This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Kinetics of bulk photo-initiated copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) polymerizations

AUTHORS: Han Byul Song\textsuperscript{1}, Austin Baranek\textsuperscript{1}, and Christopher N. Bowman\textsuperscript{*1,2}

\textsuperscript{1}Department of Chemical and Biological Engineering, University of Colorado Boulder, 596 UCB, Boulder, CO 80309-0596, United States.

\textsuperscript{2}Materials Science and Engineering Program, University of Colorado Boulder, 596 UCB, Boulder, CO 80309-0596, United States.

KEY WORD: Photopolymerization; CuAAC; step-growth polymerization; kinetics; click chemistry; real-time FTIR.

ABSTRACT: Photoinitiation of polymerizations based on the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction enables spatio-temporal control and the formation of mechanically robust, highly glassy photopolymers. Here, we investigated several critical factors influencing photo-CuAAC polymerization kinetics via systematic variation of reaction conditions such as the physicochemical nature of the monomers; the copper salt and photoinitiator types and concentrations; light intensity; exposure time and solvent content. Real time Fourier transform infrared spectroscopy (FTIR) was used to monitor the polymerization kinetics \textit{in situ}. Six different di-functional azide monomers and four different tri-functional alkyne monomers containing either aliphatic, aromatic, ether and/or carbamate substituents were synthesized and polymerized. Replacing carbamate structures with ether moieties in the monomers enabled an increase in conversion from 65\% to 90\% under similar irradiation conditions. The carbamate results in stiffer monomers and higher viscosity mixtures indicating that chain mobility and diffusion are key factors that determine the CuAAC network.
formation kinetics. Photoinitiation rates were manipulated by altering various aspects of the photoreduction step; ultimately, a loading above 3 mol% per functional group for both the copper catalyst and the photoinitiator showed little or no rate dependence on concentration while a loading below 3 mol% exhibited 1st order rate dependence. Furthermore, a photoinitiating system consisting of camphorquinone resulted in 60% conversion in the dark after only 1 minute of 75 mW/cm² light exposure at 400-500nm, highlighting a unique characteristic of the CuAAC photopolymerization enabled by the combination of the copper(I)’s catalytic lifetime and the nature of the step-growth polymerization.

INTRODUCTION

Owing to the “click” nature of being a robust, orthogonal, and efficient reaction, the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction has been widely utilized in bio-conjugation, surface functionalization, as a coupling chemistry for labeling and in polymer synthesis, particularly in the formation of complex polymer architectures. Mechanistic and kinetic investigations of the CuAAC reactions have generally been performed in highly dilute, solution-based systems, where small molecules bearing alkyne and azide functional groups were evaluated in an attempt to improve the efficiency, yield, and rate of the CuAAC reaction by varying an array of reaction conditions, including solvent types and catalyst concentrations. Vast arrays of ligands, copper salts, alkynes and azide moieties have been screened at varying concentrations to optimize and understand the kinetics of the CuAAC reaction, to define a general rate law, or to assess a mechanistic aspect of the reaction. However, the conclusions from these experiments as well as the detailed kinetic constant measurements are highly sensitive to the reaction conditions that were used, making it difficult to draw conclusions about kinetic behavior, particularly for the significant extrapolation necessary for bulk CuAAC polymerizations in which the azide and alkyne concentrations are dramatically higher and where the solubility of copper, diffusion and mobility
of reacting species, and the heat of reaction all play a crucial role in the reaction/polymerization kinetics.

Since the discovery of the CuAAC reaction in 2001 by Meldal and Sharpless, the direct addition of copper(I) salts and/or a 3 to 10 equivalent excess of a reducing agent such as sodium ascorbate with copper(II) salts have been widely used to initiate the CuAAC reaction. The insolubility of sodium ascorbate in organic media and the lack of temporal control when using copper(I) salts has hindered the development of homogeneous bulk polymers using solvent-free CuAAC. Few studies have attempted the CuAAC polymerization in bulk or investigated kinetics and properties of the resulting polymers. In 2004 and 2007, Liu et al. performed CuAAC polymerizations using solutions of multifunctional alkyne and azide monomers on copper substrates in order to analyze adhesive properties of CuAAC polymers. Later in 2010, Sheng et al. made solvent-free CuAAC linear polymers by the direct addition of copper(I) salts with limited concentrations of copper used due to solubility issues. The discovery and implementation of the photo-reduction of copper(II) upon light exposure from several research groups promoted CuAAC polymerization as a means to enhance the spatio-temporal control of the reaction. In 2006, Ritter and König presented the photogeneration of copper(I) by the reduction of copper(II) using an excitation of the chromophore in the presence of an electron donor. In 2009, Poloukhtine et al. discovered the photo-medicated copper-free azide-alkyne reaction using light to decompose cyclopropenones into cyclooctynes, which then proceed via a cycloaddition reaction with azides. Adzima et al. implemented spatio-temporal control of photo-CuAAC reactions as well as photo-polymerizations of multi-functional monomers using a visible light photoinitiator to reduce copper(II), and Tasdelen et al. introduced UV-initiated CuAAC reactions based on electron charge transfer from amine ligands to copper(II). Building on these approaches to the photoinduced reduction of copper, bulk photoinitiated CuAAC polymerization of crosslinked networks was successfully demonstrated in homogeneous and stable resin mixtures that contained multi-functional...
alkynes and azides. Specifically, Gong et al. reported kinetic profiles of bulk CuAAC polymerizations initiated by light in the presence of visible light photoinitiators, and Sandmann et al. presented photo-reduction of copper(II) acetates via light without the presence of photoinitiators on the CuAAC resins containing at least 15 weight % methanol.

