ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

DIELS-ALDER REACTION FOR THE PREPARATION OF POLYCARBONATE BLOCK COPOLYMERS

M.Sc. THESIS

Pınar Sinem OMURTAG

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JANUARY 2013

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Pınar Sinem OMURTAG, a **M.Sc.** student of ITU **Graduate School of Science Engineering and Technology** student ID **509111026**, successfully defended the **thesis** entitled "**DIELS-ALDER REACTION FOR THE PREPARATION OF POLYCARBONATE BLOCK COPOLYMERS",** which he/she prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

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Date of Submission : 17 December 2012
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To my precious family,

FOREWORD

This master study has been carried out at Istanbul Technical University, Chemistry Department of Science & Letter Faculty.

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ABBREVIATIONS

^{1}H NMR **:** Hydrogen Nuclear Magnetic Resonance Spectroscopy
^{13}C NMR **:** Carbon Nuclear Magnetic Resonance Spectroscopy
ATRP **:** Atom Transfer Radical Polymerization
CH_2Cl_2 **:** Dichloromethane
$CDCl_3$ **:** Deuterated chloroform
CuAAC **:** Copper catalyzed azide-alkyne cycloaddition
DA **:** Diels-Alder
DMF **:** *N*,*N*-dimethylformamide
ε-CL **:** ε-caprolactone
EtOAc **:** Ethyl acetate
GPC **:** Gel Permeation Chromatography
MWD **:** Molecular Weight Distribution
PCL **:** Poly(ε-caprolactone)
PEG **:** Poly(ethylene glycol)
PC **:** Poly(carbonate)
PMMA : Poly(methylmetacrylate)
PDI **:** Polydispersity Index
PMDETA **:** *N, N, N',N'', N''*-Pentamethyldiethylenetriamine
RAFT **:** Reversible Addition Fragmentation Chain Transfer
NMP **:** Nitroxide Mediated Polymerization
r-DA **:** retro-Diels-Alder
TEA **:** Triethylamine
THF **:** Tetrahydrofuran
UV **:** Ultra Violet

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DIELS-ALDER REACTION FOR THE PREPARATION OF POLYCARBONATE BLOCK COPOLYMERS

SUMMARY

Diels-Alder (DA) reaction is one of the most common reactions used in organic chemistryand invented by Otto Diels and Kurt Alder who recieved the Nobel Prize in 1950 for their discovery [118].The Diels-Alder reaction is a concerted [4π+2π] cycloaddition reaction of a conjugated diene and a dienophile to yield a 6-membered ring. This reaction is one of the most powerful tools used in the synthesis of important organic molecules.

These DA reactions are suitable for green chemistry because of the absance of metal catalyst in reaction medium. DA "click" reactions can be combined with the living /controlled polymerization methods such as RAFT, NMRP, ATRPand ROP. By using simple and efficient DA cycloaddition reactions, linear thermoplastic, thermosetting polymers and telechelic polymers can be synthesized.

Biodegradable polymers have been widely used and have greatly promoted the development of biomedical fields because of their biocompatibility and biodegradability. Synthetic biodegradable polymers have found more versatile and diverse biomedical applications because of their tailorable designs or modifications. Furthermore, aliphatic polycarbonates have good biocompatibility, low toxicity and good biodegradability [112,113]. High molecular weight aliphatic polycarbonates can be prepared by the ROP of cyclic carbonates. Most commonly used degradable materials for the preparation of clinical devices are aliphatic polyesters and copolyesters. From this point, aliphatic polycarbonates are good materials because they have functionalizable side chains (OH, NH_2, COOH, etc.) can easily meet the need for functionalization of biomaterials.

In this study, the Diels-Alder reaction as a modular ligation strategy is applied to the preparation of well-defined polycarbonate (PC)-block copolymers. Well-defined α-anthracene-terminated polycarbonate (PC-anthracene) is prepared using 9-anthracene methanol as an initiator in the ring opening polymerization of benzyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate in CH_2Cl_2 at room temperature for 5 h. Next, well-defined α-furan protected maleimide-terminated poly(ethylene glycol) (PEG_{11}-MI or PEG_{37}-MI), poly(methyl methacrylate) ($PMMA_{26}$-MI), and poly(ε-caprolactone) (PCL_{27}-MI) were clicked with PC-anthracene at reflux temperature of toluene to yield their corresponding PC-based block copolymers (PC-*b*-PEG, PC-*b*-PMMA, and PC-*b*-PCL). The homopolymer precursors and their block copolymers were characterized by using the GPC, NMR and UV analysis.

DIELS-ALDER CLICK TEPKİMELERİ İLE POLİKARBONAT BLOK KOPOLİMERLERİNİN SENTEZİ

ÖZET

Üstün özellikler gösteren ileri polimer malzemelerin sentezi konusunda yoğun çaba harcanmaktadır. Mekanik ve fiziksel özellikleri birarada bulundurmalarından dolayı blok kopolimerler en çok rağbet edilen ileri malzemelerdir. Çok geniş uygulama alanları olmasına karşın, blok kopolimerlerin sentezlenmesi halen bir meseledir.

Kontrollü/ Yaşayan‖ Polimerizasyon yöntemlerinin iyi tanımlanmış ve kompleks yapılı polimerlerin sentezinde birçok açıdan faydalar sağladığı bilinmektedir. Atom transfer radikal polimerleşmesi (ATRP), nitroksit ortamlı radikal polimerleşmesi (NMP), ve tersinir eklenme-ayrılma zincir transfer polimerleşmesi (RAFT) en yaygın kullanım alanı olan Kontrollü/ Yaşayan‖ Polimerizasyon yöntemleridir. Bu üç standart Kontrollü/ Yaşayan‖ Polimerizasyon metodundan ATRP en sık kullanılanıdır.

Kontrollü/ Yaşayan Radikal Polimerizasyon yöntemlerinin arasında Atom Transfer Radikal Polimerizasyonu (ATRP) ve Nitroksit Ortamlı Radikal Polimerizasyonu (NMP) kompleks yapılı polimerlerin sentezinde en etkili yöntemlerdir. ATRP ve NMP metotlarının her ikisi de aktif ve kararlı zincirler arasındaki hızlı dinamik dengeye dayanır ki kontrolü de sağlayan aslında budur. ATRP ve NMP gibi kontrollü polimerizasyon tekniklerinin bir avantajı da elde edilen polimerin molekül ağırlığının ve zincir uç grubu fonksiyonalitesinin kontrol edilebilir olmasıdır. Bu teknikler sayesinde polimer uç gruplarına çok çeşitli fonksiyonellikler kazandırılabilir bu da herhangi bir transformasyon reaksiyonu gerektirmeden iyi tanımlı polimerlerin eldesine izin verir.

On yıl öncesine kadar, blok kopolimerlerin kontrollü olarak sentezinde yaşayan iyonik polimerleşme (anyonik ve katyonik) metotları kullanılmaktaydı. Diğer bir yandan, zor deney koşulları iyonik polimerleşme yöntemlerinin geniş ölçekli kullanımlarını sınırlamıştır. Daha sonraları, polimerden yalnızca blok kopolimerlerin değil aynı zamanda düz zincirli polimerlerden daha karmaşık yapılara kadar olan polimerlerin sentezinde kullanılan kontrollü/yaşayan radikal polimerleşme (C/LRP) yöntemlerinin hızlı büyümesine tanıklık ettiğini görmekteyiz. Son zamanlarda biyolojik olarak uyumluluk, kolay parçalanabilme veya yüksek emilim gibi bazı özelliklere sahip polimerlere olan ilgi artmıştır. Bu polimerler medikal implantlar ve ilaç-taşıma sistemleri gibi biyomedikal ve çevresel uygulama alanlarında kullanılmaktadır. Yüzey erozyonunun bir çeşidi olan biyo çözünür malzemelerin bir çeşidi olan alifatik polikarbonatlar genellikle halka açılma polimerizasyonu (ROP) metoduyla elde edilir. Ayrıca sahip oldukları biyolojik uyumluluk, kolay parçalanabilme ve toksik olmama özelliklerinden dolayı biyomedikal ve ilaç uygulamalarında tercih edilir. Halka açılma polimerizasyonu (ROP) siklik monomerin lineer polimer oluşturmak üzere açıldığı tek polimerizasyon metottur. Lactide, karbonat gibi siklik esterlerin halka açılma polimerizasyonu kontrollü poliester sentezinde genel ve etkin bir metottur.

Polimerizasyon yöntemlerine ek olarak, düşük polidispersite indisleri ve uç gruplarda yüksek uyumluluk gibi birçok gelişmiş uygulama, ağır metaller gibi istenmeyen kirliliklerin katalizörlerden uzaklaştırılmasını gerektirir. Bu amaçla siklik esterlerin metalsiz halka açılma reaksiyonlarına organokatalitik yaklaşımlarda bulunulmuştur.

Çok yönlü, verimli, özel ve enerji olarak tercih edilen kimyasal reaksiyonlar anlamına gelen "click" terimi ilk sentetik kimyada daha sonraları polimer ve malzeme biliminde son derece popüler evrensel araçlar haline gelmiştir. Günümüzde, "click kimyası" terimi altında sınıflandırılan Diels-Alder (DA) ve bakır katalizli azid-alkin siklokatılma (CuAAC) tepkimeleri blok ve aşı kopolimerlerden karmaşık makromoleküler yapılara kadar değişen birçok polimerik malzemenin sentezinde başarılı bir şekilde uygulandı ve blok, aşı ve yıldız polimerlerin eldelerinde güçlü bir alternatif yöntem olarak ortaya çıktı.

Click kimyası hızlı, etkin, güvenilir ve seçici olmak gibi özelliklere sahip olmasının yanı sıra yeni ilaç araştırma ve biyokimya çalışmalarında geniş olarak kullanılır. Click kimyasında en popüler reaksiyonlardan biri Huisgen 1,3-dipolar siklik katılması reaksiyonudur. Oda sıcaklığında olan azid ve alkin nin reaksiyonunda Cu(I) kataliz olarak kullanılır. Bu reaksiyonun çok tercih edilmesinin sebebi reaksiyon şartlarının basit olması, yan ürün olmaması, verimin yüksek olması ve saflaştırmanın kolay olmasıdır. Bu reaksiyon mekanizması ile ilgili Emrick in yaptığı ilk çalışmalardan bu yana, biyolojik olarak ile ilgili olarak click kimyası ve halka açılma polimerizasyonu metotlarının kullanıldığı bir çok çalışma yapılmıştır. Fakat, click kimyası kullanılarak polikarbonatların modifikasyonun içeren çalışmaların sayısı azdır.

Kopolimerizasyon, polimerik malzemelerin özelliklerini değiştirme ve ayarlama da kullanılan önemli bir yöntemdir. İki polimerin tek olacak şekilde bir araya gelmesi, kopolimerlerin orijinal polimerin meritlerine kadar girebilmesi nedeniyle avantajlıdır. Aşı kopolimerler, moleküler fırça olarak da bilinirler, sahip oldukları özellikler ve şekilleri sayesinde oldukça popülerdirler.

Basit halka açılma kopolimerizasyonu ile kontrollü olarak fiziksel ve mekanik özellikleri belirlenebilen polikarbonat kopolimerler elde edilir. Karbonatların halka açılma polimerizasyonu ile yüksek kaliteli (yüksek moleküler ağırlık ve düşük polidispersite) polikarbonatların elde edilmesi oldukça oldukça efektif bir metottur. Bu çalışmada, belirlenebilir moleküler ağırlığa ve yapıya sahip olan PC-Anth aşı kopolimerlerinin dizaynı ve sentezi konu edilmiştir ve antresan-maleimid-bazlı DA "click reaksiyonu" aşı kopolimer hazırlanmasında kullanılmıştır.

Bu çalışmada, bilinen polikarbonat (PC)-blokkopolimerler hazırlamak için moduler bağlanma stratejisi olarak Diels-Alder tepkimesi uygulandı. α-antrasen sonlu polikarbonat (PC), benzil 5-metil-2-okso-1,3-dioksan-5-karboksilat monomerinin halka açılma polimerizasyonunda, başlatıcı olarak 9-antrasen metanol kullanılmasıyla ve CH_2Cl_2 solventi içerisinde oda koşullarında 5 saatte hazırlandı. Daha sonra, α-furan korumalı maleimid-sonlu polimerler sentezlendi. Sentezlenen α-furan korumalı maleimid-sonlu öncü homopolimerler poli(etilen glikol) (PEG_{11}-MI veya PEG_{37}-MI), poli(metil metakrilat) ($PMMA_{26}$-MI), ve poli(ε-kaprolakton) (PCL_{27}-MI)'dur. Uygun PC-bazlı blok kopolimerleri elde etmek için α-furan korumalı maleimid-sonlu poli(etilen glikol) (PEG_{11}-MI veya PEG_{37}-MI), poli(metil metakrilat) ($PMMA_{26}$-MI), ve poli(ε-kaprolakton) (PCL_{27}-MI) refluks sıcaklığında toluende PC-antrasenle click reaksiyonu ile bağlandı.

Öncü homopolimerler ve onların PC-bazlı blok kopolimerlerinin karakterizasyonu GPC, NMR, DSC ve UV analizleri ile yapıldı.

1. INTRODUCTION

Aliphatic polycarbonates (PCs) have achieved increasing attention for use in a wide range of different applications such as surgical sutures, bone fixation materials and controlled drug delivery due to their biocompatibility, very low toxicity and biodegradability [1-2]. PCs may be mainly synthesized using three different methods, e.g. the polycondensation of diol compounds via phosgene or dialkylcarbonates, the copolymerization of oxiranes with carbondioxide and the ring opening polymerization (ROP) of cyclic carbonate monomers [2]. The latter seems to be the most efficient preparation method when compared to the formers, which suffer from many drawbacks such as poor control on the chemical structures, the limitation of molecular weights and the formation of byproducts [2]. The ROP of cyclic carbonates has been proceeded by anionic polymerization using conventional anionic initiators or coordination-insertion polymerization catalyzed by various organometallic compounds. Recently, metal-free catalysts such as several amines and phosphines have been extensively used for an efficient synthesis of aliphatic PCs [2-10].

The introduction of functional pendant groups, such as pentafluorophenylester [11], azide [14-15], allyl [17], alkyl halide [18], hydroxyl [20], (meth)acrylate [21], styrene [22], furan[23], and maleimide [24], vinyl [29] to cyclic carbonate monomers allows a precise control over the physical, chemical and biological properties of the resulting PCs. Further reaction on these pendant groups of the resulting PCs that can be realized using highly efficient chemistries, such as click chemistry [30-32, 37-38,47-50] would lead to PCs with well-defined structures for final needs and applications[14,15,21,23,29]. Thiol-ene, and copper catalyzed azide-alkyne cycloaddition (CuAAC) reactions have been utilized only for the postpolymerization functionalization of the PCs[14,15,21,24]. Recently, we applied Diels-Alder reaction to the preparation of well-defined PC-graft copolymers[122].In this study, the PC with anthracene pendant groups was clicked with a variety of well-defined α-furan protected maleimide terminated polymers at reflux temperature of toluene for 36 h.

The Diels-Alder grafting efficiencies were found to be over 97% using UV spectroscopy.

Unfortunately so far these click reactions have not found any role in the preparation of well-defined PC-block copolymers. It should be noted that PC-block copolymers have been generally synthesized using a hydroxyl terminated macroinitiator (either PC or another polymer block) in the ROP of either another monomer or cyclic carbonate, respectively [88]. However this methodology is limited to monomers, which can be polymerized using only ROP.

The promising results from the previous work on the PC-graft copolymers enabled us to use for the first time Diels-Alder reaction as a modular ligation strategy in the preparation of well-defined PC-block copolymers. Thereby, well-defined α-anthracene-terminated PC (PC-anthracene) is synthesized and subsequently ligated with a variety of α-furan protected maleimide-terminated poly(ethylene glycol) (PEG_{11}-MI or PEG_{37}-MI), poly(methyl methacrylate) ($PMMA_{26}$-MI), poly(ε-caprolactone) (PCL_{27}-MI), and at reflux temperature of toluene to yield their corresponding PC-based block copolymers (PC-*b*-PEG, PC-*b*-PMMA, and PC-*b*-PCL) (Scheme 1).

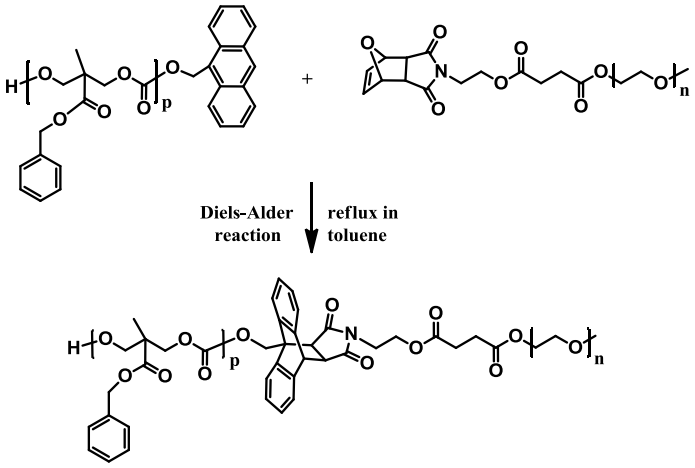


Figure 1.1: Preparation of PC-*b*-PEG copolymer via Diels-Alder reaction of α-anthracene-terminated polycarbonate (PC_{30}-anthracene) with α-furan protected-maleimide terminated-PEG (PEG_{11}-MI or PEG_{37}-MI) in toluene at 110 ^{o}C for 48 h.

2. THEORETICAL PART

2.1 Controlled/ ‘‘Living” Polymerizations

Conventional free radical polymerization (FRP) has many advantages over other polymerization processes. FRP does not require rigid process conditions and can be used for the copolymerization of wide range of vinyl monomers [96].The major limitation of FRP is poor control over some of the key elements of process that would allow the preparation of well-defined polymers with controlled molecular weight, polydispersity, composition, chain architecture, and site-specific functionality [97]

Living radical polymerizations was started in the mid-1990s; radical polymerization was thought to be a mature process with relatively little left to discover. Chain polymerizations without chain-breaking reactions are called as living polymerization by Szwarc [98].

Well-defined polymers, can only be synthesized by living ionic polymerizations or controlled/ “living” radical polymerization (C/LRP) methods [25]. Until recently, ionic polymerizations (anionic or cationic) were the only living techniques that efficiently controlled the structure and architecture of vinyl polymers. These polymerization techniques ensure low polydispersity materials, controlled molecular weight and defined chain ends but they are not useful for the polymerization and copolymerization of a wide range of functionalized vinylic monomers [26]. Furthermore, these techniques require stringent reaction conditions and pure reagents. To overcome all these limitations polymer chemists developed new concepts. These new concepts are often called controlled radical polymerization, living radical polymerization, control/“living” radical polymerization [27, 28]. Living or controlled/”living” polymerization techniques allow the synthesis of well-defined polymers with controlled molecular weight, polydispersities, and terminal functionalities. The polymerization proceeds until all of the monomer has been consumed, and further additions of monomer result in continued polymerization.

Living or controlled/"living" polymerization can proceed by anionic, cationic, group transfer, metathesis, Ziegler-Natta or radical mechanisms [99].

Living polymerization provides end-group control and enables the synthesis of block copolymers by sequential monomer addition. Living polymerization would be demandable because of allowing the synthesis of block copolymers by sequential addition of different monomers. A reactive species I* initiates polymerization of monomer A (equation 2.1).

$$I^* \xrightarrow{A} I\text{-}A_n^* \xrightarrow{B} I\text{-}A_n\text{-}B_m \qquad (2.1)$$

When the polymerization of monomer A is complete, the reactive centers are intact owing to the absence of chain-breaking reactions. Addition of a second monomer B culminate in the formation of a block copolymer containing a long block of A repeat units followed by a long block of B repeat units.

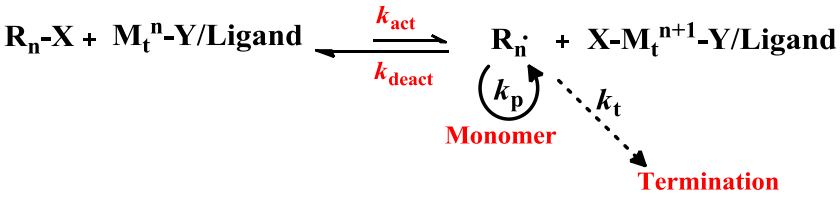
Block copolymers have commercial potential for obtaining products that can include demandable properties of two or more homopolymers. Living radical polymerizations have good commercial potential for materials synthesis because many more monomers undergo radical polymerization [98]. However, it does not necessarily provide polymers with molecular weight (MW) control and narrow molecular weight distribution (MWD). To obtain well defined polymers the initiator should be consumed at early stages of polymerization and that the exchange between species of various reactivities should be at least as fast as propagation [29-31]

2.1.1 Controlled/ ''living"radical polymerizations

Living free radical polymerizations have achieved a following in polymer chemistry. A great deal of effort has been made to develop and understand different living free radical polymerization (LFRP) methods. Georges and co-workers first introduced true nitroxide mediated polymerization (NMP) in 1993, Matyjaszewski and Sawamoto developed metal catalzed (Cu, Ru) living radical polymerization also called atom transfer radical polymerization (ATRP) in 1995, and Moad, Rizzardo and Thang reported reversible addition-fragmentation chain transfer polymerization (RAFT) in 1998 [7, 8, 9, 12].

2.1.2 Atom transfer radical polymerization (ATRP)

Atom transfer radical polymerization (ATRP) is a living radical polymerization process, which is consisting of the monomer, initiator, and catalyst composed of transition metal species with any suitable ligand. ATRP is a facile technique, which allows the preparation of well-defined polymers with narrow molecular weight distribution, predictable chain length, controlled microstructure, defined chain-ends and controlled architecture [100]. The ATRP system is consisting of the monomer, initiator, and catalyst composed of transition metal species with any suitable ligand. ATRP, which is the most versatile method of the controlled radical polymerization system, uses a wide variety of monomers, catalysts, solvents, and reaction temperature. ATRP is one of the most convenient methods to synthesize well-defined low molecular weight polymers [32].



(2.2)

A general mechanism for ATRP shown in equation 2.2. The radicals the propagating species $R_n\cdot$, are generated through a reversible redox process catalyzed by a transition metal complex. Radicals react reversibly with the oxidized metal halide complexes, $X–M_t^{n+1}$ / ligand, the deactivator, to reform the dormant species and the activator. These processes are fast, and the dynamic equilibrium that is established favors the dormant species. By this way, all chains can begin growth at the same time, and the concentration of the free radicals is quite low, resulting in reduced amount of irreversible radical-radical termination. Since the deactivation rate constant is substantially higher than that of the activation reaction$\boldsymbol{k_{eq}} = \frac{k_{act}}{k_{deact}} \sim \mathbf{10^{-7}}$

each polymer chain is protected by spending most of the time in the dormant state, and thereby the permanent termination via radical coupling and disproportionation is substantially reduced [33]. ATRP will not occur or occur very slowly if the equilibrium constant is too small. On the contrary, too large an equlibrium constant will cause to a large amount of termination because of a high radical concentration [101].

Polymer chains grow by the addition of the free radicals to monomers in a manner similar to a conventional radical polymerization, with the rate constant of propagation, k_p. Termination reactions (k_t) also occur in ATRP, mainly through radical coupling and disproportionation. However, in a well-controlled ATRP, only several percents of the chains become dead via termination [33]. Polydispersities in ATRP decrease with conversion, with the rate constant of deactivation and also with the concentration of deactivator.

