ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

THIOL-BENZOXAZINE CHEMISTRY AS A NOVEL THIOL-X REACTION FOR THE SYNTHESIS OF BLOCK COPOLYMER

M.Sc. THESIS

Abdulrahman MUSA

Department of Chemistry

Chemistry Programme

MAY 2014

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

THIOL-BENZOXAZINE CHEMISTRY AS A NOVEL THIOL-X REACTION FOR THE SYNTHESIS OF BLOCK COPOLYMER

M.Sc. THESIS

Abdulrahman MUSA
(509121039)

Department of Chemistry

Chemistry Programme

Thesis Advisor: Prof. Dr. Yusuf YAĞCI

May 2014

İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

BLOK KOPOLİMERLERİN SENTEZİ İÇİN YENİ BİR SENTETİK YÖTEM: TİYOL BENZOKSAZİN KİMYASI

YÜKSEK LİSANS TEZİ

Abdulrahman MUSA
(509121039)

Kimya Anabilim Dalı

Kimya Programı

Tez Danışmanı: Prof. Dr. Yusuf YAĞCI

MAYIS 2014

Abdulrahman Musa, an **M.Sc.** student of ITU **Graduate School of Science Engineering and Technology** student ID **509121039** successfully defended the **thesis** entitled "**THIOL-BENZOXAZINE CHEMISTRY AS A NOVEL THIOL-X REACTION FOR THE SYNTHESIS OF BLOCK COPOLYMER**", which he prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

Thesis Advisor :	**Prof. Dr. Yusuf YAĞCI** Istanbul Technical University	....
Jury Members :	**Prof. Dr. Okan SİRKECİOĞLU** Istanbul Technical University	....
	Prof. Dr. Nihan NUGAY Boğaziçi University	....

Date of Submission : 05 May 2014
Date of Defense : 29 May 2014

To my family,

FOREWORD

I will like to thank all the personalities that have contributed, either directly or indirectly, towards the success of this project.

I want to start by extending my sincere thanks and appreciation to my supervisor, Prof. Dr. Yusuf YAGCI, for broadening my knowledge and understanding of polymer synthesis and for his constant guidance, friendship and motivation during this project.

I owe a debt of gratitude to, Asst. Prof. Baris KISKAN, without whom the success of this project wouldn’t have come to a reality.

I also want to express my special thanks to my laboratory colleagues for all their help, support and assistance. They include; Ali Gorkem Yilmaz, Omer Suat Taskin, Sajjad Dadashi Silab, Mustafa Cifci, Muhammad Aydin, Mustafa Arslan, Cansu Aydogan, Elyesa Murtezi, Sean Doran, Huseyin Akbulut, Semih Erdur, Elif Semerci, and Senem Körk among others.

Finally, I want to reserve a special thanks to my parents, brothers and sisters for their continuous support, understanding, love and encouragement throughout my academic struggle.

.

May 2014 Abdulrahman MUSA

(Chemist)

TABLE OF CONTENTS

ABBREVIATIONS

^{1}H-NMR : Nuclear Magnetic Resonance Spectroscopy
AIBN : 2,2'-Azobis(2-methylpropionitrile)
ATRP : Atom Transfer Radical Polymerization
B-Prg : Propargyl Benzoxazine
Bpy : 2,2'-Bipyridine
COLBERT : Catalytic Opening of the Lateral Benzoxazine Rings by Thiol
CRP : Controlled Radical Polymerization
CTA : Chain Transfer Agent
DMF : Dimethylformamide
EBiB : Ethyl-2-Bromoisobutyrate
FTIR : Fourier Transform Infra Red
GPC : Gel Permeation Chromatography
MA : Methyl Acrylate
PEG : Poly(ethylene glycol)
PEG-N$_3$: Poly(ethylene glycol) with azide end-group
PMA : Poly(methyl acrylate)
PMA-N$_3$: Poly(methyl acrylate) with azide end-group
PS : Polystyrene
PS-TCT : Polystyrene with thiocarbonylthio end-group
RAFT : Reversible Addition Fragmentation Chain Transfer
SFRP : Stable Free Radical Polymerization
THF : Tetrahydrofuran

LIST OF TABLES

Page

LIST OF FIGURES

Page

THIOL-BENZOXAZINE CHEMISTRY AS A NOVEL THIOL-X REACTION FOR THE SYNTHESIS OF BLOCK COPOLYMER

SUMMARY

Recent advances in the field of polymer science and technology has provided diverse approaches to the synthesis of different polymer products which have been used to modify the standard of our modern life today. Synthesis of most of these polymeric materials with well-defined and modified architecture were only possible due to advances in the concept of controlled radical polymerization. The most efficient of this synthetic approach include; Atom Transfer Radical Polymerization (ATRP), Reversible Addition-Fragmentation chain Transfer (RAFT) process, and stable radical mediated polymerization. These controlled radical polymerization methods have helped in the expansion of the synthetic approaches towards production of copolymers with desired molecular weights, structures and novel properties.

This thesis reports a novel approach towards the preparation of a block copolymer using the concept thiol-Benzoxazine chemistry which is an example of click reaction. In this work, a benzoxazine moiety with an alkyne functional group was synthesized by the reaction of formaldehyde, phenol and propargyl amine. This product was used as a click linking agent to couple two different polymer chains, (polystyrene with thiol end group and poly(methyl acrylate) with azide functional group), together ,by ring opening of benzoxazine, and azide-click reactions respectively. In the first step, the polystyrene with thiol end functional group was reacted with the benzoxazine click linker leading to ring opening of benzoxazine with the preservation of alkyne group of the latter. In the second step, polymethyl acrylate with an azide end functionality was used to couple this polymer to the alkyne arm of the click linker leading to the synthesis of the block copolymer. The success of this synthetic approach was investigated using both ^{1}H-NMR and infrared spectroscopic techniques. The spectrum of the block copolymer PS-*b*-PMA clearly showed resonance characteristic peaks of polystyrene (7.21 ppm), and poly(methyl acrylate) (3.71 ppm). The IR spectrum also showed the complete disappearance of the azide stretch at 2100 cm^{-1}.

BLOK KOPOLİMERLERİN SENTEZİ İÇİN YENİ BİR SENTETİK YÖTEM: TİYOL BENZOKSAZİN KİMYASI

ÖZET

Polimerler yaşamımızı kolaylaştırmak için kullanılan önemli materyellerdir. Bilim ve teknolojideki gelişmelerde polimer bilimi önmeli bir yer tutmaktadır. Her gün gelişen yeni polimer sentez yöntemleri sayesinde elde edilmiş binlerce polimere hergün yenileri ilave edilmektedir. Günlük hayatın hemen her alanında rastlanan polimerik malzemeler, hayatın vazgeçilmez parçaları olmuşlardır.Polimerik malzemelrin bu kadar geniş kullanım alanlarına sahip olmalarının nedeni, yapısal özelliklerinin istenildiği gibi ayarlanabilir olmasından ve ekonomik olarak elde edilebilmelerinden kaynaklanmaktadır. Yapısal özelliklerinin istenildiği gibi ayarlanabilir olması, monomerlerin kendi kendileriyle ve diğer monomerlerle bağlanmalarında, bağlanma şekillerinin ve bağlanma miktarlarının fazlalığının bir sonucudur. Ayrıca istenilen fonksiyonlara sahip polimerler de uygun fonksiyonel gruplu monomerler kullanılarak kolayca hazırlanabilir. Doğrusal bir polimer, yeterince yüksek sıcaklıklarda amorf, kauçuksu bir eriyiktir. Zincirler birbiri içine giren yumak görünümünde olup, bir konformasyondan öbürün rastgele dönme ve bükülme hareketleri yapar. Yeterince düşük sıcaklıklada ise aynı polimer sert bir katıdır. Bir polimer soğutulduğunda birbirinden farklı iki mekanizma ile kristallenir. Bunlardan biri kristallenme diğeri ise camsılaşmadır. Bir polimerik maddenin ne tür pratik uygulamaya elverişli olduğu belirleyen faktörlerden biri Te (kristal erime noktası) ve Tg (camsı geçiş sıcaklığı) ile belirlenir.

Uzun zincirler halinde bulunan lineer ya da dallanmış zincirlerden oluşan polimer sistemlerine aynı zamanda termoplastik adı da verilmektedir. Yüksek oranda çapraz bağ içeren sistemler ise termosetting olarak tanımlanır. termoplastik bir malzeme sıcaklık artışı ile eriyerek şeklini değiştirebilir ve böylece kalıplara dökülebilmesi mümkün olur. Oysa yüksek oranda çapraz bağ içeren bir yapının sıcaklık artışı ile böyle bir değişim geçirmesi, zincirlerin hareketli olmayışı nedeniyle zordur ve sıcaklığın artışı bu tür malzemelerin erimesine değil, malzemenin parçalanmasına neden olur.

Tek tür birimlerden oluşan polimer zinciri homopolimer, iki ya da daha fazla monomer içeren polimerler ise kopolimer olarak adlandırılırlar. Kopolimerler genellikle farklı monomerlerin düzensiz birleşmesinden oluşarak rastgele (random) kopolimeri oluştururlar. Bununla beraber, alternatif, blok, graft kopolimerleri de mevcuttur. Alternatif kopolimerde monomer birimleri birbiri ardına gelir. Blok kopolimer farklı homopolimerlerin uzun segmentlerini içerir. Blok kopolimerlerin kullanımı gün geçtikçe artmaktadır. Bu artışın sebebi sadece farklı sentetik metotlara uygunluğundan değil aynı zamanda yaşayan polimerizasyondaki gelişmelerden de kaynaklanmaktadır. Graft kopolimer ya da diğer bir deyimle aşı kopolimer ise asıl mevcut bir polimer

zinciri üzerinde bir dallanma olarak ikinci bir monomer içerir. Polimerler lineer, dallanmış ve ağ olarak da tanımlanırlar. Lineer polimerde hiçbir dallanma yoktur.
Graft Kopolimerler dallanmış polimerlerin bir örneğidir. Ağ (Network) polimerler, difonksiyonlu monomerler yerine, polifonksiyonlu monomerler kullanıldığında meydana gelirler. Ağ polimerler ayrıca çapraz bağlı polimerleri de kapsarlar. Çünkü çapraz bağlanmayla polimer zincirleri hareketliliklerini kaybederler.
Benzoksazinler birincil amin, fenol ve formaldehit kullanılarak elde edilen organic moleküllerdir. Bu moleküller birçok polimer sentezinde kullanılabilir. Halka açılma polimerizasyonu ile polibenzoksazinleri oluştururlar. Polibenzoksazinler, yeni tip fenolik reçine olup, fenol formaldehit reçinelerinin birçok özelliğini barındırmakla beraber, çok az su tutması, kürlenme işleminde boyut değiştirmemesi ve yüksek termal karalılığından dolayı büyük ilgi uyandırmıştır. Ayrıca polibenzoksazinler, ilginç bir çok özellikleri ile novalak ve resol tipi fenolik reçinelerine daha üstün gelen yeni geliştirilmiş fenolik sistemlerdir. Bu malzemeler (i) kürleme sırasında hemen hemen hacimsel değişime uğramayışı (ii) düşük su absorpsiyonu (iii) bazı polibenzoksazinler için Tg (camsı geçiş sıcaklığı) kürlenme sıcaklığından yüksek oluşu (iv) yüksek yanma ürünü yüzdesi (v) kürleme için asit gerektirmemesi (vi) kürleme sırasında yan ürün oluşturmaması gibi özellikler gösterirler. Polibenzoksazinlerin moleküler yapıları kürlenmiş malzemelerin özelliklerini farklı uygulamalar için geniş bir aralıkta değiştirme imkanı tanır. Benzoksazin monomerleri ve karışımları, polimerizasyon mekanizmaları, kürlenmiş malzemelerin yapı özellik ilişkileri çeşitli araştırma grupları tarafından araştırılmıştır. Fakat saf polibenzoksazin kimyasının (i) yüksek kürleme sıcaklığı (~ 200°C veya üstü), (ii) işleme zorluğu ve (iii) kırılganlık gibi dezavantajları vardır. Bu dezavantajların üstesinden gelmek için birçok araştırmacı değişik stratejiler denemiştir. (i) Çeşitli fonksiyolu gruplarla modifiye edilmiş benzoksazin sentezi, (ii) polimerik benzoksazin sentezi, (iii) dolgu maddeleri, fiberler veya başka yüksek perfrmanslı polimerlerle karıştımak denenmiştir.

Polimer bilimindeki ve teknolojisindeki son gelişmeler, yüksek hayat standartları sunan polimerik malzemelerin sentezi ve hazırlanışı için yeni metotlar sunmuştur. Molekül ağırlığı ve yapısı kontrol edilebilir özellikteki bu polimerlerin sentezi kontrollü polimerizasyon yöntemlerinin kullanımı ile mümkün olabilmiştir. Bu sentetik yaklaşımların en önemlileri Atom Transfer Radikal Polimerizasyonu (ATRP), Tersinir Eklenme, Ayrılma, Zincir Transferi (RAFT) Polimerizasyonu ve kararlı radikal aracılığı ile olan polimerizasyonlardır. Bu kontrollü radikal polimerizasyonn yöntemleri, istenilen molekül ağırlık özelliğinde ve yapısal özellikteki kopolimerlerin sentezini sağlayan yaklaşımlar olmuştur.
Bu tez, bir “çıt çıt” tepkimesi olan “tiyol-benzoksazin kimyası” yöntemi ile blok kopolimerlerin sentezini va karakterizasyonunu konu almaktadır. Bu çalışmada, formaldehit, fenol ve propargil aminin tepkimesi ile alkin fonksiyonel grubuna sahip bir benzoksazin molekülü sentezlenmiştir. Bu molekül iki farklı fonksiyonel grup taşıyan iki farklı polimeri (tiyol uçlu polistiren ve azit uçlu polimetil akrilat) iki farklı “çıt çıt” tepkimesi ile (tiyol-benzoksazin halka açılması ve bakır katalizli azit alkin halka katılması) bağlamak üzere kullanılmıştır. İlk aşamada tiyol uçlu polistiren molekülü benzoksazin molekülü ile halka açılma tepkimesine girmiş ve alkin grubu

korunmuştur. İkinci aşamada, azit uçlu polimetil akrilat, oluşan poimerik yapıdaki alkin ucu ile tepkimeye girerek blok kopolimerin ikinciş segmentini oluşturmuştur. Oluşan yapı ^{1}H-NMR, FT-IR gibi spektroskopik yöntemlerle incelenmiş ve kullanılan yöntemin başarısı ortaya konmuştur. ^{1}H-NMR spektrumu, polistirene ait aromatik pikleri ve polimetil akrilata ait ester pikini taşımaktadır. FT-IR spektrumu da 2100 cm^{-1} civarındaki azit pikinin kaybolduğunu göstermektedir.