Scheme 1. Proposed reaction diagram of one approach to photoinitiated CuAAC-based polymerizations:

(a) photoinitiation, copper reduction to form Cu(I), and cycloaddition between azides and alkynes. (b) Side reactions that can potentially occur during the course of the reaction: radical coupling, copper disproportionation, copper oxidation, and alkyne coupling reactions.

Scheme 1 presents the photo-CuAAC reaction scheme that occurs when using a radical generating photoinitiator along with several plausible side reactions in four distinct stages: initiation, reduction of copper, cycloaddition, and termination. Initiation, in this case, involves the cleavage of photo-responsive compounds to generate radicals upon UV or visible light irradiation. Subsequently, the reduction of the copper(II) species into catalytically active copper(I) occurs parallel to other competing reactions, such as re-oxidation of copper(I) to copper(II), further reduction of copper(I) to copper(0), and disproportionation of copper(I) to copper(II) and copper(0). The cycloaddition step itself is a complex, multi-step mechanism involving copper diffusion, σ- and π-coordination with
alkynes, six-membered ring formation between copper-acetylide and azides, and the ultimate release of copper. Termination takes place when copper(I) loses its catalytic activity by oxidation or disproportionation. Previously, other mechanistic studies dealing with either experimental or computational modeling confirmed that the CuAAC reaction rate had a second order dependence on copper concentration, the formation of six-member rings during cycloaddition was a rate determining step, and other plausible side reactions such as alkyne coupling hindered the reaction rate by forming inactive species though all of these conclusions depend at least somewhat on the reaction conditions used.

The nature of step-growth polymerizations enables the CuAAC polymerization to form relatively homogeneous polymer networks, where the rigid-aromatic triazole adducts formed throughout the network as a product of the CuAAC reactions exhibit excellent thermal and chemical stability, while also increasing the polymer stiffness and glass transition temperature. However, the azide moieties can be explosive when sufficiently concentrated; therefore, designing higher molecular weight azide monomers is essential to enable bulk polymerizations to be performed safely and efficiently. In addition, the solubility of copper in organic substrates is often insufficient, either requiring an addition of chelating ligands to increase solubility or only allowing for minimal concentrations of copper to be incorporated into the resin mixtures. Due to the aforementioned challenges, previous investigations of the CuAAC polymerization kinetics in bulk are limited. Herein, we explore the effects of monomer structure, copper and photoinitiator concentrations, light exposure conditions, temperature, solvent, light intensity, and irradiation times on the rate of bulk CuAAC polymerization to understand this complex polymerization and enable the determination of optimal polymerization conditions for spatially and temporally controlled formation of photopolymerized CuAAC thermosets.

EXPERIMENTAL SECTION
1. Materials

1,3-Bis(isocyanatomethyl)cyclohexane, 4,4-methylenebis(cyclohexyl isocyanate), 1,3-bis(2-isocyanatopropan-2-yl)benzene, 4,4’-methylenebis(phenyl isocyanate), bis(4-hydroxyphenyl)methane, 6-chloro-1-hexanol, dibutyltin dilaurate, sodium azide, 1,1,1-tris(hydroxymethyl)propane, pentaerythritol, 1,3,5-tris(bromomethyl)benzene, phloroglucinol, propargyl alcohol, sodium hydride, diethyl azodicarboxylate, tetrabutylammonium iodide, N,N,N’,N’,N”-pentamethyldiethylenetriamine (PMDETA), copper(II) chloride, triphenylphosphine, 2,2-dimethoxy-2-phenylacetophenone (DMPA), propargyl bromide, camphorquinone (CQ), tetrahydrofuran, and acetonitrile were used as received from Sigma Aldrich. 2,2,4,4-tetramethyl-1,3-cyclobutanediol, 5-Hexyn-1-ol, hexyl isocyanate, 6-chloro-1-hexyne, 1-phenyl-1,2-propanedione (PPD), 2,2-bis(bromomethyl)-1,3-propanediol, sodium hydroxide, potassium carbonate, potassium hydroxide, hydrochloric acid, methanol, acetone, methylene chloride, and dimethylformamide were used as received from Fisher Scientific. Diphenyl(2,4,6-trimethylbenzoyl)-phosphine oxide (Lucirin-TPO) was used as received from VWR International. Bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide (I819) was used as received from BASF. All azides were synthesized according to the azide safety rules and handled with appropriate care and precaution, and generally working with the monomers, resins and polymers in small quantities. Three facile reaction schemes, alcoholsysis of isocyanates, Mitsunobu, and Williamson ether, were used to synthesize difunctional azides and tri-functional alkynes as indicated below. All NMR measurements and yields of monomers are presented in the supporting information.
Figure 1. Monomer libraries with systematic structural variations for difunctional azides 2a-2f and multifunctional alkynes 3-8, photoinitiators, and copper catalysts used in the bulk photo-CuAAC photopolymerizations studied here.