The molecular conversion and the amount of initiator used, $\boldsymbol{DP} = \frac{\Delta[\boldsymbol{M}]}{[\boldsymbol{I}]_{\boldsymbol{0}}}$; polydispersities are low, $\frac{\boldsymbol{M_w}}{\boldsymbol{M_n}} < \mathbf{1,3}$ [34].

ATRP was growed by designing a suitable catalyst (transition metal compound and ligands), using an initiator with the suitable structure, and adjusting the polymerization conditions such that the molecular weights increased lınearly with conversion and the polydispersities were typical of a living process [102,103]. This allowed for an unprecendented control over the chain topology (stars, combs, branched), the composition (block, gradient, alternating, statistical), and the end functionality for a wide distribution of radically polymerizable monomers [104-106].

Components of ATRP

ATRP is a multicomponent system, which is comprises of the monomer, an initiator with transferable (pseudo)halogen.

Monomers

A variety of monomers have been used for atom transfer radical polymerization. The typical monomers are methacrylates, acrylonitriles, styrenes, acrylates and (meth)acrylamides in bulk, solution using organics or water as solvents, and emulsion, supercritical carbon dioxide, producing polymers with well-controlled molecular weights and structures [35].

Each monomer has its own intrinsic radical propagation rate. Therefore, for a specific monomer, the concentration of propagating radicals and rate of radical deactivation need to be adjusted to maintain polymerization control [101].

Initiators

In ATRP, alkyl halides are typically used as the initiator and the rate of the polymerization is first order with respect to the concentration of alkyl halides.

To obtain well-defined polymers with narrow molecular weight distributions, the halide group X, must rapidly and selectively migrates between the growing chain and the transition-metal complex. Thus far, bromine and chlorine are the halogens that afford the best molecular weight control [36-39]. Iodine works well for acrylate polymerizations; however, in styrene polymerizations the heterolytic elimination of hydrogen iodide is too fast at high temperatures [40]. Flourine is not used because the C-F bond is too strong to undergo homolytic cleavage [101].

It should be noted that R-X bonds can be cleaved not only homolytically but also heteroytically, which depends mostly on the initiator structure and the choice of the transition metal catalyst.

The amount of the initiator in the ATRP determines the final molecular weight of the polymer at full monomer conversion. The main role of the initiator is to determine the number of growing polymer chains. If initiation is fast and transfer and termination negligible, then the number of growing chains is constant and equal to the initial initiator concentration. The theoretical molecular weight or degree of polymerization (DP) increases reciprocally with the initial concentration of initiator in a living polymerization (equation 2.3).

$$\boldsymbol{DP = \frac{[M_0]}{[Initiator]_0} \times conversion} \qquad \textbf{(2.3)}$$

Simultaneously, polydispersities decrease with the conversion (equation 2.4).

$$\boldsymbol{Polydispersity = \left(M_w / M_n \right)} \qquad \textbf{(2.4)}$$

The most frequently used initiator types used in the atom transfer radical polymerization systems are, 1-Bromo-1-phenyl ethane (Styrene), 1-Chloro-1-phenyl ethane (Styrene), Ethyl-2-bromo propionate (Methyl methacrylate) and Ethyl-2-bromo isobutyrate (Methyl methacrylate). 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 [5].

Catalysts

Catalyst is another important component of ATRP. Catalyst determines the position of the atom transfer equilibrium and the dynamics of exchange between the dormant and active species. There are several prerequisites for an efficient transition metal catalyst. First, the catalyst should react with initiator fast and quantitatively to ensure that all the polymer chains start to add monomer at the same time. Second, the catalyst must have moderate redox potential to ensure an appropriate equilibrium between dormant and active species. In general, a low redox potential of the catalyst leads to formation of the high Cu(II) concentration (equilibrium is shifted toward transient radicals). Consequently, a fast and uncontrolled polymerization is observed. In contrast, high redox potential strongly suppresses Cu(II) formation (equilibrium is shifted toward dormant species) via a halogen atom abstraction process leading to very slow polymerization. Third, the catalyst should be less sterically hindered, because large steric congestion around the metal center of catalyst results in a reduction of the catalyst activity. Fourth, a good catalyst should not afford side reactions such as Hoffman elimination, β-H abstraction, and oxidation/reduction of radicals [41].

A variety of transition metal complexes with various ligands have been studied as ATRP catalysts. The majority of work on ATRP has been conducted using copper as the transition metal. Apart from copper-based complexes, iron, nickel, rhenium, ruthenium, rhodium, and palladium have been used to some extent [6, 57, 63-66]. Recent work from Sawamoto and co-workers shows that the Ru-based complexes can compete with the Cu-based systems on many fronts. A specific Fe-based catalyst has also been reported to polymerize vinyl acetate via an ATRP mechanism [42].

Ligands

The main role of the ligand in ATRP is to solubilize the transition-metal salt in the organic media and to adjust the redox potential and halogenophilicity of the metal center forming a complex with an appropriate reactivity and dynamics for the atom transfer. The ligand should complex strongly with the transition metal, should also allow expansion of the coordination sphere, and should allow selective atom transfer without promoting other reactions.

Nitrogen ligands have been used in copper- and iron-mediated ATRP. For copper-mediated ATRP, nitrogen-based ligands work particularly well. In contrast, sulfur, oxygen, or phosphorus ligands are less effective due to in appropriate electronic effects or unfavorable binding constants.

For copper-based ATRP, the coordination chemistry of the transition-metal complex greatly affects the catalyst activity. The electronic ans steric effects of ligands are also important [101].

The most common ligands for ATRP systems are substituted bipyridines, alkyl pyridylmethanimines and multidentate aliphatic tertiary amines such as N,N,N′,N″,N″ pentamethyldiethylenetriamine (PMDETA), and tris[2-(dimethylamino) ethyl]amine (Me_6-TREN) [7,43]. In addition to those commercial products, it has been demonstrated that hexamethyltriethylene tetramine (HMTETA) provides better solubility of the copper complexes in organic media and entirely homogeneous reaction conditions [44]. Since copper complexes of this new ligand are almost insoluble in water, ATRP technique can be employed in preparing poly(acrylate esters) in aqueous suspensions [45].

In ATRP, also phosphorus-based ligands can be used to make complex most transition metals containing rhenium, ruthenium, iron, rhodium, nickel and palladium, however not copper [101].

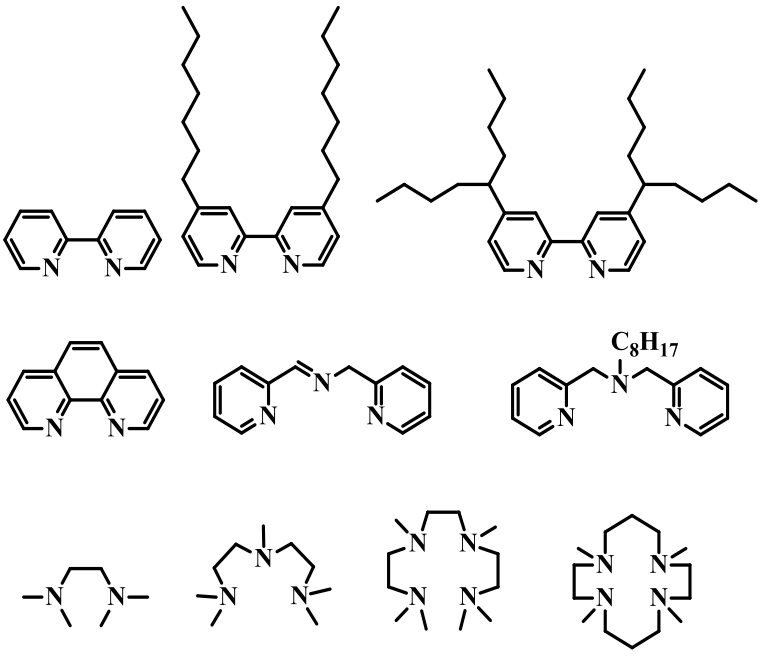


Figure 2.1: The most common ligands for ATRP systems.

Solvents

ATRP can be carried out either in bulk, in solution or in a heterogeneous system (e.g., emulsion, suspension). Various solvents such as benzene, toluene, anisole, diphenyl ether, ethyl acetate, acetone, dimethyl formamide (DMF), ethylene carbonate, alcohol, water, carbon dioxide and many others have been used for different monomers. A solvent is sometimes necessary especially when the obtained polymer is insoluble in its monomer [46].

2.2 Ring-Opening Polymerization (ROP)

Polylactones and polylactides can be prepared by two different approaches, by the polycondensation of hydroxycarboxylic acids or by the ring-opening polymerization. The polycondensation technique is less expensive than ROP. However, it is hard to get high molecular weight polymers, to success specific end groups, and to prepare well-defined copolyesters [107]. Ring-opening polymerization (ROP) is a unique polymerization process, in which a cyclic monomer is opened to generate a linear polymer. It is fundamentally different from a condensation polymerization in that there is no small molecule byproduct during the polymerization. Polymers with a wide variety of functional groups can be produced by ring-opening polymerizations. Preparation of cyclic monomers, studies of catalysis and mechanisms are active areas of research both in industry and academia [13-16].

Nowadays, increasing attention is paid to degradable and biodegradable biocompatible polymers for applications in the biomedical and pharmaceutical fields, primarily because after use they can be eliminated from the body via natural pathways and also they can be a solution to problems concerning the global environment and the solid waste management. Aliphatic polyesters are among the most promising materials as biodegradable polymers.

The most remarkable aspect of ROP was theoretically cleared by Flory; the invariant number of propagating chains in the ROP results in the generation of polymerization (DP). the advanteges of ROP in conjuction with a “living” method have facilitated the controlled synthesis of block, graft, and star polymers, which leads to a present consensus that living ROP is a powerful and versatile addition-polymerization method [108].

Tradationally, mechanisms for ROP are divided into cationic and anionic polymerization in terms of the ionic charge of active propagating species. A special case is “coordination-insertion” mechanism, which involves metal-catalyzed ROPs. this mechanism is formed from coordination of monomer to metal of a catalyst and insertation of the monomer to the to the metal-oxygen bond [108].

2.2.1 Controlled ring-opening polymerization of cyclic esters

The ring opening polymerization (ROP) of lactones and lactides to produce poly(ester)s provides versatile biocompatible and biodegradable polymers possessing good mechanical properties.

These advantages have seen aliphatic poly(ester)s receive increasing attention over the last few years driven by their application as biodegradable substitutes for conventional commodity thermoplastics and applications in the biomedical field [52].

There are some reasons for studying the polymerization of cyclic esters. Firstly, to take advantage of the potential of preparing variety of polymers with control of the major variables affecting polymer properties in synthetic polymer. In addition, there are some important factors such as economy, toxicology, and technical apparatus development. Secondly, ROP facilitates to synthesise various advanced macromolecules, involving homopolymers with well-defined structures or end groups, or copolymers such as block, graft or star copolymers[107].

If aliphatic poly(ester)s are synthesized by polycondensation of hydroxyl-carboxylic acids, yield of resulting polyesters is low molecular weight polyesters (M_n<30.000) with poor control of specific end groups [53]. In contrast, high molecular weight aliphatic polyesters can be prepared in short periods by ROP. There has been much research directed towards the controlled ROP of commercially available cyclic esters including glycolide, lactide and ε-caprolactone resulting in aliphatic poly(ester)s with high molecular weights [54].

In practice, the ROP of lactones and lactides requires an appropriate catalyst to proceed in reasonable conditions and to afford polymers with controlled properties (2.3).

Since the pioneering work of Kleine et al. in the 1950s metal-based catalytic systems have been the focus of considerable attention for the polymerization of cyclic esters, and numerous studies have been carried out to elucidate the mechanism of such coordination polymerizations. Through variation in the nature of the metal center and of the surrounding ligands, a broad range of initiators have been prepared and evaluated [55, 56, 58, 59].

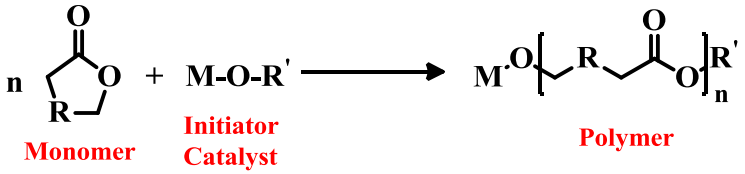


Figure 2.2: Schematic reprensantation of the ROP of a cyclic ester R=$(CH_2)_{0-3}$ and/or ($CHR^{'}$)

Besides the coordination-insertion mechanism, alternative strategies based on anionic, nucleophilic, or cationic promoters have also been recently (re)evaluated, the preliminary results reported in these fields being rather promising [60, 61].

Catalysts

A large variety of organometallic compounds, such as metal alkoxides and metal carboxylates, has been studied as initiators or catalysts in order to achieve effective polymer synthesis [56]. The covalent metal alkoxides with free p or d orbitals react as coordination initiators and not as anionic or cationic initiators [62]. The most widely used complex for the industrial preparation of polylactones and polylactides is undoubtedly tin(II)2-ethylhexanoate, commonly referred as stannous octoate [$Sn(Oct)_2$]. It has been approved as a food additive by the American Food and Drug Administration (FDA) [107]. It is also commercially available, easy to handle and soluble in common organic solvents and in melt monomers. It is highly active and allows for the preparation of high-molecular-weight polymers in the presence of an alcohol [63]. Aluminum alkoxides have also proved to be efficient catalysts for the ROP of cyclic esters. The common example, namely, aluminum (III) isopropoxide, $Al(Oi\text{-}Pr)_3$, has been largely used for mechanistic studies. However, it has been revealed to be significantly less active than $Sn(Oct)_2$ [64]. Moreover, an induction period of a few minutes is systematically observed with $Al(Oi\text{-}Pr)_3$ attributed to aggregation phenomenon [65].

For all these reasons, $Al(Oi\text{-}Pr)_3$ is much less used for the preparation of biodegradable polyesters, and especially since aluminum ions do not belong to the human metabolism and are suspected of supporting Alzheimer's disease.

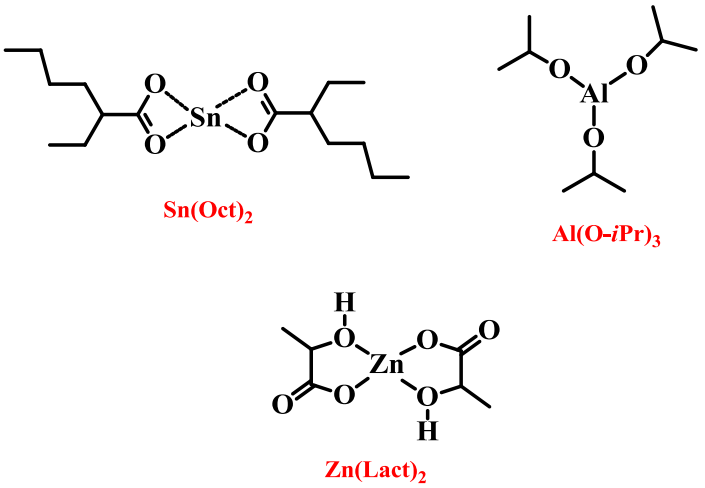


Figure 2.3: Catalysts of Ring Opening Polymerization

Much interest has been devoted to zinc derivatives as potential nontoxic catalysts. Zinc powder itself is a relatively good polymerization catalyst that is used industrially [66]. With reaction times of several days at 140 °C in bulk, it is roughly as active as $Al(Oi\text{-}Pr)_3$. Numerous zinc salts have also been investigated [67].

Although polymerization of alifatic cyclic carbonetes has been reported using organometallic catalysts (MAO, IBAO, $Sn(Oct)_2$ and $Al(Oi\text{-}Pr)_3$) and as well as enzymes, there are some metal-free catalysts polymerizations of carbonetes and other cyclic monomers such as lactones.

Simple organic molecules like 4-dimethylaminopyridine (DMAP), 4-pyrrolidinopyridine (PPY) and some phosphines have shown to support ROP of cyclic monomers in the presence of a proper nucleophilic initiator. Most of these catalysts have the advantages of being commercially available or readily synthesized [109-110].

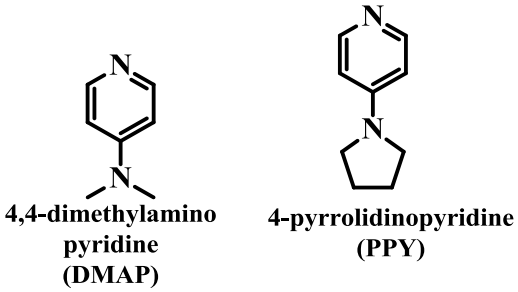


Figure 2.4: Metal-free Catalysts of Ring Opening Polymerization

N-heterocyclic carbenes (NHCs) become a new class of highly active catalysts owing to their high nucleophility. Their important reactivity for transesterification reactions are manifested in their ability to catalyze ROP of lactones and carbonates [111].

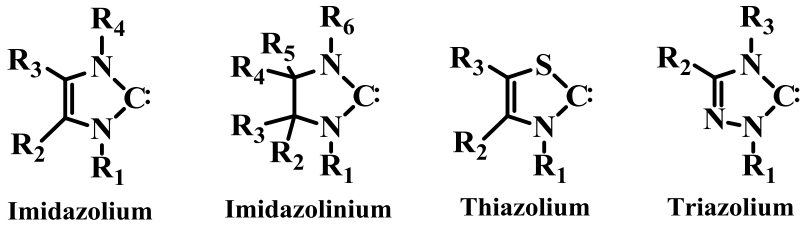


Figure 2.5: N-heterocyclic Carbenes Catalysts for Ring Opening Polymerization

Other organic catalysts have been developed that supply electrophilic and nucleophilic activations. Amine substituted ureas and thioureas proved to be highly selective for the ROP of cyclic carbonetes to give predictable molecular weights, narrow polydispersities along with end-group fidelty.

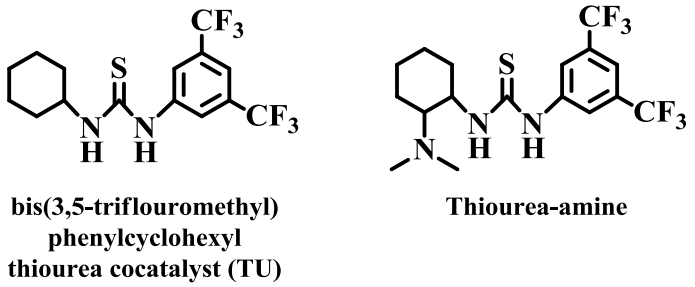


Figure 2.6: Amine Substituted Ureas and Thioureas Catalysts for ROP

Both using bis(3,5-triflouromethyl) phenylcyclohexyl thiourea cocatalyst (TU) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) caused to quantitative monomer conversion in much shorter times while maintainng the excellent control over the polyester molecular parameters [111].

2.2.2 Cationic ring-opening polymerization

For the ROP of a variety of cyclic heterocycles, cationic polymerization has been applied. the cationic ROP of lactones has been achieved using alkylating agents, acylating agents, Lewis acids, and protic acids.

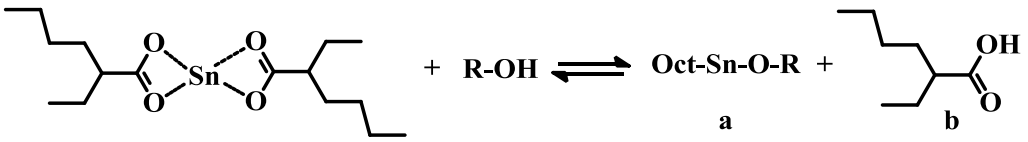
Early 1970s, it was reportted by Dittrich and Schultz that LA polymerization with cationic compounds were unsuccessfull. In 1986, Kricheldorf and co-workers screened a variety of acidic compounds, among which triflouromethanesulfonic acid (triflic acid, HOTf) and methyl triflate (MeOTf) proved to be useful initiators for cationic ROP of LA [108].

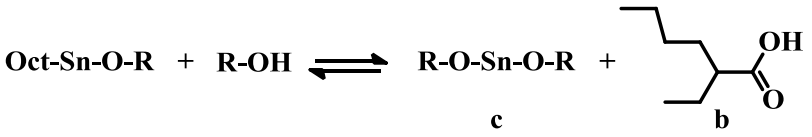
2.2.3 Anionic ring-opening polymerization

The anionic polymerization of lactones with Li or K alkoxides is well-known. However, less work has been done on the anonic ROP of strained heterocycles with organic counterions [108].

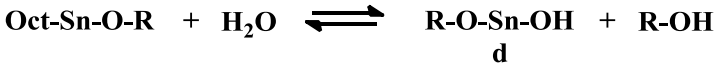
2.2.4 Coordination-insertion ring opening polymerization

Covalent metal carboxylates, particularly tin(II) bis(2-ethylhexanoate) usually referred to as tin(II) octanoate, $Sn(Oct)_2$ belong to the most frequently used initiators for polymerization of cyclic esters due to its low cost, low toxicity, and high efficiency. Although, there are controversial reports in the literature about the nature of $Sn(Oct)_2$ activity in the polymerization of lactones, two basic types of mechanism have been proposed. The first one is directly catalytic type where the catalyst serves to activate monomer through coordination with its carbonyl oxygen [68, 69]. The second mechanism is the monomer insertion type mechanism where the catalyst acts as co-initiator along with either purposely added or adventitious hydroxyl impurities, and polymerization proceeds though an activated stannous alkoxide bond [70,71].



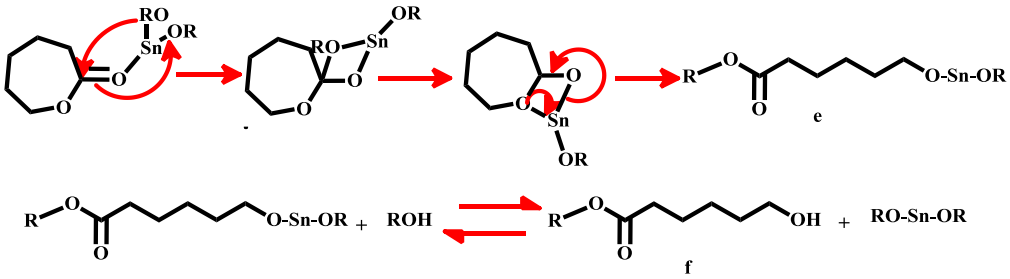


(2.5)



Kricheldorf and co-workers have recently illustrated how the structure of the alcohol initiator may influence the strength of the catalyst/alcohol interaction [69, 71]. According to these authors, this interaction, in the early stages of reaction, is responsible for formation of the "true" initiating species, subsequent ring opening, and formation of the active, propagating chain end. Prior to the beginning of polymerization, adventitious hydroxyfunctional impurities (e.g., water) or purposely added alcohol first complex and subsequently react with $Sn(Oct)_2$ producing a

stannous alkoxide species (a) and free 2-ethylhexanoic acid (b) as shown in 2.5. Further reaction with a second equivalent of alcohol produces the stannous dialkoxide initiator (c) and releases a second equivalent of 2-ethylhexanoic acid (b) as depicted in 2.5 [71, 72]. Adventitious water, meanwhile, serves mainly as a catalyst deactivator via a reversible reaction with a or c, thereby decreasing the concentration of active initiator and producing a stannous alcohol derivative (d), such as shown in 2.5, which is more thermodynamically stable than the stannous dialkoxide and is less efficient as an initiator [71].



