"Designed Macromolecular Architectures by Controlled Polymerization Methods"

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in

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By

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National Chemical Laboratory

Pune- 411 008

August 2012

To

My family

For their patience and

encouragement

Declaration by the Supervisor

Certified that the work incorporated in the thesis entitled "**Designed Macromolecular Architectures by Controlled Polymerization Methods**" submitted by Mr. Prakash Sudhir Sane was carried out under my supervision. Such material as has been obtained from other sources has been duly acknowledged in this thesis.

August, 2012 **P. P. Wadgaonkar**
Pune **(Research Guide)**

Declaration by the Candidate

I declare that the thesis entitled "**Designed Macromolecular Architectures by Controlled Polymerization Methods**" is my own work conducted under the supervision of Dr. P. P. Wadgaonkar, at Polymer Science and Engineering Division, National Chemical Laboratory, Pune.

I further declare that to the best of my knowledge, this thesis does not contain any part of work, which has been submitted for the award of any degree either of this University or any other University without proper citation.

August 2012

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Abstract

End-functionalized polymers and miktoarm copolymers are of interest due to their applications in several areas. More specifically, end-functionalized polymers are useful as building blocks for synthesis of block, graft and star copolymers. These polymers also have potential applications such as surface modification, coatings, adhesives, as well as compatibilization of polymer blends. Miktoarm star copolymers are promising materials due to their ambivalent properties and find applications in areas such as thermoplastics, associative polymers containing hydrophilic and hydrophobic segments, etc.

For the synthesis of these polymers, living polymerization methods *viz* anionic, cationic, group transfer and controlled radical polymerizations (CRP) such as reversible-addition fragmentation termination (RAFT), nitroxide mediated polymerization (NMP), and Atom Transfer Radical Polymerization (ATRP) have been developed and demonstrated to provide a high degree of control. Amongst the CRP methods, ATRP is a powerful technique to prepare polymers with predictable molecular weight. The increasing interest in ATRP technique is due to relatively mild reaction conditions and a broad choice of monomers, initiators, catalysts, etc. Functional groups can be introduced easily at the chain ends either through functionalized ATRP initiators or halogen displacement. Using ATRP technique, a variety of polymer architectures and compositions is accessible, e.g., block, graft copolymers, and hyperbranched polymers.

Because of various applications, particularly in biomedical field due to their biodegradability, aliphatic polyesters such as poly ε-caprolactones have been the subject of great interest. The absence of any functional groups limits aliphatic polyesters from many potential applications. Now-a-days, significant efforts are devoted to synthesis of different types of functional aliphatic polyesters in order to anchor the active agent to polymer structures by means of physical interactions or by covalent linkages, and hence the functionalization of aliphatic polyester becomes a topic of great interest. Ring opening polymerization (ROP) of lactones constitutes a method of choice for the synthesis of aliphatic polyesters.

The overall objective of the work was to design and synthesize new macromolecular architectures employing controlled polymerization methods. In this context, it was of interest to design and synthesize initiators containing different functional groups for ROP and ATRP as well as different multifunctional initiator (MFI) cores possessing different types and specific number of initiating sites for preparation of miktoarm copolymers. Commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid were used as the starting materials. Both 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid

contain phenolic and acid groups, which were effectively utilized in various aspects of chemical transformations for synthesis of the desired ROP and ATRP initiators as well as MFI cores.

The thesis has been divided into the following six chapters:

Chapter 1.Introduction

This chapter deals with brief introduction to CRP methods, with emphasis on ATRP. Furthermore, brief introduction to Ring Opening Polymerization (ROP) and "Click Chemistry" is presented. The synthesis of end-functionalized polymers and miktoarm copolymers by above mentioned techniques is discussed.

Chapter 2. Scope and Objectives

The **s**cope and objectives of the present thesis are outlined in this chapter.

Chapter 3. Functional Initiators: Synthesis and Characterization is sub-divided in two sections

Chapter 3a. Functional Initiators for ROP: Synthesis and Characterization

This section details synthesis of seven new functional initiators for ROP starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid.

i) 4, 4'-Bis (4-(allyloxy)phenyl)pentan-1-ol

ii) 4, 4'-(((5-Hydroxypentane-2, 2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde

iii) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl)pentan-1-ol

iv) 4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

v) 4-(4-(2-(4-(Allyloxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde

vi) 4-(4-(Allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol, and

vii) 4-(4-(2-(4-(2-Azidoethoxy) phenyl)-5-hydroxypentan-2-yl) phenoxy) benzaldehyde

Chapter 3b. Functional Initiators for ATRP: Synthesis and Characterization

This section describes synthesis of five new functional initiators for ATRP starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid.

i) 4, 4'-Bis (4-(allyloxy) phenyl)pentyl 2-bromo-2-methylpropanoate

ii) 4, 4'-Bis (4-(4-formylphenoxy) phenyl)pentyl 2-bromopropanoate

iii) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl)pentyl 2-bromopropanoate

iv) 4-(4-(Allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate, and

v) 4, 4'-Bis (4-(2-azidoethoxy) phenyl)pentyl 2-bromo-2-methylpropanoate

Chapter 4. End-Functionalized Polymers: Synthesis, Characterization and Chemical Modification

This chapter is sub-divided in two sections

Chapter 4a. End-Functional Polymers by ROP: Synthesis, Characterization and Chemical Modification

α, α'-Homobifunctionalized poly ε-caprolactones containing functional groups *viz;* bis-aldehyde, bis-allyloxy, bis-propargyloxy, bis-azido and α, α'-hetero bifunctionalized poly ε-caprolactones possessing allyloxy-aldehyde, allyloxy-azido, and aldehyde-azido functional groups were synthesized using appropriately substituted ROP initiators in the presence of $Sn(Oct)_2$ in toluene. The reactivity of functional groups was demonstrated by carrying out reactions specific to the functional group present on the polymers.

Chapter 4b. End-Functionalized Polymers by ATRP: Synthesis, Characterization and Chemical Modification

This section describes the synthesis α, α'-homobifunctionalized poly (methyl methacrylate)s containing bis-allylloxy, bis-azido, and bis-propargyloxy and α, α'-heterobifunctionalized poly (methyl methacrylate)s containing allylloxy-aldehyde functional groups using appropriately substituted ATRP initiators. Preparation of α, α'-homobifunctionalized polystyrenes containing different functional groups *viz;* bis-aldehyde, bis-allyloxy is also discussed. Kinetic studies of styrene and methyl methacrylate polymerization with selected ATRP initiators indicated controlled polymerization behavior. The reactivity of functional groups was demonstrated by carrying out reactions specific to the functional group present on the polymers.

Chapter 5. Miktoarm Star Copolymers: Synthesis and Characterization

This chapter is sub-divided in two sections

Chapter 5a. MFI- Cores for Preparation of Miktoarm Star Copolymers: Synthesis and Characterization

This section encompasses the synthesis of new MFI-cores, starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid using simple organic transformations and click chemistry. MFI-cores such as AB_2, A_2B, A_2B_2, A_3B, and ABC having different and specific number of initiating sites for ROP and ATRP were synthesized.

Chapter 5b. Mikto-arm Copolymers: Synthesis and Characterization

This section describes the synthesis of A_2B type PS-$(PCL)_2$ or AB_2 type PCL-$(PS)_2$, A_2B_2 type $(PCL)_2$-$(PMMA)_2$, A_3B type $(PCL)_3$-PMMA, and ABC type (PCL)-PEG-PS mikto arm star copolymers by utilizing synthesized MFI-cores. Synthesis of $(PCL)_2$-PEG or PCL-$(PEG)_2$, $(PCL)_2$-PLLA or $(PLLA)_2$-PCL copolymer employing coupling onto approach is also included. The structures of the synthesized polymers were confirmed by ^{1}H-NMR spectroscopy.

Chapter 6. Summary and Conclusions

This chapter summarizes the results, salient conclusions of the investigations and perspectives of the work.

Glossary

GPC- Gel permeation chromatography

ROP-Ring Opening Polymerization

ATRP- Atom Transfer Radical Polymerization

PMDETA- N, N', N', N", N" Pentamethyldiethylenetriamine

MMA-Methyl methacrylate

PMMA-Poly (methyl methacrylate)

PS-Polystyrene

ε-CL- ε-Caprolactone

PCL-Poly caprolactone

m-CPBA-3-Chloroperoxybenzoic acid

DSC-Differential Scanning Calorimetry

TGA-Thermogravimetric Analysis

WAXD-Wide angle X-ray diffraction

THF-Tetrahydrofuran

TEA-Triethylaluminium

DMF-N, N-Dimethylformamide

DCM-Dichloromethane

EDTA-Ethylenediaminetetraaceticacid

LAH-Lithium aluminium hydride

$CDCl_3$-Deuterated chloroform

DMSO- d_6- Deuterated dimethylsulfoxide

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Chapter 1

Introduction

1.1. General Introduction

1.1.1. Polymers

Polymers. Try to imagine modern life without them. No clothes, no cars, no computers, no glue, no television, the list is endless. But there is more than that. Try to imagine life itself without polymers. Indeed, without polymers Earth would be just another lump of bare, dead rock flying through the universe. DNA, the database of life, and proteins, the compounds that regulate all the chemical processes in a living being, are natural polymers. Wood, fur, cotton, all these materials are composed of natural polymers. Ever since man has discovered the fascinating properties of polymers, even without having the slightest idea of what they exactly were used them in daily life. Moreover, being an intelligent creature, man made attempts to modify these materials to improve their properties, and later on succeeded in creating fully synthetic polymers, although at that time the exact structure of these materials was still a mystery. The first fully synthetic polymer was commercialized in 1910 under the trade name Bakelite®. It took some ten years more, however, before Staudinger postulated that both natural and synthetic polymers are giant molecules that are composed of small, covalently bonded molecules, and that polymers differ from "ordinary" molecules primarily only in size. This is also where the name polymer stems from, which is derived from Greek and literally means many parts. Since then, synthetic polymer chemistry and polymer technology has taken on a high flight, and polymers evolved from the poor man's cheap replacement for natural fibers etc. to a high-tech material with properties far beyond the reach of traditional materials like metals, wood and ceramics. The usefulness of polymers to a great extent is controlled by the molecular architecture.

There is continuing need for research on new synthetic methods for producing macromolecules of precise size, composition, architecture, and shape, and with controlled homo or heterogeneity to support emerging technologies that demand increasing complexity in the polymer systems. Increasing the sophistication of molecular design in polymers through the exploitation of organic chemistry concepts and tool, is, therefore, a major direction of materials research with considerable potential for cross fertilization between disciplines. The most profound recent developments in polymer chemistry are based on this growing synergy between advanced organic chemistry and polymer synthesis. Creative approaches using organic chemistry are required to control every facet of macromolecular structures. Modern polymer chemistry allows for the synthesis of a wide range of highly complex polymer architectures- some scientist even suggest that at current state any architectural design can be achieved within certain limits of molecular weight and end group fidelity. Most of the popular polymerization techniques used in academia today were discovered at the end of the 20th century. For instance, ring opening metathesis polymerization, controlled/living radical

polymerization, click chemistry, bio-orthogonal ligation and bio-conjugations are all very recent developments in polymer chemistry.

This chapter deals with brief introduction to living radical polymerization methods, with emphasis on Atom Transfer Radical Polymerization (ATRP). Furthermore, brief introduction to Ring Opening Polymerization (ROP) and "Click Chemistry" is presented. The synthesis of end-functionalized polymers and miktoarm copolymers by above mentioned techniques is discussed.

1.1.2. End functional polymers

Telechelic polymers are polymers that bear either same or different functional groups at one or both chain ends **(Figure 1.1)**, and are important class of polymers due to their potential applications as building blocks for block copolymers, surfactants, macromonomers[1-9], etc..

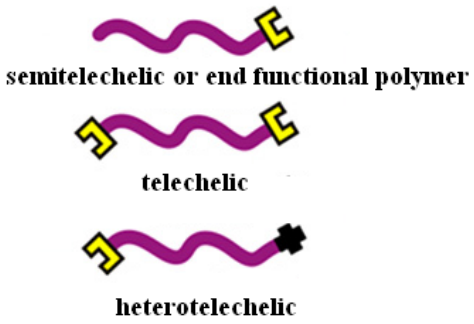


Figure 1.1: Schematic representation of end functional and telechelic polymers

The exploration of synthetic methods to obtain macromolecules with special end functionality has been an active area of research for many years as functional macromolecules are important precursors for preparation of well-defined block copolymers, graft copolymers, and star copolymers. Various architectures that could be obtained by the reaction of telechelics as represented in **Figure 1.2**

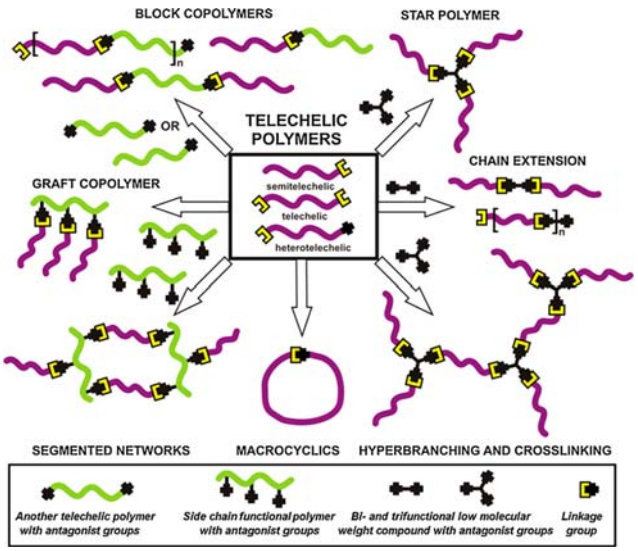


Figure 1.2: Various architectures obtained by the reactions of telechelics[10]

Different methods have been developed for the synthesis of functional polymers[11]. The synthetic strategies include the direct initiation method using a functional initiator, functional end capping[11], free radical chain transfer reaction and living polymer deactivation[12].The direct initiation method by living polymerization using functional initiator is of special interest since every polymer chain produced has initiator's functional group. In addition, living polymerization offers a good control over the polymer structure and molecular weight with low molar mass distribution. However, living polymerizations based on anionic and cationic techniques are very sensitive to moisture and impurities and in some cases they are sensitive to the functional groups to be incorporated, thus, are very difficult to use routinely. On the other hand, free radical polymerization is flexible and less sensitive to the polymerization conditions and functional groups.

1.1.3. Free-radical polymerization

Polymers can be synthesized *via* many pathways, but a clear distinction should be made between the polymerization mechanisms leading to these polymers. The most widely used process for polymer synthesis now a days is free-radical polymerization[13] which is a chain-growth polymerization process. Free-radical polymerization has the major advantage that it is much less sensitive to traces of impurities than other polymerization techniques, like e.g. ionic or coordination polymerizations. Furthermore, a wide range of vinyl monomers with general structure $CH_2=CR_1R_2$ can be polymerized *via* free-radical polymerization. The process involves the generation of free radicals from an initiator, which are then added to the monomer. Addition of monomer to the growing chain radical continues until either two growing chains meet and terminate with each other, or when the growing chain transfers its radical to another species (e.g. to monomer, polymer, solvent, etc.) which then in its turn will initiate the formation of a new macromolecule which will grow until again bimolecular termination or transfer takes place. Both in the case of transfer and termination, so-called dead chains are formed. The term dead stems from the fact that these chains have lost their active center, and cannot add monomer anymore, unless chain transfer to these dead polymer chains takes place. The lifetime of a growing polymer chain in free-radical polymerization is in the order of seconds, and as radicals are generated from the initiator continuously throughout the polymerization reaction, new chains are initiated, grow and are terminated also throughout the polymerization reaction. This implies that polymer chains do not grow simultaneously. It will be evident from these characteristics that, although free-radical polymerization is a very powerful, fast and cheap technique for polymer synthesis, conventional free-radical polymerization exhibits very little control over the molecular weight distribution and the chemical composition of the polymer chain. Also the synthesis of fancy macromolecular architectures, such as block copolymers, star polymers or comb polymers, is not possible with conventional free-radical polymerization.

1.1.4. Controlled radical polymerization

However, as the saying goes, power is nothing without control also holds for polymer chemistry. Although for many applications no strict control over the molecular weight, the molecular weight distribution or the chemical composition of the polymer is required, there is a large interest in architectures such as block copolymers, which cannot be made *via* conventional free-radical polymerization. Block copolymers are generally applied as adhesives, compatibilizers, thermoplastic elastomers, etc. Traditionally, block copolymers have always been synthesized *via* living anionic polymerization. A living process implies that all polymer chains start growing simultaneously; while during chain growth no termination or chain transfer takes place. Consequently, all chains grow for a similar period, and a narrow molecular weight distribution is obtained. When all monomer has been consumed, the active center persists, and upon addition of a new batch of monomer, polymerization continues to form a block copolymer. Anionic polymerization, however, requires very stringent reaction conditions, as the carbanion is very sensitive to traces of impurities. Industrially, anionic polymerization is therefore not frequently used. In the last decade, some polymerization techniques that combine the versatility of free radical polymerization with the control of anionic polymerization emerged. These techniques are referred to as controlled radical polymerizations (CRP), and are based on two principles: reversible termination and reversible transfer. Examples of reversible termination are Nitroxide-Mediated Polymerization (NMP)[14, 15] and Atom Transfer Radical Polymerization (ATRP)[16-19] while Reversible Addition-Fragmentation chain Transfer (RAFT)[20] is an example of reversible transfer. In reversible termination, the polymer chain is end-capped with a moiety that can reversibly undergo homolytical cleavage. In NMP, this moiety is a nitroxide {**Fig 1.3 scheme a**}, while in ATRP, a halide is reversibly transferred to a transition-metal complex {**Fig 1.3 scheme b**}. In processes based on reversible transfer, there is fast exchange of growing radicals *via* a transfer agent. In the RAFT process, dithiocarboxylates are responsible for this exchange, which proceeds *via* an intermediate radical {**Fig 1.3 scheme**. **c}**. Of the three available techniques to mediate a controlled radical polymerization, the ATRP process is the most robust. It tolerates traces of impurities, and is compatible with the broadest range of monomers and reaction conditions. In order to extend the lifetime of the propagating chains, each of these methods relies on establishing a dynamic equilibrium between a low concentration of active propagating chains and a predominant amount of dormant chains that are unable to propagate or terminate. In the case of SFRP or ATRP, the equilibrium is pushed to the left-hand side (deactivated, K_{deact}), forming an excess of dormant species as a result of the persistent radical effect[21]. In all radical polymerizations, radical termination occurs at a rate, Rt, which is dependent on the concentration of radicals, [P*], where Rt = kt[P*].

a. SFRP or NMP

Thermal dissociation of dormant species (K_{act}) provides a low concentration of radicals

b. ATRP

Transition metal activation (K_{act}) of a dormant species with a radically transferable atom

c. RAFT

Majority of chains are dormant species that participate in transfer reactions with a low concentration of active radicals

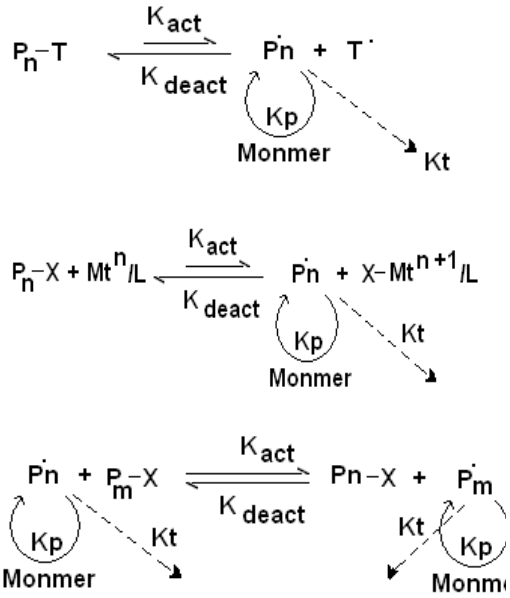


Figure 1.3: Representative examples of three main CRP methods

Therefore, at the same polymerization rate (the same [P*]), essentially the same number of chains terminate regardless of being in conventional or CRP systems. However, in the conventional process all chains are terminated, whereas in CRP, as a result of the greater number of growing chains, the terminated chains constitute a small fraction of all the chains (~1-10%). The remaining chains are dormant species, capable of reactivation, functionalization, and chain extension to form block copolymers, etc. Thus, CRP behaves as a 'living' system[22, 23]. Additionally, relatively fast initiation, at least as fast as propagation, gives control over molecular weight (the degree of polymerization is defined by the ratio of concentrations of the consumed monomer to the introduced initiator, $DPn = \Delta[M]/[I]_0$) and a narrow molecular weight distribution. **Figure 1.4** presents the cumulative number of papers published during the past 15 years on overall reversible-deactivation radical polymerization (RDRP) processes[24].

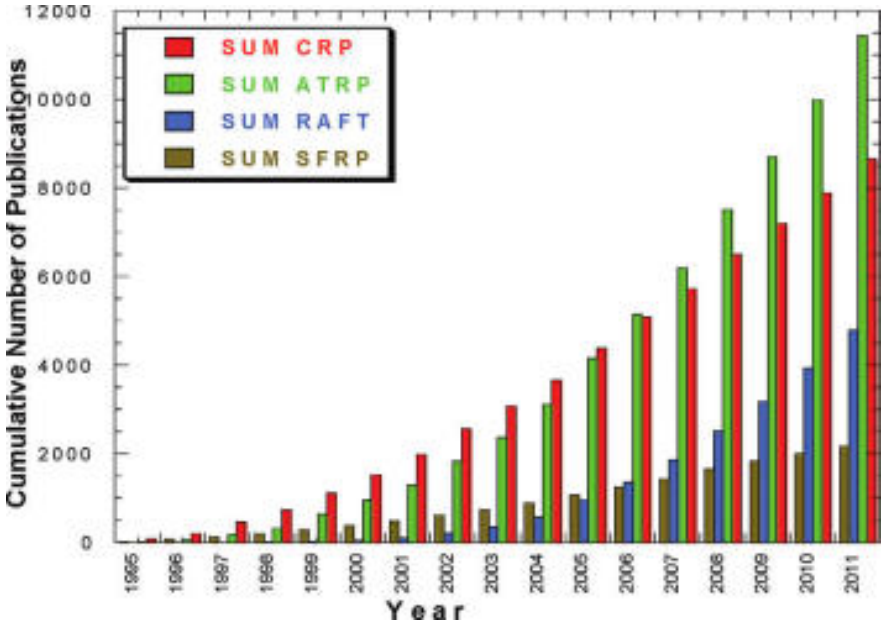
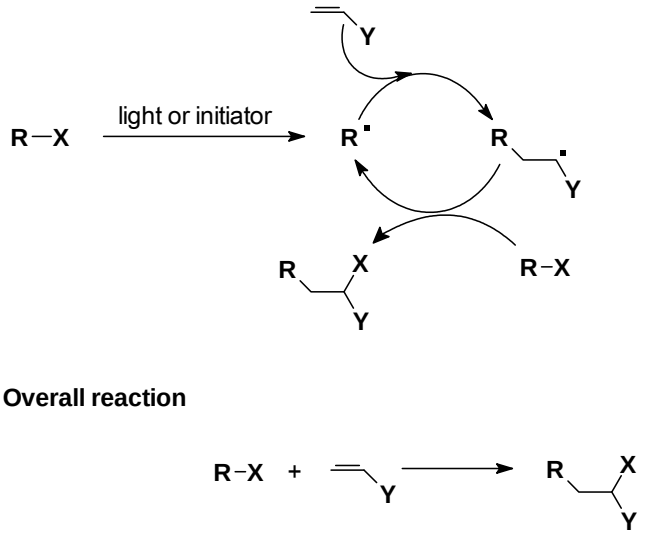


Figure 1.4 Results of SciFinder search on various RDRP systems as of December 30, 2011[24]

The growth in the number of publications in all areas of RDRP reflects the increasing interest in this field.

1.2. Atom transfer radical polymerization

Matyjazewski et al[17] and Sawamoto et al[16] introduced ATRP in 1995 simultaneously. The principle is based on the Kharasch reaction, the Atom Transfer Radical Addition (ATRA), which is widely used by organic chemists for carbon-carbon bond formation[25] **(Scheme 1.1).**



Scheme 1.1: Atom transfer radical addition reaction

The control in an ATRP system is induced by the presence of an organic halide initiator and a transition metal complex. The reversible exchange of the halogen atom between the growing

polymer chain and the transition metal complex (in its higher oxidation state) ensures the control over the polymerization.

1.2.1. Components in ATRP

1.2.1.1. Catalysts

The most important component of ATRP is the catalyst. The key function of catalyst in ATRP is to determine the position of the atom transfer equilibrium and the dynamics of the exchange between the dormant and active species[26-28]. There are several prerequisites for an efficient transition metal catalyst.

a} Metal center must have at least two accessible oxidation states by 1 electron

b) Metal center should have reasonable affinity towards halogen

c) Coordination sphere around the metal should be expandable on oxidation

d) Eventually, the position and dynamics of ATRP equilibrium should be appropriate for the particular system. To differentiate ATRP from the conventional redox-initiated polymerization and induce a controlled process, the oxidized transition metal should rapidly deactivate the propagating polymer chains to form the dormant species.

A variety of transition metal complexes with various ligands have been studied as ATRP catalysts. Transition metals such as copper[17, 29], ruthenium[16, 30, 31] molybdenum[32], manganese, rhenium, iron[33, 34], cobalt, nickel[35], rhodium[36] and palladium have been studied for ATRP. The catalyst has to be complexed in order to be active and be able to control the polymerization. This is achieved using nitrogen-containing ligands, e.g. (substituted) 2,2'-bipyridines[37], Schiff bases[38], multidentate tertiary amines, etc.

1.2.1.2. Monomers

A variety of monomers such as (meth) acrylates, styrenes, (meth) acrylamides, acrylonitrile, etc.[40] have been successfully polymerized using ATRP. Methyl methacrylate is one of the most studied monomers by ATRP using catalytic systems based on copper, ruthenium, nickel, iron, palladium and rhodium. Other methacrylate esters that have been successfully polymerized include 2-(dimethylamino) ethyl methacrylate (DMAEMA), 2-hydroxy ethyl methacrylate (HEMA), glycidyl methacrylate, silyl protected HEMA, methacrylic acid in its alkyl protected form or as its sodium salt, methacrylates with a long oligo(ethylene oxide) substituent and fluorinated methacrylic esters.

1.2.1.3. Ligands

The main roles of the ligand in ATRP are

1) To solubilize the transition metal salt in the organic media

2) To adjust the redox potential and halogenophilicity of the metal center forming a complex with an appropriate reactivity and dynamics for the atom transfer[39].

3) The ligands should complex strongly with the transition metal.

4) It should also allow expansion of the coordination sphere and should allow selective

atom transfer without promoting other reactions.

Nitrogen containing ligands are most extensively used and work well (**Figure 1.5)**

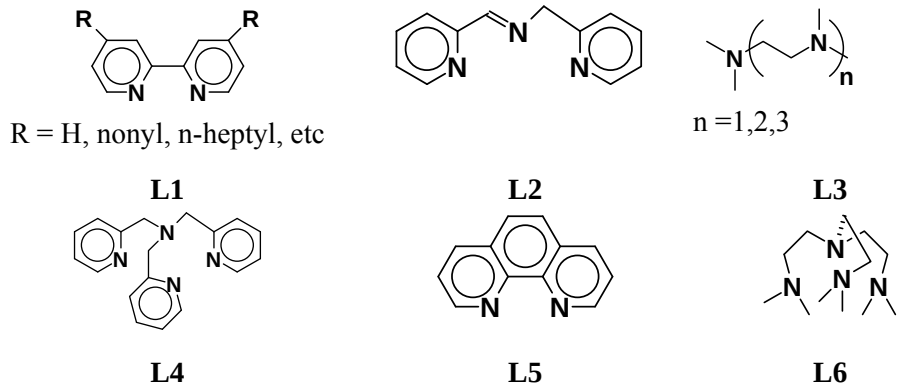


Figure 1.5: Selected nitrogen containing ligands used in ATRP

1.2.1.4. Initiators

Initiator plays important role in ATRP. Initiator forms an initiating radical species *via* homolytic cleavage of labile C-halogen bond with the help of metal catalyst. Initiator is chosen such that it should initiate fast in comparison with propagation, quantitative initiation and the probability of side reaction should be minimum[1].

Most of the successful initiators employed in ATRP are organic halides with a potentially active carbon-halogen bond, which can easily generate a radical species through electronic and steric effects of their substituents. An organic halide, the structure of which is similar to that of the dormant chain end of the polymer, is preferentially used so that the activity of the carbon-halogen bond in the initiator is similar to that of the dormant polymer terminal. The general order of bond strength in the alkyl halides is R-Cl > R-Br > R-I. Thus, alkyl chlorides should be the least efficient initiators and alkyl iodides the most efficient. However, the use of alkyl iodides requires special precautions. They are light sensitive, can form metal iodide complexes with an unusual reactivity (e.g., CuI_2 is thermodynamically unstable and cannot be isolated), the R-I bond may possibly be cleaved heterolytically and there are potential complications of the ATRP process by degenerative transfer. The alkyl chlorides and bromides have been widely employed initiators in the ATRP. Haloalkanes, allyl halides, (haloalkyl) benzenes, haloketones, haloesters, haloamides, halonitriles, sulfonyl halides, etc. are utilized in ATRP.

1.2.1.5. Solvents

ATRP can be carried out either in bulk, in solution, or in a heterogeneous system (emulsion, suspension, dispersion). Many solvents such as toluene, anisole, diphenyl ether, ethyl acetate, acetone, N, N-dimethylformamide, ethylene carbonate, alcohols, water, supercritical carbon dioxide, etc.[26] were utilized to carry out ATRP.

Several factors affect solvent choice. Chain transfer to solvent should be minimal. In addition, potential interactions between solvent and the catalytic system should be considered. Catalyst poisoning by the solvent such as carboxylic acid and solvent assisted side reactions, such as elimination of HX from polystyryl halide, which is more pronounced in a polar solvent, should be minimized. The possibility that the structure of the catalyst may change in different solvents should also be considered.

1.2.1.6. Additives

Occasionally, polymerizations are slow in most cases due to low concentration of the radical species, as required by the general principle. Use of additive is unique solution for this problem. Some additives are needed for acceleration and/ or better control of the polymerizations. Additives most probably can effectively reduce the metal species in higher oxidation states or form more efficient catalysts *via* coordination.

For example, zero-valent metals such as Cu(0) and Fe(0) can effectively reduce $CuBr_2$ and $FeBr_3$ into active CuBr and $FeBr_2$, respectively, to dramatically increase the polymerization rate[41]. This allows the controlled radical polymerization even in the presence of oxygen or without purification of the monomer, where Cu(0) and Fe(0) can reduce the generated Cu(II) and Fe- (III) species into active Cu(I) and Fe(II), respectively[42]. Phenols usually serve as radical inhibitors in conventional radical polymerization but can enhance the polymerizations of MMA[43]. Similar effects were observed for 4-methoxyphenol, phenol, and 2,6-di-*tert*-butylphenol[44].

1.2.1.7. Limitations of ATRP

A number of functional groups are not tolerated in ATRP including carboxylic acid[45], amine, ketone [46] and certain ionic groups, that react with the catalyst, thereby impeding the establishment of the equilibrium. However, carboxylic acid groups can be introduced by polymerization of the carboxylic acid salt instead or in protected form. Some monomers can be polymerized by this method but with great difficulty[47], because the formed radical is not stabilized enough, which is the case for monomers such as vinyl acetate and halogenated alkenes. The main problem in using ATRP for syntheses, industrial or otherwise, is removal of the catalyst [48]. The metal catalyst–ligand complex is undesired in the product, as the transition metal induces aging in the polymer, but also for aesthetic (coloration) and toxicological reasons removal is important. Catalyst removal is both difficult and costly, but several methods have been reported for catalyst removal in the literature, which include the use of a special solvent for separation, extraction, precipitation and dialysis[49, 50]. The most widely used procedure for copper removal is the use of an adsorbent column containing alumina or silica, or, in some cases, ion exchange resin[18].One procedure is to immobilize the catalyst by having it attached to solid supports such as clay[51] during reaction.

1.2.2. Mechanistic developments of ATRP

Much research has been devoted to the development of more active catalysts which could be used to reduce the total amount of catalyst needed and/or to polymerize less reactive monomers with strong alkyl–halide bond strengths[52]. However, such systems are inherently less oxidatively stable, as the catalysts are more reducing. These systems often require special handling procedures to remove all oxygen and oxidants so as to avoid

forming the redox conjugate of the catalyst that will shift the ATRP equilibrium towards the dormant state and significantly reduce the rate of the reaction. Mainly four approaches have been established **(Scheme 1.2).** Those are documented by Matyjaszewski et.al[28]

a) Reverse ATRP

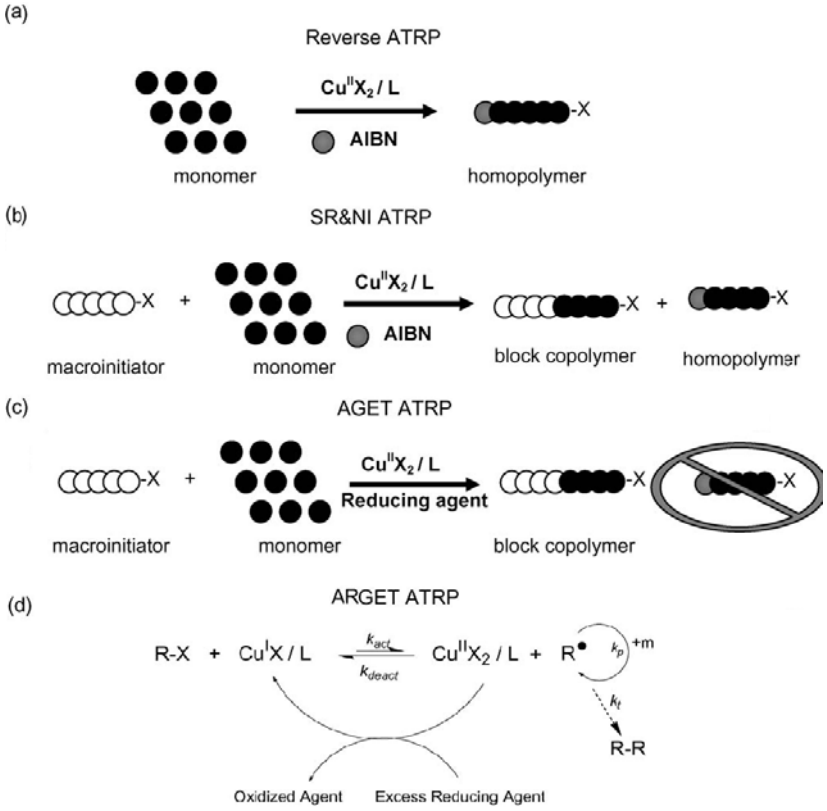
b) Simultaneous reverse and normal initiation (SR&NI) ATRP

c) Activator generated by electron transfer (AGET) ATRP

d) Activators regenerated by electron transfer (ARGET) ATRP

1.2.2.1. Reverse ATRP

In this technique, the ATRP initiator and lower oxidation state transition metal activator Cu(I) are generated *in situ* from conventional radical initiators and the higher oxidation state deactivator Cu(II)[53]. The initial polymerization components are less sensitive to oxygen, and yet the same equilibrium between active and dormant species can ultimately be established **(Scheme 1.2a)**.



Scheme 1.2: Schematic presentation of mechanistic developments in ATRP[28]

This technique would therefore be more compatible with commercial processes. However, there are several drawbacks associated with reverse ATRP: (1) because the transferable halogen atom or group is added as a part of the copper salt, the catalyst concentration must be comparable to the concentration of initiator and therefore cannot be independently reduced; (2) block copolymers cannot be formed; (3) Cu (II) complexes are typically much less soluble in organic media than those complexes of Cu (I), often resulting in a heterogeneous (and poorly controlled) polymerization

1.2.2.2. Simultaneous reverse and normal initiation (SR&NI) ATRP

In contrast to reverse ATRP, SR&NI ATRP utilizes a dual initiation system comprised of standard free radical initiators and the higher oxidation state metal complex as well as initiators with a transferable atom or group[54]. This provides the advantage of allowing highly active catalyst complexes to be added to the reaction as the higher oxidation state catalyst in lower concentration relative to the initiator, unlike in reverse ATRP, because the transferable atom is not solely a part of the catalyst salt. The radicals generated by the free radical initiator are deactivated by a Cu (II)X/L complex forming Cu(I)/L and some halogenated chains **(Scheme 1.2b).** The Cu (I)/L can then activate the alkyl halide initiator (which may be present in excess) and concurrently mediate normal ATRP. However, there are some limitations to this method, particularly with the production of block copolymers. Because a conventional free radical initiator is used to form radicals that reduce the Cu (II) complex, homopolymer chains initiated by these radicals will always be present, which can lead to a partial loss of control over functionality and topology in the synthesis of block copolymers.

1.2.2.3. Activator generated by electron transfer (AGET) ATRP

In this technique, electron transfer rather than organic radicals are used to reduce the higher oxidation state transition metal complex. This way, no homopolymers are produced during block copolymerization as in SR&NI ATRP. The principle was demonstrated with a number of Cu (II) complexes using tin (II) 2-ethylhexanoate[55] and ascorbic acid[56] as the reducing agents, which reacted with the Cu (II) complex to generate the Cu (I) ATRP activator **(Scheme 1.2c).** Normal ATRP then proceeded in the presence of alkyl halide initiators or macromonomers.

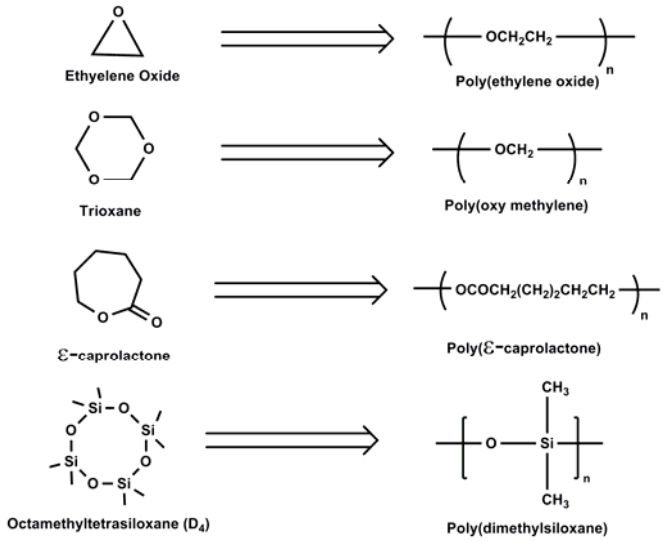
1.2.2.4. Activators regenerated by electron transfer (ARGET) ATRP

In principle, the absolute amount of copper catalyst can be reduced under normal ATRP conditions without affecting the polymerization rate, a rate which is governed by a ratio of the concentrations of Cu (I) to Cu (II) species **(Scheme 1.2d).** In ARGET ATRP, the relative concentration of catalyst to initiator can be reduced much lower than under normal ATRP conditions.

Overall, ATRP is a robust technique for synthesis of various polymer architectures, which are useful in different fields.

1.3. Ring opening polymerization (ROP)

Aliphatic polyesters occupy a key position in the field of polymer science because they exhibit the remarkable properties of biodegradability and biocompatibility, which opens up a wide range of applications as environmentally friendly thermoplastics and biomaterials. One of the routes by which such materials could be prepared is ROP of cyclic monomers such as ε-caprolactone and lactide. ROP is an important polymerization technique, along with other step and chain polymerization techniques, for production of polymers. Studies of ROP have been active areas of industrial and academic research[57]. This polymerization technique has provided a number of commercially important materials. **Scheme 1.3** illustrates some of those examples.



Scheme 1.3: Representative examples of ROP

A wide variety of aliphatic cyclic monomers have been successfully polymerized by the ring opening polymerization. This includes cyclic esters (lactones), amines, sulfides, olefins, cyclotriphosphazenes, *etc*., besides those mentioned in **Scheme 1.3.** The polymerizability of a cyclic monomer depends on both thermodynamic and kinetic factors. Kinetically, polymerization requires that there be an available mechanism for the ring to open and undergo reaction. The presence of a heteroatom in the ring provides a site for nucleophilic or electrophilic attack by an initiator species, resulting in initiation and subsequent propagation by ring opening. The most important factor that one may often deal with, however, is the thermodynamic factor, that is, the relative stabilities of the cyclic monomer. Small rings, such as 3- and 4-membered rings, are highly strained and, accordingly, have a large exothermic enthalpy associated with the ring opening. In these cases, enthalpy is the major factor in determining the free energy of polymerization. The large enthalpy (negative) ensures that the equilibrium between monomer and product favors the product. By contrast,

less strained medium rings, such as 5- to 9-membered rings, are certainly less favorable, because the enthalpy now is smaller, about equal to the entropy (both are negative), and the free energy becomes less negative accordingly. Ring opening polymerization could be achieved by either of polymerization mechanisms[58]

1) Anionic 2) Cationic 3) Coordination 4) Organocatalytic 5) Enzymatic

Out of these mechanisms, ring opening polymerization by coordination mechanism is most robust.

1.4. Click chemistry

The "click" concept, proposed by Sharpless in 2001, is undeniably one of the most noticeable synthetic trends in the research area of chemistry and material science of this new century[59, 60].The catchy term "click" refers to energetically favored, specific and versatile chemical transformation, which leads to a single reaction product. In other words, the essence of click chemistry is simplicity and efficiency. Click chemistry is therefore not a new type of chemistry, but rather a term used for a class of reactions that can create complex molecules in a very efficient manner. This exciting concept seems to perfectly answer the needs of modern scientists working in research areas as diverse as molecular biology, drug design, biotechnology, macromolecular chemistry or materials science[61, 62]. It is indeed noteworthy that over recent years, complicated reactions requiring either complex apparatus or harsh experimental conditions, have been less frequently studied than in the last century and gradually replaced by simpler tools. In this context, the straightforward click reactions have become tremendously popular.

Click chemistry describes chemistry tailored to generate substances quickly and reliably by joining small units together as nature does **(Figure 1.6).** It is defined as a fast, modular, process driven approach to irreversible connections of the substrates involved in click reactions. Click chemistry uses only the most reliable reactions to build complex molecules from olefins, electrophiles, and heteroatom linkers. Click reactions in organic solvents have also a high significance in polymer and material science. The bonds generated in the product should be chemically stable under a range of physiological conditions.

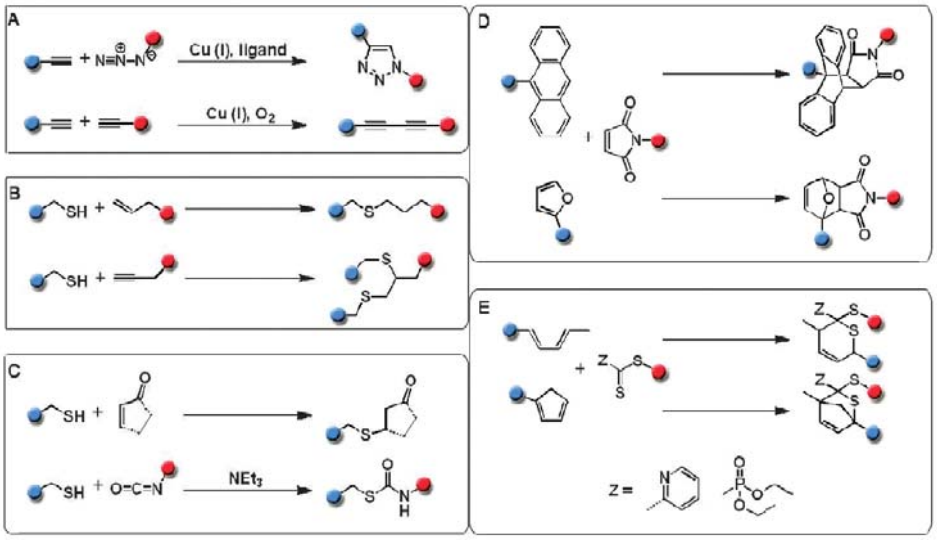


Figure 1.6: Schematic representation of the ''click'' reactions[63]

Additionally, for click reactions involved in polymerizations, the counter functionalities of the reagents should be unreactive under free radical polymerization conditions or be easily protected during the polymerization stage and functionalized afterwards.

1.4.1. Azide-alkyne reaction

Of all currently identified click reactions, the heteroatom cycloaddition class of reactions is the most reliable and versatile category. Within this category, the Huisgen 1, 3-dipolar cycloaddition of azides and alkynes is known for being closest to an "ideal" click reaction. Cu (I)-catalyzed Huisgen 1, 3-dipolar cycloaddition of azides and alkynes yields 1, 2, 3-triazole products. Traditionally, uncatalyzed cycloadditions of azides and alkynes require long reaction times, high temperatures and result in the formation of two products, 1, 4- and 1, 5- regioisomers as shown in **Figure 1.7.**

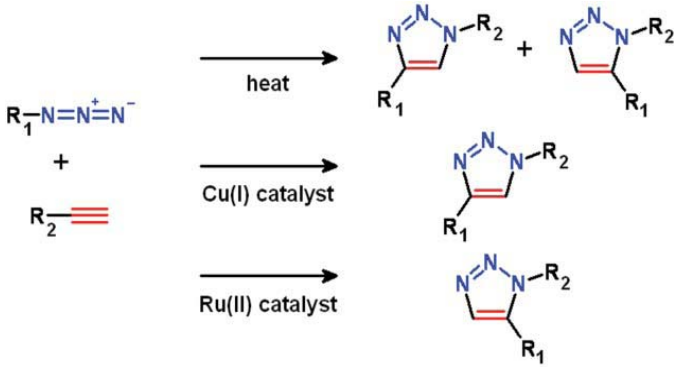


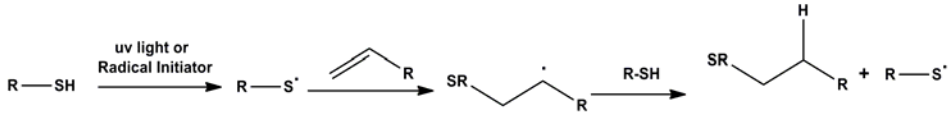
Figure 1.7: Possible regiomers during azide-alkyne click reaction[64]

This breakthrough led to a remarkable renaissance of Huisgen cycloadditions in synthetic chemistry. Hence, research in this direction has led to its widespread application in all fields of polymer chemistry and biochemistry over the last few years[65, 66].

Moreover, azide–alkyne chemistry provides platform for the functionalization or ligation of biomaterials, such as stationary phases for bioseparation, site-specific modified proteins or viruses, drug- or gene-delivery carriers, protein or oligonucleotide microarrays, and functionalized cell surfaces[67].

1.4.2. Thiol-ene reaction

The radical addition of thiols to double bonds is – under certain conditions – a highly efficient method used for polymerizations, curing reactions, grafting reactions and for the modification of polymers[68]. The mechanism for photochemical or radical induced click reaction is presented in **Scheme 1.4** and schematic presentation of thermal and photochemical thiol-ene reaction is reproduced in **Figure 1.8.**



Scheme 1.4: The mechanistic presentation of thiol-ene radical reaction[69]

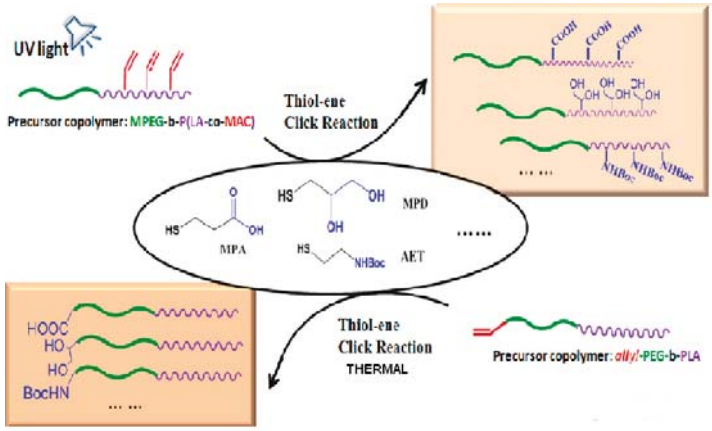
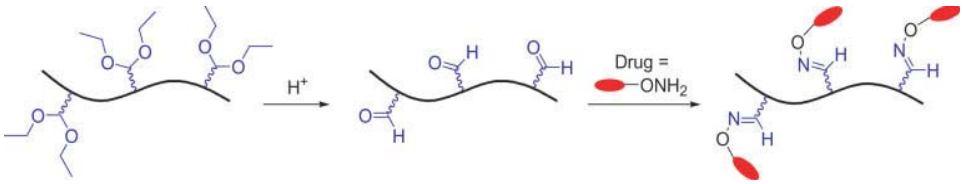


Figure 1.8: Schematic representation of thermal and photochemical thiol-ene reaction

1.4.3. Aldehyde-aminooxy click chemistry

Aldehyde- aminooxy is another reaction that comes under the category of metal free click reaction where aldehyde group can undergo click addition reaction with aminooxy functionality without any catalyst **(Scheme 1.5)**.



Scheme 1.5: Schematic presentation of aldehyde-aminooxy click reaction

Aldehyde-aminooxy type of click reaction comes under specific category "reversible covalent reactions" as the reaction can be reversed very easily by temperature or by addition of small aminooxy compounds[70]

1.4.4. The combination of living radical polymerization (LRP) and 'click' chemistry

Since the discovery of LRP, the possibilities of designing new polymer architectures has significantly improved, in particular in combination with high yield reactions for post-polymerization modification[71].This is due to compatibility of different LRP reactions with click chemistry and that is why the number of reports on the combination of click chemistry and LRP has been growing rapidly in the past years[64, 72].

1.4.4.1. ATRP and click chemistry

The combination of ATRP and click chemistry has been reported extensively[73]. This combination is very popular because ATRP and click chemistry can both be carried out with the same copper catalyst and the halogen terminus of polymer chains obtained *via* ATRP can easily be converted into the corresponding azide derivative[74]. The first report on the combination of click chemistry and ATRP was in 2004 by Matyjaszewski and coworkers[75]. End-group functionalization *via* click chemistry of polymers (suitable for click chemistry) has been reported. Functional groups like carboxylic acids, alkenes, and alcohols have been introduced[76]. Polymer end-group functionalization allows for the synthesis of macromonomers *via* ATRP[77]

1.4.4.2. NMP and click chemistry

The first article reporting on the combination of NMP and click chemistry was published in 2005[78].With the combination of NMP, click chemistry and other reactions, polymers with multiple functionalities were synthesized[78]. Click chemistry has been used in different ways. Alkoxyamine initiators functionalized with alkyne and azide groups have been reported and used for the synthesis of functionalized polymers and block copolymers[79].

1.4.4.3. RAFT and click chemistry

The combination of RAFT and click chemistry has been reported in a number of ways[80]. Alkyne and azide functional monomers, based on acrylic acid, were polymerized *via* RAFT mediated polymerization by Caruso et al[81].The polymers obtained from this polymerization were used to produce an ultrathin polymer multilayer by applying click chemistry to these polymers

1.5. Miktoarm star copolymers

Miktoarm star copolymers (sometimes called asymmetric star polymers, heteroarm star polymers, or simply miktoarm polymers) are star-shaped polymers where any number of various types of polymer arms emanates from a core. These polymer arms should vary by chemical identity and/or molecular weight **(Figure 1.9).** Miktoarm polymers are a relatively new and unique class of macromolecules, and constitute a topical area of research due to their intriguing properties which can be tailored by varying their polymer arms. Much emphasis has been placed in the recent past in developing synthetic methodologies to these star polymers, and examining their self-assembly in solution[82].

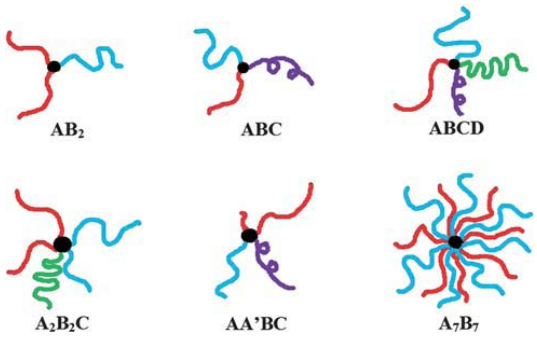


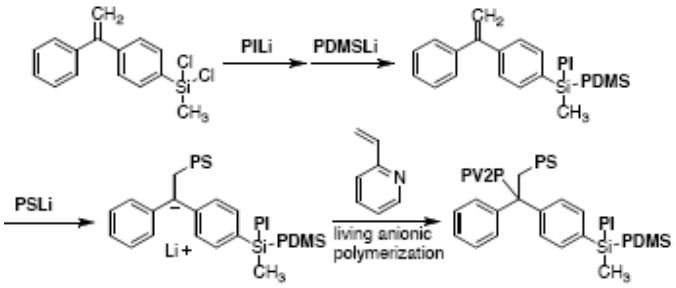
Figure 1.9: Different types of miktoarm polymers, whose polymer arms vary by the chemical identity[82]

Miktoarm star polymers are a synthetically challenging class of polymers. Multiple protection/deprotection strategies, orthogonality, and combination of different polymerization methods are typically necessary for the synthesis of these polymers, regardless of the specific type of desired miktoarm star polymer (A_2B, ABC, AB_2C_2, etc.). Considerable advances in synthetic strategies, self-assembly and applications have recently occurred, making scientific community become increasingly aware of the potential of miktoarm polymers. Synthetic methods used to prepare this kind of miktoarm copolymers are described below in brief.

1.5.1. Strategies for the preparation of miktoarm copolymers

1.5.1.1. Chlorosilane compounds

One of the most established synthetic strategies for miktoarm stars involves linking chlorosilane compounds (which serve as a core) with polymers containing reactive chain ends synthesized using living anionic polymerization. Hadjichristidis and coworkers[83] used tetrachlorosilane to synthesize an $A(AB)_3$-type miktoarm polymer, composed of polystyrene (PS) and polystyrene-b-polyisoprene. One notable feature of the chlorosilane method is the necessity of carefully reacting the living chain end of a polymer with the Si-Cl bond, for achieving controlled addition of a polymer arm onto the chlorosilane compound. This is often done by adding the chlorosilane compound in excess to ensure monosubstiution, and the unreacted byproduct is easily removed by vacuum. Finally, it is important to note that the chlorosilane methodology involves stringent reaction conditions, such as moisture-free conditions and complicated reactors that typically involve break-seal technology (due to its dependence on living anionic polymerization). Sometimes, it is beneficial to combine chlorosilane chemistry with other types of coupling reactions to build the desired miktoarm star. To this end, Hadjichristidis's group[84] created a core composed of two chlorosilane groups and diphenylethylene for the synthesis of an ABCD-type miktoarm star with four mutually incompatible arms: polystyrene, polyisoprene, poly(dimethylsiloxane) (PDMS), and poly(2-vinylpyridine) (P2VP) **(Scheme 1.6).**

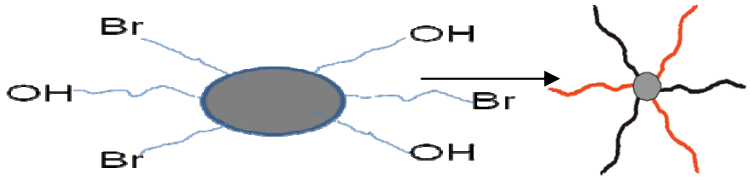


Scheme 1.6: Combination of two synthetic strategies—chlorosilane groups and diphenylethylene (a vinylic compound)—in a single core for the attachment of four different polymers[84].

Even though the use of chlorosilane linking agents is one of the oldest strategies for making miktoarm star polymers, it still is an effective strategy and continues to be employed in the synthesis of miktoarm stars.

1.5.1.2. Core-first method

There are many examples throughout the literature where the ‘‘core-first’’ method is used as a synthetic strategy[82]. The first step in this methodology requires the synthesis of a multifunctional initiator, also called a ‘‘multifunctional core,’’ or simply a ‘‘core’’ containing orthogonal initiating sites. From this core, each arm is grown outwards through a combination of different polymerization techniques **(Scheme 1.7)**.

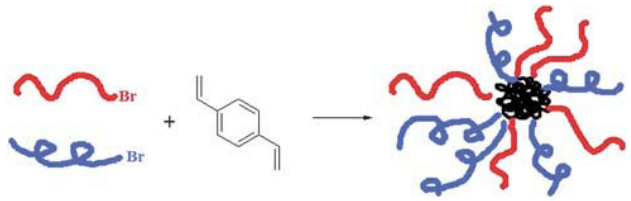


Scheme 1.7: General synthesis of a miktoarm polymer by the ‘‘core-first’’ method

such as living anionic polymerization, ring-opening polymerization (ROP)[85], or a variety of controlled/ ‘‘living’’ radical polymerization (CRP)[86] techniques including atom transfer radical polymerization (ATRP)[87], nitroxide mediated polymerization (NMP)[14], reversible addition fragmentation chain transfer (RAFT) polymerization[88], etcBecause of the combination of different polymerization methods, it is easy to introduce a wide variety of monomers into the final polymeric structure. Also, orthogonality plays a key role in the design of the multifunctional initiator—a successful synthesis of miktoarm stars requires one to polymerize a single type of initiating site on the core while leaving the other sites intact, thus ensuring that each polymerization occurs as intended on the core. Because of this nature of the multifunctional initiator, the number of polymerization initiating sites on the core is the same as the number of polymeric arms on the final miktoarm star. For instance, a multifunctional core with two ATRP initiating sites and one ROP initiating site will yield an A_2B miktoarm star polymer.

1.5.1.3. Arm first method

Although the ‘‘arm-first’’ method had typically been used to create homoarm star polymers[89], Gao and Matyjaszewski were the first to use it to demonstrate the synthesis of miktoarm star polymers, where miktoarm stars with many different arms were synthesized using either two or five different types of polymers. Generally, in this methodology, the chain ends of many linear macroinitiators, which are formed from a number of CRP methods, are used to polymerize a divinyl compound, typically divinylbenzene (DVB) **(Scheme 1.8).**

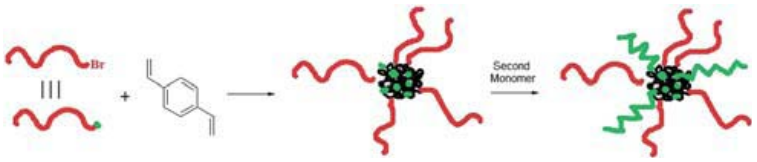


Scheme 1.8: General synthesis of a miktoarm polymer by the ‘‘arm-first’’method[82]

Many polymers were used to initiate this polymerization in a one-pot fashion to yield miktoarm stars in high yields. The final miktoarm polymer consisted of a crosslinked microgel core composed of DVB, which ties together the many polymer arms that initiated the DVB polymerization, with the polymers emanating outwards.

1.5.1.4. In–out method

The ‘‘in–out’’ method of miktoarm polymer synthesis can be seen as a cross between the ‘‘core-first’’ and ‘‘arm-first’’ methodologies. Here, a ‘‘living’’ macroinitiator (typically made by CRP methods such as ATRP) initiates the polymerization of a crosslinking agent (such as DVB) to form a homoarm star polymer with polymer arms emanating from the core. As initiating sites in macroinitiator are preserved within the core, these initiating sites can be used for subsequent polymerization of a second type of monomer to produce a miktoarm star **(Scheme 1.9).**



Scheme 1.9: General synthesis of a miktoarm star by the ‘‘in–out’’ method[82]

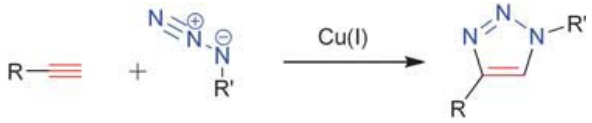
Unlike the ‘‘core-first’’ or ‘‘arm-first’’ technique, only AnBm-type miktoarm polymers can be built, i.e., only two types of polymer arms can exist in a miktoarm star polymer synthesized by the ‘‘in–out’’ technique[90, 91].

1.5.1.5. Coupling method

Coupling methods have become very widespread for the synthesis of miktoarm polymers in the past decade due to facile synthetic methodologies that have become available, and as these methods help to ensure the overall integrity of the final structure[92]. This method is highlighted by coupling of the reactive end of at least one polymer arm to a multifunctional core

using highly efficient and orthogonal reactions. The remaining arms on a miktoarm polymer are typically grown using CRP methods,

and often by ROP, living anionic polymerization, etc. The popularity of the coupling methods can partially be attributed to the rising popularity of ‘‘click’’ chemistry in macromolecular synthesis[93]. ‘‘Click’’ reactions are characterized by many features that lend themselves to macromolecular synthesis, such as simple reaction conditions, orthogonality to a variety of functional groups, simple workups, relatively simple purifications, insensitivity to different solvents, and high yields. Many different ‘‘click’’ reactions have been used to this end, such as thiol–ene[94] and Diels–Alder[95]. The most popular reaction, the so called ‘‘cream of the crop’’ is the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of an azide to an alkyne to yield a 1,2,3-triazole ring[96] **(Scheme 1.10).** This specific ‘‘click’’ reaction has found widespread use throughout the synthesis of miktoarm polymers through a coupling strategy.



Scheme 1.10: The azide–alkyne Huisgen cycloaddition, a 1,3-dipolar cycloaddition which yields a 1,2,3-triazole ring[82]

1.6. Concluding remarks

The ground-breaking discovery of living anionic polymerization by Szwarc in the year 1956 opened the route to the synthesis of model macromolecules and inspired polymer chemists to develop controlled/living routes for a range of monomers. These methods and their combinations serve as powerful tools for the synthesis of well-defined polymeric materials with predetermined properties and a rich variety of applications.

The advent of controlled radical polymerization methods, which include NMP, ATRP and RAFT, has further opened up new avenues to various advanced materials with precisely controlled molecular architectures. Of the various controlled radical polymerization methods, ATRP is very robust and versatile synthetic technique. ATRP allows preparation of molecular brushes, stars, multisegmented block copolymers, and end functional polymers with high chain end fidelity and precisely controlled structure.

Owing to the remarkable properties of biodegradable aliphatic polyesters, which are obtained by ROP of cyclic monomers such as ε-caprolactone, increasing attention has been paid to their development over the last few decades. Aliphatic polyesters with functional groups are of importance in order to anchor the active agent to polymer structures by means of physical interactions or by covalent linkages, and hence the functionalization of aliphatic polyester becomes a topic of great interest.

Miktoarm polymers are a relatively new and unique class of macromolecules, and constitute a contemporary area of research due to their intriguing properties. Much emphasis has been placed in the recent past in developing synthetic methodologies to these star polymers, and examining their self-assembly in solution. Not only has controlled radical polymerizations found increasingly widespread use in miktoarm polymer synthesis in recent years, but also has ‘‘click’’ chemistry due to its efficiency, orthogonality to other functional moieties present, simple workup, and compatibility with controlled radical polymerizations techniques. Nonetheless, careful design of synthetic protocols has been highly beneficial, as increasingly complicated miktoarm polymers are easier to build now than they were ten or fifteen years ago.

Precisely controlled synthesis of (co)polymers with designed complex architectures has enabled preparation of many advanced materials with new targeted properties that already have found or will soon find applications of commercial relevance.

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Chapter 2

Scope and Objectives

2.1. Scope and Objectives

Controlled synthesis of polymers with well-defined end groups and various architectures continues to be a synthetic challenge in polymer chemistry. End-functionalized polymers are important precursors for synthesis of block copolymers, graft copolymers, star-branched and networked structures[1-4]. End-functional polymers have potential applications in areas such as surface modification, coatings, adhesives, as well as compatibilization of polymer blends[5, 6].

Miktoarm star copolymers are promising materials for widespread applications due to their self-assembly properties[7] either in the solid state or in a selective solvent of one block,[8] which provides a great variety of morphologies in the nanometer size range.[9-13] The multifaceted role played by these materials make them useful as compatibilizers, viscosity modifiers, dispersants to stabilize colloidal suspensions, nanocarriers for the encapsulation[14, 15] and controlled release of drugs and templates for mineralization and supports for catalysis.[16-18] These polymers also find applications in areas such as thermoplastics,[19, 20] associative polymers containing hydrophilic and hydrophobic segments[12], etc.

A wide range of controlled polymerization techniques are available for synthesis end-functionalized polymers.[10, 21-23]. The term controlled polymerization introduced by A. Muller and K. Matyjaszewski[24] can be defined as a synthetic method to prepare polymers, which are well defined with respect to topology, terminal functionality, composition, and arrangement of comonomers and which have molecular weights predetermined by the ratio of concentration of reacted monomer to introduced initiator as well as designed molecular weight distribution. During the last two decades, Atom Transfer Radical Polymerization (ATRP) has been developed as one of the most successful controlled polymerization techniques to polymerize (meth) acrylates, styrene or substituted styrenes and a variety of other monomers, yielding polymers with predetermined molecular weight and designed molecular weight distribution[25, 26]. There are several advantages of ATRP over other controlled polymerization methods such as reversible-addition fragmentation termination (RAFT),[27] nitroxide mediated polymerization (NMP),[28, 29] anionic,[30] cationic[31] and group transfer polymerization (GTP)[32]. One of the notable advantages of ATRP is that a wide range of functional groups can be introduced in polymers using appropriate functional initiator[33]. A large number of ATRP initiators possessing functional groups such as hydroxyl[34], azide[35], acid[36], pyrrole[37], oxazoline[38], pyrene[39], bipyridene[40], norbornenyl[41], thiol[42], maleic anhydride[43], epoxy[44], etc. have been reported for synthesis of corresponding functional polymers at one chain end and halide at the other chain end. The halide end group of polymers obtained *via* ATRP can be transformed to other useful functionalities using nucleophilic substitution reactions or electrophilic addition reactions.[45]

Ring opening polymerization (ROP) is a polymerization technique by which strained

cyclic monomers such as ε-caprolactone (ε-CL), lactide (LLA) and glycolide (GA) can be ring opened. Aliphatic polyesters occupy a key position in the field of polymer science because they exhibit the remarkable properties of biodegradability and biocompatibility, which opens up a wide range of applications as environmentally friendly thermoplastics and biomaterials[46]. The absence of any functional groups limits aliphatic polyesters from many potential applications. Now-a-days, significant efforts have been devoted to synthesis of different types of functional aliphatic polyesters in order to anchor the active agent to polymer structures by means of physical interactions or by covalent linkages, and hence the functionalization of aliphatic polyesters becomes a topic of great interest [47].

With the advent of click chemistry by Sharpless and co-workers [48] in 2001, many academic and industrial scientists have widely explored this innovative approach for various research areas as a result of its versatility, efficiency and inertness towards functional groups[49, 50].

The overall objective of the work was to design and synthesize new macromolecular architectures employing controlled polymerization methods and their structural characterization by spectroscopic techniques. In this context, it was of interest to design and synthesize new initiators containing different functional groups for ROP and ATRP as well as different multifunctional initiator (MFI) cores possessing different types and specific number of initiating sites for preparation of miktoarm copolymers. Commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid, which in turn is derived from levulenic acid –a platform chemical obtained from biomass- and 5-hydroxy isophthalic acid were used as the starting materials. Both 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid contain phenolic and acid functional groups, which were effectively utilized in various aspects of chemical transformations for synthesis of the desired ROP and ATRP initiators as well as different MFI cores.

The first objective of the research programme was to develop a general methodology that would allow the introduction of various functional groups into initiators for ROP as well as for ATRP. Towards this end, allyloxy, propargyloxy, azido, and aldehyde functionalities were introduced. The second goal of the present study was to synthesize different end-functionalized poly ε-caprolactones and poly ε-caprolactone macromonomers by ROP. ATRP technique was used to synthesize end-functionalized poly (methyl methacrylate) / polystyrene and poly (methyl methacrylate) / polystyrene macromonomers making use of appropriate ATRP initiators. The further objective of this work was to utilize core-first approach to prepare miktoarm copolymers. Towards this end, different MFI cores possessing different types and specific number of initiating sites for preparation of AB_2-type PCL-$(PS)_2$, A_2B-type $(PCL)_2$-PS, A_2B_2-type $(PCL)_2$-$(PMMA)_2$, ABC-type PCL-PEG-PS and A_3B-type $(PCL)_3$-(PMMA) miktoarm copolymers were synthesized. Another strategy used for synthesis of

miktoarm copolymers such as $(PCL)_2$-PEG or PCL-$(PEG)_2$, $(PCL)_2$-PLLA was coupling onto approach wherein specifically placed functionalities on the prepolymers were used to couple different types of polymer arms. Based on these objectives, the following specific work was chosen for the present thesis.

1. To design and synthesize new initiators containing various functional groups such as allyloxy, propargyloxy, azido, and aldehyde for ROP.
2. To design and synthesize new initiators containing various functional groups such as allyloxy, propargyloxy, azido, and aldehyde for ATRP.
3. To utilize functionalized ROP initiators for the synthesis of α, α'-homobifunctional poly **ε**-caprolactones containing allyloxy, aldehyde, propargyloxy, and azido functional groups and α, α'- heterobifunctional poly **ε** -caprolactones containing allyloxy-aldehyde, allyloxy-azido, and azido-aldehyde functional groups and to study reactivity of the functional groups by carrying out specific reactions related to that particular functional group.
4. To utilize functionalized ATRP initiators for the synthesis of α, α'-homobifunctional poly (methyl methacrylate)s possessing allyloxy, propargyloxy, and azido functional groups and α, α'-heterobifunctional poly (methyl methacrylate)s containing aldehyde-allyloxy functional groups and to study the reactivity of functional groups by carrying out specific reactions related to that particular functional group.
5. To synthesize α, α'-homobifunctional poly styrene possessing allyloxy, and aldehyde functional groups and to study the reactivity of functional groups by carrying out specific reactions related to that particular functional group.
6. To design and synthesize new MFI cores comprising of different types and specific number of initiating sites viz., AB_2, A_2B, A_2B_2, A_3B, and ABC for preparation of miktoarm copolymers.
7. To utilize synthesized MFI cores for the synthesis of AB_2–type (PCL)-$(PS)_2$ or A_2B-type $(PCL)_2$-(PS), A_2B_2-type $(PCL)_2$-$(PMMA)_2$, A_3B-type $(PCL)_3$-PMMA, and ABC-type PCL-PEG-PS mikto arm star copolymers.
8. To synthesize $(PCL)_2$-PEG or PCL-$(PEG)_2$, $(PCL)_2$-PLLA copolymers utilizing coupling onto approach.

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Chapter 3

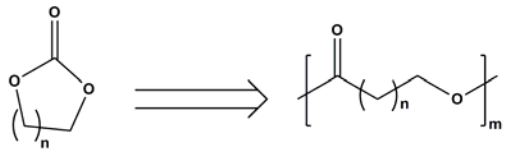
Functional Initiators: Synthesis and Characterization

Chapter 3a
Functional Initiators for ROP: Synthesis and Characterization

3a.1. Introduction

Aliphatic polyesters such as poly ε-caprolactone (PCL), poly lactic acid (PLA), and poly glycolic acid (PGA), occupy a key position in the field of polymer science because they exhibit the remarkable properties of biodegradability and biocompatibility, which opens up a wide range of applications as environmentally friendly thermoplastics and biomaterials[1]. The hydrolytical degradation, coupled with favorable mechanical properties accounts for the use of these materials in temporary medical devices. The absence of functional groups limits aliphatic polyesters from many probable applications. Now-a-days, significant efforts have been devoted to synthesis of different types of functional aliphatic polyesters in order to anchor the active agent to polymer structures by means of physical interactions or by covalent linkages, and hence the functionalization of aliphatic polyesters becomes a topic of great interest [2]. Three different mechanisms of polymerization can be implemented to synthesize aliphatic polyesters: (1) ROP of cyclic ketene acetals 2) step-growth polymerization and (3) ROP of lactones.

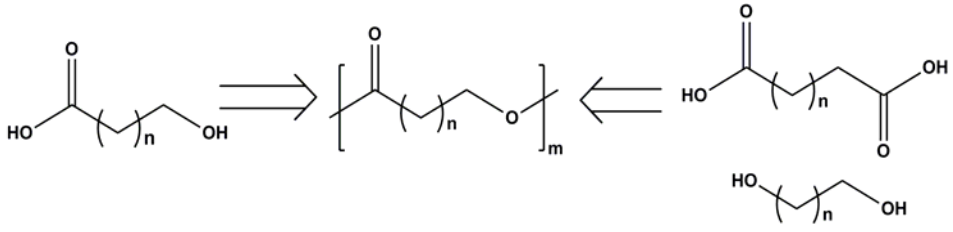
The first approach is based on ring opening of cylic ketene acetals[3-5], **(Scheme 3a.1)** where electron rich double bond is prone to react with radicals and electrophiles. Therefore, this class of monomers can undergo polymerization by radical or cationic polymerization.



Scheme 3a.1: Synthesis of aliphatic polyesters from cyclic ketene acetal[1]

Although this approach has been known for a long time, its development remained limited, most probably due to the low selectivity of the polymerization and to the difficult synthesis of this class of monomers[3]. Nevertheless, it is worth noting the unusual low crystallinity of aliphatic polyesters synthesized by the ROP of cyclic ketene acetals due to a high content of branching[6, 7] .

The second approach is step-growth polymerization which is far more used than the ROP of cyclic ketene acetals. The step-growth polymerization relies on the esterification reaction of diacids and diols or, more directly, on the esterification of hydroxy-acids **(Scheme 3a.2).** A main advantage of this technique is the easy availability of a very wide range of acid and alcohol precursors of aliphatic polyesters.



Scheme 3a.2: Synthesis of aliphatic polyesters by step-growth polymerization[1]

However, this polymerization presents severe limitations. It is mandatory to reach conversion very close to 100% for high degree of polymerization. The esterification reaction has to be carried out at high temperature. Moreover, it is also difficult to predetermine the molar mass, and its polydispersity index is quite broad. Although some important progress has been made, the synthesis of aliphatic polyesters with a high molar mass is still challenging.

All these limitations were overcome by implementing a third approach based on the ROP of lactones[8, 9]. High molar mass aliphatic polyesters with low polydispersity indices can thus be synthesized. The most typical lactones are ε-caprolactone (ε-CL) and γ̃-butyrolactone, whose polymerization was reported in 1934 by Carothers[10] **(Figure 3a.1)**.

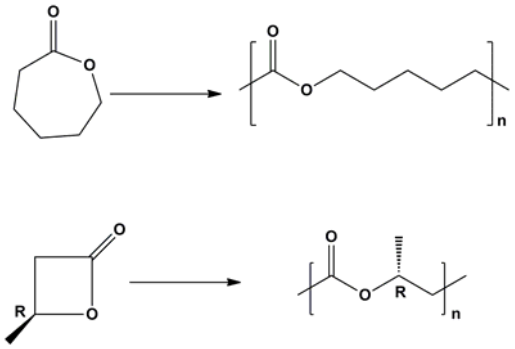


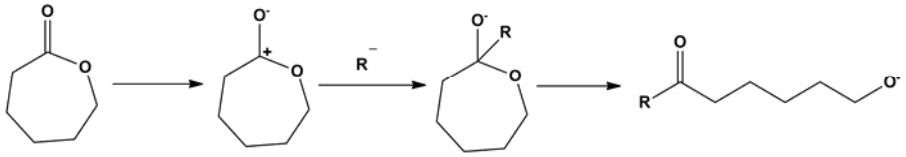
Figure 3a.1: Polymerization of ε-caprolactone and γ̃-butyrolactone[1]

3a.1.1. General mechanism of polymerization of lactones by ring opening

Four main mechanisms for the ROP of lactones exist, and they depend on the catalyst: anionic, cationic, monomer-activated and coordination– insertion ROP[11].

3a.1.1.1. Anionic ROP of ε-caprolactone

Anionic ROP **(Scheme 3a.3)** involves the formation of an anionic species which attacks the carbonyl carbon of the monomer.

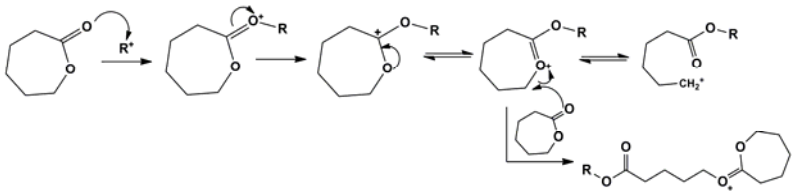


Scheme 3a.3: Mechanism for anionic ROP of ε-caprolactone[1]

The monomer is opened at the acyl–oxygen bond and the growing species is an alkoxide[12]. The main drawback of this method is the occurrence of significant intramolecular transesterification, also called ‘‘back-biting’’, in the later stages of the polymerisation. This results either in low molecular weight polymers, if the polymerisation is stopped before back-biting can occur, or in cyclic polymers.

3a.1.1.2. Cationic ROP of ε-caprolactone

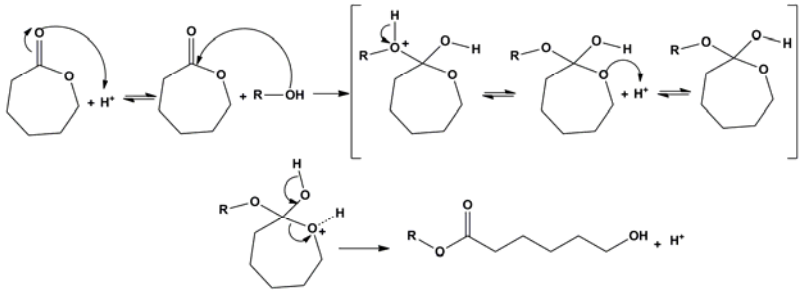
Cationic ROP **(Scheme 3a.4)** involves the formation of a cationic species which is attacked by the carbonyl oxygen of the monomer through a bimolecular nucleophilic substitution (SN^2) reaction[13].



Scheme 3a.4: Mechanism for cationic ROP of ε-caprolactone[1]

***3a.1.1.3. Monomer-activated ROP of* ε-caprolactone.**

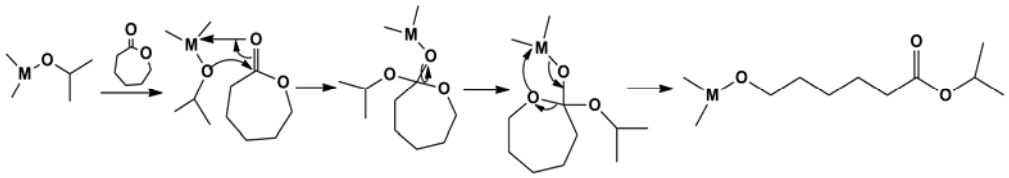
Monomer activated ROP **(Scheme 3a.5)** involves the activation of the monomer molecules by a catalyst, followed by the attack of the activated monomer onto the polymer chain end[14, 15].



Scheme 3a.5: Mechanism for monomer activated ROP of ε-caprolactone[1]

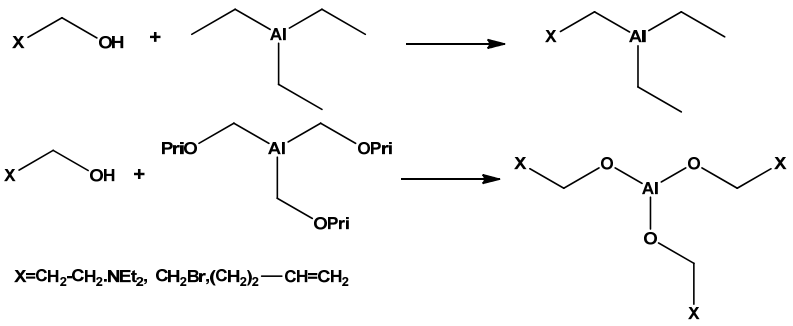
***3a.1.1.4. Coordination ROP of* ε-caprolactone**

In order to impart a better control of the polymerization, less reactive and thus more selective organometallic derivatives of metals with d-orbitals of favorable energy were substituted for anionic initiators [16]. The first work was carried out by Teyssie´ and coworkers using bimetallic μ-oxo-alkoxides[17, 18] **(Scheme 3a.6).**



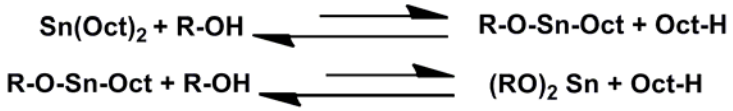
Scheme 3a.6: Mechanism for coordination-insertion ROP of ε-caprolactone[1]

Control of the ROP of lactones was improved by using aluminum alkoxides instead of their anionic counterpart, as witnessed by the increase of the selectivity factor in the case of the polymerization of ε-CL. The lower reactivity of aluminum alkoxides compared to their anionic counterparts is shown by the decrease in the rate of propagation of the polymerization (Kp). A wide range of aluminum alkoxides can easily be synthesized by the reaction of alcohols with triethylaluminum. These alcohols can even be substituted by compatible functional groups such as bromides, olefins, and tertiary amines **(Scheme 3a.7)** [19, 20]. An alternative route towards aluminum alkoxides relies on the reaction of the alcohols with aluminum isopropoxide in toluene. Isopropanol formed during this reaction is withdrawn by the distillation of the azeotrope made up of toluene and isopropanol.



Scheme 3a.7: Synthesis of functionalized aluminium alkoxides[1]

Currently, tin (II) (2-ethylhexanoate), also referred as tin octoate, is the most widely used catalyst for ROP of lactones. The popularity stems from its acceptance by the American Food and Drug Administration (FDA) for the formulation of polymer coatings in contact with food. Moreover, tin octoate is less sensitive towards water and other protic impurities than aluminum alkoxides, which facilitates its use in the laboratory and in industry. The mechanism of the tin octoate -mediated ROP of lactones remained a matter of controversy for many years, and many different mechanisms were proposed. Indeed, tin octoate is not made up of alkoxides but of carboxylates, known as poor initiators for the ROP of lactones. Penczek and coworkers[9] made a major contribution in this field. They reported that, if the polymerization is carried out in THF at 80 °C, then tin octoate is converted *in situ* into a new tin alkoxide by the reaction with either an alcohol, purposely added in the reaction medium, or with any other protic impurity present **(Scheme 3a.8)**[21].

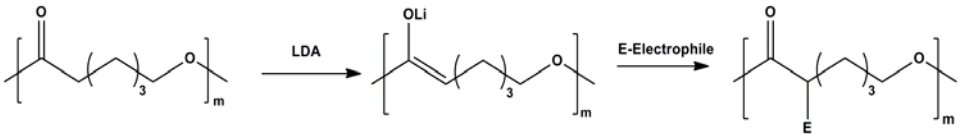


Scheme 3a.8: Initiation of the ROP of lactones by tin octoate[1]

Tin alkoxides formed *in situ* are the real initiators of the polymerization, which takes place according the usual insertion–coordination mechanism.

3a.1.2. Functional aliphatic polyesters

Aliphatic polyesters with functional group are of importance in order to anchor the active agent to polymer structures by means of physical interactions or by covalent linkages, and hence the functionalization of aliphatic polyester becomes a topic of great interest[2].Recently, two main strategies have been reported for the synthesis of functional group containing aliphatic polyesters[22]. In the first approach, PCL is reacted with lithium amides for the formation of a poly(enolate), which is then reacted with an appropriate electrophile[23]**(Scheme 3a.9).**



Scheme 3a.9: Schematic representation of functionalization of polyesters by enolate formation route[1]

The problem is the unavoidable degradation of the polyester chains by the nucleophilic sites.The second strategy relies on the ROP of α-or γ- substituted caprolactone **(Figure 3a.2),** mainly in γ-position, by various functional groups, e.g. acrylate[24], protected carboxylic acid [25, 26], protected alcohol [27, 28] , ketal [29], ketone [30] and halogen [31, 32].

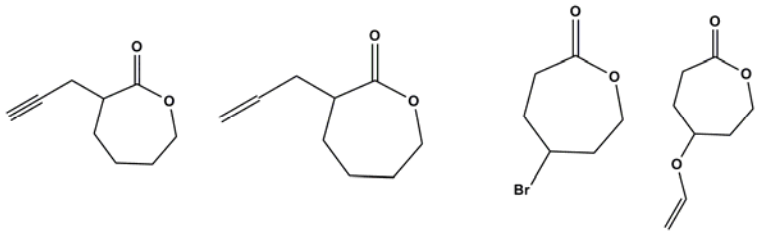


Figure 3a.2: Representative examples of functional monomers

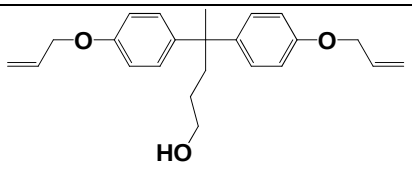
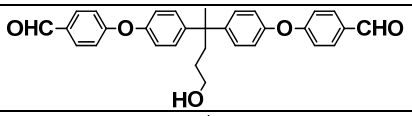
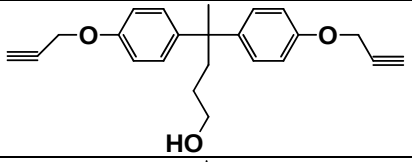
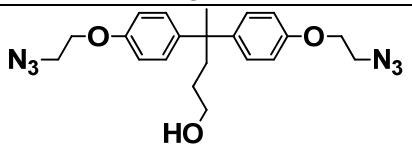
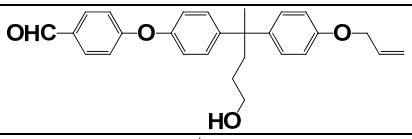
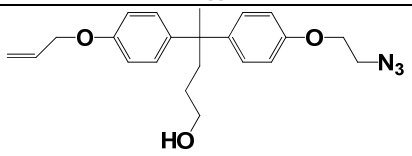
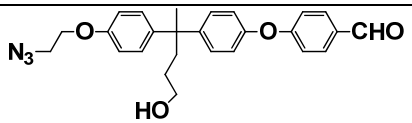
A limitation may, however, be found in the limited yield of a multi-step process. Moreover, aluminum and tin alkoxide-mediated ROP is not tolerant of hydroxyl, carboxylic acid and epoxy groups. In these specific cases, hydroxyl and carboxylic acid groups must be protected before ROP and deprotected afterwards, whereas post-polymerization epoxidation has to be considered for grafting epoxides along the chains[33-35].For all these reasons, straightforward strategies are highly desirable to prepare aliphatic polyesters with pendant hydroxyl, carboxylic acid and epoxide groups, respectively. α, ω, as well as γ-Functionality could be introduced on polycaprolactone using different approaches. α-Functionality can be introduced in a controlled way by the use of functional aluminium alkoxide initiators prepared by reaction of triethylaluminium ($AlEt_3$) with an alcohol[36, 37]. In addition, functional initiators have been synthesized through the exchange of the alkoxy group of (Al $(O^iPr)_3$) with the desired functional alcohol[38].

End functionalization of polycaprolactones with different functionalities has been demonstrated using initiation and termination reaction by Iversen et al.[39]. Alternatively, Jerome and coworkers[34] demonstrated that ω-hydroxy functionality could be introduced *via* coordination-insertion mechanism of the polymerization initiated by aluminium tri isopropoxide (Al $(O^iPr)_3$). End group modification of ω-hydroxy functionality was also demonstrated by Hedrik and coworkers[40]. Using aluminium alkoxide mediated ROP of γ-functional monomers, Hilborn et al.[41] reported γ-functionalized poly ε-caprolactone. To date, chain end functionalized aliphatic polyesters with allyl[35, 37, 39], amino[42], thiol[38, 43, 44], hydroxyl, carboxyl, epoxy[45], propargyl[46], etc either through post modification of polyesters or *via* use of functional initiators have been reported in the literature.

The present chapter deals with synthesis and characterization of seven functionalized ROP initiators **(Table 3a.1)** starting from common precursor 4,4'-bis (4-hydroxyphenyl) pentanoic acid, which in turn is derived from levulinic acid –a platform chemical obtained from biomass. 4, 4'-Bis (4-hydroxyphenyl) pentanoic acid contains acid and phenolic groups, which were effectively utilized in various aspects of chemical transformations for synthesis of the desired ROP initiators. Thus, α, α'-homo bifunctionalized initiators possessing allyloxy,

aldehyde, propargyloxy, and azido and α, α'-hetero bifunctionalized initiators featuring allyloxy-aldehyde, allyloxy-azido, and azido-aldehyde functional groups were synthesized. Consideration was given to the fact that functional groups present in the initiators are compatible under typical ROP conditions of ε-caprolactone. The choice of functional groups was made by taking into account their ability to participate in various efficient organic transformations including different types of "click" reactions. For example, allyloxy group could undergo thiol-ene reaction, while azido and propargyloxy group could take part in the well-known azide-alkyne click reaction. The rationale behind introduction of aldehyde group is that it could be further utilized in chemical modification by metal-free aldehyde-aminooxy click reaction.

