Part A

THE USE OF NONIONIC ASSOCIATIVE POLYMERS FOR THE THICKENING
AND EMULSIFYING OF PERSONAL CARE PRODUCTS

Part B

THE SYNTHESIS OF A MANGANESE SOD MIMETIC FOR REACTIVE
COATINGS

A Project Report

presented to

the Faculty of California Polytechnic State University

San Luis Obispo

In Partial Fulfillment

Of the Requirements of the Degree

Master of Science in Polymers and Coatings

by

Mallory Lynn McMahon

June 2011

© 2011

Mallory Lynn McMahon

ALL RIGHTS RESERVED

COMMITTEE MEMBERSHIP

TITLE: Part A: THE USE OF NONIONIC ASSOCIATIVE
POLYMERS FOR THE THICKENING AND
EMULSIFYING OF PERSONAL CARE
PRODUCTS
Part B: THE SYNTHESIS OF A MANGANESE
SOD MIMETIC FOR REACTIVE COATINGS

AUTHOR: Mallory Lynn McMahon

DATE SUBMITTED: June 2011

COMMITTEE CHAIR: Ray Fernando, Professor

COMMITTEE MEMBER: Mark Paczkowski, Ph.D.

COMMITTEE MEMBER: Philip Costanzo, Assistant Professor

PART A

ABSTRACT

THE USE OF NONIONIC ASSOCIATIVE POLYMERS FOR THE THICKENING AND EMULSIFYING OF PERSONAL CARE PRODUCTS

The use of nonionic associative thickeners was proposed for personal care applications. Various limitations of current rheology modifiers used in personal care were discussed. Nonionic associative polymers were examined as both thickeners and emulsifiers. The structure/property relationship for nonionic polymers and their ability to thicken and emulsify were fully examined. Results showed an increase in thickening efficiency for nonionic associative polymers with higher $\log(P)$ (partition coefficient) values. This was due to the formation of smaller aggregates and increased bridging between aggregates. The connection between oil polarity, $\log(P)$ of the associative polymer, and emulsion stability showed no relationship however; as the $\log(P)$ value of the polymer decreased, emulsion stability increased. The effects of nonionic associative polymer molecular weight and thickening efficiency proved to be positive; as molecular weight increased, thickening efficiency increased. Specific interactions between nonionic associative thickeners and common ingredients in personal care products were also explored. The interaction between nonionic associative thickeners and surfactants proved to be dependent on surfactant type as well as hydrophobe shape and size on the associative thickener. There appeared to a clear effect of salt on the thickening and emulsifying capabilities of the nonionic associative polymers but the exact interaction was not yet determined.

ACKNOWLEDGEMENTS

I would like to give special acknowledgement to Lubrizol Advanced Materials for providing the funding for this research project. I would like to thank Chris Murphy for inviting me to spend six months working on site at Lubrizol in Brecksville, Ohio. Most of all, I would like to thank Mark Paczkowski for guiding me through the research process, not only as a manager, but as a mentor as well.

PART B

ABSTRACT

THE SYNTHESIS OF A MANGANESE SOD MIMETIC FOR REACTIVE COATINGS

Superoxide dismutation (SOD) chemistry pertaining to manganese enzymes was explored. A series of manganese SOD mimetic enzymes were synthesized and their SOD activity was examined. The McCord-Fridovich Assay showed mimetic enzymes containing secondary amine bonds and electron deficiency around bonding sites had higher SOD activity. Click chemistry was used for the synthesis of a 1,4-triazole containing tridentate ligand. The ideal reaction conditions chosen for the click reaction was a solvent blend of 1:1 dichloromethane and water with copper sulfate and sodium ascorbate as a catalyst. The tridentate ligand was grafted onto azido-functionalized polystyrene. Infrared spectroscopy was used to confirm the completion of the click reaction. The azide peak at 2100 cm^{-1} was removed after the click reaction was performed on the azido-functionalized polystyrene.

ACKNOWLEDGEMENTS

I would like to give a special thanks to Dr. Phil Costanzo who guided me through this research and taught me how to be a better synthetic chemist. I would also like to thank Matt Mackenzie and Billy Grau for preparing the model compounds and performing the SOD analysis.

TABLE OF CONTENTS

	Page
LIST OF TABLES	xi
LIST OF FIGURES	xii
LIST OF SCHEMES	xiv
CHAPTER	
Part A	1 - 66
1. BACKGROUND INFORMATION	1
1.1. Rheology Overview	1
1.2. Rheology Modifiers	5
1.2.1. Conventional Thickeners	5
1.2.2. Associative Thickeners	7
1.3. Nonionic Associative Thickeners	8
1.3.1. Nonionic Associative Polymer Structure in Solution	9
1.3.2. Structure/Property Relationship for Nonionic Associative Polymers	14
2. RHEOLOGY MODIFIERS IN THE PERSONAL CARE INDUSTRY	17
2.1. Current Rheology Modifiers	17
2.2. Nonionic Associative Polymers in Personal Care	20
2.3. Nonionic Associative Polymers as Emulsifiers	21
2.4. Surfactant Interactions	22
2.4.1. Surfactants	22
2.4.2. Nonionic Associative Thickeners and Surfactants	25

3.	EXPERIMENTAL WORK AND RESULTS	29
3.1.	Structure Property Relationships	29
3.1.1.	Partition Coefficient	29
3.1.2.	Thickening Efficiency and log(P)	31
3.1.3.	Log(P) and Turbidity	33
3.1.4.	Log(P) and the Emulsification of Oil	35
3.1.5.	Log(P) and the Thickening Efficiency of Various Oils	38
3.1.6.	Molecular Weight Effects on Viscosity	39
3.2.	pH Tolerance of Nonionic Associative Thickeners	42
3.3.	Surfactant Interactions of NIATs	43
3.3.1.	Anionic Surfactants	43
3.3.2.	Surfactant Blends	48
3.4.	Salt Effects on Nonionic Associative Thickeners	52
4.	CONCLUSION	59
5.	FUTURE WORK	61
	BIBLIOGRAPHY	62
	Part B	67-86
1.	INTRODUCTION	67
1.1.	SOD Chemistry	67
1.2.	Click Chemistry	71
2.	METHODS AND MATERIALS	75
2.1	Experimental Work	75
2.1.1.	Preparation of Benzyl Azide	75

2.1.2. Preparation of Alkyne	75
2.1.3. Preparation of Ligand Via Click Reaction	76
2.1.4. Preparation of 4-Vinyl Benzyl Azide	76
2.1.5. Preparation of t-Butyl Acrylate-4-Vinyl Benzyl Azide Copolymer	77
2.6. Formation of Ligand on Copolymer	77
3. RESULTS/DISCUSSION	79
4. CONCLUSION	85
BIBLIOGRAPHY	86

LIST OF TABLES

Table	Page
Part A	
3.1: Partition Coefficient of the NIATs	30
3.2: Emulsion Stability Measured by % Volume Separation	
After 7 Days at 60 °C	36
3.3: Emulsion Stability Measured by % Volume Separation After	
7 Days at 60 °C and Centrifugation	37
3.4: Viscosity as a Function of Oil Type and log(P)	39
3.5: Salt Effects on Emulsion Stability Measured By % Volume Separation	55
Part B	
3.1: IC ₅₀ and Rate Values for Amine Ligand Library	80

LIST OF FIGURES

Figure	Page
Part A	
1.1: The Shear Stress vs. Shear Rate Curve of a Bingham Plastic	3
1.2: The Viscosity Curve of a Pseudo-Plastic Material	3
1.3: An Example of a Viscosity Curve of a Shear Thickening Material	4
1.4: Alkali-Swellable Emulsion Type Thickener	6
1.5: An Example Structure of a Nonionic Associative Polymer	8
1.6: Nonionic Associative Polymer Structure in a Dispersion	10
1.7: Rheology Profile of a HEUR Polymer	13
2.1: Surfactant Effect on NIAT Aggregates	27
3.1: Rheogram for NIAT Polymers at 2 wt% in Water	32
3.2: Viscosity (2 wt% NIAT in water) as a Function of log(P)	33
3.3: Turbidity (1 wt% NIAT in water) as a Function of log(P)	34
3.4: Effects of Molecular Weight on Thickening Efficiency and Average Aggregate Size	41
3.5: pH Effects on Viscosity	43
3.6: SLS Effects on NIAT-145 (1 wt%)	44
3.7: SLS Effects on NIAT-146 (1 wt%)	45
3.8: SLS Effects on NIAT-147 (1 wt%)	47
3.9: The Effects of SLS on Various NIATs	48
3.10: SLES/CAPB Effects on NIAT-138	50
3.11: SLES/CAPB Effects on NIAT-148	51

3.12: SLES/CAPB Differing Effects on 138 and 148	52
3.13: Salt Effects on Emulsion Viscosity	54
3.14: The Effects of Salt on Aqueous NIAT Fluid Viscosity	56
Part B	
1.1: SOD Process of Seven Coordinate Manganese Mimetic	69
1.2: Eukarion-134 Mn-SOD Mimetic	70
1.3: The Proposed Ligand Set	70
1.4: The Proposed Manganese Complex	71
3.1: Model Amine Ligand	79

LIST OF SCHEMES

Scheme	Page
Part B	
1.1: Catalysis of Superoxide Dismutation by Manganese	68
2.1: Click Chemistry for the Formation of a Triazole	72
2.2: Copper Catalyzed Click Reaction for 1,4-Triazole	73
3.1: Formation of Manganese Complex	79
3.2: Synthesis of Compound 1	81
3.3: Synthesis of Compound 2	81
3.4: Synthesis of Compound 3 Using Click Chemistry	81
3.5: Synthesis of Compound 4	82
3.6: Synthesis of Polymer 1	82
3.7: Formation of Polymer 2	83
3.8: Formation of Compound 5	83

1. Background Information

1.1 Rheology Overview

Run a Google search on “rheology” and the links that return are guaranteed to show diversity. Rheology of materials is an important aspect and therefore a wide range of research is performed to better understand it. Industries such as paints, coatings, plastics, and chemical-processing have always shown a need for an understanding of rheology. Since the 1950’s, rheology has become an important aspect in the production of food, pharmaceuticals, and biotechnology. This has spawned fields of study such as biorheology, which studies the rheology of manufactured materials in biotechnology (Barnes, 1989). With rheology playing a large role in society’s key industries, it only makes sense that it would be a concern in personal care.

Rheology is most literally defined as “the study of the deformation and flow of matter”, which was coined in 1929. Rheology studies all aspects of a material’s flow properties including its viscosity; its internal friction and resistance to flow. Rheology allows this viscosity to be measured under an array of deformations and under varying forces. Rheology also examines both the viscous and elastic characteristics of a material (Barnes, 1989).

Depending on the type of structure, materials can display a wide variety of rheological behaviors. The most simplistic system is Newtonian fluids. Newtonian fluids are defined by Equation 1.

$$\eta = \frac{\tau}{\dot{\gamma}} \quad \text{where } \eta = \text{viscosity, } \dot{\gamma} = \text{shear rate, } \tau = \text{shear stress} \quad \text{Equation 1.1}$$

As shown in Equation 1.1, for Newtonian fluids, viscosity is purely a function of the shear stress and the shear rate, and the relationship between shear stress and shear rate is linear. For this reason, Newtonian fluids have a viscosity independent of shear rate and time. It should be noted that Newtonian fluids can have viscosity dependence on temperature and pressure.

While the Newtonian model for materials is simple, a large majority of fluids have higher order effects that cause the relationship between shear stress and shear rate to diverge from linearity. This can lead to changes in viscosity in response to both shear rate and time. Fluids made from emulsions, polymer melts, surfactant systems, and suspensions all exhibit these more complex rheological behaviors. Of the more complex rheologies, it will be important to focus on those which are most common in emulsion systems used in personal care. Particularly, systems containing polymers will be the focus. Thixotropy, which describes the time dependence on viscosity, can often be witnessed in polymer solutions. This results from the formation and elimination of viscosity building structures which, after high shear, take a certain amount of relaxation time to return to equilibrium. Along with time dependence, many non-Newtonian fluids exhibit viscosities which show dependence on shear stress or rate. There are three main types of shear rate and stress dependent fluids: Bingham plastics, dilatant fluids, and pseudo-plastics. For Bingham plastics, the fluid requires a minimum shear stress or yield stress, in order to begin flowing. Once this yield stress is met, the fluid will usually act as a Newtonian fluid in which the shear rate becomes proportional to the applied shear stress (Tanner, 1985). A graphical depiction of the relationship between shear stress and shear rate for a Bingham plastic is shown in Figure 1.1.

Figure 1.1: The Shear Stress vs. Shear Rate Curve of a Bingham plastic

The key feature of Bingham plastics is the non-zero y-intercept for shear stress vs. shear rate associated with the yield stress.

Pseudo-plastic or shear-thinning behavior is another common non-Newtonian rheology which shows strong prevalence in polymer solutions. For pseudo-plastics, the ratio between shear stress and shear rate does not remain constant but instead shows a decrease at increasing shear rates. Shear-thinning is most commonly seen in paints and coatings as well as emulsions used in personal care (Tanner, 1985). Figure 1.2 displays the relationship between shear rate and viscosity for a pseudo-plastic.

Figure 1.2: The Viscosity Curve of a Pseudo-Plastic Material

For pseudo-plastic materials the viscosity decreases as shear rate increases. The slope of the decrease can be very gradual or steep depending on the fluid.

On the opposite end of the spectrum are dilatant or shear-thickening materials. These materials have a shear stress to shear rate ratio that increases with increasing shear rate. An example of the viscosity vs. shear rate curve for a dilatant material is shown in Figure 1.3.

Figure 1.3: An Example of a Viscosity Curve of a Shear Thickening Material

In Figure 1.3, the viscosity is shown increasing in response to increasing shear rates. As with pseudo-plastics, this increase can have a very small slope or a very steep one.

Although three distinct types of non-Newtonian fluids can be described, rarely are they exclusive. Many complex systems are combinations of shear dependent fluids combined with time-dependence (Tanner, 1985). With all of the unique rheologies available, research is constantly being done to produce the perfect rheology for each application. Depending on the desired flow properties, there are various rheology modifiers and thickeners available.

