Abstract

Blackburn, Jennifer Lyn. Helical Polyguanidines: Influences and Consequences of a Biased Helix. (Under the direction of Bruce M. Novak)

We have been interested in polymers that adopt extended chain helical conformations. The polyguanidines are helical polymers that can be induced to form a biased helical sense by incorporation of enantiomerically pure chiral groups in the side chains of the polymer. We have shown that polyguanidines can show amplification in their optical properties compared to their chiral monomers, but this is not true in all cases. We have shown evidence of both cooperative and non-cooperative polyguanidine systems. We have shown that the inversion barrier of a copolymer is dependent upon the ratio of comonomers. Because the ratio of comonomers is something we have some control over, we can influence a polymer's inversion barrier to some extent.

For some applications external control of the helical conformation is desirable. This control is possible if, in addition to chiral groups, the side chains of the polymer contain switching elements such as azobenzene units. We have prepared several new carbodiimide monomers for the polymerization of polyguanidines. Among these are monomers bearing chiral substituents, azobenzene groups, or both. Initial studies of polyguanidines from these monomers proved difficult due to solubility problems. After
trying unsuccessfully to overcome these problems by annealing and protonating the polymers, we developed a new approach to molecular switching in helical polymers. We ran into significant problems in relation to the thermal stability of the isomeric forms of our switching element, azobenzene. We have determined that for future work towards molecular switching new switching elements that are not thermally sensitive should be explored.
Helical Polyguanidines: Influences and Consequences of a Biased Helix

by

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A dissertation submitted to the Graduate Faculty of North Carolina State University in partial fulfillment of the requirements for the Degree of Doctor of Philosophy

Department of Chemistry

Raleigh
2004

Approved By:

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Bruce M. Novak, Chairman    Daniel L. Feldheim

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Daniel L. Comins              T. Brent Gunnoe
Dedication

This work is dedicated to my parents, John and Pat, my sister Melissa, and to Rich.

Thank you for all of your love, support, and encouragement.
Biography

The author was born on February 6, 1974 in Georgetown, Kentucky. She has one sister, Melissa. Jennifer grew up in Georgetown and attended Georgetown College before transferring to the Georgia Institute of Technology as part of a dual degree program. She earned bachelors degrees in Engineering Arts and Chemical Engineering from Georgetown College and Georgia Tech respectively. In 1998 she began her graduate education at North Carolina State University under the direction of Bruce Novak. During the course of her graduate studies Jennifer developed an interest in patent law. She passed the patent bar exam in May of 2003 and became a registered patent agent. Upon completion of her PhD in chemistry Jennifer plans to attend Duke Law School and pursue a career as a Patent Attorney.
Acknowledgements

I would like to thank my parents, John and Pat, and my sister, Melissa, who have always provided support, encouragement, and advice. I could not have reached this point without such a wonderful family. I also thank the Latta family for their support.

I would like to thank my advisor Bruce Novak for guidance and financial support during my graduate studies. He provided excellent facilities and resources and created an outstanding environment in which to study chemistry. The current and past members of the Novak group have been a blessing, and I thank them all for their advice, encouragement and friendship.

Thanks also go out to Dr. Ed Bowden and Dr. Jerry Whitten. As Director of Graduate Studies, Dr. Bowden provided advice and helped with various administrative matters. Dr. Whitten serves as the faculty advisor to Phi Lambda Upsilon. His guidance during my terms as vice president and his support of the organization are appreciated.

Many people have kept things running smoothly both in and outside of the lab. These people include Eddie Barefoot, Leonard Page, Tony Radford, Jan Singhass, Glen Hennessee, Jeff Cable, Crissy Williams-Brown, and Teresa Henline.

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<th>Symbol</th>
<th>Definition</th>
<th>Symbol</th>
<th>Definition</th>
</tr>
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<tr>
<td>Å</td>
<td>angstrom(s)</td>
<td>ΔG°</td>
<td>Gibbs free energy</td>
</tr>
<tr>
<td>α</td>
<td>optical rotation</td>
<td>GPC</td>
<td>gel permeation chromatography</td>
</tr>
<tr>
<td>[α]</td>
<td>specific optical rotation</td>
<td>ΔH°</td>
<td>enthalpy</td>
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<tr>
<td>br</td>
<td>broad</td>
<td>Hz</td>
<td>hertz</td>
</tr>
<tr>
<td>c</td>
<td>concentration</td>
<td>IR</td>
<td>infrared</td>
</tr>
<tr>
<td>°C</td>
<td>degrees Celsius</td>
<td>K</td>
<td>degrees Kelvin</td>
</tr>
<tr>
<td>calcd</td>
<td>calculated</td>
<td>K_{eq}</td>
<td>equilibrium constant</td>
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<tr>
<td>CD</td>
<td>circular dichroism</td>
<td>l</td>
<td>path length</td>
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<tr>
<td>cm⁻¹</td>
<td>wavenumber</td>
<td>m</td>
<td>multiplet</td>
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<tr>
<td>d</td>
<td>doublet</td>
<td>µ</td>
<td>micro</td>
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<tr>
<td>δ</td>
<td>chemical shift</td>
<td>Me</td>
<td>methyl</td>
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<tr>
<td>D</td>
<td>sodium D-line, 589 nm</td>
<td>MHz</td>
<td>megahertz</td>
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<tr>
<td>dd</td>
<td>doublet of doublets</td>
<td>mmol</td>
<td>millimole</td>
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<tr>
<td>DMF</td>
<td>N,N-dimethylformamide</td>
<td>N</td>
<td>normality</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
<td>MW</td>
<td>molecular weight</td>
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<tr>
<td>ee</td>
<td>enantiomeric excess</td>
<td>nm</td>
<td>nanometer</td>
</tr>
<tr>
<td>eq</td>
<td>equivalent; equilibrium</td>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
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<tr>
<td>FAB</td>
<td>fast atom bombardment</td>
<td>q</td>
<td>quartet</td>
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<tr>
<td>FT</td>
<td>Fourier transform</td>
<td>R</td>
<td>rectus (right); ideal gas constant</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>rt</td>
<td>room temperature</td>
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<tr>
<td>s</td>
<td>singlet</td>
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<tr>
<td>S</td>
<td>sinister (left)</td>
<td></td>
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<tr>
<td>$\Delta S^\circ$</td>
<td>entropy</td>
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<tr>
<td>t</td>
<td>triplet</td>
<td></td>
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<tr>
<td>T</td>
<td>absolute temperature</td>
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<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
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<tr>
<td>UV</td>
<td>ultraviolet</td>
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Chapter 1: The Chirality of Helical Polymers

1.1 A Brief Overview of Chirality

Chirality is an important concept in many facets of life. An object is chiral if it is not superimposable on its mirror image. Hands are classic examples of chiral objects, thus chiral objects are often referred to as having handedness. Some other familiar chiral objects are scissors, screws, and spiral staircases. Chirality is also present at the atomic and microscopic levels where left- and right-handed chiral materials often have differing biological consequences. For example, the left- and right-handed forms of carvone have distinctly different smells, and while the right-handed form of dextromethorphan is a common ingredient in cough syrup, the left-handed form of that compound is a highly potent narcotic.

Chirality began to attract the attention of scientists in the 1800’s with the discovery of plane-polarized light in 1809 and the subsequent realization that certain substances could rotate the plane of polarization of that light. In 1848 Louis Pasteur isolated the left- and right-handed forms of tartaric acid and went on to propose a connection between dissymmetry and life:

I am inclined to think that life, as manifested to us, must be a function of the dissymmetry of the universe and of the consequences it produces.... Life is dominated by disymmetrical actions. I can even forsee that all living species are primordially, in their structure, in their external forms, functions of cosmic dissymmetry.
At the end of the nineteenth century Lord Kelvin defined chirality and chiral objects as we know them today:

I call any geometrical figure, or group of points, chiral, and say that it has chirality if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself.\(^9\)

The importance of chirality in current scientific research cannot be overstated. This is particularly true in the pharmaceutical industry where chirality can be the difference in whether a drug will affect a person in a positive way, a negative way or not at all.\(^3,4,10\) Of all drugs on the market, over 30% are optically active chiral materials and that number is increasing every year.\(^3,11,12\) The property of chirality is also becoming increasingly important in other areas such as the food and beverage industry, agricultural chemicals, and electronics chemicals.\(^11,13\)

1.1.1 Enantiomers

A chiral object or material and its mirror image are enantiomers,\(^14\) Figure 1.1.

![Figure 1.1: Enantiomers of a chiral alcohol.](image-url)
Enantiomers are equal in energy and have all of the same physical properties except the direction to which they rotate plane polarized light. One way to differentiate between two enantiomers is to observe the rotation of plane-polarized light. A chiral material is optically active, i.e. it will rotate the plane of polarization of plane-polarized light. The degree of rotation is called the optical rotation, $\alpha$, of the enantiomer. Optical rotation depends on the solvent, the wavelength and temperature at which the measurement is taken, the concentration of the compound, and the path length of the light as it traverses the sample. By converting to specific optical rotation $[\alpha]$ through Equation 1.1, where $\alpha$ and $[\alpha]$ are in degrees, $l$ is the path length in decimeters, and $c$ is the concentration in grams/100mL, two of these variables, concentration and path length, are eliminated. Solvent, temperature, and wavelength are usually reported along with specific optical rotation for chiral compounds.

Optical activity is a property unique to chiral materials; however, the absence of optical rotation does not prove that no chiral structure is present. Optical rotation will be to an equal extent for each enantiomer of a chiral compound, but in opposite directions. If a mixture contains an equal amount of each enantiomer that mixture is racemic and will have an optical rotation of zero. A mixture of enantiomers is generally characterized by referring to its enantiomeric excess, Equation 1.2, which is zero for a racemic mixture.

$$\% \text{ Enantiomeric Excess} = \frac{[R] - [S]}{[R] + [S]} \times 100$$

(1.2)
1.1.2 **Diastereomers**

Diastereomers are similar to enantiomers in that they are two or more compounds whose atoms are connected in the same order, but they are not superimposable. While enantiomers are mirror images of each other, diastereomers are not. For example, if a compound has two asymmetric centers, its enantiomeric mirror image will have corresponding asymmetric centers of opposite configuration. The diastereomer of that same compound will have one of the chiral centers of the same configuration and the other of opposite configuration, Figure 1.2.

![Figure 1.2: Enantiomers vs. diastereomers.](image)

Unlike enantiomers, diastereomers can have very different physical properties. In fact, one way to separate enantiomers is to convert them to diastereomers via chemical reaction, separate the diastereomers via solubility or polarity differences, and convert the diastereomers back to enantiomers. This method is called diastereomeric resolution. Diastereomers are also thermodynamically inequivalent. So at any given temperature one
diastereomer will be lowest in energy, and that diastereomeric conformation will be thermodynamically preferred.

1.2 Configurational vs. Conformational Chirality

There are two situations that may lead to chirality in a molecule. First the molecule may have an atom that is asymmetrically substituted. This leads to configurational chirality. For example, the chiral molecule (S)-(−)-2-butanol in Figure 1.1 on page 2 contains a carbon atom bearing four different substituents. This atom is, therefore, a chiral center, and the entire molecule is chiral. On the other hand, a molecule may be chiral by virtue of its geometry or conformation. Hexahelicene,\textsuperscript{17} Figure 1.3, is an example of a conformationally chiral molecule. Some conformationally chiral molecules are chiral simply due to restricted rotation about a bond. These molecules are called atropisomers, and 6,6'-dinitro-2,2'-diphenic acid\textsuperscript{18} is an example of this type of chiral molecule, Figure 1.4.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{hexahelicene.png}
\caption{Left- and right-handed forms of hexahelicene.}
\end{figure}
1.2.1 Configurational Chirality

Several factors affect the magnitude of the optical activity of a configurationally chiral molecule. These factors include the placement of the asymmetric atom within the molecule and the size of the substituents. Among a series of structural isomers the optical activity can change significantly depending on the placement of the chiral center.\textsuperscript{19,20} This is shown in Figure 1.5 for structural isomers of octanol. It is the relative sizes of the substituents that lead to this difference in optical activities. Substituents that are similar in size will lead to smaller observed optical activities while larger optical activities are seen.
for molecules with chiral centers having substituents which vary in size to a greater extent.

Although specific optical rotation can increase as the ratio of molecular weights of the substituents increases, this ratio must be varied by moving the chiral center rather than simply increasing the length of one of the substituents. The optical activities of a homologous series can actually decrease with increasing molecular weight, Figure 1.6. This is because optical activities depend on the local region of the asymmetric center. Consequently, chiral compounds having asymmetrically substituted atoms whose substituents are very long chains may show zero specific optical rotations although they are chiral. This phenomena is due to the manner in which optical activities are measured. Specific optical rotation is inversely proportional to the weight percent of the compound in solution. So, as molecular weight increases the specific optical rotation $[\alpha]$ may decrease, Figure 1.6.

![Chemical structure of a chiral compound](image)

<table>
<thead>
<tr>
<th>$n$</th>
<th>3</th>
<th>7</th>
<th>11</th>
<th>14</th>
</tr>
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<tbody>
<tr>
<td>$[\alpha]^{20}_D$ (neat)</td>
<td>8.13°</td>
<td>6.25°</td>
<td>5.53°</td>
<td>4.77°</td>
</tr>
</tbody>
</table>

**Figure 1.6:** Specific optical rotations for selected members of a homologous series.

### 1.2.2 Conformational Chirality

The topics just discussed, placement of the chiral center, local region of the asymmetric atom, and molecular weight effects, apply only to configurationally chiral...
compounds. In a conformationally chiral compound there may be no chiral center because it is not necessary that there be an asymmetrically substituted atom. Thus placement and local region of the chiral center are incongruous with the concept of conformational chirality. Due to the nature of the chiral structure a conformationally asymmetric compound can have an optical activity that is much greater than a configurationally chiral compound, Figure 1.7.

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} \\
\text{HO} & \quad \text{HO}
\end{align*}
\]

(S)-(+)-2-Butanol \hspace{1cm} [\alpha]^{20}_D + 13^o \ (\text{neat})

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} \\
\text{HO} & \quad \text{HO}
\end{align*}
\]

(+)-Hexahelicene \hspace{1cm} [\alpha]^{25}_D + 3707^o \ (c \ 0.08, \ CHCl_3)

**Figure 1.7:** Comparison of the specific optical rotations of a configurationally chiral molecule and a conformationally chiral molecule.\textsuperscript{15,17}

In addition to the larger optical activities attainable by conformationally chiral compounds there is a more fundamental difference in the two types of chirality that is quite significant. The conformation of a molecule is dynamic. It can be affected by such influences as light, heat, and pH.\textsuperscript{23,24} So, the asymmetry of a conformationally chiral compound can often be manipulated by convenient means. On the other hand, the asymmetry of a configurationally chiral molecule can only be manipulated or destroyed by chemically breaking bonds within the molecule.
1.3 Helical Polymers

Macromolecules can adopt many different conformations some of which are asymmetric.\textsuperscript{23,25} We have been studying chiral helical polymers. A helix is the path traversed by combined translation and rotation about a line and is a conformationally chiral structure. Macromolecules having a purely one-handed helical sense can have many potentially advantageous properties including improved thermal stability in the solid state,\textsuperscript{26} rod vs. random coil conformations in solution,\textsuperscript{27} and uniform vs. aggregated adsorption on surfaces. One-handed helical polymers can form cholesteric liquid crystalline phases, while nematic phases are formed by the analogous racemic polymers.\textsuperscript{28} Helical polymers have applications as optical devices and biomimetic polymers. Their chirality can be exploited in chiral separations\textsuperscript{29} and as asymmetric catalysts. Helical polymers can be used in high strength materials and as recyclable polymers.

Naturally occurring helical polymers usually form single handed helical chains. Many synthetic helical polymers, however, have chains that are made up of alternating regions of left- and right-handed helical segments separated by helix reversals.\textsuperscript{30} This can be explained using simple thermodynamics. Left- and right-handed helices are enantiomers, Figure 1.8, which are necessarily equal in energy. Consequently, there is no thermodynamic preference for either helical sense. So, in the absence of an additional chiral influence a helical polymer chain will exist as a racemic mixture of left- and right-handed helices. This is unfortunate because the advantageous properties of helical
polymers mentioned previously apply to single-handed or at least biased helices. Also, the applications cited require a polymer having at least a biased helical sense.

A biased or single-handed helix can be created if the left- and right-handed helical senses can be rendered unequal in energy. If enantiomerically pure chiral monomers are used to synthesize a helical polymer the polymer will have side chains containing asymmetric centers. Consequently, the left- and right-handed helical senses of that polymer will be diastereomers, and one helical sense will be thermodynamically preferred, Figure 1.9. As a result, the polymer will be biased towards that helical sense.

**Figure 1.8:** Enantiomeric right- and left-handed helices.

**Figure 1.9:** Energy diagrams for enantiomeric and diastereomeric helices.
1.3.1 Amplification

The inherent chirality of a helical polymer is interesting due in part to the property of amplification. The differences in configurational and conformational chirality have been discussed. An excellent example of the differences in the optical activities of these two types of chiral compounds arises from the polymerization of a monomer that is configurationally chiral into a conformationally chiral helical polymer, Scheme 1.1. The chiral monomer in this example has a specific optical rotation of only $-0.04^\circ$ (neat). The conformationally chiral helical polymer has a much larger specific optical rotation of $+302^\circ$ (hexane). The increase in $[\alpha]$ is called amplification due to the dramatic increase in the observed optical properties upon polymerization.

**Scheme 1.1: Polymerization of a helical polymer from a chiral monomer.**

1.3.2 Cooperativity

Chiral monomers can be both expensive and time consuming to prepare. Fortunately, many helical polymers show cooperativity, which refers to interactions between monomer units that allow a single chiral perturbation in the polymer to influence
the regional conformation of that polymer, Figure 1.10. The length scale over which the interactions occur determines the degree of cooperativity of the polymer. Cooperativity of various polymers has been probed using chiral end groups, molecular chaperones, non-racemic mixtures of enantiomers (majority rules), and combinations of chiral and achiral comonomers. Polymers having a high degree of cooperativity can form nearly single handed helical structures with very few chiral perturbations.

**Figure 1.10:** Cooperativity in copolymers.
One way to determine the level of cooperativity of a polymer system is through polarimetry measurements. A cooperative polymer system will show an increase in specific optical rotation disproportionate to the number of chiral perturbants present, e.g. chiral monomers in a copolymer, Figure 1.11. Eventually the specific optical rotation will reach a plateau value where additional chiral perturbations have no further effect. This plateau value corresponds to the specific optical rotation of a single-handed helix. A non-cooperative system will have an optical rotation that changes linearly with concentration of chiral perturbant.

**Figure 1.11:** Comparison of specific optical rotation trends for a cooperative polymer and a non-cooperative polymer.
1.3.3 Helix Reversals and Inversion Barrier

Areas separating left- and right-handed helical segments are referred to as helix reversals. These reversals are at a higher energy than either the right- or left-handed helical regions, so lower temperature favors fewer reversals. This is apparent from polarimetry measurements of biased helices at various temperatures. There are fewer helix reversals at lower temperatures, so at lower temperatures higher rotations are observed. Helix reversals can be removed from a polymer chain by movement to the chain end or by cancellation through combination with a neighboring reversal, Figure 1.12. Conversely, new reversals can form in the reverse manner.

Figure 1.12: Dynamic interconversion of helix reversals.

Helix reversals are in constant motion along the polymer backbone and are constantly being created and destroyed. Evidence for this lies in the racemization of a
helical polymer formed by a chiral catalyst. Immediately upon polymerization with the chiral catalyst the polymer exists as a single-handed helix. Over time, however, helix reversals form, and the polymer backbone racemizes into left- and right-handed regions, Scheme 1.2. The kinetics of this racemization can reveal the helix inversion barrier.

**Scheme 1.2: Polymerization by a chiral catalyst and subsequent racemization.**

The inversion barrier is the activation energy required to switch between a left- and right-handed helix. This barrier depends on several factors including the size and steric nature of the side chains and the inherent stiffness of the polymer backbone. A polymer with a high inversion barrier will racemize slowly, while a lower inversion barrier leads to faster racemization.
1.4 Synthetic Helical Polymers

Several synthetic polymer systems including polysilanes,(polyacetylenes, poly[(triarylmethyl) methacrylates], polyaldehydes, polyisocyanides, polyisocyanates, and polyguanidines are known to display a helical conformation in solution as well as in the solid state. Polyisocyanides, polyisocyanates, and polyguanidines will be discussed. The current research deals with polyguanidines, however both polyisocyanides and polyisocyanates are of particular interest and relevance to the current work.

