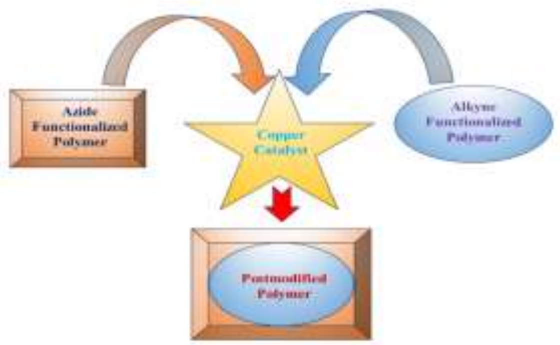
A REVIEW ON APPLICATIONS OF COPPER CATALYZED AZIDE ALKYNE CLICK CHEMISTRY IN POSTMODIFICATION OF POLYMERS

Abstract

In recent years, there has been a lot of interest in the progress of polymers through modification into graft copolymers. Click chemistry was used to synthesize graft copolymers, mostly through the Copper catalyzed Azide-Alkyne cycloaddition process, in order to get a high yield of product quickly. For postmodification, the clickable group on the polymer backbone was grafted by different polymer or chains. This succinct review emphasizes the most recent research on grafted copolymers produced by copper catalyzed azide alkyne click chemistry.

Keywords: Click chemistry, Copper catalyzed Azide-Alkyne cycloaddition, Graft polymer.

Graphical Abstract:



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I. INTRODUCTION

Postmodification of polymers is an interdisciplinary phenomenon encompassing materials science, engineering, physics, and other fields in order to teach the best experience of existing qualities to desired end-goal applications. Graft polymer synthesis typically entails two steps- polymerization and their grafting [1]. The purpose of postmodification of polymers molecular structure is often to improve its response, thermal durability, natural sensitivity and reactivity, connection, physical impact response, mobility, stiffness, and other properties [2]. In general, innovative postmodification originate from highly efficient and effective click reactions that are aided by easily available multifunctionalized monomers and effective catalysts [3].

The term "click chemistry” refers by Sharpless and his coworkers to a class of nearly perfect reactions that are highly efficient with atom economy and stereospecific. Click reactions generally requires simple conditions, easily accessible reactants and generates harmless by-products which can be easily removed [4]. Further, Sharpless and Meldal reported a new Huisgen-type [3+2] azide-alkyne cycloaddition in 2002. In this reaction $CuSO_4$/sodium ascorbate used as a catalyst and resulted in the high yield production of 1, 4-disubstituted 1, 2, 3-triazoles [5-6]. According to study of W. H. Binder and his colleague, CuAAC has been widely used in the grafting of polymers, due to its superior properties. CuAAC has been developed into an efficient polymerization technology while still meeting the aforementioned criteria for an organic reaction to evolve into a polymerization reaction. Fig. 1 depicts the reaction mechanism of copper catalyzed azide-alkyne Cycloaddition [7].