1.2 Rheology Modifiers

1.2.1 Conventional Thickeners

For polymeric rheology modifiers there are two main types: conventional and associative. Conventional thickeners are most often times water soluble polymers of high molecular weight that rarely contain hydrophobic groups. This type of conventional thickener is usually a polysaccharide derivative, of biological origin, or a synthetic hydrocarbon. They thicken by mechanisms of chain entanglement, hydrodynamic volume and flocculation of dispersed components. These polymers, which have a broad range of molecular weights, occupy a lot of volume when dissolved in solution. This limits the motion of water molecules and leads to an increase in viscosity that is dependent on temperature and polymer concentration. As the molecular weight of the water soluble polymer increases, there is a resulting increase in the viscosity of the polymer solution (Shulz, 1991).

When polymers are dissolved in aqueous solutions, the crowded polymer chains entangle with one another. Under levels of low shear, the crowded polymer chains begin to entangle with one another, causing resistance to flow. Under high enough shear rates, these entanglements are broken leading to shear-thinning characteristics. Along with entanglements and hydrodynamic volume, conventional polymer thickeners also cause flocculation of the dispersed phase. This can be seen in bridging flocculation, in which the polymer chain attaches two separate colloids thus bringing them together. Also, there is depletion flocculation, in which the size and concentration of the polymer leads to a concentration gradient which causes polymer rich and dispersed phase rich domains in

solution. Both of these types of flocculation ultimately lead to further thickening. Depending on the chain length, molecular weight, and flexibility of the polymer backbone, a range of viscosities can be observed. One of the more common conventional thickeners used in personal care would be polyethylene glycol (Koleske, 1995).

Another important type of conventional thickener would be the alkali-swellaible (ASE) polymers. ASE polymers are usually acrylate or acrylic acid species that can be crosslinked or not. A graphic display of a crosslinked ASE type polymers is represented in Figure 1.4.

Figure 1.4: Alkali-Swellaible Emulsion Type Thickener

The acrylic acid based polymer is lightly crosslinked (as represented by the dotted lines). Under neutralized conditions (pH 5.5 or greater), the carboxyl groups on the polymer repulse one another. Because of the crosslinking between polymer chains, the carboxyl groups cannot adequately avoid one another causing the polymer to swell and form viscous gel-like solutions. These are also very common rheological modifiers that are used in the personal care industry and have trade names such as Carbopol and Carbomer (Koleske, 1995).

1.2.2 Associative Thickeners

Another class of thickeners along with conventional thickeners is associative thickeners. This class contains polymers which modify the rheology of a fluid through associative interactions between polymer chains, the dispersed phase, and the medium. Unlike conventional thickeners, associative thickeners are often times lower molecular weight polymers containing both hydrophilic and hydrophobic regions. The hydrophobic regions are then able to associate with the hydrophobic moieties while the hydrophilic regions are able to associate with the hydrophilic moieties. This can lead to a network formed within a mixture leading to high viscosities and unique rheological properties. Associative polymers have been a research topic since the 1950s as their applications involve industries such as paints, coatings, personal care, and colloid stabilization. While there are many different types of associative thickening polymers, some common ones are hydrophobically modified conventional thickeners (Zhang, 2001).

Although the list of associative thickeners is growing everyday, it is important to address some of the more common ones used in industry today. First, there are hydrophobically modified cellulose associative thickeners, which are derived from hydrophilically modified cellulose. Examples of this include carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC) and methyl cellulose (MC). Hydrophilically modified cellulose is commonly used as a thickener because its long polymer chains participate in chain entanglement, ultimately leading to thickening and shear thinning qualities. However, hydrophobically and hydrophilically

modified cellulose can show greater thickening as well as emulsifying abilities. This is because the hydrophilic and hydrophobic regions of the polymer chains are able to associate at the water/oil interface thus stabilizing emulsions and preventing oil droplets from coalescing (Sun, 2007).

Hydrophobically modified alkali-swelling emulsion (HASE) thickeners are the associative analog to alkali-swelling emulsion (ASE) conventional thickeners. Like the ASE thickeners, HASE polymers are usually comprised of acrylic acid, acrylate, and other electrolytic backbones. However, unlike typical ASE types, HASE polymers contain hydrophobic “pendants” which are commonly attached via polyethylene oxide chains. HASE polymers are unique associative thickeners; they have relatively high molecular weights, an ionic charge, and they do not contain as many hydrophobic modifications as other associative thickeners. Instead, they thicken mostly by means of hydrodynamic volume both due to their size as well as their charge repulsion under basic conditions. The hydrophobic regions instead allow the HASE thickeners to create uniform emulsions by stabilizing hydrophobic moieties (Kostansek, 2005).

1.3 Nonionic Associative Thickeners

Non-ionic associative thickeners (NIAT) are one of the most popular types of associative thickeners used in the paints and coatings industry. They are nonionic polymers with a general structure following Figure 1.5.

Figure 1.5: An Example Structure of a Nonionic Associative Polymer

NIAT polymers contain three key features: a coupling agent (as represented by bolded bonds and X group), hydrophilic regions commonly made up of polyethylene oxide (PEO) derivatives and hydrophobic alcohol or amine chain ends and pendants (represented by the R groups).

An example of a nonionic associative polymer is a hydrophobically modified ethoxylated aminoplast (HEAT). For these particular thickeners, the hydrophilic polymer backbone is polyethylene glycol and the coupling agent used is an ethoxylated aminoplast. These thickeners, which are not researched as widely as many other associative thickeners, result in Newtonian rheology profiles when used in aqueous systems (Manion, 2011).

There are a variety of non-ionic associative thickeners and a widely researched type is hydrophobically modified ethoxylated urethane (HEUR) thickeners. For HEUR thickeners, the coupling agent used is a diisocyanate and the hydrophilic regions are poly(ethylene oxide) chains. The nonionic associative polymers used in this project behave similarly to HEUR type thickeners. It will be assumed that the nonionic associative thickeners in this project follow the same trends shown in the research on HEUR polymers.

1.3.1. Nonionic Associative Polymer Structure in Solution

Hydrophobically modified ethoxylated urethane polymers are usually lower molecular weight species with broad molecular weight distributions. HEUR polymers, like all non-ionic associative thickeners, modify rheology in solution by association between the hydrophobic and hydrophilic regions and this is accomplished in two ways. At low concentrations, hydrophobic end groups associate intramolecularly and

intermolecularly to form aggregates. This is accomplished by the “looping” of hydrophilic groups into a conformation that allows hydrophobic end groups of the same polymer chain to reside in the same aggregate thus building floret or flower-like structures. These floret structures build hydrodynamic volume leading to an increase in viscosity. At higher polymer concentrations, hydrophobic end groups begin to “link” aggregates by associating with two different florets. Figure 1.6 shows a schematic depiction of the association between chains.

Figure 1.6: Nonionic Associative Polymer Structure in a Dispersion

As the number of links, as shown in Figure 1.6, increases, eventually a network of florets is created with relaxation times corresponding to hydrophobes detaching from an aggregate (Tam, 1998; Annable, 1994).

It was previously speculated that the loop structure of HEUR polymers in solution was implausible. Research from Brinke and Hadzidioannou showed that it was extremely unlikely for ABA block copolymers of similar structure to undergo a loop formation in solution if end groups were not properly solvated (Ten Brinke, 1987). This has since been refuted as it has been shown that loop formations are energetically favored. While the association between hydrophobic chain ends requires a free energy of ~67 kJ/mol to stretch chain backbones into looping formations, the resulting binding

enthalpy between hydrophobic ends is ~ 71 kJ/mol. This means not only is the floret association energetically favored, but the probability of a hydrophobic chain end not being involved in an aggregation is very low (Yekta, 1995). This can be generally stated for all non-ionic associative polymers with poly(ethylene glycol) and poly(propylene glycol) backbones. Both of these polymers provide flexible backbones that allow the formation of loops. HEC polymers, on the other hand, cannot form the floret structure due to their rigid cellulosic polymer backbone.

At low HEUR concentrations (~ 0.2 wt% in water), a considerable increase in viscosity is observed due to the formation of floret shaped micelles. Work has been done to determine the number of hydrophobic moieties necessary to form a floret. This is also referred to as the aggregation number (N_A). Particularly, it has been of interest whether the aggregation number of HEUR chains in a floret is a set number or grows with increasing HEUR concentration. Research groups such as Maechling-Strasser et al. have concluded that associative thickener micelle systems are “open”; the number of HEUR chain hydrophobes aggregating in one floret continues to grow as the concentration in solution increases. This conclusion was made after light scattering measurements showed the weight averaged molecular weight (M_w) of HEUR polymers in an aqueous solution increased as the concentration increased. Conversely, research using spectroscopy to measure aggregation between HEUR chains has shown polymer association at concentrations lower than observable by diffusion and viscosity measurements by more than an order of magnitude. This has been used to assume that HEUR aggregates contain only a small number of aggregating hydrophobes with $N_A < 10$ (Maechling-Strasser, 1992).

Research has used florescent probes to better understand the associating phenomenon. This has been done using pyrene probes which emit florescent excimers upon formation of dipyme, a water insoluble molecule which becomes soluble within the hydrophobic floret core of HEUR aggregates. This allows for the number of formed florets in solution to be monitored. These studies, which have been carried out by Yekta et al. have shown that HEUR aggregation numbers are roughly 15-30 hydrophobes per floret. Therefore, roughly 10-15 polymer chains participate in the formation of one floret. This number is approximated and further depends on polymer chain length as well as hydrophobe size. It is important to point out that an aggregation number of 15-30 is threefold smaller than that of most surfactants, which also form micellar structures. Along with this, Yekta was able to prove from fluorescent probe experiments that N_A for HEUR type polymers remains constant as concentration increases thus the floret formation is considered a “closed” system (Yekta, 1998). According to Vorobyova et al., many fluorescent probe experiments vary in the results for the aggregation number of HEUR polymers. This is mainly due to the large polydispersity of the polymer. As the length of the ethylene oxide segment increases, hydrophobe aggregation number decreases. Because many HEUR type polymers have polydispersities of 2 or greater, the aggregation number of a particular HEUR polymer in solution usually falls within a range rather than a set value (Vorobyova, 2000).

Although floret size does not increase, there is a steep increase in viscosity between 0.1 wt% and 0.8 wt% HEUR in water. Studies conducted by Annable credit this to the building of localized networks formed by HEUR strands linking multiple florets. According to Annable, at increasing concentrations of HEUR the linking of florets

becomes entropically favorable and leads to an increase in viscosity, relaxation time, and elastic modulus of the solution (Annable, 1993).

The ability of HEUR chains to participate in both looping to form floret aggregates as well as linking between florets creates a very unique rheology profile. Although the likelihood of a hydrophobe to participate in a loop compared to a link is equal, under shear this equilibrium tilts to favor loops. Therefore, increasing shear transforms concentrated HEUR solutions from a gel-like substance to a viscous fluid. Also, there is a shear thickening phenomenon observed at moderate shear rates. This is distinctive of HEUR thickeners and has been associated to shear induced deformations, aggregations, as well as stretching of the linking chains (Tam, 1998; Annable, 1994). Figure 1.7 presents the structure-viscosity relationship at various shear rates as proposed by Yekta et al.

Figure 1.7: Rheology Profile of a HEUR Polymer (Yekta, 1995)

At low shear stresses both the linking and looping of HEUR strands is relatively unaffected and an increased viscosity following Newtonian behavior is noticed. The signature shear induced thickening then occurs as the linking polymers begin to stretch at

increasing shear stresses. Lastly, at high enough shear stresses, the equilibrium between links and loops shifts to favor loops and the micro-gel network is broken, leading to a large decrease in viscosity (Tam, 1998; Yekta, 1995).

1.3.2. Structure/Property Relationship for Nonionic Associative Polymers

A large area of research surrounding HEUR thickeners relates to structure-property relationships. Structure-property relationships focus on how specific changes to the polymer structure affect the aggregation number, thickening efficiency and elastic modulus. Although most HEUR thickeners have similar general structures comprised of a polyethylene oxide backbone with urethane linkages and hydrophobic segments, the size, shape, and placement of the hydrophobic regions strongly dictates hydrophobic associations. Various studies have been done to evaluate these structure effects by both altering hydrophobe position and type.

In the research done by Alexandridis et al., the size of the hydrophobic and hydrophilic region was varied to monitor the effect on aggregation number. It was found that increasing the size of the hydrophobic regions, thus making the polymer more insoluble in water, caused an increase in aggregation number of equal proportion. Likewise, as the size of the hydrophilic regions was increased, the aggregation number of the polymer decreased. Finally, as hydrophilic regions of the chain were increased, they imparted less of an effect on the aggregation number. Alexandridis concluded that the size of the aggregating moieties had a larger influence on aggregation numbers than that of the soluble moieties on the polymer (Alexandridis, 2000).

In studies by Kaczmariski and Glass, HEUR polymers were analyzed by their efficiency at aggregating and building viscosity. Aggregation efficiency was monitored

using fluorescence spectroscopy, as heavy aggregation between polymer chains causes a large increase in fluorescent emission intensity. Kaczmariski and Glass also determined the efficiency of various HEUR polymers by measuring the relationship between polymer concentration in solution and viscosity, as an increase in aggregation and association between HEUR chains should cause large increases in viscosity. Their studies showed that in order for HEUR polymers to thicken through mechanisms of association and aggregation, there must be hydrophobic segments located terminally on the polymer. When hydrophobes are located at the ends of the HEUR chains, they are able to best aggregate and associate with one another and therefore lead to drastic increases in viscosity at relatively low concentrations. Kaczmariski and Glass also found that HEUR thickening efficiency increased as terminal hydrophobe size increased. Along with that, it was found that as the size of the hydrophobic segments increased, lower concentrations of polymer were necessary for association and aggregation. Kaczmariski and Glass also concluded that increasing molecular weight of the HEUR polymers without changing the size of the hydrophobic group lowers the thickening efficiency of the polymer (Kaczmariski, 1994).

The latter studies done by Elliot and Glass showed similar results. Using fluorescent probe experiments, Elliot et al. found that branched, bulkier terminal hydrophobic groups on HEURs have an average lower aggregation number. The floret core of branched hydrophobic groups is also more hydrophilic than the core of linear hydrophobic groups. Along with this, it was found through dynamic light scattering studies that in order for a sharp increase in viscosity to occur, HEUR aggregates must reach ~500nm in solution. This size is reached at lower concentrations with branched

hydrophobic moieties as well as longer poly(ethylene oxide) regions. This leads to an initial increase in viscosity at lower concentrations for HEURs with branched hydrophobic end groups. However, it was found that at higher HEUR concentrations, linear hydrophobic groups are more viscosifying than branched hydrophobic groups on HEUR polymers (Elliot, 2003).

