

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE
ENGINEERING AND TECHNOLOGY

SYNTHESIS OF CLICKABLE HYDROGELS AND LINEAR POLYMERS BY
***TYPE II* PHOTOINITIATION**

M.Sc. THESIS

Eljesa MURTEZI

Department of Chemistry

Chemistry Programme

MAY 2014

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE
ENGINEERING AND TECHNOLOGY

**SYNTHESIS OF CLICKABLE HYDROGELS AND LINEAR POLYMERS BY
TYPE II PHOTOINITIATION**

M.Sc. THESIS

**Eljesa MURTEZI
(509111042)**

Department of Chemistry

Chemistry Programme

Thesis Advisor: Prof. Dr. Yusuf YAĞCI

MAY 2014

İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

***II. TİP* FOTABAŞLATICILARI KULLANARAK ÇİT ÇİT KİMYASINA
UYGUN HİDROJEL VE LİNEER POLİMERLERİN SENTEZİ**

YÜKSEK LİSANS TEZİ

**Eljesa MURTEZİ
(509111042)**

Kimya Anabilim Dalı

Kimyagerlik Programı

Tez Danışmanı: Prof. Dr. Yusuf YAĞCI

MAYIS 2014

To my family,

FOREWORD

First of all, I would like to express my sincere thanks to my advisor, Prof. Dr. Yusuf Yađcı for giving me the opportunity to work with him and for his support and guidance. He was a constant inspiration, and his assistance and suggestions were invaluable towards the completion of this work.

I would also like to thank the members of my exam comitee. I wish also to acknowledge and thank İlim Yayma Vakfı for the supprot and accomodation and the Turkish governmental presidency of YTB (Yurtıřı Trkler ve Akraba Toplulukları Bařkanlıđı) for the scholarship support and the various opportunities that have helped to make this journey an educational as well as an enjoyable one.

Special thanks go Mustafa ifti for his advices on handling problems, dealing with them and his patience from the very beginning.

I was also quite fortunate for having the opportunity to interact with the colleagues of our Yađcı Lab research group. I deeply appreciate Hseyin Akbulut who never hesitated to put forward his valuable support. I also wish to thank Cansu Aydođan, Sajjad Dadashi Silab, mer Suat Tařkın, Mustafa Arslan, Semiha Bektař Bozdemir, Betl Hanbeyođlu Yavař, Ali Grkem Yılmaz, Muhammed Aydın, Seán Doran, Assist. Prof. Dr. Binnur Aydođan, Assoc. Prof. M. Atilla Tařdelen, Assoc. Prof. Barıř Kıřkan, Abdurrahman Musa, Semih Erdur, Eliften Semerci, Senem Krk, Faruk Oytun, Umut Uđur zkse, Hatice řahin and Sinem Yener. With all of you it has really been a great pleasure.

Finally, I would like to dedicate this research work to my family. To my parents, for their never-ending love, sacrifice and support who have always encouraged me to pursue my goals.

May 2014

Eljesa MURTEZI
(Chemist)

TABLE OF CONTENTS

	<u>Page</u>
FOREWORD	ix
TABLE OF CONTENTS	xi
ABBREVIATIONS	xiii
LIST OF TABLES	xv
LIST OF FIGURES	xvii
SUMMARY	xix
ÖZET	xxi
1. INTRODUCTION	1
2. THEORETICAL PART	3
2.1 Photochemistry.....	3
2.2 Photopolymerization.....	4
2.3 Types of photopolymerization.....	5
2.3.1 Photoinitiated free radical polymerization.....	5
2.3.1.1 <i>Type I</i> photoinitiators (Unimolecular photoinitiator system).....	7
2.3.1.2 <i>Type II</i> photoinitiators (Bimolecular photoinitiator system).....	9
2.3.1.3 Effect of oxygen on photopolymerization.....	12
2.3.1.4 Crosslinking free radical polymerization.....	12
2.3.1.5 Monomers.....	13
2.3.2 Photo-induced anionic polymerization.....	14
2.3.3 Photo-induced cationic polymerization.....	15
2.4 Hydrogels.....	15
2.5 Poly(ethylene glycol) (PEG) as suitable material for hydrogel synthesis.....	16
2.6 Atom transfer radical polymerization (ATRP).....	16
2.6.1 Mechanism.....	16
2.6.2 Radicals as propagating species.....	17
2.6.3 Removal of copper.....	18
2.7 Block copolymers.....	18
2.8 “Click” chemistry.....	19
2.8.1 Thiol-based “Click” reaction.....	21
2.8.2 Diels-Alder cycloaddition.....	21
2.8.3 Azide-alkyne cycloaddition (Copper Catalyzed Alkyne-Azide cycloaddition (CuAAC)).....	22
3. EXPERIMENTAL PART	23
3.1 Materials.....	23
3.1.1 Solvents.....	23
3.1.2 Chemicals.....	24
3.2 Characterization.....	26
3.2.1 ¹ H Nuclear magnetic resonance spectroscopy (¹ H-NMR).....	26
3.2.2 Infrared spectroscopy.....	26
3.2.3 Gel-permeation chromatography.....	26

ABBREVIATIONS

ATRP	: Atom Transfer Radical Polymerization
DMF	: Dimethylformamide
DMSO	: Dimethylformamide
COI	: Co-initiator
CQ	: Camphorquinone
CRP	: Controlled radical polymerization
CuAAC	: Copper(I)-catalyzed Azide-Alkyne Cycloaddition
FT-IR	: Fourier Transform Infra Red
GPC	: Gas Permeation Chromatography
ISC	: Intersystem crossing
MMA	: Methyl Methacrylate
PEG	: Poly(ethylene glycol)
PEGDA	: Poly(ethylene glycol) diacrylate
PEGMA	: Poly(ethylene glycol) methyl ether methacrylate
PMDETA	: <i>N,N,N',N'',N'''</i> - Pentamethyldiethylenetriamine
PMMA	: Polymethyl Methacrylate
PMMA-Ac	: Acetylene functional poly(methyl methacrylate)
PI	: Photoinitiator
PS	: Polystyrene
PS-<i>b</i>-PMMA	: Polystyrene Methyl Methacrylate block copolymer
TBAF	: Tetrabutylammonium fluoride
THF	: Tetrahydrofuran
ΔG	: Gibbs Energy Change
¹H-NMR	: Nuclear Magnetic Resonance Spectroscopy

LIST OF TABLES

	<u>Page</u>
Table 2.1 : Structures of typical <i>Type I</i> radical photoinitiators.....	8
Table 2.2 : Structures of typical <i>Type II</i> radical photoinitiators.....	9
Table 4.1 : Molecular weight characteristics of PS-N ₃ , PMMA and PS- <i>b</i> -PMMA..	37

LIST OF FIGURES

	<u>Page</u>
Figure 2.1 : Jablonski diagram. The excited singlet state (S_1) undergoes intersystem crossing (ISC) to a triplet state (T_1), which leads to various photochemical reactions. (Image adapted from reference 56.).....	4
Figure 2.2 : Elementary reactions in free radical photopolymerization.....	6
Figure 2.3 : Formation of initiating radicals from decomposition of a <i>Type I</i> photoinitiator.	7
Figure 2.4 : Formation of initiating radicals from photolysis of <i>Type II</i> photoinitiator in the presence of suitable hydrogen donor.....	11
Figure 2.5 : Comphorquinone/Alcohol Initiation Reaction	12
Figure 2.6 : Crosslinking by free radical polymerization	13
Figure 2.7 : An examble of photoinitiated anionic polymerization.	14
Figure 2.8 : General Scheme of Photoinitiated Cationic Polymerization.....	15
Figure 2.9 : Representation of ATRP mechanism.	17
Figure 2.10 : Different types of block copolymers	19
Figure 2.11 : Overview and classification of some types of “click” reactions.	20
Figure 2.12 : Azyde-alkyne cycloaddition.....	22
Figure 3.1 : Schematic representation for hydrogel functionalization.....	28
Figure 3.2 : Synthesis of PS- N_3	28
Figure 3.3 : Synthesis of 3-(trimethylsilyl)propargyl alcohol.....	29
Figure 4.1 : Synthesis of clickable PEG crosslinked hydrogels by photoinitiated free radical polymerization and their functionalization	31
Figure 4.2 : a) FT-IR spectra of the acetylene functional hydrogel b) 2-azidomethyl pyrene and c) functionalized hydrogel via “click” reaction.....	32
Figure 4.3 : Azidation of 1-pyrenemethanol.....	33
Figure 4.4 : Flourescence spectra of PEG hydrogels a) before and b) after “click” reaction with Py- N_3 in water	33
Figure 4.5 : Photographs of clickable PEG hydrogels before (a) and after (b) click reaction with 2-azidomethyl pyrene under irradiation with a 366-nm UV lamp.....	34
Figure 4.6 : Photoinduced synthesis of protected PMMA and its deprotection	35
Figure 4.7 : 1H NMR spectra of protected and deprotected PMMA.....	35
Figure 4.8 : 1H NMR spectra of PS- <i>b</i> -PMMA.....	36
Figure 4.9 : “Click” reaction between PS and PMMA	36
Figure 4.10 : GPC traces of PS- N_3 , PMMA-Ac and PS- <i>b</i> -PMMA. “Click” reaction between PS and PMMA	37

SYNTHESIS OF CLICKABLE HYDROGELS AND LINEAR POLYMERS BY *TYPE II* PHOTOINITIATION

SUMMARY

Photoinitiated polymerization is a well-known technique exploited in many technologically important areas. Compared with the corresponding thermal processes, the light induced polymerization offers a number of advantages, including rapid polymerization rates at room temperature, and spatial and sequential control of the polymerization. Despite these advantages, photoinitiated polymerization processes lack the control of the final polymer properties and structurally well-defined polymers. There currently exist only a few examples, photochemical initiation can be applied to all conventional controlled/living radical polymerizations including iniferter, nitroxide mediated radical, atom transfer radical polymerization and reversible addition-fragmentation chain transfer polymerizations. The photochemical initiation not only enables the easy control of the polymerization under ambient temperature even for heat-sensitive monomers but also tends to minimize side reactions like chain transfer or depolymerization. The concentration of initiating species and finally growing polymer chains may be conveniently adjusted by choosing appropriate light intensities.

A photoinitiator or photoinitiator system is defined as a molecule or combinations of molecules that, upon absorption of light, initiate the polymerization. Photoinitiators for radical polymerization are classified as cleavage (*Type I*) and H-abstraction type (*Type II*) initiators. The majority of *Type I* photoinitiators are aromatic carbonyl compounds. *Type II* photoinitiators or bimolecular photoinitiators are photoinitiating systems consist of a photoinitiator such as benzophenone, thioxanthone or quinone and a coinitiator such as alcohol or amine. Photoinitiation by these compounds is based on the reaction of their triplet (excited) states with a hydrogen donor thereby producing an initiating radical. In view of applications, the selection of the co-initiator is undoubtedly of great importance. Mostly, amines are used because of their high efficiency and their relatively low price. The bimolecular hydrogen abstracting type photoinitiating systems, acting in the visible range, are wellknown.

On the other side, hydrogels as crosslinked hydrophilic polymers, are studied and synthesized by *Type II* photoinitiator polymerization system. Some types of hydrogels can be photopolymerized *in vivo* and *in vitro* in the presence of photoinitiators using visible or ultraviolet (UV) light.

Photopolymerization is used to convert a liquid monomer or macromer to a hydrogel by free radical polymerization in a fast and controllable manner under ambient conditions. Photopolymerized hydrogels have been investigated for a number of biomedical applications. Camphorquinone in conjunction with an alcohol is a typical example for the respective system. Their functionalization opens the way to modify or to manipulate with their properties towards many fields. Herein the “Click”

chemistry is chosen as an approach to modify the hydrogels after their functionalization.

Atom Transfer Radical Polymerization (ATRP) is among the most effective and most widely used methods of controlled radical polymerization (CRP). ATRP is an exceptionally robust way to uniformly and precisely control the chemical composition and architecture of polymers as well as the uniform growth of every polymer chain, while employing a broad range of monomers. ATRP is based on an inner sphere electron transfer process, which involves a reversible homolytic (pseudo)halogen transfer between a dormant species, an added initiator or dormant propagating chain end ($R-X$ or $R-P_n-X$) and a transition metal complex in the lower oxidation state (Mt^m/Ln), resulting in the formation of propagating radicals (R^\bullet) and the metal complex in the higher oxidation state with a coordinated halide ligand (e.g. $X-Mt^{m+1}/Ln$). The active radicals form with a measurable rate constant of activation k_{act} , subsequently propagate with a rate constant k_p and are reversibly deactivated k_{deact} , but, since ATRP is a radical based process, the active species can also terminate with a rate constant k_t .

“Click” chemistry, one of the subjects of this thesis, is a modular synthetic approach towards the assembly of new molecular entities. This powerful strategy relies mainly upon the construction of carbon–heteroatom bonds using spring-loaded reactants. Its growing number of applications are found in nearly all areas of modern chemistry from drug discovery to materials science. The copper(I)-catalysed 1,2,3-triazole forming reaction between azides and terminal alkynes has become a standard of “click” chemistry due to its reliability, specificity and biocompatibility. By using the efficient “click” reaction, different architectures of macromolecules such as dendrimers, dendronized linear polymers, hydrogels, supra-polymers and novel conjugated polymers can be created. “Click” chemistry strategy has also been implemented for the preparation of segmented copolymers of monomers polymerizable by different mechanisms.

In this thesis, a simple and convenient photochemical method of preparing hydrogels possessing reactive acetylenic sites is presented. In order to demonstrate the success of the process and confirm the presence of desired functional groups, a model reaction was performed. Thus, a fluorescent molecule, azido-pyrene was used as the antagonist “click” component and conjugated onto the hydrogel by “Click” reaction. The applicability of the described system on linear polymers was also demonstrated by click blocking of photochemically prepared acetylene functional poly(methyl methacrylate) (PMMA-Ac) with azidated polystyrene (PS-N₃) prepared by means of a controlled polymerization, namely Atom Transfer Radical Polymerization (ATRP).

II. TİP FOTOBAŞLATICILARI KULLANARAK ÇİT ÇİT KİMYASINA UYGUN HİDROJEL VE LİNEER POLİMERLERİN SENTEZİ

ÖZET

Son zamanlarda, fotobaşlatılmış polimerizasyon pek çok ekonomik ve ekolojik beklentiyi biraraya getirdiği için hayli ilgi çekmektedir. Oda sıcaklığında yüksek polimerizasyon hızı, düşük enerji tüketimi, çözücüsüz ortamda polimerizasyon, uygulanacak yüzey alanı ve uygulama süresinin kontrol edilebilmesi gibi avantajlar sağlamaktadır. Fotopolimerizasyon radikalik, katyonik ve anyonik olarak başlatılabilir de çok sayıda fotobaşlatıcının ve yüksek reaktivitedeki monomerlerin bulunulabilirliği açısından radikalik sistemlere daha fazla ilgi duyulmaktadır.

Kontrollü radikal polimerizasyonların avantajları olarak molekül ağırlığının polimer dönüşümüyle doğrusal bağıntı içinde olması, dolayısıyla istenilen molekül ağırlığının elde edilmesi, monodisperse yakın dar bir molekül ağırlığı dağılımı elde edilmesi, zincir sonunda fonksiyonel gruplara sahip polimerler elde edilmesi (telekelik polimerler), polimer moleküler mimari yapısının kontrol edilmesi (blok kopolimerler), sayılabilir. Günümüzde kullanılan kontrollü radikal polimerizasyon metodlarının çoğu termal olarak başlatılmaktadır. Fotopolimerizasyon yönteminde ise bu amaç için ısı yerine ışık kullanılmaktadır.

Basitçe ışıkla başlatılmış polimerizasyon reaksiyonlarına fotopolimerizasyon denir. Fotobaşlatıcının uygun bir dalga boyundaki ışık absorpsiyonu sonucunda oluşan primer radikaller tek fonksiyonlu monomerlerin polimerizasyonunu sağlarken çok fonksiyonlu monomerlerinde çapraz bağlı yapılara dönüştürülmesini sağlar. Fotobaşlatıcılar, radikal oluşturma mekanizmalarına göre (birinci tip fotobaşlatıcılar) ve (ikinci tip fotobaşlatıcılar) fotobaşlatıcılar olmak üzere iki ayrı sınıfa ayrılır.

Birinci tip fotobaşlatıcılar, radikal vermek üzere doğrudan fotoparçalanmaya uğrayan çeşitli fonksiyonel gruplar içeren aromatik karbonil bileşiklerdir. Genellikle fotoparçalanma aromatik karbonil grubun yanındaki bağdan (α yarılmaması) gerçekleşir. İkinci tip fotobaşlatıcılar, (α yarılmaması) için gerekli olan yeterli enerjisine sahip olmadıkları için, ancak uygun hidrojen verici moleküllere enerji aktarımı veya bu moleküllerden hidrojen koparma sonucu radikalleri üretirler. En geniş kullanımı olan serbest radikal fotobaşlatıcılar, benzoin, benzil ketalleri, asetofenon türevleri, açilfosfin oksitler (birinci tip fotobaşlatıcılar) ve benzofenon, tiyokzanton, kinon /tersiyer amin kombinasyonlarıdır (ikinci tip fotobaşlatıcılar). UV ışığıyla fotopolimerizasyon için aktive edilen birinci tip fotobaşlatıcı bileşenleri, çok

kullanışlı; fakat görünür ışık bölgesindeki kürleşmelerde yetersizlerdir. İkinci tip sistemlerde, polimerizasyonun başlaması hidrojen verici molekül üzerinde oluşan radikaller vasıtasıyla gerçekleşirken etkin olmayan ketil radikalleri birbirleriyle birleşerek ortamdan kaybolur. İkinci tip fotobaşlatıcılarda hidrojen verici moleküller olarak alkol, amin, eter ve tiyol molekülleri kullanılır.

