ISTANBUL TECHNICAL UNIVERSITY ★ INSTITUTE OF SCIENCE AND TECHNOLOGY

A_3 TYPE STAR POLYMERS VIA CLICK CHEMISTRY

M. Sc. Thesis by

Burcu YANKUL

Department: Polymer Science and Technology

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İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

CLICK KİMYASI İLE A_3 TİPLİ YILDIZ POLİMER SENTEZİ

YÜKSEK LİSANS TEZİ

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LIST of SYMBOLS

ATRP	**:** Atom Transfer Radical Polymerization
NMP	**:** Nitroxide Mediated Polymerization
RAFT	**:** Reversible Addition-Fragmentation Chain Transfer Polymerization
CRP	**:** Controlled/Living Radical Polymerization
St	**:** Styrene
MMA	**:** Methyl methacrylate
***t*BA**	**:** *tert*-butylacrylate
PEG	**:** Poly(ethylene glycol)
PS	**:** Poly(styrene)
P*t*BA	**:** Poly(tert-butyl acrylate)
R_m and R_n	**:** Propagating Radical
P_n and P_m	**:** Terminated Macromolecules
LFRP	**:** Living Free Radical Polymerization
CTA	**:** Chain Transfer Agent
TEMPO	**:** 2, 2, 6, 6- Tetramethylpiperidinoxy
PDI	**:** Polydispersity
PRE	**:** Persistent Radical Effect
M_t^n	**:** Transition metal
L	**:** Ligand
M_w/M_n	**:** The Molecular Weight Distribution
k_a	**:** Rate constant of activation
k_d	**:** Rate constant of deactivation
k_p	**:** Rate constant of propagation
THF	**:** Tetrahydrofuran
DMAP	**:** 4-dimethylaminopyridine
PMDETA	**:** *N,N,N',N'',N''* - pentamethyldiethylenetriamine
FTIR	**:** Fourier Transform Infrared
GPC	**:** Gel Permeation Chromotography
NMR	**:** Nuclear Magnetic Resonance Spectroscopy

A_3-TYPE STAR POLYMERS VIA CLICK CHEMISTRY

SUMMARY

Star polymers have attracted much attention in research over the years due to their unique-three dimensional shape and highly branched structure. There are two general strategies used to produce star polymers: the arm-first and core-first techniques. In the arm-first strategy, a polymer with a proper end-group functionality is reacted with an appropriate multifunctional core to give a star polymer. In the second strategy (core-first), the polymer chain is simultaneously grown from a multifunctional initiator. Previously, living ionic polymerization was the only system for the preparation of star polymers with controlled structures. However, in recent years, the use of controlled/living radical polymerization techniques in the synthesis of complex macromolecules (star and dendrimeric polymers) has quickly increased because of the variety of applicable monomers and greater tolerance to experimental conditions in comparison with living ionic polymerization routes. Nitroxide mediated radical polymerization based on the use of stable nitroxide free radicals and Mtn(Metat)/ligand catalyst- mediated living radical polymerization, which is often called atom transfer radical polymerization (ATRP), are versatile methods among living radical polymerizations. Recently, Sharpless and coworkers used Cu(I) as a catalyst in conjunction with a base in Huisgen's 1,3-dipolar cycloadditions ([3 + 2] systems) between azides and alkynes or nitriles and termed them click reactions. Later, click chemistry strategy was successfully applied to macromolecular chemistry, affording polymeric materials varying from block copolymers to complex macromolecular structures. Click reactions permit C–C (or C–N) bond formation in a quantitative yield without side reactions or requirements for additional purification steps.

We report a simple preparation of three-armed (A_3-type) star polymers based on the arm-first technique, using a click-reaction strategy between a well-defined azide-end functionalized polystyrene, poly(tert-butyl acrylate), or poly(ethylene glycol) precursor and a trisalkyne functional initiator, 1,1,1-tris[4-(2-propynyloxy)phenyl]-ethane. The click-reaction efficiency for A_3-type star formation has been investigated with gel permeation chromatography measurements (refractive-index detector) and FTIR measurements. The gel permeation chromatography curves have been split with the deconvolution method (Gaussian area), and the efficiency of A_3-type star formation has been found to be 87%.

CLICK KİMYASI İLE A_3 TİPLİ YILDIZ POLİMER SENTEZİ

ÖZET

Yıldız polimerler araştırmalarda üç boyutlu ve çok dallanmış yapılarından dolayı yıllardır ilgi çekmektedirler. Yıldız polimerlerin elde edilmesinde kullanılan iki genel yöntem vardır: kol öncelikli ve çekirdek öncelikli yöntemleri. Kol öncelikli yönteminde, uygun uç grup fonksiyonalitesine sahip polimer ona uygun çok fonksiyonlu bir çekirdekle yıldız polimer elde etmek için reaksiyona sokulur. İkinci yöntemde (çekirdek öncelikli) ise, polimer zinciri çok fonksiyonlu bir başlatıcıdan eşzamanlı bir şekilde büyümektedir. Önceleri yaşayan iyonik polimerizasyon, yıldız polimer hazırlanmasında kullanılan tek sistemdi. Fakat son yıllarda kompleks makromoleküllerin sentezinde kontrollü/yaşayan polimerizasyon tekniklerinin kullanılması, yaşayan iyonik polimerizasyon yöntemiyle mukayese edildiğinde deneysel koşullara çok daha toleranslı olması ve çok çeşitli monomerlere uygulanabilir olması nedeniyle hızlı bir şekilde arttı. Kararlı nitroksit serbest radikallerin kullanımına dayanan Nitroksit Ortamlı Radikal Polimerizasyonu ve genellikle Atom Transfer Radical Polimerizasyonu (ATRP) olarak bilinen Mtn(Metat)/ligand kataliz ortamlı radikal polimerizasyonu yaşayan radikal polimerizasyon yöntemleri arasında çok yönlü metotlardır. Son yıllarda, Sharpless ve arkadaşları azidler ve alkin/nitriller arasındaki Huisgen 1,3-dipolar siklokatılmalarda ([3 + 2] sistemi) Cu(I)'i baz ile birleştirip kataliz olarak kullandılar ve bu reaksiyonu click reaksiyonu olarak adlandırdılar. Daha sonra click kimyası blok kopolimerlerden karmaşık makromoleküler yapılara kadar değişen birçok polimerik malzemenin yapılmasına kadar makromolekül kimyasında başarılı bir şekilde uygulandı. Click reaksiyonları, yan reaksiyonlara sebebiyet vermeyecek ve ilave saflaştırma işlemlerine gereksinim duyulmayacak bir şekilde kantitatif verimle C–C (veya C–N) bağ oluşumuna izin vermektedir.

Bu çalışmada, ucu azid fonksiyonlu iyi tanımlanmış polistiren, politersiyerbütilakrilat ve polietilenglikol ile üç kollu, ucu alkin fonksiyonlu başlatıcı (1,1,1-tris[4-(2-propynyloxy)phenyl]- ethane) arasındaki click reaksiyonu kullanılarak kol öncelik tekniğine dayanan basit bir 3-kollu (A_3-tipi) yıldız polimer hazırlandı. A_3-tipli yıldız polimer oluşumu için click reaksiyonun verimi jel geçirgenlik kromatografisi (refraktif indeks detektörü) ve FTIR spektrometresi ile incelendi. Jel geçirgenlik kromatografisi eğrileri deconvolution metoduyla (Gauss alanı) ile bölündü ve A_3-tipli yıldız polimer oluşumu verimi %87 olarak bulundu.

1. INTRODUCTION

A star structure is defined as a nonlinear polymer that consists of multiple backbone chains existing from junction points [1]. Star polymers show different crystalline, mechanical, and viscoelastic properties in comparison with their corresponding linear analogues.

Interest in star polymers arises from their compact structure and globular shape, which predetermines their low viscosity when compared to linear analogues and makes them suitable materials for several applications. Synthesis of star polymers, which began in the 1950s with living anionic polymerization, has recently received increased attention due to the development of controlled/living radical polymerization (CRP) [2,3]. Typically, star polymers are synthesized via CRP by one of two strategies: core-first and arm-first. The arm-first strategy can be further subcategorized according to the procedure employed for star formation. One method is chain extension of a linear arm precursor with a multivinyl crosslinking agent, and the other is coupling linear polymer chains with a multifunctional linking agent or "grafting-onto" a multifunctional core. Although both methods were successfully used for star synthesis in anionic polymerization, to date only the former procedure, using a multivinyl cross-linking agent, has been applied in CRP for synthesis of star polymers containing multiple arms and/or functionalities [4,5].

Atom transfer radical polymerization (ATRP) is a particularly attractive CRP process for synthesis of chain-endfunctionalized polymers [6,8]. The polymers produced by ATRP preserve terminal halogen atom(s) that can be successfully converted into various desired functional chain-end groups through appropriate transformations, especially nucleophilic substitutions. The modified chain-end group, such as a hydroxyl group or an amino group, cannot react with itself but can react with an appropriate functional group on the multifunctional coupling agent, such as a carboxylic acid group by esterification, to form a star polymer. However, a

commonly encountered drawback, when using such a method, is a low yield of star products due to the slow and inefficient reactions between the modified polymer chain ends and multifunctional linking agents. In other words, highly efficient site-specific organic reactions are required in order for star synthesis to be highly successful [5].

In the past few years, “click reactions”, as termed by Sharpless et al., have gained a great deal of attention due to their high specificity, quantitative yields, and near-perfect fidelity in the presence of most functional groups. The most popular click chemistry reaction is the copper-catalyzed Huisgen dipolar cycloaddition reaction between an azide and an alkyne leading to 1,2,3-triazole [9-12].

In this work, by combination of ATRP and click reaction strategy, we prepared three-armed (A_3-type) star polymers based on the arm-first technique, using a click-reaction strategy between a well-defined azide-end-functionalized polystyrene (PS–N_3), azide-end functionalized poly (tert-butyl acrylate) (P*t*BA–N_3), or azide-end-functionalized poly(ethylene glycol) (PEG–N_3) and a trisalkyne- functional initiator, 1,1,1-tris[4-(2-propynyloxy) phenyl]ethane (**1**). The click-reaction efficiency for A_3-type star formation has been investigated with gel permeation chromatography measurements (refractive-index detector) and FTIR measurements. The gel permeation chromatography curves have been split with the deconvolution method (Gaussian area), and the efficiency of A_3-type star formation has been found to be 87%.

2. THEORETICAL PART

2.1. Conventional Free Radical Polymerizations

Conventional free radical polymerization (FRP) has many advantages over other polymerization processes. First, FRP does not require stringent process conditions and can be used for the (co)polymerization of a wide range of vinyl monomers. Nearly 50% of all commercial synthetic polymers are prepared using radical chemistry, providing a spectrum of materials for a range of markets [13]. However, the major limitation of FRP is poor control over some of the key elements of the process that would allow the preparation of well-defined polymers with controlled molecular weight, polydispersity, composition, chain architecture, and site-specific functionality.

As chain reactions, free radical polymerizations proceed via four distinct processes:

1. *Initiation*. In this first step, a reactive site is formed, thereby "initiating" the polymerization.

2. *Propagation*. Once an initiator activates the polymerization, monomer molecules are added one by one to the active chain end in the propagation step. The reactive site is regenerated after each addition of monomer.

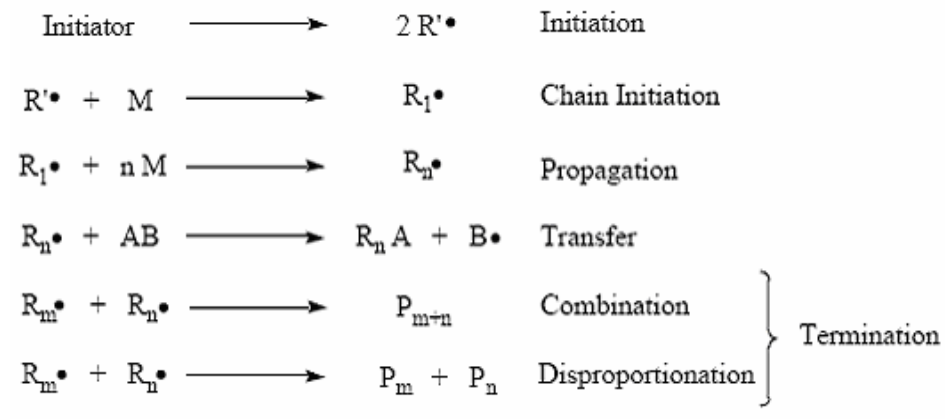
3. *Transfer*. Transfer occurs when an active site is transferred to an independent molecule such as monomer, initiator, polymer, or solvent. This process results in both a terminated molecule (see step four) and a new active site that is capable of undergoing propagation.

4. *Termination*. In this final step, eradication of active sites leads to "terminated," or inert, macromolecules. Termination occurs via coupling reactions of two active centers (referred to as combination), or atomic transfer between active chains (termed disproportionation).

The free radical chain process is demonstrated schematically below (2.1): $R^{\cdot}$ represents a free radical capable of initiating propagation; M denotes a molecule

of monomer; R_m and R_n refer to propagating radical chains with degrees of polymerization of *m* and *n*, respectively; AB is a chain transfer agent; and $P_n + P_m$ represent terminated macromolecules.

Because chain transfer may occur for every radical at any and all degrees of polymerization, the influence of chain transfer on the average degree of polymerization and on polydispersity carries enormous consequences. Furthermore, propagation is a first order reaction while termination is second order. Thus, the proportion of termination to propagation increases substantially with increasing free radical concentrations. Chain transfer and termination are impossible to control in classical free radical processes, a major downfall when control over polymerization is desired.



(2.1)

Figure 2.1 General Free Radical Polymerization Mechanism

2.2. Conventional Living Polymerizations

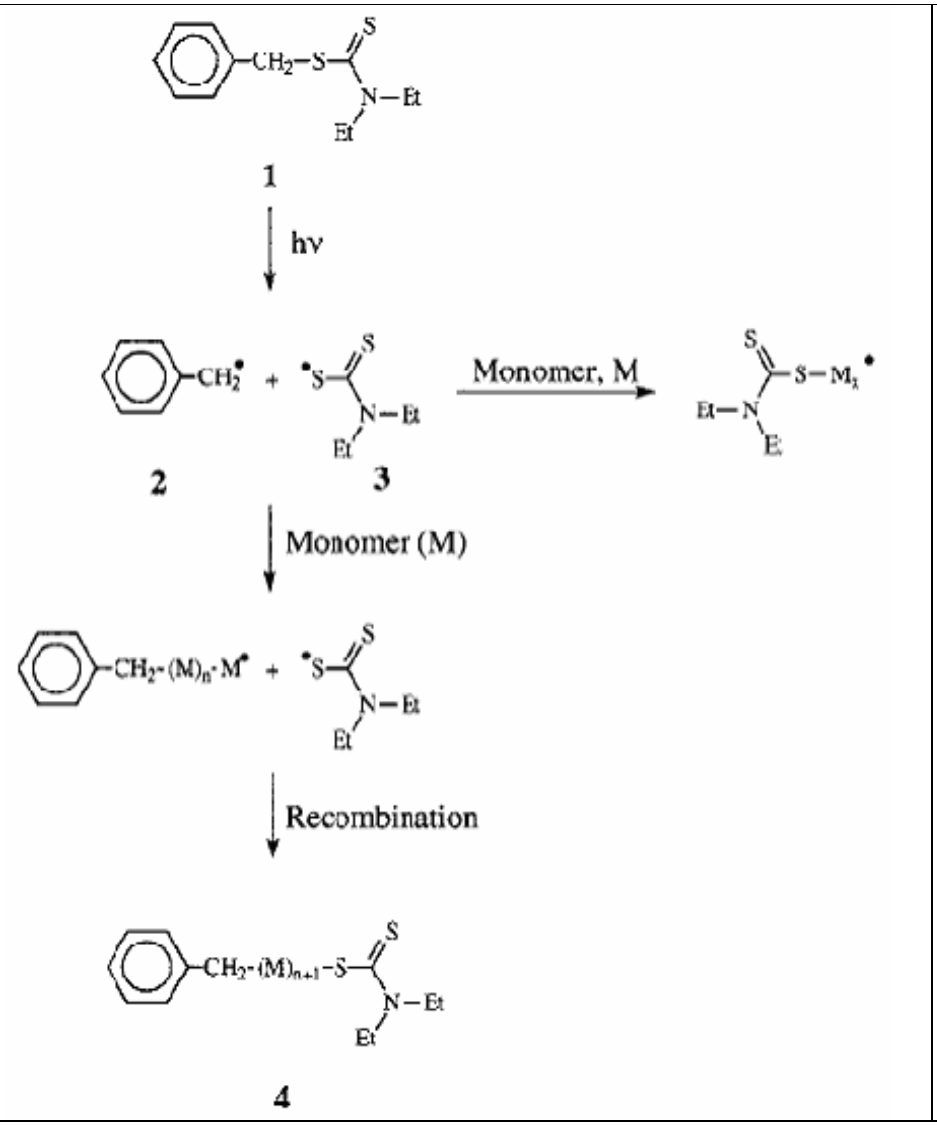
Living polymerizations are characterized by chain growth that matures linearly with time. Inherent in this definition are two characteristics of ionic polymerizations that both liken and distinguish ionic routes from the aforementioned free radical route. In order to grow linearly with time, ionic polymerizations must proceed by a chain mechanism in which subsequent monomer molecules add to a single active site; furthermore, addition must occur without interruption throughout the life of the active site. Thus, the chain transfer mechanisms described above must be absent. Living polymerizations may include slow initiation, reversible formation of species with various activities and lifetimes, reversible formation of inactive (dormant) species, and/or reversible transfer [14]. Living polymerizations must not include

irreversible deactivation and irreversible transfer. Classical living polymerizations occur by the formation of active ionic sites prior to any significant degree of polymerization. A well-suited initiator will completely and instantaneously dissociate into the initiating ions. Dependent on the solvent, polymerization may then proceed via solvent pairs or free ions once a maximum number of chain centers are formed. Solvents of high dielectric constants favor free ions; solvents of low dielectric constants favor ionic pairs. Termination by coupling will not occur in ionic routes due to unfavorable electrostatic interactions between two like charges. Furthermore, chain transfer routes are not available to living polymerizations, provided the system is free of impurities. Polymerization will progress until all of the monomer is consumed or until a terminating agent of some sort is added. On the flip side, ionic polymerizations are experimentally difficult to perform: a system free of moisture as well as oxygen, and void of impurities is needed. Moreover, there is not a general mechanism of polymerization on which to base one's experiment: initiation may occur in some systems before complete dissociation of initiator. Knowledge of the initiating mechanism must be determined *a priori* to ensure a successful reaction. Despite the advantage of molecular control of living systems, the experimental rigor involved in ionic polymerization is often too costly for industrial use and free radical routes are preferred.