1.4.1 Polyisocyanides

Polyisocyanides, Figure 1.13, were first synthesized via catalytic synthetic procedure and characterized by Millich and Sinclair in 1965. The polymerization of an optically active monomer gave a polymer that showed an optical rotation much larger than that of the monomer suggesting a regular configuration for polyisocyanides. Since then studies have proven that the regular configuration of polyisocyanides is a helix.

Molecular orbital calculations have shown that the helix arises in polyisocyanides due to nitrogen lone pair repulsion. The repulsions favor a departure from planarity of
the carbon backbone. This is similar to the lone pair repulsions in polyketones, which are isoelectronic to polyisocyanides and also have a helical conformation. Hindered rotation in the carbon main chains also contributes to the helical conformation of polyisocyanides. The angle of rotation out of planarity can be influenced by the R-group, Figure 1.13. Small R groups, for example R=H, allow a broader range of angles, but as the steric bulk of that group grows that range of angles narrows quickly to an angle indicative of a 4-fold helix.

Studies have shown that the 4/1 helix formed by polyisocyanides, i.e. four monomer units are required for one turn of the helix, has a pitch of 4 Å. Chiral groups in the side chains of the polymers can influence the handedness of this helix. As seen by Millich and co-workers polymerizing an optically active monomer can yield a polymer whose optical properties are amplified. The preference for one helical sense imposed by the chiral side chains is related to the placement of the side chains in comparison to the polymer backbone. This preference is smaller when the chiral group is further from the polymer backbone.

The rigid backbones of helical polyisocyanides give the polymers high inversion barriers. Consequently, once the polymer is formed the ratio of left- and right-handed helices does not change appreciably. This is apparent in the polymerization of poly(tert-butyl isocyanide) with a chiral catalyst. The equilibrium conformation of this polymer is a racemic mixture of right- and left-handed helices; however, the biased helix formed during the asymmetric polymerization does not racemize, Scheme 1.3. In addition to
**Scheme 1.3:** Stable helix formed by polyisocyanides.

having high inversion barriers these polymers have short persistence lengths. The persistence length of a polymer is the distance traversed along the polymer backbone until the backbone changes direction by 90°. Polyisocyanides have persistence lengths of around 30 Å. Consequently, even low molecular weight polymer chains assume wormlike conformations in solution.

**1.4.2 Polyisocyanates**

In the early 1960's it was assumed that polyisocyanates, Figure 1.14, form a helical conformation both in the solid state and in solution. In 1969 that assumption was confirmed. Goodman and Chen reported the first synthesis of an optically active polyisocyanate one year later. The polymer they synthesized showed an optical rotation

**Figure 1.14:** A polyisocyanate.
of increased magnitude and of the opposite sign as their chiral monomer indicating that the polymer assumes a preferred conformation. The first living polymerization to form a polyisocyanate with an organotitanium (IV) catalyst was reported in 1991.53

A combination of electronic and steric effects is responsible for the helical conformation of polyisocyanates, which is that of an 8/3 helix.52 Unlike the polyisocyanides, the polyisocyanates have long persistence lengths ranging from 200 Å to 600 Å depending upon the side chains and solvent.54,55 These long persistence lengths make polyisocyanates of modest molecular weight stiff-chain, rod-like polymers in solution; however, at high molecular weights a more worm-like behavior results. The helix reversals between the left- and right-handed helical segments have been shown to contribute to the worm like behavior of high molecular weight polyisocyanates.56 Consequently, an optically active polymer with a preferred helical conformation and few helix reversals can form a more extended chain than its more wormlike racemic analog.

The helical conformation of a polyisocyanate is very sensitive to chirality in the side chain. This is evidenced by the large helical bias in a polyguanidine whose only chiral center is a consequence of deuterium substitution,57 Figure 1.15. Despite the favorable response of polyisocyanates to chiral perturbants, chiral induction through the use of chiral catalysts has been unsuccessful due to the low inversion barriers of the polyisocyanates. In addition to their difference in persistence lengths polyisocyanides and polyisocyanates have different inversion barriers. A low inversion barrier leads to rapid
Figure 1.15: Specific optical rotation of a polyisocyanate with side chain chirality.

racemization of the helical senses, so achiral isocyanates polymerized with a chiral catalyst will have a specific rotation of zero.\textsuperscript{58}

The cooperativity of polyisocyanates is well known.\textsuperscript{31,36,37,59} As little as 1.2 mole percent of a chiral comonomer can influence these highly cooperative polymers to form a nearly single-handed helix.\textsuperscript{36} When two comonomers are enantiomers, only a slight enantiomeric excess is required to create helical bias.\textsuperscript{35,60} Cooperativity is dependent upon the nature and placement of the chiral center in relation to the polymer backbone. As a result, if a chiral center in the side chain of a polyisocyanate is attached to an isomerizable functional group, such as an azobenzene group, the reversible isomerization of that group can have a direct effect on the helicity of the polymer backbone, and polyisocyanates may be suitable for molecular switching applications.\textsuperscript{59,61}
1.4.3 Polyguanidines

A third class of polymers known to form a helical structure is the polyguanidines, Figure 1.16. Polyguanidines, also called polycarbodiimides, were first reported by Robinson in 1964. Early routes to polyguanidines depended on anionic techniques to polymerize a carbodiimide monomer. These anionic systems gave no control over the polymerizations and yielded only low molecular weight polymers. In 1994 Goodwin reported the living polymerization of carbodiimide monomers using titanium (IV) catalysts. These new living systems enabled the synthesis of polyguanidines having uniform chain ends, precisely controlled molecular weights, and narrow molecular weight distributions.

The structure of a polyguanidine can be thought of as a hybrid of a polyisocyanide and a polyisocyanate. Due to the similarities among the three structures it is not surprising that the polyguanidines also form extended-chain helical conformations. Polyguanidines assume a 6/1 helix both in solution and in the solid state. Polyguanidines have long persistence lengths similar to the polyisocyanates, however their high inversion barriers resemble those of the polyisocyanides.
Like the previously discussed polymers, polyguanidines can be influenced to form biased helical senses through chiral groups in their side chains.\textsuperscript{34,64} Chiral catalysts have also been successfully used to induce a biased helical sense in the polyguanidines.\textsuperscript{65} Unlike the polyisocyanates which racemize quickly, the stability of the polyguanidine helix formed is highly dependent upon the side chains of the polymer. In many cases a slow racemization is observed; however, bulky side chains can lead to a stable biased helical conformation even when those side chains are achiral.\textsuperscript{65}

The cooperativity of polyguanidines has been shown through both majority rules experiments and molecular chaperoning.\textsuperscript{34,38} In the molecular chaperone experiment when a chiral acid was added to a solution of a racemic polyguanidine a biased helix was induced. The extent of bias in that helix was dependent upon the ratio of chiral acid to monomer repeat unit. This relationship was non-linear suggesting cooperativity among the monomer units in the polymer backbone. This experiment showed that the helical conformation of a polyguanidine can be manipulated by an external influence. This molecular chaperone effect piqued our interest and led to the current goals in our ongoing studies of polyguanidines.

Knowing that the polyguanidines can form preferred helical structures and having investigated some of the structure property relationships among both preferred helical and unbiased helical polyguanidines, the next step is to study ways in which the preferred helical sense can be influenced. We are interested in studying the reversible manipulation of the helical sense of polyguanidines.
1.5 References and Notes


15 Loudon, G. M. *Organic Chemistry*; Addison-Wesley: Reading, MA, 1983.


Chapter 2: Towards Photoswitchable Polymers

2.1 Introduction

A helical polymer can form a biased helix if chiral centers are present in the side chains of that polymer. Furthermore, due to the cooperativity observed in many helical macromolecules, a copolymer with only a small amount of chiral monomer can form a one-handed helix.\textsuperscript{1,2} A helical polymer is a conformationally chiral molecule with the left- and right-handed helical senses in a dynamic equilibrium. Because the conformation of a molecule can be affected by external influences, the equilibrium between the two helical senses can be manipulated by those influences as well.\textsuperscript{3,4} Helical polymers may find applications in molecular switching if they can be reversibly switched between left- and right-handed helical senses in response to an external stimulus.

2.1.1 Motivations for Adding Azobenzene Side Chains

Our current research is focused on reversibly manipulating the biased helical sense of a polyguanidine and doing so without altering the physical composition of the polymer. Common tools for influencing the conformation of a molecule include light and heat. Often a combination of these two stimuli can affect the reversible geometric isomerization of a functional group in a molecule causing a change in that molecule’s optical and spectroscopic properties.

The influence of a chiral side chain on the helical sense of a polymer is strongly dependent upon the amount of interaction between the chiral group and the polymer.
backbone. A weak interaction can lead to a nearly racemic mixture of helices, while a strong interaction can give a nearly one-handed helix.\textsuperscript{4} The level of interaction is related to the placement of the chiral group in relation to the polymer backbone.\textsuperscript{5} The size of the chiral group is also important in that a larger chiral center often leads to a more pure helix with a higher specific optical rotation. Smaller chiral centers often reduce the thermal stability of the biased helix.\textsuperscript{6} These points are illustrated by several polyisocyanates where the size and placement of the chiral group is varied, Figure 2.1 and Figure 2.2.

\[
\begin{array}{c}
\text{Figure 2.1:} \quad \text{Effect of the placement of a chiral center on the magnitude of the specific optical rotation of a polymer (measured in } n\text{-hexane).}\textsuperscript{5}
\end{array}
\]

In studying molecular switching in the polyguanidines, we do not want to change the physical composition of the polymer so we must attempt to control and manipulate the spatial orientation of the chiral group. One way to do this is to add a photoisomerizable “switching” group to the side chains of the polymer.\textsuperscript{3} The switching group we have chosen is an azobenzene, which undergoes \textit{cis} → \textit{trans} photoisomerization, then relaxes back to \textit{cis} in a thermally controlled back isomerization,\textsuperscript{7} Figure 2.3. This isomerization can be followed by UV spectroscopy by
Figure 2.2: Effect of the size of a chiral center on the magnitude of the specific optical rotation of a polymer. Variation of the specific optical rotation with temperature (measured in chloroform).

\[
\begin{array}{c|c|c}
\alpha_D^{10} & -450^\circ & -498^\circ \\
\alpha_D^{25} & -367^\circ & -485^\circ \\
\alpha_D^{47} & -258^\circ & -480^\circ \\
\end{array}
\]

watching $\lambda_{\text{max}}$ for the $\pi \rightarrow \pi^*$ transition of the trans form decrease while $\lambda_{\text{max}}$ for the $n \rightarrow \pi^*$ transition of the cis form increases. The values of $\lambda_{\text{max}}$ for each conformation depend on the substitution of the aromatic rings,$^8,^9$ so they will be different for different polymers.

Figure 2.3: Isomerization of an azobenzene group.
2.1.2 Related Work

In related research Muller and Zentel have shown that the helical sense of copolyisocyanates can be manipulated through the isomerization of chiral azobenzene units in the side chains of one of the comonomers.\textsuperscript{3,4} In their studies they exploited the cooperativity of the polyisocyanates by using only small amounts of chiral comonomer in the copolymers. Those chiral comonomers also contained azobenzene functional groups. The optical properties of the copolymers were studied before and after isomerization of the azobenzene group. In some cases a change in the specific optical rotation of the polymer was observed after that isomerization,\textsuperscript{4} Figure 2.4.

![Chemical structure diagram](image.png)

\[ R^* = \text{CH}_2\text{CH(CH}_3\text{)}\text{CH}_2\text{CH}_3 \]

**Figure 2.4:** Specific optical rotation of a polysiocyanate before (●) and after (□) photochemical \textit{trans} → \textit{cis} azobenzene isomerization.\textsuperscript{10}

The rational for these observations is once a polymer’s helical sense is biased by the chiral center in the side chains, isomerization of the azobenzene unit changes the
spatial relationship between the chiral group and polymer backbone, which can lead to either a more pure or more racemic helix, Figure 2.5. The effect of the isomerization

![Diagram showing isomerization between R\text{trans} and R\text{cis}](image)

**Figure 2.5:** Side chain azobenzene isomerization effect.

varies depending on the nature and placement of the chiral group. In some cases the effect is further dependent on the concentration of the chiral azo monomer in the copolymer.

Unfortunately, simply including a chiral group and an azobenzene unit in the side chain of a helical polymer is not sufficient to ensure either a transfer of chirality or the ability to manipulate a biased helix. The connectivity of the different functional groups is
also of importance. Zentel found that for any transfer of chirality to occur, the polyisocyanate backbone and the chiral group must be attached to the same phenyl ring of the azobenzene. In fact, the closer they are attached, the greater is the transfer of chirality,\textsuperscript{4} Figure 2.6.

![Chemical structure](image)

No evidence of a biased helix
No effect of azo isomerization

![Chemical structures](image)

Slightly biased helix
Small isomerization effect

Large helical bias
Larger isomerization effect

**Figure 2.6:** Effect of side chain chirality for a series of copolyisocyanates (copolymerized with hexylisocyanate).\textsuperscript{4}

Polyguanidines are similar to polyisocyanates in that they have long persistence lengths. Different amounts of chiral material incorporated into polyguanidines can lead to varying degrees of helical bias,\textsuperscript{11} showing that, like the polyisocyanates, the polyguanidines can be cooperative. Polyguanidines are different from the polyisocyanates in that they have higher inversion barriers.\textsuperscript{12} These high inversion
barriers can result in more stable helices that may be advantageous for some applications.

We are interested in investigating the response of polyguanidines to side chain azobenzene isomerization and comparing that response to that of the polyisocyanates.

2.2 Materials and Methods

2.2.1 Photoswitchable Monomers

In designing our chiral switching monomer we followed Zentel’s lead. So, for our first chiral azo monomer our carbodiimide and chiral center are attached to the azobenzene in the same manner as in Zentel’s most successful polyisocyanate experiment. Initially seven carbodiimide monomers were synthesized, Figure 2.7. Of primary importance was the chiral-azo monomer, 1. The role of this monomer was both to bias and to manipulate the helical sense of the polymer. Monomers 2 and 3 also contain azobenzene groups for photochemical switching and were synthesized for comparison to 1. Of those two monomers, 2 is racemic and 3 is achiral. Monomers 4 - 6 are analogs to the first three but did not contain the switching group. The final monomer, di-n-hexylcarbodiimide, 7, was a simple achiral alkyl carbodiimide to be used as a comonomer that functions as a spacer. This monomer was used to determine how much of the azo monomer was necessary for a biased helix.
Figure 2.7: Target monomers.
Our azobenzene containing monomers can be represented by Figure 2.8 where the alkyl groups are labeled for discussion purposes. Notable differences in our monomers and the Zentel monomers are the hexyl group $R^3$ and the butyl group $R^1$. The additional alkyl group $R^3$ is necessitated due to the tertiary nature of the nitrogen of the carbodiimide compared to the oxygen of the isocyanate. A six-carbon alkyl chain was used to create similarity between that substituent of monomers 1 - 6 and the alkyl groups of the achiral spacer monomer, 7. The long alkyl chain is also believed to promote solubility of the polymer. The butyl group $R^1$ was also added to enhance the solubility of the polymer.

### 2.2.2 Monomer Synthesis

The syntheses of 1 - 3 began with the saponification of commercially available dihydrocoumarin and subsequent diazotization with a diazonium salt generated in situ from commercially available 4-butyl aniline. After esterification of the resulting acid, one of three tosylates, one chiral, one achiral, and one racemic, was used in each of three alkylations. After saponification, the acid chlorides were generated by the addition of
oxalyl chloride. Then each acid chloride reacted with azidotrimethylsilane to form an acyl azide, which was converted to an isocyanate via a Curtius rearrangement. The isocyanates reacted with hexylamine to form ureas, and the ureas were dehydrated with dibromotriphenylphosphorane to give carbodiimides 1, 2, and 3. These syntheses are shown in Scheme 2.1.

The only difference in the syntheses of 1 - 3 and 4 - 6 is the absence of the diazotization step for 4 - 6. All other steps are virtually identical, Scheme 2.2. Di-n-hexyl carbodiimide was synthesized by the dehydration of di-n-hexylurea which was generated through the quantitative reaction of commercially available hexylisocyanate and hexylamine, Scheme 2.3.

The reactions involved in the syntheses were generally facile conversions and were largely high yielding. The downside to this sequence of reactions is that many of the intermediate products were oils that had decent solubility in most organic solvents, so purification was generally difficult and recrystallization was often impossible. The difficulties experienced in purifying these compounds are only magnified by the large scales required for generating large amounts, i.e. several grams, of the final compounds for polymerizations.
Scheme 2.1: Syntheses of monomers 1 - 3.

1. NaOH/H₂O
   \[ \text{C}_4\text{H}_9\text{N} - \text{N} + \text{H}_2\text{O} \]

2. NaH
   \[ \text{NaOH} \rightarrow \text{DMF} \rightarrow \text{EtOH} \]

3. (COCl)₂
   \[ \text{COCl} \rightarrow \text{toluene} \]

4. (Me)₃SiN₃
   \[ \text{Cl} \rightarrow \text{toluene} \]

5. C₆H₄NH₂
   \[ \text{CHCl}_3 \rightarrow \text{CH}_2\text{Cl}_2 \]

1: R=CH₃ (S)
2: R=CH₃ (R/S)
3: R=H
Scheme 2.2: Synthesis of monomers 4 - 6.

1. $\text{NaOH} \quad \text{H}_2\text{O}$
2. $\text{EtOH} \quad \text{CHCl}_3 \quad \text{H}_2\text{SO}_4$
3. $\text{NaOH} \quad \text{H}_2\text{O} \quad \text{EtOH}$
4. $\text{DMF}$
5. $\text{toluene}$
6. $\text{toluene}$
7. $\text{PPh}_3, \text{Br}_2 \quad \text{Et}_3\text{N} \quad \text{CH}_2\text{Cl}_2$

4: $R=\text{CH}_3 \quad \text{(S)}$
5: $R=\text{CH}_3 \quad \text{(R/S)}$
6: $R=\text{H}$
The final carbodiimide compounds were, perhaps, the most difficult to purify. Carbodiimides of modest molecular weight, e.g. di-\textit{n}-hexylcarbodiimide, are easily purified by vacuum distillation over calcium hydride. For carbodiimides of higher molecular weight such as 1 - 6 vacuum distillation is not a viable technique. This is because carbodiimides undergo a disproportionation reaction at high temperatures, Scheme 2.4. For example, as 1 was heated during a vacuum distillation the molecule disproportionated into di-\textit{n}-hexyl carbodiimide and di-(3-(1-((\textit{S})-2-mey)-4-(4'\textit{'}-butylphenylazo)-2-phenyl)-ethyl) carbodiimide, and very pure di-\textit{n}-hexylcarbodiimide immediately distilled. Unable to find a way to remove the byproduct triphenylphosphine from the higher molecular weight carbodiimides, most polymerizations were performed with small amounts of this impurity present.
Scheme 2.4: Mechanism for carbodiimide metathesis.
2.2.3 *Catalysts for Carbodiimide Polymerization*

A number of catalysts are effective for the polymerization of carbodiimides, Figure 2.9. The first catalyst developed for the living polymerization of carbodiimides, I is extremely reactive, and the polymerization is highly exothermic.\textsuperscript{13} For better control II and III were developed. The reactivity of these catalysts is determined to a large extent by the steric demands of the monomer.\textsuperscript{13} Catalyst IV is similar to II and III, but is more active due to the replacement of the cyclopentadienyl ligand of III with a chlorine which decreases steric encumbrance and increases the Lewis acidity of the metal center.\textsuperscript{14} These titanium catalysts are all very sensitive to air and moisture and must be handled in the inert atmosphere of a dry box.

In a search for more robust catalysts that are tolerant to air and moisture, several copper catalysts were developed.\textsuperscript{15} These catalysts were active for living polymerizations of carbodiimides even in the presence of air and moisture, but were slightly less active than the titanium catalysts, and a slow termination by water was observed in wet solvents.
Figure 2.9: Catalysts for carbodiimide polymerization.
2.2.4 Polymerizations

Initial studies utilized catalyst III, which is considered moderately active for the polymerization of carbodiimides and catalyzes a living polymerization with good control. The polymerization likely proceeds by a coordination-insertion mechanism, Scheme 2.5. The polymerization is initiated by insertion of one of the carbon-nitrogen double bonds into the titanium-amide bond to form an amidinate species. The polymerization continues with successive monomer insertions in a living fashion until it is terminated by hydrolysis.

