# STUDIES ON ALL POLYMERIC OXIDATION METHODS

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**I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.**

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## ABSTRACT

### STUDIES ON ALL POLYMERIC OXIDATION METHODS

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Green chemistry is a concept in chemistry of increasing significance. Applying fundamental organic syntheses in lieu with the pursuit of an understanding of green chemistry is therefore a challenging and yet prominent necessity. Selective oxidation of primary alcohols to aldehyde derivatives is one of such synthesis in organic chemistry. In this study, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) radical and a commercially available chlorinated hydantoin containing polymer were used together in the interest of the selective oxidation of primary alcohols. Afterwards, TEMPO attached polymers were designed and synthesized to be facilitated in oxidation reactions. Therefore, the polymer could be easily separated from the reaction media. Each of these polymers was combined with chlorinated hydantoin containing polymers so as to form relatively green and all polymeric reagents. The all polymeric reagents could each time be regenerated and reused in other reactions. Primary alcohols containing different functional groups were utilized to test the performance of the catalyst mixtures. The effect of altered solvent systems was also examined. With all these in mind, an easy and relatively green method was developed for oxidation of alcohols.



Keywords: green chemistry, alcohol oxidation, TEMPO attached polymers, hydantoin containing polymers

# ÖZ

## TAMAMI POLİMERİK OKSİDASYON SİSTEMLERİ ÜZERİNE ÇALIŞMALAR

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Çevreci ve sürdürülebilir kimya anlayışı, kimyada önemini gittikçe artırmaktadır. Temel organik sentezleri çevreci bir anlayışla uygulamak, zorlayıcı olsa da öne çıkan bir gerekliliktir. Organik kimyada, bu sentezlerden birisi de, alkollerin seçici olarak aldehit türevlerine yükseltgenmesidir. Bu çalışmada, 2,2,6,6-tetrametilpiperidin 1-okzil (TEMPO) ve piyasada var olan hidantoin içeren bir polimer, birincil alkollerin seçici olarak yükseltgenmesinde birlikte kullanılmıştır. Daha sonrasında, yükseltgenme tepkimelerinde kullanılmak üzere TEMPO içeren polimerler tasarlanmış ve sentezlenmiştir. Bu polimerlerden her biri klorlanmış hidantoin içeren polimerle birlikte, yükseltgenme tepkimelerini katalize edebilecek, görece olarak yeşil ve tamamı polimerik birer sistem oluşturmuştur. Bu polimer karışımları her tepkime sonrasında tekrar kullanılabilmektedir. Bu sistemlerin performansı, farklı işlevsel gruplar içeren birincil alkollerle test edilmiştir. Çözücülerin tepkimeler üzerindeki etkisi de araştırılmıştır. Bütün bunlar göz önünde bulundurulduğunda alkol yükseltgenme tepkimesi için kolay ve görece yeşil bir yöntem geliştirilmiştir.

Anahtar Kelimeler: yeşil kimya, alkol yükseltgenmesi, TEMPO içeren polimerler, hidantoin içeren polimer

To the loving memory of my grandfather,

Ali Rıza Öztürk

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## TABLE OF CONTENTS

## LIST OF SCHEMES

## LIST OF FIGURES

### FIGURES

## LIST OF TABLES

### TABLES

## LIST OF EQUATIONS

### EQUATIONS

# CHAPTER 1

# INTRODUCTION

## 1.1.Green Chemistry

There is an emerging abuse of nature especially due to urbanisation and industrialization and their impacts on the earth such as, green house gases, global warming and extinction of wildlife. Alongside, the tremendous consumption rates and exploitation of natural resources, considering the increase in population, are serious issues. The urgency to realize and deal with their outcomes has legitimately appeared. Thus, with rising environmental consciousness, the demand for nature adapted processes in all fields is becoming more and more significant.

Chemical industry has always had a bad reputation, especially due to chemicals causing health defects and chemical accidents resulting in loss of thousands of lives. However, the first to bring up the adverse effects of chemicals was Rachel Carson in the 1960's. In her book Silent Spring, Carson was addressing the ruinous effects of DDT (dichloro-diphenyl-trichloroethane), a very famous and powerful pesticide, on the ecosystem and human health.[1] Carson pointed out that the chemical spraying entered the food chain inducing cancer risk and genetic damages both in human and animals. Until then, DDT was accepted as prominent due to it's ability to kill high variety of insects. Undoubtedly, Carson experienced personal attacks and was sued by the "influential" chemical companies, yet her integrity was soon understood and finally the use of DDT in agriculture was banned in 1972.[2] The public outcry and environmental movements had an important impact on the boycott and this incident paved the way of public awareness on public safety and environmental sustainability.

In the following years deleterious chemical disasters took place in different parts of the world all of which ignited realization among the society. Thus, the jeopardous consequences of these accidents and the increasing environmental pollution pointed out the emergency of a revolution in chemistry. As the public awareness raised, U.S. Environmental Protection Agency (EPA) was authorized. The major aim of this agency was to provide public and environmental health. In the following years, the mission of EPA was widened and international debates on environmental issues were executed. Hence, EPA contrived the term "green chemistry" in 1997, a term first introduced by Paul Anastas in 1991.[3] Green chemistry is a field in chemistry that eagers to change chemical processes thoroughly and accustom chemistry to nature. The term "green" is also affirmed as an approach which refers to environmentally compatible, and it is adapted to further areas as well. At first green chemistry was not expected to be widespread and accepted since it challenged to change traditional way of performing chemistry. However, as all the above mentioned problems related to environment and human health became obvious, the seriousness of reliable and clean chemistry was admitted. Nowadays, green chemistry education has become essential and studies on green chemistry are being awarded with prestigious rewards. Thus, in order to make the adoptance of chemical processes to green chemistry less complicated, 12 principles which summarized the concept of green chemistry were classified by Anastas and Warner.

### 1.1.1. Understanding Green Chemistry in 12 Principles

Green chemistry principles were introduced in 1998 by Paul Anastas and John C. Warner in their book Green Chemistry: Theory and Practice.[4] These principles were described as a checklist for chemists during the design of a "green" chemical process especially in chemical industry. Although each principle seems particular, they unite to construct a sustainable process at the end.

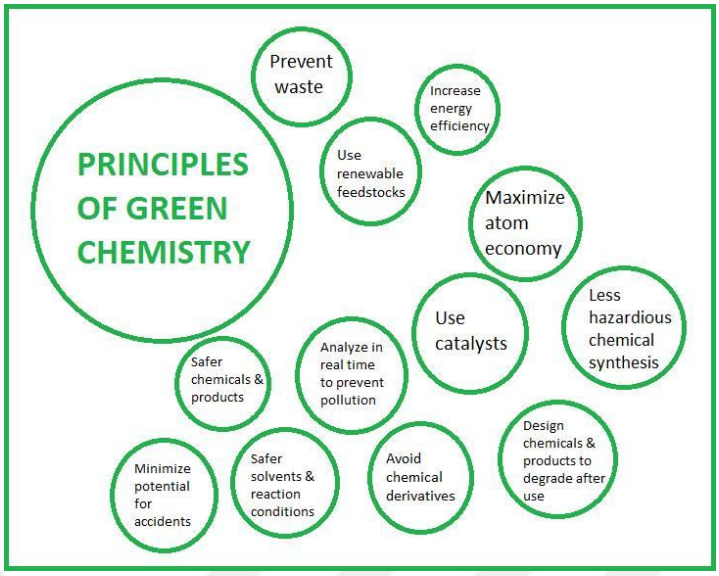



**Figure 1**. 12 Green Chemistry Principles

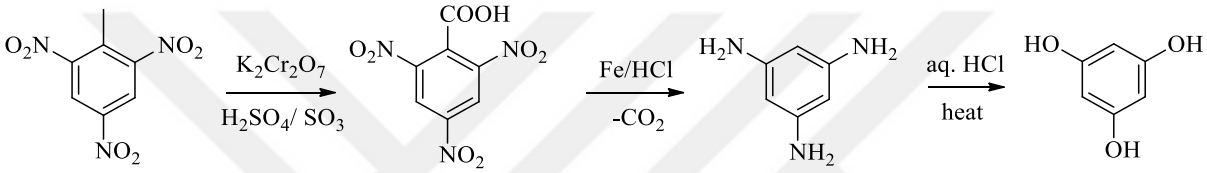
#### 1.1.1.1. Prevention

Waste management has been a vast problem after and during chemical processes. It is a serious concern in chemistry since its consequences are environmental and financial. Here, it is important to make an adequate explanation of waste for chemical processes. The environmental effects of wastes are not always directly proportional with their amount, rather the nature of waste should be analyzed. For this, a term EQ (environmental quotient) is defined. The environmental quotient is the multiplication of the E-factor, *vide infra*, with an arbitrary number Q. This number is relative to the recycling, disposal abilities and toxicity of the waste.[5] So, a comparison of the environmental impact of wastes can be done by examining their EQ. For example, inorganic wastes have higher EQ than organic wastes due the difficulty of disposal and long persistence time.[6]

According to the green chemistry approach, rather than finding a way to handle and treat waste, the aim is to prevent it from existence. The ultimate goal is to design chemical processes in a way that the "waste" of a reaction is the solvent or reactant of another or to design the process so that no waste is formed.

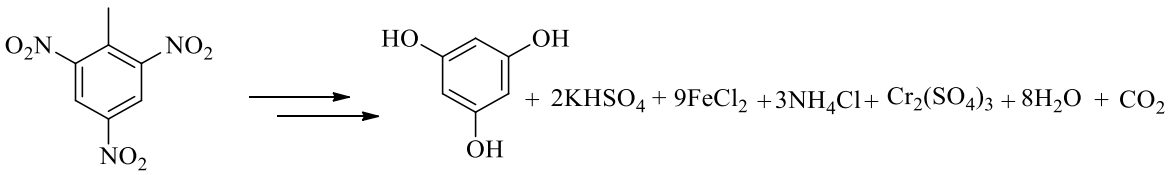
#### 1.1.1.1.1. E-factor (Environmental Factor)

It is hard to calculate the exact environmental impact of a chemical process. Rather, a measurement that compares the processes with each other can be developed. The E-factor is a metric system that measures the amount of waste produced in a process. In the simplest way, it is the ratio of total waste to the product desired. It includes all components in all steps that can be counted as waste, even the energy that is used.[7] By analyzing the concept of E-factor it can be concluded that the separation, purification, neutralization steps generate more waste than the reaction itself.[8] Hence, higher E-factor indicates higher waste production.




**Scheme 1.** Synthesis of phloroglucinol[9]

Sheldon accounts the birth of E-factor concept for the closure of a phloroglucinol plant at Oce Andeno due to the extreme waste disposal expenditure. This incident, awakened the industry on the significance of waste problem. Phloroglucinol (1,3,5-benzenetriol), an important pharmaceutical intermediate and starting material for explosives, had been synthesized starting from TNT (trinitrotoluene) until 1980's. The widely accepted 3 step process, shown in Scheme 1, was regarded as efficient due to over 90% yield with respect to the starting material.




**Scheme 2.** Stoichiometric equation of the synthesis of phloroglucinol[9]

In point of fact, it was not "efficient". When the stoichiometric equation of the overall process (Scheme 2) is examined, it is evident that 20 kgs of waste per 1 kg of

phloroglucinol will be generated. Also when all the work-up and disposal steps are taken into consideration the amount of waste increases excessively. Indeed, the process was generating 40 kg solid waste per 1 kg desired compound including chromium waste for which costly disposal methods were required.[9] Since environmental aspects were not taken into consideration the process could be viewed as efficient. However, as sustainability became more of an issue in chemistry the demand for new methods got more obvious. This actually is an outstanding example on how the perception on chemical designs changed by way of increasing environmental consciouss.

#### 1.1.1.2. Atom Economy

The efficiency of a chemical synthesis has always been regarded as determining during the adopting of a pathway. Conforming to the traditional view, efficiency is counted as the selectivity and isolated yield of the reaction. Chemoselectivity, regioselectivity as well as diastereo and enantioselectivity have been decisive parameters for the efficiency of the method.[10] These aspects regulate the number of steps for the pathway to the target compound. However, selectivity is not the only criterion for the decision of the efficiency of a design. To overcome this the term atom economy (AE) was first introduced by Trost in 1991.[11] The extent of reactant atoms appearing in the product, which is regarded as the atom economy is another feature of efficiency.[11]

$$\%\text{reaction yield} = \frac{\text{quantity ofisolated product}}{\text{theoretical quantity of product}} * 100$$

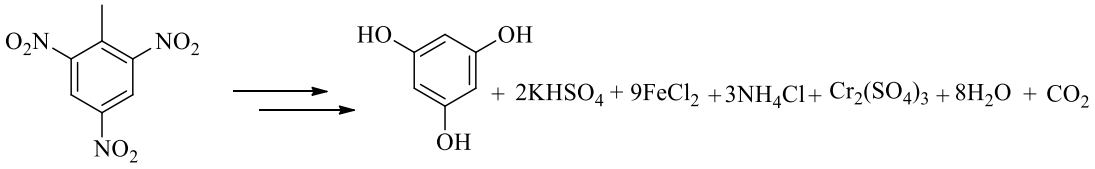
Equation 1. Calculation of % reaction yield

$$\%\text{atom efficiency} = \frac{\text{molar mass of desired product}}{\text{total molar mass of reactants}} * 100$$

Equation 2. Calculation of % atom efficiency

The atom efficiency is not about the yield of the isolated product of the reaction, rather it is related to the contribution of atoms of reactants in the desired product. Although they get confused with each other, reaction yield and atom efficiency are entirely distinct concepts that are quantified with different equations, which can be

seen above. Again, the phloroglucinol synthesis is a suitable example to examine the difference between reaction yield and atom efficiency. As mentioned before, the reaction yield is more than 90% for this process. On the other hand, in Scheme 3, where the atom efficiency is calculated, it can be seen that % atom efficiency for this process is only 5%.

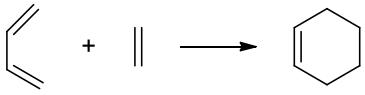



$$\%\text{atom efficiency} = \frac{126}{126 + 392 + 272 + 1143 + 160.5 + 44 + 144} = ca\ 5\%$$

**Scheme 3.** Calculation of Atom Economy for Phloroglucinol Synthesis[9]

The atom efficiency equation is only based on the stoichiometric equation so all the other reagent, solvent and energy consuming steps during work-up are excluded, in order to examine these the E-factor of the process should be considered.

In a 100% atom efficient reaction all the atoms of the reactants would be seen in the product that is formed, thus no by-products would form. For example, Diels-Alder type reaction fits to an ideal atom efficient process. In the reaction (Scheme 4) all the diene and dienophile atoms, 1,3-butadiene and ethene, respectively, are incorporated in the formation of the product. However, such simple addition reactions are not frequent in chemical synthesis.



**Scheme 4.** Diels Alder reaction of 1,3-butadiene and ethene

For these reasons, catalytic reagents that provide the activation of reactants are utilized. The great tendency of transition metals to activate organic molecules is being regarded as promising for high atom efficient reactions with high selectivity.[11] Still, it is hard to meet the selectivity and atom efficiency demands together for most

of the chemical processes. Thus, the intent is to revise or redesign synthetic methods in a way that they are both selective and atom efficient. The importance of atom economy has been understood lately and still has a long way to go. The increasing environmental pollution and decrease in natural feedstocks actually highlight the importance of reactions that eliminate the formation of by-products.

#### 1.1.1.3. Less Hazardous Chemical Synthesis

Chemical processes have the potential to cause overwhelming consequences both for human health and environment. By a safer design, this risk can be reduced or eliminated. So, the toxicity of reagents and products should be reduced as much as possible in order to be viewed as a green design. For a long time, PCC (pyridinium chlorochromate) oxidation was a widely approved method for the conversion of primary alcohols to aldehydes. However, the process requires care during handling since Cr(IV) containing species are highly toxic.[12] Hence, green alternatives for this process were proposed and are being used.[13,14] To such a degree, for a green design reagents with high toxicity should be replaced with safer derivatives whenever possible. However, the efficiency preservence should always be considered during such alterations.

#### 1.1.1.4. Designing Safer Chemicals

As the knowledge on chemical syntheses widens, the ability to forsee their perilous effects on environment and human health also increases. It is crucial to have high awareness of the characteristics of chemicals that are synthesized.[15] Resulting compounds should have relevant nature with the scope of synthesis. Meanwhile the harmful outcomes should always tried to be lowered. In this way, mechanistic toxicology studies on the results and risks of chemical exposure in living organisms. The vulnerability estimations of chemicals are still being studied.[16] Having these in hand, alterations made in synthetic design may result in the reduction of toxicity of the final products. For this purpose, degradable polymers as well as dyes that do not include heavy metals were synthesized. Although the function of pesticides is

harmful, their environmental hazard was decreased by improving selectivity in synthesis.[17]

#### 1.1.1.5. Safer Solvents and Auxillaries

Solvents are ubiquitous in chemical synthesis not only for the reaction medium but also for the separation, purification steps. Yet when environmental concerns are taken into consideration solvents are regarded as waste. Because of their volatility solvents first mix in the atmosphere and then to ground water. So, choosing the solvent of a green design is a key point in less hazardous chemical synthesis. Although it is recommended to switch to greener solvents from toxic ones, not all the reactions offer the opportunity to choose. Unfortunately, in such cases revising traditional methods is not effective, rather entirely new methods can be seeked for.[18] Also, recycling organic solvents for another reaction is a way to reduce the use of toxic solvents. However, the risk of contamination and consumption of energy is still a concern.

Most organic solvents have severe effects on human health and environment. In the guidline of The Food and Drug Administration (FDA), published in 2012, the solvents that are involved in pharmaceutical synthesis are classified according to their environmental and health impacts. Consequently, Class 1 includes solvents unauthorized to be used in pharmaceutical processes due to deleterious effects. Class 2 includes solvents with inherent toxicity for which the employment is limited. Thus Class 3 solvents are relatively less toxic than Class 2 solvents. The consequences of solvent exposure should also be recognized during chemical synthesis processes. Hence, some solvents which are significantly come upon during organic synthesis are listed below.

**Table 1.** 2012 FDA Guidline for Solvent Classification in Pharmaceutical Synthesis

| Class 1 | | Class 2 | Class 3 |
|---|---|---|---|
| Benzene | Cyclohexane | DMF | Acetic acid |
| Carbon tetrachloride | Toluene | Hexane | Acetone |
| 1,2-dichloroethane | Methanol | Pyridine | Ethanol |
| 1,1-dichloroethene | Acetonitrile | | Ethyl Acetate |
| 1,1,1-trichloroethane | Chloroform/DCM | | DMSO |

Recent studies have focused on solventless systems or non-toxic solvent utilization.[19] Among non-toxic solvents; especially supercritical solvents and water attract attention. Supercritical solvents, *e.g.* $CO_2$, are green, cheap and easily available. Yet, the special equipment requirements and employment at high temperature and pressure are some disadvantages of such solvents.[20] On the other hand, the most privileged solvent among all is water of course. Water is the only natural solvent that exists, so the widespread of its use is favored in green chemistry. Water provides several advantages as solvent due to its unique features. It is in liquid state for a long temperature range due to its heat capacity, has high hydrogen bonding abilities, *etc*. Thus, many organic reactions could be conducted in the presence of water with proper catalysts and conditions.[21] As the solvent choice of nature, water is the cheapest and most easily accessed solvent. However, the high boiling point of water, troublesome separation and solubility problems of organic species cause difficulty.

After all, safer solvents and auxillaries include all the solvents utilized during the process. However, it should be noticed that the solvent choice of a reaction is important but not the sole component of the environmental impact of a process. The energy requirements, atom economy, E-factor of the system that is the overall efficiency should always be taken into consideration.

#### 1.1.1.6. Design for Energy Efficiency

Designing synthetic methods in an energy efficient manner is the most underestimated principle of green chemistry. The reason for this is that only the energy required during the reaction is recognized, which is temperature and pressure control. For this reason, all reactions conducted at ambient temperature and pressure are accepted as "green". However, the largest amount of energy is consumed during the isolation of the desired product from the impurities, by-product. This isolation includes many cooling, heating and pumping steps each of which require energy.[22] As indicated before, consumed energy is also regarded as waste.[23] The energy here refers to fossil fuel based energy. The energy cycle of fossil fuel is pretty inefficient indeed. Only 1% of energy is applicable after the whole process.[24] Also it is in danger of depletion and alternative energy sources are being searched. Thus, these lead to both environmental and economical problems and many synthetic pathways offer a weak enegy efficiency from this perspective. All in all, design for energy efficiency should be as considered a critical design parameter as all others.

#### 1.1.1.7. Use of Renewable Feedstocks

The depletion of raw materials is a major problem in our earth. There is a demand for new methodologies that spark the utilization of renewable feedstocks.[24] In chemical processes it is essential for both raw materials and energy production. Considerable amount of energy and carbon based chemicals are produced from fossil fuels, petroleum sources which are finite source as a matter of fact. According to today's consumption rate, petroleum and natural gas sources will last 100 years.[3] Therefore, these sources should immediately be replaced with sustainable sources. Bio-mass which is available in living organisms *e.g.* agriculture residue, crops, can be regarded as a good alternative for these depleting feedstocks.[23] Again it is chemistry's responsibility to provide suitable chemical designs to obtain this energy selectively and efficiently. Also, in the production of raw materials alternative prospects are being introduced. For instance, lignin, waste of paper production, was used as starting material for the synthesis of DMSO and humic acid.[23] Thus, while waste of a process was decreased, depleting natural resources could be recovered.

#### 1.1.1.8. Reduce Derivatives

Derivatization in chemical synthesis includes additional reaction steps which are mostly encountered during multi-step chemical syntheses. Reducing derivatives refers simply to shorten the synthesis. Traditional synthesis is classified as covalent derivatization.[23] Covalent derviatization includes many reaction steps in which each step requires various solvents and reagents.[25] The compounds require purification after each step all of which generate waste and result in excessive cost. Protection and deprotection of sensitive functional groups are extra steps that consume energy and raw materials while produce waste. Also temporary physical transformations such as converting organic molecules to corrsesponding salts in order to assist their separation, are counted as derivatives.[22] For these reasons direct syntheses, syntheses without protection as well as executing tandem and flow reactions are recommended. Moreover, directing chemical transformations through weak-forces, reducing bond breaking and forming steps, is getting more attractive.[23]

#### 1.1.1.9. Catalysis

Catalysts are unalterable components of most chemical transformations. Their ability to decrease the energy requirement of the process, enhance the rate by decreasing the activation barrier, increase selectivity and the efficiency provoke their significance.[26] The amount of waste decreases extensively when shifted from stoichiometric amounts of reagents to suitable catalysts. As the extent of reagents lessen, the consumption of feedstocks is also cut down while the atom efficiency increases.[23]Additionally, the selectivity and reaction conditions of the methodology are particularly based on the catalysts used. As selectivity of the reaction increases the need for purification steps decrease accordingly which is directly related to less energy consumption.[27] Accordingly, they are fundamental in the construction of a green and sustainable design. However, their nature, synthesis, handling and disposal processes are also of environmental consideration.[26] For a catalyst to be green, other aspects should be taken into consideration as well. Besides the features mentioned above, green catalysts should be easily separated and recovered, maximize desired product while minizing waste, decrease energy requirements and more important it

should be non-toxic and have no dentrimental effects on human health. Consequently, it is possible to achieve an entirely green process by using the appropriate catalyst.[22] Environmentally benign catalysts for selective oxidation of alcohols will be further discussed, in the forthcoming parts of this chapter.

#### 1.1.1.10. Design for Degradation

The life cycle of chemicals incorporated in a chemical process is decisive on the sustainability of that process. To design an environmentally benign synthesis for a substance is important yet to recognize the impacts after decomposition is as important. In a perfect cycle the substance should degrade to another subtance that can easily accomodate in nature. Here the term biodegradation should be clarified. Biodegradation is defined as the decomposition of a substance by the assistance of microorganisms. The persistence of chemicals in the environment causes serious difficulties such as exposure and bioaccumulation. Especially halogenated species, quarternary carbons along with tertiary amines have a long persistence time. For this, studies are focused on alterations that enhance biodegradability, such as introducing ester and amide groups to long chain compounds.[23]

#### 1.1.1.11. Real Time Analysis for Pollution Prevention

The aim of green chemistry is to avoid the generation of waste rather than proposing techniques to clean them up. Moreover, use of excess reagents, unnecessarily long duration times lead to weak designs from a sustainable point of view. For this, being able to monitor the reactions instantenously, predict the outcomes and their effects with environmentally safe analytical tools is desired. Analytical tools should be utilized during the determination of the hazardness of the by-products and wastes that will be produced. Safe analytical tools are especially favored since analytical techniques generate large amount of waste and utilize toxic chemicals during analyses.[15] Green analytical chemistry intents to meet environmental demands while attaining accurate and reliable measurements. Thus, chemical transformations consider monitoring and with sustainable methods.

### 1.1.1.12. Inherently Safer Chemistry for Accident Prevention

Accidents are situations which in most cases are irresistable. Thus, chemical industry has witnessed countless amounts of accidents, some listed in Table 2, that took a toll on thousands of lives.

**Table 2.** Major accidents in the chemical industry[3]

| Chemical Substance Involved in Incident | Location | Year |
|---|---|---|
| Phosgene release | Hamburg, Germany | 1928 |
| Chlorine | Rauma, Finland | 1947 |
| Mercury/ dimethyl mercury chronic poisoning | Minamata Bay, Japan | 1965 |
| Ammonia | Potchefstroom, South Africa | 1973 |
| Explosion in caprolactam plant | Flixborough, UK | 1974 |
| Dioxin release and toxic poisoning | Seveso, Italy | 1976 |
| Chlorine | Pasadena, USA | 1976 |
| Propylene gas explosion | San Carlos, Spain | 1978 |
| Explosion in LPG storage tank | Mexico city, Mexico | 1984 |
| Methyl isocyanate | Bhopal, India | 1984 |
| Benzene, nitrobenzene | Jilin, China | 2005 |
| Bauxite, sodium hydroxide | Ajkai, Hungary | 2010 |
| Oil spillage | Gulf of Mexico, USA | 2010 |

On this account, since trying to prevent inevitable accidents is worthless, diminishing the hazards of their repercussions is prefered. Green and sustainable chemistry intents to reduce the toxicity of chemicals used, possible hazardous consequences of processes while being in harmony with nature. All the 12 principles of green chemistry, work collectively for this common goal. Not only for its own progress but

chemistry has the potential also to change the world. Creativity is the most ruling tool in inducing paradigm shifts. Along with, there is an urgent need for a change in chemical processes from ground up. Accordingly, there are promising studies of green organic processes. Hence, in the next chapter, studies towards green oxidation of alcohols will be discussed.

## 1.2. Oxidation

The biosphere contains mainly the elements; carbon, nitrogen, oxygen and hydrogen which endlessly encounter alterations, modifications and lead to adverse kinds of formations.[28] One of the most fundemental transformations that endures the existence of life on earth is oxidation. Oxidation was previously defined as the addition of oxygen to a specie. When involved in such a reaction; oxygen functions as the oxidizing agent leading the specie to be oxidized. As oxygen is quite reactive; combustion, food spoilage are observable examples of parallel processes. However, the oxidation definition could be widened to reactions that do not particularly involve oxygen. Thus, oxidation is the process in which a molecule, atom or ion loses electrons which leads to an increase in that species oxidation state. The complemetary of oxidation is reduction and together they constitute redox processes.

