated Tetrathiafulvalene (TTF) Derivatives and Their Charge Transfer Complexes and Radical Ion Salts. *J Mater Chem* **2001**, *11* (9), 2181–2191. https://doi.org/10.1039/b101866n.

(105) -Liedholm, B., Copper (I) Catalysed Replacement of Iodine by Chloride Ion _. *Acta Chem. Scand.* **1971**. 25(1).

(106) Siwach, A.; Verma, P. K. Synthesis and Therapeutic Potential of Imidazole Containing Compounds. *BMC Chem* **2021**, *15* (1), 12. https://doi.org/10.1186/s13065-020-00730-1.

(107) Kumar, M.; Kumar, D.; Raj, V. Studies on Imidazole and Its Derivatives with Particular Emphasis on Their Chemical/Biological Applications as Bioactive

Molecules/Intermediated to Bioactive Molecule. *Curr Synth. Syst. Biol* **2017**, *05* (01). https://doi.org/10.4172/2332-0737.1000135.

(108) Gueiffier, A.; Mavel, S.; Lhassani, M.; Elhakmaoui, A.; Snoeck, R.; Andrei, G.; Chavignon, O.; Teulade, J.-C.; Witvrouw, M.; Balzarini, J.; De Clercq, E.; Chapat, J.-P. Synthesis of Imidazo[1,2- *a*]Pyridines as Antiviral Agents. *J Med Chem* **1998**, *41* (25), 5108–5112. https://doi.org/10.1021/jm981051y.

(109) Verevkin, S. P.; Zaitsau, D. H.; Emel'yanenko, V. N.; Paulechka, Y. U.; Blokhin, A. V.; Bazyleva, A. B.; Kabo, G. J. Thermodynamics of Ionic Liquids Precursors: 1-Methylimidazole. *J Phys Chem B* **2011**, *115* (15), 4404–4411. https://doi.org/10.1021/jp201752j.

(110) Gomar-Nadal, E.; Rovira, C.; Amabilino, D. B. Synthesis of Optically Active Amphiphilic Tetrathiafulvalene Derivatives. *Tetrahedron* **2006**, *62* (14), 3370–3379. https://doi.org/10.1016/j.tet.2006.01.056.

(111) Khodorkovsky, V., Edzifna, A. and Neilands, O. Electron-donating ability of tetrathiafulvalene derivatives investigated by cyclic voltammetry. *Journal of Molecular Electronics* **1989**, *5*(1). 33-36.

(112) Marshallsay, G. J., Synthesis of highly functionalised tetrathiafulvalenes, Durham theses, Durham University. Available at Durham E-Theses. **1994** Online: http://etheses.dur.ac.uk/5505/.

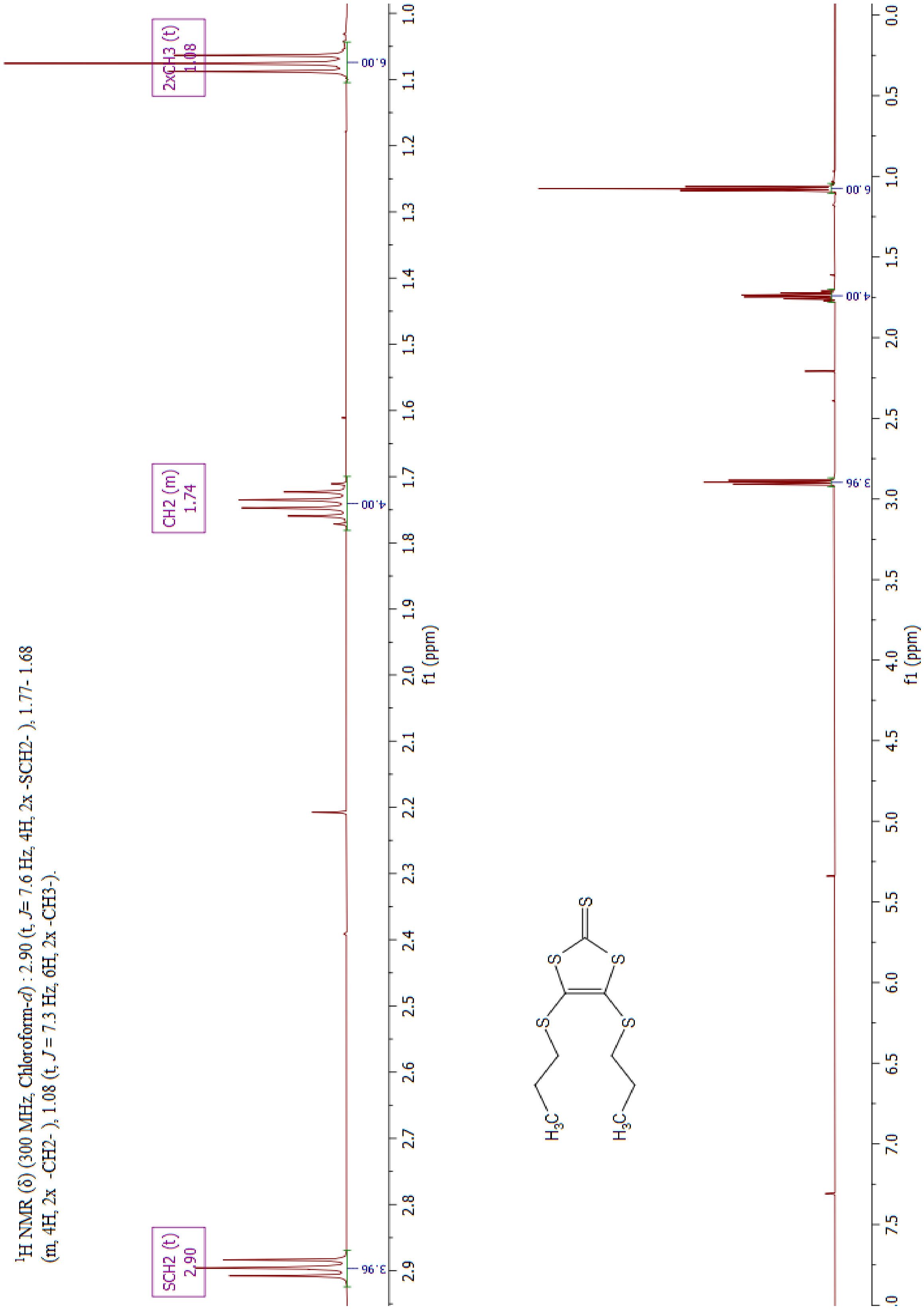
(113) Charlton, A.; Underhill, A. E.; Williams, G.; Kalaji, M.; Murphy, P. J.; Hibbs, D. E.; Hursthouse, M. B.; Malik, K. M. A. 4,4′,5,5′-Tetrakis(2-Thienyl)Tetrathiafulvalene [TT-TTF]: Synthesis and First X-Ray Crystal Structure of a Thiophene-Substituted TTF Electron Donor. *Chem. Commun.* **1996**, No. 21, 2423–2424. https://doi.org/10.1039/CC9960002423.

(114) Mizuno, M.; Garito, A. F.; Cava, M. P. 'Organic Metals': Alkylthio Substitution Effects in Tetrathiafulvalene–Tetracyanoquinodimethane Charge-Transfer Complexes. *J. Chem. Soc., Chem. Commun.* **1978**, No. 1, 18–19. https://doi.org/10.1039/C39780000018.

Appendices

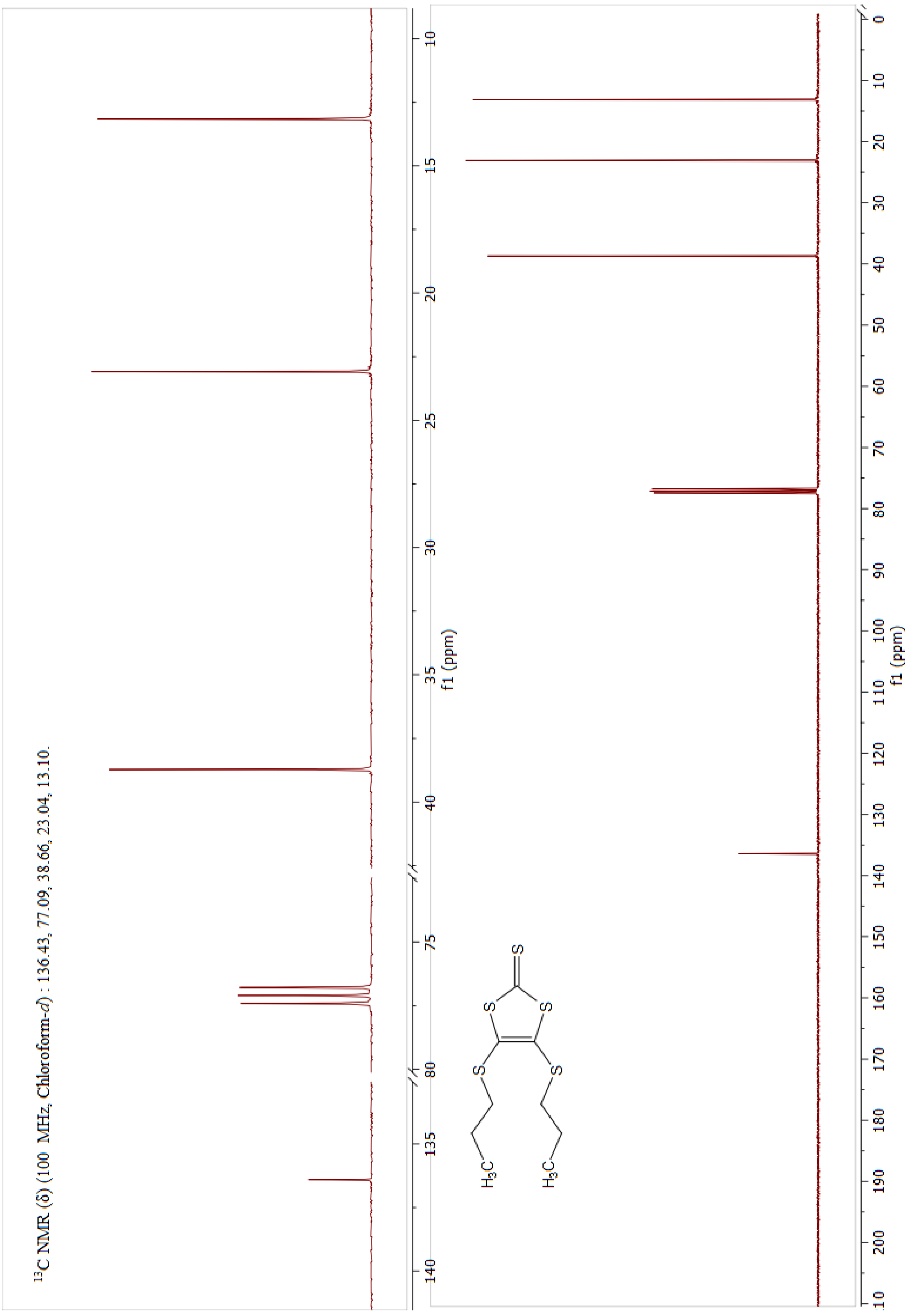
^{1}H NMR, ^{13}C NMR and MS spectra

^{1H} NMR and ^{13}C NMR spectra



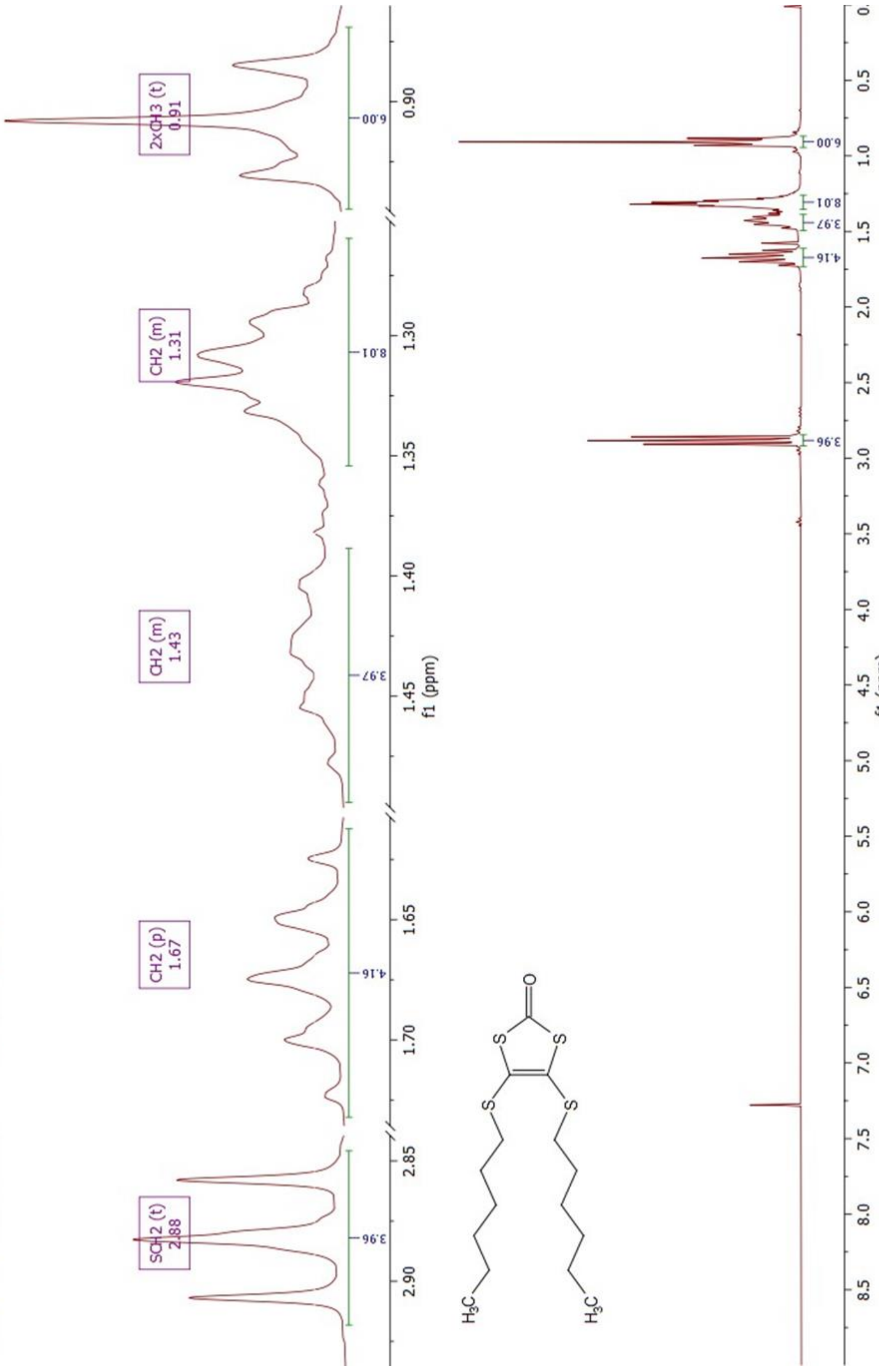
^{1}H NMR (δ) (300 MHz, Chloroform-*d*) : 2.90 (t, *J*= 7.6 Hz, 4H, 2x -SCH2-), 1.77- 1.68 (m, 4H, 2x -CH2-), 1.08 (t, *J* = 7.3 Hz, 6H, 2x -CH3-).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(propylthio)-1,3-dithiole-2-thione **11**


^{13}C NMR (δ) (100 MHz, Chloroform-*d*) : 136.43, 77.09, 38.66, 23.04, 13.10.