The general polymerization procedure is as follows: Under the inert atmosphere of a dry box, each monomer was weighed into a small vial. A stir bar was added to the vial and a small amount of a catalyst solution in anhydrous CHCl$_3$ was added. A screw cap was placed on the vial, and the vial was removed from the dry box. The polymerization stirred at room temperature until the reaction mixture formed a gel and stirring ceased. At this time it was assumed that the polymerization was complete. The cap was removed from the vial, and wet toluene was added to terminate the polymerization and dissolve the polymer. The toluene solution was poured into a beaker of rapidly stirring methanol, and the polymer precipitate was collected by filtration.
Scheme 2.5: Mechanism for carbodiimide polymerization.
The homopolymerization of 7 worked well with III, taking place in about 16 hours, Table 2.1. Copolymerizations of various amounts of 7 (85%-99%) and 1 (15%-1%) were successful; however, polymerization time increased with increasing azo monomer concentration as determined by monomer feed, e.g. up to 24 days for $P(1_{15-co-7_{85}})$. This consistent increase in polymerization time could be an indication that the polymers were forming blocky structures; however, we were unable to homopolymerize 1 with III, so it is unlikely that this monomer formed blocks of any significant size. For this reason we believe the comonomers were incorporated randomly into the polymers.

The inability to homopolymerize 1 did not initially seem significant because the anticipated result was that of high optical rotations with only a small proportion of 1, so we were satisfied with the copolymers prepared.

Table 2.1: Polymerization results catalyst III.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer (%)</th>
<th>Monomer (%)</th>
<th>Catalyst</th>
<th>Mon:Cat</th>
<th>CHCl₃ (mL)</th>
<th>Polymerization Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>P7</td>
<td>7 (100)</td>
<td>III</td>
<td>24:1</td>
<td>Neat</td>
<td>12 hours</td>
<td></td>
</tr>
<tr>
<td>$P(1_{1-co-7_{99}})$</td>
<td>1 (1)</td>
<td>7 (99)</td>
<td>III</td>
<td>140:1</td>
<td>0.5</td>
<td>2.5 days</td>
</tr>
<tr>
<td>$P(1_{4-co-7_{96}})$</td>
<td>1 (4)</td>
<td>7 (96)</td>
<td>III</td>
<td>124:1</td>
<td>0.5</td>
<td>6 days</td>
</tr>
<tr>
<td>$P(1_{7-co-7_{93}})$</td>
<td>1 (7)</td>
<td>7 (93)</td>
<td>III</td>
<td>143:1</td>
<td>0.5</td>
<td>7.5 days</td>
</tr>
<tr>
<td>$P(1_{10-co-7_{90}})$</td>
<td>1 (10)</td>
<td>7 (90)</td>
<td>III</td>
<td>114:1</td>
<td>0.5</td>
<td>10 days</td>
</tr>
<tr>
<td>$P(1_{15-co-7_{85}})$</td>
<td>1 (15)</td>
<td>7 (85)</td>
<td>III</td>
<td>141:1</td>
<td>0.5</td>
<td>24 days</td>
</tr>
<tr>
<td>P1</td>
<td>1 (100)</td>
<td>III</td>
<td>145:1</td>
<td>Neat</td>
<td>------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>
Although 1 could not be homopolymerized with III, oligomers of the analogous achiral monomer, 3, were successfully formed with a reaction time of 5 days. This indicates that the chiral center plays an important role in the polymerization. Another interesting result is the dramatic increase in polymerization time required for the copolymer containing seven percent of racemic monomer 5, 10 days, compared to the time required for the polymerization of the polymer containing the same ratio of homochiral monomer 4, 1.5 days, Table 2.2.

**Table 2.2:** Polymerization results catalyst III, monomers 4 and 5.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer (mole %)</th>
<th>Monomer (mole %)</th>
<th>Catalyst</th>
<th>Mon:Cat</th>
<th>CHCl₃ (mL)</th>
<th>Polymerization Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(4₇-co-7₉₃)</td>
<td>4 (7)</td>
<td>7 (93)</td>
<td>III</td>
<td>145:1</td>
<td>0.5</td>
<td>1.5 days</td>
</tr>
<tr>
<td>P(5₇-co-7₉₃)</td>
<td>5 (7)</td>
<td>7 (93)</td>
<td>III</td>
<td>145:1</td>
<td>0.5</td>
<td>10 days</td>
</tr>
</tbody>
</table>

Several trends can be observed from these data. Achiral monomers polymerize faster than chiral, and chiral monomers polymerize faster than racemic. Also, non-azo containing monomers polymerize faster than their corresponding azo containing monomers. Eager to test the optical properties of these polymers and explore their response to azobenzene isomerization, we did not exhaustively study these trends at this time.
2.3 Initial Optical Studies: Annealing and Acid Protonation

Once chiral-azo copolymers were prepared we began studying their optical properties. Helical polymers are commonly studied with circular dichroism (CD) spectroscopy. Polyguanidines, however, often have limited solubility. Solvents that are good for polyguanidines, typically toluene, THF, and chloroform, preclude CD measurements due to solvent effects in the short wavelength region where the polyguanidine backbone absorbs light. We, therefore, used polarimetry to determine both if a helical bias existed in our systems and the extent of that helical bias. These initial studies were complicated by the poor solubility of the copolymers in all solvents used. We determined that the best solvent is chloroform; however, even low concentrations of the copolymers yielded viscous solutions. Polarimetry studies of the copolymer solutions gave specific optical rotation data that was not significantly different from zero and that had standard deviations that were higher than expected. For example, the 95% confidence interval for $\text{P(1$_4$-co-7$_9$)}$ is $[\alpha]_{D}^{25}$ -2 ± 1°, Figure 2.10. The accepted 95% confidence interval for the instrument under these conditions is ± 0.2. 16

2.3.1 Annealing the Polymers

From our past experience with polyguanidines we know that often as carbodiimide monomers are polymerized the polymer assumes a kinetically controlled conformation. This conformation may or may not show amplification. Upon annealing the polymer can orient into its thermodynamically controlled preferred helix. 11 This orientation results in a biased helical structure with amplified optical properties;
accordingly, the copolymers were annealed at a temperature of 45 °C for 3 days. Over this time period no change was observed in either the specific optical rotation or the standard deviation, Figure 2.11.

2.3.2 Acid Protonation of the Polymers

Due to the unexpectedly high viscosities and the large standard deviations in the optical rotation, data we hypothesized that the polymers were forming aggregates that showed birefringence. When Robinson studied the first polyguanidines, he determined that these polymers are stable to hydrochloric and acetic acids. In previous work we utilized this stability and exploited the basicity of the guanidine units by adding chiral camphorsulfonic acid that acts as a molecular chaperone to bias the helical sense. Drawing on our previous experience with protonating polyguanidines, we decided to try
Figure 2.11: Specific optical rotation of P(14-co-796) over one minute after annealing at 45 °C for 17 hours (c 0.24, CHCl₃).

protonating the polymer backbone with an achiral acid with the hope that the positively charged polymer chains would repel each other, thus breaking up the aggregates. An additional consequence of acid protonation is that it tends to catalyze the helix reversal allowing the polymer to more easily assume its thermodynamically preferred helical conformation.

Solutions of copolymers were made in CHCl₃. Several milliliters of each solution were placed into volumetric flasks. A solution of tosic acid in CHCl₃ was added to each flask, and CHCl₃ was used to dilute to volume. The best results were realized using concentrations of polymer and acid of 0.24 g/100 mL polymer and 1 acid equivalent to 1.5 monomer units.

Upon addition of tosic acid, the polymer solutions did begin to show specific optical rotations of increased magnitude; however, their standard deviations actually
increased at the same time, \([\alpha]_D^{25} +79 \pm 6^\circ\), and the measurements were not reproducible, Figure 2.12. Clearly the situation was more complicated than we first anticipated. It was at this point that we decided to revisit the homopolymerization of the chiral-azo monomer. We thought that studying the homopolymer could yield insight into the properties of the copolymers.

![Graph showing specific optical rotation over time](image)

**Figure 2.12:** Specific optical rotation of \(P(1_{4-co-7_{90}})\) over one minute at room temperature after addition of 1.5 eq tosic acid/monomer unit \((c 0.24, \text{CHCl}_3)\).

### 2.4 Chiral Homopolymers

Catalyst IV is more active and has successfully polymerized a wider range of monomers than III, especially monomers with more sterically bulky side chains.\(^{14}\) Homopolymerization of 1 had been unsuccessful with III, so, we tried to homopolymerize 1 with IV. The polymerization was complete in 24 hours, Table 2.3. A copolymerization of 50% 1 and 50% 7 with IV, however, was not as successful. The
reaction mixture became cloudy and viscous within minutes after adding the catalyst solution (40 µL in toluene); however, over the next two days there was no visible change in the viscosity. The polymerization mixture never gelled which is the usual indication that the reaction is complete. The polymerization was quenched after 48 hours, and the polymer was precipitated by the usual procedure. The initial cloudiness of the polymerization mixture and incomplete polymerization indicated precipitation of the growing polymer chains, which means that the polymer is not soluble in the monomer. The reaction was repeated in toluene in hopes of avoiding that precipitation of the polymer; however, no change in viscosity was observed over two days and no polymer was recovered.

**Table 2.3: Polymerization results catalyst IV.**

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer (mole %)</th>
<th>Monomer (mole %)</th>
<th>Catalyst</th>
<th>Mon:Cat</th>
<th>Solvent (mL)</th>
<th>Polymerization Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P(1_{50\text{-co-7}_{50}}))</td>
<td>1 (50)</td>
<td>7 (50)</td>
<td>IV</td>
<td>131:1</td>
<td>0.04</td>
<td>&lt; 2 days</td>
</tr>
<tr>
<td>(P(1_{50\text{-co-7}_{50}}))</td>
<td>1 (50)</td>
<td>7 (50)</td>
<td>IV</td>
<td>131:1</td>
<td>1.00</td>
<td>--------</td>
</tr>
<tr>
<td>P1</td>
<td>1 (100)</td>
<td></td>
<td>IV</td>
<td>375:1</td>
<td>0.04</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

**2.4.1 Polymer Solubility**

Solubility properties of the chiral azo homopolymer, \(P(1)\), were quite surprising. We expected the homopolymer to show only limited solubility as was found for the previous copolymers of 1 and 7. Instead, the homopolymer was quite soluble in both
chloroform and toluene. The 50% copolymer, P(150-co-750), had good solubility as well. This indicates that the poor solubility seen with previous copolymers of lower azo concentration was probably due to the di-n-hexyl carbodiimide comonomer, which is surprising considering that the homopolymer of this monomer is generally considered to be one of the more soluble polyguanidines. The improved solubility seen for P1 enabled polarimetry studies to be conducted on solutions more concentrated than in previous studies.

2.4.2 Optical Studies

Initially P1 showed a specific optical rotation that was not very different from it's monomer, +4.6 ± 0.3°. Once again we attempted to promote evolution to a thermodynamically controlled biased helix through annealing. After annealing a solution of P1 in CHCl₃ for 19 hours at 50 °C the specific optical rotation had dropped to +0.568 ± 0.3°. After 7 days at 50 °C the specific rotation was –11.9 ± 0.3°. An identical solution that sat at room temperature over the same 7-day period had a specific optical rotation of +6.9 ± 0.3°.

The results for the 50% chiral azo copolymer, P(150-co-750) were discouraging. Upon dissolution in toluene the specific optical rotation of P(150-co-750) was –4.198 ± 0.7°, which is opposite in sign to the rotation of the chiral monomer, but not greatly amplified. After annealing for three days an increase in magnitude was expected, similar to the homopolymer. There was actually a slight decrease in magnitude to –2.4 ± 0.1°. This is discouraging because even a non-cooperative copolymer should show an optical
rotation that is half of that of the chiral homopolymer. In a cooperative system a comonomer with less than 50 percent chiral monomer may have an optical rotation nearly equal to the chiral homopolymer which is assumed to be a single handed helix.\textsuperscript{5,12} It is possible given the relatively low specific optical rotation for P1 that, for some reason, that polymer is not a single-handed helix. Due to the low rotations seen for both polymers it is not possible to determine the extent of helicity in either polymer or to say with certainty that no cooperativity is present. If it does exist, however, the cooperativity is to a very small extent. Remembering that we were originally trying to exploit the high cooperativity of these polymers and because cooperativity is not apparent in our system we decided that it would be advantageous at this time to revise that system.

2.5 Conclusions

A number of conclusions can be drawn based on the preceding studies. Difficulties in homopolymerizing 1 and 2 probably arose due to the steric demands of the chiral/racemic alkyl group. This was overcome by changing to a catalyst with a less encumbered and more Lewis acidic metal center. Furthermore, the differences in polymerization time for 4 and 5 show that monomers with the racemic alkyl group are more difficult to polymerize than monomers with the chiral alkyl group. Solubility problems with these polymers made CD spectroscopy impossible and made polarimetry studies difficult. According to our data a biased helical structure is present in homopolymer P1 as evidenced by the difference in sign and amplification of the absolute value of the specific optical rotation of P1 compared to 1, although this amplification is
lower than expected. Contrary to our hopes and expectations more than 15% of 1 is required to see amplification. Even beyond 15% of 1 the cooperativity of this polymer system is questionable.

Several modifications to our system were suggested in hopes of achieving better results. One possibility is a new comonomer for 1 to improve the solubility of the system. Increased solubility of the copolymers could lead to less uncertainty in optical rotation measurements. This could elucidate subtle differences in specific optical rotation of various copolymers which could confirm or disprove cooperativity. One possible monomer is \( N \)-hexyl-\( N' \)-phenyl carbodiimide. A new comonomer, however, will not improve the amplification observed for the homopolymer. Another option is to choose completely new monomers. We modeled our first monomers on previously studied isocyanates, but we thought that it might be advantageous to look to carbodiimide monomers previously studied in our group. Although we have seen some interesting results that have not been fully explored, the time and money involved in synthesizing material on which to perform further experiments potentially outweighs the knowledge to be gained from such experiments. Due to difficulties and length of time involved in synthesizing the monomers we decided that experimenting with new chiral monomers would be a more productive use of our resources.
2.6 Experimental

2.6.1 General Procedures and Characterizations

Reagents and solvents from commercial sources were used directly. All reactions involving air and moisture sensitive compounds were performed in oven-dried glassware under dry nitrogen using standard Schlenk techniques. All polymerizations were set up in an MBraun UNILab drybox under nitrogen atmosphere using dry solvents (MBraun solvent system).

$^1$H and $^{13}$C NMR spectra were obtained using a Varian Mercury 300 (300 MHz) or Varian Mercury 400 (400 MHz) spectrometer as specified. Chemical shifts are reported in $\delta$ (ppm) and are referenced to selected residual proton peaks for the solvents as follows: For $^1$H NMR solvent residual peaks were 7.26 ppm for CDCl$_3$ and 2.50 ppm for DMSO-d$_6$. For $^{13}$C NMR solvent residual peaks were 77.23 for CDCl$_3$ and 39.51 for DMSO-d$_6$. Significant $^1$H NMR data are tabulated in the following order: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hertz, number of protons.

Infrared spectra were obtained using a Jasco FT/IR-410 spectrometer as thin films on NaCl disks and are uncalibrated. IR data are reported in wavenumbers (cm$^{-1}$).

Optical rotation measurements were obtained on a Jasco P-1010 polarimeter at 589 nm in a 1 dm cell at 25 °C unless noted otherwise. Annealing experiments were conducted in a thermostated 1 dm cell at the specified temperature where temperature control is accurate to ± 0.1 °C.
Mass spectra were obtained at the Mass Spectrometry Laboratory for Biotechnology. Partial funding for the Facility was obtained from the North Carolina Biotechnology Center and the National Science Foundation.

Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia.

### 2.6.2 Procedures

**3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid.** A 250 mL round bottom flask was charged with a stir bar and a solution of sodium hydroxide (6.2 g, 150 mmol) in H$_2$O (50 mL). Dihydrocoumarin (6.4 ml, 50 mmol) was dissolved in the basic solution, the flask was fitted with a reflux condenser, and the solution was heated at reflux with stirring for 1.5 hours. The reaction mixture cooled to room temperature and was then transferred to a second 250 mL round bottom flask charged with a stir bar and a solution of sodium carbonate (11.31 g, 106.7 mmol) in H$_2$O (30 mL) which was subsequently cooled in an ice bath to $< 5 \degree$C.

Concurrently, a separate 250 mL round bottom flask was charged with a stir bar and 4-butylaniline (7.9 mL, 50 mmol), and 1 N HCl (60 mL) was added dropwise. The solution stirred at room temperature for 20 min before being cooled in an ice bath to $< 5 \degree$C. Then a solution of sodium nitrite (3.46 g, 50.1 mmol) in H$_2$O (10 mL) was added portionwise. The resulting solution stirred 30 minutes at $< 5 \degree$C and was then added to the sodium carbonate solution.
The entire reaction mixture stirred at < 5 °C for one hour and then was acidified with 3 N HCL causing a red-orange product to precipitate. The crude product was dissolved in 250 mL of boiling EtOH/H2O (1:1 v/v). After the solution cooled to room temperature the precipitate was removed by filtration. Distillation removed two-thirds of the liquid, and upon slow cooling to room temperature, the product precipitated as an orange solid. Yield: 80%; IR (neat) 3367, 2956, 2917, 2856, 1688, 1598, 1430, 1093, 837 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 10.35 (s, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 2.4 Hz, 1H), 7.64 (dd, J = 2.4, 8.4 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 1H), 2.83 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), 2.55 (t, J = 7.6 Hz, 2H), 1.59 (m, 2H), 1.33 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 174.0, 158.7, 150.4, 145.3, 145.1, 129.2 (2C), 127.9, 124.2, 123.0, 122.1 (2C), 115.3, 34.7, 33.3, 33.0, 25.5, 21.8, 13.8; Anal Calcd. For C₁₉H₂₂N₂O₃: C, 69.92; H, 6.79; N, 8.58; O, 14.71. Found: C, 70.16; H, 7.04; N, 8.38; O, 14.50.

3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid ethyl ester. A 500 mL round bottom flask was charged with a stir bar and a mixture of EtOH (30 mL) and CHCl₃ (100 mL). 3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid (8.85 g, 27.1 mmol) was dissolved in the mixture and concentrated sulfuric acid (1 mL) was added slowly. The flask was fitted with a reflux condenser, and the reaction mixture was heated at reflux with stirring for 16 hours. After cooling to room temperature the product solution was washed consecutively with H₂O (2 x 100 mL), saturated sodium bicarbonate (2 x 100 mL), and H₂O (2 x 100 mL). The organic phase was dried over magnesium sulfate and the solvent was removed leaving an orange solid. Yield: 91%; IR
(neat) 3360, 2957, 2931, 2858, 1734, 1275, 1095, 841 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 10.35 (s, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.65 (m, 2H), 7.36 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 1H), 4.04 (q, J = 7.2 Hz, 2H), 2.87 (t, J = 7.6 Hz, 2H), 2.63 (m, 4H), 1.59 (m, 2H), 1.32 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 172.4, 158.7, 150.4, 145.3, 145.1, 129.2 (2C), 127.5, 124.0, 123.4, 122.1 (2C), 115.2, 59.8, 34.6, 33.2, 33.0, 25.5, 21.8, 14.1, 13.8; Anal Calcd. For C₂₁H₂₆N₂O₃: C, 71.16; H, 7.39; N, 7.90; O, 13.54. Found: C, 71.43; H, 7.36; N, 7.76; O, 13.77.

**(S)-2-Methyl-1-butyl tosylate.** A 500 mL round bottom flask was charged with a stir bar and pyridine (180 mL) and was placed in an ice bath. (S)-(−)-2 Methyl-1-butanol (10 mL, 92 mmol) was dissolved in the pyridine, and tosyl chloride (35.4 g, 186 mmol) was added slowly. The resulting solution stirred for 30 minutes in the ice bath before being placed in a refrigerator for 16 hours. H₂O (200 mL) was added and the reaction stirred in an ice bath for 2 hours. The reaction mixture was extracted with Et₂O (2 x 120 mL). The organic layers were combined and washed with cold 6 N HCl (2 x 150 mL) and H₂O (3 x 150 mL). The organic layer was dried over magnesium sulfate and potassium carbonate and the solvent was removed leaving a clear liquid. Yield: 99%; [α]²⁵_D +11.1° (c 0.48, CHCl₃); IR (neat) 2966, 2879, 1599, 1360, 1188, 1176, 964, 667, 555 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 7.78 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 3.84 (m, 2H), 2.42 (s, 3H), 1.62 (m, 1H), 1.29 (m, 1H), 1.07 (m, 1H), 0.79 (d, J = 6.4 Hz, 3H), 0.75 (t, J = 7.4 Hz, 3H). ¹³C NMR (100 MHz, DMSO-d₆) δ 144.9, 132.4, 130.2 (2C), 58
127.6 (2C), 74.7, 33.7, 24.8, 21.1, 15.6, 10.8; Anal Calcd. For C\textsubscript{12}H\textsubscript{18}O\textsubscript{3}S: C, 59.47; H, 7.49; O, 19.81; S, 13.23. Found: C, 59.62; H, 7.64; O, 19.97; S, 13.07.

