SYNTHESIS OF TEMPO CONTAINING CHIRAL POLYMERS FOR KINETIC RESOLUTION OF SECONDARY ALCOHOLS

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Approval of the thesis:

THESIS TITLE

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ABSTRACT

SYNTHESIS OF TEMPO CONTAINING CHIRAL POLYMERS FOR KINETIC RESOLUTION OF SECONDARY ALCOHOLS

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Optically pure secondary alcohols are important building blocks for the synthesis of chemicals used in pharmaceutical sciences. Kinetic resolution of secondary alcohols through selective oxidation of one enantiomer to the corresponding ketone is a classical and efficient method to obtain enantiopure alcohols. An oxidative kinetic resolution is achieved by exploiting two enantiomers' unequal rates of oxidation reaction with a chiral reagent or catalyst. The general approach towards a kinetic resolution via alcohol oxidation utilizes nitroxyl radicals on a chiral environment. The oxidations with these radicals are highly efficient catalytic oxidations due to fast and efficient turnover and the use of inexpensive oxidants. In this study, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) containing chiral polymers were synthesized via ring opening metathesis polymerization. Afterwards, the synthesized polymers were used as catalysts for the oxidative kinetic resolution of 1-phenyl ethanol. Morever, a TEMPO containing polymer was employed as a cathode material in the construction of a organic radical battery.

Keywords: Oxidation, Kinetic Resolution, TEMPO Radical

ÖZ

TEMPO İÇEREN KİRAL POLİMERLERİN İKİNCİL ALKOLLERİN KİNETİK RESOLÜSYONUNDA KULLANIMLASI İÇİN SENTEZİ

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Optikçe saf ikincil alkoller ilaç endüstrisinde kullanılan kimyasalların sentezinde temel yapı taşlarıdır. Enantiyosaf alkollerin eldesinde, ikincil alkollerin bir enantiomerinin seçici olarak ketonlara oksitlenip kinetik olarak ayrılmaları klasik ve etkili bir metotdur. Oksidatif kinetik ayrılma, iki enantiyomerin kiral bir reaktif veya katalizör ile verdikleri oksidasyon reaksiyonu hızlarının farklı olmasından faydalanarak gerçekleştirilir. Alkollerin oksidasyon ile kinetik olarak ayrılmalarında kullanılan genel yaklaşım, nitroksil radikallerinin kiral ortamlarda kullanılmasıdır. Hızlı ve etkili dönüşüm sağladıkları ve ucuz oksidanlar kullandıkları için bu radikaller ile yapılan oksidasyonlar oldukça etkili katalitik oksidasyonlardır. Bu çalışmada, 2,2,6,6-tetrametilpiperidin-1-oksil (TEMPO) grubu bağlanmış kiral bir merkez içeren yeni polimerler, halka açma metatez polimerizasyonu kullanılarak sentezlenmiştir. Sonrasında, sentezlenen polimerlerin 1-fenil etanolü oksitlemedeki enantioseçicilikleri test edilmiştir. Bunlara ek olarak, TEMPO içeren bir polimer oganik radikal pili yapımında katot malzemesi olarak kullanılmıştır.

Anahtar Kelimeler: Oksidasyon, Kinetik Ayırma Yöntemi, TEMPO Radikali

To all those who have ever taught me something: *ancora imparo.*

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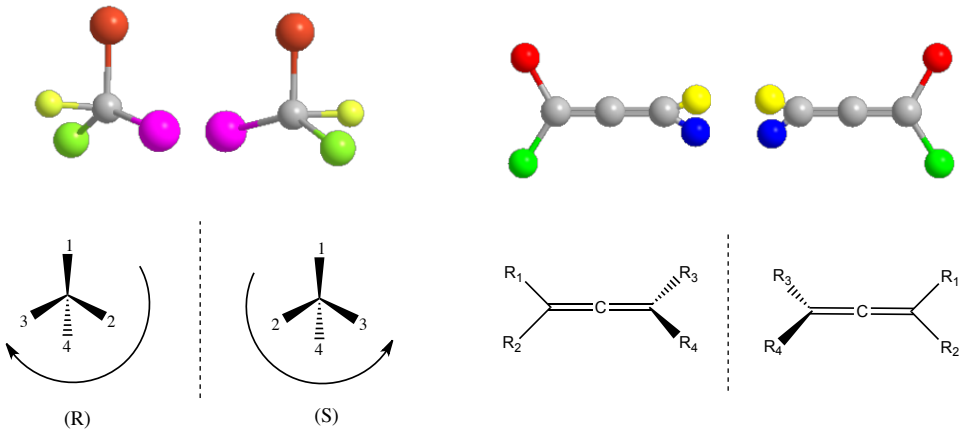
CHAPTER 1

INTRODUCTION

1.1 Chirality and Enantiomers

Derived from the Greek word for 'hand', the term chiral is used for the molecules which are nonsuperimposable with their mirror image, *i.e.* molecules without improper axis of rotation (S_n). Chirality can arise from either chiral centers or chiral axes. Central chirality is used for molecules having at least one tetrahedral atom attached to four different substituents [Figure 1a]. Axial chirality, on the other hand, arises when a molecule holds four groups placed in two different planes by pairs [Figure 1b].[1] Most of the molecules of importance like amino acids, sugars, nucleic acids are chiral.[2]



a **b**

Figure 1a. General representation of a chiral center: colors indicate different substituents. 1b. Allene as an example of axially chiral structure.

Chiral molecules, like a pair of hands, can exist as isomers called enantiomers. Enantiomers have the same physical properties except for their optical activity and same chemical properties except when they are in a chiral environment. These properties are exploited, mainly in connection with their pharmacological,[2] agricultural,[3] metabolic,[4] and toxicologic activity.[5] As an example, the two enantiomers of the amphetamine molecule is given below, these enantiomers show major difference in their biological activities. In fact, *D*-amphetamine has been increasingly prescribed to treat amphetamine abusers. Illicitly-produced, or 'street' amphetamine is a mixture of the two isomers whereas prescribed *D*-amphetamine used for the treatment is predominantly the *D*-isomer [Figure 2].[6]

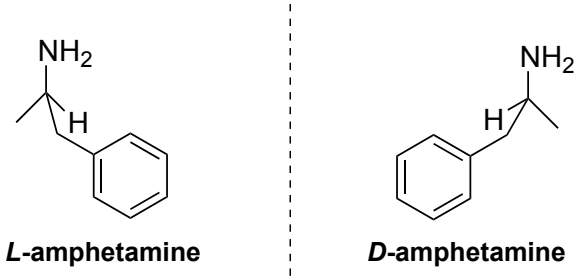


Figure 2. The two enantiomers of the amphetamine molecule

1.1.1 Preparation of Enantioenriched Compounds

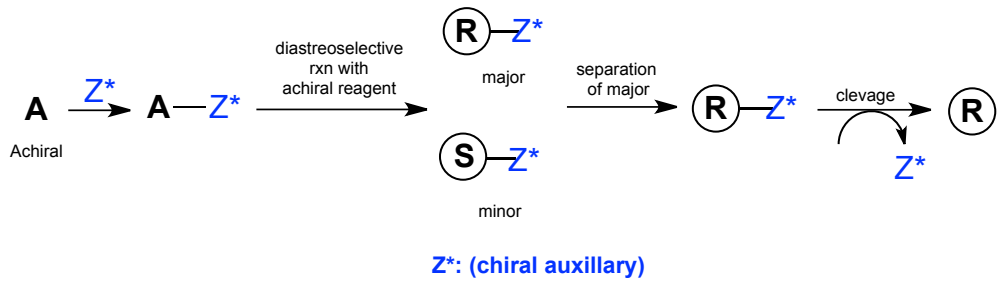
The interest for the preparation of optically pure isomers has not been faded since the discovery of the importance of chirality in biological processes. Great attention has been devoted to the preparation of enantiomerically enriched compounds for decades.[7] Two main strategies for the preparation of enantiopure compounds include asymmetric synthesis and resolution of a racemic mixture. The basic principles of these methods are well-established as a result of one hundred years of research.[8]

1.1.1.1 Enantioenriched Compounds through Asymmetric Synthesis

Asymmetric synthesis is a method for the selective synthesis of one enantiomer of the desired optically pure molecule using a chiral reagent. Asymmetric synthesis can be devided into two classes: diostereoselective ones and enantioselective ones.[8]

1.1.1.1.1 Diastereoselective Asymmetric Synthesis

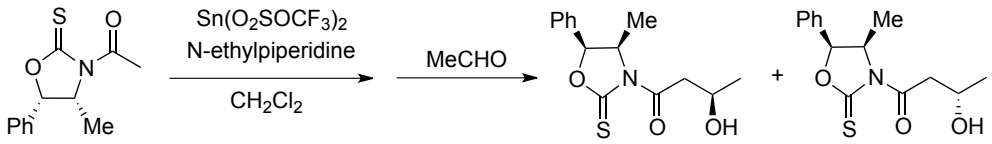
In a diastereoselective asymmetric synthesis, a chiral auxillary is first bound to an achiral substrate. The two faces of the substrate then become diastereotopic, so their reactions with a reagent may differ. After the reaction is complete, the diastereomers formed are converted to stereoenriched compounds by the removal of the chiral auxillary attached [Scheme 1].[8]



Scheme 1. Representative diastereoselective asymmetric synthesis

One of the most important methods mediated by chiral auxillaries is considered to be the asymmetric aldol condensation. Among the auxillaries, variants of Evans' oxazolidinones have proven to be highly efficient.[9]

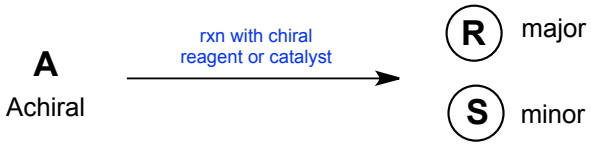
The first study utilizing chiral N-acyl oxazolidinethiones was reported by Nagao *et al*. in 1985. This study described an effective diastereoselective synthesis of aldols by the use of chiral 3-acyl-1,3-oxazolidine-2-thiones [Scheme 2].[10] Such reactions are reviewed in the literature cummulatively.[11]



Scheme 2. Nagao's chiral oxazolidinethiones in aldol-type reactions

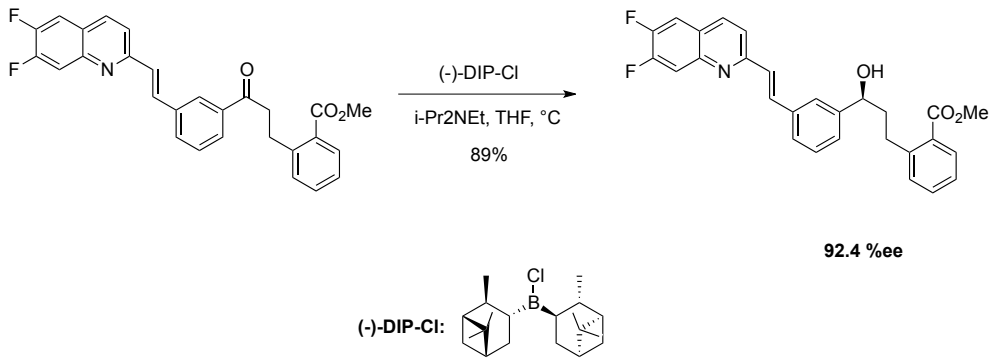
1.1.1.1.2 Enantioselective Asymmetric Synthesis

In an enantioselective asymmetric synthesis, a chiral catalyst or reagent which may differentiate between the two enantiotopic faces of an achiral substrate is used. This differentiation then provides the formation of desired enantiomer of the product [Scheme 3].[8]



Scheme 3. Representative enantiostereoselective asymmetric synthesis

Among many reported studies, one of the most studied one facilitates Brown's B-chlorodiisopinocampheylborane (DIP-Cl) for about 20 years. Several groups employed DIP-Cl for asymmetric reduction of ketones and observed reliably high enantioselectivities [Scheme 4].[12]



Scheme 4. Synthesis of the LTD_4 antagonist using (-)-DIP-Cl reduction of ketone

1.1.1.2 Enantioenriched Compounds through Enantiomeric Resolution

Enantiomeric resolution is achieved by the seperation of an equimolar mixture of racemates using physical or chemical methods. Racemic mixtures can be resolved**,** or seperated into their pure enantiomers by four methods: chromatographic resolution, resolution by crystallization, resolution by chiral derivatization and kinetic resolution.

1.1.1.2.1 Chromatographic Resolution

Chromatographic seperation is achieved by exploiting the different affinities of racemates to the stationary phase and the mobile phase. Most of chiral separations use columns packed with chiral stationary phases (chiral columns) with achiral solvents. Chromatographic methods may offer distinct advantages in the separation and analysis of enantiomers for moderate-scale separations, however they are impractical for preparative purposes. In addition, the chiral columns used for such seperations are costly and the method requires use of a high amount of solvent.[13] Chiral separation techniques using chromatography includes HPLC, GC and TLC.

1.1.1.2.2 Resolution by Crystallization

Being the oldest method for seperating the enantiomers, resolution by crystallization was first introduced by Louis Pasteur in 1848. While working on the crytallization of sodium ammonium tartarate, he realized that the crystals formed to be either left-handed or right-handed.[14] After his discovery, it was proved that two enantiomers of a racemate can be seperated if they crystallize as separate mirror imaged crystals. This type of compunds are called conglomerates and the seperation of such compounds is achieved manually. Only about 10% of racemates crystallize as conglomerates, so this method is limited to molecules with such behaviour.[15]

Examples of useful resolution by crystallization include particular compounds like *DL*-Threonine, *DL*-Adrenaline and *DL*-Glutamic Acid. Since the first reported

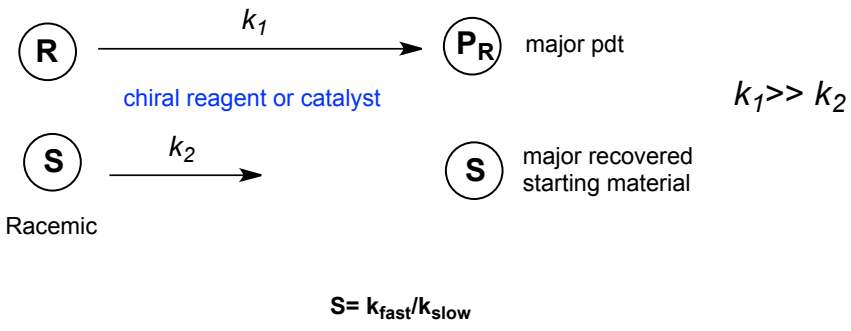
resolution by crystallization, there has been a lack of study to predict when resolution is possible by this method and when it is not. Thus, most of the studies on the crystallization phenomenon have relied mostly on empirical approaches.[14]

1.1.1.2.3 Resolution by Chiral Derivatization

A racemate with at least one functional group (amino, carbonyl, hydroxyl, thiol, epoxy, etc.) can be seperated by the reaction with a derivatizing agent. The diastereoisomers formed will have different physical or chemical properties and can be seperated by chromatography. Finally, diastereomers are treated with appropiate reagents to regenerate the original enantiomers.[16] Resolution by chiral derivatization is used for many biochemically imporant compounds, especially for aminoacids.[17]

1.1.1.2.4 Kinetic Resolution

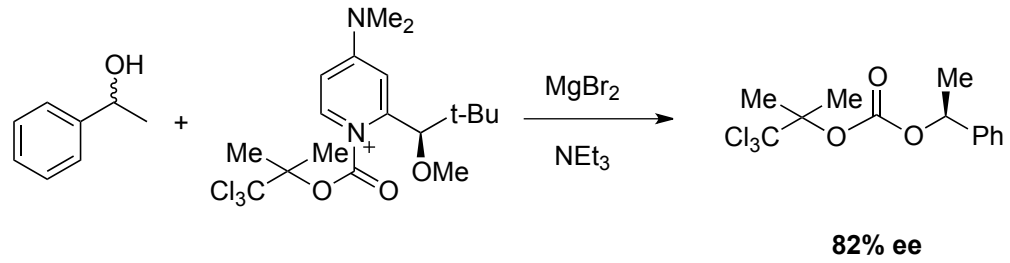
Enantiomers may display different kinetics in their reaction with chiral reagents or catalysts (*vide supra*). So, they will be resolved stereoseletively by the difference in reaction rates. One enantiomer reacts faster with the enantiopure agent, while the other one reacts slowly. If the process is efficient, one of the enantiomers is converted to the product while the other remains unchanged. Therefore, enantioenriched materials will be separated employing kinetics [Scheme 5].[18]



Scheme 5. Representative kinetic resolution

Using kinetic resolution for the preparation of enantiopure compounds is an efficient method and it is studied extensively for both enzymatic and nonenzymatic seperation processes. Numerous protocols have been developed for many reaction types including oxidation, acylation, silylation, cycloaddition etc.[19]

A common kinetic resolution method uses modified variations of dimethylaminopyridine (DMAP) as an acyl transfer agent. Vedejs utilized a DMAP derived salt as a resolving agent for a racemic alcohol. The resulting selectivity in this reaction appears to be primarily due to the steric hindrance of the pyridine ring and also the carbonyl group. This theory was further proven by the increase in selectivity as the substituent of the phenyl ring of the alcohol gets larger [Scheme 6].[20]



Scheme 6. Kinetic resolution using a DMAP derived salt

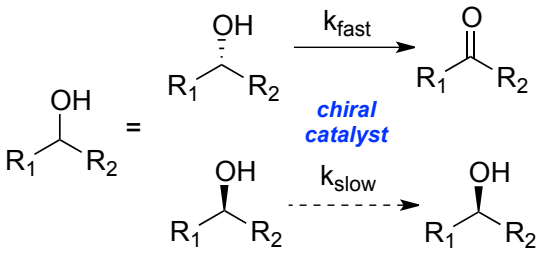
The selectivity factor (S) of a resolution is the most commonly-applied criterion to assess the efficiency of a kinetic resolution and is defined as the ratio of the rate constant of the fast reaction to the rate constant of the slow reaction. Generally, a catalyst is considered to be synthetically useful if its S factor is greater than 20.[21]

In literature, kinetic resolution techniques have been studied and applied to resolve mixtures of allylic alcohols,[22] terminal epoxides,[23] α-stereogenic carbonyl compounds[24] and secondary alcohols.[20]

1.1.1.2.4.1 Oxidative Kinetic Resolution of Secondary Alcohols

Enantiopure secondary alcohols are an important class of chiral building blocks for the synthesis of pharmaceutical, agrochemical, and fine chemicals.[25] From last decades, several approaches were reported for the kinetic resolution on secondary alcohols. These studies mostly involve kinetic resolution via acylation[21] or epoxidation.[22] Selective oxidation of one enantiomer to the corresponding ketone is another classical and efficient method for the preparation of chiral alcohols.

An oxidative kinetic resolution is achieved by exploiting two enantiomers' unequal rates of reaction with a chiral oxidizing agent or catalyst. One enantiomer is oxidized faster by the enantiopure oxidizing agent, while the other one is oxidized slowly. After the oxidation, the remaining enantioenriched starting material and the product is separated using basic standard techniques [Scheme 7].[26]



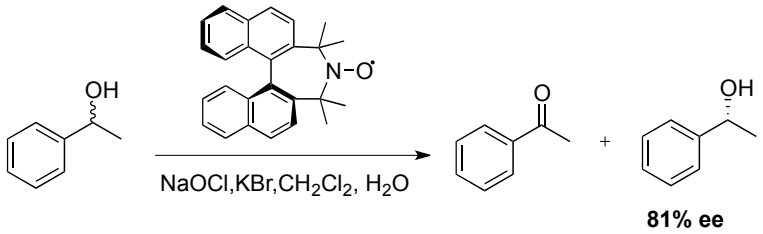
Scheme 7. Oxidative Kinetic Resolution of secondary alcohols

In the last two decades, numerous studies which use effective catalysts for oxidative kinetic resolution of secondary alcohols were reported. These studies utilized either transition metal catalysts with chiral ligands[27] or chiral organocatalysts.[28]

Among the chiral organocatalyst approaches, the most widely used one involves the use of stable nitroxyl radicals, which form the active N-oxoammonium species under oxidative conditions.

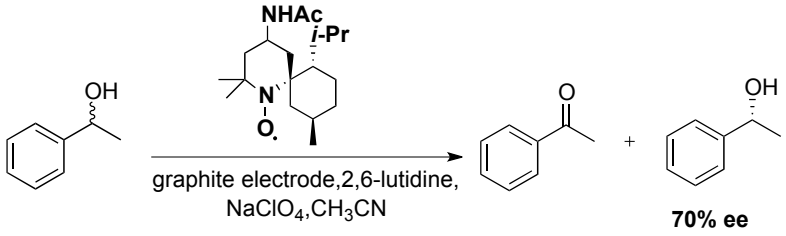
1.1.1.2.4.2 Use of Nitroxyl Radicals for Oxidative Kinetic Resolution of Secondary Alcohols

There has been several reports utilizing nitroxyl radicals for the oxidative kinetic resolution of alcohols. The first kinetic resolution via alcohol oxidation was reported by Rychnovsky's research group, and involved the use of a chiral nitroxyl radical. This system employed sodium hypochlorite as the primary oxidant (co-oxidant) and represented the first example of a nonenzymatic catalytic oxidative kinetic resolution of secondary alcohols to the corresponding ketones. The system achieved modest selectivities across a range of substrates [Scheme 8].[29]



Scheme 8. Rychnovsky's chiral TEMPO-based oxidation

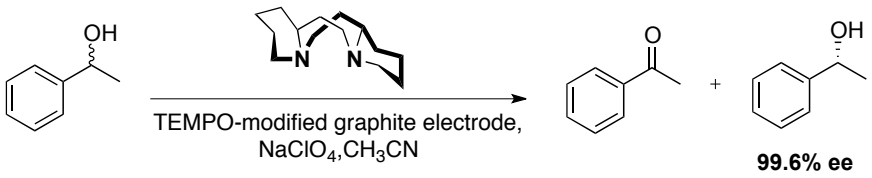
Electrolytic oxidation of alcohols using nitroxyl radicals was also achieved. Tanaka performed oxidative kinetic resolution of alcohols using Rynchovsky's chiral N-oxyl with a graphite electrode. Again, the selectivities was modest for a range of substrates [Scheme 9].[30]



Scheme 9. Oxidative kinetic resolution under electrolysis

Achiral nitroxyl radicals have also been used together with a TEMPO-modified graphite electrode and chiral diamine for the oxidative kinetic resolution of alcohols. *(-)*-sparteine serves as a chiral base in the oxidation. With this method, Osa and

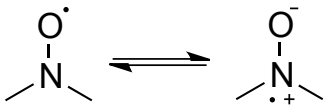
Bobbitt managed to recover a highly enantioenriched alcohol mixture with appreciable selectivities [Scheme 10].[31]



Scheme 10. Oxidative Kinetic Resolution with a chiral base

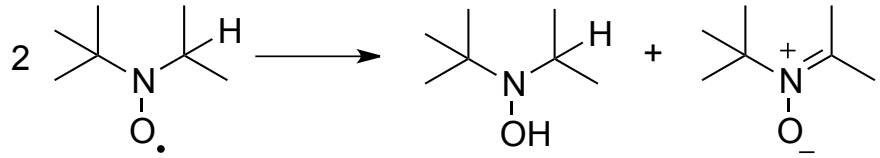
1.2 Stable Nitroxyl Radicals

Nitroxyl radicals, NO moiety with an unpaired electron on it, are compounds with trivalent nitrogen. Thermodynamically, these radicals are highly stable due to the delocalization of the free electron over the NO bond which results in a resonance stabilization [Scheme 11].[32] Due to their stability, these radicals can be handled at ambient conditions.



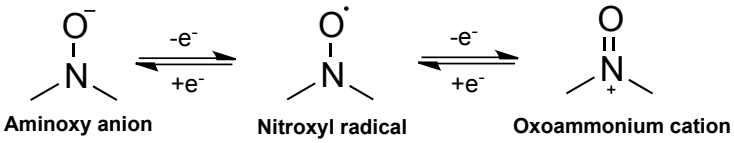
Scheme 11. Resonance structures of a nitroxyl radical

A kinetic stabilization is exerted to the nitroxyl radicals that lack hydrogens at the α position. For those nitroxyl radical with α-H-atoms, disproportionation reactions occur, forming hydroxylamine and nitrone. Thus, the majority of nonconjugated organic nitroxyl radicals are synthesized with stable tertiary alkyl groups [Scheme 12].[33]



Scheme 12. Disproportionation of nitroxyl radicals containing α-H-atoms

Nitroxyl radicals display two redox couples that play an important role in their activity. They can reversibly undergo oxidation and reduction by one electron; forming oxoamonium cations and aminoxy anions, respectively [Scheme 13].[34]



Scheme 13. Redox behaviour of a nitroxyl radical

Examples of stable nitroxyl radicals include di-tert-butyl nitroxide, 2,2,5,5-tetramethyl-1-pyrrolidinyloxy (PROXYL) and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) [Figure 3]. Among these radicals, TEMPO is widely employed due to its easy synthesis and accesibility.

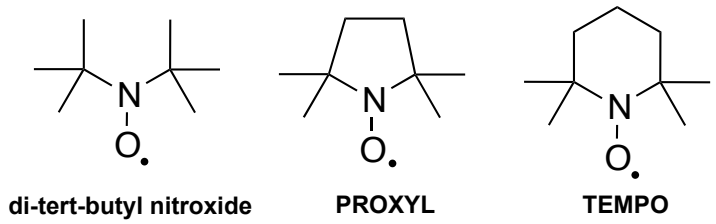


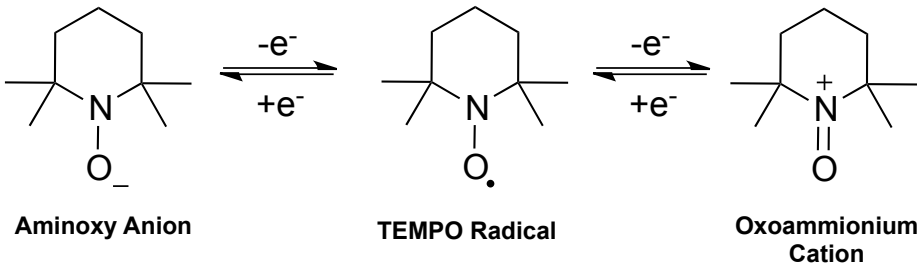
Figure 3. Examples of stable nitroxyl radicals

1.2.1 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) Radical

TEMPO is a well- known, stable nitroxyl radical used in green oxidation of alcohols.[35] It has attracted much attention due to its metal-free nature and unique redox behaviour. These radicals are commercially available and used as spin labels

for biological systems,[36] radical scavengers of organic materials[37] and oxidizing agents.[38]

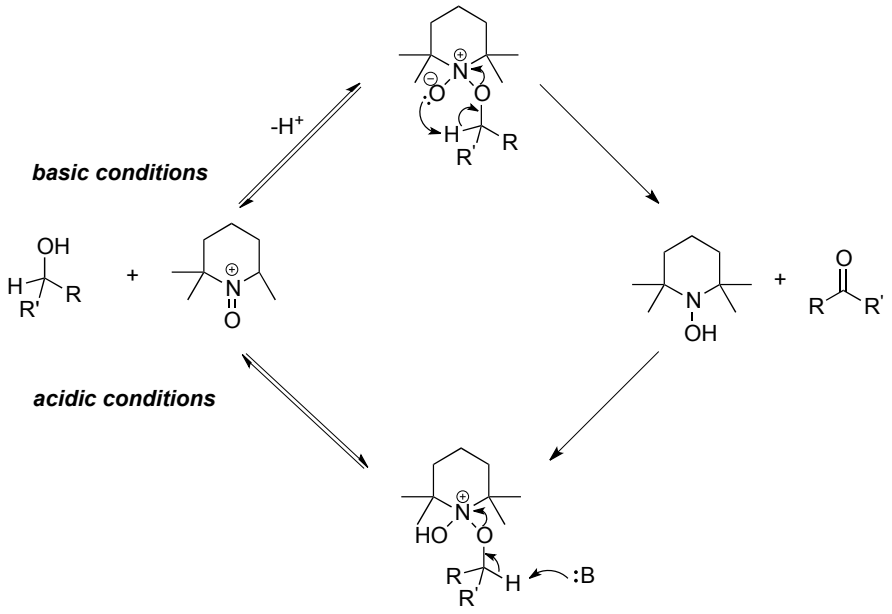
The two redox couples of TEMPO radical are shown in Scheme 14. The oxidation product of the nitroxyl radical is the oxoammonium cation and the reduction product is the aminoxy anion.



Scheme 14. The two redox couples of TEMPO radical

In oxidation reactions, TEMPO is generally used in minute amounts, and it is regenerated in the catalytic cycle shown in Scheme 15. The oxidation of alcohols is performed by oxoammonium cation, which is generated by a primary oxidant such as NaOCl,[39] *m*-CPBA,[40] and NCS [41]. The alcohol then acts as a nucleophile and attaches to the oxoammium cation to form an intermediate, which then fragments to the corresponding carbonyl compound and the hydroxylamine.

The mechanisms for TEMPO catalyzed oxidation of alcohols have also been widely studied and different reaction mechanisms were proposed for oxidations under basic and acidic conditions. Under basic conditions, TEMPO selectively oxidizes primary alcohols over secondary alcohols due to the large steric effect of the secondary alcohol. On the other hand, the oxidation of secondary alcohols is favored over primary alcohols in acidic conditions due to the possible hyride transfer between TEMPO and the alcohol [Scheme 15].[42]



Scheme 15. Proposed mechanisms for TEMPO catalyzed alcohol oxidations under basic and acidic conditions

1.2.1.1 TEMPO Incorporated Polymers

TEMPO containing compounds have also been extended to their polymeric forms to overcome the limitations in the application of small molecule systems. Such compounds were studied as probes,[43] chemical scavengers [44] and organic radical battery materials.[45] Mild oxidation of alcohols to the corresponding carbonyl compounds was also accomplished by such polymers. Using polymeric reagents not only simplify the work-up of reactions and purification of products, but it also allows facile separation and consequently the regenaration of the catalyst material.[46] Thus, the use of such reagents are considered to be relatively 'greener'.

TEMPO functionalized polymers include poly(2,2,6,6-tetramethylpiperidine-4-yl-1-oxyl methacrylate) (PTMA), poly(2,2,6,6-tetramethylpiperidine-N-oxyl-4-vinyl ether) (PTVE) and TEMPO-containing poly(norbornene) (PTNB) [Figure 4].

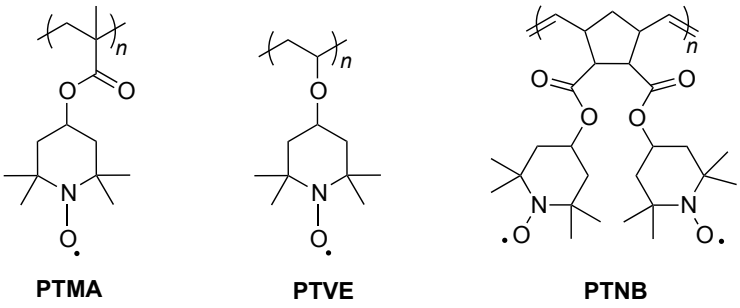
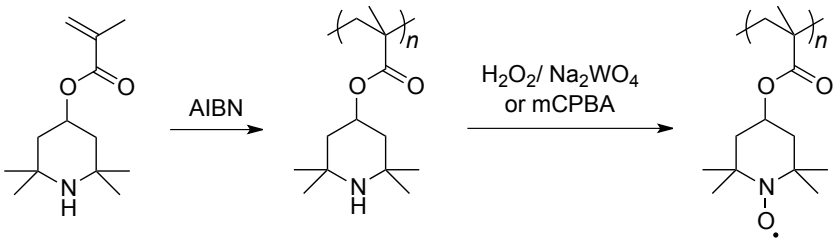


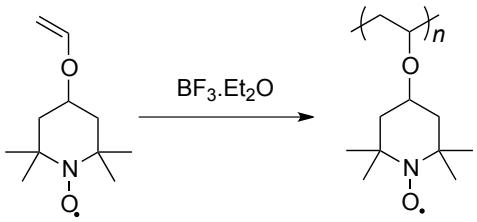
Figure 4. Examples of TEMPO incorporated polymers

The most commonly known TEMPO attached polymer is poly (TEMPO methacrylate) (PTMA). The polymer has been studied as an energy storage material because it shows sufficient electrical conductivity. The synthesis of PTMA is commonly accomplished by the polymerization 2,2,6,6-tetramethylpiperidine methacrylate, followed by the subsequent oxidation of the secondary amines [Scheme 16].[34]



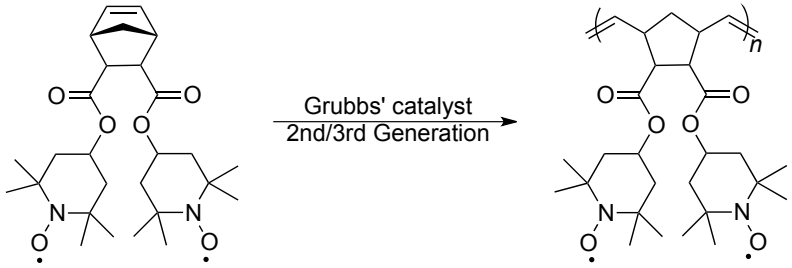
Scheme 16. Preparation of PTMA

Nakagara et al. reported a synthesis of radical polymers by cationic polymerization. In this work, the polymerization of TEMPO-vinyl ether to yield poly(TEMPO vinyl ether) (PTVE) was reported. All reported studies in the literature used PTMA as an electrode material and observed charge/discharge capacities comparable with the existing work [Scheme 17].[47]



Scheme 17. Cationic polymerization of TEMPO-vinyl ether

Another frequently prepared nitroxyl polymer is PTNB, with two TEMPO moeities per repeating unit. This polymer was also used for energy applications and featured a theoretical capacity of 109 mA h g^{-1}. The preparation of the polymer is achieved by the ROMP of the monomer 2,3-bis(2′,2′,6′,6′-tetramethylpiperidin-1′-oxyl-4′-oxycarbonyl)-5-norbornene [Scheme 18].[48]



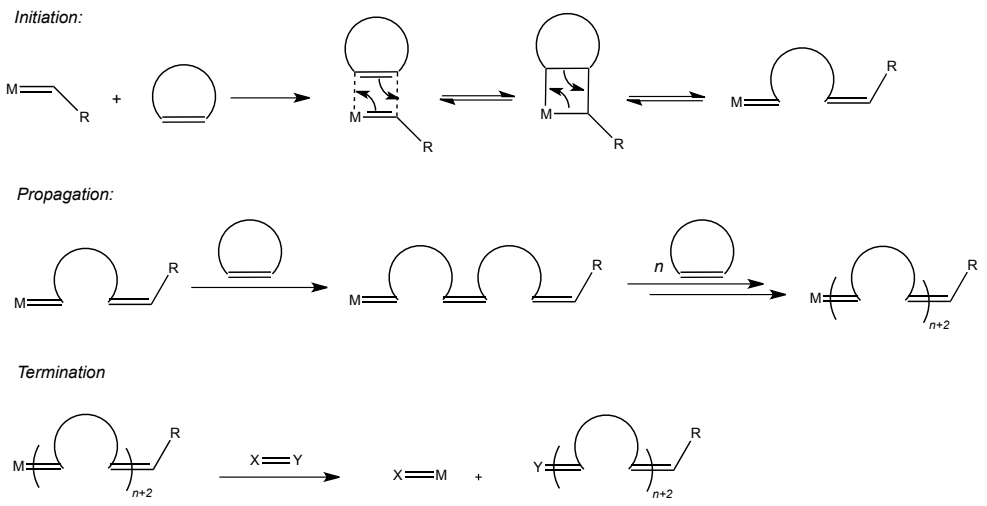
Scheme 18. Synthesis of PTNB through ROMP

Due to the inherent radical scavenging properties of nitroxyl radicals, the direct preparation of TEMPO containing polymers poses a particular challenge. The unavailability of the most common free radical polymerization as a polymerization method, has led scientists to employ alternative synthetic routes for the preparation of TEMPO incorporated polymers. In addition, the paramagnetic character of the resulting polymers complicates the structural elucidation of the synthesized structures with nuclear magnetic resonance (NMR) spectroscopy. As a result, polymerization methods which do not rely on radical intermediates are adapted. These methods include direct polymerization methods such as transition metal catalyzed polymerization, anionic polymerization, cationic polymerization, and the most widely used ring opening metathesis polymerization (ROMP).[49]

1.3 Ring Opening Metathesis Polymerization (ROMP)

ROMP is a type of olefin metathesis polymerization which provides various polymers with useful functions and unique structures. The polymerization begins with the coordination of the metal alkylidene complex into the cyclic olefin, that is the monomer. In the next step, a metallacyclobutane intermediate is formed through a [2+2] cycloaddition reaction. Then, this intermediate undergoes a retro cycloaddition to afford another metal alkylidene. The propogation step is repeated until the monomer is completely reacted, the reaction reaches equilibrium or the reaction is terminated. The reaction is generally quenched by the addition of a type of a vinylic ether, which reacts with the metallacarbene species of the growing chain, removing the metal from the polymer [Scheme 19]. [50]

In ROMP, cyclic olefins are converted into linear polymers by the release of the ring strain in the cyclic monomer, with an accompanying decrease in entropy. Thus, the monomers used in ROMP are types of cyclic olefins with relatively high ring strain, such as norbornene, cyclobutene, cyclopentene and cis-cyclooctene [Figure 5].