Synthesis of dicarbamate halide intermediates (1a-1d): A solution of diisocyanate - 1,3-bis(isocyanatomethyl)cyclohexane (a), 4,4-methylenebis(cyclohexyl isocyanate) (b), 1,3-bis(2-isocyanatopropan-2-yl)benzene (c), or 4,4′-methylenebis(phenyl isocyanate) (d) (4.09 mmol) - and dibutyltin dilaurate (5 drops) in THF (3 mL) was added in a round bottom flask and purged under nitrogen. The reaction mixture was cooled to 0°C in an ice bath, followed by dropwise addition of 6-chloro-1-hexanol (8.60 mmol, 1.17 g). Removal of the ice bath allowed the reaction mixture to stir at room temperature for 12 h. The reaction mixture was then flowed through a silica plug with excess THF and purified by column chromatography if necessary. The product – dicarbamate chlorides or bromides - was dried in vacuo as a colorless oil (1a-1c) or white solid (1d).

Synthesis of dicarbamate halide intermediates (1f): A solution of hexyl isocyanate (34.3 mmol, 5 ml) and dibutyltin dilaurate (5 drops) in THF (20 mL) was added in a round bottom flask and purged under nitrogen. The reaction mixture was cooled to 0 °C in an ice bath, followed by dropwise addition of a
solution of 2,2-bis(bromomethyl)-1,3-propanediol (f) (17.2 mmol, 4.5 g) in THF (10 ml). Removal of the
ice bath allowed the reaction mixture to stir at room temperature for 12 h. The reaction mixture was then
flowed through a silica plug with excess THF. The product was recrystallized in ethyl acetate as a white
solid (1f).

**Synthesis of carbamate diazides (2a-2d, 2f):** A solution of dicarbamate chlorides or bromides (1a-1d, 1f) (4.15 mmol) and sodium azides (16.6 mmol, 1.08 g) in DMF (30 ml) was added to a round bottom
flask connected with a reflux condenser. The reaction mixtures containing (1a-1d) were stirred at 80°C
for 12 h and for (1f) for 30 h. The product was extracted with ethyl acetate and water, dried with
Na₂SO₄, purified by column chromatography if necessary, and dried *in vacuo* as a colorless oil (2a-2c) or a white solid (2d,2f).

**Synthesis of ether diazides, (2e):** A solution of bis(4-hydroxyphenyl)methane (4.99 mmol, 1 g), 6-
chloro-1-hexanol (14.9 mmol, 2.05 g), and triphenylphosphine (14.9 mmol, 3.93 g) in THF (5 ml) was
added to a round bottom flask and placed in an ice bath inside a sonicator. After dropwise addition of
diethyl azodicarboxylate (14.9 mmol, 5.88 ml of a 40% solution in toluene) at 0°C, the reaction mixture
was sonicated for 2 h and then stirred for 12 h at room temperature. Triphenylphosphine was removed
from the reaction mixture by crystallization in ethyl acetate. The product - diether chlorides - was dried
in vacuo as a colorless oil, and sodium azides (20.6 mmol) in DMF (60 ml) was added to a round
bottom flask connected with a reflux condenser. The reaction mixture was stirred at 80°C for 12 h. The
product was extracted with ethyl acetate, water, and 1M NaOH, dried with Na₂SO₄, purified by column
chromatography if necessary, and dried *in vacuo* as a colorless oil.

**Synthesis of trialkynes, (3):** A solution of 1,1,1-tris(hydroxymethyl)propane (14.7 mmol, 1.97 g) and 40
w/w% NaOH/water in DMSO (15 ml) was added in a round bottom flask and stirred for 1 h at room
temperature. After dropwise addition of propargyl bromide (94 mmol, 8.9 ml of 80% solution in
toluene), the reaction mixture was stirred for 5 days. The product was extracted with diethyl ether and
water, dried with Na$_2$SO$_4$, purified by column chromatography if necessary, and dried *in vacuo* as a colorless oil.