**3-(1-((S)-2-Methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid.**

A 500 mL round bottom flask was charged with a stir bar and sodium hydride (0.66 g, 27 mmol), flushed with nitrogen, and sealed with a rubber septum with a nitrogen purge. DMF (50 mL) was added through the septum via syringe, and the suspension was placed in an ice bath. A separate round bottom flask was charged with 3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid ethyl ester (7.46 g, 21.1 mmol), flushed with nitrogen, and sealed with a rubber septum with a nitrogen purge. DMF (40 mL) was added through the septum via syringe. The 3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid ethyl ester/DMF solution was added to the sodium hydride/DMF suspension via cannulation. The reaction mixture was allowed to warm to room temperature and stirred at room temperature for 1 hour. A third round bottom flask was charged with (S)-2-methyl-1-butyl tosylate (5.03 g, 20.8 mmol), flushed with nitrogen, and sealed with a rubber septum with a nitrogen purge. DMF (40 mL) was added through the septum via syringe. The (S)-2-methyl-1-butyl tosylate/DMF solution was added to the reaction mixture via cannulation and the resulting mixture was heated in an 80 °C oil bath for 1 hour. The reaction mixture was poured into a 500 mL beaker containing a mixture of 1 N HCL (100 mL) and crushed ice (50 g). The resulting mixture was extracted with EtOAc/Et\textsubscript{2}O (50:50 v/v) (2 x 100 mL). The organic layers were combined and washed with 0.5 N sodium hydroxide (2 x 150 mL) and brine (2 x 150 mL). The organic phase was dried over magnesium sulfate and the solvent was removed leaving the crude product.
3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid ethyl ester.

The ethyl ester was dissolved in EtOH (18 mL) in a 100 mL round bottom flask containing a stir bar. A solution of sodium hydroxide (2.4 g, 60 mmol) in H₂O (6.0 mL) was added, the flask was fitted with a reflux condenser, and the solution was heated at reflux for 1.5 hours. After cooling to room temperature the solution was concentrated using a rotovap (removing most of the EtOH), 20 mL H₂O was added, and the solution was acidified with 6 N HCl. Upon acidification an orange oil separated. The mixture was extracted with Et₂O (2 x 50 mL). The organic layers were combined and washed with 0.5 N sodium hydroxide (2 x 50 mL) (removing the product and leaving any remaining R-OTs in the Et₂O). The basic layer was acidified with 6 N HCl and the oil that separated was pure product. The product was extracted with Et₂O (2 x 75 mL), the organic layers were dried over magnesium sulfate and the solvent was removed. Yield: 89% (two steps); [α]²⁵_D +8.1 (c 0.38, CHCl₃); IR (neat) 2960, 1708, 1598, 1493, 1465, 1103, 815 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 7.75 (m, 4H), 7.36 (d, J = 7.6 Hz, 2H), 7.13 (d, J = 8.8 Hz, 1H), 3.92 (m, 2H), 2.88 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 1.86 (m, 1H), 1.56 (m, 3H), 1.31 (m, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.92 (t, J = 7.8 Hz, 3H), 0.90 (t, J = 8.2 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 173.9, 159.3, 150.3, 145.6 (2C), 129.8, 129.2 (2C), 123.8, 123.0, 122.3 (2C), 111.5, 72.5, 34.7, 34.2, 33.5, 33.0, 25.7, 25.6, 21.8, 16.5, 13.8, 11.2; HRMS (FAB) calced for C₂₄H₂₃N₂O₃ (MH⁺) 397.2491. Found 397.2498.

N-Hexyl-N’-(3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl)-ethyl) urea. A tube shaped flask with a side arm was charged with a stir bar and 3-(1-
[((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid (5.85 g, 14.8 mmol). A rubber septum was placed on the flask and the flask was evacuated via the side arm before being filled with nitrogen. Dry toluene (30 mL) was added to the flask through the septum via syringe and then oxalyl chloride (6.5 mL, 75 mmol) was added in the same manner. The reaction stirred at room temperature for 2 hours and was then placed in a 60 °C oil bath where it stirred for 1 hour. After cooling to room temperature solvent and excess oxalyl chloride were removed in vacuo leaving the crude product, 3-((1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionyl chloride. IR (neat) 2960, 1801, 1599, 1492, 1465, 1255, 1104, 816 cm⁻¹. Dry toluene (30 mL) was added to the flask through the septum via syringe. In the same manner azidotrimethylsilane (8.0 mL, 60 mmol) was added to the flask. The reaction stirred at 45 °C for 24 hours. After cooling to room temperature solvent and excess azidotrimethylsilane were removed in vacuo leaving the crude product, 3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl)-ethyl isocyanate. IR (neat) 2960, 2270, 1598, 1493, 1465, 1256, 1106, 815 cm⁻¹. CHCl₃ (60 mL) was added to the flask and the solution was cooled in an ice bath. Hexylamine (2.0 mL, 15 mmol) was added slowly and the reaction stirred at < 5°C for 30 minutes. Yield: 91% (three steps); [α]²⁵_D +12.0 (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.81 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.8 Hz, 1H), 3.90 (m, 2H), 3.50 (t, J = 6.6 Hz, 2H), 3.09 (t, J = 7.4 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.93 (m, 1H), 1.60 (m, 3H), 1.37 (m, 11H), 1.06 (d, J = 6.8 Hz, 3H), 0.98 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 0.84 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 159.7, 158.6, 146.6, 146.2, 142.5, 129.3 (2C), 128.4, 125.5, 124.1, 122.7
N-Hexyl-N’-(3-(1-((S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) carbodiimide. (1) A 250 mL round bottom flask was charged with a stir bar and 2.06 g, 7.86 mmol of triphenylphosphine. CH$_2$Cl$_2$ (26 mL) was added and the solution was cooled in an ice bath. To a pressure equalizing addition funnel was added CH$_2$Cl$_2$ (5 mL) and bromine (0.4 mL, 7.8 mmol). This solution was added to the cold triphenylphosphine/CH$_2$Cl$_2$ solution dropwise. The resulting white suspension stirred for 30 minutes after the addition was complete. Triethylamine (2.3 mL, 17 mmol) was added to the reaction mixture and N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) urea (3.06 g, 6.19 mmol) was added in small portions over 1 hour. The reaction stirred one hour after the last addition. The reaction mixture was washed with H$_2$O (1 x 100 mL). The organic phase was dried over magnesium sulfate. The volume of the organic phase was reduced with a rotary evaporator (almost all solvent was removed) and pentane (130 mL) was added causing a reddish precipitate to form. After filtration the solvent was removed and the product, a red oil, was dried in vacuo. Yield: 92%; [α]$^{25}$D +7.5 (c 0.10, CHCl$_3$); IR (neat) 2958, 2127, 1597, 1492, 1465, 1254, 1105, 815 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.81 (m, 4H), 7.32 (m, 2H), 6.95 (d, $J = 8.4$ Hz, 1H), 3.89 (m, 2H), 3.49 (t, $J = 7.2$ Hz, 2H), 3.04 (t, $J = 7.0$ Hz, 2H), 3.00 (t, $J = 6.8$ Hz, 2H), 2.67 (t, $J = 7.6$ Hz, 2H), 1.92 (m, 1H), 1.60 (m, 3H), 1.30 (m, 11H), 1.07 (d, $J = 6.4$ Hz, 3H), 0.98 (t, $J = 7.6$ Hz, 3H), 0.94 (t, $J = 7.4$ Hz, 3H), 0.85 (t, $J = 7.4$ Hz, 3H), 0.83 (t, $J = 7.4$ Hz, 2H).
Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 159.7, 151.2, 146.5, 145.2, 140.7, 129.2 (2C), 128.0, 124.7, 124.2, 122.7 (2C), 111.0, 73.1, 46.9, 46.3, 35.7, 35.0, 33.7, 33.1, 31.6, 31.4, 26.6, 26.4, 22.7, 22.5, 17.0, 14.2, 14.1, 11.6; HRMS (FAB) calcd for C$_{30}$H$_{44}$N$_4$O (MH$^+$) 477.3593. Found 477.3574.

**$^{(R/S)}$-2-Methyl-1-butyl tosylate.** An identical procedure for the preparation of ($S$)-2-methyl-1-butyl tosylate was employed. The quantities of reagents used were 10 mL, 92 mmol of ($R$/S)-2-methyl-1-butanol, 150 mL of pyridine, 34.6 g, 180 mmol of tosyl chloride, and 200 mL of H$_2$O. Yield: 91%. This compound displayed identical spectral characteristics to the chiral ($S$)-2-methyl-1-butyl tosylate. Anal Calcd. For C$_{12}$H$_{16}$O$_3$S: C, 59.47; H, 7.49; O, 19.81; S, 13.23. Found: C, 59.60; H, 7.65; O, 19.91; S, 12.99.

**3-(1-$^{(R/S)}$-2-Methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid.** An identical procedure for the preparation of 3-(1-($S$)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid was employed. The quantities of reagents used were 0.10 g, 4.2 mmol sodium hydride, 50 mL DMF, 1.01 g, 2.84 mmol 3-(1-Hydroxy-4-(4'-butyl-phenylazo)-2-phenyl) propionic acid ethyl ester, 10 mL DMF, 0.78 g, 3.2 mmol ($R$/S)-2-methyl-1-butyl tosylate, and 10 mL DMF. In the second step quantities of reagents used were 5 mL ethanol, 0.41 g, 10.25 mmol NaOH, 10 mL H$_2$O, and 10 mL additional H$_2$O. Yield: 80% (two steps). This compound displayed identical spectral characteristics to the chiral 3-(1-($S$)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid. Anal Calcd. For C$_{24}$H$_{32}$N$_2$O$_3$: C, 72.70; H, 8.13; N, 7.06; O, 12.10. Found: C, 71.85; H, 8.14; N, 6.76; O, 11.95.
\textit{N-Hexyl-\textit{N’}-(3-(1-((R/S)-2-methylbutoxy)-4-(4’-butyl-phenylazo)-2-phenyl)-ethyl) urea.} An identical procedure for the preparation of \textit{N-hexyl-\textit{N’}-(3-(1-((S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) urea} was employed. The quantities of reagents used were 2.45 g, 6.18 mmol 3-(1-((R/S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl) propionic acid, 15 mL dry toluene, and 1.7 mL, 19 mmol oxalyl chloride. The crude product was 3-(1-((R/S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl) propionyl chloride. IR (neat) 2960, 1799, 1599, 1495, 1464, 1255, 1105, 816 cm\(^{-1}\). In the second step the quantities of reagents were 15 mL dry toluene, and 2.5 mL, 29 mmol azidotrimethylsilane. The crude product was 3-(1-((R/S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl isocyanate. IR (neat) 2960, 2270, 1598, 1496, 1465, 1255, 1106, 816 cm\(^{-1}\). In the final step 25 mL CHCl\(_3\), and 0.8 mL, 6.2 mmol hexylamine were used. Yield: 90\% (three steps). This compound displayed identical spectral characteristics to the chiral \textit{N-hexyl-\textit{N’}-(3-(1-((S)-2-methylbutoxy)-4-(4’-butyl-phenylazo)-2-phenyl)-ethyl) urea}. HRMS (FAB) calcd for C\(_{30}\)H\(_{46}\)N\(_4\)O\(_2\) (MH\(^{+}\)) 495.3699. Found 495.3700.

\textit{N-Hexyl-\textit{N’}-(3-(1-((R/S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) carbodiimide.} (2) An identical procedure for the preparation of \textit{N-hexyl-\textit{N’}-(3-(1-((S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) carbodiimide} was employed. The quantities of reagents used were 2.09 g, 7.98 mmol triphenylphosphine, 25 mL CH\(_2\)Cl\(_2\), 0.4 mL, 7.8 mmol bromine, 5.0 mL CH\(_2\)Cl\(_2\), 2.2 mL, 16 mmol triethylamine, 3.09 g, 6.25 mmol \textit{N-hexyl-\textit{N’}-(3-(1-((R/S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl)-ethyl) urea}, 100 mL H\(_2\)O, and 200 mL pentane. Yield: 90\%.

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This compound displayed identical spectral characteristics to the chiral $N$-hexyl-$N'$-(3-((S)-2-methylbutoxy)-4-((4'-butylphenylazo)-2-phenyl)-ethyl) carbodiimide. HRMS (FAB) calcd for C$_{30}$H$_{44}$N$_4$O (MH$^+$) 477.3593. Found 477.3615.

**Butyl tosylate.** An identical procedure for the preparation of (S)-2-methyl-1-butyl tosylate was employed. The quantities of reagents used were 8.3 mL, 91 mmol of 1-butanol, 74 mL of pyridine, 34.7 g, 182 mmol of tosyl chloride, and 100 mL of H$_2$O. Yield: 97%; IR (neat) 2962, 2875, 1599, 1176, 939, 663, 555 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.78 (d, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.0$ Hz, 2H), 4.00 (t, $J = 6.4$ Hz, 2H), 2.41 (s, 3H), 1.52 (m, 2H), 1.23 (m, 2H), 0.78 (t, $J = 7.6$ Hz, 3H). $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 144.8, 132.5, 130.2 (2C), 127.6 (2C), 70.6, 30.2, 21.1, 18.1, 13.2; Anal Calcd. For C$_{11}$H$_{16}$O$_3$: C, 57.87; H, 7.06; O, 21.02; S, 14.05. Found: C, 57.95; H, 7.24; O, 21.38; S, 13.70.

**3-(1-Butoxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid.** An identical procedure for the preparation of 3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid was employed. The quantities of reagents used were 3.64 g, 87.4 mmol sodium hydride, 130 mL DMF, 23.83 g, 67.23 mmol 3-(1-Hydroxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid ethyl ester, 130 mL DMF, 16.7 g, 73.2 mmol butyl tosylate, and 130 mL DMF. In the second step quantities of reagents used were 56 mL ethanol, 6.9 g, 170 mmol sodium hydroxide, 20 mL H$_2$O, 100 and mL additional H$_2$O. Yield: 79% (two steps); IR (neat) 2933, 1712, 1599, 1493, 1466, 1252, 1103, 841 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 7.76 (m, 3H), 7.72 (d, $J = 2.4$ Hz, 1H), 7.37 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 8.4$ Hz, 1H), 4.10 (t, $J = 6.4$ Hz, 2H), 2.87 (t, $J = 7.6$ Hz, 2H),
2.66 (t, J = 7.6 Hz, 2H), 2.55 (t, J = 7.6 Hz, 2H), 1.76, (m, 2H), 1.59 (m, 2H), 1.49 (m, 2H), 1.33 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 173.9, 159.2, 150.3, 145.6 (2C), 129.7, 129.2 (2C), 123.8, 122.9, 122.2 (2C), 111.6, 67.7, 34.7, 33.3, 33.0, 30.8, 25.6, 21.8, 18.8, 13.8, 13.7; Anal Calcd. For C$_{23}$H$_{30}$N$_2$O$_3$: C, 72.22; H, 7.91; N, 7.32; O, 12.55. Found: C, 71.94; H, 7.86; N, 7.32; O, 12.45.

$N$-Hexyl-$N'$-(3-(1-butoxy-4-(4'-butylphenylazo)-2-phenyl)-ethyl) urea. An identical procedure for the preparation of $N$-hexyl-$N'$-(3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl)-ethyl) urea was employed. The quantities of reagents used were 20.11 g, 52.58 mmol 3-(1-butoxy-4-(4'-butylphenylazo)-2-phenyl) propionic acid, 100 mL dry toluene, and 22.8 mL, 261 mmol oxalyl chloride. The crude product was 3-(1-butoxy-4-(4'-butylphenylazo)-2-phenyl)-ethyl isocyanate. IR (neat) 2958, 2931, 2871, 1801, 1599, 1495, 1466, 1254, 1105 cm$^{-1}$. In the second step the quantities of reagents used were 100 mL dry toluene, and 27.8 mL, 209 mmol azidotrimethylsilane. The crude product was 3-(1-butoxy-4-(4'-butylphenylazo)-2-phenyl)-ethyl isocyanate. IR (neat) 2958, 2931, 2871, 2270, 1599, 1495, 1466, 1254, 1107 cm$^{-1}$. In the final step 210 mL CHCl$_3$, and 6.9 mL, 52 mmol hexylamine were used. Yield: 95% (three steps); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.79 (m, 4H), 7.30 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.0 Hz, 1H), 4.55 (bs, 2H), 4.07 (t, J = 6.4 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 3.09 (t, J = 7.2 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.64 (m, 2H), 1.44 (m, 2H), 1.26 (m, 10H), 1.00 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 0.84 (t, J = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 159.7, 158.6, 146.6, 146.2, 142.5, 129.3
(2C), 128.4, 124.9, 124.1, 122.7 (2C), 111.4, 68.4, 41.0, 40.6, 35.8, 33.7, 31.7, 31.5, 31.3, 30.2, 26.7, 22.6, 19.6, 14.2 (2C), 14.1; Anal Calcd. For C$_{29}$H$_{44}$N$_{4}$O$_{2}$: C, 72.46; H, 9.23; N, 11.66; O, 6.66. Found: C, 72.04; H, 9.21; N, 11.67; O, 6.89.

*N*-Hexyl-*N'*- (3-(1-butoxy-4-(4'-butyl-phenylazo)-2-phenyl)-ethyl) carbodiimide. (3) An identical procedure for the preparation of *N*-hexyl-*N'*- (3-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl)-ethyl) carbodiimide was employed. The quantities of reagents used were 11.48 g, 43.75 mmol triphenylphosphine, 145 mL CH$_2$Cl$_2$, 2.3 mL, 45 mmol bromine, 30 mL CH$_2$Cl$_2$, 12.5 mL, 89.7 mmol triethylamine, 16.65 g, 34.64 mmol N-hexyl-N'-(3-(1-butoxy-4-(4'-butylphenylazo)-2-phenyl)-ethyl) urea, 200 mL H$_2$O, and 200 mL pentane. Yield: 90%; IR (neat) 2127, 1695, 1597, 1496, 1465, 1253, 1105, 813 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (m, 4H), 7.33 (m, 2H), 6.96 (d, $J$ = 8.4 Hz, 1H), 4.07 (t, $J$ = 6.2 Hz, 2H), 3.51 (t, $J$ = 7.2 Hz, 2H), 3.05 (t, $J$ = 7.2 Hz, 2H), 3.01 (t, $J$ = 7.2 Hz, 2H), 2.68 (t, $J$ = 7.6 Hz, 2H), 1.84 (m, 2H), 1.66 (m, 2H), 1.55 (m, 2H), 1.40 (m, 2H), 1.24 (m, 8H), 1.02 (t, $J$ = 7.6 Hz, 3H), 0.96 (t, $J$ = 7.2 Hz, 3H), 0.86 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 159.7, 151.2, 146.5, 145.9, 140.6, 129.2 (2C), 127.9, 124.7, 124.2, 122.7 (2C), 111.1, 68.1, 46.9, 46.3, 35.7, 33.7, 33.0, 31.6, 31.5, 31.4, 26.6, 22.7, 22.5, 19.6, 14.2, 14.1 (2C) HRMS (FAB) calcd for C$_{29}$H$_{42}$N$_{4}$O (MH$^+$) 463.3437. Found 463.3401.

3-(1-Hydroxy-2-phenyl) propionic acid. A 250 mL round bottom flask was charged with a stir bar and dihydrocoumarin (13.0 mL, 100 mmol). A solution of sodium hydroxide (12 g, 300 mmol) in H$_2$O (100 mL) was added slowly and the flask was fitted with a reflux condenser. The reaction stirred at reflux for 1.5 hours. After cooling to $< 5$
9°C in an ice bath the reaction mixture was acidified with 6 N HCl and the product precipitated as a white powder. Yield: 99%; $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 12.06 (s, 1H), 9.34 (s, 1H), 7.05 (dd, $J = 7.2$, 1.6 Hz, 1H), 7.00 (dd, $J = 8.0$, 7.6, 1.6 Hz, 1H), 6.77 (d, $J = 8.0$ Hz, 1H), 6.69 (dd, $J = 7.6$, 7.2 Hz, 1H), 2.73 (t, $J = 7.6$ Hz, 2H), 2.46 (t, $J = 7.6$ Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 174.2, 155.1, 129.7, 127.1, 126.8, 118.8, 114.8, 33.6, 25.5; Anal Calcd. For C$_9$H$_{10}$O$_3$: C, 65.05; H, 6.07; O, 28.88. Found: C, 64.78; H, 6.00; O, 28.66.