Respiration of both humans and plants which convert oxygen to yield energy are examples of naturally occuring oxidation reactions. Photosynthesis, the complementary process of plant respiration, provides oxygen and carbohydrates. In human metabolism, the energy production is illustrated by the tricarboxylic acid (TCA) cycle, also known as krebs or citric acid cycle. During each energy yielding step, oxidation of $CO_2$ takes place. The aging of human can be regarded as a redox reaction as well. Oxygen molecules entering the body lead to the weakening of immune system by electrons taken from cell membranes which results in the aging of those cells. As in naturally occuring processes, transformation by oxidation is crucial for synthetic processes. Hence, oxidation of alcohols to carbonyl derivatives are one of these processes.

### 1.2.1. Oxidation of Alcohols

Oxidation reactions of alcohols are elemental steps in organic reactions. The selectivity of these oxidations are crucial. In oxidation of primary alcohols, the aldehydes formed have the potential activity to be further oxidized to the carboxylic acid derivatives.[29,30]As in most of the organic reactions, specific reagents have an essential role in the prevention of the overoxidation product to be formed.[5] To attain such goals, many reagents were developed and discovered. These can be divided into two: metal containing reagents and organic reagents.

#### 1.2.1.1. Selective Oxidation of Primary Alcohols to Aldehydes

##### 1.2.1.1.1. Metal Containing Reagents

Studies on alcohol oxidations to carbonyl derivatives have been focused on reagents containing metals.[13] Due to the environmental concerns, studies leaned toward organic reagents.[26] This thesis also concerns non-metal reagents. Therefore, the metals will not be discussed further.

##### 1.2.1.1.2. Non Metal Reagents

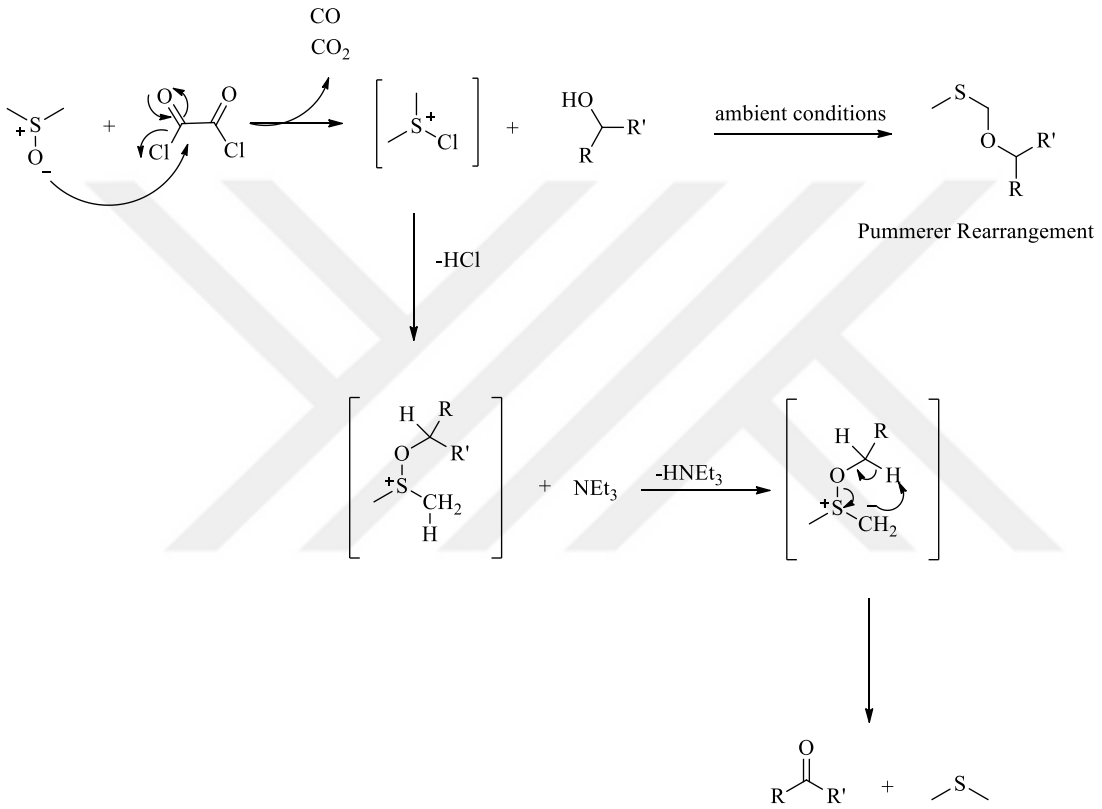
As the concept of sustainable and green design got more influencial, the importance of non-metal catalysts also grew. These catalysts are superior to metal containing catalysts also due to their oxidative resistance.[27] Hence, environmentally accepted catalysts are being synthesized and used for the oxidations of alcohols more frequently. Below, such reagents will be elaborated on.

###### 1.2.1.1.2.1. "Activated" Dimethyl Sulfoxide

The use of "activated" dimethyl sulfoxide (DMSO) for the selective oxidation of alcohols to carbonyl compounds has been widely studied. The reagent attracted extensive attention since the oxidation of primary alcohols terminated at aldehyde stage without the need for heavy metal catalysts, in fact relatively mild reagents were facilitated.

In 1965, Albright and Goldman reported that DMSO/acid anhydride mixture could be used in the oxidation of sterically hindered alcohols to carbonyl derivatives.[31] Not

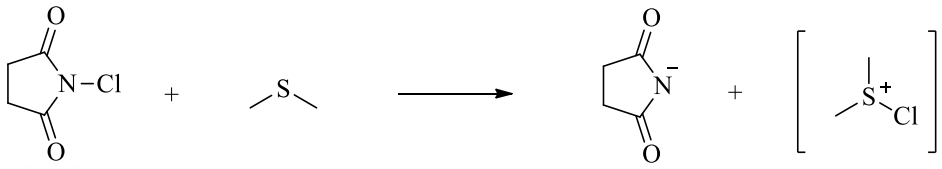
late from this, Doering reported DMSO and N,N'-dicyclohexylcarbodiimide (DCC) mixture as another mild reagent for the same purpose.[32] Swern and co-workers widened the field by oxidizing different kinds of alcohols, *i.e.* long chain alcohols, as well as examining new activation reagents, trifluoroacetic acid, $SOCl_2$, oxalyl chloride[33] *etc.*, for DMSO.[34] Thus, the DMSO/oxalyl chloride oxidation is also known as Swern oxidation.




**Scheme 5.** Mechanism of Swern oxidation

The mechanism has been proposed to be: First, DMSO reacts with oxalyl chloride to form dimethyl sulfonium chloride, which is called activation of DMSO. The sulfonium chloride has two pathways to follow in the presence of an alcohol. When temperature is raised to room temperature a Pummerer rearrangement takes place. The other one is the $S_N2$ reaction on sulfonium chloride that leads to oxidation at lower temperatures. This reaction needs a base such as triethyl amine for the completion of the oxidation process (Scheme 5).[35]

Moreover, the oxidation reaction accomplished by activated DMSO favors the oxidation of sterically hindered alcohols aside from the electrophilic activator that is used.[36] Besides, the formation of sulfonium chloride should be conducted at a temperature range of -60 $^{o}$C to -20 $^{o}$C. If it is below -60 $^{o}$C,[37] the conversion of DMSO to the intermediate may not take place whereas if it is above -20 $^{o}$C as mentioned before, Pummerer rearrangement might take place.



**Scheme 6.** Reaction between DMS and NCS to form dimethyl sulfonium chloride

Along with these Corey and Kim reported another sulphur based reagent, generated by dimethyl sulfide (DMS) and N-chlorosuccinimide (NCS). The reaction pathway was similar to that of "activated" DMSO, except the formation of dimethyl sulfonium chloride. As seen in Scheme 6, NCS and DMS were used to obtain dimethyl sulfonium chloride and relatively clean by-products were generated.[38]

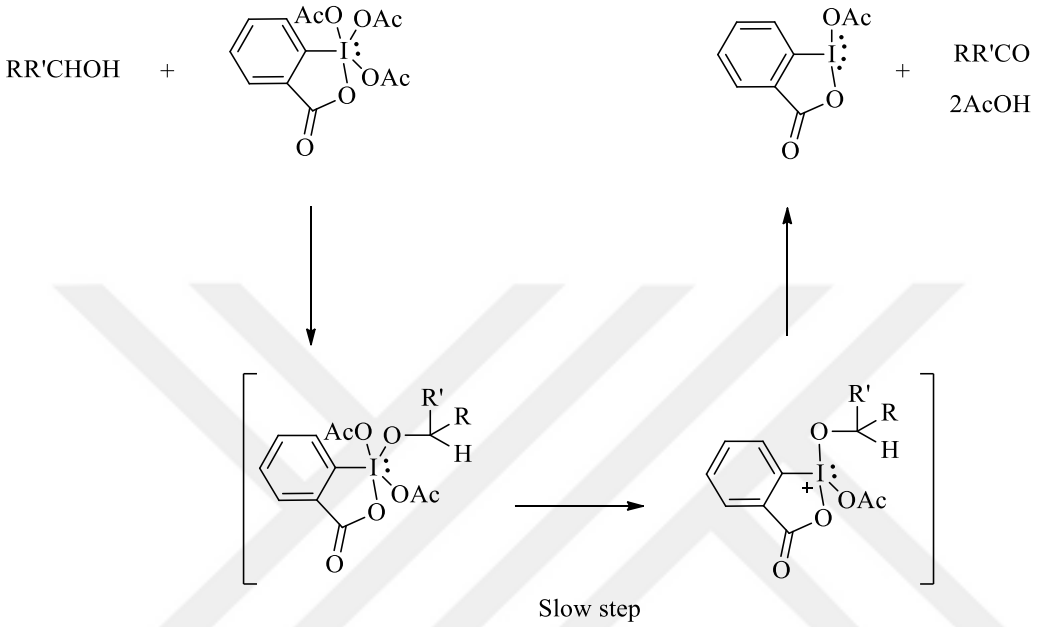
Although mild and selective, the volatility of dimethyl sulfide as well as the abnoxious smell, lessened the preferability of these reagents. To meet these concerns, studies concentrated on substitutes of these reagents that will generate nonvolatile and odorless by-products.[39,12] Also, polymer supported Swern oxidation reagents, that enabled recycling and easy separation, were synthesized.[40,41]

These revisions enhanced the sulphur based selective oxidation of alcohols. Yet, the preparation of the reagents immediate before their use and cautious handling at very low temperatures, caused difficulty. Thus, the studies tilted toward developing better reagents for the variations of Swern oxidation. Meanwhile, other reagents have been utilized in oxidation reactions.

#### 1.2.1.1.2.2. Hypervalent Iodine

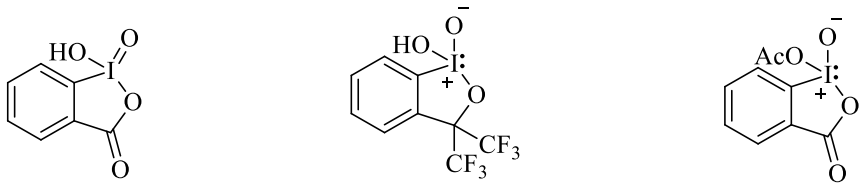
As the interest towards non-metal reagents for the selective oxidation of alcohols grew, similar methods were designed. In 1983, Dess and Martin introduced the

treatment of alcohols with 12-I-5 alkoxyperiodinane to afford aldehydes and ketones. The method provided mild oxidation of alcohols without the utilization of any toxic specie. Thus, primary and secondary alcohols were oxidized to aldehydes without the overoxidation to carboxylic acids and ketones.[42]




**Scheme 7.** Mechanism of oxidation with hypervalent iodine compounds

As shown in Scheme 7, the overall reaction commences with the fast reaction taking place between Dess-Martin periodinane and the alcohol, to form alkoxydiacetoxyperiodinane. Then, it proceeds by the formation of alkoxyperiodinane, which is the slow step (rate determining step) of the reaction. Finally, the carbonyl compound is synthesized with 10-I-3 acetoxyiodiane compound and acetic acid as by-products.[43]




IBX

**Figure 2.** Some hypervalent iodine compounds used in the oxidation of alcohols

For the selective oxidation of alcohols, other hypervalent iodinane compounds were also synthesized. It was observed that some 10-I-4 iodinane oxide reagents *vide supra* had compatible oxidizing properties with 12-I-5 alkoxyperiodinane.[44] Especially 2-iodobenzoic acid (IBX), standed out through the chemoselective oxidation of various compounds under mild conditions.[45,46] The tolerance towards moisture and water of IBX was also remarkable since in case of Dess-Martin periodinane long term exposure resulted in hydrolysis of the compound.[44] Thus, inactivation of the reagents.

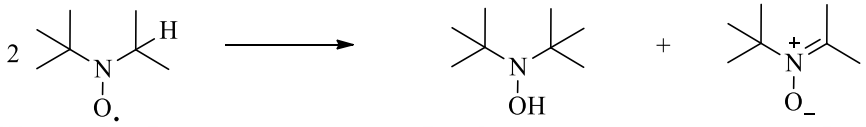
Both "activated DMSO" and hypervalent iodine are remarkable reagents in the mild and selective oxidation of primary alcohols to aldehydes, also in a manner of being regarded as sustainable designs. However, the weak atom efficiency, generation of by-products and large amounts of waste, decrease the environmental acceptance of them. Preferably, stable organic nitroxyl radicals are catalytic reagents, used extensively in green oxidations.[47]

#### 1.2.1.1.2.3. Green Oxidation with Organic Nitroxyl Radicals

Nitroxyl radicals, NO moiety with an unpaired electron on it, are compounds with trivalent nitrogen. These radicals possess relatively high stability, meaning the radicals can be handled at ambient conditions. Nitroxyl radicals can be bonded to bonds that can conjugate with, or simple bonds.[48] The radicals, which have the ability to conjugate, have lower oxidation strength, while others have higher oxidation strength. This observation was explained by stating that the unpaired electron is delocalized through the conjugated bonds. In the case of nonconjugated compounds, the electron is only localized on the NO-group which enables them to participate in oxidation rections.[49] The first examples of nonconjugated stable nitroxyl radicals; 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) radical (**a**) was synthesized by Lebedev and Kazarnovskii (Figure 3). To further increase the knowledge on NO radicals, Hoffmann and Henderson[50] synthesized di-tert-butyl-N-oxyl radical (**b**). These radicals are proved to be stable.

**a** **b**

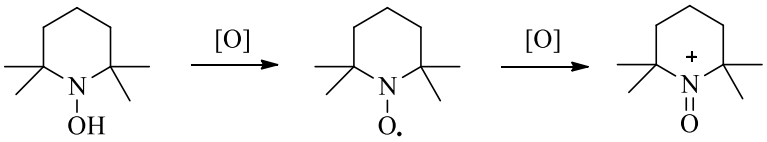
**Figure 3**. First examples of nonconjugated stable nitroxyl radicals



**c** **$c_1$** **$c_2$**

**Scheme 8.** Disproportionation of nitroxyl radicals containing α hydrogen

As can be seen in Figure 3, the stable radicals **a** and **b** do not contain hydrogens at the α position which actually inhibits a possible disproportionation reaction. Meanwhile when the radical contains a hydrogen as radical **c**, the disproportion products (Scheme 8), hydroxylamine $\mathbf{c_1}$ and nitrone $\mathbf{c_2}$, are capable of causing other reactions to take place.[51] Thus, a high majority of nonconjugated organic nitroxyl radicals are synthesized as di-tert-alkyl type.



**$a_2$** **a** **$a_1$**

**Scheme 9.** Oxidation and reduction products of organic nitroxyl radicals

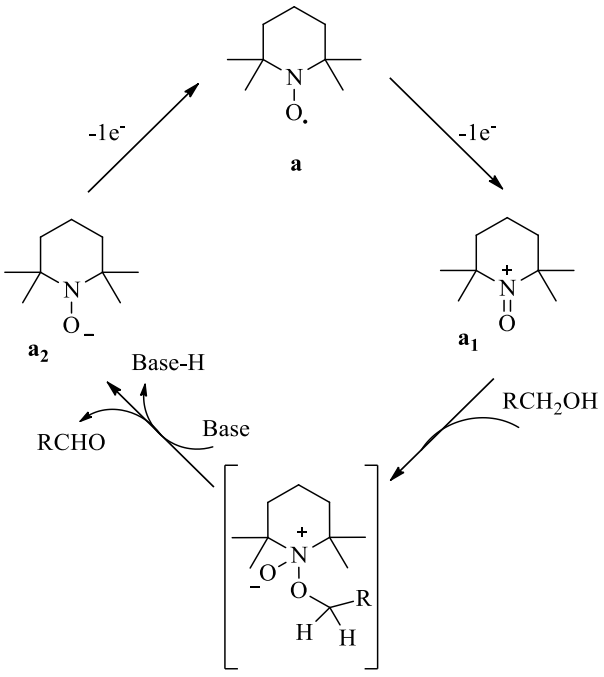
Nitroxyl radicals have reversible redox behaviors which depend on one electron transfers. In Scheme 9, the oxidation and reduction of TEMPO are shown. The oxidation product of the nitroxyl radical is oxoammonium cation $\mathbf{a_1}$ and N-hydroxylamine $\mathbf{a_2}$ is the reduced form of TEMPO, these molecules are also named as oxopiperidinium and 1-hydroxypiperidine respectively.[52]

Due to the reversible redox ability and long life time as the radical, these nonconjugated radicals have a wide application area both in chemistry and biology. Yet, among these they are well-known for their participation in oxidation reactions, especially the first synthesized nitroxyl radical TEMPO **(a)** and its analogues.

### 1.2.1.1.2.3.1. TEMPO (2,2,6,6-Tetramethyl-piperidine 1-oxyl) Radical

TEMPO radical has been extensively used in green oxidation reactions of alcohols. The metal free nature, accordance with ambient conditions and simple synthesis induced a great interest on TEMPO, as a green catalyst. Thus, the regioselectivity towards primary alcohols and selective synthesis of aldehydes established further superiority among other reagents that are used in alcohol oxidations.[53]

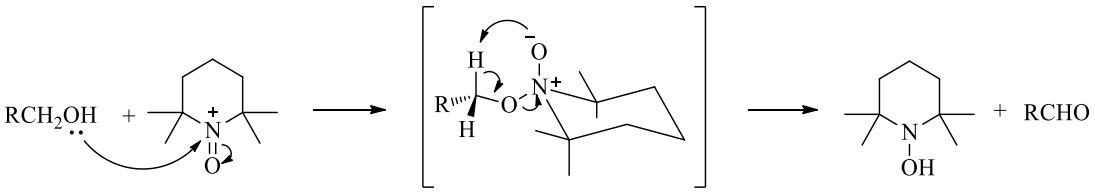
In TEMPO catalyzed oxidation reactions, TEMPO can both be used in stoichiometric and catalytic amounts. In case it is used in stoichiometric amount with respect to the alcohol, the oxoammonium cation is synthesized and than it is isolated in order to participate the oxidation reaction as a reactant. However, the isolation of the highly reactive specie is problematic. After all if TEMPO is used in catalytic amount, the oxoammionium cation is formed *in situ* without the requirement of isolation.[54]




**Scheme 10.** General representation of TEMPO catalyzed alcohol oxidations

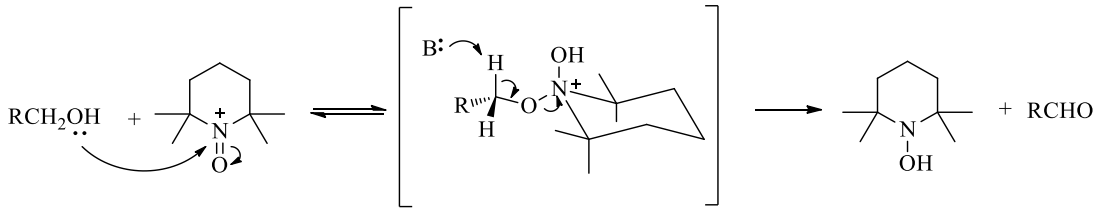
When used in catalytic amounts, TEMPO engages in the oxidation by the catalytic cycle *vide supra* in Scheme 10. Although TEMPO radical can serve as an oxidant by itself, the corresponding oxoammonium cation form of TEMPO is a stronger oxidant.[54] Hence it participates the oxidation reactions as a reactant. In an ordinary oxidation reaction of a primary or secondary alcohol, first the oxoammonium cation **$a_1$** is formed *in situ*. For the conversion of TEMPO to the oxoammonium cation a reagent which serves as an electron acceptor is demanded. This reagent is either referred as co-oxidant or primary oxidant, thus it will be referred as co-oxidant in this study. mCPBA[55], NaOCl[56], $PhI(OAc)_2$[57], NCS[58], N-Cl containing polymers[59] are examples of co-oxidants used for this purpose. During the reaction, the alcohol acts as a nucleophile and attaches to the oxoammonium cation leading to the intermediate structure. Finally, this intermediate fragments to the corresponding carbonyl compound and N-hydroxylamine derivative of TEMPO **$a_2$**.[60]

Besides their nature, the mechanism of TEMPO catalyzed oxidation reactions have been widely studied. Consequently, different mechanisms for reactions under acidic and alkaline conditions have been proposed.




**Scheme 11**. Mechanism of TEMPO catalyzed alcohol oxidation in basic medium

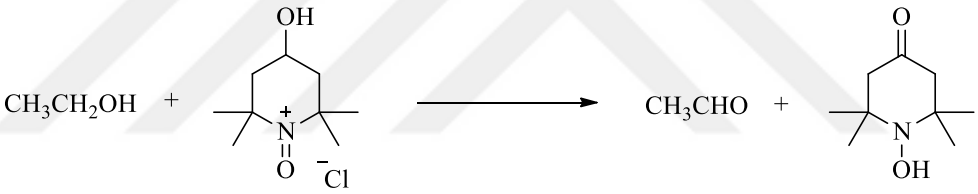
Scheme 11 shows the 5-membered transition state proposed for the oxidation reaction conducted under alkaline conditions. The sterically demanding transition state causes a high selectivity towards primary alcohols.[61]



**Scheme 12.** Mechanism of TEMPO catalyzed alcohol oxidation in acidic medium

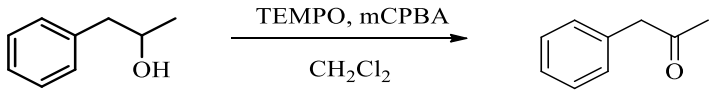
In acidic medium, the plausible mechanism is quite different than that of alkaline conditions. A linear transition state which can be seen in Scheme 12 is proposed. This transition state provides no selectivity as it is sterically less hindered.[61]

The leading study on the use of oxoammonium salts in oxidation reactions of alcohols was done by Golubev et al. in 1965. In the study, the oxoammonium salt of 4-hydroxy-TEMPO was used to catalyze the oxidation of ethanol to acetaldehyde (Scheme 13).



**Scheme 13.** First study of oxoammonium salts used in oxidation of alcohols

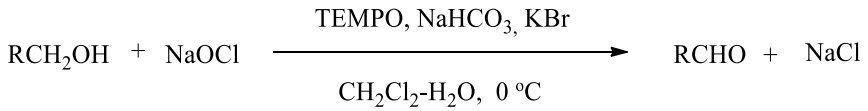
With these observations, Cella and co-workers concentrated on the mild oxidation of alcohols by peracids in the presence of TEMPO. By that time, peracids have been known as convenient reagents for mild oxidation of many functional groups yet were inactive towards alcohols. During their studies, the peracid oxidation of amino alcohol resulted in the formation of keto nitroxide. This observation was a clue that the peracid oxidation of alcohols could be achieved through the presence of a nitroxyl radical.[55]



**Scheme 14.** Mild oxidation of alcohols by TEMPO and mCPBA

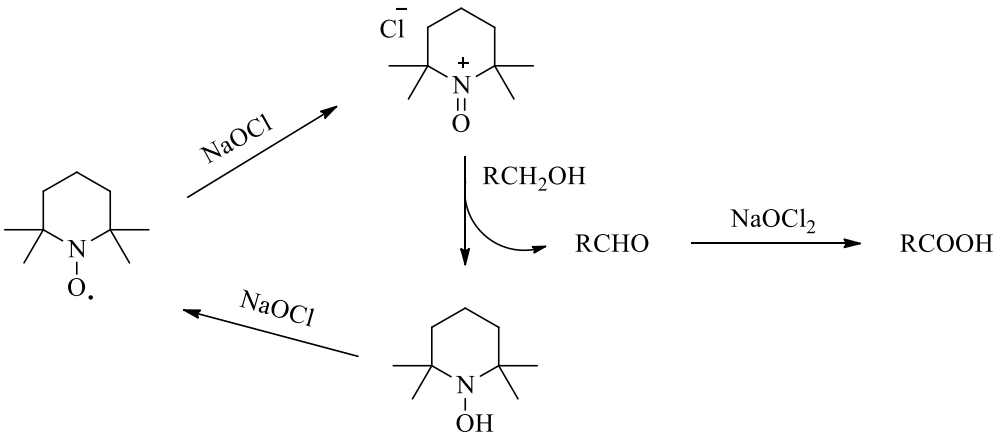
Thus, the acid catalyzed oxidation of alcohols in the presence of mCPBA and TEMPO afforded their carbonyl derivatives (Scheme 14). Yet, this method could not be applied to alcohols containing peracid sensitive functional groups.[55]

Afterwards many reagents were used as co-oxidants for TEMPO in oxidation reactions.



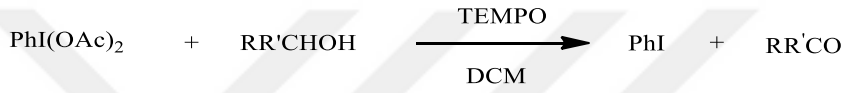

**Scheme 15.** Oxidation of alcohols to aldehydes by TEMPO/NaOCl system

TEMPO/bleach system, *vide supra,* is a very commonly used method in oxidation reactions of alcohols. It was Montarani's group to report this method, known as both Montarani protocol and Anelli's oxidation, in 1987[62]. According to the protocol, the electron transfer is enabled by NaOCl and the oxoammonium cation is continuosly regenarated. Hence alcohols can be oxidized in a short time to carbonyl derivatives with high yields and selectivity. Montarani protocol is still an attractive method in organic chemistry since it is cheap, selective and provides high yields.[63] The drawback of this method is that NaOCl forms HOCl, which is able to chlorinate sensitive reagents.[56] Moreover, such co-oxidants further oxidize aldehydes to carboxylic acid depending on the reaction time.