*Synthesis of tetraalkynes, (4)*: A solution of pentaerythritol (73.45 mmol, 10 g), KOH (1016 mmol, 57 g), and TBAI (0.95 mmol, 0.35 g) in THF (250 ml) was added to a round bottom flask connected with a reflux condenser under a nitrogen purge. After dropwise addition of propargyl bromide (691 mmol, 65.45 ml of 80% solution in toluene), the reaction mixture was stirred for 3.5 h at 70 °C. The reaction mixture was extracted with ethyl acetate, water, and 1M NaOH, dried with Na$_2$SO$_4$. The product was recrystallized in ethyl acetate at 0 °C as a yellow solid.

*Synthesis of trialkynes, (5)*: A solution of propargyl alcohol (4.51 mmol, 0.25 g) and 60% NaH (4.51 mmol, 0.18 g) oil dispersion in DMF (15 ml) was added in a round bottom flask under a nitrogen purge at 0 °C in an ice bath. After 10 min of stirring, 1,3,5-tris(bromomethyl)benzene (1.40 mmol, 0.50 g) was added to the reaction mixture and stirred for 24 h at room temperature. The reaction mixture was neutralized with HCl. The product was extracted with ethyl acetate and water, dried with Na$_2$SO$_4$, purified by column chromatography if necessary, and dried *in vacuo* as a yellow oil.

*Synthesis of trialkynes, (6)*: A solution of phloroglucinol (79.3 mmol, 10.0 g) and K$_2$CO$_3$ (476 mmol, 65.8 g) in DMF (500 ml) was added in a round bottom flask connected with a reflux condenser under a nitrogen purge. After dropwise addition of propargyl bromide (560 mmol, 53 ml of an 80% solution in toluene), the reaction mixture was stirred for 24 h at 80 °C. The reaction mixture was extracted with ethyl acetate, water, and 1M NaOH, dried with Na$_2$SO$_4$. The product was recrystallized in methanol as a white solid.

*Synthesis of trialkynes, (7)*: A solution of phloroglucinol (7.93 mmol, 1.0 g) and K$_2$CO$_3$ (47.6 mmol, 6.58 g) in DMF (50 ml) was added in a round bottom flask connected with a reflux condenser under a nitrogen purge. After dropwise addition of 6-chloro-1-hexyne (55.50 mmol, 6.8 ml), the reaction
mixture was stirred for 24 h at 100 °C. The reaction mixture was extracted with ethyl acetate, water, and 1M NaOH, dried with Na₂SO₄, purified by column chromatography, and dried in vacuo as a white solid.

Synthesis of dialkynes, (8): A solution of 2,2,4,4-tetramethyl-1,3-cyclobutanediol (6.93 mmol, 1 g), KOH (47.15 mmol, 2.65 g), and TBAI (0.048 mmol, 17.5 mg) in THF (20 ml) was added to a round bottom flask connected with a reflux condenser under a nitrogen purge. After dropwise addition of propargyl bromide (27.74 mmol, 3 ml of 80% solution in toluene), the reaction mixture was stirred for 3.5 h at 70 °C. The reaction mixture was extracted with ethyl acetate, water, and 1M NaOH, and dried with Na₂SO₄. The product was flowed through a silica plug with hexane/ethyl acetate solvent system (9:1) and recrystallized from methanol as a white solid.

Preparation of CuCl₂[PMDETA] complex: 1:1 molar mixture of CuCl₂ and PMDETA (N,N,N′,N′,N′-pentamethyldiethylenetriamine) in acetonitrile was stirred overnight at room temperature and dried in vacuo to a blue-green solid.

2. Methods

Sample preparation. Stoichiometric mixtures of a diazide, trialkyne (1:1 N₃:alkyne), and various mole percentages of CuCl₂[PMDETA] and photoinitiator per functionality were prepared. Methanol, DCM, or acetone was used to homogenize the mixture, depending on the solubility of the resin mixtures with copper, and was later removed in vacuo. The solvent content of each resin was verified by ¹H-NMR using a Bruker Avance-III 400 MHz spectrometer with 16 scans/sec⁻¹ and 1 s of relaxation time prior to any polymerization.

Fourier Transform Infrared Spectroscopy. An FTIR spectrometer (Nicolet 8700, Fisher Scientific) incorporated with a heating stage was used to monitor the real-time polymerization kinetics of the functional group conversion in transmission mode. Irradiation was performed using a light guide connected to a mercury lamp (Acticure 4000, EXFO) with either a 365 nm or 400-500 nm bandgap filter, depending on the photoinitiator used. Samples were placed between NaCl plates, and the azide
peak was monitored in the absorption range between 2300-2000 cm\(^{-1}\) having the alkane C-H stretching bonds as a reference peak between 2980-2840 cm\(^{-1}\) with 12 scans sec\(^{-1}\) and 2 cm\(^{-1}\) resolution.

