Herow RIZA

M.S. Thesis In Chemistry

July - 2010

# SYNTHESIS AND CHARACTERIZATION OF NOVEL AMPHIPHILIC POLYMERS VIA CONTROLLED RADICAL POLYMERIZATION METHODS AND CLICK REACTIONS

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Herow RIZA

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# APPROVAL PAGE

**Student** **:** Herow RIZA

**Institute** **:** Institute of Sciences and Engineering

**Department** **:** Chemistry

**Thesis Subject:** Synthesis and Characterization of Novel Amphiphilic Polymers via Controlled Radical Polymerization Methods and Click Reactions

**Thesis Date** **:** July 2010

I certify that this thesis satisfies all the requirements as a thesis for the degree of Master of Science.

________________________

Prof. Ayhan BOZKURT
**Head of Department**

This is to certify that I have read this thesis and that in my opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

________________________

Assist. Prof. Ali Ekrem MÜFTÜOĞLU
**Supervisor**

## Examining Committee Members

Assist. Prof. Ali Ekrem MÜFTÜOĞLU ____________________

Assoc. Prof. Serkan ÇALIŞKAN ____________________

Assist. Prof. Ergün GONCA ____________________

It is approved that this thesis has been written in compliance with the formatting rules laid down by the Graduate Institute of Sciences and Engineering.

________________________

Assoc. Prof. Nurullah ARSLAN
**Director**

# SYNTHESIS AND CHARACTERIZATION OF NOVEL AMPHIPHILIC POLYMERS VIA CONTROLLED RADICAL POLYMERIZATION METHODS AND CLICK REACTIONS

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Supervisor: Assist. Prof. Ali Ekrem MÜFTÜOĞLU

## ABSTRACT

Amphiphilic polymers, composed of hydrophilic and hydrophobic parts, receive great interest due to their micelle forming character. In an aqueous medium, the hydrophobic blocks of the copolymer form the core of the micelle while the hydrophilic blocks form the corona or outer shell, in which manner, hydrophobic agents can be made water-soluble. This unique feature has resulted in their utilization in many applications such as drug delivery. Click chemistry gives the opportunity to prepare block and graft polymers when used in conjunction with Controlled Polymerization Routes. Click reactions occur between terminal acetylenes and azides by metal catalysts at room temperature. Click reactions are preferable reactions for modification because of moderate reaction conditions, high yields, short reaction periods, high selectivity, tolerance for functional groups, and insensitivity to solvents.

In this study, poly(styrene-*b*-PEG-*b*-styrene) amphiphilic block copolymer and poly(MMA-*g*-2-dimethylaminoethyl methacrylate) amphiphilic graft copolymer were synthesized by using combined Atom Transfer Radical Polymerization (ATRP) and “Click” chemistry approaches. Synthesis of the former involves click coupling of azide-functional polystyrene, obtained by ATRP, with propionyl terminated PEG, prepared via Steglich esterification, in the presence of CuBr and PMDETA. The latter copolymer was prepared in the same analogy. Azide-functional hydrophilic poly(2-dimethylaminoethyl methacrylate) was grafted onto a hydrophobic acetylene side-functional PMMA backbone via a “Click” reaction. The polymers were characterized by $^1$H-NMR, and FT-IR.

**Keywords:** Amphiphilic polymer, Polyethylene oxide, Polystyrene, “Click” Reaction, Atom Transfer Radical Polymerization (ATRP)

# KONTROLLÜ POLİMERİZASYON YÖNTEMLERİ VE KLİK TEPKİMESİYLE YENİ AMFİFİLİK POLİMERLERİN SENTEZİ VE KARAKTERİZASYONU

Herow RIZA

Yüksek Lisans Tezi – Kimya Bölümü
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Tez Yöneticisi: Yrd.Doç.Dr. Ali Ekrem MÜFTÜOĞLU

## ÖZ

Hidrofilik ve hidrofobik kısımlardan oluşan amfifilik polimerler misel oluşturma özellikleri nedeniyle büyük ilgi çekmektedir. Sulu ortamlarda, hidrofobik bloklar miselin iç bölgesini oluştururken, hidrofilik bloklar kabuk kısmını oluştururlar ki bu sayede hidrofobik ajanlar suda çözünebilmektedir. Bu sıradışı özellikleri nedeniyle hidrofiller, ilaç taşıma sistemleri gibi birçok uygulamada kullanılmaktadırlar.“Klik” kimyasının Kontrollü Polimerizasyon Yöntemleriyle birlikte kullanılmasıyla blok ve aşı polimerler hazırlanabilir. Klik tepkimeleri metal katalizörler varlığında asetilen ve azid uç grupları arasında oda sıcaklığında gerçekleşirler. “Klik” tepkimelerinin polimer modifikasyonunda tercih edilme sebepleri arasında ılımlı tepkime şartları, yüksek verim, kısa tepkime süreleri, yüksek seçicilik, diğer fonksiyonel grupları iyi tolere etme ve çözücülere karşı reaktif olmama gibi etkenler sayılabilir.

Bu çalışmada, Atom Transfer Radikal Polimerizasyonu (ATRP) ve “Klik” kimyasının birlikte kullanılmasıyla poli(stiren-*b*-PEG-*b*-stiren) amfifilik blok kopolimeri ve poli(MMA-*g*-2-dimetilaminoetil metakrilat) amfifilik aşı kopolimeri sentezlendi. ATRP ile elde edilen azid fonksiyonlu polistirenle, Steglich esterleşmesiyle elde edilen propiyonil sonlu PEG’in CuBr ve PMDETA varlığında gerçekleştirilen “Klik” tepkimesiyle blok kopolimer hazırlandı. Aşı kopolimer ilkine benzer yaklaşımla sentezlendi. Azid-fonksiyonlu hidrofilik poli(2-dimetilaminoetil metakrilat) asetilen yan-fonksiyonlu hidrofobik PMMA zincirine “Klik” tepkimesiyle aşılandı. Polimerler $^{1}$H-NMR ve FT-IR ile karakterize edildi.

**Anahtar Kelimeler:** Amfifilik polimer, Polietilen oksit, Polistiren, “Klik” Tepkimesi , Atom Transfer Radikal Polimerizasyonu (ATRP)

To my family

# ACKNOWLEDGEMENT

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Finally, I am thankful to my family for all their support, patience and understanding.

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# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| $R^{\cdot}$ | : | Radical |
| M | : | Monomer |
| I | : | Initiator |
| $M_n$ | : | The number of average molecular weight |
| $M_w$ | : | The weight average molecular weight |
| $M_w$ / $M_n$ | : | The molecular weight distrubition |
| $k_{act}$ | : | Rate constant of activation step of the initiation in radical polymerization |
| $k_{deact}$ | : | Rate constant of deactivation step of the initiation in radical polymerization |
| $k_p$ | : | Rate constant of propagation step |
| $k_t$ | : | Rate constant of termination step |
| $M_t^n$ | : | Transition metal |
| R-X | : | Alkyl halide |
| CRP | : | Controlled Radical Polymerization |
| ATRP | : | Atom Transfer Radical Polymerization |
| MMA | : | Methyl methacrylate |
| RHMA | : | Alkyl a -(Hydroxymethyl)acrylate |
| EHMA | : | Ethyl a -(Hydroxymethyl)acrylate |
| BHMA | : | n-Butyl a -(Hydroxymethyl)acrylate |
| TBHMA | : | tert-Butyl a -(Hydroxymethyl)acrylate |
| PMDETA | : | *N,N,N,N',N'*-pentamethyldiethylenetriamine |
| EBiB | : | Ethyl 2-bromoisobutyrate |
| DMAP | : | 4-Dimethylaminopyridine |
| DCC | : | Dicyclohexylcarbodiimide |
| THF | : | Tetrahydrofuran |
| GPC | : | Gel Permation Chromatography |

| | | |
|---|---|---|
| UV | : | Ultra Violet |
| NMR | : | Nuclear Magnetic Resonans Spectroscopy |
| $T_g$ | : | Glass Transition Temperature |
| TLC | : | Thin Layer Chromatography |

# CHAPTER 1

# INTRODUCTION

## 1.1 GENERAL INFORMATION ABOUT AMPHIPHILIC POLYMERS

Amphiphilic polymers, which are composed of hydrophilic "water-loving" and hydrophobic "water-hating" segments, attract great interest due to their micelle forming character in aqueous media. [1-10] These materials have found utilization in many application potential e.g. in the stabilization of latex particles, emulsions, dispersions, separations and also as drug and gene delivery vehicles. [11-19]

In amphiphilic polymers synthesis, controlled radical polimerization routes such as atom transfer radical polimerization (ATRP) and also click reactions can be used.[20,21]

## 1.2 CONTROLLED RADICAL POLYMERIZATION

Radical polymerization (RP) is a very important important commercial process for preparing high molecular weight polymers because it can be used for numerous vinyl monomers under mild reaction conditions, requiring an oxygen free medium, but tolerant to water, and large temperature ranges (-80 to 250$^{o}$C). [22] In addition, many monomers can easily copolymerize radically leading to an infinite number of copolymers with properties dependent on the proportions of the comonomers. The disadvantages of conventional radical polymerization is the poor control of macromolecular structures including degrees of polymerization, polydispersity index (1.5 or 2.0), and also the practical impossibility to synthesize block copolymers, and other advanced structures. Various processes have been developed to control of free radical polymerization during the last decade and thus polymers with low polydispersities, compositions, architectures and functionalities were synthesized.

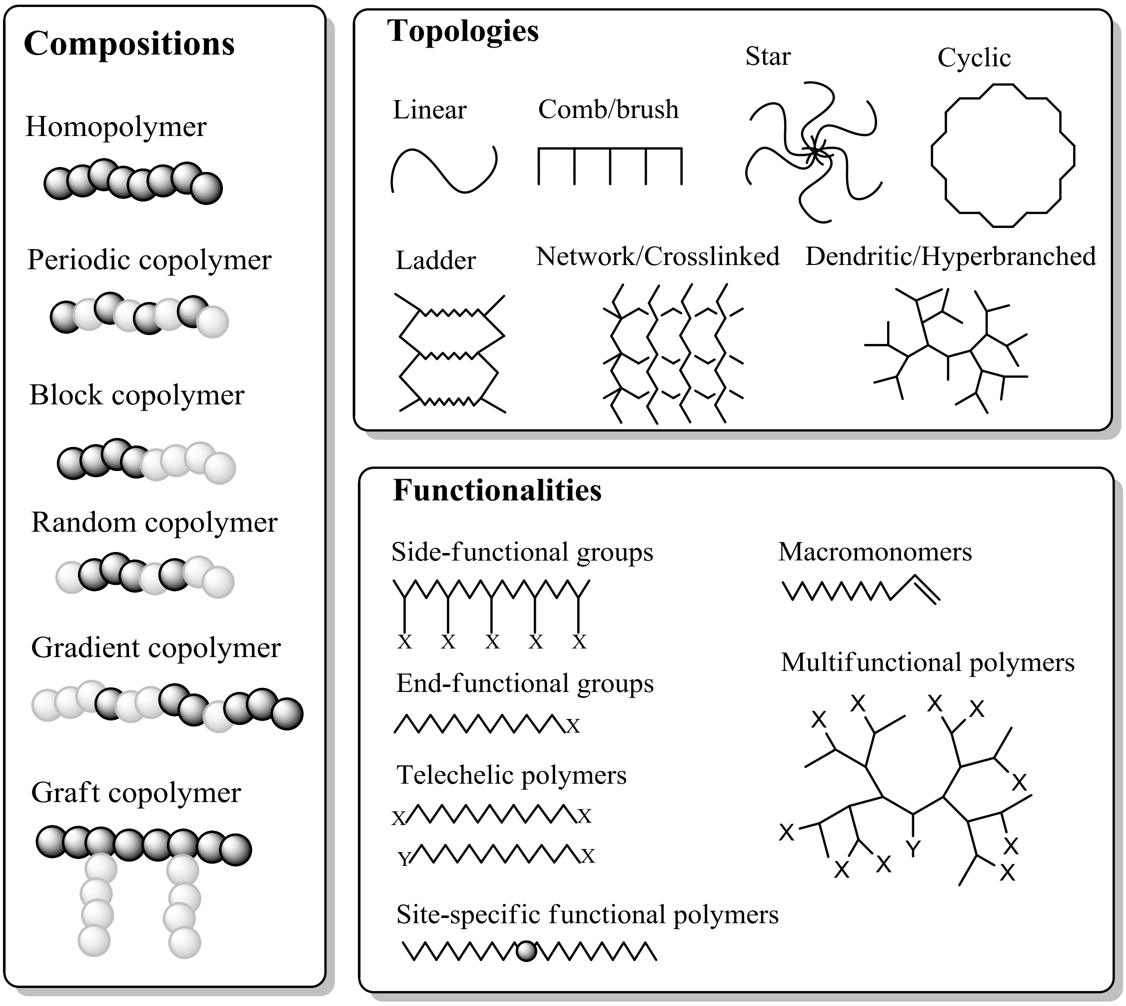


**Figure 1.1** Polymers obtained by Controlled Free Radical Polymerization (CRP) routes.

The mechanism invoked in CRP processes to extend the lifetime of growing radicals utilizes a dynamic equilibration between dormant and active sites with rapid exchange between the two states. Unlike conventional radical processes, CRP requires the use of persistent radical (deactivator) species, or highly active transfer agents to react with propagating radicals. These persistent radicals/transfer agents react with radicals (deactivation or transfer reactions with rate constant, $k_{deact}$) to form the dormant species. Conversely, propagating radicals are generated from the dormant species by an activation reaction (with rate constant, $k_{act}$). [23] The mechanism is shown below.

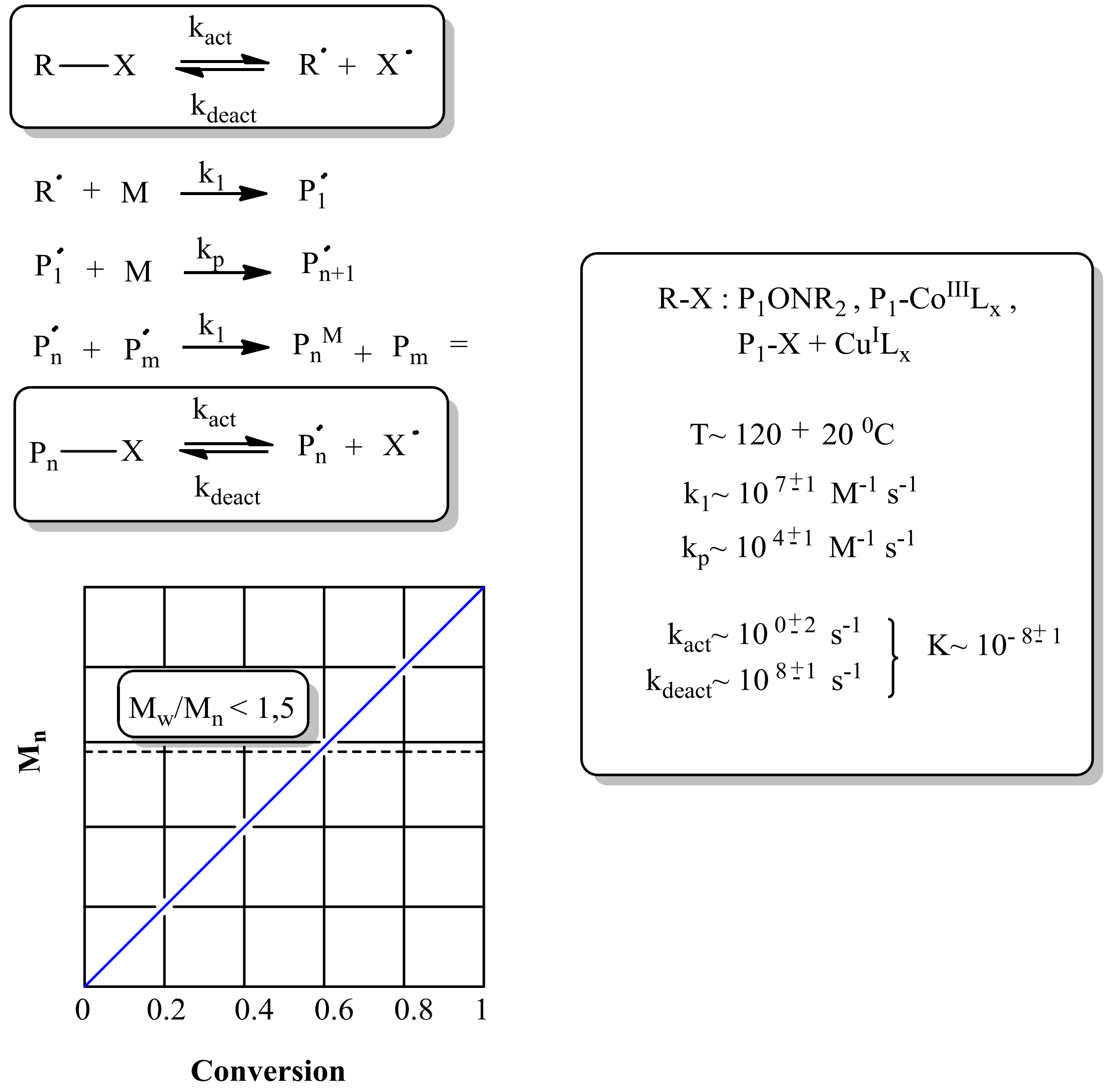


**Figure 1.2** Mechanism of Controlled Radical Polymerization.

In the 1990s, several methods were developed that enable controlled radical polymerization. These methods include: stable free-radical polymerization (SFRP), best represented by polymerization mediated with TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl) [24], metal-catalyzed atom transfer radical polymerization (ATRP) [25], reversible addition–fragmentation chain transfer (RAFT) [26] and Diphenylethene method (DPE). [27] Using these polymerization methods, the molecular weight of the polymers linearly increases with conversion and the polydispersities are well below 1.5.

## 1.3 ATOM TRANSFER RADICAL POLYMERIZATION

Atom transfer radical polymerization (ATRP) is one of the most efficient controlled/living radical polymerization (CRP) method.[28] Well-defined polymers with low polydispersities and complex architectures can be achived by ATRP.[29]

A typical ATRP requires an activated halide (RX) as initiator, a transition metal in its lower oxidation state ($M_t^n$), a ligand that complexes with the metal and finally a monomer (M).[28]

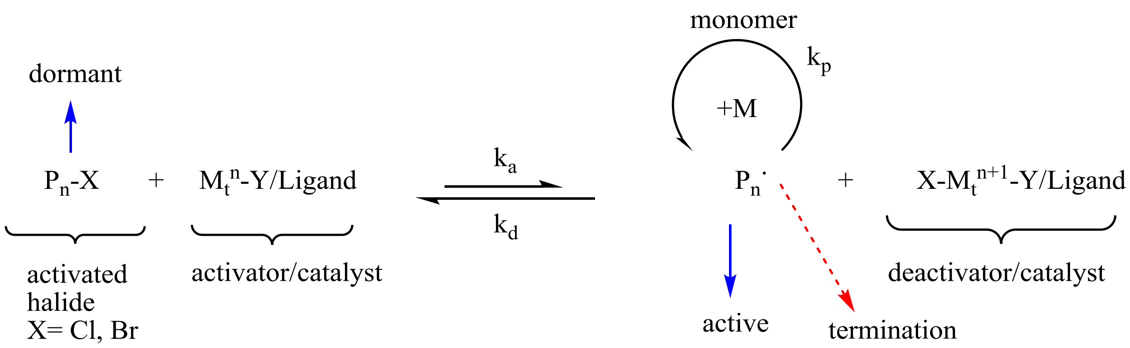


**Figure 1.3** The mechanism of ATRP.

In ATRP process, the propagating radicals, $P_n^{\cdot}$, are generated through a reversible redox process catalyzed by a transition metal complex (activator, $M_t^n$-Y/Ligand, where Y may be another ligand or a counterion) which undergoes a one-electron oxidation with concomitant abstraction of a halogen atom, X, from a dormant species, R-X ($P_m$-X). Radicals react reversibly with the oxidized metal complexes, X-$M_t^{n+1}$/ ligand, the deactivator, to reform the dormant species and the activator.This process occurs with a rate constant of activation, $k_a$, and deactivation $k_d$, respectively. Polymer chains grow by the addition of the free radicals to monomers in a manner similar to a conventional 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 percent percent of the polymer chains undergo termination. Elementary reactions consisting of initiation, propagation, and termination are showed below. Figure 1.4.