1. INTRODUCTION

Polymers are important raw materials in all walks of human life, and they are used to manufacture different products that are necessary for man’s modern activities in a way that makes living comfortable as it is today. The advances in science and technology made in recent decades owe much to development of polymer science. The synthesis and designing of new polymeric materials to achieve specific physical properties and specialized applications, and attempt to find interesting applications involving advanced structures, are in continuous development in the field of the polymer science. Polymer chemists have a variety of synthetic processes to choose from when planning a particular synthesis.

Block copolymers have become increasingly important in recent years. This importance is not only due to the availability of various synthetic methods but also due to recent developments in controlled/ living polymerization. Polymerization of two monomers in a sequential manner using controlled/ living polymerization methods, allow preparation of block copolymers with well-defined structure and chain lengths. However, depending on specific targeted applications, it is often required to combine monomers polymerized by different mechanisms. The transformation polymerization appears to be a model method to combine diverse polymerization mechanisms. This way, many monomers with different chemical structures can be polymerized to yield block copolymer with novel properties.

Recent advances in controlled radical polymerization have been applied to synthesis of wide range of well-defined specific polymer architecture. Several methods such; ATRP, stable radical mediated polymerization and RAFT processes have been accepted to be the most efficient of these methods. These controlled radical polymerization technique have helped in the expansion of the synthetic approaches towards production of copolymers.

Benzoxazines are a class of organic molecules formed by the reaction of primary amines, phenols and formaldehydes in either solvent or solventless system. This particular organic compound have been used for many polymer synthesis processes. They can be polymerized by thermal ring-opening reactions to form polybenzoxazine, which is a family of phenolic resins that has attracted significant attention in the field of polymer synthesis. This development stemmed from the fact that, the formed polybenzoxazines overcome many shortcomings associated with traditional phenolic resins such as releasing condensation by-products and using strong acids as catalyst.

In this work, a benzoxazine compound having an acetylene functional group was synthesized from phenol, propargylamine and formaldehyde. This benzoxazine precursor was used to couple two polymer chains together in a way that makes it satisfies the characteristics of a typical click reaction, not just giving a better product yield, but the reaction was successfully conducted at ambient temperature in easily removable solvents. Poly(methyl acrylate) (PMA), was synthesized via ATRP after which the bromide end group of this polymer was converted to an azido end functionality using sodium azide. RAFT process was used to synthesize Polystyrene PS with a dithiobenzoate end funtionality which was later transformed to a thiol end group by reduction using 1, 2-ethanedithiol. By taking the advantage of benzoxazine chemistry, particularly the COLBERT reaction, benzoxazines can be used as a linker between the two different polymers forming a block copolymer. The present work aims at exploiting and introduction of a new thiol-X chemistry for macromolecular synthesis based on COLBERT reaction occurring between benzoxazine ring and thiol compounds. This objective is accomplished with additional synthetic strategy that will provide its compatibility with well-established Huisgen type click reaction. As will be shown below, independently prepared thiol and azido end-functional polymers were coupled by using propargyl functional benzoxazine via COLBERT and Huisgen type click reactions in one-pot and also in sequential steps. FTIR and NMR and GPC spectroscopic techniques were used to investigate the success of the formed copolymer.

2. THEORETICAL PART

2.1 Benzoxazine Chemistry

Benzoxazines are organic molecules that consist of a single benzene ring fused to another six-membered heterocycle containing one oxygen and a nitrogen atom [1]. The first synthesis of this type molecules was recorded in the works of Cope and Holly in 1940s [2]. He used condensation reaction of primary mines, formaldehyde and phenol to obtain the products. Since that time, a lot of academic and industrial research interest into the chemistry of this class of organic molecules have increased [3, 4]. Typically, benzoxazine monomers are synthesized by using phenol, formaldehyde and amines (aliphatic or aromatic), as starting materials, (Figure 2.1).

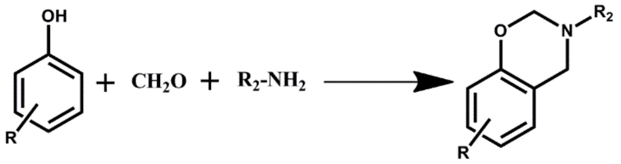


Figure 2.1 : General scheme for the synthesis of benzoxazines.

and the possible ring formation mechanisms that are proposed are illustrated in (Figure 2.2). Benzoxazine ring stability is strongly effected from the substituents on the ring. When there is more than one reactive ortho position in the starting product, it may lead to another aminoalkylation reaction. Ortho substituent having phenols provide higher yields in produced benzoxazines. Several types of benzoxazine monomers can be obtained by using different phenols and amines. Substitution groups of these phenol and amines may serve as additional polymerizable sites which may effect the curing process. Accordingly, polymeric materials with chosen properties can be prepared by using adjusted monomers. Their synthesis are carried-out using either solvent or solventless method. Many of the works on solventless method are recorded in the works of Ishida et al [5]. However, in practical application, some limitations emerged from the use of benzoxazine monomer precursor, since fabrication of films from mono functional benzoxazines are difficult because the formed films are brittle due to their low molecular weight and non-flexibility of the work structure [6-10].

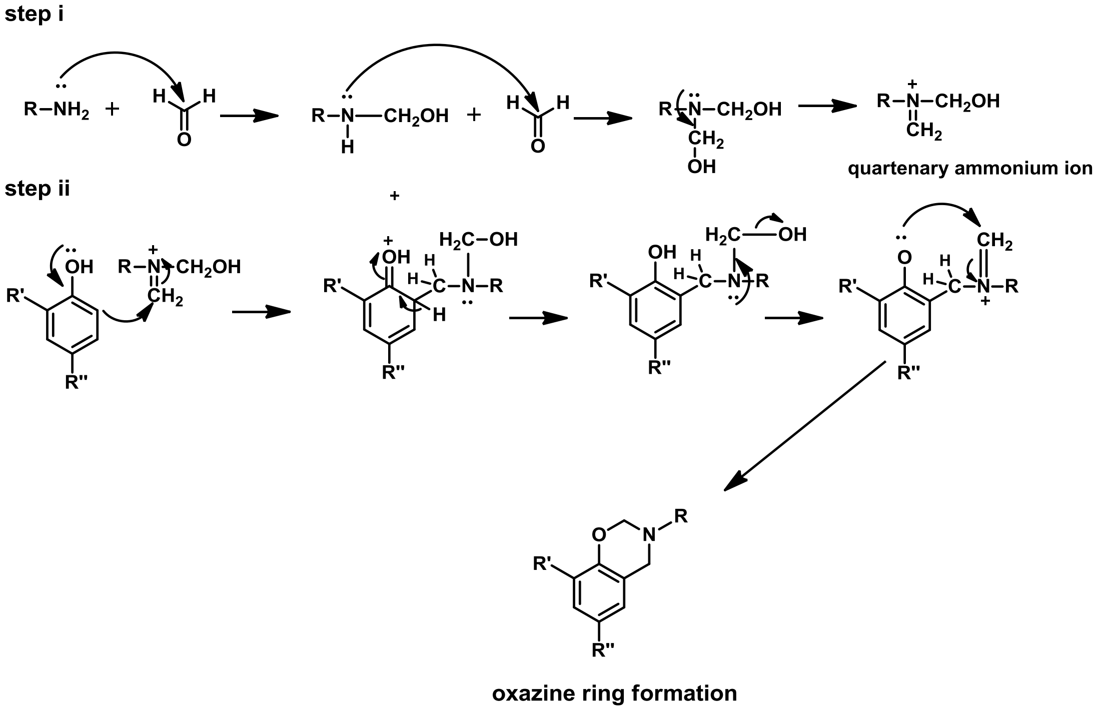


Figure 2.2 : Possible mechanism of benzoxazine ring formation.

To overcome these problems, new benzoxazine monomers with additional polymerizable groups were developed to increase the crosslinking, density and glass temperature properties of these set monomers [11-14]. These benzoxazine monomers when polymerized, form phenolic systems with fascinating features which overcome several short comings of convectional novalac and resole type phenolic resins (Figure 2.3). Some of their attractive properties include; low water absorption, dimensional stability, chemical resistivity and flame resistance [15, 16].The above mentioned properties of benzoxazine derivatives made them have wide range applications such as; used as composite material [17], manufacture of commodity materials and in high technology aerospace industries.

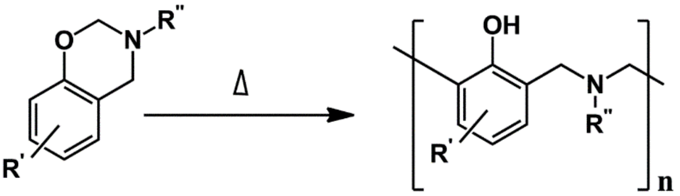


Figure 2.3 : Thermal polymerization of benzoxazine

In related work from this laboratory, we have reported various methodologies to introduce benzoxazine moieties into mesoporous and nano structures, and polymers as main chain or side chain functional groups using conventional and controlled radical polymerizations as well as step-growth polymerization methods, and Huisgen type click chemistry. This way, several specific properties of benzoxazines such as processability, film forming and toughness are enhanced. During the course of our attempts to photochemically crosslink bifunctional ally-benzoxazines with multifunctional thiols, it soon became evident that besides the expected thiol-ene reaction, the benzoxazine ring was opened with thiols even in dark at room temperature. Such novel thiol reaction with 1,3-benzoxazines that proceed through a catalytic ring opening at ambient conditions was previously noted by Gorodisher et al. The process was named as Catalytic Opening of the Lateral Benzoxazine Rings by Thiols (COLBERT reaction) which presumably proceeds by an acid catalyzed nucleophilic addition and simultaneous ring-opening reaction. In the first step, thiol protonates the amine of benzoxazine ring and an ionic intermediate is formed. Then, the resulting thiolate attacks the methylene carbon adjacent to N and O atoms and concurrent ring-opening of the benzoxazine occurs (Figure 2.4).

2.2 Controlled Radical Polymerization

Free radical polymerization is very important commercial process for preparing high molecular weight polymers because it can be used for the polymerization of many vinyl monomers under mild conditions, requiring the absence of oxygen but tolerant to water, and large temperature ranges (20^o C – 200^o C). In addition, many monomers can easily copolymerize radically leading to an infinite numbers of copolymers with properties depending on the comonomers. The only disadvantage of this method when compared with convectional radical polymerization is the poor control of macromolecular structures including degrees of polymerization, polydispersities, end functionalities, chain architecture and compositions. The synthesis of well-defined polymers has long been of great interest in polymer chemistry. Typically, living polymerization techniques are employed where the polymerizations proceed in the absence of irreversible chain transfer and chain termination. The development during the last decade of various processes for the control of free radical polymerization (CRP) has led to new ways of synthesizing polymers with low polydispersity, new architecture, composition, functionalities and molecular composition [18]. In recent years, synthesis of polymers using this concept are reported in the works of Haddleton and co-workers as well as Thang et al [19].

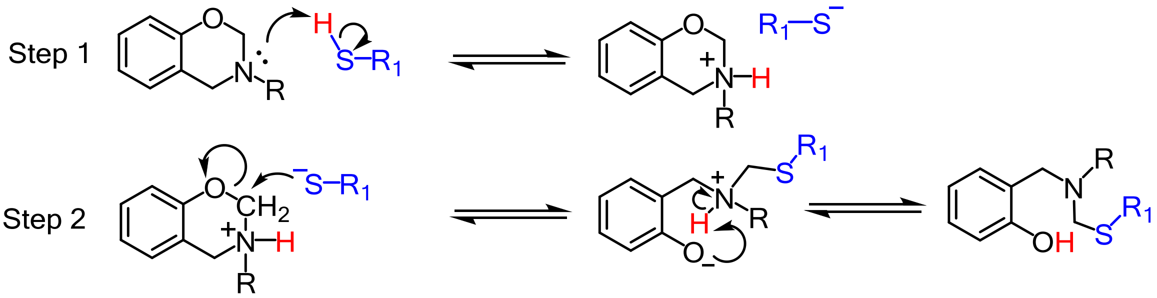


Figure 2.4 : Proposed reaction mechanism of catalytic opening of the lateral benzoxazine rings by thiols.

The most widely used of the CRP methods are ATRP [20, 21], RAFT [22], and Nitroxide-mediated radical polymerization NMRP [23]. The synthesis of polymers using ATRP approach is more versatile because, it is a simple polymerization procedure, compatible with most functional groups and allows for synthesis of polymers with very good architectural and molecular weight control.

2.2.1 Atom Transfer Radical Polymerization.

ATRP is of the methods of controlled radical polymerization used for the synthesis of polymers based on the reversible transfer of halogen atoms, or pseudo-halogens, between a dormant species (P_n–X) and a transition metal catalyst (M_nt /L) by redox chemistry. The name comes from the atom transfer step, which is the elementary reaction responsible for the uniform growth of the polymeric chains. The use of ATRP is the simplest and most versatile methods of CRP because the method works with readily accessible inexpensive initiators whose active end groups normally consist of simple halogens (Figure 2.5), and also its ability to polymerize a wide range of monomers. Although the direct polymerization of vinyl acetate and acrylic acids has not yet been successful. ATRP has been carried out in bulk, solution, dispersion and emulsion at temperatures ranging from -20^o C to 130^0 C. Some tolerance to oxygen has been reported in the presence of zero-valent metals [24]. During ATRP process, the alkyl (pseudo)halides are reduced to active radicals and transition metals are oxidized via an inner sphere electron transfer process [25]. In the most studied system, the role of the activator is played by a copper (I) species complexed by two bipyridine ligands and the role of deactivator by the corresponding copper (II) species. Here, the key step in controlling the polymerization is the transfer of an atom (or group) between the dormant chain and the transition metal catalyst in a lower oxidation state forming an active chain end and a transition metal deactivator in a higher oxidation state [26-28]. The general mechanism of ATRP is depicted in Figure 2.6.

