# MODULAR SYNTHESIS OF AMPHIPHILIC NETWORKS WITH GUEST-HOST CAPABILITIES

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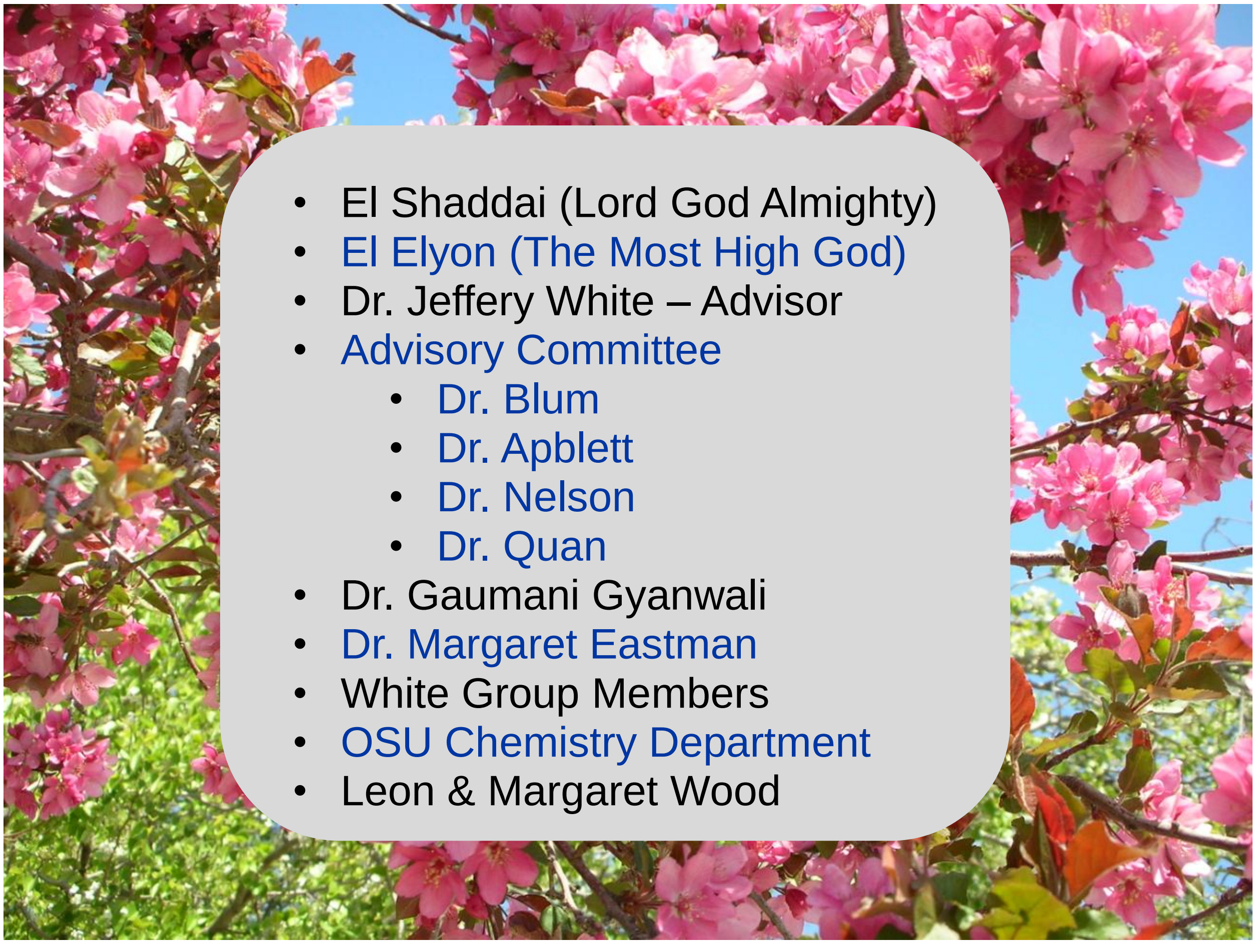

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Abstract: Herein is described a controlled modular method for nanoscopic polymer network synthesis. Nodal points, such as cyclodextrins, are well defined, as are the cross-linking tie chains (e.g. polyethylene oxide), which are of known molecular weight, and lead to species with guest-host complexation abilities. Tie chains are varied by length and nature, that is, nonpolar or polar, resulting in hydrophobic or amphiphilic networks, respectively. Methods of functionalization can result in the stoichiometric control of network densities, and nodal points, chain orientation and chemistry can be regulated. When formed into films, these networks can sequester small molecules, such as $C_{60}$ fullerene, through guest-host interactions. Interrogation of mono-functionalized and polymerized products was undertaken by solid state nuclear magnetic resonance experiments. Networked materials, though insoluble in common solvents, swell to varying degrees in nonpolar, polar protic, polar aprotic and halogenated solvents. Simple modular assembly methods for synthesizing amphiphilic polymer networks with specific linker lengths between cross-link sites, tailored hydrophilicity versus hydrophobicity, and active nodes are detailed.

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| | |
|---|---|
| AIBN | Azoisobutyronitrile |
| ATRP | Atom Transfer Radical Polymerization |
| $C_{60}$ | $C_{60}$-Fullerene |
| CD | Cyclodextrin |
| $CH_2Cl_2$ | Dichloromethane/Methylene Chloride |
| $CHCl_3$ | Chloroform |
| CP | Cross-Polarization |
| DBDD | 1, 12-Dibromododecane |
| DBH | 1, 6-Dibromohexane |
| DMF | Dimethyl Formamide |
| DMSO | Dimethyl Sulfoxide |
| EGDE | Ethylene Glycol Diglycidyl Ether |
| EtOH | Ethanol |
| $H_2O$ | Water |
| IUPAC | International Union for Pure and Applied Chemistry |
| MAS | Magic Angle Spinning |
| MBH | Monobromohexane/1-Bromohexane |
| MeOH | Methanol |

| | |
|---|---|
| NaH | Sodium Hydride |
| NaOH | Sodium Hydroxide |
| NMR | Nuclear Magnetic Resonance |
| PEGDE | Polyethylene Glycol Diglycidyl Ether |
| PEO | Polyethylene Oxide |
| RAFT | Reversible Addition Fragmentation Chain Transfer |
| TEM | Transmission Electron Microscopy |
| TGA | Thermogravimetric Analysis |
| UV-Vis | Ultraviolet-Visible Spectroscopy |

# CHAPTER I

# INTRODUCTION

**1.1 Cross-linked Polymer Networks.** Comprised of low molecular mass repeating units resulting in relatively high molecular mass macromolecules, also referred to as polymer molecules, networks are highly branched structures.[1] IUPAC defines a cross-linked polymer network as having small regions from which at least four chains emanate. Linear or branched polymers of different forms are less diverging in structure (Figure 1.1). An illustration of the practicality of cross-linking is seen in the improvement of the physical properties of naturally occuring polybutadienes, where sulfur is used to cross-link polymer chains resulting in network formation. Another example of cross-linked networks are polyepoxides, or epoxide resins, which are used as resistant coatings or strong adhesives.

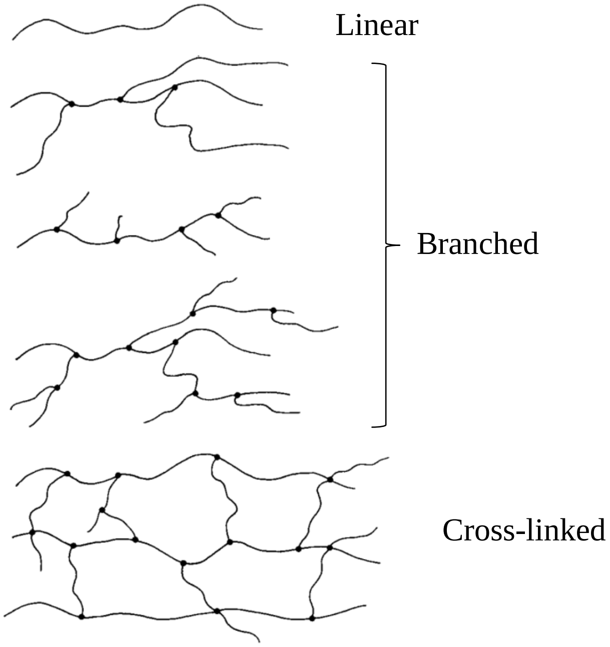


**Figure 1.1.** Structure of a cross-linked network and less diverging linear and branched polymers.[2]

Traditionally, polymer networks have been made using three methods: free radical polymerization (FRP)[3]; polycondensation[4]; and cross-linking of linear or branched polymers[5]. In FRP, the high reactivity of the radicals results in a high quantity of unwanted side reactions leading to considerable branching and uncontrolled molecular weight of linkages in the polymer.[6] Chains of a variety of lengths result, with unsystematic cross-linking node arrangements. An example of FRP is with acrylic acid monomer using *N,N'*-methylenebis(acrylamide) (MBA) as the cross-linker, initialized by AIBN (Figure 1.2).

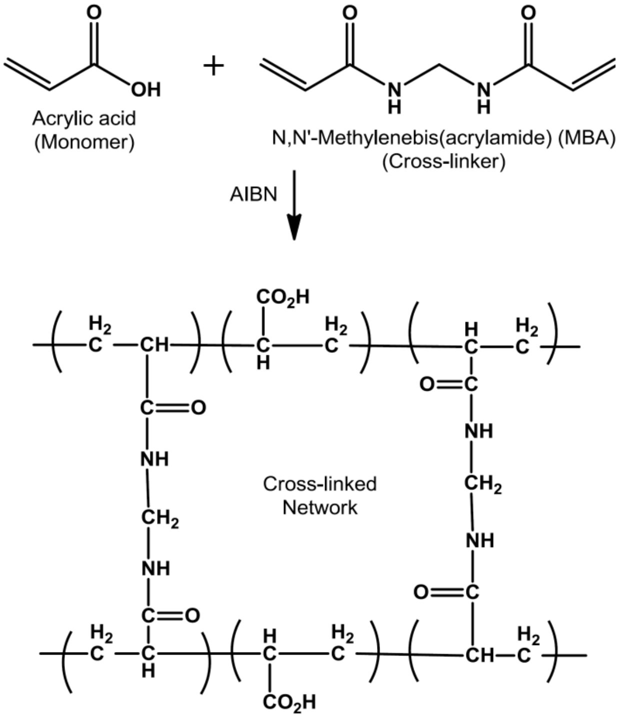


**Figure 1.2.** Free radical polymerization of acrylic acid and *N*,*N'*-methylenebis(acrylamide) initiated by AIBN.[7]

Polycondensation polymerization is used extensively in industry to generate polyesters and polyamides. The step-wise growth of polymer chains progresses via condensation reactions between functional groups of two molecules. Therefore, the polydispersity of the polymers formed is often great, and byproducts are produced at times.[8] An example of this challenge is seen in resins where, remaining a task to be generated as monodispersed spheres,[9] phenol-formaldehyde resins were among the first cross-linked polymers to be produced by step-growth polymerization (Figure 1.3).

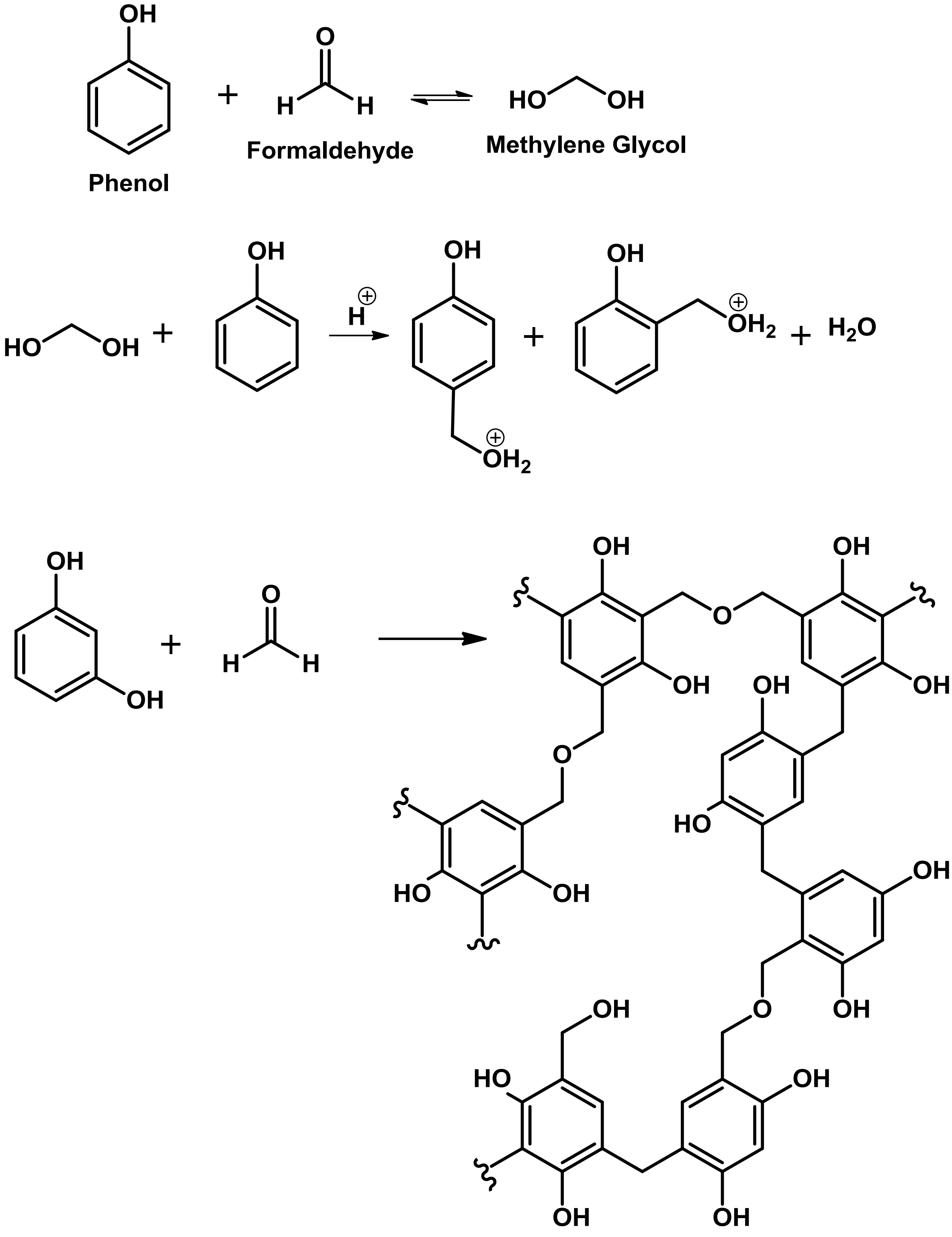


**Figure 1.3.** Formation of phenol-formaldehyde resins using the polycondensation process[10,11]

An example of the creation of polymers by cross-linking of linear chains is vulcanization, which endures as a much used means of producing polymer networks. Cross-linking agents, such as sulfur, connect polymer chains resulting in a random polymerization with a high degree of pendant chains. Molecular weight distribution between crosslinking is wide ranging. Figure 1.4 represents an idealized version of the process, but entanglements and other imperfections are common.

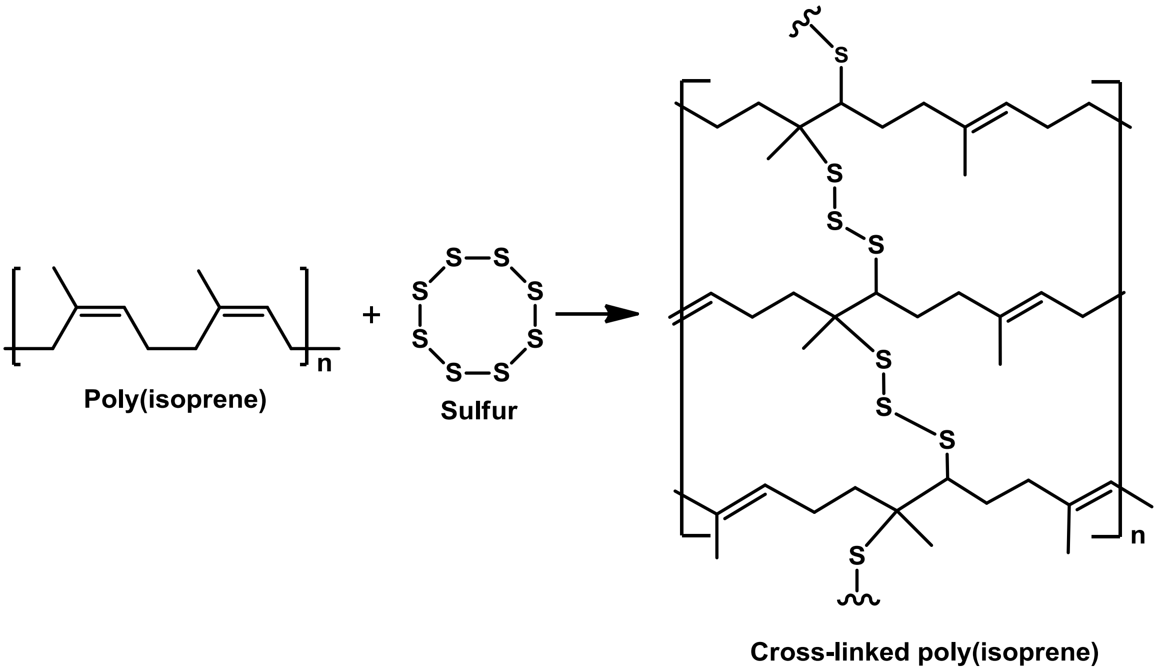


**Figure 1.4.** Vulcanization process for treatment of natural rubber[12]

There is minimal control over the architectural parameters of networks with these three conventional methods. These parameters include length of chain segments, molar mass, and polydispersity between crosslinks. The lack of control results in randomly cross-linked polymer networks. In order to better regulate these parameters, better polymerization procedures have been implemented toward the end of controlling network architecture.

These processes aim to produce polymer networks with chains of specific length and branch points with the same functional groups.

**1.2 Modular Approach.** It is the aim of this dissertation to present a modular approach for developing well defined homogenous polymer networks. The networks are made of quantifiable cross-linking linear chains with constant molar mass, and having unique guest-host capabilities. In order to do so, we will use covalent interactions between modules. The cross-linked nodes are unlike those of conventional networks in that upon connection in one direction, connection in the orthogonal direction is also available. The three components of this approach and the idealized representation of the resulting polymer network are presented in Figure 1.5. The networks have the following distinctions from most conventional cross-linked macromolecules:

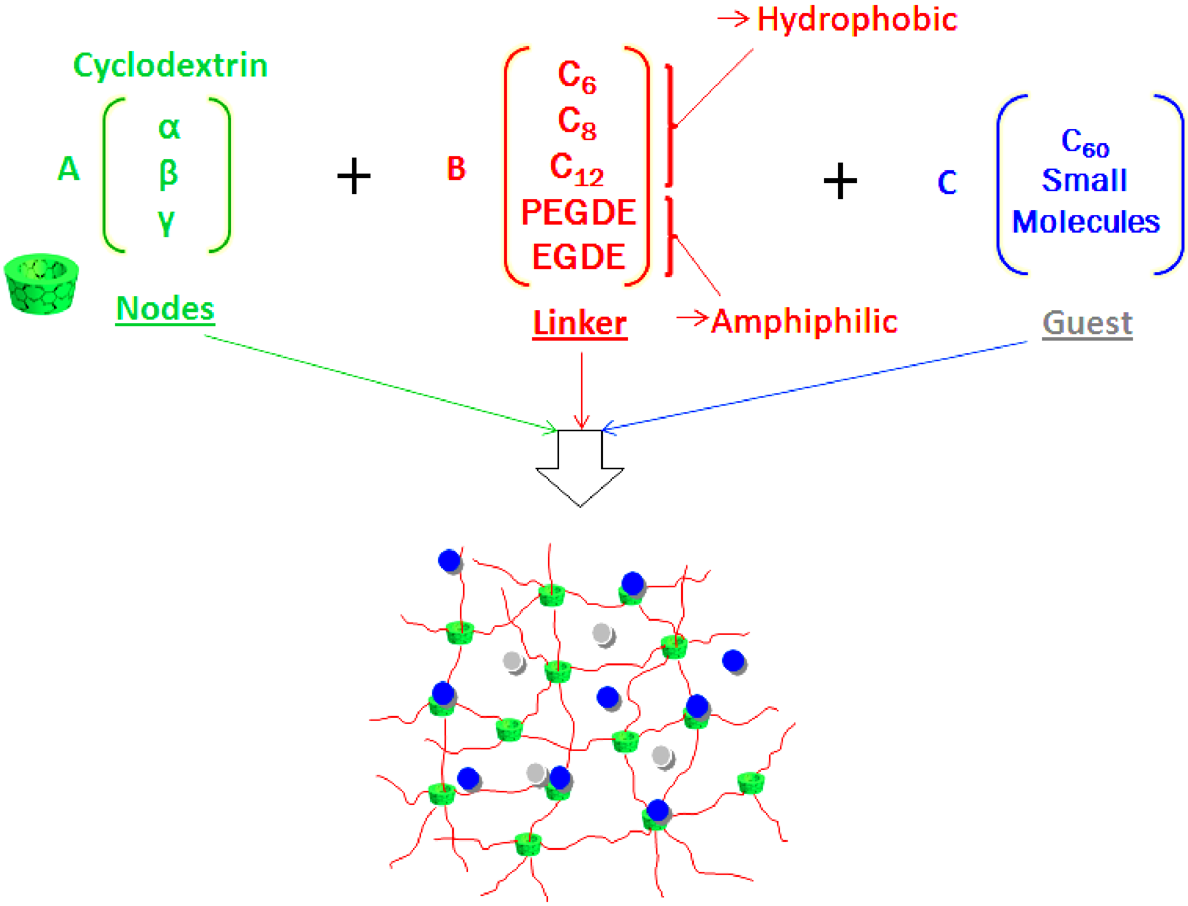


**Figure 1.5.** Modular approach to creating polymer networks using *α*-, *β*-, and *γ*-CD nodes connected by hydrophobic or hydrophilic linkers, with guest-host capabilities. Guests are represented in the network as grey and blue circles.

a) The molecular mass between crosslinks ($M_c$) is fixed;

b) The network possesses host-guest capabilities;

c) The number of tie chains in the product is known;

d) The nodal points are true molecules of distinct shape, size, and with fixed numbers of reactive functional groups;

e) The hydrophobicity/hydrophilicity of the network can be controlled based on the chemistry of the tie chains.

