# AZIDE AND ALKYNE FUNCTIONAL SILOXANES

# NEW ROUTES TO FUNCTIONAL SILOXANES:

# APPLICATIONS OF THE THERMAL AZIDE-ALKYNE CYCLOADDITION

# FOR THE SILICONE CHEMIST

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**Lay Abstract**

Polydimethylsiloxane (PDMS or silicone) fluids and elastomers are materials that find use in many applications owing to the many desirable properties they possess; personal care products, electrical insulators, sealants and biomedical are examples of products containing silicone. Native PDMS is highly hydrophobic (water repellent) and certain applications require silicones that are more compatible in environments containing water. Methods have been developed to modify both fluid and elastomeric silicones; incorporation of different molecules or polymers can enhance the properties of silicone for various applications or create unique materials. However, many of these methods have certain drawbacks: the use of sophisticated equipment, expensive ingredients, or a lack of permanence. For this reason, a new method to modify fluid and elastomeric silicones has been developed. The new method is based on the concept of 'Click' chemistry and has overcome some of challenges associated with other modification methods.

**Abstract**

Silicone oils (polysiloxane) and elastomers are a class of hydrophobic polymers with an extensive range of uses. While the high hydrophobicity can be beneficial in a variety of applications, it is not universally the case. Modification strategies for both fluid and elastomeric polydimethylsiloxane (PDMS) must be employed to create silicones with the appropriate properties for a given application, including enhanced hydrophilicity. Derivatization of PDMS leads to functional silicones with unique properties and added value.

Strategies have been developed to modify both fluid and elastomeric PDMS, however, they all have varying degrees of drawbacks: the use of sophisticated equipment or expensive catalysts, restrictions to certain types of solvents, cumbersome multi-step synthetic procedures and surface reversion are some of the challenges faced. There is an opportunity to develop a simple and generic method for the controlled functionalization of PDMS.

The Sharpless concept of 'Click' chemistry was an ideal approach to solving some of these challenges. Following nature's lead, these reactions that are modular, wide in scope, high yielding, have simple reaction conditions and generate inoffensive byproducts. Herein, a synthetic method to functionalize silicones using the thermal Huisgen 1,3-dipolar cycloaddition of azides to alkynes is described. Initial exploration focused on the creation of inherently reactive elastomers that could be modified with a model hydrophilic moiety, poly(ethylene

glycol). This was extended to the creation of amphiphilic multi-functional polysiloxanes and amphiphilic networks. Furthermore, the ‘Click’ approach was used to solve challenges faced in applications where silicones find use.

The method described overcomes silicone modification challenges. The cycloaddition reaction is tolerant to many reaction conditions, is orthoganol to a variety of chemical reactions, does not require the use of a catalyst, the starting functional groups and bonds formed are stable and the reaction is high yielding, positioning the Huisgen ‘click’ reaction is an exceptional synthetic tool for the silicone chemist.

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**List of all Abbreviations and Symbols**

| | |
|---|---|
| AFM | Atomic force microscopy |
| ATR/ATIR | Attenuated total reflectance IR |
| BSA | Bovine serum albumin |
| CA | Contact angle |
| CD | Cyclodextrin |
| $CDCl_3$ | Deuterated chloroform |
| CMC | Critical micelle concentration |
| CuAAC | Copper catalyzed azide-alkyne click |
| $D_4$ | 1,1,3,3,5,5,7,7-Octamethylcyclotetrasiloxane |
| DCM | Dichloromethane |
| DMSO | Dimethylsulfoxide |
| DOSY | Diffusion ordered NMR spectroscopy |
| DSC | Differential scanning calorimetry |
| GC-MS | Gas chromatography–mass spectrometry |
| G’ | Storage modulus (elastic modulus) |
| G’’ | Loss modulus (viscous modulus) |
| GPC | Gel permeation chromatography |
| HEL | Hen egg lysozyme |
| HRMAS | High resolution magic angle spinning |
| IR | Infrared spectroscopy |
| LVE | Linear viscoelastic |
| Mn | Number average molecular weight |
| MW | Molecular weight |
| Mw | Weight average molecular weight |
| NMR | Nuclear magnetic resonance |
| kPa | kiloPascals |
| PDI | Polydispersity index |
| PDMS | Polydimethylsiloxane |
| PEG | Poly(ethylene glycol) |
| PEO | Poly(ethylene oxide) |
| PSI | Pounds per square inch |
| Pt | Platinum |

| | |
|---|---|
| RTV | Room-temperature vulcanization |
| SEC | Size exclusion chromatograpahy |
| Tg | Glass-transition temperature |
| TEM | Transmission electron microscopy |
| TEOS | Tetraethyl orthosilicate |
| TGA | Thermogravimetric analysis |
| THF | Tetrahydrofuran |
| TPE | Thermoplastic Elastomer |
| UV | Ultraviolet |
| wt | Weight |

**Declaration of Academic Achievement**

*Published Manuscripts*

1. **Rambarran, T**.; Bertrand, A.; Gonzaga, F.; Boisson, F.; Bernard, J.; Fleury, E.; Ganachaud, F.; Brook, M.A. "Sweet Supramolecular Elastomers: Hydrogen Bonding-Induced Phase Separation of PDMS-Cyclodextrin triblocks," *Chemical Communications,* **2016**, 52, 6681-6684**.**

2. **Rambarran, T**.; Gonzaga, F.; Brook, M.A.; Lasowski, F.; Sheardown, H. *"*Amphiphilic Elastomers from Metal-Free, Click Crosslinking of PEG-Grafted Silicone Surfactants,*" Journal* of *Polymer Science Part A: Polymer Chemistry,* **2015,** 53, 1082-1093.

3. Gonzaga, F.; Sadowski, L.; **Rambarran, T.**; Grande, J.; Adronov, A.; Brook, M.A. *"*Improved divergent synthesis of dendrimers *via* metal-free "click" chemistry,*" Journal* of *Polymer Science Part A: Polymer Chemistry*, **2013,** 51, 1272-1277.

4. **Rambarran, T**.; Gonzaga, F.; Brook, M.A. *"*Multifunctional Amphiphilic Siloxane Architectures Using Sequential, Metal-Free Click Ligations,*"* *Journal* of *Polymer Science Part A: Polymer Chemistry*, **2013,** 51, 855-864. (Article Spotlighted)

5. **Rambarran, T**.; Gonzaga, F.; Brook, M.A. *"*Generic, metal-free crosslinking and modification of silicone elastomers using click ligation,*"* *Macromolecules,* **2012**, 45, 2276–2285.

6. Gonzaga, F.; **Rambarran, T**.; Brook, M.A. "Reactive, functional silicone elastomers via metal free click chemistry," *Polymer Preprints,* **2012**, 53, 495-496.

*Manuscripts in Preparation*

1. **Rambarran, T**.; Gonzaga, F.; Fatona, A.; Moran Mirabal, J.; Coulson, M.; Brook, M.A. *"*Thermal Adhesion of Silicones Using Huisgen Cyclization,*"* *ACS Applied Materials and Interfaces,* **2016**.

**Preface**

On the first page of each body chapter, a footnote contains a breakdown of each author's contribution to the multi-authored chapters. The work for the five body chapters was completed between 2011 and 2016 (over the course my graduate degree). I led the investigations described in these chapters, performed most of the experimental work, wrote the first draft of all of the work and helped with editing and responding to reviewers' comments. As such, I was the first author on all of the published work included in this thesis. For this reason, the work was deemed suitable to include in the thesis. Co-authors were acknowledged when they helped with an experiment that contributed to the research project, for helpful discussion or for being in a supervisory role. Work done over the course of my PhD where I contributed only an experiment or two was not included in this document.

# Chapter 1:
# Introductory Chapter

## 1.1 Silicones

Silicones are a class of polymer based on a repeating unit of (RR'SiO). Originally discovered in the 1920's by Kipping and made commercially available in the 1940's due to the development of a viable route to industrial preparation, silicones are currently produced on the scale of several billions of kilograms each year.[1] The most commonly used and most commercially relevant silicone is poly(dimethylsiloxane) (PDMS) containing methyl groups attached to the silicon atom (Figure 1.1); other aryl and alkyl silicones are available as well.

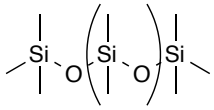



Figure 1.1: Polydimethylsiloxane

Silicones possess exceptional properties that cannot be matched by their carbon-based counterparts. In addition to exceptionally low toxicity, they are: able to mold very fine features;[2] optically transparent; gas permeable; thermally stable in the absence of acid or base; electrically resistant due to the low relative permittivity in silicone fluids; and very mobile (Tg < - 120 °C) due to their highly flexible backbone, which imparts unique properties.[1b] For these reasons, silicones find use in an extensive array of industries ranging from coatings, sealants and potting materials to almost every aspect of medicine in products ranging from drug delivery, implantable devices and topical devices such as contact lenses.[3]

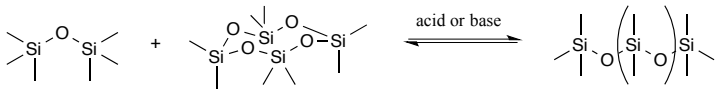
They are increasingly important in diagnostic applications, for example in 'lab-on-a-chip' devices.[4]

Silicones are hydrophobic in nature. While low surface energy materials are ideal in particular applications, such as release coatings, for example, many uses of polysiloxanes require surfaces with enhanced hydrophilicity or other interfacial properties. Consequently, modification of the polymer backbone of fluid and elastomeric PDMS is required in certain circumstances; the addition of different functional groups can change the properties of the polymers and/or provide a chemical handle for further manipulation. Functionalizing PDMS can make a material more compatible for the target application, while in other cases, combining silicones with different molecules or polymers create new high(er) value materials with unique properties. The modification of silicone surfaces can be difficult since one has to overcome the chemical stability noted above. Fortunately, there are methods to introduce functionality onto both fluid polysiloxanes and elastomeric silicone surfaces. Synthetic routes to create fluid and elastomeric silicones, techniques to functionalize them and some of the synthetic challenges with these approaches will be highlighted.

**1.2 Traditional Synthesis of Fluid Siloxanes**

The starting material for methylsilicone production is dichlorodimethylsilane, produced through the Direct Process.[1b] Hydrolysis and condensation of the chlorosilanes produces linear and cyclic siloxane oligomers. The most common cyclic siloxane, octamethylcyclotetrasiloxane ($D_4$), can be combined with a

disiloxane end-cappers in an acid or base catalyzed equilibration reaction to grow higher molecular weight polymer chains of polydimethylsiloxane (PDMS, Figure 1.2). The resultant molecular weight is dependent on the ratio of the two starting materials and the polymers obtained possess a broad molecular weight distribution. Polymerizing silicones using a kinetic mechanism enables greater control over the molecular weight; anionic ring opening polymerization using an anionic initiator and $D_3$ (hexamethylcyclotrisiloxane – which possesses ring strain) if done carefully can result in silicones with a low polydispersity. [1b]



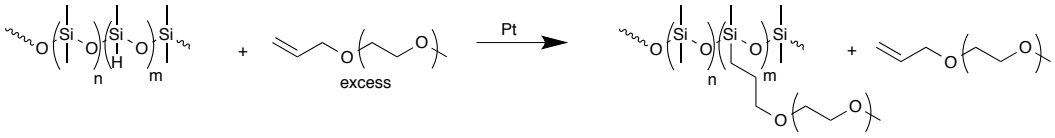

**Disiloxane** **$D_4$** **PDMS**

Figure 1.2: Equilibration reaction to grow PDMS chains

If one (or more) of the methyl groups on the disiloxane or $D_4$ starting material is substituted with a functional group, polysiloxanes with terminal or pendant functionality, are produced.[1b] The siloxane backbone is sensitive to acid and base, which can lead to depolymerization, restricting the chemistries available for modification.

Methylhydrosiloxanes are common functional silicone starting materials; the reactive Si-H group can be used to further graft a wide range of alkyl functional groups or polymers of interest containing a carbon-carbon double bond through a platinum-catalyzed hydrosilylation reaction. Functional silicones (epoxides, amines, alcohols, alkyl halides) can be prepared commercially, giving polymers with a synthetic handle for further chemical manipulation.

PDMS-g-PEG (PEG: polyethylene glycol) surfactants are prepared through hydrosilylation of allyl-functional PEG onto a hydrosiloxane rich backbone.[5] An excess of PEG is used to ensure complete conversion of the hydrosiloxane groups (Scheme 1.1) since they can undergo side reactions in the presence of the platinum catalyst, such as dehydrogenative coupling, which can lead to a loss of polymer integrity. Using an excess of the allyl/vinyl functional molecules or polymer is common when modifying PDMS through hydrosilylation and it consequently necessitates the removal of the excess or the siloxane polymer contains the excess in the final product.




Scheme 1.1: Pt catalyzed hydrosilylation of PEG onto a hydrosiloxane copolymer

While the hydrosilylation reaction is efficient, this approach has some weaknesses; the use of expensive platinum catalysts and issues with its removal, restriction of the reaction to organic solvents, and the issues noted above pose a challenge in creating multifunctional polymers or performing sequential reactions. As well, there is the possibility for side reactions to occur with certain allyl-functional molecules.[6] There are opportunities to develop methods to create polysiloxanes with stable intermediary reactive groups that allow for facile modification.

**1.3 Silicone Elastomer Synthesis**

There are three traditional methods used to crosslink fluid silicones to prepare

elastomers. Room temperature vulcanization (moisture cure) traditionally proceeds by reacting silanol-terminated PDMS with tri- or tetra-alkoxy functional silanes through hydrolysis and condensation. Acid, base, tin or titanium and ambient moisture are used to catalyze the crosslinking process, with tin based catalysts being the predominant choice.

High temperature vulcanization uses radicals to initiate a high temperature curing mechanism through two different types of processes. Radicals can abstract hydrogen from methyl silicone to produce $SiCH_2\bullet$, which can subsequently couple to produce a two-carbon bridge or, starting from PDMS containing vinyl functionality, in a 3-carbon bridge. The latter reaction (use of vinyl) can be accomplished with less reactive radicals at lower temperatures. The efficiency of the radical cure process drops as the viscosity increases and an additional disadvantage is that the final product requires the starting peroxides to be heat stripped.

The gold standard for the preparation of silicone elastomers, addition cure, uses a platinum-catalyzed hydrosilylation between complimentary polymers, one containing Si-H groups and the other containing $Si\text{-}CH{=}CH_2$ groups. This method is widely used for silicone elastomer preparation. Residual platinum remains trapped in the material, which can cause the material to yellow over time.[1b, 7]

### 1.3.1 Modification of Silicone Elastomers

As previously mentioned, silicone elastomers are highly hydrophobic, which is beneficial when used in certain products such as sealants, moisture barriers and

so forth. However, many applications require surface modification to adjust the interfacial properties, for example, to make surfaces more hydrophilic for biomaterials or microfluidic applications. Methylsilicones lack a functional chemical handle for modification posing a synthetic challenge; many approaches have been developed to address this issue.

Two strategies are commonly used to introduce hydrophilicity onto PDMS surfaces. More aggressive high-energy modification methods include plasmas, coronas, ultraviolet or ultraviolet ozone (UV or UVO), which oxidize surface methyl groups to give polar silanol groups. Milder, controlled surface modification techniques involving physical or chemical introduction of hydrophilic organic or polymeric moieties onto PDMS.

#### 1.3.1.1 Modification Using High Energy Methods

Traditional methods to modify the surface or PDMS rely on high-energy oxidation of the surface with corona, UV and most commonly plasmas.[4] The treatment of polymers with plasmas ($O_2$, Ar, $N_2$ and $NH_3$) has long been used as a selective surface modification method to enhance silicone hydrophilicity[8]. Plasma-functionalized PDMS surfaces find use in anti-fouling[9] and biomaterials[10] applications. Exposing silicones to glow discharge air or oxygen plasma leads to an increase in the polar character (via the introduction of oxygen containing moieties) onto the PDMS surface. Only short periods of irradiation are required to render the surface hydrophilic through the creation of surface silanol groups, which can condense to form silica.[11] Plasma treatment is a powerful technique

that may render the surface layer brittle; the silica layer formed can crack or wrinkle, so care has to be taken. One drawback of this technique is that the hydrophilic character disappears when the samples are kept over time in air, a phenomena called hydrophobic recovery, where the hydrophilically-modified surface returns to a hydrophobic state (discussed further below).

PDMS surfaces can also be modified by exposure to UV and ozone. UV treatment of PDMS surfaces cause PDMS chains near the surface to undergo scission, forming radical species that can recombine to form a more wettable network,[12] for example, through to the introduction of hydroxyl or carboxylic acid groups.[13] The addition of molecular oxygen and ozone created by exposing atmospheric oxygen to UV radiation removes part of the organic portions of polymers and imparts numerous hydrophilic groups (namely hydroxyl) onto the surface.[14] UVO treatment is considered a milder form of modification compared to plasma. It leads to analogous surface changes, but requires much longer times to process. Similar to plasma treatment, a silica-like layer forms on the PDMS surface with increasing exposure to UV and ozone,[15] and the surface can also undergo hydrophobic recovery .

Corona treatment can be used under ambient conditions, which has both benefits and drawback. The influence of temperature and humidity can alter the corona discharge and/or surface oxidation. Electrical discharge from a Tesla coil reacting with air converts the surface of PDMS to a higher energy more hydrophilic surface that can subsequently be modified.[13] This process, however,

can lead to significant surface damage. The hydrophobic recovery of surfaces modified by corona discharge is well established.[16]

The oxidative processes described above can dramatically increase the surface energy of silicone elastomers such that essentially zero degree contact angles of water droplets can be achieved (native PDMS surfaces have a contact angle > 100° due to unfavourable interactions of water with the hydrophobic surface).[17] However, the hydrophilic surfaces created are not stable, thus, hydrophilic surfaces formed by oxidation must be used or further modified rapidly before surface reversion occurs.

It has been suggested that hydrophobic recovery can arise from a few different mechanisms: the polymers can reorient polar groups from the surface to the bulk, pre-existing low molecular weight silicones can migrate to the air interface, hydroxyl groups on the surface can condense to give disiloxanes, and in some cases, low molecular weigh species – created in situ as the surface is modified – can also migrate to the surface.[16a] This phenomenon is a function of the silicone chain mobility that results from the large Si-O-Si bond angle (145°) and the fact that it is thermodynamically favourable for the silicone methyl groups to be located at the gas/air interface.[1b, 18]

Over recent years, significant research on the modification of PDMS surfaces had been undertaken. The outcomes of these methods still exhibit a number of drawbacks. Studies have shown that the treatment can penetrate hundreds of nanometers below the surface, causing permanent chemical changes that lead to

brittle silica-like surfaces that are prone to cracking and whose properties differ from the bulk of the material.

#### 1.3.1.2 Modification Using Physical Adsorption

Alternative strategies to oxidation have been developed to overcome the challenges associated with hydrophobic recovery. One approach takes advantage of silicone's hydrophobic surface and uses physical adsorption of amphiphilic molecules, polymers or protein to change the surface properties.[19,20] The hydrophobic portion of the surface modifier anchors onto the hydrophobic silicone surface through van der Waals forces and hydrophobic interactions, leaving hydrophilic portions on the surface. Such layered structures are more stable to hydrophobic recovery and can lower the contact angle of water on the surface. Physisorption of polyelectrolytes[21], neutral polymers[20c], proteins[22] and surfactants[23] onto PDMS to modify surfaces properties have been investigated. Another strategy for surface modification is to physically adsorb molecules onto the surface that are capable of initiating polymerization of a molecule of interest.[24]

Physical blending of silicone with hydrophilic polymers has been used to modify the properties of elastomers, however, this also changes the bulk properties.[25] While modifying silicones with hydrophilic materials prior to cure, using physical interactions, is simple there are several drawbacks. The interactions between the silicone and the modifier are weak, consequently there are potential issues with leaching and these methods may not be suitable in wet environments or for biomaterials applications. These techniques do not work well

for materials that require a high density of functionality. For this reason, there is an extensive area of research dedicated to the covalent modification of PDMS.

**1.3.1.3 Covalent Modification from Surface Oxidation**

There are several approaches to covalently incorporating groups onto PDMS surfaces. One modification strategy takes advantage of the reactive surface that is created when PDMS is exposed to high-energy irradiation, discussed above. Silanol groups formed on the surface layer of PDMS may be treated with silanes containing reactive groups to prepare functional PDMS surfaces. These surfaces can then further undergo organic transformations to graft hydrophilic polymers, reducing the effect of hydrophobic recovery,[8, 26,27] leaving the modified surface with a stable hydrophilic coating. These treatments can lead to an increase surface roughness of the material and may not permit high graft density of the hydrophilic polymers. Plasma polymerization, a dry room temperature surface modification procedure, of various molecules can also be used to generate functional surfaces for further modification.[26, 28] Isopropyl acrylamide (IPAAm) can be polymerized onto plasma treated PDMS, growing the polymers from the surface through a radical mechanism[29] or polymers (such as hydroxyethyl methacrylate) can be grafted to plasma treated surfaces.[8]

An analogous modification method is to oxidize the surface using a strong acid with hydrogen peroxide or a basic catalyst (NaOH)[30] to activate the surface and subsequently immobilize silanes that can be using to couple polymers or molecules of interest[31]. However, these aggressive conditions can damage both

the surface and bulk PDMS, so care has to be taken.

The use of high-energy irradiation and strong acid or base to chemically modify the surface overcomes some challenges associated with the physical adsorption physical adsorption method and such techniques have been successful in creating hydrophilic surfaces. However, the strong reaction conditions can lead to damage of the PDMS surfaces, therefore softer methods for surface modification are sought after.

**1.3.1.4 Other Modification Strategies**

The incorporation of excess reactive groups during (or after) the curing process that can be used to modify the surface properties after crosslinking has been explored for the modification of PDMS surfaces. One nice example of surface modification is achieved by incorporating PEG-siloxane tethers onto PDMS surfaces (a tether being PEG attached to an oliogmeric or low molecular weight siloxane block acting as a spacer between the PEG and the PDMS surface). These were made via $H_3PO_4$ catalyzed sol gel crosslinking in various molar ratios, producing hydrophilic interfaces.[32] However, much of the literature focuses on hydrosilylation chemistry. One example incorporates additional Si-H containing polymers in a silicone polymer formulation prior to curing, producing an Si-H functional surface that could be use to graft allyl-functional PEG post curing (Figure 1.3).[33] A similar method described by Guo et al. used commercial PDMS preparation (Sylgard 184) and crosslink the components in off ratios (addition cured silicones normally are mixed, just prior to cure, in equimolar

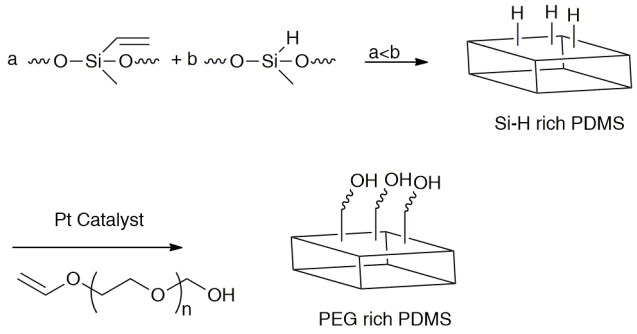



Figure 1.3: Functionalization of Si-H rich surfaces with PEG through hydrosilylation

ratios of SiH/SiCH=$CH_2$ groups), incorporating excess reactive Si-H groups that could be used to subsequently graft allyl-functional PEG, rendering the surface more hydrophilic and reducing the adsorption of proteins.[34] While these methods have the benefit of avoiding surface damage that can come along with higher energy modification techniques, the presence unreacted Si-H groups and the platinum catalyst trapped within the elastomer can lead to changes in the properties of the material over time as a result of dehydrogenative coupling (e.g., between hydrosilane and silanols that can form from hydrolysis over time).[7, 35]

A milder version of PDMS modification using acid/base takes advantage of the fact that polysiloxanes equilibrate in such conditions as a function of the ionic nature of the Si-O bonds. Controlled surface etching by subjecting a silicone surface to acid or base in a bad solvent for PDMS can be used to modify the PDMS surface; when completed in the presence of hydrosiloxanes, reactive Si-H functional groups are incorporated to the surface for further chemical manipulation.[30]

Strategies utilizing different types of chemistry have also been employed to

modify PDMS to enhance surface hydrophilicity (although not just the surface is modified). The incorporation of hydrophilic polymers into the PDMS elastomers during the curing process has been carried out using traditional room temperature vulcanization; monofunctional PEO (various molecular weights) modified with alkoxysilyl groups [$Si(OEt)_3$] underwent classic RTV cure using a tin-catalyzed moisture cure process with hydroxyl-terminated PDMS and TEOS ($Si(OEt)_4$).[36] No PEO could be removed by an aqueous extraction process following the synthesis, signifying that functional PEO was fully incorporated into the PDMS network. Protein adsorption studies were carried out and it was found that lower molecular weight PEO led to the greatest protein rejection.

In an analogous investigation, both mono- and bi- functional PEO were used as additives in the elastomer formulations to yield silicones with PEO-rich surfaces, enhanced hydrophilicity in aqueous conditions and reduced protein adsorption.[37]

### 1.3.2 Challenges

As described above, there have been a variety of synthetic approaches developed to address the modification of fluid and elastomeric PDMS. They all have specific merits: high-energy or surface oxidation methods can be performed quickly and have been highly studied, physisorption or incorporation of excess reactive groups are simple and gentle methods and blending PDMS with hydrophilic polymer circumvents hydrophobic recovery. However, there are various shortcomings with the methods discussed:

- Plasma oxidation can cause damage to the surface and surfaces can undergo hydrophobic recovery.
- Surfaces modified by physical adsorption are not very stable and are only suitable for certain environments.
- Examples of incorporating excess reactive groups using hydrosiloxanes and platinum-catalyzed addition cure can lead to long term changes in the properties of the material as a result of side reactions of the remaining Si-H groups and platinum. As well, the use of hydrosilylation chemistry has restrictions in which solvents can be used for surface modification and restrictions in the molecule or polymer that can be used to modify the surface due to functional group intolerance or potential side reactions.
- Many of these techniques require multiple synthetic steps to achieve surface modification.

Given the importance of silicones and their use in so many different applications, there remains an opportunity to develop innovative synthetic methods to modify fluid and elastomeric polysiloxanes that overcomes several of the challenges noted above.

**1.4 Objectives**

The objectives of this project are to develop new synthetic routes to create and modify fluid and elastomeric silicones. Specifically, it would be ideal to create a method to functionalize fluid polysiloxanes that readily enables the ligation of a variety of molecules or polymers and permits multifunctional polysiloxanes to be

created. Such a method would be even more powerful if it permitted the modification of silicones with molecules or polymers that would normally be challenging to achieve with traditional modification methods. A method that is compatible with a broad range of functional groups (orthogonal reactivity) could circumvent the necessity for protection and deprotection steps.

It is also desirable to develop a method in which polysiloxanes can be crosslinked into elastomers that have inherently stable and reactive interfaces. The surfaces could subsequently be modified with polymers or molecules through covalent reactions that do not damage the surface of the material. The ability to also create silicone materials that can have a different polymer of interest covalently crosslinked into the network would be an added benefit (circumventing the issues with non covalent physical blending noted above). It would be ideal for this method to be synthetically applicable in a broad sense and to overcome other synthetic challenges that exist for different applications in which silicones find use.

Effectively, we wanted to develop a synthetic methodology with the following characteristics:

1. One that uses reactive groups that are robust, reactions can be performed under a variety of conditions, and is tolerant to the presence of different functional groups.
2. The method should use reactive groups that are stable under most conditions so there is minimal concern about side reactions or degradation

if functional groups are left unreacted.

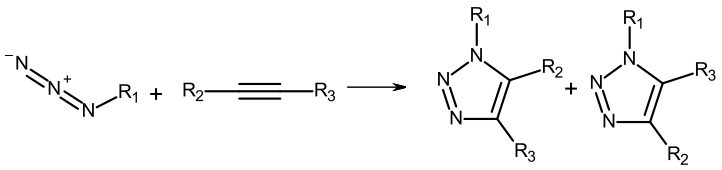
3. The method should also have near quantitative yields and reactions can be completed with stoichiometric quantities of reagents (not requiring a large excess of one reagent for the reaction to reach completion).
4. While the use of platinum metal in reactions has a record of safety, there is increasing concern of metals remaining in materials destined for human contact. Additionally, the use of tin-based catalysts may adverse health effects and are currently being phased out.[38] Ideally, the modification method would not produce offensive byproducts nor would it require a metal catalyst in the final stages of reaction (which would necessitate removal or remain in the polymer or material).

**1.5 The Strategy: Click Chemistry**

In searching for the appropriate synthetic method to explore, the Sharpless' concept of 'Click' chemistry was the ideal starting point; following nature's lead, Sharpless and coworkers' goal was to develop a set of reactions that are "modular, wide in scope, give very high yields, generate only inoffensive byproducts that can be removed by non-chromatographic methods…[with] simple reaction conditions (ideally, the process should be insensitive to oxygen and water)".[39]

Of the reactions described, the Huisgen 1,3-dipolar of azides to alkynes in particular was an attractive reaction to consider since it is regarded as the "cream of the crop" of click reactions (Scheme 1). The use of this reaction has exploded

over the years and it is used expansively in many fields of synthetic chemistry for a wide variety of applications; a simple Web of Science™ search of the topics "click chemistry" and "azide and alkyne" yields well over 3000 articles and 200 reviews in the last 10 years. Selective labelling of biomolecules such as proteins[40], polysaccharides[41], and nucleic acids[42] with either azides or alkynes has been demonstrated. It has also become a premier synthetic tool for polymer and material scientists owing to its versatility and many attractive attributes[43] and has been used a great deal as a method to modify various surfaces[44]. The Huisgen cycloaddition reaction can be performed thermally, however, the discovery of the copper-catalyzed version (copper catalyzed azide-alkyne cycloadditions or CuAAC for short) is one reason the reaction has increased in popularity over the years.[45] Using copper, the reaction can be completed quickly at ambient conditions and only produces one isomer. However, as noted above, the ideal method would not use a metal catalyst and it preferable to avoid the use of heavy metals in materials destined for human contact, which many applications of silicones are. The reaction can also be carried out using strained alkynes (in Strain Promoted Azide-Alkyne Cycloaddition or SPAAC for short), an efficient reaction that avoids the use of copper. The Bertozzi group has extensively studied the SPAAC, labelling various molecules in living cells and other biological environments.[46]



Scheme 1.2: Huisgen 1,3-Dipolar Cycloaddition of Azides to Alkynes

We judged that, compared to strained alkynes, the use of electron deficient alkynes with azides in a Huisgen cyclisation was the simplest method for initial exploration of silicone modification. In the reaction, the azide is the dipole and the alkyne is the dipolarophile and they undergo a thermal cycloaddition to form a stable triazole linker. The formation of the aromatic ring renders the reaction essentially irreversible, since the energy barrier to the reverse reaction is too high. Only one example of a reversible reaction has been demonstrated under very particular conditions in a publication in *Science* entitled "Unclicking the click: Mechanically facilitated 1,3-dipolar cycloreversions"[47], however, this article has since been retracted after an investigation demonstrated unreliable data and scientific misconduct. Unlike the copper-catalyzed click reaction, with the thermal cycloaddition, two isomers are formed; if a terminal alkyne is used, a 1,4 or 1,5 isomer is formed (Figure 1.4).

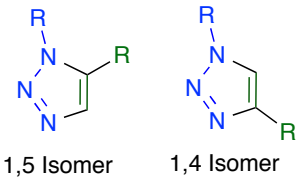



Figure 1.4: Isomers formed from the thermal cycloaddition

The use of azides as the 1,3-dipole has numerous advantages: aliphatic azides

are stable toward dimerization, hydrolysis and are orthogonal to a range of other synthetic reactions. Electron deficient alkynes are more reactive towards the cycloaddition. This is a function of the reactive groups' Frontier Molecular Orbitals (FMO).[48]

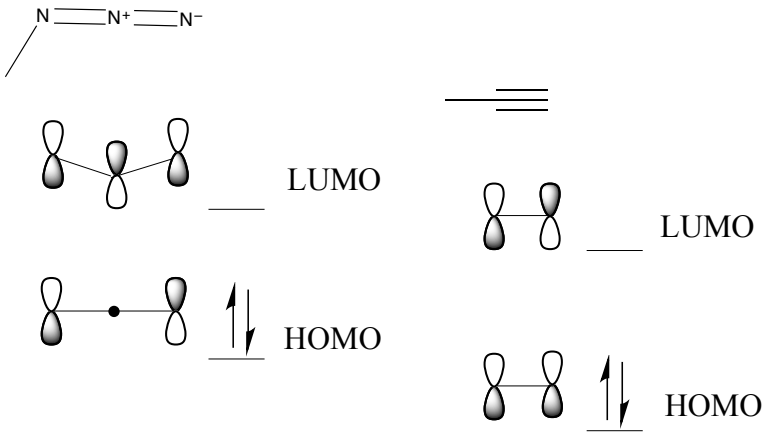



Figure 1.5: FMO of Azide and Alkyne

Both HOMO-LUMO pairs of an azide and alkyne possess the correct symmetry for interactions, however, the $HOMO_{azide}$ and $LUMO_{alkyne}$ have the smallest energy separation when using electron deficient alkynes (Figure 1.5).[49] Alkynes with adjacent electron withdrawing groups are more reactive towards the cycloaddition reaction since the energy of the $LUMO_{alkyne}$ is lowered. The reaction has been used to thermally functionalize[50] or crosslink silicones,[51] without the use of a catalyst, at low temperatures and without generating any by-products. The Huisgen 1,3-dipolar cycloaddition of azides to alkynes represents, in our view, the ideal synthetic tool to use for the objectives set out in this thesis.

**1.6 Thesis Focus I: New Routes to Functional Fluid and Elastomeric PDMS**

The first and main focus of this thesis was to develop a new method to create

functional polysiloxanes and elastomers using the Huisgen 1,3-dipolar cycloaddition of azides to alkynes. In the development of this method, PEG, a hydrophilic carbon based polymer, was chosen as the polymer modifier since its properties differ significantly from silicone. Successful ligation of PEG onto fluid or elastomeric should produce obvious changes in properties. Characterization of the copolymer product should be straightforward, since PEG is soluble in many of the same solvents as silicone. Moreover, PEG is inexpensive and has been used extensively to modify silicones for biomaterials application and to create siloxane surfactants; as a standard hydrophilic modifier it represents as great material to use in the development of a new synthetic strategy.

### 1.6.1 Chapter 2: Reactive Elastomers

The first goal and the first body chapter of this thesis focuses on the development of a simple and generic method that would enable fluid siloxanes to be crosslinked into elastomers possessing a reactive surface ready for subsequent modification, all using the Huisgen cycloaddition. The strategy proposed would first require synthesis of azido- and alkynyl- functionalized polysiloxanes that can be thermally crosslinked using off stoichiometric ratios such that an excess of one reactive group would be present in the final material. Such materials could then be functionalized with a molecule or polymer (as noted above, PEG) containing a complimentary reactive group, changing the surface properties of the material (in this case, enhancing hydrophilicity, Figure 1.6). Such a method would be very powerful since it does not require the use of multiple chemistries in the synthetic

process nor would the resultant materials contain a metal catalyst trapped within it from the crosslinking process. Additionally, the method would be simple and efficient since it does not require multiple synthetic steps to activate the surface for functionalization, it should not undergo surface reversion and it should not cause observable damage to the surface as a softer method.

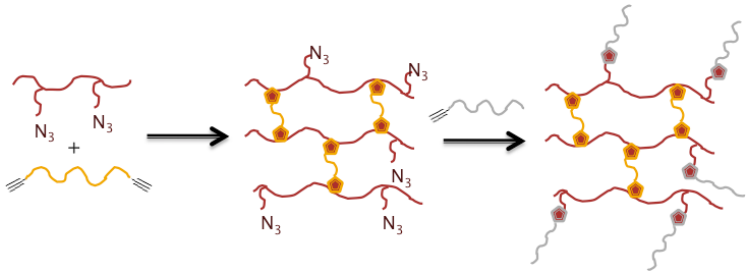



Figure 1.6: Strategy to create reactive elastomers (red and yellow = PDMS, gray = PEG)

### 1.6.2 Chapter 3: Amphiphilic Polysiloxanes

The next chapter focuses on the development of a method to synthesize multifunctional fluid polysiloxanes using the metal free azide-alkyne cycloaddition. One strategy to accomplish this would be to first create an azido-functional polysiloxane that can be reacted with different molecules or polymers containing an alkyne group (Figure 1.7). The high efficiency of the reaction should permit quantitative ligation of the starting materials in near stoichiometric reaction conditions. Additionally, because azido groups are stable, it should be possible to only functionalize a portion of the azides leaving the remaining groups to be reacted in a sequential manner to build multi-functional polysiloxanes. Since the thermal reaction circumvents the use of catalysts and the click reaction does not produce byproducts, the procedure should not require work-up steps after the

ligation rendering it simple, high yielding and suitable for a wide variety of applications.

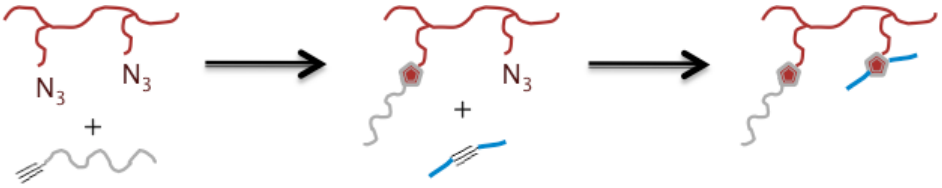



Figure 1.7: Building multi-functional polysiloxanes (red = PDMS, gray = PEG, blue = small molecule)

### 1.6.3 Chapter 4: Amphiphilic Materials

Chapter 2 discusses the development of a method to modify silicones after cure to enhance the hydrophilicity of the surface. However, in certain cases, it may be desirable to incorporate a hydrophilic polymer covalently into the material during the curing process to create materials that are inherently more wettable and do not undergo hydrophobic recovery. Chapter 4 focuses on combining the concepts explored in the previous two chapters to create such amphiphilic materials. Chapter 3 explores creating PDMS-g-PEG containing reactive groups for sequential ligation. The fluid PDMS functionalized with a less than stoichiometric amount of PEG (i.e., after reaction there are remaining reactive azido groups), could alternatively be used to crosslink alkyne-terminated PDMS (Figure 1.8) to create an amphiphilic elastomers containing dangling PEG chains within the siloxane network. Using this method to create such networks would allow the experimentalist to confirm complete ligation of PEG to PDMS using standard characterization techniques ($^1$H NMR) prior to crosslinking, which would reduce the propensity of PEG to leach of the network in aqueous

environments (which can happen in network made using physical interactions or those which cure all of the components together at once). There are also many synthetic parameters that can be varied to modify the properties of the resultant materials (PEG molecular weight, amount of PEG, crosslink density, molecular weight of the terminal PDMS).

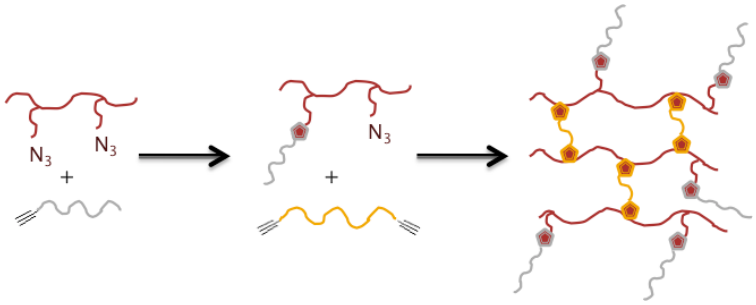



Figure 1.8: Creating amphiphilic networks (red and yellow = PDMS, gray = PEG)

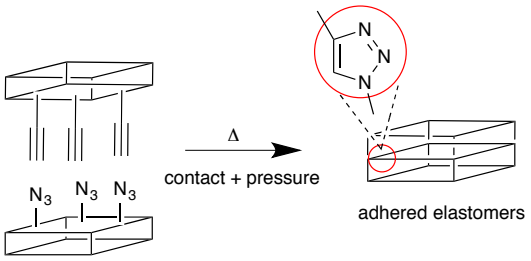
## 1.7 Thesis Focus II: Applications of Click Silicones

The first three chapters focus on developing a synthetic method, the use of the azide-alkyne cycloaddition, to modify fluid and elastomeric PDMS (namely with PEG). The focus of the final two chapters of the thesis is to apply this method more broadly. The motivation was to determine if the 'click' approach to modifying silicones could be used with other molecules or polymers and to establish if the method could be used to solve challenges in applications where silicones are used.

### 1.7.1 Chapter 5: Adhesive Elastomers for Microfluidic Applications

Silicone is an attractive material to use in the fabrication of microfluidic devices, made by bonding two PDMS components together (more details about microfluidic devices may be found in chapter 5).[52] One challenge in the design of

such devices is finding a method that can strongly bond the PDMS interfaces together. We reasoned that complimentary 'click' reactive elastomers (one elastomer containing excess alkynes and one elastomer containing excess azides) could be used as a new method to strongly adhere silicone interfaces together through a thermal welding process (Scheme 1.3).




Scheme 1.3: Click bonding of PDMS

### 1.7.2 Chapter 6: Cyclodextrin Functional Silicones

Finally, the last chapter focuses on interfacing PDMS with a hydrophilic material other than PEG. There has been increasing interest in interfacing silicones with carbohydrates, which are a renewable natural resource. The properties of PDMS are so different from carbohydrates that ligation of the two components can create new materials with unique properties. In particular, cyclodextrin, a cyclic polysaccharide, was an attractive molecule to investigate, since it can form inclusion complexes with lipophilic molecules. There was an attempt by Noomen et al. to functionalize PDMS with native cyclodextrin using hydrosilylation chemistry, however, this was unsuccessful since side reactions led to crosslinking.[53] The Huisgen cycloaddition should be the perfect tool to interface native or modified cyclodextrin with PDMS since it is robust and

tolerant to variety of functional groups and reaction conditions. Chapter 6 focuses on creating telechelic cyclodextrin functional PDMS and the resultant outcomes.

Throughout this thesis, we hope to demonstrate the utility of the Huisgen 1,3-dipolar cycloaddition of azides to alkynes for the synthesis and modification of fluid and elastomeric PDMS. Its efficiency and ease of use make it a valuable tool for the silicone chemist.

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# Chapter 2:
# Generic, metal-free crosslinking and modification of silicone elastomers using click ligation[†]

## 2.1 Abstract

Silicone elastomers are widely used in a variety of biomaterials applications. Their high hydrophobicity can, in some cases, compromise their utility. There exist few convenient, efficient and metal-free processes to introduce hydrophilic groups onto the elastomer surface. We describe the utilization of the metal-free click reaction between azido- and alkynyl-modified silicones to both crosslink and functionalize silicone elastomers. Initial crosslinking at, optionally, reduced or elevated temperatures depending on the alkyne used, results in elastomers whose moduli and tackiness can be controlled by manipulation of crosslink density through use of different chain length constituents: the systematic capping of azides on the azide-rich partner provides a level of control of both crosslinking and residual functionality after crosslinking. The residual azides or alkynes resulting from non-stoichiometric mixing of the starting materials can be used for

[†] This chapter is reproduced from Talena Rambarran, Ferdinand Gonzaga, Michael A. Brook, in Macromolecules, 2012, 45, 2276-2285 with permission from the American Chemical Society, Copyright 2012 American Chemical Society. Rambarran designed the experimental procedure with assistance from Dr. Gonzaga. Rambarran performed all experiments (with the exception of the synthesis of PEG propiolates **9a** and **9b** which Dr. Gonzaga made), and Dr. Gonzaga helped troubleshoot challenging experiments. Rambarran wrote the majority of the manuscript with additions, edits and guidance provided by Dr. Gonzaga and Dr. Brook.

sequential functionalization of the elastomer as shown through the improved wettability that results from the grafting of alkyne-functional PEG to azide-rich silicone elastomers: contact angles decrease from ~105° for the pure silicone elastomers to 85° for the azide-rich silicone elastomer, and to as low as 41° for the PEG-modified product. It is possible to modify the entire elastomer body or only the surface by judicious choice of the solvent used for the hydrophilic modification.

## 2.2 Introduction

Considerable advances have been made in understanding the factors that are associated with compatibility of biomedical devices in certain biological environments. These can include surface modulus,[1] roughness, hydrophilicity, and the presence of target biomolecules,[2] among others. Silicone elastomers are widely used in a variety of biomedical applications where their electrical stability, gas permeability, flexibility and biocompatibility in various sites in the body are particularly beneficial.[3,4] However, even in the applications where they are widely used (e.g., silicone hydrogel contact lenses) their high hydrophobicity can result in significant lipid and protein adsorption onto the surface,[3,5,6] which can be problematic. In more challenging environments, such as catheters in contact with blood, the situation is much worse: extensive biofouling occurs. In spite of an exemplary record of safety, concern has also been raised in some instances about the metallic catalysts – typically tin- or platinum-based – that are used to crosslink silicone elastomers used as biomaterials.

The ideal silicone elastomer for a given biomaterials application cannot currently be predicted. Advances toward materials that have better surface characteristics are hindered by the traditional paradigm for biomaterials synthesis, which involves "one-off" preparation and characterization of materials and surfaces. Some examples of generic surfaces, which can be readily and systematically modified by a related series of compounds, have been reported. For example, monofunctional poly(ethylene glycol)(PEG) can be tethered to silicone surfaces.[7,8] After functional group conversion of the terminal alcohol into an activated ester, the surface can react readily with a wide variety of (bio)functional amines, including proteins. However, such protocols are not sufficiently explicit to be useful in developing surface character/biological response relationships – it is not possible to control which amine on the protein will react. Thus, there remains a need to develop versatile generic methods to modify the surfaces of silicone elastomers.

The utility of copper-catalyzed azide–alkyne 1,3-dipolar cycloaddition (CuAAC) has been shown in a wide variety of applications, including the functionalization of polymeric materials.[9] Selective labelling of biomolecules such as proteins,[10,11,12,13] polysaccharides,[14,15] and nucleic acids,[16] with either azides or alkynes has been demonstrated. We reasoned that if complementary silicone elastomers could be prepared, which possessed controlled concentrations of azide and alkynes internally within the elastomer body and at the external interface, it would be possible to perform high-throughput synthesis of modified silicone

elastomers, which could then be assessed for biocompatibility in various biological tests: specific biomolecules and/or groups that deliver different properties like charge, non-ionic hydrophiles (e.g., PEG[7,8]) and other materials could be systematically added to the silicone.

As noted above, it is preferable to avoid the use of heavy metals in materials destined for human contact. The necessity of a copper (I) catalyst[17] for the azide/alkyne click reaction would therefore be disadvantageous. Recently, it has been shown that the Huisgen 1,3-dipolar cycloaddition of azides to alkynes ('click' chemistry) can be used to thermally functionalize[18] or crosslink silicones,[19] without the use of a catalyst, at low temperatures and without generating any by-products. Here, we extend the straightforward methodology to prepare functional silicone elastomers that optionally contain an excess of alkynes, or azides that can be secondarily functionalized using another click reaction. Subsequent click chemistry using these reactive groups permits further chemical modification of the silicone rubbers. The process is illustrated by the internal and external grafting of various hydrophilic polymers (PEG of different molecular weights), leading to a substantial reduction in the hydrophobic character of 'click' crosslinked elastomers. This simple, versatile and efficient methodology allows crosslinking and functionalization of silicone elastomers with great control over many experimental parameters, including temperature of cure, stoichiometry, crosslink density, and composition, extending the range of potential applications of siloxane elastomers.

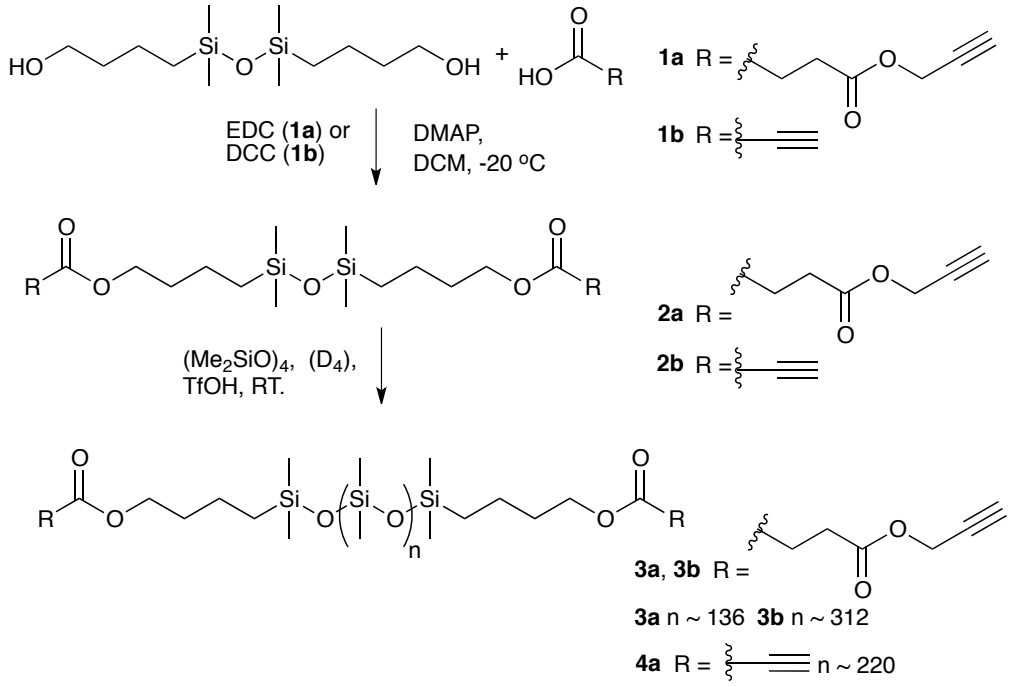
## 2.3 Results and Discussion

### *2.3.1 Synthesis of functional polymers to optimizing crosslink density*

The preparation of functional silicone elastomers that can participate in the Huisgen 1,3-dipolar cycloaddition first required the synthesis of alkyne- and azido-functionalized silicone precursors, respectively. A variety of alkyne- and azide-modified building blocks were synthesized to permit control over the cure process and also over the final mechanical properties of the elastomers *via* manipulation of both the crosslink density and the residual functionality.

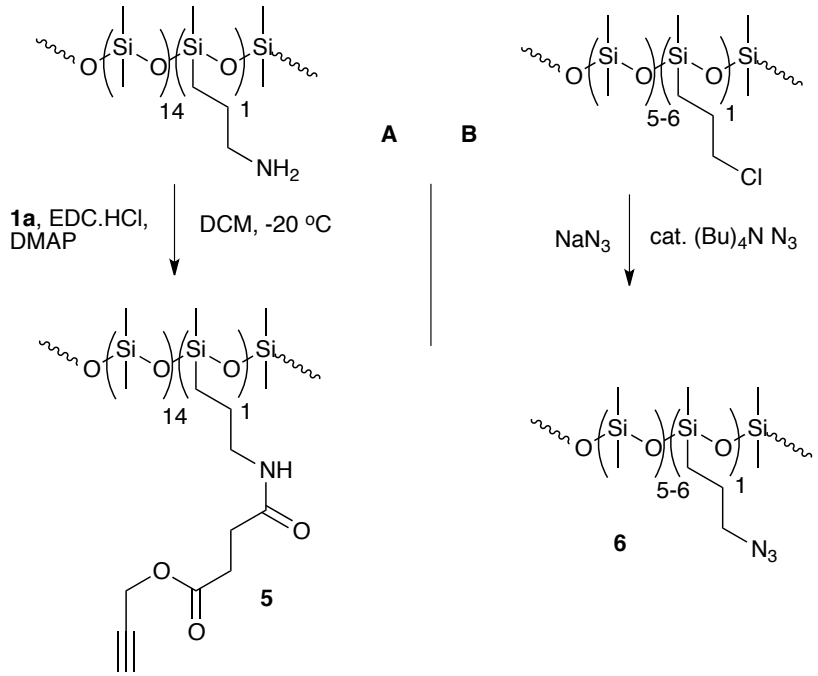
Several alkyne-terminated polysiloxanes, which varied in the nature of their molecular weights and the alkyne terminal group (both activated or non-activated), were prepared as reaction partners for the azidoalkylsilicone. First, non-activated (propargyl) or activated (propiolate) alkyne-terminated disiloxanes were prepared, as shown in Scheme 2.1. The esterification of acids **1a**[60] or **1b** with 1,3-bis(hydroxybutyl)tetramethyl disiloxane, catalyzed by EDC, yielded the alkyne-terminated disiloxanes **2a** and **2b**, respectively. With these compounds as end groups, acid-catalyzed equilibration of **2a** and **2b** with various amounts of $D_4$ ($(Me_2SiO)_4$) was used to grow the PDMS chains, giving the propargyl-terminated polysiloxane **3a** (81% yield; MW 10,600 $g{\cdot}mol^{-1}$), **3b** (77% yield; MW 23,700 $g{\cdot}mol^{-1}$), and propiolate-terminated **4a** (85% yield; MW 16,500 $g{\cdot}mol^{-1}$), respectively. Molecular weights were determined by $^1H$ NMR using end group analysis. The method was validated by gel permeation chromatography (GPC) for

compound **3b,** which gave an $M_n$ of 17,000 g·mol$^{-1}$, in good agreement with values determined by $^1$H NMR (less than 3% error).




Scheme 2.1: Synthesis of alkyne-terminated polysiloxanes

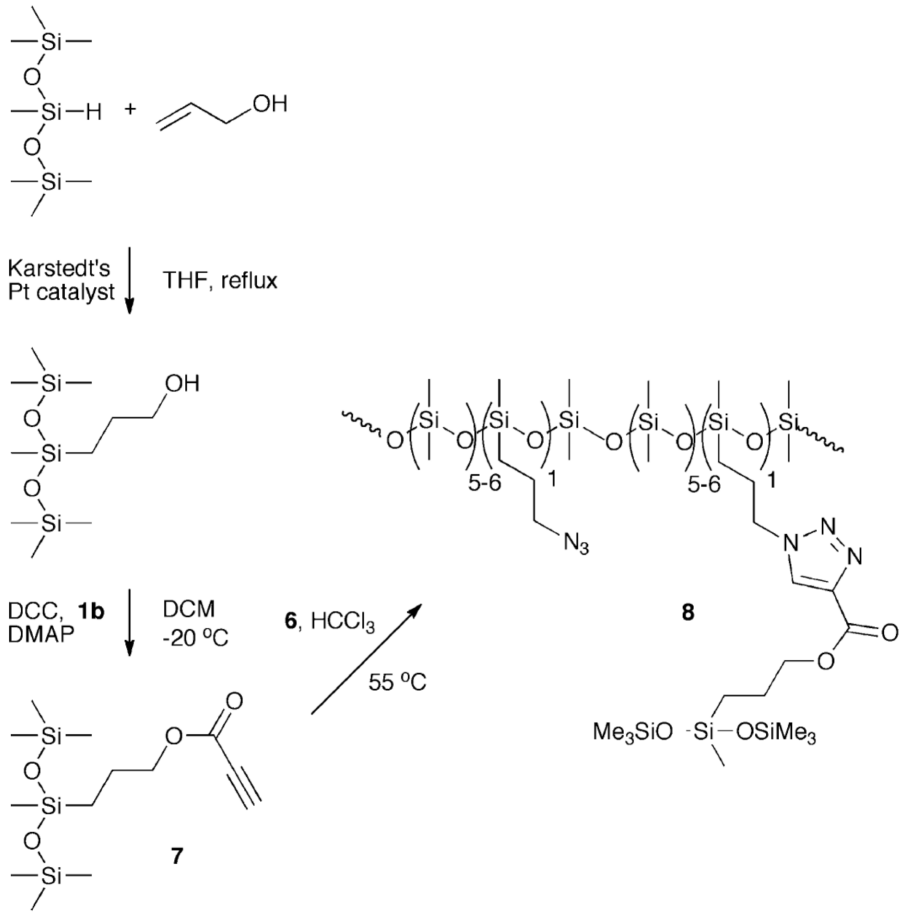
Alternatively, a polysiloxane with multiple pendant alkyne groups was prepared using an EDC coupling reaction between a commercially available (aminopropyl)methylsiloxane-dimethylsiloxane copolymer (MW 3000-6000 g·mol$^{-1}$; 6-7 mol% (aminopropyl)methyl-siloxane unit, trimethylsiloxy-terminated) and non-activated **1a** (Scheme 2.2A). The resultant polymer **5** was obtained in an 84% yield.




Scheme 2.2: A: Synthesis of poly(alkyne)siloxane **5. B:** Synthesis of poly(azidopropyl)siloxane **6**

A multifunctional poly(dimethylsiloxane)-co-(methyl(azidopropyl)siloxane) was prepared from a commercially available poly(dimethylsiloxane)-co-((chloropropyl)methylsiloxane) (MW:7,500-10,000 g·mol$^{-1}$; 14-16 mol % chloropropyl units, trimethylsiloxy-terminated) using azide anions in refluxing THF, with tetra-*n*-butylammonium azide as a phase transfer catalyst (Scheme 2.2B). The resulting polysiloxane **6** with multiple azido functionalities was obtained in an almost quantitative yield; an average molecular weight of 537.8 g·mol$^{-1}$ per repeat unit was calculated from proton NMR. The number of active azido groups, which correlates to the crosslink density, could be controlled by 'capping' a selected fraction with a monoalkyne-terminated trisiloxane **7** as

shown in Scheme 2.3, yielding polymer **8**, in which about 50% of the available azides have been converted to the a trisiloxane-substituted triazole ring.




Scheme 2.3: Synthesis of monoalkyne-trisiloxane **7** and its click reaction with polymer **6** to yield poly(azidopropyl)siloxane **8**

*2.3.2 Elastomer Synthesis*

The thermal 'click' reaction between alkyne- and azido-modified polysiloxanes led to crosslinked elastomeric networks with stable aromatic triazole rings connecting the precursors (Figure 2.1 step A). A total of four different types of reactive elastomers were created using experimental methodologies that differed

only in temperature: three of them contained excess azido functional groups (Series **I**, **II**, and **III**) and one containing excess alkyne-functionality (Series **IV**). Three series of elastomers: **I**, **II** and **III** containing excess azide functionality were created by crosslinking **6** with dialkyne-terminated polysiloxanes **3a, 3b** and **4a**, respectively. Series **IV** resulted from the reaction of **5** with **8**.

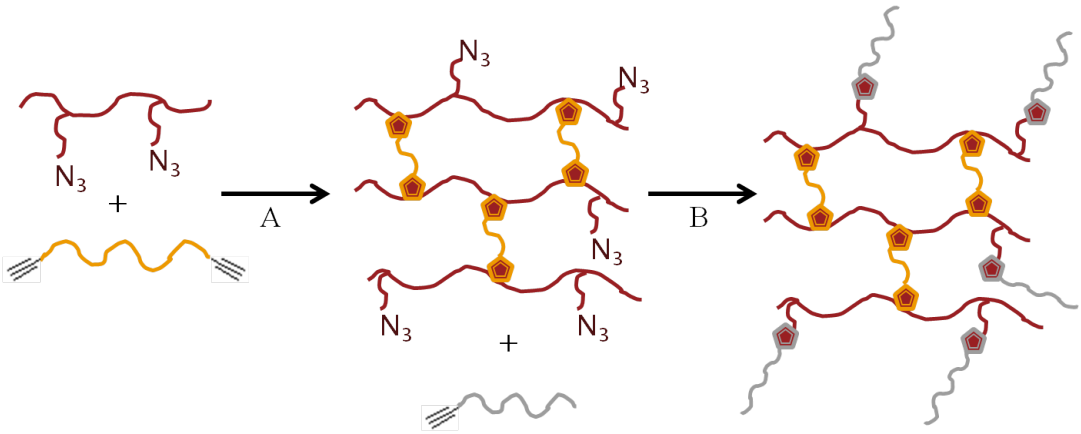



Figure 2.1: Schematic representation showing: A: crosslinking B: grafting alkynyl PEG to the residual azide groups.

The onset temperature for a thermal, metal-free 'click' reaction depends on the electronic properties of the alkyne being used.[20] The presence of electron-withdrawing groups adjacent to the alkyne lowers the energy level of the LUMO. The alkyne activation manifests itself in cycloaddition reactions that occur at lower temperatures than non-activated alkynes: we,[18,19] and others,[21,22,23] have shown that esters of propiolic acid or acetylene dicarboxylic acid can "click" at or near room temperature within a few hours, and without the need of any catalyst. Recently, we applied this metal-free, activated alkyne to azide cycloaddition to prepare elastomeric silicones.[19] When combined with ring strain effects (first

discovered by Wittig),[24] the reaction is even more facilitated (strain-promoted alkyne-azide cycloaddition or SPAAC) and is increasingly being applied in covalent modifications of living systems,[25] in-vivo imaging,[26] lipid[27] and peptide[28] labelling, hydrogel crosslinking, [29] and polymer [30 , 31] or dendrimer [32] functionalization.

The choice of non-activated alkynes **3a**, **3b** (of different molecular weights) or activated alkyne **4a** allowed control over both the temperature and time of the curing process and the mechanical properties of the resulting rubbers by changing the crosslink density. The crosslinking of **6** with **3a** to give Series **I** was performed at 90 °C for 48 h using a 2, 4, 6, 8 or 10 fold excess of the azido functionality, respectively, to leave various quantities of residual reactive groups in the resultant elastomers. Small amounts of toluene or $CHCl_3$ were used to homogenize the pre-elastomer mixture. In general, crosslinking resulted in transparent, colourless monolithic elastomers. However, the entire Series **I** of elastomers obtained were mechanically fragile. For example, when attempting to remove them from their curing vessel, the elastomers cracked or fragmented completely. Low tear resistance and resistance to crack propagation is a common feature of unfilled silicones (those not reinforced with a mineral filler, typically silica[33]). To reduce the crosslink density, an analogous series of elastomers, Series **II**, was created using the higher molecular weight propargyl-terminated PDMS **3b** and **6** while maintaining the same molar quantities of reactive groups. The resulting monolithic rubbers **IIA-IIE** were mechanically more robust but sticky

elastomers, completely unlike the previous crack-prone Series, **IA-IE**. As expected, the hardness of elastomers in Series **II** tracked with crosslink density (Table 2.1). Rubbers prepared with a twofold excess of azide were firm with a Shore OO hardness of 56 (corresponding approximately to a Shore A hardness of 10), the elastomer containing a tenfold excess of azido groups was extremely soft with a Shore OO hardness of only 18, and elastomers prepared at other alkyne/azide ratios fell between these two extremes: the larger the difference in stoichiometry between azide- and alkyne reactive groups, the more reactive groups that were left over, and the lower crosslink density in the obtained material.