Scheme 19. Representative ROMP

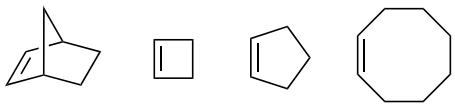


Figure 5. Examples of ROMP monomers

Starting from the mid-1970s, the studies on this subject have increased exponentially. This, in turn, has led to a vast amount of knowledge in structures that catalyze these systems. Among the designed catalysts to date, the Group VI (Schrock-type) and Group VIII (Grubbs-type) ones have remarkably broadened the limits of olefin methathesis research [Figure 6]. In fact, Grubbs and Schrock were awarded the Nobel Prize in 2005 for their contribution to the metathesis method in organic synthesis.

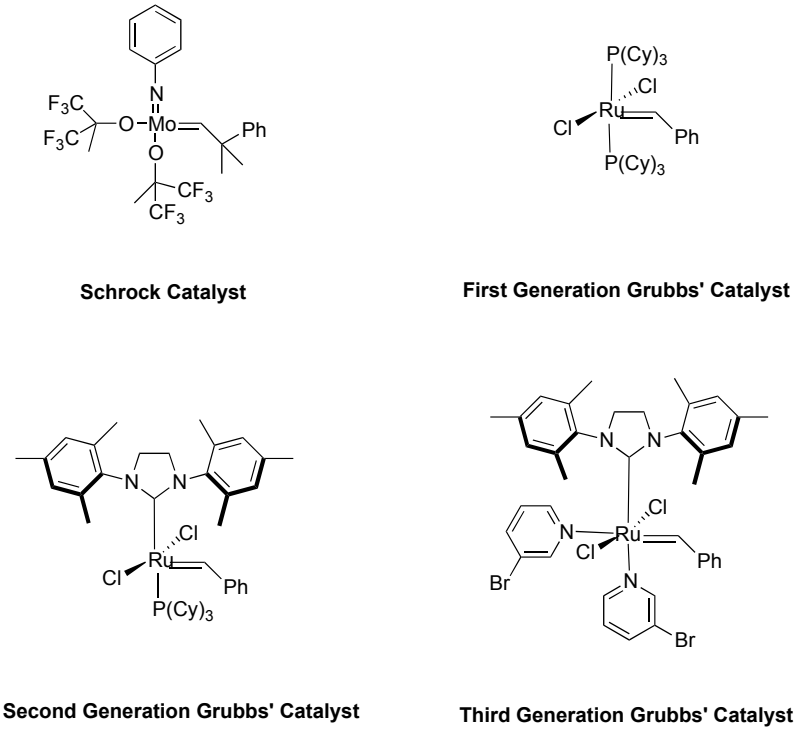
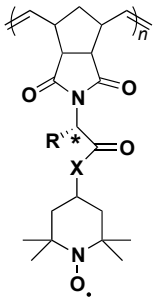


Figure 6. Examples of catalysts used for ROMP

CHAPTER 2

AIM OF THE STUDY

Optically pure secondary alcohols are pivotal building blocks in synthetic organic chemistry. Oxidative kinetic resolution of secondary alcohols catalyzed by chiral catalysts has been extensively studied. Among numereous systems that are developed, recent studies focus on the use of organocatalysts. In this study, we intent to report the synthesis of new 2,2,6,6- tetramethylpiperidine (TEMPO) containing chiral polymers for this purpose [Figure 7]. The polymers will be used as catalysts for the oxidative kinetic resolution of 1-phenylethanol. The hypothesis is that the chiral backbone provides chiral environment which will prevent one of the enantiomers from approaching the TEMPO. This hypothesis will be tested under Anelli's conditions. The advantage of this method will be the possible regenaration of the polymers after an oxidation reaction. In addition, the synthesis of a simple TEMPO containing polymer will be repeated to investigate its electrochemical properties by constructing a primitive organic radical battery.



polA: R=Me, X=O
polB: R=Me, X=NH
polC: R=Bn, X=O
polD: R=Bn, X=NH

Figure 7. Synthesized TEMPO containing chiral polymers

CHAPTER 3

RESULTS AND DISCUSSION

3.1 TEMPO Attached Chiral Polymers

3.1.1 Design of the TEMPO Attached Chiral Polymers

In the literature, there have been several reports utilizing nitroxyl radicals for oxidative kinetic resolution of secondary alcohols.[29,30,31] To induce selectivity in oxidation of one enantiomer, (this in the literature is refered as *enantioselective oxidation* which is misused in our opinion (advisor and the author)) these nitroxyl radicals should be used in a chiral environment. To achieve the chiral environment, research groups synthesized types of chiral nitroxyl radicals,[29,30] or nitroxyl radicals were used together with other chiral reagents.[31] The preparation of such catalysts are cumbersome. Moreover, to our best knowledge, none of them included nitroxyl radical attached chiral polymeric backbones to create a chiral environment for such purpose. With these, our efforts mainly focused on designing polymeric reagents with TEMPO moieties attached to them. Environmentally benign TEMPO seemed to be an obvious alternative as a nitroxyl radical and it is widely used for the mild oxidation of secondary alcohols. Withal, polymeric reagents are user friendly due to their alterable physical properties like solubility. Further, polymeric reagents could simply be separated and regenerated for further oxidation reactions.

To test the effect of chiral sidechains on polymers, four new TEMPO attached chiral polymers were targeted to be used in kinetic resolution of secondary alcohols [Figure 8]. Chirality was introduced to these polymers with easily accessible, affordable enantiopure amino acids. Chiral sidechains are shown to enforce helicity to polymers.[51] Consecutively, this helicity could provide the TEMPO unit with the chiral environment that is needed for enantioselectivity in oxidation.

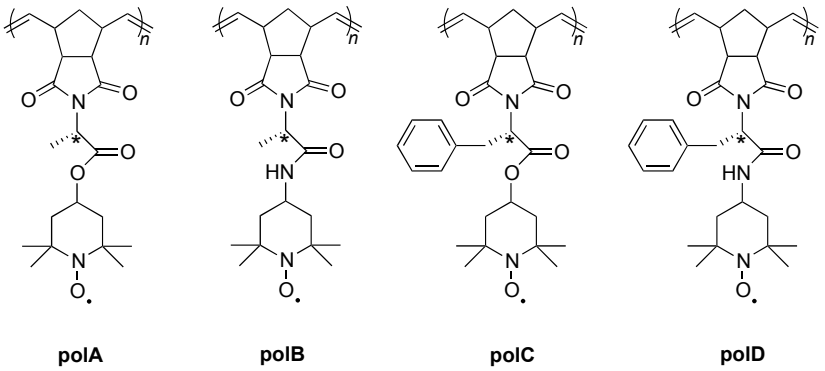
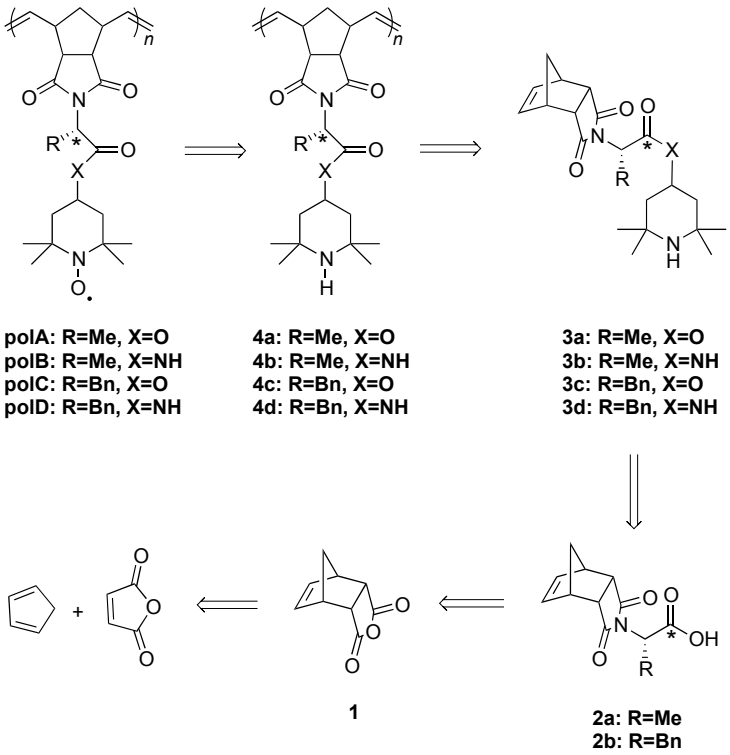


Figure 8. Designed TEMPO attached chiral polymers

Polymers **polA** and **polB** will have *L*-alanine, polymers **polC** and **polD** will have *L*-phenyl alanine as chirality inducing agent. Phenyl alanine has sterically more hindered side chain than alanine. Furthermore, ester and amide (linkage where piperidinyl unit is bonded to the aminoacid unit) structure-property relationship will be observed through examining **polA** and **polC** versus **polB** and **polD**.

3.1.2 Synthesis of the TEMPO Attached Chiral Polymers

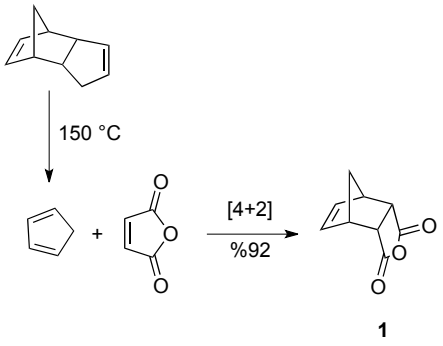
The retrosynthetic analyses of the polymers revealed a synthesis with total of 5 steps for each polymer [Scheme 20]. All four of the designed polymers were synthesized in the same manner. Syntheses start with the formation of norbornene skeletons by Diels-Alder reaction of cyclopentadiene with maleic anhydride. Then, chiral amino acids were incorporated to the resulting carbic anhydride. Substantial esterification or amidation of the carboxylic acids with 2,2,6,6-tetramethylpiperdine derivatives afford the desired monomeric structures. Monomers were then polymerized by ring opening metathesis polymerization (ROMP) and the double bonds on the resulting polymers were hydrogenated. Finally, the polymers were oxidized to obtain TEMPO containing chiral reagents.



Scheme 20. Retrosynthetic analysis of the synthesized polymers

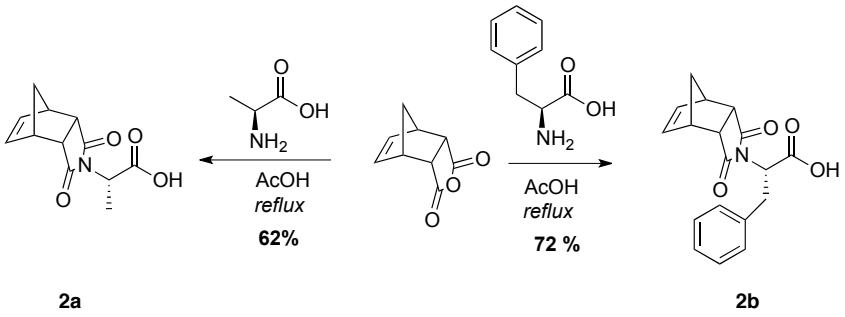
3.1.2.1 Synthesis of the Monomers

Synthesis of the monomers required three steps. In the first step, carbic anhydride structure was obtained as [4+2] Diels Alder adduct of maleic anhydride and cyclopentadiene. Cyclopentadiene dimer was cracked at 170 °C to get cyclopentadiene which was collected by distillation into a flask cooled to -78 °C to prevent dimerization. The freshly distilled diene was treated with maleic anhydride to give carbic anhydride as a white precipitate, with a yield over 90 % [Scheme 21]. The compound **1** did not need further purification. ^{1}H NMR and melting point of the product were consistent with the previously reported data.[52]



Scheme 21. Synthesis of carbic anhydride (**1**)

In the second step, chiral alanine derivatives were incorporated to the norbornene skeletons. For this, the Diels Alder adduct **1** was treated with either *L*-Alanine or *L*-Phenyl alanine in acetic acid [Scheme 22]. The resulting carboxylic acids **2a** and **2b** were analyzed using ^{1}H NMR and the assigned protons in the structures are given in Figure 9. The vinylic protons of the *L*-Alanine containing acid **2a** appear to be identical, showing a multiplet at 6.1 ppm for two protons. On the other hand, *L*-Phenyl alanine containing structure suggested two different vinylic protons which showed two different shifts. This was observed for compounds **3a** and **3c** as well, and the origin of this observation is discussed below.



Scheme 22. Synthesis of compound **2**

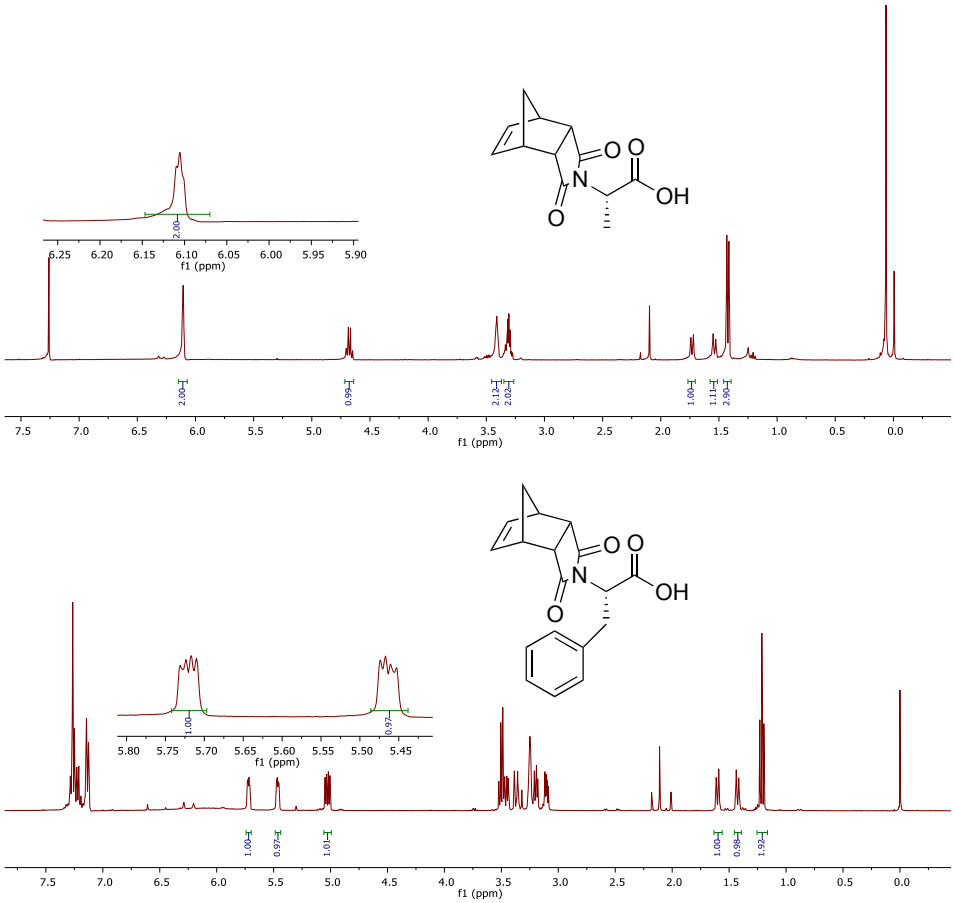
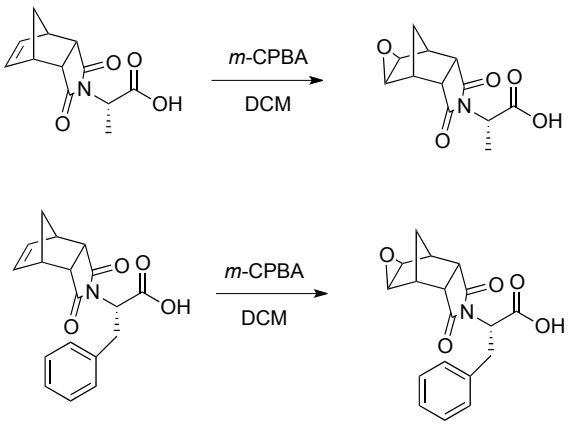


Figure 9. ^{1}H NMR of compound **2a** and **2b**

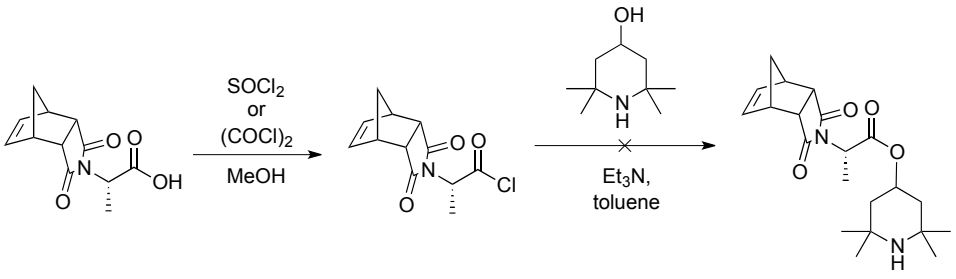
The methyl groups are smaller compared to the phenyl group. In an epoxidation reaction one might expect that epoxidation of **2a** with *m*-CPBA will result in diastereomic mixture, while for **2b**, one might expect the product to be a single diastereomer. Despite these expectations, the treatment of **2a** and **2b** in dichloromethane with *m*-CPBA, yielded single diastereomer for both as judged by ^{1}H NMR [Scheme 23].



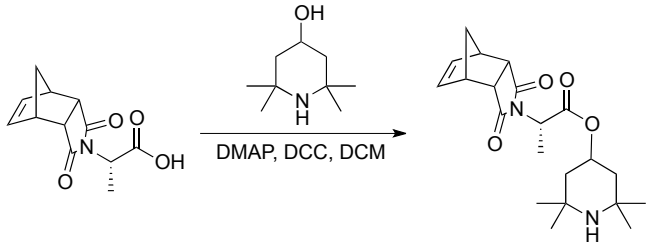
Scheme 23. Epoxidation reactions of **2a** and **2b**

Finally, TEMPO precursor piperidines were incorporated to the acids to obtain four different chiral monomers **3**. In **3a** and **3c**, piperidine is incorporated into the structures through ester bonds; while in **3b** and **3d** the linkage is an amide.

In our first attempts to form ester bond in **3a, 2a** was first converted to the acyl chloride derivatives by the treatment with thionyl chloride, and oxalyl chloride. The resulting chlorides were too reactive that they were easily hydrolysed when exposed to the moisture in the atmosphere [Scheme 24]. Therefore, we decided to run the esterifcation reactions by employing DCC coupling. In this reaction the acid **2a** was treated with 4-hydroxy-2,2,6,6-tetramethyl piperdine in the presence of N,N′-Dicyclohexylcarbodiimide (DCC) [Scheme 25]. Although this experiment furnished the desired compound **3a,** the side product, dicyclohexylurea (DCU), could not be removed from the product despite many column chromatography efforts.

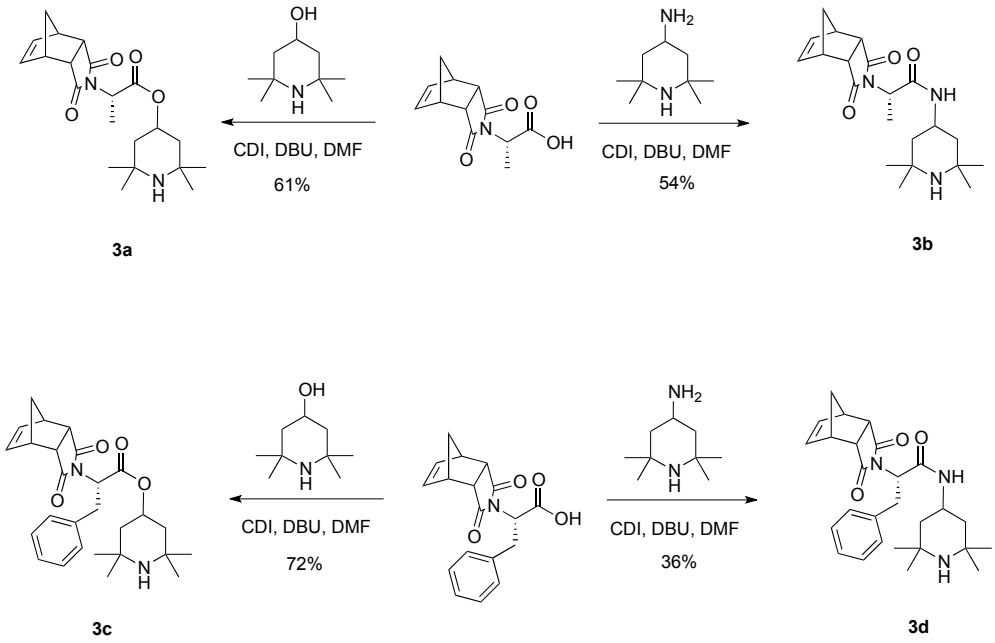


Scheme 24. Acylation of carboxylic acids, followed by esterification



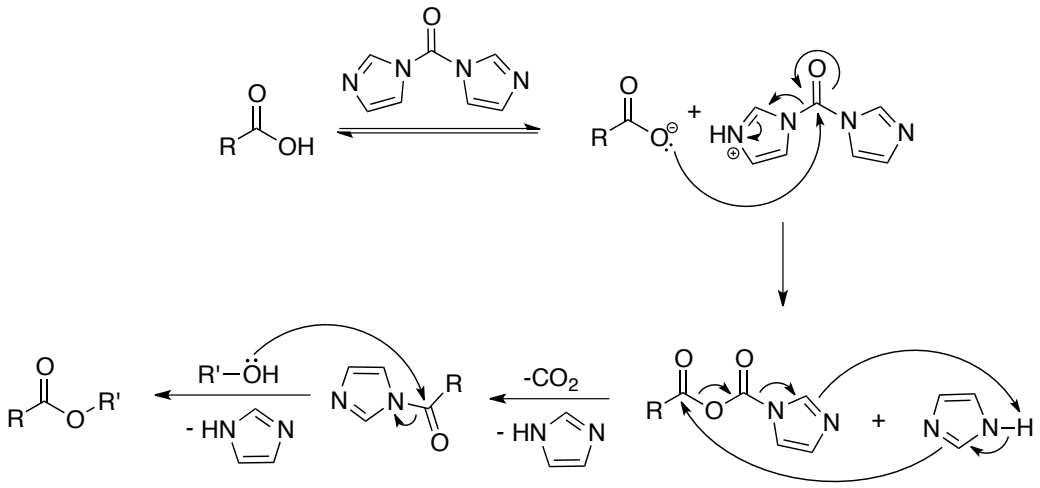
Scheme 25. DCC coupling of **2a** with 4-hydroxy-2,2,6,6-tetramethyl piperidine

With these in mind, we searched for alternative ways to get compound **3a**. The widely used N,N'-Carbonyldiimidazole (CDI) was considered to be a suitable reagent for such couplings on paper. To run the reaction, CDI was added in portions to carboxylic acid **2a** in DMF and the resulting solution was stirred for 1 hour at room temperature. Subsequently, 4-hydroxy-2,2,6,6-tetramethyl piperidine was added and the solution was stirried at 60 °C for 4 hours. Water was added to cease the reaction, then the product was extracted into ethyl acetate [Scheme 26]. This reaction furnished a pure compound, without a need for column chromatography for further purificatiın. Compounds **3b**, **3c**, and **3d** were obtained in similar manner.



Scheme 26. Esterification and amidation of carboxylic acids

A representative general mechanism of CDI esterification is shown in Scheme 27. First, the treatment of carboxylic acids with CDI at room temperature yields imizolides with the liberation of CO_2. Then, esters or amides are formed by the addition of alcohols or amines; respectively.



Scheme 27. A representative mechanism for CDI esterification

In the ^{1}H NMR of the products **3a** and **3b**, the vinylic protons were observed to resonate at same chemical shift [Figure 10]. However, for products **3c** and **3d** two different chemical shifts were seen on the spectra. To understand this difference, NOESY experiments were run for both compounds **3a** and **3b**. This showed that the protons on phenyl groups are close to one vinylic proton while far from the other one. This is probably causing these two protons to resonate at two different chemical shifts. That is, one proton is shielded more than the other one due to the interaction with the phenyl ring. The effect of the phenyl ring is circled in red in Figure 11.

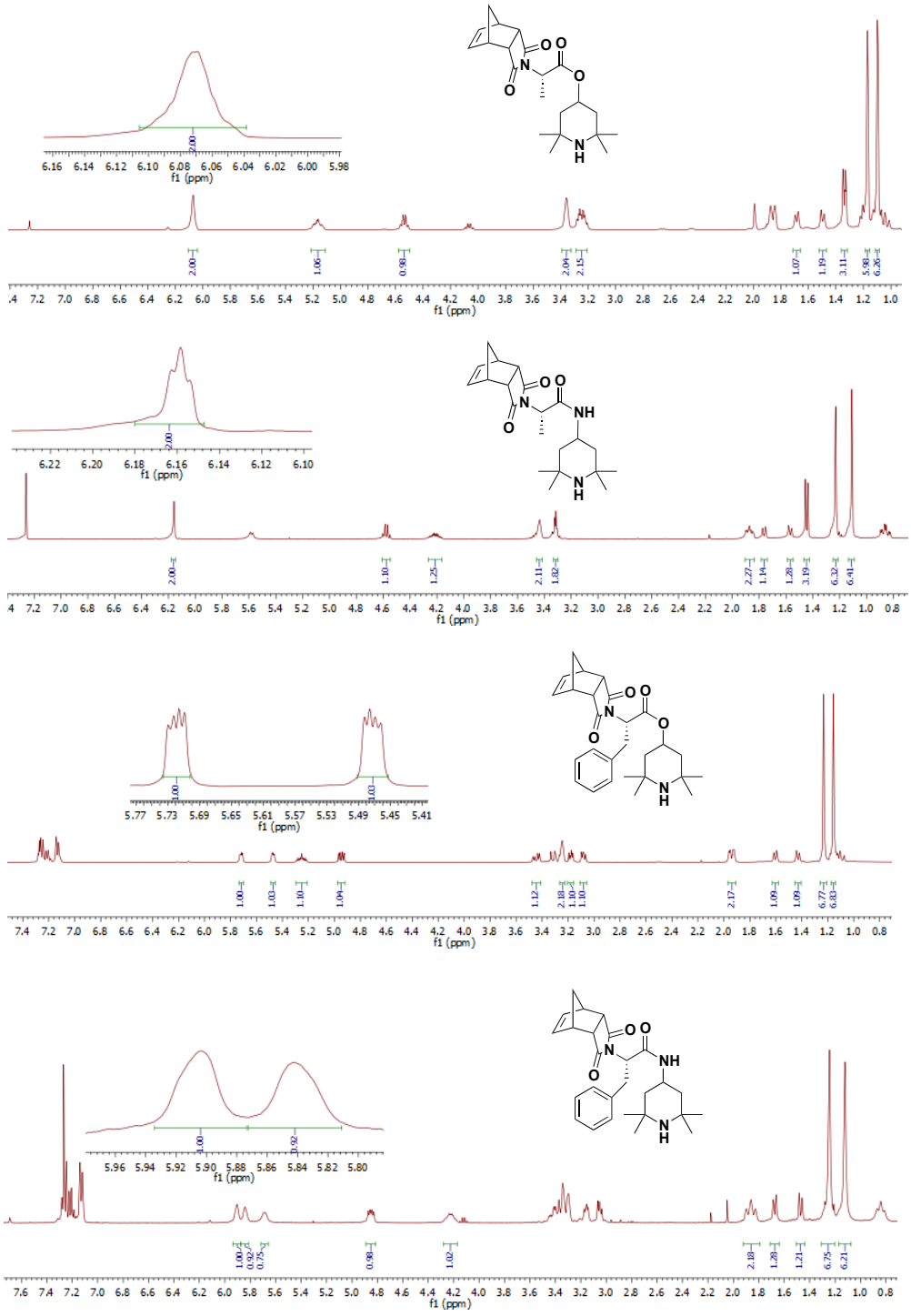


Figure 10. Difference in vinylic protons of alanine and phenyl alanine derivatives

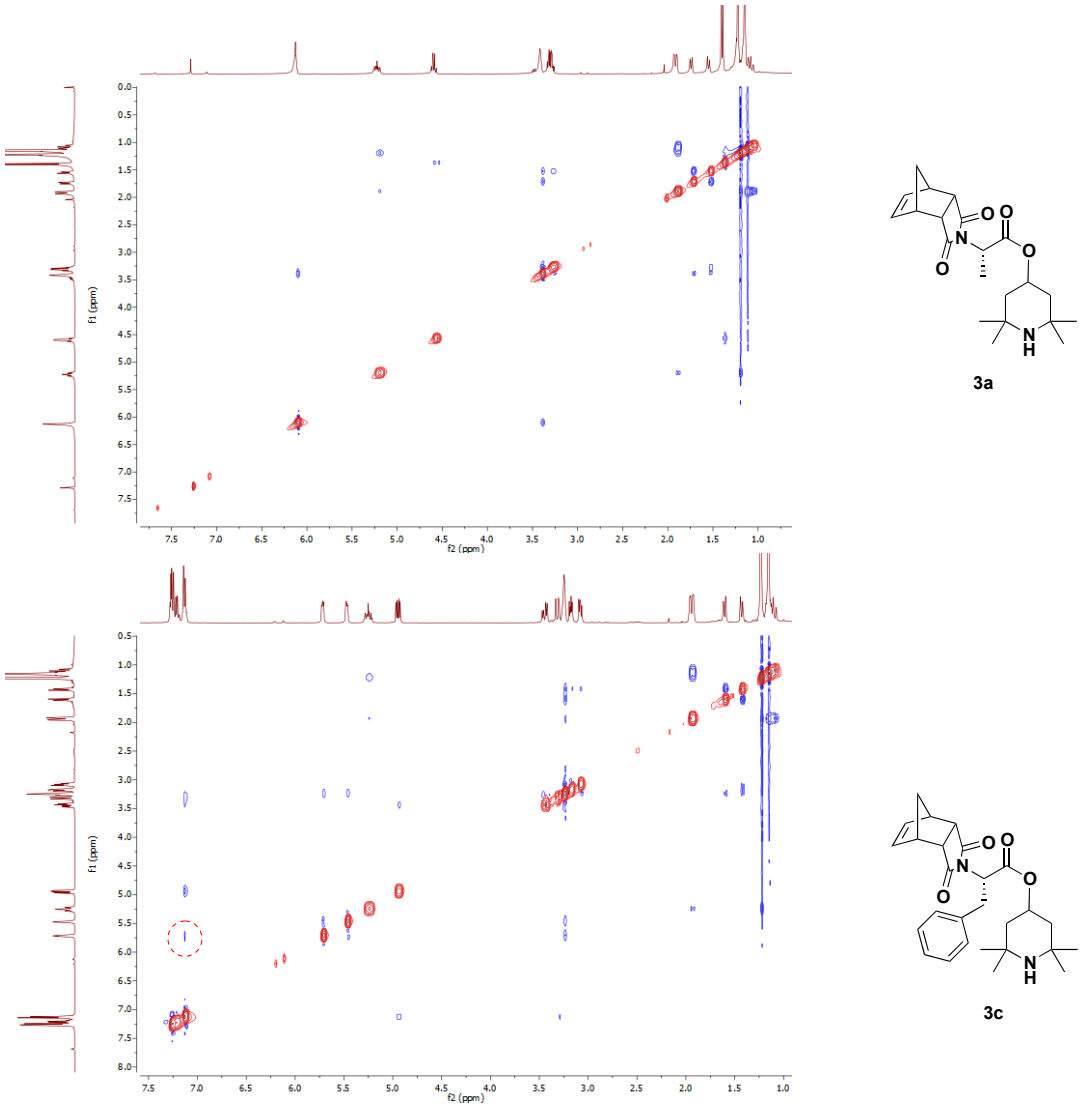


Figure 11. NOESY NMR Spectra of **3a** and **3b**.