The work done by Glass and Kaczmariski was also examined by Barmar et al. by testing rheological differences in HEUR polymers with identical hydrophobic end groups but varying hydrophilic chain lengths. Much like Kaczmariski and Glass, Barmar et al. found an increased efficiency at thickening for the HEURs with lower hydrophilic chain lengths. Barmar also found an increase in the storage modulus as hydrophilic chain lengths on HEUR polymers decreased. This translates to a higher association between hydrophobic end groups and a more elastic solution when hydrophilic chain length is decreased and hydrophobic chain length is kept constant. It was also found that as the polydispersity of the HEUR polymer increased, thickening efficiency decreased (Barmar, 2004).

2. Rheology Modifiers and the Personal Care Industry

A common outlook in the personal care industry is that it is based solely on aesthetics. People want a particular look so they purchase a product which will give them that look. However, many products recite the same claims and even contain many of the same active ingredients so how do consumers differentiate between the good and the bad? Although many different products may deliver the same set of ingredients to accomplish an alleged function, how these ingredients are delivered can make a complete difference in the overall performance of a product. Much like two paints of the same color by different companies, one of the factors that separates the ordinary from extraordinary is the rheology. Not only does the rheology of a personal care product help to determine its application, but it decides how the product will be used, where it will be used, and how thick the product will deposit onto the substrate. The personal care industry requires a wide range of rheological properties. Whether the formulator is making a spray, serum, gel, wax, cream, lotion, or paste, a number of flow factors need to be controlled. Rheology modifiers in personal care need to not only control viscosity, but also the elastic modulus, the viscous modulus, any yield stress, and response to shear. With control of these attributes, formulators can control product shelf life, performance, and application. For this reason, it is comparable to the paint industry and therefore requires similar technologies for “tailor-made” rheology profiles of various products.

2.1. Current Rheology Modifiers

There is a variety of rheology modifiers currently in use today in personal care products. Carbohydrate based thickeners make up a large majority and include natural thickening agents such as guar gum derivatives, cellulose, xanthan gum, pectin, cassia

and agar (Rosen, 2005). These thickeners, which are high molecular weight species, build viscosity through hydrodynamic volume and chain entanglement mechanisms. For this reason, they often exhibit pseudoplastic rheologies and shear thinning. They are highly hydrophilic leading them to swell in the presence of water, however they cannot be used in formulations containing less than 90% aqueous phase. This is due to solubility of the polymers, which require large amounts of water for proper dispersion. Also, because of their high molecular weights they often require low concentrations (<1 weight percent) to build reasonable viscosities (Karsheva, 2007). Depending on the carbohydrate thickener, their viscosity and clarity can depend greatly on temperature, salt content, pH, and method of dispersion. There are also issues, particularly with the natural gums, of price, availability, as well as microbial contaminants (Kirk, 1978). There are also a few protein based thickeners used. Much like carbohydrates, these are usually naturally derived and include albumin, gelatin, keratin, and milk, fish, wheat, soy, and silk proteins (Rosen, 2005).

A large amount of synthetic polymeric thickeners are used in cosmetic products and this class contains polymers such as polyvinyl pyrrolidone vinyl acetate copolymer (PVP/VA), alkylene and alkylene oxides, and polyacrylic acid and acrylate derivatives (Rosen, 2005). Of these synthetic thickeners, one of the most widely used is the poly(acrylic acid) thickeners (Carbopol®/Carbomer®). These crosslinked polymers, which are considered ASE thickeners, contain carboxyl groups along the polymer backbone and are easily solubilized in water. Under neutralized conditions of pH 5.5 or higher, the carboxyl groups ionize and repel one another. Because of the crosslinking, water is trapped within the polymer forming hydrogels upon repulsion induced swelling.

These thickeners have shown great efficiency at thickening an array of personal care products such as hair gels, lotions, creams, and body washes. Also, because of the crosslinked microgel structure, insoluble particulates and inorganics are trapped and can be dispersed and suspended indefinitely. Although ASE type thickeners have been revolutionary to rheology modifying in personal care, there are some limitations. First off, many biologically active ingredients (actives) used in skin care are acidic and as a result, more formulations are slightly acidic. This inhibits the electrostatic repulsion between neutralized anionic groups thus preventing the polymer from swelling. For this reason, poly(acrylic acid) based thickeners are not useful in low pH formulations. Also, these thickeners have low electrolyte and salt tolerance. Under high electrolyte concentrations, charge shielding occurs around the –OH groups and prevents repulsion. This also causes a large decrease in viscosity. For this reason, many formulations made with ASE thickeners lose their viscosity upon contact with skin, which contains salt (Annable, 1994).

Along with organic soluble thickeners, there are also a few types of inorganic thickeners used in personal care. This includes silica and various magnesium silicates, organoclays, bentonite, hectorite, and quaternium-18 derivatives (Rosen, 2005). For inorganic thickeners, if there is no interaction between particles, the viscosity profile remains Newtonian with increased viscosity. However, those thickeners that do have particle interaction create unique rheology profiles. Instead, the viscosity profile will be only Newtonian at low thickener concentrations and will become highly elastic and gelatinous at high concentrations (Paye, 2006). These thickeners are limited in their use;

not only do they require hydration time, but they must be used in higher concentrations and often pull large quantities of water from the aqueous phase (Koleske, 1995).

Although there are a variety of rheological modifiers available in the personal care industry, there is need for improvement. As the green movement gains momentum, consumers demand shorter and safer formulation lists which exclude many of the long time “go-to” ingredients. In turn, as product competition increases, clients demand ingredients which are multifunctional. This drives the search for new rheology modifiers which not only build viscosity, but also emulsify, aid in film formation, are pH and electrolyte insensitive, and create a sensory profile that’s beyond just satisfactory. This is the void that nonionic associative thickeners (NIAT) are set to fill.

2.2. Nonionic Associative Polymers in Personal Care

In order for NIAT polymers to be accepted and utilized as thickeners in the personal care industry, there needs to be proof that they outperform what is already available. NIAT thickeners need to not only solve the shortcomings of current thickeners, but also show comparable performance in formulation. Not only are NIAT polymers expected to solve problems associated with electrolyte concentration and pH, but they should also show to be a multifunctional ingredient for formulators, acting as both thickeners and emulsifiers.

Amphiphilic block copolymers which aggregate in solution are generally considered to be salt tolerant. The effects of salt on the aggregating process at low concentrations, in theory, should be synergistic. Alexandridis et al. found that at low concentrations of NaCl, the dissociated ions migrated to the aggregate corona of the aggregating associative polymers and assisted in the formation of larger florets. This was due to the shielding of the electrostatic repulsion between hydrophilic regions in the

corona by the salt ions (Alexandridis, 2000). For the hydrophobically modified polyurethanes, salt sensitivity is largely determined by the nature of the hydrophilic regions. Noble found that ionic HEUR polymers showed a greater reaction to the addition of salt, however nonionic HEUR polymers showed no evidence of salt sensitivity (Noble, 1997). All of the polymers proposed in this paper for the personal care industry are nonionic and therefore should be salt insensitive. This would allow NIAT polymers to be an ultimate replacement for many of the salt sensitive polymers currently used in personal care applications.

2.3. Nonionic Associative Polymers as Emulsifiers

It is ideal to not only introduce a new thickener to the personal care industry, but a multifunctional one with emulsifying capabilities as well. A personal care product can be generally described in one of the four ways: an aqueous gel, an oil in water emulsion, a water in oil emulsion, and a neat oil. An emulsion is a two liquid component system in which the two components are immiscible with one another. Therefore, a compound that disperses and stabilizes one of the liquids in the other is required to keep the two components mixed and prevent coalescing of emulsified droplets. Emulsions are commonly used in the personal care industry to alter the less than desirable feeling of actives and emollients. Many active ingredients and emollients are oils and deliver a greasy feel which can be a negative attribute for the consumer. By dispersing the oils in an aqueous environment, the sensory can be altered so it is more favorable to consumers. Emulsions usually contain emulsifiers in conjunction with thickeners to provide stability between the two phases with the appropriate viscosity. Most emulsifiers are amphiphilic molecules with segments that are soluble in both phases so they can adsorb at the

interface of the two liquids thus lowering the interfacial tension and preventing coalescence. Various surfactants and cetyl alcohol are common emulsifiers used today (Laba, 1993). Because of the amphiphilic nature of hydrophobically modified thickeners, they can be synthesized in a way that may allow them to be good emulsifiers also. Hydrophobic moieties could reside in the oil phase while hydrophilic moieties would remain in the aqueous phase. This should both assist in lowering interfacial tension as well as preventing coalescence through steric stabilization; large polymer strands should prevent oil droplets from coming too close together (Tadros, 2008). The ability to adequately emulsify as well as thicken would provide HEUR polymers with an extra advantage over today's top thickening agents.

2.4. Surfactant Interaction

An important aspect of nonionic associative thickeners will be their interaction with other important cosmetic formulation ingredients. One of the most common ingredients used in personal care products are surfactants. Surfactants, much like associative thickeners, build very unique structures in solution that lead to lower interfacial tensions as well as unique rheology profiles. The interactions between surfactants and HEURs have been examined in detail in the paints and coatings industry as well as academia; however specifics regarding the cosmetic industry are still somewhat uncharted territory. It is therefore necessary to fully understand the associations between HEURs and surfactants prior to using NIATs in formulation.

2.4.1. Surfactants

Before the relationship between surfactants and NIATs can be investigated, it is important to first adequately describe the characteristics surrounding surfactants.

Surfactants most literally are defined as “surface active agents” because of their tendency to initially migrate to interfaces. The most defining feature about surfactants is that they are amphiphilic and contain at least two types of segments, both soluble in different types of solvents. For this reason, surfactants tend to position themselves at medium interfaces to allow lyophilic portions to remain in solvent while lyophobic portions avoid the bulk solvent. This leads to a decrease in surface tension and surfactants in this category can be referred to as “unimers”. As surfactant concentration begins to increase, the unimers will align themselves at the surface until a critical concentration is met and the unimers aggregate together to form micelles. This critical concentration is known as the “critical micelle concentration”(CMC), is unique to each surfactant, and the concentration of unimers in solution will rarely exceed this value (Holmberg, 2007; Myers, 2006).

Some interesting changes occur in solution at the CMC. The osmotic pressure, which is relatively stable leading up to the CMC, begins to linearly decline once the critical value is met. Also, surface tension will continue to decrease as surfactant concentration increases until the CMC is met, at which point it levels out. Finally, upon addition of surfactant to a mixture, turbidity will slowly increase. However, at the critical micelle concentration and above, turbidity will rapidly increase. All of these changes are used by scientists to quantify the CMC for each surfactant (Holmberg, 2007; Myers, 2006).

At the critical micelle concentration, the first aggregation structure to be formed by surfactant molecules is a sphere. The number of surfactant molecules in one micelle is known as the “aggregation number” and is dependent on the structure and charge on the surfactant molecule. This is because the radius of the micelle, which is influenced by the

length of an extended surfactant molecule as well as the hydrophobe, determines the aggregation number. For simple surfactant systems which have “closed” micelles, this number will not change after the CMC. For more complex/open surfactant systems which form shapes different than spheres, the aggregation number can continue to grow after the CMC in order to form shapes like cylinders, rods, ovals, and wormlike threads (Holmberg, 2007; Myers, 2006).

When discussing the surfactants used in personal care, the specific shape of the surfactant micelles becomes more complicated. In cleansing applications such as detergents, shampoos, and soaps, more than one type of surfactant is usually used. Cosurfactant systems usually have lower CMC values than either surfactant alone. This allows the formation of viscosity building micelles at much lower surfactant concentrations which reduces the irritancy of many cleansers used on the skin and hair. Along with this, lower CMC values for surfactant blends leads to superior foaming, lathering and emulsifying properties. The most common surfactant blend used in personal care applications is a blend of an anionic and zwitterionic surfactant. Frequently this involves an anionic such as a sulfate surfactant along with an alkylbetaine/alkylamidobetaine zwitterionic surfactant. These mixtures give rise to unique micelle shapes which start as mixed spherical micelles. Christov et al. looked closely at the shape transitions of sodium dodecyl sulfate (SDS) and cocoamidopropyl betaine (CAPB) in solution and noticed a sharp increase in viscosity pertaining to the transition into rod shaped spheres. This transition occurs at a concentration less than ten-fold of the concentration of SDS alone (Christov, 2004). Even more unique are the micelles of CAPB and sodium lauryl ether sulfate (SLES), a common cleansing

application cosurfactant mixture. Petekidis et al. describes the surfactant molecules as initially forming mixed spherical micelles which then grow into cylinders and eventually become a wormlike structure which entangle much like polymer chains in solution. The transition into wormlike micelles results in a distinct change in solution characteristics largely due to the ease in breaking and reforming the wormlike strands. Along with this, Petekidis noted that the size distribution between the wormlike micelles is exponentially large as well as concentration dependant. This results in a unique rheology profile at various ranges of SLES/CAPB concentrations (Petekidis, 2002).

2.4.2. NIATs and Surfactants

The behaviors of surfactants and associative thickeners in solution have both been described using similar jargon; aggregation number, hydrophobicity and micelle shape are important features of each material. Both surfactants and NIATs form structures and networks in solution that build viscosity and are able to emulsify by entrapping lyophobic moieties in their micelle cores. Although surfactants and NIATs are used in conjunction with one another frequently in the coatings industry, it is relatively unexplored territory in the personal care industry. There has been an especially large amount of work done involving HEUR thickeners and surfactants in solution since both are used together in paint formulations. Prior knowledge of this specific interactions will serve purpose in discovering the balance necessary to allow the surfactants and NIATs to work synergistically in a cosmetic formulation.