Table 3a.1: Functionalized ROP initiators

Sr. No.	Name of Initiator	Structure
1	4,4'-Bis(4-(allyloxy)phenyl)pentan-1-ol	
2	4,4'-(((5-Hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde	
3	4,4'-Bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol	
4	4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentan-1-ol	
5	4-(4-(2-(4-(Allyloxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde	
6	4-(4-(Allyloxy)phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol	
7	4-(4-(2-(4-(2-Azidoethoxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde	

3a.2. Experimental

3a.2.1. Materials

4, 4'-Bis (4-hydroxyphenyl) pentanoic acid, lithium aluminium hydride (LAH), 4-fluoro benzaldehyde, 2-chloroethanol, and *p*-toluene sulphonyl chloride (Aldrich), were used as received. Allyl bromide, and propargyl bromide were distilled prior to the use. Tetrahydrofuran (S.D. Fine-Chem) was stirred over calcium hydride for 12 h, filtered and distilled. Further, it was refluxed over sodium-benzophenone complex for 2 days, distilled and used. Dichloromethane (S.D. Fine-Chem) was stirred over calcium hydride and distilled before use. Triethyl amine and pyridine were stirred over sodium hydroxide, distilled and stored over sodium hydroxide. Sodium sulphate, potassium hydroxide, sodium hydrogen carbonate, sodium azide, bromine, methanol, sulphuric acid and chloroform, all received from S.D. Fine-Chem. Ltd., India were used as received.

3a.2.1.1. Synthesis of 2-azidoethyl 4-methylbenzenesulfonate

3a.2.1.1.1. Synthesis of 2-azidoethanol

Into a 1L two necked round-bottom flask equipped with a dropping funnel were charged, 2-chloroethanol (20 g, 250 mmol) and water (250 mL). The reaction mixture was stirred for 20 minutes. The solution of sodium azide (80 g, 1250 mmol) in water (350 mL) was added dropwise over a period of 30 minutes. The reaction mixture was refluxed for 8 h, allowed to attain room temperature and then extracted with ethyl acetate (3 x 250 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and ethyl acetate was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as an eluent. The removal of the solvent yielded 18.0 g (89 %) of 2-azidoethanol as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2108

^1H NMR ($CDCl_3$, δ/ppm): 3.73 (t, 2H), 3.39 (t, 2H), 2.87(bs, 1H).

3a.2.1.1.2. Synthesis of 2-azidoethyl 4-methylbenzenesulfonate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2-azidoethanol (9.0 g, 103 mmol), pyridine (8.13 g, 103 mmol), and dry dichloromethane (70 mL). The reaction mixture was cooled to 0 °C. The solution of *p*-toluenesulphonylchloride (19.63 g, 103 mmol) in dry chloroform (50 mL) was added drop-wise under constant stirring at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature overnight. The reaction mixture was washed with 5% $NaHCO_3$ (3 x 100 mL) and water (3 x 100 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and chloroform was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (10:90, v/v) as eluent. The removal of the solvent yielded 23.50 (95 %) of 2-azidoethyl 4-methylbenzenesulfonate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 2110

^{1}H NMR ($CDCl_3$, δ/ppm): 7.72 (d, 2H), 7.29 (d, 2H), 4.07 (t, 2H), 3.39 (t, 2H), 2.37 (s, 3H).

3a.2.2. Characterization and measurements

FTIR spectra were recorded on a Perkin-Elmer Spectrum *GX* spectrophotometer in chloroform.NMR spectra were recorded on a Bruker 200 MHz spectrometer at resonance frequencies of 200 MHz for ^{1}H-NMR and 50 MHz for ^{13}C-NMR measurements using $CDCl_3$ or DMSO-d_6 as a solvent. ESI-MS were obtained using an API-Q-Star Applied Biosynthesis spectrometer. Elemental analyses were carried out on a Carlo Erba CHNS-O analyzer.

3a.3. Synthesis

3a.3.1. Synthesis of 4, 4'-bis (4-(allyloxy)phenyl)pentan-1-ol

3a.3.1.1. Synthesis of methyl 4, 4' –bis (4-hydroxyphenyl) pentanoate

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4'-bis (4-hydroxyphenyl) pentanoic acid (20 g, 70 mmol), and methanol (300 mL). The reaction mixture was stirred for 15 minutes, followed by addition of concentrated sulphuric acid (1 mL). The reaction mixture was refluxed for 8 h. Methanol was removed under reduced pressure and ethyl acetate (300 mL) was added to the reaction mixture. The ethyl acetate solution was washed with saturated brine solution (3x50 mL) and dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (50:50, v/v) as eluent to afford 19 g (90 %) of methyl 4, 4' –bis (4-hydroxyphenyl) pentanoate.

IR ($CHCl_3$, cm^{-1}): 3150, 1730

^{1}H NMR (DMSO-d_6 δ/ppm): 9.24 (s, 2H, phenolic OH), 6.97 (d, 4H, Ar-H *meta* to phenolic OH), 6.69 (d, 4H, Ar-H *ortho* to phenolic OH), 3.53 (s, 3H, OCH_3), 2.31-2.23 (m, 2H, -CH_2-CH_2), 2.08-2.01 (m, 2H, -CH_2-CH_2), 1.47 (s, 3H, -CH_3).

3a.3.1.2. Synthesis of methyl 4, 4'–bis (4-(allyloxy) phenyl) pentanoate

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, methyl 4, 4'–bis (4-hydroxyphenyl) pentanoate (18 g, 60 mmol), K_2CO_3 (12.3 g, 90 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of allyl bromide (18.1 g, 150 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), water (2 x 50 mL), and dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 21.7 g (95 %) of methyl 4, 4'–bis (4-(allyloxy) phenyl) pentanoate as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 1730, 1250

^{1}H NMR ($CDCl_3$, δ/ppm): 7.11 (d, 4H, Ar-H *meta* to ether linkage), 6.84 (d, 4H, Ar-H *ortho* to ether linkage), 6.11-5.97 (m, 2H, CH =CH-), 5.43 (q, 4H, C=CH_2), 4.52 (d, 4H, O-CH_2),

3.61 (s, 3H, OCH_3), 2.42-2.36 (m, 2H, $-CH_2-CH_2$), 2.12-2.06 (m, 2H, $-CH_2-CH_2$), 1.57 (s, 3H,$-CH_3$).

3a.3.1.3. Synthesis of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol

Into a 250 mL two necked round-bottom flask equipped with a reflux condenser and a dropping funnel were charged, LAH (5.6 g, 160 mmol) and dry THF (100 mL). The solution of methyl 4, 4'–bis (4-(allyloxy) phenyl) pentanoate (16 g, 42 mmol) in dry THF (40 mL) was added over a period of 30 minutes. Effervences were observed during the addition. Reaction mixture was refluxed for 8 h, cooled and then moist sodium sulfate was added to deactivate LAH. The reaction mixture was filtered and THF was evaporated. The precipitate was dissolved in dilute HCl (25 mL) and the solution was extracted with ethyl acetate (3 x 50 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), and water (2 x 50 mL). The ethyl acetate layer was separated, dried over sodium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (40:60, v/v) to afford 10.4 g (70 %) of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 1250

^{1}H NMR ($CDCl_3$, δ/ppm): 7.09 (d, 4H, Ar-H *meta* to ether linkage), 6.80 (d, 4H, Ar-H *ortho* to ether linkage), 6.12-5.95 (m, 2H, C=CH-), 5.43-5.24 (m, 4H, $C=CH_2$), 4.49 (d, 4H, $-OCH_2$), 3.58 (t, 2H,$-CH_2OH$), 2.12- 2.06 (m, 2H, $-CH_2$), 1.58 (s, 3H,$-CH_3$), 1.39- 1.31 (m, 2H,$-CH_2$).

^{13}C-NMR ($CDCl_3$, δ/ppm): 156.0, 139.8, 132.4, 128.4, 117.6, 114.3, 72.4, 63.8, 42.5, 42.2, 30.9, 23.5.

3a.3.2. Synthesis of 4, 4'-(5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy)dibenzaldehyde

3a.3.2.1. Synthesis of 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol

Into a 250 mL two necked round-bottom flask equipped with a reflux condenser and a dropping funnel were charged, LAH (5.6 g, 162 mmol) and dry THF (150 mL). The solution of methyl 4, 4' –bis (4-hydroxyphenyl) pentanoate (16.2 g, 54 mmol) in dry THF (50 mL) was slowly added over a period of 30 minutes. Effervesces were observed during the addition. Reaction mixture was refluxed for 8 h, cooled and then moist sodium sulfate was added to deactivate LAH. Dilute HCl (25 mL) was added to dissolve the formed salt and ethyl acetate (250 mL) was added. The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), and water (2 x 50 mL). The ethyl acetate layer was separated, dried over sodium sulfate, filtered and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (40:60, v/v) to afford 10.4 g (71 %) of 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3150

^{1}H NMR (Acetone-d_6, δ/ppm): 8.28 (s, 2H, phenolic OH), 7.05 (d, 4H, Ar-H *meta* to phenolic OH), 6.75 (d, 4H, Ar-H *ortho* to phenolic OH), 3.53 (t, 2H,-CH_2OH), 2.10- 2.06 (m, 2H, -CH_2), 1.56 (s, 3H,-CH_3), 1.39- 1.31 (m, 2H,-CH_2)

3a.3.2.2. Synthesis of 4, 4'-(5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy)dibenzaldehyde

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol (16.3 g, 60 mmol), K_2CO_3 (12.3 g, 90 mmol) and acetone (150 mL) and the reaction mixture was stirred for 10 min. The solution of 4-fluorobenzaldehyde (18.6 g, 150 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure. The product was taken up in ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), and water (2 x 50 mL). The ethyl acetate layer was separated, dried over sodium sulfate, filtered and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 23 g (80 %) of 4,4'-(4,4'-(5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy)dibenzaldehyde as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3150, 1710

^{1}H- NMR ($CDCl_3$, δ/ppm): 9.85 (s, 2H, aldehyde), 7.79 (d, 4H, Ar-H *ortho* to aldehyde), 7.18 (d, 4H, Ar-H *ortho* to ether linkage), 6.98-6.91 (m, 8H, Ar-H *ortho* to ether linkage and *meta* to ether linkage), 3.60 (t, 2H,-CH_2OH), 2.17- 2.06 (m, 2H, -CH_2), 1.62 (s, 3H,-CH_3), 1.39-1.31 (m, 2H,-CH_2)

^{13}C-NMR ($CDCl_3$, δ/ppm): 191.4, 162.4, 154.7, 140.2, 139.8, 131.4, 130.4, 129.7, 126.9, 122.5, 118.3, 114.9, 63.8, 42.5, 42.2, 30.7, 23.8

3a.3.3. Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol (16.3 g, 60 mmol), K_2CO_3 (12.3 g, 125 mmol) and dry acetone (150 mL). The reaction mixture was stirred for 10 minutes. The solution of propargyl bromide (14.75 g, 125 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL) and water (2 x 50 mL). The ethyl acetate layer was dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 19.4 g (93 %) of 4,4'-bis(4-(prop-2-yn-1-yloxy) phenyl)pentan-1-ol as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2123, 1250.

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.10 (d, 4H, Ar-H *meta* to ether linkage), 6.86 (d, 4H, Ar-H *ortho* to ether linkage,), 4.65 (d, 4H, O-CH_2), 3.59 (t, 2H, O-CH_2), 2.51 (t, 2H, acetylene proton), 2.13-2.06 (m, 2H, -CH_2-CH_2), 1.58 (s, 3H, -CH_3), 1.39-1.30 (m, 2H, CH_2-CH_2).

^{13}C-NMR ($CDCl_3$, δ/ppm): 156.0, 139.8, 128.2, 114.5, 81.0, 77.8, 69.4, 63.8, 42.5, 42.2, 30.9, 23.5

3a.3.4. Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol **(**15 g, 55 mmol**),** K_2CO_3 **(**15.6 g**,** 115 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of 2-azidoethyl 4-methylbenzenesulphonate (27.7 g, 115 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), and water (2 x 50 mL). The ethyl acetate layer was dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 20.75 g (92 %) of 4,4'-bis(4-(2-azidoethoxy) phenyl)pentan-1-ol as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2108, 1250.

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.04 (d, 4H, Ar-H *meta* to ether linkage), 6.74 (d, 4H, Ar-H *ortho* to ether linkage), 4.05 (d, 4H, O-CH_2), 3.60-3.40 (m, 6H, -OCH_2 +-CH_2N_3), 2.13-2.03 (m, 2H, -CH_2-CH_2), 1.51 (s, 3H, -CH_3), 1.32-1.27 (m, 2H, -CH_2-CH_2).

^{13}C-NMR ($CDCl_3$, δ/ppm): 156.0, 139.5, 128.1, 114.5, 68.5, 63.8, 51.3, 42.5, 42.6, 30.9, 24.2

3a.3.5. Synthesis of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde

3a.3.5.1. Synthesis of 4-(2-(4-(allyloxy) phenyl) 5-hydroxy pentan-2-yl) phenol

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol (16.3 g, 60 mmol), K_2CO_3 (8.1 g, 60 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of allyl bromide (7.25 g, 60 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), water (2 x 50 mL), and dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 15.9 g (85%) of 4-(2-(4-(allyloxy) phenyl)5-hydroxy pentan-2-yl)phenol as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3130, 1250

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.08-6.96 (m, 4H, Ar-H *meta* to ether linkage and Ar-H *meta* to phenol), 6.79-6.66 (m, 4H, Ar-H *ortho* to ether linkage and Ar-H *ortho* to phenol), 6.11-5.97 (m, 1H, CH =CH-), 5.43-5.23 (q, 2H, C=CH_2), 4.49 (d, 2H, O-CH_2), 3.58 (t, 2H, OCH_2), 2.12-2.05 (m, 2H, -CH_2-CH_2), 1.54 (s, 3H,-CH_3), 1.40-1.35 (m, 2H, -CH_2-CH_2).

3a.3.5.2. Synthesis of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4-(2-(4-(allyloxy) phenyl) 5-hydroxy pentan-2-yl) phenol (18.72 g, 60 mmol), K_2CO_3 (8.2 g, 60 mmol) and dry DMF (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of 4-fluoro benzaldehyde (7.45 g, 60 mmol) in DMF (50 mL) was added over a period of 30 minutes. The reaction mixture was heated at 100 °C for 8 h, cooled and filtered. DMF was evaporated under vacuum and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), water (2 x 50 mL), and dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 22.25 g (89 %) of 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxy)pentan-2-yl)phenoxy)
benzaldehyde as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 1715, 1250.

^{1}H-NMR ($CDCl_3$, δ/ppm): 9.91 (s, 1H, CHO), 7.84 (d, 2H, Ar-H *ortho* to aldehyde), 7.25-6.82 (m, 10H, Ar-H), 6.13-5.99 (m, 1H, CH =CH-), 5.45-5.26 (q, 2H, C=CH_2), 4.53 (d, 2H, -OCH_2), 3.63 (t, 2H, OCH_2), 2.16-2.08 (m, 2H, -CH_2-CH_2), 1.64 (s, 3H,-CH_3), 1.46-1.39 (m, 2H, -CH_2-CH_2).

^{13}C-NMR ($CDCl_3$, δ/ppm): 191.4, 162.3, 156.0, 155.6, 154.7, 140.2, 139.8, 139.2, 133.4, 131.4, 130.4, 129.7, 128.1, 126.9, 122.5, 118.3, 114.9, 114.5, 71.7, 63.8, 42.5, 42.2, 30.7, 23.8

3a.3.6. Synthesis of 4-(4-(allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4-(2-(4-(allyloxy) phenyl) 5-hydroxy pentan-2-yl) phenol (18.72 g, 60 mmol), K_2CO_3 (8.2 g, 60 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of 2-azidoethyl 4-methylbenzenesulfonate (14.45 g, 60 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), water (2 x 50 mL), and dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 20.8 g (91%) of 4-(4-(allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2108, 1250.

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.11-7.06 (m, 4H, Ar-H *meta* to ether linkage), 6.80 (d, 4H, Ar-H *ortho* to ether linkage), 6.12-5.98 (m, 2H, CH =CH-), 5.43-5.23 (q, 4H, $C=CH_2$), 4.49 (d, 4H, $O-CH_2$), 4.11 (t, 2H, OCH_2), 3.59-3.54 (m, 4H, OCH_2 and CH_2-N_3), 2.13-2.07 (m, 2H, $-CH_2-CH_2$), 1.58 (s, 3H,$-CH_3$), 1.36-1.31 (m, 2H, $-CH_2-CH_2$).

^{13}C-NMR ($CDCl_3$, δ/ppm): 156.0, 155.4, 139.8, 139.2, 133.4, 128.1, 126.9, 118.3, 114.9, 114.5, 72.4, 68.5, 63.8, 51.3, 42.5, 42.2, 30.7, 23.8

3a.3.7. Synthesis of 4-(4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl)phenoxy)benzaldehyde

3a.3.7.1. Synthesis of 4-(2-(4-(2-azidoethoxy) phenyl) 5-hydroxy pentan-2-yl) phenol

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4, 4' – (5-hydroxypentane-2, 2-diyl) diphenol (16.3 g, 60 mmol), K_2CO_3 (8.1 g, 60 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of 2-azidoethyl 4-methylbenzenesulphonate (14.21 g, 60 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), water (2 x 50 mL), and dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 15.75 g (77 %) of 4-(2-(4-(2-azidoethoxy) phenyl)5-hydroxy pentan-2-yl)phenol as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3120, 2108.

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.11-7.00 (m, 4H, Ar-H *meta* to ether linkage and Ar-H *meta* to phenol), 6.81-6.67 (m, 4H, Ar-H *ortho* to ether linkage and Ar-H *ortho* to phenol), 5.72(bs, 1H, phenolic OH) 4.10 (t, 2H, $O-CH_2$), 3.59-3.54 (m, 4H, OCH_2 and CH_2-N_3), 2.13-2.07 (m, 2H, $-CH_2-CH_2$), 1.76 (bs, 1H, alcoholic OH), 1.58 (s, 3H,$-CH_3$), 1.36-1.31 (m, 2H, $-CH_2-CH_2$).

3a.3.7.2. Synthesis of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2-yl)phenoxy)benzaldehyde

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl) phenol (12 g, 35 mmol), K_2CO_3 (4.8 g, 35 mmol) and DMF (150 mL) and the reaction mixture was stirred for 10 min. The solution of 4-fluorobenzaldehyde (4.35 g, 35 mmol) in DMF (50 mL) was added over a period of 30 minutes. The reaction mixture was heated at 100 °C for 8 h, cooled and filtered. DMF was evaporated under vacuum. The product was taken up in ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL), and water (2 x 50 mL). The ethyl acetate layer was separated, dried over sodium sulfate, filtered and solvent was evaporated under reduced

pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 10.6 g (81%) of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2- yl)phenoxy)benzaldehyde as a thick yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2108, 1715, 1250.

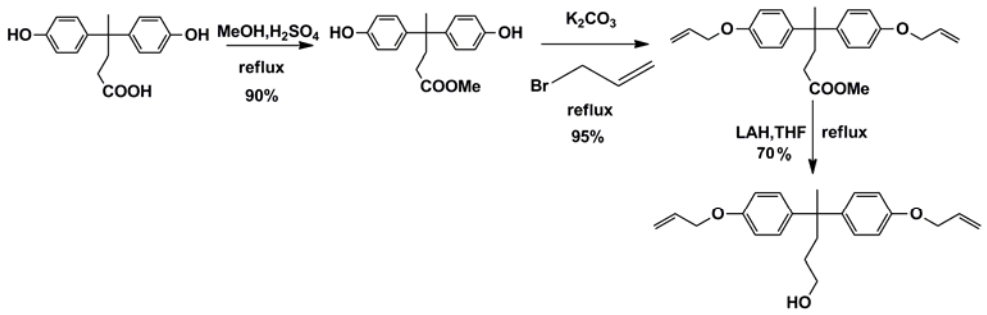
^{1}H-NMR ($CDCl_3$, δ/ppm): 9.91 (s, 1H, CHO), 7.84 (d, 2H, Ar-H *ortho* to aldehyde), 7.25-6.83 (m, 10H, Ar-H), 4.14 (t, 2H, -OCH_2), 3.70-3.50 (m, 4H, CH_2N_3+ CH_2OH), 2.19-2.12 (m, 2H, -CH_2-CH_2), 1.64 (s, 3H,-CH_3), 1.46-1.39 (m, 2H, -CH_2-CH_2).

^{13}C-NMR ($CDCl_3$, δ/ppm): 191.4, 162.3, 156.0, 154.7, 140.2, 139.2, 131.4, 130.4, 127.7, 126.7, 122.3, 118.3, 114.9, 67.7, 63.8, 51.3, 42.5, 42.2, 30.7, 23.8

3a.4. Results and Discussion

3a.4.1. Synthesis of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol

Scheme 3a.10 depicts route for **t**he synthesis of new ROP initiator, namely, 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol. Synthesis of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol was achieved in three steps starting from commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid



Scheme 3a.10: Synthesis of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol

In the first step, 4, 4'-bis (4-hydroxyphenyl) pentanoic acid was esterified using methanol in the presence of a catalytic amount of concentrated sulphuric acid to yield methyl ester of 4, 4'-bis (4-hydroxyphenyl) pentanoic acid. Next, the methyl ester was subjected to allylation reaction using allyl bromide in the presence of K_2CO_3 in acetone to obtain methyl 4, 4'–bis (4-(allyloxy) phenyl) pentanoate. The LAH reduction of 4, 4'–bis (4-(allyloxy) phenyl) pentanoate yielded the corresponding alcohol 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol.

4, 4'–Bis (4-(allyloxy) phenyl) pentan-1-ol and the intermediates involved in its synthesis were purified by silica gel column chromatography and were characterized using FTIR, ^{1}H NMR and ^{13}C NMR spectroscopy. FT-IR spectrum of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol showed absorption band at 3200 cm^{-1} and at 1250 cm^{-1} which correspond to asymmetric stretching of alcohol functionality and to ether linkage, respectively. ^{1}H-NMR spectrum of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol along with assignments is reproduced in **Figure 3a.3.** The aromatic protons *meta* to allyloxy group exhibited as a doublet at 7.09 ppm while aromatic protons *ortho* to allyloxy group appeared as a doublet at 6.80 ppm. The presence of allyloxy functionality was confirmed by the appearance of multiplets in the range

6.12-5.95 ppm, and 5.43-5.24 ppm corresponding to methine and vinyl protons, respectively. The protons of methylene groups attached to oxygen in ether linkage exhibited a doublet at 4.49 ppm. The spectral data corresponding to other protons was in good agreement with the proposed structure.

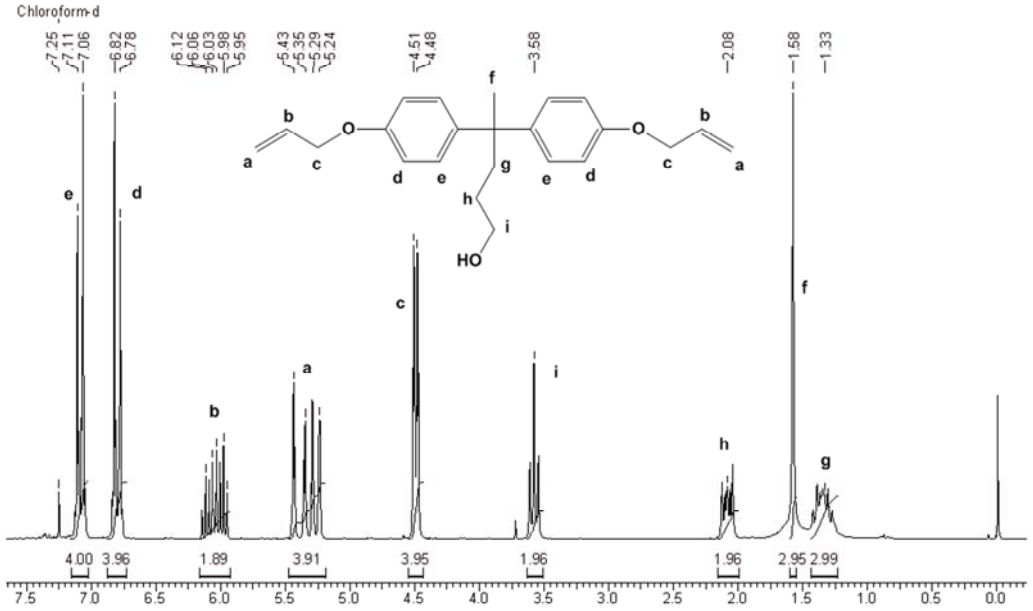
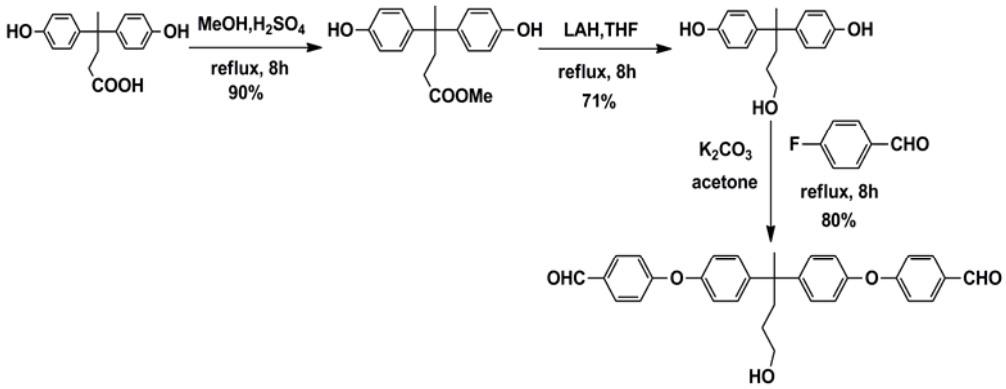


Figure 3a. 3: ^{1}H-NMR spectrum of 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol in $CDCl_3$

In ^{13}C-NMR spectrum, peaks due to allyloxy carbon atoms were observed at 132.4 and 117.6 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3a.4.2. Synthesis of 4, 4'- (((5-hydroxypentane 2, 2-diyl) bis (4,1-phenylene))bis(oxy) dibenzaldehyde

Scheme 3a.11 depicts route for the synthesis of 4, 4'- (((5-hydroxypentane 2, 2-diyl)bis(4,1- phenylene))bis(oxy) dibenzaldehyde. The new initiator was synthesized starting from commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid. In the first step, 4, 4'-bis (4-hydroxyphenyl) pentanoic acid was esterified using methanol to yield methyl ester of 4, 4'-bis (4-hydroxyphenyl) pentanoic acid which on LAH reduction afforded 4, 4'-(5-hydroxypentane-2,2-diyl)-diphenol.



Scheme 3a.11: Synthesis of 4, 4'- (((5-hydroxypentane 2, 2-diyl)bis(4,1-phenylene)) bis(oxy) dibenzaldehyde

The nucleophilic substitution reaction of 4-fluorobenzaldehyde with 4, 4'-(5-hydroxypentane-2,2-diyl)-diphenol in dry DMF using K_2CO_3 as a base yielded 4, 4'- (((5-hydroxypentane 2,2-diyl)bis(4,1-phenylene))bis(oxy) dibenzaldehyde. The product was purified by column chromatography and was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy.

FT-IR spectrum of 4, 4'- (((5-hydroxypentane 2,2-diyl)bis(4,1- phenylene))bis(oxy) dibenzaldehyde showed absorption bands at 3150 cm^{-1} which corresponds to asymmetric stretching of alcohol functionality and at 1710 cm^{-1} that corresponds to aldehyde group, respectively. **Figure 3a. 4** represents ^{1}H-NMR spectrum of 4, 4'- (4,4'-(5-hydroxypentane 2,2-diyl bis(4,1- phenylene)bis(oxy) dibenzaldehyde along with the assignments.

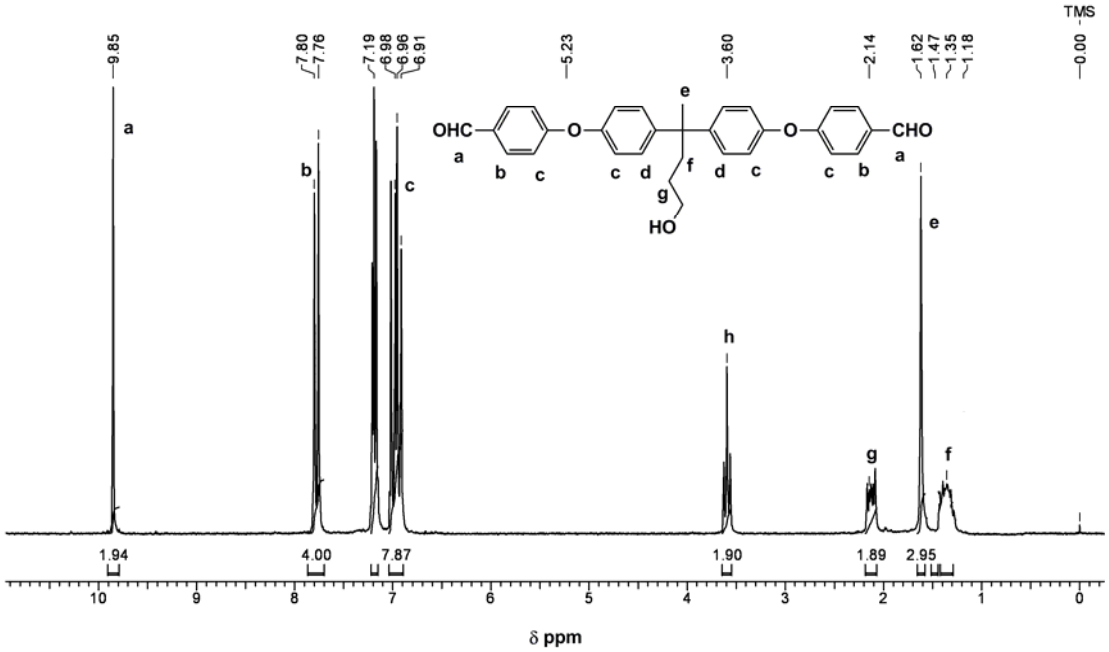
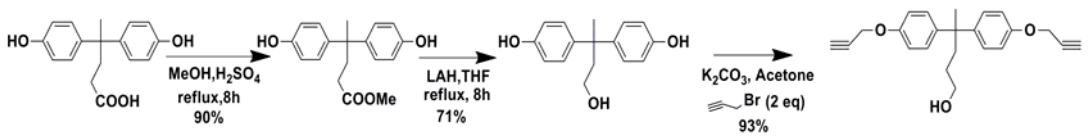


Figure 3a. 4: ^{1}H-NMR spectrum of 4, 4'- (((5-hydroxypentane 2,2-diyl)bis (4,1- phenylene))bis(oxy) dibenzaldehyde in $CDCl_3$

The presence of aldehyde functionality was confirmed by the appearance of a singlet at 9.85 ppm. The aromatic protons *ortho* to aldehyde group were deshielded and appeared as a doublet at 7.79 ppm. The spectral data corresponding to other protons was in good agreement with the proposed structure. In ^{13}C-NMR spectrum, a peak due to aldehyde carbonyl carbon was observed at 191.4 ppm, The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3a.4.3. Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol

Scheme 3a.12 depicts route for the synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol. The new initiator was synthesized starting from methyl ester of 4, 4'-bis (4-hydroxyphenyl) pentanoic acid. The LAH reduction of the methyl ester yielded the corresponding alcohol 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol which was subjected to propargylation reaction using propargyl bromide in the presence of K_2CO_3 in acetone to obtain 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol.



Scheme 3a.12: Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol

4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol and the intermediates involved in its synthesis were purified by silica gel column chromatography and were characterized using FTIR, ^{1}H NMR and ^{13}C NMR spectroscopy. FT-IR spectrum of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol showed absorption bands at 3200 cm^{-1} and 2123 cm^{-1} which correspond to asymmetric stretching of alcohol functionality and propargyloxy functionality, respectively. ^{1}H-NMR spectrum of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol along with assignments is reproduced in **Figure 3a.5.**

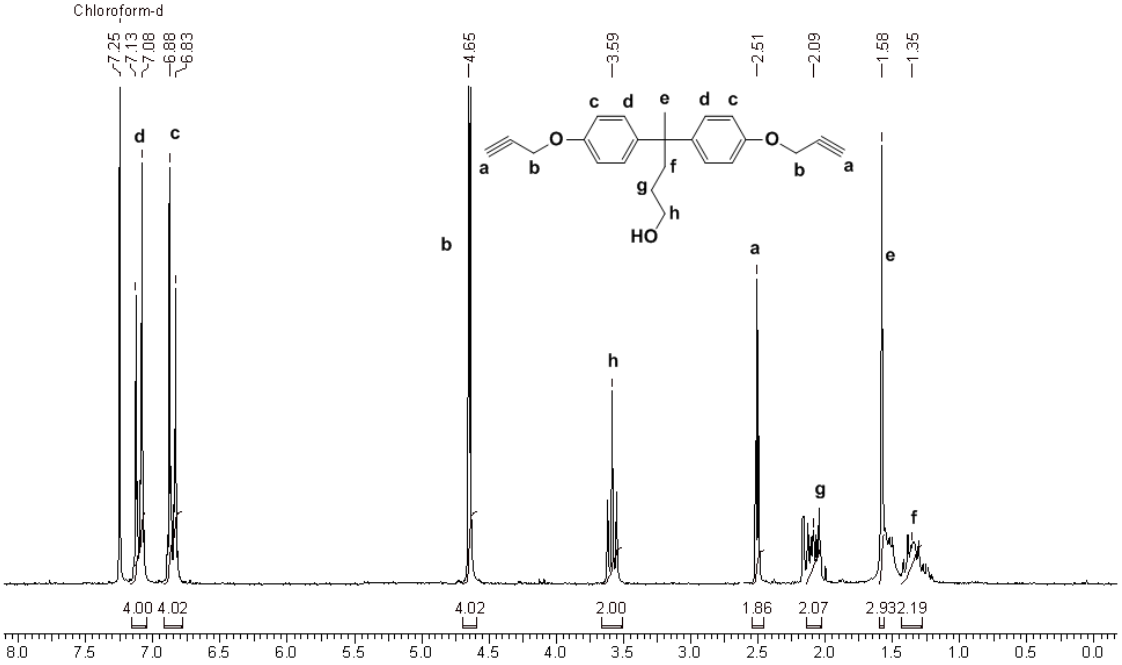
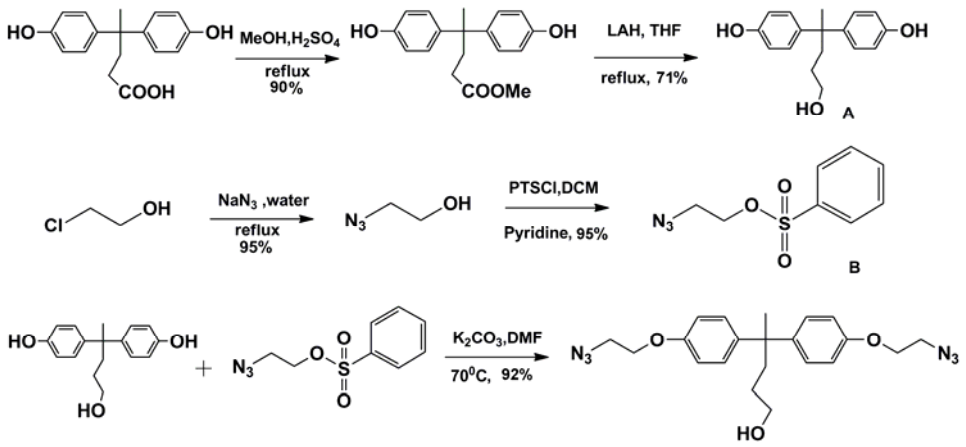


Figure 3a. 5: ^{1}H-NMR spectrum of 4,4'-bis(4-(prop-2-yn-1-yloxy) phenyl)pentan-1-ol in $CDCl_3$

The aromatic protons *meta* to propargyloxy group were observed as a doublet at 7.10 ppm while aromatic protons *ortho* to propargyloxy group appeared as a doublet at 6.86 ppm. The protons of methylene groups attached to oxygen in ether linkage exhibited a doublet at 4.65 ppm. The presence of propargyloxy functionality was confirmed by the appearance of a triplet at 2.51 ppm, corresponding to acetylene proton. The spectral data corresponding to other protons was in good agreement with the proposed structure.In ^{13}C-NMR spectrum, peaks due to propargyloxy carbon atoms were observed at 81.0 and 77.8 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3a.4.4. Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

Scheme 3a.13 depicts route for synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol.



Scheme 3a.13: Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

The synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol was carried out from 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol **(**synthesis of 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol is discussed in **Section 3a.4.2)**. In a sepearte step, 2-azidoethyl 4-methylbenzenesulphonate was synthesized from 2-chloro ethanol. 2-Azido ethanol was prepared from commercially available 2-chloroetanol by reacting it with sodium azide in water. Chemical transformation was monitored by FT-IR, the peak at 2108 cm^{-1} confirmed the conversion. In the next step, 2-azido ethanol was treated with tosyl chloride in dichloromethane using pyridine as an acid scavenger to obtain 2-azidoethyl 4-methylbenzenesulfonate. The product was purified by column chromatography. Next, 4, 4'-(5-hydroxypentane-2, 2-diyl) diphenol was subjected to alkylation reaction using 2 equivalent of 2-azidoethyl 4-methylbenzenesulphonate in the presence of K_2CO_3 in acetone to obtain 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol. The product was purified by column chromatography and was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4, 4'-bis(4-(2-azidoethoxy) phenyl)pentan-1-ol showed absorption band at 3200 cm^{-1} which corresponds to asymmetric stretching of alcohol functionality, and a characteristic peak at 2108 cm^{-1} corresponding to asymmetric stretching of azido functionality, respectively. **Figure 3a.6** represents ^{1}H-NMR spectrum of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol along with the assignments.

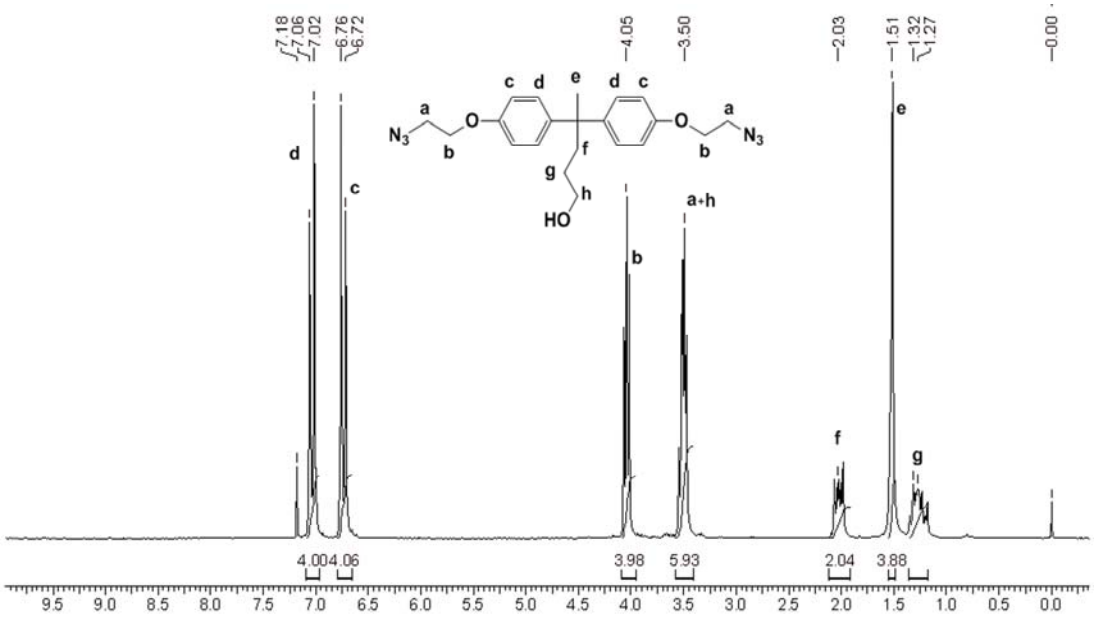
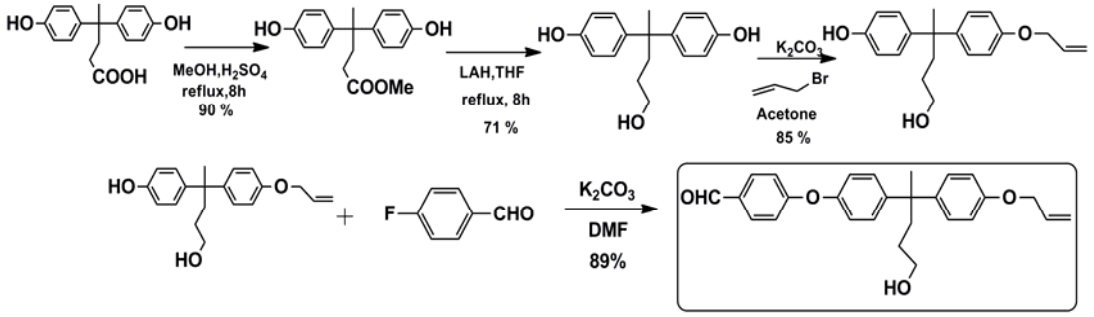


Figure 3a.6: ^{1}H-NMR spectrum of 4, 4'-bis(4-(2-azidoethoxy) phenyl)pentan-1-ol in $CDCl_3$

In ^{1}H-NMR spectrum, peaks due to aromatic protons appeared as doublets at 7.04 and 6.74 δ ppm. The spectral data corresponding to other protons was in good agreement with the proposed structure. In ^{13}C-NMR spectrum, a peak due to carbon atom adjacent to azide functionality was observed at 51.3 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3a.4.5. Synthesis of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde

Scheme 3a.14 depicts the route for synthesis of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde.



Scheme 3a.14: Synthesis of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde

We first envisaged the construction of versatile heterobifunctional initiator for ROP by considering the fact that orthogonality of functional groups should remain intact. 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol (synthesis of 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol is discussed in **Section 3a.4.2)** was used as the starting material for the synthesis of new

initiator. Allylation reaction using 1 equivalent of allyl bromide in the presence of K_2CO_3 was carried out. In order to minimize the formation of di-allyloxy substituted compound, addition of allyl bromide was performed slowly. However, the crude reaction product was found to be a mixture of desired mono-allyloxy product and minor amount of di-allyloxy compound. Column chromatography was found to be essential for seperation of mono allyloxy product 4-(2-(4-(allyloxy) phenyl) (5-(hydroxypentan-2-yl) phenol. The next step in the synthesis involved nucleophilic substitution reaction of 4-fluorobenzaldehyde with 4-(2-(4-(allyloxy) phenyl) (5-(hydroxypentan-2-yl) phenol in dry DMF using K_2CO_3 as a base to obtain 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde.

The product was purified by column chromatography and was characterised by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde showed absorption band at 3200 cm^{-1} which corresponds to asymmetric stretching of alcohol functionality, and a characteristic peak at 1715 cm^{-1} that corresponds to asymmetric stretching to aldehyde functionality, respectively. **Figure 3a.7** represents ^{1}H-NMR spectrum of 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde along with the assignments. The presence of aldehyde functionality was confirmed by the appearance of a singlet at 9.91 ppm. The aromatic protons *ortho* to aldehyde group were deshielded and appeared as a doublet at 7.84 ppm.

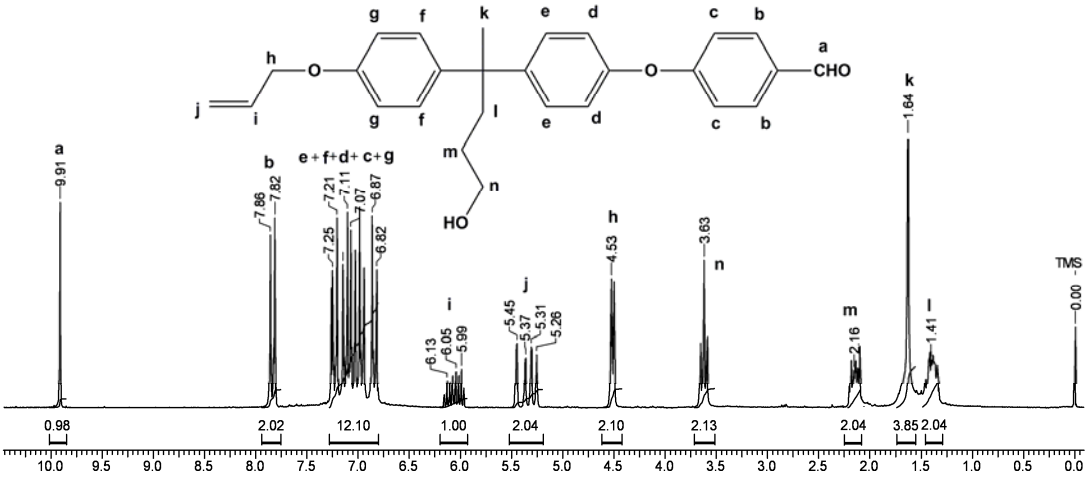
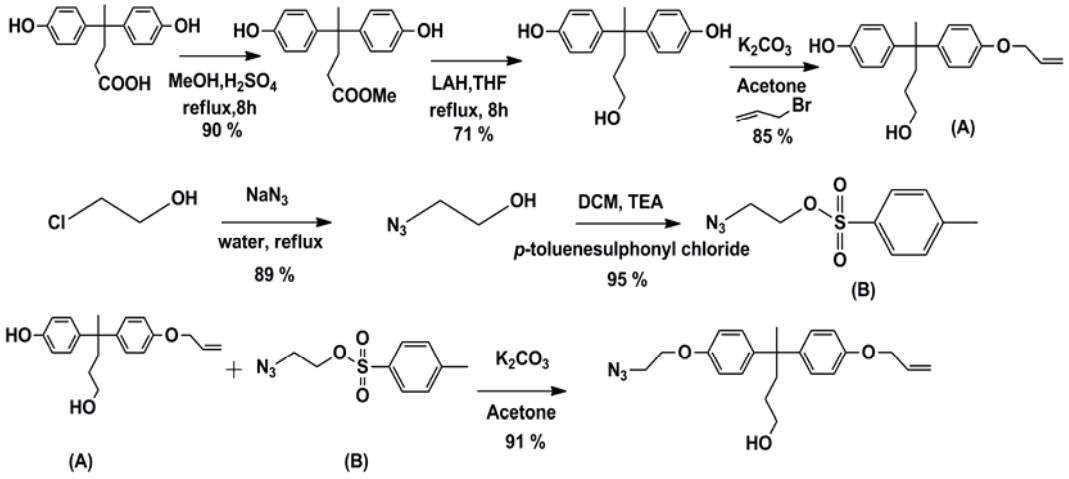


Figure 3a.7: ^{1}H-NMR spectrum of 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde in $CDCl_3$

The presence of allyloxy functionality was confirmed by the appearance of multiplets in the range 6.13-5.99 ppm, and 5.45-5.26 ppm corresponding to methine and vinyl protons, respectively. The spectral data corresponding to other protons was in good agreement with the proposed structure. In ^{13}C-NMR spectrum, the peaks corresponding to carbon atoms in allyloxy functionality appeared at 133.4 and at 118.3 ppm.

3a.4.6. Synthesis of 4-(4-(allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol

Scheme 3a.15 depicts route for the synthesis of 4-(4-(allyloxy) phenyl)-4-(4-2-azidoethoxy) phenyl) pentan-1-ol. We first visualized the construction of versatile heterobifunctional initiator for ROP by considering the fact that orthogonality of functional groups should remain intact. The synthesis of new initiator was commenced from 4-(2-(4-(allyloxy) phenyl) (5-(hydroxypentan-2-yl) phenol which was prepared from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid **(section 3a.4.5)**.



Scheme 3a.15: Synthesis of 4-(4-(allyloxy)phenyl)-4-(4-(2- azidoethoxy)phenyl) pentan-1-ol

The next step in the synthesis involved nucleophilic substitution reaction of 2-azidoethyl 4-methylbenzenesulphonate **(synthesis is discussed in section 3a.4.4)** with 4-(2-(4-(allyloxy) phenyl) (5-(hydroxypentan-2-yl) phenol in dry DMF using K_2CO_3 as a base to obtain 4-(4-(allyloxy)phenyl)-4-(4-(2-azidoethoxy)phenyl)pentan-1-ol.

The product was purified by column chromatography and was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4-(4-(allyloxy)phenyl)-4-(4-(2-azidoethoxy)phenyl)pentan-1-ol showed absorption band at 3200 cm^{-1} and 2108 cm^{-1} which correspond to asymmetric stretching of alcohol functionality, and to asymmetric stretching of azido functionality, respectively. **Figure 3a.8** represents ^{1}H-NMR spectrum of 4-(4-(allyloxy) phenyl)-4-(4-(2- azidoethoxy) phenyl) pentan-1-ol along with the assignments. The presence of allyloxy functionality was confirmed by the appearance of multiplets in the range 6.12-5.98 ppm, and 5.43-5.23 ppm corresponding to methine and vinyl protons, respectively. The spectral data corresponding to other protons was in good agreement with the proposed structure.

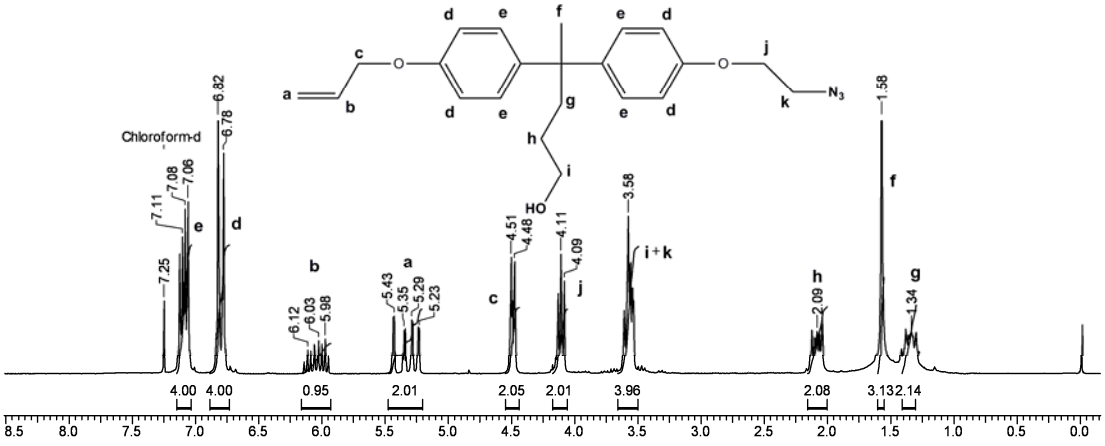
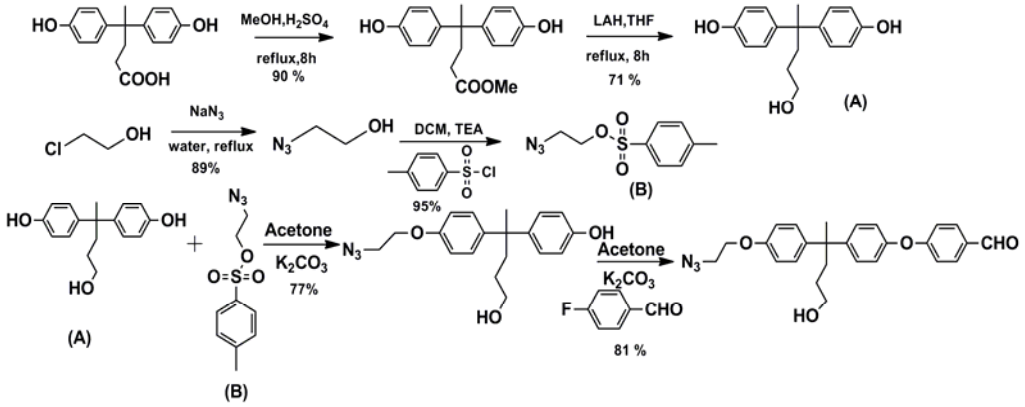


Fig. 3a.8: ^{1}H-NMR spectrum of 4-(4-(allyloxy)phenyl) -4-(4-(2-azidoethoxy) phenyl) pentan-1-ol in $CDCl_3$

In ^{13}C-NMR spectrum, the peaks corresponding to carbon atoms in allyloxy functionality appeared at 133.4 and at 118.3 ppm while the carbon atom attached to azido functionality appeared at 51.3 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3a.4.7. Synthesis of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan-2- yl)phenoxy)benzaldehyde

Scheme 3a.16 depicts route for synthesis of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2- yl) phenoxy) benzaldehyde.



Scheme 3a.16: Synthesis of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan -2- yl)phenoxy)benzaldehyde

The new initiator was synthesized starting from 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol **(**synthesis of 4, 4'-(5-hydroxypentane-2, 2-diyl)-diphenol was discussed in **section 3a.4.2)**. 4, 4'-(5-Hydroxypentane-2, 2-diyl)-diphenol was subjected to alkylation reaction using 1 equivalent of 2-azidoethyl 4-methylbenzenesulphonate **(**synthesis is discussed in **section 3a.4.4)** in the presence of K_2CO_3 in acetone. In order to minimize the formation of di-substituted compound, addition of 2-azidoethyl 4-methylbenzenesulphonate was carried out slowly. However, the crude reaction product was found to be a mixture of desired mono-substituted and minor amount of di-substituted compound. Column chromatography was

found to be essential for seperation of mono substituted product. The nucleophilic substitution reaction of 4-fluorobenzaldehyde with 4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl) phenol in dry DMF using K_2CO_3 as a base yielded 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2- yl) phenoxy)benzaldehyde. The product was purified by column chromatography and was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2-yl)phenoxy)benzaldehyde showed absorption bands at 3200 cm^{-1}, 2108 cm^{-1}, and 1715 cm^{-1} which correspond to asymmetric stretching of alcohol functionality, asymmetric stretching of azido functionality and aldehyde asymmetric stretching, respectively. **Figure 3a.9** represents ^{1}H-NMR spectrum of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2- yl) phenoxy)benzaldehyde along with the assignments. The presence of aldehyde functionality was confirmed by the appearance of a singlet at 9.91 ppm. The aromatic protons *ortho* to aldehyde group were deshielded and appeared as a doublet at 7.84 ppm. The spectral data corresponding to other protons was in good agreement with the proposed structure.

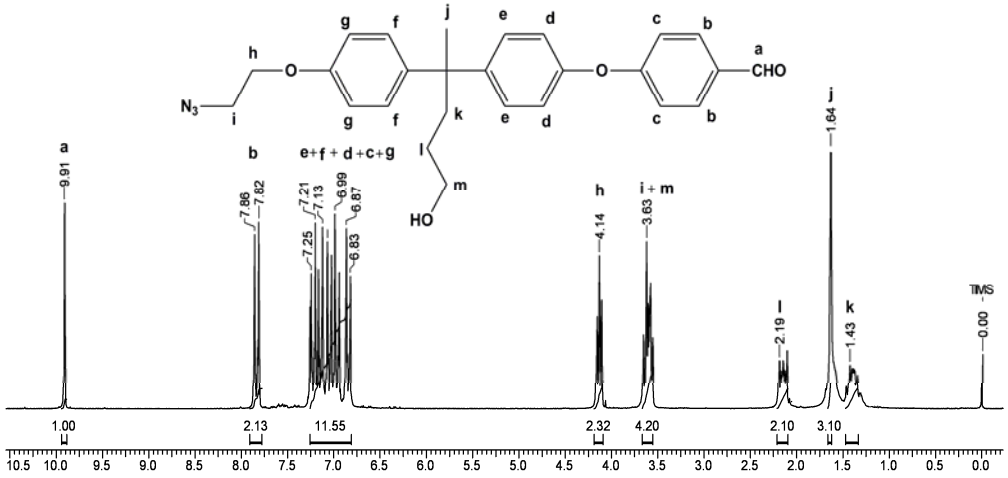


Figure 3a.9: ^{1}H-NMR spectrum of 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan-2- yl)phenoxy)benzaldehyde in $CDCl_3$

In ^{13}C-NMR spectrum, a peak due to carbonyl carbon of aldehyde group was observed at 191.4 ppm, and the peak corresponding to carbon atoms attached to azido functionality appeared at 51.3 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure. The peak assignments in ^{13}C-NMR spectrum were confirmed by DEPT spectrum.

3a.5. Conclusions

- ✓ The following seven new ROP initiators containing functional groups were synthesized starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid.
  1) 4, 4'-Bis (4-(allyloxy) phenyl) pentan-1-ol
  2) 4, 4'-(((5-Hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde
  3) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol,
  4) 4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentan-1-ol,
  5) 4-(4-(2-(4-(Allyloxy) phenyl)-5-hydroxypentan-2-yl) phenoxy) benzaldehyde,
  6) 4-(4-(Allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol, and
  7) 4-(4-(2-(4-(2-Azidoethoxy) phenyl)-5-hydroxypentan-2-yl) phenoxy) benzaldehyde
- ✓ The initiators Serial number 1-4 and Serial number 5-7 are potentially useful for preparation of α, α'-homo bifunctional and α, α'-hetero bifunctional polymers, respectively by ROP of cyclic monomers such as ε-caprolactone.

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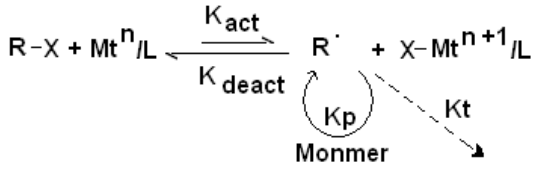
Chapter 3b
Functional Initiators for ATRP: Synthesis and Characterization

3b.1. Introduction

Atom transfer radical polymerization (ATRP) has emerged as one of the most powerful synthetic techniques in polymer science. Similar to well established living polymerization methods such anionic, cationic, etc, ATRP allows synthesis of polymers with predetermined molecular weight, narrow molecular weight distribution and desired composition[1, 2]. Moreover, with the help of functional ATRP initiators it is possible to obtain polymers with well-defined end groups[3].

3b.1.1. Initiators

The initiator is a very important component in ATRP due to its key role in controlling the equilibrium as well as rate of initiation. The amount of initiator determines molecular weight of the polymer and its efficiency determines the number of chains initiated. As shown in **Scheme 3b.1**, in the initiation step, the transition metal complex abstracts halogen from the organic halide (RX), creating a radical R· that adds to double bond of the monomer and the sequence continues[4].



Scheme 3b.1: Schematic representation of ATRP mechanism[1]

Structural adjustment of the alkyl part R and the leaving group X in order to make the R-X bond more labile than the propagating polymer-X bond provides a handle to fine-tune the rate of initiation in ATRP system**.** The basic criteria for selection of initiator is that initiation should be fast in comparison with propagation, quantitative initiation and the probability of side reaction should be minimum. Also, incorporation of the alkyl group R at one chain end and halogen at the other chain end provides a route to synthesize end-functional polymers using initiators containing functional groups **(Figure 3b.1).**

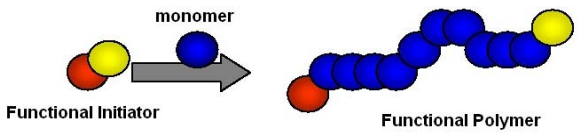
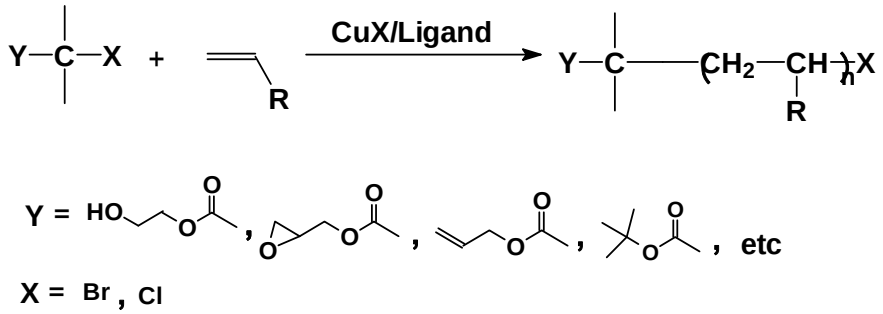


Figure 3b.1: Schematic representation of synthesis of end-functional polymers using functional initiators

Most of the successful initiators employed in ATRP are organic halides with a potentially active carbon-halogen bond, which can easily generate a radical species through electronic and steric effects of their substituent[1]. An organic halide, the structure of which is similar to that of the dormant chain end of the polymer, is preferentially used so that the activity of the carbon-halogen bond in the initiator is similar to that of the dormant polymer

terminal. Alkyl chlorides and bromides have been widely employed initiators in ATRP. Haloalkanes, allyl halides, (haloalkyl) benzenes, haloketones, haloesters, haloamides, halonitriles, sulfonyl halides, etc. are utilized successfully in ATRP[5] **(Scheme 3b. 2).**



Scheme 3b.2: Approach to synthesize end-functionalized polymers by ATRP

Different types of halogenated compounds are useful initiators for ATRP and are discussed below based on their structure.

3b.1.1.1. Halogenated alkanes

Halogenated alkanes, such as $CHCl_3$ or CCl_4, are typically used in atom transfer radical addition and were among the first studied ATRP initiators[6, 7] **(Figure 3b.2.)**.

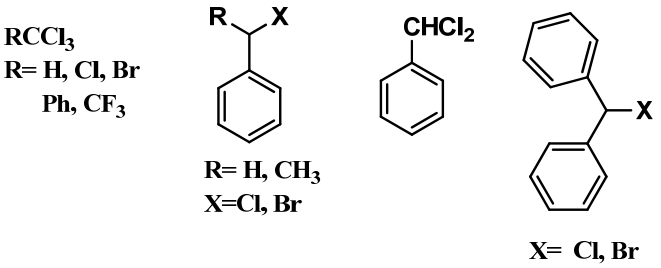


Figure 3b.2: Some halogenated alkanes and benzylic halides used as ATRP initiators[1]

In the ruthenium-catalyzed ATRP of MMA, molecular weight of the polymer increased linearly with the conversion; however, at high monomer conversion, the molecular weight deviated from the theoretical values[8]. The polymers obtained were monomodal with low polydispersities (ca. 1.3). In contrast, di- or monochloromethanes were not able to polymerize MMA under similar conditions[9].

3b.1.1.2. Benzylic halides

Benzyl-substituted halides **(Figure 3b.2.)** are useful initiators for the polymerization of styrene and its derivatives due to their structural resemblance. However, they fail in polymerization of more reactive monomers in ATRP such as MMA. For example, using CuCl- $(dNbpy)_2$ as the catalyst, inefficient initiation was observed when 1-phenylethyl chloride was employed as the initiator for the polymerization of MMA[10].

3b.1.1.3. α-Haloesters

Various α-haloesters have been successfully employed to initiate well-controlled ATRP **(Figure 3b.3.)**. In general, α-haloisobutyrates produce initiating radicals faster than the corresponding α-halopropionates due to better stabilization of the generated radicals after the halogen abstraction step. Thus, slow initiation will generally occur if α-halopropionates are

used to initiate the polymerization of methacrylates. In contrast, α-bromopropionates are good initiators for ATRP of acrylates due to their structural resemblance.

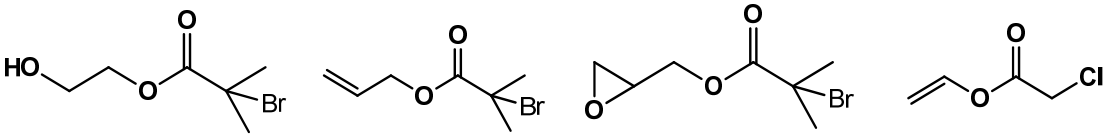


Figure 3b.3: Representative functional ATRP initiators derived from α-haloesters[1]

***3b.1.1.4*. α-Haloketones**

An α-bromoketone has been used to initiate the controlled polymerization of MMA catalyzed by Ni{*o,o'*-$(CH_2NMe_2)_2C_6H_3$}Br[11] and Ni$(PPh_3)_4$[12]. Polyhalogenated α-haloketones (e.g., CCl_3COCH_3 and $CHCl_2COPh$) are among the best initiators for the ATRP of MMA catalyzed by ruthenium complexes[13-16]. The stronger electron-withdrawing power of the carbonyl group of ketone induces further polarization of the carbon-chlorine bond, which is attributed to the faster initiation observed with the ketones than with the ester counterparts.

3b.1.1.5. α-Halonitriles

α-Halonitriles are fast radical generators in ATRP, due to the presence of the strong electron-withdrawing cyano group. Moreover, the radical formed after halogen abstraction is sufficiently reactive, which leads to fast initiation through rapid radical addition to monomer. Of the initiators studied for the polymerization of acrylonitrile catalyzed by copper complexes, 2-bromopropionitrile resulted in polymers with the lowest polydispersities[17]. However, α-halonitriles were not used in ruthenium-catalyzed ATRP as the cyano group deactivates the catalyst by forming a strong complex with ruthenium.

***3b.1.1.6.* Sulfonyl halides**

As ATRP initiators, sulfonyl chlorides yield a much faster rate of initiation than monomer propagation[18].The apparent rate constants of initiation are about four (for styrene and methacrylates) and three (for acrylates) orders of magnitude higher than those for propagation. As a result, well-controlled polymerizations of a large number of monomers have been obtained in copper-catalyzed ATRP[19]. End-functional polymers have been prepared using sulfonyl chlorides where functionalities were introduced onto the aromatic ring[20] **(Figure 3b.4.)**.

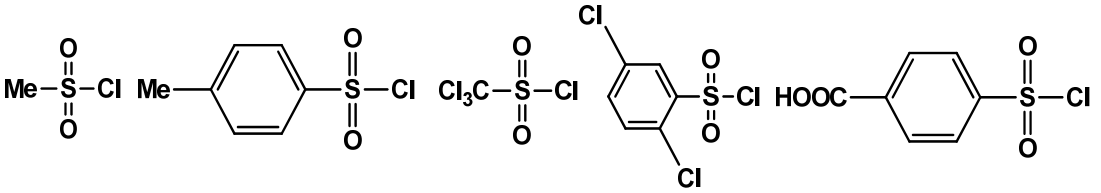


Figure 3b.4: Representative examples of sulfonyl chlorides used as ATRP initiators[1]

3b.1.1.7. General comments on the initiator structure in ATRP

Two parameters are important for a successful ATRP initiating system. First, initiation should be fast in comparison with propagation. Second, the probability of side reactions should be minimized. Analogous to the "living" carbocationic systems, the main

factors that determine the overall rate constants are the equilibrium constants rather than the absolute rate constants of addition[21]. There are several general considerations for the initiator choice.

(1) The stabilizing group order in the initiator is roughly CN > C(O)R > C(O)OR > Ph > Cl > Me. Multiple functional groups may increase the activity of the alkyl halide, e.g., carbon tetrachloride, benzhydryl derivatives, and malonates. Tertiary alkyl halides are better initiators than secondary ones, which are better than primary alkyl halides. These have been partially confirmed by recent measurements of activation rate constants[22-24]. Sulfonyl chlorides also provide faster initiation than propagation.

(2) The general order of bond strength in the alkyl halides is R-Cl > R-Br > R-I. Thus, alkyl chlorides should be the least efficient initiators and alkyl iodides the most efficient. However, the use of alkyl iodides requires special precautions. They are light sensitive, can form metal iodide complexes with an unusual reactivity (e.g., CuI_2 is thermodynamically unstable and cannot be isolated), the R-I bond may possibly be cleaved heterolytically, and there are potential complications of the ATRP process by degenerative transfer[25, 26].By far, bromine and chlorine are the most frequently used halogens. In general, the same halogen is used in the initiator and the metal salt (e.g., RBr/CuBr); however, the halogen exchange can sometimes be used to obtain better polymerization control[27]. In a mixed halide initiating system, R-X/Mt-Y (X, Y) (Br or Cl), the bulk of the polymer chains are terminated by chlorine due to the stronger alkyl-chloride bond. Thus, the rate of initiation is increased relative to propagation and ethyl 2-bromoisobutyrate/CuCl leads to a better controlled polymerization of MMA in comparison to using ethyl 2-bromoisobutyrate/CuBr. A similar result has also been observed in Ru-based ATRP[28]. The halogen exchange method also enables the use of alkyl halides of apparently lower reactivities in the polymerization of monomers with apparently higher equilibrium constants. This is especially important for the formation of block copolymers[29-32]. Pseudohalogens (e.g., SCN) have also been used in ATRP[33]. Initiation using benzyl thiocyanate is slow for both styrene and MA, and M_n higher than the theoretical values are obtained. Better results are obtained when alkyl halides are used as the initiators and CuSCN as the catalyst. Similarly, transition metal dithiocarbamates have been employed in the presence of AIBN to induce controlled reverse ATRP of styrene at 120 °C. Good agreement between theoretical and experimental M_n values were obtained with Mw/Mn in the range 1.15-1.30

(3) Successful initiation in ATRP can depend strongly on the choice of catalyst. For example, 2-bromoisobutyrophenone initiates the controlled polymerization of MMA catalyzed by ruthenium or nickel complexes but has not been successfully used in the copper-mediated ATRP[34].

(4) The method or order of reagent addition can be crucial. For example, slow addition of the benzhydryl chloride initiator to the CuCl $(dNbpy)_2$-catalyzed ATRP of MMA generates a lower concentration of benzhydryl radicals[34] and thus reduces the rate of termination between the radicals. The diethyl 2-bromomalonate/CuBr system initiates the ATRP of styrene, and the polymerization was well controlled when the catalyst was added slowly to the initiator/monomer solution. This avoided the potential reduction of the malonyl radical by the copper (I) species. It may also be surprising, but the heterogeneous catalytic systems may provide more efficient initiation than homogeneous ones when very reactive alkyl halide initiators are used, most likely due to slow dissolution of the catalyst and hence its lower instantaneous concentration. For example, CCl_4 is a good initiator for styrene and MMA with CuBr $(bpy)_3$ as the catalyst[34], but the same is not true using the CuBr $(dNbpy)_2$ catalytic system. The initiation efficiency increased when the catalyst solution was added slowly to the initiator solution[35].

3b.1.1.8. Initiator efficiency

In general, the same halogen is used in the initiator and the metal salt (e.g., RBr/CuBr), however, the halogen exchange can sometimes be used to obtain better polymerization control[29]. The initiator efficiency is especially important for the formation of block copolymers, functionalized polymers and telechelic polymers. The lowering of initiator efficiency for a particular initiating system is caused due to the factors like the functionality of initiator, concentration of initiator in reaction and temperature of the reaction. For example, Lu et al.[36] showed that 5-chloromethyl-2-hydroxy-benzaldehyde **(Figure 3b.5, a)** as initiator in ATRP of styrene in presence of CuCl/PMDETA as catalyst resulted with initiator efficiency in the range 0.08 to 1.02.

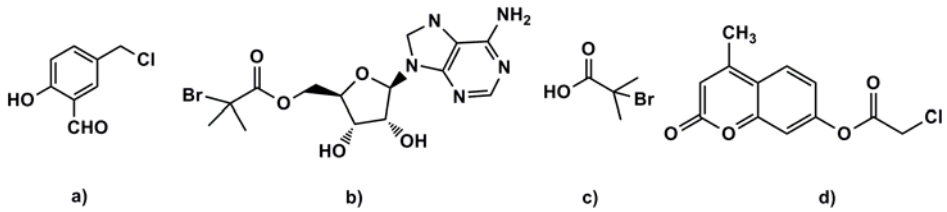


Figure 3b.5: Structures of a) 5-chloromethyl-2-hydroxy-benzaldehyde b) unprotected uridine derived initiator c) alpha halocarboxylic acid and d) coumarin functionalized initiator

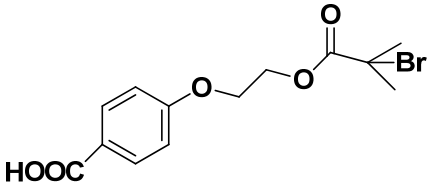
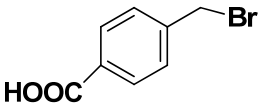
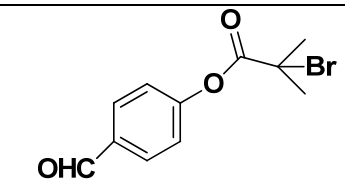
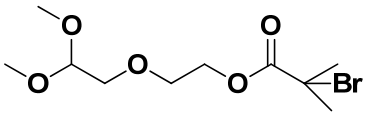
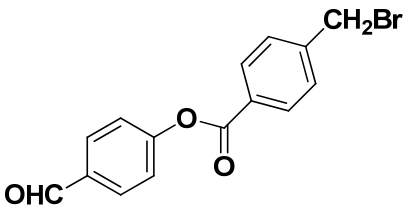
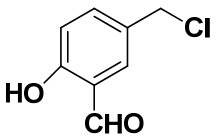
With decreasing monomer to initiator ratio, efficiencies of the initiator reduced and the MWD of polystyrene expanded. Haddleton et al[37] reported that the initiator efficiency of unprotected uridine derived **(Figure 3b.5, b)** initiator in ATRP of MMA using CuBr/ *N*-(*n*-pentyl)-2-pyridylmethanimine as catalyst was lower (0.46) as the M_n is increased. Matyjazewski et al[5] observed the lower initiator efficiency in ATRP of styrene using α-halocarboxylic acids **(Figure 3b.5, c)** as initiator in presence of CuBr/PMDETA as catalyst, which was attributed to intramolecular cyclization reaction forming γ-butyrolactone. Liu et al[38] studied the ATRP of styrene in presence of CuBr/bipyridine as catalyst using coumarin

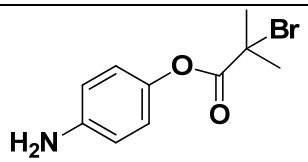
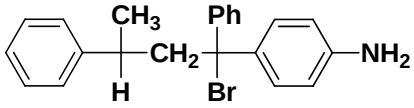
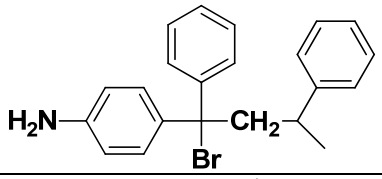
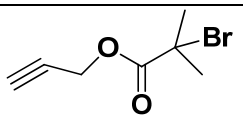
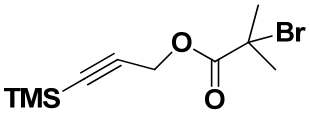
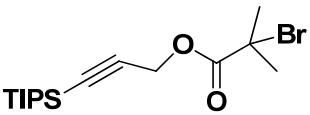
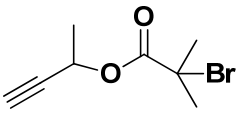
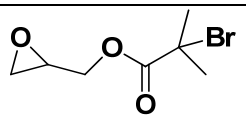
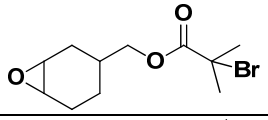
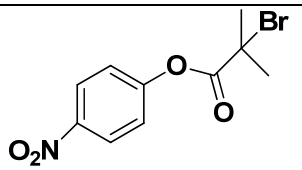
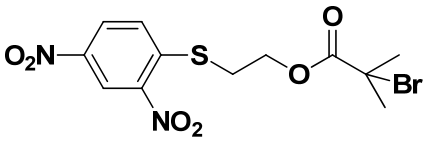
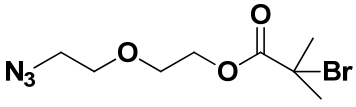
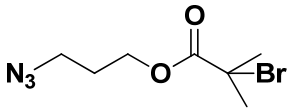
functonalized **(Figure 3b.5, d)** initiator. The initiator efficiency was found to decrease with increasing monomer to initiator ratio and temperature**.**

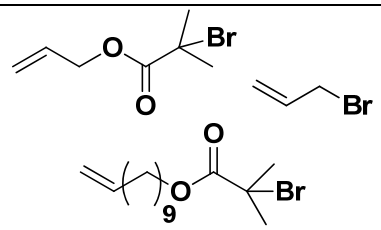
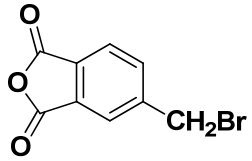
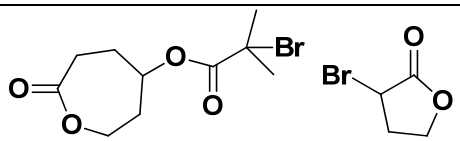
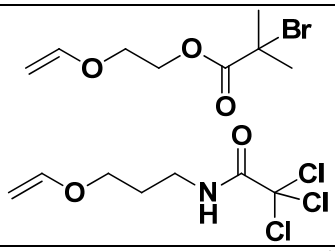
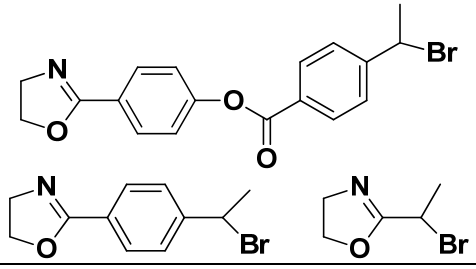
3b.1.2. ATRP initiators containing functional groups

Taking advantage of the tolerance of ATRP for functional groups, a variety of functionalized initiators have been synthesized and used for preparation of end functionalized polymers. A large number of initiators with different functionalities have been documented by Yagci et. al.[39] and Matyjaszewski et. al[40]. Representative functionalized ATRP initiators employed for synthesis of end-functionalized polymers are presented in **Table 3b.1.**

Table 3b.1: Representative examples of functionalized ATRP initiators

Sr. No.	Functionality	Initiator	Monomer polymerized
1.	Acid	 	Styrene[5] Styrene
2.	Aldehyde	   	MMA[41] OEGMA[42] Styrene[43, 44] Styrene [36]

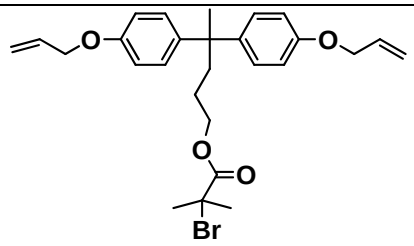
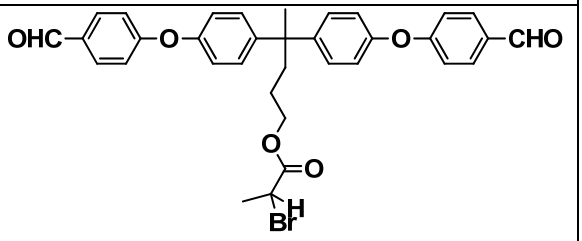
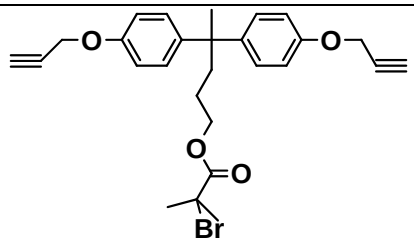
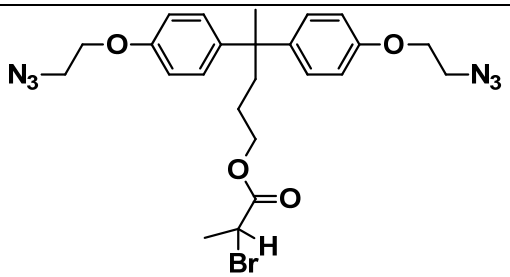
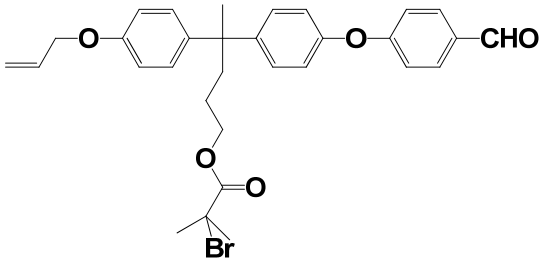
Sr. No.	Functionality	Initiator	Monomer polymerized
3.	Amine		MMA[41]
			Styrene[45]
			Styrene[46]
4.	Alkyne		DMAEMA[47]
			Styrene[48], MMA[49], HEMA[50]
			Styrene[51], MA[52],
			MMA[53], Styrene[54, 55]
5.	Epoxy		MMA, Styrene [56]
			Styrene[57]
6.	Nitro		MMA[58]
			MMA[59]
7.	Azide		DMAEMA[47]
			Styrene[60]

Sr. No	Functionality	Initiator	Monnomer polymerized
8.	Allyl		DMAEMA[61] MMA, Styrene[62-65]
9.	Anhydride		Styrene[66]
10	Lactone		MMA[67] Styrene[56]
11.	Vinyloxy		MMA[64] DMAEMA,MMA[68]
12	Oxazoline		Styrene[69]

A survey of literature revealed that major focus has been centered on the synthesis of α-functional ATRP initiators with little efforts on the preparation of α, α' homobifunctional and α, α' hetero bifunctinal ATRP initiators.

The present work deals with design and synthesis of α, α' homobifunctional and α, α' hetero bifunctinal ATRP initiators **(Table 3b.2)** starting from common precursor 4,4'-bis (4-hydroxyphenyl) pentanoic acid, which in turn is derived from levulinic acid- a platform chemical obtained from biomass.

Table 3b.2: Functionalized ATRP initiators synthesized

Sr. No.	ATRP initiator	Structure
1	4,4'-Bis(4-(allyloxy)phenyl)pentyl 2-bromo-2-methylpropanoate	
2	4,4'-Bis(4-(4-formyl phenoxy)phenyl)pentyl 2-bromopropanoate	
3	4,4'-Bis(4-(prop-2-yn-1-yloxy)phenyl)pentyl 2-bromo2-methylpropanoate	
4	4,4'-Bis(4-(2-azidoethoxy)phenyl)pentyl 2-bromopropanoate	
5	4-4-(Allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methylpropanoate	

Thus, four α, α'-homo bifunctional ATRP initiators containing allyloxy, aldehyde, propargyloxy, and azido functionality and a α, α'-hetero bifunctional ATRP initiator featuring allyloxy-aldehyde functional groups were synthesized. The choice of functional groups was made by considering their ability to take part in various efficient organic transformations including different types of "click" reactions. For example, allyloxy group could undergo thiol-ene reaction, while azido and propargyloxy group could take part in the well-known azide-alkyne click reaction. The rationale behind introduction of aldehyde group is that it

could be further utilized in chemical modification by metal-free aldehyde-aminooxy click reaction.

3b.2. Experimental

3b.2.1. Materials

Synthesis of 4, 4'-bis(4-(allyloxy)phenyl)pentan-1-ol, 4,4'-(((5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde, 4,4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol, 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol, and 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde has been discussed in **Chapter 3a.** 2-Bromoisobutyryl bromide and 2-bromopropanoyl bromide were purchased from Aldrich and were used as received. Sodium chloride, anhydrous sodium sulphate, potassium hydroxide, sodium hydrogen carbonate, sodium hydroxide, ethanol, methanol and chloroform, all received from S.D. Fine-Chem. Ltd., India were used as received. Tetrahydrofuran was stirred over calcium hydride for 12 h, filtered and distilled. Further it was refluxed over sodium-benzophenone complex for 2 days, then distilled and used. Dichloromethane was stirred over calcium hydride and distilled before use. Triethyl amine was stirred over potassium hydroxide, distilled and stored over potassium hydroxide.

3b.2.2. Characterization and measurements

FTIR spectra were recorded on a Perkin-Elmer *Spectrum GX* spectrophotometer in chloroform. NMR spectra were recorded on a Bruker 200 MHz spectrometer at resonance frequencies of 200 MHz for ^{1}H-NMR and 50 MHz for ^{13}C-NMR measurements using $CDCl_3$ as a solvent.

3b.3. Synthesis

3b.3.1. Synthesis of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol (10.2 g, 29 mmol), triethylamine (3. 5 g, 35 mmol), and dry chloroform (50 mL). The reaction mixture was cooled to 0 ^{O}C in an ice salt bath. The solution of 2-bromoisobutyryl bromide (8.0 g, 35 mmol) in dry chloroform (20 mL) was added dropwise into the reaction mixture under stirring at 0 ^{o}C over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and then stirred overnight. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL).The organic layer was dried over anhydrous sodium sulfate, filtered and ethyl acetate was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate/pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 12.7 g (88%) of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 1730, 1250

^{1}H NMR ($CDCl_3$, δ/ppm): 7.12 (d, 4H, Ar-H *meta* to ether linkage), 6.84 (d, 4H, Ar-H *ortho* to ether linkage), 6.11- 5.97 (m, 2H, C=CH-), 5.44-5.25 (q, 4H, C=CH_2), 4.52 (d, 4H, -OCH_2-

), 4.12 (t, 2H, -CH_2-O-CO), 2.12- 2.06 (m, 2H, -CH_2), 1.92 (s, 6H,-$(CH_3)_2$), 1.59 (s, 3H,-CH_3), 1.51- 1.45 (m, 2H, -CH_2).

^{13}C NMR ($CDCl_3$, δ/ppm): 171.5, 156.4, 141.6, 133.4, 128.1, 117.5, 114.7, 68.7, 64.3, 53.9, 44.6, 33.7, 27.8, and 24.1.

ESI-MS (m/z): 523 [M+Na^+]

Anal. Calcd for $C_{27}H_{33}BrO_4$, C-64.67, H-6.63, Br-15.93, O-12.76, found: C-64.22, H-6.89, Br-15.38, O-13.51

3b.3.2. Synthesis of 4, 4'-bis (4-(4- (formylphenoxy) phenyl) pentyl 2-bromopropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4,4'-(4,4'-(5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy)dibenzaldehyde (10 g, 21 mmol), triethylamine (2.52 g, 25 mmol), and dry chloroform (100 mL). The reaction mixture was cooled to 0 °C and the solution of 2-bromopropanoyl bromide (5.40 g, 25 mmol) in dry chloroform (30 mL) was added dropwise into the reaction mixture under stirring over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and stirred for 12 h. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL).The organic layer was dried over anhydrous sodium sulfate, filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate/pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 11.8 g (92 %) of 4, 4'-bis (4-(4- (formylphenoxy) phenyl) pentyl 2-bromopropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 1735, 1710

^{1}H NMR ($CDCl_3$, δ/ppm): 9.85 (s, 2H, aldehyde), 7.78 (d, 4H, Ar-H *ortho* to aldehyde), 7.19 (d, 4H, Ar-H *meta* to ether linkage), 7.02-6.92 (m, 8H, Ar-H *ortho* to ether linkage and *meta* to ether linkage), 4.37-4.25 (q, 1H,-OCOCHBr), 4.13-4.08 (m, 2H, CH_2OCO), 2.16- 2.06 (m, 2H, -CH_2), 1.75 (d, 3H, $OCOCHCH_3$) 1.61 (s, 3H,-CH_3), 1.39-1.31 (m, 2H,-CH_2)

^{13}C NMR ($CDCl_3$, δ/ppm): 191.3, 169.5, 162.6, 154.4, 141.6, 131.4, 128.1, 122.2, 118.5, 65.7, 41.6, 39.8, 30.7, 27.8, and 24.1.

ESI-MS (m/z): 651 [M+Na^+]

3b.3.3. Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl)pentyl 2-bromo2-methylpropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4,4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol (10 g, 29 mmol), triethylamine (3.5 g, 35 mmol), and dry chloroform (50 mL). The reaction mixture was cooled to 0 °C. and the solution of 2-bromopropanoyl bromide (8 g, 35 mmol) in dry chloroform (30 mL) was added dropwise into the reaction mixture under stirring over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and stirred for 12 h. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL). The organic layer was dried over anhydrous sodium sulfate,

filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 12.3 g (88 %) of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo2-methylpropanoate as a pale yellow liquid.