Termal polimerizasyonla karşılaştırıldığında fotopolimerizasyon oda sıcaklığında hızlı, zamansal ve mekan kontrollü olmasından dolayı büyük avantajlara sahiptir. Fakat bu avantajların yanında fotopolimerizasyonla elde edilen polimerin molekül ağırlığı, molekül ağırlık dağılımı ve fonksiyonallitesi gibi özelliklerin kontrolü mümkün değildir. Bundan dolayıda blok ve aşırı gibi kopolimerlerin sentezi fotopolimerizasyonla gerçekleşmesi kısıtlıdır. Günümüzde kullanılan iniferter, nitroksitle büyütülmüş radikal polimerizasyon ve atom transfer radikal polimerizasyon (ATRP) gibi kontrollü/yaşayan termal polimerizasyon tekniklerinin fotokimyasal başlatılmış birkaç örnekleri mevcuttur. Fotokimyasal olarak başlatılan kontrollü/yaşayan polimerizasyonlarda zincir transfer ve depolimerizasyon gibi yan reaksiyonların minimize edilmesinden dolayı daha düşük molekül ağırlık dağılımına sahip polimerler elde edilmektedir. Ayrıca uygun ışık şiddeti seçilerekte hem başlatıcı konsantrasyonu hem de polimer zincirlerinin boyu ayarlanabilir.

Hidrojeller, polimer ağları olarak, fiziksel veya kimyasal olarak birbirine çapraz bağlı üç boyutlu bir yapıya sahiptir. Bu çözünmeyen çapraz bağlı yapı aynı zamanda aktif maddelerin immobilizasyonunu ve biyomoleküllerin etkinliğini maddelerin spesifik olarak salması özelliğiyle sağlar. Hidrojeller, kısmen temel ilkeler sebeplerden kısmen de geniş uygulama sebeplerinden dolayı uzun yıllar boyunca büyük ilgi çekmiştir. Gerek yüksek su tutma özellikleri, gerekse de buldukları ortamın şartlarına bağlı olarak su tutma kapasitelerinin büyük oranda değişebilmesi, hidrojellerin birçok alanda kullanımına imkan tanımaktadır. Ayrıca hidrojeller, içeriğinin yüksek su içermesi özelliğinden ve buna bağlı biyolojik uyumluluğundan dolayı biyomedikal alanlarda başarılı bir şekilde kullanılmaktadır. Sentetik polimerlere dayanan hidrojeller, doğal biyomalzemelere nazaren çok yönlü kullanılabilirliği ve düşük maliyeti sayesinde çeşitli biyomedikal ve endüstri alanlarında kullanılmaktadır. Özellikle PEG hidrojelleri son yıllarda toksik olmama, hidrofilik ve vücuda uyumlu yapıları nedeniyle dikkat çekmeye başlamıştır.

Son yıllarda sıkça gündeme gelen, temelleri 2001 yılında Sharpless ve çalışma arkadaşları tarafından sağlamaştırılan “klik” kimyası organik sentez dünyasına yeni bir yaklaşım getirmiştir. “Klik” kimyası Huisgen reaksiyonu da olarak bilinmektedir. “Klik” reaksiyonları terminal asetilenler ve azidler arasında gerçekleşen reaksiyonlardır. “Klik” reaksiyonlarının tercih edilmesinin sebepleri arasında; makul reaksiyon koşullarında gerçekleştirilebilmeleri, yüksek verim alınabilmesi, yüksek seçicilik ile gerçekleşmeleri, fonksiyonel grup çeşitliliğine olanak sağlamaları, kısa reaksiyon sürelerine sahip olmaları ve kullanılan çözücülere karşı hassas olmamaları gösterilebilir. “Klik” reaksiyonlarının uygulama alanları kullanılacak polimer tiplerine bağlı olarak çeşitlendirilebilir.

Bu alıřmada, reaktif asetilen grubu ieren hidrojelilerin basit ve uygun fotokimyasal yntemiyle sentezi anlatılmaktadır. İstenilen fonksiyonel grupların varlıđını kanıtlamak ve kullanılan yntemin bařarısının gstermek amacıyla model bir reaksiyon gerekleřtirildi. Bylece, azido-piren floresans molekl antagonist “klik” bileřeni olarak kullanılarak “klik” reaksiyonuyla hidrojele konjuge edilmiřtir. Ayrıca, bahsedilen sistemin lineer polimerler zerinde uygulanabiliriliđi de fotopolimerizasyon yntemi ile elde edilen asetilen fonksiyonlu polimetilmetakrilatın bir kontroll polimerizasyon eřidi olan ATRP ile sentezlenip azid fonksiyonlandırılan polistiren ile blok kopolimerizasyonuyla gsterildi.

1. INTRODUCTION

Hydrogels are chemically and/or physically cross-linked three-dimensional hydrophilic macromolecular networks that are capable of absorbing large amounts of water or biological fluids. Over the past few decades, hydrogels/hydrophilic polymers prepared by various polymerization methods and organic reactions have received significant interest because of their potentials in areas such as pharmaceuticals, biology, chemistry, medicine and so on.[1-6] These networks possessing three dimensional structure, were formed either physically or chemically. Traditionally, hydrogels are prepared by photo- or redox polymerization of water-soluble vinyl monomers, and crosslinking of hydrophilic macromonomers. Hydrogels in the micro- and nano- form may be produced by solution polymerization under selected conditions.[7-10] Recently, chemoselective crosslinking reactions induced by simply mixing polymer component solutions have become a common method for the preparation of such materials. Several biocompatible coupling reactions such as those between aldehyde and hydrazide[11, 12] as well as, Michael additions of thiols[13, 14], have successfully been employed for the formation of hydrogels.

Cu(I)-catalyzed azide-alkyne cycloaddition, commonly known as “Click Chemistry,” has proven to be the most influential method for the preparation of complex macromolecular structures[15, 16], polymeric networks, and biomaterials.[17] In our laboratory, particularly CuAAC click reactions were successfully used for the preparation of functional polymers and networks.[18-25] Such reactions have also been employed in the synthesis of hyperbranched-type complex structures.[26] We have focused on the use of these types of “click” reactions for the synthesis of various macromolecular architectures.[27-33] It seemed that click chemistry could be an important tool for extending possible combinations of conventional polymers with polyconjugated systems.

The reported approaches for the preparation of hydrogels using “Click” Chemistry are based on crosslinking of acetylene or azide-functionalized polymers under mild

conditions. Depending on the previously reported studies associated with diverse actions of “click” reactions, we envisioned that clickable sites could be incorporated into hydrogels during the preparation step under particular conditions. The difference between the reactivity of olefinic and acetylenic bonds towards radicals governs the selective formation of hydrogel with alkyne functional groups,[34] which are the key components of subsequent “click” reaction.

Photopolymerization has several advantages compared to thermal polymerization such as low energy requirement, spatial control, and fulfillment of green chemistry demands since polymerization processes may operate without solvent.[35-37] Free radical photopolymerization is based on the photochemical generation of initiating species through two main processes, namely, cleavage (*Type I*) or hydrogen abstraction (*Type II*) reactions. In *Type II* systems, initiating radicals are generated by bimolecular interactions of compounds whose triplet (excited) states readily react with hydrogen donors.[38-44] Many thioxanthone and camphorquinone based photoinitiators were developed and successfully used in various applications.[45-54]

2. THEORETICAL PART

2.1 Photochemistry

Initially, a photon needs to be absorbed for any subsequent photochemical reaction to occur in a molecule. Numerous aspects are necessary for a photochemical reaction to occur: (i) overlap must exist between the spectral emission of the light source and the absorption spectra of the targeted chromophore, (ii) the absorbed photon must have sufficient energy to enable the desired reaction, and (iii) the energy must ultimately lead to appropriate orbital transitions in the target molecule to cause the desired reaction. Formulations used in photoinitiated processes thus must contain a photosensitive molecule that has an absorption in the wavelength range in which the process is to be conducted. For an effective reaction to occur, a photon is absorbed either directly by a molecule that also contains the targeted reactive functional group or by a molecule that generates reactive intermediates (e.g., generation of radical/ionic intermediates for polymerization/crosslinking reactions). It also can be absorbed by a photosensitizing molecule that interacts with other molecules in the formulation while in its excited state (*i.e.*, photosensitization) to cause one of the former reactions.

Photon absorption promotes an electron from its ground state (S_0) to its excited singlet state (S_1), which is described in a typical Jablonski diagram (Figure 2.1).[55] In the absence of any photochemical processes, S_1 , representing the excited singlet state of the chromophore, either deactivates to S_0 by fluorescence emission or through internal conversion by heat dissipation. Alternatively, it undergoes intersystem crossing (ISC) to a triplet state (T_1). T_1 either deactivates to S_0 by phosphorescence emission or by ISC. These photophysical processes are in competition with photochemical processes, which include the various targeted reactions.

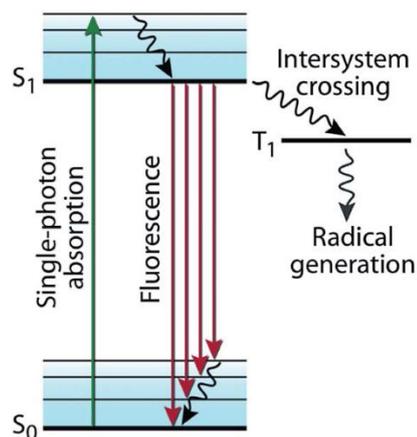


Figure 2.1 : Jablonski diagram. The excited singlet state (S_1) undergoes intersystem crossing (ISC) to a triplet state (T_1), which leads to various photochemical reactions.

2.2 Photopolymerization

Photopolymerization is concerned with absorption of ultraviolet radiation to produce an unstable excited species. Subsequent formation of a free radical by rearrangement, fragmentation or energy transfer, followed by attack to a monomer, leads to polymerization. The photoinitiated polymerization of monomers and oligomers to form crosslinked higher molecular weight material is the basis for most of the commercial applications of photopolymer technology. Photopolymerization is one of the most rapidly expanding processes for materials production. The reactive monomeric materials that are most commonly used are low molecular weight unsaturated acrylate or methacrylate monomers that can be made to crosslink with the use of a radical generating photoinitiator.[56] Cationic initiated crosslinking of monomeric materials with epoxy and/or vinyl ether functionality has increased in practicality with the development of new higher efficiency photoinitiators that generate cationic species (e.g. strong acids) upon exposure.[57] Typical photopolymer formulations contain a photoinitiator system, monomers and oligomers, a polymer or polymers to provide specific physical and/or processing properties and a variety of additives to modify the physical properties of the light sensitive composition or the final properties of the cured photopolymer. Photopolymerization chemistry is commercially utilized in a wide variety of applications (e.g. coatings, adhesives, sealants, printing plates and so on). Since a free-radical mechanism is involved in photopolymerization, to the typical conditions governing thermal polymerization must be added the many factors (e.g., irradiation

source, photoinitiator, wavelength screening, catalyst, temperature, solvent, presence of oxygen, etc.) associated with ultraviolet-induced polymerization. The excited species is formed by subjecting the photoinitiator or photosensitizer to ultraviolet radiation. PI*, the excited molecule, possesses more energy than the ground state and is, therefore, capable of transferring energy to another substance or a monomer which then undergoes bond cleavage to give a free-radical initiation site. PI* is then returned to the ground-state energy level PI and is no longer available to transfer energy to form active sites. Disappearance of PI* may also occur without initiation; it may take the form of thermal energy, fluorescence, or energy transfer. (Figure 2.2).

Photo-induced polymerization has also been used for the preparation of block and graft copolymers. Funt and Collins[58] applied the techniques of focusing a beam of intense ultraviolet radiation on a stream of monomer containing a free-radical initiator. The polymer chain grows to a certain block length which still possesses active end groups and this block is permitted to fall into a second monomer reservoir. Polymers containing functional groups susceptible to photolysis also provide initiation sites for the synthesis of block and graft copolymers.

2.3 Types of photopolymerization

2.3.1 Photoinitiated free radical polymerization

Photoinitiated free radical polymerization is one of the most widely employed route in industrial applications because of its applicability to a wide range of formulations based on acrylates, unsaturated polyesters, and polyurethanes and the availability of photoinitiators having spectral sensitivity in the near-UV or visible range.

It consists of four distinct steps:

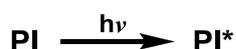
i) **photoinitiation** step involves absorption of light by a photosensitive compound or transfer of electronic excitation energy from a light absorbing sensitizer to the 5 photosensitive compound. Homolytic bond rupture leads to the formation of a radical that reacts with one monomer unit.

ii) **propagation** step involves repeated addition of monomer units to the chain radical produces the polymer backbone.

iii) *chain transfer* step involves termination of growing chains by hydrogen abstraction from various species (e.g., from solvent) and formation of new radicals capable of initiating other chain reactions.

iv) *termination* step involves termination of chain radicals by disproportionation or recombination reactions. Termination can also occur by recombination or disproportionation with any other radical including primary radicals produced by the photoreaction.

Photoinitiation:



Propagation:



Transfer:



Termination:



Figure 2.2 : Elementary reactions in free radical photopolymerization.

The role that light plays in photopolymerization is restricted to the very first step, namely the absorption and generation of initiating radicals. The reaction of these radicals with monomer, propagation, transfer and termination are purely thermal processes; they are not affected by light. In most cases of photoinduced

polymerization, initiators are used to generate radicals. Photoinitiators are generally divided into two classes, *Type I* and *Type II*, according to the process by which initiating radicals are formed.

2.3.1.1 *Type I* photoinitiators (Unimolecular photoinitiator system)

Photoinitiators termed unimolecular are so designated because the initiation system involves only one molecular species interacting with the light and producing free-radical active centers. These substances undergo a homolytic bond cleavage upon absorption of light.

Initiating radicals, formed by direct photofragmentation process (α or less common β cleavage) of *Type I* photoinitiators upon absorption of light, are capable of triggering polymerization. As illustrated in Figure 2.3, the photoinitiator forms an excited singlet state, which then undergoes rapid intersystem crossing to form a triplet state. In the triplet state, two radicals (benzoyl and benzyl radicals) are generated by α -cleavage fragmentation. The benzoyl radical is the major initiating species, while, in some cases, the benzyl radical may also contribute to the initiation.

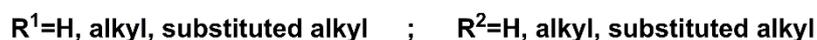
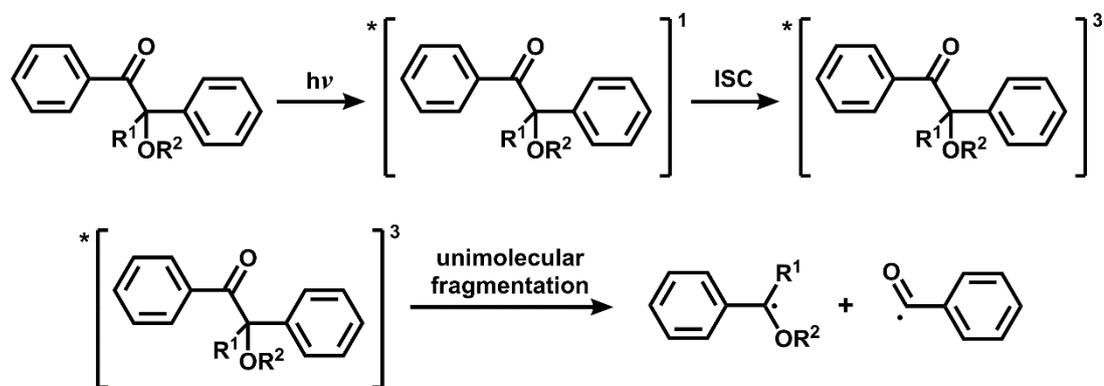
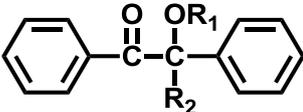
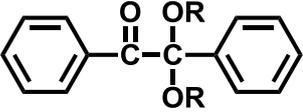
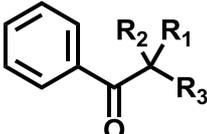
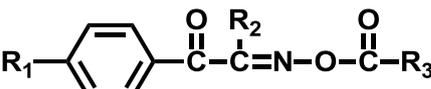
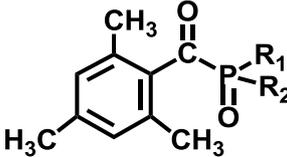


Figure 2.3 : Formation of initiating radicals from decomposition of a *Type I* photoinitiator.

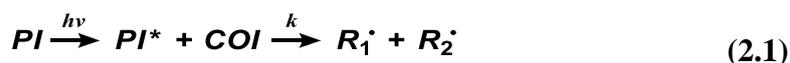
Most of the *Type I* photoinitiators are aromatic carbonyl compounds with appropriate substituents. Benzoin ether derivatives, benzil ketals, hydroxylalkylphenones, α -aminoketones and acylphosphine oxides are the most efficient ones (Table 2.1).[59-62]

Table 2.1 : Structures of typical *Type I* radical photoinitiators.