3-(1-Hydroxy-2-phenyl) propionic acid ethyl ester. A 500 mL round bottom flask was charged with a stir bar and a mixture of EtOH (60 mL) and CHCl$_3$ (200 mL). 3-(1-Hydroxy-2-phenyl) propionic acid (14.19 g, 85.37 mmol) was dissolved in the mixture, and concentrated sulfuric acid (5 mL) was added slowly. The flask was fitted with a reflux condenser, and the reaction mixture was heated at reflux with stirring for 16 hours. After cooling to room temperature the product solution was washed with H$_2$O (2 x 200 mL), saturated sodium bicarbonate (2 x 200 mL), and H$_2$O (2 x 200 mL). The organic phase was dried over magnesium sulfate, and the solvent was removed leaving a white solid. Yield: 89%; $^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 9.39 (s, 1H), 7.00 (m, 2H), 6.75 (d, $J = 8.1$ Hz, 1H), 6.67 (t, $J = 7.4$ Hz, 1H), 4.01 (q, $J = 7.0$ Hz, 2H), 2.74 (t, $J = 7.6$ Hz, 2H), 2.51 (t, $J = 7.6$ Hz, 2H), 1.13 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (75 MHz, DMSO-d$_6$) $\delta$: 172.6, 155.2, 129.8, 127.3, 126.5, 118.9, 114.9, 59.8, 33.6, 25.3, 14.2; Anal Calcd. For C$_{11}$H$_{14}$O$_3$: C, 68.02; H, 7.27; O, 24.71. Found: C, 68.14; H, 7.22; O, 24.81.

3-(1-((S)-2-Methylbutoxy)-2-phenyl) propionic acid. An identical procedure for the preparation of 3-(1-((S)-2-methylbutoxy)-4-(4′-butylphenylazo)-2-phenyl)
propionic acid was employed. The quantities of reagents used were 2.58 g, 108 mmol sodium hydride, 150 mL DMF, 12.53 g, 64.51 mmol 3-(1-hydroxy-2-phenyl) propionic acid ethyl ester, 50 mL DMF, 15.65 g, 64.67 mmol (S)-2-methyl-1-butyl tosylate, and 50 mL DMF. In the second step quantities of reagents used were 50 mL ethanol, 6.0 g, 150 mmol sodium hydroxide, 15 mL H₂O, and 40 mL additional H₂O. Yield: 64% (two steps); [α]²⁵D +8.5 (c 0.83, CHCl₃); IR (neat) 2962, 1709, 1495, 1454, 1244, 1111, 750 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 7.14 (m, 2H), 6.91 (d, J = 8.0 Hz, 1H), 6.83 (dt, J = 0.8, 7.2 Hz, 1H), 3.83 (m, 2H), 2.78 (t, J = 7.8 Hz, 2H), 2.46 (t, J = 7.8 Hz, 2H), 1.82 (m, 1H), 1.52 (m, 1H), 1.27 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 174.1, 156.5, 129.6, 128.7, 127.5, 120.0, 111.2, 71.9, 34.3, 33.8, 25.7, 25.6, 16.6, 11.3; Anal Calcd. For C₁₄H₂₀O₃: C, 71.16; H, 8.53; O, 20.31. Found: C, 71.10; H, 8.54; O, 20.23.

*N*-Hexyl-*N'*-(3-((S)-2-methylbutoxy)-2-phenyl)-ethyl) urea. An identical procedure for the preparation of *N*-hexyl-*N'*-(3-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl)-ethyl) urea was employed. The quantities of reagents used were 8.17 g, 34.6 mmol 3-((S)-2-methylbutoxy)-2-phenyl) propionic acid, 70 mL dry toluene, and 10.0 mL, 115 mmol oxalyl chloride. The crude product was 3-((S)-2-methylbutoxy)-2-phenyl) propionyl chloride. IR (neat) 2962, 2929, 2875, 1799, 1495, 1456, 1246, 1038, 752 cm⁻¹. In the second step the quantities of reagents used were 70 mL dry toluene, and 15.0 mL, 113 mmol azidotrimethylsilane. The crude product was 3-((S)-2-methylbutoxy)-2-phenyl)-ethyl isocyanate. IR (neat) 2274, 1494, 1456, 1244, 1118, 752 cm⁻¹. In the final step 150 mL CHCl₃, and 4.6 mL, 35 mmol hexylamine were
used. Yield: 99% (three steps); IR (neat) 3335, 2959, 1635, 1494, 1454, 1244, 1120, 750 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.15 (td, J = 7.6, 1.6 Hz, 1H), 7.09 (dd, J = 7.6, 1.6 Hz, 1H), 6.92 (dd, J = 7.6, 1.6 Hz, 1H), 6.84 (td, J = 7.6, 1.6 Hz, 1H), 5.76 (t, J = 5.6 Hz, 1H), 5.73 (t, J = 5.6 Hz, 1H), 3.78 (m, 2H), 3.18 (td, J = 6.8, 5.6, Hz, 2H), 2.95 (td, J = 7.2, 5.6 Hz, 2H), 2.65 (t, J = 7.2 Hz, 2H), 1.8 (m, 1H), 1.5 (m, 1H), 1.3 (m, 9H), 1.0 (d, J = 6.8 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 156.7, 130.0, 127.6, 127.4, 120.0, 111.3, 71.9, 39.4, 39.2, 34.3, 31.1, 30.9, 30.0, 26.1, 25.7, 22.1, 16.6, 13.9, 11.2; Anal Calcd. For C₂₀H₃₄N₂O₂: C, 71.81; H, 10.25; N, 8.37; O, 9.57. Found: C, 72.08; H, 10.31; N, 8.26; O, 9.40.

**N-Hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide.** (4) An identical procedure for the preparation of N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-4-(4'-butylphénylazo)-2-phenyl)-ethyl) carbodiimide was employed. The quantities of reagents used were 12.40 g, 47.29 mmol triphenylphosphine, 150 mL CH₂Cl₂, 2.2 mL, 43 mmol bromine, 30 mL CH₂Cl₂, 12.4 mL, 89.0 mmol triethylamine, 1.50 g, 34.3 mmol N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) urea, 200 mL H₂O, and 250 mL pentane. Yield: 87%; IR (neat) 2959, 2127, 1494, 1454, 1245, 1118, 751 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.18 (m, 2H), 6.86 (m, 2H), 3.80 (m, 2H), 3.43 (t, J = 7.2 Hz, 2H), 3.07 (t, J = 7.0 Hz, 2H), 2.92 (t, J = 7.0 Hz, 2H), 1.89 (m, 1H), 1.53 (m, 3H), 1.31 (m, 7H), 1.05 (d, J = 6.4 Hz, 3H), 0.96 (t, J = 7.6 Hz, 3H), 0.89 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.4, 130.9, 128.0, 127.3, 120.3, 111.1, 72.6, 46.9, 46.6, 35.1, 33.1, 31.6, 31.4, 26.7 (2C), 26.4, 22.8, 17.0, 14.3, 11.6; HRMS (FAB) calcd for C₂₀H₃₂N₂O (MH⁺) 317.2593. Found 317.2598.
3-(1-((R/S)-2-Methylbutoxy)-2-phenyl) propionic acid. An identical procedure for the preparation of 3-(1-((S)-2-methylbutoxy)-4-(4'-butylphenylazo)-2-phenyl) propionic acid was employed. The quantities of reagents used were 2.42 g, 101 mmol sodium hydride, 200 mL DMF, 15.99 g, 82.33 mmol 3-(1-Hydroxy-2-phenyl) propionic acid ethyl ester, 30 mL DMF, and 20.81 g, 85.97 mmol (R/S)-2-methyl-1-butyl tosylate, 20 mL DMF, 20 mL ethanol, 8.17 g, 204 mmol sodium hydroxide, 65 mL H₂O, and 60 mL additional H₂O. Yield: 64% (two steps). This compound displayed identical spectral characteristics to the chiral 3-(1-((S)-2-methylbutoxy)-2-phenyl) propionic acid. Anal Calcd. For C₁₄H₂₀O₃: C, 71.16; H, 8.53; O, 20.31. Found: C, 71.22; H, 8.53; O, 20.31.

N-Hexyl-N’-(3-(1-((R/S)-2-methylbutoxy)-2-phenyl)-ethyl) urea. An identical procedure for the preparation of N-hexyl-N’-(3-1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) urea was employed. The quantities of reagents used were 12.25 g, 46.33 mmol 3-(1-((R/S)-2-methylbutoxy)-2-phenyl) propionic acid, 80 mL dry toluene, and 12 mL, 140 mmol oxalyl chloride. The crude product was 3-(1-((R/S)-2-methylbutoxy)-2-phenyl) propionyl chloride. IR (neat) 2962, 1800, 1496, 1456, 1246, 1038, 752 cm⁻¹. In the second step the quantities of reagents were 80 mL dry toluene, and 15 mL, 110 mmol azidotrimethylsilane. The crude product was 3-(1-((R/S)-2-methylbutoxy)-2-phenyl)-ethyl isocyanate. IR (neat) 2963, 2275, 1603, 1496, 1455, 1245, 752 cm⁻¹. In the final step 180 mL CHCl₃, and 6.1 mL, 46 mmol hexylamine were used. Yield: 96%; (three steps) This compound displayed identical spectral characteristics to the chiral N-hexyl-N’-(3-(1-(S)-2-methylbutoxy)-2-phenyl)-ethyl) urea. Anal Calcd. For C₂₀H₃₄N₂O₂: C, 71.81; H, 10.25; N, 8.37; O, 9.57. Found: C, 71.65; H, 10.27; N, 8.23; O, 9.81.

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**N-Hexyl-N’-(3-1-((R/S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide. (5)**

An identical procedure for the preparation of N-hexyl-N’-(3-1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide was employed. The quantities of reagents used were 6.19 g, 23.6 mmol triphenylphosphine, 20 mL CH₂Cl₂, 1.2 mL, 23 mmol bromine, 5 mL CH₂Cl₂, 6.5 mL, 47 mmol triethylamine, 6.06 g, 18.1 mmol N-hexyl-N’-(3-1-((R/S)-2-methylbutoxy)-2-phenyl)-ethyl) urea, 50 mL H₂O, and 100 mL pentane. Yield: 93%; This compound displayed identical spectral characteristics to the chiral N-hexyl-N’-(3-1-(S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide. HRMS (FAB) calcd for C₂₀H₃₂N₂O (MH⁺) 317.2593. Found 317.2597.

**3-(1-Butoxy-2-phenyl) propionic acid.** An identical procedure for the preparation of 3-1-((S)-2-methylbutoxy)-4-(4’-butylphenylazo)-2-phenyl) propionic acid was employed. The quantities of reagents used were 0.57 g, 24 mmol sodium hydride, 70 mL DMF, 3.02 g, 15.6 mmol 3-(1-hydroxy-2-phenyl) propionic acid ethyl ester, 15 mL DMF, and 3.56 g, 15.6 mmol butyl tosylate, 15 mL DMF, 3 mL ethanol, 0.41 g, 10 mmol sodium hydroxide, 1.0 mL H₂O, and 10 mL additional H₂O. Yield: 68% (two steps); IR (neat) 2960, 2873, 1709, 1495, 1454, 1244, 752 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 12.08 (s, 1H), 7.14 (m, 2H), 6.92 (d, J = 8.0 Hz, 1H), 6.83 (t, J = 7.4 Hz, 1H), 3.96 (t, J = 6.4 Hz, 2H), 2.77 (t, J = 7.8 Hz, 2H), 2.46 (t, J = 7.8 Hz, 2H), 1.71 (m, 2H), 1.46 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 174.0, 156.5, 129.5, 128.6, 127.5, 120.1, 111.3, 67.0, 33.7, 30.9, 25.5, 18.9, 13.8; Anal Calcd. For C₁₃H₁₆O₃: C, 70.24; H, 8.16; O, 21.59. Found: C, 70.29; H, 8.25; O, 21.44.
**N-Hexyl-N’-(3-(1-butoxy-2-phenyl)-ethyl) urea.** An identical procedure for the preparation of N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) urea was employed. The quantities of reagents used were 0.47 g, 2.1 mmol 3-(1-butoxy-2-phenyl) propionic acid, 5 mL dry toluene, and 1.0 mL, 11 mmol oxalyl chloride. The crude product was 3-(1-butoxy-2-phenyl) propionyl chloride IR (neat) 2960, 2935, 2873, 1799, 1495, 1456, 1246, 1028, 956, 752 cm\(^{-1}\). In the second step the quantities of reagents were 5 mL dry toluene, and 1.2 mL, 9.0 mmol azidotrimethylsilane. The crude product was 3-(1-butoxy-2-phenyl)-ethyl isocyanate. IR (neat) 2960, 2274, 1495, 1454, 1244, 1119, 752 cm\(^{-1}\). In the final step 10 mL CHCl\(_3\), and 0.3 mL, 2.2 mmol hexylamine were used. Yield: 95% (three steps); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 7.15 (td, \(J = 7.6, 1.6\) Hz, 1H), 7.09 (dd, \(J = 7.6, 1.6\) Hz, 1H), 6.92 (dd, \(J = 7.6, 1.6\) Hz, 1H), 6.84 (td, \(J = 7.6, 1.6\) Hz, 1H), 5.76 (t, \(J = 5.6\) Hz, 1H), 5.72 (t, \(J = 5.6\) Hz, 1H), 3.95 (t, \(J = 6.4\) Hz, 2H), 3.17 (td, \(J = 7.2, 5.6\) Hz, 2H), 2.95 (td, \(J = 6.8, 5.6\) Hz, 2H), 2.64 (t, \(J = 6.8\) Hz, 2H), 1.79 (m, 2H), 1.50 (m, 2H), 1.28 (m, 8H), 0.94 (t, \(J = 7.6\) Hz, 3H), 0.86 (t, \(J = 6.8\) Hz, 3H); \(^13\)C NMR (100 MHz, DMSO-d\(_6\)) \(\delta\) 158.0, 156.6, 130.0, 127.6, 127.4, 120.1, 111.4, 67.1, 39.4, 39.2, 31.1, 30.9 (2C), 30.0, 26.1, 22.1, 18.9, 14.0, 13.8; Anal Calcd. For C\(_{19}\)H\(_{32}\)N\(_2\)O\(_2\): C, 71.21; H, 10.06; N, 8.74; O, 9.98. Found: C, 71.02; H, 10.15; N, 8.97; O, 10.18.

**N-Hexyl-N’-(3-(1-butoxy-2-phenyl)-ethyl) carbodiimide.** (6) An identical procedure for the preparation of N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide was employed. The quantities of reagents used were 0.64 g, 2.4 mmol triphenylphosphine, 8.0 mL CH\(_2\)Cl\(_2\), 0.12 mL, 2.3 mmol bromine, 1.5 mL CH\(_2\)Cl\(_2\), 0.66 mL, 4.7 mmol triethylamine, 0.49 g, 1.5 mmol N-hexyl-N’-(3-(1-butoxy-2-phenyl)-ethyl)
urea, 40 mL H$_2$O, and 20 mL pentane. Yield: 90%; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18 (m, 2H), 6.87 (m, 2H), 3.97 (t, $J = 6.4$ Hz, 2H), 3.43 (td, $J = 7.4$ Hz, 2H), 3.06 (t, $J = 6.8$ Hz, 2H), 2.91 (t, $J = 7.4$ Hz, 2H), 1.79 (m, 2H), 1.50 (m, 4H), 1.28 (m, 6H), 0.99 (t, $J = 7.4$ Hz, 3H), 0.89 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.3, 130.9, 128.0, 127.2, 120.3, 111.2, 67.6, 46.9, 46.5, 33.0, 32.4, 31.6, 31.4, 26.7 (2C), 22.8, 19.6, 14.2, 14.1; HRMS (FAB) calcd for C$_{19}$H$_{30}$N$_2$O (MH$^+$) 303.2436. Found 303.2422.

**Di-n-hexyl urea.** In a 250 mL round bottom flask charged with a stir bar hexyl isocyanate (3.0 mL, 21 mmol) was dissolved in CHCl$_3$ (80 mL). The solution was cooled in an ice bath and then hexyl amine (2.7 mL, 21 mmol) was added. The reaction stirred for 30 minutes. The solvent was removed leaving a white solid that was dried in vacuo. No further purification was required. Yield 99% $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 5.71 (t, $J = 5.6$ Hz, 2H), 2.94 (q, $J = 6.4$ Hz, 4H), 1.29 (m, 16H), 0.86 (t, $J = 6.8$ Hz, 6H); $^{13}$C NMR (400 MHz, DMSO-d$_6$) $\delta$ 158.1, 39.2 (2C), 31.1 (2C), 30.0 (2C), 26.1 (2C), 22.1 (2C), 13.9 (2C).

**Di-n-hexyl carbodiimide.** (7) An identical procedure for the preparation of N-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl-ethyl) carbodiimide was employed. The quantities of reagents used were 3.58 g, 13.7 mmol triphenylphosphine, 46 mL CH$_2$Cl$_2$, 0.7 mL, 13 mmol bromine, 10 mL CH$_2$Cl$_2$, 4.0 mL, 27 mmol triethylamine, 2.50 g, 10.9 mmol di-n-hexyl urea. Yield: 93% IR (neat) 2929, 2129, 1439, 1121, 721 cm$^{-1}$.

**General polymerization procedure for the preparation of homo- and copolymers.** Poly(di-n-hexyl guanidine), P7. Under the inert atmosphere of a dry box, 134 mg, 0.637 mmol of di-n-hexyl carbodiimide, 7, was weighed into a screw-capped
vial. A stir bar was added to the vial, and the vial was put on a magnetic stir plate. 5.7 mg, 26 \( \mu \)mol of bischloro-\( \eta^5 \)-cyclopentadienyl-dimethylamido titanium IV, III, was added to the vial and the cap was screwed on tightly. After addition of the catalyst a screw cap was placed on the vial and the vial was removed from the dry box. The polymerization stirred at room temperature until the reaction mixture formed a gel and stirring ceased. At this time it was assumed that the polymerization was complete. The cap was removed from the vial, and wet toluene (0.5 mL) was added to terminate the polymerization and dissolve the polymer. The toluene solution was poured into a beaker of rapidly stirring methanol (250 mL), and the polymer precipitate was collected by filtration. Yield 70-90\% IR (neat) 2929, 2129, 1439, 1121, 721 cm\(^{-1}\).

In the case of a copolymerization the comonomers were mixed well before the addition of any catalyst. In the cases where the polymerization was done in a solvent a stock solution of catalyst was prepared in either dry chloroform or dry toluene and a small amount of that solution was added to the monomer mixture. The amount of wet toluene varied for each polymerization and in each case was just enough to dissolve the polymer (0.5 to 10 mL).
2.7 References and Notes


10 Adapted from reference 4.


16 Instrument accuracy for optical rotation is ± 0.002°. Converting to specific optical rotation with a path length of 50 mm and a concentration of 2.4 mg/mL gives a standard deviation of ±1.6°. Converting this standard deviation to confidence interval via CI = σ* t/√(N) where σ is standard deviation, t is the t-value for 30 degrees of freedom, 0.68, and N is the number of measurements, 31, the confidence interval is ± 0.2°.
Chapter 3: A Modified Approach to Photoswitchable Copolymers

3.1 Introduction

Polyguanidines are known to have a helical backbone, and chiral side chains can lead to a biased helical sense.\textsuperscript{1,2} We have prepared several new carbodiimide monomers. These monomers include chiral, achiral, and racemic versions of monomers that have azobenzene functional groups and analogous monomers without azobenzene groups. We have also synthesized various homopolymers and copolymers of these monomers. For the polymers prepared so far we have seen some evidence of a biased helix, although amplification in the optical properties of the polymers has been less than expected.

We have thus far only observed amplification through the specific optical rotations of the polymers. We have been unable to use circular dichroism (CD) spectroscopy to observe helicity in these polymers due to the insolubility of the polymers in solvents suitable for that measurement. In addition to preventing CD measurements poor solubility of the polymers has caused other problems. Viscous solutions have made polarimetry measurements difficult. In some cases annealing the polymer solutions led to specific rotations indicating the presence of biased helices, but very little or no cooperativity was observed.

Due to the difficulties we encountered with the polymers and in light of the relatively long monomer synthesis compared to other carbodiimide monomers with which our group has worked,\textsuperscript{1} we chose to pursue new target monomers. In modifying our approach we had three goals. First, we wanted to use monomers that were easier to
synthesize and purify. A second goal was to structurally simplify the monomers and consequently the polymers. Polymers with bulky side chains may have more difficulty orienting into a helix. Our third goal was to improve the solubility of the polymers, because a major problem with our studies up to this point was the solubility of the polymers.

### 3.1.1 New Monomers

The solubility problems with copolymers of 1 and 7, Figure 2.7 on page 34, did not extend to the homopolymer of 1. We cannot explain why 1 and 7, each of which forms a soluble homopolymer, lead to a copolymer of low solubility. In an attempt to improve the solubility of the polymers we changed the spacer monomer to \( N \)-hexyl-\( N' \)-phenylcarbodiimide, 8. The homopolymer of 8 is soluble in CHCl₃, toluene, and benzene. The regiospecific polymerization of 8 may also be advantageous.