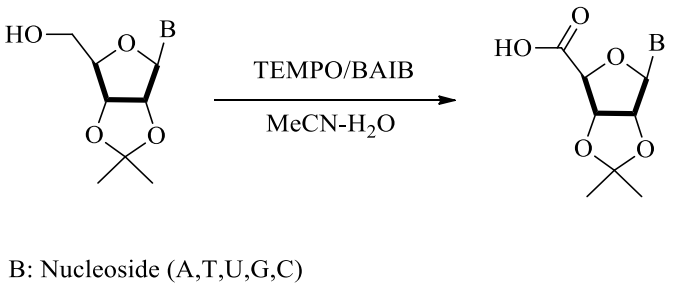

**Scheme 16.** Oxidation of alcohols to carboxylic acids by TEMPO/NaOCl system

Although TEMPO/bleach system can be used in the synthesis of carboxylic acids, further modifications to attain the acids have been applied. Zhao and coworkers revised Anelli's method for the oxidation of primary alcohols to carboxylic acid derivatives. In this method, NaOCl oxidizes TEMPO to the oxoammonium salt. Thus, the primary alcohol is converted to the aldehyde derivative, (Scheme 16). Afterwards, the aldehyde is oxidized to the carboxylic acid by $NaOCl_2$. As NaOCl is used in catalytic amount rather than stoichiometric, the posibility of chlorination is reduced.[64] It should be noted that, TEMPO is used for the conversion of the alcohol to aldehyde derivative. For the carboxylic acid to be formed, $NaOCl_2$ is needed.[64]




**Scheme 17.** Oxidation with TEMPO and hypervalent iodine compounds

In another early example of TEMPO catalyzed oxidations, $PhI(OAc)_2$, a hypervalent iodine compound, was utilized as the electron acceptor for the oxoammonium salt formation (Scheme 17). In their work, Piancatelli et al. reported high conversion yields of alcohols to carbonyl compounds. This method was more environmentally benign when compared to the previous works since there was no demand for inorganic salts. Hence, relatively less by-products are formed.[57]



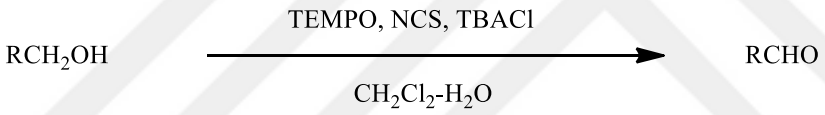

B: Nucleoside (A,T,U,G,C)

**Scheme 18.** Modifications on TEMPO/hypervalent iodine catalyst ixture

Again for the the further oxidation to the carboxylic acid, Epp and Widlanski used a modified procedure of Piancatelli, by using iodobenzene diacetate (BAIB). As shown in Scheme 18, the experiments were conducted in MeCN/water mixture rather than halogenated solvents. As a result, carboxylic acids from primary alcohols could be

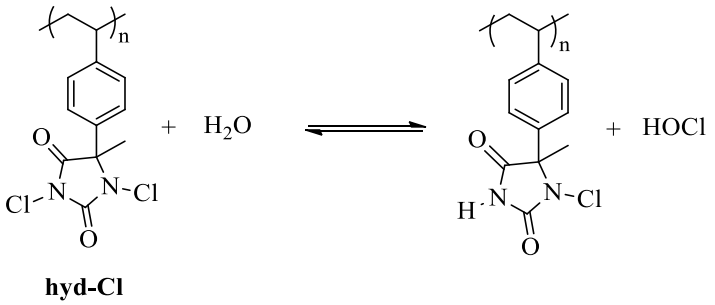
synthesized untroublesome, in high yields.[65] Use of acetonitrile under alkaline conditions could complicate the reaction. (See Results and Discussions part of this thesis.)

The use of molecular oxygen as co-oxidant in TEMPO oxidations has also attracted attention. Molecular oxygen is being highligted as a green oxidant due to its clean, non-toxic and environmentally accepted character.[66,67] Aerobic TEMPO oxidations have been employed by the participation of several metal catalysts, mostly, palladium, ruthenium, copper containing reagents.[5] Although the results are promising, ensuring catalyst activity for alcohols with different reactivities is still point at issue. Moreover, the organic solvent requiring designs are likely to be inflammable, so reactions conducted in the presence of water or solventless systems provide safer synthesis.[27] Hence, attempts to obtain safe and efficient oxidation of alcohols with molecular oxygen are in progress.




**Scheme 19.** Oxidation of alcohols to aldehydes catalyzed with TEMPO and NCS

Einhorn and co-workers employed NCS and tetrabutylammonium chloride (TBACl) with TEMPO for the formation of oxoammonium salt in situ. By this method (Scheme 19), they achieved high chemoselectivity in the oxidation of primary alcohols to aldehydes without any overoxidation.[58] Following this procedure, we accomplished oxidation of primary alcohols to corresponding aldehydes with N-Cl containing polymer as co-oxidant (Scheme 20). This method has the advantage of recovering and regenerating the co-oxidant. Moreover, no further oxidation of the aldehyde to the carboxylic acid is observed.[59]



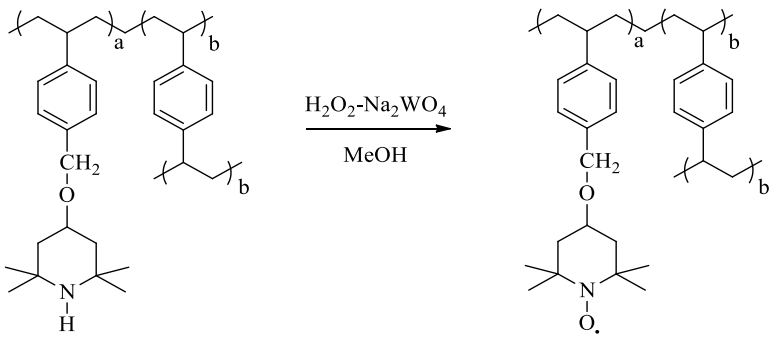

**hyd-Cl**

**Scheme 20.** TEMPO catalyzed oxidation of alcohols to aldehydes with recoverable polymer

Although TEMPO was used in minute amounts during most of the reactions, products needed purification. Therefore, studies concentrated on solid supported TEMPO reagents.

### 1.2.1.1.2.3.2. Solid Supported TEMPO Radicals

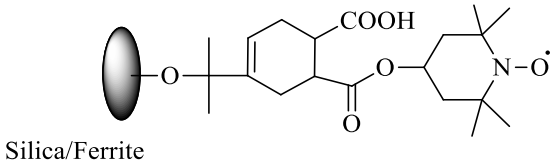
The development of solid supported organic catalysts are accepted as prominent in distinctive areas of chemistry.[68] TEMPO incorporated polymers, a member of this class, have been synthesized for various purposes; oxidation, spin labelled compounds, polymer stabilizers, organic radical batteries.[69] Thus, oxidation of alcohols to corresponding carbonyl compounds have been accomplished by these polymers.[70] The preference of these polymers can be explained by their facile separation and reusability[71]. Consequently, sustainable methods could be designed with TEMPO attached polymers for such oxidations.




**Scheme 21.** TEMPO containing polymers used in alcohol oxidations

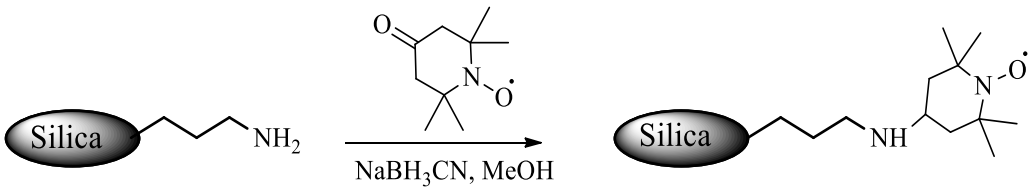
In 1985, Endo and co-workers synthesized hydrophilic and hydrophobic polymers containing TEMPO moieties (Scheme 21). They employed these polymers in the

oxidation of benzyl alcohol in the presence of Fe(III) as oxidant.[72] In 1988, the same group utilized these polymers for the same purpose only with Cu(II) as oxidant. They also reported the effectiveness of monomeric and polymeric nitroxyl radicals compared for catalytic activity in oxidation reactions. According to the study, the results for low loaded polymeric nitroxyl radicals were remarkably better.[73]




**Scheme 22.** TEMPO moities restrained on ferrrite and silica surfaces

Non-toxicity and recyclability could also be attained with TEMPO containing oxidation catalysts. TEMPO moieties were restrained on ferrite and silica surfaces (Scheme 22) leading to non-volatile and insoluble powders. These reagent-supported powders were employed with Cu(II) in oxidations of alcohols. They could be reused after each oxidation with promoted separation. Thus, a sustainable method for the oxidation of alcohols with TEMPO as the catalytic reagent, was introduced.[74]




Scheme 23. TEMPO supported on silica surface

As well as the activity change of the catalysts, attaining chemoselectivity after being attached on a surface or polymer is a crucial issue. In such manner, TEMPO supported on silica surface (Scheme 23) was employed with bleach to yield carbonyl derivatives of primary and secondary alcohols. Anelli's protocol was selected for the oxidation reactions since it was mild and highly selective for primary alcohols.[56] Subsequently, a mixture of 1-phenylethanol and benzylalcohol was conducted in Anelli's reaction conditions with TEMPO attached on silica surface. Thus, even after

10 recycles, the catalyst showed high selectivity towards benzylalcohol[75], which also provides further evidence for a 5-membered transition state for the TEMPO moiety.[61]

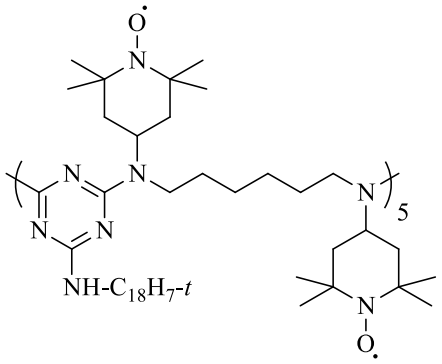
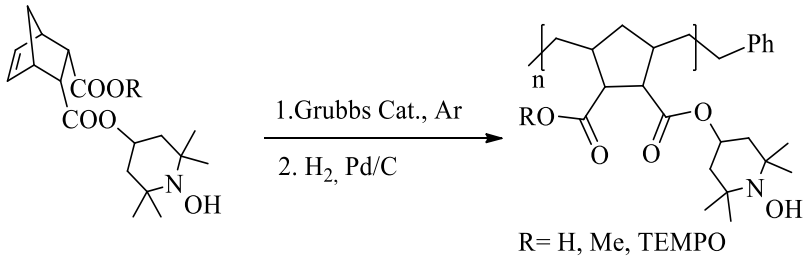



**Figure 4.** Structure of polyamine immobilized piperidinyl oxyl (PIPO)

Greener methods for selective oxidation of alcohols could be achieved by conducting TEMPO immobilized polymers. Sheldon and coworkers handled a readily available polymer containing a hindered amine to obtain polyamine immobilized piperidinyl oxyl also known as PIPO (Figure 4). Resultantly, the oxidation reactions were catalyzed by PIPO and bleach, in the abscence of any chlorinated solvent as well as the co-oxidant bromide, again with high selectivity.[76] Soon after, another environmentally benign process for PIPO catalyzed oxidation reactions was reported. In the aerobic oxidation with CuCl, benzyl alcohol could be converted to benzaldehyde with good yields yet the method was limited to activated benzylic and allylic alcohols.[77]

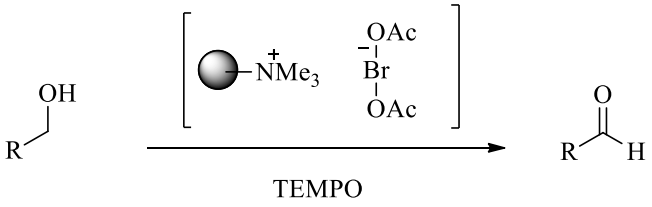



**Scheme 24.** Norbornene anchored TEMPO attached polymers

For the same purpose, Tanyeli and co-workers synthesized norbornene anchored polymers shown in Scheme 24. After the synthesis they conducted Anelli's oxidation

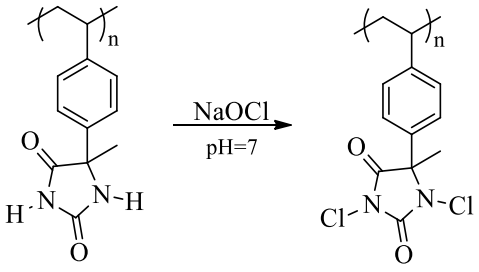
by the presence of these polymers as catalyst. Thus, primary alcohols were converted to aldehyde derivatives by this method.[78]

With various methods for immobilized TEMPO in hand, the search for immobilized (solid supported) co-oxidants started, which indeed is a relatively new search.




**Scheme 25.** Polymer supported non metal reagent used as co-oxidant

Kirschning reported the use of polymer supported non metal reagent as co-oxidant in TEMPO oxidation, *vide supra*. The polymer provided easy separation of the carbonyl compounds.[79] In like manner, in our study we used N-Cl containing polymers as co-oxidant for TEMPO mediated selective alcohol oxidations as mentioned before. These polymers are commercially available polystyrene based hydantoin containing polymers, which were synthesized for sanitization purposes.[80] The acidic protons on the hydantoin moiety can easily be exchanged with chlorine atoms at neutral pH (Scheme 26). The chlorinated hydantoin containing polymer provides mild release of oxidative chlorine generated *in situ*. By this, mild and selective oxidation of alcohols without chlorination possibility on sensitive functional groups was be accomplished. The solid supported oxidant could each time be regenerated by household bleach, and reused with enduring activity.




**hyd-Cl**

**Scheme 26.** Chlorination of hydantoin containing polymer at neutral pH

# CHAPTER 2

## AIM OF THE STUDY

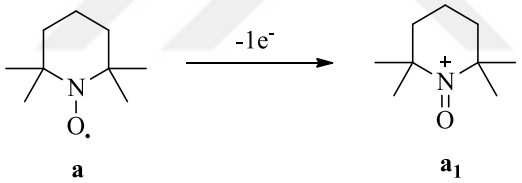
Mild oxidation of primary alcohols to aldehyde derivatives has been extensively studied. Recent studies that are also summarized in the introduction part have focused on the adaption of the methods to green chemistry. Simplicity, sustainability and environmental acceptance are important criteria of this concept. In this study, our intent is to design a simple and reusable all polymeric system that will have reduced environmental hazard. The system will be used for the oxidation of primary alcohols to aldehyde derivatives. The polymers will easily be separated from the reaction medium by simple filtration and will be used in further reactions. 2,2,6,6-tetramethylpiperidine (TEMPO) radical, a relatively green and selective catalyst, will be used as the secondary oxidant for the oxidation reaction. TEMPO incorporated polymers will be synthesized starting from 4-amino-2,2,6,6-tetramethylpiperidine. Together with, commercially available chlorinated hydantoin containing polymers will be used as the co-oxidant. With the experience from our previous studies, we await the hydantoin polymers to be a good alternative for this purpose. These two polymers will be used collectively in a biphasic solvent system to obtain aldehyde derivatives of primary alcohols. Unlike in Anelli's method further oxidation to carboxylic acid is not expected due to the mild "$Cl^{+}$" release of chlorinated hydantoin containing polymer regardless of the amount. The all polymeric system will be applied to primary alcohols with different functional groups.

# CHAPTER 3

# RESULTS AND DISCUSSIONS

## 3.1. Polymeric Co-Oxidant for Selective TEMPO Oxidation

Our study towards the green oxidation of alcohols began with slight modifications on Anelli's method. In their method, NaOCl was used as co-oxidant in TEMPO catalyzed oxidation. NaOCl (household bleach) generates oxidative chlorine "$Cl^+$" *in situ* which acts as an electron acceptor for the conversion of TEMPO radical to oxoammonium cation (Scheme 27). After this conversion, the oxoammonium cation catalyzes the oxidation reaction to form the desired oxidation product.



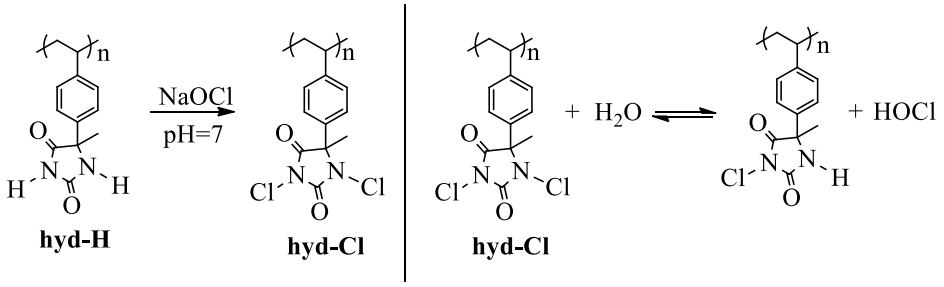

**a** **$a_1$**

**Scheme 27.** Conversion of TEMPO radical to oxoammonium cation

Anelli's method could be used in the oxidation of primary alcohols to aldehyde derivatives in alkaline conditions. However, the shortcoming of this method is that NaOCl, the co-oxidant, has the ability to further oxidize aldehydes to carboxylic acids. For this reason, a milder co-oxidant should be used.

**Figure 5.** poly(5-methyl-5-(4'-vinylphenyl)hydantoin polymer

At the beginning of this study, a polymer that could provide mild release of oxidative chlorine was sought. With this, the problem of further oxidation to carboxylic acid would be solved. Moreover, since the reagent is a polymer it would easily be separated from the reaction medium and the purification steps would be reduced. Thus, poly(5-methyl-5-(4'-vinylphenyl)hydantoin **hyd-H**, an antimicrobial polymer[81], was selected for this purpose (Figure 5). The prevention of further oxidation is due to the equilibrium between chlorinated hydantoin containing polymer and hypochlorous acid. That is, there is a minute amount of hypochlorous acid in the medium. This equilibrium is depicted in Scheme 28.




**Scheme 28.**Chlorination of hydantoin polymer at neutral pH and equilibrium in water

Poly(5-methyl-5-(4'-vinylphenyl)hydantoin) **hyd-H**, could each time be chlorinated with stoichiometric amount of NaOCl to form the desired **hyd-Cl** polymer (Scheme 28). The chlorination of hyd-H polymer was completed in a buffer solution at *ca.* pH=7 attained by NaOCl and $CH_3COOH$. The level of chlorination was determined with iodometric titration.

### 3.1.1. Iodometric Redox Titration of Chlorinated Hydantoin Polymer

The stability of the polymer to hold oxidative chlorine was also examined. This was tested by iodometric redox titration as well as the level chlorination. The polymers were titrated with standardized $Na_2S_2O_3$ at slightly acidic conditions.

$$Cl^+ (aq) + 3I^- (aq) + H^+ (aq) \longrightarrow HCl (aq) + I_3^- (aq)$$

$$I_3^- (aq) + 2S_2O_3^{2-} (aq) \longrightarrow 3I^- (aq) + S_4O_6^{2-} (aq)$$

**Scheme 29**. Redox reactions in iodometric titration of **hyd-Cl**

In the test, first of all the analyte **hyd-Cl**, is treated with excess iodide ion. Thus by the redox reaction, the analyte is reduced and iodide ion is oxidized to elemental iodine. Then, elemental iodine reacts with iodide ion to form triiodide ion. This cycle continues until all elemental iodine is consumed. Meanwhile, the triiodide that is formed is titrated with sodium thiosulfate. The end-point of the reaction is detected by the color dissappearence of starch indicator which forms a blue complex with triiodide.

$$\text{Weight \% } Cl^+ = \left(\frac{35.45 \times N \times V}{2 \times W}\right) \times 100$$

N: normality of $Na_2S_2O_3$ V:volume of $Na_2S_2O_3$ W: weight of analyte

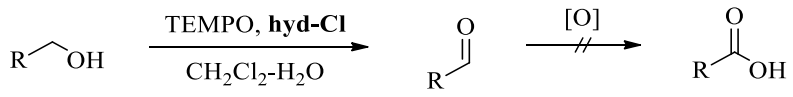
**Equation 3.** Calculation of $Cl^+$ content

The $Cl^+$ content of the polymer was calculated by Equation 3 shown above. The theoretical $Cl^+$ content was again determined by this equation to be 25 w%. The experimental Cl content was calculated as 19.17 w%. The $Cl^+$ release was observed to be continuing a day long. Significant changes were not observed within 2 weeks in dark and no moist conditions.

### 3.1.2. Oxidation of Primary Alcohols with Hydantoin Polymer and TEMPO

In the oxidation of primary alcohols to aldehydes, we followed the same procedure set by Anelli[56] with only one modification: instead of hypochlorous acid, we used

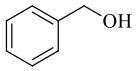
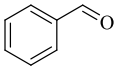
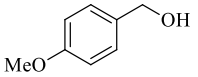
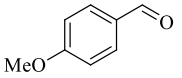
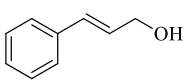
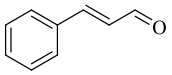
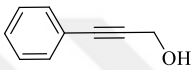
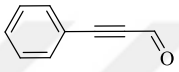
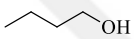
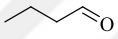
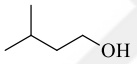
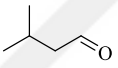
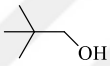
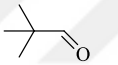
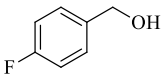
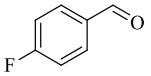
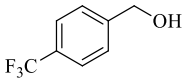
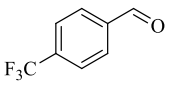
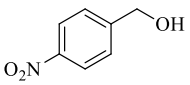
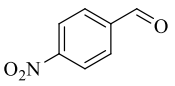
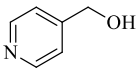
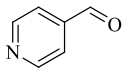
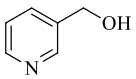
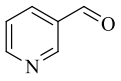
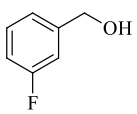
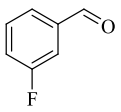
chlorinated hydantion containing polymer **hyd-Cl**. TEMPO, **hyd-Cl**, $NaHCO_3$ and the primary alcohol was mixed in water:dichloromethane (Scheme 30). The reactions were completed as judged by TLC in the given time intervals (Table 3).




**Scheme 30.** Oxidation of primary alcohols with hydantoin polymer and TEMPO[59]

The **hyd-Cl** polymer released only catalytic amount of $Cl^+$ to the reaction medium and no further oxidation to carboxylic acid was observed even at long durations (Table 4). $Cl^+$ release is governed by Le Chatellier Principle (Scheme 28).

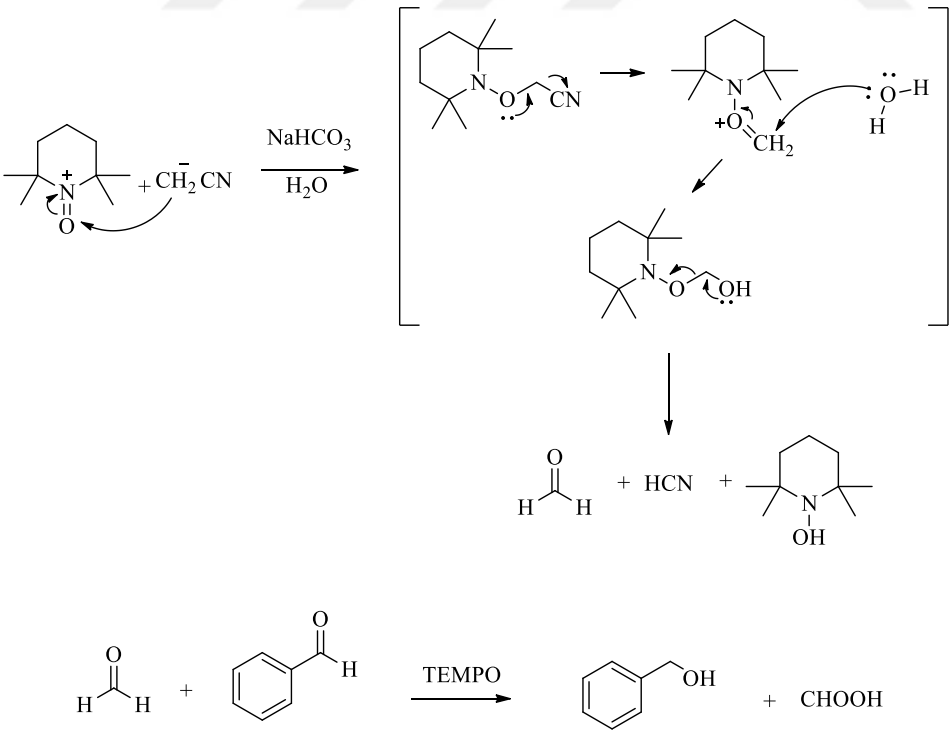
**Table 3.** Primary alcohols oxidized to aldehyde derivatives

| Alcohol | Aldehyde | Isolated Yield (reaction time) |
|---|---|---|
|  |  | 96% (3h) |
|  |  | 90% (3h) |
|  |  | 90% (3h) |
|  |  | 85% (3h) |
|  |  | 75% (3h) |
|  |  | 70% (3h) |
|  |  | 75% (3h) |
|  |  | 85% (6h) |
|  |  | 90% (8h) |
|  |  | 90% (8h) |
|  |  | 85% (6h) |
|  |  | 85% (6h) |
|  |  | 85% (3h) |

The reactions were conducted in a biphasic solvent system, water/dichloromethane at alkaline conditions. Biphasic solvent system was preferred due to enhanced contact of oxoammonium salt and the alcohol.[59] Since the scope of this study is to develop a relatively green method, environmentally less hazardous solvent systems were also sought

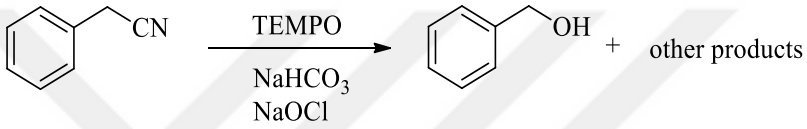
### 3.1.3. Alternative Solvent System for the Oxidation

The ultimate goal of this study is to achieve green oxidation of alcohols relatively green organic solvents were sought rather than using halogenated solvents. For this reason, the reaction was tested in acetonitrile/water system. However we observed that the conversion yield of the primary alcohols was very low. Benzoic acid formation was also detected. This observation needed an explanation: Based on literature[82], we proposed the following mechanism shown in Scheme 31. Thus, decrease in yields occurs since there is another reaction running simultaneously.




**Scheme 31.** Reaction of oxoammonium salt and acetonitrile

Based on our proposal, acetonitrile loses a proton at alkaline conditions. Then, it attaches the oxygen of the oxoammonium salt, to generate a protected cyanohydrin structure. The reason for this attachment to happen from the oxygen can be explained by the hard sof acid base theory (HSAB). Accordingly, the acetonitrile acts as a soft base preferring to attach the oxygen rather than the nitrogen which is harder. Afterwards, by the elimination of hydrogen cyanide and the attachment of a water molecule, formaldehyde and hydroxyl amine derivative of TEMPO are formed. Afterwards a cross cannizaro reaction[83] occurs between the benzaldehyde and formaldehyde, leading the formation of formic acid and benzyl alcohol (Scheme 31).




**Scheme 32.** Anelli Oxidation of benzyl cyanide

To affirm our assumption, we conducted Anelli's method with equivalent amounts of TEMPO and benzyl cyanide (Scheme 32). We expected to observe the existence of benzaldehyde due to the explanation mentioned above. Thus, the crude NMR signal at *ca.*10 ppm indicated that benzaldehyde was formed after the reaction. Therefore, the reactions were decided to be conducted in dichloromethane/water mixture.