IR (CHCl3, cm-1): 2123, 1731

^{1}H NMR ($CDCl_3$, δ/ppm): 7.11 (d, 4H, Ar-H *meta* to ether linkage), 6.86 (d, 4H, Ar-H *ortho* to ether linkage), 4.66 (d, 4H, -OCH_2-), 4.12 (t, 2H, -CH_2-O-CO), 2.51 (t, 2H, acetylene proton), 2.16-2.08 (m, 2H, -CH_2), 1.91 (s, 6H,-$(CH_3)_2$), 1.58 (s, 3H, ,-CH_3), 1.48-1.42 (m, 2H, -CH_2) ppm.

^{13}C NMR ($CDCl_3$, δ/ppm): 171.1, 155.4, 140.6, 128.1, 114.5, 78.7, 76.3, 66.7, 62.3, 51.2, 41.6, 34.0, 30.7, and 24.1.

3b.3.4. Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl)pentyl 2-bromopropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4, 4'-bis(4-(2-azidoethoxy) phenyl)pentan-1-ol (10.20 g, 25 mmol), triethylamine (3.0 g, 30 mmol), and dry chloroform (100 mL). The reaction mixture was cooled to 0 °C and the solution of 2-bromopropanoyl bromide (6.45 g, 30 mmol) in dry chloroform (30 mL) was added dropwise into the reaction mixture under stirring over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and stirred for 12 h. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL).The organic layer was dried over anhydrous sodium sulfate, filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 11.9 g (85%) of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 2110, 1725

^{1}H NMR ($CDCl_3$, δ/ppm): 7.10 (d, 4H, Ar-H *meta* to ether linkage), 6.82 (d, 4H, Ar-H *ortho* to ether linkage), 4.40-4.30 (q, 1H, -OCOCH), 4.20-4.10 (m, 6H,O-CH_2), 3.57 (t, 4H, CH_2N_3), 2.12- 2.06 (m, 2H, -CH_2), 1.81 (d, 3H,-$OCOCH_3$), 1.59 (s, 3H,-CH_3), 1.51- 1.45 (m, 2H, -CH_2).

^{13}C NMR ($CDCl_3$, δ/ppm): 172.6, 155.4, 139.6, 128.1, 114.6, 68.5, 66.7, 51.2, 49.8, 42.6, 34.0, 30.7, and 24.1.

3b.3.5. Synthesis of 4-4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methylpropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde (10.40 g, 25 mmol), triethylamine (3 g, 30 mmol), and dry chloroform (100 mL). The reaction mixture was cooled to 0 °C and the solution of 2-bromoisobutyryl bromide (6.80 g, 30 mmol) in dry chloroform (30 mL) was added dropwise into the reaction mixture under stirring over a

period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and was stirred for 12 h. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL).The organic layer was dried over anhydrous sodium sulfate, filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate/pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 12.6 g (90 %) of 4-4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl)pentyl 2-bromo-2-methylpropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 1735, 1710

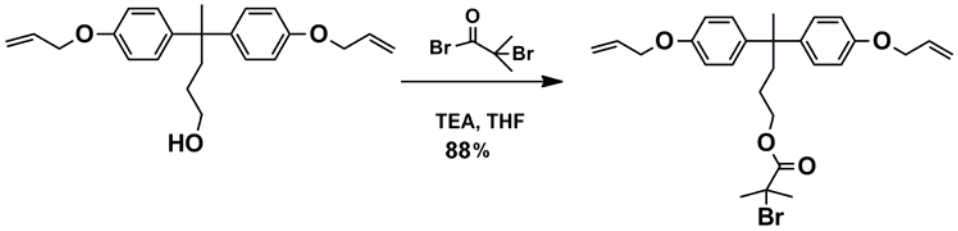
^1H NMR ($CDCl_3$, δ/ppm): 9.92 (s, 1H, aldehyde), 7.84 (d, 2H, Ar-H *ortho* to aldehyde), 7.15-6.83 (m, 10H, Ar-H), 6.16-5.99 (m, 1H, CH =C-), 5.45-5.25 (q, 2H, $C=CH_2$), 4.52 (d, 2H, -OCH_2), 4.15 (t, 2H, CH_2OCO), 2.16- 2.06 (m, 2H, -CH_2), 1.93 (s, 6H, $OCOC(CH_3)_2$) 1.64 (s, 3H,-CH_3), 1.53- 1.47 (m, 2H,-CH_2)

^{13}C NMR ($CDCl_3$, δ/ppm): 191.3, 170.5, 162.8, 155.2, 154.4, 141.6, 140.6, 134.0, 131.4, 128.1, 122.2, 118.5, 114.3, 70.4, 65.7, 51.3, 41.6, 39.8, 30.7, and 24.1.

3b.4. Results and Discussion

3b.4.1. Synthesis of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

The synthesis of new ATRP initiator, namely, 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate was carried out by esterification reaction of 4, 4–bis (4-(allyloxy) phenyl) pentan-1-ol with 2-bromoisobutyryl bromide **(Scheme 3b.3).**



Scheme 3b.3: Synthesis of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

The product was purified by column chromatography and was characterized by FT-IR, ^1H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate showed absorption band at 1730 cm^{-1} that corresponds to ester carbonyl asymmetric stretching and the absorption band at 1250 cm^{-1} corresponding to ether linkage. In ^1H-NMR spectrum (**Figure 3b.6)** of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate., the presence of allyloxy functionality was confirmed by the appearance of multiplets in the range 6.11- 5.97 ppm, and 5.44-5.25 ppm corresponding to methine and vinyl protons, respectively. The singlet appeared at 1.92 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

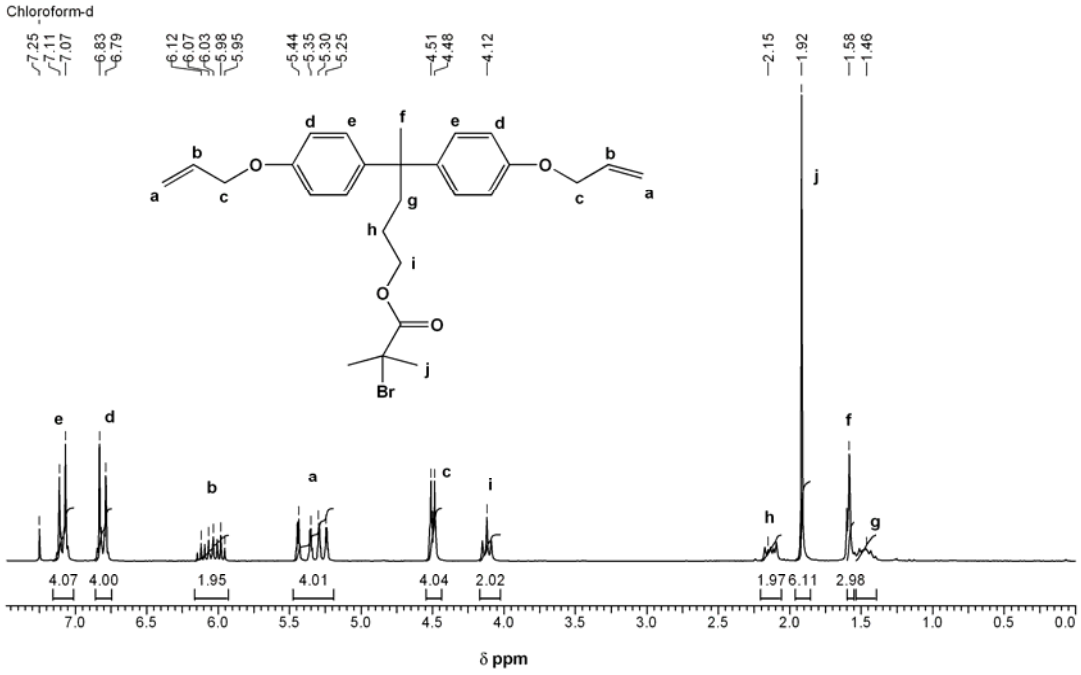
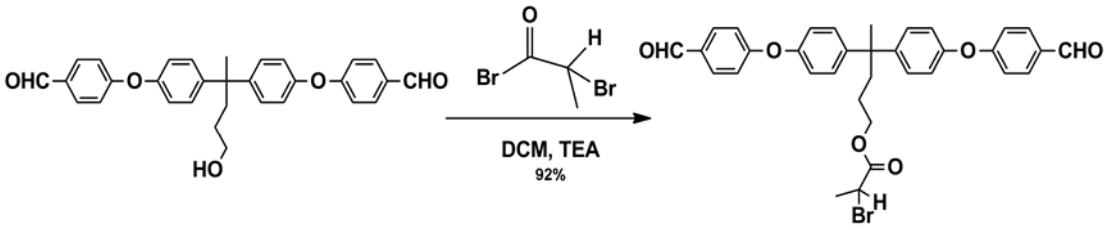


Figure 3b.6: ^{1}H-NMR spectrum of 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate in $CDCl_3$

In ^{13}C-NMR spectrum, a peak due to ester carbonyl carbon was observed at 171.5 ppm and the carbon atoms corresponding to allyl group appeared at 133.4 and 117.5 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure. The peak assignments in ^{13}C-NMR spectrum were confirmed by DEPT spectrum.

3b.4.2. Synthesis of 4, 4'-bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate

4,4'-Bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate was synthesized by esterification of 4, 4'- (4,4'-(5-hydroxypentane 2,2-diyl bis(4,1- phenylene)bis(oxy) dibenzaldehyde with 2-bromopropanoyl bromide in dry chloroform **(Scheme 3b.4).** The product was purified by silica gel column chromatography and was characterized using FT-IR, ^{1}H- NMR and ^{13}C- NMR spectroscopy.



Scheme 3b.4: Synthesis of 4, 4'-bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate

FT-IR spectrum of 4, 4'-bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate, exhibited absorption bands at 1735 cm^{-1} that corresponds to ester carbonyl asymmetric stretching and the absorption band at 1710 cm^{-1} corresponding to aldehyde group.

^{1}H-NMR spectrum of 4, 4'-bis (4-(4- (formylphenoxy) phenyl) pentyl 2-bromopropanoate along with assignments is shown in **Figure 3b. 7.**

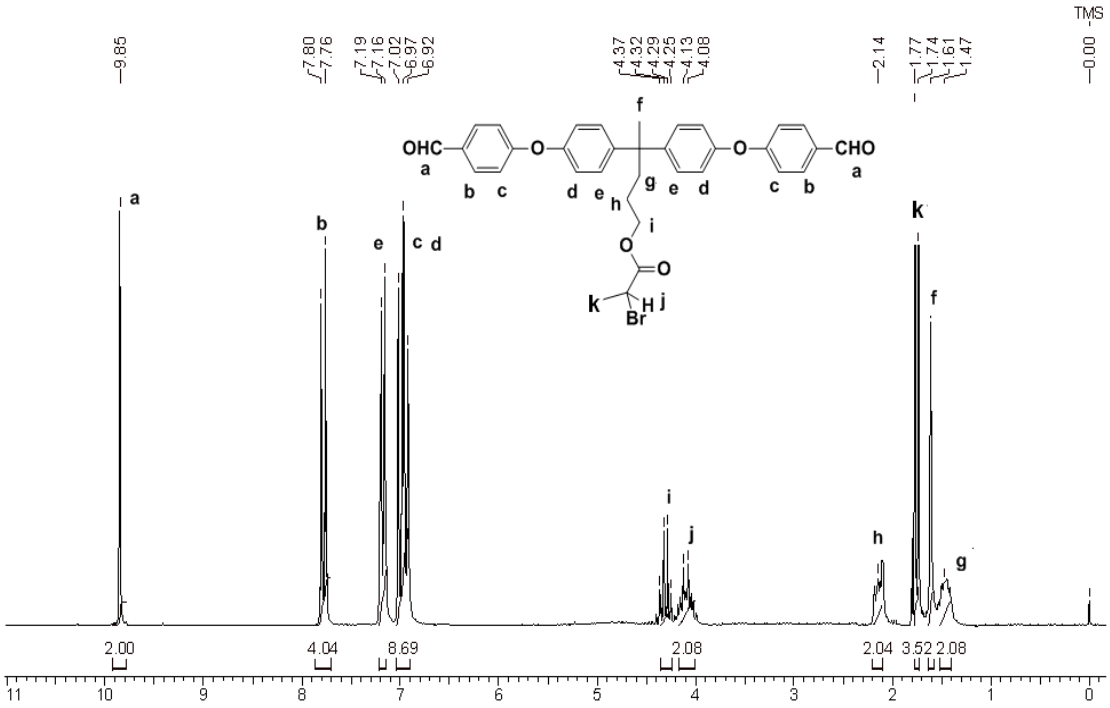
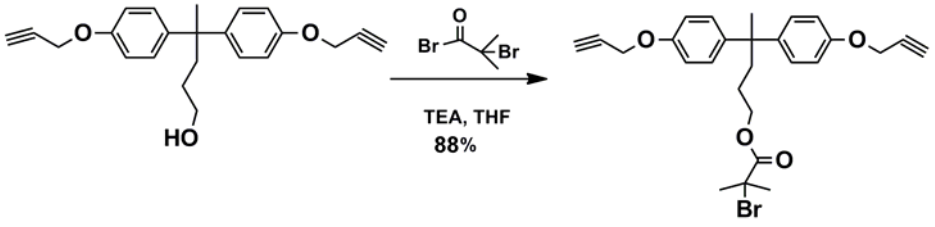


Figure 3b.7: ^{1}H-NMR spectrum of 4, 4'-bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate in $CDCl_3$

The presence of aldehyde functionality was confirmed by the appearance of a singlet at 9.85 ppm. The aromatic protons *ortho* to aldehyde group were deshielded and appeared as a doublet at 7.78 ppm. The quartet corresponding to methylene protons attached to halo ester appeared at 4.37-4.25 ppm. The doublet appeared at 1.75 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure. In ^{13}C-NMR spectrum, a peak corresponding to carbonyl carbon of aldehyde group was observed at 191.3 ppm and peak due to ester carbonyl carbon was observed at 169.5 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure. The peak assignments in ^{13}C-NMR spectrum were confirmed by DEPT spectrum.

3b.4.3. Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

Synthesis of new ATRP initiator, *viz*, 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromopropanoate was carried out by esterification of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol with 2-bromoisobutyryl bromide **(Scheme 3b.5).**



Scheme 3b.5: Synthesis of 4, 4'-bis (4-(prop-2-yn-1-yloxy)phenyl)pentyl 2-bromo 2-methylpropanoate

The product was purified by column chromatography and was characterized by FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. FT-IR spectrum of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo2-methylpropanoate showed absorption bands at 2123, and 1731 cm^{-1} that correspond to propargyloxy and ester carbonyl asymmetric stretching, respectively. In ^{1}H-NMR spectrum of 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo-2-methylpropanoate (**Figure 3b.8)**, the presence of propargyloxy functionality was confirmed by the appearance of a triplet at 2.51 ppm. The singlet appeared at 1.91 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

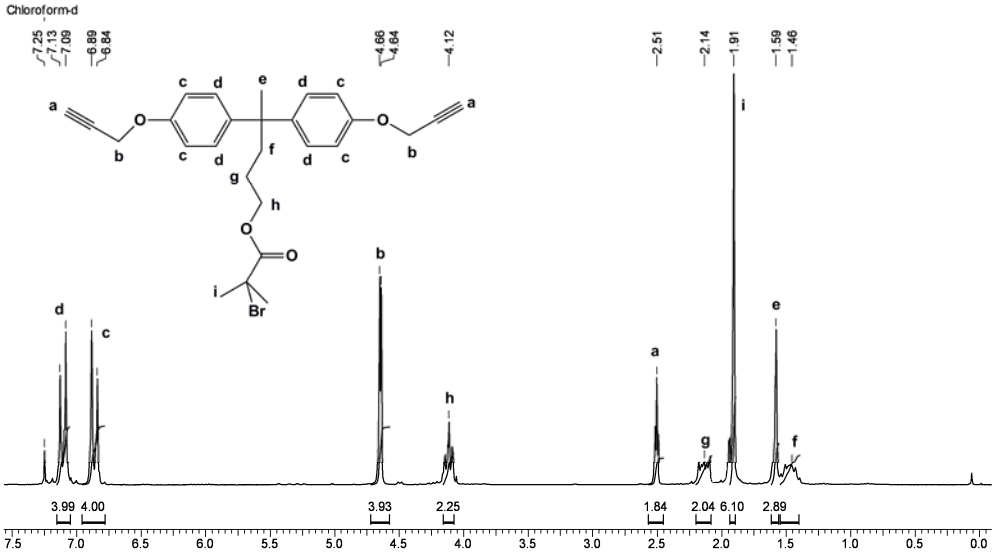
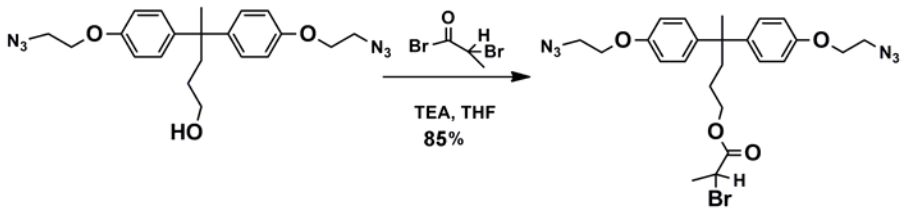


Figure 3b.8: ^{1}H-NMR spectrum of 4, 4'-bis (4-(prop-2-yn-1-yloxy)phenyl) pentyl 2-bromo2-methylpropanoate in $CDCl_3$

In ^{13}C-NMR spectrum, a peak due to ester carbonyl carbon was observed at 171.1 ppm and the carbons corresponding to propargyloxy group appeared at 78.7 and 76.3 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3b.4.4. Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl)pentyl 2-bromopropanoate

4, 4'-Bis (4-(2-azidoethoxy) phenyl)pentyl 2-bromopropanoate was synthesized by esterification of 4,4'-bis(4-(2-azidoethoxy) phenyl)pentan-1-ol with 2-bromopropanoylbromide in dry chloroform **(Scheme 3b.6).** The product was purified by silica gel column chromatography and was characterized using FT-IR, ^{1}H-NMR spectroscopy.



Scheme 3b.6: Synthesis of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromo-propanoate

In FT-IR spectrum, the absorption peak at 2110 cm^{-1} confirmed the azido functionality. In ^{1}H-NMR spectrum of 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromo-propanoate (**Figure 3b.9)**, the appearance of triplet at 3.57 ppm could be attributed to the methylene protons attached to azido functional group. The doublet appeared at 1.81 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

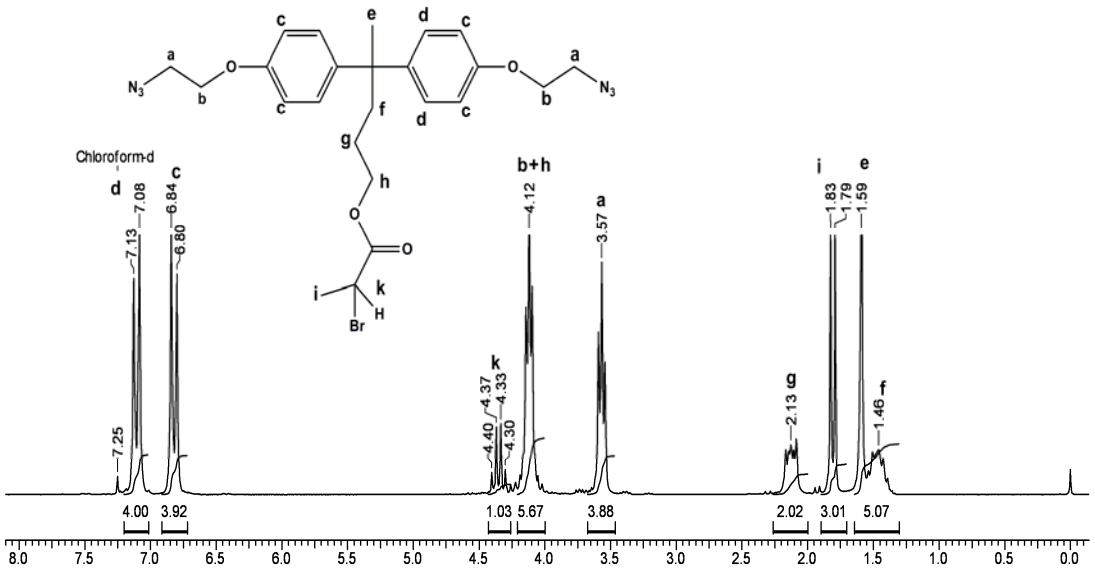
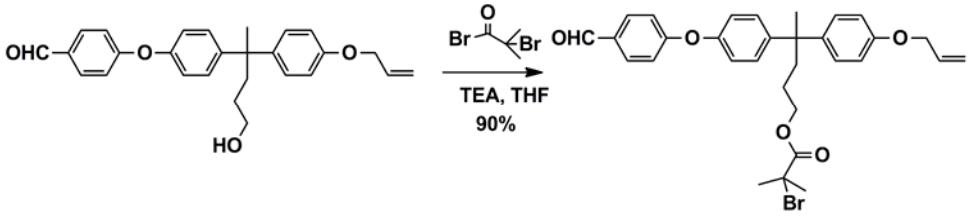


Figure 3b.9: ^{1}H-NMR spectrum of 4,4'-bis(4-(2-azidoethoxy)phenyl)pentyl 2-bromo-propanoate in $CDCl_3$

In ^{13}C-NMR spectrum, a peak due to ester carbonyl carbon was observed at 172.6 ppm and the carbons attached to azido group appeared at 49.8 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure. The peak assignments in ^{13}C-NMR spectrum were confirmed by DEPT spectrum.

3b.4.5. Synthesis of 4-(4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methyl propanoate

4-(4-(Allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methyl propanoate was synthesized by esterification of 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde with 2-bromoisobutyryl bromide in dry chloroform **(Scheme 3b.7).** The product was purified by silica gel column chromatography and was characterized using FT-IR, ^{1}H-NMR and ^{13}C- NMR spectroscopy.



Scheme 3b.7: Synthesis of 4-(4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl)pentyl 2-bromo-2-methyl propanoate

FT-IR spectrum of 4-(4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy) phenyl)pentyl 2-bromo-2-methyl propanoate showed absorption bands at 1735, and 1710 cm^{-1} that correspond to ester carbonyl and aldehyde asymmetric stretching, respectively. ^{1}H-NMR spectrum of 4-(4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate along with assignments is shown in **Figure 3b.10**

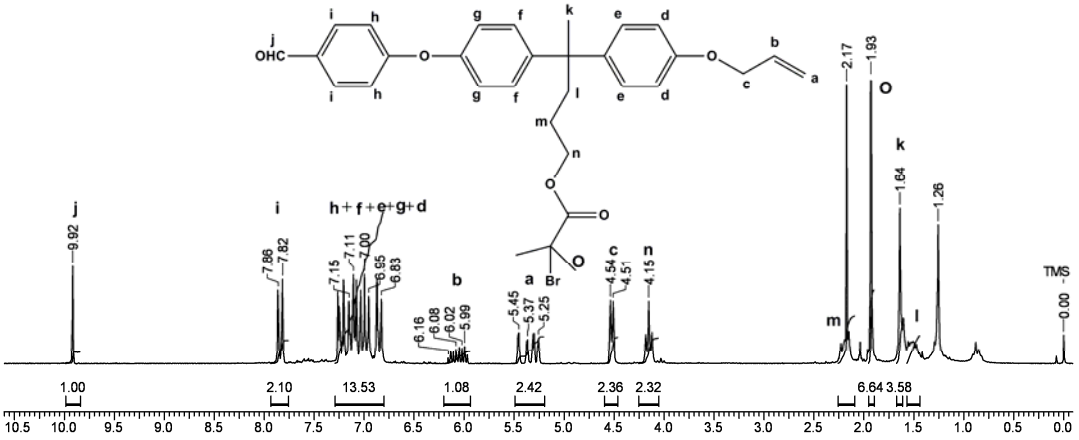


Figure 3b.10: ^{1}H-NMR spectrum of 4-(4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate in $CDCl_3$

The presence of aldehyde functionality was confirmed by the appearance of a singlet at 9.92 ppm. The presence of allyloxy functionality was confirmed by the appearance of multiplets in the range 6.16-5.99 ppm, and 5.45-5.25 ppm corresponding to methine and vinyl protons, respectively. The singlet appeared at 1.93 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure. In ^{13}C-NMR spectrum, a peak corresponding to carbonyl carbon of aldehyde group was observed at 191.3 ppm and peak due to ester carbonyl carbon was observed at 170.5 ppm. The carbon atoms corresponding to allyl group appeared at 134 and 118.5 ppm. The spectral data corresponding to other carbon atoms was in good agreement with the proposed structure.

3b.5.Conclusions

- ✓ The following five new ATRP initiators containing functional groups were synthesized, starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid.
  1) 4, 4'-Bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate
  2) 4, 4'-Bis (4-(4'- (formylphenoxy) phenyl) pentyl 2-bromopropanoate
  3) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo-2-methylpropanoate
  4) 4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate, and
  5) 4-(4-(Allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate
- ✓ The initiators serial number 1-4 and serial number 5 are potentially useful for preparation of α, α'-homo bifunctional and α, α'-hetero bifunctional polymers respectively, by ATRP of monomers such as methyl methacrylate and styrene.

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Chapter 4

End-Functionalized Polymers: Synthesis Characterization and Chemical Modification

Chapter 4a

End-Functionalized Polymers by ROP: Synthesis, Characterization and Chemical Modification

4a.1. Introduction

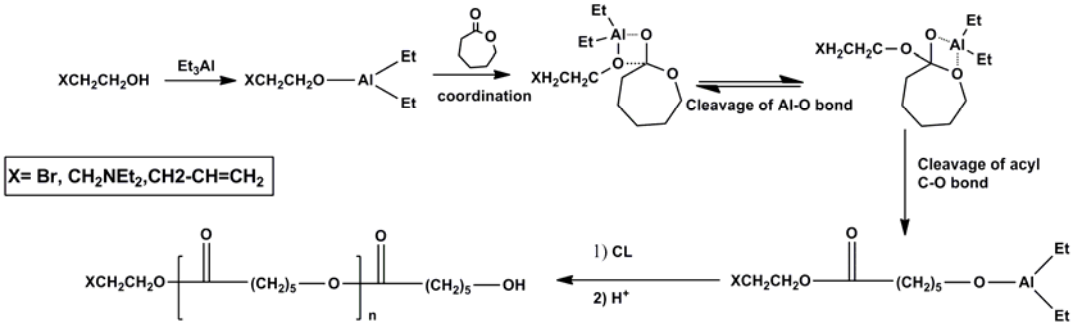
Aliphatic polyesters based on ε-caprolactone, lactide, and glycolide are of interest for medical and pharmaceutical applications by virtue of their biocompatible and biodegradable properties[1, 2]. Current targets for these materials include degradable sutures, resorbable implant materials, tissue engineering scaffolds, and drug delivery vehicles[3-5]. While suitable for many applications, such polyesters are hydrophobic, semi-crystalline solids that lack functionality for further modification and tailoring. The preparation of functionalized aliphatic polyesters is a synthetic challenge, irrespective of whether the functionality is introduced at the monomer stage or in post polymerization chemistry. In the former case, such functionality must be compatible with the polymerization conditions, while in the latter case the desired transformations must be achieved without degradation of the polyester backbone[6-9].

4a.1.1. Poly ε-caprolactone containing different types of functional groups

Functionality at α-, ω-, as well as γ-position could be introduced on poly ε-caprolactone using different approaches. 1) α-functionality can be introduced in a controlled way by the use of appropriate functional initiators 2) ω-functionalized poly ε-caprolactone could be prepared by post modification reaction and 3) γ-functionalized poly ε-caprolactone might be accessible by use of γ-functionalized cyclic monomers.

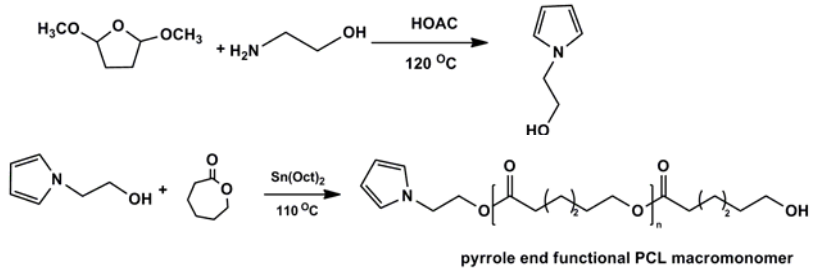
4a.1.1.1. Poly ε-caprolactone containing functionality at α-position

Functionality at α- position could be introduced in a controlled way by the use of functional initiators e.g aluminium alkoxide initiators prepared by reaction of triethylaluminium ($AlEt_3$) with an alcohol[10]. Aluminium alkoxides [Al $(OCH_2CH_2X)_3$] carrying a functional group (X- Br, CH_2NEt_2, $CH_2CH{=}CH_2$) have been used as efficient initiators for ring opening polymerization (ROP) of lactones, lactides and glycolides. Hydrolysis of active aluminium alkoxide bond leads to the formation of an asymmetric telechelic aliphatic polyester, the end groups being X and OH, respectively. The reaction proceeds through the coordination of aluminium to the exocyclic carbonyl oxygen of ε-caprolactone, followed by the acyl-oxygen cleavage of the monomer and insertion into the Al-O bond of the initiator **{Scheme 4a.1}**.



Scheme 4a.1: α-Functionalization of poly ε-caprolactones using functional initiators[10]

In addition, functional initiators have been synthesized through the exchange of the alkoxy group of (Al ($O^iPr)_3$) with the desired functional alcohol[11] or even macromonomers or end functional aliphatic esters could be synthesized by properly placing appropriate functional groups on alcoholic substrate[12]**{Scheme 4a.2}**.

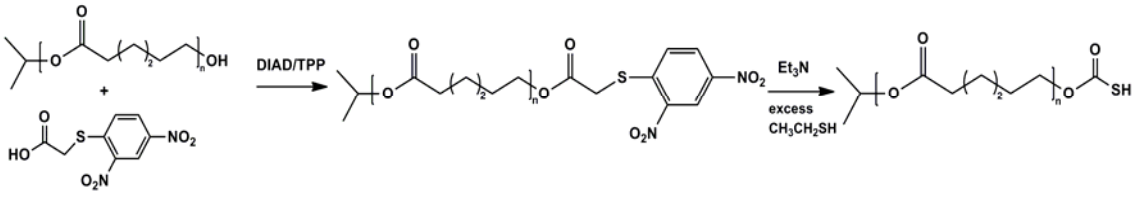


Scheme 4a.2: α-Functionalization of poly ε-caprolactones by initiator approach[12]

Lipase catalyzed ROP was used to synthesize α-end functionalized poly ε-caprolactone with different functionalities such as vinyl, phenol, ether, ester using respective functionalized alcohols[13].

4a.1.1.2. Poly ε-caprolactone containing functionality at ω -position

ω-Functionalized poly ε-caprolactone could be prepared by post modification reaction. Representative example is depicted in **Scheme 4a.3.** Coupling reactions are mainly used to couple OH-functionaized poly ε-caprolactone but one need to consider the reaction conditions which must not affect polymer chain[14].



Scheme 4a.3: ω- Functionalized poly ε-caprolactones by end group modification[14]

4a.1.1.3. Poly ε-caprolactone containing functionality at β- or γ *-position*

β- or γ-Functionalized poly ε-caprolactone could be accessible by the use of β- or γ-functionalized cyclic monomers. Various functionalities could be introduced at β- or γ-position by appropriately placed functionality on cyclic monomers. Representative examples of functional ε-caprolactone monomers are depicted in **Figure 4a.1.**

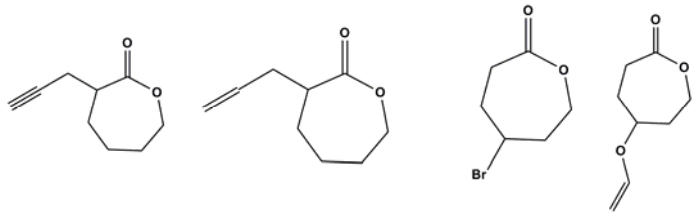
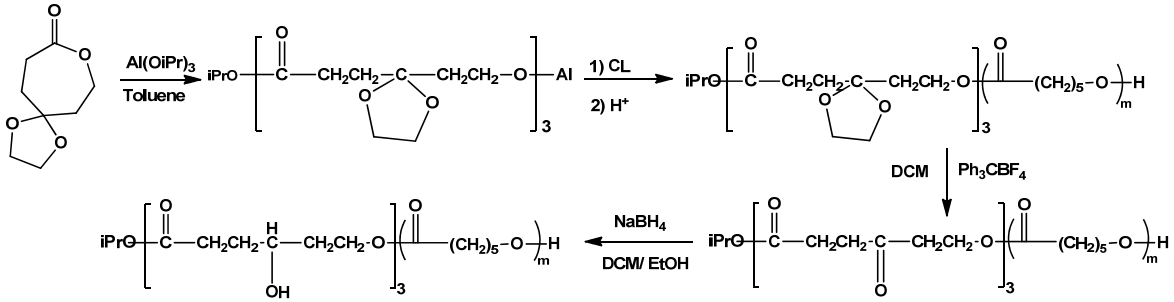


Figure 4a.1: Representative examples of functional caprolactone monomers

Unfortunately, this strategy presents severe drawbacks. Firstly, several of these lactones are not commercially available and several steps are often necessary for their synthesis. Moreover, it is mandatory to rigorously purify theses lactones before polymerization, especially if sensitive alkoxides are used as initiators, which is sometimes a difficult task. Accordingly, the total yield of the synthesis is sometimes low and the functionalized lactone is thus quite expensive. Several functional groups such as epoxides, alcohols, and carboxylic acids are not tolerated by propagating species such as aluminum and tin (IV) alkoxides. To introduce such functionalities which are not compatible to ROP reaction conditions by this route, one has to use protected functional monomer and after polymerization protected group could be selectively deprotected into desired functionality. But it is not always easy to have deprotection conditions where no degradation takes place. After deprotection step, particular functionality could be converted into different functional groups. Jerome et al.[10] reported synthesis of ketone functionalized polyester by deacetalization of ethylene ketal pendant group (**Scheme 4a.4).** which was further converted into alcohol functionality by carrying out reduction.

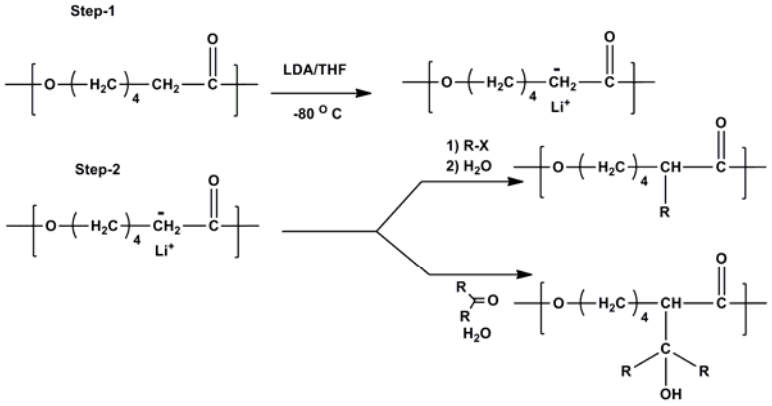


Scheme 4a.4: γ-Functionalized poly ε-caprolactones by chemical modification[10]

4a.1.2. Functionalization of poly ε-caprolactone by chemical modification

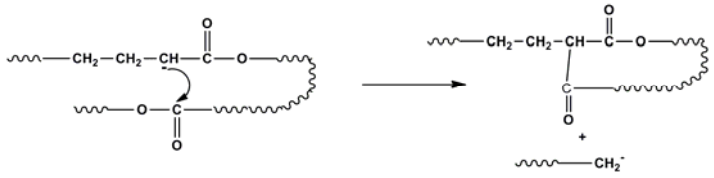
4a.1. 2.1. Chemical modification using anionic route

The most direct route towards functionalized aliphatic polyesters is based on the functionalization of polyester chains[10]. This approach is very appealing because a wide range of functionalized aliphatic polyesters could then be made available from a single precursor. This approach was implemented by Vert and coworkers[15] using a two-step process. First, poly ε-caprolactone was metallated by lithium diisopropylamide with formation of a poly (enolate). Next, the poly (enolate) was reacted with an electrophile (**Scheme 4a.5)** such as naphthoyl chloride[16], benzylchloroformate, acetophenone[16], or carbon dioxide[17]. The implementation of this strategy is, however, difficult because of a severe competition between chain metallation and chain degradation. Moreover, the content of functionalization is quite low (<30%), even under optimized conditions.



Scheme 4a.5: Chemical modification of poly ε-caprolactones chain using anionic route[15]

Substitution reactions *via* the α hydrogen of an ester have not been extended to aliphatic polyesters so far, probably because of the sensitivity of these macromolecules to lysis and intramolecular autocondensation (**Scheme 4a.6)** reaction of poly ε-caprolactone.

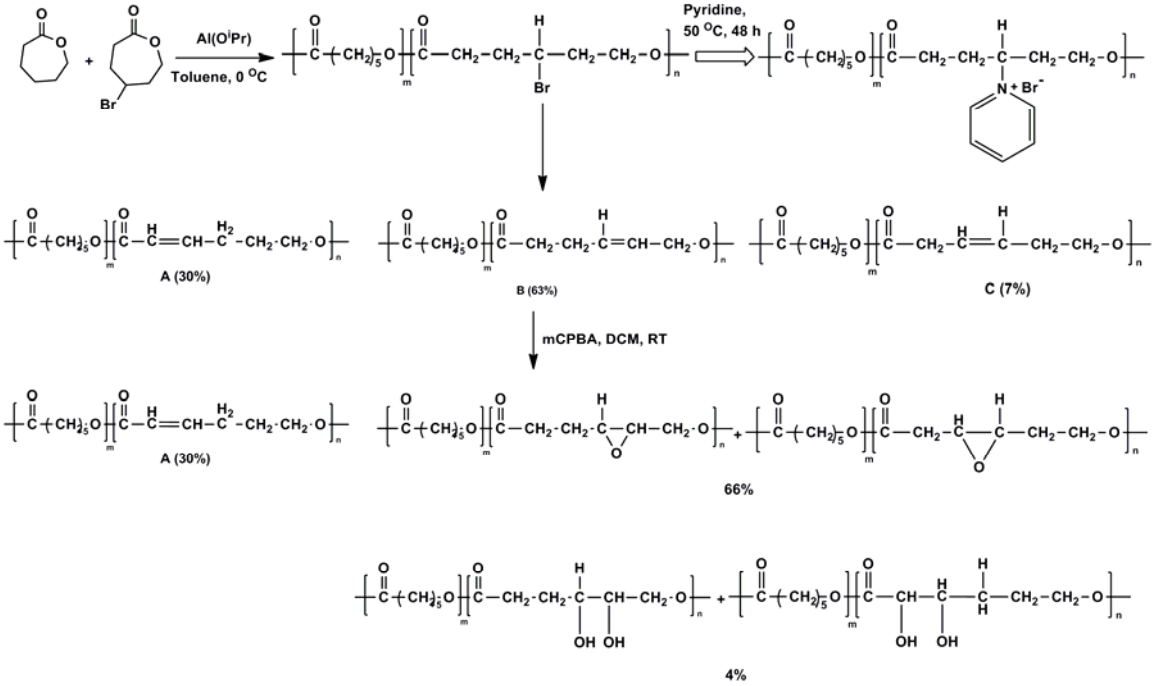


Scheme 4a.6: Intramolecular autocondesation reaction of poly ε-caprolactones[15]

4a.1.2.2. Copolymerization and end functional modification

Reactivity of γ-bromo substituent allows for the new functional polyesters to be prepared[10]. A polycationic poly ε-caprolactone has been made available by reaction of pyridine and poly (ε-CL-co-γBrCL) .The quaterenization is close to completeness. This functionalization

opens the way to the synthesis of hydrosoluble polyester (**Scheme 4a.7)**. The reaction of 1, 8-diazabicyclo [5.4.0] undec-7-ene (DBU) with poly (ε-CL-co-γBrCL) in toluene at 80 °C leads to unsaturated polyester. The elimination reaction is not selective as a mixture of non-conjugated and conjugated olefin units is formed.

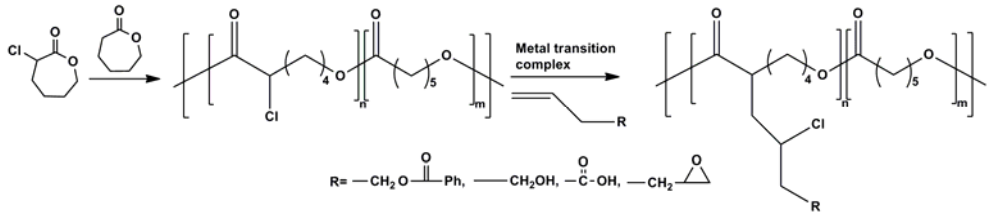


Scheme 4a.7: Chemical modification of poly ε-caprolactones by quaternization and elimination

The quantitative epoxidation of the non-conjugated double bonds has been carried out with *3*-chloroperbenzoic acid. It must be noted that the epoxidation reaction doesn't lead to degradation and provides versatile intermediates for further functionalization of the polyester backbone.

4a.1.2.3. Chemical substitution using atom transfer radical addition (ATRA)

Aluminum and tin alkoxides mediated ROP is not tolerant of hydroxyl, carboxylic acid and epoxy groups. In these specific cases, hydroxyl and carboxylic acid groups must be protected before ROP and deprotected afterwards[18 19, 20], whereas post-polymerization epoxidation has to be considered for grafting epoxides along the chains[21-23]. For all these reasons, straightforward strategies are highly desirable to prepare aliphatic polyesters with pendant hydroxyl, carboxylic acid and epoxide groups[24]. Substitution of radical species for the anionic ones used in the 'poly (enolate)' strategy is an alternative worth being tested (**Scheme 4a.8)**, because of the much higher tolerance of the aliphatic polyesters to radicals compared to nucleophiles[16].



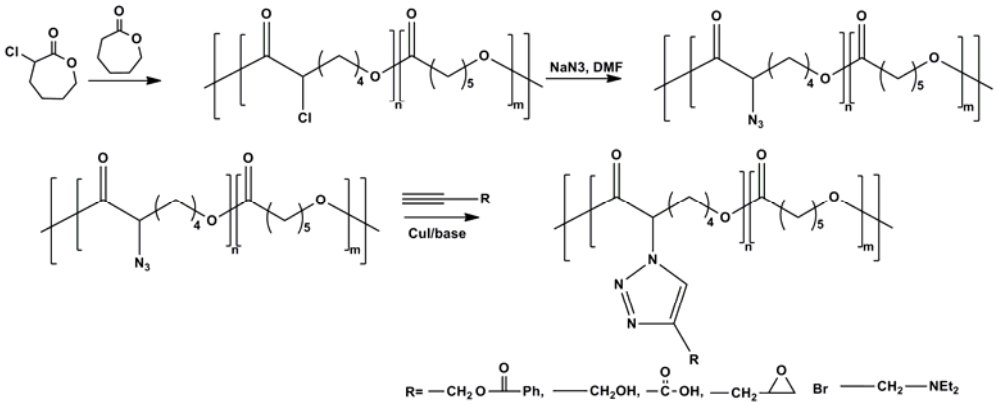
Scheme 4a.8: Schematic representation of chemical modification of poly ε-caprolactones by ATRA[24]

4a.1.2.4. Chemical modification using click chemistry

"Click" chemistry has emerged as an attractive and promising tool to synthesis of novel polymers with well-defined architectures[25]. The great success of this process relies on its simplicity, efficiency and selectivity, wide applicability regardless of the reagents, molecular complexity and ability to take place under aerobic conditions[26].

4a.1.2.4.1. Azide-alkyne click chemistry

Since the pioneering work of Sharpless[27], highly regioselective copper-mediated 1,3-dipolar cycloaddition of alkynes and azides, known as a "click" reaction[28], is extensively used in macromolecular engineering[29-32]**(Scheme 4a.9)**. Substitution of the pendent chlorides of poly (αClεCL-*co*-εCL) random copolymers by sodium azide, followed by the Huisgen's 1, 3-dipolar cycloaddition of alkynes (functional and/ or polymeric), is a valuable technique for grafting a variety of substituents onto poly ε-caprolactone.

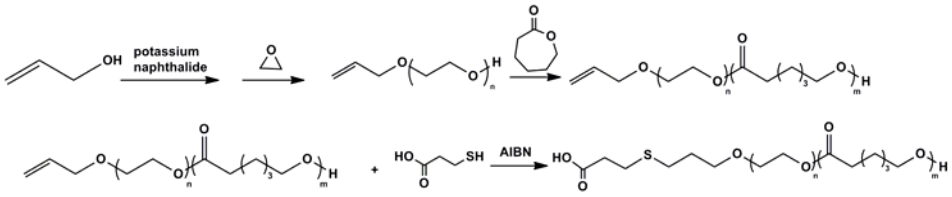


Scheme 4a.9: Chemical modification of poly ε-caprolactones by azide-alkyne click chemistry[33, 34]

4a.1.2.4.2. Thiol-ene click chemistry

Another reaction that is recently emerging as an attractive "click" process is the addition of thiols to alkenes (**Scheme 4a.10)**, which is called thiol-ene click reaction[35-38]. Thiol-ene

chemistry has many of the attributes of alkyne-azide click chemistry, such as tolerance to many different reaction conditions, facile synthetic strategies and clearly defined reaction pathways. Therefore, the thiol-ene click reaction has been utilized for a range of applications, including cross-linked polymeric matrices, such as hydrogels[39], polymer and nanoparticle functionalization[40], dendrimer synthesis[41], and nanoprinting and patterning[42].



Scheme 4a.10: Chemical modification of poly ε-caprolactones by thiol-ene click chemistry

4a.1.2.5. Chemical modification using Michael addition reaction

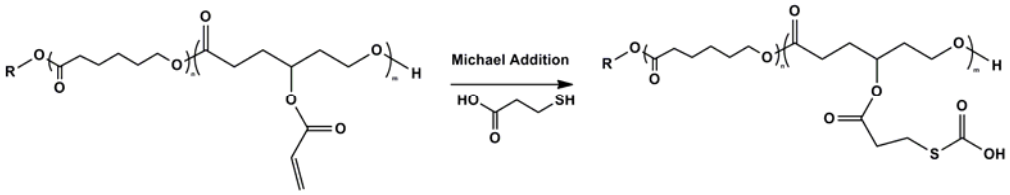
The Michael-type addition of thiol compounds onto γ-acryloyloxy ε-caprolactone unit is a very straightforward technique of functionalization and grafting of poly ε-caprolactone with the advantage of high reactivity and chemoselectivity of the reactants[43]. (**Scheme 4a.11)** and which is tolerant to a variety of functional groups and does not require intermediate protection/deprotection steps[44].

The characteristic features of this reaction are

(i) occurrence under very mild conditions (preventing the polyester degradation),

(ii) tolerance to a wide range of functional groups (avoiding protection/deprotection steps),

(iii) no need for metallic catalyst, and thus no contamination that could be a problem for biomedical applications



Scheme 4a.11: Chemical modification by Michael addition reaction[44]

The easy synthesis and living (co) polymerization of γ-acryloyloxy-ε-caprolactone (ACL) makes it easy to have double bonds distributed along polyester backbones of different architectures[45] and enable Michael-type addition.

To date, numerous successful modification examples have been reported, including chain end functionalized aliphatic polyesters with allyl[10, 46, 47] , amino[48], thiol[14, 49, 50], hydroxyl,

carboxyl, epoxy[24] , propargyl[51-53], and azide[54] by ROP initiated by the functional group containing initiators or through post modification of polyesters.

A survey of literature revealed that major attention has been paid to the synthesis of α-, ω-, or α, ω-functionalized aliphatic polyesters by modification route or by use of functional initiator approach with little efforts on the preparation of α, α'-bifunctionalized polymers. Keeping these points in mind, synthesis of different α, α'-homobifunctionalized poly ε-caprolactones, possessing allyloxy, propargyloxy, azide and aldehyde functionality and α, α'-hetero bifunctionalized poly ε-caprolactones, featuring allyloxy-aldehyde, allyloxy-azido, and azido-aldehyde functionality was undertaken. End-functionalized polymers were characterized by FTIR and NMR spectroscopy and size exclusion chromatography. End functionality on the polymer was demonstrated by carrying out specific reactions of that particular functional group present on polymer.

4a.2. Experimental

4a.2.1. Materials

4,4'-Bis(4-(allyloxy)phenyl)pentan-1-ol, 4,4'-(((5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde, 4,4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol, 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol, 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde, 4-(4-(allyloxy)phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol and 4-(4-(2-(4-(2-azidoethoxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde were synthesized as per the procedures described in **chapter 3a**. ε-Caprolactone (Aldrich), was stirred over calcium hydride for 4 h and distilled under reduced pressure. Toluene was dried over sodium wire. 3-Chloroperoxybenzoic acid, phenyl acetylene, stannous (II) octoate, 3-mercaptopropionic acid and azobisisobutyronitrile were received from Lancaster and were used as received. Sodium sulphate, potassium hydroxide, sodium hydrogen carbonate, methanol, chlorobenzene and chloroform, all received from S.D. Fine-Chem. Ltd., India, were used as received.

4a.2.2. Characterization and measurements

FTIR spectra were recorded on a Perkin-Elmer Spectrum *GX* spectrophotometer. NMR spectra were recorded on a Bruker 200 MHz spectrometer for ^{1}H-NMR and 125 MHz for ^{13}C-NMR measurements using $CDCl_3$, $CDCl_3$ without TMS or DMSO-d6 as a solvent. Molecular weight and molecular weight distribution of polymers were determined using GPC analysis at a flow rate of 1 mL min^{-1} in chloroform at 30 °C (Thermoseparation product) equipped with spectra

series UV 100 and spectra system RI 150 detectors. Two 60 cm PSS SDV-gel columns (102 – 105 A^O and 100 A^O) were used at 30 °C. The sample concentration was 2 to 3 mg mL^{-1} and the injection volume was 50 mL. HPLC grade chloroform was used as eluent at room temperature with a flow rate of 1 mL min^{-1}. Polystyrene was used as the calibration standard.

4a.2.3. Synthesis of functional poly ε-caprolactones

α, α'-Homo- as well as hetero-bifunctional poly ε-caprolactones having different functional groups were synthesized by ROP of ε-caprolactone using respective functional initiators in toluene in the presence of stannous (II) octoate as catalyst.

4a.2.3.1. Synthesis of α, α' -bisallyloxy functionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (4.0 g, 35 mmol), stannous (II) octoate (0.8 mg, 0.0019 mmol), 4, 4'–bis (4-(allyloxy) phenyl) pentan-1-ol (134 mg, 0.38 mmol) and toluene (15 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the rection mixture to room temperature, diluted with dichloromethane (15 mL) and poured into cold methanol (150 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.06 (d, Ar-H *meta* to ether linkage), 6.79 (d, Ar-H *ortho* to ether linkage), 6.11-5.97(m, =CH), 5.43-5.23 (q, $=CH_2$), 4.49 (d, $-OCH_2$), 4.04 (t, $-CH_2OOC$ from poly ε-caprolactone), 2.29 (t, - CH_2CH_2CO from poly ε-caprolactone), 1.64-1.57 (m, $-CH_2CH_2$ from poly ε-caprolactone + protons from initiator fragment), 1.39- 1.34 (m, $-CH_2CH_2$ from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.1.1. Chemical transformation of α, α'- bisallyloxy functionalized poly ε-caprolactone into bis-epoxide functionalized poly ε-caprolactone

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, bis-allyloxy functionalized poly ε-caprolactone (810 mg, 0.1 mmol) and dichloromethane (15 mL) and the solution was cooled to 0 °C with ice water. The solution of 3-chloroperoxybenzoic acid (86 mg, 0.5 mmol) in dichloromethane (10 mL) was added over a period of 30 minutes. After completion of addition, the reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 24 h. The reaction mixture was washed with aqueous 5%

$NaHCO_3$ solution (3 x 15 mL) and de-ionized water (3 x 15 mL). The polymer was precipitated into methanol (50 mL), filtered and was dried under vacuum at 50 °C for 8 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.06 (d, Ar-H *meta* to ether linkage), 6.80 (d, Ar-H *ortho* to ether linkage), 4.04 (t, -CH_2OOC from poly ε-caprolactone), 2.91 (bs, -CH_2O), 2.73 (bs, -CH_2O), 2.61-2.55 (m, -CH_2O), 2.33 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.64-1.58 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.37 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.2. Synthesis of α, α'- bisaldehyde functionalized poly ε-caprolactones

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (2.85 g, 25 mmol), stannous (II) octoate (2 mg, 0.005 mmol), 4,4'-(4,4'-(5-hydroxypentane-2,2-diyl) bis(4,1-phenylene)) bis(oxy) dibenzaldehyde (480 mg, 1.0 mmol) and toluene (30 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. The polymerization was carried out at 110 °C. After a given time, the polymerization mixture was cooled to room temperature, diluted with dichloromethane (20 mL) and poured into cold methanol (200 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730, 1710

^{1}H NMR ($CDCl_3$, δ/ppm): 9.86 (s, aldehyde), 7.78 (d, Ar-H *ortho* to aldehyde), 7.20-7.15 (d, Ar-H *meta* to ether), 7.02-6.92 (m, Ar-H), 3.99 (t, -CH_2OOC from poly ε-caprolactone), 2.24 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.58-1.53 (m, -CH_2CH_2 from poly ε-caprolactone+ protons from initiator fragment), 1.34-1.31 (m, -CH_2CH_2 from poly ε-caprolactone+ protons from initiator fragment)

4a.2.3.2.1. Chemical transformation by aldehyde-aminooxy click reaction

4a.2.3.2.1.1. Synthesis of O-(2-azidoethyl) hydroxylamine

4a.2.3.2.1.1.1. Synthesis of 2-azidoethanol

Synthesis of 2-azidoethanol was carried out as discussed in **Chapter 3a Section 3a.2.1.1.1.**

4a.2.3.2.1.1.2. Synthesis of 2-azidoethyl 4-methylbenzenesulfonate

Synthesis of 2-azidoethyl 4-methylbenzenesulfonate was carried out as discussed in **Chapter 3a Section 3a.2.1.1.**

4a.2.3.2.1.1.3. Synthesis of 2-(2-azidoethoxy) isoindoline-1, 3-dione

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2-azidoethyl 4-methylbenzenesulfonate (8.9 g, 37 mmol), triethylamine (5.0 g, 56 mmol), and dry THF (70 mL). The reaction mixture was cooled to 0 °C. The solution of N-hydroxy phthalimide (9.15 g, 56 mmol) in dry THF (20 mL) was added drop-wise into the reaction mixture under constant stirring at 0 °C. The reaction mixture was stirred at 80 °C for 24 h. The reaction mixture was cooled, THF was evaporated under vacuum and chloroform (50 mL) was added. The chloroform solution was washed with 5% $NaHCO_3$ (3 x 100 mL) and de-ionized water (3 x 100 mL). The chloroform solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (10:90, v/v) as eluent. The removal of the solvent yielded 6.10 (71 %) of 2-(2-azidoethoxy) isoindoline-1, 3-dione a white solid

IR ($CHCl_3$, cm^{-1}): 2108, 1690.

^1H NMR ($CDCl_3$, δ/ppm): 7.87-7.83 (m, 2H), 7.78-7.74 (m, 2H), 4.34 (t, 2H), 3.65 (t, 2H).

4a.2.3.2.1.1.4. Synthesis of O-(2-azidoethyl) hydroxylamine

Into a 250 mL single necked round-bottom flask were charged, 2-(2-azidoethoxy) isoindoline-1, 3-dione (3.0 g, 12 mmol), and dichloromethane (50 mL). The solution of hydrazine hydrate (3.6 g, 72 mmol) in dichloromethane (20 mL) was added drop-wise into the reaction mixture under stirring. The reaction mixture was stirred at room temperature overnight. The reaction mixture was filtered and washed with 5% $NaHCO_3$ (3 x 100 mL) and de-ionized water (3 x 100 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and dicholoromethane was evaporated under reduced pressure to obtain O-(2-azidoethyl) hydroxylamine 750 mg (60 %) as a slight yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3100, 2110

^1H NMR ($CDCl_3$, δ/ppm): 5.18 (bs, 2H), 3.77 (t, 2H), 3.39 (t, 2H).

4a.2.3.2.1.2. Reaction of α, α'-bisaldehde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, bis-aldehyde functionalized poly ε-caprolactone (360 mg, 0.2 mmol), dichloromethane (10 mL) and a pinch of sodium sulfate. The solution of O-(2-azidoethyl) hydroxylamine (250 mg, 20 mmol) dissolved in dichloromethane (5 mL) was added and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was precipitated into cold hexane (50 mL). The polymer was filtered and dried under vacuum at 50 °C for 8 h.

IR ($CHCl_3$, cm^{-1}): 2110, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 8.11 (s, -CH=N), 7.56 (d, Ar-H *ortho* to oxime), 7.16 (d, Ar-H *meta* to ether linkage), 7.02-6.92 (m, Ar-H), 4.35 (t, $-OCH_2$) 4.06 (t, $-CH_2CH_2OOC$ from poly ε-caprolactone), 3.57 (t, CH_2N_3), 2.31 (t, $-CH_2CH_2CO$, from poly ε-caprolactone), 1.65-1.61 (m, $-CH_2CH_2$, from poly ε-caprolactone+ protons from initiator fragment), 1.41- 1.35 (m, $-CH_2CH_2$, from poly ε-caprolactone+ protons from initiator fragment)

4a.2.3.3. Synthesis of α, α'-bispropargyloxy functionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged, ε-caprolactone (3.76 g, 33 mmol) with, stannous (II) octoate (1 mg, 0.0025 mmol), PMDETA (17 mg, 0.1 mmol), 4, 4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol (174 mg, 0.5 mmol) and toluene (30 mL) under nitrogen atmosphere. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, diluted with dichloromethane (25 mL) and poured into cold methanol (250 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 7.09 (d, Ar-H *meta* to ether linkage), 6.85 (d, Ar-H *ortho* to ether linkage), 4.64 (d, $-OCH_2$), 4.04 (t, $-CH_2OOC$, from poly ε-caprolactone), 2.51 (t, acetylene proton), 2.29 (t, - CH_2CH_2CO, from poly ε-caprolactone), 1.64-1.59 (m, $-CH_2CH_2$, from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.37 (m, $-CH_2CH_2$, from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.3.1. Chemical transformation of α, α'-bispropargyloxy functionalized poly ε-caprolactone

4a.2.3.3.1.1. Reaction of α, α'-bis-propargyloxy functionalized poly ε-caprolactone with 2-azidoethyl 4-methylbenzenesulfonate

Schlenk tube equipped with a magnetic stir bar was charged with, bis-propargyloxy functionalized poly ε-caprolactone (530 mg, 0.1 mmol), CuBr (15 mg, 0.1 mmol), 2-azidoethyl 4-methylbenzenesulfonate (450 mg, 2 mmol), DMF (20 mL) and N, N, N', N', N"-pentamethyldiethylenetriamine (20 μL, 0.85 mmol) under nitrogen atmosphere. The Schlenk tube was sealed and the reaction mixture was degassed three times by freeze-pump-thaw cycles and kept stirring for 24 h at room temperature. After the reaction time, DMF was removed under reduced pressure and reaction mixture was diluted with dichloromethane (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was filtered and dried at room temperature under vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730

^1H NMR ($CDCl_3$, δ/ppm): 7.80 (d, *ortho* to sulfonate), 7.64 (d, *meta* to sulfonate), 7.37 (s, triazole ring proton), 7.04 (d, Ar-H *meta* to ether linkage), 6.80 (d, Ar-H *ortho* to ether linkage), 5.13 (d, -OCH_2), 4.59 (d, -OCH_2), 3.99 (t, -CH_2OOC, poly ε-caprolactone), 2.24 (t, - CH_2CH_2CO, from poly ε-caprolactone), 1.58-1.53 (m, -CH_2CH_2, from poly ε-caprolactone + protons from initiator fragment), 1.34-1.31 (m, -CH_2CH_2, from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.4. Synthesis of α, α'-bisazido functionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (2.36 g, 20.75 mmol), stannous octoate (1 mg, 0.002 mmol), 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol, (170 mg, 0.415 mmol) and toluene (30 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, diluted with dichloromethane (25 mL) and poured into cold methanol (250 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 2108, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 7.08 (d, Ar-H from initiator), 6.85 (d, Ar-H from initiator), 4.04 (t, -CH_2OOC from poly ε-caprolactone + $OCH_2CH_2N_3$ protons from initiator fragment), 2.29 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.63-1.59 (m, -CH_2CH_2 from poly ε-caprolactone), 1.39-1.33 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.4.1. Chemical transformation α, α'- bisazido functionalized poly ε-caprolactones

4a.2.3.4.1.1. Reaction of α, α'- bis-azido functionalized poly ε-caprolactone with phenyl acetylene

Schlenk tube equipped with a magnetic stir bar was charged with, α, α'-bisazido functionalized poly ε-caprolactone (490 mg, 0.1 mmol), CuBr (15 mg, 0.1 mmol), phenyl acetylene (204 mg, 2 mmol), DMF (20 mL) and N, N, N', N', N"-pentamethyldiethylenetriamine (20 μL, 0.1 mmol) under nitrogen atmosphere. The Schlenk tube was sealed and the reaction mixture was degassed three times by freeze-pump-thaw cycles and kept stirring for 24 h at room temperature. After the reaction time, DMF was removed under reduced pressure and reaction mixture was diluted with dichloromethane (50 mL) the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into methanol (500 mL) to precipitate the polymer. The polymer was filtered and dried at room temperature under vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 7.94 (s, Ar-H attached to triazole ring), 7.80 (d, Ar-H attached to triazole ring + triazole proton), 7.44-7.38 (m, Ar-H attached to triazole ring), 7.03 (d, Ar-H from initiator), 6.77 (d, Ar-H from initiator), 4.78 (t, -CH_2), 4.35 (t, -CH_2), 4.04 (t, -CH_2OOC from poly ε-caprolactone), 2.29 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.65-1.57 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.39- 1.34 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.5. Synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (5.68 g, 50 mmol), stannous (II) octoate (1 mg, 0.002 mmol), 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl) phenoxy) benzaldehyde (172 mg, 0.415 mmol) and toluene (30 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated

by cooling the reaction mixture to room temperature, diluted with dichloromethane (20 mL) and poured into cold methanol (200 mL). The polymer was collected by filtration and dried at rrom temperature in vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730, 1710

^1H NMR ($CDCl_3$, δ/ppm): 9.90 (s, -CHO), 7.84 (d, Ar-H *ortho* to aldehyde), 7.25-6.86 (m, Ar-H), 6.13-5.99 (m, $-CH_2-CH=CH_2$), 5.45-5.24 (q, $-HC=CH_2$), 4.50 (d, $-OCH_2$), 4.04 (t, $-CH_2OOC$ from poly ε-caprolactone), 2.29 (t, - CH_2CH_2CO from poly ε-caprolactone), 1.58-1.53 (m, - CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.34-1.31 (m, $-CH_2CH_2$ from poly ε-caprolactone)

4a.2.3.5.1. Chemical modification of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones

4a.2.3.5.1.1. Aldehyde-aminooxy click reaction

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones (970 mg, 0.1 mmol), dichloromethane (10 mL) and a pinch of sodium sulfate. Then, solution of O-(2-azidoethyl) hydroxylamine (125 mg, 10 mmol) dissolved in dichloromethane (5 mL) was added and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was precipitated into cold hexane (50 mL). The obtained polymer was filtered and dried under vacuum at 50 °C for 8 h.

IR ($CHCl_3$, cm^{-1}): 2110, 1730

^1H NMR ($CDCl_3$, δ/ppm): 8.07 (s, -CH=N), 7.52 (d, Ar-H *ortho* to oxime), 7.11-6.80 (m, Ar-H), 6.12-6.00 (m, $-CH=CH_2$), 5.45-5.24 (q, $-HC=CH_2$), 4.50 (d, $-OCH_2$), 4.05 (t, $-CH_2CH_2OOC$ from poly ε-caprolactone), 2.29 (t, - CH_2CH_2CO, from poly ε-caprolactone), 1.61-1.53 (m, $-CH_2CH_2$ from poly ε-caprolactone + protons from initiator fragment), 1.39- 1.31 (m, $-CH_2CH_2$ from poly ε-caprolactone)

4a.2.3.5.1.2. Thiol-ene thermal click reaction

Into a clean and dry Schlenk tube were charged, allyloxy functionalized poly ε-caprolactone (490 mg, 0.05 mmol), 3- maracptopropionic acid (53 mg, 0.5 mmol), AIBN (82 mg,

0.5 mmol) and chlorobezene (20 mL). The mixture was degassed *via* three freeze-pump-thaw cycles and subsequently vacuum sealed. The Schlenk tube was heated at 80 °C for 6 h. The reaction was quenched by cooling the reaction mixture at 0 °C. Chlorobenzene was removed under reduced pressure. The polymer was dissolved in dichloromethane (20 mL) and precipitated into cold methanol (200 mL) and purified by carrying out precipitation for another 2 times into cold methanol. The polymer was dried under vacuum at 50 °C and was characterized by ^{1}H - NMR spectroscopy.

^{1}H NMR ($CDCl_3$, δ/ppm): 8.05 (s, -CH=N), 7.51 (d, Ar-H *ortho* to oxime), 7.11-6.78 (m, Ar-H), 4.01 (t, -CH_2CH_2OOC from poly ε-caprolactone), 2.89 (t, S-CH_2), 2.75 (t, S-CH_2), 2.63 (t, CH_2-COOH), 2.31 (t, - CH_2CH_2CO, from poly ε-caprolactone), 1.69-1.63 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.35 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.6. Synthesis of α-allyloxy, α'- azido heterobifunctionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (3.78 g, 33.2 mmol), stannous (II) octoate (1 mg, 0.002 mmol), 4-(4-(allyloxy)phenyl)-4-(4-(2-azidoethoxy)phenyl)pentan-1-ol (158 mg, 0.415 mmol) and toluene (30 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, diluted with dichloromethane (20 mL) and poured into cold methanol (200 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 2108, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 7.06 (d, Ar-H *meta* to ether linkage), 6.80 (m, Ar-H *ortho* to ether linkage), 6.06-5.97 (m, -CH =CH_2), 5.45-5.25 (q, HC=CH_2), 4.50 (d, -OCH_2), 4.04 (t, -CH_2OOC from poly ε-caprolactone), 2.29 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.65-1.55 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.39- 1.31 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.6.1. Chemical modification of α-allyloxy, α'- azido heterobifunctionalized poly ε-caprolactones

4a.2.3.6.1.1. Azide-alkyne click reaction

Schlenk tube equipped with magnetic stir bar was charged with, α- allyloxy α'-azido heterobifunctionalized poly ε-caprolactone (730 mg, 0.1 mmol), CuBr (15 mg, 0.1 mmol), phenyl acetylene (106 mg, 1 mmol), DMF (20 mL) and N, N, N', N', N"-pentamethyldiethylenetriamine (20μL, 0.1 mmol) under nitrogen atmosphere. The Schlenk tube was sealed and the reaction mixture was degassed three times by freeze-pump-thaw cycles and kept stirring for 24 h at room temperature. After the reaction time, DMF was removed under reduced pressure and reaction mixture was diluted with dichloromethane (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was isolated by filtration and dried at room temperature under vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730

^1H NMR ($CDCl_3$, δ/ppm): 7.94 (s, Ar-H attached to triazole ring), 7.80 (d, Ar-H attached to triazole ring), 7.45-7.35 (m, Ar-H attached to triazole ring + triazole ring proton) 7.04 (d, Ar-H *ortho* to ether linkage from initiator), 6.75 (d, Ar-H *meta* to ether linkage from initiator), 6.12-5.95 (m, CH_2-CH =CH_2), 5.44-5.23 (q, -CH=CH_2), 4.78(t, OCH_2), 4.50 (d, -OCH_2), 4.04 (t, -CH_2OOC from poly ε-caprolactone), 2.29 (t, - CH_2CH_2CO from poly ε-caprolactone), 1.65-1.53 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.34-1.31 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment)

4a.2.3.6.1.2. Thiol-ene thermal click reaction

Into a clean and dry Schlenk tube, α- allyloxy α'-azido heterobifunctionalized poly ε-caprolactone (370 mg, 0.05 mmol), 3- maracptopropionic acid (53 mg, 0.5 mmol), AIBN (82 mg, 0.5 mmol) and chlorobezene (20 mL) were mixed. The reaction mixture was degassed *via* three freeze-pump-thaw cycles and subsequently vacuum sealed. The schlenk tube was heated at 80 °C for 6 h. The reaction was quenched by cooling the reaction mixture at 0 °C. Chlorobenzene was removed under reduced pressure. The polymer was dissolved in dichloromethane (20 mL) and precipitated into cold methanol (200 mL) and purified by caring out precipitation for another 2 times into cold methanol. The polymer was dried under vacuum at 50 °C.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.94 (s, Ar-H attached to triazole ring), 7.80 (d, Ar-H attached to triazole ring), 7.45-7.35 (m, Ar-H from phenyl acetylene + triazole ring proton) 7.04 (d, Ar-H *ortho* to ether linkage from initiator fragment), 6.77 (d, Ar-H *meta* to ether linkage from initiator fragment), 4.78 (t, OCH_2), 4.04 (t, -CH_2OOC from poly ε-caprolactone), 2.89 (t, S-CH_2), 2.75 (t, S-CH_2), 2.63 (t, CH_2-COOH), 2.29 (t, - CH_2CH_2CO from poly ε-caprolactone), 1.65-1.53 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.34- 1.31 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.7. Synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones

Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (5.68 g, 50 mmol), stannous (II) octoate (50 mg, 0.002 mmol), 4-(4-(2-(4-(2- azidoethoxy) phenyl)-5-hydroxypentan- 2- yl)phenoxy)benzaldehyde (184 mg, 0.415 mmol) and toluene (30 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, diluted with dichloromethane (20 mL) and poured into cold methanol (200 mL). The polymers were collected by filtration and dried at room temperature in a vacuum for 24 h.

IR ($CHCl_3$, cm^{-1}): 1730, 1710

^{1}H NMR ($CDCl_3$, δ/ppm): 9.92 (s, -aldehyde), 7.85 (d, Ar-H *ortho* to aldehyde), 7.19-6.98 (m, Ar-H), 4.06 (t, -CH_2OOC from poly ε-caprolactone), 2.31 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.66-1.58 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.38 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.7.1.Chemical modification of α-aldehyde, α'-azido heterobifunctional poly ε-caprolactones

4a.2.3.7.1.1. Azido-alkyne click reaction

Schlenk tube equipped with a magnetic stir bar was charged with, α-aldehyde, α'-azido heterobifunctional poly ε-caprolactone (1.21 g, 0.1 mmol), phenyl acetylene (106 mg, 1 mmol), CuBr (15 mg, 0.1 mmol), PMDETA (20 μL, 0.1 mmol) and DMF (20 mL). The reaction mixture was degassed *via* three freeze-pump-thaw cycles and subsequently vacuum sealed. The Schlenk tube was heated at 80 °C for 6 h. DMF was removed under reduced pressure. The polymer was

dissolved in dichloromethane (15 mL) and purified by precipitation in cold methanol (150 mL). The polymer was collected by filtration and dried at 50 ^{0}C under vacuum for 18 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 9.92 (s, aldehyde), 7.94 (s, triazole ring proton), 7.90 (d, Ar-H attached to triazole ring) 7.85 (d, Ar-H *ortho* to aldehyde), 7.45-7.35 (m, Ar-H attached to triazole ring), 7.19-6.96 (m, Ar-H), 4.06 (t, -CH_2OOC from poly ε-caprolactone), 2.31 (t, -CH_2CH_2CO from poly ε-caprolactone), 1.65-1.58 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.38 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.2.3.7.1.2. A*ldehyde-aminooxy click reaction*

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, α-aldehyde, α'-azido heterobifunctional poly ε-caprolactone (605 mg, 0.05 mmol), dichloromethane (10 mL) and a pinch of sodium sulfate. Solution of O-(2-azidoethyl) hydroxylamine (102 mg, 1 mmol) dissolved in dichloromethane (5 mL) was added and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was precipitated into cold hexane (50 mL). The obtained polymer was filtered and dried under vacuum at 50 °C for 8 h.

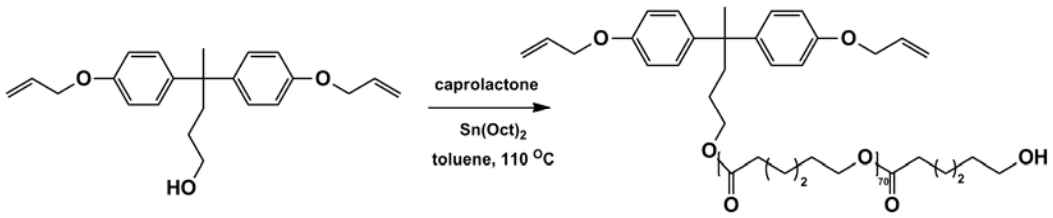
IR ($CHCl_3$, cm^{-1}): 2110, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 8.07 (s, -CH=N), 7.94 (s, Ar-H attached to triazole ring) 7.90 (d, Ar-H attached to triazole ring) 7.85 (d, Ar-H attached to triazole ring), 7.48-7.40 (m, Ar-H attached to triazole ring and proton from triazole ring) 7.19-6.96 (m, Ar-H), 4.06 (t, -CH_2CH_2OOC from poly ε-caprolactone), 2.31 (t, -CH_2CH_2CO, from poly ε-caprolactone), 1.65-1.61 (m, -CH_2CH_2 from poly ε-caprolactone + protons from initiator fragment), 1.41- 1.35 (m, -CH_2CH_2 from poly ε-caprolactone)

4a.3. Results and Discussion

4a.3.1. Synthesis of α, α'-bisallyloxy functionalized poly ε-caprolactones

Scheme 4a.12 depicts the ROP of ε-caprolactone using 4, 4'-bis(4-(allyloxy)phenyl)pentan-1-ol as the initiator.



Scheme 4a.12: Synthesis of α, α'-bisallyloxy functionalized poly ε-caprolactones

The conditions and results of synthesis of bis-allyloxy functionalized poly ε-caprolactones are summarized in **Table 4a.1**

Table 4a.1: Reaction conditions and results for synthesis of α, α'-bisallyloxy functionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n,\ theo}$	[d]$M_{n,\ NMR}$	[e]$M_{n,\ GPC}$	M_w/M_n
1	45:1	8	71	4000	4500	6000	1.38
2	90:1	16	76	8100	7900	10300	1.46
3	135:1	24	81	12800	13500	19400	1.33

(Temperature-110 °C Solvent: toluene) [CL]/ $[Sn(Oct)_2]$=200

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator],

b- Gravimetry

c- $M_{n,theo}$= $\{\frac{[M]_O}{[I]_O}$ x (% Conv.) x Mol. Wt. of monomer (114)$\}$ + mol. wt. initiator(352)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

Three different monomer/initiator ratios were utilized to obtain α, α'-bisallyloxy functionalized poly ε-caprolactones with different molecular weights. ^{1}H-NMR spectrum of α, α'-bisallyloxy functionalized poly ε-caprolactone featuring allyloxy functional groups is reproduced in **Figure 4a.2**. The appearance of multiplet in the range 6.11-5.97 ppm and 5.43-5.39 ppm confirmed the presence of allyloxy functionality. Molecular weights could be calculated for α, α'-bisallyloxy functionalized poly ε-caprolactones by ^{1}H-NMR spectroscopy.

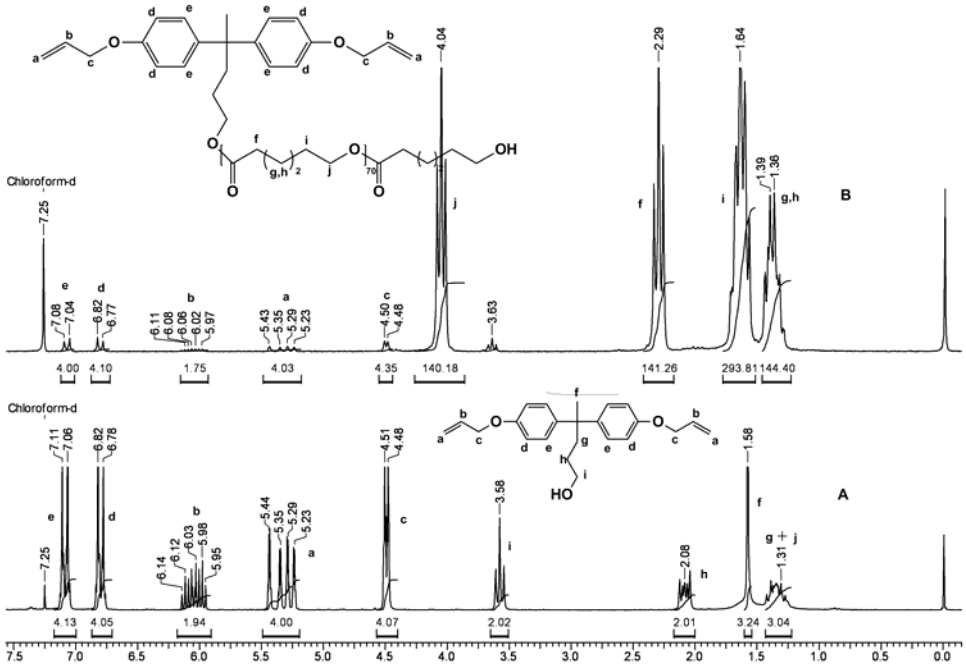


Figure. 4a.2: ^{1}H-NMR spectra of A) 4, 4'-bis (4-(allyloxy) phenyl) pentan-1-ol

B) α, α'-bisallyloxy functionalized poly ε-caprolactones in $CDCl_3$

$M_{n,\ NMR}$ of α, α'-bisallyloxy functionalized poly ε-caprolactones was calculated by comparing the intensity of multiplet in the range 6.11-5.97 ppm for allyloxy group to a peak belonging to $-OCH_2$ in PCL at 4.04 ppm.

$Dpn = [I_{4.04}/2/ (I_{6.11\text{-}5.97\ (alllyloxy\ proton)}/2)]$

Molecular weights were calculated using the equation,

$M_{n,\ NMR}$= [Dpn x 114 (mol. wt. of monomer)] + 352 (mol. wt. of initiator)

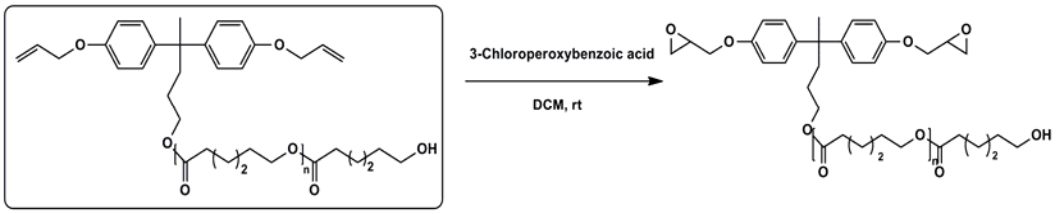
Molecular weights of α, α'-bisallyloxy functionalized poly ε-caprolactones calculated by ^{1}H-NMR spectroscopy ($M_{n,NMR}$: 4500-13500) were in close agreement to the molecular weights calculated from the monomer-to-initiator ratio ($M_{n,theo}$). In addition, GPC trace was found to be monomodal with PDI values in the range 1.33-1.46 for α, α'-bisallyloxy functionalized poly ε-caprolactones.

Thus, 4, 4'-bis (4-(allyloxy) phenyl) pentan-1-ol was demonstrated to be a useful ROP initiator for synthesis of α, α'-bisallyloxy functionalized poly ε-caprolactones.

4a.3.1.1. Chemical modification of α, α'*-bis-allyloxy functionalized poly ε-caprolactone*

4a.3.1.1.1. Chemical modification of α, α'*-bis-allyloxy functionalized poly ε-caprolactone by epoxidation reaction*

In order to illustrate the reactivity of allyloxy functionality, the organic reaction of allyloxy group such as epoxidation of bis-allyloxy functionalized poly ε-caprolactone with *3*-chloroperoxybenzoic acid as an oxidant was carried out **(Scheme 4a.13).**



Scheme 4a. 13: Chemical modification of α, α'- bisallyloxy functionalized poly ε-caprolactones

The epoxidised product was characterized by ^{1}H-NMR spectroscopy (**Figure 4a. 3B**).

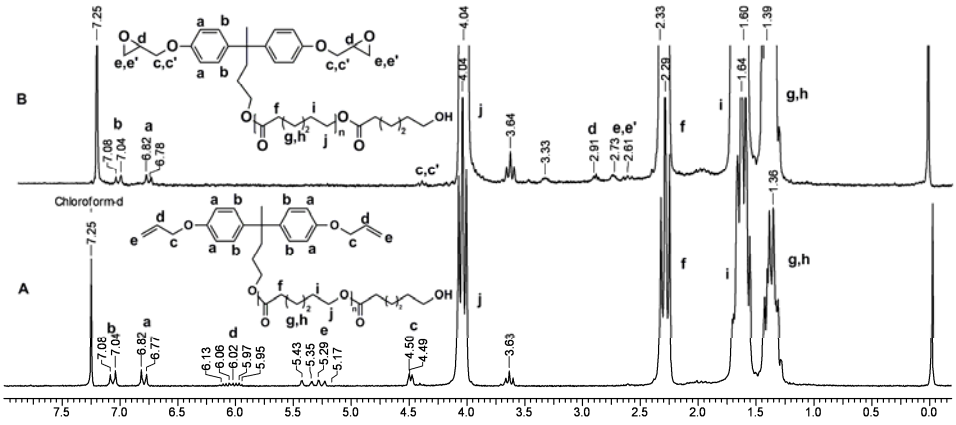


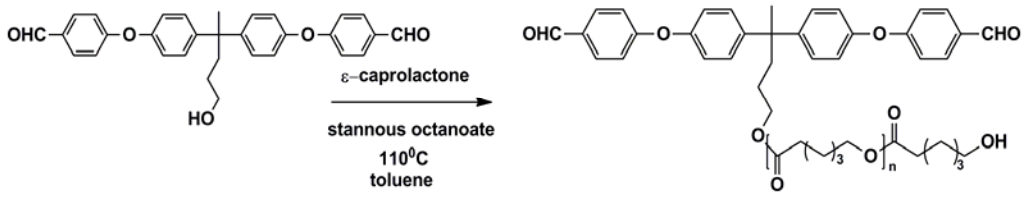
Figure 4a. 3: ^{1}H-NMR spectra of A) α, α'-bis-allyloxy functionalized poly ε-caprolactone B) α, α'-bis-epoxide functionalized poly ε-caprolactone in $CDCl_3$

The complete disappearance of the resonances corresponding to allyloxy group protons and the appearance of new signals corresponding to oxirane ring protons at 2.91, 2.73 and 2.61-2.55 ppm indicated complete conversion of bis-allyloxy into bis-epoxy functionalized poly ε-caprolactone macromonomer. These epoxy functionalized poly ε-caprolactone could find application as an

impact modifier in conventional epoxy resins[55]. The photoinduced cationic polymerization of epoxy type of macromonomers could lead to different types of block and graft copolymers [56].

4a.3.2. Synthesis of α, α'-bisaldehyde functionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using, 4, 4'-(5-hydroxypentane 2,2-diyl bis(4,1-phenylene)bis(oxy) dibenzaldehyde as the initiator (**Scheme 4a.14)**.



Scheme 4a.14: Synthesis of α, α'-bisaldehyde functionalized poly ε-caprolactones

The conditions and results of synthesis of bis-aldehyde functionalized polycaprolactones are summarized in **Table 4a.2.**

Table 4a.2: Reaction conditions and results for synthesis of α, α'-bisaldehyde functionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n\ theo}$	[d]$M_{n,NMR}$	[e]M_{nGPC}	M_w/M_n
1	25:1	8	70	2500	2100	2600	1.37
2	85:1	16	85	8700	8800	10800	1.33
3	135:1	24	91	14500	14500	19400	1.47

(Temperature-110 °C, Solvent: toluene) [CL]/ $[Sn(Oct)_2]$=200

a-$[M]_O$ / $[I]_O$: [Monomer]:[Initiator]

b- Gravimetry

c- $M_{n,theo}= \{\frac{[M]_O}{[I]_O} \times (\%\ Conv.) \times$ mol. wt. of monomer (114)$\}$ + mol. wt. initiator(480)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

Polycaprolactones possessing molecular weights ($M_{n,NMR}$) from 1800 to 14500 were synthesized by varying monomer to initiator ratio. ^{1}H-NMR spectrum of α, α'-bisaldehyde functionalized poly ε-caprolactone is reproduced in **Fig. 4a.4**. The appearance of a singlet at 9.86 ppm confirmed the presence of aldehyde functionality.

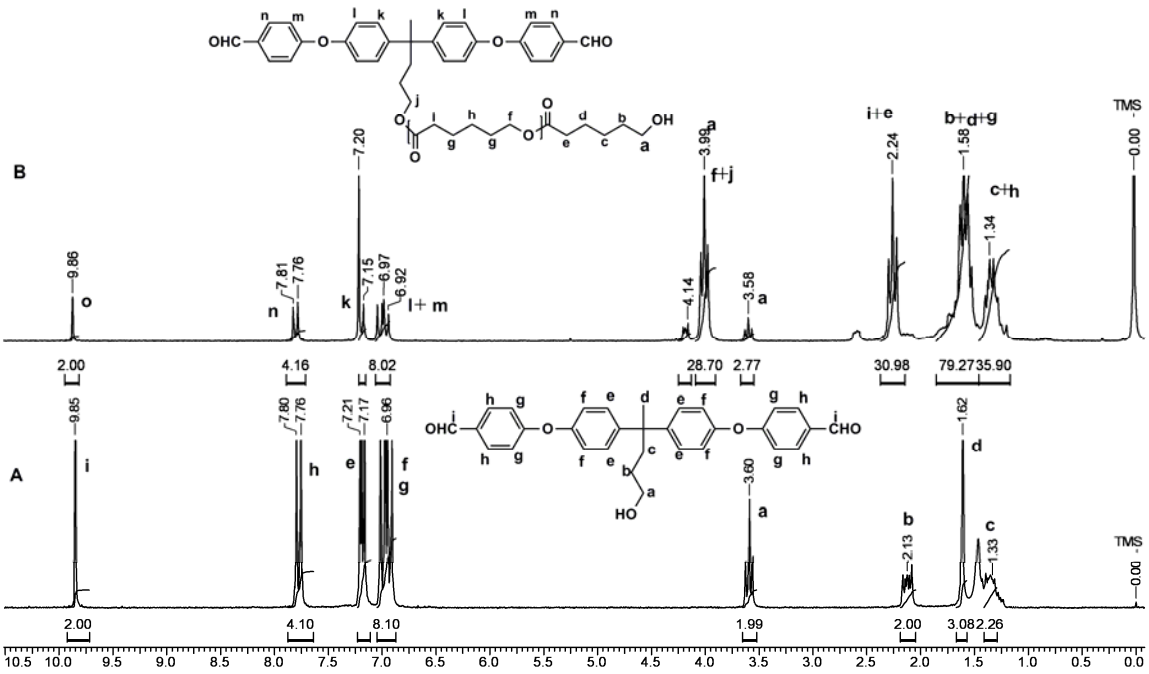


Figure 4a. 4: ^{1}H-NMR spectra of A) 4, 4'-(4, 4'-(5-hydroxypentane 2,2-diyl bis(4,1-phenylene)bis(oxy) dibenzaldehyde B) α, α'-bisaldehyde functionalized poly ε-caprolactone in $CDCl_3$

Molecular weights for bis-aldehyde functionalized poly ε-caprolactone were determined by ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $-OCH_2$ in poly ε-caprolactone at 3.99 ppm to a singlet at 9.86 ppm corresponding to aldehyde groups. The degree of polymerization was calculated from NMR analysis using the relation,

$Dpn = (I_{3.99/2})/I_{9.86/2\ (aldehyde\ proton)}$

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x 114 (mol. wt. of monomer)] + 480 (mol. wt. of initiator)

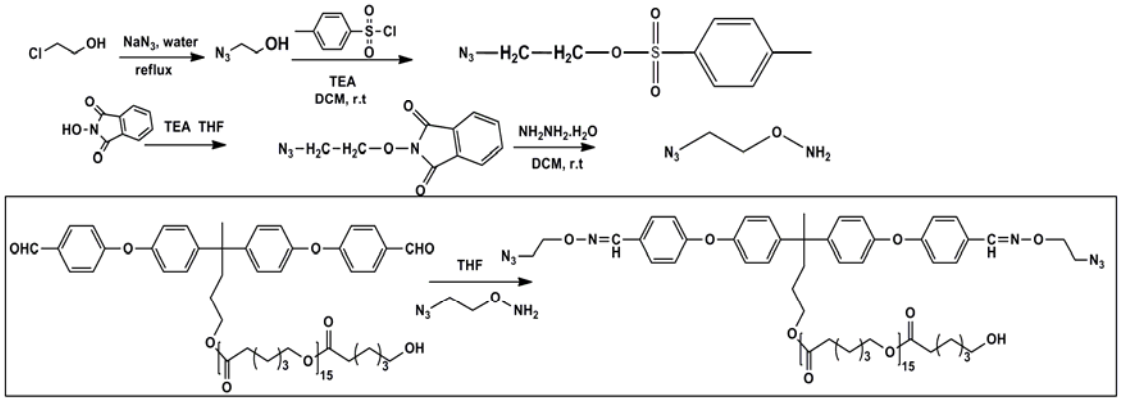
$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) calculated from the monomer to initiator ratio. In addition, GPC data revealed monomodal distribution with PDI values 1.33-1.47 for poly ε-caprolactones.