Photoinitiator	Structure	λ_{\max}
Benzoin ethers	 <p>$R_1 = \text{H, alkyl}$ $R_2 = \text{H, substituted alkyl}$</p>	323
Benzyl ketals	 <p>$R = \text{CH}_3, \text{C}_3\text{H}_7, \text{CH}_2$</p>	365
Acetophenones	 <p>$R_1 = \text{OCH}_3, \text{OC}_2\text{H}_5$ $R_2 = \text{OCH}_3, \text{H}$ $R_3 = \text{C}_6\text{H}_5, \text{OH}$</p>	340
Benzyl oxymes	 <p>$R_1 = \text{H, SC}_6\text{H}_5$ $R_2 = \text{CH}_3, \text{C}_6\text{H}_{13}$ $R_3 = \text{C}_6\text{H}_5, \text{OC}_2\text{H}_5$</p>	335
Acylphosphine oxides	 <p>$R_1 = \text{SCH}_3, \text{morpholine}$ $R_2 = \text{CH}_3, \text{CH}_2\text{Ph, C}_2\text{H}_5$ $R_3 = \text{N}(\text{CH}_3)_3, \text{morpholine}$</p>	380

2.3.1.2 Type II photoinitiators (Bimolecular photoinitiator system)

The excited states of certain compounds do not undergo *Type I* reactions because their excitation energy is not high enough for fragmentation (i.e., their excitation energy is lower than the bond dissociation energy). The excited molecule can however react with another component of the polymerization mixture (co-initiator (COI)) to produce initiating radicals (eq. 2.1). In this case, radical generation follows second-order kinetics (eq. 2.2).



$$\frac{d[R_1]}{dt} = \frac{d[R_2]}{dt} = k[PI^*][COI] \quad (2.2)$$

Typical *Type II* photoinitiators include aromatic carbonyls such as benzophenone and derivatives[63-66], thioxanthone and derivatives[67-72], benzil[63], quinines[63], and organic dyes[72-77], whereas alcohols, ethers, amines, and thiols are used as hydrogen donors.

Alternative approach concerns the attachment of both chromophoric and hydrogen donating groups into polymer chains. This way, the odor and toxicity problems observed with the conventional photoinitiators and amine hydrogen donors were overcome.

Table 2.2 : Structures of typical *Type II* radical photoinitiators.

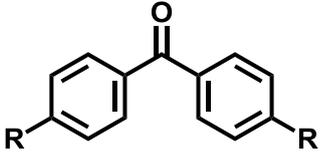
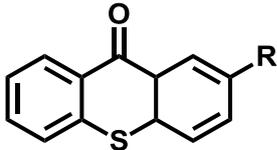
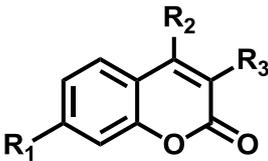
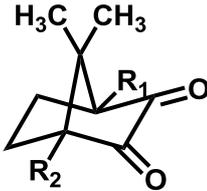
Photoinitiator	Structure	λ_{max}
Benzophenones	 <p>$R_1 = H, OH, N(C_2H_5)_2, C_6H_5$</p>	335
Thioxantones	 <p>$R = H, Cl, isopropyl$</p>	390

Table 2.2 : Structures of typical *Type II* radical photoinitiators (continued)

Coumarins		370
	$R_1 = \text{N}(\text{C}_2\text{H}_5)_2, \text{N}(\text{CH}_3)_2$ $R_2 = \text{CH}_3, \text{cyclopentane}$ $R_3 = \text{benzothiazole, H}$	
Camphorquinones		470
	$R_1 = \text{CH}_3, \text{H}$ $R_2 = \text{H, CH}_3$	

In fact, photoinitiators with higher wavelength absorption characteristics are desired as they cost lower energy and are defined to be “green”. Typical photoinitiators for *Type II* system are listed in Table 2.2.

Radical generation by *Type II* initiating systems has two distinct pathways:

Photoinduced electron transfer reactions and subsequent fragmentation

Photoinduced electron transfer is a more general process, which is not limited to a certain class of compounds and is more important as an initiation reaction comprising the majority of bimolecular photoinitiating systems. The photoexcited compounds (sensitizer) can act as either an electron donor with the coinitiator as an electron acceptor or vice-versa. The radical ions obtained after the photoinduced electron transfer can generally undergo fragmentation to yield initiating radicals (eq. 2.3-2.5)

The electron transfer is thermodynamically allowed, if Gibbs Energy Change (ΔG) calculated by the Rehm-Weller equation (eq. 2.6) is negative.[78]





$$\Delta G = F[E_{1/2ox}(D/D^{\cdot+}) - E_{1/2red}(A/A^{\cdot-})] - E_s + \Delta E_c \quad (2.6)$$

Where F = Faraday constant,

$E_{1/2ox}(D/D^{\cdot+}) - E_{1/2red}(A/A^{\cdot-})$ = Redox potentials of the donor and acceptor,

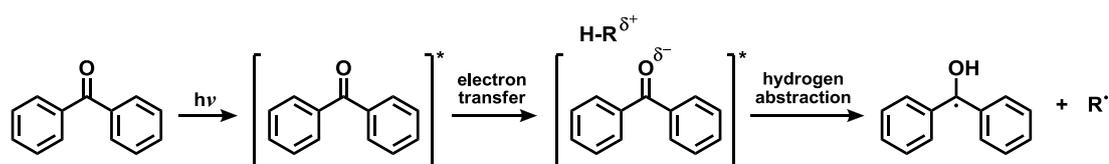
E_s = Excitation state of the reactive site of the sensitizer; $E_s = h\nu$,

ΔE_c = Coulomb stabilization energy

Electron transfer is often observed for aromatic ketone/amine, aromatic/alcohol pairs and with dye/coinitiator systems.

Hydrogen abstraction from a suitable hydrogen donor

Bimolecular hydrogen abstraction is limited to diaryl ketones.[79] The free radical generation process is the H-abstraction reaction of triplet photoinitiator from hydrogen donors (R-H) such as amines and alcohols. The radical derived from the donor can initiate the polymerization, whereas ketyl radicals stemming from aromatic carbonyl compound are usually not reactive toward vinyl monomers because of bulkiness, the delocalization of the unpaired electrons, or both. The overall process is depicted in the example of benzophenone in Figure 2.4.



R = amines, alcohols, ethers, thiols

Figure 2.4 : Formation of initiating radicals from photolysis of *Type II* photoinitiator in the presence of suitable hydrogen donor.

Many efforts have been addressed towards the development of very efficient photoinitiators[80], oligomers[81] and monomers[82]. 1,2-Diketones, such as camphorquinone in combination with an appropriate co-initiator are most used initiators. These diketones exhibit low intensity $n\pi^*$ transitions in the range between 400 and 500 nm. Alcohols are used as co-initiators in these systems. The α -alcohol-radicals initiate the polymerization reaction, while the ketyl radical mainly dimerizes

or disproportionates. As the diketone is destroyed by photochemical reduction (Figure 2.5), these initiators start the formation of crosslinks.

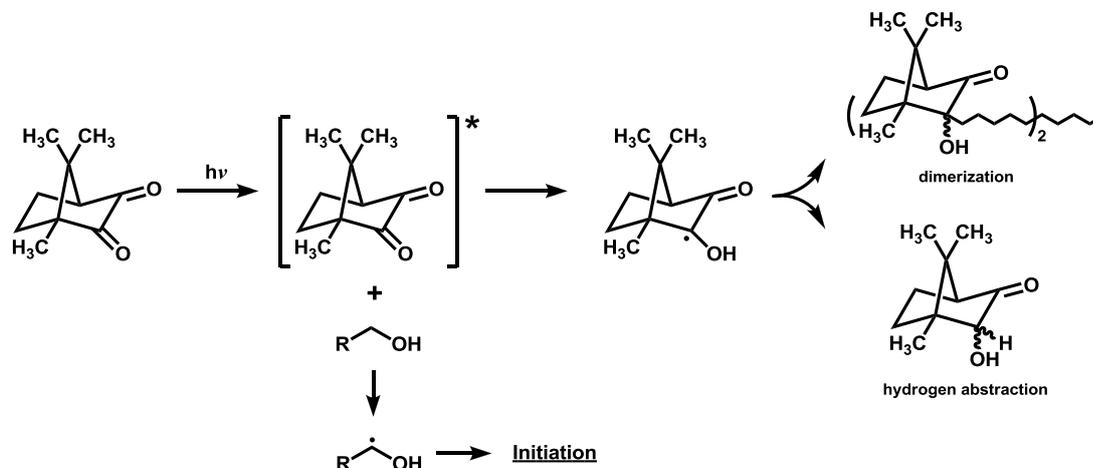


Figure 2.5 : Comphorquinone/Alcohol Initiation Reaction

2.3.1.3 Effect of oxygen on photopolymerization

Oxygen is a well-known strong inhibitor of radical-induced polymerizations due to its high reactivity towards radicals. By scavenging the initiator radicals, oxygen reduces the rate of polymerization, thus longer exposure time is required.[83] One of the first examples of the effects of oxygen on photocuring was described by Wight.[84]

2.3.1.4 Crosslinking free radical polymerization

The free radical copolymerization of a monomer M with a bis-unsaturated monomer N is of special interest as it yields crosslinked species, which have found a wide variety of applications. When the process starts, the system is binary and it can be treated as a regular free radical copolymerization. However, as soon as some N units have been added to radical sites, pendent double bonds are formed (Figure 2.6), which exhibit their own reactivity. From there, the system involves three different polymerizable constituents: M monomer, N monomer and the pendant unsaturations; the system has become ternary.

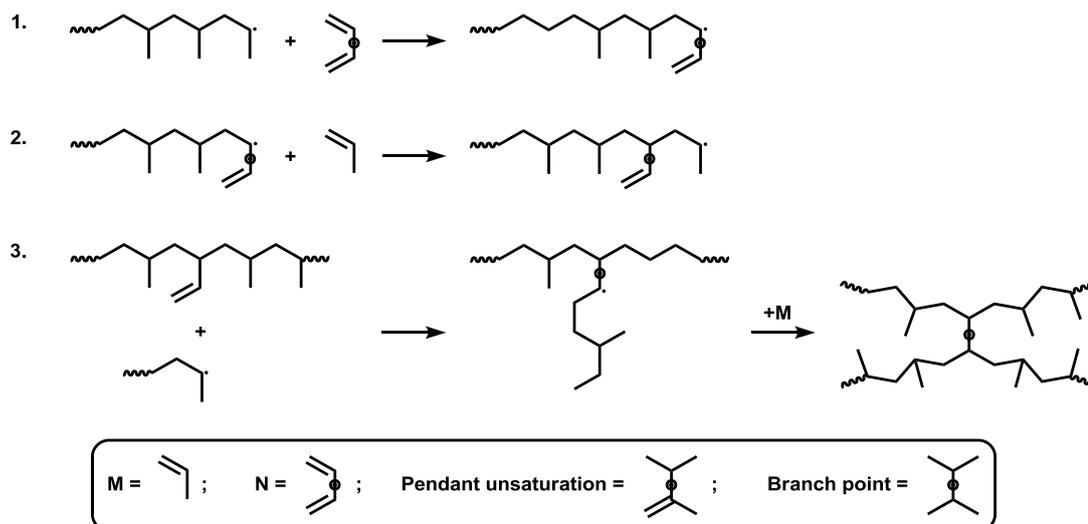


Figure 2.6 : Crosslinking by free radical polymerization

2.3.1.5 Monomers

Unsaturated monomers, which contain a carbon–carbon double bond (C=C), are used extensively in free radical photopolymerizations. The free-radical active center reacts with the monomer by opening the C=C bond and adding the molecule to the growing polymer chain. Most unsaturated monomers are able to undergo radical polymerization because free-radical species are neutral and do not require electron-donating or electron-withdrawing substituents to delocalize the charge on the propagating center, as is the case with ionic polymerizations. Commercial consideration in formulation development is therefore given to the final properties of the polymer system, as well as the reactivity of the monomer. Acrylate and methacrylate monomers are by far most widely used in free-radical photopolymerization processes. These monomers have very high reaction rates, with acrylates having an even faster reaction rate than their methacrylate counterparts.[85] This makes them especially amenable for high speed processing needed in the films and coatings industry.

Multiacrylates increase the mechanical strength and solvent resistance of the ultimate polymer by forming cross-linked networks rather than linear polymer chains, whereas monoacrylates reduce the viscosity of the prepolymer mixture for ease of processing.[85, 86] One of the drawbacks of acrylate and methacrylate systems is their relatively large polymerization shrinkage. Shrinkage is caused by the formation of covalent bonds between monomer molecules. When a covalent bond is formed

between two monomer molecules, the distance between them is approximately half as much as that between two molecules experiencing van der Waal's forces in solution. This shrinkage causes stresses in the polymer parts, which can affect their ultimate performance, especially in applications such as stereo lithography, dentistry, and coatings.

2.3.2 Photo-induced anionic polymerization

There are a wide range of reactions that could be catalyzed by a base, including urethane formation from alcohols and isocyanates, ring opening reaction of epoxies by nucleophilic species and Michael addition reactions. Several of these reactions are important in industrial applications. Most base-catalyzed processes are inert to oxygen and moisture, which is a great advantage for applications in coatings, in contrast to radical and cationic photopolymerizations due to their inhibition by oxygen and moisture, respectively.

The primary limitation on the implementation of base catalyzed reactions is a lack of suitable photoinitiating systems. Most photoinitiators, or photolabile bases, that are reported to date, suffer either from low catalytic activity and long-term stability or solubility in the organic media and limited availability.

Yagci and co-workers[87-89] demonstrated that weak base generating photoinitiator systems can be used to initiate zwitterionic polymerization of cyano acrylates. *N*-Alkoxy pyridinium and *N*-Phenacylpyridinium type salts were shown to be effective initiators for such zwitterionic polymerization. Manners[90] reported that sila[1]ferrocenophanes undergo ring-opening polymerization when treated with Na[C₅H₅] and UV light (Figure 2.7).

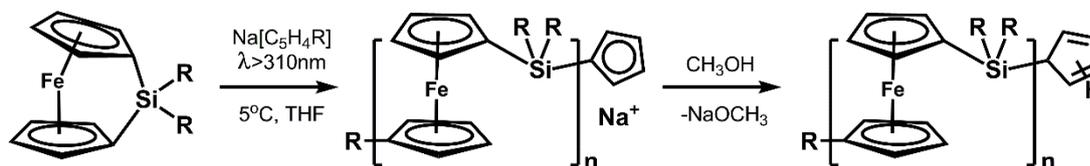


Figure 2.7 : An example of photoinitiated anionic polymerization.

2.3.3 Photo-induced cationic polymerization

Epoxy and vinyl ether based monomers that are prone to cationic polymerization are of low volatility and negligible toxicity and possess good rheological properties.[91] In contrast to free radical polymerization, molecular oxygen does not inhibit the polymerization, and hence films can be cured in the presence of dry air. Moisture generally terminates the polymerization.

Photoinitiated cationic polymerizations are generally accomplished with the aid of onium salts. The past two decades have seen a rapid growth in the research of new photoinitiators for cationic polymerization. Among them, the onium-type photoinitiators such as iodonium[92], sulfonium[93, 94], and alkoxy pyridinium[95-97] salts are important due to their thermal stability, solubility in most of the cationically polymerizable monomers, and efficiency in generating reactive species upon photolysis.[98]

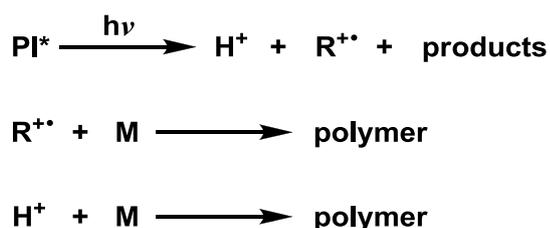


Figure 2.8 : General scheme of photoinitiated cationic polymerization

A photo-sensitive compound, namely photoinitiator (PI), absorbs incident light and undergoes decomposition leading to production of initiating species. Active species, namely a radical cation ($\text{R}^{+\bullet}$) in turn, react with cationic polymerizable monomers (M), and yield polymer (Figure 2.8).

Photoinduced decomposition and subsequent reaction of the radical cation with solvent or monomer lead to the formation of Bronsted acid, which is responsible for further initiation.

2.4 Hydrogels

Hydrogels are defined as three-dimensional networks of hydrophilic polymers that are able to absorb up to hundreds of times their dry weight in water. Hydrogels based on synthetic polymers, thanks to their versatility and low costs compared with natural

biomaterials, have been successfully employed in a variety of biomedical applications, ranging from ophthalmic and vascular prostheses to drug delivery and soft-tissue replacement.[99-101] They are water swollen polymer matrices, with a tendency to imbibe water when placed in aqueous environment. This ability to swell, under biological conditions, makes it an ideal material for use in drug delivery and immobilization of proteins, peptides, and other biological compounds. Due to their high water content, these gels resemble natural living tissue more than any other type of synthetic biomaterial.[102] These networks, have a three dimensional structure, crosslinked together either physically, or chemically. This insoluble crosslinked structure allows immobilization of active agents, biomolecules effectively, and allows for its release in well-defined specific manner. Thus the hydrogels' biocompatibility and crosslinked structure are responsible for its varied applications.

2.5 Poly(ethylene) glycol (PEG) as suitable material for hydrogel synthesis

It is known that hydrophilic monomers provide a distinct advantage in both fabrication and application of hydrogels. The premier material used today for both drug delivery, cell encapsulation and as adhesion promoters is Poly (ethylene glycol) hydrogels. PEG is nontoxic, thus ideal for biological applications, and can be injected into the body without adverse effects.

It is also an FDA approved materials for use in humans. Acrylate monomers are esters containing vinyl groups, that is two carbon atoms double bonded to each other, directly attached to the carbonyl atom. On exposure to UV radiation, the photoinitiator, photofragments to yield radicals. These radicals initiate polymerization, by attacking the C=C double bonds present in the acrylate groups. In linear chain formation, branched as well as crosslinked structures are also formed, thus forming an insoluble three dimensional polymer network. This polymer network is the hydrogel, which can be used further on different fields and purposes.

