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Copper-Catalyzed Azide Alkyne Cycloaddition Polymer Networks

by

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The final copy of this thesis has been examined by The signatories, and we find that both the content and the form meet acceptable presentation standards of scholarly work in the above mentioned discipline.
Abstract

The click reaction concept, introduced in 2001, has since spurred the rapid development and reexamination of efficient, high yield reactions which proceed rapidly under mild conditions. Prior to the discovery of facile copper catalysis in 2002, the thermally activated azide-alkyne or Huisgen cycloaddition reaction was largely ignored following its discovery in large part due to its slow kinetics, requirement for elevated temperature and limited selectivity. Now, arguably, the most prolific and capable of the click reactions, the copper-catalyzed azide alkyne cycloaddition (CuAAC) reaction is extremely efficient and affords exquisite control of the reaction. The orthogonally and chemoselectivity of this reaction enable its wide utility across varied scientific fields. Despite numerous inherent advantages and widespread use for small molecule synthesis and solution-based polymer chemistry, it has only recently and rarely been utilized to form polymer networks. This work focuses on the synthesis, mechanisms, and unique attributes of the CuAAC reaction for the fabrication of functional polymer networks.

The photo-reduction of a series of copper(II)/amine complexes via ligand metal charge transfer was examined to determine their relative efficiency and selectivity in catalyzing the CuAAC reaction. The aliphatic amine ligands were used as an electron transfer species to reduce Cu(II) upon irradiation with 365 nm light while also functioning as an accelerating agent and as protecting ligands for the Cu(I) that was formed. Among the aliphatic amines studied, tertiary amines such as triethylamine (TEA), tetramethyldiamine (TMDA), N,N,N’,N”,N”-
pentamethyldiethylenetriamine (PMDTA), and hexamethylenetetramine (HMTETA) were found to be the most effective. The reaction kinetics were accelerated by increasing the PMDETA : Cu(II) ratio with a ratio of ligand to Cu(II) of 4:1 yielding the maximum conversion in the shortest time. The sequential and orthogonal nature of the photo-CuAAC reaction and a chain-growth acrylate homopolymerization were demonstrated and used to form branched polymer structures.

A bulk, organic soluble initiation system consisting of a Cu(II) salt and a primary amine was also examined in both model reactions and in bulk polymerizations. The system was shown to be highly efficient, leading to nearly complete CuAAC polymerization at ambient temperature. Increasing the ratio of amine to copper from 1 to 4 increases the CuAAC reaction rate significantly from 4 mM/min for 1:1 ratio of Cu(II):hexylamine to 14mM/min for 1:4 ratio. The concentration dependence of the amine on the reaction rate enables the polymerization rate to be controlled simply by manipulating the hexylamine concentration.

Sequential thiol–acrylate and photo-CuAAC click reactions were utilized to form two-stage reactive polymer networks capable of generating wrinkles in a facile manner. The click thiol-Michael addition reaction was utilized to form a cross-linked polymer with residual, reactive alkyne sites that remained tethered throughout the network. The latent, unreacted alkyne sites are subsequently reacted with diazide monomers via a photoinduced Cu(I)-catalyzed alkyne–azide cycloaddition (CuAAC) reaction to increase the cross-link density. Increased cross-linking raised the modulus and glass transition temperature from 1.6 MPa and 2 °C after the thiol–acrylate reaction to 4.4 MPa and 22 °C after the CuAAC reaction, respectively. The double click reaction approach led to micro-wrinkles with well-controlled wavelength and amplitude of 8.50 ± 1.6 and 1.4 μm, respectively, for a polymer with a 1280 μm total film thickness. Additionally, this approach further enables spatial selectivity of wrinkle formation by photo-patterning.
The CuAAC-based polymerization was also used to design smart, responsive porous materials from well-defined CuAAC networks, which possesses a high glass transition temperature ($T_g = 115^\circ$C) due to the formation of the triazole linkages. The toughness, recovery, fixity, and shape memory attributes of this material were examined. The unique recovery behavior of the porous CuAAC material is characterized by its ability to recover plastic deformation upon heating. The tough and stiff nature of the glassy CuAAC polymer networks translates into desirable high compressive strain shape memory foams. The CuAAC foam exhibited excellent shape-memory behavior and was able to recover through each of five successive cycles of 80% compression at ambient temperature, presenting a significant volume change and resistance to fracture. In addition, the glassy CuAAC foam was able to withstand more than 10 cycles of compression to 50% strain and subsequent recovery at ambient temperature, indicative of ductile behavior in the glassy state.
To my mother and father, for your endless love and support
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# Table of Contents

List of Schemes ............................................................................................................................. ix
List of Figures .................................................................................................................................. xi
Chapter 1: Introduction and Background ...................................................................................... 1
Chapter 2: Objectives .................................................................................................................... 26
Chapter 3: Evaluation and Development of Novel Photoinitiator Complexes for Copper-Catalyzed Azide-Alkyne Cycloaddition Reaction ....................................................... 28
Chapter 4: Hexylamine initiates bulk-polymerization of copper-Catalyzed azide-alkyne cycloaddition reaction ................................................................................................................... 52
Chapter 5: Photo-CuAAC Induced Wrinkle Formation in a Thiol–Acrylate Elastomer via Sequential Click Reactions .................................................................................................................. 68
Chapter 6: Unique recovery and toughness behavior of glassy copper-catalyzed azide alkyne foam .................................................................................................................................... 94
Chapter 7: Conclusions and future directions ................................................................................ 120
Bibliography ................................................................................................................................... 124
List of Schemes

Schemes

1.1. Thermal Huisgen 1,3-dipolar cycloadditions..........................................................2

1.2. The Cu(I)-catalyzed azide-alkyne cycloaddition reaction, CuAAC..........................3

1.3. Some poly-triazole based ligands that prove to be efficient in the CuAAC..............5

1.4. Equilibrium between inactive polymeric copper(I) acetylides and active monomeric copper(I) acetylides..............................................................6

1.5. The first class of cyclooctyne-based structures were developed to enable the copper-free azide alkyne cycloaddition reaction........................................7

1.6. The first proposed mechanism for the CuAAC reaction. This scheme was adapted from reference 40 and 43...........................................................9

1.7. The dinuclear proposed mechanism for the CuAAC reaction. This scheme was adapted from reference 44..............................................................9

1.8. Thiol-ene reaction mediated either by a base (Thiol-Michael addition) or by radicals (radical-mediated thiol-ene).........................................................11

1.9. The copper catalyzed azide-alkyne reaction is shown across the bottom of the scheme. The catalytic Cu(I) required for the CuAAC reaction is generated by the radical mediated reduction of Cu(II)..........................................................16

3.1. The photo-mediated CuAAC reaction is shown with two possible photoinitiating pathways (A and B) where in both cases the catalytic Cu(I) required for the CuAAC reaction is generated by the reduction of Cu(II) to Cu(I). The electron for reduction is either donated by (A) aliphatic tertiary amine ligands or (B) from radicals generated via a conventional radical photoinitiator...32
4.1. (a) CuAAC monomers used for polymer network. (b) Schematic representation of the polymerization of diazide and tri-alkyne monomers to form a cross-linked polymer network.

5.1 Process of Wrinkle Formation via a Dual Click Reaction Approach. Monomers (a) pentaerythritol tetramercaptopropionate (PETMP) and trimethylolpropane triacrylate (TMPTA) were reacted with propargyl acrylate (PA) catalyzed by triethylamine to produce a (b) thiol–acrylate network with a uniform cross-link density and latent alkyne moieties. The elastomer also contained Bisphenol A di(3-azido-2-hydroxypropan-1-ol) ether (BPADA) and a visible-light photoinitiator (bis(2,4,6-trimethylbenzoyl)phenylphosphineoxide, I819) (c) by immersing the first stage polymer in a solution of copper(II) sulfate which gradually diffused into the film and exposing the polymer to irradiation, the photoinitiator cleaves to form radicals which subsequently reduce copper(II) to copper(I). As a result, copper(I) initiates the reaction between the azide and the alkyne (second stage polymerization). The diffusion-limited presence of copper(I) limits the second polymerization to a thin skin layer at the surface. (d) Upon deswelling of the solvent, wrinkles are formed across the surface of the material.

6.1. (a) The chemical structure of the monomers used to synthesize the CuAAC foam. (b) The chemical structure of the monomers used to synthesize the epoxy-amine foam. (c) A general scheme for the cyclization of an alkyne/azide system for a CuAAC polymer.
List of Figures

Figures
3.1 (a) Real time infrared spectroscopy shows the conversion of 200 mM benzylazide as it reacts with 200 mM phenylacetylene and 10 mM CuCl_2 complexed with either 10 mM of N,N,N',N'-Tetramethylethylenediamine (tertiary amine, open squares), N,N'-Dimethylethylenediamine (secondary amine, open circles), or ethylenediamine (primary amine, filled circles). The samples were exposed to 5mW/cm^2 of light centered around 365 nm for 100 minutes. The tertiary amine ligand was found to accelerate the reaction 40% more than the secondary amine. However, the primary amine was unreactive toward the photo-CuAAC. (b), A proposed path for photolysis process of Cu(II)-N base ligands is summarized. Here, the Cu(II)(amine) undergoes LMCT upon irradiation. The primary products of the photolysis are Cu(I) and an intermediate radical (L').

3.2 Chemical structures of aliphatic tertiary amine ligands used in this study.

3.3 The average reaction rate of the photo-CuAAC reaction is presented under both light and dark curing conditions in the presence of different tertiary amine dentate ligands. The plot indicates that under dark curing excess amines do not reduce Cu (II) by themselves to any significant extent, other than for TEA. The reaction mixture consisted of a solution of 200 mM benzyl azide, 200 mM phenylacetylene and 10 mM CuCl_2/tertiary amine ligand at a ratio of 1:4. Light cured samples were exposed to 5mW/cm^2 of light centered around 365 nm.

3.4 (a), Cu(II) concentrations obtained from EPR as a function of the irradiation time for various 3.5mM CuCl_2/ tertiary amine ligands at a ratio of 1:4 in DMF. (b), UV-Vis absorbance at 800 nm as a function of time for 3.5 mM CuCl_2/ tertiary amine ligand with a ratio of 1:4 in DMF. Samples were irradiated with 365 nm at 20 mW/cm^2.

3.5 Real time infrared spectroscopy shows the conversion of 200 mM benzylazide as it reacts with 200 mM phenylacetylene and 6.7 mM CuCl_2/PMDETA in various atmospheres including the addition of a radical scavenger (open triangles), in ambient atmosphere (open triangles), in the presence of pure oxygen (open circles) and argon sparging (filled circles).

3.6 Average reaction rates (M/min) at different stoichiometric ratios of ligand to metal ranging from 1:1 to 1:15 Cu:PMDETA. The reaction rate accelerates until it reaches a maximum at a ratio of ligand to metal of 4:1 with respect to the Cu concentration.
3.7 (a), Cu(II) concentrations obtained from EPR as a function of the irradiation time for 3.5mM CuCl\(_2\)/PMDETA with a ratio of 1:4 and 1:1 in DMF. (b), UV-Vis absorbance at 800 nm as a function of time for 3.5 mM CuCl\(_2\)/PMDETA with a ratio of 1:4 and 1:1 in DMF. Samples were irradiated with 365 nm at 20 mW/cm\(^2\). Both mixtures showed very similar photo-reduction rate.

3.8 \(^1\)H NMR spectra of a sequential photo-CuAAC reaction and acrylate indicating the formation of the triazole via CuAAC and then radical homopolymerization of the acrylate: (a) a mixture of benzyl azide and propargyl acrylate before reaction, (b) Upon UV-irradiation LMCT promoted CuAAC click reaction between the benzyl azide and the alkyne group of propargyl acrylate (c) followed by thermal initiation using heating to 65 °C to polymerize the acrylate group of the propargyl acrylate and form a linear polymer. The reaction mixture was 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl\(_2\)-PMDETA, and 2 wt % AIBN in DMF-d.

3.9 Functional group conversion (azide for the photo-CuAAC and acrylate) as a function of time for the sequential photo-CuAAC reaction and radical-mediated acrylate polymerization. The CuAAC reaction is initiated using 365 nm light for 50 minutes (cross), followed by heating to 65 °C to initiate the radical-mediated acrylate polymerization. The reaction mixture contained 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl\(_2\)-PMDETA, 2 % wt AIBN, and 10 % wt DMSO.

4.1 Mid-IR kinetic study of the azide conversion as a function of time in a thin sample of neopentyldiazide, trialkyne-ether, CuCl\(_2\)/PMDETA, and hexylamine. The mole ratio based on functional groups is 50:50:1 of azide: alkyne: copper with varying the mole ratio of hexylamine to Cu: zero (open diamond), 1 (cross), 3 (open circle), 4 (open square). No reaction was observed in the absence of amine while increasing the mole ratio of the amine increased the reaction rate significantly.

4.2 Mid-IR kinetic study of the azide conversion as a function of time of a thin sample of neopentyldiazide, trialkyne-ether, CuCl\(_2\)/PMDETA, and amine. The molar ratio based on functional groups is 50:50:1:4 of azide: alkyne: copper: amine.

4.3 Mid-IR kinetic study of the azide conversion as a function of time of a thin sample of benzylazide, phenylacetylene, Cu(I) iodide, and amine. The mole ratio based on functional groups is 50:50:1:4 of azide: alkyne: copper: amine.

4.4. Average reaction rate of the CuAAC reaction as a function of hexylamine concentrations for a thin sample of 0.2M phenylacetylene, 0.2M benzylazide, 0.02M copper(II)Cl\(_2\)/PMDETA in methanol.
4.5 (a) Precipitation of Cu(I) acetylide after the addition of phenylacetylene to a solution of Cu(II) and hexylamine. (b) UV-Vis absorbance for 1.0 mM CuSO$_4$ with hexylamine with a ratio of 1:4 in methanol. (c) UV-Vis absorbance for 1.0 mM CuSO$_4$, 1.0 mM CuSO$_4$ and hexylamine with a ratio of 1:4, 1.0 mM CuSO$_4$ with hexylamine, and phenylacetylene with a ratio of 1:4:5 in methanol.

5.1 FT-IR spectroscopy—attenuated total reflectance-kinetics data of the (a) the unreacted monomers spectra shows the stretch thiol vibration at 2575 cm$^{-1}$ and the stretch azide vibration at 2100 cm$^{-1}$ (b) neat polymer of stage 1 thiol–acrylate Michael addition reaction shows the complete absence of the thiol stretching vibrations peak at 2575 cm$^{-1}$ at the end of the reaction, indicating that the thiols are consumed completely to form the first stage polymer network, while the azides and the alkynes remain unreacted. (c) The spectra of a neat polymer of stage 2 photo-CuAAC reaction which was quantified via the decreasing of the stretching vibrations peak area at 2100 cm$^{-1}$ suggests that the limited quantities of azides have reacted and that the average azide–alkyne conversion within the penetration depth of the ATR–FTIR, which is 6 μm, is 25%. The second photopolymerization was initiated via exposure of the polymer film in 1 M CuSO$_4$ solution to 400–500 nm irradiation and 2 mW/cm$^2$ intensity for 1 h at 75 °C. The thiol to acrylate functional group ratio was maintained at 1:1. The homogeneous mixture contained 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, and 0.96 mmol PA. The initiator system was composed of 0.5 wt % TEA and 4.0 wt % I$_{819}$. 

5.2 Glass transition temperature, T$_g$, (a) and rubbery storage modulus (b) were measured for a stage 1 thiol–acrylate network and a stage 2 thiol–acrylate-CuAAC combined network, after the formation of the photo-CuAAC “skin” on the surface of the thiol–acrylate elastomer. The stage 1 network was formed via a stoichiometric thiol (PETMP) and acrylate (TMPTA) click reaction showing a narrow glass transition peak. The mixture contained a 1:1 mol ratio of thiol to acrylate, a 1:1 mol ratio of azide to alkyne, 0.5 wt % TEA, and 4.0 wt % I$_{819}$. To initiate the stage 2 photopolymerization the sample was cured in a hot aqueous solution of CuSO$_4$ to 400–500 nm irradiation and 2 mW/cm$^2$ intensity at 75 °C for an hour. The second stage polymer also formed a homogeneous network with a narrow glass transition temperature.

5.3 (a) SEM image of wrinkles generated via sequential click reactions on an elastomer in which after the initial network is generated via the thiol-Michael reaction, the second stage photopolymerizations was initiated via visible light initiator (I$_{819}$) in heated solution of 1 M CuSO$_4$ with 400–500 nm irradiation and 2 mW/cm$^2$ intensity at 75 °C for an hour. (b) A typical topography of wrinkled film is captured using AFM, using the same conditions as image (a).

5.4 (a) SEM image and (b) AFM images of the thiol-acrylate film, stage 1 polymerization, proven the flatness of the surface.
5.5 SEM image of wrinkles generated via sequential click reactions on an elastomer in which after
the initial network is generated via the thiol-Michael reaction, the second stage polymerizations
was initiated via a thermal initiator azobisisobutyronitrile (AIBN) in a heated solution of 1 M
CuSO4 at 75 °C for an hour.................................................................78

5.6 SEM images of a control sample wherein the second stage polymerization was conducted in
the absence of Cu with 400-500 nm irradiation and 2mW/cm² intensity at 75 °C for an hour. The
control sample indicates that wrinkles are only formed in the presence of copper.................80

5.7 SEM images of a control sample wherein the second stage polymerization was conducted via
immersion the polymer in 1 M CuSO4 at 75 °C for an hour in the dark. The flatness of the surface
indicates that light is necessary to initiate the second stage photopolymerization.................80

5.8 (a) and (b) SEM images of wrinkles on both side of the film (surface 1, a) (surface 2, b) of the
sample. All samples contain 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, 0.96
mmol PA, 0.5 wt % TEA, and 4.0 wt % I819. Wrinkles generated via the second stage CuAAC
polymerizations which was conducted in a solution of 1 M CuSO4 with 400–500 nm irradiation
and 2 mW/cm² intensity at 75 °C for an hour.................................................................81

5.9 (a) shows the influence of the thiol–acrylate film thickness on wrinkle wavelength generated
on the two surfaces. (b) The influence of the thiol–acrylate film thickness on the wrinkle amplitude
was calculated using AFM measurements. It is observed that the wrinkle wavelength and
amplitude increase as a function of increasing polymer thickness. (c) The influence of thickness
of thiol–acrylate polymer on surface modulus (Young’s modulus) is plotted. All samples contain
0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, 0.96 mmol PA, 0.5 wt % TEA, and
4.0 wt % I819. Wrinkles generated via the second stage CuAAC polymerizations which was
conducted in a solution of 1 M CuSO4 with 400–500 nm irradiation and 2 mW/cm² intensity at 75
°C for an hour. SEM images and ImageJ software were used to calculate the average wavelength
of the wrinkles.................................................................83

5.10 SEM image of wrinkles that formed in a pattern after selectively consuming radicals via prior
exposure of the sample through a photomask in which it was selectively irradiated with UV or
visible wavelengths for 15 min at 15 mW/cm² intensity to consume radicals in the exposed regions
(a). The polymer was subsequently immersed in a 1 M CuSO4 solution and further irradiated at
400–500 nm wavelength and 2 mW/cm² intensity at 75 °C for 1 h. The smooth, unwrinkled area
indicates the region in which the radicals were consumed during the initial exposure, and thereby
the catalyst, Cu(I), is not generated (b). Wrinkles are formed in areas where the film was unexposed
to irradiation (c)..........................................................................................................................85
6.1 IR kinetic study of the azide conversion of a thin sample of 1:1 mole ratio of trilkayne-ether: bisphenoldiazide, and CuCl$_2$/PMDETA with 2mol% CuCl$_2$ and 8 wt % hexylamine as a catalyst system……………………………………………………………………………………………………98

6.2 Glass transition temperature, $T_g$, and storage modulus were measured for a CuAAC foam. The CuAAC foam was formed via a stoichiometric mole ratio of bisphenoldiazide, trialkyne ether, 2 mole % CuCl$_2$/PMDETA, and 8 wt % hexylamine with 80 % porosity via click reaction showing a narrow glass transition peak with a $T_g$= 115 °C , and a rubbery modulus = 1.0 MPa…………98

6.3 Tensile shape memory behavior of 1 mm CuAAC foams. The sample was strained to almost 11% at 140 °C and was subsequently cooled to -10 °C to fix the shape. The applied stress was then unloaded at -10 °C ($R_f$ = 99%) and was heated up to 140 °C to determine its shape recovery behavior ($R_r$ = 99%). The CuAAC foam was formed from a stoichiometric mixture of bisphenoldiazide, trialkyne ether, 2 mole % CuCl$_2$/PMDETA, and 8 wt % hexylamine with 80 % porosity……………………………………………………………………………………….….99

6.4 (a) Average toughness for 4 specimen of foams. Each specimen was compressed to 80% strain for 5 successive cycle at ambient temperature ($T<<T_g$) with a strain rate of 0.01 mm/s. (b) A typical stress-strain responses for 5 successive compression tests performed on a single specimen of the CuAAC foams. The cylindrical CuAAC foam was compressed consecutively to 80% at ambient temperature with a strain rate of 0.01 mm/s. The foam showed the ability to recover over multiple compression cycles. The toughness or energy to 80% strain was calculated after the first cycle to be 850 MJ/m$^3$……………………………………………………………………..……………101