Another series of azido-rich elastomers, Series **III**, was created by crosslinking the activated alkyne polymer **4a** with **6** using a 2, 4, 6, 8 and 10 fold molar excess of azido groups, respectively. As before, toluene and/or chloroform were initially added to homogenize the mixture of polymers prior to crosslinking, which was completed at 60 °C in only 12 hours, or in less than 8 hours at 70 °C. The resultant elastomer Series **III** exhibited improved properties over the previous two Series **I** and **II**: the rubbers were flexible yet firm and neither sticky nor gummy (Table 2.1). This series was comparable, in terms of mechanical properties, to lightly crosslinked conventional silicone elastomers obtained via platinum-catalyzed addition cure: the Shore A hardness value for **IIIA** was 12 (**IIA** had a Shore A value of 9). In Series **III**, the distance between crosslinks (~16,000 $g \cdot mol^{-1}$) provided by the dipropiolate-terminated alkyne **4a** was optimal with respect to mechanical and surface properties when compared to the lower MW

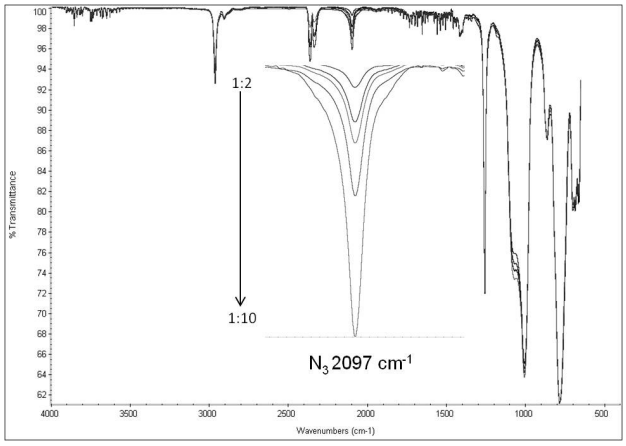
propargyl-terminated polysiloxanes **3a** (10,600 $g \cdot mol^{-1}$; mechanically weak products resulted) and higher MW **3b** (23,700 $g \cdot mol^{-1}$, soft/sticky materials resulted).

To ensure that the integrity of the residual functional groups was preserved during the curing process, excess azido Series **I**, **II** and **III** were analyzed using ATR-IR: the asymmetric azide stretch presents an intense band at 2097 $cm^{-1}$. Taking Series **III** as an example, it was observed qualitatively that the signal corresponding to the azide stretch was larger with increasing azide concentration in the formulations, correlating across the series with the amount of excess of the incorporated azido groups theoretically present (Figure 2.2A). Additionally, setting the $SiMe_2$ signal at 1260 $cm^{-1}$ in the silicone elastomers as an internal standard (as its signal remains constant throughout the series of elastomers[34]), the ratio of relative areas between the standard $SiMe_2$ band and the azide band versus the calculated stoichiometry were plotted for every formulation. A linear correlation was observed, indicating that as the formulation moves away from a stoichiometric ratio of alkyne/azide, more and more azide moieties are retained in the final elastomer (Figure 2.2B). This confirms that the curing process did not degrade the excess azido reactive groups.

Table 2.1: Summary of the various elastomeric materials prepared.

| Entry | Alkyne | Azide | Ratio (RC≡CR':$N_3$) | Cure Conditions | Outcome | Shore OO hardness |
|---|---|---|---|---|---|---|
| **IA** | **3a** | **6** | 1:2 | | Readily cracked | 51±2 |
| **IB** | | | 1:4 | 5 mL toluene | Systematically varies | 48±2 |
| **IC** | | | 1:6 | | | 43±4 |
| **ID** | | | 1:8 | 90 °C, 48h | between **IA** and **IE** | 37±3 |
| **IE** | | | 1:10 | | Soft/gummy | 28±2 |
| **IIA** | **3b** | **6** | 1:2 | | Very flexible | 54±2 |
| **IIB** | | | 1:4 | | Systematically varies | 49±2 |
| **IIC** | | | 1:6 | 5 mL toluene | | 41±2 |
| **IID** | | | 1:8 | | between **IIA** and **IIE** | 23±2 |
| **IIE** | | | 1:10 | 90 °C, 48h | Soft, sticky, gummy | 18±1 |
| **IIIA** | **4a** | **6** | 1:2 | 3 mL toluene | Firm | 68±3 |
| **IIIB** | | | 1:4 | | Systematically varies | 57±4 |
| **IIIC** | | | 1:6 | 60 °C, 12h | | 47±3 |
| **IIID** | | | 1:8 | or | between **IIIA** and **IIIE** | 35±4 |
| **IIIE** | | | 1:10 | 3 mL toluene 70 °C, 8h | Softer | 22±3 |
| **IVA** | **5** | **8** | 4:1 | | More firm | 56±1 |
| **IVB** | | | 6:1 | | Systematically varies | 45±2 |
| **IVC** | | | 8:1 | 1 mL toluene | | 35±1 |
| **IVD** | | | 10:1 | | between **IVA** and **IVE** | 18±6 |
| **IVE** | | | 12:1 | 90 °C, 12h | More flexible, soft | 7±3 |

A




B

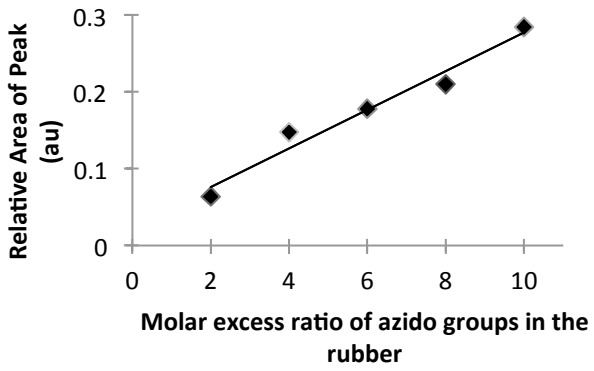



Figure 2.2: A: FT-IR of Series **III** showing an increase of residual azides in the product elastomers, B: Relative area under the azide peak

To show the versatility of this synthetic approach, a series of elastomers, Series **IV**, containing excess alkyne (rather than azide) functionality was also prepared. First, **6** was reacted with a propiolate-containing trisiloxane, **7**, at 55 °C for 20 hours to consume ~ 50% of the azido groups (Scheme 2.3), giving polysiloxanes **8** in quantitative yields (MW ~1408 $g{\cdot}mol^{-1}$ per repeat unit). This pre-functionalization reduced the number of possible crosslink units in the resulting elastomer. Polymers **5** and **8** were mixed in offset ratios to give a 4, 6, 8, 10 and 12 fold molar excess, respectively, of alkyne functional groups and crosslinked at

90 °C. After a few hours, elastomeric gels had already formed and transparent, faint yellow monolithic elastomers, **IVA-IVE**, were obtained after 12 hours. Although these elastomers were created using a non-activated alkyne functionality, similar to **3a** and **3b**, the gelation process occurred in a much shorter time, due to the fact that both precursors are multifunctional and thus present higher densities of reactive groups, leading to enhanced cycloaddition rates. The samples were cooled to room temperature after 12 hours, at which time the resultant elastomers (**IVA-IVE**) were flexible, firm and strong (although it was possible to measure Shore OO hardness, some of the elastomers cracked when attempting to measure Shore A hardness, Table 2.1), and easy to work with: they could be removed from the curing vessel without tearing, surface modification or adhesion to the glass (by contrast, elastomers prepared with **3a** and **3b** were either extremely soft or had barely gelled at this time point). Moreover, as both precursors **5** and **8** were multifunctional, the improved curing process permitted the preparation of elastomers containing an even higher molar excess of reactive groups (ratio 1:12, azide:alkyne) than the elastomers derived from difunctional polymers **3a**, **3b** or **4a**, without being detrimental to the final mechanical properties of the elastomers.

It is instructive to compare the mechanical properties of the four different Series of elastomers (Table 2.1). The trends of Shore OO hardness within a given Series and between Series are very similar, as are the absolute values. However, the importance of network structures on elastomer mechanical properties was evident from the differences in the ability to simply manipulate the materials. Here, the

pure network structure manifests itself. Series **III** and **IV** have appropriate crosslink densities, to give mechanically robust materials. They also exhibit fewer dangling chains, when compared to the Series **II**, resulting in much less tacky materials. For practical application, these materials would normally be reinforced by silica fillers to improve the intrinsically poor tear resistance exhibited by silicones, as is exemplified by the behaviour of Series **I**.

*2.3.3 Functionalization of Elastomers using Poly(ethylene glycol)(PEG)*

Chemical modification of the elastomer Series **III** was performed using monopropiolate-terminated poly(ethylene glycol)s (PEG) **9a** and **9b** (MW = 750 and 2000 g $mol^{-1}$)(Figure 2.1, step B). PEG, a highly hydrophilic polymer, was chosen to demonstrate the efficiency with which the hydrophobic silicone elastomer can be synthetically modified: wettability of the resulting polymers can be easily monitored by contact angle measurements. Two strategies were used. In the first, the elastomer was modified either with PEG in water or neat: in neither case does the silicone effectively swell,[35,36] such that only modification of the surface would occur. In the second process the entire elastomer body was modified by reacting an excess of PEG and the elastomers in refluxing chloroform for 24 hours. During this process, the disks swelled to several times their original volume. The functionalized elastomers of Series **III** were purified by Soxhlet extraction to remove any ungrafted PEG and were dried at 50 °C for 1 day, during which time the rubbers shrunk back to their original size.

Upon visual inspection of the elastomers, it was in some cases immediately apparent that modification had occurred: some elastomers were transformed from transparent and colourless to slightly opaque or whitish after the modification (Figure 2.3). To characterize the materials and obtain an estimation of the amount of grafted PEG, an NMR of a rubber **IIIE** modified with **9a** was obtained by swelling the material in deuterated chloroform. The resulting $^{1}$H NMR (Figure 2.4A) displayed two broad signals, one at 0.08 ppm corresponding to the methyl protons of the polysiloxane chains -((C$H_3$)$_2$SiO)- and a signal at 3.66 ppm corresponding to the -C$H_2$- repeating unit of the PEG chains, confirming successful functionalization. By comparing the relative integration of these 2 signals, it was estimated that about 20% of the azido groups had undergone the click reaction. In addition to a noticeable reduction in the azido signal at 2097 cm$^{-1}$ in the IR, there was the emergence of a small signal at 1737 cm$^{-1}$ corresponding to the carbonyl group of the grafted PEG-monopropiolate ester (Figure 2.4B).

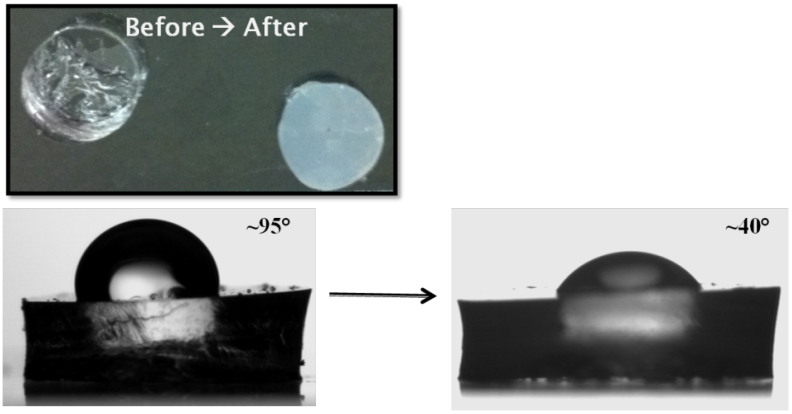



Figure 2.3: Compound **IIID** and **IIID-PEG9b** Left photograph; Right: Sessile drop contact angles after at t=0 and ~30 minutes, 40° (Rubber **IIID**)

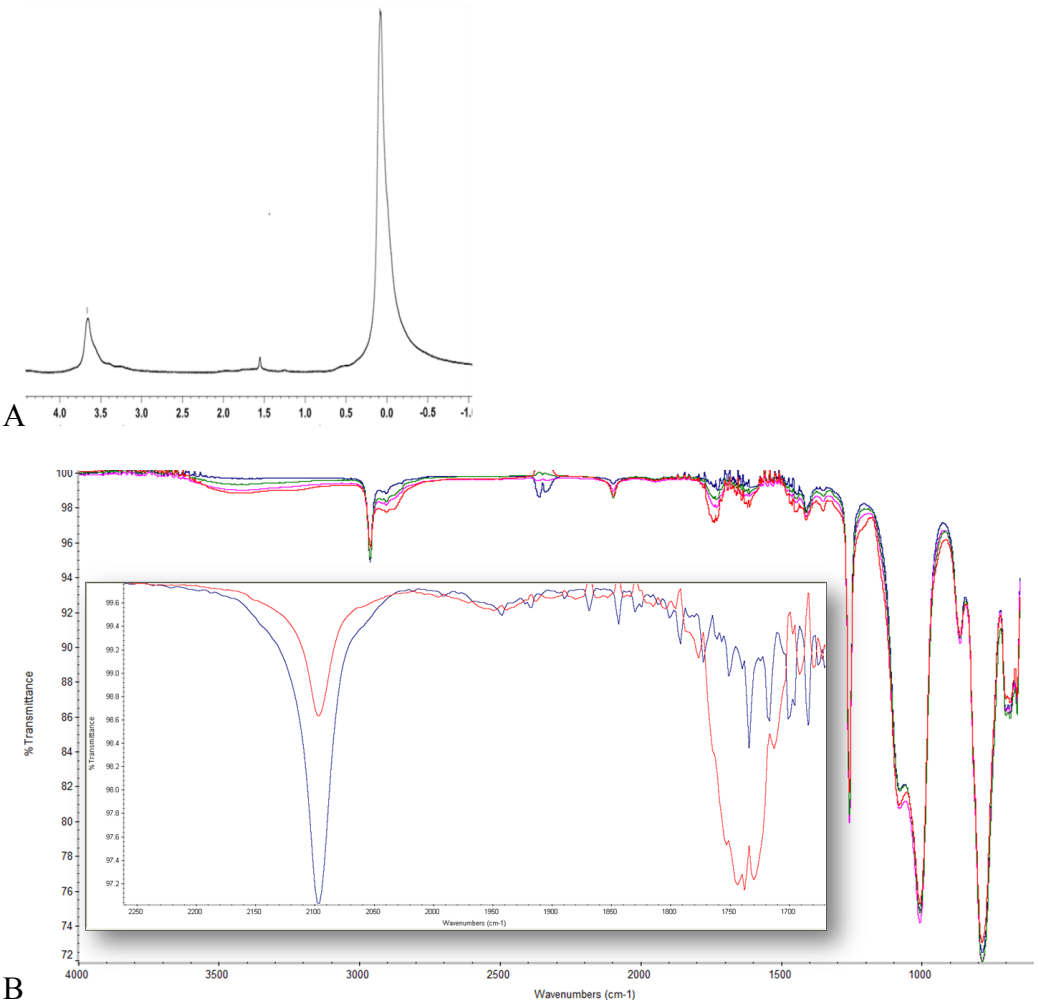



Figure 2.4: A: NMR of **IIIE** after modification with 9a showing the introduction of PEG at 3.66 ppm. B: IR of the III-9a series, Inset spectrum – Expanded IR spectra of IIIE (blue) and IIIE-9a (red), showing the disappearance of 2079 $cm^{-1}$ azide signal and appearance of the 1737 $cm^{-1}$ carbonyl signal.

Hydrophobic surfaces, such as pristine PDMS rubbers, have a high contact angle (normally > 100°):[37] the water droplet beads up because of differences in energy between the water and the silicone as a result of hydrophobic interactions. Even relatively subtle changes, such as the addition of azide groups, can increase wettability. For example, elastomer **IIID** saw a decrease in contact angle from 103° to a plateau value of 83° over 30 minutes. This slightly lower contact angle

value, when compared to non-functionalized PDMS, may be attributed to the presence of numerous azido groups. We note that contact angles are also affected by surface roughness.[38,39] The pre-elastomers are fluids and flow to give very low roughness surfaces.

Much more hydrophilic silicone surfaces can be generated by modification with PEG.[5,7,8,40-45] Static contact angle measurements in air at two time points were made in triplicate of the Series **III** elastomers that had been modified with **9b** PEG swollen in chloroform (Table 2.2). Samples that initially contained a larger quantity of azido groups were found, after modification by PEG, to have lower initial and final contact angles than those with fewer azides. For example, the initial contact angle of **IIIA-PEG9b** was 98° while for **IIID-PEG9b** it was 80° and final values (after 30 minutes) were 87° and 55°, respectively. These changes can be attributed to two different phenomena. First, and obviously, an increasing concentration of water soluble PEG will reduce the water contact angle. Secondly, elastomers in a given Series initially containing a larger excess of azido groups have lower crosslink densities. A more flexible network allows for better diffusion of PEG into the swelled elastomers during grafting and, thus, a higher grafting density of hydrophilic chains. In addition, after grafting, the same flexible network will permit the grafted PEG chains to have higher mobility, and thus a better ability to reorganize to the surface, allowing the water droplet to more rapidly wet out.[34,46]

Table 2.2: Advancing contact angles of Series III elastomers modified with **9a** or **9b**.

| Elastomer<br>Series **III + 9b** | Ratio<br>Alkyne:Azide | Initial (°) | 60s (°) | 30 min (°) |
|---|---|---|---|---|
| **IIIA-PEG9b** | 1:2 | 98±6 | n/a | 87±6 |
| **IIIB-PEG9b** | 1:4 | 87±5 | 81±9 | 69±8 |
| **IIIC-PEG9b** | 1:6 | 86±3 | 73±9 | 61±7 |
| **IIID-PEG9b** | 1:8 | 80±3 | 66±8 | 55±6 |
| **IIIE-PEG9b** | 1:10 | 74±1 | 62±1 | 55±1 |
| After soaking in water, rinsing in acetone and drying under $N_2$ | | | | |
| Rubber | Ratio | Final (°) | | |
| **IIIB-PEG9b** | 1:4 | 57±3 | | |
| **IIIB-PEG9a** | 1:4 | 46±5 | | |
| **IIID-PEG9b** | 1:8 | 51±2 | | |
| **IIID-PEG9a** | 1:8 | 41±6 | | |
| **IIID no PEG** | 1:8 | 85±3 | | |
| Surface functionalization: absence of swelling solvents | | | | |
| **IIIC-PEG9a** (60 °C in water) | 1:6 | 61±5 | | |
| **IIIC-PEG9a** (60 °C neat) | 1:6 | 70±1 | | |
| **IIIC-PEG9a** (21 °C in water) | 1:6 | 68±4 | | |

To allow comparisons of changes in wettability between elastomers bearing different length PEG chains, contact angle measurements were performed for the elastomers **IIIB** and **IIID** modified with **9a** or **9b**, respectively. The elastomers were soaked for an hour in water, rinsed with acetone and dried under a nitrogen

flow prior to measurement. It was observed that the contact angle values (Table 2.2) were lower when the elastomers were first soaked in water, which has also been observed by Murthy et al.;[47] for example, the contact angle of **IIIB-PEG9b** dried in air reached a value of 69° whereas the same sample pre-soaked for an hour in water reached a value of 57°. Shorter PEG chains allowed the modified rubbers to reach lower contact angle values: **IIIB-PEG9a** reached a lower contact angle (46°) than **IIIB-PEG9b** (57°). The lower contact angle can be rationalized by steric considerations; shorter PEG chains should be more easily grafted and the corresponding material may contain a higher density of hydrophilic PEG chains. Shorter hydrophilic chains should also have a higher mobility within the silicone to rearrange to the surface as has been previously observed.[5,7,8] Furthermore, as previously observed by Fortuniak et al.,[39] water sorption onto the surface of siloxane elastomers can change the surface roughness additionally impacting the contact angle.

Elastomers modified by PEG in poor solvents (water and neat: at 60 ºC and at room temperature) for silicone similarly showed improved wettabilities (Table 2.2). The increase in wettability, over the series studied, unsurprisingly showed a correlation between available residual azide concentration in the elastomer and wettability of the PEG-modified elastomers. It is thus possible to 'dial in,' within limits, the desired degree of surface/bulk functionalization simply by manipulating the nature of the pre-elastomer starting materials. More importantly, the ability to perform the metal-free click process in both hydrophobic and

hydrophilic solvents extends the utility of the reaction for the surface modification of silicone elastomers.

The manipulation of surfaces of silicone-based elastomers is non-trivial. Strategies to increase surface hydrophilicity include the addition of a new polymer layer, for example, by plasma polymerization,[48] by surface oxidation, again typically using a plasma or other high energy techniques[49 - 57] or by the introduction of functional groups that can be used to tether hydrophiles including biomolecules.[5,7,8] With the former process, hydrophilization can be quite efficient, but it is challenging to control the introduction of specific quantities of hydrophiles in specific orientations; subsequently tethering additional (bio)molecules adds its own challenges. Plasma oxidation renders silicone elastomers hydrophilic for short periods of time. However, the process of surface reversion, in which highly mobile chains are able to migrate to the air interface, is extremely efficient and soon returns the surface to a hydrophobic state.[52] In our experience, it is difficult to reproducibly trap the silanols formed during oxidation at the interface.

It is possible to graft hydrophiles, such as PEG, on the surface using combinations of organic transformations that may (e.g., platinum-catalyzed hydrosilylation),[7,8] or may not (e.g., Michael addition[58,59]) require the use of metal catalysts. The advantages of the surface grafting approach is that, under ideal conditions, the graft density, graft thickness and types of (bio)molecules that modify the surface can be controlled. Often, however, conditions are not ideal.

For example, the use of Michael group acceptors is problematic with protein grafting- any of the available free amine groups could intervene.

The use of azide/alkyne click reactions[9,60] offers significant benefits for the controlled modification of silicone elastomers. As demonstrated above, without the need for catalysts – metal-based or not – and in a reaction that produces no by-products, it is possible to efficiently control both silicone elastomer formation and surface functionalization. The properties of the initially formed silicone elastomer are controlled by simply varying the ratio of simple and readily available azide-/alkyne-containing building blocks. Thus, network morphology, crosslink density, and the concentration of residual functional groups in the elastomer are all readily manipulated. In addition, the temperature used to initiate the reaction can be controlled. While low temperature processes would normally be perceived to be of highest utility, the use of higher temperature processes allows much more working time after mixing of the functionalized prepolymers.

The ability to specifically label (bio)molecules with azides or alkynes has previously been demonstrated.[10-16] Alkyne- or azide-rich silicone elastomer surfaces should make excellent targets as a biomaterials support, as it is possible to modify the functional elastomers throughout using good solvents for silicone (alkanes, aromatics, halocarbons, isopropanol) or preferentially at the external interface using poorer solvent (water, methanol). The latter route is particularly useful for polar biomolecules as it should be possible to avoid the use of protection/deprotection strategies and directly couple suitably modified

biomolecules to the silicone surface in water. The development of click functional silicone elastomers as high-throughput biomaterials' supports will form the basis of future reports.

**2.4 Conclusions**

Simple, efficient metal-free click reactions can be used both to crosslink azide- and alkyne-modified silicones, and to facilitate their subsequent chemical modification with hydrophilic species. Silicone elastomers were prepared by reacting compounds selected from a series of di- and multi-alkyne functionalized polysiloxanes of varying reactivities with one of several poly(azide)-containing siloxanes. After curing, and depending on the ratios of the starting materials, alkyne- or azide-rich elastomers resulted. The process allows extensive control over the quantity and nature of the excess reactive groups incorporated into the elastomers, as well as the conditions under which the elastomers are cured, such as the temperature and time required to crosslink the precursors. Further chemical modification of the elastomers was demonstrated by the click ligation of alkyne-modified PEGs of various chain lengths either at the interface, or throughout the entire body of the elastomer. After PEG modification, the wettability of the elastomers was considerably increased. The ability to use metal-free 'click' reaction both for crosslinking and surface modification in two simple, sequential reactions should be applicable to high-throughput preparation of potential biomaterials surfaces.

## 2.5 Experimental Section

### *2.5.1 Materials and Methods*

(Chloropropyl)methylsiloxane-dimethylsiloxane copolymer (14-16 mol % (chloropropyl)methylsiloxanes, MW 7,500-10,000 $g \cdot mol^{-1}$, trimethylsiloxy-terminated), (aminopropyl)methylsiloxane-dimethylsiloxane copolymer (6-7 mol % (aminopropyl)methyl-siloxanes, MW 3,000-6,000 $g \cdot mol^{-1}$, trimethylsiloxy-terminated), octamethylcyclotetrasiloxane ($D_4$), and 1,3-bis(hydroxybutyl)tetramethyldisiloxane were obtained from Gelest. Propiolic acid (95%), propargyl alcohol (99%), succinic anhydride (99%), *N*-(3-dimethylaminopropyl)-*N*′-ethyl-carbodiimide hydrochloride (EDC·HCl, commercial grade), sodium azide and dimethylaminopyridine (DMAP, 99%) were obtained from Sigma-Aldrich. Tetra-*n*-butylammonium azide was obtained from TCI. All materials were used as received. Compound **1a**, the monopropargyl ester of butanedioic acid was prepared according to a published procedure.[61] 1,3-Bis(propiolatobutyl)tetramethyl-disiloxane (2**b**) was synthesized following the procedure by Gonzaga et al. [19]

IR analyses were made with a Bio-Rad infrared spectrometer (FTS-40). $^1H$ NMR were recorded at room temperature on a Bruker AC-200 spectrometer (at 200 MHz for $^1H$ and 50 MHz for $^{13}C$) or a Bruker AV 600 spectrometer (at 600 MHz for $^1H$ and 150 MHz for $^{13}C$) using deuterated solvents ($CDCl_3$). Contact angle measurements were performed using a Kruss DSA Contact Angle

Apparatus using 18.1 mΩ·cm (MilliQ) water. GPC analysis was performed on a Viscoteck GPCmax VE-2001 chromatograph using toluene as the eluent.

*2.5.2 Alkyne Synthesis*

Synthesis of propargyl-terminated disiloxane **2a**

Compound **1a** (1.05 g, 6.7 mmol) and bis(4-hydroxybutyl)tetramethyldisiloxane (0.89 g, 3.2 mmol) were solubilized in dry dichloromethane (DCM, 30 mL) in a 50 mL round-bottomed flask. The mixture was cooled at -20 °C in a dry ice/acetone bath and then a catalytic amount of DMAP (0.10 g, 0.8 mmol) was added. EDC·HCl (1.29 g, 6.7 mmol) was slowly added and the reaction was allowed to stir under a positive pressure of nitrogen for 24 h. Cooling at -20 °C was maintained for 8 h, then the mixture was allowed to return to room temperature. The DCM was evaporated and the mixture was dissolved in diethyl ether (30 mL). The organic phase was washed with 2 x 20 mL of 0.08 M aqueous HCl followed by 2 x 25 mL 5% $NaHCO_3$ solution. The organic phase was dried over $MgSO_4$ and gravity filtered. Diethyl ether (40 mL) and activated charcoal (1 g) were added and the mixture was allowed to stir for 12 h. The suspension was filtered and the volatiles removed in vacuo to yield 2.10g (76% yield) of pure propargyl-terminated disiloxane, **2a**.

$^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.01 (s, 12H, SiC*H*$_3$); 0.49 (t, 4H, *J*=8.2 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.37 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.62 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.46 (s, 2H, C≡C*H*); 2.63 (m, 8H, O=CC*H*$_2$C*H*$_2$C=O); 4.06 (t, 4H, *J*=6.0 Hz, SiCH$_2$CH$_2$CH$_2$C*H*$_2$); 4.67 (s, 4H, C*H*$_2$C≡CH). $^{13}$C NMR ($CDCl_3$,

150.9 MHz, δ): 0.2 (SiC*H*$_3$); 17.7 (Si*C*H$_2$CH$_2$CH$_2$CH$_2$); 19.5 (SiCH$_2$*C*H$_2$CH$_2$CH$_2$); 28.8 (SiCH$_2$CH$_2$*C*H$_2$CH$_2$); 31.8 (CH≡CCH$_2$OO=C*C*H$_2$CH$_2$C=O); 52.0 (*C*H$_2$C≡CH); 64.4 (SiCH$_2$CH$_2$CH$_2$*C*H$_2$); 74.9 (C≡*C*H); 77.4 (*C*≡CH); 171.9, 171.3 (O=*C*CH$_2$CH$_2$*C*=O). MS (ES-positive mode): *m/z* [M + $NH_4^+$] calculated = 572.2711; [M + $NH_4^+$] found = 572.2739.

Synthesis of propargyl-terminated polysiloxanes **3a** and **3b**

Octamethylcyclotetrasiloxane ($D_4$, 8.10 g, 27.3 mmol) and **2a** (0.55 g, 1.0 mmol) were placed in a 50 mL round-bottomed flask fit with a septum and purged with nitrogen. The mixture was agitated with a magnetic stirrer followed by the addition of triflic acid (200 μL, 2.3 mmol). The mixture was stirred for 1 d at room temperature, after which time magnesium oxide (1.00 g) was added followed by dry hexanes (25 mL). The slurry was stirred for 1 h. An additional 25mL of hexanes was added, and then the mixture was filtered through a short pad of Celite on a fritted funnel, vacuum was applied to speed up the filtration. Volatiles were removed in vacuo to yield 8.10 g of crude product, which was purified by kugelrohr distillation (2 h at 140 °C). The polymer was re-dissolved in diethyl ether (100 mL), 1.00 g of activated carbon was added, and the slurry was stirred for 20 h, at which time the suspension was filtered though a short pad of Celite on a fritted funnel, vacuum was applied to speed up the filtration. Volatiles including excess $D_4$ were removed *in vacuo* (< 0.1 mm) at 140 °C to yield 6.90 g of a transparent colourless oil, **3a**. $^1$H NMR spectroscopy indicated that the resulting polysiloxane chain was comprised of ~136 dimethylsiloxane units

(relative integration of the 8H (OC=C$H_2$C$H_2$C=O protons at 2.66 ppm) and 4H (O=COC$H_2$CH$_2$CH$_2$CH$_2$Si protons at 4.09 ppm) versus 818 for dimethylsiloxane (SiCH$_3$ at 0.07 ppm)), which corresponds to an average molecular weight of ~10,600 g·mol$^{-1}$ (yield: 81%). The same procedure using a larger amount of octamethylcyclotetrasiloxane ($D_4$, 18.08 g, 61 mmol) and **2a** (0.60 g, 1.1 mmol) yielded 14.14 g of a polysiloxane chain **3b** constituted of 313 dimethylsiloxane units, which correspond to an average molecular weight of 23,700 g·mol$^{-1}$ (yield: 77%).

$^1$H NMR ($CDCl_3$, 200 MHz, δ): 0.01 (s, 818H for **3a** and 1875H for **3b**, SiC$H_3$); 0.49 (t, 4H, *J*=8.2 Hz, SiC$H_2$CH$_2$CH$_2$CH$_2$); 1.37 (m, 4H, SiCH$_2$C$H_2$CH$_2$CH$_2$); 1.62 (m, 4H, SiCH$_2$CH$_2$C$H_2$CH$_2$); 2.46 (s, 2H, C≡C$H$); 2.63 (s, 8H, O=CC$H_2$C$H_2$C=O); 4.06 (t, 4H, *J*=6.0 Hz, SiCH$_2$CH$_2$CH$_2$C$H_2$); 4.67 (s, 4H, C$H_2$C≡CH).

Synthesis of propiolate-terminated polysiloxane **4a**

1,3-Bis(propiolatobutyl)tetramethyldisiloxane (**2b**) was synthesized following the procedure by Gonzaga et al. [19] The same equilibration methodology as outlined in the above procedure (synthesis of **3a** and **4a**) was followed, but using **2b** (0.78 g, 2.0 mmol) as the end group, with $D_4$ (34.09 g, 115.0 mmol) and triflic acid (200 μL, 2.3 mmol), yielding 29.77 g of propiolate-terminated polysiloxane, **4a**. The polysiloxane chain was constituted of 220 dimethylsiloxane units, corresponding to an average molecular weight of 16,500 g·mol$^{-1}$ (yield: 85%) determined by $^1$H NMR and confirmed by GPC ($M_n$= 17,000 g·mol$^{-1}$; PDI = 1.6).

$^1$H NMR ($CDCl_3$, 200 MHz, δ): 0.07 (s, 1320H, SiC*H*$_3$); 0.56 (t, 4H, *J*=8.3 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.37 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.68 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.86 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, SiCH$_2$CH$_2$CH$_2$C*H*$_2$).

Synthesis of poly(alkyne)-functionalized polymer **5**

In a 100 mL round-bottomed flask, (aminopropyl)methylsiloxane-dimethylsiloxane copolymer (6-7 mol % (aminopropyl)methylsiloxane, 11.30 g, 10.1 mmol) and **1a** (1.89 g, 12.1 mmol) were dissolved in dry DCM (50 mL). The mixture was cooled at -20 °C in a dry ice/acetone bath, and a catalytic amount of DMAP (0.02 g, 0.2 mmol) was added. EDC·HCl (2.33 g, 12.1 mmol) and additional DCM (15 mL) were slowly added. The reaction was covered, purged with nitrogen and allowed to stir under a positive pressure of nitrogen for 48 h. The mixture was then washed with 2 x 50 mL of 0.1 M HCl (it took several hours for the mixture to phase separate) followed by 2 x 25 mL of distilled water. The organic phase was dried over $MgSO_4$, gravity filtered and the volatiles removed in vacuo to yield 10.60 g (84% yield) of the title compound as a faint yellow oil.

$^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.07 (s, 84H, SiC*H*$_3$); 0.50 (m, 2H, SiC*H*$_2$CH$_2$CH$_2$N); 1.53 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$N); 2.47 (m, 3H, O=CCH$_2$C*H*$_2$C=ON and C≡C*H*); 2.72 (m, 2H, O=CC*H*$_2$CH$_2$C=ON); 3.22 (m, 2H, SiCH$_2$CH$_2$C*H*$_2$N); 4.68 (s, 2H, C*H*$_2$C≡CH). $^{13}$C NMR ($CDCl_3$; 150 MHz): δ = -0.33, 1.25, 1.99, 14.12, 23.40, 31.10, 42.57, 52.33, 75.14, 171.02, 172.40.

Synthesis of propiolate functional trisiloxane **7**

In a round-bottomed flask were successively introduced allyl alcohol (4.36 g, 75.0 mmol), bis(trimethylsiloxy)methylsilane (5.56 g, 25.0mmol), and dry toluene (25 mL). Karstedt's platinum hydrosilylation catalyst (platinum-divinyltetramethyl-disiloxane complex, solution in xylenes: 0.05 mL) was added, and the mixture was stirred at 50 °C in a dry atmosphere (connected to a Drierite tube) for 16 h. The volatiles were then removed *in vacuo*, and the light brown oily residue was directly esterified as follow: propiolic acid (3.50 g, 50.0 mmol) in dry dichloromethane (40 mL) was added, and the solution was cooled at -20 °C using a dry ice/acetone bath. A catalytic amount of DMAP (0.10 g, 0.8 mmol) was added, followed by small portions addition of DCC (6.19 g. 30.0 mmol). Cooling at -20 °C was maintained for 8 h. The mixture was then allowed to return to room temperature (overnight). The DCM was evaporated *in vacuo*, and the residue re-dissolved in dry diethyl ether. The insoluble dicyclohexyl urea was removed by filtration. The filtrate was concentrated *in vacuo* and the resulting oil was chromatographed over silica gel eluting using 1% ethyl acetate in hexanes to afford 6.54 g (79% for the 2 steps) of the title compound as a colorless oil.

$^{1}$H NMR ($CDCl_3$; 200MHz, δ): 0.02 (s, 3H, SiC$H_3$); 0.08 (s, 18H, Si(C$H_3$)$_3$); 0.47 (m, 2H, SiC$H_2$CH$_2$CH$_2$O); 1.69 (m, 2H, SiCH$_2$C$H_2$CH$_2$O); 2.87 (s, 1H, C≡C$H$); 4.14 (t, 2H, $J$=7.0 Hz, SiCH$_2$CH$_2$C$H_2$O). $^{13}$C NMR ($CDCl_3$; 150 MHz, δ): -0.2 (Si$C$H$_3$); 2.0 (Si($C$H$_3$)$_3$); 13.5 (Si$C$H$_2$CH$_2$CH$_2$O); 22.4 (SiCH$_2$$C$H$_2$CH$_2$O); 68.8 (SiCH$_2$CH$_2$$C$H$_2$O); 74.5 (C≡$C$H); 75.0 ($C$≡CH); 153.0 ($C$=O). HRMS (EI): *m/z* [M+] calculated = 332.1295, found = 332.1279.

Synthesis of propiolate-terminated PEOs **9a** (750 MW) and **9b** (2000 MW)

Propiolate-terminated monomethoxy poly(ethylene oxide) **9a**: in a round-bottomed flask containing monomethoxypoly(ethylene-oxide) *(av. mol. wt: 750*) (15.0 g, 20.0 mmol), was successively added propiolic acid (4.2 g, 60.0 mmol), toluene (90 mL) and a catalytic amount of *p*-toluenesulfonic acid (0.5 g, 2.6 mmol). The flask was equipped with a Dean-Stark apparatus, and heated to reflux with azeotropic removal of water. Completion of the reaction was monitored by $^{1}$H NMR, by comparison of the 3 protons of terminal methoxy with the appearance of the methylenic ester protons at 4.34 ppm (*ca.* 20 h). The solution was then cooled to room temperature, and washed three times with 50 mL of an aqueous potassium carbonate solution. The organic phase was then dried over magnesium sulfate, concentrated *in vacuo*, and the crude product directly loaded onto a chromatography column packed with silica gel. Elution started with pure dichloromethane, then increasing amounts of methanol were added to the eluent (up to 5%, v:v). The fractions containing the propiolate ester were combined, evaporated under reduced pressure to afford pure monopropiolate-terminated monomethoxy poly(ethylene oxide), (12.1 g, 77 % yield).

$^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 4.34 (t, 2H, -COOC$H_2$-, $J$ = 6.0 Hz), 3.74 to 3.55 (m, ~ 60H, -OC$H_2$C$H_2$O-), 3.37 (s, 3H, OC$H_3$), 2.89 (s, broad, 1H, *H*CCCOO). $^{13}$C NMR ($CDCl_3$, 125 MHz, δ): 152.68, 75.67, 74.56, 71.94, 70.57, 68.57, 65.24, 59.03. HRMS (ES Positive mode): *m/z* [$M+NH_4^+$] calculated = 806.4749, found = 806.4768.

Monopropiolate-terminated monomethoxy poly(ethylene oxide) **9b**: in a round-bottomed flask containing monomethoxy poly(ethylene oxide) *(av. mol. wt: 2000*) (20.0 g, 10 mmol), was successively added propiolic acid (2.8 g, 40 mmol), toluene (70 mL) and a catalytic amount of *p*-toluenesulfonic acid (0.75 g, 3.9 mmol). The flask was equipped with a Dean-Stark apparatus, and heated with azeotropic removal of water. Completion of the reaction was monitored by $^{1}$H NMR, by comparison of the 3 protons of terminal methoxy with to the appearance of the methylenic ester protons at 4.27 ppm. Once the reaction was complete, the mixture was then concentrated in vacuo, and the crude product was dissolved in a minimal amount of dichloromethane. The mixture was then added dropwise to a beaker containing ice-cold diethyl ether (150 mL). Once complete, the mixture was allowed to stir for a further 20 min to ensure complete precipitation. The precipitate was then collected using a fritted funnel and dried under reduced pressure. The white powder was redissolved in DCM, and the precipitation procedure (drop by drop addition into ice-cold diethyl ether) was repeated. The precipitate was collected in a fritted funnel, dried under reduced pressure in a desiccator to afford the title compound (16.8g; 82%) as a white powder.

$^{1}$H NMR ($CDCl_3$, 500 MHz, δ): 4.27 (t, 2H, -COOC*H*$_2$-, *J* = 5.0 Hz), 3.47 to 3.68 (m, ~ 233H, -OC*H*$_2$C*H*$_2$O-), 3.31 (s, 3H, -OC*H*$_3$), 3.01 ppm (s, 1H, *H*CCCOO). $^{13}$C NMR ($CDCl_3$, 125 MHz, δ): 152.59, 75.62, 74.48, 71.88, 70.60, 68.50, 65.14, 58.97 ppm. HRMS (ES Positive mode): m/z $[M+H]^+$ calculated = 2065.2008, found = 2065.1916.

*2.5.3 Azide Synthesis*

Synthesis of Poly(azidopropylmethyl)-co-(dimethylsiloxane) **6**

The preparation of **6** is an improvement of the previously published method by Gonzaga et al. [19] (Chloropropylmethyl)siloxane-dimethylsiloxane copolymer (14-16 mol % (chloropropyl)methylsiloxane, by $^1$H NMR ($(Me_2SiO)_{5.5}(Cl(CH_2)_3MeSiO)_1)_n$; 543.45 g/mol repeat unit) 20.00 g, 36.8 mmol of chloropropyl groups), $NaN_3$ (3.62 g, 55.7 mmol) and ($n$-butyl)$_4NN_3$, (0.50 g, 1.8 mmol) were dissolved in dry THF (60 mL). The mixture was refluxed with stirring for 24 h. At this stage, the reaction was found to be almost complete by $^1$H NMR spectroscopy. Additional ($n$-butyl)$_4NN_3$ (0.30 g, 1.00 mmol) was therefore added, and the mixture was refluxed an additional 24 h. THF was removed *in vacuo*. The mixture was redissolved in diethyl ether (60 mL) and filtered though neutral alumina. Volatiles were removed in vacuo to yield 19.43 g (96% yield) of the title compound. Characterization by $^1$H and $^{13}$C NMR was in agreement with previously reported values.[19] In subsequent elastomer synthesis, $^1$H NMR spectroscopy was to calculate the molecular weight of an average repeat unit using the ratio of azide (using the $CH_2$ adjacent to $N_3$ at 3.26 ppm as a diagnostic) to alkyne groups.

$^1$H NMR ($CDCl_3$, 200 MHz, δ): 0.07 (s, 35H, $SiCH_3$); 0.56 (m, 2H, $SiCH_2CH_2CH_2N_3$); 1.62 (m, 2H, $SiCH_2CH_2CH_2N_3$); 3.24 (t, J=6.9 Hz, 2H, $SiCH_2CH_2CH_2N_3$).

Synthesis of polymer **8**: poly(azido)siloxane with a reduced (by 50%) amount of azido groups

Compound **6** (3.00 g, 5.6 mmol), **7** (0.93 g, 2.80 mmol) and chloroform (1 mL) were added to a vial and stirred for 20 h at 55 °C, at which time volatiles were removed to give the title compound in quantitative yield. The resulting polymer was characterized by $^{1}$H NMR, which confirmed that about half of the initial azide functional groups had reacted to form triazole rings with trisiloxane blocking groups.

$^{1}$H NMR ($CDCl_3$; 600 MHz, δ): 0.07 (s, 101H, $SiCH_3$); 0.3 (m, 6H, $SiCH_2$); 1.63 (m, 2H, $SiCH_2CH_2CH_2N_3$); 1.79 (m, 2H, $SiCH_2CH_2CH_2$-triazole); 1.95 (m, 2H, $SiCH_2CH_2CH_2O$); 3.21 (t, 2H, J=6.9 Hz, $SiCH_2CH_2CH_2N_3$); 4.30 (m, 2H, $O{=}COCH_2CH_2CH_2Si$); 4.37 (m, 2H, $CH_2$-triazole); 8.03, 8.08 (s, 1H, C=CH).

*2.5.4 Elastomer Synthesis*

Four distinct series of elastomers were prepared (**I**, **II**, **III** and **IV**), as summarized in Table 2.1. These different series differ in the precursors used: alkynes **3a**, **3b, 4a**, and **5**; azides **6** and **8**. Different alkyne to azide ratios were used in each series, generating elastomers with various amounts of residual reactive azide or alkyne groups. According to the alkyne used, the crosslinking process could be performed at different temperatures, as stated in Table 2.1. Finally, the Shore OO hardness (durometer) of the elastomers were determined.

The general procedure is illustrated by the synthesis of a reactive elastomer containing an excess of azide that was formed by a crosslinking reaction between

**3b** and **6** with an alkyne to azide ratio of 1:2 respectively (**IIa**). Polymer **6** (0.38 g, 0.7 mmol of azido functional units) was placed in a small glass Petri dish followed by dialkyne **3b** (4.16 g, 0.35 mmol of alkyne), and toluene (5 mL). After vigorous mixing, a homogeneous and transparent mixture resulted. The dish was then covered and placed in an oven at 90 °C for 48 h. The initially formed solution turned into a monolithic elastomer during this time. The same procedure was followed using molar ratios of alkyne:azide functional groups (**3b:6**) of 1:4, 1:6, 1:8 and 1:10, respectively, to give **IIB**, **IIC**, **IID** and **IIE** (Table 1).

The above procedure was repeated using **6** and dialkyne **3a** to give more rigid elastomers **IA-IE** compared to Series **II**. An analogous series was made using **4a** with **6** and toluene (3 mL); crosslinking at 60 °C occurred after 12 h to yield colourless and transparent monolithic elastomers **IIIA-IIIE**. Slightly higher temperatures (70 °C) led to more rapid curing (8 h). Finally, a series of elastomers **IVA-IVE** using a molar excess of alkyne functional groups were made on a smaller scale; crosslinking of **5** and **8** on a 1 g scale in 10 mL beakers using toluene (600 μL) to homogenize the mixture was performed with molar ratios of azide:alkyne (**8**:**5**) of: 1:4, 1:6, 1:8, 1:10 and 1:12, respectively. The mixtures were cured at 90 °C for 12 h to form monolithic elastomers that were transparent and slightly yellow, **IVA**, **IVB**, **IVC**, **IVD** and **IVE** respectively.

All elastomers were removed from their respective vessels, cut into smaller cylindrical disks and characterized by IR then stored in the dark in plastic petri dishes until further use.

Table 2.1 below summarizes the precursors used, stoichiometry ratios, curing conditions, and outcome of the different cross-linking processes we performed.

*2.5.6 PEG-Functionalized Silicones*

Elastomers of Series **IIIA-IIIE** were functionalized using with **9a** and **9b**, respectively. The general procedure is outlined for the elastomer **IIIA** using **9b**. Four elastomer disks (total mass of 0.23 g) were placed into a 50 mL round-bottomed flask fit with a condenser under a positive pressure of nitrogen. The weight ratio of **6** used in the formation of each elastomer was determined to ensure that an excess of PEG was used during the functionalization process; elastomer **IIIA** contained 13% **6** by mass (0.03 g, 0.06 mmol). Chloroform (20 mL) and excess **9b** (0.11 g, 0.05 mmol) were added to the flask and the elastomers were refluxed with stirring for 24 h. The rubbers swelled to several times their original volume. Purification was carried out by Soxhlet extraction using DCM for 24 h. The elastomers were dried in a glass Petri dish at 50 °C for several days yielding slightly opaque, whitish elastomers that had shrunk back to their original size. This procedure was repeated using **IIIB – IIIE** with **9b** as well as with **IIIA-IIIE** modified with **9b** using a 3 x molar excess. The resultant modified elastomers were characterized using IR and contact angle measurements; **IIID-9b** was characterized by $^{1}$H NMR (**Figure 4**A).

Elastomers **IIIC** were also functionalized with **9a** via 3 different methods in poor solvents for silicones. **IIIC** (1 disk) and **9a** (300 mg) were placed in a vial with 0.5 mL of distilled water and stir bar. The rubber-PEG mixture was stirred at

60 °C for 72 h then purified by a Soxhlet extraction with methanol for 24 h. The rubber was then placed in a glass Petri dish to air dry at room temperature for 30 min. This process was also repeated with fresh **IIIC** elastomers at room temperature as well as in neat **9a** at 60 °C. After extraction and air drying the rubbers were characterized by static contact angle measurements (Table 2.2).

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# Chapter 3:
# Multifunctional Amphiphilic Siloxane Architectures Using Sequential, Metal-Free Click Ligations[†]

## 3.1 Abstract

Polysiloxanes or silicones are a class of macromolecules widely used in commerce because of their exceptional properties. Their derivatization leads to functional silicones with added value and properties, such as surfactants and liquid crystals, amongst many others. However, most silicone surfactants are mono-functional, due to the synthetic challenges associated with the introduction of multiple functional groups onto the hydrolytically-sensitive siloxane backbone. Thus, general routes to surface-active silicones with multiple and different functional groups are not available. Herein, a synthetic strategy is reported that permits sequential derivatization of silicones with hydrophiles including oligo(ethylene oxides), carboxylic acids and bromoalkylesters using a simple metal-free Click reaction: the process benefits from mild conditions, extremely

[†] This chapter is reproduced from Talena Rambarran, Ferdinand Gonzaga, Michael A. Brook, in the Journal of Polymer Science Part A: Polymer Chemistry, 2013, 51, 855-864 with permission from Wiley, Copyright 2013 Wiley Periodicals, Inc., A Wiley Company. Rambarran designed the experimental procedure with assistance from Dr. Gonzaga. Rambarran performed most of the experiments (with the exception of the synthesis of PEG propiolates which Dr. Gonzaga made), and Dr. Gonzaga helped troubleshoot experiments. Rambarran and Dr. Gonzaga wrote the the manuscript with additions, edits and guidance provided by Dr. Brook.

high yields and does not generate any by-products, allowing the facile preparation of di- and tri-functional silicones that could not be readily obtained using traditional methods. The products exhibit amphiphilic characteristics as demonstrated through interfacial tension measurements that yielded the critical aggregation concentration of selected compounds.

**3.2 Introduction**

The development of (multi)functional soft materials, and particularly of (multi)functional polymers, precisely engineered in term of architecture, reactivity, functionality, solubility and polarity, has attracted considerable interest due to their application in nanotechnology and their contribution to industrial and academic research related to health or energy issues.[1] The synthesis of such macromolecules presents multiple challenges, including the number, type, variety and/or density of functional groups, limitations of available purification techniques, solubility of hydrophilic/hydrophobic partners in a single solvent, and so on.[2,3] In order to address these difficulties, efficient organic transformations, such as the copper(I)-catalyzed 1,3-dipolar cycloaddition of azides and alkynes, known as Click chemistry,[4,5,6] have been developed. Near quantitative yield, regiospecific conversion, and compatibility with a broad range of functional groups (orthogonality) has made this process an ideal tool for the construction of block copolymers[7], dendrimers[8,9] and the coupling of telechelic polymers prepared by ATRP[10], but also for the quantitative derivatization of linear polymer chain termini[11,12], backbones[13,14,15,16], and dendrimers[17]. Multiple Click-

functionalizations using a simultaneous strategy or a cascade strategy have been previously described.[3] In the simultaneous strategy, a polymer backbone having multiple copies of different functional groups undergoes distinct and independent reactions to yield, in a single step, a new polyfunctional polymer. In the cascade strategy, a monofunctional polymer backbone undergoes multiple reactions, in a single step but at different reactive sites using two sets of complimentary molecules, the linker and the terminator.

Some polymer backbones are inherently labile, which prevents the use of particular reagents and/or modification strategies and thus impairs functionalization. Polysiloxanes, or silicones, in particular, are sensitive to acid- and base-catalyzed redistribution (leading to depolymerization via the formation of small cyclic monomers) and other degradation reactions.[18] Thus, functional silicones are generally prepared through hydrosilylation, the platinum-catalyzed addition of hydrosilanes to unsaturated carbon-carbon bonds,[19] or through modification of functional silicones obtained initially via hydrosilylation (such as amino-, hydroxy- and epoxy-silicones). However, the process suffers from limitations such as the use of expensive metal catalysts (and the issues associated with removal and potential leaching from final products[20]) and the restriction to organic solvents (which often involves tedious protection-deprotection steps for polar reagents): finding a common solvent makes it particularly challenging to prepare amphiphilic silicones due to the large differences in polarities between hydrophilic moieties and very hydrophobic silicones. Additionally,

hydrosilylation reactions are usually performed with an excess of alkene (or alkyne) to ensure the complete conversion of reactive hydrosilanes and prevent their further hydrolysis and condensation. It is often not possible to remove excess reagents after the reaction. These procedures do not allow sequential derivatization of silicones with different functional moieties, and thus restrict the ability to prepare polyfunctional silicones using sequential reactions. Last but not least, side reactions such as dehydrogenative coupling (e.g., between hydridosilane and silanols, generating hydrogen gas) result in the loss of polymer backbone integrity and sometimes to crosslinking[21] in the case of modifications of poly(methylhydro)siloxanes. For all these reasons, there are very few examples of polyfunctional silicones, particularly when compared to the tremendous progress achieved in the synthesis of their carbon analogs.

It was reasoned that the Click synthetic strategies, extremely mild and efficient, would be highly valuable for the modification of polysiloxanes. Conventional (copper-catalyzed) Click strategies have been applied to silicone derivatization: an initial report by Fleury *et al.* showed that copper-catalyzed Click chemistry allows the coupling of low-molecular weight saccharides to mono- or difunctional silicones in a homogenous reaction medium,[22] while Rieger *et al.* used CuAAC to prepare thermoplastic silicone elastomers.[23] The approach was further improved, showing that by using electron-deficient alkynes (that are activated towards the Huisgen 1,3-dipolar cycloaddition, and thus able to react with azides at low or room temperature) and polyazido-siloxanes, it was possible to synthesize complex

peptide- or carbohydrate-based silicone polymers[24], cross-link elastomers at mild or even room temperature[25], and functionalize silicone elastomers without the need of any metal catalyst[26,27].

In this report, it is demonstrated that metal-free, azide to alkyne cycloadditions performed at low temperatures – even at room temperature – allow the sequential, multiple functionalization of silicone polymers with different small molecules or polymers of various hydrophilicity to yield multifunctional amphiphilic architectures. The strength of the methodology described relies on two crucial synthetic advantages. First, the efficiency of the mild, uncatalyzed cycloaddition permits complete and quantitative ligation of the starting building blocks in stoichiometric or near stoichiometric conditions, as demonstrated in a first part. Second, it is shown that, using lower than stoichiometric alkyne-to-azide ratios, the reaction occurs efficiently without affecting the residual azides. These remaining azides can be used for additional metal-free ligation, in a sequential way, to obtain di- or even tri-functional polysiloxanes. The proposed strategy is simple, high yielding, does not generate any by-products and eliminates the need to remove any metal catalyst from the reaction products, making it suitable for a wide range of potential (bio)applications.

## 3.3 Experimental

### 3.3.1 Materials

(Chloropropyl)methylsiloxane-dimethylsiloxane copolymer (MW: 7,500-10,000 $g.mol^{-1}$; 14-16 mol % (chloropropyl)methyl-siloxane) was obtained from Gelest.

Propiolic acid (95%), monomethoxy poly(ethylene oxide) (av. mol. wt: 2000), monomethoxy poly(ethylene oxide) (av. mol. wt: 750), monomethoxy poly(ethylene oxide) (av. mol. wt: 350), acetylene dicarboxylic acid (**5**; 95%), sodium azide (99.5%), (dimethylamino)pyridine (DMAP, 99%) and tetra-*n*-butylammonium azide were obtained from Sigma-Aldrich. All materials were used as received.

### 3.3.2 Instrumentation

IR analyses were performed on a Bio-Rad infrared spectrometer (FTS-40). $^{1}H$ and $^{13}C$ NMR were recorded at room temperature on a Bruker AV600 spectrometer (at 600 and 150 MHz, respectively), using deuterated solvents ($CDCl_3$, $CD_3OD$). Contact angles and CMC's were measured on a Kruss DSA Contact Angle Apparatus using 18.1 mΩ·cm water. GPC analyses were performed on a Waters Alliance GPC System using tetrahydrofuran as the eluent and calibrated with a polystyrene calibration kit S-M-10 (Lot 85) from Polymer Laboratories. Differential scanning calorimetry was carried out on a General V4.1C DuPont 2100 apparatus with a heating rate of 15.0 °C/min.

### 3.3.4 Synthesis

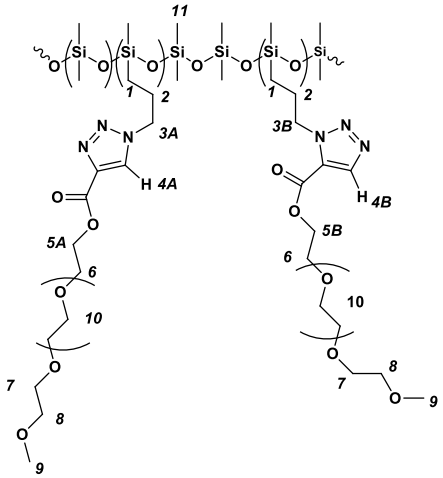
Poly(azidopropylmethyl)-co-(dimethylsiloxane) **1** was prepared as previously described.[27] $^{1}H$ NMR spectroscopy was used to determine the average molecular of a repeating unit: for every azidopropyl chain (with a characteristic triplet at 3.23 ppm corresponding to the methylene unit in α to the azido group), 33.53 protons were integrated for the methylsiloxane moieties, corresponding to an

average molecular weight of 503.5 g $mol^{-1}$ per repeating unit. The molecular weight was determined using GPC (Daltons): $M_n$ = 8000, $M_w$ = 13760, PDI = 1.72. IR (KBr $cm^{-1}$): 2962, 2097 (asym. stretch azide), 1261, 1089, 800.

Mono-propiolate-terminated PEG **2** (MW 385, estimated by $^1$H NMR), **3** (MW 840, estimated by $^1$H NMR), and **4** (MW 2140, estimated by $^1$H NMR), were prepared according to a previously described procedure. [28] Bis(bromopropyl)acetylene dicarboxylate **6** was prepared as previously described.[29]

***Synthesis of mono-functional PEG silicones 7, 8 and 9***

A representative procedure for the synthesis of silicone amphiphiles **7**, **8** and **9**, in which all azido groups were reacted with the same propiolate-terminated PEG, is illustrated below for the synthesis of **7**: polymers **1** (0.311g, 0.62mmol) and **2** (0.252g, 0.65mmol, 1.06 eq.) were weighed into a vial followed by the addition of $CHCl_3$ (0.5mL). The mixture was heated at 55 °C with stirring for 48 h, at which time the reaction was found to be complete by $^1$H NMR. Solvents were removed *in vacuo* to yield 0.563g (quantitative) of **2** as a viscous oil. The same procedure was used for the synthesis of **8** (quant.) and **9** (quant.; reaction required additional 24 h), using monopropiolate-terminated PEGs **3** and **4**, respectively.



**7 (**1,4 isomer (A), 1,5 isomer (B)): $^{1}$H NMR ($CDCl_3$, 600 MHz) δ: 0.06 (s, 33.5 H, SiC*H*$_3$, *11*), 0.48-0.51 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.90-1.97 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.37 (s, 3H, -OC*H*$_3$, *9*), 3.54 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.63-3.65 (m, 19H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.66-3.68 (m, 2H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.82 (m, 2H, -COOCH$_2$C*H*$_2$-, *6*), 4.36,4.66 (m, 2H, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.43, 4.48 (2H, -COOCH$_2$ -, *5A, 5B*), 8.08 to 8.13 (multiple singlets, 1H, *H*CCCOO, *4A, 4B*).; $^{13}$C NMR ($CDCl_3$, 150 MHz, δ): -0.42, 0.92, 1.18, 1.42, 1.92, 14.32, 24.44, 31.06, 53.27, 59.16, 64.20, 65.39, 68.90, 69.08, 70.71, 72.07, 127.58, 139.87, 160.85; IR (KBr) *v* = 3128, 2961, 2877, 2110, 1734, 1541, 1456, 1349, 1261, 1226, 1198, 1097, 1043, 1023, 951, 803 cm$^{-1}$; GPC (Daltons): $M_n$ = 4970, $M_w$ = 6520, PDI=1.31. Contact angle of a thin film on glass: 15° (after 60s).

***Synthesis of di-functional PEG silicones 10, 11 and 12***

A representative procedure for the synthesis of silicone amphiphiles **10**, **11** and **12**, in which all azido groups were simultaneously reacted with a mixture of two different propiolate-terminated PEGs *in a one-pot process*, is illustrated below by the synthesis of **10** (using a 1:0.53:0.53 of **1**:**2**:**3**): polymer **1** (0.252g, 0.5mmol of functional repeating unit), monopropiolate-terminated PEG **2** (0.102g, 0.265mmol, 0.53 equiv.) and monopropiolate-terminated PEG **3** (0.222g, 0.265mmol, 0.53 equiv.) were weighed into a vial followed by the addition of the minimal amount of $CHCl_3$ to obtain a clear solution (approximately 1.5mL). The mixture was heated at 55 °C with stirring for 48 h, at which time the reaction was found to be complete by $^{1}$H NMR. Solvents were removed *in vacuo* to yield

0.576g (quantitative) of **10** as a highly viscous yellow oil. The same procedure was used for the synthesis of **11** (quant.) and **12** (quant.), using (molar) stoichiometric ratios of 1:0.53:0.53 for **1**:**2**:**4** and **1**:**3**:**4**, respectively.

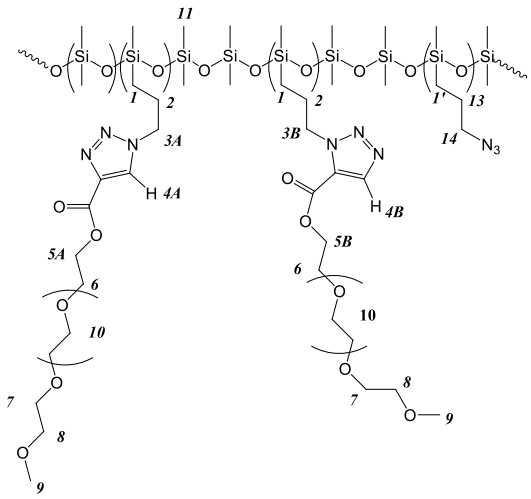
*Major 1,4 isomer (A ~ 80%, see structure above), Minor 1,5 isomer (B ~20%, see structure above)*

**10**: $^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.04-0.08 (m, 33.5 H, SiC*H*$_3$, *11*), 0.47-0.50 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.93-1.97 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.36 (s, 3H, -OC*H*$_3$, *9*), 3.53 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.59-3.64 (m, 43H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.66-3.68 (m, 2H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.81 (m, 2H, -COOCH$_2$C*H*$_2$-, *6*), 4.37,4.67 (m, 2H, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.43, 4.48 (2H, -COOCH$_2$-, *5A, 5B*), 8.06 to 8.15 (multiple singlets, 1H, *H*CCCOO, *4A, 4B*).; $^{13}$C NMR ($CDCl_3$, 150 MHz, δ): -0.45, 0.89, 0.99, 1.15, 1.90, 14.27, 24.40, 53.24, 59.14, 64.16, 64.68, 65.34, 68.65, 68.86, 69.03, 70.42, 70.67, 72.03, 127.53, 127.71, 138.11, 139.82, 160.81; IR (KBr) $v$ = 3520 (hygroscopic compound), 3126, 2959, 2868, 2107, 1946, 1732, 1652, 1538, 1458, 1349, 1260, 1197, 1099, 1025, 952, 852, 805, 700 cm$^{-1}$.

***Synthesis of 50% (PEG or diacid)-functionalized poly(azidopropylmethyl)-co-(dimethylsiloxane) 13, 14, 15 and 16***

A representative procedure for the synthesis of silicone amphiphiles **13** - **16**, in which only 50% of the azide moieties are used for Click ligation, is illustrated by the synthesis of **13**: in a glass scintillation vial were introduced **1** (0.252g, 0.5 mmol of repeating unit), **2** (0.096g, 0.25mmol) and the minimal amount of $CDCl_3$ to obtain a clear solution (*ca*. 1mL). The mixture was heated at 55 °C with

stirring for 36 h, at which time the reaction was found to be complete by $^1$H NMR. Solvents were removed *in vacuo* to yield 0.348g (quantitative) of **13** as a viscous pale oil. The same procedure was used for the synthesis of **14**, **15** and **16**, using alkynes **3**, **4** and **5** respectively, in lieu of **2**. For **16**, the reaction was performed in a small amount of diethyl ether (in which the diacid is extremely soluble) at room temperature for 48 h.