The above mentioned difference in ^{1}H NMR was further investigated by DFT calculations. The calculations were run at the level of M06/6-311G(d) level of theory as implementedin Gaussian 09.[53] Calculation revealed that the methyl group has no effect on the vinylic protons [Figure 12]. However, phenyl groups in **3c** has an effect on the vinylic protons that one proton seems to be more shielded. Morever, **3c** could have two conformers due to the free rotation around chiral center and the benzylic carbon, resulting in structures **3c_1** and **3c_2**. **3c_2** is more stable by 1.07 kcal/mol according to the calculations.

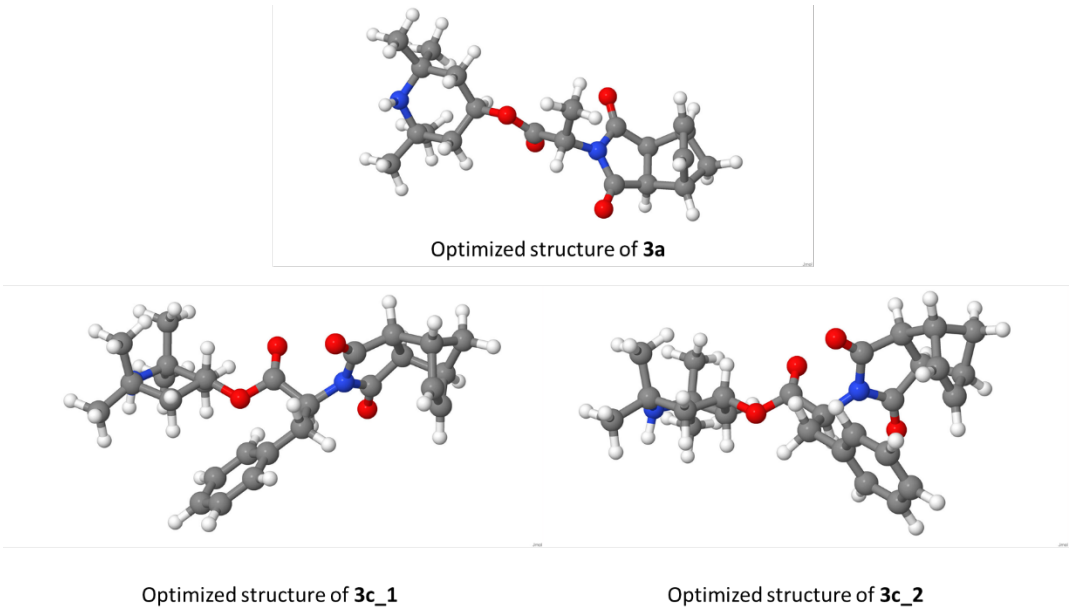
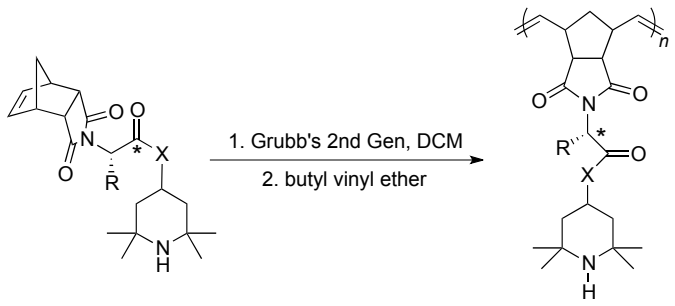


Figure 12. 3D structures of compound **3a** and **3c**

3.1.2.2 ROMP of the Monomers

The monomers were successfully synthesized and then they were polymerized by ROMP. Grubbs' 2nd generation catalyst was preffered over the first generation because this catalyst is reported to be more effective for the polymerization of such structures.[54] In the literature, ruthenium based catalysts are reported to exhibit enhanced air and light stability over other catalyst. [55] Still, the polymerizations were done under inert Argon atmosphere. The color of the solutions turned from yellow to brown and the viscosities have increased after 2 days. For the termination, butyl vinyl ether was used and the polymers were washed with diethyl ether and water for purification [Scheme 28].



3a: R=Me, X=O
3b: R=Me, X=NH
3c: R=Bn, X=O
3d: R=Bn, X=NH

4a: R=Me, X=O
4b: R=Me, X=NH
4c: R=Bn, X=O
4d: R=Bn, X=NH

Scheme 28. ROMP of the monomers

Different catalyst loadings were employed under the same conditions for the synthesis of the polymers. It was concluded that a catalyst loading of at least 1.0 mol % is required for the synthesis of *L*-alanine containing polymers, whereas for *L*-phenyl alanine containing ones this ratio should be doubled. This was explained with the steric effects of the phenyl ring exerted on the double bonds, blocking the catalyst for the initiation step (*vide supra*).

The initial indication for a possible polymerizations were the appearent decrease in viscocity observed during the course of the reactions. After doing the workup for the reactions, the ^{1}H NMR spectra of the monomers and polymers were compared. The disapearence of the peaks belonging to the vinylic protons on the monomers, supported the polymerization of the monomers. The difference in ^{1}H NMR data for **3a** and **4a** is shown in Figure 13. For **3b** and **4b**, please see Apendices. NMR analyses for the remaining polymers, **4c** and **4d**, were not possible due to solubility problems of the polymers.

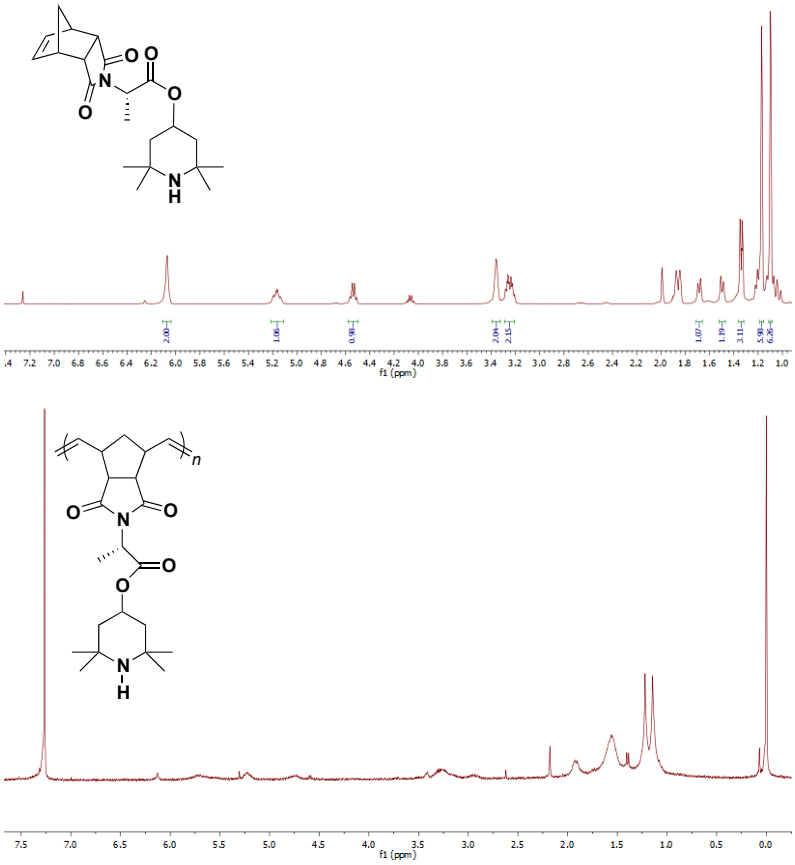
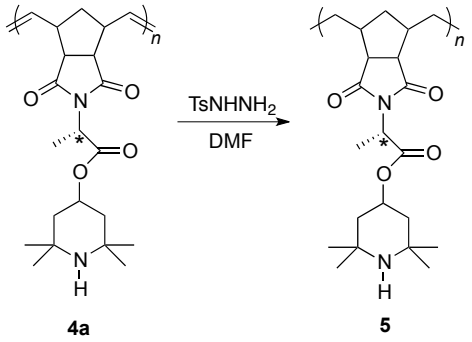


Figure 13.[1]H NMR of **3a** and **4a**

3.1.2.3 Hydrogenation of the Polymer 4a

The olefinic groups on the polymers **4** are prone to oxidation and can also be oxidized to form epoxides or hydroxylated compounds in the oxidation of piperidines to TEMPO radicals. This may deviate our attention from our primary goal. To observe the effect of the double bonds on the backbone of the polymers, polymer **4a** was hydrogenated. The hydrogenation method used for this study facilitates stochiometric amount of *p*-toluenesulfonyl hydrazide ($TSNHNH_2$) as reducing agent.[56] Polymer was dissolved in DMF and the reducing agent was added. The solution was allowed to reflux for 4 hours. With the addition of diethylether, the polymer precipitated from the reaction mixture and the resulting side product, *p*-toluenesulfonic acid, was removed by washing with methanol [Scheme 29]. The resulting polymers were

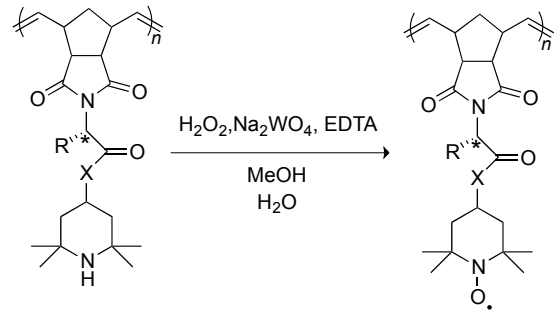
compared, and no appearent difference was observed in their reactivities in an oxidation reactions. Thus, for the remaining polymers **4b**, **4c**, **4d** hydrogenation was not performed.



Scheme 29. Hydrogenation of the polymer **4a**

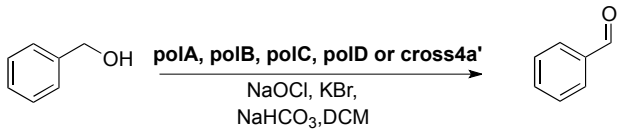
3.1.2.4 Oxidation of Piperidines to TEMPO Radicals

Hydrogenated polymers were subjected to oxidation to yield the desired TEMPO radicals on the structures. Polymers were dissolved in MeOH/water mixture in round bottomed flasks. To the stirring solutions, $Na_2WO_4.2H_2O$ and EDTA were added. H_2O_2 was introduced to the solutions in portions during 4 days of oxidation. The resulting orange/brown polymers were then collected by simple fitration [Scheme 30].



Scheme 30. Oxidation of the piperidines to TEMPO radicals

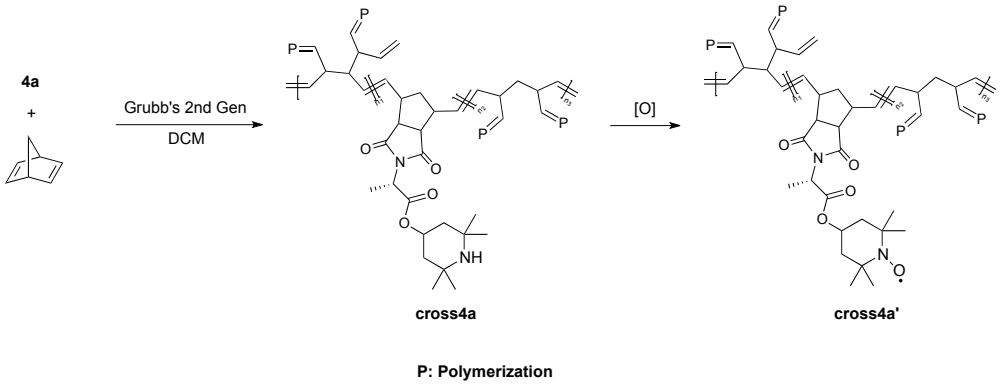
Characterization of the resulting polymeric structures using NMR Spectroscopy is troublesome due to the presence of paramagnetic electron on the TEMPO. Thus, an alternative approach was taken. To examine the existence of TEMPO units in the their structures, polymers were tested as catalysts in Anelli oxidation.[39] Conversion of benzyl alcohol to the corresponding aldehyde confirmed the existence of TEMPO units in the structures [Scheme 31]. This method was employed in our previous studies for the existence of TEMPO radical.[54,57]



Scheme 31. Anelli oxidation using the synthesized polymers

3.1.2.5 Crosslinking of Polymer 4a

Polymer **4a** was also crosslinked with norbornadiene in 1:1 ratio and under the same conditions discussed above to give **cross4a** [Scheme 32]. This was done so to obtain a rigid polymer with significantly reduced solubility. Such a polymer, may contain chiral pockets which may induce enantioselectivity in an alcohol oxidation. Moreover, the recovery of the polymer after the oxidations is easier for such structures. When we compare the SEM images of polymers with the crosslinked ones, it was seen that crosslinked polymers have crystallinity while the other polymers showed no crystallinity [Figure 14].



Scheme 32. Synthesis of crosslinked polymer**, cross4a**

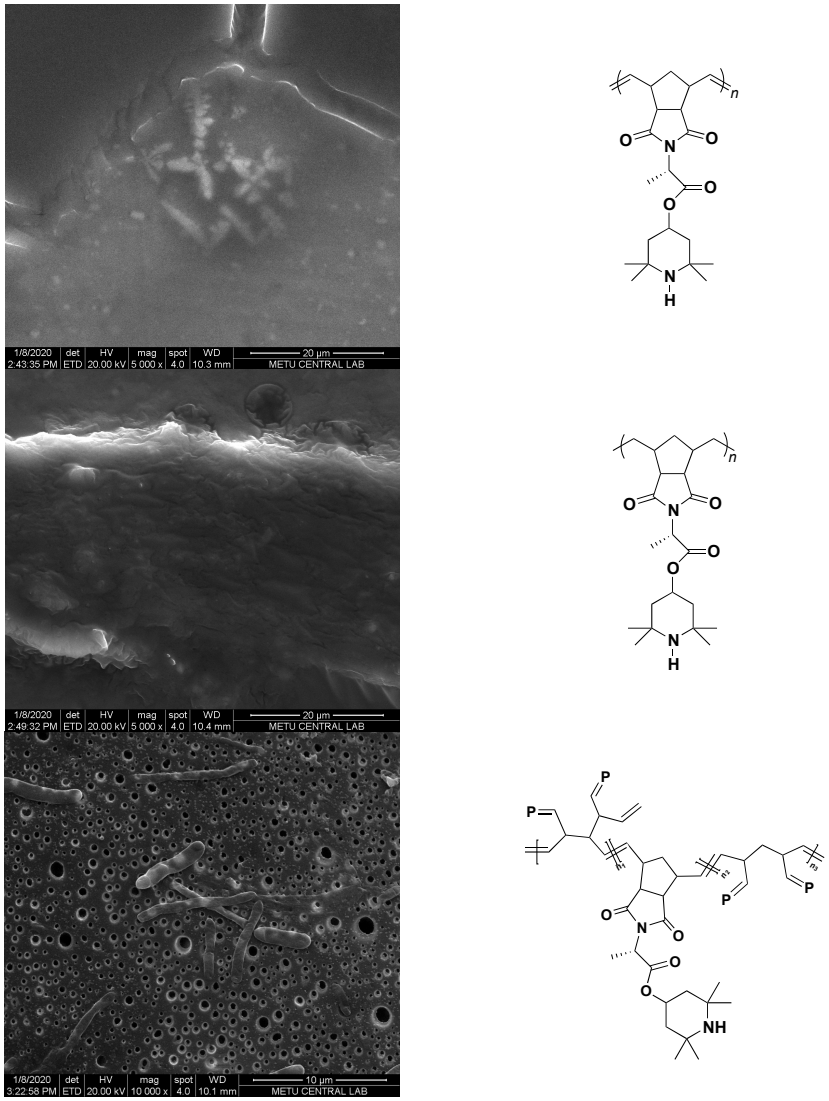
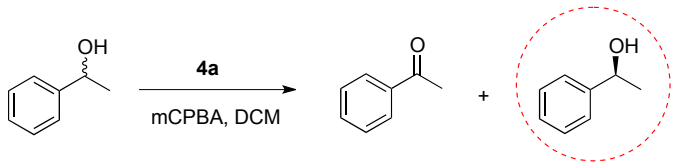


Figure 14. SEM Images of **4a**, **5**, and **cross4a**

3.1.2.6 Studies on Use of the Chiral Polymers for Oxidative Kinetic Resolution of Secondary Alcohols

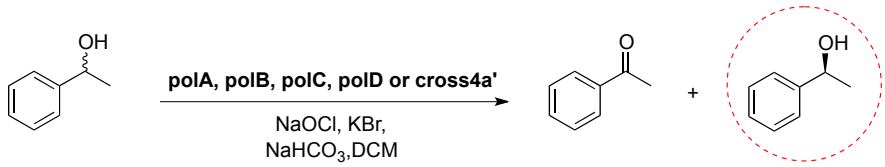
In the literature, kinetic resolution of racemic 1- Phenyl ethanol as a secondary alcohol is the most studied one.[30] This is due to the existence of the phenyl ring, crowdening the environment around the alcohol. This effect may result in enantioselectivity in oxidation. Therefore, in this study, 1-Phenyl ethanol was chosen as a substrate and subjected to oxidation using the synthesized polymers as catalysts for kinetic resolution.

First, oxidation under acidic conditions was performed in the presence of mcPBA as the primary oxidant. TEMPO containing polymers were used in minute amounts and the reactions were monitored using TLC. After 2 hours of stirring, the product mixture was seperated using column chromatography [Scheme 33]. Obtained alcohol mixture was analyzed using chiral HPLC. Using a Chiralcel OD column, enantiomers of the alcohols were seperated. However, there were no considerable enantiomeric excess in the resulting mixture.



Scheme 33. Oxidation under acidic conditions

Reviewing the mechanisms involved in TEMPO mediated oxidations, it was concluded that performing oxidations under basic conditions is a better alternative for kinetic resolution. This is due to the steric demand in such oxidations. Thus, 1-Phenyl ethanol was also oxidized under basic conditions with NaOCl as the primary oxidant (Anelli's protocol). Synthesized TEMPO containing polymers were again used and the solutions were stirred for 2 hours [Scheme 34]. The resulting mixture was analyzed once again with the Chiralcel OD column, however there were no considerable enantiomeric excess.



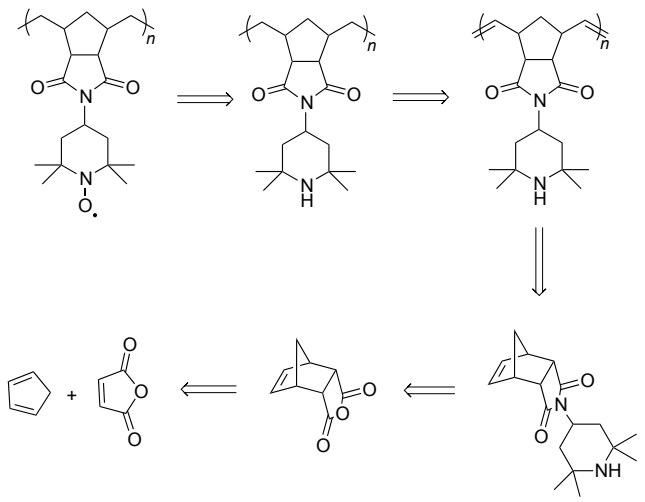
Scheme 34. Oxidation under basic conditions

3.2 TEMPO Attached Polymers for Organic Radical Battery Application

TEMPO attached polymers have also been used for the selective oxidation of alcohols to aldehydes. Tanyeli and coworkers used such polymers under Anelli's conditions for the oxidation of primary alcohols to corresponding aldehydes, and reported oxidation potentials comparable with the monomeric TEMPO units.[58]

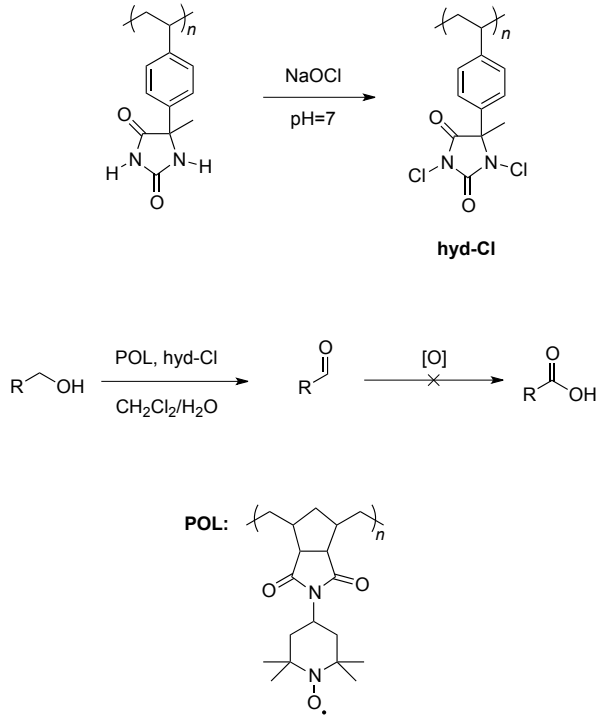
In our previous study, we reported the synthesis of new TEMPO attached polymers to be used together with readily available hydantoin polymer beads **hyd-H**, for TEMPO mediated oxidation of primary alcohols to aldehydes. The system used all polymeric reagents which could simply be separated and regenerated to be used for other oxidation reactions.[57]

The synthesis starts with the Diels-Alder reaction of maleic anhydride with cyclopentadiene to give [4+2] Diels Alder adduct. Resulting carbic anhydride was reacted with 2,2,4,4-tetramethylpiperidine to furnish the monomer, and the monomer was polymerized by ROMP with Grubbs' 2nd generation catalyst. The double bonds in the polymeric structure were hydrogenated using Pd as catalyst in a high pressure reactor at 60 bar. The partially hydrogenated polymer was then exposed to oxidation to get the nitroxyl radical [Scheme 35]. The synthesized monomer was also crosslinked with norbornadiene to yield polymers with lower solubilities to be used as a heterogeneous catalyst. Furthermore, it was shown that these polymers can be recovered and reused for consecutive oxidations of primary alcohols.[57]



Scheme 35. Synthetic scheme of the previously synthesized polymer

The TEMPO mediated oxidation reactions were conducted at the same conditions for various alcohols. These reactions provided selectively aldehydes within 3-6 hours. After completed reactions, the polymeric mixture was filtered off and regenerated by chlorination with aqueous NaOCl solution [Scheme 36].



Scheme 36. General scheme for the selective oxidation of alcohols to aldehydes

With the TEMPO containing functional polymer in hand, the adventures of these polymers remained to be tested; organic functional polymers have been developed as alternatives to inorganic materials because of their light weight, flexibility, thin film-forming ability, processability, metal-free or environmentally benign nature, and no limitation in organic resources. With these in mind, the organic nitroxide radical containing polymers are great candidates for the production of organic radical batteries. These batteries are characterized by their excellent electrochemical properties such as high charging/discharging rate and long cycle stability.

A primitive test cell of an organic radical battery was also assembled with the TEMPO attached polymer described above [Figure 15]. In a glove bag filled with Argon gas, the battery was constructed. For the cathode material, synthesized TEMPO-containing polymer powder was mixed with 40% of charcoal as a conductive additive and 10% of cellulose as the binder. The mixture was dissolved in N-Methyl-2-pyrrolidone (NMP), and the resulting slurry was spread over an aluminum plate. The aluminum plate was then heated on a hot plate to remove the solvent. As the anode material, a Li wire was chosen. A maximum of 2.5 V was achieved in a 0.1 M of $LiClO_4$ in acetonitrile solution as the electrolyte.

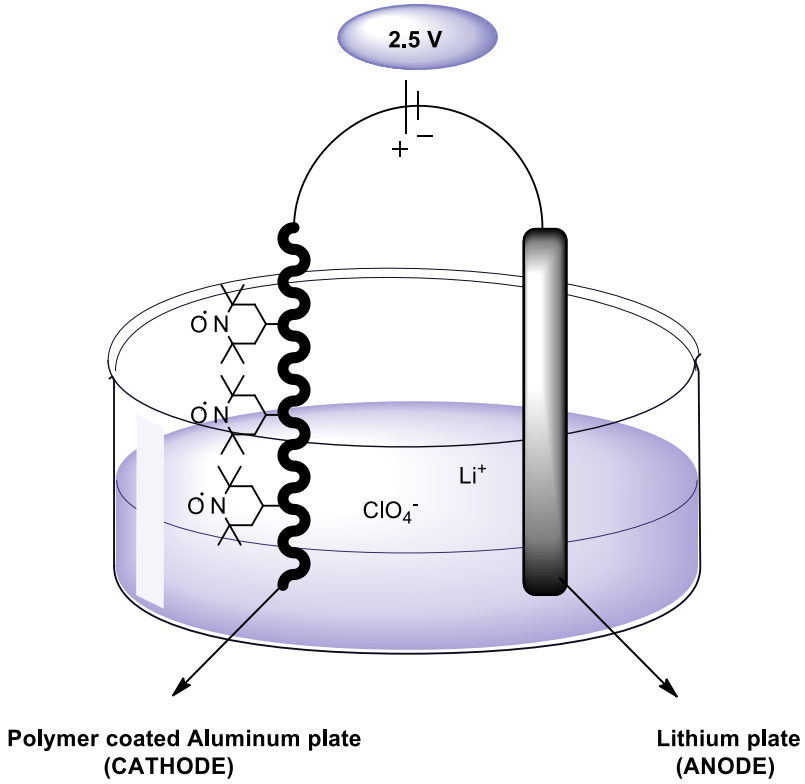


Figure 15. Schematic representation of the assembled cell

Compared with the well known PTMA containing batteries, the assembled primitive cell shows promising performance. This study is still under investigation for further improvements and an all organic battery is the ultimate goal for such a study.

CHAPTER 4

CONCLUSION

In the first part of this thesis, four new TEMPO containing polymers were synthesized and characterized. The polymers were designed to have chiral sidechains to enforce helicity on their structures. Thus, commercially available chiral alanine derivatives were used to induce chirality on the monomers. ^{1}H NMR spectra of the synthesized alanine and phenyl alanine containing monomers were consistent with the structures. Consequitive ROMP of the synthesized monomers with Grubbs' 2nd generation catalyst afforded the desired polymers. However, to achieve polymerization of phenyl alanine containing monomers, catalyst loading had to be at least twice as much as the one used for the alanine containing one. This was thought to be the result of the presence of the phenyl ring, effecting the coordination of the catalyst to the double bond. After the polymerization, piperidine moeities on the polymers were oxidized to yield the desired TEMPO containing chiral polymers. Afterwards, synthesized polymers were tested as catalysts for oxidative kinetic resolution of 1-phenyl ethanol. Anelli's protocol was employed and the secondary alcohol was partially oxidized to the corresponding ketone. Unreacted alcohol mixture was seperated from the reaction mixture using column chromatography and the enantiomers were analyzed using chiral HPLC. However, the expected selectivity was not observed under the experimental conditions employed. The helicity of the polymer should be provided for the kinetic resolution of alcohols. This remains a challange in our studies for now.

In the second part of this thesis, synthesis of another TEMPO containing polymer (previously synthesized in our laboratory) was repeated to be used as cathode material in the construction of a primitive organic radical battery. A maximum of 2.5 Voltage was achieved against Li anode, which is comparable with the previously reported organic radical battery materials. This is promising and deserves a further study.

CHAPTER 5

EXPERIMENTAL

5.1 Methods and Material

All starting materials and solvents except ethyl acetate and hexane were purchased from Sigma Aldrich and were used without further purifications. Solvents used for Flash Chromatography were distilled prior to use (EtOAc and Hexane over $CaCl_2$). The reactions were monitored by thin layer chromatography (TLC) (Merck Silica Gel 60 F254) and visualized by UV light at 254 nm.

Structural evaluation of the synthesized compounds was accomplished with the instruments stated below:

Melting points were measured using Stuart SMP11 Instrument. All reported melting points were uncorrected.

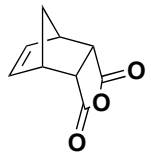
^{1}H and ^{13}C nuclear magnetic resonance spectra of the compounds were recorded in $CDCl_3$ with Bruker Avance III Ultrashield 400 Hz NMR spectrometer. The chemical shifts were stated in parts per million (ppm) with tetramethylsilane (TMS) as internal reference. Spin multiplicities were indicated as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), tt (triplet of triplet), m (multiplet) and coupling constants (J) were reported as in Hz (Hertz). Raw ^{1}H and ^{13}C NMR spectra of products were given in Appendix A. NMR spectra were processed with MestReNova program.

Infrared (IR) Spectra were recorded with Thermo Scientific Nicolet iS10 ATR-IR spectrometer. Signal locations were reported in reciprocal centimeter (cm^{-1}). The IR spectra of the compounds synthesized are given in Appendix B. IR spectra were processed with OriginPro 2015 program.

High Resolution Mass Spectra (HRMS) are given in Appendix C. Spectra were processed in positive mode on (ES+) using Time of Flight mass analyzer.

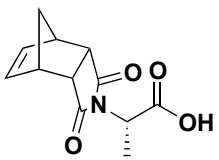
5.2 Synthesis of the TEMPO Attached Polymers

5.2.1 Synthesis of Carbic Anhydride (1)[59]



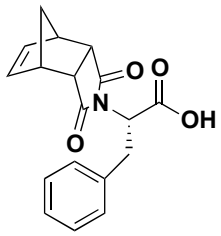
A 50-ml round-bottomed flask containing cyclopentadiene dimer (30.00 ml) was attached to a fractional distillation setup. The dimer was heated on an oil bath to approximately 170 °C. The cracked cyclopentadiene was collected in another round-bottomed flash which was cooled to -78 °C using dry ice-acetone mixture. Maleic anhydride (9.00 g, 91.78 mmol) was dissolved in ethyl acetate-hexane mixture (15:20) upon heating. This solution was cooled on an ice bath, prior to the addition of the cracked cyclopentadiene. To the cooled solution, freshly prepared cyclopentadiene (6.68 g, 101.07 mmol) was added dropwise. After all the cyclopentadiene was added, white crystals were formed which were filtered to obtain the product. (15.30 g, 92.2%) m.p: 165 °C. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.33-6.30 (m, 2H), 3.60-3.57 (m, 2H), 3.54-3.48 (m, 2H), 1.79 (d, *J*=9.0, 1H), 1.58 (d, *J*=9.2, 1H).

5.2.2 Synthesis of (*S*)-2-((3a*R*,4*S*,7*R*,7a*S*)-1,3-dioxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoisoindol-2(3*H*)-yl)propanoic acid (2a)[60]



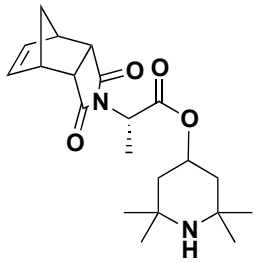
Compound **1** (6.00 g, 36.55 mmol) was mixed with *L*-alanine (3.30 g, 37.04 mmol) in a 250-ml round-bottomed flask. The solution was refluxed in acetic acid (150.00 ml) overnight. Subsequently, acetic acid was evaporated and the residue was extracted with diethyl ether and water. The organic phase was separated and dried over Na_2SO_4. White crystals were obtained after evaporation under vacuum. (6.12 g, 71.2%) m.p: 137 °C. $[\alpha]_{589}^{20\,°C}$ = -45.4° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.04 (t, *J*=1.9, 2H), 4.61 (q, *J*= 14.5, 7.2, 1H), 3.38-3.32 (m, 2H), 3.28-3,21 (m, 2H), 1.67 (dt, *J*= 8.8, 1.7, 1H), 1.49 (d, *J*= 8.8 1H), 1.36 (d, *J*=7.2, 3H). IR: 3255 cm^{-1} (O-H stretching), 2976 cm^{-1} (C-H stretcing), 1767 cm^{-1} (C=O stretching), 1738 cm^{-1} (C=O stretching), 1666 cm^{-1} (C=O stretching).

5.2.3 Synthesis of (*S*)-2-((3a*R*,4*S*,7*R*,7a*S*)-1,3-dioxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoisoindol-2(3*H*)-yl)-3-phenylpropanoic acid (2b)[60]



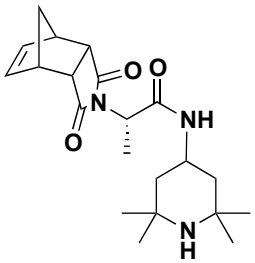
Compound **1** (6.00 g, 36.55 mmol) was mixed with *L*-phenylalanine (6.00 g, 36.32 mmol) in a 250-ml round-bottomed flask. The solution was refluxed in acetic acid (150.00 ml) overnight. Subsequently, acetic acid was evaporated and the residue was extracted with diethyl ether and water. The organic phase was separated and dried over Na_2SO_4. White crystals were obtained after evaporation under vacuum. (8.12 g, 71.8%) m.p: 132 °C. $[\alpha]_{589}^{20\,°C}$ = -56.7° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.29-7.11 (m, 5H), 5.73-5.70 (m, 1H), 5.48-5.45 (m, 1H), 5.03 (dd, *J*= 11.5, 5.3 1H), 3.53-3.44 (m, 2H), 3.25 (m, 2H), 3.22-3.17 (m, 1H), 3.13-3.08 (m, 1H),1.60 (d, *J*= 8.8, 1H), 1.43 (d, *J*= 8.7, 1H). IR: 3248 cm^{-1} (O-H stretching), 2985cm^{-1} (C-H stretching), 1772 cm^{-1} (C=O stretching), 1749 cm^{-1} (C=O stretching), 1695 cm^{-1} (C=O stretching).