Thus, 4, 4'-(4, 4'-(5-hydroxypentane 2, 2-diyl bis(4,1- phenylene)bis(oxy) dibenzaldehyde was found to be a useful ROP initiator for synthesis of α, α'-bisaldehyde functionalized poly ε-caprolactone

4a.3.2.1. Chemical modification of α, α'-bisaldehyde functionalized poly ε-caprolactone

4a.3.2.1.1. Reaction of α, α'-bisaldehyde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine

The aldehyde functionality is known to undergo aldehyde-aminooxy click reaction[57]. The reactivity of aldehyde functionality was illustrated by carrying out click reaction with O-(2-azidoethyl) hydroxylamine on α, α'-bisaldehyde functionalized poly ε-caprolactone at room temperature. (**Scheme 4a.15**). The conversion was assessed by FT-IR and ^{1}H-NMR spectroscopy. In FT-IR spectrum, in addition to the peak corresponding to poly ε-caprolactone at 1730 cm^{-1}, characteristic peak corresponding to azido functionality appeared at 2110 cm^{-1} confirming the coupling reaction.



Scheme 4a.15: a) Synthesis of O-(2-azidoethyl) hydroxylamine

b) reaction of α, α'- bisaldehyde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine

Figure 4a.5 represents ^{1}H-NMR spectra of α, α'-bisaldehyde functionalized poly ε-caprolactone ($M_{n,NMR}$: 1800) and its click reaction product with O-(2-azidoethyl) hydroxylamine. ^{1}H-NMR spectra showed complete disappearance of the peak corresponding to aldehyde functionality and

appearance of a new peak at 8.11 ppm (-CH=N-O) which indicated oxime formation without disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone. The model aldehyde-aminooxy click reaction study with O-(2-azidoethyl) hydroxylamine introduces azido moiety on poly ε-caprolactone chain which further opens up plethora of opportunities to introduce different types of functional groups on poly ε-caprolactone by well known azide-alkyne click reaction[58].

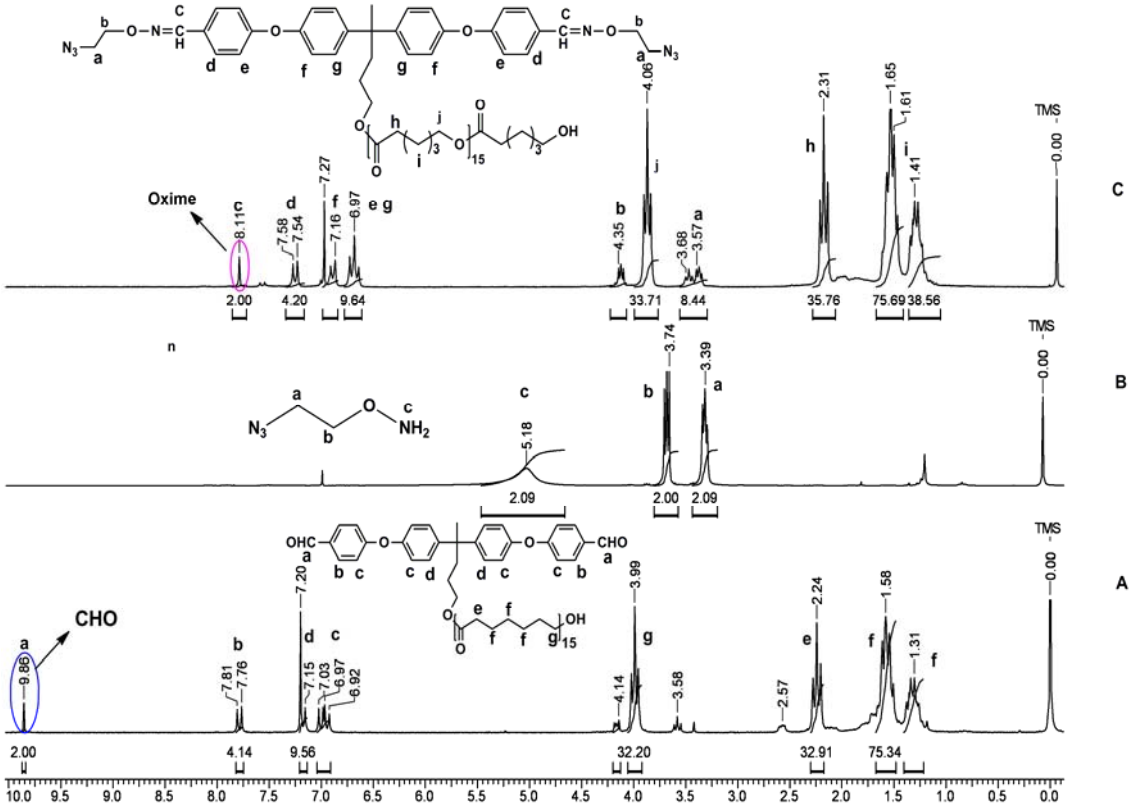
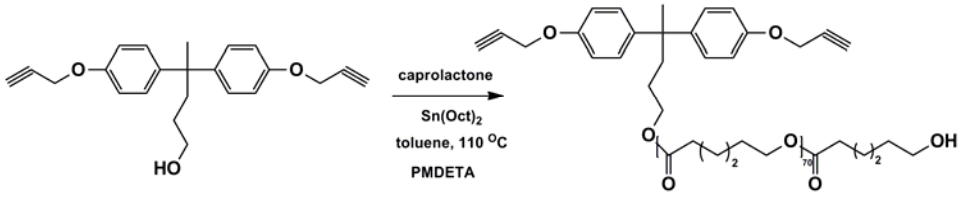


Figure 4a.5: ^{1}H-NMR spectra of A) O-(2-azidoethyl) hydroxylamine B) α, α'-bisaldehyde functionalized poly ε-caprolactone and C) the product formed by reaction of α, α'-bisaldehyde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine in $CDCl_3$

4a.3.3. Synthesis of α, α'-bis propargyloxy functionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using, 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol as the initiator in the presence of PMDETA (**Scheme 4a.16)**. As propargyl groups are reactive, the synthesis of propargyl terminated poly ε-caprolactone at high temperature still proves to be challenging. The reactivity issue of propargyl group could be suppressed by the use

of PMDETA in polymerization system whose huge steric hindrance provides the protective effect[61]. Therefore, PMDETA was deliberately added in the polymerization system.



Scheme 4a.16: Synthesis of α, α'-bispropargyloxy functionalized poly ε-caprolactones

The conditions and results of synthesis of bis-propargyloxy functionalized poly ε-caprolactones are summarized in **Table 4a.3**. Poly ε-caprolactones with molecular weights of 5300 and 11800 ($M_{n,NMR}$) were synthesized by varying monomer to initiator ratio.

Table 4a.3: Reaction conditions and results for synthesis of α, α'-bis propargyloxy functionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n,theo}$	[d]$M_{n,NMR}$	[e]$M_{n,GPC}$	M_w/M_n
1	65:1	12	60	4800	5300	5900	1.24
2	130:1	24	68	10500	11800	13500	1.33

(Temperature-110 °C Solvent: toluene) [CL]/ $[Sn(Oct)_2]$=200

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator]

b- Gravimetry

c- $M_{n,theo}= \{\frac{[M]_O}{[I]_O} \times (\%\ Conv.) \times$ mol. wt. of monomer (114)$\}$ + mol. wt. initiator (348)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

^{1}H-NMR spectrum of α, α'-bis propargyloxy functionalized poly ε-caprolactones is reproduced in **Figure 4a.6.**

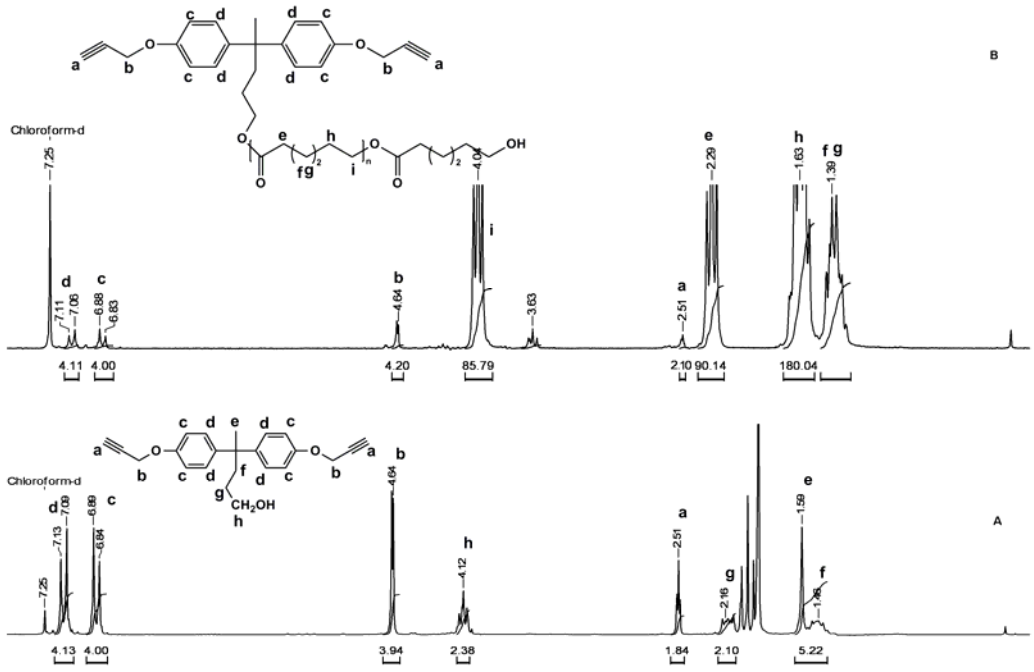


Figure 4a.6: ^{1}H-NMR spectra of a) 4,4'-bis(4-(prop-2-yn-1-yloxy) phenyl)pentan-1-ol

b) α, α' bis-propargyloxy functionalized poly ε-caprolactone in $CDCl_3$

The appearance of a triplet at 2.51 ppm confirmed the presence of propargyloxy functionality. Molecular weights for α, α'-bis propargyloxy functionalized poly ε-caprolactones were determined using ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $-OCH_2$ in poly ε-caprolactone at 4.04 ppm to a triplet at 2.51 ppm corresponding to propargyloxy groups. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = [I_{4.04} / 2 / (I_{2.51} / 2)]$$ *(propargyloxy proton)*

Where $I_{4.04}$ and $I_{2.51}$ are integrals of the signals positioned at 4.04 and 2.51 ppm for CH_2 of poly ε-caprolactone chain and propargyloxy functionality, respectively.

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x 114 (mol. wt. of monomer)] + mol.wt. initiator

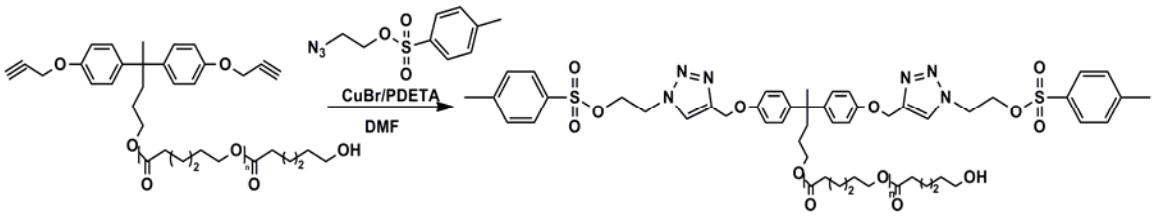
$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) calculated from the monomer to initiator ratio. In addition, GPC data revealed monomodal distribution with PDI values of 1.24-1.33 for poly ε-caprolactone.

Thus, 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol was found to be a useful ROP initiator in the presence of PMDETA for synthesis of α, α' bis-propargyloxy functionalized poly ε-caprolactones.

4a.3.3.1. Chemical modification of α, α'-bis propargyloxy functionalized poly ε-caprolactones

4a.3.3.1.1. Reaction of α, α'-bis propargyloxy functionalized poly ε-caprolactones with 2-azidoethyl 4-methylbenzenesulfonate

It is well known that propargyloxy functionality undergoes azide-alkyne click reaction[58]. The reactivity of propargyloxy functionality was illustrated by carrying out click reaction with 2-azidoethyl 4-methylbenzenesulfonate on α, α' bis-propargyloxy functionalized poly ε-caprolactone in the presence of CuBr/PMDETA (**Scheme 4a.17)**.



Scheme 4a.17: Reaction of bis-propargyloxy functionalized poly ε-caprolactone with 2-azidoethyl 4-methylbenzenesulfonate

The transformation was assessed by FT-IR and ^{1}H-NMR spectroscopy. In FT-IR spectrum, the characteristic peak corresponding to ester group of poly ε-caprolactone at 1730 cm^{-1} retained while the peak belonging to propargyloxy functionality at 2310 cm^{-1} completely disappeared confirming the coupling reaction without any backbone degradation. **Figure 4a.7** represents ^{1}H-NMR spectra of α, α'-bis propargyloxy functionalized poly ε-caprolactones ($M_{n,NMR}$: 5300) and its click reaction product with 2-azidoethyl 4-methylbenzenesulfonate. ^{1}H-NMR spectra revealed complete disappearance of the peak corresponding to propargyloxy functionality and appearance of a new peak at 8.11 ppm (proton corresponding to triazole ring) which indicated triazole ring formation without disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone.

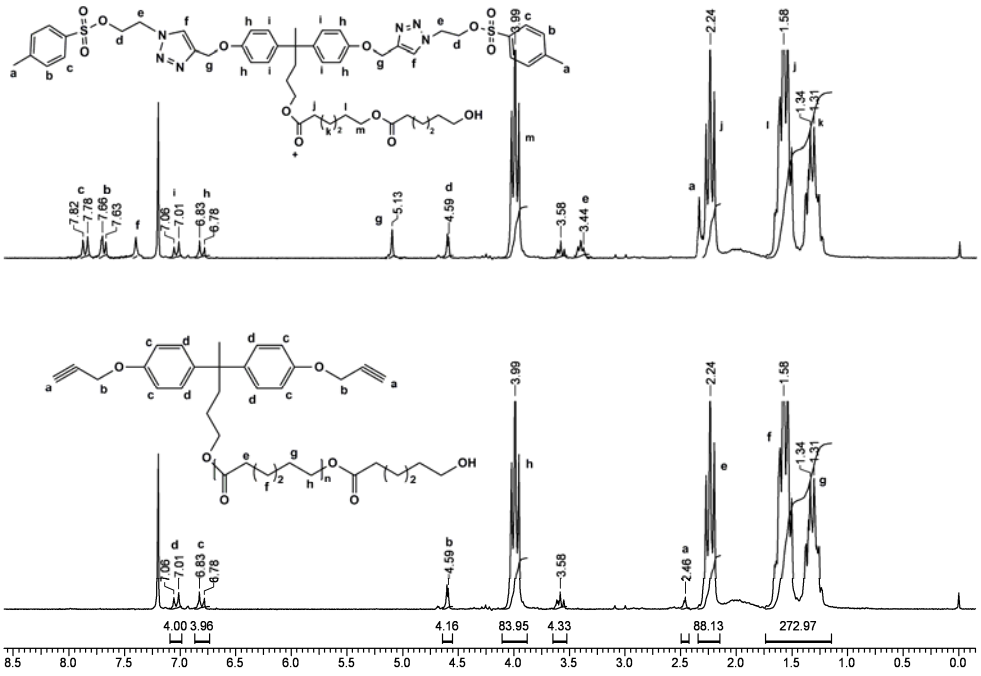
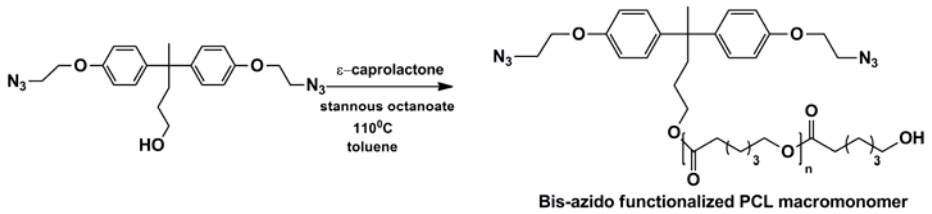


Figure 4a.7: ^{1}H-NMR spectra of A) α, α'-bis propargyloxy functionalized poly ε-caprolactones B) product formed by reaction of α, α'-bis propargyloxy functionalized poly ε-caprolactone with 2-azidoethyl 4-methylbenzene sulfonate in $CDCl_3$

Model click reaction with azido compound opens up the possibilities of click reaction for functionalization of poly ε-caprolactone with different useful functional groups just by making use of appropriately substituted azido compounds.

4a.3.4. Synthesis of α, α'-bisazido functionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using, 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol as the initiator (**Scheme 4a.18)** under the conditions reported for ε-caprolactone polymerization in the presence of azido group containing initiator[59]



Scheme 4a.18: Synthesis of α, α'-bisazido functionalized poly ε-caprolactones

The conditions and results for synthesis of α, α'- bis-azido functionalized poly ε-caprolactones are summarized in **Table 4a.4**. Poly ε-caprolactones with molecular weights ($M_{n,NMR}$) ranging from 4900 to 14600 were synthesized by varying monomer to initiator ratio.

Table 4a.4: Reaction conditions and results for synthesis of α, α'-bisazido functionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n,theo}$	[d]$M_{n,NMR}$	[e]$M_{n,GPC}$	M_w/M_n
1	50:1	8	64	4100	4900	5400	1.24
2	100:1	16	61	7400	8400	13500	1.33
3	150:1	24	70	12400	14600	18600	1.28

(Temperature-110 °C Solvent: toluene) [CL]/ $[Sn(Oct)_2]$=200

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator]

b- Gravimetry

c- $M_{n,theo}$= $\{\frac{[M]_O}{[I]_O}$ x (% Conv.) x mol. wt. of monomer (114)} + mol. wt. initiator (410)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

^{1}H-NMR spectrum of α, α'-bisazido functionalized poly ε-caprolactone is reproduced in **Figure 4a.8.** Molecular weights for α, α'-bisazidofunctionalized poly ε-caprolactones were determined by ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $–OCH_2$ in ε-caprolactone at 4.04 ppm to a doublet at 7.08 ppm corresponding to aromatic protons from initiator fragment. The degree of polymerization was calculated from NMR analysis using the relation,

$Dpn = [(I_{4.04}/2)/(I_{7.08}/4)_{(aromatic\ proton)}]$

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [*Dpn* x 114 (mol. wt. of monomer)] + mol. wt. initiator

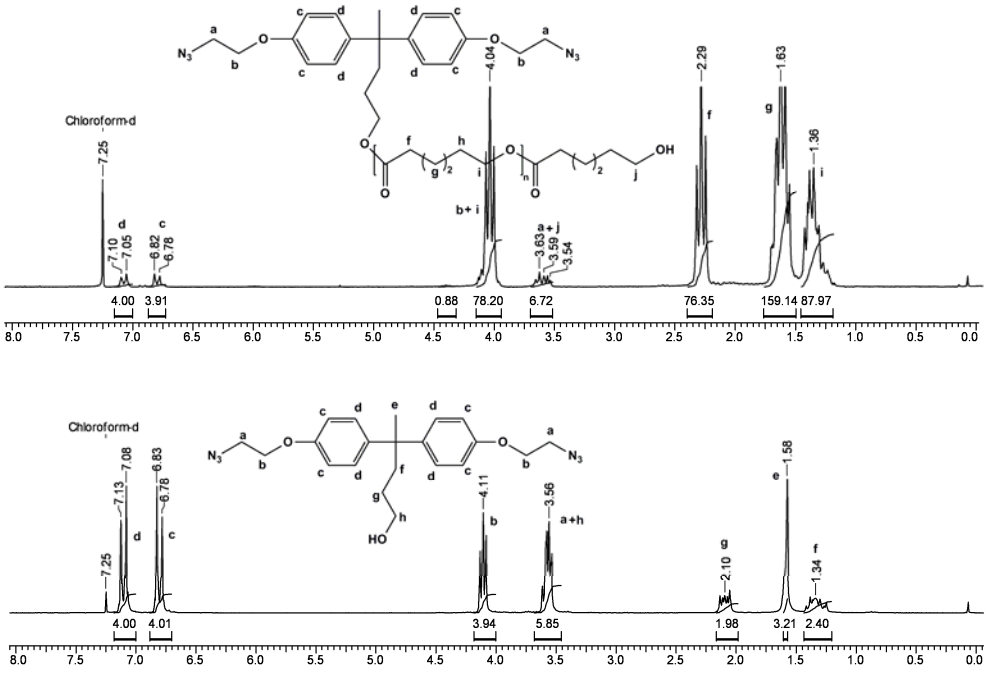


Figure 4a.8: ^{1}H-NMR spectra of a) 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

b) bis-azido functionalized poly ε-caprolactone in $CDCl_3$

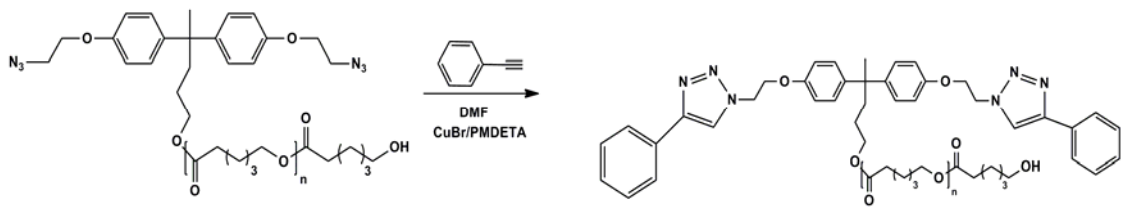
$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights ($M_{n\ th}$) calculated from the monomer to initiator ratio. In addition, GPC data revealed monomodal distribution for poly ε-caprolactone. The PDIs were in the range 1.24-1.33.

Thus, 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol was found to be a useful ROP initiator for synthesis of α, α'-bisazido functionalized poly ε-caprolactones under our experimental conditions.

4a.3.4.1. Chemical modification of α, α'-bisazido functionalized poly ε-caprolactones

4a.3.4.1.1. Reaction of α, α'-bisazido functionalized poly ε-caprolactones with phenyl acetylene

The azido functionality is well known for azide-alkyne click reaction[58]. The reactivity of azido functionality was illustrated by carrying out click reaction with phenyl acetylene on α, α'-bisazidofunctionalized poly ε-caprolactones at room temperature (**Scheme 4a.19**).



Scheme 4a.19: Reaction of α, α'- bis-azido functionalized poly ε-caprolactone with phenyl acetylene

The transformation was characterized by FT-IR and ^{1}H-NMR spectroscopy. In FT-IR spectrum, the peak corresponding to poly ε-caprolactone at 1730 cm^{-1} was retained while the characteristic peak corresponding to azido functionality at 2108 cm^{-1} completely disappeared confirming coupling reaction without backbone degradation. **Figure 4a.9** represents ^{1}H-NMR spectra of azido-terminated poly ε-caprolactone ($M_{n,NMR}$: 4900) and its click reaction product with phenyl acetylene.

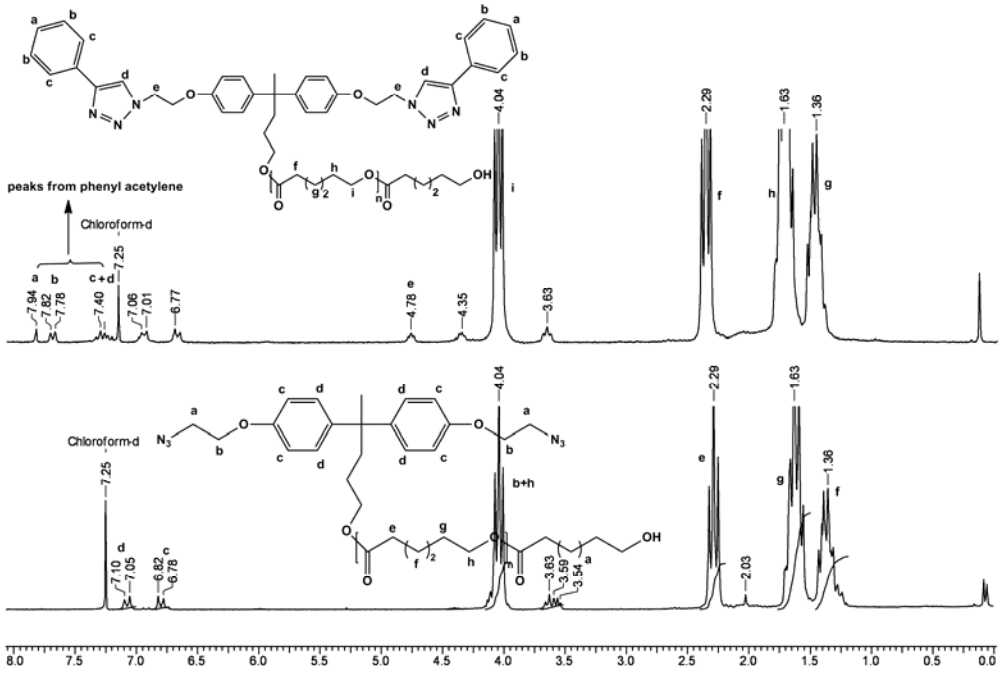


Figure 4a.9: ^{1}H-NMR spectra of A) α, α'-bis-azido functionalized poly ε-caprolactone B) product formed by reaction of α, α'-bis-azido functionalized poly ε-caprolactone with phenyl acetylene in $CDCl_3$

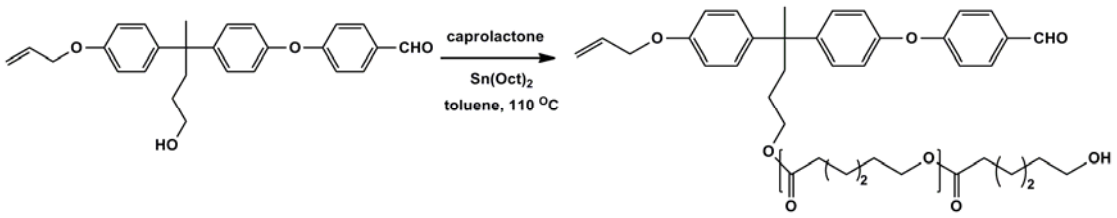
^{1}H-NMR spectra indicated appearance of new peaks at 7.94, 7.80, 7.40 ppm (proton corresponding to phenyl ring + triazole ring) which elucidated triazole formation without

disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone.

Model click reaction with phenyl acetylene opens up a simple methodology to functionalize poly ε-caprolactone with those functional groups which are otherwise difficult to introduce on poly ε-caprolactone just by making use of appropriately substituted acetylene compounds.

4a.3.5. Synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using, 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde as the initiator (**Scheme 4a.20)**.



Scheme 4a.20: Synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones

The conditions and results of synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones are summarized in **Table 4a.5.** Poly ε-caprolactones with molecular weights ($M_{n,NMR}$) ranging from 5100 to 23000 were synthesized by varying monomer to initiator ratio.

Table 4a.5: Reaction conditions and results for synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n\ theo}$	[d]M_{nNMR}	[e]M_{nGPC}	M_w/M_n
1	60:1	8	61	4600	5100	5900	1.43
2	120:1	16	71	10100	9700	11800	1.34
3	240:1	24	69	19300	23000	29000	1.26

(Temperature-110 °C Solvent: Toluene) [CL]/ $[Sn(Oct)_2]$=200

a-$[M]_O$ / $[I]_O$: [Monomer]:[Initiator] ,

b- Gravimetry

c- $M_{n,theo}$= $\{\frac{[M]_O}{[I]_O}$ x (% Conv.) x mol. wt. of monomer(114)} + mol. wt. initiator (416)

d- $M_{n,NMR}$= Determined from NMR,

e- $M_{n,GPC}$-; Polystyrene standard; $CHCl_3$ eluent

[1]H-NMR spectrum of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone is represented in **Figure 4a.10.** The appearance of a singlet at 9.91 ppm and multiplets in the range 6.11-5.97 ppm, and 5.43-5.39 ppm confirmed the presence of aldehyde functionality and allyloxy functionality, respectively on poly ε-caprolactone.

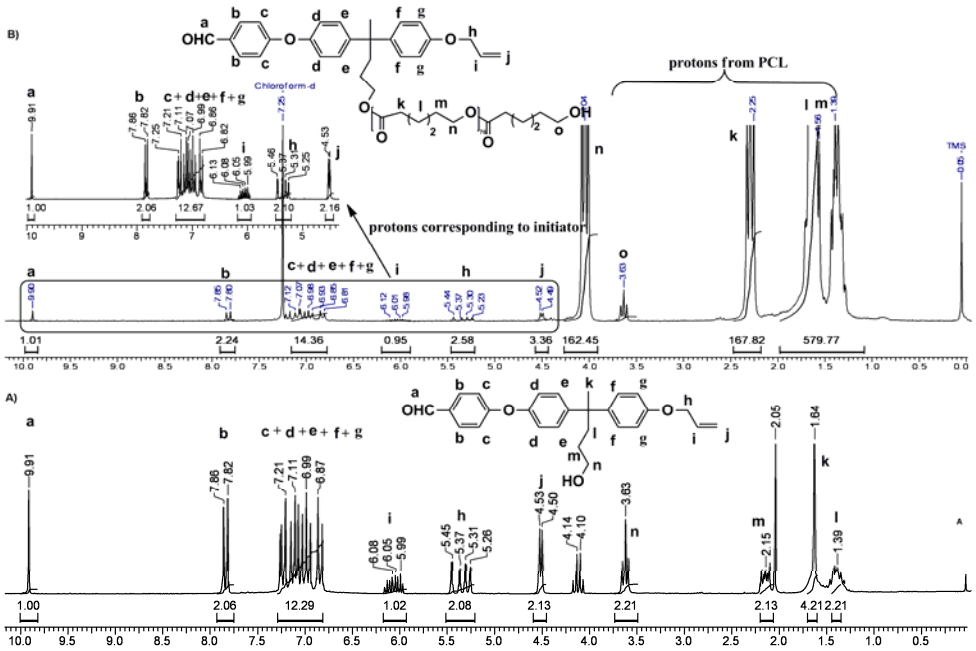


Figure 4a. 10: ^{1}H-NMR spectra of A) 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxy)pentan-2-yl)phenoxy)benzaldehyde and B) α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone in $CDCl_3$

Molecular weights for aldehyde-allyloxy hetero functionalized poly ε-caprolactones were determined by ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $-OCH_2$ in poly ε-caprolactone at 4.04 ppm to a singlet at 9.91 ppm corresponding to aldehyde group. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = [I_{4.04/2} / (I_{9.91/1})_{(aldehyde\ proton)}]$$

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x mol. wt. of monomer (114)] + mol.wt.inititor

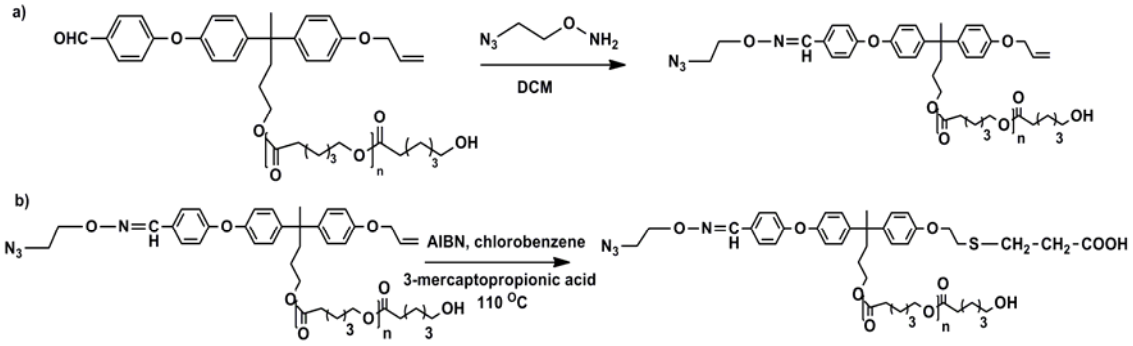
$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) calculated from the monomer to initiator ratio. In addition, GPC data revealed monomodal distribution with PDI values in the range 1.26-1.43, for poly ε-caprolactone. Thus, 4-(4-(2-(4-(allyloxy) phenyl)-5-hydroxy) pentan-2-yl)phenoxy)benzaldehyde was found to be a useful ROP initiator for synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones.

4a.3.5.1. C*hemical modification of* α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone

The aldehyde and allyloxy functionalities are known to undergo different types of click reactions without use of any metal catalyst. Aldehyde group is known to undergo aldehyde - aminooxy click reaction[57] while allyloxy group can undergo thiol-ene addition click reaction. We first performed aldehyde-aminooxy click reaction by considering the fact that aldehyde would undergo addition reaction with thiols and then thiol–ene click reaction was performed.

4a.3.5.1.1. Reaction of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone *with O-(2-azidoethyl) hydroxylamine*

The reactivity of aldehyde functionality was illustrated by carrying out click reaction with O-(2-azidoethyl) hydroxylamine on poly ε-caprolactone at room temperature (**Scheme 4a (21a)**).



Scheme 4a.21: a) Reaction of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine b) reaction of α-azido, α'-allyloxy functionalized poly ε-caprolactone with 3-mercaptopropionic acid

In FT-IR spectrum, in addition to the peak corresponding to poly ε-caprolactone at 1730 cm^{-1}, characteristic peak corresponding to azido functionality at 2110 cm^{-1} appeared confirming introduction of azido group *via* formation of oxime. **Fig. 4a.11** represents ^{1}H-NMR spectra of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone ($M_{n,NMR}$: 9700) and its click reaction product with O-(2-azidoethyl) hydroxylamine. ^{1}H-NMR spectra showed complete disappearance of the peak corresponding to aldehyde functionality and appearance of a new peak at 8.07 ppm (-CH=N-O) which elucidated oxime formation without disturbing peaks related to

poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone. The model aldehyde-aminooxy click reaction study with O-(2-azidoethyl) hydroxylamine introduces azido moiety on poly ε-caprolactone chain which further opens up plethora of opportunities to introduce different types of functional groups on poly ε-caprolactone by well known azide-alkyne click reaction [60].

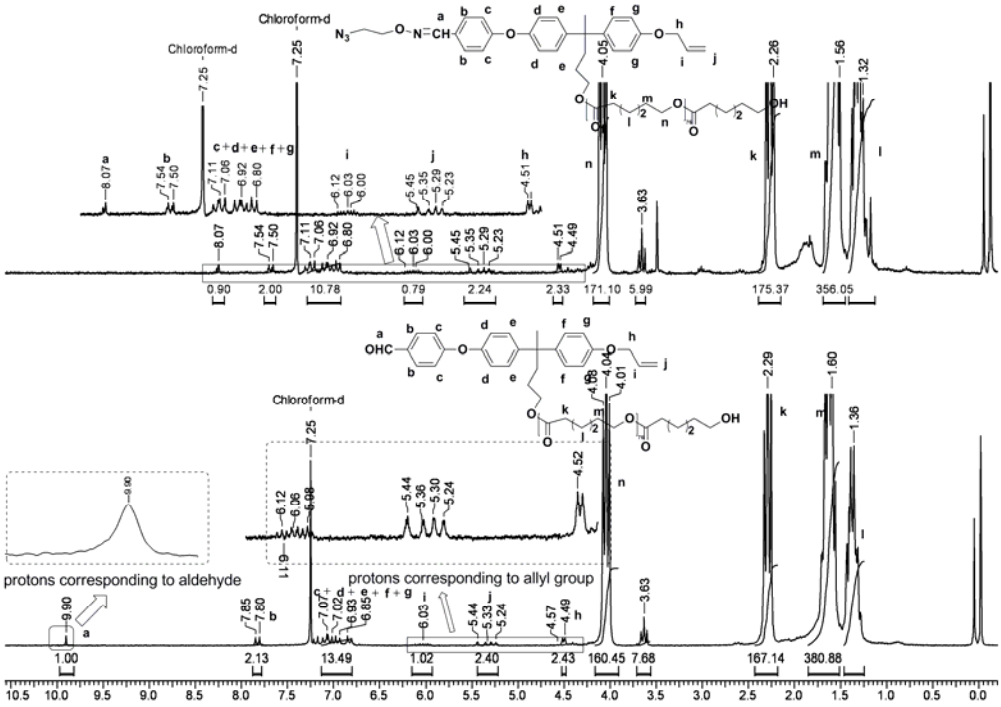


Figure 4a.11: ^{1}H-NMR spectra of A) α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone B) product formed by reaction of α-aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine in $CDCl_3$

4a.3.5.1.2. Reaction of* α-azido, α'-allyloxy functionalized poly ε-caprolactone *with 3-mercaptopropionic acid

The presence of allyloxy functionality was illustrated by carrying out click reaction with 3-mercaptopropionic acid in the presence of AIBN at 110 °C in chlorobenzene (**Scheme 4a.21b)**. The transformation was characterized by ^{1}H-NMR spectroscopy. **Figure 4a.12** depicts ^{1}H-NMR spectra of α-azido, α'-allyloxy functionalized poly ε-caprolactone ($M_{n,NMR}$: 9700) and its thiol-ene click reaction product. Complete disappearance of the peak corresponding to allyloxy

functionality and appearance of new peaks at 2.79, 2.75, 2.69 ppm indicated addition of thiol without any side reaction such as degradation of poly ε-caprolactone backbone.

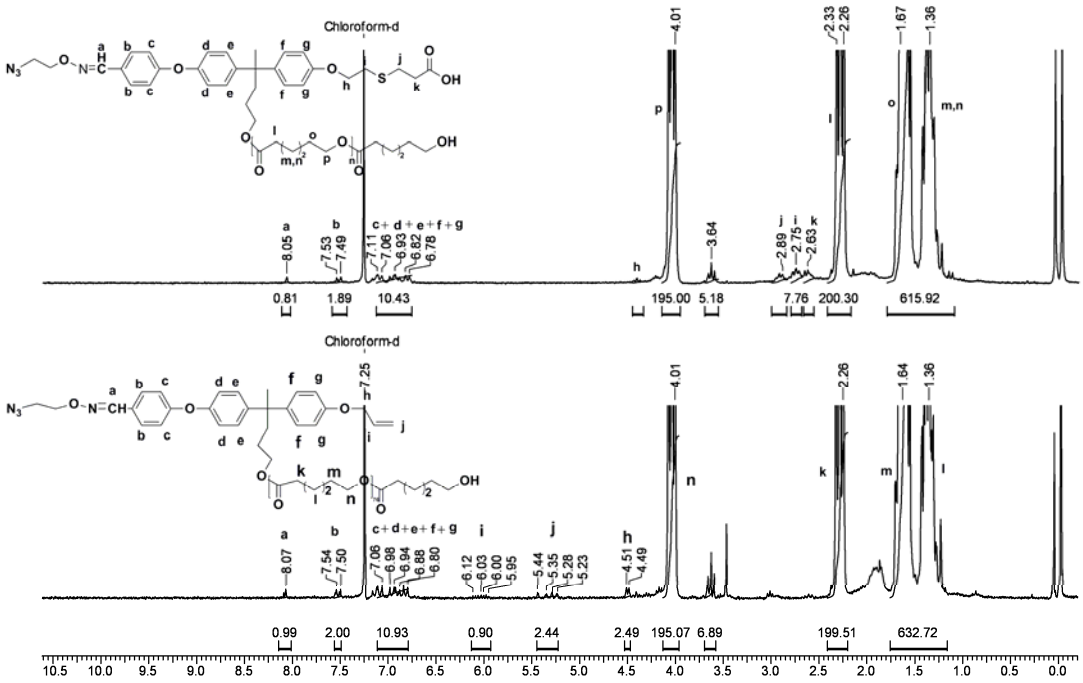
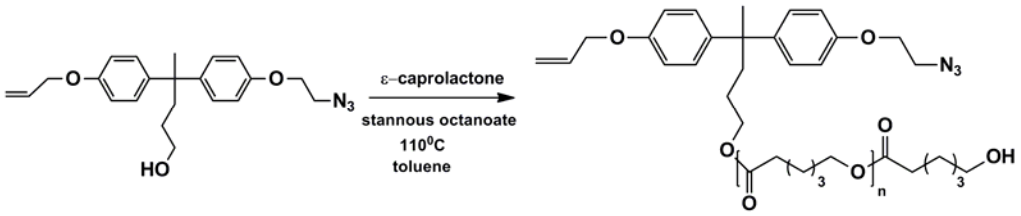


Figure 4a.12: ^{1}H-NMR spectra of A) α-azido, α'-allyloxy functionalized poly ε-caprolactone B) product of reaction of α-azido, α'-allyloxy functionalized poly ε-caprolactone with 3-mercaptopropionic acid in $CDCl_3$

The presence of aldehyde and allyloxy functionalities engenders opportunities to introduce various types of useful functionalities by carrying out different types of click reactions.

4a.3.6. Synthesis of α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using, 4-(4-(allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol as the initiator (**Scheme 4a.22)**.



Scheme 4a.22: Synthesis of α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones

The conditions and results of synthesis of α-allyloxy, α'-azido heterobifunctional poly ε-caprolactones are summarized in **Table 4a.6.**

Table 4a.6: Reaction conditions and results for synthesis of α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones

Sr. No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n,theo}$	[d]$M_{n,NMR}$	[e]$M_{n,GPC}$	M_w/M_n
1	50:1	12	76	4200	4800	5900	1.43
2	80:1	24	71	6900	7300	10500	1.34

(Temperature-110 °C Solvent: toluene) [CL]/ $[Sn(Oct)_2]$=200

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator]

b- Gravimetry

c- $M_{n,theo} = \{\frac{[M]_O}{[I]_O} \times (\%\ Conv.) \times$ mol. wt. of monomer+ mol. wt. initiator (381)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

Poly ε-caprolactones with molecular weights of 4800 and 7300 ($M_{n,NMR}$) were synthesized by varying monomer to initiator ratio. ^{1}H-NMR spectrum of ***α***-allyloxy, α'-azido heterobifunctional poly ε-caprolactone is represented in **Figure 4a.13.** The appearance of multiplets in the range 6.06-5.97 ppm and 5.43-5.23 ppm, confirmed the presence of allyloxy functionality.

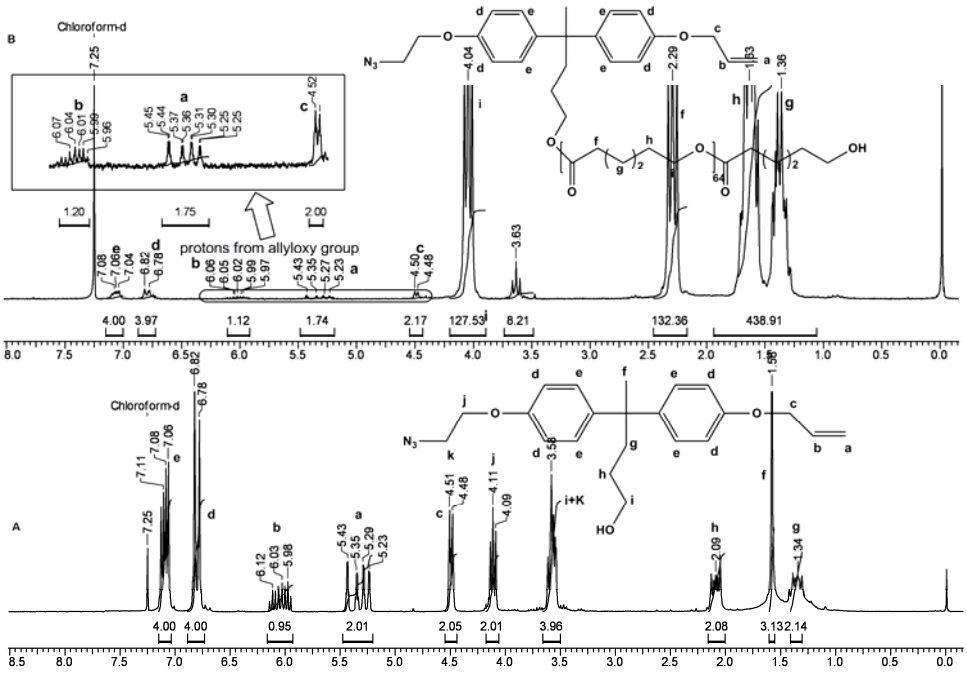


Figure 4a.13: ^{1}H-NMR spectra of A) 4-(4-(allyloxy)phenyl)-4-(4-(2- azidoethoxy) phenyl)pentan-1-ol B) α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactone in $CDCl_3$

Molecular weights for α-allyloxy, α'-azido heterobifunctional poly ε-caprolactones were determined by ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $-OCH_2$ in poly ε-caprolactone at 4.04 ppm to a singlet at 6.06-5.97 ppm corresponding to allyloxy groups. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = [I_{4.04/2}/(I_{6.06\text{-}5.9/1})]$$ *(allyloxy proton)*

Molecular weights were calculated using the equation,

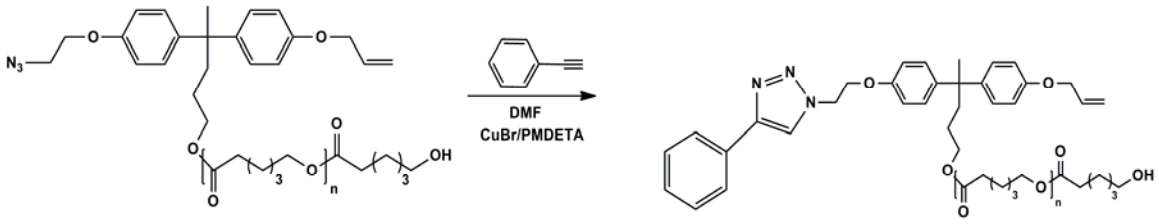
$M_{n,\,NMR}$= [Dpn x 114 (mol. wt. of monomer)]

$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights (M_{ntheo}) calculated from the monomer to initiator ratio. In addition, GPC data revealed monomodal distribution with PDI values of 1.34 and 1.43 for poly ε-caprolactone. Thus, 4-(4-(allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol was found to be a useful ROP initiator for synthesis of α-allyloxy, α'-azido heterobifunctional poly ε-caprolactones.

4a.3.6.1. Chemical modification of α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones

4a.3.6.1.1. Reaction of α-allyloxy, α'-azido functionalized poly ε-caprolactone with phenyl acetylene

The azido functionality is known to undergo azide-alkyne click reaction[58]. The reactivity of azido functionality was illustrated by carrying out click reaction with phenyl acetylene on poly ε-caprolactone containing allyloxy and azido functional groups at room temperature. (**Scheme 4a.23**). In FT-IR spectrum, the peak corresponding to poly ε-caprolactone at 1730 cm^{-1} was retained while the characteristic peak corresponding to azido functionality at 2108 cm^{-1} completely disappeared confirming the coupling reaction without backbone degradation.



Scheme 4a.23: Reaction of α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones with phenyl acetylene

Figure 4a. 14 depicts ^{1}H-NMR spectra of α-allyloxy, α'-azido heterobifunctional poly ε-caprolactones ($M_{n,\ NMR}$: 7300) and its click reaction product with phenyl acetylene. ^{1}H-NMR spectra indicated appearance of new peaks at 7.94, 7.80, 7.40 ppm (proton corresponding to phenyl ring + triazole ring) which elucidated triazole formation without disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone.

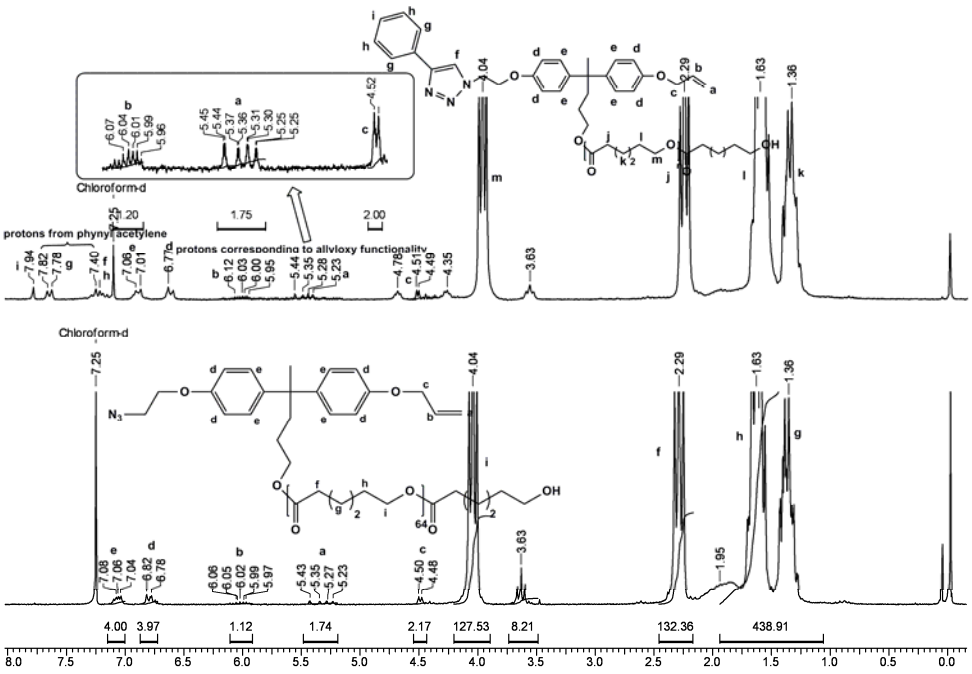


Figure 4a.14: ^{1}H-NMR spectra of A) α-allyloxy, α'-azido heterobifunctionalized poly ε-caprolactones B) product formed by the reaction of α-allyloxy, α'-azido functionalized poly ε-caprolactone with phenyl acetylene in $CDCl_3$

4a.3.6.1.2. Reaction of α-allyloxy functionalzed poly ε-caprolactones with 3-mercaptopropionic acid

The reactivity of allyloxy functionality was illustrated by carrying out click reaction with 3-mercaptopropionic acid on poly ε-caprolactone in the presence of AIBN at 110 °C in chlorobenzene as a solvent (**Scheme 23 (b)**). The conversion was assessed by ^{1}H-NMR spectroscopy. **Figure 4a.15** represents ^{1}H-NMR spectra of α-allyloxy terminated poly ε-caprolactone ($M_{n,\ NMR}$: 7300) and its thiol-ene click reaction product with 3-mercaptopropionic acid. ^{1}H-NMR spectra showed complete disappearance of the peak corresponding to allyloxy functionality and appearance of new peaks at 2.79, 2.75, 2.69 ppm which illustrated addition of thiol without disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone.

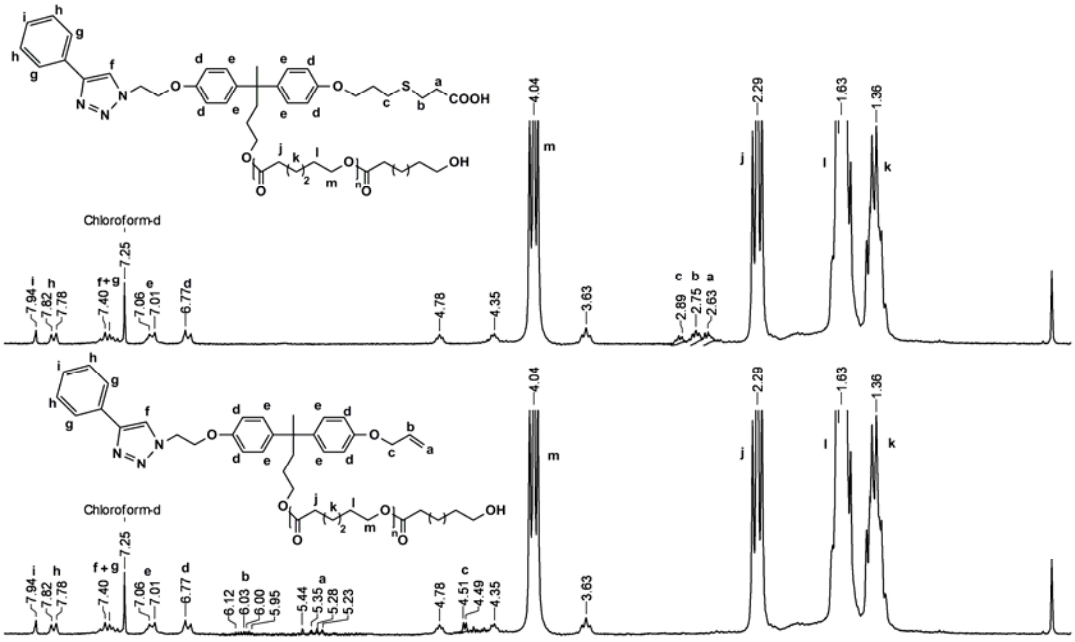
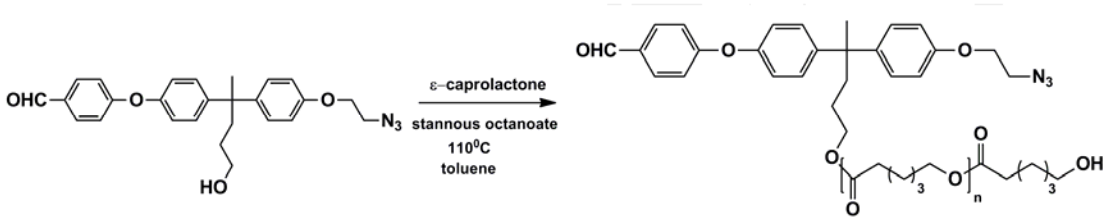


Figure 4a.15: ^{1}H-NMR spectra of A) α-allyloxy functionalized poly ε-caprolactone B) the product formed by reaction of α-allyloxy functionalized poly ε-caprolactone with 3-mercaptopropionic acid in $CDCl_3$

Thus, poly ε-caprolactone with azido and allyloxy functionalities provide an opportunity to introduce functional groups by azido-propargyloxy and thiol-ene click reactions.

4a.3.7. Synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones

ROP of ε-caprolactone was carried out using 4-(4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde as the initiator (**Scheme 4a.24)**.



Scheme 4a.24: Synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones

The reaction conditions and results of synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones are summarized in **Table 4a.7.**

Table 4a.7: Reaction conditions and results for synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n,theo}$	[d]$M_{n,NMR}$	[e]$M_{n,GPC}$	M_w/M_n
1	60:1	12	67	5000	5600	5900	1.21
2	120:1	24	71	10200	11800	13500	1.36

(Temperature-110 °C Solvent: toluene) $[CL]/[Sn(Oct)_2] = 200$

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator]

b- Gravimetry

c- $M_{n,theo} = \{\frac{[M]_O}{[I]_O} \times (\%\ Conv.) \times$ mol. wt. of monomer$\}$ + mol. wt. Initiator (445)

d- $M_{n,NMR}$ = Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

Poly ε-caprolactones with molecular weights of 5600 and 11800 ($M_{n,NMR}$) were synthesized by varying monomer to initiator ratio. ^{1}H-NMR spectrum of α-aldehyde, α'-azido hetero bifunctionalized poly ε-caprolactone is represented in **Figure 4a.16**. The appearance of a singlet at 9.92 ppm confirmed aldehyde functionality. Molecular weights were determined by ^{1}H-NMR spectroscopy by comparing integral intensity of peak belonging to $-OCH_2$ in poly ε-caprolactone at 4.06 ppm to a singlet at 9.92 ppm corresponding to aldehyde groups.

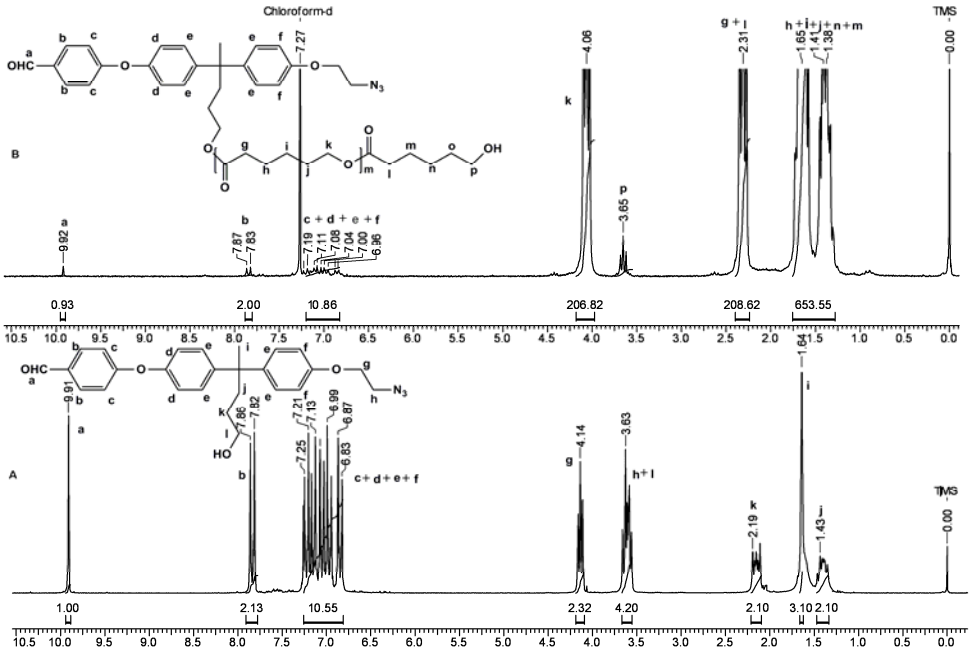


Figure 4a. 16: ^{1}H-NMR spectra of A) 4-(4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde B) α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones in $CDCl_3$

Degree of polymerization was calculated from NMR analysis using the relation,

$Dpn = [I_{4.06/2} / (I_{9.92/1})]$ *(aldehyde proton)*

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x mol. wt. of monomer (114)] + mol.wt.inititor (445)

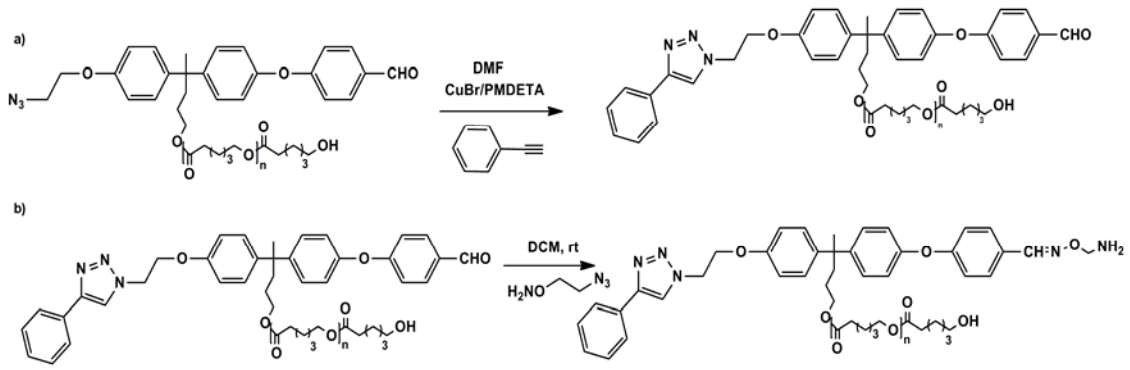
$M_{n,NMR}$ values were in reasonably good agreement with theoretical molecular weights ($M_{n\ theo}$) calculated from the monomer to initiator ratio. In addition, GPC dara revealed monomodal with PDI values of 1.21 and 1.36, for poly ε-caprolactones.

Thus, 4-(4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl) phenoxy) benzaldehyde was found to be a useful ROP initiator for synthesis of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones.

4a.3.7.1 Chemical modification of α- aldehyde, α'- azido heterobifunctionalized poly ε-caprolactone

4a.3.7.1.1. Reaction of α- aldehyde, α'- azido heterobifunctionalized poly ε-caprolactone with phenyl acetylene

The azido functionality is well known for azide-alkyne click reaction[58]. The reactivity of azido functionality was illustrated by carrying out click reaction with phenyl acetylene on poly ε-caprolactone containing aldehyde and azido functional groups at room temperature. (**Scheme 4a.25**).



Scheme 4a.25: Reaction of α-aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones a) with phenyl acetylene

b) with O-(2-azidoethyl) hydroxylamine

In FT-IR spectrum, the peak corresponding to poly ε-caprolactone at 1730 cm^{-1} was retained while the characteristic peak corresponding to azido functionality at 2108 cm^{-1} completely disappeared confirming the coupling reaction. **Figure 4a.17** represents ^{1}H-NMR spectra of poly ε-caprolactone containing aldehyde-azido functional groups ($M_{n,NMR}$: 11800) and its click reaction product with phenyl acetylene.

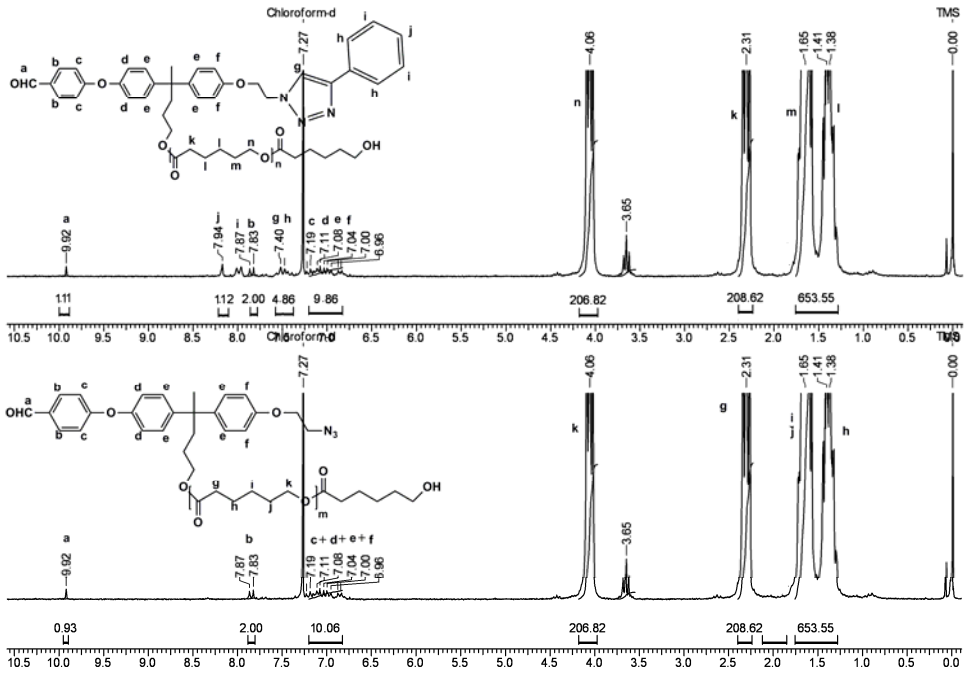


Figure 4a.17: ^{1}H-NMR spectra of A) α- aldehyde, α'- azido heterobifunctionalized poly ε-caprolactone B) product formed by reaction of α- aldehyde, α'- azido heterobifunctionalized poly ε-caprolactone with phenyl acetylene in $CDCl_3$

^{1}H-NMR spectra showed appearance of new peaks at 7.94, 7.80, 7.40 ppm (proton corresponding to phenyl ring + triazole ring) in addition to the peaks corresponding to poly ε-caprolactone which indicated triazole formation without disturbing peaks related to poly ε-caprolactone attesting completion of the reaction without any side reaction such as degradation of poly ε-caprolactone backbone.

4a.3.7.1.2. Reaction of α- aldehyde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine

The aldehyde functionality is known to undergo aldehyde-aminooxy click reaction[57]. The reactivity of aldehyde functionality was illustrated by carrying out click reaction with O-(2-azidoethyl) hydroxylamine on poly ε-caprolactone at room temperature (**Scheme 4a.25(b)**). The transformation was characterized by FT-IR and ^{1}H-NMR spectroscopy. In FT-IR spectrum, the peak corresponding to poly ε-caprolactone at 1730 cm^{-1} was retained while the characteristic peaks corresponding to aldehyde functionality at 1710 cm^{-1} completely disappeared confirming the coupling reaction. **Figure 4a.18** represents ^{1}H-NMR spectra of poly ε-caprolactone containing

aldehyde-azido functional groups ($M_{n,NMR}$: 11800) and its click reaction product with O-(2-azidoethyl) hydroxylamine.

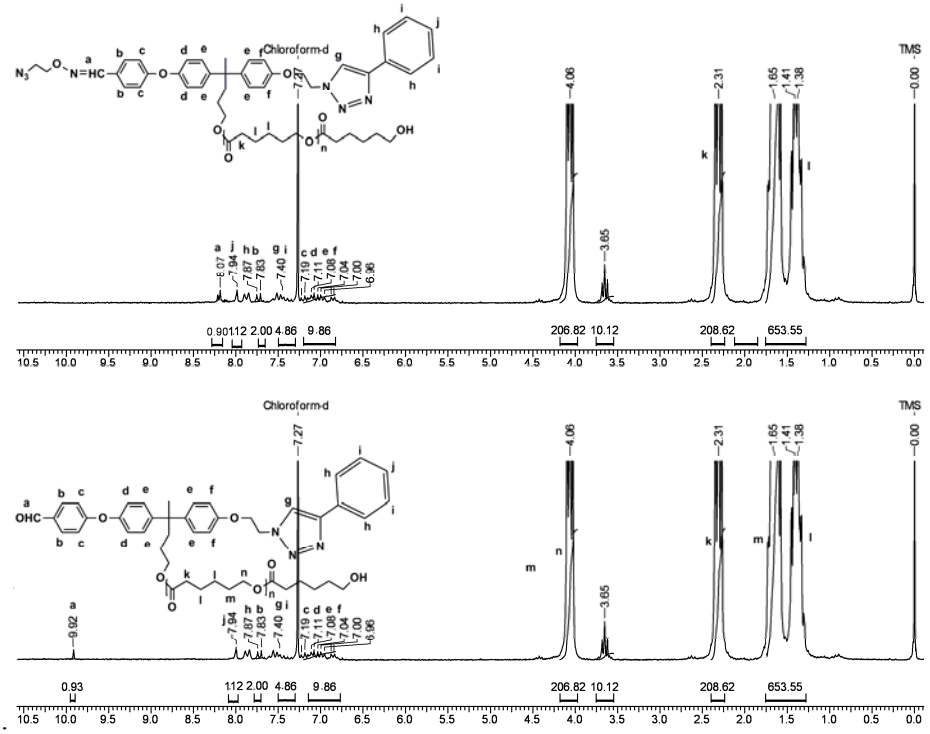


Figure 4a.18: ^{1}H-NMR spectra of A) α- aldehyde functionalized poly ε-caprolactone B) product fromed by reaction of α- aldehyde functionalized poly ε-caprolactone with O-(2-azidoethyl) hydroxylamine in $CDCl_3$

Thus, advantage of availability of azido and aldehyde heterofunctionality on polycaprolactone could be taken for functionalization of polycaprolactone by azido-propargyloxy and aldehyde-aminooxy click reaction is demonstrated.

4a.4. Conclusions

- ✓ Functionalized ROP initiators were demonstrated to be useful initiators for the synthesis of α, α'- homo and α, α'- hetero bifunctionalized poly ε-caprolactones

  1) α, α'- Homo bifunctionalized polycaprolactones containing allyloxy, aldehyde, azido, and propargyloxy functional groups possessing different molecular weights were prepared.

  2) α, α'- Hetero bifunctionalized poly ε-caprolactones featuring allyloxy-aldehyde, allyloxy- azido and azido-aldehyde with different molecular weights were prepared.
- ✓ Reactivity of end functional groups on the poly ε-caprolactones was demonstrated by carrying out specific reactions of that particular functional group present on polymer without backbone degradation.
- ✓ Poly ε-caprolactones possessing clickable end functional groups represent valuable precursors for synthesis of Y-shaped miktoarm star copolymers

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Chapter 4b

End-Functionalized Polymers by ATRP: Synthesis, Characterization and Chemical Modification

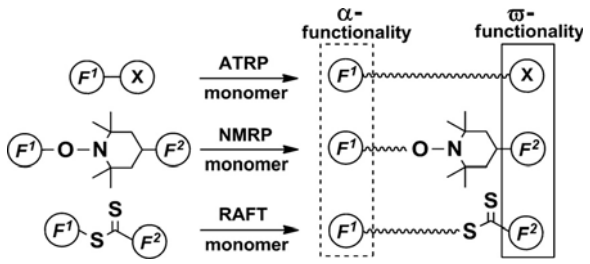
4b.1. Introduction

A major concern of polymer and material scientists is to design functional materials with properties tuned to match the needs of expanding technology. In particular, end-functional polymers have an important position because of their potential applications as components in the synthesis of block copolymers, thermoplastic elastomers, polymer networks, surfactants, macromonomers, etc[1]. According to the IUPAC, end-functional polymers are defined as polymeric molecules with reactive end groups that have the capacity to enter into further polymerization or other reactions. Pioneering work on the synthesis of functional polymers, their conversion to the final products with specific properties by reacting with functional groups may be dated to 1947[2]. However, the concept was not fully recognized until 1960[3]. Significant contributions to the development of this class of polymeric materials prolong in the current literature[4, 5]. In the last two decades there has been a rapid growth in the development and understanding of controlled/living radical polymerizations (C/LRP)[6]. Precise control of functionality, molecular weight, and uniformity (molecular weight distribution) can now be made not only by living ionic polymerization routes but also by newly developed controlled/living radical polymerization techniques.

4b.1.1 Synthesis of telechelic/end-functionalized polymers by CRP

Accurate control of polymerization process is an important aspect for the preparation of well-defined telechelics and end-functionalized macromolecules[7]. Such control of chain ends was traditionally accomplished using living ionic polymerization techniques. But it is well known that the ionic processes suffer from rigorous synthetic requirements and in some cases they are sensitive to the functional groups to be incorporated. On the other hand, free radical polymerization is flexible and less sensitive to the polymerization conditions and functional groups. However, conventional free radical processes yield polymers without control of molecular weight and chain end. Competing coupling and disproportionation steps and the inefficiency of the initiation step lead to functionalities less than or greater than those theoretically expected. Recent developments in controlled/living radical polymerization provided the possibility to synthesize well-defined telechelic polymers with controlled functionality[8]. As described below, all the controlled/living radical polymerization methods, namely atom transfer radical polymerization (ATRP)[9, 10], nitroxide mediated radical polymerization (NMP) also called as stable free radical mediated polymerization (SFRP)[11], reversible addition-fragmentation chain transfer polymerization (RAFT)[12], iniferters[13], iodine transfer polymerization[14] (ITP) can be used for preparation of telechelic/end-functional polymers. There are two strategies for synthesizing telechelic polymers using the widely used C/LRP methods including ATRP, RAFT, or NMP processes[15, 16]. Functionality can be incorporated onto the initiating segment of ATRP, RAFT, or

NMP initiators which afford α-functional polymers. Equally, functionality can be affixed to the terminating portion of initiators which provides ω-functional polymer **(Scheme 4b.1).**

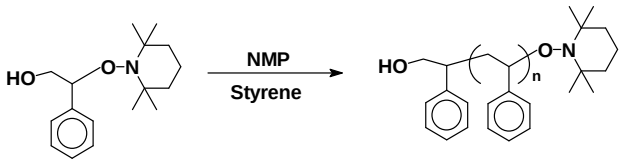


Scheme 4b.1: General synthetic strategies for telechelic polymers by ATRP, NMP and RAFT methods[17].

Polymers can be functionalized at one end (semi-telechelic), both ends (telechelic), or possess differing functionality at the ends (heterotelechelic). As an alternative, functionalization of polymer can be achieved by post-polymerization reactions.

4b.1.1.1. End-functionalized polymers by NMP

NMP was reported as a successful method to obtain end-functional polymers[17]. The utilization of functional alkoxyamine during polymerization generally gives functional polymers. Several examples are reported where functionalities such as acid[18-21], azide[22, 23], alcohol[24, 25], protected amine[26, 27], halide[28, 29] were introduced in polymers. The use of TEMPO with a hydroxyl-functional initiator gives hydroxyl-terminated polymers[30] **(Scheme 4b.2)**.



Scheme 4b.2: Synthesis of hydroxyl-terminated polystyrene using NMP

4b.1.1.2.End-functionalized polymers by RAFT polymerization

RAFT polymerization is an extremely versatile process and has been utilized in the preparation of narrow MWD polymers or copolymers from most monomers amenable to radical polymerization. There is compatibility with a wide range of functionality in monomers, solvents and initiators. Due to its compatibility with functional groups, it is also known for the synthesis of end-functionalized polymers *via* functional RAFT agent. In RAFT polymerization, an easy way to synthesize end-functionalized polymers is the polymerization in the presence of functionalized RAFT agents. A variety of functionalities such as alcohol[31, 32], acid[33, 34], amine[35], azide[36, 37], alkyne[38, 39], allyl[40, 41],epoxy[42] could be introduced in polymers *via* functional RAFT agents. **Figure 4b.1** shows selected functionalized RAFT agents utilized in preparation of end-functional

polymers through RAFT polymerization[40, 43-45]. There are certain reported difficulties with RAFT polymerization such as retardation and poor control which is frequently attributable to inappropriate choice of RAFT agent for the monomers and reaction conditions. RAFT agents that perform well under a given set of circumstances are not necessarily optimal for all circumstances.

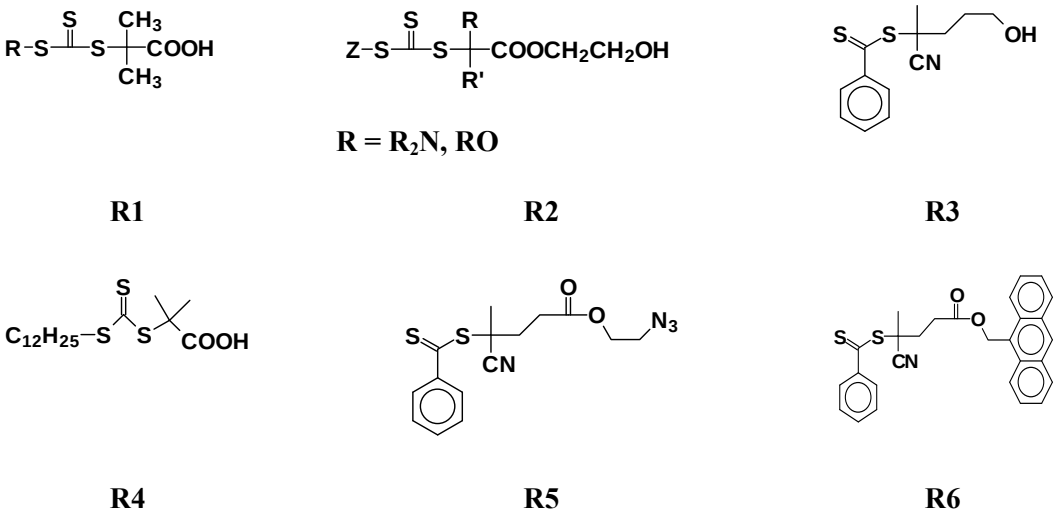
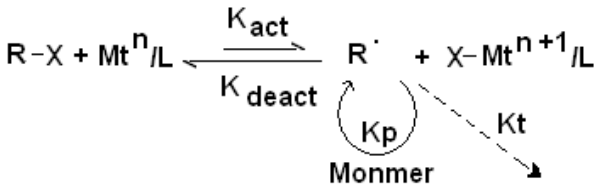


Figure 4b.1: Selected functionalized RAFT agents

4b.1.1.3. End-functionalized polymers by ATRP

Matyjazewski et al[46] and Sawamoto et al[47] introduced ATRP in 1995 simultaneously. The principle is based on the Kharasch[48] reaction, the Atom Transfer Radical Addition (ATRA)[49], which is widely used by organic chemists for carbon-carbon bond formation. The control in an ATRP system is induced by the presence of an organic halide initiator and a transition metal complex. The reversible exchange of the halogen atom between the growing polymer chain and the transition metal complex (in its higher oxidation state) ensures the control over the polymerization **(Scheme 4b.3)**. As in other living polymerizations, ATRP process can be effectively employed for the synthesis of end-functionalized polymers. Compared to NMP and RAFT polymerization, ATRP is known to be the most promising polymerization technique for synthesis of end-functionalized polymers on the basis of the present vast amount of literature[17,50]



Scheme 4b.3: Mechanism of ATRP

Four major routes for functional polymers *via* ATRP have been reported **(Figure 4b.2):**

1) Use of functional initiators

2) Substitution of the terminal halogen atom

3) Direct polymerization of functional monomers

4) Polymerization of "protected" monomers, followed by post-polymerization

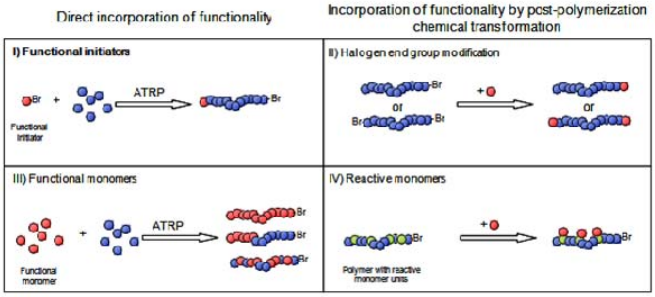


Figure 4b.2: Major strategies for functional polymers *via* ATRP

The first two approaches yield end-functionalized polymers whereas the last two yield polymers with multiple functionalities along the backbone. To this end, using functional initiators, two general methods are employed to synthesize functional polymers a) using functional initiator having functional group on α, chain end b) halide displacement method. In the former, polymerization is initiated with a functionalized organic halide initiator coupled with a metal catalyst to form polymers with an α-end (head) functionality[51]. In the latter, end-functionalization is achieved through transformation of a stable carbon-halogen terminal bond[52].

4b.1.1.3.1. Polymerization of functional monomers

The simplest approach to a functional polymer is the direct polymerization of a monomer containing the desired functionality[53]. ATRP is generally tolerant to many polar functional groups and this route has often been successfully used. Water-soluble monomers (both neutral and ionic) can be polymerized in a controlled fashion by ATRP directly in protic (aqueous) media, provided that some basic rules for catalyst selection are obeyed[54]. In some cases, polar monomers especially those that are strongly coordinating (basic, nucleophilic or acidic)-can react with the ATRP catalyst, the alkyl halide-type initiator or the polymeric dormant species. In these cases, monomers with 'protected' groups should be used. They can be transformed into the desired polar functionalities after the polymerization[55, 56].

4b.1.1.3.2. Use of functional ATRP initiators

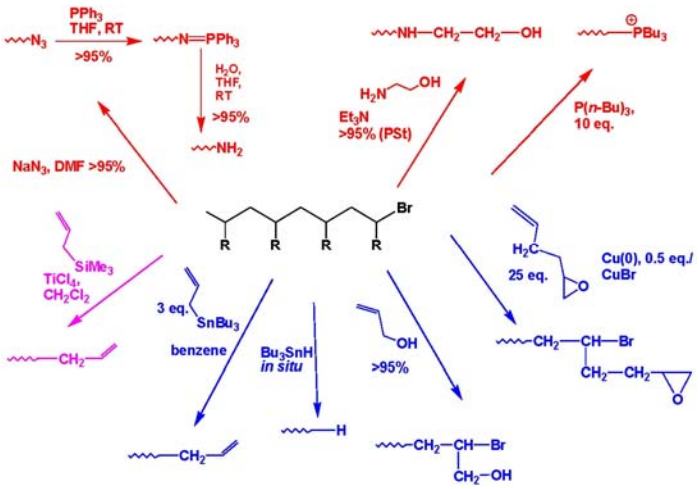
In ATRP, the incorporation of α-functional groups is achieved by making use of appropriately functionalized initiators. It should be pointed out that besides the desired functionality, the initiators need to be equipped with a radical stabilizing group on the α-carbon atom such as aryl, carbonyl, nitrile to ensue successful ATRP. Taking advantage of the tolerance of ATRP for functional groups, a variety of functionalized initiators have been synthesized and

used for preparation of end functionalized polymers. Functional ATRP initiators have been documented by Yagci et. al[17] and Matyjaszeweski et al[10]

4b.1.1.3.3. End-functionalized polymers via halide displacement

This is another important method for the synthesis of end-functionalized polymers by ATRP[10]. Polymers obtained by ATRP contain a halogen atom as end group, if termination and transfer reactions are essentially absent. The halogen atom can be replaced through a variety of reactions leading to end functional polymers. A common method of dehalogenation is, reaction of polymer synthesized by ATRP with trialkyltin hydride[49, 52].

Such substitutions are often desirable for high-temperature applications where some evidence for halogen loss has been described[57]. By replacing tributyltin hydride with allyl tri-*n*-butylstannane, polymers with allyl end groups were produced[58]. The terminal halogen can also be displaced by other methods such as nucleophilic substitution, cyclo-addition, free-radical chemistry, or electrophilic addition catalyzed by Lewis acids. **(Scheme 4b.4)**



Scheme 4b.4: End-functionalized polymers synthesized by displacement of terminal halogen atom using electrophilic substitution, nucleophilic substitution, cyclo addition and radical addition reactions[59]

A survey of literature revealed that α- or ω-functional polymers have been frequently reported in the literature employing the appropriate strategies which have been summarized in previous sections. Scant attention has been paid to synthesize α, α' homo bifunctional and α, α'-heterobifunctional polymers by ATRP technique. The present study encompasses synthesis of different end-functionalized polymers viz. polystyrene and poly (methyl methacrylate). α, α'-Homobifunctional polystyrene and poly (methyl methacrylate) having different functionalities such as allyloxy, aldehyde, propargyloxy, azido and α-aldehyde, α'-allyloxy heterobifunctional poly (methyl methacrylate) with different molecular weights were prepared using appropriate initiators. FT-IR, NMR spectroscopy and GPC techniques were used to characterize end-

functionalized polymers. End functionality on the polymer was demonstrated by carrying out specific reactions of that particular functional group present on polymer.

4b.2. Experimental

4b.2.1. Materials

4,4'-Bis(4-(allyloxy)phenyl)pentyl 2-bromo-2-methylpropanoate, 4,4'-bis(4-(4-formylphenoxy)phenyl)pentyl 2-bromopropanoate, 4,4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentyl-2-bromo2-methylpropanoate, 4-4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methylpropanoate, and 4,4'-bis(4-(2-azidoethoxy)phenyl)pentyl 2-bromopropanoate, were synthesized starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid as described in **chapter 3b**. Synthesis of O-(2-azidoethyl) hydroxylamine has been detailed in **chapter 4a**. N, N, N', N', N"-Pentamethyldiethylenetriamine (PMDETA), 2-bromoisobutyryl bromide (98%), phenyl acetylene (Aldrich), cholorobenzene, AIBN (Spectochem), bromine (Loba), chloroplatinic acid monohydrate, *3*-chloroperoxybenzoic acid, lithium aluminium hydride (LAH), and triethylsilane were used as received. Copper (I) bromide (Aldrich, 99.9%) was washed with glacial acetic acid in order to remove any soluble oxidized species, filtered, washed with ethanol, and dried. Methyl methacrylate (MMA) and styrene were stirred over calcium hydride for 4 h and distilled under reduced pressure just before use.

4b.2.2. Characterization and measurements

FTIR spectra were recorded on a Perkin-Elmer Spectrum *GX* spectrophotometer. NMR spectra were recorded on a Bruker 200 MHz spectrometer for ^{1}H-NMR and 125 MHz for ^{13}C-NMR measurements using $CDCl_3$, $CDCl_3$ without TMS as a solvent. Molecular weight and molecular weight distribution of polymers were determined using GPC analysis at a flow rate of 1 mL min^{-1} in chloroform at 30 °C (Thermoseparation product) equipped with spectra series UV 100 and spectra system RI 150 detectors. The sample concentration was 2 to 3 mg mL^{-1} and the injection volume was 50 mL. HPLC grade chloroform was used as eluent at room temperature with a flow rate of 1 mL min^{-1}. Polystyrene and PMMA were used as the calibration standards.

4b.2.3. Synthesis of functional polystyrenes and poly (methyl methacrylate)s

4b.2.3.1. Synthesis of α, α'- bis-allyloxy functionalized polystyrenes and poly (methyl methacrylate)s

ATRP of styrene in bulk at 110 °C and that of methyl methacrylate in anisole at 80 °C was carried out. In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (120 mg, 0.85 mmol). The Schlenk tube was thoroughly flushed with argon.

4,4'-Bis(4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate (425 mg, 0.85 mmol) was dissolved in styrene (11.0 g, 106 mmol) in a separate sample vial, degassed and was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and PMDETA (173 μL, 0.85 mmol) was rapidly added. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 110 °C. Kinetic study was performed by taking aliquots at regular intervals. After the reaction time, polymerization was quenched by cooling the reaction mixture in a liquid nitrogen bath. The reaction mixture was diluted with THF (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was dried under reduced pressure for 24 h. The monomer conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.07 (d, Ar-H from initiator), 6.80 (d, Ar-H from initiator), 6.09-5.98 (m, =CH), 5.45-5.23 (q, $=CH_2$), 4.49 (d, $-OCH_2$), 3.58 (s, $-OCH_3$ from poly (methyl methacrylate), 1.87-0.81 (m, CH_2, -CH from poly (methyl methacrylate) + protons from initiator)

^{1}H NMR ($CDCl_3$, δ/ppm): 7.05-6.39 (m, Ar-H from polystyrene + Ar-H from initiator), 6.09-5.95 (m, 2H, =CH), 5.45-5.23 (q, $=CH_2$), 4.49 (d, $-OCH_2$), 1.86-1.43 (m, $-CH_2$,-CH- from polystyrene + protons from initiator)

4b.2.3.1.1. Chemical modification of α, α'- bis-allyloxy functionalized polystyrene

4b.2.3.1.1.1. Reaction of α, α'- bis-allyloxy functionalized polystyrene with bromine

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, α, α'- bis-allyloxy functionalized polystyrene (730 mg, 0.066 mmol, M_{nNMR}-11100) and carbon tetrachloride (10 mL). The solution of bromine (2.5 mL) in carbon tetrachloride (5 mL) was added until solution turned to red and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was precipitated into methanol (100 mL). The obtained polymer was dried under vacuum at 50 °C for 8 h and was characterized by ^{1}H NMR spectroscopy.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.12-6.39 (m, Ar-H from polystyrene + Ar-H from initiator), 4.59-4.52 (m, CH_2Br and CHBr), 1.86-1.43 (br, $-CH_2$, -CH- from polystyrene)

4b.2.3.1.1.2. Hydrosilylation reaction of α, α'- bis-allyloxy functionalized polystyrene with triethylsilane using chloroplatinic acid monohydrate as a catalyst

Into a 100 mL two necked round-bottom flask equipped with a dropping funnel were charged, solution of chloroplatinic acid monohydrate (560 mg, 1.36 mmol,) in acetonitrile (5

mL), triethyl silane (2.30 g, 1.36 mmol) in acteonitrile (5 mL) and α, α'- bis-allyloxy functionalized polystyrene (730 mg, 0.066 mmol, M_{nNMR}-11100) in dry toluene (15 mL) under the stream of argon. The reaction mixture was stirred at room temperature for 30 minutes. The dark green colored solution was precipitated in cold methanol and the polymer was separated by filtration. The polymer was dried under vacuum at 50 °C for 8 h and was characterized by ^{1}H – NMR spectroscopy.