**1.2.1 Nodes.** The nodes of our system are molecular tie points and play a key role in the properties of the final network. Glucose-based cyclic oligomeric compounds, commonly known as ‘cyclodextrins’, have been proposed by us as nodes in the formation of the networks. However, the scope of this approach is not limited to cyclodextrins. Similar types of cyclic molecules having appropriate functional groups and networking possibilities can be alternate candidates as nodal points. For example, cycloparaphenylenes[13] or cyclophanes[14] can play important roles as such alternate nodes.

**1.2.1.1 Cyclodextrin.** Cyclodextrin (CD) is an oligomer comprising of D-glucopyranose units in a ring. The most commonly occuring CDs are *α*-, *β*-, and *γ*-CD corresponding to six, seven, and eight D-glucopyranose units, respectively, as shown in Figure 1.6.

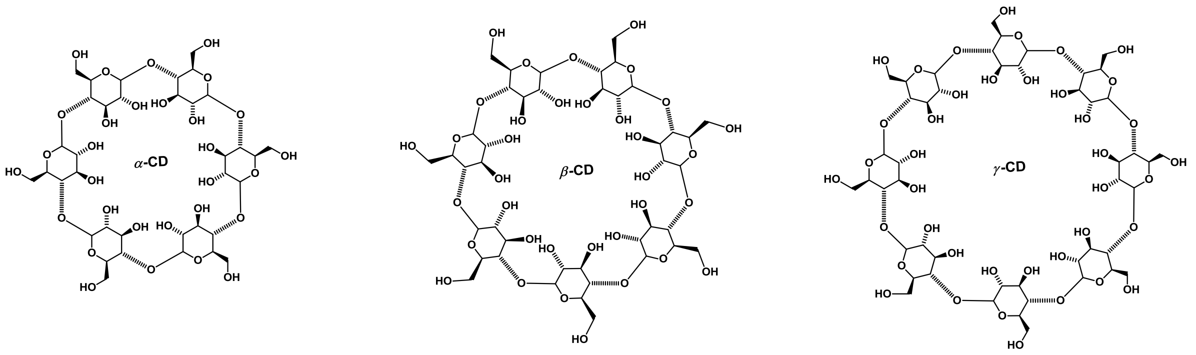
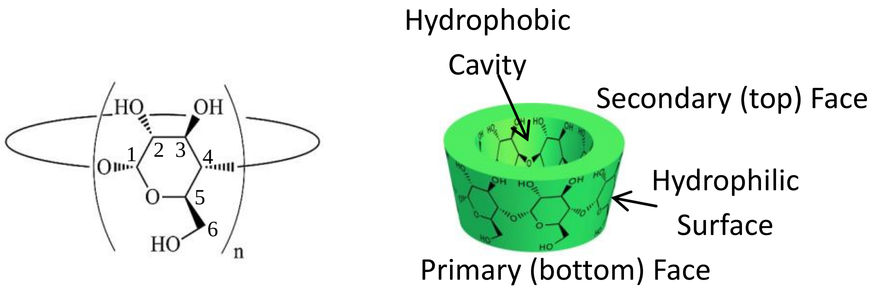


**Figure 1.6.** Molecular structures of *α*-, *β*-, and *γ*-CD

Possibly because of steric contraints, accounts of cyclodextrins with less than six glucose units have not been published, but those of more than eight units have been produced. In each sugar unit there is a primary hydroxyl in the C-6 position and secondary hydroxyls in the C-2 and C-3 positions. There is covalent bonding between units of the CD molecule via $\alpha$-1,4 ether linkages (Figure 1.7). The secondary hydroxyls are on the secondary face of the CD molecule, that is, the face of greater diameter. The primary hydroxyls, however, are on the primary face of the molecule as shown in Figure 1.7. The polar hydroxyl hydrogens are oriented outward, and the non-polar C-3 and C-5 hydrogens and ether oxygens are oriented inward resulting in cyclodextrin's hydrophilic perifery and hydrophobic cavity (Figure 1.7).[15,16]



D-glucopyranose unit

**Figure 1.7.** Cyclodextrin D-glucopyranose unit and hydrophobic and hydrophilic domains.

Harata reported hydrogen bonding between C-2 hydroxyls of one glucopyranose unit with C-3 hydroxyls of adjacent glucopyranose units.[17] In $\alpha$-CD four such hydrogen bonds are established since one glucopyranose unit is configured with a slight distortion. In $\beta$-CD, there is a continuous band of hydrogen bonding around the CD ring, rendering hydroxyls less available for hydrogen bonding with water. The eight unit ring in $\gamma$-CD affords more ring flexibility and less of such a hydrogen bond band. These properties contribute to the relative solubilities of the CD rings, with $\beta$-CD being the least soluble.[18] Some chemical–physical properties of $\alpha$-, $\beta$-, and $\gamma$-CDs are summarized in Table 1.1.

**Table 1.1.** Chemical–physical properties of $\alpha$-, $\beta$-, and $\gamma$-CDs[19]

| | $\alpha$-CD | $\beta$-CD | $\gamma$-CD |
|---|---|---|---|
| Number of glucopyranose units | 6 | 7 | 8 |
| Molecular weight | 972 | 1135 | 1297 |
| Solubility in water (% w/v) 25°C | 14.5 | 1.85 | 23.2 |
| Inner cavity diameter (nm) | 0.47–0.53 | 0.60–0.65 | 0.75–0.83 |
| Outer cavity diameter (nm) | 1.46 | 1.54 | 1.75 |
| Cavity height (nm) | 0.79 | 0.79 | 0.79 |
| Cavity volume ($nm^3$) | 0.174 | 0.262 | 0.472 |
| Crystal water content (wt.%) | 10.2 | 13.2–14.5 | 8.13–17.7 |
| Water molecules in cavity | 6 | 11 | 17 |
| Melting temperature range (°C) | 255–260 | 255–265 | 240–245 |

**1.2.1.2 Cyclodextrin Chemical Reactivity.** The reactive functional groups of CDs are the secondary hydroxyl groups at the C-2 and C-3 positions of the glucopyranose ring, and the primary hydroxyl groups at the C-6 position. The three hydroxyl groups often compete for reagents because of their similar reactivities, therefore selectivity is difficult. The C-6 hydroxyls are the most nucleophilic and the least sterically hindered groups. Therefore, they are most likely to attack an electrophile or a reagent with a bulky group(s) under normal circumstances, usually under weak basic conditions.[20]

The C-2 hydroxyls are the most acidic and are most easily deprotonated under strong basic condition to form a more nucleophilic oxyanion.[21] The C-3 hydroxyl hydrogen bonds to that of C-2, which, in addition to steric hindrance, contributes to the C-3 hydroxyls being least reactive.[22] CD-hydroxyl reactivities have been summarized based on reaction conditions and reagent type and are shown in Figure 1.8.[23]

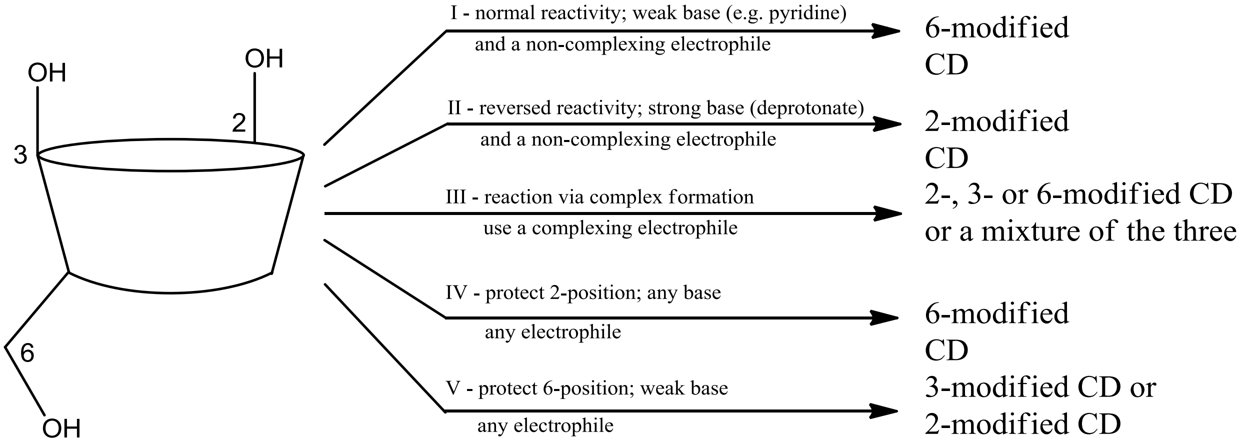


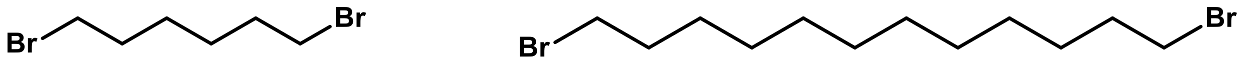
**Figure 1.8.** Chemical reactivity of CD hydroxyls.[23]

Reagent reactivity plays an important role in determining the substitution of the product. For example, trimethylsilyl chloride (TMSCl) reacts with cyclodextrins less selectively and forms products functionalized at all three OH positions, while trityl chloride ($(C_6H_5)_3CCl$) is selectively attacked by the C-6 oxyanion.[24]

**1.2.1.3 Cyclodextrin Chemical Stability.** CD $\alpha$-1,4-linkages are hydrolyzed to form linear dextrins at high temperatures and acid concentrations, though stable under neutral, basic and dilute acid conditions at room temperature. Hydrolysis of $\beta$-CD in 1.15M HCl solution at

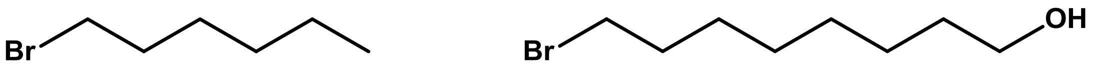
$100^{o}C$ into its simpler sugar was observed by Szejtli who also investigated CD ring opening versus glycosidic bond breakage.[25] At lower temperatures ($0^{o}C$), however, higher concentrations of HCl (5N, 10N) resulted in the formation of stable CD-HCl-$H_2O$ complexes with no hydrolysis observed.

**1.2.2 Tie Chains.** Bi-functional molecules such as simple alkyl chains, linear oligomers, or polymer chains are examples of tie chains used as cross-linking units in the networks. These cross-linkers form the network matrix, and displace a large percentage of the polymer. This document outlines the use of simple chemistry toward a controlled approach of establishing linkers of varied lengths and composition between nodes. Terminal functionalities of alkyl bromides and diglycidyl ethers are used as leaving groups in nucleophilic substitution reactions. Figure 1.9 illustrates the linker molecules used in the reactions.



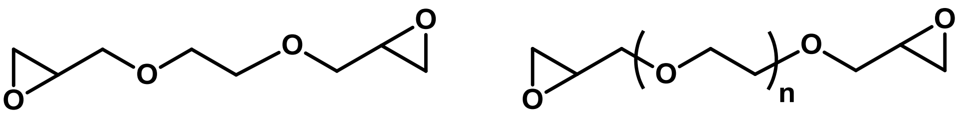
1,6-dibromohexane (DBH)

1,12-dibromododecane (DBDD)



1-bromohexane (MBH)

8-bromooctan-1-ol

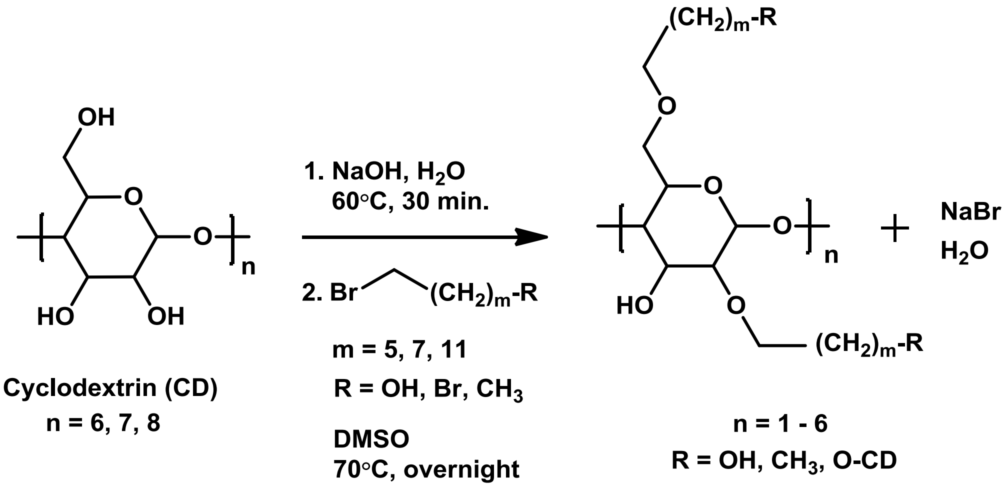


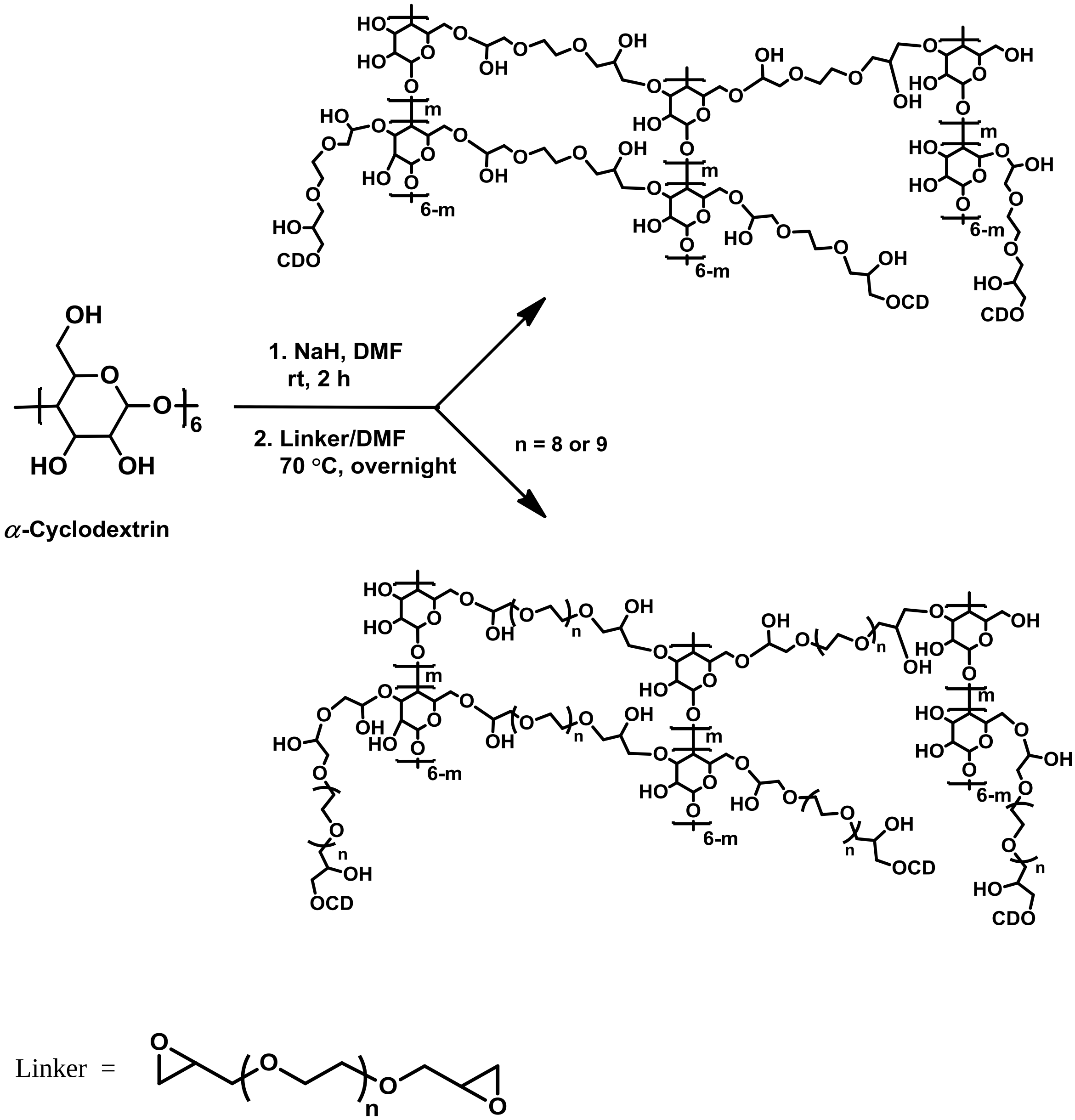
Ethylene glycol diglycidyl ether (EGDE)

$PEG_{500}$ diglycidyl ether (PEGDE)

**Figure 1.9.** Linker molecules used in reactions

**1.2.2.1 Reaction of Linkers with Nodes to Form Polymer Networks.** Alkyl dibromides and diglycidyl ethers provide terminal leaving groups and are appropriately sized to allow easy entry and exit from the CD cavity. The nucleophilic reaction occurs following formation of cyclodextrin oxyanions by a suitable base. The functionalization chemistry employed is given in Scheme 1.1.





Linker =

Ethylene Glycol Diglycidyl Ether (n = 1)
PEG Diglycidyl Ether (n = 8 or 9)

**Scheme 1.1.** The functionalization chemistry employed in formation of networks. CD is ionized by NaOH or NaH, followed by a dropwise diluted linker addition.

The eighteen to twenty-four hydroxyls oriented three-dimensionally around the rings of the three CDs allow for good connectivity at the nodes. Cyclodextrin polymers result from linking of CD nodes via tie chains. Figure 1.10 shows different forms of CD polymers.[26] The branched and linear polymers are generated by functionalizing polymeric backbones with CDs via monofunctional linkers, or linking CDs linearly via tie chains. Similar to the networked polymer in Figure 1.10, cross-linked polymer networks can be prepared by linking CD oligomers via tie chains three-dimensionally. Of note is that the CD guest-host capability is maintained with all the aforementioned CD polymer types.

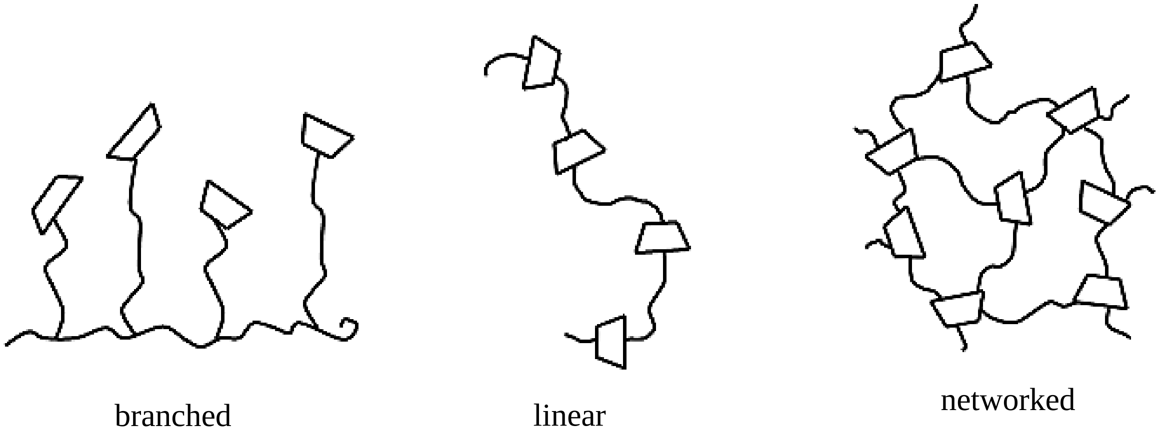


**Figure 1.10.** Variations in CD polymer forms showing branched, linear, and networked CD polymers.

Widespread interest across industries in CD-network polymers resulting from their potential applications in energy, medicine, agriculture, pharmacy and food production is ongoing.[27] Epichlorohydrin cross-linking chemistry in NaOH solution has led to swellable cyclodextrin polymer networks.[28-30] Additionally, CD-polyurethane resins were synthesized for chromatographic separation of aromatic amino acids using isocyanate-based cross-linkers.[31] The gel structure of these networks was deformed under high pressure due to the high flexibility and compressibility, limiting use in separation columns.[32] Furthermore, the length between the cross-links and the cross-link density cannot be controlled. Robust hydrogels with controlled strength and stability[33-35] have been made using fixed molecular weight cross-linkers, primarily employing di-isocyanate based chemistry.[36]

**1.2.3 The Guests.** Guests are molecules that interact with the CD cavity, which acts as the host. Non-covalent interactions are present in this type of molecular complexation of two or more bound molecules. Inclusion complexes result from small molecules residing in, or capping the cavity of the CD.

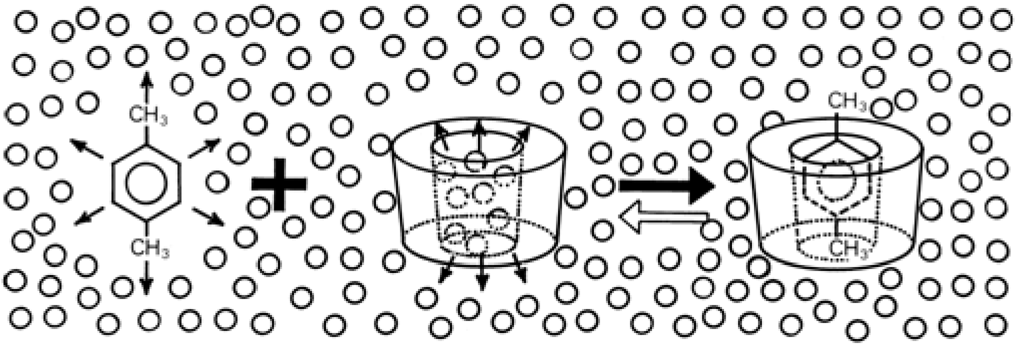


**Figure 1.11.** Schematic representation of guest-host interaction between *p*-Xylene (guest) and CD (host) in water (circles).[37] Xylene's hydrophobicity drives the equilibrium to the right since the CD cavity, being also hydrophobic, allows for hydrophobic interactions.