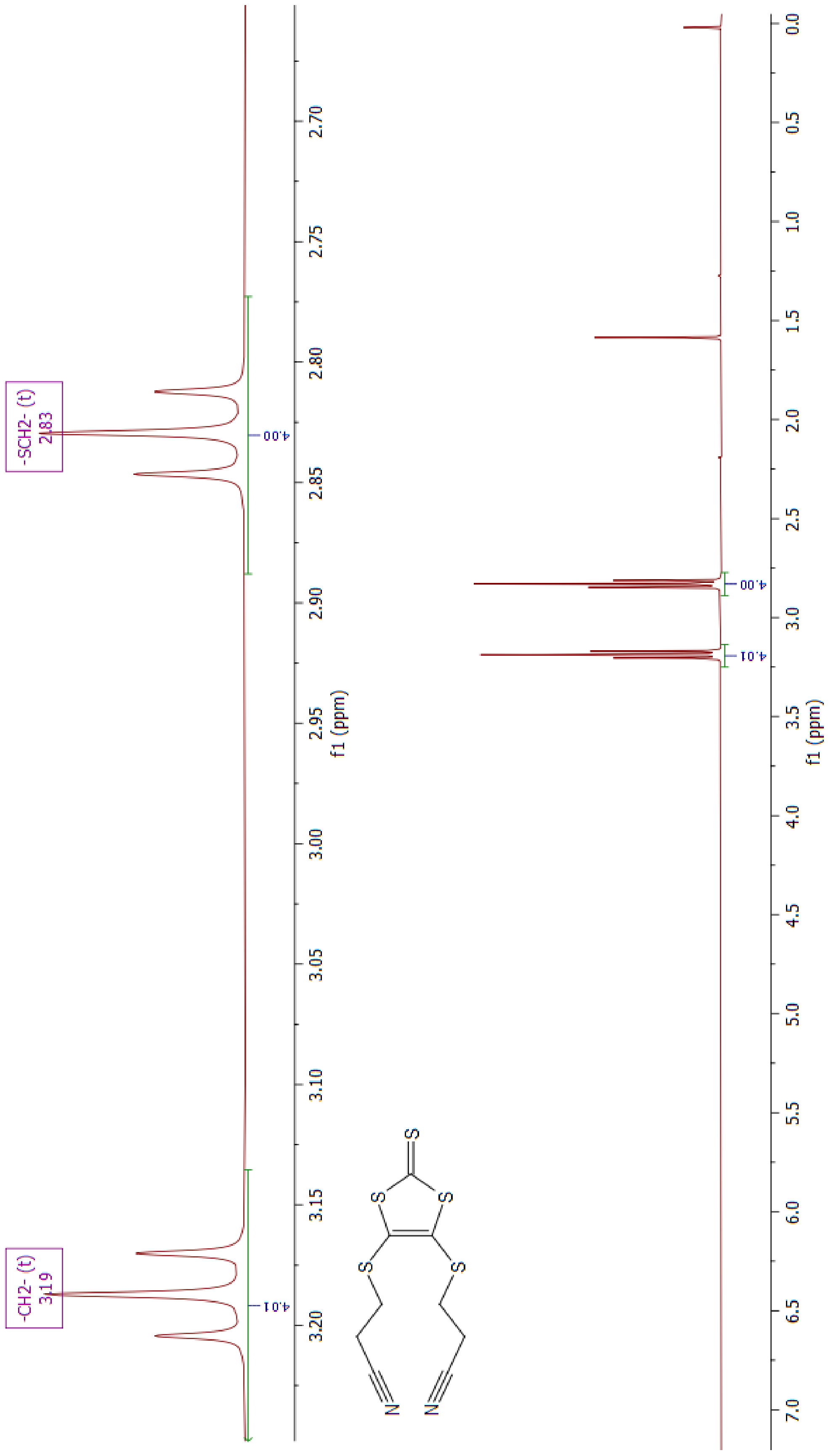
^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(propylthio)-1,3-dithiole-2-thione **11**

^1H NMR (δ) (300.18 MHz, Chloroform-*d*) : 2.88 (t, *J* = 7.0 Hz, 4H, -SCH_2-), 1.67 (p, *J* = 8.2 Hz, 4H, -CH_2-), 1.49 – 1.38 (m, 4H, -CH_2-), 1.34 – 1.27 (m, 8H, -CH_2-), 0.91 (t, *J* = 7.0 Hz, 6H, 2x -CH_3).

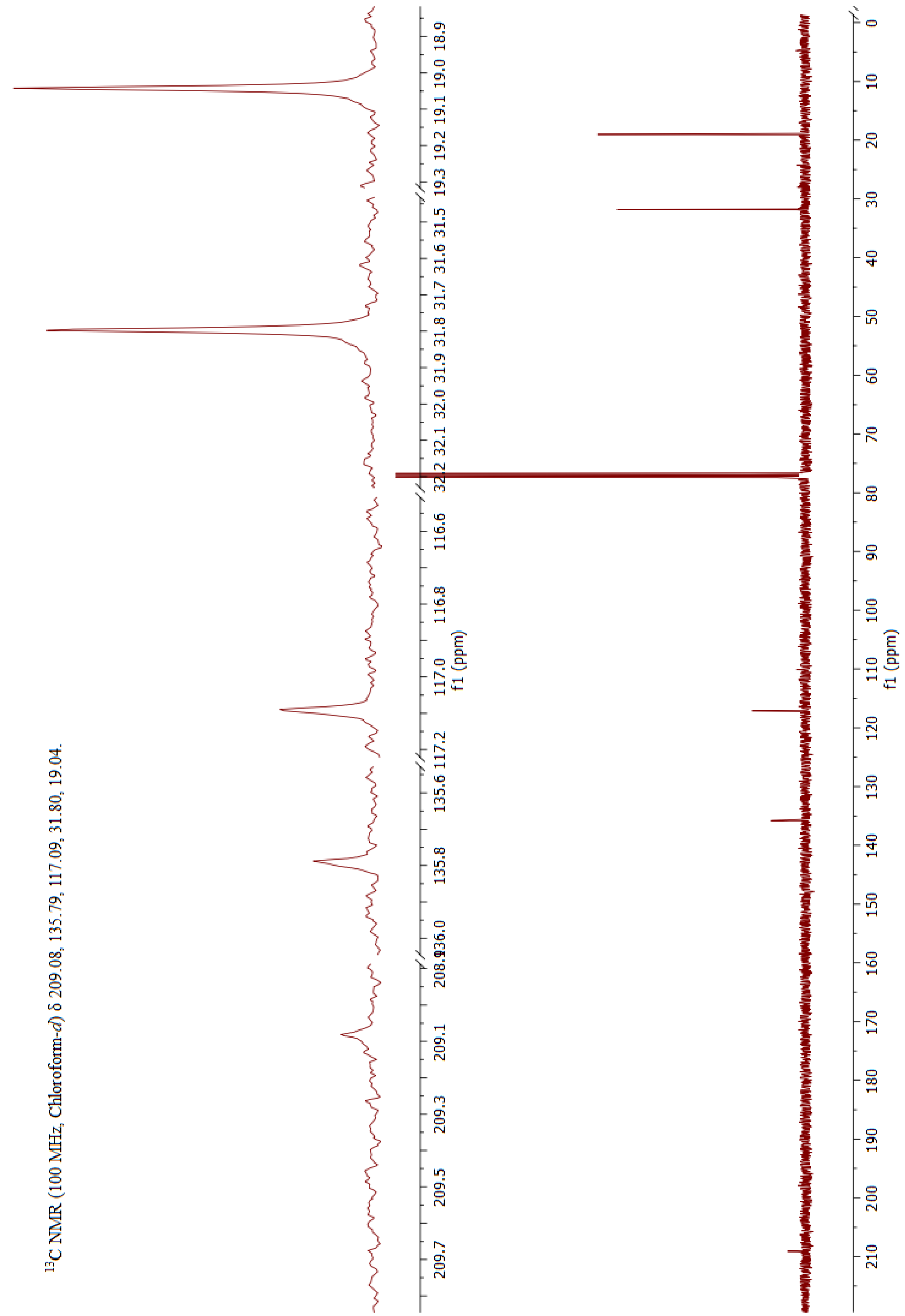


^1H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(hexylthio)-1,3-dithiole-2-thione **11**

^1H NMR (400 MHz, Chloroform-*d*) δ 3.19 (t, *J* = 6.8 Hz, 4H, CH2 x2), 2.83 (t, *J* = 6.9 Hz, 4H, SCH2 x2).

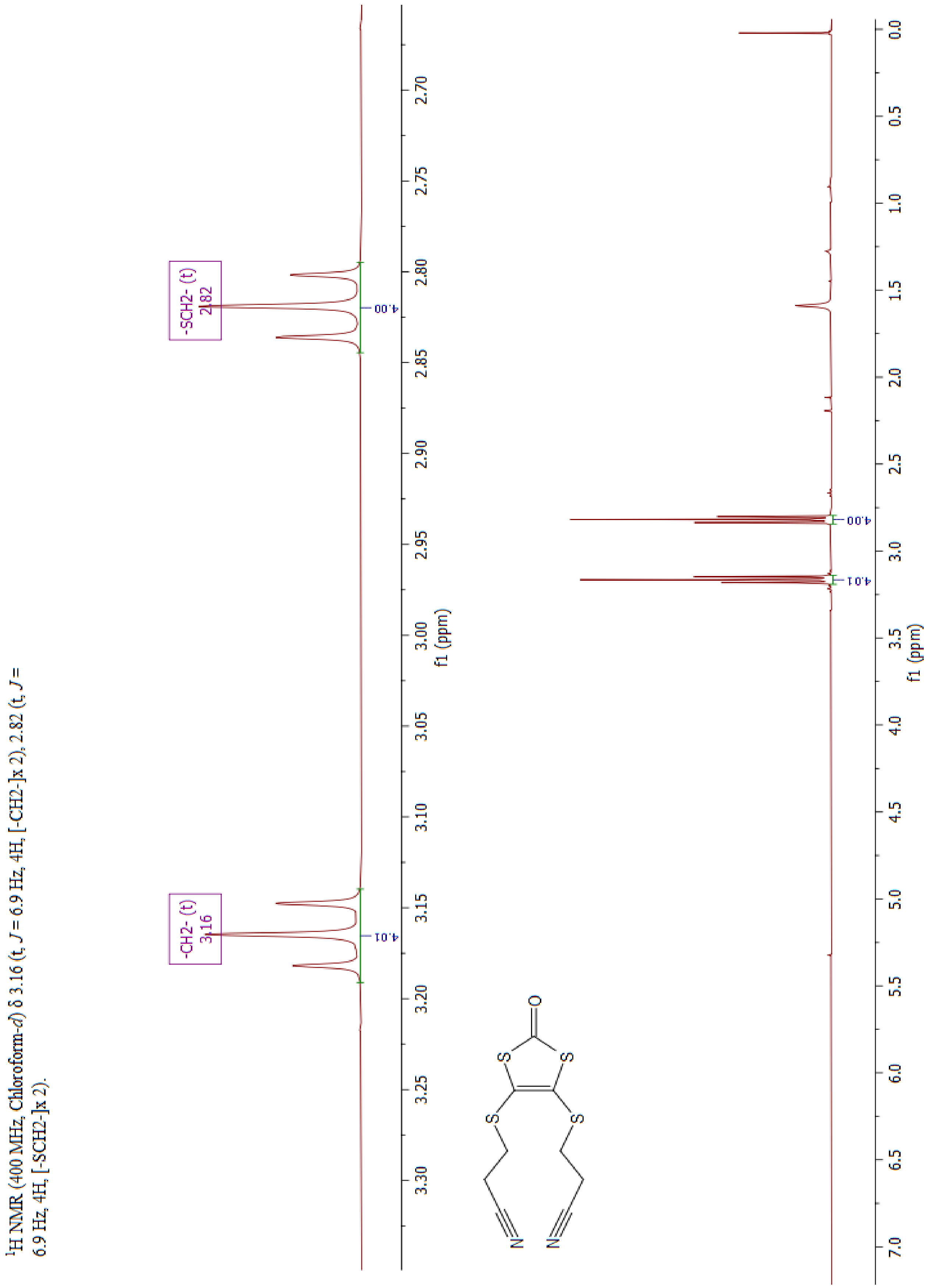


^1H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-thione **12**



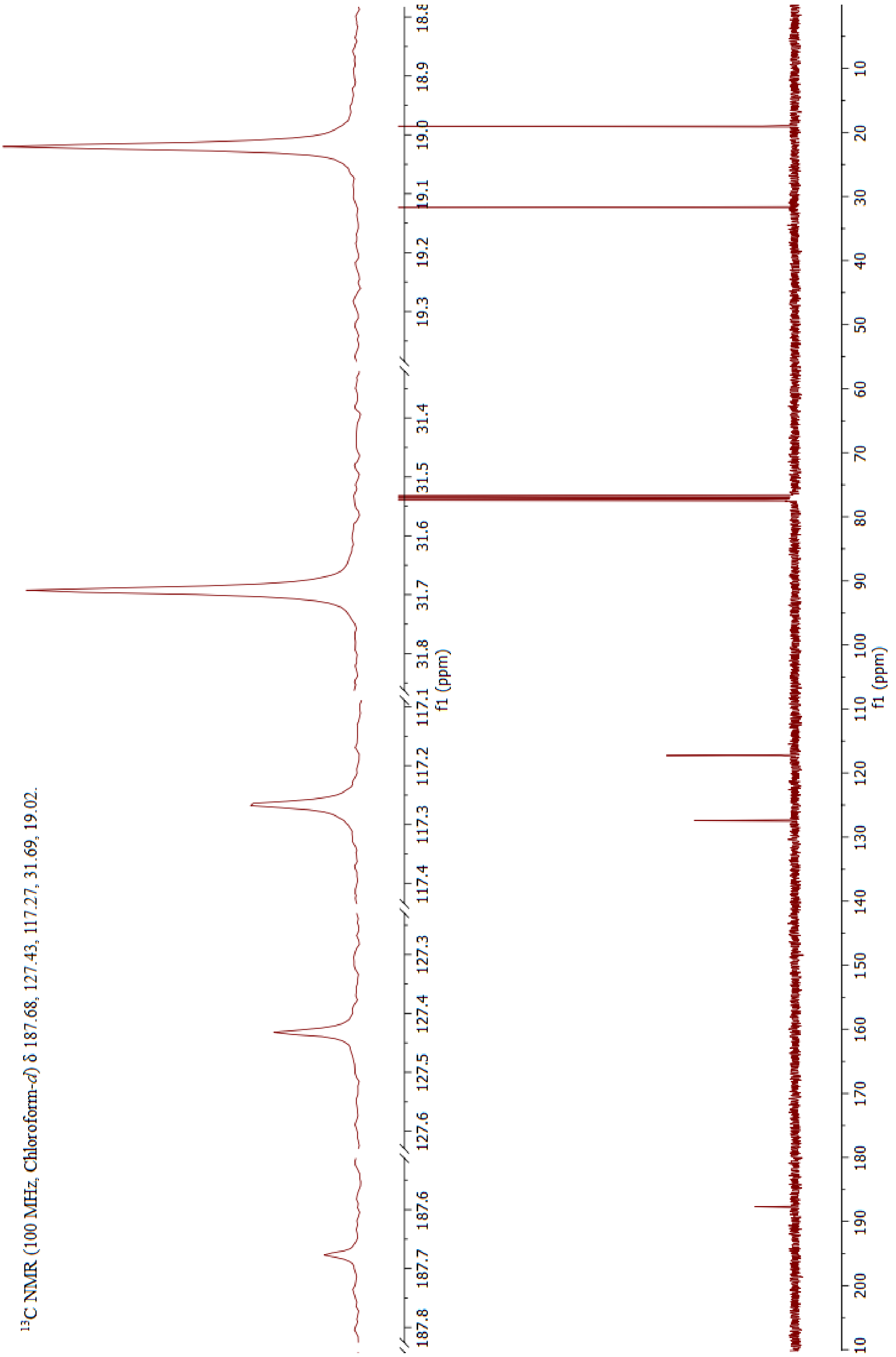
^{13}C NMR (100 MHz, Chloroform-*d*) δ 209.08, 135.79, 117.09, 31.80, 19.04.