5.2.4 Synthesis of Compound 3a



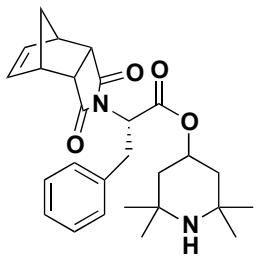
CDI (4.22 g, 26.00 mmol) was added in small portions to a stirred solution of **2a** (5.69 g, 24.20 mmol) in DMF (10.00 ml). The solution was stirred for an hour at room temperature. To the mixture, was then added 2,2,6,6-Tetramethyl-4-piperidinol (3.81 g, 24.20 mmol) and DBU (3.68 g, 24.20 mmol). The solution was stirred overnight at 60 °C. In the morning, the solution was concentrated under vacuum and diethyl ether was added to the residue. Precipitation occurred and white crystals were collected by filtration. (5.55 g, 61.2%) m.p: 106 °C. R_f: 0.23 in EtOAc. $[\alpha]_{589}^{20\,^{\circ}C}$ = -1.4° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 5.95-5.83 (m, 2H), 5.04-4.91 (m, 1H) 4.41-4.29 (m, 1H), 3.23-3.01 (m, 4H), 1.73-1.60 (m, 2H), 1.55-1.44 (m, 1H), 1.38-1.29 (m, 1H), 1.20-1.10 (m, 3H), 1.05-0.86 (m, 14H). ^{13}C NMR ($CDCl_3$) δ (ppm): 175.98, 175.87, 134.14, 133.88, 70.04, 51.79, 51.02, 47.36, 45.44, 45.21, 44.70, 44.57, 43.13, 34.31, 28.62. IR: 3323 cm^{-1} (N-H stretching), 2953 cm^{-1} (C-H stretching), 1778 cm^{-1} (C=O stretching), 1738 cm^{-1} (C=O stretching), 1701 cm^{-1} (C=O stretching). HRMS: (TOF-MS) m/z: $[M+H]^+$ Calcd for $C_{21}H_{31}N_2O_4^+$ 375.2284, found 375.2284.

5.2.5 Synthesis of Compound 3b



CDI (4.38 g, 27.01 mmol) was added in small portions to a stirred solution of **2a** (6.00 g, 25.51 mmol) in DMF (10.00 ml). The solution was stirred for an hour at room temperature. To the mixture, was then added 4-Amino-2,2,6,6-tetramethylpiperidine (3.99 g, 25.51 mmol) and DBU (3.88 g, 25.51 mmol). The solution was stirred overnight at 60 °C. Subsequently, the solution was concentrated under vacuum and diethyl ether was added to the residue. A precipitate formation was observed as white crystals which were collected by filtration. (5.18 g, 54.1%) m.p: 177 °C. R_f: 0.08 in EtOAc. $[\alpha]_{589}^{20\,^{\circ}C}$ = -1.5 ° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.13-6.07 (m, 2H), 5.24-5.15 (m, 1H), 4.56 (dd, *J*=14.4, 7.2, 1H), 3.42-3.36 (m, 2H), 3.32-3.22 (m, 2H), 1.93-1.86 (m, 2H), 1.72 (d, *J*=8.8, 1H), 1.52 (d, *J*=8.7, 1H), 1.37 (d, *J*=7.2, 3H), 1.21-1.18 (m, 6H), 1.13-1.10 (m, 8H). ^{13}C NMR ($CDCl_3$) δ (ppm): 177.27, 177.09, 167.85, 135.23, 134.79, 52.55, 51.21, 50.01, 45.92, 45.77, 45.40, 45.20, 43.23, 35.13, 28.69. IR: 3367 cm^{-1} (N-H stretching), 3323 cm^{-1} (N-H stretching), 2970 cm^{-1} (C-H stretching), 1761 cm^{-1} (C=O stretching), 1689 cm^{-1} (C=O stretching), 1660 cm^{-1} (C=O stretching). HRMS: (TOF-MS) m/z: $[M+H]^+$ Calcd for $C_{21}H_{32}N_3O_3^+$ 374.2444, found 374.2445.

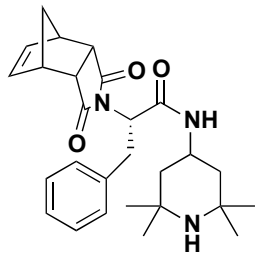
5.2.6 Synthesis of Compound 3c



CDI (1.72 g, 10.61 mmol) was added in small portions to a stirred solution of **2b** (3.00 g, 9.64 mmol) in DMF (10.00 ml). To the mixture, was then added 2,2,6,6-Tetramethyl-4-piperidinol (1,52 g, 9.64 mmol) and DBU (1.47 g, 9.64 mmol). The solution was stirred overnight at 60 °C. Subsequently, the solution was concentrated under vacuum and diethyl ether was added to the residue. A precipitate formation was observed as white crystals which were collected by filtration. (3.11 g, 71.6 %)

m.p: 116 °C. R_f: 0.29 in EtOAc. $[\alpha]_{589}^{20\,°C}$ = -2.6 ° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.29-7.11 (m, 5H), 5.74-5.71 (m, 1H), 5.49-5.45 (m, 1H), 5.30-5.21 (m, 1H), 4.95 (dd, *J*=11.4, 5.4, 1H), 3.48-3.28 (m, 2H), 3.28-3.22 (m, 2H), 3.21-3.14 (m,1H), 3.11-3.06 (m, 1H), 1.94 (d, *J*=11.8, 2H), 1.60 (d, *J*=8.8, 1H), 1.43 (d, *J*=8.7, 1H), 1.23 (s, 8H), 1.56 (m, 6H). ^{13}C NMR ($CDCl_3$) δ (ppm): 176.87, 176.78, 168.09, 136.67, 134.37, 134.29, 129.19, 128.47, 126.96, 70.96, 53.16, 52.27, 51.66, 45.99, 45.76, 44.92, 44.71, 43.81, 43.78, 34.92, 34.89, 34.00, 29.06, 29.04. IR: 3454 cm^{-1} (N-H stretching), 2970 cm^{-1} (C-H stretching), 1772 cm^{-1} (C=O stretching), 1738 cm^{-1} (C=O stretching), 1695 cm^{-1} (C=O stretching). HRMS: (TOF-MS) m/z: $[M + H]^+$ Calcd for $C_{27}H_{35}N_2O_4^+$ 451.2597, found 451.2558.

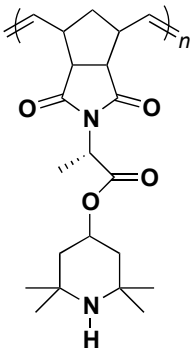
5.2.7 Synthesis of Compound 3d



CDI (0.77 g, 4.73 mmol) was added in small portions to a stirred solution of **2b** (1.34 g, 4.30 mmol) in DMF (5.00 ml). To the mixture, was then added 4-Amino-2,2,6,6-tetramethylpiperidine (0.67 g, 4.30 mmol) and DBU (0.65 g, 4.30 mmol). The solution was stirred overnight at 60 °C. Subsequently, the solution was concentrated under vacuum and diethyl ether was added to the residue. A precipitate formation was observed as white crystals which were collected by filtration. (0.70 g, 36.1 %) m.p: 182 °C. R_f: 0.09 in EtOAc. $[\alpha]_{589}^{20\,°C}$ = -3.2 ° in DCM. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.30- 7.10 (m, 5H), 5.94, 5.89 (m, 1H), 5.89-5.81 (m, 1H), 5.72-5.65 (m, 1H), 4.85 (dd, *J*=11.0, 6.0, 1H), 4.29-4.17 (m, 1H), 3.46-3.28 (m, 4H), 3.19-3.13 (m, 1H), 3.09-3.03 (m, 1H), 1.93-1.80 (m, 2H), 1.67 (d, *J*= 9.2, 1H), 1.47 (d, *J*= 8.8, 1H), 1.29-1.21 (m, 8H), 1.17-1.09 (m, 6H). ^{13}C NMR ($CDCl_3$) δ (ppm): 177.43, 177.14, 167.16, 136.76, 134.95, 134.74, 129.07, 128.60, 127.04, 55.70, 52.46, 51.19, 45.77, 45.58,

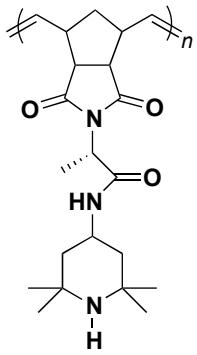
45.06, 44.91, 43.11, 33.89. IR: 3344 cm^{-1} (N-H stretching), 3311 cm^{-1} (N-H stretching), 2964 cm^{-1} (C-H stretching), 1761 cm^{-1} (C=O stretching), 1678 cm^{-1} (C=O stretching), 1633 cm^{-1} (C=O stretching). HRMS: (TOF-MS) m/z: $[M + H]^+$ Calcd for $C_{27}H_{36}N_3O_3^+$ 450.2757, found 450.2758.

5.2.8 Synthesis of Compound 4a



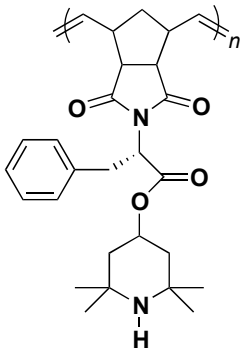
Compound **3a** (1.00 g, 2.67 mmol) was put in a 25-ml round-bottomed flask and dissolved in DCM (5.00 ml). The flask was flushed with Ar gas prior to the addition of the Grubbs' second generation catalyst (0.0227 g, 0.0267 mmol). The catalyst was added and the solution was stirred under Ar atmosphere. During the 3 days it was stirred, the colour of the solution turned black and the viscosity of the solution increased. Ethyl vinyl ether (2.00 ml) was added to cease the polymerization and the solution was stirred for an additional hour. DCM was evapored and brownish solid was obtained (0.92 g) which were washed three times with diethyl ether. With the melting point apparatus, melting started at 98 °C. IR: 2958 cm^{-1} (C-H stretching), 1772 cm^{-1} (C=O stretching), 1701 cm^{-1} (C=O stretching).

5.2.9 Synthesis of Compound 4b



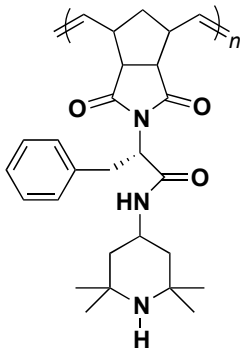
Compound **3b** (1.00 g, 2.68 mmol) was put in a 25-ml round-bottomed flask and dissolved in DCM (5.00 ml). The flask was flushed with Ar gas prior to the addition of the Grubbs' second generation catalyst (0.0227 g, 0.0268 mmol). The catalyst was added and the solution was stirred under Ar atmosphere. During the 3 days it was stirred, the colour of the solution turned black and the viscosity of the solution increased. Ethyl vinyl ether (2.00 ml) was added to cease the polymerization and the solution was stirred for an additional hour. DCM was evapored and brownish solid was obtained (0.90 g) which were washed three times with diethyl ether. With the melting point apparatus, melting started at 160 °C. IR: 3317 cm^{-1} (N-H stretching), 2958 cm^{-1} (C-H stretching), 1772 cm^{-1} (C=O stretching), 1695 cm^{-1} (C=O stretching).

5.2.10 Synthesis of Compound 4c



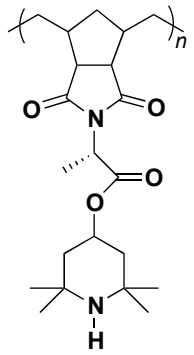
Compound **3c** (0.500 g, 1.11 mmol) was put in a 25-ml round-bottomed flask and dissolved in DCM (5.00 ml). The flask was flushed with Ar gas prior to the addition of the Grubbs' second generation catalyst (0.0188 g, 0.0222 mmol). The catalyst was added and the solution was stirred under Ar atmosphere. During the 3 days it was stirred, the colour of the solution turned black and the viscosity of the solution increased. Ethyl vinyl ether (2.00 ml) was added to cease the polymerization and the solution was stirred for an additional hour. DCM was evapored and brownish solid was obtained (0.11 g) which were washed three times with diethyl ether. With the melting point apparatus, melting started at 126 °C. IR: 2937 cm^{-1} (C-H stretching), 1738 cm^{-1} (C=O stretching), 1702 cm^{-1} (C=O stretching).

5.2.11 Synthesis of Compound 4d



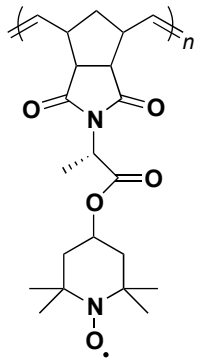
Compound **3d** (0.50 g, 1.11 mmol) was put in a 25-ml round-bottomed flask and dissolved in DCM (5.00 ml). The flask was flushed with Ar gas prior to the addition of the Grubbs' second generation catalyst (0.0188 g, 0.0222 mmol). The catalyst was added and the solution was stirred under Ar atmosphere. During the 3 days it was stirred, the colour of the solution turned black and the viscosity of the solution increased. Ethyl vinyl ether (2.00 ml) was added to cease the polymerization and the solution was stirred for an additional hour. DCM was evapored and brownish solid was obtained (0.05 g) which were washed three times with diethyl ether. With the melting point apparatus, melting started at 170 °C. IR: 3344 cm^{-1} (N-H stretching), 2941 cm^{-1} (C-H stretching), 1766 cm^{-1} (C=O stretching), 1695 cm^{-1} (C=O stretching).

5.2.12 Synthesis of Compound 5



In a 50-ml round-bottomed flask, the polymer **4a** (0.60 g) and $TsNHNH_2$ (0.89 g, 4.80 mmol) were refluxed in DMF (15.00 ml). After 3 hours of reflux, the hydrogenated polymer was precipitated by the addition of diethyl ether and collected by filtration. (0.40 g) IR: 3439 cm^{-1} (N-H stretching), 2941 cm^{-1} (C-H stretching), 1738 cm^{-1} (C=O stretching), 1695 cm^{-1} (C=O stretching).

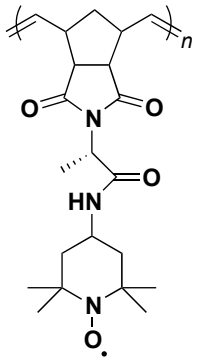
5.2.13 Synthesis of Compound polA



To a solution of the compound **4a** (0.31 g) in water-methanol mixture (10:10) was added $Na_2WO_4.2H_2O$ (0.40 g, 1.21 mmol) and EDTA (0.35 g, 1.20 mmol). K_2CO_3 (0.50 g, 3.62 mmol) was added after, to attain the basicity and the solution was stirred until all the reagents were dissolved, except for the polymer. H_2O_2 (15.00 ml) was introduced to the solution in 3 portions during the 2 days it was stirred. The color of the solution turned from white to orange and the oxidized polymer was collected by

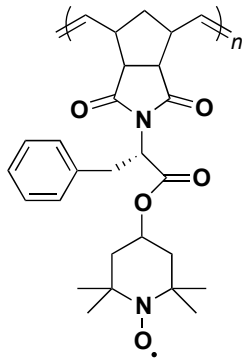
filtration (0.28 g). With the melting point apparatus, melting started at 164 °C. IR: 3434 cm^{-1} (O-H stretching), 2942 cm^{-1} (C-H stretching), 1740 cm^{-1} (C=O stretching), 1700 cm^{-1} (C=O stretching).

5.2.14 Synthesis of Compound polB



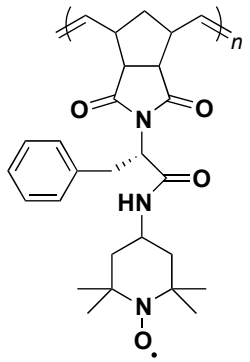
To a solution of the compound **4b** (0.89 g) in water-methanol mixture (10:10) was added $Na_2WO_4.2H_2O$ (0.39 g, 1.18 mmol) and EDTA (0.35 g, 1.20 mmol). K_2CO_3 (0.5 g, 3.62 mmol) was added after, to attain the basicity and the solution was stirred until all the reagents were dissolved, except for the polymer. H_2O_2 (15.00 ml) was introduced to the solution in 3 portions during the 2 days it was stirred. The color of the solution turned from white to orange and the oxidized polymer was collected by filtration (0.98 g). With the melting point apparatus, melting started at 182 °C. IR: 3338 cm^{-1} (O-H stretching), 2935 cm^{-1} (C-H stretching), 1772 cm^{-1} (C=O stretching), 1772 cm^{-1} (C=O stretching).

5.2.15 Synthesis of Compound polC



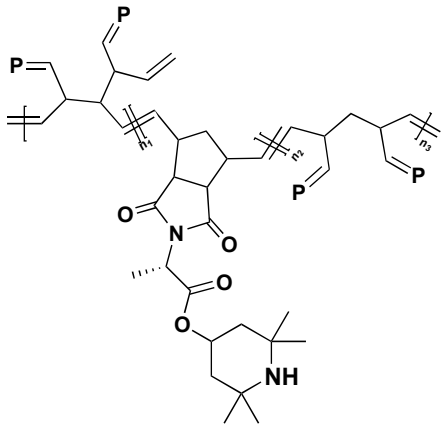
To a solution of the compound **4c** (0.63 g) in water-methanol mixture (10:10) was added $Na_2WO_4.2H_2O$ (0.14 g, 0.42 mmol) and EDTA (0.14 g, 0.48 mmol). K_2CO_3 (0.10 g, 0.72 mmol) was added after, to attain the basicity and the solution was stirred until all the reagents were dissolved, except for the polymer. H_2O_2 (15.00 ml) was introduced to the solution in 3 portions during the 2 days it was stirred. The color of the solution turned from white to orange and the oxidized polymer was collected by filtration (0.42 g). With the melting point apparatus, melting started at 135°C. IR: 3490 cm^{-1} (O-H stretching), 2976 cm^{-1} (C-H stretching), 1741 cm^{-1} (C=O stretching), 1700 cm^{-1} (C=O stretching).

5.2.16 Synthesis of Compound polD



To a solution of the compound **4d** (0.03 g) in water-methanol mixture (5:5) was added $Na_2WO_4.2H_2O$ (0.04 g, 0.14 mmol) and EDTA (0.04 g, 0.14 mmol). K_2CO_3 (0.05 g, 0.36 mmol) was added after, to attain the basicity and the solution was stirred until all the reagents were dissolved, except for the polymer. H_2O_2 (5.00 ml) was introduced to the solution in 3 portions during the 2 days it was stirred. The color of the solution turned from white to orange and the oxidized polymer was collected by filtration (0.02 g). With the melting point apparatus, melting started at 180 °C. IR: 3383 cm^{-1} (O-H stretching), 2931 cm^{-1} (C-H stretching), 1695 cm^{-1} (C=O stretching), 1772 cm^{-1} (C=O stretching).

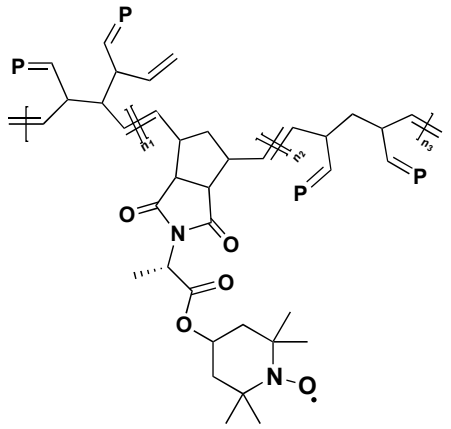
5.2.17 Synthesis of the Crosslinked Polymer, cross4a



P: Polymerization

Compound **4a** (1.0 g, 2.67 mmol) and norbornadiene (0.25 g, 2.67 mmol) were dissolved in DCM (10.00 ml) in a 25-ml round-bottomed flask. The flask was flushed with Ar gas prior to the addition of the Grubbs' second generation catalyst (0.0297g, 0.0349 mmol). The catalyst was added and the solution was stirred under Ar atmosphere. During the 2 days it was stirred, the viscosity of the solution increased and gel formation is observed. Butylvinyl ether (2.00 ml) was added to cease the polymerization and the solution was stirred for an additional hour. DCM was evapored and brownish solid was obtained (1.10 g) which were washed three times with diethyl ether. IR: 2953 cm^{-1} (C-H stretching), 1737 cm^{-1} (C=O stretching), 1701 cm^{-1} (C=O stretching).

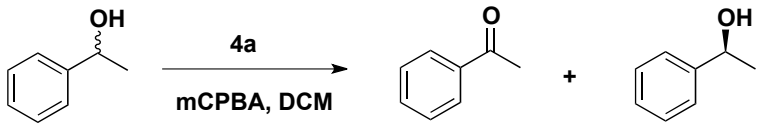
5.2.18 Oxidation of the Crosslinked Polymer, cross4a'



To a solution of the crosslinked polymer (1.8 g) in water-methanol mixture (10:10) was added $Na_2WO_4.2H_2O$ (0.4 g, 1.21 mmol) and EDTA (0.35 g, 1.20 mmol). K_2CO_3 (0.5 g, 3.62 mmol) was added after, to attain the basicity and the solution was stirred until all the reagents were dissolved, except for the polymer. H_2O_2 (15.00 ml) was introduced to the solution in 3 portions during the 2 days it was stirred. The color of the solution turned from white to orange and the oxidized polymer was collected by filtration (1.7 g). IR: 3427 cm^{-1} (O-H stretching), 2935 cm^{-1} (C-H stretching), 1738 cm^{-1} (C=O stretching), 1701 cm^{-1} (C=O stretching).

5.3 Oxidative Kinetic Resolution of 1-Phenyl ethanol

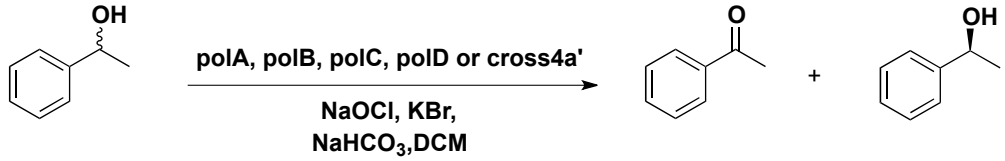
5.3.1 Oxidation under Acidic Conditions



A 50-ml round-bottomed flask was charged with DCM (15.00 ml). To the solution, was then added 1-Phenyl ethanol (0.61 g, 5.00 mmol) and catalytic amount of **4a**. A solution of mCPBA (1.04 g, 6.00 mmol) in DCM (10.0 ml) was prepared and added to the alcohol solution with a dropping funnel and the solution was stirred at room

temperature for 1.5 hours. The reaction was quenched by the addition of 1.0 N NaOH solution (25.00 ml). The layers were seperated and the aqueous layer was extracted with brine, dried over Na_2SO_4 and concentrated.

5.3.2 Oxidation under Basic Conditions



1-Phenylethanol (0.15 g, 1.23 mmol) was dissolved in DCM (2.00 ml). To the mixture, catalytic amount of synthesized polymer and KBr were added and the mixture was cooled to °C on ice bath. A solution of NaOCl (0.44 g in 2.00 ml water) was adjusted to pH~ 8.0 using $NaHCO_3$. This solution was then added to the alcohol mixture at °C. Finally, TBAI as phase transfer reagent was added and the solution was stirred for 120 mins. The layers were separated and extracted with DCM, dried over Na_2SO_4 and concentrated.

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APPENDICES

A. NMR Spectra

NMR spectra were recorded at Bruker Avance III Ultrashield 400 Hz. $CDCl_3$ was used as solvent in all records.