**1.2.3.2 Small Molecular Complexes.** Small organic molecules are renowned for being encapsulated by cyclodextrins. In aqueous media, hydrophobic guest molecules capitalize on the unique amphiphilic CD property, residing in the hydrophobic cavity and being transported by means of the host's hydrophilic exterior. This capability has led to CDs' common utility in drug delivery. The food and cosmetic industries use CD encapsulation of volatile and odorous molecules for product enhancement. Hydrogen bonding, electrostatic interactions, van der Waals interactions, and hydrophobic interactions are the forces that allow these CD guest-host complexations.[38] Guest-host inclusion and exclusion undergo dynamic equilibrium when in solution. Water molecules reside in the CD cavity in aqueous solution (Figure 1.11).[37] Water molecules are displaced by the guest molecule during complexation.

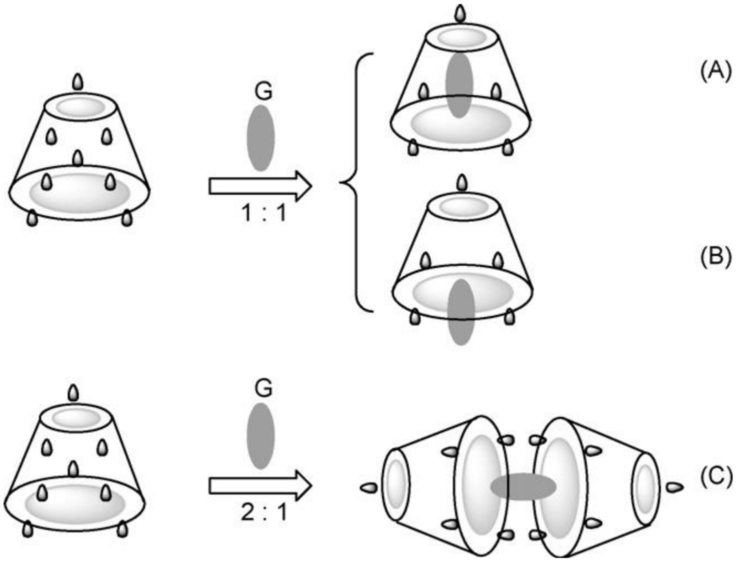


**Figure 1.12.** Schematic sketches of three modes of complexation of small molecules with cyclodextrin.[39]

Guest-host interactions occur in three common modes between small molecules and cyclodextrins.[39] Complexations where the guest is completely inserted in the CD cavity is shown in Figure 1.12A. Examples of such interactions are with para-substituted phenyl ring compounds,[40] methanol,[41] and other small molecules. Bulkier phenyl analogs form associative complexes as shown in Figure 1.12B, where the guest molecule is partially included in the CD cavity. Larger molecule guests, such as ferrocenes,[42] metal salts,[43] and fullerenes,[44] form complexes where the guest is capped and sandwiched by two CD molecules (Figure 1.12C).

**1.2.3.3 Fullerene.** Carbon atoms in fullerences are bonded to three neighboring carbons with $sp^2$ hybridization. The molecule contains only carbon atoms and resembles a soccer ball. Fullerenes vary by the number of carbon atoms in the molecule and range from 20 ($C_{20}$) carbons to 720 ($C_{720}$). Common fullerenes are $C_{60}$ (Buckminster fullerene) and $C_{70}$. Buckminister fullerene (Figure 1.13) is comprised of 12 pentagonal and 20 hexagonal rings. This spherical molecule of 0.7 nm diameter has sixty single and thirty double bonds.[45] $C_{60}$ is highly strained, and because of poor π-electron delocalization, is not aromatic.[46]

**Figure 1.13.** Structure of fullerene ($C_{60}$) used as a guest to synthesize nanocomposites with CD networks.

**1.3 Objectives.** The main goal of this research is to develop techniques for creating homogenous polymer networks having well defined cross-link lengths and densities with covalently and non-covalently (guest-host) interacting molecular nodes. Short-chain functionalized alkanes, ethers, cyclic oligomers, and polymers were emphasized in order to gain control of network architecture and properties. These modules resulted in molecular frameworks of different shapes and sizes. Focus was placed on the use of inexpensive reagents and methods, and mild reaction conditions. Some project specific objectives were to:

1. Design an inexpensive and easy cyclodextrin functionalization method and work-up to ultimately make polymer networks with fixed cross-link lengths and stoichiometrically regulated cross-link densities.

2. Prepare inclusion complexes using cyclodextrin networks and small molecular guests.

3. Investigate the sequestration properties of the networks by preparation of their films and membranes.

**1.4 Summary.** The following three chapters of this dissertation present three areas of the research project. Chapter II describes simple functionalization chemistry to create derivatized cyclodextrins, ultimately leading to hydrophobic nanoscopic polymer networks. Chapter III presents the synthesis of membranes from the hydrophobic networks that have sequestered fullerene molecules, yielding a unique polymer composite. Chapter IV's focus is on the extension of the Chapter II work by making amphiphilic networks using hydrophilic linkers.

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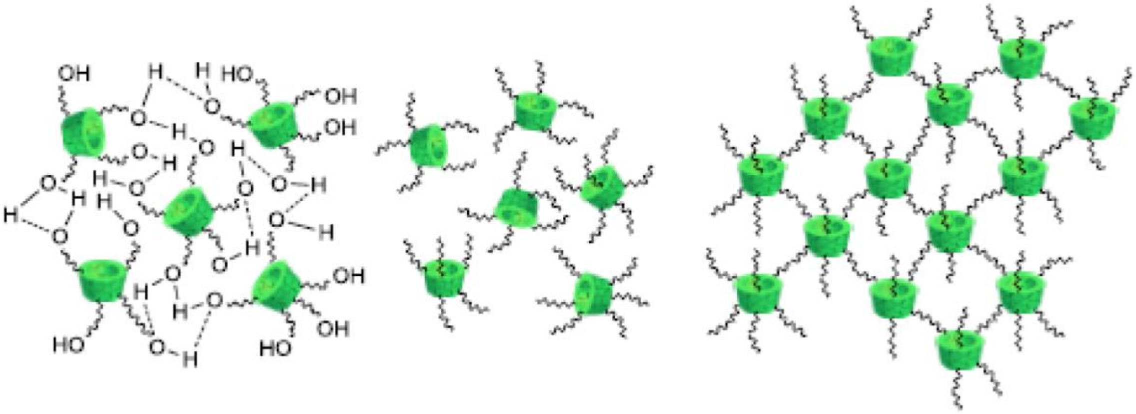
# CHAPTER II

# CYCLODEXTRIN DERIVITIZATION: SIMPLE ROUTES TO SOLUBILITY AND NANOSCOPIC POLYMER NETWORK DESIGN

**Abstract.** Opportunities arise to generate materials with new solubility, phase transfer, guest-host, and network properties by chemically functionalizing cyclodextrins in a systematic fashion. These substances can be used in polymer science, in making templates or scaffolds for synthesis of new materials, including free-volume modifiers, and as stabilizers or compatibilizers. The selective functionalization of cyclodextrin rings with short- and long-chain alkyl derivatives of varying polarity by easily purified, inexpensive, and simple one-pot methods are described herein. The use of bifunctional cross-linking reagents results in cyclodextrin-based polymer networks. The type and extent of functionalization, which may be controlling devices for swelling and solubility, are revealed by solution and solid-state NMR experiments. The average number of methylenes per CD ring is an expression of the degree of alkyl chain functionalization. With an average of up to sixteen methylenes, water soluble products result, but at a value of 32 these materials become water insoluble.

**2.1 Introduction.** It is our belief that functionalized CDs have potential in polymer science as tunable surfactants, scavengers, free-volume modifiers, and network formation templates if systematic and economical derivitization routes are available. With possible use in biphasic catalysis, drug delivery or drug recovery from wastestreams, and nanostructure templating, many amphiphilic compounds can result from CD modification.[1-4] Silylated,[1] alkylated,[2,4-7] sulfonated,[5,8] carboxylated,[9] and ethylene-oxide-functionalized[10,11] CDs have been reported in the literature. Polystyrene-functionalized CDs have found use as compatibilizers for polystyrene and polydimethylsiloxane solutions.[12] Sodium hydride (NaH) in dimethylformamide, tetrahydrofuran, or dimethylsulfoxide (DMSO) is used for alkyl halide functionalization.[2,4,5] Since anhydrous conditions are required for NaH use, preparation for reaction is more involved. The controlled methylation at *β*-CD's 2-*O*-position starting from its 6-bromo-6-deoxy derivative in the presence of $BaO/Ba(OH)_2 \cdot 8H_2O$ and dimethyl sulfate are other recent examples.[6,7] This reaction requires a multi-step work-up to isolate pure products. Amphiphilic CD derivatives including 2-hydroxypropyl and 2-hydroxyl-3-betainpropyl-functionalized *β*-CDs have been recently discussed.[13,14] Substrates with epoxide moieties were reacted with ionized CDs to synthesize these derivatives. Aqueous NaOH concentrations by volume of up to 30% at 60 °C were the conditions for making the *β*-CD oxyanions. The stability of CD oligomeric chains can be affected by such strongly basic conditions, which may also require neutralization at high acid concentrations. Hydroxyethyl modified CDs[15] and osmium tetroxide-catalyzed modified CD oxidation are also recent examples. Amphiphilic *β*-CDs with ethylene oxide functionality were generated by reacting ethylene carbonate and per-alkylthio *β*-CDs to give a 2-*O*-position-modified product with 1 to 3 oligo-ethoxy groups per ring.[11] Biphasic catalysts were produced following a multistep synthesis involving poly(ethylene oxide) modified CDs.[10] To do this, 2,3-*O*-dialkyl CD derivatives were obtained by Takeo's and Kuge's method,[7] and a Fugedi[2] protocol enabled 6-*O*-position protection. Diphenylmethyl potassium initiator brought about anionic ring opening polymerization of the functionalized rings. Documentations of CD modifications, mainly with applications in biology and pharmaceuticals, were presented in a recent review.[16]

This account offers a straightforward method for the preparation of alkyl-chain-modified $\alpha$- and $\beta$-CD's. Heating the CD in basic aqueous solution results in oxyanion formation. The addition of diluted haloalkane further lowers the reaction mixture concentration. The dilute reaction mixture also results in CD oxyanions at room temperature. This simple one-pot synthesis, without the aid of NaH or needing strong acid work-up, because of very low NaOH concentration, yields alkyl-functionalized or networked CDs. Monofunctional alkyl reagents lead to the alkyl-functionalized CDs, and the bifunctional to networked materials. Products generated by this simple inexpensive process are easily purified and stored as dry powders. Quantitative solid-state NMR experiments show that the degree of functionalization, and therefore solubility, is easily controlled. Finally, we illustrate that novel cross-linked networks of CD rings can be formed using bifunctional haloalkane reagents. Scheme 2.1 shows three different structure types accessible using our NaOH-mediated syntheses, with detailed structures and characterization described in the following sections.



**Scheme 2.1.** Representations of **(left)** hydroxyoctyl functionalized CDs, depicted with hydrogen bonding, **(center)** hexyl functionalized CDs, and **(right)** cross-linked networks formed in the dibromohexane/CD reaction. In the latter case, the network is three-dimensional and amorphous, with the cyclodextrin rings less spatially ordered than shown.

## 2.2 Experimental

**2.2.1 Materials.** *α*- and *β*-CDs were purchased from Cyclodextrin Technologies Development Inc., and used after re-crystallization from their saturated solutions in de-ionized water, followed by drying overnight at 80 °C. 8-bromo-1-octanol was purchased from TCI America, and DMSO was obtained from Sigma Aldrich Chemical Company; both were used without purification.

**2.2.2 Hydroxyoctyl Functionalization with 8-Bromo-1-octanol.** To 243 mg (0.25mmol) *α*-CD in 0.30-0.35M NaOH solution (60 mg in 5 mL water, 1.5 mmol) at 60 °C was added 8-bromo-1-octanol (1.5 mmol) dissolved in 5 mL DMSO dropwise. The temperature was raised to 70 °C and stirring continued for 9 h. Cream-colored solids formed upon cooling to room temperature. The solid was filtered and washed several times with acetone to remove DMSO and other soluble components. The filtrate, along with the acetone used for washing, was kept in the fume hood for several hours, inducing further solid precipitation as acetone slowly evaporated.  This residue was similarly filtered and washed with acetone.  This process was repeated until no further precipitation occurred. The final product was obtained as a white solid.

For reference, we define equimolar as one reagent molecule per CD ring. However, since there are six ($\alpha$-CD) or seven ($\beta$-CD) glucose units per CD ring, and we assume that at least one reactive hydroxyl group exists per glucose unit, a minimum ratio of 1:6 or 1:7 CD:bromooctanol would be required for $\alpha$- and $\beta$-CD, respectively.  Overall product yields for the bromooctanol/CD derivatives were, on average, 20%.  Yields were calculated based on the mass of the final dried products.

**2.2.3 Hexyl Group Functionalization with 1-Bromohexane.** $\alpha$-CD (0.5 mmol) was dissolved in 5 mL of 1.2N NaOH (240 mg) solution and stirred at 60 °C for 3 h.  The temperature of the reaction mixture was increased to 70 °C and 840 μL (6 mmol) 1-bromohexane (MBH) dissolved in 5 ml DMSO was added dropwise.  The clear reaction mixture after reagent addition turned white, and product precipitation was observed after continuous heating.  The solvents were decanted and the product was washed several times with acetone followed by water, and dried in a vacuum oven.  Overall product yields for the monobromohexane/CD derivatives ranged from 80 to 90 %.  Yields were calculated based on the mass of the final dried products.

**2.2.4 Bifunctional Derivatization with 1,6-Dibromohexane.** For a product possessing an $\alpha$-CD:DBH molar ratio of 1:6, $\alpha$-CD (0.5 mmol) was dissolved in 5 mL of 0.6N NaOH solution and stirred at 60 °C for 2 h.  The temperature was then increased to 70 °C and 0.46 mL (3 mmol) of 1,6-dibromohexane (DBH) dissolved in 5 ml DMSO was added dropwise. Stirring continued for 9 h and the reaction mixture was allowed to cool to room temperature with stirring for an additional 2 h. Addition of acetone precipitated a white solid, which was filtered, washed with acetone, and vacuum oven dried, followed by crushing to produce shiny white crystals.

Similarly, a 1:12 molar ratio of $\alpha$-CD:DBH network was synthesized as follows: $\alpha$-CD (0.5 mmol) was dissolved in 5 mL of 1.2N NaOH solution and stirred at 60 °C for 3 h. The temperature was then increased to 70 °C and 0.92 mL (6 mmol) of 1,6-dibromohexane (DBH) dissolved in 5 mL DMSO was added dropwise. The reaction mixture appeared creamy white in color upon addition of the DBH solution. Stirring continued for 10 h following which the reaction mixture was allowed to cool to room temperature with stirring for an additional 2 h. The product precipitated out of the reaction mixture and the supernatant was decanted. The residue was washed several times with acetone and finally dried under vacuum. The “tough” lumps were crushed to obtain a white powder. Overall product yields for the dibromohexane/CD networks ranged from 35 to 45 percent. Yields were calculated based on the mass of the final dried products.

Analyses of products and the extent of reaction on $\alpha$-CD and $\beta$-CD were carried out using spectroscopic and chemical methods. Solution $^{1}$H NMR measurements were acquired by dissolving the products (when soluble) in DMSO, and spectra were acquired on a 400 MHz spectrometer. As networked materials are an ultimate goal of our synthetic efforts, characterization methods suitable for insoluble derivatives are required. Therefore, in addition to solution NMR, $^{1}$H-decoupled (75-kHz decoupling field strength) solid-state $^{13}$C MAS (magic-angle spinning) NMR spectra of the dried final products, obtained using a Bruker DSX-300 spectrometer operating at 7.05 Tesla field strength (300 MHz $^1$H Larmor frequency), were collected to investigate the product nature and reaction extent. $^{13}$C single-pulse (90° pulse width) data with $^1$H decoupling were recorded for the samples at 5-kHz MAS speeds, with a 120 second recycle time between each pulse.

Wet chemical tests with $AgNO_3$ were used to determine if bromoalkanes reacted, by observation of AgBr precipitates, therefore indicating that free bromide ions were generated. $AgNO_3$ confirmed the formation of free $Br^-$ ions in functionalization reactions, as the AgBr resulted in the reaction mixture turning a milky off-white color. A gray precipitate, resulting from AgOH formation was also observed following addition of dilute NaOH. No change was observed when $AgNO_3$ was mixed with bromooctanol with no NaOH or CD present.

**2.3 Results and Discussion.** Four key questions need to be addressed in assessing the reaction scheme: (1) can hydrophilicity/hydrophobicity be controlled to produce solubility variance; (2) how does the reaction stoichiometry affect the extent of functionalization per CD ring; (3) does the reaction yield a stable product; and (4) where does functionalization occur? Our main interest in undertaking this synthetic route focuses on the inexpensive production of functionalized solid-state CDs, which would then be easily available for a range of possible uses in materials and polymers, such as guest–host scavengers, free-volume modifying additives, network nodes, or compatibilizers. Solid-state NMR is suitable to characterize products since removal of unreacted starting materials and byproducts following multiple drying/washing steps can be tracked in insoluble materials. Additionally, applicable solid-state NMR experiments can provide quantitative data on the degree of functionalization or cross-linking depending on reagents, reaction conditions, and CD type.

**2.3.1 Monofunctional Derivatization via C8 Chain Bearing Polar End Group.** Figure 2.1 shows solution $^1$H NMR spectra for pure CD (1a) and 8-bromo-1-octanol functionalized CD with CD:bromooctanol ratios of 1:1 (1b) and 1:6 (1c), in DMSO. Peak assignments for pure CD are given in the insertion.

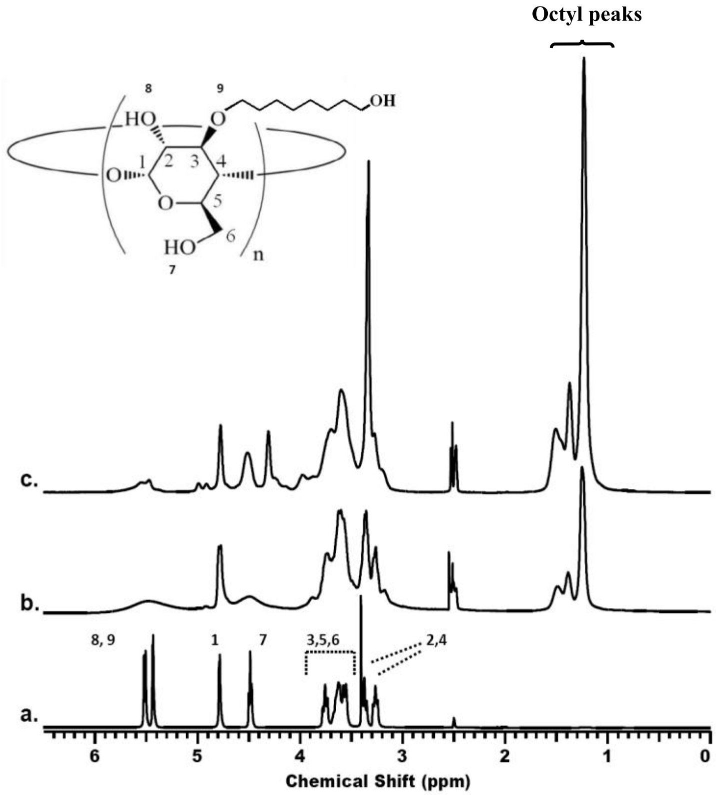


**Figure 2.1.** $^1$H solution NMR spectra of **a)** pure *α*-cyclodextrin **b)** 1:1 *α*-cyclodextrin/8-bromo-1-octanol adduct and **c)** 1:6 *α*-cyclodextrin/8-bromo-1-octanol adduct. The intense narrow peak at 3.4 ppm in a) is due to an impurity in DMSO. The peak assignments in 2.1a correspond to the numbered protons in the inset structure.

The literature values known for sugars and CDs[17,18] are consistent with those shown of pure CD and are in agreement with experimentally measured integrals and *J*-coupling splittings. The proton in the 1-position on the ring is used as an internal reaction and intensity standard since it is non-reactive. Peak 1 broadens slightly with reaction, but no change in chemical shift, splitting, or intensity is observed (2.1b and 2.1c). Bromooctanol should react with the two secondary and one primary hydroxyl groups on the CD ring, yielding free bromide and the derivatized ring in the process. As stated in the experimental section, we confirmed production of free bromide in all cases via reaction with $AgNO_3$ to yield the presence of AgBr. The reaction is nonspecific, that is, both primary and secondary CD hydroxyls react equally as shown by changes in the total line shape and intensity for peaks 7, 8, and 9 in Figure 2.1(b,c). Based on comparison to peak 1 these three hydroxyl peaks decrease in total intensity by 50% in the 1:1 reaction relative to pure CD (2.1b vs. 2.1a). An increase in peak intensities in the 3.5–4 ppm region is observed, while an expected corresponding decrease in the region downfield of 4 ppm takes place as the reaction proceeds. Whereas the primary hydroxyl peak (peak 7 at 4.5 ppm) increases in intensity in 2.1c compared to 2.1b or 2.1a, the secondary hydroxyl peaks (peaks 8 and 9 ca. 5.5 ppm) decrease an additional 30% in 2.1c over 2.1b. This difference is attributed to the H7 in pure CD having the same approximate chemical shift as the hydroxyl of the octanol. The spectra also show an increase in intensity of the octyl methylene peaks in the 1–2 ppm region. As expected from the reaction scheme, increased intensities for the signals in the 3–4 ppm range in 2.1b and 2.1c is consistent with CD hydroxyl derived ether linkages.