2.6 Atom transfer radical polymerization (ATRP)

2.6.1 Mechanism

ATRP is controlled by an equilibrium between propagating radicals and dormant species, predominately in the form of initiating alkyl halides/macromolecular species

(P_nX). The dormant species periodically react with the rate constant of activation (k_{act}) and with transition metal complexes in their lower oxidation state, Mt^m/L . Acting as activators Mt^m represents the transition metal species in oxidation state m and L is a ligand) and deactivators transition metal complexes in their higher oxidation state, coordinated with halide ligands $X-Mt^{m+1}/L$ (Figure 2.9).

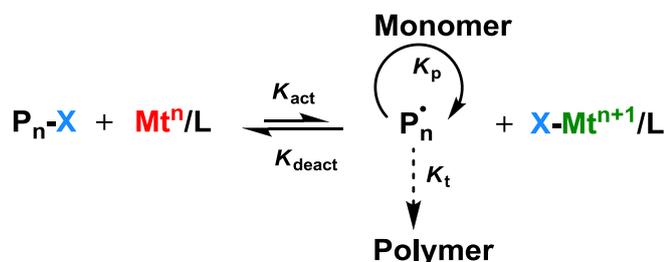


Figure 2.9 : Representation of ATRP mechanism.

The deactivator reacts with the propagating radical in a reverse reaction (k_{deact}) to reform the dormant species and the activator. ATRP is a catalytic process and can be mediated by many redox-active transition metal complexes (Cu^I/L and $X-Cu^{II}/L$ has been the most often used transition metal but other studied metals include Ru, Fe, Mo, Os, etc.).[103]

The rate of an ATRP depends on the rate constant of propagation and on the concentrations of monomer and growing radicals. The structure of the ligand and monomer/dormant species as well as reaction conditions (solvent, temperature, and pressure) can strongly influence the values of the rate constants, k_{act} [104] and k_{deact} [105], and their ratio, K_{ATRP} . [106, 107] Rates of ATRP increase with catalysts activity (K_{ATRP}) but under some conditions may decrease, due to radical termination and a resulting low $[Cu^I/L]/[X-Cu^{II}/L]$ ratio, due to buildup in the concentration of deactivator via the persistent radical effect.[108] ATRP is a very robust and versatile synthetic technique for preparation of polymers with precisely controlled architecture and site specific functionality. ATRP is a very robust and versatile synthetic technique for preparation of polymers with precisely controlled architecture and site specific functionality.

2.6.2 Radicals as propagating species

The “living” nature of ATRP originates in fast initiation, concurrent growth of all chains via intermittent activation of dormant species catalyzed by Cu complexes,

resulting in a small fraction of terminated chains. Although non radical active species were proposed in ATRP[109], there is abundant evidence that ATRP operates via a radical mechanism.

2.6.3 Removal of copper

One limitation of the “early” ATRP procedures was associated with the relatively high concentration of catalyst, often equimolar to initiator. This high concentration of catalyst was required to overcome radical termination reactions.[110, 111] Purification methods included passing the polymer solution through silica or neutral alumina columns[112], stirring with an ion-exchange resin[113], clay[114], precipitation of polymers into a nonsolvent[115], or the use of a heterogeneous catalyst that could be isolated after polymerization.[116]

2.7 Block copolymers

Block copolymers comprise two or more homopolymer subunits linked by covalent bonds. The union of the homopolymer subunits may require an intermediate non-repeating subunit, known as a junction block. Block copolymers with two or three distinct blocks are called diblock copolymers and triblock copolymers, respectively.

Copolymers may also be described in terms of the existence of or arrangement of branches in the polymer structure. Linear copolymers consist of a single main chain whereas branched copolymers consist of a single main chain with one or more polymeric side chains.

Block copolymers are made up of blocks of different polymerized monomers. For example, PS-*b*-PMMA is short for polystyrene-*b*-poly(methyl methacrylate) and is usually made by first polymerizing styrene, and then subsequently polymerizing MMA from the reactive end of the polystyrene chains. This polymer is a "diblock copolymer" because it contains two different chemical blocks. Triblocks, tetrablocks, multiblocks, etc. can also be made. Diblock copolymers are made using living polymerization techniques, such as atom transfer free radical polymerization (ATRP), reversible addition fragmentation chain transfer (RAFT), ring-opening metathesis polymerization (ROMP), and living cationic or living anionic polymerizations.[117]

Block copolymers are normally prepared by controlled polymerization of one monomer, followed by chain extension with a different monomer[118] to form AB or ABC block copolymers. Halogen exchange is recommended for the preparation of block copolymers when one is moving from a macroinitiator of lower activity, such as a styrene or an acrylate, to continue the polymerization with a monomer that forms a more reactive dormant species, such as a methacrylate or acrylonitrile if one desires to obtain a narrow polydispersity for the second block. The following diagram shows the arrangement of blocks in an AB diblock (1), an ABA triblock (2), an ABC triblock (3), and a starblock (4) (Figure 2.10).

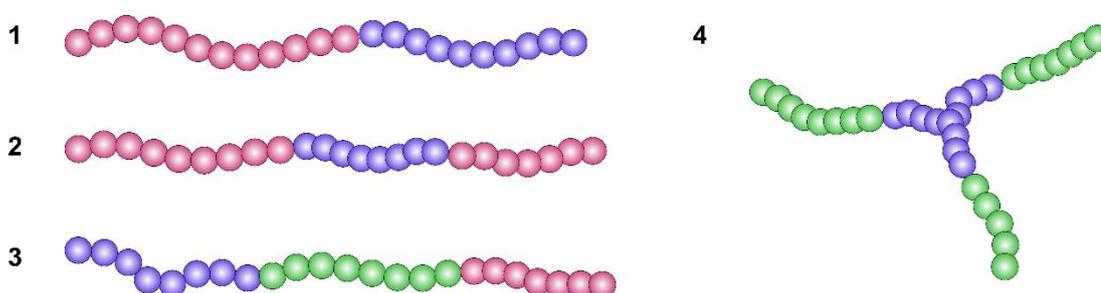


Figure 2.10 : Different types of block copolymers

2.8 “Click” chemistry

In 2001, Sharpless introduced the concept of “click” chemistry, one of the most versatile and modular approaches to couple two reactive partners in a facile, quick, selective, reliable and high yield reaction under mild conditions.[17]

“Click” chemistry also provides a powerful and versatile tool for materials synthesis owing to its simplicity, selectivity, efficiency, and tolerance of various functional groups. Consequently, a wide range of controlled-architecture materials have been synthesized through various “click” reactions, including block polymers, micelles, dendrimers, gels, and networks. An alternative and elegant strategy to incorporate clickable groups on polymer chains is to functionalize the polymerization initiator with a click reactant (such as an azide or alkyne), thus avoiding the necessity for post-polymerization modification prior to ligation.

In 2006, Barner-Kowollik and co-workers employed clickable groups into RAFT initiator structures by synthesizing azide- and alkyne-modified, conventional RAFT agents to mediate the polymerization of styrene and vinyl acetate.[119] Besides the

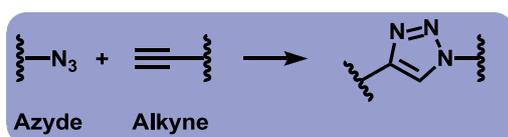
widely used azide and alkyne functional groups, other click type reactants, such as aldehydes and aminoxy, have been utilized for the facile synthesis of complex polymer architectures, such as star copolymers.

Although the simplicity and efficiency of “click” chemistry has been extensively explored in linear/cyclic block copolymer synthesis, it has also found utility as an effective tool in preparation of materials with complex architectures. Nischang et al. employed radical-mediated thiol-ene click chemistry to functionalize hierarchically structured cubic polyhedral silsesquioxanes.[120]

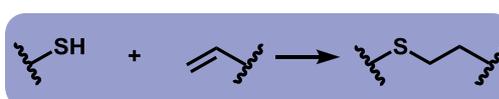
“Click” chemistry has also been applied to the formation of polymer networks. Indeed, “click” reactions are particularly well suited for the synthesis and modification of hydrogels to achieve tunable properties. By applying click reactions to form a hydrogel and subsequently using light to spatially pattern chemical functionality through photo-click and photo-cleavage reactions, they have demonstrated the ability to pattern physical characteristics in three dimensions throughout the hydrogel.[121]

Thiol-click reaction, diels-alder and azide-alkyne cycloaddition reaction are selected here as representatives because of their fast reaction kinetics and wide utility in applications. Each of the selected reactions has recently been implemented and is particularly versatile in the context of material synthesis and functionalization.[122]

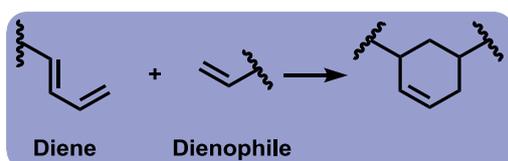
Azide Alkyne Cycloaddition



Thiol-vinyl addition



Diels-Alder addition



Thiol-yne

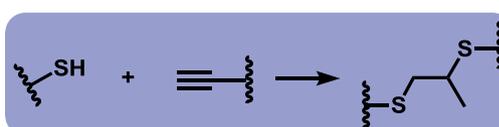


Figure 2.11 : Overview and classification of some types of “click” reactions.

2.8.1 Thiol- based “Click” reaction

Despite the azide-alkyne cycloaddition reaction, there exists a constellation of thiol reactions that have also been considered to be “click reactions and that have been broadly applied in materials science. Among this thiol-X family of reactions, one particularly common thiol-based click reaction is the radical-mediated addition of a thiol to a vinyl.

The radical-mediated thiol-ene reaction is also an excellent example of the importance of reaction conditions in determining under what circumstances a reaction behaves in a manner consistent with the click paradigm. Thiol-ene click reactions comprise another class of powerful tools in imprint and lift-off lithography. In 2008, Hawker and co-workers used thiol-ene chemistry to fabricate tunable PEG- and polysiloxane-based, cross-linked elastomers.[123]

Recently, the radical-mediated thiol-ene mechanism has been complemented by the thiol-yne mechanism wherein a thiol and alkyne are coreacted in a 2:1 ratio with each alkyne capable of reacting with two thiols in an alternating chain transfer and propagation process that is mechanistically equivalent to the thiol-ene reaction.[124-127]

2.8.2 Diels-Alder cycloaddition

The Diels-Alder cycloaddition is one of the most powerful and widely used reactions in organic synthesis and has been employed extensively in polymer chemistry applications such as block copolymer synthesis, formation of highly cross-linked networks, and self-healing materials.[128-132] The Diels-Alder reaction, first described by Otto Diels and Kurt Alder in 1928, is a [4+2] cycloaddition reaction between a diene and a dienophile to form a cyclohexene adduct. One attractive characteristic of the Diels-Alder reaction that has been exploited in polymer chemistry is its thermal reversibility, which can be utilized in temperature-controlled reversible polymer network formation, particularly in self-healing applications.[133]

2.8.3 Azide-alkyne cycloaddition of copper catalyzed alkyne-azide cycloaddition (CuAAC)

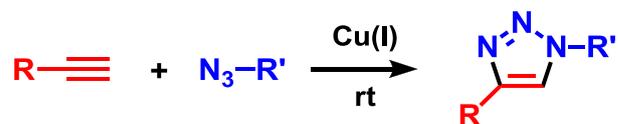


Figure 2.12 : Azide-alkyne cycloaddition

The 1,3-dipolar cycloaddition of azides with alkynes was first discovered by Huisgen in 1963. However, it did not attract much interest until it was demonstrated that this high temperature reaction could also be carried out under mild conditions using Cu(I) as the catalyst, and with tremendous regio-selectivity. This was discovered simultaneously and independently by Meldal and his group in Denmark, and Fokin and Sharpless in USA.[134-137]

The CuAAC reaction has been successfully introduced in many different scientific areas, and its potential has been demonstrated in materials chemistry[138], polymers[139, 140], nanoparticle synthesis[141] etc.

3. EXPERIMENTAL PART

3.1 Materials

3.1.1 Solvents

Chloroform (CHCl₃, VWR, 99,2%)

It was used as received.

Toluene (Merck, 99,9%)

It was used as received.

Diethyl ether (J.T. Baker)

It was used as received.

Methanol (Merck, 99,9%)

It was used as received.

1,4 dioxane (Riedel-deHaen,99,5%)

It was used as received.

Dimethylformamide (DMF, Aldrich)

It was used as received.

Pyridine (Aldrich, ≥99.0%)

It was used as received.

Tetrahydrofuran THF (HiPerSolv CHROMANORM® for HPLC)

It was used as received.

Cyclohexane laboratory reagent (Aldrich, $\geq 99.8\%$)

It was used as received.

3.1.2 Chemicals

Methyl methacrylate (MMA, Aldrich, 99%)

It was passed through a short neutral activated aluminum oxide (0.063-0.200 mm) column before use.

Styrene (Aldrich, 99%)

It was passed through a short neutral activated aluminum oxide (0.063-0.200 mm) column before use.

Camphorquinone (97%, Aldrich)

It was used as received.

Poly(ethylene glycol) methyl ether methacrylate (PEGMA; Aldrich, $M_n=300$)

It was used as received.

Poly(ethylene glycol) diacrylate (PEGDA; Aldrich, average $M_n=575$)

It was used as received.

Bromoethane ($\geq 98\%$, Aldrich)

It was used as received.

Chlorotrimethylsilane ($\geq 98\%$, Aldrich)

It was used as received.

Sulfuric acid (95-97%, Aldrich)

It was used as received.

Magnesium sulfate anhydrous (for analysis EMSURE®)

It was used as received.

N,N,N',N',N'' pentamethyldiethylenetriamine (PMDETA; 99%)

It was used as received.

Ethyl 2-bromopropionate (EtBP) (98%)

It was used as received.

Copper(I) bromide (Aldrich, ≥98%)

It was used as received.

Sodium azide (99%)

It was used as received.

Propargyl alcohol (PA, 99%, Aldrich)

It was used as received.

p-Toluenesulfonyl chloride (Aldrich, ≥99.0%)

It was used as received.

1-Pyrenemethanol (Aldrich, 98%)

It was used as received.

Tetrabutylammonium fluoride solution (Aldrich, 1 M in THF)

It was used as received.

2-Azidomethyl pyrene

It was used as received.

3-(trimethylsilyl)propargyl alcohol[142]

Was synthesized according to the previously reported procedure.[142]

3.2 Characterization

3.2.1 ¹H-Nuclear magnetic resonance spectroscopy (¹H-NMR)

¹H NMR measurements were recorded using an Agilent VNMRS 500 MHz instrument.

3.2.2 Infrared spectroscopy (FT-IR)

The FTIR spectra are recorded at Perkin Elmer Spectrum One with an ATR accessory (ZnSe, Pick Miracle Accessory) and cadmium telluride (MCT) detector. Resolution was 4 cm⁻¹ and 12 scans with 0.2 cm/s scan speed

3.2.3 Gel permeation chromatography (GPC)

Molecular weights and molecular weight distributions were determined by SEC performed in THF as eluent. The apparent molecular weights (M_n) and polydispersities (M_w/M_n) were determined by gel permeation chromatography (GPC) using a Viscotek GPCmax auto-sampler system consisting of a pump, three ViscoGEL GPC columns (G2000HHR, G3000HHR and G4000HHR) (7.8 mm internal diameter, 300 mm length), and a Viscotek differential refractive index (RI) detector with THF as eluent at a flow rate of 1.0 mL/min at 30°C. The effective molecular weight separations of the columns are ranging as 456–42,800 g/mol for G2000HHR; 1050–107,000 g/mol for G3000HHR; and 10,200– 2,890,000 g/mol for G4000HH. The detector was calibrated with polystyrene standards having narrow molecular weight distribution and the quoted molecular weights of the polymers therefore are expressed in terms of polystyrene equivalents. Data were analyzed using Viscotek OmniSEC Omni-01 software.

3.3 Synthesis

3.3.1 Synthesis of alkyne functional hydrogels

Hydrogels were synthesized through light-induced free radical polymerization. A typical procedure for the preparation of the gels is as follows. A DMF solution of PEGMA (1.05 mmol), PEGDA (5.25 x 10⁻² mmol), camphorquinone (5.25 x 10⁻² mmol) and propargyl alcohol (5.25 x 10⁻² mmol) was purged with nitrogen gas for

4-5 minutes and transferred into a special silicon material piece tightly jammed between two microscope glass slides. After sealing with paraffin, 45-minute irradiation from a KER-Vis blue photoreactor equipped with 6 lamps (Philips TL-D 18 W) emitting light nominally at 400–500 nm at room temperature resulted in the formation of the desired hydrogel. After polymerization, the glassware mold was gently opened and removed, and the formed gel was kept in deionized water at room temperature for at least two days for the removal of unreacted reagents.

3.3.2 Synthesis of 2-azidomethyl pyrene (Py-N₃)

The synthesis of azide functionalized pyrene (Py-N₃) was adapted from the literature[143, 144] (Figure 4.3). 1-Pyrenemethanol (0.847 g, 3.65 mmol) was dissolved in 10mL chloroform under nitrogen atmosphere and cooled down in an ice bath (0°C) and pyridine (0.6 mL, 7.3 mmol) was added. Then, toluene-4-sulfonyl chloride (1.040 g, 5.48 mmol) dissolved in 10mL of chloroform was slowly added to the reaction flask at cold. The reaction mixture was stirred overnight at room temperature. The solvent was removed under vacuum and the obtained viscous liquid tosylate was used in azidation reaction without any purification. Sodium azide (0.202 g, 3.1 mmol) was added to solution of the obtained tosylate (0.400 g, 1.04 mmol) in DMF and the reaction mixture was stirred for 2 days at 65°C. After extraction of the crude product with CH₂Cl₂/water, the organic layer was dried with anhydrous MgSO₄ and solvent was evaporated by rotary evaporator. The oily product was precipitated in cold water and centrifuged. The yellow product was dried under vacuum.