^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-thione **12**

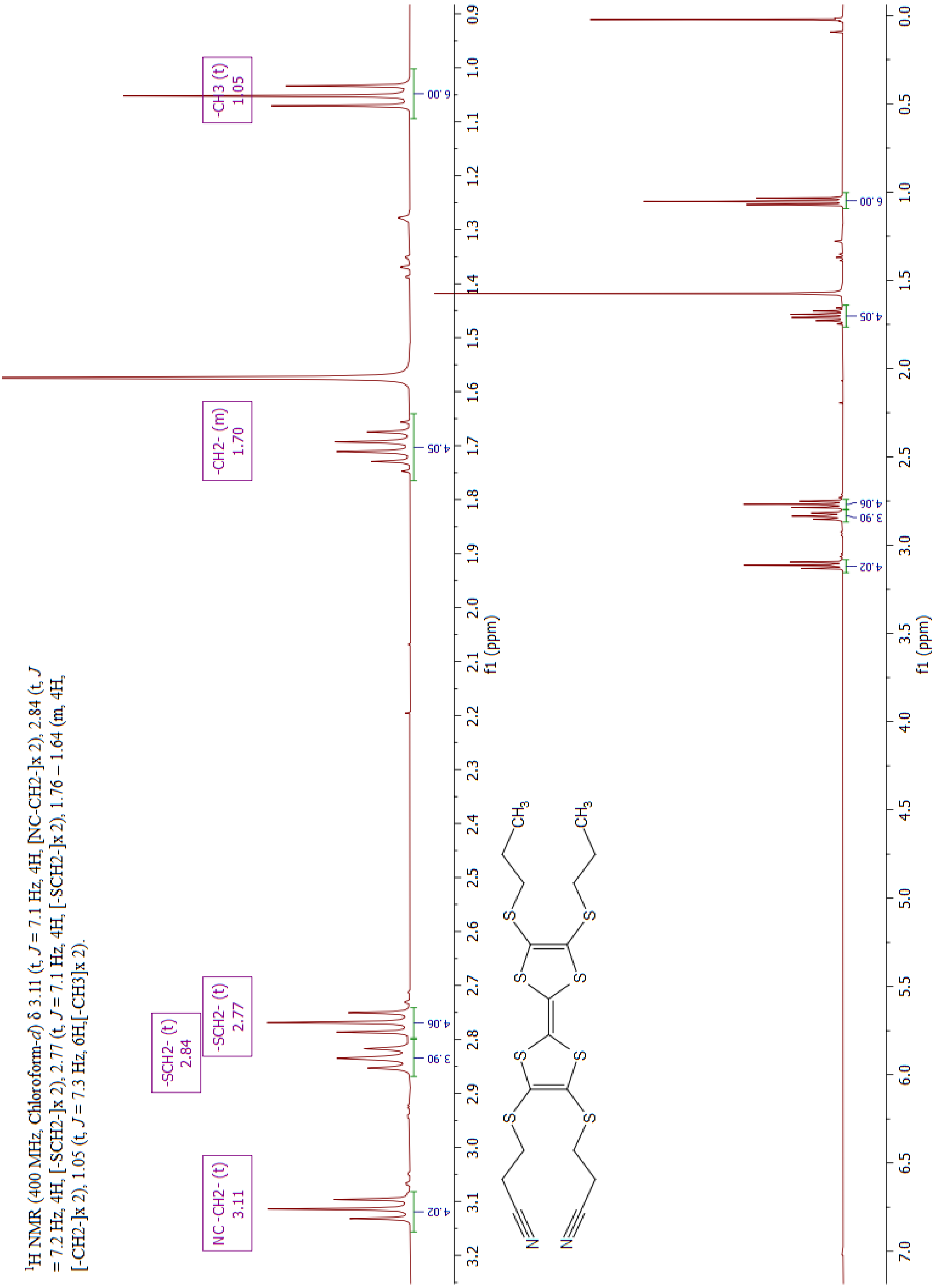


^1H NMR (400 MHz, Chloroform-*d*) δ 3.16 (t, *J* = 6.9 Hz, 4H, [-CH2-]x 2), 2.82 (t, *J* = 6.9 Hz, 4H, [-SCH2-]x 2).

^1H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16**



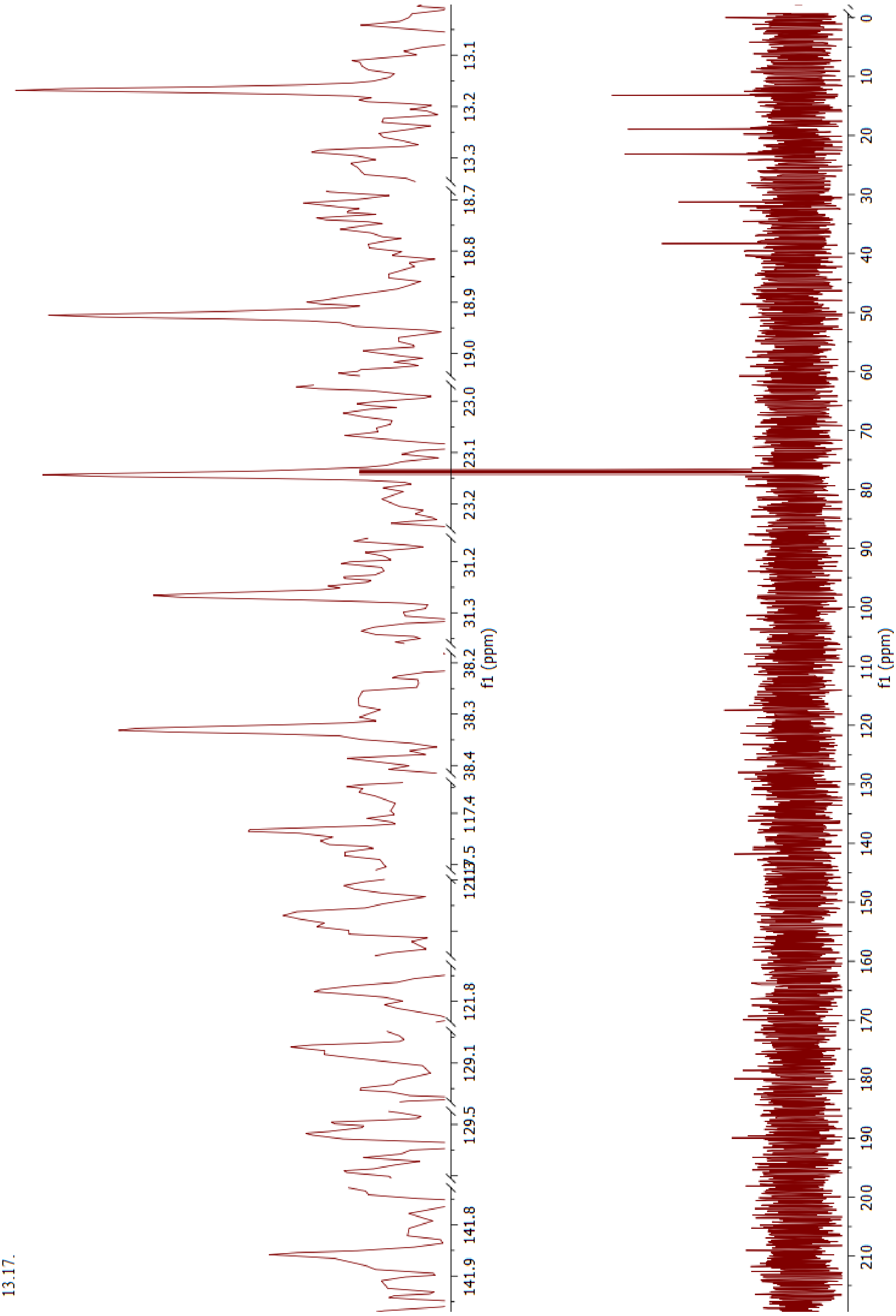
^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(cyanoethylthio)-1,3-dithiole-2-one **16**



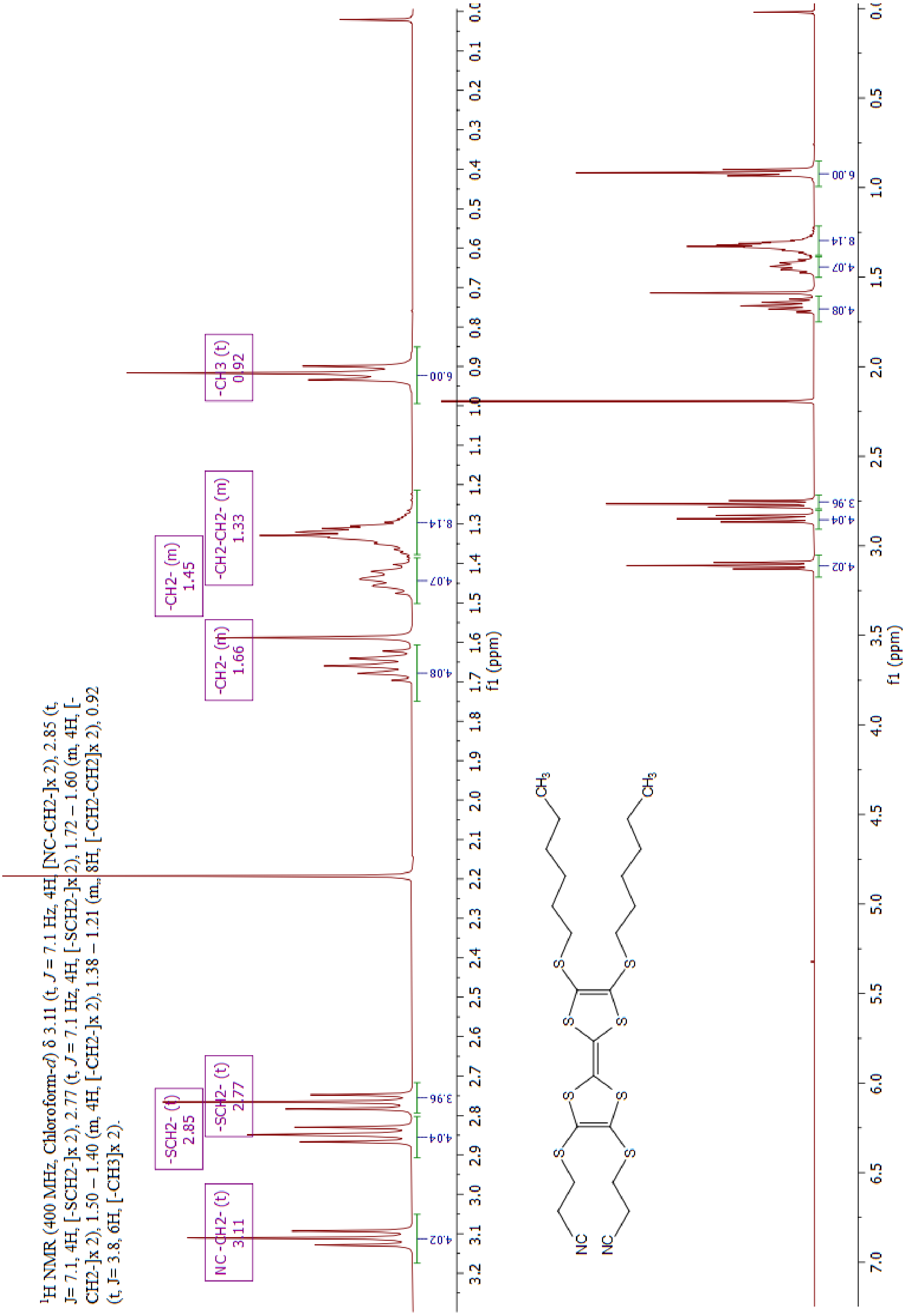
^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.11 (t, *J* = 7.1 Hz, 4H, [NC-CH2-]x 2), 2.84 (t, *J* = 7.2 Hz, 4H, [-SCH2-]x 2), 2.77 (t, *J* = 7.1 Hz, 4H, [-SCH2-]x 2), 1.76 – 1.64 (m, 4H, [-CH2-]x 2), 1.05 (t, *J* = 7.3 Hz, 6H,[-CH3]x 2).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 2,3-bis(cyanoethylthio)-6,7-bis(propylthio)tetrathiafulvalene **17a**

^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.9, 129.5, 118.5, 38.33, 31.27, 23.14, 18.93, 13.17.

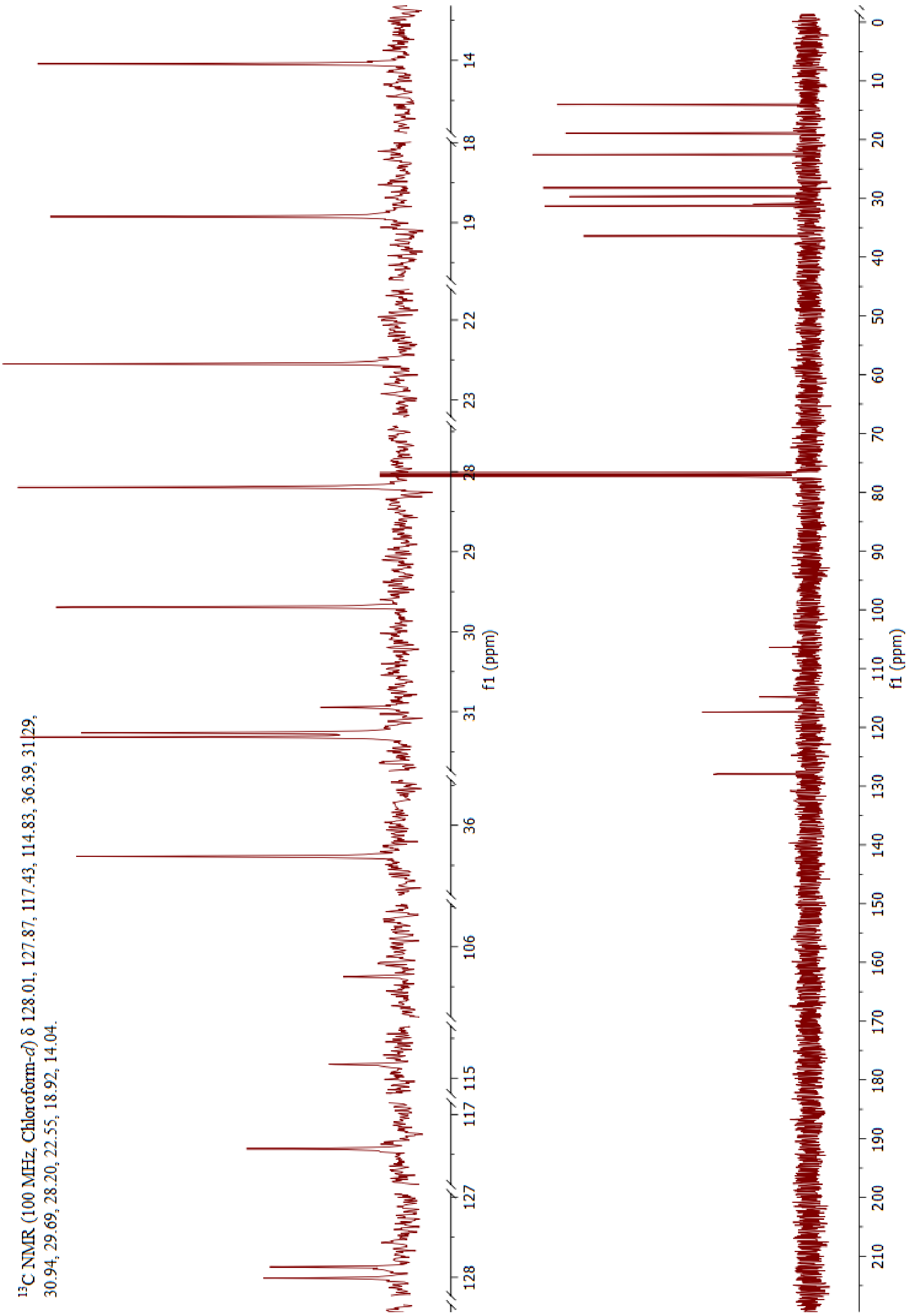


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 2,3-bis(cyanoethylthio)-6,7-bis(propylthio)tetrathiafulvalene **17a**