^{1}H NMR ($CDCl_3$ without TMS, δ/ppm): 7.12-6.39 (m, Ar-H from polystyrene + Ar-H from initiator), 4.31 (t, -CH_2O), 1.86-1.43 (m, -CH_2,-CH from polystyrene), 0.84-0.79 (m, -CH_3), 0.49-0.44 (m, Si-CH_2)

4b.2.3.1.1.3. Transformation of α, α'- bis-allyloxy functionalized polystyrene into α, α'- bis-epoxide functionalized polystyrene

Into a 100 mL two necked round-bottom flask equipped with a dropping funnel was charged, α, α'- bis-allyloxy functionalized polystyrene (730 mg, 0.066 mmol, $M_{n,NMR}$-11100) dissolved in dichloromethane (10 mL) and the solution was cooled to 0 °C with ice water. The solution of *3*-chloroperoxybenzoic acid (1.0 g, 6.8 mmol) in dichloromethane (25 mL) was slowly added over a period of 30 minutes. After completion of addition, the reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 24 h. The solution was washed with aqueous 5% $NaHCO_3$ solution (3 x 100 mL) and de-ionized water (3 x 100 mL). The polymer was precipitated into methanol (25 mL). The polymer was dried under vacuum at 50 °C for 8 h and was characterized by ^{1}H-NMR spectroscopy.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.12-6.39 (m, Ar-H in polystyrene + Ar-H in initiator), 3.15-3.13 (m, -CH_2O), 2.74-2.70 (m, -CH_2O), 2.59-2.55 (m, 2H, CH_2O), 1.86-1.43 (br, -CH_2, -CHPh- from polystyrene)

4b.2.3.2. Synthesis of α, α'-bisaldehyde functionalized polystyrene

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (120 mg, 0.85 mmol) and the tube was thoroughly flushed with argon. 4, 4'-Bis (4-(4-(formylphenoxy) phenyl) pentyl 2-bromopropanoate (0.52 g, 0.85 mmol) was dissolved in styrene (3.1 g, 29.75 mmol) in a separate sample vial, degassed and the solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and N, N, N', N', N"-pentamethyldiethylenetriamine (173 μL, 0.85 mmol) was added rapidly. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 110 °C. Kinetic study was performed by taking aliquots at regular intervals. After appropriate time;

polymerization was quenched by cooling reaction mixture in liquid nitrogen bath. The reaction mixture was diluted with tetrahydrofuran (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was dried under reduced pressure for 24 h and weighed. The monomer conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$ δ/ppm): 9.85 (s, 2H, aldehyde), 7.77 (d, Ar-H *ortho* to aldehyde), 7.02-6.50 (m, Ar-H from polystyrene + Ar-H from initiator), 2.12-1.99 (m, -CH_2 from polystyrene + protons from initiator fragment), 1.75-1.50 (m, -CH from polystyrene + protons from initiator fragment)

4b.2.3.3. Synthesis of α, α'-bis propargyloxy functionalized poly (methyl methacrylate)s

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (120 mg, 0.85 mmol) and the tube was thoroughly flushed with argon. 4, 4'-Bis (4-(prop-2- ynyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate (420 mg, 0.85 mmol) was dissolved in methyl methacrylate (2.65 g, 25.5 mmol) in a separate sample vial, degassed and the solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and N, N, N', N', N"-pentamethyldiethylenetriamine (173 µL, 0.85 mmol) was added. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 80 °C. After appropriate time; polymerization was quenched by cooling reaction mixture in liquid nitrogen bath. The reaction mixture was diluted with tetrahydrofuran (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was dried under vacuum for 24 h and weighed. The monomer conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$ δ/ppm): 7.08 (d, Ar-H from initiator fragment), 6.86 (d, Ar-H from initiator fragment) 4.65 (t, -OCH_2 from initiator fragment), 3.58 (s, -OCH_3 from poly (methyl methacrylate) and -OCH_2 from initiator fragment), 2.52 (t, acetylene proton), 1.85- 0.82 (m, CH_2, -CH_3 from poly (methyl methacrylate + protons from initiator fragment))

4b.2.3.4. Synthesis of α, α'-bisazido functionalized poly (methyl methacrylate)s

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (120 mg, 0.85 mmol) and the tube was thoroughly flushed with argon. 4,4'-Bis(4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate (470 mg, 0.85 mmol) was dissolved in methyl methacrylate (6.8 g, 68 mmol) in a separate sample vial, degassed and the solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction

mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and N, N, N', N', N"-pentamethyldiethylenetriamine (173 μL, 0.85 mmol) was added rapidly. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 80 °C. Kinetic study was performed by taking aliquots at regular intervals. After appropriate time; polymerization was quenched by cooling reaction mixture in liquid nitrogen bath. The reaction mixture was diluted with tetrahydrofuran (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into excess methanol (500 mL) to precipitate the polymer. The polymer was filtered, dried under vacuum for 24 h and weighed. The monomer conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$ δ/ppm): 7.09 (d, Ar-H from initiator fragment), 6.81 (d, Ar-H from initiator fragment) 4.12 (t, -OCH_2 from initiator fragment), 3.58 (s, -OCH_3 from poly (methyl methacrylate) and -OCH_2 from initiator fragment), 1.85-0.83 (m, CH_2, -CH_3 from poly (methyl methacrylate + protons from initiator fragment))

4b.2.3.4.1. Chemical modification of α, α'- bis-azido functionalized poly (methyl methacrylate)s

4b.2.3.4.1.1. Reaction of α, α'- bis-azido functionalized poly (methyl methacrylate)s with phenyl acetylene

In a typical experiment, Schlenk tube equipped with a magnetic stir bar were charged with, α, α'- bis-azido functionalized poly (methyl methacrylate) (750 mg, 0.1 mmol), CuBr (30 mg, 0.2 mmol), phenyl acetylene (204 mg, 2 mmol), N, N, N', N', N"-pentamethyldiethylenetriamine (20 μL, 0.1 mmol) and DMF (20 mL) under nitrogen atmosphere. The Schlenk tube was sealed and the reaction mixture was degassed three times by freeze-pump-thaw cycles and kept stirring for 24 h at room temperature. After reaction time, DMF was removed under vacuum and reaction mixture was diluted with dichloromethane (50 mL). The solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into cold methanol (500 mL) to precipitate the polymer. The polymer was filtered and dried under vacuum for 24 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.94 (s, Ar-H attached to triazole ring), 7.80 (d, Ar-H attached to triazole ring), 7.44-7.38 (m, Ar-H attached to triazole ring + triazole ring proton), 7.08 (d, Ar-H from initiator), 6.80 (d, Ar-H from initiator), 4.78 (t, -CH_2), 4.35 (t, -CH_2), 3.58 (s, -OCH_3 from poly (methyl methacrylate) and -OCH_2 from initiator fragment), 1.85-0.83 (m, CH_2, -CH_3 from poly (methyl methacrylate + protons from initiator fragment))

4b.2.3.5. Synthesis of α-aldehyde, α'-allyloxy heterobifunctionalized poly (methyl methacrylate)s

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (120 mg, 0.85 mmol) and the tube was thoroughly flushed with argon. 4-4-(Allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methylpropanoate (480 mg, 0.85 mmol) was dissolved in methyl methacrylate (4.25 g, 42.5 mmol) in a separate sample vial, degassed and the solution was transferred *via* argon-purged syringe to the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under argon atmosphere, the reaction mixture was opened and N, N, N', N', N"-pentamethyldiethylenetriamine (173 μL, 0.85 mmol) was added. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 80 °C. Kinetic study was performed by taking aliquots at regular intervals. After appropriate time; polymerization was quenched by cooling reaction mixture in liquid nitrogen bath. The reaction mixture was diluted with tetrahydrofuran (50 mL) and the solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into cold methanol (500 mL) to precipitate the polymer. The polymer was filtered, dried under vacuum for 24 h and weighed. The monomer conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$ δ/ppm): 9.93 (s, aldehyde from initiator), 7.85 (d, Ar-H *ortho* to aldehyde from initiator), 7.14-6.84 (m, Ar-H from initiator), 6.14-6.00 (m, -CH =C-), 5.46-5.26 (q, -C=CH_2), 4.53 (d, -OCH_2), 3.60 (s, -OCH_3 from poly (methyl methacrylate), 1.90-0.84 (m, CH_2, -CH from poly (methyl methacrylate + protons from initiator fragment))

4b.2.3.5.1. Chemical modification of α-aldehyde, α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)

4b.2.3.5.1.1. Aldehyde- aminooxy click reaction

Into a 50 mL two necked round-bottom flask equipped with a dropping funnel were charged, α-aldehyde, α'-allyloxy hetero bifunctionalized poly (methyl methacrylate) (740 mg, 0.2 mmol), dichloromethane (10 mL) and a pinch of sodium sulfate. The solution of O-(2-azidoethyl) hydroxylamine (1.02 g, 10 mmol) dissolved in dichloromethane (5 mL) was added and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was precipitated into cold hexane (50 mL). The obtained polymer was filtered and dried under vacuum at 50 °C for 8 h.

IR ($CHCl_3$, cm^{-1}): 2110, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 8.11 (s, -CH=N), 7.56 (d, Ar-H *ortho* to oxime), 7.14-6.82 (m, Ar-H from initiator fragment), 6.19-6.02 (m, -CH =C-), 5.46-5.31 (q, -C=CH_2), 4.54 (d, -OCH_2), 4.30 (t, OCH_2), 3.60 (s,-OCH_3 from poly (methyl methacrylate)), 1.91-0.81 (m, -CH_2, -CH from poly (methyl methacrylate + protons from initiator fragment)).

4b.2.3.5.1.2 Thiol-ene thermal click reaction

Into a clean and dry Schlenk tube α-allyloxy α'-azido functionalized poly (methyl methacrylate) (185 mg, 0.05 mmol), 3-mercaptopropanoic acid (53 mg, 0.5 mmol) and AIBN (82 mg, 0.5 mmol) were dissolved in chlorobezene (20 mL). The mixture was degassed *via* three freeze-pump-thaw cycles and subsequently vacuum sealed. The Schlenk tube was heated at 80 °C for 6 h. The polymer was purified by precipitation in cold methanol. The polymer was dried at 50 °C under vacuum for 18 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 8.11 (s, -CH=N), 7.56 (d, Ar-H *ortho* to oxime), 7.14-6.82 (m, Ar-H from initiator), 4.54 (d, -OCH_2), 4.30 (t, OCH_2), 3.60 (s, -OCH_3 from poly (methyl methacrylate), 1.87-0.81 (m, CH_2, -CH from poly (methyl methacrylate).

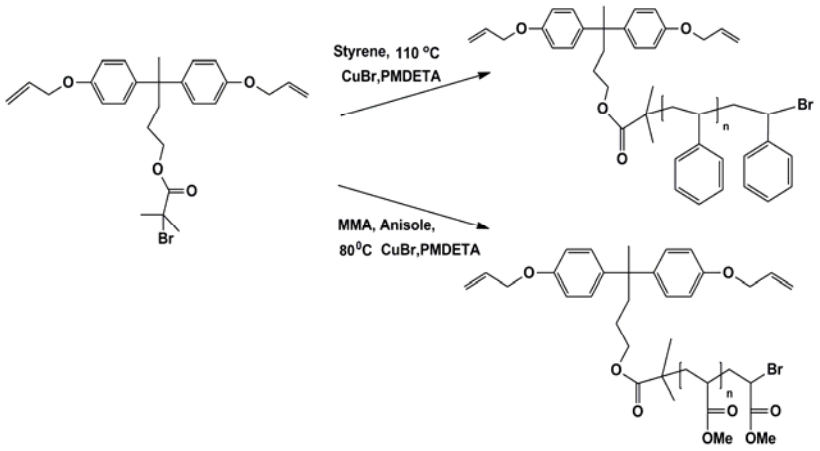
4b.3. Results and Discussion

ATRP technique has been routinely employed for the synthesis of polymers with α-, ω- and α, ω-functional end groups and a wide variety of functional groups have been introduced. However, there are limited examples of synthesis of α, α'-homobifunctional polymers such as dihydroxyl[60], dicarboxylic acid[61], di(4-fluorobenzoyl)[62], and di(aromatic bromo)[63] using initiator approach. To the best of our knowledge, there are no reports on synthesis of α, α'–hetero bifunctionalized polymers using ATRP initiators.

In the present work, we report synthesis of α, α'–homo- and α, α'–hetero bifunctionalized polymers using initiator approach. The functionalities introduced on polymers such as allyloxy, propargyloxy, azido and aldehyde were chosen by considering the fact that all these functionalities are capable of undergoing click reactions.

4b.3.1. Synthesis of α, α'-bisallyloxy functionalized polystyrenes and poly (methyl methacrylate)s

ATRP of styrene in bulk and that of methyl methacrylate in anisole was carried out using bis-allyloxy functionalized ATRP initiator *viz*, 4,4'-bis(4-(allyloxy) phenyl)pentyl 2-bromo-2-methylpropanoate (**Scheme 4b.5).**



Scheme 4b.5: Synthesis of α, α'-bisallyloxy functionalized polystyrenes and poly (methyl methacrylate)s

The reaction conditions and results of synthesis of α, α'-bis-allyloxy functionalized poly (methyl methacrylate)s and polystyrenes are summarized in **Tables 4b.1** and **Table 4b.2**, respectively.

Table 4b. 1: Reaction conditions and results for synthesis of α, α'-bis allyloxy functionalized poly (methyl methacrylate)s

Sr. No.	[a]$[M]_0$: [I] : [Cu]: [L]	[b]Conv. (%)	[c]$M_{n,\ theo}$	$M_{n,\ NMR}$	[d]$M_{n,\ GPC}$	M_w/M_n	[e]I^{eff}
1	100:1:1:1	74	7900	9000	10100	1.34	0.87
2	200:1:1:1	43	9100	11900	10500	1.32	0.76
3	300:1:1:1	38	11900	12000	11700	1.23	0.98
4	500:1:1:1	32	16500	21500	18500	1.23	0.76

(Time-8 h, Temperature- 80 °C solvent: Anisole 50 % w/v w.r.t. monomer)

a- [M]:[I]:[Cu]:[L] = [Monomer]:[Initiator]:[CuBr]:[PMDETA]
b- Gravimetry
c- Mol. wt. monomer x [Mo] / $[I_O]$ x % conv. + mol. wt. initiator (500)
d- PMMA standard
e- $I^{eff} = M_{n,theo}/M_{n,NMR}$

Different ratios of $[M_0]$ / $[I_0]$ with same reaction interval were chosen so as to obtain polymers with different molecular weights. The conversions were determined by gravimetric analysis. The reaction conversions were kept low (32 – 74%) so as to avoid potential side reactions involving allyloxy groups. Molecular weights of poly (methyl methacrylate)s ($M_{n,NMR}$: 9000-21500) were in close agreement to the molecular weights calculated from the monomer-to-

initiator ratio. In addition, GPC data revealed PDI values in the range 1.23-1.34 for poly (methyl methacrylate).

Table 4b. 2: Reaction conditions and results for synthesis of α, α'- bis-allyloxy functionalized polystyrenes

Sr. No.	[a]$[M]_0$: [I] : [Cu]: [L]	[b]Conv. (%)	[c]$M_{n,\ theo}$	$M_{n,\ NMR}$	[d]$M_{n,GPC}$	M_w/M_n	[e]I^{eff}
1	125:1:1:1	68	9300	11100	13600	1.09	0.83
2	300:1:1:1	61	18800	19800	16990	1.06	0.94
3	500:1:1:1	51	26000	29600	28300	1.07	0.87

(Time – 8 h, Temperature-110 °C in bulk)

a- [M]:[I]:[Cu]:[L] = [Monomer]:[Initiator]:[CuBr]:[PMDETA]

b- Gravimetry

c- Mol. wt. monomer x [Mo] / $[I_O]$ x % conv. + mol. wt. initiator (500)

d- PS standard

e- $I^{eff} = M_{n,theo}/M_{n,\ NMR}$

Different ratios of $[M_0]$ / $[I_0]$ with same reaction interval were chosen so as to obtain polymers with different range of molecular weights. The conversions were determined by gravimetric analysis. The reaction conversions were kept low (51–68%) so as to avoid potential side reactions involving allyloxy groups. Molecular weights of polystyrenes ($M_{n,NMR}$: 11100-29600) were in close agreement to the molecular weights calculated from the monomer-to-initiator ratio. In addition, GPC trace **(Figure 4b.3)** revealed monomodal distribution with PDI values in the range 1.07-1.09 for polystyrene. The PDIs were relatively narrow, which is in good agreement with a controlled polymerization method.

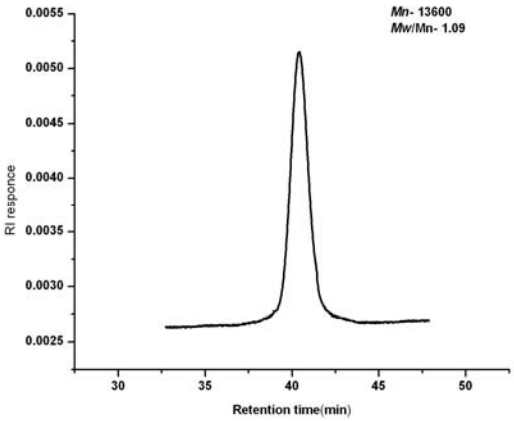


Figure 4b.3 GPC trace of α, α'-bis-allyloxy functionalized polystyrene

A kinetic study was performed to verify the control over the polymerization of styrene. The linearity of plot of ln (M_0/M_t) *vs* polymerization time, **(Figure 4b.4)** where M_0 and M_t are initial and the actual monomer concentration indicated the pseudo first order kinetics.

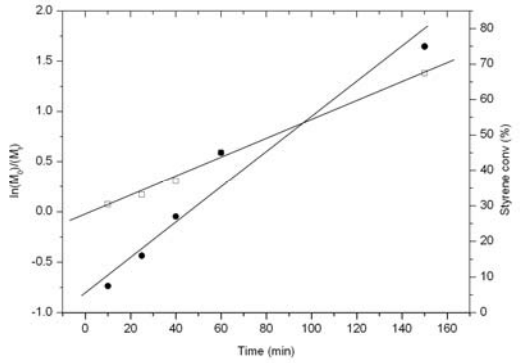


Figure 4b.4: Relationships between ln ($[M_0]/[M_t]$) and the polymerization time for ATRP of styrene at 110 °C in bulk

The concentration of radicals remained constant during the polymerization reaction and therefore it can be concluded that no detectable side reactions occurred during polymerization. The linear increase of molecular weight with increasing conversion and PDI below 1.4 (**Figure 4b.5**) represents an additional indication for a controlled polymerization mechanism.

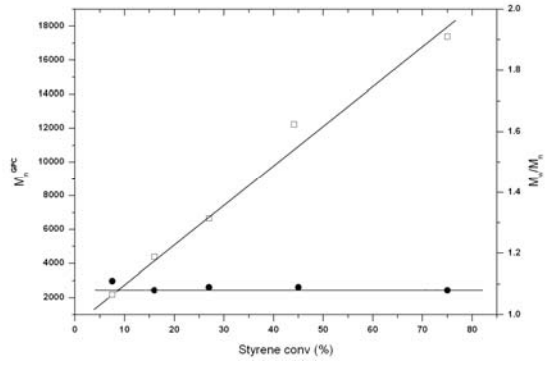


Figure 4b.5: Dependence of number-average molecular weight and PDI on monomer conversion for ATRP of styrene at 110 °C in bulk

These results are consistent with the results previously reported using allyl group containing ATRP initiators[64,65]. ^{1}H-NMR spectra of α, α'-bis-allyloxy functionalized poly (methyl methacrylate) and polystyrene are reproduced in **Figure 4b.6** and **Figure. 4b.7**, respectively.

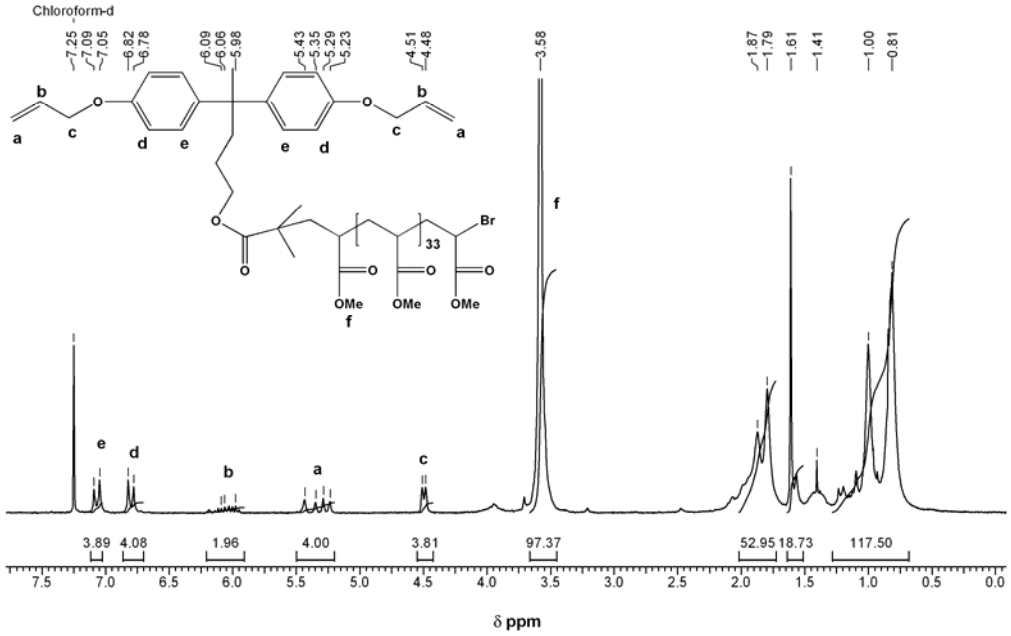


Figure 4b. 6: ^{1}H-NMR spectrum of α, α'- bisallyloxy functionalized poly(methyl methacrylate) in $CDCl_3$

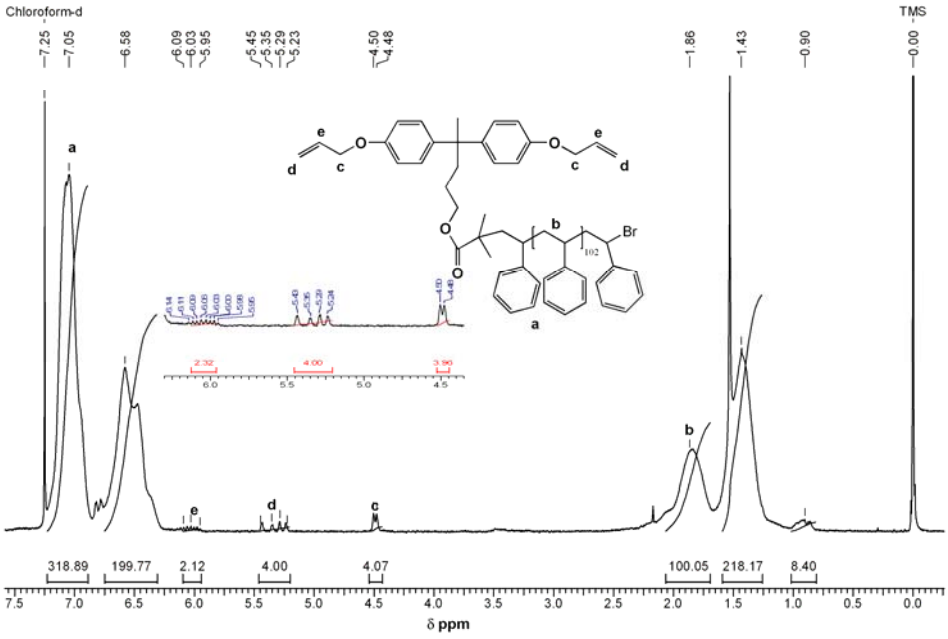


Figure 4b. 7: ^{1}H-NMR spectrum of α, α'-bisallyloxy functionalized polystyrene in $CDCl_3$

The appearance of multiplets in the range 6.09-5.95 ppm and 5.43-5.23 ppm confirmed the presence of allyloxy functionality. Molecular weights can be calculated for bis-allyloxy functionalized polystyrene and poly (methyl methacrylate) by ^{1}H-NMR spectroscopy. $M_{n,NMR}$ of poly (methyl methacrylate) was calculated by comparing integrated intensity of peak belonging to -OCH_3 in PMMA at 3.58 ppm to a multiplet in the range 6.09-5.95 ppm corresponding to allyloxy functionality.

$$Dpn = [I_{3.58}/3/ (I_{5.95\ (alllyloxy\ proton)}/2)]$$

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x 100 (mol. wt. of monomer)] + 500 (mol. wt. of initiator)

$M_{n,NMR}$ of allyloxy- functionalized PS was calculated by comparing integrals of phenyl ring protons with methylene protons attached to ether linkage.

$$Dpn = [I_{7.05\text{-}6.39}/5/ (I_{5.97\ (alllyloxy\ proton)}/2)]$$

Molecular weights were calculated using the equation,

$M_{n,NMR}$= [Dpn x 104 (mol. wt. of monomer)] + 500 (mol. wt. of initiator)

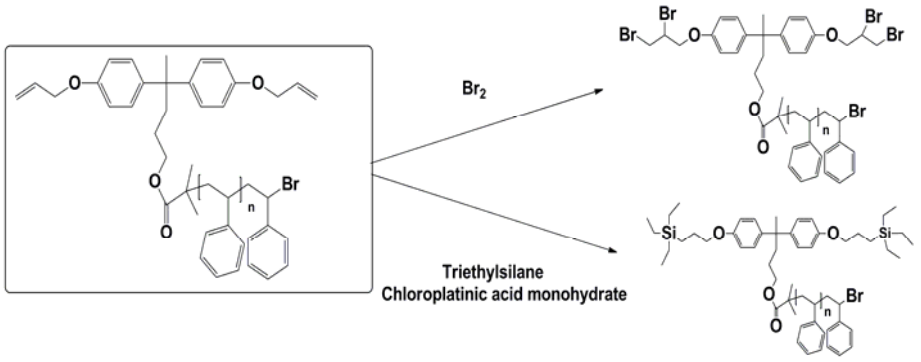
Molecular weights calculated by ^{1}H-NMR spectroscopy (M_{nNMR}) were in reasonably good agreement with theoretical molecular weights ($M_{n,\ theo}$) indicating good initiator efficiency (I^{eff} = 0.83-0.94).

Thus, 4, 4'-bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate was found to be useful ATRP initiator for controlled polymerization of methyl methacrylate and styrene under specified conditions.

4b.3.1.1. Chemical modification

4b.3.1.1.1. Reaction of* α, α'- bisallyloxy functionalized *polystyrene with bromine and triethylsilane

In order to illustrate the reactivity of allyloxy functionality, the organic reactions of allyloxy group such as addition of bromine and hydrosilylation were studied on polystyrene (**Scheme 4b.6**). α, α'- Bis-allyloxy functionalized polystyrene was treated with bomine in order to study general and simple diagnostic reaction for unsaturation.



Scheme 4b.6: Reactions of α, α'- bisallyloxy functionalized polystyrene

The brominated product was characterized by ^{1}H-NMR spectroscopy **(Figure 4b.8 B)**. ^{1}H-NMR spectrum revealed complete disappearance of the signal corresponding to allyloxy functionality (6.09-5.95 and 5.43-5.23 ppm) confirming the completion of reaction. Furthermore, hydrosilylation reaction using triethylsilane was carried out on bis-allyloxy functionalized polystyrene in the presence of chloroplatinic acid monohydrate as a catalyst. The reaction product was characterized by ^{1}H-NMR spectrum (**Figure 4b.8D**) in which total disappearance of the peaks corresponding to allyloxy protons in the range 6.09-5.95 and 5.43-5.23 ppm indicated completion of reaction.

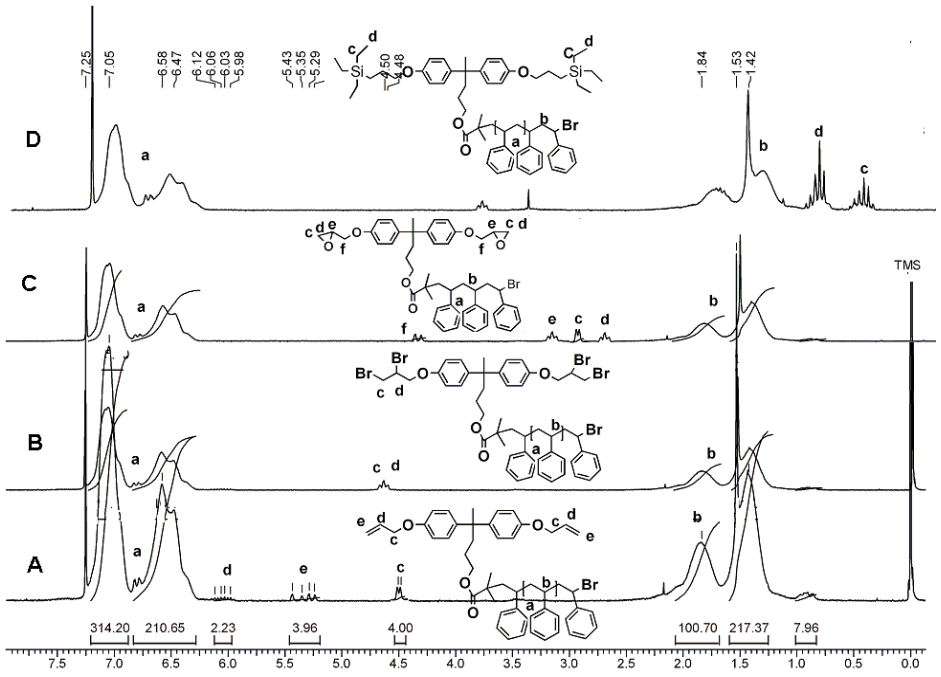
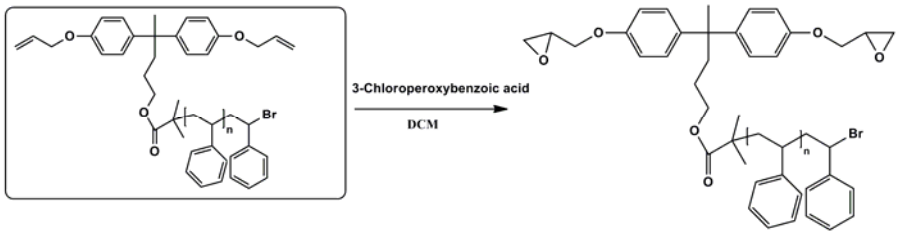


Figure 4b.8: ^{1}H-NMR spectra of A) bis-allyloxy functionalized polystyrene B) polystyrene after bromination C) bis-epoxide functionalized polystyrene in $CDCl_3$ D) hydrosilylation product of bis-allyloxy functionalized polystyrene in $CDCl_3$ without TMS

The model hydrosilylation study with triethylsilane opens up further detailed investigation of hydrosilylation reaction with mono- and di-hydride-terminated polydimethylsiloxane to yield Y-shaped miktoarm copolymer PS-b-$(PDMS)_2$ and PDMS -g- PS, respectively.

4b.3.1.1.2. Transformation of α, α'- *bisallyloxy functionalized polystyrene into α, α'bis- epoxy functionalized polystyrene*

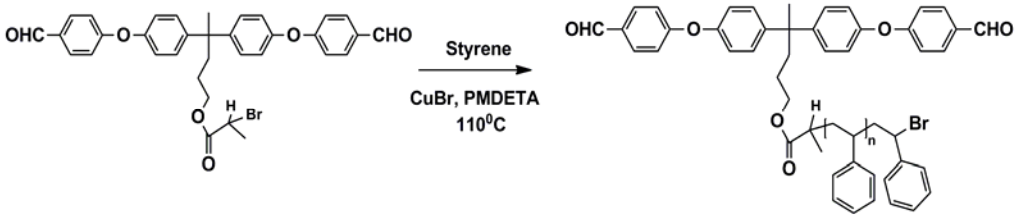
Epoxidation of bis-allyloxy functionalized polystyrene with *3*-chloroperoxybenzoic acid as an oxidant was carried out (**Scheme 4b.7**). The epoxidised product was characterized by ^{1}H-NMR spectroscopy **(Figure 4b.8 C).** The complete disappearance of the resonances corresponding to allyloxy group protons and the appearance of new signals corresponding to oxirane ring protons at 3.15-3.13, 2.74-2.70 and 2.59-2.50 ppm indicated complete conversion of bis-allyloxy into bis-epoxy functionalized polystyrene.



Scheme 4b.7 Chemical transformation of α, α'-bis-allyloxy functionalized polystyrene into α, α'-bis- epoxy functionalized polystyrene

4b.3.2. Synthesis of α, α'- bis-aldehyde functionalized polystyrenes

ATRP of styrene in bulk was carried out using 4, 4'-bis (4-(4- (formylphenoxy) phenyl) pentyl 2-bromopropanoate as an initiator **Scheme 4b.8**



Scheme 4b.8: Synthesis of α, α'- bis-aldehyde functionalized polystyrenes

The conditions and results of synthesis of α, α'-bisaldehyde functionalized polystyrene are summarized in **Table 4b.3.**

Table 4b.3: Reaction conditions and results for synthesis of α, α'- bis-aldehyde functionalized polystyrenes

Sr. No.	[a] $[M]_0$: [I] : [Cu]: [L]	Time (h)	[b] Conv (%)	[c] $M_{n,theo}$	$M_{n,NMR}$	[d] $M_{n,GPC}$	M_w/M_n	[e] Ieff
1	35:1:1:1	3	64	2900	3100	3800	1.16	0.93
2	120:1:1:1	5	73	9700	10900	12000	1.14	0.88
3	225:1:1:1	8	76	18400	21500	28200	1.11	0.85

(Temperature-110 °C in bulk)

a- [M]:[I]:[Cu]:[L] = [Monomer]:[Initiator]:[CuBr]:[PMDETA]

b- Gravimetry

c- [Mol. wt. of monomer x $\frac{[M]_O}{[I]_O}$ x (% conv.)] + mol. wt. initiator (614)

d- Polystyrene standard,

e- $I^{eff} = M_{n,theo}/M_{n,NMR}$

Different ratios of $[M_0]$ / $[I_0]$ with same reaction interval were chosen so as to obtain polymers with a range of molecular weights combined with convenient polydispersity. The conversions were determined by gravimetric analysis. ^{1}H-NMR spectrum of bis-aldehyde functionalized polystyrene is reproduced in **Figure 4b.9.** The appearance of a singlet at 9.85 ppm confirmed the presence of aldehyde functionality.

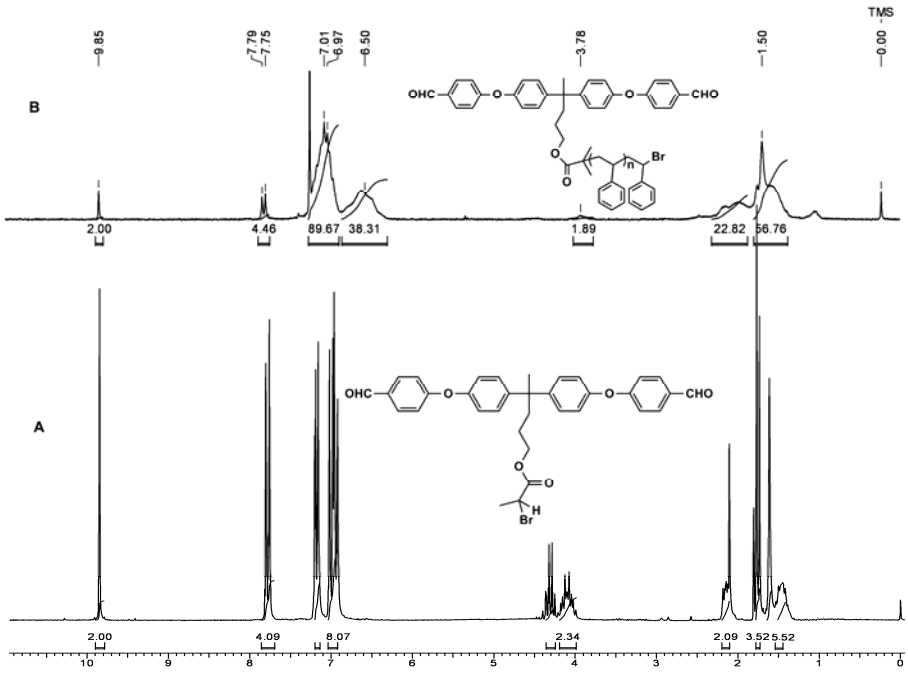


Figure 4b.9: ^{1}H-NMR spectra of A) 4,4'-bis (4-(4- (formylphenoxy) phenyl) pentyl 2-bromopropanoate B) α, α'- bis-aldehyde functionalized polystyrene in $CDCl_3$

Integration of signals for aldehyde functionality and comparison with the integration values for phenyl ring protons in polystyrene allows molecular weight to be determined. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = (I_{7.01\text{-}6.50}/5)/(I_{9.85}/2_{\text{(aldehyde proton)}})$$

Where $I_{7.01\text{-}6.50}$ corresponds to integration of phenyl ring protons of polystyrene chain. The contribution of aromatic ring protons from initiator fragment was subtracted from the total integration of the peaks appearing in the range 7.01-6.50 ppm. $I_{9.85}$ represents integration of the signal positioned at *9.85 ppm* corresponding to aldehyde protons.

Molecular weights were calculated by using equation,

$M_{n,\,NMR}$ = [Dpn x 104 (Mol. Wt. of monomer)] + 614 (Mol. Wt. of initiator)

Molecular weights determined by ^{1}H-NMR spectroscopy ($M_{n,NMR}$) were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) (**Table 4b.3)** indicating good initiator efficiency (I^{eff} = 0.85-0.93). In addition, GPC trace revealed monomodal distribution with PDI values in the range 1.11-1.16 for polystyrene. The PDIs were relatively narrow, which is a characteristic behavior of a controlled radical polymerization method.

A kinetic study was performed to verify the control over the polymerization of styrene. The linearity of plot of ln (M_0/M_t) *vs* polymerization time, (**Figure 4b.10**) where M_0 and M_t are initial and the actual monomer concentration indicated the pseudo first order kinetics.

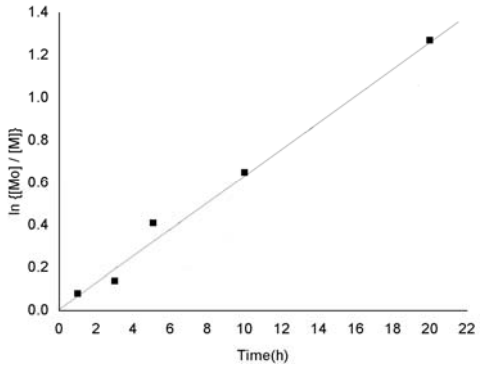


Figure 4b.10: Relationship between ln ($[M_0]/[M_t]$) and the polymerization time for ATRP of styrene at 110 °C in bulk

The concentration of radicals remained constant during the polymerization reaction and therefore it can be concluded that no side reactions occurred during polymerization. The linear increase of molecular weight with conversion and PDI below 1.3 (**Figure 4b.11**) represents an additional indication for a controlled polymerization mechanism.

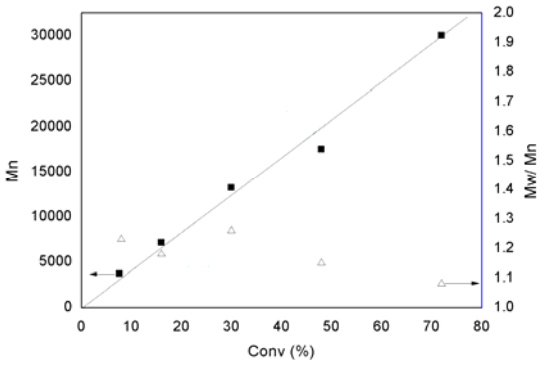
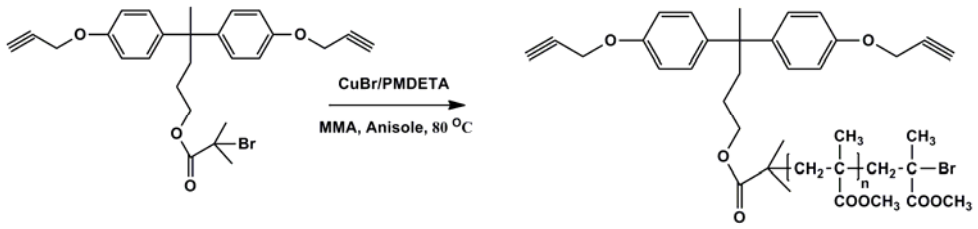


Figure 4b.11: Dependence of number-average molecular weight and PDI on monomer conversion for ATRP of styrene at 110 °C in bulk

Thus, 4, 4'-bis (4-(4- (formyl phenoxy) phenyl) pentyl 2-bromopropanoate was found to be useful ATRP initiator for controlled polymerization of styrene under specified conditions.

4b.3.3. Synthesis of α, α'- bis-propargyloxy functionalized poly (methyl methacrylate)s

ATRP of methyl methacrylate in anisole was carried out using 4, 4'-bis (4-(prop-2-yn-1-yloxy)phenyl)pentyl 2-bromo-2-methylpropanoate as an initiator (**Scheme 4b.9).**



Scheme 4b.9: Synthesis of α, α'-bis-propargyloxy functionalized poly (methyl methacrylate)s

The conditions and results of synthesis of α, α'-bis-propargyloxy functionalized poly (methyl methacrylate)s are summarized in **Table 4b.4**

Table 4b.4: Reaction conditions and results for synthesis of α, α'-bis-propargyloxy functionalized poly (methyl methacrylate)s

Sr. No.	[a] [M]:[I]: [Cu]:[L]	Time (h)	[b]Conv (%)	[c]$M_{n,theo}$	$M_{n,NMR}$	[d]$M_{n,GPC}$	M_w/M_n	[e] I^{eff}
1	[30] : [1]:[1]:[1]	3	65	2500	3900	7600	1.59	0.64
2	[140] : [1]:[1]:[1]	6	73	10700	15700	25800	1.50	0.68
3	[210] : [1]:[1]:[1]	9	66	14400	22300	32900	1.46	0.64

(Temperature-80 °C solvent: Anisole (50%, w/v w.r.t monomer))

a- [M]:[I]:[Cu]:[L] = [Monomer]:[Initiator]:[CuBr]:[PMDETA]

b- Gravimetry

c- $[\text{mol. wt. of monomer} \times \frac{[M]_O}{[I]_O} \times (\% \text{ conv.})] + \text{mol. wt. initiator (496)}$

d- Polystyrene standard

e- $I^{eff} = M_{n,theo}/M_{n,NMR}$

Different ratios of $[M_0]$ / $[I_0]$ with different reaction interval were chosen so as to obtain polymers with different molecular weights. The conversions were determined by gravimetric analysis. ^{1}H-NMR spectrum of α, α'- bis-propargyloxy functionalized poly (methyl methacrylate) is reproduced in **Figure 4b.12.**

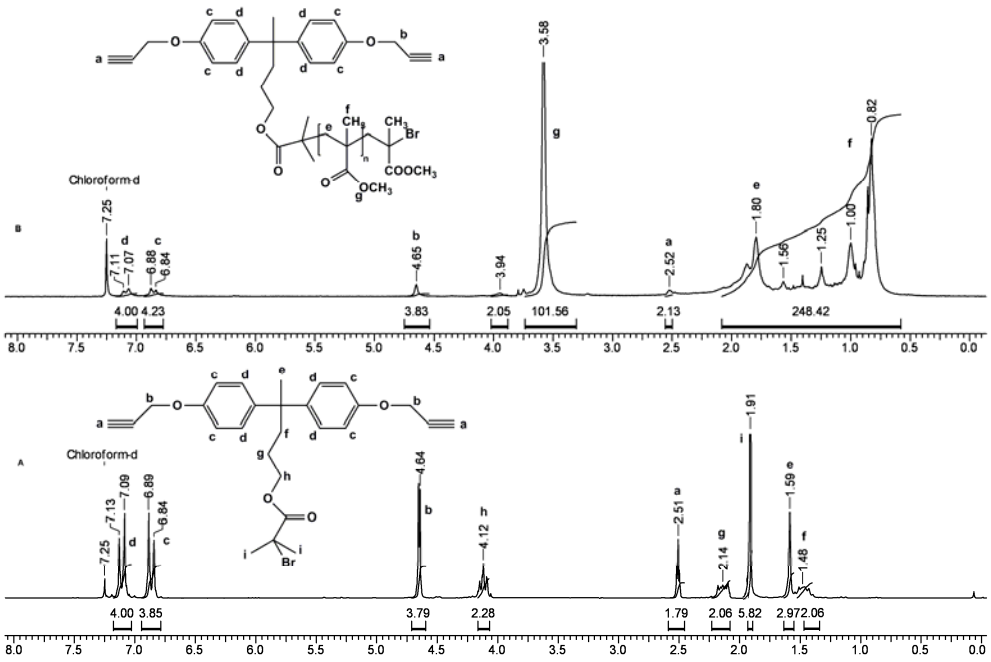


Figure 4b.12: ^{1}H-NMR spectra of A) 4,4-bis(4-(prop-2-yn-1-yloxy)phenyl)pentyl 2-bromo2-methylpropanoate B) α, α'- bis-propargyloxy functionalized poly(methyl methacrylate) in $CDCl_3$

The appearance of a triplet at 2.52 ppm confirmed the presence of propagyloxy functionality. It was presumed that two propargyloxy groups are present per polymer chain. Integration of signals for propargyloxy functionality and comparison with the integration values for methoxy protons in poly (methyl methacrylate) allows the molecular weight to be determined. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = (I_{3.58}/3)/(I_{2.52(acetylene\ proton)}/2)$$

Where $I_{3.58}$ corresponds to integration of methoxy protons of poly (methyl methacrylate). $I_{2.52}$ represents integration of the signal positioned at 2.52 ppm corresponding to acetylene protons.

Molecular weights were calculated using equation,

$M_{n,NMR}$ = [Dpn x 100 (mol. wt. of monomer)] + 496 (mol. wt. of initiator)

It was observed that molecular weights determined by ^{1}H-NMR spectroscopy ($M_{n,NMR}$) were higher than theoretical molecular weights ($M_{n,theo}$) indicating lower initiator efficiency (I^{eff} = 0.64-0.68). In addition, GPC trace revealed broad distribution with PDI values in the range 1.46-1.59 for poly (methyl methacrylate). The PDIs were relatively on higher side, which indicated some deviation from characteristic behavior of a controlled radical polymerization method. A kinetic study was performed to verify the control over the polymerization of methyl methacrylate. The

plot of ln (M_0/M_t) *vs* polymerization time, (**Figure 4b.13**) where M_0 and M_t are initial and the actual monomer concentration indicated deviation from linearity and hence, the deviation from pseudo first order kinetics.

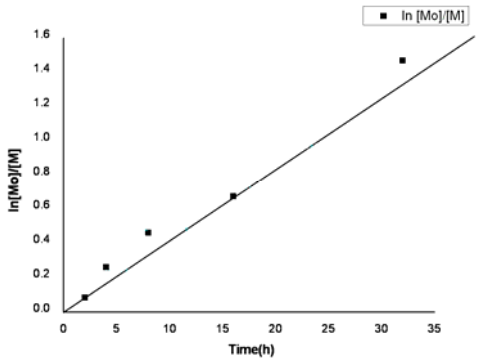


Figure 4b.13: Relationship between ln ($[M_0]/[M_t]$) and the polymerization time for ATRP of methyl methacrylate at 80 °C in anisole

The concentration of radicals may vary during the polymerization reaction and therefore it can be concluded that some sort of side reactions involving propargyloxy functionality occurred during polymerization. However, no efforts were made to probe the nature of such side reactions. The linear increase of molecular weight with increasing conversion and PDI above 1.4 (**Figure 4b. 14**) represents an additional point to substantiate the occurrence of side reaction during polymerization. This could be attributed to the complexation of copper catalyst with alkyne functionality[66].

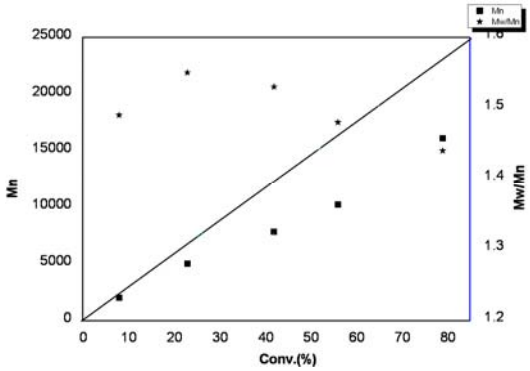


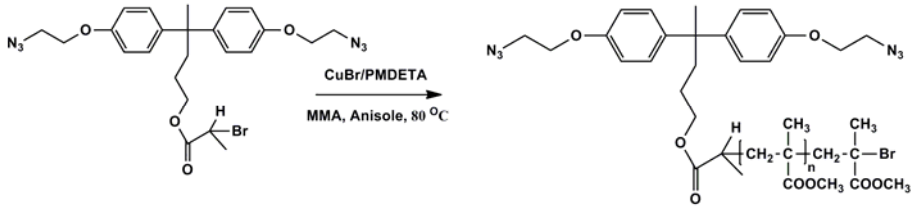
Figure 4b.14: Dependence of number-average molecular weight and PDI on monomer conversion for ATRP of methyl methacrylate at 80 °C in anisole

4b.3.4. Synthesis of α, α'-bis-azido functionalized poly (methyl methacrylate)s

ATRP initiators containing azido functional group(s) have been successfully employed for synthesis of corresponding azido-terminated polymers under carefully designed conditions[67,

[68]. Care needs to be taken in selecting the reaction conditions as azido groups are known to be thermally labile and shock sensitive. Furthermore, depending on the initiator structure there is a possibility of participation of azido group in intramolecular cyclisation reaction.

ATRP of methyl methacrylate was carried out in anisole using 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate as the initiator (**Scheme 4b.10)**.



Scheme 4b.10: Synthesis of α, α'- bis-azido functionalized poly (methyl methacrylate)s

The conditions and results of synthesis of α, α'-bis-azido functionalized poly (methyl methacrylate)s are summarized in **Table 4b.5**

Table 4b.5: Reaction conditions and results of synthesis of α, α'-bis-azido functionalized poly (methyl methacrylate)s

Sr. No.	[a] $[M]_0$: [I] : [Cu]: [L]	Time (h)	[b] Conv (%)	[c] $M_{n,theo}$	$M_{n,NMR}$	[d] $M_{n,GPC}$	M_w/M_n	[e] Ieff
1	80:1:1:1	3	66	5800	7500	8200	1.24	0.77
2	160: 1:1:1	7	62	10500	12600	17600	1.28	0.83
3	240:1:1:1	9	59	14700	18700	26000	1.17	0.78

(Temperature-80 °C Solvent: Anisole (50%, w/v w.r.t monomer)))

a- [M]:[I]:[Cu]:[L] = [Monomer]:[Initiator]:[CuBr]:[PMDETA]
b- Gravimetry
c- [Mol. wt. of monomer x $\frac{[M]_O}{[I]_O}$ x (% conv.)] + mol. wt. initiator (558)
d- Polystyrene standard,
e- $I^{eff} = M_{n,theo}/M_{n,NMR}$

Different ratios of $[M_0]$ / $[I_0]$ with different reaction intervals were chosen so as to obtain polymers with different molecular weights. The conversions were determined by gravimetric analysis. ^{1}H-NMR spectrum of α, α'-bis-azido functionalized poly (methyl methacrylate) is reproduced in **Figure. 4b.15.** Integration of signals for aromatic functionality and comparison with the integration values for methoxy protons in poly (methyl methacrylate) allows the molecular weight to be determined. The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = \{(I_{3.58}/3)/I_{7.09}/4_{(aromatic\ proton)}\}$$

Where $I_{3.58}$ and $I_{7.09}$ are integrals of the signals positioned at *3.58* corresponds to methoxy protons of poly (methyl methacrylate) and 7.09 ppm for aromatic protons, respectively.

Molecular weights were calculated by ^{1}H-NMR spectroscopy using equation,

$M_{n,NMR}$ = [Dpn x 100 (mol. wt. of monomer)] + mol. wt. initiator (558)

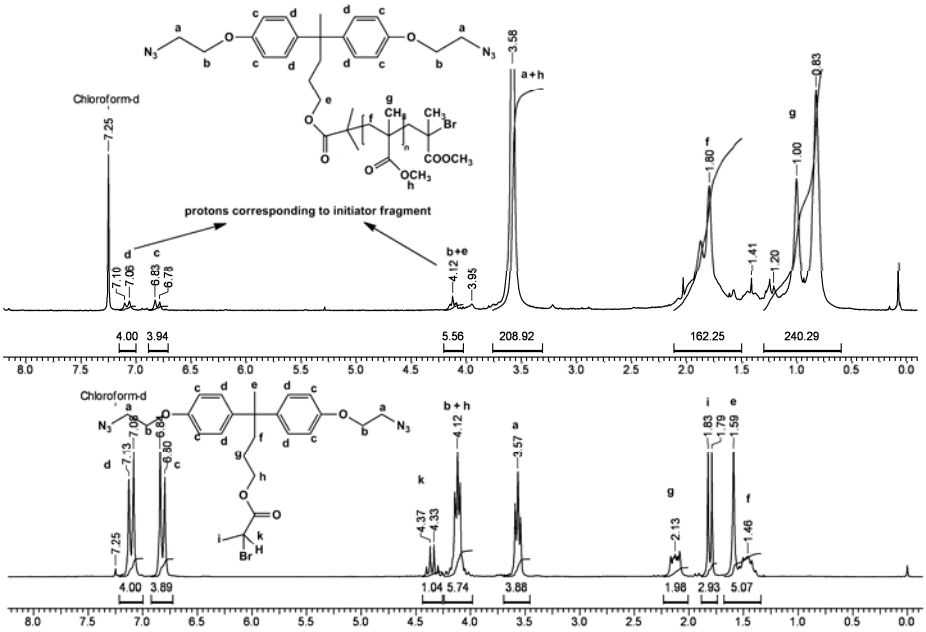


Figure 4b. 15: ^{1}H-NMR spectra of A) 4,4'-bis(4-(2-azidoethoxy)phenyl)pentyl 2-bromopropanoate and B) α, α'-bis-azido functionalized poly (methyl methacrylate) in $CDCl_3$

Molecular weights determined by ^{1}H-NMR spectroscopy ($M_{n,NMR}$) were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) indicating good initiator efficiency (I^{eff} = 0.77-0.83). In addition, GPC study revealed monomodal distribution with PDI values in the range

1.17-1.28 for poly (methyl methacrylate). The PDIs were relatively narrow, which is a characteristic behavior of a controlled radical polymerization method. A kinetic study was performed to verify the control over the polymerization of methyl methacrylate. The linearity of plot of ln (M_0/M) *vs* polymerization time, (**Figure 4b.16**)

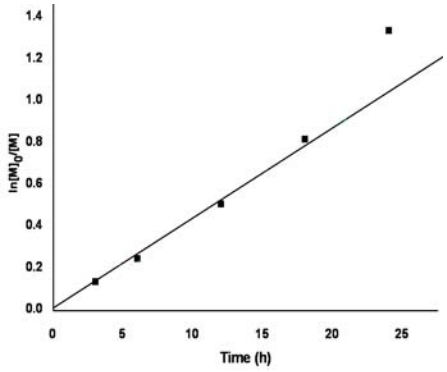


Figure 4b. 16: Relationship between ln ([M_0] / [M]) and the polymerization time for ATRP of methyl methacrylate at 80 °C in anisole

Where M_0 and M_t are initial and the actual monomer concentration indicated the pseudo first order kinetics. The concentration of radicals remained constant during the polymerization reaction and therefore it can be concluded that no detectable side reactions occurred during polymerization. The linear increase of molecular weight with increasing conversion and PDI below 1.3 (**Figure 4b. 17**) represents an additional indication for a controlled polymerization mechanism.

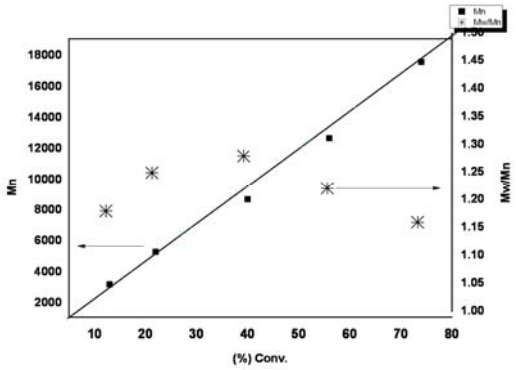


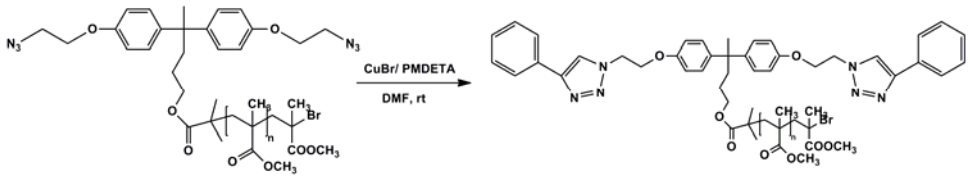
Figure 4b. 17: Dependence of number-average molecular weight and PDI on monomer conversion for ATRP of methyl methacrylate at 80 °C in anisole

Thus, 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate was found to be a useful ATRP initiator for controlled polymerization of methyl methacrylate under the specified reaction conditions.

4b.3.4.1. Chemical modification of α, α'- bis-azido functionalized poly (methyl methacrylate)s

4b.3.4.1.1. Azide-alkyne click reaction of α, α'- bis-azido functionalized poly (methyl methacrylate) with phenyl acetylene

The reactivity of α, α'-azido functionality on poly (methyl methacrylate) was illustrated by carrying out click reaction with phenyl acetylene (**Scheme 4 b. 11**).



Scheme 4b.11: Post-functionalization of α, α'-bis-azido functionalized poly (methyl methacrylate) by azide-alkyne click rection

In FT-IR spectrum, characteristic peak corresponding to azido functionality disappeared while the peak corresponding to carbonyl group of poly (methyl methacrylate) was retained at 1730 cm^{-1} confirming completion of the coupling reaction, The coupling reaction was characterized by ^{1}H-NMR spectroscopy (**Figure 4b. 18)**. In addition to the peaks corresponding to aromatic protons, a characteristic peak corresponding to triazole ring was observed at 7.94 ppm.

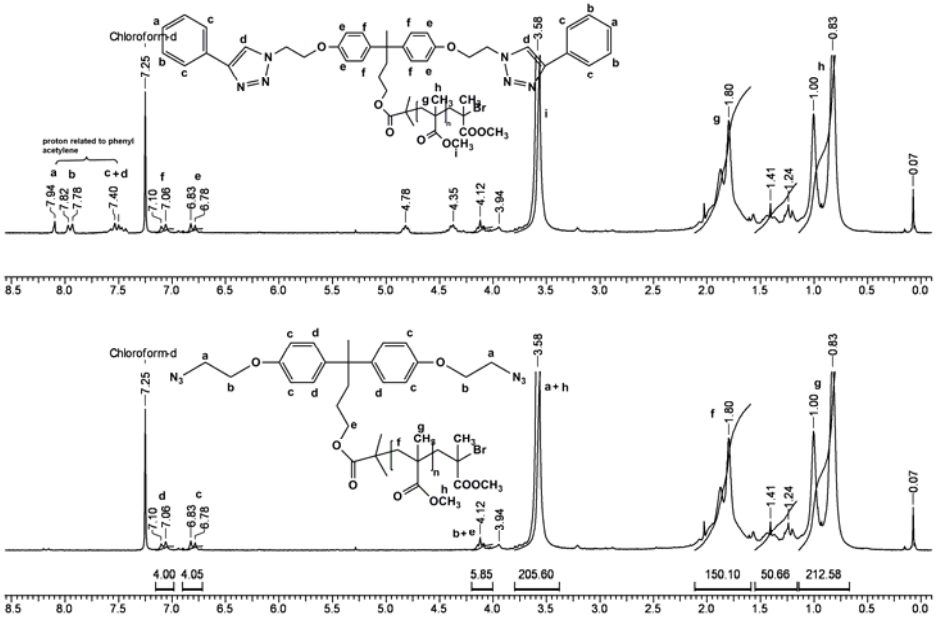
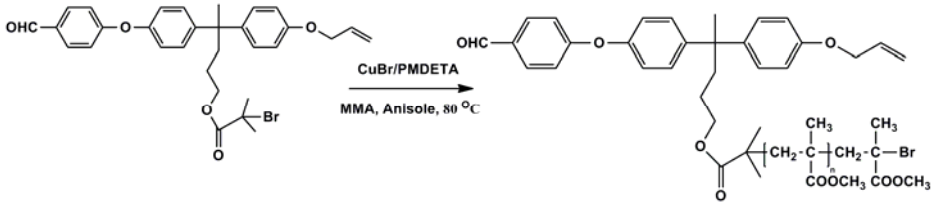


Figure 4b. 18: ^{1}H-NMR spectra of A) α, α'-bis-azido functionalized poly (methyl methacrylate) and B) product of the reaction of α, α'-bis-azido functionalized poly (methyl methacrylate) with phenyl acetylene in $CDCl_3$

4b.3.5. Synthesis of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)s

ATRP of methyl methacrylate was carried out using 4-4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methylpropanoate as the initiator (**Scheme 4b.12)**.



Scheme 4b. 12: Synthesis of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)s

The conditions and results of synthesis of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)s are summarized in **Table 4b.6**

Table 4b.6: Reaction conditions and results of synthesis of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)s

Sr.No.	[a]$[M]_0/[I]_0$	Time (h)	[b]Conv. (%)	[c]$M_{n\ theo}$	[d]$M_{n,NMR}$	[e]$M_{n,GPC}$	M_w/M_n	I^{eff}
1	50:1	3	55	3300	3700	5300	1.21	0.89
2	100:1	5	60	6600	7800	12100	1.25	0.84
3	200:1	8	67	14000	19700	28800	1.19	0.71

(Temperature-80 °C, Solvent: Anisole (50%, w/v w.r.t monomer)))

a- $[M]_O$ / $[I]_O$: [Monomer]:[Initiator]
b- Gravimetry

c- $M_{n,th}$= $\{\frac{[M]_O}{[I]_O}$ x (% Conv.) x mol. wt. of monomer$\}$ + mol. wt. initiator (565)

d- $M_{n,NMR}$= Determined from NMR

e- $M_{n,GPC}$- Determined from GPC; Polystyrene standard; $CHCl_3$ eluent

Different ratios of $[M_0]$ / $[I_0]$ with different reaction interval were chosen so as to obtain polymers with range of molecular weights. The conversions were determined by gravimetric analysis. The reaction conversions were kept in the range 55 – 67% in order to ensure avoidance

of potential side reactions related to allyloxy functional group. ^{1}H-NMR spectrum of α-aldehyde, α'-allyloxy functionalized poly (methyl methacrylate) is reproduced in **Figure 4b.19.** The appearance of a singlet at 9.93 ppm confirmed the presence of aldehyde functionality. The appearance of multiplets in the range 6.14-6.00 ppm and 5.46-5.26 ppm confirmed the presence of allyloxy functionality. Integration of signals for aldehyde functionality and comparison with the integration values for methoxy protons in poly (methyl methacrylate) allows the molecular weight to be determined.

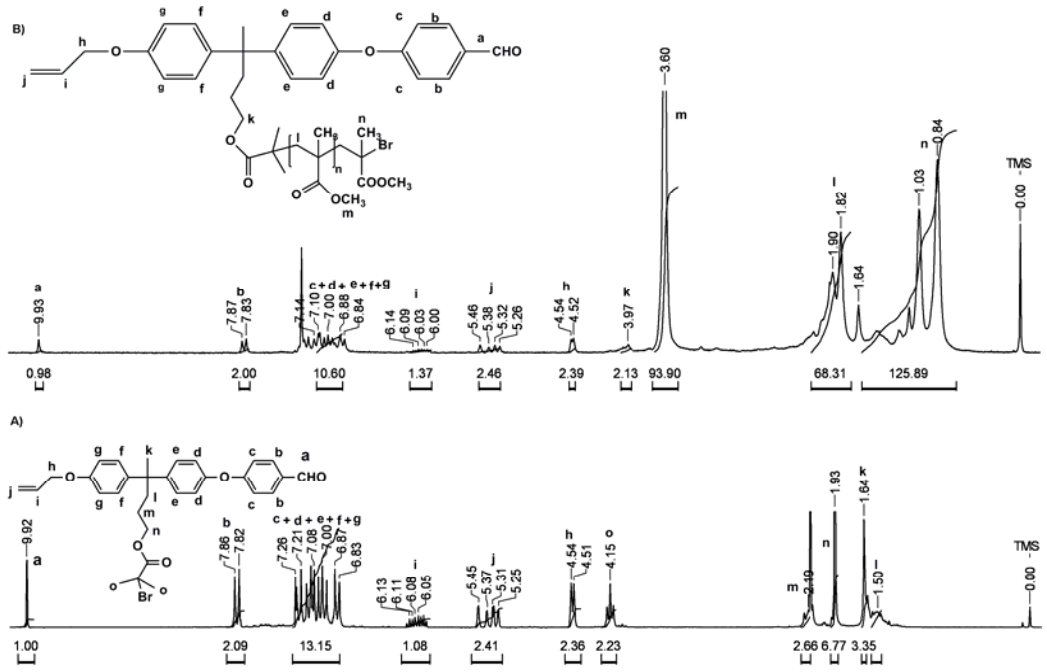


Figure 4b. 19: ^{1}H-NMR spectra of A) 4-(4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy) phenyl)pentyl 2-bromo-2-methyl propanoate and B) α- aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate) in $CDCl_3$

The degree of polymerization was calculated from NMR analysis using the relation,

$$Dpn = \{(I_{3.58}/3)/I_{9.93/1\ (aldehyde\ proton)}\}$$

Where $I_{3.58}$ and $I_{9.93}$ are integrals of the signals positioned at 3.58 corresponds to methoxy protons of poly (methyl methacrylate) and 9.93 ppm for aldehyde functionality, respectively.

Molecular weights were calculated by ^{1}H-NMR spectroscopy using equation,

$$M_{n,NMR} = [Dpn \times 100\ (mol.\ wt.\ of\ monomer)] + mol.\ wt.\ initiator\ (565)$$

Molecular weights determined by ^{1}H-NMR spectroscopy ($M_{n,NMR}$) were in reasonably good agreement with theoretical molecular weights ($M_{n,theo}$) indicating good initiator efficiency (I^{eff} =

0.71-0.89). In addition, GPC trace revealed monomodal distribution with PDI values in the range 1.19-1.25 for poly (methyl methacrylate). The PDIs were relatively narrow, which is a characteristic behavior of a controlled radical polymerization method. A kinetic study was performed to verify the control over the polymerization of styrene. The linearity of plot of ln (M_0/M_t) *vs* polymerization time (**Figure 4b.20**)

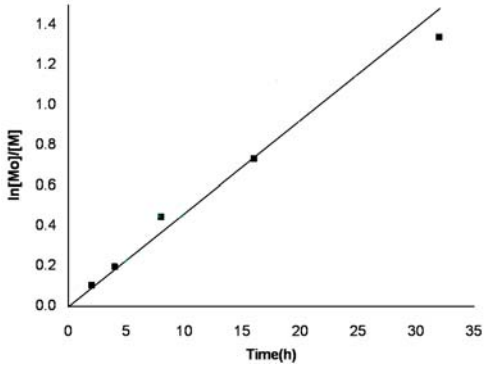


Figure 4b. 20: Relationship between ln ($[M_0]$ / $[M_t]$) and the polymerization time for ATRP of methyl methacrylate at 80 °C in anisole

where M_0 and M_t are initial and the actual monomer concentration indicated the pseudo first order kinetics. The concentration of radicals remained constant during the polymerization reaction and therefore it can be concluded that no detectable side reactions occurred during polymerization. The linear increase of molecular weight with increasing conversion and PDI below 1.25 (**Figure 4b. 21**) represents an additional indication for a controlled polymerization mechanism.

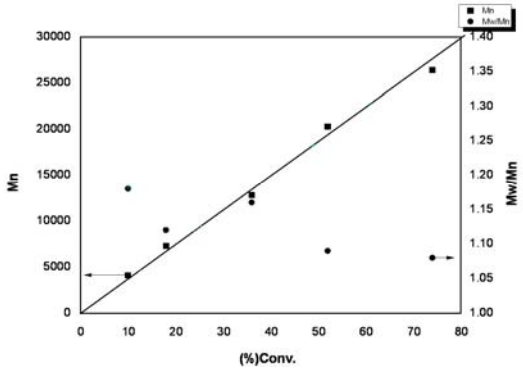


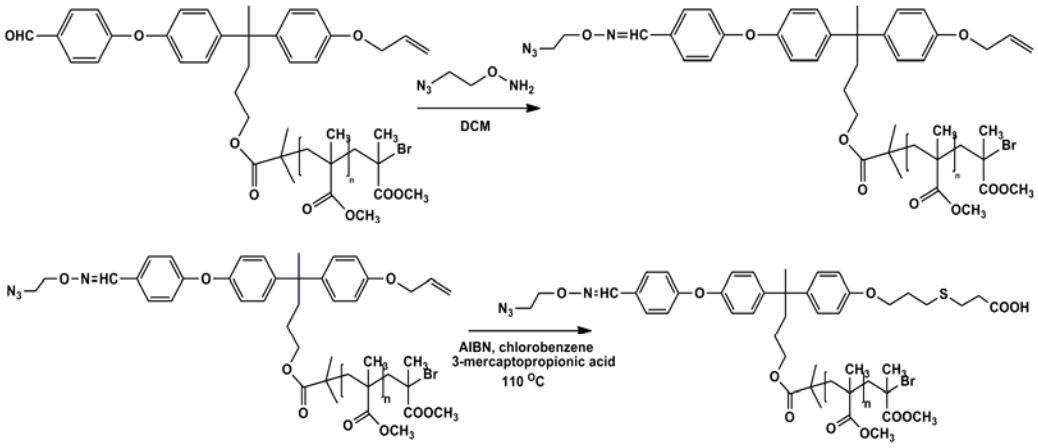
Figure 4b. 21: Dependence of number-average molecular weight and PDI on monomer conversion for ATRP of methyl methacrylate at 80 °C in anisole

Thus, 4-(4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl)pentyl 2-bromo-2-methyl propanoate was found to be an useful ATRP initiator for controlled polymerization of methyl methacrylate under specified conditions.

4b.3.5.1. Chemical modification of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate)s

4b.3.5.1.1. Aldehyde-aminooxy click reaction of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate) with O-(2-azidoethyl) hydroxylamine

The reactivity of aldehyde functionality was illustrated by carrying out click reaction with O-(2-azidoethyl) hydroxylamine at room temperature (**Scheme 4 b.13**).



Scheme 4b. 13: Post-functionalization of α-aldehyde α'-allyloxy hetero bifunctionalized poly (methyl methacrylate) by A) aldehyde-aminooxy click reaction
B) thiol-ene click reaction

In FT-IR spectrum, in addition to the peak corresponding to poly (methyl methacrylate) at 1730 cm^{-1}, characteristic peak corresponding to azido functionality appeared at 2110 cm^{-1} confirming formation of oxime by the coupling reaction. **Figure 4b.22** represents ^{1}H-NMR spectra of aldehyde terminated poly (methyl methacrylate) ($M_{n,NMR}$: 3700) and its click reaction product with O-(2-azidoethyl) hydroxylamine. ^{1}H-NMR spectra showed complete disappearance of the peak corresponding to aldehyde functionality and appearance of a new peak at 8.11 ppm (-CH=N-O) which elucidates oxime formation without affecting peaks related to poly (methyl methacrylate) attesting completion of the reaction without any side reaction such as degradation of poly (methyl methacrylate) backbone.

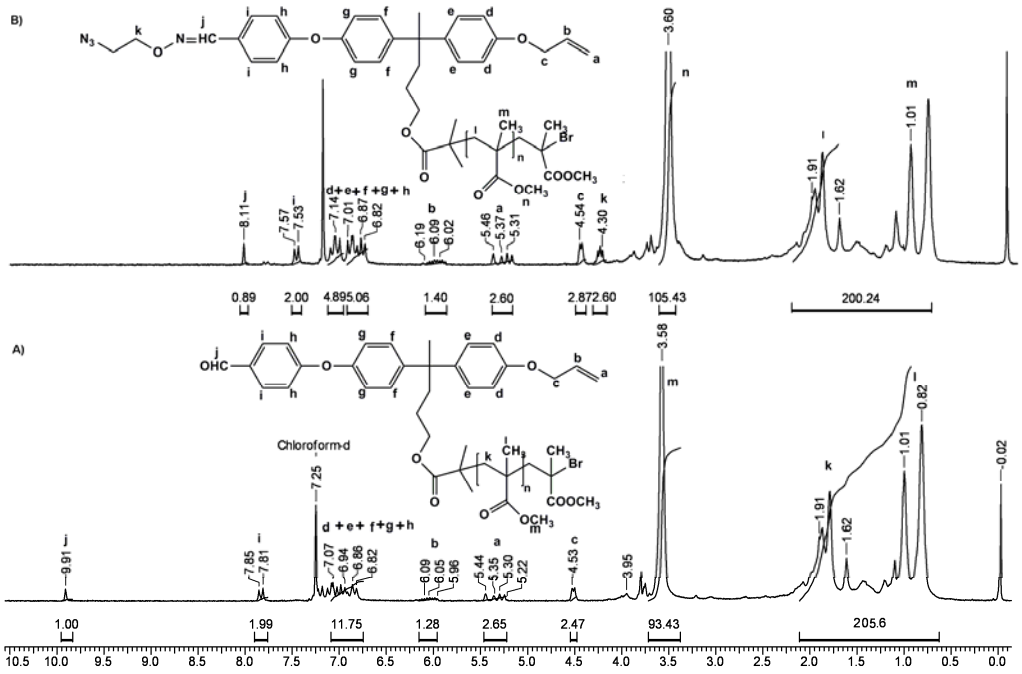


Figure 4b. 22: ^{1}H-NMR spectra of A) α-aldehyde α'-allyloxy hetero bifunctional poly (methyl methacrylate) and B) product of reaction of α-aldehyde α'-allyloxy hetero bifunctional poly (methyl methacrylate) with O-(2-azidoethyl) hydroxylamine in $CDCl_3$

The model aldehyde-aminooxy click reaction study with O-(2-azidoethyl) hydroxylamine introduces azido moiety on poly (methyl methacrylate) chain which further opens up plethora of opportunities to introduce different types of functional groups on poly (methyl methacrylate) by well known azide-alkyne click reaction[69].

4b.3.5.1.2 Thiol-ene click reaction of α-allyloxy, α'-azido heterobifunctionalized poly (methyl methacrylate)s

The reactivity of allyloxy functionality was illustrated by carrying out click reaction with 3-mercaptopropionic acid on poly (methyl methacrylate) in presence of AIBN at 110 °C in chlorobenzene as a solvent (**Scheme 4b.13)**. The conversion was assessed by ^{1}H-NMR spectroscopy. ^{1}H-NMR spectra of allyloxy functionalized poly (methyl methacrylate) (M_{nNMR}: 3700) and its click reaction product with 3-mercaptopropionic acid is shown in **Figure 4b.23.**

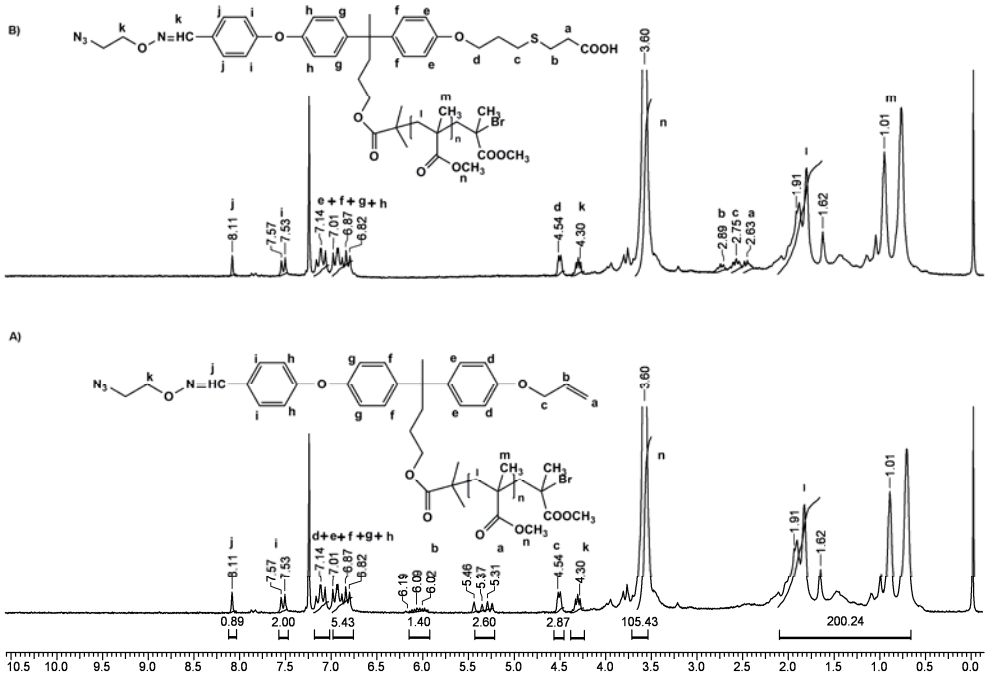


Figure 4b. 23: ^{1}H-NMR spectra of A) α-allyloxy, α'-azido hetero bifunctionalized poly (methyl methacrylate) and B) the product of thiol-ene click reaction in $CDCl_3$

From ^{1}H-NMR spectrum, it is observed that the peak corresponding to allyloxy functionality disappeared completely and appearance of new peaks at 2.79, 2.75, 2.69 ppm indicated addition of thiol without any side reaction such as degradation of poly (methyl methacrylate) backbone.

4b.4. Conclusions

- ✓ α, α'- Homo and α, α'- hetero bifunctionalized polystyrenes and poly (methyl methacrylate)s having different molecular weights were synthesized using appropriate ATRP initiators.

  1) α,α'-Bis allyloxy-terminated polystyrenes and poly (methyl methacrylate)s were synthesized by ATRP using 4,4'-bis(4-(allyloxy) phenyl)pentyl 2-bromo-2-methylpropanoate as the initiator and reactivity of allyloxy functionality was demonstrated by carrying out bromination, epoxidation and hydrosilylation reaction.

  2) α,α'-Bis-aldehyde terminated polystyrenes were synthesized by ATRP using 4,4'-bis(4-(4-formylphenoxy)phenyl)pentyl 2-bromopropanoate as the initiator.

  3) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl)pentyl 2-bromo-2-methylpropanoate was studied as the ATRP initiator for polymerization of methyl methacrylate which resulted into poor control over molecular weight and broader molecular weight distribution of PMMA.

  4) α,α'-Bisazido terminated poly (methyl methacrylate)s were synthesized by ATRP using 4,4'-bis(4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate as the initiator and the reactivity azido functionality was demonstrated by carrying out azido-propargyl click reaction with phenyl acetylene.

  5) α -Aldehyde,α'- allyloxy hetero bifunctionalized poly (methyl methacrylate)s were synthesized using4-(4-(allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate as the ATRP initiator and the reactivity aldehyde and allyloxy functionality was demonstrated by carrying out aldehyde-aminooxy and thiol-ene click reactions, respectively.

- ✓ Polystyrenes and poly (methyl methacrylate)s possessing clickable end functional groups represent valuable precursors for synthesis of Y-shaped miktoarm star copolymers

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Chapter 5

Miktoarm Star Copolymers: Synthesis and Characterization

Chapter 5a

MFI- Cores for Preparation of Miktoarm Star Copolymers: Synthesis and Characterization

5a.1. Introduction

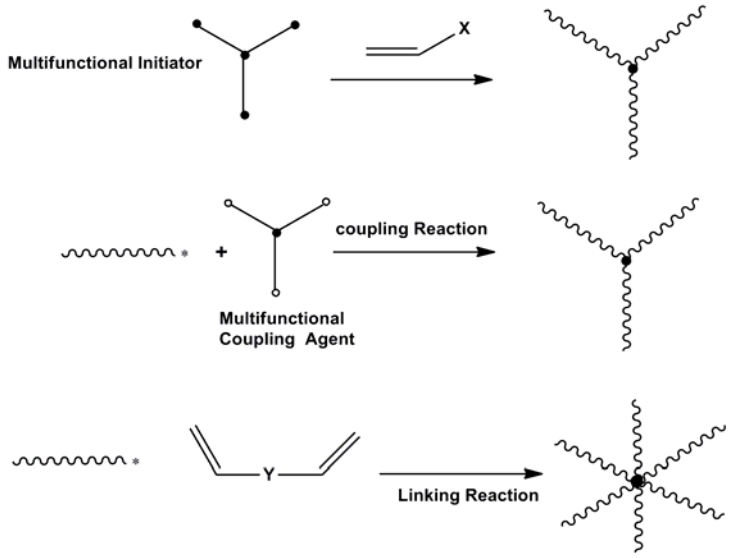
Miktoarm polymers are a relatively new and unique class of macromolecules and constitute a contemporary area of research due to their intriguing properties which can be tailored by varying their polymer arms. Much emphasis has been placed in the recent past in developing synthetic methodologies to these star polymers, and examining their self-assembly in solution. The different synthetic strategies to construct a variety of miktoarm star polymers are reported in the literature and each methodology strikes a balance between ease of synthesis and control over the final architecture[1].

5a.1.1. Star polymers

Star polymers consist of several linear polymer chains connected at one point[2]. Their compact structure and globular shape provide them with a set of unique properties, such as low solution viscosity, and the core shell architecture which enables several potential applications spanning a range from thermoplastic elastomers[3] to drug carriers[4]. Based on the chemical compositions of the arm species, star polymers can be classified into two categories: symmetric (or homoarm) star polymers or asymmetric (or heteroarm) star copolymers. Star polymers prepared by anionic polymerization were examined prior to the development of controlled radical polymerization (CRP)[1]. However, due to the limitations of ionic polymerization such as very stringent reaction conditions, purity and compatibility issue with some functional groups, the composition and functionality of the materials were limited. With the advent of CRP in the last two decades, star copolymers with different architectures could now be possible.

5a.1.1.1. Symmetric stars

Symmetric star polymers are branched polymers consisting of several identical linear chains linked to a central core. The synthesis of well-defined star polymers has been the subject of numerous studies to date[5]. Three general synthetic methods, as outlined in **Scheme 5a.1,** *viz.,* 1) multifunctional initiator approach 2) coupling reaction and 3) linking reaction have been developed.



Scheme 5a.1: General methods for synthesis of symmetric star polymers[1]

5a.1.1.2. Asymmetric stars

Miktoarm star copolymers (sometimes called asymmetric star polymers, heteroarm star polymers, or simply miktoarm polymers) are star-shaped polymers where any numbers of various types of polymer arms emanate from a core. These polymer arms should vary by chemical identity **(Figure 5a. 1).** Multiple protection/deprotection strategies, orthogonality, and combination of different polymerization methods are typically necessary for synthesis of these polymers, regardless of the specific type of desired miktoarm star copolymers (A_2B, A_2B_2, AB_2C_2, etc).

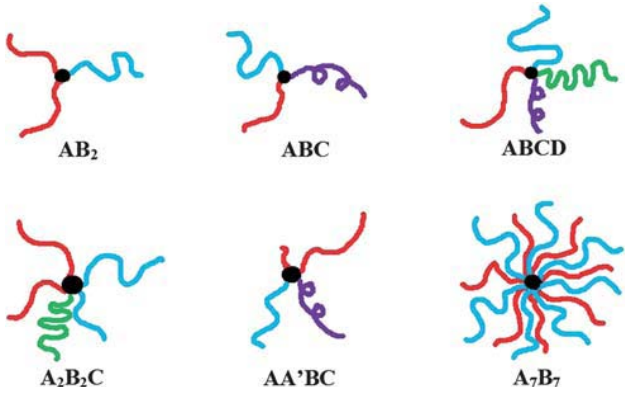


Figure 5a.1: Different types of miktoarm star copolymers[6]

Considerable advances in synthetic strategies, self-assembly and applications have recently occurred, making scientific community increasingly aware of the potential of miktoarm polymers.

Generally, five strategies have been reported in the literature to prepare miktoarm star copolymers.

1. Chlorosilane compounds.

2. Core-first approach

3. Arm-first approach

4. In-out method

5. Coupling method

These five strategies have been briefly discussed in **Chapter 1 Section 1.5.1**. Out of these five approaches, core first approach is studied in detail in the literature and is discussed below.