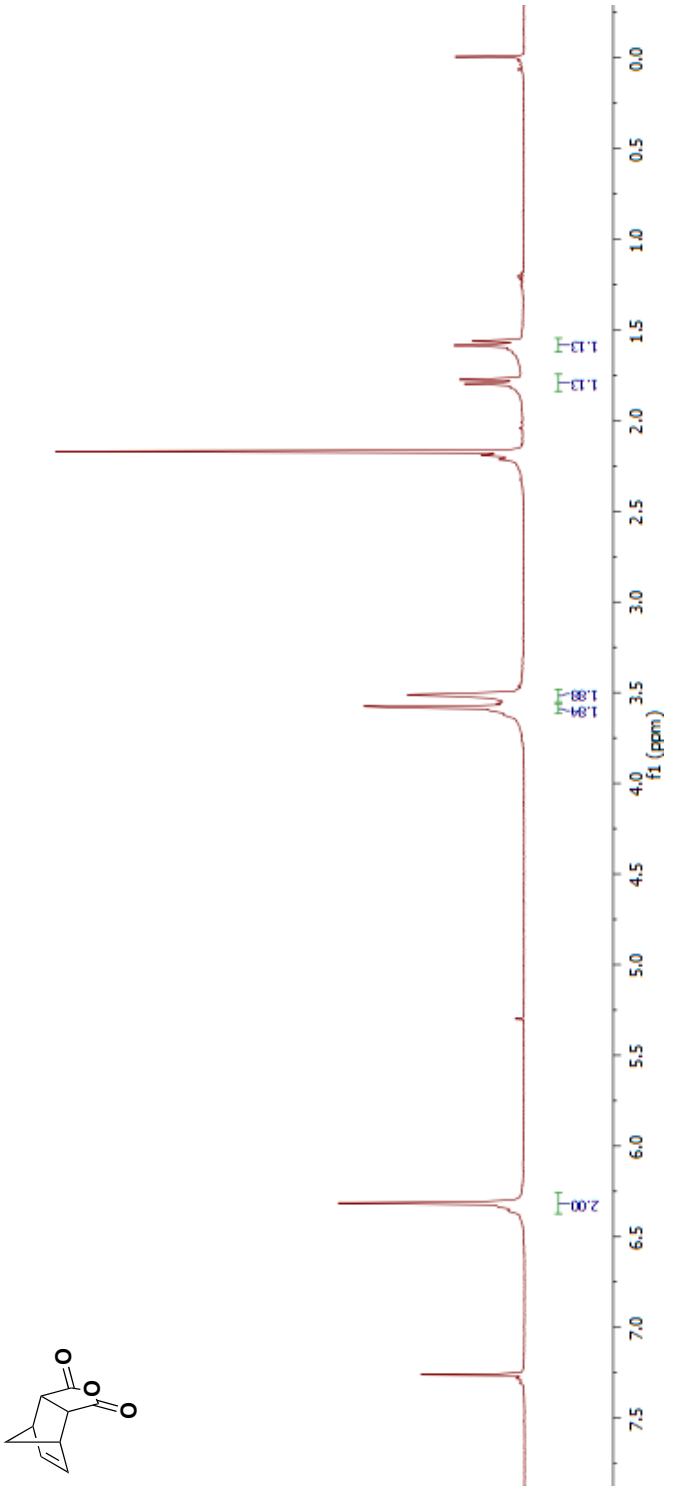

Figure 16. ^{1}H NMR Spectrum of Compound **1**

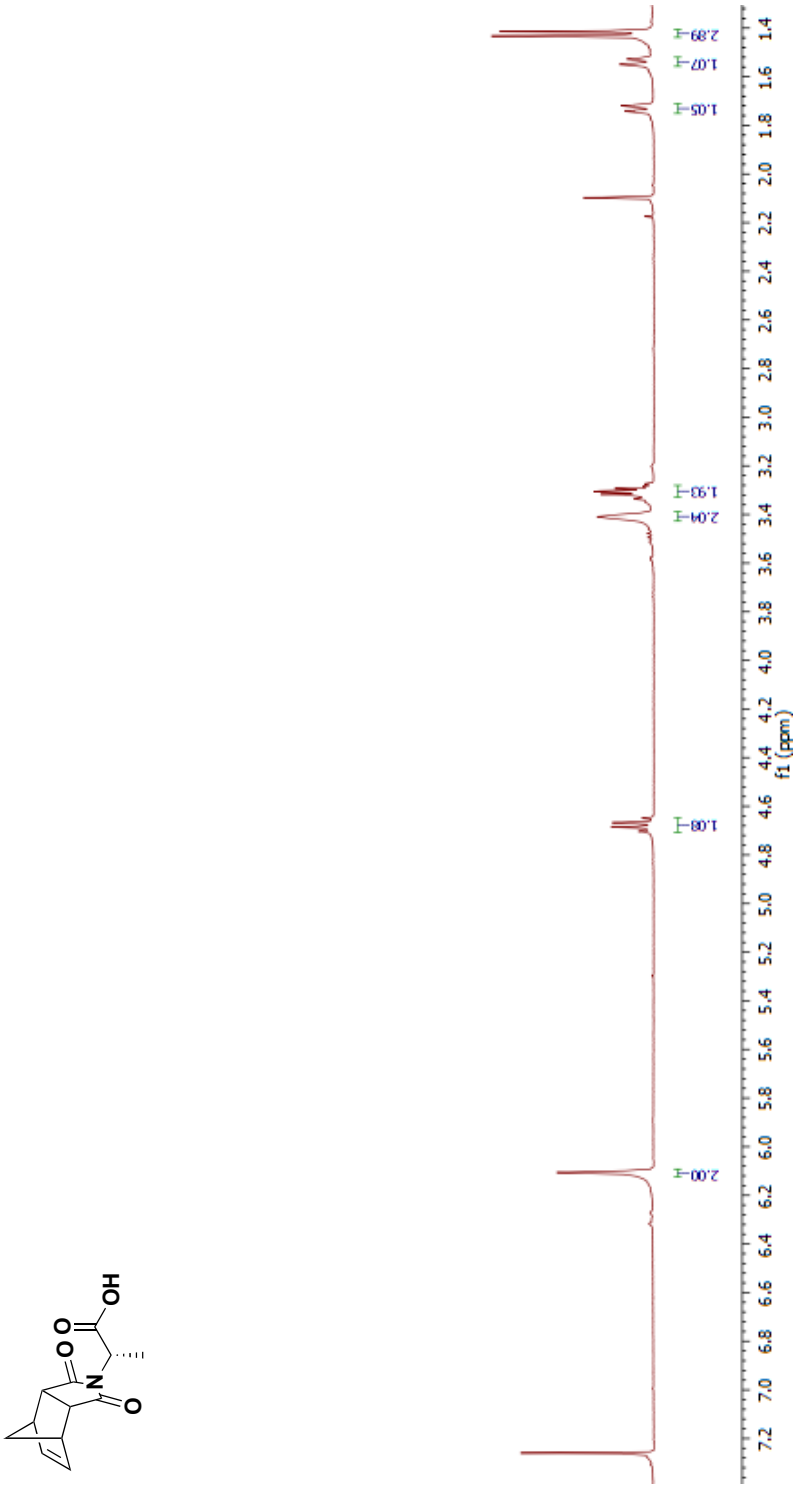

Figure 17. ^{1}H NMR Spectrum of Compound **2a**

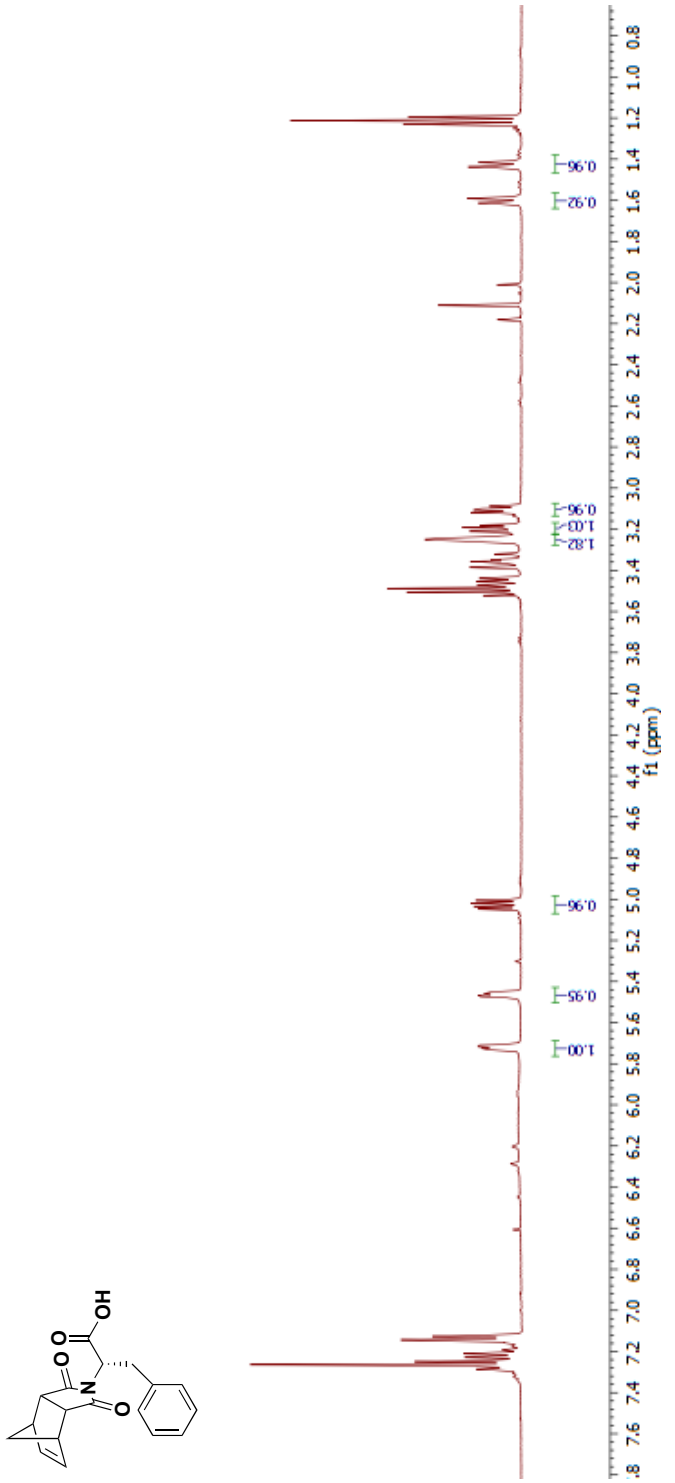

Figure 18. [1]H NMR Spectrum of Compound **2b**

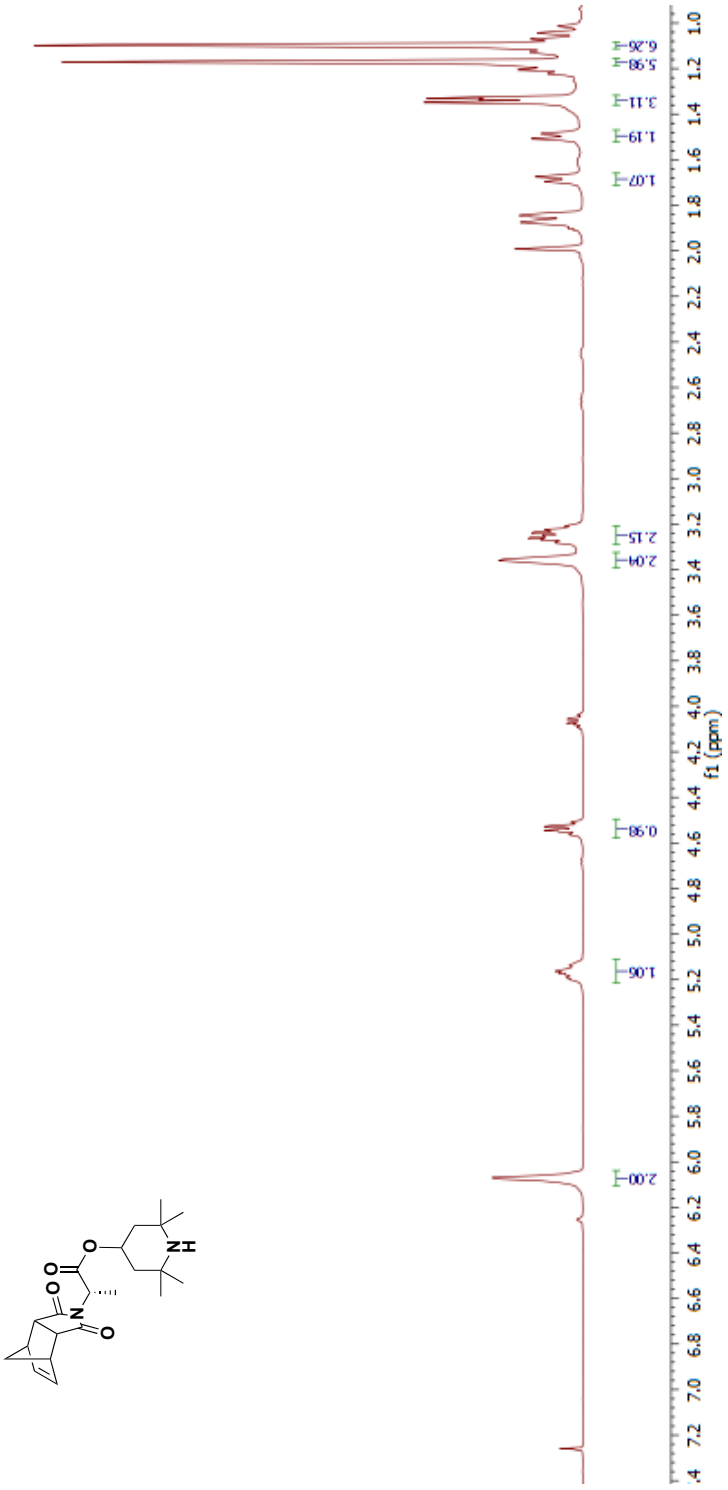

Figure 19. ^{1}H NMR Spectrum of Compound **3a**

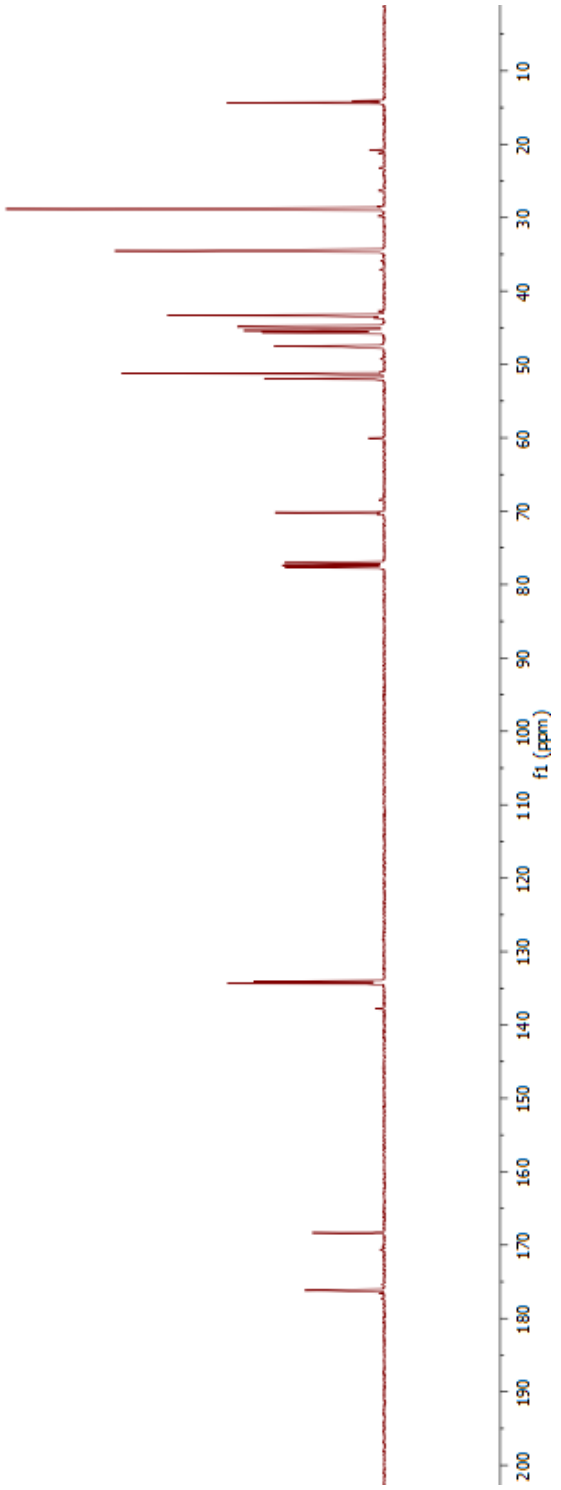

Figure 20. ^{13}C NMR Spectrum of Compound **3a**

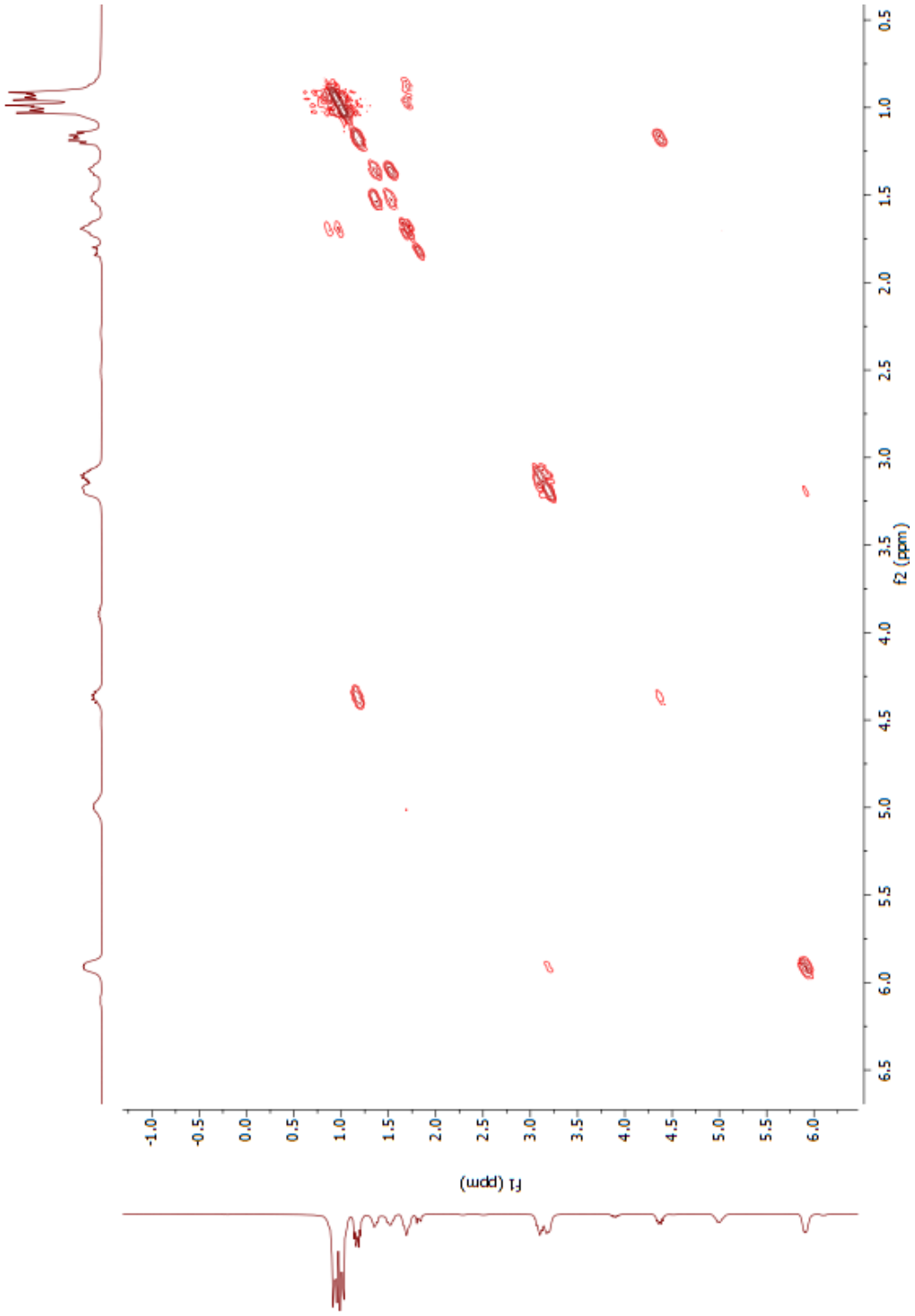

Figure 21. COSY NMR Spectrum of Compound **3a**

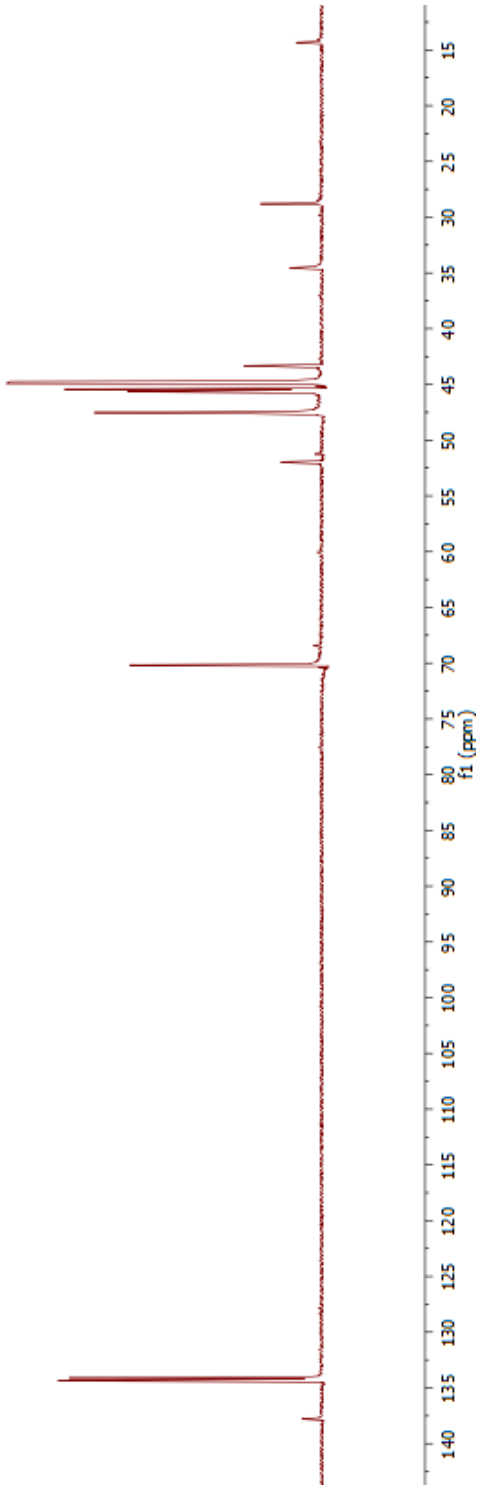

Figure 22. DEPT 90 NMR Spectrum of Compound **3a**

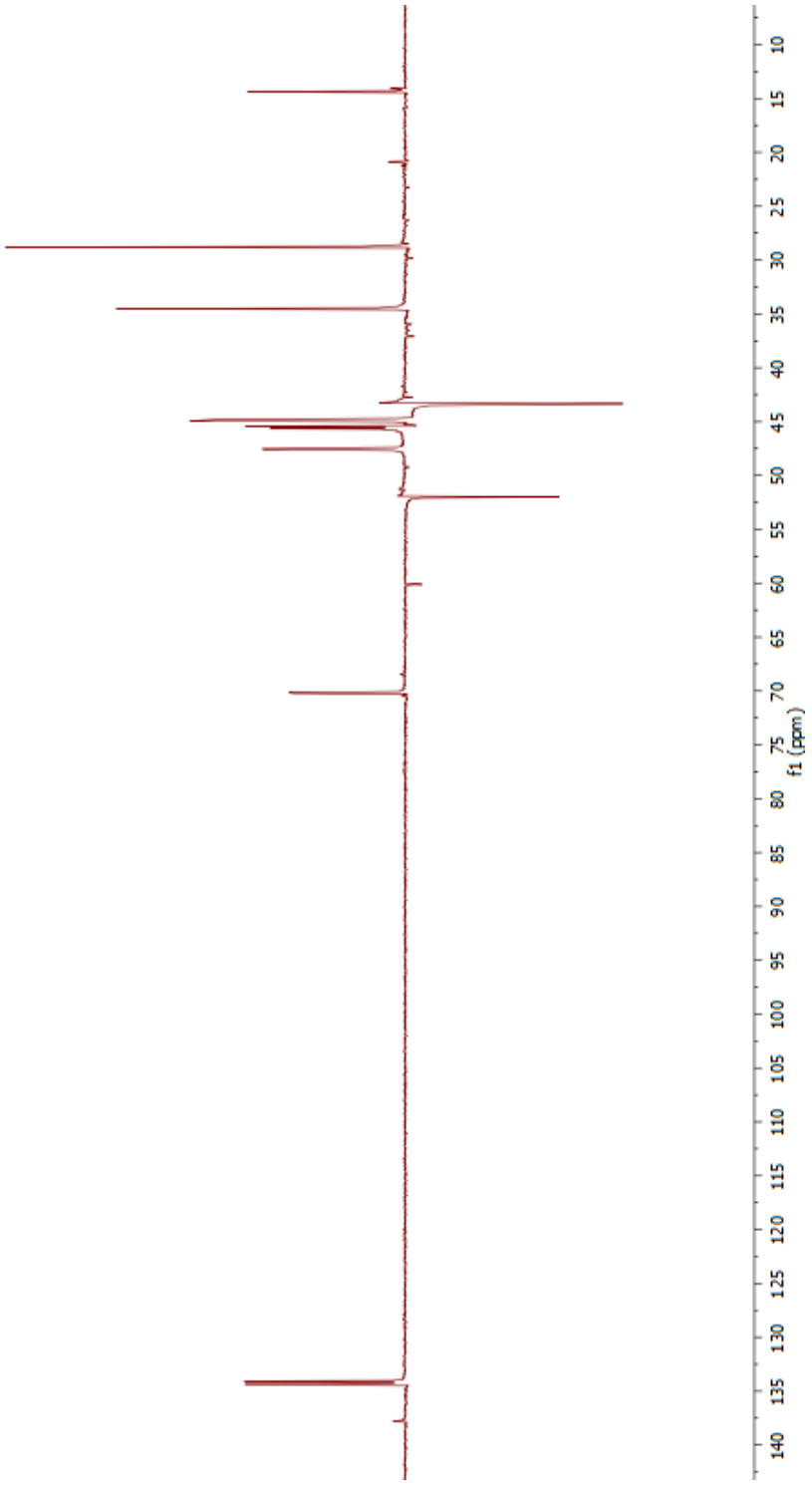

Figure 23. DEPT 135 NMR Spectrum of Compound **3a**

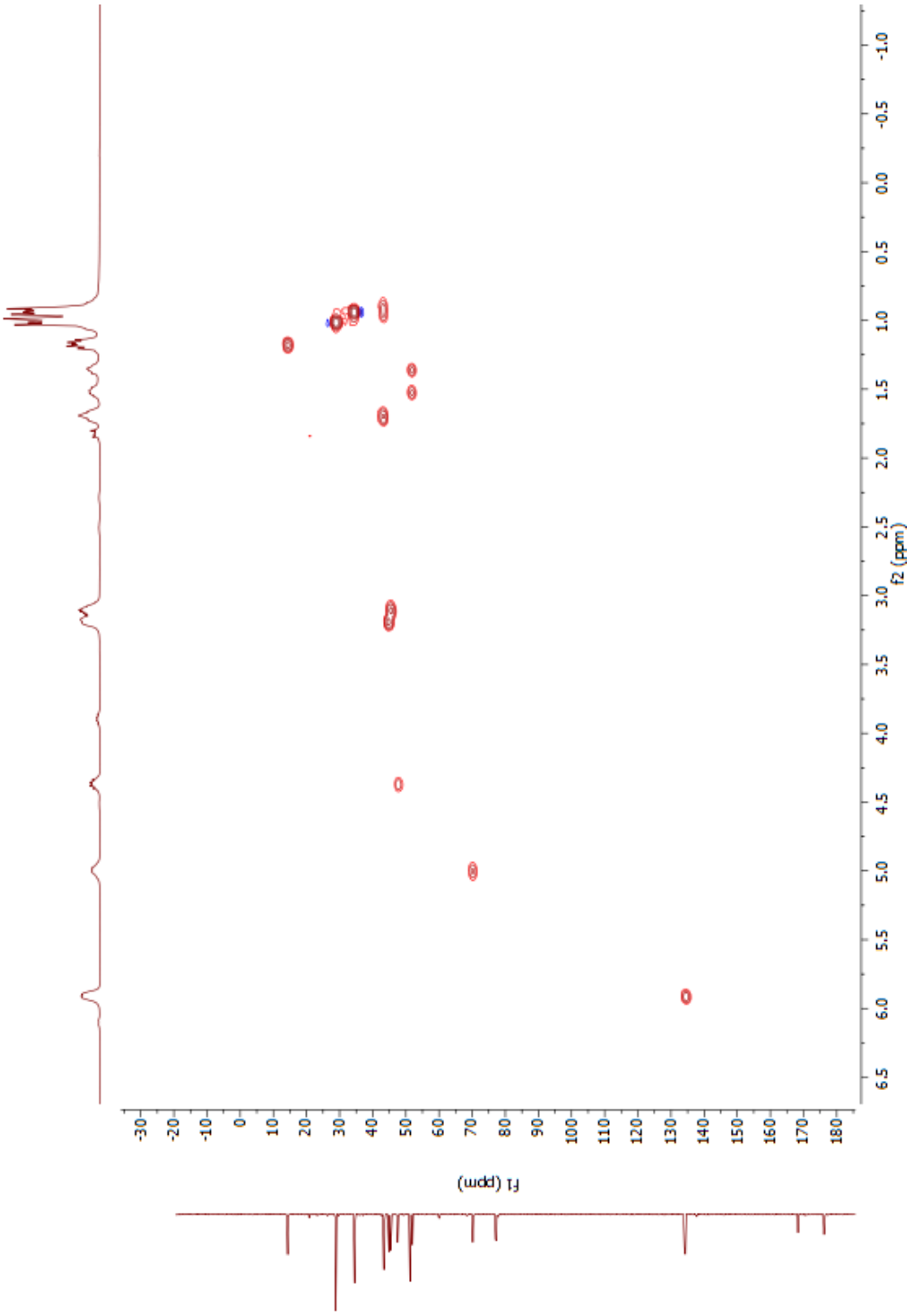

Figure 24. HSQC NMR Spectrum of Compound **3a**

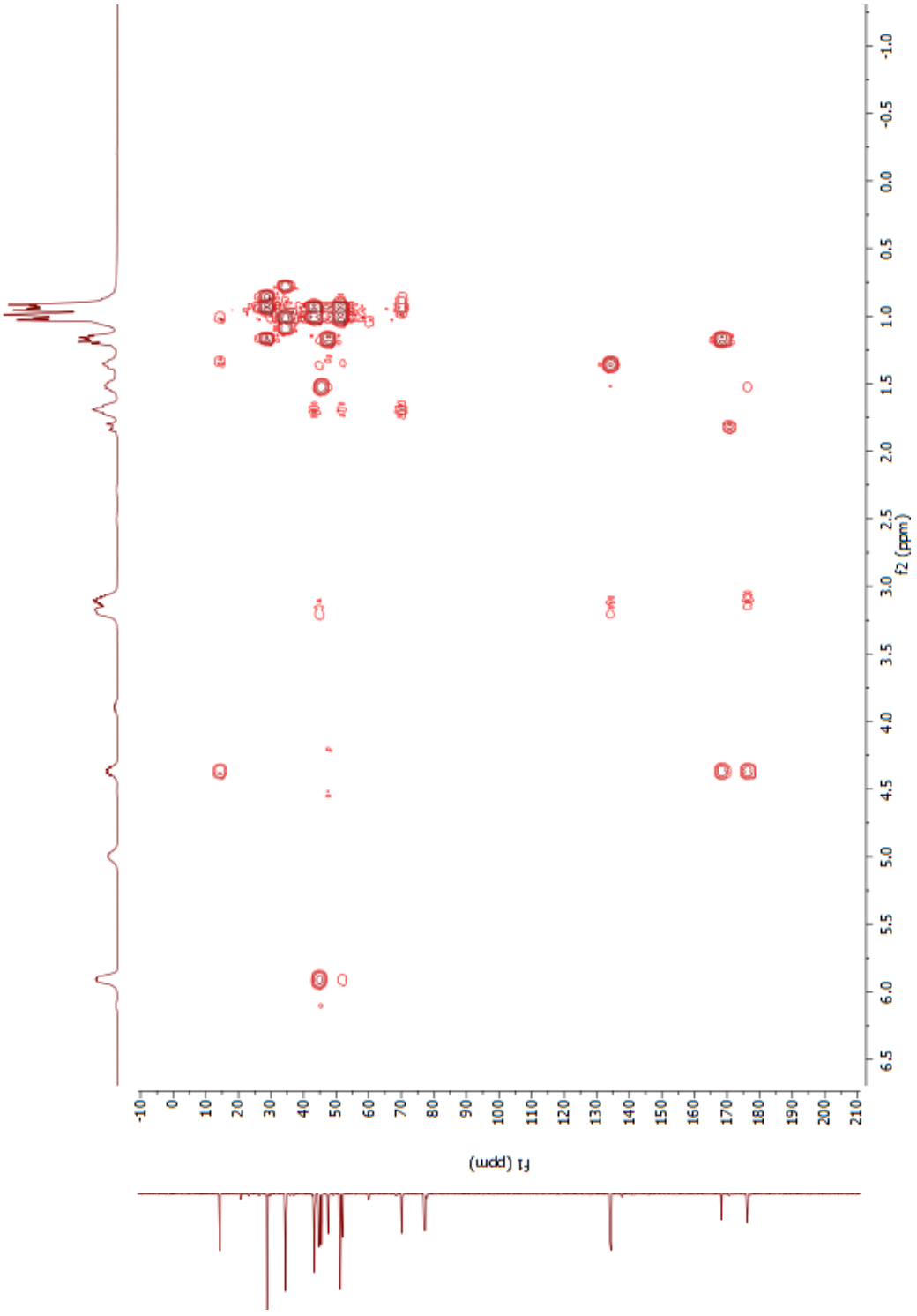

Figure 25. HMBC NMR Spectrum of Compound **3a**

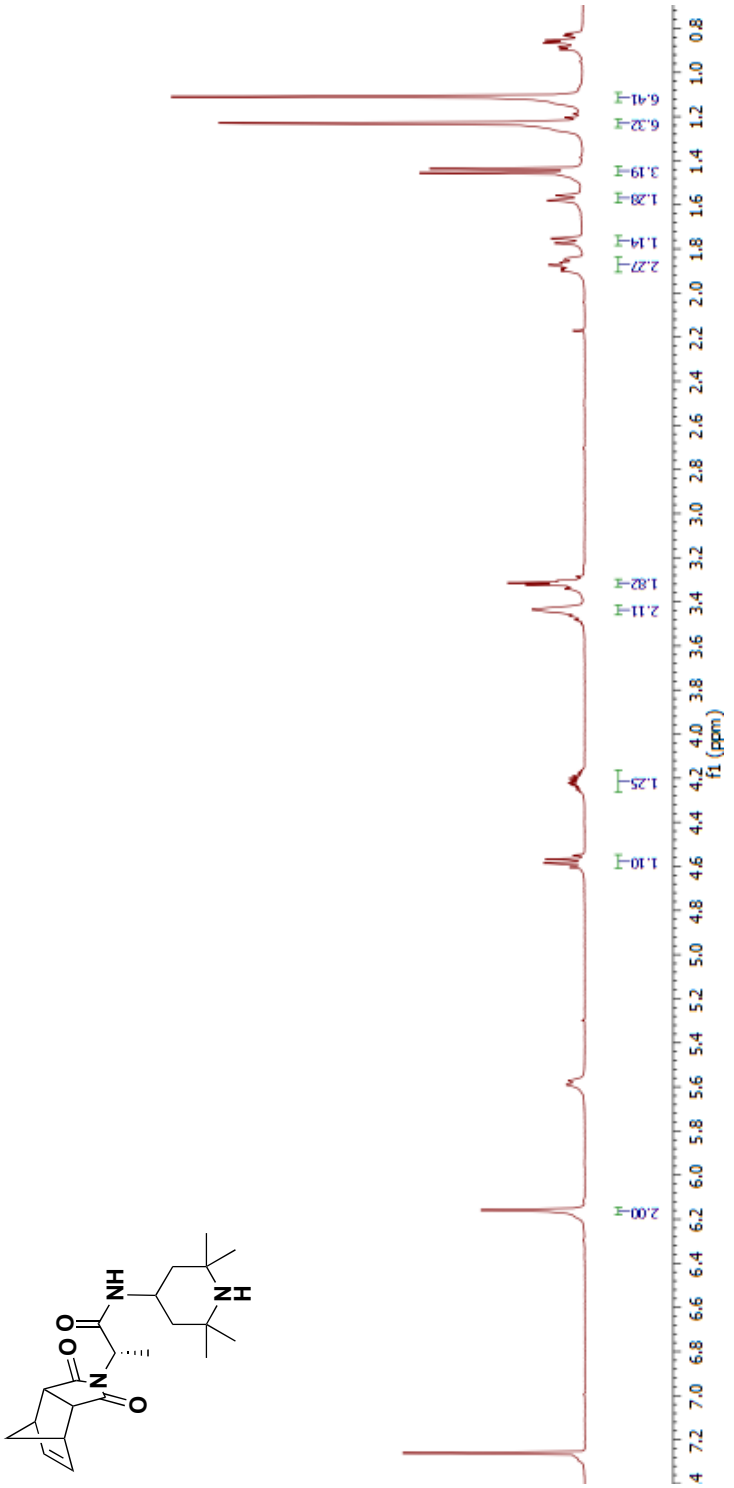

Figure 26. [1]H NMR Spectrum of Compound **3b**

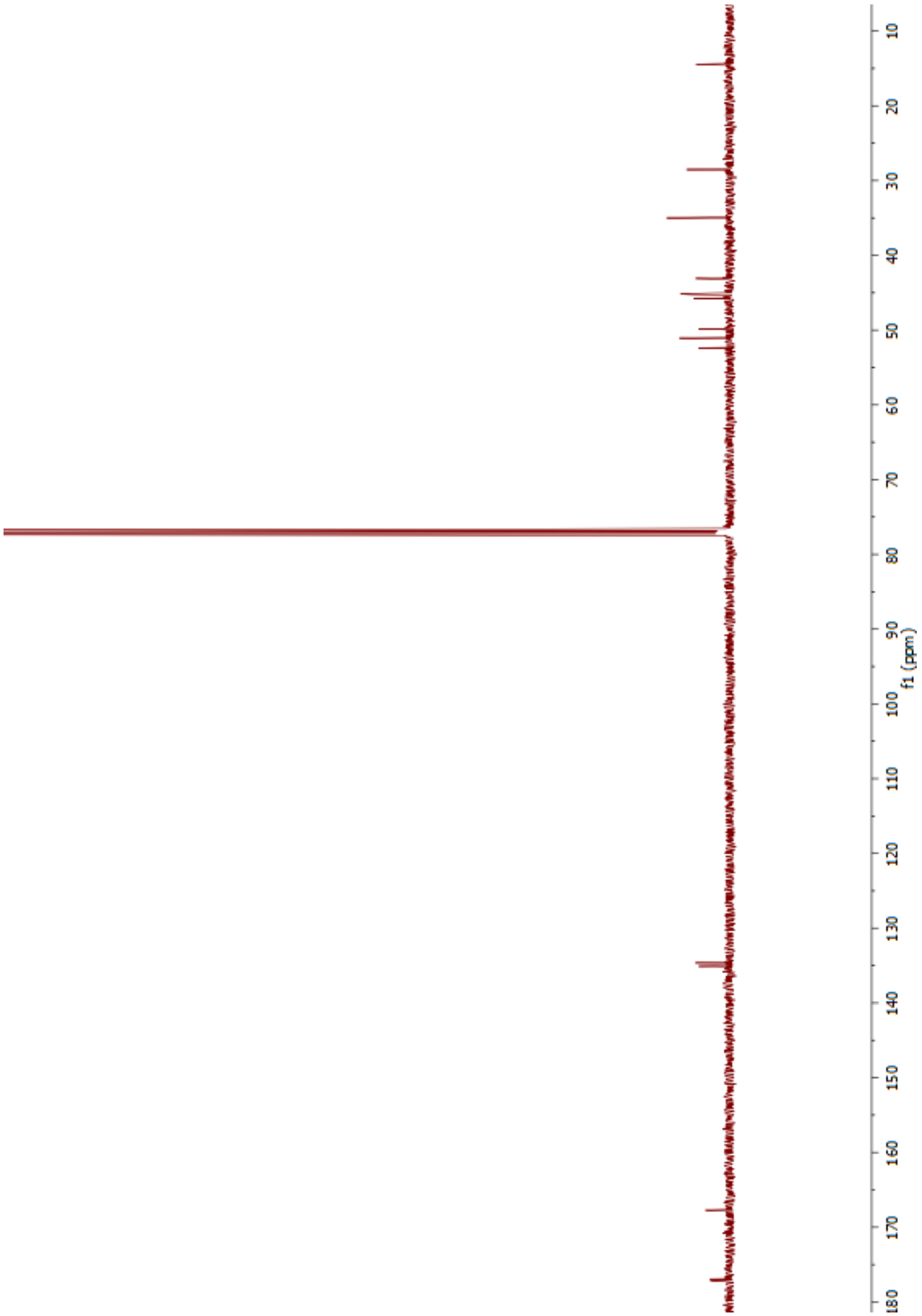