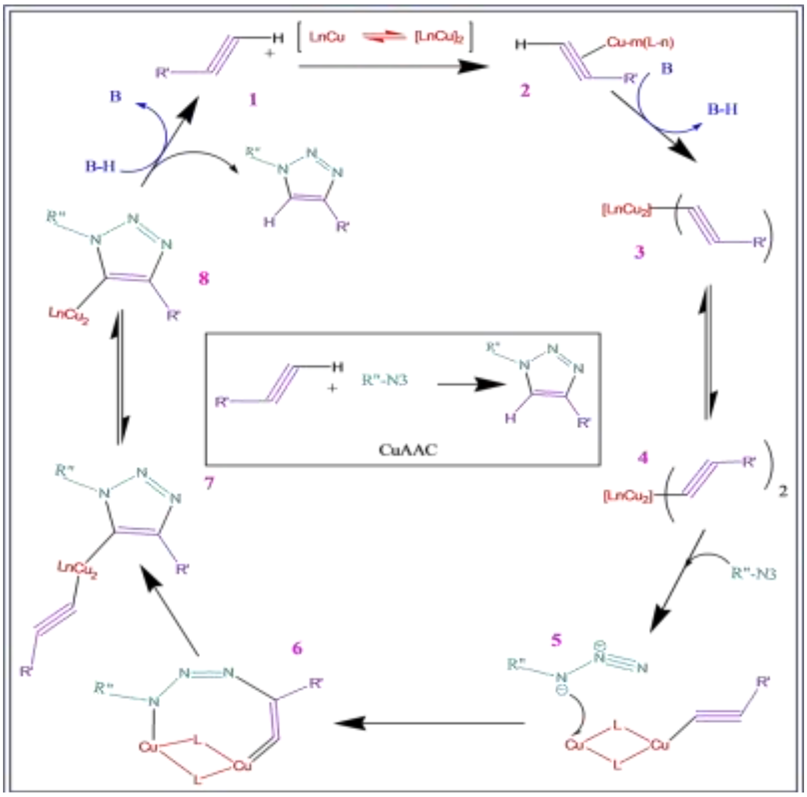


Figure 1: Reaction Mechanism of CuAAC Click Reaction.

II. ABBREVIATIONS

β-CD	β-cyclodextrin
(β-CD)-g- HPEG	(β-cyclodextrin)-graft-Methyl allylpolyoxyethylene
CuAAC	Copper catalyzed Azide-Alkyne Cycloaddition
CuNPs	Copper nanoparticles
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
HMTETA	Hexamethylenetetramine
HA-FA	Hyaluronic acid- Ferulic acid
HA-FA-g-HEG	Hyaluronic acid- Ferulic acid-graft- Hexa(ethylene glycol)
HEG	Hexa(ethylene glycol)
HPEG	Methyl AllylPolyoxyenthylene
HMTETA	Hexamethyltriethylenetetramine
P3HT	Poly(3-hexylthiophene)
PCL	Polycaprolactone
PCL-b-PDMA	Polycaprolactone-block-poly(2-dimethylaminoethyl methacrylate)
PDMA	Poly(2-dimethylaminoethyl methacrylate)
PECH	Poly(epichlorohydrin)
PECH-g-PMMA	Poly(epichlorohydrin)-graft-Poly(methylmethacrylate)
PEG	Poly(ethylene glycol)
PEG-g-PPX	Poly(ethylene glycol))-graft-Poly(p-xylylenes)
PEO	Poly(ethylene oxide)
PEtOx	poly(2-ethyl-2-oxazoline)
P(GMA)	Poly(Glycidyl methacrylate)
PHEA	Poly(2-hydroxyethyl acrylate)
PHEA-g-PEG	Poly(2-hydroxyethylacrylate)-graft-Poly(ethylene glycol)
Plina	Poly(linoleic acid)
PLina-g-PCL	Poly(linoleic acid)-g-poly(caprolactone)
PMDETA	N,N,N′,N’,N″pentamethyldiethylenetriamine
P(MeOx-co-PentOx	Poly(2-methyl-2-oxazoline-co-2-pentyl-2-oxazoline)
P(MeOx-co-PentOx)-g-PEtOx	Poly(2-methyl-2-oxazoline-co-2-pentyl-2 oxazoline)- graft-poly (2-ethyl-2-oxazoline)
PMMA	Poly(methylmethacrylate)
PNIPAAm	Poly(n-isopropylacrylamide)
PNIPAAm-g-PPX	Poly(n-isopropylacrylamide)-graft-Poly(p-xylylenes)
PPA	Poly (propargyl 2-ylidene-acetate)
PPO	Poly(propylene oxide)
PPO-g-PVA	poly(propyleneoxide)-graft-Poly(vinyl alcohol)
PPT	Poly(thiophene)