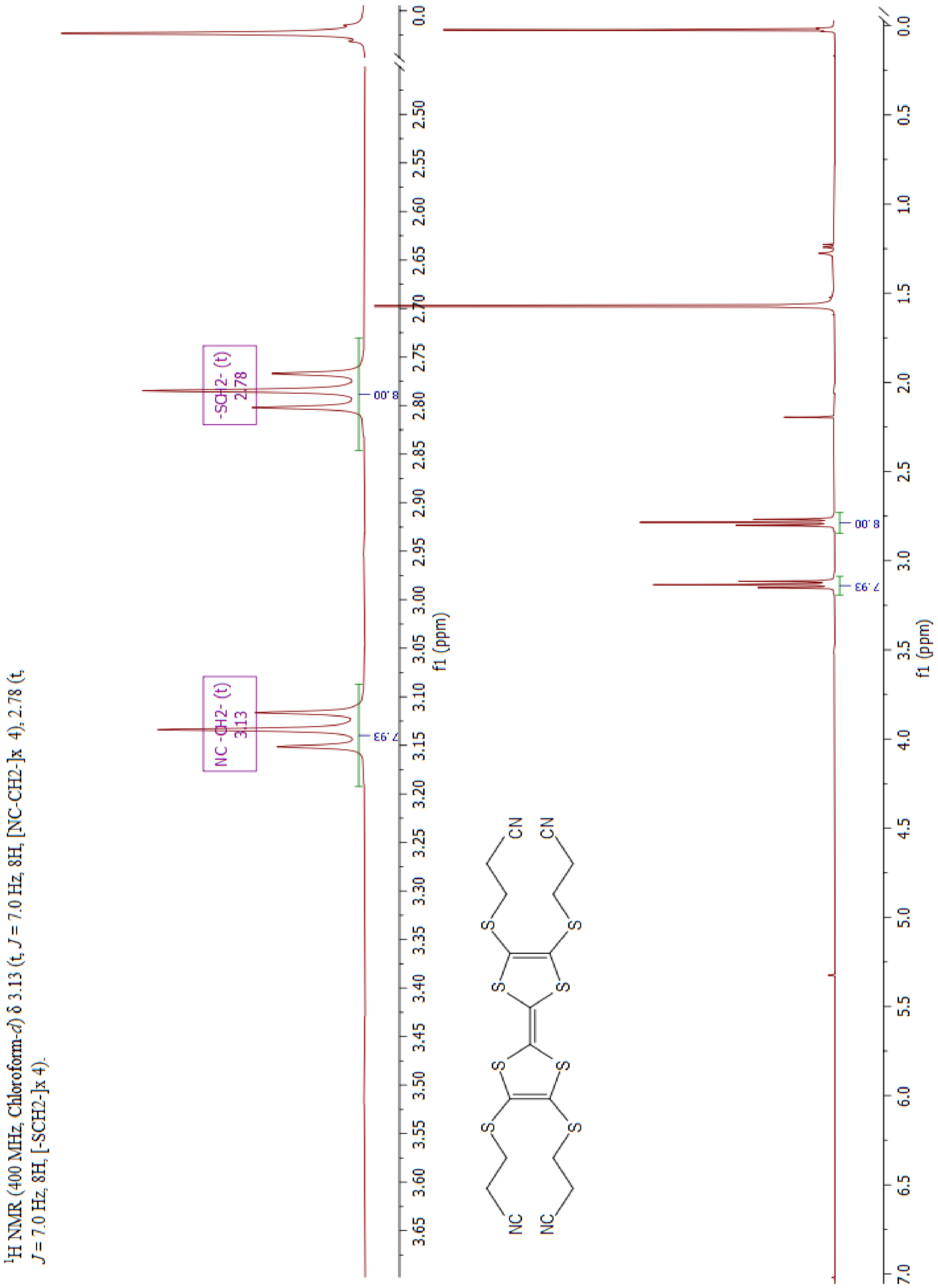


^1H NMR (400 MHz, Chloroform-*d*) δ 3.11 (t, *J* = 7.1 Hz, 4H, [NC-CH2-]x 2), 2.85 (t, J= 7.1, 4H, [-SCH2-]x 2), 2.77 (t, *J* = 7.1 Hz, 4H, [-SCH2-]x 2), 1.72 – 1.60 (m, 4H, [-CH2-]x 2), 1.50 – 1.40 (m, 4H, [-CH2-]x 2), 1.38 – 1.21 (m, 8H, [-CH2-CH2]x 2), 0.92 (t, J= 3.8, 6H, [-CH3]x 2).

^1H NMR (300 MHz, Chloroform-d) spectrum of 2,3-bis(cyanoethylthio)-6,7-bis(hexylthio)tetrathiafulvalene **17b**

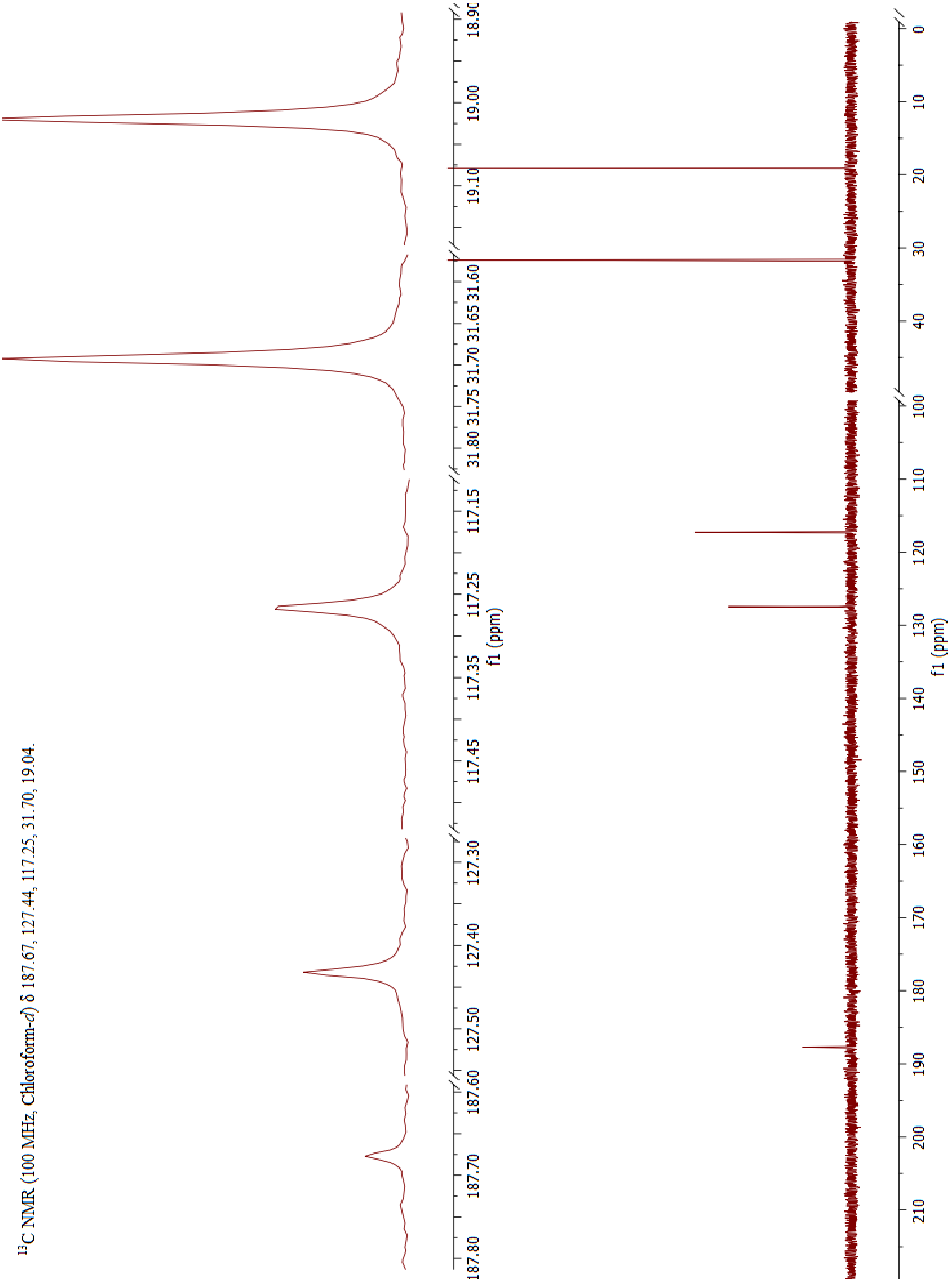


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 2,3-bis(cyanoethylthio)-6,7-bis(hexylthio)tetrathiafulvalene **17b**



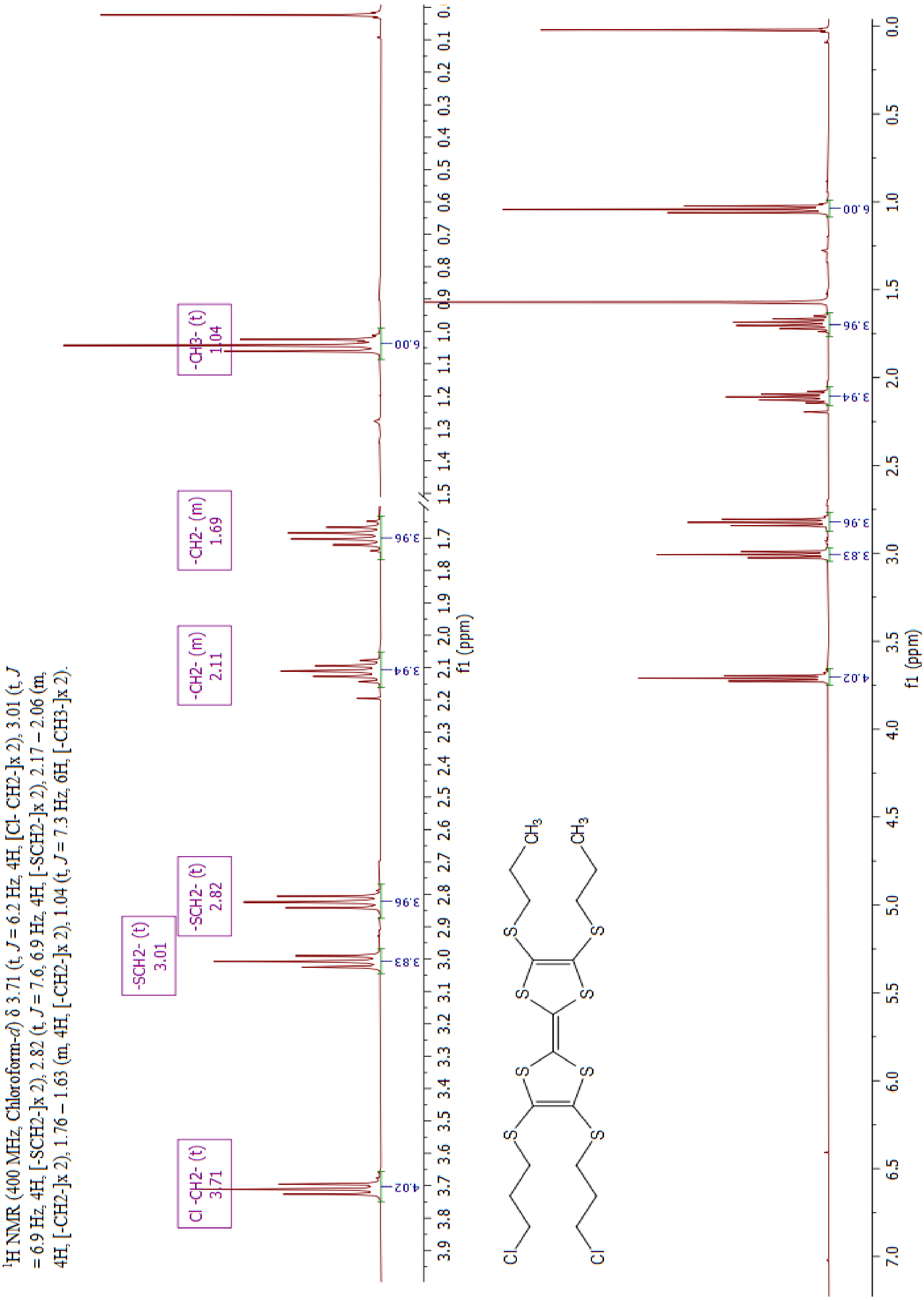
^1H NMR (400 MHz, Chloroform-*d*) δ 3.13 (t, *J* = 7.0 Hz, 8H, [NC-CH2-]x 4), 2.78 (t, *J* = 7.0 Hz, 8H, [-SCH2-]x 4).