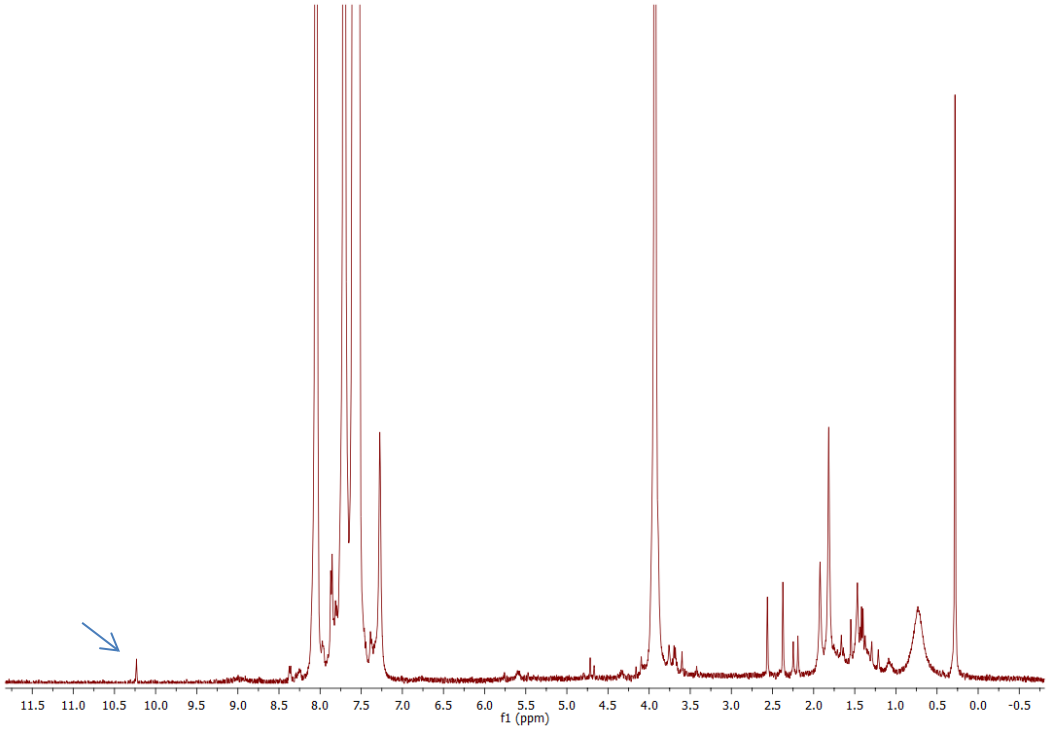



**Figure 6.** Crude NMR data of Anelli Oxidation of benzyl cyanide

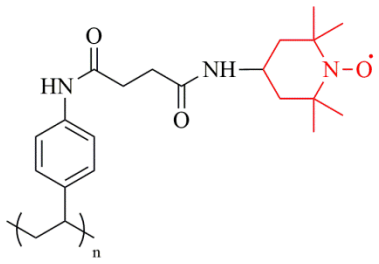
Hence, primary alcohols with different functional groups could be succesfully oxidized to their aldehyde derivatives (Table 3). Even though the reactions could be accomplished with high yields, the system failed for the difficult separation of TEMPO, which required column chromatography *etc*.[59] To address this question certain polymers were designed in which TEMPO was attached to the backbone.

### 3.2. Design and Synthesis of TEMPO Attached Polymers

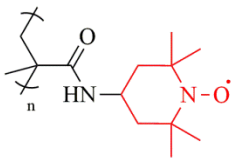
Even though TEMPO attached polymers exist in the literature, we decided to synthesize such polymers to gain insight about them. Therefore, three different polymers were targeted (Figure 7). The synthesis of polymers were intuitively thought to be simple, synthesized from readily available chemicals, and resistant to oxidative conditions. These polymers were expected to function like TEMPO radical in alcohol oxidation reactions.

The first polymer synthesized was **TEMPOL-PS**, because the abundance of polystyrene. The second one was **TEMPOL-MET** due to the synthesis being

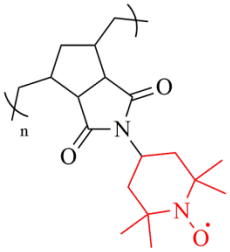
described in the literature. The third polymer **TEMPOL-NORB** was chosen because of the synthetic simplicity.



**TEMPOL-PS**



**TEMPOL-MET**



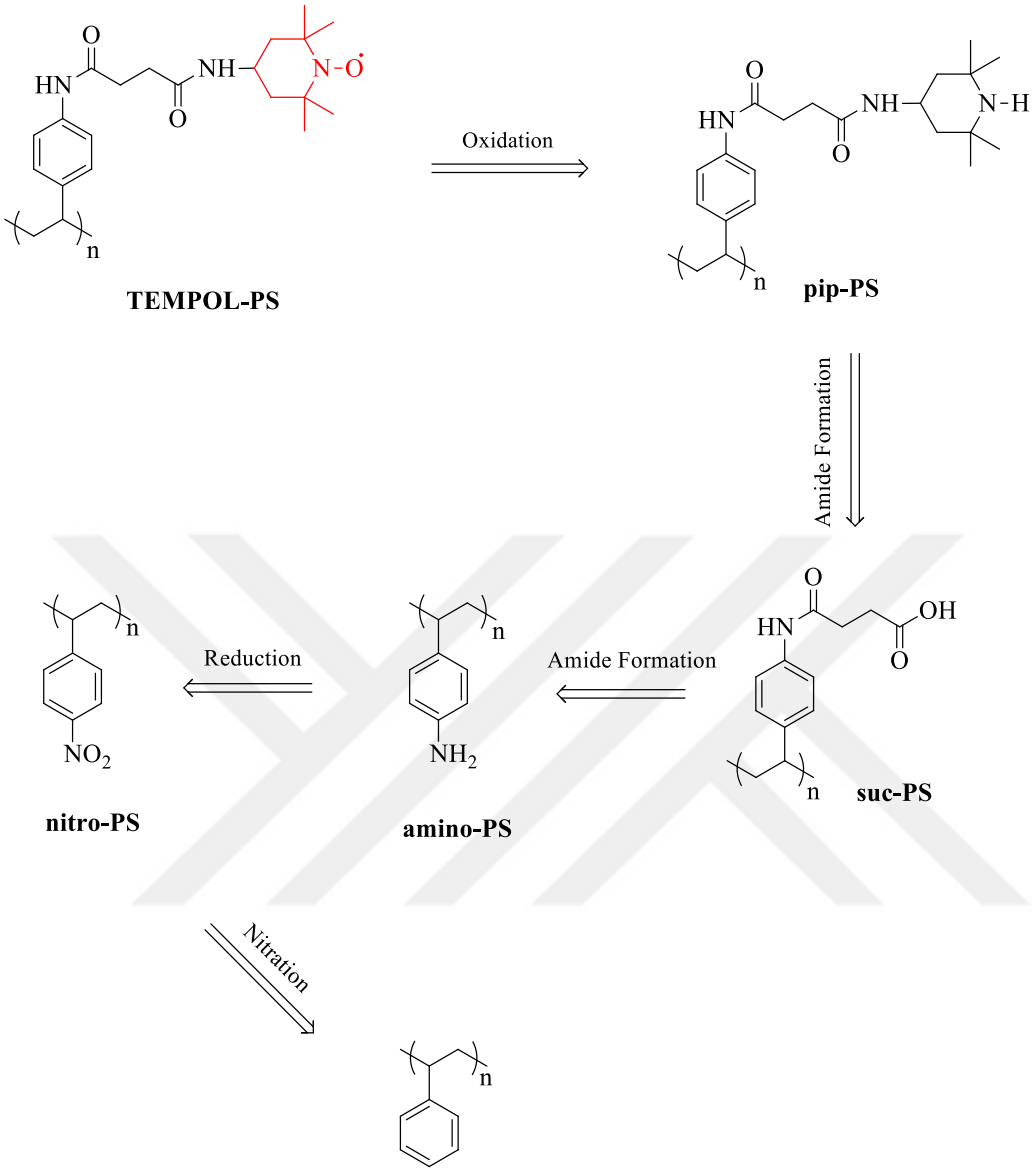
**TEMPOL-NORB**

**Figure 7.** Designed TEMPO attached polymers

In general, the existence of nitroxyl radical in the structure of the polymers was primarily tested with Anelli's method and the results were supported with IR analysis. Six membered nitroxyl radicals are observed to show IR vibrations between 1400 $cm^{-1}$ and 1340 $cm^{-1}$.[84] Also, ESR (Electron Spin Resonance) results confirmed the existance of nitroxyl radicals on these polymers.

### 3.2.1. Synthesis of TEMPOL-PS

The 5 step synthesis of **TEMPOL-PS** started with readily available polystyrene beads. In order to modify the polymer, nitro groups were introduced to the structure. Then, the nitro groups were reduced to obtain **amino-PS**. The synthesis continued with the reaction of **amino-PS** with succinic anhydride and the attachement of 4-amino-2,2,6,6-tetramethylpiperidine. Finally the piperidine was oxidized to a nitroxyl radical (Scheme 33). Each step will be discussed below.

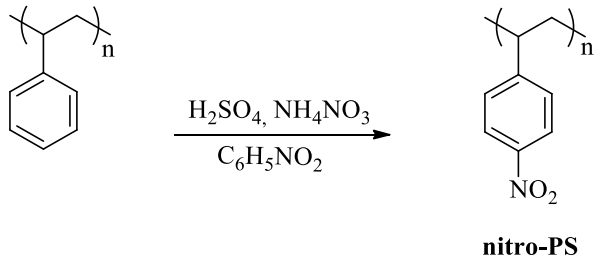



**Scheme 33.** Retrosynthetic pathway of **TEMPOL-PS**

### 3.2.1.1. Nitration of Polystyrene

Nitration of polystyrene was first completed with direct nitration method. The nitration was carried out in nitric acid/sulfuric acid solution. However, the yield of nitration was low since the concentration of nitric acid was low. That is why, a more effective method for nitration was applied. Poly(4-nitrostyrene) **(nitro-PS)** was obtained by ammonium nitrate and sulfuric acid mixture in high yields. The reaction of sulfuric acid and ammonium nitrate provides 100% nitric acid, which is the reason

for the method being more effective (Scheme 34). The IR spectrum of the polymer was in accordance with the structure.[85]

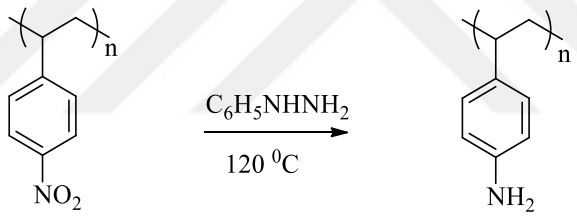



**nitro-PS**

**Scheme 34.** Nitration of Polystyrene with Ammonium Nitrate and Sulfuric Acid

### 3.2.1.2. Reduction of Nitro Groups

The modification of polystyrene continued with the reduction of nitro groups to amino groups. The amino groups would function as nucleophilic centers during the further steps of the synthesis of **TEMPOL-PS**.

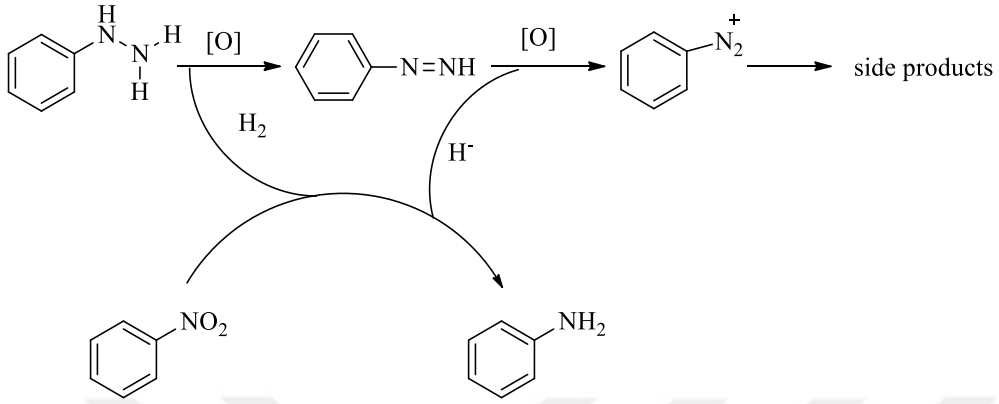



**nitro-PS** **amino-PS**

**Scheme 35.** Reduction of **nitro-PS**

The reduction of nitro-PS was accomplished by mixing the polymer with $PhNHNH_2$ at 120 $^oC$ over night (Scheme 35). An organic reagent, phenylhydrazine was used for the reduction of **nitro-PS** rather than heavy metals. By this, the environmental spoil of the method was reduced. However, the separation of $PhNHNH_2$ was burdensome. Therefore the polymer was kept several days in EtOH in order to get rid of the reagent. The IR spectrum of the structure revealed amine peaks at 3418 $cm^{-1}$ and 3343 $cm^{-1}$[186] however a total reduction could not be achieved. The mechanism of this reaction is depicted in Scheme 36. This mechanism is proposed to proceed through two successive oxidations of phenylhydrazine which produces hydrogen and hydride.

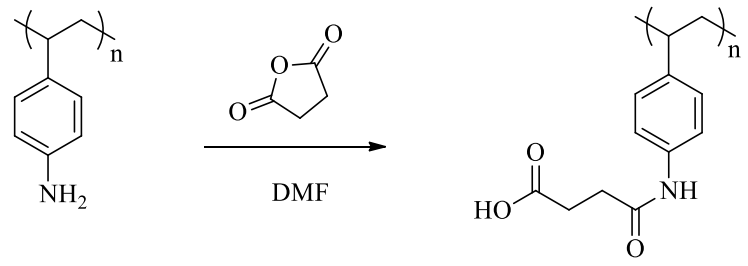
These species, thus, reduce the nitro group. A similar mechanism was proposed by Balci et al.[87]




**Scheme 36**. Proposed mechanism of reduction of poly(4-nitrostyrene) with phenylhydrazine

### 3.2.1.3. Reaction with Succinic Anhydride

The target of the synthesis was to introduce a nitroxyl radical to the structure of the polymer. So the next step was the attachment of an in-between group that would provide electrophile functionality for the reaction with 4-amino-2,2,6,6-tetramethylpiperidine. Thus, **amino-PS** was dissolved in DMF and reacted with excess succinic anhydride to form **suc-PS** (Scheme 37).

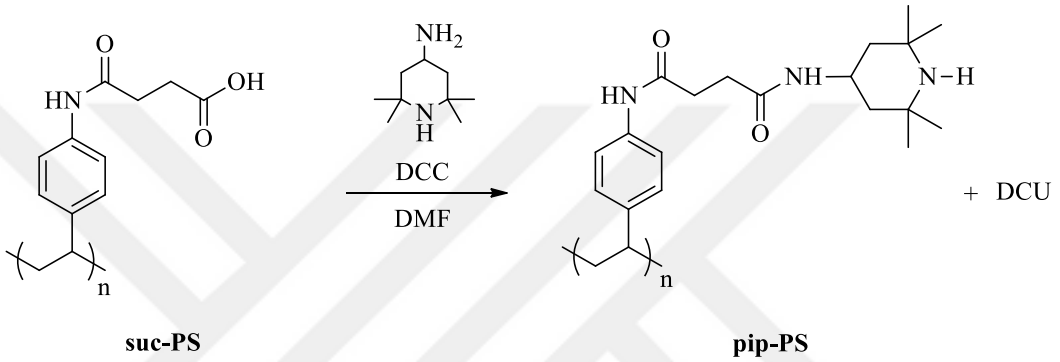



**Scheme 37.** Synthesis of **suc-PS**

The electrophile functionality which would be used in the next step was attained with the carboxylic acid end of the structure. Hence, the existence of the carboxylic acid and amide were confirmed with the peaks at 2922 $cm^{-1}$, 1653 $cm^{-1}$ and 1510 $cm^{-1}$ in the IR data.

### 3.2.1.4. Reaction with 4-amino-2,2,6,6-tetramethylpiperidine

The reaction occuring between a carboxylic acid and an amine to form an amide is not spontaneous at room temperature. Thus, the reaction should either be conducted at high temperature or a coupling agent that can activate the carboxylic acid should be used[88]. Likewise, in the reaction of 4-amino-2,2,6,6-tetramethylppiperidine and **suc-PS**, an amide bond would be formed. Hence, DCC was used to activate the carboxylic acid functionality that is involved in the structure of **suc-PS**.

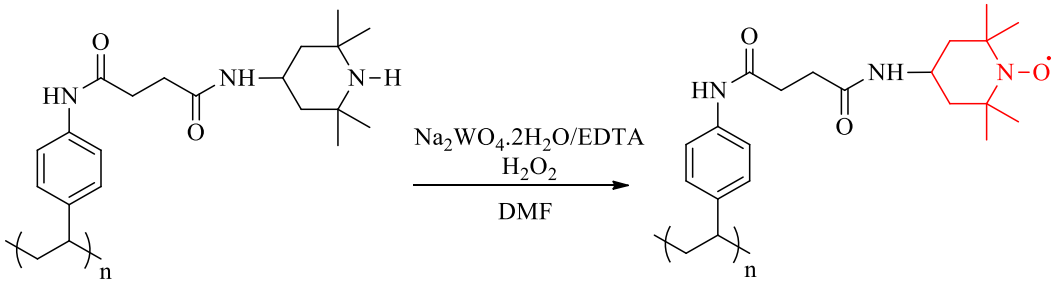



**suc-PS** **pip-PS**

**Scheme 38.** Synthesis of **pip-PS**

The first step is the reaction between DCC and carboxylic acid to convert the hydroxy group to a better leaving group. First of all, suc-PS was dissolved in DMF and cooled to 0 $^{o}$C. Then DCC was introduced to the solution. The reaction was conducted at low temperature in order to inhibit the conversion of DCC to dicyclohexylurea (DCU) before the activation of carboxylic acid. Then, 4-amino-2,2,6,6-tetramethylpiperidine was added and the solution was stirred at room temperature (Scheme 38). The byproduct of the coupling reaction is DCU which is hard to remove from the reaction medium. In this case the desired product was a polymer, **pip-PS**. Hence, DCU could be eliminated by washing the polymer with solvents in which DCU is soluble. Thus, the polymer was washed several times with MeOH to remove DCU and dichloromethane to remove unreacted DCC.

### 3.2.1.5. Formation of Nitroxyl Radical by Oxidation




**pip-PS** **TEMPOL-PS**

**Scheme 39.** Synthesis of **TEMPOL-PS**

The last step of the synthesis was the oxidation of piperidine to form a nitroxyl radical. As shown in Scheme 39, the polymer was dissolved in DMF. To the stirring solution, $Na_2WO_4.2H_2O$ and EDTA dissolved in water were introduced. Finally $H_2O_2$ was added and the solution was stirred for 5 days.[89]

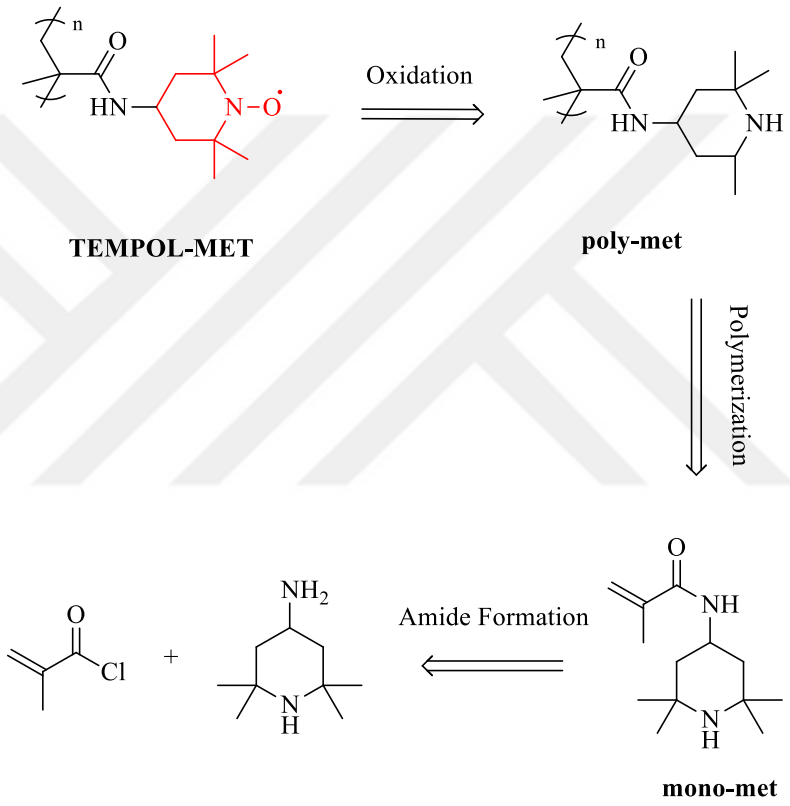
Figure 8. Picture of **TEMPOL-PS**

Oxidation of the polymer yielded orange **TEMPOL-PS** (Figure 8). IR data were utilized to prove the existence of nitroxyl radical (Figure 24). To be sure of the existence of TEMPO radical, an Anelli Oxidation for benzyl alcohol was performed, and positive results indicated the presence of the nitroxyl radical moiety.

### 3.2.2. Synthesis of TEMPOL-MET

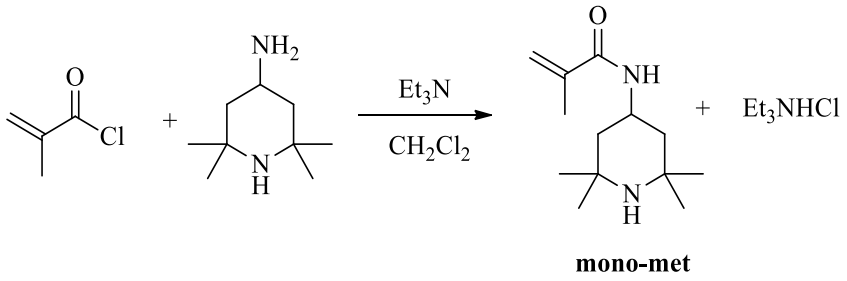
#### 3.2.2.1. Trial Pathway for synthesis of TEMPOL-MET

The second polymer **TEMPOL-MET** was designed due to the existence of this polymer in the literature.[90,91] Examining the literature revealed that the synthesis should be straightforward. However, this turns out to be not the case in our hands. Our first design for the synthesis of the polymer was shown in Scheme 40.




**Scheme 40.** Retrosynthetic pathway of the first attempt for **TEMPOL-MET**

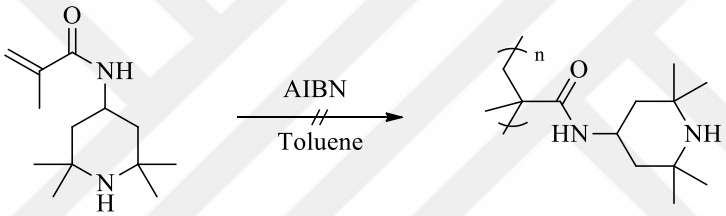
The synthesis of **mono-met** happened to be problematic in our hands. The reaction was prepared and perfomed several times, yet the monomer could not be synthesized. Rather, signs of polymerization (oligomer formation) were observed in NMR data. The reason for this might be the 4-amino-2,2,6,6-tetramethylpiperidine acting as an initiator for the polymerization of metacryloyl moiety. In order to inhibit this possibility, the reaction should be conducted at a temperature below 0 $^{0}$C.




**mono-met**

**Scheme 41.** Synthesis of **mono-met**

With these in mind, the reagents were cooled below -10 $^0$C in freezer prior to use. Again after the reagents shown in Scheme 41, were mixed dropwise, the mixture was kept in freezer. The monomer was cleaned by eluting it through a column. The NMR spectrum was in accordance with the literature.[90]



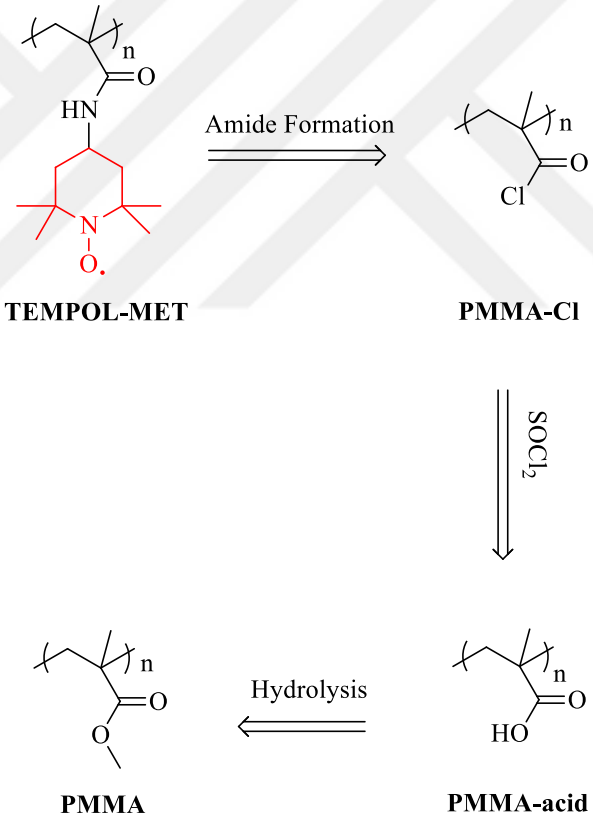

**mono-met** **poly-met**

**Scheme 42.** Polymerization of **mono-met**

The monomer was subjected to polymerization by free radical polymerization with azobisisobutyronitrile (AIBN) as radical initiator. Free radical polymerization was chosen because of the chance that a crosslinked polymer could be obtained through back-biting or chain transfer mechanism[92], high molecular weights were expected as well. The reaction was conducted under inert atmosphere(Argon atmosphere) at 70$^0$C and lasted 20 hours, after 3 times of freeze-pump cycle. However, at this point the NMR spectrum showed that the polymerization could not be accomplished. With all these difficulties in mind, an efficient and easy way was sought for obtaining **TEMPOL-MET**.

### 3.2.2.2. TEMPOL-MET Synthesis Through Modification of PMMA

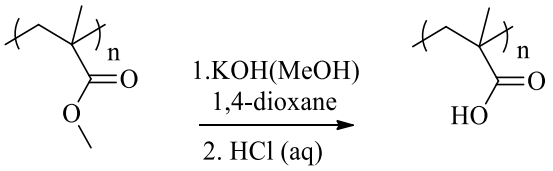
The new synthesis of **TEMPOL-MET** was planned to be concluded in 3 steps. Commercially available poly(methyl methacrylate) **(PMMA)** beads were utilized as starting material. The retrosynthetic pathway was designed to the extent of the insertion of nitroxyl radical moiety to the structure (Scheme 43). Thus, the methyl ester was decided to be converted to acyl chloride and the reaction with 4-amino-TEMPO was expected to yield **TEMPOL-MET** (Scheme 43). However, the process described above is not going to yield 100 % of conversion. The polymer will have esters amides and imine groups present in the structure. Yet we still call and show this polymer as **TEMPOL-MET** for simplicity.




**Scheme 43.** Retrosynthetic pathway of **TEMPOL-MET**

### 3.2.2.2.1. Synthesis of PMMA-Cl

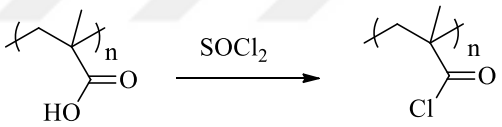
The hydrolysis of PMMA was conducted at alkaline conditions. The **PMMA** beads were refluxed in 1,4-dioxane and methanolic KOH solution over night (Scheme 44). The polymer was precipitated in excess HCl solution to yield partially hydrolyzed **PMMA**, **PMMA-acid**.