**13** *Major 1,4-isomer (A ~80%), Minor 1 5-isomer (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz) δ: 0.05 to 0.09 (s, 33.5H, SiC*H*$_3$, *11*), 0.47-0.51 (m, 1H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.53-0.59 (m, 1H, C*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.61-1.67 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.91-1.99 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 3.22 (t , *J*=6.0 Hz, 1H, C*H*$_2$N$_3$, *14*), 3.37 (s, 1.5H, -OCH$_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, C*H*$_2$OCH$_3$, *8*), 3.64-3.65 (m, ~10H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.68 (m, 1H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.79-3.84 (m, 1H, -COOCH$_2$C*H*$_2$, *6*), 4.35,4.66 (m, 1Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45, 4.48 (1Htotal, -COOC*H*$_2$ -, *5A, 5B*), 8.07-8.15 (multiple singlets, 0.5H, *H*CCCOO, *4A, 4B*). $^{13}$C NMR ($CDCl_3$, 150 MHz) δ: -0.41, 0.91, 1.01, 1.17, 1.91, 14.32, 14.63, 22.90, 24.44, 53.28, 54.26, 59.16, 64.21, 69.08, 70.71, 72.08, 127.54, 139.86, 160.84; IR (KBr) *v* = 3126, 2959,

2903, 2873, 2099, 1735, 1724, 1449, 1410, 1346, 1260, 1097, 1016, 852, 800, 703 $cm^{-1}$; GPC (Daltons): $M_n$ = 6500, $M_w$ = 8630, PDI = 1.32.

***Synthesis of di-functional PDMS (50% acetylene dicarboxylic acid/50% PEG) 17, 18, and 19***

A representative procedure for the synthesis of bi-functional silicone amphiphiles **17** - **19** is illustrated by the synthesis of **17**: in a glass scintillation vial were introduced **13** (0.348g, 0.25 mmol of remaining azide moieties), **5** (0.030g, 0.265mmol, 1.06 equiv.) and the minimal amount of $CDCl_3/Et_2O$ to obtain a clear solution (*ca*. 1mL). The mixture was heated at 35 °C in an open vial for 12 h, and for 24 h at 55 °C, at which time the reaction reached completion, as determined by $^1$H NMR. Solvents were removed *in vacuo* to yield 0.378g (quantitative) of **17** as a transparent gel-like material. The same procedure was used for the synthesis of **18** using **14** as the starting azide (pale yellow gel; quantitative yield). **19** was prepared using **16** as the starting azide, dissolved in 1 mL $CDCl_3$, to which was added 1.06 equiv. of alkyne **2** (relative to the remaining 50% azide groups) in a minimum of diethyl ether. The mixture was heated at 35 °C in an open vial for 12 h, and for 24 h at 55 °C, at which time the reaction had reached completion, as determined by $^1$H NMR, to yield **19** quantitatively (**19** and **17** being isostructural, their identical spectroscopic characterizations are given below).

**17 (and 19)**: $^1$H NMR ($CDCl_3$ + $CD_3OD$, 600 MHz) δ: -0.01 (s, 33.5H, SiC$H_3$), 0.44 (m, 2H, SiC$H_2$$CH_2$$CH_2$triazole), 1.88 (m, 2H, $CH_2$C$H_2$$CH_2$triazole), 3.30 (s, 1.5H, -OC$H_3$), 3.47 (1H, PEG chain overlapping $CD_3OH$), 3.61-3.68 (m, 12H,

PEG chain), 3.75 (br. s, 1H, PEG chain), 4.325,4.61 (2 br. s, 1Htotal (0.8 and 0.2), $SiCH_2CH_2CH_2$triazole PEG), 4.41 (br. s, 1H, -$COOCH_2$), 4.74 (br. s, 1H, $SiCH_2CH_2CH_2$triazole diacid), 8.04-8.21 (multiple singlets, 0.5H, *H*CCCOO); $^{13}C$ NMR ($CDCl_3$, 150 MHz) δ: -1.69, -0.62, 0.65, 0.77, 0.98, 1.20, 1.70, 13.76, 14.16, 24.27, 53.22, 53.99, 58.90, 64.12, 68.74, 68.91, 70.10, 70.47, 75.31, 127.71, 130.83, 139.52, 160.74; IR (KBr) $\nu$ = 3439, 3131, 2959, 2904, 2881, 2496, 1940, 130, 1635, 1546, 1455, 1410, 1346, 1263, 1202, 1105, 1016, 852, 800, 700 $cm^{-1}$.

***Synthesis of tri-functional silicone using sequential Click ligations***

The syntheses of tri-functional silicones **21** and **22** were performed using the methodology previously described for mono- or difunctional silicones: polyazide **1** (0.126g, 0.25mmol of repeating unit) and PEG **4** (0.134g, 0.0625mmol, 0.25 equiv.) were dissolved in a scintillation vial with the minimum amount of $CDCl_3$ and the solution was heated at 55 °C until completion (between 24 and 36 h) to obtain the di-functional silicone **20** (0.260g; quantitative). Aliquots were used for characterization by NMR. The 2$^{nd}$ Click ligation was performed directly, in the same vial, by adding alkyne **6** (0.022g, 0.0625mmol, 0.25equiv.) and 0.5mL of $CDCl_3$, and the solution was heated at 55 °C for 48 h, to yield **21** (0.282g; quant.). The third Click ligation was performed by adding alkyne **5** (0.015g, 0.1325mmol, 1.06 equiv. relative to the 0.125mmol of azide left) in a minimum of diethyl ether at 35 °C for 6 h in the open vial followed by 24 h at 55 °C to yield the tri-functional silicone **22** (0.297g; quantitative).

**20**: *Major 1,4-isomer (A ~ 80%), Minor 1,5-isomer (B ~20%):* $^{1}$H NMR ($CDCl_3$, 600 MHz) δ: 0.04 to 0.11 (m, 33.5H, SiC*H*$_3$, *11*), 0.49-0.52 (m, 0.5H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.54-0.57 (m, 1.5H, SiC*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.62-1.66 (m, 1.5H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.90-1.99 (m, 0.5H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 3.22 (m, 1.5H, C*H*$_2$N$_3$, *14*), 3.38 (s, 0.75H, -OCH$_3$, *9*), 3.55 (t, *J*=6.0 Hz, 0.5H, C*H*$_2$OCH$_3$, *8*), 3.60-3.69 (m, ~47H, -OC*H*$_2$C*H*$_2$O-, 7, *10*), 3.80-3.83 (m, 0.5H, -COOCH$_2$C*H*$_2$, *6*), 4.37 and 4.66 (m, 0.5Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45 and 4.50 (m, 0.5Htotal, -COOC*H*$_2$, *5A, 5B*), 8.06-8.15 (multiple singlets, 0.25H, *H*CCCOO, *4A, 4B*). $^{13}$C NMR ($CDCl_3$, 150 MHz) δ: —0.55, -0.42, 0.90, 1.02, 1.17, 1.41, 1.91, 14.31, 14.63, 22.89, 24.43, 53.27, 54.25, 59.18, 64.20, 68.90, 70.70, 72.07, 127.53, 138.23, 160.84; IR (KBr) 3423 (hygroscopic compound), 2962, 2901, 2870, 2096, 1732, 1643, 1455, 1346, 1299, 1260, 1099, 1016, 952, 847, 802 cm$^{-1}$.

**21**: $^{1}$H NMR ($CDCl_3$, 600 MHz) δ: 0.02 to 0.08 (m, 33.5H, SiC*H*$_3$, *11*), 0.47-0.54 (m, 2H, SiC*H*$_2$CH$_2$CH$_2$, *1 and 1'*), 1.60-1.63 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.90-1.96 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 2.27-2.32 (m, 1H, COOCH$_2$C*H*$_2$CH$_2$Br), 3.22 (m, 1H, C*H*$_2$N$_3$, *14*), 3.35 (s, 0.75H, -OCH$_3$, *9*), 3.50-3.55 (m, 1.5H, COOCH$_2$CH$_2$C*H*$_2$Br and C*H*$_2$OCH$_3$, *8*), 3.62-3.68 (m, ~47H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.78-3.83 (m, 0.5H, -COOCH$_2$C*H*$_2$, *6*), 4.35 and 4.66 (m, 1Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.43 and 4.47-4.55 (m, 1.5Htotal, -COOC*H*$_2$-, *5A, 5B* and COOC*H*$_2$CH$_2$CH$_2$Br ), 8.06-8.15 (multiple singlets, 0.25H, *H*CCCOO, *4A, 4B*); $^{13}$C NMR ($CDCl_3$, 150 MHz) δ: -0.55, -0.47, 0.84, 0.96, 1.12, 1.36, 1.86,

14.31, 14.57, 22.84, 24.38, 29.14, 29.27, 31.31, 31.65, 53.20, 54.20, 59.11, 63.57, 64.41, 64.68, 68.85, 69.02, 70.66, 72.02, 127.47, 129.65, 139.82, 139.92, 158.43, 160.20, 160.79; IR (KBr) 3525, 2962, 289, 2740, 2695, 2243, 2096, 1952, 1738, 1638, 1555, 1460, 1416, 1358, 1341, 1283, 1260, 1199, 1147, 1113, 1019, 963, 919, 841, 805, 733cm$^{-1}$.

**22**: 0.03 to 0.06 (m, 33.5H, SiC*H*$_3$, *11*), 0.45-0.51 (m, 2H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 1.88-1.94 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 2.25-2.30 (m, 1H, CH$_2$C*H*$_2$CH$_2$Br), 3.34 (s, 0.75H, -OCH$_3$, *9*), 3.47-3.52 (m, 1.5H, COOCH$_2$CH$_2$C*H*$_2$Br and C*H*$_2$OCH$_3$, *8*), 3.60-3.68 (m, ~47H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.78-3.83 (m, 0.5H, -COOCH$_2$C*H*$_2$, *6*), 4.35 and 4.66 (m, 1Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.43 and 4.46-4.55 (m, 1.5Htotal, -COOC*H*$_2$ -, *5A, 5B* and COOC*H*$_2$CH$_2$CH$_2$Br), 4.79 to 4.81 (m, 1H, SiCH$_2$CH$_2$C*H*$_2$triazole from acetylene dicarboxylate alkyne), 8.06-8.15 (multiple singlets, 0.25H, *H*CCCOO,*4A, 4B*); $^{13}$C NMR ($CDCl_3$, 150 MHz) δ: -1.57, -0.76, -0.61, -0.54, 0.80, 0.88, 1.06, 1.31, 1.81, 13.81, 14.08, 14.24, 14.51, 22.79, 24.26, 29.10, 29.27, 31.25, 31.55, 53.21, 54.13, 59.02, 61.54, 63.59, 64.12, 64.48, 64.63, 68.59, 68.78, 68.98, 69.77, 70.20, 70.55, 71.93, 72.68, 75.42, 127.59, 128.01, 129.69, 130.85, 138.49, 139.67, 139.81, 152.96, 156.54, 158.35, 160.12, 160.75, 166.79; IR (KBr) 3437, 2962, 2904, 280, 2745, 2493, 1949, 17732, 1635, 1549, 1466, 1410, 1355, 1260, 1205, 1097, 1013, 955, 852, 808, 700cm$^{-1}$.

### 3.4 Results and Discussion

Before undertaking the synthesis of multifunctional silicone amphiphiles using sequential metal-free Click chemistry, it was necessary to ensure that two crucial conditions were fulfilled: first, the metal-free cycloaddition could be performed at moderate temperatures, in stoichiometric or near stoichiometric conditions, and afford the coupling products in high yields and second, that any residual azides would not be affected by the process and thus remain available for secondary reactions. This hypothesis was tested by performing the reaction between poly(azidopropylmethyl)-co-(dimethylsiloxane) **1** and several activated alkynes whose structures are summarized in Chart 3.1. The first tests were performed with monopropiolate-terminated PEG of various molecular weights (**2**, **3** and **4**), to give graft-PEG silicones **7**, **8** and **9**, respectively, as shown in Scheme 3.1.

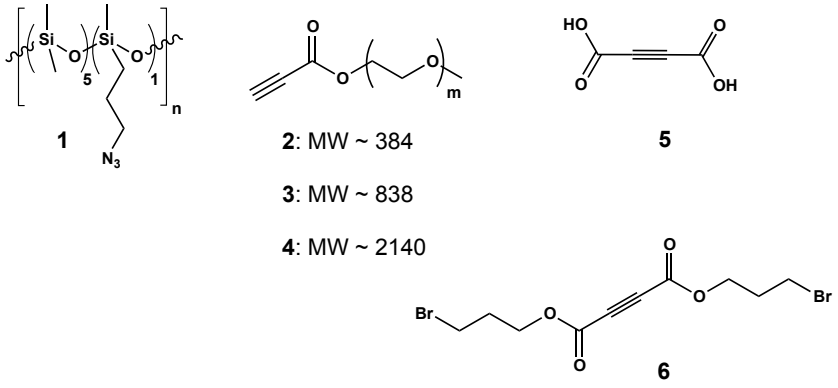
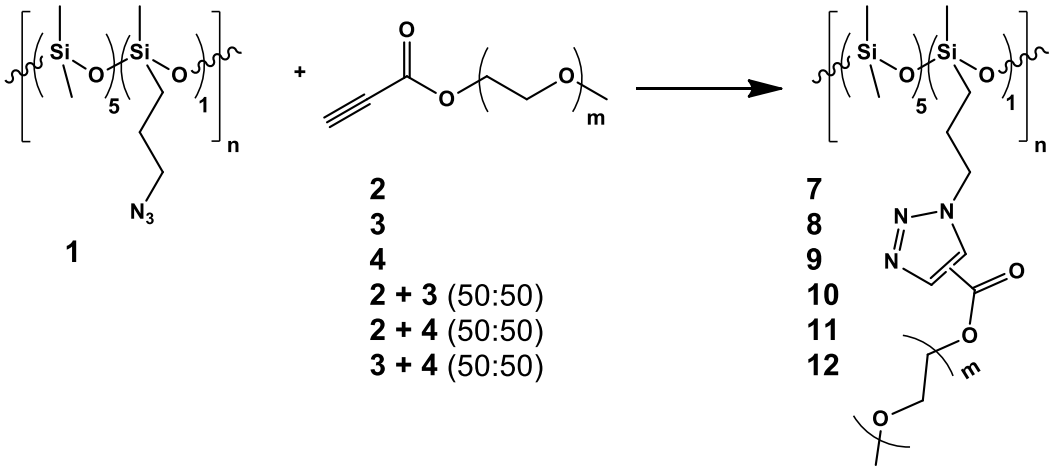



Chart 3.1: Summary of polysiloxane azide (**1**) and activated alkynes (**2**-**6**) used in the study.

A summary of the mono- and poly-functional silicones that were prepared is given in Table 3.1. The reactions were performed under ambient conditions (in

air), at 55 °C in glass vials. Considering that the molecular weights of the different reagents were estimated by proton NMR, it was decided to use 1.06 equivalents of (readily removable) alkyne per azido group (assuming a ±3% uncertainty during integration of each reagent). A minimum amount of solvent ($CDCl_3$) was used to homogenize the reagents mixture, allowing for reaction monitoring using proton NMR.




Scheme 3.1: Synthesis of mono- and di-functional PEG silicones using metal-free Click chemistry.

The results were very promising; under the described conditions, reaction completion was reached in 48 hours for the click reaction of **1** with **2** or **3**, while the reaction of **1** and **4** (the highest molecular weight PEG-alkyne) required 72 hours. Several signals in the NMR were indicative of a complete reaction: the multiplet at 1.64 ppm (methylene β to the azido moiety in the starting polyazide) totally disappeared, and was replaced by a multiplet at 1.94 ppm; and, complete disappearance of the triplet corresponding to the methylene group in α of the

Table 3.1: Summary of mono- and poly-functional silicones prepared, their composition and the synthetic methodology involved in their preparation.

| Entry | Azide | Alkyne(s) | Product number | Stoichiometry (azide: alkyne) | Type of silicone (functional groups) | Process |
|---|---|---|---|---|---|---|
| 1 | **1** | **2** | **7** | 1 : 1 | Monofunctional (PEG **2**) | Single |
| 2 | **1** | **3** | **8** | 1 : 1 | Monofunctional (PEG **3**) | Single |
| 3 | **1** | **4** | **9** | 1 : 1 | Monofunctional (PEG **4**) | Single |
| 4 | **1** | **2 + 3** | **10** | 1: 0.5 : 0.5 | Difunctional (PEGs **2** and **3**) | Single |
| 5 | **1** | **2 + 4** | **11** | 1: 0.5 : 0.5 | Difunctional (PEGs **2** and **4**) | Single |
| 6 | **1** | **3 + 4** | **12** | 1: 0.5 : 0.5 | Difunctional (PEGs **3** and **4**) | Single |
| 7 | **1** | **2** | **13** | 1: 0.5 | Difunctional (azide and PEG **2**) | Sequential |
| 8 | **1** | **3** | **14** | 1: 0.5 | Difunctional (azide and PEG **3**) | Sequential |
| 9 | **1** | **4** | **15** | 1: 0.5 | Difunctional (azide and PEG **4**) | Sequential |
| 10 | **1** | **5** | **16** | 1 : 0.5 | Difunctional (azide and diacid) | Sequential |
| 11 | **13** | **5** | **17** | 1: 0.5: 0.5 | Difunctional (PEG **2** and diacid) | Sequential |
| 12 | **14** | **5** | **18** | 1: 0.5: 0.5 | Difunctional (PEG **3** and diacid) | Sequential |
| 13 | **16** | **2** | **19 (=17)** | 1: 0.5: 0.5 | Difunctional (diacid and PEG **2**) | Sequential |
| 14 | **1** | **4** | **20** | 1: 0.25 | Difunctional (azide and PEG **4**) | Sequential |
| 15 | **20** | **6** | **21** | 1:0.25:0.25 | Trifunctional (azide, PEG **4**, dibromo) | Sequential |
| 16 | **21** | **5** | **22** | 1:0.25:0.25:0.5 | Trifunctional (PEG **4**, dibromo, diacid) | Sequential |

azido moiety (at 3.23ppm) was observed. Evidence of the formation of the triazole ring came from the new signals corresponding to the new aromatic protons of the triazole (multiple singlets between 8.07 and 8.12 ppm; the two potential isomers, corresponding to the 1,4- and 1,5-isomers, were formed in a ~4:1 ratio; see Supporting Information for full spectra); new signals corresponding to the methylene units α to the formed triazole rings (4.36 and 4.66ppm); and the presence of the peaks at 127.58 and 139.87ppm corresponding to the 2 carbons in the triazole ring indicate a successful cycloaddition. Additionally, complete conversion was confirmed by IR spectroscopy: the IR spectrum of polyazide **1** displayed an intense signal at 2097$cm^{-1}$ corresponding to the asymmetric stretch of the azide moiety. After reaction, analysis of the products confirmed complete disappearance of the azide stretch, and the presence of the carbonyl stretch from the grafted propiolate-PEGs (Figure 3.1). These results clearly demonstrate that metal-free click reactions between alkylazidosilicones and monopropiolate-terminated PEG occur quantitatively under mild conditions to yield silicone-graft-PEG surfactants.

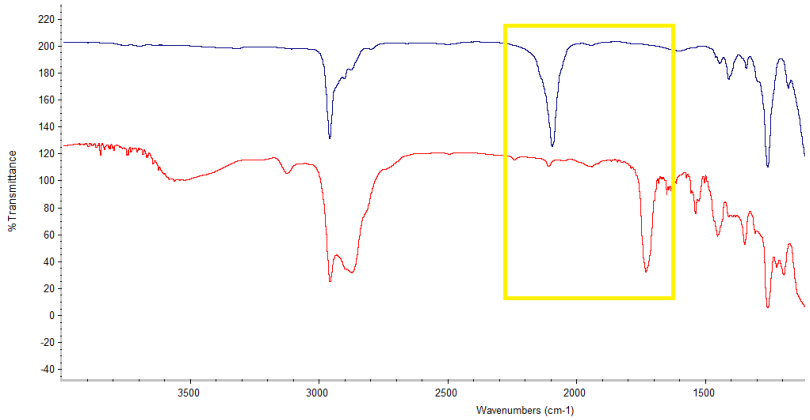



Figure 3.1: Offset IR spectra of 1 (top) and 7 (bottom), highlighting in the box the disappearance of the azide stretch at 2097 $cm^{-1}$ and the appearance of the carbonyl stretch at ~1735 $cm^{-1}$.

Using the same methodology, amphiphilic silicones bearing two types of PEG, varying in their chain length, were also obtained quantitatively: surfactants **10**, **11** and **12** result from the ligation of polyazide **1** with equimolar amounts of **2** and **3**, **2** and **4**, and **3** and **4**, respectively (see Table 3.1 for a complete listing of the prepared samples). The ability to synthesize such PEG-based silicone surfactants, without the need for a metal-catalyst, under mild experimental conditions and in stoichiometric ratios is highly valuable, as these amphiphilic silicones are known to have remarkable surface-activity properties.[30] Superwetters, for example (commonly used to disperse agricultural chemicals on leaves), represent a class of silicone-PEG surfactants unmatched by their aliphatic counterparts.[31] This new synthetic route allows facile access to PEG-silicone surfactants, and permits the hydrophilic/hydrophobic ratio to be tailored simply by manipulating the molecular weight and ratios of different PEG chains.

The second challenge, necessary for sequential functionalization of silicones using metal-free Click chemistry, was to demonstrate that azide groups were

preserved when the reactions were performed away from stoichiometric ratios (i.e., when the alkyne reagent was in deficit compared to the azide). To test this hypothesis, the metal-free Click reaction between PDMS-azide **1** and the same 3 monopropiolate-terminated PEGs **2**, **3** and **4** were performed, and also with acetylene dicarboxylic acid **5** using a stoichiometry of 2:1 (in other words, using 0.5 equivalent of alkyne compared to the azide) to give the corresponding polysiloxanes **13** (50% PEG-385), **14** (50% PEG-840), **15** (50% PEG-2140) and **16** (50% acetylene dicarboxylic acid), respectively (see Table 3.1). Under the previously described conditions, the reaction was complete in 24 hours: the integration of the proton NMR clearly indicates that 50% of the azide groups were successfully converted into triazole rings. The signals characteristic of the triazole rings, for example, corresponding to the methylene α to the triazole rings were observed, however, while the triplet corresponding to the methylene α to the azide groups was still present its intensity was reduced by 50%. IR spectroscopy fully confirmed that the integrity of the remaining, unreacted azide groups were preserved: the intense characteristic band at 2097cm$^{-1}$ was still present, signifying that unreacted azide groups were not affected by the first Click reaction, and were thus available for subsequent derivatization. Another very interesting feature is that identical results were obtained when the Click reaction was performed at room temperature: despite longer reaction times (48 to 120 hours depending on the PEG-alkyne molecular weight), the procedure yielded the corresponding amphiphilic silicones bearing 50% of remaining azide groups.

The remaining azide groups of polymers were then reacted with a different alkyne than the one used in the first Click reaction, to yield difunctional polysiloxane amphiphiles. The residual azides of **13** and **14** were reacted with acetylene dicarboxylic acid **5** to give **17** and **18**, respectively. Polymer **16** (functionalized with 50% acetylene-dicarboxylic acid) was reacted with **2** to give **19**. Polymer **19**, with 50% of the azide groups clicked to PEG **2** and 50% clicked to acetylene dicarboxylic acid **5**, is isostructural with polymer **17**: the only difference relies in the order in which the two Click reactions were performed (PEG first for **17**, diacid first for **19**). Reactions were performed at 35 °C then 55 °C in a minimal amount of $CDCl_3$ and diethyl ether (used for the initial solubilization of diacid **5**) for 48 hours to reach completion. Successful and complete ligations were demonstrated by analysis of $^1H$ NMR and IR spectra: the triplet at 3.23ppm corresponding to the α-methylene group to the azide moieties completely vanishes, as well as the characteristic signature of the azido group at $2097cm^{-1}$.

The flexibility of the described synthetic route is worth mentioning. Compounds **17** and **19**, two isostructural silicone amphiphiles who present identical NMR and IR, could be obtained by thermally grafting the PEG chain or the diacid first, at the will of the experimentalist. This provides additional synthetic flexibility as, for example, the carboxylic acid could be esterified or amidified with biologically relevant molecules, prior to or after PEGylation (or the grafting of another biological tag, for example). Due to the versatility of Click reactions, the possibility to perform sequential, independent Click ligation on the same substrate

and in any desired order opens up new opportunities for the synthesis of multifunctional silicones.

Supplementary characterizations were performed on the amphiphilic PEG-silicones. First, the molecular weight changes of the polymers were investigated using Gel Permeation Chromatography (GPC) as a function of increasing numbers of grafted PEG chains onto the starting polyazide. The results are summarized in Table 3.2.

Table 3.2: Gel Permeation Chromatography analysis of **1** and clicked amphiphilic silicones **7** and **13**.

| Entry | Polymer | $M_n$ [a] | $M_w$ [a] |
|---|---|---|---|
| 1 | **1** | 8000 | 13760 |
| 2 | **7** | 4970 | 6520 |
| 3 | **13** | 6500 | 8630 |

[a] From GPC.

The starting polysiloxane-azide **1** has a $M_n$ of 8000 and $M_w$ of 13,760 Daltons and a polydispersity index (PDI) of 1.72. As alkynyl PEG **2** was clicked onto the backbone, one would expect to see an increase in molecular mass. Counterintuitively, $M_n$ and $M_w$ obtained from the GPC data decreased with the addition of PEG: when reacting 50% of azido groups to form **13** both $M_n$ and $M_w$ values decreased (6500 and 8630 Daltons, respectively). This effect was even more pronounced when all the azide groups were clicked with PEG, as shown in the GPC analysis of polymer **7** ($M_n$ and $M_w$ of 4970 and 6520 Daltons, respectively). Considering that both $^{1}H$ and $^{13}C$ NMR and IR spectroscopies

confirmed the successful ligation of the PEG chains to the siloxane backbone, such results were initially surprising. However, such phenomena (i.e., the large difference between the additive calculated values and the ones determined by GPC) have been previously described for graft-PEG silicones prepared using hydrosilylation, with either $CHCl_3$ or toluene as eluant.[32,33] Increased PEG chain lengths elicited a similar behavior: as the PEG chains increased in length, the apparent molecular weights determined by GPC decreased. Since the same phenomenon is observed in solvents that can efficiently solvate both the silicone backbone and the PEG grafts (chloroform) or solvents that are better for just the backbone (toluene, and THF in our case), the possibility of a more coiled polymer due to the insolubility of the PEG grafts seems unlikely. As this phenomenon was also observed for other amphiphilic copolymers, it was postulated that the possible absorption of polar segments on the packing material in the analytical columns could be responsible of the discrepancies between the GPC results and the calculated values.[34,35]

The amphiphilicities of the PEG-graft polymers **7**, **8** and **9** were established by measuring contact angles of thin films of polymers **7-9** that were prepared on glass slides by dissolving the polymer in small amounts of dichloromethane and allowing slow evaporation of the solutions. The procedure yielded smooth, ~1 mm thick polymer films. Figure 3.2 displays the decrease in contact angle over time for the 100% PEG grafted copolymers. Silicones are strongly hydrophobic, and typically present contact angle values higher than 100°.[36] The grafting of PEG

chains onto the siloxane backbone strongly affects their wettability: more highly wettable structures were associated with the shorter PEG chain, with an immediate drop to CA values to a plateau at 27°, a behavior analogous to silicone superwetters.[30] With the intermediate PEG chain length, the decrease in CA was slower, with a value of 33° at 1 minute, indicating a slower reorganization of the hydrophilic moieties at the surface due to increased length. Finally, with the highest molecular weight PEG on PDMS, an extremely slow decrease in CA value was observed, from 56° to 52° after 1 minute, due to the solid nature of the longer PEG chains. The solid nature of the product is demonstrated by the higher melting point of PDMS-g-PEG with increased PEG length; **7**, **8** and **9** have melting points of 39.8 ºC, 41.9 ºC and 50.5 ºC, respectively, as determined by DSC.

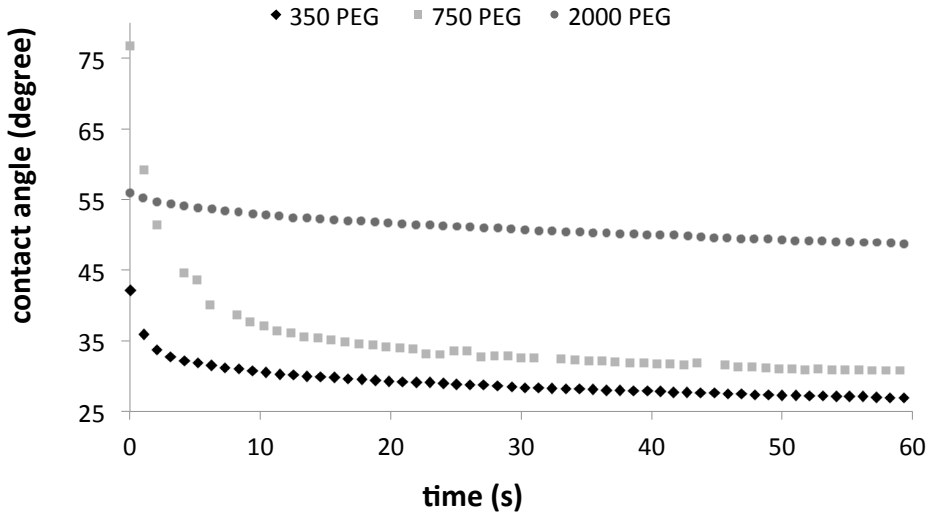



Figure 3.2: Evolution of contact angles with time for thin films of PEG-Silicones 7 (100% grafted PEG 2), 8 (100% grafted PEG 3) and 9 (100% grafted PEG 4).

The process of time dependent surface reorganization to increase surface wettability has been demonstrated for many polymer systems. Silicones are known to undergo surface reversion: even highly wettable surfaces revert to hydrophobic surfaces once water is removed,[37] but can recover to a degree when re-exposed to water. The magnitude of the change described above is higher than other silicones with which we have previously worked. Wong et al.[38] observed surface reorganization on poly(styrene) to reveal hydrophilic carboxylic acid ends upon exposure to water vapor. Similarly Horinouchi et al.[39] demonstrated increased wettability of poly(methylmethacrylate) surfaces due to surface rearrangement when in contact with water, which was attributed to the changing orientation of carbonyl moieties.

Another property expected from amphiphilic PEG-graft-silicones is the ability to self-assemble in water, or micellize. The Critical Micelle Concentration (CMC) was measured for polymers **9** and **15** (100% and 50% of azides clicked with PEG **4**). Plots of surface tension versus concentrations are shown in Figure 3.3. The CMC values were found to be 0.18 weight % for **9**, and 0.067% weight % for **15**. As expected, keeping constant the hydrophilic moiety (PEG **4**), the CMC decreased (in wt %) with an increase of the hydrophobic moiety. These results demonstrate that Click ligations are an effective and easy route to prepare PEG-silicone surfactants, and that the method is versatile enough to fine-tune the amount of PEG chains introduced to control amphiphilicity and aggregation behavior.

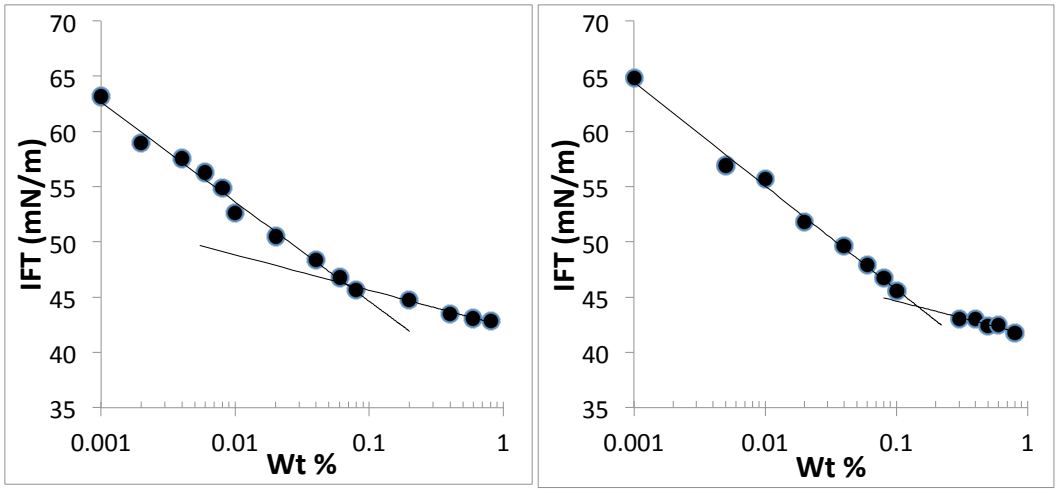


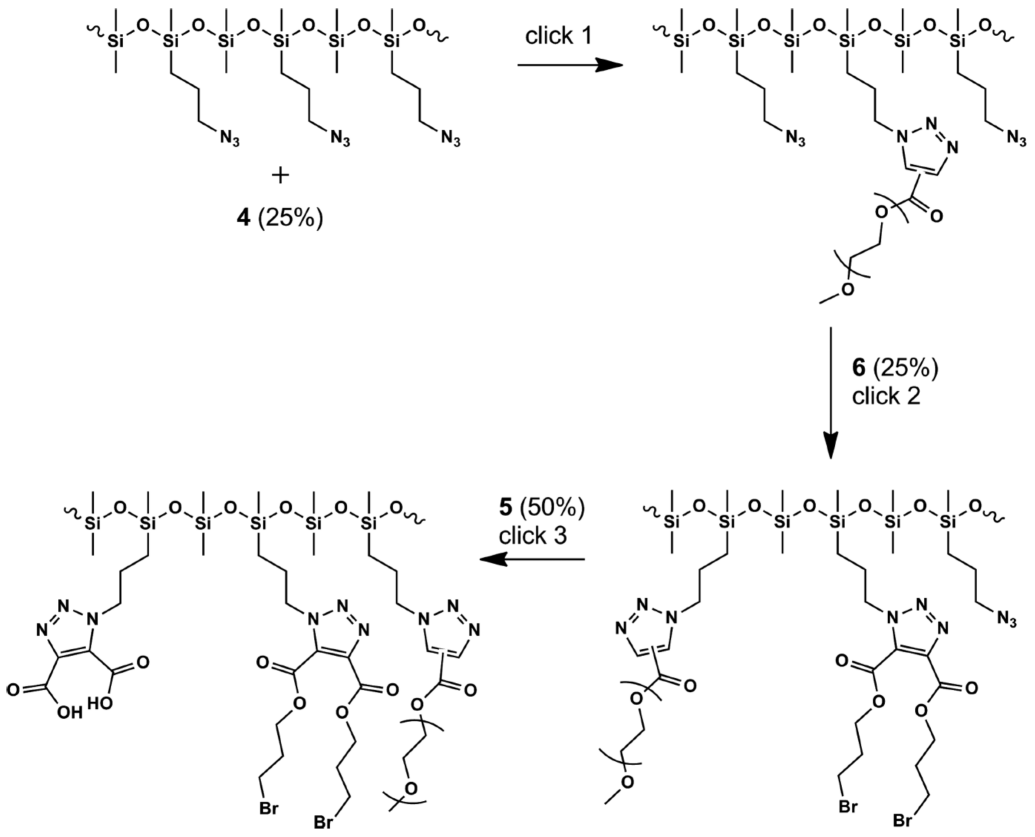

Figure 3.3: Plots of interfacial tension versus concentration for surfactants **9** (100% grafted PEG **4**; left) and **15** (50% grafted PEG **4**; right).

Finally, to further demonstrate the efficiency and versatility of the sequential Click strategy, a tri-functional silicone bearing PEG, bromo-alkyl and carboxylic acid functionalities was assembled, as illustrated in Scheme 3.2. In the first Click reaction 25% of the available azide groups in **1** were reacted with PEG **4** to yield polymer **20**: after one day at 55 °C, the reaction was found to be complete.

Proton and carbon NMR confirmed the successful ligation as observed previously with the 100% and 50% samples (polymers **9** and **15**, respectively). The only difference could be seen in the integration of the signals by NMR: a new set of peaks in the $^{1}$H NMR appears, arising from the protons in positions α and β of the triazole ring, and their relative integration agrees with a 1:3 ratio compared to the same protons in positions α and β of the unreacted azido moieties. Additionally, the corresponding peaks in position α to the triazole ring are visible, along with the proton on the triazole ring itself. The changes in the $^{1}$H NMR spectra following sequential metal-free Click ligations are shown in Figure 3.4. In a

second step, bis(bromopropyl)acetylene dicarboxylate **6** was clicked onto a fraction of the remaining azide groups of polymer **20**, at 55 °C: this led quantitatively to the trifunctional polymer (bromo-alkyl, PEG and azide) **21** in quantitative yield.

Proton NMR shows the appearance of new methylene group α to the newly formed triazole rings, while the integration of the methylene α to the azido moiety decreased by the same amount. Additionally, 3 sets of signals corresponding to the bromopropyl moieties are clearly distinguishable in the $^{1}$H NMR, integrating for 1 proton each (4 protons according to the formula, multiplied by a factor 0.25 due to the 25% relative stoichiometry; see Figure 3.4). In the carbon NMR, the different carbons of the 2 sets of triazole (127.47, 129.65, 139.82 and 139.92ppm), and the different carbonyls from the 2 different esters (propiolate and acetylene dicarboxylate), are easily differentiated (158.43, 160.20 and 160.79ppm). In the 3$^{rd}$ sequential Click reaction, the remaining azido moieties were reacted with acetylene dicarboxylic acid **5** in a mixture diethyl ether/chloroform to yield the tri-functional amphiphilic silicone **22**. Figure 3.4 clearly shows the total disappearance of the methylene protons in position α of the azido moieties (now all reacted) and the corresponding new signals from the methylene group in α of the new triazole rings, substituted with 2 carboxylic acid functionalities (at 4.8ppm; Figure 3.4, signal d3').




Scheme 3.2: Synthesis of a tri-functional polysiloxane using sequential metal-free Click ligation

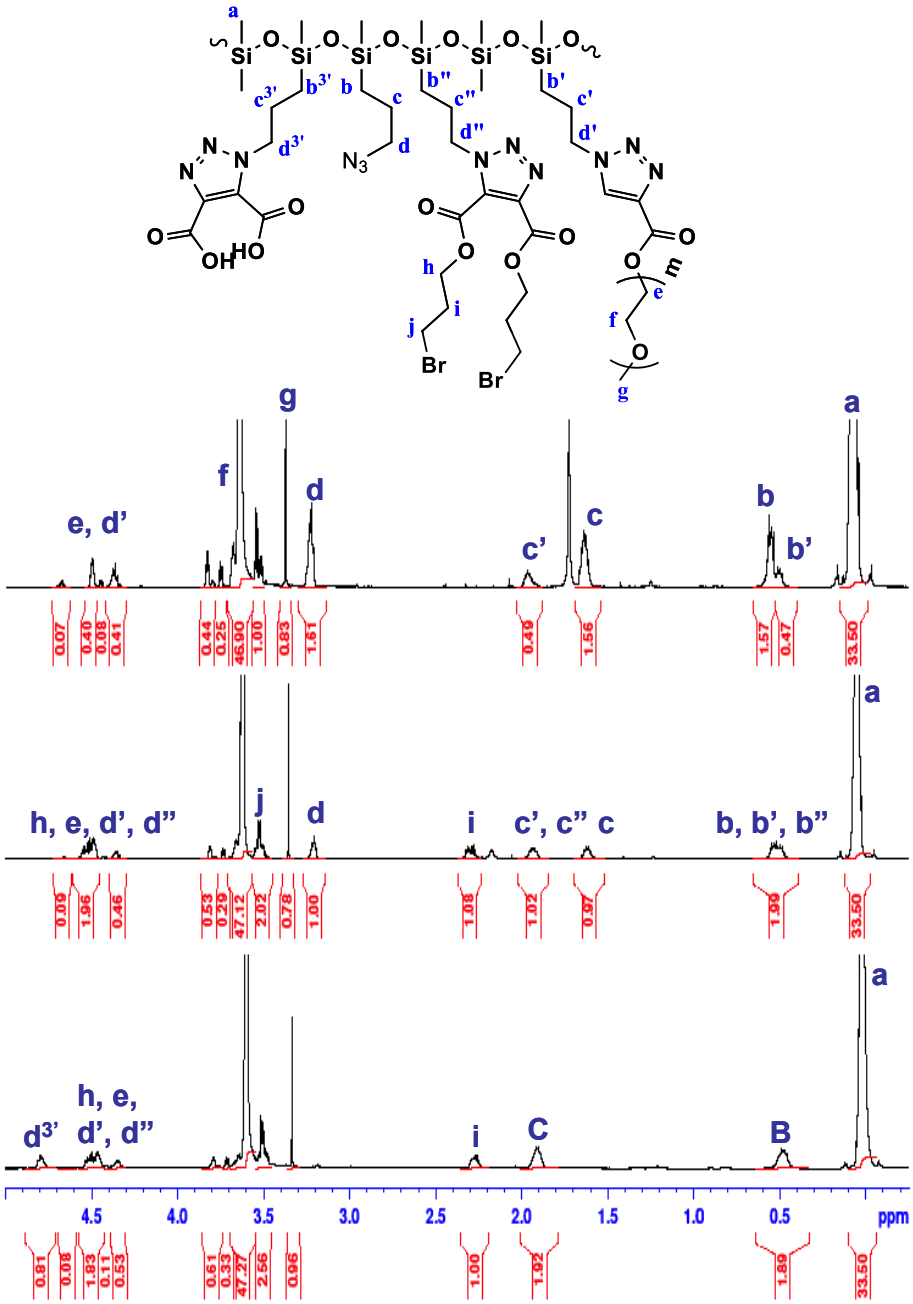



Figure 3.4: Evolution of NMR spectra upon sequential, tri-functionalization of polyazide 1 with 25% (molar) of PEG 4 (top spectrum; polymer 20), 25% PEG 4 and 25% dibromoacetylene dicarboxylate 6 (middle spectrum; polymer 21), and 25% PEG 4, 25% 6 and 50% acetylene dicarboxylic acid 5 (bottom spectrum; polymer 22).

Traditional routes to functional silicones typically involve hydrosilylation, with its attendant disadvantages. By contrast, metal-free Click chemistry provides a more flexible synthetic route. A broader number of functional groups are tolerated; the reactions are straightforward to perform and, under the mild thermal conditions used, the azides do not appear to undergo any undesired side reactions – any residual azides can be capped by small molecules or used for crosslinking or other purposes.[27] Thus, the degree and type of functionalization is up to the researcher, as shown by the three sequential reactions that lead to compound **22** without the need for protecting groups.

### 3.5 Conclusions

A synthetic strategy that permits sequential derivatization of silicones with different hydrophilic entities using a simple metal-free Click reaction was presented. The methodology presented overcomes synthetic challenges associated with preparing polyfunctional silicones and yields control over the sequence of functionalization to the experimentalist. The ability to synthesize such PEG-based silicone surfactants, without the need for a metal-catalyst and in stoichiometric ratios is highly valuable, as these amphiphilic silicones are known to have interesting surface-activity properties. The process benefits from mild conditions, extremely high yields and does not generate any by-products, allowing the facile preparation of di- and tri-functional silicones that could not be obtained using traditional methods.

### 3.6 Acknowledgments

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# Chapter 4:
# Amphiphilic Thermoset Elastomers from Metal-Free, Click Crosslinking of PEG-Grafted Silicone Surfactant[⊥]

## 4.1 Abstract

The hydrophobicity of silicone elastomers can compromise their utility in some biomaterials applications. Few effective processes exist to introduce hydrophilic groups onto a polysiloxane backbone and subsequently crosslink the material into elastomers. This problem can be overcome through the utilization of metal-free click reactions between azidoalkylsilicones and alkynyl-modified silicones and/or PEGs to both functionalize and crosslink silicone elastomers. Alkynyl-functional PEG was clicked onto a fraction of the available azido groups of a functional polysiloxane, yielding azido reactive PDMS-g-PEG rake surfactants. The reactive polymers were then used to crosslink alkynyl-terminated PDMS of different molecular weights. Using simple starting materials, this generic yet versatile method permits the preparation and characterization of a library of amphiphilic

[⊥] This chapter is reproduced from Talena Rambarran, Ferdinand Gonzaga, Michael A. Brook, Frances Laowski and Heather Sheardown in the Journal of Polymer Science Part A: Polymer Chemistry, 2015, 53, 1082-1093 with permission from Wiley, Copyright 2015 Wiley Periodicals, Inc., A Wiley Company. Rambarran designed the experimental procedure with assistance from Dr. Gonzaga. Rambarran synthesized all of the starting materials and elastomers (with the exception of the synthesis of the two higher molecular weight PEG propiolates which Dr. Gonzaga made). Lasowski performed the protein adhesion study and wrote the portion of experimental and results corresponding to the protein work. Rambarran performed all other characterization and wrote the the manuscript with additions, edits and guidance provided by Dr. Brook.

thermoset elastomers that vary in their composition, crosslink density, elasticity, hydrogel formation, and wettability. An appropriate balance of PEG length and crosslink density leads to a permanently highly wettable silicone elastomer that demonstrated very low levels of protein adsorption.

**4.2 Introduction**

Polysiloxanes (PDMS) are a class of materials that find use in an extensive range of applications, including microfluidic devices[1] and biomaterials,[2] due to their broad range of desirable properties including high gas permeability, high flexibility, optical transparency, very low toxicity, high thermal stability, and moldability.[3] However, the high hydrophobicity of silicones can limit their use in biomaterials applications. For example, significant lipid and protein adsorption[3,4,5] onto hydrophobic surfaces can be problematic in the eye;[6] in the most serious cases, extensive biofouling can lead to ocular diseases.

Numerous strategies to modify the surface of silicones to yield improved wettability have been reported. In some cases, strong chemical treatments can cause oxidative surface damage that can lead to reduced biocompatibility.[7,8,9,10] Alternative strategies utilize surface passivation by a variety of hydrophilic polymers, notably poly(ethylene glycol)(PEG).[11] Irrespective of the process used to render silicones hydrophilic, the surfaces generally suffer from hydrophobic recovery (an initially hydrophilic surface becomes hydrophobic over time). Amphiphilic copolymer networks, in which both the surface and the interior of the siloxane network possess enhanced hydrophilicity, represent a new class of

promising materials for a range of applications,[12,13] including in biomaterials applications: [14,15,16,17] the silicone hydrogels used in contact lenses fall into this category.

The incorporation of dangling PEG chains into a silicone network to improve water wettability has been reported; however, the procedures for their preparation generally require dry reagents and inert conditions, [18] and/or leave potentially harmful metal catalysts trapped within the material.[19,20] For example, the copper-catalyzed azide-alkyne 1,3-dipolar cycloaddition, known as 'click' chemistry (CuAAC),[21,22,23,24] has been utilized in a wide variety of applications, including the functionalization of polymeric materials[25] and the synthesis of amphiphilic hydrogels.[26] This highly efficient process that leads to a variety of interesting materials is catalyzed by Cu(I) salts, the toxicity of which can be a drawback for biological applications. Despite the excellent safety record of the silicone elastomers used as biomaterials, concerns have been raised when metallic catalyst residues (tin-, copper- or platinum-based) remain in the materials.

Alternative metal-free 'click' strategies have been employed for biological or polymer functionalization, notably the creative use of ring strained alkynes.[27,28] Recently, it has been shown that the Huisgen[29] 1,3-dipolar cycloaddition of azides to alkynes ('click' chemistry) can be used to thermally functionalize and crosslink silicones, without the use of a catalyst, at low temperatures and without generating any by-products.[30] This strategy was used to create thermoset elastomers (referred to as elastomers hereafter) containing excess reactive groups

(azido- or alkynyl-) that could subsequently graft hydrophilic macromolecules and polymers (such as alkynyl-PEG) to create a more hydrophilic elastomer surface.[31] It was also demonstrated that alkynyl-PEG could be grafted onto an azido-functional PDMS backbone using the metal-free strategy at less than stoichiometric ratios, preserving reactive groups for controlled sequential functionalization.[32]

Herein, we report an extension of the metal-free methodology for the preparation of amphiphilic silicone-PEG networks that involves first creating PDMS-g-PEG surfactants containing reactive azido groups that can subsequently be used to crosslink alkyne-terminated PDMS. We reasoned that grafting PEG chains throughout the entire elastomer network would increase the inherent wettability and, if appropriately formulated, could circumvent the possibility of hydrophobic recovery over time, as the material, a silicone hydrogel when water swollen, would ideally be homogenous throughout its entire body. The simple, versatile and efficient methodology allows control over a range of experimental parameters, including the molecular weight of PEG, the graft density, the PDMS molecular weight and, subsequently, the crosslink density and ability to form a hydrogel.

## 4.3 Experimental

### 4.3.1 Materials

(Chloropropyl)methylsiloxane-dimethylsiloxane copolymer (14-16 mol % (chloropropyl)methylsiloxanes, MW 7,500-10,000 $g \cdot mol^{-1}$, trimethylsiloxy-

terminated), octamethylcyclotetrasiloxane ($D_4$), and 1,3-bis(hydroxybutyl)tetramethyldisiloxane were obtained from Gelest. Propiolic acid (95%), monomethoxy poly(ethylene oxide) (av. mol. wt: 2000), monomethoxy poly(ethylene oxide) (av. mol. wt: 750), monomethoxy poly(ethylene oxide) (av. mol. wt: 350), poly(ethylene oxide) (av. mol. wt: 400), propiolic acid (95%), sodium azide (99.5%), (dimethylamino)pyridine (DMAP, 99%) and tetra-*n*-butylammonium azide were obtained from Sigma-Aldrich. All materials were used as received.

### 4.3.2 Methods

IR analyses were performed on a Bio-Rad infrared spectrometer (FTS-40). $^{1}H$ and $^{13}C$ NMR spectra were recorded at room temperature on a Bruker AV600 spectrometer (at 600 and 150 MHz, respectively) or Bruker AC-200 spectrometer (at 200 MHz for $^{1}H$), using deuterated solvents ($CDCl_3$).

Contact angles were measured on a Kruss DSA 100 using 18.1 mΩ·cm water (Easypure® II, RF ultrapure water system). Samples were submerged in deionized water for 2 weeks prior to being measured and all measurements were performed in triplicate.

The % water uptake of the samples was measured after soaking in deionized water for 1 day and 14 days, respectively. Samples were placed in separate vials in 5 mL of deionized water for either 1 or 14 d and their masses were measured (wet mass – $m_w$). Each sample was then dried in vacuo for 24 h and the mass was

measured (dry mass – $m_d$). The % water uptake is defined as $(m_w-m_d)/m_d*100$. The reported values are the average of triplicate experiments.

Rheological measurements were undertaken using an ARES 4X733707T-CE using 7 mm parallel plates. Dynamic strain sweep experiments at frequency 1 Hz were performed for all samples to determine the linear dynamic range of the strain. Dynamic frequency sweep (stain controlled) experiments were performed for all samples in triplicate, using a strain in the linear dynamic range (1, 5 or 10).

Atomic force microscopy (AFM, Veeco Dimension Icon) was measured using Scan Asyst mode (the resonance frequency = 0.4 N/m and scanning frequency 2 Hz) with a silicon tip. The roughness factor ($R_Q$) was determined for an area of 5 x 5 $\mu m^2$.

The quantity of water soluble extractables was determined by placing pre-weighed samples ($m_i$) that had been dried (in vacuo for 24 h at 60 °C, 56 mmHg) into deionized water for 24 h. The elastomers were removed from the water/extracts and dried in vacuo (24 h at 60 °C, 56 mmHg) and the final mass was determined ($m_f$). The % aqueous extractables were calculated as: % extractable = $(m_i – m_f)/m_i *100$. All samples were measured in triplicate.

The quantity of organic soluble extractables was determined by placing pre-weighed samples ($m_i$) that had been dried (in vacuo for 24 h at 60 °C, 56 mmHg) into a sealed vial with dichloromethane for 24 h. The elastomers were removed from the DCM/extracts and dried in vacuo (24 h at 60 °C, 56 mmHg) and the final

mass was determined ($m_f$). The % organic extractables were calculated as: % extractable = $(m_i - m_f)/m_i * 100$. All samples were measured in triplicate.

**4.3.3 General Synthesis**

A representative example of the synthesis is detailed below. Detailed experimental procedures for all of the polymers and materials, including an elastomer created with α,ω-propiolated PEG (Figure 4.1), are provided in the Supporting Information along with characterization; this includes images of the materials, storage modulus plots from rheological characterization, infrared spectra, quantity of aqueous and organic extractables, water uptake and an experimental section for the protein adhesion study.

***4.3.3.1 Azidoalkylsilicones***

Poly(azidopropylmethyl)-co-(dimethylsiloxane) **1** was prepared as previously described[31] starting from commercially available (chloropropyl)methylsiloxane-dimethylsiloxane copolymer. $^1$H NMR spectroscopy was used to determine the average molecular weight of a repeating unit: for every azido propyl chain (with a characteristic triplet at 3.23 ppm corresponding to the methylene unit in α of the azido group), 34.86 protons were integrated for the methylsiloxane moieties, corresponding to an average molecular weight of 537g·mol$^{-1}$ per repeating unit (i.e., $(Me(N_3(CH_2)_3)SiO)_1(Me_2SiO)_5$).

***4.3.3.2 α,ω-Silicone propiolates***

Propiolate-terminated disiloxane was synthesized from 1,3-bis(hydroxybutyl)tetramethyldisiloxane and propiolic acid according to the

previously published procedure of Rambarran et al.[31] Higher molecular weight propiolate-terminated PDMS was grown from the disiloxane (end groups) via acid-catalyzed equilibration using $D_4$ to yield propiolate-terminated polysiloxane **2** (MW of 3,600 g·mol$^{-1}$), **3** (MW 7,800 g·mol$^{-1}$) and **4** (MW of 16,200 g·mol$^{-1}$); MW was determined by $^1$H NMR.[31]

#### *4.3.3.3 PEG-monopropiolates*

PEG mono-propiolate **5** (MW of 406 g·mol$^{-1}$, determined by $^1$H NMR), **6** (MW of 813 g·mol$^{-1}$, determined by $^1$H NMR), and **7** (MW of 2060 g·mol$^{-1}$, determined by $^1$H NMR) were prepared from monomethoxy poly(ethylene oxide) according to a previously described procedure.[33]

***Synthesis of low molecular weight* 5 *PEG (406 g·mol$^{-1}$) -modified, functional silicones* 8, 9 *and* 10**

The syntheses of silicone amphiphiles **8**, **9** and **10** were carried out by reacting polymer **1** with propiolate-terminated PEG **5** in non-stoichiometric ratios such that 25, 50 or 75% (respectively for **8**, **9** and **10**) of the available azido groups were 'clicked', i.e., reacted with, PEG-monopropiolates. A representative procedure is illustrated below for the synthesis of **8**: polymers **1** (0.73 g, 1.36 mmol) and **5** (0.14 g, 0.34 mmol, 0.25 eq.) were placed into a vial followed by the addition of 1.5 mL of $CHCl_3$. The vial was sealed and the mixture was heated at 60 °C with stirring for 18 h, at which time the reaction was found to be complete by $^1$H NMR (0.87 g, quant.). The solvent was removed from the reaction by blowing a stream of nitrogen over the mixture.

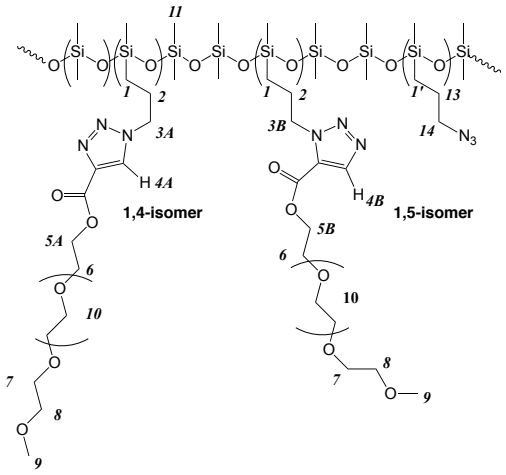
**1** (1.09 g, 2.03 mmol) and **5** (0.42 g, 1.03 mmol), homogenized with 4 mL of $CHCl_3$, were reacted to produce **9** (1.51 g, quant.).

**1** (1.62 g, 3.02 mmol) and **5** (0.92 g, 2.25 mmol), homogenized with 5 mL of $CHCl_3$, were reacted to produce **10** (quant.; reaction required additional 24 h).

**8***:* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, SiC*H*$_3$, *11*), 0.47-0.51 (m, 0.5H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.53-0.59 (m, 1.5H, C*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.61-1.67 (m, 1.5H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.91-1.99 (m, 0.5H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 1.5H, C*H*$_2$N$_3$, *14*), 3.37 (s, 0.75H, -OCH$_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, C*H*$_2$OCH$_3$, *8*), 3.64-3.65 (m, ~5H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.68 (m, 0.5H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.79-3.84 (m, 0.5H, -COOCH$_2$C*H*$_2$, *6*), 4.35,4.66 (m, 0.5H total, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45, 4.48 (0.5H total, -COOC*H*$_2$ -, *5A, 5B*), 8.07- 8.15 (multiple singlets, 0.25H, *H*CCCOO,*4A, 4B*).

**9:** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, SiC*H*$_3$, *11*), 0.47-0.51 (m, 1H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.53-0.59 (m, 1H, C*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.61-1.67 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.91-1.99 (m, 1H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 1H, C*H*$_2$N$_3$, *14*), 3.37 (s, 1.5H, -OCH$_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, C*H*$_2$OCH$_3$, *8*), 3.64-3.65 (m, ~10H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.68 (m, 1H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.79-3.84 (m, 1H, -COOCH$_2$C*H*$_2$, *6*), 4.35,4.66 (m, 1H total, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45, 4.48 (1H total, -COOC*H*$_2$ -, *5A, 5B*), 8.07-8.15 (multiple singlets, 0.5H, *H*CCCOO,*4A, 4B*).

**10:** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, SiC*H*$_3$, *11*), 0.47-0.51 (m, 1.5H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.53-0.59 (m, 0.5H, C*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.61-1.67 (m, 0.5H, SiCH$_2$C*H*$_2$CH$_2$N$_3$, *13*), 1.91-1.99 (m, 1.5H, SiCH$_2$C*H*$_2$CH$_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 0.5H, C*H*$_2$N$_3$, *14*), 3.37 (s, 2.25H, -OCH$_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1.5H, C*H*$_2$OCH$_3$, *8*), 3.64-3.65 (m, ~15H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.68 (m, 1.5H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.79-3.84 (m, 1.5H, -COOCH$_2$C*H*$_2$, *6*), 4.35,4.66 (m, 1.5H total, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45, 4.48 (1.5H total, -COOC*H*$_2$ -, *5A, 5B*), 8.07- 8.15 (multiple singlets, 0.75H, *H*CCCOO,*4A, 4B*).




***Medium molecular weight 6 PEG (PEG-800 g·mol$^{-1}$)-modified functional silicones* 11*,* 12 *and* 13 *and high molecular weight* 7 *PEG-modified (PEG 2060 g·mol$^{-1}$) functional silicone* 14**.

See Supporting Information for details.

***Synthesis of Elastomers* 15*,* 16*,* 17*: PEG 5 (400 g·mol$^{-1}$)-functional networks crosslinked with PDMS 3 (7,800 g·mol$^{-1}$)***

A representative procedure for the synthesis of PEG-functional PDMS networks **15-17** is illustrated by the synthesis of **15**. **8** (0.87 g, 0.34 mmol of alkynyl PEG, 1.02 mmol of azido groups) and **3** (3.98 g, 1.02 mmol of alkyne) were mixed with

5 mL toluene and stirred vigorously to homogenize the mixture. The mixture was poured into a 5 cm Pyrex Petri dish, covered and placed in a 55 °C oven for 18 h, at which time the rubber had cured. The temperature was increased to 90 °C for an additional hour to ensure that the rubber was adequately crosslinked, and then removed from the heat and allowed to cool. An analogous process was repeated reacting **9** and **10** with **3** to create elastomers **16** and **17**, respectively (amounts of the reagents used can be found in Table 4.1). The materials were characterized by Shore OO hardness, IR, and rheology; **15** and **16** were additionally characterized by water contact angle (Table 4.2) and swellability in water, (Figure 4.3 B).

***Synthesis of Elastomers* 18, 19, 20*: PEG* 5 *(400g·mol$^{-1}$)-functional networks crosslinked with PDMS* 4 *(16,200 g·mol$^{-1}$)***

See Supporting Information for details.

***Synthesis of Elastomers* 21*, 22*: *PEG* 6 *(800 g·mol$^{-1}$)-functional networks crosslinked with PDMS 3 (7800 g·mol$^{-1}$)***

See Supporting Information for details.

***Synthesis of Elastomers* 23*, 24 *PEG 6 (800 g·mol$^{-1}$)-functional networks crosslinked with PDMS 4 (16200 g·mol$^{-1}$)***

See Supporting Information for details.

***Synthesis of Elastomers* 25*, 26*, 27*: PEG 5 (400 g·mol$^{-1}$)-functional networks crosslinked with PDMS* 2 *(3600 g·mol$^{-1}$)***

A representative procedure for the synthesis of PEG and azide functional PDMS networks, **25-27**, is illustrated by the synthesis of **25**. **8** (1.94 g, 0.81 mmol of

alkynyl PEG, 2.19 mmol of azido groups) and **2** (2.02 g, 1.12 mmol of alkyne) were mixed with 2 mL of $CHCl_3$ and stirred vigorously to homogenize the mixture. The mixture was poured into a 5 cm Pyrex Petri dish, covered and placed in a 60 °C oven for 18 h. The temperature was increased to 90 °C for an additional hour to ensure that the rubber was fully cured and then removed from the heat and allowed to cool.

**26**: **9** (2.58 g, 1.76 mmol alkynyl PEG, 1.70 mmol azido groups) and **2** (1.55 g, 0.86 mmol) were mixed (6 mL $CHCl_3$) to produce elastomer **26** (4.13g).

**27**: **10** (3.38 g, 3.01 mmol alkynyl PEG, 1.00 mmol azido groups) and **2** (0.96 g, 0.53 mmol) were mixed (7 mL $CHCl_3$) to produce elastomer **27** (4.34 g).

A similar process was used to make rubber **28** from PEG **6** (813 $g \cdot mol^{-1}$) and PDMS **2** (3600 $g \cdot mol^{-1}$) and rubber **29** from PEG **7** (2060 $g \cdot mol^{-1}$) and PDMS **2** (3600 $g \cdot mol^{-1}$)

See Supporting Information for details.

### *Synthesis of α,ω-PEG propiolates,* **30**, *and example elastomer with α,ω-Silicone and α,ω-PEG propiolates,* **31**

See Supporting Information for details.