^1H NMR (300 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(2'cyanoethylthio)tetrathiafulvalene **18**



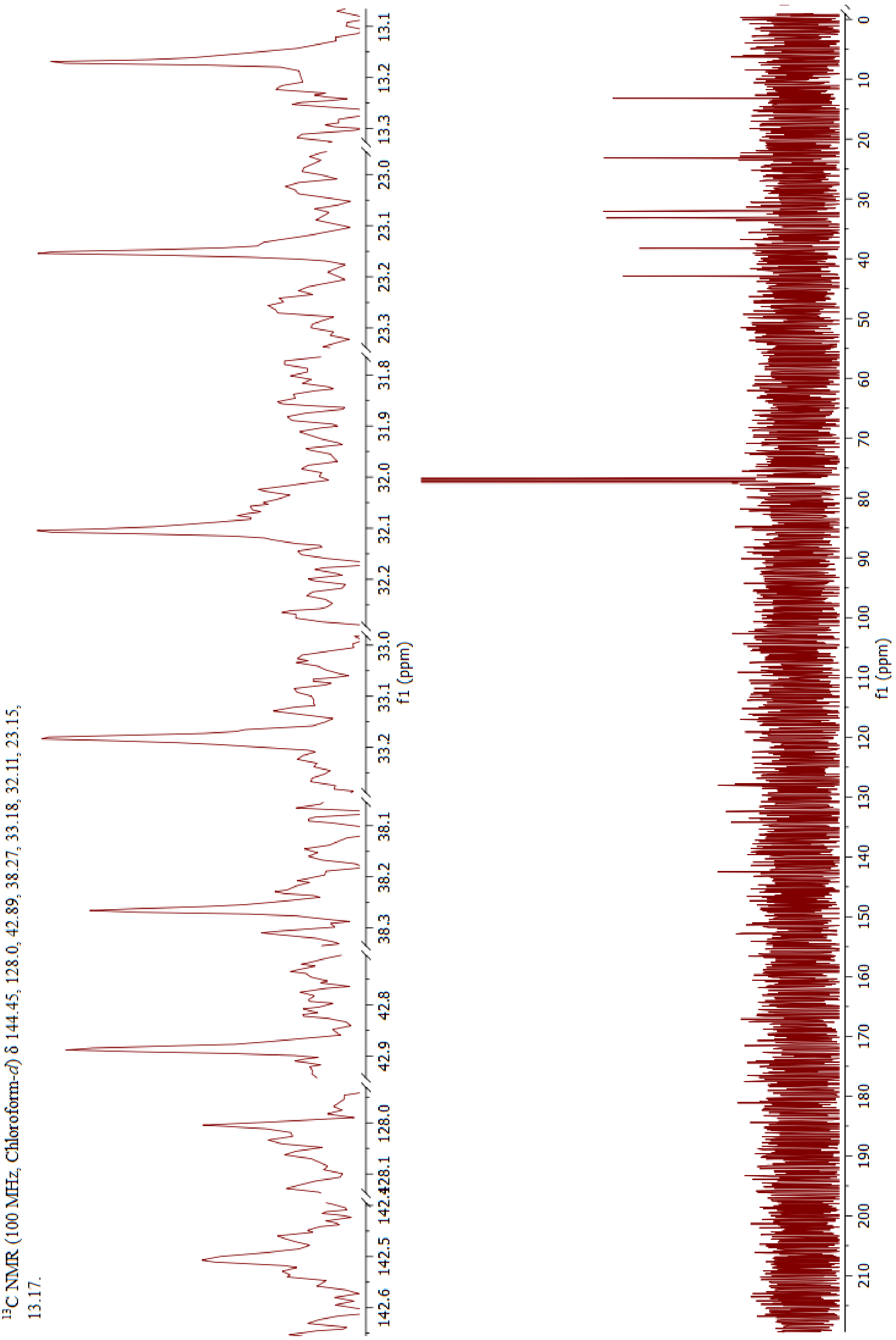
^{13}C NMR (100 MHz, Chloroform-*d*) δ 187.67, 127.44, 117.25, 31.70, 19.04.

^{13}C NMR (100 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(2’cyanoethylthio)tetrathiafulvalene **18**



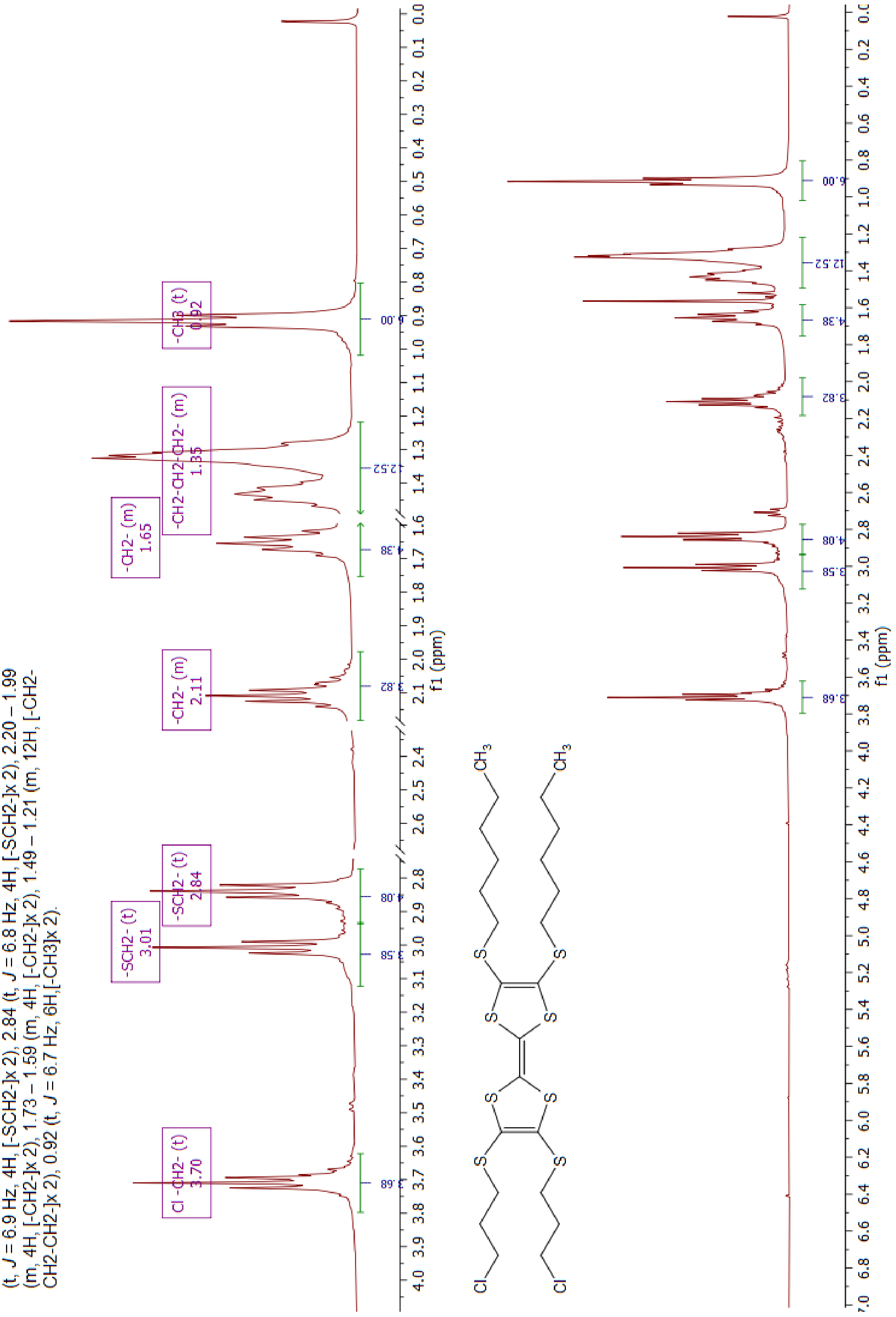
^1H NMR (400 MHz, Chloroform-*d*) δ 3.71 (t, *J* = 6.2 Hz, 4H, [Cl- CH2-]x 2), 3.01 (t, *J* = 6.9 Hz, 4H, [-SCH2-]x 2), 2.82 (t, *J* = 7.6, 6.9 Hz, 4H, [-SCH2-]x 2), 2.17 – 2.06 (m, 4H, [-CH2-]x 2), 1.76 – 1.63 (m, 4H, [-CH2-]x 2), 1.04 (t, *J* = 7.3 Hz, 6H, [-CH3-]x 2).

^1H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(3’-chloropropylthio)-6,7-bis(propylthio)tetrathiafulvalene **20a**



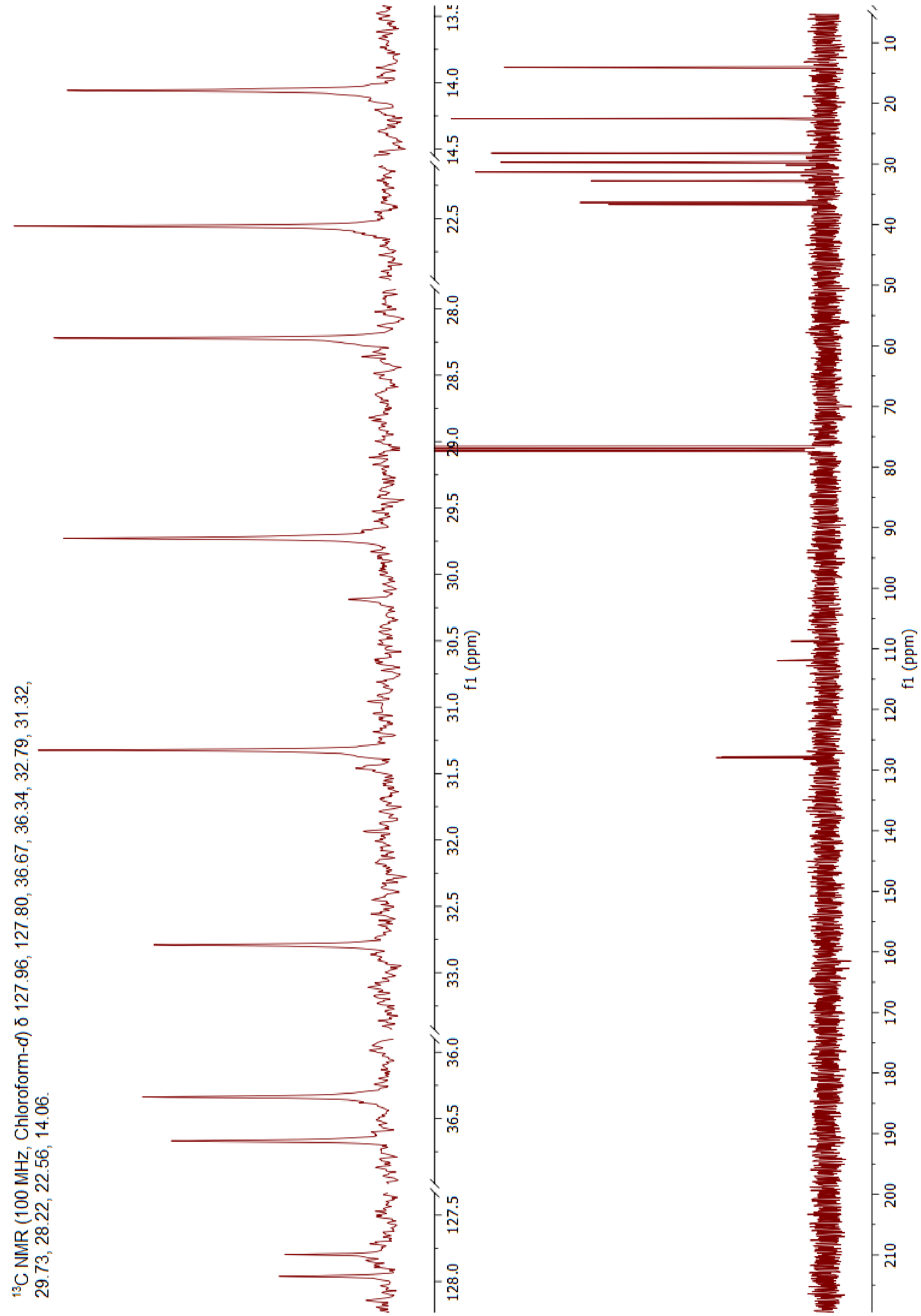
^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.45, 128.0, 42.89, 38.27, 33.18, 32.11, 23.15, 13.17.

^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(3'-chloropropylthio)-6,7-bis(propylthio)tetrathiafulvalene **20a**

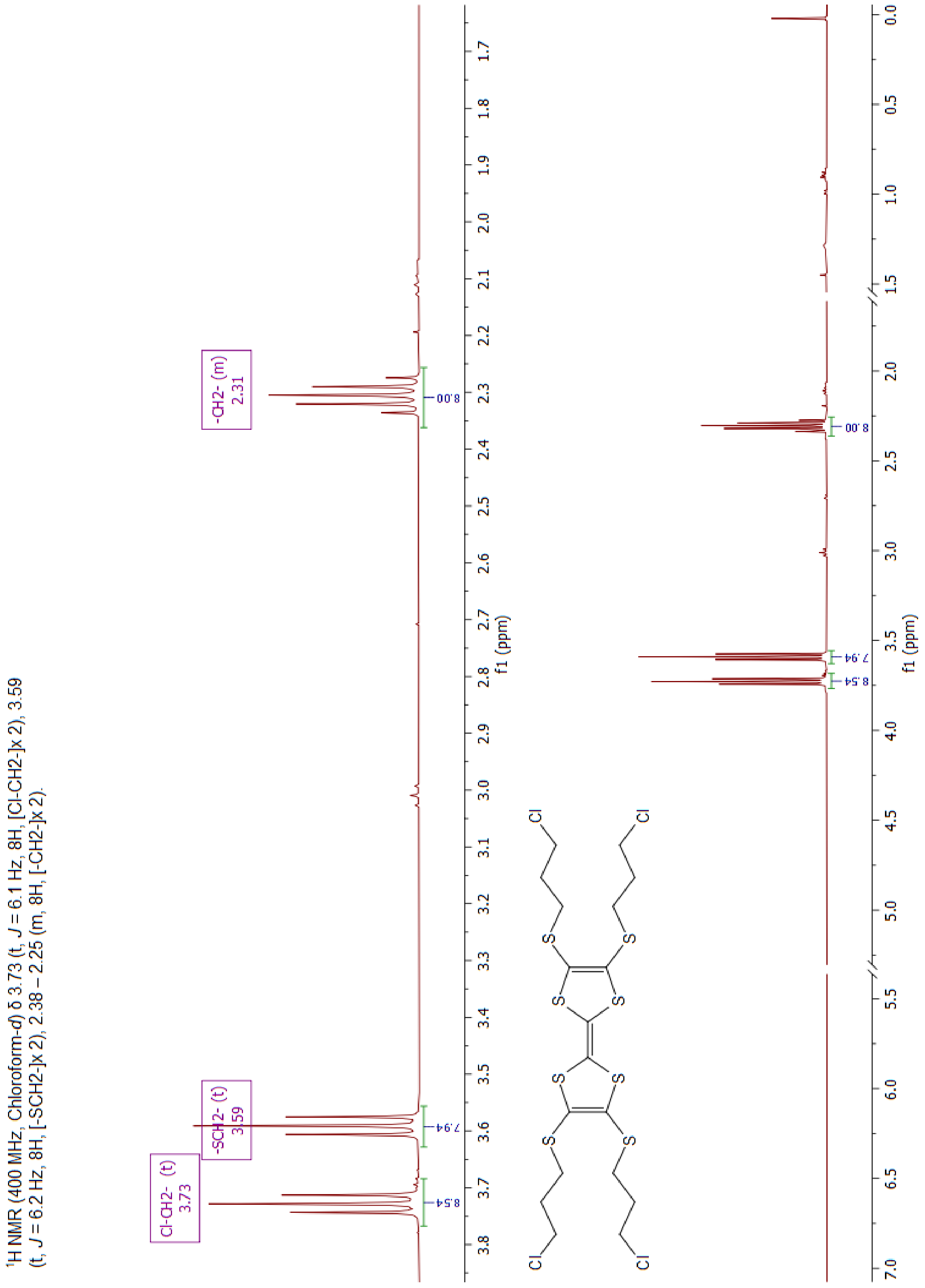


^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.70 (t, *J* = 6.2 Hz, 4H, [Cl-CH2-]x 2), 3.01 (t, *J* = 6.9 Hz, 4H, [-SCH2-]x 2), 2.84 (t, *J* = 6.8 Hz, 4H, [-SCH2-]x 2), 2.20 – 1.99 (m, 4H, [-CH2-]x 2), 1.73 – 1.59 (m, 4H, [-CH2-]x 2), 1.49 – 1.21 (m, 12H, [-CH2-CH2-CH2-]x 2), 0.92 (t, *J* = 6.7 Hz, 6H,[-CH3]x 2).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(3'-chloropropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **20b**