(2.6)

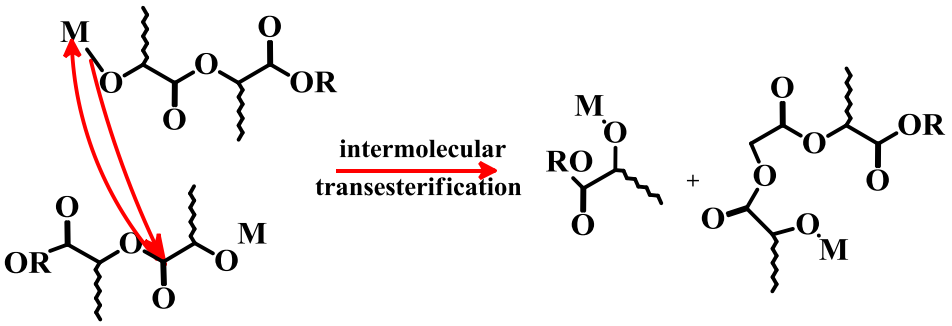
Reaction of c with monomer by means of coordination- insertion generates the first actively propagating chain end (e) consisting of not only the initiating alcohol fragment but also the active propagating center derived from the first monomer unit and stannous alkoxide. The e species may either propagate or undergo rapid intermolecular exchange of the stannous alkoxide moiety for a proton from either hydroxyl groups of initiator (if remaining) or another hydroxy chain end, either e or polymeric in nature. This rapid exchange of protons and stannous alkoxide moieties results in a dynamic equilibrium between activated and deactivated chain ends as depicted in 2.6, where R= unreacted alcohol initiator or hydroxy chain ends generated in situ. This process eventually consumes the remaining unreacted alcohol initiator not involved in the initial formation of c. ROP based on coordination-insertion mechanism has been thoroughly investigated since it may yield well-defined polyesters through living polymerization [62, 73].

In such coordination-insertion polymerizations, the efficiency of the molecular-weight control depends from the ratio $k_{propagation}/k_{initiation}$ but also from the extent of transesterification side reactions. These transesterification reactions can occur both intramolecularly (backbiting leading to macrocyclic structures and shorter chains) and intermolecularly (chain redistributions) (2.7-2.8) [74].

Intermolecular transesterification reactions modify the sequences of copolylactones and prevent the formation of block co-polymers. Intramolecular transesterification reactions cause degradation of the polymer chain and the formation of cyclic oligomers.

The polymerization/depolymerization equilibrium should also be taken into account as a particular case of intramolecular transesterification reaction. All of these side reactions result in broader molecular-weight distributions, sometimes making the molecular weights of the resulting polymers irreproducible. The extent of these undesirable transesterification reactions was found to strongly depend on the metallic initiator [64]. Side reactions occur from the very beginning of the polymerization with $Sn(Oct)_2$, leading to rather broad MWD (PDI indexes around 2) but only at high or even complete conversion with $Al(O\textit{i}\text{-}Pr)_3$, yielding lower PDI indexes (less than 1.5) [64,75].

Parameters that influence the number of transesterifications are temperature, reaction time, and type and concentration of catalyst or initiator. Depending on the metal used, the initiator is more or less active towards transesterification reactions [75].



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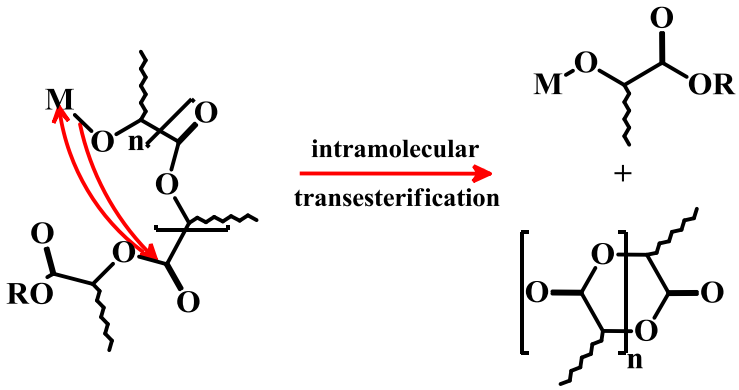


(2.8)

The promising results obtained with $Sn(Oct)_2$, $Al(Oi\text{-}Pr)_3$, and $Zn(Lact)_2$ have given rise to a growing interest in metal-based initiators that would display higher catalytic activity and better control the extent of the undesirable transesterification reactions.

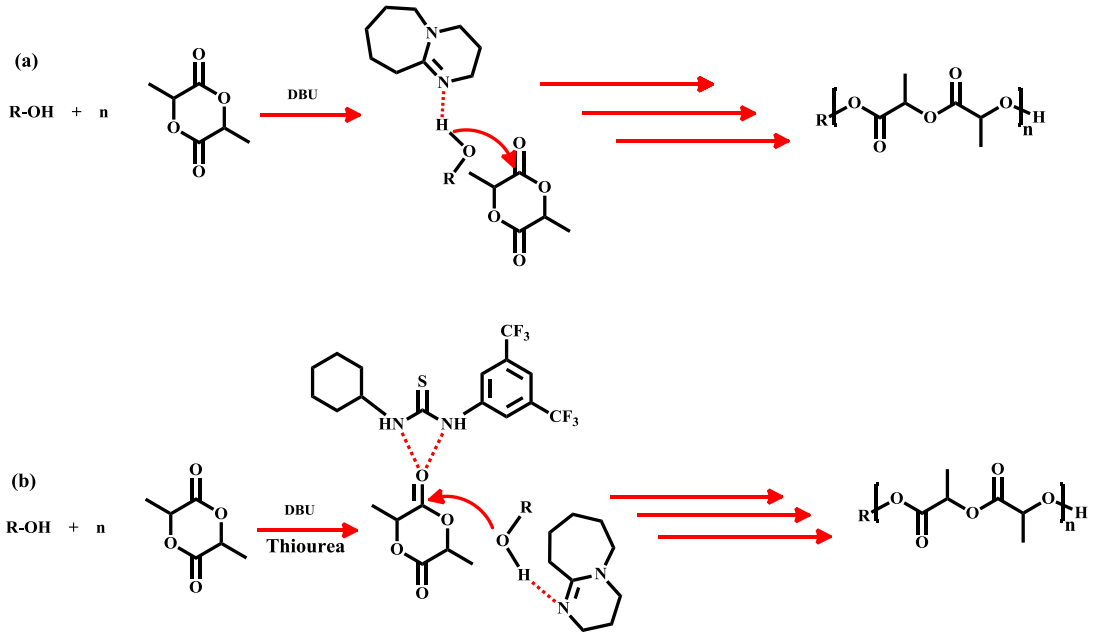


Figure 2.7:(a) Chain-end/general base activation in the presence of LA and DBU and **(b)** bifunctional activation of LA in the presence of ROH from an equimolar mixture of thiourea and DBU [111].

Poly(ε-caprolactone)

Poly(ε-caprolactone) (PCL) is a semicrystalline polymer which represents one of several aliphatic polyesters that undergo degradation and absorbtion in vivo [76, 77]. The repeating molecular structure of PCL homopolymer consists of five non-polar methylene groups and a single relatively polar ester group. Although not produced from renewable raw materials, PCL is a fully biodegradable thermoplastic polymer due to the presence of the hydrolytically unstable aliphatic-ester linkage. PCL has good water, oil, solvent and chlorine resistance.

PCL has some unusual properties, including a low Tg (~ –60 °C) and Tm (~ 60 °C) and a high thermal stability. These properties are related to PCL's chain of carbons, as longer chains are give rise to less mobility and lower Tm's and Tg's. PCL is also highly permeable, which results from its low Tg and subsequent rubbery state at room temperature.

PCL is one of biodegradable polymers which have been used to prepare functional materials [78].

Copolymers containing poly(ε-caprolactone) (PCL) are especially interesting because they are miscible with a wide range of polymers, and they have features like crystallizability, lack of toxicity, ability to disperse pigments, low-temperature adhesiveness, and printability [79].

PCL has been increasingly studied in the scientific community and applied for drug delivery and tissue engineering [80]. Owing to its high crystallinity and strong hydrophobicity of polymer backbone, PCL homopolymer usually show slow biodegradation and drug-release rate [81].

PCL is compatiable with numerous other polymers, has the possibility of blending this aliphatic polyester with a number of commercial polymers such as poly(vinyl chloride) and bisphenol A polycarbonate. PCL is of interest as a packaging material and in biomedical applications since it is degradable and its degredation products are non-toxic. PCL and other copolymers have been evaluated for medical uses such as drug delivery systems, an external casting material for broken bones, as a material for use in making custom dental impression trays.

In addition to above, it is used mainly in thermoplastic polyurethanes, resins for surface coatings, adhesives and synthetic leather and fabrics. It also serves to make stiffeners for shoes and orthopedic splints, and fully biodegradable compostable bags, sutures, and fibres. Because the homopolymer has a degradation time on the order of 2 years, copolymers have been synthesized to accelerate the rate of bioabsorption. In Sweden there has been an attempt to produce PCL bags, but they degraded before reaching the customers.

Polycarbonates

Biodegradable polymers have been widely used and have greatly promoted the development of biomedical fields because of their biocompatibility and biodegradability. Synthetic biodegradable polymers have found more versatile and diverse biomedical applications because of their tailorable designs or modifications.

Most commonly used degradable materials for the preparation of clinical devices are aliphatic polyesters and copolyesters. From this point, aliphatic polycarbonates are good materials because they have functionalizable side chains (OH, NH_2, COOH, etc.) can easily meet the need for functionalization of biomaterials.

Furthermore, aliphatic polycarbonates have good biocompatibility, low toxicity and good biodegradability [112,113]. High molecular weight aliphatic polycarbonates can be prepared by the ROP of cyclic carbonates.

The most commonly used cyclic carbonates for ROP are five- ans six-membered cyclic monomers. A great variety of functional cyclic carbonate monomers have been successflly used for homopolymerization and copolymerization with various heterocyclic monomers through ROP [114].

Recently, Hedrick et. al. surveyed a Lewis base (1,8-diazabicyclo[5.4.0]undec-7-ene, DBU) for the ROP of trimethylenecarbonate (TMC) based on organocatalysis and synthesized a variety of functional polycarbonates [115]. Since DBU is purely organic, it is particularly suitable for use in the synthesis of biomaterials [116].

2.3 Click Chemistry

In 2001, Sharpless and coworkers introduced “click” chemistry, a new approach in organic synthesis that involves a handful of almost perfect chemical reactions [19]. Click chemistry can be summarized only one sentence: Molecules that are easy to make. Requirements for click reactions involving one or more polymeric reagents, which orginally defined by Sharpless, are high yields, stable compounds, modular, wide in scope, chemoselective, single reaction trajectory. There are other adapted requirements, which are related to synthetic polymer chemistry, like equimolarity, large-scale purification, fast timescale [117].

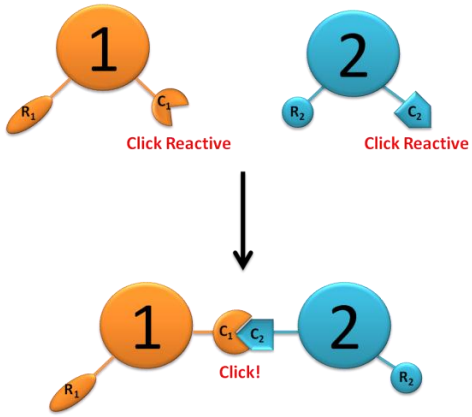


Figure 2.8: General notation of click chemisty

Nowadays there are several processes have been identified under this term in order to meet these criterias such as nucleophilic ring opening reactions; non-aldol carbonyl chemistry; thiol additions to carbon–carbon multiple bonds (thiol-ene and thiol-yne); and cycloaddition reactions.

Among these selected reactions, copper(I)-catalyzed azide-alkyne (CuAAC) and Diels-Alder (DA) cycloaddition reactions and thiol-ene reactions have gained much interest among the chemists not only the synthetic ones but also the polymer chemists.

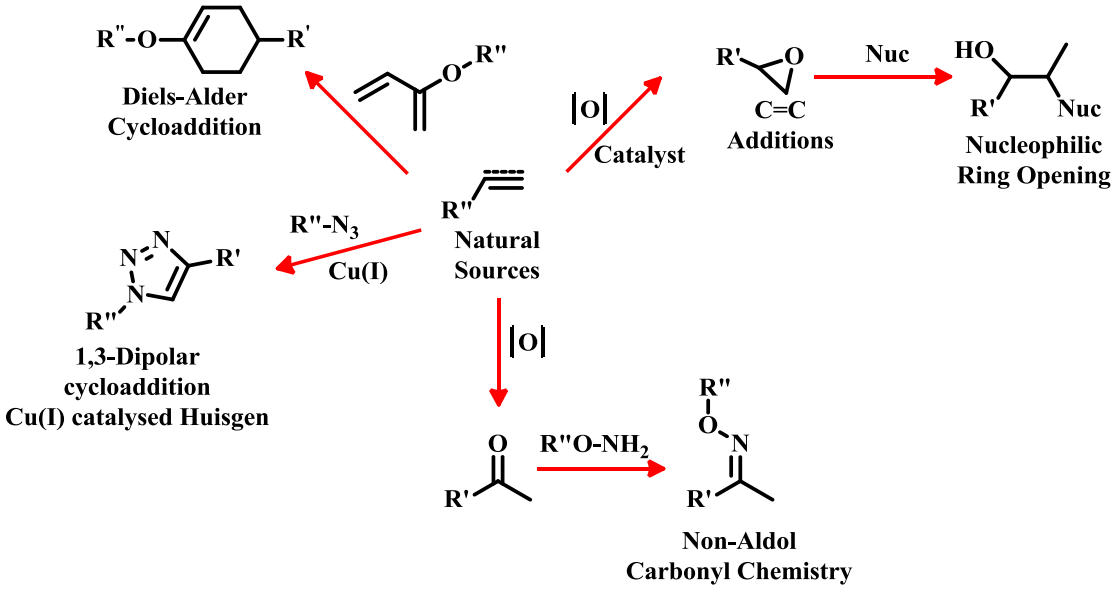


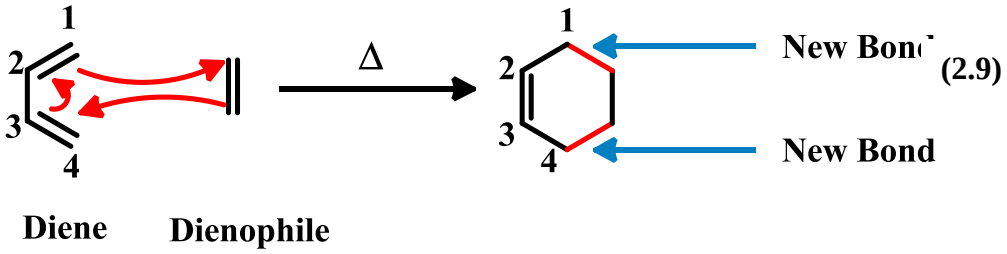
Figure 2.9: A selection of reactions which match the Click Chemistry criteria

During the last years, “click” cycloadditions became also very popular in polymer chemistry, as a tool for functionalizing synthetic macromolecules [100].

2.3.1 Diels-Alder reaction

Diels-Alder (DA) reaction is one of the most common reactions used in organic chemistryand invented by Otto Diels and Kurt Alder who recieved the Nobel Prize in 1950 for their discovery [118].The Diels-Alder reaction is a concerted [4π+2π] cycloaddition reaction of a conjugated diene and a dienophile to yield a 6-membered ring. This reaction is one of the most powerful tools used in the synthesis of important organic molecules. The three double bonds in the two starting materials are converted into two new single bonds and one new double bond to afford cyclohexenes and related compounds (equation 2.9).

This reaction is named for Otto Diels and Kurt Alder, who received the 1950 Nobel prize for discovering this useful transformation [82-84].



DA cycloaddition reaction forms not only carbon-carbon bonds but also heteroatom-hetroatombonds (hetero-Diels-Alder, HDA) and it is widely used synthetically to prepare siz-membered rings [119]. Typically, the DA reaction works best when either the diene is substituted with electron donating groups (like -OR, -NR2, etc) or when the dienophile is substituted with electron-withdrawing groups (like -NO2, -CN, -COR, etc) [85].

Some attractive features of DA reactions (retro-Diels-Alder, rDA) are thermal reversibility and decomposition reaction of the cyclic system that can be controlled by temperature[120].

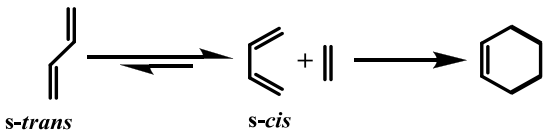
Figure 2.10: General mechanism of Diels-Alder/retro Diels-Alder reactions of dienophile and dien

These DA reactions are suitable for green chemistry because of the absance of metal catalyst in reaction medium. DA “click” reactions can be combined with the living /controlled polymerization methods such as RAFT, NMRP, ATRPand ROP. By using simple and efficient DA cycloaddition reactions, linear thermoplastic, thermosetting polymers and telechelic polymers can be synthesized.

In brief, DA “click” reactions show great potential for the prepration of tailor-made functional materials such as telechelic polymers, block, graft, star, star-block, H-shaped polymers, dendirimers, bioconjugates and hybris materials. DA “click” chemistry has some advantages such as water-solubility, high reaction yields, no detectable side-reactions and no requirement for additional catalysts [121].

Stereochemistry of Diels-Alder reaction

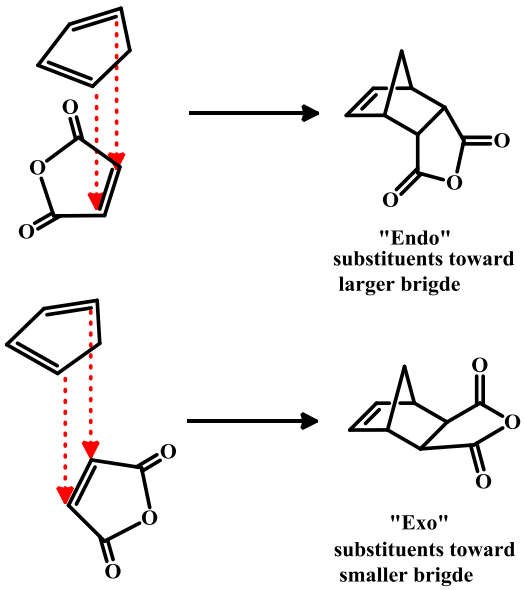
There are stereochemical and electronic requirements for the DA reaction to occur smoothly. First, the diene must be in an s-cis conformation instead of an s-trans conformation to allow maximum overlap of the orbitals participating in the reaction (equation 2.10).



(2.10)

The "s" in s-cis and s-trans refers to "sigma", and these labels describe the arrangement of the double bonds around the central sigma bond of a diene. Dienes often exist primarily in the lower energy s-trans conformation, but the two conformations are in equilibrium with each other. The s-cis conformation is able to react in the DA reaction and the equilibrium position shifts towards the s-cis conformer to replenish it. Over time, all the s-trans conformer is converted to the s-cis conformer as the reaction proceeds.

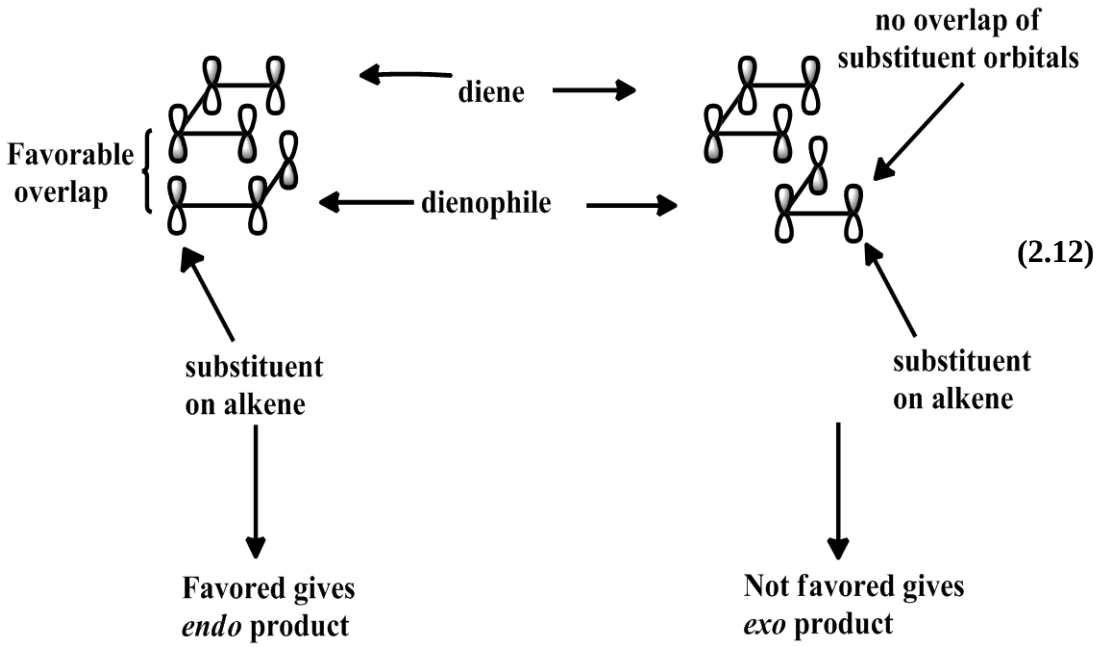
A unique type of stereoselectivity is observed in DA reactions when the diene is cyclic. In the reaction of maleic anhydride with cyclopentadiene, for example, the endo isomer is formed (the substituents from the dienophile point to the larger bridge) rather than the exo isomer (the substituents from the dienophile point away from the larger bridge) (equation 2.11).



(2.11)

The preference for endo–stereochemistry is "observed" in most DA reactions. The fact that the more hindered endo product is formed puzzled scientists until Woodward, Hoffmann, and Fukui used molecular orbital theory to explain that overlap of the p orbitals on the substituents on the dienophile with p orbitals on the diene is favorable, helping to bring the two molecules together [86, 87].

Hoffmann and Fukui shared the 1981 Nobel Prize in chemistry for their molecular orbital explanation of this and other organic reactions. In the illustration below, notice the favorable overlap (matching light or dark lobes) of the diene and the substituent on the dienophile in the formation of the endo product (equation 2.12):



(2.12)

Oftentimes, even though the endo product is formed initially, an exo isomer will be isolated from a DA reaction. This occurs because the exo isomer, having less steric strain than the endo, is more stable, and because the DA reaction is often reversible under the reaction conditions. In a reversible reaction, the product is formed, reverts to starting material, and forms again many times before being isolated.

The more stable the product, the less likely it will be to revert to the starting material. If the reaction is not reversible under the conditions used, the kinetic product will be isolated. However, if the first formed product is not the most stable product and the reaction is reversible under the conditions used, then the most stable product, called the thermodynamic product, will often be isolated.

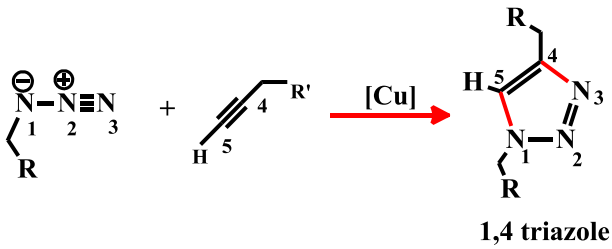
2.3.2 Copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC)

Huisgen's 1,3-dipolar cycloaddition of alkynes and azides yielding triazoles is, undoubtedly, the premier example of a click reaction [88]. Recently, 1,3-dipolar cycloadditions, such as reactions between azides and alkynes or nitriles, have been applied to macromolecular chemistry, offering molecules ranging from the block copolymers to the complexed macromolecular structures [89].