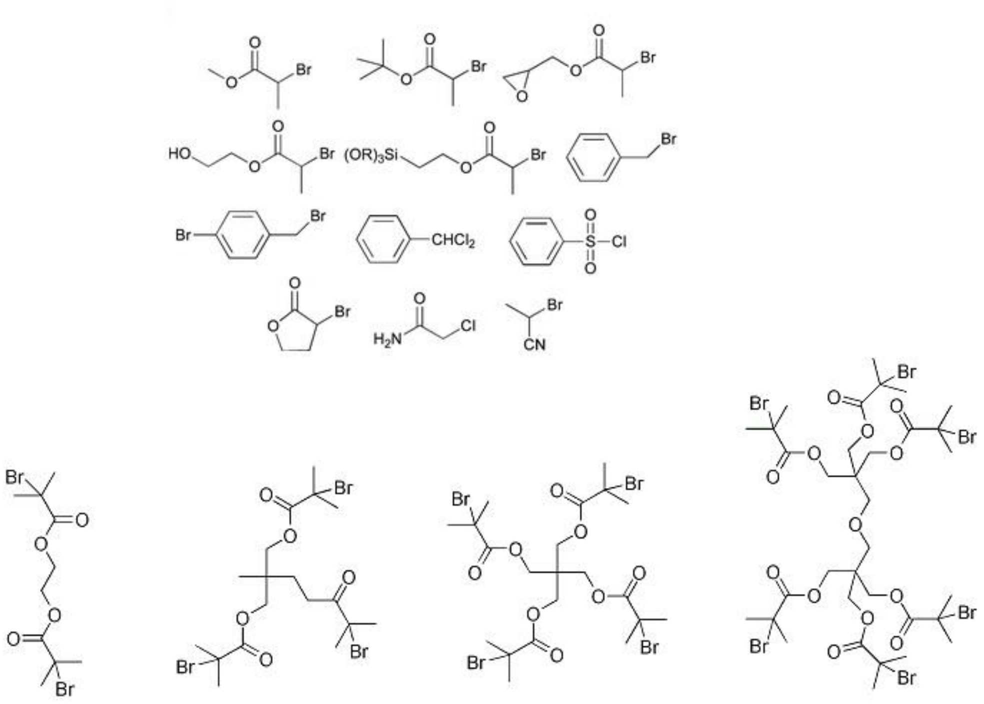


Figure 2.5 : Example of ATRP initiator

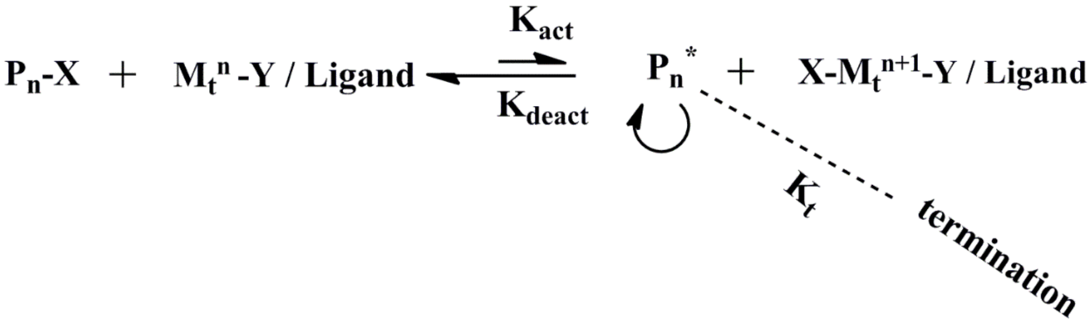
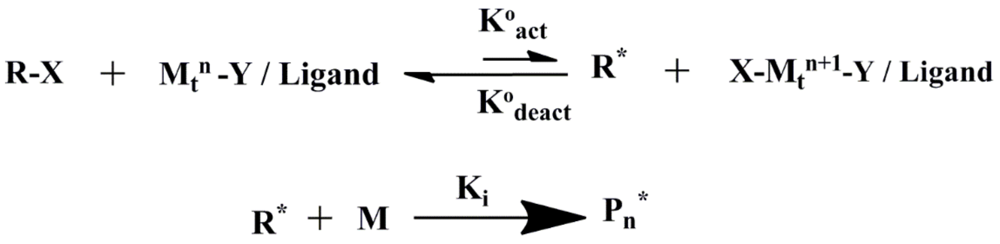


Figure 2.6 : General mechanistic pathway of ATRP method

In ATRP, polymer chains grow by the addition of the free radical to monomers in a manner similar to a convectional radical polymerization, with the rate constant of propagation, K_p. Termination reactions, K_t, also occur in ATRP mainly through radical coupling and disproportionation; however, in a well-controlled ATRP, no more than a few percentage of the polymer chains undergo termination. The elementary reactions consisting of initiation, propagation, and termination are shown in (Figures 2.7, 2.8, and 2.9). Other side reactions may additionally limit the achievable molecular weights. Typically, no more than 5% of the total growing polymer chains terminate during the initial, short, nonstationary stage of the polymerization. This process generates oxidized metal complexes, the deactivators, which behave as persistent radicals to reduce the stationary concentration of growing radicals and thereby minimize the contribution of termination at later stages [29]. A successful ATRP will have not only small contribution to terminated chains but also uniform growth of all the chains which is accomplished through fast initiation and rapid reversible deactivation.

2.2.1.1 Initiation

Initiation involves the development of an active side by the monomer. This may occur spontaneously by the absorption of heat, light, or high energy irradiation. The double of monomer breaks apart, monomer bond to free radical and the free electron is transferred to the outside carbon atom in this reaction.



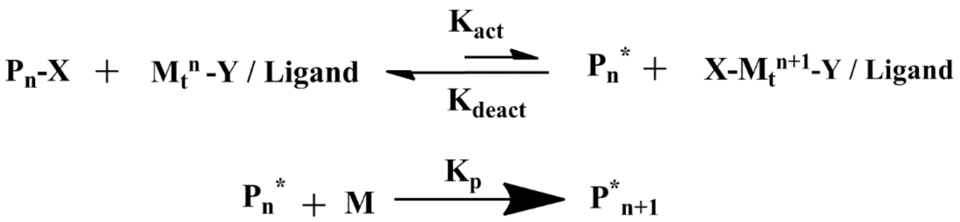
$$\mathbf{R\text{-}X} + \mathbf{M_t^{n}\text{-}Y / Ligand} \underset{K^{o}_{deact}}{\overset{K^{o}_{act}}{\rightleftharpoons}} \mathbf{R^{*}} + \mathbf{X\text{-}M_t^{n+1}\text{-}Y / Ligand}$$

$$\mathbf{R^{*}} + \mathbf{M} \xrightarrow{K_i} \mathbf{P_n^{*}}$$

Figure 2.7 : ATRP initiation step

2.2.1.2 Propagation

In this step, the initiated monomer adds to the other monomer. Addition of free radical to the double bond of monomer, with regeneration of another radical. The active center is thus continuously relocated at the end of growing polymer chain. Propagation is able to occur consistently because the energy in the chemical system is lowered as the chain grows. This step continues until the growing chain radical is deactivated by chain termination.



$$P_n\text{-}X + M_t^n\text{-}Y / \text{Ligand} \underset{K_{deact}}{\overset{K_{act}}{\rightleftharpoons}} P_n^* + X\text{-}M_t^{n+1}\text{-}Y / \text{Ligand}$$

$$P_n^* + M \xrightarrow{K_p} P^*_{n+1}$$

Figure 2.8 : ATRP propagation step

2.2.1.3 Termination

The last step Termination the growth activity of a polymer chain radical is destroyed by reaction with another free radical in the system to produce polymer molecules. Termination reactions are more important in polymer production are combination and disproportionation. In termination by combination, two growing polymer chain react with each other and destruct the growing activity. In disproportionation, unstable atom transferred from one polymer chain to the other. Coupling reactions generate a single polymer whereas disproportionation generates two polymers from two reacting polymer chain radicals. The dominant termination depends on nature of the reactant monomer. Disproportionation needs energy to break the chemical bonds and take place at high reaction temperatures. Combination of growing polymer radicals predominates at low temperatures.

$$P_n^* + P_m^* \xrightarrow{K_t} P_{n+m} \quad \text{or} \quad P_n^= + P_m^H$$

Figure 2.9 : ATRP Termination Step

2.2.2 Raft Polymerization

RAFT is among the most successful CRP processes due to its large applicability to a wide range of monomers. Exchange reactions in this technique are also very fast, which lead to well controlled systems. Successful application of the RAFT process requires the appropriate selection of a RAFT reagent for a particular monomer. In contrast to ATRP, the RAFT technique does not require any metal catalyst. Instead, thiocarbonylthio compounds, such as dithioesters, dithiocarbamates, trithiocarbonates, and xanthates (MADIX) are employed in order to mediate the polymerisationvia a reversible chain-transfer process. These reagents are called chain transfer agents (CTA). The mechanism itself is complex. It is based on two chain-transfer and two chain-propagation equilibria which establish control over the radical polymerization. Various dithioesters, dithiocarbamates, trithiocarbonates and xanthates have been effectively used as transfer agents to control molecular weights, molecular weight distributions, and even molecular architecture [22, 30]. Reversible chain transfer may, in principle, involve homolytic substitution, or addition-fragmentation (RAFT) or some other transfer mechanism. An essential feature is that the product of chain transfer is also a chain transfer agent with similar activity to the precursor transfer agent. The overall process has also been termed degenerate or degenerative chain transfer since the polymeric starting materials and products have equivalent properties and differ only in molecular weight (Figure 2.10).

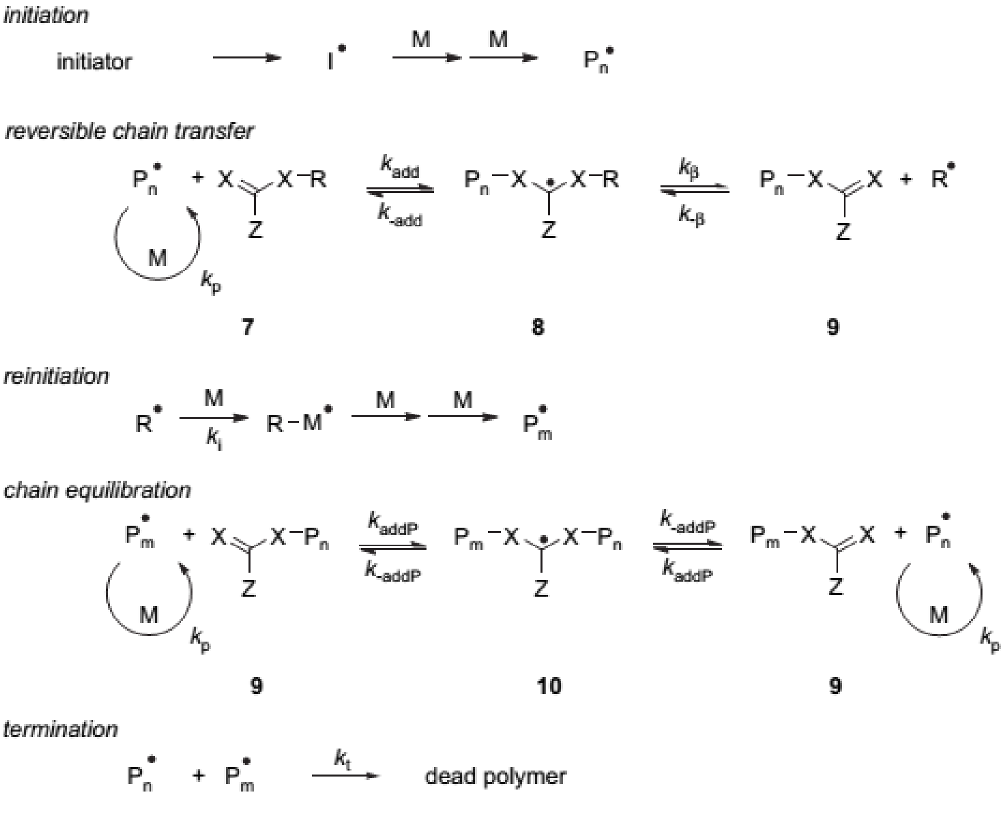


Figure 2.10 : Mechanism of RAFT polymerization

2.3 Thiol Chemistry

Thiol Chemistry is an important concept in organic chemistry which can be applied for the synthesis of functional polymers using post polymerization modification (PPM). This synthetic approach is easily achieved using thiols because, they can react with many groups including; acrylates, enes, ynes, halogens, epoxy and many others

[31-35] (Figure 2.11). One of the earliest systematic studies regarding the post-polymerization modification of polyBu via radical thiol addition was reported by Serniuk and coworkers in 1948 [36]. They proposed that only the vinyl groups generated by 1, 2-addition of butadiene units (i.e., pendant vinyl groups) were functionalized. Since these early studies, thiol–ene post-polymerization modification has developed into a powerful synthetic tool. Radicals that mediate the thiol–ene addition can either be generated by thermal or photochemical initiation. Hawker and coworkers illustrated that, although both initiation pathways lead to the complete conversion of pendant alkenes, milder conditions and shorter reaction times are sufficient when photoinitators are used [37]. Furthermore, they also demonstrated the orthogonality of the radical thiol addition and CuAAC and the compatibility of the alkene group with controlled radical polymerization (CRP) techniques. Recently, Heise reported the preparation of an unsaturated polyester (polyGI) via enzymatic ring-opening polymerization (ROP) of the corresponding cyclic ester monomer containing backbone alkene groups. He demonstrated that these backbone alkene groups are also susceptible to post-polymerization modification via thiol–ene addition, but near-quantitative conversion of these groups is only possible when a high excess of thiol is used, as these backbone alkene groups have decreased reactivity compared to pendant alkenes [38]. Owing to the fact that, this thiol reactions are facile and rapid, macromolecular structures with thiol functionalities can be easily converted to desired telechelic structures or materials [39]. The demand of well-defined polymers with thiol functionalities has increased in different areas, such as optics, microelectronics, and biotechnology, since the mercapto group establishes specific interactions with metals as gold, silver, and cadmium [40]. However, thiols are highly unstable species and not compatible with radical polymerization. This is because, they can cause side reactions with active species, monomers and catalyst. Hence, polymers with thiol functionalities need to be protected and used immediately after production or stored in a well-protected form. If properly and successfully synthesized, thiols have many

applications, including the production of biomaterials, hydrogels, thin films, cross-linked networks, self-healing coating and so on [41-47].