2.3. Controlled/Living Free Radical Polymerizations

Conventional free radical polymerization techniques are inherently limited in their ability to synthesize resins with well-defined architectural and structural parameters. Free radical processes have been recently developed which allow for both control over molar masses and for complex architectures. Such processes combine both radical techniques with living supports, permitting reversible termination of propagating radicals. In particular, three controlled free radical polymerizations which are atom transfer radical polymerization (ATRP), nitroxide mediated polymerization (NMP), and reversible addition fragmentation chain transfer (RAFT) have been well investigated. Each of these techniques is briefly presented below and all are based upon early work involving the use of initiator-transfer agent-terminators to control irreversible chain termination of classical free radical process.

In 1982, Otsu et al. extended the idea of living polymerizations to free radical systems in the use of initiator-transfer agent-terminators, or iniferters [15]. Such initiators act both as primary radicals to initiate polymerization (R'•, Fig. 2.1) and as radical chain terminators (R_m• or R_n•, Fig. 2.1), consequently permitting a near linear increase of molar mass with time and percent conversion [16]. However, the similarities between living anionic systems and Otsu's iniferter reaction end there. The iniferter mechanism (Fig. 2.2) yields radicals that can initiate new chains throughout the course of the reaction [17]. The iniferter systems also show significant loss of active end groups from the growing polymers [17b]. Consequently, these systems display relatively large polydispersities with a substantial amount of homopolymer being formed in conjunction with block copolymer [17a].



(2.2)

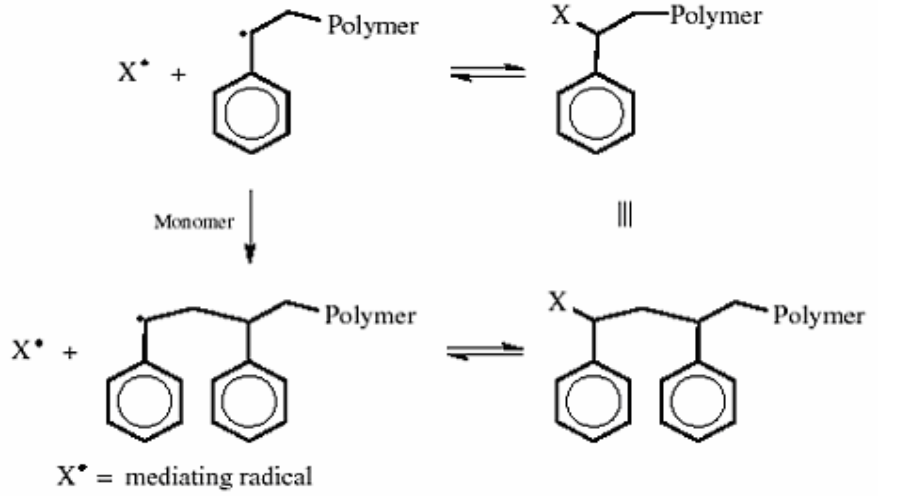
Figure 2.2 The iniferter mechanism

2.3.1. Nitroxide-Mediated Living Radical Polymerizations

This pioneering work was one of the seminal contributions that provided the basis for the development of living free radical polymerization (LFRP), and it is interesting to note the similarity between the iniferter mechanism outlined in Figure 2.2 and the general outline of a living free-radical mechanism (Fig. 2.3). In this general mechanism, the reversible termination of the growing polymeric chain is the key step for reducing the overall concentration of the propagating radical chain end. In the absence of other reactions leading to initiation of new polymer chains (i.e., no reaction of the mediating radical with the vinylic monomer), the concentration of reactive chain ends is extremely low, minimizing irreversible termination reactions,

such as combination or disproportionation. All chains would be initiated only from the desired initiating species and growth should occur in a pseudoliving fashion, allowing a high degree of control over the entire polymerization process with well-defined polymers being obtained.

The identity of the mediating radical, $X^{\bullet}$, is critical to the success of living free radical procedures and a variety of different persistent, or stabilized radicals have been employed [18–22]. However the most widely studied and certainly most successful class of compounds are the nitroxides and their associated alkylated derivatives, alkoxyamines. Interestingly, the development of nitroxides as mediators for radical polymerization stems from pioneering work by Solomon, Rizzardo, and Moad into the nature of standard free-radical initiation mechanisms and the desire to efficiently trap carbon-centered free radicals [23].



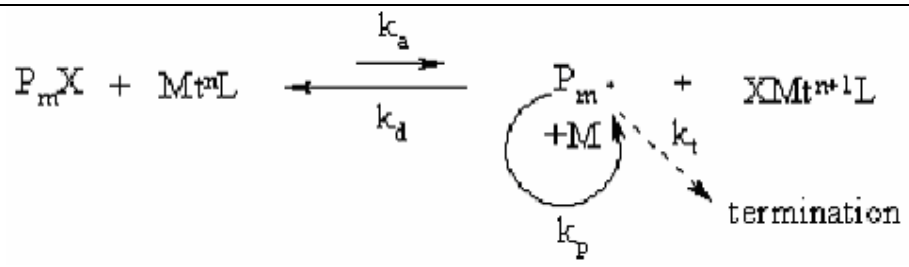
(2.3)

Figure 2.3 The general outline of the free-radical mechanism

2.3.2. Atom Transfer Radical Polymerization (ATRP)

ATRP is one of the most versatile controlled radical polymerization method. This method utilizes a reversible halogen atom abstraction step in which a lower oxidation state metal (M_t^n complexed by ligands L) reacts with an alkylhalide (P_m-X) to generate a radical ($P_m^{\bullet}$) and a higher oxidation state metal complex ($XM_t^{n+1}L$). This radical then adds monomer to generate the polymer chain (k_p). The higher oxidation state metal can then deactivate the growing radical to generate a dormant chain and the lower oxidation state metal (k_d) as seen in (Fig. 2.4). The molecular weight is controlled because both initiation and deactivation are fast, allowing for all the

chains to begin growing at approximately the same time while maintaining a low concentration of active species. Termination cannot be totally avoided; however, the proportion of chains terminated compared to the number of propagating chains is small [24]. Several metal/ligand systems have been used to catalyze this process and a variety of monomers including styrene, methacrylates, and acrylonitrile have been successfully polymerized [25-27].



(2.4)

Figure 2.4 The mechanism of ATRP

The rate of ATRP is internally first order in monomer, externally first order with respect to initiator and activator, Cu(I), and negative first order with respect to deactivator, XCu(II). The actual kinetics depends on many factors including the solubility of activator and deactivator, their possible interactions, and variation of their structures and reactivities with concentrations and composition of the reaction medium.

One of the most important parameters in ATRP is the dynamics of exchange, especially the relative rate of deactivation. If the deactivation process is slow in comparison with propagation, then a classic redox initiation process operates leading to conventional, and not controlled, radical polymerization. Polydispersities in ATRP decrease with conversion, with the rate constant of deactivation, k_d, and also with the concentration of deactivator, [XCu(II)]. They, however, increase with the propagation rate constant, k_p, and the concentration of initiator, $[RX]_o$. This means that more uniform polymers are obtained at higher conversion, when the concentration of deactivator in solution is high and the concentration of initiator is low. Also, more uniform polymers are formed when deactivator is very reactive and monomer propagates slowly (styrene rather than acrylate) [28].

2.3.2.1. Monomers

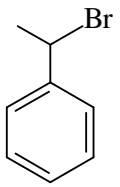
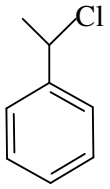
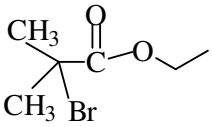
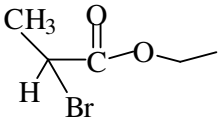
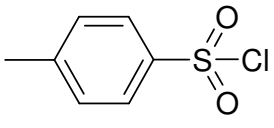
A variety of monomers have been successfully polymerized using ATRP. Typical monomers include styrenes (meth) acrylates, (meth) acrylamides, and acrylonitrile, which contain substituents that can stabilize the propagating radicals. Even under the same conditions using the same catalyst, each monomer has its own unique atom transfer equilibrium constant for its active and dormant species. In the absence of any side reactions other than radical termination by coupling or disproportionation, the magnitude of the equilibrium constant $(K_{eq}=k_{act}/k_{deact})$ determines the polymerization rate.

2.3.2.2. Initiators

The main role of the initiator is to determine the number of growing polymer chains. Two parameters are important for a successful ATRP initiating system. First, initiation should be fast in comparison with propagation. Second, the probability of the side reactions should be minimized.

In ATRP, alkylhalides (RX) are typically used as initiator and the rate of polymerization is first order with respect to the concentration of RX. 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 bromine or chlorine, the molecular weight control is the best. Flourine is not used because the C-F bond is too strong to undergo homolytic cleavage.

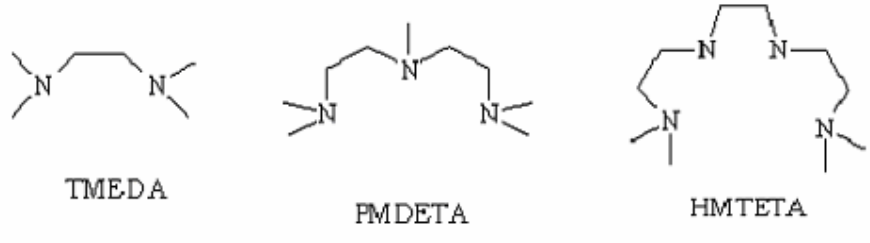
Table 2.1. The most frequently used initiator types in ATRP systems

• Initiator	• Monomer
 1-Bromo-1-phenyl ethane	Styrene
 1-Chloro-1-phenyl ethane	Styrene
 Ethyl-2-bromo isobutyrate	Methyl methacrylate
 Ethyl-2-bromo propionate	Methylacrylate and other acrylates
 p-toluene sulphonyl chloride	Methyl methacrylate

2.3.2.3. Ligands

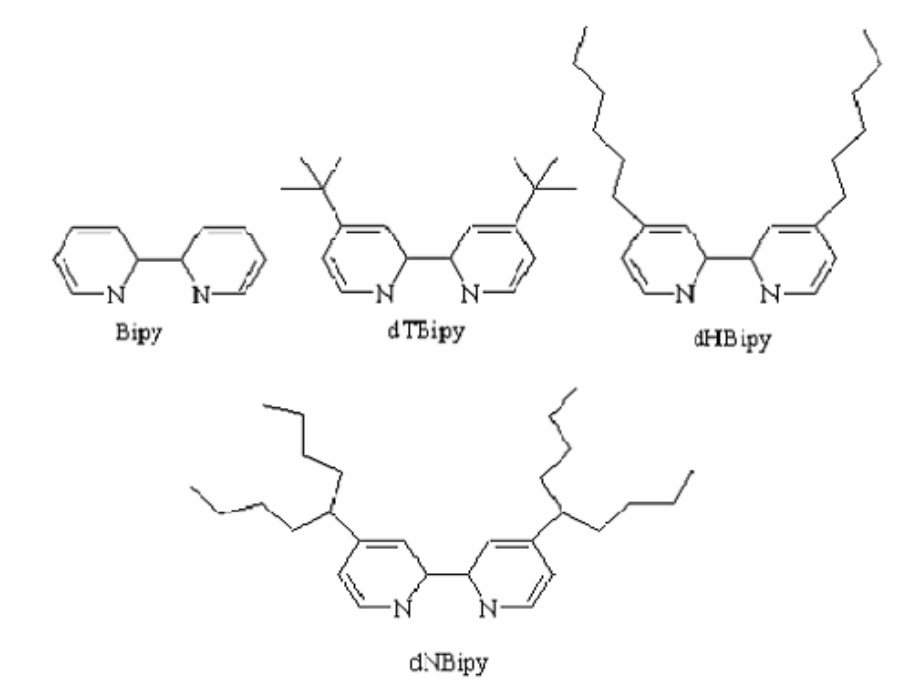
The main role of the ligand in ATRP is to solubilize the transition metal salt in the organic media and to adjust the redox potential of the metal center for the atom transfer. There are several guidelines for an efficient ATRP catalyst. First fast and quantitative initiation ensures that all the polymer chains start to grow simultaneously. Second, the equilibrium between the alkylhalide and the transition metal is strongly shifted toward the dormant species side. This equilibrium position will render most of the growing polymer chains dormant and produce a low radical concentration. As a result, the contribution of radical termination reactions to the

overall polymerization is minimized. Third 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. Fourth relatively fast activation of the dormant polymer chains provides a reasonable polymerization rate. Fifth, there should be no side reactions such as β-H abstraction or reduction/oxidation of the radicals.



(2.5)

Figure 2.5 Nitrogen based ligands



(2.6)

Figure 2.6 Derivatives of 2,2-bipyridine

The most widely used ligands for ATRP systems are the derivatives of 2,2-bipyridine and nitrogen based ligands such as *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA), tetramethylethylenediamine (TMEDA), 1,14,7,10,10-hexamethyltriethylenetetraamine (HMTETA), tris[2-(dimethylamino) ethyl]amine (Me_6-TREN) and alkylpyridylmethanimines are also used.

2.3.2.4. Transition Metal Complexes

Catalyst is the most important component of ATRP. It is the key to ATRP since it determines the position of the atom transfer equilibrium and the dynamics of exchange between the dormant and active species. There are several prerequisites for an efficient transition metal catalyst. First, the metal center must have at least two readily accessible oxidation states separated by one electron. Second the metal center should have reasonable affinity toward a halogen. Third the coordination sphere around the metal should be expandable upon oxidation to selectively accommodate a (pseudo)-halogen. Fourth the ligand should complex the metal relatively strongly.

The most important catalysts used in ATRP are; Cu(I)Cl, Cu(I)Br, $NiBr_2(PPh_3)_2$, $FeCl_2(PPh_3)_2$, $RuCl_2(PPh_3)_3$/ $Al(OR)_3$.

2.3.2.5. Solvents

ATRP can be carried out either in bulk, in solution or in a heterogeneous system (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.

2.3.2.6. Temperature and Reaction time

The rate of polymerization also determines the rate of polymerization by effecting both propagation rate constant and the atom transfer equilibrium constant. The k_p/k_t ratio increase as a result of higher temperature thus enables us better control over the polymerization. However this may also increase the side reactions and chain transfer reactions. The increasing temperature also increases the solubility of the catalyst. Against this, it may also poison catalyst by decomposition. Determining the optimum temperature; monomer, catalyst and the targeted molecular weight should be taken into consideration.