Sharpless and co-workers have identified a number of reactions that meet the criteria for click chemistry, arguably the most powerful of which discovered to date is the Cu(I)-catalyzed variant of the Huisgen 1,3-dipolar cycloaddition of azides and alkynes to afford 1,2,3-triazoles [90]. Because of Cu(I)-catalyzed variant of the Huisgen 1,3-dipolar cycloaddition of azides and alkynes reactions' quantitative yields, mild reaction condition, and tolerance of a wide range of functional groups, it is very suitable for the synthesis of polymers with various topologies and for polymer modification [91]. Because of these properties of Huisgen 1,3-dipolar cycloaddition, reaction is very practical. Moreover, the formed 1,2,3-triazole is chemically very stable [92].

In recent years, triazole forming reactions have received much attention and new conditions were developed for the 1,3-dipolar cycloaddition reaction between alkynes and azides [93]. 1,2,3-triazole formation is a highly efficient reaction without any significant side products and is currently referred to as a click reaction [94].

Copper(I)-catalyzed reaction sequence which regiospecifically unites azides and terminal acetylenes to give only 1,4-disubstituted 1,2,3 triazoles (2.13).



(2.13)

In fact, the discovery of Cu(I) efficiently and regiospecifically unites terminal alkynes and azides, providing 1,4-disubstituted 1,2,3-triazoles under mild conditions, was of great importance. On the other hand, Fokin and Sharpless proved that only 1,5-disubstituted 1,2,3-triazole was obtained from terminal alkynes when the catalyst switched from Cu(I) to ruthenium(II) [92].

3. EXPERIMENTAL WORK

3.1 Materials

Methyl methacrylate (MMA, 99%, Aldrich) was passed through basic alumina column to remove inhibitor and then distilled over CaH_2 in vacuum prior to use. ε-Caprolactone (ε-CL, 99 %, Aldrich) was distilled from CaH_2 in vacuum. Poly(ethylene glycol monomethyl ether) (PEG-OH) (M_n= 550 g/mol, Acros, M_n = 2000 g/mol, Fluka) was dried over anhydrous toluene by azeotropic distillation. *N,N,N',N'',N''*-Pentamethyldiethylenetriamine (PMDETA, 99%, Aldrich) was distilled over NaOH prior to use. *N,N'*-Dicyclohexylcarbodiimide (DCC, 99%, Aldrich), 4-dimethylaminopyridine (DMAP, 99%, Acros), CuCl (99.9 %, Aldrich), 9-anthracene methanol (97%, Aldrich), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 99%, Aldrich), *N,N'*-dicyclohexylcarbodiimide (DCC, 99%, Aldrich), 4-dimethylaminopyridine (DMAP, 99%, Acros), benzyl alcohol (99.8%, Aldrich), and ethyl chloroformate (97%, Aldrich) were used as received. Dichloromethane (CH_2Cl_2, Aldrich) was used after distillation over P_2O_5. Tetrahydrofuran (THF; 99.8%, J.T. Baker) was dried and distilled over benzophenone-Na. Solvents unless specified here were purified by conventional procedures. All other reagents were purchased from Aldrich and used as received without further purification.

3.2 Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on an Agilent VNMRS 500 (500 MHz for proton and 125 MHz for carbon) and on a Bruker AC-250 spectrometer (250 MHz for proton). The conventional gel permeation chromatography (GPC) measurements were carried out with an Agilent instrument (Model 1100) consisting of a pump, refractive index (RI) detector and four Waters Styragel columns (guard, HR 5E, HR 4E, HR 3, and HR 2), (4.6 mm internal diameter, 300 mm length, packed with 5 μm particles). The effective molecular weight ranges are 2000-4,000,000, 50-100,000, 500-30,000, and 500-20,000 g/mol, respectively. THF and toluene were used as eluent at a flow rate of 0.3 mL/min at 30 °C and as an internal standard, respectively.

The apparent molecular weights ($M_{n,GPC}$ and $M_{w,GPC}$) and polydispersities (M_w/M_n) were determined with a calibration based on linear PS standards using PL Caliber Software from Polymer Laboratories. UV spectra were recorded on a Shimadzu UV-1601 spectrophotometer in CH_2Cl_2. The differential scanning calorimetry (DSC) measurements were performed on a DSC Q1000 (TA Instruments) instruments with a heating rate of 10 ^oC /min under nitrogen.

3.3 Synthetic Procedures

4,10-Dioxatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione **(1)** [123], 4-(2-hydroxyethyl)-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione **(2)** [123, 2-bromo-2-methyl propionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-en-4-yl) ethyl ester **(3)** [123], 4-(2-(1,3-dioxo-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindol-2(3H)-yl)ethoxy)-4-oxobutanoic acid **(4)** [123], 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea **(5)** [124] were prepared according to published procedures. Furan protected maleimide end functionalized PEG (PEG-MI, M_n= 550 and M_n = 2000), was prepared according to published procedure [125]. PEG (PEG-MI, M_n= 550 and M_n = 2000), was prepared according to published procedure.

3.3.1 Synthesis of 4,10-dioxatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione (1)

Maleic anhydride (30 g, 0.30 mol) was suspended in 150 mL of toluene and the mixture warmed to 80 °C. Furan (33.4 mL, 0.45 mol) was added via syringe and the turbid solution stirred for 6 h. The mixture was then cooled to ambient temperature white solids formed during standing were collected by filtration and washed with 2 × 30 mL of petroleum ether and once with diethyl ether (50 mL) yielding **1** as white needless. (Yield= 44.4 g, 87%). Mp: 114-115 ^oC (DSC). ^1H NMR ($CDCl_3$, δ) 6.57 (s, 2H, C*H*=C*H*, bridge protons), 5.45 (s, 2H, -C*H*O, bridge-head protons), 3.17 (s, 2H, C*H*-C*H*, bridge protons). ^{13}C NMR ($CDCl_3$, δ) 170.18, 137.29, 82.46, 48.88. Mass spectrometry (+EI) *m*/*z* (%): 167 [MH+] (50), 144 (35), 130 (20).

3.3.2 Synthesis of 4-(2-hydroxyethyl)-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5- dione (2)

The adduct **1** (10 g, 60 mmol) was suspended in methanol (150 mL) and the mixture was cooled to 0 °C. A solution of ethanolamine (3.6 mL, 60 mmol) in 30 mL of methanol was added dropwise (10 min) to the reaction mixture.

And the resulting solution was stirred for 5 min at 0 °C, then 30 min at ambient temperature, and finally refluxed for 8 h. After cooling the mixture to ambient temperature, solvent was removed under reduced pressure, and residue was dissolved in 150 mL of CH_2Cl_2 and washed with 3 × 100 mL of water. The organic layer was separated, dried over Na_2SO_4 and filtered. Removal of the solvent under reduced pressure gave white-off solid which was further purified by flash chromatography eluting with ethylacetate (EtOAc) to give the product as a white solid. (Yield= 4.9 g, 40%). Mp = 138-139 °C (DSC). ^{1}H NMR ($CDCl_3$, δ) 6.51 (s, 2H, C*H*=C*H*, bridge protons), 5.26 (s, 2H, -C*H*O, bridge-head protons), 3.74-3.68 (m, 4H, NCH_2CH_2OH), 2.88 (s, 2H, C*H*-C*H*, bridge protons). ^{13}C NMR ($CDCl_3$, δ) 177.03, 136.60, 81.09, 60.53, 47.74, 42.03. Mass spectrometry (+EI) *m*/*z* (%): 210 [MH+] (50), 145 (22), 142 (100), 124 (17).

3.3.3 Synthesis of 2-bromo-2-methyl propionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo [5.2.1.0^{2,6}] dec-8-en-4-yl) ethyl ester (3)

In a 250 mL of round bottom flask were added **2** (2.0 g, 9.55 mmol) and Et_3N (1.44 mL, 10.54 mmol) in 100 mL of THF. The mixture was cooled to 0 °C, and a solution of 2-bromo isobutyryl bromide (2.34 g, 10.0 mmol) in 25 mL of THF was added dropwise (30 min) to the reaction mixture. The white suspension was stirred for 3 h at 0 °C and subsequently at ambient temperature for overnight. The ammonium salt was filtered off and the solvent was removed under reduced pressure to give a pale-yellow residue that was further purified by column chromatography over silica gel eluting with EtOAc/hexane (1/4) to give **3** as a white solid. (Yield= 1.86 g, 55%). Mp = 81-82 °C (DSC). ^{1}H NMR ($CDCl_3$, δ) 6.49 (s, 2H, C*H*=C*H*, bridge protons), 5.24 (s, 2H, -C*H*O, bridge-head protons), 4.31 (t, *J* = 5.2 Hz, 2H, NCH_2CH_2OC=O), 3.79 (t, *J* =5.2 Hz, 2H, NC$H_2$$CH_2$OC=O), 2.85 (s, 2H, C*H*-C*H*, bridge protons), 1.87 (s, 6H, C(CH_3)$_2$-Br). ^{13}C NMR ($CDCl_3$, δ) 176.12, 171.55, 136.83, 81.09, 62.36, 55.96, 47.74, 37.69, 30.83. Mass spectrometry (+EI) *m*/*z* (%): 360 [MH+] (100).

3.3.4 4-(2-(1,3-dioxo-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindol-2(3H)-yl)ethoxy)-4-oxobutanoic acid (4)

2 (5 g, 23.9 mmol) was dissolved in 150 mL of 1,4-dioxane. To the reaction mixture were added Et_3N (16.58 mL, 119.6 mmol), DMAP (4.38 g, 35.8 mmol), and succinic anhydride (9.56 g, 95.6 mmol) in that order.

The reaction mixture was stirred for overnight at 50 ^{o}C, then poured into ice-cold water and extracted with CH_2Cl_2. The organic phase was washed with 1 M HCl, dried over Na_2SO_4 and concentrated. The crude product was crystallized from ethanol to give **4** as white crystal. Yield: 5.9 g (80%). M.p. = 122-123 ^{o}C (DSC). ^{1}H NMR ($CDCl_3$, δ) 6.50 (s, 2H, C*H*=C*H*, bridge protons), 5.25 (s, 2H, -C*H*O, bridge-head protons), 4.25 (t, *J* = 5.2 Hz, 2H, $NCH_2CH_2OC=O$), 3.74 (t, *J* =5.2 Hz, 2H, $NCH_2CH_2OC=O$), 2.87 (s, 2H, C*H*-C*H*, bridge protons), 2.66-2.53 (m, 4H, $C=OCH_2CH_2C=OOH$). ^{13}C NMR ($CDCl_3$, δ) 177.26, 176.35, 172.01, 136.83, 81.09, 61.22, 47.74, 37.92, 29.24. Mass spectrometry (+EI) *m*/*z* (%): 310 [MH+] (100), 242 (100), 142 (18), 124 (13).

3.3.5 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea) (5)

Cyclohexylamine (1.85 g, 18.5 mmol) was added dropwise at room temperature to a stirring solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (5.0 g, 19 mmol) in THF (20 mL). After the solution was stirred for 4 h, the solvent was evaporated. The white residue was recrystallized from hexane to give TU as a white powder. Yield: 5.90 g (86%).

3.3.6 Preparation of benzyl functional carbonate monomer

Benzyl functional carbonate monomer was prepared in two step.

3.3.7 Benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate (6)

2,2 bis(dihydroxymethyl)propionic acid (5.0 g, 0.037 mol) and KOH (2.6 g, 0.045 mol) in 40 mL of THF were added into a 100 mL of three-neck round bottom flask. After the solution was stirred at 100˚C for 1 h, the temperature was decreased to 45°C and benzyl bromide (5.0 mL, 0.042 mol) was added drop-wise to the solution. The white suspension was further stirred at 45 °C overnight. The salt was filtered off and the mixture was extracted with CH_2Cl_2 (250 mL) and three times distilled water (50 mL). After evaporation of solvent, the remaining yellow residue was further purified by crystallization from ethyl acetate/hexane (1/1) to give benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate as white powder. The compound was further dried at 40 ºC in a vacuum oven for 24 h (Mp = 77.8 °C, DSC). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.40-7.30 (m, 5H, Ar*H*), 5.21 (s, 2H, PhCH_2O), 3.94 (d, 2H, *J* = 10 Hz,

CC*H*$_2$OH), 3.74 (d, 2H, *J* = 10 Hz, CC*H*$_2$OH), 2.88 (bs, 1H, CH$_2$O*H*), 1.08 (s, 3H, C*H*$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ) 175.72 (PhCH$_2$O*C*=O), 135.66 (Ar*C* of Ph), 128.62 (Ar*C* of Ph), 128.31 (Ar*C* of Ph), 127.85 (Ar*C* of Ph), 68.31 (C*C*H$_2$OH), 66.69 (Ph-*C*H$_2$O), 49.25 (*C*CH$_3$), 17.11 (C*C*H$_3$).

3.3.8 Synthesis of monomer (benzyl 5-methyl-2-oxo-1,3-dioxane-5- carboxylate) (7)

Previously obtained benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate (5.0 g, 0.022 mol) was added in a 250 mL of three-neck round bottom flask and dissolved in 100 mL of THF. The solution was cooled to 0 °C and a solution of ethyl chloroformate (4.2 mL, 0.044 mol) in 25 mL of THF was added dropwise to the reaction mixture. Next a solution of triethylamine (9.3 mL, 0.066 mol) in 25 mL of THF was added dropwise to the reaction mixture for 20 min. The white suspension was stirred at 0 °C for 2 h and subsequently at ambient temperature overnight. The ammonium salt was filtered off and the solvent was removed under reduced pressure. The remaining residue was further purified by crystallization from ethyl acetate/hexane (1/1) to give **1** as a white powder and finally dried at 40 ºC in vacuum oven for 24 h (Yield = 4 g (80%); Mp = 72.2 °C, DSC). ^{1}H NMR (500 MHz, CDCl$_3$, δ) 7.40-7.30 (m, 5H, Ar*H*), 5.22 (s, 2H, PhC*H*$_2$O), 4.71 (d, 2H, *J* = 10 Hz, CC*H*$_2$OC=O), 4.20 (d, 2H, *J* = 10 Hz, CC*H*$_2$OC=O), 1.33 (s, 3H, C*H*$_3$). ^{13}C NMR (125 MHz, CDCl$_3$, δ) 170.90 (PhCH$_2$O*C*=O), 147.38 (O*C*=OO), 134.74 (Ar*C* of Ph), 128.78 (Ar*C* of Ph), 128.76 (Ar*C* of Ph), 128.23 (Ar*C* of Ph), 72.95 (*C*H$_2$OC=OO), 67.94 (Ph*C*H$_2$O), 40.24 (*C*CH$_3$), 17.62 (C*C*H$_3$).

3.3.9 Preparation of α-anthracene-terminated polycarbonate (PC$_{30}$-anthracene)

PC$_{30}$-anthracene was prepared by ROP of **7** (2 g, 8 mmol) using DBU (0.038 mL, 0.27 mmol) and TU (0.098 g, 0.27 mmol) as catalyst and 9-anthracene methanol (0.055 g, 0.26 mmol) as an initiator in CH$_2$Cl$_2$ at room temperature for 5 h. The degassed monomer in CH$_2$Cl$_2$ (14 mL), catalyst, and initiator were added to a 25 mL two-neck round bottom flask that had been flame-dried under vacuum and purged with argon. The tube was degassed with three freeze-pump-thaw (FPT) and left in vacuum. After the polymerization, the mixture was concentrated and precipitated into an excess amount of methanol at ambient temperature.

The recovered polymer was redissolved in THF and precipitated in methanol/diethyl ether (1/1), and then THF/methanol. The purified polymer was finally dried at 40 ºC in a vacuum oven for 24 h (Yield: 1.84 g, 92%; $M_{n,theo}$= 7130 g/mol, $M_{n,NMR}$ = 7710 g/mol, $M_{n,UV}$ =7665 g/mol, $M_{n,GPC}$ = 5000 g/mol, M_w/M_n= 1.32, relative to PS standards). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 8.49 (s, 1H, Ar*H* of anthracene), 8.33 (d, 2H, Ar*H* of anthracene), 7.99 (d, 2H, Ar*H* of anthracene), 7.60-7.20 (m, Ar*H* of anthracene and Ar*H* of Ph), 6.17 (s, 2H, CH_2-anthracene), 5.13 (bs, PhCH_2O of PC), 4.29 (bs, CH_2OC=O of PC), 3.71 (bs, 2H, CH_2OH, end-group of PC), 1.23 (bs, CH_3 of PC).

3.3.10 Preparation of furan-protected maleimide-end-functionalized PEG (PEG_{11}-MI)

Me-PEG_{11} (M_n = 550) (2.0 g, 3.63 mmol) was dissolved in 50 mL of CH_2Cl_2. To the reaction mixture were added DMAP (0.044 g, 0.363 mmol) and 4 (2.24 g, 7.27 mmol) in that order. After stirring 5 min at room temperature, a solution of DCC (1.49 g, 7.27 mmol) in 10 mL of CH_2Cl_2 was added. Reaction mixture was stirred for overnight at room temperature. After filtration off the salt, the solution was concentrated and the viscous brown color product was purified by column chromatography over silica gel eluting with CH_2Cl_2/EtOAc mixture (1:1, v/v) and then with CH_2Cl_2/methanol (90:10, v/v) to obtain MI-PEG as viscous brown oil. Yield: 2.7 g (88%). ^{1}H NMR ($CDCl_3$, δ) 6.50 (s, 2H, C*H*=C*H* as bridge protons), 5.25 (s, 2H, -C*H*O, bridge-head protons), 4.23 (m, 4H, CH_2OC=O), 3.75-3.51 (m, OCH_2CH_2 repeating unit of PEG, C=ONCH_2, and CH_2-PEG repeating unit), 3.36 (s, 3H, PEG-OCH_3), 2.87 (s, 2H, C*H*-C*H*, bridge protons) 2.61-2.56 (m, 4H, C=OCH_2CH_2C=O).

3.3.11 Preparation of furan-protected maleimide-end-functionalized PEG (PEG_{37}-MI)

PEG_{44}-OH (M_n = 2000) (2.0 g, 1 mmol) was dissolved in 80 mL of CH_2Cl_2. To the reaction mixture were added DMAP (0.13 g, 1.0 mmol) and 10 (0.62 g, 2 mmol) in that order. After stirring 5 min at room temperature, a solution of DCC (0.41 g, 2.0 mmol) in 10 mL of CH_2Cl_2 was added.

Reaction mixture was stirred overnight at room temperature. After filtration off the urea byproduct, the mixture was precipitated into diethyl ether for three times to obtain pure MI-PEG as a pale white solid. (Yield= 1.9 g, 83%).

^{1}H NMR ($CDCl_3$, δ) 6.50 (s, 2H, C*H*=C*H* as bridge protons), 5.25 (s, 2H, -C*H*O, bridge-head protons), 4.23 (m, 4H, CH_2OC=O), 3.75-3.51 (m, OCH_2CH_2 repeating unit of PEG, C=ONCH_2, and CH_2-PEG repeating unit), 3.36 (s, 3H, PEG-OCH_3), 2.87 (s, 2H, C*H*-C*H*, bridge protons) 2.61-2.56 (m, 4H, C=OCH_2CH_2C=O).

3.3.12 Preparation of furan-protected maleimide-end-functionalized PMMA ($PMMA_{26}$-MI)

In a 25 mL of Schlenk tube, MMA (5.0 mL, 47 mmol), PMDETA (0.20 mL, 0.94 mmol), CuCl (0.093 g, 0.94 mmol), toluene (5 mL), and 2-bromo-2-methyl-propionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-en-4-yl)-ethyl ester (0.34 g, 0.94 mmol) were added, and the reaction mixture was degassed by FPT cycles, and left in argon. The tube was then placed in a thermostated oil bath at 40 °C for a predetermined time. The polymerization mixture was diluted with THF, passed through a basic alumina column to remove the catalyst, and precipitated into hexane. The polymer was dried for 24 h in a vacuum oven at 40 °C ($M_{n,theo}$ = 2800 g/mol, $M_{n,NMR}$ = 2900 g/mol, $M_{n,GPC}$=2700 g/mol, M_w/M_n = 1.32). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 6.54 (s, 2H, C*H*=C*H*, bridge protons), 5.27 (s, 2H, -C*H*O, bridge-head protons), 4.17 and 4.12 (m, 2H, NCH_2CH_2OC=O), 3.75-3.50 (m, OCH_3 of PMMA and NCH_2CH_2OC=O), 2.91 (s, 2H, C*H*-C*H*, bridge protons), 2.20-0.75 (m, aliphatic protons of PMMA).

3.3.13 Preparation of furan-protected maleimide-end-functionalized PCL (PCL_{27}-MI)

PCL_{27}-MI was prepared by ROP of ε-CL (5.0 mL, 0.045 mol) using both DBU (0.168 mL, 1.13 mmol) and TU (0.417 g, 1.13 mmol) as catalyst and 2 (0.235 g, 1.13 mmol) as an initiator at 40 °C for 4 h. The degassed monomer in CH_2Cl_2 (8 mL), catalyst, and initiator were added to a previously flamed schlenk tube equipped with a magnetic stirring bar in the order mentioned. The tube was degassed with three freeze-pump-thaw (FPT) and left in vacumm. After the polymerization, the mixture was diluted with THF, and precipitated into an excess amount of cold methanol.

The purified polymer was isolated by filtration and dried at 40 ºC in a vacuum oven for 24 h (Yield = 3.49 g, 67 %, $M_{n,theo}$ = 3100 g/mol, $M_{n,NMR}$ = 3300 g/mol, $M_{n,GPC}$ = 5750 g/mol, M_w/M_n= 1.08, relative to PS standards). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.52 (s, 2H, C*H*=C*H*, vinyl protons), 5.26 (s, 2H, -C*H*O, bridge-head protons), 4.22 (t, 2H, NCH_2CH_2OC=O), 4.06 (t, CH_2OC=O of PCL), 3.78-3.60 (m, 4H, NCH_2CH_2OC=O and CH_2OH end-group of PCL), 2.87 (s, 2H, C*H*-C*H*, bridge protons), 2.31 (t, C=OCH_2 of PCL), 1.85-1.25 (m, CH_2 of PCL).

3.3.14 Preparation of PC-*b*-PEG copolymer via Diels-Alder click reaction between PC_{30}-anthracene and PEG_{11}-MI

PC_{30}-anthracene (0.10 g, 0.013 mmol, $M_{n,NMR}$ = 7710 g/mol, 1 equiv) and PEG_{11}-MI (0.016 g, 0.019 mmol, $M_{n,theo}$ = 840 g/mol, 1.5 equiv) were dissolved in 30 mL of toluene. Next, the mixture was bubbled with nitrogen for 30 min and refluxed at 110 ^{o}C for 48 h in the dark. After this specified time, solution was evaporated to dryness and the residual solid was dissolved in THF, and subsequently precipitated in methanol. This dissolution-precipitation procedure was repeated two times and the obtained product was dried in a vacuum oven at 40 ºC for 24 h (Yield = 0.10 g). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.60-7.00 (m, Ar*H* of benzyl and Diels-Alder adduct), 5.64 (bs, CH_2-Diels-Alder adduct), 5.13 (bs, PhCH_2O of PC), 4.76 (m, C*H*, bridge head proton), 4.28 (bs, CH_2OC=O of PC and C=OOCH_2CH_2), 3.80-3.00 (m, OCH_2CH_2, PEG repeating unit, C=OOCH_2CH_2N, C=OOCH_2CH_2N, OCH_3 end-group of PEG and C*H*-C*H* bridge protons), 2.62 and 2.52 (br, C=OCH_2CH_2C=O), 1.22 (bs, CH_3 of PC).