Initiation

$$R{-}X \;+\; M_t^{n}\text{-}Y\,/\,\text{Ligand} \;\rightleftharpoons\; R \;+\; X\text{-}M_t^{n+1}\text{ - }Y\,/\,\text{Ligand}$$

$$R \;+\; M \;\xrightleftharpoons{k_i}\; P_1$$

Propogation

$$P_n{-}X \;+\; M_t^{n}\text{-}Y\,/\,\text{Ligand} \;\xrightleftharpoons[k_d]{k_a}\; P_n \;+\; X\text{-}M_t^{n+1}\text{ - }Y\,/\,\text{Ligand}$$

$$P_n \;+\; M \;\xrightleftharpoons{k_p}\; P_{n+1}$$

Termination

$$P_n \;+\; P_m \;\xrightleftharpoons{k_t}\; P_{n+m}$$

**Figure 1.4** Elementary reactions consisting of initiation, propagation, and termination.

ATRP is a multi-component system, so concentrations and the structures of all these compounds affect the polymerization rate and the properties of the resulting polymer. Basic components of ATRP, monomers, a specific initiator, metal, ligands, temperature, reaction time and solvent should be selected.

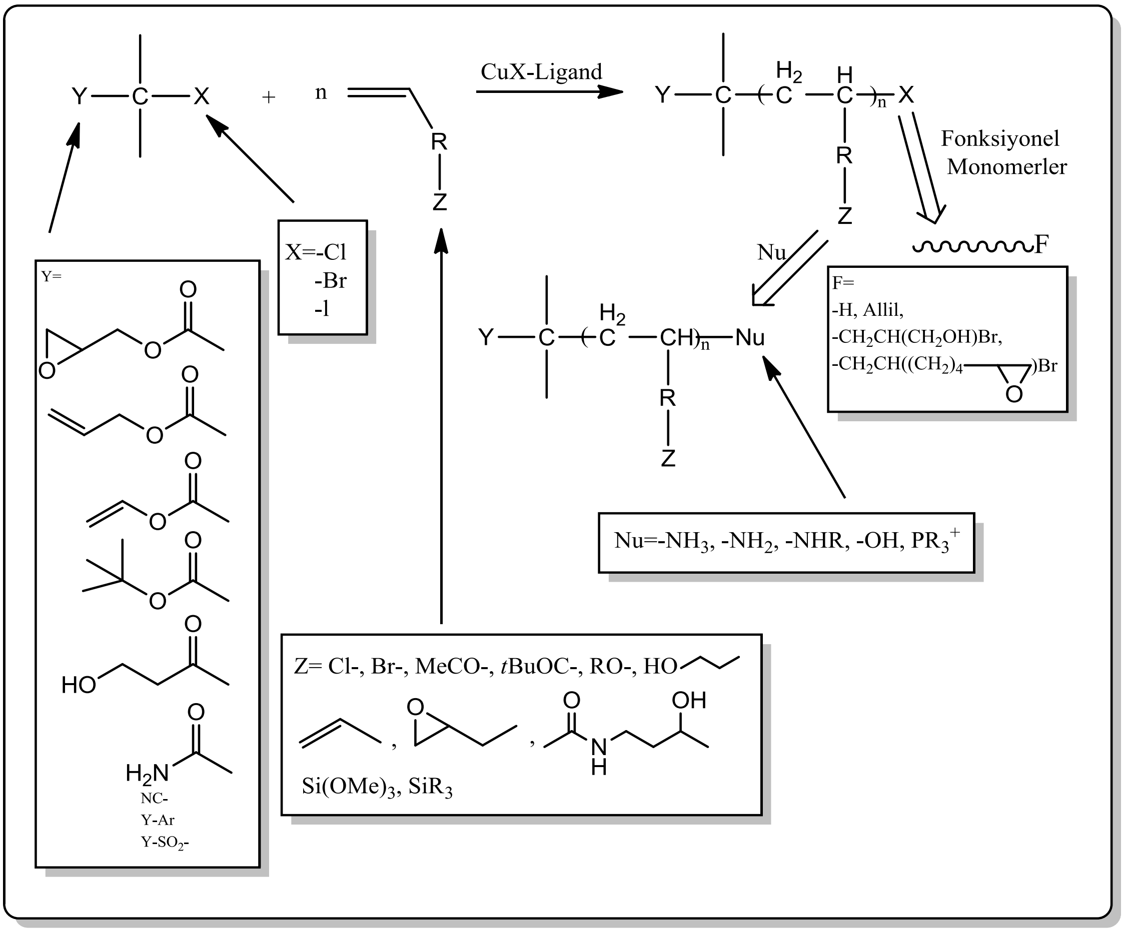


**Figure 1.5** Synthesis functional polymers via ATRP

## 1.3.1 COMPONENTS OF ATRP

### 1.3.1.1 Monomers

In ATRP, various monomers, such as styrenes, (meth)acrylates, (meth)acylamides, acrylonitrile, diens, N-vinylpridine and other monomers can be used to obtain well-defined polymers. Generally, styrene and MMA are used in ATRP.

Styrene: Styrene ATRP is usually conducted at 110 $^0$C for bromide-mediated polymerization and 130 $^0$C fort the chloride-mediated polymerization [30] and the most frequently preferred system is bulk.

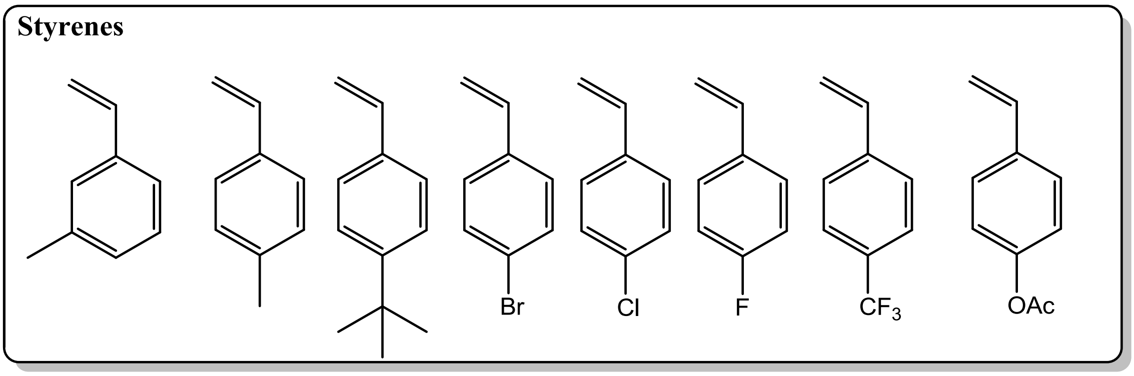


**Figure 1.6** Styrene derivates used as ATRP monomers.

Methyl Methacrylate: The standard conditions for ATRP of methyl methacrylate are similar to those of ATRP of styrene except that less copper (I) catalyst is needed and the polymerizations are conducted in %50 solution (dimethoxy benzene or diphenyl ether) at 90 $^0$C.

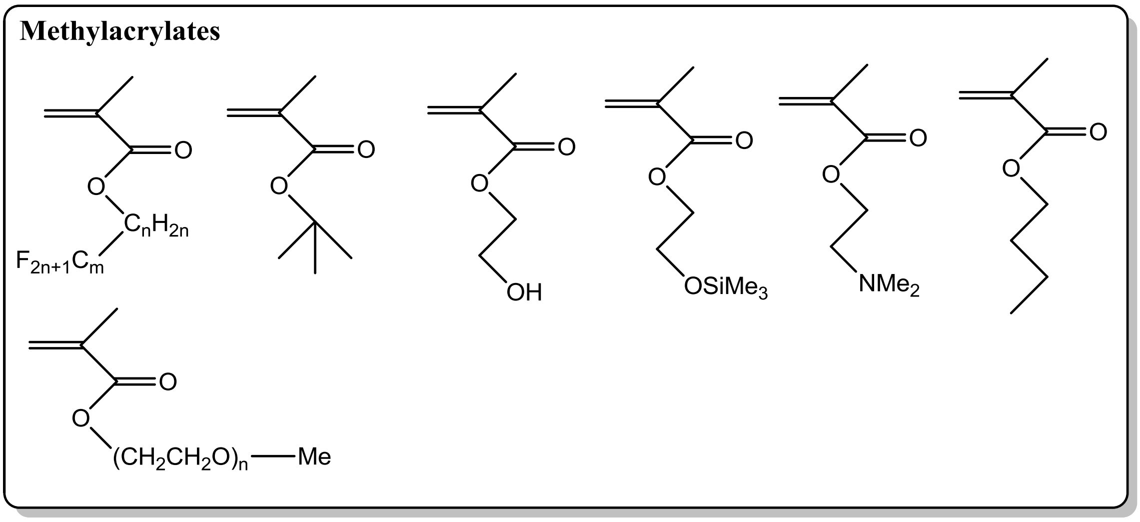


**Figure 1.7** Methacrylates used as ATRP monomers.

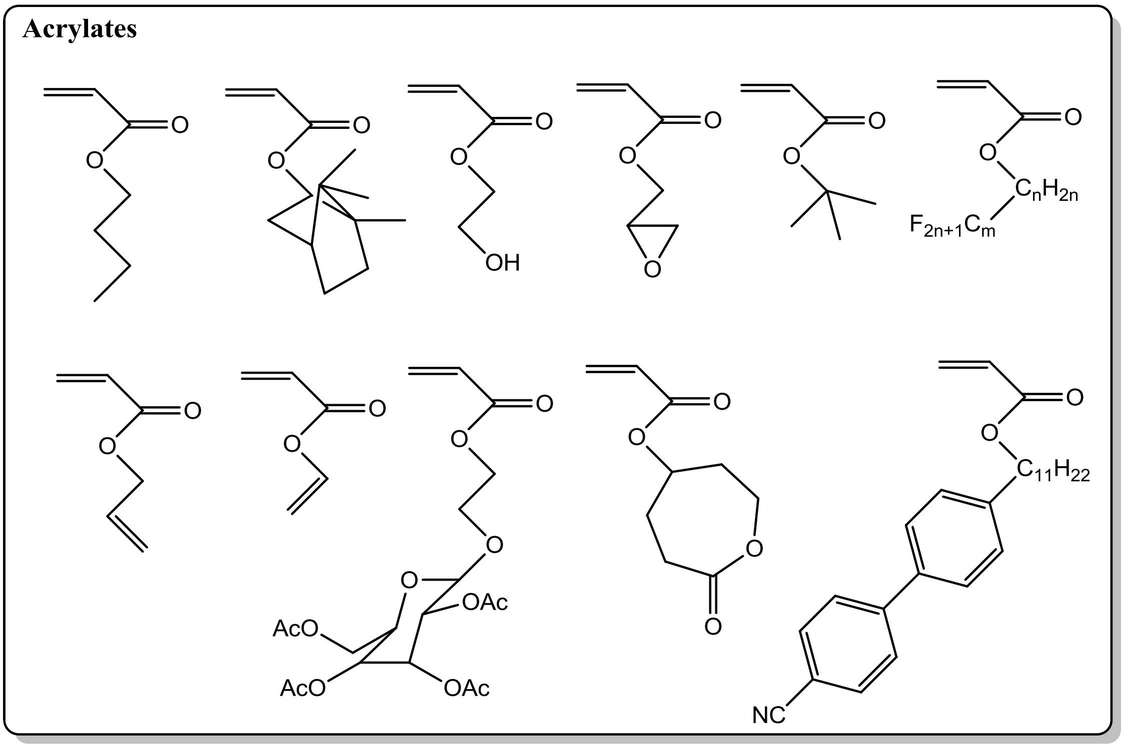


**Figure 1.8** Acrylates used as ATRP monomers.

### 1.3.1.2 Initiators

The main role of the initiator is to determine the number of growing polymer chains. A varitey of activated alkyl halides (RX) are characteristic used as initiator and the rate of the polymerization is first order with respect to the concentration of RX in ATRP systems. Initiation is accomplished with homolytic cleavage of activated halides and addition of generated radicals to monomer as depicted in Figure 1.7. To obtain well-defined polymers with narrow molecular weight distributions, the halide group, X, must rapidly and selectively migrate between the growing chain and the transition metal complex. When X is either bromide or chloride, the molecular weight is well controlled.[31,32]

$$\mathrm{R\text{-}X} \quad + \quad \mathrm{M_t^{n}} \,/\, \mathrm{Ligand} \quad \rightleftharpoons \quad \mathrm{R.} \quad + \quad \mathrm{.\,X\text{-}M_t^{n+1}} \,/\, \mathrm{Ligand}$$

$$\mathrm{R.} + \mathrm{M} \quad \longrightarrow \quad \mathrm{RM.}$$

**Figure 1.9** Initiation in ATRP.

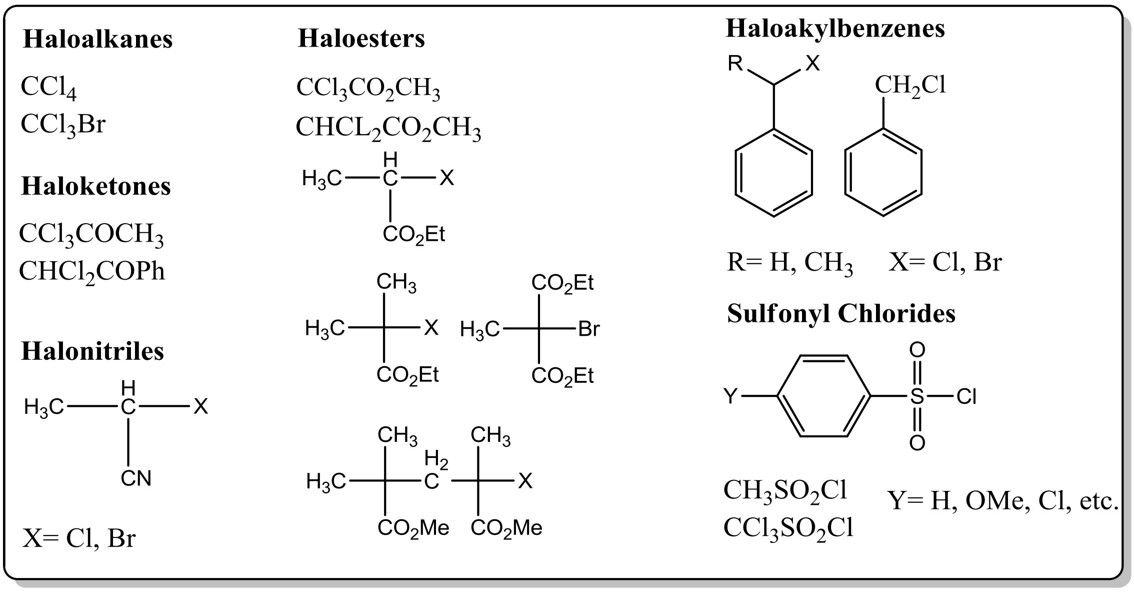


**Figure 1.10** The most commonly used intiators in ATRP systems.

### 1.3.1.3 Transition Metals

Perhaps the most important component of ATRP is the catalyst. It is the key to ATRP since it determines the position of the atom transfer equilibrium and tje dynamics of exchange between the dormant and active species. There are several prerequisites that a transition metal has to satisfy to result in a succesfull ATRP process:

- The metal center must have at least two readily accessible oxidation states separated by one electron.
- The metal center should have reasonable affinity toward a halogen.
- The coordination sphere around the metal should be expandable upon oxidation to selectively accommodate a (pseudo) halogen.
- The ligand should complex the metal relatively strongly.
- Position and dynamics of the ATRP equilibrium should be appropriate for the particular system. To differentiate ATRP from the conventinal redox-initiated polymerization and induce a controlled process, the oxidized transition metal should rapidly deactive the propagating polymer chains to from the dormant species.[33]

A variety of transition metal complexes with various ligands have been studied as ATRP catalysts. The majority of wrok on ATRP has been conducted using copper as the transtion metal. A part from copper-based complexes, Fe [34], Ni [35], Ru [36],etc have been used to some extent. Recent work from Sawamoto and co-workers shows that the Ru-based complexes can compete with the Cu-based systems on many fronts. A specific Fe-based catalyst has also been reported to polymerize vinyl acetate via an ATRP mechanism.[37]

#### 1.3.1.4 Ligands

There are two main roles of ligands in ATRP. The first role is to solubilize the transition metal salt in the organic media. They control solubilities and ensure stability of the complex in different monomers, solvents and temperatures. Polymers with lower polydispersities are usually obtained with a homogenous catalyst due to fine-tuning of the equilibrium. The second role is to adjust the redox potential of the metal center for appropriate reactivity and dynamics for the atom transfer. Another words, the ligand playes a crucial role in tuning the activity of the related catalyst in the activation and deactivation steps of the ATRP mechanism. Fast deactivation of the active radicals by halogen transfer ensures that all polymer chains are growing at approximately the same rate, leading to a narrow molecular weight distribution. Relatively fast activation of the dormant polymer chains provides a reasonable polymerization rate.[38]

The most common ligands for ATRP systems are substituted bipyridines, alkyl pyridylmethanimines and multidentate aliphatic tertiary amines such as N,N,N$^{'}$,N$^{''}$,N$^{''}$ pentamethyldiethylenetriamine (PMDETA), and tris[2-(dimethylamino) ethyl]amine ($Me_6$-TREN). [39,40]