Figure 27. ^{13}C NMR Spectrum of Compound **3b**

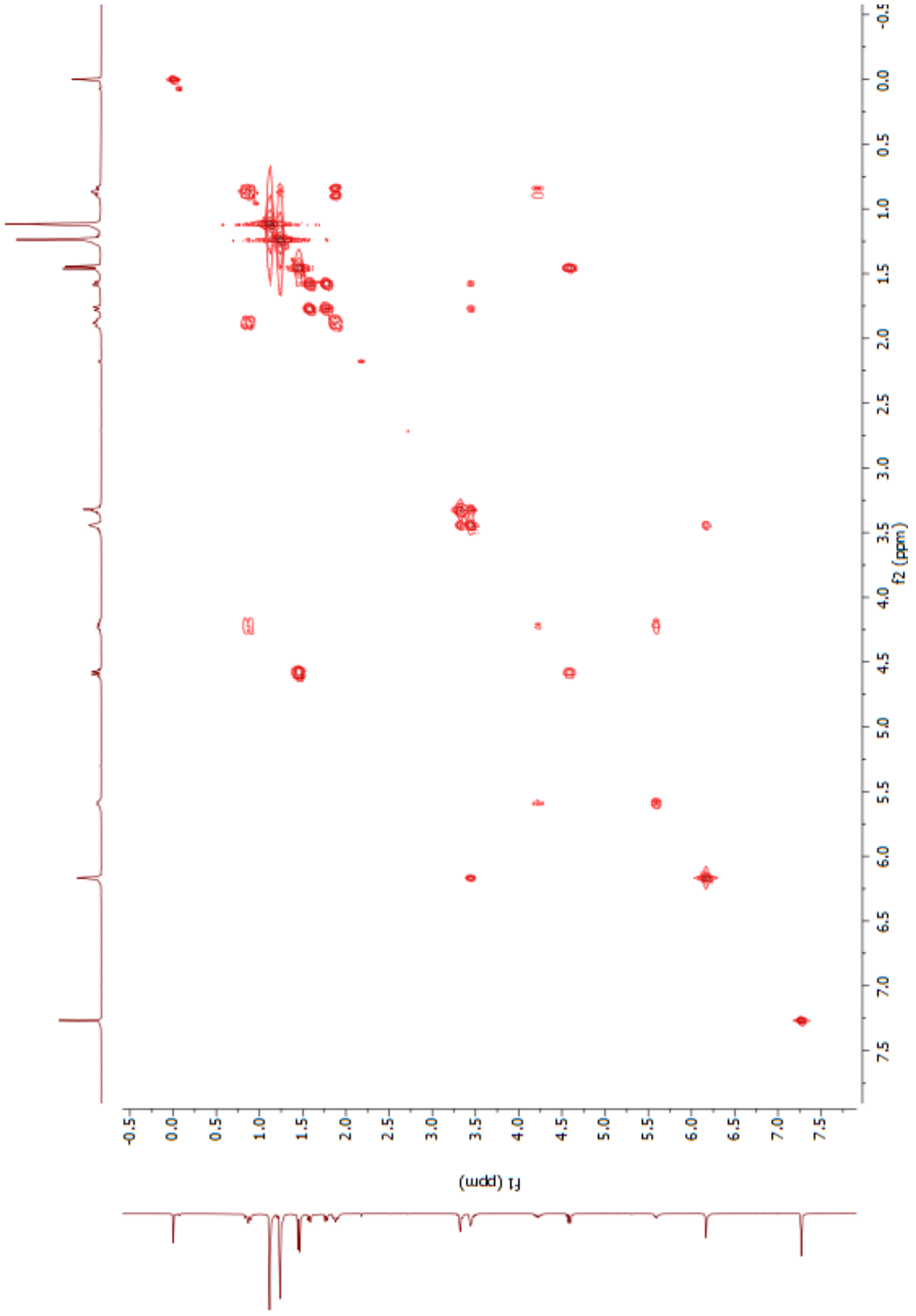

Figure 28. COSY NMR Spectrum of Compound **3b**

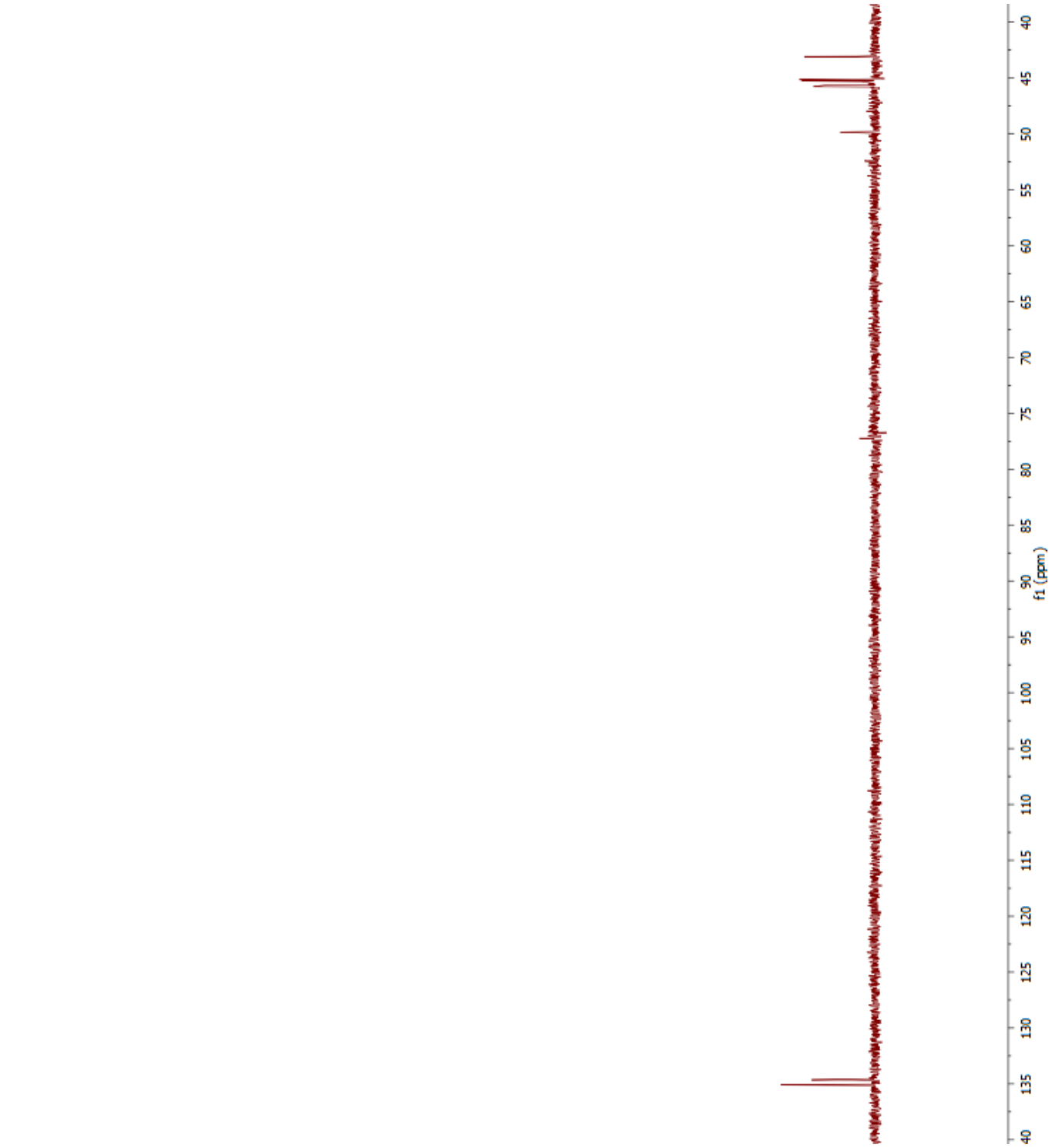

Figure 29. DEPT 90 NMR Spectrum of Compound **3b**

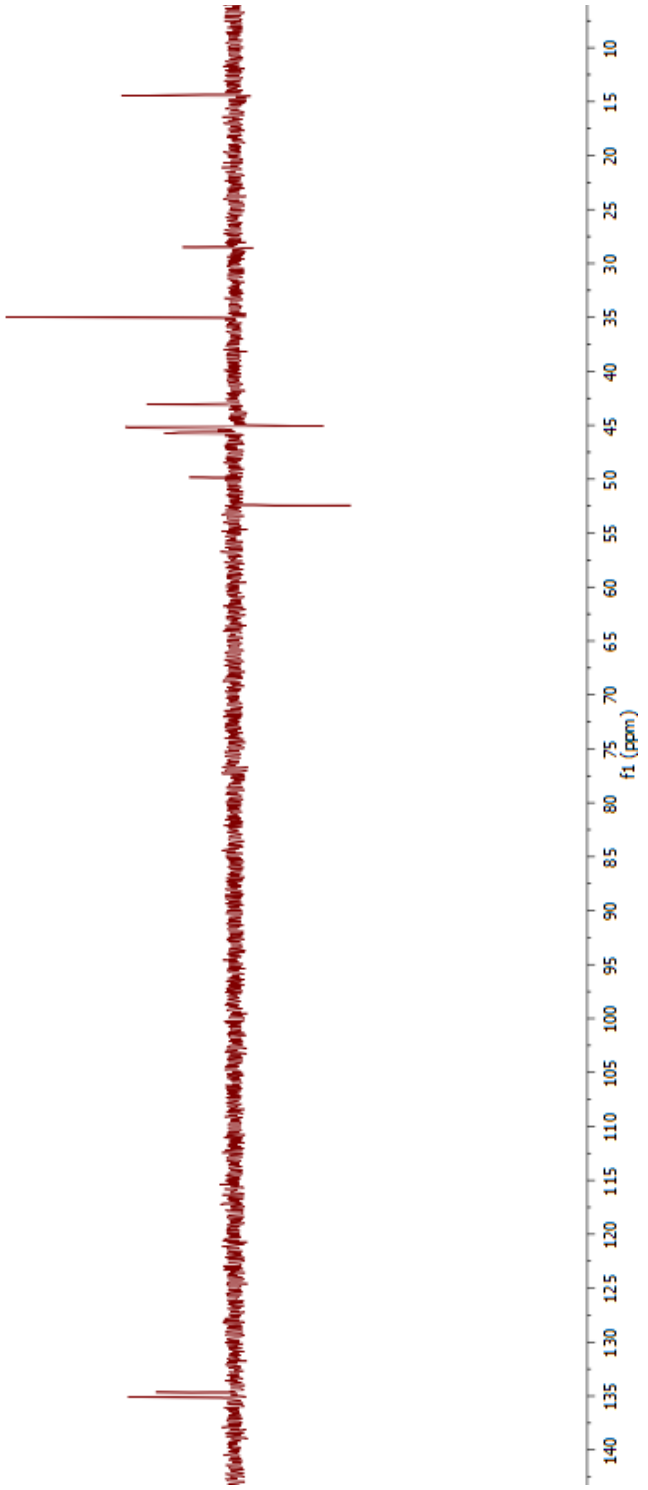

Figure 30. DEPT 135 NMR Spectrum of Compound **3b**

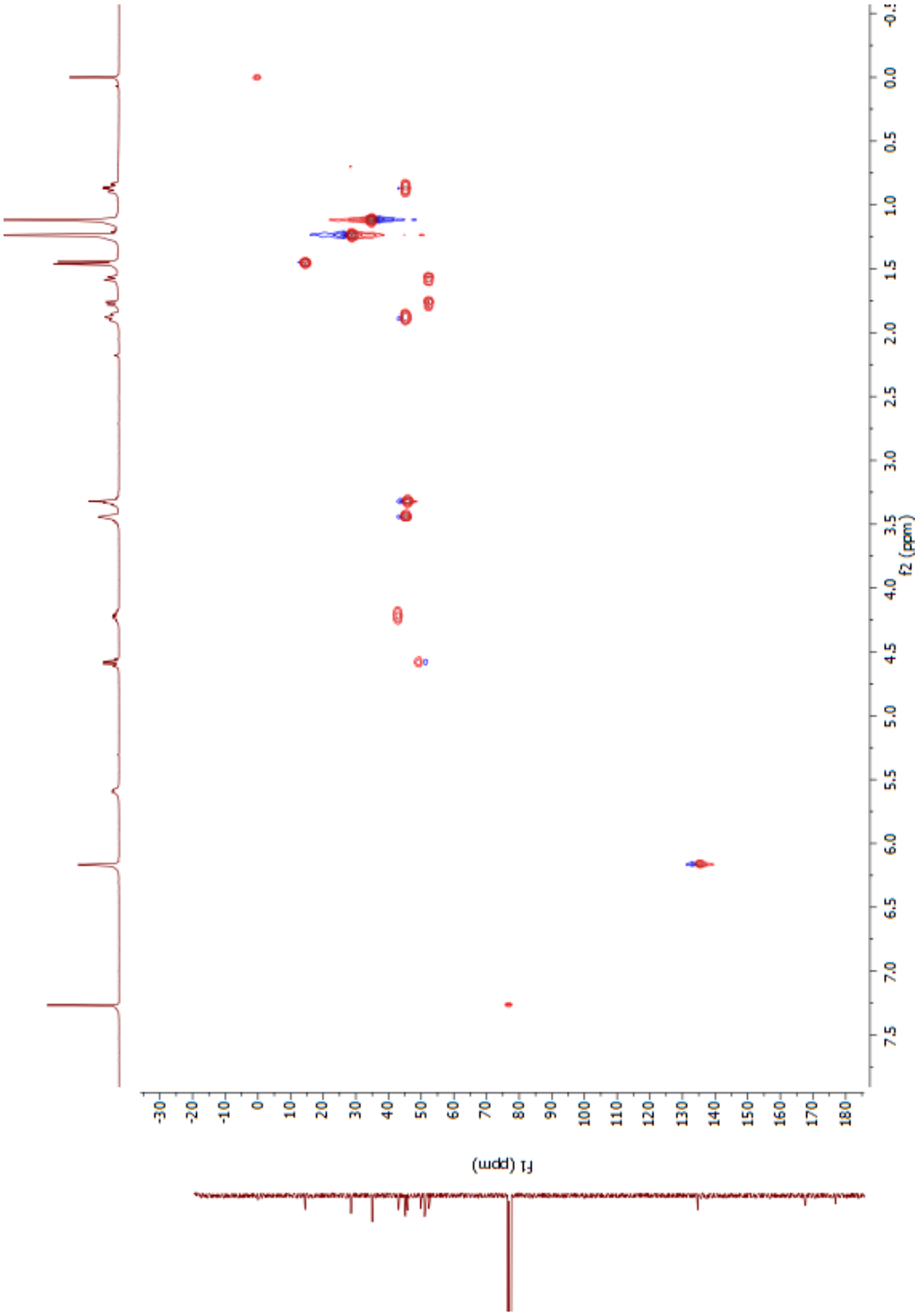

Figure 31. HSQC NMR Spectrum of Compound **3b**

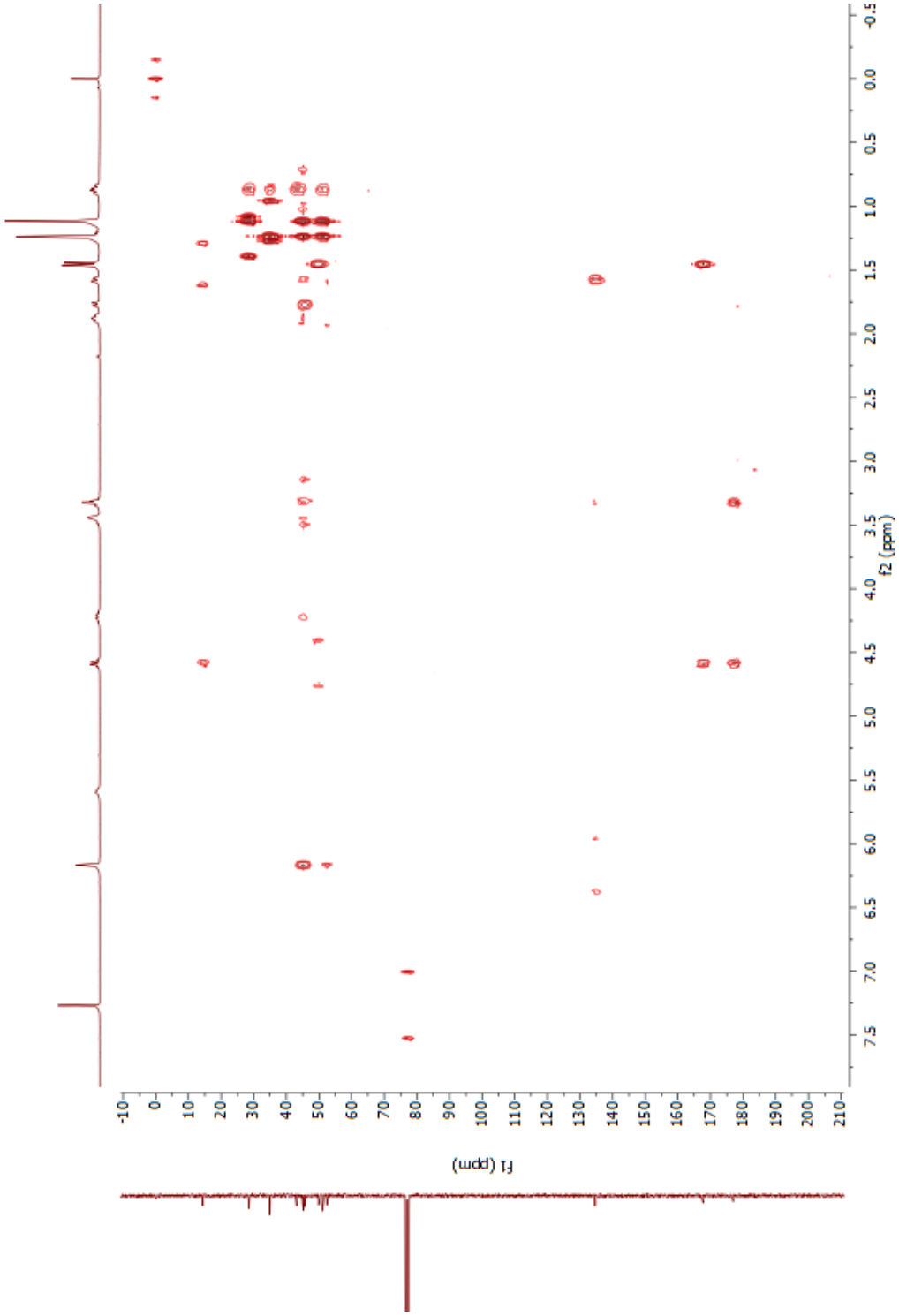

Figure 32. HMBC NMR Spectrum of Compound **3b**

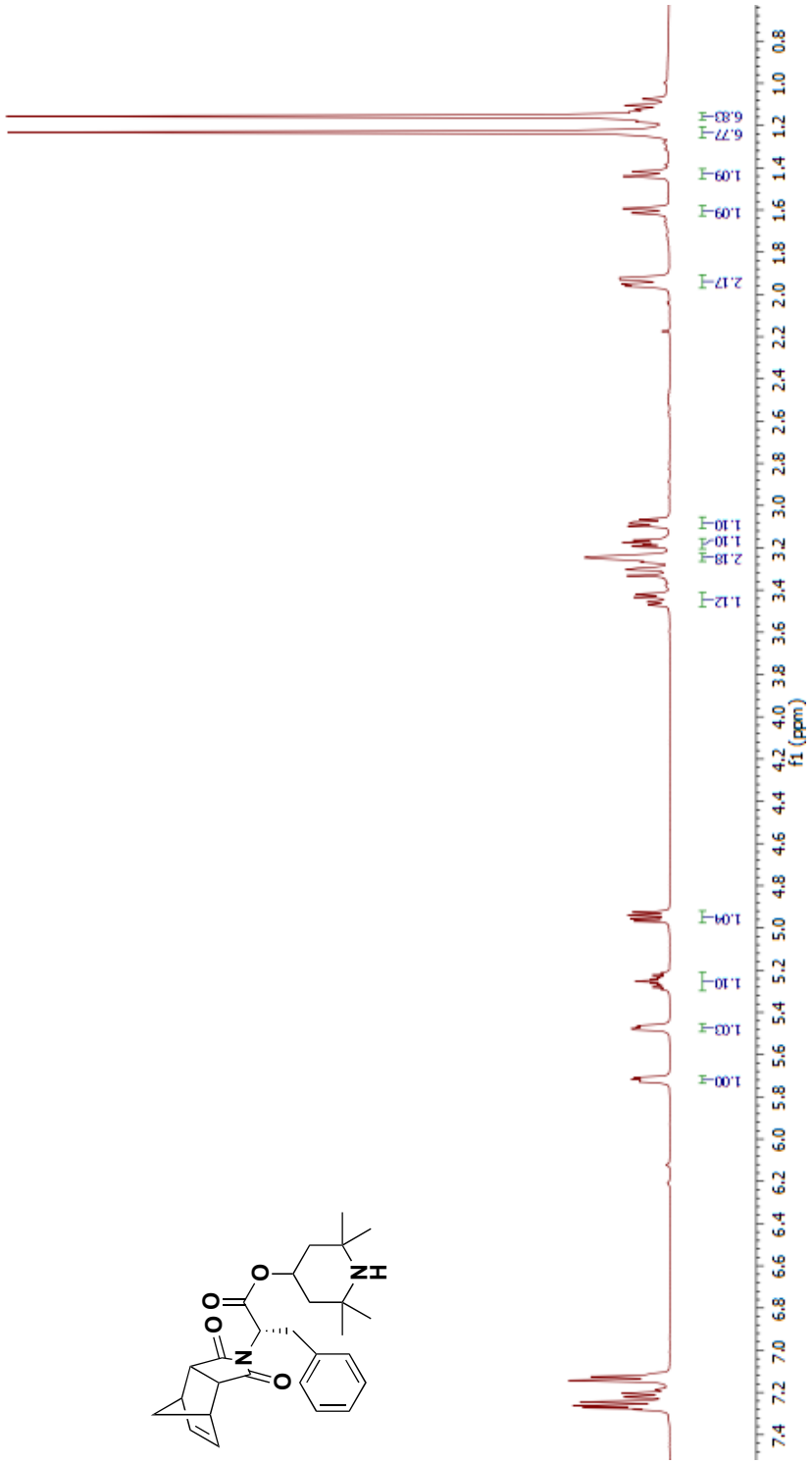

Figure 33. ^{1}H NMR Spectrum of Compound **3c**

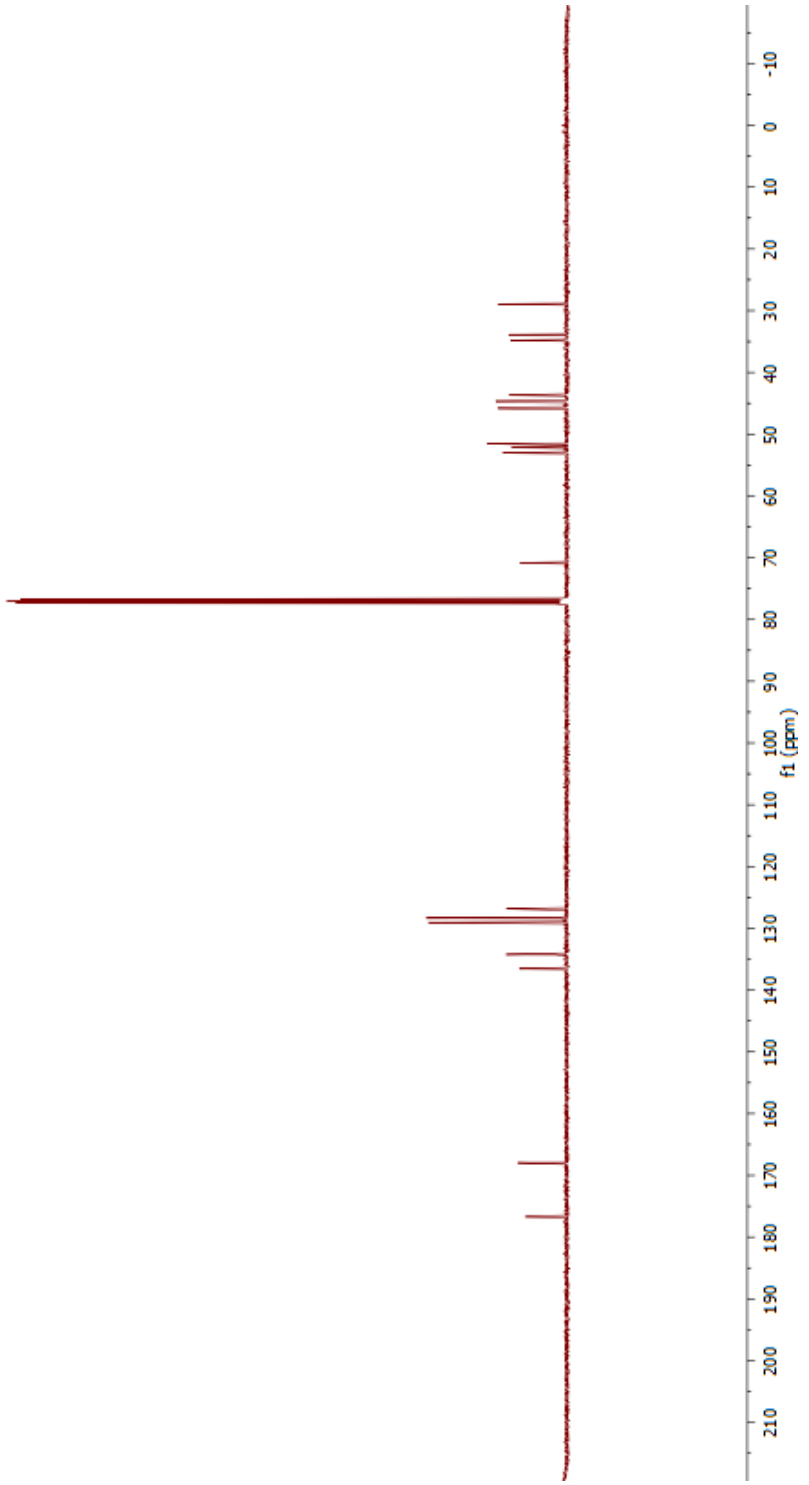

Figure 34. ^{13}C NMR Spectrum of Compound **3c**

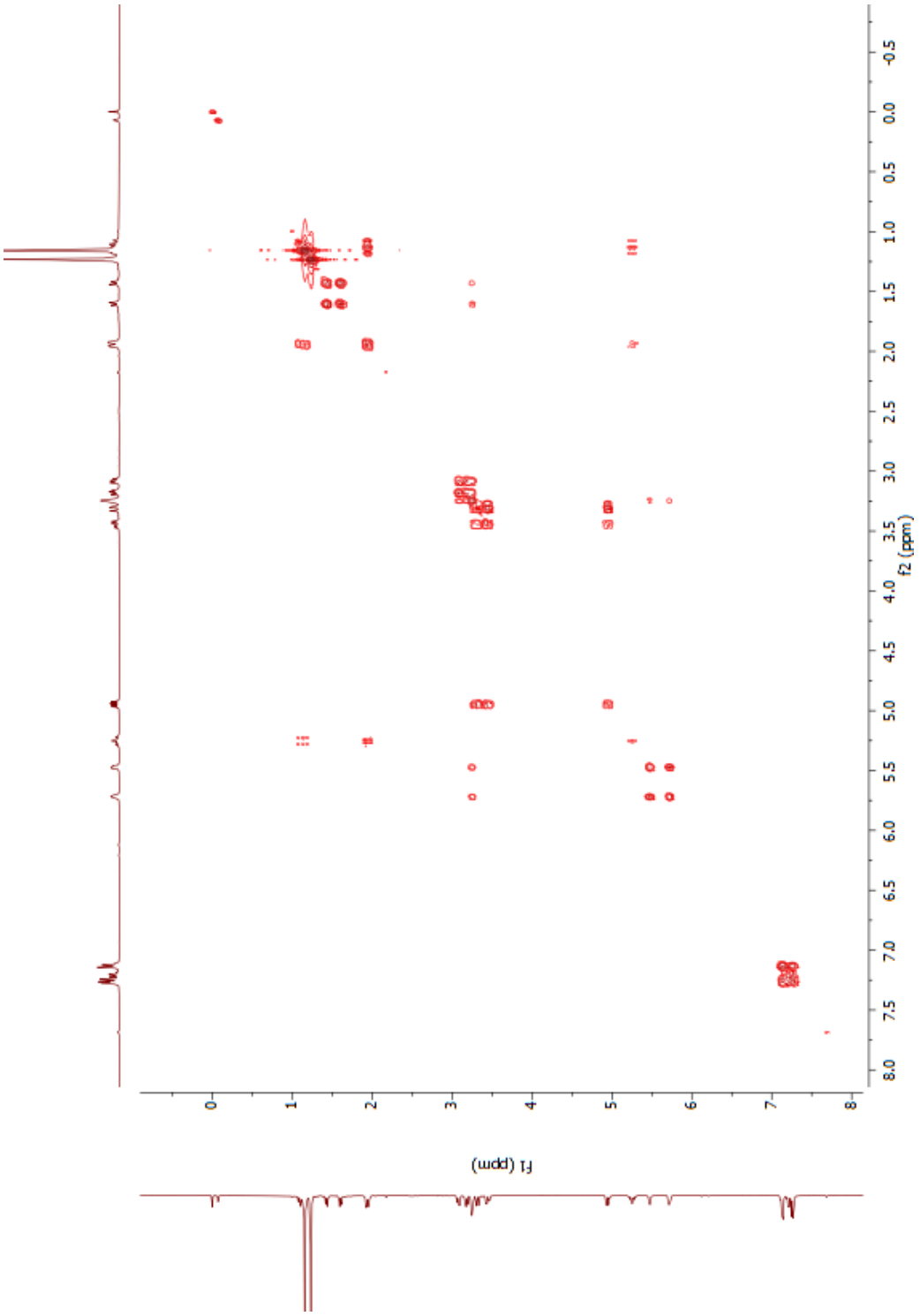

Figure 35. COSY NMR Spectrum of Compound **3c**

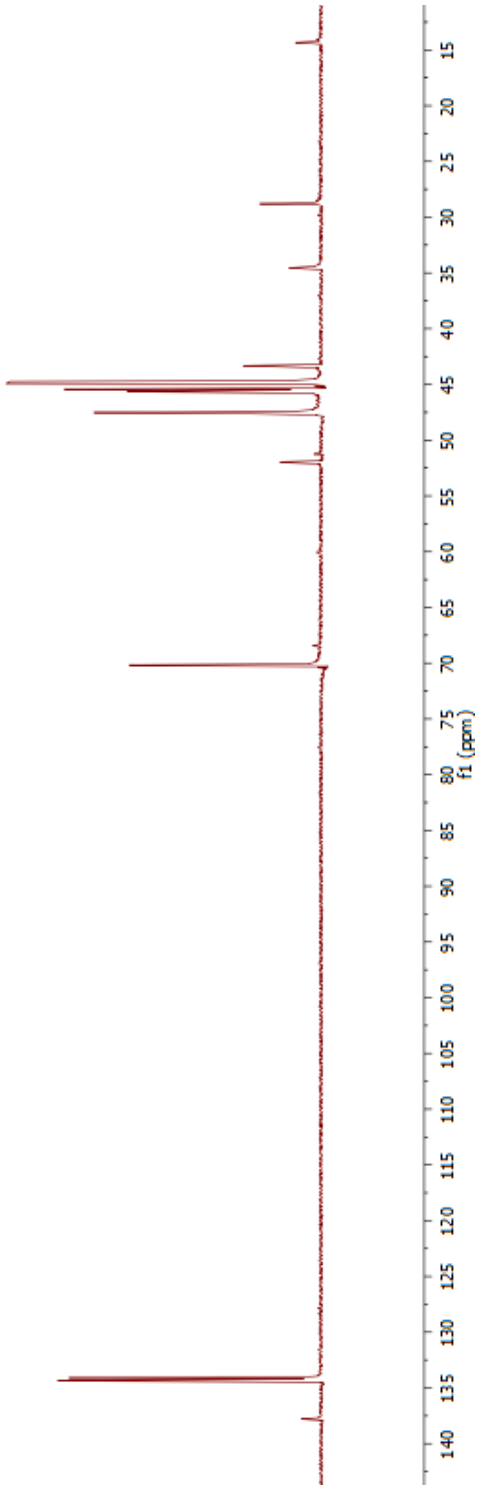

Figure 36. DEPT 90 NMR Spectrum of Compound **3c**

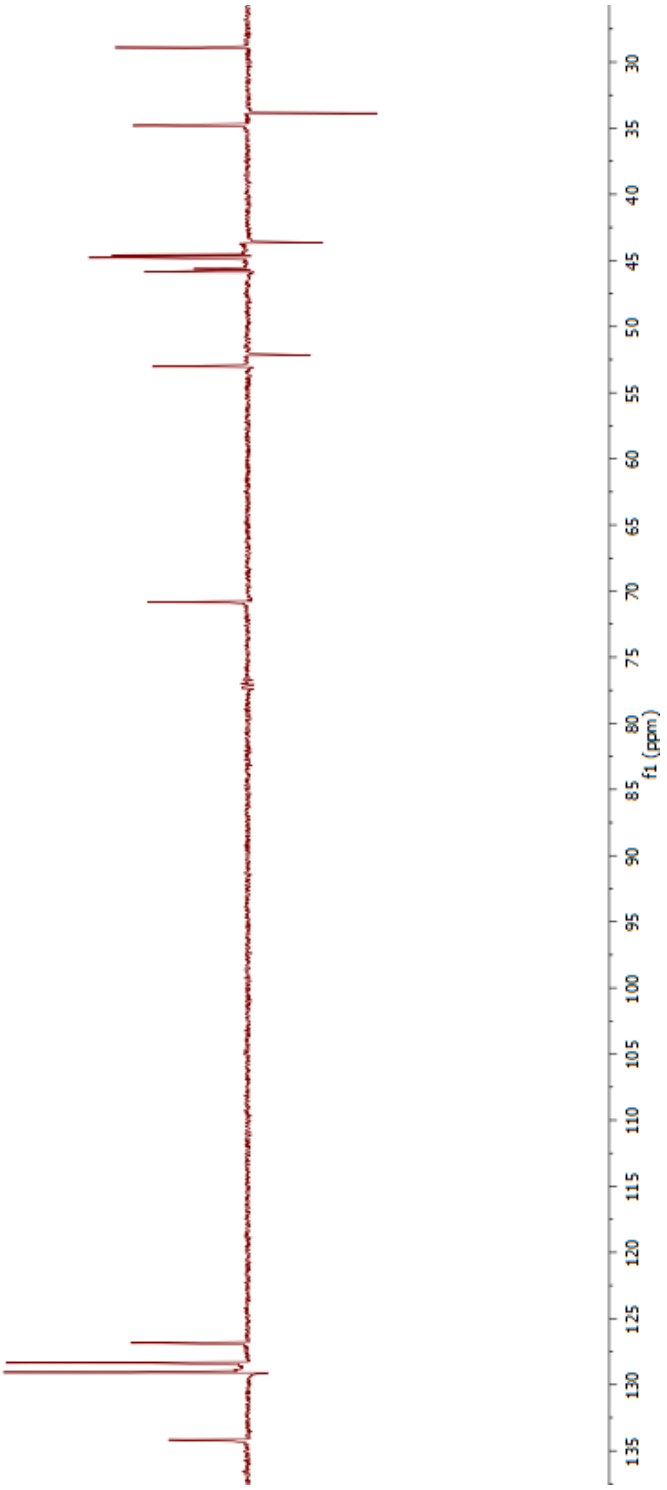

Figure 37. DEPT 135 NMR Spectrum of Compound **3c**

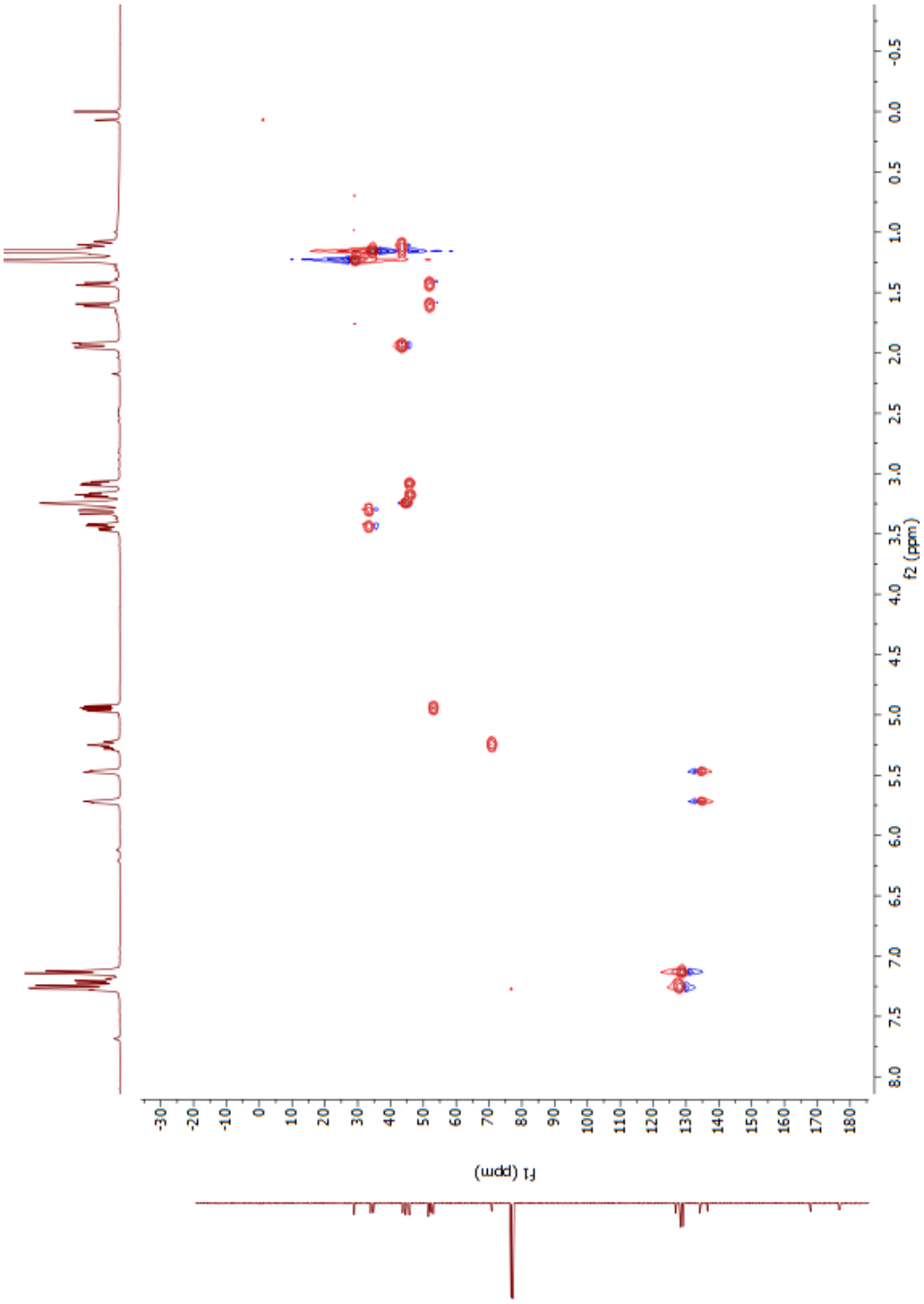