**RESULTS AND DISCUSSION**

*Monomer Structural Variations.* Combinations of azide and alkyne monomers containing monomers of various structure and functionality were examined while maintaining all other reaction conditions the same, including the copper loading, photoinitiator concentration, light exposure time and intensity, and temperature. The resulting CuAAC polymerization kinetics are shown in Figures 2 and 3. Generally, despite being initiated by relatively low light intensities (only 10 mW/cm\(^2\)), these polymerizations are largely complete after only 2-5 minutes of irradiation though persistent polymerization does occur well after exposure is complete, indicative of the long lifetime of the catalytic Cu(I) species formed during the exposure period.

As shown in Figure 2, structural elements within the azide monomers such as the presence of either aromatic or non-aromatic cores and either the carbamate or ether linkages in the monomer backbones affect both the initial polymerization rate and final conversion significantly. Azides having cyclohexane cores, \(2a\) and \(2b\), resulted in slightly more rapid initial polymerization rates and approximately 6.5% higher final conversion after 30 minutes, as compared to azides bearing aromatic cores, \(2c\) and \(2d\). Similarly, an azide monomer \(2e\) containing an ether linkage in contrast to a carbamate linkage as in monomer \(2d\), showed a two-fold increase in the initial polymerization rate during the first 2 minutes of irradiation and resulted in approximately 20% higher maximum conversion after 30 minutes. From the viscosity measurement for the pure azides at 50 °C via rheometry, the viscosity of the azide monomers with a single ring core, \(2a\) and \(2c\), was 0.18 Pa·s, while the viscosity of the azide monomers having two ring cores, \(2b\) and \(2d\), was 5.8 Pa·s at a shear rate of 20 s\(^{-1}\) (See Table S1). Similarly, the azide monomer \(2e\) containing an ether linkage had a viscosity of 0.05 Pa·s, approximately 100 times less viscous than the azide monomer \(2d\) with a carbamate linkage (Table S1). By correlating
the viscosity of the monomers with the kinetic profiles from Figure 2, it is clear that increasing the monomer viscosity results in a reduction of both the initial rate of polymerization and the maximum conversion. The effect of viscosity on the polymerization rate is likely caused by diffusional limitations, either of the initiation reaction or of the CuAAC reaction itself. A similar effect of increasing viscosity was also observed in resins with azides 2f and 2d as shown in Figure 2.

Azide 2f contains two azide functional groups held in close proximity by sterically hindered carbamate side groups. This short distance between the two azides has previously been reported to accelerate the CuAAC reaction, proposing that the formation of a first triazole works as a ligand to aid copper coordination for the very proximate neighboring azide. However, no significant difference in kinetics was observed between azides 2d and 2f, suggesting that this proximal effect is of minimal importance in these bulk, highly concentrated reaction environments.

Figure 2. Bulk photo-CuAAC polymerization kinetics as measured by FTIR. 1:1 azide:alkyne mixture with varying azide structures, including 2a (closed square), 2b (open triangle), 2c (closed triangle), 2d (closed circle), 2e (open square), 2f (open circle). Each azide was polymerized stoichiometrically with alkyne 3 in the presence of 2 mol% CuCl₂[PMDETA], 4 mol%
DMPA per azide functional group, and <0.5 wt% methanol (<0.5 wt% acetone for 2e). Each mixture was irradiated for 5 min (gray shaded area) at 50 °C with 10 mW/cm² of 365 nm light following 3 minutes in the dark as a baseline measuring period.