3.3.15 Preparation of PC-*b*-PEG copolymer via Diels-Alder click reaction between PC_{30}-anthracene and PEG_{37}-MI

PC_{30}-anthracene (0.25 g, 0.032 mmol, based on $M_{n,NMR}$ = 7710 g/mol, 1 equiv) and PEG_{37}-MI (0.115 g, 0.05 mmol, $M_{n,theo}$ = 2300 g/mol, 1.5 equiv) were dissolved in 40 mL of toluene. Then, the reaction mixture was bubbled with nitrogen for 30 min and refluxed at 110 ^{o}C in the dark for 48 h. After this specified time, the solution was evaporated to dryness and the residual solid was dissolved in THF, and subsequently precipitated in methanol. This dissolution-precipitation procedure was repeated two times and the recovered product was dried in a vacuum oven at 40 ºC for 24 h

(Yield = 0.22 g). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.60-7.00 (m, Ar*H* of benzyl and Diels-Alder adduct), 5.63 (br, CH_2-Diels-Alder adduct), 5.12 (bs, PhCH_2O of PC), 4.75 (m, C*H*, bridge head proton), 4.27 (bs, CH_2OC=O of PC and C=OOCH_2CH$_2$),

3.80-3.00 (m, OCH_2CH_2, PEG repeating unit, C=OOCH_2CH$_2$N, C=OOCH$_2$CH_2N, OCH_3 end-group of PEG and C*H*-C*H* bridge protons), 2.61 and 2.52 (br, C=OCH_2CH_2C=O), 1.22 (bs, CH_3 of PC).

3.3.16 Preparation of PC-*b*-PMMA copolymer via Diels-Alder click reaction between PC_{30}-anthracene and $PMMA_{26}$-MI

PC_{30}-anthracene (0.20 g, 0.026 mmol, $M_{n,NMR}$ = 7710 g/mol, 1 equiv) and $PMMA_{26}$-MI (0.098 g, 0.033 mmol, $M_{n,NMR}$ = 2900 g/mol, 1.3 equiv) were dissolved in 20 mL of toluene. Subsequently, the mixture was bubbled with nitrogen for 30 min and refluxed at 110 ^{o}C for 48 in the dark h. After this specified time, solution was evaporated to dryness and the residual solid was dissolved in THF, precipitated in methanol and methanol/diethyl ether mixture, respectively (1/1, v/v). The obtained product was dried in a vacuum oven at 40 ºC for 24 h (Yield = 0.25 g).

^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.60-7.00 (m, Ar*H* of benzyl and Diels-Alder adduct), 5.60 (br, CH_2-Diels-Alder adduct), 5.12 (bs, PhCH_2O of PC), 4.76 (m, C*H*, bridge head proton), 4.27 (m, CH_2OC=O of PC and C=OOCH_2CH$_2$), 3.80-3.00 (m, OCH_3 of PMMA, C=OOCH$_2$CH_2N, and C*H*-C*H* bridge protons), 2.20-0.60 (CH_2 and CH_3 of PMMA and CH_3 of PC).

3.3.17 Preparation of PC-*b*-PCL copolymer via Diels-Alder click reaction between PC_{30}-anthracene and PCL_{27}-MI

PC_{30}-anthracene (0.25 g, 0.033 mmol, based on $M_{n,NMR}$ = 7710 g/mol, 1 equiv) and PCL_{27}-MI (0.14 g, 0.043 mmol, $M_{n,NMR}$ = 3300 g/mol, 1.3 equiv) were dissolved in 40 mL of toluene. Subsequently, the mixture was bubbled with nitrogen for 30 minutes and refluxed at 110^{o}C in the dark for 48 h. After this specified time, solution was evaporated to dryness and the residual solid was dissolved in THF, precipitated in methanol and methanol/diethyl ether mixture, respectively (1/1, v/v). The obtained product was dried in a vacuum oven at 40 ºC for 24 h (Yield = 0.23 g). ^{1}H NMR (500 MHz, $CDCl_3$, δ) 7.60-7.00 (m, Ar*H* of Ph and Ar*H* of Diels-Alder adduct), 5.61 (br, CH_2-Diels-Alder adduct), 5.12 (br, 2H, PhCH_2O of PC), 4.75

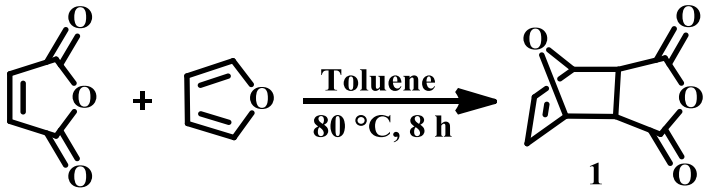
(m, C*H*, bridge head proton), 4.27 (m, CH_2OC=O of PC and C=OOCH_2CH$_2$), 4.06 (t, CH_2OC=O of PCL), 3.80-3.60 (m, NCH_2CH$_2$OC=O, CH_2OH end-group of PC and CH_2OH end-group of PCL), 3.32 (m, C*H*-C*H*, bridge protons), 2.31 (t, 2H, C=OCH_2 of PCL), 1.80-1.15 (m, CH_2 of PCL and CH_3 of PC).

4. RESULTS AND DISCUSSION

Herein we studied Diels-Alder reaction strategy for the production of a wide variety of PC based block copolymers. Although the PC based block copolymers have been generally prepared by the growing a second block (PC or other polymer) from the hydroxyl-terminated macroinitiator (other polymer or PC) via only ROP, the Diels-Alder reaction as a modular click reaction strategy has been successfully adapted to the synthesis of the PC-based block copolymers via the ligation of an α-anthracene-terminated PC with a wide variety of α-furan protected-maleimide-terminated homopolymers (PEG_{11}-MI, and PEG_{37}-MI, $PMMA_{26}$-MI and PCL_{27}-MI).

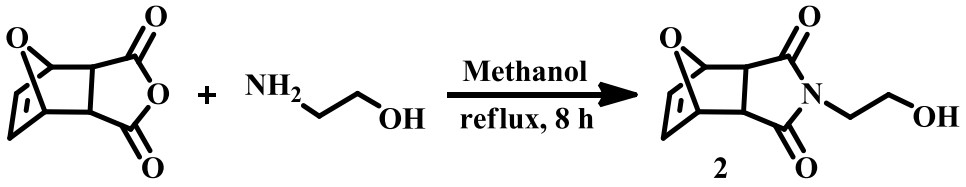
4.1 Synthesis of Initiators

First of all, maleic anhydride and furan were reacted in toluene at reflux temperature for 8 h to give 4,10-Dioxatricyclo[5.2.1.02,6]dec-8-ene-3,5-dione **(1)** (equation 4.1). The anhydride **1** was obtained as small white needless.



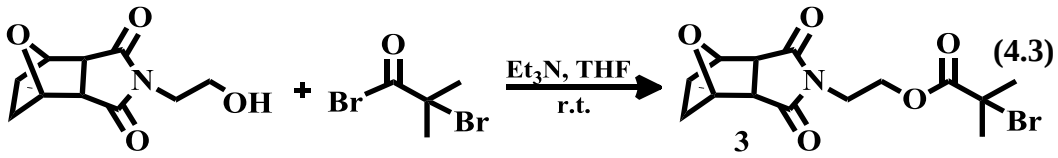
(4.1)

The reaction of the anhydride **1** was then carried out to give the 4-(2-Hydroxyethyl)-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-ene-3,5- dione **(2).** In this reaction, the anhydride **1** was suspended in MeOH and a solution of ethanolamine in MeOH was added at 0 ^{o}C, then the mixture refluxed for 8 h (equation 4.2). Finally, compound **2** was obtained as a white solid.



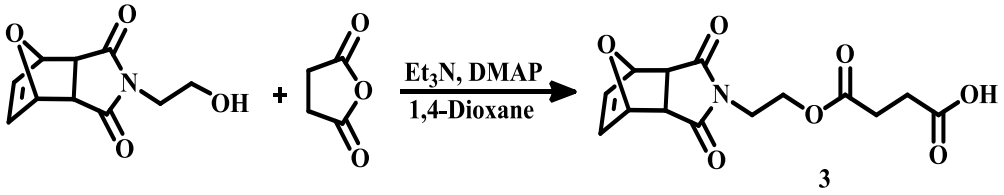
(4.2)

The synthesis of 2-bromo-2-methyl-propionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-en-4-yl) ethyl ester **(3)** was obtained via an esterification reaction between **2** and 2-bromoisobutryl bromide in THF at room temperature (equation 4.3). Thus, the initiators with proper functionalities for DA reaction were first prepared.



(4.3)

The hydoxyl functionality of **2** was converted to carboxylic acid via a reaction with succinic anhydride in the presence of Et_3N/DMAP catalyst system and 1,4-dioxane as solvent in order to give the 4-(2-{[(3-acetyl-7-oxabicyclo[2.2.1]hept-yl)carbonyl]amino}ethoxy)-4-oxobutanoic acid **(4)** (equation 4.4).



(4.4)

From overlay ^{1}H NMR spectra Figure 4.1 of **4**, methylene protons next to the ester ($NCH_2CH_2OC{=}O$) and methylene protons adjacent to nitrogen ($NCH_2CH_2OC{=}O$) appeared at 4.25 ppm and 3.74 ppm respectively. Moreover, the multiplet peaks around 2.66-2.53 ppm confirmed successful conversion of hydroxyl group to carboxylic acid. From spectrum (c), it is clearly seen that the methyl protons next to Br were detected at 1.87 ppm and the methylene protons next to the ester unit at 4.31 ppm. Moreover, the characteristic protons of the adduct were also detected at 6.49 ppm (bridge vinyl protons), 5.24 ppm (bridge-head protons) and 2.85 ppm (bridge protons) respectively. These results confirmed that the synthesis of **3** was achived.

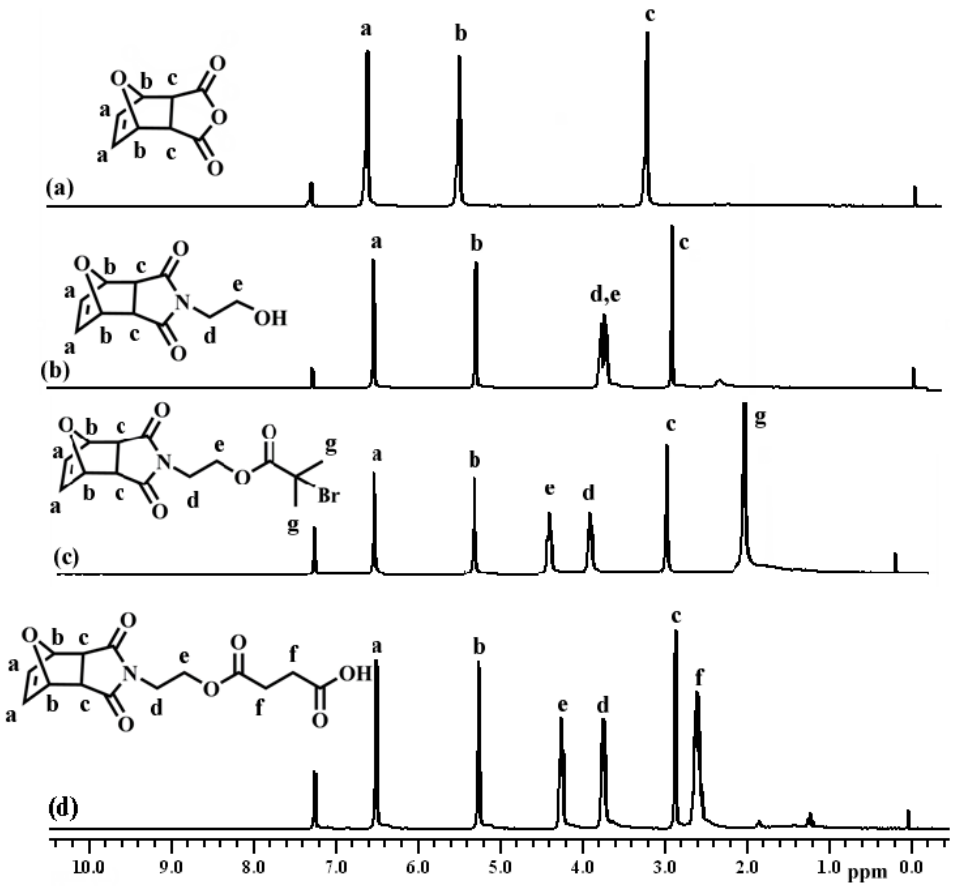
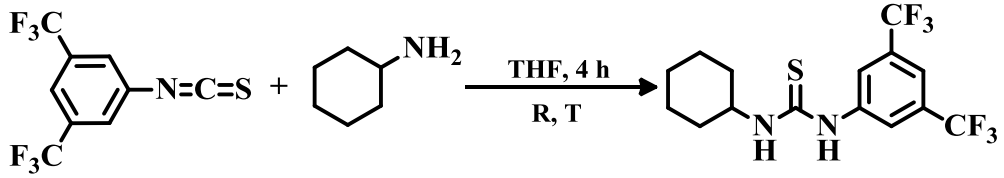


Figure4.1: ^{1}H NMR spectra of: **a**) 3-acetyl-N-(2-hydroxyethyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid **(1)**; **b**) 3-acetyl-N-(2-hydroxyethyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxamide (**2)**; **c)** 2-bromo-2- methyl-propionic acid 2-(3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-en-4-yl) ethyl ester **(3)**; **d**) 4-(2-{[(3-acetyl-7-oxabicyclo[2.2.1]hept-yl)carbonyl]amino}ethoxy)-4-oxobutanoic acid **(4)** in $CDCl_3$.

To synthesize 1-(3,5-bis(trifloromethyl)phenyl)-3-cyclohexylthiourea) is in other world co-catalyst (TU), cyclohexylamine and 3,5-bis(trifluoromethyl)phenyl isothiocyanate were reacted in THF at room temperature for 4h (equation 4.6). Finally, compound **5** was obtained as a white solid.



(4.6)

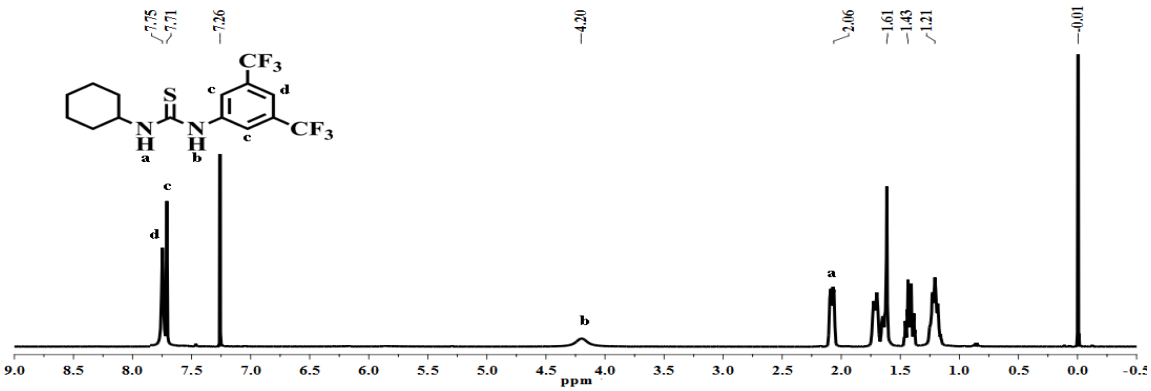
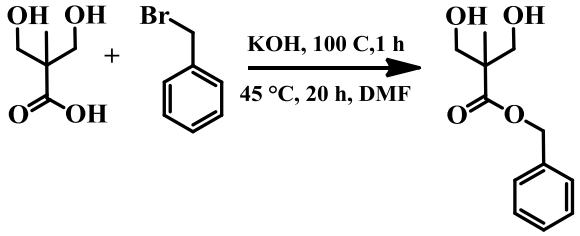


Figure4.2: ^{1}H NMR spectrum of 1-(3,5-bis(triflоromethyl)phenyl)-3-cyclohexylthiourea) in $CDCl_3$ (500 MHz).

4.2 Preparation of Benzyl Functional Carbonate Monomer

Initially, benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate **(6)** was synthesized by this way; 2, 2-bis (hydroxymethyl)-propanoic acid was reacted with KOH to become potassium salt of benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate in DMF at 100°C. After 1h temperature was decreased in 45°C, than benzylbromide added to reaction mixture. Process is given below schematically (equation 4.7).



(4.7)

^{1}H NMR spectroscopy confirmed clearly the structure of **6** by appearance of characteristic signals of phenyl 7.4-7.3 ppm. It is obviously seen that the peak of methylene protons neighbouring to hydroxyl group is between 3.72 and 3.94 ppm.

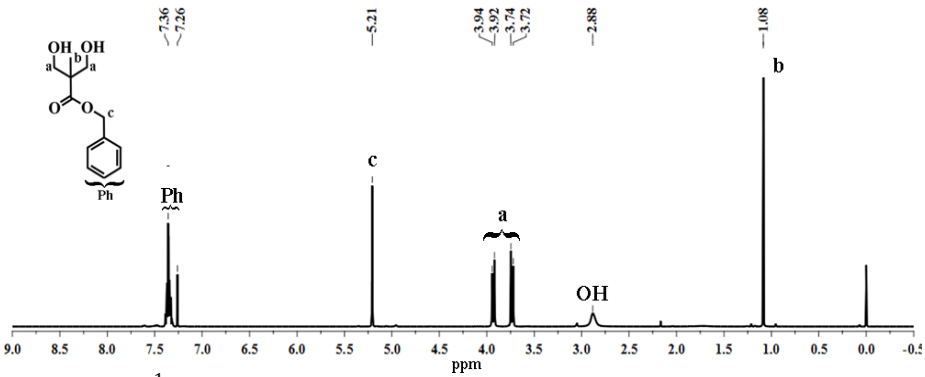
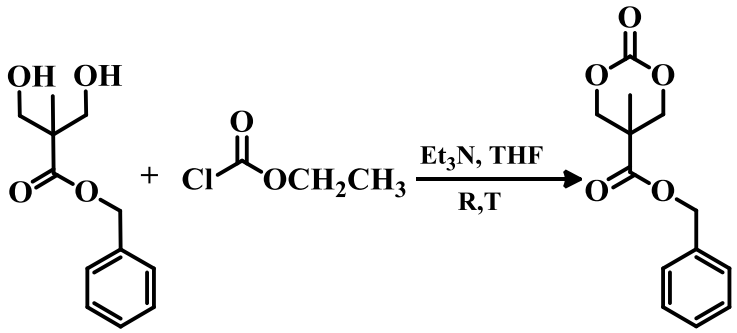


Figure4.3: ^{1}H NMR spectrum of benzyl 3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate in $CDCl_3$ (500 MHz).

In the following step, benzyl-carbonate monomer (benzyl 5-methyl-2-oxo-1,3-dioxane-5- carboxylate) was synthesized **(4.8).** The cyclization was performed in the presence of ethyl chloroformate in dilute anhydrous THF solution via dropwise addition of triethylamine.



(4.8)

^{1}H NMR spectroscopy confirmed clearly the structure of **7** by appearance of characteristic signals of phenyl (δ 7.4-7.3). The double doublets at δ 4.19/4.72 were attiributable to the methylene protons next to the carbonate. Importantly, no peak at δ 3.72-3.94 assignable to the methylene protons adjacent to the hydroxyl group was detected.

The ^{1}H NMR and elemental analysis of Benzyl-carbonate showed similar outcome.

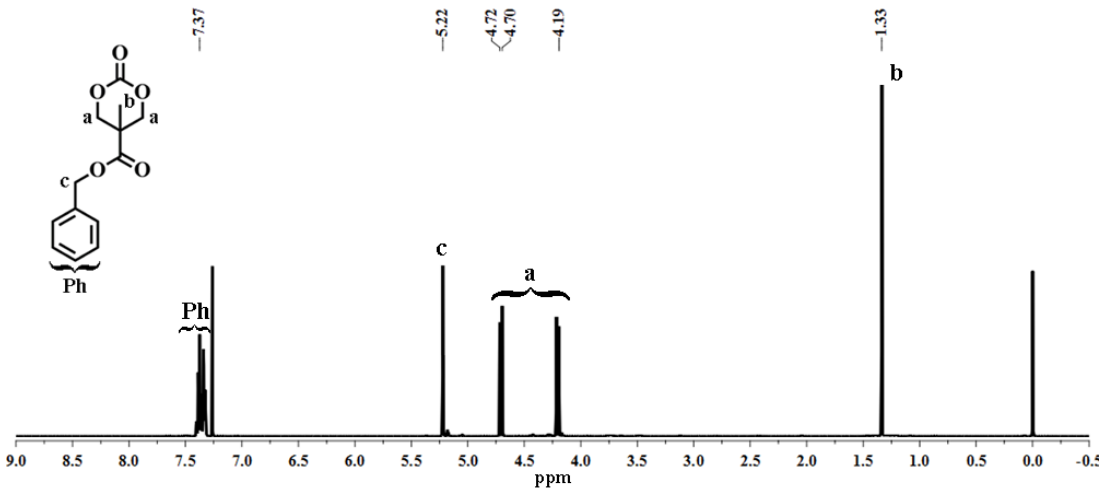


Figure4.4: ^{1}H NMR spectrum of benzyl 5-methyl-2-oxo-1,3-dioxane-5- carboxylate in $CDCl_3$ (500 MHz).

In addition, ^{13}C NMR spectroscopy indicated a peak at 147.38 ppm that proved the cyclic carbonate formation.

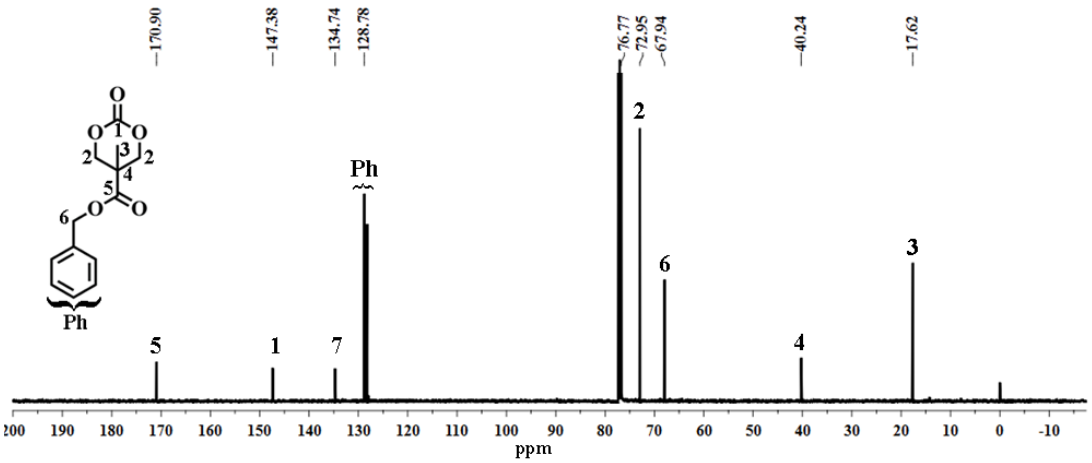
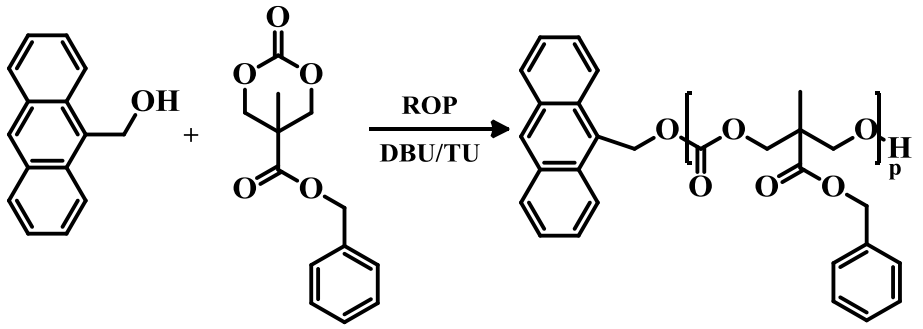


Figure4.5: ^{13}C NMR spectrum of benzyl 5-methyl-2-oxo-1,3-dioxane-5- carboxylate in $CDCl_3$ (500 MHz).