**PMMA** **PMMA-acid**

**Scheme 44**. Hydrolysis of PMMA

The carboxylic acid functionality in the structure was confirmed with IR data (Figure 9). Then, the partially hydrolized PMMA was chlorinated in order to convert the hydroxy group to a better leaving group. Hence, the polymer was refluxed in thionyl chloride to yield **PMMA-Cl** (Scheme 45).

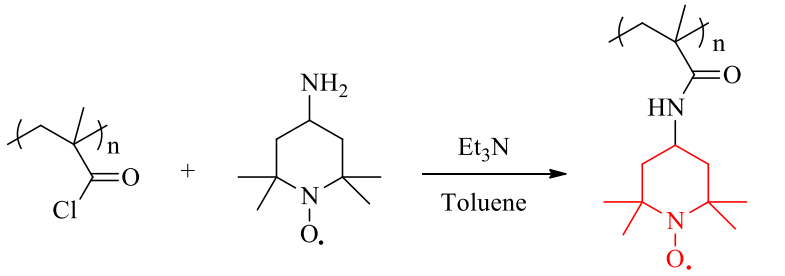



**PMMA-acid** **PMMA-Cl**

**Scheme 45.** Chlorination of PMMA-acid

### 3.2.2.2.2. Insertion of Nitroxyl Radical Moiety

The reaction of **PMMA-Cl** with 4-amino-TEMPO formed an amide bond. The reaction did not require a coupling agent since the activation barrier was low due to the good leaving group ability of chloride. Thus, the polymer was dissolved in toluene and refluxed with 4-amino-TEMPO to yield **TEMPOL-MET** (Scheme 46).




**PPMA-Cl** **TEMPOL-MET**

**Scheme 46**. Synthesis of TEMPOL-MET

The structure of the polymer was determined by IR data at each step of the synthesis. To characterize the polymers, the IR spectrum of PMMA was taken as the reference. The changes observed for each modification of the polymer on IR was recorded. IR spectrum of PMMA acid showed –OH stretching due to the carboxylic acid groups. Upon treatment of the acid with thionyl chloride, the –OH stretching peaks dissappear. Thus, different kinds of carbonyl peaks appeared around 1700 $cm^{-1}$ due to the formation of anhydride and acyl chloride.

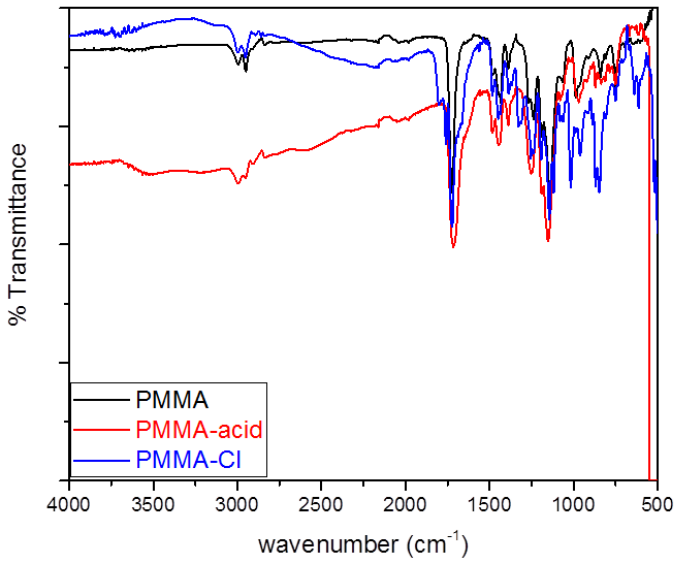


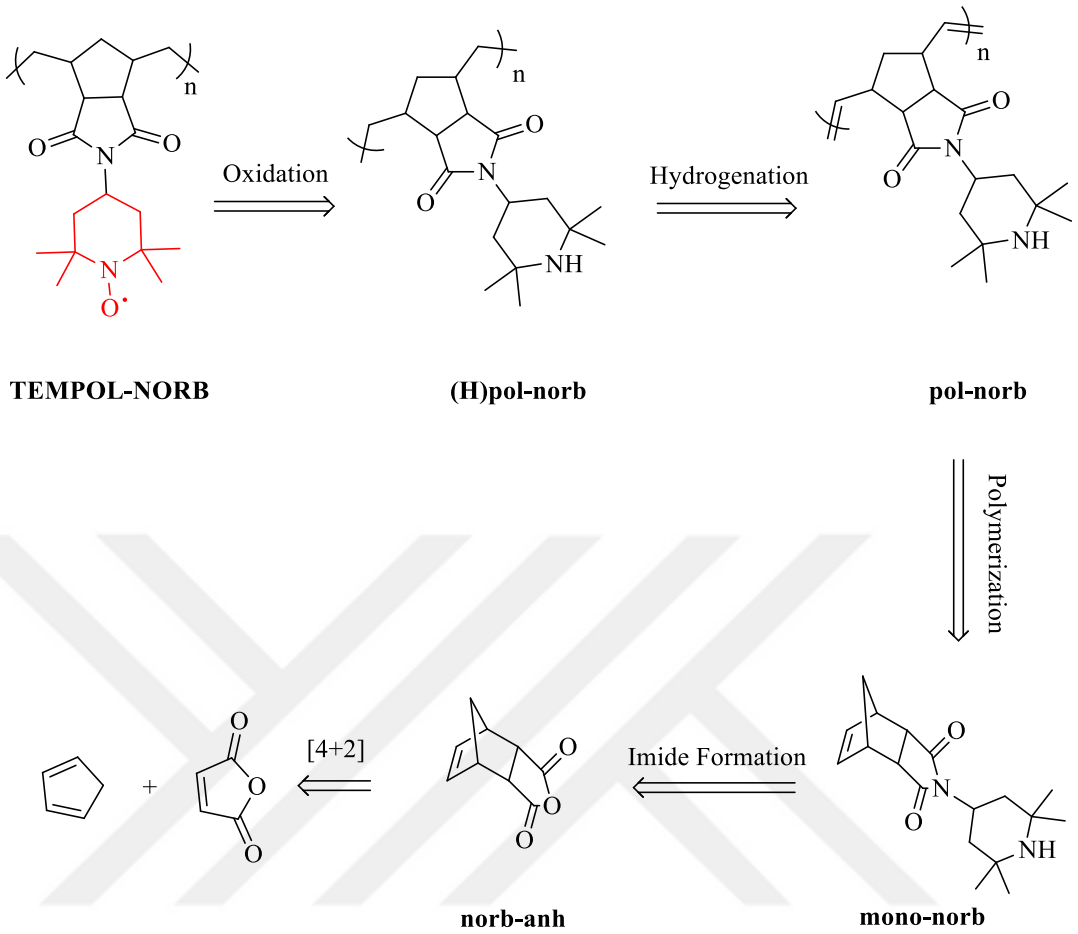

**Figure 9.** IR Spectra of PMMA, PMMA-acid and PMMA-Cl

The brown solid, **TEMPOL-MET** (Figure 10) that was obtained by the synthesis was analyzed with IR spectrometry. The existence of nitroxyl radical was confirmed with Anelli oxidation of benzyl alcohol.

Figure 10. Picture of **TEMPOL-MET**

### 3.2.3. Synthesis of TEMPOL-NORB

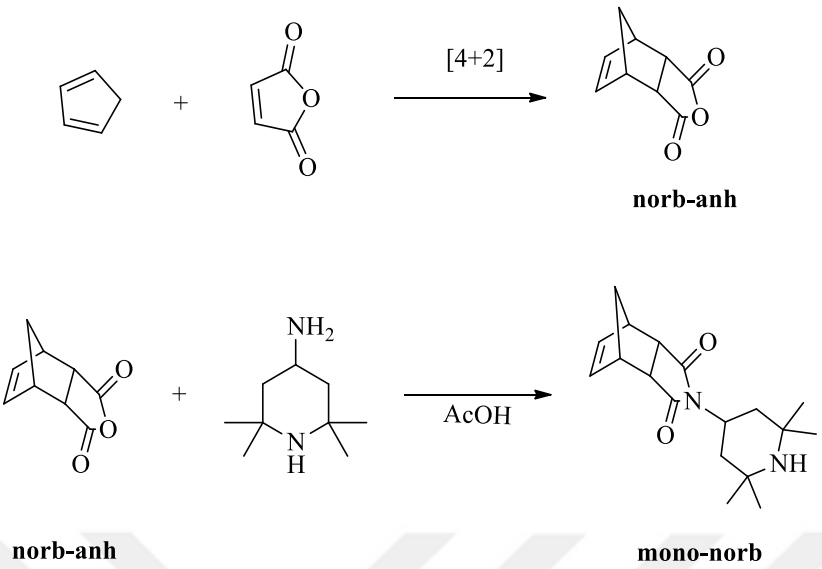
The last TEMPO attached polymer studied in this thesis, **TEMPOL-NORB** was envisioned to be synthesized in five steps (Scheme 47). The retrosynthesis of this polymer revealed that the monomer which contains norbornene skeleton **mono-norb** could be obtained by Diels-Alder reaction of **maleic anhydride** with cyclopentadiene. The monomer could be polymerized by ring opening metathesis polymerization (ROMP) to yield **pol-norb** and could be hydrogenated to form **(H)pol-norb**. Finally, polymer **(H)pol-norb** could be oxidized to attain **TEMPOL-NORB** which contains nitroxyl radical in the structure (Scheme 47).




**Scheme 47.** Retrosynthetic pathway of **TEMPOL-NORB**

### 3.2.2.1. Synthesis of the mono-norb

The synthesis of **mono-norb** required two steps (Scheme 48). *cis*-5-Norbornene-*endo*-2,3-dicarboxylic anhydride was synthesized by [4+2] conjugate addition of maleic anhydride and cyclopentadiene. For this, the cyclopentadiene dimer was cracked via retro Diels-Alder reaction at 170 $^{o}$C, the distillate was collected and saved in a flask at -78 $^{o}$C. The distallate was then mixed with maleic anhydride to get a solid compound simultaneously. Hence, the compound **norb-anh** was synthesized with a high yield of 94%.




**Scheme 48.** Synthesis of mono-norb

**norb-anh** was treated with 4-amino-2,2,6,6-tetramethylpiperidine in AcOH to yield 1-(2,2,6,6-tetramethylpiperidin-4-yl)-1H-pyrrole-2,5-dione **mono-norb** (Scheme 48). The assigned protons in the structure are shown in the NMR spectrum in Figure 11. The two protons that gave signals at 1.9 ppm and 1.3 ppm belong to the unlabelled – $CH_2$ group. These protons distinct from each other by being axial and equatorial protons. Due to the dihedral angle, the equatorial ones shows up as tripletat 1.9 ppm. Whereas the proton at 1.3 ppm gives a doublet of doublet ($J$=8.8 Hz) due to axial-axial interaction with $H_F$. The cosy NMR results were also in accordance with the structure.

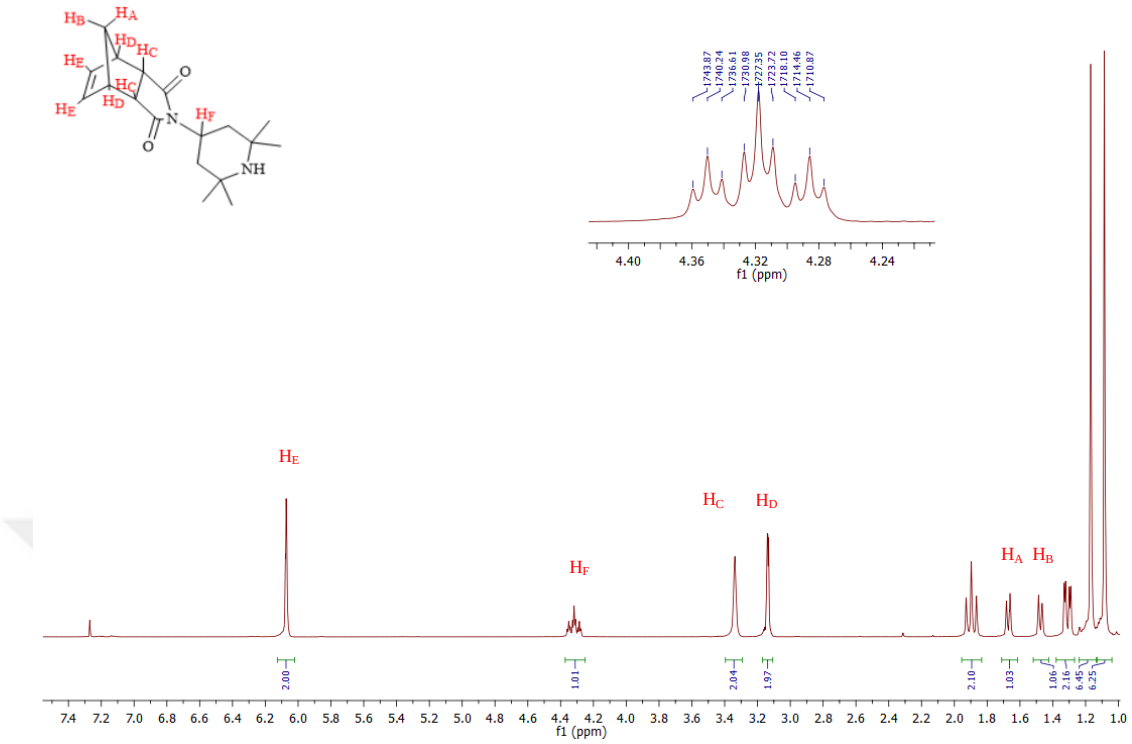
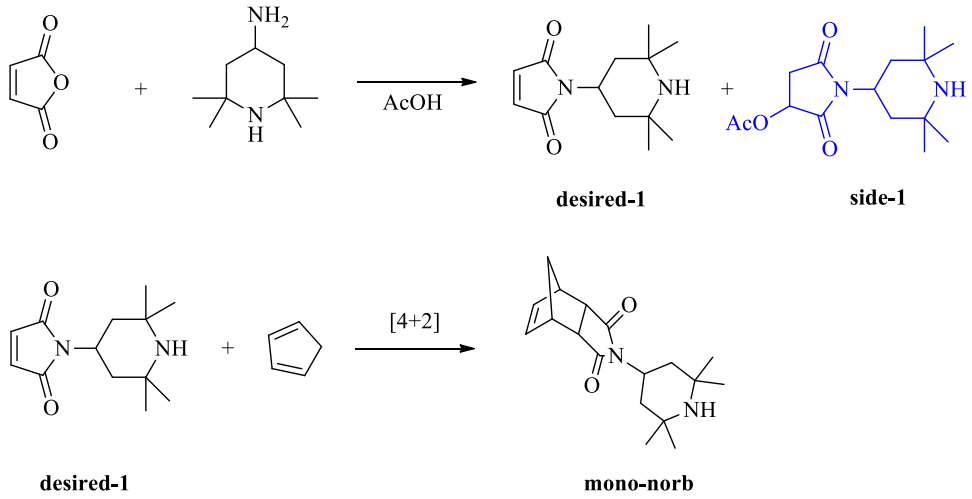



**Figure 11.** NMR Spectrum of **mono-norb**

To simplify the characterization, the monomer was decided to be synthesized by the synthetic pathway shown in Scheme 49. According to the pathway, first of all compound **desired-1** would be synthesized and then it would be reacted with cyclopentadiene to yield **mono-norb**.




**Scheme 49.** Trial for the synthesis of **mono-norb**

Maleic anhydride and 4-amino-2,2,6,6-tetramethylpiperidine were again treated in AcOH solution to form 1-(2,2,6,6-tetramethylpiperidin-4-yl)-1H-pyrrole-2,5-dione, **desired-1**. However, two different compounds were observed in TLC analysis. Hence, the NMR data supported this observation. When the NMR data were examined (Figure 12), the other compound was understood to be 2,5-dioxo-1-(2,2,6,6-tetramethylpiperidin-4-yl)pyrrolidin-3-yl acetate, **side-1**. The proton $H_X$ gave a doublet of doublet signal at low field, *ca*. 5.4 ppm which was caused by being next to an acetoxy group and another carbonyl group. Each of the protons $H_B$ and $H_A$, which were next to a carbonyl group, gave rise to different doublets at *ca*. 3.1 ppm and 2.7 ppm. The coupling constants of the coupled protons were observed to be similar.

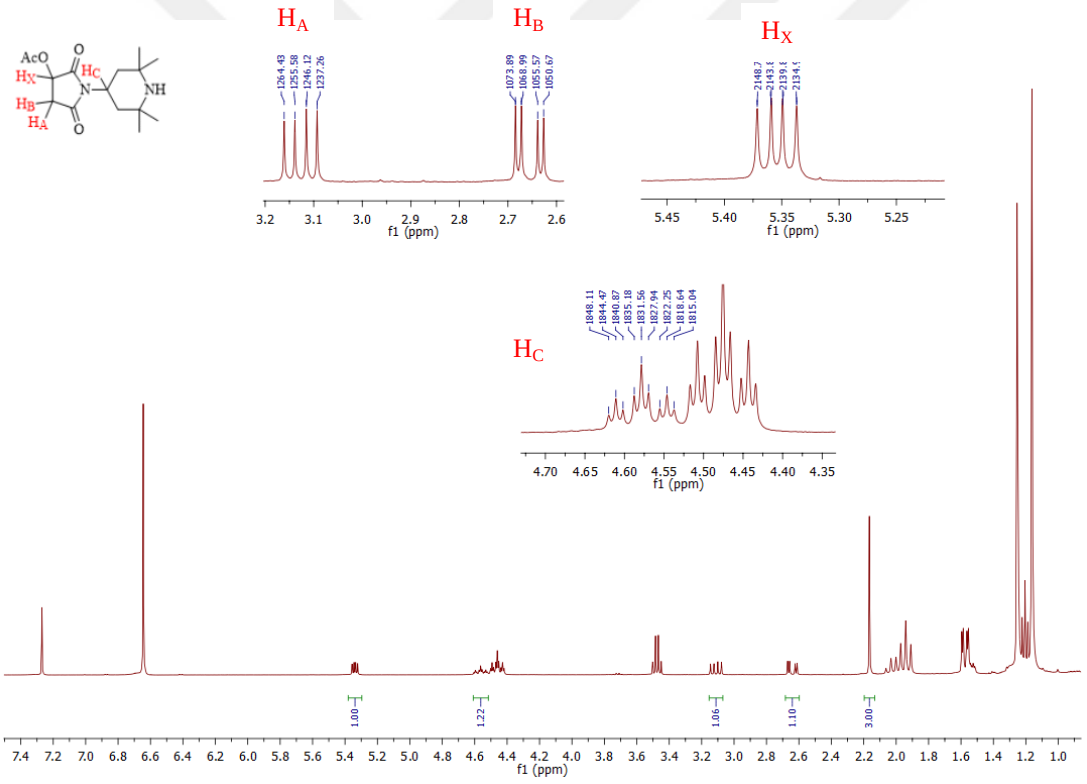
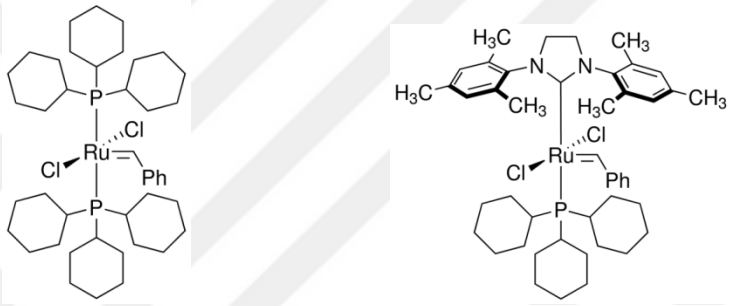



**Figure 12.** NMR Spectrum of **side-1** and **desired-1** mixture

The interesting thing about the side product was the possibility of 1,4-addition of AcOH, which in this case was used as solvent, to maleic anhydride. This interesting finding needs further investigation.

### 3.2.2.2. Ring Opening Metathesis Polymerization of Monomer

The monomer, **mono-norb** was succesfully synthesized and then it was polymerized by ring opening metathesis polymerization (ROMP). ROMP is stimulated by the ring strain that occurs due to the norbornene structure.[93] Catalysts are used to initiate and control the polymerization. In our study we used Grubbs catalyst for this purpose. The first generation Grubbs catalyst *vide infra*, was tried yet no satisfactory results could be obtained. Actually, previous studies showed that the use of second generation Grubbs catalyst (Figure 13) is more favoured in such strained structures. This is grounded on the fact that these structures require a slower initiation step due to handling difficulties.[94] Thus, this can be provided by second generation catalyst.

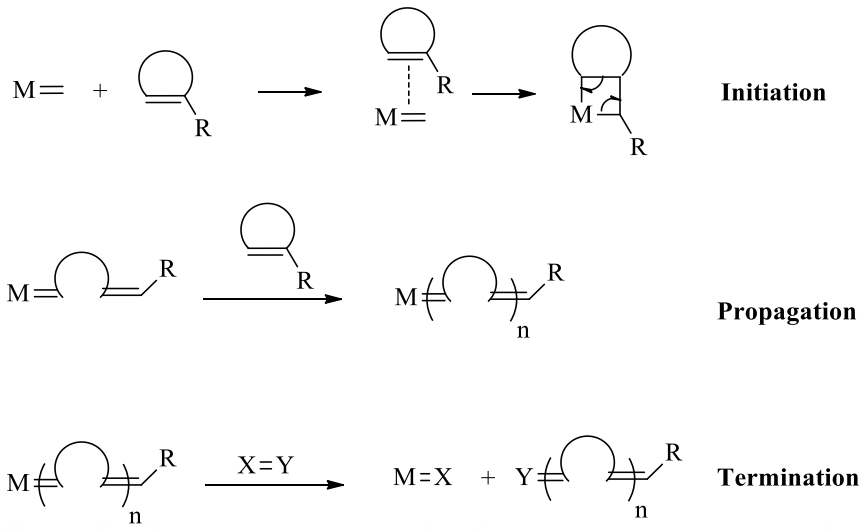



1st generation Grubbs Catalyst

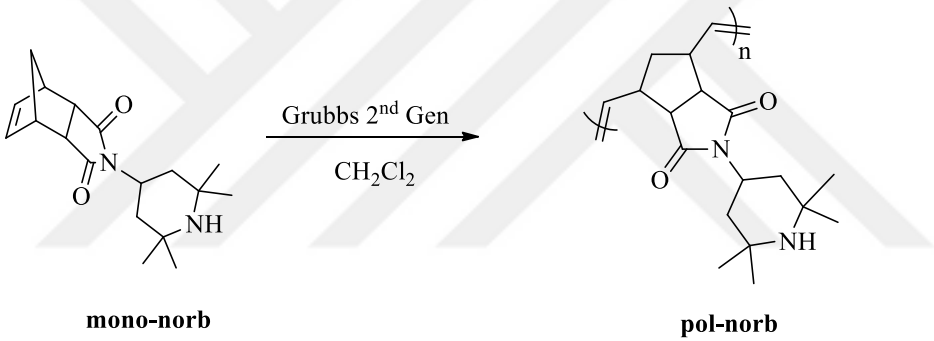
2nd Generation Grubbs Catalyst

**Figure 13.** Grubbs 1st and 2nd Generation Catalysts

The mechanism of ring opening metathesis polymerization has been extensively studied.[93] As shown in Scheme 50, the metal alkylidinium complex, in this case Grubbs 2nd generation catalyst, binds to the cyclic olefin that is the monomer. A [2+2] cycloaddition reaction takes place between them to form a metallocyclobutane intermediate.[95] Then, the metallocyclobutane structure opens by retro cycloaddition to generate another metal alkylidinium complex with active sides for polymerization. The initiation and propagation steps are repeated for each new monomer molecule. In the termination step, a new olefin is introduced to the medium in order to form a different metal alkylidinium complex. With this, the polymer gets discharged from the metal catalyst.[95]




**Scheme 50.** Mechanism of Ring Opening Metathesis Reaction[93]




**mono-norb** **pol-norb**

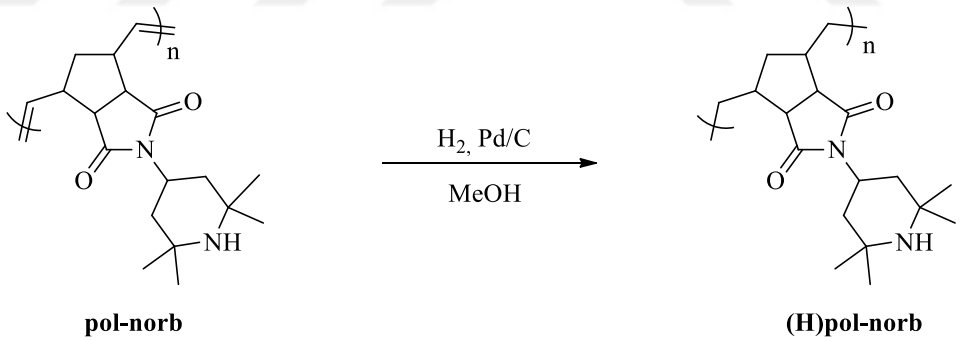
**Scheme 51.** Polymerization of **mono-norb**

Consequently, more active Grubbs 2nd Generation catalyst was used for the polymerization (Scheme 51). Although the catalyst is reported to have no air and light sensitivity, the polymerization was conducted under inert conditions maintained by Ar atmosphere. For the first few trials, an efficient polymerization was not observed. The color of the solution changed from purple to black within a day. However the viscosity of the solution did not increase even after 12 days. Also, the GPC analysis of the compound showed that it exhibited rather an oligomer structure with a molecular weigth of 2794 Da. Then, the amount of the catalyst was decided to be decreased in order to have a longer chain polymer. Favorably, after this alteration the viscosity of the solution increased in 3 days. Then *t*-butylvinyl ether was added to the solution in order to terminate polymerization. During the purification of the

polymer, vacuum filtration was observed to cause loss of compound due to the relatively small pore size of celite, which was used to remove the metal from medium. Therefore, **pol-norb** was washed several times with diethyl ether and and water[53] to obtain a greyish polymer.

### 3.2.2.3. Hydrogenation of the Polymer

With the **pol-norb** in hand, it could be subjected to oxidation in order to acquire nitroxyl radicals in the structure. However, the olefinic groups in the repeating unit had also potency to be oxidized to epoxides and other oxidized products. Therefore, the olefinic parts of the polymer were subjected to hydrogenation. The first trial experiment was conducted in a high pressure reactor. **pol-norb** was dissolved in MeOH and Pd/C was added as a catalyst. The solution was kept in reactor at 20 barr pressure 40 $^{o}$C temperature for 6 hours. Yet, NMR results showed that the olefinic bonds were not hydrogenated. Afterwards, hydrogenation was performed at ambient pressure with $H_2$ balloon. The solution was kept under $H_2$ for five days, however the results did not change.