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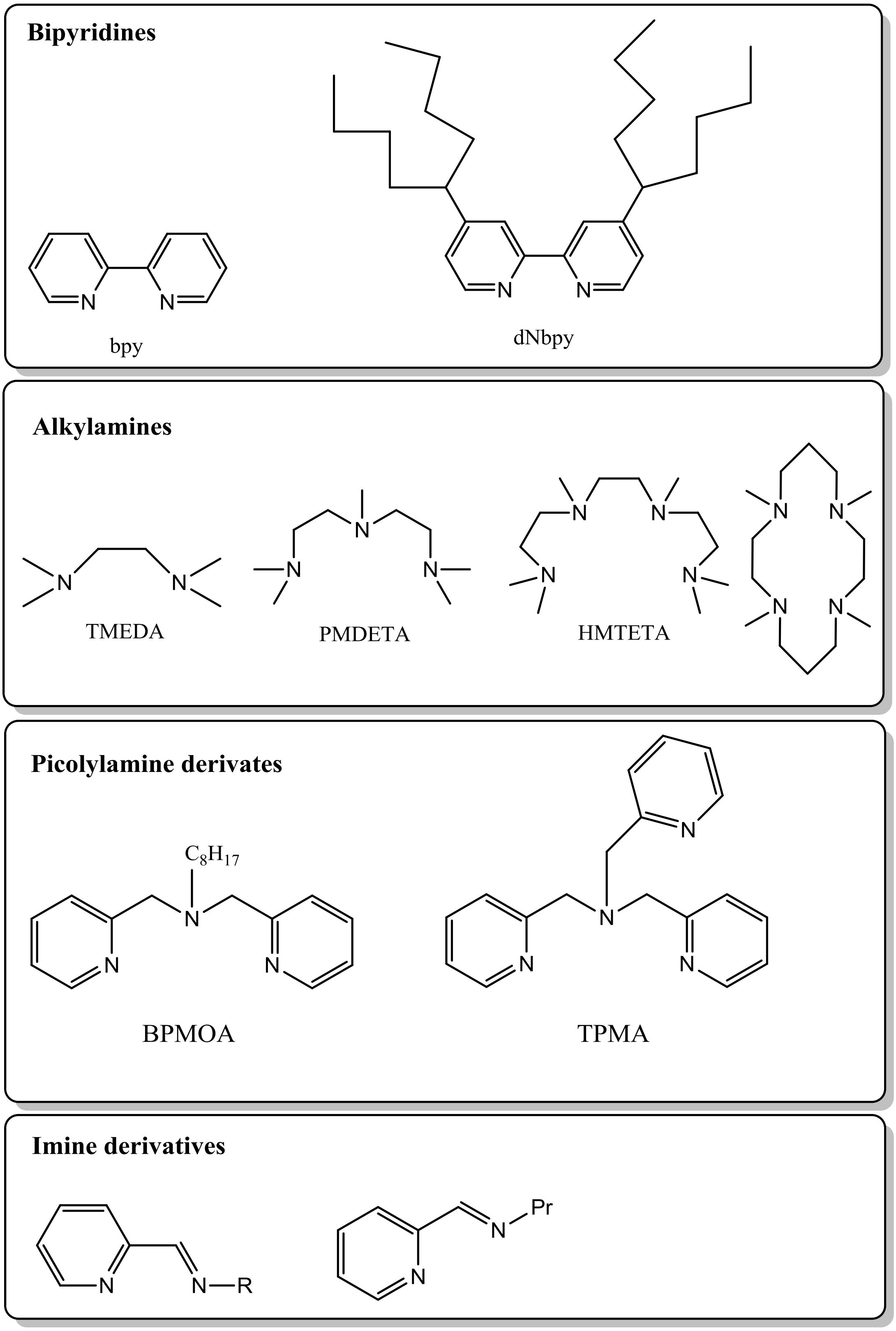


**Figure 1.11** Examples of ligands used in copper-mediated ATRP are illustrated

### 1.3.1.5 Solvents

ATRP can be carried out in bulk, in solution or in heterogeneous systems (e.g., emulsion, suspension). Various solvents, such as benzene, toluene, anisole, diphenyl ether, ethyl acetate, acetone, dimethyl formamide (DMF), ethylene carbonate, alcohol, water, carbon dioxide, and many others, have been used for different monomers. A solvent is sometimes necessary, especially when the obtained polymer is insoluble in its monomer (e.g., polyacrylonitrile). Several factors affect the solvent choice. Chain transfer to solvent should be minimal. In addition, interactions between solvent and the catalytic system should be considered. Catalyst poisoning by the solvent (e.g., carboxylic acids or phosphine in copper-based ATRP) and solvent-assisted side reactions, such as elimination of HX from polystyryl halides, which is more pronounced in a polar solvent, should be minimized.[41,42]

### 1.3.1.6 Temperature and Reaction time

The rate of polymerization in ATRP increases with increasing temperature due to the increase of both the radical propagation rate constant and the atom transfer equilibrium constant. As a result of higher the rate of radical propagation than the rate of radical termination, higher $k_p/k_t$ ratios and better control "livingness" may be observed at higher temperatures. However, chain transfer and other side reactions become more pronounced at elevated temperatures. In general, the solubility of the catalyst increases at higher temperatures; however, catalyst decomposition may also occur with the temperature increase. The optimal temperature depends mostly on the monomer, the catalyst and the targeted molecular weight.

At high monomer conversions, the rate of propagation slows down considerably; however, the rate of any side reaction does not change significantly, as most of them are monomer concentration independent. Prolonged reaction times leading to nearly complete monomer conversion may not increase the polydispersity of the final polymer but will induce loss of end groups. Thus, to obtain polymers with high end-group functionality or to subsequently synthesize block copolymers, conversion must not exceed 95% to avoid endgroup loss. [43]

## 1.4 CLICK CHEMISTRY

Click chemistry gives the opportunity to attach ligands onto polymers for modification is called click reaction and it is also known as Sharpless ‘click’ reaction.[44,45]

This modification process provides;
- often quantitative yields,
- a high tolerance of functional groups
- an insensitivity of the reaction to solvents
- reaction at various types of interfaces such as solid/liquid, liquid/liquid, or even solid/solid interfaces. [45].

Click reactions are preferable reactions for modification because of moderate reaction conditions, high yields, short periods of reaction times and high selectivity.[44,46,47] There is a wide range of application field of this reaction, which varies with the sort of polymers.[48]

Click reactions, which are derivatives of Huisgen 1, 3 dipolar cyloaddition reactions, occurs between terminal acetylenes and azides by metal catalyst at room temperature.[49-51] The click reaction is illustrated below.

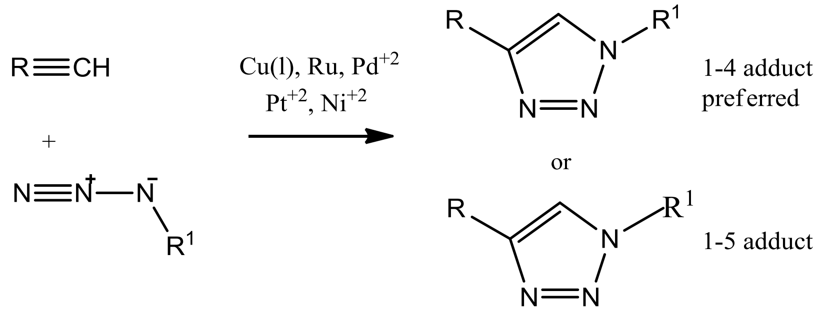


**Figure 1.12** Click reaction

### 1.4.1 Suitable Compounds for Click Chemistry

Exceptions of self-reactive reagents and materials that can produce stable complexes with Cu (I), all functional groups are suitable for click reactions.[52,53] The figure shows the compounds, which are not suitable for, azide/alkyne-type click reactions because of the Huisgen 1, 3 dipolar cyloaddition side reactions.[54,55]

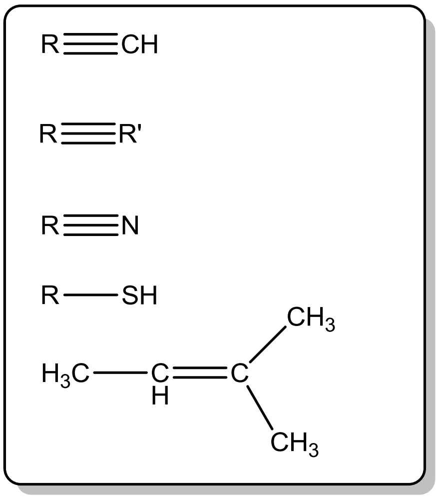


**Figure 1.13** Unsuitable compounds for click reaction

### 1.4.2. Mechanism of Click Reactions

As it mentioned before click reactions occurs between terminal acetylenes and azide by metal catalyst. The mechanism of click reactions first explained by Meldal and co-workers and Sharpless and co-workers. [48,52,53] Multifarious catalytic systems are present to affect the 1, 3-dipolar cycloaddition process. Cu (I) salts can be directly used or Cu (I) species can be obtained from the reduction of Cu (II) by sodium ascorbarte or metallic copper in catalytic systems. [52,53,56] The mechanism of click reactions, shown below, depends on the Cu-acetylide formation. [52,53]

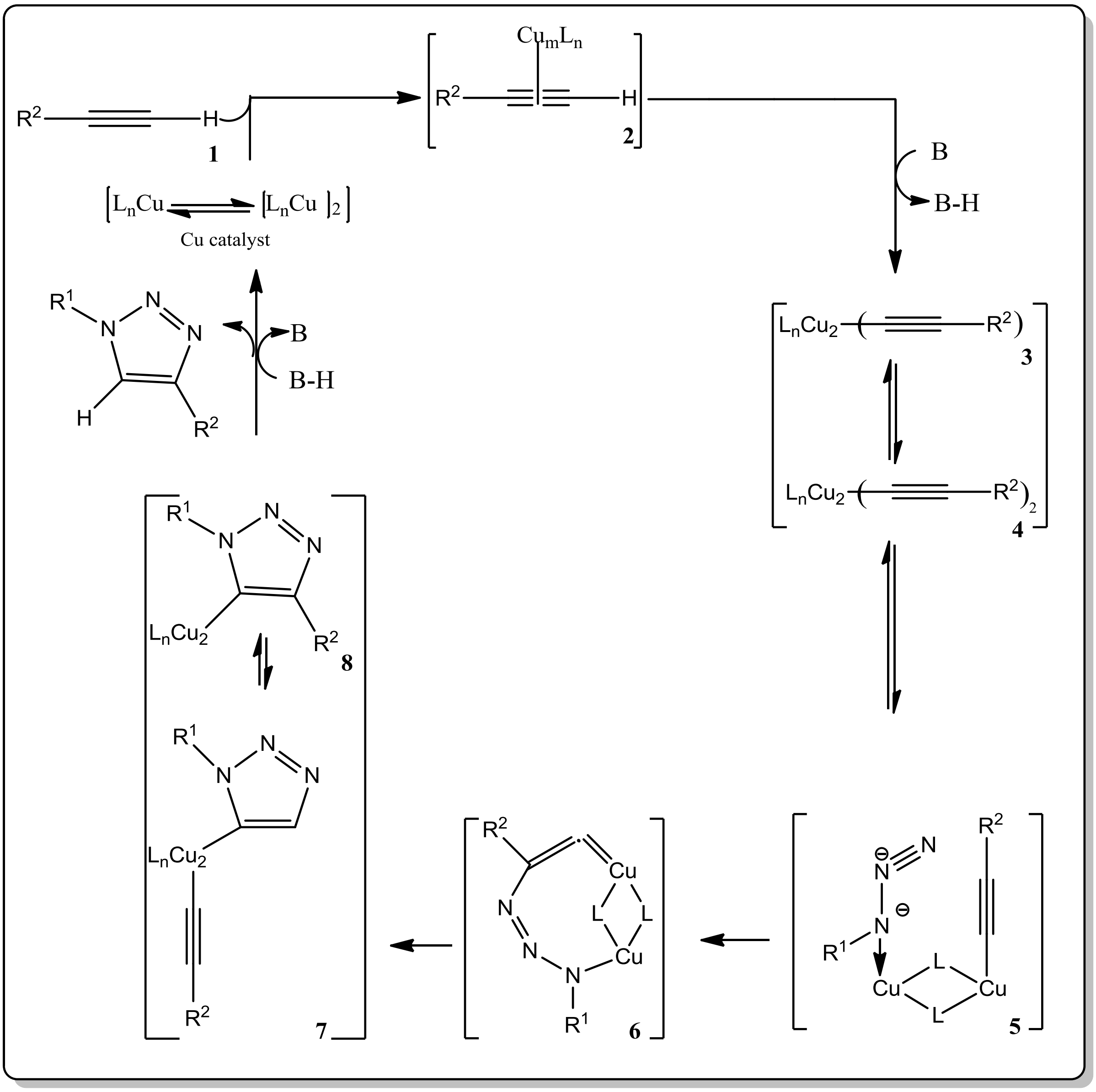


**Figure 1.14** Mechanism of Click reaction

Terminal alkynes and Cu (I) particles produce a π-complex (Cu-acetylide) to lower pKa value of the terminal alkynes that allow attack onto C-H bond. [46-48] In addition, 1-5 equivalents of base have positive influences on the formation of the copper (I)-acetylide. THF, diethyl ether, DMF, DMSO or halogenated solvents are applicable for click reactions. And also, water/alcohol or water/toluene systems can give excellent results. [57-59]

# CHAPTER 2

# EXPERIMENTAL PART

## 2.1 CHEMICALS

The monomers, methyl methacrylate (MMA), dimethylaminoethyl methacrylate (DMAEMA), 2-hydroxyethyl methacrylate (HEMA), styrene were purchased from Aldrich and they were distilled over $CaH_2$ under decreased pressure prior to use. Propiolic acid (Acetylene-carboxylic acid) was purchased from Merck and was used as received. PMDETA (N,N,N′,N″,N″-Pentamethyldiethylenetriamine, 99%), bipyridine (bpy), HMTETA (hexamethyltriethylenetetramine) were purchased from Aldrich. DCC (N,N'-Dicyclohexylcarbodimide, 99% ) and DMAP (4-Dimethylamino) pyridine, 99%) were purchased from Aldrich. Toluene and dichloromethane ($CH_2Cl_2$) were purified by distillation over $CaH_2$ under decreased pressure. Tetrahydrofuran (THF), hexane, methyl alcohol ($CH_3OH$) and dimethylformamide (DMF) were used without further purification. Copper (I) bromide (CuBr), Copper (I) chloride, p-Tosyl chloride (p-TsCl) and sodium azide ($NaN_3$) were purchased from Sigma-Aldrich. Ethyl-2-bromo isobutyrate (EBIB) was purchased from Aldrich and it was used as received. Polyethleneglycol (PEG-3000) was purchased from Sigma-Aldrich.

## 2.2 INSTRUMENTATION

$^1$H-NMR spectra was recorded on a Bruker AM 400 or an AC 200 instrument for solutions in $CDCl_3$. Chemical shifts are reported in ppm relative to TMS as internal standard for the $^1$H spectra. Multiplicities are described using the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet and br=broad. FT-IR spectra were recorded on a Bruker Alpha-P in the range of 400-4000cm$^{-1}$.

GPC measurements were performed on tetrahydrofuran (THF) solutions of the polymers (on the THF soluble parts of the polymer) using a GPC 1100 (Agilent) instrument. The measurements were standardized against THF solutions of a polystyrene standard.

## 2.3 CHEMICAL SYNTHESIS AND PREPARATION

### 2.3.1 Synthesis of PEG-Alkyne

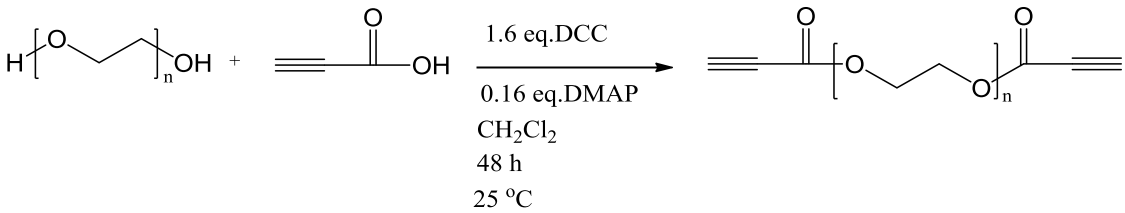


**Figure 2.1** Synthesis of PEG-alkyne.

Firstly, PEG-3000 (1g , $3.33 \times 10^{-4}$ mol ) was dissolved in $CH_2Cl_2$ (20 mL). Then propiolic acid (62 μL, $5 \times 10^{-4}$ mol), DCC (0.100 g, 5.33 x $10^{-4}$mol) and DMAP (6.5 mg, $5.33 \times 10^{-5}$ mol) were added to the solution, which was then allowed to stir at room temperature for 48 hours. The polymer was precipitated in diethyl ether, filtered and dried under vacuum at 40°C. (yield 94 %) (see Figure 2.1). $^1$H-NMR ($CDCl_3$, ppm, δ): 4.39 ( 2H,-O-**$CH_2$**- $CH_2$-), 3.68 (2H, -$CH_2$**$CH_2$**O-), 2.65 (**HC**≡C-CO-O- , PEG –alkyne). Mn: 3322 g/mol from $^1$H-NMR. For PEG-OH, FT-IR ($cm^{-1}$): 3440, 2882, 1967, 1461, 1337, 1091, 1056. For PEG-alkyne, FT-IR($cm^{-1}$): 2886, 2746, 2112, 1967, 1711, 1461, 1342, 1091, 1051.

### 2.3.2 Synthesis of Polystyrene (PS)

CuBr (0.0626 g, $4.37 \times 10^{-4}$ mol), PMDETA (91μL, $4.37 \times 10^{-4}$ mol), ethyl 2-bromo isobutyrate ( 128 μL, $8.73 \times 10^{-4}$ mol) as an initiator , styrene (10 mL, 0.0873 mol )were introduced in a Schlenck tube and the reaction mixture was degassed by three freze-pump-thaw cycles and left vacuo. The tube was stirred at 110 °C for 3 hours. Then, the mixture was diluted with THF, and passed through a silica column to remove the complex salts. The resulting polymer was precipitated in methanol and collected by vacuum filtration and the poymer was dried under vacuum at 40 $^0$C for 24 h as depicted in Figure 2.2. (yield, 75 %). $^1$H-NMR ($CDCl_3$, ppm, δ): 7.02-6.39 (5H, m, from aromatic ring), 3.68 (2H, $CH_3\boldsymbol{CH_2}$-O-), 2.55 ($CH_3CH_2OCOC(CH_3)_2$-$\boldsymbol{CH_2}$CH-), 1.18 ($\boldsymbol{CH_3}CH_2$-O-), GPC: Mn= 2400, PDI: 1.28 FT-IR ( cm$^{-1}$) : 3026, 2918, 2846, 1482, 1467, 756, 699.