As subsequent discussion will reveal, where functionalization leads to cross-linked CD networks, solution NMR resolution is inadequate. It is therefore necessary to use solid-state NMR, and though some adducts were soluble, solid-state data for all CD products were collected in order to accrue ample data for future work. CP MAS spectra of materials presented in Figure 2.1 in solution are shown in Figure 2.2 in the dry solid state. The multiplicity due to the inequivalent and crystallographically rigid environments assumed by the glucose rings of pure $\alpha$-CD are shown in Figure 2.2a.[19]

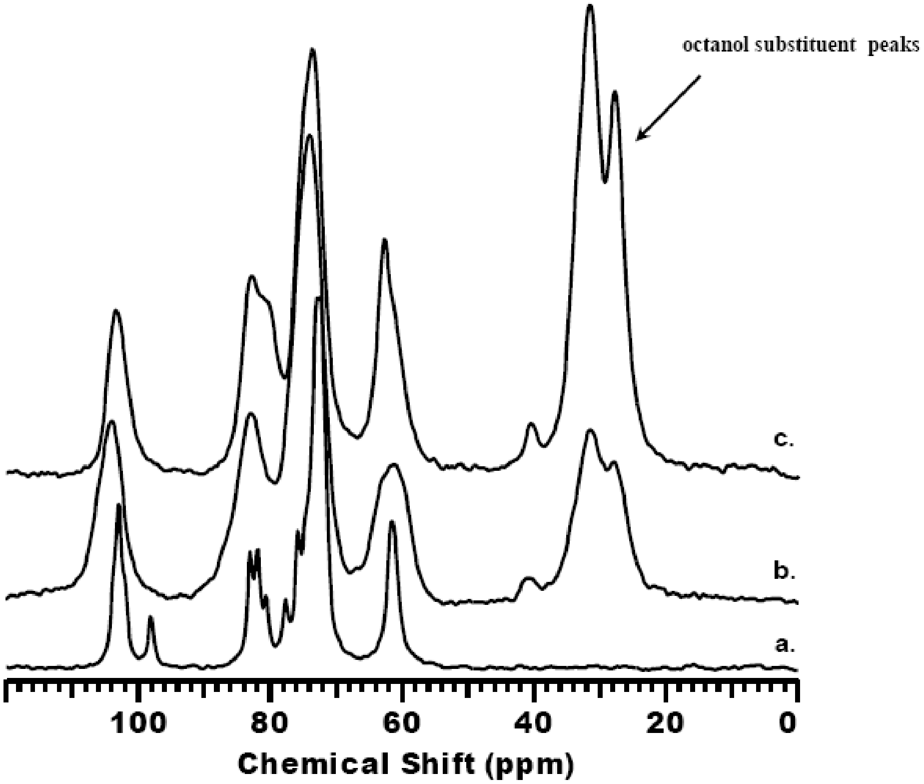


**Figure 2.2.** $^{13}$C CP MAS NMR spectra for **a)** pure $\alpha$-CD**; b)** multiple washed and dried product with 1:1 $\alpha$-CD:8-bromo-1-octanol molar ratio in the reaction mixture; **c)** same reaction product obtained using 1:6 molar ratio. The primary peaks resulting from alkyl chain incorporation on the CD rings are centered at 30 ppm. The small peak at 41 ppm arises from residual DMSO. All spectra were collected using $^1$H decoupling.

The CD peaks in the 70–105 ppm region transform into single broad signals because the reaction destroys the crystalline structure. The octyl methylene peaks, as a result of reaction with the CD hydroxyls, are observed around 30 ppm in Figure 2.2(b,c). Additional contributions from the octyl appendage are observed in the 60–62 ppm region, arising from the methylene alpha to the hydroxyl at the chain end.

Signal acquisition suggests that the chains attached to the CD ring are rigid, as would be expected for true covalent bonding to the ring. A physical mixture results in different spectra, as will be discussed in later sections. Comparisons of spectra from different NMR experiments revealed no significant differences in the type and intensity of signals, indicating that the product is homogeneous. Regular solution NMR experiments do not afford this discriminator.

Figure 2.3 shows spectra of results for reactions designed to verify that dilute NaOH was actually the factor affecting reactivity, and that simply heating the reaction mixture was not leading to the desired product. From the bottom spectrum in Figure 2.3, we conclude that the dilute NaOH is required for successful functionalization of the CD hydroxyls via reaction with bromooctanol. Figure 2.3 also reveals additional spectral features at 61–63 ppm and 81–83 ppm, which are overlapping with CD peaks.

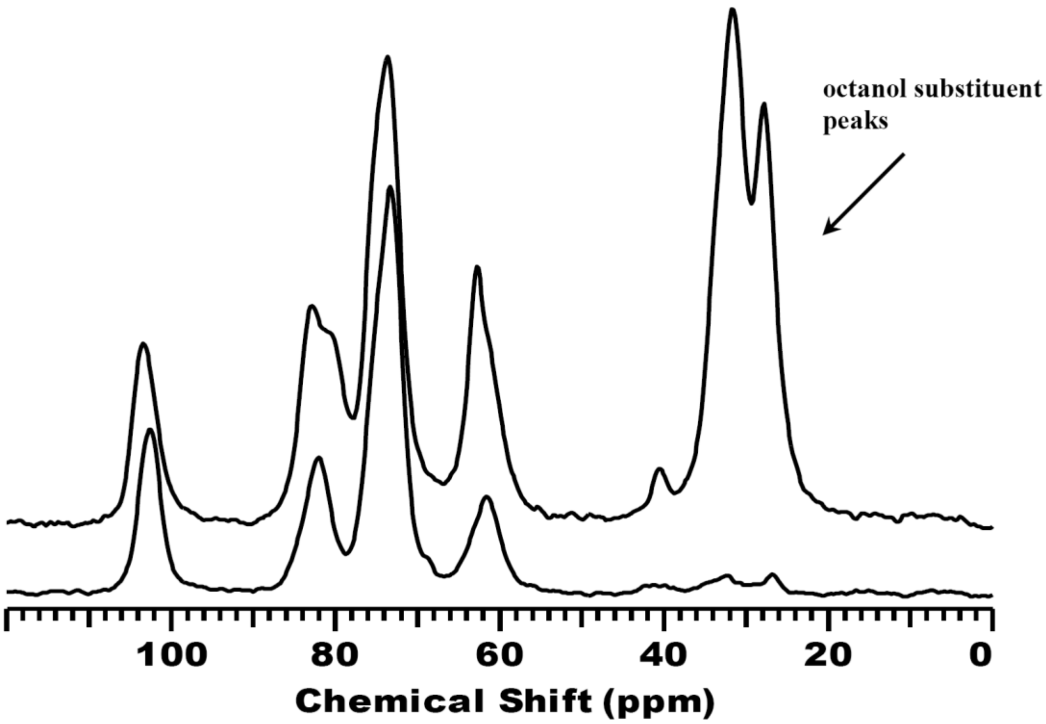


**Figure 2.3.** Comparison of $^{13}$C CP MAS NMR spectra for **top)** the 1:6 molar ratio product of $\alpha$-CD and 8-bromo-1-octanol obtained using dilute NaOH, versus **bottom)** the same reactants, stoichiometry, and reaction conditions but without addition of the NaOH to the reaction mixture. In both cases, the reaction temperature was 70 °C.

The influence of temperature was examined by reducing the reaction temperature to 23 °C from 70 °C (as used for the materials in Figs. 2.1–2.3). The results of this experiment are shown in Figure 2.4, where CP MAS spectra for $\alpha$-CD products obtained at the different temperatures, using equimolar CD:bromooctanol are compared. It is interesting that the reaction occurs even at room temperature, though with about half the yield of when heated. The bottom spectrum in Figure 2.4 indicates that oxyanions form at room temperature even in dilute NaOH.

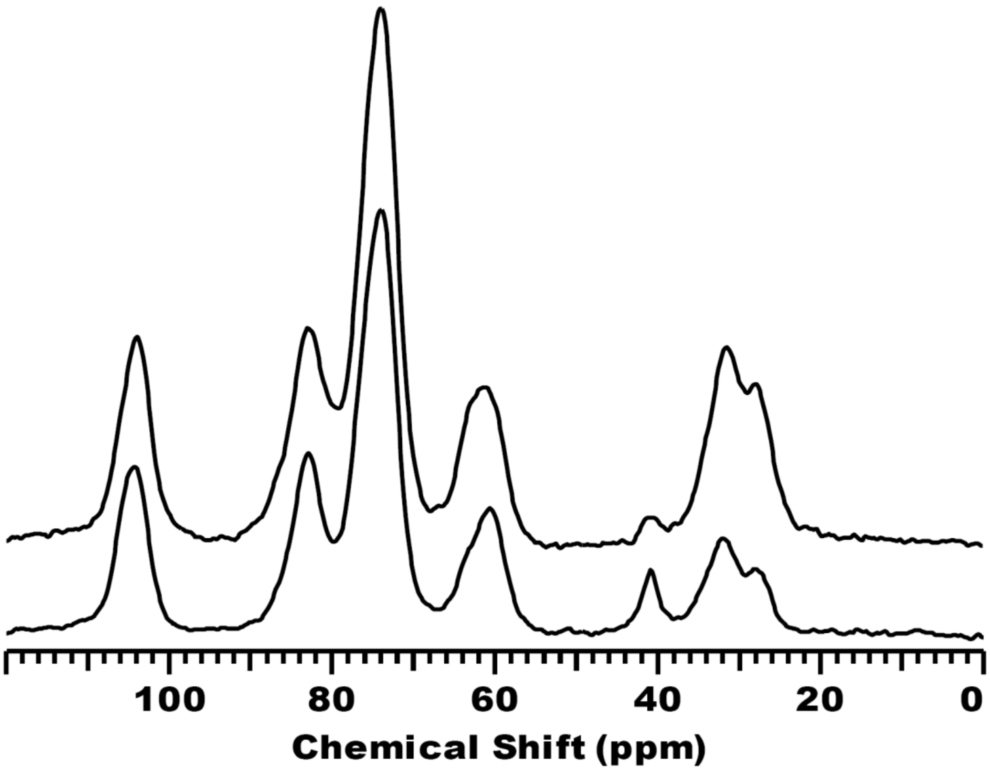


**Figure 2.4.** $^{13}$C CP MAS NMR spectra for **top)** product with 1:1 $\alpha$-CD:8-bromo-1-octanol molar ratio reaction carried out in the presence of NaOH for 9 h at 70 °C; **bottom)** same reaction as above, but at 23 °C. The small peak at 41 ppm arises from residual DMSO.

Physical mixtures of bromooctanol and CD in solvent (without NaOH), followed by drying, were used to exclude the possibility that unreacted reagent contributed to the signals in the aforementioned spectra. The results of this control experiment are shown in Figure 2.5, where remaining bromooctanol peaks bear no resemblance to those in Figures 2.2–2.4. For clarity, the spectra in Figures 2.2–2.4 were obtained via CP methods, whereas the sample in Figure 2.5 yielded CP signals in the 20–40 ppm region that were negligible, indicating ‘‘free’’ bromooctanol molecules. The narrow peak widths also suggest freely reorienting small molecules, and it is known that molecules (including macromolecules) inside the nonpolar CD cavities can rapidly reorient.[20] It is not evident, however, if the bromooctanol is acting as a guest in the CD cavity or is hydrogen bonding with the CD hydroxyls on the periphery. In the event that inclusion complexation occurs, spectra should show sharp peaks as in Figure 2.5, as opposed to the broader peaks resulting from covalently bonded chains (Figure 2.4).

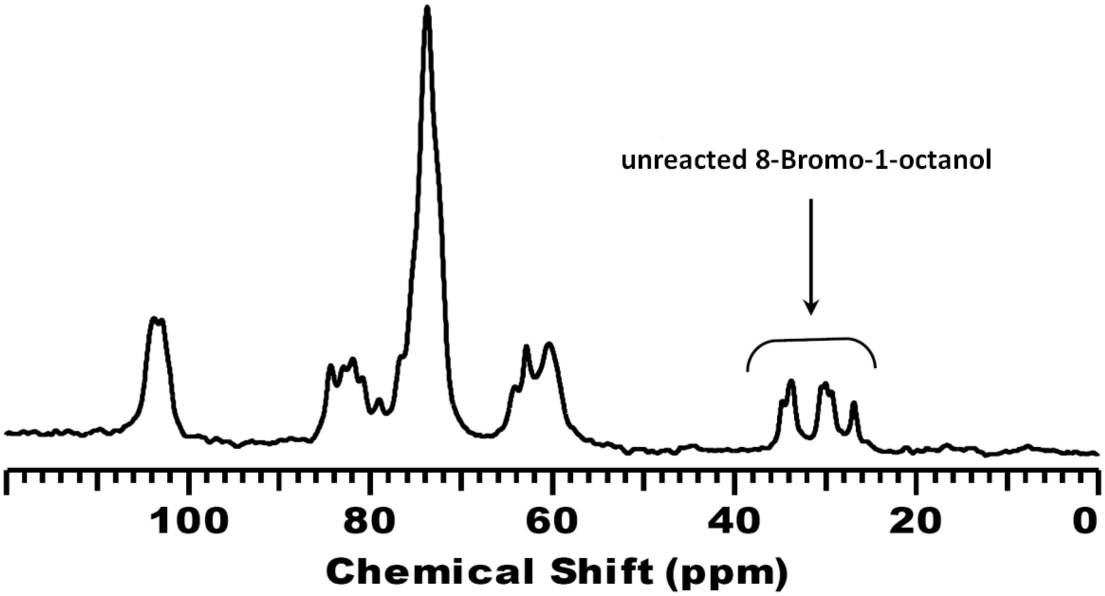


**Figure 2.5.** $^{13}$C single-pulse MAS NMR spectra for physical mixtures of the bromooctanol reagent and $\beta$-CD, demonstrating that the degree to which inclusion compounds can form in the larger $\beta$-CD cavities does not yield product spectra of the type shown in Figures 2.2-2.4.

The tertiary carbon C-1 of each glucose ring, with a chemical shift of 103-ppm, is non-reactive and is used as an internal standard. Quantitative solid-state NMR Bloch decay experiments can determine the number of CD hydroxyls functionalized by alkyl chains. For example, spectral deconvolution and lineshape fitting on the Bloch decay spectrum of the 1:6 $\alpha$-CD product showed that each CD ring was modified with an average of 4–5 hydroxyoctyl chains.

**2.3.2. Monofunctional Derivatization via C6 Chain Bearing Non-Polar End Group.** In addition to the derivatives described above with side chains which are hydroxyl

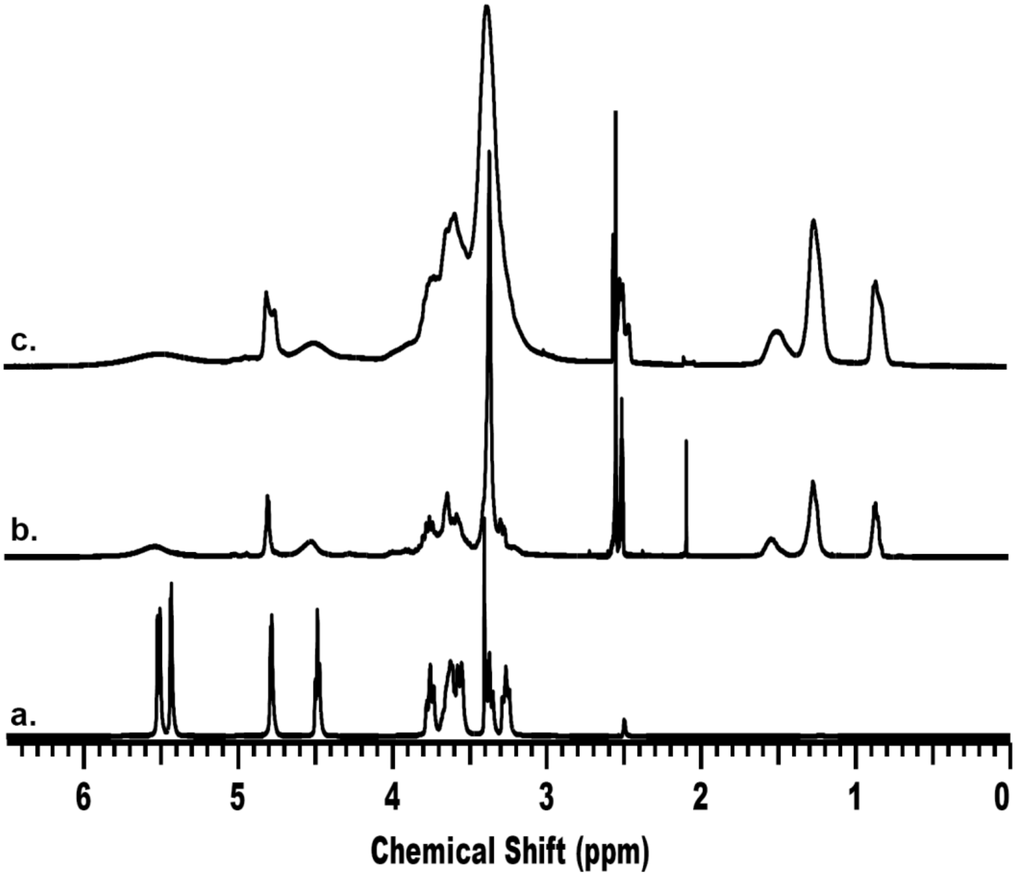


**Figure 2.6.** $^1$H solution NMR spectra of **a)** pure $\alpha$-cyclodextrin **b)** $\alpha$-cyclodextrin/ 1-bromohexane 1:6 reaction product and **c)** $\alpha$-cyclodextrin/1-bromohexane 1:12 reaction product.

terminated, nonpolar-functionalized CDs were also synthesized. Reacting CD with 1-Bromohexane is expected to convert the polar exterior of the CD ring to a non-polar species. Figure 2.6 shows $^1$H solution NMR spectra of derivatives prepared in this manner. The decrease in CD hydroxyl peak intensities and associated increase in CD ether linkage signals (3–4 ppm), as well as alkyl methyl/methylene signals (0.5–1.5 ppm) with increasing number of hexyl chains functionalizing the rings were observed, as previously with other analogs (Figure 2.1). The solid-state NMR spectrum of the 1:12 reaction product shown in Figure 2.6c is rendered in Figure 2.7. Peaks from the hexyl

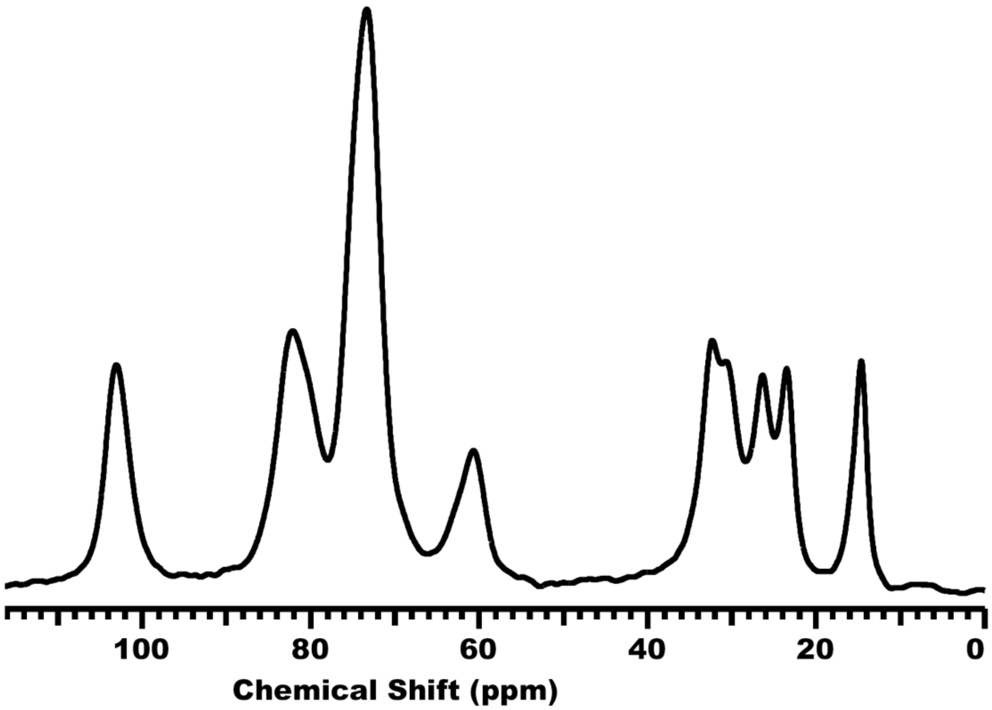


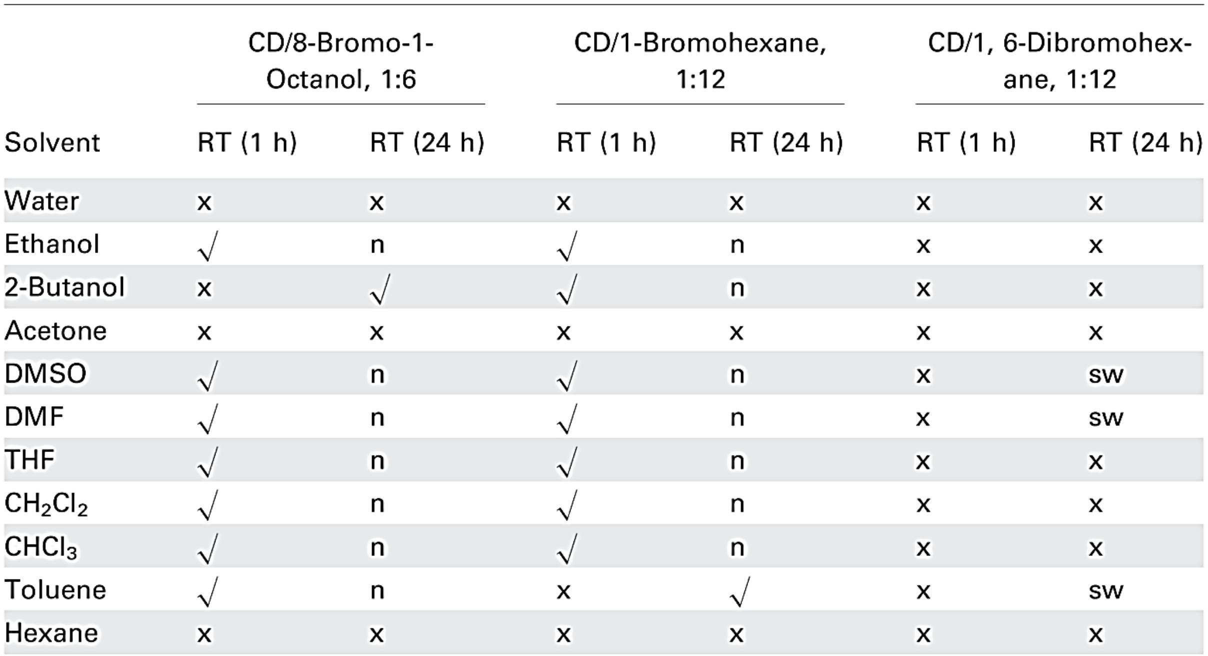
**Figure 2.7.** $^{13}$C CP MAS NMR spectrum of the dried product resulting from the reaction of $\alpha$-CD with 1-Bromohexane (MBH) in the presence of 0.12N NaOH at 70 °C for 16 h. The molar ratio was $\alpha$-CD:NaOH:MBH=1:12:12.

side chain functionalizing the CD ring are clearly resolved. The product contains covalently bonded side chains, as indicated by Bloch decay spectra being identical to the CP spectra. If the side chains were not bonded, they would be very mobile, and peaks would be of relatively lower magnitude in CP than Block decay spectra, because of poor CP efficiency. Peaks in the 20–40 ppm region are notably narrower than those seen for the bromooctanol groups in Figures 2.2–2.4, however, which indicates that the latter are possibly participating in hydrogen bonding through the hydroxyl termini. For this product, 8–9 hexyl chains per CD ring are obtained, which was slightly less than the 12 chains per ring targeted in the stoichiometry.