PPX	Poly(p-xylylenes)
PSB	Poly(sulfobetaine methacrylate)
PSB-g-PPX	Poly(sulfobetaine methacrylate) -graft-Poly(p-xylylenes)
PSf	Polysulfone
PSf-g- PDMA	Polysulfone-graft-poly(2dimethylaminoethyl methacrylate)
PSf-g-PNIPAAm	Polysulfone-graft- Poly(n isopropylacrylamide)
PT-g-(PCL-b-PDMAEMA	Polythiophene-graft-poly(caprolactone-block-dimethylaminoethyl methacrylate)
PT-g-PEO	Poly(thiophene)-graft-poly(ethylene oxide)
PT-g-P3HT	Poly(thiophene)-graft-poly(3hexylthiophene)
PT-g-PMMA	Poly(thiophene)-graft poly(methylmethacrylate)
PVA	Poly(vinyl alcohol)
PVC	Polyvinyl chloride
PVC-g-PCL	Polyvinyl chloride-graft- Polycaprolactone
PVC-g-PMMA	Polyvinylchloride-graft- poly(methylmethacrylate)
TPOM	tetrakis (2-propynyloxymethyl)-methane

III. LITERATURE REVIEW

In order to create grafted polymers, A. E. Masucci and his colleagues developed a versatile method for side chain engineering. Grafted copolymers were produced by different alkynyl PEO, PMMA, and P3HT side chains conjugate with azido PT backbones via CuAAC click reactions. The grafting-to technique was used to create the PT-g-PEO, PT-g-PMMA and PT-g-P3HT. Following postmodification, nanoprecipitation techniques were utilized to convert into nanoparticles. These grafted copolymer architectures can enhance the fluorescence of polymer nanoparticles. Additionally, this gives the potential to serve as materials for various therapies, sensors, and imaging applications [8].

P. Chen and his coworkers utilize the CuAAC to conjugate azido PSB, PEG and PNIPAAm on substrates of alkynyl PPX through chemical vapor deposition. It has enhanced the PSB, PEG, and PNIPAAm-modified surfaces ability to resist cellular and platelet adherence. According to their research, using grafted polymers to create antifouling surfaces on a range of substrates is an easy way to create surfaces for use in immunoassay, biosensor, biomaterial, and other diagnostic applications [9].

By varying the amount of succinic-acid substitution, T. Nishimura and another researcher created the amphiphilic grafted copolymers through CuAAC. This grafted polymer was consisted of succinic-acid-modified (PPO-g-PVA) with a range of varied main-chain persistence lengths. UV or visible light is not absorbed by this grafted copolymer, which means there is no spectroscopic absorbance interference between the membrane proteins and the surfaces of the discs. As a result, succinic-acid-modified (PPO-g-PVA) grafted copolymer nanodiscs might be useful as a cutting-edge tool for understanding the work of proteins membrane [10].

According to research by H. Salehi and his colleagues, using azido PSf with alkynyl PNIPAAm synthesized the amphiphilic PSf-g-PNIPAAm via CuAAC. PSf-g-PNIPAAm used for the production of thermo-responsive thin film composite-forward osmosis membranes [11]. Similar to this, azido PSf with alkynyl PDMA created the hydrophilic PSf-g-PDMA via CuAAC. PSf-g-PDMA used for the manufacture of pH-responsive thin film composite-forward osmosis membranes [12]. Both grafted copolymers were characterized highly porous, hydrophilic.

U. Haldar and his coworkers constructed graft copolymer by click chemistry. Azido PT as the backbone conjugated with alkynyl PCL-b-PDMAEMA through CuAAC click reaction. PT-g-(PCL-b-PDMAEMA) are extremely pH responsive, water soluble, and exhibit pH-dependent aggregation, forming micelles, vesicles, and multivesicular aggregates as the pH is raised from 3 to 7 to 10. For the creation of next-generation bioelectronic, opto-electronic, and energy storage devices, the organic mixed electronic and ionic conductivity property of their grafted copolymer was particularly intriguing [13].

M. Saletti and his colleagues developed a click reactions crosslinking technique to obtain cross-linked HA derivatives for use in the production of hydrogels. Alkynyl functionalized HA-FA coupled with Azido functionalized HEG via CuAAC were quickly crosslinked. The shear-thinning ratio of HA-FA-g-HEG is totally within the range of a healthy synovial fluid shear-thinning ratio (70-250), making it appear to be a potential treatment for osteoarticular diseases. They demonstrated the perfect biocompatibility of the HA-FA grafted copolymers [14].