4.3 Preparation of the Block Copolymers via Combination of ROP and Diels-Alder Click Reaction

The α-anthracene-terminated polycarbonate (PC_{30}-anthracene) was prepared from the ROP of benzyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (**7**) using 9-anthracene methanol as initiator and TU/DBU as catalyst in CH_2Cl_2 at room temperature for 5 h (4.9). The structure of the PC_{30}-anthracene was confirmed by ^{1}H NMR and UV spectroscopy. From ^{1}H NMR spectroscopy, two doublets (4.72 and 4.19 ppm) corresponding to the CH_2 adjacent to the carbonate group in **7** disappeared and a new broad singlet signal at 4.29 ppm that is assigned to the CH_2OC=O of PC appeared in association with the characteristic signals of the anthracene and CH_2 linked to the anthracene at 8.49-7.31 and 6.17 ppm, respectively (Figure 4.59).



(4.9)

The number-average molecular weight ($M_{n,NMR}$ = 30 (DP_n) X 250 g/mol + MW of end-groups (208 g/mol) = 7710 g/mol) of the PC-anthracene could be calculated by comparing integrated signals of the main backbone CH_2OC=O protons (4H) -098t 4.29 ppm and the anthracene protons (5H) between 8.49 and 7.99 ppm.

Furthermore, monitoring by UV spectroscopy, the characteristic five-finger absorbance of the anthracene end-group at 300-400 nm gave the $M_{n,UV}$ = 7665 g/mol, therefore confirming that every PC backbone is terminated with one anthracene functionality. Next, the $M_{n,theo}$ was determined according to the following equation, $M_{n,theo}$ = ($[M]_0/[I]_0$) X MW of **7** (250 g/mol) X conv. % + MW of end-groups (208 g/mol) = 7130 g/mol and found to be consistent with the $M_{n,NMR}$ and $M_{n,UV}$. The GPC analysis of PC_{30}-anthracene displayed a monomodal GPC trace with narrow polydispersity ($M_{n,GPC}$ = 5000 g/mol, M_w/M_n = 1.32 with respect to PS standards).

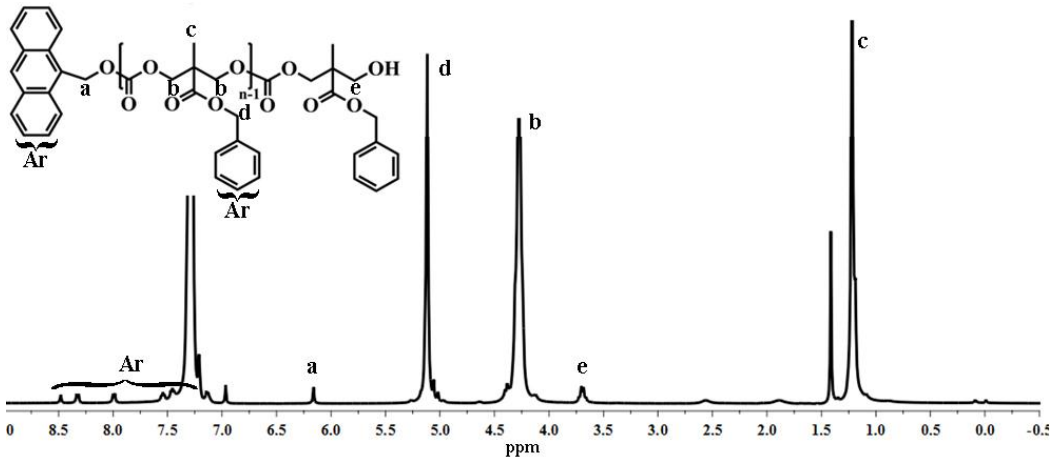
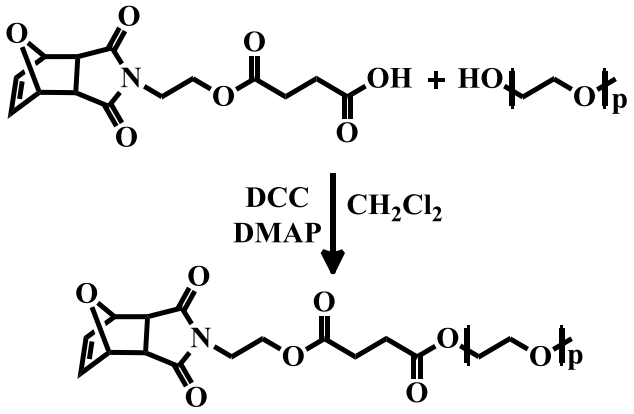


Figure4.6: ^{1}H NMR spectrum of α-anthracene-terminated polycarbonate (PC_{30}-anthracene) and cyclic carbonate in $CDCl_3$ (500 MHz).

Before ATRP of the precursor polymers, condensation reactions of PEG_{11} precursor was carried out. First, PEG_{11}-MI was obtained via an esterification reaction between Me-PEG (M_n=550) and excess amount of **4** in the presence of DCC as a coupling agent and DMAP as a catalyst (4.10).



(4.10)

From ^{1}HNMR spectrum of the polymer, the bridge and bridge-head protons were detected at 6.49, 5.24 and 2.86 ppm respectively.

The $M_{n,NMR}$= 750 of MI-PEG was determined from a ratio of integrated peaks at 3.62 ppm (OCH_2CH_2 protons of PEG) to 6.49 ppm (vinyl end protons).

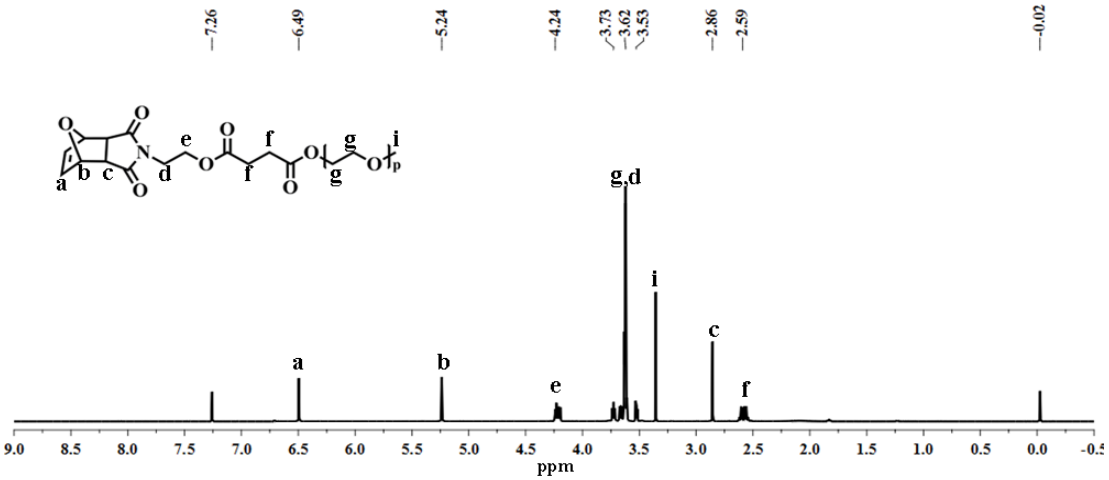


Figure4.7: ^{1}H NMR spectrum of PEG_{11}-MI in $CDCl_3$ (500 MHz).

Then, the commercially available PEG-OH (M_n = 2000 g/mol) was reacted with **4** affording PEG_{44}-MI. The structure of the desired PEG-MI could be fully identified by ^{1}H NMR (Figure 4.8). The characteristic protons of PEG-MI, such as vinyl (C*H*=C*H*), bridge-head (C*H*CH=CHC*H*), repeating unit of PEG (OCH_2CH_2) and bridge $CH_2N(C=O)C$*H-CH*) were assigned at 6.5, 5.2, 3.5-3.9 and 2.8 ppm, respectively. The $M_{n,NMR}$ was determined by comparing the integral of vinyl end group signal (δ 6.5) to those of repeating unit of PEG and N-CH_2 (δ 3.9-3.5), while including the MW of **4**. $M_{n,NMR}$ fit well with the $M_{n,theo}$ indicating a quantitative maleimide end-group functionalization (Table 4.1).

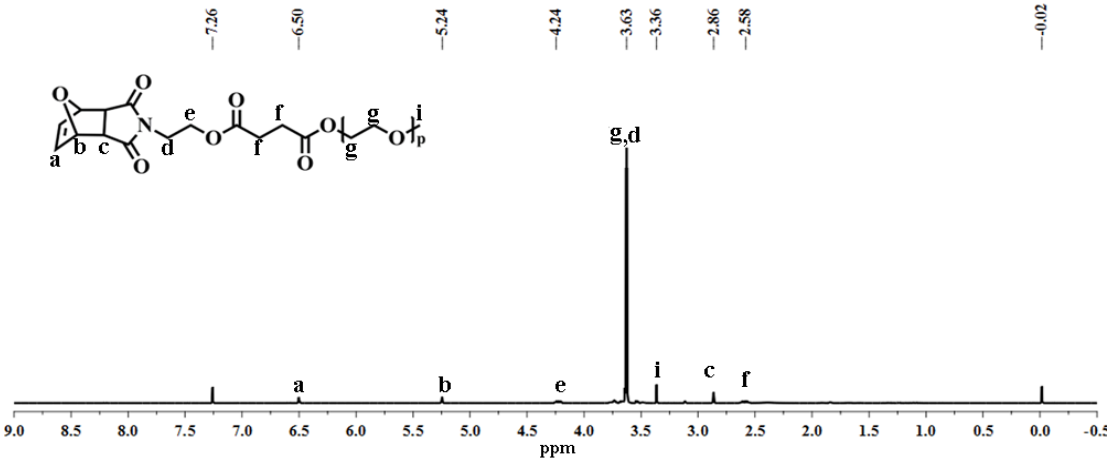
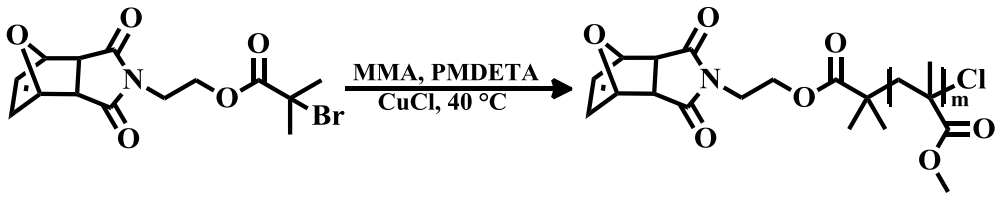


Figure4.8: ^{1}H NMR spectrum of PEG_{37}-MI in $CDCl_3$(500 MHz).

Then compound **3** was used as an initiator in ATRP of MMA in the presence of CuCl/PMDETA as a catalyst system at 40 ºC to obtain PMMA-MI **(4.11).** The maleimide functional group of the **3** was protected with furan in order to prevent radical copolymerization of maleimide with MMA during polymerization. The polymerization temperature was deliberately kept low avoiding furan deprotection at elevated temperatures. Number-average molecular weight calculated by GPC ($M_{n,GPC}$) of PMMA-MI was in fairly good agreement with the theoretical one ($M_{n,theo}$) indicating that the initiation was not quantitative under these polymerization conditions.



(4.11)

The $M_{n,NMR}$ of PMMA-MI (Figure 4.8) was determined from a ratio of integrated peaks at 3.59 ppm (OCH_3 protons of MMA) and N-CH_2 (δ 3.8 -3.4) to that of a signal at 6.5 ppm assignable to vinylic two protons, while being included the molecular weight of initiator (357 g/mol) (4.11). The number-average molecular weight obtained by GPC ($M_{n,GPC}$ = 2685 g/mol, relative to linear PMMA standarts) is an excellent agreement with $M_{n,NMR}$, thus indicating that the quantitative maleimide end-group functionalization of the PMMA was successful. Moreover, M_w/M_n = 1.31 calculated from GPC displays narrow molecular weight distribution.

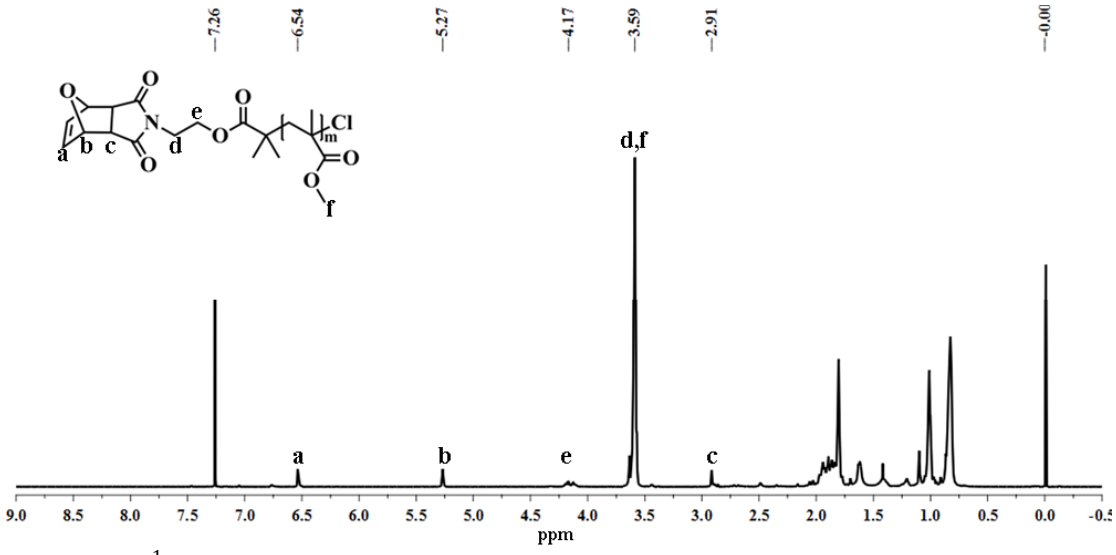
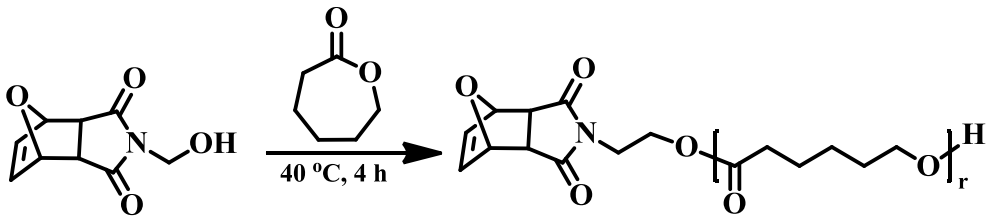


Figure4.9: ^{1}H NMR spectrum of PMMA-MI in $CDCl_3$ (500 MHz).

Then compound **2** was used as an initiator in ROP of ε-CL in the presence of both DBU and TU as a catalyst system at 40 ºC, 4h to obtain PCL-MI (4.12). The maleimide functional group of the **2** was protected with furan in order to prevent radical copolymerization of maleimide with ε-CL during polymerization. The polymerization temperature was deliberately kept low avoiding furan deprotection at elevated temperatures.



(4.12)

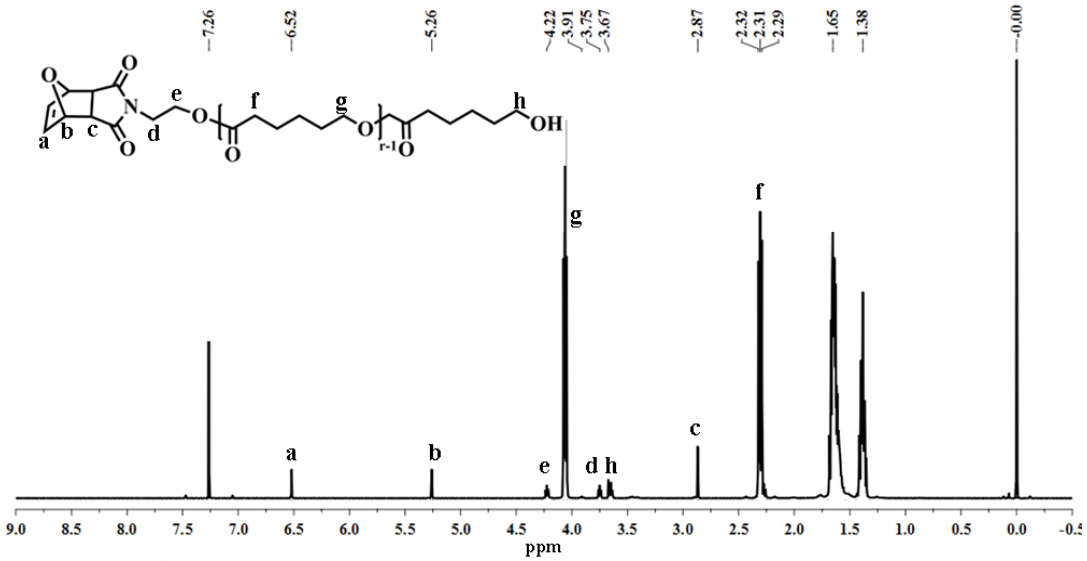


Figure4.10: ^{1}H NMR spectrum of PCL-MI in $CDCl_3$ (500 MHz).

Polymer was determined accordingly from the integration of the peaks at 4.03 ppm related to PCL repeating unit protons and N-CH_2 (δ 3.8 -3.4) to that of a signal at 6.5 ppm assignable to vinylic two protons.

Four samples of furan protected maleimide end-functionalized polymers were easily prepared using ATRP, condensation reaction as described before and ROP. Besides, $M_{n,NMR}$ of PC-Anth was calculated by comparing of the integrals of the aromatic protons of PC at 6.0-7.5 ppm and that of two protons of anthracene end group at 7.9 ppm. Furthermore, $M_{n,UV}$ of PC-Anth was calculated by assuming that ε of anthryl end goup was the same as that of 9-antracene methanol (ε = 5385 at 367 nm in CH_2Cl_2).

From Table 4.1, It was found good agreement between $M_{n,theo}$ $M_{n,NMR}$, $M_{n,GPC}$ and $M_{n,UV}$ values. The results of the linear polymers used for the synthesis of block copolymers were tabulated in Table 4.1.

Table 4.1: The results of linear polymers used in DA click reactions.

Polymer	$M_{n,GPC}$[f] (g/mol)	M_w/M_n	$M_{n,theo}$ (g/mol)	$M_{n,NMR}$[i] (g/mol)	$M_{n,UV}$ (g/mol)
PC_{30}-anthracene[a]	5000	1.32	6960[g]	7710	7665[j]
$PMMA_{26}$-MI[b]	2685	1.31	2800[g]	2915	-
PCL_{27}-MI[c]	2800[k]	1.08	3100[g]	3290	-
PEG_{11}-MI[d]	550	1.09	840[h]	860	-
PEG_{37}-MI[e]	3000	1.05	2300[h]	2800	-

[a] Synthesized by ROP of **(7)** in CH_2Cl_2 using DBU as a catalyst and 9-anthracene methanol as an initiator at 25 °C. $[M]_0:[I]_0 = 30$

[b] $[M]_0:[I]_0:[CuCl]:[PMDETA] = 50:1:1:1$; polymerization was carried out at 40 °C. MMA/toluene = 1/1 (v/v).

[c] Synthesized by ROP of ε-CL in CH_2Cl_2 using DBU as a catalyst and **(5)** as an initiator at 40 °C. $[M]_0:[I]_0 = 40$

[d] Obtained by an esterification reaction between compound PEG-OH (550) and **(4).**

[e] Obtained by an esterification reaction between compound PEG-OH (2000) and **(4).**

[f] Determined by using conventional GPC (RI detection) in THF at 30 ºC relative to PS standards except MI-PMMA relative to PMMA standards.

[g] $M_{n,theo} = ([M]_0/[I]_0)$ X conversion % X MW of monomer + MW of initiator.

[h] $M_{n,theo} = M_n$ of PEG-OH + MW of **(4).**

[i] Determined by ^1H NMR.

[j] The molecular weight of PC-Anth was calculated by employing UV-spectroscopy assuming that the molar extinction coefficient (ε=5385 L mol^{-1} cm^{-1} at 367 nm in CH_2Cl_2) of anthryl end group in the obtained polymer was the same as that of 9-anthracene methanol.

[k] Determining more precise the molecular weight for PCL, a correction formula was used $M_{n,PCL} = 0.259$ X $M_{n,GPC}^{1.073}$ where $M_{n,GPC}$ is the molecular weight determined from GPC using PS standards [126].

The PC_{30}-anthracene homopolymer was subsequently ligated with a variety of well-defined α-furan-protected maleimide-terminated linear polymers, PEG_{11}-MI, PEG_{37}-MI, $PMMA_{26}$-MI and PCL_{27}-MI in order to yield well-defined PC based block copolymers under Diels-Alder reaction conditions. The 1.3 and 1.5 equiv of the α-furan protected maleimide-terminated homopolymers with respect to the PC_{30}-anthracene were deliberately chosen to ensure the reaction completion, as well as easy elimination from the reaction mixture. The Diels-Alder adduct formation for all block copolymerization was monitored by UV spectroscopy by following the disappearance of the characteristic five-finger absorbance of the anthracene moiety at 300-400 nm and thereby, their Diels-Alder efficiencies (DA_{eff}) were calculated to be in the range of 90-95% (Table 4.2).

Table 4.2: Characteristics of PC-block copolymers

Polymer	$M_{n,GPC}$[c] (g/mol)	M_w/M_n[c]	$M_{n,theo}$[b] (g/mol)	$M_{n,NMR}$[e] (g/mol)	%DA_{eff}[d]
PC-*b*-PEG_{11}[a]	4200	1.26	8560	8565	91
PC-*b*-PEG_{37}[b]	4800	1.25	10500	9540	90
PC-*b*-$PMMA_{26}$	6400	1.31	010615	10520	94
PC-*b*-PCL_{27}	9800	1.14	10990	10600	95

[a]From PEG_{11}-MI. [b]From PEG_{37}-MI. [c]Determined by GPC (RI detection) in THF at 30 °C using PS calibration. [d]$M_{n,theo}$ = Sum of $M_{n,NMR}$ of the precursor polymer. [e]$M_{n,NMR}$ of the block copolymers were calculated by taking into account a ratio of integrated values of the PC_{30}-anthracene (DP_n = 30) to the PEG, PMMA, and PCL blocks. [e]DA_{eff} % = [1-(A_t/A_0)] X 100.