Table 4.1: Amounts of reagents used

| Azide **1** g: mmol per azide | PEG- g: mmol | Azide-PEG | Stoichio-metry (azide: PEG) | PDMS Alkyne- g: mmol per alkyne | Product number |
|---|---|---|---|---|---|
| 0.73: 1.36 | **5**-0.14: 0.34 | **8** | 1:0.25 | **3**-3.98: 1.02 | **15** |
| 1.09: 2.03 | **5**-0.42/1.03 | **9** | 1:0.5 | **3**-4.02: 1.03 | **16** |
| 1.62: 3.02 | **5**-0.92: 2.25 | **10** | 1:0.75 | **3**-2.99: 0.77 | **17** |
| 0.41: 0.76 | **5**-0.07: 0.17 | **8** | 1:0.25 | **4**-4.76: 0.59 | **18** |
| 0.54: 1.00 | **5**-0.20: 0.49 | **9** | 1:0.5 | **4**-4.00: 0.49 | **19** |
| 1.10: 2.05 | **5**-0.62: 1.52 | **10** | 1:0.75 | **4**-4.26: 0.53 | **20** |
| 0.68: 1.27 | **6**-0.25: 0.31 | **11** | 1:0.25 | **3**-3.76: 0.96 | **21** |
| 0.87: 1.62 | **6**-0.68: 0.84 | **12** | 1:0.5 | **3**-3.13: 0.80 | **22** |
| 0.37: 0.69 | **6**-0.14: 0.17 | **11** | 1:0.25 | **4**-3.94: 0.51 | **23** |
| 0.49: 0.91 | **6**-0.36: 0.44 | **12** | 1:0.5 | **4**-3.52: 0.47 | **24** |
| 1.61: 3.00 | **5**-0.33: 0.81 | **8** | 1:0.25 | **2**-2.02: 1.12 | **25** |
| 1.86: 3.46 | **5**-0.72: 1.76 | **9** | 1:0.5 | **2**-1.55: 0.86 | **26** |
| 2.15: 4.00 | **5**-1.23: 3.01 | **10** | 1:0.75 | **2**-0.96: 0.53 | **27** |
| 1.50: 3.03 | **6**-0.62: 0.76 | **11** | 1:0.25 | **2**-2.08: 1.15 | **28** |
| 1.21: 2.25 | **7**-1.27: 0.62 | **14** | 1:0.25 | **2**-1.71: 0.83 | **29** |

## 4.4 Results and Discussions

### 4.4.1 Starting Materials

Three distinct constituents were used to create PEG-modified silicone elastomers: pendant azidoalkylsilicones; dialkyne-terminated silicone chains; and monoalkyne-terminated PEG (Figure 4.1A). Polyfunctional poly(dimethylsiloxane)-co-(methyl(azidopropyl)siloxane) **1** was prepared from

commercially available starting materials according to the procedure by Rambarran et al.[31]; the average molecular weight of 537 g·mol$^{-1}$ per azide monomer unit was determined by $^1$H NMR (i.e., $(Me(N_3(CH_2)_3)SiO)_1(Me_2SiO)_5$). Alkyne (propiolate)-terminated PDMS was synthesized using activated esters in three different molecular weights as previously described[31]; **2** ($M_n$=3,600 g·mol$^{-1}$, 93% yield), **3** ($M_n$=7,800 g·mol$^{-1}$, 90% yield), and **4** ($M_n$=16,200 g·mol$^{-1}$, 88% yield) were obtained as colorless oils. Monoalkyne (propiolate)-functional PEG was also synthesized in three different molecular weights from commercially available starting materials as previously described;[33] the average molecular weights of **5** (408 g·mol$^{-1}$), **6** (813 g·mol$^{-1}$), and **7** (2060 g·mol$^{-1}$) were determined by $^1$H NMR using end group analysis. α,ω-Propiolate PEG was prepared following a modified method of Rambarran et al.[31]

**4.4.2 Pendant PEG-PDMS polymers**

The azide-functional silicones were first modified with monofunctional PEG to create reactive silicone-PEG graft copolymers (**8-14,** Figure 4.1B). Propiolate-functional PEGs of three different MW were attached onto the PDMS backbone in three different ratios, leaving residual reactive groups (Figure 4.1B).

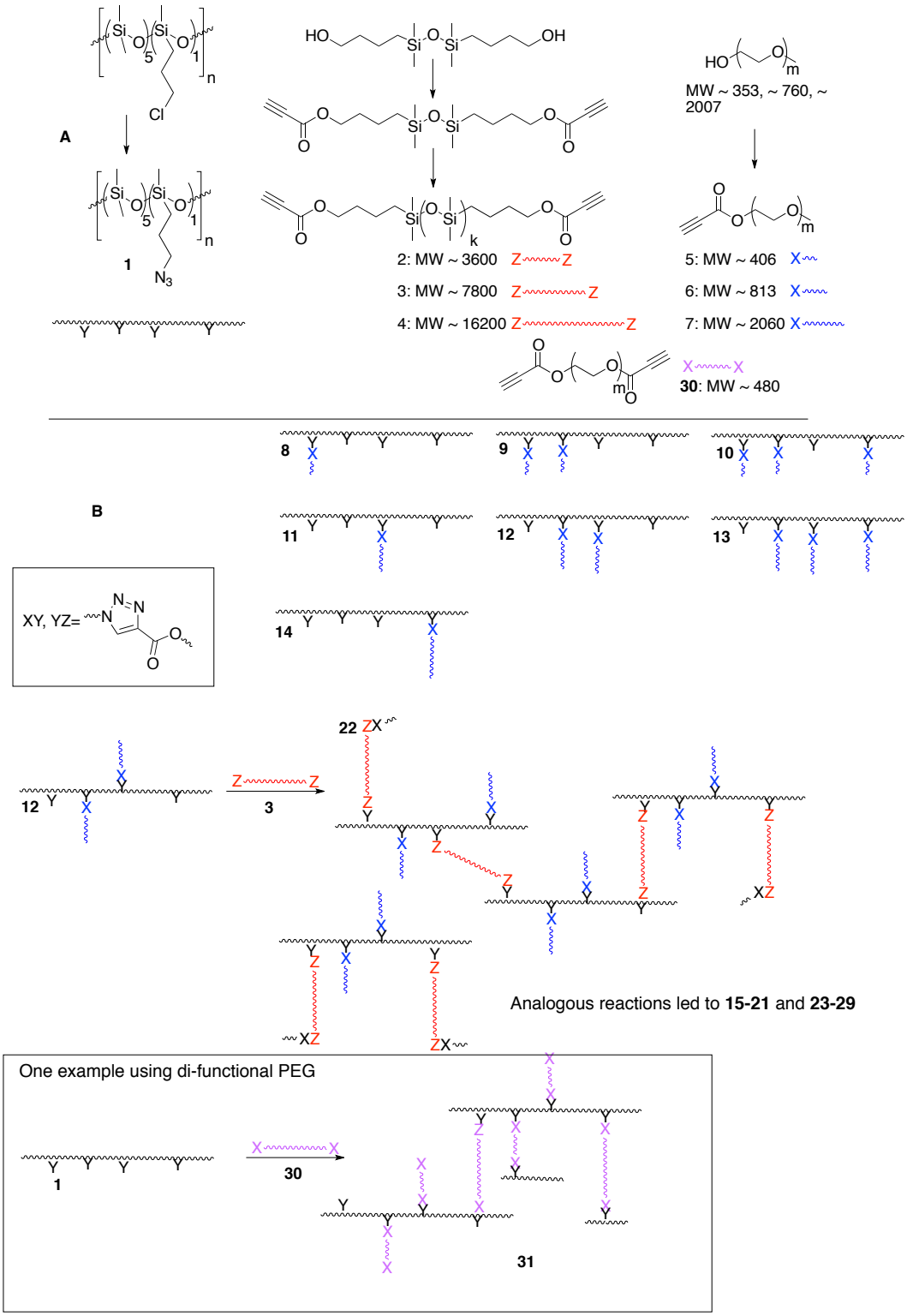



Figure 4.1: Functionalizing and crosslinking PEG-PDMS

For example, PEG monopropiolate, **5** (408 g·mol$^{-1}$) was grafted onto polymer **1** (azido-PDMS) at a 25, 50 or 75% molar equivalent of the available azido groups by mixing the appropriate amount of each reagent (see Supporting Information) with a small amount of solvent (chloroform or toluene) and heating them to 60 °C for 18 - 24 hours, at which time the reactions were found to be complete by $^{1}$H NMR, giving **8**, **9** or **10**. Analogous reactions were performed with longer PEG **6** (813 g·mol$^{-1}$), yielding polymers **11**, **12** or **13**. In these cases slightly longer reaction times (~12 hours) and additional solvent was required to homogenize the mixtures. (Note that in the absence of a small amount of solvent inconsistent and irreproducible mixing led to lower yields and more complex product mixtures). In a single example, **1** was functionalized with a 25% equivalent of the higher molecular weight PEG **7** (2060 g·mol$^{-1}$) in $CHCl_3$ and toluene at 60 °C for 24 h with stirring to yield polymer **14**. The products were pure (uncontaminated with reagent polymers) after removal of the solvent by evaporation: the thermal reaction between pendant azido groups on the reactive polysiloxane backbone and PEG occurred in near quantitative yields (Supporting Information).

This process constitutes a simple strategy to synthesize a variety of rake style silicone polyethers with differing molecular weights and PEG content. Such polymers are used in a variety of applications, including stabilization of polyurethane foams. The residual azide groups can be used in a subsequent Huisgen reaction for further functionalization. This was demonstrated in a previous investigation by modifying a polymer analogous to **11** with acetylene

dicarboxylic acid, where an examination of the surfactancy of these intermediates is reported.[32]

### 4.4.3 Amphiphilic silicone elastomers

The same synthetic strategy was used to create 15 amphiphilic thermoset elastomers that differed in composition and structure (**15-29**, Figure 4.1C). Shorter propiolate-terminated PDMS **3** (~8,000 g·mol$^{-1}$) was used to bridge crosslinkers **8**, **9** or **10** at a ratio sufficient to consume the available azido groups. The pre-polymer mixtures were homogenized with a small amount of $CHCl_3$ and/or toluene, cast in a glass Petri dish and allowed to cure in a 60 °C oven for 24 hours, followed by 1 hour at 90 °C to ensure complete cure, yielding **15**, **16**, or **17**, respectively. IR data confirmed the complete disappearance of the 2097 cm$^{-1}$ that arises from unreacted azide moieties (Supporting Information). Analogous elastomers were prepared from the reaction of **8**, **9** or **10** with higher molecular weight PDMS, **4** (~16,200 g·mol$^{-1}$) to yield elastomers **18**, **19**, or **20**, respectively. Polymers with medium molecular weight PEG side chains **11** or **12** (25 and 50% equiv. of PEG **6**, 813 g·mol$^{-1}$) were also crosslinked with an equivalent amount of **3** (~8,000 g·mol$^{-1}$) to yield **21** or **22**, or crosslinked with **4** (~16,200 g·mol$^{-1}$) to yield **23** or **24**, respectively. In a single example, an elastomer was formed from crosslinking **1** with a telechelic PEG with propiolate termini, **30**, using the same reaction conditions to create an elastomer, **31**.

It was also possible to prepare elastomers with residual reactive azide groups: shorter propiolate terminated PDMS **2** (~3,600 g·mol$^{-1}$) was used to bridge

crosslinkers. For example, compounds **8**, **9**, or **10** were homogenized in a small amount of solvent with **2** and thermally cured to produce elastomers **25**, **26** or **27**. In these elastomers approximately half of the remaining azide groups (i.e., 37.5, 25 and 12.5 % of the original amount, respectively) were used for crosslinking and the other half remained free in the network, as confirmed by ATR-IR. The resultant materials were transparent, easy to manipulate, firm, neither tacky nor brittle, and had smooth surfaces. This procedure was repeated by crosslinking the more PEG-rich **11** with **2** to give **28**. Because of the longer PEG chain, this material was softer and more water absorbent than its lower molecular weight PEG counterpart, **25**. Finally, one functional elastomer was prepared that contained nearly 30% PEG by weight by reacting **7** with PDMS **2** in a mixture of toluene and chloroform and allowing partial cure with stirring for several hours prior to the final cure in the oven (see next section). The resultant material was hard, somewhat brittle, opaque and waxy. A summary of the materials is contained in Table 4.2. Amounts of the reagents used and the IR spectra can be found in the Supporting Information. As previously shown, the networks can be further functionalized by performing a Huisgen reaction with either the surface bound or all the azides.[31]

Two competing processes were observed during cure: crosslinking due to azide-alkyne cycloaddition, and phase separation between the alkynyl-PDMS and the graft copolymers. Different network morphologies could result depending on the relative kinetics of the two processes. Therefore, to enhance the reproducibility of

Table 4.2: PDMS-g-PEG elastomers and properties.

| PEG | Azide -PEG | Ratio (azide: PEG) | PDMS Alkyne | Product number | Tan d 0.1 Hz/ 100Hz | G'(kPa) 0.1Hz/ 100Hz | PEG Wt % | Description | Contact Angle (@300s) | Shore OO |
|---|---|---|---|---|---|---|---|---|---|---|
| **5** | **8** | 1:0.25 | **3** | **15** | 0.067/ 0.07 | 93.6/ 96.8 | 2.8 | Slightly opaque, flexible, not tacky | 101±3 | 77±2 |
| **5** | **9** | 1:0.5 | **3** | **16** | NA/ 0.03 | 95.9/ 110.5 | 7.6 | Transparent, flexible, not tacky | 92±5 | 71±2 |
| **5** | **10** | 1:0.75 | **3** | **17** | 0.009/ 0.296 | 12.7/ 24.1 | 16. 6 | Transparent, gel, very tacky | - | 45±4 |
| **5** | **8** | 1:0.25 | **4** | **18** | 0.011/ 0.073 | 53.9/ 68.7 | 1.4 | Slightly opaque, flexible, slightly tacky | 109±3 | 66±1 |
| **5** | **9** | 1:0.5 | **4** | **19** | 0.009/ 0.094 | 34.0/ 44.7 | 4.6 | Transparent and mildly white, very tacky, prone to cracks, flexible | 101±6 | 57±1 |
| **5** | **10** | 1:0.75 | **4** | **20** | 0.070/ 0.078 | 67.8/ 100.0 | 10. 4 | Transparent, soft, very tacky | 87±6 | 67±4 |
| **6** | **11** | 1:0.25 | **3** | **21** | 0.004/ 0.124 | 115.3/ 115.8 | 5.4 | Slightly opaque, flexible, not tacky | 107±1 | 74±2 |
| **6** | **12** | 1:0.5 | **3** | **22** | 0.026/ 0.223 | 95.8/ 98.2 | 14. 4 | Transparent (over time turned very slightly opaque), flexible, not tacky | 76±6 | 70±2 |
| **6** | **11** | 1:0.25 | **4** | **23** | 0.045/ 0.156 | 64.8/ 74.2 | 3.1 | Opaque, flexible, not tacky | 45±4 | 70±2 |
| **6** | **12** | 1:0.5 | **4** | **24** | 0.212/ 0.476 | 48.6/ 74.7 | 9.3 | Transparent, uneven, very tacky | 67±2 | 59±1 |
| **5** | **8** | 1:0.25 | **2** | **25** | 0.073/ 0.606 | 63.2/ 67.2 | 8.4 | Transparent, firm, not tacky | 50±2 | 68±1 |
| **5** | **9** | 1:0.5 | **2** | **26** | 0.020/ 0.170 | 84.0/ 81.1 | 17. 6 | Transparent, flexible | 68 | 65±1 |
| **5** | **10** | 1:0.75 | **2** | **27** | 0.044/ 0.232 | 30.0/ 38.2 | 28 | Transparent, flexible, tacky | 60±5 | 55±2 |
| **6** | **11** | 1:0.25 | **2** | **28** | 0.000/ 0.061 | 5.3/ 22.7 | 14. 6 | Slightly opaque, very flexible, stretchy, a little tacky | 57±2 | 36±4 |
| **7** | **14** | 1:0.25 | **2** | **29** | n/a | n/a | 30. 4 | Opaque, waxy | 57±2 | 83±3 |

the outcomes, small amounts of solvents were used to homogenize the polymers to avoid phase separation during cure. For each pre-elastomer, the volume of solvent was adjusted until clear mixtures and a clear crosslinked gel was obtained. In some instances, it was necessary to partly 'pre-cure' the material with stirring for some time and then finish the curing process in the oven. This utilization of solvent allowed some chemical bonds to form during mixing, which kept the dispersion homogenous, before finally curing the polymers (without agitation) under conditions where phase separation could not compete kinetically with the cure. The resultant materials ranged from colorless to pale yellow and transparent to hazy depending on the PEG/silicone ratio (Table 4.2, Supporting Information).

### 4.4.4 Characterization

#### 4.4.4.1 Shore OO Hardness

Durometer (resistance to indentation) is a common way to characterize elastomeric materials. Shore OO measurements, which are particularly useful for the characterization of the viscoelastic properties of soft materials, demonstrated that the Huisgen process allows for customizable silicone materials. Unsurprisingly, for elastomers in which the monofunctional PEG and difunctional PDMS lengths are held constant, the hardness was observed to decrease with decreasing crosslink density and increase with backbone-grafted PEG (Figure 4.2a). The use of shorter difunctional PDMS while holding the PEG concentration fixed led to harder materials as the longer PDMS spacers imparted more flexibility into the network (Figure 4.2b).

More subtle changes were observed when the PEG molecular weight was changed while holding the number of crosslinks constant (25, 50, 75%). With ~8,000 g/mol difunctional PDMS spacers, formulations with 400 MW PEG, **15** and **16**, were slightly harder than those with 800 MW PEG, **21** and **22**; the opposite was true with ~16,000 g/mol difunctional PDMS spacers, where 400 MW PEG **18** and **19** were slightly softer than 800 MW PEG **23** and **24** (Figure 4.2c). PEG can help to reinforce the network via crystallization of the PEG segments,[18] which could explain the change in hardness with increasing PEG length within the network.

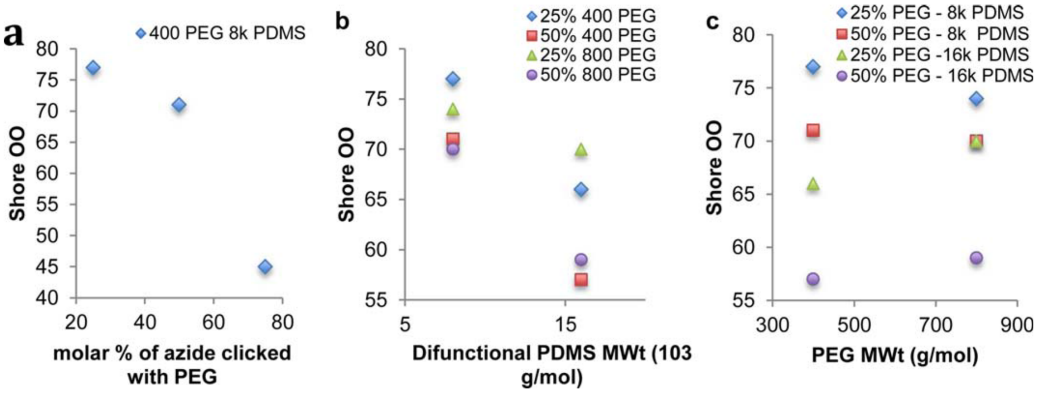



Figure 4.2: Changes in elastomer hardness: a) as a function of the quantity of grafted PEG, b) with increasing difunctional PDMS molecular weight, c) with increased PEG molecular weight.

These materials, such as **20** and **24**, possess enhanced hardness when compared to analogous unfilled silicone elastomers that do not contain PEG. In a previous investigation, an elastomer analogous to **20** in terms of PDMS spacer length and amount of crosslinks but without PEG in the network, possessed a Shore OO value of 35±4,[31] which is nearly half the hardness of its PEG containing counterpart described above (Shore OO for **20** = 67±4). This supports the

assertion that the PEG contained in the network can enhance the physical hardness. With shorter PEG as with materials **18** and **19**, there may be insufficient PEG chain length for enhanced crystallization, but sufficient length to facilitate repulsion between silicone and PEG in the network, leading to a softer gel-like network. Note that the quantity of polar extractables (using water) within the network was low (<2%), confirming that the PEG is efficiently grafted onto the PDMS backbone prior to crosslinking (Supporting Information). Very small amounts of organic extractables (less than 15%) were observed for the majority of the elastomers (Supporting Information). Compounds **17**, **19** and **28** demonstrated higher amounts of organic extractables.

#### 4.4.4.2 Rheology

The ability to tune properties of these elastomers was also shown from rheological experiments. The linear viscoelastic (LVE) region was determined by performing a dynamic strain sweep at constant frequency. Dynamic frequency sweeps were then performed choosing a strain within the LVE regions. The storage modulus (G') of the elastomers generated varied over a wide range – 5,000-115,000 Pa: both flat and responsive effects of frequency were observed (Figure 4.3a, Table 4.2 and Supporting Information). Many of the elastomers displayed a frequency-independent G' during the frequency sweep at constant strain (in the LVE range) and had essentially the same elastic response independent of the changing frequency, which is the characteristic behavior of an ideal elastomer or gel.[34,35]

Some networks displayed a frequency-dependent G' (the modulus increased with increasing frequency), a property typical of highly branched polymers or of gels containing polymers that are not bound into the network.[34] The materials with higher amount of organic extractables demonstrated low G'; **17** and **28** also had significant frequency dependent moduli, suggesting there may have been incomplete curing of these materials. Sequestered monografted α,ω-silicone propiolates can contribute to this effect. At low frequencies, the gel network and sol fractions can rearrange to accommodate stress: the observed properties resemble the equilibrium elastic deformation of the network because polymer entanglement lifetimes are shorter than the oscillation period.[36] As the frequencies increase, the oscillation becomes faster than the time it takes for physical entanglements to rearrange resulting in stored elastic energy, which leads to an observable increase in the storage modulus.

Rheological properties (G') of unfilled silicone elastomers made using traditional platinum-catalyzed addition cure (hydrosilylation of Si-H and Si-vinyl functional PDMS) exhibited comparable elastic properties to the 'click' silicones described above. Robert et al. has demonstrated that unmatched ratios of functional groups yield elastomers with lower storage modulus resulting from a less cross-linked network, similar to our thermoset elastomer structures.[37] A 20% - 90% excess of a functional groups within the PDMS network produced G' values between 900 and 9 kPa. The authors noted that dangling chains connected to the network at only one end could act as plasticizers of the silicone network.[37] Larsen et al. also

investigated the elastic properties of non-stoichiometrically cured PDMS rubbers (from hydrosilylation) and found G' values between 158 – 30 kPa for elastomers with 15 – 50% excess of one type of functional group.[38]

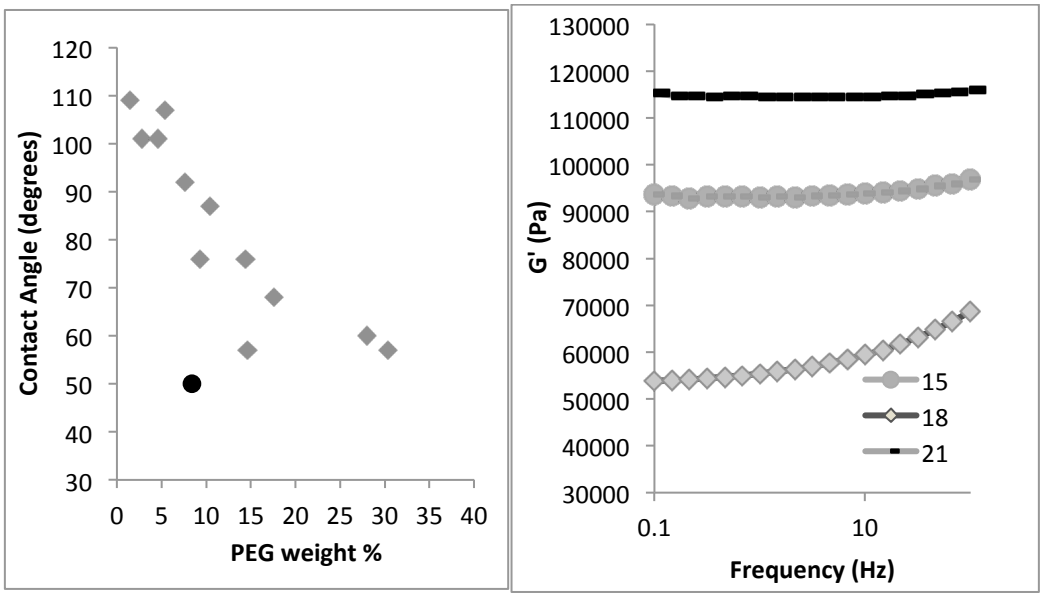



Figure 4.3: A Left: Contact angle vs. PEG weight percent (The outlier (•) represents the wettable elastomer **25**) B Right: Example storage modulus of elastomers/gels.

**4.4.4.3 Water Uptake**

One of the objectives of this work was to make materials that had potential utility in biomaterials' applications. In light of this objective it was important to characterize the response of the materials to water as hydrogels are used in biomedical applications ranging from contact lenses to wound dressings. The amount of water uptake into the networks was measured at two time points, 24 hours and 14 days. While most of the elastomers remained relatively unchanged during the water equilibration stage, others took up significant amounts of water (from 1 – 61 wt% over 24 hours, Supporting Information Figure 4S). After 2

weeks, the water uptake increased significantly in several of the elastomers, ranging from 3 – 113 wt%. Surprisingly, the water uptake was not directly proportional to the PEG content in the network. Instead, networks that were more gel like, with longer PEG chains and had increasing G' with frequency in the rheological experiments, tended to swell more with water. This observation is likely a reflection of the network structure; for example, **28** (made with PEG 750 $g \cdot mol^{-1}$), swelled substantially more than **25** (made with PEG 350 $g \cdot mol^{-1}$), its lower PEG counterpart. From these data it is clear that these reactions permit the design of silicone-PEG hydrogels.

#### 4.4.4.4 Contact Angle

Static water contact angles were measured to analyze how the incorporation of PEGs (of various chain length and grafting density) in the elastomer body affected wettability, compared to pure silicone elastomers that have contact angles >100°.[39] When PEG is grafted using the Huisgen reaction onto the surface of elastomers containing excess azido groups, enhanced surface wettability was observed, with decreases in contact angle ranging from 41 – 87° at 30 minutes).[31] Prior to measuring contact angles on the rubbers described above, they were soaked in deionized water for several days to ensure the PEG chains were fully hydrated. In the absence of this conditioning, surface effects involving hydration and adsorption/absorption of water can affect the observed angles. The contact angles were measured at time = 300 s, in triplicate for each rubber (see Table 4.2).

It was anticipated that all of the elastomers would display a decrease in contact angle arising from the quantity of PEG found within the network.

The results varied across the different elastomers and gels, contact angles ranging between 45±4° (elastomer **25**) and 109±3° (elastomer **18**), with the majority falling under 70°. These changes were not the result of changes in surface roughness, which were small (Supporting Information). There is a rough correlation between the amount of PEG in the network and the decrease in the contact angel (Figure 4.3B). Compound **25** was exceptional, exhibiting both rapid and significant decrease in contact angle to ~35° in air after 5 minutes (Figure 4.4). This high wettability is apparently a consequence both of the molecular weight of the PEG and its mobility. A network analogous to **25** but incorporating α,ω-propiolate-PEG (i.e., tethered at both ends) of low molecular weight **30** was created for comparison (Supporting Information); this elastomer was found to have a water contact angle from air of 62±2° at 300s.

Lin et al. have previously created silicone networks using the Sn-catalyzed room temperature condensation of silanols and alkoxy silanes (RTV), separately incorporating two different molecular weight dangling PEG chains within the network. They found that elastomers made with ~ 6 – 9 PEG units had water contact angles that decreased down to 40°, while those made with 4 – 6 PEG units decreased only to 80°.[19] Ding and coworkers made analogous networks using platinum-catalyzed hydrosilylation, similarly incorporating ~ 300 $g \cdot mol^{-1}$ dangling PEG chains into the network at loadings from 11 – 25 wt% and found decreases in

contact angle to 55 – 95°, respectively.[20] Taken with our previous finding that PDMS modified with 750 g·mol$^{-1}$ PEG created more wettable surfaces than those modified with 2000 g·mol$^{-1}$ PEG, the data suggests that shorter, but not shorter than about 300 MW molecular weight PEG, incorporated into or on silicone elastomers yields more wettable surfaces. Similar effects have been observed with so-called superwetting surfactants that exhibit maximum surface activity at 6-8 PEG units.[40]

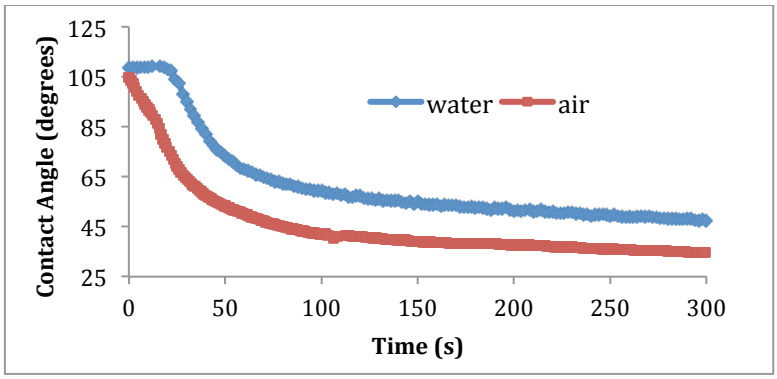



Figure 4.4: Contact angle of **25** before (air) and after soaking in water for 24 hours

The results suggest that not only does the amount and length of PEG incorporated into the network influence the wettability, but the crosslink density of the material also plays a key role. For example, **25** and **15**, which vary in the amount of crosslinks and the length of difunctional PDMS, have contact angle values of ~50° and ~100°, demonstrating how relatively subtle changes in the crosslinking can drastically impact the wettability of the surface.

As previously noted, silicones surfaces with enhanced hydrophilicity are necessary in some biomaterials applications to minimize lipid and protein

adsorption and subsequent conformational changes. Exemplar materials were selected to confirm the assertion that higher wettability surfaces correlates with decreased protein adsorption, a key step in surface fouling. Figure 4.5 depicts the hen egg lysozyme (HEL) and bovine serum albumin (BSA) adsorption results of four materials, as determined by radiolabeling: Sylgard 184, click elastomer with no PEG, material **22** (low wettability), and material **25** (high wettability). The control materials, Sylgard 184 and the 'click' elastomer with no PEG, showed similar amounts of protein adsorption; it is expected these levels correspond to a protein monolayer forming on the surface during the 3 hour incubation time. The elastomer with low wettability, **22**, showed similar adsorption to the controls for BSA but higher protein deposition levels for HEL. Given that this material showed greater swelling than the control materials, and that HEL is smaller than BSA, it is likely that some of this smaller HEL protein penetrated into the material to account for higher HEL loading.

The highly wettable elastomer **25** substantially reduced the adsorption of both HEL and BSA relative to the control materials, as expected. This is likely due to the mobile nature of these PEG chains creating a large, hydrated, protective layer on the silicone surface. These results are promising and demonstrate that these amphiphilic 'click' materials can yield silicone surfaces that have improved interfaces in biological environments.

The azide/alkyne click reaction offers significant advantages for the creation of modified silicone networks over traditional technologies. As demonstrated herein,

without the need for a catalyst, metal based or not, and with no byproducts, it is possible to efficiently functionalize and sequentially crosslink silicone elastomers to create amphiphilic networks that, at high PEG content, are hydrogels.

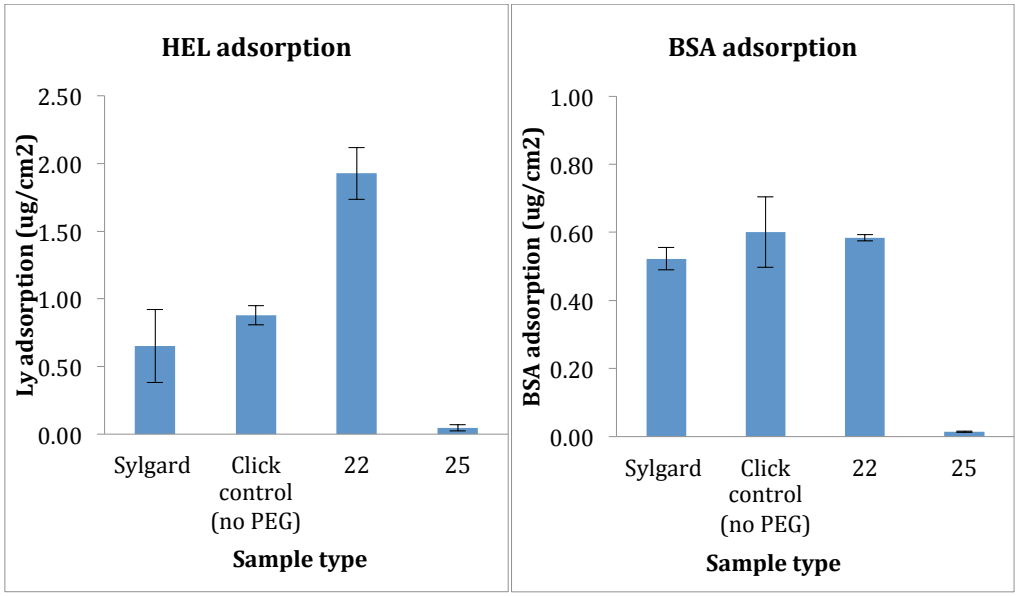



Figure 4.5: HEL and BSA Adsorption of different silicone surfaces (n=4 for each material)

The properties of the elastomers can be controlled by simply varying the ratio and composition of the azido and alkyne functional building blocks. The network structure, surface chemistry and wettability, crosslink density, length and amount of PEG functional groups can be easily manipulated.

Elastomers for biomaterials applications are frequently made in "one off" processes, which is inherently inefficient when one is trying to identify the optimal hardness, wettability, water content and, in the case of ophthalmic materials, oxygen permeability. As seen from the range of materials described

above, it is trivial to make elastomers that traverse the hard/soft, wettable/water repellent surfaces, hydrogel/dehydrated silicone spectrum using thermal linking of PEG and silicone. Importantly, the system permits additional functionalization on the surface or thorough the body of the object in subsequent Huisgen reactions.

**4.5 Conclusions**

The catalyst-free (metal-free) Huisgen reaction can be used for the creation of amphiphilic silicone networks containing PEG (1.4 – 46 wt%). The mild and efficient reaction can be used to both PEG-functionalize and crosslink azide- and alkyne-modified silicones to create novel amphiphilic materials. The metal-free synthesis is simple and high yielding, with no by-products or work up required and represents a highly efficient method for preparing silicone-PEG networks. Silicone surfactants containing dangling (pendant) PEG throughout the bulk of the network were created by first grafting monoalkynyl-PEG on an azido-functional PDMS backbone to give PDMS-g-PEG polymers, while preserving unreacted azido groups. Subsequent crosslinking with α,ω-alkynyl-PDMS permitted control over the weight% PEG in the final material, the crosslink density of the network and, consequently, a variety of physical properties of the materials, including viscoelastic properties and wetting. The residual azide groups are also available for further functionalization if desired. One highly wettable material with an advancing contact angle of 35° relies on a balance of mobile PEG chains at relatively low concentration and a median crosslink density for this behavior. The

simple synthetic platform can create materials with antifouling properties as a result of the pendant PEG within the network as demonstrated by the low protein adsorption in demonstrated for the most wettable materials.

### 4.6 Acknowledgements

We thank the Natural Sciences and Engineering Research Council of Canada and the 20/20 NSERC Ophthalmic Materials Network for financial support of this research. T.R. also thanks NSERC for the award of the Julie Payette Research Scholarship and the Alexander Graham Bell Canada Graduate Scholarship D Level. We would like to thank Prof. M. Howlader for use of the contact angle machine and Mrs. Fangfang Zhang for help with the AFM imaging.

### 4.7 Supporting Information

Synthesis and characterization of PEG dipropiolate **30**, functional polymers **1** – **14**, and elastomers **15** – **29**, **31** (including contact angles, images, IR data. Details of protein adsorption, AFM, and rheological data.

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# Chapter 5:
# Thermal Bonding of Silicones For Microfluidics Using Huisgen Cyclization[⊥]

## 5.1 Abstract

The bonding of layers of silicones during manufacture of microfluidic devices, for example, is normally accomplished using plasma oxidation. The process can be costly, may require a clean room and materials that ensure the flatness of the bonding layers. The presence of hydrophobic recovery can lead to high variability in the degree of adhesion. The Huisgen 1,3-dipolar cycloaddition of azides to alkynes – a metal-free reaction – readily occurs at the interface of silicones bearing excess alkynes and azides, respectively. The same reaction can be used to crosslink the PDMS and to bond one PDMS layer to another. After bonding simply by heating, unfilled elastomers underwent cohesive failure (at ~145 kPa) during delamination tests without adhesive failure. The synthetic method described can be used in multilayer soft lithography for microfluidic device

[⊥] This chapter is currently being edited for submission into ACS Applied Materials and Interfaces. The co-authors on this paper are: Talena Rambarran, Ferdinand Gonzaga, Ayodele Fatona, Jose Moran-Mirabal, Michael Coulson, and Michael A. Brook. Rambarran led the investigation and performed most of the experimental work (with the exceptions listed below). Dr. Gonzaga helped with the initial synthetic design, Coulson (under Rambarran's supervision) helped to recreate some materials for peel tests (not discussed in this chapter) and Fatona made and tested the Sylgard controls and helped with burst measurements. Rambarran wrote the manuscript with additions, edits and guidance provided by Dr. Brook and helpful discussion and edits from Dr. Moran-Mirabal.

fabrication, with lower stringency on laboratory environment and fabrication material requirements, and renders the microfluidic channel functional, with residual reactive azide and/or alkyne groups available for subsequent modification.

**5.2 Introduction**

Microfluidic devices increasingly find use in many important applications, such as the miniaturization of analytical systems, clinical analysis and environmental testing. The ability to work on a small scale reduces the amount of reagents required, enables portability of testing devices and reduces the analysis time required.[1] Soft lithography is a fast and economical method for the fabrication of microfluidic devices and silicone elastomers are ideal materials for such devices, as they are inexpensive compared to silicon or glass, can be easily processed, are non-toxic, thermally stable, gas permeable, and optically transparent.[2,3]

PDMS (polydimethylsiloxane) devices are typically manufactured by touch-bonding a premolded elastomer containing the microchannel profiles to a flat sheet of silicone or glass. An important consideration when using PDMS is the bond strength between the component layers. Bonding to PDMS substrates typically involves surface modification by oxygen plasma, creating silanol groups that can form covalent bonds on contact.[1-2, 4] However, there are several disadvantages to the plasma bonding approach: the method may require a cleanroom facility adding to the cost and time of fabrication, the more rigid oxidized surface can crack under stress, and the material can undergo

hydrophobic recovery where PDMS from the bulk migrates to the surface prior to contact with the second surface, leading to weaker and inconsistent adhesion.[5] Therefore, improving the simplicity and reliability of PDMS/PDMS adhesion for microfluidic and other applications is an outstanding challenge.

There are many different approaches in the literature to bonding PDMS to various substrates.[6] Edding et al. compared PDMS-PDMS bonding using an oxygen plasma, corona discharge, partial curing and off ratio mixtures (i.e., [SiH]/[Si-vinyl]) in platinum-catalyzed addition cure ($R_3SiH + H_2C{=}CH\text{-Silicone} \rightarrow R_3SiCH_2CH_2\text{Silicone}$): the latter two chemical methods led to stronger bonding than the standard oxygen plasma.[7] However, the authors reported that off ratio silicone mixtures could lead to cohesively weak, sticky materials. An additional consideration with this approach is that residual hydrosilanes can undergo hydrolysis over time under ambient conditions changing both polymer modulus and bond adhesion. Oxidative surface etching with Piranha solution, the use of which has safety issues, has also been examined.[8]

Other strategies for PDMS bonding involve organic chemistry. For example, amine and epoxide groups[9] have been used to bond PDMS interfaces, and carboxyl-amine bonding has been used to bond PDMS to glass and gold.[10-11] Such organofunctional groups were incorporated onto the interface by chemically modifying the surface of pre-cured elastomers or other substrates. The amino-epoxide bonding method had comparable bond strengths to traditional plasma methods of bonding PDMS, however, the synthetic methodology required several

steps and still used plasma oxidization to create the reactive silanol groups that were modified with amino or epoxide groups. It would be ideal to have a simple and low cost fabrication method that can generate a strong bond between PDMS interfaces and subsequently enables the targeted modification of microfluidic channels, if desired.

Previously, our group demonstrated that it is possible to create stable PDMS elastomers from alkyne- and azide- modified polysiloxanes.[12] Herein, we extend this methodology to demonstrate that reactive elastomers made with complimentary reactive azide- or alkyne- groups can be thermally bonded in the absence of catalysts to produce strong adhesion between the PDMS constituents. This synthetic method is advantageous when compared to other methods because the reactive interface is created during the curing process, circumventing multiple synthetic steps to introduce reactive groups to the surface. The synthetic method described herein has the additional benefit that, if used to create microfluidic devices using multi-layered soft lithography, the reactive azido- or alkynyl- groups remain present on the channel providing synthetic handles for further modification.

**5.3 Results and Discussion**

The synthesis of silicone elastomers having an inherently reactive interface first required the synthesis of azido- and alkynyl- functional polysiloxane building blocks, which could be crosslinked using off stoichiometric ratios to leave residual functional groups in the material, including at the interface. A desirable

elastomer would be transparent and mechanically robust while providing excess reactive groups for secondary bonding to complimentary PDMS interfaces. Attempts to prepare elastomers from alkynyl- and azido-alkylsilicones derived from a common glycidylsilicone starting polymer failed: phase separation during cure compromised the crosslinking process (Supporting Information). Therefore, telechelic alkyne-terminated PDMS was synthesized by first esterifying 1,3-bis(hydroxybutyl)tetramethyl disiloxane with propiolic acid,[13] following a previously published procedure.[12] This compound served to provide end groups when equilibrated with $D_4$ ($(Me_2SiO)_4$) to grow the PDMS chain,[14] yielding propiolate-terminated PDMS **1**; the molecular weight was determined by $^1$H NMR using end group analysis (75% yield; MW 4860 $g \cdot mol^{-1}$, Supporting Information). A polysiloxane copolymer containing multiple pendant alkyne groups was prepared using an EDC coupling reaction between a commercially available (aminopropyl)methylsiloxane-dimethylsiloxane copolymer and the monopropargyl ester of butanedioic acid. The alkyne pendant polysiloxane, **2**, was obtained in an 87% yield with a molecular weight (per alkynyl- functional) group of 1315 $g \cdot mol^{-1}$ (1 alkynyl methyl siloxane unit to every ~14 dimethylsiloxane units).

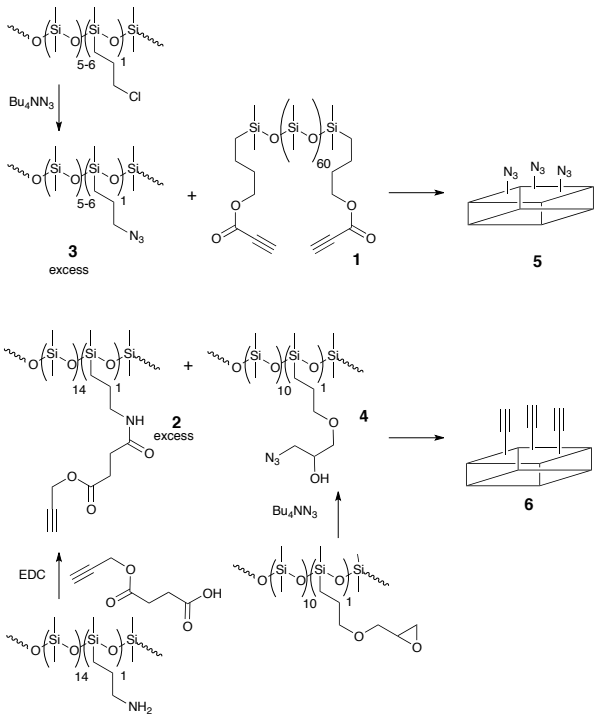
A multifunctional poly(methyl(azidopropyl)siloxane)-co-(dimethylsiloxane) was prepared by refluxing a commercially available poly(dimethylsiloxane)-co-((chloropropyl)methylsiloxane) with sodium azide and tetra-*n*-butylammonium azide in THF. The resulting multiple azido- functional polysiloxane **3** had an

average molecular weight of 530 g·mol$^{-1}$ per azido group (as calculated from $^{1}$H NMR) and was obtained in a 90% yield (i.e., $[N_3(H_2C)_3SiMeO]/[Me_2SiO]_5$ in an average repeating unit). A second azido- functional polymer, containing less functionality along the backbone, was synthesized from a commercially available glycidyl ether functionalized polysiloxane copolymer, acid catalyst and sodium azide, adapted from the previously reported procedure.[15] Polymer **4** was obtained in a 79% yield as a colorless transparent oil with a MW of ~1130 g·mol$^{-1}$ per azido group as calculated from $^{1}$H NMR ($[N_3CH_2(OH)CHCH_2O(H_2C)_3SiMeO]$ $/[Me_2SiO]_{10}$, Supporting Information).

The synthesis of the azido- and alkynyl- reactive silicone elastomers was carried out by first homogenizing the pre-polymer mixture (~4.7 g) in a glass vial with 1 mL of solvent (chloroform and/or toluene). The excess azido-elastomer was synthesized by mixing polymer **1** and **3** using a 6-fold stoichiometric excess of azido- groups to create elastomer **5** (1:6 ratio of alkyne:azide groups). Similarly, the excess alkynyl- elastomer was made by mixing **2** and **4** using a 6-fold stoichiometric excess of alkyne groups to create elastomer **6** (Scheme 5.1). A small amount of hydrophobized silica (with $Me_3Si$ groups on the surface, <2% by weight; reinforced silicones can contain >20 wt% $SiO_2$) was added to the excess azido-elastomer formulation **5** to increase its strength, since tubing required for the delamination experiments (see below) was cured into it. Analogous rubbers were prepared using lower excesses of reactive groups: elastomer **7** is analogous to elastomer **5**, but with a 3-fold molar excess of azido groups and **8** is analogous

to elastomer **6** but with a 2-fold molar excess of alkyne groups. Control silicone elastomers were also made from a commercial Sylgard 184 kit, which are highly reinforced.

The uncured mixtures were placed in glass Petri dishes coated with Parylene. While it was possible to cure the rubbers directly on the glass, the polymer coating facilitated removal of the elastomers post-curing. Pieces of tubing plugged with metal wire (to prevent ingress of liquid polymer, Supporting Information) were placed upright in the Petri dish holding the excess azido- mixture **5** prior to curing. Curing the tubing into the elastomer ensured a sealed inlet with a tight pressure fit that was needed for high-pressure delamination experiments. The excess alkyne-containing elastomer formulation **6** was cured as is, without any tubing/wires. The polymer mixtures were placed in a 100 °C oven. Although cure appeared to be complete after 6 h, the polymers were kept at elevated temperature for a total of 18 hours to ensure thorough crosslinking: transparent, monolithic elastomers 3 mm thick resulted. The presence of the reactive groups on the surface of the material throughout the curing process were demonstrated using ATIR specroscopy.[12]



Scheme 5.1. Synthesis of reactive elastomers from functional polysiloxanes

Elastomer **5** was carefully removed from the Petri dish. A ~2.5 cm square was cut around the tubing, the wire was carefully removed from the tubing channel, and a needle of the same diameter as the inner opening of the tubing (18G) was pressed through the channel and out of the bottom of the elastomer to ensure there were no obstructions that would affect the pressure measurements (Figure 5.1B). Alkyne rich elastomer **6** was used as is in the Petri dish.

Adhesion of **5** to **6** simply required contact and removal of air bubbles that were present, which was ensured with gentle pressure using the tip of a spatula. The tubing cured into the azido-rich elastomer protruded ~1 cm from the adhesive interface (Figure 5.1B). The layered materials were then placed into a

conventional oven at 100 °C at atmospheric pressure for 20 h, then allowed to cool to room temperature.

Adhesion of the PDMS/PDMS interface was measured using air pressure: this delamination method is commonly used determine the bond strength between two interfaces.[6a, 7, 11] However, a simplified version of process that could be readily exploited without advanced instrumentation was utilized; it must be noted that for this simple approach, no end chamber was molded into the device. A blunt needle tip was inserted into the device tubing and connected through a Luer Lock to an Endotek Big 60 Inflation Device (large syringe-like device fit with a pressure gauge), which was used to slowly increase the pressure to ~145 kPa, at which point the material failed cohesively, while the adhesion of the two layers was not disrupted. Star like fissure cracks (image in Supporting Information) formed in the top and/or bottom layers of the laminate, but two layers remained bonded.

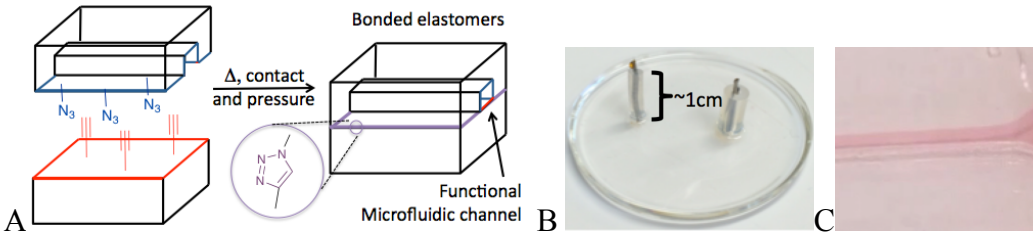



Figure 5.1: A: Schematic of adhesion of functional PDMS B: Elastomer **5** showing inserted tubing with wire and C: colored water through the channel

The bonding strength results were confirmed using an alternative, more sophisticated procedure. The tubing was connected to a nitrogen line, coupled to a digital pressure gauge, and the material was submerged in water. The nitrogen pressure was slowly increased until bubbles erupted from the material. Inspection

of the device following these tests also showed cohesive failure: the top layer 3 mm thick containing the Luer lock tube had cracked to relieve the pressure (Supporting Information).

Adhesion via van der Waals forces is suitable for low pressure applications (≤ 40 kPa)[1]; high pressure/flow applications require stronger bonding, with some devices needing to withstand pressures of >140 kPa.[16] A comparison of the adhesion as a function of functional group concentration demonstrated that adhesion could be tuned using the Huisgen method. At a low excess of reactive groups (elastomers **7** and **8**) weak adhesion between the two layers was observed and the material failed at the adhesive interface at ~46 kPa. Materials with more functional groups (**5** and **6**) had stronger adhesion at the interface; the adhesion was stronger than the cohesive strength of the material itself (>145 kPa), which underwent cohesive failure during the delamination experiment. (Supporting Information).

Traditional plasma oxidation of the PDMS surface can be costly, may require a clean room and exhibits large variability in resulting bond strengths; the plasma bonded Sylgard controls demonstrated inconsistency in bond strength in this investigation (145±62 kPa). Note that the failure mode in this case was at the adhesive bond, unlike the Huisgen bonded materials. Various alternative methods have been developed including acids to etch the surface[8] and/or incorporate surface organic functional groups.[9] While these methods can lead to improved

adhesion (97-200 kPa) they require several steps and the later example also uses plasma oxidation to incorporate the functional groups on the surface.

The Huisgen method of PDMS/PDMS bonding has the advantages of being simple and not requiring any specialized equipment. The strength of the thermal Huisgen bonding (>145 kPa) is comparable to or better than other methods of post curing silicone-silicone bonding and is suitable for higher-pressure applications. Note that the system chosen was designed to be forgiving and readily subject to optimization depending on need. The silicone elastomers were cured on comparatively rough glass, not flat silicone wafers. In addition, the elastomers were either lightly filled or unfilled with reinforcing agents, unlike the Sylgard 'standard'. The pressure at which failure occurred, in light of these facts, is surprisingly high. Perhaps more importantly, the results obtained are more reproducible than those with plasma bonding. This is a consequence of hydrophobic recovery of silicone surfaces. For plasma and other methods that oxidize the surface of PDMS, the interface can revert back to being hydrophobic in as little as ~30 minutes due to the highly mobile PDMS chains. By contrast, both the azide and alkyne-rich silicones surfaces are stable, so one could theoretically create molded silicone components and bond the surface at a later stage: comparable adhesion results were obtained on freshly made samples and those that had been left on the bench for a few weeks. It is also possible to have differential levels adhesion of these surfaces by mating a surface with one reactive group concentration with other combinations of surfaces with different partner

reactive group concentrations. The tunability of adhesive properties of silicone surfaces is something that cannot be achieved with many other surface modification protocols.

Microfluidic channels based on silicone often suffer from poor wettability with water, which retards flow of analytes.[17] Manipulating these surfaces can be challenging.[18] The azide/alkyne surfaces described above, once in a microchannel, will remain chemically reactive: three walls containing one functional group and the fourth wall containing another functional group, a situation also described by Lee and Cheung.[9] These groups allow for facile chemical modification of the internal channel surfaces (Figure 5.1). This approach was demonstrated by casting the azide-rich silicone on a silicon mold with a 700 x 230 micron feature to form a microfluidic layer (elastomer **5**). Bonding to a flat alkyne-rich silicone (elastomer **6**) led to functional microchannels within the elastomer (**5**+**6**).

## 5.4 Conclusions

In this manuscript, azido- and alkynyl- modified polysiloxanes were used 'off ratio' to crosslink silicone elastomers, while leaving residual azide or alkyne groups on the surface for subsequent bonding. Thermal bonding of complimentary azide + alkyne PDMS surfaces lead to strong interfacial adhesion, even when the devices were fabricated under low stringency conditions. When subjected to air pressure delamination experiments, the material failed at 145 kPa, showing that the bond at the interface is stronger then the material itself. The synthetic method described is simple and a valuable platform for the construction of functional

microfluidic or other devices through soft lithography. An additional benefit, arising from the use of azide and alkyne groups that remain present on the surface of the channel, is the ability to undertake further in-channel modification.

## 5.5 Supporting Information

Detailed synthetic procedures and characterization for the polymers (an attempted alternative synthesis is also described) and elastomers, and detailed of adhesion experiments and a listing of burst strengths, including a photo of a cracked-under-pressure elastomer, preparation of microchannel containing elastomers from photolithographic molds. The Supporting Information is available free of charge on the ACS Publications website.

## 5.6 Acknowledgements

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# Chapter 6:

# Sweet Supramolecular Elastomers from α,ω(β-Cyclodextrin terminated) PDMS[†]

## 6.1 Abstract

Azido β-cyclodextrins were attached to propiolate-functionalized polydimethylsiloxanes by metal-free click chemistry. The obtained telechelic copolymers spontaneously produced elastomeric gums. Demixing and supramolecular associations are the driving forces for the construction of these strongly associated (but reversible) physical networks.

## 6.2 Introduction

Materials chemistry research has seen a dramatic expansion in the development of smart materials relying on dynamic crosslinking methodologies. Non-covalent crosslinking techniques, such as π-π stacking,[1] ionic pairing (e.g., with ionomers),[2] metal-ligand association[3] and, predominantly, hydrogen-bonding

[†] This chapter is reproduced from Talena Rambarran, Arthur Bertrand, Ferdinand Gonzaga, Fernande Boisson, Julien Bernard, Etienne Fleury, François Ganachaud, Michael. A. Brook, in Chemical Communications, 2016, 52, 6681-6684 with permission from the Royal Society of Chemistry, Copyright 2016 RSC. Rambarran designed the experimental procedure and Rambarran performed all of the experiments and characterization with the following exceptions: Bertrand synthesized the first batch of azido cyclodextrin and Boisson performed the DOSY experiments. Rambarran wrote the majority of the manuscript with additions, edits and guidance provided by Dr. Brook and Dr. Ganachaud. Boisson wrote the experimental section corresponding to the DOSY experiments. Gonzaga is acknowledged for useful discussions and Bernard and Fluery for a supervisory role (along with Ganachaud and Brook).

interactions,[4] have been particularly developed. Many of these strategies rely on the facile modification of polymers with functional groups that can further combine through explicit strong associations,[4a,4c] or interact weakly together leading to phase separation from the bulk polymer.[4e,4f] Such systems are advantageous because crosslinking is generally reversible, such that the polymers may be easily recycled or repurposed.

Polydimethylsiloxane (PDMS) constitutes a class of hydrophobic polymer with a broad range of applications thanks to the various chemistries available for functionalization.[5] Dynamic associations of functional polydimethylsiloxanes have been described using pyrene,[6] coumarin,[7] thiol-silver interactions,[8] and via urea,[9] urea-imidazolidone derivatives[10] or ureidopyrimidinones[4a,11]. These latter moieties specifically dimerize and clusterize to form long fibres leading to non-covalent networks.[11] We also recently reported Lewis acid/Lewis base complexes between amino- and boronato-functional PDMSs,[12] or model fluoro-PDMS oligomers that were strongly physically-crosslinked by aggregated polar silanol groups.[13] Industrially, GENIOMER© poly(siloxane-urea) sold by Wacker Chemie are filler-free elastomers that show remarkable mechanical properties and transparency.

Recently, there has been increasing interest in interfacing PDMS with carbohydrates, as their combination imparts unique properties to resulting materials.[14] Cyclodextrins (CD) are model cyclic oligosaccharides of various cage sizes that can solubilize lipophilic drugs by inclusion in their cavity.[15] As such,

they are used in an extensive variety of applications[16] ranging from separation science,[17] cosmetics,[18] food additives,[19] pharmaceuticals,[20] drug delivery[21] and many other chemical industries. CD-PDMS inclusion complexes, however, have hardly been studied: cyclosiloxanes[22] can be trapped by the different cages (α-, β- and γ-CDs) whereas low molar mass PDMSs form polyrotaxanes only with γ-CDs,[23] the crosslinking of which allows the production of so-called sliding-ring gels[24]. To our knowledge, only two teams have reported the grafting of acylated β-CD on PDMS by means of hydrosilylation.[25] However, this method is inefficient for unprotected CD because hydroxyl groups undergo dehydrogenative coupling leading to crosslinking. Recently, the thermal Huisgen 1,3-dipolar cycloaddition ('click' chemistry) was used to crosslink mixtures of alkyne- and azido-functionalized polysiloxanes,[26] and to facilitate the ligation of PDMS to hydrophilic poly(ethylene glycol).[27] This method was chosen here to prepare α,ω-CD-functionalized PDMS by thermal cycloaddition of β-CD with alkyne-terminated PDMS chains. It was discovered that the ligation reaction leads to the formation of self-supporting elastomers (see photos in the graphical abstract). This communication describes a series of experiments undertaken to characterize PDMS/CD hybrid materials and aims at identifying the parameters that are behind the formation of these PDMS-based elastomers.

### 6.3 Results and Discussion

The synthesis of PDMSs end-capped by CD first required functionalization of the two starting materials. Mono-6-deoxy-6-azido-β-cyclodextrin **1** was synthesized according to a previously published procedure and purified accordingly.[28]

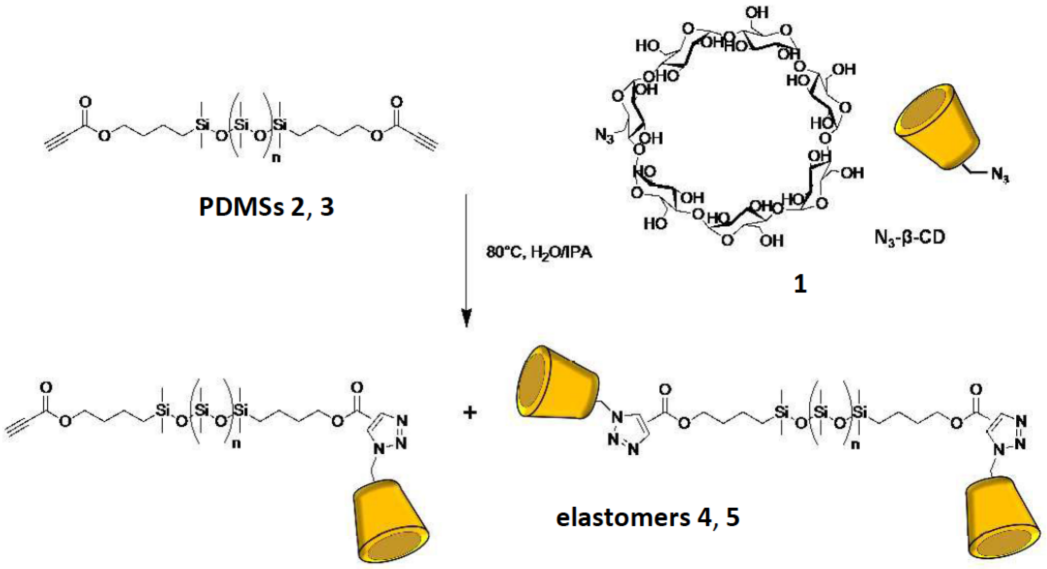


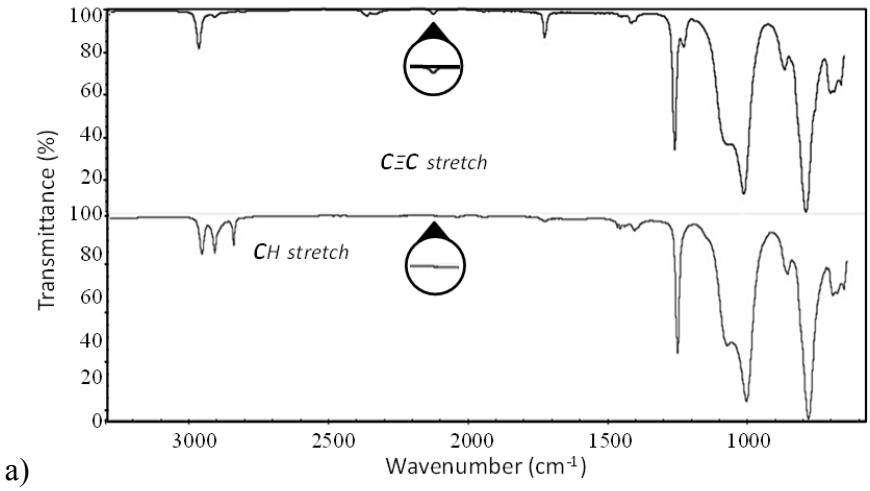

Figure 6.1: Synthesis of β-cyclodextrin functional PDMS.

Two polymers with electron-deficient alkyne chain-ends were prepared following the procedure by Rambarran *et al*. to ensure ligation through a catalyst-free click reaction.[29] 1,3-bis(propiolatobutyl)-capped polydimethylsiloxanes **2** and **3** have molar masses of 4,100 and 8,600 g.mol$^{-1}$, respectively, as determined by $^{1}$H NMR (for full characterization of these starting materials, see ESI and Figs. S1-S4).

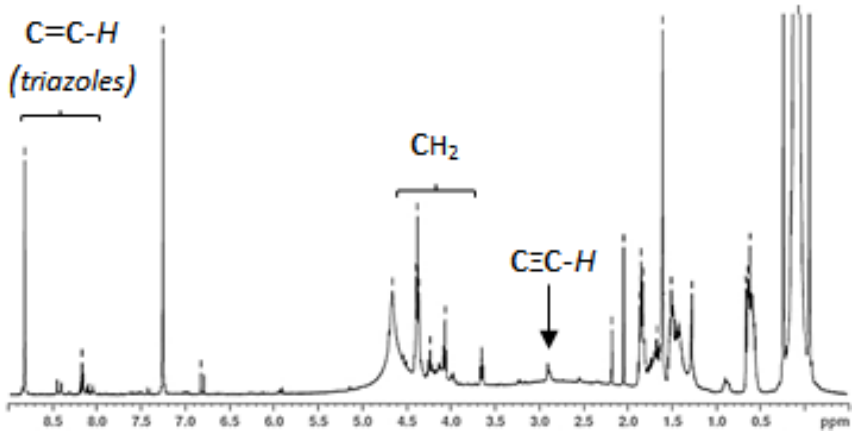
The first challenge arose in bringing the two reagents together. PDMS is highly hydrophobic and CDs are intrinsically hydrophilic, although β-CD is the least water-soluble derivative of the family. A mixture of 1:1 water:isopropanol was chosen as the dispersing medium, a compromise that partly solubilizes CD,[30]

while the isopropanol helps to disperse the PDMS. Mixtures of azido-β-CD **1** with either propiolate-terminated PDMS **2** or **3** (1:1 azide:propiolate stoichiometry), were reacted together in dilute solution at 80 °C (Figure 6.1). After 5 days of stirring with heating, monolithic pieces of soft viscoelastic polymers phase-separated from the solution, giving **4** and **5**, respectively. For comparison, the reaction between **1** and **2** was also performed in the presence of a copper catalyst to give **6**. Whereas isomers are not the same for thermal and CuAAC click reactions, both efficiently gave an insoluble elastic material.[31‡,$]

The polymeric materials **4** and **5** were difficult to characterize since they swelled up to 20x their mass in typical solvents for PDMS, i.e. THF, chloroform, DCM, and $D_4$, but did not dissolve in any of them. A variety of techniques generally performed for cross-linked elastomers, namely spectroscopy (infrared, HRMAS-NMR), thermal analyses (thermogravimetry and DSC) and rheology were applied to characterize these hybrid PDMSs (after removal of the extractables). Subtle differences were observed between the infrared spectra of **2** versus **4** (Figure 6.2a).




a)




b)

Figure 6.2: (a) IR comparing PDMS before (2 = upper curve) and after the thermal click reaction with 1 (4 = bottom curve); (b) 1H HRMAS NMR in CDCl3 of 4.