5a.1.1.2.1. Core-first method

In the core-first method or growing-from approach, a multifunctional initiator core (MFI) is used[7,8,9]. Multifunctional initiator cores (MFI)s are compounds capable of simultaneously initiating several polymerizations to form the arms of the star polymer, while the remaining moiety composes the core of the star. A MFI core has to fulfill the following requirements in order to produce well-defined star polymers with uniform arms, low molecular weight distribution and controllable molecular weights: (a) all the initiation sites must be equally reactive (b) the initiation rate must be higher than the propagation rate and c) the polymerization of different monomers by different mechanisms should be possible to be performed in sequence. In these cases, controlled radical polymerizations are frequently used. There are many examples throughout the literature where the ‘‘core-first’’ method is used as a synthetic strategy[10-12]. The first step in this methodology requires the synthesis of a MFI core, or simply a ‘‘core’’ containing orthogonal initiating sites. From this core, each arm is grown outwards through a combination of different polymerization techniques **(Figure 5a.2).**

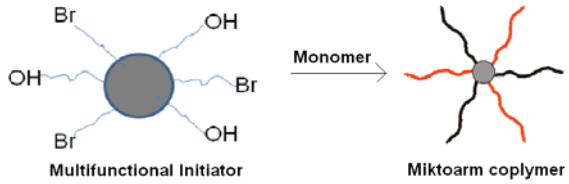
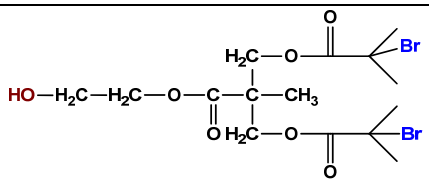
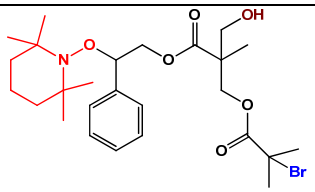
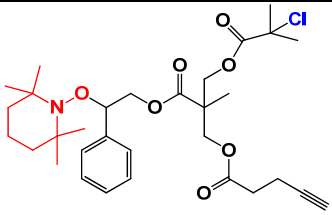
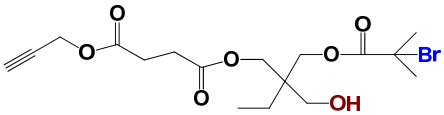
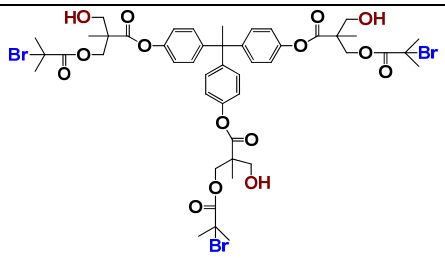
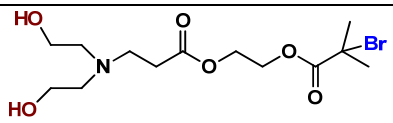
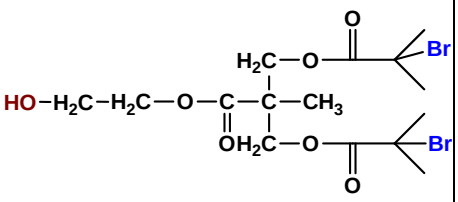
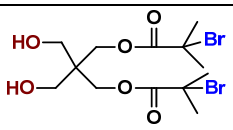
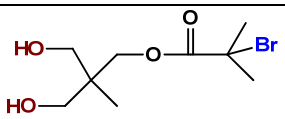
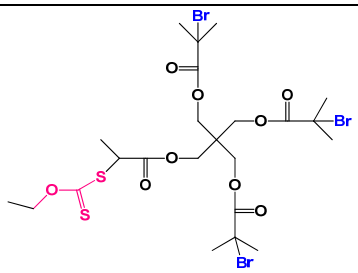
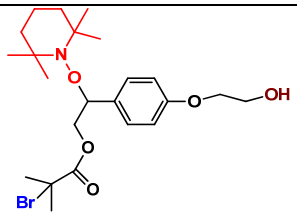


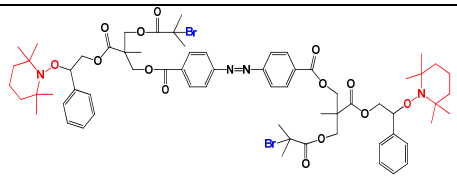
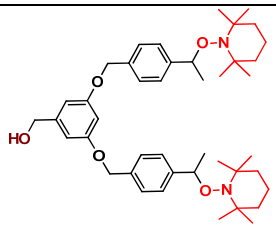
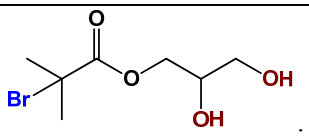
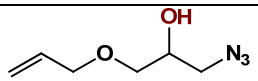
Figure 5a.2: General synthesis of a miktoarm polymer by the core-first approach

Because of the nature of the multifunctional initiator, the number of polymerization initiating sites on the core is the same as the number of polymeric arms on the final miktoarm star. For instance, a multifunctional core with two ATRP initiating sites and one ROP initiating site will yield an A_2B miktoarm star polymer. For example, a novel trifunctional initiator was proposed by Tunca et al[10] to produce a three-arm PCL-$(PtBuA)_2$. Different techniques such as ring-opening polymerization (ROP)[13] or a variety of controlled/ ‘‘living’’ radical polymerization (CRP)[14] techniques including atom transfer radical polymerization (ATRP)[15], nitroxide mediated polymerization (NMP)[16], reversible addition– fragmentation chain transfer (RAFT) polymerization[17], *etc* could be used. Because of the combination of different polymerization methods, it is easy to introduce a wide variety of monomers into the final polymeric structure. Also, orthogonality plays a key role in the design of the multifunctional initiator—a successful synthesis of miktoarm stars requires one to polymerize a single type of initiating site on the core while leaving the other sites intact, thus ensuring that each polymerization occurs as intended on the core. Thus, core could be designed according to the requirement. Symmetric star copolymers could be obtained by proper design and synthesis of the core having initiating sites which undergo initiation by same polymerization mechanism or core with different initiating sites could be designed and synthesized for its utilization in preparation of asymmetric or miktoarm star copolymers. Some literature examples of different types of MFI-cores utilized for synthesis of miktoarm copolymers are listed in **Table 5a.1.**

Table 5a.1: Representative examples of MFI-cores reported in literature for preparation of miktoarm copolymers

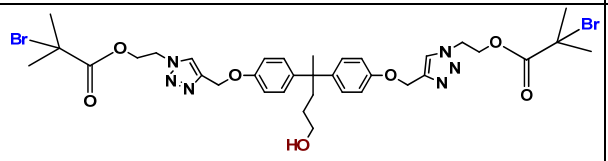
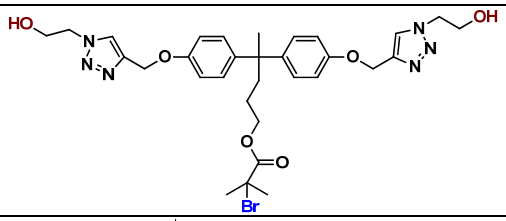
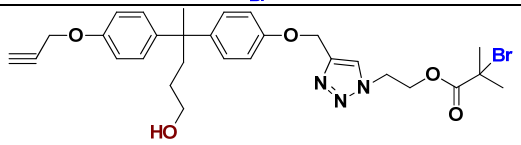
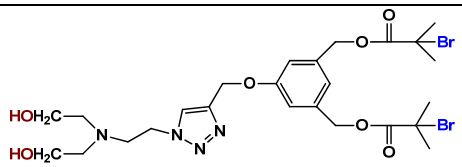
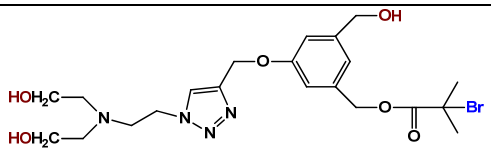
Sr. No.	Core Structure	Type of polymerization techniques	Miktoarm copolymers
1.		ROP, ATRP	AB_2-type (PCL)(PtBuA)$_2$[10]
2.		ROP, NMP, ATRP	ABC-type (PCL)(PS)(PtBuA)[11]
3.		NMP, ATRP, Alkyne homocoupling	A_2B_2-type (PS)$_2$(PMMA)$_2$
4.		ROP, ATRP, Click	ABC –type PCL-PDMA-PEG[12]
6.		ATRP, ROP	$(AB)_3$ –type (PMMA-PCL)$_3$[7]

Sr. No.	Core Structure	Type of polymerization techniques	Miktoarm copolymers
7.		ROP, ATRP	A_2B-type $(PCL)_2$-PDMA[18]
		ROP, ATRP	AB_2-type PCL-$(PDMA)_2$[18]
8.		ROP, ATRP	A_2B_2-type $(PCL)_2$-$(PS)_2$[19]
9.		ROP, ATRP	A_2B-type $(PCL)_2$-(PMMA)[20]
11.		SET-LRP, RAFT	A_3B-type $(PNIPAAM)_3$-PVK[21]
12.		ATRP, NMP, ROP	ABC-type (PMMA)-(PS)-PCL[9]

Sr. No.	Core Structure	Type of polymerization techniques	Miktoarm copolymers
13.		ATRP, NMP	A_2B_2-type $(PMMA)_2$-$(PS)_2$[22]
14.		ROP, NMP	AB_2-type (PCL)-$(PS)_2$[23]
15.		ATRP, ROP, ROP	ABC- type PS-PCL-PLLA[24]
16.		Thiol-ene click, ROP, Azide-alkyne click	ABC-type PS-PCL-PEG[25]

Although several multifunctional initiator cores are reported in the literature, there exists scope for design and synthesis of new multifunctional initiator cores possessing different types and varying number of initiating sites. In the present study, synthesis of five new multifunctional initiator cores (**Table 5a.2.)** based on two commercially available starting materials namely, 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxyisophthalic acid is described. Synthesis of MFI-cores was carried out using simple organic transformations and click chemistry. Consideration was given to the criteria discussed in **Section 5a.1.1.2.1** *viz* orthogonality of different initiating sites in the design of MFI- cores. **Table 5a.2** represents five different types of new MFI-cores synthesized.

Table 5a.2: MFI-cores synthesized in the present work

Sr. No.	MFI-Core	MFI-core Abbreviation	Type of polymerization techniques
1.		**AB_2-type OH-Ini-$(Br)_2$**	ROP, ATRP
2.		**A_2B-type $(OH)_2$-Ini-Br**	ROP, ATRP
3.		**ABC-type Br-Ini-(OH)-propargyl**	ROP, Azide-alkyne Click Chemistry, ATRP
4.		**A_2B_2-type $(OH)_2$-Ini-$(Br)_2$**	ROP, ATRP
5.		**A_3B-type $(OH)_3$-Ini-Br**	ROP, ATRP

5a.2. Experimental

5a.2.1. Materials

Synthesis of 2-azido ethanol, 2-azidoethyl 4-methylbenzenesulfonate, methyl 4, 4' –bis (4-hydroxyphenyl) pentanoate, and 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol, has been reported in **Chapter 3a.** 4, 4'-Bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate was synthesized as per the procedure reported in **Chapter 3b**. 2-Bromoisobutyryl bromide (98%),

N, N, N', N', N"-pentamethyldiethylenetriamine (PMDETA) (Aldrich, 99%), lithium aluminium hydride (LAH) and propargyl bromide were used as received. Triethyl amine (TEA) was distilled prior to the experiments. 2-Chloroethanol, sodium azide, cupric sulphate, sodium L(+) ascorbate, dichloromethane (DCM), tetrahydrofuran (THF), sodium sulphate, potassium hydroxide, sodium hydrogen carbonate, methanol and chloroform, all received from S.D. Fine-Chem. Ltd., India and were used as received.

5a.2.2. Characterization and measurements

FT-IR spectra were recorded on a Perkin-Elmer Spectrum *GX* spectrophotometer. NMR spectra were recorded on a Bruker 200 MHz spectrometer for ^{1}H-NMR and 125 MHz for ^{13}C-NMR measurements using $CDCl_3$, DMSO-d_6 and Acetone-d_6 as a solvent.

5a.3. Synthesis

5a.3.1. Synthesis of trifunctional initiator core

5a.3.1.1. Synthesis of AB_2-type trifunctional initiator core-OH-Ini-$(Br)_2$

5a.3.1.1.1. Synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol

4, 4'–Bis (4-(propargyloxy) phenyl) pentan-1-ol was synthesized as described in **Chapter 3a, Section 3a.3.3**

5a.3.1.1.2. Synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2-azidoethanol (5.0 g, 58 mmol), triethylamine (5.25 g, 58 mmol), and dry chloroform (50 mL). The reaction mixture was cooled to 0 °C. The solution of 2-bromoisobutyryl bromide (13.2 g, 58 mmol) in dry chloroform (20 mL) was added dropwise into the reaction mixture under stirring at 0 °C over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and then stirred overnight. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and water (3 x 100 mL).The organic layer was dried over anhydrous sodium sulfate, filtered and ethyl acetate was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 12.25 g (90 %) of 2-azidoethyl 2-bromo-2-methylpropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 2110, 1730

^1H NMR ($CDCl_3$, δ/ppm): 4.21 (t, 2H, OCH_2), 3.39 (t, 2H, NCH_2), 1.92 (s, 6H, $2(CH_3)$)

5a.3.1.1.3. Synthesis of AB_2-type trifunctional initiator core OH -Ini-$(Br)_2$

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol (1.75 g, 5 mmol), 2-azidoethyl 2-bromo-2-methylpropanoate (2.35 g, 10 mmol) and acetonitrile: *tert*-butanol: water (3:1:1 v/v) (50 mL). The reaction mixture was stirred for 20 minutes. Cupric sulphate (125 mg, 0.5 mmol), and sodium L(+) ascorbate (99 mg, 0.5 mmol) were added to the reaction mixture with constant stirring. The reaction mxture was refluxed overnight. The reaction mixture was allowed to cool to room temperature and dichloromethane (25 mL) was added to the reaction mixture. Organic layer was repeatedly washed with saturated solution of sodium salt of EDTA to remove copper residue. The solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum to afford 3.35 g (82 %) of MFI-core OH-Init-$(Br)_2$

IR ($CHCl_3$, cm^{-1}): 3200, 1730

^1H NMR ($CDCl_3$, δ/ppm): 8.10 (s, 2H, triazole ring protons), 7.13 (d, 4H, Ar-H *meta* to ether linkage), 6.91 (d, 4H, Ar-H *ortho* to ether linkage), 5.12 (s, 4H, $OCH_2C{=}C$), 4.78 (t, 4H, OCH_2 CH_2) 4.61 (t, 4H, CH_2CH_2N), 4.33 (bs, 1H, -OH), 3.48 (t, 2H, $-CH_2OH$), 2.15-2.08 (m, 2H, $-CH_2$), 1.84 (s, 12H, $2(CH_3)_2$), 1.56 (s, 3H, CH_3), 1.36-1.27 (m, 2H, $-CH_2$)

5a.3.1.2. Synthesis of A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br

5a.3.1.2.1. Synthesis of 2-azidoethanol

2-Azidoethanol was synthesized as reported in **Chapter 3a, Section 3a.2.1. 1.1**

5a.3.1.2.2. Synthesis of 4, 4'-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-

2-methylpropanoate

4, 4'-Bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate was synthesized as reported in **Chapter 3b, Section 3b.3.3**

5a.3.1.2.3. Synthesis of A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2-azidoethanol (0.87 g, 10 mmol), 4, 4'-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate (2.48 g, 5 mmol) and acetonitrile: *tert*-butanol: water (3:1:1 v/v) (50 mL). The reaction mixture was stirred for 20 minutes. Cupric sulphate (125 mg, 0.5 mmol) and sodium L(+) ascorbate (99 mg, 0.5 mmol) were added to the reaction mixture with constant stirring. The reaction mxture was refluxed overnight. The reaction mixture was allowed to cool to room temperature and dichloromethane (25 mL) was added to the reaction mixture. The organic layer was repeatedly washed with saturated solution of sodium salt of EDTA to remove copper residue. The solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum to afford 2.88 g (86 %) of MFI-core $(OH)_2$-Init-Br

IR ($CHCl_3$, cm^{-1}): 3200, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 8.04 (s, 2H, triazole ring protons), 7.15 (d, 4H, Ar-H *meta* to ether linkage), 6.95 (d, 4H, Ar-H *ortho* to ether linkage), 5.12 (s, 4H, $OCH_2C{=}C$), 4.50-3.97 (m, 12H OCH_2 and alcoholic protons), 2.27-2.19 (m, 2H, $-CH_2$), 1.91 (s, 6H, $(CH_3)_2$), 1.60 (s, 3H, CH_3), 1.56- 1.47 (m, 2H, $-CH_2$)

5a.3.1.3. Synthesis of ABC-type trifunctional initiator core-(OH)-Ini-Br-propargyloxy

5a.3.1.3.1. Synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol

4, 4'–Bis (4-(propargyloxy) phenyl) pentan-1-ol was synthesized as reported in **Chapter 3a, Section 3a.3.3.**

5a.3.1.3.2. Synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate

2-Azidoethyl 2-bromo-2-methylpropanoate was synthesized as reported in **Section 5a.3.1.1.2.**

5a.3.1.3.3. Synthesis of ABC-type trifunctional initiator core Br-Ini-(OH)-propargyloxy

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol (1.75 g, 5 mmol), 2-azidoethyl 2-bromo-2-methylpropanoate (1.17 g, 5 mmol) and acetonitrile: *tert*-butanol: water (3:1:1 v/v) (50 mL). The reaction mixture was stirred for 20 minutes. Cupric sulphate (125 mg, 0.5 mmol) and sodium L(+) ascorbate (99 mg, 0.5 mmol) were added to the reaction mixture with constant

stirring. The reaction mxture was refluxed overnight. The reaction mixture was allowed to cool to room temperature and dichloromethane (25 mL) was added to the reaction mixture. The organic layer was repeatedly washed with saturated solution of sodium salt of EDTA to remove copper residue. The solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum to afford 2.18 g (75%) of MFI-core.Br-Init-(OH)-propargyl

IR ($CHCl_3$, cm^{-1}): 3200, 2123, 1730.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.77 (s, 1H, triazole ring protons), 7.10 (d, 4H, Ar-H *meta* to ether linkage), 6.86 (d, 4H, Ar-H *ortho* to ether linkage), 5.18 (s, 2H, OCH_2C=C), 4.65 (m, 4H, OCH_2), 4.56 (m, 2H, -CH_2N), 3.49 (s, 2H, -CH_2OH), 2.51(t, 1H, -CH_2), 2.39-2.27 (m, 2H, CH_2CH_2), 2.16-2.09 (m, 2H, CH_2CH_2), 1.86 (s, 6H, $(CH_3)_2$), 1.60 (s, 3H, CH_3).

5a.3.2. Synthesis of tetra functional initiator core

5a.3.2.1. Synthesis of A_2B_2 - type tetra functional initiator core $(OH)_2$-Ini-$(Br)_2$

5a.3.2.1.1. Synthesis of (5-(prop-2-yn-1-yloxy)-1, 3-phenylene) bis(methylene)bis(2-bromo-2-methylpropanoate)

5a.3.2.1.1.1. Synthesis of dimethyl-5-hydroxyisophthalate

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, 5-hydroxyisophthalic acid (10.0 g, 55 mmol), and methanol (300 mL). The reaction mixture was stirred for 15 minutes, followed by addition of concentrated sulphuric acid (1 mL). The reaction mixture was refluxed for 8 h. Methanol was removed under reduced pressure and ethyl acetate (300 mL) was added to the reaction mixture. The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL) and water (3 x 50 mL). The organic layer was separated, dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (50:50, v/v) as eluent to afford 10.97 g (95 %) of dimethyl-5-hydroxyisophthalate as a light yellow solid.

^{1}H NMR (Acetone-d6 δ/ppm): 8.04 (s, 1H, Ar-H *para* to phenolic OH), 7.64 (d, 2H, Ar-H *ortho* to phenolic OH), 3.88 (s, 6H, OCH_3)

5a.3.2.1.1.2. Synthesis of dimethyl-5-(prop-2-yn-1-yloxy) isophthalate

Into a 500 mL two necked round-bottom flask equipped with a reflux condenser were charged, dimethyl-5-hydroxyisophthalate (8.10 g, 40 mmol), K_2CO_3 (6.80 g, 50 mmol) and dry acetone (150 mL) and the reaction mixture was stirred for 10 minutes. The solution of propargyl bromide (5.90 g, 50 mmol) in acetone (50 mL) was added over a period of 30 minutes. The reaction mixture was refluxed for 8 h, cooled and filtered. Acetone was evaporated under reduced pressure and the reaction mixture was diluted with ethyl acetate (150 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL) and water (2 x 50 mL). The organic layer was separated, dried over sodium sulfate, filtered and evaporated. The crude product was purified by column chromatography using ethyl acetate:pet ether (20:80, v/v) to yield 8.82 g (89 %) of dimethyl-5-(prop-2-yn-1-yloxy) isophthalate as a white solid.

IR ($CHCl_3$, cm^{-1}): 2123, 1730.

^{1}H NMR ($CDCl_3$, δ/ppm): 8.28 (s, 1H, Ar-H *para* to ether linkage,), 7.79 (d, 2H, Ar-H *ortho* to ether linkage), 4.76 (d, 4H, O-CH_2), 3.91 (s, 6H, OCH_3), 2.50 (t, 2H, acetylene proton)

5a.3.2.1.1.3. Synthesis of (5-(prop-2-yn-1-yloxy)1, 3-phenylene) dimethanol

Into a 250 mL two necked round-bottom flask equipped with a reflux condenser and a dropping funnel were charged, LAH (2.60 g, 70 mmol) and dry THF (100 mL). The solution of dimethyl-5-(prop-2-yn-1-yloxy) isophthalate (4.0 g, 14 mmol) in dry THF (40 mL) was added over a period of 30 minutes. Effervences were observed during the addition. Reaction mixture was refluxed for 8 h, cooled and then moist sodium sulfate was added to deactivate LAH. The reaction mixture was filtered and THF was evaporated. The precipitate was dissolved in dilute HCl (25 mL) and the solution was extracted with ethyl acetate (3 x 50 mL). The ethyl acetate solution was washed with saturated brine solution (3 x 50 mL), sodium bicarbonate solution (3 x 50 mL) and water (2 x 50 mL). The organic layer was separated, dried over sodium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate:pet ether (40:60, v/v) to afford 2.15 g (80 %) of 5-(prop-2-yn-1-yloxy)1, 3-phenylene dimethanol as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2123.

^{1}H NMR (Acetone-d6, δ/ppm): 6.98 (s, 1H, Ar-H *para* to ether linkage,), 6.91 (d, 2H, Ar-H *ortho* to ether linkage), 4.78 (d, 2H, O-CH_2), 4.62 (d, 4H, O-CH_2), 4.06 (br, 2H, OH), 3.07 (t, 2H, acetylene proton)

5a.3.2.1.1.4. Synthesis of (5-(prop-2-yn-1-yloxy)-1, 3-phenylene) bis(methylene)bis(2-bromo-2-methylpropanoate)

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, (5-(prop-2-yn-1-yloxy) 1, 3-phenylene) dimethanol (3.84 g, 20 mmol), triethylamine (3.64 g, 40 mmol), and dry chloroform (50 mL). The reaction mixture was cooled to 0 °C in an ice salt bath. The solution of 2-bromoisobutyryl bromide (9.16 g, 40 mmol) in dry chloroform (20 mL) was added dropwise into the reaction mixture under stirring at 0 °C over a period of 30 minutes. The reaction mixture was stirred at 0 °C for 2 h, allowed to attain room temperature and then stirred overnight. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and water (3 x 100 mL). The organic layer was separated, dried over anhydrous sodium sulfate, filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 8.9 g (91 %) of (5-(prop-2-yn-1-yloxy)-1, 3-phenylene) bis(methylene)bis(2-bromo-2-methylpropanoate) as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 2123, 1730

^{1}H NMR ($CDCl_3$, δ/ppm): 8.28 (s, 1H, Ar-H *para* to ether linkage,), 7.79 (d, 2H, Ar-H *ortho* to ether linkage), 4.76 (d, 4H, O-CH_2), 3.91 (s, 6H, OCH_3), 2.50 (t, 2H, acetylene proton), 1.92 (s, 12H,-2 $(CH_3)_2$).

5a.3.2.1.1.5. Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2, 2'-azanediyldiethanol (2.1 g, 20 mmol) and dry THF (70 mL). The reaction mixture was stirred for 15 minutes. The solution of 2-azidoethyl 4-methylbenzenesulfonate (2.41 g, 10 mmol) in THF (50 mL) was added drop-wise under constant stirring at room temperature. The reaction mixture was heated at 80 °C for 8 h. The reaction mixture was cooled to room temperature. THF was removed to get thick solution which was dissolved in water (100 ml) and then extracted with dichloromethane (500 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate: pet ether (10:90, v/v) as

eluent. The removal of solvent yielded 1.13 (65%) of 2, 2'-((2-azidoethyl) azanediyl) diethanol as a light brown liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2110.

^1H NMR ($CDCl_3$, δ/ppm): 3.60 (t, 4H, CH_2OH), 3.38 (t, 2H, CH_2N_3), 2.96 (bs, 2H, OH), 2.75-2.65 (m, 6H, CH_2N).

5a.3.2.1.1.6. Synthesis of A_2B_2-type tetrafunctional initiator-$(OH)_2$-Ini-$(Br)_2$

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2,2'-((2-azidoethyl)azanediyl)diethanol (1.74 g, 10 mmol), 4, 4'-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate (4.9 g, 10 mmol) and mixture of acetonitrile: *tert*-butanol: water (3:1:1 v/v) (50 mL). The reaction mixture was stirred for 20 minutes. Cupric sulphate (250 mg, 1 mmol) and sodium L (+) ascorbate (200 mg, 1 mmol) were added to the reaction mixture with constant stirring. The reaction mxture was heated at 80 °C for 8 h, allowed to cool to room temperature and then dichloromethane (25 mL) was added to the reaction mixture. Dicholoromethane layer was repeatedly washed with saturated solution of sodium salt of EDTA to remove copper residue. The dichloromethane solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum to afford 5.5 g (83%) of MFI-core $(OH)_2$-Init-$(Br)_2$.

IR ($CHCl_3$, cm^{-1}): 3200, 1715

^1H NMR ($CDCl_3$, δ/ppm): 7.84 (s, 1H, triazole ring proton), 6.94 (s, 3H, Ar-H), 5.20 (s, 2H, -CH_2N), 5.16 (s, 4H, -CH_2OCO), 4.45 (s, 4H, -$OCH_2C{=}C$), 3.72-3.66 (bs, CH_2OH 4H), 3.42 (bs, 2H, NCH_2 , 3.01 (bs, 2H, OH), 2.66 (bs, 4H, $(NCH_2(CH_2OH))_2$), 1.94 (s, 12H, 2 $(CH_3)_2$).

5a.3.2.2. Synthesis of A_3B-type tetra functional initiator core $(OH)_3$-Ini-Br

5a.3.2.2.1. Synthesis of (3-hydroxymethyl)-5-(prop-2-yn1-ynyloxy) benzyl 2-bromo-2-methylpropanoate

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, (5-(prop-2-yn-1-yloxy) 1, 3-phenylene) dimethanol (3.84 g, 20 mmol), triethylamine (1.82 g, 20 mmol), and dry chloroform (50 mL). The reaction mixture was cooled to 0 °C. The solution of 2-bromoisobutyryl bromide (4.60 g, 20 mmol) in dry chloroform (20 mL) was added drop wise into the reaction mixture under stirring at 0 °C over a period of 30 minutes. The

reaction mixture was stirred at 0 °C for 2 h. The reaction mixture was allowed to attain room temperature and then stirred overnight. The reaction mixture was washed with 5% aqueous $NaHCO_3$ solution (3 x 100 mL) and water (3 x 100 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate:pet ether (25:75, v/v) as eluent. The removal of the solvent yielded 4.75 g (70%) of (3-hydroxymethyl)-5-(prop-2-yn1-ynyloxy) benzyl 2-bromo-2-methylpropanoate as a pale yellow liquid.

IR ($CHCl_3$, cm^{-1}): 3200, 2123, 1730.

^1H NMR ($CDCl_3$, δ/ppm): 8.28 (s, 1H, Ar-H *para* to ether linkage,), 7.79 (d, 2H, Ar-H *ortho* to ether linkage), 5.19 (d, 2H, O-CH_2), 4.70 (d, 4H, OCH_2), 2.50 (t, 2H, acetylene proton), 1.96 (s, 6H, - $(CH_3)_2$)

5a.3.2.2.2. Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol

Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol was carried out as reported in **Section 5a.3.2.1.1.5.**

5a.3.2.2.3. Synthesis of A_3B-type tetrafunctional initiator-$(OH)_3$-Ini-Br

Into a 250 mL two necked round-bottom flask equipped with a dropping funnel were charged, 2,2'-((2-azidoethyl)azanediyl)diethanol (1.75 g, 10 mmol), (3-hydroxymethyl)-5-(prop-2-yn1-ynyloxy) benzyl 2-bromo-2-methylpropanoate (3.41 g, 10 mmol) and a mixture of acetonitrile: *tert*-butanol: water (3:1:1 v/v) (50 mL). The reaction mixture was stirred for 20 minutes. Cupric sulphate (250 mg, 1 mmol) and sodium L(+) ascorbate (200 mg, 1 mmol) were added to the reaction mixture with constant stirring. The reaction mxture was heated at 80 °C for 8 h. The reaction mixture was allowed to cool at room temperature and then dichloromethane (25 mL) was added to the reaction mixture. Organic layer was repeatedly washed with saturated solution of sodium salt of EDTA to remove copper residue. The dichloromethane solution was dried over anhydrous sodium sulfate, filtered and solvent was evaporated under vacuum to afford 4.0 g (79 %) of MFI-core $(OH)_3$-Ini-Br.

IR ($CHCl_3$, cm^{-1}): 3200, 1715,

^1H NMR ($CDCl_3$, δ/ppm): 7.81 (s, 1H, triazole ring proton), 6.96 (s, 1H, Ar-H), 6.88 (s, 2H, Ar-H) 5.21 (s, 2H, -OCH_2), 5.12 (s, 2H, -OCH_2), 4.59 (s, 2H, -OCH_2), 4.39 (t, 2H, -NCH_2), 3.34 (m,

7H, OCH_2+-NCH_2) 3.42 (bs, 4H), 2.93 (bs, 2H, -OH protons), 2.58 (t, 4H, -NCH_2), 1.94 (s, 6H, (-$CH_3)_2$).

5a.4. Results and Discussion

5a.4.1. Synthesis of trifunctional initiator Core

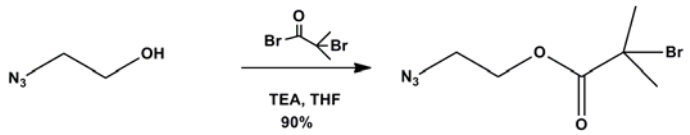
5a.4.1.1. Synthesis of AB_2-type trifunctional initiator OH-Ini-$(Br)_2$

5a.4.1.1.1. Synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol

The synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol has been described in **Chapter 3a, Section 3a.4.3**

5a.4.1.1.2. Synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate

Scheme 5a.2 depicts the route for synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate. The esterification reaction of 2-azidoethanol with 2-bromoisobutyryl bromide yielded the desired 2-azidoethyl 2-bromo-2-methylpropanoate which was purified by silica column chromatography and was characterized using FTIR, ^{1}H NMR spectroscopy.



Scheme 5a.2: Synthesis of 2-azidoethyl 2-bromo 2-methylpropaonate

FT-IR spectrum of 2-azidoethyl 2-bromo-2-methylpropanoate exhibited absorption bands at 2110 and 1730 cm^{-1} which correspond to azido group and asymmetric stretching of carbonyl of ester, respectively. In ^{1}H-NMR spectrum **(Figure 5a.3)**, singlet at 1.92 ppm could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

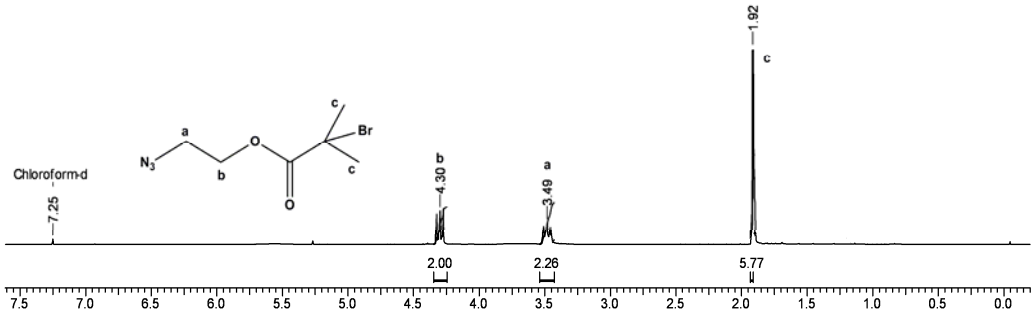
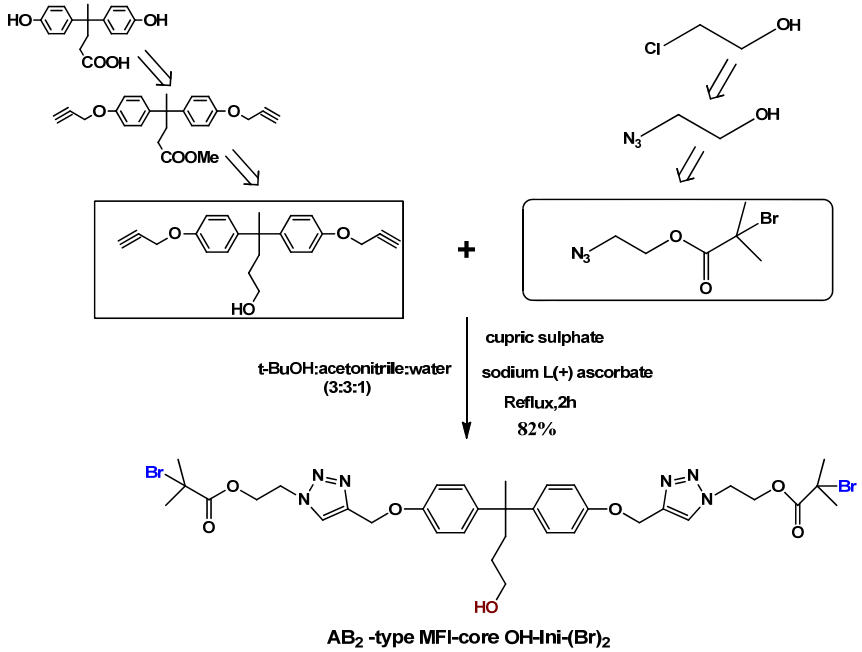


Figure 5a.3: ^{1}H-NMR spectrum of 2-azidoethyl 2-bromo 2-methylpropaonate in $CDCl_3$

5a.4.1.1.3. Synthesis of trifunctional initiator core OH-Ini-(Br)$_2$

Scheme 5a.3 depicts the route for synthesis of trifunctional initiator core OH-Init-(Br)$_2$ using click chemistry. Click reaction between bis-propargyloxy functionalized alcohol, namely, 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol, and 2-azidoethyl 2-bromo 2-methylpropaonate was performed in the mixture of acetonitrile; *tert*-butanol: water (3:1:1, v/v) in the presence of cupric sulphate and sodium L(+) ascorbate as a catalyst system to afford trifunctional initiator core OH-Ini-(Br)$_2$.



Scheme 5a.3: Synthesis of AB$_2$-type trifunctional initiator core OH-Ini-(Br)$_2$

In FT-IR spectrum of AB_2-type trifunctional initiator core OH-Ini-$(Br)_2$ the peaks corresponding to alkyne group and an azide groups disappeared, while retaining characteristic peaks of alcohol and ester at 3200 and 1730 cm^{-1}, respectively indicating the completion of ‘‘click’’ reaction. ^{1}H-NMR spectrum of trifunctional initiator (**Figure 5a.4**) exhibited characteristic resonance of triazole ring proton at 8.10 ppm. The singlet appeared at 1.84 ppm for twelve protons could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

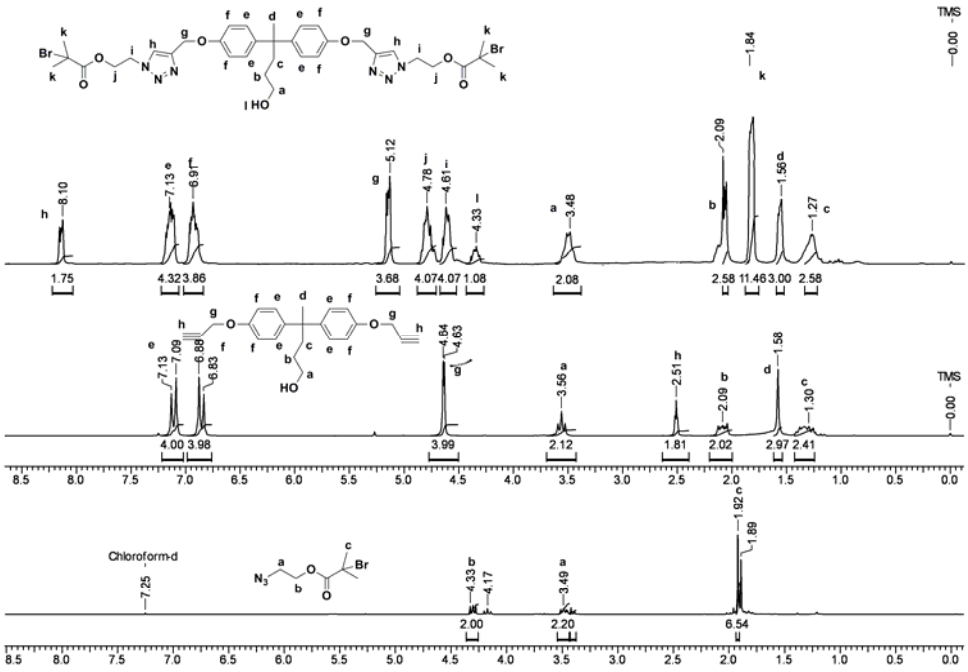


Figure 5a. 4: ^{1}H-NMR spectra of A) 2-azidoethyl 2-bromo-2-methylpropanoate B) 4, 4’–bis (4-(propargyloxy) phenyl) pentan-1-ol C) trifunctional initiator core OH-Ini-$(Br)_2$ in $CDCl_3$

5a.4.1.2. Synthesis of A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br

5a.4.1.2.1. Synthesis of 4, 4’-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

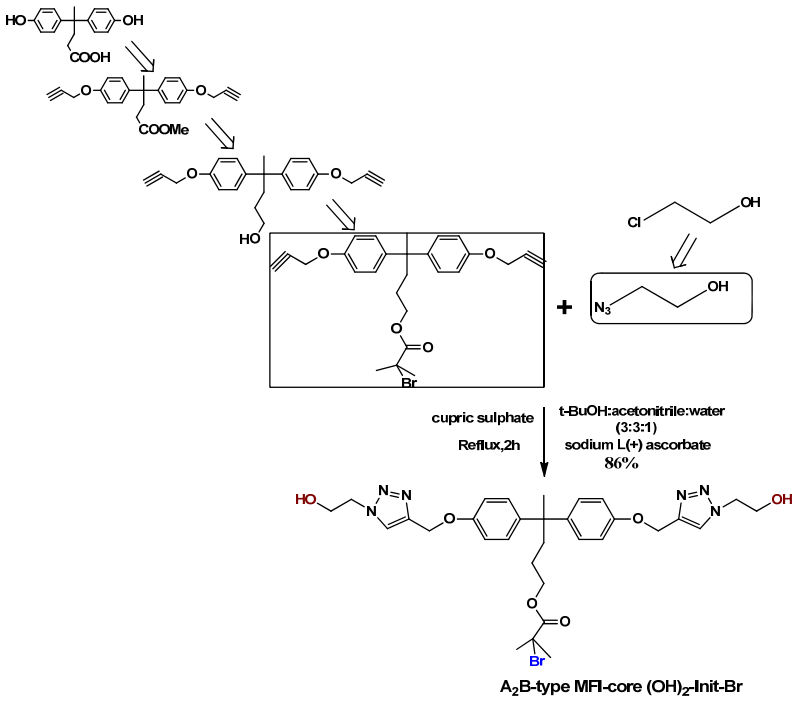
The synthesis of 4, 4’-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate has been described in **Chapter 3b, Section 3b.4.1**.

5a.4.1.2.2. Synthesis of 2-azidoethanol

The synthesis of 2-azidoethanol has been described in **Chapter 3a**, **Section 3a.2.1. 1.1**

5a.4.1.2.3. Synthesis of trifunctional initiator core $(OH)_2$-Ini-Br

Scheme 5a.4 depicts the route for synthesis of trifunctional initiator core $(OH)_2$-Init-Br using click chemistry. Click reaction between bis-propargyloxy functionalized ATRP initiator, namely, 4, 4'-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate and 2-azidoethanol was performed in acetonitrile: *tert*-butanol: water (3:1:1, v/v) in the presence of cupric sulphate and sodium L(+) ascorbate as a catalyst system to afford trifunctional initiator $(OH)_2$-Init-Br. In FT-IR spectrum of A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br the peaks corresponding to alkyne group and an azide groups disappeared, while retaining characteristic peaks of alcohol and ester at 3200 and 1730 cm^{-1}, respectively indicating the completion of ''click'' reaction.



Scheme 5a.4: Synthesis of A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br

^{1}H-NMR spectrum of trifunctional initiator core (**Figure 5a.5**) revealed characteristic resonance of triazole ring proton at 8.04 ppm, the singlet appeared at 1.91 ppm for six protons could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

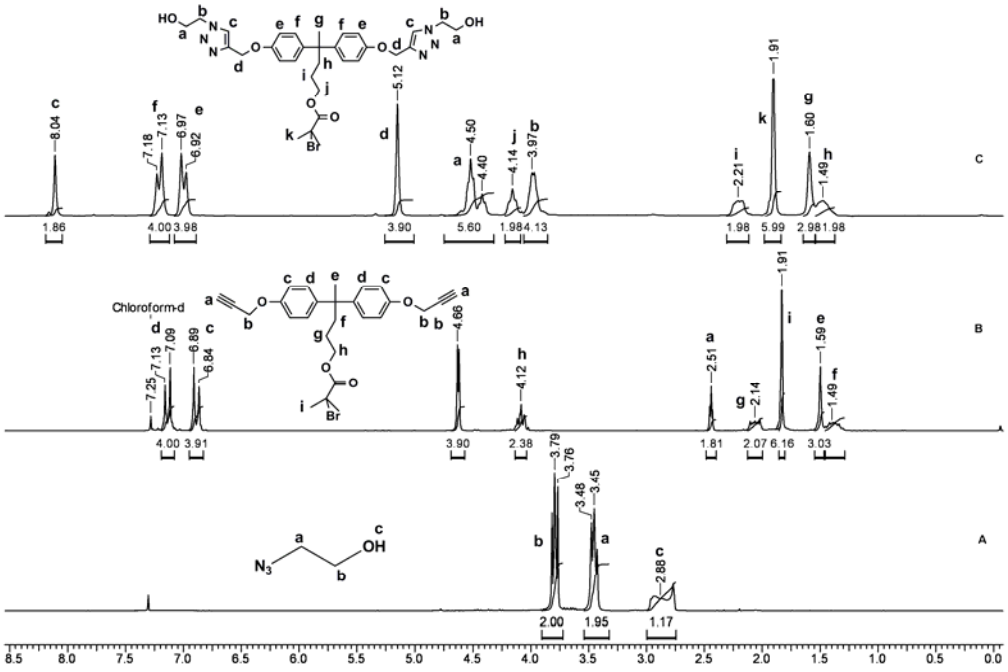


Figure 5a. 5: ^{1}H-NMR spectra of A) azidoethanol B) 4, 4'-bis (4-(propargyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate C) trifunctional initiator core $(OH)_2$-Ini-Br in $CDCl_3$

5a.4.1.3. Synthesis of ABC-type trifunctional initiator core (OH)-Ini-(Br)-propargyloxy

5a.4.1.3.1. Synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol

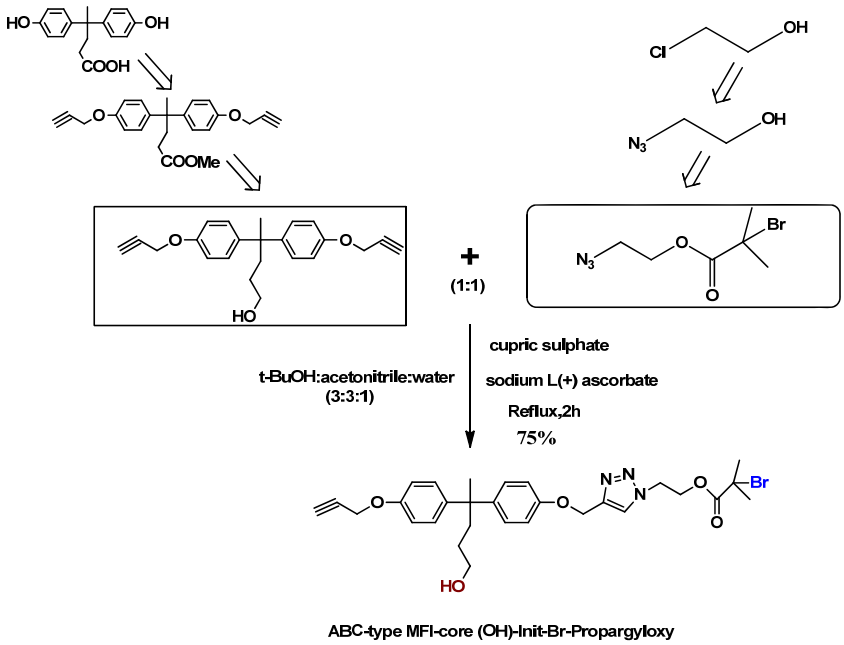
The synthesis of 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol has been described in **Chapter 3a Section 3a.3.3**

5a.4.1.3.2. Synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate

The synthesis of 2-azidoethyl 2-bromo-2-methylpropanoate has been described in **section 5a.4.1.1.2.**

5a.4.1.3.3. Synthesis of trifunctional initiator core Br-Ini-(OH)-propargyloxy

As shown in **Scheme 5a. 5,** click reaction between bis-propargyloxy functionalized alcohol, namely, 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol and 1 equivalent of 2-azidoethyl 2-bromo-2-methylpropanoate was performed in acetonitrile : tert-butanol: water (3:3:1, v/v) in the presence of cupric sulphate and sodium L(+) ascorbate as a catalyst system to afford trifunctional initiator Br-Ini-(OH)-propargyloxy.



Scheme 5a.5: Synthesis of ABC-type trifunctional initiator core Br-Ini-(OH)-propargyloxy

In order to minimize the formation of di- substituted compound, addition of 2-azidoethyl 2-bromo-2-methylpropanoate was carried out slowly. However, the crude reaction product was found to be a mixture of desired mono product and minor amount of di-substituted compound. Column chromatography was found to be essential for seperation of mono substituted product. In FT-IR spectrum of ABC-type trifunctional initiator core Br-Ini-(OH)-Propargyl, the peak corresponding to an azide group disappeared, while retaining characteristic peaks of alcohol and ester at 3200 and 1730 cm^{-1}, respectively. ^{1}H-NMR spectrum **(Figure 5a.6)** showed characteristic resonance of triazole ring proton at 7.77 ppm. The presence of propargyloxy functionality was confirmed by the presence of a triplet at 2.51 ppm. The singlet appeared at 1.86 ppm for six protons could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

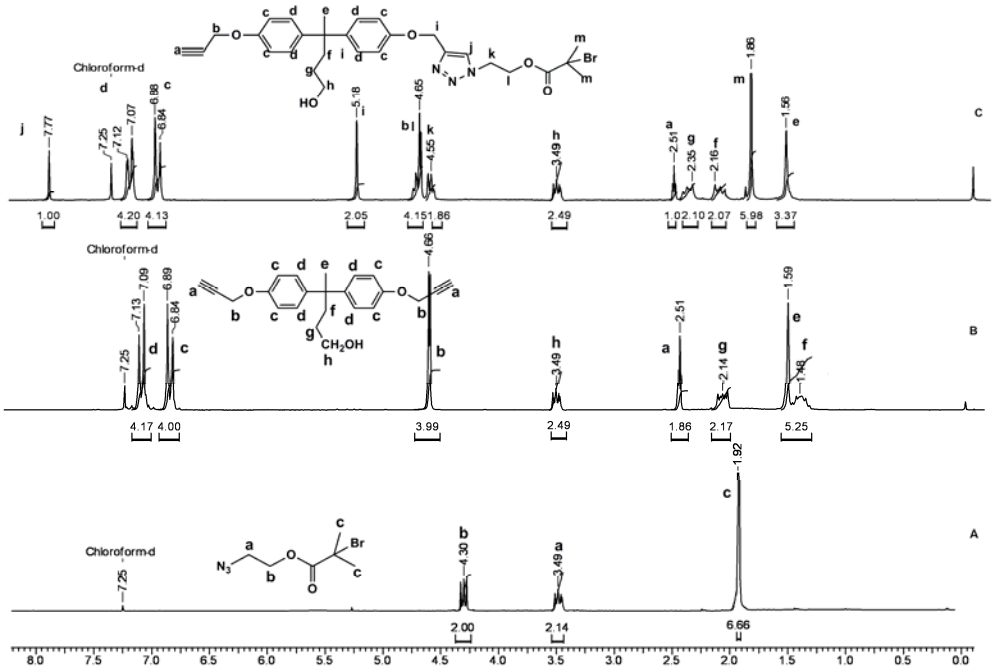


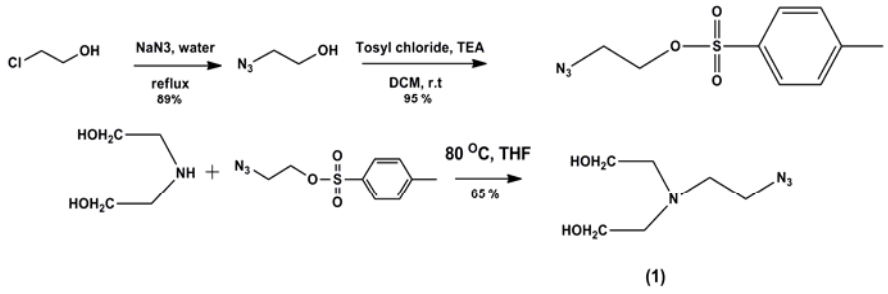
Figure 5a. 6: ^{1}H-NMR spectra of A) 2-azidoethyl 2-bromo-2-methylpropanoate B) 4, 4'–bis (4-(propargyloxy) phenyl) pentan-1-ol C) trifunctional initiator core Br-Ini-(OH)-propargyloxy in $CDCl_3$

5a.4.2. Synthesis of tetrafunctional initiator

5a.4.2.1. Synthesis of A_2B_2 –type tetrafunctional initiator $(OH)_2$-Ini-$(Br)_2$

5a.4.2.1.1. Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol

Scheme 5a. 6 depicts the route for synthesis of 2, 2'-((2-azidoethyl)azanediyl) diethanol, which involved three steps. In the first step, 2-chloroethanol was converted into 2-azidoethanol by nucleophilic substitution reaction with sodium azide.



Scheme 5a. 6: Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol

Further, 2-azidoethyl 4-methylbenzenesulfonate was prepared from 2-azidoethanol by carrying out reaction with *p*-toluene sulphonyl chloride in dichloromethane at room temperature. The product was purified by silica gel column chromatography. In the third step, 2-azidoethyl 4-methylbenzenesulfonate was coupled with 2, 2'azanediyldiethanol in THF at 80 °C. The product was purified by silica gel column chromatography and was characterized using FT-IR, ^{1}H-NMR spectroscopy. FT-IR spectrum of 2, 2'-((2-azidoethyl) azanediyl) diethanol showed absorption band at 3200 cm^{-1} which corresponds to asymmetric stretching of alcohol functionality and a characteristic peak at 2110 cm^{-1} corresponding to asymmetric stretching of azido functionality, respectively. In ^{1}H-NMR spectrum **(Figure 5a.7),** the triplet appeared at 3.60 ppm could be attributed to methylene protons attached to alcohol group while triplet appeared at 3.38 ppm could be accredited to methylene protons attached to azido functional group. The spectral data corresponding to other protons was in good agreement with the proposed structure.

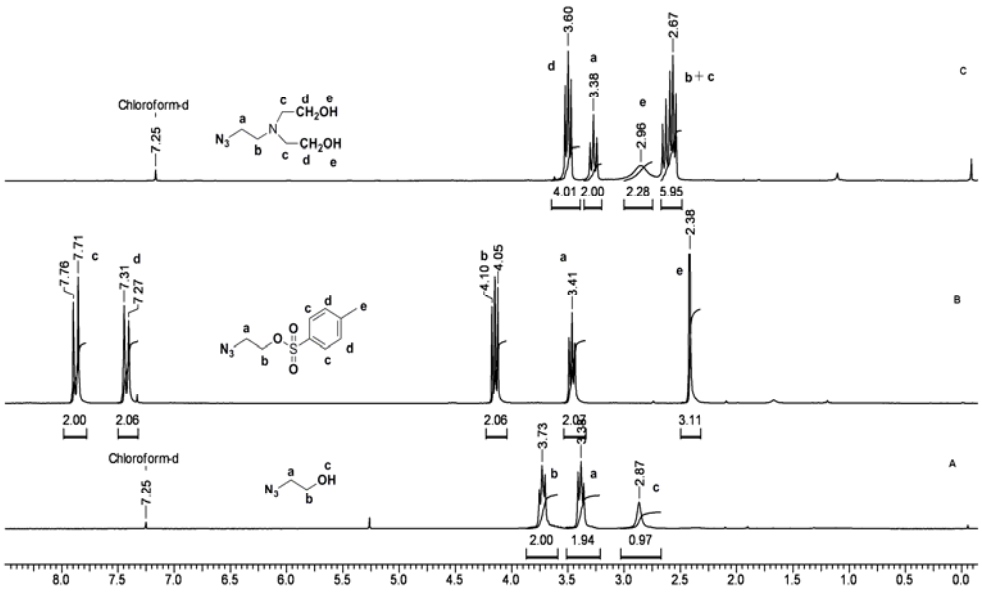
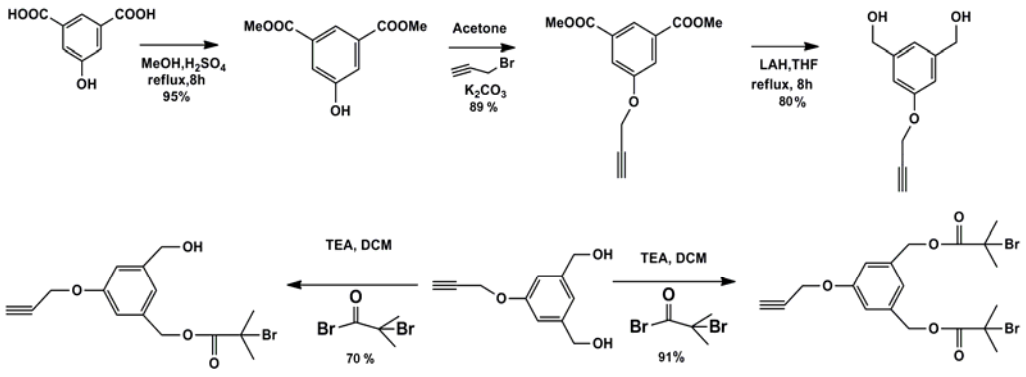


Figure 5a. 7: ^{1}H-NMR spectra of A) 2-azidoethanol B) 2-azidoethyl 4-methylbenzenesulfonate C) 2, 2'-((2-azidoethyl) azanediyl) diethanol in $CDCl_3$

***5a.4.2.1.2. Synthesis of* (5-(prop-2-yn-1-yloxy)-1,3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate)**

The synthesis of (5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate) was carried out in four steps starting from commercially available 5-hydroxyisophthalic acid as outlined in **Scheme 5a.7**.



Scheme 5a. 7: Synthesis of 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate) and (3-hydroxymethyl)-5-(prop-2-yn1-ynyloxy) benzyl 2-bromo-2-methylpropanoate

5-Hydroxyisophthalic acid was esterified using methanol in the presence of a catalytic amount of concentrated sulphuric acid to yield dimethyl 5-hydroxyisophthalate. The dimethyl ester was subjected to propargylation to obtain dimethyl 5-(prop-2-yn1-yloxy) isophthalate which on LAH reduction yielded 5-(prop-2-yn1-yloxy)-1, 3,-phenylene) dimethanol. The esterification of 5-(prop-2-yn1-yloxy)-1, 3,-phenylene) dimethanol with 2-bromoisobutyryl bromide yielded the desired (5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate). (5-(Prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate) and the intermediates involved in its synthesis were purified by silica gel column chromatography and were characterized using FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopy.

FT-IR spectrum of 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate) displayed absorption band at 2323 cm^{-1} which corresponds to asymmetric stretching of propargyloxy functionality and a peak at 1725 cm^{-1} which corresponds to asymmetric stretching of carbonyl of ester functionality, respectively.

In ^{1}H-NMR spectrum of 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis(2-bromo-2-methylpropanoate) (**Figure 5a.8**), aromatic protons appeared as a multiplet in the range 6.94-6.90 ppm. The methylne protons flanked between ester group and aromatic ring displayed a peak at 5.12 ppm while the methylene protons attached to aromatic ring and acetylene group appeared at 4.64 ppm. The presence of propargyloxy functionality was confirmed by the appearance of a triplet at 2.46 ppm. The singlet appeared at 1.89 ppm for twelve protons could be attributed to protons corresponding to methyl group of halo ester.

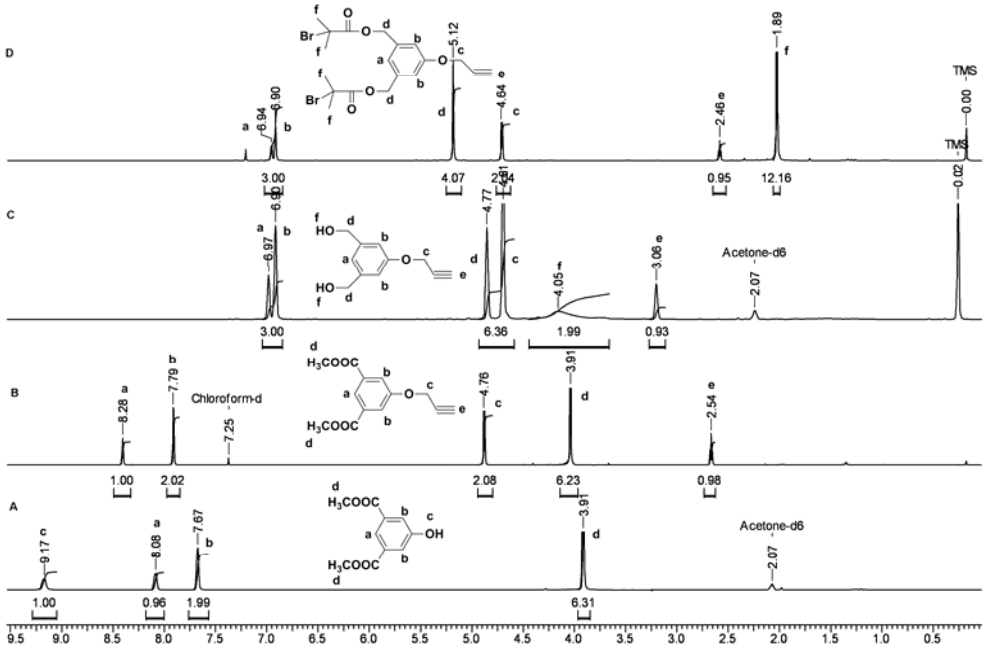
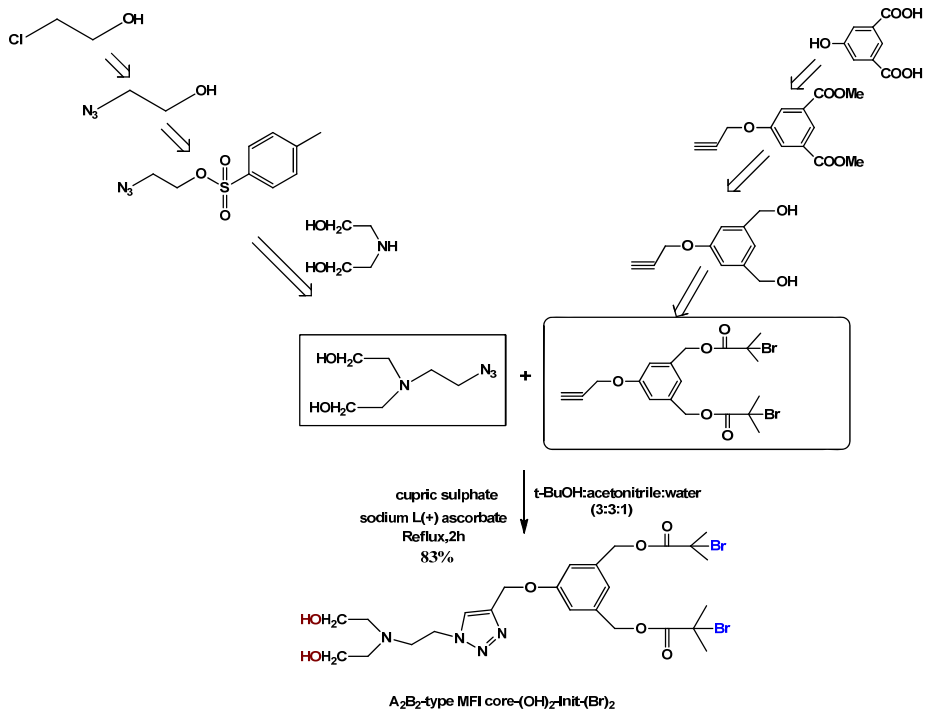


Figure 5a. 8: ^{1}H-NMR spectra of A) dimethyl 5-hydroxyisophthalate B) dimethyl 5-(prop-2-yn-1-yloxy)isophthalate C) 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)dimethanol D) 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)bis(methylene)bis (2-bromo-2-methylpropanoate) in $CDCl_3$

5a.4.2.1.3. Synthesis of A_2B_2-type tetrafunctional initiator core-$(OH)_2$-Ini-$(Br)_2$

The click reaction between 5-(prop-2-yn-1-yloxy)-1, 3-phenylene) bis (methylene)bis(2-bromo-2- methyl propanoate) and 2, 2'-((2-azidoethyl) azanediyl) diethanol was performed in acetonitrile: *tert*-butanol: water (3:1:1) in the presence of cupric sulphate and sodium L(+) ascorbate as a catalyst system to obtain tetrafunctional initiator $(OH)_2$-Ini-$(Br)_2$ (**Scheme 5a. 8).**



Scheme 5a. 8: Synthesis of A_2B_2–type multifunctional core $(OH)_2$-Ini-$(Br)_2$

Click reaction product was characterized by FT-IR and ^{1}H-NMR spectra. In FT-IR spectrum of A_2B_2-type tetrafunctional initiator core $(OH)_2$-Ini-$(Br)_2$ the peaks corresponding to alkyne group and an azide groups disappeared, while retaining characteristic peaks of alcohol and ester at 3200 and 1725 cm^{-1}, respectively.

^{1}H-NMR spectrum (**Figure. 5a.9**) exhibited characteristic resonance of triazole ring proton at 7.84 ppm, the singlet appeared at 1.94 ppm for twelve protons could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

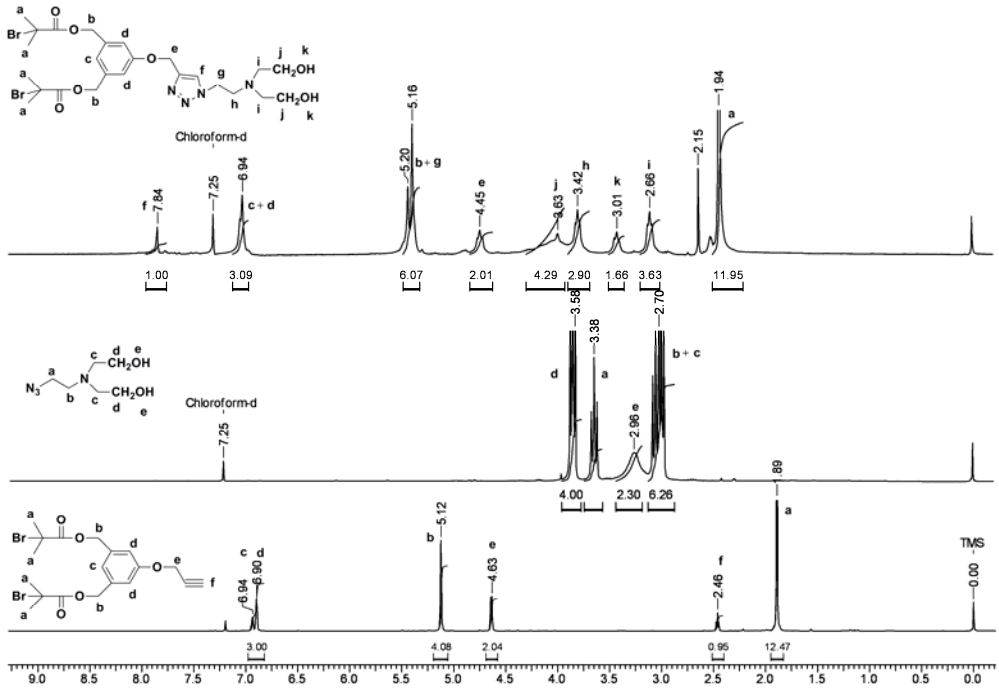


Figure 5a. 9: ^{1}H-NMR spectra of A) 5-(prop-2-yn-1-yloxy)-1, 3-phenylene) bis(methylene)bis(2-bromo-2-methylpropanoate)

B) 2, 2'-((2-azidoethyl) azanediyl) diethanol

C) tetrafunctional initiator A_2B_2-type core $(Br)_2$-Ini-$(OH)_2$ in $CDCl_3$

5a.4.2.2. Synthesis of A_3B-type tetrafunctional initiator-$(OH)_3$-Ini-Br

5a.4.2.2.1. Synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol

The synthesis of 2, 2'-((2-azidoethyl) azanediyl) diethanol has been described in **Section 5a.4.2.1.1.**

5a.4.2.2.2. Synthesis of 3-(hydroxymethyl)-5-(prop-2-yn-1-yloxy) benzyl 2-bromo-2-methylpropanoate

As shown in **Scheme 5a.7** synthesis of 3-(hydroxymethyl)-5-(prop-2-yn-1-yloxy)benzyl 2-bromo-2-methylpropanoate was carried out by esterification reaction of 5-(prop-2-yn1-yloxy)-1,3,-phenylene) dimethanol with 1 equivalent of 2-bromoisobutyryl bromide. 3-(Hydroxymethyl)-5-(prop-2-yn-1-yloxy) benzyl 2-bromo-2-methylpropanoate was purified by silica gel column chromatography and was characterized using FT-IR and ^{1}H-NMR spectroscopy. In ^{1}H-NMR spectrum, (**Figure 5a.10**), aromatic protons were observed at 7.0-6.93 ppm, while the

methylene protons attached to ester group appeared at 5.19. The methylene protons attached to –OH group and the methylene protons of propargyloxy functionality observed together in the range 4.71-4.69 ppm. The presence of propargyloxy functionality was confirmed by the appearance of a triplet at 2.53 ppm. The singlet appeared at 1.96 ppm for six protons could be attributed to methyl group of halo ester.

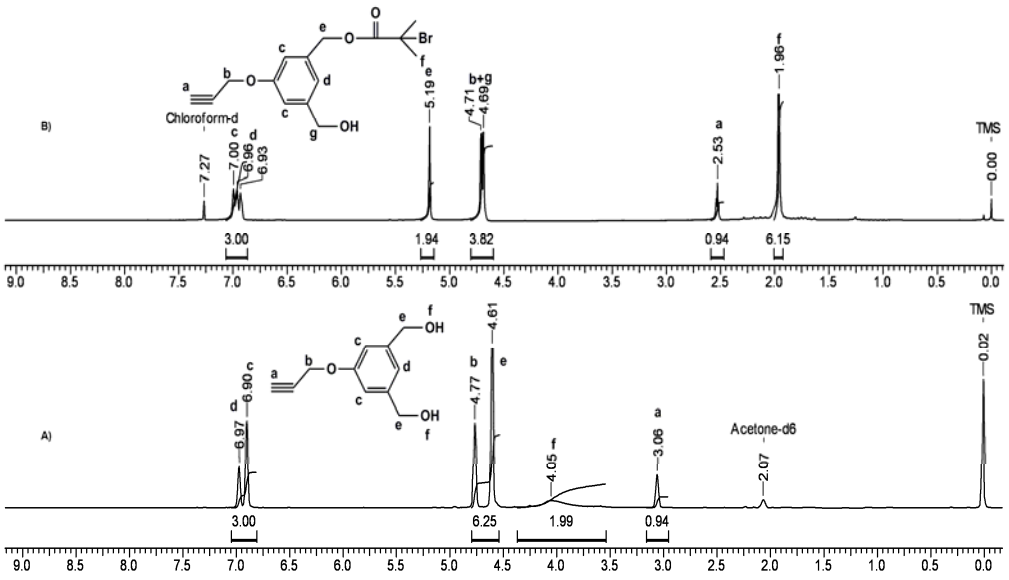
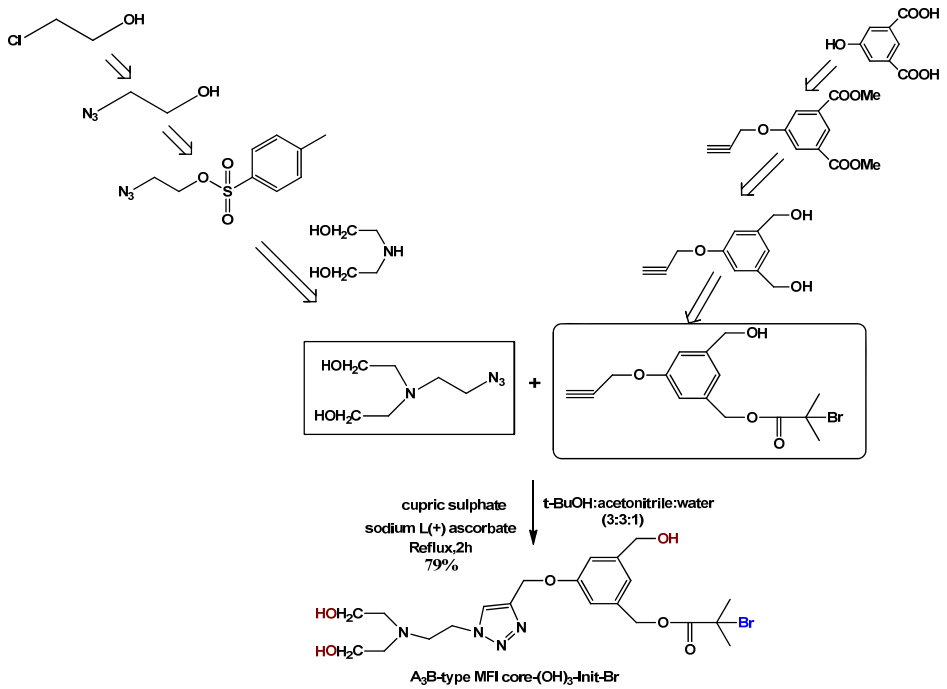


Figure 5a. 10: ^{1}H-NMR spectra of A) 5-(prop-2-yn-1-yloxy)-1, 3-phenylene)dimethanol B) 3- (hydroxymethyl)-5-(prop-2-yn-1-yloxy)benzyl 2-bromo-2-methylpropanoate in $CDCl_3$

5a.4.2.2.3. Synthesis of A_3B-type tetrafunctional initiator core $(OH)_3$-Ini-Br

As shown in **Scheme 5a. 9,** click reaction between 3-(hydroxymethyl)-5-(prop-2-yn-1-yloxy) benzyl 2-bromo-2-methylpropanoate and 2, 2'-((2-azidoethyl) azanediyl) diethanol was performed in acetonitrile: *tert*-butanol: water (3:1:1) in the presence of cupric sulphate and sodium L(+) ascorbate as a catalyst system to afford tetrafunctional initiator core $(OH)_3$-Ini-Br.



Scheme 5a. 9: Synthesis of A_3B-type tetra functional core $(OH)_3$-Ini-Br

In FT-IR spectrum of A_3B-type tetrafunctional initiator core $(OH)_3$-Ini-Br the peaks corresponding to alkyne group and an azide group disappeared, while retaining peaks of alcohol at 3150 cm^{-1} and carbonyl of ester at 1725 cm^{-1}, respectively indicating the completion of ''click'' reaction. ^{1}H-NMR spectrum of tetra functional A_3B-type $(OH)_3$-Ini-Br initiator core (**Figure. 5a.11**) exhibited characteristic resonance of triazole ring proton at 7.81 ppm, the singlet appeared at 1.93 ppm for six protons could be attributed to protons corresponding to methyl group of halo ester. The spectral data corresponding to other protons was in good agreement with the proposed structure.

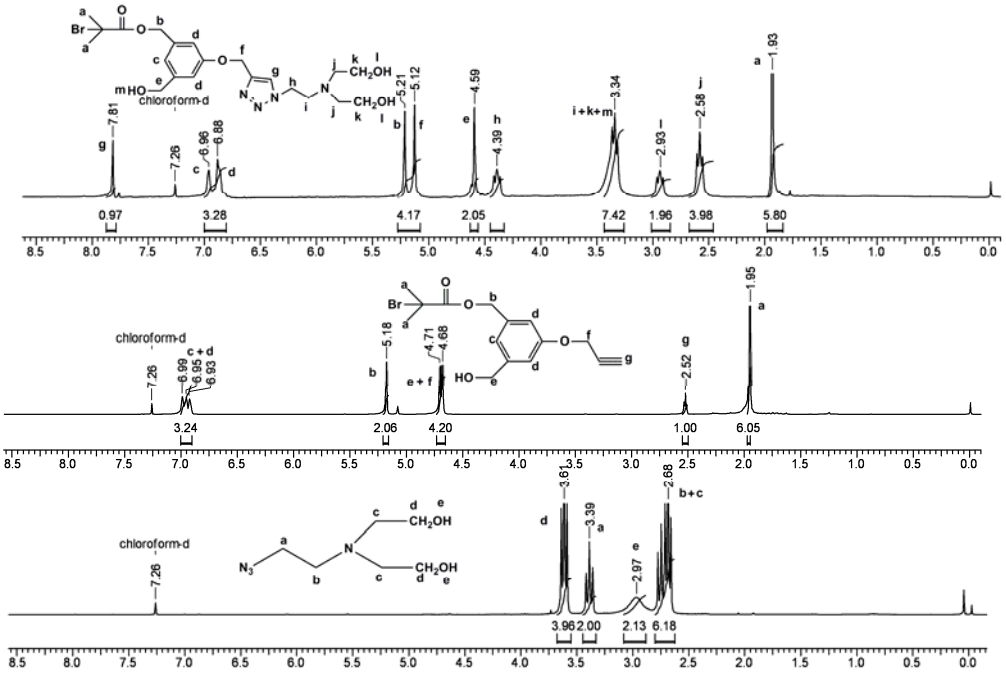


Figure 5a. 11: ^{1}H-NMR spectra of A) 2, 2'-((2-azidoethyl) azanediyl) diethanol B) 3-(hydroxymethyl)-5-(prop-2-yn-1-yloxy) benzyl 2-bromo-2-methylpropanoate C) tetrafunctional A_3B-type initiator core $(OH)_3$-Ini-Br in $CDCl_3$

5a.5. Conclusions

- ✓ The following five new multifunctional initiator (MFI)-cores featuring different types and specific number of initiating sites were synthesized using combination of simple organic transformations and click chemistry starting from two commercially available materials, 4,4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid.

  i) AB_2-type trifunctional initiator OH-Ini-$(Br)_2$

  ii) A_2B-type trifunctional initiator $(OH)_2$-Ini-Br

  iii) ABC-type trifunctional initiator Br-Ini- (OH)-Propargyl

  iv) A_2B_2-type tetrafunctional initiator $(OH)_2$-Ini-$(Br)_2$

  v) A_3B-type tetrafunctional initiator $(OH)_3$-Ini-Br

- ✓ These MFI-cores are potentially useful for preparation of miktoarm copolymers using techniques such as ROP, ATRP and click chemistry.

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Chapter 5b

Mikto-arm Copolymers:

Synthesis and Characterization

5b.1. Introduction

Miktoarm star polymers (sometimes called asymmetric star polymers, heteroarm star polymers, or simply miktoarm polymers) are star-shaped polymers composed of different number of various types of polymer arms emanating from a core[1] **(Figure 5b.1)**. The term mikto is derived from the Greek word mikto μικτος, meaning mixed.

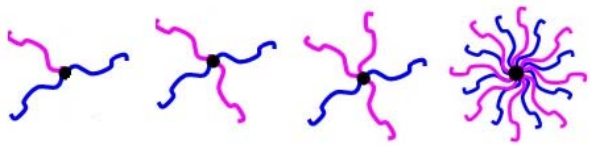


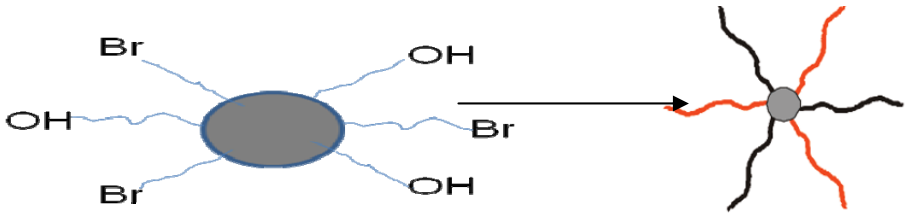
Figure 5b.1: Representative examples of miktoarm copolymers

These polymer arms should vary by chemical identity. Miktoarm copolymers are a relatively new and unique class of macromolecules, and constitute a contemporary area of research due to their intriguing properties which can be tailored by varying their polymer arms[1]. Much emphasis has been placed in the recent past in developing synthetic methodologies to these star polymers, and examining their self-assembly in solution. Miktoarm star polymers are a synthetically challenging class of polymers. Multiple protection/deprotection strategies, orthogonality, and combination of different polymerization methods are typically necessary for the synthesis of these polymers, regardless of the specific type of desired miktoarm star polymer (A_2B, ABC, AB_2C_2, etc.)[1]. Considerable advances in synthetic strategies, self-assembly and applications have recently occurred, making scientific community increasingly aware of the potential of miktoarm polymers[1]. Various approaches such as coupling of chlorosilane compounds with reactive chain ends of prepolymers, core-first method, arm-first method, in-out method, and coupling method could be used to prepare miktoarm copolymers out of which, core-first and coupling method approach have been studied by several research groups[2-4].

5b.1.1.Core-first approach

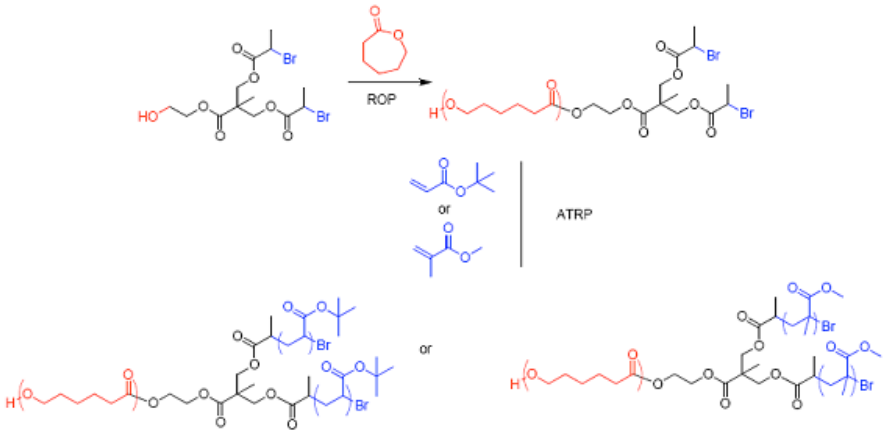
There are many examples throughout the literature where the ‘‘core-first’’ method is used as a synthetic strategy for preparation of miktoarm copolymers[5-7]. The first step in this methodology requires the synthesis of a multifunctional initiator (MFI), also called a ‘‘multifunctional core,’’ or simply a ‘‘core’’ containing orthogonal initiating sites. From this core, each arm is grown outwards through a combination of different polymerization techniques (**Scheme 5b.1**), such as living anionic polymerization[8], ring-opening polymerization (ROP)[9], or a variety of controlled/ ‘‘living’’ radical polymerization (CRP)[10] techniques including atom transfer radical polymerization (ATRP)[11], nitroxide mediated polymerization (NMP)[12], reversible

addition– fragmentation chain transfer (RAFT) polymerization[13], etc. Because of the combination of different polymerization methods, it is easy to introduce a wide variety of monomers into the final polymeric structure.



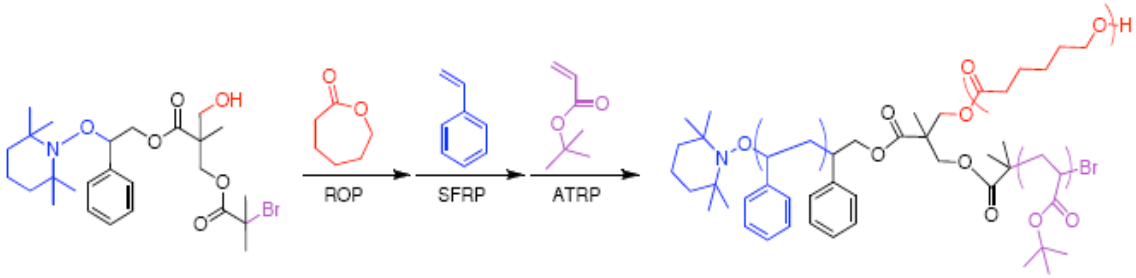
Scheme 5b.1: General synthetic representation of a miktoarm polymer by the ''core-first''method

Also, orthogonality plays a key role in the design of the multifunctional initiator—a successful synthesis of miktoarm stars requires polymerization from single type of initiating site on the core while leaving the other sites intact, thus ensuring that each polymerization occurs as intended on the core. Because of this nature of the multifunctional initiator, the number of polymerization initiating sites on the core is the same as the number of polymeric arms on the final miktoarm star. For instance, a multifunctional core with two ATRP initiating sites and one ROP initiating site will yield an A_2B miktoarm star polymer. Using the "core-first" method, Tunca and coworkers[14] built an AB_2 miktoarm star polymer, in which the first step was the synthesis of a multifunctional initiator designed for sequential ROP and ATRP (**Scheme 5b.2**). Furthermore, the core was used for ROP of ε-caprolactone through the alcohol to generate a polymer functionalized with two bromine end groups. These sites were polymerized *via* ATRP using either *tert*-butyl acrylate or methyl methacrylate to create two different types of AB_2-type miktoarm star polymers. Other types of polymers can be built in a similar manner.



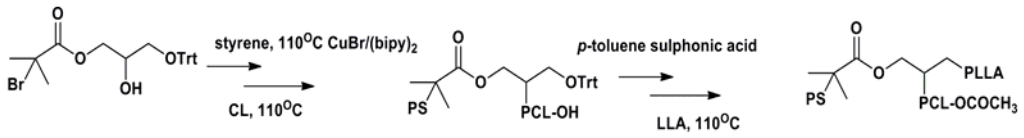
Scheme 5b.2: AB_2 miktoarm star polymer made with the "core-first" method by sequential ROP and ATRP[1]

Though the synthesis of ABC miktoarm stars requires a greater deal of sophistication in the synthetic strategy, this can still be easily accomplished using the "core-first" method. Hizal and coworkers[15] synthesized a multifunctional initiator with three different initiating sites for ATRP, ROP, and stable free-radical polymerization (SFRP) to create an ABC miktoarm star polymer where each polymerization step does not require end-group modification for subsequent polymerization reactions **(Scheme 5b.3)**. Because of the variety of polymerization methods and their accompanying choice of monomers, it is easy to see why the "core-first" technique is a versatile and efficient synthetic strategy[16, 17]. A simple substitution of one monomer for another can lead to a library of ABC-type miktoarm stars. For instance, ROP of ε-caprolactone could just as easily be replaced with the ROP of glycolic acid or lactide to create different miktoarm stars.



Scheme 5b.3: Synthesis of ABC miktoarm star polymer made with the ''core-first'' method by three different polymerization methods[1]

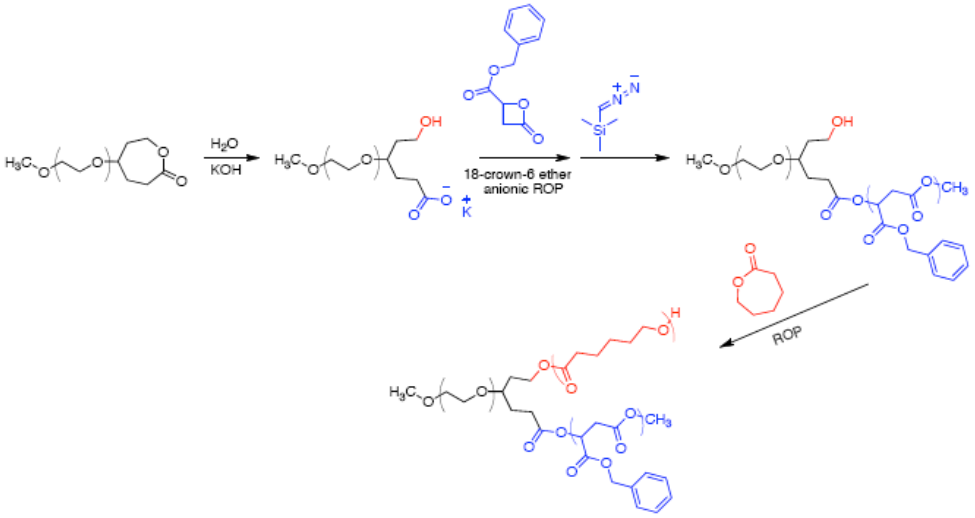
Variations to the "core-first" strategy have become prevalent throughout the literature. For example, it is possible to employ two ROP and one ATRP from a multifunctional initiator to create an ABC miktoarm star provided that protection/deprotection strategies are used[18]. In this regard, a core compound composed of one bromide chain-end and two alcohols—one protected with a triphenylmethyl group and the other deprotected was prepared **(Scheme 5b.4).**



Scheme 5b.4: Strategy for the synthesis of ABC miktoarm copolymer from the heterotrifunctional initiator

ROP of the deprotected alcohol using ε-caprolactone as monomer followed by ATRP with styrene yielded a diblock copolymer. Because the final step involved is ROP, it was necessary to functionalize the chain-end of the PCL arm with a protecting group in order to avoid subsequent ROP reactions on both the PCL chain-end as well as the third alcohol. Finally, acidic conditions were employed to deprotect the alcohol at the core so that subsequent ROP with L-lactide could occur, yielding an ABC miktoarm star composed of PS, PLLA, and PCL.

Another more commonly seen variation of the "core-first" strategy involves functionalization of the chain-end of a polymer arm, sometimes called the linear macroinitiator. The functional group at the chain end contains multiple types of initiating sites, thus serving as a branching point for successive polymerization reactions, and eventually yielding the final miktoarm star. This variation of "core-first" approach is an attractive strategy because the synthesis of a core designed to polymerize *n* arms is replaced by the synthesis of a chain-end functionalized polymer which allows the growth of *n-1* arms[19, 20]. Jérôme and coworkers[21] used this strategy (**Scheme 5b.5**). to create a novel, fully-biocompatible ABC-type miktoarm star with poly ethylene glycol, poly ε-caprolactone, and poly benzyl ß-malolactonate arms.



Scheme 5b.5: Synthesis of ABC miktoarm star by functionalization of a linear macroinitiator (PEG) followed by successive ring opening polymerizations[1]

5b.1.2. Coupling method

Coupling methods have become very widespread for the synthesis of miktoarm polymers in the past decade due to facile synthetic methodologies that have become available, and as they retain the overall integrity of the final structure[22-24]. This method is highlighted by coupling of the reactive end of at least one polymer arm to a multifunctional core using highly efficient and orthogonal reactions. The remaining arms on a miktoarm polymer are typically grown using CRP methods, and often by ROP, living anionic polymerization, etc. The popularity of the coupling methods can partially be attributed to the rising popularity of "click" chemistry in macromolecular synthesis[25, 26]. "Click" reactions are characterized by many features that lend themselves to macromolecular synthesis, such as simple reactions conditions, orthogonality to a variety of functional groups, simple workups, relatively simple purifications, insensitivity to different solvents, and high yields. Many different "click" reactions have been used to this end,

such as thiol-ene[27] and Diels-Alder[28]. The most popular reaction, the so-called "cream of the crop" is the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of an azide to an alkyne to yield a 1,2,3-triazole ring[29, 30] (**Figure 5b.2**). This specific "click" reaction has widespread use throughout the synthesis of miktoarm polymers through a coupling strategy. One of the examples of the coupling technique was reported by Tunca and coworkers[31].