**2.3.3 Solubilities.** Depending on the nature and extent of functionalization, CD modification is expected to lead to variations in solubility. Bulk solubility data are summarized in Table 2.1 for the CD derivatives prepared. Whereas bromooctanol and bromohexyl CD derivatives were both soluble in water at a 1:1 starting material molar ratio, increasing the chain density per CD ring to 1:6 CD:chain resulted in both derivatives being insoluble in water while maintaining solubility in ethanol. Using low cost reagents, the hydrophilic exterior of CD can be made insoluble with minor modification, as these data demonstrate. Table 2.1 summarizes differential solubility at the higher side-chain concentrations for three different synthetic routes. It was observed that these synthetic methods can generate a wide range of final products, with different solubilities and dispersions in a variety of solvents.

In general, quantitative solid-state NMR experiments show water solubility decreasing within the 16–32 methylene range added per CD ring in $\alpha$-CD, with adducts

**Table 2.1.** Bulk solubility of derivatized cyclodextrins in a variety of common solvents at room temperature.



| | CD/8-Bromo-1-Octanol, 1:6 | | CD/1-Bromohexane, 1:12 | | CD/1, 6-Dibromohexane, 1:12 | |
|---|---|---|---|---|---|---|
| Solvent | RT (1 h) | RT (24 h) | RT (1 h) | RT (24 h) | RT (1 h) | RT (24 h) |
| Water | x | x | x | x | x | x |
| Ethanol | √ | n | √ | n | x | x |
| 2-Butanol | x | √ | √ | n | x | x |
| Acetone | x | x | x | x | x | x |
| DMSO | √ | n | √ | n | x | sw |
| DMF | √ | n | √ | n | x | sw |
| THF | √ | n | √ | n | x | x |
| $CH_2Cl_2$ | √ | n | √ | n | x | x |
| $CHCl_3$ | √ | n | √ | n | x | x |
| Toluene | √ | n | x | √ | x | sw |
| Hexane | x | x | x | x | x | x |

For the products denoted as insoluble or swollen, increasing the temperature to 80 °C did not result in solubility. All were tested at the fixed concentration of 5 mg product per mL solvent. x, not soluble; ✓, soluble; n, not tested; and sw, swelling observed.

in solution at about 16 groups, and insolubility at 32 groups per CD ring. The use of a dibromo-terminated alkyl group to generate CD-based networks is discussed in subsequent sections.

**2.3.4 Bifunctional Derivatization and Network Formation.** It is our desire to synthesize polymer networks that have varying tie chain polarity, controlled cross-link densities, and which incorporate the novel guest–host properties present in CDs. Preliminary endeavors comprise extending the monobromohexyl modifications of the previous section to include bifunctional DBH in the reaction scheme. CD-alkyl chain networks are produced by the reaction, as presented in Scheme 2.1. Figure 2.8 shows the solid-state $^{13}$C CP MAS NMR spectra for modified CD prepared using 1:12 and 1:6 CD:DBH ratios. Solid-state NMR methods were necessary for this material, as the solution $^{1}$H NMR spectra (acquired in a manner similar to those shown in Figures 2.1 and 2.6) showed no peaks due to motional constraints, which is consistent with polymer network formation. Though the spectra in Figure 2.8 are not quantitative, the approximate area of the hexyl chain signals in the 20–40 ppm region does appear to increase with the higher DBH concentration. The C-1 methine signal (Scheme 2.2) at 103 ppm has been normalized to equal intensity in the spectra. The relative heights of all

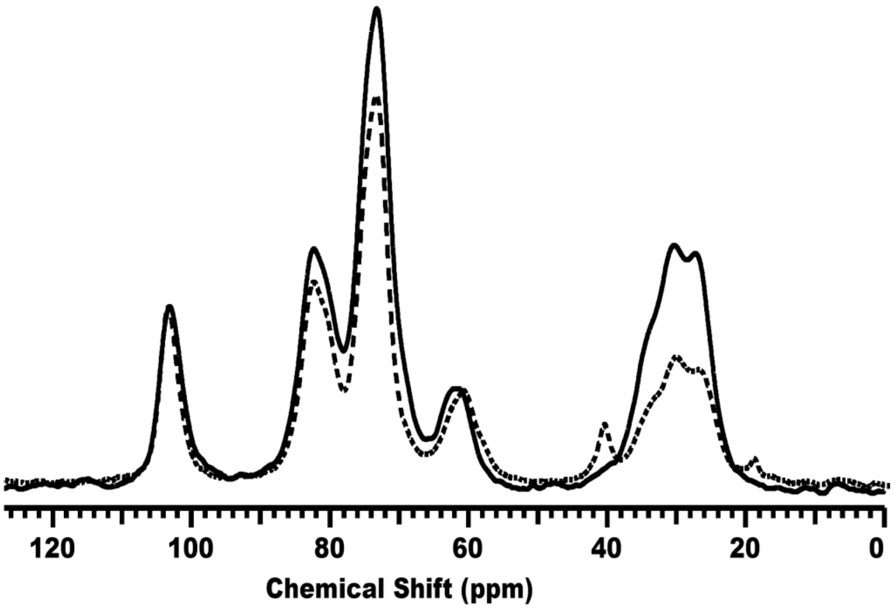
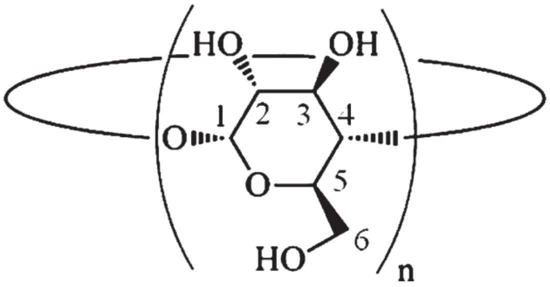


**Figure 2.8.** $^{13}$C CP MAS NMR spectra of washed and dried products from the reaction of $\alpha$-CD with dibromohexane (DBH) in the presence of 1.2N NaOH at 70 °C for 10 h, using the molar ratio $\alpha$-CD:NaOH:DBH =1:12:12 **(solid top trace)** compared to the molar ratio 1:6:6 **(bottom dashed trace)**.

signals in the spectra are consistent with the expectation for increased functionalization in the 1:12 over the 1:6 product. Quantitative peak area calculations from the Bloch decay spectrum of the 1:12 reaction product revealed that an average of six hexyl chains were attached per $\alpha$-CD ring out of a targeted 12 appendages, yielding a total functionalization conversion of 50%. Similar results were obtained with ionized $\beta$-CD as the nucleophile.



**C1:** 103 ppm
**C2-C5:** 72 ppm
**C4:** 83 ppm
**C6:** 62 ppm

**Scheme 2.2.** Representation of cyclodextrin repeat unit, where n = 6, 7, or 8 for $\alpha$, $\beta$, and $\gamma$ CD, respectively. Quantitative Bloch decay NMR spectra obtained as a function of reagent loading indicate that oxyanion formation and reaction occurs at C2, C3 and C6 sites. However, C2 and C3 carbons are not resolved in the NMR spectra, so specific reactivity differentiation between the two sites is not possible.

As evidenced by the signals in the 20–40 ppm region being of significantly larger line widths (Figure 2.8), the individual methylene groups in the hexyl side chains are more constrained relative to the side chains in the MBH product (Figure 2.7). Furthermore, the side chain methylene signals are larger in Figure 2.8 than those presented prior in Figures 2.2 and 2.3 resulting from bromooctanol derivatization, though the average number of side chains per CD ring is about equal. These observations are strong substantiation for network formation.

Solubility studies on the CD/DBH products afforded clear evidence that the bifunctional reagent leads to cross-linked networks. These products were insoluble in all solvents tested, covering a range of solvent polarities from water to toluene, and including polar aprotic solvents (Table 2.1). Swelling was observed in toluene which is a nonpolar solvent (Figure 2.9). This approach has been extended to vary the length and polarity of the linker chains between CD rings, resulting in altered network densities with controlled guest-host and swelling properties.

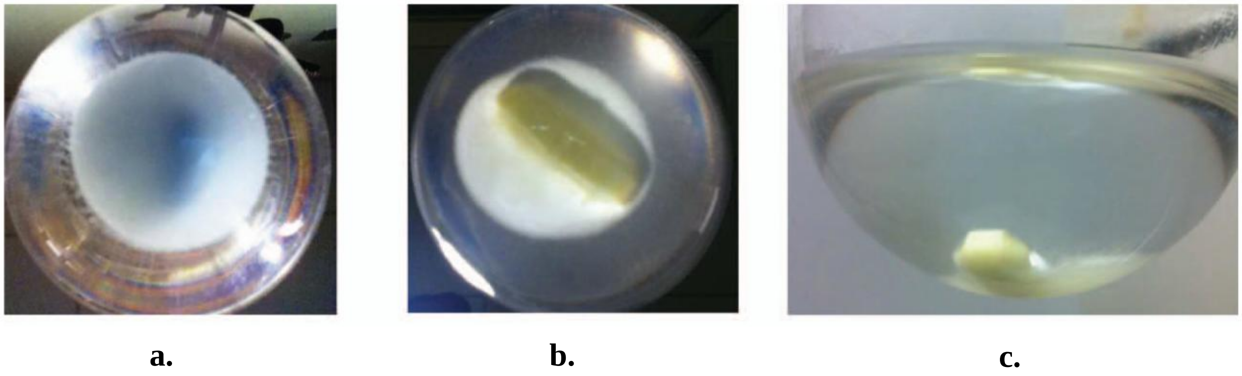

**a.** **b.** **c.**

**Figure 2.9.** Photographs illustrating behavior of materials made using the molar ratio $\alpha$-CD:NaOH:dibromohexane = 1:12:12 in **(a)** acetone, **(b)** toluene, and **(c)** a side view of sample (b). The swollen translucent appearance in (b) and (c) is noteworthy where the stir bar is clearly visible, whereas in (a) the unswollen solid prevents light transmission.

**2.4 Conclusions.** A simple one-pot synthesis has been used to functionalize CDs with dilute NaOH as the reagent of note for generating CD oxyanions toward modification by alkyl chains. These reaction conditions generate CDs of varying polarity and solubility. Solid-state NMR experiments indicate that the degree of functionalization of the stable products can be controlled by reaction conditions. Water solubility decreases along the range of 16–32 methylene groups added per CD ring, with complete solubility at about 16, and insolubility at about 32 and more. Additionally, simple routes for polymerization of CD cores to produce aliphatic chain cross-linked networks have been presented. This method has potential to be extended and generate polymeric networks that contain true macromolecular linkers between the CD cores, including both nonpolar (alkane) and polar (e.g., polyethylene glycol) connecting chains in the network structure.

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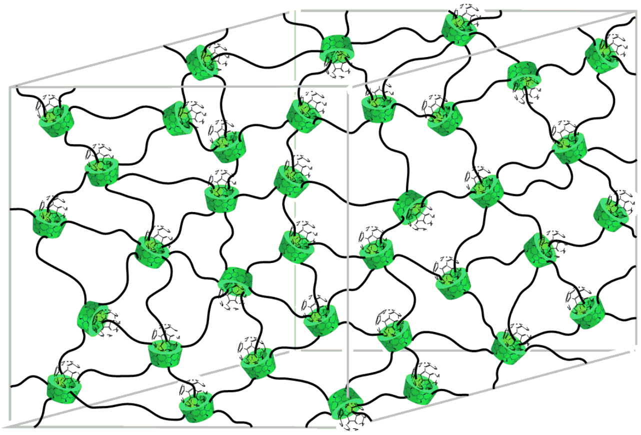
# CHAPTER III

# FULLERENE-NANOSCOPIC POLYMER NETWORK COMPOSITES

**Abstract.** Cyclodextrin rings represent the network nodes or tie points, which enable the polymer network to possess guest−host capabilities. Stable $C_{60}$-occupied polymer networks with improved mechanical properties result from $C_{60}$ homogeneous intercalation via van der Waals guest-host interactions of the fullerene with hydrophobic $\gamma$-cyclodextrin cavities. Such stable $C_{60}$ interactions do not occur when $\gamma$-cyclodextrin is replaced by the lower inner cavity diameter $\alpha$-cyclodextrin. Multiple toluene extractions reveal that stable $C_{60}$ concentrations are retained by the composite network, as shown by characterization. Applications for this composite could include $C_{60}$ removal from solvents. A modular approach for the synthesis of these polymer networks with well-defined node and cross-linking dimensions is described. A number of different guests other than $C_{60}$ should respond similarly using this preparation method.

**3.1 Introduction.** Industries such as biomedicine, energy, and consumer products have created a need for new synthetic strategies toward novel hybrid materials to comply with performance parameters. Several recent reviews have pointed out that a growing niche in materials science involves organic macromolecules with inorganic fillers as constituents of polymer composites and nanocomposites.[1-4] Silsesquioxanes, clays, and mesoporous silicates have arisen as such inorganic fillers used in polymer nanocomposites within the materials science field. $C_{60}$ provides a nanoscopic filler function with structural uniformity and improved mechanical properties.[5-8] Possible applications for $C_{60}$ polymer composites include photovoltaics and energy transfer advantages for light harvesting.[9-11] The process of producing $C_{60}$ homogeneously dispersed polymer matrices has garnered much attention of late.[12-15] Fillers strengthen networks and are dispersed in the cross-linked polymer matrix, rendering the network unique topologically. For some time polyisobutylenes, polybutadienes, polyisoprenes, as well as other synthetic elastomers, have been regularly reinforced with silica or carbon black in industry. Variations in polymer chain molecular weight distribution between cross-linking locations, as well as particle size and filler dispersion heterogeneity have often plagued these systems.[16] The motivation for creating monodispersed $C_{60}$, and other well defined nanoscopic filler compatible polymer networks stems from our previous interest in elastomer networks[17-19] and polymer blends[20-22]. We describe in this contribution $C_{60}$–polymer network composites formed by cross-linking $\gamma$-CD molecules with dodecyl chains. The result is a covalently bonded polymer matrix with CD cavities at regular intervals, and of suitable size, capable of accommodating $C_{60}$. Mixtures of CD and $C_{60}$ have shown interactions between the hydrophobic $\gamma$-CD cavity, which has the largest cavity dimension relative to

$\alpha$- and $\beta$-CD, and $C_{60}$.[23,24] Relatively few reports have outlined $C_{60}$ based polymer composites in which the $C_{60}$ is unmodified or in some manner unchanged chemically, and discussions on using this particular guest−host interaction as a means toward polymer composite networks have not been reported. Discussion on the synthesis, characterization, and properties of the $C_{60}$−CD polymer nanocomposite networks follow. These synthesized materials have (1) monodisperse filler sizes due to $C_{60}$, (2) monodisperse 12-carbon tie chain lengths, and (3) guest−host capabilities resulting from CD nodes and are graphically presented in Scheme 3.1.



**Scheme 3.1.** Representation of $C_{60}$/$\gamma$-cyclodextrin/dodecyl polymer network with each $\gamma$-CD ring functionalized with an average of five C12 chains.

## 3.2 Experimental

**3.2.1 Materials.** Technical grade $\beta$- and $\gamma$-CDs (both ~98.4% pure) were purchased from Cyclodextrin Technologies Development Inc., Gainesville, FL. Sublimed 99.9% pure $C_{60}$ was obtained from MER Corporation, Tucson, AZ. Dimethyl sulfoxide (DMSO) was purchased from Sigma-Aldrich Chemical Company, St. Louis, MO. 1,12-dibromododecane (98% pure) (DBDD) was purchased from Alfa Aesar Company. All other reagents and solvents were of analytical grade. All chemicals were used as received, without further purification.

**3.2.2 Synthesis of Dodecyl/$\gamma$-Cyclodextrin Networks.** In a typical reaction, 324 mg (250 µmol) $\gamma$-CD was dissolved in 4 mL water, 80 mg (2 mmol) NaOH added and the resulting mixture heated at 70 °C for half an hour. Separately, 657 mg (2 mmol) DBDD was dissolved in 4 mL DMSO by heating at 50 °C. The DBDD solution was added dropwise to the CD solution and the temperature raised to 100 °C, following which the reaction mixture was stirred for 18 h. The final ratio of the reagents was CD:NaOH:DBDD = 1:8:8. The reaction mixture was allowed to cool to room temperature and acetone was added to further precipitate the product. The mixture was filtered, and to ensure removal of all unreacted starting materials and byproducts, acetone washing of filtrand was repeated, followed by washing with ethanol and water. The resulting solid was dried under vacuum overnight. Theoretical yields were calculated based on functionalization of one hydroxyl per glucose unit and eight per CD ring. Yields based on mass of products were about 30%. An average of five dodecyl linkers per CD ring was calculated from solid state NMR spectra.

**3.2.3 Formation of $C_{60}$/Dodecyl/$\gamma$-Cyclodextrin Nanocomposite Networks.** 20 mg (10.1 mmol) of the dried dodecyl/$\gamma$-CD product was swollen by 5 mL dimethyl formamide (DMF), and 2 mg (2.7 mmol) of $C_{60}$ was dissolved in 5 mL of DMF separately. In addition to this $C_{60}$:CD ratio, reactions using 1:1 and 2:1 ratios were also done. Mixtures were stirred separately at room temperature overnight, followed by heating at 60 °C for 30 min, then combining of the two mixtures. Heating of the resulting mixture continued for an additional 3 h, followed by stirring at room temperature for 15 h. Vacuum filtration of the mixture using glass micro-fiber filter paper resulted in a film that was air dried overnight at room temperature. Free $C_{60}$ was removed by toluene washing, the film dried, and removed from the filter paper. This dark brown to black $C_{60}$/polymer composite network, henceforth referred to as “as prepared”, was subjected to additional toluene washes to determine the $C_{60}$ stability. Control experiments with toluene replacing DMF for network swelling and $C_{60}$ dissolution showed no significant $C_{60}$ intercalation, with membranes showing a near white coloration.

**3.3 Characterization.** $^{1}$H-decoupled (75-kHz decoupling field strength) solid-state $^{13}$C MAS (magic angle spinning) NMR spectra were recorded for the network products and membranes using a Bruker DSX-300 spectrometer operating at 7.05 Tesla field strength (300 MHz $^{1}$H Larmor frequency). $^{13}$C single-pulse (90° pulse width) data with $^{1}$H decoupling were recorded for most of the samples. Unless otherwise stated, 5-kHz MAS speeds were used in all cases, and recycle times between each pulse were typically 120 seconds for the networks and 160 seconds for the $C_{60}$ composite samples.

Thermal gravimetric analysis (TGA) was used to probe the thermal stability of the composite networks. TGA data were acquired on a TA 2950 instrument, using a ramp rate of 10 °C/min, in air, up to a final temperature of 400 °C. UV−vis spectroscopy was used to examine the nature of $C_{60}$ in solution, and data were acquired on filtrates using a Cary 100 spectrometer.

## 3.4 Results and Discussion

**3.4.1 *γ*-CD/Dibromododecane Networks.** Well defined networks that can homogeneously incorporate discrete molecular components such as $C_{60}$ motivated the choice of *γ*-CD as a functional node and dodecyl chains as cross-linkers. Previously we have described NaOH mediated *α*-CD/dibromohexane cross-linked network formation,[25]

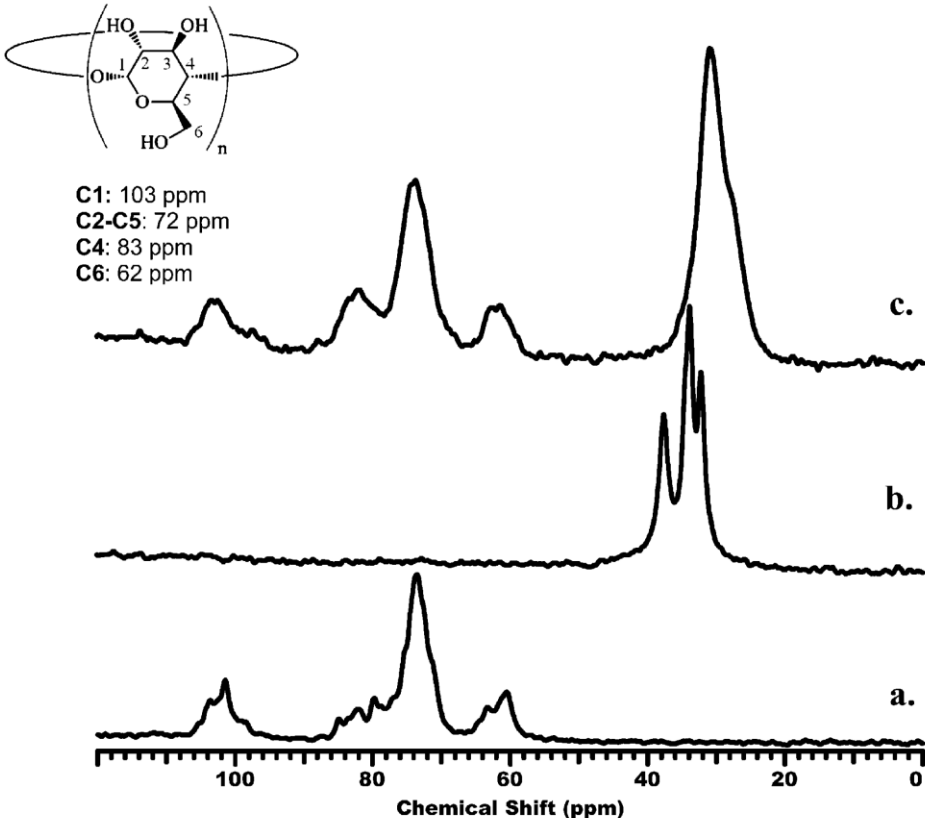


**Figure 3.1.** $^{13}$C MAS single-pulse spectra for **(a)** pure *γ*-CD, **(b)** pure DBDD, and **(c)** the dodecyl/*γ*-CD network formed from the reaction of DBDD and *γ*-CD. The inset shows the carbons labeled by their respective chemical shifts for the CD region (60−110 ppm) of the spectrum. The DBDD and dodecyl signals are in the 20−40 ppm region of (b) and (c), respectively.

however, these networks do not result in stable incorporation of $C_{60}$. Solid-state MAS NMR spectroscopy showed the degree of CD ring functionalization through good resolution and dynamic discrimination between network moieties. The solid-state $^{13}C$ MAS NMR spectra of pure DBDD and the dodecyl/$\gamma$-CD network product are shown in Figure 3.1, and peak assignments are pointed out in the structure inset. The pure CD spectrum is given as a reference in Figure 3.1a, in which the crystallographically inequivalent carbon signals for each chemical moiety, that disappear following reaction, are observed.[26] Any unnetworked CD/DBDD inclusion complexes were removed by several washings of the dried network with hot water.[26]

No residual unreacted crystalline DBDD appears in the network as evidenced by a comparison of the chemical shifts and line widths for DBDD peaks in the 20-40 ppm region of the product to those of pure DBDD. With respect to peak widths and peak intensities, the quantitative single-pulse spectrum (Figure 3.1c) looks nearly identical to the CP MAS spectrum, which is not shown here, for the same sample. This similarity indicates that all dodecyl chains are covalently bonded to CD rings and incorporated in the network because CP preferentially emphasizes rigid moieties. Integrations of the Figure 3.1 signals reveal an average of five dodecyl chains per CD ring.