These include the appearance of a C-H stretch band at 2930 $cm^{-1}$ and a slight broad signal at 3290 $cm^{-1}$ arising from the hydroxyl groups of the CD (see zoom in Fig. 11S5), and a diminution of the intensity of the 2120 $cm^{-1}$ signal corresponding to the alkyne stretch. Figure 6.2b shows the HRMAS $^{1}H$ NMR spectrum of **4** swelled in $CDCl_3$. The signals corresponding to the -$CH_2$- of butyl end groups of PDMS were found in the 4-4.4 region (three peaks corresponding to the $CH_2$ attached to the two triazole and residual alkyne polymer, see precise

assignments in the ESI†); there was a corresponding diminution of the CH alkyne signal (at 2.9 ppm), and the appearance of C-H aromatic signals for the 1,4 and 1,5 triazole motifs (above 8 ppm). This technique demonstrates that, after extraction of unreacted PDMS, a fraction of PDMS chains that have reacted at only one end remained in the elastomer (~70% of the alkynes in the product **4** had undergone the cycloaddition reaction, Figure 6.2b; for compound **5**, ~65%, Fig. 11S6).[£]

The DSC thermogram for rubber **4** did not show glass transition or melting/crystallization events between -50 and 300 °C (Fig. 11S7). Thermogravimetric analyses (TGA) of the unextracted material showed two separate steps of decomposition (Fig. 11S8): cyclodextrin degradation[32] at 325-460 °C and PDMS degradation between 460 and 550 °C, at somewhat higher temperature than expected (see TGA of starting materials in Fig. 11S4).[33] Based on residue quantitation, the molar ratio of cyclodextrin:PDMS in the elastomeric product was ~75 % and ~65 % for **4** and **5**, in good agreement with NMR data.

Dynamic frequency sweep tests were carried out to measure storage ($G'$) and loss ($G''$) moduli in the linear viscoelastic regime. Propiolate-functionalized PDMSs **2** and **3** behave as Newtonian fluids, as expected (see Fig. 11S9). Whereas for **4** and **5** elastomers, a plateau of *G'* and *G''* at low frequency in oscillatory shear experiments was observed (Figure 6.3), similar to Botterhuis's physically crosslinked UPy PDMSs.[11] These viscoelastic materials (G'>G'' on the full frequency range) show moduli typical of unfilled materials (*G'* in the range of few

kPa). Also, the more functionalized the polymer, the more elastic the resultant material. Temperature sweeps show that G' moduli increase linearly with temperature up to 100 °C (see an example for **4** in Fig. 11S10), after which some dehydration/degradation reactions start to occur. This confirms the theory of elasticity that supposes a direct relationship between the G' moduli and the temperature. Finally, the complex viscosity of these materials decreases dramatically with increasing frequency, typical of a shear-thinning behaviour expected for physically-associated materials (Fig. 11S11).

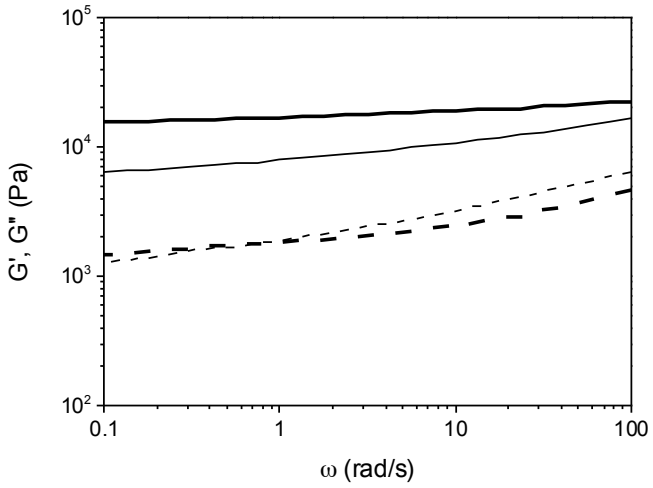



Figure 6.3: Frequency sweeps rheology measurements, giving G' (solid lines), and G'' (dot lines) for **4** (thick lines) and **5** (thin lines).

Transmission electron microscopy (TEM) analysis was obtained for both elastomers stained with ruthenium oxide (see ESI). Two levels of aggregates are seen: small dense dots of about 2 to 5 nm in size throughout the entire material and randomly spaced large dark, spherical aggregates (diameter = 18±9 nm) (Figure 6.4). The outer diameter of β-CD is ~1.53 nm,[34] giving a theoretical

molecular volume of ~ 2 $nm^3$. This implies the CD aggregation number is on the order of a few or hundreds of molecules in these small and large aggregates, respectively. Analogous conclusions can be drawn for elastomer **5**, which however possesses smaller clusters (Fig. 11S12).

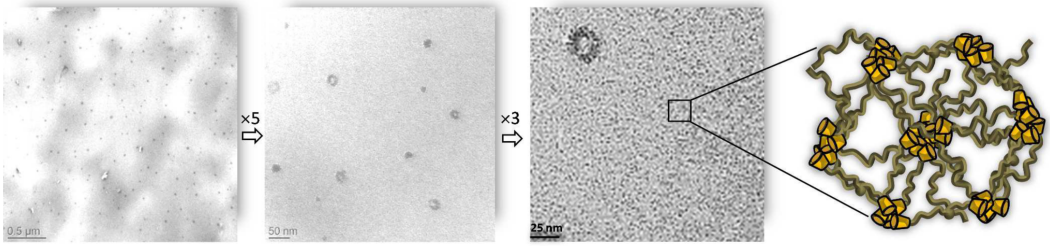



Figure 6.4: TEM images ($RuO_4$ stain) of microtomed **4** elastomer at three increasing zooms (see scale bars on photos). The PDMS material is strengthened by big aggregates (around 40 nm in size) and tightened by numerous small clusters (of about 2 to 5 nm). Right: schematized networks formation by CD clusterization.

The origin of the physical cross-linking is ascribed to CD-CD interactions. The hydroxyl dominated rim of CD may explicitly aggregate to form a network of hydrogen bonds, as is known to occur in solution.[35] The thermal reaction between **2** and 3-azido-1-propanol in place of **1** led to an oil (ESI†).

The reaction of fully acetylated **1**, mono-(6-deoxy-6-azido)-peracylated-β-CD with **2** gave a highly viscous liquid that dissolves in typical solvents for PDMS (for synthesis and NMR characterization, see Fig. 11S13-S14, ESI†). These two experiments confirm that CD clustering builds viscosity of the bulk material, whereas multiple H-bonding between CD units are compulsory to form elastomers.

A chaotropic agent known to disrupt non-covalent interactions was used to dissolve these aggregates.[13] A few drops of a 1:3 mixture of tetramethylguanidine (TMG) and trifluoroacetic acid (TFA) was added to a THF solution containing pieces of rubbers. After 24 hours the solid chunks had disappeared.[§] A SEC comparison of the molar mass distributions of PDMS precursors and clicked materials **4** and **5** (Fig. 11S15) highlighted a significant shift of the SEC traces (to lower retention volumes) for the dissolved elastomers confirming the attachment of CDs on the PDMS chain termini. Noteworthy, SEC traces of materials **4** and **5** were somewhat larger in mass (≈ 30K) than expected for α,ω-CD-functionalized PDMS suggesting the formation of aggregates due to poor solubility of CD units in THF.

In regard with the construction of these elastomers, a last point to elucidate concerns the inclusion capabilities of the hydrophobic β-CD cavity and the possible generation of sliding gels. Inclusions of PDMS into β-CDs have been previously described in the literature: different PDMS-based polyrotaxanes[23a,b] were produced with oligosiloxanes of less than 9 $Me_2SiO$ units whereas another team[36] proposed that longer PDMS chains (up to about 40 units) with an epoxide end-functionality could form complexes with β-CDs. Whatever the degree of polymerization of the PDMS, both agreed that the maximum number of accommodated molecules is 2, which means that the β-CDs are not sliding along the chains but rather act as chain end capping components (obstructing the reaction of the included alkynes). In this context, even assuming that inclusions

occur in our system, the formation of the PDMS/CD hybrid elastomers through threading of azido-β-CDs **1** onto PDMS chains and concomitant click ligation with non CD-included alkyne-functionalized PDMS chains can be discarded, as PDMS chain end capping with azido-β-CDs and simultaneous click ligation reactions would produce linear supramolecular chain-extended PDMS. In addition, DOSY NMR investigations (see Fig S16 and S17, ESI) gave no evidence of the formation of complexes between β-CD derivatives and 1,3-bis(propiolatobutyl)-ended polydimethylsiloxanes. Altogether, these results suggest that the generation of larger molar mass aggregates is not due to cage entrapment or catenation, but solely to H-bonding interactions and phase demixing.

### 6.4 Conclusions

β-CD has been grafted to PDMS chains using a metal-free click reaction. Bonding of β-CD to PDMS was apparent from the $^{1}$H NMR HRMAS spectra and TGA analyses, which demonstrated partial (>65%) ligation. Elastomer formation arises from the strong incompatibility of PDMS and CD causing CD/CD physical associations within the PDMS matrix through H-bonding interactions, even at temperatures up to 100°C. Incorporation of a chaotropic agent competing with CD/CD physical interactions resulted in the destruction of the elastomers. We anticipate using these “all-soft” elastomers as patches releasing active principle.

**6.5 Acknowledgements**

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**6.6 Notes and references**

‡ Coupling of azido-β-CD to non-activated alkyne-terminated PDMS was unsuccessful even in the presence of copper.

£ From the $^{1}$H NMR of product **4**, one can roughly deduce the amounts of about 90% of the 1,4 addition and 10% of the 1,5 addition, which is not expected for catalyst-free click reaction.[26] We attribute this preferred addition to the bulkiness of the CD molecules that promotes the generation of 1,4 isomers. Similar ratio was observed for the click reaction of acetylated CD.

§ To check that PDMS is not undergoing chemical redistribution in the presence of TFA/TMG salt, the salt was mixed with PDMS alone. SEC traces exhibited no changes in molar mass or dispersity from the starting material after 2 days.

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# Chapter 7:
# General Conclusions

Fluid and Elastomeric silicones are an important class of materials that find use in numerous applications owing to their exceptional properties; thermal and chemical stability, transparency, gas permeability, flexibility and so forth. However, many applications of silicones require the materials to be functionalized, improving their properties or making the materials more compatible in different environments. While many strategies have been developed to modify both fluid and elastomeric PDMS, there are some shortcomings associated with these methods. There remains a requirement to develop simple and generic methods to modify polysiloxanes of various forms and address other synthetic challenges for applications where silicones are used.

The focus of this thesis was the development of different ways to modify fluid and elastomeric PDMS using 'Click' chemistry, specifically the use of the thermal Huisgen 1,3-dipolar cycloaddition of azides to alkynes. This reaction has many attractive attributes that can overcome some of the synthetic challenges associated with modifying silicones (as noted in the introduction).

Chapter 2 focused on the development of a methodology to create reactive elastomers that could subsequently be functionalized with a hydrophilic polymer. It was demonstrated that azido- and alkynyl- functionalized polysiloxanes could be crosslinked, incorporating an excess of one type of reactive group into the

material (excess azides being the focus). The excess reactive groups were stable and preserved during the curing process, producing elastomers that were ready for subsequent modification with PEG. Successful ligation of alkynyl-PEG was demonstrated through various characterization techniques and the PDMS surfaces possessed enhanced hydrophilicity compared to native PDMS. This synthetic method had many advantages: the thermal cyclization did not leave any residual metal catalyst trapped in the material and could be used for both crosslinking and subsequent modification, reducing the number of synthetic steps necessary to achieve surface functionalization. PEG grafting could be carried out in both organic and aqueous solvent, owing to the reaction's tolerance to a variety of conditions. The simple method could be applied broadly, to functionalize silicones with a variety of molecules or polymer of interest.

Chapter 3 demonstrated the utility of Huisgen cyclization in functionalizing fluid polysiloxanes. The method allowed multifunctional polysiloxanes to be prepared in a sequential fashion (owing to the stable intermediary reactive group) with stoichiometric ratios of reagents (owing to the reaction's efficiency), overcoming challenges associated with the classical methods to prepare such materials. Other benefits of this method include that it did not require a copper catalyst, nor did it produce any byproducts and afforded high yields.

Chapter 4 extends the utility of the azide-alkyne 'Click' silicone modification method, combing elements of the work described in Chapters 2 and

3. In certain instances, it may be desirable to have a defined amount of a hydrophilic modifier within the siloxane network. Azido-PDMS was functionalized with varying amounts of different molecular weight PEG's (in less than stoichiometric ratios, leaving residual azides). The reactive graft-copolymers were subsequently be used to crosslink alkyne terminated PDMS of different molecular weights. The method is versatile and provides many synthetic parameters that can be altered to change the properties of the resultant amphiphilic materials.

While the initial chapters focus on the generic development of silicone modification using the Huisgen reaction, the final two chapters move beyond fundamental methodology development and aim to apply the Huisgen cyclization to interface silicones with different materials and address synthetic challenges in applications where silicones find use. Chapter 5 focuses on developing a method to bond silicone interfaces together, a challenge faced in building PDMS based microfluidics devices which require strong bonding between the PDMS components. Crosslinking azido- and alkynyl- polymers with an excess of one type of reactive group produced complimentary PDMS interface, containing either alkyne and azide rich surfaces. The reactive surfaces were stable and the materials were thermally bonded. Delamination experiments demonstrated the strength of the adhesion between the bonded interfaces was stronger than the materials themselves, and stronger than traditional methods to adhere silicones (such as subjecting the material to oxygen plasmas).

Chapter 6 focused on interfacing PDMS with unmodified cyclodextrin (a cyclic saccharide with interesting properties), something that was not possible using hydrosilylation chemistry due to the nature of the saccharide. Successful ligation was demonstrated through a variety of characterization techniques and produced elastomeric materials through aggregation and phase separation of cyclodextrin in the PDMS matrix.

Overall, the thermal Huisgen 1,3-dipolar cycloaddition of azides to alkynes has proven to be a powerful tool for the synthetic silicone chemist. The robust reaction can be used to modify fluid and elastomeric silicones in a variety of reaction conditions. The reaction does not generate byproducts nor does it require the use of a catalyst that can remain trapped in the materials (or necessitating subsequent removal). The reaction is high yielding and highly efficient, allowing stoichiometric amounts of reagents to be used (in contrast to other methods which require an excess of one type of reagent). The reactive azide and alkyne groups are stable, allowing sequential manipulation of the polymer, whether that is to modify elastomer surfaces, to build multifunctional polymers or crosslink graft copolymers to create amphiphilic materials. While the method was used to create hydrophilicly modified elastomer surfaces and PEG-siloxane surfactants (two common uses of silicones), it was demonstrated that this could be extended further. Silicones could be interfaced with carbohydrates (a synthetically challenging combination) and it was also demonstrated that materials could be

strongly thermally bonded at their interface, highly useful in the creation of microfluidic devices.

While no synthetic method is perfect and there are surely limitations to the method described throughout this thesis, limitations do not negate the value of the "Click" method to synthetic silicone chemistry. Having presented this work at numerous silicone conferences, there has always been excitement about the utility of the metal-free "Click" reaction applied to silicones from academic researchers and silicone industries alike. Considering the importance of silicones and their extensive range of uses, it is essential to continue to find new and innovative ways to synthesize and modify siloxane-based materials. While this thesis focused strictly on 'click' functional materials (i.e. we used our own azide and alkyne functionalized prepolymers), this concept can be extended. Benefits of the modification methods described herein can possibly be incorporated into commercial silicone formulations, merging this fundamental research into real world of industrial silicone chemistry. This thesis provides a foundation and the initial exploration of applying the Huisgen cyclization to address some of the synthetic challenges of interfacing silicones with other material. The possibilities of extending this research are boundless and are only contingent on the creativity and drive of those who desire to explore this work further.

# Chapter 8: Appendix 1

# Supporting Information for Chapter 3: Multifunctional Amphiphilic Siloxane Architectures Using Sequential, Metal-Free Click Ligations

## 8.1 Experimental

### 8.1.1. Monofunctional Silicones: Polymers 7, 8 and 9

The general synthetic procedure is given in the manuscript, as well as the spectroscopic characterization for polysiloxane **7**. Spectroscopic characterizations for **8** and **9** are given below:

**8**: $^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.04 to 0.09 (s, 33.5 H, SiC*H*$_3$,*11*), 0.48-0.51 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.97 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.37 (s, 3H, -OC*H*$_3$, *9*), 3.54 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.63-3.65 (m, 66H, -OC*H*$_2$C*H*$_2$O-, *10 and 7*), 3.82 (m, 2H, -COOCH$_2$C*H*$_2$-, *6*), 4.38,4.68 (m , 2H total, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.44, 4.46 (2H total, -COOCH$_2$ -, *5A, 5B*), 8.06 to 8.19 (multiple singlets, 1H, *H*CCCOO,*4A, 4B*).; $^{13}$C NMR ($CDCl_3$, 150 MHz, δ): -0.41, 1.18, 1.47, 14.32, 24.44, 53.28, 59.17, 64.19, 64.77, 68.90, 69.07, 70.71, 72.08, 127.57, 129.75, 139.89, 160.84; IR (KBr) 3511 (hygroscopic compound), 3126, 2956, 2870, 1730, 1655, 1541, 1458, 1346, 1279, 1099, 1038, 950, 850, 805, 739 cm$^{-1}$.

Contact angle of a thin film on glass: 35º (at 60s).

**9**: $^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.08 (m, 33.5 H, SiC*H*$_3$,*11*), 0.43-0.55 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.8-1.98 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.36 (s, 3H, -OC*H*$_3$,

*9*), 3.54 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.60-3.75 (m, 178H, -OC*H*$_2$C*H*$_2$O-, *10 and 7*), 3.81 (m, 4H, -COOCH$_2$C*H*$_2$-, *6*), 4.38,4.68 (m , 2H total, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.43, 4.49 (2H total, -COOCH$_2$ -, *5A, 5B*), 8.06 to 8.15 (multiple singlets, 1H, *H*CCCOO,*4A, 4B*); $^{13}$C NMR (CDCl$_3$, 150 MHz, δ): -0.45, 1.15, 1.89, 14.29, 24.40, 53.25, 59.14, 61.81, 63.14, 64.16, 68.97, 69.04, 70.40, 70.67, 72.05, 72.70, 127.54, 140.02, 160.81, 161.09; IR (KBr): 3423 (hygroscopic compound), 2956, 2909, 2873, 2101, 1957, 1718, 1649, 1469, 1457, 1352, 1299, 1260, 1102, 1036, 950, 844, 805 cm$^{-1}$.

Contact angle of a thin film on glass: 43º (at 60s).

### 8.1.2. Difunctional PEG Silicones Prepared in a One Pot Process: Polymers 10, 11 and 12

Graft-polymer bearing 2 different PEG chains were synthesized using molar ratios 1:0.53:0.53 for **1:2:3**, **1:2:4**, **1:3:4** respectively to create surfactants **10**, **11** and **12**. The general synthetic procedure is given in the manuscript, as well as the spectroscopic characterization for polymer **10**. Spectroscopic characterizations for **11** and **12** are given below:

*Major isomer 1, 4 (A ~ 80%), Minor isomer 1, 5 (B ~20%)*

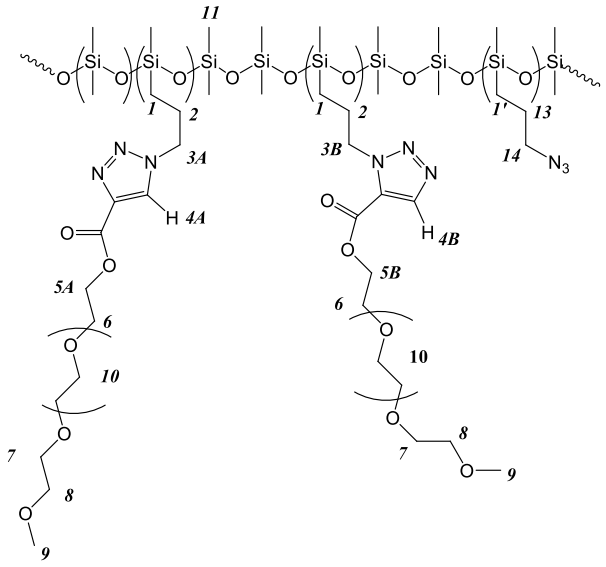
**11**: $^{1}$H NMR (CDCl$_3$, 600 MHz, δ): 0.04-0.08 (m, 33.5 H, SiC*H*$_3$,*11*), 0.43-0.52 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.88-1.98 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.35 and 3.36 ( two s., total 3H, -OC*H*$_3$, *9*), 3.53 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.58-3.64 (m, 107H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.66-3.68 (m, 3H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.81 (m, 2H, -COOCH$_2$C*H*$_2$-, *6*), 4.37,4.66 (m , 2H, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.43, 4.48 (2H, -COOCH$_2$ -, *5A, 5B*), 8.06 to 8.17 (multiple singlets, 1H, *H*CCCOO,*4A, 4B*).; $^{13}$C

NMR ($CDCl_3$, 150 MHz, δ): -0.46, 0.89, 0.99, 1.14, 1.90, 14.26, 24.39, 53.23, 59.13, 64.15, 64.66, 65.33, 68.86, 69.02, 70.66, 72.03, 127.49, 139.82, 160.81; IR (KBr) *v* = 3437 (hygroscopic compound), 2956, 2906, 2873, 2101, 1949, 1730, 1641, 1544, 1352, 1297, 1260, 1197, 1108, 1030, 952, 850, 808 $cm^{-1}$.

**12**: $^1H$ NMR ($CDCl_3$, 600 MHz, δ): 0.05-0.08 (m, 33.5 H, SiC*H*$_3$,*11*), 0.43-0.54 (m, 2H, SiC*H*$_2$CH$_2$, *1*), 1.88-1.98 (m, 2H, SiCH$_2$C*H*$_2$CH$_2$, *2*), 3.36 (s., 3H, -OC*H*$_3$, *9*), 3.53 (m, 2H, C*H*$_2$OCH$_3$, *8*), 3.58-3.64 (m, 130H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.66-3.68 (m, 3H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.81 (m, 2H, -COOCH$_2$C*H*$_2$-, *6*), 4.36,4.66 (m , 2H, SiCH$_2$CH$_2$C*H*$_2$N$_3$, *3A, 3B*), 4.43, 4.48 (2H, -COOCH$_2$ -, *5A, 5B*), 8.06 to 8.17 (multiple singlets, 1H, *H*CCCOO,*4A, 4B*).; $^{13}C$ NMR ($CDCl_3$, 150 MHz, δ): -0.46 1.14, 1.89, 14.26, 24.39, 53.23, 59.13, 64.14, 68.64, 68.85, 69.01, 70.65, 72.02, 127.50, 139.81, 160.80; IR (KBr) *v* = 3520 (hygroscopic compound), 2956, 2906, 2870, 2102, 1949, 1732, 1643, 1538, 1455, 1352, 1297, 1260, 1199, 1099, 1027, 952, 852, 802 $cm^{-1}$.

### 8.1.3. 50% PEG or Diacid-Functionalized Silicones 13, 14, 15 and 16

The general synthetic procedure to prepare graft polymers where only 50% of the azide groups are reacted with an activated alkyne is given in the manuscript, as well as the spectroscopic characterization for polymer **13**. Spectroscopic characterizations for **14**, **15** and **16** are given below:



**14** *(Major isomer 1, 4 (A ~ 80%), Minor isomer 1, 5 (B ~20%) :* $^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.04 to 0.09 (m, 33.5H, SiC*H*$_3$,*11*), 0.48-0.51 (m, 1H, SiC*H*2CH2CH2triazole, *1*), 0.53-0.58 (m, 1H, C*H*2CH2CH2N$_3$, *1'*), 1.61-1.65 (m, 1H, SiCH2C*H*2CH2triazole, *2*), 1.91-1.98 (m, 1H, SiCH2C*H*2CH2N$_3$, *13*), 3.22 (t , *J*=6Hz, 1H, C*H*$_2$N$_3$, *14*), 3.37 (s, 1.5H, -OCH$_3$, *9*), 3.54 (m, 1H, C*H*$_2$OCH$_3$, *8*), 3.64-3.67 (m, ~30H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.68 (m, 1H, C*H*$_2$CH$_2$OCH$_3$, *7*), 3.82-3.84 (m, 1H, -COOCH$_2$C*H*$_2$, *6*), 4.37,4.67 (m , 1Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.45, 4.49 (1Htotal, -COOC*H*$_2$ -, *5A, 5B*), 8.06- 8.17 (multiple singlets, 0.5H, *H*CCCOO,*4A, 4B*). $^{13}$C NMR ($CDCl_3$, 150 MHz, δ): -0.55, -0.42, 0.92, 1.01, 1.17, 1.41, 1.91, 14.32, 14.62, 22.90, 24.43, 53.27, 54.26, 59.17, 64.19, 69.07, 70.71, 72.08, 127.53, 139.89, 160.84; IR (KBr) 3126, 2962, 2901, 2870, 2099, 1946, 1732, 1544, 1455, 1416, 1347, 1260, 1197, 1094, 1016, 847, 805, 703 cm$^{-1}$.

**15** *(Major isomer 1, 4 (A ~ 80%), Minor isomer 1, 5 (B ~20%) :* $^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.03 to 0.07 (m, 33.5H, SiC*H*$_3$,*11*), 0.47-0.51 (m, 1H, SiC*H*2CH2CH2triazole, *1*), 0.52-0.56 (m, 1H, C*H*2CH2CH2N$_3$, *13*), 1.60-1.65 (m, 1H, SiCH2C*H*2CH2triazole, *2*), 1.90-1.98 (m, 1H, SiCH2C*H*2CH2N$_3$, *13*), 3.21

(t , *J*=6Hz, 1H, C*H*$_2$N$_3$, *14*), 3.36 (s, 1.5H, -OCH$_3$, *9*), 3.53 (m, 1H, C*H*$_2$OCH$_3$, *8*), 3.63-3.68 (m, ~94H, -OC*H*$_2$C*H*$_2$O-, *10*), 3.82-3.84 (m, 1H, -COOCH$_2$C*H*$_2$, *6*), 4.36,4.66 (m , 1Htotal, SiCH$_2$CH$_2$C*H*$_2$triazole, *3A, 3B*), 4.44, 4.49 (1Htotal, -COOC*H*$_2$ -, *5A, 5B*), 8.06- 8.15 (multiple singlets, 0.5H, *H*CCCOO,*4A, 4B*). $^{13}$C NMR (CDCl$_3$, 150 MHz, δ): -0.45, 0.89, 0.99, 1.14, 14.27, 14.58, 22.85, 24.40, 53.24, 54.21, 59.14, 64.16, 69.03, 70.66, 72.03, 127.55, 139.85, 160.84; IR (KBr) 3428 (hygroscopic compound), 2962, 2901, 2870, 2096, 1952, 1727, 1641, 1458, 1349, 1297, 1263, 1099, 955, 850, 802cm$^{-1}$.

**16**: $^1$H NMR (CDCl$_3$ + 1drop CD$_3$OD, 600 MHz, δ): 0.03 to 0.09 (m, 33.5H, SiC*H*$_3$,*11*), 0.50-0.55 (m, 2H, SiC*H*2CH2CH2, *1 and 1'*), 1.63 (m, 1H, SiCH2C*H*2CH2triazole, *2*), 1.95 (m, 1H, SiCH2C*H*2CH2N$_3$, *13*), 3.21 (t , *J*=6Hz, 1H, C*H*$_2$N$_3$, *14*), 4.84 (SiCH$_2$CH$_2$C*H*$_2$triazole, *3A = 3B*), 4 to 6 (broad, 2H, COO*H*); $^{13}$C NMR (CDCl$_3$, 150 MHz, δ): -0.54, -0.44, 0.83, 0.95, 1.13, 1.38, 1.87, 14.27, 14.60, 22.87, 24.33, 54.25, 54.35, 75.43, 130.93, 138.35, 153.33, 156.31, 166.69; IR (KBr) 3600 to 3000, 2967, 2909, 2645, 2498, 2096, 1752, 1638, 1549, 1457, 1413, 1280, 1097, 847, 802, 697cm$^{-1}$.

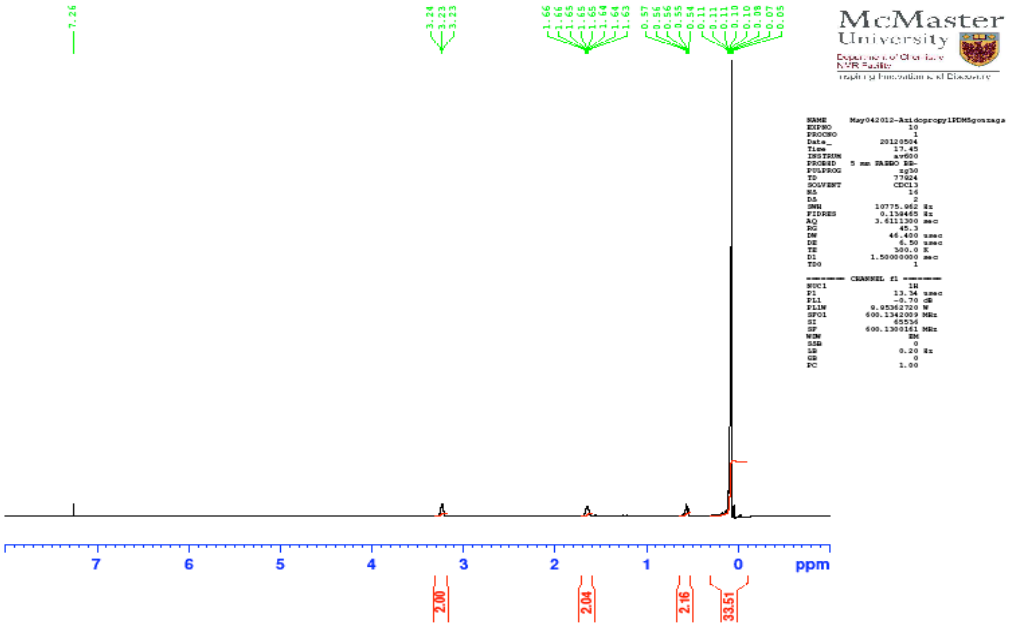
### 8.1.4. Difunctionalized Silicones 17, 18 and 19

The general synthetic procedure to prepare graft polymers where 50% of the azide groups are reacted with PEG or acetylene dicarboxlic acid, and the remaining azides reacted with acetylene dicarboxylic acid or PEG, respectively, is given in the manuscript for the iso-structural polymers **17** and **19**. Spectroscopic characterizations for polymer **18** are given below:

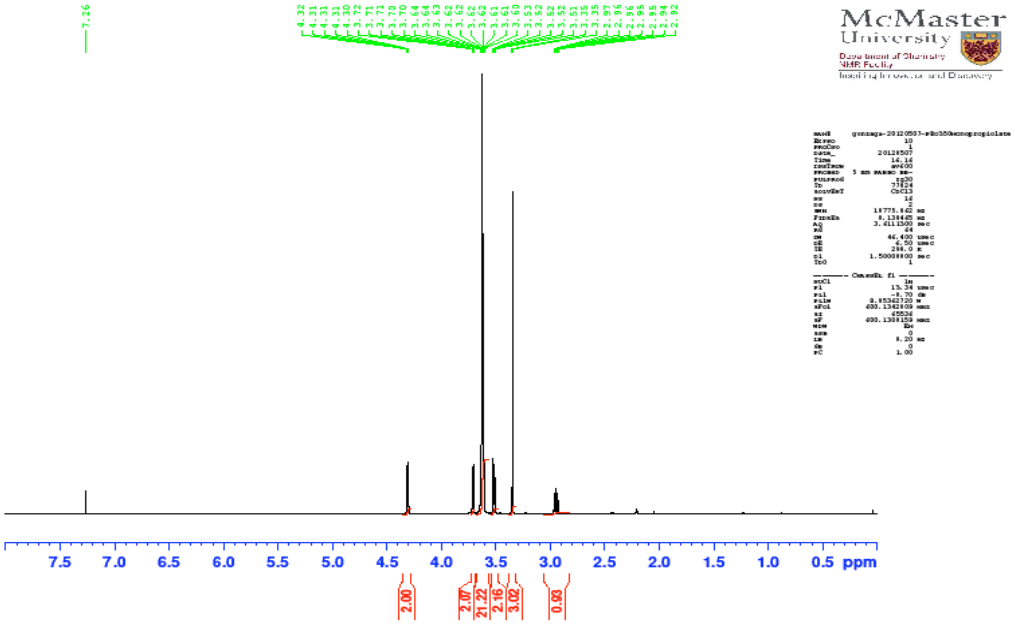
**18**: $^{1}$H NMR ($CDCl_3$ + $CD_3OD$, 600 MHz) δ: 0.00 to 0.06 (br.s, 33.5H, SiC$H_3$), 0.40-0.52 (m, 2H, SiC$H_2$CH$_2$CH$_2$triazole), 1.92 (m, 2H, CH$_2$C$H_2$CH$_2$triazole), 3.34 (s, 1.5H, -OC$H_3$), 3.49 (1H, PEG chain overlapping $CD_3OH$), 3.61-3.68 (m, 33H, PEG chain), 3.79 (m, 1.5H, PEG chain), 4.36 and 4.64 (2 m, 1Htotal (0.8 and 0.2), SiCH$_2$CH$_2$C$H_2$triazole PEG), 4.46 (m, 1H, -COOC$H_2$), 4.79 (m, 1H, SiCH$_2$CH$_2$C$H_2$triazole diacid), 8.04- 8.21 (multiple singlets, 0.5H, *H*CCCOO); $^{13}$C NMR ($CDCl_3$, 150 MHz) δ: -1.56, -0.60, -0.53, 0.77, 0.81, 0.88, 1.07, 1.31, 1.81, 13.82, 14.21, 24.28, 24.32, 53.24, 54.05, 59.02, 61.53, 64.14, 64.67, 68.79, 68.99, 70.18, 70.55, 71.93, 72.73, 75.42, 127.65, 130.93, 139.67, 153.15, 160.76; IR (KBr) *v* = 3450, 3131, 2965, 2904, 2870, 2498, 1946, 1732, 1632, 1546, 1457, 1413, 1349, 1260, 1199, 1108, 1022, 944, 852, 805, 700 cm$^{-1}$.

.

Polymer **1**:




PEG **2**:



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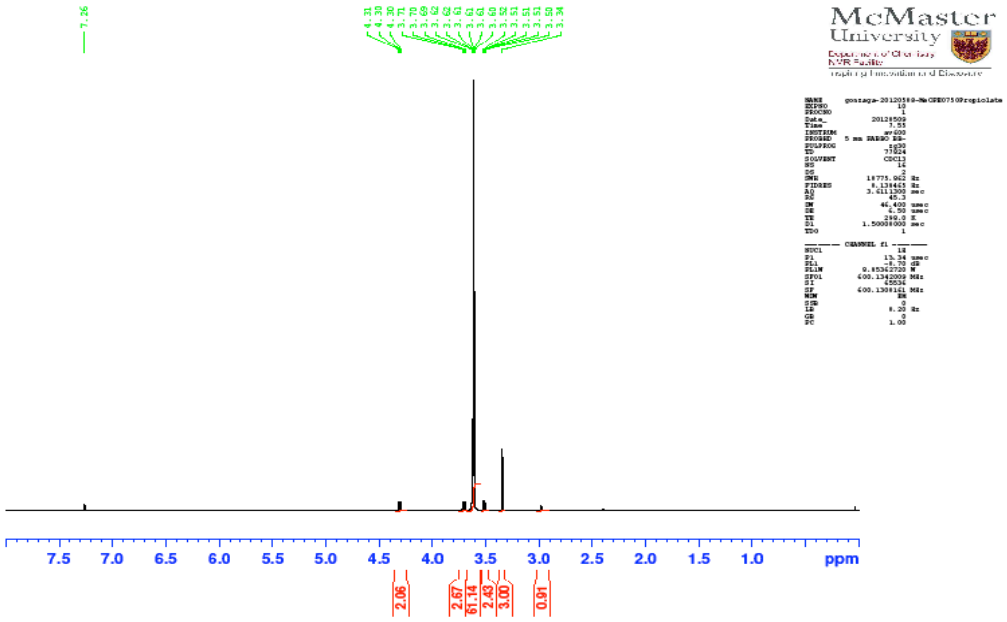
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4.30
4.30
3.71
3.70
3.69
3.62
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3.62
3.61
3.61
3.60
3.55
3.51
3.51
3.50
3.34
McMaster
University
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
1.0
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2.67
61.14
2.43
3.00
0.91

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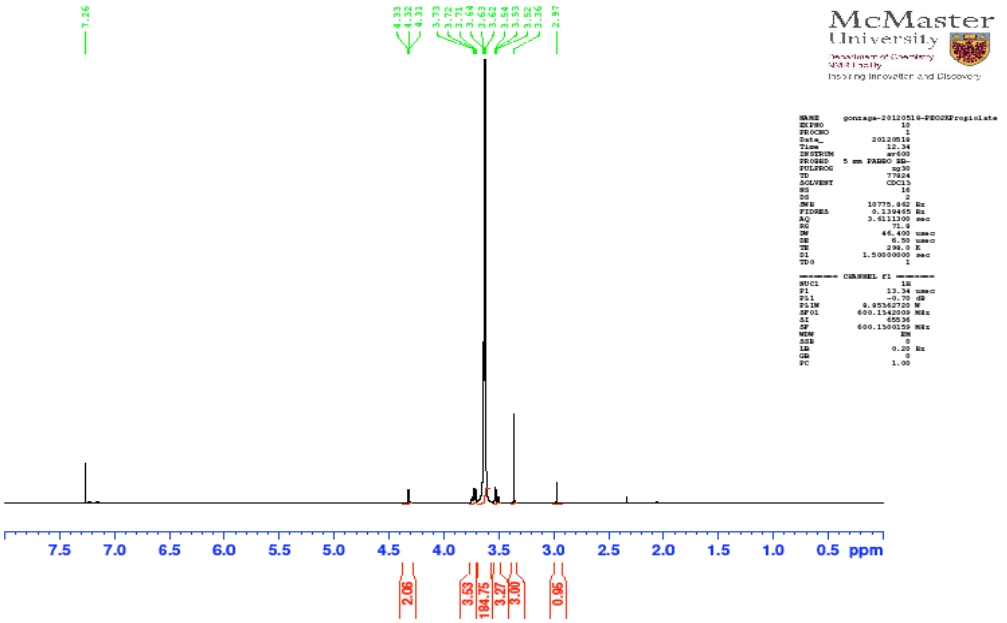
7.26
4.33
4.32
4.31
3.73
3.72
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3.54
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3.52
3.36
2.97
McMaster
University
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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ppm
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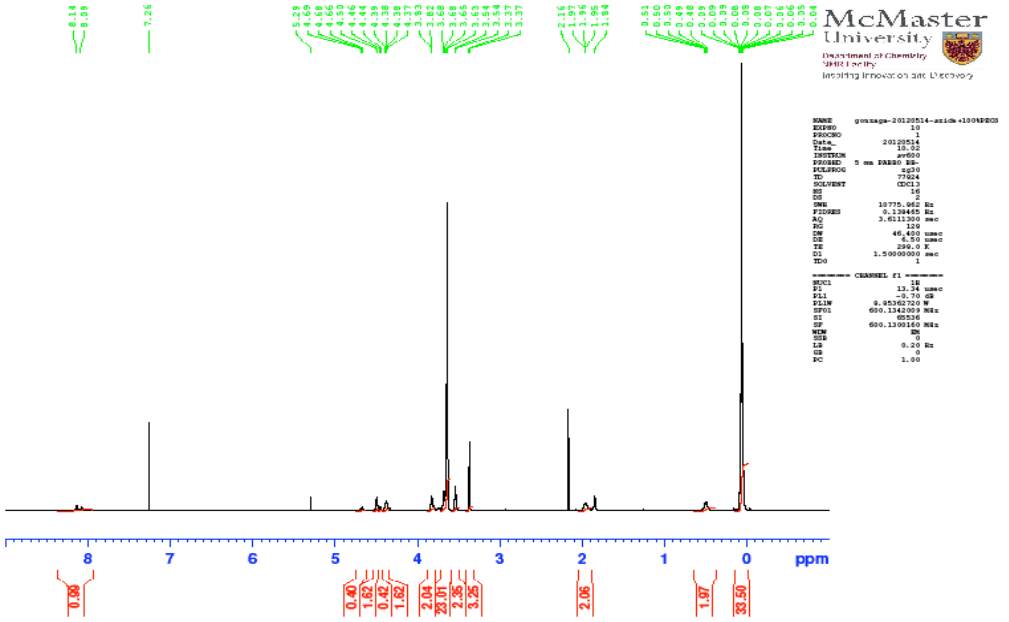
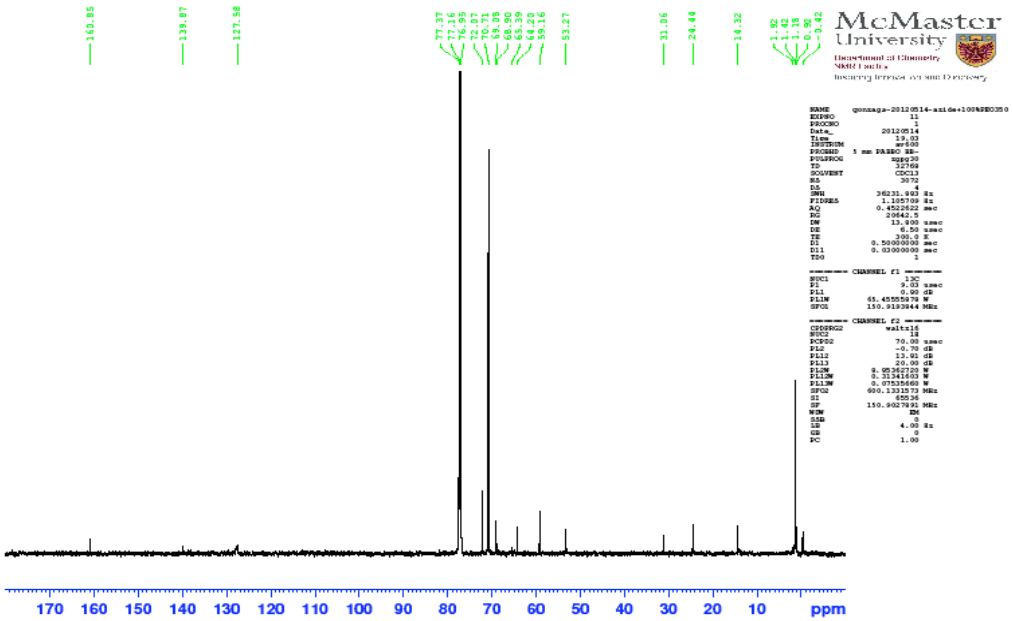
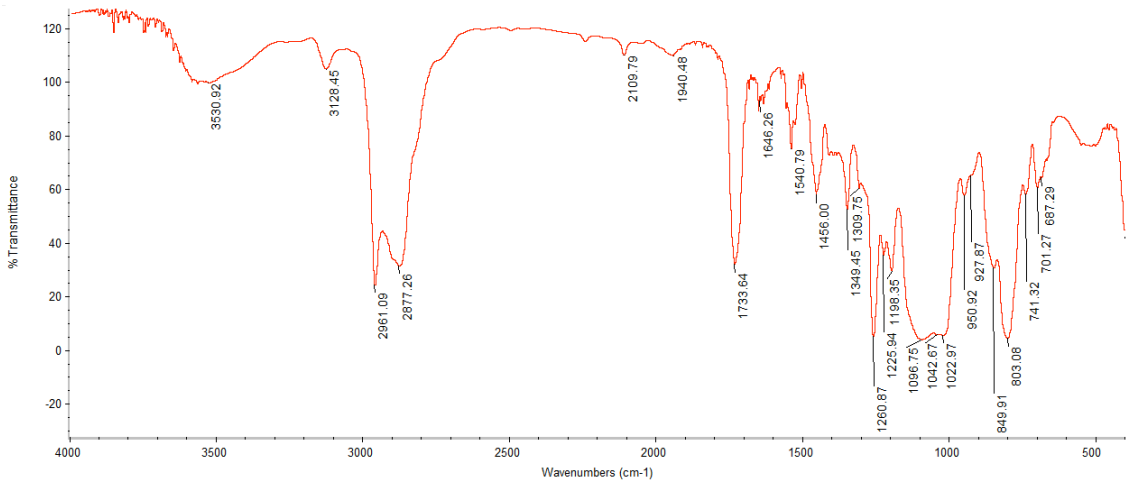
Polymer **7**: $^{1}$H NMR




Polymer **7**: $^{13}$C NMR



Polymer **7**: IR

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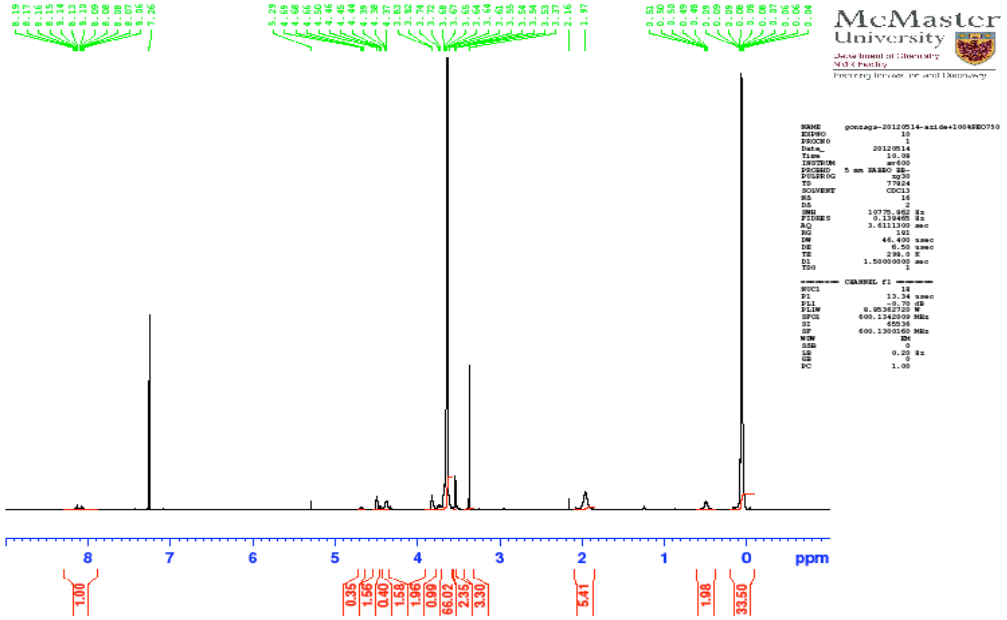
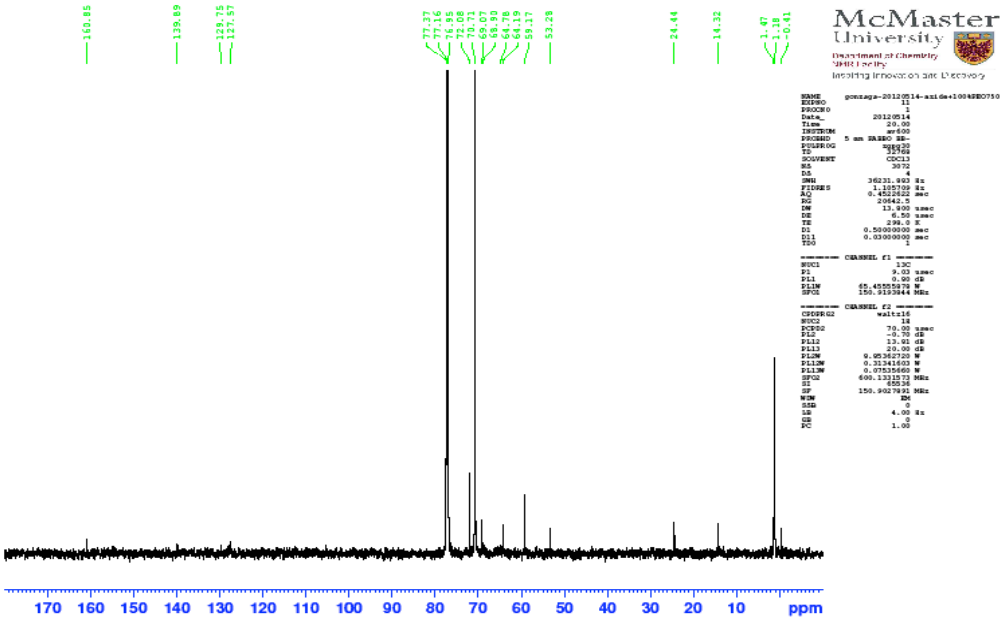
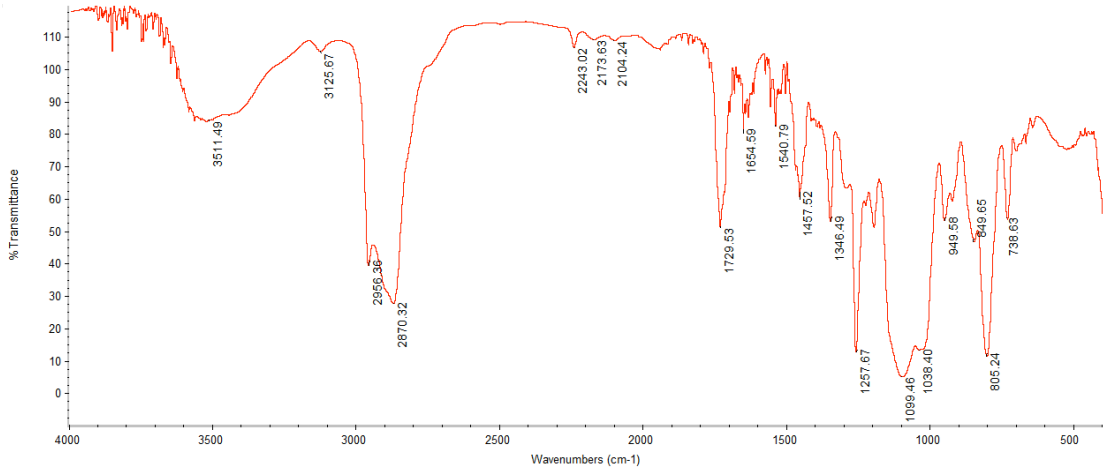


Polymer **8**: $^{13}$C NMR




Polymer **8**: IR



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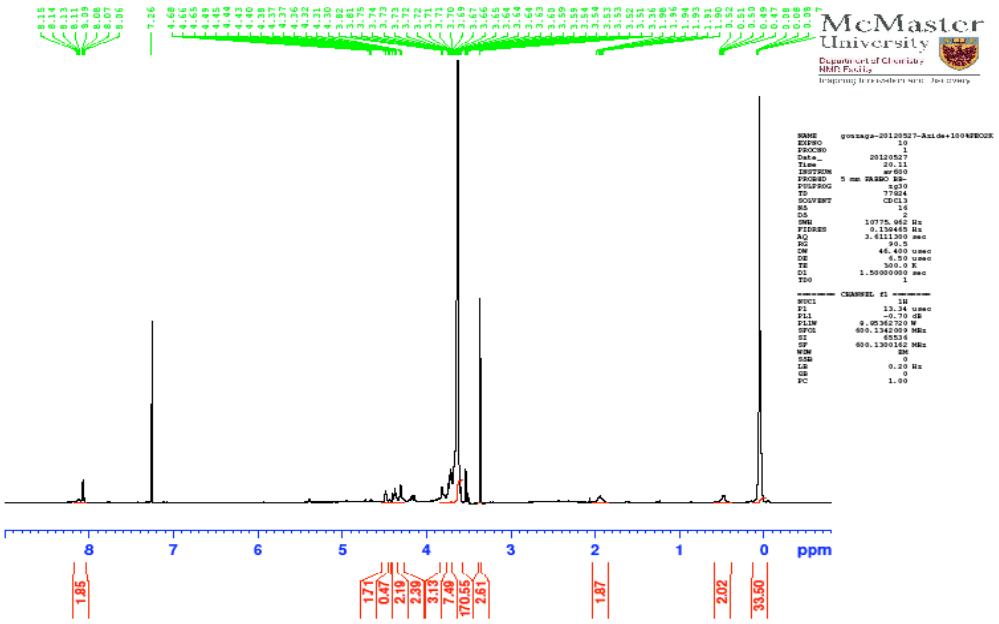
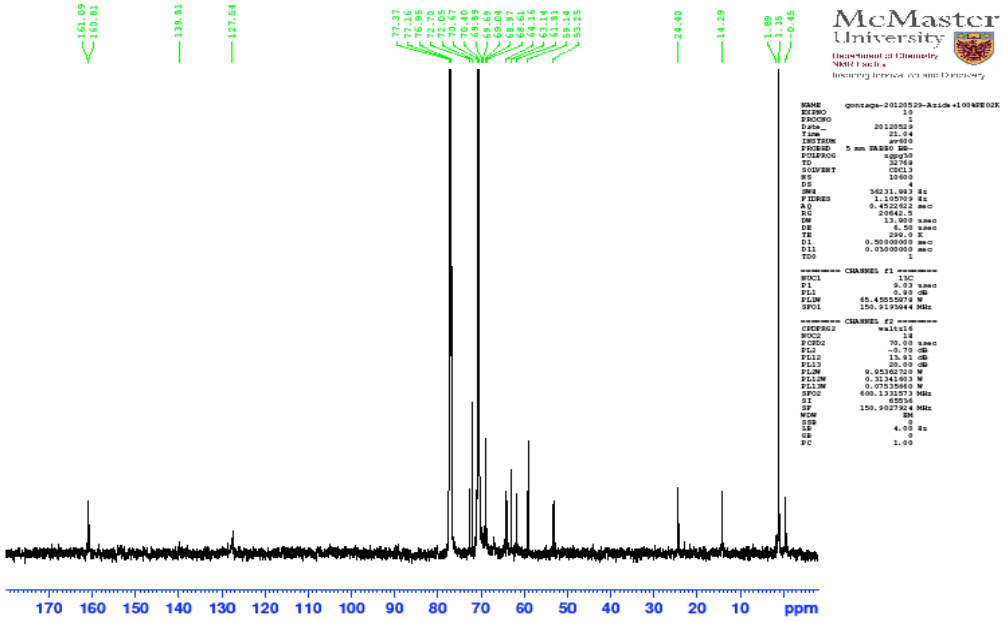
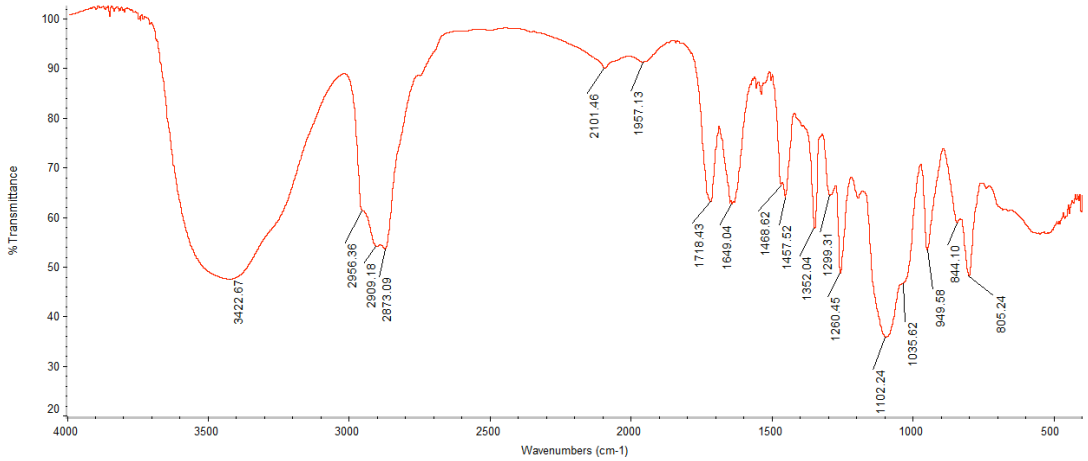