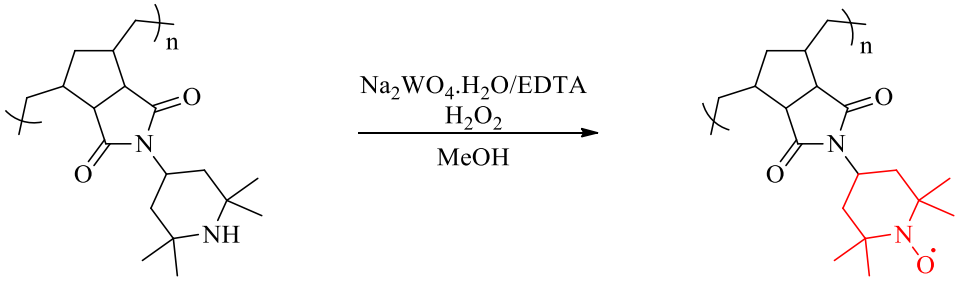

**pol-norb** **(H)pol-norb**

**Scheme 52.** Hydrogenation of **pol-norb**

Finally, the reaction conditions of the reaction conducted in high pressure reactor were elavated. The pressure was increased to 60 barr and the temperature was raised to 66 $^{o}$C, above the boiling point of MeOH (Scheme 52). This time, more than 35% hydrogenation was accomplished in 3 hours. This result was affirmed by NMR with the integration value of the triplet like signal at *ca*. 6 ppm that belong to the hydrogens attached to the olefinic bond.

### 3.2.2.4. Formation of Nitroxyl Radical by Oxidation

The hydrogenated polymer, **(H)pol-norb** was oxidized to attain nitroxyl radicals in a similar procedure described for the previous polymers (Scheme 53).




**(H)pol-norb** **TEMPOL-NORB**

**Scheme 53.** Oxidation of **(H)pol-norb**

Figure 14. Picture of TEMPOL-NORB

The solution was stirred 5-7 days to yield orange/pink **TEMPOL-NORB (**Figure 14). However the IR data did not reveal N-O stretching peak, rather the nitroxyl radical existed in hydroxylamine form. Anelli oxidation of benzyl alcohol yielded benzaldehyde, which confirmed that the hydroxylamine could be oxidized to the oxoammonium cation by electron transfer in *situ*.

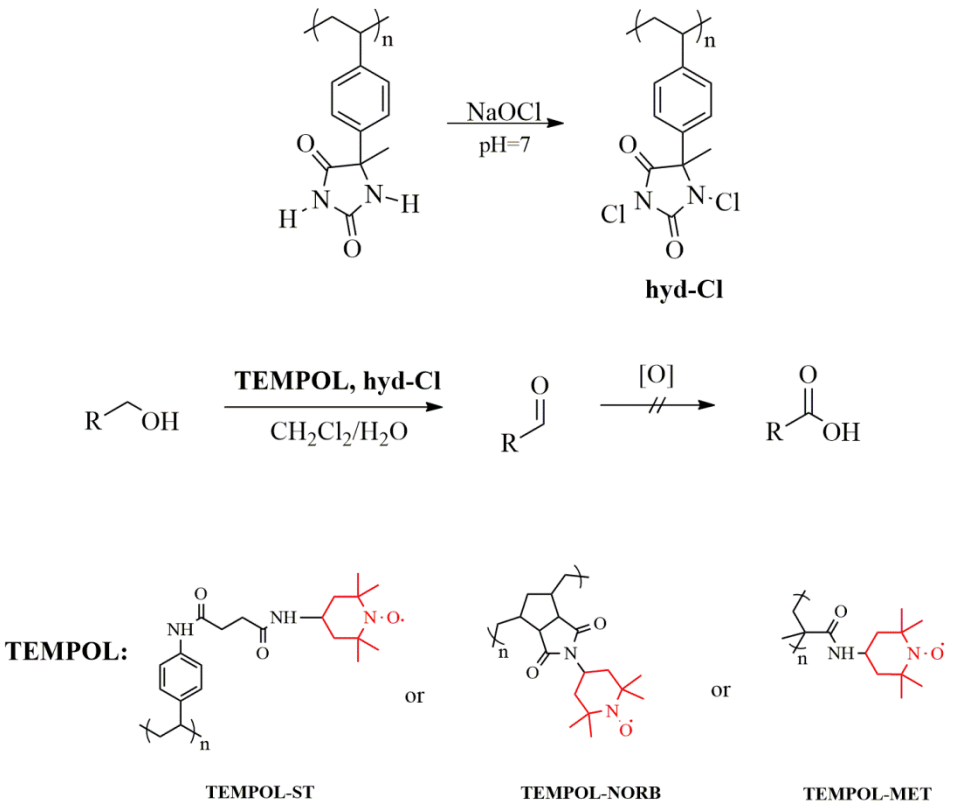
### 3.2.2.5. Crosslinking Attempts

The polymer **TEMPOL-NORB** was observed to be soluble in dichloromethane. Although the polymer could be recovered by reprecipitation from diethyl ether this would increase the use of solvent and generation of waste. So, the strength of the polymer was decided to be enhanced by crosslinking the olefin functionality in the

structure. The compound was subjected to thiol-ene photopolymerization by dissolving in dichloromethane and the addition of octane-1,8-dithiol. The reaction mixture was exposed to UV light for 10 days yet precipitation of the polymer was not observed. Then crosslinking with dicumyl peroxide was tried yet again a satisfying result was not achieved. Consequently, the oxidation reactions were conducted in dichloromethane. These studies needs further investigations and these are beyond the scope of this thesis.

### 3.3. Oxidation of Primary Alcohols to Aldehydes with Polymer Mixtures

Primary alcohols were subjected to oxidation by all polymeric reagents: **hyd-Cl** and TEMPO attached polymers (Scheme 54). In order to avoid the use of halogenated solvents as explained before, relatively green solvents were searched for the oxidation reactions. For the **TEMPOL-PS** polymer, ethyl acetate and acetone were selected. **TEMPOL-PS** was observed to be insoluble in either of these solvents. However, only limited conversion to the aldehyde was observed. Therefore, the reactions were conducted in dichloromethane/water solvent mixture. Oxidation reaction with **TEMPOL-NORB** was conducted in diethyl ether, as the polymer was insoluble in this solvent. However, as in the case of **TEMPOL-PS** slight conversions were observed even after long durations. Thus, dichloromethane was decided to be used throughout this thesis.



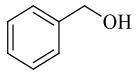
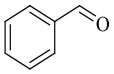
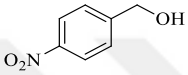
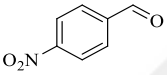
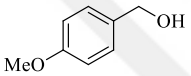
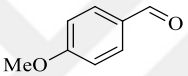
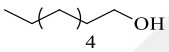
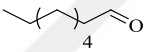
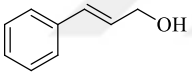
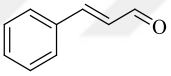

**Scheme 54.** Oxidation of primary alcohols to aldehydes catalyzed by polymeric mixture

The reactions were conducted at the same conditions with the oxidations mentioned at the beginning of the Results and Discussions part of the thesis, *vide supra*. Each polymeric mixture was tested with: benzyl alcohol, 4-nitrobenzyl alcohol, 4-methoxybenzyl alcohol, 1-octanol and cinnamyl alcohol (Table 4). The alcohols were selected according to their electronic nature. The conditions were identical in all oxidation reactions except for the type of the TEMPO containing polymer being used.

The activities of the polymers were examined in 1 hour by $^{1}$H NMR data. However, the results showed that the amount of alcohols were too much considering the other reagents included in the systems. The results of 4-methoxybenzaldehyde and cinnamaldehyde showed difference between the activities of polymers. This may have resulted due to the different partical sizes of the polymers. **TEMPOL-NORB** was larger in size (lower density) which might have effected the collision possibility. All of the polymers showed enhanced activity with 4-nitrobenzyl alcohol. This can

be explained by the electron withdrawing goup attached to the aromatic ring. The electron density on the $–CH_2$ group attached to the OH decreases, which eases the abstraction of a proton at alkaline conditions.

**Table 4.** Conversion of Primary Alcohol to Aldehyde in 1 Hour

| | | Conversion in 1 hour based on $^1$H NMR data | | |
|---|---|---|---|---|
| Alcohol (300 mg) | Product | **TEMPOL-ST** | **TEMPOL-MET** | **TEMPOL-NORB** |
|  |  | 15 % | 9% | 12% |
|  |  | 23 % | 28% | 37% |
|  |  | 14% | 11% | 6% |
|  |  | 1% | 1% | 1% |
|  |  | 30% | 11% | 6% |

# CHAPTER 4

# CONCLUSIONS

In this study, polymeric reagents were faciliated toward green oxidation of alcohols. The first part of the study included the utilization of a chlorinated hydantoin based polymer, **hyd-Cl** as a co-oxidant for TEMPO mediated oxidation of primary alcohols to aldehyde derivatives. Oxidation of pimary alcohols containing different functional groups were accomplished by TEMPO/ **hyd-Cl** system. Iodometric redox titration was employed in order to test the chlorination capacity and stability of **hyd-Cl**. The results showed that the polymer preserves the chlorine content at no light and no moist conditions.

In the second part, three different TEMPO containing polymers were succesfully synthesized to be used on behalf of TEMPO in oxidation reactions. The first polymer, **TEMPOL-PS** was synthesized by the modification of readily available polystyrene. The five step synthesis was concluded by the attachment of 4-amino-2,2,6,6-tetramethylpiperidine and oxidation of the polymer to yield **TEMPOL-PS**. The second polymer, **TEMPOL-MET** was at first tried to be synthesized starting from methacryloyl choride and 4-amino-2,2,6,6-tetramethylpiperidine. Although this monomer could be synthesized, the polymerization could not be accomplished. Therefore, the polymer **TEMPOL-MET** was obtained by the modification of PMMA beads. The third polymer **TEMPOL-NORB** was synthesized by the ROMP of the norbornene skeleton of the monomer. On account of its functionality, Grubbs 1$^{st}$ generation catalyst was used for the polymerization. However, an efficient polymerization could not be achieved. Consequently, more active Grubbs 2$^{nd}$ generation catalyst was utilized. This time the polymerization was accomplished.

The polymer was hydrogenated and oxidized to obtain **TEMPOL-NORB**. All these polymers were subjected to Anelli oxidation of benzyl alcohol and full conversion to benzaldehyde was observed.

These polymers were separately used with **hyd-Cl** in the oxidation of primary alcohols to aldehyde derivatives. It was shown that these polymers can overcome such a task. The polymers were each time filtered with simple filtration and chlorinated for another oxidation reaction. Hence, different kinds of primary alcohols were tested with these systems. The percent conversion of each alcohol to aldehyde derivative based on $^{1}$H NMR was examined for all three polymers. However, the activities of the polymers will be more clearly understood after full oxidation of alcohols. The systems need further optimization for the full oxidation of alcohols.

The employment of easily separable polymeric reagents in oxidation of primary alcohols provided enhanced atom economy for the reactions. This is an important step towards a green process. However, the use of halogenated solvents should be avoided. This is also a future endavour.

As future study, the search for environmentally accepted solvents will continue. Full oxidations of alcohols will be accomplished. Moreover, the employment of the TEMPO containing polymers as organic radical batteries will be investigated.

# CHAPTER 5

# EXPERIMENTALS

## 5.1. Methods and Materials:

All starting materials and solvents were purchased from Sigma Aldrich and were used without further purifications.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.

$^{1}H$ 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). $^{1}H$ 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.

### 5.2. General Procedure for Oxidation of Alcohols with TEMPO and hyd-Cl

$NaHCO_3$ solution (10.00 mL, 5.00 w%) was placed into a round bottomed flask and catalytic amount of KBr was also added. Chlorinated hydantoin polymer (2.00 g) and TEMPO radical (20.00 mg) were put in the solution. Finally, primary alcohol in dichloromethane (10.00 mL) was introduced and the biphasic mixture was stirred 3 hours at room temperature. The organic phase was separated and the aqueous phase was extracted with dichloromethane. The organic phase was dried over $Na_2SO_4$ and the solvent was evaporated.

### 5.3. Iodometric Redox Titration

#### 5.3.1. Standardization of $Na_2S_2O_4$

$Na_2S_2O_4$ (15.81 g, 0.10 moles) was dissolved in boiled and recooled distilled water (1.00 L). The solution was placed in a burette. In an erlenmeyer flask, $KIO_4$ (0.13 g, 0.62 mmole) and KI (2.00 g, 12.05 mmoles) were dissolved in distilled water (75.00 mL). The solution in the flask was titrated with $Na_2S_2O_4$ solution. Titration continued until the color of the solution turned from brown to pale yellow. Then, starch solution (0.50 g) was added and the color turned to blue. The blue solution was titrated again with $Na_2S_2O_4$ until the color dissappeared. The amount of consumed titrant was recorded. The titration was repeated three times and the molarity of the solution was calculated by the mean value of these results.

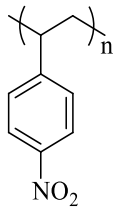
#### 5.3.2. Iodometric Titration of hyd-Cl beads

Polymeric beads were weighed and put into a solution of acetic acid/ethanol (10.00 v%). KI (0.25 g, 1.51 mmoles) was introduced to the solution and the color turned to yellow-brown. The solution was titrated with standardized $Na_2S_2O_4$ solution (9.76 mM) until the brown color turned to pale yellow. Then starch solution was added and the color changed to violet. Titration was continued until the color dissappeared. The volume of titrant was recorded.

## 5.4. Synthesis of TEMPO-Attached Polymers

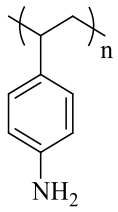
### 5.4.1. Synthesis of TEMPOL-PS

5.4.1.1. Poly(4-nitrostyrene) **(nitro-PS)**



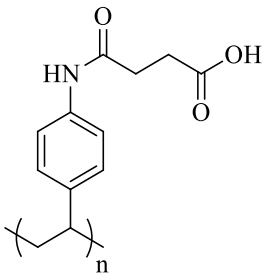

A round bottomed flask was charged with polystyrene beads (0.50 g). Nitrobenzene was added to the flask and the solution was stirred until complete dissolution was achieved. Ammonium nitrate (5.00 g, 0.06 mmole) was introduced to the stirring solution and the flask was put into an ice bath. Afterwards, $H_2SO_4$ (5.00 ml) was added in slow portions and reprecipitation of the polymer occured. The solution was stirred at room temperature over night. The solution was added to excess water and reprecipitation of the polymer occured. The yellow solid was separated from the reaction medium by decantation and it was washed several times with water and ethanol. (0.80 g) IR: 1510 $cm^{-1}$ ($NO_2$ antisym stretching), 1340 $cm^{-1}$ ($NO_2$ sym stretching)

5.4.1.2. Poly(4-aminostyrene) **(amino-PS)**



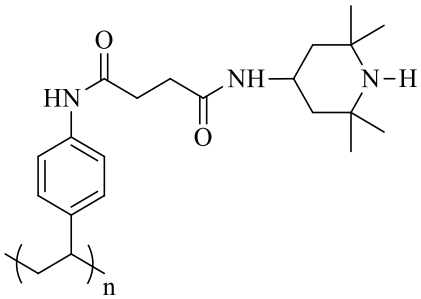

Poly-p-nitrostyrene (0.80 g) was dissolved in $PhNHNH_2$ (80.00 ml) and placed in a round bottomed flask. The flask was equiped with a condenser and the solution was refluxed at 120 $^oC$ over night. Methanol was added to reprecipitate the polymer and $PhNHNH_2$ was separated by decantation. The orange solid was washed several times with ethanol. (0.35g) IR: 3418 $cm^{-1}$, 3343 $cm^{-1}$ (N-H stretching)

5.4.1.3. Poly(4-oxo-4-((4-styrene)amino)butanoic acid) (**suc-PS)**



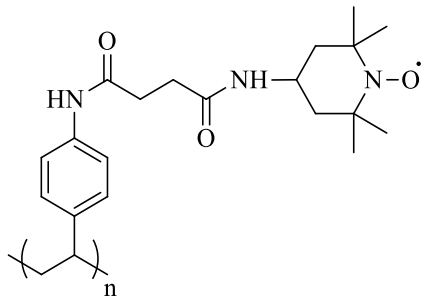
Poly-p-aminostyrene (5.00 g, 42.02 mmoles) was installed in a round bottomed flask and DMF (100.00 ml) was added with stirring to dissolve the polymer. When the polymer dissolved, succinic anhydride (6.00 g, 59.96 mmoles) was added and the solution was stirred under $N_2$ atm over night. The orange product was reprecipitated from water and washed several times with ethanol and water. (6.80 g) IR: 3296 $cm^{-1}$ (N-H stretching), 2922 $cm^{-1}$ (N-H stretching), 1693 $cm^{-1}$ (C=O stretching)

5.4.1.4. Poly($N^1$-(2,2,6,6-tetramethylpiperidine-4-yl)-$N^4$-(4-styrene) succinamide) **(pip-PS)**



Polymer **suc-PS** (13.60 g) was placed in a round bottomed flask was dissolved in DMF. The flask was placed in an ice bath. When the temperature was cooled down below 5 $^oC$, DCC (8.00 g, 38.77 mmole) was slowly added to the solution. Afterwards 4-amino-2,2,6,6-tetramethylpiperidine (7.11 g, 45.52 mmole) was dropwise added and the solution was allowed to stir at room temperature over night. The polymer was reprecipitated from DMF by MeOH. Then, it was washed several times with each of the following solvents: MeOH, water and $CH_2Cl_2$. (0.70 g)

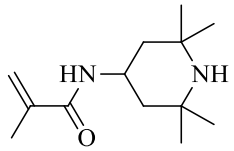
5.4.1.5. Poly($N^1$-(2,2,6,6-tetramethylpiperidine-4-oxyl)-$N^4$-(4-styrene) succinamide) **(TEMPOL-PS)**



Polymer **pip-PS** (0.70 g) was dissolved in DMF. To the solution EDTA (0.50 g, 1.71 mmole) and $Na_2WO_4.2H_2O$ (0.50 g, 1.63 mmole) were added. Then $H_2O_2$ (30.00 ml) was added with time intervals in 3 days. Afterwards the orange solid was reprecipitated from the solution by water and washed several times with water. (0.70 g) IR: 3298 $cm^{-1}$ (N-H strecthing), 1343 $cm^{-1}$ (N-O stretching)

5.4.2. Synthesis of **TEMPOL-MET**

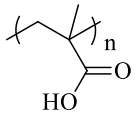
5.4.2.1. N-(2,2,6,6-tetramethylpiperidine-4-yl) methacryl-amide **(mono-met)**



4-Amino-2,2,6,6-tetramethylpiperidine (2.01 g, 12.84 mmole) was dissolved in $CH_2Cl_2$ (40.00 ml). To the solution, $NEt_3$ (2.59 g, 25.60 mmole) was added and the solution was put into freezer. Meanwhile, metacryloyl chloride (1.22 g, 11.68 mmole) was also cooled in the freezer. After both the solution and metacryolyl chloride were cooled to -20 $^oC$, metacryloyl chloride was added dropwise to the solution. When gas evolution finished, the solution was sealed and put again to freezer. After an hour, the solution was washed with water and extracted with $CH_2Cl_2$. The organic phase was dried over $Na_2SO_4$ and $CH_2Cl_2$ was evaporated at reduced pressure. Excess $NEt_3$ was removed by a vacuum pump. The pale yellow viscose liquid was flushed with Ar gas and sealed before it was put into the freezer

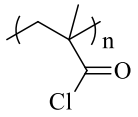
again. Column chromatography with ethyl acetate:hexane (1:1) yielded white crystals. (0.70 g, 27%)

5.4.2.3. Poly(methacrylic acid), **(PMMA acid)**



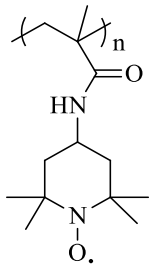

PMMA (6.20 g) was dissolved in 1,4-dioxane (100.00 ml). To the solution methanolic solution of KOH (50.00 ml) was added and the solution was refluxed over night. The flask was cooled and the hydrolyzed polymer was precipitated in excess aqueous HCl. The polymer was washed several times with water, filtered and dried under vacuum. (4.50 g) IR: 3400 $cm^{-1}$ (O-H stretching), 1713 $cm^{-1}$ (C=O stretching)

4.4.2.4. Poly(metacryloyl chloride), **(PMMA-Cl)**




**PMMA-acid** (4.50 g) was dissolved in $SOCl_2$ (40.00 ml) and a few drops of DMF was added to the solution. The solution was refluxed for 2 hours. $SOCl_2$ was evaporated and the polymer was dried under vacuum. 1768 $cm^{-1}$ (C=O stretching)

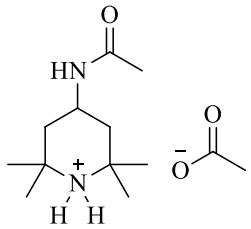
4.4.2.5. N-(2,2,6,6-tetramethylpiperidine-4-oxyl) methacryl-amide




**PMMA-Cl** (1.00 g) was dissolved in toluene (30.00 ml). To the solution 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (0.34 g, 1.98 mmoles) was added and the solution was refluxed for 2 hours. The solvent was evaporated and the polymer was

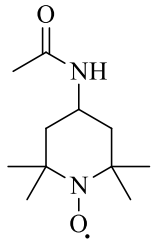
washed several times with MeOH to yield brown solids. (0.50 g) IR: 1761 $cm^{-1}$ (C=O stretching), 1374 $cm^{-1}$ (N-O stretching)

4.4.2.6. 4-Acetamido-2,2,6,6-tetramethylpiperidine



4-Amino-2,2,6,6-tetramethylpiperidine (4.56 g, 29.18 mmole) in diethyl ether (10.00 ml) was put into a round bottomed flask. The flask was placed in an ice bath and the solution was cooled down below 8 $^{o}$C. Acetic anhydride (10.80 g, 0.10 mole) in diethyl ether (10.00 ml), was dropwise added to the stirring solution in 1 hour period. The solution was stirred for 24 hours at room temperature. The acetic acid salt of the compound was collected as white precipitate, filtered under vacuum and washed with diethyl ether. (5.30 g, 91%) $^{1}$H NMR ($CDCl_3$): δ 5.95 (s, 3H), 4.32 (m, 1H), 2.00 (d, *J*=11.8, 6H), 1.86 (dd, *J*=13.21, 3.85, 2H), 1.55 (t, *J*=12.65, 2H), 1.44 (s, 6H), 1.35 (s, 6H)

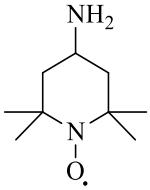
4.4.2.7. 4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl



4-Acetamido-2,2,6,6-tetramethylpiperidine (5.00 g, 25.21 mmole) in distilled water (50.00 ml) was put into a round bottomed flask. To the solution $Na_2WO_4.2H_2O$ (0.50 g, 1.63 mmole) and EDTA (0.50 g, 1.71 mmole) were also added and the solution was stirred. $H_2O_2$ (10.00 ml) was added in portions and the solution turned from yellow to orange. The solution was stirred at room temperature for 4 days to yield orange crystals. The crystals were washed several times with water. (5.00 g,

86%) IR: 3312 $cm^{-1}$ (N-H stretching), 1646 $cm^{-1}$ (C=O stretching), 1364 $cm^{-1}$ (N-O stretching)

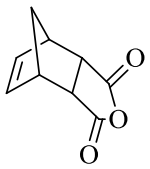
4.4.2.8. 4-Amino-2,2,6,6-tetramethylpiperidine-1-oxyl



4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (0.25 g, 1.96 mmole) was put into a round bottomed flask and mixed with aqueous KOH solution (20.00 ml, 15.00 w%). The flask was equipped with a condenser and the solution was refluxed for 20 hours. Afterwards, the cooled solution was basified with $K_2CO_3$ and extracted with diethyl ether. The organic phase was dried over $MgSO_4$ and the solvent was evaporated at reduced pressure. (0.14 g, 42%) IR: 3352 $cm^{-1}$, 3279 $cm^{-1}$ (N-H stretching),1358 $cm^{-1}$ (N-O stretching)

5.4.3. Synthesis of **TEMPOL-NORB**

5.4.3.1. *cis*-5-Norbornene-*endo*-2,3-dicarboxylic anhydride **(norb-anh)**

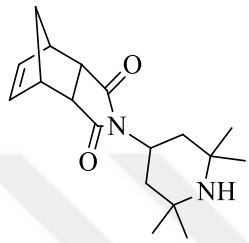


Cyclopentadiene dimer in a round bottomed flask was suited with distillation apparatus. The dimer was heated to 160-170 $^oC$. Cracked cyclopentadiene was collected to another round bottomed flask cooled to -78 $^oC$ by dry ice/acetone mixture.

Maleic anhydride (6.00 g, 61.19 mmole) was dissolved in ethyl acetate (16.00 ml) upon heating until 55-60 $^oC$. To the homogeneous solution, hexane (20.00 ml) was added and the flask was placed in an ice bath. When the solution was cooled down to room temperature, cyclopentadiene (6.00 g, 90.77 mmole) was added dropwise.