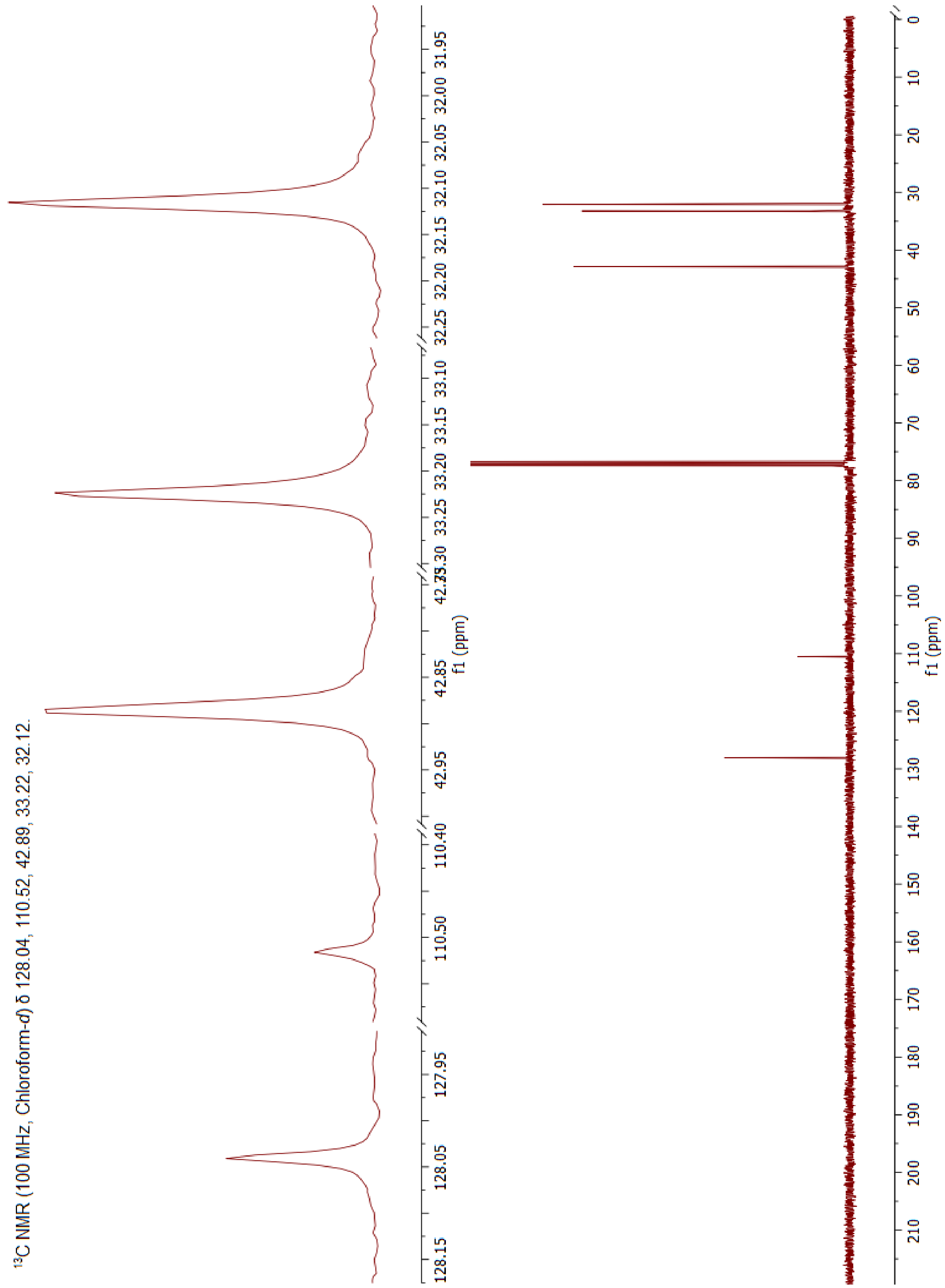


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(3'-chloropropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **20b**

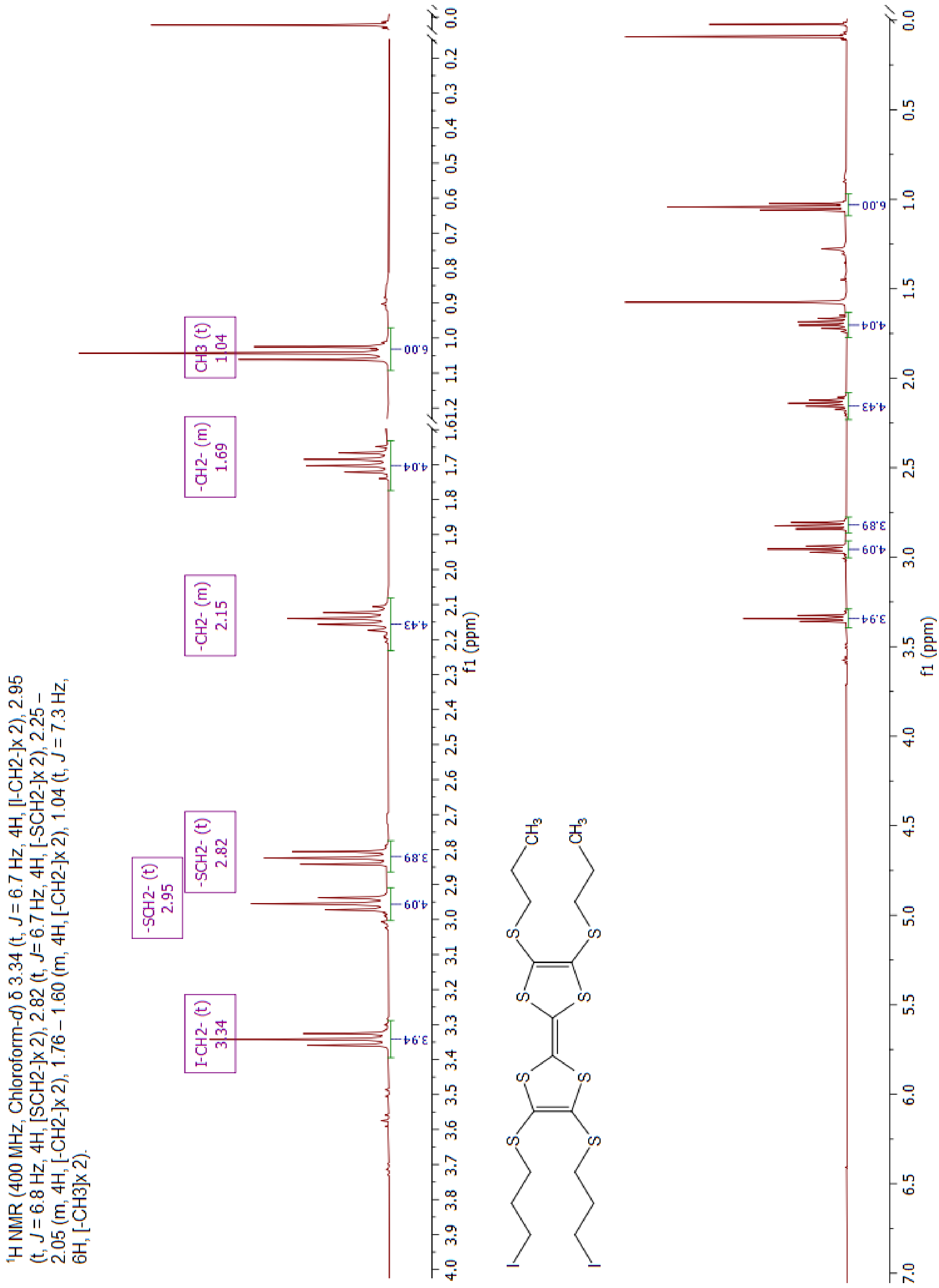


^1H NMR (400 MHz, Chloroform-*d*) δ 3.73 (t, *J* = 6.1 Hz, 8H, [Cl-CH2-]x 2), 3.59 (t, *J* = 6.2 Hz, 8H, [-SCH2-]x 2), 2.38 – 2.25 (m, 8H, [-CH2-]x 2).

^1H NMR (300 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(3-Chloropropylthio)tetrathiafulvalene **31**

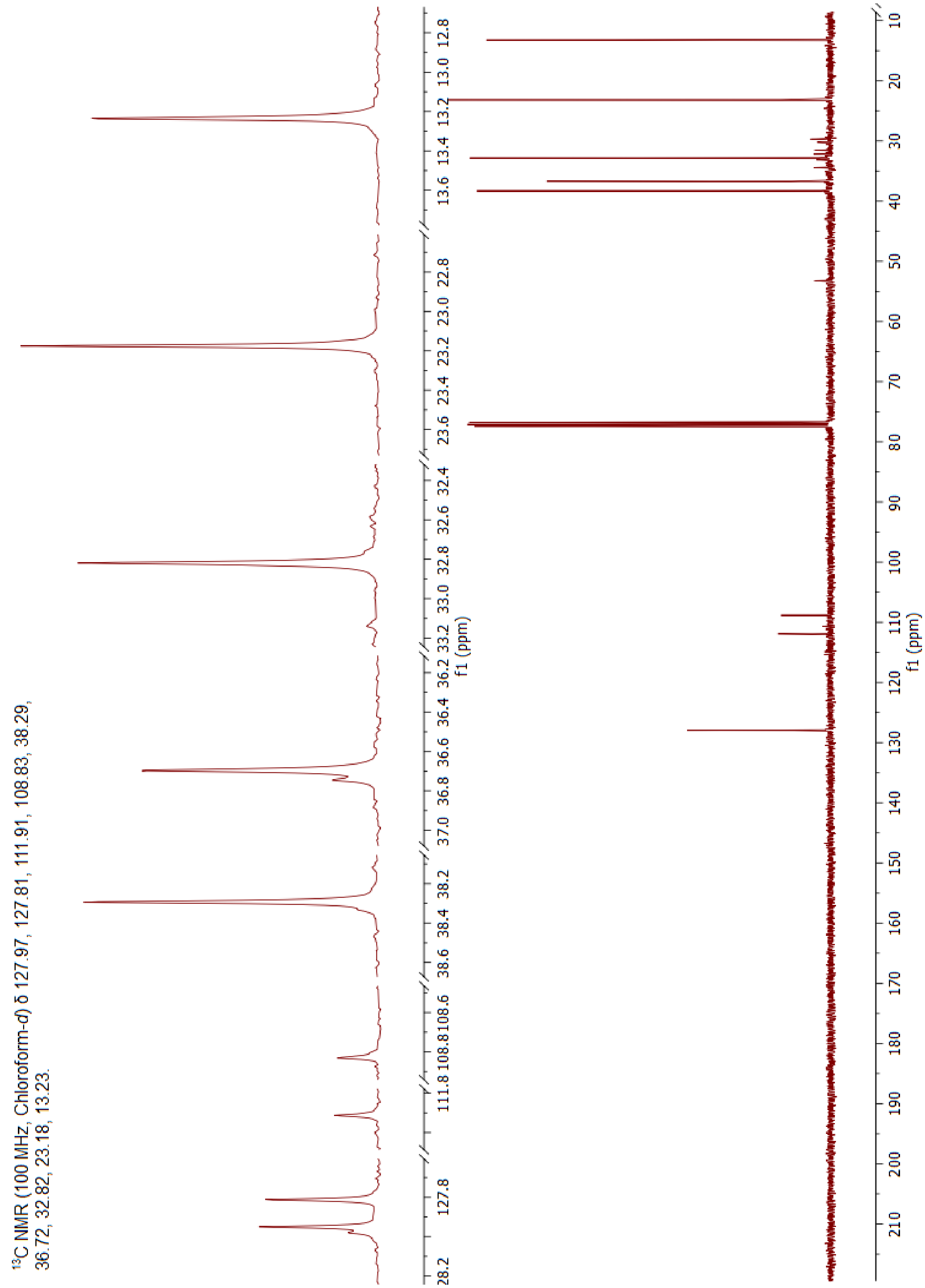


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(3-Chloropropylthio)tetrathiafulvalene **31**



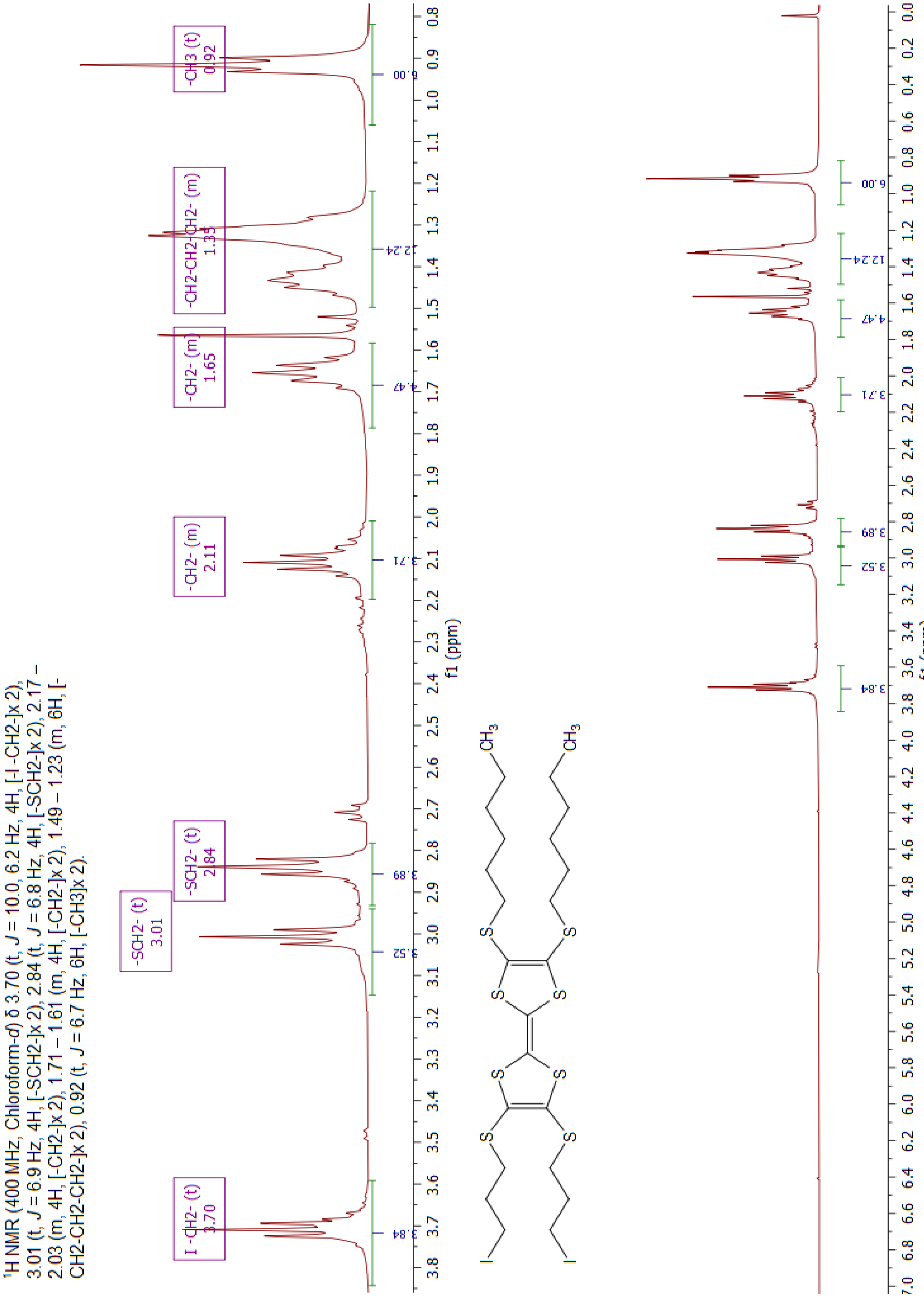
^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.34 (t, *J* = 6.7 Hz, 4H, [I-CH2-]x 2), 2.95 (t, *J* = 6.8 Hz, 4H, [SCH2-]x 2), 2.82 (t, *J*= 6.7 Hz, 4H, [-SCH2-]x 2), 2.25 – 2.05 (m, 4H, [-CH2-]x 2), 1.76 – 1.60 (m, 4H, [-CH2-]x 2), 1.04 (t, *J* = 7.3 Hz, 6H, [-CH3]x 2).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(3'-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene **32a**