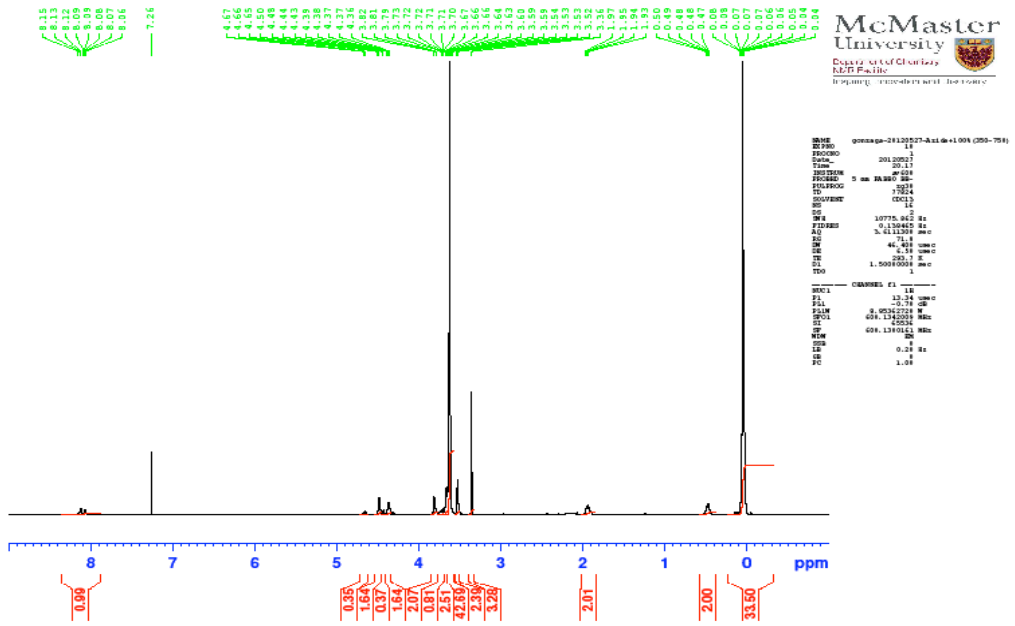

Polymer **9**: $^{13}$C NMR



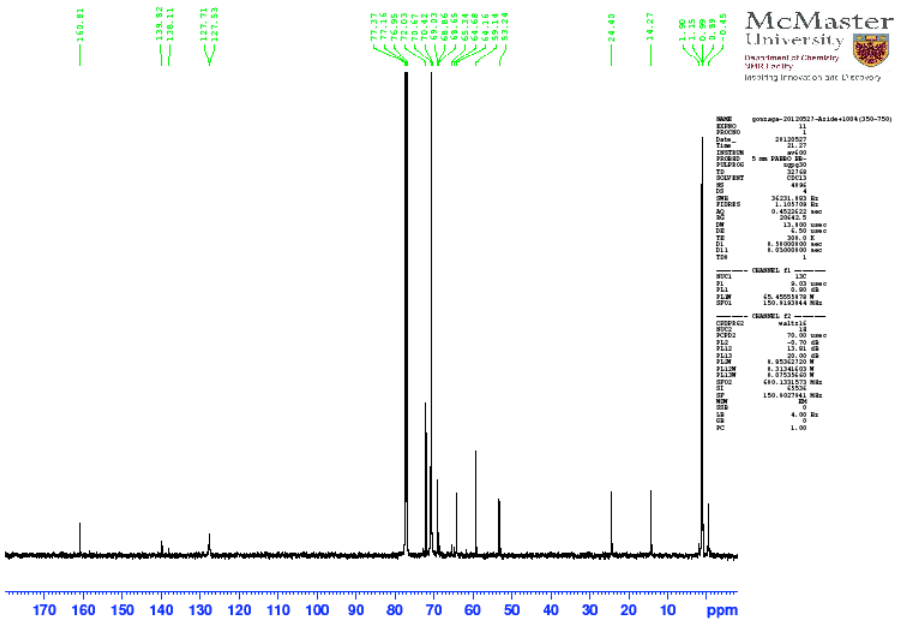
Polymer **9**: IR



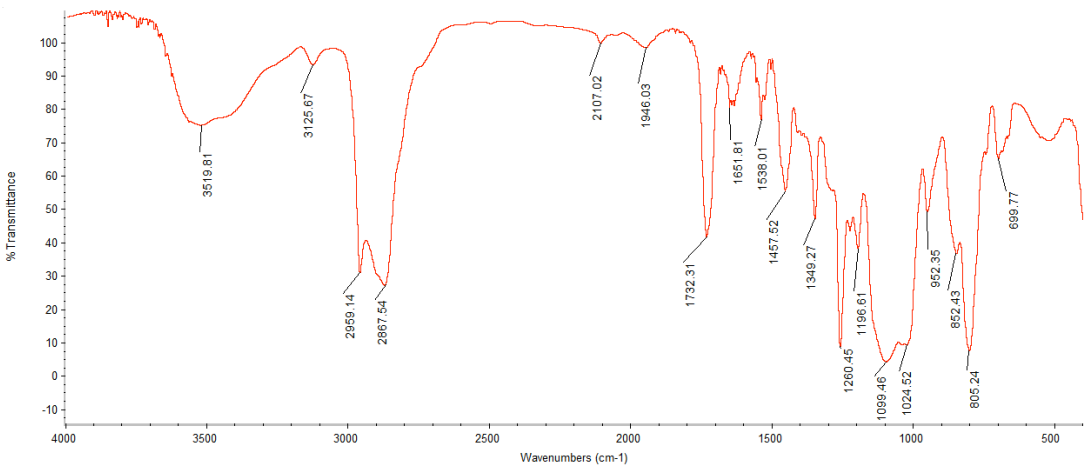

Polymer **10**: $^{1}$H NMR



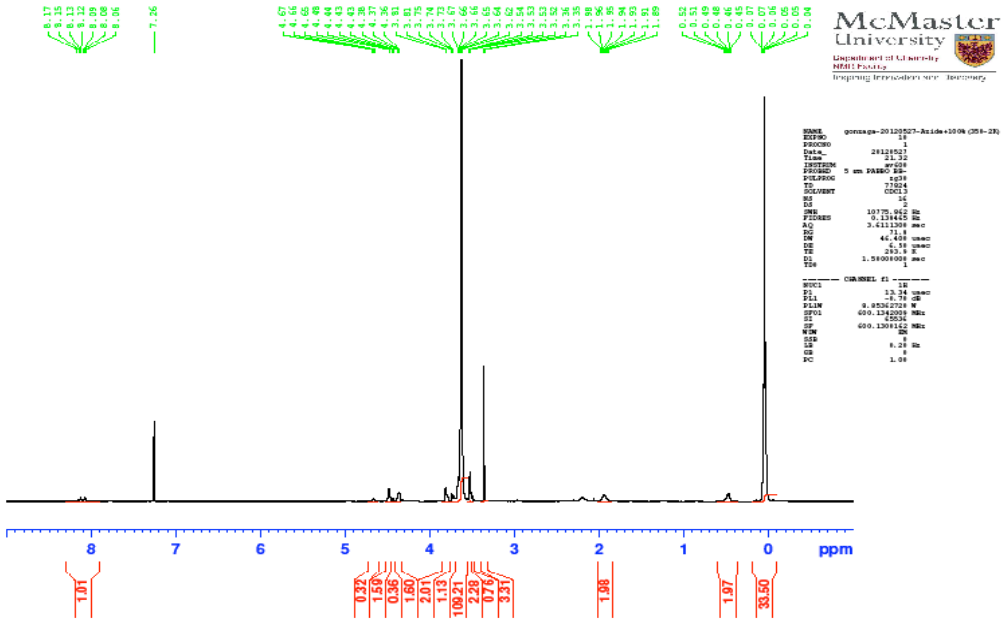
Polymer **10**: $^{13}$C NMR



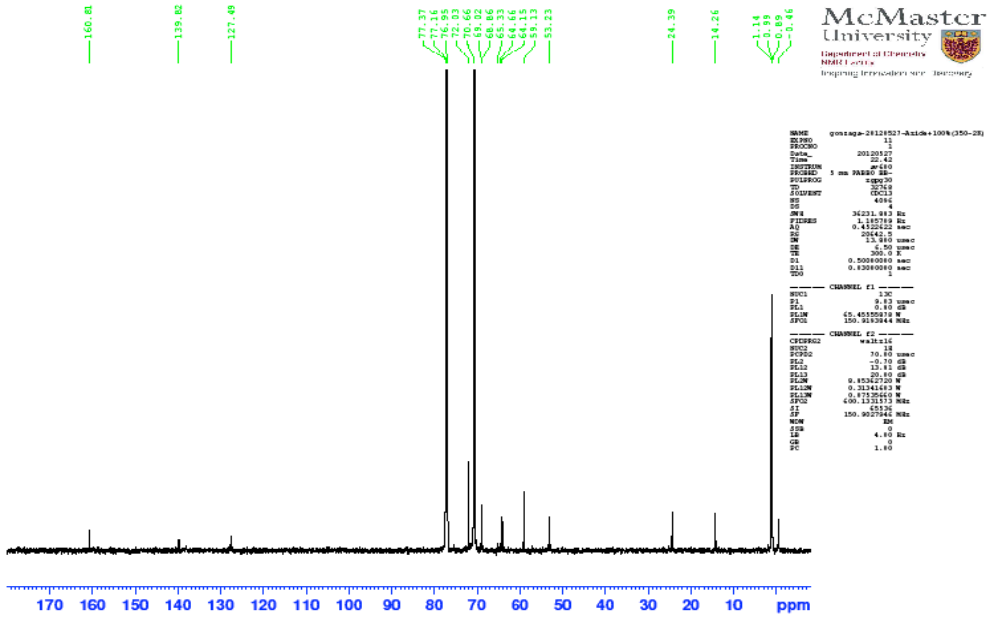

Polymer **10**: IR



Polymer **11**: $^{1}$H NMR




Polymer **11**: $^{13}$C NMR



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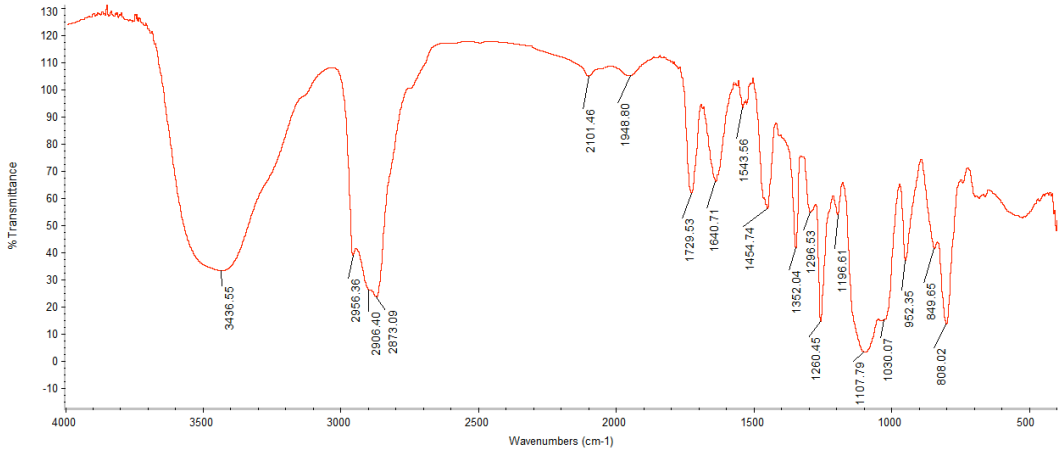
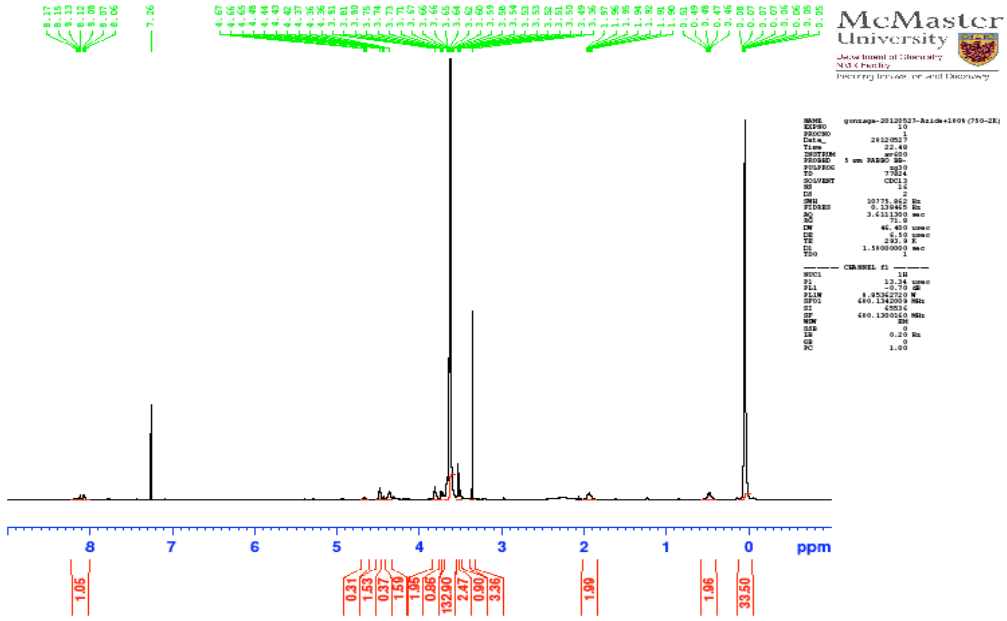



Polymer **12**: $^{1}$H NMR



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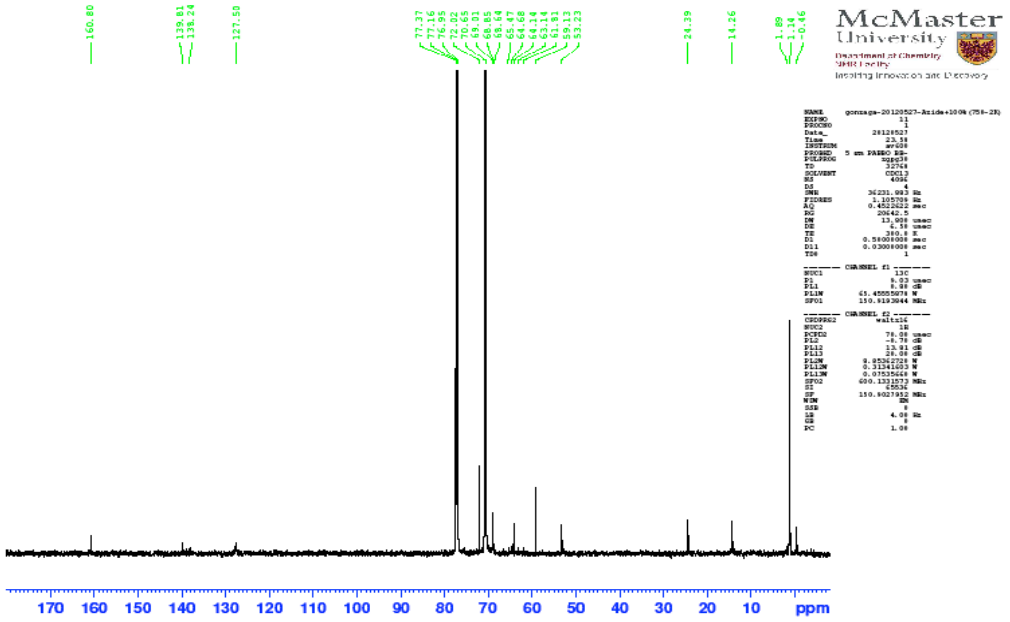
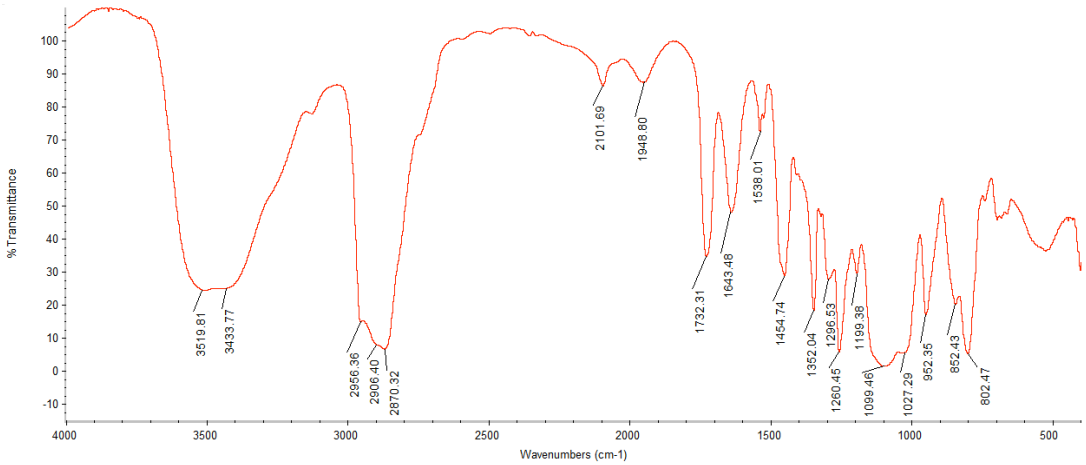
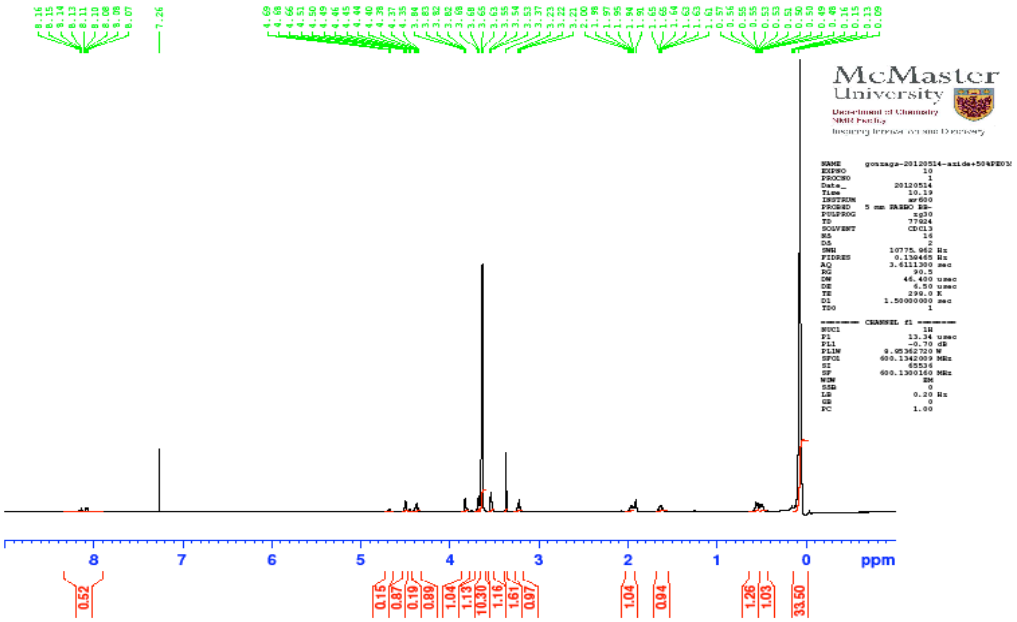



Polymer **12**: IR



Polymer **13**: $^{1}$H NMR

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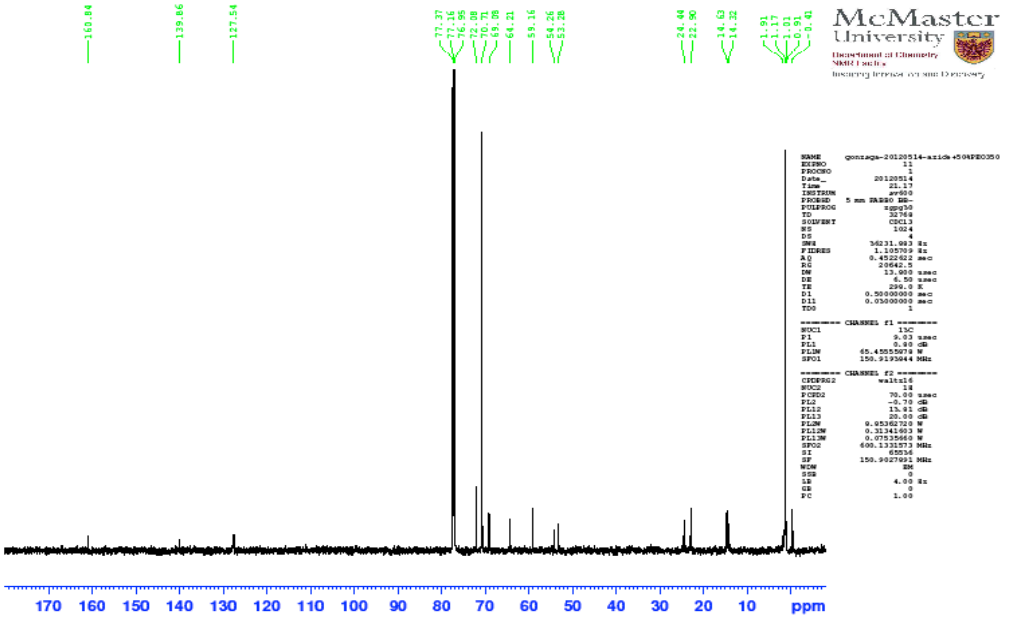
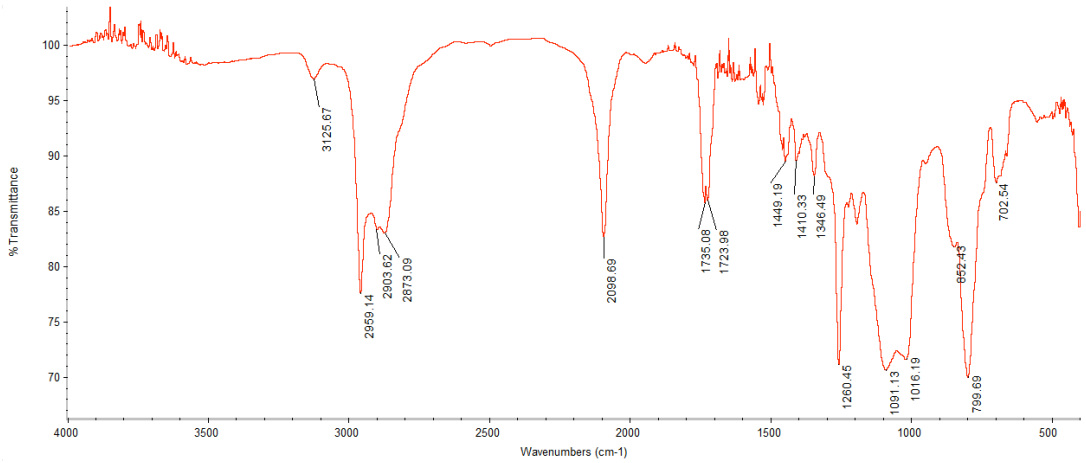


Polymer **13**: IR

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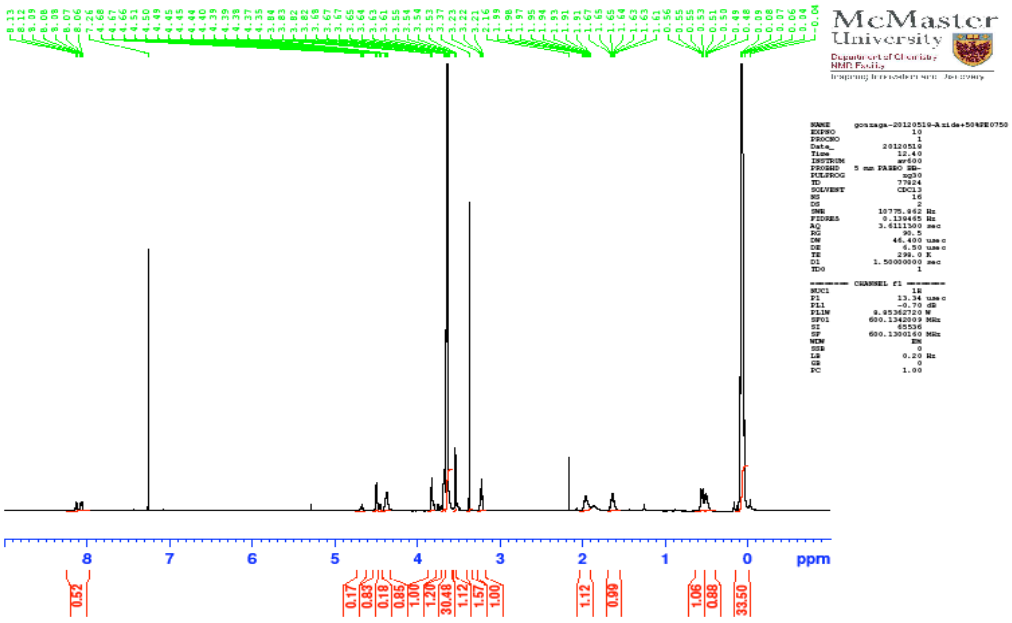
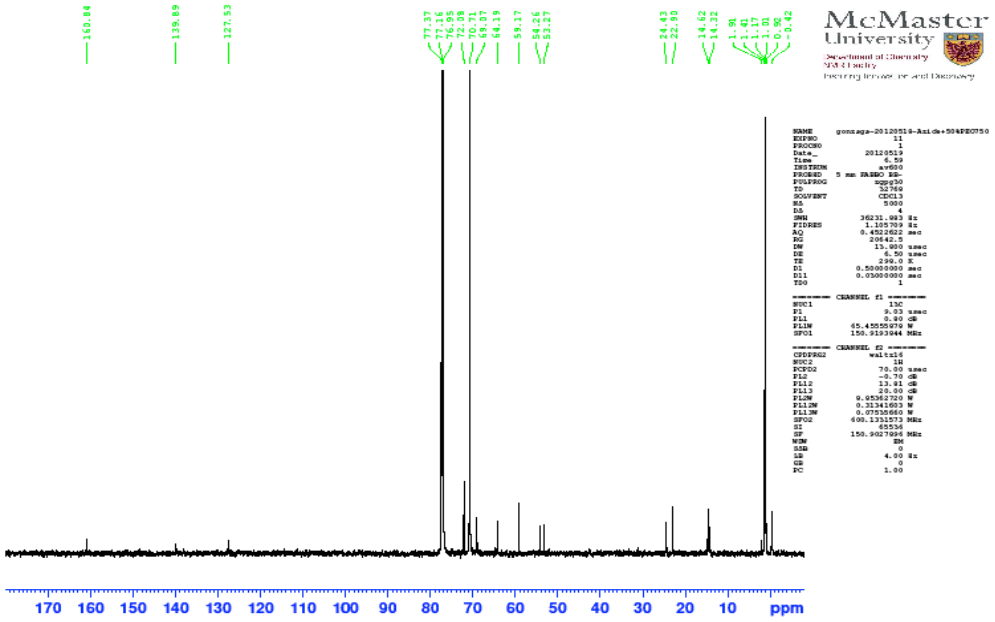
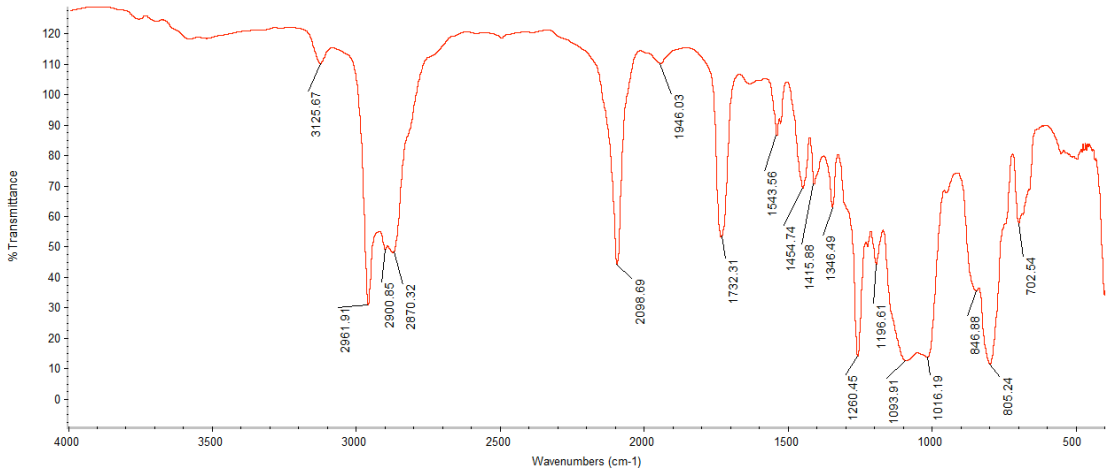


Polymer **14**: $^{13}C$ NMR




Polymer **14**: IR



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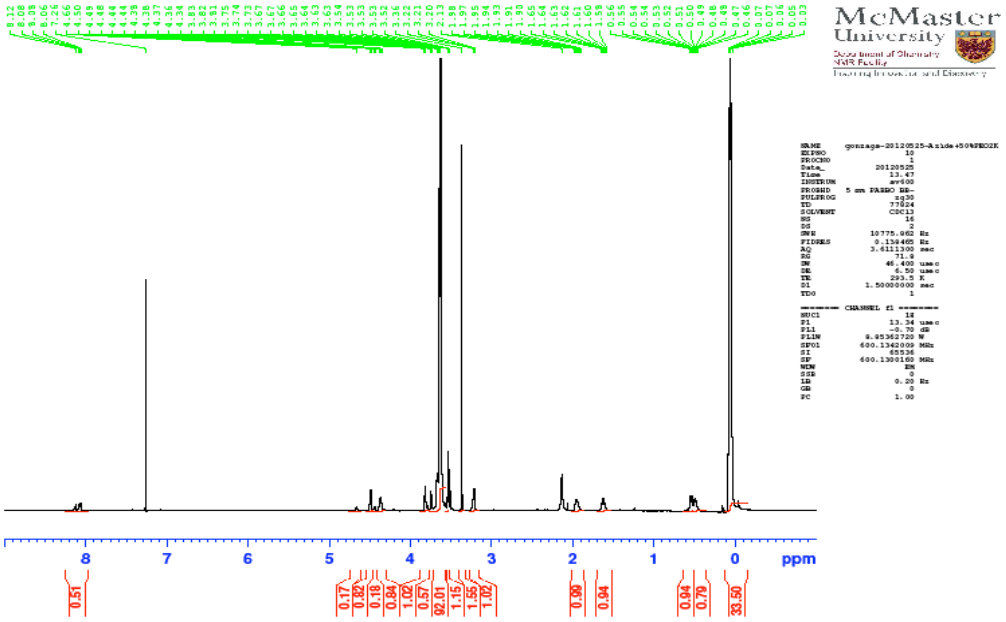
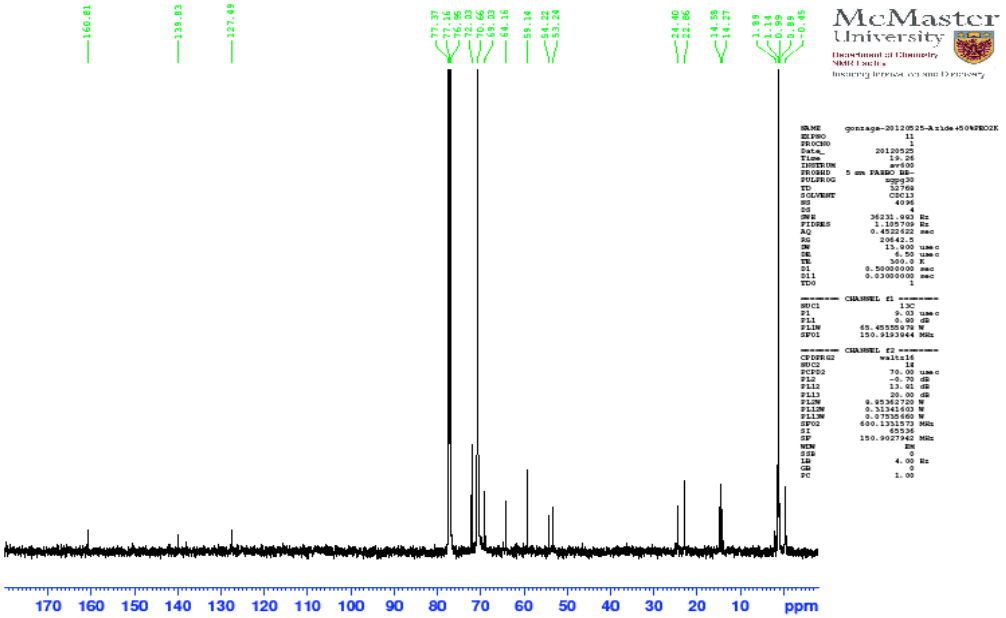



Polymer **15**: $^{13}$C NMR



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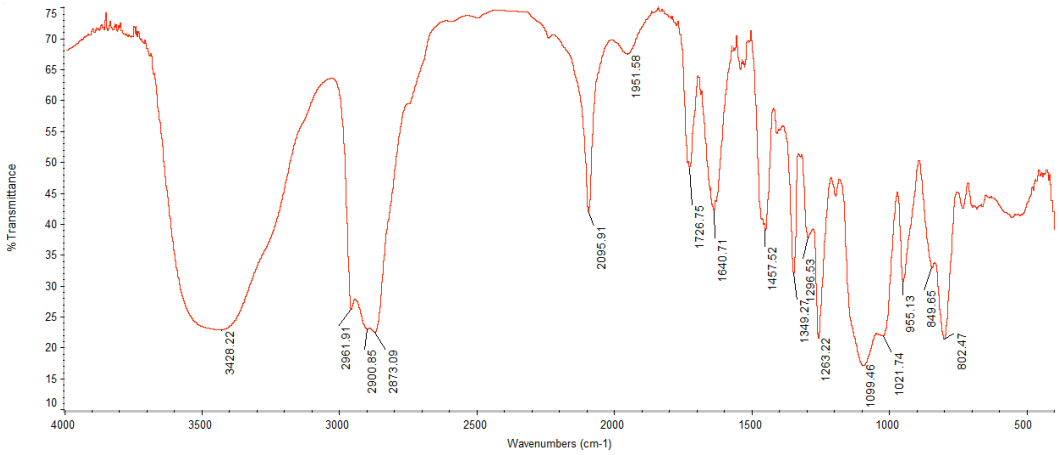


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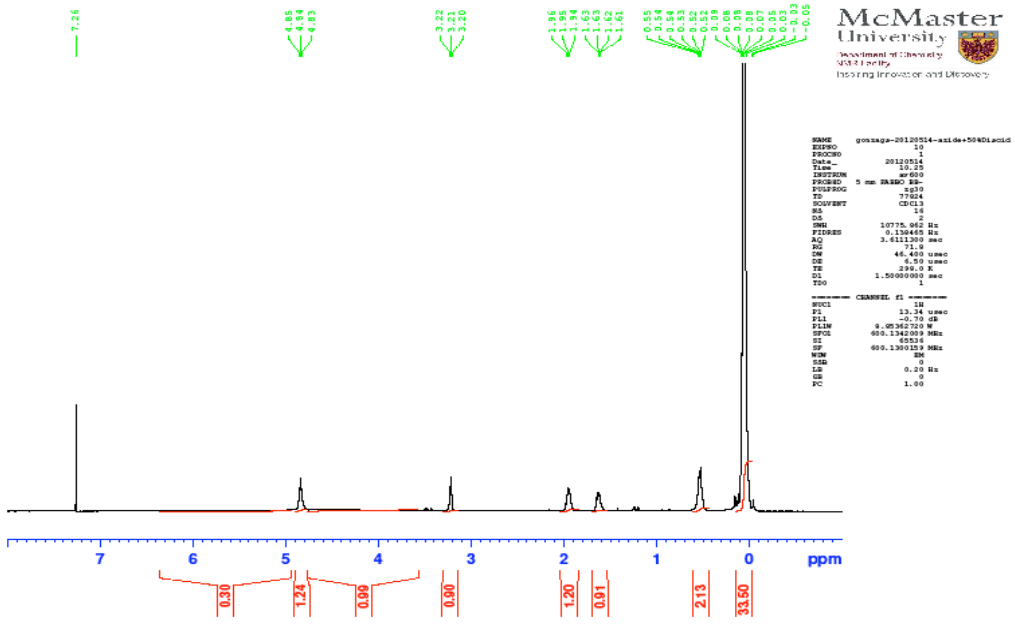
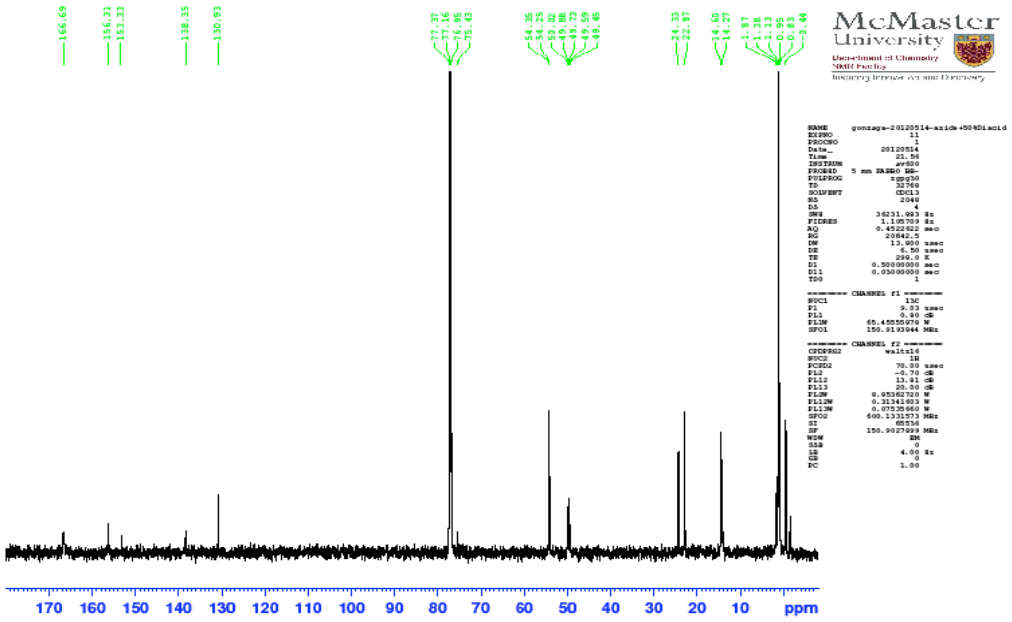
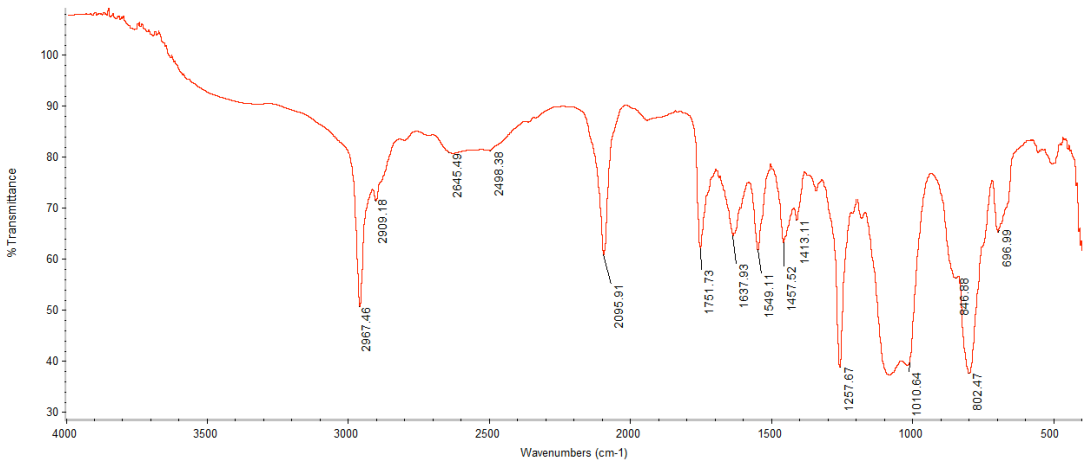


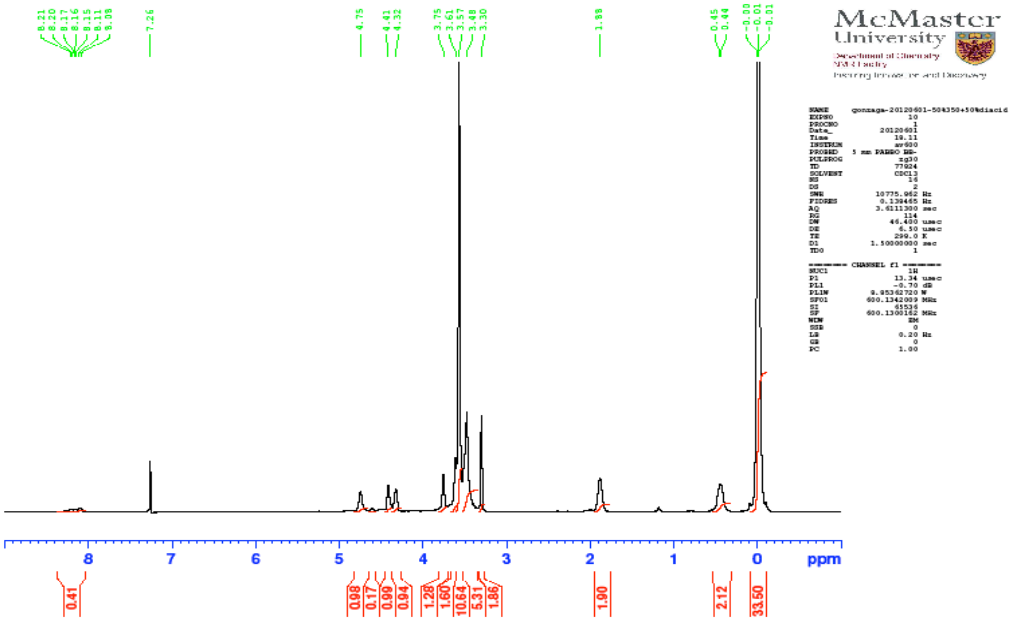
Polymer **16**: $^{13}$C NMR



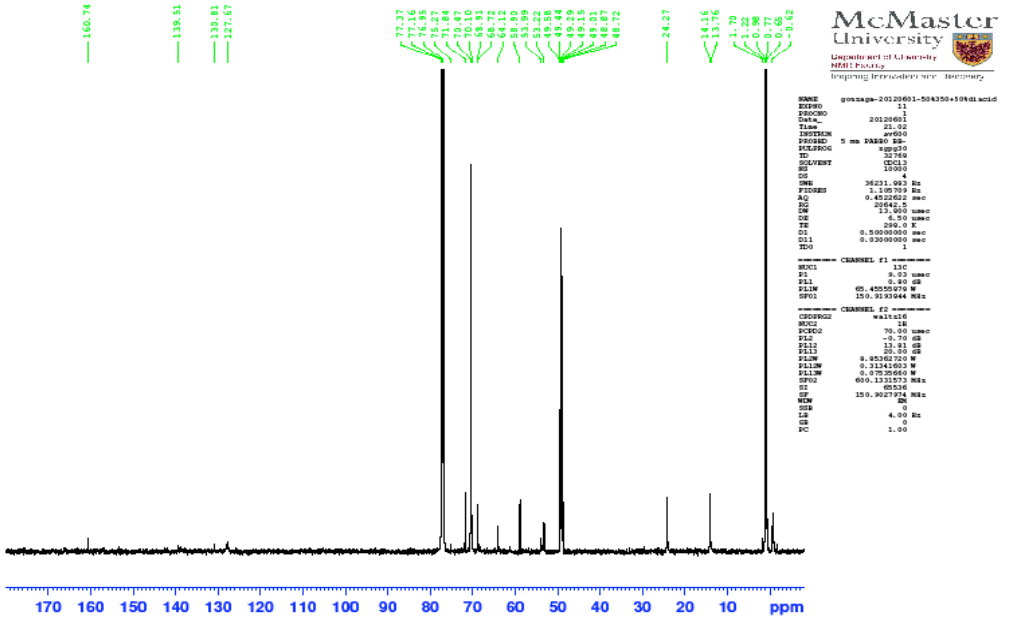

Polymer **16**: IR



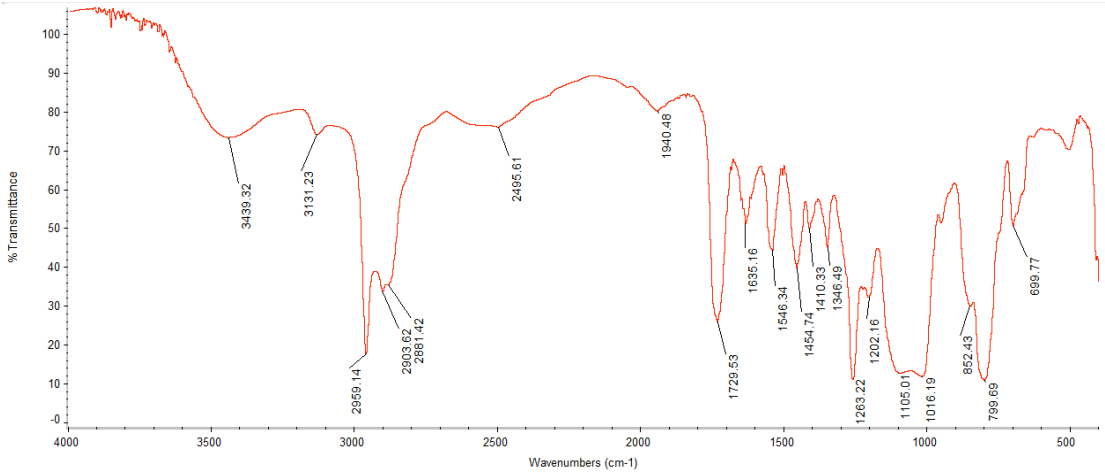
Polymers **17** and **19**: $^{1}$H NMR



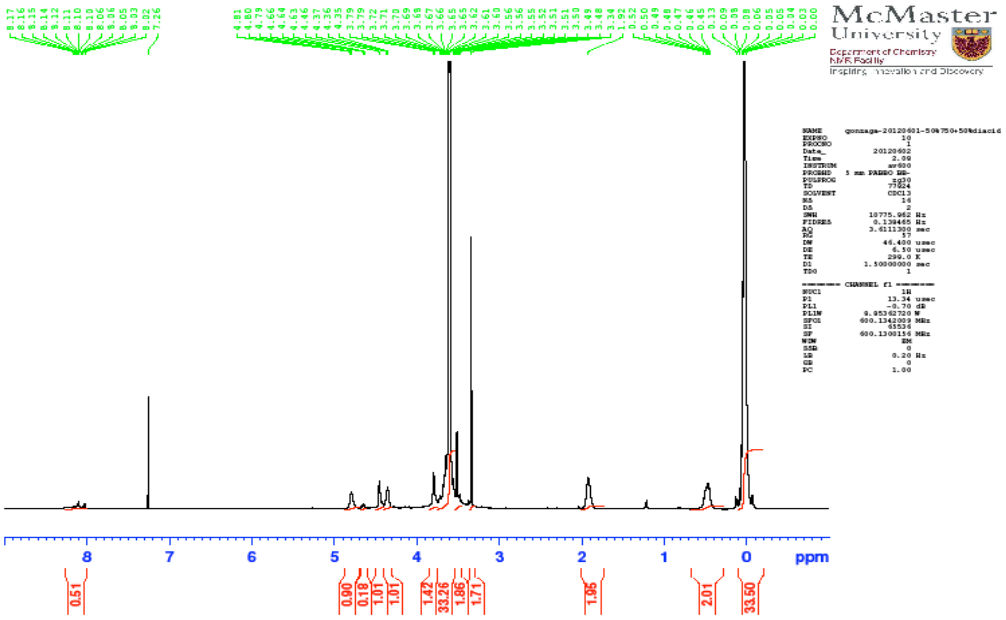

Polymers **17** and **19**: $^{13}$C NMR



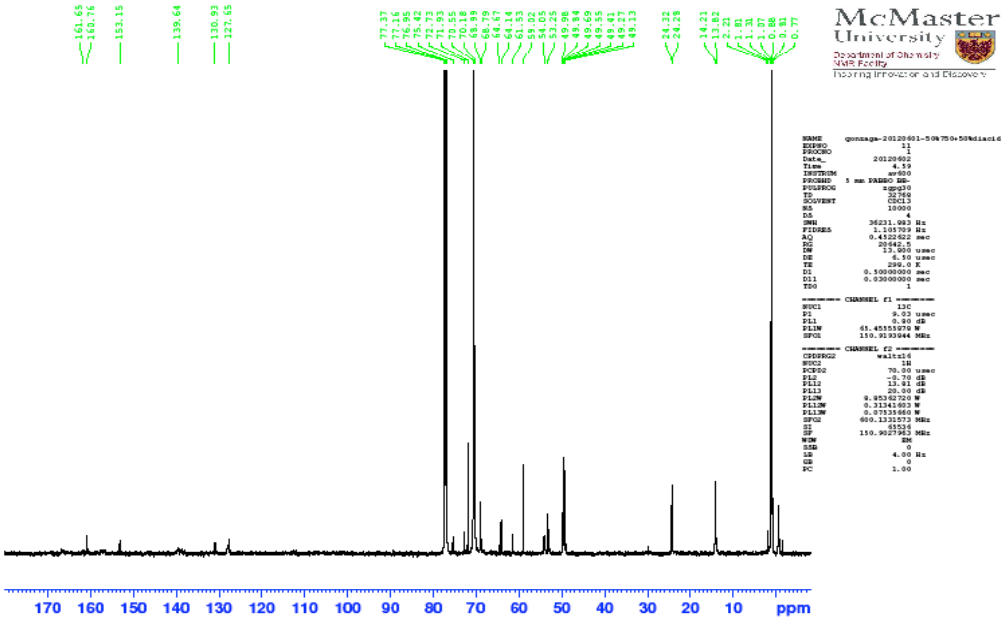
Polymers **17** and **19**: IR



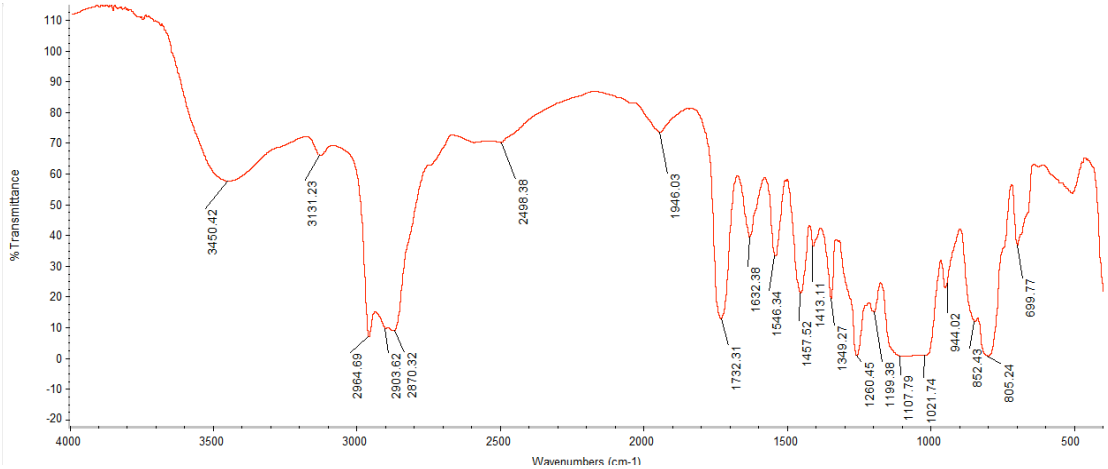

Polymer **18**: $^{1}$H NMR



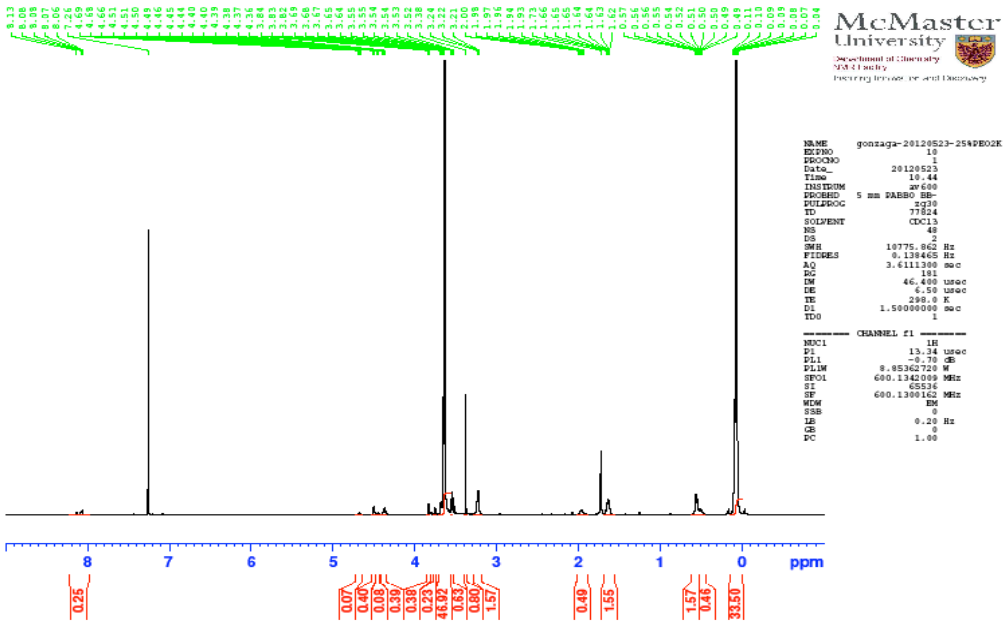
Polymer **18**: $^{13}$C NMR



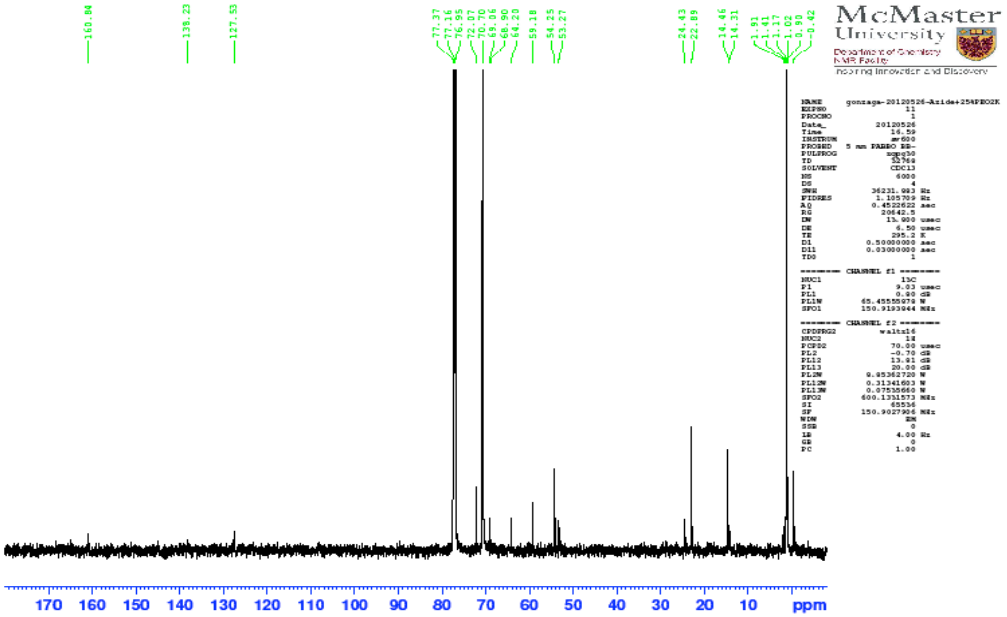

Polymer **18**: IR



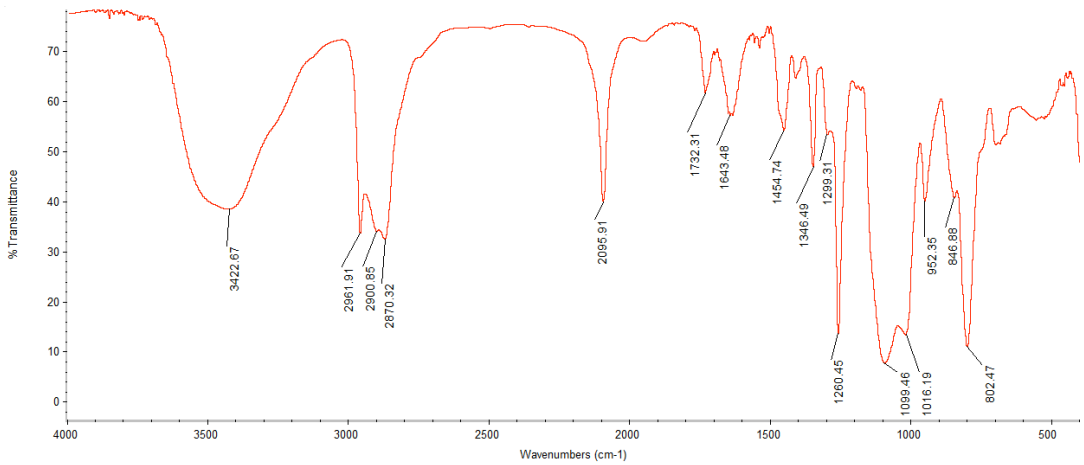
Polymer **20**: $^{1}$H NMR



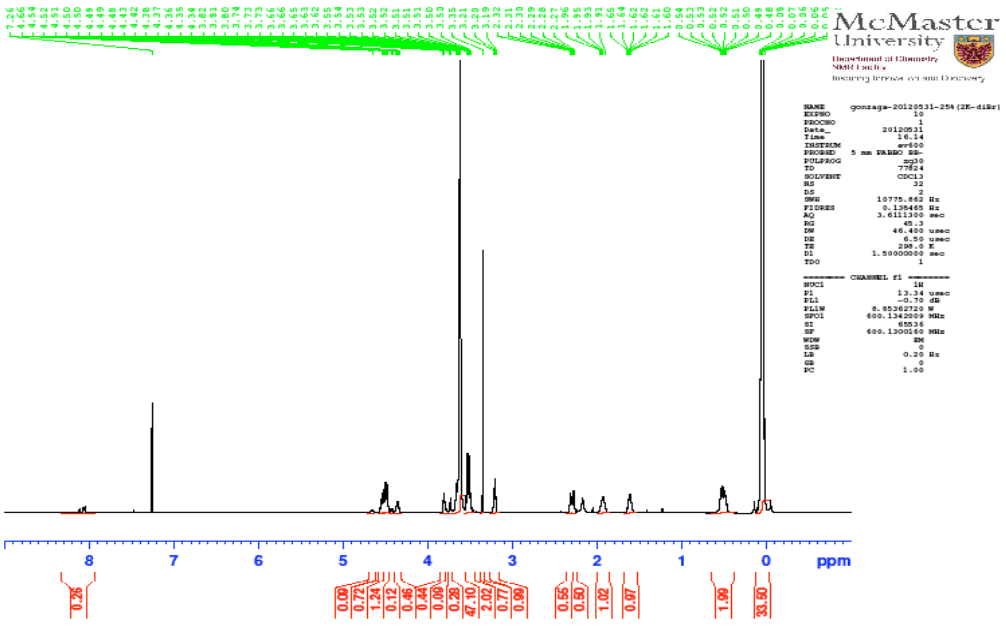

Polymer **20**: $^{13}$C NMR



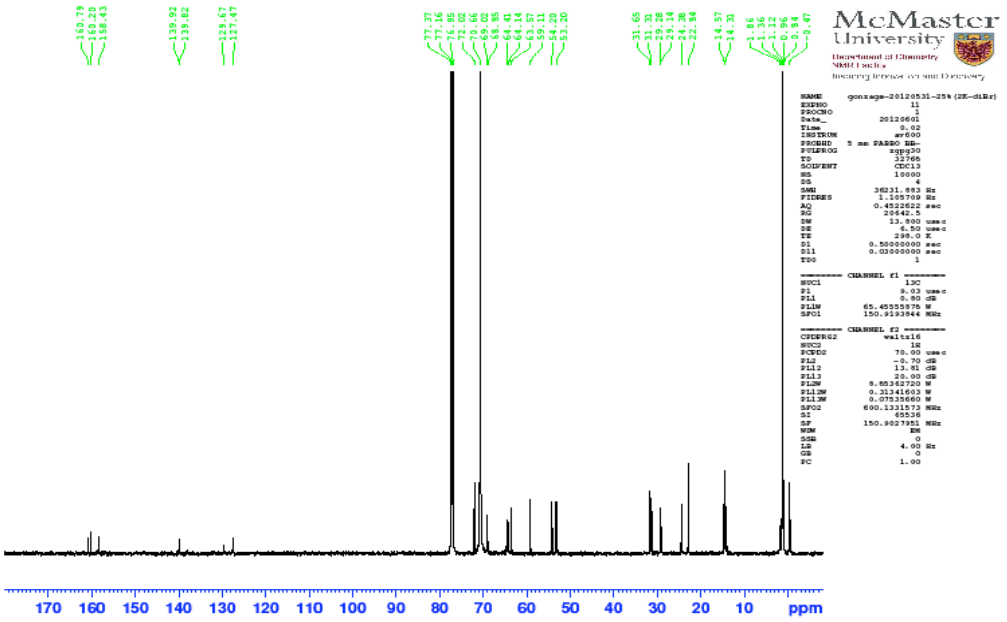
Polymer **20**: IR



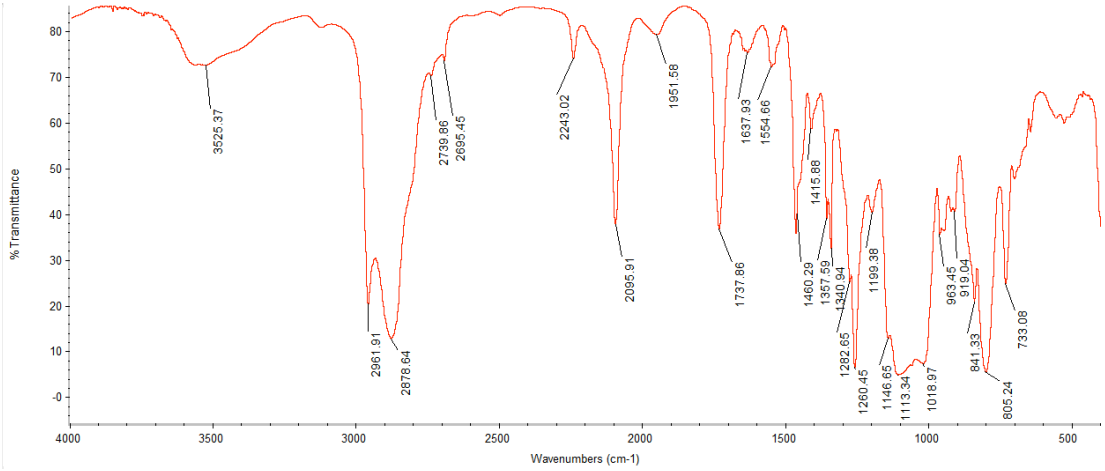

Polymer **21**: $^{1}$H NMR



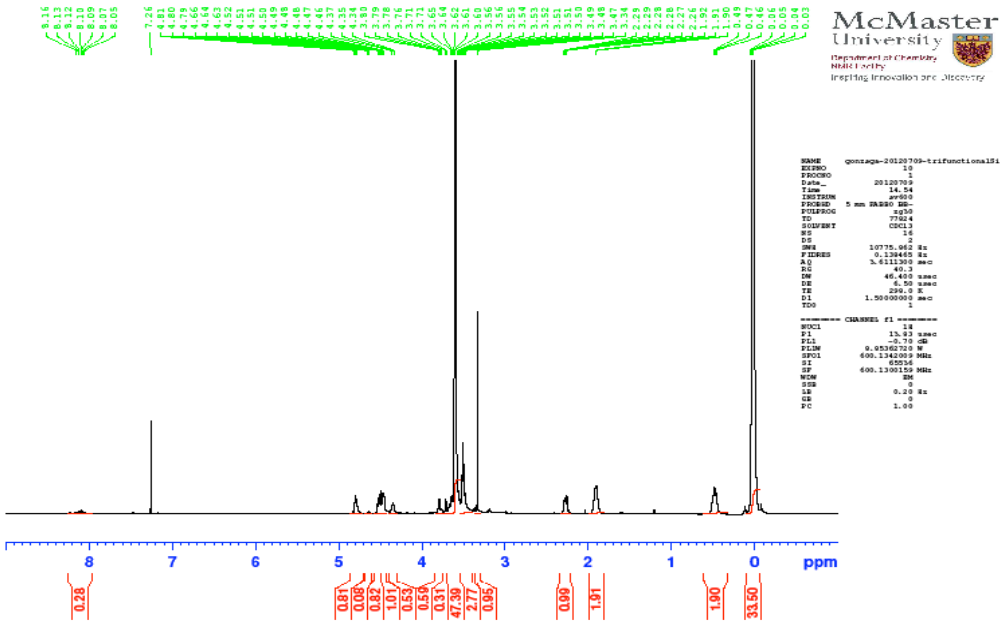
Polymer **21**: $^{13}$C NMR



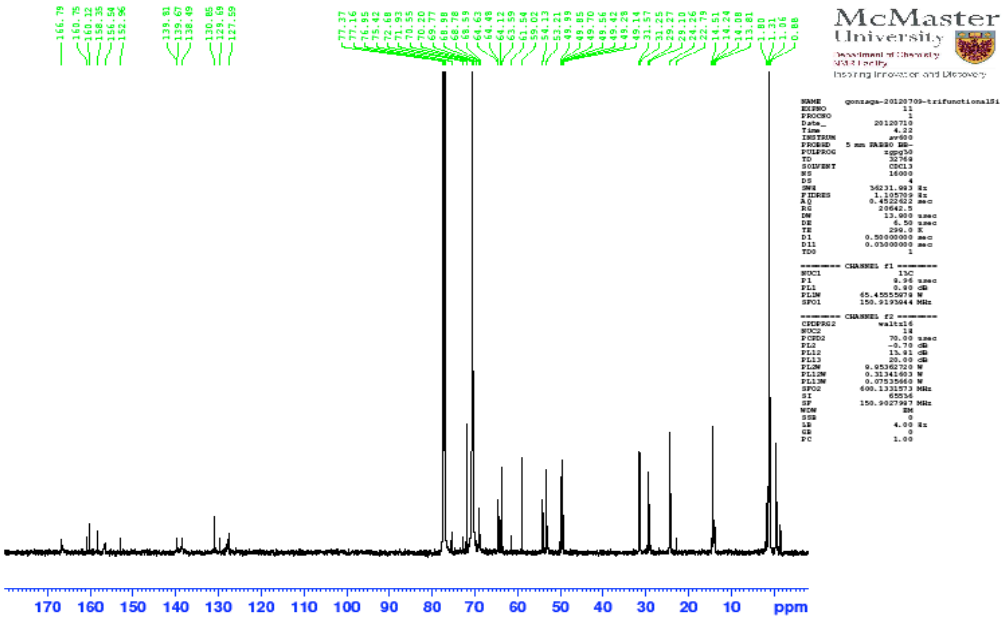

Polymer **21**: IR



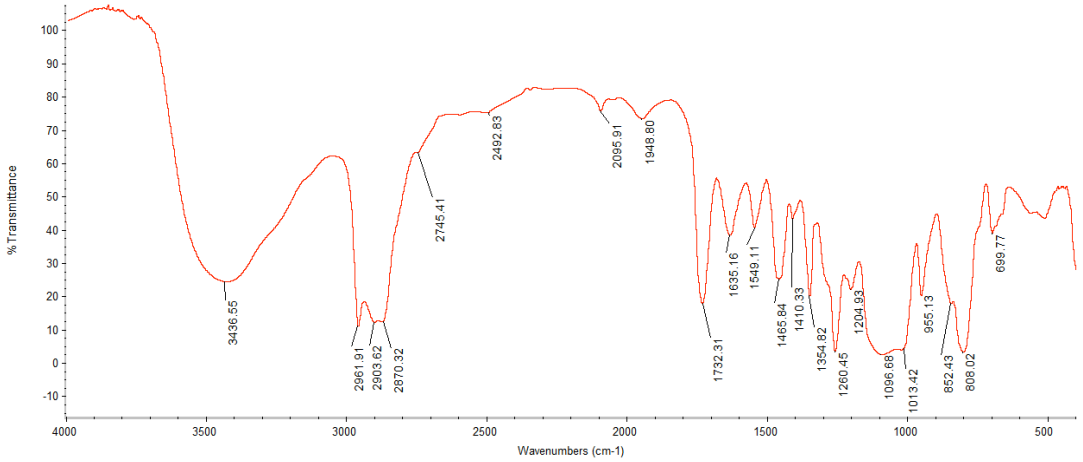
Polymer **22**: $^{1}$H NMR




Polymer **22**: $^{13}$C NMR



Polymer **22**: IR



# Chapter 9: Appendix 2

# Supporting Information for Chapter 4: Amphiphilic Elastomers from Metal-Free, Click Crosslinking of PEG-Grafted Silicone Surfactants

## 9.1 Experimental Synthesis

### 9.1.1 α,ω-Silicone propiolates

Propiolate-terminated disiloxane was synthesized from 1,3-bis(hydroxybutyl)tetramethyldisiloxane and propiolic acid. **2** (MW of 3,600 $g \cdot mol^{-1}$), **3** (MW 7,800 $g \cdot mol^{-1}$) and **4** (MW of 16,200 $g \cdot mol^{-1}$, MW determined by $^1H$ NMR), respectively. **2**: $^1H$ NMR ($CDCl_3$, 200 MHz, δ): 0.07 (s, 273H, $SiC\mathit{H_3}$); 0.56 (t, 4H, *J*=8.3 Hz, $SiC\mathit{H_2}CH_2CH_2CH_2$); 1.37 (m, 4H, $SiCH_2C\mathit{H_2}CH_2CH_2$); 1.68 (m, 4H, $SiCH_2CH_2C\mathit{H_2}CH_2$); 2.86 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, $SiCH_2CH_2CH_2C\mathit{H_2}$). **3**: $^1H$ NMR ($CDCl_3$, 200 MHz, δ): 0.07 (s, 605H, $SiC\mathit{H_3}$); 0.56 (t, 4H, *J*=8.3 Hz, $SiC\mathit{H_2}CH_2CH_2CH_2$); 1.37 (m, 4H, $SiCH_2C\mathit{H_2}CH_2CH_2$); 1.68 (m, 4H, $SiCH_2CH_2C\mathit{H_2}CH_2$); 2.86 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, $SiCH_2CH_2CH_2C\mathit{H_2}$). **4**: $^1H$ NMR ($CDCl_3$, 200 MHz, δ): 0.07 (s, 1295H, $SiC\mathit{H_3}$); 0.56 (t, 4H, *J*=8.3 Hz, $SiC\mathit{H_2}CH_2CH_2CH_2$); 1.37 (m, 4H, $SiCH_2C\mathit{H_2}CH_2CH_2$); 1.68 (m, 4H, $SiCH_2CH_2C\mathit{H_2}CH_2$); 2.86 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, $SiCH_2CH_2CH_2C\mathit{H_2}$).