6.5 (a) Average fixity and recovery for 4 specimen of foams. The. Each specimen was compressed to 80% strain for 5 successive cycle at ambient temperature ($T<<T_g$) with a strain rate of 0.01 mm/s. The recovery and fixity was calculated after each cycle of compression. (b) The permanent shape (left) of a CuAAC foam and the 80% compressed foam (middle). Heating the foam above its $T_g$ results in complete recovery of its original shape (right)…………………………………………………………………………………………….102

6.6 The CuAAC foam after 5 successive compression cycles to 80% strain…………………..102

6.7 SEM image of the CuAAC foam………………………………………………………………………………………………………..104

6.8 Four sequential cycles of compression and recovery for a CuAAC foam. The foam was compressed to 80% strain at ambient temperature with a strain rate of 0.01 mm/s, followed by recovery of the compressed sample upon heating to $T_g+ 40$ °C with a heating rate of 3 °C / min under preload (0.15N). Samples were held isothermal at 150 °C for 10 minutes between cycles.
The same sample was compressed four times with monitoring of the recovery as a function of temperature after each compression cycle. The CuAAC foam was formed via a stoichiometric mole ratio of bisphenol diazide, trialkyne ether, 2 mole % CuCl$_2$/PMDETA, and 8 wt % hexylamine with 80 % porosity……………………………………………………………………………………………………105

6.9 FTIR kinetic study of the Epoxy conversion of a 1 mm thickness of 1:0.5:0.5 mole ratio of bisphenol A Diglycidyl Ether, 1,6-diaminohexane, and aniline. FTIR was used to monitor the disappearance of the C-H stretching at 4530 cm$^{-1}$. The sample was heated to 100 °C for 5 hours…………………………………………………………………………………………………………………………106

6.10 (a) Glass transition temperature, $T_g$, and storage modulus were measured for the epoxy amine foam. The epoxy-amine network was formed with a mole ratio of 1:0.5:0.5 bisphenol A diglycidyl ether, 1,6-diaminohexane, and aniline with 80% porosity via click reaction showing a narrow glass transition peak with a $T_g=125$ °C and a rubbery modulus = 1.2 MPa. (b) Stress-strain curve obtained by compressing the epoxy-amine foam to 80% strain with a strain rate of 0.01 mm/s at ambient temperature. The epoxy-amine energy to 70% strain was calculated after the first cycle to be 300 MJ/m$^3$. The image in the left corner shows the epoxy-amine foam severely damaged after the first cycle of compression……………………………………………………………………………………………………107

6.11: Average toughness or energy to 50 % strain for 4 specimen of CuAAC foams and 4 epoxy amine foams. Each specimen was compressed successively to 50% strain until failure at ambient temperature ($T$<<$T_g$) with a strain rate of 0.01 mm/s. The CuAAC foam was able to recover 13 successive cycle of compressions while the epoxy-amine failed only after 2 cycles of 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Chapter 1

Introduction and Background

1.1. The click concept

Traditional organic synthesis is a highly useful tool to synthesize new materials; however, it is often expensive and time consuming. Many synthetic strategies are based on inefficient reactions with side products that require multistep purification with large solvent consumption in purification and column chromatography steps. While these methodologies sharpen the skill of chemists, they can delay the discovery of new materials due to the synthetic challenges. The demand for synthesized materials with unique properties that expand and/or enable the advancement in many fields is great across materials science, biotechnology, medicine and energy, and yet, under many circumstances, this development is limited by the synthetic approaches necessary for producing novel materials and novel material behavior.

To address this shortcoming and spur the development of new molecules and materials, Kolb, Finn and Sharpless in 2001 introduced the “click” chemistry’ paradigm.¹ They identified a list of criteria for reactions and processes that would enable simple, robust synthesis of molecules and/or materials. Further, they also identified a set of reactions that meet these criteria including reactions that proceed chemoselectivity to completion with high yield, create one product that is easy to remove without chromatography, are wide in scope, tolerate various conditions, and are simple to perform. Any reaction that meets these criteria was referred to as a “click reaction”. Many illustrations of click reactions were presented in Sharpless 2001 review, most of which are based on the formation of heteroatom-carbon bonds that are thermodynamically-favored reactions, and lead specifically to one product. Because of the simplicity of this concept, it has had a dramatic
impact on organic chemistry. This concept brought back the urgency to organic chemistry to rely on simple, efficient reactions that could be used to create new compounds. The click chemistry paradigm has been extended broadly to various fields including polymer and materials chemistry, biotechnology and bioconjugation, drug discovery, nanomaterials, and surface modification among many others.

1.2. Thermally Activated Azide-Alkyne Huisgen Cycloaddition

The traditional 1,3 dipolar cycloaddition between a terminal alkyne and an organic azide results in the formation of a mixture of 1,4 triazole adducts and 1,5 triazole adducts (Scheme 1.1). Rolf Huisgen was the first to understand this reaction, and he did extensive work in this area. The reaction between the 1,3-dipolar azide, and the dipolarophile alkyne requires elevated temperature to enable the reaction. This reaction is usually sluggish, even at elevated temperatures, owing to its high activation energy (25–26 kcal/mol for methyl azide and propyne). Although the azide is not the most reactive 1,3 dipolar compound, it is favorable because it is nearly devoid of side reactions when reacting with the alkyne and it has stability toward oxygen, water and under a majority of organic synthesis conditions.

![Scheme 1.1 Thermal Huisgen 1,3-dipolar cycloadditions](image)

Prior to the development of Cu(I) catalysis, the Huisgen Cycloaddition reaction had been relatively unused due to the low reactivity of the reaction, prolonged reaction times, and the fears
of the explosive nature of azides when used at elevated temperatures. The development of Cu(I) catalysis of this reaction by the Sharpless and Meldal groups in 2002 has largely been responsible for the ubiquitous use that it now enjoys.\textsuperscript{18,19}

1.3. An Introduction to the Copper(I)-Catalyzed Azide–Alkyne Cycloaddition, CuAAC

Shortly after the development of the “click” concept, in 2002, Valery V. Fokin and K. Barry Sharpless at the Scripps Research Institute in California\textsuperscript{18} and Morten Meldal in the Carlsberg Laboratory in Denmark\textsuperscript{19} independently reported the discovery of a highly robust copper(I)-catalyzed cycloaddition of terminal alkynes and organic azides, i.e., the CuAAC reaction, which selectively forms the 1,2,3-triazole (\textbf{Scheme 1.2}). Fokin and Sharpless stated in their original report that, “…this new catalytic process seems to offer an unprecedented level of selectivity, reliability, and scope for those organic synthesis endeavors which depend on the creation of covalent links between diverse building blocks.”\textsuperscript{1}

\textbf{Scheme 1.2} The Cu(I)-catalyzed azide-alkyne cycloaddition reaction, CuAAC.

The catalyzed reaction proceeds in a variety of aqueous and organic mixtures at ambient temperatures under mild conditions, and tolerates many functional groups, giving nearly quantitative yields of the stable triazole connection in a robust, relatively process independent manner. Moreover, this reaction is bio-orthogonal in which the azide and the alkyne react only with each other even in the presence of numerous other functional groups, as neither the azide nor the alkyne groups are present in natural systems. This unique ability facilitated the rapid spread
of this reaction across the field of biological applications where orthogonally is critical due to the presence of various endogenous biological functionalities. 6,7,20

Typically, the catalyst, copper(I), is formed by the reduction of a copper(II) salt such as CuSO₄ in situ via ascorbic acid or sodium ascorbate in aqueous media or a mixture of water and an organic solvent to give the active form of the catalyst, Cu(I). Alternatively, Cu(I) salts such as copper(I) halide, copper(I) triflate or tetrakis (acetonitrile), copper(I) hexafluorophosphate are used directly; however; poor solubility often limits their implementation. The Cu(I) catalysis is responsible for a dramatic rate acceleration relative to the uncatalyzed cycloaddtion – often proceeding seven orders of magnitude more rapidly 21,22.

Copper exists in several different oxidation states, Cu⁺¹, Cu⁺², and Cu⁰. Cu(I) is the least stable oxidation state, and it oxidizes by reacting with dissolved oxygen to form Cu⁺², or by disproportionation (2Cu⁺¹ to Cu⁺² and 2Cu⁰). To stabilize Cu(I) oxidation, ligands are usually employed to prevent these side reactions. Sharpless and co-workers reported that (tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine, TBTA) significantly reduces these side reactions, enabling a lower catalyst loading (i.e., 1%) , while simultaneously improving the reaction rate. The biocompatibility of CuAAC in bioconjugation reactions was also repeated using the TBTA ligand. 23,24,25 This ligand was proposed to act as tetradentate ligand to block all copper(I) sites, so there could be no oxidant attack. The tertiary amine’s nitrogen atom was assumed to coordinate the metal, while the three triazole arms could temporarily dissociate to allow copper(I) coordination with an alkyne to form the active copper(I)-acetylide species that starts the catalytic cycle. Screening various analogous ligands reveals similar efficiency to other tris-triazole based ligands (Scheme 1.3). Over the years, these poly-triazole based ligands were developed to work under various reaction conditions, such as increasing solubility in water. BTTP = 3-[4-{(bis[1-tert-butyl-
1H-1,2,3-triazol-4-yl)methyl]amino)methyl},-1H-1,2,3-triazol-1-yl]propanol,\textsuperscript{26} BTTPS = 3-[4-\{(bis[(1-tert-butyl-1H-1,2,3-triazol-4-yl)methyl]amino)methyl}]-1H-1,2,3-triazol-1-yl]propyl hydrogen sulfate,\textsuperscript{26} BTTES = 2-[4-\{(bis[(1-tert-butyl-1H-1,2,3-triazol-4-yl)methyl]amino)methyl}]-1H-1,2,3-triazol-1-yl]propyl hydrogen sulfate,\textsuperscript{26} and BTTAA = 2-[4-\{(bis[(1-tert-butyl-1H-1,2,3-triazol-4-yl)methyl]amino)methyl}]-1H-1,2,3-triazol-1-yl]acetic acid\textsuperscript{28} were all developed for use in aqueous media (Scheme 1.3). Cyclic voltammetry studies showed that these ligands increase the redox potential of C(I)/Cu(II) by almost 300 mV,\textsuperscript{23} and envelop and protect the Cu(I) species to stabilize it and keep it active. The unique reactivity of polytriazole ligands can be understood from their interference in early stages of the CuAAC reaction when forming the copper(I) acetylides. Fokin proposed that non-aggregated copper(I) acetylides are active towards the CuAAC reaction, while the aggregated copper(I) acetylides are inactive. It is believed that the polytriazole ligands prevent copper(I) acetylide aggregation by preventing nucleation of the aggregated copper(I) acetylides\textsuperscript{29} (Scheme 1.4).

Scheme 1.3 Some poly-triazole based ligands that proved to be efficient in the CuAAC reaction.
Scheme 1.4 Equilibrium between inactive polymeric copper(I) acetylides and active monomeric copper(I) acetylides.

Inspired by the fact that the cycloaddition of organic azides and alkynes can proceed at mild conditions including ambient temperature, be chemoselective, be inert nature to biological functionalities, and be insensitive to water, several groups have utilized this reaction in biological settings. The primary negative associated with implementation of CuAAC in biological environments is the copper toxicity where the facile redox potential of copper makes it easy to lose or gain an electron that can lead to the formation of reactive oxygen species that may damage proteins and/or oligonucleotides.30

Towards eliminating the Cu(I) catalyst, Bertozzi and co-workers noted that cyclooctynes reacted “like an explosion” when mixed with phenyl azide to form the triazole product. They subsequently developed difluorocyclooctynes 1.1 (Scheme 1.5) in which the difluoride improved the reactivity further31. The strained alkyne has increased reactivity at ambient temperature due to the release of 18 Kcal/mol of ring strain energy – thus enabling reactivity even in the absence of copper. This reaction is now referred to as Cu-free click chemistry. The reactivity of the difluorocyclooctynes is vastly accelerated in comparison to a linear alkyne; however, the reactivity
is still slower than the copper mediated reaction. Therefore, Bertozzi and co-workers developed further strained cyclooctynes 1.2 which demonstrated even higher reactivity towards azides.\textsuperscript{32} Since then, various cyclooctyne-based structures have been developed to increase reactivity with more accessible synthetic approaches. This cyclooctyne approach has been successful in enabling free-copper azide alkyne reaction in biological environments with an ever-growing list of applications.\textsuperscript{33-38}

Scheme 1.5 The first class of cyclooctyne-based structures were developed to enable the copper-free azide alkyne cycloaddition reaction.

1.4. Mechanism of the Cu(I) catalyzed azide-alkyne cycloaddition reaction.

The CuAAC reaction has been employed widely in various fields of science due to its robustness, simplicity, and forgiving nature. Despite its wide utility, the mechanism of this reaction is complex, and details of the reaction mechanism remained unclear and controversial. Sharpless reported the first proposed mechanism\textsuperscript{39} (Scheme 1.6) in which the alkyne is deprotonated by a base, and coordinates to copper(I), the active catalyst. If there is a free coordination site on copper(I), an azide would coordinate to that site as well. A double bond is formed between the copper(I) and the C\textsubscript{1} of the acetylide, and then this unusual six-member ring undergoes a transannular ring contraction to yield the triazolide copper which protonates to release the copper(I) ion and form the triazole. Different studies focused on understanding the mechanism and designing experiments to reveal the details of the reaction.\textsuperscript{40-42,21,24,25} Finn and Fokin did kinetic
measurements, and they found that the rate law of the reaction is second order in the concentration of the copper(I). They suggested two copper atoms participate to assist the formation of the C-N bond between the azide and the alkyne. The DFT calculations strongly supported that hypothesis, and Finn and Fokin proposed another mechanism (Scheme 1.7).\textsuperscript{43} Recently, Fokin and co-workers presented direct evidence for the dinuclear formation of the copper(I) intermediate.\textsuperscript{44} The authors used a real-time flow calorimetry to monitor the reaction between copper(I) acetylide and benzyl azide, and no reaction was observed. When 5 mol % of copper(I) was added, the reaction proceeds to completion within 20 minutes. This experiment demonstrated that the sigma bond between copper(I) and the acetylide is not enough to initiate the cycloaddition, and the formation of a pi-bond with the second copper activates that species toward the cycloaddition reaction.

Although there has been extensive investigation of the CuAAC mechanism,\textsuperscript{40-42,21,24,25} the structure of the active species are controversial. The structure, nature and concentration of the active copper(I) species likely change over the course of the reaction; therefore, kinetic experiments are useful but provide only limited information about the mechanism and active species.
Scheme 1.6 The first proposed mechanism for the CuAAC reaction. This scheme was adapted from reference 40 and 43.

Scheme 1.7 The dinuclear proposed mechanism for the CuAAC reaction. This scheme was adapted from reference 44.

1.5. Ruthenium catalyzed azide-alkyne cycloaddition reaction (RuAAC).

An alternative catalyst system to Cu(I) for the azide alkyne cycloaddition reaction is ruthenium which participates in the analogous ruthenium-catalyzed azide alkyne cycloaddition
reaction, RuAAC, to yield the 1,5 substituted-triazole, instead of the 1,4 substituted-triazole that results from the CuAAC reaction. Unlike the CuAAC reaction in which only terminal alkynes react, triazoles generated from RuAAC can be synthesized via terminal alkynes or from an internal alkyne. The RuAAC rate is unaffected by the alkyne substitution; however, it is highly dependent on the azide structure where primary azides result in high yield, while secondary azides react more slowly. Tertiary azides are hardly clickable by the RuAAC reaction. In addition, the RuAAC rate is affected by the catalyst choice, and up to now only limited catalytic system can be used to achieve high selectivity and yield.

1.6. Polymers Clicked by CuAAC

Since the advancements in click chemistry, particularly the CuAAC reaction, this concept has been incorporated rapidly into the field of macromolecular synthesis owing to the simplicity and efficiency of this concept which not only allows for the synthesis of well-known polymers, but also enables the preparation of complex structures that were previously inaccessible. Arguably, the click concept has far more impact in polymer synthesis than small molecule synthesis. Unlike small molecules synthesis, efficiency in polymer synthesis is more demanding in a process where a simple separation of the unreacted functional groups to get a pure product in many instances has not previously existed.

Thiol click chemistry is another reaction family within the click chemistry paradigm (Scheme 1.8). The thiol-vinyl reaction is mediated either by radicals (radical-mediated thiol-ene reaction) or by a base/nucleophile (thiol-Micheal addition reaction). Thiol chemistry has been used extensively to construct various polymer structures including the synthesis of cross-
linked polymers, post-functionalization of polymers and surfaces, and construction of well-defined polymer architectures, among others. This chemistry has proven to be powerful and robust in macromolecular synthesis with the benefit of its insensitivity to water and oxygen. One of the biggest advantages of thiol-based chemistry for polymer network synthesis is the step-growth mechanism. Unlike chain growth polymerizations, polymer chains grow homogeneously, resulting in narrow glass transition temperatures that lead to desirable features such as delayed gelation, low shrinkage, and low shrinkage stress.

![Scheme 1.8](image.png)

Scheme 1.8 Thiol-ene reaction mediated either by a base (Thiol-Michael addition) or by radicals (radical-mediated thiol-ene)

Among the click chemistry toolbox, the CuAAC reaction is the most efficient and robust. Thus, this reaction is often referred to as “the” click reaction. Over the last decade, numerous studies have focused on employing this powerful click reaction in the construction of sophisticated structures with well defined chain length and end group functionality. In this section, applications and implementations of the CuAAC reaction in polymer science are described in detail with several examples, mainly focusing on construction of linear and dendritic polymer architectures, copolymers and functional network polymers.

The CuAAC reaction has been utilized in polymer synthesis in two fundamental ways either to construct new materials or to modify existing polymers, including the functionalization or decorating of polymers as used to achieve various structures and properties. The most important requirements to simple decoration and functionalization of a material are chemoselectivity (to
functionalize only the desire site) and quantitative yield (to ensure complete, stoichiometric functionalization). These two requirements are ideally fulfilled by the chemistry of the CuAAC reaction.

1.6.1. Linear and block copolymers

Both the azide and the alkyne groups have relatively limited reactivity toward other functional groups which has enabled the CuAAC reaction to be utilized to construct linear polymers and to make end-functionalized macromolecules. Finn and co-workers were the first to explore CuAAC reaction to construct linear and three dimensional polymer networks which were explored as a novel adhesion material for copper surfaces, as the triazoles that were formed have a strong propensity to bind to transition metals.\(^6\) Linear telechelic polymers with well defined end groups have frequently been prepared by combining atom transfer radical polymerization (ATRP) and CuAAC reactions, where following ATRP, the halogen end groups are replaced by azide groups, and subsequently used in the CuAAC reaction, for example in block copolymer ligation.\(^6\)-\(^9\) The robustness and chemoselectivity of the CuAAC reaction in macromolecular synthesis were demonstrated by designing structures that otherwise are difficult to prepare by other means like preparing macrocycles from linear polymers\(^7\),\(^8\), and connecting block copolymers of varies structures together by coupling azide- and alkyne-functionalized segments.\(^7\),\(^2\),\(^7\)

1.6.2. Dendritic polymer architectures

Different groups have employed CuAAC to construct dendrimeric structures.\(^7\),\(^4\)-\(^7\) The dendrimer synthesis relies on clickable reactions where these idealized structures require highly efficient reactions for each of the repeated steps to ensure quantitative conversion as the dendrimer
grows. Hawker, Fokin, and Sharpless were among the first to highlight the chemoselectivity and efficiency of the CuAAC reaction for dendrimer synthesis, and they found this chemistry to be a straightforward strategy for large scale synthesis of these ideal structures.\(^{74}\)

### 1.6.3. Network polymers

The CuAAC reaction has also been utilized to construct polymer networks which possess unique properties.\(^{78,79}\) Analogous to the thiol chemistry highlighted above, CuAAC-based polymer networks are formed via a step-growth mechanism resulting in a homogeneous network with narrow glass transition temperatures, which leads to beneficial properties such as delayed gelation and low shrinkage. However, the CuAAC reaction has the added advantage of forming rigid triazole junctions as a result of the polymerization which significantly influences the ultimate material properties.

The azide alkyne cycloaddition reaction has proven useful for the synthesis of a range of cross-linked polymer networks though most were synthesized in the presence of a large amount of solvent to form a gel rather than in bulk. Hawker and co-workers cross-linked bi-functional alkyne-PEGs and tetra-functional azide-PEGs to form a hydrogel with a well-defined network and with improved mechanical properties, where the hydrogel strength was about 10 times greater than a hydrogel that was cross-linked by conventional chain growth polymerization reactions.\(^{79}\) The CuAAC reaction also enables the facile formation of a hydrogel with residual azide or alkyne groups, simply by reacting with a stoichiometric excess of one component, that are useful for subsequent clickable reactions that have been used to decorate the hydrogel with various compounds including imaging moieties, peptides, and drugs.\(^{80-82,8,9}\)
As mentioned above, the bulk polymerization of CuAAC was first demonstrated by Finn and coworkers where multifunctional azides and alkynes were polymerized between two plates of copper.\textsuperscript{66} Taking advantage of the affinity of triazoles to transition metals, the polymer network yielded adhesives which were twice as strong as a commercially available metal adhesives. Several other groups later used Cu(I) salts to initiate the bulk azide alkyne reaction to construct polymer networks.\textsuperscript{83,84} The bulk polymerization has been much less developed, likely due to the azide safety concerns\textsuperscript{85,86} as well as difficulties in finding soluble catalyst species in bulk where most of the commercially available inorganic copper salts have very limited solubility in organic media.