After purification the PC based block copolymers, a clear shift to the higher molecular weight region was detected from GPC measurements while maintaining narrow polydispersity index (M_w/M_n) and monomodal distribution, except for PC-*b*-PEG copolymer (from PEG_{11}-MI), in which a negligible change to the higher molecular weight occurred (Fig. 11 and 12).

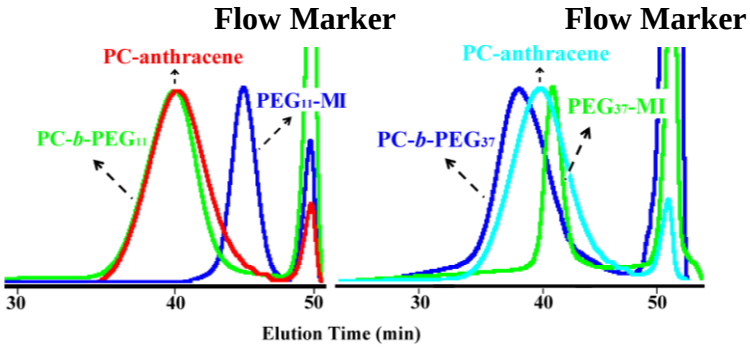


Figure 4.11: Overlay of GPC traces of PC_{30}-anthracene, PEG_{11}-MI, PEG_{37}-MI and their block copolymers in THF at 30°C

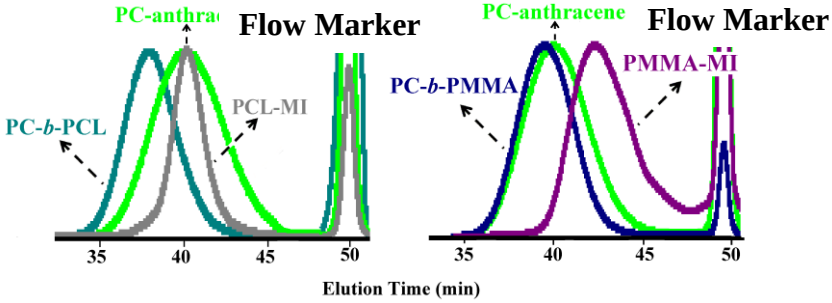


Figure 4.12: Overlay of GPC traces of PC_{30}-anthracene, $PMMA_{26}$-MI, PCL_{27}-MI and their block copolymers in THF at 30°C

Moreover, ^{1}H NMR spectroscopy clearly evidenced the structures of the target block copolymers. A rough examination of the ^{1}H NMR spectra of all block copolymers

proved the disappearance of the characteristic anthracene signals from 8.49 to 7.20 ppm coupled with the appearance of the C*H* (bridge-head proton) (*ca.* δ 4.75) and the CH_2-Diels-Alder adduct (*ca.* δ 5.64), indicating that the Diels-Alder reactions had successfully occurred. Also, the ^{1}H NMR spectroscopy analysis obviously showed the characteristic signals for the CH_2OC=O of the PC (4.27 ppm), the CH_2CH_2O of the PEG (3.64 ppm), the OCH_3 of PMMA (3.60 ppm) and the CH_2OC=O of PCL (4.06 ppm) segments in the corresponding block copolymers.

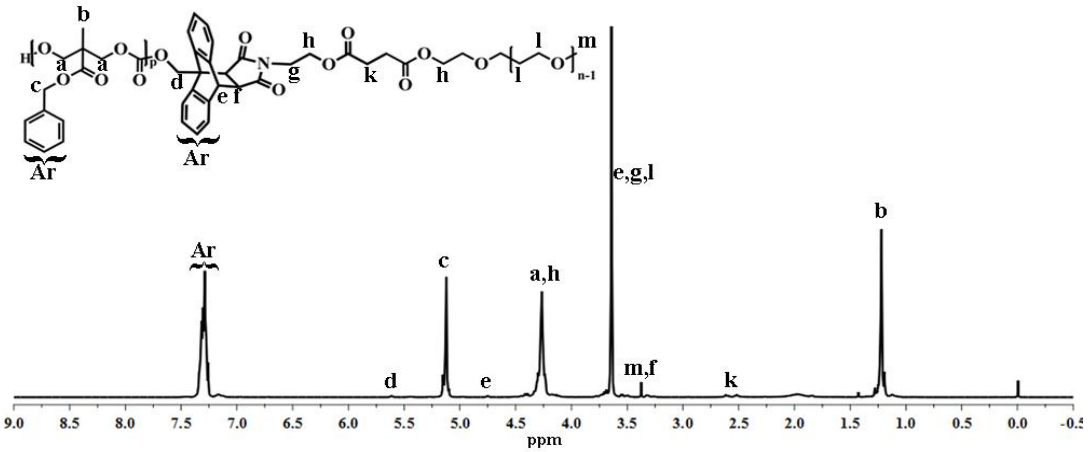


Figure 4.13: ^{1}H NMR spectrum of polycarbonate-*b*-poly(ethylene glycol) (PC-*b*-PEG) copolymer (from PC_{30}-anthracene and PEG_{11}-MI) in $CDCl_3$ (500 MHz).

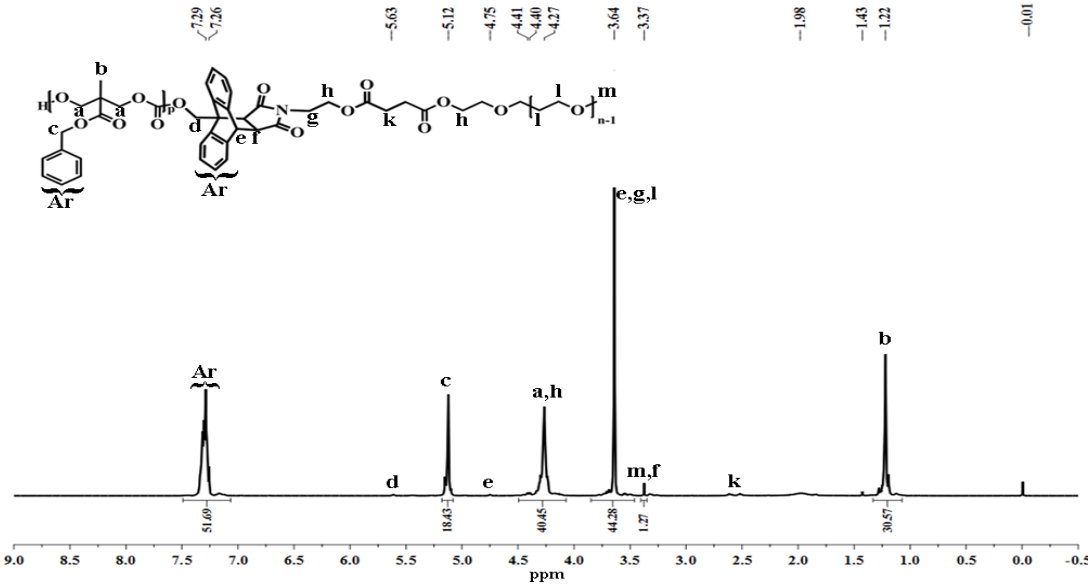


Figure 4.14: ^{1}H NMR spectrum of polycarbonate-*b*-poly(ethylene glycol) (PC-*b*-PEG) copolymer (from PC_{30}-anthracene and PEG_{37}-MI) in $CDCl_3$ (500 MHz).

From the NMR spectrum of the PC-*b*-PEG copolymer (from PEG_{11}-MI), the DP_n of the PEG segment present in the block copolymer was calculated from a ratio of integrated signals at 3.65 (OCH_2CH_2 of PEG) to 5.13 ppm (PhCH_2O of PC).

And it found to be 10.6, assuming the DP_n of the PC-anthracene is 30. Using analogous calculations, the DP_n of the PEG in the PC-*b*-PEG copolymer (from PEG_{37}-MI) is calculated to have 36 being consistent with the DP_n = 37 of the linear PEG precursor, while assuming that the DP_n of the PC is 30 (Fig. 4.13 and 4.14). It is noted that these calculated DP_ns confirm the quantitative incorporation of the PEG blocks into the PC chain via Diels-Alder reaction.

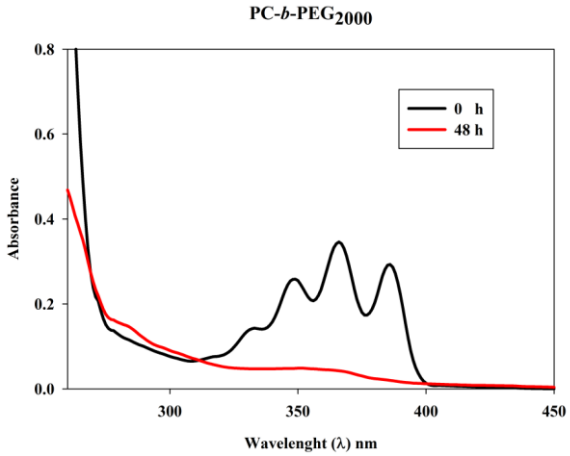


Figure4.15: UV-Vis spectra of PC-*b*-PEG copolymer (C_0 = 5.2 X 10^{-5} M in CH_2Cl_2).

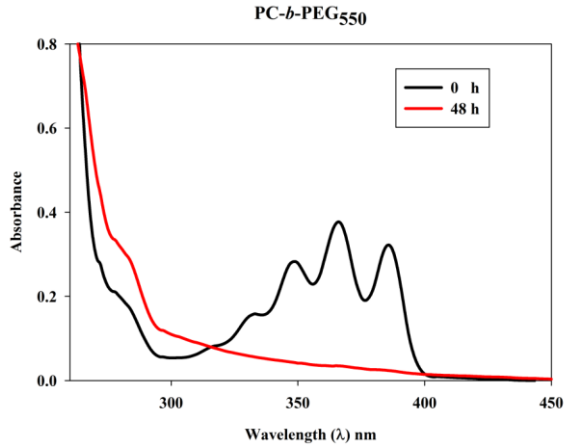


Figure4.16: UV-Vis spectra of PC-*b*-PEG copolymer (C_0 = 8.1 X 10^{-5} M in CH_2Cl_2)

Next, ^{1}H NMR analysis of the PC-*b*-PMMA copolymer also confirmed the quantitative conjugation of the $PMMA_{26}$-MI with the PC_{30}-anthracene based on integral comparison of the OCH_3 signal (PMMA) with the PhCH_2O signal (PC) at 3.60 and 5.12 ppm, respectively, yielding the DP_n = 25.5 of the PMMA block (assuming the DP_n of the PC-anthracene is 30) (Fig. 4.17).

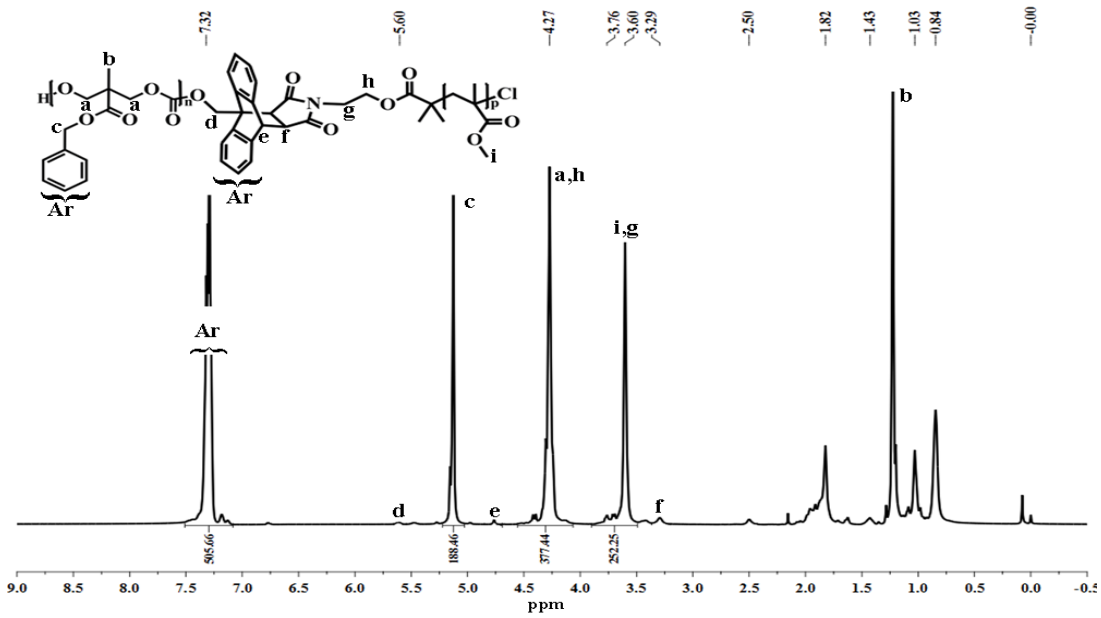


Figure 4.17: ^{1}H NMR spectrum of polycarbonate-*b*-poly(methyl methacrylate) (PC-*b*-PMMA) copolymer in $CDCl_3$ (500 MHz).

Finally, for the case of PC-*b*-PCL copolymer, an integrated ratio of the PhCH_2O of the PC at 5.12 ppm to the CH_2OC=O of the PCL at 4.06 ppm gave the calculated DP_n = 25 of the PCL block that is comparable to that of the PCL-MI precursor (DP_n = 27) (Fig. 4.18).

Additionally, it is noted that the calculated DP_ns from the ^{1}H NMR are consistent with the DA_{eff} data obtained from the UV measurements.

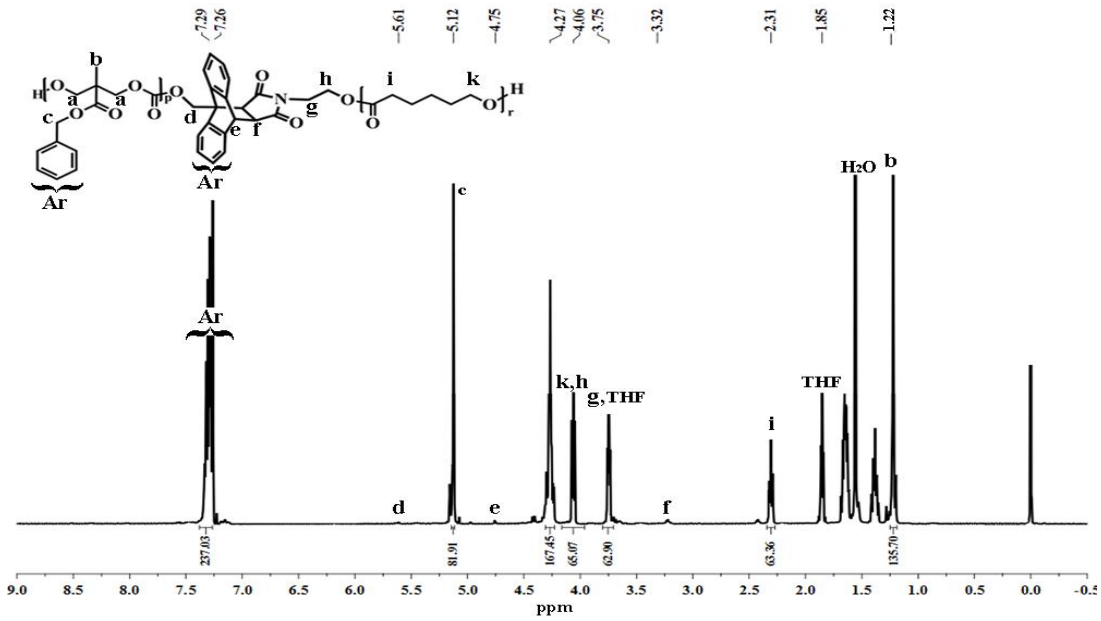


Figure 4.18: ^{1}H NMR spectrum of polycarbonate-*b*-poly(ε-caprolactone) (PC-*b*-PCL) copolymer in $CDCl_3$ (500 MHz).

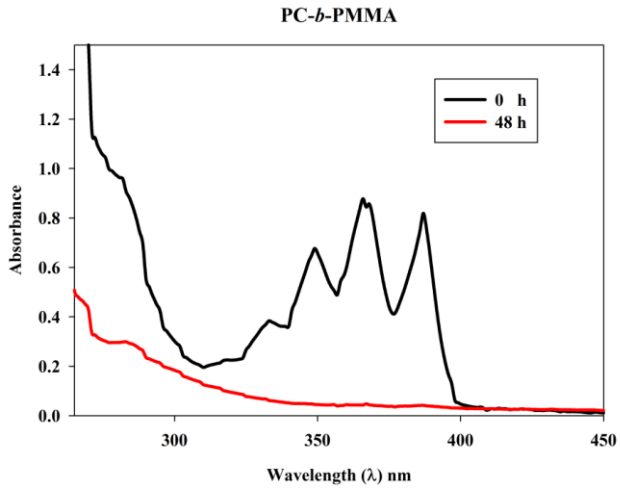


Figure 4.19: UV-Vis spectra of PC-*b*-PMMA copolymer (C_0 = 6.5 X 10^{-5} M in CH_2Cl_2).

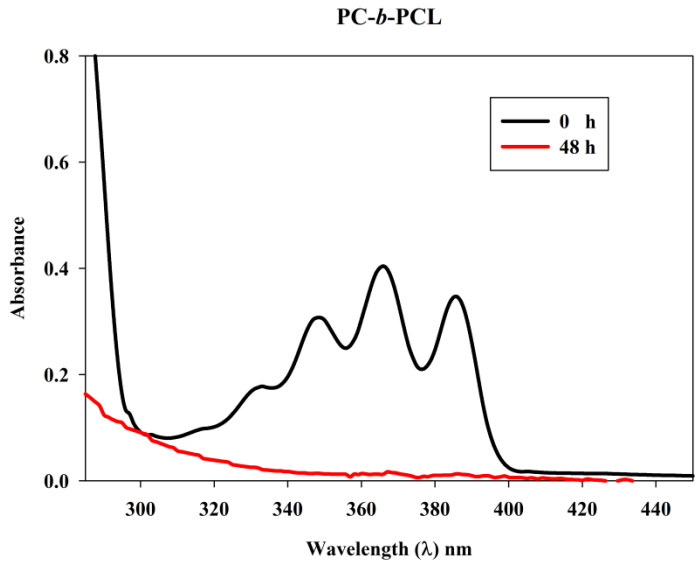


Figure 4.20: UV-Vis spectra of PC-*b*-PCL copolymer (C_0 = 8.1 X 10^{-5} M in CH_2Cl_2).

5. CONCLUSION

In this study, we described for the first time the synthesis of well-defined PC-based block copolymers using the Diels-Alder click reaction of the PC_{30}-anthracene with a variety of the α-furan protected maleimide-terminated polymers (PEG_{11}-MI, PEG_{37}-MI, $PMMA_{26}$-MI and PCL_{27}-MI). The UV, NMR and GPC measurements revealed that Diels-Alder click reaction displayed an efficient and an alternative pathway for the synthesis of a wide variety of PC-block copolymers via polymer-polymer conjugation. Therefore, the Diels-Alder click reaction is found to be superior over the classical preparation of PC-block copolymers via growing a second block from the hydroxyl-terminated macroinitiator using only ROP. Notably, Diels-Alder reaction becomes a more prominent particularly for the preparation of a variety of biocompatible polymers (such as PC), because it does not use any toxic copper catalyst compared to the CuAAC.

REFERENCES

[1] **Feng, J.; Zhuo, R.-X.; Zhang, X.-Z.** *Prog. Polym. Sci*. **2012**, 37, 211-236.

[2] **Suriano, F.; Coulembier, O.; Hedrick, J. L.; Dubois, P**. *Polym. Chem.* **2011**, 2, 528-533.

[3] **Guillaume, S. M.; Carpentier, J.-F.** *Catal. Sci. Technol.* **2012**, 2, 898-906.

[4] **Kamber, N. E.; Jeong, W.; Waymouth, R. M.; Pratt, R. C.; Lohmeijer, B. G. G.; Hedrick, J. L.** *Chem. Rev.* **2007,** 107, 5813-5840.

[5] **Matyjaszewski, K. and Xia, J.H.**, 2001, Atom transfer radical polymerization, *Chemical Reviews*, **101,** 2921-2990.

[6] **Matyjaszewski, K., Gnanou, Y., and Leibler, L.**, 2007. *Macromolecular Engineering: Precise Synthesis, Materials Properties, Applications*. Weinheim, Wiley-VCH.

[7] **Wang, J.S. and Matyjaszewski, K.**, 1995, Controlled living radical polymerization - atom-transfer radical polymerization in the presence of transition-metal complexes, *Journal of the American Chemical Society*, **117,** 5614-5615.

[8] **Kato, M., Kamigaito, M., Sawamoto, M., and Higashimura, T.**, 1995, Polymerization of methyl-methacrylate with the carbon-tetrachloride dichlorotris (triphenylphosphine) ruthenium(ii) methylaluminum bis(2,6-di-tert-butylphenoxide) initiating system - possibility of living radical polymerization, *Macromolecules*, **28,** 1721-1723.

[9] **Georges, M.K., Veregin, R.P.N., Kazmaier, P.M., and Hamer, G.K.**, 1993, Narrow molecular-weight resins by a free-radical polymerization process, *Macromolecules*, **26,** 2987-2988.

[10] **Helou, M.; Miserque, O.; Brusson, J.-M.; Carpentier, J.-F.; Guillaum, S. M.** *Chem. Eur. J.* **2010**, 16, 13805-13813.

[11] **Sanders, D. P.; Fukushima, K.; Coady, D. J.; Nelson, A.; Fujiwara, M.; Yasumoto, M.; Hedrick, J. L.** *J. Am. Chem. Soc.* **2010**, 132, 14724–14726.

[12] **Chiefari, J., Chong, Y.K., Ercole, F., Krstina, J., Jeffery, J., Le, T.P.T., Mayadunne, R.T.A., Meijs, G.F., Moad, C.L., Moad, G., Rizzardo, E., and Thang, S.H.**, 1998, Living free-radical polymerization by reversible addition-fragmentation chain transfer: The RAFT process, *Macromolecules*, **31,** 5559-5562.

[13] **Ivin, K, J., and Saegusa, T,** eds. 1984. *Ring-opening Polymerization*, Vols. 1-3, Elsevier, London.

[14] **Zhang, X.; Zhong, Z.; Zhuo, R.** Macromolecules 2011, 44, 1755-1759.

[15**] Xu, J.; Prifti, F.; Song, J.** *Macromolecules* **2011**, 44, 2660-2667.

[16] **Brunelle, D. J.,** Ed. 1993. *Ring-opening Polymerization: Mechanisms, Catalysis, Structure, Utility,*Carl Hanser Verlag, NY.

[17] **Tempelaar, S.; Mespouille, L.; Dubois, P.; Dove, A. P.** *Macromolecules* **2011**, 44, 2084–2091.

[18] **Mindemark, J.; Bowden, T.** *Polymer* **2011**, 52, 5716-5722.

[19] **Kolb, H.C., Finn, M.G., and Sharpless, K.B.**, 2001, Click chemistry: Diverse chemical function from a few good reactions, *Angewandte Chemie-International Edition*, **40,** 2004-2021.

[20] **Parzuchowski, P. G.; Jaroch, M.; Tryznowski, M.; Rokicki, G.** *Macromolecules* **2008**, 41, 3859-3865.

[21] Chen**, W.; Yang, H.; Wang, R.; Cheng, R.; Meng, F.; Wei, W.; Zhong, Z.** *Macromolecules* **2010**, 43, 201–207.

[22] **Miyagawa, T.; Shimizu, M.; Sanda, F.; Endo, T.** *Macromolecules* **2005**, 38, 7944-7949.