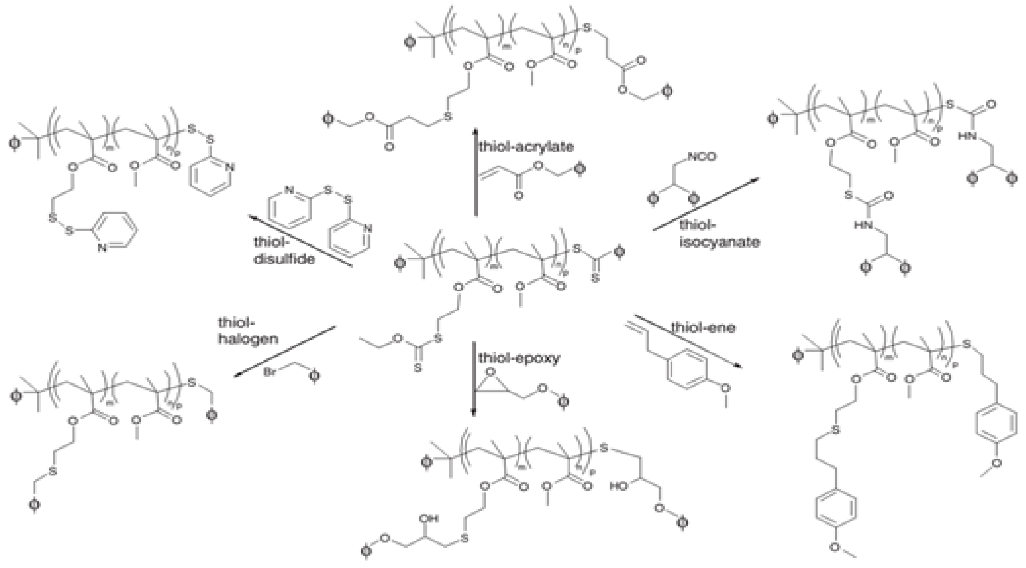


Figure 2.11 : One pot deprotection and functionalization of protected polythiol copolymer via different thiol-x- reactions

2.4 Click Chemistry

Click chemistry is a concept used to describe a class of reactions that have certain characteristics in common. For a reaction to be classified as a 'click', it has to be modular, wide in scope, highly yielding, generate in-offensive by-products that can easily be removed by non-chromatographic methods and should also be stereospecific. The concept was introduced by K. Barry Sharpless to refer to reactions that can generate desired products using easy and fast reaction conditions [48]. The most prominent example of click reaction is based on the well-established copper (1)-catalyzed Huisgen 1, 3-dipolar cycloaddition (CuAAC) reaction between azides and terminal alkynes [48, 49]. Other reactions which satisfy the criteria of a click chemistry include, nucleophilic ring-opening reactions of strained heterocyclic electrophiles [50], reactions of non-aldo carbon compounds (involving urea, oximes and hydrazones) [51], Diels-Alders Reaction [52-54], and addition to carbon-carbon multiple bonds (especially Thiol-ene chemistry and Michael additions) [37]. Click reactions possess chemoselective and single reaction trajectory characteristics, which are of great importance for the synthetic community. Indeed, chemists are increasingly focusing on the high yields, which can be achieved on a fast-time scale under mild conditions even when equimolar substrates are reacted. In these processes, only negligible concentration of easily removable by-products may be formed. Another feature of the concept concerns orthogonality since they are generally insensitive to moisture, oxygen, or any other contamination in the reaction media [55]. Applications of click reactions have had a profound effect on diverse areas of research. For example, over 5000 scientific articles have been published since 2001 regarding the use of click reactions for preparative organic synthesis, bio-conjugation, drug discovery, polymer and material sciences, and nanotechnology From these studies, it is clear that novel polymeric materials may be fabricated from new monomers, for example, monomers differing in chemical nature from “classical” monomers. Because most “classical” monomers are inexpensive and readily available, their utilization for the production of novel materials deserves intense consideration from a practical point of view. In addition, click chemistry has attracted worldwide interest for its potential to embed desired properties into conventional polymers, particularly when combined with controlled/living polymerization processes. However, in some applications that feature surface patterns or three-dimensional scaffolds, these reactions may not be adequate, particularly when spatial and temporal controls are also required [56]. Click chemistry in general has received considerable attention as a powerful modular synthesis approach. It has been used in the synthesis of polymers with different composition and topology, ranging from linear (telechelic [57], and block copolymer [58], to non-linear macromonomer structure [59-61]). Click chemistry has found numerous application in polymer chemistry, drug discovery, material science and many more [48, 62]. However, it has some limitations which include the need for metal catalyst [63], and inability to control by external stimulator or to conduct the reaction in the absence of solvent [64]. To enhance the concept of click chemistry as an important synthetic approach, the discovery of alternative robust, efficient and orthogonal click reaction is necessary.

2.4.1 Copper Catalyzed Azide-Alkyne Cycloaddition

This reaction is also known as copper (I)-catalyzed Huisgen 1, 3-dipolar cycloaddition (CuAAC) reaction between azides and terminal alkynes. This reaction dramatically accelerates the combination of azides with terminal alkynes. It is very robust, general, insensitive, and orthogonal to most other chemistries used in synthesis of polymers.

Unlikely uncatalyzed cycloadditions of azides and alkynes, Cu(I) catalyzed reactions allows very fast and regioselective formation of only the 1,4-triazoles at mild reaction conditions such as low temperatures and absence of side products. The general scheme for azide click reaction is shown in (Figure 2.12).

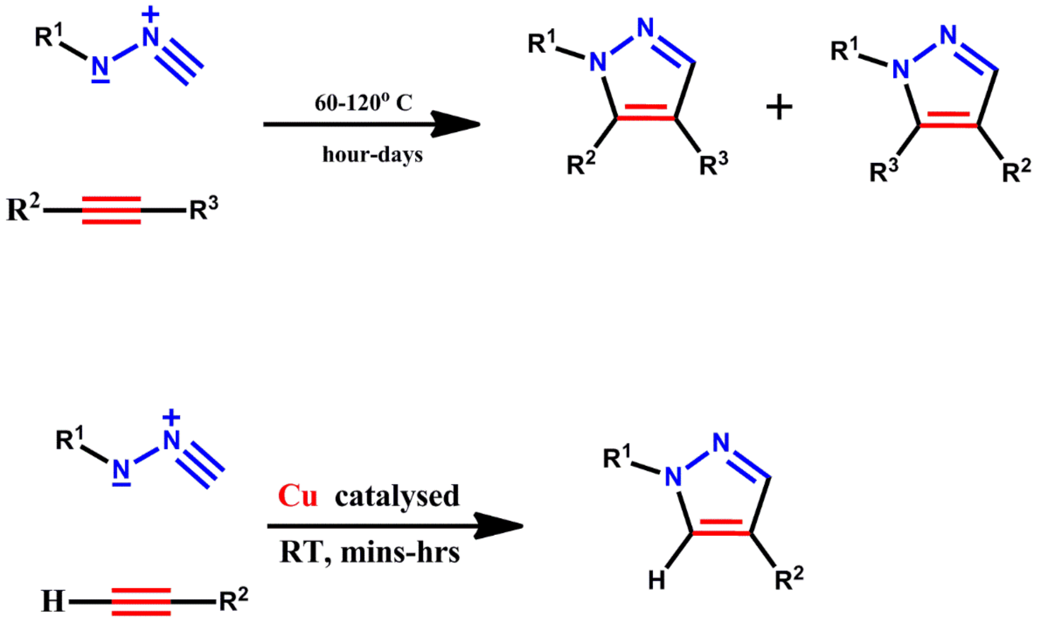


Figure 2.12 : General representation of thermal and copper catalyzed cycloaddition

2.4.2 Diels-Alder Click Chemistry

This type of click reaction was discovered by professor Otto Diels and his student Kurt Alder in 1950 [65]. The Diels-Alder (DA) reaction is one of the most common reactions used in organic chemistry and is a type of cycloaddition reactions. Two in a diene and one in a dienophile, totally three p bonds, recompose to give a six-membered ring in all Diels-Alder reactions. Although Diels-Alder reaction are used in organic chemistry for many years, it gained popularity in the field of materials science with the discovery of “click chemistry”. The majority of “click” reactions generally create new carbon-heteroatom bonds, whereas Diels-Alder “click” reactions create new carbon-heteroatom bonds and carbon-carbon bonds. This property increases the interest on this reaction at the chemistry world. The DA reaction, shown its general form in (figure 2.13), involves a [4+2] cycloaddition reaction between an electron-rich diene (furan and its derivatives, 1, 3 cyclopentadiene and its derivatives etc.) and an electron-poor dienophile (maleic acid and its derivatives, vinyl ketone etc.) to form a stable cyclohexene adduction [66, 67].

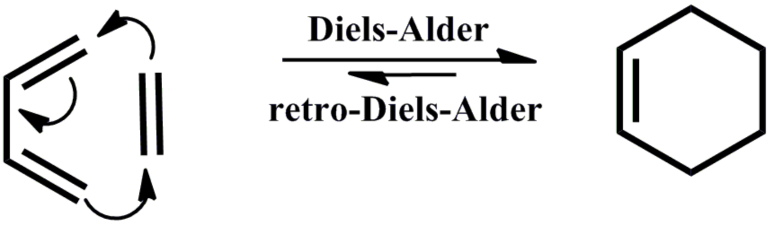


Figure 2.13 : General Mechanism of Diels-Alder/retro Diels-Alder reactions of dienophile and diene.

2.4.3 Thiol-Ene Click Chemistry

The radical addition of thiols to carbon-carbon double bonds is called as thiol-ene reaction and was discovered in the early 1900s by Posner. In thiol-ene reactions (Figure 2.14), S-H bonds formed to a double or triple bond by either a free radical or ionic mechanism. During the process, a typical chain initiation, propagation and termination take place (Figure 2.15). At the Initiation stepthiol interact with photoinitiator, on light exposure, resulting in the formation of a thiyl radical, RS˙. Propagation steps incorporate with attachment of thiyl radical to the C=C bond and hydrogen abstraction of a thiol group by a carbon-centered radical resulting the synchronous generation of a new thiyl radical, respectively and lastly Termination takes place radical–radical coupling processes. Basically sulfur version of the hydrosilylation reaction is called Thiol-ene reactions. Thiols are also known as transfer agents and their reaction with alkenes conducted under radical conditions, photochemically and thermally [32, 68, 69] absence of side reactions. Thiol-ene reactions are considered as “click” reactions because of high yielding, efficient reactions, tolarence of solvents and functional groups.

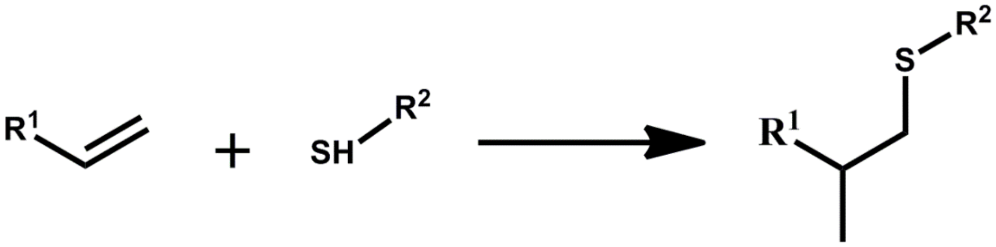


Figure 2.14 : Example of conglomeration of thiol-ene

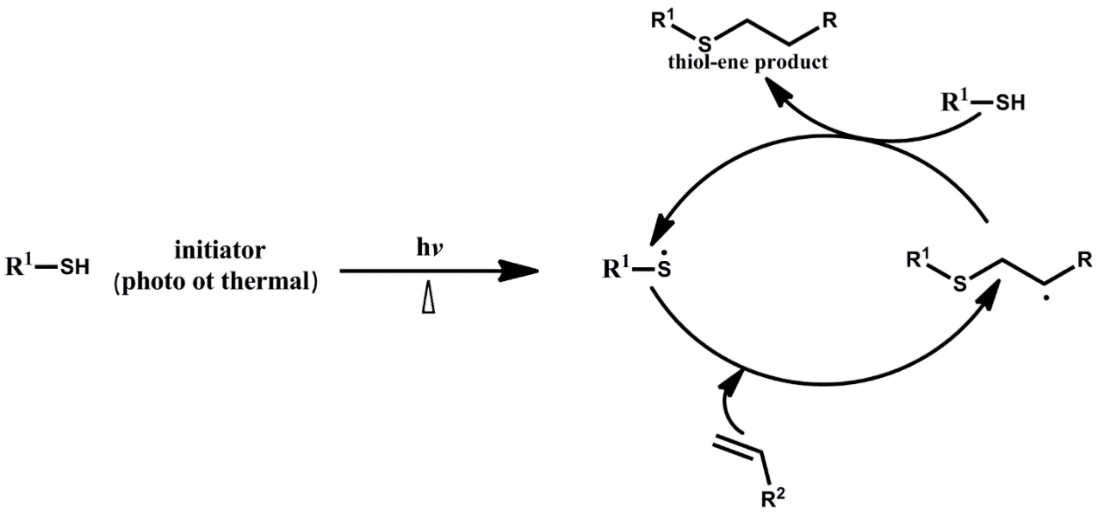


Figure 2.15 : Schematic diagram of cross-linking

3. EXPERIMENTAL PART

3.1 Materials and Chemicals

3.1.1 Reagents

Propargylamine (Sigma-Aldrich,98%), phenol (≥99%, Sigma-Aldrich), formaldehyde (38% w/v J.T Baker), ethyl 2-bromopropionate (99%, Aldrich) , copper (I) bromide (98%, Acros), anhydrous magnesium sulfate (99%, Sigma-Aldrich), triethylamine (Sigma-Aldrich, ≥99 %), diethyl ether (Sigma-Aldrich, ≥99 %), copper (II) bromide (98%, Acros), 2,2'-Bipyridyl (bpy) (Aldrich,99%), poly(ethylene glycol) methyl ether (Aldrich, M_n≈2000), sodium azide (NaN_3) (Sigma-Aldrich, ≥99.5 %), tosyl chloride (TsCl) (Fluka, ≥99 %), sodium hydroxide, (≥97.0%, Sigma-Aldrich) HCl (37%, Sigma-Aldrich), 1,2-ethanedithiol (Merck,99%) and 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid (CTA) (Sigma-Aldrich, ≥97%), and were used as received. 2,2'-Azobis(2-methylpropionitrile) (AIBN, 98%, Fluka) was recrystallized from acetone prior to use and ethyl 2-bromoisobutyrate (EBiB) (Aldrich, 98%) was purified through vacuum distillation. Styrene and methyl acrylate monomers were passed though basic alunina column to remove the inhibitor before usage.