1.7. Photopolymerization of CuAAC

The broad implementations of the CuAAC in material science, as highlighted above, and the nature of the CuAAC reaction, as a simple, controllable and efficient reaction with the invisibility of the azides and alkynes to many functional groups, enhances the critical need to achieve spatiotemporal control. Here, the CuAAC is catalyzed by Cu(I), which is typically generated by chemical reduction of Cu(II) to Cu(I) via sodium ascorbate or directly by the addition of Cu(I).\textsuperscript{1-5} Unfortunately, these approaches lack spatiotemporal control, and the CuAAC reaction proceeds spontaneously when they are mixed. From the small molecule synthetic point of view, spatiotemporal control is relatively unimportant. However, for applications such as dental materials, 3D printing, coatings, adhesives, contact lenses, and many biomaterials applications, spatiotemporal control is crucial where materials must be initiated on demand. Spatiotemporal control is often achieved by utilizing light, i.e., photoinitiation. Controlling the generation of catalyst, Cu(I), by a photochemical process enables initiation of the reaction at specific times and
locations. The combination of the classic advantages of click reactions with photochemical initiation further enhances this powerful reaction.

Spatial control of the CuAAC reaction has been achieved partially, using techniques such as scanning-probe lithography,\textsuperscript{87,88} microcontact printing,\textsuperscript{89,90} and electroclick chemistry.\textsuperscript{91,92} However, each one of these approaches is limited to reactions on surfaces. Initial attempts to control the reaction photochemically used a combination of electron donor and redox-active chromophore where light was used in the photoreduction of the chromophore, which in turn generated a strong reducing agent that worked to reduce Cu(II) to Cu(I).\textsuperscript{93} Following this work, Popkin and co-workers demonstrated the photogeneration of cyclooctynes from cyclopropenones upon light exposure, which rapidly undergoes copper free azide alkyne reaction though this reaction is limited to a maximum of one azide-alkyne reaction per photon that is absorbed\textsuperscript{94}. Later, several groups sought to photochemically generate copper(I) \textit{in situ} from copper (II) using different approaches including electron transfer from photosensitizer,\textsuperscript{95-97} ligand-metal charge transfer,\textsuperscript{98} photolysis of copper(II) complexes,\textsuperscript{99} and copper containing photoinitiators\textsuperscript{100}. In considering the photoinitiated CuAAC reaction, it was reported that radicals are capable of reducing and oxidizing copper (II) species.\textsuperscript{101,102} Inspired by this work, Adzima \textit{et al.} presented a simple platform where light was used to generate Cu(I) species \textit{in situ} simply by the addition of a radical-generating photoinitiator to a Cu(II) salt (Scheme 1.9).\textsuperscript{103} Upon light exposure, the photoinitiator generates radicals, which reduce Cu(II) to Cu(I), and subsequently catalyzes the CuAAC reaction. This approach has proven to be simple, efficient, and versatile. The diverse capability of this technique was demonstrated in patterning hydrogels,\textsuperscript{104} synthesis of macromolecules,\textsuperscript{105-107} block copolymers,\textsuperscript{108} and high-performance cross-linked polymer networks with unique mechanical properties.\textsuperscript{78,79}
Scheme 1.9 The copper catalyzed azide-alkyne reaction is shown across the bottom of the scheme. The catalytic Cu(I) required for the CuAAC reaction is generated by the radical mediated reduction of Cu(II).

Research Overview

In this thesis, research was conducted to explore the utility of copper-catalyzed azide-alkyne reactions for the synthesis of polymer networks. Spectroscopic measurements were conducted to evaluate this reaction and explore its mechanism, while mechanical measurements examined the relationship between the underlying reactions and the polymer properties. The CuAAC reaction was utilized in the fabrication of functional materials owing to its efficiency and tolerance of other functional groups, which enable fabrication of novel materials for various applications.

Following this introduction and objectives laid out in the next chapter, chapter three and four detail the use of a new catalytic system for the CuAAC reaction. Fourier transfer infrared (FTIR) spectroscopy was used to determine the conversion and kinetics of the CuAAC reaction. UV-spectroscopy, and electron paramagnetic resonance (EPR) spectroscopy were used to determine the active catalyst concentrations. Chapter three focuses on photo-reduction of copper complexes via ligand-metal charge transfer, and their use to initiate the CuAAC reaction with potential uses to fabricate a brush polymer. Chapter five describes a novel catalyst system for bulk polymerization using copper salts with primary amines to initiate the CuAAC reaction.
Chapter five examines the manipulation of surface features on a thiol-acrylate film. The sequential thiol-acrylate and CuAAC click reactions were used to create gradient in the cross-linking densities where the thiol–acrylate reaction is used for initial network formation and subsequently the CuAAC reaction locally increases the cross-link density. This gradient in the cross-link density along the film results in micro-wrinkles on the surface. Control over the wavelength and amplitude of these wrinkles using the resin film thickness is further demonstrated by studying the surface profiles using scanning electron microscopy (SEM) and atomic force microscopy (AFM). The spatial selectivity of wrinkle formation was also presented.

Chapter six presents the use of the CuAAC chemistry to form a porous material with a high glass transition temperature. The mechanical properties of the network under compression were tested. The shape memory of the glassy material was examined, and compared to an epoxy-amine foam as a control. The CuAAC foam compacts in volume up to 80% of its original length, and fully recovers when it is reheated through several cycles.
References


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Chapter 2
Objectives

This thesis explores methods for controlling and utilizing the copper(I) catalyzed azide alkyn cycloaddition (CuAAC) reaction as a polymerization that is useful in forming cross-linked polymer networks. Different catalytic systems are employed for initiating this reaction, which is also utilized for functional materials: photo-directed micro-wrinkles and porous high strain capacity shape memory polymers. The overall objective of this thesis is to enhance the understanding, control, development and implementation of the CuAAC reaction in the formation of cross-linked polymer networks with unique capabilities associated with that reaction. More specifically, the aims of this research were to:

1) Examine several pathways for copper(II) reduction to copper(I) as a method for catalyzing the CuAAC reaction, and understand the capabilities and mechanism of the Cu(II) reduction and

2) Use the CuAAC reaction to form polymer networks of varying form and function including to

i) Form photo-directed micro-wrinkles using a sequential thiol-acrylate and CuAAC click reactions and

ii) Synthesize tough, porous CuAAC-based polymers and examine their shape memory characteristics, recovery and toughness under low strain and high strain compression tests.
The CuAAC reaction has been extensively used for small molecules synthesis, macromolecular synthesis and functionalization in solution, but it has seldom been utilized for three dimensional polymer network formation. The synthesis of cross-linked polymer networks faces the challenge of finding a soluble, and efficient catalytic system. The typical reaction conditions under which the CuAAC reaction is used include the addition of copper(II) sulfate and sodium ascorbate in aqueous media or a mixture of organic and aqueous components. This catalytic system has been successful and is widely used for numerous implementations of the click reaction. However, the solubility of this system in organic media is limited. Thus, the first part of this thesis focuses on the development and understanding of new catalytic systems that work efficiently and with high selectivity for the CuAAC reaction, including both photo-catalytic and conventional bulk redox catalyst systems. The second objective seeks to understand the impact of the underlying chemistry on the material properties. CuAAC-based polymer networks possess unique attributes due to the formation of rigid triazole linkages throughout the polymer network, and these attributes were utilized to create functional materials of varying characteristics. The stiff nature of the CuAAC polymer network was useful here in combination with rubbery networks to create variation of the surface modulus which resulted in buckling. The stiff and tough behavior of porous CuAAC based polymer network was also examined to create high compressive strain shape memory materials that are capable of repeatedly recovering from extensive plastic deformation.
Chapter 3

Evaluation and Development of Novel Photoinitiator Complexes for Photoinitiating the Copper-Catalyzed Azide-Alkyne Cycloaddition Reaction

Abstract

Here, several distinct approaches for photoinitiation and subsequent utilization of the Copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction are developed. In particular, Cu (II) - ligand complexes were synthesized that enabled direct photoreduction of the Cu (II). The sequential and orthogonal nature of the photo-CuAAC reaction and a chain-growth acrylate homopolymerization were demonstrated and used to form branched polymer structures. The efficiency of the photo-initiated Cu (II) complexes in regards to their ability to initiate the CuAAC reaction was examined by reacting a variety of amino-functional ligands with Cu(II) halides to form complexes capable of forming Cu(I) upon light irradiation. When irradiated with 365 nm light, the ligand donates an electron to Cu(II) to reduce it to Cu(I) which subsequently initiates the azide–alkyne cycloaddition (i.e., Photo-CuAAC) reaction with exquisite spatiotemporal control. Aliphatic amine ligands were found to be the most efficient ligands in promoting photoreduction of Cu(II) and stabilizing Cu(I), once formed. Among the aliphatic amines studied, tertiary amines such as triethylamine (TEA), tetramethyldiamine (TMDA), N,N,N’,N”,N”-pentamethyldiethylenetriamine (PMDTA), and hexamethylenetetramine (HMTETA) were found to be the most effective. In addition, the Cu(II)-amine complexes were insensitive to oxygen, indicating that the catalytic Cu (I) is largely prevented from re-oxidation by complexation with the amine ligand and/or the triazole. The reaction kinetics were accelerated by increasing the PMDETA : Cu(II) ratio with a ratio of ligand to Cu(II) of 4:1 yielding the maximum conversion in the shortest time.
Introduction

The emergence of the Click Chemistry concept as put forward by Sharpless and coworkers has led to the identification of a set of highly efficient, reliable and selective reactions that readily meet the demands and desires for the synthesis of new materials. Specifically, the copper catalyzed azide-alkyne cycloaddition (CuAAC) reaction has been prominently established as the ideal click reaction due to its simplicity, orthogonality and regioselectivity relative to other organic reactions. The desirable attributes of this reaction have led to its extensive implementation in materials science, surface functionalization, biomaterials, and conventional organic synthesis.

The CuAAC reaction is typically catalyzed by Cu (I) where the means of generating Cu(I) has ranged from the direct addition of Cu(I) to the reduction of Cu(II) in situ using different reducing agents to the generation of Cu(I) electrochemically to several other less frequently used approaches. Although the different approaches have been applied successfully to generate Cu(I), most suffer from a lack of spatiotemporal control which has the potential for limiting the CuAAC reaction, particularly in several areas of materials science. The CuAAC reaction using any one of the conventional methods for generation of Cu(I) species proceeds rapidly once the precursors are mixed. The reaction kinetics often limit the implementation of this reaction in applications that vary from photolithography to industrial coatings as well as photoresists, just to name a few, where spatiotemporal control is crucial. The importance and ubiquitous nature of photoinitiated click reactions was recently highlighted for a number of different reaction types and applications.7

Unlike conventional approaches using Cu(I) salts, reducing agents, or copper turnings, a photo-mediated technique for generating Cu(I) in situ affords comprehensive spatial and temporal control of the CuAAC reaction, wherein the generation of Cu(I) is limited to selectively irradiated
regions in both time and space. In addition to the spatiotemporal control, the photo-induced 
CuAAC reaction offers a facile means to control the reaction rate simply by changing the light 
intensity or photoinitiator concentration. Thus, the photo-mediated CuAAC reaction represents a 
powerful technique that effectively combines the benefits of this powerful click reaction with the 
myriad advantages of a photoinduced process. A previous method for initiating the CuAAC 
reaction using light used the CuAAC reaction to mimic biological signal transduction processes. 
Light was used in the photoreduction of a chromophore, which in turn generated a strong reducing 
agent that worked to reduce Cu(II) to Cu(I). However, the reducing agent was observed to be 
unstable and was consumed within a short irradiation period. An additional study examined the 
implementation of a Cu-complex involving copper halides and an amine ligand, PMDETA, to 
generate a photosensitive complex that exhibits the desired photo-reduction properties upon 
irradiation. While successful in demonstrating the photoinitiation capabilities of this system, the 
reaction often took hours to reach completion. Another reported photo-catalyst system for the 
CuAAC reaction is copper(II) tren ketoprofenate complex developed by Vincent and co-workers. 
The complex was shown to catalyze the CuAAC reaction upon UV irradiation and oxygen 
exposure which demonstrated temporal control over the reaction. Subsequent work demonstrated 
that an efficient means to initiate the CuAAC reaction involves first photogenerating an active 
radical intermediate that could reduce Cu(II) to generate the active form of the catalyst Cu(I). 
This approach to initiate the photo-click CuAAC reaction has been shown to have high modularity 
and versatility as a new platform and can be used in bulk polymerizations to synthesize polymers 
containing triazole links throughout their structure. The control afforded by the photo-CuAAC 
reaction opens up avenues for the CuAAC reaction to be implemented in a range of materials 
science fields that vary from macromolecule synthesis to hydrogel micropatterning.
The CuAAC reaction can be photoinitiated by Cu(II) complexes that exhibit direct photoinduced reduction or by using a variety of radical generators with Cu(II) salts with subsequent reduction of the Cu(II), as shown in scheme 3.1. Many Cu(II) complexes are known to be sensitive to light and they undergo photoinduced reduction via Ligand-Metal-Charge Transfer (LMCT). The result of the LMCT is the ligand oxidation and the reduction of the Cu(II) to Cu(I). Different Cu(II) complexes have been shown to promote LMCT upon irradiation such as copper (II) (3,5-diisopropyl salicylic acid), copper (II) malonate, copper(II) quercetin, copper(II) rutin, and Cu(II)-pentamethyldiethylenetriamine. However, the stability of Cu(I) after the photolysis process was an issue where Cu(II) malonate, for example, on irradiation produced Cu(I) and a methyl radical which was then capable of reacting further with Cu(I) to re-oxidize it back to Cu(II). Among these complexes, the Cu(II)-amine complex was shown to promote LMCT and the CuAAC reaction at the same time, suggesting that Cu(I) is stabilized by the amine. Therefore, the focus here is to examine aliphatic amines that more effectively produce the active catalytic form of Cu(I).

The amine ligand here not only works to provide an electron to reduce Cu(II) upon irradiation, but it also increases the solubility of the Cu(II) in most organic solvents. Also, importantly, the amine serves to stabilize Cu(I) once it is formed. Each of these factors plays a role in controlling the efficiency and effectiveness of the photo-initiated CuAAC reaction.

In this study we demonstrate both spatial and temporal control over the CuAAC by the photoinduced generation of the active form of the catalyst Cu(I) to initiate the CuAAC reaction. The efficiency and kinetics of the photo-CuAAC reaction are shown to be comparable to other traditional CuAAC reaction approaches, and the reaction timescale and progress are evaluated under a range of different initiation and reaction conditions such as different photoreduction
mechanisms and complexing ligands.

Scheme 3.1 The photo-mediated CuAAC reaction is shown with two possible photoinitiating pathways (A and B) where in both cases the catalytic Cu(I) required for the CuAAC reaction is generated by the reduction of Cu(II) to Cu(I). The electron for reduction is either donated by (A) aliphatic tertiary amine ligands or (B) from radicals generated via a conventional radical photoinitiator.

Additionally, the mechanism of catalyst turnover for the Cu- Complexes system was characterized. We demonstrate the selectivity and versatility of this overall approach via a sequential and orthogonal photo-CuAAC step growth reaction that is followed by chain growth acrylate homopolymerization.

Results and Discussion

The photo-CuAAC reaction has been shown to be simple and robust with high yields and is ideally suited for further development and implementation. Due to its recent development, this approach has not been explored in detail and to-date, few papers have been published regarding this technique, particularly in examining the role of the amine type and how that affects the photo-initiation and CuAAC reaction.

As the stability of Cu(I) generated from different Cu(II) complexes varied based on the instability of the radicals that are formed during the photolysis process, it was expected that the
Cu(I) stability would also vary with the radicals produced from a tertiary amine to a primary amine. Mixtures of Cu(II) chloride with either a primary, secondary or tertiary amine ligand were formed and tested. As shown in Figure 3.1, the tertiary amine, tetramethylethylenediamine and the secondary amine, dimethylethylene diamine, initiated the CuAAC reaction between benzyl azide and phenylacetylene as observed by the FTIR results. On the other hand no reaction was observed when a primary amine, ethylenediamine, was used as the ligand. This observation implies that the primary amine was not able to lead to the desired Cu(I) catalyst. Interestingly, it has been previously reported that when aliphatic amine ligands chelate to Cu(II), they undergo LMCT upon UV irradiation, and the primary products of the photolysis are Cu(I) and an intermediate radical.\textsuperscript{15} With these unreactive amines, it is possible that the reverse reaction between the primary products of the photolysis results in re-oxidization of Cu(I) back to Cu(II). This kind of back electron transfer has been reported previously in copper photochemistry.\textsuperscript{21,22,23} It is inferred that the stability of the generated radicals is one critical element necessary to have successful and fast ligation. Secondary, and even more so tertiary, amines produce radicals that are more stable than primary radicals, thus allowing the Cu(I) to persist in solution, resulting in subsequent catalysis of the CuAAC reaction. FTIR results also show that when the secondary amine/Cu(II) complex is used to initiate the reaction, the initial reaction rate is similar to the tertiary amine. Then, the reaction rate starts to change, and the average reaction rate is 40% slower than when the analogous tertiary amine is used. These results indicate that although the aliphatic amine-based ligands are able to promote LMCT and allow for the benefit of a controllable catalyst system to initiate the CuAAC reaction, the stability of the radicals formed is also of importance in dictating the overall reaction.
Figure 3.1 (a) Real time infrared spectroscopy shows the conversion of 200 mM benzylazide as it reacts with 200 mM phenylacetylene and 10 mM CuCl$_2$ complexed with either 10 mM of N,N,N',N'-Tetramethylethylenediamine (tertiary amine, open squares), N,N'-Dimethylethylenediamine (secondary amine, open circles), or ethylenediamine (primary amine, filled circles). The samples were exposed to 5mW/cm$^2$ of light centered around 365 nm for 100 minutes. The tertiary amine ligand was found to accelerate the reaction 40% more than the secondary amine. However, the primary amine was unreactive toward the photo-CuAAC. (b) A proposed path for photolysis process of Cu(II)-N base ligands is summarized. Here, the Cu(II)(amine) undergoes LMCT upon irradiation. The primary products of the photolysis are Cu(I) and an intermediate radical (L').

Various tertiary amine ligands, as presented in Figure 3.2, were used in the photoreduction of Cu(II). When mixed with Cu(II)Cl$_2$, all the tertiary amines were shown to catalyze the CuAAC reaction successfully, though at rates that differed by nearly an order of magnitude. The average reaction rate of these catalyst systems was measured using FTIR and is shown in Figure 3.3. The reaction rates along with the initiation times for the CuAAC reaction between benzyl azide and phenylacetylene varied upon exposure. The initiation times were 300 minutes in all samples. Generally, the reactions start slowly in the first 10 minutes followed by a rate acceleration followed by a plateau after 250 minutes. The results indicate that as the number of nitrogen atoms on the ligand increases, the CuAAC reaction rate also increases until it reaches a maximum with the tri-
dentate amine ligand, PMDETA. However, the reaction rate is observed to slow down again when an amine with four nitrogen atoms (HMTETA) is used to initiate the reaction.

We hypothesize that, at least through the triamine, the increased number of amines increases the ligand-metal complex strength and binding, resulting in an increase in the quantum yield of the photolysis process which leads to higher Cu(I) concentrations and more rapid reaction kinetics. However, by monitoring the photoreduction of Cu(II) to Cu(I) by EPR and UV-Vis, we observed that the concentration of Cu(I) in the reaction mixture is not the only factor necessary to achieve efficient, rapid cycloaddition, as shown in Figure 3.4. Both UV-vis and EPR experiments exhibit similar trends. HMTETA (hexamethyl-triethylenetetramine) showed only a 5% reduction in Cu(II) concentration to Cu(I) after 40 minutes of irradiation. However, mixing CuCl₂ with excess TEA spontaneously reduces Cu(II) to Cu(I) entirely as evidenced by EPR and UV-Vis data, consistent with previous studies.²⁴

Figure 3.2 Chemical structures of aliphatic tertiary amine ligands used in this study.
Figure 3.3 The average reaction rate of the photo-CuAAC reaction is presented under both light and dark curing conditions in the presence of different tertiary amine dentate ligands. The plot indicates that under dark curing excess amines do not reduce Cu (II) by themselves to any significant extent, other than for TEA. The reaction mixture consisted of a solution of 200 mM benzyl azide, 200 mM phenylacetylene and 10 mM CuCl$_2$/tertiary amine ligand at a ratio of 1:4.

Light cured samples were exposed to 5mW/cm$^2$ of light centered around 365 nm.