As described in Section 1.3.1, the structure of HEURs in solution involves the formation of flower-like aggregates with a hydrophobic core formed from “looped” polymer chains. These florets are then “linked” together at high polymer concentrations

by associations of one chain in multiple micelles. The balance between links and loops, if left unsheared, is in equilibrium; the relaxation time corresponding to both links and loops is merely the time for a hydrophobe to leave an aggregation. In the work done by Annable et al., rheology was used to determine the structural changes occurring when surfactants are added to HEUR solutions. Through measurements of the storage and loss moduli it was found that under the addition of surfactant, HEUR solutions could no longer be described as having one relaxation time and instead consisted of a distribution of relaxation times. Along with that, upon the addition of a low concentration of surfactant, an increase in the storage modulus as well as an even larger increase in the overall relaxation time of the material occurred. These increases were noticed at surfactant concentrations well below the CMC of the surfactant used. From these results, Annable et al. concluded that as surfactant concentration increases, the equilibrium between links and loops initially shifts to favor links. Therefore, the number of chains participating in only one micelle decreases. This shift from loops to links causes an initial increase in the storage modulus, since an increase in links leads to a larger network and more microgels. However, as surfactant concentration is increased beyond the modulus maximum, the number of looped polymer chains decreases so much that the network falls apart and ultimately the viscosity is drastically decreased (Annable, 1994).

In more recent work by Dai et al., the specific interactions occurring between HEUR polymers and surfactants was explored using microcalorimetry and laser light scattering. Dai performed a series of titration experiments varying the concentration of HEUR and sodium dodecyl sulfate and identified three important concentrations. Dai

described the interactions between SDS and HEUR polymers using the graphical depiction in Figure 2.1.

Figure 2.1: Surfactant effect on NIAT aggregates (Dai, 2001)

At zero to low concentrations of SDS, as represented by (a) and (b), SDS molecules associate with the hydrophobic core of HEUR molecules in an uncooperative manner. The CAC, critical aggregation concentration as shown in (c), is the concentration of surfactant in a HEUR solution at which the surfactant and polymer molecules begin to interact. This initial interaction involves the hydrophobes on surfactant molecules participating in and strengthening the HEUR florets. This eventually leads to surfactant molecules replacing HEUR hydrophobes in the florets, allowing more HEUR hydrophobes to participate in linking between florets. As concentrations of SDS increase as shown in (d), there is an increased number of unassociated hydrophobes in solution which results in a shift from SDS hydrophobes participating in HEUR florets to HEUR hydrophobes being solubilized within SDS micelles. The C_2 , second critical concentration, occurs once the HEUR hydrophobes are fully saturated with SDS. This

ultimately represents the destruction of the HEUR network and a rapid decrease in viscosity. Increasing concentrations of SDS then result in the formation of SDS free micelles in solution as shown in (e). This is known as the C_m and at this stage the hydrophilic portions of the HEUR polymer wrap around the SDS micelle corona (Dai, 2001).

Research has also been done involving surfactant interactions with nonionic associative thickeners of the HEAT class. In the research done by Manion et al., the interactions between HEAT type thickeners and surfactants comprised of ethoxylated octyl phenols (Triton X series surfactants) was explored. As stated in Section 1.3, HEAT thickeners result in fluids with Newtonian rheology profiles however; in the presence of Triton X surfactants, these fluids show shear thinning, shear thickening, thixotropy, and antithixotropy behavior. This unusual rheology profile is due to interactions between surfactant molecules and HEAT polymer chains. The weak interaction between the two molecules leads to an initial shear thinning rheology as the interactions are easily disturbed at low shear rates. At increased shear rates, a second interaction occurs between thickener hydrophobes and surfactant hydrophobes and this interaction is driven by increased accessibility of the hydrophobic groups due to shear. These secondary interactions lead to thixotropy, as the intermolecular hydrophobic association is stable and maintains structure during decreasing shear rates (Manion, 2011).

3. Experimental Work and Results

3.1. Structure/Property Relationship

Because the use of nonionic associative thickeners in personal care applications is relatively new, there has been very little research done on the relationship between polymer structure and behavior in personal care type formulations. Depending on the personal care product, the desired thickening and emulsifying capabilities can change. Any changes on the polymer structure that result in changes of emulsifying and thickening efficiency must be fully explored. It is also important to examine the effects of oil polarity on the emulsifying and thickening capabilities of the polymer, since a wide range of oil phase products are used. This will allow minor changes in the polymer to be adjusted depending on the specific personal care application.

3.1.1. Partition Coefficient

Because the exact structures of the nonionic associative thickeners are a trade secret, they will instead be described as telechelic polymers with hydrophobic end caps which differ in shape and characteristic partition coefficient. The partition coefficient refers to the concentration ratio of a compound in two immiscible solvents. These solvents can be different phases such as water and air or two immiscible liquids. Most frequently, the partition coefficient, P , refers to the concentration ratio of a compound in water and octanol. In this particular case, the $\log(P)$ value is then a measurement of hydrophilicity and hydrophobicity. The equation that defines the $\log(P)$ value is described in Equation 3.1.

$$\log P_{oct/water} = \log \left(\frac{[solute]_{octanol}}{[solute]_{water}^{un-ionized}} \right) \quad \text{Equation 3.1}$$

It is important when calculating log(P) that the water used in “un-ionized”. This is due to the change in water structure under the presence of various ions leading to changes in solute solubility (“Hofmeister Series”). Using the equation in Figure 3.1, it can be determined that low log(P) values relate to more hydrophilic compounds, while high log(P) values relate to more hydrophobic compounds (Leo, 1971). The hydrophilicity of each of the NIAT polymers’ hydrophobe used in this study has been calculated as a reference for how water-soluble the polymers are. The polymers used in this study were all synthesized in the same manner and only differed in hydrophobic end groups. Unless otherwise noted, molecular weights and polydispersities are the same amongst the NIAT polymers used. The log(P) values are outlined in Table 3.1.

Table 3.1: Partition Coefficients of the NIATs

Thickener	log(P)
138	5.98
145	7.39
146	6.81
147	5.96
148	9.30
149	7.63

As shown in Table 3.1, the hydrophilicity of the polymers varies; 147 represents the most hydrophilic NIAT while 148 represents the most hydrophobic NIAT. Differences in the NIAT's performance based on $\log(P)$ values will be observed and analyzed.

3.1.2. Thickening Efficiency and $\log(P)$

The effects of the hydrophilicity, or $\log(P)$, on the thickening efficiency of a NIAT polymer were fully explored. Although literature states the effects of hydrophobe size and shape or hydrophilic segment size on viscosity, there has never been a direct link between a NIAT polymer's $\log(P)$ value and its thickening efficiency. The relationship was examined between $\log(P)$ and viscosity using NIAT polymers synthesized at Lubrizol Advanced Materials. The polymers were used at 2 wt% in water and allowed to dissolve into solution in a 54°C oven overnight. Polymer solutions were homogenized using an IKA Ultraturrax T25 homogenizer for 5 minutes at 11000 rpm. The solutions were left to equilibrate overnight. Viscosity was tested on an AR-1000 Rheometer at 25°C. Samples were equilibrated for 3 minutes and then measured on a continuous ramp from 1 to 1000 s^{-1} over the course of 5 minutes.

Figure 3.1: Rheogram for NIAT Polymers at 2 wt% in Water

The viscosity profile of the NIAT polymers in water changes as the $\log(P)$ value changes. For polymers with hydrophobes of a lower $\log(P)$ value (NIAT 147, 138, 146), the viscosity profile can be described as relatively Newtonian. However, as the $\log(P)$ value increases, the viscosity profile of the NIAT in water becomes more pseudo-plastic. To further examine the trend between thickening efficiency and $\log(P)$ value, viscosity readings were taken from 5 s^{-1} for the six polymers. Figure 3.2 displays the trend between $\log(P)$ and viscosity.

Figure 3.2: Viscosity (2 wt% NIAT in water) as a Function of log(P)

As shown in Figure 3.2, there is an increase in viscosity as log(P) increases. This means as the NIAT polymer becomes more hydrophobic, its thickening efficiency increases. This is in agreement with the work done by Barmar et al. and Glass and Kazmarski. Both research groups found an increase in thickening efficiency for polymers with larger hydrophobe groups or shorter hydrophilic segments.

3.1.3. Log(P) and Turbidity

Other than the varying viscosities between the NIAT polymers in water, clarity of the solutions was another noticeable difference. The difference in clarity for the polymers in water was measured using a HF Scientific Micro 100 Benchtop Turbidity Meter. NIAT polymer solutions were diluted to 1 wt% in water to increase clarity of the more turbid solutions. The results for the change in turbidity as a function of log(P) is shown in Figure 3.3.

Figure 3.3: Turbidity (1 wt% NIAT in water) as a Function of log(P)

Figure 3.3 shows a decrease in NIAT in water turbidity as the log(P) value of the NIAT polymer increases. Turbidity of a fluid usually represents the polymer structure in the fluid. To further examine the difference in aggregation shape and size of the NIAT polymers in solution, dynamic light scattering experiments were performed on a Zetasizer Nano Series Instrument. This instrument can measure the size of particles and molecules using NIBS technology and dynamic light scattering. As shown above in Figure 3.3, the turbidity of the NIAT in water solutions increases due to an increase in aggregate size. It is also shown that aggregate size increases as the hydrophilicity of the polymer increases. This supports the claims made by Elliot et al., that aggregation number decreased as hydrophobic moieties became bulkier. A decreased aggregation number would translate to a smaller aggregate size while an increase in hydrophobe size would translate to a higher log(P) value. These results are intuitive; as a polymer becomes more hydrophobic, it is going to be less stable in solution and therefore be more willing to

aggregate at lower concentrations. Less polymer hydrophobes in a single aggregate would cause the aggregates to be smaller. This would increase the clarity of the solution. Also, with smaller aggregates, the number of polymer chains in solution necessary to begin bridging florets would decrease as well. For this reason, higher viscosities are observed as NIAT polymers become more hydrophobic.

3.1.4. Log(P) and the Emulsification of Oil

In the personal care industry, a wide range of oils are used. This includes more polar vegetable and plant based oils such as olive and avocado oil, as well as highly non-polar oils like mineral oil. Also, many silicone oils like polydimethylsiloxane (dimethicone) are used in personal care products to increase lubrication and softness. Silicones are highly non-polar and often more difficult to emulsify than other oils (Kasprzak, 1994). Ergo, it is of value to look closely at the oil polarity effects on thickening and emulsifying efficiency of NIAT polymers. Because NIATs can be created with varying log(P) values and varying polarities, emulsion stability has been examined as a function of both oil polarity and log(p) of the NIAT polymer.

Emulsions were made using three different NIAT polymers made by Lubrizol Advanced Materials. NIAT polymers 138, 145, and 148 have log(P) values of 5.98 , 7.39, and 9.3 respectively. Oil (25 wt%) in water emulsions were made with vegetable oil, mineral oil, or dimethicone with the NIAT polymers (2 wt%). Interfacial tension values (IFT) between water and vegetable oil, mineral oil, and dimethicone were 18 mN/m, ~30 mN/m, >30 mN/m respectively. These interfacial tension values between the oil and water can be relate to the relative polarity of the oils; as the interfacial tension increases, oil polarity decreases. Emulsions were homogenized using an IKA Ultraturrax

T25 homogenizer for 5 minutes at 11,000 rpm. A 20 mL portion of each emulsion was placed in a plastic centrifuge tube. Emulsions were centrifuged for 1 hour at 3000 rpm. No separation was detected for any emulsion and the centrifuge tubes were placed in an oven at 60°C for 7 days. Emulsion stability, measured by percent volume of separation, was tabulated after 7 days in the oven is presented in Table 3.2.

Table 3.2: Emulsion Stability Measured by % Volume Separation After 7 Days at 60 °C

	Thickener/ Emulsifier		
Oil	138	145	148
Log(P)	5.98	7.39	9.3
Vegetable Oil			
IFT ~ 18 mN/m	0 %	0 %	2.5 %
Mineral Oil			
IFT ~ 30 mN/m	2.5 %	2.5 %	0 %
Dimethicone			
IFT > 30 mN/m	0 %	0 %	2.5 %

As shown in Table 3.2, a trend can be noticed between the log(P) value of the NIAT polymer and oil polarity for emulsion stability. Polymer 138, which has the lowest log(P) value and the highest hydrophilicity, has shown to have the highest stability in vegetable oil which is the most polar oil. Conversely, polymer 148, which has the highest log(P) value is shown to be best at stabilizing emulsions made with more nonpolar oils like mineral oil. It can also be noted that polymer 145, with a log(P) of 7.39, is still not hydrophobic enough to efficiently stabilize emulsions of the nonpolar mineral oil.

Finally, it can be concluded that hydrophilic NIAT polymers are better at emulsifying dimethicone in water than highly hydrophobic NIAT polymers. To further investigate this trend, the emulsions were centrifuged for 1 hour at 3000 rpm after removal from the oven.

Table 3.3: Emulsion Stability Measured by % Volume Separation After 7 Days at 60 °C and Centrifugation

	Thickener/ Emulsifier		
Oil	138	145	148
Log(P)	5.98	7.39	9.3
Vegetable Oil	0 %	5 %	2.5 %
Mineral Oil	2.5 %	10 %	5 %
Dimethicone	2.5 %	5 %	10 %

From Table 3.3, it can be pointed out that as log(P) increases, a NIAT polymer's ability to emulsify dimethicone in water decreases. However, the exact relationship between log(P) and emulsifying capabilities of the NIAT are somewhat unclear. As the log(P) value of a NIAT polymer decreases, its emulsion stabilizing efficiency increases when comparing NIAT-138 and NIAT 148. This is evident in the data, which shows polymer 138 with more stable emulsions, regardless of oil polarity. However, as log(P) increases from 5.98, emulsion stabilizing efficiency goes through a minimum at log(P) ~7. Emulsion stability begins to increase as log(P) increases beyond this value, however does not return to the efficiency of the more hydrophilic NIAT polymer. This could be due to the polymer associating with the water phase stronger at low log(P) values leading

to increased stability. At high $\log(P)$ values, the polymer associates stronger with the oil phase; however, since the oil phase is not continuous, it does not have as large an impact on the overall emulsion stability.

Another aspect to consider with emulsifying stability is hydrophobe shape. NIAT-138 has a linear shaped hydrophobe, NIAT-145 has a plate shaped hydrophobe, and NIAT-148 has a branched shaped hydrophobe. These different shaped hydrophobes will aggregate differently and perhaps the linear shaped hydrophobes can pack closer together than branched or plate shaped hydrophobes around oil droplets. This tighter packing between hydrophobes could allow NIAT-138 to align at the interface between water and oil droplets, thus providing better emulsion stability.