Figure 38. HSQC NMR Spectrum of Compound **3c**

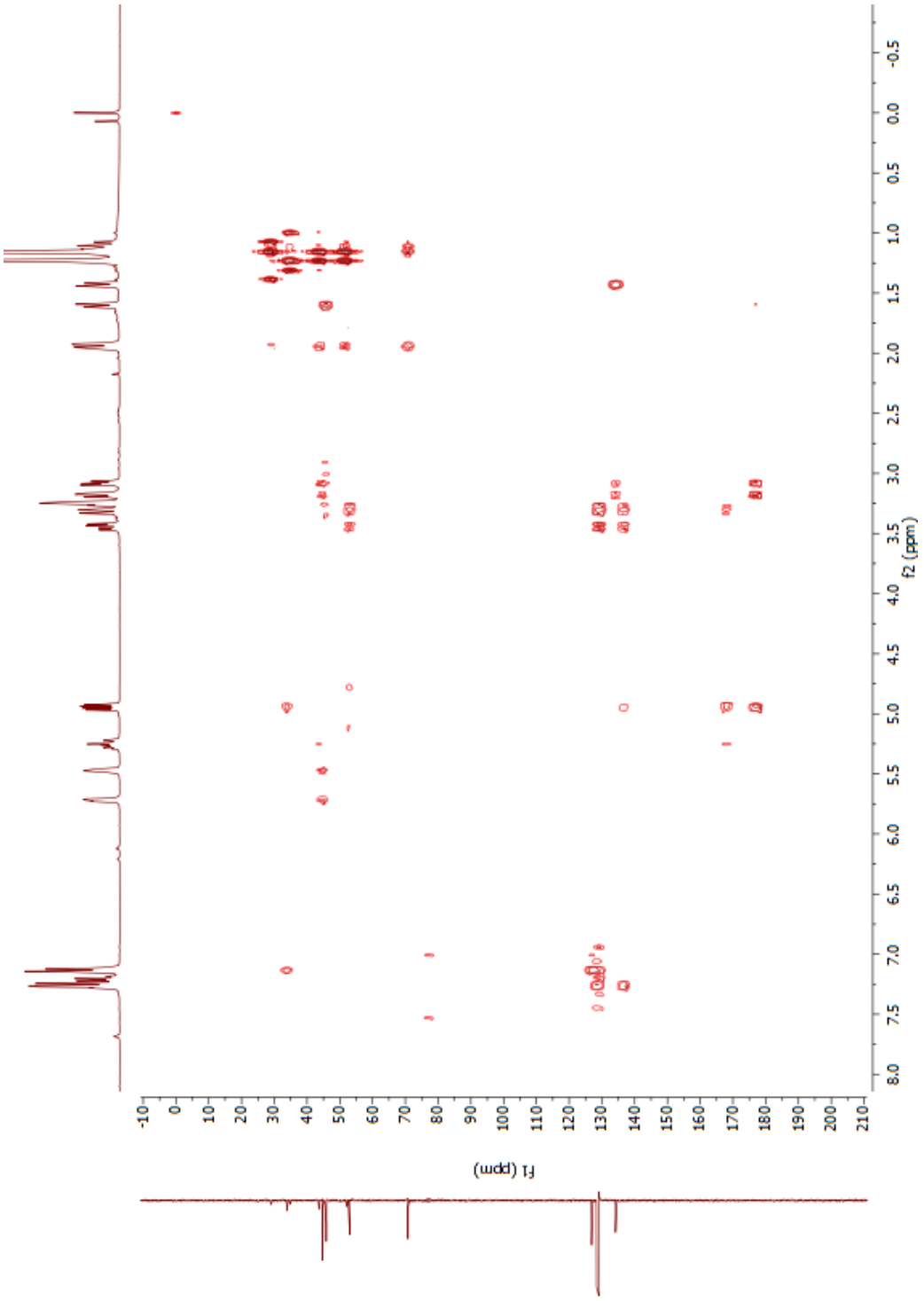

Figure 39. HMBC NMR Spectrum of Compound **3d**

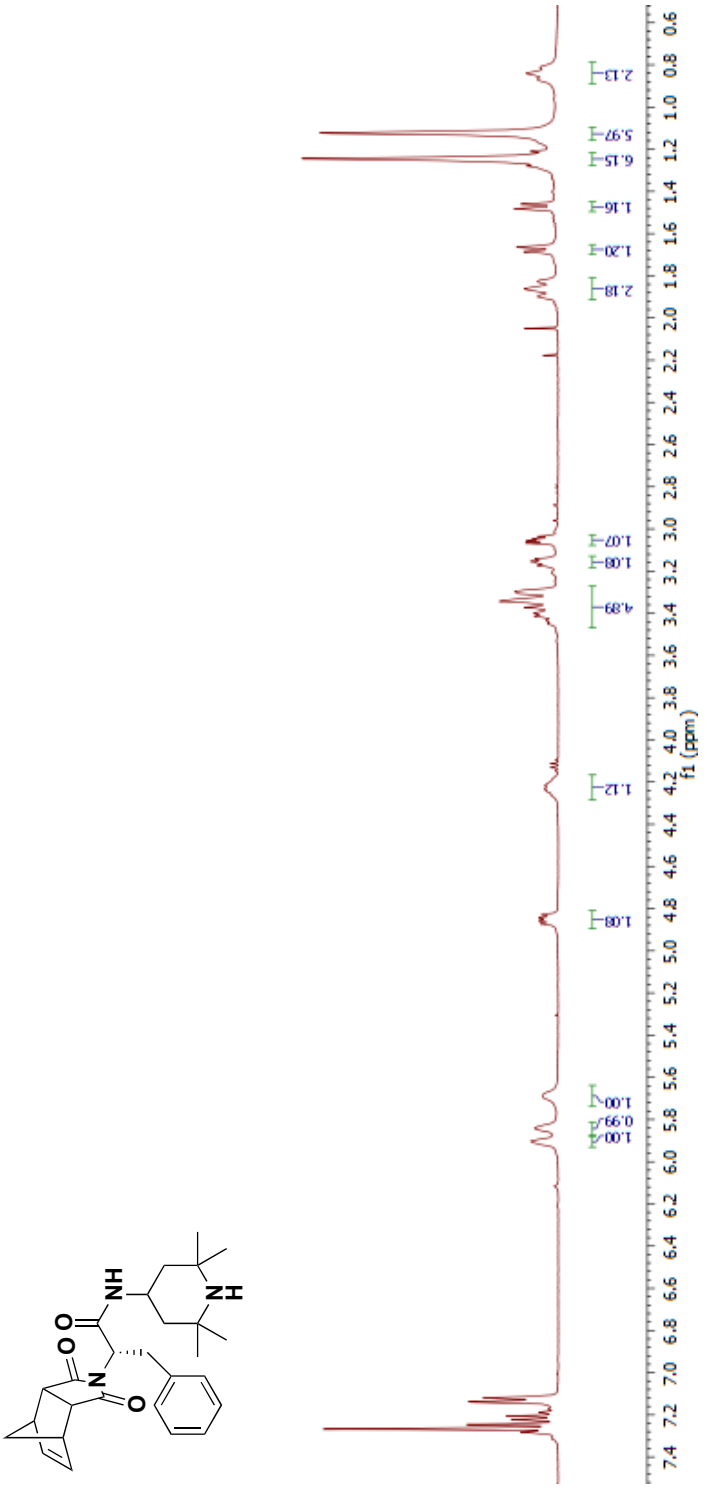

Figure 40. ^{1}H NMR Spectrum of Compound **3d**

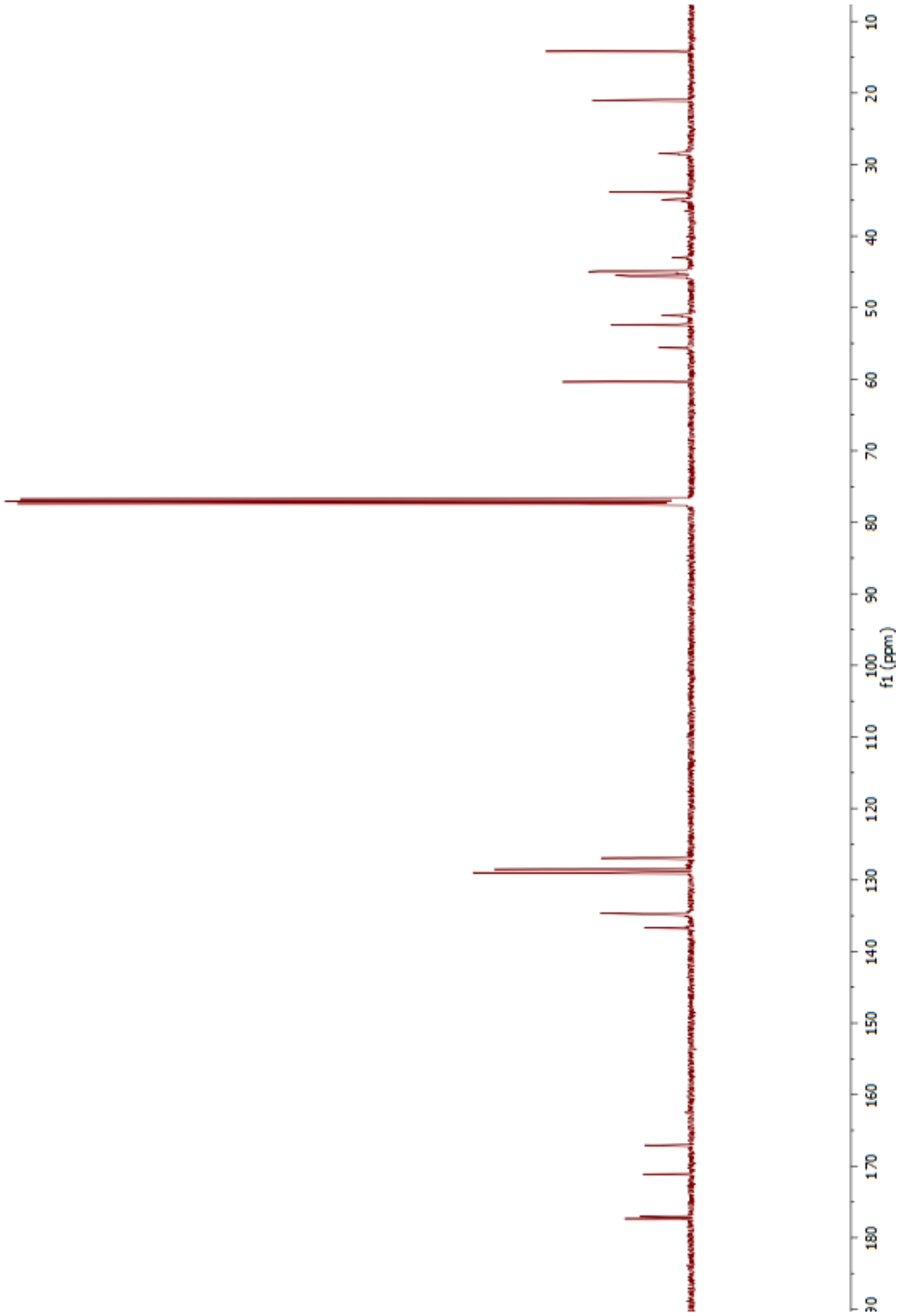

Figure 41. ^{13}C NMR Spectrum of Compound **3d**

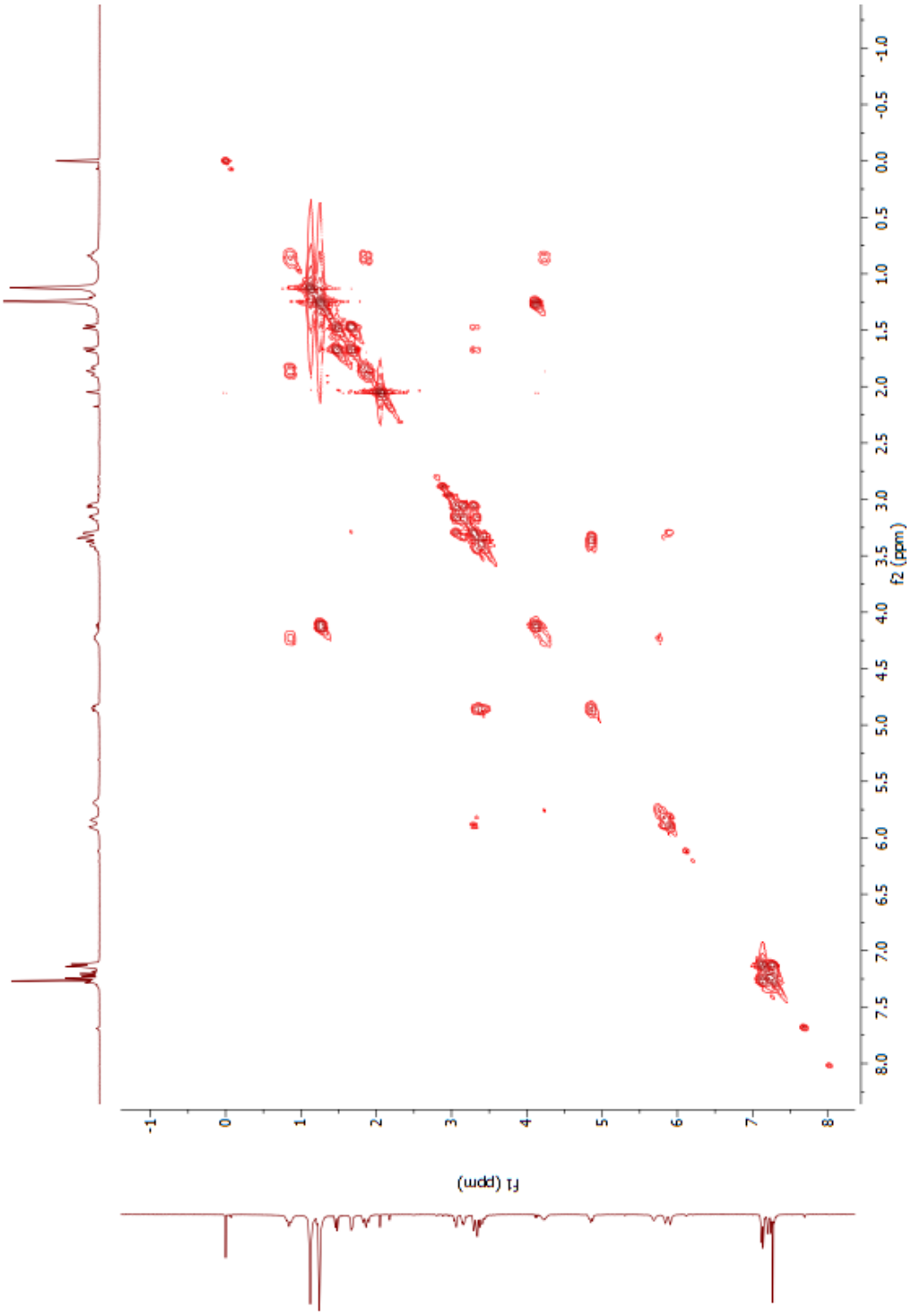

Figure 42.COSY NMR Spectrum of Compound **3d**

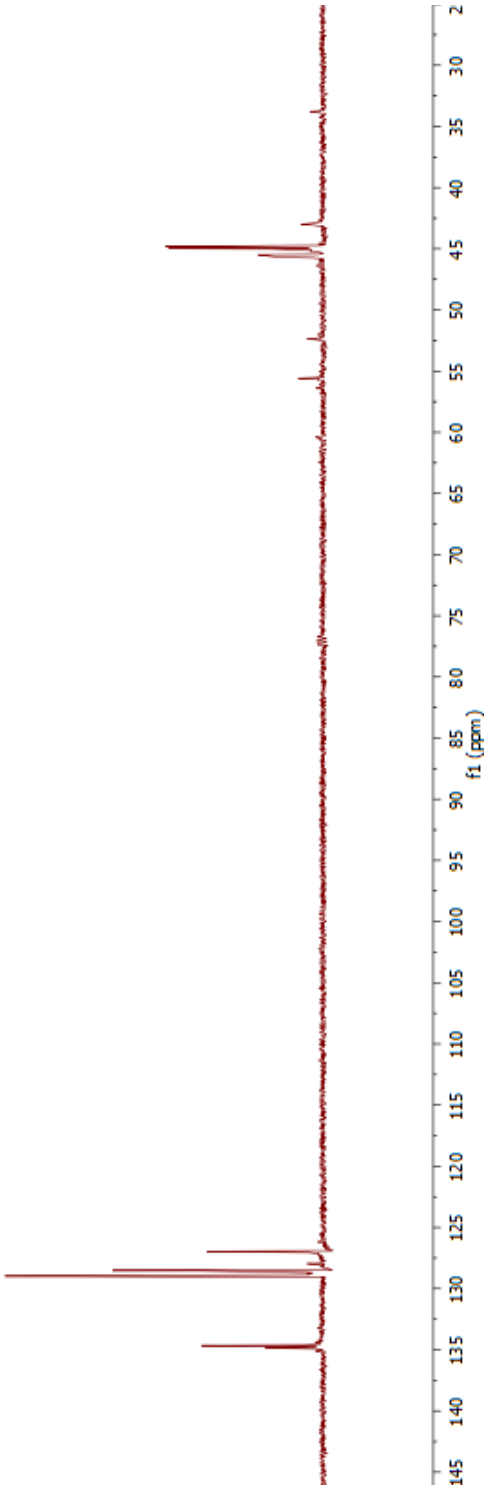

Figure 43. DEPT 90 NMR Spectrum of Compound **3d**

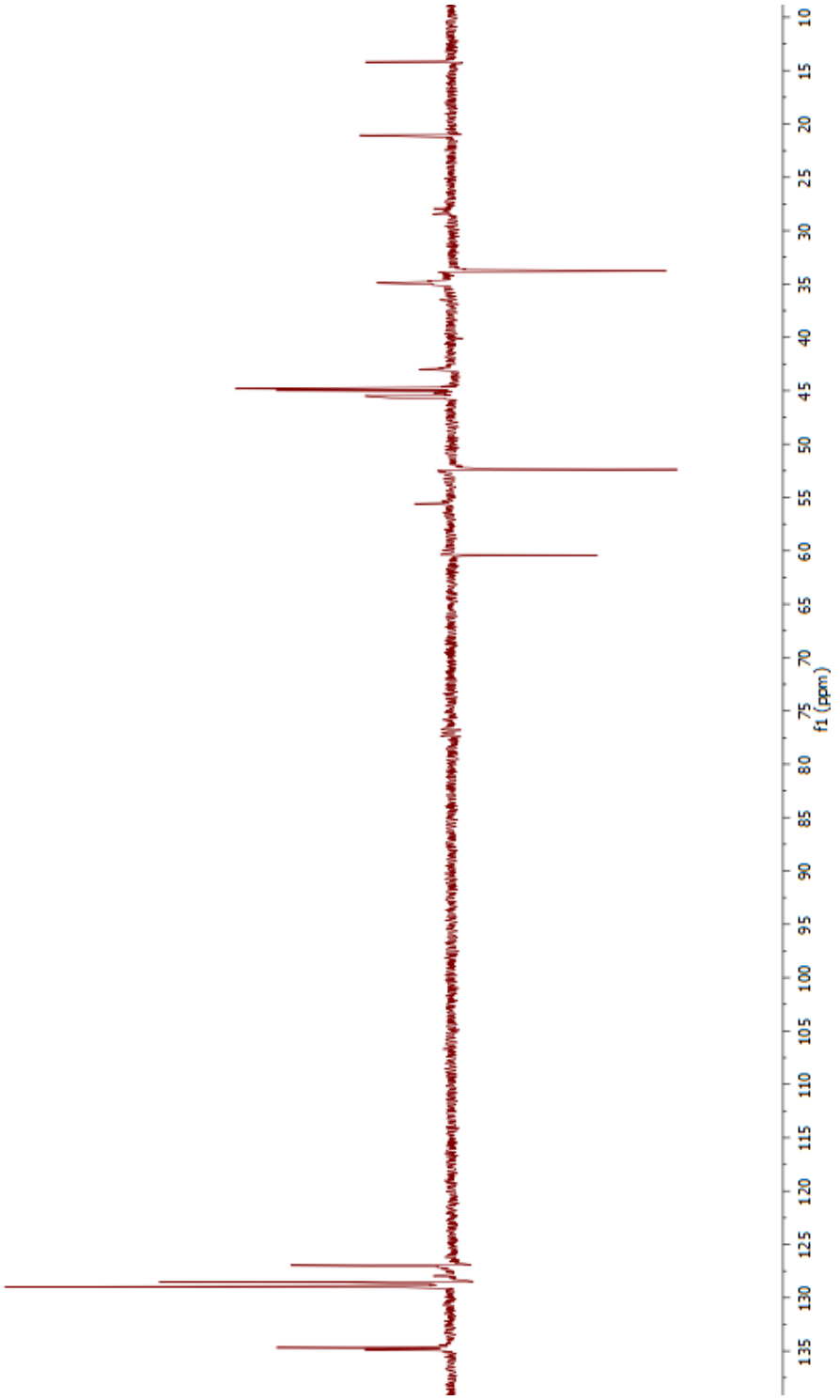

Figure 44. DEPT9 135 NMR Spectrum of Compound **3d**

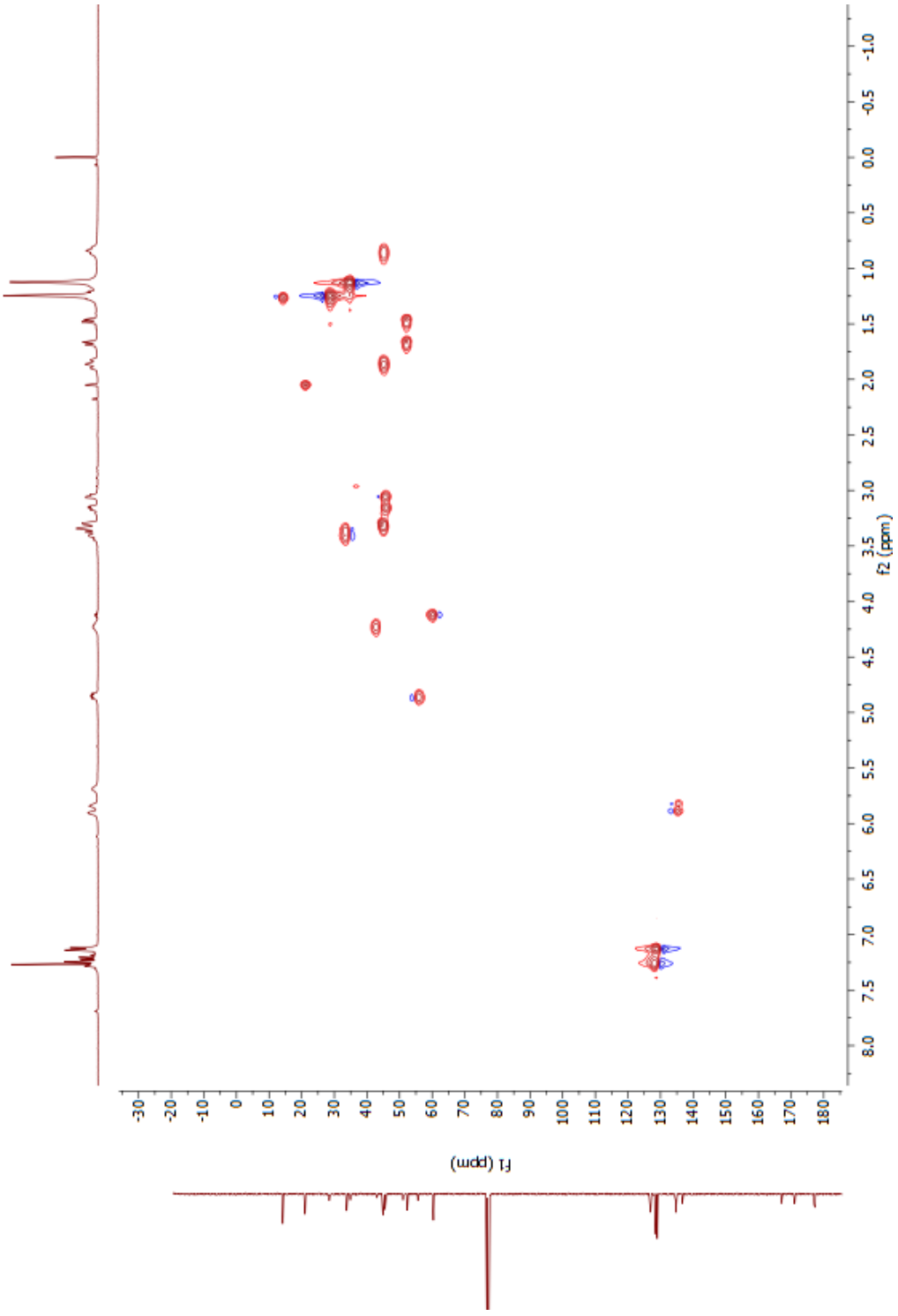

Figure 45. HSQC NMR Spectrum of Compound **3d**

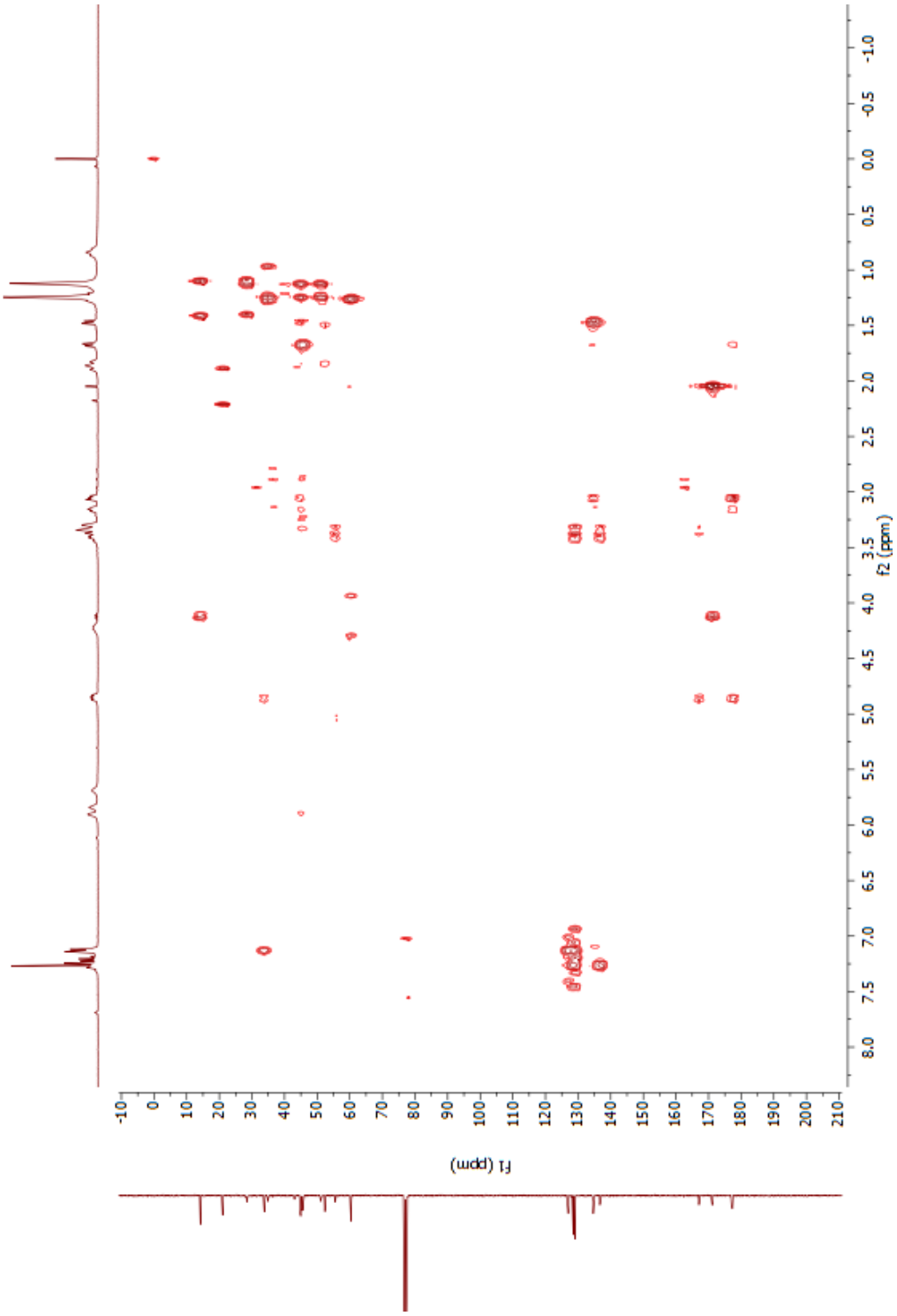

Figure 46. HMBC NMR Spectrum of Compound **3d**

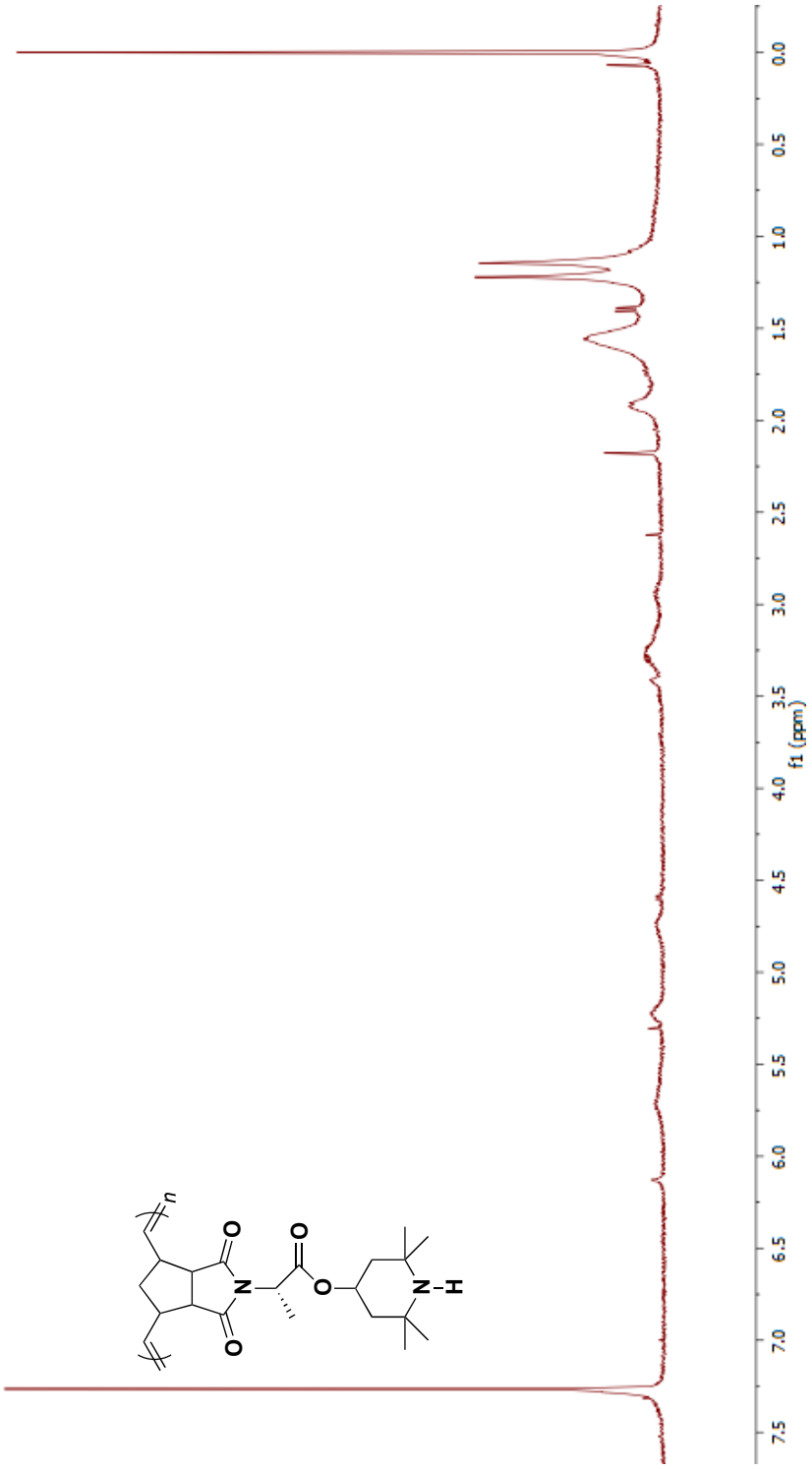

Figure 47.[1]H NMR Spectrum of Compound **4a**

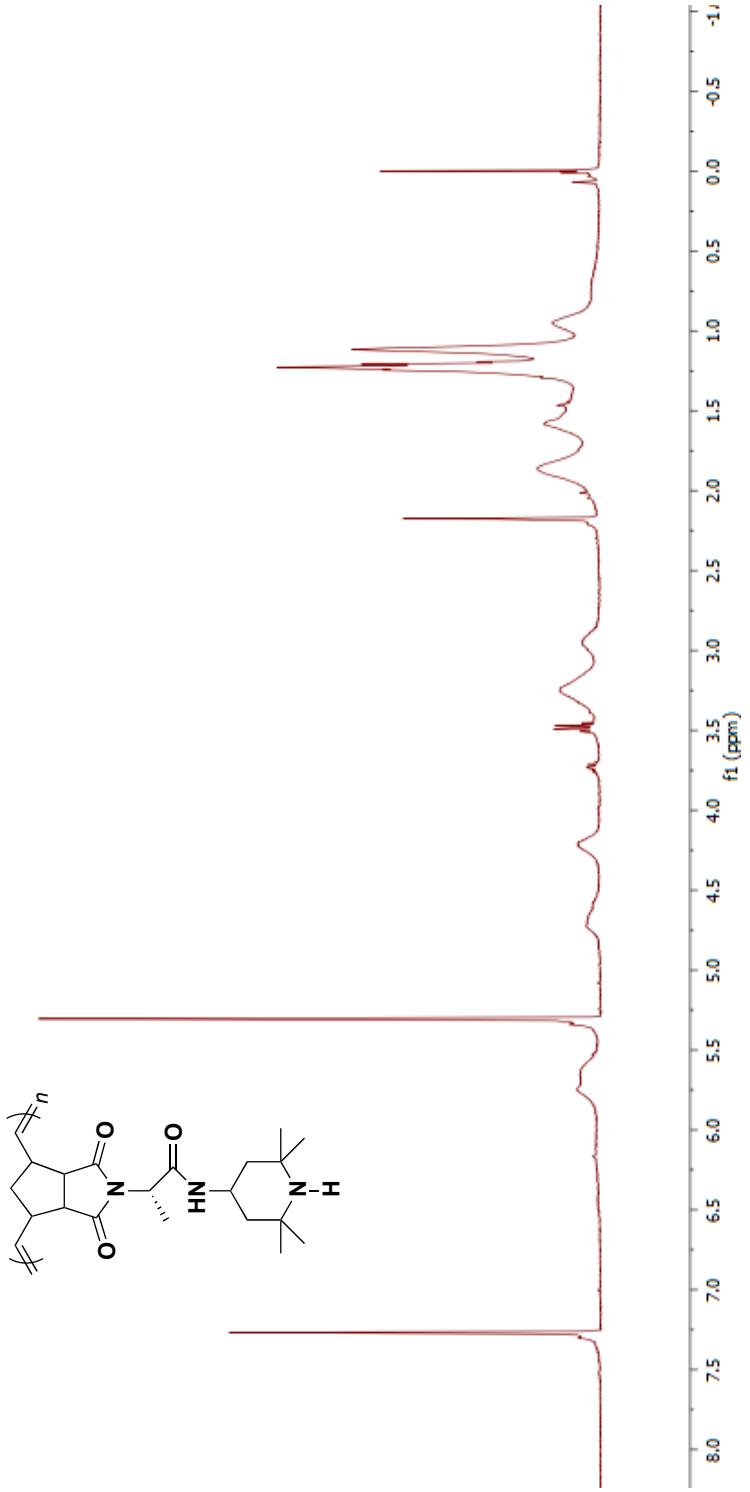

Figure 48. ^{1}H NMR Spectrum of Compound **4b**

B. IR Spectra

IR spectra were recorded at Thermo Scientific Nicolet iS10 ATR-IR spectrometer.