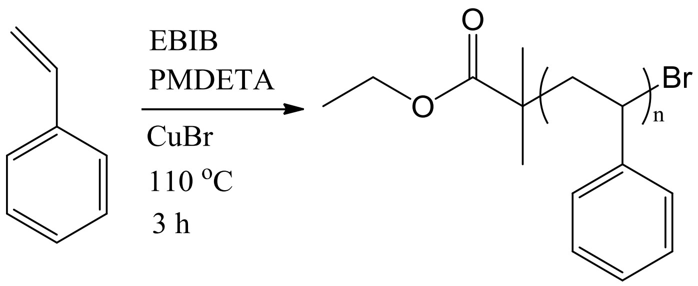


**Figure 2.2** Synthesis of Polystyrene (PS).

### 2.3.3 Synthesis of Azide-Functional Polystyrene (PS-$N_3$)

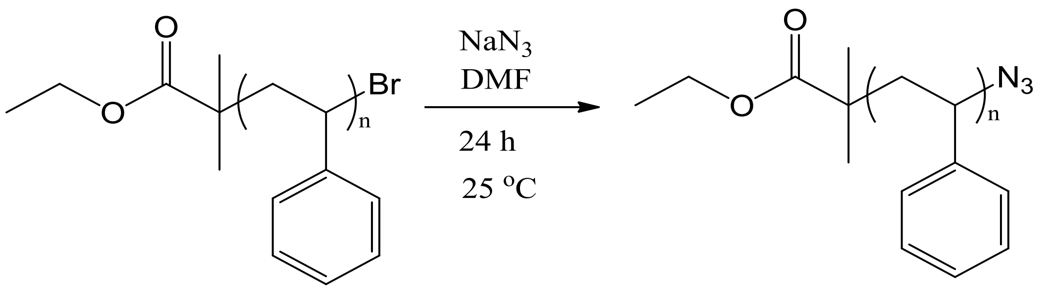


**Figure 2.3** Synthesis of azide-functional polystyrene.

A typical procedure for the preparation PS-$N_3$ is as follows. PS (3g, 3.75 $\times 10^{-4}$ mol) was dissolved in 50 mL N,N- dimethylformamide (DMF) and $NaN_3$ (0.0317 g, 4.88 $\times 10^{-4}$ mol ) was added in a Schlenk tube. The resulting solution was allowed to stir at 25 °C 24 hours. Then, DMF was removed with rotary evaporator and the polymer was dissolved in $CH_2Cl_2$.Then, it was extracted with distilled water three times, then it was precipitated in methanol, collected by vacuum filtration and dried at 40 °C in a vacuum oven for 24 h. $^1$H-NMR ($CDCl_3$, ppm, δ): 7.02-6.39 (5H, m, from aromatic ring), 3.68 (2H, $CH_3\boldsymbol{CH_2}$-O-), 2.45($CH_3CH_2OCOC(CH_3)_2$-$\boldsymbol{CH_2}$CH-), 1.18($\boldsymbol{CH_3}CH_2$-O ), GPC: Mn: 2800, PDI: 1.22, FT-IR ( $cm^{-1}$) : 3027, 2917, 2851, 2094, 1492, 1448, 753, 691.

### 2.3.4 Synthesis of Poly(Styrene-*b*-PEG-*b*-Styrene) by using Click Reaction

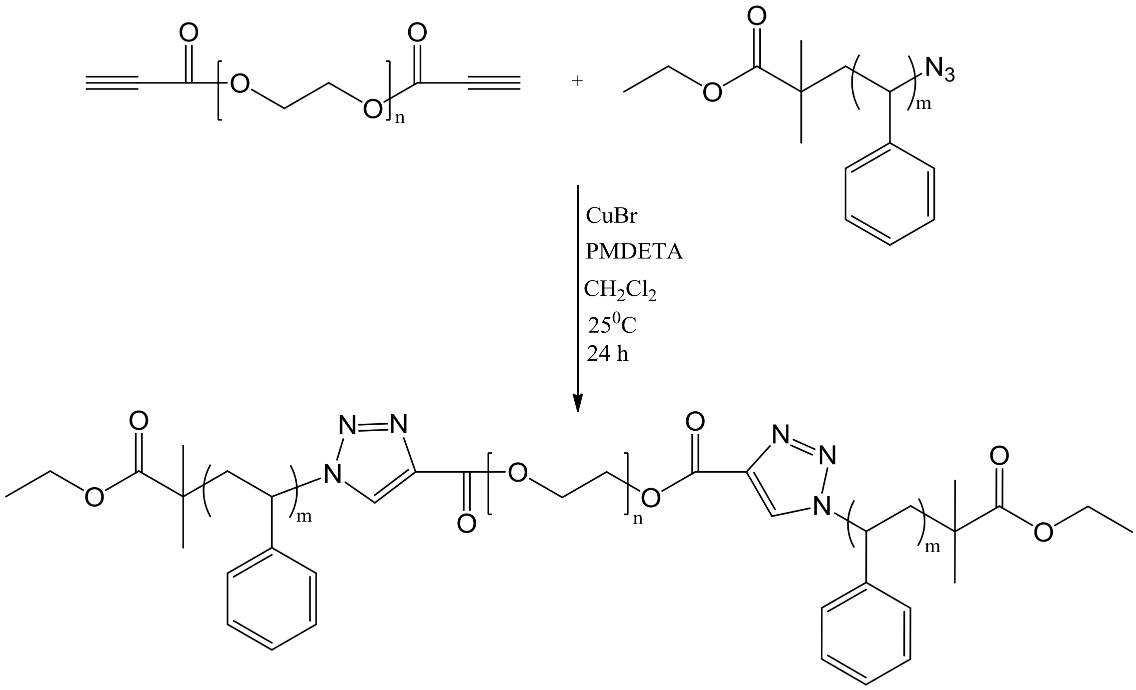


**Figure 2.4** Synthesis of Poly(Styrene-*b*-PEG-*b*-Styrene) by Click Reaction

A typical procedure for the click reaction was as follows: ([PS-$N_3$]/[PEG-alkyne]/[CuBr]/[PMDETA] - [2,2]:[1]:[20]:[20], $25^oC$) as depicted in Figure (2.4). 0.8 g ($10^{-4}$ mol) of PSt-$N_3$, 0.15g ($4.55x10^{-5}$mol) of PEG-alkyne, 0.132g ($4.55x10^{-4}$mol) of CuBr and 25ml $CH_2Cl_2$ were added into a Schlenk flask with a magnetic bar. The mixture was bubbled with nitrogen for 15 min. Three vacuum- purge nitrogen were performed then PMDETA was added. The mixture was stirred overnight at room temperature. After the reaction, the mixture was further diluted with THF, and passed through a silica-gel column to remove the catalyst. The product was precipitated in diethyl ether, and dried at room temperature in a vacuum oven for 48 h. $^1$H-NMR ($CDCl_3$, ppm, δ): 7.45 (s, 1H, from triazole group), 7.02-6.38(m, 5H, from aromatic rings), 4.51 (s, 2H, ($CH_3CH_2OCOC(CH_3)_2$-$CH_2$***CH***-), 3.59 (t, 2H, -$CH_2$**$CH_2$**O-, from PEG), 2,54 (s, **HC**≡C-CO-O-, PEG-alkyne), 2.29 (m, 2H, $CH_3CH_2OCOC(CH_3)_2$-

***CH*$_2$**CH-), 1.35 (t, 3H, ***CH*$_3$**$CH_2$-O-). FTIR(cm-1): 3031, 2922, 2851, 2100, 1727, 1596, 1493, 1449, 1025, 759, 694. GPC : Mn = 6600 PDI = 1.35

### 2.3.5 Synthesis of Poly(hydroxyethyl methacrylate-*co*-methyl methacrylate) p( HEMA-*co*-MMA)

CuCl ( 0.0726 g, 7.33 x $10^{-4}$ mol ), bipyridine (bpy) (0.2862 g, 1.83x$10^{-3}$ mol), ethyl 2-bromo isobutyrate (190 µL, 7.33 x $10^{-4}$mol ) as an initiator, HEMA (1.6 mL, 0.0132 mol) and MMA (6.4 mL, 0.0601 mol) and 5.3 mL methanol were introduced in a Schlenck tube and the reaction mixture was degassed by three freze-pump-thaw cycles. The tube was stirred at 22 $^{o}$C for 14 hours. Then, the mixture was diluted with THF, and passed through a silicagel column to remove the complex salts. The resulting copolymer was precipitated in hexane and collected by vacuum filtration and the copolymer was dried under vacuum at 60 $^{0}$C for 24 h. (conv.: 68 %) $^{1}$H-NMR ($CDCl_3$, ppm, δ): 4.10 (2H,-COO**$CH_2$**-), 3.82 (2H, -COO$CH_2$**$CH_2$**OH), 3.60 (3H, -COO**$CH_3$**), 2.64 (-$CCH_3$**$CH_2$**- , PMMA), 1.92 (-**$CH_2$**$CCH_3$, PHEMA), 1.41(6H,-C(**$CH_3$**)$_2$ ), 1.24 (3H,**$CH_3$**$CH_2$OCO-). FT-IR ( $cm^{-1}$) : 3528, 2996, 2948, 1721, 1443, 1148. GPC : Mn : 5800; PDI : 1.29.

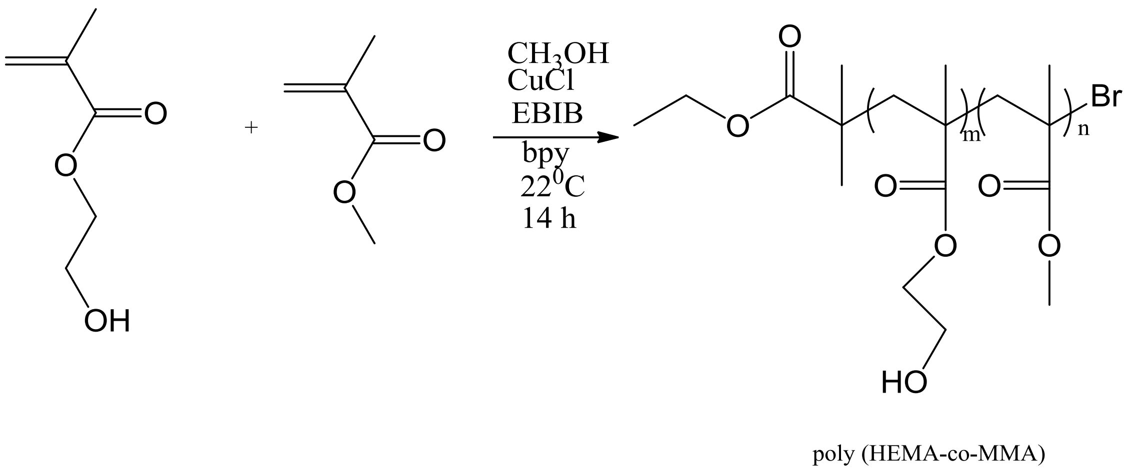


**Figure 2.5** Synthesis of p(HEMA-*co*-MMA).

### 2.3.6 Synthesis of Poly(alkyne-hydroxyethyl methacrylate-*co*-methyl methacrylate)

Firstly, copolymer (2g, 3.43x$10^{-4}$ mol) was dissolved in $CH_2Cl_2$ (30 mL). Then propiolic acid (32 µL, 5.15 x $10^{-4}$ mol), DCC ( 0.113 g, 5.49 x $10^{-4}$mol) and DMAP

(6.7 mg, $5.49 \times 10^{-5}$ mol) were added to the solution, which was then allowed to stir at room temperature for 48 h. The polymer was precipitated in hexane, filtered and dried under vacuum at 40 $^{o}$C for 48 h (yield 75%). $^{1}$H-NMR (CDCl$_3$, ppm, δ): 4.06 (2H, -COO**CH$_2$**-), 3.78 (2H, -COOCH$_2$**CH$_2$**O-), 3.53 (3H, -COO**CH$_3$**) , 2.55 (H, -O-CO-C≡**CH**, PHEMA-alkyne) 2.10 (-**CH$_2$**CCH$_3$, PHEMA), 1.36 (6H, -C(**CH$_3$**)$_2$), 1.19 (3H, **CH$_3$**CH$_2$OCO-). FT-IR (cm$^{-1}$): 3537, 2996, 2948, 2112, 1721, 1448, 1144.

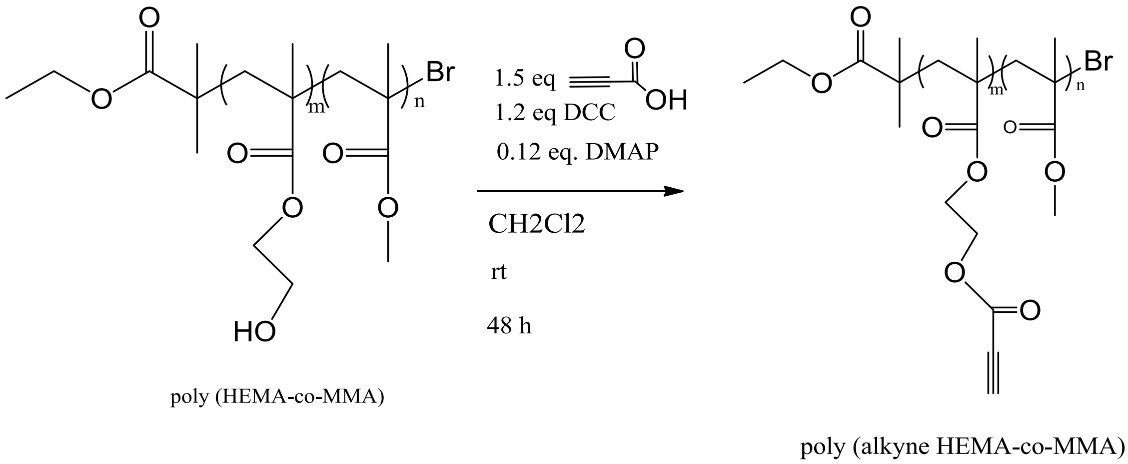


**Figure 2.6** Synthesis of p( alkyne-HEMA-co-MMA)

### 2.3.7 Synthesis of Poly(Dimethylaminoethyl methacrylate) p(DMAEMA)

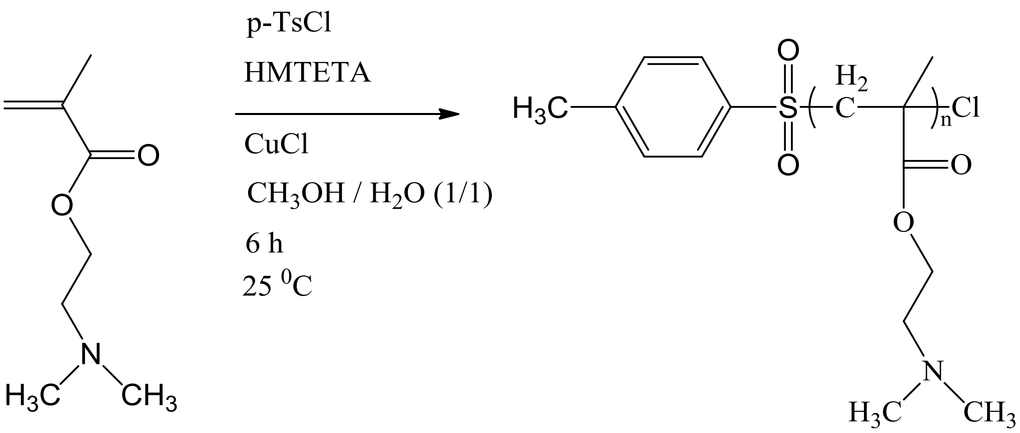


**Figure 2.7** Synthesis of Poly(Dimethylaminoethyl methacrylate) p(DMAEMA)

CuCl (0.0359g, $3.63 \times 10^{-4}$ mol) was added to a dry 50 mL Schlenk flask was evacuated and flushed with $N_2$(g). Distilled DMAEMA (2 mL, 0.0121 mol), HMTETA (99 μL, $3.63 \times 10^{-4}$ mol), methanol (2 mL, dry) and distilled water (2 mL) were added to the Schlenk flask using degassed syringes. The mixture was stirred for 10 minutes and then degassed by three freze-pump-thaw cycles, then p-TsCl (0.0231g, $1.21 \times 10^{-4}$ mol) was added and the reaction mixture was stirred for 6 h at 25 $^0$C. The polymerization was terminated by exposing the reaction vessel to air and 10 mL THF was added. The solution was passed through a basic alumina column. Then, the volume of the solution was reduced using a rotary evaporator and the concentrated solution was poured into hexane for precipitation and the polymer was dried under vacuum at 25 $^0$C for 24 h. $^1$H-NMR ($CDCl_3$, ppm, δ): 7.10-6.84 (m, 4H, from aromatic ring), 4.18(t, 2H, -COO***CH₂***$CH_2N(CH_3)_2$),3.89(-***CH₂***-C-,from DMAEMA), 3.42 (COO $CH_2$***CH₂***$N(CH_3)_2$), 2.51 (s, 6H, -N(***CH₃)₂***), 2.38(s, 3H, ***CH₃***-Ph-). FT-IR ( cm$^{-1}$): 2943, 2825, 2767, 1721, 1457, 1395, 1267, 1144, 1017, 964, 854, 775.

### 2.3.8 Synthesis of Azide-functional Poly(Dimethylaminoethyl methacrylate) p(DMAEMA-$N_3$)

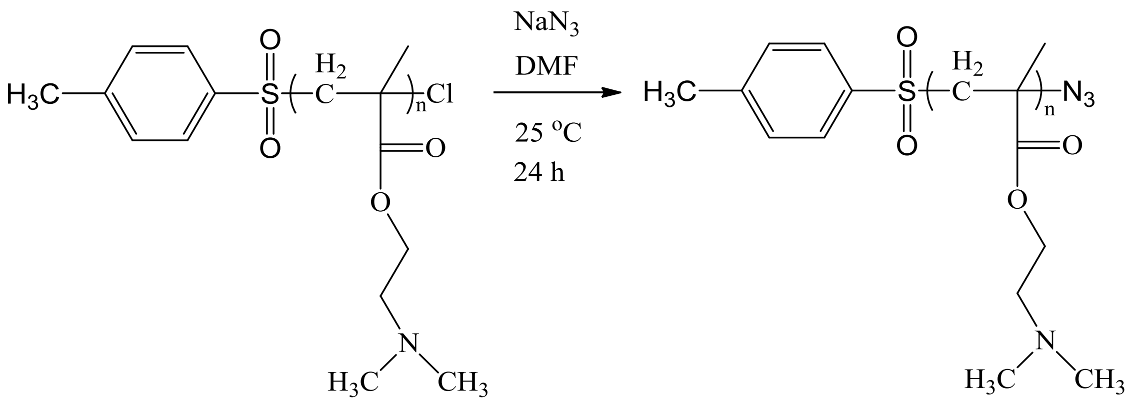


**Figure 2.8** Synthesis of Azide-functional Poly(Dimethylaminoethyl methacrylate) p(DMAEMA-$N_3$)

A typical procedure for the preparation of DMAEMA-$N_3$ is as follows. P-DMAEMA (0.7 g, $7\times10^{-5}$ mol) was dissolved in 30 mL *N*,*N*-dimethylformamide (DMF) and $NaN_3$ (10 mg, $12 \times10^{-5}$ mol) was added in a Schlenk tube. The resulting solution was allowed to stir at 25 °C 24 h. Then, DMF was removed with rotary evaporator and the polymer was dissolved in $CH_2Cl_2$. After having been extracted with distilled water three times, it was precipitated in hexane, and collected by vacuum filtration. Finally, it was dried at 25 °C in a vacuum oven for 24 h.

$^1$H-NMR ($CDCl_3$, ppm, δ): 7.10-6.84 (m, 4H, from aromatic ring), 4.18(t, 2H,-COO$\boldsymbol{CH_2}CH_2N(CH_3)_2$),3.89(-$\boldsymbol{CH_2}$-C-,from DMAEMA), 3.42 (COO $CH_2\boldsymbol{CH_2}N(CH_3)_2$), 2.51 (s, 6H, -N($\boldsymbol{CH_3)_2}$), 2.38(s, 3H, $\boldsymbol{CH_3}$-Ph-). FT-IR ($cm^{-1}$) : 2940, 2827, 2768, 2093, 1726, 1459, 1392, 1225, 1142, 959, 851, 783.