2.3.2.7. Molecular weight and molecular weight distribution

We can determine the average molecular weight of the polymer by the ratio of consumed monomer and the initiator as in a typical living polymerization ($DP_n=\Delta[M]/[I]_o$, DP=degree of polymerization) while there is a narrow molecular weight distribution ($1.0 < M_w/M_n < 1.5$).

The molecular weight distribution or polydispersity M_w / M_n is the index of the polymer chain distribution. In a well-controlled polymerization, M_w / M_n is usually less than 1.1.

$\mathbf{M_w / M_n = 1 + [[RX]_o k_p / k_d [D]] . [(2/p) - 1]}$	(2.7)

Figure 2.7 The polydispersity index in ATRP in the absence of chain termination and transfer

Where, D: Deactivator, k_p: Propagation rate constant, k_d: Deactivation rate constant, p: Monomer conversion

When a hundred percent of conversion is reached, in other words p=1, it can be concluded that;

i) Polydispersities (molecular weigh distributions) decrease, if the catalyst deactivates the chains faster (smaller k_p / k_d)

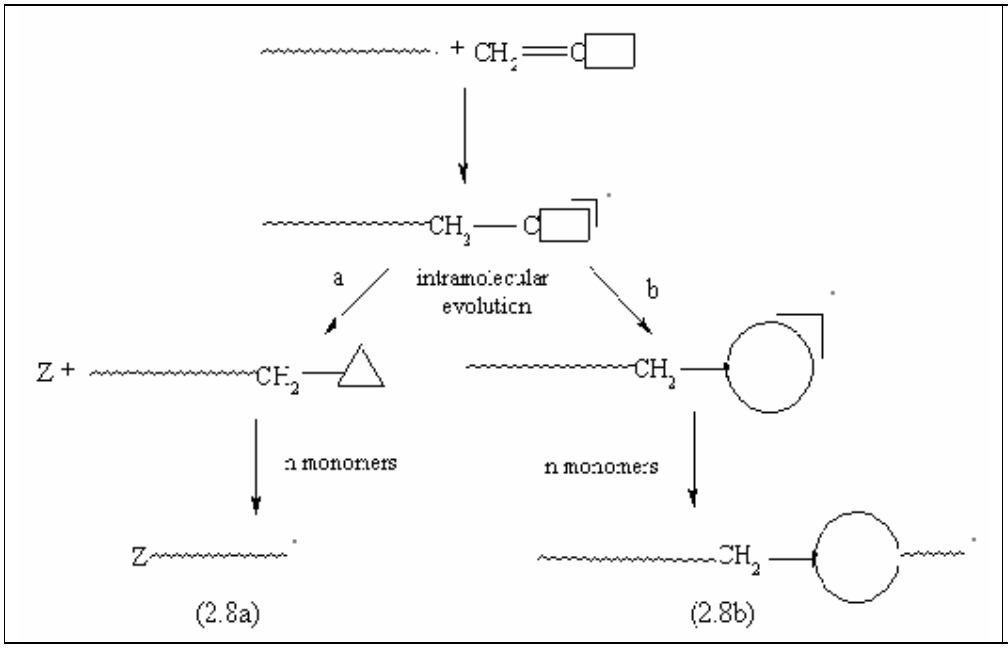
ii) For the smaller polymer chains, higher polydispersities are expected to obtain because the smaller chains include little activation-deactivation steps resulting in little control of the polymerization.

iii) Polydispersities decrease as the concentration of the deactivator decreases. (For example, the addition of a small amount of Cu(II) halides in copper-based ATRP decreases the reaction rate thus leads to better controlled polymerizations)

2.3.3. Addition –Fragmentation Polymerization (RAFT)

An addition-fragmentation process is said to occur in free radical polymerization whenever a growing polymer chain reacts with a compound bearing both an activated site of unsaturation and a weak bond located somewhere else in the molecule. The intermediate radical formed by the addition of propagating radical on the transfer agent undergoes fragmentation involving the weak bond generating

another radical which can enter the polymerization cycle. Such a process occurs with the formation of a functional group on the backbone of the polymer (which carried also radical, (Fig. 2.8a) or at the end of the polymer chain (the radical resting another molecule (Fig. 2.8b). The former case involves the use of an addition-fragmentation monomer and the latter the introduction of an addition-fragmentation chain transfer agent in the polymerization medium (Fig. 2.8).



(2.8)

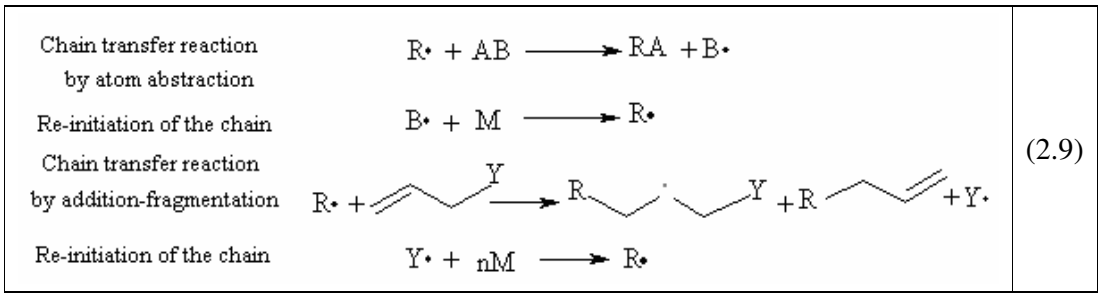
Figure 2.8 An addition-fragmentation process

Many monomer and transfer agents based on these types of skeleton have already been developed. However the actual use of an addition-fragmentation chain transfer agent or of an addition-fragmentation monomer in industrial applications is still limited at the present time, because of various problems arising from their synthesis, polymerizability and properties, although such compounds could inherently be useful in most industrial applications.

The control of molar mass in free radical polymerization is usually achieved by the addition of a chain transfer agent in the polymerization medium. When a chain carrying radical is trapped by another specific compound XY to produce a radical Y• which is also reactive, this radical Y• can re-initiate a new radical chain. In this case XY is called a chain transfer agent. Two kinds of chain transfer agents can be distinguished according to their mode of action:

1. Atom or group transfer agents operating by an abstraction pathway (Fig. 2.9). These additives are generally solvents such as CCl_4, mercaptans, substituted disulfides which react in the medium as atom donors to the growing macro radicals, thus terminating the polymer chain and generating, respectively a trichloromethyl a thiyl radical, able to re-initiate polymerization [29-30].

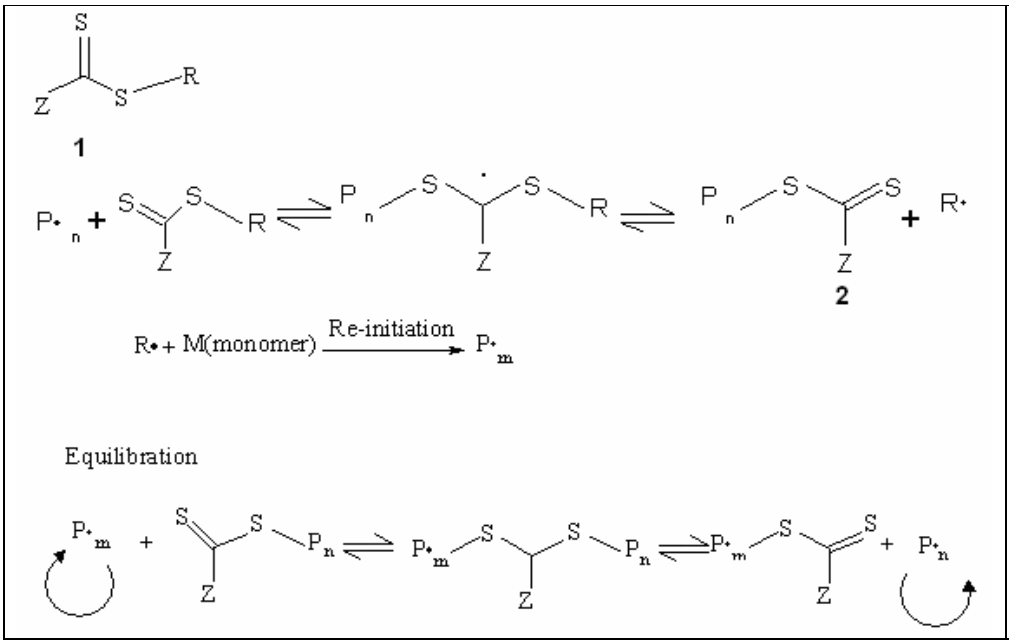
2. Addition-fragmentation chain transfer agents (Fig. 2.9). The chain transfer agents which follow the addition-fragmentation mechanism are particular interest in organic and polymer chemistry. Recently many studies have shown that allyl, acrylyl and allenyl transfer to alkyl halides represent powerful synthetic tolls to prepare sophisticated molecules. Such a process was also identified as an effective means for controlling the molar mass of vinyl polymers, avoiding the use of conventional chain transfer agents based on thioderivatives.



(2.9)

Figure 2.9 Addition-fragmentation chain transfer agents

Thiocarbonylthio compounds of general structure 1 in (Fig. 2.10) confer living characteristics to radical polymerization [31-32]. These reagents function by establishing a dynamic equilibrium between propagating radicals ($P_n^{\bullet}$) and dormant chains 2 in (Fig. 2.10) by a mechanism of reversible addition –fragmentation chain transfer (raft) as shown in (Fig. 2.10). RAFT agents 1 in (Fig. 2.10) function effectively only when the substituent on sulfur (R) is good homolytic leaving group when compared to the polymer chain P_n. With appropriate choice of the RAFT agent 1 in (Fig. 2.10) a wide range of polymers of predetermined M_W and narrow polydispersity can be prepared [31-32-33]. The versatility and convenience of this process offer distinct advantages over other forms of living radical polymerization [34-35].



(2.10)

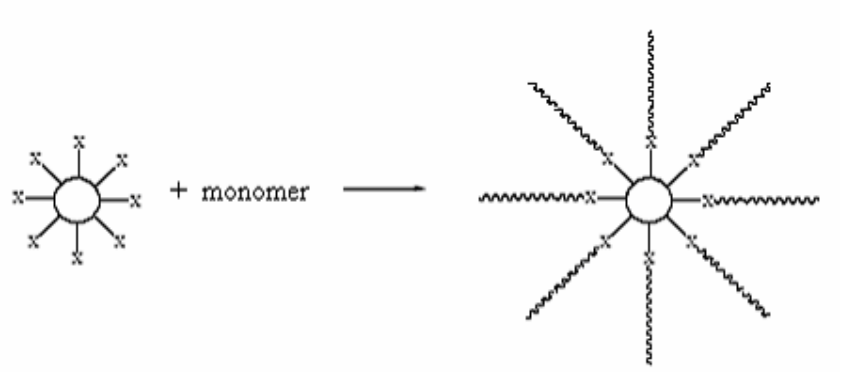
Figure 2.10 Mechanism of reversible addition –fragmentation chain transfer (RAFT)

2.4 Synthesis of Star-Shaped Polymers

2.4.1 Introduction

Elucidation of structure-property relationships remains an ongoing field of study in polymer science. The introduction of long chain branching is known to affect polymer physical properties and processability as a result of changing the melt, solution, and solid-state properties of polymers [36]. It has been shown that branching results in a more compact structure in comparison to linear polymers of similar molecular weight, due to their high segment density, which alters the crystalline, mechanical, and viscoelastic properties of the polymer. While it is well-known that long chain branching greatly influences polymer physical properties, a fundamental understanding of structure-property relationships remains difficult due to the complexity of branched polymer structures. A branched polymer structure was described as a nonlinear polymer with multiple backbone chains radiating from junction points [37]. Star-shaped macromolecules constitute the simplest form of branched macromolecules, comprising only one branch point, and as such, have received significant attention in the elucidation of structure property relationships [38]. Although star polymers constitute the simplest branched structure, their synthesis remains challenging, and star polymers are often difficult to synthesize in a

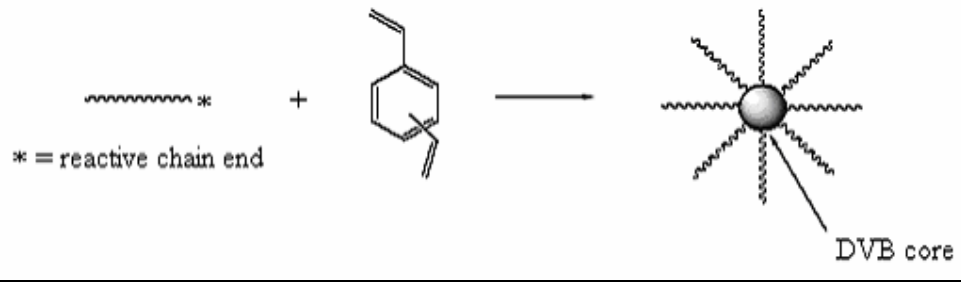
well-controlled manner. Due to the complex nature of these macromolecules, controlled polymerization techniques, such as anionic, cationic, living free radical, and group transfer (GTP) polymerization have typically been used to obtain well-defined star-shaped macromolecules. Star polymers are typically synthesized using either a core-first approach, or an arm-first approach. In the core-first synthetic method, a multifunctional initiator is used and the number of arms is proportional to the number of functionalities on the initiator (Fig. 2.11) [39].



(2.11)

Figure 2.11 The core-first synthetic method

Using the core-first method, well-defined star-shaped macromolecules can be synthesized as long as initiation is rapid relative to propagation. While this approach was used in the first cationic synthesis of star-shaped polymers, containing three or four arms, it tends to yield polymers with broadened molecular weight distributions [40]. In the arm-first synthetic method, linear arm polymers are synthesized and then coupled using a multifunctional linking agent or divinyl compound. In this case, the number of arms depends on the linking efficiency of the arm polymer to the multifunctional core and an alternative method is used to determine the number of arms (Fig. 2.12). This approach is typically used in both living anionic and cationic syntheses of star-shaped polymers [41].



(2.12)

Figure 2.12 The arm-first synthetic method

As discussed previously, living anionic chain ends are very reactive and are used in a variety of chain end functionalization strategy. This characteristic of living chain ends makes living anionic polymerization ideal for the synthesis of complex architectures using chain end coupling reactions. The synthesis of star-shaped polymers using living anionic polymerization has been achieved using a variety of linking agents. Typical linking reagents for coupling of living anionic chain ends are chlorosilanes and their derivatives. However, these types of endcapping reagents are limited in their utility by the necessity for equal reactivity and accessibility of all reactive sites on the linking agent. Use of both silicon tetrachloride and chloromethylated benzenes have been hampered by these limiting factors. Other linking agents are dimethyl phthalate, trisallyloxytriazines, and divinylbenzene. In some cases, the number of arms using the arm first approach is controlled by the number of functionalities on the linking agent, such as trichloromethylsilane or tetrachlorosilane.

In other cases, such as divinylbenzene, the linking agent undergoes homopolymerization to form the core and the number of arms is greater than the functionality of the linker molecule. While the arm-first method is typically used in conjunction with living anionic polymerization to form well-defined star-shaped macromolecules, the core-first methodology has also been used. The core-first method requires the generation of a reactive core molecule prior to polymerization and this oftentimes leads to undesired coupling reactions between core molecules. As the arms grow out from the core, the tendency to couple decreases. The main advantage to the core-first methodology is the ease of chain end functionalization at the star periphery.

More recently, several of the techniques discussed above have been used in conjunction with one another to synthesize novel macromolecular architectures. For example, Muller et al. reported the use of both cationic and anionic polymerization to synthesize star-shaped block copolymers [42]. The polymerization of isobutylene was initiated using 1,3,5-tricumylchloride and terminated using diphenylethylene and methanol to yield a diphenylethylene methoxy group. This group was then transformed into an initiator for the anionic polymerization of methyl methacrylate using a K/Na alloy.

Star-branched structures in which the arms are comprised of different polymer backbones were achieved using the arm-first approach and a difunctional diphenylethylene derivative. In this approach, the first monomer was polymerized using living anionic techniques and then terminated with the difunctional diphenylethylene derivative. The second monomer was then polymerized from the residual functionality on the diphenylethylene molecule to yield A_2B_2 type macromolecules. When macromolecules with less defined cores are synthesized, a variety of techniques have been employed, including the use of a bromomethylbenzene derivative in the synthesis of *t*-butyl methacrylate star-shaped macromolecules, hyperbranched cores, main chain functional graft sites, and convergent coupling of arm polymers to synthesize dendritically branched polystyrene.