3.1.2 Solvents

Tetrahydrofuran (THF) (Sigma-Aldrich, ≥99.9%), N, N-dimethylformamide (DMF) (Sigma-Aldrich, 99.8%), chloroform (Sigma, ≥99%), methanol (Merck, 99.9%), ethanol (Sigma-Aldrich, ≥99.8%), dichloromethane (Sigma-Aldrich, 99.7%) and were used as received.

3.2 Characterization

3.2.1 ^{1}H-Nuclear magnetic resonance spectroscopy (^{1}H-NMR)

^{1}H NMR spectra of 5–10 % (w/w) solutions in $CDCl_3$ with $Si(CH_3)_4$ as internal standard were recorded at room temperature at Agilent VNMRS 500 MHz spectrometer.

3.2.2 Fourier transform infrared spectroscopy (FT-IR)

FT-IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum One-B spectrometer**.**

3.2.3 Gel-permeation chromatography (GPC)

Gel permeation chromatography (GPC) measurements were obtained from a Viscotek GPCmax Autosampler system consisting of a pump, a Viscotek UV detector and Viscotek a differential refractive index (RI) detector. Three ViscoGEL GPC columns (G2000HHR, G3000HHR and G4000HHR), (7.8 mm internal diameter, 300 mm length) were used in series. THF was used as an eluent at flow rate of 1.0 mL min^{-1} at 30 °C. Both detectors were calibrated with PS standards having narrow molecular weight distribution. Data were analyzed using Viscotek OmniSEC Omni-01 software. Molecular weights were calculated with the aid of polystyrene standards

3.3 Preparation Methods

3.3.1 Preparation of propargyl benzoxazine (B-Pr) as Click Linker

In a 250 ml flask, formaldehyde (37% solution in water) (5.7 mL, 70 mmol) in 100 ml chloroform was cooled in an ice bath, to this solution, propargylamine (1.93 g, 35 mmol), was added portion-wise. The solution was kept stirring for 15 min below 5 °C. Thereafter, a solution of phenol (3.3 g, 35 mmol) in 25 ml chloroform was added. The solution was refluxed for 6 h. After this reaction time, the content of the flask cooled and was washed twice with a cold 0.1 M sodium hydroxide solution and three times with cold distilled water. Afterwards, the chloroform layer was dried with anhydrous magnesium sulfate and solvent was removed with a rotary evaporator, yielding a pale yellow viscous fluid (yield 65 %). ^{1}H NMR($CDCl_3$): □= 2.30 (t, J=2.5 Hz, 1H,–CH_2–C≡CH), 3.58 (d, J=2.5 Hz, 2H,–CH_2–C≡CH), 4.09 (s, 2H, Ar–CH_2–N), 4.89 (s, 2H, –O–CH_2–N), 6.68–6.95 (3H, –C_6H_3–) ppm.

3.3.2 Synthesis of bromo functional poly(methyl acrylate) (PMA-Br) by ATRP

In a dry Schlenk flask with a magnetic stirrer, CuBr (63 mg, 0.44 mmol), bpy (206 mg, 1.32 mmol), EBiB (65 µL, 0.44 mmol), and MA (9.1 mL, 0.101 mol), were added and deoxygenated followed by three freeze-pump-thaw cycle. The Schlenk flask was immersed in an oil bath at 100 °C for 7 h. After the described time, the tube was cooled down to room temperature rapidly and THF (25 mL) added. The solution was passed through a short path neutral alumina column to remove the copper catalyst. Then, the polymer was precipitated in excess of methanol (200 mL), and then dried at 40 °C in vacuum oven for 48 h..

3.3.3 Synthesis of azido-terminated poly(methyl methacrylate) (PMA-N_3)

PMA-Br (1.9 g) was reacted with NaN_3 (100 mg, 1.54 mmol) for 3 h at room temperature in DMF (3 mL) to functionalize PMA with azide groups. The polymer was precipitated from methanol-water mixture then the collected solid was dissolved in THF (15 mL) and re-precipitated in methanol (200 mL). The azido terminated polymer (PMA-N_3) was dried under vacuum at room temperature for 48 h.

3.3.4 Synthesis of polystyrene with thiocarbonylthio end-group (PS-TCT) by RAFT Polymerization

In a dry Schlenk flask with a magnetic stirrer, AIBN (12 mg, 0.073 mmol), CTA (40.5 mg, 0.145 mmol), styrene (9.06 g, 0.087 mol), and dry DMF (3 mL) were added. The reaction mixture was degassed by three freeze-pump-thaw cycle. The tube was heated at 80 ˚C for 24 hr. After the given time, the mixture was cooled down to room temperature and diluted with THF. The polymer was precipitated in methanol. After filtration the solid was collected and dried under vacuum at room temperature for 24 h to give polystyrene with thiocarbonylthio end-group (PS-TCT).

3.3.5 Synthesis of thiol end-functional polystyrene (PS-SH)

Into a two neck flask equipped with a stirrer, DMF (8 mL), PS-TCT (0.5 g), and metallic zinc (9.75 mg, 0.149 mmol) were added under N_2 atmosphere. Next, 1, 2-ethandithiol (47 mg, 0.5 mmol) was added to the reaction mixture by a syringe. The reaction mixture was stirred for 3 h and the polymer was precipitated ten-fold excess methanol/water mixture (10:1) containing 1-2 drops of *conc.* HCl. The polymer was dried under vacuum at room temperature and PS-SH obtained as white-powder.

3.3.6 Tosylation of poly(ethylene glycol) methyl ether

Poly(ethylene glycol) methyl ether (2.00 g) was dissolved in DCM (20 mL), and toluene-4-sulfonyl chloride (1.91 g, 10.0 mmol) and triethylamine (1.00 g, 10.0 mmol) were then added. The reaction mixture was stirred for 20 h at room temperature. After this period, the product was filtered and concentrated, and then the polymer was precipitated from cold diethyl ether, dried under vacuum at room temperature to give the desired product (PEG-Ts).

3.3.7 Azide functionalized poly(ethylene glycol) methyl ether (PEG-N_3)

PEG-Ts (1.5 g, 1.00 mmol) was dissolved in DMF (8 mL) and NaN_3 (453 mg, 10.00 mmol) was added. The reaction mixture was stirred for 22 h at room temperature. DCM (25 mL) was added and the reaction mixture was washed three times with cold distilled water, twice with cold 6 M HCl solution and twice with cold distilled water. The organic layer was dried with anhydrous magnesium sulfate then concentrated. The polymer was precipitated from cold diethyl ether yielding a white solid product (PEG-N_3)

3.3.8 Synthesis of propargyl end-functional polystyrene (PS-B-Prg) by COLBERT reaction

In to a dark reaction flask, PS-Thiol (150 mg, 1 equiv.), and B-Prg (64.9 mg, 5 eq.), were dissolved in a mixture of THF and methanol (3:1) (v/v) (5 mL) as solvent. This mixture was stirred at RT for 5 h. After this reaction time, PS-B-Prg was precipitated in cold methanol (100 mL) and the polymer was dried under vacuum at room temperature for 48 h.

3.3.9 Synthesis of polystyrene-block-poly(methyl acrylate) (PS-b-PMA)

In to a dark reaction flask, PS-SH (0.30 mmol), and B-pr (5 equiv), were dissolved in 5 mL mixture of THF and methanol (3:1) as solvent. There after, PMA-N_3 (0.30 mmol), Bpy (2.40 mmol), and CuBr (0.30 mmol) were added. This mixture was stirred at room temperature for 24 h. After the reaction time, the final mixture was diluted in THF and passed through short alumina column in order to remove copper catalyst. The solvent was concentrated by rotary evaporation and polymer was isolated by precipitation from methanol. The click product was dried at 40°C in vacuum oven overnight.

3.4.0 One-pot two step synthesis of polystyrene-block- poly(ethylene glycol) methyl ether (PS-b-PEG)

In to a dark reaction flask, PS-Thiol (150 mg, 1 equiv.), and B-Prg (64.9 mg, 5 eq.), were dissolved in a mixture of THF and methanol (3:1) (v/v) (5 mL) as solvent. This mixture was stirred at RT for 5 h. After this reaction time, a mixture of PEG-N_3 (128 mg, 1.2 equiv.), bpy (14.6 mg, 0.1 mmol), and CuBr (13.4 mg, 0.1 mmol) in THF (5 mL) was injected into the reaction flask and the whole mixture was stirred at RT for further 20 h. After this period of time, the final solution was passed through short alumina column using THF as eluent in order to remove copper complex. The solution was concentrated by rotary evaporation and copolymer was isolated by precipitation from methanol.

4. RESULTS AND DISCUSSION

As stated in the introduction section, our synthetic approach toward the direct preparation of block copolymers is based on “double click” chemistry strategy combining 1,3-dipolar azide-alkyne and benzoxazine-thiol COLBERT reactions in one pot. We have previously employed double click strategy for the preparation of polymeric photoinitiators and graft copolymers through combination of azide-alkyne and Diels-Alder reactions. It was predicted that propargyl benzoxazine (B-Prg) would act as a click linker for the coupling of two distinct polymers to form desired block copolymers. First, propargyl benzoxazine (linker molecule) was successfully synthesized according to the literature [70], from the reaction of phenol, propargyl amine and formaldehyde using 1,2-dioxane as solvent (Figure 4.1).

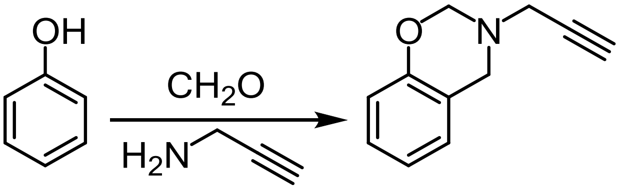


Figure 4.1 : Synthesis of Propargyl Benzoxazine

To access the block structure, two polymers with different backbone chemistries were end-functionalized with a highly reactive thiol and azide functionalities. For the synthesis of parent azide functionalized polymer, we first prepared bromo end-functional poly(methyl acrylate) (PMA–Br) via atom transfer radical polymerization (ATRP) of methyl acrylate (MA) and then, quantitatively converted into poly(methyl acrylate)-azide (PMA–N_3) in the presence of NaN_3/DMF at room temperature (Scheme 4 (1)). On the other hand, we synthesized tosylated poly(ethylene glycol) monomethyl ether starting from poly(ethylene glycol) using a well-known tosylation procedure and subsequent azidation yielded azido functional poly(ethylene glycol) (PEG-N_3) (Figure 4.2).

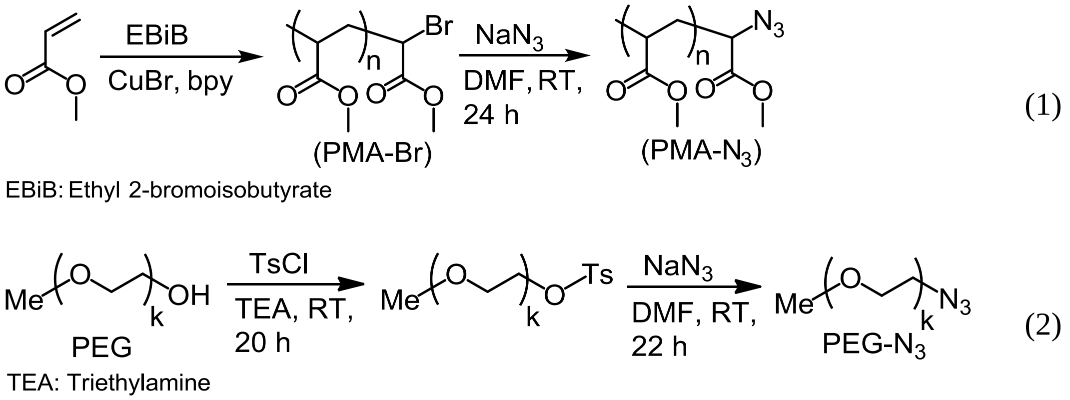


Figure 4.2 Synthesis of azido functional poly(methyl acrylate) (PMA–N_3) and poly(ethylene glycol) (PEG-N_3)

Successful azidations was confirmed by the presence of azide stretching band at 2094 and 2100 cm^{-1} in the IR spectra of PMA-N_3 and PEG-N_3, respectively (Figures 4.3 and 4.4).

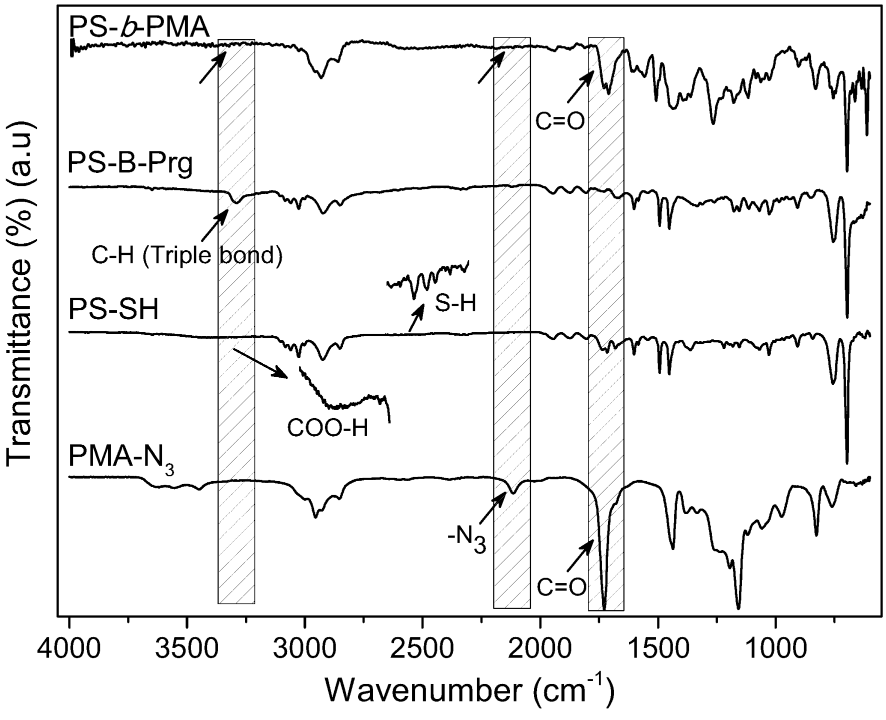


Figure 4.3. FT-IR spectra of azido functional poly(methyl acrylate) (PMA-N_3), thiol functional polystyrene (PS-SH), benzoxazine-functional polystyrene (PS-B-Prg) and final block copolymer (PS-*b*-PMA).