The PLina-g-PCL grafted copolymers were developed by S. Alli using azido PLina and alkynyl PCL. CuAAC click reactions enabled the production of PLina-g-PCL in large quantities and with high molecular weights. By adopting this technique, graft copolymers can be produced quickly and efficiently. This approach is particularly useful for preparing PLina with functional groupings. These results and the biocompatibility of PLina and biodegradability of PCL were used to promote the utilization of PLina-g-PCL grafted copolymers in the biomedical field [15].

A novel monovinyl β-CD monomer is used to create polycarboxylate superplasticizers, β-CD grafted on the end of the side chain, according to B. Li's research. As the first attempted to combine the steric hindrance effects of polyoxyethylene and β-CD during the synthesis of polycarboxylate superplasticizer. (β-CD)-g- HPEG is created by grafting azido (β-CD) on the Alkynyl polyoxyethylene (HPEG) via a CuAAC click reaction [16].

B. Savaş and his colleagues used a "click" chemistry to graft terminally Alkynyl PMMA to azido PECH in order to produce the PECH-g-PMMA comb-type graft copolymers via CuAAC click reaction. Through the use of polymers containing PECH and PMMA units, this work can give well-characterized materials with a variety of biomedical application possibilities [17]. Similar to this, they created the PVC-PMMA grafted copolymer by using a CuAAC to graft azido PVC to terminally alkynyl PMMA [18]. Further, T. Öztürk's research indicates that CuAAC was used to make PVC-g-PCL brush-type graft copolymers utilizing alkynyl PVC and terminally azido PCL. FT-IR, 1H-NMR, SEM, TGA, and GPC studies were used to characterize this graft copolymer [19].

Through post-modifications of block copolymers, P. Shang and associates synthesized hydrogel. In this work, azido mPEG block copolymer was grafted with the alkynyl P(GMA) block copolymer and TPOM via CuAAC. This hydrogel itself was responsive to temperature and was also used for repairing tissue injuries [20].

CuAAC was used by S. Nagane and his colleagues to postmodify azido co-polyester with alkynyl phenyl acetylene and ethynyl-4-nitrobenzene. Stress-strain measurements were used to characterize the postmodified polyesters and compared to a similar azido co-polyester. The cross-linked polymers showed lower percentage elongation at break and higher tensile strength and Young's modulus [21]. Postmodified PHEA-g-PEG was created by L. Xiao and associates through grafting the azido PEG side chain using the CuAAC click reaction onto the alkynyl PHEA portion of the backbone. The AFM image revealed the shapes of cylinders, spheres, and "beads on a string" belonging to the random distribution of PHEA-g-PEG and PEG. While the GPC and 1H NMR data confirmed that the grafting density was 100% [22].

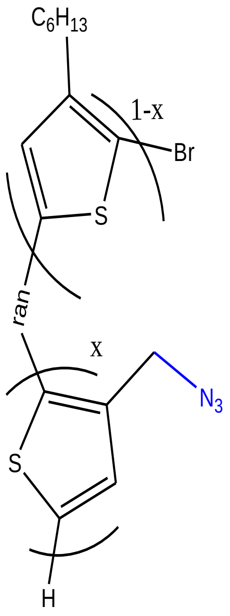
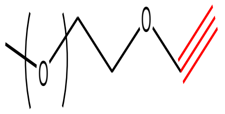
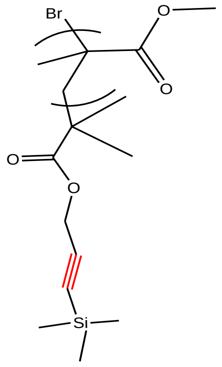
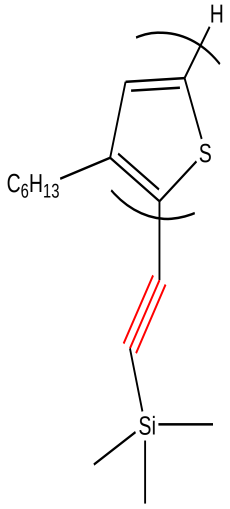
Li and colleagues used CuAAC to post-modify alkynyl-functionalized PPA with different azido compounds, including benzyl azide and 1-azido-2,3,4,5,6-pentafluorobenzene, among others. It was established that the CuAAC reaction to PPA is a highly successful method for post-modification. Also, it has demonstrated good functional group tolerance with a broad substrate scope and practically quantitative conversions (90%) [23].