2.4.2 Synthesis of Functional Star-Shaped Polymers

Chain-end functionalization is an additional challenge in the synthesis and characterization of complex polymer architectures. As discussed previously, living anionic polymerization methodologies are typically used to synthesize star-shaped macromolecules due to the controlled nature of these reactions. Functionalized alkyllithium initiators provide quantitative chain end functionalization and are an attractive alternative to electrophilic terminating reagents for the synthesis of chain-end functionalized polymers. Functionalized initiators facilitate the synthesis of telechelic and heterotelechelic polymers, functionalized block polymers, and star-shaped polymers with functional groups on each arm terminus [43]. The use of the functional initiator 3-(*t*-butyldimethylsilyloxy)-1-propyllithium (*t*BDMSPrLi) was reported in the synthesis of a variety of polymers with various architectures, such as polyisoprene, polybutadiene, poly(methyl methacrylate), and poly(1,3-cyclohexadiene), to yield hydroxyl chain end functionalized polymers. While living anionic polymerization using functional initiation has proven an excellent pathway to chain-end functional polymers, other researchers have reported various methodologies for the preparation of star-shaped macromolecules with diverse chain-end functionalities.

Hedrick et al. reported the core-first synthesis of star-shaped poly(ε-caprolactone) hydroxyl terminated macroinitators with six arms using ring opening polymerization

and the subsequent transformation into ATRP initiators [44]. The macroinitiators were then used to polymerize several monomers, including methyl methacrylate, hydroxyethyl methacrylate, or ethylene oxide. There are several parameters in an ATRP that should be controlled carefully in order to maximize the yield of stars and prevent star-star coupling reactions. Some detailed studies have been carried out on the coupling of monofunctional polystyrenes and polyacrylates with DVB and di(meth)acrylates to prepare star polymers and the following guidelines have been developed:

- The ratio of difunctional reagent to growing chains seems to be optimal in the range of 10-20
- Monomer conversion (or reaction time) has to be carefully controlled and stopped before star-star coupling occurs.
- Higher yields of stars are observed for polyacrylates than for polystyrenes. This may be attributed to a higher proportion of terminated chains in styrene polymerization.
- The choice of the difunctional reagent is important and reactivity should be similar to, or lower than that of the arm-building monomers.
- Halogen exchange slightly improves efficiency of star formation.
- Solvent, temperature, catalyst concentration should be also optimized [45].

In a similar fashion, using living cationic polymerization, Gnanou and coworkers synthesized star-shaped polystyrenes and used functional group transformation to transform the chain-end functionality to either hydroxyl of amino at the periphery. The hydroxyl terminated samples were also utilized as macroinitiators for ethylene oxide polymerization. In several cases, ATRP was used in acrylic polymerizations to yield polymers with hydroxyl, epoxy, amino, bromide, or cyano functionalized star polymers.

Utilizing a different approach, Hirao et al. have introduced functionality to star polymers using living anionic polymerization in conjunction with functionalized diphenylethylene (DPE) derivatives and organic functional group transformations [46]. Using this approach, functionality was introduced at the α-terminus, at block junctions, or at the core. Quirk et al. pioneered this work and Hirao et al. based their research on this work [47]. Fréchet and Hawker et al. have also reported the use of nitroxide mediated polymerization in the synthesis of functionalized star polymers

[48]. They reported the synthesis of a series of compounds, ranging from simple to complex, and have focused on homo, block, and random copolymers with both apolar and polar vinylic repeat units and functional group integration in diverse positions. Ishizu et al. have also reported on the functionalization of polyisoprene star polymers with p-chloro styrene to yield a periphery of reactive styrene groups, capable of forming a crosslinked network [49]. While both functional polymers and star-shaped polymers are prevalent in the literature, the combination of well-defined thermoreversible chain end interactions, such as multiple hydrogen bonding interactions, and star-shaped macromolecules is limited. Hadjichristidis et al. studied the synthesis and characterization of well-defined linear and star-shaped polystyrenes, polyisoprenes, and polybutadienes bearing both sulfo- and phosphoro-zwitterionic groups, which have a thermoreversible nature [38]. While these studies have made great strides in delineating structure-property relationships for these materials, the reversible interaction is ionic and it is anticipated that their behavior will significantly differ from a multiple hydrogen bonding interaction. Meijer et al. have recently reported the synthesis of model low molar mass poly (ethylene oxide-*co*-propylene oxide) three arm star polymers bearing pendant quadruple hydrogen bonding functionalities [50]. These polymers were compared with three arm star polymers bearing urea chain ends, non-functional chain ends, and with a chemically crosslinked network and the influence of chain end functionality was studied. However, due to the hydrophilic nature of the parent polymer, the effect of atmospheric moisture on the polymer physical properties was not excluded. The introduction of thermally reversible interactions at the chain ends of star-shaped polymers is only one of the interesting families to which chain end functionalized polymers serve as a precursor. Organic functional groups, such as hydroxyl and amino serve as stepping stones to diverse and rich functionalization strategies.

2.5. Click Chemistry

Click chemistry is a concept introduced by K. Barry Sharpless in 2001 and describes chemistry tailored to generate substances quickly and reliably by joining small units together as nature does.

Following nature's lead, the purpose is to generate substances by joining small units together with heteroatom links (C–X–C). The term "click chemistry", the foundation of this approach, is defined a set of stringent criteria that a process must meet to be useful in this context.

A chemical transformation that is part of click chemistry obeys the following criteria:

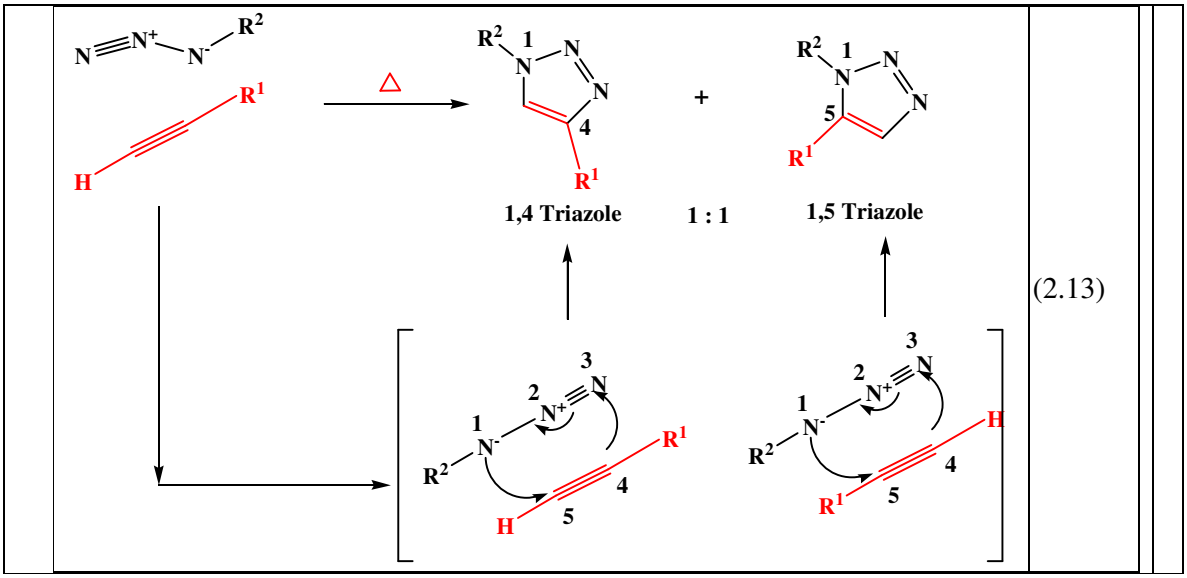
- application modular and wide in scope
- obtains high chemical yield
- generates inoffensive byproducts
- is stereospecific
- simple reaction conditions
- has readily available starting materials and reagents
- no solvent involved or a benign solvent (preferably water)
- easy product isolation by crystallisation or distillation but not preparative chromatography
- physiologically stable
- large thermodynamic driving force > 84 kJ/mol for a fast reaction with a single reaction product. A distinct exothermic reaction makes a reactant "spring loaded".
- high atom economy

Chemical reactions that fit the bill are:

- cycloaddition reactions, particularly the Huisgen 1,3-dipolar cycloaddition (and the Cu(I) catalyzed azide-alkyne cycloaddition) as well as Diels-Alder reactions
- nucleophilic substitution especially to small strained rings like epoxy and aziridine compounds (ring opening reactions)
- carbonyl-chemistry-like formation of ureas and amides but reactions of the non-aldol type due to low thermodynamic driving force.
- addition reactions to carbon - carbon double bonds like epoxidation and dihydroxylation [51].

Huisgen 1,3-dipolar cycloadditions are exergonic fusion processes that unite two unsaturated reactants and provide fast access to an enormous variety of five-membered hetero-cycles. The cycloaddition of azides and alkynes to give triazoles is arguably the most useful member of this family [52,53]. Because of its quantitative yields, mild reaction condition, and tolerance of a wide range of functional groups, it is very suitable for the synthesis of polymers with various topologies and for polymer modification [54]. The copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction has emerged as the best example of "click chemistry," characterized by extraordinary reliability and functional group tolerance [55]. In macromolecular science Cu(I) catalysed method is reported to have high yields and practically no side reactions. The formed triazole ring has a strong dipolar moment and can form H-bonds giving some hydrophilicity while being stable under biological conditions [56]. An acceleration of the reaction rate of approximately seven orders of magnitude has been observed using Cu(I) [57]. Such reactions were proven to be very practical, because they can be performed in high yield, in multiple solvents (including water), and in the presence of numerous other functional groups. Moreover, the formed 1,2,3-triazole is chemically very stable [58]**.** Because azides and alkynes are essentially inert to most biological and organic conditions, including highly functionalized biological molecules, molecular oxygen, water, and the majority of common reaction conditions in organic synthesis [59]**.** Azides usually make fleeting appearances in organic synthesis: they serve as one of the most reliable means to introduce a nitrogen substituent through the reaction $-R-X \rightarrow [R-N_3] \rightarrow R-NH_2$. The azide intermediate is shown in brackets because it is generally reduced straightaway

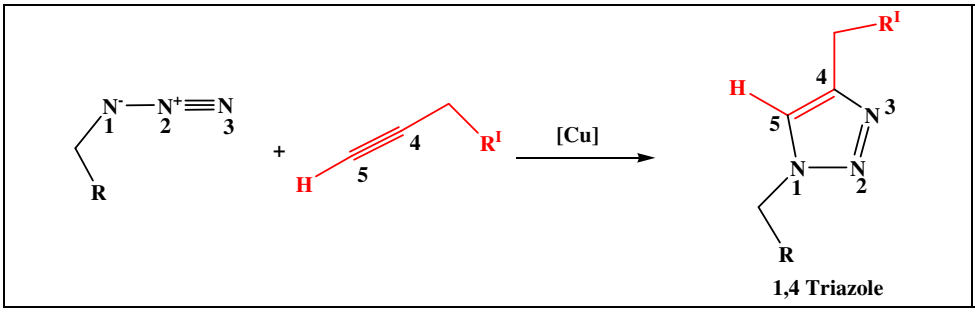
to the amine. Despite this azidophobia, this have been learned to work safely with azides because they are the most crucial functional group for click chemistry endeavors. Ironically, what makes azides unique for click chemistry purposes is their extraordinary stability toward H_2O, O_2 , and the majority of organic synthesis conditions. The spring-loaded nature of the azide group remains invisible unless a good dipolarophile is favorably presented. However, even then the desired triazole forming cycloaddition may require elevated temperatures and, usually results in a mixture of the 1,4 and 1,5 regioisomers (Fig. 2.13) [60].



(2.13)

Figure 2.13 Huisgen's [1,3] dipolar cycloaddition between azides and acetylenes to form triazoles

Copper(I)-catalyzed reaction sequence which regiospecifically unites azides and terminal acetylenes to give only 1,4-disubstituted 1,2,3 triazoles. (Fig. 2.14).



(2.14)

Figure 2.14 Regioselectivity of click chemistry with addition of Cu(I) catalyst

The discovery of Cu(I) catalysis of this process has opened a myriad of applications in bioconjugation, organic synthesis, materials and surface science, and combinatorial chemistry [61]. Since the initial discovery of Cu(I)-catalyzed alkyne–

azide coupling, numerous successful examples have been recorded in the literature, but as of yet, no systematic study of optimal conditions has been reported. Further, conditions have varied widely, particularly with respect to generation of the active Cu(I) species. Sources of Cu(I) include Cu(I) salts, most commonly copper iodide, in-situ reduction of Cu(II) salts, particularly Cu(II) sulfate, and comproportionation of Cu0 and Cu(II) . Recent reports suggest that nitrogen-based ligands can stabilize the Cu(I) oxidation state under aerobic, aqueous conditions and promote the desired transformation. Steric factors and electronic effects may also play a role in the success of this click chemistry [59]. The copper-catalyzed reaction is thought to proceed in a stepwise manner starting with the generation of Cu(I) acetylide (Fig. 2.15).

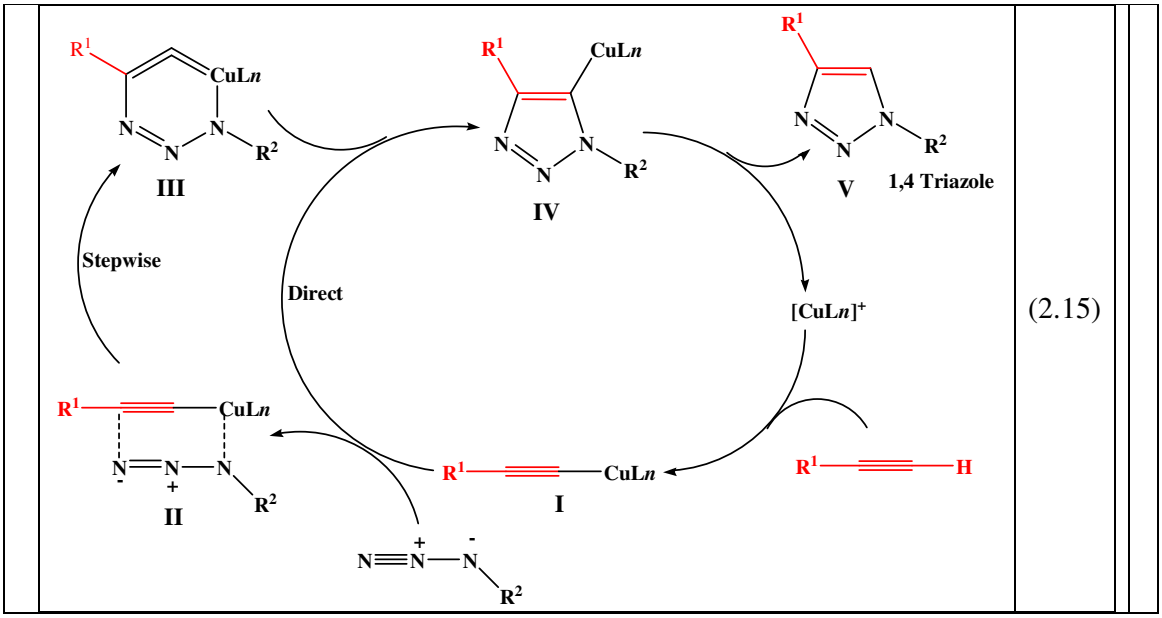
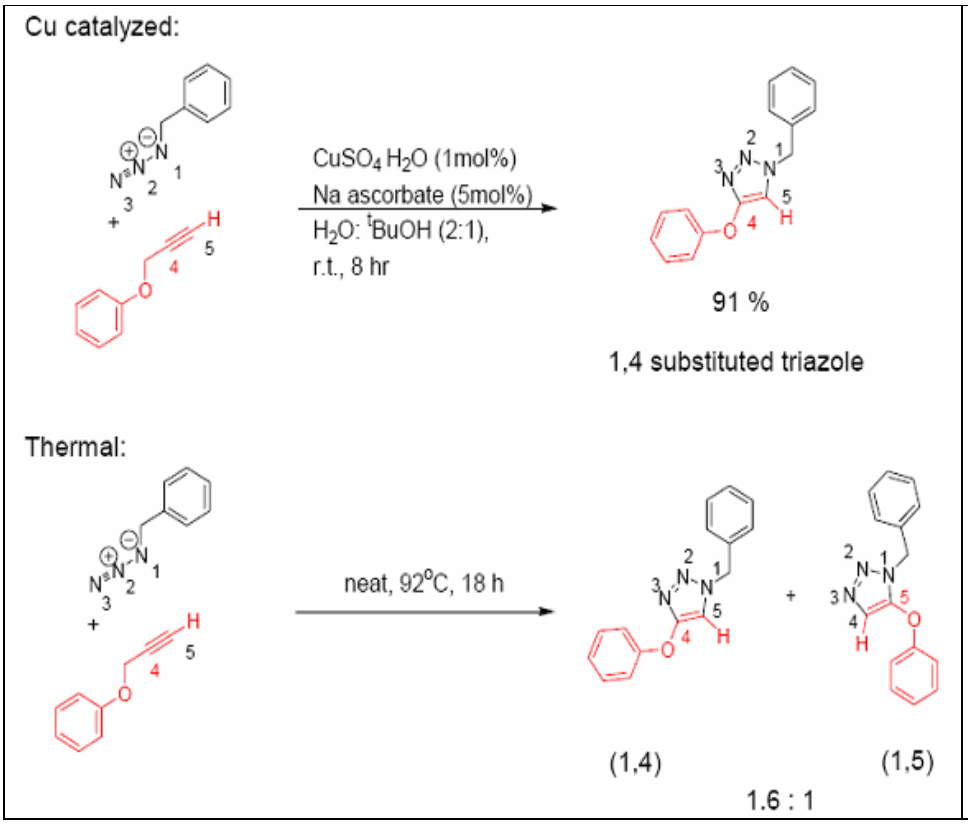


Figure 2.15 Proposed catalytic cycle for Cu(I)-catalyzed ligation

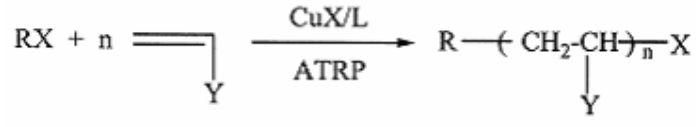
Comparison of the thermal reaction between benzyl azide and phenyl propargyl ether with the copper-catalyzed reaction of the same substrates demonstrates the importance of copper catalysis (Fig. 2.16). The thermal reaction leads to the formation of two disubstituted triazole isomers while the Cu(I)-catalyzed reaction selectively produces the 1,4-isomer in 91% yield after 8 hours [60-61-62].