3.3.3 Functionalization of hydrogels by “Click” reaction

In a typical click reaction, after drying by lyophilization above obtained gel, CuBr (0.156 mmol), PMDETA (0.156 mmol), 2-azidomethyl pyrene (0.104 mmol) and 5 mL of DMSO were placed in a Schlenk tube. The reaction mixture was degassed by three freeze-pump-thaw cycles and stirred at 40°C. After 24 h, the modified hydrogel was placed in deionised water; NH₃ solution and water, consecutively, to remove unreacted reagents, especially CuBr.

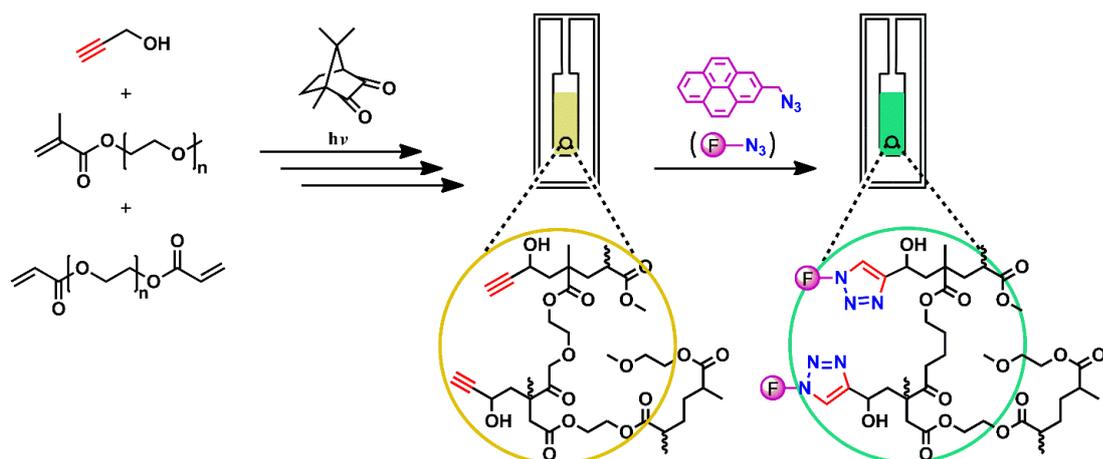


Figure 3.1 : Schematic representation for hydrogel functionalization

3.3.4 Synthesis of azide end-functional polystyrene (PS-N₃)

Copper bromide (24.8 mg, 0.17 mmol), styrene (2 mL, 17 mmol), PMDETA (59.96 mg, 0.35 mmol), and EtBP (31.3 mg, 0.17 mmol) were added to a Schlenk tube, which was then sealed and degassed by three freeze-pump thaw cycles. The mixture was heated and stirred at 110°C in an oil bath. After 3h, the polymerization was ceased by opening the flask and exposing the catalyst to air. The final mixture was diluted in THF and passed through a short neutral alumina column in order to remove copper catalyst. The mixture was concentrated by rotary evaporation and subsequently precipitated in methanol. The precipitated polystyrene was filtered and dried under vacuum. The obtained bromine end-functional polystyrene (8800 g/mol, 0.17 mmol), sodium azide (0.17 mmol) and 3 mL of DMF were added in a flask. The clear homogeneous solution was stirred at room temperature for 24 h. Then, polystyrene was precipitated in methanol, filtered and dried under vacuum.

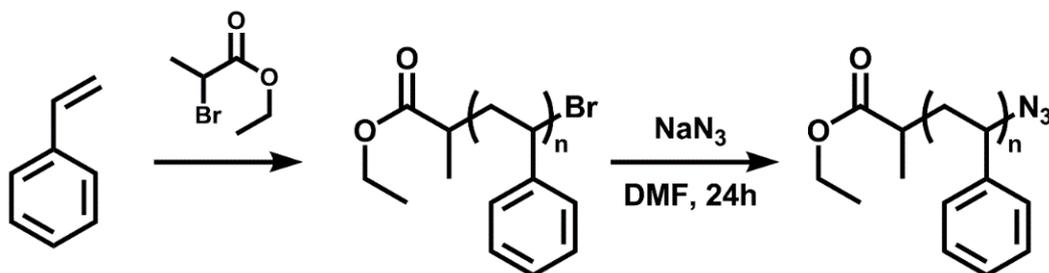


Figure 3.2 : Synthesis of PS-N₃

3.3.5 Preparation of 3-(trimethylsilyl)propargyl alcohol

300 mL, three-necked, round-bottomed flask (equipped with a mechanical stirrer and a thermometer) is fitted with a Claisen adapter on which is mounted a 25 mL pressure-equalizing addition funnel and a reflux condenser. The apparatus is flushed with nitrogen and then charged with 4.87 g (2.0 mol) of magnesium turnings and 100 mL of dry THF. To the stirred suspension is added dropwise 14.95 mL (2.0 mol) of bromoethane over 180 min. while maintaining the temperature at 50°C or less. After complete addition, the gray-green solution is heated at 50°C for 60 min. and then cooled to 5°C on ice. A solution of 4.16 mL (0.72 mol) of propargyl alcohol in 4.2 mL of THF is cautiously added dropwise to the gray suspension over 75 min. while maintaining the temperature at 10°C or less. The addition funnel is rinsed with 2.5 mL of THF and the gray-green suspension is stirred overnight. The resulting solution is cooled to 5°C on ice and the addition funnel is charged with 25.4 mL (2.0 mol) of chlorotrimethylsilane. This is added dropwise to the stirred solution over 60 min. while maintaining the temperature at 25°C or less by external cooling with ice. After complete addition, the mixture is heated to reflux for 120 min. with a heating mantle. The suspension is cooled to 20°C on ice and then 80 mL of 1.4 M aqueous sulfuric acid is cautiously added over 45 min. so that the temperature remains below 45°C. The resulting solution is stirred for 5 min. and then 60 mL of ether is added. Both phases are transferred to a 500 mL separatory funnel and the layers are separated. The aqueous phase is extracted twice with 40 mL portions of ether and all ether layers are individually washed in series with two 100 mL portions of water and once with 80 mL of saturated sodium chloride solution. The combined organic extracts are dried over magnesium sulfate and concentrated by rotary evaporation. The yellow-brown residue is purified by short path distillation to afford 8.2–8.6 g (91–94% yield) of 3-(trimethylsilyl)propargyl alcohol as a clear, colorless liquid, bp 76°C.[142] (Scheme 3.3).

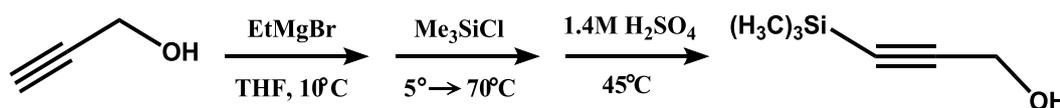


Figure 3.3 : Synthesis of 3-(trimethylsilyl)propargyl alcohol

3.3.6 Preparation of acetylene functional poly(methyl methacrylate) (PMMA-Ac)

MMA (0.963 g, 9.61 mmol), camphorquinone (0.0159 g, 9.61×10^{-2} mmol) and 3-(trimethylsilyl)propargyl alcohol (0.0123 g, 9.61×10^{-2} mmol) were added to a Pyrex tube, which was purged with gaseous nitrogen and then sealed. The mixture was irradiated under the conditions described for hydrogel preparation for 60 min. At the end of the reaction, the final mixture was diluted with THF and subsequently precipitated in methanol. The precipitated polymer was filtered and dried under vacuum ($M_n = 17\,200 \text{ g mol}^{-1}$, $M_w/M_n = 1.65$). A suspension of above obtained polymer (2.89×10^{-2} mmol) was dissolved in THF containing 5% water under an inert atmosphere, and 1M TBAF solution (1.44 mmol) was added. The mixture was stirred for 150 min. at room temperature. The polymer was subsequently precipitated in 10-fold excess of methanol, washed sequentially with MeOH, H₂O, and again with MeOH and finally dried again in vacuum oven.

3.3.7 “Click” coupling of PS-N₃ and PMMA-Ac

In a Pyrex tube, PS-N₃ (300 mg, 0.051 mmol), copper bromide (0.155 mmol), PMDETA (0.155 mmol), alkyne functional PMMA (0.155 mmol) and THF (3 mL) were added. The tube was capped with a septum and purged with nitrogen. The mixture was stirred overnight at room temperature. The product was precipitated in methanol, filtered and dried under vacuum.

4. RESULTS AND DISCUSSION

Synthetic strategy applied in this study is based on the hydrogen abstraction reactions of excited *Type II* photoinitiators from alcohols. In the process, CQ was used as the *Type II* photoinitiator due to its strong absorption in the visible range which does not interfere with that of the components and formed gel. This way, any possible photodegradation of the formed gel by prolonged irradiation time is eliminated. Photoinitiated polymerization of poly(ethylene glycol)methyl ether methacrylate (PEGMA) in the presence of poly(ethylene glycol) diacrylate (PEGDA as cross-linker in DMF at visible range using CQ and propargyl alcohol as photoinitiator and co-initiator, respectively was performed. Since radicals stemming from the hydrogen abstraction from propargyl alcohol by photoexcited CQ are responsible for the initiation, the gels thus formed are expected to possess acetylenic groups in the structure (Figure 4.1).

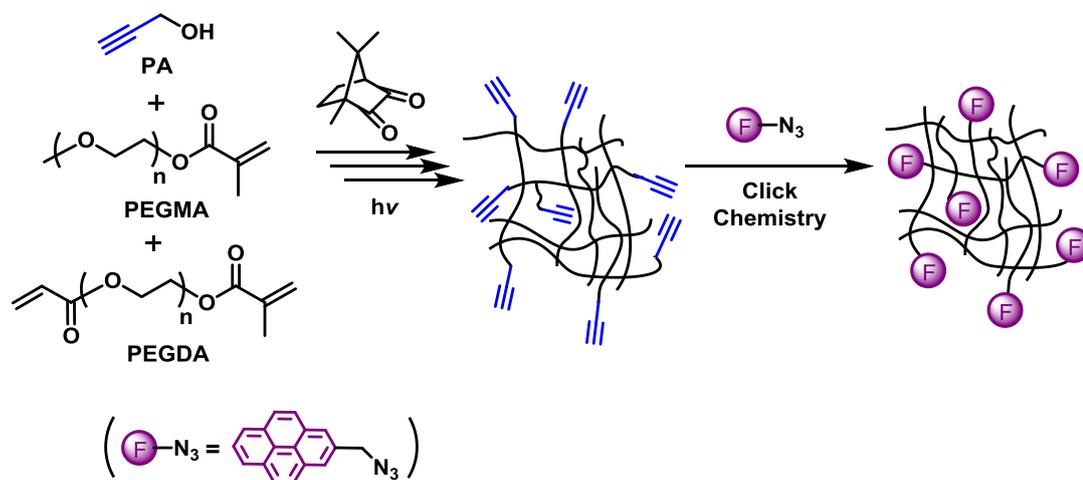


Figure 4.1 : Synthesis of clickable PEG crosslinked hydrogels by photoinitiated free radical polymerization and their functionalization.

In the process, the reactivity of the initiating and propagating radicals towards acetylenic group of the co-initiator should be considered. Although the rate constants for these particular radicals are not known, it is expected that they react predominantly with the acrylate and methacrylate groups. In a related study from the authors' laboratory, it was found that the rate constants for the reaction of

photochemically generated phosphonyl radicals with triple bonds is two orders of magnitude lower than that of double bonds.[145] Another important issue that needs to be considered is the possibility of hydrogen abstraction of the excited CQ from polyether segments of the monomer and cross-linker. It is known that *Type II* photoinitiators are known to undergo hydrogen abstraction with ethers such as poly(ethylene oxide)[146] to form initiating radicals. Although not presented here, such reaction would only increase the cross-linked density of the gels formed and not impede acetylene functionality. Incorporation of acetylenic groups into hydrogels was confirmed by FT-IR spectral analysis. As can be seen from Figure 4.2.a, the stretching band of alkyne groups appear at 2150 cm^{-1} .

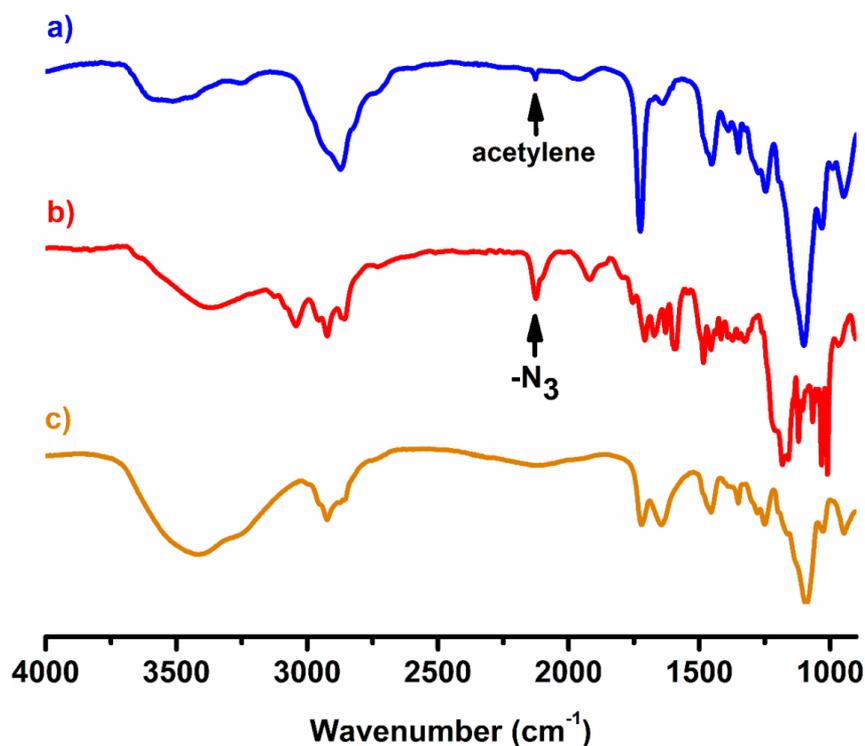


Figure 4.2 : a) FT-IR spectra of the acetylene functional hydrogel b) 2-azidomethyl pyrene and c) functionalized hydrogel via “click” reaction.

For convenience, 2-azidomethyl pyrene (Py-N₃) was selected as the antagonist click component so as to have efficient characterization of cross-linked material because of its attractive fluorescent properties. For this purpose, 1-pyrenemethanol was converted to Py-N₃ by tosylation and subsequent azidation process according to the following reaction (Figure 4.3) as described previously. The post-functionalization of the hydrogel obtained by photopolymerization efficiently proceeded at room temperature with Py-N₃ in the presence of CuBr and PMDETA.

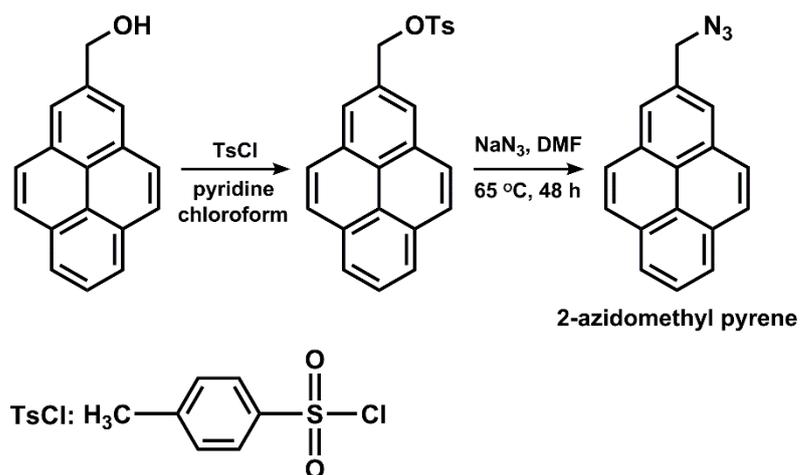


Figure 4.3 : Azidation of 1-pyrenemethanol

The success of the click reaction was confirmed by spectral analysis. As can be seen from the FT-IR spectrum of the click product (Figure 4.2.c) both the azide and alkyne peaks at around 2100 cm^{-1} and 2150 cm^{-1} , respectively disappeared completely. Thus, the applied click reaction was efficient and quantitative for the conversion of alkyne and azides to triazoles. The incorporation of the pyrene group was further supported by fluorescence measurements. As can be seen from Figure 4.4 the fluorescence emission spectra of the hydrogel before and after the click reaction are quite different. The unmodified hydrogel exhibits almost no emission. In complete contrast, the fluorescence emission spectra of the clicked gel displays structured broad excited state and excimer emissions in the range of 400- 600 nm with a maximum at 500 nm.

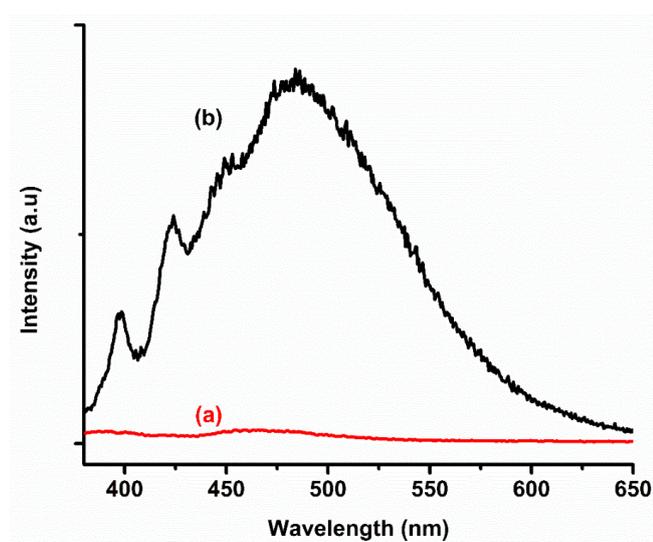


Figure 4.4 : Fluorescence spectra of PEG hydrogels a) before and b) after “click” reaction with Py- N_3 in water.