### 2.3.9 Synthesis of Poly(MMA-*g*-2-Dimethylaminoethyl methacrylate-*g*-Styrene) by using Click Reaction

0.14 g ($1.75x10^{-5}$mol) of P(DMAEMA-$N_3$), 0.105g ($1.75x10^{-5}$ mol) of (PS-$N_3$), 0.0204g ($3.5x10^{-5}$mol) of P(alkyne-HEMA-*co*-MMA), 0.050g ($3.5x10^{-4}$mol) of CuBr and 25ml $CH_2Cl_2$ were added into a Schlenk flask with a magnetic bar. The mixture was bubbled with nitrogen for 15 min. Three vacuum-purge nitrogen were performed then 0.0730 mL PMDETA was added. The mixture was stirred overnight at room temperature. After the reaction, the mixture was further diluted with THF, and passed through a silica-gel column to remove the catalyst. The product was precipitated in diethyl ether, and dried at room temperature in a vacuum oven for 48 h.

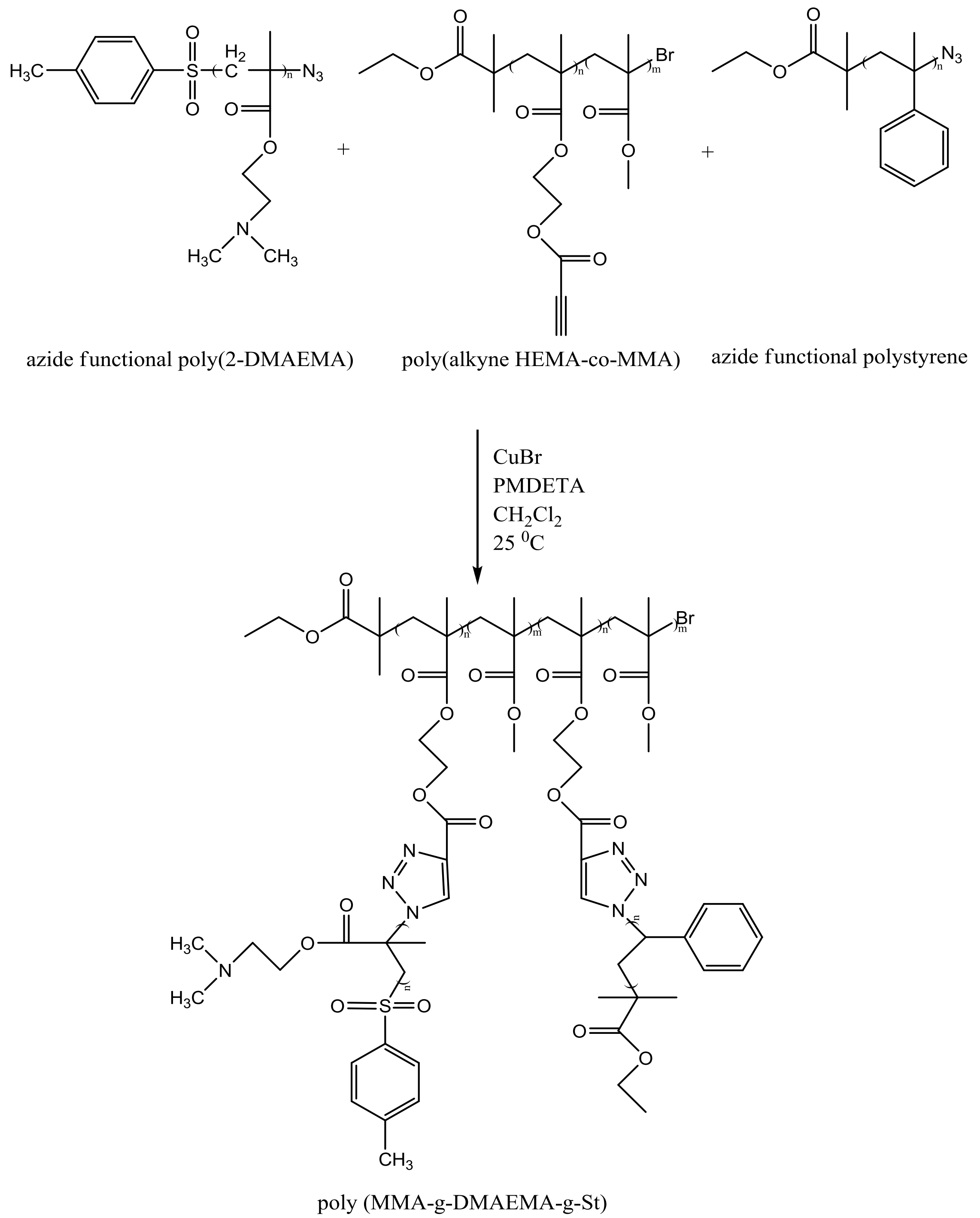


**Figure 2.9** Synthesis of poly(MMA-g-2-DMAEMA-g-St).

# CHAPTER 3

# RESULTS AND DISCUSSION

Amphiphilic ABA type block copolymer and amphiphilic graft copolymer were synthesized via a controlled radical polymerization (CRP), in particular Atom Transfer Radical Polymerization (ATRP) and then by using ‘‘Click Chemistry’’. These procedures involve the preparation of the skeletal polymers, azide functional p(DMAEMA) and PS-$N_3$ possessed with the appropriate click components. Polyethylene glycol (PEG-3000) was purchased commercially. First, alkyne di-terminal functional poly(ethylene glycol) was synthesized by Steglich Esterification in the presence of DCC/DMAP at room temperature. Also, alkyne terminal functional poly(hydroxyethyl-co-methylmethacrylate) p(HEMA-*co*-MMA) was synthesized by Steglich Esterification.The other components, namely polystyrene and poly(dimethylaminoethyl methacrylate) were synthesized via Atom Transfer Radical Polymerization (ATRP). Then, bromide and chloride groups were quantitatively converted into azide-functional polystyrene and azide-functional p(DMAEMA) in the presence of $NaN_3$/DMF at room temperature, respectively. The terminal chloride and bromide groups were easily transformed into azide groups to produce PS-$N_3$ and p(DMAEMA-$N_3$), respectively. The four click reactive molecules were then combined in couples to obtain the targeted amphiphilic polymers. The results will be discussed further below.

### 3.1 Synthesis of PEG-Alkyne

First, propionyl terminated PEG-alkyne was prepared with Steglich Esterification in the presence of DCC/DMAP at room temperature as depicted in Figure 3.1. The molecular weight was determined by using $^{1}$H-NMR spectroscopy.

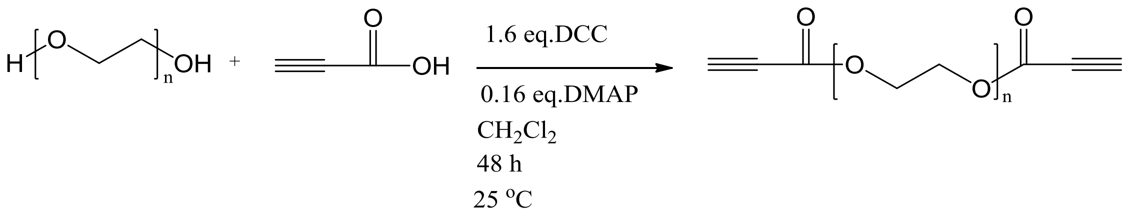


**Figure 3.1** Synthesis of PEG-alkyne.

Fourier transform infrared spectroscopy is used to study the formation of PEG-alkyne. A representative FT-IR spectrum for the system PEG and PEG-alkyne are shown in Figure 3.2. The FT-IR spectrum for PEG shows the characteristic absorption bands for -C-O- C- stretching vibration at 1091 $cm^{-1}$ and -OH stretching vibration at 3440 $cm^{-1}$. After Steglich Esterification, the ester wavenumber carbonyl stretching and -C≡CH stretching vibration were observed at 1711 and 2112 $cm^{-1}$, respectively and the -OH stretching vibration at 3440 $cm^{-1}$ disappeared. All the above results confirm the formation of the PEG-alkyne.

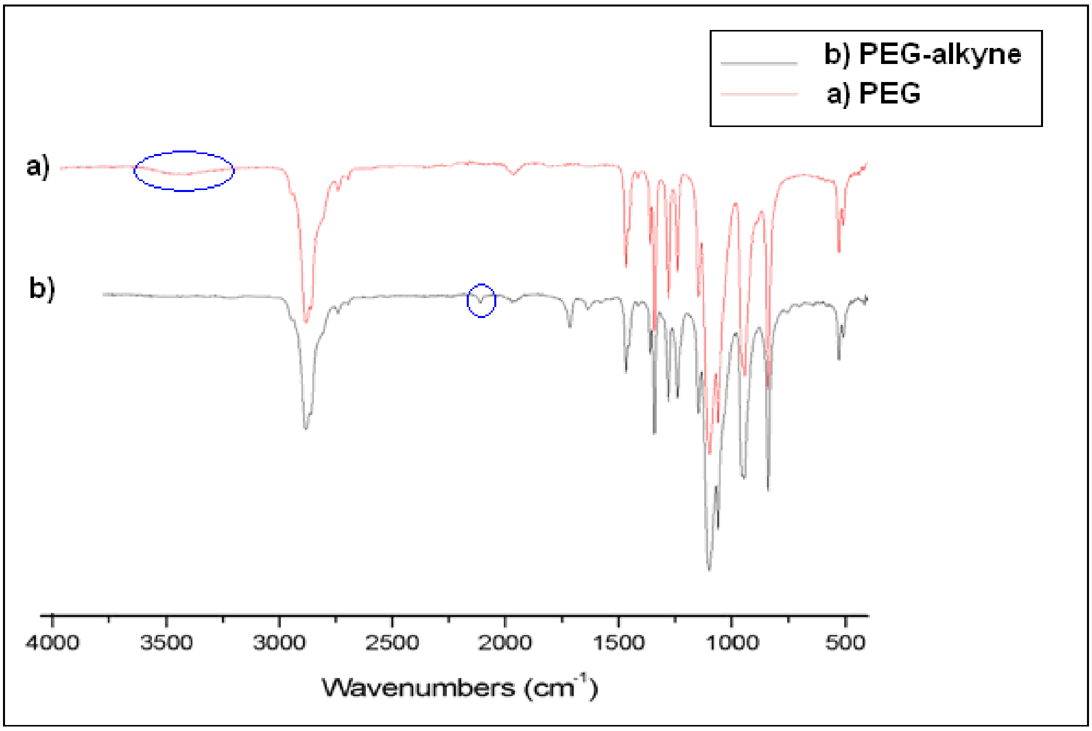


**Figure 3.2** The FT-IR spectrum of a) PEG, b) PEG-alkyne.

Also, $^{1}$H-NMR spectroscopy supports to prove the formation of the PEG-alkyne. A typical NMR spectrum of the system PEG-alkyne is shown in Figure 3.3. The $^{1}$H-NMR spectrum (see Figure 3.3) exhibits a-hydrogen peaks of the ether linkages and terminated alkyne group at 3.68 and 2.65 ppm, respectively.

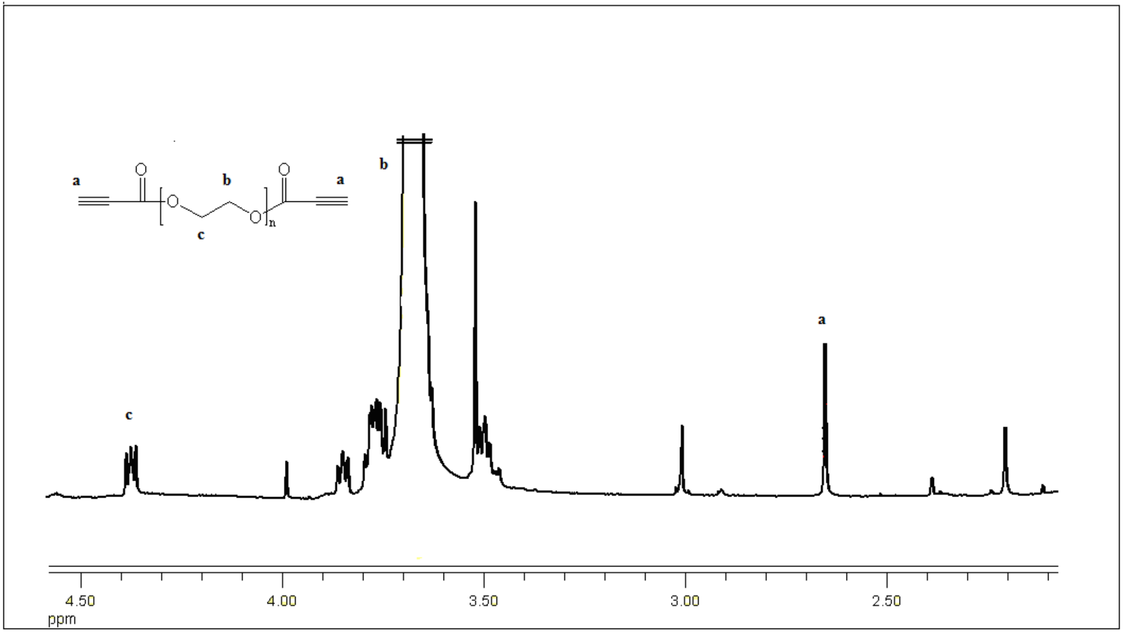


**Figure 3.3** The $^{1}$H-NMR spectrum of  PEG-alkyne.

### 3.2 Synthesis of Polystyrene (PS)

Polystyrene was synthesized via Atom Transfer Radical Polymerization (ATRP) in the presence of EBIB, PMDETA and CuBr as depicted in Figure 3.4. In this step, ethyl 2-bromoisobutyrate (EBIB), N,N,N',N'',N''-Pentamethyldiethylenetriamine (PMDETA), copper bromide(CuBr) were used as initiator, ligand and catalyst, respectively and the ratio of [Monomer]/[Initiator]/[Catalyst]/[Ligand] is 100/1/0.5/0.5, respectively. All of peaks confirm the formation of the PS in Figure 3.6.

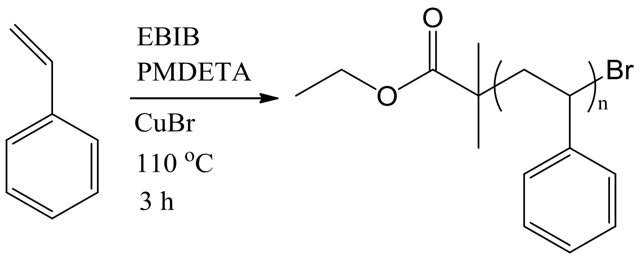


**Figure 3.4** Synthesis of Polystyrene.

Also, the signals at 7.02, 3.68, 2.45 and 1.18 ppm are respectively assigned to the resonanceof($C_6H_5$-),($CH_3$***$CH_2$***-O-),($CH_3CH_2OCOC(CH_3)_2$-***$CH_2$***CH-),(***$CH_3$***$CH_2$-O-) phenyl groups, methylene,methylene, methyl protons from polystyrene.

## 3.3 Synthesis of Azide-Functional Polystyrene (PS-$N_3$)

Firstly, Polystyrene was synthesized via Atom Transfer Radical Polymerization (ATRP).Then, bromide group was quantitatively converted via nucleophilic substitution into azide-functional polystyrene in the presence of $NaN_3$/DMF at room temperature as depicted in Figure 3.5. The FT-IR spectral analysis also supports this result. Compared to the FT-IR spectrum of PS, the spectrum of PS-$N_3$ exhibits an obvious peak at 2094 $cm^{-1}$ (see Figure 3.6).

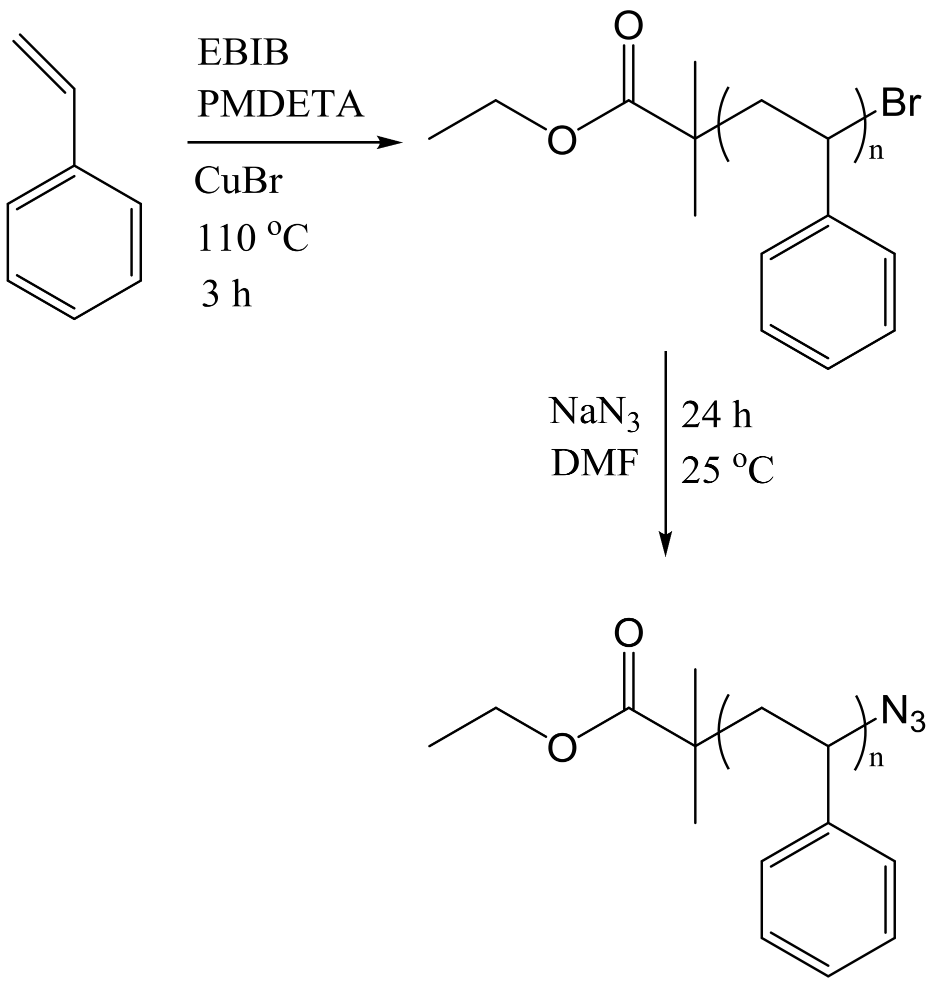


**Figure 3.5** Synthesis of Azide-functional Polystyrene.

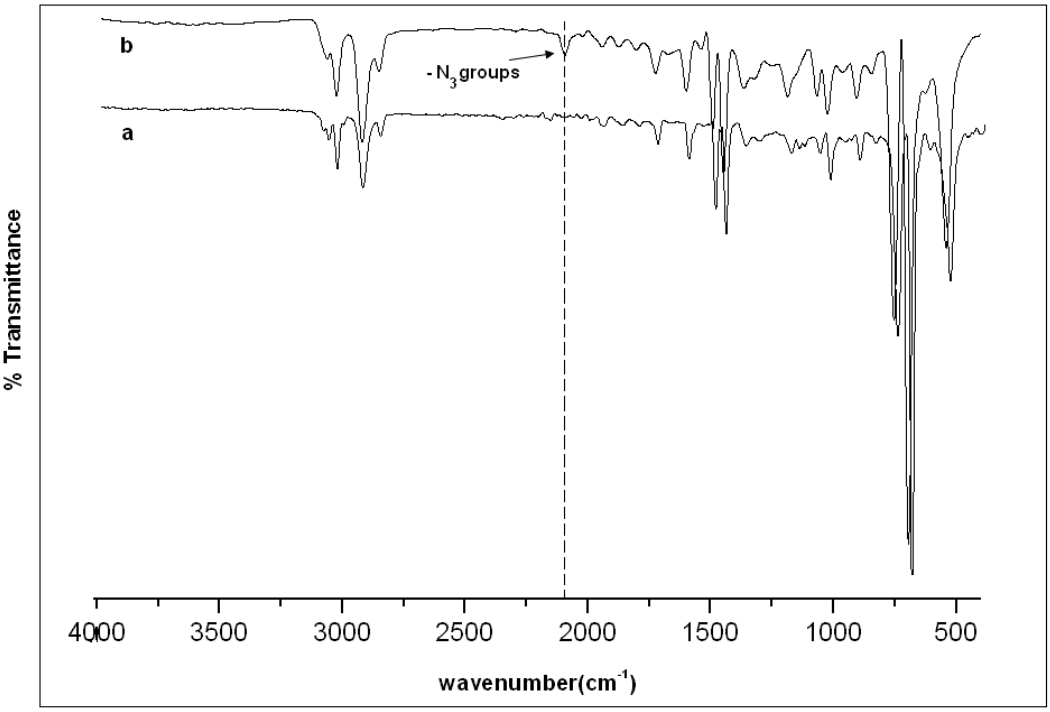


**Figure 3.6** The FT-IR spectra of a) Polystyrene (PS), b) azide-functional polystyrene(PS-$N_3$).

### 3.4 Synthesis of Poly(Styrene-*b*-PEG-*b*-Styrene) by using Click Reaction

Finally, the click coupling occurs between the azido side-functional polystyrene and PEG-alkyne to obtain amphiphilic ABA type block copolymer of the two, as depicted in Figure 3.7. The azide stretching band at around 2094 $cm^{-1}$ disappears almost completely. The triazole units show several medium or strong peaks in the 1490-1650 $cm^{-1}$ range due to ring C=N, C-N vibrations. Aromatic ring in polystyrene shows absorption at nearly 1650 $cm^{-1}$ and the aliphatic C-H stretchings were observed at 2800-3000 $cm^{-1}$ regions. The aromatic C-H stretchings were observed at 3000-3100 $cm^{-1}$ regions (See Figure 3.8).