(2.16)

Figure 2.16 Regioselectivity using Cu(I)

The development of the Cu(I)-catalyzed cycloaddition reaction between azides and terminal alkynes has led to many interesting applications of click reactions including the synthesis of natural product derivatives. Although azides and alkynes display high mutual reactivity, individually these functional groups are two of the least reactive in organic synthesis. They have been termed bioorthogonal because of their stability and inertness towards the functional groups typically found in biological molecules. This bioorthogonality has allowed the use of the azide-alkyne [3 + 2] cycloaddition in various biological applications including target guided synthesis and activity-based protein profiling [63-64]. Moreover, ATRP shares a number of important features with click chemistry including robustness, versatility and excellent tolerance towards many functional-groups, including water [57]. Polymers synthesized by ATRP have well-defined chlorine or bromine end groups (Fig. 2.17).



(2.17)

Figure 2.17 ATRP polymers with halogen end group

The halogen end group can be converted to other functional groups using standard organic procedures. However, the transformation is preferably carried out under mild conditions, as the substitution must be as free of side reactions as possible and the yield of the transformation reaction must be quantitative. According to the model reactions of these compounds with sodium azide, the displacement of the halogen end group by azide in dimethylformamide is a very efficient method to obtain azide end functionalized polymers. The reaction proceeds fast, especially when the leaving group is bromine and the selectivity of the reaction approaches 100%. Bromine end functionalized polystyrene as well as polyacrylate were efficiently converted to azide end functionalized polymer. Bromine terminated pMMA reacted slower under the same reaction conditions. However, with a 10-fold excess of sodium azide, complete conversion was obtained within 12 hours at room temperature The functionalized polymers can find many applications, for example as macromonomers, telechelics or other specialty polymers. Azides are interesting end functional groups because they can be converted to amino end groups [65]. Another benefit of conducting Cu(I) catalyzed click reactions with polymers prepared by ATRP is that the predetermined molecular weight and narrow molecular weight distribution facilitate analysis of the reaction products. Although methods such as gas chromatography and NMR are frequently employed to characterize the products of Cu(I)-catalyzed click reactions of low-molecular-weight compounds, these techniques are generally incompatible with polymer coupling reactions due to high molecular weight of starting materials and products. However, polymer click coupling reactions can be easily monitored by size exclusion chromatography (SEC) and quantitatively analyzed by Gaussian multipeak fitting of the resulting chromatogram (Fig. 2.18). Therefore, polymer click coupling reactions are an attractive way to investigate the optimal conditions under which these reactions should be performed, particularly for polymer and materials chemistry applications [66].

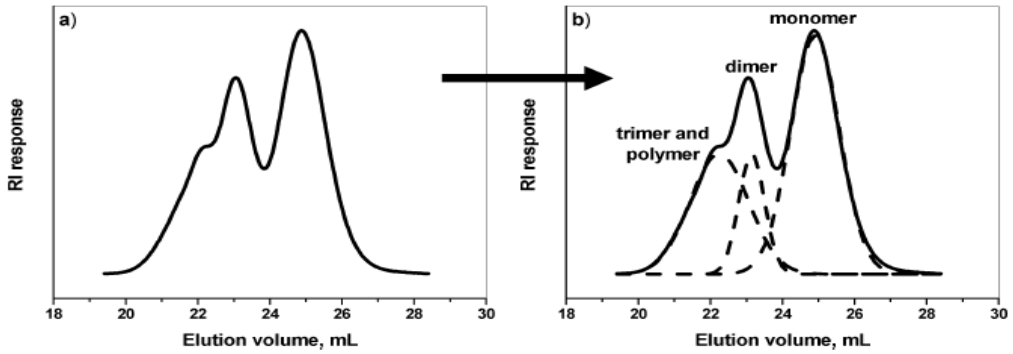


Figure 2.18. SEC trace for click coupling reaction of diazidopolystyrene (0.1 M -N_3) with propargyl ether (0.1 M -C–CH) using CuBr (0.05 M) as catalyst and TPMA (0.05 M) as ligand after 3 h, showing (a) original chromatogram and (b) chromatogram after Gaussian multipeak fitting.

Some click reactions have already been successfully used in polymer and materials chemistry. The efficient preparation of well-defined polymeric tetrazoles, or dendrimers, amphiphilic block copolymers, cross-linked block copolymer vesicles, and adhesives with triazole units has been reported. Click reactions were also used in the synthesis of functionalized poly(oxynorbornenes) and block copolymers and are a convenient alternative to other coupling reactions applied to polymers prepared by ATRP (such as atom transfer radical coupling or reversible thiol oxidative coupling) for the preparation of high molecular weight polymeric materials [67].

In summary, click chemistry has proven to be a powerful tool in biomedical research, ranging from combinatorial chemistry and target-templated *in situ* chemistry for lead discovery, to bioconjugation strategies for proteomics and DNA research. Azides and acetylenes are stable across a broad range of organic reaction conditions and in biological environments, yet they are highly energetic functional groups. Their irreversible combination to triazoles is highly exothermic, albeit slow. The full potential of this ligation reaction was unleashed with the discovery of Cu(I) catalysis. Benefiting from more than a million-fold rate acceleration, this process proceeds in near-quantitative yields in water, and because no protecting groups are used, the products are screened directly from the reaction mixture. This triazole-forming process, and click chemistry in general, promise to accelerate both lead finding and lead optimization, due, above all, to its great scope, modular design, and reliance on extremely short sequences
of near-perfect reactions [63].

3. EXPERIMENTAL WORK

3.1. Materials

St (99%, Merck), *t*BA (99%, Aldrich), *tert*-butylacrylate (*t*BA, 99%, Aldrich) were passed through a basic alumina column to remove the inhibitor and then distilled over CaH_2 *in vacuo* before use. *N,N,N',N'',N''*-Pentamethyldiethylenetriamine (PMDETA, Aldrich) was distilled over NaOH before use. Poly(ethylene glycol) (PEG) (M_n = 2000, Acros) with monohydroxy end group was dried over anhydrous toluene by azeotropic distillation. Tetrahydrofuran (THF, 99.8%, J.T. Baker) was dried and distilled over $LiAlH_4$. Other solvents were purified by conventional procedures. All other reagents were purchased from Aldrich and used as received.

3.2. Instrumentation

^1H NMR spectra was recorded on a Bruker NMR Spectrometer (250 MHz) in $CDCl_3$. Gel permeation chromatography measurements were obtained from an Agilent instrument (Model 1100) consisting of a pump, a refractive index (RI) detector, and four Waters Styragel columns (HR 5E, HR 4E, HR 3, and HR 2). THF was used as eluent at a flow rate of 0.3 mL/min at 30 ^oC. Toluene was as an internal standard. Data analyses were performed with PL Caliber Software. The molecular weight of the polymers was calculated on the basis of linear polystyrene standards (Polymer Laboratories). Peak Fit program (version 4.12, Seasolve) was used for the deconvolution of the GPC curves. Fourier transform infrared (FTIR) analysis was carried out with a Perkin Elmer Spectrum One FTIR spectrometer.

3.3. Synthesis of 1,1,1-tris[4-(2-propynyloxy) phenyl] ethane Initiator, 1

1,1,1-tris (4-hydroxy-phenyl) ethane (0.75 g, 2.45 mmol) was dissolved in DMF (10 mL) and propargyl bromide (80% in toluene) (0.97 mL, 9 mmol) and K_2CO_3 (2.4 g, 17.5 mmol) were added to the mixture. The reaction mixture was stirred for 24 hours at 110 ^oC. After the reaction is completed, the mixture is filtered and evaporated in vacuum to remove dimethyl formamide (DMF). CH_2Cl_2 (200 mL) was added and the reaction mixture was washed three times with distilled water (100 mL x 3). The combined organic phase was dried over Na_2SO_4, filtered and evaporated. The remaining product was purified by column chromatography over silica gel eluting with ethylacetate / hexane (1:9) to obtain pure **1** yielding yellow-green colored liquid (0.684 g, 67 %). ^1H NMR ($CDCl_3$) 7.01-6.96 (m, 6H, ArH), 6.88-6.82 (m, 6H, ArH), 4.66 (d, J = 2.4 Hz, 6H, HC≡C-CH_2) 2.50 (t, J = 2.4 Hz, 3H, HC≡C-CH_2) 2.09 (s, 3H, CH_3).

3.4. Preparation of azide end-functionalized P*t*BA (P*t*BA-N_3)

P*t*BA was prepared by ATRP of *t*BA using ethyl-2-bromoisobutyrate (EiBr) as an initiator. Into a 10 mL of Schlenk tube, *t*BA (8 mL, 54.6 mmol), PMDETA (0.057 mL, 0.27 mmol), CuBr (0.04 g, 0.27 mmol), and EiBr (0.04 mL, 0.27 mmol) were added in that order. The tube was degassed by three freeze-pump-thaw cycles, left *in argon* and placed in a thermostated oil bath at 80 ^oC for 40 min. Subsequently the polymerization mixture was diluted with THF, passed through a basic alumina column to remove the catalyst, and precipitated in methanol:distilled water (1:4) mixture in cold. After the precipitation it was decanted. CH_2Cl_2 was added and the reaction mixture was washed three times with distilled water. The organic layer was dried with anhydrous Na_2SO_4 and solvent was removed in vacuum, yielding white solid. The polymer was dried for 24 h in a vacuum oven at 25 ^oC. ($M_{n,GPC}$ = 6700; M_w/M_n= 1.29; $[M]_o/[I]_o$ = 200; conv. 25 %; $M_{n,theo}$ = 6600; $M_{n,NMR}$ = 7200).

Thus obtained P*t*BA (2 g, 0.27 mmol) was dissolved in (DMF) (15 mL) and sodium azide (0.7 g, 10.8 mmol) was added. The reaction mixture was stirred for 24 hours at room temperature. It was filtered and evaporated to remove DMF. CH_2Cl_2 (100 mL) was added and the reaction mixture was washed three times with distilled water. The

organic layer was dried with anhydrous Na_2SO_4 and solvent was removed in vacuum, yielding white solid (1.9 g, 95 %).

3.5. Preparation of azide end-functionalized PS (PS-N_3)

PS was prepared by ATRP of styrene using ethyl-2-bromoisobutyrate (EiBr) as an initiator. Into a 10 mL of Schlenk tube, styrene (9.36 mL, 81.6 mmol), PMDETA (0.086 mL, 0.41 mmol), CuBr (0.058 g, 0.41 mmol), and EiBr (0.06 mL, 0.41 mmol) were added and the reaction mixture was degassed by three freeze-pump- thaw cycles and left in *vacuum*. The tube was then placed in a thermostated oil bath at 110 ^oC for 30 min. The dark-green polymerization mixture was diluted with THF, passed through a basic alumina column to remove the catalyst, and precipitated in methanol. The polymer was dried for 24 h in a *vacuum* oven at 25 ^{o} C. ($M_{n,GPC}$ = 3450; M_w/M_n= 1.10; $[M]_o/[I]_o$ = 200; conv. 15 %; $M_{n,theo}$ = 3300; $M_{n,NMR}$ = 3500)

Previously obtained PS (1,9 g, 0.54 mmol) was dissolved in DMF (15 mL) and sodium azide (1.40 g, 21.71 mmol) was added. The reaction mixture was stirred for 24 hours at room temperature. It was filtered and evaporated to remove DMF. CH_2Cl_2 (100 mL) was added and the reaction mixture was washed three times with distilled water. The organic layer was dried with anhydrous Na_2SO_4 and solvent was removed in vacuum. Polymerization mixture was diluted with THF and precipitated in methanol. The polymer was dried for 24 h in a *vacuum* oven at 25 ^{o} C, yielding white solid (1.8 g, 95%).

3.6. Preparation of azide end-fuctionalized PEG (PEG-N_3)

PEG (M_n = 2000) (2.00 g, 1 mmol) with mono hydroxyl group was dissolved in CH_2CI_2 (15 mL), triethylamine (2.78 ml, 20 mmol), 4-(dimethylamino) pyridine (DMAP) (1.22 g, 10 mmol) and toluene-4-sulfonyl chloride (tosyl chloride) (1.91 g, 10.0 mmol) were added to the solution. The reaction mixture was stirred for 24 hours at room temperature and then poured into cold 4M hydrochloric acid solution. The product was extracted with CH_2Cl_2 and solvent was removed in *vacuum.* The remaining product was purified by column chromatography over silica gel eluting first with CH_2CI_2 / ethylacetate (1:1) to remove unreacted DMAP and tosyl chloride,

and then with methanol / CH_2CI_2 (1:10) to obtain pure polymer. The polymer is dissolved in THF, precipitated in cold diethyl ether and dried for 24 h in a vacuum oven at 25 ^oC (1.84, 92 %).

Thus obtained mono tosylated PEG (1.84 g, 0.84 mmol) was dissolved in DMF (15 mL) and sodium azide (2.18 g, 0.033 mmol) was added to the solution. The reaction mixture was stirred for 24 hours at room temperature. CH_2Cl_2 (100 mL) was added and the reaction mixture was washed three times with distilled water. Solvent was removed in vacuum and precipitated in cold diethyl ether. The polymer was dried in a vacuum oven for 24 h at 25 ^oC (1.75 g, 95%).

3.7. Preparation of P*t*BA$_3$ star via click reaction between 1 and P*t*BA-N$_3$ (1 : 3)

1 (0.007 g, 0.0162 mmol) and P*t*BA-N_3 (0.35 g, 0.048 mmol) were dissolved in nitrogen-purged DMF (5 mL) in a Schlenk tube. CuBr (3.58 x 10^{-3} g, 0.025 mmol) and PMDETA (5.2 µL, 0.025 mmol) were added in order and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in *argon* and stirred at room temperature for 24 h. Solution was passed through alumina column to remove copper salt, precipitated in cold methanol: water (4:1) mixture. After the precipitation it was decanted and extracted with CH_2Cl_2. The organic layer was dried with anhydrous Na_2SO_4, filtered and solvent was removed in vacuum. At last, it was dried in vacuum oven at 25 ^oC.

3.8. Preparation of PS$_3$ star via click reaction between 1 and PS-N$_3$ (1 : 3)

1 (0.008 g, 0.0189 mmol) and azide end- functionalized PS (0.198 g, 0.056 mmol) were dissolved in 5 mL of nitrogen-purged DMF in a Schlenk tube. CuBr (4.0 x 10^{-3} g, 0.028 mmol) and PMDETA (6 µL, 0.028 mmol) were added and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in *argon* and stirred at room temperature for 24 h. Polymer solution was passed through alumina column to remove copper salt, precipitated in methanol and dried in vacuum oven at 25 ^oC.