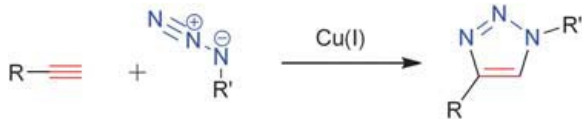
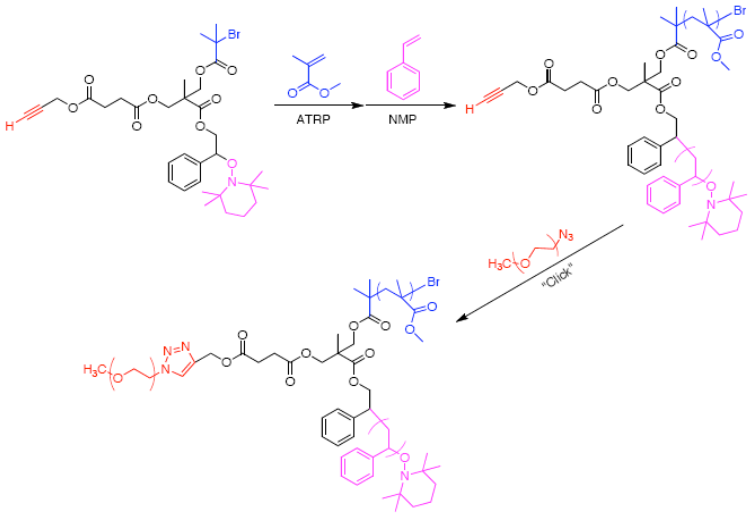


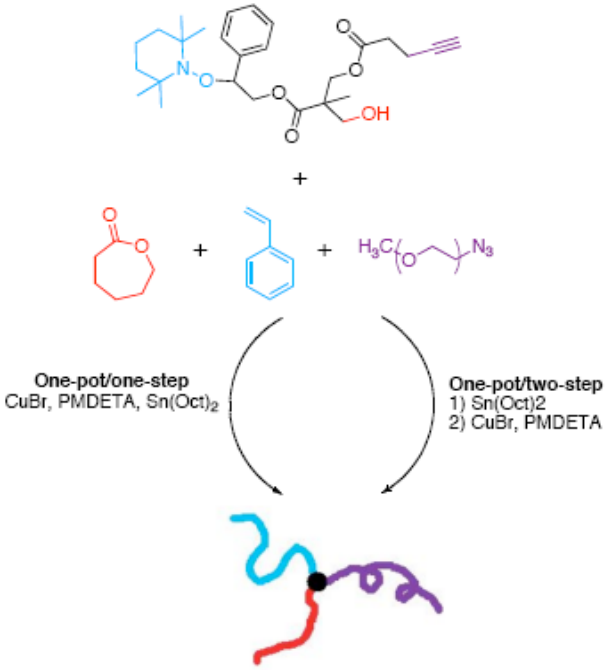
Figure 5b.2: The azide–alkyne Huisgen cycloaddition, a 1,3-dipolar cycloaddition which yields a 1,2,3-triazole ring[1]

In their study, ATRP and NMP were used to polymerize PMMA and PS, respectively from a trifunctional core, leaving a block copolymer with an alkyne as the only remaining functionality which is located at the junction. Subsequent "click" reaction with either azide-terminated PEG or P*t*-BA yielded an ABC-type miktoarm star polymer (**Scheme 5b.6**). In considering the fact that these two polymers were made by coupling two different azide-terminated polymers to a block copolymer precursor, these results suggest that a "click" reaction can efficiently couple a variety of azide-terminated polymers to a block copolymer scaffold to create a miktoarm star polymer. It was demonstrated that the azide-alkyne "click" reaction can efficiently couple the chain-end of a polymer to the congested core of a block copolymer. Furthermore, the orthogonality of "click" coupling allows tolerance of initiating groups from prior polymerization reactions, the bromide atom from ATRP or the alcohol from ROP for instance, which obviates the need for protection/deprotection strategies for these functionalities.



Scheme 5b.6: Synthesis of ABC-type miktoarm star from a trifunctional core by ATRP, NMP, and click chemistry[1]

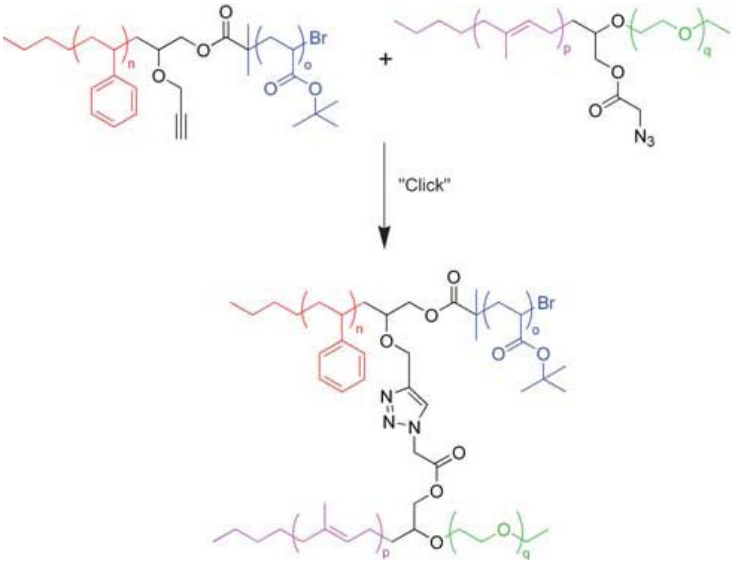
However, it should be noted that the "click" coupling method is only possible through the careful control of reaction conditions, including prolonged reaction times (often 24 h) and high concentration of macroinitiator, as well as a purification strategy for separating a miktoarm star from its polymeric precursors.Monteiro et. al[32] demonstrated in an excellent study that facile synthesis of miktoarm AB_2 stars can be easily achieved by optimizing the "click" coupling reaction conditions, resulting in low PDI and high yield in relatively short reaction times. Liu and coworkers[33] combined the "click" reaction between an azide and an alkyne with ROP and ATRP to synthesize an ABC miktoarm polymer composed of PCL, poly((2-dimethylamino)ethyl methacrylate) (PDMA) and either PS or PEG in a one-pot fashion. Similarly, the group of Tunca[34] has created an ABC miktoarm polymer in a one-pot fashion by combining NMP (instead of ATRP), ROP, and the "click" coupling reaction. NMP was used to grow PS, ROP for PCL, and azide-functionalized PtBA, PMMA, or PEG were clicked to the core to yield the final star (**Scheme 5b.7**).



Scheme 5b.7: One-pot synthesis of ABC miktoarm star[1]

The NMP and ROP reactions were simultaneously conducted prior to addition of azide-terminated polymer (one-pot/two-step); or the NMP, ROP, and "click" reaction were all allowed to proceed simultaneously (one-pot/one-step). Compared to the work of Liu and coworkers[33], longer reaction time and higher temperature was used to obtain miktoarm stars. It is evident from these two studies that a variety of conditions and polymers can be used to create a library of

miktoarm stars in a one-pot fashion, as long as a well-defined multifunctional core is synthesized. The studies mentioned for the coupling method so far have been used to make relatively simple miktoarm stars—AB_2 and ABC—which could also be made using a variety of other techniques, such as the "core-first" method or through the use of chlorosilane compounds. While many synthetic benefits from the coupling method have become evident relative to these other techniques, including a wider variety of monomers, it is important to note that any useful synthetic protocol for the synthesis of miktoarm stars must allow increasingly complex structures to be formed. In one example, ABCD miktoarm star polymers (rarely found in the literature due to stringent reaction conditions) were made by simply coupling two diblock copolymers together through azide-alkyne "click" chemistry (**Scheme 5b.8**)[4].



Scheme 5b.8: Synthesis of ABCD miktoarm star polymer by ''click'' coupling between two diblock copolymers[1]

An excess of azido-functionalized diblocks was deliberately used (~1.5:1) to ensure the completion of reaction, leaving behind both the 4-arm miktoarm polymer and a single type of unreacted diblock copolymer. The different solubilities of these two types of polymers in water were taken advantage of during the separation of these two polymers, yielding a purified ABCD-type miktoarm star polymer in approximately 70 % yield. The same strategy of coupling two block copolymers together through "click chemistry" to create the final miktoarm star was employed to yield unique H-shaped miktoarm star composed of five different arms (PS, PCL, PtBA, PEG, and PMMA) in moderately high yield[35].

Though most examples of miktoarm polymer synthesis in the literature that employ a coupling strategy by utilizing the Cu(I)-catalyzed Huisgen cycloaddition between an azide and an alkyne, there are other reactions that are available to achieve efficient coupling and a facile synthetic route[36]. Other popular variants of the "click" reaction that are widespread in

macromolecular synthesis include thiol-ene coupling reaction[37] and Diels-Alder reaction[28]. Altintas *et al*[38] coupled PCL functionalized with anthracene to PtBA functionalized with maleimide in a Diels-Alder reaction to create a block copolymer, so that subsequent NMP of PS followed by free radical photopolymerization of PMMA from the diblock copolymer junction yielded the final ABCD miktoarm star. The Diels-Alder reaction has also been used to make ABC miktoarm polymers[39]. Though coupling reactions outside of the classification of "click" reactions are rather sparse, one notable example arose recently where an A_2B_2 miktoarm polymer was made by coupling two diblock copolymers together at their junction points in an alkyne-alkyne homocoupling reaction[40]. Yields and polydispersity were comparable to those already described by the Huisgen "click" reaction. Thus, literature data demonstrates the enormous possibility of synthesis of different types of miktoarm copolymers possessing variety of polymer arms just by combination of techniques.

This chapter deals with synthesis and characterization of different types of miktoarm copolymers such as A_2B type $(PCL)_2$-PS, $(PCL)_2$-PEG, $(PCL)_2$-PLLA and AB_2 type PCL-$(PEG)_2$, PCL-$(PS)_2$ Y-shaped miktoarm copolymers, A_3B type such as $(PCL)_3$- PMMA, A_2B_2 type $(PCL)_2$-$(PMMA)_2$ using multifunctional initiator (MFI) core approach and coupling onto approach. The idea behind synthesizing $(PCL)_2$-PS, PCL-$(PS)_2$, $(PCL)_3$-PMMA or $(PCL)_2$-$(PMMA)_2$ is that it gives opportunity to have a copolymer system where one semicrystalline and biodegradable aliphatic polyester flexible arm will be covalently bonded with amorphous PS or PMMA. Porous templates of PS or PMMA could be prepared by selective degradation of PCL arm from these copolymers. These porous templates could further be used as supports for catalytic reactions. The philosophy behind synthesizing $(PCL)_2$-PEG or PCL-$(PEG)_2$ was that arms of the copolymers are biocompatible and biodegradable and constitute the amphiphilic system which could self assemble differently in different solvents and can be utilized as vehicles in drug delivery. Synthesis of $(PCL)_2$-PLLA was carried out by considering advantages and some limitations associated with individual homopolymers. Advantages associated with PCL are it is flexible and more ductile and thus exhibits high elongation at break. PCL is biodegradable and permeable to many drugs. But the disadvantages related with PCL are due to high flexibility, its mechanical strength is poor and its bio-degradation is slow. On the other hand, if PLLA is considered, advantages are its degradation is fast; it is biocompatible and has good modulus and strength. Thus, by combining these two polymers in single polymer system properties could be tuned. As these two polymers are immiscible with each other even in melt, covalent coupling is the preferred route for synthesis of miktoarm copolymers consisting of PCL and PLLA arms.

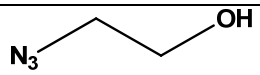
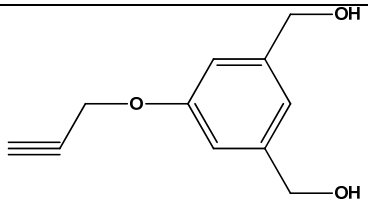
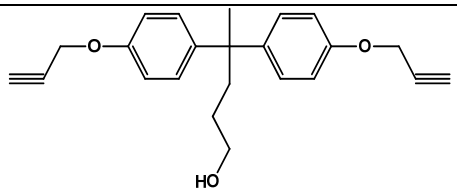
5b.2. Experimental

5b.2.1. Materials

Synthesis of 2-azidoethanol and 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl)pentan-1-ol has been described, respectively, in **Chapter 3a** and **Chapter 4a** while **s**ynthesis of A_2B, AB_2, ABC, A_2B_2, A_3B-type MFI cores and (5-(prop-2-yn-1-yloxy)1,3-phenylene) dimethanol, has been described in **Chapter 5a.** Styrene, ε-caprolactone, methyl methacrylate, and N, N-dimethyl formamide (DMF) were stirred over CaH_2 for 4 h and distilled under reduced pressure. N, N, N', N', N"-Pentamethyldiethylenetriamine (PMDETA) was used as received. Copper (I) bromide (Aldrich, 99.9%) was washed with glacial acetic acid in order to remove any soluble oxidized species, filtered, washed with ethanol, and dried.

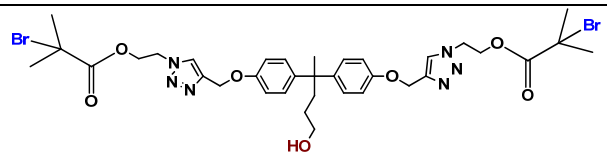
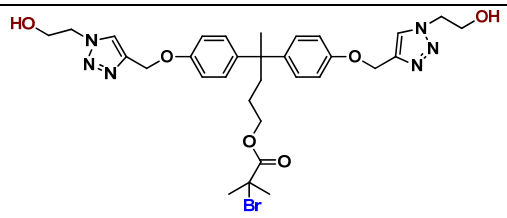
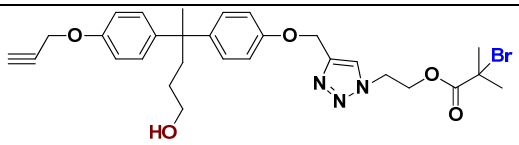
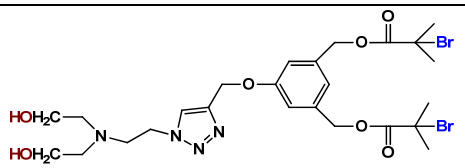
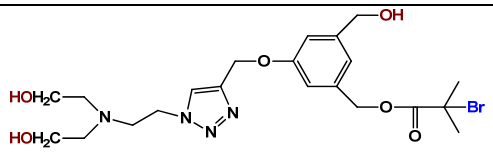
Initiators used in the preparation of functional prepolymers are listed in **Table 5b.1.**

Table 5b.1: Initiators used in preparation of functional prepolymers

Initiator Structure	***Initiator***	***Prepolymer synthesized***
	**Azidoethanol**	**Azido-functional PLLA**
	**Mid-chain mono-propargyloxy functional ROP initiator**	**Mid-chain mono-propargyloxy functionalized PCL**
	**Bis-Propargyloxy functionalized ROP initiator**	**α, α'-Bis-propargyloxy functionalized PCL**

Multifunctional initiator core used in the preparation of miktoarm copolymers are listed in **Table 5b.2**

Table 5b.2: MFI cores used in preparation of miktoarm copolymers

Initiator Structure	*Abbreviation*	*Polymer synthesized*
	**AB_2-type OH-Ini-$(Br)_2$**	**AB_2-type PCL-$(PS)_2$**
	**A_2B-type $(OH)_2$-Ini-Br**	**A_2B-type $(PCL)_2$-PS**
	**ABC-type (OH)-Init-propargyl-Br**	**ABC-type PCL-PEG-PS**
	**A_2B_2-type $(OH)_2$-Init-$(Br)_2$**	**A_2B_2-type $(PCL)_2$-$(PMMA)_2$**
	**A_3B-type $(OH)_3$-Init-Br**	**A_3B-type $(PCL)_3$-PMMA**

5b.2.2. Characterization and measurements

FT-IR spectra were recorded on a Perkin-Elmer Spectrum *GX* spectrophotometer. NMR spectra were recorded on a Bruker 200 MHz spectrometer for ^{1}H-NMR and 125 MHz for ^{13}C-NMR measurements using $CDCl_3$, DMSO-d_6 or acetone-d_6 as a solvent. Molecular weight and molecular weight distribution of polymers were determined using GPC analysis at a flow rate of 1 mL min^{-1} in chloroform at 30 °C (Thermoseparation product) equipped with spectra series UV 100 and spectra system RI 150 detectors. The sample concentration was 2 to 3 mg / mL and the

injection volume was 50 µL. HPLC grade chloroform was used as eluent at room temperature with a flow rate of 1 mL / min. Polystyrene was used as the calibration standard.

5b.2.2.1. WAXD analysis

WAXD analysis was performed over the 2θ range 10 to 40^{O} on a Bruker AXS: D8 Focus equipped with graphite monochromatized Cu Kα radiation (λ = 1.54056 Å).

5b.3. Synthesis of miktoarm copolymers

5b.3.1. Miktoarm copolymer synthesis by core-first approach

5b.3.1.1. Synthesis of $(PCL)_2$-PS, Y-shaped miktoarm star copolymers

5b.3.1.1.1. Synthesis of poly ε-caprolactone macroinitiator using trifunctional initiator $(OH)_2$ - Ini -Br

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (3.0 g, 26.4 mmol), stannous (II) octoate (0.5 mg, 0.0012 mmol), A_2B-type MFI (164 mg, 0.24 mmol) and toluene (20 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles and then the tube was immersed into preheated oil bath at 110 °C. After appropriate time, the polymerization was terminated by cooling the reaction mixture to room temperature. Toluene was removed under vacuum, diluted with dichloromethane (20 mL) and poured into cold methanol (200 mL). The polymer was collected by filtration and dried at room temperature in vacuum for 24 h. % Conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$, δ/ppm): 8.13 (s, triazole ring proton), 7.18-6.83 (m, Ar-H), 5.36 (bs, -OCH_2-from initiator fragment), 4.78 (bs, -OCH_2-from initiator fragment), 4.55 (bs, -OCH_2-from initiator fragment), 4.04 (t, $COOCH_2$ from poly ε-caprolactone + protons from initiator), 2.29 (t, CH_2COO from poly ε-caprolactone + protons from initiator), 1.91(s, from initiator fragment) 1.67-1.62 (m, $COOCH_2CH_2CH_2CH_2CH_2$-COO from poly ε-caprolactone + protons from initiator), 1.39-1.35 (m, $COOCH_2$-$CH_2CH_2CH_2CH_2COO$ from poly ε-caprolactone + protons from initiator)

5b.3.1.1.2. Synthesis of $(PCL)_2$- PS Y-shaped miktoarm copolymer

In a typical experiment, the Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (10 mg, 0.075 mmol). The Schlenk tube was thoroughly flushed with argon. Poly ε-caprolactone macroinitiator [$(PCL)_2$-Br] (1.05 g, 0.075 mmol) and styrene (0.40 g, 3.75 mmol) were dissolved in toluene (15 mL) in separate sample vials, degassed and solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture

was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and PMDETA (20 μL, 0.075 mmol) was added. The Schlenk tube was sealed with a stopper and was kept in an oil bath at 110 °C. After appropriate time, the polymerization was terminated by cooling and exposing reaction mixture to atmosphere, and diluted by addition of THF (50 mL). The solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into cold methanol (500 mL) to precipitate the polymer. The polymer was collected by filtration and dried at room temperature in vacuum for 24 h. % Conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.15-6.40 (m, Ar-H, from polystyrene + Ar-H, from MFI-core), 4.06 (t, from poly ε-caprolactone), 2.29 (t, from poly ε-caprolactone), 1.67-1.62 (m, from polystyrene + poly ε-caprolactone), 1.39-1.35 (m, from polystyrene + from poly ε-caprolactone)

5b.3.1.1.3. Procedure for degradation of PCL arm in $(PCL)_2$-PS Samples

The degradation of poly ε-caprolactone was carried out according to the procedure described in the literature[41]. A 0.5 M solution was prepared by dissolving 2.0 g of sodium hydroxide (Aldrich) in an 40/60 (v/v) solution of methanol/water (total volume of 100 mL). The degradation was carried out by placing $(PCL)_2$-PS sample (0.5 g) in the solution and then stirring in an oil bath at 65 °C. Typically reaction was carried out for about a week. The reaction mixture was cooled to room temperature, the precipitate was filtered and was washed with water and was then dried under vacuum for 14 h at room temperature. The degradation of PCL from the sample was confirmed by ^{1}H- NMR spectroscopy and GPC analysis.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.15-6.40 (m, Ar-H from polystyrene), 1.39- 1.35 (m, -CH_2,-CH_2, from poly styrene)

5b.3.1.2. Synthesis of PCL-$(PS)_2$, Y-shaped miktoarm star copolymers

5b.3.1.2.1. Synthesis of poly ε-caprolactone macroinitiator using trifunctional initiator OH - Ini-$(Br)_2$

Synthesis of poly ε-caprolactone macroinitiator using trifunctional initiator OH-Init-$(Br)_2$ was carried out by similar procedure as reported in **Section 5b.3.1.1.1.**

5b.3.1.2.2. Synthesis of PCL-$(PS)_2$ Y-shaped miktoarm copolymers

Synthesis of PCL-$(PS)_2$ Y-shaped miktoarm copolymer was carried out by employing ATRP of styrene on poly ε-caprolactone macroinitiator [PCL–$(Br)_2$] by similar procedure as reported in **Section 5b.3.1.1.2.**

5b.3.1.3. Synthesis of $(PCL)_2$-$(PMMA)_2$ miktoarm star copolymers

5b.3.1.3.1. Synthesis of poly ε-caprolactone macroinitiator using tetra-functional initiator $(OH)_2$-Ini-$(Br)_2$

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (4.50 g, 40 mmol), stannous (II) octoate (0.5 mg, 0.0013 mmol), tetra functional initiator core A_2B_2-type $(Br)_2$-Ini-$(OH)_2$ (137 mg, 0.26 mmol) and toluene (25 mL) under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles and then the tube was immersed into preheated oil bath at 110 °C. After appropriate time, the polymerization was terminated by cooling the reaction mixture to room temperature. Toluene was removed under vacuum, diluted with dichloromethane (25 mL) and poured into cold methanol (250 mL). The polymer was collected by filtration and dried at room temperature in a vacuum for 24 h. % Conversion was determined by gravimetry.

^{1}H-NMR ($CDCl_3$, δ/ppm): 7.77 (s, triazole ring proton), 6.95 (s, Ar-H, from initiator fragment), 5.15 (s, -OCH_2-from initiator fragment), 4.04 (t, from poly ε-caprolactone), 2.29 (t, from poly ε-caprolactone), 1.67-1.62 (m, from poly ε-caprolactone + from initiator fragment), 1.39-.35 (m, from poly ε-caprolactone)

5b.3.1.3.2. Synthesis of $(PCL)_2$-$(PMMA)_2$ miktoarm star copolymers by ATRP

In a typical experiment, the Schlenk tube equipped with a magnetic stir bar was charged with CuBr (10 mg, 0.07 mmol). The Schlenk tube was thoroughly flushed with argon. Poly ε-caprolactone macroinitiator (1.0 g, 0.07 mmol) and methyl methacrylate (700 mg, 7 mmol) were dissolved in toluene (15 mL) in separate sample vials, degassed and the solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and PMDETA (14 μL, 0.07 mmol) was added. The Schlenk tube was sealed with a rubber septum and was kept in an oil bath at 110 °C under continuous stream of argon. After appropriate time, the polymerization was terminated by cooling and exposing reaction mixture to atmosphere and diluted with THF (50 mL). The solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into cold methanol (500 mL) to precipitate the polymer. The polymer was collected by filtration and dried at room temperature in vacuum for 24 h. % Conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$, δ/ppm): 4.06 (t, $COOCH_2$ from poly ε-caprolactone macroinitiator), 3.60 (s, -OCH_3, from poly (methyl methacrylate)) 2.29 (t, -CH_2COO from poly ε-caprolactone macroinitiator), 1.67-1.62 (m, $COOCH_2CH_2CH_2CH_2CH_2$-COO from poly ε-caprolactone

macroinitiator + poly (methyl methacrylate)), 1.39- 1.35 (m, $COOCH_2$-$CH_2CH_2CH_2CH_2COO$ from poly ε-caprolactone + poly (methyl methacrylate)).

5b.3.1.3.3. Procedure for hydrolysis of the PCL arm in $(PCL)_2$-$(PMMA)_2$ miktoarm copolymer

Hydrolysis of copolymer was carried out following the procedure reported by Howdle et.al.[42] $(PCL)_2$-$(PMMA)_2$ miktoarm copolymer (1 g) was dissolved in 1, 4-dioxane (30 mL) at 85 °C. Concentrated hydrochloric acid (2 mL, 37 wt % HCl in water) was added to the solution, which was left stirring for 20 h. The reaction mixture was cooled to room temperature. The reaction mixture was precipitation in cold petroleum ether (300 mL). The polymer was collected by filtration and dried at room temperature in vacuum for 24 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 3.60 (s, OCH_3, from poly (methyl methacrylate)), 1.87-0.81 (m, -CH_2,-CH,-CH_3 from poly (methyl methacrylate))

5b.3.1.4 Synthesis of $(PCL)_3$-(PMMA) miktoarm copolymers

5b.3.1.4.1. Synthesis of poly ε-caprolactone macroinitiator using tetra functional initiator $(OH)_3$-Ini-Br

Synthesis of poly ε-caprolactone macroinitiator using trifunctional initiator $(OH)_3$-Init-(Br) was carried out by similar procedure as reported in **Section 5a.3.1.3.1.**

5b.3.1.4.2. Synthesis of miktoarm copolymers by ATRP

Synthesis of $(PCL)_3$-PMMA miktoarm copolymer was carried out employing ATRP of methyl methacrylate on poly ε-caprolactone macroinitiator [$(PCL)_3$–Br] by similar procedure as reported in **Section 5a.3.1.3.2.**

5b.3.2. Miktoarm copolymer synthesis by coupling method

5b.3.2.1. Synthesis of PCL-$(PEG)_2$, and $(PCL)_2$-(PEG) Y-shaped miktoarm star copolymers

5b.3.2.1.1. Synthesis of mid-chain mono-propargyloxy and bis-propargyloxy end functionalized PCL

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (6.0 g, 52 mmol), stannous (II) octoate (3.5 mg, 0.0086 mmol) 5-(prop-2-yn-1-yloxy) 1, 3-phenylene)dimethanol (330 mg, 1.73 mmol) and toluene (20 mL) under nitrogen atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, diluted with dichloromethane (25 mL) and

poured into cold methanol (250 mL) to precipitate polymer. The polymer was filtered and dried in vacuum for 24 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.11 (d, Ar-H *meta* to ether linkage, from initiator fragment), 6.83 (d, Ar-H *ortho* to ether linkage, from initiator fragment), 4.64 (d, -OCH_2, from initiator fragment), 5.19 (s, OCH_2, from initiator fragment), 5.07 (s, OCH_2 from initiator fragment), 4.65 (s, OCH_2 from initiator fragment), 4.04 (t, from poly ε-caprolactone), 2.50 (t, acetylene proton, from initiator fragment), 2.29 (t, from poly ε-caprolactone), 1.67-1.62 (m, from poly ε-caprolactone), 1.39-1.35 (m, from poly ε-caprolactone)

Following the same procedure α, α'- bispropargyloxy end-functionalized poly (ε-caprolactone)s with different molecular weights were synthesized

5b.3.2.1.2. Preparation of azido-end functionalized PEG (PEG-N_3)

Azide-end functionalized PEG with different chain lengths were prepared from commercially available α-methoxy-ω-hydroxy poly (ethylene glycol) according to procedure reported in the literature[43, 44].

Into a 500 mL three-necked flask, PEG (Mn = 5000, 5.0 g, 1.0 mmol) with mono-hydroxyl end group was dissolved in 250 mL of toluene. Traces of water were removed by azeotropic distillation and 30-40 mL of toluene was removed under reduced pressure. The reaction mixture was cooled to 0 °C and triethylamine (1.25 mL, 10 mmol) was added. 2-Bromoisobutyryl bromide (2.31 g, 10 mmol) was added drop wise *via* syringe over a period of 30 minutes, and the reaction mixture was stirred overnight at room temperature. The stirred solution was treated with charcoal, which was subsequently removed by filtration, and most of the toluene was removed under vacuum and polymer was dissolved in dichloromethane (50 mL) and precipitated into diethyl ether (500 mL). The polymer was dried under vacuum, dissolved in water at pH 8-9, and then extracted with dichloromethane (150 mL). The organic layer was dried over Na_2SO_4, filtered and removal of the solvent under vacuum afforded bromine end functionalized PEG.

Thus obtained bromine end functionalized PEG (2.75 g, 0.53 mmol) was dissolved in DMF (15 mL) and sodium azide (344 mg, 5.3 mmol) was added to the solution. The reaction mixture was stirred for 24 h at room temperature. DMF was removed under reduced pressure and the residue was dissolved in water at pH 8-9, and then extracted with dichloromethane (150 mL), precipitated in cold diethyl ether. Azido terminated PEG was dried for 24 h in a vacuum oven at 25 °C.

^{1}H NMR ($CDCl_3$, δ/ppm): 3.63 (s, -OCH_2CH_2), 1.47 (s, CH_2-N_3)

Following the same procedure PEG-N_3 (1000 and 2000) were synthesized.

5b.3.2.1.3. Click reaction between PEG-N_3 and mid-chain mono-propargyloxy functionalized PCL

Mid-chain monopropargyloxy poly ε-caprolactone (0.77 g, 0.1 mmol) and an azide end-functionalized PEG (585 mg, 0.12 mmol) were dissolved in nitrogen-purged DMF (10 mL) in a Schlenk tube. CuBr (14 mg, 0.1 mmol) and PMDETA (20 µL, 0. 1 mmol) were added and the reaction mixture was degassed by three freeze-pump-thaw cycles and stirred at room temperature for 24 h. DMF was removed under vacuum, polymer was dissolved in dichloromethane (20 mL) passed through alumina column to remove copper, precipitated into cold diethyl ether (200 mL), filtered and dried in vacuum at 40 °C.

^{1}H NMR ($CDCl_3$, δ/ppm): 4.05 (t, $COOCH_2$), 3.64 (s, PEG-backbone), 2.31 (t, CH_2COO), 1.65 (m, $COOCH_2CH_2CH_2CH_2CH_2$-COO), 1.38 (m, $COOCH_2$-$CH_2CH_2CH_2CH_2COO$).

5b.3.2.2. Synthesis of $(PCL)_2$-(PLLA) Y-shaped miktoarm star copolymers

5b.3.2.2.1 Synthesis of mid-chain mono-propargyloxy functionalized poly ε-caprolactone

Synthesis of mid-chain monopropargyloxy functionalized poly ε-caprolactone was carried out as reported in **section 5b.3.2.1.1**.

5b.3.2.2.2 Synthesis of azido end functionalized PLLA

In a typical experiment, Schlenk tube equipped with magnetic stir bar was charged with, (+) LLA (5.75 g, 40 mmol), stannous (II) octoate (2 mg, 0.004 mmol), 2-azidoethanol (70 mg, 0.8 mmol) and toluene (15 mL) under nitrogen atmosphere. The reaction mixture was degassed by three freeze-pump-thaw cycles. The (+) LLA polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, toluene was removed under vacuum, diluted with dichloromethane (25 mL) and poured into cold methanol (250 mL) to precipitate polymer. The polymer was filtered and dried in vacuum for 24 h.

FT-IR: 2110, 1735 cm^{-1}

^{1}H NMR ($CDCl_3$, δ/ppm): 5.17-5.13 (q, OCH), 4.39- 4.31 (m, -OCH_2), 3.48 (t, CH_2N_3, from initiator), 1.56 (d, -$CHCH_3$).

5b.3.2.2.3 Click reaction between PLLA-N_3 and mid-chain mono propargyloxy functionalized poly ε-caprolactone

Mid-chain mono propargyloxy functionalized PCL (3.1 g, 1.0 mmol) and an azide end-functionalized PLLA (6.1 g, 1.2 mmol), CuBr (143 mg, 1.00 mmol) and PMDETA (20 µL, 1.0

mmol) were taken in nitrogen-purged DMF (20 mL) in a Schlenk tube and the reaction mixture was degassed by three freeze-pump-thaw cycles and left under argon and stirred at room temperature for 24 h. DMF was removed under vacuum and polymer was dissolved in dichloromethane (50 mL). Polymer solution was passed through alumina column to remove copper residue, precipitated into cold methanol (500 mL) filtered and dried in vacuum oven.

^{1}H NMR ($CDCl_3$, δ/ppm): 5.17-5.13(q, $OCHCH_3$ from PLLA), 4.04 (t, $COOCH_2$ from poly ε-caprolactone), 2.29 (t, CH_2COO from poly ε-caprolactone), 1.59-1.55 (m, from poly ε-caprolactone + from PLLA), 1.41-1.36 (m, from poly ε-caprolactone)

5b.3.3. Synthesis of ABC-type PCL-PEG-PS copolymers by core first and coupling approach

5b.3.3.1. Synthesis of poly ε-caprolactone containing mono propargyloxy and ATRP initiating site

In a typical experiment, Schlenk tube equipped with a magnetic stir bar was charged with, ε-caprolactone (6.0 g, 52 mmol), stannous (II) octoate (0.5 mg, 0.0013 mmol), ABC-type OH-Ini-(Br)-propargyloxy MFI-core (151 mg, 0.26 mmol) and toluene (25 mL) under nitrogen atmosphere. The reaction mixture was degassed by three freeze-pump-thaw cycles. ε-CL polymerization was carried out at 110 °C. After a given time, the polymerization was terminated by cooling the reaction mixture to room temperature, toluene was removed under vacuum, diluted with dichloromethane (50 mL) and poured into cold methanol (500 mL) to precipitate polymer. The polymer was filtered and dried under vacuum for 24 h. % Conversion was determined by gravimetry.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.78 (s, triazole ring proton), 7.11 (d, Ar-H *meta* to ether linkage, from initiator fragment), 6.83 (d, Ar-H *ortho* to ether linkage, from initiator fragment), 5.19 (s, OCH_2), 4.65 (d, -OCH_2, from initiator fragment), 4.05 (t, from PCL), 2.50 (t, 1H, alkyne proton, from initiator fragment), 2.30 (t, from poly ε-caprolactone), 1.67-1.62 (m, from poly ε-caprolactone + from initiator fragment), 1.39-1.35 (m, from poly ε-caprolactone + from initiator fragment)

5b.3.3.2. Click reaction between PEG-N_3 and poly ε-caprolactone containing mono propargyloxy and ATRP initiating site

Poly ε-caprolactone containing mono propargyloxy, and ATRP initiating site (2.0 g, 0.1 mmol), an azide end-functionalized PEG (132 mg, 0.12 mmol), CuBr (14 mg, 0.1 mmol) and PMDETA (20 μL, 0. 1 mmol) were taken in nitrogen-purged DMF (20 mL) and the reaction mixture was degassed by three freeze-pump-thaw cycles and left under argon and stirred at room temperature for 24 h. Reaction was terminated and DMF was removed under vacuum. Polymer was dissolved in dichloromethane (20 mL) and polymer solution was passed through alumina column to remove

copper salt, precipitated into cold diethyl ether (200 mL). The polymer [PCL-PEG macroinitiator] was filtered and dried under vacuum for 12 h.

^{1}H NMR ($CDCl_3$, δ/ppm): 4.06 (t, from poly ε-caprolactone macro initiator), 3.65 (s, PEG-backbone), 2.31 (t, from poly ε-caprolactone macro initiator), 1.65-1.61 (m, from poly ε-caprolactone macro initiator), 1.40-1.36 (m, from poly ε-caprolactone macro initiator).

5b.3.3.3. Synthesis of ABC-type PCL-PEG-PS copolymers by ATRP

In a typical experiment, the Schlenk tube equipped with a magnetic stir bar was charged with, CuBr (10 mg, 0.072 mmol). The Schlenk tube was thoroughly flushed with argon. PCL-PEG macroinitiator (1.52 g, 0.072 mmol) and styrene (3.4 g, 32.5 mmol) were dissolved in toluene (15 ml) in separate sample vials, degassed and the solution was transferred *via* argon-purged syringe into the Schlenk tube under argon atmosphere. The reaction mixture was degassed three times by freeze-pump-thaw cycles. Under an argon atmosphere, the reaction mixture was opened and PMDETA (15 μL, 0.072 mmol) was added. The Schlenk tube was sealed with a stopper under vacuum and was kept in an oil bath at 110 °C. After appropriate time, the polymerization was terminated by cooling and exposing reaction mixture to atmosphere and diluted with THF (50 mL). The solution was passed through neutral alumina column to remove copper residue. The solution was concentrated and poured into cold methanol (500 mL) to precipitate the polymer. The polymer was filtered and dried under vacuum for 24 h. % Conversion was determined gravimetrically.

^{1}H NMR ($CDCl_3$, δ/ppm): 7.05-6.48 (m, Ar-H from PS + Ar-H from MFI), 4.06 (t, - from poly ε-caprolactone in PCL-PEG macroinitiator), 3.65 (s, from PEG chain in PCL-PEG macroinitiator), 2.31 (t, from poly ε-caprolactone in PCL-PEG macroinitiator), 1.67-1.62 (m, from poly ε-caprolactone in PCL-PEG macroinitiator), 1.39- 1.35 (m, from poly ε-caprolactone + from PS)

5b.4. Results and Discussion

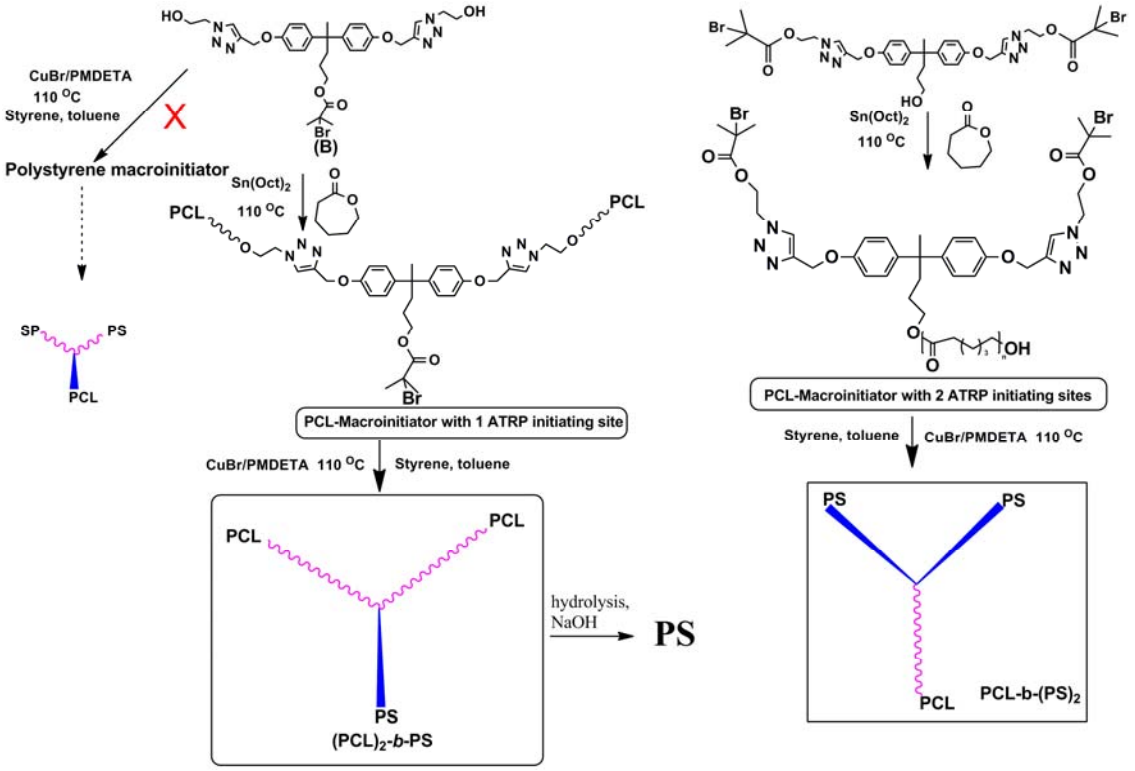
5b.4.1. Miktoarm copolymer synthesis by core-first approach

5b.4.1.1. Synthesis of $(PCL)_2$-(PS) and PCL-$(PS)_2$ Y-shaped miktoarm star copolymers

5b.4.1.1.1. Synthesis of poly ε-caprolactone based ATRP macroinitiators by ROP

MFI-core $(OH)_2$-Ini-Br was found to be insoluble in styrene monomer and solvents such toluene and anisole-which are commonly used as reaction media for ATRP of styrene. Therefore, ATRP of styrene using $(OH)_2$-Init-Br was abandoned. MFI-core $(OH)_2$-Ini-Br was found to be soluble in ε-caprolactone monomer. Therefore, ROP of ε-caprolactone using $(OH)_2$-Ini-Br as the initiator was carried out to obtain PCL-macro initiator. Poly ε-caprolactone macroinitiators

containing one or two ATRP initiating sites were synthesized by ROP of ε-CL in toluene at 110 °C using $(OH)_2$-Init-Br and (OH)-Init-Br_2, respectively as the initiators (**Scheme 5b.9**).



Scheme 5b.9: Synthesis of $(PCL)_2$-(PS) and PCL-$(PS)_2$ Y-shaped miktoarm copolymers

The reaction conditions and results of synthesis of poly ε-caprolactone macroinitiators are summarized in **Table 5b.3** and **Table 5b.4**

Table-5b.3: Reaction conditions and results for synthesis of PCL- macro initiators using A_2B MFI-core

Sr. No.	Macro initiator	Time (h)	$[M]_O/[I]_O$	[a]Conv. (%)	M_n			M_w/M_n
					[b]Theo	[l]H-NMR	[c]GPC	
1	PCL-I	12	110	76	10200	13800	18500	1.38
2	PCL-II	24	225	67	17800	20600	26200	1.27

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- % Conv. = Gravimetric

b- $M_{n,\,Theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol. wt. of initiator (670)

c- GPC- PS standard

Table-5b.4: Reaction conditions and results for synthesis of PCL-macro initiators using AB_2 MFI-core

Sr. No.	Macro initiator	Time (h)	$[M]_O/[I]_O$	[a] Conv. (%)	M_n			M_w/M_n
					[b] Theo	^{1}H-NMR	[c] GPC	
1	PCL-III	12	140	72	12300	14300	16500	1.42
2	PCL-IV	24	280	81	26600	d	31500	1.37

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- % Conv. = Gravimetric

b- $M_{n\ theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol. wt. of initiator (818)

c- GPC- PS standard

d - Not determined

^{1}H-NMR spectrum of poly ε-caprolactone macroinitiator is shown in **Figure 5b.3b**. In ^{1}H-NMR spectrum, peaks related to MFI fragment and poly ε-caprolactone chain were observed. The appearance of peak at 8.13 ppm and 7.18-7.0 ppm confirmed the presence of triazole and aromatic rings, respectively. Number average molecular weights of PCL- macroinitiators were calculated from ^{1}H-NMR spectroscopy by comparing the intensity the methylene protons (OCH_2, 4.05 ppm) to the peaks belonging to triazole protons from initiator at 8.13 ppm.

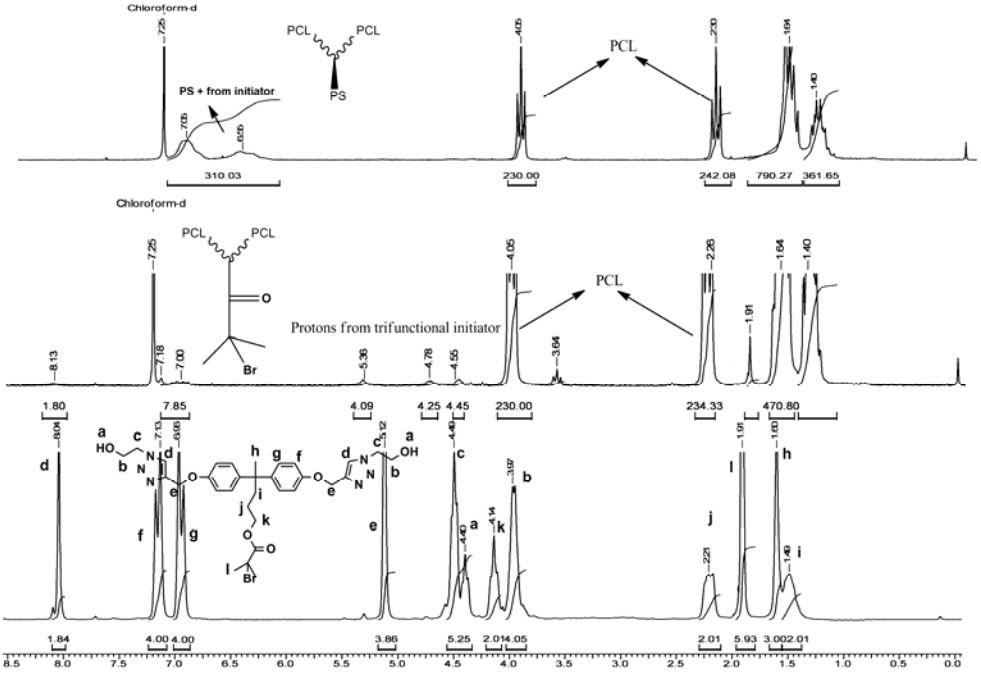


Figure 5b. 3: ^{1}H-NMR spectra of A) A_2B-type tri functional initiator B) PCL macro initiator C) $(PCL)_2$-PS A_2B-type star shaped copolymer in $CDCl_3$

Calculations of $M_{n,NMR}$ for macroinitiator $(PCL)_2$-Br

$$= \left(\frac{A_b}{2} \times \frac{2}{A_a} \right) \times \text{mol. wt. of monomer (114)} + \text{mol. wt. of MFI-core (670)}$$

$M_{n,NMR}$ was in good agreement with the theoretical molecular weights, (**Table 5b.3 and 5b.4**). Number–average molecular weights, Mn, were determined to be 13800 for PCL-I, 20600 for PCL-II, and 14300 for PCL-III, respectively. The degree of polymerization (DP), of the PCL block was determined from ^{1}H-NMR spectra. The obtained PCL-I: $(PCL_{60})_2$-Br, PCL-II: $(PCL_{90})_2$-Br and PCL-III PCL_{125}-Br_2 were subsequently employed as ATRP macroinitiators for the polymerization of styrene.

5b.4.1.1.2. Synthesis of miktoarm star copolymers by ATRP

As depicted in **Scheme 5b.9** PCL-I and PCL-II were employed as macroinitiators for ATRP of styrene in toluene at 110 °C using CuBr/PMDETA complex as the catalyst. ^{1}H-NMR spectrum of $(PCL)_2$-PS synthesized using PCL-I macroinitiator is reproduced in **Figures 5b 3c.** ^{1}H-NMR spectrum exhibited the characteristic NMR resonances of PS and PCL and all signals were assigned. Molecular weight of the resulting miktoarm star copolymer was determined by comparing the integral ratio of peaks at δ = 7.05-6.40 ppm characteristic of polystyrene after deducting contribution of protons from MFI fragment to that of peak at δ = 4.04 ppm due to OCH_2 of PCL chain.

Molecular weight of A_2B-type miktoarm by NMR:

Molecular weight of miktoarm copolymer could be obtained by using following equation

$$= \left(\frac{Aa}{5} \times \text{mol. wt of monomer (104)} \right) + \text{Mol. wt. of PCL macroinitiator } (M_{n,\,NMR})$$

Molecular weight and molecular weight distribution data of the miktoarm copolymers obtained are included in **Tables 5b.5.**

Table 5b.5: Reaction conditions and results for synthesis of Y-shaped A_2B-type $(PCL)_2$-(PS) miktoarm copolymers

Sr. No	Macro initiator (Mn by NMR)	Time (h)	[a]$[M]_O/[I]_O$ /[Cu]/[L]	[b]Conv (%)	Mn			Mw/ Mn	Miktoarm copolymer formed
					[c]Theo	^{1}H-NMR	[d]GPC		
1	PCL-I (13800)	12	65:1:1:1	61	18000	20300	31800	1.25	$(PCL_{60})_2$-PS_{63}
2	PCL- I (13800)	20	130:1:1:1	58	21600	24000	35400	1.34	$(PCL_{60})_2$-PS_{98}
3	PCL- II (20600)	12	150:1:1:1	53	28900	32400	41500	1.26	$(PCL_{90})_2$-PS_{113}
4	PCL- II (20600)	20	250:1:1:1	48	33100	39200	51000	1.23	$(PCL_{90})_2$-PS_{178}

a-$[M]_O$ / $[I]_O$ / [Cu] /[L]= [Monomer]:[Macroinitiator]:[CuBr]:[Ligand]

b- % conv= Gravimetric

c- $M_{n,theo}$ = $[M]_O$/ $[I]_O$ x % Conv x mol. wt . monomer + mol. wt. PCL macroinitiator

d- $M_{n,\,GPC}$ = PS standard

It was observed that, molecular weights determined by ^{1}H-NMR were higher than GPC analysis; which could be due to the hydrodynamic volume factor of miktoarm star copolymers. GPC traces of the PCL-II macroinitiator and $(PCL_{90})_2$-PS_{178} are shown in **Figure 5b.4** which were mono-modal and symmetric.

It was observed that the GPC peak clearly got shifted to higher molecular weight after the ATRP of styrene compared to the PCL-based macroinitiator and no peak corresponding to PCL-macroinitiator was detected in GPC trace of $(PCL_{90})_2$-PS_{178}.

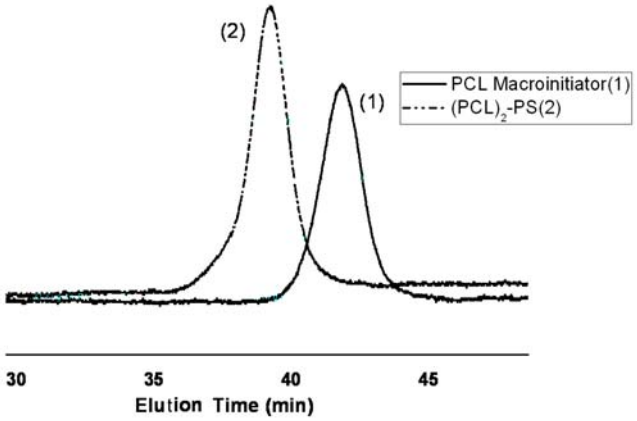


Figure 5b.4: GPC traces of (1) PCL macro initiator and (2) $(PCL)_2$ – PS A_2B-type miktoarm copolymer

5b.4.1.1.2.1. Degradation of PCL arm in $(PCL)_2$-PS samples

To demonstrate mikto copolymer formation, the miktoarm copolymer $(PCL_{90})_2$-PS_{178} was hydrolyzed in an alkaline medium to degrade the PCL arm. GPC traces of the miktoarm copolymer before and after hydrolysis are presented in **Figure 5b.5.** GPC trace of product obtained after alkali hydrolysis corresponds **to** molecular weight of 16800 (PS-standard) which apparently matches closely with theoretical molecular weight of polystyrene block.

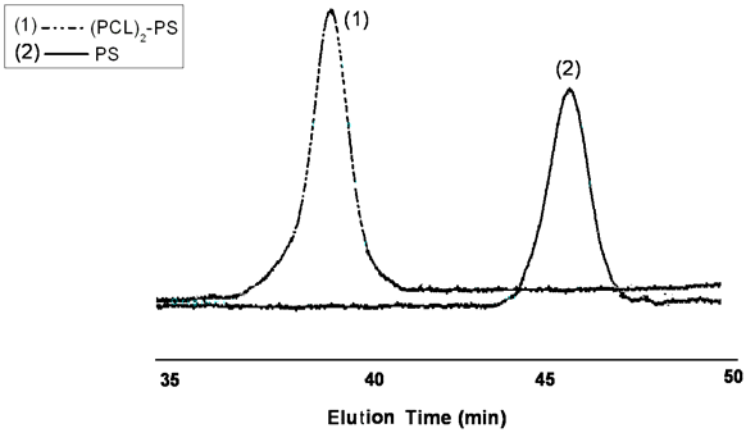


Figure 5b.5: GPC traces of 1) $(PCL)_2$-PS miktoarm copolymers before hydrolysis 2) product after hydrolysis

The degradation of the PCL arm from the miktoarm copolymer after hydrolysis was also confirmed by NMR analysis (**Figure 5b. 6**).

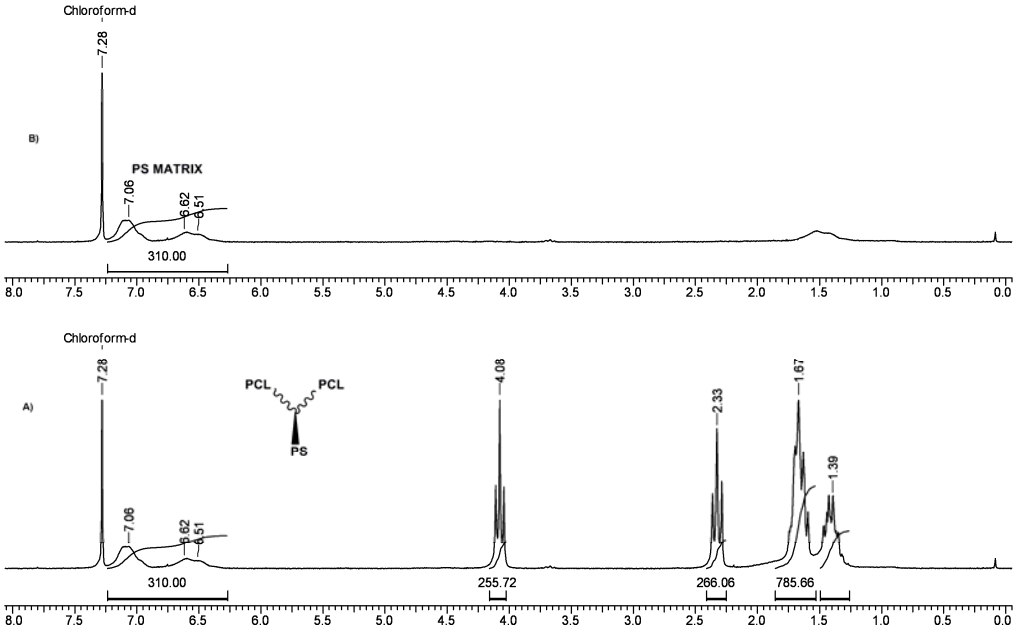


Figure 5b. 6: ^{1}H-NMR spectra of A) $(PCL)_2$-PS A_2B-type star shaped copolymer
B) product obtained after hydrolysis in $CDCl_3$

From ^{1}H-NMR spectrum, it was observed that peaks corresponding to PCL arm (**Figure 5b.6A**) in the miktoarm copolymer, were absent in the spectrum of the hydrolyzed product (**Figure 5b.6B**) and NMR spectrum matches with that of polystyrene.

5b.4.1.1.2.2. Crystallinity study

Crystallinity study of the polymers was investigated using WAXD measurements. As shown in **Figure 5b.7**, WAXD pattern of PCL macroinitiator (**Figure 5b.7a)** showed prominent diffraction peaks at $2\theta = 21.4$ and 23.8^O suggesting the semi-crystalline nature. As can be seen from **Figure 5b.7b** for $(PCL_{90})_2$-PS_{113}, copolymer showed peaks related to PCL chain while the intensity of the peaks decreased marginally suggesting decrease in the crystallinity. For $(PCL_{90})_2$-PS_{178} (**Figure 5b.7c)** as the polystyrene content in miktoarm copolymer $(PCL_{90})_2$-PS_{178} is more, it was observed that amorphous phase of polystyrene restricted the crystallization of PCL chain and resulted into amorphous nature of $(PCL_{90})_2$-PS_{178} as evidenced from the hollow broad peak in WAXD.

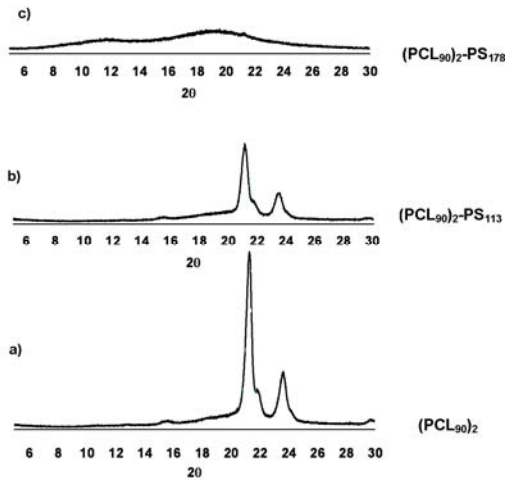


Figure 5b.7: WAXD patterns of A) PCL-macro initiator B) $(PCL_{90})_2$-PS_{113} C) $(PCL_{90})_2$-PS_{178} miktoarm copolymer

5b.4.1.1.2.3. Differential scanning calorimetric studies

Thermal transition parameters of PCL-macroinitiator and $(PCL_{90})_2$-PS_{113} were determined using DSC study. As a representative example, DSC cooling scan from the melt and subsequent heating scan for both poly ε-caprolactone macroinitiator and $(PCL_{90})_2$-PS_{113} are presented in **Figure 5b.8 and Figure 5b.9**, respectively.

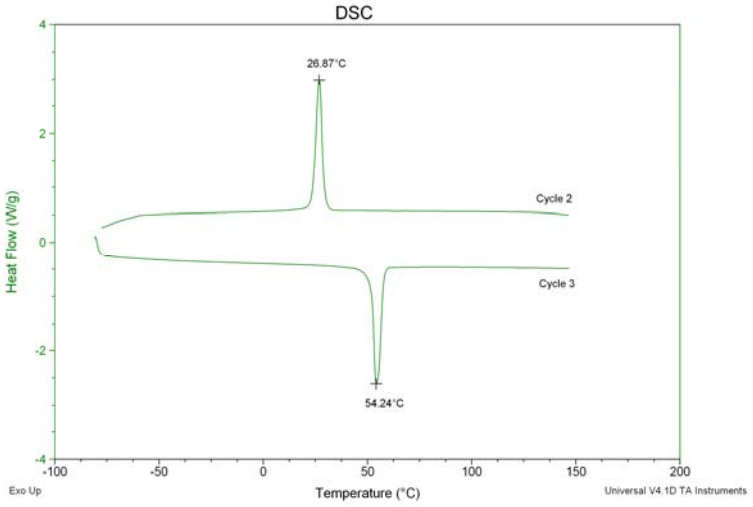


Figure 5b.8: DSC curves of PCL-macro initiator during cooling (cycle-2) and heating cycles (cycle-3)

As can be seen in **Figure 5b.8** sharp melting endotherm at 54.24 °C, corresponding to the melting transition and sharp exotherm at 26.87 °C, corresponding to the crystallization temperature of the semi-crystalline poly ε-caprolactone macroinitiator segment were observed.

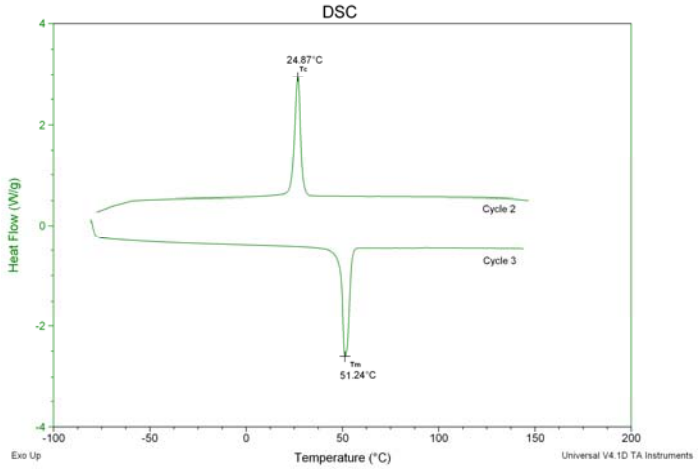


Figure 5b.9: DSC curves of $(PCL_{90})_2$-PS_{113} 1) cooling (cycle-2) 2) heating cycles (cycle-3)

In case of $(PCL_{90})_2$-PS_{113}, **(Figure 5b.9)** peaks corresponding to melting and crystallization temperature were observed at 51.24 and at 24.87 °C, respectively. As in the miktoarm copolymers, the morphological confinement due to polystyrene increases, Tm and Tc values decreased. A decrease in the melting transition indicated that the previous crystallization process was somewhat impaired (i.e., it occurred at lower temperatures where thinner lamellar crystals that melt at lower temperatures are produced)[45]. The glass transition of the PS component was observed for the $(PCL_{90})_2$-PS_{113} miktoarm star copolymers **(Figure 5b.10)**, at 100.96 °C. This transition can only be observed if the samples were previously quenched (at 60 °C/min) from the melt until 70 °C (where the $(PCL)_2$ component does not crystallize),and then heated at 40 °C/min

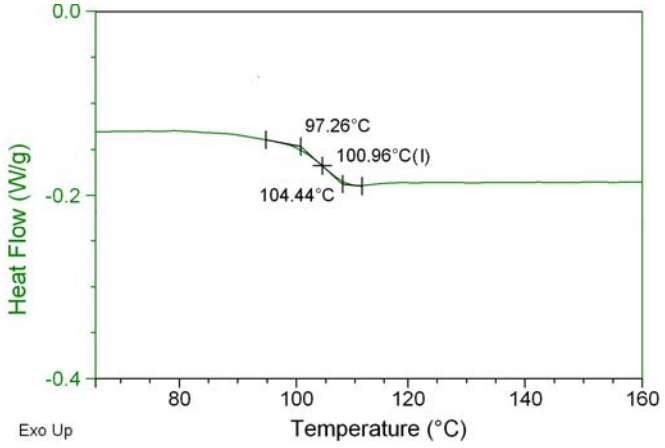


Figure 5b.10: Heating DSC scans (40 °C/min) for the $(PCL_{90})_2$-PS_{113} miktoarm copolymer after a fast cooling (60 °C/min) from 120 to 70 °C

to 120 °C[45]. With this simple DSC procedure, the glass transition of the PS component could be easily distinguished during the heating scan.

Poly ε-caprolactone macroinitiators containing two ATRP initiating sites (Table 5b.3) were employed for ATRP of styrene to obtain Y shaped AB_2-type (PCL)-$(PS)_2$ miktoarm star

copolymers. Reaction conditions and results of synthesis of Y shaped AB_2-type (PCL)-$(PS)_2$ miktoarm star copolymers are presented in **Table 5b.6**

Table 5b.6: Reaction conditions and results for synthesis of Y shaped AB_2-type (PCL)-$(PS)_2$ miktoarm copolymers

Sr. No	Macro initiator ($M_{n,\ NMR/GPC}$)	Time (h)	[a]$[M]_O/[I]_O$ /[Cu]/[L]	[b]Conv (%)	Mn			Mw/Mn	Miktoarm copolymers formed
					[c]Theo	^{1}H-NMR	[d]GPC		
1	PCL- III (14300)	12	100:1:1:1	53	19800	21200	24300	1.28	PCL_{125}-$(PS_{30})_2$
2	PCL- III (14300)	20	200:1:1:1	56	25900	31700	36200	1.37	PCL_{125}-$(PS_{83})_2$
3	PCL-IV (30500)	12	100:1:1:1	58	36500	e	51000	1.32	PCL_{267}-$(PS_{99})_2$
4	PCL-IV (30500)	20	200:1:1:1	54	41700	e	63500	1.23	PCL_{267}-$(PS_{159})_2$

a- $[M]_O$ / $[I]_O$ / [Cu] /[L]= [Monomer]:[Macroinitiator]:[CuBr]:[Ligand]

b- % conv= Gravimetric

c- $M_{n,theo}$ = $[M]_O$/ $[I]_O$ x % Conv x mol. wt . monomer + mol. wt. macroinitiator

d- $M_{n,\ GPC}$ = PS standard

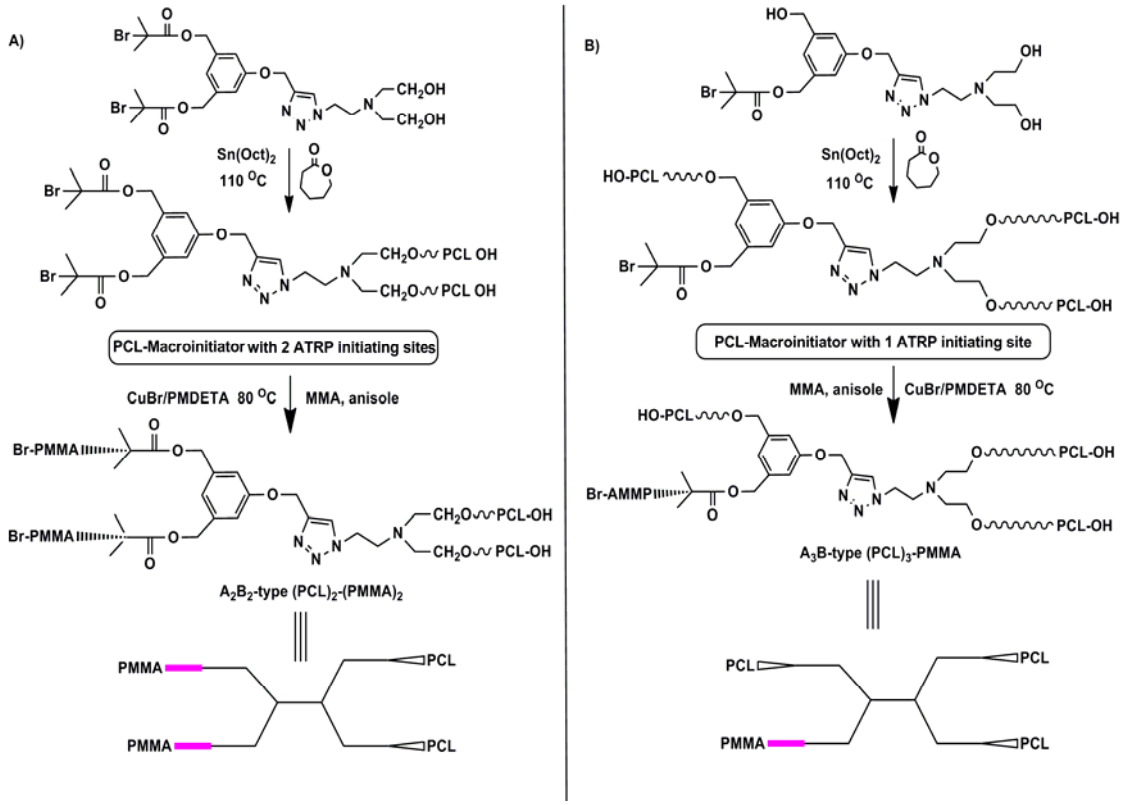
e- Not determined

The present study was limited to demonstrate the utility of poly ε-caprolactone macroinitiators containing two ATRP initiating sites for synthesis of Y shaped AB_2-type (PCL)-$(PS)_2$ miktoarm star copolymers. Characterization of miktoarm copolymers was carried out by NMR-spectroscopy.

5b.4.1.2. Synthesis of $(PCL)_2$-$(PMMA)_2$ and $(PCL)_3$-PMMA miktoarm star copolymers

5b.4.1.2.1. Synthesis of poly ε-caprolactone based ATRP macroinitiators by ROP

Poly ε-caprolactone based ATRP macroinitiators containing one or two ATRP initiating sites were prepared by ROP of ε-CL in toluene at 110 °C using A_3B-type $(OH)_3$-Init-Br and A_2B_2-type $(OH)_2$-Init-Br_2 as initiators, respectively **(Scheme 5b.10).**



Scheme 5b.10: Synthesis of A) $(PCL)_2$-$(PMMA)_2$ and B) $(PCL)_3$-PMMA

The reaction conditions and results of synthesis of poly ε-caprolactone macroinitiators are summarized in **Tables 5b.7 and 5b.8.**

Table 5b.7: Reaction conditions and results for synthesis of PCL- macro initiators using A_2B_2 MFI-core

Sr. No.	Macro initiator	Time (h)	$[M]_O/[I]_O$	[a]Conv (%)	M_n			M_w/M_n
					[b]Theo	[1]H-NMR	[c]GPC	
1	PCL-1	12	150	62	11300	14100	19500	1.46
2	PCL-2	24	300	65	22900	27500	32600	1.41

Temperature: 110 °C, Solvent: Toluene

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- % Conv. = gravimetric

b- $M_{n\ theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol wt of initiator (662)

c- GPC- PS standard

Table 5b.8: Reaction conditions and results for synthesis of PCL-macro initiators using A_3B MFI core

Sr. No.	Macro initiator	Time (h)	$[M]_O/[I]_O$	[a]Conv (%)	M_n			M_w/M_n
					[b]Theo	[1]H-NMR	[c]GPC	
1	PCL-3	12	150	72	12800	16300	21300	1.48
2	PCL-4	24	250	66	19300	d	28500	1.50

Temp: 110 °C, Solvent: Toluene

[Initiator] / $[Sn(Oct)_2]$ = 200

a- % Conv. = gravimetric

b- $M_{n\ theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol wt of initiator (514)

c- GPC- PS standard

d- Not determined

[1]H-NMR spectrum of poly ε-caprolactone based macroinitiator is shown in **Figure 5b.11b**,

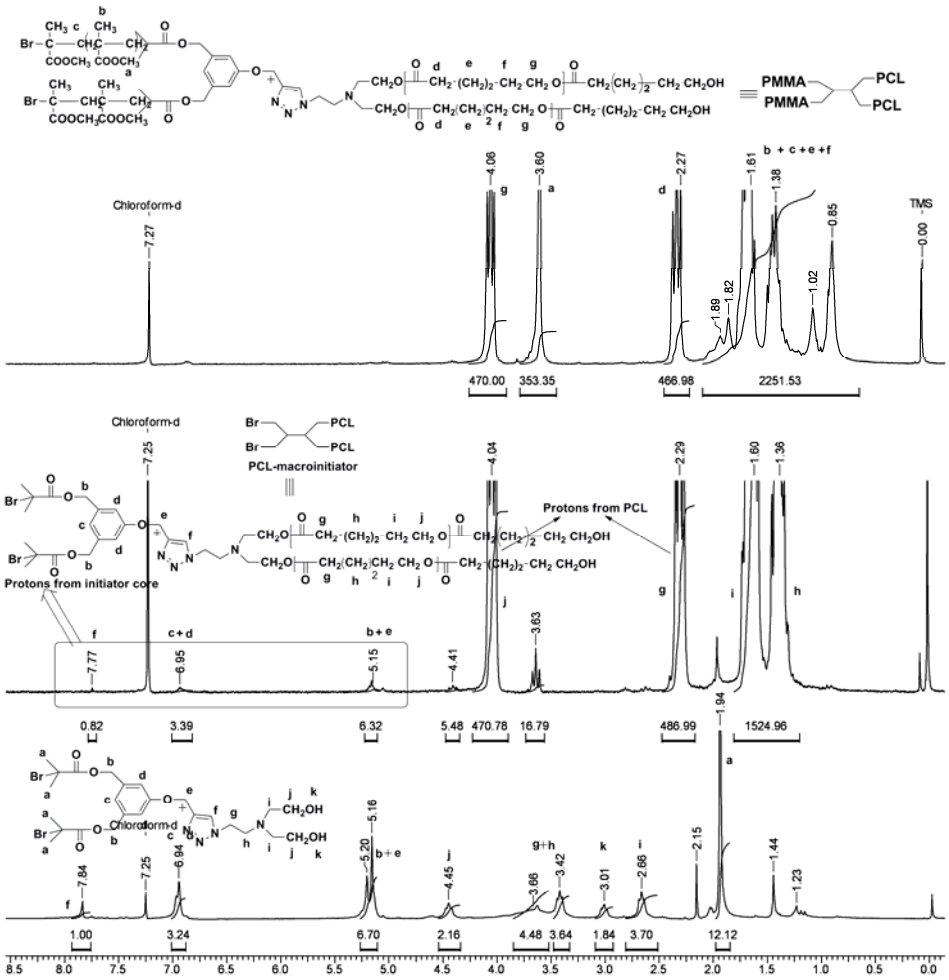


Figure 5b.11: ^{1}H-NMR spectra of A) A_2B_2 multifunctional core B) PCL-based macro initiator C) $(PCL)_2$-$(PMMA)_2$ miktoarm copolymer in $CDCl_3$

^{1}H-NMR spectrum exhibited resonances, corresponding to MFI-core and poly ε-caprolactone chain. The appearance of peak at 7.77 ppm and 6.95 ppm confirmed the presence of triazole and aromatic rings from initiator, respectively. $M_{n,NMR}$ of PCL-based macroinitiators were determined from ^{1}H-NMR, by comparing the intensity of the methylene protons ($COO\underline{CH_2}CH_2CH_2$, 4.04 ppm) in poly ε-caprolactone and to the peaks at 7.70 ppm belonging to triazole ring proton from initiator.

Calculations of $M_{n,NMR}$ for macroinitiator $(PCL)_2$-Br_2 =

$$\left(\frac{Aj}{2} \times \frac{1}{Af} \times \text{mol. wt. of monomer (114)} + \text{mol. wt. of initiator (514)}\right)$$

$M_{n,NMR}$ values were in good agreement with the theoretical molecular weights, and were found to be 14100 for **PCL-1**:$(PCL)_2$-Br_2, 27500 for **PCL-2**:$(PCL)_2$-Br_2 and 16300 for **PCL-3**: $(PCL)_3$-Br. Degree of polymerization (DP), of the PCL arm was determined from ^{1}H-NMR. The obtained **PCL-1**: $(PCL_{62})_2$-Br_2, **PCL-2**: $(PCL_{120})_2$-Br_2 **PCL-3**: $(PCL_{48})_3$-Br were subsequently employed as macroinitiators for polymerization of methyl methacrylate.

5b.4.1.2.2. Synthesis of miktoarm star copolymers by ATRP

PCL-1: $(PCL_{120})_2$-Br_2 was employed as macroinitiators (**Scheme 5b.10)** for ATRP of methyl methacrylate in anisole at 80 °C using CuBr/PMDETA complex as the catalyst system. Reaction conditions and results of synthesis of A_2B_2-type $(PCL)_2$-$(PMMA)_2$ miktoarm copolymers are incorporated in **Tables 5b.9.**

Table 5b.9: Reaction conditions and results for synthesis of A_2B_2-type $(PCL)_2$-$(PMMA)_2$ miktoarm copolymers

Sr. No	Macro initiator (Mn by NMR)	Time (h)	[a]$[M]_O$/ $[I]_O$/ [Cu]/ [L]	[b]Conv. (%)	Mn			Mw/ Mn	Miktoarm copolymer
					[c]Theo	^{1}H-NMR	[d]GPC		
1	PCL-1 (27500)	12	75:1:1 :1	51	31300	34400	45800	1.54	$(PCL_{120})_2$-$(PMMA_{34})_2$
2	PCL-1 (27500)	20	150:1: 1:1	57	36000	39300	53400	1.49	$(PCL_{120})_2$-$(PMMA_{60})_2$

a- $[M]_O$ / $[I]_O$/ [Cu]/[L]= [Monomer]:[Macroinitiator]:[CuBr]:[Ligand]

b- % conv= Gravimetric

c- $M_{n\ theo}$ = $[M]_O$/ $[I]_O$ x % conv x mol. wt . monomer + mol. wt. of PCL-macroinitiator

d- $M_{n\ GPC}$ = PS standard

^{1}H-NMR spectrum of $(PCL)_2$-$(PMMA)_2$ is reproduced in **Figures 5b. 11c.** ^{1}H-NMR spectrum exhibited characteristic resonances of PCL and PMMA. D_Pn of poly (methyl methacrylate) arm of the resulting miktoarm star copolymers was determined by comparing the integral ratio of peaks at δ= 3.60 ppm characteristic of methoxy of poly (methyl methacrylate) to that of peak at δ= 4.04 ppm due to OCH_2 of PCL chain.

Calculations of $M_{n,NMR}$ for $(PCL)_2$-$(PMMA)_2$ miktoarm copolymer =

$$\left(\frac{Aa}{3} \text{ x mol. wt. of monomer (100)} + \right) \text{mol. wt. of PCL-macroinitiator } (M_{n,NMR})$$

Molecular weights determined by GPC were higher than calculated from ^{1}H-NMR spectra which might be attributed to the different hydrodynamic volume of miktoarm copolymers. GPC traces

of PCL-based macroinitiator and $(PCL)_2$-$(PMMA)_2$ are shown in **Figure 5b.12.** GPC trace of miktoarm copolymer showed tailing indicating broader polydispersity.

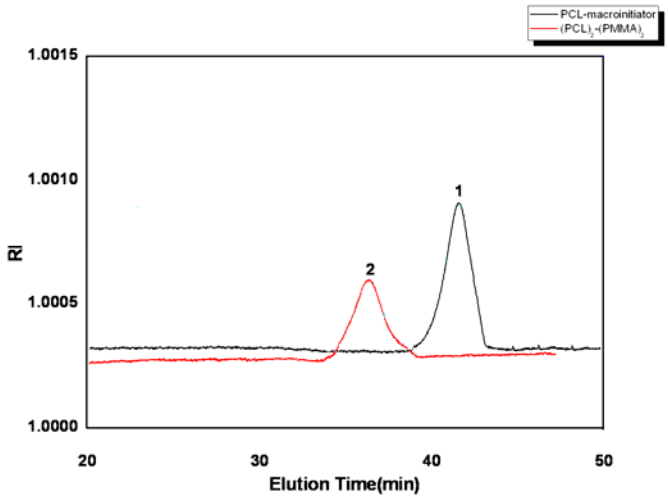


Figure 5b.12: GPC traces of 1) PCL macro initiator 2) $(PCL)_2$-$(PMMA)_2$ miktoarm copolymer

5b.4.1.2.2.1. Degradation of PCL arm in $(PCL)_2$-$(PMMA)_2$ samples

To demonstrate miktoarm copolymer formation, miktoarm copolymer $(PCL_{120})_2$-$(PMMA_{60})_2$ was hydrolyzed in acidic medium to degrade PCL block. GPC traces of the miktoarm copolymer before and after hydrolysis are presented in **Figure 5b. 13**. The peak eluting at shorter time is due to miktoarm copolymer. After hydrolysis, the peak eluted at much longer time with a molecular weight of 9300 (PS-standard) and could be attributed to PMMA arm.

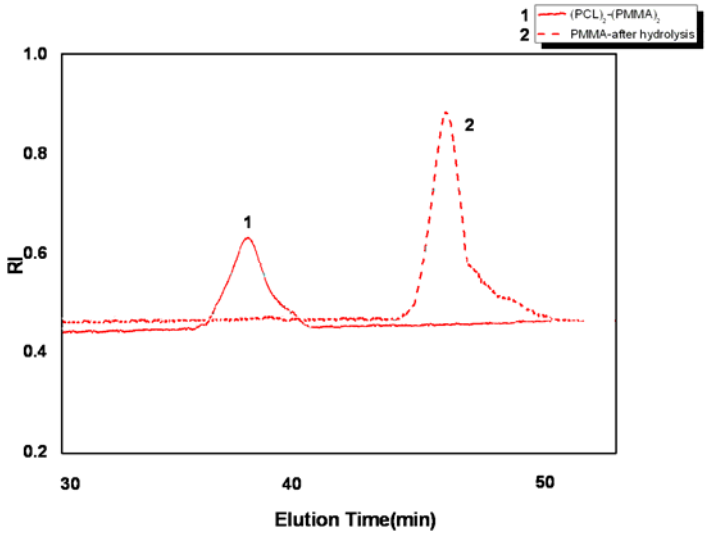


Figure 5b.13: GPC traces of 1) $(PCL)_2$-PMMA miktoarm copolymers before hydrolysis 2) product after hydrolysis

The degradation of the PCL arm from the miktoarm copolymer after hydrolysis was confirmed by ^{1}H-NMR. A comparison of NMR-spectra of miktoarm copolymer **Figure 5b.14.A** and hydrolysed product **(Figure 5b.14.B)** indicated that peaks corresponding to PCL-arm were absent in the NMR spectrum of hydrolysed product and the spectrum matched with that of PMMA.

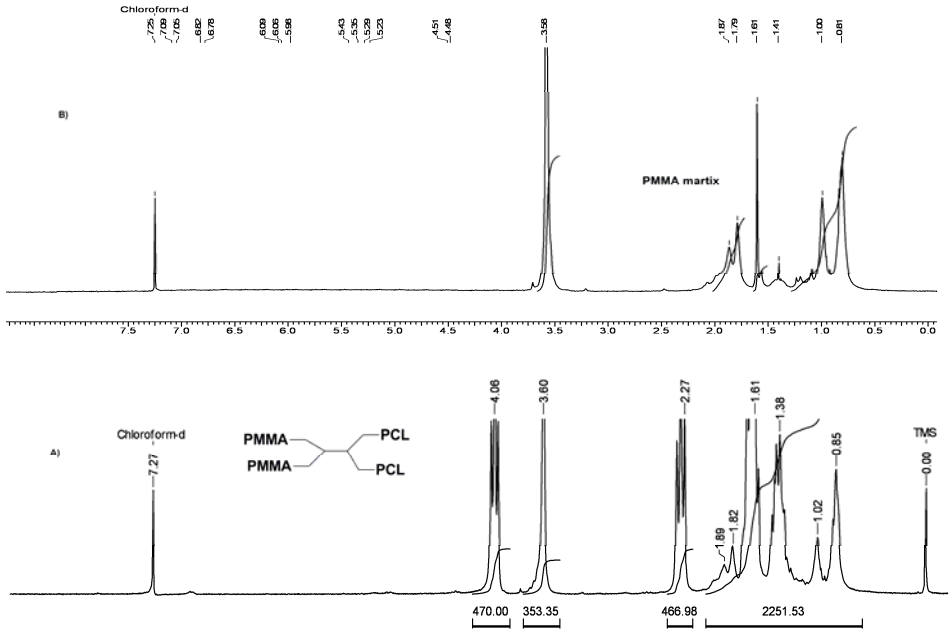


Figure 5b. 14: ^{1}H-NMR spectra of A) $(PCL)_2$-$(PMMA)_2$ A_2B_2-type miktoarm star copolymer B) product obtained after hydrolysis in $CDCl_3$

5b.4.1.2.2.2. Differential scanning calorimetric studies

DSC curves of the miktoarm copolymer $(PCL_{120})_2$-$(PMMA_{60})_2$ are presented in **Figure 5b.15**.

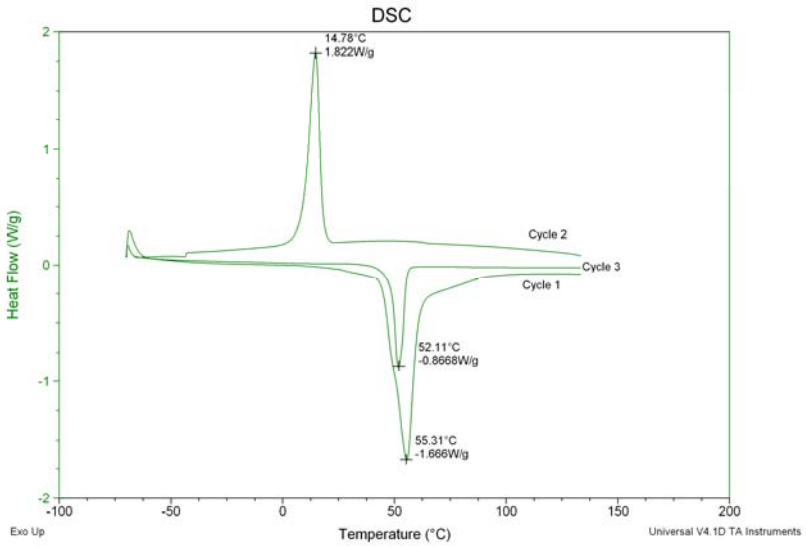


Figure 5b.15: DSC curves of $(PCL_{120})_2$-$(PMMA_{60})_2$ during heating (cycle-1), cooling (cycle-2) and heating cycles (cycle-3)

The thermograms of the miktoarm copolymer $(PCL_{120})_2$- $(PMMA_{60})_2$ exhibited a melting transition assignable to the PCL block at 55.3 °C (*T*m), (cycle-1). No Tg was observed for PCL or for PMMA. An exotherm was observed at 14.78 °C which could be attributed to crystallization temperature of semi-crystalline PCL arm. Poly ε-caprolactone macroinitiators containing one ATRP initiating site (Table 5b.7) were employed for ATRP of methyl methacrylate to obtain A_3B-type $(PCL)_3$-PMMA miktoarm star copolymers. Reaction conditions and results of synthesis of A_3B-type $(PCL)_3$-PMMA miktoarm star copolymers are presented in **Table 5b.10.**

Table 5b.10: Reaction conditions and results for synthesis of A_3B-type $(PCL)_3$-PMMA miktoarm copolymers

Sr. No	Macroinitiator (Mn by NMR)	Time (h)	[a]$[M]_O$/ $[I]_O$/ [Cu]/ [L]	[b]Conv (%)	Mn			Mw/ Mn	Miktoarm copolymer
					[c]Theo	^{1}H-NMR	[d]GPC		
1	PCL-3 (16300)	12	75:1:1 :1	52	20200	23100	36000	1.58	$(PCL_{48})_3$-$PMMA_{68}$
2	PCL-3 (16300)	24	150:1: 1:1	59	25100	30300	48200	1.56	$(PCL_{48})_3$-$PMMA_{140}$

a- $[M]_O$ / $[I]_O$/ [Cu]/[L]= [Monomer]:[Macroinitiator]:[CuBr]:[Ligand]

b- % conv = Gravimetric

c- $M_{n\ theo}$ = $[M]_O$/ $[I]_O$ x % conv x mol. wt . monomer + mol. wt. macroinitiator (NMR)

d- $M_{n\ GPC}$ = PS standard

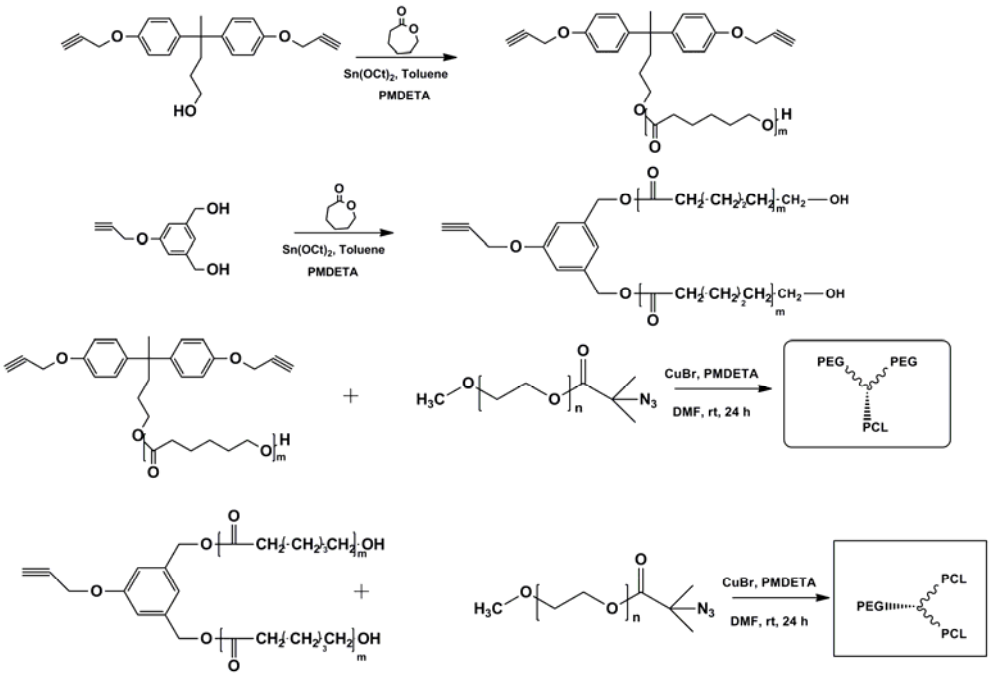
The present study was limited to demonstrate the utility of poly ε-caprolactone macroinitiators containing one ATRP initiating site for synthesis of A_3B-type $(PCL)_3$-PMMA miktoarm star copolymers. Characterization of miktoarm copolymers was carried out by NMR-spectroscopy.

5b.4.2. Miktoarm copolymer synthesis by coupling method approach

5b.4.2.1. Synthesis of PCL-(PEG)$_2$, and (PCL)$_2$-(PEG) Y-shaped miktoarm star copolymers

5b.4.2.1.1. Synthesis of propargyloxy-functionalized poly ε-caprolactone

ROP of ε-caprolactone was carried out using mono as well as bis-propargyloxy functionalized ROP initiators as shown in **Scheme 5b.11**.



Scheme 5b.11: Synthesis of PCL-(PEG)$_2$, and (PCL)$_2$-(PEG) Y-shaped miktoarm copolymers

Mid-chain mono-propargyloxy functionalized poly ε-caprolactones were obtained by employing (5-(prop-2-yn-1-yloxy)-1, 3-phenylene) dimethanol as the initiator. α, α'-Bispropargyloxy functionalized poly ε-caprolactones were obtained using 4, 4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol as the initiator as reported in **Chapter 4a Section 4a.3.1.**

The reaction conditions and results of synthesis of mid-chain monopropargyloxy functionalized poly ε-caprolactones are summarized in **Table 5b.11**. Different ratios of $[M_0]$ / $[I_0]$ were chosen so as to obtain polymers with different range of molecular weights. The conversions were determined by gravimetric analysis.