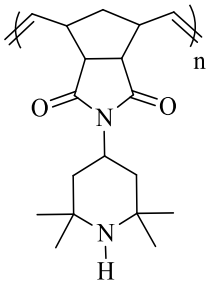
After the complete addition of cyclopentadiene, the flask was placed in an ice bath and crystallization occured. The white crystals were filtered and washed with ethyl acetate. (11.28 g, 94%) $^{1}$H NMR ($CDCl_3$): δ 6.31 (t, *J*= 1.7, 2H), 3.60-3.56 (m, 2H), 3.51 (dt, *J*= 4.8, 1.6, 2H), 1.78 (dt, *J*= 9.2, 4.8, 1H), 1.57 (s, 1H) IR: 3010 $cm^{-1}$ (C=C stretching), 1835 $cm^{-1}$ (C=O antisym stretching), 1762 $cm^{-1}$ (C=O sym stretching)

5.4.3.2. 1-(2,2,6,6-Tetramethylpiperidin-4-yl)-1H-pyrrole-2,5-dione **(mono-norb)**



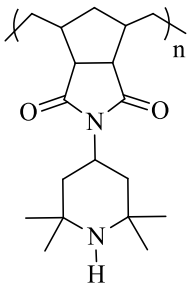

*cis*-5-Norbornene-*endo*-2,3-dicarboxylic anhydride (1.00 g, 6.09 mmole) was mixed with 4-amino-2,2,6,6-tetramethylpiperidine (0.95 g, 6.08 mmole) in a round bottomed flask. The flask was equipped with a condenser and the solution was refluxed in glacial acetic acid (20.00 ml) over night. The day after, acetic acid was evaporated under vacuum. The residue was basified with NaOH and extracted with diethyl ether. The organic phase was dried over $Na_2SO_4$ and the solvent was evaporated to yield red-orange crystals. (1.55 g, 84.30%) m.p.: 139 $^{o}$C $^{1}$H NMR ($CDCl_3$) δ (ppm) 6.08 (t, *J*=1.8, 2H), 4.32 (tt, *J*=12.9, 3.6, 1H), 3.34 (m, 2H), 3.17-3.11 (m, 2H), 1.90 (t, *J*=12.6, 2H), 1.68 (dt, *J*= 8.7, 1.6, 1H) 1.48 (d, *J*=8.7, 1H) 1.32 (dd, *J*=12.7, 3.6, 2H), 1.17 (s, 6H), 1.09 (s, 6H) $^{13}$C NMR ($CDCl_3$) δ (ppm): 177.63, 134.37, 54.91, 52.02, 45.12, 43.38, 38.27, 31.73, 25.70. IR: 3017 $cm^{-1}$ (C=C stretching), 1680 $cm^{-1}$ (C=O stretching)

5.4.3.3. Polymerization of **mono-norb, pol-norb**



Monomer (1.55 g, 5.63 mmole) was dissolved in dichloromethane (10.00 ml). To the solution Grubbs catalyst 2$^{nd}$ generation (0.01 g, 0.01 mmole) was added and the solution was stirred under inert Argon atmosphere. The color of the solution turned from purple to black within a day and during the 4 days it was stirred, the viscosity of the solution increased. The reaction was monitored with TLC and t-butylvinyl ether (1.00 ml) was added to cease polymerization. After the solution was stirred for another hour dichloromethane was evaporated. The grayish solid was washed several times with diethyl ether and water. (1.51 g) IR: 3000 cm$^{-1}$ (C-H stretching), 1700 cm$^{-1}$ (C=O stretching)

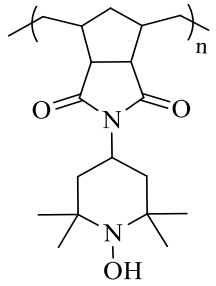
5.4.3.4. Hydrogenation of **pol-norb, (H)pol-norb**



Polymer (0.30 g) was dissolved in ethanol (50.00 ml) and placed in a high pressure reactor. To the solution Pd/C (0.11 g) was added and the tightly closed reactor was heated to 66 $^{o}$C. Hydrogen gas was allowed to enter the reactor until the pressure reached 60 barr and the reactor was kept at this pressure for 6 hours. After the reaction was completed the reactor was cooled down to room temperature and the catalyst was filtered. The solvent was evaporated and the gray solid reprecipitated

form the residue by the addition of diethyl ether. (0.30 g) IR: 2976 $cm^{-1}$ (C-H stretching), 1693 $cm^{-1}$ (C=O stretching)

5.4.3.5. Oxidation of **(H)pol-norb, TEMPOL-NORB**



Hydrogenated polymer (0.30 g) was put in a round bottomed flask and dissolved in distilled water (25.00 ml). Methanol (10.00 ml) was added to the solution and precipitation occured. To the solution EDTA (0.35 g, 1.20 mmole) and $NaWO_4.2H_2O$ (0.4 g, 1.21 mmole) were added. Finally, anhydrous potassium carbonate (0.5 g, 3.62 mmole) was added to attain basicity and the solution was kept stirring until the reagents were totally dissolved. $H_2O_2$ (15.00 ml 35.00 v%) was introduced slowly to the solution and foaming occured. Additionall $H_2O_2$ (25.00 ml, 35 v%) was introduced in 3 days. The solution turned from yellow to pink and the polymers were separated by decantation after 5 days. The pink solid was washed several times with water. (0.31 g) IR: 3506 $cm^{-1}$ (OH stretching), 2963 $cm^{-1}$ (C=C stretching), 1700 $cm^{-1}$ (C=O stretching)

## 5.5. Oxidation of Alcohols with Polymer Mixtures

5.5.1. General Procedure for Oxidation with **TEMPOL** Polymers/**hyd-Cl**

$NaHCO_3$ (10.00 ml, 5.00 w%) solution was placed into a round bottomed flask and catalytic amount of KBr was also added. Chlorinated hydantoin polymer (2.00 g) and **TEMPOL** (15.00 mg) were put in the solution. Finally primary alcohol in dichloromethane (10.00 ml) was introduced and the biphasic mixture was stirred 1 hour at room temperature. The organic phase was separated and the aqueous phase was extracted with dichloromethane. The organic phase was dried over $Na_2SO_4$ and the solvent was evaporated.