3.9. Preparation of PEG_3 star via click reaction between 1 and PEG-N_3 (1 : 3)

1 (0.014 g, 0.033 mmol) and azide end- functionalized PEG (0.198 g, 0.99 mmol) were dissolved in 5 mL of nitrogen-purged DMF in a Schlenk tube. CuBr (7.2×10^{-3} g, 0.05 mmol) and PMDETA (12 µL, 0.05 mmol) were added and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in argon and stirred at room temperature for 24 h. Polymer solution was passed through alumina column to remove copper salt, precipitated in cold diethyl ether and dried in vacuum oven at 25 ^{o}C.

3.10. Preparation of P*t*BA_3 star via click reaction between 1 and P*t*BA-N_3 (1 : 3,6)

Azide end-funtionalized P*t*BA (0.35 g, 0.0486 mmol) and **1** (0.0056 g, 0.0135 mmol) were dissolved in nitrogen-purged DMF (5 mL) in a Schlenk tube. CuBr (2.32×10^{-3} g, 0.016 mmol) and PMDETA (3.4 µL, 0.016 mmol) were added in order and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in *argon* and stirred at room temperature for 24 h. Solution was passed through alumina column to remove copper salt, precipitated in cold methanol : water (4:1) mixture. After the precipitation it was decanted and extracted with CH_2Cl_2. The organic layer was dried with anhydrous Na_2SO_4, filtered and solvent was removed in vacuum. At last, it was dried in vacuum oven at 25 ^{o}C.

3.11. Preparation of PS_3 star via click reaction between 1 and PS-N_3 (1 : 3,6)

1 (0.0066 g, 0.0159 mmol) and azide end- functionalized PS (0.2 g, 0.057 mmol) were dissolved in 5 mL of nitrogen-purged DMF in a Schlenk tube. CuBr (2.73×10^{-3} g, 0.019 mmol) and PMDETA (3.97 µL, 0.019 mmol) were added and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in *argon* and stirred at room temperature for 24 h. Polymer solution was passed through alumina column to remove copper salt, precipitated in methanol and dried in vacuum oven at 25 ^{o}C.

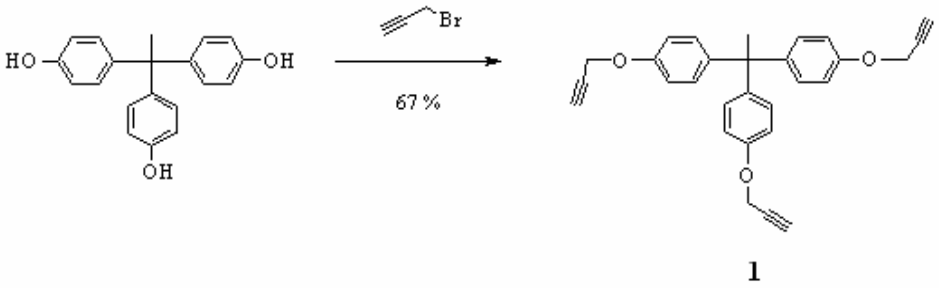
3.12. Preparation of PEG_3 star via click reaction between 1 and PEG-N_3 (1 : 3,6)

1 (0.012 g, 0.028 mmol) and azide end- functionalized PEG (0.2 g, 0.1 mmol) were dissolved in 5 mL of nitrogen-purged DMF in a Schlenk tube. CuBr (4.78×10^{-3} g, 0.033 mmol) and PMDETA (6.95 µL, 0.033 mmol) were added and the reaction mixture was degassed by three freeze-pump-thaw cycles and left in argon and stirred at room temperature for 24 h. Polymer solution was passed through alumina column to remove copper salt, precipitated in cold diethyl ether and dried in vacuum oven at 25 ^{o}C.

4. RESULTS and DISCUSSION

4.1. Synthesis of Initiator

First of all, trisalkynyl-functional compound **1** was prepared in a 67% yield via an etherification reaction between 1,1,1-tris(4-hydroxyphenyl)ethane and propargyl bromide. The structure of **1** was confirmed by ^{1}H NMR and elemental analysis. In the ^{1}H NMR spectrum of **1**, it was evident that C*H*$_2$ protons of propargyl bromide at 3.86 were shifted to 4.66 ppm as a doublet signal of C*H*$_2$O indicating an etherification reaction (Fig. 4.2).



1 (4.1)

Figure 4.1 Etherification reaction between 1,1,1-tris(4-hydroxyphenyl)ethane and propargyl bromide

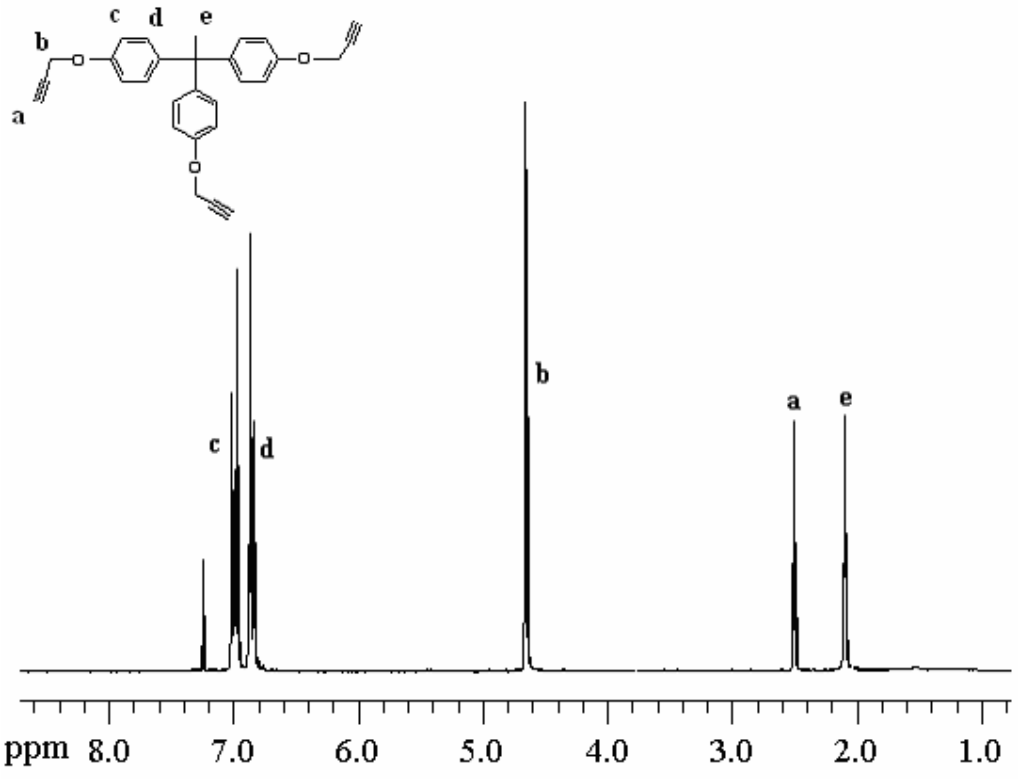
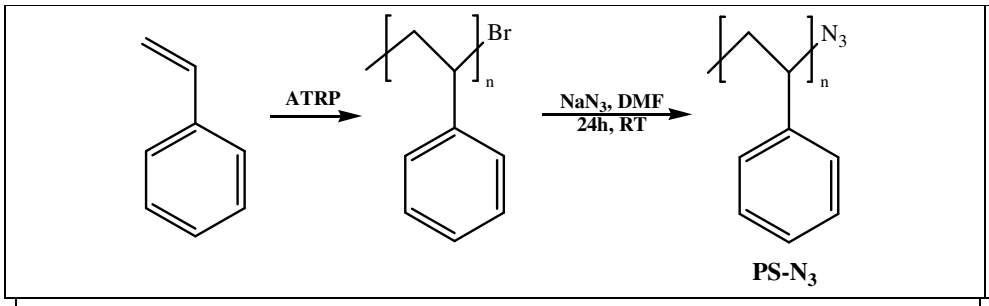


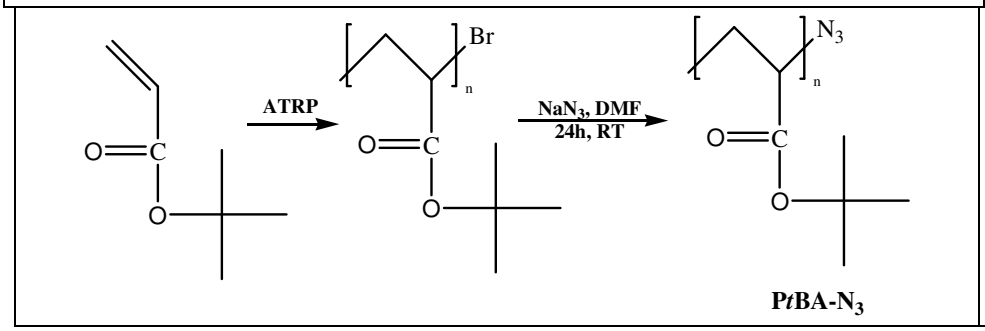
Figure 4.2. ^{1}H NMR spectrum of **1** in $CDCl_3$.

4.2. Synthesis of azide end-functionalized PS, P*t*BA and PEG

Well-defined PS and P*t*BA were obtained from the ATRP of the related monomers. Their bromide end groups were quantitatively converted to the azide form with a wellknown procedure. The ω-azide end functionality of both PS and P*t*BA was confirmed with ^{1}H NMR. For PS–N_3, a signal at 4.5 ppm, assigned to C*H*–Br, disappeared, and a new peak appeared at 3.9 ppm, indicating C*H* linked to the azide end group. For P*t*BA–N_3, the C*H*–N_3 end-functional group was detected at 3.6–3.8 ppm, whereas C*H*–Br was detected at 4.1 ppm.



(4.3)

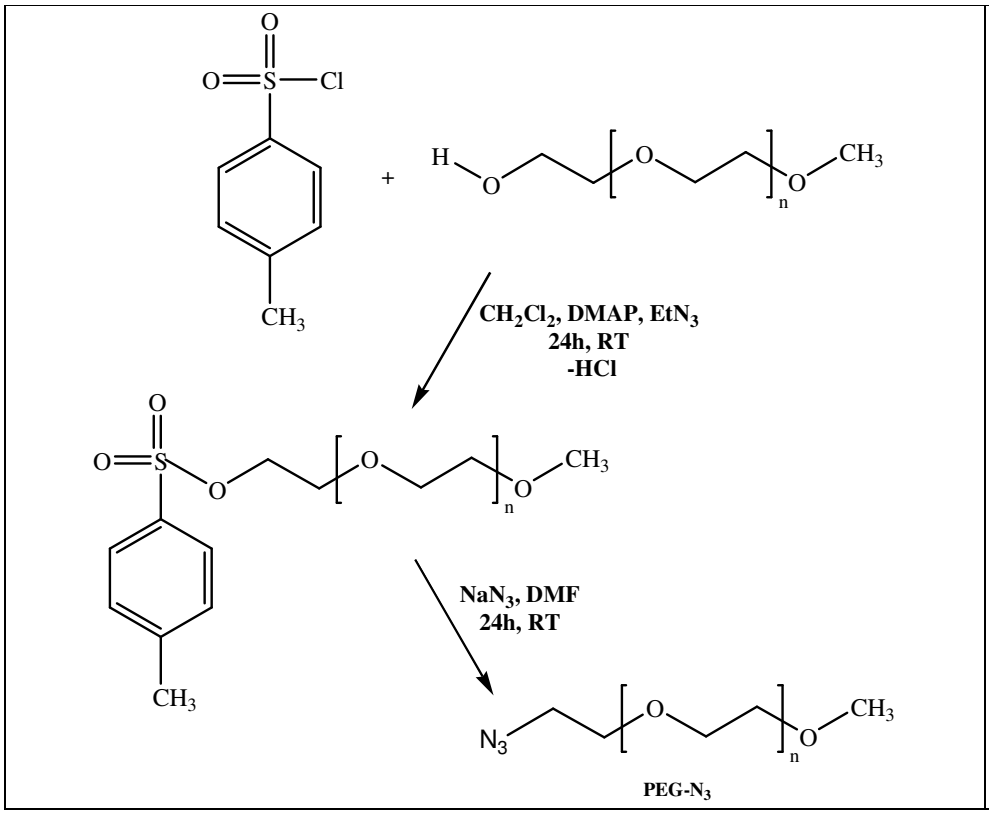


(4.4)

Figure 4.3 Synthesis of azide end funtionalized polystyrene

Figure 4.4 Synthesis of azide end funtionalized poly(tert-butyl acrylate)

Commercially available PEG with a monohydroxyl end group was first tosylated and then converted to azide. The C*H*–N_3 end group of PEG was observed at 3.9 ppm from the ^{1}H NMR spectrum.

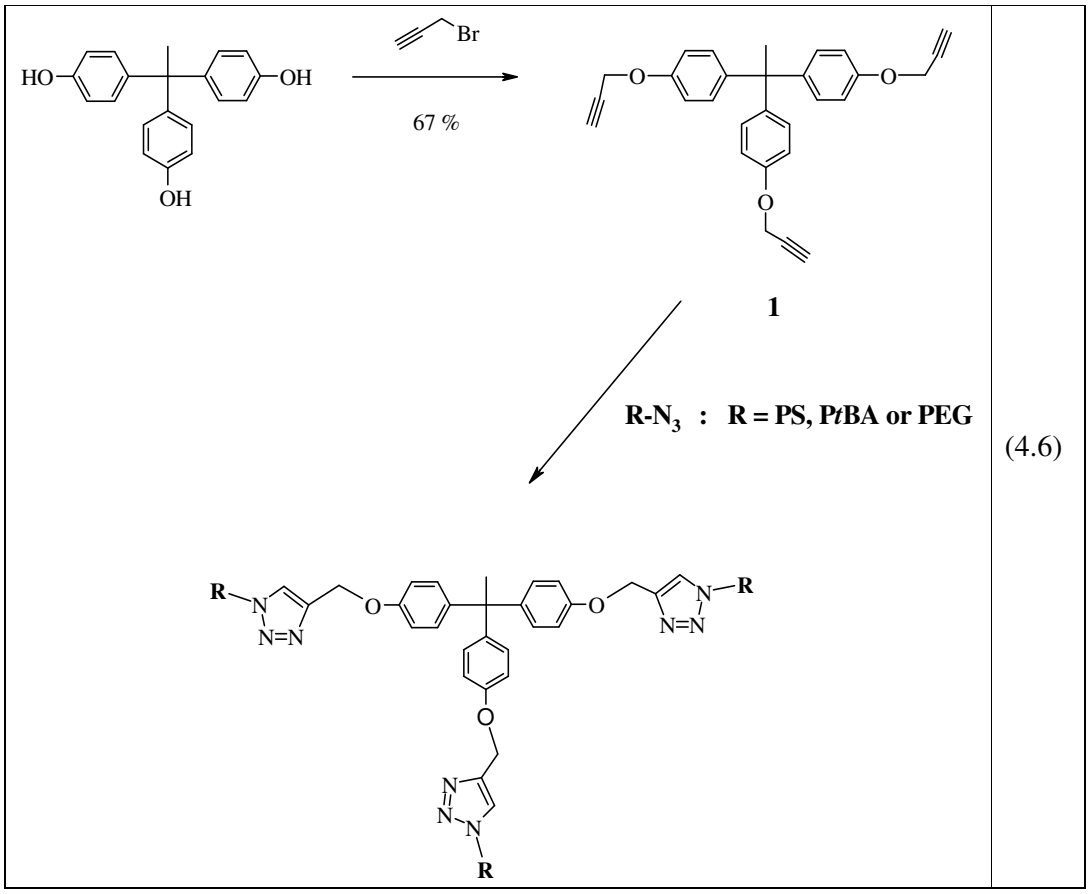


(4.5)

Figure 4.5. Synthesis of azide end funtionalized poly(ethyleneglycol)

4.3. Synthesis of A_3-type star polymers through click reactions

Well-defined PS, P*t*BA, or PEG with azide-end-functional groups was reacted with **1** to give the corresponding star polymers. Click reactions were carried out with equimolar amounts of the reactants ([azide]/[trisalkyne] = 3/1) and nonequimolar amounts of the reactants ([azide]/[trisalkyne] = 3,6/1) in DMF with CuBr/PMDETA for 24 h at room temperature.



(4.6)

Figure 4.6 Synthesis of A_3-type star polymers through click reactions

Star formation in all cases was monitored with GPC measurements. From GPC traces, it was clearly observed that the reaction mixture contained mainly A_3 star polymer and less A_2 block copolymer and A_1 homopolymer (Figs. 4.7–4.12). The molar percentages of A_3, A_2, and A_1 were calculated from the GPC traces with the deconvolution method (Gaussian area) via the Peak Fit program.