As observed in Figure 3, structural variations in the alkyne monomers have a pronounced effect on the initial polymerization rate and the final conversion. Alkynes 3, 4, 5, 6, and 8 showed a noticeable increase in the average initial polymerization rate, as compared to alkyne 7, during the first 2 minutes of irradiation, mainly due to the higher reactivity of an alkyne functional group next to an ether linkage compared to a hydrocarbon linkage. The alkyne reactivity was also confirmed through a study of small molecule model compound reactivity in solution by FTIR, using a 2 M solution in DMF of propargyl alcohol or 5-hexyn-1-ol, difunctional azides 2c, 2% CuCl₂[PMDETA], and 4% DMPA, irradiated at ambient temperature (Figure S1). The average initial reaction rate using propargyl alcohol was 4.5 mol/(L·min) while the average initial rate using 5-hexyn-1-ol was only 1.7 mol/(L·min), suggesting approximately 2.6 times higher reactivity of propargyl alcohol towards the CuAAC reaction under these conditions. However, despite a slower average initial polymerization rate as compared with alkyne 6, a resin containing alkyne 7 reached 97% conversion after 50 minutes, as compared to alkyne 6 which reached only 82% conversion after 50 minutes. Longer hydrocarbon linkages between the alkyne functional groups in 7 in contrast to 6 provide flexibility to the resin, which aids in increasing the final conversion, as long as the copper(I) species are able to remain active. Furthermore, by increasing the alkyne functionality from 3 to 4, alkyne 4 yielded only 82% conversion after 50 minutes while alkyne 3 achieved 90% conversion after the same time. However, when the alkyne functionality was further reduced to 2, alkyne 8 only exhibited 87% conversion after 50 minutes, where the number average degree of polymerization is predicted to be 8 repeat units using the Carothers equation, which corresponds to a number average molecular weight of 6000 (PDI = 1.9). Clearly, the final conversion is strongly affected by vitrification and structural elements of the monomer that impact the final glass transition temperature of the polymer will have a significant effect on the final conversion as well.
Specifically, the correlation between conversion and the structural rigidity of monomers, rather than the reactivity of functional groups, suggests that the kinetics of CuAAC bulk polymerizations are highly diffusion-limited, especially at the later stages of polymerization.

![Bulk photo-CuAAC polymerization kinetics using FTIR.](image)

**Figure 3.** Bulk photo-CuAAC polymerization kinetics using FTIR. 1:1 azide:alkyne mixture with varying alkyne structures, including 3 (open triangle), 4 (closed triangle), 5 (closed circle), 6 (open square), 7 (closed square), 8 (open circle). Each alkyne was polymerized stoichiometrically with azide 2c in the presence of 2 mol% CuCl$_2$[PMDETA], 4 mol% DMPA per azide functional group, and <0.5 wt% methanol. Each mixture was irradiated for 5 min (gray shaded area) at 50 °C with 10 mW/cm$^2$ of 365 nm light following 3 minutes in the dark as a baseline measuring period.

Figure 4 illustrates the effect of the presence of solvent on the final conversion of the CuAAC polymerization via variations in methanol concentration within a single resin mixture. With increasing methanol content, one expects the initial viscosity and final glass transition temperature for the polymer to be reduced. Here, the primary effect was found to be the plasticization of the methanol which increases chain mobility.$^{56}$ The conversion after 10 minutes reaction time was increased dramatically by the presence of the methanol with a negligible influence on the initial polymerization rate. In addition,
the effect of methanol content on polymerization conversion was only significant at ambient temperature, while negligible differences were observed at elevated temperature, 50 °C.

Figure 4. Bulk photo-CuAAC polymerization kinetics using FTIR. 1:1.2 azide:alkyne mixture with varying methanol concentration ranging from 0.1 to 12.8% by weight. Azide 2c was polymerized with alkyne 3 in the presence of 2 mol% CuCl₂[PMDETA], 4 mol% DMPA per azide functional group, and methanol. Each mixture was irradiated for 5 min (gray shaded area) at (top) ambient temperature and (bottom) 50 °C with 10 mW/cm² of 365 nm light following 3 minutes in the dark as a baseline measuring period.
Visible light photoinitiators. In Figure 5, a variety of visible light photoinitiators, including CQ (camphorquinone), PPD (1-phenyl-1,2-propanedione), I819 (bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide), and Lucirin TPO (2,4,6-trimethylbenzoyl-diphenylphosphine oxide) – were tested to examine their effectiveness in initiating the CuAAC polymerization. A 1:1 stoichiometric mixture of azide 2c and alkyne 3 with 2 mol% CuCl$_2$[PMDETA] and 2 mol% visible light photoinitiators was polymerized using 10 mW/cm$^2$ of 400-500 nm light. For all cases, over 60% conversion was achieved with substantially different initial polymerization rates under the same condition tested. The most obvious behavior observed was that rapid initial polymerization rates were only achieved for photoinitiators with higher molar extinction coefficient such as TPO and I819; however, relatively high conversions were obtained using the CQ initiation system over an extended time period, indicative of the versatility of copper reduction by nearly any radical initiator and the longevity of the copper(I) catalyst that is formed.

![Figure 5. Bulk photo-CuAAC polymerization kinetics using FTIR. 1:1 azide:alkyne mixture with varying photoinitiators, including TPO (open triangle), I819 (closed triangle), PPD (open circle), CQ (closed circle). Azide 2c was polymerized stoichiometrically with alkyne 3 in the presence of 2 mol% CuCl$_2$[PMDETA], 2 mol% photoinitiators per azide functional](image)
group, and <1 wt% DCM. Each mixture was irradiated continuously (gray shaded area) at 35 °C with 10 mW/cm² of 400-500 nm light following 3 minutes in the dark as a baseline measuring period.