3.1.5. $\log(P)$ and the Thickening Efficiency of Various Oils

Because these associative polymers are going to be used as both thickeners and emulsifiers in personal care products, any effects of oil polarity on their thickening efficiency must be examined. For this study, the same 9 solutions studied in “Emulsion Stability” were examined. All nine solutions were tested on an AR-1000 Rheometer on a continuous ramp from 1 to 1000 s^{-1} in 5 minutes at 25°C. Viscosity measurements were used at 5 s^{-1} . Table 3.4 displays the resulting viscosity measurements as a function of thickener and oil type.

Table 3.4: Viscosity (mPa*s at 5 s⁻¹) as a Function of Oil Type and log(P)

	Thickener/ Emulsifier		
Oil	138	145	148
Log(P)	5.98	7.39	9.3
Vegetable Oil IFT ~ 18 mN/m	4,500	35,000	40,000
Mineral Oil IFT ~ 30 mN/m	4,700	30,000	30,000
Dimethicone IFT > 30 mN/m	5,000	40,000	50,000

The results in Table 3.4 allude to a possible connection between oil polarity and log(P) of the thickener used. For all three thickeners, an increase in viscosity was noticed for dimethicone, the oil with the lowest polarity (highest IFT value). On the other hand, for NIAT-138 and 148, the emulsion made with the most polar oil (vegetable oil) had the lowest viscosity measurements. This would appear to follow a trend: as oil polarity decreases, thickening efficiency of the NIAT polymers increases for emulsions. NIAT-145 does not follow this particular trend though so the specific relationship between log(P) of the NIAT polymer and polarity of the oil used in an emulsion cannot yet be determined.

3.1.6. Molecular Weight Effects on Viscosity

Although a fair amount of research has been done on thickening efficiency as a function of NIAT molecular weight, there are some contradicting results. As stated earlier, Kaczmariski and Glass found that increasing molecular weight of NIAT polymers

without proportionately increasing hydrophobe size led to an overall decrease in thickening efficiency (Kaczmariski, 1994). However, according to Elliot et al., viscosity increases of NIAT solutions are shown once aggregate size reaches 500 nm and above. This critical size can be reached at lower concentrations by either increasing hydrophobe branching or increasing the length of the poly(ethylene oxide) chain (Elliot, 2003). By increasing the poly(ethylene oxide) chain length, molecular weight would increase without increasing hydrophobe size which disagrees with Kaczmariski's claims. Therefore, it is imperative to determine the ultimate effects of increasing the molecular weight of a NIAT-type polymer without changing the hydrophobe shape and size.

To examine this, three NIAT type polymers were synthesized. All three contained identical terminal hydrophobe groups and varied in the length of the internal chains. The molecular weights increased from 33,000 g/mol to 52,000 g/mol. Each polymer was dissolved in deionized water at 1.82×10^{-5} mol/100 g water. Viscosity was measured using an AR-1000 Rheometer on a continuous ramp from 1 to 1000 s^{-1} in 5 minutes at 25°C. Figure 3.4 shows the resulting viscosities taken from 5 s^{-1} .

Figure 3.4: Effects of Molecular Weight on Thickening Efficiency and Average Aggregate Size

A sharp increase in viscosity is observed as the molecular weight of the NIAT type polymer increases. This appears to be in agreement with Elliot et al. and in order to confirm this, the aggregate size for each of the solutions was measured. From the aggregation size data, it can be concluded that as the molecular weight of the NIAT polymer increases, the aggregation size increases. This directly corresponds to an increase in viscosity. It is expected that as the length of the poly(ethylene oxide) chain increases, the size of the loops on the floret-shaped aggregates would increase. This would lead to a larger overall aggregate size, as reflected in the data. Larger aggregates would contribute to an increase in viscosity because increasing hydrodynamic volume of a polymer in a fluid increases fluid viscosity. Therefore it can be concluded that

increasing the molecular weight of the polymer without changing the hydrophobe shape and size leads to an overall increase in thickening efficiency due to larger aggregate size.

3.2. pH Tolerance of Nonionic Associative Thickeners

Because the NIAT-type polymers synthesized for this study are non-ionic, it is expected for them to be pH tolerant. This tolerance, if true, would make NIAT type polymers extremely advantageous as thickeners in personal care. Many of the actives used in personal care (i.e. lactic acid, salicylic acid) are acidic and therefore many formulations need to be made at slightly acidic pH values. A versatile thickener that does not lose its efficiency at low pH values is necessary.

To test the pH sensitivity of the NIAT-type polymers, simple water and oil emulsions were made at pH 2.5-5.5. A citric acid buffer solution was used to tailor the pH of the DI water in the emulsions. Vegetable oil (25 wt%) was emulsified with each of the buffered water solutions using an IKA Ultraturrax T25 homogenizer for 5 minutes at 11,000 rpm. Differences in the rheology profiles of the emulsions at different pH values was measured using an AR-1000 Rheometer on a continuous ramp from 1 to 1000 s⁻¹ in 5 minutes at 25°C. The rheogram for the various buffer solution emulsions is shown in Figure 3.5.

Figure 3.5: pH Effects on Viscosity

The pH of the emulsion does not change the rheology profile of a thickened emulsion using a NIAT type polymer. From these results, it can be determined that NIATs would allow personal care products to be formulated at a range of pH values and would not lose viscosity from the addition of various active ingredients.

3.3. Surfactant Interactions on NIATs

3.3.1. Anionic Surfactants

It is already known that anionic surfactants interact with associative thickeners both synergistically and antagonistically. At low enough concentrations, anionic surfactant molecules participate in associative polymer aggregates resulting in the formation of larger networks and increasing viscosities. However, at higher

concentrations, surfactant molecules solubilize associative polymer hydrophobes and completely destroy the network and thickening mechanism. What has not yet been widely researched is how the surfactant and associative polymer interaction changes in response to different shaped hydrophobes on the polymer. Different shaped hydrophobes will cause variations in aggregation number as well as aggregate size. Both of these qualities should affect how surfactant molecules interact with the associative polymer network and possibly change the CAC and the C_2 (see Figure 2.1) .

To examine this, three different shaped hydrophobes were chosen: linear (NIAT-146), plate (NIAT-145), and branched (NIAT-147). Each NIAT was dissolved in water at 1 wt%. Rheology data was collected as sodium lauryl sulfate concentration ranged from 0 wt% to 0.3 wt%. Note: CMC of SLS is 0.2 wt%. The effects of anionic surfactants on a plate shaped hydrophobically modified urethane are shown in Figure 3.6.

Figure 3.6: SLS Effects on NIAT-145 (1 wt%)

The first noticeable feature from Figure 3.6 is the dramatic decrease in viscosity at SLS concentrations greater than 0.05 wt%. From 0 – 0.05 wt%, the interaction between SLS and NIAT-145 appears to be synergistic, as shown by the increase in viscosity with increasing SLS concentration. The CAC for SLS and a NIAT with a plate shaped hydrophobe appears to be between 0 and 0.01 wt% since an increase in viscosity can be observed at 0.01 wt% at low shear rates. This pertains to the formation of mixed SLS/NIAT micelles and the increasing shift from loops to links. At a 0.1 wt% SLS level, the polymer network is completely destroyed. Not only does the distinctive shear thinning quality become Newtonian, but the viscosity is reduced more than 100-fold. This is most likely due to the solubilization of hydrophobes by SLS molecules and the destruction in NIAT aggregates. Therefore, the C_2 exists somewhere between 0.05 wt% and 0.1 wt% SLS. The effects of an anionic surfactant on a linear shaped hydrophobically modified nonionic polymer are in Figure 3.7.

Figure 3.7: SLS Effects on NIAT-146 (1 wt%)

When compared to NIAT-145 with a plate shaped hydrophobe, immediately it can be noticed that NIAT-146 in water has a very different viscosity profile. Unlike NIAT-145 which shows dramatic and immediate shear thinning, NIAT-146 shows the expected rheology profile including the Newtonian plateau, slight shear thickening, followed by shear thinning. This is expected from linear shaped hydrophobe NIAT polymers because they were the type used by Tam et al. to characterize the rheology profile. NIAT-146 is most likely aggregating in the proposed manner of florets linked together to form microgels and a network. As with NIAT-145, the CAC for SLS interacting with a linear shaped hydrophobe NIAT is between 0 and 0.01 wt%. This is shown by the increase in viscosity from 0 wt% SLS to 0.01 wt% SLS and represents the synergistic interaction between anionic surfactant molecules and NIAT aggregations. However, at 0.05 wt% SLS, the NIAT network is destroyed as represented by the Newtonian rheology profile at a decreased viscosity. Therefore the C_2 for NIAT-146 is somewhere between 0.01wt% and 0.05 wt% SLS. This is roughly half of the C_2 for NIAT-145 which alludes to different interaction mechanisms between plate shaped hydrophobes and linear hydrophobes on a NIAT polymer.

NIAT-147, which contains branched shaped hydrophobes, was the last associative thickener to be examined with SLS. The effects of SLS on this particular type of NIAT polymer is shown in Figure 3.8.

Figure 3.8: SLS Effects on NIAT-147 (1 wt%)

As shown in Figure 3.8, the neat polymer and water solution for NIAT-147 shows a vastly different rheology profile than NIAT-145 or NIAT-146. While both NIAT-146 and NIAT-145 show shear thinning due to the destruction of floret linkages at high shear rates, NIAT-147 shows a Newtonian rheogram. This could be due to the branched hydrophobes not participating in floret-floret linking at 1 wt% and therefore there is no larger network to break up. This would also explain the SLS effects. While both NIAT-146 and NIAT-145 saw >20 fold decrease in viscosity from high SLS additions, NIAT-147 showed <10 fold viscosity decrease. This would also be due to the fact that there is less of a NIAT structure and network for SLS to destroy. Like NIAT-146 and 145, the CAC for a branched shaped hydrophobe is somewhere between 0 and 0.01 wt% SLS. Also, the C_2 , or the point at which SLS starts negatively interacting with NIAT

aggregations, occurs somewhere between 0.01 and 0.05 wt% anionic surfactant. A summary of SLS effects on various NIAT polymers is displayed in Figure 3.8.

Figure 3.9: The Effect of SLS on Various NIATs

From Figure 3.9, the following generalizations can be made regarding ionic surfactants and nonionic associative thickeners:

- 1) For NIAT in water concentrations of 1 wt%, anionic surfactant interactions are synergistic between 0 and 0.01 wt%
- 2) At concentrations of anionic surfactant above 0.01 wt%, viscosity begins to decrease as the surfactant molecules begin to break apart NIAT associations
- 3) Thickening efficiency of NIAT-type polymers with plate shaped hydrophobes show higher tolerance for anionic surfactants than other shaped hydrophobes

3.3.2. Surfactant Blends

Although SLS is used in many home care applications, surfactant blends of anionic and zwitterionic surfactants are more common in cosmetic applications.

Cocoamidopropyl betaine (CAPB) and sodium laureth sulfate (SLES) is a common surfactant blend used for many cleansing applications such as body washes and face washes. As mentioned earlier, CAPB and SLES form unique structures in solution like rods and wormlike micelles. While SLS interactions with associative thickeners have been studied in depth by various groups, the interaction between CAPB/SLES and associative thickeners is relatively unknown. Therefore, it is necessary to explore this particular interaction so NIAT-type polymers may be used in cleansing applications.

The interaction between SLES/CAPB and NIAT was examined with two different polymers, NIAT-138 (linear shaped hydrophobe) and NIAT-148 (branch shaped hydrophobe). SLES/CAPB was used at a ratio of 3:1 in solution. Polymer concentration was held constant at 1 wt% in water, and total surfactant concentration varied from 0 to 15 wt%. These values were chosen based on typical surfactant concentrations in cleansing applications. All rheology measurements were taken on an AR-1000 Rheometer using a continuous ramp from 1 to 1000 s⁻¹ in 5 minutes at 25 °C. Surfactant concentrations 0 to 10 wt% showed no changes in polymer/water solution therefore surfactant concentration 10-15 wt% was examined closely.

The relationship between the viscosity profile of NIAT-138 (linear hydrophobe, low log(P) value) in water and SLES/CAPB is shown in Figure 3.10.

Figure 3.10: SLES/CAPB Effects on NIAT-138

Both NIAT-138 (at 1wt%) and SLES/CAPB (at 15wt%) have relatively Newtonian rheology profiles with low thickening efficiency. However, when the two are combined in a mixture, the resulting viscosity is approximately 1000 fold higher with shear thinning characteristics. This is directly related to the unique aggregations that the NIAT and surfactant blend make in solution. As Petekidis et al. described (see 2.4.1), SLES and CAPB blends form wormlike micelles in solution. When hydrophobically modified polymers interact with the wormlike micelles the structure in the solution is reinforced, as shown by the rapid and drastic increase in viscosity. This alludes to NIAT/surfactant interacting which could involve the bridging of wormlike micelles by NIAT chains or the participation of SLES and CAPB molecules in NIAT aggregations.

NIAT-148, which has a branched shaped hydrophobe and a high log(P) value, was also observed under the presence of SLES/CAPB surfactant blend. The results are outlined in Figure 3.11.

Figure 3.11: SLES/CAPB Effects on NIAT-148

Figure 3.11 shows a distinct difference in the interaction between SLES/CAPB with NIAT-148 compared to NIAT-138. Although NIAT-148 displays a shear thinning rheology profile, the addition of 0-12.5 wt% of SLES/CAPB causes the viscosity to drastically drop and become Newtonian. This relates to SLES/CAPB surfactant molecules destroying the aggregation structure of the NIAT molecules in solution. However, at 14 wt% SLES/CAPB, a new structure begins to form as shown by the rapid increase in viscosity and shear-thinning. This most likely is the concentration of surfactant at which the density of wormlike micelles in solution becomes high enough to allow NIAT assisted bridging between wormlike “strands”. It is important to note that at

surfactant concentrations of 15wt%, the original low shear rate viscosity of the neat NIAT in water solution is nearly matched. For the NIAT only solution, a drastic shear thinning is observed meaning the structure is relatively weak. However, at 14 wt% and 15 wt% SLES/CAPB and 1 wt% NIAT-148, shear thinning is less drastic meaning the new structure formed is stronger than that of NIAT alone. A graph comparing the effects of SLES/CAPB on 138 and 148 is shown in Figure 3.12.

Figure 3.12: The Effects of SLES/CAPB on the Viscosity of NIAT-138 and 148 Mixtures

It can be seen by Figure 3.11 that NIAT-148 and SLES/CAPB do not show as efficient thickening as NIAT-138 and SLES/CAPB. This could be largely due to the shape of the NIAT-148 hydrophobe; being branched and bulky, the hydrophobe does not easily fit the SLES/CAPB micellar structure which appears to be dominating in the mixture.