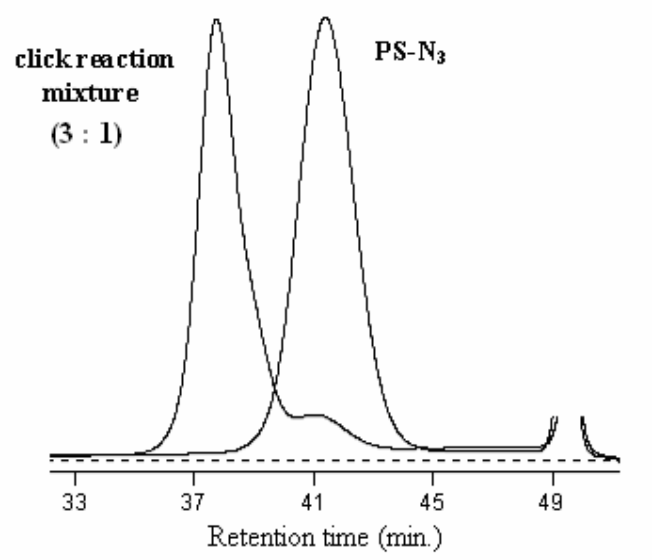


Figure 4.7. GPC curves of PS–N_3 and click reaction mixture of PS–N_3 and **1** (RI detector)

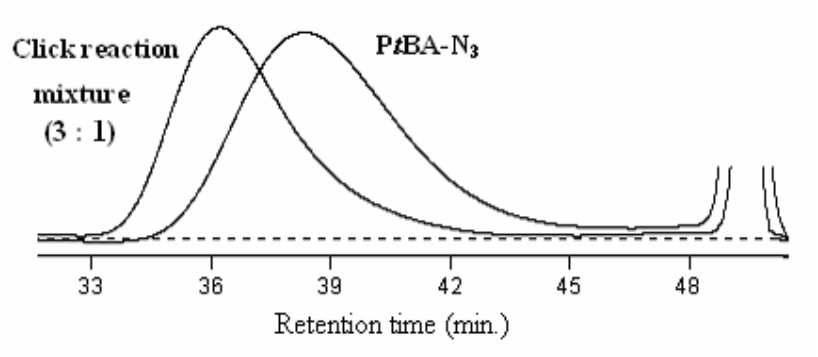


Figure 4.8. GPC curves of P*t*BA–N_3 and click reaction mixture of P*t*BA–N_3 and **1** (RI detector).

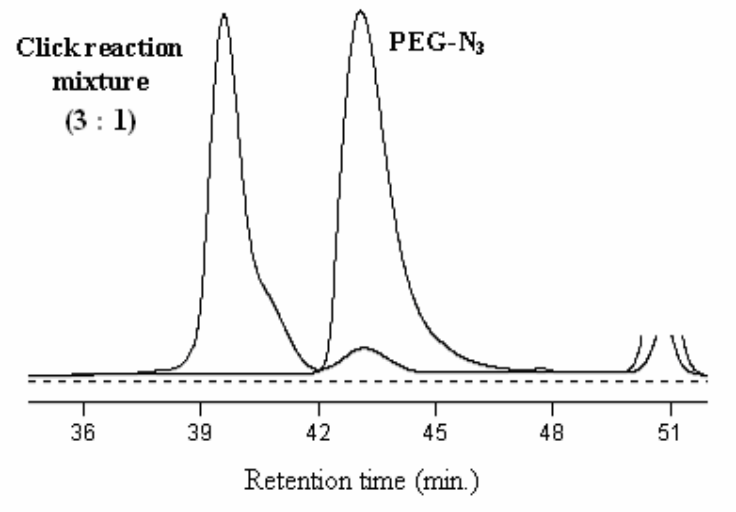


Figure 4.9. GPC curves of PEG–N_3 and click reaction mixture of PEG–N_3 and **1** (RI detector).

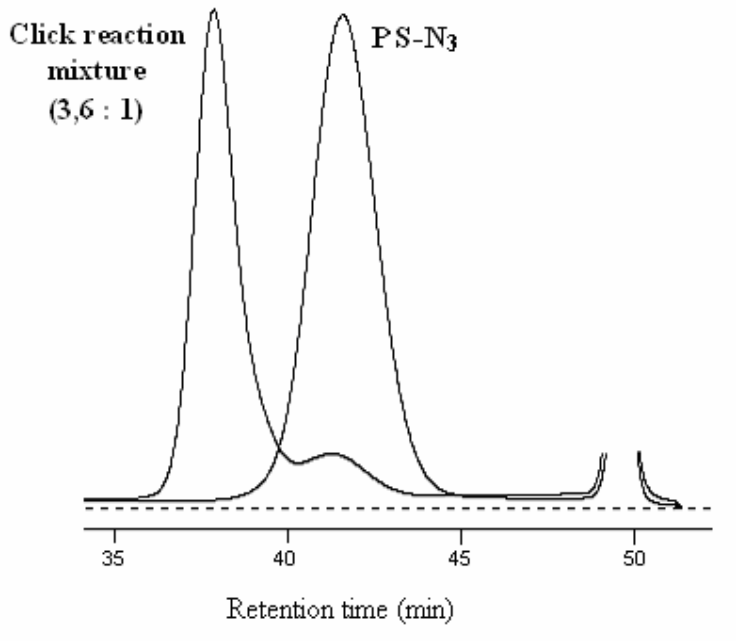


Figure 4.10. GPC curves of PS–N_3 and click reaction mixture of PS–N_3 and **1** (RI detector)

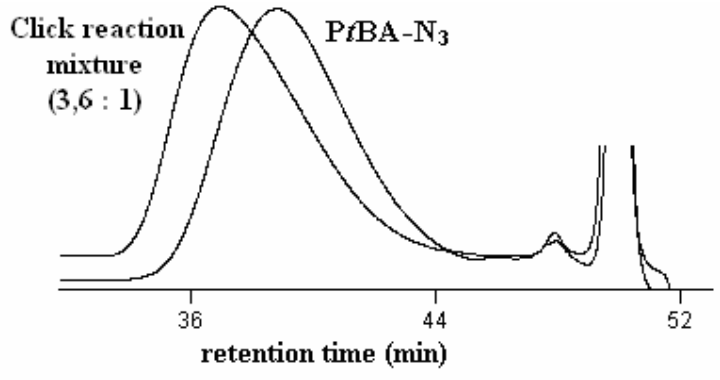


Figure 4.11. GPC curves of P*t*BA–N_3 and click reaction mixture of P*t*BA–N_3 and **1** (RI detector)

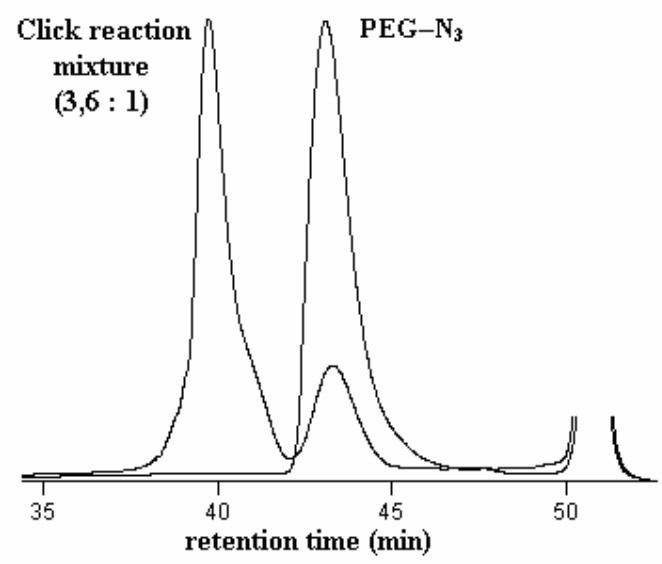


Figure 4.12. GPC curves of PEG–N_3 and click reaction mixture of PEG–N_3 and **1** (RI detector)

Moreover, the splitting of GPC traces with the deconvolution method (Gaussian area) is displayed in Figures 4.13–4.18.

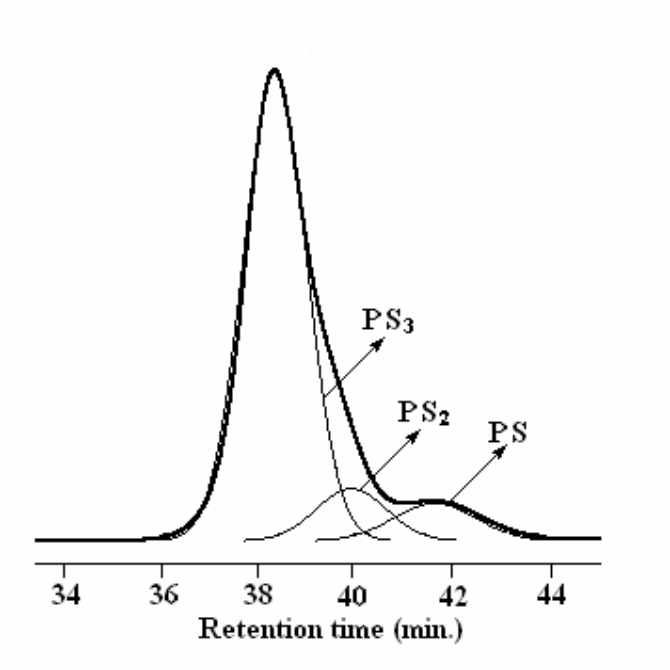


Figure 4.13. Splitting of GPC curves (click reaction mixture of PS–N_3 and **1** (3 : 1)) using deconvolution method (Gaussian area).

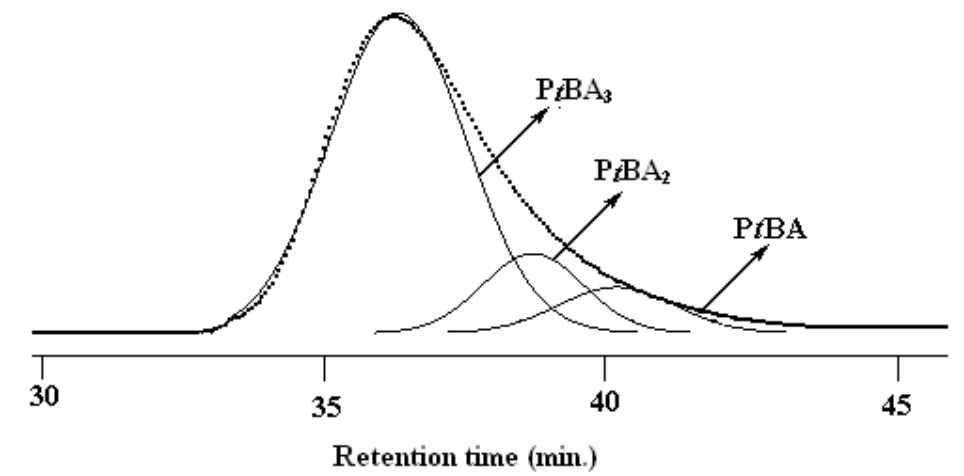


Figure 4.14. Splitting of GPC curves (click reaction mixture of P*t*BA–N_3 and **1** (3 : 1)) using deconvolution method (Gaussian area).

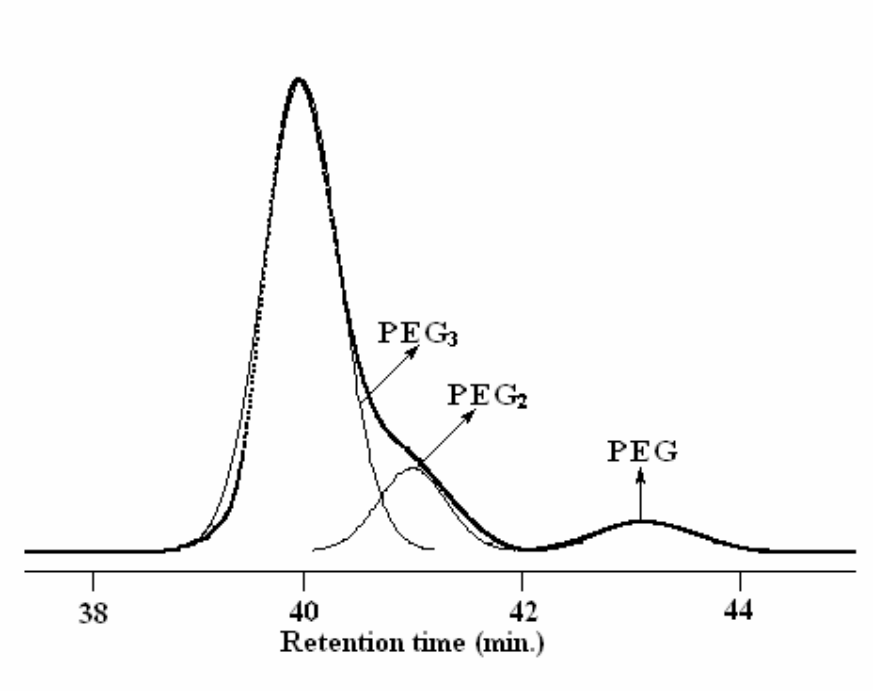


Figure 4.15. Splitting of GPC curves (click reaction mixture of PEG–N_3 and **1** (3 :1)) using deconvolution method (Gaussian area).

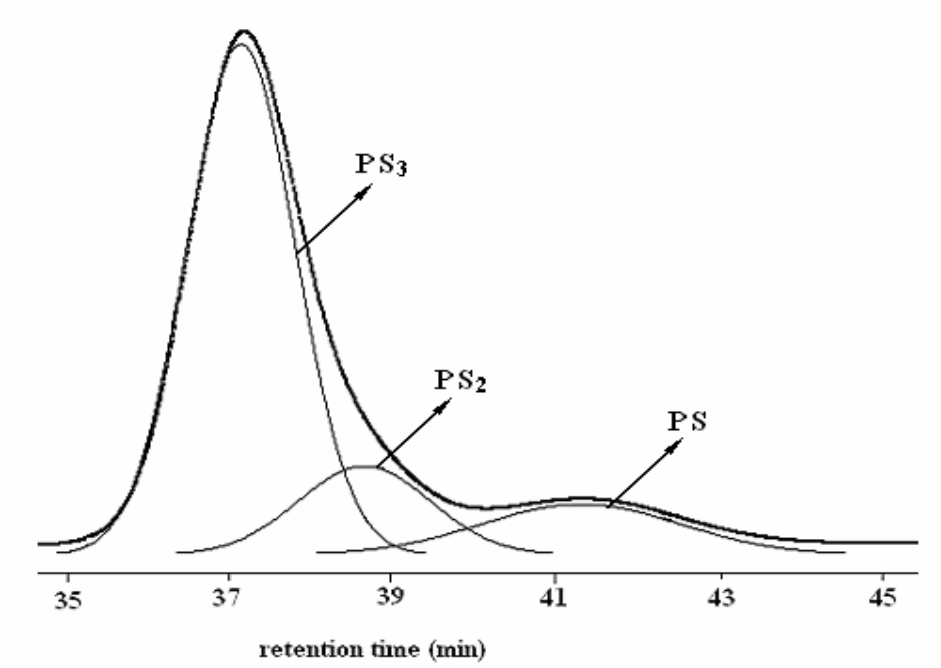


Figure 4.16. Splitting of GPC curves (click reaction mixture of PS–N_3 and **1** (3,6 : 1)) using deconvolution method (Gaussian area).

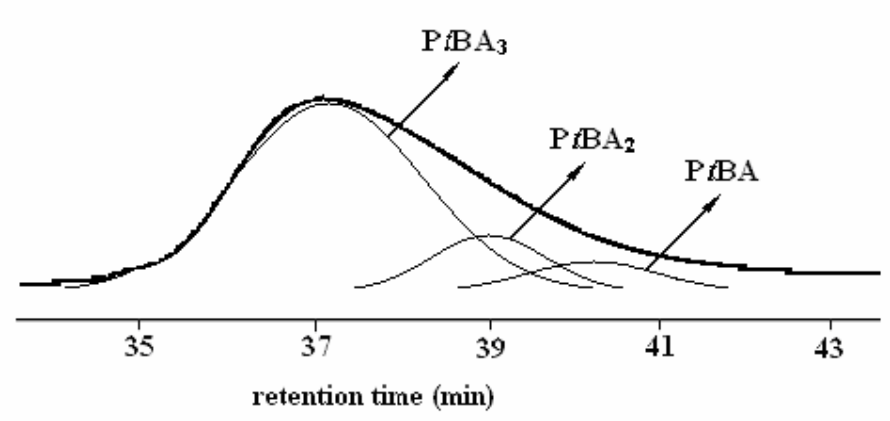


Figure 4.17. Splitting of GPC curves (click reaction mixture of P*t*BA–N_3 and **1** (3,6 : 1)) using deconvolution method (Gaussian area).