This behavior is expected since alkyne groups (consequently pyrene groups) are incorporated into the gel randomly during the photochemical process. While isolated pyrene chromophores contribute to the excited state emission, the strong interactions of the excited pyrene moieties with those in their ground states in the close proximity cause excimer emission around 480 nm. Similar fluorescence behavior resulting from the restraints imposed by the polymeric structures with different topologies was previously shown.[147-149]

The fluorescence property of the clicked hydrogel was also confirmed by a visual observation of the emission recorded with irradiation from a UV lamp at 366 nm (Figure 4.5).

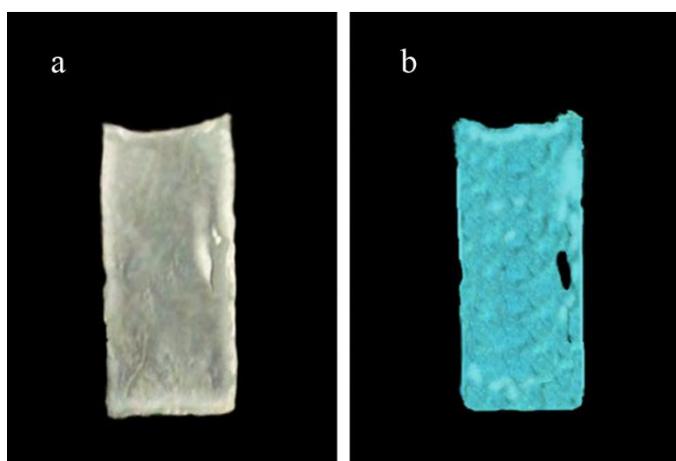


Figure 4.5 : Photographs of clickable PEG hydrogels before (a) and after (b) click reaction with 2-azidomethyl pyrene under irradiation with a 366-nm UV lamp.

In order to demonstrate the versatility and efficiency of the described photochemical method in synthetic polymer chemistry, we have performed experiments in block copolymer formation. Thus, a block copolymer formation was attempted between acetylene end-functionalized poly(methyl methacrylate) (PMMA-Ac) and azide end-functionalized polystyrene (PS-N₃). PMMA-Ac was prepared *Type II* photoinitiation in a manner similar to that described for hydrogels except that the co-initiator, propargyl alcohol was protected. This was necessitated in order to obtain polymers with high alkyne functionality. Any reaction of the initiating and propagating radicals with the alkyne groups would lead to the formation of polymers without click functionality. Thus, polymerization of MMA using CQ and 3-trimethylsilyl-2-propyn-1-ol as photoinitiator and co-initiator, respectively resulted in the formation of polymers with protected acetylene groups. The obtained polymer was

subsequently deprotected by treatment with TBAF in THF using the established procedure to yield PMMA-Ac (Figure 4.6).

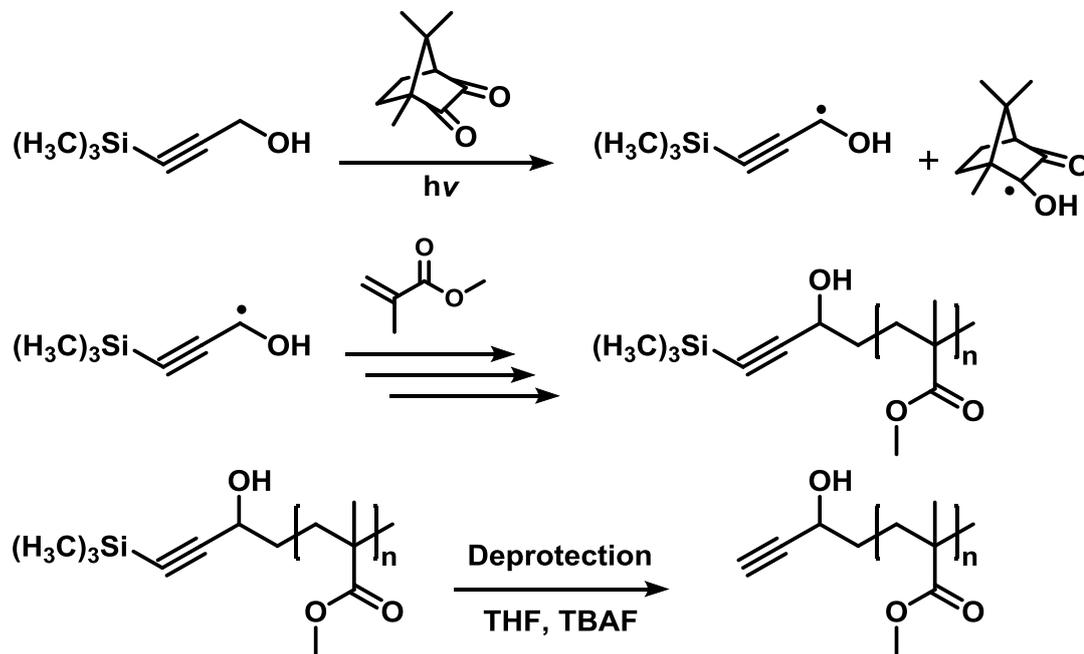


Figure 4.6 : Photoinduced synthesis of protected PMMA and its deprotection

The $^1\text{H-NMR}$ analysis of the products before and after deprotection clearly confirms successful obtainment of PMMA-Ac (Figure 4.7). The antagonist click polymer click component, namely PS- N_3 was prepared by the usual ATRP followed by azidation processes.

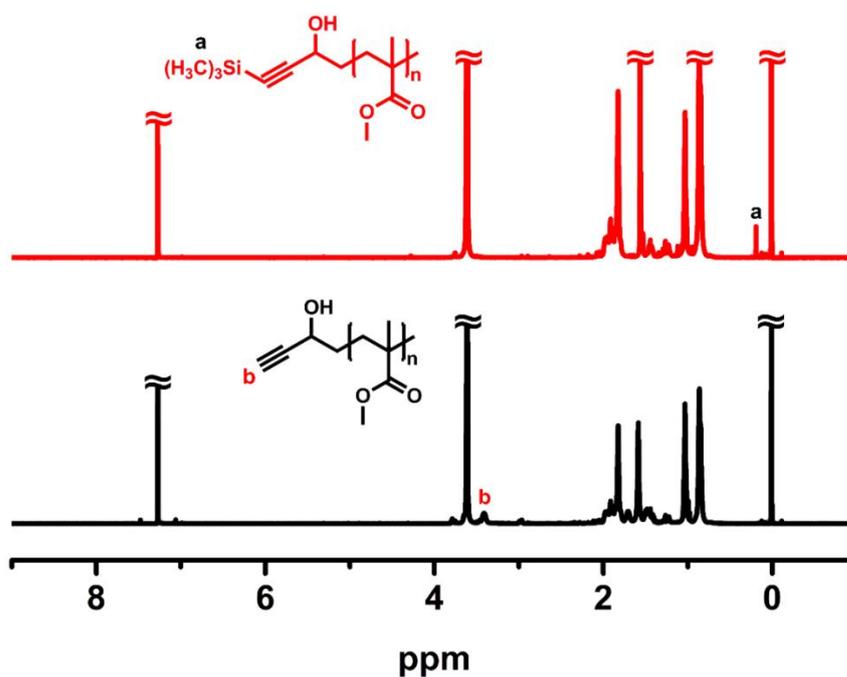


Figure 4.7 : $^1\text{H NMR}$ spectra of protected and deprotected PMMA.

The “click” reaction between PMMA-Ac and PS-N₃ was performed under similar experimental conditions as with the hydrogel (Figure 4.8). The formation of block copolymer was evidenced by spectral and GPC analyses (Figure 4.10). The ¹H NMR spectrum of block copolymer obtained by “click” reaction indicated characteristic peaks of both precursors (Figure 4.8).

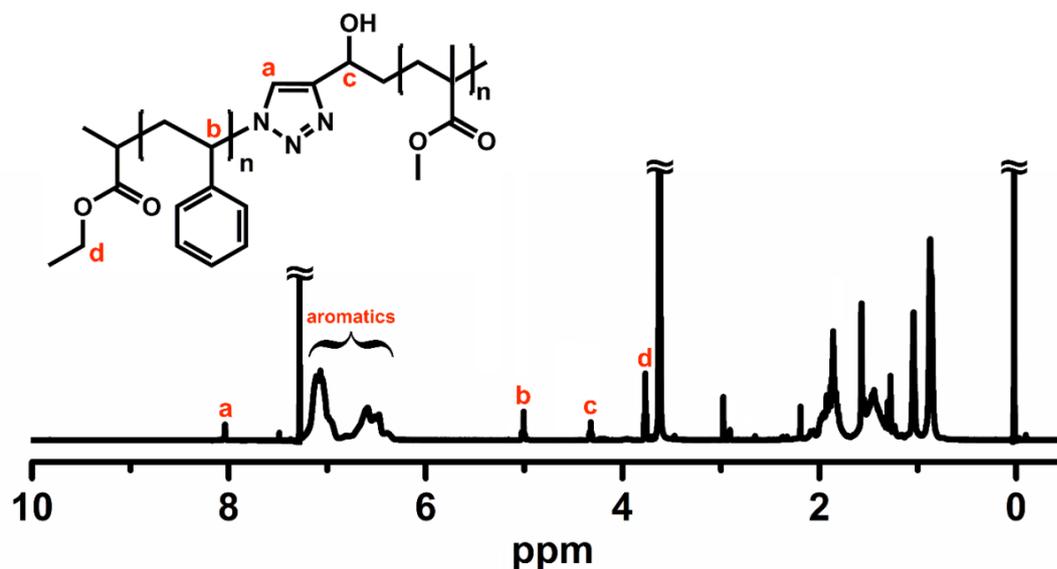


Figure 4.8 : ¹H NMR spectra of PS-*b*-PMMA

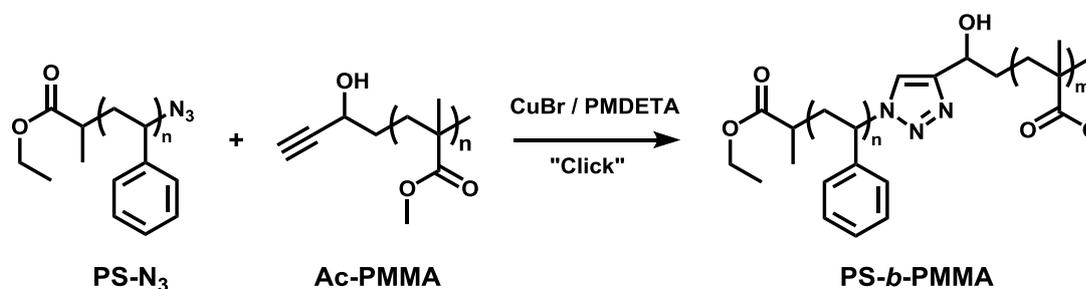


Figure 4.9 : “Click” reaction between PS and PMMA

In Figure 4.10, the GPC traces of the “click” precursor polymers as well as of the resulting block copolymer were shown. It should be pointed out that the PMMA-Ac has a relatively broader molecular weight distribution due to the nature of the photopolymerization process. During the photolysis, polymers with different chains lengths are formed. In the chromatogram of the block copolymer, however, a clear shift toward higher molecular weight region was observed. Notably, the peaks corresponding to the precursor polymers disappeared completely. The molecular

weight characteristics of the initial polymers and the resulting block copolymer collected in Table 4.1 also confirm the successful click process.

Table 4.1 : Molecular weight characteristics of PS-N₃, PMMA and PS-*b*-PMMA

Polymers	M_n (gmol ⁻¹)	M_n/M_w
PS-N ₃	8800	1.38
PMMA-Ac	17 200	1.65
PS- <i>b</i> -PMMA	27 300	1.84

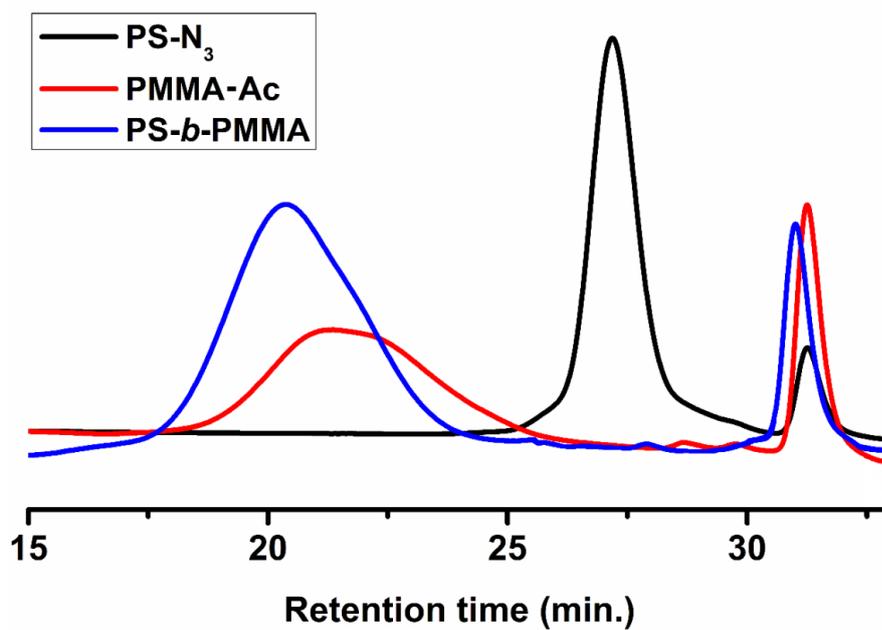


Figure 4.10 : GPC traces of PS-N₃, PMMA-Ac and PS-*b*-PMMA.

5. CONCLUSION

In conclusion, a mild and highly versatile photochemical method for the preparation of clickable macromolecular structures, i.e., hydrogels and linear polymers via hydrogen abstraction type photoinitiation using aromatic carbonyl compounds such as CQ in conjunction with functional co-initiators has been developed. The subsequent model click reactions for functionalization of hydrogels and block copolymer formation clearly confirms the success of the protocol which may easily be implemented in the biological and material sciences.

REFERENCES

- [1] Langer, R. and Tirrell, D. A., 2004. Designing Materials for Biology and Medicine. *Nature*, **428** 487-492.
- [2] Stevens, M. M., Flynn, N. T., Wang, C., Tirrell, D. A. and Langer, R., 2004. Coiled-Coil Peptide-Based Assembly of Gold Nanoparticles. *Advanced Materials*, **16** 915-918.
- [3] Rocha, S., Cardoso, I., Boerner, H., Pereira, M. C., Saraiva, M. J. and Coelho, M., 2009. Design and Biological Activity of Beta-Sheet Breaker Peptide Conjugates. *Biochemical and Biophysical Research Communications*, **380** 397-401.
- [4] Prasath, R. A., Gokmen, M. T., Espeel, P. and Du Prez, F. E., 2010. Thiol-Ene and Thiol-Yne Chemistry in Microfluidics: A Straightforward Method Towards Macroporous and Nonporous Functional Polymer Beads. *Polymer Chemistry*, **1** 685-692.
- [5] Lin, D. M. and Che, J. F., 2010. Hydrogel-Modified Bio-Electrodes. *Progress in Chemistry*, **22** 1195-1202.
- [6] Naghash, H. J. and Okay, O., 1996. Formation and Structure of Polyacrylamide Gels. *Journal of Applied Polymer Science*, **60** 971-979.
- [7] Oh, J. K., Siegwart, D. J., Lee, H.-i., Sherwood, G., Peteanu, L., Hollinger, J. O., Kataoka, K. and Matyjaszewski, K., 2007. Biodegradable Nanogels Prepared by Atom Transfer Radical Polymerization as Potential Drug Delivery Carriers: Synthesis, Biodegradation, in Vitro Release, and Bioconjugation. *Journal of the American Chemical Society*, **129** 5939-5945.
- [8] Hamidi, M., Azadi, A. and Rafiei, P., 2008. Hydrogel Nanoparticles in Drug Delivery. *Advanced Drug Delivery Reviews*, **60** 1638-1649.
- [9] Oh, J. K., Drumright, R., Siegwart, D. J. and Matyjaszewski, K., 2008. The Development of Microgels/Nanogels for Drug Delivery Applications. *Progress in Polymer Science*, **33** 448-477.
- [10] Funke, W., Okay, O. and Joos-Muller, B., 1998. Microgels - Intramolecularly Crosslinked Macromolecules with a Globular Structure. *Microencapsulation - Microgels - Iniferters*, **136** 139-234.
- [11] Jha, A. K., Hule, R. A., Jiao, T., Teller, S. S., Clifton, R. J., Duncan, R. L., Pochan, D. J. and Jia, X., 2009. Structural Analysis and Mechanical Characterization of Hyaluronic Acid-Based Doubly Cross-Linked Networks. *Macromolecules*, **42** 537-546.
- [12] Ossipov, D. A., Piskounova, S., Varghese, O. P. and Hilborn, J., 2010. Functionalization of Hyaluronic Acid with Chemoselective Groups Via a Disulfide-Based Protection Strategy for in Situ Formation of Mechanically Stable Hydrogels. *Biomacromolecules*, **11** 2247-2254.
- [13] Dhanasingh, A., Salber, J., Moeller, M. and Groll, J., 2010. Tailored Hyaluronic Acid Hydrogels through Hydrophilic Prepolymer Cross-Linkers. *Soft Matter*, **6** 618-629.