Copper & Photoinitiator Concentration. Figure 6 presents the effects of the photoinitiator and copper concentration on the average initial polymerization rate, as measured by the time required to react from 10% to 30% conversion. In order to minimize the number of variables affecting the polymerization rate other than the concentration of copper and photoinitiator, one specific reaction condition was chosen as follows: azide 2c and alkyne 3 were polymerized stoichiometrically with CuCl₂[PMDETA] as a catalyst, and CQ as a visible light photoinitiator, with continuous irradiation at a light intensity of 75 mW/cm², wavelength range of 400-500 nm, and a temperature of 35 °C. It should be noted that the absorption efficiency of the photoinitiator, molar extinction coefficient of the photoinitiator, the solubility of copper(II), the stability of copper(I) and several other factors are all also important factors controlling initiation and copper reduction that are intended to be preserved by using a single polymerization condition.

For both PI:Cu ratios cases, the average initial polymerization rates increased linearly as the copper concentration varied from 0 mol% to 3 mol%, indicating that the initial rate is first order in copper concentration under these circumstances. However, as the concentration of copper increased from 3 mol% to 5 mol%, either a subtle increase or a plateau in the average polymerization rate was observed. It is worth noting that precipitation of copper catalysts started to appear for resin formulations containing higher copper loadings above 4 mol% several hours after mixing. This slight increase or plateau in the rate regardless of higher copper and photoinitiator loadings is possibly due to phenomena associated with various CuAAC reactions. First, at higher copper concentrations, disproportionation of copper(I), aggregation and/or precipitation of insoluble copper species can occur rapidly, and each one promotes the formation of inactive copper species. Furthermore, at higher photoinitiator concentrations, a higher density of radicals generated from the photoinitiator increases radical-radical
recombination/termination reactions which then eliminates radicals that would otherwise be available to reduce copper.

For the case when the PI concentration is 1 mol%, the average initial polymerization rates remained constant as the copper concentration varied from 1 mol% to 6 mol%. This constant rate over a wide range of copper loadings indicates that copper reduction which strongly dictates the average initial polymerization rates is highly restricted by insufficient amounts of photoinitiator relative to the copper.

![Figure 6](image_url)

**Figure 6.** The average initial polymerization rate taken between 10% to 30% conversion from FTIR as a function of the copper concentration. A 1:1 azide:alkyne mixture with varying copper and photoinitiator concentration. Azides 2c was polymerized stoichiometrically with alkynes 3 in the presence of different molar ratio of CuCl₂[PMDETA] and CQ per azide functional group, and <1 wt% methanol. Each mixture was irradiated for continuous at 35 °C with 75 mW/cm² of 400-500 nm light following 3 minutes in the dark as a baseline measuring period. [PI]/[Cu]=1 (closed square) and [PI]/[Cu]=2 (closed circle) indicate the molar ratio of the photoinitiator to copper (PI:Cu) is fixed at 1 and 2 while [PI]=1 (closed triangle) represents when the photoinitiator concentration is fixed at 1 mole % with varying copper concentration.

**Light Exposure.** To probe the influence of light intensity and exposure dose on the polymerization rate, a single resin formulation consisting of a 1:1 stoichiometric mixture of azide 2c and alkyne 3 with 2 mol% CuCl₂[PMDETA] and 2 mol% CQ was polymerized using different light intensities and exposure...
times. Figure 7 demonstrates the effects of light intensity on the polymerization kinetics. The initial polymerization rate was significantly improved by increasing light intensity using CQ, mainly because the lower molar extinction coefficient of CQ requires higher light intensity to effectively generate radicals without the presence of excess amine as a co-initiator.\textsuperscript{58} It must be noted that at 75 mW/cm\textsuperscript{2}, a 5 °C temperature increase was observed, due to the heat generated at the higher light intensity. The small increase in temperature also serves to accelerate the CuAAC polymerization, though not enough to significantly increase conversion. Interestingly, the lag time between the start of irradiation and the maximum rate of polymerization increased monotonically with decreasing light intensity, ranging from 3 minute to 26 minutes under the conditions tested. After 60 minutes of irradiation, all samples with different light intensities resulted in a conversion over 60%.