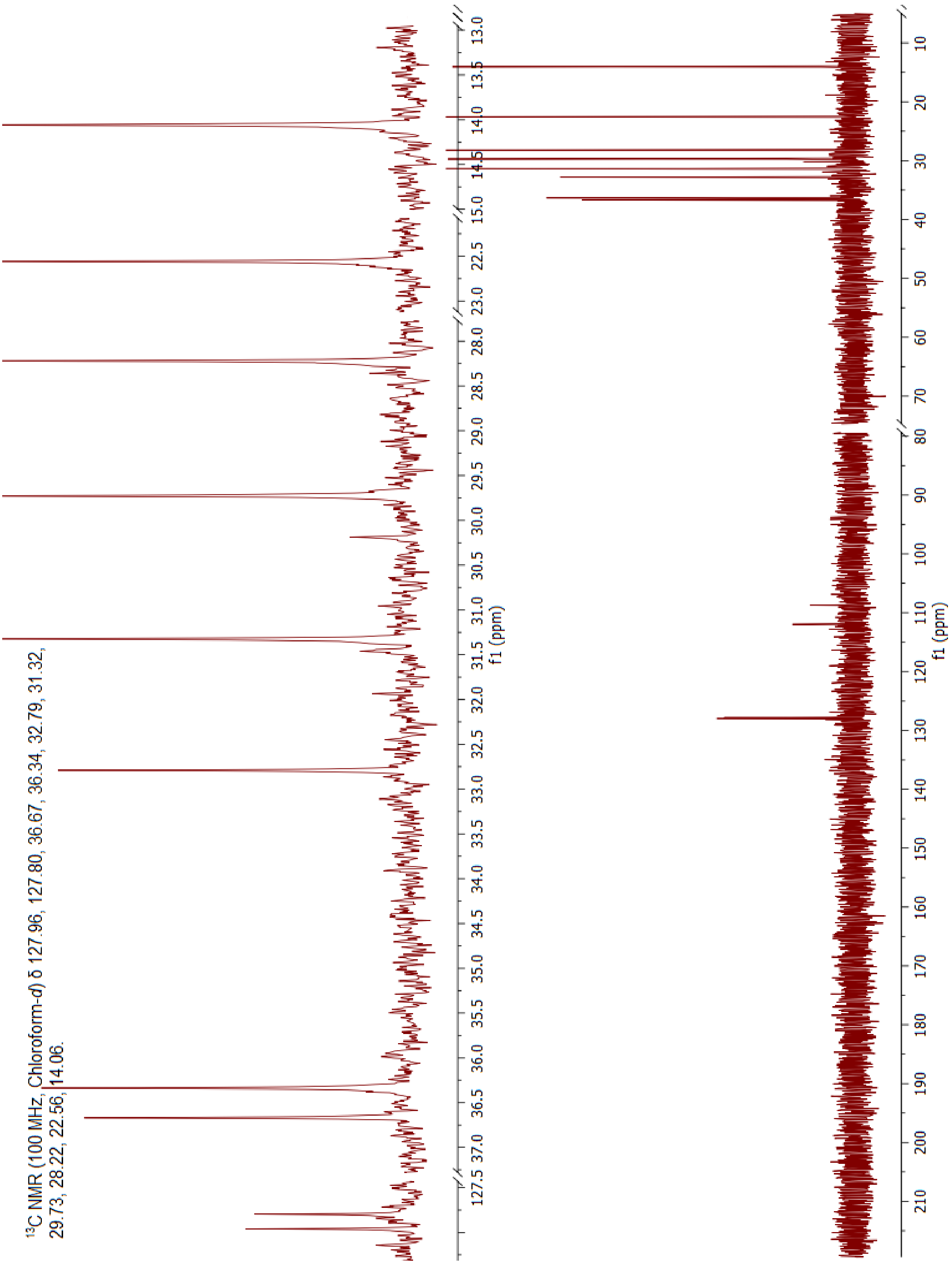
^{13}C NMR (100 MHz, Chloroform-*d*) δ 127.97, 127.81, 111.91, 108.83, 38.29, 36.72, 32.82, 23.18, 13.23.

^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(3'-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene **32a**

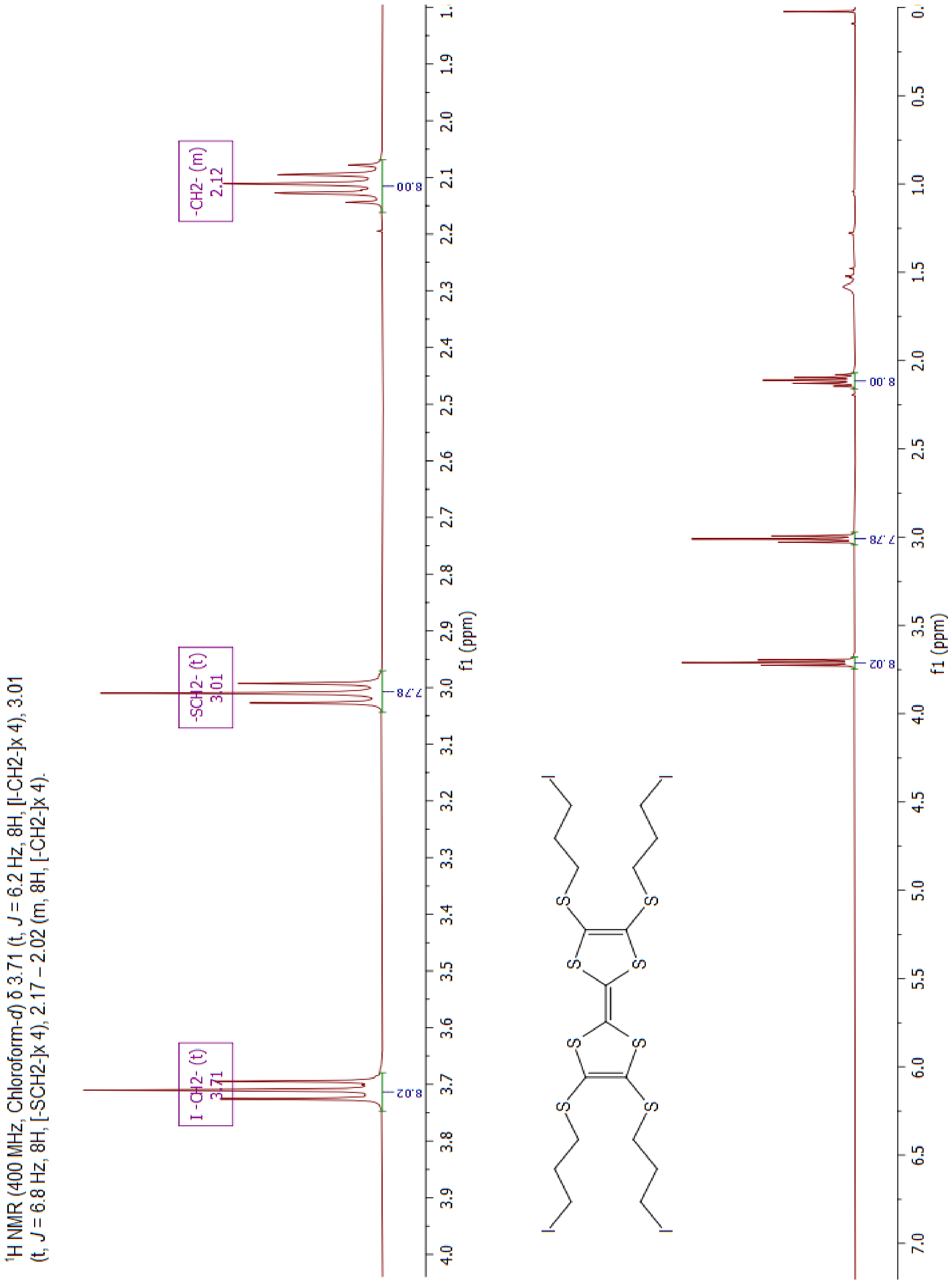


^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.70 (t, *J* = 10.0, 6.2 Hz, 4H, [-I -CH2-]x 2), 3.01 (t, *J* = 6.9 Hz, 4H, [-SCH2-]x 2), 2.84 (t, *J* = 6.8 Hz, 4H, [-SCH2-]x 2), 2.17 – 2.03 (m, 4H, [-CH2-]x 2), 1.71 – 1.61 (m, 4H, [-CH2-]x 2), 1.49 – 1.23 (m, 6H, [-CH2-CH2-CH2-]x 2), 0.92 (t, *J* = 6.7 Hz, 6H, [-CH3]x 2).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(3’-iodopropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **32b**

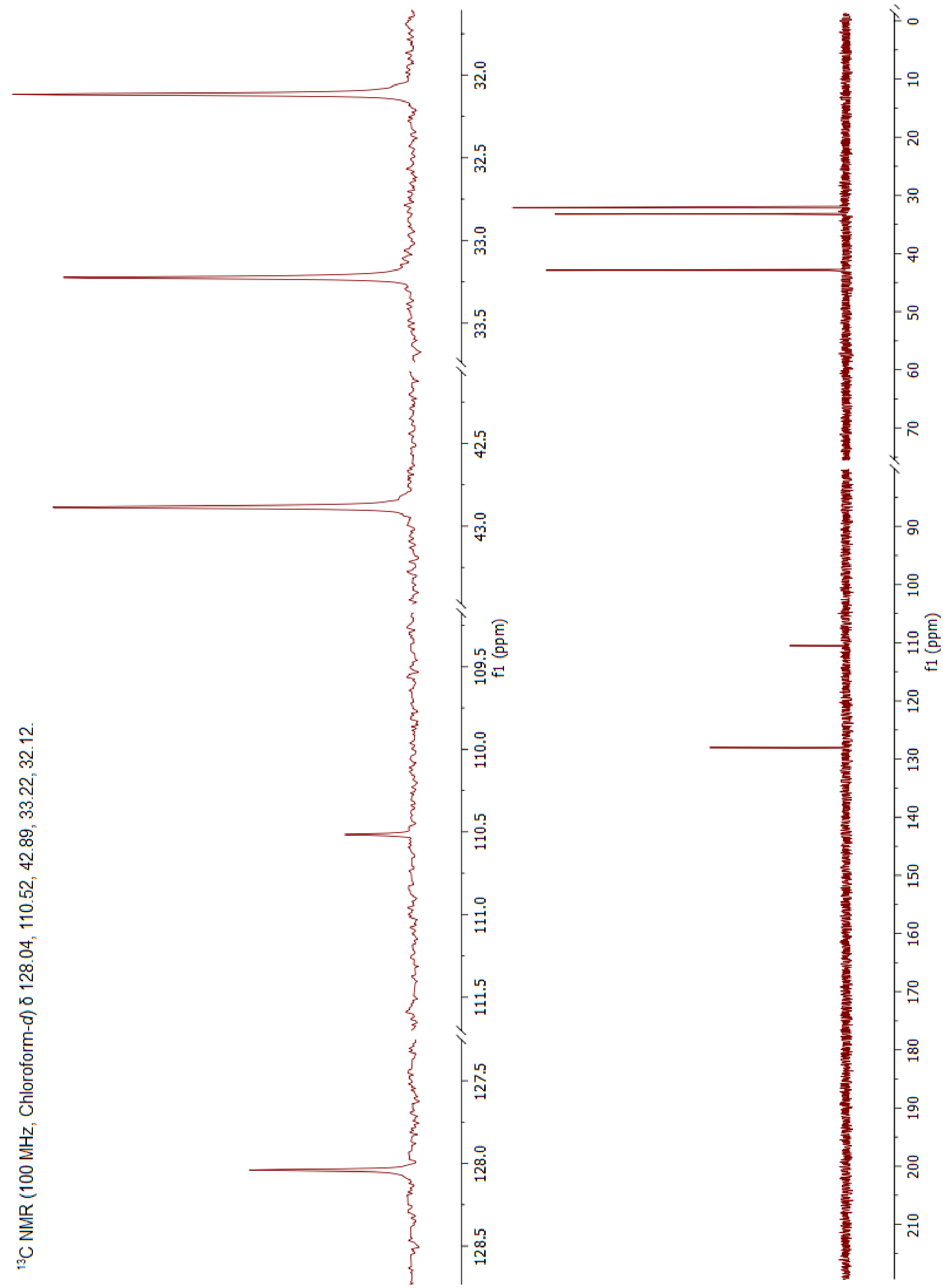


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 4,5-bis(3'-iodopropylthio)-6,7-bis(hexylthio)tetrathiafulvalene **32b**

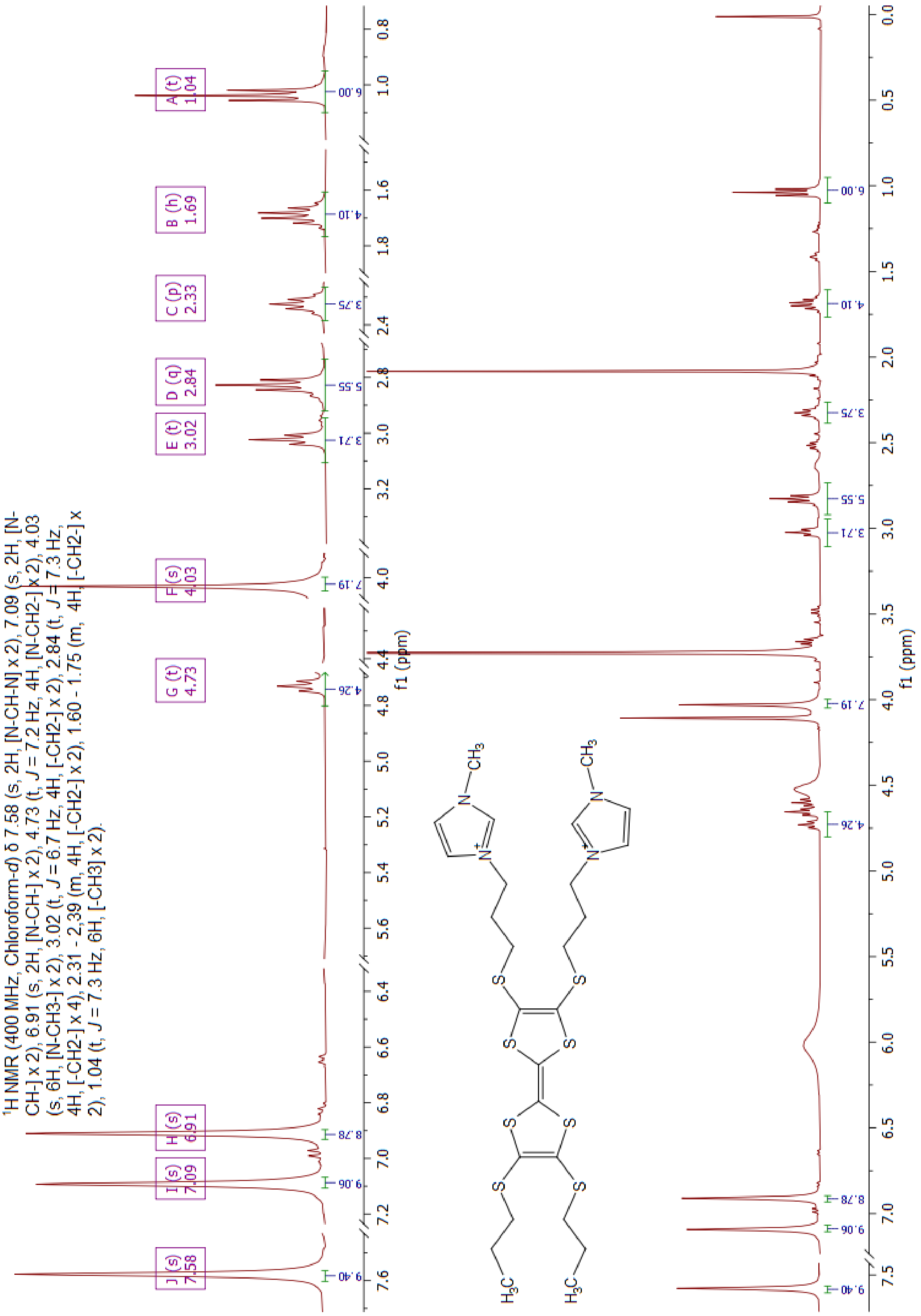


^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.71 (t, *J* = 6.2 Hz, 8H, [I-CH2-]x 4), 3.01 (t, *J* = 6.8 Hz, 8H, [-SCH2-]x 4), 2.17 – 2.02 (m, 8H, [-CH2-]x 4).