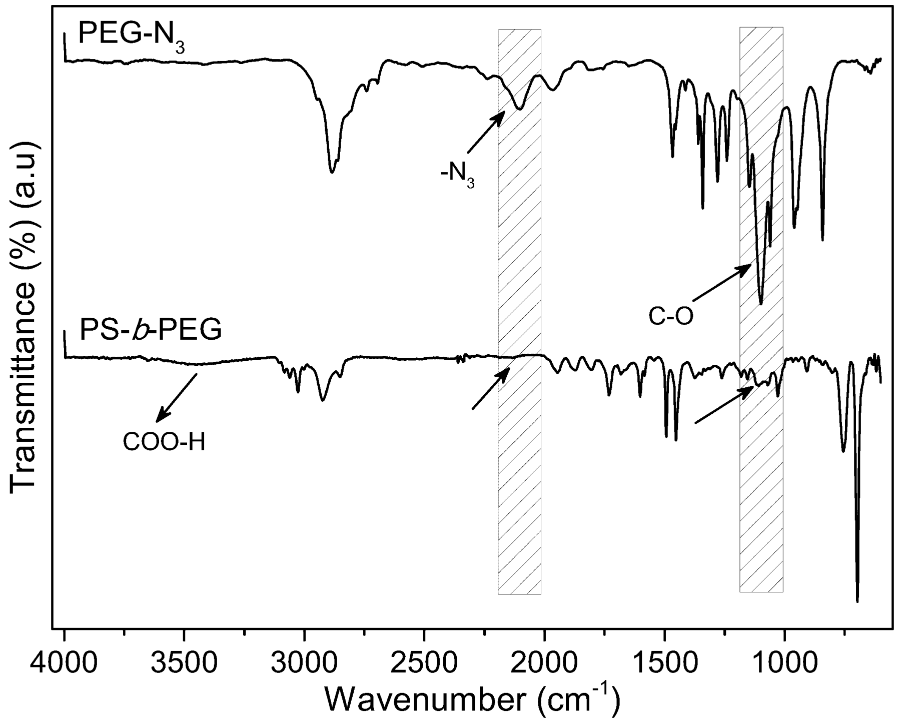


Figure 4.4. FT-IR spectra of azido functional poly(ethylene glycol) (PEG-N_3), and final block copolymer (PS-*b*-PEG).

The precursor for the second segment of the block copolymer was synthesized by two consecutive reactions starting from Reversible Addition Fragmentation chain Transfer (RAFT) polymerization to yield polystyrene with thiocarbonylthio end-group (PS-TCT). These end-groups can be considered as a masked thiol and therefore, RAFT polymers are useful sources specifically for thiol-X chemistries. The RAFT based polystyrene–thiol (PS–SH) is easily accessible by treatment of the thiocarbonylthio RAFT group with metallic zinc and 1, 2-ethandithiol (Figure 4.5). The structure of the PS–SH was confirmed by ^{1}H NMR spectrum (Figure 4.6) as –SH proton can be detected at 3.49 ppm. Moreover, the protons of methylene alongside the carboxylic acid of the CTA initiator are visible at 2.37 ppm.

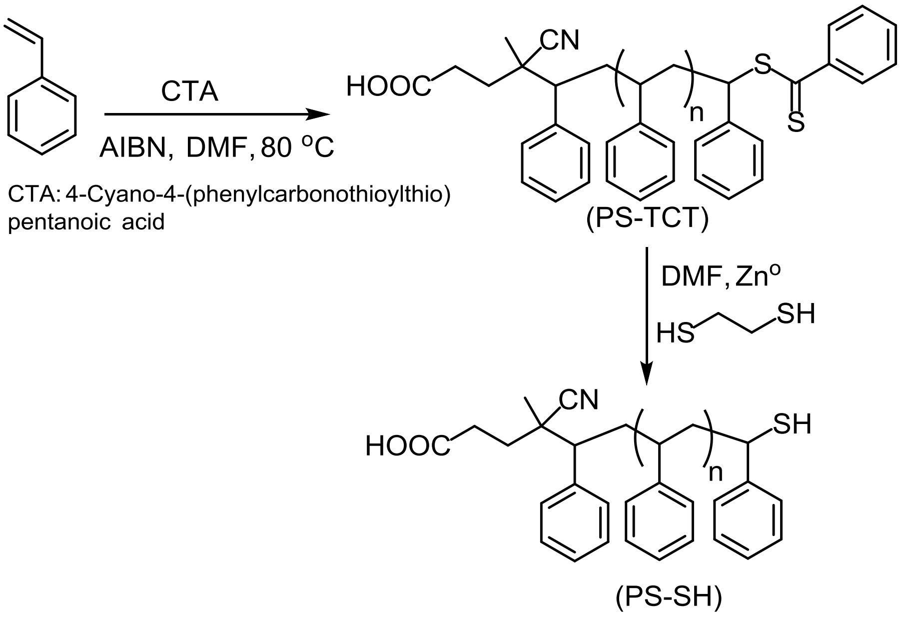


Figure 4.5: Sequential synthesis of thiol functional polystyrene (PS-SH).

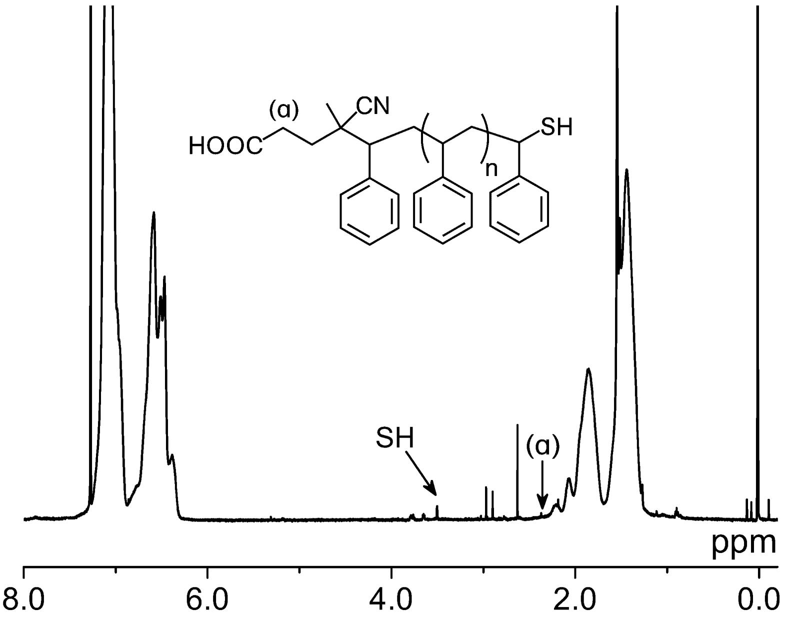


Figure 4.6. ^{1}H-NMR spectrum of thiol functional polystyrene (PS-SH) in $CDCl_3$

After the completion of the synthesis of click linker B-Prg, thiol and azido functional polymers, all these components were reacted in both sequential and one-pot two step manner as depicted (Figure 4.7). While PMA-N_3 was used in sequential reaction method to produce PS-*b*-PMA, one-pot two step procedure was applied to only PEG-N_3 to form PS-*b*-PEG.

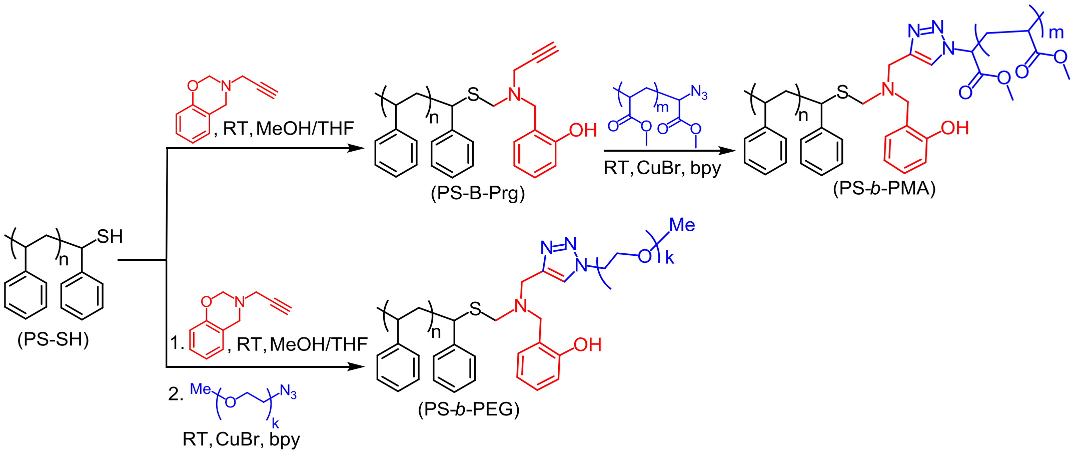


Figure 4.7. Sequential and one-pot two step synthesis of PS-*b*-PMA and PS-*b*-PEG, subsequently. (Note that the end functionality 4-cyanopentanoic acid of PS is omitted in the scheme for better clarity)

After removing the Cu (I) catalyst, the polymers were precipitated and dried under vacuum. The extent of linking of the azido and thio functional polymers was monitored by FT-IR and ^{1}H NMR spectroscopy. In the IR spectrum of the PS-*b*-PMA (Figure 4.3), the complete disappearance of the azide band at 2094 cm^{-1} and the preservation of carbonyl group band at 1723 cm^{-1} are noted. Moreover, in (Figure 4.4), the conversion of azide of PEG-N_3 is also detectable from the vanishing azide band at 2100 cm^{-1}. Additionally, C-O band of PEG at 1099 cm^{-1} remains in the IR spectrum of PS-*b*-PEG evidencing the incorporation of PEG to the block copolymer structure. In the corresponding ^{1}H-NMR spectra (Figures 4.8 and 4.9), the proton of the triazole ring at ≈7.48 ppm is clearly detectable. These spectral observations confirm efficient Huisgen type click reaction. The parallel thiol-benzoxazine reaction also proceeds competently. In the process, thiol end groups are consumed as evidenced by NMR analysis; the proton of –SH was diminished after the coupling reaction (Figure 4.8). Herein, a question can be raised whether the thiol group is susceptible to react with triple bond of the propargyl under the applied reaction conditions. Previous studies focusing on the reaction of benzoxazines with thiols and the methods to prevent the thiol−benzoxazine ring-opening reaction revealed that the thiol−benzoxazine reaction was catalyzed with the acidic proton of thiol and inhibited by the addition of bases since the protonation of the amine plays an important role in the thiol−benzoxazine ring opening process (*vide ante*, Scheme 1). Hence, in order to divert thiol to triple bond basic conditions is required.

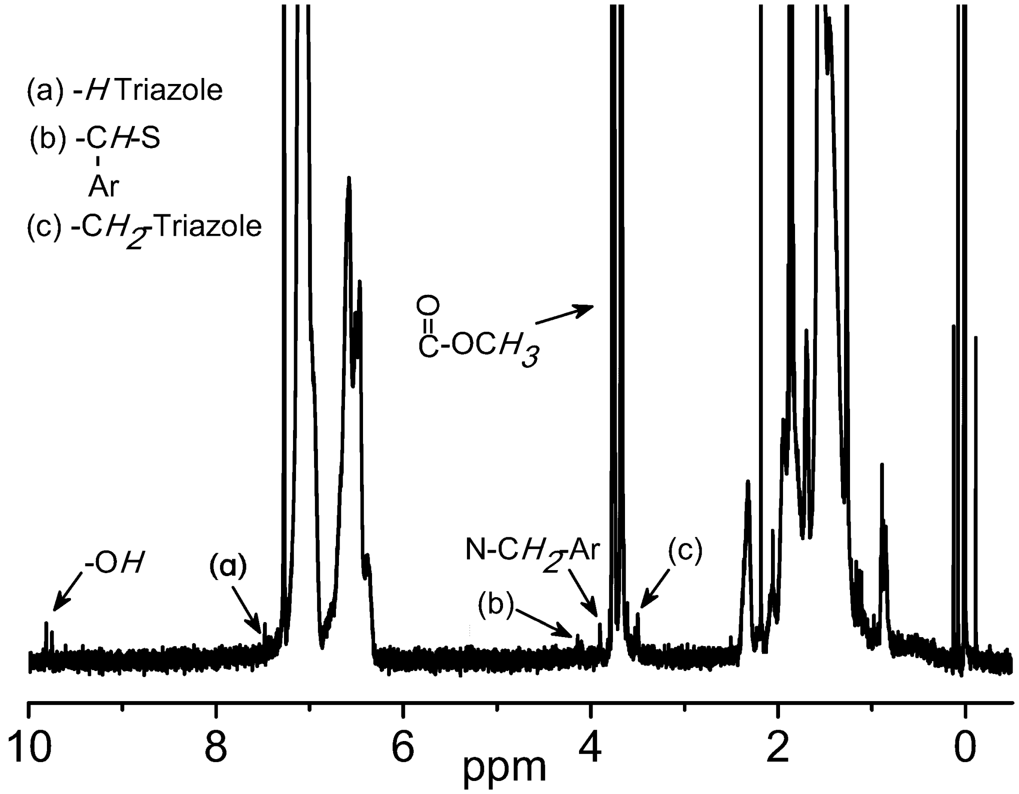


Figure 4.8: ^{1}H-NMR spectrum of polystyrene-*block*-poly(methyl acrylate) (PS-*b*-PMA)) in $CDCl_3$.