3.4. Salt Effects on Nonionic Associative Thickeners

If a new type of emulsifier and thickener is going to be introduced into personal care, it needs to solve the problems of the current products used. Salt sensitivity of thickeners, particularly ASE-types, is a main concern for formulators. Salt sensitivity of a formulation is important in skin care applications because the human skin naturally contains small amounts of salt. For cleansing applications, various types of salt are often added to finished formulations to promote small increases in viscosity, as salt and surfactants act synergistically as thickeners. For hair care applications, salt sensitivity of products is a concern because of the ion content in tap water. Depending on the region, different types of tap water contain different salts and the effects of tap water on a hair care product greatly determine the feel of the hair while it is wet. Although NIAT type polymers are not known to be salt sensitive, it is imperative to do appropriate testing to confirm the areas of personal care in which NIAT polymers can be utilized for thickening and emulsifying.

For each of the following tests, vegetable oil in water emulsions were made with 2.5 wt% NIAT polymer. The rheology profile and stability of the emulsions was tested at 0-10 wt% (0 - ~0.2 mol%) salt concentrations. Ammonium chloride and magnesium chloride were both provided by EMD Chemicals and are ACS Grade. Sodium chloride was provided by BHD Chemicals Ltd. and is ACS Grade. Rheology testing was done on an AR-1000 Rheometer using a continuous ramp from 1 to 1000 s^{-1} in 5 minutes at 25°C. Emulsion stability was tested under centrifugation for 30 minutes at 3000 rpm.

The effects of salt on the viscosity at 5 s^{-1} of a NIAT-138 thickened emulsion is displayed in Figure 3.13.

Figure 3.13: The Effects of Salt Concentration on Viscosity of an NIAT Emulsion

The effects of salt on NIAT emulsions, as shown in Figure 3.12, are relatively shocking. Being non-ionic in nature, it would be expected that various types of salt would have little to no effect on the thickening mechanism of a NIAT polymer. However, as shown in Figure 3.12, there is an obvious effect that appears to be salt type dependent. Under high levels of sodium chloride, ~0.175 mol% NaCl, a viscosity decrease of more than half is observed. Conversely, under moderate levels of magnesium chloride, ~0.10 mol% MgCl_2 , the viscosity of the NIAT emulsion is more than tripled. Finally, ammonium chloride appears to have the least effect on emulsion viscosity, causing only a small viscosity decrease at ~0.2 mol% NH_4Cl . To further investigate this, emulsion stability under various salt levels was observed.

The results of emulsion stability in the presence of salt after 30 minutes of centrifugation at 3000 rpm are listed in Table 3.5.

Table 3.5: Salt Effects on Emulsion Stability Measured By % Volume Separation

	Weight Percent of Salt					
Salt	0 %	2 %	4 %	6 %	8 %	10 %
NaCl	0 %	0 %	0 %	2.5 %	2.5 %	50 %
NH ₄ Cl	0 %	0 %	0 %	0 %	0 %	0 %
MgCl ₂	0 %	0 %	0 %	0 %	0 %	0 %

As shown in Table 3.5, once again the effects of salt on NIAT emulsions are dependent on salt type. Neither magnesium chloride nor ammonium chloride affect the stability of a biphasic system emulsified with a NIAT-type polymer. Sodium chloride, on the other hand, causes phase separation when used at weight percents above 6%. The change in emulsion stability alludes to a change in the interfacial tension between the oil and water phase due either to changes in surface tension or water polarity. To better understand the specific changes occurring under the addition of salt, surface tension measurements were collected from literature. According to measurements made by Jarvis et al., all three salts used in this study increase the surface tension of water. However, ammonium chloride has the least effect on increasing the surface tension of water, while magnesium chloride has the largest effect at increasing the surface tension of water (Jarvis, 1968). This trend does not coincide directly with the emulsion stability results since NaCl falls right in the middle for changing surface tension but is the only salt that causes drastic separation.

The changes in surface tension also directly correspond to the re-ordering of water molecules under the presence of salt. As the surface tension of water decreases, the water becomes less polar leading to less hydrophilic interactions. As the surface tension of the water increases, the water becomes more polar leading to more hydrophilic interactions. Because the NIAT polymers used are amphiphilic, any changes in the polarity of the water will directly affect the solubility and structure of the NIATs in water. To directly measure this relationship, the effects of salt on a NIAT viscosity in water was measured. The results are shown in Figure 3.14.

Figure 3.14: The Effects of Salt on Aqueous NIAT Fluid Viscosity

There appears to be a relationship between salt type, concentration, and the thickening efficiency of a NIAT polymer in pure water. All three salts cause an increase in thickening efficiency of the NIAT polymers in water with MgCl₂ having the largest impact. This is due to the re-ordering of water molecules in the presence of various salts.

Because the effects of salt on NIAT thickened solutions vary depending on the type of salt, it can be concluded that there is a relationship to the Hofmeister Effect. The Hofmeister Effect, as discovered by Franz Hofmeister in 1888, describes the ability of a salt to precipitate a protein out of water. For anions, the ability to “salt out” a protein is: $\text{SO}_4^{2-} > \text{HPO}_4^{2-} > \text{acetate} > \text{Cl}^- > \text{NO}_3^- > \text{Br}^- > \text{ClO}_3^- > \text{I}^- > \text{ClO}_4^- > \text{SCN}^-$. For cations, the ability to “salt out” a protein is as:

$\text{NH}_4^+ > \text{K}^+ > \text{Na}^+ > \text{Li}^+ > \text{Mg}^{2+} > \text{Ca}^{2+} > \text{guanidinium}$. As the series moves to the left, the structure of water becomes more disordered, hydrophobic aggregations are destabilized, and proteins are “salted out”. As the series moves to the right, the structure of water becomes more ordered, the solubility of hydrophobes decreases and therefore hydrophobic aggregations are stabilized and proteins are “salted in” (“Hofmeister Series”).

The effect of salt type on NIAT solutions is trickier than that of a regular protein however, because NIAT polymers contain both insoluble and soluble portions. When exposed to “salting in” salts like magnesium chloride, the hydrophilic portions of the polymer become more stable in solution and the hydrophobic portions of the polymer become less soluble in solution leading to aggregation stability and increasing viscosities (shown in Figure 3.13). However, in the presence of “salting out” salts such as ammonium chloride, the hydrophobic moieties become more soluble in solution leading to less stable hydrophobic aggregations while the hydrophilic regions are less solubilized in solution. This leads to decreasingly stable emulsions because the hydrophobe aggregations coating the oil droplets are less stable. It can be assumed by the results in Figure 3.12 that the salting out of hydrophobic moieties has a larger effect than the

salting out of hydrophilic moieties as shown by the very minor decreasing viscosity under high levels of ammonium chloride. Finally, in the presence of NaCl, which does not strongly stabilize either moiety on the NIAT polymer in water, an overall salting out effect is observed as shown by the decrease in emulsion stability and the decreasing viscosity in Figure 3.13.

Although the Hofmeister series could be used to defend the effects of salt on a NIAT thickened emulsion in which a hydrophobic and hydrophilic solvent are present, it leaves room for argument when an oil phase is absent. Although the Hofmeister series states that NH_4Cl should cause water to become more disordered and in turn destabilize hydrophobic aggregations, the data does not support this claim. Unlike the NIAT thickened oil-in-water emulsions, increasing viscosities are seen for all three salt types when NIAT is used in water only. It cannot be determined why an opposite effect on viscosity is observed between emulsions and neat NIAT in water solutions. This could be due to the integrity of the materials used, although all three salts were ACS Grade.

4. Conclusion

The personal care industry, which is constantly changing due to new consumer demands, is in need of a new type of rheology modifiers. If formulators want to develop a product at low pH, limit the number of ingredients by using multifunctional ones, or create thickened and stable emulsions under the presence of salt, there needs to be a new class of materials available to solve these problems. Nonionic associative thickeners show promise in solving every one of these issues.

Nonionic associative thickeners have shown superior thickening ability. Depending on the log(P) value of the polymer, the hydrophobe shape and size, and the length of the hydrophile, very specific rheologies can be created. This is largely due to changes in aggregate size which, in turn, affects the loop to link ratio of the NIAT structure in solution. This allows formulators the ability to develop different NIAT polymers to fit different applications, whether it be a hair gel, lotion, or cream. The rheology profile of a cosmetic product could be 100% tailor made.

Not only do NIAT polymers allow the construction of unique and diverse rheologies, but they show stability in areas other thickeners fall short. As it was shown in Section 3.2, nonionic associative thickeners are stable under a broad range of pH values. This would allow formulators to use NIATs to thicken cosmetic products containing acid based active ingredients.

Nonionic associative thickeners, besides providing rheology modification, have also shown to be excellent emulsifiers. The amphiphilic structure of NIAT, which resembles the amphiphilic nature of many surfactants and emulsifiers, allows them to disperse hydrophobic moieties in hydrophilic environments. These emulsions are stable,

even under the most harsh testing conditions and therefore completely eliminate the need for outside emulsifiers to be used. Although these nonionic polymers are referred to as thickeners, they are multifunctional ingredients that emulsify just as well.

It can also be assumed that nonionic associative thickeners can be utilized in a variety of applications such as hair care, skin care, and even cleansing applications. The synergistic thickening effect between the NIAT polymers and the common SLES/CAPB surfactant blend allow for a variety of body washes and soaps to be thickened with NIATs. This gives formulators the freedom of having a thickener that is compatible with a variety of other ingredients and can be used in multiple applications.

The only area in which the performance of nonionic associative thickeners is not completely understood is their interaction with salts. Because they are nonionic, it was expected that salts would have little to no effect on their performance as both thickeners and emulsifiers. It is perplexing that all three salt types increased the viscosity of aqueous NIAT solutions yet had varying effects on NIAT emulsions. Not only did NaCl decrease emulsion viscosity, but also emulsion stability. It can be pointed out that any negative effects of salt on NIAT solutions is still incomparable to salt effects on other common thickeners and emulsifiers. For example, ionic thickeners often observe a 50% decrease in viscosity under merely 2 wt% salt. The negative effects of salt on the NIATs was after 8-10 wt%, an amount that will rarely be encountered in personal care products. Also, the negative effects of NaCl on emulsion stability were still not as drastic as the effects of NaCl on commonly used emulsifiers which can show phase separation under 4 wt% NaCl. Although the NIATs did not perform as expected, they still outperform the other products on the market in terms of salt stability.

5. Future Work

As stated previously, NIATs have shown superior performance as multifunctional ingredients proving they are suited for personal care applications. Before their usage in personal care formulations, there are still a few aspects of their interactions that need to be understood. First, the effect salt has on the associations between NIAT polymers needs to be closely examined. Although all of the salts used were ACS grade, this is still not as pure as salt would be if present on the skin or in tap water. Therefore the use of pharmaceutical grade salt would produce more accurate results.

It would also be ideal to perform emulsion stability testing and viscosity testing with other salts from the Hofmeister series including salts that should strongly “salt in” and strongly “salt out” to observe any potential patterns. Dynamic light scattering experiments should also be performed on the aqueous NIAT solutions in the presence of salt to determine whether thickening/thinning is occurring due to changes in aggregation size. Finally, the ability for these polymers to form films will need to be looked at. Depending on the personal care application, film forming of a product can be desired or unwanted. Therefore, a series of drawdowns on various substrates will be necessary to confirm the effect these NIAT polymers have on the applied surface.

BIBLIOGRAPHY

- Alexandridis, Paschalis, and Bjorn Lindman. *Amphiphilic Block Copolymers: Self-assembly and Applications*. Amsterdam: Elsevier, 2000.
- Annable, Tom, Richard Buscall, Rammile Ettelaie, and Diane Whittlestone. "The Rheology of Solutions of Associating Polymers: Comparison of Experimental Behavior with Transient Network Theory." *Journal of Rheology* 37.4 (1993).
- Annable, Tom, Richard Buscall, Rammile Ettelaie, Philip Shepherd, and Diane Whittlestone. "Influence of Surfactants on the Rheology of Associating Polymers in Solution." *Langmuir* 10.4 (1994): 1060-070.
- Barmar, Mohammad, Mehdi Barikani, and Babak Kaffashi. "The Effect of Molecular Weight on the Behaviour of Step-Growth Hydrophobically Modified Ethoxylated Urethane (S-G HEUR) End-capped with Dodecyl Alcohol." *Iranian Polymer Journal* 13.3 (2004): 241-46.
- Barnes, Howard A., J. F. Hutton, and Kenneth Walters. *An Introduction to Rheology*. Amsterdam: Elsevier, 1989.
- Christov, N. C., N. D. Denkov, P. A. Kralchevsky, K. P. Ananthapadmanabhan, and A. Lips. "Synergistic Sphere-to-Rod Micelle Transition in Mixed Solutions of Sodium Dodecyl Sulfate and Cocoamidopropyl Betaine." *Langmuir* 20.3 (2004): 565-71.
- Dai, S., K. C. Tam, and R. D. Jenkins. "Binding Characteristics of Hydrophobic Ethoxylated Urethane (HEUR) and an Anionic Surfactant: Microcalorimetry and Laser Light Scattering Studies." *The Journal of Physical Chemistry B* 105.42 (2001): 10189-0196.

- Elliott, Peter T., Lin-lin Xing, Wylie H. Wetzel, and J. Edward Glass. "Influence of Terminal Hydrophobe Branching on the Aqueous Solution Behavior of Model Hydrophobically Modified Ethoxylated Urethane Associative Thickeners." *Macromolecules* 36.22 (2003): 8449-460.
- "Hofmeister Series." London South Bank University. Web. Apr. 2011.
<<http://www.lsbu.ac.uk/water/hofmeist.html>>.
- Holmberg, Krister, B. Jonsson, B. Kronberg, and B. Lindman. *Surfactants and Polymers in Aqueous Solution*. Chichester [u.a.: Wiley, 2007.
- Jarvis, Neldon L., and Milton A. Scheiman. "Surface Potentials of Aqueous Electrolyte Solutions." *The Journal of Physical Chemistry* 72.1 (1968): 74-78. Print.
- Kaczmariski, J. Philip, and J. Edward Glass. "Synthesis and Characterization of Step Growth Hydrophobically-Modified Ethoxylated Urethane Associative Thickeners." *Langmuir* 10.9 (1994): 3035-042.
- Karsheva, M., S. Georgieva, and S. Handijieva. "The Choice Of The Thickener - A Way To Improve the Cosmetics Sensory Properties." *Journal of the University of Chemical Technology and Metallurgy* 42.2 (2007).
- Kasprzak, Kenneth A. Silicone Containing Personal Care Products. Dow Corning Corporation, assignee. Patent 5,302,382. 12 Apr. 1994.
- Kim, Jong-Yun, Jun-Yeob Song, Eun-Joo Lee, and Seung-Kyu Park. "Rheological Properties and Microstructures of Carbopol Gel Network System." *Colloid & Polymer Science* 281.7 (2003): 614-23.
- Kirk, Raymond E., Donald F. Othmer, Martin Grayson, and David Eckroth. "Gums." *Encyclopedia of Chemical Technology*. New York: Wiley, 1978.