### 9.1.2 PEG-monopropiolates

PEG mono-propiolate **5** (MW of 406 g·mol$^{-1}$, determined by $^1$H NMR), **6** (MW of 813 g·mol$^{-1}$), and **7** (MW of 2060 g·mol$^{-1}$)(MW determined by $^1$H NMR) were prepared from monomethoxy poly(ethylene oxide) according to a previously described procedure.[i] **5**: $^1$H NMR ($CDCl_3$, 600 MHz): δ 4.34 (t, 2 H's, -COOC**H$_2$**-, *J* = 6.0 Hz), 3.74 to 3.55 (m, ~ 29 H's, -OC**H$_2$**C**H$_2$**O-), 3.37 (s, 3 H's, $OCH_3$), 2.89 (s, broad, 1H, **H**CCCOO). **6**: $^1$H NMR ($CDCl_3$, 600 MHz): δ 4.34 (t, 2 H's, -COOC**H$_2$**-, *J* = 6.0 Hz), 3.74 to 3.55 (m, ~ 66 H's, -OC**H$_2$**C**H$_2$**O-), 3.37 (s, 3 H's, $OCH_3$), 2.89 (s, broad, 1H, **H**CCCOO). **7**: $^1$H NMR ($CDCl_3$, 600 MHz): δ 4.34 (t, 2 H's, -COOC**H$_2$**-, *J* = 6.0 Hz), 3.74 to 3.55 (m, ~ 180 H's, -OC**H$_2$**C**H$_2$**O-), 3.37 (s, 3 H's, $OCH_3$), 2.89 (s, broad, 1H, **H**CCCOO).

### 9.1.3 Medium molecular weight 6 PEG-modified (PEG-800 g·mol$^{-1}$) functional silicones *11*, *12* and *13*

**1** (1.07 g, 1.99 mmol of azide) and **6** (0.41 g, 0.50 mmol of alkyne, 0.25 eq.) were homogenized with 2 mL of chloroform to produce **11** (1.48 g, quant.).

**1** (0.87 g, 1.62 mmol of azide) and **6** (0.68 g, 0.84 mmol of alkyne, ~0.50 eq.) were reacted in 5 mL of toluene to yield **12** (1.55 g, quant.).

**1** (1.48 g, 3.00 mmol of azide) and **6** (1.83 g, 2.25 mmol of alkyne, ~0.75 eq.) were reacted in 5 mL of toluene to yield **13** (3.31 g, quant.; reaction required additional 12 h).

**11** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, SiC*H*$_3$, *11*), 0.47-0.51 (m, 0.5H, SiC*H*$_2$CH$_2$CH$_2$triazole, *1*), 0.53-0.59 (m, 1.5H, C*H*$_2$CH$_2$CH$_2$N$_3$, *1'*), 1.61-1.67 (m,

1.5H, $SiCH_2CH_2CH_2N_3$, *13*), 1.91-1.99 (m, 0.5H, $SiCH_2CH_2CH_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 1.5H, $CH_2N_3$, *14*), 3.37 (s, 0.75H, $-OCH_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, $CH_2OCH_3$, *8*), 3.64-3.65 (m, ~15H, $-OCH_2CH_2O-$, *10*), 3.68 (m, 0.5H, $CH_2CH_2OCH_3$, *7*), 3.79-3.84 (m, 0.5H, $-COOCH_2CH_2$, *6*), 4.35,4.66 (m, 0.5H total, $SiCH_2CH_2CH_2$triazole, *3A, 3B*), 4.45, 4.48 (0.5H total, $-COOCH_2-$, *5A, 5B*), 8.07- 8.15 (multiple singlets, 0.25H, *H*CCCOO,*4A, 4B*).

**12** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, $SiCH_3$, *11*), 0.47-0.51 (m, 1H, $SiCH_2CH_2CH_2$triazole, *1*), 0.53-0.59 (m, 1H, $CH_2CH_2CH_2N_3$, *1'*), 1.61-1.67 (m, 1H, $SiCH_2CH_2CH_2N_3$, *13*), 1.91-1.99 (m, 1H, $SiCH_2CH_2CH_2$triazole, *2*), 3.22 (t , *J*=6.0 Hz, 1H, $CH_2N_3$, *14*), 3.37 (s, 1.5H, $-OCH_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, $CH_2OCH_3$, *8*), 3.64-3.65 (m, ~29H, $-OCH_2CH_2O-$, *10*), 3.68 (m, 1H, $CH_2CH_2OCH_3$, *7*), 3.79-3.84 (m, 1H, $-COOCH_2CH_2$, *6*), 4.35,4.66 (m, 1H total, $SiCH_2CH_2CH_2$triazole, *3A, 3B*), 4.45, 4.48 (1H total, $-COOCH_2-$, *5A, 5B*), 8.07-8.15 (multiple singlets, 0.5H, *H*CCCOO,*4A, 4B*).

**13** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, $SiCH_3$, *11*), 0.47-0.51 (m, 1.5H, $SiCH_2CH_2CH_2$triazole, *1*), 0.53-0.59 (m, 0.5H, $CH_2CH_2CH_2N_3$, *1'*), 1.61-1.67 (m, 0.5H, $SiCH_2CH_2CH_2N_3$, *13*), 1.91-1.99 (m, 1.5H, $SiCH_2CH_2CH_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 0.5H, $CH_2N_3$, *14*), 3.37 (s, 2.25H, $-OCH_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1.5H, $CH_2OCH_3$, *8*), 3.64-3.65 (m, ~34H, $-OCH_2CH_2O-$, *10*), 3.68 (m, 1.5H, $CH_2CH_2OCH_3$, *7*), 3.79-3.84 (m, 1.5H, $-COOCH_2CH_2$, *6*), 4.35,4.66 (m, 1.5H

total, $SiCH_2CH_2CH_2$triazole, *3A, 3B*), 4.45, 4.48 (1.5H total, -$COOCH_2$ -, *5A, 5B*), 8.07- 8.15 (multiple singlets, 0.75H, *H*CCCOO,*4A, 4B*).

The same procedure was used to make reactive functional silicone **14** from higher molecular weight PEG **7**, PEG 2060 g·mol$^{-1}$) functional silicones polymers **1** (1.21 g, 2.44 mmol) and **7** (1.27 g, 0.62 mmol, 0.25 eq.) yielding **14** (2.48 g, quant.).

**14** *(Major isomer 1,4 (A ~ 80%), Minor isomer 1,5 (B ~20%):* $^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.05 to 0.09 (s, 31.9H, $SiCH_3$, *11*), 0.47-0.51 (m, 0.5H, $SiCH_2CH_2CH_2$triazole, *1*), 0.53-0.59 (m, 1.5H, $CH_2CH_2CH_2N_3$, *1'*), 1.61-1.67 (m, 1.5H, $SiCH_2CH_2CH_2N_3$, *13*), 1.91-1.99 (m, 0.5H, $SiCH_2CH_2CH_2$triazole, *2*), 3.22 (t, *J*=6.0 Hz, 1.5H, $CH_2N_3$, *14*), 3.37 (s, 0.75H, -$OCH_3$, *9*), 3.55 (t, *J*=6.0 Hz, 1H, $CH_2OCH_3$, *8*), 3.64-3.65 (m, ~43H, -$OCH_2CH_2O$-, *10*), 3.68 (m, 0.5H, $CH_2CH_2OCH_3$, *7*), 3.79-3.84 (m, 0.5H, -$COOCH_2CH_2$, *6*), 4.35,4.66 (m, 0.5H total, $SiCH_2CH_2CH_2$triazole, *3A, 3B*), 4.45, 4.48 (0.5H total, -$COOCH_2$ -, *5A, 5B*), 8.07- 8.15 (multiple singlets, 0.25H, *H*CCCOO,*4A, 4B*).

### 9.1.4 Synthesis of Elastomers *15*, *16*, *17*: PEG *5* (400 g·mol$^{-1}$) functional networks crosslinked with PDMS *3* (7,800 g·mol$^{-1}$)

The materials were characterized by; Shore OO hardness, IR, rheology; **15** and **16** were additionally characterized by water contact angle and swellability in water (for images, see Table 9.1S).

### 9.1.5 Synthesis of Elastomers *18*, *19*, *20*: PEG 5 (400g·mol$^{-1}$) functional networks crosslinked with PDMS 4 (16,200 g·mol$^{-1}$)

**18**: **8** (0.48 g, 0.17 mmol of alkynyl PEG, 0.59 mmol of azido groups) and **4** (4.76 g, 0.59 mmol of alkyne) were reacted (6 mL of toluene and 3 mL $CHCl_3$) to produce elastomer **18** (5.24 g).

**19**: **9** (0.74 g, 0.49 mmol of alkynyl PEG, 0.51 mmol of azido groups) and **4** (4.00 g, 0.49 mmol of alkyne) were reacted (5 mL of toluene and 5 mL $CHCl_3$) to produce elastomer **19** (4.74 g).

**20**: **10** (1.72 g, 1.52 mmol of alkynyl PEG, 0.53 mmol of azido groups) and **4** (4.26 g, 0.53 mmol of alkyne) were reacted (5 mL of toluene and 5 mL $CHCl_3$) to produce elastomer **20** (5.98 g).

The materials were characterized by Shore OO hardness, IR, rheology, water contact angle and swellability in water (for images, see Table 9.1S).

### 9.1.6 Synthesis of PEG 6 (800 g·mol$^{-1}$)-based functional networks

The polymeric/solvent mixtures were sealed, and allowed to pre-cure with stirring at 60 °C for 2 h prior to being cured at 70 °C for 24 h, and 90 °C for 1 h.

***Crosslinked with PDMS* 3 *(7800 g·mol$^{-1}$)***

**21**: **11** (0.93 g, 0.31 mmol alkynyl PEG, 0.96 mmol azido groups) and **3** (3.76 g, 0.96 mmol alkynyl groups) were reacted (3 mL of toluene and 5 mL $CHCl_3$) to produce **21** (4.69 g).

**22**: **12** (1.55 g, 0.84 mmol alkynyl PEG, 0.78 mmol azido groups) and **3** (3.13 g, 0.80 mmol alkynyl groups) were reacted (10 mL of toluene) to produce **22** (4.68 g).

***Crosslinked with PDMS 4 (16200 g·mol$^{-1}$)***

**23**: **11** (0.51 g, 0.17 mmol alkynyl PEG, 0.51 mmol azido groups) and **4** (3.94 g, 0.51 mmol alkynyl groups) were reacted (10 mL of toluene and 2 mL $CHCl_3$) to produce **23** (4.45 g).

**24**: **12** (0.85 g, 0.44 mmol alkynyl PEG, 0.47 mmol azido groups) and **4** (3.52 g, 0.47 mmol alkynyl groups) were reacted (6 mL of toluene) to produce **24** (4.37 g).

The materials were characterized by Shore OO hardness, IR, water contact angle and swellability in water (for images, see Table 9.1S).

### 9.1.7 Synthesis of Elastomers *25*, *26*, *27*: PEG *5* (400 g·mol$^{-1}$)- functional networks crosslinked with PDMS *2* (3600 g·mol$^{-1}$)

**28**: **11** (2.12 g, 0.76 mmol alkynyl PEG, 2.27 mmol azido groups) and **2** (2.08 g, 1.15 mmol) were mixed (1 mL toluene + 3 mL $CHCl_3$) to produce elastomer **28** (4.20 g).

**29**: **14** (2.48 g, 0.62 mmol of alkynyl PEG, 1.63 mmol of azido groups) and **2** (1.71 g, 0.83 mmol of alkyne) were mixed (6 mL toluene + 5 mL $CHCl_3$) to produce **29**, 4.19 g).

The materials were characterized by Shore OO hardness, IR, rheology, water contact angle and swellability in water (for images, see Table 9.1S).

### 9.1.8 Example Elastomer with α,ω- PEG

#### 9.1.8.1 Synthesis of α,ω-PEG propiolates, 30

The synthetic process for dipropiolate terminated poly(ethylene glycol) was modified from Gonzaga et al.[i] Propiolic acid (14.52 g, 207 mmol), toluene (25 mL), and a catalytic amount of *p*-toluenesulfonic acid (0.05 g, 2.6 mmol) were

successively added in a round-bottomed flask containing poly(ethylene glycol) (aver. mol wt: 370, 10.27 g, 55 mmol of -OH). The flask, equipped with a Dean Stark apparatus, was heated with azeotropic removal of water. Completion of the reaction was monitored by $^1$H NMR spectroscopy (about 40 h). The solution was then cooled to room temperature, and washed three times with an aqueous potassium carbonate solution (50 mL). The PEG formed a separate phase and the crude brown product was directly loaded onto a chromatography column packed with silica gel. Elution started with pure dichloromethane, then increasing amounts of methanol were added to the eluent (up to 5% v:v). The fractions containing the propiolate ester were combined, evaporated under reduced pressure to afford pure propiolate-terminated poly(ethylene oxide) (7.91 g, 60% yield) as a yellow oil.

$^1$H NMR ($CDCl_3$, 600 MHz): δ = 4.23 (t, J = 6.0 Hz, 4H; COOC**H**$_2$-), 3.63 (t, J = 6.0 Hz, 4H; COOCH$_2$C**H**$_2$-), 3.57 to 3.54 (m, ≈ 25H; -C**H**$_2$C**H**$_2$-), 3.05 to 3.02 (s, broad, 2H; **H**CCCOO).

**9.1.8.2 Elastomer with α,ω-Silicone and α,ω-PEG propiolates, 31**

Compounds **1** (1.02 g, 2.00 mmol azide), **30** (0.24 g, 1.01 mmol alkyne) and **2** (0.73 g, 0.36 mmol alkyne) were homogenized with 1000 μL of $CHCl_3$ and 400 μL of toluene in a glass scintillation vial and placed to cure in a 60 °C oven. After 2 h, the polymers were mixed again and left to cure for another 18 h. At this time, the polymers had cured into a firm, slightly opaque yellow elastomer; the temperature was increased to 90 °C for an additional 12 h to ensure complete

crosslinking. The elastomer was cooled to room temperature and removed from the curing vessel and ¼ inch diameter circular disks were punched for contact angle measurements. Water contact angles were measured in triplicate for the elastomer from air (62±2°) and after soaking in deionized water for 24 h (60±2°).

**9.2 Protein Adsorption**

The adsorption on silicone elastomers of hen egg lysozyme (HEL; Sigma-Aldrich, St. Louis, MO) and bovine serum albumin (BSA; Sigma-Aldrich), respectively, were investigated by radiolabeling. HEL and BSA were conjugated to $I^{125}$ using the iodine monochloride method, as previously described.[ii,iii] Briefly, radiolabeled protein solution was passed through two columns packed with AG 1-X4 (Bio-Rad, Hercules, CA) to remove unbound $I^{125}$; the columns were subsequently rinsed with phosphate buffered saline (PBS) to ensure all labeled protein was removed. Free iodide was determined using trichloroacetic acid precipitation, and was found to be less than 1.1% for both proteins. The materials, having a surface area of 0.633 $cm^2$, were then incubated for 3 h in a 1 mg/mL solution of either HEL or BSA, which were comprised of 10% radiolabeled protein and 90% unlabeled protein. They were subsequently rinsed in PBS three times, for 5 minutes each time, and counted using an automated gamma counter (1470 Wallac Wizard; PerkinElmer, Woodbridge, ON). Adsorption of protein was measured using 4 discs for each protein solution. The radioactivity on each material was converted into micrograms of protein per $cm^2$ for quantification.

## 9.3 Additional Results

### 9.3.1 Atomic Force Microscopy

Increased surface roughness as a result of water sorption to the surface of the silicone elastomers can influence observed contact angle values (rough surfaces tend to have higher contact angles).[iv] The elastomers/gels were soaked in water for several days, and some did have appreciable water uptake, which could contribute to the to the higher than anticipated contact angles. Even soaking normal silicone elastomers in water can lead to enhanced roughness.[v] The elastomers described herein, synthesized from fluid polymer precursors, had smooth surfaces and low surface roughness in air. However, after swelling in water, atomic force microscopy demonstrated small increases in surface roughness, but not enough to significantly affect the contact angle. Elastomer **22** had a surface roughness ($R_q$) = 6.7 and elastomer **25** $R_q$ = 1.9 dry; after soaking in water the $R_q$ values increased to 12.5 and 15.1, respectively. The water contact angles for dry **22** and **25** changed from 78±4° and 34±3° at 300 s, respectively, while the water soaked samples exhibited values of 76±6° and 50 ±2°.

Compound **25** is of particular interest because of its highly responsive nature. The compound was made by reacting 25% of the available azido groups with PEG **5** (350 g/mol) and crosslinking with the shorter PDMS **2** (3,600 g/mol), leaving residual azide groups. The change in contact angle over time was rapid and greater than any of the other compounds prepared, both from a dry and wet state. This result was initially counterintuitive because many of the other materials, **22** for example, have more PEG, both with respect to graft density and PEG chain

length and were expected to be more highly wettability. However, we and others have observed analogous outcomes for PEG-containing networks: the key is PEG chain length.

### 9.3.2 Rheology

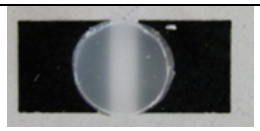
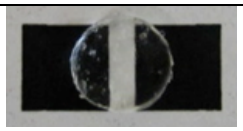
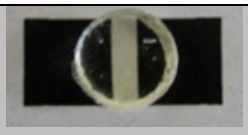
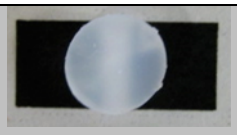
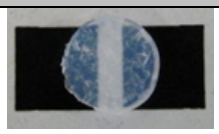
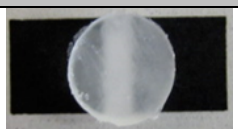
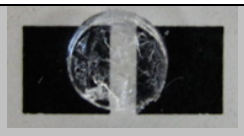
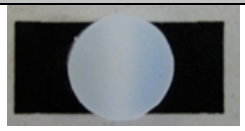
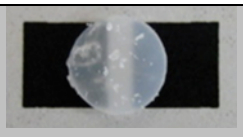
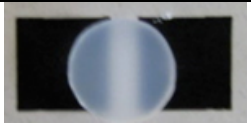
Generally, G' decreased with increasing alkynyl-PDMS chain length. As anticipated, a more flexible network resulted, reducing the stored elastic energy: e.g., **15** with the PDMS length ~8,000 $g \cdot mol^{-1}$ had a G' of 94 kPa compared to elastomer **18** with the PDMS length ~16,000 $g \cdot mol^{-1}$ whose G' was 54 kPa at 0.1 Hz.

When increasing the PEG length for elastomers/gels created with the same crosslink density (i.e., 25, 50 or 75% of the azido groups reacted) while maintaining the same alkynyl-PDMS linker length, an increase in the storage modulus was observed: e.g., going from **15** made with ~400 $g \cdot mol^{-1}$ PEG to **21** made with ~800 $g \cdot mol^{-1}$ PEG, the modulus increased from 94 kPa to 115 kPa, suggesting the PEG interactions (crystallization) adds to the elastic energy in the material.


A B

Figure 9.1S: Photographs of PEG/silicone elastomers produced using the Huisgen reaction: A: **22** (left), B: **23** (right)

Table 9.1S: Images of Rubbers

| | | | |
|---|---|---|---|
| 15 |  | 24 |  |
| 16 |  | **25** |  |
| 17 |  | **26** |  |
| 18 |  | **27** |  |
| 19 |  | **28** |  |
| 20 |  | **29** |  |
| 21 |  | **30** |  |
| 22 |  | **31** |  |
| 23 |  | | |

### 9.3.3 Aqueous Extractables

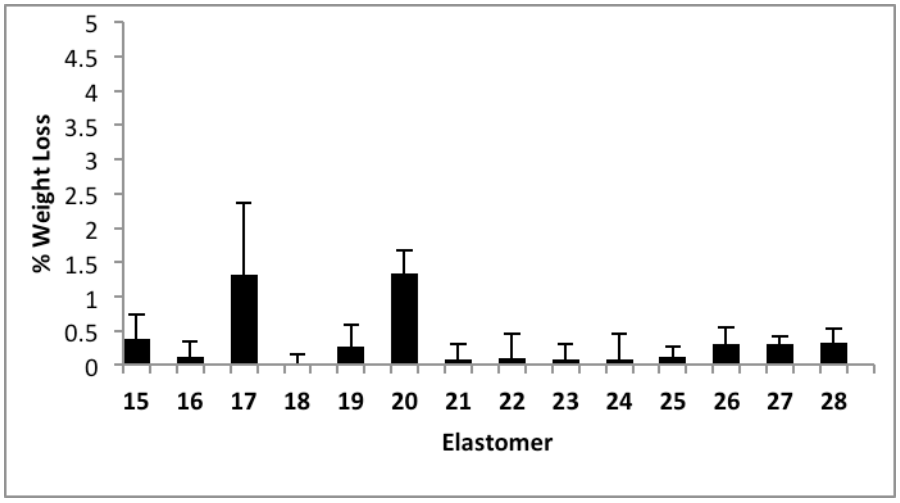



Figure 9.2S: Aqueous extractables from the elastomers.

### 9.3.4 Organic Extractables

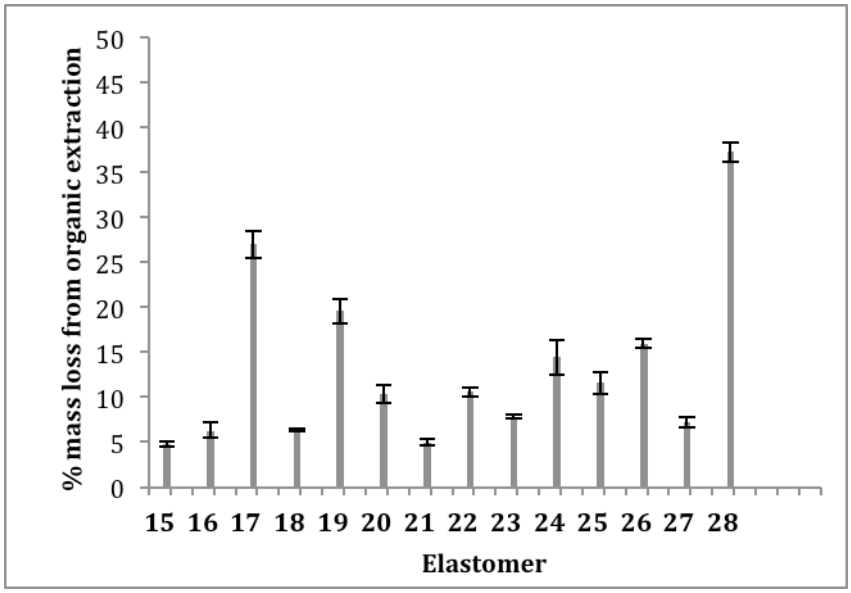



Figure 9.3S: Organic extractables from the elastomers.

### 9.3.5 Water Uptake

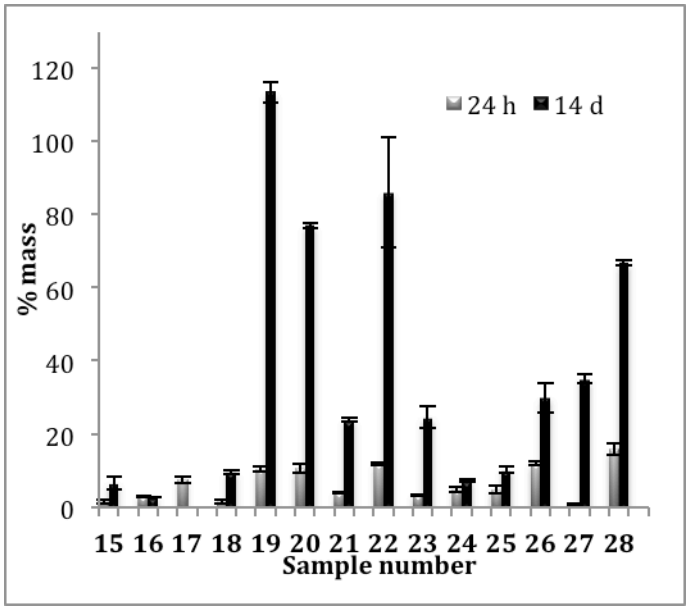



Figure 9.5S: Water uptake (wt%) at 24 hours and 14 days

### 9.3.6 AFM of Select Elastomers

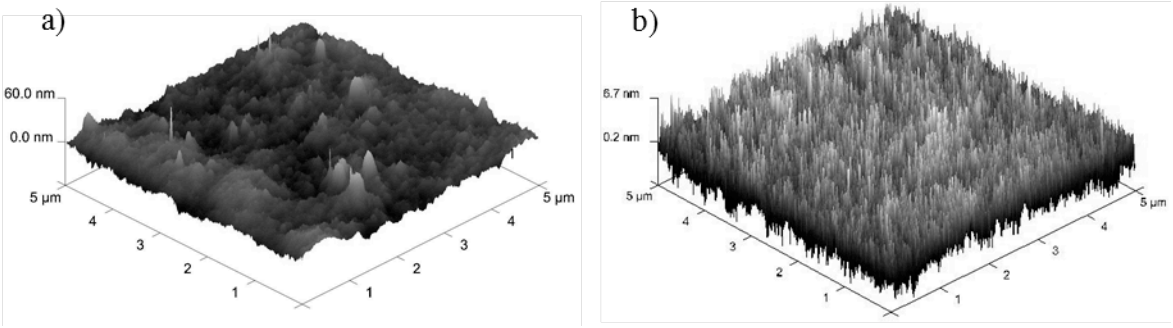



Figure 9.6S: AFM of rubbers **22** (a) $R_q$ = 6.7 and **25** (b) $R_q$ = 1.9

### 9.3.7 Rheological Data

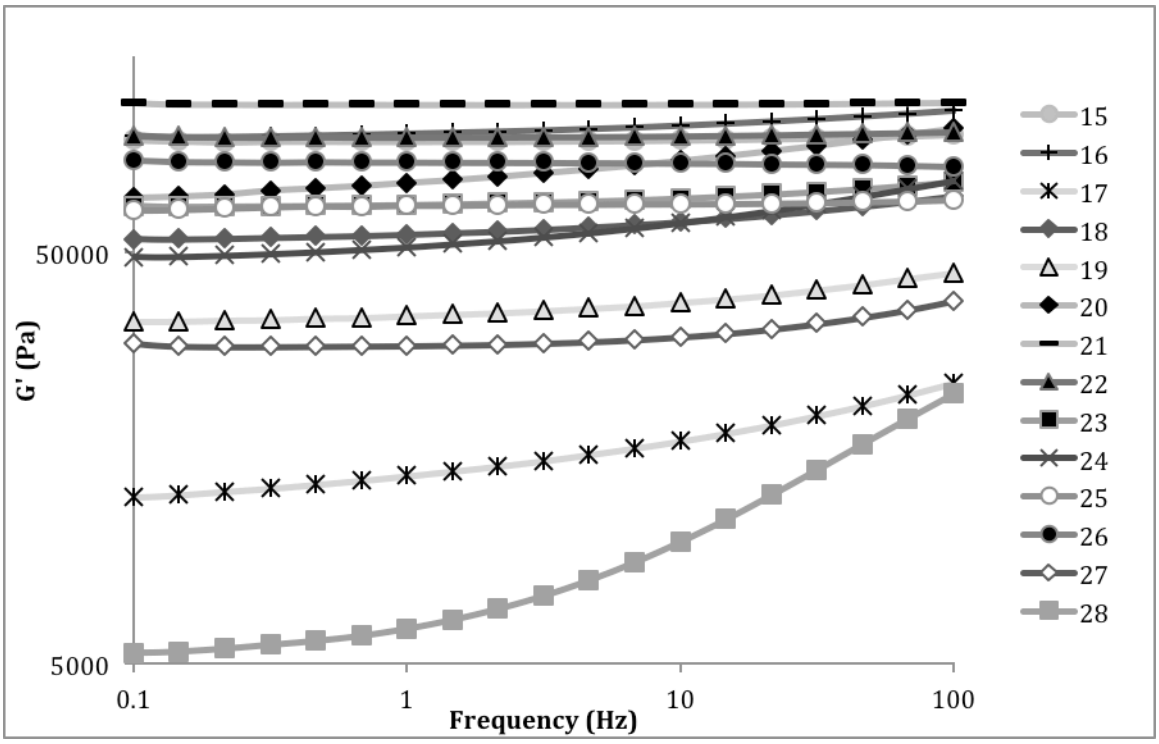
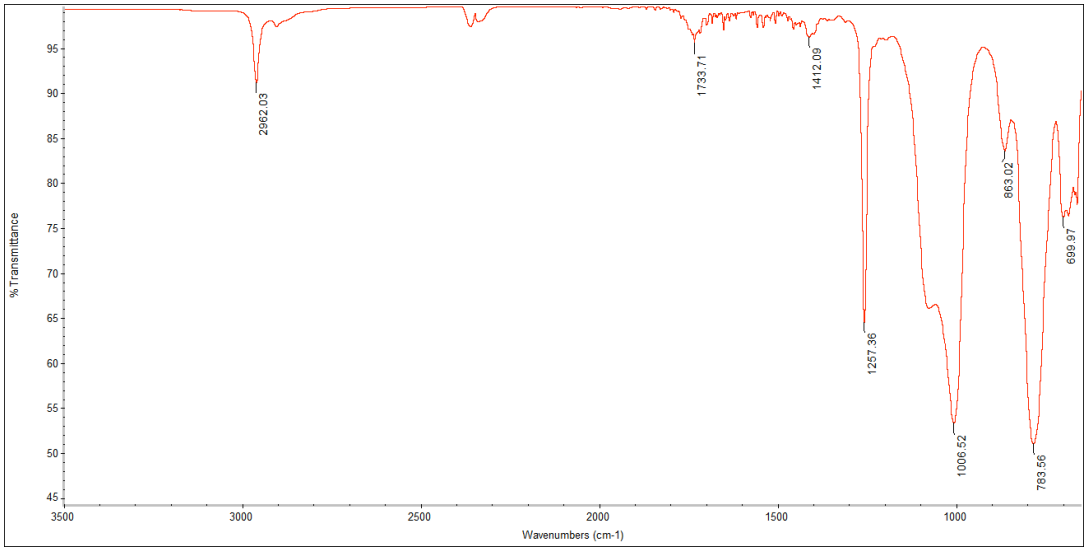



Figure 9.7S: Storage modulus of elastomers/gels

### 9.3.8 Infrared Spectra

**15**

IR (ATR) ν = 2962, 1733, 1412, 1257, 1006, 863, 783, 699 $cm^{-1}$



**16**

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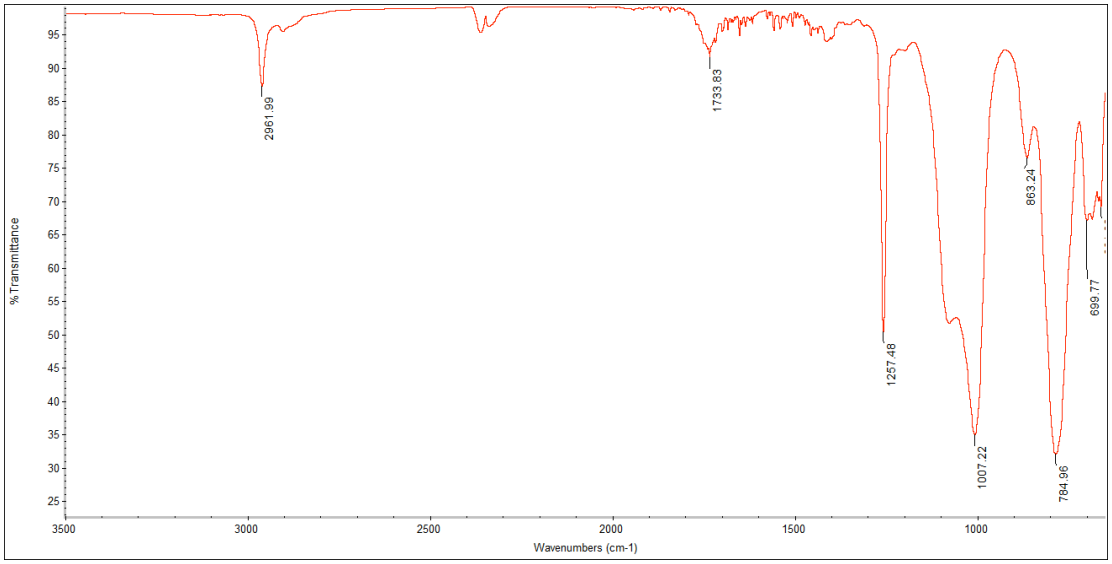


**17**

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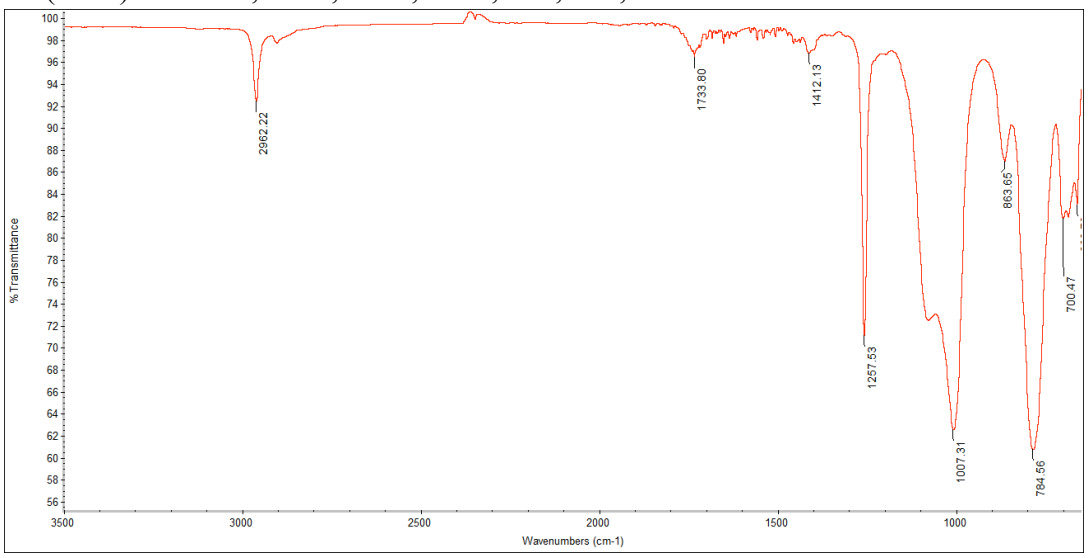
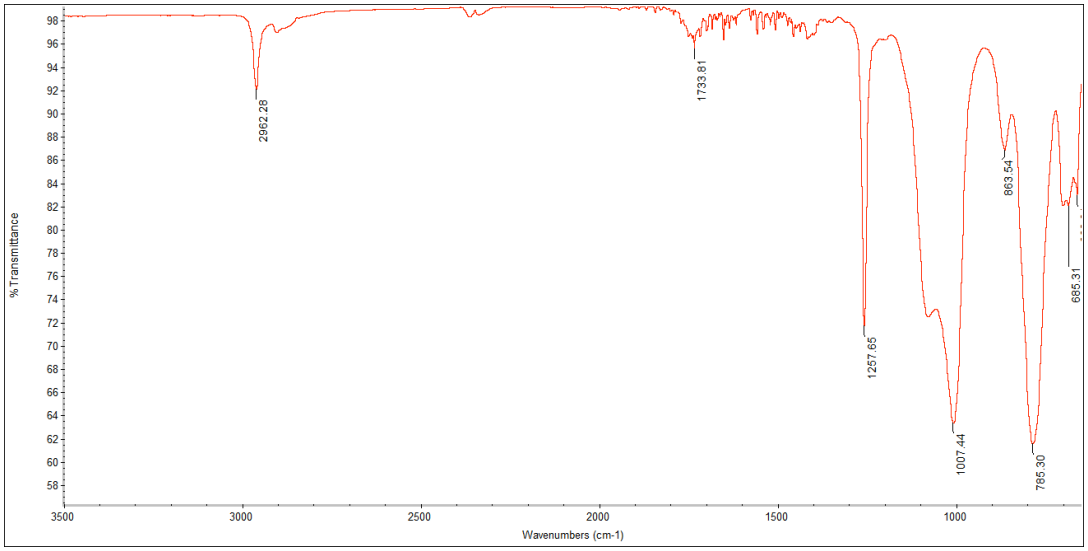


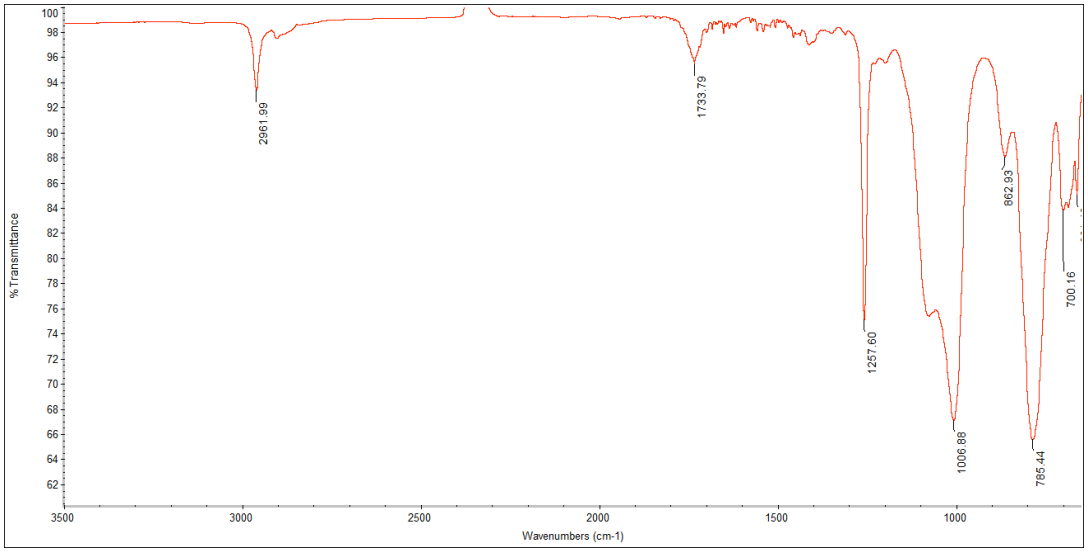
**19**

IR (ATR) ν = 2962, 1734, 1257, 1007, 863, 785, 685 $cm^{-1}$



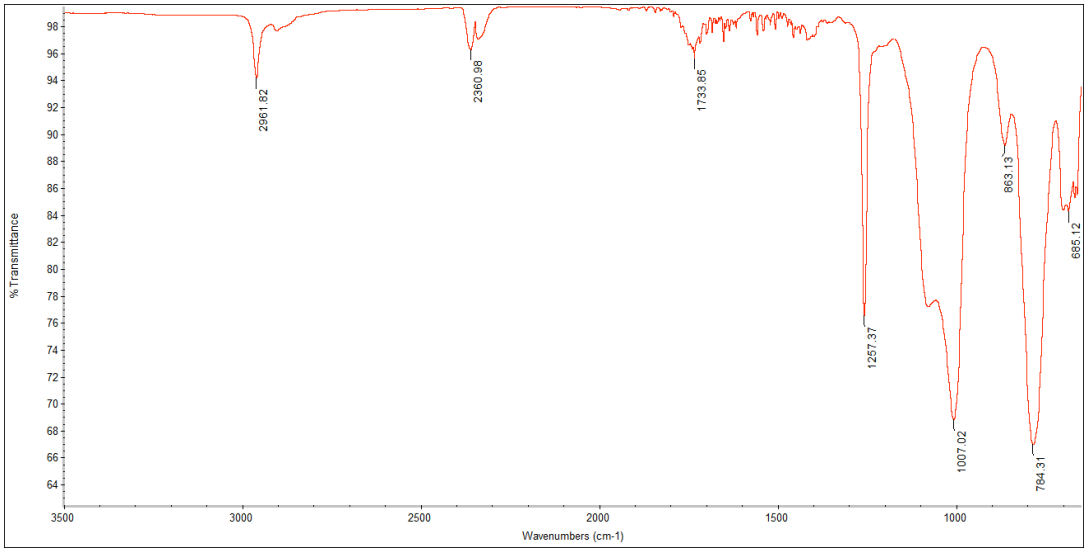

**20**

IR (ATR) ν = 2962, 1734, 1257, 1007, 863, 785, 700 $cm^{-1}$



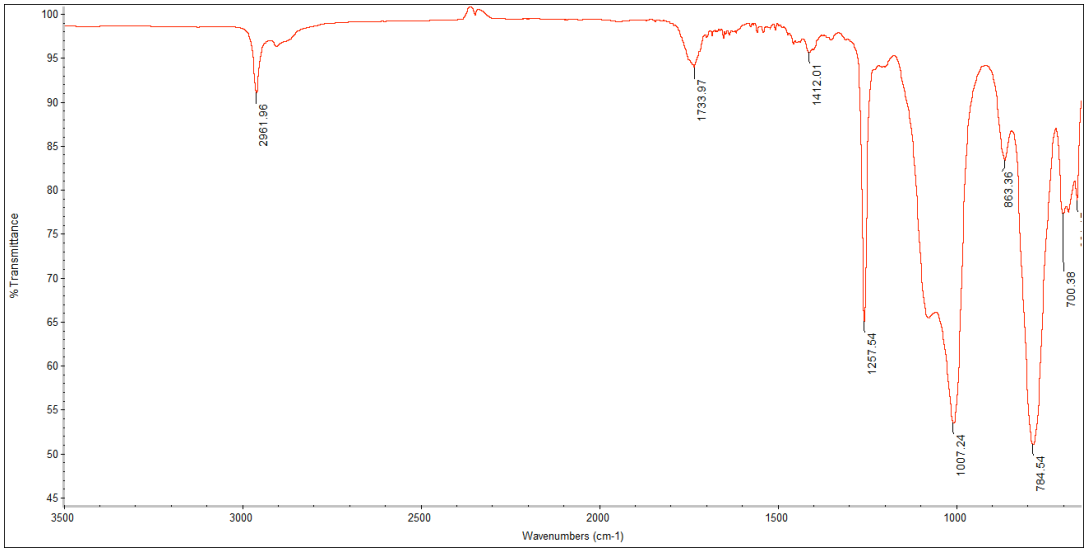
**21**

IR (ATR) ν = 2962, 1734, 1257, 1007, 863, 785, 685 $cm^{-1}$



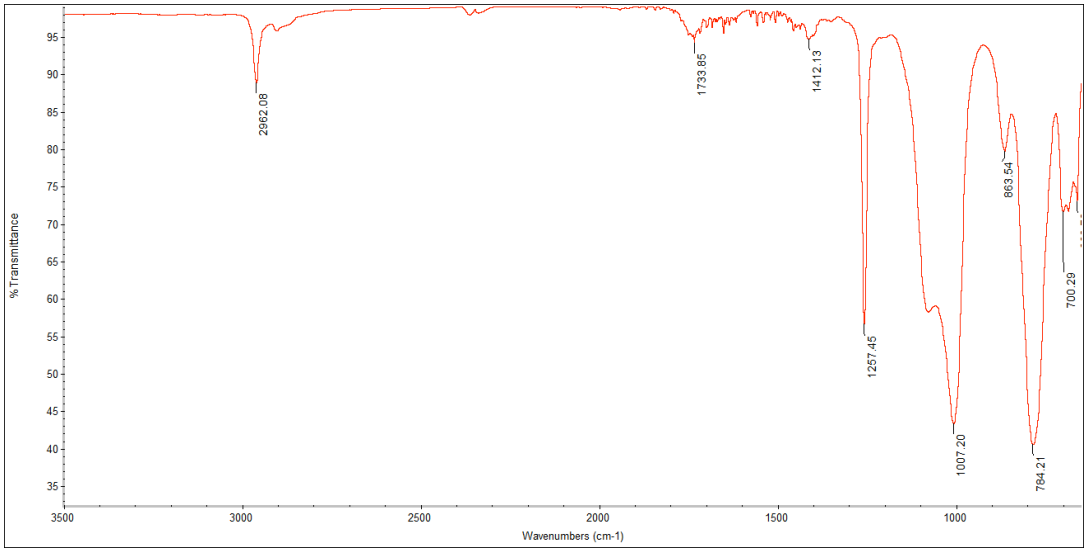

**22**

IR (ATR) ν = 2962, 1734, 1412, 1257, 1007, 863, 785, 700 $cm^{-1}$



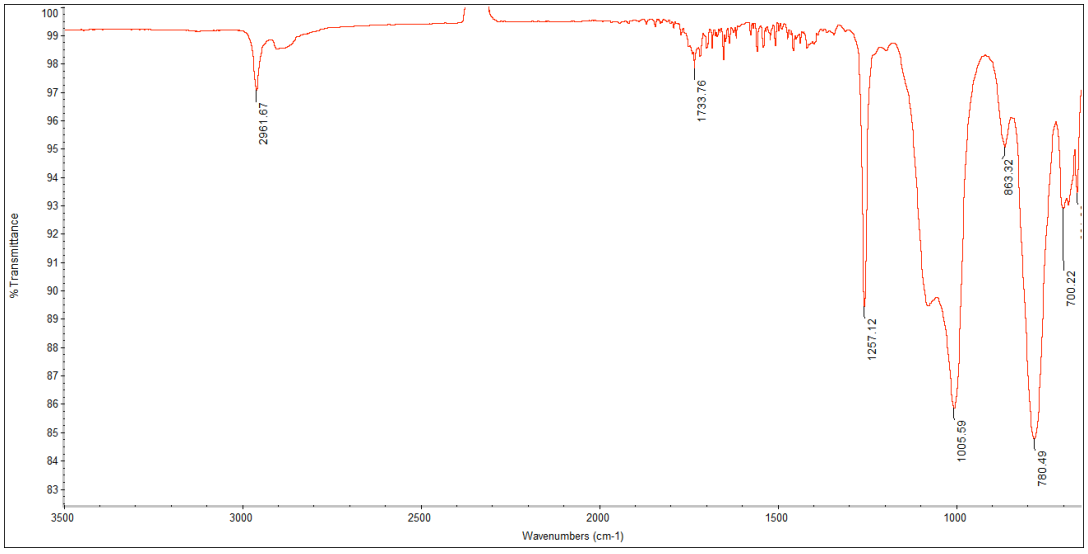
**23**

IR (ATR) ν = 2962, 1734, 1412, 1257, 1007, 863, 785, 700 $cm^{-1}$



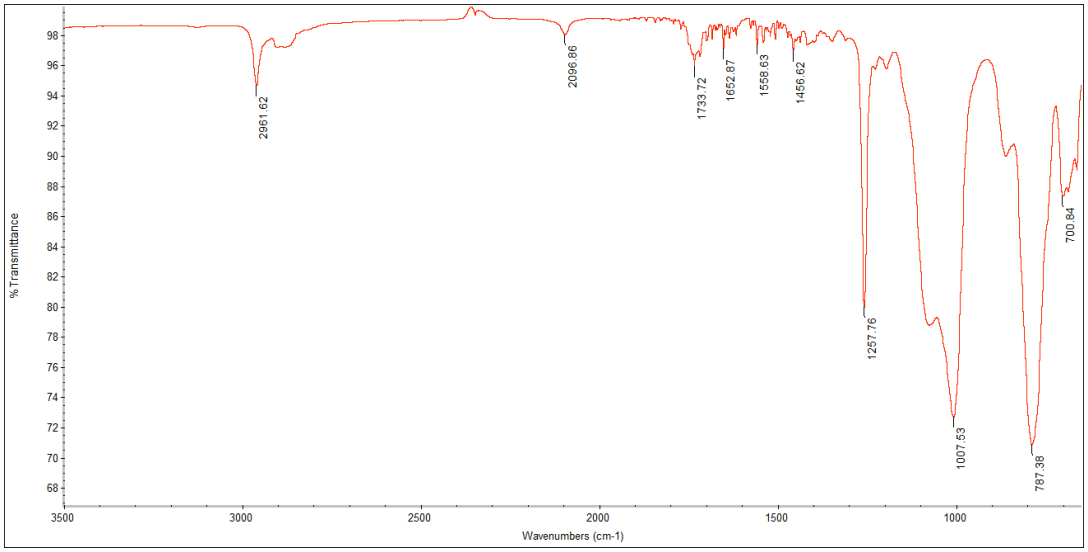

**24**

IR (ATR) ν = 2962, 1734, 1257, 1006, 863, 780, 700 $cm^{-1}$



**25**

IR (ATR) ν = 2962, 2097, 1734, 1257, 1006, 863, 780, 700 $cm^{-1}$




**26**

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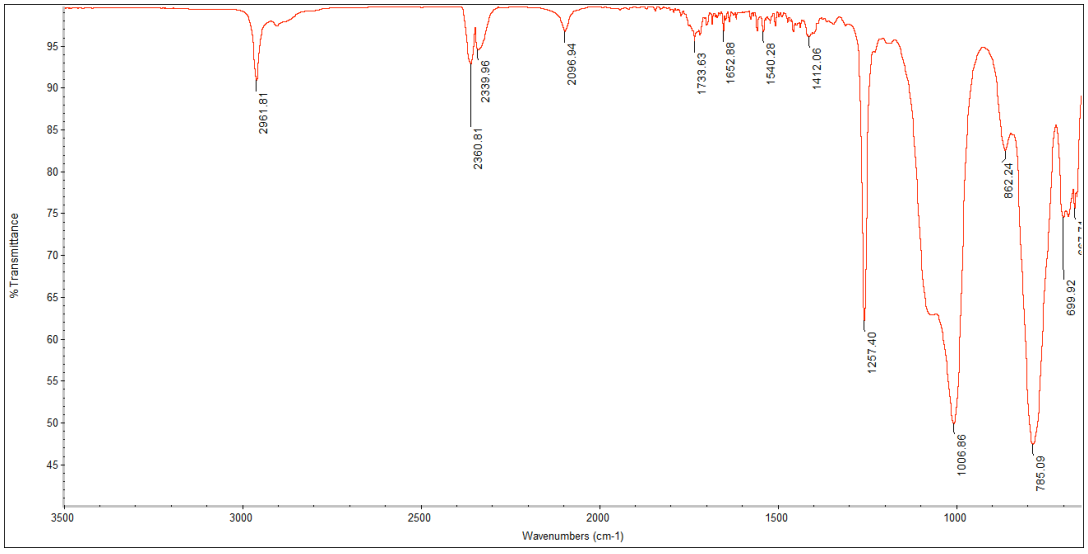
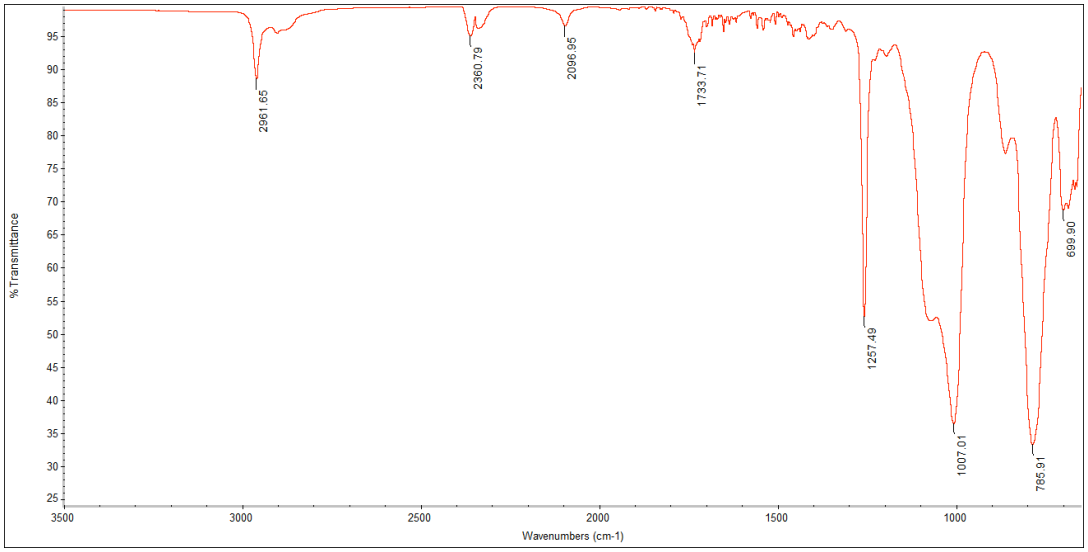


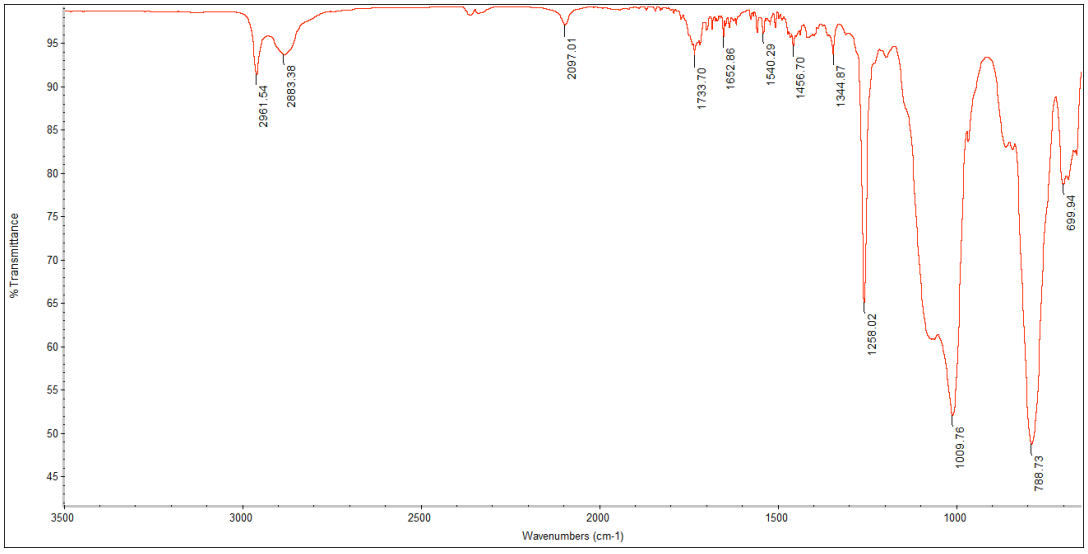
**27**

IR (ATR) ν = 2962, 2097, 1734, 1257, 1007, 786, 700 $cm^{-1}$




**28**

IR (ATR) ν = 2961, 2883, 2097, 1734, 1258, 1009, 788, 699 $cm^{-1}$



**29**

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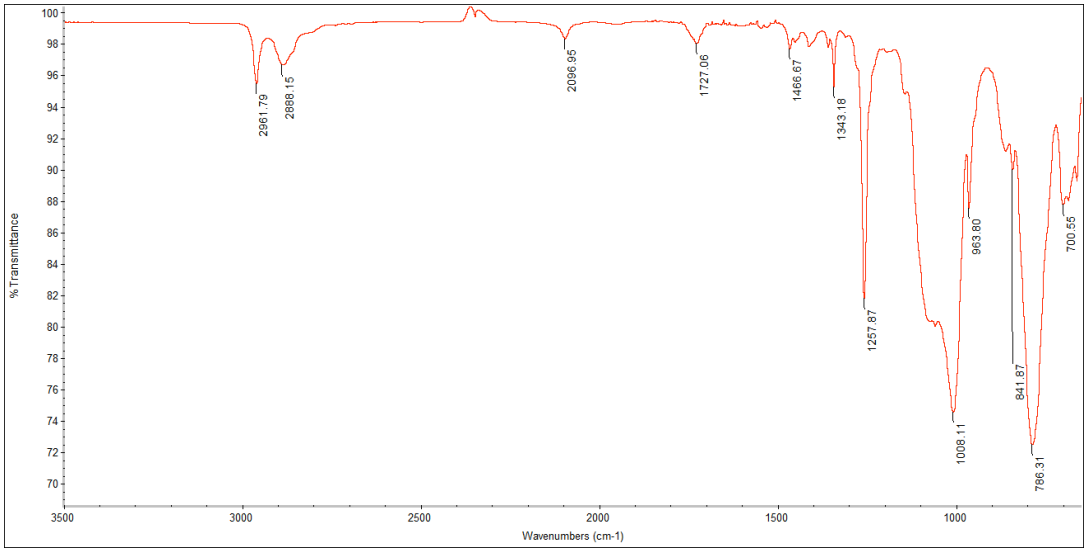


## 9.4 References

[i] F. Gonzaga, J. B. Grande, M. A. Brook, *Chem. Eur. J.,* **2012**, 18, 1536-1541.
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# Chapter 10: Appendix 3
# Supporting Information for Chapter 5: Thermal Bonding of Silicones for Microfluidics Using Huisgen Cyclization

## 10.1 Experimental Section

### 10.1.1 Materials

(Chloropropyl)methylsiloxane-dimethylsiloxane copolymer ($Me_3SiO(Me_2SiO)_n(Me(Cl(CH_2)_3)\text{-}SiO)_mSiMe_3$, 14-16 mol % (chloropropyl)methylsiloxanes, MW 7,500-10,000 $g \cdot mol^{-1}$, trimethylsiloxy terminated), (aminopropyl)methylsiloxane-dimethylsiloxane copolymer ($Me_3SiO(Me_2SiO)_n(Me(H_2N(CH_2)_3)SiO)_mSiMe_3$, 6-7 mol % (aminopropyl)methyl-siloxanes, trimethylsiloxy-terminated), octamethylcyclotetrasiloxane ($D_4$), and 1,3-bis(hydroxybutyl)tetramethyldisiloxane were obtained from Gelest. (Glycidyl-ether)methylsiloxane-dimethylsiloxane copolymer ($Me_3SiO(Me_2SiO)_n(Me(OCH_2CH)\text{-}CH_2O(CH_2)_3)SiO)_mSiMe_3$Silmer EP J10 MW 9,300 $g \cdot mol^{-1}$) was obtained from Siltech. Propiolic acid (95%), propargyl alcohol (99%), succinic anhydride (99%), sodium azide (99.5%) and dimethylaminopyridine (DMAP, 99%) and trifluoromethanesulfonic acid (99%) were obtained from Sigma-Aldrich. *N*-(3-dimethylaminopropyl)-*N′*-ethyl-carbodiimide hydrochloride (EDC·HCl, commercial grade) was obtained from Alfa Aesar. Tetra-*n*-butylammonium azide was obtained from TCI. Sylgard 184

was obtained from Dow Corning. Aerosil R8200 was obtained from Evonik. Parylene was obtained from Specialty Coating Systems and deposited using a Labcoter® 2 Parylene Deposition Unit Model PDS 2010. All materials were used as received.

### 10.1.2 Characterization

$^1$H NMR were recorded at room temperature on a Bruker AV 600 spectrometer (at 600 MHz for $^1$H) using deuterated solvent $CDCl_3$. Air pressure delamination experiments were performed using an Endotek Big 60 Inflation Device (syringe fit with a pressure gauge) by MeritMedica or using a MediaGauge™ MGA-9V (digital gauge for gases) from SSI Technologies Inc. attached to Wilkerson regulator and a house nitrogen line. GPC were run on an Alliance Waters 2695 Separation Module using THF as the eluent.

### 10.1.3 General Synthesis

#### *10.1.3.1 Alkyne Synthesis*

*Synthesis of propiolate-terminated polysiloxane* **1**

1,3-Bis(propiolatobutyl)tetramethyldisiloxane was synthesized following the procedure by Gonzaga et al.[1] and was used to make propiolate-terminated PDMS following the procedure from Rambarran et al.[2] An equilibration reaction to grow the polymer chains was performed using 1,3-bis(propiolatobutyl)tetramethyldisiloxane (4.80 g, 12.57 mmol) as the end group, with $D_4$ (49.90 g, 168.58 mmol) and triflic acid (200 μL, 2.3 mmol), yielding 40.75 g of propiolate-terminated polysiloxane, **1**. The polysiloxane chain

contained on average 62 dimethylsiloxane units, corresponding to an average molecular weight of 4862 g·mol$^{-1}$ (yield: 75%) determined by $^1$H NMR.

$^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.07 (s, 374 H, SiC*H*$_3$); 0.56 (t, 4H, *J*=8.3 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.37 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.68 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.86 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, SiCH$_2$CH$_2$CH$_2$C*H*$_2$).

*Synthesis of (4-(propylamino)-4-oxo-, 2-propyn-1-yl ester butanoic acid)methylsiloxane-dimethylsiloxane copolymer* **2**

The synthesis of a pendant alkyne functional copolymer was adapted from the previously published procedure.[2] In a 100 mL round-bottomed flask, (aminopropyl)methylsiloxane-dimethylsiloxane copolymer (6-7 mol % (aminopropyl)methylsiloxane, 30.39 g, 27.65 mmol) and the monopropargyl ester of butanedioic acid (5.055 g, 32.37 mmol), made following the previously published procedure,[3] were dissolved in dry DCM (40 mL). The mixture was cooled at -10 °C in a dry ice/acetone bath. EDC·HCl (5.91 g, 30.8 mmol) and additional DCM (10 mL) were slowly added followed by a catalytic amount of DMAP (0.04 g, 0.2 mmol). The reaction was covered, purged with nitrogen and allowed to stir under a positive pressure of nitrogen for 24 h. The mixture was then washed with 2 x 20 mL of 0.1 M HCl followed by 2 x 20 mL of brine (NaCl in distilled water). The organic phase was dried over $MgSO_4$, gravity filtered and the volatiles removed in vacuo to yield 29.77 g (87% yield) of the title compound, a viscous, pale yellow oil. The polymer molecular weight was determined by GPC,

Mn=13050 g·mol$^{-1}$ and the molecular weight per alkyne was determined by $^{1}$H NMR (1315 g·mol$^{-1}$).

$^{1}$H NMR ($CDCl_3$, 600 MHz, δ): 0.07 (s, 89H, SiC*H*$_3$); 0.50 (t, *J* = 8.4 Hz 2H, SiC*H*$_2$CH$_2$CH$_2$N); 1.53 (p, *J* = 7.8 Hz, 2H, SiCH$_2$C*H*$_2$CH$_2$N); 2.47 (m, 3H, O=CCH$_2$C*H*$_2$C=ON and C≡C*H*); 2.72 (m, 2H, O=CC*H*$_2$CH$_2$C=ON); 3.22 (m, 2H, SiCH$_2$CH$_2$C*H*$_2$N); 4.68 (s, 2H, C*H*$_2$C≡CH).