Figure 5.0 and 5.1 show GPC traces of the precursor polymers and final block copolymers. Clearly, after the two successive coupling reactions and one-pot method, the GPC traces shift to higher molecular weights. In sequential synthesis GPC indicates polymer precursors is reacted each other completely. However, in one-pot two step method, there is unconsumed PEG-N_3 left in the final polymer. The molecular weight characteristics of the polymers are presented in Table 1. The relatively lower molecular weight distribution of the block copolymer is another indication of the complete coupling processes at both stages.

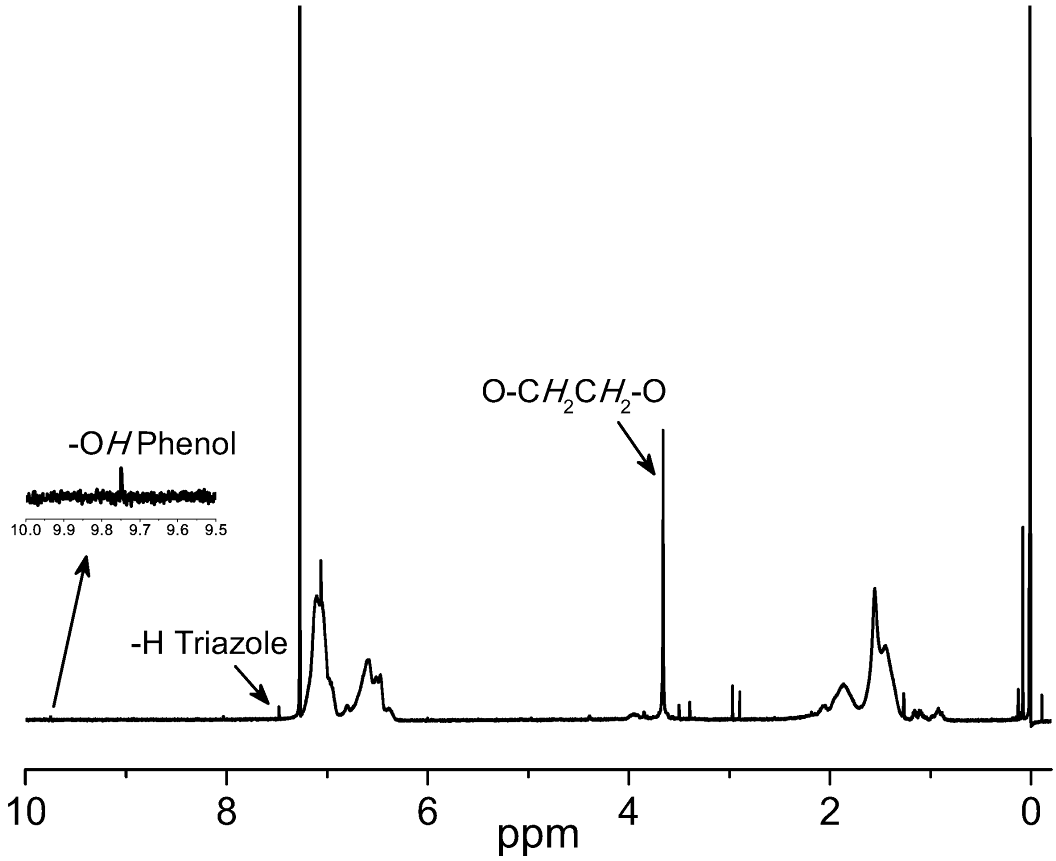


Figure 4.9: ^{1}H-NMR spectrum of polystyrene-*block*-poly(ethylene glycol) (PS-*b*-PEG)) in CDCl$_3$.

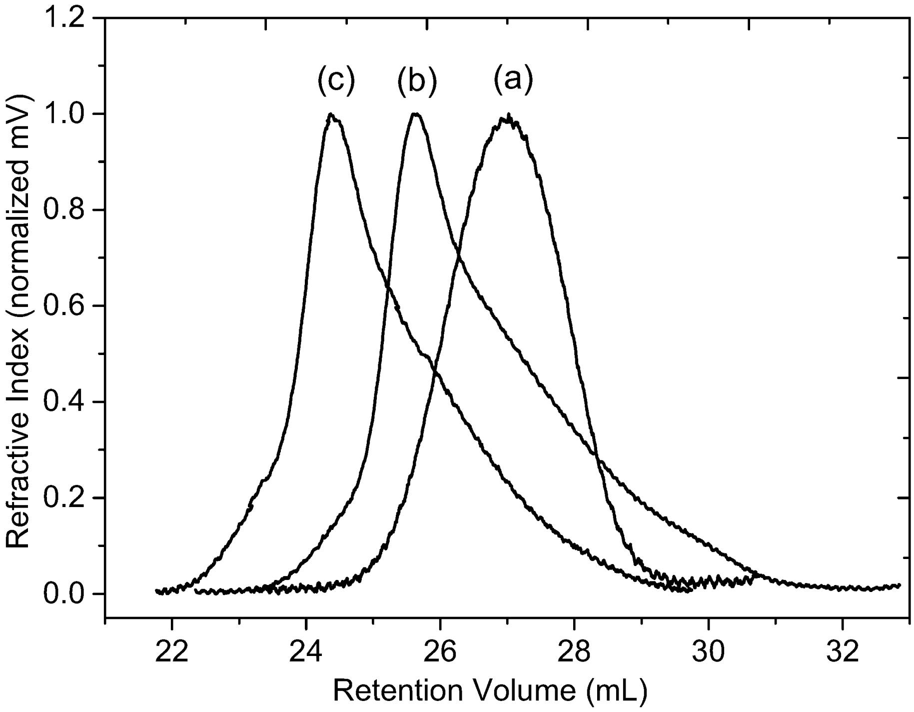


Figure 5.0: GPC traces of PMA-N$_3$ (a), PS-SH (b) and PS-*b*-PMA (c).

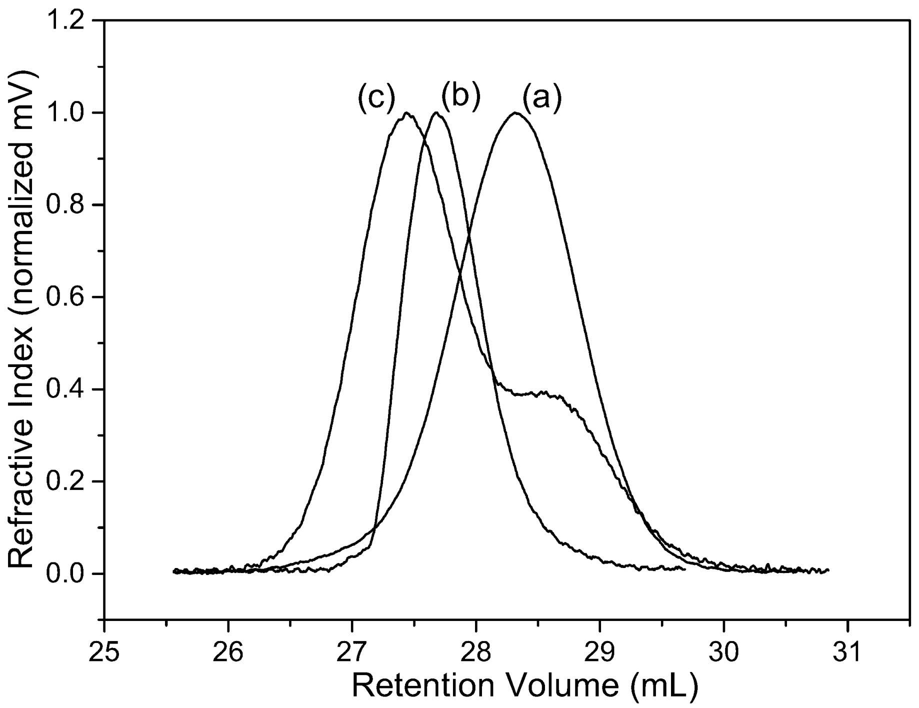


Figure 5.1: GPC traces of PEG-N_3 (a), PS-SH (b) and PS-*b*-PEG (c).

Table 4.1 : Molecular weight characteristics of the polymers

Polymer	M_n[a]	M_w/M_n[a]
PMA-N_3	10.300	1.38
PEG-N_3	1950	1.21
PS-SH[b]	16.800	1.95
PS-SH[c]	2555	1.40
PS-*b*-PMA	23.100	1.54
PS-*b*-PEG	5760	1.50

[a] Determined by GPC according to polystyrene standards

[b] Used in sequential synthesis

[c] Used in one-pot two step synthesis

5. CONCLUSIONS AND RECOMMENDATIONS

In conclusion, we have established a new thiol-X coupling reaction based on the ring opening of benzoxazine molecules with thiols. Its applicability to macromolecular syntheses was demonstrated on block copolymer formation of PS with PMA or PEG. The precursors PMA-N_3 and PEG-N_3 were prepared by azidation processes. The accomplishment of RAFT and subsequent reaction with 1,2 ethanedithiol in the presence of metallic zinc gave the other click component PS-SH. Propargyl containing benzoxazine was synthesized and successfully used as a click linker for both thiol–benzoxazine and Huisgen type click reactions in sequential or one–pot manner to give desired block copolymer. It appears from this study that properly functionalized macromolecules, when introduced in the benzoxazine-thiol system, could give various possibilities in macromolecular architecture. The ease of benzoxazine synthesis and its design flexibility also are additional advantages in targeting polymers in such way, since there are various commercially available primary amines and phenols present. Moreover, phenolic –OH formed after thiol–benzoxazine reaction is a suitable platform for further functionalization that could yield mictoarm star polymers and more. Further studies in this line together with the combination of benzoxazine-thiol chemistry with other click reactions are now in progress.

REFERENCES

[1] Kasapoglu, F., Cianga, I., Yagci, Y. and Takeichi, T., 2003. Photoinitiated Cationic Polymerization of Monofunctional Benzoxazine. *Journal of Polymer Science Part A: Polymer Chemistry,* **41(21),** 3320-3328.

[2] Holly, F. W. and Cope, A. C., 1944. Condensation Products of Aldehydes and Ketones with O-Aminobenzyl Alcohol and O-Hydroxybenzylamine. *Journal of the American Chemical Society,* **66(11),** 1875-1879.

[3] Burke, W. J., 1949. 3,4-Dihydro-1,3,2h-Benzoxazines. Reaction of P-Substituted Phenols with N,N-Dimethylolamines. *Journal of the American Chemical Society,* **71(2),** 609-612.

[4] Riess, G. S., M.; Guth, G.; Roche, M.; and **Lande, B.**, In *Advances in Polymer Synthesis,* Culbertson, B. M. a. M., J. E.,, Ed. Plenum: New York, 1985.

[5] Ishida, H. U.S. Patent 5,543,516, May 18, 1996..

[6] Altinkok, C., Kiskan, B. and Yagci, Y., 2011. Synthesis and Characterization of Sulfone Containing Main Chain Oligobenzoxazine Precursors. *Journal of Polymer Science Part A: Polymer Chemistry,* **49(11),** 2445-2450.

[7] Ates, S., Dizman, C., Aydogan, B., Kiskan, B., Torun, L. and Yagci, Y., 2011. Synthesis, Characterization and Thermally Activated Curing of Polysulfones with Benzoxazine End Groups. *Polymer,* **52(7),** 1504-1509.

[8] Aydogan, B., Sureka, D., Kiskan, B. and Yagci, Y., 2010. Polysiloxane-Containing Benzoxazine Moieties in the Main Chain. *Journal of Polymer Science Part A: Polymer Chemistry,* **48(22),** 5156-5162.

[9] Demir, K. D., Tasdelen, M. A., Uyar, T., Kawaguchi, A. W., Sudo, A., Endo, T. and Yagci, Y., 2011. Synthesis of Polybenzoxazine/Clay Nanocomposites by in Situ Thermal Ring-Opening Polymerization Using Intercalated Monomer. *Journal of Polymer Science Part A: Polymer Chemistry,* **49(19),** 4213-4220.

[10] Kiskan, B., Aydogan, B. and Yagci, Y., 2009. Synthesis, Characterization, and Thermally Activated Curing of Oligosiloxanes Containing Benzoxazine Moieties in the Main Chain. *Journal of Polymer Science Part A: Polymer Chemistry,* **47(3),** 804-811.

[11] Agag, T. and Takeichi, T., 2003. Synthesis and Characterization of Novel Benzoxazine Monomers Containing Allyl Groups and Their High Performance Thermosets. *Macromolecules,* **36(16),** 6010-6017.

[12] Koz, B., Kiskan, B. and Yagci, Y., 2011. A Novel Benzoxazine Monomer with Methacrylate Functionality and Its Thermally Curable (Co)Polymers. *Polymer Bulletin,* **66(2),** 165-174.

[13] Sponton, M., Estenoz, D., Lligadas, G., Ronda, J. C., Galia, M. and Cadiz, V., 2012. Synthesis and Characterization of a Hybrid Material Based on a Trimethoxysilane Functionalized Benzoxazine. *Journal of Applied Polymer Science,* **126(4),** 1369-1376.

[14] Takeichi, T., Nakamura, K., Agag, T. and Muto, H., 2004. Synthesis of Cresol-Based Benzoxazine Monomers Containing Allyl Groups and the Properties of the Polymers Therefrom. *Designed Monomers and Polymers,* **7(6),** 727-740.

[15] **Ghosh, N. N., Kiskan, B. and Yagci, Y.,** 2007. Polybenzoxazines - New High Performance Thermosetting Resins: Synthesis and Properties. *Progress in Polymer Science,* **32(11),** 1344-1391.

[16] **Ning, X. and Ishida, H. S.,** 1994. Phenolic Materials Via Ring-Opening Polymerization of Benzoxazines - Effect of Molecular-Structure on Mechanical and Dynamic-Mechanical Properties. *Journal of Polymer Science Part B-Polymer Physics,* **32(5),** 921-927.

[17] **Kiskan, B., Ghosh, N. N. and Yagci, Y.,** 2011. Polybenzoxazine-Based Composites as High-Performance Materials. *Polymer International,* **60(2),** 167-177.

[18] **Matyjaszewski, K.,** 2000. Preface. In *Controlled/Living Radical Polymerization,* American Chemical Society.