^{1}H NMR (300 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(3-Iodopropylthio)tetrathiafulvalene **33**

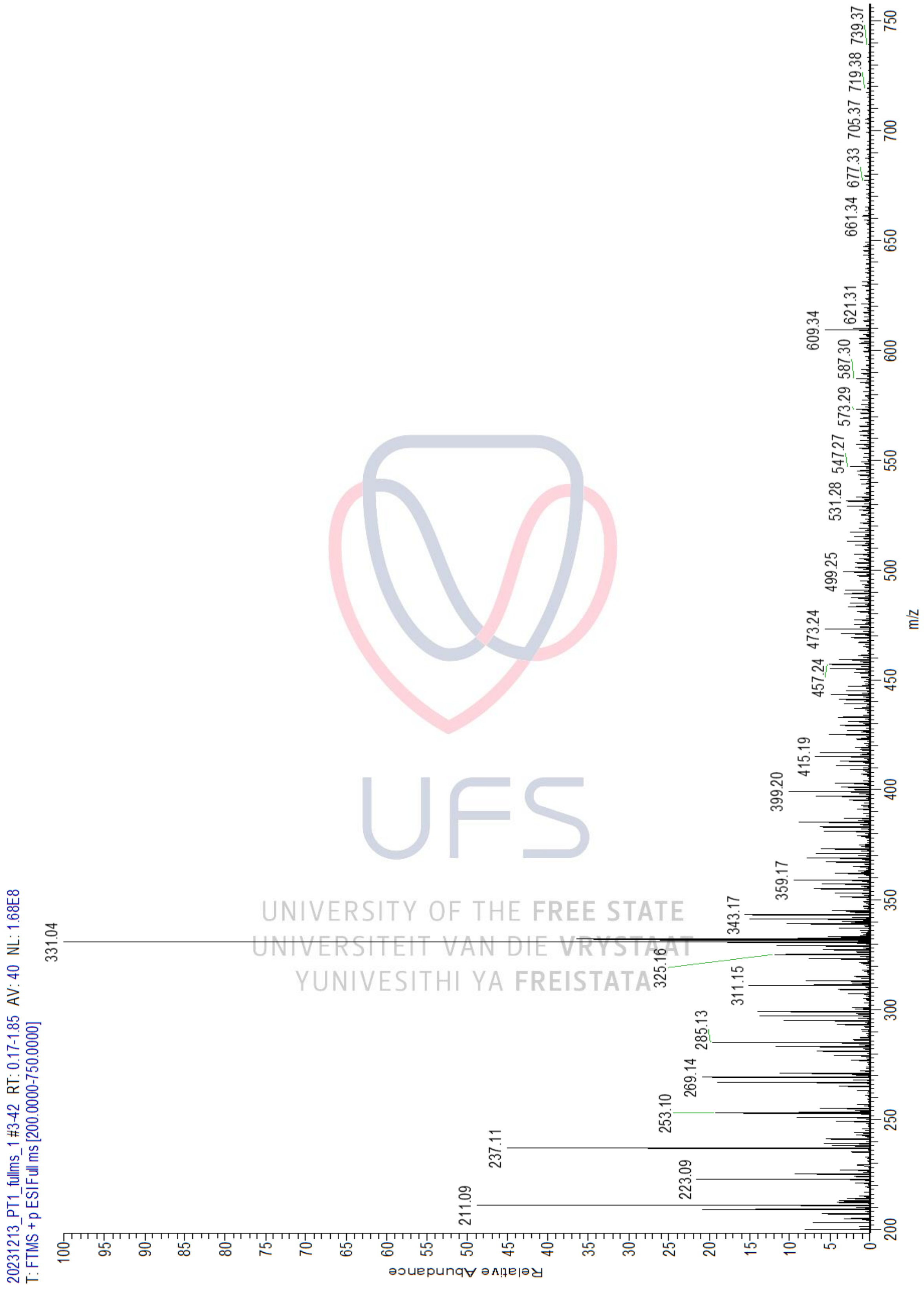


^{13}C NMR (100 MHz, Chloroform-d) spectrum of 2,3,6,7-Tetrakis(3-Iodopropylthio)tetrathiafulvalene **33**



^1H NMR (400 MHz, Chloroform-*d*) δ 7.58 (s, 2H, [N-CH-N] x 2), 7.09 (s, 2H, [N-CH-] x 2), 6.91 (s, 2H, [N-CH-] x 2), 4.73 (t, *J* = 7.2 Hz, 4H, [N-CH2-] x 2), 4.03 (s, 6H, [N-CH3-] x 2), 3.02 (t, *J* = 6.7 Hz, 4H, [-CH2-] x 2), 2.84 (t, *J* = 7.3 Hz, 4H, [-CH2-] x 4), 2.31 - 2,39 (m, 4H, [-CH2-] x 2), 1.60 - 1.75 (m, 4H, [-CH2-] x 2), 1.04 (t, *J* = 7.3 Hz, 6H, [-CH3] x 2).

^1H NMR (300 MHz, Chloroform-d) spectrum of 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene **4a**, with trace of impurities. However, successful preparation of the highly polar derivative is confirmed by MS results.


2023121З_PT1_fullms_1 #3-42 RT: 0.17-1.85 AV: 40 NL: 1.68E8
T: FTMS + p ESI Full ms [200.0000-750.0000]
Relative Abundance
m/z
331.04
211.09
237.11
223.09
253.10
269.14
285.13
325.16
311.15
343.17
359.17
399.20
415.19
457.24
473.24
499.25
531.28
547.27
573.29
587.30
609.34
621.31
661.34
677.33
705.37
719.38
739.37
100
95
90
85
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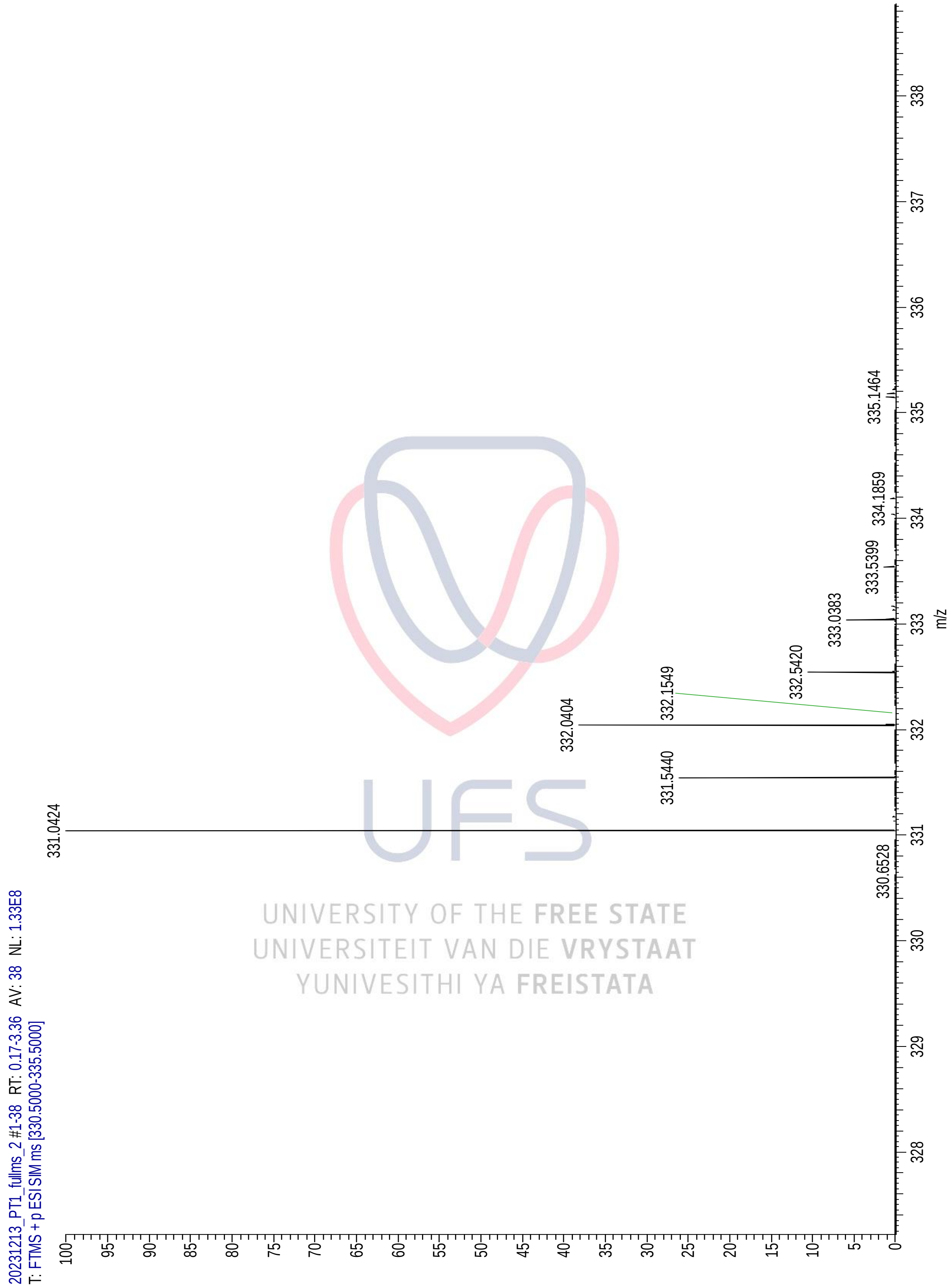
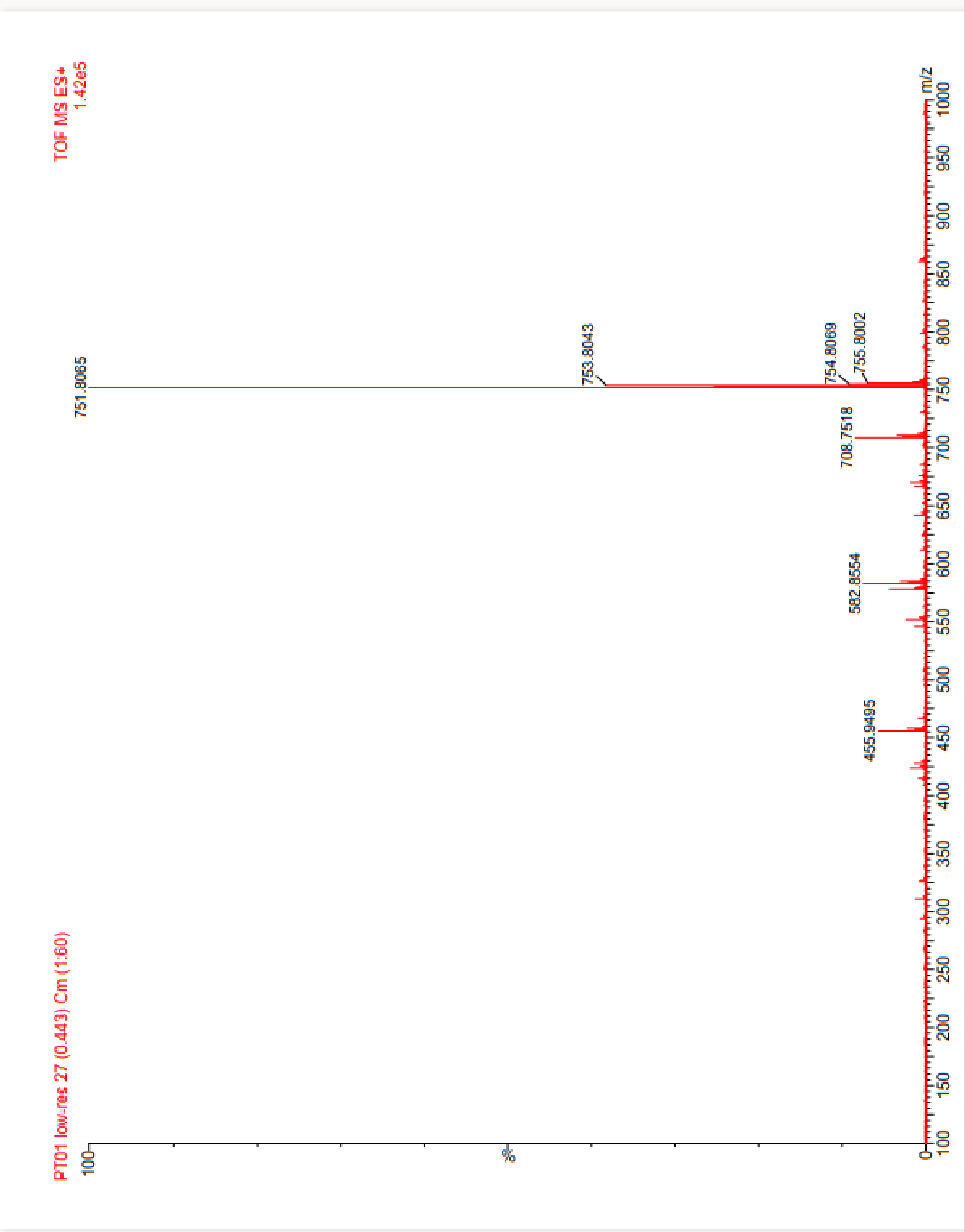


Previous and current spectra: High resolution mass spectrum of 4,5-bis(1-methylimidazole-3-propylthio)-6,7-bis(propylthio)tetrathiafulvalene **4a**.

FT-MS (ESI): *m/z* = 335.0424 (M+); calcd. for $C_{26}H_{38}N_4S_8^{2+}$, 331.0431 (M+).



Low resolution mass spectrum of 4,5-bis(3’-iodopropylthio)-6,7-bis(propylthio)tetrathiafulvalene **32a**, of MS (TOF ESI+): *m/z* (%) = 751.8065 (M+).