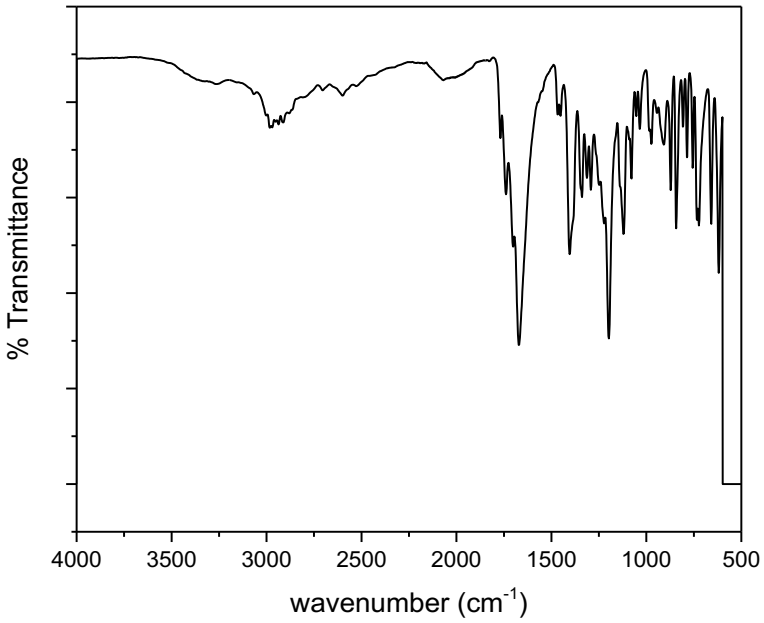

Figure 49. IR Spectrum of Compound **2a**

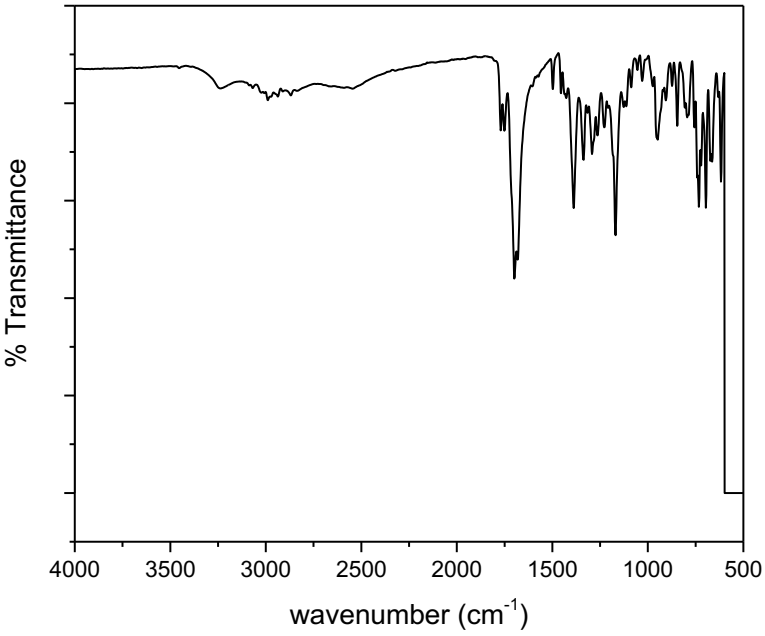

Figure 50. IR Spectrum of Compound **2b**

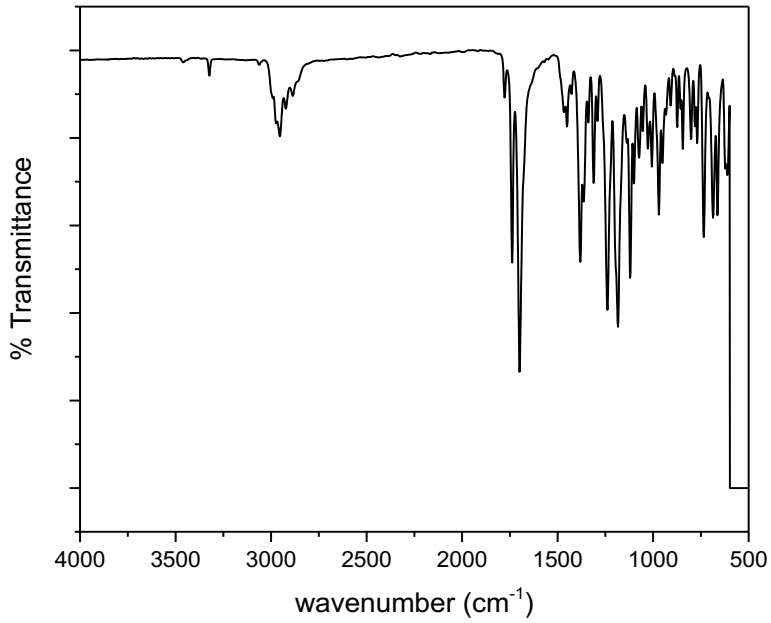

Figure 51. IR Spectrum of Compound **3a**

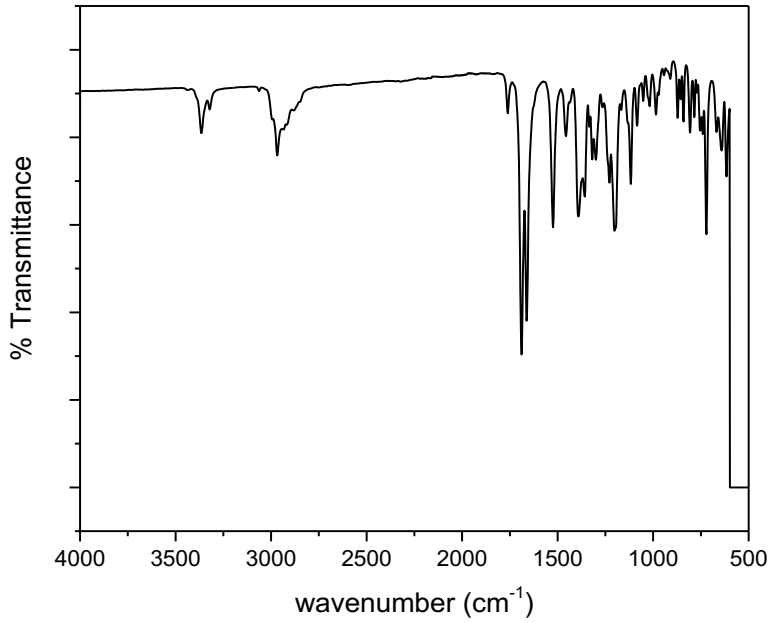

Figure 52. IR Spectrum of Compound **3b**

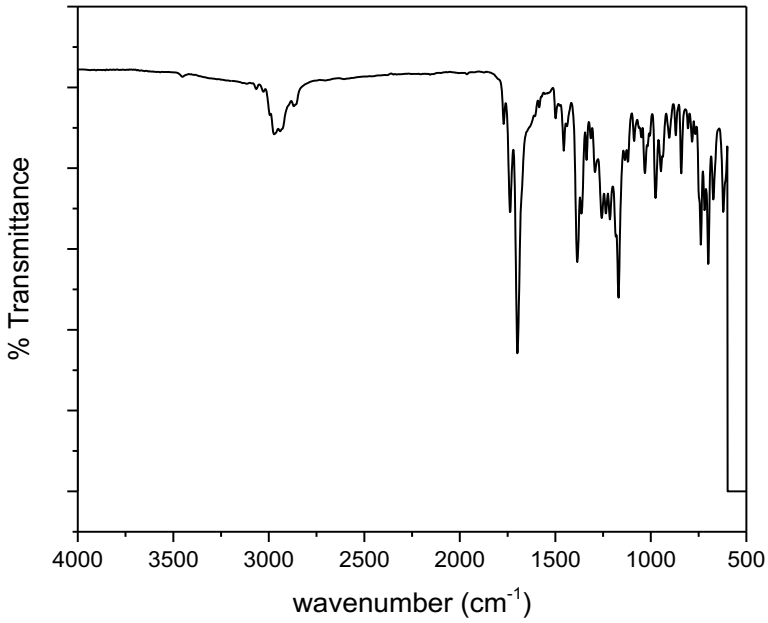

Figure 53. IR Spectrum of Compound **3c**

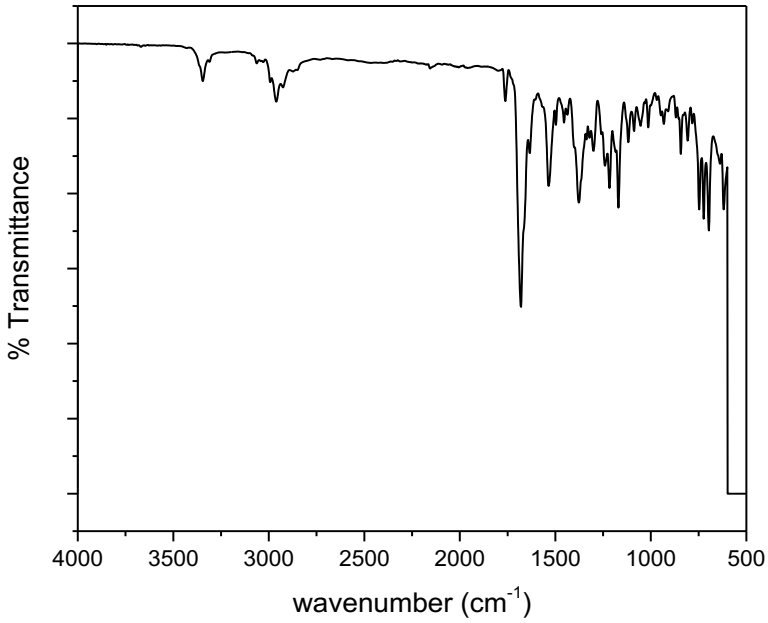

Figure 54. IR Spectrum of Compound **3d**

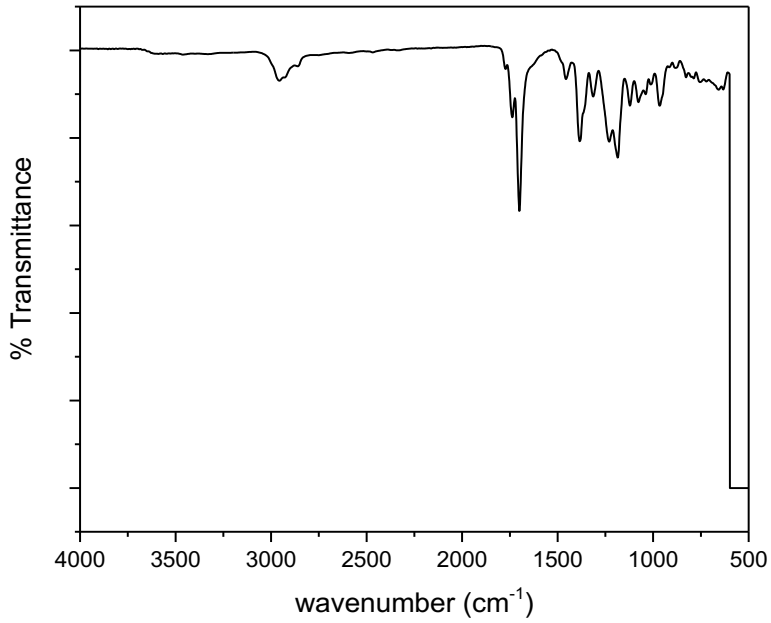

Figure 55. IR Spectrum of Compound **4a**

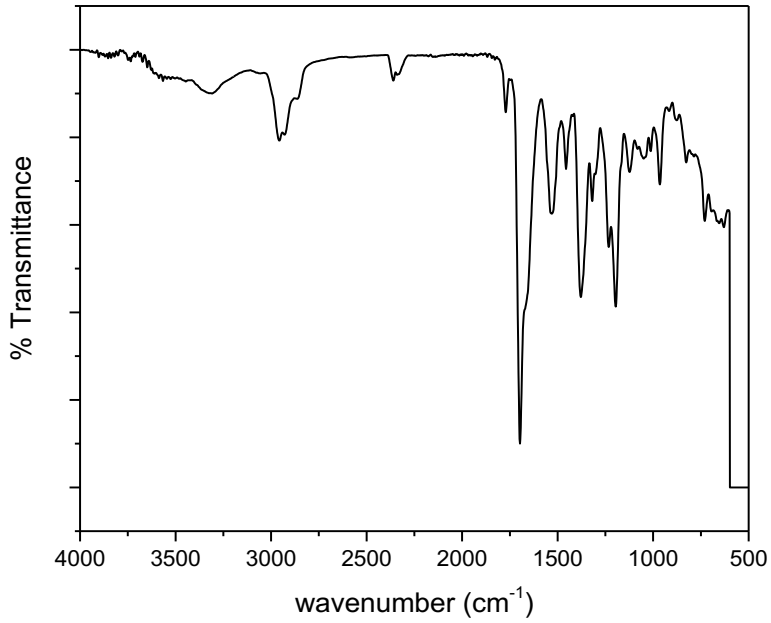

Figure 56. IR Spectrum of Compound **4b**

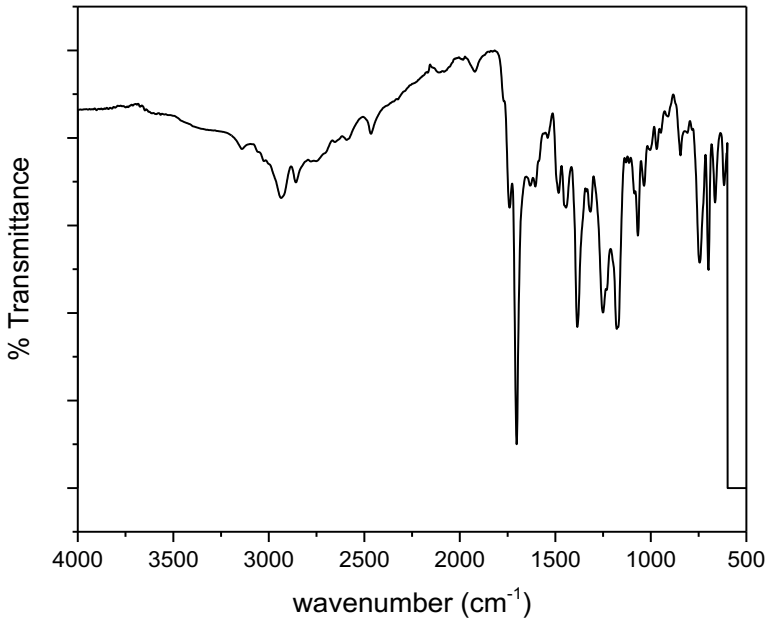

Figure 57. IR Spectrum of Compound **4c**

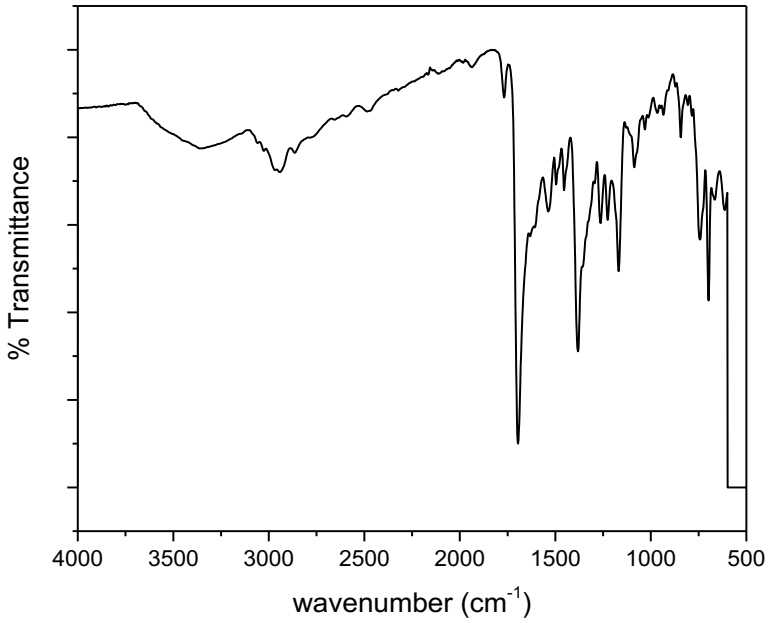

Figure 58. IR Spectrum of Compound **4d**

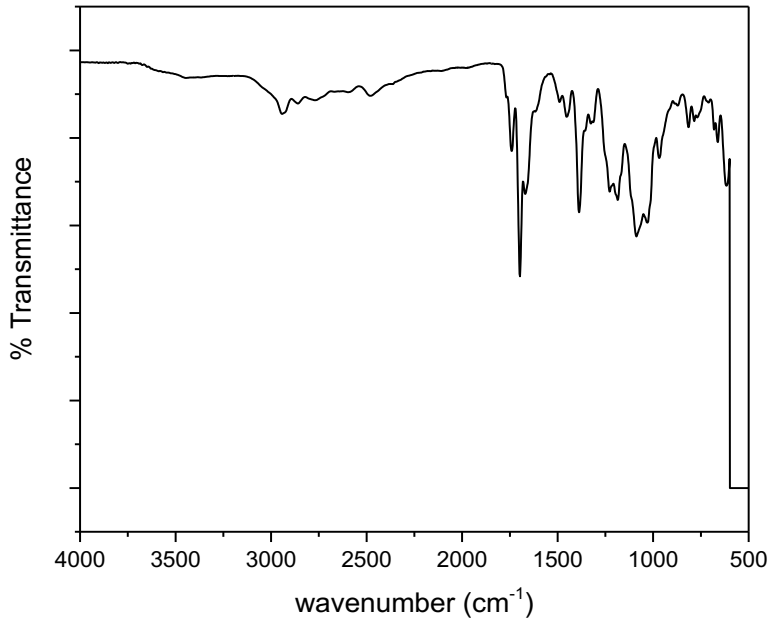

Figure 59. IR Spectrum of Compound **5**

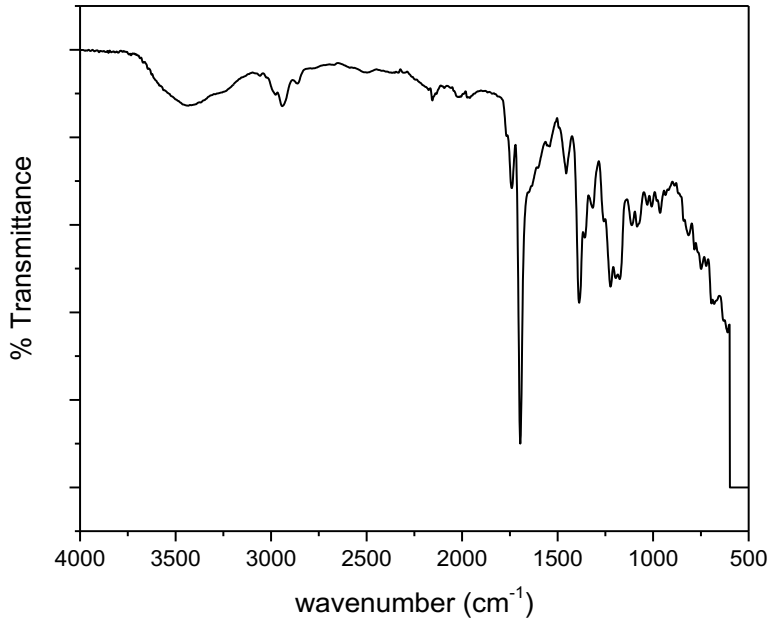

Figure 60. IR Spectrum of Compound **polA**

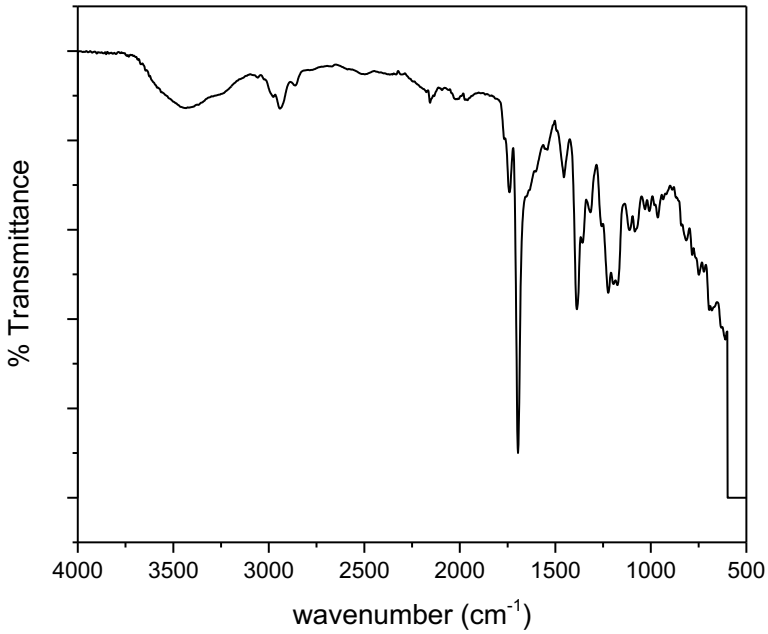

Figure 61. IR Spectrum of Compound **polB**

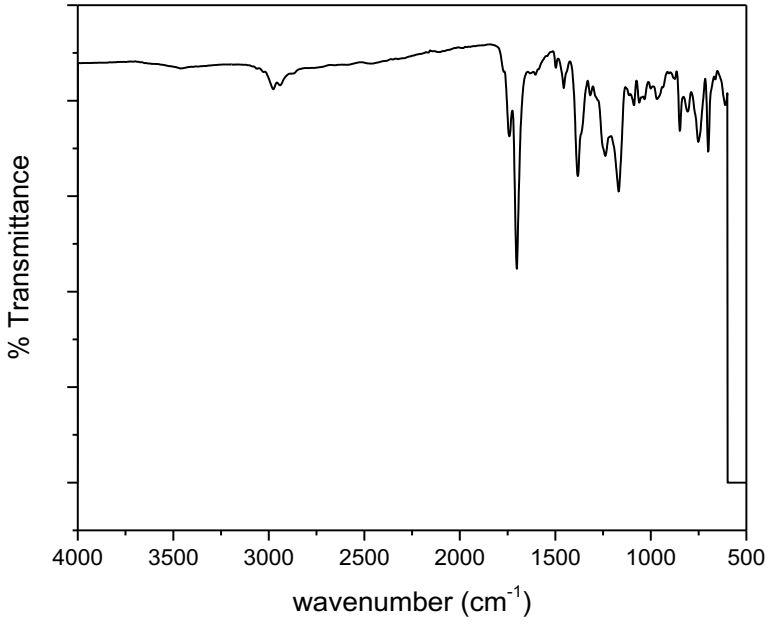

Figure 62. IR Spectrum of Compound **polC**

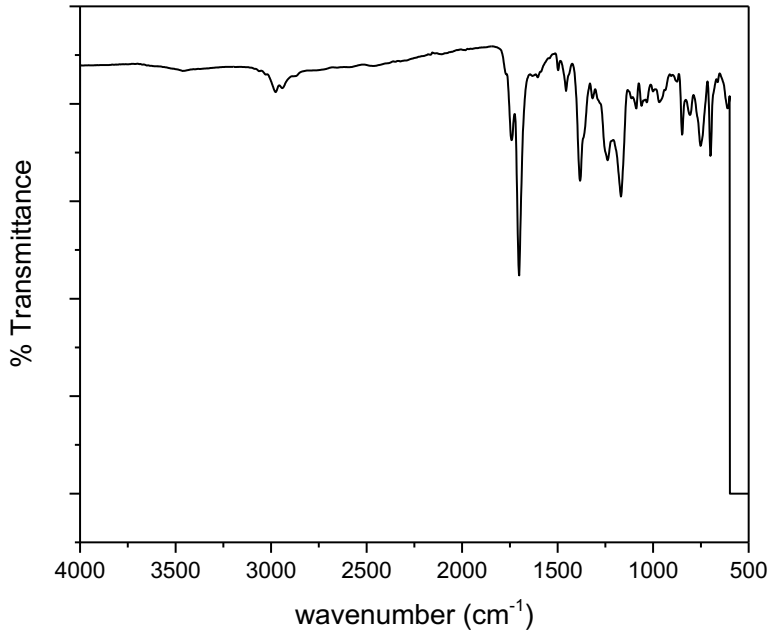

Figure 63. IR Spectrum of Compound **polD**

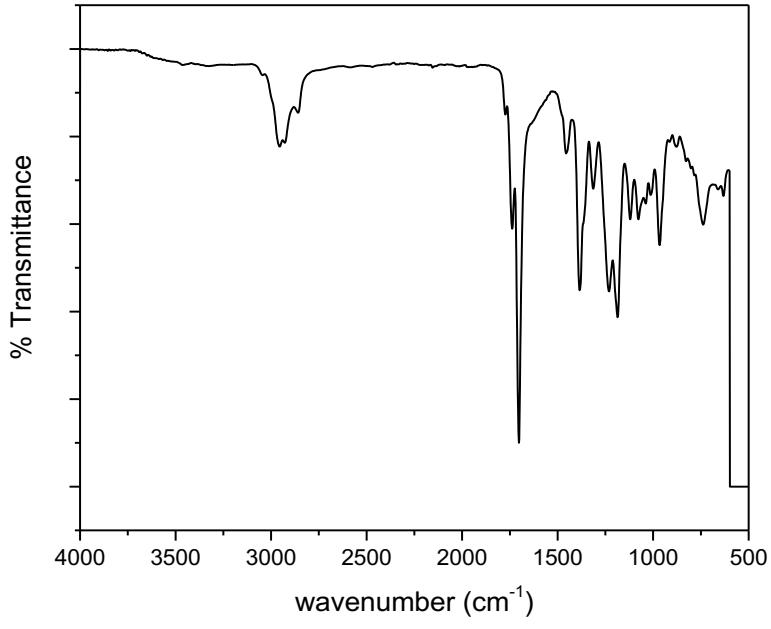

Figure 64. IR Spectrum of Compound **cross4a**

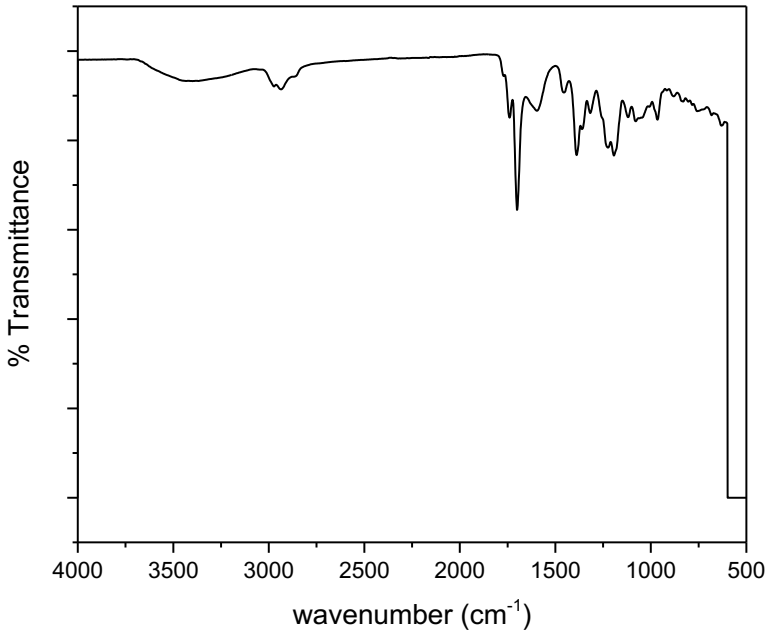

Figure 65. IR Spectrum of Compound **cross4a'**

C. HRMS Spectra

High Resolution Mass Spectra (HRMS) Spectra were processed in positive mode on (ES+) using Time of Flight mass analyzer.

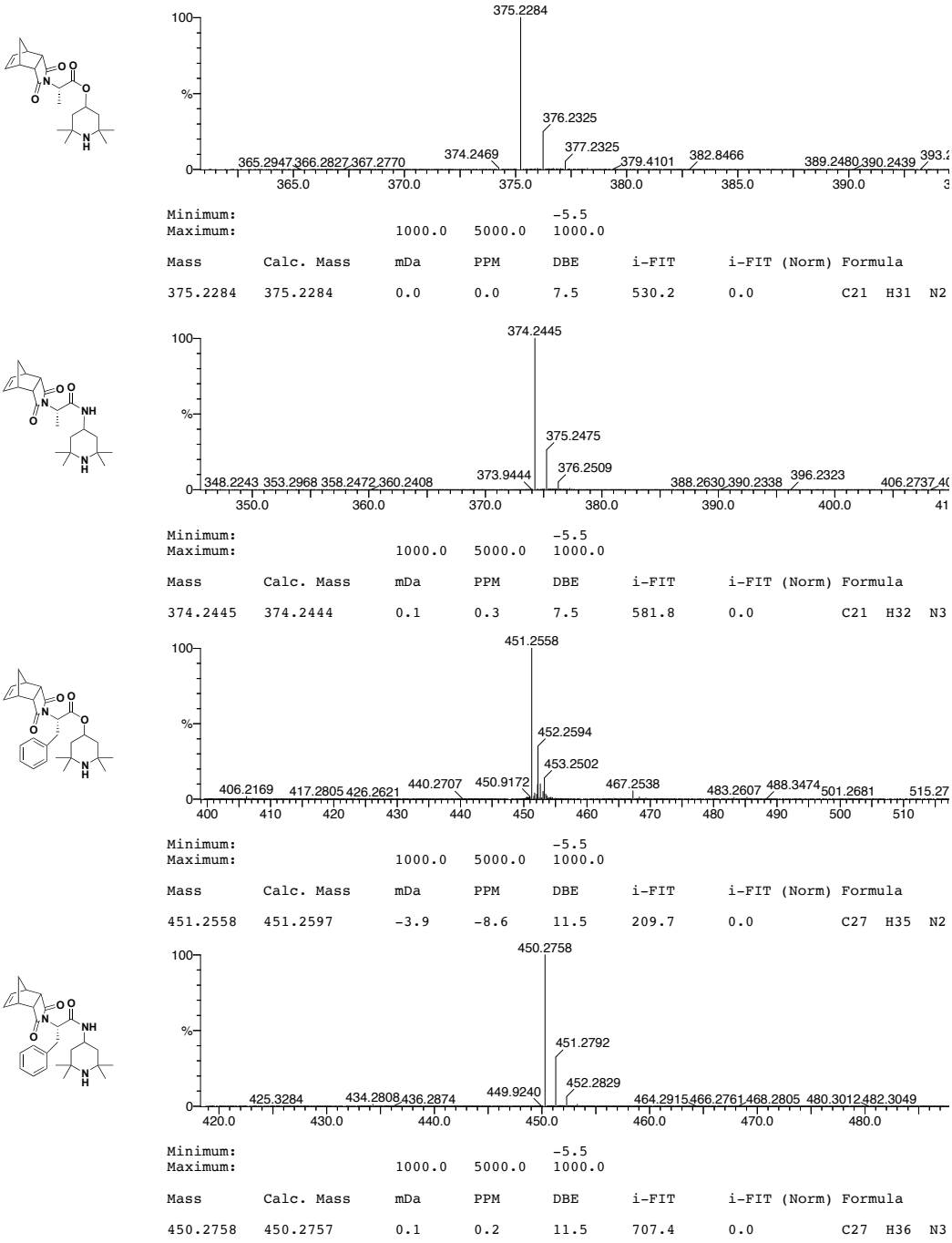

Figure 66. HRMS Spectra of the Synthesized Monomers