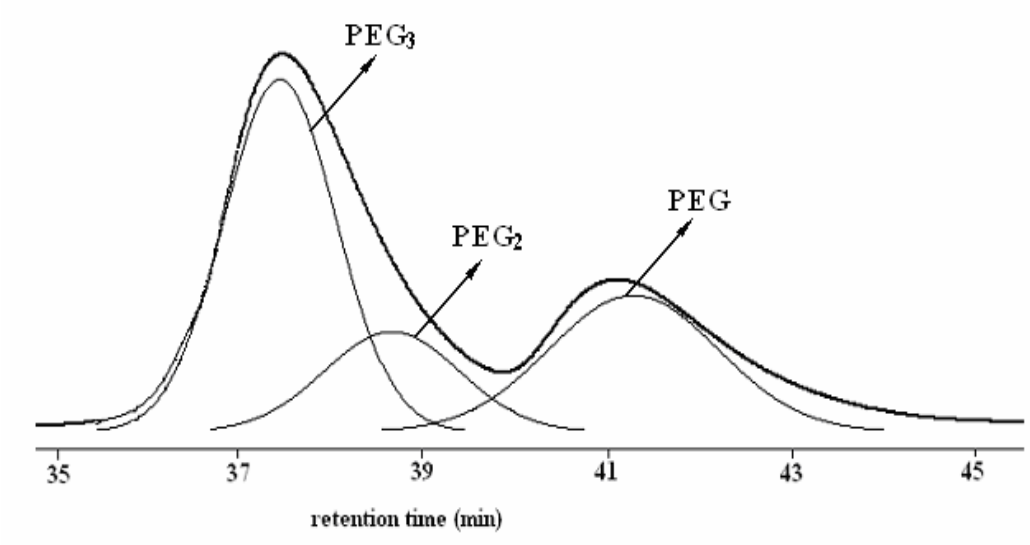


Figure 4.18. Splitting of GPC curves (click reaction mixture of PEG–N_3 and **1** (3,6 :1)) using deconvolution method (Gaussian area).

All data for star formation via click cycloaddition reactions are collected in Table 4.1.

Table 4.1. A_3 star polymers via click reaction between azide end-functionalized polymers and **1.**

Polymer type	P-N_3 : trialkine	Azide end-functionalized polymer precursors		Area % in GPC traces from click reaction		
		M_n	M_w/M_n	A_3 (star polymer)	A_2 (block copolymer)	A (unreacted homopolymer)
PS	3 : 1	3450	1.10	87	8	5
P*t*BA	3 : 1	6700	1.29	85	10	5
PEG	3 : 1	2650	1.07	82	12	6
PS	3,6 : 1	3450	1.10	85	10	5
P*t*BA	3,6 : 1	6700	1.29	80	15	5
PEG	3,6 : 1	2650	1.07	75	10	15

Eighty seven percent of the PS–N_3 chains were reacted with **1** (3 : 1) to give the PS_3 star, and the remaining 8 and 5% represented the PS_2 block copolymer and PS homopolymer, respectively.

Highly efficient click reactions were also observed for P*t*BA_3 and PEG_3 star formation. The A_3-type star formation efficiency was found to be 85 and 82% for P*t*BA and PEG, respectively. The efficiency of click reactions between azide end-funtionalized polymers and **1** with 3,6 : 1 ratio were also studied. As a result, 85% of click reaction mixture was the PS_3 star polymer for PS, 80 and 75% was the P*t*BA_3 and the PEG_3 star polymers respectively.

Star formation through the coupling of azide and alkyne groups was also confirmed by ^{1}H NMR measurements. From the spectrum of the PS_3 star, C*H* linked to the azide end group of PS at 3.9 ppm was removed, and a new broad signal assigned to C*H*– of PS and OCH_2– of the core, both linked to the triazole ring, was detected at 5.0 ppm.

Moreover, the –OCH_2CCH group was noted at 4.6 ppm, due to the remaining unreacted alkyne group of the core. For the P*t*BA_3 star, a new peak was assigned to C*H* of the triazole ring (δ = 7.7 ppm), along with the appearance of the C*H* signal as an end group of P*t*BA and the OCH_2– signal of the core at 5.1 ppm, both linked to the triazole ring. The ^{1}H NMR spectrum of the PEG_3 star clearly displayed signals at 7.8, 5.1, and 4.5 ppm assignable to C*H* of the triazole ring, OCH_2– of the core, and the CH_2– end group of PEG, respectively (Fig. 4.19).

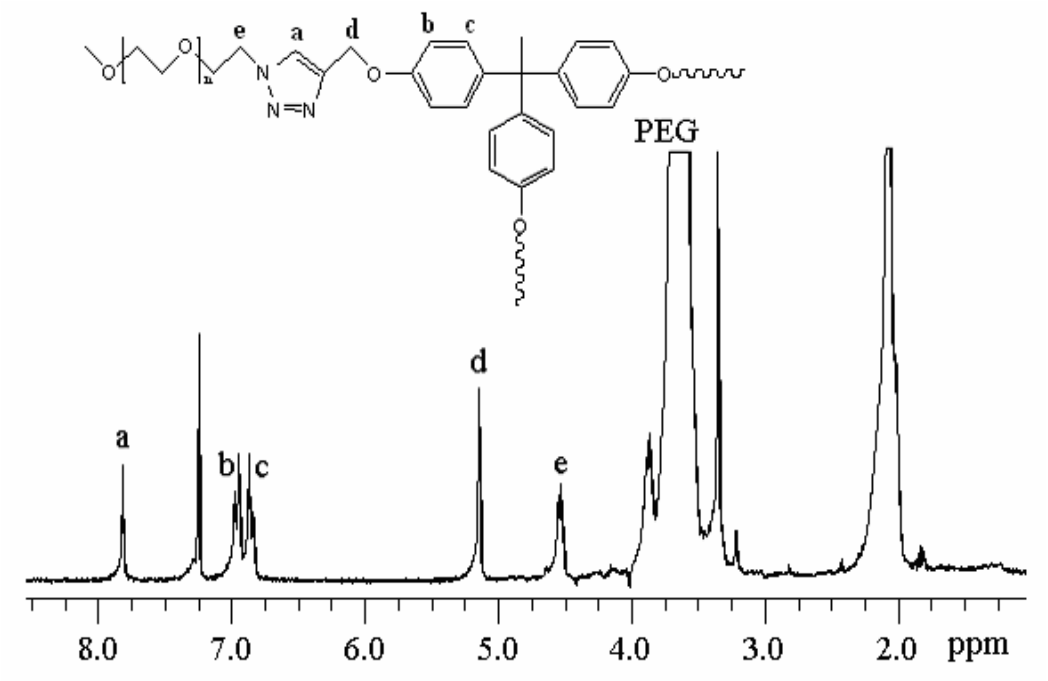


Figure 4.19. ^{1}H NMR spectrum of the PEG_3 star polymer (through a click reaction between PEG–N_3 and **1**) in $CDCl_3$.

Notably, FTIR analysis of the star polymers revealed the complete disappearance of the azide stretching frequencies ranging from 2094 to 2112 cm^{-1} (Fig. 4.20-4.22).

Although the azide functionality was seen at 2094 cm^{-1} for PS–N_3, it was disappeared in the PS_3 star polymer FTIR spectrum. Also in two spectrum we could see the aromatic C–*H* strecthing frequencies of both styrene and core agent at 2977 cm^{-1} (Fig. 4.20).

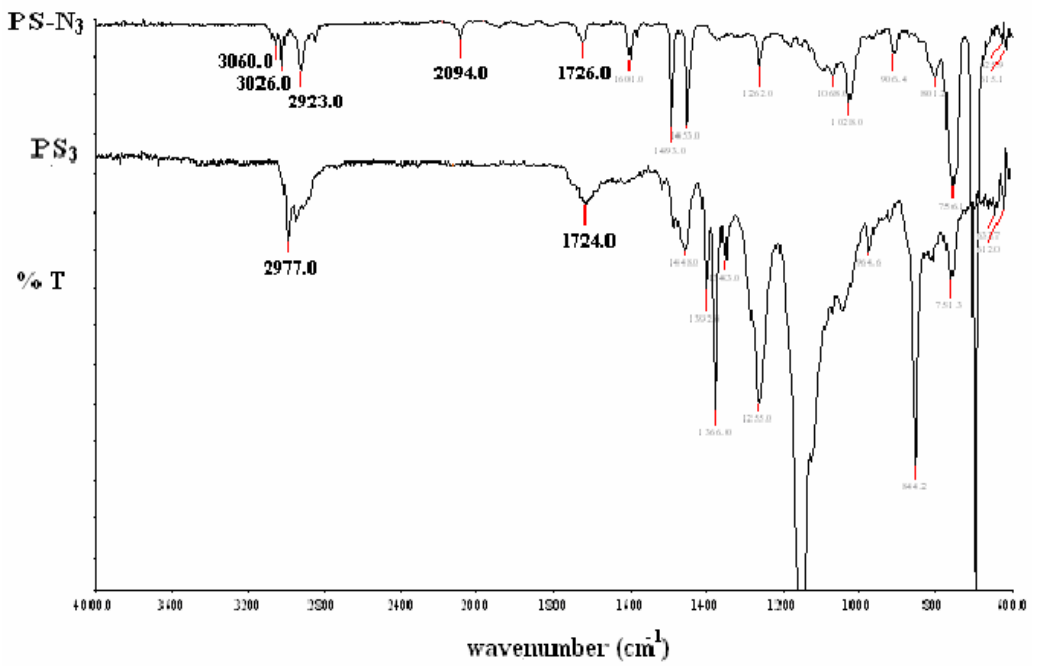


Figure 4.20. FTIR spectrum of the PS–N_3 and PS_3 star polymer (through a click reaction between PS–N_3 and **1**)

When we looked at the FTIR spectrum of both P*t*BA–N_3 and P*t*BA_3 star polymer, the azide funtionality could be seen at 2113 cm^{-1}. As the click reaction was completed this peak was absent in the P*t*BA_3 star polymer FTIR spectrum. Moreover, in both spectrum –C=O stretching of P*t*BA was seen at 1723 cm^{-1} (Fig. 4.21).

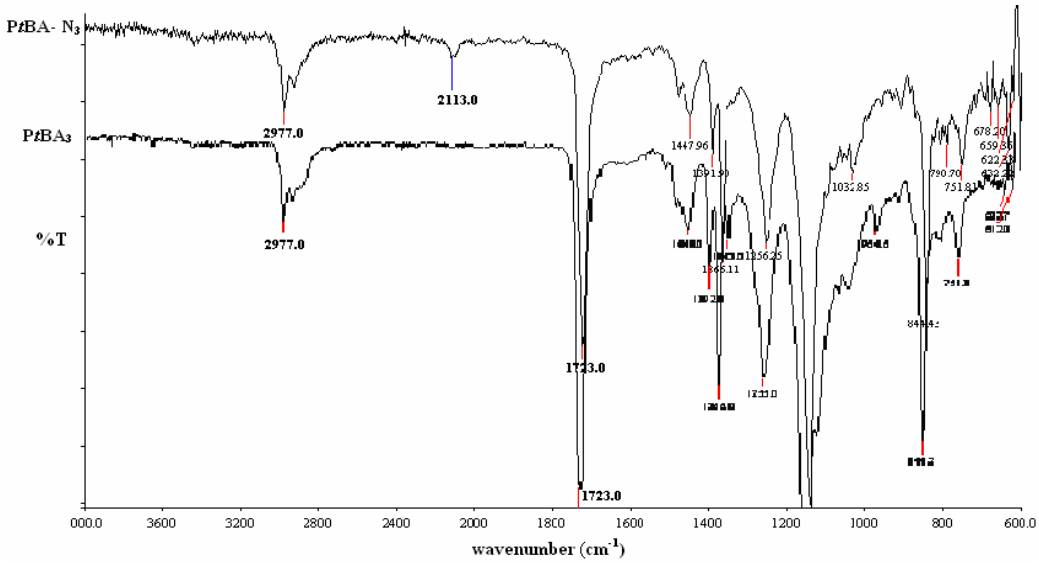


Figure 4.21. FTIR spectrum of the P*t*BA–N_3 and P*t*BA_3 star polymer (through a click reaction between P*t*BA–N_3 and **1**)

The azide funtionality was seen at 2101 cm^{-1} for PEG–N_3, and it was disappeared in PEG_3 star polymer FTIR spectrum (Fig. 4.22).

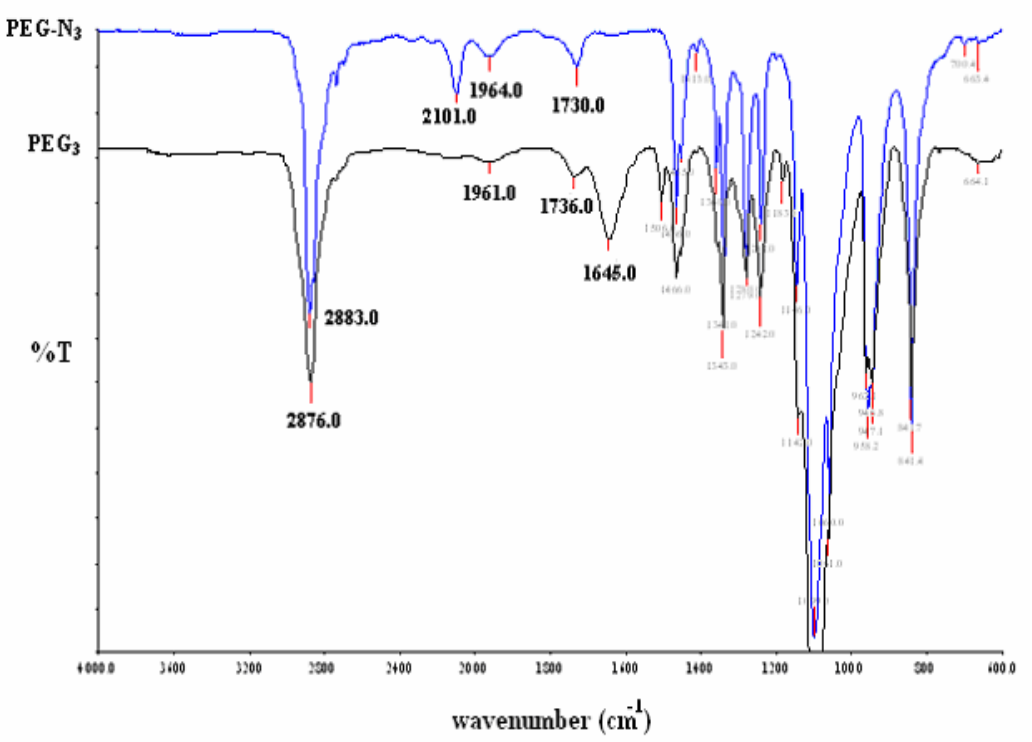


Figure 4.22. FTIR spectrum of the PEG–N_3 and PEG_3 star polymer (through a click reaction between PEG–N_3 and **1**)

Several parameters may affect the efficiency of the click reaction for A_3-type star formation, such as the reaction solvent, alkyne/azide ratio, molecular weight of the azide-end-functionalized polymers, catalyst, base, and temperature.

CONCLUSION

In conclusion, we applied a click-chemistry strategy to the formation of A_3-type star polymers such as PS_3, P*t*BA_3, and PEG_3. For this purpose, first, trisalkyne-functional initiator, 1,1,1-tris[4-(2-propynyloxy) phenyl]ethane (**1**) was synthesized. Then well defined polymers such as polystyrene, poly(tert-butyl acrylate) and poly(ethylene glycol) were synthesized. After the polymerizations, polymers were reacted with NaN_3 in order to give well defined azide end-funtionalized polymers. The initiator (**1**) obtained was used in the click reaction with well-defined azide-end-functionalized polystyrene ($PS–N_3$), azide-end functionalized poly (tert-butyl acrylate) (P*t*$BA–N_3$), or azide-end-functionalized poly(ethylene glycol) ($PEG–N_3$) in order to give A_3-type star polymer. Click reactions were carried out with equimolar amounts of the reactants ([azide]/[trisalkyne] = 3/1) and nonequimolar amounts of the reactants ([azide]/[trisalkyne] = 3,6/1).

The click-reaction efficiency for A_3-type star formation has been investigated with gel permeation chromatography measurements (refractive-index detector) and FTIR measurements. The gel permeation chromatography curves have been split with the deconvolution method (Gaussian area), and the A_3-type star polymers were recovered in yields as high as 87% because of the highly efficient click reaction.

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