Figure 3.2 shows images for dry and solvent-swollen films prepared from the dodecyl/$\gamma$-CD network. Solvent-swollen networks are translucent (Figure 3.2a) and maintain clarity after drying (Figure 3.2b). The networks are insoluble in other common laboratory solvents, but swell in DMF, DMSO, and toluene. These networks are fragile swollen or when dried, lacking adequate toughness to be handled as a single film (Figure 3.2), and result in fragments.

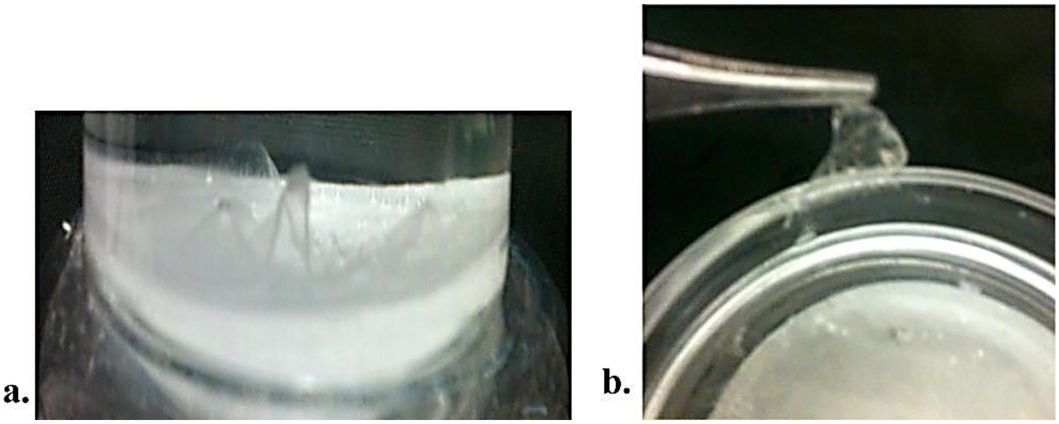


**Figure 3.2.** Images of **(a)** the swollen dodecyl/$\gamma$-CD network film in DMF and **(b)** the same film after casting and drying. The dry film in (b) is brittle and lacks sufficient toughness to be lifted from the Petri dish without breaking into several pieces.

Different physical properties were exhibited by the as-prepared and dried $C_{60}$/dodecyl/$\gamma$-CD composite networks in comparison to the networks lacking $C_{60}$. Figure 3.3 shows images of the swollen composite films (Figure 3.3a) and after drying. In the swollen state, adequate structural integrity remains, allowing films to be repeatedly handled without fragmenting (Figure 3.3b). Homogeneous dispersion of stabilized $C_{60}$ was maintained with several soakings of the as-prepared composites in excess toluene for 24 h. Each membrane in Figure 3.3 was toluene soaked six times, each soaking for 24 h, which indicates that $C_{60}$ was stably intercalated into the network. Toluene is excellent at solubilizing $C_{60}$, and is known to sever fullerene aggregated clusters into individual $C_{60}$ molecules,[27] suggesting that competitive binding of $C_{60}$ with the dodecyl/γ-CD network occurs.

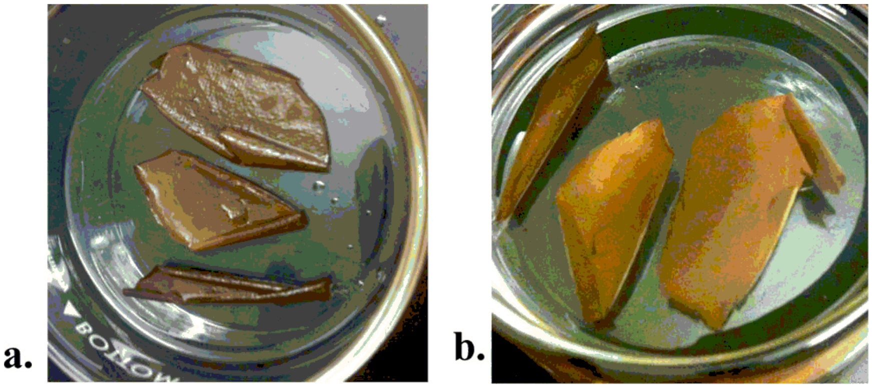


**Figure 3.3.** Images of **(a)** the $C_{60}$/dodecyl/$\gamma$-CD network membranes immediately after removal from DMF and placed in a dry container and **(b)** the same films after reimmersion in toluene. These membranes were obtained after six separate 24 h washings in toluene; note that the membrane is still intact and homogeneous with respect to $C_{60}$ distribution. Note that the field of view here is ca. 2.5−3 times larger than in Figure 3.2.

Solid-state $^{13}C$ MAS NMR data were collected for both the as-prepared $C_{60}$/dodecyl/$\gamma$-CD composite network and the network after multiple 24 h toluene washings in order to quantify the nature of $C_{60}$ binding in the network. Additionally, to assess the quantity and nature of $C_{60}$, UV−vis data were collected on the toluene extracts. Figure 3.4 shows the NMR results for pure $C_{60}$, pure dodecyl/$\gamma$-CD network, and the composites as a function of number of toluene extractions. The sample shown in Figure 3.4 was prepared with a $C_{60}$:CD ratio of 1:3.6. Quantitative evaluation of peak areas in Figure 3.4b-d revealed that 91, 73, and 66% of $C_{60}$ remained in the membrane for one, three, and six toluene washings, respectively. It is noteworthy to point out that 91% of $C_{60}$ remains incorporated in the network after one toluene wash of the as-prepared membrane, which results in a 14 wt % $C_{60}$ composite network. Soaking for 144 h in the

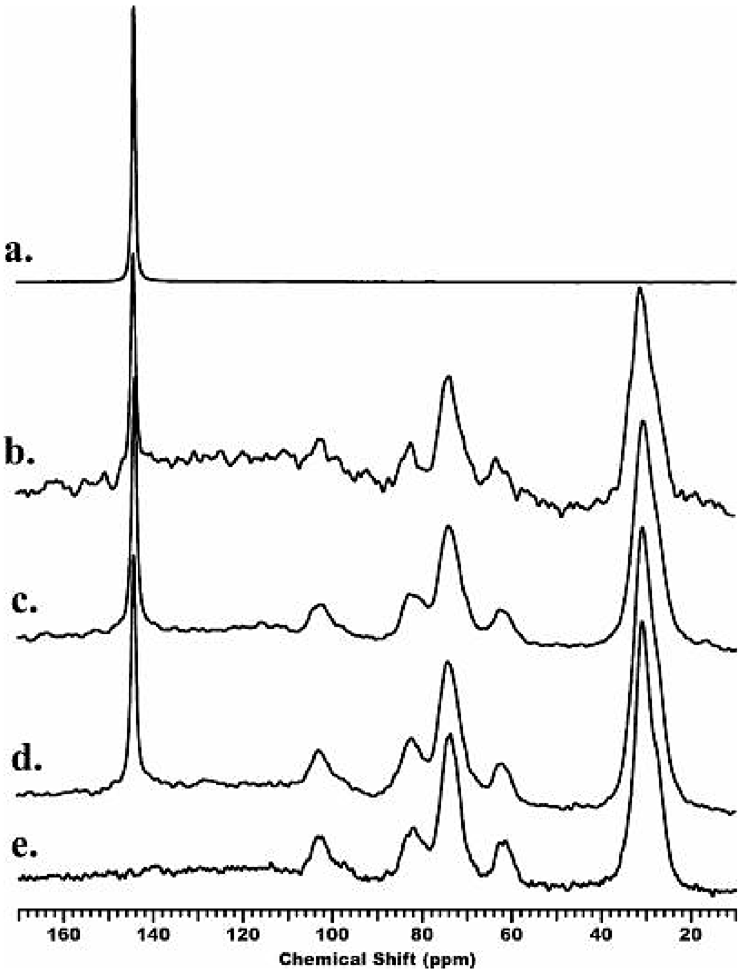


**Figure 3.4.** $^{13}C$ solid-state MAS NMR spectra of **(a)** pure $C_{60}$, compared with the membranes after **(b)** one, i.e., as-prepared, **(c)** three, and **(d)** six 24 h toluene washings. The dodecyl/*γ*-CD network is shown in **(e)** for reference.

excellent $C_{60}$ solvent, toluene, allows two-thirds of the $C_{60}$ to be maintained (9 wt %) in the thin (ca. 500 µm) film composite. There was an observed 100 °C raise in onset of detectable mass loss in the dried multiple washed $C_{60}$/dodecyl/*γ*-CD network membranes, which occurred at 190 °C, over the pure dodecyl/γ-CD networks as indicated by TGA data (Figure 3.5).

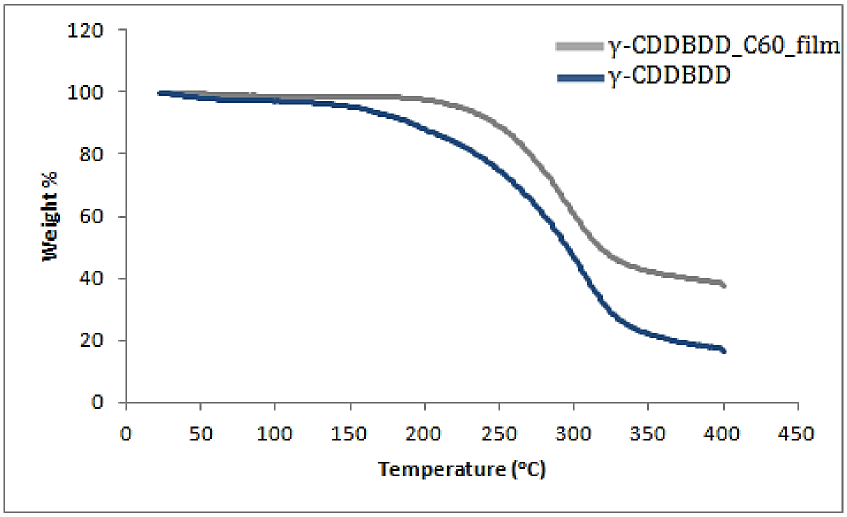


**Figure 3.5.** TGA results of the network materials and of the film after sequestration of $C_{60}$. The trace labeled γ-CDDBDD is from the dried network powder while the γ-CDDBDD_$C_{60}$_film is the membrane after sequestration of $C_{60}$.

Toluene extracts were subjected to UV-vis analysis following each wash of the composites. Figure 3.6 shows the two, three, and six wash data. The light purple color of the toluene extracts indicate that isolated $C_{60}$ molecules are present, rather than aggregated clusters.[28] No additional $C_{60}$ was extracted from the composite following six washes (Figure 3.6), which corresponds to 66% of the original $C_{60}$ remaining intercalated in the network, and this is also supported by NMR data (Figure 3.4). Pure $C_{60}$ absorbs at 336 nm, as does the extracted $C_{60}$, indicating that $C_{60}$ remains unmodified during composite preparation, consistent with the purple extract color.

**3.4.2. Mechanism of $C_{60}$ Incorporation in the Network.** As shown in Scheme 3.1, $C_{60}$ can selectively bind to the CD cavities in the dodecyl/γ-CD network. Alternatively, nonselective adsorption within the swollen network free-volume between dodecyl cross-

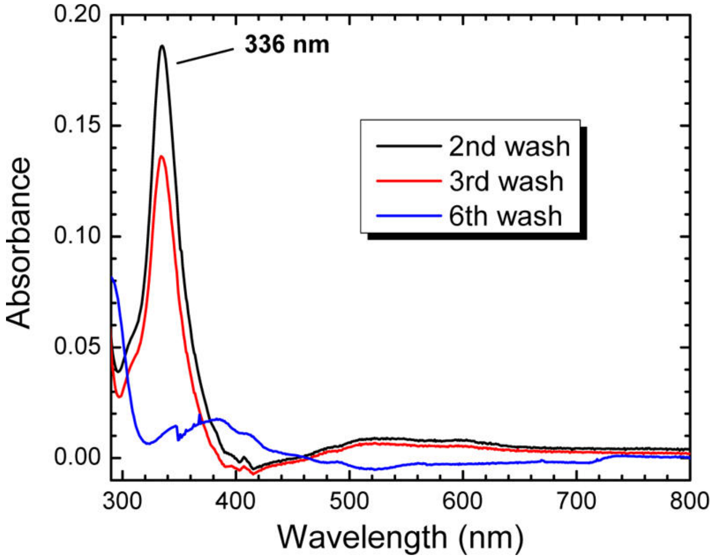


**Figure 3.6.** UV−vis spectroscopy results for toluene extracts from the $C_{60}$/dodecyl/$\gamma$-CD networks as a function of the number of extractions.

linking chains can occur. Though good evidence for strong $C_{60}$/CD noncovalent interactions, the above data from toluene extractions are not conclusive. Networks using $\alpha$-CD and dibromododecane were synthesized in order to ascertain whether the $C_{60}$/dodecyl/$\gamma$-CD composite networks interaction was guest−host in nature. Whereas $\gamma$-CD has an inner cavity diameter of 0.83 nm, sufficient to accommodate $C_{60}$ of 0.68 nm diameter, $\alpha$-CD has a diameter of 0.57 nm. Figure 3.7 shows differences between the $C_{60}$/dodecyl/$\gamma$-CD and $C_{60}$/dodecyl/$\alpha$-CD composites, each having an average of five dodecyl chains per CD ring in the network. These networks differ only with the node, $\gamma$- or $\alpha$-CD, and are otherwise the same. Figures 3.7a and 3.7c show that after preparation, the *γ*-CD and *α*-CD color and texture appear different. With a smooth, dark appearance, the $C_{60}$/dodecyl/*γ*-CD membrane (Figure 3.7a) contrasts with the $C_{60}$/dodecyl/*α*-CD, which has a rough appearance lacking uniformity in color (Figure 3.7c). The $C_{60}$/dodecyl/*α*-CD is voided of $C_{60}$ after 1 h of toluene extraction (Figure3.7d), while a similar treatment of the *γ*-CD network causes minimal $C_{60}$ loss (Figure 3.7b). As outlined above, about 67% of $C_{60}$ is maintained in the $C_{60}$/dodecyl/*γ*-CD membrane, shown in Figure 3.7a, following five additional toluene washes, whereas a single wash results in the smaller cavity *α*-CD membrane practically voided of $C_{60}$.

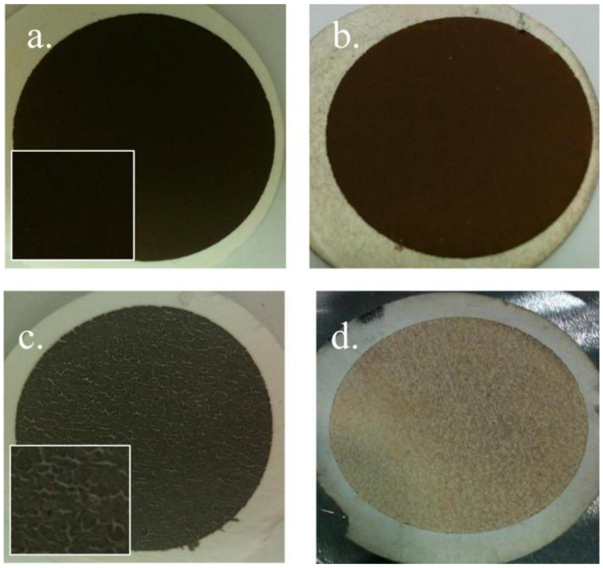
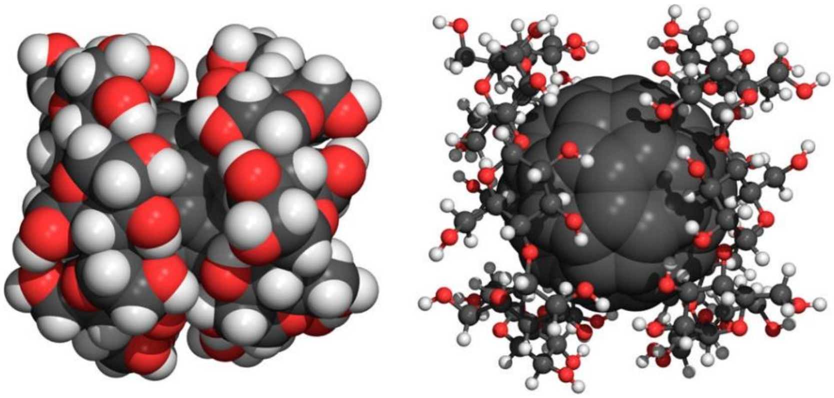


**Figure 3.7.** Comparison of as-prepared dry membranes with those obtained after washing in excess toluene for 1 h: **(a)** *γ*-CD/dodecyl network after $C_{60}$ incorporation and before wash; **(b)** same membrane as in (a) after toluene wash; **(c)** *α*-CD/dodecyl network membrane after $C_{60}$ incorporation and before wash; **(d)** same membrane as in (c) after toluene wash. The insets in the lower left of (a) and (c) are 10× zoomed images.

Four conclusions may be drawn from these data. First, the dodecyl/*γ*-CD networks incorporate strongly bound $C_{60}$, but the smaller cavity dodecyl/*α*-CD membranes do not. With $C_{60}$ intercalated, dodecyl/*γ*-CD networks form continuous membranes, which are discontinuous in the absence of $C_{60}$. With washing or soaking in toluene, the majority of $C_{60}$ remains in dodecyl/*γ*-CD networks, though some is removed. These results are good evidence for the arrangement in Scheme 3.1, particularly for networks that have undergone several toluene washes for removal of $C_{60}$ that is in the polymer matrix and not in the CD cavities. It appears as though $C_{60}$ behaves as a cross-linker to mechanically toughen the dodecyl/*γ*-CD networks through interactions with CD, as is implied by Figure 3.2 and Figure 3.7c,d, in which discontinuous and fragile networks occur when $C_{60}$ and CD are not proximate. In other reports, for both the *γ*- and *β*-oligomers, $C_{60}$ coordinates with the cavities of two unnetworked CDs in a bicoordinate or bicapped complex.[29,30] It is not certain whether bicoordinate or single-coordinate (Scheme 3.1)



**Scheme 3.2.** Space-filling **(left)** and partial ball-and-stick **(right)** structures of $C_{60}$ and *γ*-cyclodextrin complexes in solution, calculated via geometry optimization using the MM+ molecular mechanics potential in HyperChem 7.52.

$C_{60}$/CD complexes occur with the covalently networked CDs reported herein. Space-filling and hybrid ball-and-stick structures of calculated bicoordinate $C_{60}$/CD complexes are presented in Scheme 3.2. Seridi described interactions of $C_{60}$ and *β*-CD,[31] and MM+ molecular mechanics calculations were modified for *γ*-CD to produce energy-minimized structures. Literature accounts and these energy-minimized structures point to $C_{60}$ stabilizing network integrity through CD bicoordinate or bicapping relationships. With the CDs being linked with dodecyl tie chains, it is unlikely that this bicoordinate form of association exists for all $C_{60}$s in the network. Such coordination may be occurring between parts of the network, however, where tie chain density is at a level too low to bestow the necessary physical toughness for membrane formation to occur without $C_{60}$. This phenomenon could explain the data seen in Figures 3.3 and 3.7a,b as opposed to the pure CD networks in Figure 3.2.

**3.5 Conclusions.** A method for synthesizing networks whose CD-facilitated guest-host properties enable stable and homogeneous incorporation of $C_{60}$ has been described. Known CD modification approaches can be applied to vary the length and kind of chain, other than the nonpolar dodecyl linkers used in this contribution. In addition, CDs could be grafted into existing polymer chain structures[32] and not necessarily incorporated as nodes in the network. Furthermore, the CD type may be altered, accessing varied inner cavity dimensions. Nanoporous CD polymers or “nanosponges”, which should be capable of accommodating guests forming nanocomposite networks, have been described using other methods.[33,34] The routes used within should be applicable generally for monodisperse filler incorporation to strengthen networked composites.

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# CHAPTER IV

# MODULAR ASSEMBLY OF DISCRETE POLYMER NETWORKS WITH AMPHIPHILIC GUEST-HOST PROPERTIES

**Abstract.** A modular assembly procedure for producing amphiphilic polymer networks containing specific linker lengths between cyclodextrin (CD) cross-link sites is described. The linker type and length can be selected to tune the relative hydrophilicity/hydrophobicity of the network, and the size of the guest-host binding site can be varied by using either $\alpha$-, $\beta$-, or $\gamma$-CD as the node. The two-step, one-pot reaction sequence produces well-defined networks with stable ether linkages that can be purified by simple washing and filtration steps. Short ethylene glycol versus long polyethylene oxide linkers result in networks that are generally insoluble in common organic solvents, but which swell to varying degrees in polar protic, polar aprotic, and chlorinated solvents such as water, methanol, ethanol, dimethylsulfoxide (DMSO), dimethylformamide (DMF), methylene chloride, and chloroform. All networks swell in water and present a hydrophobic CD cavity that is available for binding non-polar molecules. The networks should be applicable to the removal of hydrophobic contaminants, e.g. pharmaceutical molecules, from water or wastewater streams.