- Koleske, J. V. "Thickeners and Rheology Modifiers." *Paint and Coating Testing Manual: Fourteenth Edition of the Gardner-Sward Handbook*. Philadelphia, PA: ASTM, 1995. 268-83.
- Kostansek, Edward. "Associative Polymer/latex Dispersion Phase Diagrams II: HASE Thickeners." *Journal of Coatings Technology and Research* 2.6 (2005): 417-22.
- Laba, Dennis. *Rheological Properties of Cosmetics and Toiletries*. New York: M. Dekker, 1993.
- Leo, Albert, Corwin Hansch, and David Elkins. "Partition Coefficients and Their Uses." *Chemical Reviews* 71.6 (1971): 525-616.
- Maechling-Strasser, C. "Hydrophobically End-capped Poly (ethylene Oxide) Urethanes: 1. Characterization and Experimental Study of Their Association in Aqueous Solution." *Polymer* 33.3 (1992): 627-36.
- Manion, Sean J., Raymond H. Fernando, and Laura L. Johnson. "Shear-Thickening in Aqueous Surfactant-Associative Thickener Mixtures." *J. Coat. Technol. Res* 8.3 (2011): 299-309.
- Myers, Drew. *Surfactant Science and Technology*. Hoboken, NJ: J. Wiley, 2006. Print.
- Nagashima, Kazuomi, Vladimir Strashko, Peter M. Macdonald, Richard D. Jenkins, and David R. Bassett. "Diffusion of Model Hydrophobic Alkali-Swellable Emulsion Associative Thickeners." *Macromolecules* 33.25 (2000): 9329-339.
- Noble, Karl-Ludwig. "Waterborne Polyurethanes." *Progress in Organic Coatings* 32.4 (1997): 131-36.

- Paye, Marc, A. O. Barel, and Howard I. Maibach. "Rheological Additives and Stabilizers." *Handbook of Cosmetic Science and Technology*. New York: Taylor & Francis, 2006.
- Petekidis, G., L. A. Galloway, S. U. Egelhaaf, M. E. Cates, and W. C. K. Poon. "Mixtures of Colloids and Wormlike Micelles: Phase Behavior and Kinetics." *Langmuir* 18.11 (2002): 4248-257.
- Rosen, Meyer R. *Delivery System Handbook for Personal Care and Cosmetic Products*. Estados Unidos: William Andrew, 2005.
- Schulz, Donald N., and J. Edward Glass. *Polymers as Rheology Modifiers*. Washington, DC: American Chemical Society, 1991.
- Sun, Wenbin, Dejun Sun, Yunping Wei, Shangyin Liu, and Shuiyan Zhang. "Oil-in-water Emulsions Stabilized by Hydrophobically Modified Hydroxyethyl Cellulose: Adsorption and Thickening Effect." *Journal of Colloid and Interface Science* 311.1 (2007): 228-36.
- Tadros, Th F. *Colloids in Cosmetics and Personal Care*. Weinheim, Germany: Wiley-VCH, 2008.
- Tam, K. C., R. D. Jenkins, M. A. Winnik, and D. R. Bassett. "A Structural Model of Hydrophobically Modified Urethane–Ethoxylate (HEUR) Associative Polymers in Shear Flows." *Macromolecules* 31.13 (1998): 4149-159.
- Tanner, Roger I. *Engineering Rheology*. Oxford [Oxfordshire: Clarendon, 1985.
- Ten Brinke, G., and G. Hadziioannou. "Topological Constraints and Their Influence on the Properties of Synthetic Macromolecular Systems. 1. Cyclic Macromolecules." *Macromolecules* 20.3 (1987): 480-85.

- Vorobyova, Olga, and Mitchell A. Winnik. "Determination of Aggregation Numbers in Aqueous Solutions of Hydrophobically Modified Polymers by Fluorescent Probe Techniques." *Associative Polymers in Aqueous Media*. By J. E. Glass. Washington, DC: American Chemical Society, 2000.
- Yekta, Ahmad, Bai Xu, Jean Duhamel, Hendra Adiwidjaja, and Mitchell A. Winnik. "Fluorescence Studies of Associating Polymers in Water: Determination of the Chain End Aggregation Number and a Model for the Association Process." *Macromolecules* 28.4 (1995): 956-66. Print.
- Yekta, Ahmad, Vorobyova, Olga and Mitchell A. Winnik. "Fluorescent Probe Studies of the Association in an Aqueous Solution of a Hydrophobically Modified Poly(ethylene oxide)" *Macromolecules* 31.25 (1998): 8998-9007.
- Zhang, L. M. "Cellulosic Associative Thickeners." *Carbohydrate Polymers* 45.1 (2001).

PART B

1. Introduction

1.1. SOD Chemistry

Superoxide, $O_2^\bullet$, is a free radical produced by all organisms performing cellular respiration. It is biologically considered toxic due to its high reactivity and decomposition into hydroxyl radical and hydrogen peroxide, which are both toxic to organisms as well. Because almost all cells exposed to oxygen are in turn exposed to superoxide, each contains their own method of disposing of superoxide. Superoxide destroying enzymes are known as superoxide dismutase (SOD) (Dees, 2007; Muller, 2007).

Depending on the cell, there are different forms of the SOD enzyme. The four main types of SOD enzymes are copper/zinc SOD enzymes, iron SOD enzymes, manganese SOD enzymes, and nickel SOD enzymes. The copper/zinc SOD enzyme, which is utilized by eukaryotes, is a protein that binds to both copper and zinc. For this type of SOD enzyme, the ligands for the copper and zinc are an aspartate with six histidines (Tainer, 1983). The nickel SOD enzyme, which is the most recently discovered, is used in prokaryotic organisms. Research by Wuerges et al. has shown it possesses a unique gene sequence unlike any of the other SOD enzymes or protein however, Ni-SOD shows a similar catalytic rate to the other known SOD enzymes (Wuerges, 2004). Fe-SOD enzymes are a class of SOD scavenging proteins that are also used by prokaryotes as well as protists and within the mitochondria. The Fe-SOD is especially common in bacteria such as *E. coli* and in the plastids in plants.

The last important form of SOD enzymes is the Mn-SOD enzymes. Mn-SOD is found mainly in the mitochondria of plants and animals, the chloroplasts of plants, and facultative aerobes. Because of its similarity to FeSOD, many of MnSOD's functions are interchangeable with FeSOD(Beyer, 1989). The specific reaction by which manganese catalyzes superoxide dismutation is shown in Scheme 1.1.

Scheme 1.1: Catalysis of Superoxide Dismutation by Manganese

Mn-SOD participates in the oxidation of superoxide to produce oxygen. Then, the reduced Mn-SOD reacts with superoxide and hydrogen to produce hydrogen peroxide.

Although all of the different types of SOD enzymes are found naturally, they are often difficult to extract and use for medical purposes. Therefore, many synthetic SOD agents have been developed (Riley, 1994). For the purpose of this research, SOD chemistry and synthetic SOD enzymes pertaining to the manganese class will be the main focus. Of all the various SOD enzymes, manganese-SOD mimetics are shown to be the most active, particularly seven coordinate mimetics. These synthetic SOD enzymes consist of manganese(II) bound to a pentaazacyclopentadecane based ligand and two water molecules. The direct process by which these seven-coordinate Mn-SOD mimetics work is shown in Figure 1.1.

Figure 1.1: SOD Process of Seven Coordinate Manganese Mimetics (Dees, 2007)

There are two main pathways by which these mimetics function, the outer-sphere pathway and the inner-sphere pathway. The inner sphere process is pH independent and the rate determining step is the formation of a free coordination site in the axial position. The inner-sphere pathway works by binding the superoxide molecules to this axial coordination position. On the other hand, the outer sphere process is pH dependent and performs SOD chemistry using a proton-coupled electron transfer with the manganese as its rate determining step (Dees, 2007).

Although seven coordinate Mn-SOD mimetics are shown to be the most active, there are also four, five, and six coordinate Mn-SOD mimetics being created. This is mainly influenced by the natural Mn-SOD enzymes, which have been found as both five coordinate manganese and six coordinate manganese systems. Many of these mimetics have been made using tridentate nitrogen based ligands. These mimetics are commonly found having trigonal bipyramidal and pentagonal bipyramidal geometries for five and six coordinate respectively (Baffert, 2004). The five coordinate Mn-SOD mimetic that is used as a template for this research is commercially available and shown in Figure 1.2.

Figure 1.2: Eukarion-134 Mn-SOD Mimetic

The model ligand contains a phenolic/imine based structure. The goal of this research is to develop an active tridentate ligand for a Mn-SOD mimetic utilizing a similar phenolic/imine base. In order to do this, an appropriate and innovative Mn(II) ligand must be first synthesized and tested for activity. This research aims to not only produce a ligand for Mn(II) that will show SOD activity, but to also synthesize a ligand that can be grafted onto a polymer. This would allow for the creation of a reactive coating: a coating which, in the presence of manganese, can perform SOD chemistry. The proposed ligand set is shown in Figure 1.3.

Figure 1.3: The Proposed Ligand Set

The ligand in Figure 1.3, is tridentate and coordinates with manganese at the oxygen, nitrogen, and triazole nitrogen. The proposed SOD complex is shown in Figure 1.4.

Figure 1.4: The Proposed Manganese Complex

1.2. Click Chemistry

In order to synthesize the desired ligand to create an active manganese SOD enzyme, “click chemistry” is utilized. “Click chemistry”, which was started by Barry Sharpless in 2001, is a general term describing a chemical reaction in which the following conditions are met:

- Reaction is highly thermodynamically favorable (with driving forces greater than 20 kcal/mol)
- Reaction results in high yields
- Reaction does not result in or require harmful species (whether it be solvents, reactants, or reaction byproducts)
- Reaction requires relatively quick and simple purification techniques (particularly no chromatography required)
- Reaction results in stereospecific products
- Reaction has a highly selective product

Click chemistry is used for the formation of new carbon-heteroatom bonds such as cycloadditions of unsaturated species (i.e. Diels Alder reaction, the Huisgen 1,3-

dipolar cycloaddition), chemistry involving nucleophilic substitution, carbonyl chemistry (not involving aldol types), and addition to carbon-carbon double and triple bonds (Kolb, 2001). This research focuses solely on click chemistry and its applications involving the Azide-Alkyne cycloaddition.

The Azide-Alkyne cycloaddition, often referred to as *the* click reaction, involves the formation of a 1,3 or 1,4-triazole from an azide and an alkyne. The reaction sequence is shown in Scheme 2.1.

Scheme 2.1: Click Chemistry for the Formation of a Triazole

The 1,3-cycloaddition can result in two distinct products: the 1,4-triazole and the 1,5-triazole. In order to make the reaction more selective toward a specific product, the inclusion of a copper catalyst was added to the reaction. The copper-catalyzed azide-alkyne cycloaddition, unlike the cycloaddition without copper, reacts azides only at the terminal alkyne position. This results in the 1,4-triazole product exclusively. According to Sharpless et al., the mechanism by which the copper catalyst creates this product selectivity is shown in Scheme 2.2.

Scheme 2.2: Copper Catalyzed Click Reaction for 1,4-Triazole

The reaction begins with the alkyne species reacting with the copper catalyst to form a copper(I) acetylide (Product 1, Reaction A). Upon contact with the azide (Reaction B), the copper acetylide reacts through a stepwise sequence to form a six-membered ring intermediate. This intermediate (Product 3), which is favored by 12-15 kcal/mol to the direct route (Reaction C*), ultimately determines the 1,4-triazole (Product 5) selectivity of the reaction by forcing the alkyne to react at the terminal position (Rostovtsev, 2002).

The copper catalyst used in cycloaddition click reactions comes in a variety of forms. Copper(I) must be present in solution to act as a catalyst and this can be done by the addition of Cu(I) salts, Cu(0) with oxidizing agents, and Cu(II) with reducing agents. Examples of copper(I) salts include CuBr and CuI however these often require harmful co-solvents, a nitrogen base, and do not always result in high yields. Copper(0) has also

be used in conjunction with Cu(II) as an oxidizing agent however, once again, resulting yields are mediocre for a click reaction. The most successful copper catalyzed cycloadditions involve the generation of Cu(I) in situ from a Cu(II) species and a reducing agent. The most commonly used combination involves copper sulfate pentahydrate ($\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$) and sodium ascorbate as a reducing agent. Not only does this combination allow for the reaction to be done in water with small amounts of cosolvent, but it also results in yields of up to 100% (Meldal, 2008).

The majority of this research involved the click reaction between benzyl azide and a synthesized alkyne species. Although research on click chemistry claims the high success and yield rates for reactions, the specific electronics on the alkyne species led to a less favorable product. To drive the reaction forward, the appropriate reaction conditions were used from research done on other electronically instable click reactions.

In research done by Lakshman et al., click reactions were performed between alkynes and azides that were in equilibrium with a tetrazole species. In order to drive the reaction toward the tetrazole product and prevent the reaction from stopping due to tetrazole formation, various reaction conditions were tested. It was found the $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ with sodium ascorbate was the best copper catalyst, showing higher yield results than copper salts and copper (0). It was also found that the 1,4 triazole product was most stable and did not collapse into its tetrazole tautomer under solvent conditions of 1:1 dichloromethane and water. Much like the preliminary work done for this research, Lakshman et al. found that cosolvents with which water was miscible did not provide a nonpolar enough atmosphere to stabilize the desired product (Lakshman, 2010).

For this reason, a solvent blend of dichloromethane and water was used for the click reaction performed in this research.