Surprisingly, HMTETA showed the least reduction in Cu(II) concentration upon irradiation with a reaction rate that is 4 times faster than a mixture of Cu(II)/TEA. These results raise the question whether the Cu(I)-L that forms after the photolysis process has a different reactivity for forming the copper (I) acetylide. TMDA (tetramethyldiamine), and PMDETA have a significant effect on the photoreduction of Cu(II) and result in an intermediate reaction rate. In contrast to TEA, other amine ligands including TMDA, PMDTA and HMTETA show almost zero reaction in the dark within the time limit of the experiments. The difference between TEA and the other ligands initiated in the dark is significant and indicated by the fact that it is the only one that is effectively non-zero. These results also indicate that self-reduction by excess amine is limited to TEA, which strengthens the temporal control that can be achieved by the photo-CuAAC reaction using alternate Cu(II)salt/amine systems. Complete temporal control is achieved only in initiating
the start of the reaction. After shining light, it is not possible to turn the reaction off simply by extinguishing the light due to the long-lived Cu(I) catalyst. Despite this, turning off the light does significantly slow down the reaction due to reoxidation of the Cu(I) and the lack of continued generation of the catalyst.\textsuperscript{11,12}

**Figure 3.4** (a), Cu(II) concentrations obtained from EPR as a function of the irradiation time for various 3.5mM CuCl\textsubscript{2}/tertiary amine ligands at a ratio of 1:4 in DMF. (b), UV-Vis absorbance at 800 nm as a function of time for 3.5 mM CuCl\textsubscript{2}/tertiary amine ligand with a ratio of 1:4 in DMF. Samples were irradiated with 365 nm at 20 mW/cm\textsuperscript{2}.

It is well known that the active catalyst Cu(I) in its uncomplexed form is not stable and can readily oxidize through one of many reactions including that with dissolved oxygen. Since
oxidation of Cu(I) would significantly alter the reaction kinetics, the stability of Cu(I) in the photoinitiated Cu(II)salt/amine system was evaluated at various conditions. Moreover, it is well known that the redox potential of C(I) varies significantly with different ligands.\textsuperscript{25,26,27} Figure 3.5 shows that the reaction progress for samples prepared with equimolar concentrations of PMDETA and Cu(II) reacted at ambient conditions is similar to samples sparged with either argon or oxygen purges. These results indicate that the reaction rate is similar whether oxygen is present in these systems or not, implying that the Cu(I) catalyst is stable to oxidation under these conditions, likely stabilized by continued complexation with the amine ligand. This result supports previous work in which ligands were seen to stabilize Cu(I) toward oxidation by dissolved Oxygen.\textsuperscript{28} The amine here is not only working as an electron transfer center during the catalyst generation, but it also acts as a stabilizing agent for the otherwise unstable Cu(I). The ability of the Cu(II)salt/amine system to initiate the CuAAC reaction with excellent temporal control while simultaneously overcoming oxygen inhibition will enable thin film and bulk reactions where otherwise oxygen is found to inhibit the reaction.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure3_5.png}
\caption{Real time infrared spectroscopy shows the conversion of 200 mM benzylazide as it reacts with 200 mM phenylacetylene and 6.7 mM CuCl\textsubscript{2}/PMDETA in various atmospheres including the addition of a radical scavenger (open triangles), in ambient atmosphere (open triangles), in the presence of pure oxygen (open circles) and argon sparging ( filled circles).}
\end{figure}
Since the CuAAC reaction kinetics are second order relative to the concentration of the Cu(I) catalyst, any reduction in the active Cu(I) catalyst concentration is expected to have a pronounced influence on the reaction rate. As shown in Figure 3.5, the addition of a radical scavenger, hydroquinone, to the reaction mixture of CuCl₂/PMDETA leads to faster reaction rates and higher conversions of the azide. It is clear that in these Cu(II)-ligand photoinitiating systems, the radical scavenger influences the reaction rate by increasing the concentration of the active catalyst Cu(I) by preventing any reverse reaction of the radical with the Cu(I). The presence of the radical scavenger consumes the generated radicals, and thereby prevents the re-oxidation of Cu(I) which would decrease its concentration and subsequently the reaction rate.

It was also observed that varying the ratio of the metal to ligand influences the reaction rate significantly. Our results showed that as the ligand to metal ratio increased, the reaction rate accelerates until it reaches a maximum at a ratio of ligand to metal of 4 to 1, with respect to the concentration of Cu, as shown in Figure 3.6. Increasing the ligand concentration further slows the reaction, potentially due to the possibility for multiple ligands being chelated to the same Cu(II) atom. To investigate further whether increasing the ligand concentration would influence the rate of the photoreduction of Cu(II), we monitored the d-d transition at 800 nm of a mixture of CuCl₂/PMDETA using UV-Vis and the absorption of the paramagnetic Cu(II) by EPR with a 1:1 and 1:4 stoichiometric ratio of Cu:ligand when exposed to a 365 nm light source. The EPR and UV spectra showed continuous reduction of Cu(II) to Cu(I), as shown in Figure 3.7. Both samples exhibit a very similar overall reduction in the Cu(II) concentration upon irradiation. The rate acceleration seems to be solely a result of increasing the basicity of the system as shown in the previous studies.29
Figure 3.6  Average reaction rates (M/min) at different stoichiometric ratios of ligand to metal ranging from 1:1 to 1:15 Cu:PMDETA. The reaction rate accelerates until it reaches a maximum at a ratio of ligand to metal of 4 : 1 with respect to the Cu concentration.

Figure 3.7  (a), Cu(II) concentrations obtained from EPR as a function of the irradiation time for 3.5mM CuCl$_2$/ PMDETA with a ratio of 1:4 and 1:1 in DMF. (b), UV-Vis absorbance at 800 nm as a function of time for 3.5 mM CuCl$_2$/ PMDETA with a ratio of 1:4 and 1:1 in DMF. Samples were irradiated with 365 nm at 20 mW/cm$^2$. Both mixtures showed very similar photo-reduction rate.
Sequential photo-CuAAC reaction and acrylate polymerization

Photopolymerization utilizing the CuAAC reaction combining radical-based photoinitiators and copper salts to initiate the polymerization process with exquisite control of the reaction has been demonstrated in the literature by the formation of surface patterning of PEG hydrogels\textsuperscript{11,14}, bulk crosslinked triazole-containing polymers from multifunctional azide and alkyne monomers\textsuperscript{12}, and block copolymers bearing azide and alkyne functionalities.\textsuperscript{13} Polymerizations using radical-based photoinitiators as reducing agents were found to be very efficient; however, the potential for radicals of this type to initiate other reactions exists. One particular advantage of the photoinduced CuAAC via LMCT of Cu-complexes compared to other methods is that it offers spatiotemporal control with great selectivity to the CuAAC reaction in the presence of a variety of functional groups. Herein, we describe a method in which a material with two different functional groups is utilized for the orthogonal and sequential synthesis of brush polymers. The ease of this novel method comes from the nature of the dual functional groups on the same molecule that enables two orthogonal reactions to occur within the same solution. The alkyne group of propargyl acrylate participates in the photo-CuAAC reaction with benzyl azide to form a triazole via photoinduced LMCT of the Cu-PMDETA complex; whereas the acrylate group of the propargyl acrylate subsequently undergoes photopolymerization via initiation by a radical thermal initiator to produce a linear polymer with side chain triazole groups, as illustrated schematically in Figure 3.8. We mentioned earlier that one of the primary products of the photolysis process of Cu-PMDETA is an intermediate radical which can re-oxidize Cu(I) back to Cu(II). Experimentally, this radical appears to be insufficiently reactive to initiate conventional radical polymerization of the acrylate group.

In an NMR tube a mixture of benzyl azide/propargyl acrylate at a 1:1 ratio was mixed with Cu-
PMDETA and AIBN in DMF-d7. After 180 minutes of exposure to 365 nm light at 5mW/cm², more than 95% of the alkyne units were consumed to form triazoles while no acrylate groups had reacted. ¹H NMR demonstrated the formation of the triazole upon UV irradiation with 95% conversion. The successful transformation of azide and alkyne groups into triazoles was confirmed by the disappearance of the terminal proton on the alkyne (2.84 ppm) and the appearance of the proton of the triazole rings (8.20 ppm) in the ¹H NMR spectra. Further, the methylene group neighboring the azide, and the alkyne (4.41 and 4.78 ppm) shifted to (5.33 and 5.76 ppm) due to the formation of the triazole. The ¹HNMR spectra after the triazole formation shows signal broadening due to the presence of paramagnetic species in the NMR sample, as shown in Figure 3.8. (b). Upon heating to 65°C to decompose the AIBN into radicals that are capable of initiating the acrylate polymerization, the acrylate reacted to almost 80% conversion and a linear polymer was formed as evidenced by the shift of the three acrylate protons (5.95, 6.20, and 6.44 ppm to 1.9, 2.3 and 2.55 ppm, respectively) due to the formation of the polymer backbone. GPC result also confirmed the formation of the linear polymer (Mn=23,442 g/mole).

The sequential reaction was also followed by FT-IR spectroscopy. Here, the two reactions were shown to be independent of each other as indicated by essentially zero acrylate conversion occurring during the cycloaddition reaction, as shown in Figure 3.9. The LMCT of Cu-PMDETA would generate radicals via the photolysis process, but as also demonstrated by the NMR results, these radicals are unable to attack the double bond of the acrylate group as indicated by the stability of the FTIR monitored acrylate peak at 800 cm⁻¹ during the cycloaddition of the azide and the terminal alkyne. On the other hand, subsequent exposure of the product to high temperatures to initiate the acrylate homopolymerization via the thermal initiator AIBN does not impact the triazole formed via the alkyne azide reaction due to the thermal stability of the triazoles.³⁰
By enabling two sequential, orthogonal reactions as described above, we have demonstrated that selective pre-functionalization can be achieved through a Cu(I)-catalyzed click reaction that also exhibits spatiotemporal control.

Figure 3.8. $^1$H NMR spectra of a sequential photo-CuAAC reaction and acrylate indicating the formation of the triazole via CuAAC and then radical homopolymerization of the acrylate: (a) a mixture of benzyl azide and propargyl acrylate before reaction, (b) Upon UV-irradiation LMCT promoted CuAAC click reaction between the benzyl azide and the alkyne group of propargyl acrylate (c) followed by thermal initiation using heating to 65 °C to polymerize the acrylate group of the propargyl acrylate and form a linear polymer. The reaction mixture was 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl$_2$-PMDETA, and 2 wt % AIBN in DMF-d.
Figure 3.9. Functional group conversion (azide for the photo-CuAAC and acrylate) as a function of time for the sequential photo-CuAAC reaction and radical-mediated acrylate polymerization. The CuAAC reaction is initiated using 365 nm light for 50 minutes (cross), followed by heating to 65°C to initiate the radical-mediated acrylate polymerization. The reaction mixture contained 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl₂-PMDETA, 2 % wt AIBN, and 10 % wt DMSO.

Conclusions

The photo-CuAAC click reaction is a promising technique that offers tremendous control and capabilities for expanding further the potential implementations of this powerful reaction. We have evaluated and described methods for improving the efficiency of photoinitiation using Cu(II)-complexes. Tertiary aliphatic amine ligands were used as an electron transfer species to reduce Cu(II) upon irradiation while also functioning as an accelerating agent and as protecting ligands for the Cu(I). Moreover, this catalyst system was demonstrated to be effective, adaptable to organic and aqueous media, and highly selective to the CuAAC reaction. However, further work is required to optimize these systems as extended irradiation times as well as UV range that can be used remain an issue. Prolonged irradiation can decompose azides especially at high irradiation intensities and at shorter wavelengths. Uniquely, photo-CuAAC via LMCT was shown to be very selective.
towards the CuAAC reaction and was used to synthesize triazole side chain polymers using a combination of photo-CuAAC and subsequent homopolymerization of the ene with chain growth polymerization, offering sequential and orthogonal reactions within the same polymer.

**Experimental**

**Materials**

Phenylacetylene (Sigma Aldrich), Cu(II) chloride (Sigma Aldrich), copper sulfate pentahydrate (Sigma Aldrich), triethylamine (TEA) (Sigma Aldrich), tetramethyldiamine (TMDA) (Sigma Aldrich), N,N,N’,N”’,N’”-pentamethyldiethylenetriamine (PMDTA) (Sigma Aldrich), 1,1,4,7,10,10-Hexamethylenetetramine (HMTETA) (Sigma Aldrich), dimethylformamide (Sigma Aldrich), tetrahydrofuran (Sigma Aldrich), propargyl acrylate (Sigma Aldrich) were used without further purification. Benzyl azide was synthesized according to the literature.31

**Methods**

**Fourier Transform Infrared Spectroscopy (FT-IR)**

FT-IR was outfitted with a horizontal transmission stage and combined with a variable pathlength liquid cell with CaF$_2$ windows. Specimens were prepared by forming a 50 µm thin film between salt crystals. All specimens were irradiated with an EXFO Acticure high pressure mercury vapor short arc lamp equipped with either a 365 nm bandgap filters. The radiation intensity of the mercury lamp was determined using an International Light IL1400A radiometer equipped with a GaAsP detector and a quartz diffuser.

A solution of THF/DMF (4:1) was mixed with 0.2M phenylacetylene, 0.2M benzyl azide, and 0.01M 1:1 copper:ligand mixture. All reactant concentrations were kept the same in all
experiments unless otherwise mentioned. All samples were monitored by FTIR first in the dark for an hour to ensure that the reactions were not initiated in the absence of light. FTIR was used to monitor the disappearance of the azide peak in the region between 2213 and 1900 cm$^{-1}$. The azide peak is convoluted with the DMF peaks in this region. The contribution of the azide peak was calculated by subtracting the DMF spectra from the reactive solution spectra. The conversion also was calculated from the change in the azide peak throughout the reaction. The reaction rate was calculated by averaging over several minutes.

It is worth noting that, although it is well known that organic azides can photochemically decompose when irradiated with UV light below 400 nm, we found the azide decomposition rate to be very low, i.e., less than 2% when a 50 μm thin film comprised of a blank sample of azide was irradiated for 5 hours through a 365 nm bandpass filter with a light intensity of 5mW/cm$^2$. However, by utilizing Cu(II) complexes that exhibit LMCT in the visible region or using dyes to absorb visible light and reduced Cu(II) complexes, decomposition can be entirely avoided.

**NMR**

$^1$H NMR spectra were recorded on a Bruker Avance-III 300 NMR spectrometer at 25 °C in CDCl$_3$. All chemical shifts are reported in ppm relative to tetramethylsilane (TMS). NMR was used to identify the triazole product in samples of similar composition to those used for the FTIR experiments. For NMR samples, the desired reactants were combined in a 20 ml scintillation vial and stirred rapidly at ambient temperature. Samples were then irradiated with 5 mW/cm$^2$ intensity from an Acticure 4000 lamp using a 365 nm bandgap filter. The resulting mixture was extracted with diethyl ether and water. The organic layer was separated, dried using saturated sodium chloride solution and sodium sulfate anhydrous, filtered, and evaporated to give the triazole product. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.82 (ddd, $J$ = 4.2, 3.5, 1.8 Hz, 2H), 7.68 (s, 1H), 7.50 –
7.30 (m, 8H), 5.60 (s, 2H).

_Ultraviolet--Visible Spectroscopy (UV-VIS), and Electron Paramagnetic Resonance (EPR)_

In a UV cuvette or EPR tube, a fresh mixture of CuCl₂/tertiary amine ligand 0.0035 M with 1:4 or 1:1 ratio of Cu: ligand was irradiated with an EFXO Acticure high pressure mercury vapor short arc lamp equipped with a 365 nm bandgap filter at an intensity of 20.0 mW/cm². UV and EPR spectra were taken at multiple time points to follow the evolution of the absorption spectra. EPR measurements were performed on an X-band Bruker Elexsys 500 spectrometer equipped with a ultra-high sensitivity cavity (SHQE cavity, Bruker). Spin quantitation was performed by double integration of the spectra. Different concentrations of CuCl₂ in DMF were used as standards. All spectra were recorded at ambient temperature using the following parameters: microwave frequency 9.88 GHz, center field 3377 G, sweep width 1100 G, modulation amplitude 20G, modulation frequency 100 kHz, microwave power 2 mW, number of scans 2.

**Sequential photos-CUAAC reaction and acrylate.**

The ¹H NMR sample was prepared by mixing 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl₂/PMDETA and 2 wt % AIBN in DMF-d7. The NMR tube was irradiated with an EFXO Acticure high pressure mercury lamp equipped with a 365 nm bandpass filter at an intensity of 5.0 mW/cm² for almost 3 hours, following by heating the tube in an oil bath to 65 °C for several hours.

FTIR samples were prepared by mixing 0.43 mmole of benzyl azide, 0.43 mmole propargyl acrylate, 0.043 mmole of CuCl₂/PMDETA, 2 wt % AIBN, and 10 wt % DMSO. The sample was
placed between two NaCl crystals (~ 10 μm thickness) which were sealed to prevent solvent evaporation. FTIR was used to monitor the disappearance of the azide peak at 2100 cm\(^{-1}\), and the acrylate peak at 800 cm\(^{-1}\). The sample was irradiated with an EFXO Acticure high pressure mercury lamp equipped with a 365 nm bandpass filter at an intensity of 5.0 mW/cm\(^2\), and irradiation was ceased after 50 minutes. The sample then was heated in an IR heating cell for another 50 minutes.

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References


Chapter 4

Hexylamine initiates bulk-polymerization of Copper-Catalyzed azide-alkyne cycloaddition reaction

Abstract

A mixture of Cu(II) and hexylamine was used to initiate polymerization via the copper(I) catalyzed azide alkyne cycloaddition (CuAAC) reaction in bulk to form a crosslinked polymer network. The catalytic system was shown to be effective, and it enabled the polymerization to proceed to near completion at ambient temperature. Increasing the ratio of amine to copper from 1 to 4 increases the CuAAC reaction rate significantly from 4 mM/min for a 1:1 ratio of Cu(II):hexylamine to 14mM/min for a 1:4 ratio. The concentration dependence of the amine on the reaction rate enables the polymerization rate to be controlled simply by manipulating the hexylamine concentration. The rate dependence and UV-Vis measurements indicate that hexylamine does not act as the sole reducing agent, and it aids in shifting the equilibrium of Cu(II) towards a Cu(I) species that initiates the reaction.
Introduction

Bulk polymerization of multifunctional monomers to produce 3D polymer networks has a variety of advantages in processing, molding, and molecular architecture. Monomers are generally easier to process than polymers and can be polymerized in situ to a final product that requires little to no further processing. Coatings, adhesives, dental materials, and 3D prototyping apply bulk polymerization because the monomer mixture is a low viscosity liquid, and after processing becomes a rubbery or glassy solid that is ready for use. A variety of reactions have been used to bulk polymerize monomers. The copper(I)-catalyzed azide-alkyne cycloaddition reaction, CuAAC, has the advantages of being a prime example of click reaction.\textsuperscript{1,2} The CuAAC reaction is one of the most successfully implemented click reactions due to the orthogonally, chemoselectivity, fidelity, and exquisite control of reaction. These “click” attributes facilitated its widespread application in a variety of science fields such as drug discovery\textsuperscript{3,4}, surface modification\textsuperscript{5,6}, and materials science\textsuperscript{7-9} among others.

The CuAAC reaction has been utilized to construct polymer networks that possess unique properties.\textsuperscript{10-14} One of the biggest advantages of CuAAC polymer networks is that it is formed via a step-growth mechanism resulting in a homogeneous network, narrow glass transition temperatures, which leads to beneficial properties such as a delay in gelation and low shrinkage stress compared to chain-growth networks. The CuAAC reaction has the added advantage of forming rigid-aromatic triazole linkers as a result of polymerization which significantly influences the glass transition temperature, stiffness and toughness of the network.\textsuperscript{10-14} Additionally, the CuAAC chemistry allows utilizing orthogonal chemistries and a variety of azide and alkyne monomers to tune the chemical and mechanical properties.
Traditional conditions for catalyzing the CuAAC reaction utilize a Cu(II) salt, often the sulfate, and sodium ascorbate in aqueous media or in a mixture of organic and aqueous media\textsuperscript{1}. This catalytic system has been successful and widely used. However, the solubility of this system in organic media is very limited. To overcome this limitation, several groups presented different catalytic systems to initiate the reaction in organic solutions\textsuperscript{15-18}. This issue is more pronounced when dealing with bulk polymerization of multifunctional azides and alkynes which is generally carried out in neat conditions, which raised the issue of designing a catalytic system that can work effectively in this environment, protect the formed Cu(I) and prevent polynucleation of the copper-acetylide. CuAAC bulk polymerizations have been much less explored, likely due to the azide safety concerns\textsuperscript{19,20} as well as difficulties in finding soluble catalyst species in bulk where most of the commercially available inorganic copper salts have limited solubility in organic media\textsuperscript{16}.

Finn and coworkers first demonstrated bulk polymerization of multifunctional azides and alkynes between two plates of copper\textsuperscript{13}. Taking advantage of the affinity of triazoles towards transition metals, the polymer network yielded adhesives which were twice as a strong as a commercially available metal adhesive. Others initiated the bulk azide-alkyne reaction using Cu(I) salts such phosphine based copper(I) complexes and copper(I) acetate\textsuperscript{21-23}. These Cu(I) complexes exhibited better organic solubility than inorganic copper salts; however, significant amounts of undesired side-products are generated such as Staudinger reduction of azide by phosphine based ligands\textsuperscript{24}. The thermodynamically unstable Cu(I) ion can either disproportionate or be oxidized by oxygen. Consequently, the active catalyst Cu(I) for CuAAC is often generated \textit{in situ} by employing Cu(II) with a reducing agent.\textsuperscript{8} Recently our group presented a versatile method to initiate bulk polymerization in neat conditions with great spatiotemporal control.\textsuperscript{10,11} This approach involves utilizing radical generator, i.e., a photoinitiator, with Cu(II) salts. The photoinitiator generates
radicals upon light exposure and these radicals subsequently reduce C(II) to Cu(I), the active form of the catalyst.\textsuperscript{25} Despite its successful implementation, side reactions are possible when radicals are generated that react with the azide to generate nitrogen gas. Furthermore, the spatiotemporal control associated with photoinitiation is not necessary for many applications. Thus, an easy approach to process a monomer mixture containing Cu(II) and add a reducing agent that then induces polymerization will contribute to the development and implementation of CuAAC polymer networks.