[23] **Hu, Y.; Qiao, L.; Qin, Y.; Zhao, X.; Chen, X.; Wang, X.; Wang, F.** *Macromolecules* **2009**, 42, 9251–9254.

[24] **Onbulak, S.; Tempelaar, S.; Pounder, R. J.; Gok, O.; Sanyal, R.; Dove, A. P.; Sanyal, A.** *Macromolecules* **2012**, 45, 1715−1722.

[25] **Szwarc, M.,** 1956. Block copolymers, *Nature*, **178**, 1168.

[26] **Quirk, R. P., Kinning, D. J., and Fetters, L. J.,** 1989. Comprehensive Polymer Science, Aggarwal, S. L., Vol 7, p.1, Ed. Pergamon Press, London.

[27] **Matyjaszewski, K.,** 1995. Introduction to Living Polymerization, Living and/or Controlled Polymerization, *J. Phys. Org. Chem.*, **8(4),** 197-207.

[28] **Percec, V., and Tirrel, D. A.,** 2000. Living or Controlled ?, *J. Polym. Sci., Part A: Org. Ppoly Chem.*, **38(10),** 1705-1752.

[29] **Zhang, J.-F.; Ren, W.-M.; Sun, X.-K.; Meng, Y.; Du, B.-Y.; Zhang, X.-H.** *Macromolecules 2012*, 44 , 9882-988.

[30] (a) Click Chemistry for Biotechnology and Materials Science, **Lahann, J.,** Ed.; Wiley: Chichester, 2009; (b) **Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C.** J. *Chem. Rev.* **2009**, 109, 5620-5686.

[31] **Rosen, B. M.; Wilson, C. J.; Wilson, D. A.; Peterca, M.; Imam, M. R.; Percec,** V. *Chem. Rev.* **2009**, 109, 6275-6540.

[32] **Grimaud, T.; Matyjaszewski, K.,** 1997. Controlled/"Living" radical polymerization of methyl methacrylate by atom transfer radical polymerization, *Macromolecules*, **30**, 2216.

[33] **Patten, T.E. and Matyjaszewski, K.**, 1999, Copper(I)-catalyzed atom transfer radical polymerization, *Accounts of Chemical Research*, **32,** 895-903.

[34] **Sumerlin, B. S.; Vogt, A. P**. *Macromolecules* **2010**, 43, 1-13.

[35] **Youqing Shen, Huadong Tang,** 2004. Catalyst separation in atom transfer radical polymerization. Shijie Ding Department of Chemical and Petroleum Engineering, University of Wyoming, Laramie, WY, USA.

[36] **Kato, M., Kamigaito, M., Sawamoto, M., and Higashimura, T.,** 1995. Polymerization of Methyl Methacrylate with the Carbon Tetrachloride/Dichlorotris(triphenylphosphine)ruthenium(II)/Methylal

uminum Bis(2,6-di-tert-butylphenoxide) Initiating System: Possibility of Living Radical Polymerization, *Macromolecules*, **28(5),** 1721-1723.

[37] **Hoyle, C. E.; Lowe, A. B.; Bowman, C. N.** *Chem. Soc. Rev.* 2010, 39, 1355-1387.

[38] **Altintas, O.; Tunca, U.** *Chem. Asian J.* **2011**, 6, 2584-2591.

[39] **Matyjaszewski, K., Patten, T. E., and Xia, J.,** 1997. Controlled/"Living" Radical Polymerization. Kinetics of the Homogeneous Atom Transfer Radical Polymerization of Styrene, *J. Am. Chem. Soc.*, **119(4),** 674-680.

[40] **Davis, K., O'Malley, J., Paik, H. J., and Matyjaszewski, K.,** 1997. Effect of the Counteranion in Atom Transfer Radical Polymerization Using Alkyl (Pseudo) Halide Initiators, *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)*, **213(320-Poly Part 2),** 687.

[41] **Xia, J., Zhang, X., and Matyjaszewski, K.**, 2000, The Effect of Ligands on Copper-Mediated Atom Transfer Radical Polymerization, *Transition Metal Catalysis in Macromolecular Design*, 207-223.

[42] **Hizal, G.; Tunca, U.; Sanyal, A.** *J. Polym. Sci. Part A: Polym. Chem.* **2011**, 49, 4103-4120.

[43] **Durmaz, H.; Sanyal, A.; Hizal, G.; Tunca, U.** *Polym. Chem.* **2012**, 3, 825-835.

[44] **Matyjaszewski, K., Patten, T.E., and Xia, J.H.**, 1997, Controlled/"living" radical polymerization. Kinetics of the homogeneous atom transfer radical polymerization of styrene, *Journal of the American Chemical Society*, **119,** 674-680.

[45] **Matyjaszewski, K., Davis, K., Patten, T.E., and Wei, M.L.**, 1997, Observation and analysis of a slow termination process in the atom transfer radical polymerization of styrene, *Tetrahedron*, **53,** 15321-15329.

[46] **Hamley, I. W.,** 1998. The Physics of block copolymers, Oxford University Press, Oxford.

[47] **Altintas, O.; Vogt, A. P.; Barner-Kowollik, C.; Tunca, U.** *Polym. Chem.* **2012,** 3, 34-45.

[48] **Kempe, K.; Krieg, A.; Becer, C. R.; Schubert,** U. S. *Chem. Soc. Rev.* **2012**, 41, 176-191

[49] **Barner-Kowollik, C.; Du Prez, F. E.; Espeel, P.; Hawker, C. J.; Junkers, T.; Schlaad, H.; Van Camp,** W. *Angew. Chem., Int. Ed.* **2011**, 50, 60-62

[50] **Durmaz, H.; Dag, A.; Gursoy, D.; Demirel, A. L.; Hizal, G.; Tunca, U.** *J. Polym. Sci. Part A: Polym. Chem.* **2010**, 48, 1557-1564.

[51] **Durmaz, H.; Dag, A.; Erdogan, E.; Demirel, A. L.; Hizal, G.; Tunca, U.** *J. Polym. Sci. Part A: Polym. Chem.* 2010, 48, 99-108.

[52] **a) A. C. Albertsson and I. K. Varma,** 2003. *Biomacromolecules*, **4**, 1466-1486. **b) E. S. Place, J. H. George, C. K. Williams and M. M. Stevens,** 2009. *Chem.Soc. Rev*., **38**, 1139–1151.

[53] **A. C. Albertsson and I. K. Varma,** 2002. *Adv. Polym. Sci.*, **157**, 1-40.

[54] **O. Dechy-Cabaret, B. Martin-Vaca and D. Bourissou,** 2004. *Chem.Rev*., **104,** 6147-6176.

[55] **Kleine, J., and Kleine, H.-H.,** 1959. Über Hochmolekulare, İnsbesondere Optisch Aktive Polyester der Milchsäure, ein Beitrag zur Stereochemie Makromolekularer Verbindungen, *Makromol. Chem.*, **30(1),** 23-38.

[56] **Löfgren, A., Albertsson, A.C., Dubois, P. and Jerome, R.,** 1995. Recent Advances in Ring-Opening Polymerization of Lactones and Related-Compounds, *J. Macromol. Sci. Rev. Macromol. Chem. Phys.*, **C35(3),** 379-418.

[57] **Kuran, W.,** 1998. Coordination Polymerization of Heterocyclic And Heterounsaturated Monomers, *Prog. Polym. Sci.*, **23(6)**, 919-992.

[58] **Duda, A., and Penczek, S.,** 2000. In *Polymers from Renewable Resources: Biopolyesters and Biocatalysis*, ACS Symposium Series 764, American Chemical Society, Washington, D.C., p 160.

[59] **O'Keefe, B., Hillmyer, M. A., and Tolman, W. B.,** 2001. Polymerization of Lactide and Related, Cyclic Esters by Discrete Metal Complexes, *J. Chem. Soc., Dalton Trans*, 2215-2220.

[60] **Penczek, S.,** 2000. Cationic Ring-Opening Polymerization (Crop) Major Mechanistic Phenomena, *J. Polym. Sci. Polym. Chem.*, **38(11),** 1919-1933.

[61] **Penczek, S. and Slomkowski, S.,** 1987. Progress In Anionic Ring-Opening Polymerization, in "*Recent Advances in Anionic Polymerization*, Chap **19**, 275, Eds. Hogen, E.T. and Smid, J., Elsevier, New York.

[62] **Mecerreyes, D., Jerome, R. and Dubois, P.,** 1999. Novel Macromolecular Architectures Based on Aliphatic Polyesters: Relevance of the "Coordination-Insertion" Ring-Opening Polymerization, *Adv. Polym. Sci.*, **147,** 1-59.

[63] **Lundberg, R.D. and Cox, E.F.,** 1969. Lactones, in *Ring-Opening Polymerization*, Frish, K., Reegen, S., Eds, 2:247 Marcel Dekker, New York.

[64] **Kricheldorf, H. R., Berl, M., and Scharnagl, N.,** 1988**.** Poly(Lactones). 9. Polymerization Mechanism of Metal Alkoxide Initiated Polymerizations of Lactide and Various Lactones, *Macromolecules*, **21(2),** 286-293.

[65] **Kowalski, A., Duda, A., and Penczek, S.,** 1998. Polymerization of L,L-Lactide Initiated by Aluminum Isopropoxide Trimer or Tetramer, *Macromolecules*, **31(7),** 2114-2122.

[66] **Schwach, G.**, **Coudane, J., Engel, R., and Vert, M.,** 1998. Ring Opening Polymerization of D,L-Lactide in the Presence of Zinc Metal and Zinc

Lactate, *Polym.* Initiated by Aluminum Isopropoxide Trimer or Tetramer, *Macromolecules, Int.* **46(3),** 177-182.

[67] **Kreiser-Saunders, I., and Kricheldorf, H. R.** 1998. Polylactones, 39. Zn Lactate- Catalyzed Copolymerization of L-Lactide with Glycolide or ε-Caprolactone, *Macromol. Chem. Phys.,* **199(6),** 1081-1087.

[68] **Schwach, G., Coudane, J., Engle, R., and Vert, M.,** 1997. More About the Polymerization of Lactides in the Presence of Stannous Octoate, *J. Polym. Chem., Part A: Polym. Chem.,* **35(16),** 3431-3440.

[69] **Kricheldorf, H. R., Kreiser-Saunders, I., and Boettcher, C.,** 1995. Polylactones: 31. Sn(II)Octoate-Initiated Polymerization of L-Lactide: A Mechanistic Study, *Polymer,* **36(6),** 1253-1259.

[70] **Kowalski, A., Duda, A., and Penczek, S.,** 2000. Mechanism of Cyclic Ester Polymerization Initiated with Tin(II) Octoate. 2. Macromolecules Fitted with Tin(II) Alkoxide Species Observed Directly in MALDI-TOF Spectra *Macromolecules,* **33(3),** 689-695.

[71] **Kricheldorf, H. R., Kreiser-Saunders, I., and Stricker, A.,** 2000. Polylactones 48. $SnOct_2$-Initiated Polymerizations of Lactide: A Mechanistic Study, *Macromolecules*, **33(3),** 702-709.

[72] **Kowalski, A., Duda, A., and Penczek, S.,** 1998. Kinetics and Mechanism of Cyclic Esters Polymerization Initiated with Tin(II) Octoate, 1. Polymerization of Epsilon-Caprolactone, *Macromol. Rapid. Commun.* **19 (11),** 567-572.

[73] **Löfgren, A., Albertsson, A.C., Dubois, P. and Jerome, R.,** 1995. Recent Advances in Ring-Opening Polymerization of Lactones and Related-Compounds, *J. Macromol. Sci. Rev. Macromol. Chem. Phys.,* **C35(3),** 379-418.

[74] **Kricheldorf, H. R., Kreiser, S. I.,** 1996. Polylactides - Synthesis, Characterization and Medical Application, *Macromol. Symp.,* **103,** 85-102.

[75] **Dubois, P., Ropson, N., Jérôme, R. and Teyssie, P.,** 1996. Macromolecular Engineering of Polylactones and Polylactides. 19. Kinetics of Ring-Opening Polymerization of Epsilon-Caprolactone Initiated With Functional Aluminum Alkoxides, *Macromolecules,* **29(7),** 1965-1975.

[76] **Schindler, A., Jeffcoat, A. R., Kimmel, G. L., Pitt, C. G., Wall, M. E., and Zweidinger R. A.,** 1977. Biodegradable Polymers for Sustained Drug Delivery, in *Contemporary Topics in Polymer Science,* **Vol. 2**, E. M. Pearce and R. J. Schaefgen, Eds., Plenum, New York.

[77] **Pitt, C.G., Chasalow, Y.M., Hibionada, Y.M., Klimas, D.M. and Schlinder, A.,** 1981. Aliphatic Polyesters I. The Degredation of Poly(ε-caprolactone) *in vivo, J. Appl. Polym. Sci.,* **68,** 1534-1538.

[78] **Zhang Q., Remsen E.E., Wooley K.L.,** 2000. *J Am Chem Soc*, 122:3642.

[79] **Arnal M.L., Balsamo V., Lopez C.F., Contreras J., Carillo M., Schmalz H.,** et. 2001. *Macromolecules,* 34:7973.

[80] **a) Labet, M., Thielemans, W.,** 2009. *W. Chem Soc Rev*, **38**, 3484-3504. **b) Albertsson, A. C.; Varma, I. K.,** 2003. *Biomacromolecules*, **4**, 1466-1486.

[81] **a) Wang, L.; Dong, C. M.,** 2006. *J Polym Sci Polym Chem*, **47**, 3218-3228. **b) Dong C. M.; Guo, Y. Z.; Qiu, K. Y.; Gu, Z. W.; Feng, X. D.,** 2005. *J Control Release*, **107**, 53-64.

[82] **Diels, O. and Alder, K.**, 1928, Synthesen in der hydroaromatischen Reihe, *Justus Liebig's Annalen der Chemie*, **460,** 98-122.

[83] **Corey, E.J.**, 2002, Catalytic enantioselective Diels-Alder reactions: Methods, mechanistic fundamentals, pathways, and applications, *Angewandte Chemie-International Edition*, **41,** 1650-1667.

[84] **Diels, O. and Alder, K.**, 1926, Über die Ursachen der Azoesterreaktion, *Justus Liebig's Annalen der Chemie*, **450,** 237-254.

[85] **Fringuelli, F. and Taticchi, A.**, 2002. *The Diels Alder reaction : selected practical methods*. Chichester, New York, Wiley.

[86] **Woodward, R.B. and Hoffmann, R.**, 1970. *The conservation of orbital symmetry*. Weinheim/Bergstr, Verlag Chemie.

[87] **Woodward, R.B. and Hoffmann, R.**, 1965, Stereochemistry of electrocyclic reactions, *Journal of the American Chemical Society*, **87,** 395-397.

[88] (a) **Zeng, F.; Liu, J.; Allen, C.** *Biomacromolecules* **2004,** 5, 1810-1817; (b) **Xie, Z.; Guan, H.; Lu, C., Chen, X.; Jing, X.** *Acta Biomaterialia* **2005**, 1 635–641; (c) **Guan, H.-L.; Xie, Z.-G.; Zhang, P.-B.; Wang, X.; Chen, X.-S.; Wang, X.-H.; Jing, X.-B.** *J. Polym. Sci. Part A: Polym. Chem.* **2005**, 43, 4771-4780; (d**) Wu, R.; Al-Azemi, T. F.; Bisht, K. S**. *Macromolecules* **2009**, 42, 2401-241; (e) **Chiu, F.-C.; Lai, C.-S.; Lee, R.-S.** *J. Appl. Polym. Sci.* **2007**, 106, 283-292; (f) Fukushima**, K.; Pratt, R. C.; Nederberg, F.; Tan, J. P. K.; Yang, Y. Y.; Waymouth, R. M.; Hedrick,** J. L. *Biomacromolecules* **2008,** 9, 3051-3056; (g) **Zhang, X.; Chen, F.; Zhong, Z.; Zhuo, R.** *Macromol. Rapid Commun.* **2010**, 31, 2155–2159; (h) **Xu, J.; Prifti, F.; Song,** J. *Macromolecules* **2011**, 44, 2660–2667; (i) **Helou, M.; Carpentier, J.-F.; Guillaume, S. M.** *Green Chem.* **2011**, 13, 266-271; (j) **Yang, C.; Ong, Z. Y.; Yang, Y.-Y.; Ee, P. L. R.; Hedrick, J.** L. *Macromol. Rapid Commun.* **2011**, 32, 1826-1833.

[89] **Gacal, B.; Durmaz, H.; Tasdelen, M. A.; Hizal, G.; Tunca, U.; Yagci, Y.; Demirel, A. L.,** 2006. Anthracene-Maleimide-Based Diels Alder "Click Chemsitry" as a Novel Route to Graft Copolymers, *Macromolecules*, **39**, 5330-5336.

[90] **Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L.** *Macromolecules* **2006**, 39, 7863-7871.

[91] **Liu, Q.; Chen, Y.,** 2006. Synthesis of Well-Defined Macromonomers by the Combination of Atom Transfer Radical Polymerization and a Click Reaction, *Journal of Polymer Science: Part A: Polymer Chemistry*, **44**, 6103-6113.

[92] **Lutz, J. F.; Börner, H. G.; Weichencan, K.,** 2005. Combining Atom Transfer Radical Polymerization and Click Chemistry: A Versatile Method for the Preparation of End-Functional Polymers, *Macromol. Rapid Commun.*, **26**, 514-518.

[93] **Kamijo, S.; Jinb, T.; Yamamotoa, Y.,** 2004. Four-component coupling reactions of silylacetylenes, allyl carbonates, and trimethylsilyl azide catalyzed by a Pd(0)-Cu(I) bimetallic catalyst. Fully substituted triazole synthesis from seemingly internal alkynes, *Tetrahedron Letters*, **45**, 689-691.

[94] **Mantovani, G., Lecolley, F., Tao, L., Haddleton, D.M., Clerx, J., Cornelissen, J.J.L.M., and Velonia, K.** *J. Am. Chem. Soc.* **2005**, 127, 2966-2973.

[95] **Dag A.; Durmaz, H.; Hizal,G.; Tunca, U.** *J. Polym. Sci. Part A: Polym. Chem.* **2008**, 46, 302-313.

[96] **Matyjaszewski, K., and Davis, T., (eds.),** 2001, *Handbook of Radical Polymerization*, John Wiley & Sons, New Jersey

[97] **Matyjaszewski, K., Spanswick J.,** 2005, Controlled/Living Radical Polymerization, *Material Science*, 26-33.

[98] **Odian,G.**, 2004, *Principle of Polymerization*. John Wiley & Sons, New Jersey

[99] **Coca, S., Paik, H., Matyjaszewski, K.,** 1997, Block Coplymers by Transformation of Living Ring-Opening Metathesis Polymerization into Controlled/"Living" Atom Transfer Radical Polymerization, **30**, 6513-6516.

[100] **Binder, W. H.; Kluger, C**. *Macromolecules* **2004**, *37*, 9321-9330.

[101] **Matyjaszewski, K.;Xia, J.** 2001, *Chem Rev*., **101,** 2923

[102] **Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T.** 1995, *Macromolecules*, **28**, 1721.

[103] **Percec, V.; Barboiu, B.** 1995, *Macromolecules*, **28**, 7970.

[104] **Matyjaszewski, K.; Wang,** J. S. WO Pat. 9630421, U.S. Pat. 5,763,548.

[105] **Matyjaszewski, K.; Coca, S., Gaynor, S. G.; Greszta, D.; Patten, T.E.; Wang, J.; Xia, J.** WO Pat. 9718247, US. Pat. 5, 807-937

[106] **Patten, T. E.; Matyjaszewski, K.** 1999, *Acc. Chem. Res*, **32**, 895

[107] **Stridsberg, K.M.; Ryner, M.; Albertsson, A.C.** 2002, *Polym. Sci*., 157, 41-65.

[108] **Kamber, N.E.; Jeong, W.; Waymouth, R.M.** 2007, *Chem. Rev.*, 107, 5813-5840.

[109] **Myers, M.;Connor, E.F; Moller, M.; Glauser, T.; Hedrick, J.L**. 2001, *Angew. Chem*., Int. Ed., 40, 2712.

[110] **Biela,T.; Penczek, S.; Slomkowski, S.; Vogl,O.** 1983, *Makromol. Chem*., 184, 811.

[111] (a) **Dove, A. P., Pratt, R. C., Lohmeijer, G.B.G., Culkin, D. A. Hagberg , E. C., Nyce, G. W., Waymouth, R. M., Hedrick, J. L.** 2006, *Polymer* ,

47, 4018; **(b) Suriano,F.; Coulembier, O.; Hedrick,J.L; Dubois P**. *Polym. Chem*., 2011, 2, 528–533.

[112] **Zku, K.J; Hendren, R.W; Jensen, K.; Pitt, C.G.;** 1991, *Macromolecules*, 24, 1736-1740.

[113] **Rokickci, G.** 2000, *Prog. Polym. Sci*., 25, 259-342.

[114] **Tian,H.; Tang, Z.; Zhuang, X.; Chen, X.; Jing, X.** 2012, *Polym. Sci*., 37, 237-280.

[115] **Seow, W.Y, Yang, Y.Y.** 2009, *Journal of Controlled Release*, 139, 40-47.

[116] **C. B. Kowollik, F. E. Du Prez, P. Espeel, C. J. Hawker, T. Junkers, H. Schlaad, W. Van Camp,** 2010, *Angew. Chem. Int. Ed.*, 49, 2 – 5.

[117] **Diels, O.; Alder, K.; Liebigs, J.** Ann. Chem., 1928, 460, 98–122

[118] **L. F. Tietze and G. Kettschau, Top.** *Curr. Chem.*, 1997, 189, 1–120.

[119] **J. L. Ripoll, A. Rouessac and F. Rouessac,** *Tetrahedron*, 1978, 34, 19–40.

[120**] M.A. Tasdelen**, 2011, *Polym. Chem*., 2011, **2**, 2133.

[121**] Dag, A.; Aydin, M.; Durmaz, H.; Hizal, G.; Tunca,** U *J. Polym. Sci. Part A: Polym. Chem.* **2012**, 50, 4476-4483.

[122] **Mantovani, G., Lecolley, F., Tao, L., Haddleton, D.M., Clerx, J., Cornelissen, J.J.L.M., and Velonia, K.** *J. Am. Chem. Soc.* **2005**, 127, 2966-2973.

[123] **Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L.** *Macromolecules* **2006**, 39, 7863-7871

[124] **Dag A.; Durmaz, H.; Hizal,G.; Tunca, U.** *J Polym Sci Part A : Polym Chem* 2008, 46, 302-313

[125] **Dubois, P., Barakat, I., Jerome, R., and Teyssie, P.**, 1993, Macromolecular engineering of polylactones and polylactides .12. Study of the depolymerization reactions of poly(epsilon-caprolactone) with functional aluminum alkoxide end-groups, *Macromolecules*, 26, 4407-4412.

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OMURTAG, P.S., DAG, A., DURMAZ, H., GUNAY, U.S., HIZAL, G., TUNCA; "Preparation of Polycarbonate with Anthracene and Azido Pendant Groups and Its Grafting via Click Chemistry", 4th EuCheMS Chemistry Congress, Prague, Czech Republic, (August 26-30, 2012).

OMURTAG, P.S., DAG, A., DURMAZ, H., GUNAY, U.S., HIZAL, G., TUNCA; "Antrasen ve Azid Yan Fonksiyonlu Polikarbonat Zincirlerinin Sentezi ve Klick Kimyası ile Aşılanması", 26. National Chemistry Congress, Muğla, (October 1-6, 2012).