Regiospecificity is a property that may help us in our goal to form highly ordered polymers. Asymmetrically substituted carbodiimides can be polymerized via two pathways depending on which carbon-nitrogen double bond undergoes insertion, Figure 3.1. Depending upon the steric and electronic properties of the substituents, the polymerization may be more or less regiospecific. A larger difference in properties of the substituents generally leads to a more regiospecific polymer. Previous studies involving 8 have shown that the homopolymer of 8 forms a regiospecific polymer with the phenyl group in the amine position, Figure 3.2. This regiospecificity will give our polymers a very regular structure, which can promote helix formation.
Figure 3.1: Two possible insertion pathways in the polymerization of carbodiimides.
In an effort to simplify the monomer containing the chiral center and azobenzene group we looked to chiral monomers our group had previously studied. We chose to base our chiral switching monomer on $N$-methyl-$N'-(1,S)$-phenylethyl)carbodiimide, 9S, which also homopolymerizes into a regiospecific polymer.\textsuperscript{3,4} So our new target monomer was $N$-methyl-$N'-(1,S)-(4$-phenylazo$)$phenylethyl$)carbodiimide, 10S, Figure 3.3. We

\begin{center}
\begin{tikzpicture}
    % Drawing code here
\end{tikzpicture}
\end{center}

\textbf{Figure 3.3:} New chiral-switching monomer, 10S, based on previously studied chiral monomer, 9S.
thought the proximity of the chiral center to both the polymer and the azobenzene would likely enhance both the transfer of chirality and the effect of azo isomerization. This monomer is also somewhat similar to an isocyanate monomer, 4-((2,S)-isocyanatopropoxy)azobenzene, used in a more recent study by Zentel\(^5\), Figure 3.4.

![4-((2,S)-isocyanatopropoxy)azobenzene](image)

**Figure 3.4:** Chiral-azo isocyanate monomer that leads to a very high chiral induction.

In that study an extremely high chiral induction was observed and photoisomerization of the azo group had no effect on the helical sense of the polymer backbone. The large chiral induction is likely due to the proximity of the chiral group to the polymer backbone. Our chiral center is in the same position relative to the polymer backbone so we were hopeful of a high chiral induction. Our azobenzene group is closer to both the chiral center and the polymer backbone than Zentel's was, so we were hopeful that we would see some effect of the azobenzene isomerization.

### 3.1.2 Monomer Synthesis

The synthesis of 8 is a simple two-step process. Aniline and hexyl isocyanate react in chloroform at room temperature to form N-hexyl-N’-phenylurea which is then dehydrated with dibromotriphenylphosphorane, Scheme 3.1. The boiling point of 8 is
low enough that it can be purified by vacuum distillation. We initially designed a four-step synthesis for 10S beginning with commercially available (S)-1-methyl-4-nitrobenzylamine, Scheme 3.2. In the planned synthesis after reduction of the aromatic nitro group to the amine by hydrogenation, diazotization with nitrosobenzene would give 4-(1,S)-aminoethyl azobenzene. Upon urea formation and dehydration 10S would be obtained. The diazotization step proved difficult and although we could see no reason that the primary amine would impede his reaction, literature suggested that it was necessary to protect the primary amine during this step. With the protection and deprotection the synthesis grew to six steps and we were further from our goal of a simple, quick monomer synthesis.

An additional concern involving this monomer was the expected solubility, or possible insolubility, upon polymerization. While the monomer structure appears advantageous for both chiral induction and molecular switching, the homopolymer of 9S
on which 10S is based has limited solubility. It is likely that a homopolymer of 10S would be even less soluble. Initially we were willing to take a chance on 10S because the synthesis seemed simple and efficient and the structure looked so promising for chiral induction that we anticipated small amounts would be needed to bias the helix. We hoped that the solubility of a copolymer containing small amounts of 10S copolymerized with 8 would show similar solubility to a homopolymer of 8. As the synthesis grew, however, the time and monetary investment (the starting material is very expensive) grew also.
Furthermore it is likely that purification of **10S** would be difficult due to its molecular weight. Discouraged by the growing synthesis and anticipated difficulties we abandoned the pursuit of **10S** in favor of a new approach.

### 3.2 A New Strategy

The simplest way of incorporating both a chiral center and an azobenzene group into the side chains of a polyguanidine is to copolymerize one monomer that contains a chiral center with a second monomer that contains the switching group. These monomers can also be polymerized with a third monomer that acts as a spacer. It is in this way that we revised our strategy towards studying molecular switching in the polyguanidines.

Most studies involving manipulation of chiral induction through side chain isomerization including our own efforts rely on an azobenzene switching group in close proximity to both the chiral center and the polymer backbone.\(^5\,8,9\) This is based on the assumption that the spatial orientation of the chiral center relative to the polymer backbone dictates the effectiveness of the transfer of chirality from the chiral center to the polymer backbone. This orientation has been influenced in the past by manipulation of the chiral group. The chiral group was attached to the azobenzene, and isomerization of the azobenzene changed the position of the chiral group relative to the stationary polymer backbone. We wondered if the same effect could be seen by using the azobenzene to adjust the polymer backbone conformation relative to a "stationary" chiral side chain. One way to adjust a polymer backbone conformation is to change the inversion barrier of the polymer.
3.2.1 *Inversion Barrier*

Each helical polymer has a characteristic energy barrier to helix inversion. This energy barrier is the activation energy required for the polymer to orient into its thermodynamically preferred conformation.\(^2\) Inversion barrier is a property of helical polymers that has been discussed, but that we had not studied for our specific polymers. We think that the helix inversion barrier of a polymer can be affected by the isomerization of azobenzene units in the polymer side chains. The change in inversion barrier may shift the equilibrium ratio of left- and right-handed helices.

To determine the inversion barrier of the homopolymer of an achiral monomer that monomer is first polymerized with a chiral catalyst. The chiral catalyst induces a biased helical conformation in the resulting polymer.\(^{10,11}\) Because helix reversals are constantly moving along the polymer backbone and there is no thermodynamically preferred helical sense, over time the polymer backbone will racemize into a mixture of left- and right-handed helical regions of equivalent sizes. This involves inversion between the two helical senses. Modeling this as a reversible equilibrium between two states and assuming that this process follows first order kinetics we can calculate the approximate activation energy for this process.\(^{10}\)

A reversible reaction can be represented by equation 3.1 where A and B are the species in equilibrium, \(k_f\) is the forward rate constant, and \(k_b\) is the reverse rate constant.

\[
\begin{align*}
A & \underset{k_b}{\overset{k_f}{\rightleftharpoons}} B \\
(3.1)
\end{align*}
\]
In this case A represents the helical sense of the initially formed single-handed helix and B represents the opposite helical sense. The rate equation for a reversible reaction is shown in equation 3.2. Putting this equation in terms of the concentrations of A at time equal to t and at equilibrium and integrating gives equation 3.3. A detailed derivation of this equation can be found in Appendix A3.1.

\[
\text{rate} = \frac{-d[A]}{dt} = k_f[A] - k_b[B] \tag{3.2}
\]

\[
\ln \left( \frac{[A]_t - [A]_{eq}}{[A]_0 - [A]_{eq}} \right) = -(k_f + k_b)t = -k_{obs}*t \tag{3.3}
\]

We cannot directly measure the concentration of A so we let the initially measured specific optical rotation represent the initial concentration of A. The subsequent decrease in magnitude of the observed specific optical rotation is a consequence of both the decrease in concentration of A and the concurrent increase in concentration of B. These concentration changes are equal in magnitude and have identical effects on the observed specific optical rotation. So, any observed change in specific optical rotation, \([\alpha]\), is twice the change that would be expected due to the change in concentration of only A, \([\alpha_A]\). To let specific optical rotation represent concentration of A the measured \([\alpha]\) must be converted to \([\alpha_A]\) using equation 3.4, where \([\alpha]\) equals \([\alpha_A]_1\). After

\[
2\Delta[\alpha_A] = \Delta[\alpha]
\]

\[
2([\alpha_A]_{(x+1)} - [\alpha_A]_x) = [\alpha]_{(x+1)} - [\alpha]_x
\]

\[
[\alpha_A]_{(x+1)} = [\alpha_A]_x + ([\alpha]_{(x+1)} - [\alpha]_x)/2 \tag{3.4}
\]
converting each \([\alpha]\) to \([\alpha_A]\) we can use \([\alpha_A]\) to represent the concentration of A. Then the approximate rate constant for inversion at a given temperature can be calculated using equation 3.5. The subscripts o, eq, and t represent initial, at equilibrium, and at time "t" and are used to designate when \([\alpha]\) was measured. The calculated rate constant and the

\[
\ln \left( \frac{[\alpha_A]_t - [\alpha_A]_{eq}}{[\alpha_A]_0 - [\alpha_A]_{eq}} \right) = -k_{obs} t
\]

(3.5)

time are represented by \(k_{obs}\) and \(t\) respectively. As calculated \(k_{obs}\) is a function of both the forward and reverse rate constants for this equilibrium. However, in the case of a single handed helix racemizing into enantiomeric left- and right-handed helices, A and B are equal in energy, so \(k_f\) and \(k_b\) for that equilibrium must be equal, and \(k_{obs}\) is equal to \(2k_f\).

After rate constants are determined at several temperatures, an Arrhenius plot can be constructed to determine the activation energy for helix inversion. The Arrhenius equation is equation 3.6 where \(k\) is a rate constant, \(A\) is a constant, \(E_a\) is the activation energy, \(R\) is the ideal gas constant, and \(T\) is absolute temperature. The Arrhenius equation can be rearranged to equation 3.7. To determine an activation energy the natural logs of

\[
k = Ae^{(-E_a/RT)}
\]

(3.6)

\[
\ln k = \frac{-E_a}{R} \left( \frac{1}{T} \right) + \ln A
\]

(3.7)

several rate constants are plotted against the inverse of the temperature at which they were measured. The activation energy can be calculated from the slope of the graph.
3.2.2 Monomer Synthesis

For our chiral monomer we chose \(N\)-methyl-\(N'\)-((1,\(S\))-phenylethyl)carbodiimide, \(9S\). This monomer is synthesized in good yield by a two-step one-pot process, Scheme 3.3. The commercially available \((S)\)-(1)-methylbenzylamine reacts with methylisothiocyanate to form the thiourea. Upon addition of mercury (II) oxide to the reaction mixture the thiourea is converted to the carbodiimide. Monomer \(9S\) is easily purified by vacuum distillation.

The azobenzene containing monomer, \(N\)-hexyl-\(N'\)-((4-phenylazo)phenyl)carbodiimide, \(11\), was synthesized via a different two-step synthetic route, Scheme 3.4. Commercially available 4-phenylazoaniline was allowed to react with hexylisocyanate in refluxing toluene to give the \(N\)-hexyl-\(N'\)-((4-phenylazo)phenyl)urea.
Scheme 3.4: Synthesis of monomer 11.

The urea was then dehydrated using dibromotriphenylphosphorane, which was generated in situ. Monomer 11 could not be purified by vacuum distillation. Upon heating under reduced pressure 11 undergoes a disporportionation reaction which gives di-n-hexylcarbodiimide and di-(4-phenylazo)phenylcarbodiimide. This behavior has also been seen with other high molecular weight carbodiimides.\(^7\) Vacuum distillation of 11 yielded a distillate consisting of pure di-n-hexylcarbodiimide. Ultimately, 11 was used in a slightly impure form that contained a small amount of triphenylphosphine oxide.

3.2.3 Inversion Barriers of the Polymers.

To begin our studies of these polymers we homopolymerized azo monomer 11 and determined its inversion barrier. Monomer 11 was homopolymerized with the chiral catalyst (S)-[Ti(OPr\(^+\))\(_2\)(BINOLato)], VIII, Figure 3.5, generously supplied by Dr. Gonglu.
Figure 3.5: Chiral catalyst, VIII, for carbodiimide polymerization.

Tian. The polymerization was performed under neat conditions and was complete after 68 hours. The polymer was recovered by the usual procedure. Additional polymerization data for all polymers can be found in Appendix A3.2. The specific optical rotation of the first isolated polymer was $-135^o$, ($c \ 0.20$, toluene). The polymer solution was annealed at 70 °C for 3 days, and the specific optical rotation was measured to check for racemization of the helix. The solution did show an optical rotation of zero, but this was not due to racemization. An IR spectrum of the polymer solution showed that the polymer had depolymerized, Figure 3.6 (C=N=C, 2137 cm$^{-1}$). Polyguanidines are known to depolymerize at elevated temperatures,$^{12,3}$ Figure 3.7; however, most are stable up to 150 °C.
Figure 3.6: IR spectrum of P11 after annealing. The strong carbodiimide stretch is seen at 2137 cm\(^{-1}\).

Figure 3.7: Mechanism for thermal decomposition of polyguanidines.
Subsequently P11 samples were annealed at 50, 55, and 60 °C. The specific optical rotation of the polymer was followed during annealing, Figure 3.8. The changes in optical rotation with time as the helices racemized allowed calculation of the inversion barrier of this polymer by the method described in section 3.2.1, Figure 3.9 and Figure 3.10. The helix inversion barrier of P11 is 24 kcal/mol. Further details regarding inversion barrier calculations can be found in Appendix A3.3.

**Figure 3.8:** Specific optical rotation as a function of time as P11 is annealed at three different temperatures.
**Figure 3.9:** Determination of rate constant, $k_{\text{obs}}$, for helix inversion in P11 at three different temperatures.

**Figure 3.10:** Arrhenius plot for determining activation energy for helix reversal of P11.

A copolymer of 11 and 8 was synthesized, $P(8_{80}-\text{co}-11_{20})$. This copolymer contained 80% of 8 and 20% of 11 based on monomer feed and was polymerized with VIII, which was also used for P11. The homopolymer of 8, which was studied
previously,\textsuperscript{10} has an inversion barrier of 20 kcal/mol. We expected the copolymer to have an inversion barrier between 20 and 24 kcal/mol. When first isolated $P(8_{80}-co-11_{20})$ had a specific rotation of $-298^\circ$, ($c$ 0.20, toluene). This is more than twice the initial rotation of $P11$. While this may indicate a significant difference in the polymer backbone structure it could be a consequence of sample handling. Once a polymerization is complete that polymer is dissolved in toluene and then precipitated in methanol. Depending on the amount of polymer present, the amount of toluene used, and the solubility of the polymer it may take several hours or more than a day to fully dissolve the polymer. During this time in solution racemization may begin. So the initially observed specific optical rotation of the polymer may not indicate the conformation of the polymer immediately upon polymerization.

Copolymer $P(8_{80}-co-11_{20})$ was annealed at 55 °C and its annealing curve was compared to that of homopolymer $P11$, Figure 3.11. The initial slope of the annealing curve for the copolymer is less steep than the initial slope of the annealing curve for the homopolymer. The difference in the shapes of the annealing curves indicates that racemization takes place more slowly in the copolymer than in the homopolymer $P11$. A slower racemization indicates a higher inversion barrier, which is the opposite to what we expected due to the lower inversion barrier of the homopolymer of 8.
A copolymer of 8 and 9S was also synthesized. This copolymer contained 70% of 8 and 30% of 9S based on monomer feed. The copolymer P(8\textsubscript{70}-co-9S\textsubscript{30}) contains chiral side chains so its thermodynamically controlled conformation is a biased helix. This copolymer was polymerized with achiral catalyst IV which resulted in a kinetically controlled conformation. So far in the current studies we had seen only a small amount of amplification in chiral homopolymer P1, and little or no cooperativity had been observed. Our first concern with P(8\textsubscript{70}-co-9S\textsubscript{30}), even before studying the inversion barrier, was whether or not the chiral monomer could induce a biased helix in the copolymer. Initially P(8\textsubscript{70}-co-9S\textsubscript{30}) had a specific optical rotation of $-50^\circ$. After annealing at 80 °C for 5 hours the specific optical rotation was $+130^\circ$. This amplification indicated a biased helical sense. Subsequently, the copolymer was annealed at 50, 60, and 70 °C, Figure 3.12.

**Figure 3.11**: Comparison of annealing curves for homopolymer P11 and copolymer P(8\textsubscript{80}-co-11\textsubscript{20}) at 55 °C.
Figure 3.12: Specific optical rotation as a function of time as P(870-co-9S30) is annealed at four different temperatures.

For an equilibrium involving diastereomeric helices $k_f$ and $k_b$ are not equal. Using irreversible first order kinetics and only initial data the approximate forward rate constant $k_f$ can be calculated, equations 3.8-3.10. Using $\alpha_A$ as defined in section 3.2.1 we can

$$\begin{align*}
A & \xrightarrow{k_f} B \\
\text{rate} &= \frac{-d[A]}{dt} = k[A] \quad (3.9) \\
\ln [A] &= -k_{obs}t + \ln[A]_0 \\
(k_{obs} \sim k_f) \quad (3.10)
\end{align*}$$

calculate approximate rate constants at each annealing temperature, Figure 3.13. From the rate constants the activation energy for this polymer was determined to be 15 kcal/mol, Figure 3.14.
Figure 3.13: Determination of rate constant, $k_{obs}$, for helix inversion of P(870-co-9S30) at four different temperatures.

Figure 3.14: Arrhenius plot for determination of activation energy of helix inversion for copolymer P(870-co-9S30).
From these preliminary results we learned several things, but we also made several assumptions that should be verified. The chiral monomer, 9S, does induce the polymer backbone to form a biased helix, which we assumed was cooperative. We did not know at this point if the copolymer was actually cooperative i.e., if the achiral monomer units adopt the configuration preferred by the chiral monomer units. The amplification may be due only to the configuration of the chiral monomer units. To prove the cooperativity of this polymer system we needed to synthesize copolymers with varying amounts of chiral monomer.

We have also seen an indication of the effect of comonomer ratio on the inversion barrier of the copolymers. At this point we desired to both determine the inversion barrier of P9S and further study how the inversion barrier of the copolymers is affected by varying the ratios of monomers.

### 3.3 Azobenzene Photochemistry

Concurrent with the preliminary cooperativity and inversion barrier studies we performed several azobenzene isomerization experiments. In studying the photochemistry of our azobenzene polymers there are several variables to consider. Among these are solvent, irradiation wavelength, irradiation time, and sample concentration. The trans isomer of azobenzene has an intense UV absorption at 320 nm corresponding to the \( \pi \rightarrow \pi^* \) transition.\(^{13}\) The intensity of the signal at this wavelength decreases as isomerization proceeds. The cis isomer has a less intense absorption maximum at 430 nm due to the \( n \rightarrow \pi^* \) transition.\(^{13}\) Substitution of the phenyl rings can change the value of \( \lambda_{\text{max}} \) for each
of the transitions. For example, 4-[4’-(hexylphenyl)azo]phenol has a $\lambda_{\text{max}}$ of 361 nm for the $\pi \rightarrow \pi^*$ transition of the trans isomer and 445 nm for the $n \rightarrow \pi^*$ transition of the cis isomer.\textsuperscript{14} This shift in absorbance relative to azobenzene is due to the alkyl substituent and the polar hydroxy group. Poly(3-ethynylazobenzene) is an example of a polymer having an azobenzene side chain. For this polymer, $\lambda_{\text{max}}$ is 340 nm for the trans isomer while a $\lambda_{\text{max}}$ of 450 nm is observed for the cis isomer.\textsuperscript{15}

### 3.3.1 The Photostationary State

The $\text{trans} \rightarrow \text{cis}$ isomerization of an azobenzene group is a photochemical process. The reverse $\text{cis} \rightarrow \text{trans}$ isomerization can proceed either photochemically or thermally. The photostationary state is reached when the rate of $\text{trans} \rightarrow \text{cis}$ photoisomerization is equal to the combined rates of $\text{cis} \rightarrow \text{trans}$ photoisomerization and $\text{cis} \rightarrow \text{trans}$ thermal isomerization. The photostationary state will be represented herein as a percent of either the trans or cis isomer.

Zimmerman, Chow and Paik studied the photostationary state of azobenzene over a variety of conditions and found that this state is independent of concentration over the range of concentrations studied ($10^{-3} - 10^{-5}$) but is highly dependent upon the wavelength of irradiating light.\textsuperscript{16} Specifically as the wavelength of irradiating light increased from 313 nm to 436 nm the photostationary state in terms of concentration of the cis isomer decreased from 80% to 15%. That is when the sample was irradiated with light having a wavelength close to the $\text{trans} \pi \rightarrow \pi^*$ absorption wavelength at least 80% of the sample was converted to the cis isomer. For irradiating light of 365 nm, roughly midway between
the \( \lambda_{\text{max}} \) for the characteristic \textit{trans} and \textit{cis} absorptions, the photostationary state was limited to 40% cis. When the wavelength of irradiating light was very close to the \textit{cis} \( n \rightarrow \pi^* \) absorption wavelength only 15% of the \textit{cis} isomer was attained. So irradiation wavelength is a critical variable in photochemical azobenzene isomerization.