Amines have been widely used to reduce Cu(II) and drive ATRP,\textsuperscript{26} atom transfer radical polymerization. Primary amines, in particular, have been extensively employed as reducing and capping agents for metal nanoparticle synthesis\textsuperscript{27}. Inspired by these reactions, we hypothesized that primary amines in combination with Cu(II) will also catalyze CuAAC reactions including bulk polymerization. This contribution deals with the neat bulk CuAAC polymerization of multifunctional azides and alkynes using a mixture of Cu(II)/ligands and primary amine as a reducing agent. Bulk polymerization using amines has the advantage of converting easily processable monomers to a cross-linked network. Direct addition of Cu(I) has been used to start the polymerization; however, Cu(I) is sometimes difficult to dissolve and often requires heat and time. Cu(II) will not set off the reaction, decreasing the likelihood of premature polymerization. In addition, since no photoinitiator is required for polymerization, a thick film is easily formed by uniform curing throughout the depth of the material.
Results and discussion

A reaction between a trifunctional alkyne (trilkayne-ether), a difunctional azide (neopentylidiazide), and Cu(II)Cl₂/PMDETA, as a catalyst, was chosen as a model system to test the hypothesis with the structures presented in Scheme 1.4 (a). Using PMDETA as a ligand to chelate the copper where the presence of hydroxyl groups in the monomer structure improves the solubility of copper in the monomer. The azide monomer, neopentylidiazide, has a high molecular weight, making it safe to handle in such conditions though the adiabatic temperature rise of the reaction should always be considered when designing a bulk-polymerizable CuAAC reaction system. A mole ratio based on functional groups of 50:50:1 of azide: alkyne: Cu(II)Cl₂/PMDETA was used in combination with varying concentrations of the chosen amine, hexylamine, as shown in Figure 4.1. The reaction kinetics were investigated using FTIR, which was used to monitor the disappearance of the azide peak at 2100 cm⁻¹ as a function of time. Increasing the ratio of amine to copper from 1 to 4 increases the reaction rate significantly from 4 mM/min for 1:1 ratio of Cu(II):hexylamine to 14mM/min for 1:4 ratio; however, all samples achieved nearly complete conversion to yield a cross-linked polymer network, albeit requiring different reaction times. The concentration dependence of the amine on the reaction rate enables the polymerization rate to be controlled simply by manipulating the hexylamine concentration. The 1:4 mole ratio of copper:hexylamine initiates the reaction to 70% conversion in 10 minutes and requires an additional 25 minutes to reach 96% conversion. The polymerization slows due to a combination of reactant consumption and vitrification of the polymer that limits the mobility of the reacting species. In contrast, no reaction was observed within 2 hours, when no amine was used, which highlighted the amine’s role in the initiation process.
a). CuAAC monomers

\[
\text{Neopentyldiazide} \quad \text{Trialkyne-ether}
\]

**Scheme 4.1**: (a) CuAAC monomers used for polymer network. (b) Schematic representation of the polymerization of diazide and tri-alkyne monomers to form a cross-linked polymer network.

**Figure 4.1**: Mid-IR kinetic study of the azide conversion as a function of time in a thin sample of neopentyldiazide, trialkyne-ether, CuCl\textsubscript{2}/PMDETA, and hexylamine. The mole ratio based on functional groups is 50:50:1 of azide: alkyne: copper. Hexylamine concentration is varied as 0 (open diamond), 1(cross), 3 (open circle) and 4 (open square) with respect to the Cu mole ratio. No reaction was observed in the absence of amine while increasing the reaction rate increased significantly with increase in the amount of hexylamine.
Various amines were used in 50:50:1:4 azide: alkyne: copper: amine formulations to initiate the CuAAC polymerization and explore the role of the amine further as shown in Figure 4.2. Aliphatic primary amines, analogous in structure to hexylamine, such as butylamine, pentyamine and heptylamine showed similar kinetic profiles, which suggested that the alkyl group length was insignificant.

Aliphatic primary amines might initiate the CuAAC reaction by reducing the catalytically inactive copper(II) to the active form of the catalytic copper(I), while possibly simultaneously working also as capping agent that protects the Cu(I) from side reactions, and preventing polynucleation of the copper-acetylide. To evaluate this possibility, we compared the kinetic profile of hexylamine to a tertiary amine triethylamine, TEA, which is known to be a good copper(II) reducing agent and capping agent, to initiate the CuAAC reaction in bulk and with the same molar species ratios that were used for the copper(II)/hexylamine system. TEA showed much slower kinetics than when hexylamine was used to initiate the bulk polymerization. Previous studies showed that an excess TEA with respect to copper(II) is sufficient to reduce all Cu(II) completely and quickly to Cu(I). Despite the high concentration of the active form of the catalyst, copper(I), at the beginning of the polymerization process, the kinetics are still very slow. These results suggest that the nature of Cu(I)/L species is critical to enhancing the CuAAC rate.

![Figure 4.2](image.png)

**Figure 4.2**: Mid-IR kinetic study of the azide conversion as a function of time of a thin sample of neopentyl diazide, trialkyne-ether, CuCl2/PMDETA, and amine. The molar ratio based on functional groups is 50:50:1:4 of azide: alkyne: copper: amine.
To examine the reactivity of Cu(I)/hexylamine and Cu(I)/TEA, a system of 0.2M phenylacetylene, 0.2M benzylazide, 0.02M copper(I) iodide, and 0.08M of amine, hexylamine or TEA, in THF was used to test the reactivity in solution. The Cu(I)/hexylamine (reaction rate of 20mM/min) was more reactive with a reaction rate 12.5 times faster than Cu(I)TEA (reaction rate 1.6mM/min) as shown in Figure 4.3.

\[ \text{Figure 4.3.} \text{ Mid-IR kinetic study of the azide conversion as a function of time of a thin sample of 0.2M phenylacetylene, 0.2M benzylazide, 0.02M copper(I) iodide, and 0.08M of amine, (hexylamine or TEA), in THF.} \]

A system of 0.2M benzyl azide, 0.2M phenylacetylene and 0.02M of Cu(II) with varying amine concentration from 0.01M to 0.2M was used to investigate the CuAAC reaction rate as a function of the hexylamine concentration as shown in Figure 4.4. Increasing the molar ratio of hexylamine to copper from 0.5:1 to 4:1 increases the reaction rate significantly from 0.5 mM/min to 7mM/min where the reaction reached complete conversion within 25 minutes. The rate acceleration caused by increasing hexylamine leads to a plateau at molar ratios higher than 4:1 hexylamine : copper.
We observed that when phenylacetylene was added to a solution of Cu(II) and hexylamine, a yellowish solid precipitate formed almost instantly, and more precipitate is formed when additional alkyne is added, suggesting that the Cu(II) was reduced to Cu(I) and formed the Cu(I) acetylide, as shown in Figure 5.4 (a). No solid formed when phenylacetylene was added to a solution containing Cu(II) only. Measurement of the UV-Vis spectrum of Cu(II) at 650 nm which is associated with d-d transition of Cu(II) d⁹ configuration was used to monitor the Cu(II) reduction. Amines, in general, have been used to reduce Cu(II). However, a mixture of 0.01 M Cu(II)/hexylamine with a mole ratio of 1:4 of copper:hexylamine in methanol showed no change in UV-Vis spectra over 16 hours as shown in Figure 5.4(b). A decrease in the 650 nm peak which represents the transformation from the Cu(II) d⁹ configuration to the Cu(I) d¹⁰ configuration was only observed when an alkyne, e.g., phenylacetylene, was added to the Cu(II)/hexylamine mixture as shown in Figure 5.4 (c). These data suggest that hexylamine only reduces Cu(II) to Cu(I) in the presence of the alkyne.

Figure 4.4: Average reaction rate of the CuAAC reaction as a function of hexylamine concentrations for a thin sample of 0.2M phenylacetylene, 0.2M benzylazide, 0.02M copper(II)Cl₂/PMDETA in methanol.
Figure 4.5: (a) Precipitation of Cu(I) acetylide after the addition of phenylacetylene to a solution of Cu(II) and hexylamine. (b) UV-Vis absorbance for 1.0 mM CuSO$_4$ with hexylamine at a ratio of 1:4 in methanol. (c) UV-Vis absorbance for 1.0 mM CuSO$_4$, 1.0 mM CuSO$_4$ and hexylamine at a ratio of 1:4, 1.0 mM CuSO$_4$ with hexylamine, and phenylacetylene with a ratio of 1:4:5 in methanol.
On the basis of these observations and experimental results, it is proposed that Cu(II) exists in an equilibrium state with its other oxidation states. However, once the alkyne is added, the reactive Cu(I)/hexylamine species deprotonates the terminal alkynyl hydrogen, and a solid precipitate is formed which is an irreversible process shifting the equilibrium toward forming more Cu(I) species, resulting in Cu(II) reduction to Cu(I) as observed from the UV-Vis results. The amine’s role in this process is also evidenced by the positive order in hexylamine concentration observed in Figure 4.1. The rate dependence and UV-Vis measurements indicate that hexylamine does not act as the sole reducing agent, and it aids in shifting the equilibrium of Cu(II) towards a Cu(I) species.

Conclusion

In summary, the stoichiometric CuAAC reaction between an azide and alkyne is initiated by Cu(II) and hexylamine. The reaction proceeds efficiently to near completion to yield a crosslinked polymer network from appropriate multifunctional azides and alkynes at ambient temperature where the polymerization rate was controlled by controlling the amine concentration. The Cu(I)/hexylamine (or other alkyl amines) was shown to be reactive as a catalyst of the CuAAC reaction though hexylamine was not able to reduce Cu(II) to Cu(I) by itself, and only in the presence of the three component mixture of Cu(II), hexylamine and an alkyne, was reduction of Cu(II) to Cu(I) observed. This work presents a facile approach to in situ reduction of Cu(II) to Cu(I) in a bulk polymerizing resin by the addition of an alkyl amine.

Experimental

Materials

1,1,1-tris(hydroxymethyl) propane , propargyl bromide solution 80 wt% in toluene, sodium hydroxide, neopentyl glycol diglycidyl ether, lithium perchlorate, sodium azide, copper(II)
chloride, copper(I) iodide, N,N,N′,N′,N′″-pentamethyldiethylenetriamine (PMDTA), hexylamine, butylamine, pentylamine, heptylamine, triethylamine, aniline, tetrahydrofuran, dimethyl sulfoxide, and acetonitrile were obtained from Sigma-Aldrich, and were used without further purification.

**Monomers synthesis**

**Synthesis of 1-(Prop-2ynyloxy)-2,2-bis(prop-2-ynyloxy)methyl)butane**

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An aqueous solution of 40% NaOH was prepared, and then 150 mL DMSO was added to the mixture. After stirring for 20 minutes, 1,1,1-tris(hydroxymethyl) propane (4.93g, 0.037 mol) was added to the solution and stirred for additional 20 minutes. Propargyl bromide (22.25 g, 0.15 mol) was added to the mixture. The reaction was stirred at ambient temperature for 48 h, and then the brown suspension was diluted with 200 mL of distilled water and extracted with a 1:1 mixture of diethyl ether: ethyl acetate (300 mL). The mixture was washed three times with distilled water and brine, dried with anhydrous Na₂SO₄, and concentrated at reduced pressure. The crude product was purified by silica gel column chromatography using hexane:ethyl acetate (9:1) to give a pure product with 70% yield. 1H NMR (400 MHz, Chloroform-d) \( \delta \) 4.14 (d, \( J = 2.4 \) Hz, 6H), 3.42 (s, 6H), 2.42 (t, \( J = 2.4 \) Hz, 3H), 1.44 (q, \( J = 7.6 \) Hz, 2H), 0.90 (t, \( J = 7.6 \) Hz, 3H).

**Synthesis of Neopentyl glycol di(3-azido-2-hydroxyl propan-1-ol) ether**

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\begin{array}{c}
\text{N}_3 \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{N}_3 \\
\end{array}
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Neopentyl glycol diglycidyl ether (17.74 g, 82.03 mmol), and LiClO₄ (25.25 g, 0.237 mol) were added to acetonitrile (150 mL). NaN₃ (16.90 g, 0.260 mol) then was added to the mixture.
The mixture was refluxed at 90 °C and left to react overnight. The reaction mixture was cooled to ambient temperature, dissolved in 500 mL of DI water, and then extracted with ethyl acetate (4 x 150 mL). The solution was washed with brine, dried over anhydrous \( \text{Na}_2\text{SO}_4 \) and concentrated at reduced pressure. After purification, a yellowish viscous liquid was obtained with 95% yield. \( ^1 \text{H} \) NMR (400 MHz, CDCl\(_3\), \( \delta \)): 3.98-3.22 (m, 16H), 0.89 (s, 6H)

**Synthesis of CuCl\(_2\)/PMDTA**

PMDTA (2.00 g, 11.54 mmol) was added dropwise to a slurry of CuCl\(_2\) (1.55 g, 11.54 mmol) and acetonitrile (60 mL) under constant stirring. The mixture was stirred for 10 minutes to form a *turquoise solution* which was concentrated at reduced pressure to get CuCl\(_2\)/PMDETA powder.

**Characterization**

**Fourier Transform Infrared Spectroscopy (FT-IR)- Bulk polymerization**

Safety note: In the case of adding hexylamine to initiate the CuAAC reaction using 2 mol % of copper(II), spontaneous heating to high temperature has been observed at elevated hexyl amine concentrations (for these specific circumstances, above 10 mol % of hexylamine for the used monomers). Thus, caution must be used when using CuAAC reaction or any other exothermic reaction to bulk polymerize. In all instances the adiabatic temperature rise of the mixture should be considered, and only reactions with sufficiently dilute azides and alkynes should be performed, particularly when reacting any significant mass of material where heat transfer would be limited.

Neopentyldiazide (2.0 gm, 6.6 mmol) was mixed with CuCl\(_2\)/PMDETA (81.4 mg, 2.6 mmol) using a speed mixer at 2500 rpm for five minutes to form a homogenous mixture without using any solvent. This mixture was used for all IR experiments. IR samples were formulated with a 50:50:1:4 azide: alkyne: CuCl\(_2\)/PMDETA: aliphatic primary amine ratio based on the moles of functional groups. A small amount was placed between two sodium chloride crystals, using a spacer with a thickness of 50 \( \mu \)m. FTIR was used to monitor the disappearance of the azide peak at 2100 cm\(^{-1}\).
Fourier Transform Infrared Spectroscopy (FT-IR)- Solution reaction

FT-IR was outfitted with a horizontal transmission stage and combined with a variable pathlength CaF$_2$ crystal cell. Samples were prepared by forming a 50 μm thin film between salt crystals. 0.2M Phenylacetylene, and 0.2M benzyl azide, and 0.02M copper(I) iodide in THF were prepared with varying amine concentrations: 0.04M, 0.08M, and 0.12M. FTIR was used to monitor the disappearance of the azide peak in the region between 2030 and 2170 cm$^{-1}$. The reaction rate was calculated by measuring the slope of the azide conversion curve with respect to time between 10 % and 30 % conversion. It was ensured that the curve was linear between these limits.

Acknowledgments

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Chapter 5

Photo-CuAAC Induced Wrinkle Formation in a Thiol–Acrylate Elastomer via Sequential Click Reactions

Abstract

Two sequential click reactions are implemented in a facile methodology used to generate well-defined spatiotemporally controlled and persistent wrinkles on the surface of an elastomer. The click thiol-Michael addition reaction was utilized to form a cross-linked polymer with residual, reactive alkyne sites that remained tethered throughout the network. The latent, unreacted alkyne sites are subsequently reacted with diazide monomers via a photoinduced Cu(I)-catalyzed alkyne–azide cycloaddition (CuAAC) reaction to increase the cross-link density. Increased cross-linking raised the modulus and glass transition temperature from 1.6 MPa and 2 °C after the thiol–acrylate reaction to 4.4 MPa and 22 °C after the CuAAC reaction. However, the second-stage photopolymerization of the CuAAC reaction is significantly spatially restricted via limited Cu(II) ion diffusion into the thiol–acrylate elastomer, thereby creating the desired cross-linking gradient throughout the depth of the initial network and leading to the formation of a highly cross-linked skin layer. This approach leads to the formation of well-defined, persistent, reproducible wrinkles on the surface of the material with wavelength and amplitude of 8.50 ± 1.60 and 1.41 μm, respectively, for a polymer with a 1280 μm total film thickness. Control over the wavelength and amplitude of these wrinkles using the resin film thickness is further demonstrated by studying the surface profiles using scanning electron microscopy (SEM) and atomic force microscopy (AFM). Additionally, this novel technique allows the spatial selectivity of wrinkle formation with a wrinkled area that is only 8 μm wider than the photomasked area. This strategy represents a unique approach to generate photodirected wrinkling on the entire surface of the elastomer in one single step.
Introduction

Surface topography is significant for the physical interaction of surfaces with their surroundings. Nature uses topographical features to induce specific surface-mediated behaviors and appearances such as adhesion of gecko toes to walls,\textsuperscript{1} optical enhancement of the Papilio blumei butterfly wings,\textsuperscript{2} the antibacterial nature of shark skin,\textsuperscript{3} and many others. Surface topography is capable of tuning not only the surface behavior or physical appearance but also affects tactile perception. Amazingly, a human finger can discriminate topographical feature sizes as small as 13 nm.\textsuperscript{4}

Unsurprisingly then, there is an increasing interest in a wide arena of fields that take advantage of wrinkle formation to create self-organized micro/nano scale features. Researchers have found that mimicking nature’s wrinkled topography on surfaces yields materials with exquisite properties. Wrinkle formation or buckling has emerged as a simple and low cost tool to manipulate the surface topography, as compared to traditional lithographic fabrication. Additionally, it allows simple and cost efficient patterning over large surface areas. The manipulation of substrates to generate surface features has proven to be highly useful in smart adhesives,\textsuperscript{5, 6} biological applications,\textsuperscript{7} coatings for fouling-resistance,\textsuperscript{8} and controlling the surface wettability,\textsuperscript{9} among others.

One of the most common and effective approaches to generate wrinkles utilizes the introduction of mechanical failure within materials via a gradient in the stress distribution between a hard skin layer and a soft, thick foundation. A common approach to wrinkle formation involves the utilization of poly(dimethylsiloxane) (PDMS) as the underlying, foundation material as it is inexpensive and easy to manipulate via coating or processing in a variety of manners to induce wrinkling. Bowden et al.\textsuperscript{10} reported the wrinkling phenomenon when a thermally expanded PDMS
poly(dimethylsiloxane) film was coated with a thin layer of gold. Since then, several groups utilized PDMS to generate wrinkles using different techniques including solvent swelling,\textsuperscript{11} UVO treatment,\textsuperscript{12} and mechanical stretching.\textsuperscript{13} However, the long-term durability of a PDMS-based substrate is poor and the stability of the wrinkles formed using PDMS is a function of temperature, limiting high temperature applications of polymers.

\textbf{Scheme 5.1} Process of Wrinkle Formation via a Dual Click Reaction Approach. Monomers (a) pentaerythritol tetramercaptopropionate (PETMP) and trimethylolpropane triacrylate (TMPTA) were reacted with propargyl acrylate (PA) catalyzed by triethylamine to produce a (b) thiol–acrylate network with a uniform cross-link density and latent alkyne moieties. The elastomer also contained Bisphenol A di(3-azido-2-hydroxypropan-1-ol) ether (BPADA) and a visible-light photoinitiator (bis(2,4,6-trimethylbenzoyl)phenylphosphineoxide, I819) (c) by immersing the first stage polymer in a solution of copper(II) sulfate which gradually diffused into the film and exposing the polymer to irradiation, the photoinitiator cleaves to form radicals which subsequently reduce copper(II) to copper(I). As a result, copper(I) initiates the reaction between the azide and the alkyne (second stage polymerization). The diffusion-limited presence of copper(I) limits the second polymerization to a thin skin layer at the surface. (d) Upon deswelling of the solvent, wrinkles are formed across the surface of the material.
In the recent past, there have been several different approaches to wrinkle-formation that do not rely on PDMS as a substrate such as the self-swelling of acrylate monomers, utilizing liquid crystals, and shape memory polymers to generate wrinkled surfaces. In a multistep approach, Ding and co-workers used lightly cross-linked polystyrene particles as a shape memory material that could then be deformed into a compressed temporary storage configuration. The particles in this temporary configuration were coated with gold and subsequently heated above the glass transition temperature of the polymer where the constrained shape recovery of the polystyrene particles resulted in the formation of wrinkles on the surface. New strategies for forming wrinkles in the surface utilize two stage reactive polymer networks which enable tuning of the final polymer properties. Kloxin and co-workers presented an effective approach in which an off-stoichiometric, two-stage reactive network thiol–ene elastomer with excess acrylates formed an initial network containing both a photoinitiator and a photoabsorber. The elastomer was then strained and irradiated with UV light to form a highly cross-linked skin which leads to the generation of photodirected wrinkles on the surface of the material. Podgórski et al. used a similar approach where thiol-isocyanate-methacrylate two-stage reactive network polymers were used for fabrication of well-defined surface patterns and functional geometric shapes. Recently, Yagei and co-workers used photoinduced sequential thiol–ene and CuAAC click reactions to synthesize novel block copolymers.