- [14] Hiemstra, C., van der Aa, L. J., Zhong, Z. Y., Dijkstra, P. J. and Feijen, J., 2007. Rapidly in Situ-Forming Degradable Hydrogels from Dextran Thiols through Michael Addition. *Biomacromolecules*, **8** 1548-1556.
- [15] Altintas, O., Hizal, G. and Tunca, U., 2006. Abc-Type Hetero-Arm Star Terpolymers through "Click" Chemistry. *Journal of Polymer Science Part a-Polymer Chemistry*, **44** 5699-5707.
- [16] Altintas, O., Yankul, B., Hizal, G. and Tunca, U., 2007. One-Pot Preparation of 3-Miktoarm Star Terpolymers Via Click 3+2 Reaction. *Journal of Polymer Science Part a-Polymer Chemistry*, **45** 3588-3598.
- [17] 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-+.
- [18] Yilmaz, G., Kahveci, M. U. and Yagci, Y., 2011. A One Pot, One Step Method for the Preparation of Clickable Hydrogels by Photoinitiated Polymerization. *Macromolecular Rapid Communications*, **32** 1906-1909.
- [19] Odaci, D., Gacal, B. N., Gacal, B., Timur, S. and Yagci, Y., 2009. Fluorescence Sensing of Glucose Using Glucose Oxidase Modified by Pva-Pyrene Prepared Via "Click" Chemistry. *Biomacromolecules*, **10** 2928-2934.
- [20] Durmaz, Y. Y., Karagoz, B., Bicak, N., Demirkol, D. O., Yalcinkaya, E. E., Timur, S. and Yagci, Y., 2011. Modification of Polydivinylbenzene Microspheres by a Hydrobromination/Click-Chemistry Protocol and Their Protein-Adsorption Properties. *Macromolecular Bioscience*, **11** 141-150.
- [21] Okcu, S. S., Durmaz, Y. Y. and Yagci, Y., 2010. Synthesis and Characterization of Telechelic Block Co-Polymers by Combination of Atom Transfer Radical Polymerization and Click Chemistry Processes. *Designed Monomers and Polymers*, **13** 459-472.
- [22] Tasdelen, M. A. and Yagci, Y., 2013. Light-Induced Click Reactions. *Angewandte Chemie-International Edition*, **52** 5930-5938.
- [23] Durmaz, Y. Y., Sangermano, M. and Yagci, Y., 2010. Surface Modification of Uv-Cured Epoxy Resins by Click Chemistry. *Journal of Polymer Science Part a-Polymer Chemistry*, **48** 2862-2868.
- [24] Tasdelen, M. A., Yilmaz, G., Iskin, B. and Yagci, Y., 2012. Photoinduced Free Radical Promoted Copper(I)-Catalyzed Click Chemistry for Macromolecular Syntheses. *Macromolecules*, **45** 56-61.
- [25] Tasdelen, M. A. and Yagci, Y., 2010. Light-Induced Copper(I)-Catalyzed Click Chemistry. *Tetrahedron Letters*, **51** 6945-6947.
- [26] Malkoch, M., Schleicher, K., Drockenmuller, E., Hawker, C. J., Russell, T. P., Wu, P. and Fokin, V. V., 2005. Structurally Diverse Dendritic Libraries: A Highly Efficient Functionalization Approach Using Click Chemistry. *Macromolecules*, **38** 3663-3678.
- [27] Kiskan, B., Demiray, G. and Yagci, Y., 2008. Thermally Curable Polyvinyl Chloride Via Click Chemistry. *Journal of Polymer Science Part a-Polymer Chemistry*, **46** 3512-3518.
- [28] Ergin, M., Kiskan, B., Gacal, B. and Yagci, Y., 2007. Thermally Curable Polystyrene Via Click Chemistry. *Macromolecules*, **40** 4724-4727.

- [29] **Kukut, M., Kiskan, B. and Yagci, Y.,** 2009. Self-Curable Benzoxazine Functional Polybutadienes Synthesized by Click Chemistry. *Designed Monomers and Polymers*, **12** 167-176.
- [30] **Tasdelen, M. A., Van Camp, W., Goethals, E., Dubois, P., Du Prez, F. and Yagci, Y.,** 2008. Polytetrahydrofuran/Clay Nanocomposites by in Situ Polymerization and "Click" Chemistry Processes. *Macromolecules*, **41** 6035-6040.
- [31] **Iskin, B., Yilmaz, G. and Yagci, Y.,** 2011. Abc Type Miktoarm Star Copolymers through Combination of Controlled Polymerization Techniques with Thiol-Ene and Azide-Alkyne Click Reactions. *Journal of Polymer Science Part a-Polymer Chemistry*, **49** 2417-2422.
- [32] **Iskin, B., Yilmaz, G. and Yagci, Y.,** 2011. Synthesis of Abc Type Miktoarm Star Copolymers by Triple Click Chemistry. *Polymer Chemistry*, **2** 2865-2871.
- [33] **Temel, G., Aydogan, B., Arsu, N. and Yagci, Y.,** 2009. Synthesis and Characterization of One-Component Polymeric Photoinitiator by Simultaneous Double Click Reactions and Its Use in Photoinduced Free Radical Polymerization. *Macromolecules*, **42** 6098-6106.
- [34] **Barson, C. A., Bevington, J. C. and Huckerby, T. N.,** 1991. Reactivities Towards the Benzoyloxy Radical of Some Acetylenic-Compounds When Used in the Polymerization of Methyl-Methacrylate. *Polymer Bulletin*, **25** 83-86.
- [35] **Tasdelen, M. A. and Yagci, Y.,** 2011. Photochemical Methods for the Preparation of Complex Linear and Cross-Linked Macromolecular Structures. *Australian Journal of Chemistry*, **64** 982-991.
- [36] **Yagci, Y.,** 2012. New Photoinitiating Systems Designed for Polymer/Inorganic Hybrid Nanocoatings. *Journal of Coatings Technology and Research*, **9** 125-134.
- [37] **Yagci, Y., Jockusch, S. and Turro, N. J.,** 2010. Photoinitiated Polymerization: Advances, Challenges, and Opportunities. *Macromolecules*, **43** 6245-6260.
- [38] **Tasdelen, M. A., Demirel, A. L. and Yagci, Y.,** 2007. Poly(Propylene Imine) Dendrimers as Hydrogen Donor in Type Ii Photoinitiated Free Radical Polymerization. *European Polymer Journal*, **43** 4423-4430.
- [39] **Altinkok, C., Uyar, T., Tasdelen, M. A. and Yagci, Y.,** 2011. In Situ Synthesis of Polymer/Clay Nanocomposites by Type Ii Photoinitiated Free Radical Polymerization. *Journal of Polymer Science Part a-Polymer Chemistry*, **49** 3658-3663.
- [40] **Yilmaz, G., Acik, G. and Yagci, Y.,** 2012. Counteranion Sensitization Approach to Photoinitiated Free Radical Polymerization. *Macromolecules*, **45** 2219-2224.
- [41] **Kumbaraci, V., Aydogan, B., Talinli, N. and Yagci, Y.,** 2012. Naphthodioxinone-1,3-Benzodioxole as Photochemically Masked One-Component Type Ii Photoinitiator for Free Radical Polymerization. *Journal of Polymer Science Part a-Polymer Chemistry*, **50** 2612-2618.
- [42] **Tasdelen, M. A., Kiskan, B. and Yagci, Y.,** 2006. Photoinitiated Free Radical Polymerization Using Benzoxazines as Hydrogen Donors. *Macromolecular Rapid Communications*, **27** 1539-1544.

- [43] Tasdelen, M. A., Kumbaraci, V., Talinli, N. and Yagci, Y., 2006. Photochemically Masked Benzophenone: Photoinitiated Free Radical Polymerization by Using Benzodioxinone. *Polymer*, **47** 7611-7614.
- [44] Gam-Derouich, S., Lamouri, A., Redeuilh, C., Decorse, P., Maurel, F., Carbonnier, B., Beyazit, S., Yilmaz, G., Yagci, Y. and Chehimi, M. M., 2012. Diazonium Salt-Derived 4-(Dimethylamino)Phenyl Groups as Hydrogen Donors in Surface-Confined Radical Photopolymerization for Bioactive Poly(2-Hydroxyethyl Methacrylate) Grafts. *Langmuir*, **28** 8035-8045.
- [45] Yilmaz, G., Tuzun, A. and Yagci, Y., 2010. Thioxanthone-Carbazole as a Visible Light Photoinitiator for Free Radical Polymerization. *Journal of Polymer Science Part a-Polymer Chemistry*, **48** 5120-5125.
- [46] Taskin, O. S., Yilmaz, G., Tasdelen, M. A. and Yagci, Y., 2014. Photoinduced Reverse Atom Transfer Radical Polymerization of Methyl Methacrylate Using Camphorquinone/Benzhydrol System. *Polymer International*, **63** 902-907.
- [47] Esen, D. S., Temel, G., Balta, D. K., Allonas, X. and Arsu, N., 2014. One-Component Thioxanthone Acetic Acid Derivative Photoinitiator for Free Radical Polymerization. *Photochemistry and Photobiology*, **90** 463-469.
- [48] Balta, D. K., Arsu, N., Yagci, Y., Sundaresan, A. K., Jockusch, S. and Turro, N. J., 2011. Mechanism of Photoinitiated Free Radical Polymerization by Thioxanthone-Anthracene in the Presence of Air. *Macromolecules*, **44** 2531-2535.
- [49] Akat, H., Gacal, B., Balta, D. K., Arsu, N. and Yagci, Y., 2010. Poly(Ethylene Glycol)-Thioxanthone Prepared by Diels-Alder Click Chemistry as One-Component Polymeric Photoinitiator for Aqueous Free-Radical Polymerization. *Journal of Polymer Science Part a-Polymer Chemistry*, **48** 2109-2114.
- [50] Temel, G., Arsu, N. and Yagci, Y., 2006. Polymeric Side Chain Thioxanthone Photoinitiator for Free Radical Polymerization. *Polymer Bulletin*, **57** 51-56.
- [51] Balta, D. K., Arsu, N., Yagci, Y., Jockusch, S. and Turro, N. J., 2007. Thioxanthone-Anthracene: A New Photoinitiator for Free Radical Polymerization in the Presence of Oxygen. *Macromolecules*, **40** 4138-4141.
- [52] Tunc, D. and Yagci, Y., 2011. Thioxanthone-Ethylcarbazole as a Soluble Visible Light Photoinitiator for Free Radical and Free Radical Promoted Cationic Polymerizations. *Polymer Chemistry*, **2** 2557-2563.
- [53] Yilmaz, G., Beyazit, S. and Yagci, Y., 2011. Visible Light Induced Free Radical Promoted Cationic Polymerization Using Thioxanthone Derivatives. *Journal of Polymer Science Part a-Polymer Chemistry*, **49** 1591-1596.
- [54] Tunc, D., Gacal, B. and Yagci, Y., 2013. An Amphiphatic Thioxanthone-Anthracene Photoinitiator for Free-Radical Polymerization. *Turkish Journal of Chemistry*, **37** 525-537.
- [55] Scott, T. F., Kloxin, C. J., Forman, D. L., McLeod, R. R. and Bowman, C. N., 2011. Principles of Voxel Refinement in Optical Direct Write Lithography. *Journal of Materials Chemistry*, **21** 14150-14155.

- [56] Hageman, H. J., 1989. Oxygen-Inhibition in the Photoinitiated Free-Radical Polymerization and Crosslinking of Acrylates. *Abstracts of Papers of the American Chemical Society*, **197** 116-PMSE.
- [57] Tilley, M., Pappas, B., Pappas, S. P., Yagci, Y., Schnabel, W. and Thomas, J. K., 1989. Laser Flash-Photolysis Studies on Iodonium and Sulfonium Salts. *Journal of Imaging Science*, **33** 62-64.
- [58] Funt, B. L. and Collins, E., 1958. Formation of Block Polymers of Butyl Acrylate with Styrene and Vinyl Pyridine. *Journal of Polymer Science*, **28** 359-364.
- [59] Davidson, R. S., 1993. The Chemistry of Photoinitiators - Some Recent Developments. *Journal of Photochemistry and Photobiology a-Chemistry*, **73** 81-96.
- [60] Gruber, H. F., 1992. Photoinitiators for Free-Radical Polymerization. *Progress in Polymer Science*, **17** 953-1044.
- [61] Hageman, H. J., 1985. Photoinitiators for Free-Radical Polymerization. *Progress in Organic Coatings*, **13** 123-150.
- [62] Monroe, B. M. and Weed, G. C., 1993. Photoinitiators for Free-Radical-Initiated Photoimaging Systems. *Chemical Reviews*, **93** 435-448.
- [63] Davidson, R. S., 1983. The Chemistry of Excited Complexes - a Survey of Reactions. *Advances in Physical Organic Chemistry*, **19** 1-130.
- [64] Ledwith, A., Bosley, J. A. and Purbrick, M. D., 1978. Exciplex Interactions in Photoinitiation of Polymerization by Fluorenone-Amine Systems. *Journal of the Oil & Colour Chemists Association*, **61** 95-104.
- [65] Ledwith, A. and Purbrick, M. D., 1973. Initiation of Free-Radical Polymerization by Photoinduced Electron-Transfer Processes. *Polymer*, **14** 521-522.
- [66] Jauk, S. and Liska, R., 2008. Photoinitiators with Functional Groups 9: New Derivatives of Covalently Linked Benzophenone-Amine Based Photoinitiators. *Journal of Macromolecular Science Part a-Pure and Applied Chemistry*, **45** 804-810.
- [67] Catalina, F., Tercero, J. M., Peinado, C., Sastre, R., Mateo, J. L. and Allen, N. S., 1989. Photochemistry and Photopolymerization Study on 2-Acetoxy and Methyl-2-Acetoxy Derivatives of Thioxanthone as Photoinitiators. *Journal of Photochemistry and Photobiology a-Chemistry*, **50** 249-258.
- [68] Peinado, C., Catalina, F., Corrales, T., Sastre, R., Amatguerri, F. and Allen, N. S., 1992. Synthesis of Novel 2-(3'-Dialkylaminopropoxy)-Thioxanthone Derivatives - Photochemistry and Evaluation as Photoinitiators of Butyl Acrylate Polymerization. *European Polymer Journal*, **28** 1315-1320.
- [69] Balta, D. K., Temel, G., Aydin, M. and Arsu, N., 2010. Thioxanthone Based Water-Soluble Photoinitiators for Acrylamide Photopolymerization. *European Polymer Journal*, **46** 1374-1379.
- [70] Temel, G. and Arsu, N., 2007. 2-Methylol-Thioxanthone as a Free Radical Polymerization Initiator. *Journal of Photochemistry and Photobiology a-Chemistry*, **191** 149-152.
- [71] Karasu, F., Arsu, N., Jockusch, S. and Turro, N. J., 2009. Mechanistic Studies of Photoinitiated Free Radical Polymerization Using a Bifunctional Thioxanthone Acetic Acid Derivative as Photoinitiator. *Macromolecules*, **42** 7318-7323.

- [72] Balta, D. K., Karasu, F., Aydin, M. and Arsu, N., 2007. The Effect of the Amine Structure on Photoinitiated Free Radical Polymerization of Methyl Methacrylate Using Bisketocoumarin Dye. *Progress in Organic Coatings*, **59** 274-277.
- [73] Polykarpov, A. Y., Hassoon, S. and Neckers, D. C., 1996. Tetramethylammonium Tetraorganylborates as Coinitiators with 5,7-Diiodo-3-Butoxy-6-Fluorone in Visible Light Polymerization of Acrylates. *Macromolecules*, **29** 8274-8276.
- [74] Shi, J. M., Zhang, X. P. and Neckers, D. C., 1992. Xanthenes - Fluorone Derivatives .1. *Journal of Organic Chemistry*, **57** 4418-4421.
- [75] Shi, J. M., Zhang, X. P. and Neckers, D. C., 1993. Xanthenes - Fluorone Derivatives .2. *Tetrahedron Letters*, **34** 6013-6016.
- [76] Tanabe, T., Torresfilho, A. and Neckers, D. C., 1995. Visible-Light Photopolymerization - Synthesis of New Fluorone Dyes and Photopolymerization of Acrylic-Monomers Using Them. *Journal of Polymer Science Part a-Polymer Chemistry*, **33** 1691-1703.
- [77] Valdesaguilera, O., Pathak, C. P., Shi, J., Watson, D. and Neckers, D. C., 1992. Photopolymerization Studies Using Visible-Light Photoinitiators. *Macromolecules*, **25** 541-547.
- [78] Yao, H. W., Huang, M. J., Chen, Z. Y., Hou, L. S. and Gan, F. X., 2002. Optimization of Two-Monomer-Based Photopolymer Used for Holographic Recording. *Materials Letters*, **56** 3-8.
- [79] Turro, N. J., Cherry, W. R., Mirbach, M. J., Mirbach, M. F. and Ramamurthy, V., 1978. Direct Photo-Chemical, Oxygen Catalyzed and Temperature-Dependent Population of Triplet-States - Applications to Photochemistry of Cyclic Azoalkanes. *Molecular Photochemistry*, **9** 111-118.
- [80] Stone, F. S. and Liberman, R., 1987. *Journal of Radiation Curing*, **14**.
- [81] Miller, H. C., 1989. *Proc. Radiation Tech. Conf., Florence*, 429.
- [82] Decker, C. and Moussa, K., 1991. Photopolymerization of Multifunctional Monomers .4. Acrylates with Carbamate or Oxazolidone Structure. *European Polymer Journal*, **27** 403-411.
- [83] Decker, C. and Moussa, K., 1988. A New Method for Monitoring Ultra-Fast Photopolymerizations by Real-Time Infrared (Rtir) Spectroscopy. *Makromolekulare Chemie-Macromolecular Chemistry and Physics*, **189** 2381-2394.
- [84] Decker, C., 1990. Real-Time Monitoring of Polymerization Quantum Yields. *Macromolecules*, **23** 5217-5220.
- [85] Koleske, J. V., 2002. *Radiation Curing of Coatings, ASTM International, West Conshohocken*.
- [86] Roffey, C. G., 1982. *Photopolymerization of Surface Coatings*. J. Wiley: New York, USA, .
- [87] Arsu, N., Onen, A. and Yagci, Y., 1996. Photoinitiated Zwitterionic Polymerization of Alkyl Cyanoacrylates by Pyridinium Salts. *Macromolecules*, **29** 8973-8974.
- [88] Onen, A., Arsu, N. and Yagci, Y., 1999. Photoinitiated Polymerization of Ethyl Cyanoacrylate by Phosphonium Salts. *Angewandte Makromolekulare Chemie*, **264** 56-59.
- [89] Kasapoglu, F., Aydin, M., Arsu, N. and Yagci, Y., 2003. Photoinitiated Polymerization of Methyl Methacrylate by Phenacyl Type Salts.