***10.1.3.2 Azide Synthesis***

*Synthesis of Poly(azidopropylmethyl)-co-(dimethylsiloxane)* **3**

(Chloropropylmethyl)siloxane-dimethylsiloxane copolymer (14-16 mol % (chloropropyl)methylsiloxane), 61.50 g, 117.4 mmol of chloropropyl groups), $NaN_3$ (12.78 g, 196.6 mmol) and (*n*-butyl)$_4NN_3$, (0.24 g, 1.8 mmol) were dissolved in dry THF (60 mL) according to the previously published procedure.[2] The mixture was refluxed with stirring for 60 h. The reaction was found to be complete by $^{1}$H NMR spectroscopy. THF was removed *in vacuo*. The mixture was dissolved in diethyl ether (60 mL) and filtered though neutral alumina. Volatiles were removed in vacuo to yield 56.36 g (90% yield) of the title compound. Characterization by $^{1}$H NMR demonstrated the purified product. In subsequent elastomer synthesis, $^{1}$H NMR spectroscopy was to calculate the molecular weight of an average azido- containing repeat unit, 530.8 g.mol$^{-1}$. The polymer molecular weight as determined by GPC was Mn=17600 g·mol$^{-1}$.

$^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.07 (s, 34H, $SiCH_3$); 0.56 (m, 2H, $SiCH_2CH_2CH_2N_3$); 1.62 (m, 2H, $SiCH_2CH_2CH_2N_3$); 3.24 (t, 2H, $SiCH_2CH_2CH_2N_3$).

*Synthesis of [1-azido-2-propanol-3-(oxypropyl)]methylsiloxane-dimethylsiloxane copolymer* **4**

The procedure was adapted from Halila et al.[4] Silmer EPJ10 (epoxypropoxypropyl)methylsiloxane-dimethylsiloxane copolymer (16.44 g, 15.11 mmol) was weighed into a 100 mL round-bottomed flask with isopropanol (20 mL) and the mixture was stirred. $NaN_3$ (2.17 g, 33.4 mmol) was dissolved in 4 mL of distilled water and added to the silicone solution followed by glacial acetic acid (3 mL, 52.4 mmol) and the round bottom flask was placed in an oil bath fit with a condenser at 80 °C with stirring. After 22 h, the reaction was found to be complete by $^1$H NMR. The mixture was cooled and transferred to a separatory funnel, diluted with 50 mL of diethyl ether and washed with 2x 20 mL of saturated sodium bicarbonate and 2 x 20 mL of distilled water. The organic layer was dried over sodium sulfate and the solvent was removed in vacuo to yield 13.58 g of the title copolymer (79% yield, MW 1131 g.mol$^{-1}$ per repeat unit as determine by $^1$H NMR), a colourless transparent oil. The polymer molecular weight determined by GPC was Mn=8840 g·mol$^{-1}$.

$^1$H NMR ($CDCl_3$, 600 MHz, δ): 0.09 (m, 77H, 12x $Si(CH_3)_2$) 0.50 (m, 2H, $SiCH_2$), 1.63 (p, $J$ = 7.6 Hz, 2H, $SiCH_2CH_2CH_2$), 3.36 (m, 2H, $CH_2N_3$), 3.43 (m, 4H, $CH_2OCH_2$), 3.93 (m, 2H, CHOH).

### *10.1.3.4 Elastomer Synthesis*

Glass Petri dishes were used as the curing vessel for the elastomers, after being coated with Parylene using a Labcoter® 2 Parylene Deposition Unit. The general curing procedure is illustrated by the synthesis of a reactive elastomer containing an excess of azido- groups, formed by crosslinking **1** and **3** with an alkyne:azide ratio of 1:6. Polymer **3** (2.68 g, 5.06 mmol of azido- functional units) was placed in a glass vial followed by dialkyne **1** (2.03 g, 0.83 mmol of alkyne functional groups), 0.081 g of Aerosil R8200 and 1 mL of $CHCl_3$. After vigorous mixing, the homogeneous and transparent mixture was poured into the coated glass dish containing one or two pieces of tubing (standing upright) with an 18G (1.2 mm) opening plugged with metal wire. The dish was then placed in an oven at 100 °C for 18 h to cure. The mixture crosslinked into a colourless transparent monolithic elastomer, **5**, within the first 6 h, however, additional time heating (12 h) was used to ensure that thorough crosslinking occurred. The same procedure was followed using polymers **2** (4.92 g, 3.74 mol) and **4** (0.67 g, 0.59 mol) with molar ratios of alkyne:azide functional groups of 6:1 (the tubing was not included in the excess alkyne elastomers) to yield elastomer **6,** a transparent monolithic elastomer with a slight yellow tint. The synthesis of the elastomers above was repeated twice and utilizing wider tubing as well. The amount of reagents used can be found in Table 10.S1.

*Lower Functionality Huisgen Elastomer*

Huisgen elastomers with a reduced excess of azido- and alkynyl- groups in the formulation were created according to the procedure outlined above. **1** (2.45 g, 1.01 mmol of alkynyl functional groups) and **3** (1.66 g, 3.13 mmol of azido groups) were crosslinked with tubing to create elastomer **7** containing a 3:1 ratio of azide:alkyne. **2** (2.63 g, 2.00 mmol) and **4** (1.15 g, 1.02 mol) were crosslinked to create elastomer **8** containing a 2:1 ratio of alkyne:azide.

#### *10.1.3.5 Sylgard Control*

Silicone test devices were fabricated using vinyl molds as previously described.[5] Briefly, self-adhesive vinyl films (80 μm thickness, FDC-4300, FDC graphics films, SOUTH Bend, IN) were patterned via Xurography utilizing a high-resolution blade cutter (Graphtec ROBO Pro CE5000-40-CRP, Graphtec America, Inc., Irvine, CA) into 5 mm x 5 mm square negative molds adhered onto cleaned polystyrene dish. 1.2 cm Masterflex® Silicone tubing (1/16" x 0.189", Cole-Parmer Canada Inc.) was placed over each vinyl molds as in-situ inlets with tight pressure fit necessary for the high-pressure experiment. Sylgard 184 pre-polymer (10:1 wt% elastomer: hardener, mixed and degassed) was cast over the vinyl molds and allowed to cure at room temperature for 48 h.

### 10.1.4 Elastomer Adhesion and Characterization

Initial attempts to measure adhesion of the Huisgen elastomers using a 90° peel-adhesion test[6] and using an orthogonal delamination test[7] were unsuccessful, since the materials frequently did not survive the experimental test set-up. During the

90° peel test, when attempting to clamp the top rubber flap to run the measurements, the elastomer often tore. During the orthogonal delamination experiments, when attempting to clamp the aluminum pieces in place on the Instron, the adhered elastomers often delaminated from the adhesive to the aluminum. Therefore, it was necessary to find a softer method to test the adhesion of elastomers.

*Pressure Testing*

The general procedure for adhering the silicone elastomers will be illustrated by the procedure for thermally bonding the interface of elastomers **5** and **6**. Elastomer **5** was carefully removed from the glass Petri dish using a small spatula. A scalpel was used to cut a ~2.5 cm square around the tubing cured into the elastomer. The wire was very carefully removed from the center of the tubing and a 18G needle was pressed through the top of the tubing out of elastomer base. Any debris was removed from the base of the elastomer to ensure a flat surface for bonding. The elastomer with the tubing cured into it, **5**, was placed into contact with the surface of elastomer **6**. A spatula was used to depress the top elastomer onto the bottom elastomer, ensuring that the surfaces were in close contact with each other and no air bubbles were present at the interface. The elastomer was placed in a 100 °C oven for 20 h. The elastomer was removed from the heat and allowed to cool to room temperature. Testing of the adhesion was done the next day using the Endotek Big 60 Inflation Device tubing connected to an 18G needle in which the tip had been cut off leaving a flat surface. The blunted needle tip was placed in the

tubing close to the interface and was held upright. The syringe handle was depressed slowly increasing the pressure until the material or adhesion failed (total time over ~20 s).

*Sylgard Control*

After curing, silicone test devices were cut using a scalpel and bonded to flat piece of Sylgard rubber after 30 s of oxygen plasma exposure (30 sccm air inlet flow, 600 mTorr) at high power (30 W) in a PDC expanded plasma cleaner (Harrick, Ithaca, NY).

*Pressurized Testing Under Water*

A secondary method was used to test adhered elastomers **5** and **6**, **7** and **8**, and to test the Sylgard control. Regulated nitrogen pressure was attached to dead-end pressure chamber (5 x 5 x 0.08 mm) in test devices fabricated as above and immersed in a beaker of milliQ water to measure failure pressure in test devices. The nitrogen pressure started from atmospheric pressure and was increased gradually until device failure was observed visually through the bubbling of nitrogen gas into milliQ water as a result of test device bond layer delamination or material failure (Figure 10.S1). Note: An enhanced material strength of silicone elastomer can be achieved by adding a mineral filler, typically silica.[8] The use of appropriate Teflon connector at the silicone tubing interconnect ensured no nitrogen losses during the course the failure pressure measurement.

Figure 10.S1: Huisgen bonded interface after the delamination experiment, star/fissure cracks through the material (background, sky)

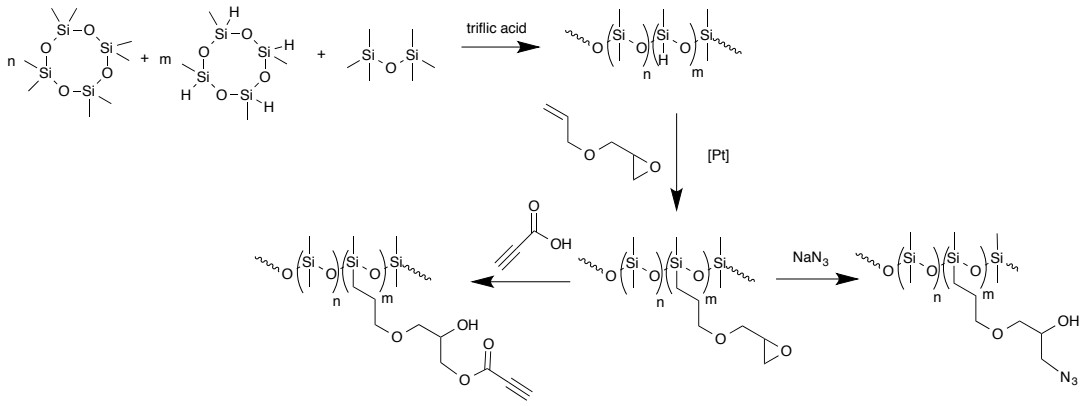
Table 10.S1: Elastomer composition and burst strength[a]

| Elastomer | $N_3$ (g:mmol[a]) | ≡ (g:mmol[b]) | Ratio $[N_3]$:[≡] | Burst Strength (PSI) |
|---|---|---|---|---|
| **5** | **3** (2.67:5.03) | **1** (2.03:0.84) | 6:1 | 22, 21, 20 |
| **6** | **4** (0.67:0.59) | **2** (4.94:3.75) | 1:6 | |
| **5** | **3** (2.69:5.07) | **1** (2.02:0.83) | 6:1 | 17, 20 |
| **6** | **4** (0.52:0.46) | **2** (3.88:2.95) | 1:6 | |
| **5** | **3** (2.63:4.96) | **1** (2.12:0.87) | 6:1 | 24 |
| **6** | **4** (0.52:0.46) | **2** (3.92:2.98) | 1:6 | |
| **7** | **3** (1.66:3.13) | **1** (2.45:1.01) | 3:1 | 6 |
| **8** | **4** (1.15:1.02) | **2** (2.63:2.00) | 1:2 | |
| **7** | **3** (1.64:3.10) | **1** (2.43:1.00) | 3:1 | 4, 10 |
| **8** | **4** (1.00:0.88) | **2** (2.43:1.84) | 1:2 | |
| **Sylgard** | n/a | n/a | 18, 13, 14, 37, 32, 17, 18, 18 | 21±9 |

[a] None of the laminates, **5** and **6**, underwent adhesive failure. The control elastomers, **7** and **8**, and Sylgard, underwent adhesive failure.

[b] g/mmol per azido or alkynyl group.

## 10.2 Unsuccessful Synthetic Approach




Scheme 10.S1: Glycidyl ether approach azido and alkynyl functional polymers.

The initial synthetic approach to create adhesive materials was to first create (or purchase) (methylhydrosiloxane)-dimethylsiloxane copolymer with 1:5 ratio of Si-H to $SiMe_2$ constituents in which allyl glycidyl ether could be hydrosilylated onto the backbone to impart epoxide functionality. The functional polymers could then optionally be modified with azido- or alkynyl- groups (Scheme 10.S1). These could then be used to crosslink analogously functionalized telechelic polymers (glycidyl ether-terminated PDMS functionalized with azido- or alkynyl- groups) leaving excess reactive groups in the material that could be used to subsequent bonding. This approach was unsuccessful; the glycidyl ether functional starting material once azide or alkyne modified did not crosslink into nice materials. The resultant elastomers were tacky, soft and opaque. This likely arose from the incompatibility of the telechelic and pendant polymers; the pendant polymers have a significant amount of carbon based organic functionality that can lead to

phase separation when attempting to crosslink with a telechelic polymer, mostly silicone based.

**10.3 Click Bonded PDMS with Microfluidic Channel**

Azido- and Alkynyl- PDMS were bonded together with a linear microfluidic channel imprint (trench) on the excess azide PDMS.

**1** (1.12 g, 0.5 mmol) and **3** (1.58 g, 3.0 mmol) were mixed vigorously with 0.27 g of Aerosil R 8200 and 0.5 g of $D_4$ as the solvent. The mixture was poured onto a silicon wafer containing a rectangular microfluidic channel profile on the surface made of PMMA photoresist via conventional photolithography methods (channel dimensions: width 700 μm, depth 200 μm). Surrounding the channel was a Sylgard mask with a rectangular shape cut out, so the prepolymer would cure into a rectangular shape around the channel. **2** (2.25g, 1.52 mmol) and **4** (0.28g, 0.26 mmol) were mixed with 0.5 mL of toluene and poured onto a silicon wafer with a rectangular Sylgard mask. The mixtures were placed in a 95 °C oven to cure for 24 h to produce elastomers **9** and **10** respectively. The fully cured elastomers and were cut around the edge of the mold with scalpel and carefully removed from the mold. The azido rubber **9** had the channel imprint in tact, was placed face down on top of **10**, pressing the surfaces together. The elastomers were placed in an oven at 110 °C for 24 h. When removed from the heat, the rubbers were strongly adhered together. To see if the channel was intact, the top and bottom of the bonded elastomers (at the edges of the linear channel) were cut to expose the channel opening and a syringe with red water was inserted just at the top of the

channel and the liquid was pushed through the channel using the syringe. The red dye demonstrated the channel was intact, with sharp edges and the red liquid did not leak into the bonded interface after 20 minutes time.

### 10.4 References for Supporting Information

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2. Rambarran, T.; Gonzaga, F.; Brook, M. A., Generic, Metal-Free Cross-Linking and Modification of Silicone Elastomers Using Click Ligation. *Macromolecules* **2012,** *45* (5), 2276-2285.
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6. Verdier, C.; Ravilly, G., Peeling of polydimethylsiloxane adhesives: The case of adhesive failure. *Journal of Polymer Science Part B: Polymer Physics* **2007,** *45* (16), 2113-2122.
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# Chapter 11: Appendix 4

# Supporting Information for Chapter 6: Sweet Supramolecular Elastomers from α,ω(β-Cyclodextrin terminated) PDMS

## 11.1 Experimental Section

### *11.1.1 Materials*

Octamethylcyclotetrasiloxane ($D_4$, 98%), and 1,3-bis(4-hydroxybutyl)tetramethyldisiloxane (95%) were obtained from Gelest. Propiolic acid (95%), *N*-(3-dimethylaminopropyl)-*N′*-ethyl-carbodiimide hydrochloride (EDC-HCl, commercial grade), 1,1,3,3-tetramethylguanidine (TMG, 99%) and dimethylaminopyridine (DMAP, 99%) were obtained from Sigma-Aldrich. Trifluoroacetic acid (analytical grade) (TFA) was obtained from Carlo Erba Reagents. Mono-6-deoxy-6-azido-b-cyclodextrin **1** was synthesized according to a published procedure,[1] using materials purchased from Sigma Aldrich. ESI-MS and FTIR spectra are given in Figures S1 and S2, respectively. Solvents DMSO-$d_6$, $CDCl_3$, THF, isopropanol, $CH_2Cl_2$ (DCM), and toluene were all obtained from Sigma Aldrich and used as received.

### *11.1.2 Characterization*

$^1$H NMR spectra were recorded at room temperature on a Bruker AC-250 spectrometer (at 250 MHz for $^1$H), a Bruker AVANCE 500MHz Spectrometer (500 MHz for $^1$H and 125 MHz for $^{13}$C) or a Bruker AVANCE II spectrometer (at 400 MHz for $^1$H and 100.6 MHz for $^{13}$C) using deuterated solvents ($CDCl_3$ or DMSO-$d_6$). $^{13}$C chemical shifts are reported with respect to $CDCl_3$ as an internal standard, set at 77.23 ppm. $^1$H NMR chemical shifts are reported with respect to chloroform ($CHCl_3$) as an internal standard, set at 7.26 ppm or with respect to

residual proton signal of DMSO-$d_6$ set at 2.50 ppm. Coupling constants ($J$) are recorded in Hertz (Hz). The abbreviations s=singlet, d=doublet, t=triplet, m=multiplet, are used to report spectra.

DOSY experiments were performed on a Bruker Avance III 400 spectrometer equipped with a 5 mm multinuclear broad band probe (BBFO+) with z-gradient coil. A double stimulated echo sequence (DSTE) incorporating bipolar gradient pulses was used for the measurement of self-diffusion coefficients. Gradients were incremented from 0.96 G $cm^{-1}$ to 47.19 G $cm^{-1}$ in 40 steps using an exponential ramp. 64 scans were acquired with 16k data points. A gradient pulse length d/2 of 1.5 ms was used with a diffusion delay D set to 100 ms. Fourier transformation was applied in F2 with 2 Hz exponential broadening. The diffusion dimension of the 2D DOSY spectra was processed with TOPSPIN DOSY software.

Size exclusion chromatography (SEC) in THF eluent was measured on a Shimadzu apparatus equipped with a CTO-20A oven, set at 35 °C, a RID 10A refractive index detector, and a Viscotek 270 Dual detector (viscometer and light scattering). A mixture of TFA (0.342 g, 0.33 mmol) and TMG (0.115 g, 0.11 mmol) was first weighed into a vial with 1 mL of THF and mixed vigorously. The rubber (15 mg) was then placed in a vial with 3 drops of the chaotropic salt solution and 4 mL of THF solvent and left for 24 h, at which time it was found to have dissolved.

Infrared spectra were measured on a Nicolet iS10 Thermo Scientific, using the ATR mode, at room temperature. Differential scanning calorimetry and thermogravimetric analyses were measured on TA Instruments Q500 and Q20, respectively. Rheological measurements were taken on an ARES SN Rheometer from TA Instruments. All specimens were tested as 1-mm thick disks, under a nitrogen atmosphere, using 25 mm parallel plate geometry. Oscillatory sweep

measurements were taken as a function of angular frequency in the range 0.1-100 rad/s, at 3% strain, whereas temperature sweeps measurements were done between 30 and 150 °C, at constant frequency and strain (1 Hz, 3%).

Transmission electron microscopy was measured either on Philips CM120 TEM (Lyon) or on a Titan 1 FEI Titan 80-300 Cubed (Hamilton). Thin slices (~60 nm) of the elastomers were prepared by microtoming. Ruthenium tetroxide vapor (popular for heterogeneous polymer systems) was used as a stain, as it has been shown to enhance electron density contrast for polymers containing ethers, alcohols and aromatics.[2] Given the nature of cyclodextrin and the fact that it is connected to the PDMS through an aromatic linkage, cyclodextrin rich areas in the material were expected to provide greater contrast.

### *11.1.3 General Syntheses*

*Synthesis of propiolate-terminated polydimethylsiloxane 2, 3*

Two 1,3-bis(propiolatobutyl)-terminated polydimethylsiloxanes **2** and **3** (see Figure 1 in main text), which differ in molar mass, were synthesized following the procedure by Rambarran et al.[3] The polysiloxane chain **2** was constituted from ~52 dimethylsiloxane units, corresponding to an average molar mass of 4,100 $g \cdot mol^{-1}$ as determined by $^1H$ NMR and confirmed by GPC (THF: $M_n$= 4,100 $g \cdot mol^{-1}$; PDI = 2.05.). Polysiloxane **3** has ~114 dimethylsiloxane units, corresponding to an average molar mass of 8,600 $g \cdot mol^{-1}$ as determined by $^1H$ NMR and confirmed by GPC (THF: $M_n$= 7,800 $g \cdot mol^{-1}$; PDI = 1.95).

*Compound* **2**: $^1H$ NMR ($CDCl_3$, 500 MHz, δ): 0.07 (s, 312H, $SiCH_3$); 0.52 (t, 4H, *J*=8.3 Hz, $SiCH_2CH_2CH_2CH_2$); 1.38 (m, 4H, $SiCH_2CH_2CH_2CH_2$); 1.69 (m, 4H, $SiCH_2CH_2CH_2CH_2$); 2.87 (s, 2H, C≡C*H*); 4.19 (t, 4H, *J*=6.5 Hz, $SiCH_2CH_2CH_2CH_2$). See FTIR and $^1H$ NMR spectra in Figures S2 and S3, respectively.

*Compound* **3**: $^1$H NMR ($CDCl_3$, 500 MHz, δ): 0.07 (s, 684H, SiC*H*$_3$); 0.52 (t, 4H, *J*=8.3 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.38 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.69 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.87 (s, 2H, C≡C*H*); 4.20 (t, 4H, *J*=6.5 Hz, SiCH$_2$CH$_2$CH$_2$C*H*$_2$).

*Synthesis of β-CD functional PDMSs **4**, **5***

Compounds **1** (0.17 g, 0.15 mmol per azide) and **2** (0.31g, 0.075 mmol, 0.15 mmol per alkyne) were mixed in a glass vial with 8 mL of 1:1 water:isopropanol at 80 °C. The reaction was initially turbid. After 5 d, the solution became transparent and a monolithic yellow elastomer **4** (0.40 g, 82% of the original starting mass) precipitated out of the solution. **4** could be swollen in dichloromethane after a few hours but did not dissolve. Partially reacted PDMS remaining in solution was removed simply by decanting. Any material not tightly bound within the network could be extracted with DCM, reducing the mass of the rubber to 0.21 g, 43% of the original mass of the reagents. The un-extracted material was characterized by IR, $^1$H NMR (HRMAS), SEC (THF eluent), TGA, DSC, TEM and rheology.

This process was repeated starting from **3** (0.32 g 0.037 mmol, 0.074 mmol per alkyne) to create the elastomer **5** (0.28 g**,** 70% of the original mass of the reagents) taking 5 days to reach completion. After extraction with DCM, the mass was reduced to 0.25 g, 63% of the original mass of the reagents.

*Compound* **4**: $^1$H NMR ($CDCl_3$, 400 MHz, δ): 0.07 (s, 342 H, SiC*H*$_3$); 0.62 (m, 4H, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.49 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.83 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.86 (s, 0.6H, C≡C*H*); 4.37 (m, 4H, SiCH$_2$CH$_2$CH$_2$C*H*$_2$), 4.66 (broad s, $H_2O$), 8.18, 8.83 (s, 1.4H, *C-H* aromatic). Note that some of the silicone polymers reacted at only one end, such that residual SiCH$_2$CH$_2$CH$_2$CH$_2$

groups were present, with additional signals at 1.37, 1.69 and 4.23 ppm. SEC (after chaotropic salt treatment): $M_n$=28,700 g/mol, PDI=2.80.

*Compound* **5**: $^1$H NMR ($CDCl_3$, 400 MHz, δ): 0.07 (s, 654 H, SiC*H*$_3$); 0.62 (m, 4H, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.49 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.83 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$); 2.86 (s, 0.7H, C≡C*H*); 4.37 (t, 4H, SiCH$_2$CH$_2$CH$_2$C*H*$_2$), 4.66 (broad s, $H_2O$), 8.18, 8.83 (s, 1.3H, *C-H* aromatic). As noted above, peaks from residual SiCH$_2$CH$_2$CH$_2$CH$_2$ groups were present at 1.37, 1.69 and 4.23 ppm. SEC (after chaotropic salt treatment): $M_n$=30,300 g/mol, PDI=2.60.

*Click reaction with copper catalyst*

**1** (0.114 g, 56 μmol), **2** (0.059 g, 51 μmol), copper sulfate pentahydrate (99.99%, Sigma-Aldrich, 0.003g 12 μmol) and sodium ascorbate (>98%, Sigma, 0.006 g, 28 μmol) were mixed with 3mL of 1:1 $H_2O$:isopropanol. The cloudy dispersion was stirred at room temperature. After 45 min, the solution turned transparent and small drops of gels formed and stuck to the sides of the glass. The final elastomer was comparable to the thermally prepared counterpart in terms of its supramolecular state (it dissolves in THF/chaotropic salt solution, but only swells, and does not dissolve in good solvents for silicones).

*Reaction of* **2** *with 3-azido-1-propanol*

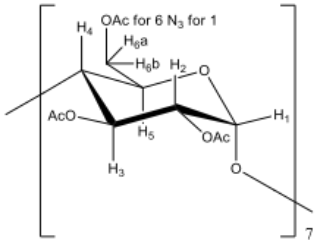
3-Azido-1-propanol was synthesized according to a previously described procedure.[4] Propiolate-terminated PDMS (0.44 g, 0.21 mmol of alkyne) and 3-azido-1-propanol (0.09 g, 0.29 mmol) were added to a scintillation vial with 7 mL of 1:1 $H_2O$:IPA and left to stir at 80 °C for 5 days at which time a viscous oil was observed that was comprised of triazole-modified silicone, as confirmed by $^1$H NMR.

$^1$H NMR ($CDCl_3$, 250 MHz, δ): 0.05 (s, 320H, SiC*H*$_3$); 0.59 (t, 4H, *J*=8.3 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.44 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.81 (m, 4H,

$HOCH_2CH_2CH_2$); 2.15 (m, 4H, $SiCH_2CH_2CH_2CH_2$); 3,65 (m, 4H, $HOCH_2CH_2CH_2$); 4.33 (t, 4H, *J*=6.5 Hz, $SiCH_2CH_2CH_2CH_2$); 4.58 (t, 4H, *J*=6.9 Hz, $HOCH_2CH_2CH_2$); 8.10, 8.11 (s, 2H, C*H aromatic*).

*Synthesis of mono-(6-deoxy-6-azido)-peracylated-β-cyclodextrin* ***6***

Mono-6-deoxy-6-azido-β-cyclodextrin was synthesized according to the previously published procedure:[5] an adaptation of the procedure by Noomen et al.[6] was used to synthesize the azido peracylated-β-cyclodextrin. Azido-β-cyclodextrin **1** (0.45 g, 0.38 mmol), DMAP (cat, 3.50 mg), acetic anhydride (3 ml ~3.24 g, 31.74 mmol) and pyridine (5 mL) were added to a 20 mL scintillation vial, sealed and stirred at 80 °C for 96 h (the mixture turned transparent upon mixing and heating). The reaction was removed from heat and allowed to cool to room temperature. Upon cooling in an ice bath, no product precipitated. The mixture was precipitated in 100 mL of cold water, vacuum filtered and allowed to dry on the filter paper and placed in a vacuum desiccator for 48 h, at which time 0.55 g of product (73% yield) was recovered.




$^1$H NMR (600 MHz): 2.10 (63 H, C$H_3$CO); 3.72 (m, 9H, $H_4$, $H_6$,$^a$, $H_6$,$^b$) 4.13-4.58 (19H, $H_5$, $H_6^a$, $H_6^b$); 4.81 (m, 7H, $H_3$); 5.09 (m, 7H, $H_1$). LRMS (ESI positive): m/z [$M^+$ :($NH_4^+$)] calculated = 2017.6, found = 2017.7, m/z [$M^{++}$:($NH_4^+$)($K^+$)] calculated = 1028.3, found = 1028.4.

*Acylated-β-Cyclodextrin-functional PDMS **7** (Thermal Cycloaddition)*

**6** (0.41 g, 0.20 mmol) and **2** (0.40 g, 0.20 mmol of alkynyl groups) were weighed into a 10 mL round-bottomed flask fit with a condenser. The reagents were homogenized with 1 mL of toluene + 1 mL of $CHCl_3$ and stirred at 90 °C. The initial reaction mixture was colorless and transparent. As the reaction progressed, the mixture turned to yellow and finally to a light brown. At 144 h, the reaction was found to be complete by proton NMR (75% conversion) as demonstrated by the disappearance of the C-H signal from the propiolate (2.87 ppm), the appearance of the C-H aromatic signals from triazole of the product (8.15 - 8.24 ppm) and the splitting pattern of the $CH_2$ a Si. Two signals were observed, one corresponding to the product integrating to 1.5 and one corresponding to the starting material integrating to 0.5. The reaction was stopped at this time to mirror the reaction progress with the non-acylated cyclodextrin. Upon removal of the solvent, the product was transparent brown solid of mass 0.74 g (91% yield). The product could be dissolved in various organic solvents.

$^1$H NMR (600 MHz): 0.07 (s, 288 H, SiC*H*$_3$); 0.58 (t, 4H, *J*=9 Hz, SiC*H*$_2$CH$_2$CH$_2$CH$_2$); 1.45 (m, 4H, SiCH$_2$C*H*$_2$CH$_2$CH$_2$); 1.81 (m, 4H, SiCH$_2$CH$_2$C*H*$_2$CH$_2$) 2.10 (126 H, C*H*$_3$CO); 3.72 (m, 18H, $H_4$, $H_{6'}^{a}$, $H_{6'}^{b}$) 4.13-4.58 (42H, $H_5$, $H_6^{a}$, $H_6^{b}$, SiCH$_2$CH$_2$CH$_2$C*H*$_2$); 4.81 (m, 14H, $H_3$); 5.09 (m, 14H, $H_1$); 8.05, 8.16 (s, 2H, C-*H aromatic*). Note that some of the silicone polymers reacted at only one end, such that residual SiCH$_2$CH$_2$CH$_2$CH$_2$OCOCH groups were present with additional signals at 0.53, 1.38, 1.68 and 2.87 ppm along with a small amount of unreacted compound **6** whose signals overlapped with the product.

## 11.2 Characterization of synthons

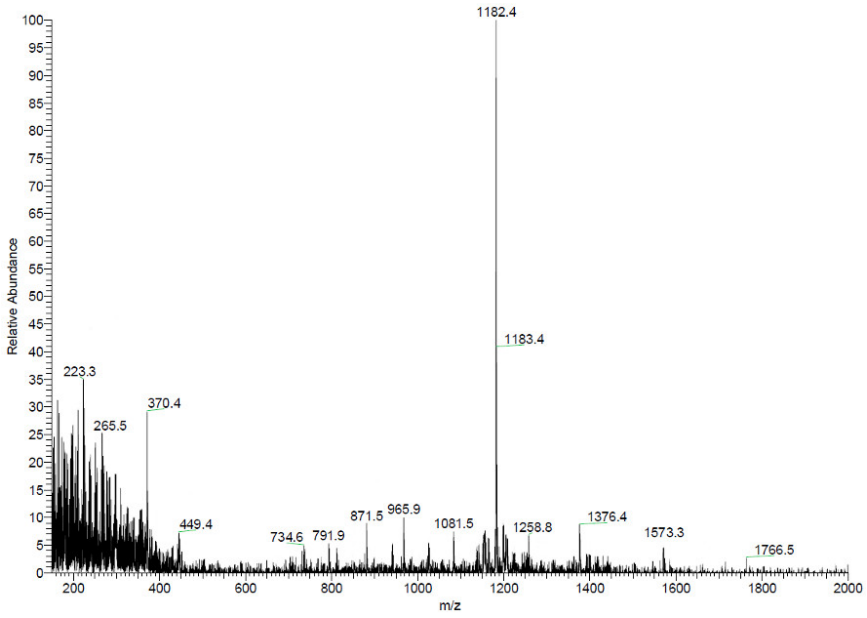



Figure 11.S1. Electrospray-mass spectrum of $N_3$-β-CD protonated by $Na^+$ (main peak at 1183.4 g/mol).

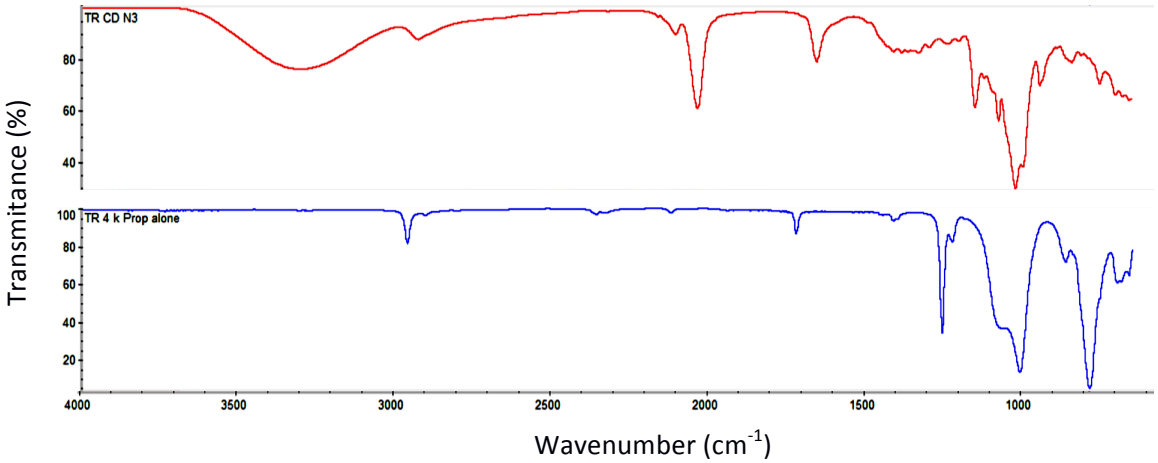



Figure 11.S2. FTIR spectra of starting material: (top) $N_3$-β-CD **1**; (bottom) Propiolate-PDMS **2**.

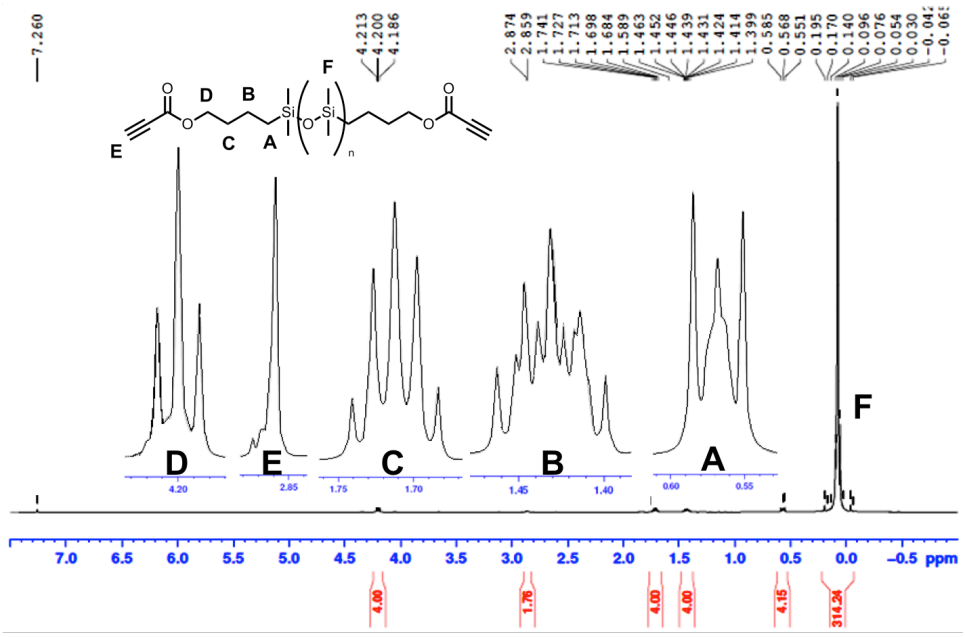



Figure 11.S3. $^{1}$H NMR spectra of propiolate-PDMS **2** in $CDCl_3$:

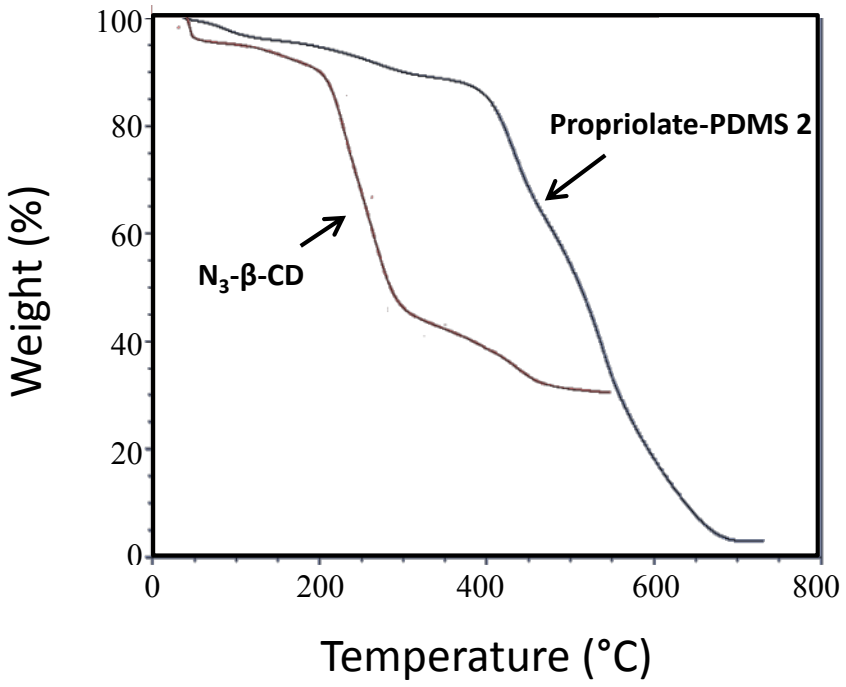



Figure S4. TGA of $N_3$-β-CD **1** and propiolate-PDMS **2**.

### 11.3 Characterization of α,ω(β-CD functionalized) -PDMS

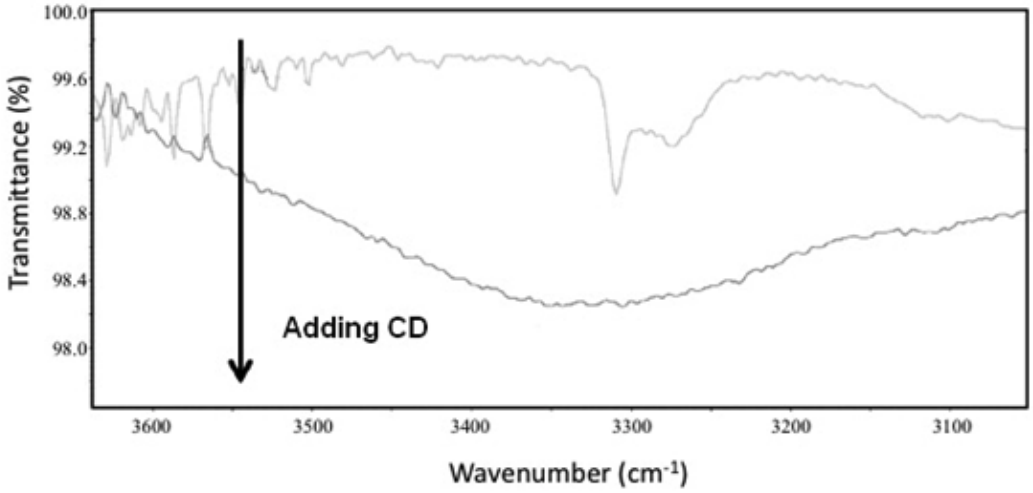



Figure 11.S5. Zoom on the FTIR region of OH stretch for propiolate PDMS **2** (top) and elastomer **4** (bottom).

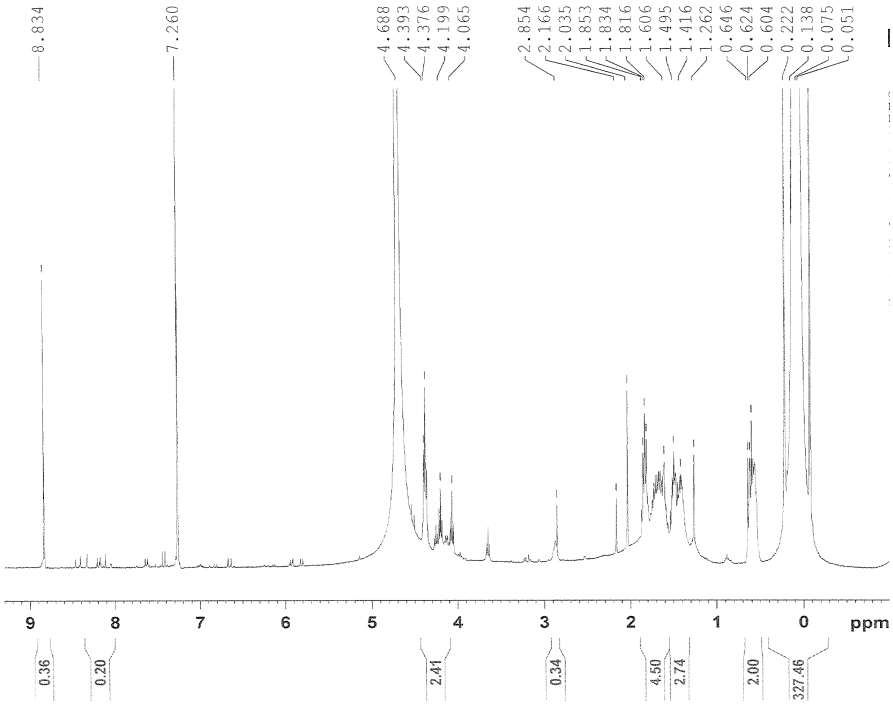



Figure 11.S6. $^{1}$H HRMAS spectrum of the elastomer **5**.

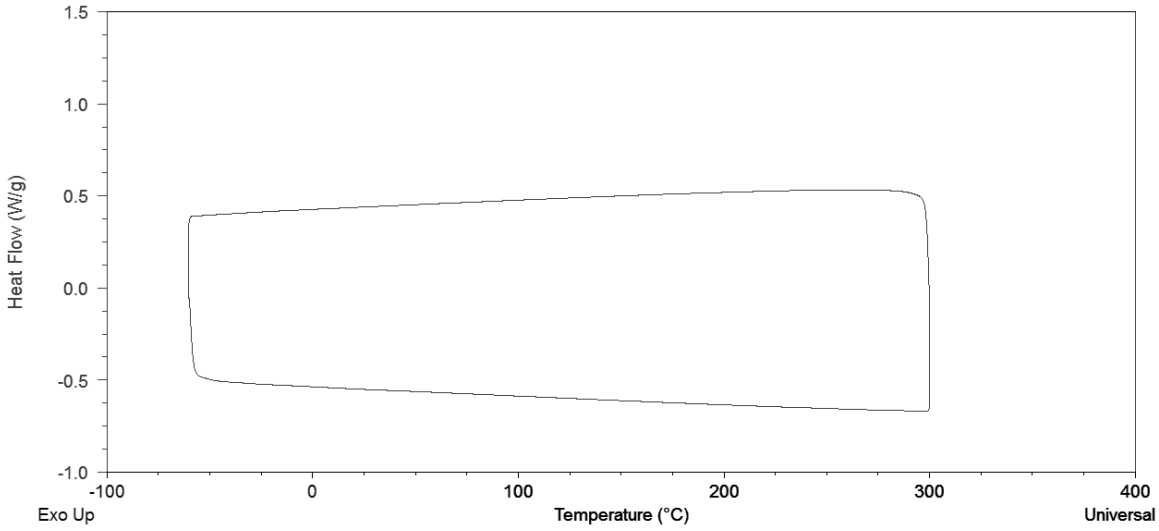



Figure 11.S7. DSC cycles of the elastomer **4.**

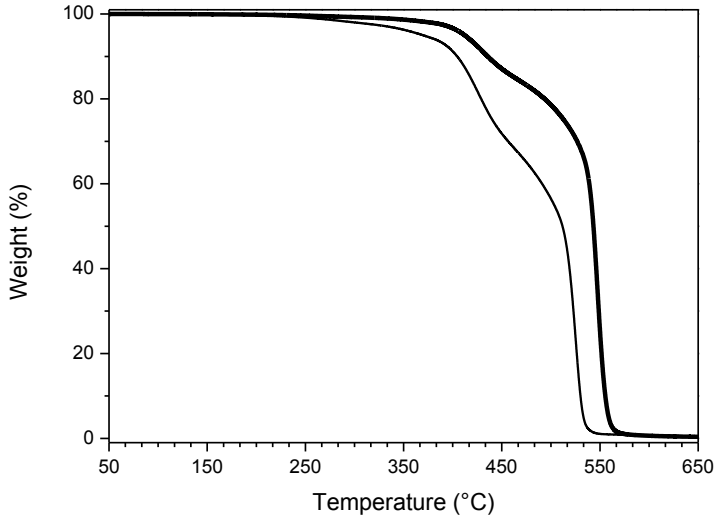



Figure 11.S8: TGA of **4** (thin line) and **5** (thick line) elastomers.

### 11.3.1 Rheology study

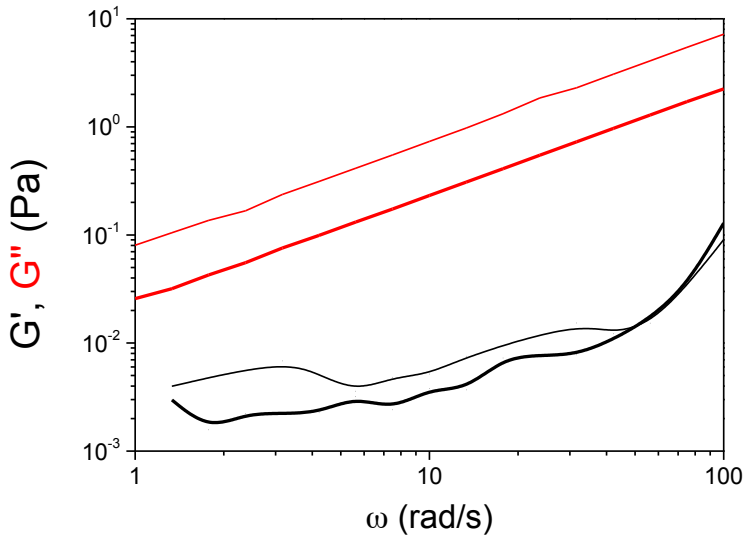



Figure 11.S9. Frequency sweeps at constant strain for propiolate-PDMSs **2** (thick line) and **3** (thin line).

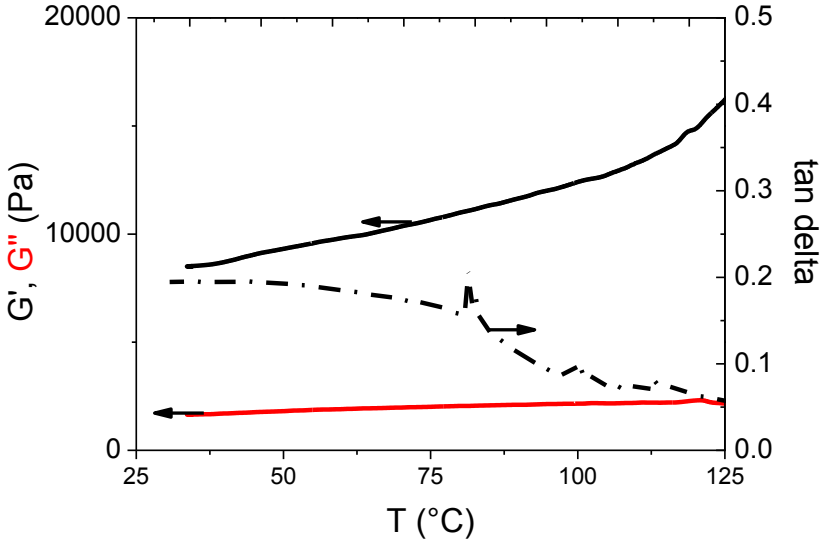



Figure 11.S10. Temperature sweeps at constant strain for elastomer **4**.

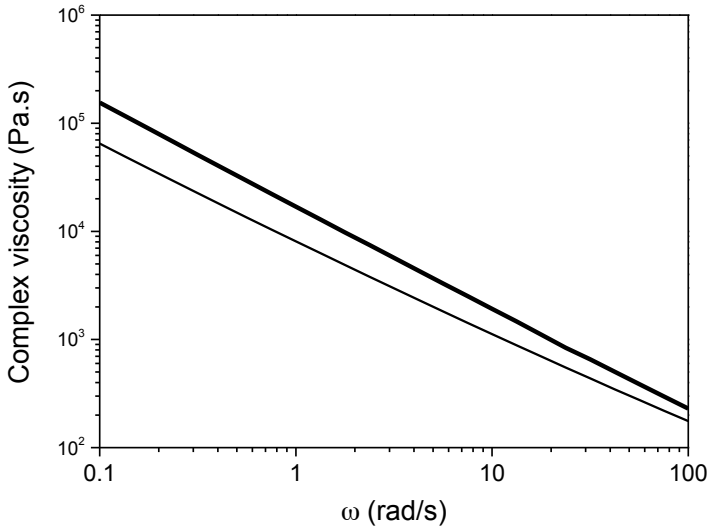



Figure 11.S11. Complex viscosity versus angular frequency for elastomers **4** (thick line) and **5** (thin line).

### 11.3.2 Microscopy study

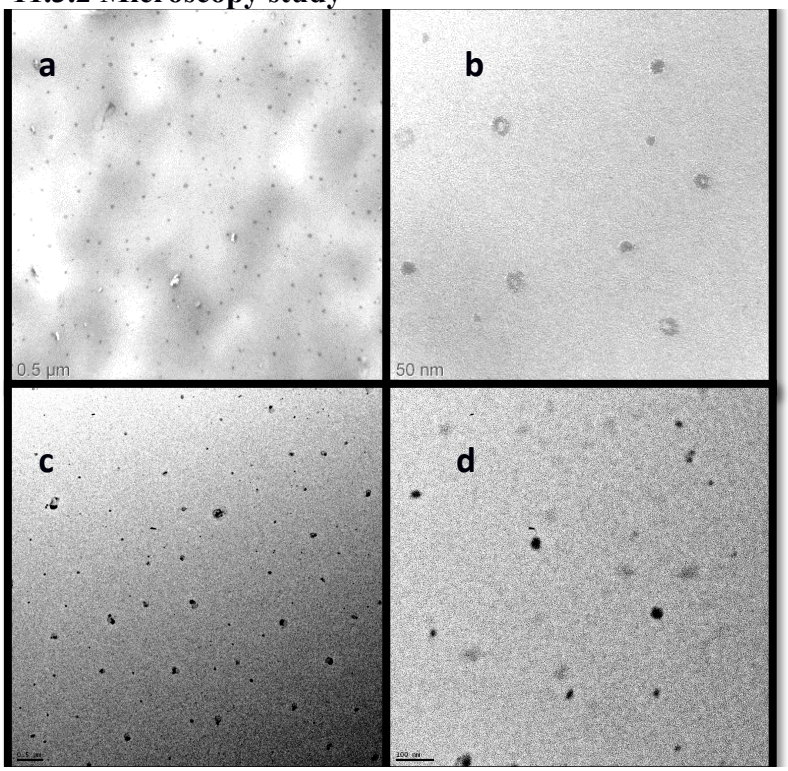



Figure 11.S12: SEM images on a conventional TEM (a,b) and High Resolution TEM (c,d) of elastomers **4** (upper row)

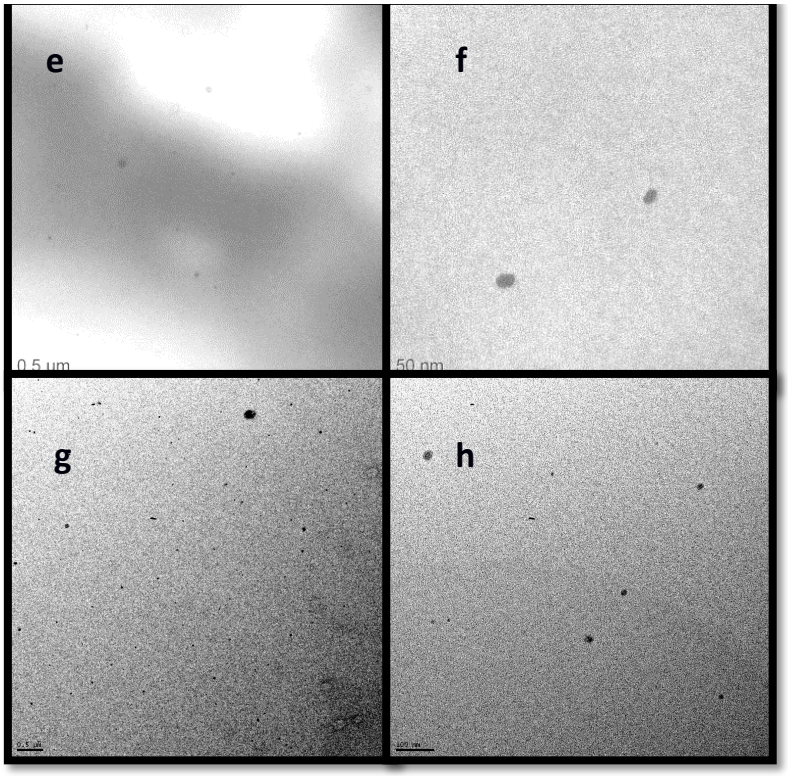



Figure 11.S12: SEM images on a conventional TEM (e,f) and High Resolution TEM (g,h) of elastomers **5** (bottom row).11.4 Complementary analyses

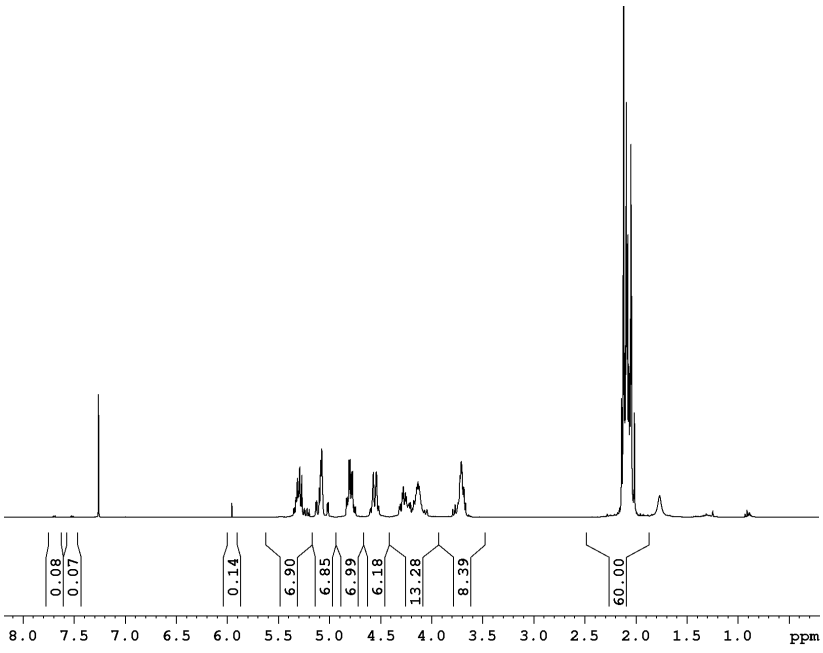



Figure 11.S13. $^{1}H$ NMR spectrum in $CDCl_3$ of acetylated β-CD **6**.

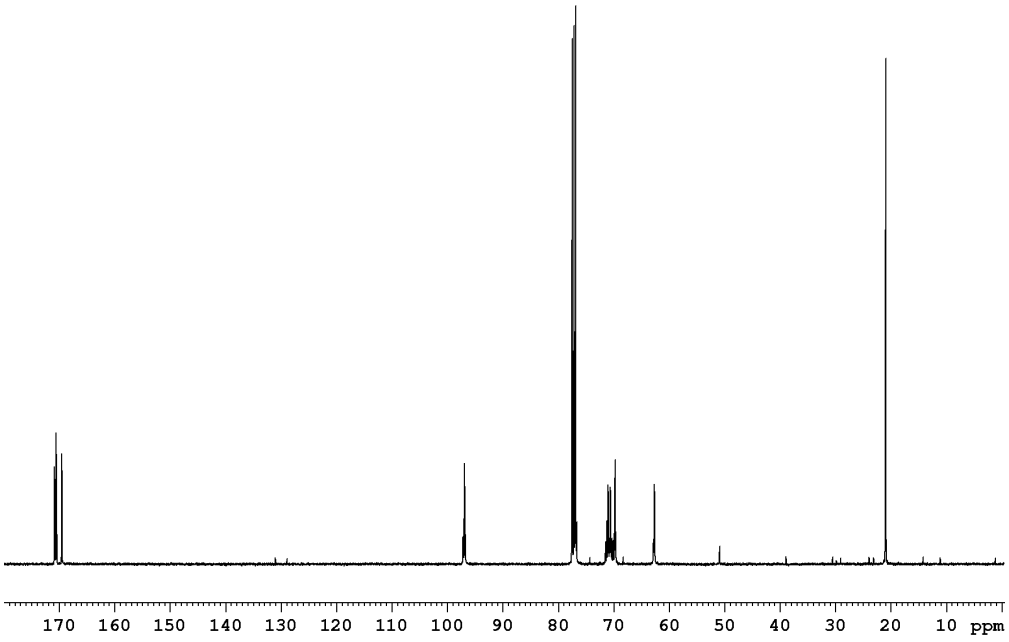



Figure 11.S14: $^{13}C$ NMR spectrum in $CDCl_3$ of acetylated β-CD **6**.

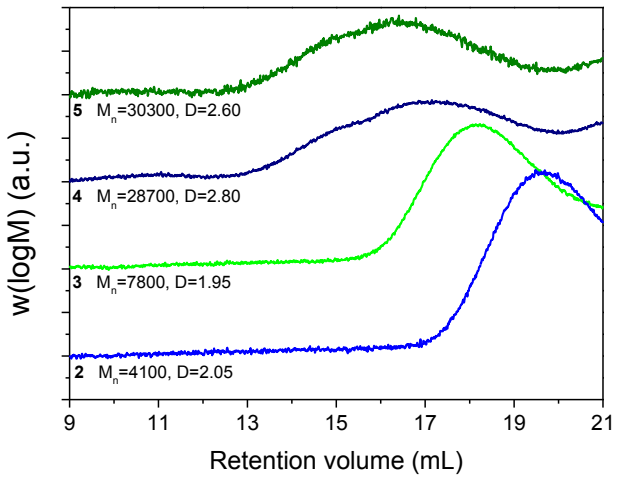



Figure 11.S15: SEC analyses in THF of the original propiolate polymers **2**, **3** and final elastomers **4** and **5** after the click reaction with **1**, and solubilization in a chaotropic salt/THF solution. The fact that the molar masses of the complexes show an increased mass suggests that some aggregation is occurring owing to the poor THF solubility of the CD end chains.

### 11.4.1 DOSY measurements and interpretation

A specific study on the interactions between acetylated cyclodextrin **6** and PDMS propiolate **2** was first carried out to check whether the cyclodextrin cage could accommodate alkyne groups or PDMS chains in its core. The mixture was first prepared in $CDCl_3$, introducing 26.6 mg of **6** and 26.5 mg of **2** in 1.15 g of deuterated solvent (1/1 molar ratio alkyne/CD). First comparison of the $^1H$ NMR spectra revealed no shifting of the protons inside the cavities, as expected for a complexed cage (signals H3 and H5, see ref. 7, for instance). The proton of the acetylene function around 3 ppm is slightly shifted, but this is due to its inherent lability (also observed with dilution). DOSY analysis was done on this mixture and compared to the polymer **7**, obtained by click reaction between **6** and **2**. 2D DOSY maps are shown in Figure 11.S16. In the mixture, the diffusion coefficients of **6** and terminal groups of **2** are close (380 vs. 290 $\mu m^2/s$, respectively). When considering the *D* ($Me_2SiO$) units of the backbone, the diffusion coefficient is slightly different (190 $\mu m^2/s$, not shown), in better agreement with the molar mass differences (2007 and 4100 g/mol for **6** and **2**, respectively). Such variation of *D* coefficients between main polymer units and terminal groups has already been pointed out.[8] Since the diffusion coefficients of both entities are clearly separated, it is concluded that under these conditions, no tight bounding between PDMS and CD through an inclusion complex was observed.

In the case of polymer **7**, all the signals of PDMS and b-CD line to a smaller value of D corresponding to the polymer ($D$ = 185 $\mu m^2/s$). Viscosity effects were excluded as the diffusion coefficient of $CHCl_3$ was found constant for both solutions. The ratio of *D* coefficients of free versus clicked b-CD can be expressed as:

$$D_{free}/D_{clicked} \approx (M_{free}/M_{clicked})^{-a}$$

where $M_i$ are the average molar mass of the considered products, and $a = 1/dF$ with $dF$ the fractal dimension of the products.[9] Assuming that the fractal

dimension of both free and clicked b-CD is the same and estimated at 2 for a polymer in a theta solvent (*a* value of 0.5), very close to the value reported for simple b-CD at 0.49.[10] With a calculated $D_{cliked}/D_{free}$ ratio of 0.49, one finds a $M_{free}/M_{clicked}$ ratio of 0.24, which corresponds to a polymer of one PDMS chain coupled with two b-CD molecules. One can see also traces of free PDMS and free CD signals.

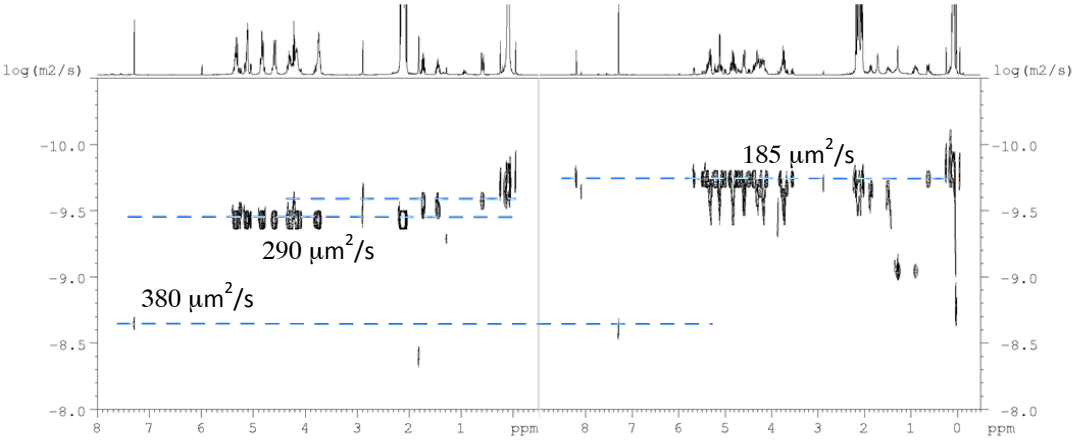



Figure 11.S16: 2D DOSY maps of (left) the acetylated b-CD **6** and the propiolate PDMS **2** mixed together in $CDCl_3$ and (right) the polymer **7** from click reaction in $CDCl_3$.

### 11.5 References for Supporting Information

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