In both of the previous two-stage reactive network approaches described, a thiol-click reaction was implemented to form the initial network that was then manipulated to form a skin and yield wrinkles. The secondary reaction was a free radical chain growth polymerization rather than a step growth click reaction. The click chemistry concept was introduced by Sharpless with the
goal of identifying processes and reactions that proceed efficiently and predictably under relatively facile reaction conditions to achieve a desired end as simply and robustly as possible. Among other aspects, click reactions are generally those that proceed rapidly to quantitative yield without side products or side reactions at ambient conditions and in an orthogonal manner. The most prolific and powerful of these reactions is the CuAAC reaction. Recently, simple approaches have been developed for photoinitiating this click reaction, enabling it to join other types of photoinitiated click reactions that all have the significant additional benefit of spatiotemporal control of the reaction. Utilizing the CuAAC click reaction as a second stage network, instead of chain growth reaction, enables further postfunctionalization of the polymer networks in which residual alkynes or azides could readily be used for subsequent reactions. Further, implementing the CuAAC in the formation of cross-linked triazole-containing polymers has the benefits of the formation of a high glass transition temperature, homogeneous cross-linked polymer.

Herein, we implement two click reactions; the thiol–acrylate click reaction is used for initial network formation and subsequently the CuAAC click reaction locally increases the cross-link density. This strategy, in several aspects similar to the two-stage reactive polymer network approaches described above, now utilizes instead two sequential click reactions. The initial click reaction results in an elastomer that is formed via a Michael addition reaction between a thiol and an acrylate. By stoichiometrically incorporating a dual functional monomer such as propargyl acrylate that contains both yne and acrylate functionalities, it is possible to design a network that also contains reactive alkyne sites tethered throughout the elastomer. This approach provides the latent ability to react the network further with free difunctional azide upon photoinduced catalyst generation. The second-stage CuAAC photopolymerization increases the cross-link density where this stage is initiated by immersing the sample in a copper solution. The reaction is limited in two
dimensions through the ability to mask the light exposure, and it is further restricted in the third dimension due to the diffusion-limited penetration of the Cu ions into the elastomer, as shown in Scheme 5.1. This technique represents a simple approach that enables photodirected wrinkling that also facilitates control over both the wrinkle wavelength and amplitude.

Results and Discussion

Thiol–acrylate and azide–alkyne cycloaddition reactions (i.e., Photo-CuAAC) were used to form two stage network polymers through a base-catalyzed reaction that proceeds stoichiometrically via the thiol–acrylate “click” reaction mechanism and a subsequent photoinduced CuAAC reaction. Specifically, a tetra-thiol (pentaerythritol tetramercaptopropionate, PETMP), a triacrylate (trimethylolpropane triacrylate, TMPTA), and a diazide (Bisphenol A di(3-azido-2-hydroxy propan-1-ol) ether, BPADA) along with a visible-light photoinitiator (bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide, I819), propargyl acrylate PA, and triethylamine (TEA) were used to form the networks as shown in Scheme 5.1. The stoichiometric mole ratio of the monomers was 1.25:1:1:2 for the tetra-thiol: triacrylate: diazide: propargyl acrylate, respectively. Utilizing a monomer such as propargyl acrylate that has both acrylate and alkyne functionality takes advantage of the orthogonality of the thiol-Michael reaction and enables only the double bonds to react in the initial thiol-Michael click reaction, leaving the alkyne unreacted and tethered to the network along with the free diazide and photoinitiator. By virtue of this approach, the oxidation of thiols by Cu to form disulfides,\(^{33}\) as well as the corresponding spontaneous reduction of Cu(II) to Cu(I), was eliminated by fully reacting the thiols in the initial network formation. Thereby, the second stage CuAAC photopolymerization reaction is not initiated spontaneously by thiol-induced Cu reduction; rather, it requires light exposure.
After the thiol–acrylate elastomer was formed, the clear substrate was immersed in a 1 M solution of copper(II) sulfate that allowed for Cu diffusion and penetration into the film. When the substrate and solution are exposed to irradiation, the visible light photoinitiator within the network cleaves to form radicals, which subsequently reduce copper(II) to copper(I) as has recently been shown to be an effective way for photoinitiat ing the CuAAC reaction.\textsuperscript{24-30} The generated copper(I) initiates the reaction between the azide functional groups and alkyne functional groups, thereby generating a stiff polymer network.

Wrinkles form due to the elastic instability between soft and stiff layers within the network when they are subject to either compression or stretching beyond a critical strain.\textsuperscript{13} During the CuAAC reaction, we form a stiff triazole-based network within the soft thiol–acrylate network with spatial variation in the modulus induced via a gradient in the catalyst diffusion and/or masked light exposure. Upon deswelling of the solvent, the polymer contracts and the surface of the polymer relaxes in the form of wrinkles due to the modulus mismatch between the soft foundation of the underlying thiol–acrylate and the stiff skin formed by the azide alkyne network. After the second stage CuAAC photopolymerization and solvent removal, the polymer network becomes relatively opaque and dull due to the surface wrinkles.

To confirm and evaluate the functional group conversions and characterize the resulting cross-linked polymer networks, both the initial and final networks were characterized physically. Figure 5.1(a) shows the ATR–FT IR spectra after the formation of the initial thiol–acrylate network, showing complete conversion of the thiol as evidenced by the complete disappearance of the peak associated with the thiol at 2550 cm\textsuperscript{-1}, while the azides and alkynes remained unreacted as evidenced by the fact that the IR signals associated with the azide at 2100 cm\textsuperscript{-1} and the C–H stretch of the alkyne at 3300 cm\textsuperscript{-1} remained unchanged. Additionally, the azide peak at 2100
cm$^1$ decreases after the second stage curing with 60 min of continuous irradiation, demonstrating a 25% average consumption of the azide within the approximately 6 μm penetration depth of the ATR–FTIR effective path length using this setup including a ZnSe crystal. Given that the skin formation is largely limited to the top 1–2 μm of the film (later analysis), this indicates that the conversion within that skin is high and potentially nearly quantitative. This high, localized CuAAC reaction leads to a dramatic increase in cross-link density that subsequently increases the modulus and Tg. Although the alkyne groups have the potential to react with the photochemically formed radicals, this reactivity is low, particularly in the presence of Cu(II). In the presence of Cu(II), the low redox potential of Cu(II), i.e., +0.34 V, results in high reactivity of the formed radicals toward Cu.$^{34}$
Figure 5.1 FT-IR spectroscopy—attenuated total reflectance-kinetics data of the (a) the unreacted monomers spectra shows the stretch thiol vibration at 2575 cm\(^{-1}\) and the stretch azide vibration at 2100 cm\(^{-1}\) (b) neat polymer of stage 1 thiol–acylate Michael addition reaction shows the complete absence of the thiol stretching vibrations peak at 2575 cm\(^{-1}\) at the end of the reaction, indicating that the thiols are consumed completely to form the first stage polymer network, while the azides and the alkynes remain unreacted. (c) The spectra of a neat polymer of stage 2 photo-CuAAC reaction which was quantified via the decreasing of the stretching vibrations peak area at 2100 cm\(^{-1}\) suggests that the limited quantities of azides have reacted and that the average azide–alkyne conversion within the penetration depth of the ATR–FTIR, which is 6 μm, is 25%. The second photopolymerization was initiated via exposure of the polymer film in 1 M CuSO\(_4\) solution to 400–500 nm irradiation and 2 mW/cm\(^2\) intensity for 1 h at 75 °C. The thiol to acrylate functional group ratio was maintained at 1:1. The homogeneous mixture contained 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, and 0.96 mmol PA. The initiator system was composed of 0.5 wt % TEA and 4.0 wt % I819.
Figure 5.2 Glass transition temperature, Tg, (a) and rubbery storage modulus (b) were measured for a stage 1 thiol–acrylate network and a stage 2 thiol–acrylate-CuAAC combined network, after the formation of the photo-CuAAC “skin” on the surface of the thiol–acrylate elastomer. The stage 1 network was formed via a stoichiometric thiol (PETMP) and acrylate (TMPTA) click reaction showing a narrow glass transition peak. The mixture contained a 1:1 mol ratio of thiol to acrylate, a 1:1 mol ratio of azide to alkyne, 0.5 wt % TEA, and 4.0 wt % I819. To initiate the stage 2 photopolymerization the sample was cured in a hot aqueous solution of CuSO$_4$ to 400–500 nm irradiation and 2 mW/cm$^2$ intensity at 75 °C for an hour. The second stage polymer also formed a homogeneous network with a narrow glass transition temperature.

The initial and final polymer properties associated with the thiol–acrylate polymer (stage I) and a composite polymer film with a skin formed by photoinitiated azide–alkyne polymerization (stage II) were evaluated using dynamic mechanical analysis (DMA). As shown in Figure 5.2, the glass transition temperature of the overall film is shifted from 2 to 22 °C by the second stage CuAAC reaction. While this second reaction is limited to a very small volume of the film as measured in DMA, its dramatically higher cross-link density as well as the presence of the stiff triazole ring structures in the skin all contribute to a significant increase in both modulus and Tg. It is expected that the skin modulus and Tg would be significantly higher than those measured here
for the entire film. Despite the increase in cross-link density being localized to a thin film on the periphery of the sample, the rubbery modulus of the overall film, as a measure of the cross-link density, increases by more than a factor of 2 from 1.6 to 4.4 MPa for the pure thiol–acrylate network and the CuAAC skin-containing network, respectively. Ultimately, as evidenced by the DMA and ATR–FTIR results, the second stage CuAAC curing is successful in forming a more cross-linked, higher modulus skin as needed for wrinkle formation.

Figure 5.3 (a) SEM image of wrinkles generated via sequential click reactions on an elastomer in which after the initial network is generated via the thiol-Michael reaction, the second stage photopolymerizations was initiated via visible light initiator (I819) in heated solution of 1 M CuSO₄ with 400–500 nm irradiation and 2 mW/cm² intensity at 75 °C for an hour. (b) A typical topography of wrinkled film is captured using AFM, using the same conditions as image (a).

Surface profiles characterized using SEM and AFM reveal the surface topography after the formation of a CuAAC skin on the surface of the thiol–acrylate substrate, as shown in
Figure 5.3 (a) and (b). The surface flatness after the first stage polymerization was demonstrated by the SEM and AFM analysis as shown in Figure 5.4. To demonstrate an analogous approach and demonstrate that photoinitiation was not necessary, azobis(isobutyronitrile) (AIBN) was used as a thermally sensitive radical generator to initiate the second stage CuAAC skin forming reaction. Generally similar, wrinkled structures were observed in films of this type as well as shown in Figure 5.5.

Figure 5.4: (a) SEM image and (b) AFM images of the thiol-acrylate film, stage 1 polymerization, proven the flatness of the surface.

Figure 5.5: SEM image of wrinkles generated via sequential click reactions on an elastomer in which after the initial network is generated via the thiol-Michael reaction, the second stage polymerizations was initiated via a thermal initiator azobisisobutyronitrile (AIBN) in a heated solution of 1 M CuSO4 at 75 °C for an hour.
It should be noted that these films do not have a well-defined CuAAC skin but rather a gradient of the CuAAC network within the thiol–acrylate network that reflects the gradient in copper concentration. Curing the thiol–acrylate elastomers under an irradiation of 2 mW/cm² at 400–500 nm light in a heated aqueous copper solution allows the Cu(II) to diffuse according to Fick’s law, establishing a concentration gradient of Cu within the network. Since the CuAAC reaction rate depends significantly on the Cu(I) concentration, regions of higher Cu(I) concentration achieve higher alkyne–azide conversions, while regions of lower concentration achieve lower azide–alkyne conversion. Accordingly, the polymerization rate is highest at the surface due to the high concentration of Cu, and the polymerization rate declines as the Cu concentration decreases through the depth of the sample. The differential polymerization rates between the surface and bulk of the thiol–acrylate substrate lead to different cross-link densities, which along with the contraction from deswelling, lead to an instability within the material which is then minimized via the formation of wrinkles on the surface of the substrate. Control experiments on films exposed to heated solutions of Cu but no light and films exposed to all of the same conditions but in the absence of Cu failed to produce any wrinkles or other surface roughness, indicative that the CuAAC surface polymerization is necessary for wrinkle formation as shown in Figures 5.6 and 5.7.
Figure 5.6: SEM images of a control sample wherein the second stage polymerization was conducted in the absence of Cu with 400-500 nm irradiation and 2mW/cm² intensity at 75 °C for an hour. The control sample indicates that wrinkles are only formed in the presence of copper.

Figure 5.7: SEM images of a control sample wherein the second stage polymerization was conducted via immersion the polymer in 1 M CuSO₄ at 75 °C for an hour in the dark. The flatness of the surface indicates that light is necessary to initiate the second stage photopolymerization.
Figure 5.8 (a) and (b) SEM images of wrinkles on both side of the film (surface 1, a) (surface 2, b) of the sample. All samples contain 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, 0.96 mmol PA, 0.5 wt % TEA, and 4.0 wt % I819. Wrinkles generated via the second stage CuAAC polymerizations which was conducted in a solution of 1 M CuSO$_4$ with 400–500 nm irradiation and 2 mW/cm$^2$ intensity at 75 °C for an hour.

Since wrinkles are formed due to the increased modulus associated with the CuAAC skin, which is in turn controlled by copper diffusion from the solution into the thiol–acylate cross-linked network, wrinkles are induced over the entire surface area of the film including the top (surface1) and bottom (surface2), as shown in Figure 5.8 (a) and (b) upon uniform light exposure. Indeed, it was observed that the immersion of the polymer into a solution of copper while stirring allows for complete contact between the polymer and the Cu, and with subsequent photoirradiation, wrinkles were formed on the entire surface of the substrate. The wavelengths and amplitudes of the wrinkles were measured by SEM and AFM, Figure 5.9 (a,b). As previously observed,$^{10,19}$ both the wrinkle wavelength and amplitude scale linearly with the thickness of the polymer film. The wrinkle wavelength and amplitude were 8.50 ± 1.60 and 1.41 μm, respectively,
for a polymer with a 1280 μm total film thickness. Tapping mode AFM was used to estimate the Young’s modulus of the surface polymer for materials before and after skin formation. The Young’s moduli of the thiol–acrylate network and photo-CuAAC network were then used to estimate the thickness of the CuAAC skin. The linear elastic buckling theory predicts that the wavelength (λ) of the resulting wrinkles follows a defined relationship \( h \approx \frac{\lambda}{2\pi}\left(\frac{3E_s}{E_f}\right)^{1/3} \), where \( E_s \) and \( E_f \) denote the Young’s modulus of the substrate and film skin, respectively. The skin thickness, \( h \), was then determined from the measurement of the two moduli (1.2 MPa for the thiol–acrylate and 14.9 MPa for the CuAAC) and found to be approximately 800 nm for a polymer with 1280 μm thickness. The calculated thickness of the CuAAC thin film suggests that the Cu penetrates only a very short distance into the network. The average swelling of copper solution into the initial polymer network was in the order of 1–3%, and this feature, combined with the polarity of the Cu, makes it reasonable that the Cu, at a sufficient level to initiate the reaction, would remain essentially only at the surface. The thickness of the CuAAC skin is controlled by the very limited penetration depth of the Cu into the thiol–acrylate film that arises from the hydrophobicity of the system. It should be noted that, while residual functional groups exist in the interior of the matrix, when the wrinkled structure was re-evaluated after three months, that there was qualitatively no change in the wrinkled structure.
Figure 5.9 (a) shows the influence of the thiol–acrylate film thickness on wrinkle wavelength generated on the two surfaces. (b) The influence of the thiol–acrylate film thickness on the wrinkle amplitude was calculated using AFM measurements. It is observed that the wrinkle wavelength and amplitude increase as a function of increasing polymer thickness. (c) The influence of thickness of thiol–acrylate polymer on surface modulus (Young’s modulus) is plotted. All samples contain 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, 0.96 mmol PA, 0.5 wt % TEA, and 4.0 wt % I819. Wrinkles generated via the second stage CuAAC polymerizations which was conducted in a solution of 1 M CuSO₄ with 400–500 nm irradiation and 2 mW/cm² intensity at 75 °C for an hour. SEM images and ImageJ software were used to calculate the average wavelength of the wrinkles.
The spatial selectivity of wrinkle formation is also demonstrated, as shown in Figure 5.10. The pattern in the figure was generated by exposing the neat polymer film of the initial network to irradiation with a photolithographic mask attached to the surface, prior to any exposure to the Cu solution. The mask contains 100 μm dark stripes and 150 μm transparent stripes. The film was then exposed to UV or visible light for 15 min to selectively consume and bleach the photoinitiator in the exposed regions. As demonstrated earlier in the control experiment, the presence of photoinitiator is necessary for the formation of wrinkles to reduce the diffused Cu(II) to the active form of the catalyst, Cu(I). After exposure to irradiation under the mask, the sample was removed and placed in the Cu solution to enable diffusion and then further irradiated uniformly (i.e., not through the mask). This approach results in localized wrinkle formation, with wrinkles only in the regions where the photoinitiator was not bleached, while the regions where the photoinitiator was bleached remain wrinkle-free and flat. The wrinkled regions were 108 μm wide, approximately 8 μm wider than the mask that was initially used to generate the initiator-free regions. Clearly, photoinitiator diffusion and replenishment of the immediate surroundings is likely responsible for the wrinkles generated in these regions.
Figure 5.10 SEM image of wrinkles that formed in a pattern after selectively consuming radicals via prior exposure of the sample through a photomask in which it was selectively irradiated with UV or visible wavelengths for 15 min at 15 mW/cm$^2$ intensity to consume radicals in the exposed regions (a). The polymer was subsequently immersed in a 1 M CuSO$_4$ solution and further irradiated at 400–500 nm wavelength and 2 mW/cm$^2$ intensity at 75 °C for 1 h. The smooth, unwrinkled area indicates the region in which the radicals were consumed during the initial exposure, and thereby the catalyst, Cu(I), is not generated (b). Wrinkles are formed in areas where the film was unexposed to irradiation (c).

Conclusions

Sequential thiol–acrylate and photo-CuAAC click reactions have been utilized to form two-stage reactive polymer networks capable of generating wrinkles in a facile manner. After an initial
homogeneous thiol–acrylate step growth network was formed, a second step-growth reaction, the CuAAC click reaction, was initiated in a gradient fashion within the thiol–acrylate network via Cu diffusion to generate microwrinkles with well-controlled wavelength and amplitude. This approach to generating surface topographies is also tunable, where the ability to change the Cu-catalyst concentration, cross-link density, light intensity, and monomer types offer many opportunities to control wrinkle generation. The wrinkling mechanism described here is nonspecific, and, indeed, this approach could be utilized to obtain controlled patterns in a broad range of two stage reactive polymer networks simply by diffusing the catalyst or the photoinitiator into a network for a controlled amount of time. Additionally, this approach further enables spatial selectivity of wrinkle formation by photopatterning.

**Experimental**

**Materials**

Pentaerythritol tetrakis(3-mercaptopropionate) (PETPM) was donated by Bruno Bock. Trimethylolpropane triacrylate (TMPTA), copper sulfate pentahydrate, triethylamine (TEA), Azobisisobutyronitrile (AIBN), and propargyl acrylate (PA) were purchased from Sigma Aldrich and used without further purification. Irgacure 819 (Bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide) was obtained from BASF.

**Synthesis of Bisphenol A di(3-azido-2-hydroxy propan-1-ol) ether (BPADA):** To a solution of bisphenol A diglycidyl ether (8.42 g, 24.735 mmol) in acetonitrile (100 mL) was added LiClO₄(8.325 g, 78.5 mmol). The mixture was stirred, and then NaN₃ (4.995 g, 77 mmol) was added in small portions. The solution was heated to 90 °C, and allowed to reflux overnight. The reaction mixture was allowed to cool down to room temperature, and the crude material was taken
up in 500 mL’s of water and extracted with ethyl acetate (4 x 150 mL). The ethyl acetate layer was washed with brine and dried over sodium sulfate, and then concentrated at reduced pressure. After purification, a yellowish viscous liquid was obtained. 1 H NMR (400 MHz, CDCl 3, δ): 7.17 (m, 4H), 6.85 (m, 4H), 4.19 (m, 2H), 3.99 (dd, 4H, J = 6.0, 1.2 Hz), 3.55 (m, 4H), 2.42 (d, 2H, J = 1.0 Hz), 1.68 (s, 6H).

**Thiol acrylate network fabrication.** In a vial PETMP/ TMPTA/ BPADA/PA with 0.6 mmol PETMP, 0.48 mmol TMPTA, 0.48 mmol BPADA, 0.96 mmol PA, and 4.0 wt % I819 were added together and mixed thoroughly. Finally, 0.5 wt % TEA was added to catalyze the Michael addition polymerization, and the mixture was placed between 2 glass microscope slides with a 0.5 mm spacer until the initial polymerization was completed. Samples were kept for a few hours to ensure that all thiol functional groups were reacted with the acrylate functional groups.