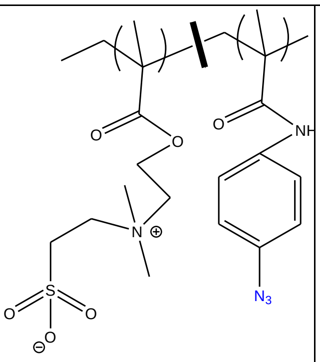
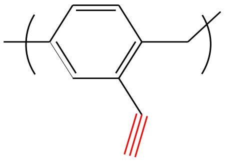
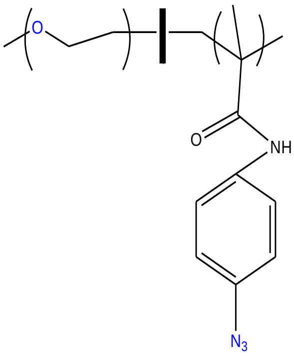
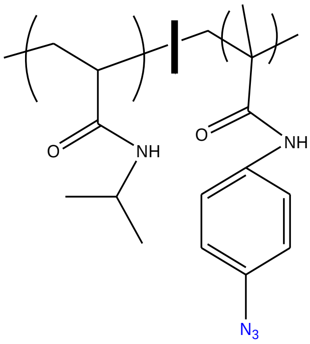
Glaive and colleagues showed how to synthesize P(MeOx-co-PentOx)-g-PEtOx through alkynyl functionalized PEtOx combined with azido P(MeOx-co-PentOx) via CuAAC. This family of hydrophilic and biocompatible copolymers has the potential to be used as bioreactors in the biomedical area due to its self-assembling characteristics [24].

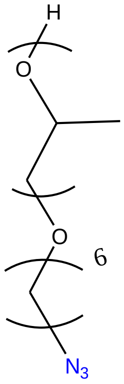
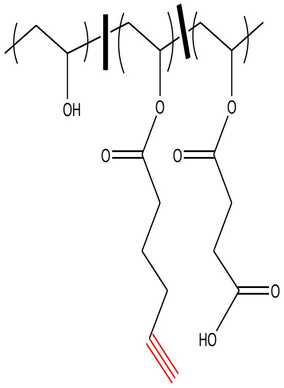
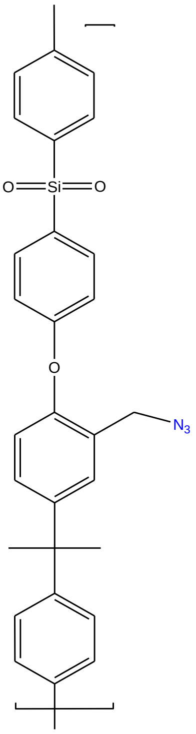
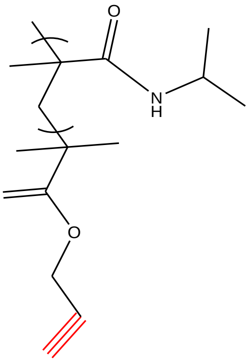
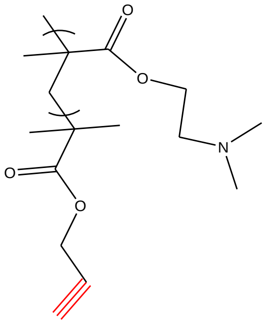
Table 1: Mostly Used Catalyst, Base and Solvent for Cuaac Click Reactions