Table 5b.11: Reaction conditions and results for synthesis of mid-chain mono-propargyloxy functionalized PCLs

Sr. No.	$[M]_O/[I]_O$	Time (h)	[a]Conv. (%)	M_n			M_w/M_n
				[b]Theo	^{1}H-NMR	[c]GPC	
1	30	10	66	2200	3100	4200	1.39
2	50	18	55	3300	4100	4600	1.34
3	100	24	56	6600	7600	9200	1.41

Temperature: 110 °C, Solvent: Toluene

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- % Conv. = gravimetric

b- $M_{n\ theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol. wt. of initiator (192)

c- GPC- PS standard

Molecular weights of poly ε-caprolactone ($M_{n,\ NMR}$: 3100-7600) were in close agreement to the molecular weights calculated from the monomer-to-initiator ratio. In addition, GPC revealed monomodal distribution with PDI values in the range 1.34-1.41 for poly ε-caprolactones. ^{1}H-NMR spectrum of mid-chain mono-propargyloxy functionalized poly ε-caprolactone is represented in **Figure 5b.16.** The appearance of triplet corresponding to acetylene proton at 2.53 ppm and doublet corresponding to methylene protons of propargyloxy ether at 4.68 ppm confirmed the presence of propargyloxy functionality. $M_{n,NMR}$ of mid-chain mono-propargyloxy-functionalized poly ε-caprolactones could be determined by comparing integrals of signals of propargyloxy protons at 4.68 ppm with that of OCH_2 protons of poly ε-caprolactone at δ 4.04 ppm.

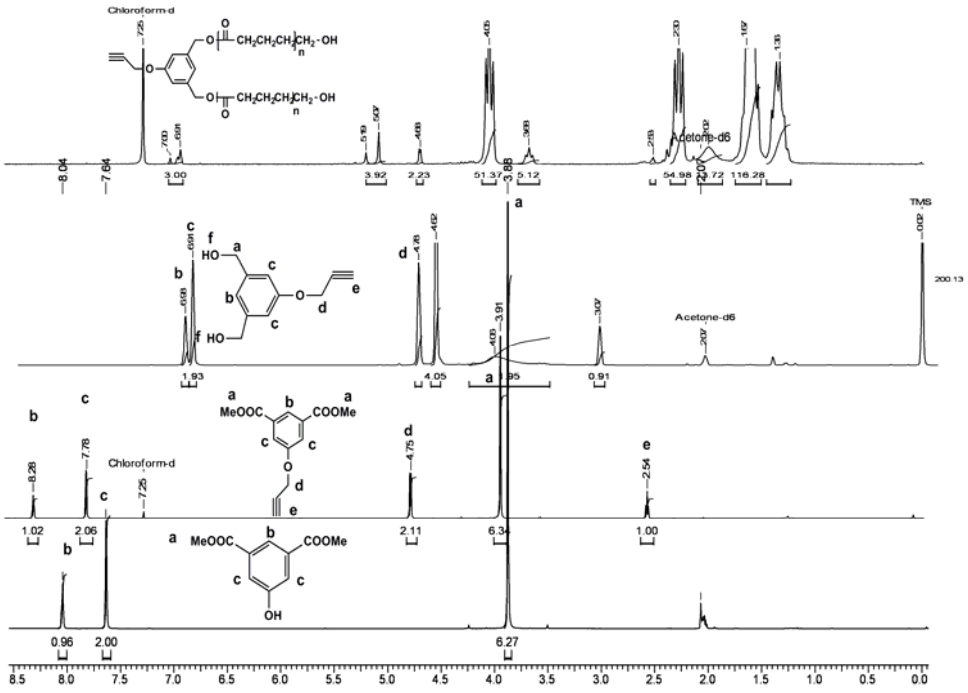


Figure 5b.16: ^{1}H-NMR spectra of A) dimethyl-5-hydroxyisophthalate B) dimethyl-5-(prop-2-yn-1-yloxy)isophthalate C) (5-(prop-2-yn-1-yloxy) 1,3-phenylene) dimethanol D) mid-chain mono-propargyloxy functionalized poly ε-caprolactone in $CDCl_3$

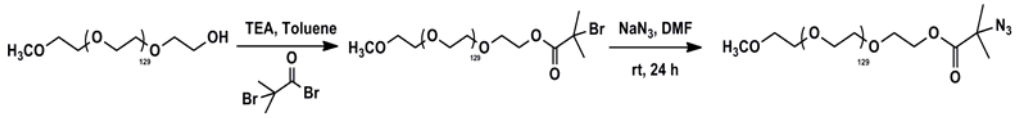
Calculations of $M_{n,NMR}$ for mid-chain monopropargyloxy-$(PCL)_2$ prepolymer

$$= \left(\frac{Ab}{2} \times \frac{2}{Aa} \right) \text{x mol. wt. of monomer (114) + mol. wt. of initiator (192)}$$

Molecular weights calculated by ^{1}H-NMR spectroscopy ($M_{n,NMR}$) were in reasonably good agreement with theoretical molecular weights ($M_{n,th}$) which indicated that the molecular weight of mid-chain mono-propargyloxy terminated poly ε-caprolactones can be well controlled by adjusting the molar ratios of the ε-CL monomer to the initiator.

5b.4.2.1.2. Synthesis of azido-end functionalized PEG (PEG-N_3)

Azide end-functionalized PEGs were synthesized from commercially available monomethoxy PEG (mPEG) (Mn = 1000, 5000) in two steps **(Scheme 5b.12).**



Scheme 5b.12: Synthesis of azido-end functionalized PEG

α-Methoxy-ω-hydroxy poly (ethylene glycol)s were first reacted with 2-bromoisobutyryl bromide to obtain $\tilde{\omega}$ bromo terminated PEG (PEG-Br). Then, the bromine end group of Br terminated PEG was converted to the azido functional group in the presence of excess NaN_3. **Figure 5b.17** represents the ^{1}H-NMR spectra of PEG-Br and PEG-N_3.

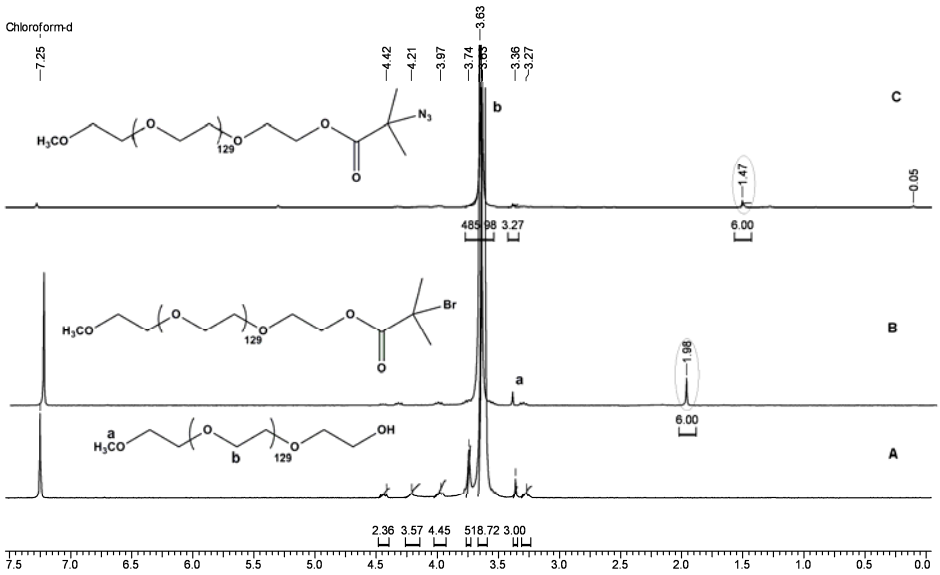


Figure 5b.17: ^{1}H-NMR spectra of A) monomethoxy PEG-OH (5000) B) monomethoxy PEG -Br C) monomethoxy PEG –N_3 in $CDCl_3$

The peaks corresponding to PEG chain could be clearly detected. The conversion of bromo to azido was confirmed by upfield shift of methylene peak adjacent to azide functionality from 1.98 to 1.47 ppm. FT-IR measurements were performed to further confirm formation of azido-terminated PEG. Compared with the IR spectrum of bromine terminated PEG, a new characteristic peak corresponding to azido group at 2108 cm^{-1} was observed which convincingly indicated the transformation of bromide group into azido functionality.

5b.4.2.1.3. Click reaction between mid-chain mono-propargyloxy poly ε-caprolactone and α, α' bis-propargyloxy functionalized PCL with PEG-N_3

''Click'' chemistry strategy was used to prepare PEG-$(PCL)_2$ and $(PEG)_2$-(PCL) miktoarm star copolymer by coupling propargyloxy functionalized poly ε-caprolactones with azido end-functionalized PEGs using CuBr/PMDETA as catalyst system in DMF at r.t. following the reported procedure[44]. The results for miktoarm star copolymers preparation *via* ''click'' cycloaddition reactions are summarized in **Table 5b.12.**

Table 5b.12: Results for synthesis of PEG-$(PCL)_2$ and $(PEG)_2$-(PCL) miktoarm copolymers

Sr. No.	Propargyloxy functionalized PCL	Azido functionalized PEG	M_n			M_w/M_n	Miktoarm copolymer
			Theo	^{1}H-NMR	GPC		
1	PCL-7600 (mid chain monopropargyloxy)	5100	12700	12800	7800	1.43	PEG_{115} - $(PCL_{33})_2$
2	PCL-5000 (bis-propargyloxy)	5100	15200	14400	9600	1.36	$(PEG_{115})_2$-PCL_{44}

12 mole % excess azide end functionalized PEG precursor was used to prepare miktoarm copolymers. After ‘‘click’’ reaction, unreacted azide end functionalized PEG was removed by dialysis. ^{1}H NMR spectrum of the synthesized PEG_{115}-$(PCL_{33})_2$ copolymer is shown in **Figure 5b.18.**

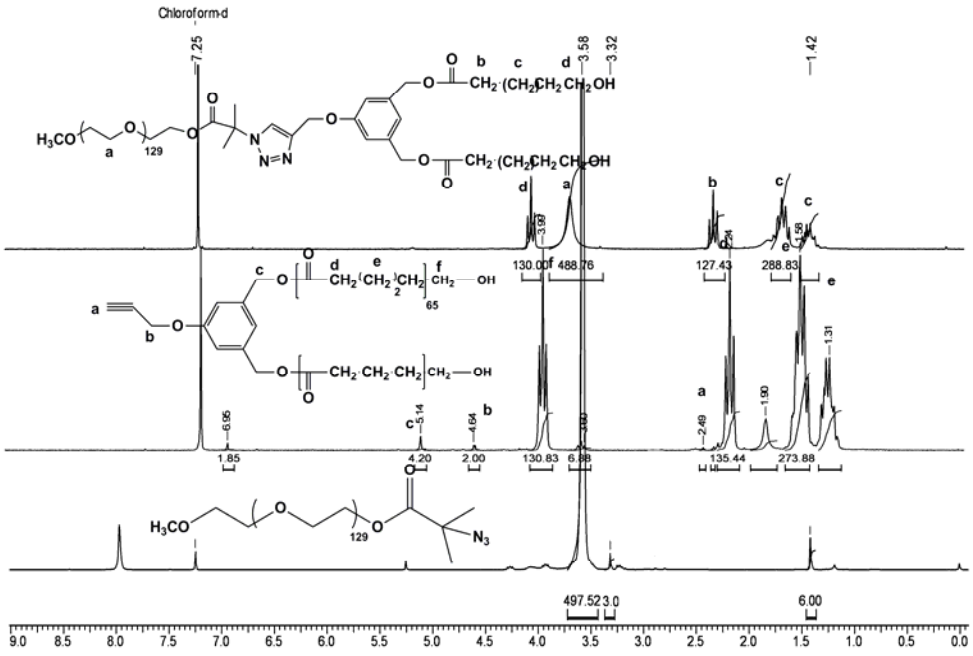


Figure 5b. 18: ^{1}H-NMR spectra of A) PEG-N_3 B) mid-chain monopropargyloxy functionalized poly ε-caprolactone C) PEG_{115}-$(PCL_{33})_2$ miktoarm copolymer in $CDCl_3$

Molecular weights of PEG_{115}-$(PCL_{33})_2$ copolymers can be calculated comparing integral ratio of the peak at 3.65 ppm corresponding to methylene protons of the PEG arm to the area peak at 4.04 ppm due to $–OCH_2$ in the poly ε-caprolactone chain. Dpn of miktoarm copolymers by ^{1}H-NMR spectroscopy could be denoted for PEG-$(PCL)_2$: as PEG_{115}-$(PCL_{33})_2$ and for $(PEG)_2$-PCL as $(PEG_{115})_2$-PCL_{44}.Molecular weights of $(PEG)_2$-PCL and PEG-$(PCL)_2$ mikto-arm star copolymers were determined from GPC (RI detector) using linear PS standards. Molecular weights calculated from GPC were lower than that calculated from ^{1}H-NMR spectroscopy. This might be due different interaction of hydrophilic PEG chain to GPC column.

5b.4.2.1.3.1. Crystallinity study

PEG-PCL amphiphilic system has been studied widely for drug delivery applications mostly due to biocompatible and biodegradable properties. Physical state, especially the crystalline structure within the micellar core, has a great influence on drug incorporation, micelle stability, as well as drug release. Whereas an amorphous structure is favorable for drug loading[46], a crystalline structure provides good kinetic stability and sustained drug release of micelles[47, 48]. Therefore, the crystallinity of the miktoarm copolymers was investigated with WAXD analysis. WAXD patterns of PEG and PCL prepolymers showed prominent diffraction peaks at 2θ = 19.1, 23.4^O (**Figure 5b.19a),** and 2θ = 21.4 and 23.8^O (**Figure 5b.19b)**, respectively, suggesting the semi-crystallinity.

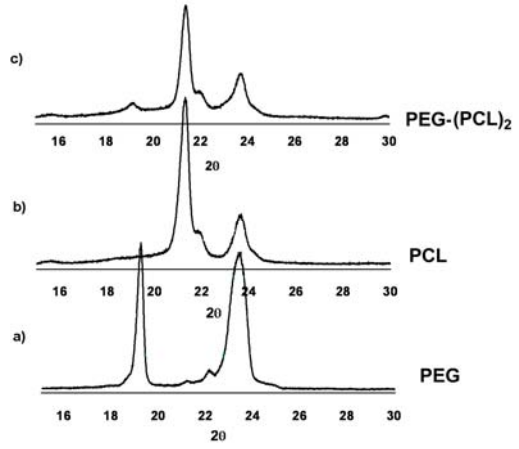


Figure 5b. 19: WAXD patterns of A) PEG-N_3 B) mid-chain monopropargyloxy functionalized poly ε- caprolactone C) PEG_{115}-$(PCL_{33})_2$ miktoarm copolymer

For PEG_{115}-$(PCL_{33})_2$, the coexistence of the characteristic diffraction peaks for both PCL and PEG was observed **(Figure 5b.19c)** suggesting semi-crystalline nature of miktoarm copolymers. It was also noted that the peaks at 2θ=23.4^O from PEG and at 23.8^O for PCL overlapped with each other. These results suggested a microphase separation in the miktoarm copolymers. Similar observations have been reported in the literature for PEG-PCL system[49, 50].

5b.4.2.1.3.2. Differential scanning calorimetric studies

The melting and crystallization behavior of PEG_{115}-$(PCL_{33})_2$ copolymer was investigated by DSC (**Figure 5b.20)**. DSC curves showed melting peaks related to PEG and PCL at 54.8 and 51.2 °C, respectively, and two exothermic peaks related to crystallization temperature were observed at 29.12 and 12.24 °C for PEG_{115}-$(PCL_{33})_2$, suggesting that two distinct crystalline domains existed in the copolymer, which is in consistent with WAXD data.

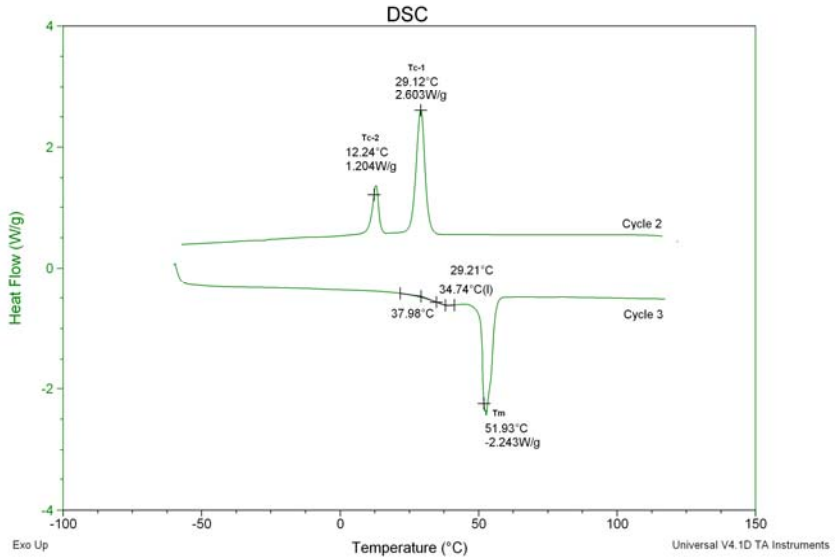


Figure 5b.20: DSC curves of PEG_{115}–$(PCL_{33})_2$ miktoarm copolymer 1) cooling (cycle-2) and 2) heating (cycle-3)

5b.4.2.2. Synthesis of $(PCL)_2$-(PLLA) Y-shaped miktoarm star copolymers

5b.4.2.2.1. Synthesis of mid-chain monopropargyloxy functionalized PCL

Results of synthesis of mid-chain monopropargyloxy functionalized PCLs have been summarized in **Section 5b.4.2.1.1**

5b.4.2.2.2. Synthesis of α-azido-end functionalized PLLA (PLLA-N_3)

ROP of (+) LLA was carried out using 2-azidoethanol as the initiator (**Scheme 5b.13)**

Scheme 5b.13: Preparation of α-azido end functionalized PLLA

The reaction conditions and results of synthesis of α-azido functionalized PLLA are summarized in **Table 5b.13.** Different ratios of $[M_0]$ / $[I_0]$ were chosen so as to obtain polymers with different range of molecular weights. The conversions were determined by gravimetric analysis. The molecular weights of PLLA ($M_{n,NMR}$: 5600 and 10200) were in close agreement with the molecular weights calculated from the monomer-to-initiator ratio. In addition, GPC data revealed monomodal distribution with PDI values of 1.39 and 1.48 for PLLA.

Table 5b.13: Reaction conditions and results for synthesis of azido functionalized PLLA

Sr. No.	$[M]_O/[I]_O$	Time (h)	[a]Conv (%)	M_n			M_w/M_n
				[b]Theo	[1]H-NMR	[c]GPC	
1	50	14	68	5000	5600	7100	1.39
2	100	24	60	8700	10200	14500	1.48

Temperature: 110 °C, Solvent: Toluene

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- $M_{n\ theo} = [M]_O/[I]_O$ x % conv. x mol. wt. of monomer + mol. wt. of initiator (87)

b- % Conv. = gravimetric

c- GPC- PS standard

^{1}H-NMR spectrum of azido functionalized PLLA is represented in **Figure. 5b.21**

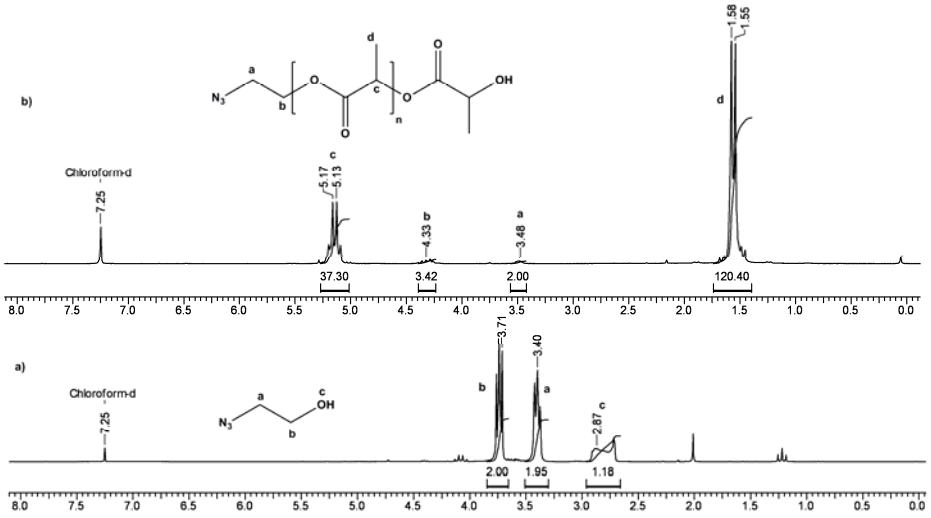


Figure 5b.21: ^{1}H-NMR spectra of A) 2-azidoethanol B) azido functionalized PLLA in $CDCl_3$

In ^{1}H-NMR spectrum, the methylene protons adjacent to azido functionality appeared as a triplet at 3.48 ppm. Molecular weights of azido terminated PLLA were determined by ^{1}H NMR. $M_{n,NMR}$ of azido-functionalized PLLA could be determined by comparing integrals of signals of methylene protons adjacent to azido functionality with those of OCH proton of PLLA at δ 5.15 ppm. Molecular weights calculated by ^{1}H-NMR spectroscopy ($M_{n,\ NMR}$) were in reasonably good agreement with theoretical molecular weights.

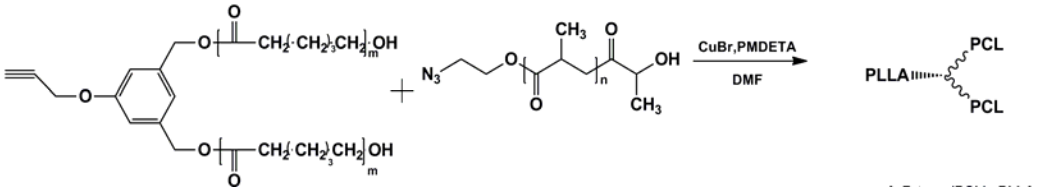
Calculations of $Mn_{\ NMR}$ for azido-functionalized PLLA=

$$\left(\frac{Ac}{1} \times \frac{2}{Aa} \right) \times \text{mol. wt. of monomer (144)} + \text{mol. wt. of initiator (87)}$$

Where Ac is intensity of peak area @ 5.15 ppm and Aa is intensity of peak area @ 3.48 ppm.

5b.4.2.2.2. Cycloaddition reaction between azido functionalized PLLA and mid-chain mono propargyloxy functionalized poly ε-caprolactone

''Click'' chemistry strategy was used to prepare $(PCL)_2$-PLLA miktoarm star copolymer. Click reaction was performed between mid-chain mono propargyloxy functionalized poly ε-caprolactone and azido functionalized PLLA using CuBr/PMDETA as catalyst system in DMF at 30 °C following the reported procedure[44] (**Scheme 5b.14**).



Scheme 5b.14: Synthesis of A_2B-type $(PCL)_2$-PLLA miktoarm copolymer

Results for preparation of $(PCL)_2$-PLLA miktoarm star copolymers *via* ''click'' cycloaddition reaction are summarized in **Table 5b.14.**

Table 5b.14: Results for synthesis of $(PCL)_2$-PLLA miktoarm copolymers

Sr. No.	Propargyloxy functionalized PCL	Azido functionalized PLLA	M_n			M_w/M_n	Miktoarm copolymer
			Theo	^{1}H-NMR	GPC		
1	PCL- 3100 (mid-chain mono-propargyloxy)	5600	8700	10800	18000	1.53	$(PCL_{14})_2$-$PLLA_{39}$
2	PCL-7600 (mid-chain mono-propargyloxy)	5600	13300	22800	27800	1.49	$(PCL_{33})_2$-$PLLA_{39}$

^{1}H-NMR spectrum of $(PCL)_2$-PLLA copolymer is shown in **Figure 5b.22.**

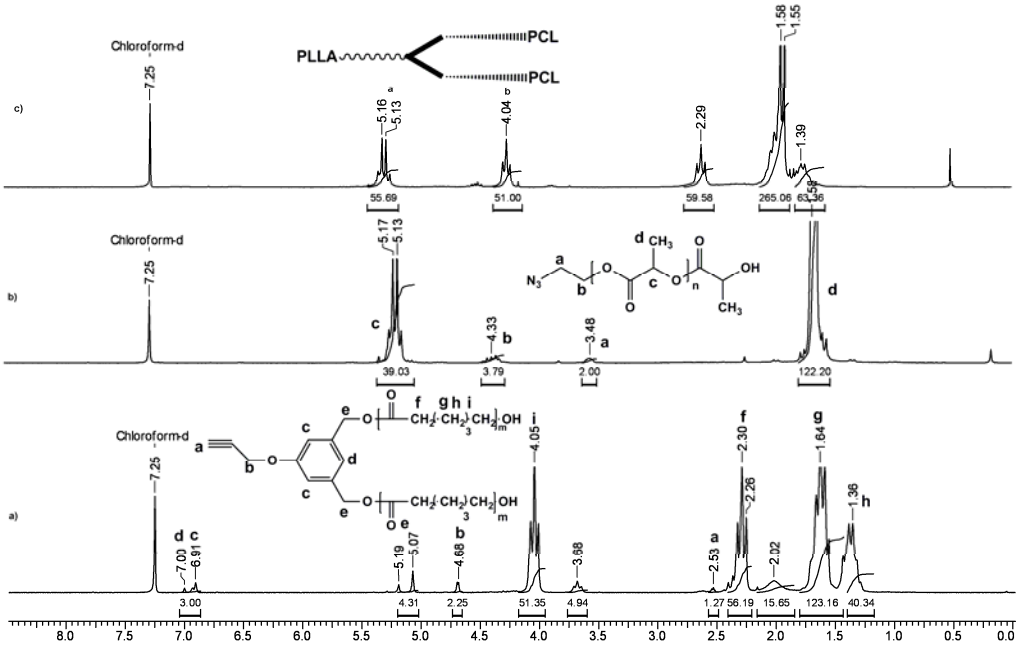


Figure 5b.22: ^{1}H-NMR spectra of A) mid-chain mono propargyloxy functionalized poly ε-caprolactone B) azido functionalized PLLA C) $(PCL_{14})_2$-$PLLA_{39}$ miktoarm copolymer in $CDCl_3$

Molecular weights of $(PCL_{14})_2$-$PLLA_{39}$ miktoarm copolymers could be determined by comparing integral ratio of the peak area at 5.16 ppm of the -OCH protons of the PLLA arm to the peak area at 4.04 ppm due to $–OCH_2$ in the poly ε-caprolactone arm.

Molecular weight of miktoarm copolymer =

$$\left\{ \frac{IA_a}{2} \text{ x mol wt. of monomer (144)} + \frac{IA_b}{2} \text{ x mol wt. of monomer (114)} \right\}$$

Molecular weights determined by GPC were higher than theoretical molecular weights which could be attributed to different hydrodynamic volume of miktoarm star copolymers. Representative GPC curves are shown in **Figure 5b.23.** After cycloaddtion, GPC trace shifted to higher molecular weights as compared to their precursors. The presence of unreacted azido terminated PLLA which was used in an amount higher than the stoichiometric ratio was also detected in GPC trace. The removal of unreacted azido terminated PLLA posed practical difficulties as chloroform, dichloromethane, tetrahydrofuran, and dimethyl formamide are good solvents for both miktoarm copolymer and azido functionalized PLLA. Thus, selective separation of azido functionalized PLLA was not possible under our experimental conditions.

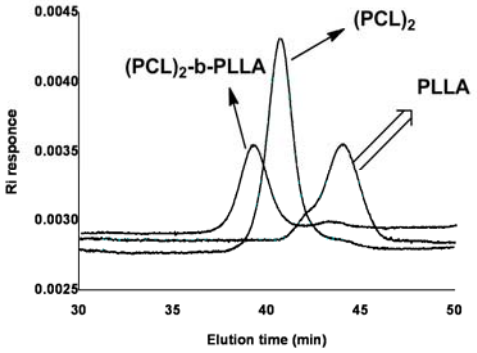


Figure 5b.23: GPC traces of A) azido functionalized PLLA B) mid-chain mono-propargyloxy functionalized poly ε-caprolactone C) $(PCL)_2$-PLLA miktoarm copolymer

5b.4.2.2.2.1. Crystallinity study

Crystallinity of the miktoarm copolymers was investigated by WAXD and DSC. As shown in **Figure 5b.24 a,b**, WAXD patterns of PLLA and PCL showed prominent diffraction peaks at $2\theta = 19.1, 23.4^O$, and $2\theta = 21.4, 23.8^O$, respectively. In case of $(PCL_{14})_2$-$PLLA_{39}$ miktoarm copolymers, peaks related to both PCL and PLLA semi-crystalline domains were clearly observed (**Figure 5b.24c**) suggesting semi-crystalline nature of miktoarm copolymer.

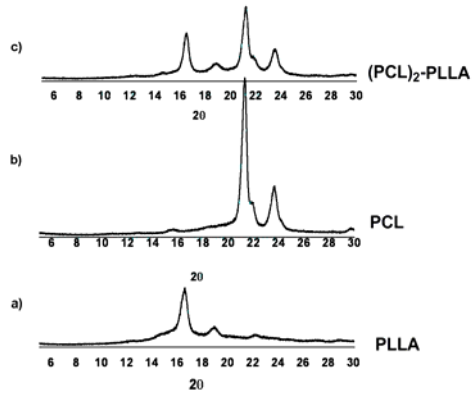


Figure 5b. 24: WAXD patterns of A) azido functionalized PLLA B) mid-chain mono-propargyloxy functionalized poly ε- caprolactone C) $(PCL_{14})_2$-$PLLA_{39}$ miktoarm copolymer

5b.4.2.2.2.2. Differential scanning calorimetric studies

DSC curves of $(PCL_{14})_2$-$PLLA_{39}$ copolymer are shown in **Figure 5b.25**. Melting peaks with Tm of 132.20 and 50.92 °C for PLLA and PCL, respectively and two exothermic peaks related to crystallization temperature were observed at 82.85 and 24.37 °C for PLLA and PCL, respectively suggesting that two distinct crystalline domains existed in the copolymer, which was consistent with the WAXD data.

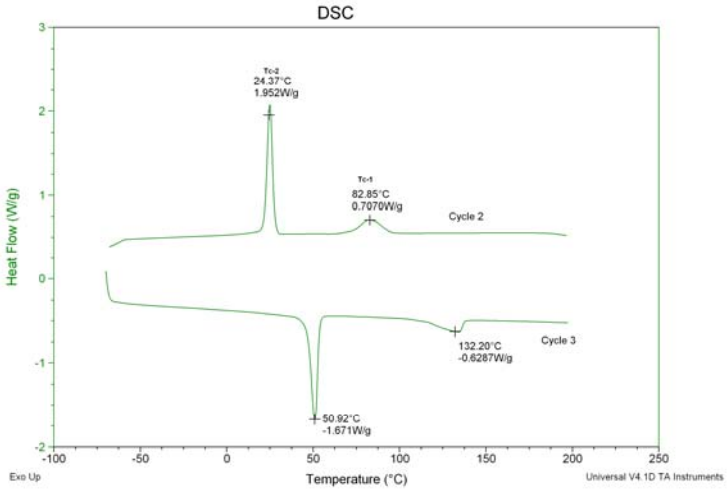


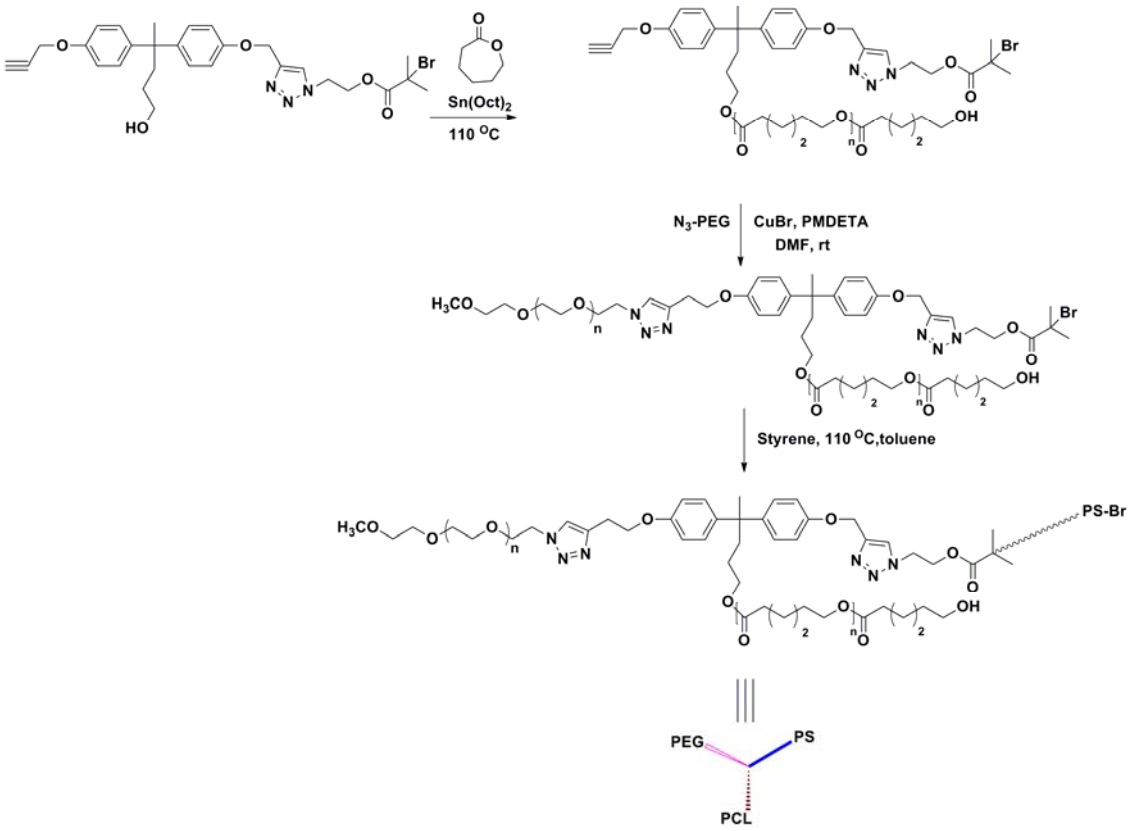
Figure 5b.25: DSC curves of $(PCL_{14})_2$ – $PLLA_{39}$ during cooling (cycle-2) and heating cycles (cycle-3)

5b.4.3. Miktoarm copolymer synthesis by core-first and coupling method approach

5b.4.3.1. Synthesis of PCL-PEG-PS miktoarm copolymers

5b.4.3.1.1. Synthesis of poly ε-caprolactone macroinitiator containing propargyloxy functionality and ATRP initiating site

ROP of ε-caprolactone was carried out using ABC-type MFI-core Br-Ini-(OH)-propargyloxy as the initiator (**Scheme 5b.15).**



Scheme 5b.15: Synthesis of ABC- type PCL-PEG-PS miktoarm copolymer

The reaction conditions and results of synthesis of poly ε-caprolactones macroinitiator containing propargyloxy functionality and ATRP initiating site are summarized in **Table 5b.15.**

Table 5b.15: Reaction conditions and results for synthesis of PCL-based macro initiators using ABC-type MFI core

Sr. No.	$[M]_O/[I]_O$	Time (h)	[a]Conv. (%)	M_n			M_w/M_n
				[b]Theo	^{1}H-NMR	[c]GPC	
1	100	12	62	7700	10200	17500	1.43
2	200	20	67	15900	19800	26200	1.47

Temperature: 110 °C, Solvent: Toluene

[Initiator] / $[Sn(Oct)_2]$ = 200.

a- % Conv. = gravimetric

b- $M_{n\ Theo} = \frac{[M]_O}{[I]_O} \times$ % conv. x mol. wt. of monomer + mol. wt. of initiator (583)

c- GPC- PS standard

Two different ratios of $[M_0]$ / $[I_0]$ were chosen so as to obtain poly ε-caprolactones with different molecular weights. The conversions were determined by gravimetric analysis. Molecular weights of poly ε-caprolactones ($M_{n,\ NMR}$: 10200 and 19800) were in close agreement with the molecular weights calculated from the monomer-to-initiator ratio. In addition, GPC traces revealed monomodal distribution with PDI values of 1.43 and 1.47 for poly ε-caprolactones. **Figure 5b.26** shows ^{1}H-NMR spectra of trifunctional initiator core Br-Init-(OH)-propargyloxy and poly ε-caprolactone macroinitiator. ^{1}H-NMR spectra clearly exhibited peaks related to initiator fragment and poly ε-caprolactone. The appearance of peaks at 7.78 ppm and 7.12-6.85 ppm confirmed the presence of triazole and aromatic ring protons from MFI-core, respectively.

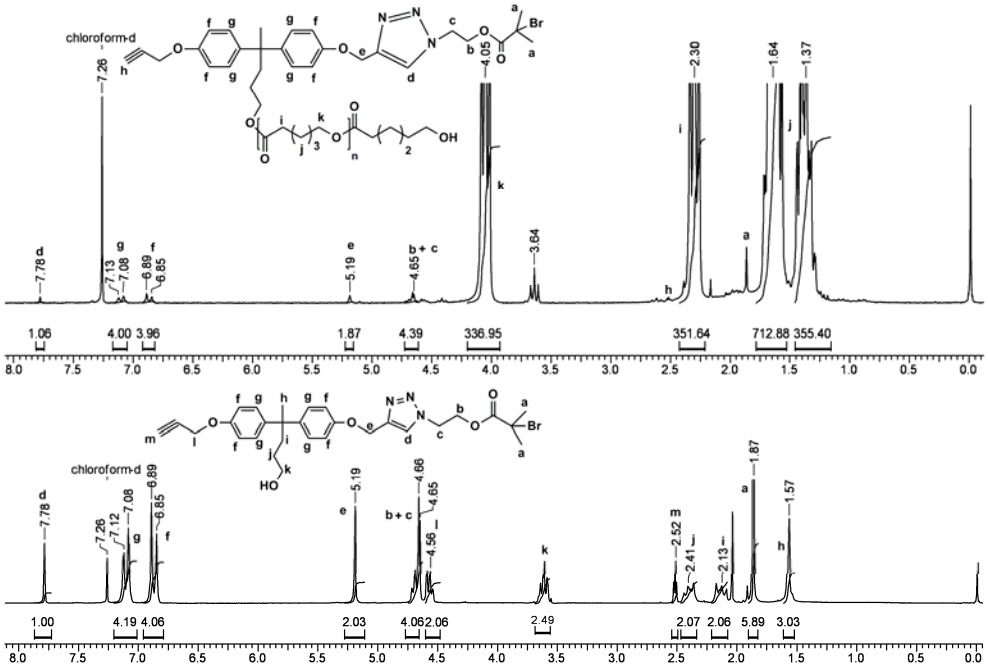


Figure 5b.26: ^{1}H-NMR spectra of A) MFI-core Br-Ini-(OH)-propargyloxy

B) poly ε-caprolactone macro initiator in $CDCl_3$

$M_{n,NMR}$, of PCL-based macroinitiators was determined by comparing the intensity of OCH_2 peak at 4.05 ppm in poly ε-caprolactone to the peaks belonging to aromatic protons from MFI-core.

Calculations of $M_{n,NMR}$ for PCL- macroinitiator

$$= \left\{ \frac{IA_k}{2} \times \frac{1}{IA_d} \right\} \times \text{mol. wt. of monomer (114)} + \text{mol. wt. of initiator (583)}$$

5b.4.3.1.2. Preparation of azido functionalized PEG-(PEG-N_3)

Synthesis of azide-end functionalized PEGs has been discussed in **section 5b.4.2.1.2**

5b.4.3.1.3. Click reaction between PEG-N_3 and propargyloxy functionalized poly ε-caprolactone macroinitiator

''Click'' chemistry strategy was used to prepare PEG-PCL macroinitiator. Click reaction was performed between poly ε-caprolactones with a propargyloxy functionality and azide end-functionalized PEG (M_n-1000) using CuBr/PMDETA as catalyst system in DMF at r.t. following the reported procedure[44] (**Scheme 5b.15**). 1.2 Equivalent of PEG was taken so as to ensure completion of cycloaddtion reaction. After the coupling reaction, the catalyst was removed by passing through a column of neutral alumina and the polymer was isolated by precipitation. After ''click'' reaction, unreacted azide end functionalized PEG was removed by dialysis[51]. Results for

preparation of PEG-PCL macroinitiators *via* ''click'' cycloaddition reaction are summarized in **Table 5b.16**.

Table 5b.16: Results for synthesis of PEG-PCL macro initiators

Sr. No.	Propargyloxy functionalized PCL	Azido functionalized PEG	M_n			M_w/M_n
			Theo	^{1}H-NMR	GPC	
1	10200	1100	11300	11100	9800	1.44
2	19800	1100	20800	20724	13600	1.49

Representative ^{1}H- NMR spectrum of PCL-PEG macroinitiator is shown in **Figure 5b.27.** $M_{n,NMR}$ of PCL-PEG macroinitiators were determined by comparing the intensity the OCH_2 peak at 4.05 ppm from poly ε-caprolactone and intensity of peak at 3.65 ppm due to OCH_2CH_2O of PEG-arm.

Calculations of $M_{n,NMR}$ for macroinitiator (PCL)-PEG macroinitiator

$$= \left\{ \frac{IA_e}{2} \text{ x x mol. wt. of monomer (114)} + \frac{IA_a}{4} \text{ x mol. wt. of monomer (44)} \right\}$$

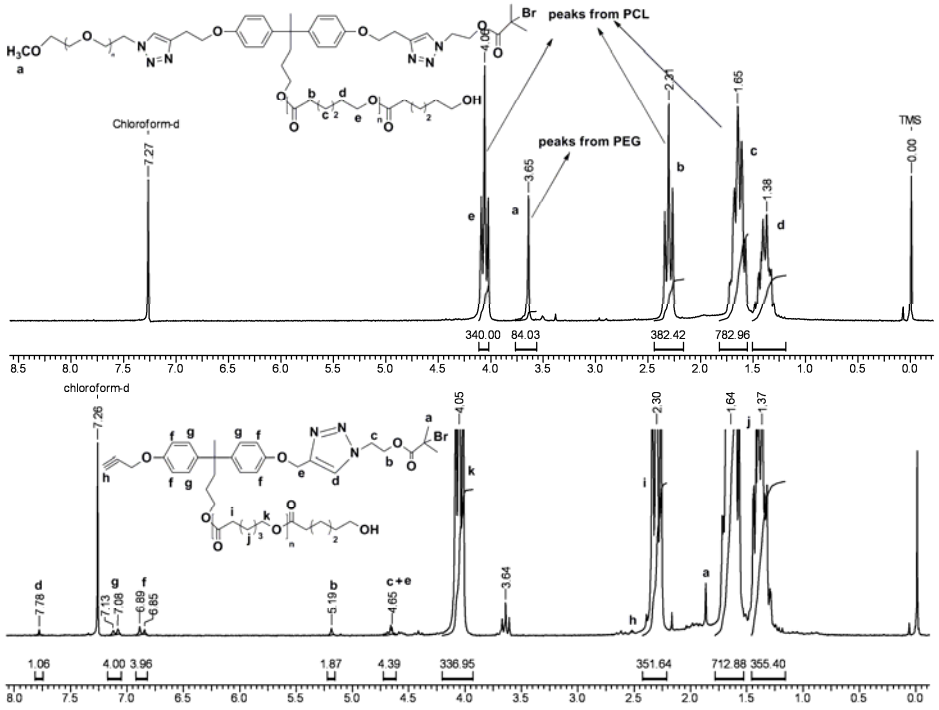


Figure 5b. 27: ^{1}H-NMR spectra of A) poly ε-caprolactone macroinitiator containing propargyloxy functional group and ATRP initiating site B) PCL-PEG macro initiator containing ATRP initiating site in $CDCl_3$

GPC data revealed molecular weight distribution values of 1.44 and 1.49 for PCL-PEG macroinitiator (**Figure 5b.28**). As compared to $M_{n,NMR}$, $M_{n,GPC}$ values were found to be lower which may be due to the different interactions of the amphilic chain with the GPC column.

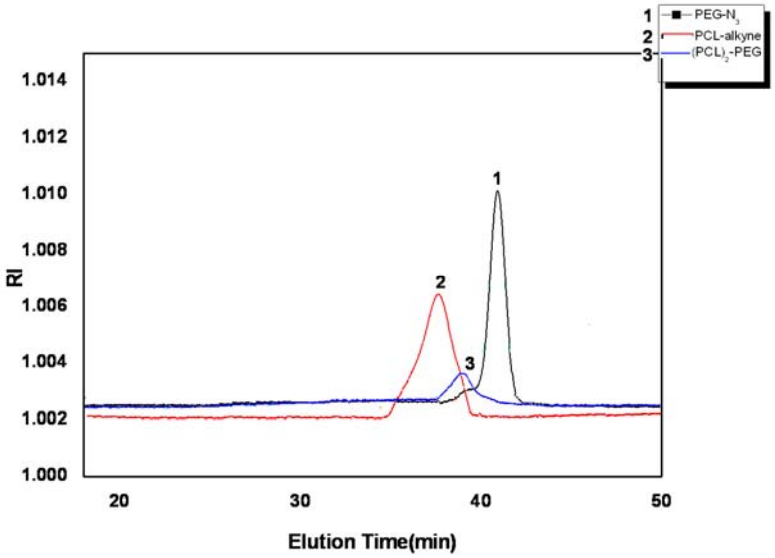


Figure 5b.28: GPC traces of 1) PEG-N_3 2) propargyloxy functionalized poly ε-caprolactone macro initiator 3) PCL-PEG-macro initiator

5b.4.3.1.4. Synthesis of ABC-type PCL-PEG-PS miktoarm copolymers

As depicted in **Scheme 5b.12** PCL-PEG-Br was employed as macroinitiator for the ATRP polymerization of styrene in toluene at 110 °C using CuBr/PMDETA complex as the catalyst. Results obtained for synthesis of PCL-PEG-PS miktoarm copolymers are included in **Table 5b.17.**

Table 5b.17: Results for synthesis of ABC-type PCL-PEG-PS miktoarm copolymers

Sr. No.	Macroinitiator (Mn by NMR)	Time (h)	$[M]_O/[I]_O/$ [Cu]/[L]	Conv (%)	Mn			Mw/ Mn	Miktoarm copolymer
					Theo	^{1}H-NMR	GPC		
1	PCL-PEG (20800)	8	225:1:1:1	50	32200	36500	48600	1.58	PCL_{173}-PEG_{21}-PS_{150}
2	PCL-PEG (20800)	14	450:1:1:1	44	41500	48000	63200	1.52	PCL_{173}-PEG_{21}-PS_{260}

$[M]_O$ / $[I]_O$/ [Cu]/[L]= [Monomer]:[Macroinitiator]:[CuBr]:[Ligand]

% Conv = Gravimetric

$M_{n\ theo}$ = $[M]_O$/ $[I]_O$ x % conv x mol. wt . monomer + mol. wt. macroinitiator

$M_{n\ GPC}$ = PS standard

^{1}H-NMR spectrum of PCL-PEG-PS is reproduced in **Figures 5b. 29.** NMR spectrum exhibited resonances corresponding to PS, PEG and PCL arms. The DP of the polystyrene branch of PCL-PEG-PS miktoarm copolymers was determined by comparing the integral intensity ratio of peaks at δ= 7.05-6.48 ppm due to aromatic protons of polystyrene and that of peak at δ = 4.06 ppm corresponding to OCH_2 of PCL chain.

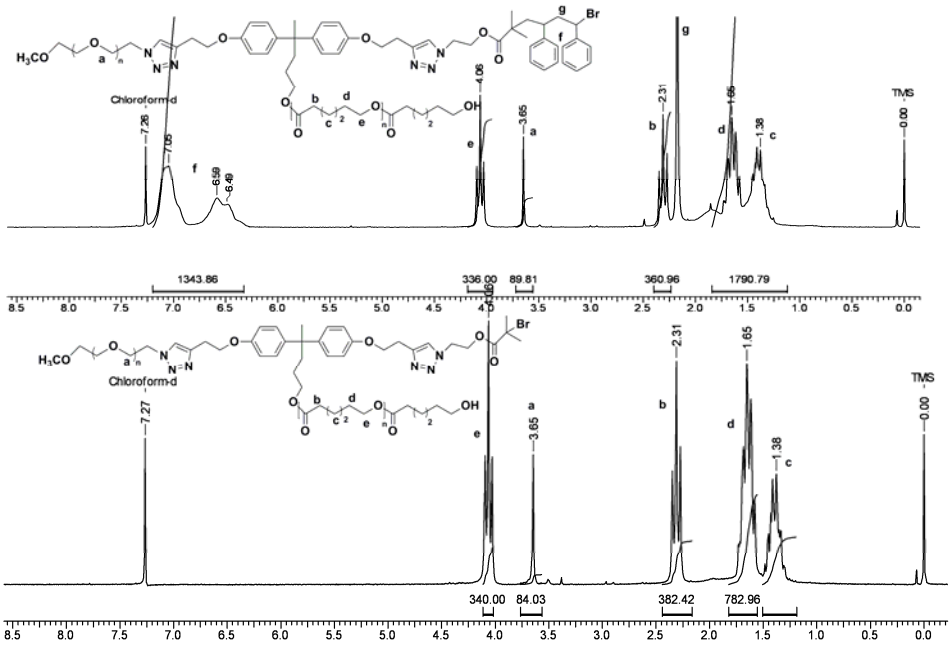


Figure 5b.29: ^{1}H-NMR spectra of A) PCL-PEG containing propargyl functionality

B) ABC-type PCL_{173}-PEG_{21}-PS_{260} miktoarm copolymer in $CDCl_3$

GPC data indicated molecular weight distribution values of 1.52 and 1.58 for PCL-PEG-PS **(Figure 5b.30)** and molecular weights were found to be higher than determined by ^{1}H-NMR which may be due to different interactions of the amphiphilic chain segment with GPC column.

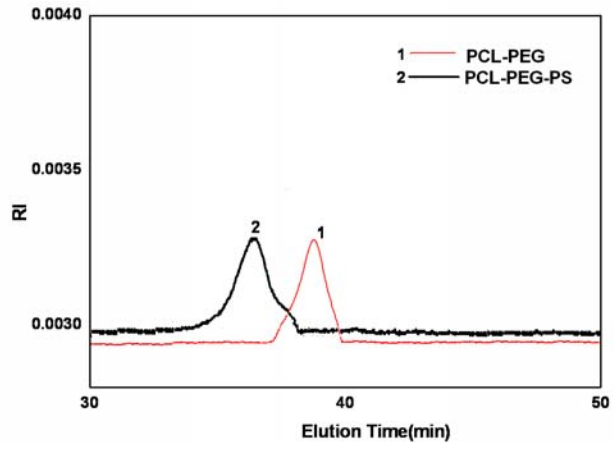


Figure 5b.30: GPC traces of 1) PCL-PEG-Br 2) PCL-PEG-PS miktoarm copolymer

5b.4.3.1.4.1. Crystallinity study

Crystallinity study of miktoarm copolymers was investigated using WAXD measurements. As shown in **Figure 5b.31**, WAXD pattern of PCL-PEG copolymers **Figure 5b.31a** showed prominent diffraction peaks at 2θ = 19.1, 21.4 and 23.8^{O} suggesting semi-

crystallinity. As ATRP of styrene was carried out and as the polystyrene content in miktoarm copolymer PCL-PEG-PS increases, it was observed that amorphous phase of polystyrene restricted the crystallization of both PCL and PEG chains and as a result, there was loss of crystallinity as evidenced by hollow broad peak (**Figure 5b.31b)**.

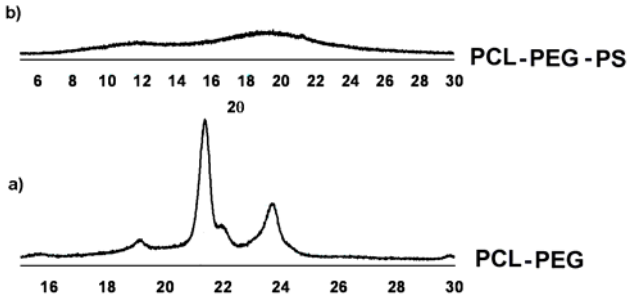


Figure 5b. 31: WAXD patterns of A) PCL-PEG macro initiator B) ABC- type PCL_{173}-PEG_{21}-PS_{260} miktoarm copolymer

5b.4.3.1.4.2. Differential scanning calorimetric studies

Thermal properties of PCL_{173}-PEG_{21}- PS_{260} miktoarm copolymer were investigated by DSC at a heating rate of 10 °C/min under nitrogen atmosphere. As observed in **Figure 5b.32**, melting transitions at 54 and 57 °C were observed which may belong to the PEG and PCL segments, respectively.

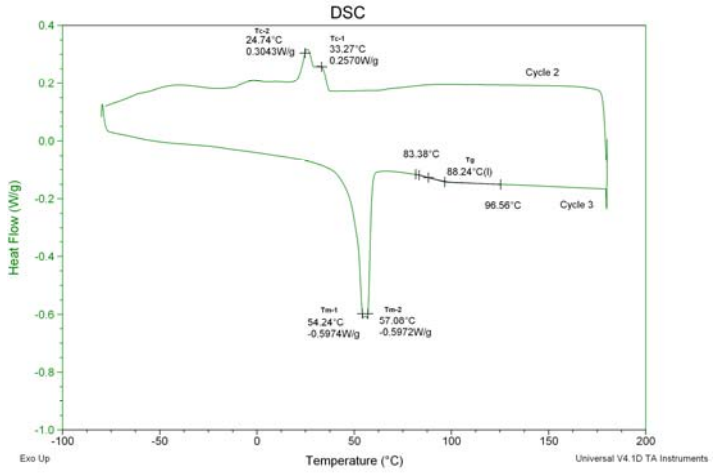


Figure 5b.32: DSC curves of PCL_{173}-PEG_{21}-PS_{260} during cooling (cycle-2) and heating cycles (cycle-3)

Two exotherms were observed at 33.27 and 24.74 which could be attributed to crystallization of PEG and PCL, respectively. Only one glass transition temperature (Tg) was detected at around 88 °C evidencing the PS fragment. This value is lower than the expected Tg value of PS (95–105 °C) probably due to the miscibility of the polymer segments. Similar observations were reported in the literature for PCL-PEG-PS system[52].

5b.5 Conclusions

- ✓ Miktoarm copolymers such as A_2B type $(PCL)_2$-PS, $(PCL)_2$-PEG, $(PCL)_2$-PLLA and AB_2 type such as PCL-$(PS)_2$, and PCL-$(PEG)_2$, A_3B type such as $(PCL)_3$-PMMA, and A_2B_2 type $(PCL)_2$-$(PMMA)_2$ were synthesized using MFI-core approach and coupling onto approach. The synthesized miktoarm copolymers were characterized by ^{1}H-NMR spectroscopy.
- ✓ These synthesized fascinating macromolecular architectures are interesting materials for studying their self assembly behavior.
- ✓ Miktoarm star copolymers could be potentially useful as viscosity modifiers, compatibilizers for blends, drug delivery vehicles, etc.

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Chapter 6

Summary and Conclusions

6.1 Summary and Conclusions

The synthesis of chain-end-functionalized polymers is of great importance due to their various practical and potential applications such as adhesives, sealants, reactive compatibilizers, etc. One of the most important applications of end-functionalized polymers is their demonstrated utility as building blocks for synthesis of block, graft and star copolymers.

The overall goal of the present work was to design and synthesize functionalized polymers and miktoarm copolymers. Towards this end, functionalized initiators for ROP and ATRP and MFI-cores for preparation of miktoarm copolymers were synthesized starting from commercially available precursors *viz,* 4, 4'-bis (4-hydroxyphenyl) pentanoic acid, which in turn is derived from levulinic acid- a platform chemical obtained from biomass- and 5-hydroxy isophthalic acid. The second objective of the work was to utilize these ROP and ATRP initiators for synthesis of functionally-terminated polymers and macromonomers. The third objective was to synthesize MFI cores and utilize *via* ATRP in combination with ROP and click chemistry or ROP in combination with click chemistry to synthesize miktoarm star copolymers using core-first and coupling method approach, respectively.

Starting from commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid, the following seven new α, α'-homo and α, α'-hetero bifunctionalized initiators for ROP (Serial Nos i-vii) and five new ATRP initiators (Serial Nos viii- xii) were synthesized,

i) 4, 4'-Bis (4-(allyloxy) phenyl) pentan-1-ol

ii) 4, 4'-(((5-Hydroxypentane-2, 2-diyl) bis (4, 1-phenylene))bis(oxy))dibenzaldehyde

iii) 4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol

iv) 4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentan-1-ol

v) 4-(4-(2-(4-(Allyloxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde

vi) 4-(4-(Allyloxy) phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol

vii) 4-(4-(2-(4-(2-Azidoethoxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde

viii) 4, 4'-Bis (4-(allyloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

ix) 4, 4'-Bis (4-(4-formylphenoxy) phenyl) pentyl 2-bromopropanoate

x) 4, 4'-Bis (4- (prop-2-yn-1-yloxy) phenyl) pentyl 2-bromo-2-methylpropanoate

xi) 4, 4'-Bis (4-(2-azidoethoxy) phenyl) pentyl 2-bromopropanoate, and

xii) 4-(4-(Allyloxy) phenyl)-4-(4-(4-formylphenoxy) phenyl) pentyl 2-bromo-2-methyl propanoate

Thus, a total of twelve functionalized initiators were designed and synthesized. All initiators were characterized by FTIR, ^{1}H-NMR and ^{13}C-NMR spectroscopy.

These functionalized initiators were utilized in the synthesis of end-functionalized polymers such as poly ε-caprolactones, poly (methyl methacrylate)s and polystyrenes. The

reactivity of functional groups on polymers was demonstrated by carrying out specific reactions of the respective functional group.

α,α'- Bis-allyloxy functionalized poly ε-caprolactones ($M_{n,GPC}$ – 6000 to 19400, M_w/M_n =1.33-1.46) were synthesized by ROP of ε-caprolactone using 4,4'-bis(4-(allyloxy)phenyl)pentan-1-ol as initiator in the presence of Sn $(Oct)_2$ in toluene. Reactivity of allyloxy functionality was demonstrated by carrying out epoxidation and thiol-ene click reaction.

α,α'- Bis-allyloxy functionalized poly (methyl methacrylate)s and polystyrenes were synthesized by ATRP of methyl methacrylate and styrene, respectively using 4,4'-bis(4-(allyloxy)phenyl)pentyl 2-bromo-2-methylpropanoate as initiator in the presence of CuBr/PMDETA as a catalyst. α,α'- Bis-allyloxy functionalized poly (methyl methacrylate)s with different molecular weights ($M_{n,GPC}$ – 10100 to 18500 with M_w/M_n = 1.23 - 1.34) were synthesized and initiator efficiency was found to be in the range 0.76 to 0.98. The kinetic study of methyl methacrylate polymerization revealed controlled polymerization behavior. α,α'- Bis-allyloxy functionalized polystyrenes with different molecular weights ($M_{n,GPC}$ – 13600 to 28300 with M_w/M_n = 1.06 - 1.09) were prepared. Initiator efficiency was found to be in the range 0.83 to 0.94. Reactivity of allyloxy functionality was demonstrated by carrying out bromination, epoxidation and hydrosilylation reaction.

α,α'- Bis-aldehyde functionalized poly ε-caprolactones ($M_{n,GPC}$ – 2600 to 19400, M_w/M_n =1.33-1.47) were synthesized using 4,4'-(((5-hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde as the initiator. Reactivity of aldehyde functionality was demonstrated by carrying out aldehyde-aminooxy click reaction.

α,α'- Bis-aldehyde functionalized polystyrenes were synthesized by ATRP of styrene using 4,4'-bis(4-(4-formylphenoxy)phenyl)pentyl 2-bromopropanoate as initiator in the presence of CuBr/PMDETA as a catalyst. Bis-aldehyde terminated polystyrenes with different molecular weights ($M_{n,GPC}$ –3800 to 28200 with M_w/M_n = 1.11 - 1.16) were synthesized. Initiator efficiency was found to be in the range 0.85 to 0.93. The kinetic study of styrene polymerization revealed controlled polymerization behavior.

α,α'- Bis propargyloxy functionalized poly ε-caprolactones ($M_{n,GPC}$ – 5900 to 13500, M_w/M_n =1.24-1.33) were synthesized using 4,4'-bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol as initiator for ROP of ε-caprolactone in the presence of PMDETA. Reactivity of propargyloxy functionality was demonstrated by carrying out propargyloxy-azido click reaction with 2-azidoethyl 4-methylbenzenesulfonate.

4, 4'-Bis (4-(prop-2-yn-1-yloxy) phenyl)pentyl 2-bromo-2-methylpropanoate was studied as the ATRP initiator for polymerization of methyl methacrylate which resulted into poor control over molecular weight and broader molecular weight distribution of PMMA. The deviation from the controlled radical polymerization behavior could apparently be due to involvement of

propargyloxy group in some side reactions. Further studies such as MALDI-TOF analysis of α,α'-bis propargyloxy functionalized poly (methyl methacrylate)s are warranted.

α,α'- Bis-azido functionalized poly ε-caprolactones ($M_{n,GPC}$ – 5400 to 18600, M_w/M_n =1.24-1.33) were synthesized using 4, 4'-bis (4-(2-azidoethoxy) phenyl) pentan-1-ol as initiator for ROP of ε-caprolactone . Reactivity of azido functionality was demonstrated by carrying out azide-alkyne click reaction with phenyl acetylene.

α,α'- Bis-azido functionalized poly (methyl methacrylate)s were synthesized by ATRP using 4,4'-bis(4-(4-formylphenoxy)phenyl)pentyl 2-bromopropanoate as initiator in the presence of CuBr/PMDETA at 80 °C in anisole. α, α'- Bis-azido functionalized poly (methyl methacrylate)s with different molecular weights ($M_{n,GPC}$ –8200 to 26000 with M_w/M_n = 1.17 - 1.28) were synthesized and initiator efficiency was found to be in the range 0.77 to 0.83. The kinetic study of methyl methacrylate polymerization revealed controlled polymerization behavior. Reactivity of azido functionality was demonstrated by carrying out azide-alkyne click reaction with phenyl acetylene.

α-Aldehyde, α'-allyloxy heterobifunctionalized poly ε-caprolactones ($M_{n,GPC}$ – 5900 to 29000, M_w/M_n =1.26-1.43) were synthesized using 4-(4-(2-(4-(allyloxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde as the initiator. Reactivity of aldehyde was demonstrated by carrying out aldehyde-aminooxy click reaction while reactivity of allyloxy functionality was demonstrated by carrying out thiol-ene click reaction.

α-Aldehyde, α'-allyloxy heterobifunctionalized poly (methyl methacrylate)s with different molecular weights ($M_{n,GPC}$ –5300 to 28800 with M_w/M_n = 1.19-1.25) were synthesized using 4-4-(allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methylpropanoate as the initiator and initiator efficiency was found to be in the range 0.71 to 0.89. The kinetic study of methyl methacrylate polymerization revealed controlled polymerization behavior. Reactivity of aldehyde functionality was demonstrated by carrying out aldehyde-aminooxy click reaction while reactivity of allyloxy functionality was demonstrated by carrying out thiol-ene click reaction.

α-Allyloxy, α'-azido heterobifunctional poly ε-caprolactones ($M_{n,GPC}$ – 5900 to 10500, M_w/M_n =1.34-1.43) were synthesized using 4-(4-(allyloxy)phenyl)-4-(4-(2-azidoethoxy)phenyl)pentan-1-ol as the initiator for ROP of ε-caprolactone. Reactivity of azido group was demonstrated by carrying out azido-propargyloxy click reaction while reactivity of allyloxy functionality was demonstrated by thiol-ene click reaction.

α-Aldehyde, α'- azido heterobifunctionalized poly ε-caprolactones ($M_{n,GPC}$ – 5900 to 13500, M_w/M_n =1.21-1.36) were synthesized using 4-(4-(2-(4-(2-azidoethoxy) phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde as the initiator for ROP of ε-caprolactone. Reactivity of aldehyde functionality was demonstrated by carrying out aldehyde-aminooxy click reaction

while reactivity of azido functionality was demonstrated by carrying out azido-propargyloxy click reaction.

Thus, the synthesized α, α'-homo and α, α'-hetero bifunctionalized initiators were found to be useful for ROP and ATRP leading to the formation of corresponding end-functional polymers.

Miktoarm star polymers (sometimes called asymmetric star polymers, heteroarm star polymers, or simply miktoarm polymers) are star-shaped polymers where number of various types of polymer arms emanates from a core. Miktoarm star copolymers are a synthetically challenging class of polymers. Synthesis of miktoarm star copolymers was carried out using two approaches: 1) Core-first and 2) Coupling method approach

Starting from two common precursors, *viz*; 4,4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid, five new multifunctional initiator (MFI) cores possessing different types and specific number of initiating sites were synthesized using a combination of simple organic transformations and click chemistry for the core-first approach,. Thus, MFI cores such as

i) AB_2-type trifunctional initiator core-OH-Ini-$(Br)_2$

ii**)** A_2B-type trifunctional initiator core $(OH)_2$-Ini-Br

iii) ABC-type trifunctional initiator core Br-Ini-(OH)-propargyl

iv) A_2B_2 - type tetra functional initiator core $(OH)_2$-Ini-$(Br)_2$, and

v) A_3B-type tetra functional initiator core $(OH)_3$-Ini-Br

were synthesized and characterized using FT-IR and NMR-spectroscopy.

Core-first approach was exploited to prepare miktoarm copolymers. Using appropriate MFI core, different molecular weight PCL-macro initiators were synthesized by ROP of ε-caprolactone possessing different number of ATRP initiating sites. Furthermore, these macroinitiators were used for ATRP of styrene and methyl methacrylate in order to prepare miktoarm copolymers such as $(PCL)_2$-PS, PCL-$(PS)_2$, and $(PCL)_2$-$(PMMA)_2$, $(PCL)_3$-PMMA, respectively. Miktoarm copolymers were characterized FT-IR and ^{1}H-NMR spectroscopy and SEC. Thermal properties were studied by DSC and crystallization study was performed using WAXD and it was concluded that crystallization of poly ε-caprolactone arm was restricted by amorphous phase of polystyrene arm.

Coupling onto approach was utilized to prepare miktoarm copolymers such as $(PCL)_2$-PEG, PCL-$(PEG)_2$, and $(PCL)_2$-PLLA. Mono and bis-propargyloxy functionalized PCLs having different molecular weights were synthesized by ROP of ε-caprolactone using 5-prop-2-yn-1-yloxy)-1, 3-phenylene) dimethanol and 4, 4'-bis (4-(prop-2-yn-1-yloxy) phenyl) pentan-1-ol as the initiators, respectively. In a separate step, azido functionalized PEG and PLLA possessing different molecular weights were prepared by chemical modification of commercially available

PEG with monohydroxyl end group (mPEG) and ROP of (+) LLA using azidoethanol as initiator, respectively. Click reaction was employed to couple

propargyloxy functionalized PCLs with azido terminated PEG or PLLA to yield miktoarm copolymers such as $(PCL)_2$-PEG, $(PCL)_2$-PLLA and PCL-$(PEG)_2$. Miktoarm copolymers were characterized FT-IR and ^{1}H-NMR spectroscopy and SEC. Thermal properties were studied by DSC and crystallization study was performed using WAXD. From these studies it was concluded that $(PCL)_2$-PEG, $(PCL)_2$-PLLA and PCL-$(PEG)_2$ contains semi-crystalline domains

Core-first and coupling onto approach was employed to synthesize ABC-type PCL-PEG-PS miktoarm copolymers. Initially, propargyloxy functionalized PCL was prepared by ROP of ε-caprolactone and then it was coupled with azido terminated PEG to yield PCL-PEG copolymer. ATRP of styrene was carried out to synthesize ABC-type PCL-PEG-PS copolymers. Miktoarm copolymers were characterized FT-IR and ^{1}H-NMR spectroscopy and SEC. Thermal properties were studied by DSC and crystallization study was performed using WAXD. From these studies it was observed that (PCL)-PEG, copolymer was crystalline in nature while (PCL)-PEG-PS miktoarm copolymer was found to be amorphous.

Thus, synthesis of different types of miktoarm copolymers such as A_2B type $(PCL)_2$-PS, $(PCL)_2$-PEG, $(PCL)_2$-PLLA and AB_2 type PCL-$(PEG)_2$, PCL-$(PS)_2$, Y-shaped miktoarm copolymers, A_3B type as $(PCL)_3$- PMMA, A_2B_2 type $(PCL)_2$-$(PMMA)_2$ was carried out by employing MFI-core approach and coupling onto approach. The structures of the synthesized polymers were confirmed by ^{1}H-NMR spectroscopy.

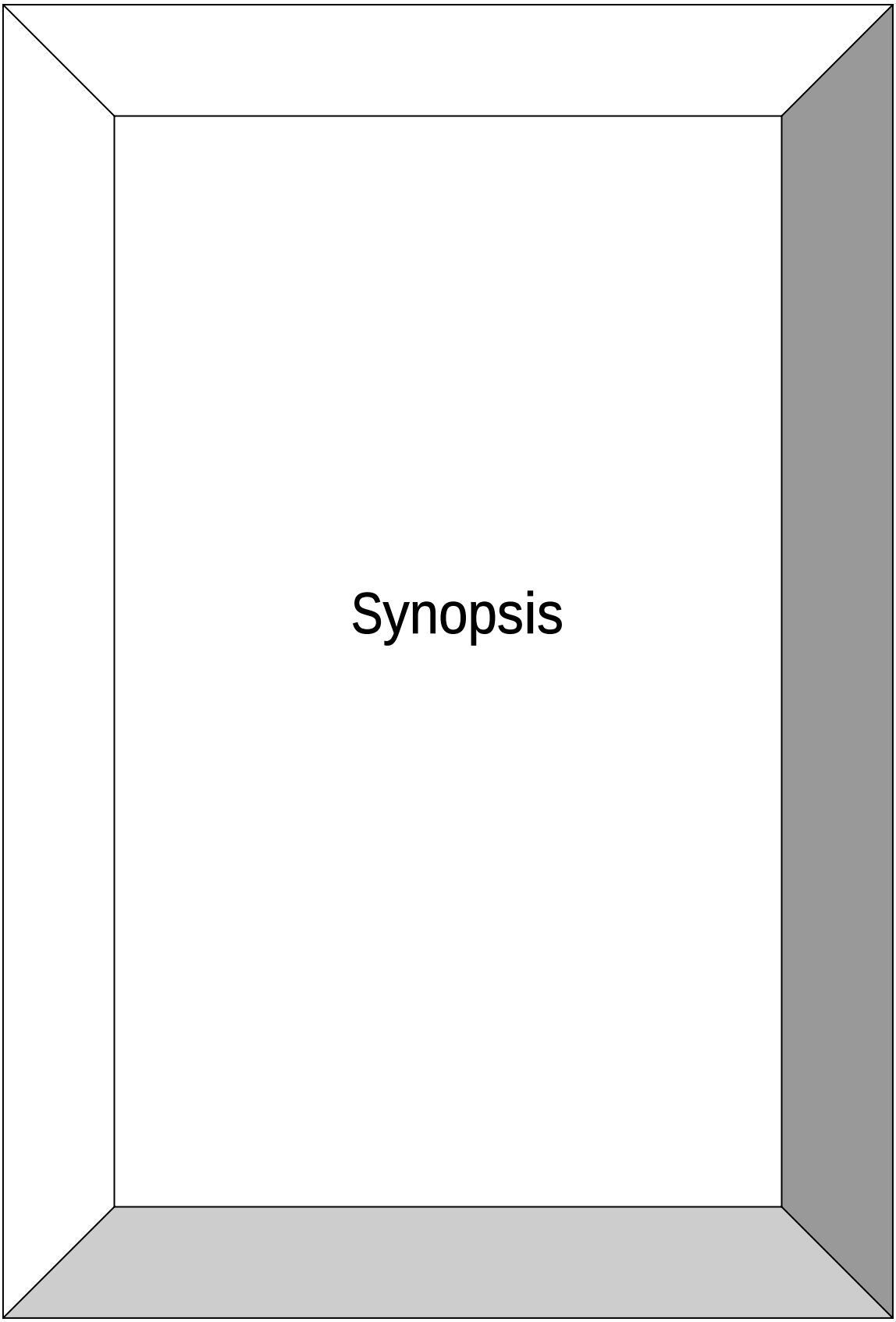
6.2 Perspectives:

The present work on design and synthesis of new functionalized initiators, end-fuctionalized polymers and miktoarm copolymers has opened up many new prospects for the future work.

- The present work on synthesis of new functionalized initiators for ROP and ATRP has expanded the range of functionalities available for the synthesis of end-functionalized polymers and macromonomers.
- The synthesized α, α'- homo- and α, α'- hetero bi functional initiators should be applicable to a variety of monomers capable of undergoing ROP and ATRP.
- Initiators containing α, α'-homo bifunctional groups are potentially useful condensation monomers for synthesis of step growth polymers by polycondensation with appropriate comonomers. Step growth polymers, thus obtained, would contain pendant initiating sites which could be further exploited for preparation of graft copolymers
- Poly ε-caprolactones, polystyrenes and poly (methyl methacrylate)s possessing clickable end functional groups represent valuable precursors for synthesis of a library of Y-shaped

miktoarm star copolymers by judicious choice of polymers possessing complimentary clickable functional groups.

- These synthesized fascinating macromolecular architectures could show some interesting properties, such as self assembly. Thus, further studies are needed to cram self assembly properties and applications of such materials.
- Mikto arm star copolymers could be potentially useful as viscosity modifiers, compatibilizers for blends, drug delivery vehicles, etc.


Synopsis

Synopsis of the Thesis Entitled

"Designed Macromolecular Architectures by Controlled Polymerization Methods"

Introduction

The exploration of synthetic methods to obtain macromolecules with predetermined molecular weight, narrow molecular weight distribution and well-defined architectures has been an active area of research for many years. The discovery of living anionic polymerization by Szwarc facilitated major developments in both synthetic polymer chemistry and polymer physics as it opened an avenue to the production of well-defined polymers with precisely designed molecular architectures and nano-structured morphologiess[1].This ground-breaking discovery inspired many researchers to develop controlled/living routes for a plethora of monomers including those not compatible with anionic polymerization. These methods and their combinations serve as an arsenal for the synthesis of well-defined polymeric materials with predetermined properties and a rich variety of applications [2].

End-functionalized polymers are a type of functional polymers and are the most important materials due to their potential applications in several areas [3]**.** More specifically, end-functionalized polymers are useful as building blocks for synthesis of block, graft and star copolymers. These polymers also have potential applications in areas such as surface modification, coatings, adhesives, as well as compatibilization of polymer blends[4]. A star polymer is a branched polymer in which a single branch point gives rise to multiple linear chains or arms. If the arms are identical the star polymer is said to be regular or homo-star polymer. If arms are composed of different repeating subunits, the star polymer molecule is said to be hetero or miktoarm copolymer. Great attention has been paid to the design and synthesis of miktoarm star copolymers due to their unique morphological and physical properties compared to their linear counterparts. Miktoarm star copolymers are mainly categorized by their three main synthesis techniques: core-first [5 6 7 8 9] coupling onto [10 11 12] and arm- first [13].

End functional polymers and miktoarm copolymers could be assessed using different techniques such as anionic and cationic polymerization but due to stringent reaction conditions and some limitations associated with these techniques, polymer chemists shifted interest to controlled radical polymerization methods such as reversible-addition fragmentation termination (RAFT)[14] nitroxide mediated radical polymerization (NMP),[15, 16], and Atom Transfer Radical Polymerization (ATRP)[17]. Amongst the controlled radical polymerization methods, ATRP is a powerful technique to prepare polymers with predictable molecular weight and narrow polydispersity. The increasing interest in ATRP technique is due to relatively mild reaction conditions and a broad choice of monomers, initiators, catalysts, etc [17-19]. With this controlled

radical polymerization method, a variety of polymer architectures and compositions is accessible, e.g., block copolymers, graft copolymers, and hyperbranched polymers. Functional groups can also be introduced easily at the chain ends either through functionalized ATRP initiators or by postmodification approach such as halogen displacement through nucleophilic substitution [20, 21].

Ring opening polymerization (ROP) is another controlled polymerization technique under specific conditions which is used to synthesize aliphatic polyesters by ring opening of cyclic monomers. Because of various applications, particularly in biomedical field due to their biocompatibility and biodegradability, aliphatic polyesters such as poly ε-caprolactone (PCL), polylactide (PLA), and polyglycolide (PGA) have been the subject of interest. A major limitation to the use of PCL, and other aliphatic polyesters, is the lack of pendant functional groups along the chains. Now-a-days, large efforts are devoted to synthesis of functional aliphatic polyesters in order to tailor a series of properties such as hydrophilicity, mechanical/thermal properties; the functionality is introduced either at the monomer stage or by post polymerization [22].

Since the introduction of click chemistry concept by Sharpless and co-workers in 2001, many academic and industrial scientists have widely explored this innovative approach for the synthesis of functional polymers and star copolymers due to its versatility, efficiency and inertness towards functional groups [23, 24].

The overall objective of the work was to design and synthesize new macromolecular architectures employing controlled polymerization methods. It was of interest to design and synthesize new initiators containing different functional groups for ROP and ATRP as well as different multifunctional initiator (MFI) cores possessing different types and specific number of initiating sites for preparation of miktoarm copolymers. Commercially available 4, 4'-bis (4-hydroxyphenyl) pentanoic acid, which in turn is derived from levulenic acid –a platform chemical obtained from biomass- and 5-hydroxy isophthalic acid were used as the starting materials. Both 4, 4'-bis (4-hydroxyphenyl) pentanoic acid and 5-hydroxy isophthalic acid contain phenolic and acid groups which were effectively utilized in various aspects of chemical transformations for synthesis of the desired initiators. New initiators for ROP and ATRP containing various functional groups such as allyloxy, aldehyde, propargyloxy, and azido were designed and synthesized. These functionalized initiators were utilized for synthesis of end-functional polymers. The MFI-cores were designed and synthesized using simple organic transformations and utilized to obtain miktoarm copolymers (A_2B, AB_2, A_2B_2, and A_3B) *via* combination of suitable polymerization techniques. By keeping the above objectives in mind, the following specific work was selected for the present thesis.

1. Synthesis of functional initiators having functionalities viz., allyloxy, aldehyde, propargyloxy, and azido for ROP.
2. Synthesis of functional initiators containing functional groups viz., allyloxy, aldehyde, propargyloxy, and azido for ATRP
3. Synthesis of poly ε-caprolactones containing different homo as well as hetero functional groups.
4. Synthesis of poly (methyl methacrylate)s and polystyrenes with different homo and hetero end functional groups.
5. Synthesis and characterization of MFI-cores with the use of simple organic reactions and click chemistry.
6. Synthesis and characterization Y-shaped miktoarm copolymers such as AB_2 type PS-$(PCL)_2$, PEG-$(PCL)_2$, and PLLA- $(PCL)_2$. A_2B type $(PS)_2$-(PCL) and $(PEG)_2$- PCL and A_2B_2-type $(PCL)_2$-$(PMMA)_2$, A_3B-type $(PCL)_3$-PMMA.

The thesis has been divided into following six chapters.

Chapter 1: Introduction

This chapter deals with brief introduction to CRP methods, with emphasis on ATRP. Furthermore, brief introduction to Ring Opening Polymerization (ROP) and "Click Chemistry" is presented. The synthesis of end-functionalized polymers and miktoarm copolymers by above mentioned techniques is discussed.

Chapter 2: Scope and Objectives

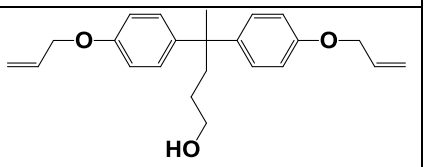
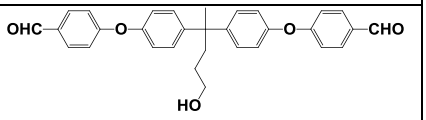
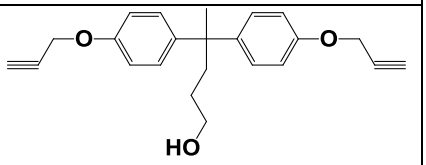
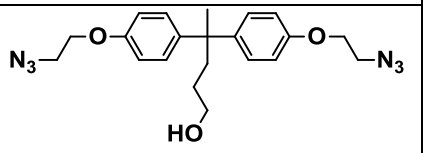
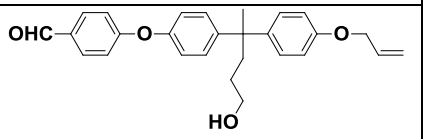
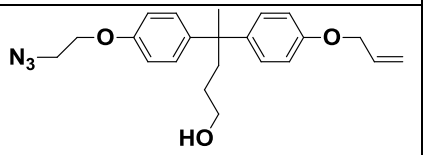
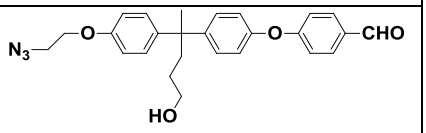
This chapter discusses scope and objectives of the thesis.

Chapter 3: Functional Initiators: Synthesis and Characterization

Chapter 3a: Functional Initiators for ROP: Synthesis and Characterization

This chapter describes synthesis of functionalized initiators for ROP **(Table 1).**

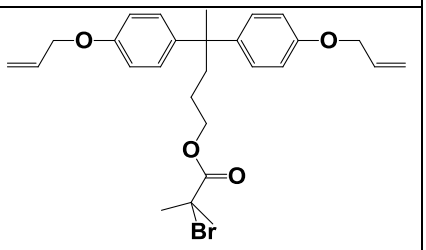
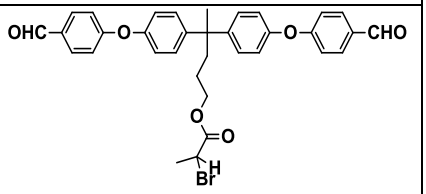
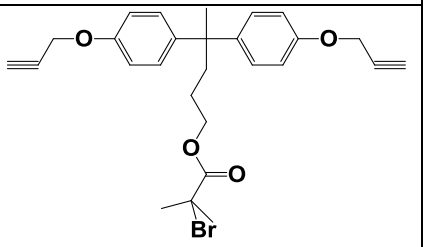
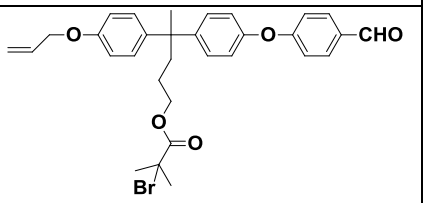
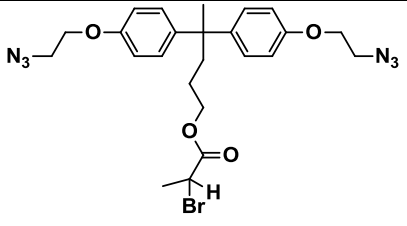
Table 1. Synthesized Functional ROP Initiators

Sr. No.	ROP Initiator	Structure
1	4,4’-Bis(4-(allyloxy)phenyl)pentan-1-ol	
2	4,4'-(((5-Hydroxypentane-2,2-diyl)bis(4,1-phenylene))bis(oxy))dibenzaldehyde	
3	4,4’-Bis(4-(prop-2-yn-1-yloxy)phenyl)pentan-1-ol	
4	4, 4’-Bis (4-(2-azidoethoxy) phenyl) pentan-1-ol	
5	4-(4-(2-(4-(Allyloxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde	
6	4-(4-(Allyloxy)phenyl)-4-(4-(2-azidoethoxy) phenyl) pentan-1-ol	
7	4-(4-(2-(4-(2-Azidoethoxy)phenyl)-5-hydroxypentan-2-yl)phenoxy) benzaldehyde	

Chapter 3b: Functional Initiators for ATRP: Synthesis and Characterization

This chapter describes synthesis of functionalized initiators for ATRP. Five new ATRP initiators were synthesized **(Table 2).**

Table 2. Synthesized Functional ATRP Initiators

Sr. No.	ATRP Initiator	Structure
1	4,4'-Bis(4-(allyloxy)phenyl)pentyl 2-bromo-2-methylpropanoate	
2	4,4'-Bis(4-(4-formylphenoxy)phenyl)pentyl 2-bromopropanoate	
3	4,4'-Bis(4-(prop-2-yn-1-yloxy)phenyl)pentyl 2-bromo-2-methylpropanoate	
4	4-(4-(Allyloxy)phenyl)-4-(4-(4-formylphenoxy)phenyl)pentyl 2-bromo-2-methyl propanoate	
5	4,4'-Bis(4-(2-azidoethoxy)phenyl)pentyl 2-bromopropanoate	

Chapter 4: **End-Functionalized Polymers: Synthesis and Characterization**

Chapter 4a: **End-Functionalized Polymers by ROP: Synthesis, Characterization and Chemical Modification**

This chapter embodies synthesis of different α, α'-homo and α, α' hetero bifunctionalized polymers, viz., allyloxy, aldehyde, azido, and propargyloxy functionalized poly ε-caprolactones, having different molecular weights using appropriate initiators. End-functionalized polymers were characterized by FTIR and NMR spectroscopy and size exclusion chromatography (SEC). End functionality on the polymer was demonstrated by carrying out specific reactions of that particular functional group present on polymer.

Chapter 4b: **End-Functionalized Polymers by ATRP: Synthesis, Characterization and Chemical Modification**

This chapter discribes synthesis of different α, α' -homo and α, α' -hetero bifunctionalized polymers, viz. poly (methyl methacrylate)s and polystyrenes with different molecular weights using appropriate initiators. FTIR, NMR, and SEC techniques were used to characterize end-functionalized polymers. End functionality on the polymer was demonstrated by carrying out specific reactions of that particular functional group present on polymer.

Chapter 5: Miktoarm Star Copolymers: Synthesis and Characterization

Chapter 5a: MFI- Cores for Preparation of Miktoarm Star Copolymers: Synthesis and Characterization

Multifunctional initiator (MFI) cores such as A_2B, AB_2, ABC, AB_3, and A_2B_2 possessing initiating sites for ROP and ATRP were synthesized either starting from 4, 4'-bis (4-hydroxyphenyl) pentanoic acid or 5-hydroxyisophthalic acid. The MFI-cores and the intermediates involved in their synthesis were characterized by FTIR and NMR spectroscopy.

Chapter 5b: Mikto-arm Star Copolymers: Synthesis and Characterization

This Section deals with synthesis and characterization of miktoarm copolymers such as, AB_2 type PCL-$(PS)_2$ and PCL-$(PEG)_2$, A_2B type $(PCL)_2$-PEG, $(PCL)_2$-PS, A_3B type as $(PCL)_3$- PMMA, A_2B_2 type $(PCL)_2$-$(PMMA)_2$ using MFI approach and coupling onto approach. The miktoarm copolymers were characterized NMR spectroscopy and SEC. Thermal properties of miktoarm copolymers were studied by DSC. Crystallization study was performed using wide angle X-ray diffractiometry.

Chapter 6: Summary and Conclusions

This chapter summarizes the results, salient conclusions and future prospects of the work reported in the thesis.

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List of Publications

1) Prakash S. Sane, Bhausaheb V. Tawade, Dnyaneshwar V. Palaskar, Shamal K. Menon, Prakash P. Wadgaonkar:
Aromatic aldehyde functionalized polycaprolactone and polystyrene macromonomers: synthesis, characterization and aldehyde-aminooxy click reaction
***Reactive and Functional polymers; 72, (2012),* 713**

2) Prakash S. Sane, Dnyaneshwar V. Palaskar, Prakash P. Wadgaonkar:
Synthesis of bis-allyloxy functionalized polystyrene and poly (methyl methacrylate) macromonomers using a new ATRP initiator
European Polymer Journal; 47, (2011), 1621

3) Dnyaneshwar V. Palaskar, Prakash S. Sane, Prakash P. Wadgaonkar:
A new ATRP initiator for synthesis of cyclic carbonate-terminated poly (methyl methacrylate)
Reactive and Functional Polymers; 70, (2010) 931

4) Arvind S. More, Prakash S. Sane, Anandrao S. Patil, Prakash P. Wadgaonkar:
Synthesis and characterization of aromatic polyazomethines bearing pendant pentadecyl chains
Polymer Degradation and Stability; 95, (2010), 1727

5) Prakash S. Sane, Bhausaheb V. Tawade, Indravadan A. Parmar, Savita Kumari, Prakash P. Wadgaonkar:
A Facile Strategy for Preparation of α-Heterobifunctional Poly ε-caprolactone and Poly (methyl methacrylate) Containing 'Click Chemistry' Compatible Aldehyde and Allyloxy Functional Groups Using Initiator Approach
Journal of Polymer Science Part-A, Polymer Chemistry (submitted)