2. Methods and Materials

All chemicals were received from Cal Poly Stockroom without any further purification. ^1H NMR was carried out on a Bruker 300 MHz NMR Spectrometer. GPC data was collected on an 1200 Series Agilent SECurity GPC System. Infrared Spectroscopy was performed on a Nicolet Nexus 470 FT-IR. Amine ligand library was prepared by Matt Mackenzie and Billy Grau.

2.1 Experimental Work

2.1.1. Preparation of Benzyl Azide (Compound 1)

To a 100 mL round bottom flask, benzyl bromide (6.00 g, 35.1 mmol) and sodium azide (2.74 g, 42.1 mmol) were dissolved in dimethyl formamide (DMF, 18.75 mL) and water (6.25 mL). A scoop of potassium carbonate was added to maintain a basic atmosphere. **WARNING:** Azide must only be added under basic conditions to avoid the formation of HN_3 , a toxic and explosive compound. The round bottom flask was left to stir overnight at room temperature. Benzyl azide was extracted from water and DMF using diethyl ether and brine was added to separate any emulsion layer. The diethyl ether was removed from benzyl azide via rotary evaporation to yield Compound 1. ^1H NMR: (ppm), 7.4 (5, q), 4.4 (2, s).

2.1.2. Preparation of Alkyne (Compound 2)

In a 25 mL round bottom flask, salicylaldehyde (15.6 mmol, 1.66 mL) and propargyl amine (15.6 mmol, 1.00 mL) were added to ethanol (25 mL). The flask was refluxed at 85 °C for 30 min in a hot oil bath. The round bottom flask was removed from heat and allowed to cool to room temperature. Sodium borohydride (15.6 mol, 0.59 g)

was added to the flask and left to stir 24 hours. Remaining sodium borohydride salts were removed using gravity filtration and ethanol was removed via rotary evaporation to yield Compound **2**. ^1H NMR: (ppm), 7.3 (1, s), 7.2 (1, t), 7.1 (1, d), 6.8 (1, q), 4.0 (2, s), 3.4 (2, s), 2.25 (1, s).

2.1.3. Preparation of Ligand Via Click Reaction (Compound **3**)

In a 500 mL Erlenmeyer flask, Compound **2** (8 mmol, 1.30g) and Compound **1** (8 mmol, 1.06 g) were dissolved in dichloromethane (140 mL) with a stir bar. Meanwhile, sodium ascorbate (8 mmol, 1.60 g) and copper sulfate pentahydrate (4 mmol, 1.00g) were dissolved in deionized water (140 mL). The aqueous mixture was then slowly added to the organic mixture with stirring. Mixture was left to react for 24 hours at room temperature with rapid stirring. Overnight, mixture changed from bright orange in color to olive green. Mixture was transferred to a 500 mL separatory funnel and left for 20 min to settle. The organic layer was then separated from the aqueous layer into an Erlenmeyer flask. The aqueous layer was back extracted with dichloromethane. The full organic layer was then washed with 1M aqueous EDTA (x6, 50 mL) to remove copper. Brine was added to each of the extractions to aid in the separation of the emulsion layer. The washed organic layer was then dried over magnesium sulfate, filtered via gravity filtration and rotary evaporated to remove solvent. Any remaining solvent was removed using high vacuum evaporation to yield Compound **3**. ^1H NMR: (ppm), 7.5-6.8 (11, b), 5.5 (2, s), 4.0-3.5 (4, b).

2.1.4. Preparation of 4-Vinyl Benzyl Azide (Compound **4**)

To a 500 mL round bottom flask, 4-vinyl benzyl chloride (0.0628 mol, 9.58 g), sodium azide (0.0785 mol, 5.10 g), DMF (200 mL), water (75 mL) and sodium carbonate (3 scoops for basic conditions) were added. **WARNING:** Azide must only be added

under basic conditions to avoid the formation of HN_3 , a toxic and explosive compound. The flask was left to stir at room temperature overnight. The mixture was then transferred to a 500 mL separatory funnel and the product was extracted from DMF and water using ether (50 mL, 10x). Rotary evaporation was then utilized to remove any trace solvent yielding Compound **4**. ^1H NMR: (ppm), 7.4 (2, d), 7.3 (2, d), 6.75 (1, d), 5.3 (1, d), 4.4 (2, s).

2.1.5. Preparation of t-Butyl Acrylate-4-Vinyl Benzyl Azide Copolymer (Polymer 1)

A 25 mL round bottom flask sealed with a septum and copper wire was used to purge t-butyl acrylate (121.52 mmol, 15.56 g), Compound **4** (3.76 mmol, 0.598 g), and tetrahydrofuran (THF, 10 mL) under nitrogen for 15 min. Meanwhile, azobisisobutyronitrile (1.25 mmol, 0.205) and a stir bar were added to a 100 mL Schlenk flask sealed with a septum and copper wire. The Schlenk flask was vacuum backfilled with nitrogen (x3). The THF solution was added to the Schlenk flask via a purged needle and the flask was lowered into a 60 °C oil bath and left to polymerize with stirring for 30 min. The polymerization was stopped by exposing the reaction to air and the viscous liquid was dissolved in THF (100 mL). The dissolved polymer was then precipitated into a 1000 mL mixture of 1:1 MeOH and ice. The majority of the ice and methanol was decanted off and the bright yellow polymer was left to dry in a 70 °C oven for 2 days yielding Polymer **1**. GPC: $M_n = 16,000$ g/mol. IR: 2100 cm^{-1} .

2.1.6. Formation of Ligand on Copolymer (Polymer 2)

In a 500 mL Erlenmeyer flask, Compound **2** (0.1 mmol, 0.0161g) and Polymer **1** (0.00313 mmol N_3 , 1.00 g) were dissolved dichloromethane (250 mL). Copper sulfate pentahydrate (1 mmol, 0.249 g) and sodium ascorbate (2 mmol, 0.396 g) were dissolved

in H₂O (2 mL). The water mixture was then added dropwise into the dichloromethane mixture and the flask was rapidly stirred for 24 hours at room temperature. The mixture was then rotary evaporated until solution volume was roughly 175 mL. The polymer solution was then precipitated into a 1750 mL solution of 1:1 ice and methanol. The majority of the ice and methanol was decanted off and the polymer solution was isolated and dried in the oven for 2 days at 70 °C yielding Polymer **2**. IR: Peak at 2100 cm⁻¹ missing.

3. Results/Discussion

The majority of this research focused on the development of a unique and novel tridentate ligand set for the formation of a six coordinate Mn-SOD mimetic. Click chemistry was utilized for the formation of the triazole group and as stated previously, click chemistry is known to produce thermodynamically favorable, high yielding, and selective reactions. A model ligand set is outlined in Figure 3.1 and was prepared to demonstrate proof of principle.

Figure 3.1: Model Amine Ligand

Click chemistry was used to produce the imine bond in high yields. Variations were made to the ligand by altering the R groups, followed by subsequent testing of the structure/function relationship. The activity of the model amine ligand group as a Mn-SOD enzyme was tested using the McCord-Fridovich Assay. Ligands were complexed with Manganese using the reaction outlined in Scheme 3.1.

Scheme 3.1: Formation of Manganese Complex

After the complex was synthesized, the McCord-Fridovich assay was used to confirm SOD activity. The McCord-Fridovich assay involves the addition of a

superoxide probe, which absorbs light at 550 nm under the presence of superoxide. From the McCord-Fridovich assay, IC₅₀ values, or the concentration of Mn-SOD mimetic at which 50% of the superoxide formation was inhibited, were calculated. Table 3.1 displays the data collected for the amine ligand library.

Table 3.1: IC₅₀ and Rate Values for Amine Ligand Library

R ₁	R ₂	IC ₅₀	k (M ⁻¹ s ⁻¹)
H	H	.45μM	7.5x10⁶
H	OCH ₃	1.1μM	3.1x10 ⁶
H	CH ₃	.80μM	4.5x10 ⁶
H	NO₂	.73μM	4.8x10⁶
H	Cl	.65μM	5.6x10 ⁶
Et ₂ N	H	5.2μM	7.0x10 ⁵

It is apparent in Table 3.1 that electron deficient R group ligands have lower IC₅₀ values and faster rates for inhibiting the formation of superoxide. This is shown by the R groups in bold, which showed low IC₅₀ values and large rate constant values.

The preliminary work done on the variety of amine based ligands provided the motivation for the synthesis of the target ligand (Polymer **2**) which was synthesized in this project. Not only does it contain the active amine group, but the R groups are hydrogens, which proved to be the most active in combination with an amine. The initial

stages of the research involved the synthesis of the Compound **3** by reacting Compound **1** with Compound **2** using click chemistry.

Scheme 3.2: Synthesis of Compound 1

Scheme 3.3: Synthesis of Compound 2

Compound **1** and **2** were reacted in a copper catalyzed click reaction to form the final 1,4-Triazole based Compound **3**. Scheme 3.2 outlines this reaction.

Scheme 3.4: Synthesis of Compound 3 Using Click Chemistry

The particular click reaction between the alkyne species and benzyl azide provided the ultimate challenge for this project. Unlike the majority of click reactions, which can be easily performed in aqueous and water miscible solvent blends, the target Mn-SOD ligand continued to collapse under similar conditions. However, once the solvent blend of water and dichloromethane with heavy stirring was implemented, the

reaction proceeded with ease. It can be assumed that the formation of the triazole depended on an organic environment for the stabilization of the product.

The target ligand of this paper was grafted onto a polystyrene copolymer once the appropriate reaction conditions were determined. In order to graft Compound **3** onto a polymer, azido-functionalized polystyrene was utilized in the click reaction. This was done by the synthesis and polymerization of Compound **4**, shown in Scheme 3.5 and 3.6.

Scheme 3.5: Synthesis of Compound 4

Scheme 3.6: Synthesis Polymer 1

Polymer **1** was then reacted with the alkyne species using the same click reaction conditions outlined in Scheme 3.4.

Scheme 3.7: Formation of Polymer 2

The reaction in Scheme 3.7 was confirmed using IR spectroscopy. Prior to performing the click reaction between the Polymer 1 and Compound 2, a large peak at 2100 cm^{-1} is present for the polymer's IR spectra due to the azide group. Therefore, after the completion of the click reaction between Polymer 1 and Compound 2, the disappearance of the 2100 cm^{-1} peak confirmed all of the azide groups were triazoles. Polymer 2, a polymer containing the ligand for the Mn-SOD mimetic, was produced in extremely low yields.

Later work complexed Compound 3 with manganese to form the Mn-SOD mimetic, Compound 5.

Scheme 3.8: Formation of Compound 5

The McCord-Fridovich assay performed on Compound **5** resulted in an IC₅₀ value of 0.301 μ M, which is lower than any of the other amine model ligands synthesized indicating that Compound **5** is a highly active Mn-SOD mimetic.

4. Conclusion

The goal of this research was to create a polymeric ligand which, when complexed with manganese, could perform superoxide dismutase. The polymeric enzyme could then lead to the formation of reactive coatings, which act as free radical scavengers. Click chemistry was chosen as a reaction route for the synthesis of the triazole species holding the ligand together and ultimately grafting it onto the polymer. Click chemistry was chosen for its reputation of thermodynamically favorable reactions leading to high yields. Once the appropriate reaction conditions were determined for the click reaction, the target Mn-SOD ligand was synthesized successfully and grafted onto a polymer. McCord-Fridovich assays showed high SOD activity for the target ligand set. Future work will need to be done to examine SOD activity changes observed for the ligand set grafted onto the polymer.

BIBLIOGRAPHY

- Baffert, Carole, Isabel Romero, Jacques Pécaut, Antoni Llobet, Alain Deronzier, and Marie-Noëlle Collomb. "Synthesis and Structural Characterization of Five-, Six-, and Seven-coordinate Mononuclear Manganese(II) Complexes with N-tridentate Ligands." *Inorganica Chimica Acta* 357.12 (2004): 3430-436.
- Beyer, Wayne F., Jacqueline A. Reynolds, and Irwin Fridovich. "Differences between the Manganese and the Iron-containing Superoxide Dismutases of Escherichia Coli Detected through Sedimentation Equilibrium, Hydrodynamic, and Spectroscopic Studies." *Biochemistry* 28.10 (1989): 4403-409.
- Dees, Anne, Achim Zahl, Ralph Puchta, Nico J. R. Van Eikema Hommes, Frank W. Heinemann, and Ivana Ivanović-Burmazović. "Water Exchange on Seven-Coordinate Mn(II) Complexes with Macrocyclic Pentadentate Ligands: Insight in the Mechanism of Mn(II) SOD Mimetics." *Inorganic Chemistry* 46.7 (2007): 2459-470.
- Kolb, Hartmuth C., M. G. Finn, and K. Barry Sharpless. "Click Chemistry: Diverse Chemical Function from a Few Good Reactions." *Angewandte Chemie International Edition* 40.11 (2001): 2004-021.
- Lakshman, Mahesh K., Manish K. Singh, Damon Parrish, Raghavan Balachandran, and Billy W. Day. "Azide–Tetrazole Equilibrium of C-6 Azidopurine Nucleosides and Their Ligation Reactions with Alkynes." *Journal of Organic Chemistry* 75.8 (2010): 2461-473.
- Meldal, Morten, and Christian Wenzel Tornøe. "Cu-Catalyzed Azide–Alkyne Cycloaddition." *Chemical Reviews* 108.8 (2008): 2952-3015.

- Muller, Florian L., Michael S. Lustgarten, Youngmok Jang, Arlan Richardson, and Holly Van Remmen. "Trends in Oxidative Aging Theories." *Free Radical Biology and Medicine* 43.4 (2007): 477-503.
- Riley, Dennis P., and Randy H. Weiss. "Manganese Macrocyclic Ligand Complexes as Mimics of Superoxide Dismutase." *Journal of the American Chemical Society* 116.1 (1994): 387-88.
- Rostovtsev, Vsevolod V., Luke G. Green, Valery V. Fokin, and K. Barry Sharpless. "A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective "Ligation" of Azides and Terminal Alkynes." *Angewandte Chemie International Edition* 41.14 (2002): 2596-599.
- Tainer, John A., Elizabeth D. Getzoff, Jane S. Richardson, and David C. Richardson. "Structure and Mechanism of Copper, Zinc Superoxide Dismutase." *Nature* 306.5940 (1983): 284-87.
- Wuerges, J. "Crystal Structure of Nickel-containing Superoxide Dismutase Reveals Another Type of Active Site." *Proceedings of the National Academy of Sciences* 101.23 (2004): 8569-574.