The photostationary state of an azo isomerization is not only a function of irradiation wavelength. Different photostationary states are accessible depending also upon the structure of the compound and its environment (i.e. small molecule solution, polymer solution, or polymeric film). For solutions of various side chain azobenzene containing polymers the range of photostationary states attained include 90% \textit{cis} in about 1 hour for an isocyanate polymer in THF irradiated at 365 nm \((\lambda_{\text{max}} = 354 \text{ nm})\)\textsuperscript{8} and about 30% \textit{cis} in 2 hours for poly(3-ethynylazobenzene) in THF irradiated at 300-400 nm \((\lambda_{\text{max}} = 340 \text{ nm})\).\textsuperscript{15} So, it is very difficult to predict either the composition of the photostationary state or the time to reach that state.

### 3.3.2 Current Work

For our experiments we used a 450 Watt medium pressure, quartz mercury vapor lamp. The lamp was cooled using a cooling well and a thermostated cooled water bath. A high pass filter (350+ nm) was used in combination with a band pass filter centered at 362 nm. The resulting band of irradiation was centered at 370 nm with a width of 40 nm, Figure 3.15. Samples were measured at room temperature.
We irradiated a solution of azobenzene in chloroform and measured a UV spectrum every 10 minutes until the photostationary state was reached at 30 minutes. The photostationary state contained about 66% cis azobenzene which is slightly greater than that obtained by Zimmerman et al. at 365 nm. We isomerized azobenzene in chloroform for comparison to previous work. Most of our polymer solutions, however, will be in toluene due to the high annealing temperatures and the desire to reduce evaporation of the solvent as much as possible. So, following the same procedure as above, measuring UV every 10 min, we irradiated a solution of 4-phenylazoaniline in toluene. 4-Phenylazoaniline has a $\lambda_{\text{max}}$ of 375 nm in toluene for the trans $\pi \rightarrow \pi^*$ transition compared to 320 nm for azobenzene in CHCl$_3$. We chose 4-phenylazoaniline because it was readily available in our lab and we expected $\textbf{P11}$ to show a UV maximum in the same region. The photostationary state was reached in less than 10 minutes and

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{transmission_spectrum}
\caption{Transmission spectrum of combined glass filters.}
\end{figure}
contained about 67% cis isomer. After irradiation additional spectra were measured at ten-minute intervals until the thermal back isomerization was complete. This took place in only 70 minutes, Figure 3.16. The fast rate of back isomerization may make studying the inversion barriers of irradiated polymers difficult.

![UV spectrum of 4-phenylazoaniline during cis → trans back isomerization at room temperature after UV irradiation at 370 nm for 10 minutes.](image)

**Figure 3.16: UV spectrum of 4-phenylazoaniline during cis → trans back isomerization at room temperature after UV irradiation at 370 nm for 10 minutes.**

### 3.3.3 Effect of Annealing on UV spectrum

The UV spectrum of an azobenzene-containing polymer can be affected by factors other than the isomerization of the azobenzene. The polyguanidines that we are using must be annealed before they reach their equilibrium helical conformation. We have seen the effect of annealing on the UV spectrum of P(879-co-920-co-111), Figure 3.17. After annealing the absorbance at 375 nm was only 35% of the pre-annealed value. A sample of 4-phenylazoaniline in toluene annealed for the same time did not show the
Figure 3.17: Azobenzene region of UV spectra of \textbf{P}(8_{76}-co-9S_{23}-co-11_{1})\), before and after annealing at 60 °C for 24 hours.

same change in spectrum. The structural changes that result from annealing likely cause a change in the extinction coefficient of the polymer. Even at room temperature an unannealed sample will begin to equilibrate slowly to its thermodynamically controlled conformation and may have a UV spectra that changes slightly as that equilibration takes place. To isolate the effect of the isomerization on the UV spectra we must isomerize polymer samples that have previously been annealed.

3.4 Discussion

Our hypothesis is that \textit{trans} \(\rightarrow\) \textit{cis} isomerization of an azobenzene in the side chain of a polymer can change the inversion barrier of that polymer. This change in inversion barrier may force the polymer into a more pure or a more racemic helical
conformation. To determine the effect of isomerization on inversion barrier we must measure the inversion barrier, *i.e.* anneal polymer solutions before and after isomerization. If we anneal the polymer after the isomerization following the back isomerization will be problematic because the UV spectrum will change as a result of both the back isomerization and the annealing. Also, the annealing process usually lasts in excess of one day. Significant if not complete back isomerization will take place during that time, so we will not truly be measuring the inversion barrier of a polymer with azobenzene side chains in the *cis* configuration.

Before we could further study our hypothesis and determine if any connection exists between azo isomerization and helix inversion barrier it was necessary to have a more through understanding of the inversion barriers of our polymers and of polyguanidines in general. There are many complexities in the system we were using including multiple monomers and multiple responses to stimuli such as heat and light. It was also important to investigate the optimum monomer ratio for these studies. Due to the complex nature of our task we thought it was best to start with a simple system and proceed from there. Since polymer inversion barrier is at the heart of our theory our next step was to design experiments to study the inversion barriers of a simple series of polymers involving only two comonomers.
3.5 Experimental

3.5.1 General Procedures and Characterizations

Reagents and solvents from commercial sources were used directly. All reactions involving air and moisture sensitive compounds were performed in oven-dried glassware under dry nitrogen using standard Schlenk techniques. All polymerizations were set up in an MBraun UNILab drybox under nitrogen atmosphere using dry solvents (MBraun solvent system).

$^1$H and $^{13}$C NMR spectra were obtained using a Varian Mercury 300 (300 MHz) or Varian Mercury 400 (400 MHz) spectrometer as specified. Chemical shifts are reported in $\delta$ (ppm) and are referenced to selected residual proton peaks for the solvents as follows: For $^1$H NMR solvent residual peaks were 7.26 ppm for CDCl$_3$ and 2.50 ppm for DMSO-d$_6$. For $^{13}$C NMR solvent residual peaks were 77.23 for CDCl$_3$ and 39.51 for DMSO-d$_6$. Significant $^1$H NMR data are tabulated in the following order: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hertz, number of protons.

Infrared spectra were obtained using a Jasco FT/IR-410 spectrometer as thin films on NaCl disks and are uncalibrated. IR data are reported in wavenumbers (cm$^{-1}$).

Optical rotation measurements were obtained on a Jasco P-1010 polarimeter at 589 nm in a 1 dm cell at 25 °C unless noted otherwise. Annealing experiments were conducted in a thermostated 1 dm cell at the specified temperature where temperature control is accurate to $\pm$ 0.1 °C.
UV measurements were obtained on a Jasco UV-Vis 410 spectrophotometer. All measurements were performed at room temperature.

Mass spectra were obtained at the Mass Spectrometry Laboratory for Biotechnology. Partial funding for the Facility was obtained from the North Carolina Biotechnology Center and the National Science Foundation.

Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia.

3.5.2 Procedures

N-Hexyl-N’-phenylurea. A 500 mL round bottom flask was charged with 5.5 mL, 60 mmol aniline and 150 mL CHCl₃. The flask was placed in an ice bath. 8.8 mL, 60 mmol hexylisocyanate was added slowly and the reaction was removed from the ice bath. The reaction stirred at room temperature for 24 hours, and the solvent was removed. The product, a white solid, was dried in vacuo. Yield 99%; ¹H NMR (400 MHz, DMSO-d₆) δ 8.35 (s, 1H), 7.36 (d, J = 7.8 Hz, 2H), 7.18 (t, J = 7.8 Hz, 2H), 6.85 (t, J = 7.8 Hz, 1H), 6.08 (t, J = 5.6 Hz, 1H), 3.05 (td, J = 7.0, 5.6 Hz, 2H), 1.36 (m, 2H), 1.27 (m, 6H), 0.85 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 155.2, 140.6, 128.6 (2C), 120.8, 117.5 (2C), 39.0, 31.0, 29.7, 26.1, 22.1, 13.9.

N-Hexyl-N’-(4-phenylazo)phenylurea. A 250 mL round bottom flask was charged with 5.42 g, 27.5 mmol 4-phenylazoaniline and 50 mL toluene. 4 mL, 27.5 mmol hexylisocyanate was added slowly, and the flask was fitted with a reflux condenser. The reaction was heated at reflux with stirring for 2 hours. The solvent was removed. The
product, a yellow solid, was dried in vacuo. Yield 89%; IR (neat) 3480, 3384, 1617, 1598, 1505, 1341, 835, 689 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 8.89 (s, 1H), 7.81 (m, 4H), 7.55 (m, 5H), 6.29 (t, \(J = 5.6\) Hz, 1H), 3.08 (td, \(J = 6.6, 5.6\) Hz, 2H), 1.42 (m, 2H), 1.27 (m, 6H), 0.86 (t, \(J = 7.0\) Hz, 3H); \(^1^3\)C NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) 154.7, 152.1, 146.1, 144.1, 130.6, 129.4 (2C), 123.9 (2C), 122.2 (2C), 117.4 (2C), 39.1, 31.0, 29.6, 26.0, 22.1, 13.9.

**N-Hexyl-N’-phenylcarbodiimide (8).** An identical procedure for the preparation of\(N\)-hexyl-N’-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide (Chapter 2) was employed. The quantities of reagents used were 18.63 g, 71.04 mmol triphenylphosphine, 50 mL CH\(_2\)Cl\(_2\), 3.5 mL, 68 mmol Br\(_2\), 25 mL CH\(_2\)Cl\(_2\), 20.0 mL, 143 mmol triethylamine, 12.00 g, 54.50 mmol \(N\)-hexyl-N’-phenylurea. Yield: 90%; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29 (m, 2H), 7.11 (m, 3H), 3.41 (t, \(J = 6.8\) Hz, 2H), 1.69 (m, 2H), 1.39 (m, 2H), 1.33 (m, 4H), 0.90 (t, \(J = 7.0\) Hz, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 140.9, 136.2, 129.5 (2C), 124.7, 123.6 (2C), 47.0, 31.5 (2C), 26.6, 22.7, 14.2; Anal Calcd. For C\(_{13}\)H\(_{18}\)N\(_2\): C, 77.18; H, 8.97; N, 13.85. Found: C, 77.27; H, 9.21; N, 13.89.

**N-Methyl-N’-((1,S)-phenylethyl)carbodiimide (9S).** A 250 mL round bottom flask was charged with 14.09 g, 192.8 mmol methylisothiocyanate, a stir bar, and 100 mL CH\(_2\)Cl\(_2\). The flask was placed in an ice bath. 24.6 mL, 193 mmol (S)-(1)-methylbenzylamine was added to the solution and the flask was removed from the ice bath. The solution stirred at room temperature for two hours. The reaction mixture was cooled in an ice bath, and to the cold solution was added 21.29 g Na\(_2\)SO\(_4\) and 86.97 g, 401.6 mmol mercuric oxide (red). The reaction flask was removed from the ice bath, and
the reaction stirred at room temperature for 1 hour. After two filtrations through celite a yellowish liquid was obtained. The solution was concentrated to about 10mL and 20mL hexane was added. The volume of the solution was again reduced to 10mL and the solution was again filtered through celite and the solvent was removed. 0.5 g CaH\textsubscript{2} was added to the crude product and the flask was placed onto a vacuum distillation apparatus. The remaining solvent was removed in vacuo and the pressure was reduced to 30 mtorr. The flask was immediately placed in a 90 °C oil bath and the crude product quickly distilled into a clean dry flask (30 mtorr, 60 °C). The purified product was flushed with nitrogen and subsequently stored in a drybox. Yield 85%; IR (neat) 3029, 2974, 2131, 1493, 1454, 1423, 1303, 1067, 700 cm\textsuperscript{-1}; NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.34 (m, 5H), 4.61 (q, \(J = 6.8\) Hz, 1H), 2.94 (s, 3H), 4.54 (d, \(J = 6.8\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 144.2, 135.0, 128.8 (2C), 127.6, 126.1 (2C), 56.8, 33.0, 25.3; Anal Calcd. For C\textsubscript{10}H\textsubscript{12}N\textsubscript{2}: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.72; H, 7.66; N, 17.37

\textit{N}-Hexyl-\textit{N'}-(4-phenylazo)phenylcarbodiimide (11). An identical procedure for the preparation of \textit{N}-hexyl-\textit{N'}-(3-(1-((S)-2-methylbutoxy)-2-phenyl)-ethyl) carbodiimide (Chapter 2) was employed. The quantities of reagents used were 3.85 g, 14.7 mmol triphenylphosphine, 20 mL CH\textsubscript{2}Cl\textsubscript{2}, 0.70 mL, 14 mmol Br\textsubscript{2}, 10 mL CH\textsubscript{2}Cl\textsubscript{2}, 4.0 mL, 29 mmol triethylamine, 4.39 g, 13.5 mmol \textit{N}-hexyl-\textit{N'}-(4-phenylazo)phenylurea. Yield: 89%; IR (neat) 2928, 2136, 1595, 1505, 1435, 1346, 1139, 845 cm\textsuperscript{-1}.

\textbf{General polymerization procedure for the preparation of homo- and copolymers}. The general polymerization procedure can be found in Chapter 2, section 2.6.2. Tabulated polymerization data are in Appendix A3.2.
3.6 References and Notes

Appendices
A3.1: Derivation of equation 3.3.

A reversible reaction:
\[ A \xrightleftharpoons[k_b]{k_f} B \]

The equilibrium constant:
\[ K_{eq} = \frac{k_f}{k_b} = \frac{[B]_{eq}}{[A]_{eq}} \]
\[ [B]_{eq} = [A]_{eq} \frac{k_f}{k_b} \]

A and B are the only species present so:
\[ [A]_0 + [B]_0 = [A]_t + [B]_t = [A]_{eq} + [B]_{eq} \]

Substituting for \([B]_{eq}\) and rearranging
\[ [A]_t + [B]_t = [A]_{eq} + [A]_{eq} \frac{k_f}{k_b} \]
\[ [B]_t = [A]_{eq} + [A]_{eq} \frac{k_f}{k_b} - [A]_t \]

The rate equation is:
\[ \text{rate} = \frac{-d[A]}{dt} = k_f[A] - k_b[B] \]

Substituting for \([B]\):
\[ \frac{-d[A]}{dt} = k_f[A]_t - k_b ([A]_{eq} + [A]_{eq} \frac{k_f}{k_b} - [A]_t) \]
\[ \frac{-d[A]}{dt} = k_f[A]_t - k_b[A]_{eq} - k_f[A]_{eq} + k_b[A]_t \]
\[ \frac{-d[A]}{dt} = (k_f + k_b)([A]_t - [A]_{eq}) \]

Integrated form:
\[ \ln \left( \frac{[A]_t - [A]_{eq}}{[A]_0 - [A]_{eq}} \right) = -(k_f + k_b)t = -k_{obs}^*t \]
A3.2: Polymerization Table

Table 3.1: Polymerization data.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer</th>
<th>mg</th>
<th>mmol</th>
<th>mol %</th>
<th>Catalyst</th>
<th>Mon:Cat</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>P11</td>
<td>11</td>
<td>512</td>
<td>1.67</td>
<td>100</td>
<td>VII</td>
<td>376:1</td>
<td>Neat</td>
</tr>
<tr>
<td>P(8&lt;sub&gt;80-co-11&lt;sub&gt;20&lt;/sub&gt;)</td>
<td>8</td>
<td>801</td>
<td>3.96</td>
<td>80</td>
<td>VII</td>
<td>468:1</td>
<td>Neat</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>208</td>
<td>0.68</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P(8&lt;sub&gt;70-co-9S&lt;sub&gt;30&lt;/sub&gt;)</td>
<td>8</td>
<td>149</td>
<td>0.74</td>
<td>70</td>
<td>VII</td>
<td>105:1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>9S</td>
<td>51</td>
<td>0.32</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P(8&lt;sub&gt;76-co-9S&lt;sub&gt;23-co-11&lt;sub&gt;1&lt;/sub&gt;)</td>
<td>8</td>
<td>805</td>
<td>3.98</td>
<td>76</td>
<td>IV</td>
<td>360:1</td>
<td>Neat</td>
</tr>
<tr>
<td></td>
<td>9S</td>
<td>198</td>
<td>1.23</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>18</td>
<td>0.06</td>
<td>1</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

A3.3: Determination of Energy Barriers to Helix Inversion

Table 3.2: Least squares calculation of rate constants for helix inversion.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Temp (°C)</th>
<th>least squares fit</th>
<th>R²</th>
<th>k&lt;sub&gt;obs&lt;/sub&gt; (s&lt;sup&gt;-1&lt;/sup&gt;)</th>
<th>Temp (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P11</td>
<td>50</td>
<td>y = -3.68E-05x + 4.81</td>
<td>0.980</td>
<td>3.68E-05</td>
<td>323</td>
</tr>
<tr>
<td></td>
<td>55</td>
<td>y = -6.52E-05x + 4.82</td>
<td>0.971</td>
<td>6.52E-04</td>
<td>328</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>y = -1.13E-04x + 4.77</td>
<td>0.968</td>
<td>1.13E-04</td>
<td>333</td>
</tr>
<tr>
<td>P(8&lt;sub&gt;70-co-9S&lt;sub&gt;30&lt;/sub&gt;)</td>
<td>50</td>
<td>y = -2.28E-04x + 4.08</td>
<td>0.995</td>
<td>2.28E-04</td>
<td>323</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>y = -4.45E-04x + 3.98</td>
<td>0.999</td>
<td>4.45E-04</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>y = -1.51E-03x + 3.99</td>
<td>0.987</td>
<td>1.51E-03</td>
<td>353</td>
</tr>
</tbody>
</table>
Table 3.3: Least squares calculation of helix inversion barriers.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>least squares fit</th>
<th>$R^2$</th>
<th>Inversion Barrier (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P11</td>
<td>$y = -12.1x + 27.1$</td>
<td>1.00</td>
<td>24 +/- 1</td>
</tr>
<tr>
<td>P($8_{70}$-co-$9S_{30}$)</td>
<td>$y = -7.19x + 13.9$</td>
<td>1.00</td>
<td>14 +/- 1</td>
</tr>
</tbody>
</table>
Chapter 4: Determining Cooperativity and Inversion Barriers

4.1 Introduction

Our present work investigating molecular switching in the polyguanidines depends in part on the cooperativity of the specific polymer systems involved. Cooperativity has been shown in the polyguanidines through both majority rules and molecular chaperoning experiments; however, a more comprehensive review of previous work in this area would be valuable before continuing with our current goals. We are also interested in investigating the kinetic energy barrier to switching between helical senses for the copolymers currently under investigation. The stiff backbone and generally high helix inversion barriers of polyguanidines are well known.\textsuperscript{1,2} These kinetic barriers may prove to inhibit the cooperativity of the polyguanidine copolymers.

We have assumed that an induced change in the conformation of the side chains can lead to a change in the preference for one helical sense based on similar results in the polyisocyanates. Thus, anything that might aid in comparing and contrasting these two types of polymers would be helpful. Further investigation of the helix inversion barriers of our copolymers combined with cooperativity studies may give us insight into the differences between polyguanidines and polyisocyanates. If possible we may also benefit from determining the thermodynamic preference for the lower energy diastereomeric helix. Before continuing with molecular switching attempts, some of this background information should be fleshed-out in more detail.
4.2 Cooperativity in the Polyguanidines

Several experiments can be conducted to probe the cooperativity of a copolymer system. Three of these, sergeants and soldiers, majority rules, and molecular chaperoning have been used with varying results to illustrate the cooperative nature of polyguanidines. In the sergeants and soldiers experiment chiral “sergeant” molecules are copolymerized with achiral “soldier” monomers. In the majority rules experiment a non-racemic mixture of enantiomers is copolymerized. In the molecular chaperone experiment chiral molecules are added to a solution of a polymer that has no chiral centers and a racemic helical backbone. Cooperativity is determined by the extent to which the sergeant monomers, the monomer units of the majority configuration, or the molecular chaperones respectively, impose their preferred helical orientation on the polymer as a whole. In all cases a non-linear relationship between the amount of chiral material and the optical properties of the polymer is an indication of cooperativity of the polymer system.

4.2.1 Sergeants and Soldiers

Polyguanidines were first tested for cooperativity using the sergeants and soldiers experiment. In this first experiment \(N-(R)-2,6\text{-dimethylheptyl}-N'\text{-hexyl carbodiimide}, \textbf{12R}, \) was the chiral sergeant monomer and di-\(n\)-hexyl carbodiimide, \textbf{7}, was the achiral soldier monomer, Figure 4.1. In this case, after annealing, the magnitude of the specific optical rotation of the polymers increased linearly with increasing mole percent sergeant monomer, Figure 4.2. A linear relationship can indicate that there is a non-cooperative
Figure 4.1: Sergeants and soldiers experiment.