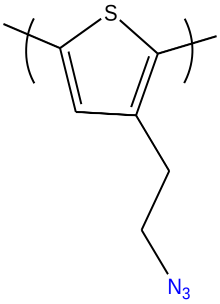
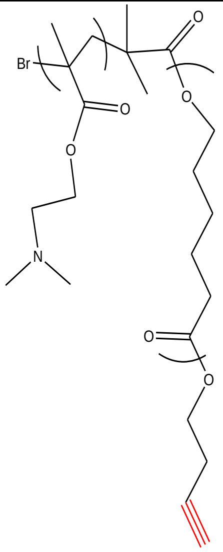
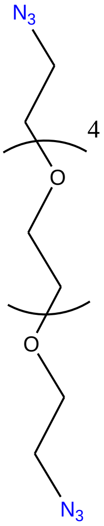
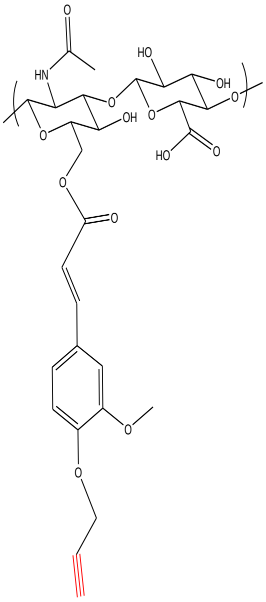
Catalyst	Base	Solvent	Ref.
CuBr	PMDETA	Tetrahydrofuran (THF)	[8]-[24]
CuCl	HMTETA	DMSO	
CuSO4.5H2O	Sodium ascorbate	DMF	
CuNPs		Deionized water tert-butanol: water (1:1)	

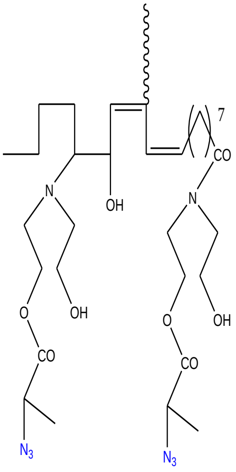
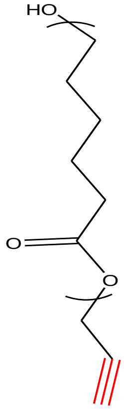
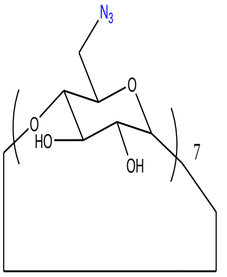
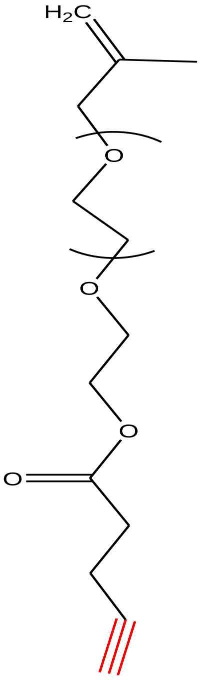
Table 2: Overview of Copper Catalysed Click reactions in Grafted Copolymers

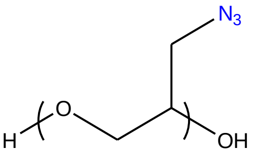
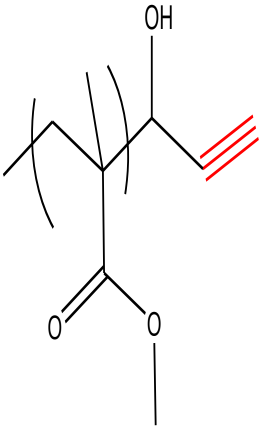
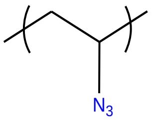
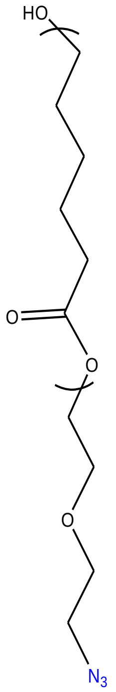
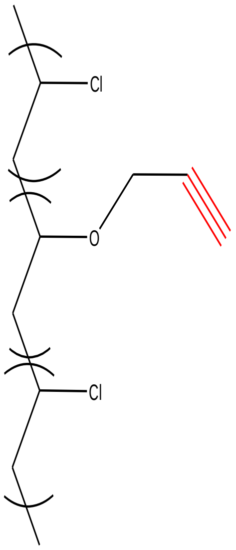
Sr. No.	Clickable groups		Catalyst/ Conditions	Grafted polymer	Ref.
	Azide	Alkyne			
1	PT 	PEO 	Cu(I)Br/ PMDETA/ THF/65°C/ 16hr	PT-g- PEO	[8]
		PMMA 		PT-g- PMMA	
		P3HT 		PT-g- P3HT	
2	PSB			PSB-g-	[9]