Also, the appearance of the peak belonging to-CH proton of the triazole ring at 7.45 ppm is a typical indication for the successful completion of click reaction. The signals at 7.45 ppm belong to the methine proton of the triazole ring, which indicates the triazole formation as depicted in Figure 3.9.

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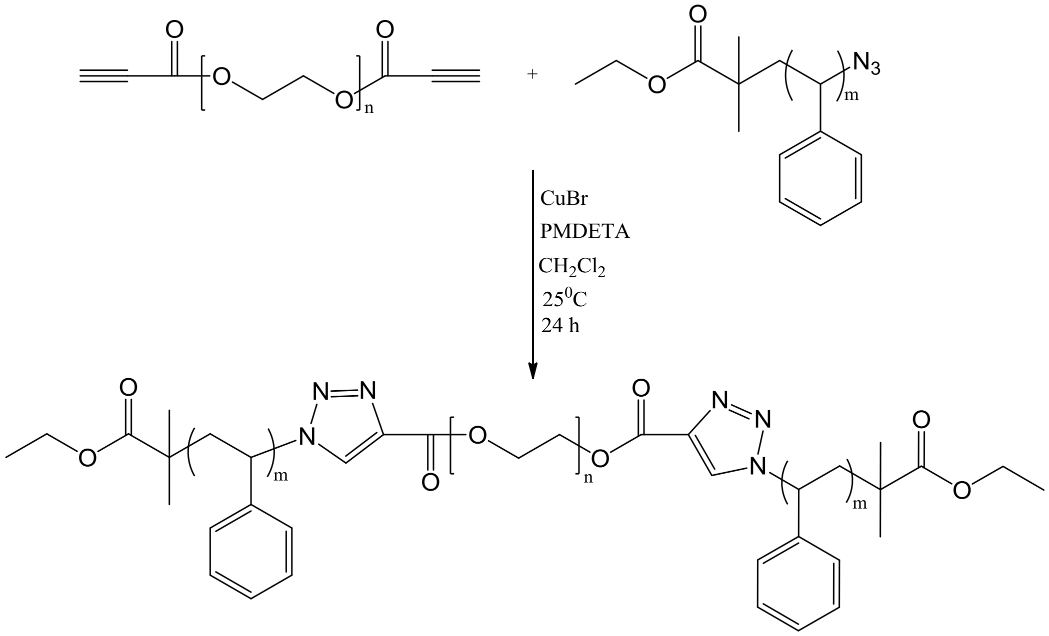


**Figure 3.7** Synthesis of poly(Styrene-*b*-PEG-*b*-Styrene).

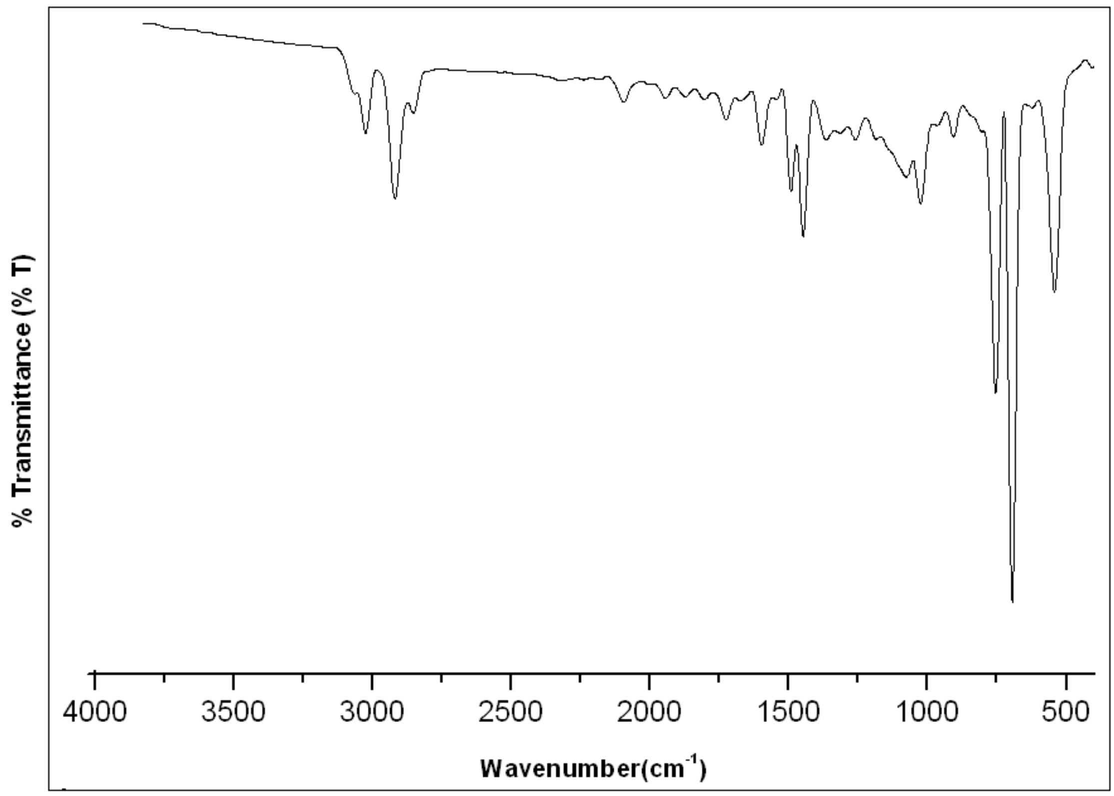


**Figure 3.8** The FT-IR spectrum of poly(Styrene-*b*-PEG-*b*-Styrene).

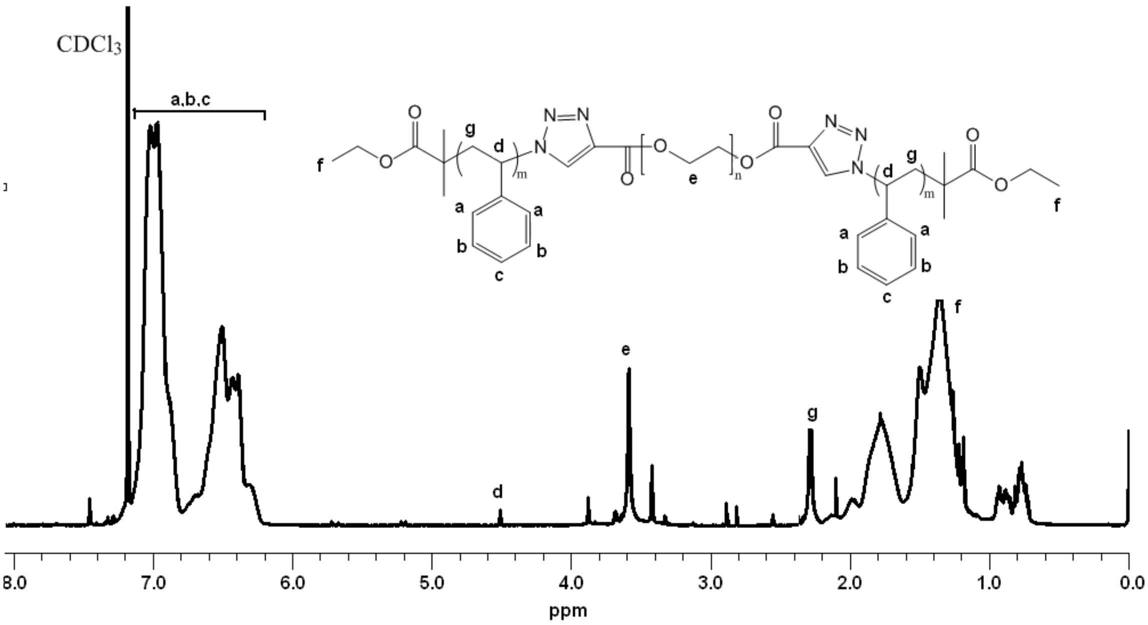


**Figure 3.9** The $^{1}$H-NMR spectrum of poly(Styrene-*b*-PEG-*b*-Styrene).

Also, the appearence of peak belonging to phenyl groups in aromatic ring between 7.02-6.38 (a,b,c) and methylene groups in polyethylene glycol (PEG) at 3.59 ppm (e) clearly show that have been obtained to amphiphilic ABA type block copolymer, see Figure 3.9.

### 3.5 Synthesis of Poly(hydroxyethyl methacrylate-*co*-methyl methacrylate)

The copolymers of methyl methacrylate (MMA) and 2-hydroxyethyl methaacrylate (HEMA) were prepared by Atom Transfer Radical Polymerization (ATRP) at 22 $^{o}$C in methanol by using ethyl-2- bromoisobutyrate and CuCl/2,2'-bipyridine as initiator and catalyst, respectively as depicted in Figure 3.10. HEMA acted as the side chain functional monomer possessing antogonist hydroxyl functionality.

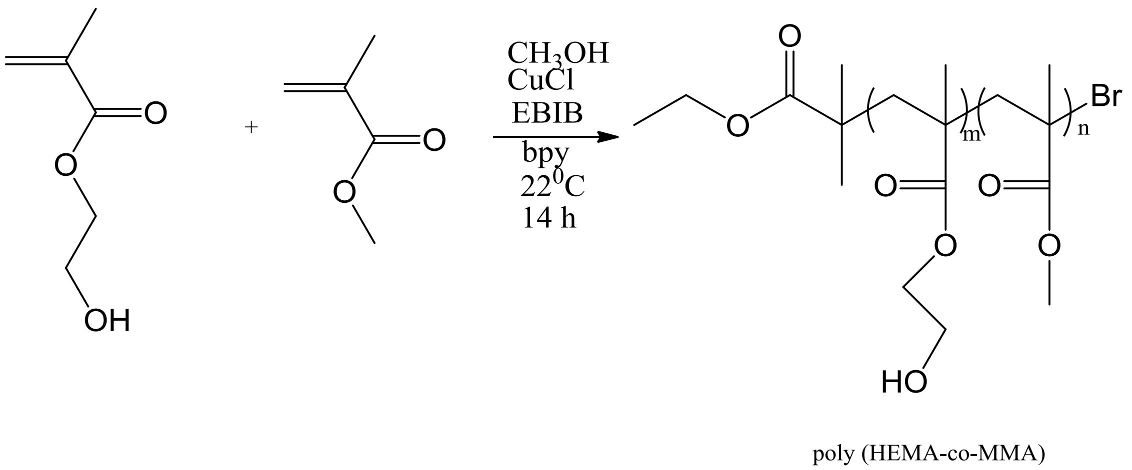


**Figure 3.10** Synthesis of poly (hydroxyethyl methacrylate-*co*-methylmethacrylate).

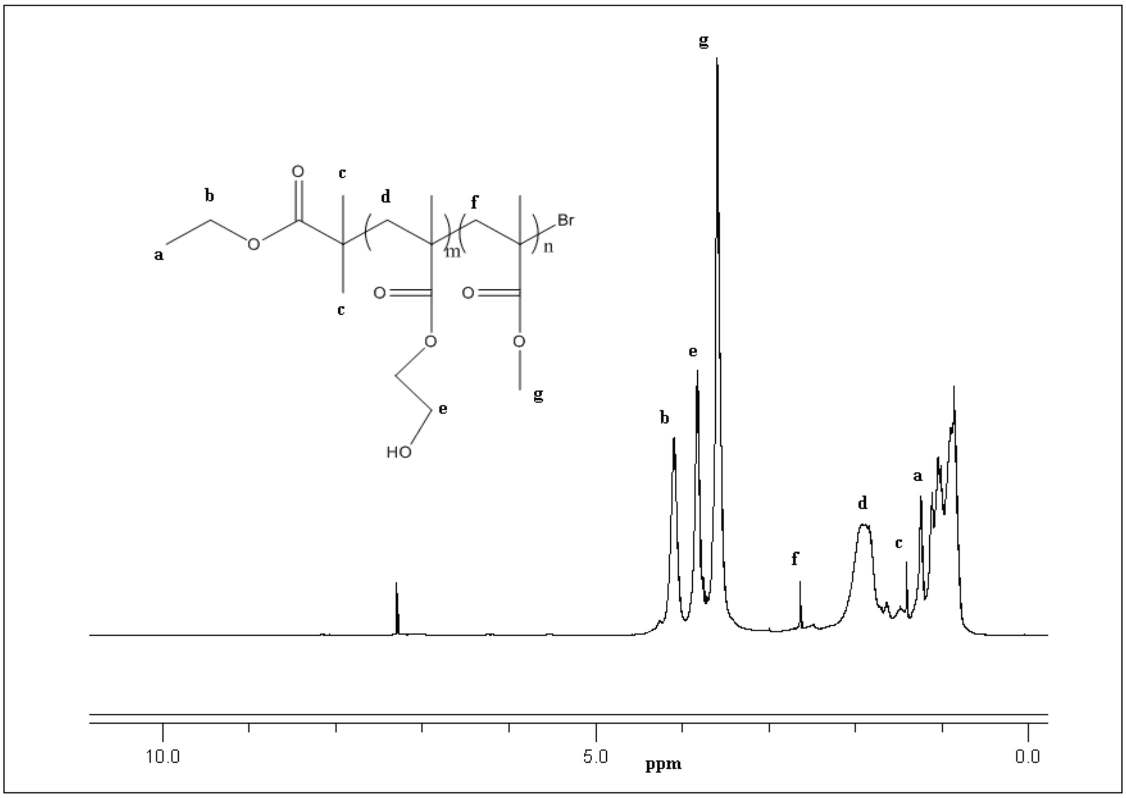


**Figure 3.11** The $^{1}$H-NMR spectra of poly(hydroxyethyl methacrylate-*co*-methylmethacrylate).

The structure of poly(HEMA-co-MMA) was analyzed by $^{1}$H-NMR spectroscopy. The $^{1}$H-NMR spectrum of poly(HEMA-co-MMA) is shown in Figure 3.11. The signals at 4.10 (b), 3.82 (e), 3.60 (g), 2.64 (f), 1.92(d), 1.41(c), 1.24(a) ppm are respectively assigned to the resonance of (-COO**CH**$_2$-),(-COOCH$_2$**CH$_2$**OH),(-COO**CH$_3$**), (-CCH$_3$**CH$_2$-**, PMMA), (-**CH$_2$**CCH$_3$, PHEMA), (-C(**CH$_3$**)$_2$), (**CH$_3$**CH$_2$OCO-) methylene, methylene, methyl, methylene, methylene, methyl protons from poly(HEMA-co-MMA).

The FT-IR spectral analysis also supports this result. The FT-IR spectrum of poly(HEMA-*co*-MMA) (see Figure 3.13) has a strong peak at 1721 cm$^{-1}$ for the ester C=O peak. The presence of a strong broad absorption in the 3000-3500 cm$^{-1}$ region is due to the O-H bond. Based on the results of $^{1}$H-NMR and FT-IR, poly(hydroxyethyl methacrylate-*co*-methyl methacrylate), p(HEMA-*co*-MMA) was prepared successfully.

### 3.6 Synthesis of Poly(alkyne-hydroxyethyl methacrylate-*co*-methyl methacrylate)

In this step, alkyne terminal functional p(HEMA-co-MMA) was prepared by ester formation between poly(hydroxyethyl methacrylate-*co*-methylmethacrylate), p(HEMA-*co*-MMA) and propiolic acid in the presence of DCC/DMAP as depicted in Figure 3.12. This reaction is called Steglich Esterification.

Compared to the FT-IR spectrums of poly (alkyne-HEMA-*co*-MMA) with poly (HEMA-*co*-MMA), a new band appear at 2112 cm$^{-1}$ in the spectrum of poly(alkyne-HEMA-*co*-MMA), which are assigned to the stretching vibration of the alkyne group. The bonds at 1721 cm$^{-1}$ are due to the formation of ester groups as depicted in Figure 3.13.

The structure of poly(alkyne-HEMA-*co*-MMA) was analyzed by $^{1}$H-NMR spectroscopy. The $^{1}$H-NMR spectrum of poly(HEMA-*co*-MMA) is shown in Figure 3.14. The signals at 4.06 (b), 3.78 (e), 3.53 (g), 2.55 (h), 2.10 (d), 1.36 (c), 1.19 (a) ppm are respectively assigned to the resonance of (-COO**CH**$_2$-),(-COOCH$_2$**CH$_2$**O),(-COO**CH$_3$**), (-O-CO-C≡**CH**, PHEMA-alkyne), -CCH$_3$**CH$_2$-**, PMMA), (-C(**CH$_3$**)$_2$), (**CH$_3$**CH$_2$OCO-) methylene, methylene, methyl,methine,methylene, methyl,methyl protons from poly(alkyne-HEMA-*co*-MMA) as depicted in Figure 3.14.