**4.1 Introduction.** Polymer networks can potentially provide tunable material properties based on the chemical composition of the linker or tie chains involved, the density of cross-link sites within the network of linkers, and whether the cross-link site (i.e. the node) is passive or presents an active chemical moeity.[1,2] Recently, networks based on cyclodextrin (CD) nodes have garnered attention for introducing non-bonded tie points through polymer/CD inclusion chemistry.[3,4] As highlighted in a recent review, the network topology choices are vast, and can be most easily differentiated based on whether the CDs are covalently attached to the rest of the network, or non-covalently incorporated through slide ring/rotaxane geometries.[5] Network topology usually would dictate network properties, which can determine their application in everyday materials.

Typical routes to covalent incorporation of CDs into the network via reaction with external hydroxyl groups on the CD ring and some monomeric network-forming reagent involve ATRP[6] or RAFT[7] chemistries. While enabling selectivity and some control of the network properties, they require more complex synthetic schemes. In other routes, CDs have been functionalized using NaOH as the base and diglycidyl ethers as the linker.[8-22] Ethylene glycol diglycidyl ether was used with NaOH concentrations ranging from 19 M[8,9] to 0.1 M[14]. In the latter case HCl neutralization of the reaction mixture was followed by exhaustive dialysis for network isolation. Other efforts employing dialysis[19,22] or lyophilization[22] in their purification include those of Moya-Ortega et al. and Liu et al. Purification methods vary, and can extend the time to product recovery by days or a week.[23-25]

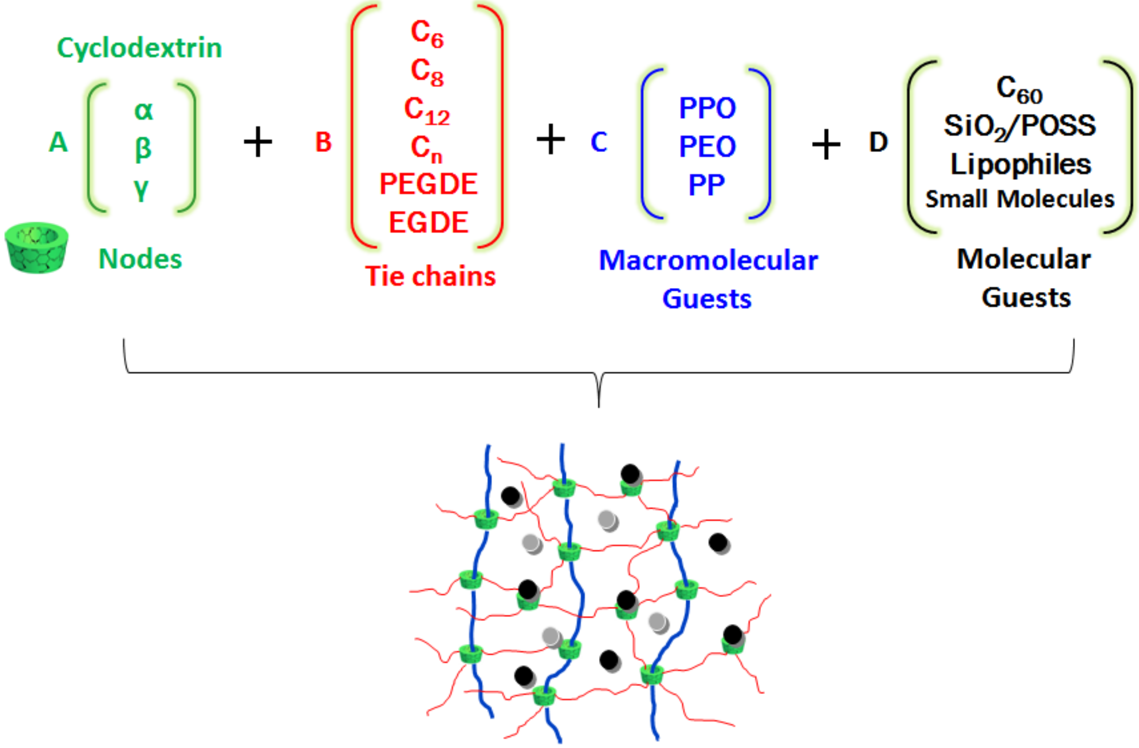
Epichlorohydrin has been frequently used for making CD amphiphilic networks.[16,18,22,26] CDs were linked by poly(γ-glutamic acid) using various bases in a one-pot synthesis.[27] Amide[22,36-38] and ester[15,16,20,24,27,28] linkages appear to be equally as common in making these networks. Methods requiring emulsifiers,[26] cellulose,[11,12,15,20,21] agar,[17] xanthan,[29] and a fluid wax[21] have been discussed. Free radical polymerization[20,29,30] and injection molding[23] were among the strategies employed toward a similar end. Networks resulting from CD-triblock copolymer inclusion complexation[28,31,32] generate networks in which the CDs are not chemically bonded. Some have been reported to behave as networks only for short time periods in aqueous environments and not stable enough for certain applications.[31] In other cases CD functionalization is required prior to reaction with the linker in order to obtain the desired network.[15,16,20,24,27,28] The aforementioned are different methods to what we will present toward amphiphilic CD cross-linked networks. The importance of these networks stems from the unique amphiphilic CD property of possessing a hydrophobic cavity, while still exhibiting miscibility and reactivity with a hydrophilic matrix.

A simple synthetic scheme that yields networks, employing as few reagents as possible, would be attractive if networks:

1. have tunable hydrophilicity and swelling in water and other solvents;
2. contain stable, covalently-bonded CDs at cross-link sites with a vacant cavity for CD guest-host chemistry;
3. contain specific network linker lengths that can be varied discretely;
4. cross-link density can be controlled via the average number of linker chains per CD node; and
5. are easily isolated and purified.

The simplicity of such a modular synthetic scheme, and the accessible range in final network properties, is depicted pictorially in Scheme 4.1. While the components labeled "A" and "B" in Scheme 4.1 are required, the addition of "C" and "D" depend on the final targets, and for hydrophobic networks (non-polar B linkers), examples have been described by us in previous work.[1]

In this contribution, the synthesis of hydrophilic *α*-CD based networks cross-linked with either PEO (polyethylene oxide) or ethylene glycol using a two-step, one-pot method is described. The approach is similar to that depicted in Scheme 4.1, with the use of telechelic epoxide-functionalized ethylene glycol-based linkers results in hydrophilic



**Scheme 4.1.** General approach for modular synthesis of discrete networks with guest-host capabilities.

rather than hydrophobic networks.[22,33] The cyclodextrin requires no prior modification, emulsifiers, cellulose, agar, or other additives. The resulting networks have stable ether linkages, as opposed to those with ester or amide linkages. The networks are well defined, since monodisperse linkers of known molecular weight are used. Purification via filtration and washing is relatively simple and inexpensive, resulting in the network in 1 - 2 days rather than several days or a week. This one-pot approach results in amphiphilic networks that exhibit significant swelling in water, i.e. hydrogels, most polar solvents, and which contains nodes that impart permanent guest-host properties to the network.

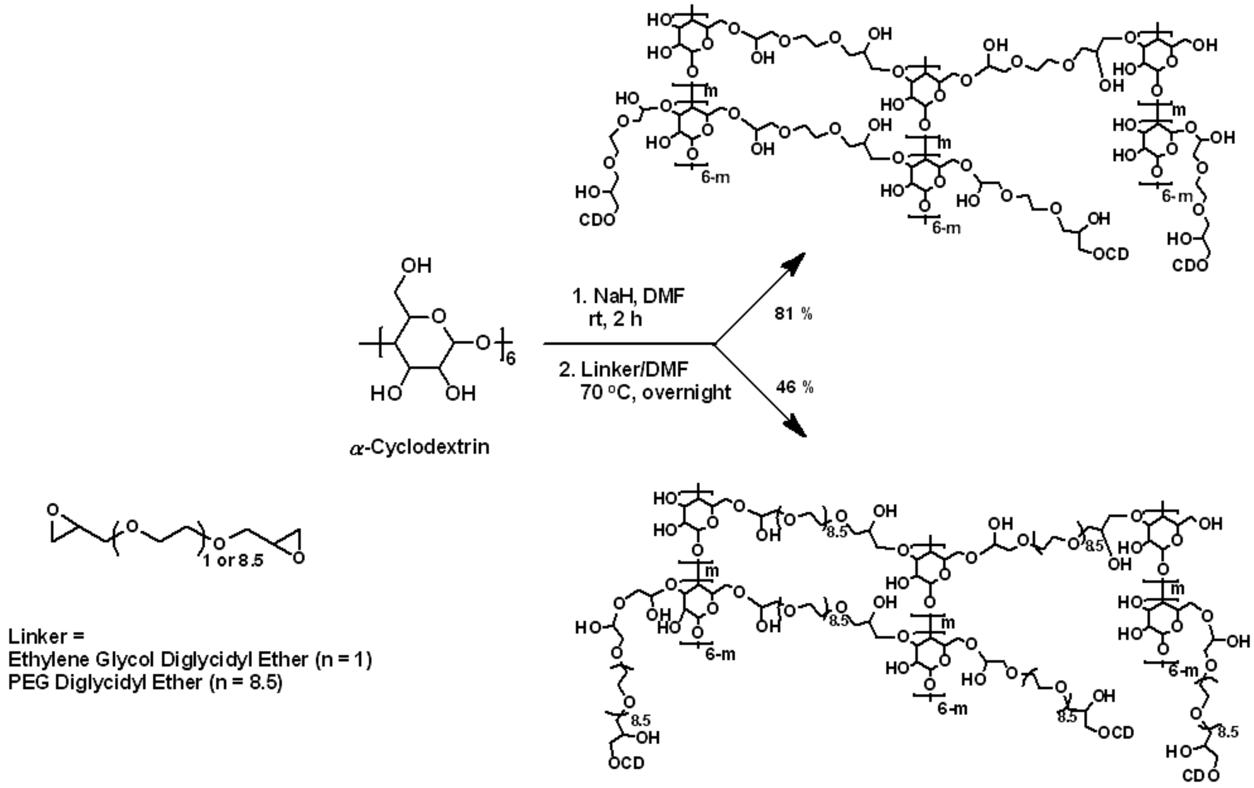
## 4.2. Experimental

**4.2.1. Materials & Methods.** $\alpha$-CD was purchased from Cyclodextrin Technologies Development Inc. and dried overnight under vacuum at 80 °C. NaH was obtained from Strem Chemicals, Inc. PEGDE (polyethylene glycol diglycidyl ether, molecular weight = 500 g/mole) was obtained from Sigma-Aldrich Co., and EGDE (ethylene glycol diglycidyl ether, molecular weight = 174 g/mole) from VWR. DMF was obtained from Pharmco-Aaper, and purified using an Innovative Technology solvent purification system. Cross polarization (CP) and direct polarization (DP) solid-state $^{13}C$ magic-angle (MAS) NMR spectra (denoted CPMAS or DPMAS) on the final dried networks were acquired using an Agilent (Varian) Inova 600 MHz NMR spectrometer, with standard acquisition and MAS parameters as reported previously.[34] Swollen-state $^{13}C$ magic-angle (MAS) NMR spectra were acquired via direct polarization following swelling to equilibrium in water. In all cases, MAS speeds of 4-6 kHz and $^{1}H$ decoupling field strengths of 45-50 kHz were used. CPMAS spectra were acquired with a 2-second delay, and quantitative DPMAS NMR data were acquired with 60-s recycle delays and used to calculate the average number of linker chains per CD ring in each network, as has been previously detailed.[34] Typically, 512-1K scans were collected.

**4.2.2. PEG Diglycidyl Ether$_{500}$/$\alpha$–CD Network Formation.** To NaH (130 mg, 5.41 mmol) under inert atmosphere was added $\alpha$-CD (220 mg, 225 µmol) dissolved in 2 mL of anhydrous DMF, and the reaction mixture was stirred for 2 h at room temperature (rt). PEGDE (1.2 mL, 1.35g, 2.71 mmol) with an average molecular weight of 500 g·mol$^{-1}$ was dissolved in 2 mL of anhydrous DMF and added to the reaction mixture dropwise. The reaction temperature was raised to 70 °C, and stirring continued overnight. The reaction mixture was quenched with 20 mL deionized (DI) $H_2O$, and stirred for several minutes. The mixture was then vacuum filtered, and the solids washed with water followed by acetone. The resulting powder was dried under reduced pressure (mechanical vacuum pump) overnight at 60 °C. The reaction yielded 409 mg of network (45.6 % conversion based on mass). To ensure no starting materials were present in the network, and as a quick test to indicate network presence, 18 mL of water was added to 10 mg of network in a 25 mL vial and the contents shaken vigorously. Solubility tests were carried out by adding 250 µL of solvent to 25 mg of network in 6 × 50 mm culture tubes.

**4.2.3. Ethylene Glycol Diglycidyl Ether /$\alpha$–CD Network Formation.** To NaH (130 mg, 5.41 mmol) under inert atmosphere was added $\alpha$-CD (220 mg, 225 µmol) dissolved in 2 mL of anhydrous DMF, and the reaction mixture was stirred for 2 h at rt. EGDE (422 µL, 472 mg, 2.71 mmol) was dissolved in 2 mL of anhydrous DMF and added dropwise. The reaction temperature was raised to 70 °C, and stirring continued overnight. The reaction mixture was quenched with 20 mL deionized (DI) $H_2O$, and stirred for several minutes. The mixture was then vacuum filtered, and solids washed with water, followed by acetone. The resulting powder was dried under reduced pressure overnight at 60 °C. The reaction yielded 368 mg of network (80.7 % conversion based on dried solid product mass). To ensure no starting materials were present in the network and as a quick test to indicate network presence, 18 mL of water was added to 10 mg of network in a 25 mL vial and the contents shaken vigorously. Solubility tests were carried out by adding 250 µL of solvent to 25 mg of network in 6 × 50 mm culture tubes.

**4.3. Results and Discussion.** Our previous work targeted the synthesis of hydrophobic networks that could be used for guest-host chemistry, e.g. $C_{60}$ incorporation into the CD cavity,[34] or for the assembly of topologically unique "orthogonal" polymer networks.[35] Linkers were composed of polymethylene units. To broaden the scope of those networks and assemble hydrophilic and/or amphiphilic networks, hydrophilic linkers were required. Linkers based on ethylene oxide/PEG repeating units were an obvious choice, but less obvious was the correct chemistry for simple covalent reaction of any length of hydrophilic linker with CD hydroxyl groups to create ether linkages. The telechelic diepoxides EGDE and PEGDE were found to be most effective, as compared to dihaloethylene glycols, for cases where the first step is CD oxyanion formation via NaH reaction. DMF was the most effective solvent choice to preclude epoxide ring-opening prior to reacting with the CD oxyanion. Trace water can lead to premature ring opening, as was observed when either NaH was replaced by NaOH, or anhydrous DMF was replaced by DMSO. The overall two-step one-pot reaction scheme is shown in Scheme 4.2. After drying, the resulting solid product was washed with water multiple times to remove any unreacted EGDE or



**Scheme 4.2.** Synthesis of α-CD networks with either EGDE or PEGDE linkers.

PEGDE linker. The solid product swelled when placed in water (*vide infra*), but did not dissolve in any solvent, indicative of networked structures. Deploying such networks as solids that will swell in water or other hydrophilic solvents presents several end-use advantages, and characterization of the networks in their solid and swollen states is required.

The insoluble products were not amenable to standard solution NMR experiments, but $^{13}C$ magic-angle spinning (MAS) NMR of the swollen networks afforded excellent resolution. Shown in Figure 4.1 are the swollen-state MAS NMR spectra for networks prepared according to Scheme 4.2. Based on the absence of signals in the 40-55 ppm range of Figure 4.1, all epoxide rings have reacted. The methine peak of the epoxy moiety shifts from about 52 ppm to about 70 ppm after ring opening. The methylene peak alpha to the epoxide shifts from ca. 66 ppm to 73 ppm, and the methylene peak in the ring shifts from 44 ppm to ca. 73 ppm when functionalized. The shifted peaks are now overlapping with the well-known CD peaks (see Figure 4.1 inset, and Figures 4.2 and 4.3 for pure CD result). Any such linker that has undergone ring opening, but is not bonded to CDs, will be removed during the washing process. Figure 4.1 indicates that an approximately 4 ppm downfield shift occurs for C2 and C4 of cyclodextrin (labeled as C2' and C4') that have been functionalized at the C2 and C6 hydroxyl positions. A similar downfield shift has been observed in monofunctionalized CDs.[36] However, since some C2 and C6 positions remain unfunctionalized, the original peaks are observed as well. In addition, the diminished C4' peak in the PEGDE network spectrum corresponds to the lower degree of functionalization in comparison to the EGDE network. It is possible that C3 is undergoing a downfield shift upon modification, but the C3' peak may be unresolved in the 68 to 77 ppm region. The minor peaks at 101.3, 81.1, 66.0, and 64.2 ppm are believed to be conformational isomers.[37] The tertiary carbon in CD, labeled C1 in Figure 4.1 inset, is known to be nonreactive, and the

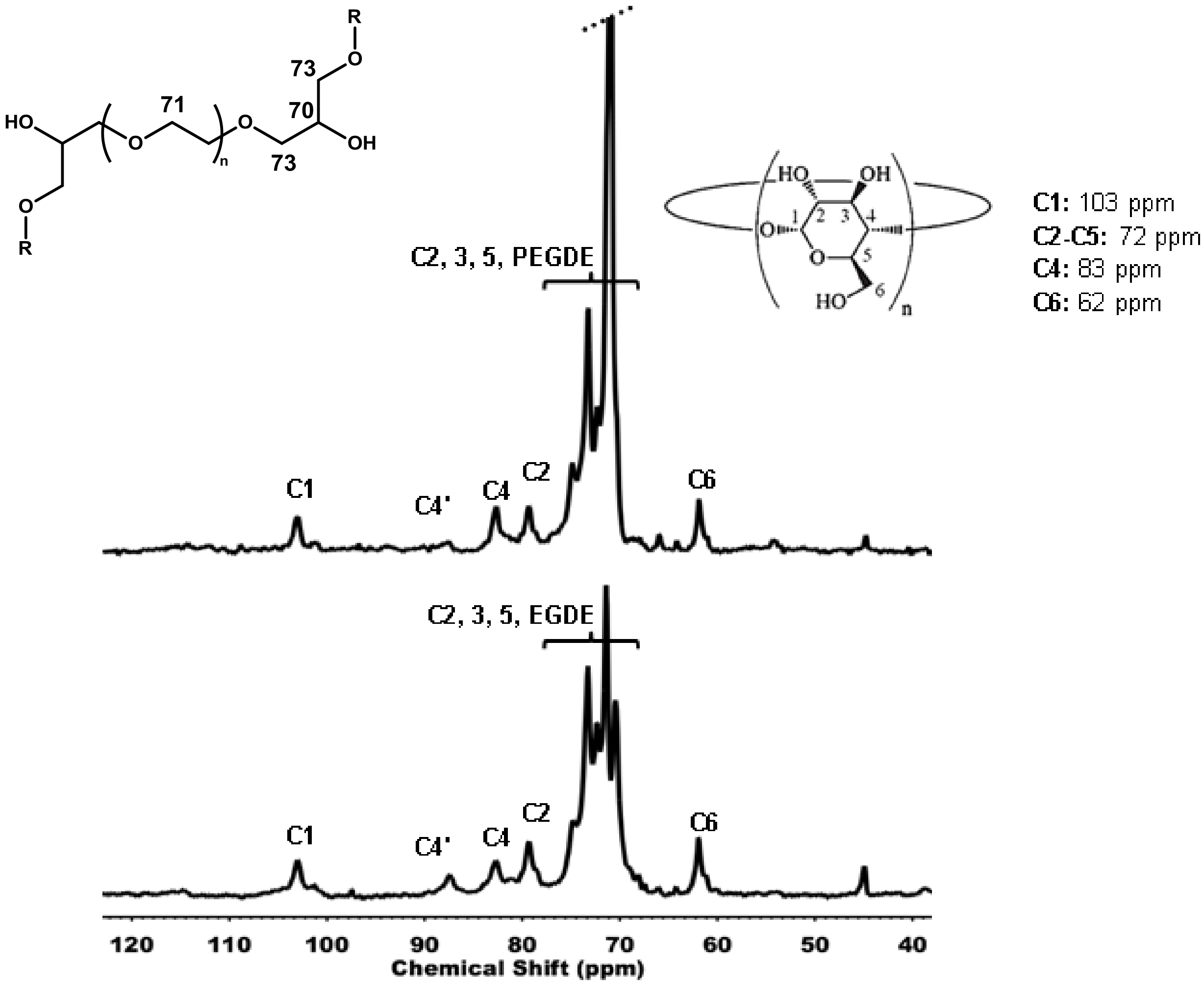


**Figure 4.1.** $^{1}$H-decoupled $^{13}$C single-pulse MAS NMR spectra of $\alpha$-CD/PEGDE (**top)** and $\alpha$-CD/EGDE (**bottom**) networks swollen in $H_2O$. The 44.8 ppm peak is from residual DMF. The highest intensity peak is shown off scale in the PEGDE spectrum for clarity. n=6 for $\alpha$-CD, as shown in the upper right inset. Chemical shifts for the linker are indicated.

corresponding 101-103 ppm peak was used as an internal standard. Subtraction of five times the 101-103 ppm area from the total integrated areas in the 60-90 ppm yields the total integral from addition of the linker. Knowing that there are six glucose rings in $\alpha$-CD (n=6 in Figure 4.1 CD structure inset), and based on the number of carbons in either the EGDE or PEGDE linkers, quantitative calculations based on the integrals yielded an average of ca. 8 linker chains per CD ring in the PEGDE network, and ca. 12 linker chains per CD ring in the EGDE network. We recognize that this does not mean these ca. 8 or ca. 12 chains per CD ring are always connected to another CD ring; some reactions may involve only reaction of one linker chain end. Unfortunately, if only one of the linker ends is connected to CD, and the other is the hydroxyl moiety resulting from ring-opening of the other epoxide, the $CH_2$ peak alpha to the hydroxyl would be in the same 70-80 ppm region as the other peaks in Figure 4.1, and cannot be resolved.