**Second stage curing:** After the formation of the stage 1 network via thiol-Michael addition, polymer films were immersed in heated 1 M CuSO 4.5H 2 O solution. An oil bath was used to control the temperature, which was set to 75°C. The polymer films were stirred for one hour while being exposed to 2 mW/cm 2 400-500 nm irradiation using an EXFO Acticure high pressure mercury vapor short arc lamp equipped with a 400-500 nm bandgap filter. After curing, the samples were removed and left to dry either at ambient temperature for 4 h or in the oven at 45 °C for 15 min.
Characterization

**Atomic Force Microscopy.** Force-displacement curves were obtained using a Nanoscope IIIa scanning probe microscope (Veeco Instruments, Inc., Santa Barbara, CA) in contact mode. A silicon cantilever with a spring constant of 6.23 N/m and an attached 20 µm borosilicate glass bead were used for indentation. The spring constant was determined using Sader’s Method \(^{35}\) before attachment of the glass bead. Optical sensitivity was determined by the average of multiple force displacement curves (n=10) taken on a hard metal disc surface. Measurements were taken in a 5 x 5 point matrix approximately 10 µm apart. The appropriate curves were fit using the Hertz equation at an indentation depth at which the polymer behaves as an elastic solid, as described by McKee *et al.*\(^{36}\). The wrinkle amplitude was taken as the average peak to valley distance in the topographic images from the AFM.

**Dynamic Mechanical Analysis (DMA).** The experiments were performed using TA instruments DMA Q800. Samples were rectangular with dimensions of (1 mm thickness × 5mm width × 9 mm height). The multi-frequency strain mode was used and the temperature was ramped at 3 °C/min with a frequency of 1 Hz and a strain of 0.01 % with temperature range of −25 to 60 °C. The glass transition temperature (Tg) was determined as the maximum point of the tan δ curve.

**FT-IR Spectroscopy—Attenuated Total Reflectance.** Reaction kinetic experiments were performed to ensure full conversion of the thiol and to determine the azide conversion. These studies were performed using a Nicolet Magna 760 spectrometer equipped with a Thermo Nicolet smart AKR ZnSe 45° attachment. Experiments were conducted on a neat polymer film. The thiol peak at 2575 cm\(^{-1}\) and the azide peak at 2100 cm\(^{-1}\) were assessed, and the conversions calculated using the carbonyl peak at 1750 cm\(^{-1}\) as an internal standard.
**Scanning Electron Microscopy** The polymer morphologies were imaged using a JEOL JSM-7401F scanning electron microscope (SEM) operating at a 20 kV accelerating voltage. The microstructures were observed at the top surface of the film. SEM images were used to calculate the average wavelength of the wrinkles using ImageJ software.

**Photopatterning.** The neat polymer film of stage 1 was placed on glass cover slides, with a photolithographic mask attached to the surface. A chrome mask was created with 100 μm dark stripes and alternating 150 μm transparent stripes. The film was exposed to a collimated light source for 15 minutes, prior to any exposure to the Cu solution, from an optical mask alignment system (Optical Associates, Inc. San Jose, Ca) using a 5 × 5 cm area collimated flood exposure source with irradiation intensity of 15 mW cm⁻² with principal output at 365 nm, or using a 400-500 nm filter on top of the mask. After consuming the photoinitiator in the exposed regions, the film was cured in hot 1 M CuSO₄.5H₂O solution, and further irradiated with light from 400-500 nm at an intensity of 2 mW/cm² intensity at 75 °C for one hour, leaving only the patterned, wrinkled polymer in the area where the photoinitiator was not consumed, 100 um.

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References


Chapter 6
Unique recovery and toughness behavior of glassy Copper-catalyzed azide alkyne foam

Abstract

This study is the first to employ the use of the copper-catalyzed azide alkyne cycloaddition reaction (CuAAC) to design a tough, stiff, porous material from a well-defined network, which possesses a high glass transition temperature ($T_g=115^\circ$C) due to the formation of the triazole linkages. The foam material exhibited excellent shape-memory behavior and was able to recover through each of five successive cycles of 80% compression at ambient temperature, presenting a significant volume change and resistance to fracture. In addition the glassy CuAAC foam was able to withstand more than 10 cycles of compression to 50% strain and subsequent recovery at ambient temperature indicative of ductile behavior in the glassy state. The CuAAC foam exhibits reversible plasticity which is a form of shape memory in which a material undergoes a significant plastic deformation when deformed below the glass transition but still recovers fully when heated above $T_g$. To investigate the effect of the network linkages, i.e., the triazoles, on the mechanical behavior at high strain, the CuAAC foam was compared to an epoxy-amine-based foam which was used as a negative control, where monomers with similar backbone structures to the CuAAC monomers were used to form the network. Both polymers have the advantage of forming via a step-growth polymerization, generating a homogenous network and having many similar mechanical properties, i.e., $T_g=115$ °C and a rubbery modulus =1.0 MPa for the CuAAC network, $T_g=125$ °C and a rubbery modulus = 1.2 MPa for the epoxy-amine network. When comparing the energy required to compress the foams to 80% strain, the CuAAC foam exhibited a toughness almost three times greater than the epoxy-amine foam (850 vs. 300 MJ/m$^3$). Additionally, the epoxy-amine foam was severely damaged after the first cycle of compression to 80% strain at ambient temperature, while the CuAAC foam compressed uniformly to 80 % of its original height to a small disc, and held the compressed shape until being heated above $T_g$.

Introduction
Shape-memory polymers (SMPs) are a class of smart polymeric materials that have the ability to store a temporary shape in a deformed state, and recover to a permanent shape upon exposure to a specific stimulus.\textsuperscript{1,2,3} SMP foams, in particular, possess several distinctive material capabilities that neat SMPs do not possess, such as lighter weight, greater volumetric expansion and dramatic permeability change upon actuation.\textsuperscript{4,6} The shape-memory behavior allows SMP foams to be compacted to extremely small volumes, compared to neat/regular SMPs,\textsuperscript{7} which provides them utility in varied applications such as deployable biomedical devices that can facilitate minimally invasive vascular treatments.\textsuperscript{8-10} These foams have potential in deployable spacecraft structures, such as solar sails, solar arrays, and sunshields, in which conservation of volume and weight is an extremely important concern when transporting structures into space.\textsuperscript{11} In addition, SMP foams have been explored as self-repairing materials where a compressed secondary shape foam was utilized to partially close or fill damaged areas via its large volumetric expansion.\textsuperscript{6} These applications all rely on large deformations during programming of the shape-memory effect. SMP foams enable these large, on-demand shape changes yet require high toughness to avoid failure upon high strain loading.

The majority of SMP foams utilize either polyurethane (PU)\textsuperscript{12-15}, or epoxy\textsuperscript{16-20}-based materials. Thermoset polyurethane SMP foams have been used extensively at ambient temperature, and they exhibit high failure strains but low glass transition temperatures ($T_g$s), limiting the high temperature applications of these polymers. Thermosetting epoxy SMP foams have been reported with a $T_g$ of up to 90 °C, but their brittle nature below $T_g$ limits their uses.\textsuperscript{16} Different techniques have been used to enhance the toughness of epoxies such as the addition of soft/thermoplastic particles,\textsuperscript{21} blending of copolymers,\textsuperscript{22} and utilization of composite materials.\textsuperscript{23,24} These approaches each have drawbacks, for example, incorporating soft particles in a glassy polymer compromises the mechanical properties, while the addition of small rigid or soft particles can also suffer from aggregation of the particles, leading to inhomogeneous dispersions. In addition, there is significant variation in results depending on the monomer systems being used, thereby making it difficult to generalize outcomes.\textsuperscript{25,26,16} Overall, it is desirable to design a tough, high $T_g$ SMP foam that is repeatedly deformable to a highly compacted state and still demonstrates full recovery.
The mechanical properties of SMP foams are dictated by the nature of their chemical bonding and pore structure, i.e. porosity. Moving away from the traditional chemistry of polyurethanes and epoxies, here, we introduce a polymer foam fabricated for the first time using a copper-catalyzed azide alkyne cycloaddition (CuAAC) reaction-based polymerization as a potential material for high strain SMP foams. Hawker and co-workers demonstrated the potential of triazole linkages to improve the strength of the network in which bifunctional alkyne-PEGs and tetrafunctional azide-PEGs formed a hydrogel via the CuAAC reaction. These materials resulted in well-defined networks with improved mechanical properties, where the CuAAC hydrogel strength was about 10 times greater than a hydrogel that was cross-linked by conventional chain growth polymerization. Although the CuAAC reaction has been studied extensively in solution, minimal work has been done to use it as a bulk polymerization reaction to form cross-linked networks with little done to understand the resulting mechanical properties.

CuAAC-based network polymerizations and polymers have unique properties. The network is formed through a step-growth mechanism, which leads to beneficial properties such as delayed gelation, low shrinkage, low shrinkage stress, and an inherently uniform polymer network as indicated by a narrow glass transition when compared to conventional chain growth polymerization methods. Polymers formed with a narrow glass transition are excellent materials for shape memory applications. Additionally, the hetero-cyclic triazole ring, which forms in molar quantities during the CuAAC polymerization, significantly influences the mechanical properties of the network due to its rigid nature. Implementing the CuAAC chemistry to form a network allows a wide range of azide and alkyne monomers and orthogonal chemistries to be used to tune the physicochemical properties of the network. Moreover, among the various reactions in the click chemistry toolbox, the CuAAC reaction is often considered to be the most capable reaction due its ideal nature. This reaction proceeds efficiently and predictably under relatively facile reaction conditions to quantitative yields at ambient temperature and in an orthogonal manner. Furthermore, simply by reacting off-stoichiometric mixtures during the original polymerization, the CuAAC reaction enables facile post-functionalization in which residual alkynes or azides are used in subsequent reactions to alter the physical or chemical properties of the polymer network.
The purpose of this study is to employ the chemistry of CuAAC reactions to create a porous material that is tough and has a well-defined network with $T_g$ values well above ambient temperature. The homogeneity and thermo-mechanical properties of the CuAAC polymer network make it an excellent candidate for SMP foams. The shape-memory behavior of this material as well as its thermo-mechanical behavior and toughness were examined and compared to traditional epoxy foams.

**Results and discussion**

Here, we explore the shape-memory behavior, recovery and toughness of rigid CuAAC foams. The homogeneous, glassy CuAAC network was formed through a Cu(II)-hexyl amine catalyzed reaction that proceeds stoichiometrically via the azide-alkyne “click” reaction. Specifically, a bisphenoldiazide (Bisphenol A di(3-azido-2-hydroxy propan-1-ol) ether), a trialkyne-ether (1-(Prop-2-ynyloxy)-2,2-bis(prop-2-ynyloxymethyl)butane), CuCl$_2$/PMDETA and hexylamine were used to form the networks, see Scheme 6.1. The monomer mixture consists of 1:1 mole ratio of trilkyne-ether, bisphenoldiazide as well as 2 mole % CuCl$_2$/PMDETA, and 8 wt% hexylamine, with respect to monomer. The ratio of 1.5: 1 monomers to solvent (methanol) lowers the overall resin viscosity which improves the salt crystal distribution as needed to form the foam.

The CuAAC foam was made by using a salt-leaching technique$^{36}$ in which salt is added to the monomer/solvent mixture: 20 wt % monomers (ratio of 1.5: 1 monomers to solvent) and 80 wt % sodium chloride. After casting by solvent evaporation and polymerization, a solid polymer with distributed salt crystals is formed. Subsequent leaching of the salt particles in water results in the formation of a polymeric foam. The foam porosity is 80% and pore sizes range from approximately 200 – 350 μm with an average pore size of 290 ± 40 μm.
a). CuAAC monomers

![Chemical structure of CuAAC monomers](image)

b). Epoxy-amine monomers

![Chemical structure of epoxy-amine monomers](image)

c). The Cu(I)-catalyzed azide-alkyne cycloaddition reaction, CuAAC

![Catalyzed cycloaddition reaction](image)

**Scheme 6.1**: (a) The chemical structure of the monomers used to synthesize the CuAAC foam. (b) The chemical structure of the monomers used to synthesize the epoxy-amine foam. (c) A general scheme for the cyclization of an alkyne/azide system for a CuAAC polymer.

The kinetic profile as measured by infrared spectroscopy, for the reaction of the trialkyne-ether and bisphenoldiazide using Cu(II) salt as a catalyst and hexylamine as a reducing agent is presented in **Figure 6.1**. The Cu(II) – hexylamine system proved to be an efficient catalyst to initiate the reaction, and the CuAAC reaction proceed to completion at ambient temperature in
approximately 40 minutes. The thermo-mechanical properties of this fully reacted CuAAC foam were then evaluated by dynamic mechanical analysis (DMA). The $T_g$ of the CuAAC foam was observed to be 115 °C with full width at half height of 10 ± 2 °C, and a rubbery modulus of 1.0 MPa, as indicated in Figure 6.2. The CuAAC reaction of these monomers produced a glassy network due to the heterocyclic triazole connections, which form during polymerization.

Figure 6.1: IR kinetic study of the azide conversion of a thin sample of 1:1 mole ratio of trilkayne-ether: bisphenoldiazide, and CuCl$_2$/PMDETA with 2mol% CuCl$_2$ and 8 wt % hexylamine as a catalyst system.

Figure 6.2: Glass transition temperature, $T_g$, and storage modulus were measured for a CuAAC foam. The CuAAC foam was formed via a stoichiometric mole ratio of bisphenoldiazide, trialkyne ether, 2 mole % CuCl$_2$/PMDETA, and 8 wt % hexylamine with 80 % porosity via
click reaction showing a narrow glass transition peak with a $T_g=115 \, ^\circ\text{C}$, and a rubbery modulus $= 1.0 \, \text{MPa}$.

The CuAAC polymer network is homogenous,$^{30,31}$ as indicated by the narrow and distinct $T_g$, making it an attractive candidate as a SMP. $^{33}$ The shape-memory capability of the CuAAC foam was verified by using a free-strain recovery test as indicated in Figure 6.3. The sample was heated to 140 °C, and deformed to 12% strain followed by fixing the shape by cooling down to -10 °C. Upon heating, the recovery profile was recovered. The foam exhibits a dramatic shape change over a narrow range of temperature as dictated by the sharp glass transition temperature. The CuAAC foam exhibits repeatable shape memory cycles with both the free strain recovery ($R_r$) and shape fixity ($R_f$) around 99%.

**Figure 6.3:** Tensile shape memory behavior of 1 mm CuAAC foams. The sample was strained to almost 11% at 140 °C and was subsequently cooled to -10 °C to fix the shape. The applied stress was then unloaded at -10 °C ($R_f = 99\%$) and was heated up to 140 °C to determine its shape recovery behavior ($R_r = 99\%$). The CuAAC foam was formed from a stoichiometric mixture of bisphenoldiazide, trialkyne ether, 2 mole % CuCl$_2$/PMDETA, and 8 wt % hexylamine with 80 % porosity.

The compression and shape-memory behavior of the CuAAC foams after multiple cycles of compression and recovery are presented in Figure 6.4. The CuAAC foams were compressed to 80% strain at a rate of 0.01 mm/s at ambient temperature ($T<<T_g$) and experienced linear elastic and/or plastic deformation as well as densification over the course of each compression cycle.
However, the samples mechanically exhibited a noticeable degree of damage between cycles 3 and 5, as indicated by the significant change in the stress-strain curve. Fixity and recovery ratios were evaluated after each cycle as shown in Figure 6.5(a). The foams maintained between 92 and 94% of the compressive strain when unloaded after each cycle. The small amount of elastic recoil is explained by the networks ability to efficiently store plastic deformation at temperatures well below $T_g$ due to limited chain mobility, as shown in Figure 6.5(b). The recovery ratios were then measured after reheating the samples above 115°C. The CuAAC foam was able to recover fully through five successive cycles of deformation to 80% of its original height upon heating, presenting a significant volume change at ambient temperature with great resistance to fracture. The ability of the glassy CuAAC network to recover five successive cycles of plastic deformation is remarkable. This unique behavior is known as “reversible plasticity” which is a form of shape memory in which a material undergoes a significant plastic deformation at ambient temperature and recovers fully when reheated. The material was able to recover both the temporal elastic, linear region, and plastic region of deformation. Although the foam sample fully recovered its original shape during the first five compression cycles, a decrease in the mechanical performance after each cycle was seen where the maximum stress decreased slightly for the first three cycles - 50, 48, 45 MPa respectively, from the first to the third cycle, while it decreased more significantly in the fourth cycle to 31 MPa. The maximum stress also declined, indicating that structural bonds are breaking after each cycle as a result of the applied strain. The foam dimensions were relatively the same even after a significant crack was initiated at the end of the fifth cycle of compression as shown in Figure 6.6.
Figure 6.4: (a) Average toughness for 4 specimens of foams. Each specimen was compressed to 80% strain for 5 successive cycles at ambient temperature ($T<<(T_g)$) with a strain rate of 0.01 mm/s. (b) A typical stress-strain response for 5 successive compression cycles performed on a single specimen of the CuAAC foams. The cylindrical CuAAC foam was compressed consecutively to 80% at ambient temperature with a strain rate of 0.01 mm/s. The toughness or energy to 80% strain was calculated after the first cycle to be 850 MJ/m$^3$. 

Figure 6.5: (a) Average fixity and recovery for 4 specimens of foams. Each specimen was compressed to 80% strain for 5 successive cycle at ambient temperature ($T_{g}$) with a strain rate of 0.01 mm/s. The recovery and fixity were calculated after each cycle of compression. (b) The permanent shape (left) of a CuAAC foam and the 80% compressed foam (middle). Heating the foam above its $T_{g}$ results in complete recovery of its original shape (right).

Figure 6.6: The CuAAC foam after 5 successive compression cycles to 80% strain.

When materials with a rigid crosslinked network and a $T_{g}$ much higher than ambient temperature are subjected to significant strains, they tend to fracture since the immobility of the
polymer chains limits their ability to dissipate energy, for example through mechanical damping via bond rotation or by breaking secondary intermolecular interactions like hydrogen bonding or pi-stacking. 38, 39 Here, the triazole linkage offers stiffness and toughness with hydrogen bonding and pi-stacking potential that might contribute to the unexpected toughness of the glassy CuAAC networks.

The stress-strain response of the CuAAC foam to compression showed a typical behavior that is representative of the compression of a porous material. The curve starts with a linear response, which is the elastic region, where the slope of the line is the Young’s modulus, followed by a plateau region in which the stress stays relatively constant until about 55-60% of the strain as shown in Figure 6.4(a). This region is associated with collapse of the pores. Once all of the pores collapse, the polymeric material itself starts to increase in density, which causes the stress to rise steeply. In the plateau region the CuAAC thin walls that are on the order of tens of microns, as shown in Figure 6.7, fold and bend without severely damaging the network. In addition, the homogeneous nature of the CuAAC network would help to distribute the stress equally through the network which is essential to minimize stress localization which would result in crack initiation. The stress compressed the 10 mm length of SMP CuAAC foam uniformly in the axial direction to form a 2 mm tall disc that, when reheated, returns to its original shape as shown in Figure 6.5 (b).

![SEM image of the CuAAC foam.](image)

**Figure 6.7:** SEM image of the CuAAC foam.
The thermal free-strain recovery behavior of the compressed foams is seen in Figure 6.8. After being programmed to 80% compressive strain at ~22°C, the samples were allowed to freely recover while being heated to $T_g + 40$°C at a rate of 3 °C/min. The samples were then held at 150°C for 10 minutes to ensure thermal equilibrium throughout the sample. In each cycle, the foams remained relatively stable up until the onset of glass transition (~100°C), as only 10% strain was recovered. After which, the foams rapidly expanded to at least 90% of its original length within the glass transition region. Full recovery was eventually achieved when the samples reached 150°C and were held isothermally. This behavior was attributed to thermal effects of the sample being in contact with the compression plates used at both ends to monitor strain. This behavior was not observed if the experiments were performed in an oven preheated to 150°C, in which recovery occurred more rapidly. While the overall recovery ratios of the samples were equal, the onset of recovery increased with each cycle. For example, the response of the 4th heating cycle was ~20°C higher compared to the 1st cycle. The delay in recovery is likely caused by the mechanical damage accumulated throughout the porous structure from cycle to cycle.

Figure 6.8: Four sequential cycles of compression and recovery for a CuAAC foam. The foam was compressed to 80% strain at ambient temperature with a strain rate of 0.01 mm/s, followed by recovery of the compressed sample upon heating to $T_g + 40$ °C with a heating rate of 3 °C /
min under preload (0.15N). Samples were held isothermal at 150 °C for 10 minutes between cycles. The same sample was compressed four times with monitoring of the recovery as a function of temperature after each compression cycle. The CuAAC foam was formed via a stoichiometric mole ratio of bisphenoldiazide, trialkyne ether, 2 mole % CuCl2/PMDETA, and 8 wt % hexylamine with 80 % porosity.