[19] **Haddleton, D. M., Maloney, D. R. and Suddaby, K. G.,** 1996. Competition between B-Scission of Macromonomer-Ended Radicals and Chain Transfer to Cobalt(Ii) in Catalytic Chain Transfer Polymerization (Cctp). *Macromolecules,* **29(1),** 481-483.

[20] **Kamigaito, M., Ando, T. and Sawamoto, M.,** 2001. Metal-Catalyzed Living Radical Polymerization. *Chemical Reviews,* **101(12),** 3689-3746.

[21] **Matyjaszewski, K. and Xia, J.,** 2001. Atom Transfer Radical Polymerization. *Chemical Reviews,* **101(9),** 2921-2990.

[22] **Chiefari, J., Chong, Y. K., Ercole, F., Krstina, J., Jeffery, J., Le, T. P. T., Mayadunne, R. T. A., Meijs, G. F., Moad, C. L., Moad, G., Rizzardo, E. and Thang, S. H.,** 1998. Living Free-Radical Polymerization by Reversible Addition−Fragmentation Chain Transfer: The Raft Process. *Macromolecules,* **31(16),** 5559-5562.

[23] **Hawker, C. J., Bosman, A. W. and Harth, E.,** 2001. New Polymer Synthesis by Nitroxide Mediated Living Radical Polymerizations. *Chemical Reviews,* **101(12),** 3661-3688.

[24] **Matyjaszewski, K., Coca, S., Gaynor, S. G., Wei, M. and Woodworth, B. E.,** 1998. Controlled Radical Polymerization in the Presence of Oxygen. *Macromolecules,* **31(17),** 5967-5969.

[25] **Wang, J.-S. and Matyjaszewski, K.,** 1995. Controlled/"Living" Radical Polymerization. Halogen Atom Transfer Radical Polymerization Promoted by a Cu(I)/Cu(Ii) Redox Process. *Macromolecules,* **28(23),** 7901-7910.

[26] **Kato, M., Kamigaito, M., Sawamoto, M. and Higashimura, T.,** 1995. Polymerization of Methyl Methacrylate with the Carbon Tetrachloride/Dichlorotris-(Triphenylphosphine)Ruthenium(Ii)/Methylaluminum Bis(2,6-Di-Tert-Butylphenoxide) Initiating System: Possibility of Living Radical Polymerization. *Macromolecules,* **28(5),** 1721-1723.

[27] **Matyjaszewski, K., Gaynor, S. and Wang, J.-S.,** 1995. Controlled Radical Polymerizations: The Use of Alkyl Iodides in Degenerative Transfer. *Macromolecules,* **28(6),** 2093-2095.

[28] **Matyjaszewski, K., Patten, T. E. and Xia, J.,** 1997. Controlled/“Living” Radical Polymerization. Kinetics of the Homogeneous Atom Transfer Radical Polymerization of Styrene. *Journal of the American Chemical Society,* **119(4),** 674-680.

[29] **Fischer, H.,** 1999. The Persistent Radical Effect in Controlled Radical Polymerizations. *Journal of Polymer Science Part A: Polymer Chemistry,* **37(13),** 1885-1901.

[30] **Moad, G., Rizzardo, E. and Thang, S. H.,** 2005. Living Radical Polymerization by the Raft Process. *Australian Journal of Chemistry,* **58(6),** 379-410.

[31] **Hoogenboom, R.,** 2010. Thiol-Yne Chemistry: A Powerful Tool for Creating Highly Functional Materials. *Angewandte Chemie-International Edition,* **49(20),** 3415-3417.

[32] **Hoyle, C. E. and Bowman, C. N.,** 2010. Thiol–Ene Click Chemistry. *Angewandte Chemie International Edition,* **49(9),** 1540-1573.

[33] **Kade, M. J., Burke, D. J. and Hawker, C. J.,** 2010. The Power of Thiol-Ene Chemistry. *Journal of Polymer Science Part A: Polymer Chemistry,* **48(4),** 743-750.

[34] **Li, H., Yu, B., Matsushima, H., Hoyle, C. E. and Lowe, A. B.,** 2009. The Thiol−Isocyanate Click Reaction: Facile and Quantitative Access to Ω-End-Functional Poly(N,N-Diethylacrylamide) Synthesized by Raft Radical Polymerization. *Macromolecules,* **42(17),** 6537-6542.

[35] **Nguyen, L.-T. T., Gokmen, M. T. and Du Prez, F. E.,** 2013. Kinetic Comparison of 13 Homogeneous Thiol-X Reactions. *Polymer Chemistry,* **4(22),** 5527-5536.

[36] **Serniuk, G. E., Banes, F. W. and Swaney, M. W.,** 1948. Study of the Reaction of Buna Rubbers with Aliphatic Mercaptans1. *Journal of the American Chemical Society,* **70(5),** 1804-1808.

[37] **Campos, L. M., Killops, K. L., Sakai, R., Paulusse, J. M. J., Damiron, D., Drockenmuller, E., Messmore, B. W. and Hawker, C. J.,** 2008. Development of Thermal and Photochemical Strategies for Thiol−Ene Click Polymer Functionalization. *Macromolecules,* **41(19),** 7063-7070.

[38] **Ates, Z., Thornton, P. D. and Heise, A.,** 2011. Side-Chain Functionalisation of Unsaturated Polyesters from Ring-Opening Polymerisation of Macrolactones by Thiol-Ene Click Chemistry. *Polymer Chemistry,* **2(2),** 309-312.

[39] **Hoyle, C. E., Lowe, A. B. and Bowman, C. N.,** 2010. Thiol-Click Chemistry: A Multifaceted Toolbox for Small Molecule and Polymer Synthesis. *Chemical Society Reviews,* **39(4),** 1355-1387.

[40] **Carrot, G., Hilborn, J., Hedrick, J. L. and Trollsås, M.,** 1999. Novel Initiators for Atom Transfer Radical and Ring-Opening Polymerization: A New General Method for the Preparation of Thiol-Functional Polymers. *Macromolecules,* **32(15),** 5171-5173.

[41] **Campos, L. M., Meinel, I., Guino, R. G., Schierhorn, M., Gupta, N., Stucky, G. D. and Hawker, C. J.,** 2008. Highly Versatile and Robust Materials for Soft Imprint Lithography Based on Thiol-Ene Click Chemistry. *Advanced Materials,* **20(19),** 3728-3733.

[42] **Ghosh, S., Basu, S. and Thayumanavan, S.,** 2006. Simultaneous and Reversible Functionalization of Copolymers for Biological Applications†. *Macromolecules,* **39(17),** 5595-5597.

[43] **Hvilsted, S.,** 2012. Facile Design of Biomaterials by 'Click' Chemistry. *Polymer International,* **61(4),** 485-494.

[44] **Such, G. K., Johnston, A. P. R., Liang, K. and Caruso, F.,** 2012. Synthesis and Functionalization of Nanoengineered Materials Using Click Chemistry. *Progress in Polymer Science,* **37(7),** 985-1003.

[45] Wong, L., Boyer, C., Jia, Z., Zareie, H. M., Davis, T. P. and Bulmus, V., 2008. Synthesis of Versatile Thiol-Reactive Polymer Scaffolds Via Raft Polymerization. *Biomacromolecules,* **9(7),** 1934-1944.

[46] Yoon, J. A., Kamada, J., Koynov, K., Mohin, J., Nicolaÿ, R., Zhang, Y., Balazs, A. C., Kowalewski, T. and Matyjaszewski, K., 2011. Self-Healing Polymer Films Based on Thiol–Disulfide Exchange Reactions and Self-Healing Kinetics Measured Using Atomic Force Microscopy. *Macromolecules,* **45(1),** 142-149.

[47] Yuan, Y. C., Rong, M. Z., Zhang, M. Q., Chen, J., Yang, G. C. and Li, X. M., 2008. Self-Healing Polymeric Materials Using Epoxy/Mercaptan as the Healant. *Macromolecules,* **41(14),** 5197-5202.

[48] Kolb, H. C., Finn, M. G. and Sharpless, K. B., 2001. Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angewandte Chemie International Edition,* **40(11),** 2004-2021.

[49] Tornøe, C. W., Christensen, C. and Meldal, M., 2002. Peptidotriazoles on Solid Phase: [1,2,3]-Triazoles by Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of Terminal Alkynes to Azides. *The Journal of Organic Chemistry,* **67(9),** 3057-3064.

[50] Kumaraswamy, G., Ankamma, K. and Pitchaiah, A., 2007. Tandem Epoxide or Aziridine Ring Opening by Azide/Copper Catalyzed [3+2] Cycloaddition: Efficient Synthesis of 1,2,3-Triazolo B-Hydroxy or B-Tosylamino Functionality Motif. *The Journal of Organic Chemistry,* **72(25),** 9822-9825.

[51] Heredia, K. L., Tolstyka, Z. P. and Maynard, H. D., 2007. Aminooxy End-Functionalized Polymers Synthesized by Atrp for Chemoselective Conjugation to Proteins. *Macromolecules,* **40(14),** 4772-4779.

[52] Franc, G. and Kakkar, A. K., 2009. Diels–Alder “Click” Chemistry in Designing Dendritic Macromolecules. *Chemistry – A European Journal,* **15(23),** 5630-5639.

[53] Hizal, G., Tunca, U. and Sanyal, A., 2011. Discrete Macromolecular Constructs Via the Diels–Alder “Click” Reaction. *Journal of Polymer Science Part A: Polymer Chemistry,* **49(19),** 4103-4120.

[54] Tasdelen, M. A., 2011. Diels-Alder "Click" Reactions: Recent Applications in Polymer and Material Science. *Polymer Chemistry,* **2(10),** 2133-2145.

[55] Binder, W. H. and Sachsenhofer, R., 2007. ‘Click’ Chemistry in Polymer and Materials Science. *Macromolecular Rapid Communications,* **28(1),** 15-54.

[56] Brieke, C., Rohrbach, F., Gottschalk, A., Mayer, G. and Heckel, A., 2012. Lichtgesteuerte Werkzeuge. *Angewandte Chemie,* **124(34),** 8572-8604.

[57] Gao, H., Louche, G., Sumerlin, B. S., Jahed, N., Golas, P. and Matyjaszewski, K., 2005. Gradient Polymer Elution Chromatographic Analysis of A,Ω-Dihydroxypolystyrene Synthesized Via Atrp and Click Chemistry. *Macromolecules,* **38(22),** 8979-8982.

[58] Durmaz, H., Colakoglu, B., Tunca, U. and Hizal, G., 2006. Preparation of Block Copolymers Via Diels Alder Reaction of Maleimide- and Anthracene-End Functionalized Polymers. *Journal of Polymer Science Part A: Polymer Chemistry,* **44(5),** 1667-1675.

[59] Binder, W. H. and Kluger, C., 2004. Combining Ring-Opening Metathesis Polymerization (Romp) with Sharpless-Type “Click” Reactions: An

Easy Method for the Preparation of Side Chain Functionalized Poly(Oxynorbornenes). *Macromolecules,* **37(25),** 9321-9330.

[60] Fu, Q., Wang, G., Lin, W. and Huang, J., 2009. One-Pot Preparation of 3-Miktoarm Star Terpolymers Via “Click Chemistry” and Atom Transfer Nitroxide Radical Coupling Reaction. *Journal of Polymer Science Part A: Polymer Chemistry,* **47(3),** 986-990.

[61] Hoogenboom, R., Moore, B. C. and Schubert, U. S., 2006. Synthesis of Star-Shaped Poly(Epsilon-Caprolactone) Via 'Click' Chemistry and 'Supramolecular Click' Chemistry. *Chemical Communications,* **38),** 4010-4012.

[62] Lutz, J.-F., 2007. 1,3-Dipolar Cycloadditions of Azides and Alkynes: A Universal Ligation Tool in Polymer and Materials Science. *Angewandte Chemie International Edition,* **46(7),** 1018-1025.

[63] Becer, C. R., Hoogenboom, R. and Schubert, U. S., 2009. Click Chemistry Beyond Metal-Catalyzed Cycloaddition. *Angewandte Chemie-International Edition,* **48(27),** 4900-4908.

[64] Adzima, B. J., Tao, Y., Kloxin, C. J., DeForest, C. A., Anseth, K. S. and Bowman, C. N., 2011. Spatial and Temporal Control of the Alkyne–Azide Cycloaddition by Photoinitiated Cu(Ii) Reduction. *Nat Chem,* **3(3),** 256-259.

[65] Diels, O. and Alder, K., 1928. Synthesen in Der Hydroaromatischen Reihe. *Justus Liebigs Annalen der Chemie,* **460(1),** 98-122.

[66] Nicolaou, K. C., Snyder, S. A., Montagnon, T. and Vassilikogiannakis, G., 2002. The Diels–Alder Reaction in Total Synthesis. *Angewandte Chemie International Edition,* **41(10),** 1668-1698.

[67] Sauer, J. and Sustmann, R., 1980. Mechanistic Aspects of Diels-Alder Reactions: A Critical Survey. *Angewandte Chemie International Edition in English,* **19(10),** 779-807.

[68] Dondoni, A., 2008. The Emergence of Thiol–Ene Coupling as a Click Process for Materials and Bioorganic Chemistry. *Angewandte Chemie International Edition,* **47(47),** 8995-8997.

[69] Morgan, C. R., Magnotta, F. and Ketley, A. D., 1977. Thiol/Ene Photocurable Polymers. *Journal of Polymer Science: Polymer Chemistry Edition,* **15(3),** 627-645.

[70] Ergin, M., Kiskan, B., Gacal, B. and Yagci, Y., 2007. Thermally Curable Polystyrene Via Click Chemistry. *Macromolecules,* **40(13),** 4724-4727.

CURRICULUM VITAE

Name Surname: **Abdulrahman MUSA**

Place and Date of Birth: **Kaduna, 03/03/81**

E-Mail: **absudais11@yahoo.com**

B.Sc.: **Ahmadu Bello University, Zaria, Kaduna, Nigeria**

PUBLICATIONS/PRESENTATIONS ON THE THESIS

- **Musa, A.**, Kışkan, B., and Yağcı, Y., 2014: Thiol-Benzoxazine Chemistry as a novel Thiol-X Reaction for the synthesis of Block Copolymer, *Polymer* (accepted for publication)