Figure 4.2 shows CPMAS spectra for the dried networks, along with the pure $\alpha$-CD spectrum for reference. Spectra in Figure 4.2 were collected using cross-polarization (CP) from $^1H$ nuclei to nearby $^{13}C$ nuclei, which requires a permanent and static dipolar coupling for effective polarization transfer. Acquired signals indicate that the linker groups attached to the CD ring are themselves rigid, as would be expected for true covalent bonding to the CD ring. A simple physical mixture of CD and linkers, even without multiple washing steps, generates vastly different spectra as has been shown previously.[1] Comparisons between CP spectra and single $\pi/2$-pulse spectra (DPMAS results in Figure 4.3) revealed no significant differences in the type and intensity of signals, indicative of a homogeneous product. Subtle differences in some of the line shapes and intensities in Figure 4.2 versus Figure 4.3 arise from the preferential emphasis of relatively rigid CD ring moieties in the CPMAS spectra due to their stronger static dipolar couplings, and simultaneous discrimination against more mobile carbons residing in the linker chains. With respect to the average amount of linker addition per CD ring, the DPMAS spectra for the solid networks in Figure 4.3 are in every way consistent with the swollen-state data in Figure 4.1. Most importantly, they demonstrate that all linkers are covalently bound, having survived multiple washing and drying steps prior to spectral acquisition. Any unreacted linker should be removed by washing.

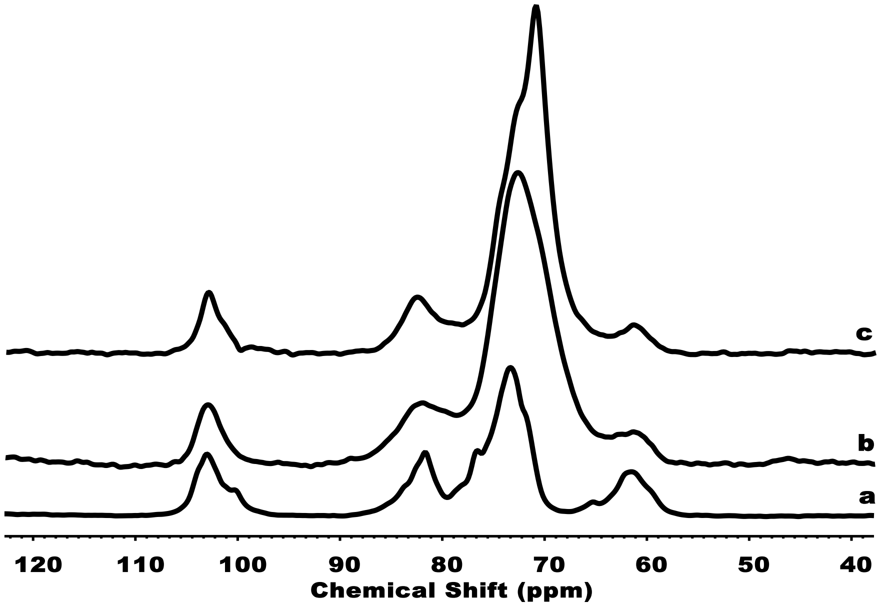


**Figure 4.2.** $^{1}$H-decoupled $^{13}$C CPMAS NMR spectra of **(a)** pure solid $\alpha$-CD, **(b)** $\alpha$-CD/EGDE network, and **(c)** $\alpha$-CD/PEGDE networks.

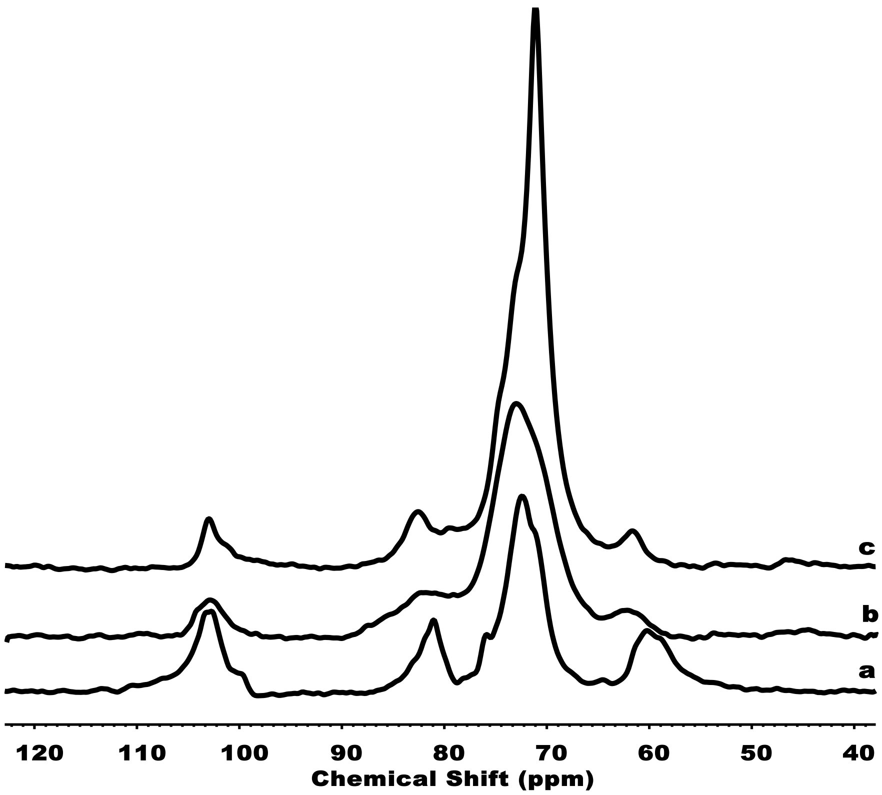


**Figure 4.3.** $^1$H-decoupled $^{13}$C single-pulse (DPMAS) NMR spectra of **(a)** pure solid $\alpha$-CD, **(b)** $\alpha$-CD/EGDE network, and **(c)** $\alpha$-CD/PEGDE

Solubility and swelling tests were carried out on the networks; similar behavior was observed at 1-hour and 24-hour solvent exposure times. As a typical test, 10 mg of the network was immersed in 18 mL of water and the combination vigorously shaken, resulting in persistence of the network. Control experiments involving reactions without NaH resulted in a clear reaction mixture with all starting materials dissolved and no precipitate. In this test, any unreacted telechelics would readily dissolve in the relatively large volume of water. These results confirm that the sample was linker-functionalized CD, and that no starting materials were present. Solubility and swelling data are summarized in Table 4.1. Swelling was observed by the CD/PEGDE network in $H_2O$, MeOH, EtOH, DMSO, DMF, $CH_2Cl_2$, and $CHCl_3$, and by CD/EGDE in $H_2O$, MeOH, EtOH, DMSO, and DMF. Swell ratios were calculated using the equation **swell ratio = $V_s/V_d$**, where $V_s$ is the volume of swollen network, and $V_d$ the volume of dry network.

**Table 4.1.** Solubilities, swelling, and swell ratios of $\alpha$-CD/PEGDE and $\alpha$-CD/EGDE networks in a number of common solvents at room temperature.

| Swollen | Swell Ratio | | Insoluble |
|---|---|---|---|
| | PEGDE | EGDE | |
| Water | 2.2 | 1.9 | 2-Propanol |
| Methanol | 2.0 | 1.6 | 2-Butanol |
| Ethanol | 1.5 | 1.2 | Acetone |
| DMSO | 1.8 | 2.7 | Acetonitrile |
| DMF | 1.7 | 2.3 | 2-Butanone |
| Dichloromethane | 1.3 | 1.0 | Ethyl Acetate |
| Chloroform | 1.4 | 1.0 | THF |
| | | | Toluene |
| | | | Ether |
| | | | Hexanes |
| | | | Cyclohexane |
| | | | Pentane |
| | | | Xylenes |

More extensive swelling tests were carried out using 25 mg of network in 250 μL of solvent, the results of which are shown in Figure 4.4. The dry network and the network in toluene (insoluble) are presented as references in each frame. In the polar protic solvents ($H_2O$, EtOH, and MeOH), the PEGDE network swelled more than did the EGDE network. On the other hand, more swelling was observed in the EGDE network than the PEGDE network by the polar aprotic solvents (DMSO and DMF). In an appropriate solvent, the total network swelling should be a function of the number of linker chains per node, the length of each linker chain, the intermolecular interactions between the solvent and the linker, and finally, the interaction between the solvent and the CD cavity. This latter characteristic is unique to these networks. Significant PEGDE network swelling by the chlorinated solvents was observed, while the EGDE network swelled only slightly. The bottom two frames of Figure 4.4 indicate that the density of the swollen networks lies somewhere between the 1.33 and 1.48 g/mL, densities of $CH_2Cl_2$ and $CH_3Cl$, respectively.

The observed differential swelling between the two networks in protic versus aprotic solvents appears to depend primarily on the linker length. Given that the PEGDE linker has 8-9 ethylene oxide repeat units versus the one unit of the EGDE linker, there are more sites for hydrogen bonding with the polar protic solvents. The increased number of polar protic solvent molecules in the network matrix results in more swelling for the PEGDE network than in the EGDE network. In contrast, the EGDE network with its shorter linkers has more CD rings per unit volume. Since the methyl groups of the polar aprotic solvents can interact with the hydrophobic CD cavity, there is more swelling in the EGDE network by the polar aprotic solvents than in the PEGDE network. This is schematically depicted in Figure 4.5. These results show that swelling ratio is a function of both the linker length and the guest-host capability of the CD node.

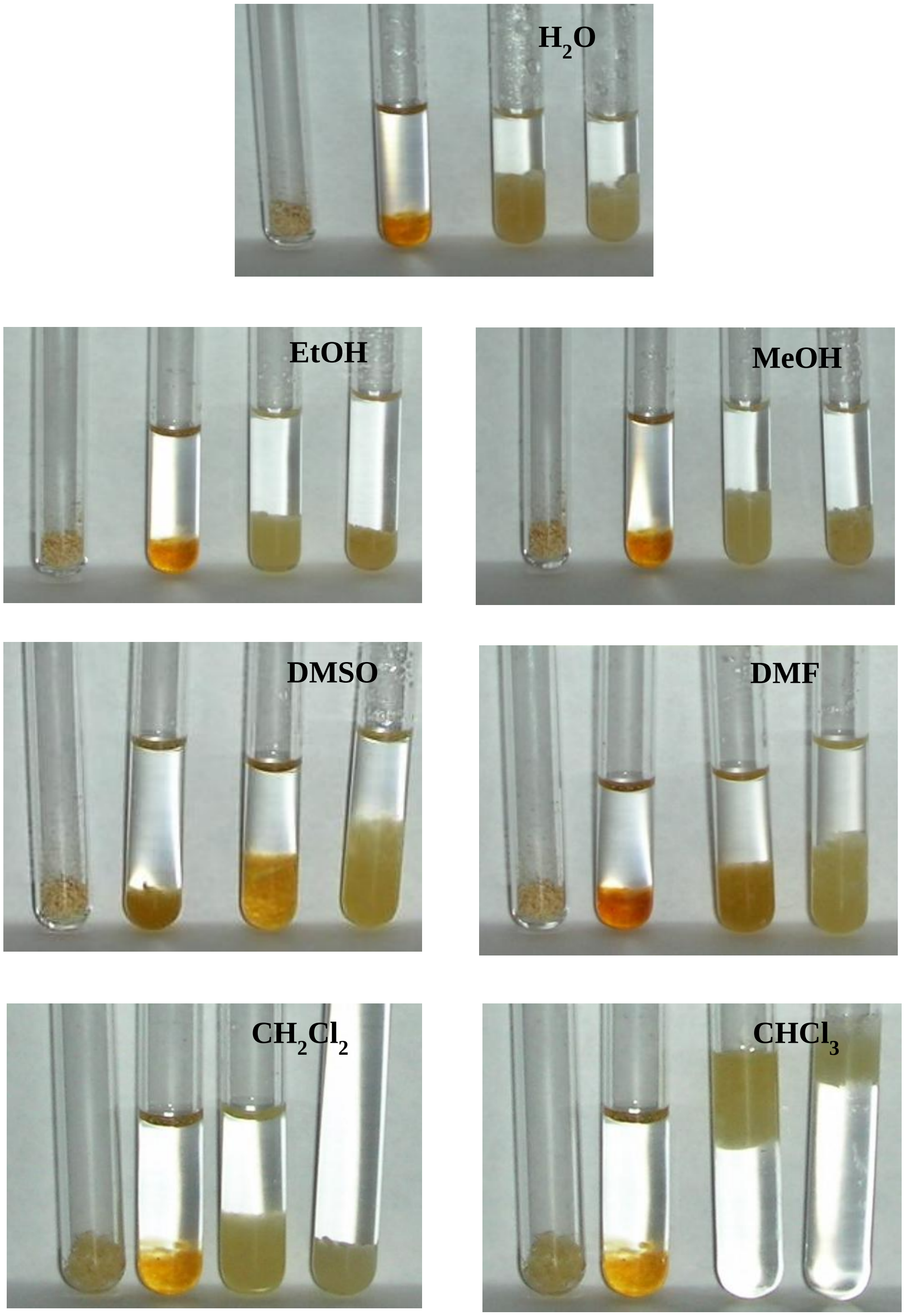


**Figure 4.4.** Swelling of amphiphilic networks **left to right** in each frame: dry network → PEGDE network in toluene (250 μL) → PEGDE network in specified solvent → EGDE network in specified solvent.

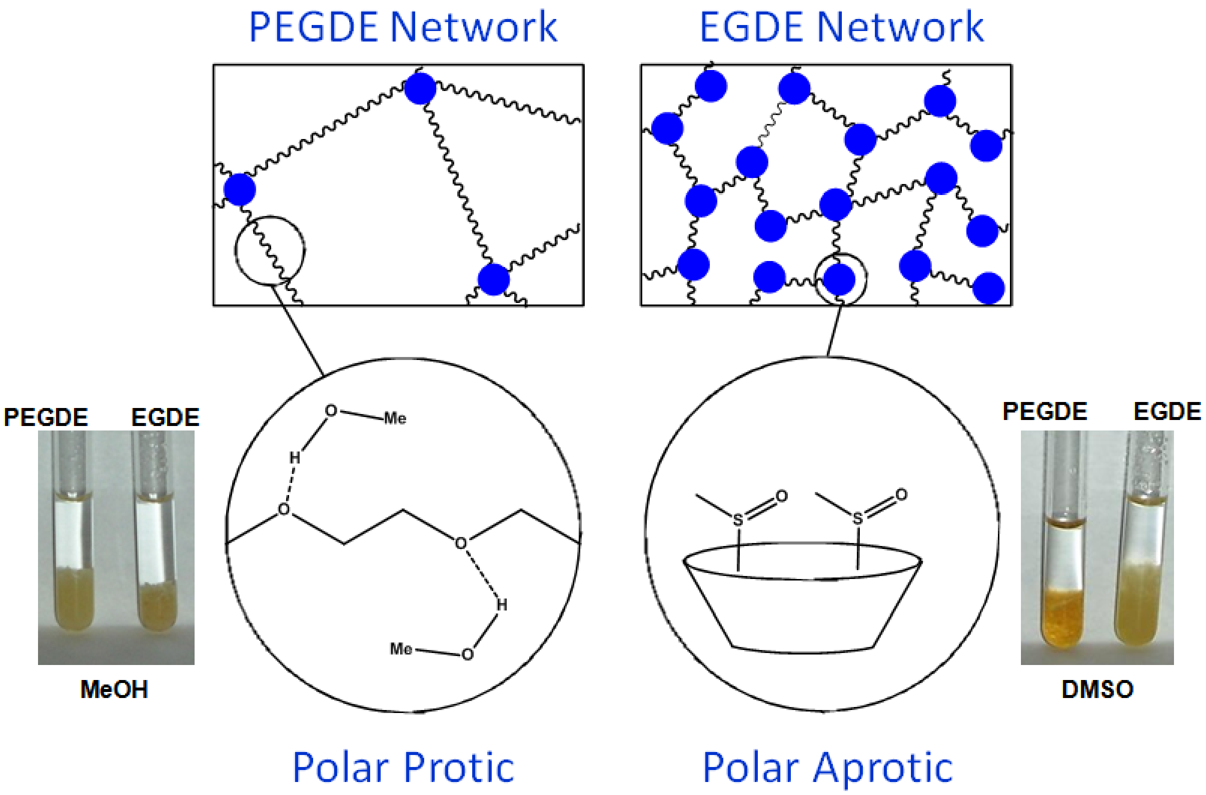


**Figure 4.5.** Proposed interactions between PEGDE and EGDE networks with polar protic versus polar aprotic solvents, as a function of network density. Methanol and dimethylsulfoxide are shown as examples.

**4.4 Conclusions.** The modular syntheses of amphiphilic polymer networks with well-defined cross-linked dimensions were carried out using CD as the node and PEGDE or EGDE as the linkers. Greater molecular weight PEGs could be used to produce networks of lower density. Using commercially available end-functionalized linkers, the syntheses were accomplished in one pot with NaH as the base, and purified by filtering and washing, followed by overnight drying. The networks are insoluble in the twenty solvents tested, but swelling is exhibited in the CD/PEGDE network by $H_2O$, MeOH, EtOH, DMSO, DMF, $CH_2Cl_2$, and $CHCl_3$, and in the CD/EGDE network by $H_2O$, MeOH, EtOH, DMSO, and DMF. The difference in network density, resulting from the linker used, is evidenced by the swelling behavior. Polar protic solvents hydrogen bond to a greater degree with the higher molecular weight PEGDE linker than with the EGDE linker. This results in more swelling in the PEGDE network in these solvents. On the other hand, more swelling is observed in the EGDE network relative to the PEGDE network by the polar aprotic solvents. The relatively greater amount of CD rings in the EGDE network than the lower density PEGDE network accounts for this phenomenon. The solvent molecule interaction with the amphiphilic networks are representative of the interaction with guests for which the networks act as hosts.[7,37] These robust amphiphilic cross-linked networks may be used as platforms for guest−host networking with applications in energy, biomedicine, consumer products, and sequestration of recyclables or contaminants from water or waste streams.

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# CHAPTER V

# CONCLUSIONS AND FUTURE DIRECTIONS

Molecular nodes were connected using a controlled modular approach by well defined, fixed tie chains of known molecular mass resulting in nanoscopic polymer networks. Cyclodextrins can be functionalized at the C2, C3, and C6 hydroxyls to form stable nodes for networks. The covalent formation of CD networks chemically connects CDs with adjacent CD nodes and helps in maintaining the rigidity of the swollen networks. $\alpha$-, $\beta$- and $\gamma$-CDs were networked using hydrophobic short and long chain alkyl halide and hydrophilic PEG and ethylene glycol linkers. Vacuum filtration was used to produce membranes or thin films from the swollen networks. The swollen hydrophobic network has sequestered $C_{60}$ molecules by interactions with the CD cavity, and membranes of this material have improved mechanical and thermal strength in comparison to membranes lacking $C_{60}$.

In the amphiphilic network, PEGs of greater molecular weight could be used to produce networks of lower density. Using commercially available end-functionalized linkers, the syntheses were accomplished in one pot with NaH as the base, and purified by filtering and washing, followed by overnight drying. Hydrophobic networks swell in DMSO, DMF, and toluene. The amphiphilic networks are insoluble in the twenty solvents tested, but swelling is exhibited in the CD/PEGDE network by $H_2O$, MeOH, EtOH, DMSO, DMF, $CH_2Cl_2$, and $CHCl_3$, and in the CD/EGDE network by $H_2O$, MeOH, EtOH, DMSO, and DMF. The difference in amphiphilic network density, resulting from the linker used, is evidenced by the swelling behavior. Polar protic solvents hydrogen bond to a greater degree with the higher molecular weight PEGDE linker than with the EGDE linker. This results in more swelling in the PEGDE network in these solvents. On the other hand, more swelling is observed in the EGDE network relative to the PEGDE network by the polar aprotic solvents. The relatively greater amount of CD rings in the EGDE network than the lower density PEGDE network accounts for this phenomenon. The solvent molecule interaction with the amphiphilic networks are representative of the interaction with guests for which the networks act as hosts. These robust amphiphilic cross–linked networks may be used as platforms for guest−host networking with applications in energy, biomedicine, consumer products, and contaminant sequestration from waste streams.

Future work on these networks entails testing their ability to host small molecule guests, such as pharmaceutical contaminants in water. This can be done using diffusion NMR studies, where the guest is expected to exhibit a slower diffusion coefficient when in the CD cavity than in the network matrix. Additionally, solution proton NMR can be used as further evidence for the guest-host interaction of these networks with small molecule guests. Allowing less than one equivalent of the guest molecule to be intercalated in the CD cavity by stirring overnight in a suitable deuterated solvent, then filtering, followed by obtaining proton NMR spectra, can show loss of the guest molecule in the solvent. Both diffusion and proton NMR experiments can be monitored using a similar cross-linked network that does not have CD, or other cavity-containing nodes, as a control. That is, the diffusion experiment on such a non-CD network is expected to show one diffusion rate since there is no cavity present to coordinate the guest molecule. Similarly, this control network is not expected to retain the guest, and the small molecule is expected to be observed in the solvent by proton NMR.

In addition to the initial guest-host interaction investigations on the current *a*-CD/PEGDE network, a range of different guests can be introduced for testing. Potential guest candidates include nicotine, epinephrine, and warfarin. Similar tests using the different solvents that are compatible with the network and the guest can be undertaken. To further expand the scope of the amphiphilic network, *β*- and *γ*-CD networks can be made using EGDE and PEGDEs of different molecular weights as linkers, and the swell ratios of these networks measured. With the exposure gained from these interrogations, a means of using the networks in a filtration cartridge can be devised, whereby prior stirring to intercalate the guest in the CD cavity is not required, but sequestration can be accomplished through direct filtering through the cartridge. Networks can be fine-tuned for these filtering devises to target specific guests, or class of guest molecules, by varying the CD, linker, and/or solvent combinations. Further, different types of nodes analogous to CD, such as cycloparaphenylenes and cyclophanes, can be used for network formation and be subjected to similar treatment as the CD networks.

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Do everything without arguing or complaining, so that you may become blameless and pure, children of God without fault in a crooked and depraved generation in which you shine like stars in the universe. Phil. 2:14,15

The Lord Himself goes before you and will be with you; He will never leave you nor forsake you. Do not be afraid, do not be discouraged. Deut. 31:8

being confident of this, that he who began a good work in you will carry it on to completion until the day of Christ Jesus. Phil. 1:6

Rejoice always, pray without ceasing, in all things give thanks, for this is the will of God in Christ Jesus concerning you. 1 Thess. 5:16-18

you are mine. Isa. 43:1e