The CuAAC reaction forms rigid triazole linkages, unlike thiol-ene and epoxy-amine reactions which form flexible linkages. To investigate the effect of the network linkage on the mechanical behavior at high strain, the CuAAC SMP foam was compared to an epoxy-amine-based foam which was used as a negative control, where monomers with similar backbone structures as in the CuAAC case were used to form the network. The epoxy amine foam was produced by the same fabrication method as the CuAAC foam, and a mole ratio of 1:0.5:0.5 bisphenol A diglycidyl Ether, 1,6-diaminohexane, and aniline with 80% porosity as shown in Scheme 6.1 (b), and Figure 6.9. A mixture of flexible diamine and rigid mono-amine was used to achieve a crosslink density similar to the CuAAC foam as indicated by the similar rubbery modulus values between these two networks. The glass transition temperature, Tg, and the rubbery modulus of the epoxy-amine foam are observed to be 125 °C and 1.2 MPa, respectively, whereas the CuAAC foam has a Tg= 115 °C with a rubbery modulus of 1.0 MPa as shown in Figure 6.2 and 6.10 (a). Both polymers have the advantage of forming via a step-growth polymerization to form a homogenous network with a narrow Tg. The CuAAC polymer network, however, has the distinction of forming a rigid triazole linkage at a high concentration throughout the network, instead of the flexible tertiary amine bond that forms as result of epoxy-amine polymerization. The epoxy-amine foam was compressed to 80 % strain with strain rate of 0.01 mm/s at ambient temperature as shown in Figure 6.10 (b) where this foam shows brittle behavior and fails at 70% strain. The image in Figure 6.10 (b) shows the epoxy-amine foam severely damaged after the first compression cycle, while the CuAAC foam compressed uniformly to 80 % of its original height fully recovered. The toughness of the CuAAC foam (850 MJ/m3) to 80% strain is almost 3 times the toughness of epoxy-amine foam (300 MJ/m3). The ductile behavior of the glassy CuAAC foam compared to the brittle behavior of the glassy epoxy-amine suggests that the triazole linkage promotes not only a stiff network but also a tough network with high strain capability in compression.
Figure 6.9: FTIR kinetic study of the Epoxy conversion of a 1 mm thickness of 1:0.5:0.5 mole ratio of bisphenol A diglycidyl Ether, 1,6-diaminohexane, and aniline. FTIR was used to monitor the disappearance of the C-H stretching at 4530 cm⁻¹. The sample was heated to 100 °C for 5 hours.
Figure 6.10: (a) Glass transition temperature, $T_g$, and storage modulus were measured for the epoxy amine foam. The epoxy-amine network was formed with a mole ratio of 1:0.5:0.5 bisphenol A diglycidyl ether, 1,6-diaminohexane, and aniline with 80% porosity via click reaction showing a narrow glass transition peak with a $T_g = 125 \, ^\circ C$ and a rubbery modulus = 1.2 MPa. (b) Stress-strain curve obtained by compressing the epoxy-amine foam to 80% strain with a strain rate of 0.01 mm/s at ambient temperature. The epoxy-amine energy to 70% strain was calculated after the first cycle to be 300 MJ/m$^3$. The image in the left corner shows the epoxy-amine foam severely damaged after the first cycle of compression.

Since the 80% deformation corresponds closely to the maximum possible compression of the CuAAC foam of 80% porosity, the energy required for deformation of the CuAAC and epoxy-amine foams was also characterized at a relatively low strain (50%), until failure at ambient temperature as shown in Figure 6.11. Again the glassy CuAAC foam demonstrated great toughness and the ability to recover plastic deformation for up to 13 cycles of compression while the epoxy-amine survived only 2 compression cycles. As expected, each foam’s mechanical performance declined with successive cycles.
Figure 6.1: Energy required to achieve 50% compression for 4 specimens of CuAAC foams and 4 epoxy amine foams. Each specimen was compressed repeatedly to 50% strain until failure at ambient temperature ($T<T_g$) with a strain rate of 0.01 mm/s. The CuAAC foam was able to recover up to 13 successive cycles of compressions while the epoxy-amine failed after only 2 cycles of compression.

The energy required for deformation of the CuAAC and epoxy-amine foam was also investigated as a function of temperature as shown in Figure 6.2. Seven foams for each system were compressed to 50% strain at a rate of 0.01 mm/s at seven different temperatures: 20, 40, 60, 80, 100, 120, and 140 °C. To ensure uniform heating, each sample was held at a constant temperature for 10 minutes at each temperature point. Energy was measured as the area under the stress-strain curve. The energy required for both the CuAAC and epoxy-amine is the highest at ambient temperature; however, the CuAAC energy to 50% strain at ambient temperature is 2.5 times higher than the energy of epoxy-amine under the same conditions. As the temperature increases, the polymer becomes more ductile leading to reduction in the deformation resistance, and the energy declines for both the CuAAC and epoxy-amine foam. This behavior is particularly pronounced at temperatures close to the $T_g$ in which both systems show a 97% reduction in energy just above the $T_g$ regions.
Figure 6.12: The energy required for 50% strain plotted as a function of temperature for CuAAC network (filled circle) and the epoxy-amine network (filled square). Seven different foam samples for each system were compressed to 50% at different temperatures: 20, 40, 60, 80, 100, 120, and 140 °C. The energy values of CuAAC foams, and epoxy-amine were calculated as the area under the stress–strain curves to 50 % strain.

Conclusions

This work has demonstrated a facile approach to fabricate foams based on CuAAC polymerizations with outstanding shape memory attributes that are formed from high toughness networks, particularly as compared to traditional epoxy-amine foams. The unique recovery with the capability for recoverable plastic deformation at ambient temperature under cyclic deformations as well as the stiffness and toughness of the glassy CuAAC network make these materials desirable as high-strain SMP foams. The CuAAC network recovered almost fully through five consecutive compression cycles of 80% of its original length and 13 consecutive cycles of deformation to 50% strain at ambient temperature, demonstrating a remarkable, reversible plasticity. The ability of the CuAAC foam to compact at ambient temperature to a small volume without fracture, having an easily tunable $T_g$ with a wide range of monomer backbone structures combined with the unique chemistry of CuAAC such as chemoselectivity and orthogonally opens the door for porous CuAAC polymers to be widely employed in various smart material applications.
Experimental

Materials

1,1,1-Tris(hydroxymethyl) propane, propargyl bromide solution 80 wt% in toluene, sodium hydroxide, sodium chloride, bisphenol A diglycidyl ether, lithium perchlorate, sodium azide, copper(II) chloride, N,N,N',N',N''-pentamethyldiethylenetriamine(PMDTA), aniline, 1,6-diaminohexane, dimethyl sulfoxide, and acetonitrile were obtained from Sigma-Aldrich, and were used without further purification.

Monomers synthesis

Synthesis of 1-(Prop-2-ynyloxy)-2,2-bis(prop-2-ynyloxy)methyl)butane

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\begin{align*}
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\text{O} & \quad \text{O}
\end{align*}
\]

A solution of 40% NaOH in water (33.30 g, 50 mL H₂O) was added to 250 mL DMSO, and the mixture was stirred for 30 minutes at ambient temperature. 1,1,1-Tris(hydroxymethyl) propane (9.86g, .073 mol) was added to the solution and stirred for 20 minutes. Propargyl bromide (44.5 g, 0.299 mol) was added in aliquots to the mixture. The reaction was left for two days, and the resulting brown suspension diluted with 400 mL of distilled water and extracted with a 1:1 mixture of diethyl ether:ethyl acetate (600 mL). The organic layer was washed three times with distilled water and brine, dried with anhydrous Na₂SO₄, and concentrated at reduced pressure. The concentrate was purified by flash chromatography (9:1 hexane:ethyl acetate) with 70% yield . 1H NMR (400 MHz, Chloroform-d) δ 4.14 (d, J = 2.4 Hz, 6H), 3.42 (s, 6H), 2.42 (t, J = 2.4 Hz, 3H), 1.44 (q, J = 7.6 Hz, 2H), 0.90 (t, J = 7.6 Hz, 3H).

Synthesis of Bisphenol A di(3-azido-2-hydroxy propan-1-ol) ether
A solution was made of bisphenol A diglycidyl ether (16.84 g, 49.47 mmol) and LiClO₄ (16.65 g, 0.157 mol) in acetonitrile (150 mL). NaN₃ (9.99 g, 0.154 mol) was added in small amounts to the suspension. The solution was heated to 90°C and refluxed overnight. The reaction mixture was cooled to ambient temperature, and the crude material dissolved in 500 mL of DI water. This mixture was then extracted with ethyl acetate (4 x 150 mL). The organic layer was washed with brine and dried over anhydrous Na₂SO₄ and concentrated at reduced pressure. After purification, a yellowish viscous liquid was obtained with 99% yield. 1 H NMR (400 MHz, CDCl₃, δ): 7.17 (m, 4H), 6.85 (m, 4H), 4.19 (m, 2H), 3.99 (dd, 4H, J = 6.0, 1.2 Hz) 3.55 (m, 4H), 2.42 (d, 2H, J = 1.0 Hz), 1.68 (s, 6H).

Synthesis of CuCl₂/PMDTA

PMDTA (2.66 g, 15.35 mmol) was added to 30 mL acetonitrile and the mixture was added dropwise to a slurry of CuCl₂ (2.1 g, 15.35 mmol) and acetonitrile (60 mL) under constant stirring. This formed a turquoise solution. The reaction mixture was stirred for 30 minutes at ambient temperature and dried under vacuum.

Foam Preparation and Polymerization

Mold fabrication

A mold was made from poly(dimethylsiloxane) (PDMS). A Teflon cylinder 6 mm in diameter and 16 mm in length was glued to the bottom of a paper cup. PDMS mixed with a 15 wt % curing agent mixture was poured into the cup. After curing at 70 °C for 3 hours, the mold was removed from the paper cup.

CuAAC foam synthesis

The CuAAC foam was made by the salt leaching method using a mixture of 20 wt % monomers (monomers to solvent, methanol, ratio was 1.5:1) and 80 wt% sodium chloride with
respect to monomer. Sodium chloride was sifted through two different sized sieves with 350 μm mesh and 212 μm mesh. The average salt size was 290±40 μm. CuAAC polymer samples were formulated with a 50:50:1 azide:alkyne: CuCl₂/PMDTA ratio based on the moles of functional groups. The reaction mixture was left to mix on a Vortex mixer while the mold and sodium chloride were being prepared. The mold was rinsed with RainX to prevent polymer adhesion to the wall of the mold, and then sodium chloride was added and compacted in the mold with a Teflon rod. A slit was made in the bottom of the mold to allow air to escape when the reaction mixture was added. Hexylamine, 8 wt% with respect to monomer, was added to the reaction mixture to reduce Cu(II) to Cu(I), mixed with a pipette, and then added drop-wise on top of the salt in the mold to completely cover the salt. The reaction was allowed to proceed until the polymer was hard enough to remove from the mold without physical deformation. The polymer was left overnight at 80°C to ensure complete curing. Cured foams were left in 500 mL of DI water at 50°C for 5 days with water changed once daily to leach the sodium chloride and the hexylamine out from the polymer. Finally foams were vacuum-dried at 100 °C for a day before using.

**Epoxy-amine foam synthesis**

The Epoxy-amine foam was made by the salt leaching method using a mixture of 20 wt% monomers (monomers to solvent, acetonitrile, ratio was 1.5:1) and 80wt% sodium chloride with respect to monomer. Epoxy-amine polymer samples were formulated with a 1:0.5:0.5 bisphenol A diglycidyl ether : 1,6-diaminohexane : aniline ratio based on the moles of functional groups. Bisphenol A diglycidyl ether was weighed into a small vial and dissolved in acetonitrile. 1,6-diaminohexane and aniline were measured into a small vial and heated to 40 °C to melt. Sodium chloride was added to a mold that was previously treated with Rain-X. The mixed amines were added to the bisphenol A diglycidyl ether solution and mixed thoroughly before being added dropwise to the sodium chloride in the mold. The mold with the reaction mixed in with the sodium chloride was allowed to cure overnight at ambient temperature. The following day, the polymers were removed from the mold, and then were left to cure at 80-100 °C for 48 hours to ensure proper conversion. Cured foams were left in 500 mL of DI water at 50°C for 5 days with water changed once daily to leach the sodium chloride out from the polymer. Finally foams were vacuum-dried at 100 °C for a day before using.

**Characterization**
Fourier Transform Infrared Spectroscopy (FT-IR)

CuAAC samples were formulated with a 50:50:1 azide:alkyne: CuCl\textsubscript{2}/PMDTA ratio based on the moles of functional groups. A few drops of methanol were added and the mixture vortexed to obtain a homogenous mixture. Methanol was removed under vacuum. Hexylamine, 8 wt% with respect to monomer, was added to the mixture, and a small amount was placed between two sodium chloride crystals, using a spacer with a thickness of 65 µm. FTIR was used to monitor the disappearance of the azide peak at 2100 cm\(^{-1}\).

Epoxy-amine samples were formulated with a 1:0.5:0.5 ratio of bisphenol A diglycidyl ether, 1,6-diaminohexane, and aniline ratio based on the moles of functional groups. The mixture was heated to obtain a homogenous mixture. A small amount of reaction mixture was placed between two glass slides, using a rubber spacer with a thickness of 1 mm. FTIR was used to monitor the disappearance of the C-H stretching at 4530 cm\(^{-1}\). The sample was heated to 100 °C for 5 hours using a heating stage that was placed inside the IR chamber while monitoring the disappearance of the C-H peak.

Dynamic Mechanical Analysis (DMA)

DMA was performed to characterize the thermo-mechanical properties of the foam. CuAAC and epoxy-amine polymers were synthesized using the methods previously described. To create rectangular samples, a mold was made for the mixture by using binder clips to hold a 1 mm thick rubber cutout between the glass slides. This mold formed a slot between the glass slides that was 1 mm thick x 6.5 mm wide x 10 mm long. The mechanical properties of the foam samples were characterized by using TA instruments DMA Q800. The rectangular samples were tested with the multi-frequency strain mode. The temperature was ramped from 25 °C to 150 °C at 3°C/min with a frequency of 1 Hz and a strain of 0.01%. The glass transition temperature \(T_g\) was determined as the maximum point of the tan δ curve.

Shape memory characterization

The shape memory behavior of the samples was characterized using several test methods. First, a low-strain, shape memory cycle under free-strain recovery was characterized using the DMA machine. Rectangular samples were heated to \(T_g + 30°C\) and stressed at a constant rate of
0.004 MPa/min to 10-20% strain. The samples were then rapidly cooled to -10°C at a rate of 20°C/min. The force was then decreases to 0.001 N and held to constant. Finally strain recovery was monitored as the sample was heated to 150 °C at a rate of 3°C/min. The shape fixity $R_f$ and shape-recovery ($R_r$) ratios were calculated as:

$$R_f(\%) = \left(\frac{\epsilon_u(N)}{\epsilon_m}\right) \times 100 \quad \text{(1)}$$

$$R_r = \left(\frac{\epsilon_u - \epsilon_p}{\epsilon_m - \epsilon_p}\right) \times 100 \quad \text{(2)}$$

Where $\epsilon_u$, $\epsilon_m$ and $\epsilon_p$ are the unloading strain, maximum strain, and permanent strain after heating, respectively. It should be noted that the term $\epsilon_p(N-1)$ is equal to zero when calculating these ratios for only one cycle (i.e. $N=1$).

Next, cyclic free-strain shape memory behavior was characterized under high strain and low deformation-temperature conditions. Cylindrical foam samples measuring approximately 6.5 mm in diameter and 10 mm in length were compressed to 80% strain at a rate of 0.01 mm/s using a uniaxial test machine (MTS Eden Prairie, MN, USA). Compression was performed at ambient temperature (22 °C). Samples were then unloaded to zero stress and heated to 125 °C and held for 10 minutes to ensure thermal equilibriu. This process was repeated for a maximum of $N=5$ cycles. The shape-fixity and recovery ratios were measured after each cycle. To monitor recovery as a function of temperature, recovery tests were also performed using a Bose-Electro-Force 3200 (Eden Prairie, MN). After each cycle of deformation to 80% at ambient temperature, as described above, the recovery was measured as the sample was heated from 25 °C to 150 °C at a rate of 3 °C/ min under constant preload (0.15N). Samples were held isothermal at 150 °C for 10 minutes to ensure equilibrium between cycles. The fixity and recovery ratio were calculated as in equations 1 and 2 above.

**Toughness characterization**

The toughness of the CuAAC and epoxy-amine foams was investigated as a function of temperature. Cylindrical samples measuring 6.5 mm in diameter and 10 mm length were compressed to 50% strain at a rate of 0.01 mm/s using a uniaxial mechanical tester. Samples were compressed at seven different temperatures: 20, 40, 60, 80, 100, 120, and 140 °C. To ensure
uniform heating, each sample was held at a constant temperature for 10 minutes at each temperature point. The toughness was measured as the area under the stress-strain curve. Finally, samples were heated at 150 °C and held isothermally for 10 minutes.

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Chapter 7
Conclusions and future directions

The copper(I) catalyzed azide alkyne cycloaddition, CuAAC, reaction has several desirable attributes both for the synthesis of small molecules and for macromolecular synthesis such as its high chemoselectivity, orthogonality to other functional groups, and a tolerance to a variety of reaction conditions. This thesis focused on investigation of the CuAAC reaction for polymer network synthesis. Different catalytic systems were developed to initiate the CuAAC reaction in solution and for bulk polymerization. The CuAAC polymer network was also utilized to form materials with various functions and structures.

In chapter 3, Cu(II)/amine complexes were employed to initiate the CuAAC reaction via ligand metal charge transfer, LMCT. The photo-reduction of these complexes was examined to determine their efficiency in catalyzing the CuAAC reaction. The aliphatic amine ligands were used as an electron transfer species to reduce Cu(II) upon irradiation while also functioning as an accelerating agent and as protecting ligands for the Cu(I). Uniquely, photo-CuAAC via ligand metal charge transfer was shown to be highly selective towards the CuAAC reaction and was used to synthesize triazole side chain polymers using a combination of photo-CuAAC and subsequent homopolymerization of the ene with chain growth polymerization, offering sequential and orthogonal reactions within the same polymer.

In chapter 4, Cu(II)/aliphatic primary amines, particularly hexylamine, were used to initiate bulk polymerization of bifunctional azides and trifunctional alkynes. The catalytic system was shown to be effective, and it catalyzed the polymerization to near completion at ambient temperature. The polymerization rate was strongly dependent on the amine concentration so that the polymerization rate could readily be controlled. The rate dependence and UV-Vis
measurements indicate that hexylamine does not act as the sole reducing agent, and it aids in shifting the equilibrium of Cu(II) towards a Cu(I) species to catalyze the CuAAC reaction, including polymerization of multiazide and multialkyne monomers.

In chapter 5, sequential thiol–acrylate and photo-CuAAC click reactions have been utilized to form two-stage reactive polymer networks capable of generating wrinkles. After an initial homogeneous thiol–acrylate step growth network was formed, a second step-growth reaction, the CuAAC click reaction, was initiated in a gradient fashion within the thiol–acrylate network via Cu diffusion into the film to generate micro-wrinkles. Control over the wavelength and amplitude of these wrinkles using the resin film thickness is further demonstrated by studying the surface profiles using scanning electron microscopy (SEM) and atomic force microscopy (AFM). Additionally, this technique was used to photopattern wrinkle formation using a photomask.

In chapter 6 the CuAAC reaction was employed to design a tough, stiff porous material, forming a well-defined network which possessed a high glass transition temperature ($T_g = 115^\circ$C) due to the formation of the triazole linkages. The shape-memory behavior of this material as well as its thermo-mechanical behavior and toughness were examined, and compared to traditional epoxy foams. The foam material demonstrated shape-memory behavior and was able to fully recover through up to five successive cycles of compressive deformation to 80% at ambient temperatures, presenting a significant volume change and resistance to fracture. The CuAAC foam exhibits reversible plasticity in which the foam recovers almost entirely from significant deformation when reheated above its glass transition.

**Future directions**

The CuAAC reaction is among the most widely implemented click reactions; however, application of this powerful chemistry in bulk polymerization is still in its infancy. The reaction
still suffers from significant limitations such as the relatively high concentration of copper, unpredictable monomer reactivity due to the complex reaction mechanism, side reactions of azides when radicals are used, and the highly exothermic nature of the reaction. At the same time the potential for the CuAAC reaction in bulk polymerization is significant because the reaction is efficient and is orthogonal to many other common reactions. The unique chemistry of the CuAAC reaction with the step-growth polymerization mechanism, opens the door to design materials with unique properties and with potential for subsequent modification and functionalization.

Lowering the copper concentration limits its cytotoxicity, and lowers the pronounced color of the final polymer. Designing highly efficient catalytic system with a reasonable reaction rate would reduce the need for high catalyst concentration. Oligomerization seems to be necessary when designing such efficient catalytic system to overcome the exothermic nature of the reaction in bulk conditions.

The synthesis and evaluation of a broader range of monomer structures and examination of the kinetics would help to discover the general trend of reactivity in this system. The synthesis of various structures of azide-containing monomers is more accessible than alkyne-containing monomers, where the azides are readily prepared using various reactions such as nucleophilic substitution of alkyl halides or tosylates with sodium azide. The synthesis of low viscosity monomers baring alkynes, with high yield and simple reactions is more challenging. We designed a simple road to synthesis of a large library of alkyne-based monomers using the click reaction of Michael addition of thiols with propargyl bromide. The synthesis proved to be simple and straightforward, with minimal purification. Moreover, the thiol-ether alkyne bond was found to be reactive toward the cycloaddition with the azides.
The Cu(II)/aliphatic primary amine system, chapter 4, is a very efficient pathway to initiate the CuAAC bulk polymerization, and it enables incorporation of groups for subsequent radical mediated polymerizations for post-polymerization modifications of the material properties.

Porous CuAAC-based materials have the potential to be used for smart materials synthesis and biomedical devices. The mechanical properties are easily manipulated by varying the monomer structures with glass transition temperatures ranging from 150-37 °C. The advantage of the large surface area of porous materials combined with the robust chemistry of the CuAAC reaction allows for the incorporation of different chemistries to designs smart materials like membranes with selective functional group modifications, shape memory materials, and controllable pores size using lyotropic liquid crystals.
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