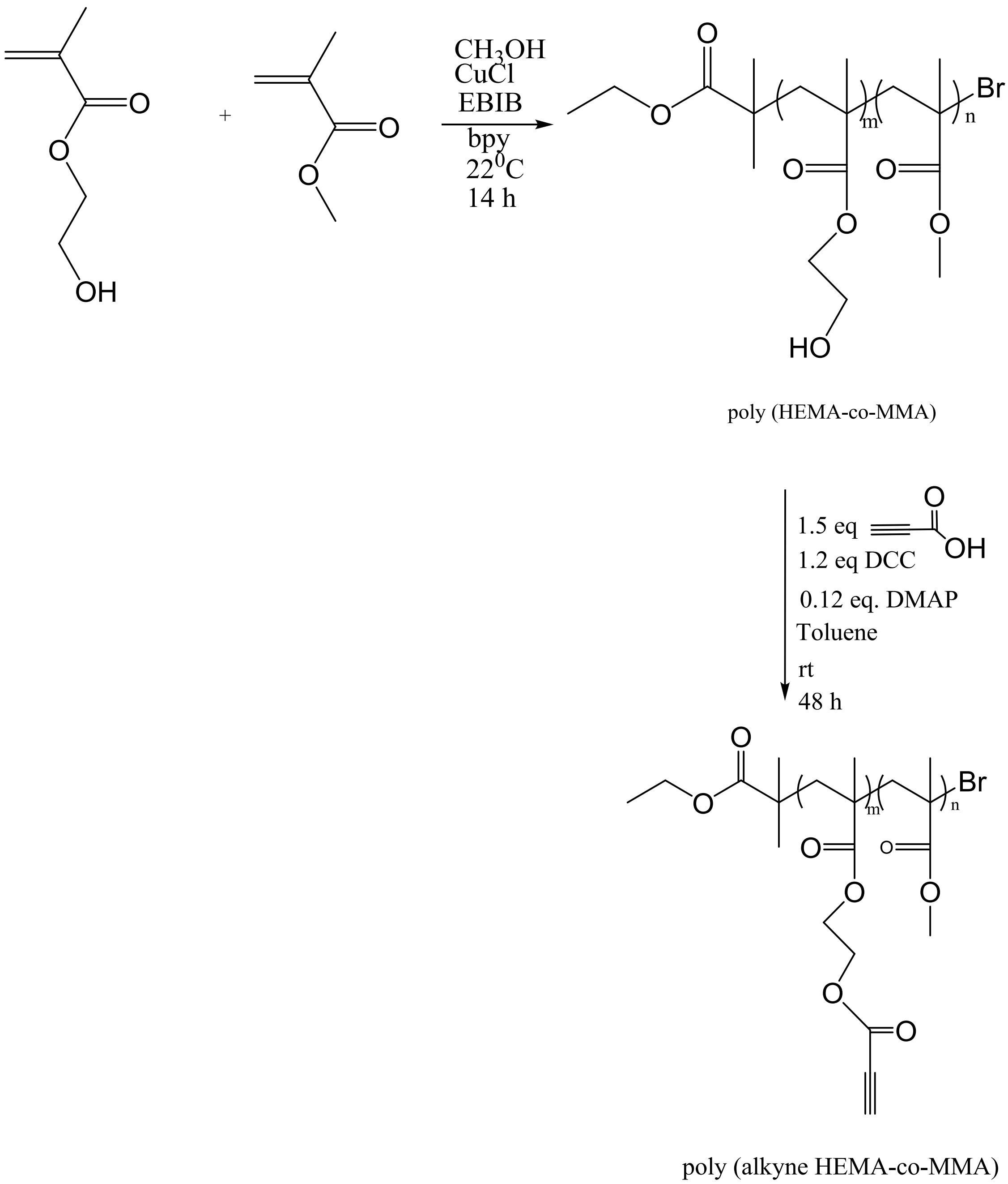


**Figure 3.12** Synthesis of poly(HEMA-*co*-MMA) and poly(alkyne HEMA-*co*-MMA)

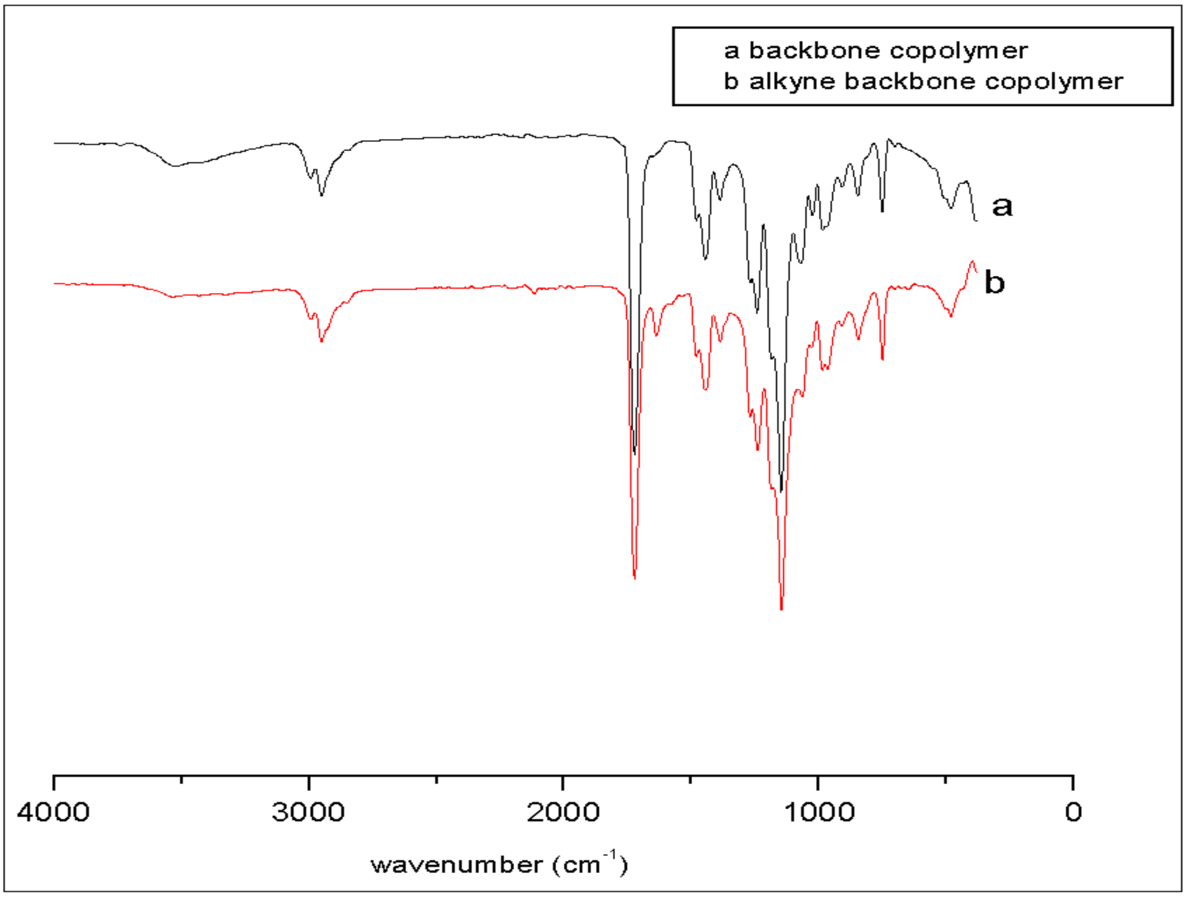


**Figure 3.13** The FT-IR spectra of a) poly(HEMA-*co*-MMA), b) poly(alkyne HEMA-*co*-MMA).

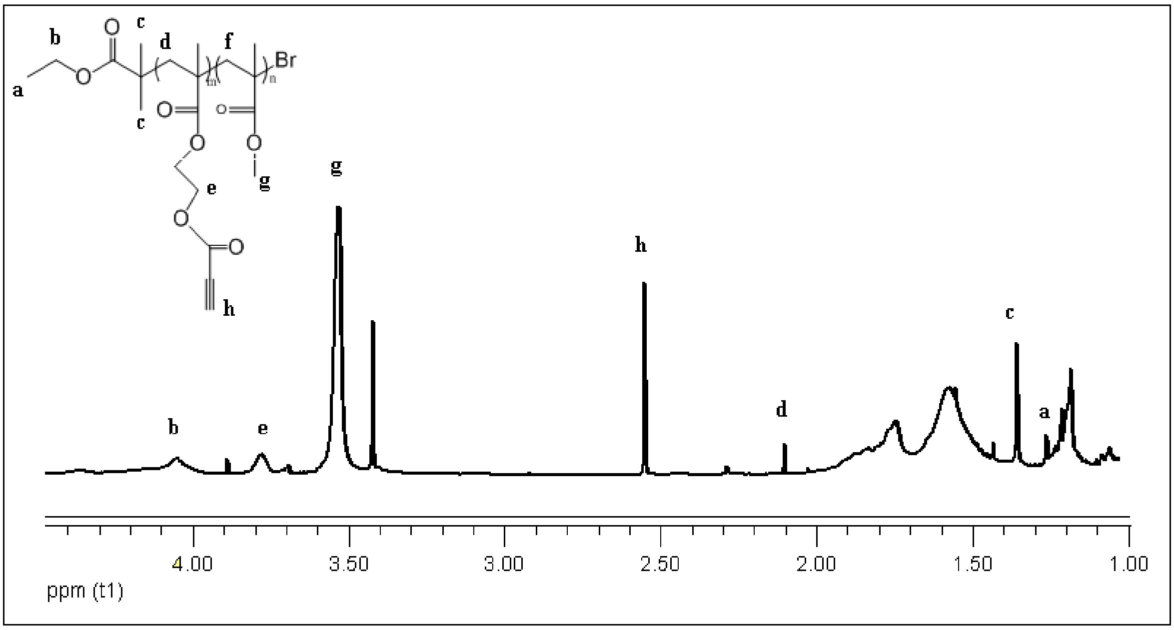


**Figure 3.14** The $^{1}$H-NMR spectra of poly(alkyne HEMA-*co*-MMA)

### 3.7 Synthesis of Poly(Dimethylaminoethyl methacrylate) p(DMAEMA)

Poly(dimethylaminoethyl methacrylate), p(DMAEMA), was synthesized via Atom Transfer Radical Polymerization (ATRP) in the presence of p-Tosyl chloride, HMTETA, CuCl and methyl alcohol as depicted in Figure 3.16. In this step, p-Tosyl chloride(p-TsCl), hexamethyltriethylenetetramine (HMTETA) copper(I) chloride (CuCl) and methyl alcohol were used as initiator, ligand, catalyst and solvent, respectively and the ratio of [Monomer]/[Initiator]/[Catalyst]/[Ligand] is 100/1/3/3, respectively. All of peaks in FT-IR spectrum, confirm the formation of the p(DMAEMA) in Figure 3.17.

Also, the signals at 7.10-6.84, 4.18, 3.89, 3.42, 2.51 and 2.38 ppm are respectively assigned to the resonance of ($C_6H_4$-, from aromatic ring), (-COO***$CH_2$***$CH_2N(CH_3)_2$), (-***$CH_2$***-C-, fromDMAEMA),(COO$CH_2$***$CH_2$***$N(CH_3)_2$),(-N(***$CH_3)_2$***), (***$CH_3$***-Ph-) methylene, methylene, methylene, methyl, methyl protons from poly(dimethylaminoethyl methacrylate), p(DMAEMA) as depicted in Figure 3.15.

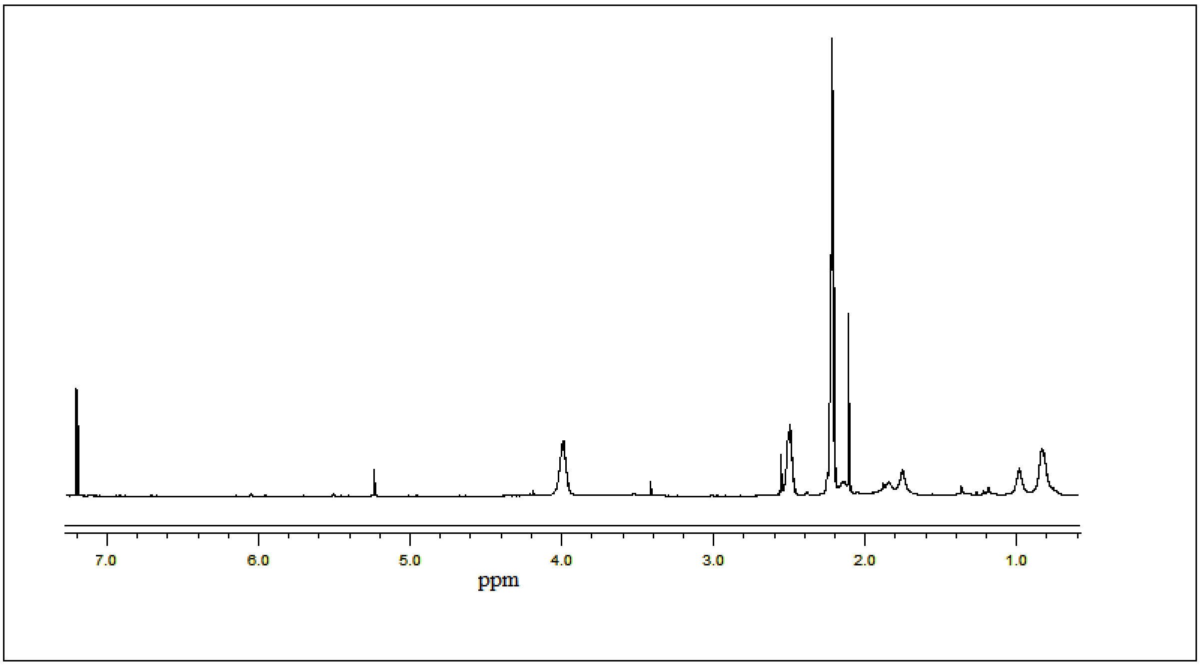


**Figure 3.15** The $^1$H-NMR-spectra of p(DMAEMA)

## 3.8 Synthesis of Azide-functional Poly(Dimethylaminoethyl methacrylate) p(DMAEMA-$N_3$)

Firstly, Poly(dimethylaminoethyl methacrylate) was synthesized via Atom Transfer Radical Polymerization (ATRP). Then, chloride groups were quantitatively converted via nucleophilic substitution into azide-functional p(DMAEMA) in the presence of $NaN_3$/DMF at room temperature as depicted in Figure 3.16. The FT-IR spectral analysis also supports this result. Compared to the FT-IR spectrum of poly (DMAEMA) with the FT-IR spectrum of poly(DMAEMA-$N_3$), a new peak exhibits at 2093 $cm^{-1}$ (see Figure 3.17).

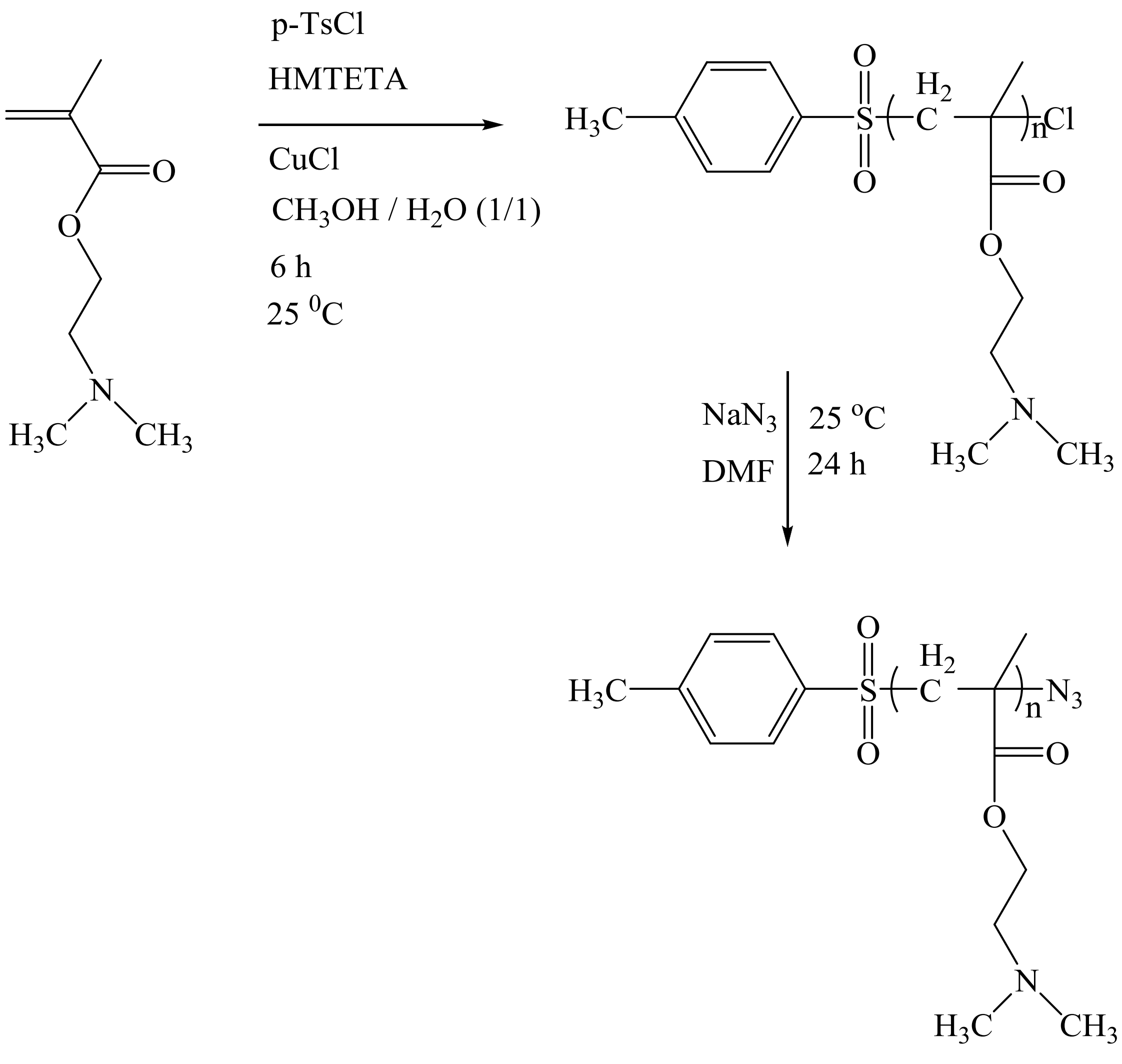


**Figure 3.16** Synthesis of poly(dimethylaminoethyl methacrylate), poly(DMAEMA), and azide-functional poly(dimethylaminoethyl methaacrylate), poly(DMAEMA-$N_3$).