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# APPENDICES

## PART A: NMR SPECTRA

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

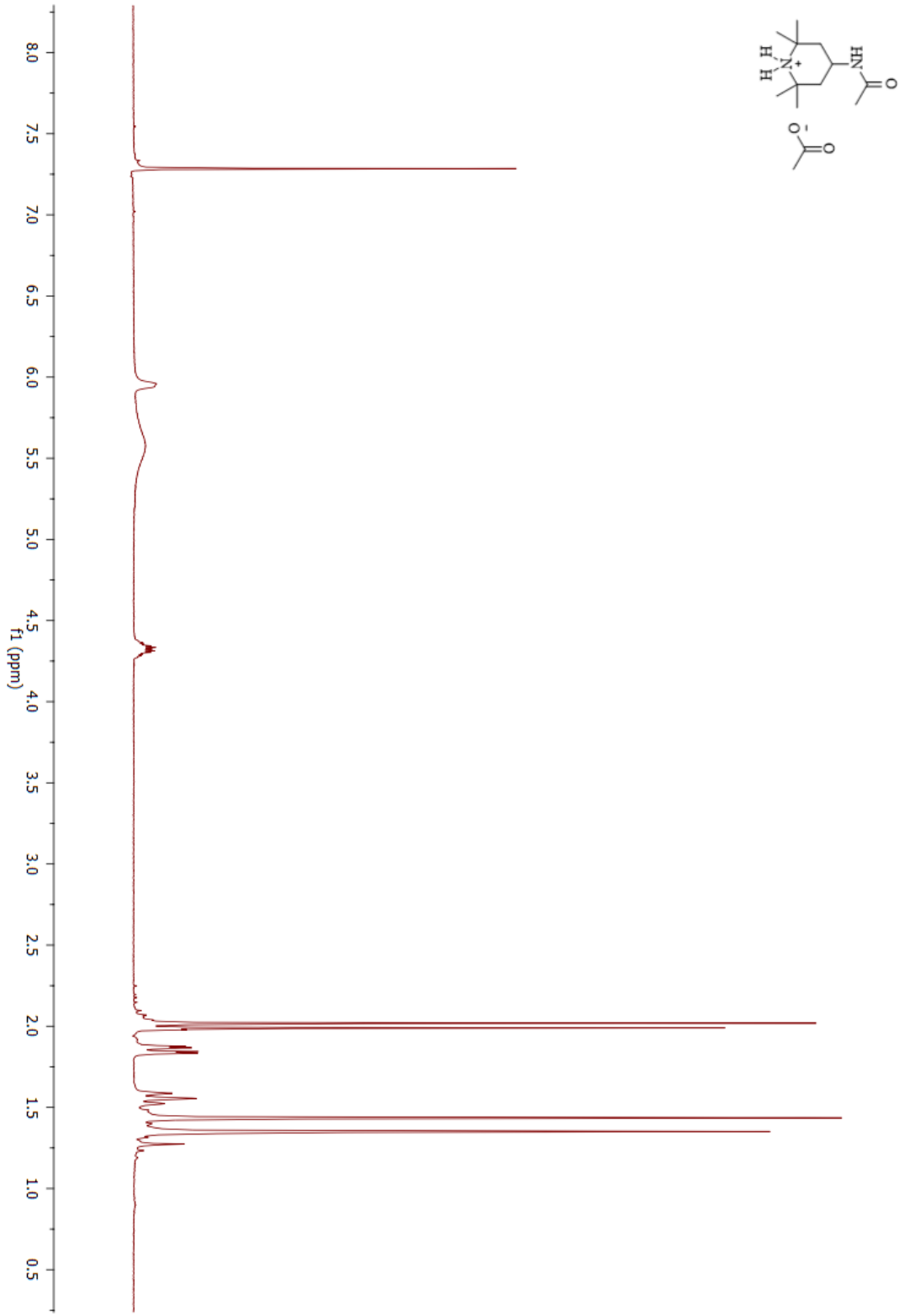


**Figure 15.** NMR Spectrum of 4-acetamido-2,2,6,6-tetramethylpiperidine

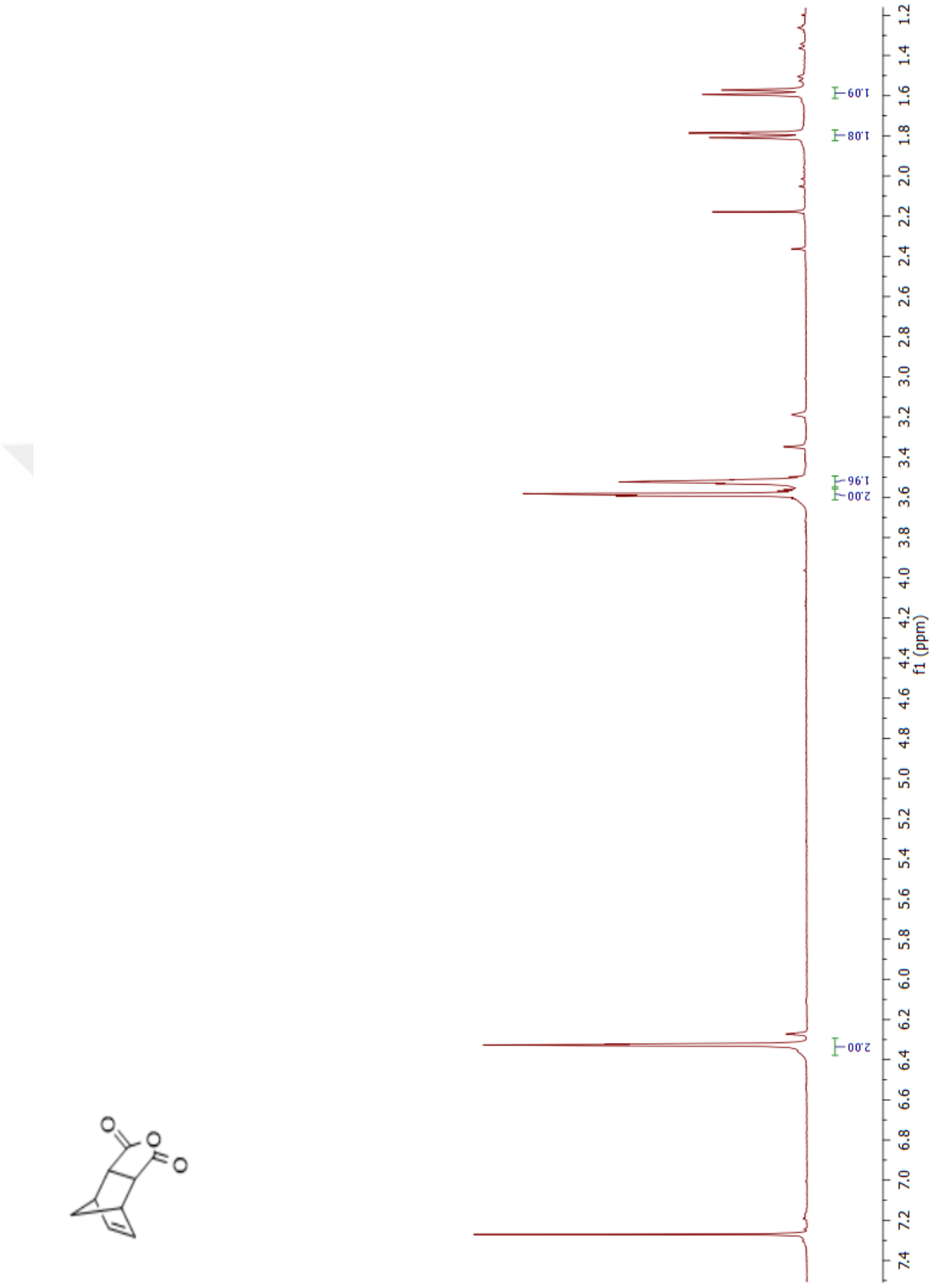


**Figure 16.** $^{1}$H NMR Spectrum of norb-anh

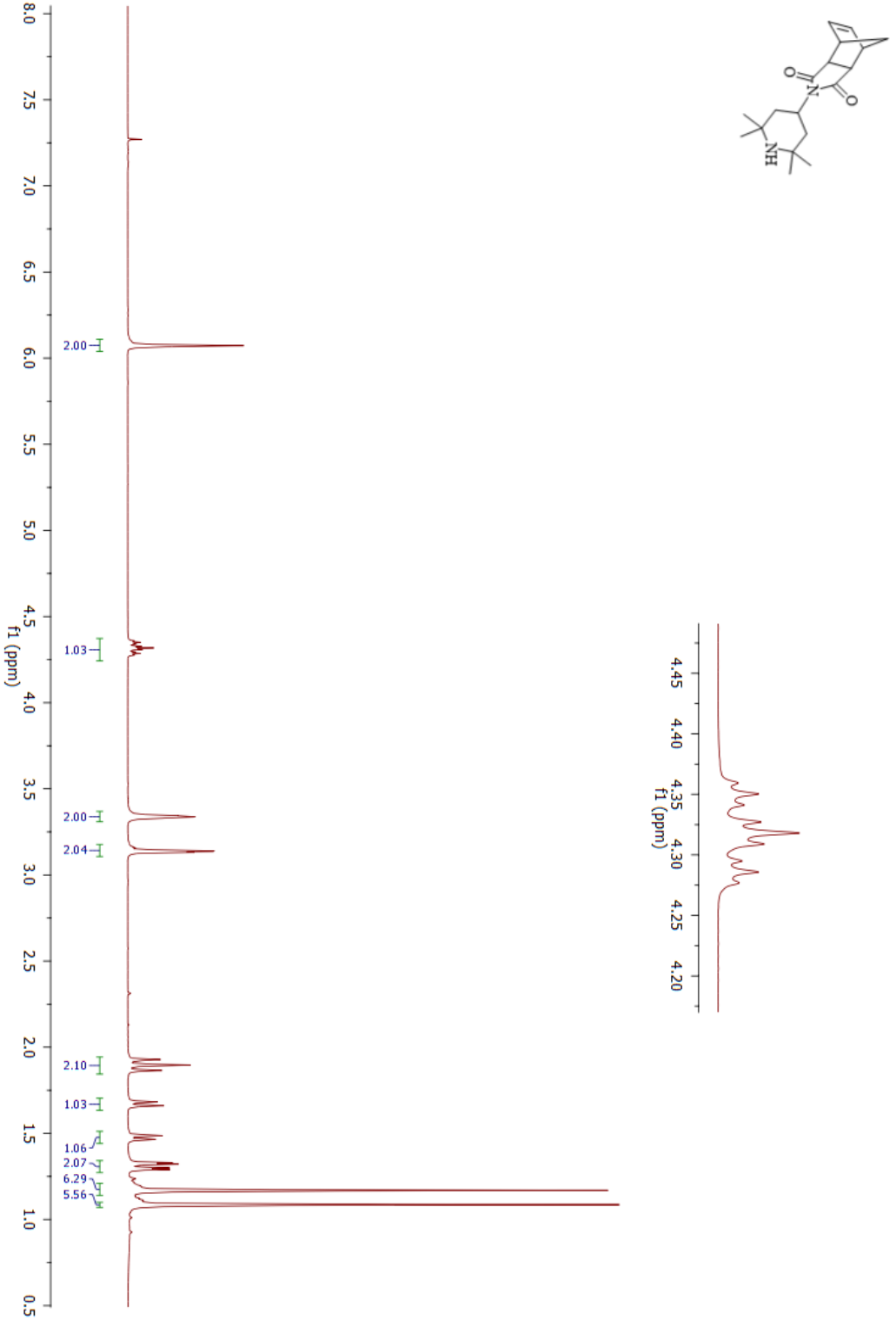


**Figure 17**. $^{1}$H NMR Spectrum of mono-norb

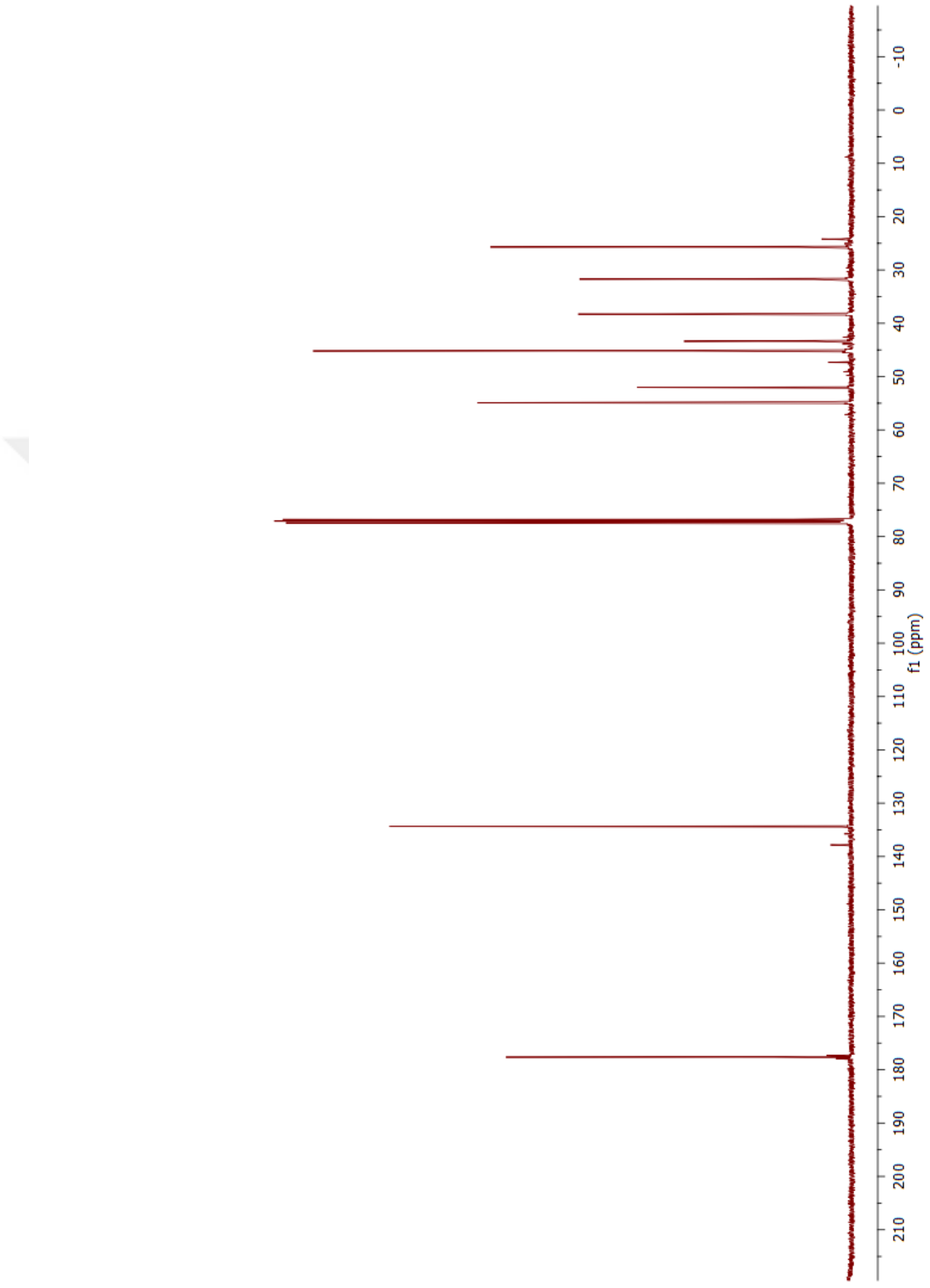


**Figure 18**. $^{13}C$ NMR Spectrum of mono-norb

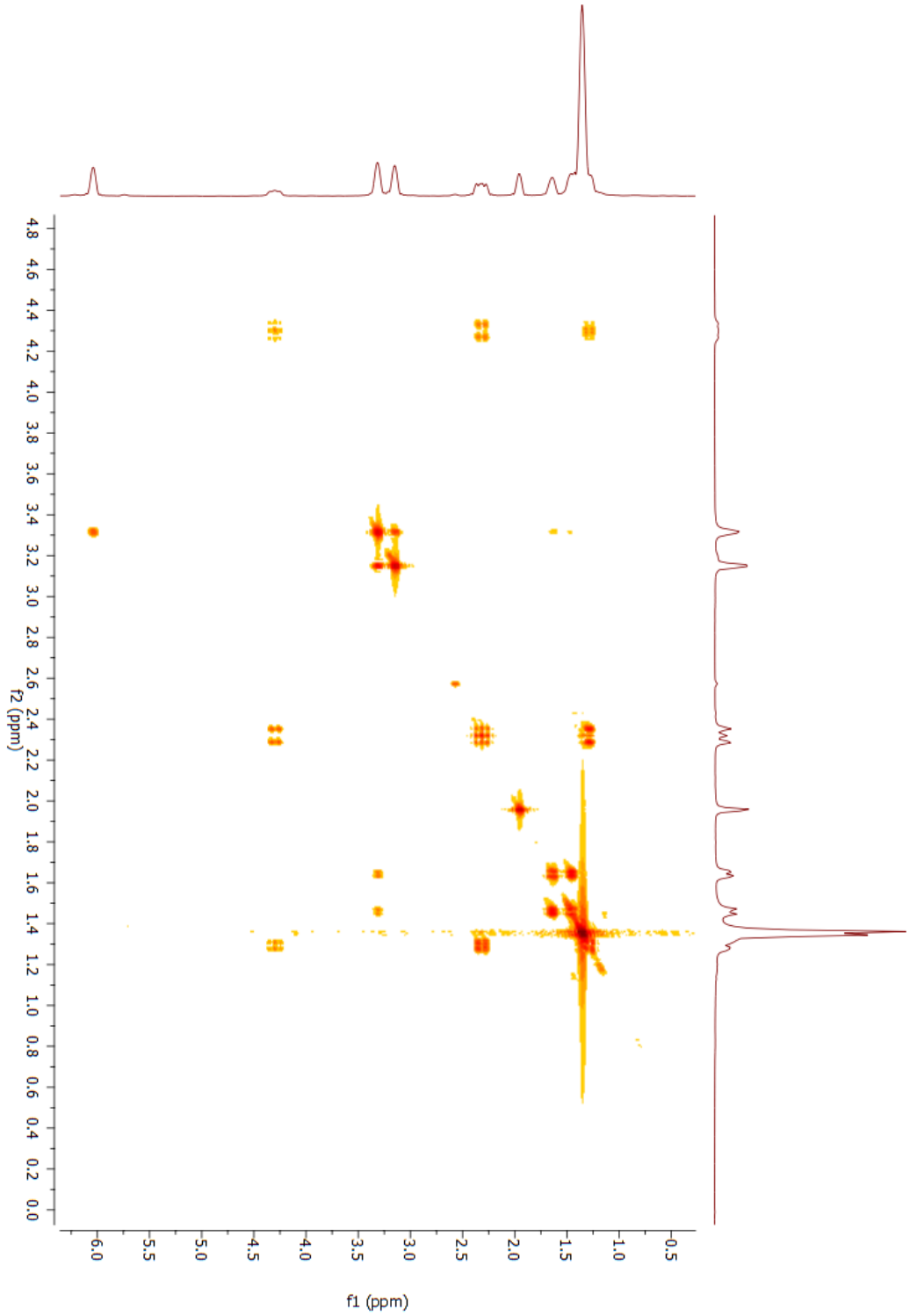


**Figure 19.** Cosy NMR Spectrum of mono-norb

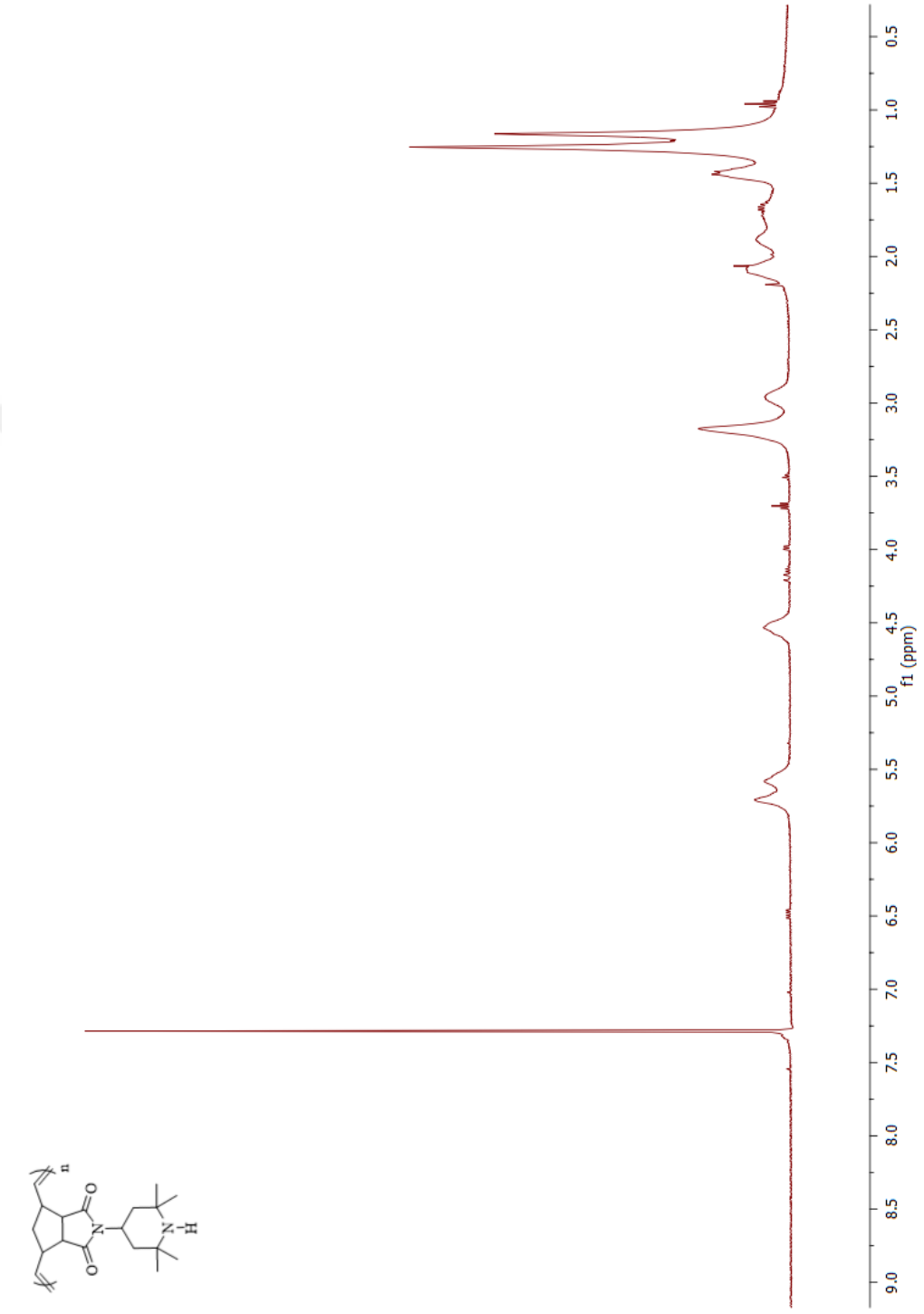


**Figure 20**. $^{1}$H NMR Spectrum of pol-norb

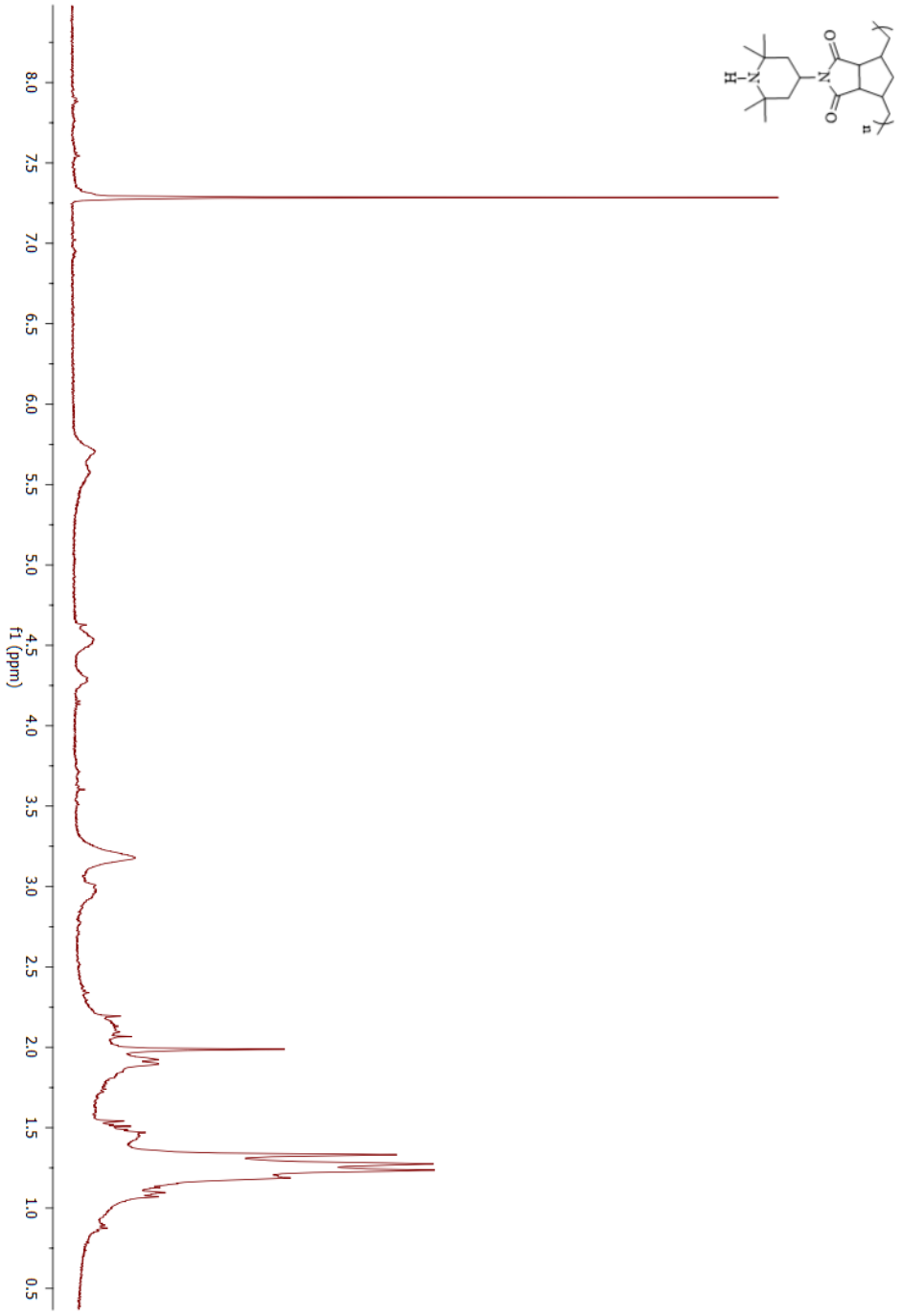


**Figure 21**. $^{1}$H NMR Spectrum of (H)pol-norb

**PART B: IR SPECTRA**

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

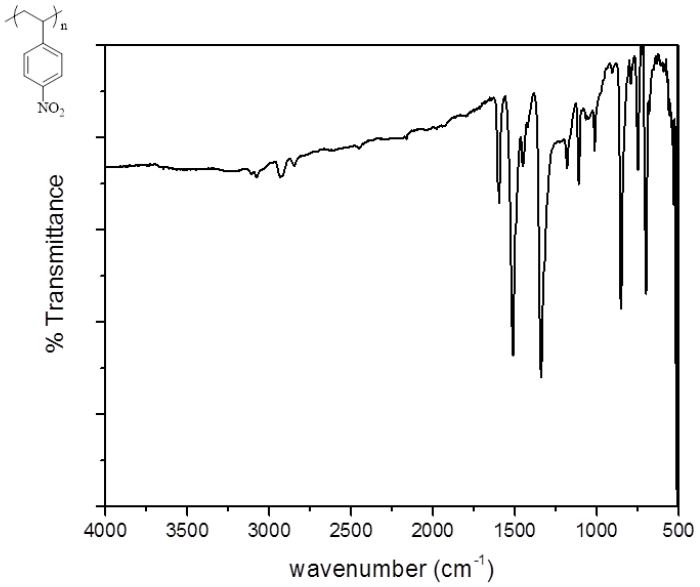


**Figure 22**. IR spectrum of **nitro-PS**

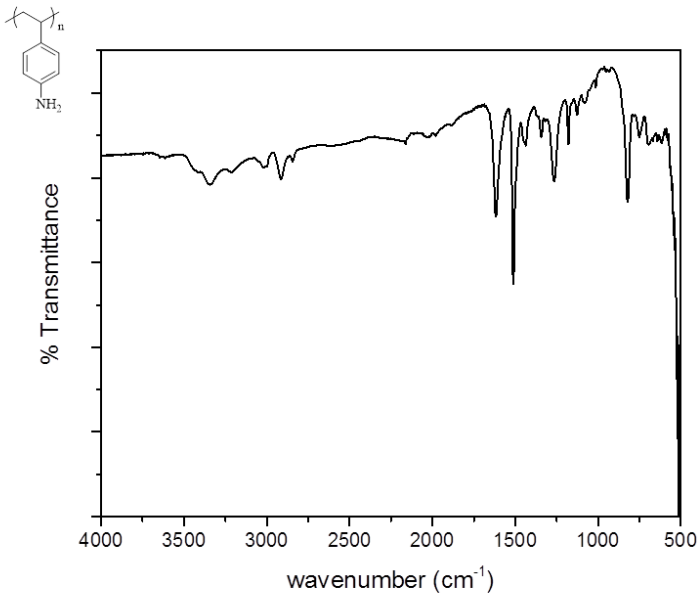


**Figure 23**. IR Spectrum of **amino-PS**

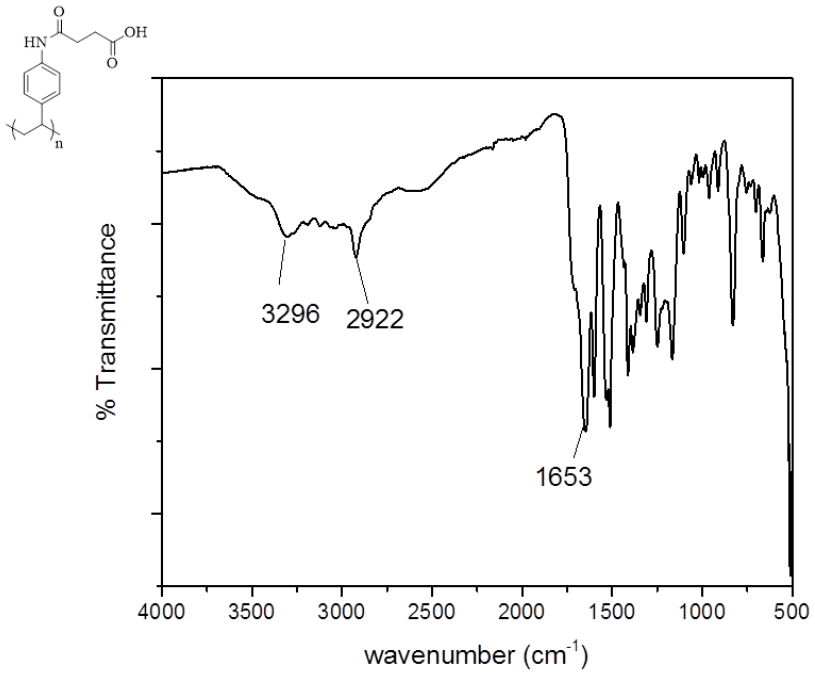


**Figure 24**. IR Spectrum of **suc-PS**

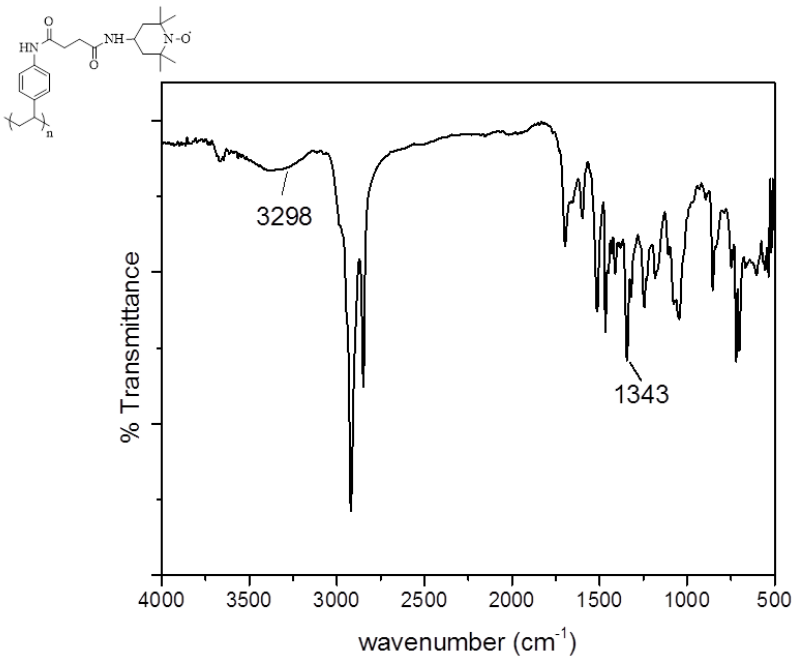


**Figure 25**. IR Spectrum of **TEMPOL-PS**

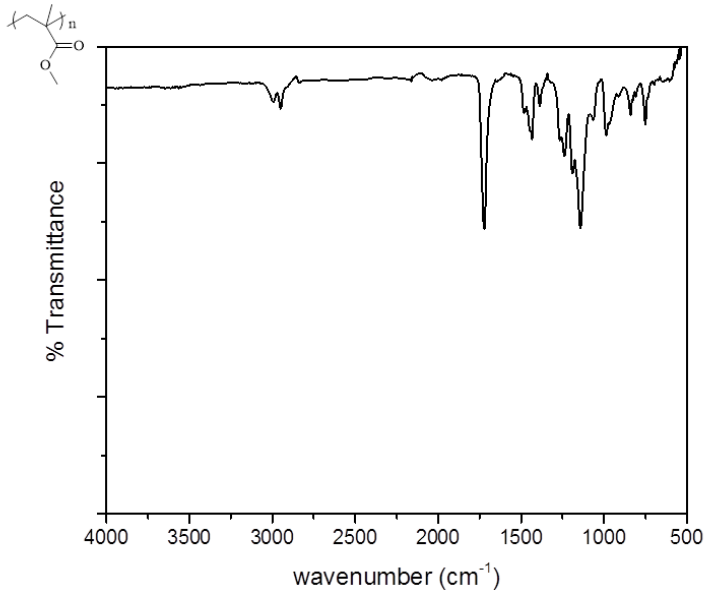


**Figure 26.** IR Spectrum of **PMMA**

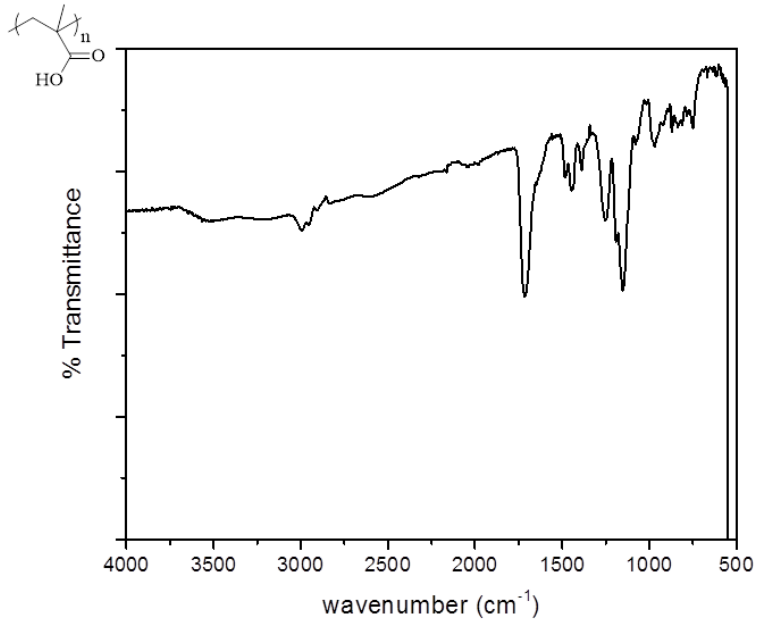


**Figure 27.** IR Spectrum of **PMMA-acid**

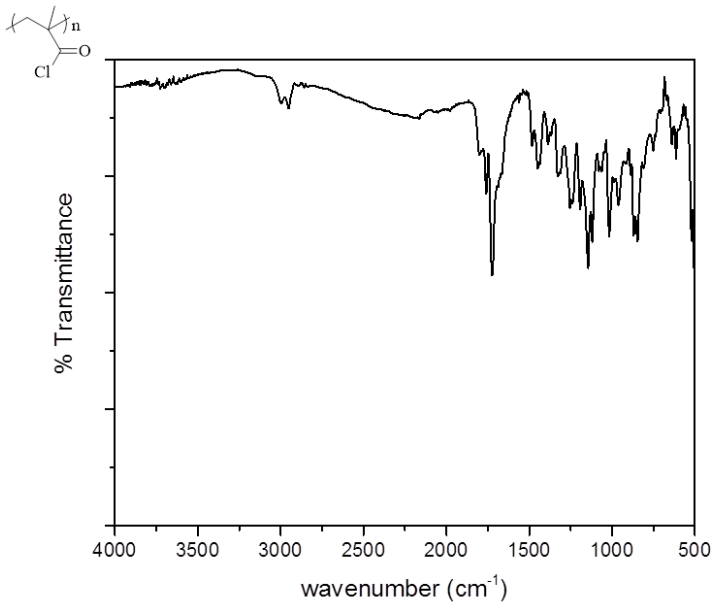


**Figure 28**. IR Spectrum of **PMMA-Cl**

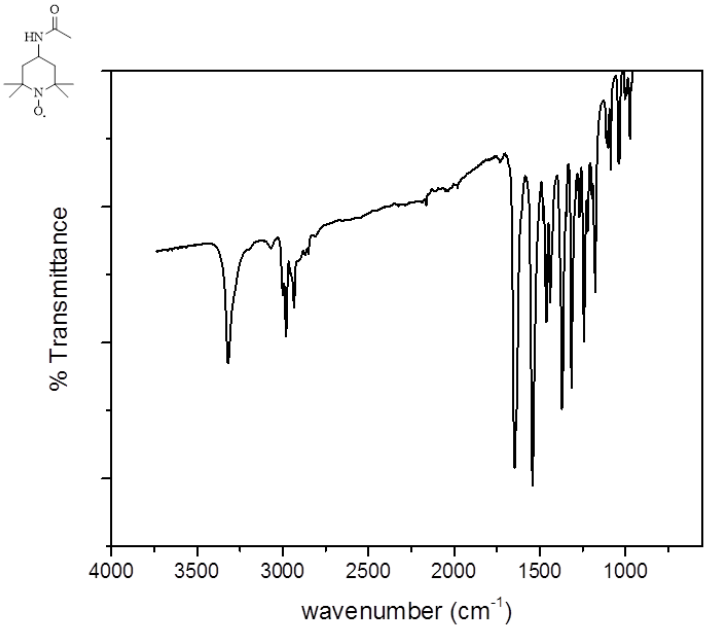


**Figure 29**. IR Spectrum of 4-acetamido-TEMPO

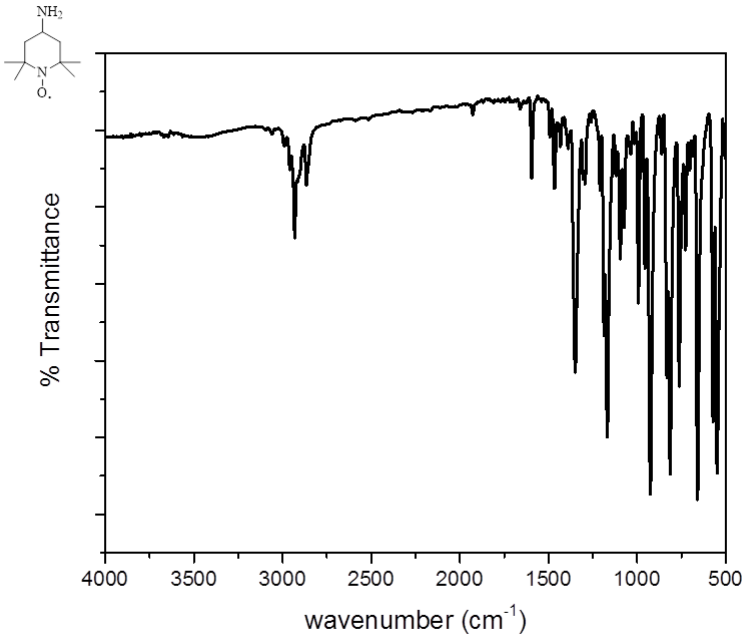


**Figure 30**.IR Spectrum of 4-amino-TEMPO

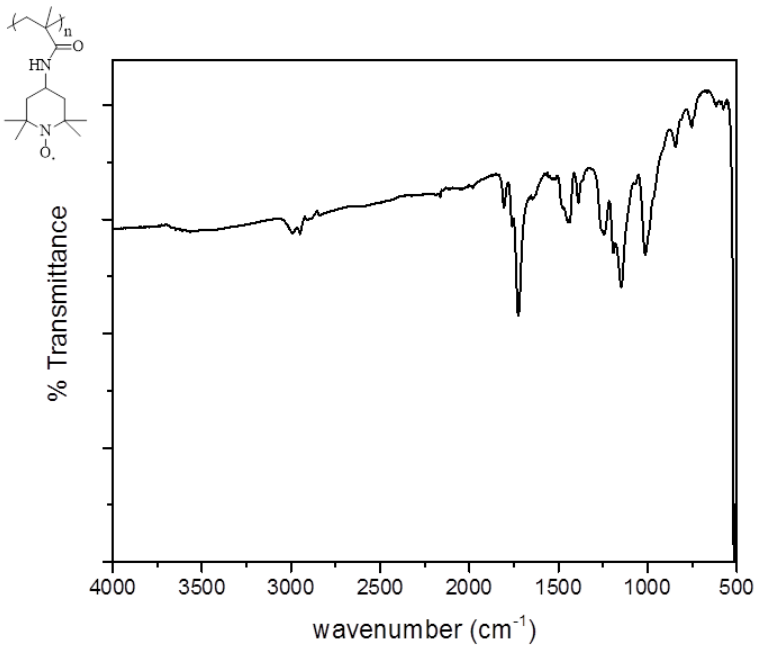


**Figure 31**. IR Spectrum of **TEMPOL-MET**

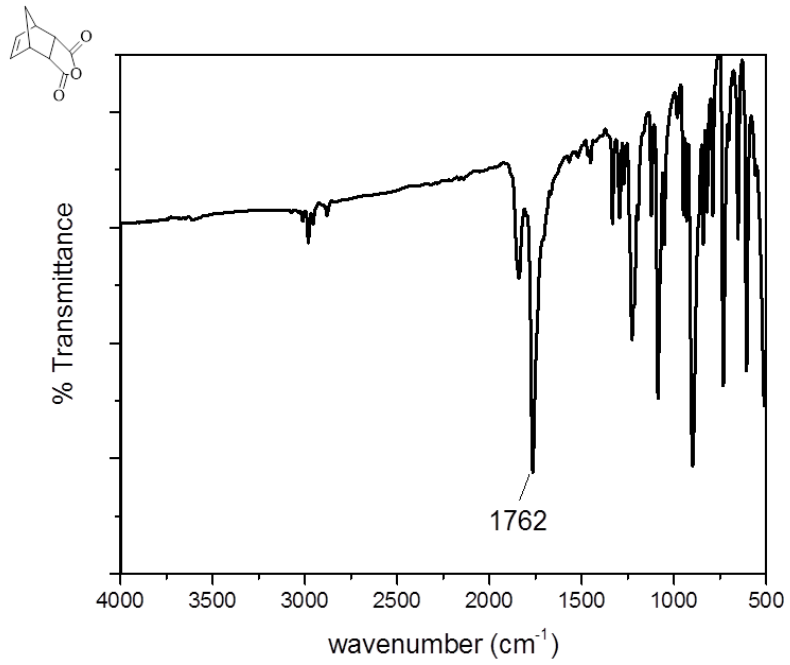


**Figure 32**. IR Spectrum of **norb-anh**

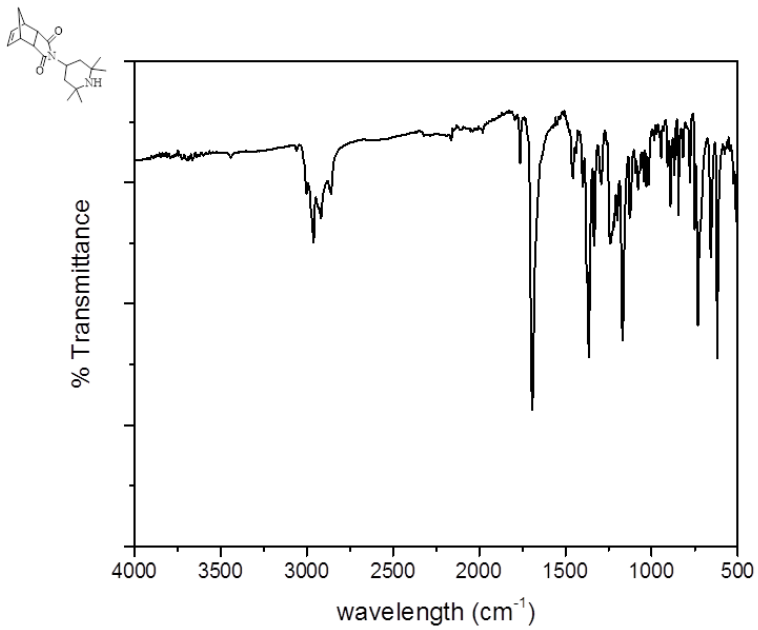


**Figure 33.** IR Spectrum of **mono-norb**

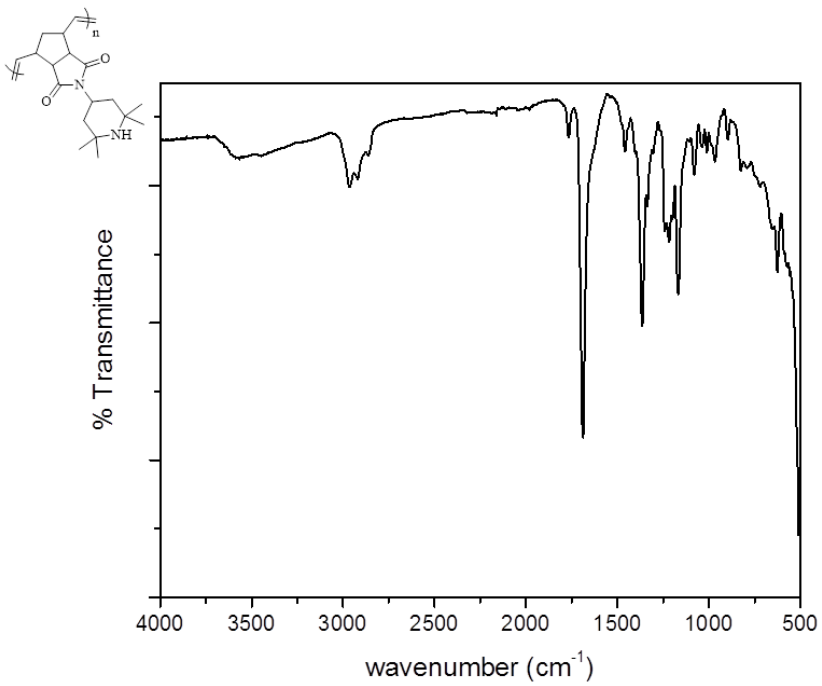


**Figure 34**.IR Spectrum of **pol-norb**

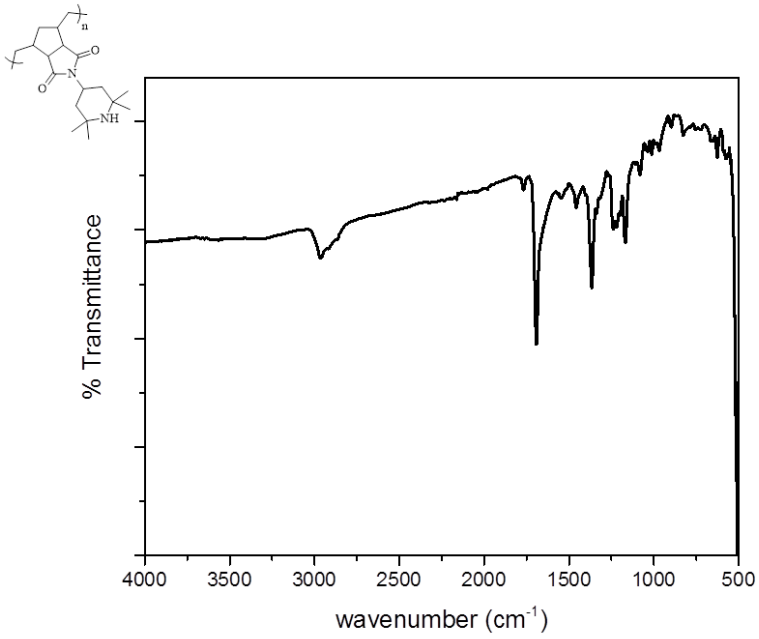


**Figure 35**. IR Spectrum of **(H)pol-norb**

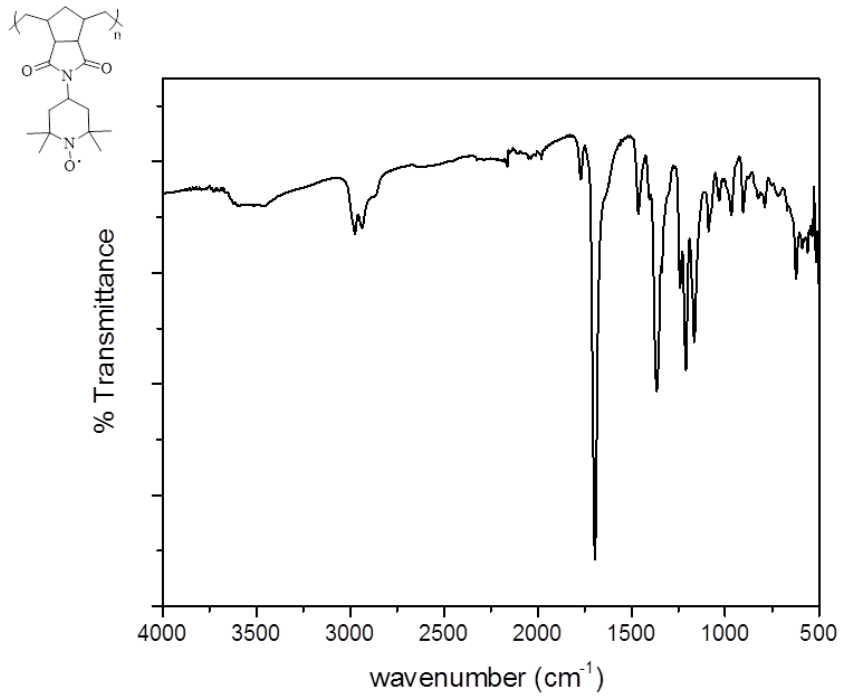


**Figure 36.** IR Spectrum of **TEMPOL-NORB**