- Journal of Photochemistry and Photobiology a-Chemistry*, **159** 151-159.
- [90] **Tanabe, M. and Manners, I.**, 2004. Photolytic Living Anionic Ring-Opening Polymerization (Rop) of Silicon-Bridged 1 Ferrocenophanes Via an Iron-Cyclopentadienyl Bond Cleavage Mechanism. *Journal of the American Chemical Society*, **126** 11434-11435.
- [91] **Yagci, Y. and Schnabel, W.**, 1988. Light-Induced Cationic Polymerization. *Makromolekulare Chemie-Macromolecular Symposia*, **13-4** 161-174.
- [92] **Crivello, J. V. and Lam, J. H. W.**, 1977. Diaryliodonium Salts - New Class of Photo-Initiators for Cationic Polymerization. *Macromolecules*, **10** 1307-1315.
- [93] **Crivello, J. V. and Lam, J. H. W.**, 1979. Photoinitiated Cationic Polymerization with Triarylsulfonium Salts. *Journal of Polymer Science Part a-Polymer Chemistry*, **17** 977-999.
- [94] **Denizligil, S., Yagci, Y. and McArdle, C.**, 1995. Photochemically and Thermally-Induced Radical Promoted Cationic Polymerization Using an Allylic Sulfonium Salt. *Polymer*, **36** 3093-3098.
- [95] **Yagci, Y., Kornowski, A. and Schnabel, W.**, 1992. N-Alkoxy-Pyridinium and N-Alkoxy-Quinolinium Salts as Initiators for Cationic Photopolymerizations. *Journal of Polymer Science Part a-Polymer Chemistry*, **30** 1987-1991.
- [96] **Yagci, Y. and Endo, T.**, 1997. N-Benzyl and N-Alkoxy Pyridinium Salts as Thermal and Photochemical Initiators for Cationic Polymerization. In *Polymer Synthesis / Polymer Catalysis*, Springer-Verlag Berlin, Berlin.
- [97] **Yagci, Y., Lukac, I. and Schnabel, W.**, 1993. Photosensitized Cationic Polymerization Using N-Ethoxy-2-Methylpyridinium Hexafluorophosphate. *Polymer*, **34** 1130-1133.
- [98] **Kasapoglu, F. and Yagci, Y.**, 2002. Photo Sensitized Cationic Polymerization of Cyclohexene Oxide Using a Phenacylanilinium Salt. *Macromolecular Rapid Communications*, **23** 567-570.
- [99] **Lee, K. Y. and Mooney, D. J.**, 2001. Hydrogels for Tissue Engineering. *Chemical Reviews*, **101** 1869-1879.
- [100] **Mann, B. K.**, 2003. Biologic Gels in Tissue Engineering. *Clinics in Plastic Surgery*, **30** 601-+.
- [101] **Mather, M. L. and Tomlins, P. E.**, 2010. Hydrogels in Regenerative Medicine: Towards Understanding Structure-Function Relationships. *Regenerative Medicine*, **5** 809-821.
- [102] **Lin, C. C. and Metters, A. T.**, 2006. Hydrogels in Controlled Release Formulations: Network Design and Mathematical Modeling. *Advanced Drug Delivery Reviews*, **58** 1379-1408.
- [103] **di Lena, F. and Matyjaszewski, K.**, 2010. Transition Metal Catalysts for Controlled Radical Polymerization. *Progress in Polymer Science*, **35** 959-1021.
- [104] **Tang, W. and Matyjaszewski, K.**, 2006. Effect of Ligand Structure on Activation Rate Constants in Atrp. *Macromolecules*, **39** 4953-4959.
- [105] **Tang, W., Kwak, Y., Braunecker, W., Tsarevsky, N. V., Coote, M. L. and Matyjaszewski, K.**, 2008. Understanding Atom Transfer Radical Polymerization: Effect of Ligand and Initiator Structures on the

- Equilibrium Constants. *Journal of the American Chemical Society*, **130** 10702-10713.
- [106] **Tang, W., Tsarevsky, N. V. and Matyjaszewski, K.**, 2006. Determination of Equilibrium Constants for Atom Transfer Radical Polymerization. *Journal of the American Chemical Society*, **128** 1598-1604.
- [107] **Matyjaszewski, K., Paik, H. J., Zhou, P. and Diamanti, S. J.**, 2001. Determination of Activation and Deactivation Rate Constants of Model Compounds in Atom Transfer Radical Polymerization. *Macromolecules*, **34** 5125-5131.
- [108] **Fischer, H.**, 2001. The Persistent Radical Effect: A Principle for Selective Radical Reactions and Living Radical Polymerizations. *Chemical Reviews*, **101** 3581-3610.
- [109] **Harrisson, S., Rourke, J. P. and Haddleton, D. M.**, 2002. C-13 Kinetic Isotope Effects in the Copper(I)-Mediated Living Radical Polymerization of Methyl Methacrylate. *Chemical Communications*, 1470-1471.
- [110] **Tsarevsky, N. V. and Matyjaszewski, K.**, 2007. "Green" Atom Transfer Radical Polymerization: From Process Design to Preparation of Well-Defined Environmentally Friendly Polymeric Materials. *Chemical Reviews*, **107** 2270-2299.
- [111] **Shen, Y. Q., Tang, H. D. and Ding, S. J.**, 2004. Catalyst Separation in Atom Transfer Radical Polymerization. *Progress in Polymer Science*, **29** 1053-1078.
- [112] **Ma, I. Y., Lobb, E. J., Billingham, N. C., Armes, S. P., Lewis, A. L., Lloyd, A. W. and Salvage, J.**, 2002. Synthesis of Biocompatible Polymers. 1. Homopolymerization of 2-Methacryloyloxyethyl Phosphorylcholine Via Atrp in Protic Solvents: An Optimization Study. *Macromolecules*, **35** 9306-9314.
- [113] **Matyjaszewski, K., Pintauer, T. and Gaynor, S.**, 2000. Removal of Copper-Based Catalyst in Atom Transfer Radical Polymerization Using Ion Exchange Resins. *Macromolecules*, **33** 1476-1478.
- [114] **Munirasu, S., Deshpande, A. and Baskaran, D.**, 2008. Hydrated Clay for Catalyst Removal in Copper Mediated Atom Transfer Radical Polymerization(a). *Macromolecular Rapid Communications*, **29** 1538-1543.
- [115] **Kasko, A. M., Heintz, A. M. and Pugh, C.**, 1998. The Effect of Molecular Architecture on the Thermotropic Behavior of Poly 11-(4'-Cyanophenyl-4"-Phenoxy)Undecyl Acrylate and Its Relation to Polydispersity. *Macromolecules*, **31** 256-271.
- [116] **Kickelbick, G., Paik, H. J. and Matyjaszewski, K.**, 1999. Immobilization of the Copper Catalyst in Atom Transfer Radical Polymerization. *Macromolecules*, **32** 2941-2947.
- [117] **Floudas, G., Pispas, S. and Hadjichristidis, N.**, 1999. Functionalized Block Copolymers: Synthesis, Structure, and Dynamics. *Abstracts of Papers of the American Chemical Society*, **218** U580-U580.
- [118] **Davis, K. A. and Matyjaszewski, K.**, 2002. Statistical, Gradient, Block, and Graft Copolymers by Controlled/Living Radical Polymerizations. *Statistical, Gradient, Block and Graft Copolymers by Controlled/Living Radical Polymerizations*, **159** 1-169.

- [119] Quemener, D., Davis, T. P., Barner-Kowollik, C. and Stenzel, M. H., 2006. Raft and Click Chemistry: A Versatile Approach to Well-Defined Block Copolymers. *Chemical Communications*, 5051-5053.
- [120] Nischang, I., Brueggemann, O. and Teasdale, I., 2011. Facile, Single-Step Preparation of Versatile, High-Surface-Area, Hierarchically Structured Hybrid Materials. *Angewandte Chemie-International Edition*, **50** 4592-4596.
- [121] Adzima, B. J., Tao, Y. H., Kloxin, C. J., DeForest, C. A., Anseth, K. S. and Bowman, C. N., 2011. Spatial and Temporal Control of the Alkyne-Azide Cycloaddition by Photoinitiated Cu(I) Reduction. *Nature Chemistry*, **3** 256-259.
- [122] Barner-Kowollik, C., Du Prez, F. E., Espeel, P., Hawker, C. J., Junkers, T., Schlaad, H. and Van Camp, W., 2011. "Clicking" Polymers or Just Efficient Linking: What Is the Difference? *Angewandte Chemie-International Edition*, **50** 60-62.
- [123] Campos, L. M., Meinel, I., Guino, R. G., Schierhorn, M., Gupta, N., Stucky, G. D. and Hawker, C. J., 2008. Highly Versatile and Robust Materials for Soft Imprint Lithography Based on Thiol-Ene Click Chemistry. *Advanced Materials*, **20** 3728-+.
- [124] Fairbanks, B. D., Scott, T. F., Kloxin, C. J., Anseth, K. S. and Bowman, C. N., 2009. Thiol-Yne Photopolymerizations: Novel Mechanism, Kinetics, and Step-Growth Formation of Highly Cross-Linked Networks. *Macromolecules*, **42** 211-217.
- [125] Fairbanks, B. D., Sims, E. A., Anseth, K. S. and Bowman, C. N., 2010. Reaction Rates and Mechanisms for Radical, Photoinitiated Addition of Thiols to Alkynes, and Implications for Thiol-Yne Photopolymerizations and Click Reactions. *Macromolecules*, **43** 4113-4119.
- [126] Hoogenboom, R., 2010. Thiol-Yne Chemistry: A Powerful Tool for Creating Highly Functional Materials. *Angewandte Chemie-International Edition*, **49** 3415-3417.
- [127] Lowe, A. B., Hoyle, C. E. and Bowman, C. N., 2010. Thiol-Yne Click Chemistry: A Powerful and Versatile Methodology for Materials Synthesis. *Journal of Materials Chemistry*, **20** 4745-4750.
- [128] Tasdelen, M. A., 2011. Diels-Alder "Click" Reactions: Recent Applications in Polymer and Material Science. *Polymer Chemistry*, **2** 2133-2145.
- [129] Nicolaou, K. C., Snyder, S. A., Montagnon, T. and Vassilikogiannakis, G., 2002. The Diels-Alder Reaction in Total Synthesis. *Angewandte Chemie-International Edition*, **41** 1668-1698.
- [130] Adzima, B. J., Kloxin, C. J., DeForest, C. A., Anseth, K. S. and Bowman, C. N., 2012. 3d Photofixation Lithography in Diels-Alder Networks. *Macromolecular Rapid Communications*, **33** 2092-2096.
- [131] Adzima, B. J., Aguirre, H. A., Kloxin, C. J., Scott, T. F. and Bowman, C. N., 2008. Rheological and Chemical Analysis of Reverse Gelation in a Covalently Cross-Linked Diels-Alder Polymer Network. *Macromolecules*, **41** 9112-9117.
- [132] Chen, X. X., Dam, M. A., Ono, K., Mal, A., Shen, H. B., Nutt, S. R., Sheran, K. and Wudl, F., 2002. A Thermally Re-Mendable Cross-Linked Polymeric Material. *Science*, **295** 1698-1702.

- [133] Liu, Y.-L. and Chuo, T.-W., 2013. Self-Healing Polymers Based on Thermally Reversible Diels-Alder Chemistry. *Polymer Chemistry*, **4** 2194-2205.
- [134] Tornøe, C. W., Christensen, C. and Meldal, M., 2002. Peptidotriazoles on Solid Phase: 1,2,3-Triazoles by Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of Terminal Alkynes to Azides. *Journal of Organic Chemistry*, **67** 3057-3064.
- [135] Rostovtsev, V. V., Green, L. G., Fokin, V. V. and Sharpless, K. B., 2002. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective "Ligation" of Azides and Terminal Alkynes. *Angewandte Chemie-International Edition*, **41** 2596-+.
- [136] Heusgen, R., 1968. Mechanism of 1,3-Dipolar Cycloadditions. Reply. *The Journal of Organic Chemistry*, **33** 2291-2297.
- [137] Huisgen, R., 1989. Kinetics and Reaction-Mechanisms - Selected Examples from the Experience of 40 Years. *Pure and Applied Chemistry*, **61** 613-628.
- [138] Iha, R. K., Wooley, K. L., Nystrom, A. M., Burke, D. J., Kade, M. J. and Hawker, C. J., 2009. Applications of Orthogonal "Click" Chemistries in the Synthesis of Functional Soft Materials. *Chemical Reviews*, **109** 5620-5686.
- [139] Dichtel, W. R., Miljanic, O. S., Spruell, J. M., Heath, J. R. and Stoddart, J. F., 2006. Efficient Templated Synthesis of Donor - Acceptor Rotaxanes Using Click Chemistry. *Journal of the American Chemical Society*, **128** 10388-10390.
- [140] Meldal, M., 2008. Polymer "Clicking" by CuAAC Reactions. *Macromolecular Rapid Communications*, **29** 1016-1051.
- [141] Boisselier, E., Diallo, A. K., Salmon, L., Ruiz, J. and Astruc, D., 2008. Gold Nanoparticles Synthesis and Stabilization Via New "Clicked" Polyethyleneglycol Dendrimers. *Chemical Communications*, 4819-4821.
- [142] Jones, T. K. and Denmark, S. E., 1986. Stereospecific Reduction of Propargyl Alcohols: (E)-3-Trimethylsilyl-2-Propen-1-ol. *Organic Syntheses*, **64** 182.
- [143] Kabalka, G. W., Varma, M., Varma, R. S., Srivastava, P. C. and Knapp, F. F., 1986. Tosylation of Alcohols. *Journal of Organic Chemistry*, **51** 2386-2388.
- [144] Parrish, B., Breitenkamp, R. B. and Emrick, T., 2005. Peg- and Peptide-Grafted Aliphatic Polyesters by Click Chemistry. *Journal of the American Chemical Society*, **127** 7404-7410.
- [145] Ciftci, M., Kahveci, M. U., Yagci, Y., Allonas, X., Ley, C. and Tar, H., 2012. A Simple Route to Synthesis of Branched and Cross-Linked Polymers with Clickable Moieties by Photopolymerization. *Chemical Communications*, **48** 10252-10254.
- [146] Tasdelen, M. A., Moszner, N. and Yagci, Y., 2009. The Use of Poly(Ethylene Oxide) as Hydrogen Donor in Type II Photoinitiated Free Radical Polymerization. *Polymer Bulletin*, **63** 173-183.
- [147] Karagoz, B., Durmaz, Y. Y., Gacal, B. N., Bicak, N. and Yagci, Y., 2009. Functionalization of Poly(Divinylbenzene) Microspheres by Combination of Hydrobromination and Click Chemistry Processes: A Model Study. *Designed Monomers and Polymers*, **12** 511-522.

- [148] **Gacal, B. N., Koz, B., Gacal, B., Kiskan, B., Erdogan, M. and Yagci, Y.,** 2009. Pyrene Functional Poly(Vinyl Alcohol) by "Click" Chemistry. *Journal of Polymer Science Part a-Polymer Chemistry*, **47** 1317-1326.
- [149] **Toiserkani, H., Yilmaz, G., Yagci, Y. and Torun, L.,** 2010. Functionalization of Polysulfones by Click Chemistry. *Macromolecular Chemistry and Physics*, **211** 2389-2395.

CURRICULUM VITAE



Name Surname: Eljesa MURTEZI

Place and Date of Birth: Skopje – 18.12.1986

Address: Istanbul Technical University, Faculty of Science and Letters, Department of Chemistry, 34469, Maslak, Istanbul / TURKEY

E-Mail: eljesa_m@hotmail.com

B.Sc.: Ss. Cyril and Methodius University of Skopje, Faculty of Natural Sciences and Mathematics, 1000, Skopje, Republic of Macedonia

PUBLICATIONS/PRESENTATIONS ON THE THESIS

- **Murtezi E.**, Yagci Y., 2014: Photoinduced *In Situ* ATRP and “Click” Reactions for the Synthesis of Block Copolymers, *Submitted to ACS Macro Letters*, June
- Doran S., **Murtezi E.**, Barlas F.B., Timur S., Yagci Y., 2014: One Pot Photo-Induced Sequential CuAAC and Thiol-ene Click Strategy for Bio-active Macromolecular Synthesis, *Macromolecules*, March 2014
- **Murtezi E.**, Ciftci M., Yagci Y., 2014; Synthesis of Clickable Hydrogels and Linear Polymers by *Type II* Photoinitiation, *Submitted to Polymer International*, Mach 2014
- Poster Presentation in the “44th WORLD CHEMISTRY CONGRESS”, Istanbul, Turkey, 2014, 11-16 August