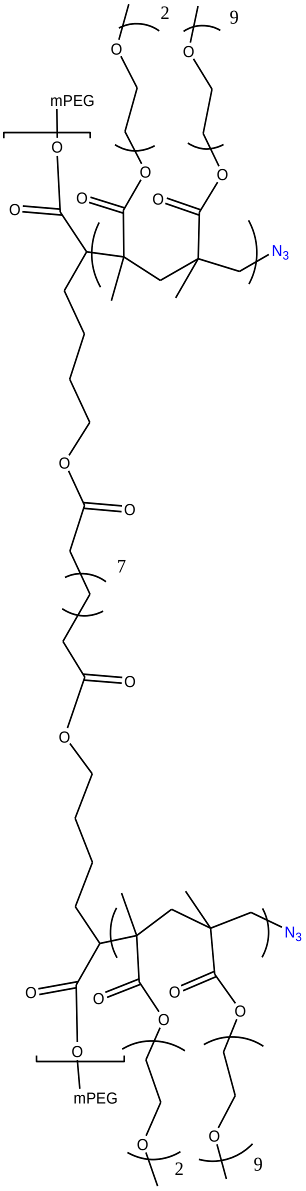
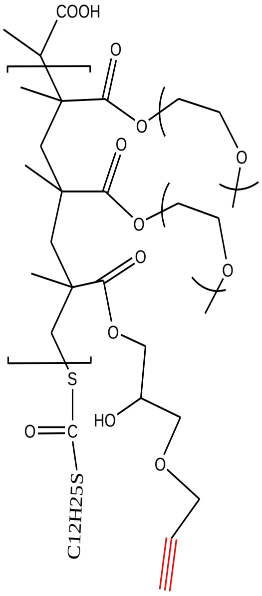
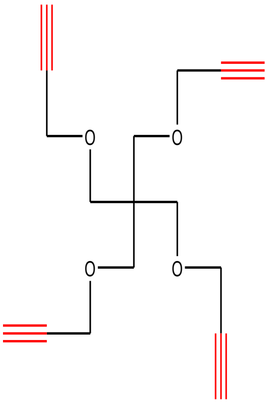
		PPX 	Copper (II) 300ulphate/ Sodium ascorbate/ Deionized water/ r.t./8hr	PPX	
	PEG 			PEG-g-PPX	
	PNIPAAm 			PNIPA-g-PPX	
3	PPO	PVA	Cu(I)Br/ PMDETA/ DMSO/	PPO-g-(PVA-COOH)	[10]

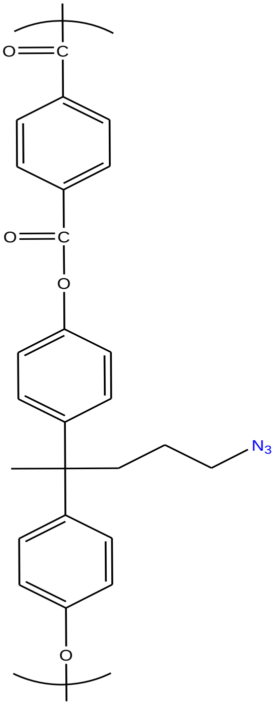
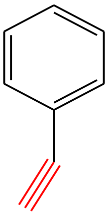
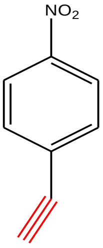
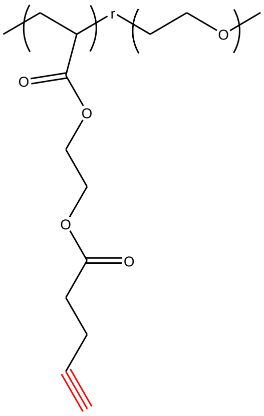
			65°C/72hr		
4	PSf 	PNIPAAm 	Cu(I)Cl/ PMDETA/ DMF/r.t./ 72hr	PSf-g-PNIPAAm	[11]
5		PDMA 		PSf-g-PDMA	[12]
6	PT	PCL-b-PDMA	Cu(I)Br/ HMTETA/ THF/r.t./24 hr	PT-g-(PCL-b-PDMAEM)	[13]