**Figure 7.** Bulk photo-CuAAC polymerization kinetics using FTIR. 1:1 azide:alkyne mixture with varying light intensity, including 75 mW/cm\textsuperscript{2} (closed triangle), 50 mW/cm\textsuperscript{2} (open triangle), 20 mW/cm\textsuperscript{2} (closed square), 10 mW/cm\textsuperscript{2} (open square). Azide 2c was polymerized stoichiometrically with alkyne 3 in the presence of 2 mol% CuCl\textsubscript{2}[PMDETA], 2 mol% CQ per azide functional group, and <1 wt% DCM. Each mixture was irradiated continuously (gray shaded area) at 35 °C with different light intensities of 400-500 nm light following 3 minutes in the dark as a baseline measuring period.
As shown in Figure 8, different exposure times at a fixed light intensity, 75 mW/cm$^2$, were screened to define an optimal exposure dose required to yield the maximum polymerization rate. Exposure times greater than 3 minutes were found to have a limited benefit, as essentially the same kinetic profiles were observed as with continuous irradiation. In order to determine the concentration of CQ after 3 minutes of light exposure, a solution containing 0.044M CQ with 0.044M PMDETA as a coinitiator in methanol was irradiated using 75 mW/cm$^2$ of light irradiation at 400-500nm (Figure S2-3) and the absorption spectra was measured at different exposure times. Approximately 70% of the CQ was bleached following 3 minutes of light exposure in the presence of PMDETA. Given that outcome in an optically thick sample, one would reasonably expect that at elevated temperatures and in the presence of monomers also bearing carbamate functionality which provide an additional coinitiator source for CQ, CQ is largely decomposed during a 3 minute irradiation period used in Figure 8. Thus, the lack of any benefit associated with continuous exposure after this period likely results from the lack of generation of any additional radicals that would be capable of reducing Cu(II) to Cu(I). Further, from the emission spectra of the mercury arc lamp with 400-500nm band pass filter and using the absorbance spectra of the CQ photoinitiator as measured by the UV/Vis spectrometer, approximately 2 moles of photons are absorbed per mole of CQ during 3 minutes of irradiation (Figure S4). With only 3 minutes of exposure time, 82% azide conversion was achieved after 60 minutes, but approximately 55% of this reaction conversion occurred after the light was turned off. Interestingly, this extended dark polymerization was also observed after as little as 1 minute of irradiation; less than 2% conversion was obtained during the first minute of irradiation, but an additional 60% conversion was achieved during 56 minutes of time in the dark. Furthermore, the cases of 1, 2, and 3 minutes of irradiation all achieved more than 50% conversion in the dark despite the differences in the initial polymerization rate and the final conversion at 60 minutes. This extent of dark polymerization highlights the longevity of the
catalytically active Cu(I) species as compared to conventional radical processes, where radical termination events cease the polymerization rapidly after initiation is halted.

Figure 8. Bulk photo-CuAAC polymerization kinetics using FTIR. 1:1 azide:alkyne mixture with varying exposure times, including 0 minute (closed circle), 0.5 minute (open circle), 1 minute (closed triangle), 2 minutes (open triangle), 3 minutes (closed square), 60 minutes (open square). Azide 2c was polymerized stoichiometrically with alkyne 3 in the presence of 2 mol% CuCl₂[PMDETA], 2 mol% CQ per azide functional group, and <1 wt% methanol. Each mixture was irradiated at 35 °C with 75 mW/cm² of 400-500 nm light following 3 minutes in the dark as a baseline measuring period. Only the start of light irradiation is highlighted in gray dotted line.

CONCLUSIONS

The kinetics of CuAAC photopolymerizations are highly influenced by the resin viscosity and the ultimate glass transition temperature of the polymer, both being strongly dictated by the monomer structure. CuAAC photopolymerizations exhibit a rapid initial rate followed by the attainment of a maximum conversion that is limited by vitrification and therefore increases dramatically with the addition of plasticizers. The most efficient photo-reduction of copper occurred here when 3 mol% of the copper per functional group were present. Of significant practical benefit, it was demonstrated that the
copper(I) catalyst persists long after irradiation is ceased causing polymerization to continue without
additional light exposure. Although this extent of dark polymerization limits the temporal control of the
photo-induced CuAAC polymerization, controlled initiation of the reaction is readily achieved. For
numerous applications, the persistence of the polymerization long after exposure is a significant benefit,
enabling dark polymerization for an extended time following only a short exposure. For example, in one
instance, approximately 50% to 60% conversion occurred in the dark after only one minute of
irradiation.

ACKNOWLEDGMENTS

The authors acknowledge financial support from the National Institutes of Health (NIH:5U01DE023774) and the National Science Foundation (NSF:CHE1214109).

*CORRESPONDING AUTHOR

Tel.: +1 303 492 3247; fax: +1 303 492 4341.

E-mail address: Christopher.bowman@colorado.edu (C.N. Bowman)

REFERENCES

7 S. Vutti, N. Buch-Månson, S. Schoffelen, N. Bovet, K. L. Martinez and M. Meldal,
8 T. Smyth, K. Petrova, N. M. Payton, I. Persaud, J. S. Redzic, M. W. Graner, P. Smith-jones and


Kinetics of bulk photo-initiated copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) polymerizations

Han Byul Song, Austin Baranek, and Christopher N. Bowman