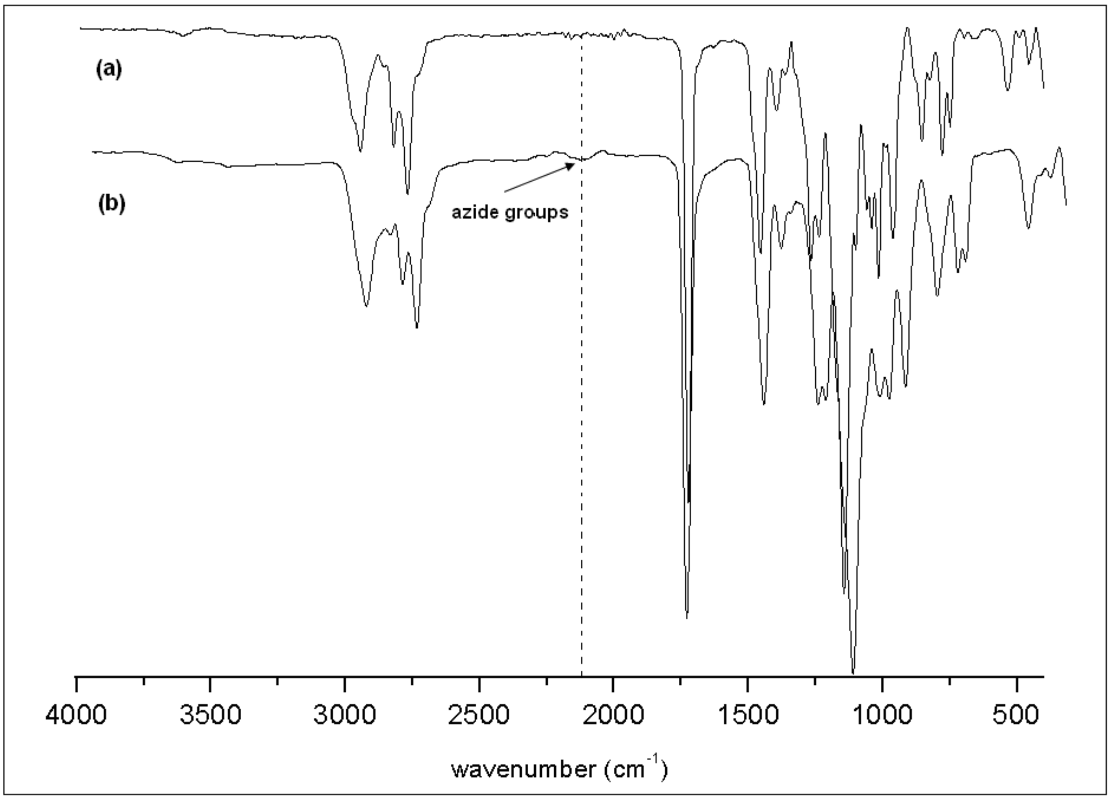


**Figure 3.17** The FT-IR spectra of a) poly(dimethylaminoethyl methacrylate), b) azide functional poly(dimethylaminoethyl methacrylate).

## 3.9 Synthesis of Poly(MMA-g-2-Dimethylaminoethyl methacrylate-g-styrene) by using Click Reaction

Finally, the click coupling occurs between the azido end-functional poly(dimethylaminoethyl methacrylate), azido end-functional polystyrene and poly(alkyne-HEMA-*co*-MMA) to obtain amphiphilic graft copolymer of the three, as depicted in Figure 3.18. In the FT-IR spectrum, the azide stretching band at around 2093 $cm^{-1}$ disappears almost completely. The triazole units show several medium or strong peaks in the 1470-1680 $cm^{-1}$ range due to ring C=N, C-N vibrations. The aliphatic C-H stretchings were observed at 2800-3000 $cm^{-1}$ region. The bands at 1726 $cm^{-1}$ are due to the formation of ester groups.

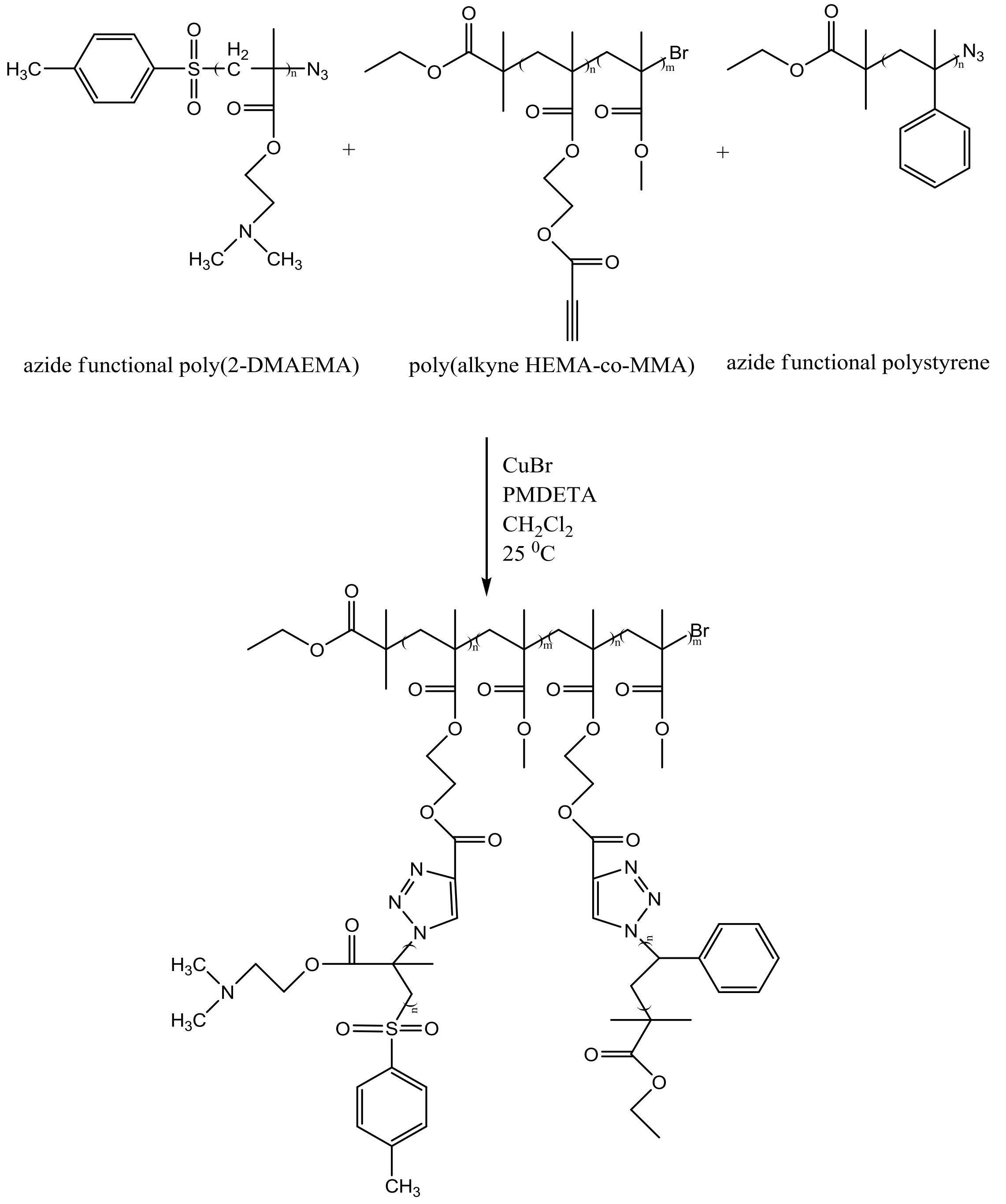


**Figure 3.18** Synthesis of Poly(methylmethacrylate-*g*-2-dimethylaminoethyl methacrylate-g-styrene), poly(MMA-*g*-2-DMAEMA-g-St).

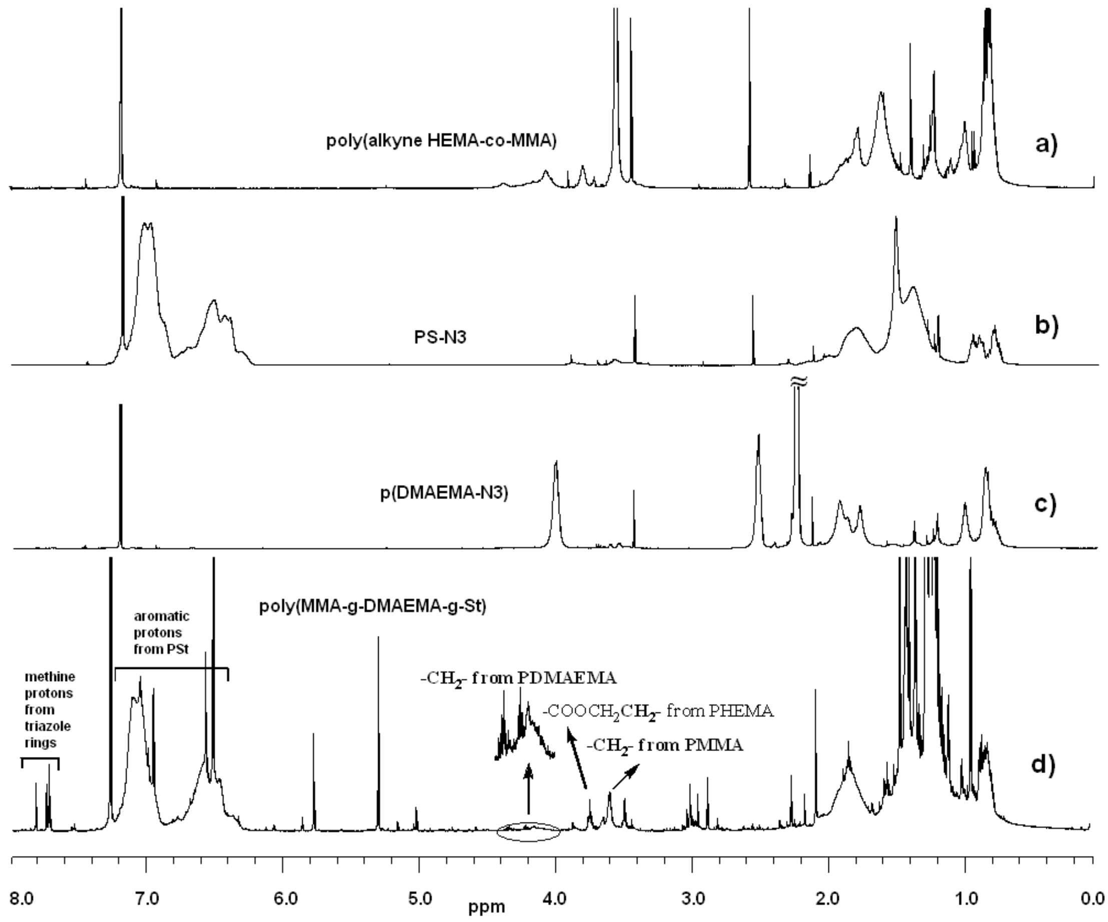


**Figure 3.19** The $^{1}$H-NMR spectra of a) poly(alkyne HEMA-co-MMA), b) PS-$N_3$, c) poly(DMAEMA-$N_3$), d) poly(MMA-g-2-DMAEMA-g-St).

In the $^{1}$H-NMR spectra, the signals at 3.60 and 3.78 ppm can be attributed to the methylene protons of MMA repeating units and methylene protons of HEMA units, respectively. The –CH proton of the triazole rings of the final product appears around 7.81-7.71 ppm, which supports the formation of the click reaction. The signals between 7.21-6.41 ppm belonging to the aromatic protons of styrene repeating units and the signal between 4.2-4.0 ppm belonging to the methylene protons of PDMAEMA prove the successful incorporation of the two chains in the click product.

Finally, further proof on the occurrence of the click reaction regarding the synthesis of poly(styrene-*b*-PEG-*b*-styrene) is obtained from GPC analysis. The GPC traces of azido-functional polystyrene(PS-$N_3$) and poly(styrene-*b*-PEG-*b*-styrene) have been provided in Figure 3.20. The shifting of initial peak (a) to lower retention time (b) shows that block formation has successfully been accomplished.

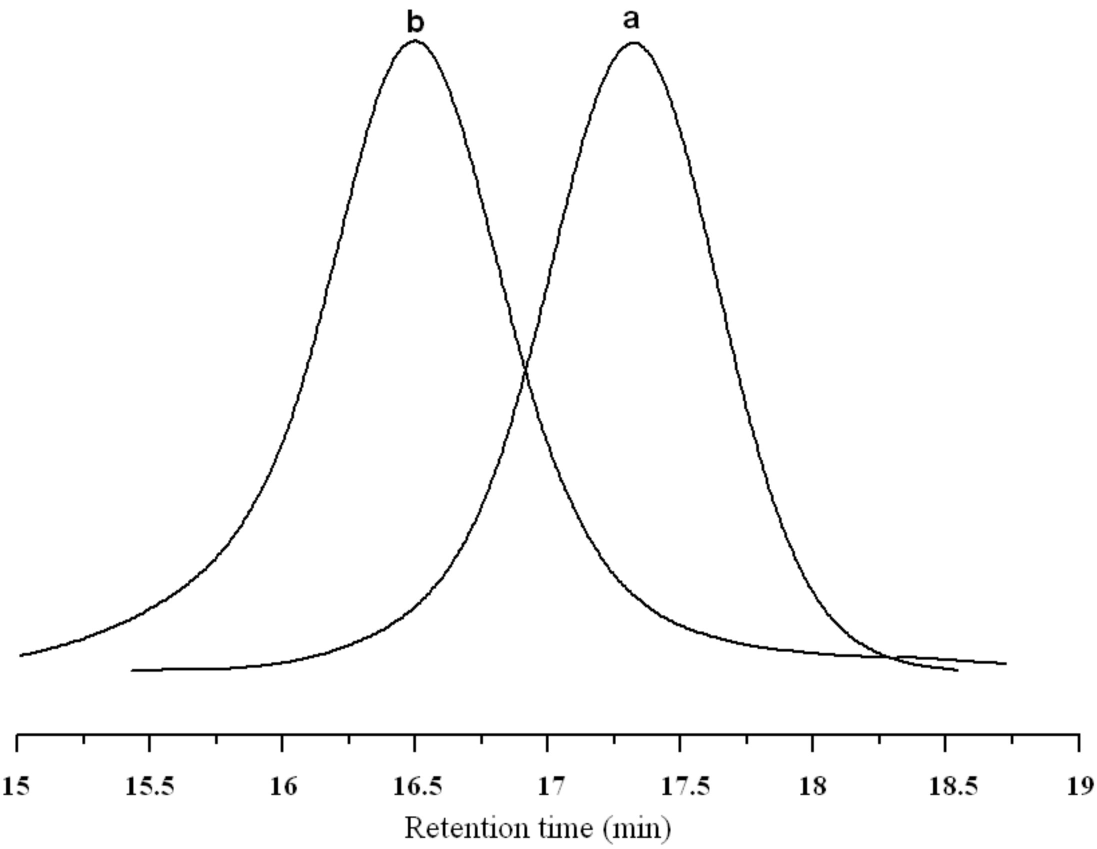


**Figure 3.20** The GPC traces of a) Azido-functional polystyrene(PS-$N_3$), b) poly(Styrene-*b*-PEG-*b*-Styrene).

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# SYNTHESIS AND CHARACTERIZATION OF NOVEL AMPHIPHILIC POLYMERS VIA CONTROLLED RADICAL POLYMERIZATION METHODS AND CLICK REACTIONS

Herow RIZA

M. Sc. Thesis in Chemistry
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Supervisor: Assist. Prof. Ali Ekrem MÜFTÜOĞLU

## ABSTRACT

Amphiphilic polymers, composed of hydrophilic and hydrophobic parts, receive great interest due to their micelle forming character. In an aqueous medium, the hydrophobic blocks of the copolymer form the core of the micelle while the hydrophilic blocks form the corona or outer shell, in which manner, hydrophobic agents can be made water-soluble. This unique feature has resulted in their utilization in many applications such as drug delivery. Click chemistry gives the opportunity to prepare block and graft polymers when used in conjunction with Controlled Polymerization Routes. Click reactions occur between terminal acetylenes and azides by metal catalysts at room temperature. Click reactions are preferable reactions for modification because of moderate reaction conditions, high yields, short reaction periods, high selectivity, tolerance for functional groups, and insensitivity to solvents.

In this study, poly(styrene-*b*-PEG-*b*-styrene) amphiphilic block copolymer and poly(MMA-*g*-2-dimethylaminoethyl methacrylate) amphiphilic graft copolymer were synthesized by using combined Atom Transfer Radical Polymerization (ATRP) and “Click” chemistry approaches. Synthesis of the former involves click coupling of azide-functional polystyrene, obtained by ATRP, with propionyl terminated PEG, prepared via Steglich esterification, in the presence of CuBr and PMDETA. The latter copolymer was prepared in the same analogy. Azide-functional hydrophilic poly(2-dimethylaminoethyl methacrylate) was grafted onto a hydrophobic acetylene side-functional PMMA backbone via a “Click” reaction. The polymers were characterized by $^1$H-NMR, and FT-IR.

**Keywords:** Amphiphilic polymer, Polyethylene oxide, Polystyrene, “Click” Reaction, Atom Transfer Radical Polymerization (ATRP)

# KONTROLLÜ POLİMERİZASYON YÖNTEMLERİ VE KLİK TEPKİMESİYLE YENİ AMFİFİLİK POLİMERLERİN SENTEZİ VE KARAKTERİZASYONU

Herow RIZA

Yüksek Lisans Tezi – Kimya Bölümü
Temmuz 2010

Tez Yöneticisi: Yrd.Doç.Dr. Ali Ekrem MÜFTÜOĞLU

## ÖZ

Hidrofilik ve hidrofobik kısımlardan oluşan amfifilik polimerler misel oluşturma özellikleri nedeniyle büyük ilgi çekmektedir. Sulu ortamlarda, hidrofobik bloklar miselin iç bölgesini oluştururken, hidrofilik bloklar kabuk kısmını oluştururlar ki bu sayede hidrofobik ajanlar suda çözünebilmektedir. Bu sıradışı özellikleri nedeniyle hidrofiller, ilaç taşıma sistemleri gibi birçok uygulamada kullanılmaktadırlar.“Klik” kimyasının Kontrollü Polimerizasyon Yöntemleriyle birlikte kullanılmasıyla blok ve aşı polimerler hazırlanabilir. Klik tepkimeleri metal katalizörler varlığında asetilen ve azid uç grupları arasında oda sıcaklığında gerçekleşirler. “Klik” tepkimelerinin polimer modifikasyonunda tercih edilme sebepleri arasında ılımlı tepkime şartları, yüksek verim, kısa tepkime süreleri, yüksek seçicilik, diğer fonksiyonel grupları iyi tolere etme ve çözücülere karşı reaktif olmama gibi etkenler sayılabilir.

Bu çalışmada, Atom Transfer Radikal Polimerizasyonu (ATRP) ve “Klik” kimyasının birlikte kullanılmasıyla poli(stiren-*b*-PEG-*b*-stiren) amfifilik blok kopolimeri ve poli(MMA-*g*-2-dimetilaminoetil metakrilat) amfifilik aşı kopolimeri sentezlendi. ATRP ile elde edilen azid fonksiyonlu polistirenle, Steglich esterleşmesiyle elde edilen propiyonil sonlu PEG’in CuBr ve PMDETA varlığında gerçekleştirilen “Klik” tepkimesiyle blok kopolimer hazırlandı. Aşı kopolimer ilkine benzer yaklaşımla sentezlendi. Azid-fonksiyonlu hidrofilik poli(2-dimetilaminoetil metakrilat) asetilen yan-fonksiyonlu hidrofobik PMMA zincirine “Klik” tepkimesiyle aşılandı. Polimerler $^{1}$H-NMR ve FT-IR ile karakterize edildi.

**Anahtar Kelimeler:** Amfifilik polimer, Polietilen oksit, Polistiren, “Klik” Tepkimesi , Atom Transfer Radikal Polimerizasyonu (ATRP)