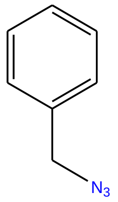
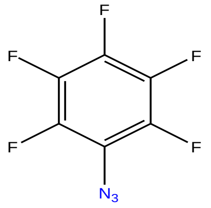
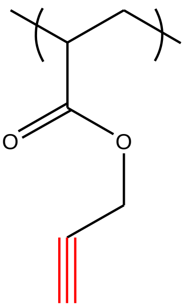
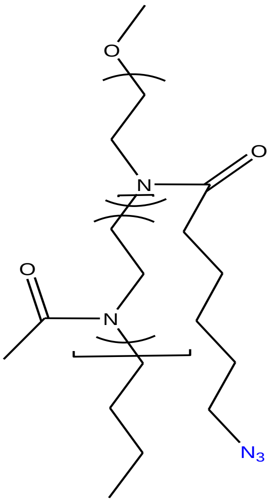
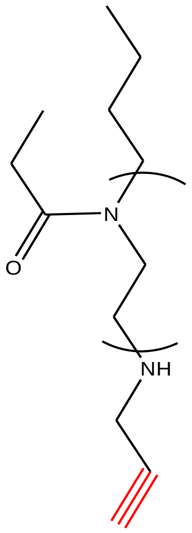
					
7	HEG 	HA-FA 	CuSO4.5H2 O / sodium ascorbate/ tert-butanol: water 1:1 /r.t./Overnight	HA-FA-g-HEG	[14]
8	Plina	PCL	Cu(I)Cl/		[15]

			PMDETA/ DMF/ 40°C /24hr	PLina-g- PCL	
9	β-CD 	HPEG 	CuSO4.5H2O / Sodium ascorbate/ DMSO: water (3:1) / 70°C /24hr	(β-CD)- g- HPEG	[16]
10	PECH	PMMA	Cu(I)Br/ PMDETA/ DMSO/	PECH-g- PMMA	[17]

			35°C/48hr		
11	PVC 		Cu(I)Br/ PMDETA/ DMF/ 35°C/72hr	PVC-g-PMMA	[18]
12	PCL 	PVC 	Cu(I)Br/ PMDETA/ DMF/35°C /72hr	PVC-g-PCL	[19]
13	PEG block copolymer	P(GMA) block copolymer			[20]

			CuSO4.5H2O / Sodium ascorbate/Deionized water/ r.t.	Hydrogel	
		TPOM 	Cu(I)Cl/ PMDETA/ DMF/r.t. /24hr		
14	Co-polyester	Phenyl acetylene			[21]

		 Ethynyl-4-nitrobenzene 	Copper (II) sulfate/ Sodium ascorbate/ DMF/r.t./ Overnight	Post-modified-Polyester	
15	PEG 	PHEA 	Cu(I)Br/ PMDETA/ DMF/50°C /12hr	PHEA-g-PEG	[22]
16	benzyl azide				[23]

	 1-azido-2,3,4,5,6-pentafluorobenzene 	PPA 	Cu(I)Br/ PMDETA/ THF/ r.t./ 24hr	Post-modified-PPA	
17	P(MeOx-co-PentOx) 	PEtOx 	CuNPs/ DMSO/ 80°C-Microwave/ 40min.	P(MeOx-co-PentOx)-g-PEtOx	[24]

IV. CONCLUSION

CuAAC has significant advantages in postmodification of polymers. It has been amply demonstrated that postmodified polymers can vary in composition, architectural style, and intended applications. Given its tremendous impact over the last few years, the CuAAC click reaction appears to have made extremely advancements in polymer science. Future click-type reactions will appear, offering strong, useful chemical tools for researching precursor materials with the possibility for post-modification by straightforward chemical processes.

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