Figure 4.2: Optical rotation for the series of copolymers in the sergeants and soldiers experiment.\(^6\)
system or that the polymer microstructure is blocky. If blocks of the individual monomers form, cooperativity or lack thereof is impossible to determine. In this case, differences in polymerization rates of the various copolymers were visibly apparent. It was concluded that the polymer was forming a blocky microstructure, thus the cooperativity of the system is still in question.

### 4.2.2 Majority Rules

After the sergeants and soldiers experiment was unsuccessful two polyguanidine systems were studied using majority rules. The first system consisted of $N$-methyl-$N'$-((R)-1-phenylethyl) carbodiimide, 9R, and its enantiomer $N$-methyl-$N'$-((S)-1-phenylethyl) carbodiimide, 9S, Figure 4.3. The specific optical rotation showed an initially linear response that began to curve toward a maximum absolute value at about 65% enantiomeric excess (ee) of the R enantiomer, Figure 4.4. This curvature is

![Figure 4.3: Majority rules experiment.](image)

$\text{Figure 4.3: Majority rules experiment.}$
characteristic of a cooperative system. The most interesting result from this study was the decrease in specific optical rotation above 65% ee. Ultimately the enantiomerically pure polymer of \(9R\) showed a specific optical rotation of about 40 degrees less than the maximum reached at 65% ee \(9R\). Subtle effects of this nature have been attributed to the optical rotation contribution of the chiral center in the side chain. Although admittedly this case showed a much more pronounced effect than seen in similar studies, this explanation seemed reasonable given that in discussing that experiment it was reported that \(9R\) has a specific optical rotation of +72° (c 0.22, CHCl\(_3\), 365nm, rt) which will act to off-set the negative rotation due to the helix. Data from this study were used to conclude that a majority rules effect was apparent and that this effect proved the cooperative nature of this system. It was admitted, however, that this system was not as well behaved as
previously studied majority rules systems. The complexities of the behavior could not be explained at that time.

The second system studied by majority rules led to more reliable results. The two enantiomeric monomers polymerized were \textbf{12R} and \textit{N-}(S)-2,6-dimethylheptyl-N'-hexyl carbodiimide, (\textbf{12S}), Figure 4.5. After the polymers were annealed a pronounced majority

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{diagram.png}
\caption{Majority rules experiment.}
\end{figure}

rules effect was apparent. As the enantiomeric excess of the \textit{R} enantiomer increased, the initially linear response in specific optical rotation curved toward a maximum value and then reached a plateau at only 60\% ee \textbf{12R}, Figure 4.6. These results indicate that a copolymer with only 60\% ee of monomer units of the majority configuration, in this case \textit{R}, has nearly the same configuration as a homopolymer of \textbf{12R}. It is interesting to note that although \textbf{12R} has an optical rotation of opposite sign of the polymer the chiral center
in the side chain does not seem to have an effect on the optical rotation of the polymer as was seen in the previous majority rules experiment. The data from this experiment are typical of a cooperative system.

**Figure 4.6:** Specific optical rotation of majority rules copolymers.⁶

### 4.2.3 Molecular Chaperones

The third method used for probing cooperativity in the polyguanidines, chiral molecular chaperoning, was designed to exploit the basicity of the polyguanidines. The polymer studied in this experiment, P7, possesses achiral side chains and exists as a racemic mixture of left- and right-handed helices at equilibrium. Solutions were made containing P7 in chloroform and varying concentrations of a chiral acid, (S)-camphorsulfonic acid. Overall acid concentration was kept constant at a molar ratio of 1:5 polymer repeats:acid using benzoic acid, Figure 4.7. Upon protonation of the polymer
backbone and ion-pairing of the polymer with the chiral anion, the polymer apparently orients into a biased helix. Specific optical rotation, normalized to negate the effects of the chiral acid, increased non-linearly toward a final maximum value of 250°, Figure 4.8. The molecular chaperone experiments showed that cooperativity is possible when the chirality is introduced through ionic interactions as well as when the chiral center is covalently bonded to the polymer backbone.

Figure 4.7: A polyguanidine protonated with camphorsulfonic acid and benzoic acid.

Figure 4.8: Specific optical rotation of P7 with varying concentrations of a chiral acid.
Investigations into the cooperativity of polyguanidines have thus far only shown that cooperativity is possible for some polyguanidine systems. It is not clear from the available data why one polyguanidine system might be cooperative while another is not or even whether the cooperative polyguanidines are as cooperative as the polyisocyanates. There is no reason to doubt the cooperativity of the copolymer of 12R and 12S as determined by majority rules; however, while the copolymer of 9R and 9S was declared to be a cooperative system the deviations from classic cooperative behavior have not been adequately explained. It is of some concern that this poorly understood system involves a monomer in our current studies.

4.3 Cooperativity in the Current Work

Because cooperativity is so vital to our current research goals, we decided to further investigate cooperativity using our current chiral and achiral monomers. To simplify the experiment no azo containing monomer was used at this time.

4.3.1 Polymers

A series of copolymers from achiral monomer 8 and chiral monomer 9S was prepared. Homopolymers of 8 and 9S were also prepared. The compositions of the copolymers in terms of percent of the chiral monomer were 0, 10, 20, 30, 50, and 100% of 9S based on monomer feed. The polymerizations were carried out in the following manner: In a dry box each monomer was weighed into a small vial, and a stir bar was
added to the vial. Subsequent stirring created a homogeneous mixture of the monomers. Then a small amount of a solution of catalyst IV in dry toluene was added. This amount was between 5 and 20 µL depending upon the amount of monomer used. Each polymerization was complete in about a minute and the polymers were recovered by the usual procedure. Due to the fast rate of polymerization for all polymers no relationship between monomer ratio and polymerization rate was visually apparent. Additional polymerization data can be found in Appendix A4.1.

Assuming that the polymers would not be in their thermodynamically controlled preferred helix immediately upon polymerization, the polymers were annealed at 50 °C until the specific optical rotation reached a plateau value indicating that the equilibrium helical conformation had been reached. The final specific optical rotation value reached for each polymer is shown in Table 4.1 and Figure 4.9 as a function of mole percent of the chiral monomer.

**Table 4.1:** Specific optical rotations of homo and copolymers of 8 and 9S.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>[α]D^50</th>
</tr>
</thead>
<tbody>
<tr>
<td>P8</td>
<td>0</td>
</tr>
<tr>
<td>P(890-co-9S10)</td>
<td>89</td>
</tr>
<tr>
<td>P(880-co-9S20)</td>
<td>193</td>
</tr>
<tr>
<td>P(870-co-9S30)</td>
<td>252</td>
</tr>
<tr>
<td>P(850-co-9S50)</td>
<td>179</td>
</tr>
<tr>
<td>P9S</td>
<td>16</td>
</tr>
</tbody>
</table>
Initially there is an increase in specific optical rotation with increasing mole percent of 9S. As the mole percent of 9S increases from 0 to 30 percent the equilibrium conformation becomes more and more biased. Above 30% of 9S there is a decrease in specific optical rotation. Clearly there is a non-linear relationship, which we would expect from a cooperative system.

4.3.2 Discussion

These results recall the majority rules experiment involving the same chiral monomer, 9S and its enantiomer, 9R. Both experiments measure the ability of one of the enantiomers to influence the helical preference of a copolymer. In both experiments there is an initial linear response to the chiral monomer followed by a slight bending toward a maximum specific rotation value and finally a decrease in specific rotation. In the present
experiment, unlike the previous experiment, the decrease in specific rotation at high chiral monomer concentrations is much greater than the expected contribution of the chiral center in the side chain. The maximum rotation reached was more than $160^\circ$ greater than that of the homopolymer, but the chiral monomer has a specific optical rotation of only $-21.5^\circ$ ($c \ 0.22$, toluene).

We believe this is evidence of a difference in the helical structures of the polymers. A helical polymer has a characteristic helical pitch. There are also characteristic dihedral angles that determine the number of repeat units required for one single turn of the helix, which is 6 for poly(di-$n$-hexyl guanidine). These characteristic properties can be different for polymers that have different side chains even if the backbone repeat unit is the same. So the helical structure formed by $9S$ clearly has properties leading to a lower specific optical rotation than that of $P(8_{70}-co-9S_{30})$. The optical rotation of $9S$ is so low that it is almost completely countered by the specific optical rotation of the side chain. In order to further investigate our system we decided to study the inversion barriers of the polymers.

4.4 Inversion Barriers

Our initial overall goal, generally stated, was to reproduce behavior in the polyguanidines that had initially been observed in the polyisocyanates. Often behavior observed in one helical polymer system can be duplicated in another similar system. The inability to do that in this case must arise from some fundamental difference between the polyisocyanates and polyguanidines. The polyisocyanates have thermodynamically
induced helicity. That is, the handedness of the helix is controlled by thermodynamics. They have stiff polymer chains but helix inversion frequently occurs due to the low inversion barriers. Therefore, a polyisocyanate will always assume its thermodynamic low energy conformation whether that conformation is a racemic mixture of left- and right-handed helices or a biased helix resulting from chiral side chains.

4.4.1 Drawing From Previous Experience

Polyguanidines are also stiff chain polymers; however, we have shown in past work that their helix inversion barriers are higher than those of the polyisocyanates.\textsuperscript{1,2} In the past we have studied inversion barriers for several homopolymers. Based on these studies we think that the inversion barrier is related to the size and steric demands of the side chains of the polymer. Specifically we believe that larger side chains contribute to a higher inversion barrier. We wanted to explore this theory by examining the relationship between monomer ratio and inversion barrier of the copolymers.

4.4.2 Homopolymers

Prior to studying the copolymers it is instructive to study each homopolymer. When achiral monomer 8 is polymerized with an achiral catalyst the homopolymer produced has a specific optical rotation of zero due to the racemic nature of the left- and right-handed helical senses. The inversion barrier of P8 was calculated by polymerizing the achiral monomer with a chiral catalyst and following the change in the specific optical rotation over time at various temperatures as the polymer backbone racemizes into
left- and right-handed regions. From an Arrhenius plot the activation energy for this process was obtained. As previously stated the inversion barrier for this homopolymer is 20 kcal/mol. Chiral monomer 9S was polymerized using achiral catalyst IV. Subsequent annealing at several temperatures promoted evolution to the thermodynamically controlled biased helix. Following this evolution at each temperature allowed us to calculate an inversion barrier of 10 kcal/mol.

4.4.3 Copolymers

The same series of copolymers used in the cooperativity studies was used to study inversion barrier. Each of these polymers was annealed at several different temperatures from 40 °C to 80 °C. We followed the specific optical rotation of each polymer at each temperature as it evolved from its less ordered kinetically controlled conformation to its more ordered thermodynamic conformation. Figure 3.12 shows data for \( \text{P}(8_{70}-\text{co}-9_{30}) \) which is representative of the data for all copolymers. Again, assuming first order kinetics, rate constants were calculated, as described in section 3.2.3, using optical rotation data at each temperature, Figure 3.13. Subsequently an Arrhenius plot was made for each copolymer the slope of which was used to calculate the activation energy for helix inversion for the corresponding copolymer, Figure 3.14.

Table 4.2 and Figure 4.10 show the energy barrier to helix inversion for each copolymer. Further details regarding inversion barrier calculations can be found in Appendix A4.2. The inversion barrier is 20 kcal/mol for the achiral homopolymer. Ten percent of 9S drops that inversion barrier by 1 kcal/mol. Additional chiral monomer
continues to decrease the inversion barrier, and as previously mentioned the helix inversion energy for the chiral homopolymer was 10 kcal/mol.

**Table 4.2:** Inversion barriers of a series of copolymers of 8 and 9S.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Inversion Barrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>P8</td>
<td>20</td>
</tr>
<tr>
<td>P(8_{90-co-9S}10)</td>
<td>19</td>
</tr>
<tr>
<td>P(8_{80-co-9S}20)</td>
<td>17</td>
</tr>
<tr>
<td>P(8_{70-co-9S}30)</td>
<td>15</td>
</tr>
<tr>
<td>P(8_{50-co-9S}50)</td>
<td>12</td>
</tr>
<tr>
<td>P9S</td>
<td>10</td>
</tr>
</tbody>
</table>

**Figure 4.10:** Energy barrier to helix inversion for a series of copolymers of 8 and 9S.

4.4.4 **Molecular Weight Effects**

Molecular weights were not experimentally determined for these polymers due to difficulties involved with those measurements. Molecular weight determination by gel
permeation chromatography (GPC) is difficult because the polyguanidines tend to adhere to GPC columns. So polymers of a single molecular weight elute over large volumes. Polyguanidines also tend to form lyotropic liquid crystals, so shear alignment of the chains makes viscosity measurements difficult to obtain. However, based on monomer to catalyst ratio all of the polymers used in this study have molecular weights of about 20,000 which is above the region in which molecular weight affects optical rotation or inversion barrier. This was proven using a series of polymers having molecular weights ranging from 12,000 to 100,000, Figure 4.11 and Figure 4.12. So slight variations in the molecular weights of different samples should have no effect on the results.

\[
\text{Figure 4.11: Constant } [\alpha] \text{ for various molecular weights of } P(88_{80}-co-9S_{20}).
\]
4.5 Thermodynamic Preference for Lower Energy Helix

To calculate helix inversion barriers we annealed each copolymer at several temperatures. The plateau value of the specific optical rotation at each temperature is an indication of the equilibrium distribution of helical senses in the copolymer at that temperature. At higher temperatures there is a more racemic mixture of left- and right-handed helices than there is at lower temperatures. Data for $\text{P}(8_{70-co-9S_{30}})$ are representative of the temperature dependence of the plateau value in the specific optical rotation, Figure 4.13.

Figure 4.12: Constant inversion barrier for various molecular weights of $\text{P}(8_{80-co-9S_{20}})$. 
In some cases similar data have been used to determine ΔG° for the left and right helical senses with the transition between the two modeled as reversible reaction. The basis for this calculation is Equation 4.1 where ΔG° is the difference in free energies of

$$\Delta G^\circ = -RT\ln K_{eq}$$\hspace{1cm}(4.1)$$

the left- and right-handed helices, R is the ideal gas constant, T is absolute temperature, and $K_{eq}$ is the equilibrium constant. Rearranging and substituting for $\Delta G^\circ$ using Equation 4.2 gives Equation 4.3. Thus, a plot of ln $K_{eq}$ vs. 1/T should yield a straight line from which $\Delta H^\circ$ and $\Delta S^\circ$ can be calculated using the slope and intercept respectively. $\Delta H^\circ$ and $\Delta S^\circ$ can then be used to calculate $\Delta G^\circ$ using Equation 4.2.

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$\hspace{1cm}(4.2)$$

Figure 4.13: Specific optical rotation as a function of temperature for $P(8_{70}-co-9S_{30})$. 

![Graph showing specific optical rotation as a function of temperature](image-url)
\[
\ln K_{\text{eq}} = - \frac{\Delta H^\circ}{R} \left( \frac{1}{T} \right) + \frac{\Delta S^\circ}{R} \quad (4.3)
\]

To do this calculation one must be able to calculate the equilibrium constant from the specific optical rotation data. This requires knowing or estimating \([\alpha]\) for a single-handed helix. Unfortunately, we do not know the specific optical rotation value of the single-handed helix of any of our copolymers. However, if we assume that the maximum optical rotation which corresponds to a single handed helix occurs at a temperature less than 20 °C, we can estimate that \(\Delta G\) for the left- and right-handed helices of \(P(8_{70}-co-9S_{30})\) is less than 1 kcal/mol.

### 4.6 Discussion

Specific optical rotation increased and then decreased as the ratio of chiral monomer in the copolymer increased. This indicates a substantial difference in the helices formed by \(P8\) and \(P9S\). The energy barrier to helix inversion showed a constant although non-linear decrease from 20 to 10 kcal/mol. We have previous data indicating that the size of the side chains of the polymer can play a part in determining the helix inversion barrier of that polymer. The small methyl side chain of the chiral monomer is likely responsible for the decrease in inversion barrier as the percentage of the chiral monomer increased.
4.7 Conclusions and Suggestions for Future Work.

We have shown that in some cases polyguanidines show amplification in their optical properties compared to their chiral monomers, but this is not true in all cases. We have shown evidence of both cooperative and non-cooperative polyguanidine systems. We have shown that the inversion barrier of a copolymer is dependent upon the ratio of comonomers. Because the ratio of comonomers is something we have some control over, we can influence a polymer's inversion barrier to some extent.

We have presented two approaches to switching between helical senses. We ran into significant problems in relation to the thermal stability of the isomeric forms of our switching element, azobenzene. For future work towards molecular switching new switching elements that are not thermally sensitive should be explored.

4.8 Experimental

4.8.1 General Procedures and Characterizations

Optical rotation measurements were obtained on a Jasco P-1010 polarimeter at 589 nm in a 1 dm cell at 25 °C unless noted otherwise. Annealing experiments were conducted in a thermostated 1 dm cell at the specified temperature where temperature control is accurate to ± 0.1 °C.

4.8.2 Procedures

Monomer synthesis is detailed in the experimental section of Chapter 3, section 3.5.2.
General polymerization procedure for the preparation of homopolymers and copolymers. The general polymerization procedure can be found in Chapter 2, section 2.6.2. Tabulated polymerization data are in Appendix A4.1.
4.9 References and Notes


6 Adapted from reference 5.
Appendices
### A4.1: Polymerization Table

**Table 4.3:** Polymerization data.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer</th>
<th>mg</th>
<th>mmol</th>
<th>mol %</th>
<th>Catalyst</th>
<th>Mon:Cat</th>
<th>Toluene (µL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(890-co-9S10)</td>
<td>8</td>
<td>462</td>
<td>2.28</td>
<td>90</td>
<td>VII</td>
<td>107:1</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>41</td>
<td>0.25</td>
<td>10</td>
<td>VII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P(880-co-9S20)</td>
<td>8</td>
<td>417</td>
<td>2.06</td>
<td>80</td>
<td>VII</td>
<td>104:1</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>83</td>
<td>0.52</td>
<td>20</td>
<td>VII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P(870-co-9S30)</td>
<td>8</td>
<td>149</td>
<td>0.74</td>
<td>70</td>
<td>VII</td>
<td>105:1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>51</td>
<td>0.32</td>
<td>30</td>
<td>VII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P(850-co-9S50)</td>
<td>8</td>
<td>112</td>
<td>0.55</td>
<td>50</td>
<td>VII</td>
<td>111:1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>89</td>
<td>0.55</td>
<td>50</td>
<td>VII</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P9S</td>
<td>9S</td>
<td></td>
<td></td>
<td>100</td>
<td>VII</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A4.2: Determination of Energy Barriers to Helix Inversion

Table 4.4: Least squares calculation of rate constants for helix inversion.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Temp (°C)</th>
<th>least squares fit</th>
<th>$R^2$</th>
<th>$k_{obs}$ (s$^{-1}$)</th>
<th>Temp (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P8</strong></td>
<td>60</td>
<td>$y = 9.35E-02x + 6.63$</td>
<td>0.980</td>
<td>9.35E-02</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>$y = 2.38E-01x + 6.57$</td>
<td>0.982</td>
<td>2.38E-01</td>
<td>343</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>$y = 3.56E-01x + 6.58$</td>
<td>0.985</td>
<td>3.56E-01</td>
<td>348</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>$y = 5.28E-01x + 6.62$</td>
<td>0.994</td>
<td>5.28E-03</td>
<td>353</td>
</tr>
<tr>
<td><strong>P(8_{90-co-9S_{10}})</strong></td>
<td>40</td>
<td>$y = -1.82E-05x + 3.09$</td>
<td>0.349</td>
<td>1.82E-05</td>
<td>313</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>$y = -1.12E-04x + 3.05$</td>
<td>0.716</td>
<td>1.12E-04</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>$y = -2.51E-04x + 3.32$</td>
<td>0.935</td>
<td>2.51E-04</td>
<td>343</td>
</tr>
<tr>
<td><strong>P(8_{80-co-9S_{20}})</strong></td>
<td>50</td>
<td>$y = -1.13E-03x + 2.45$</td>
<td>0.821</td>
<td>1.13E-03</td>
<td>323</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>$y = -2.49E-03x + 2.77$</td>
<td>0.749</td>
<td>2.49E-03</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>$y = -1.12E-02x + 2.93$</td>
<td>0.997</td>
<td>1.12E-02</td>
<td>353</td>
</tr>
<tr>
<td><strong>P(8_{70-co-9S_{30}})</strong></td>
<td>50</td>
<td>$y = -2.28E-04x + 4.08$</td>
<td>0.995</td>
<td>2.28E-04</td>
<td>323</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>$y = -4.45E-04x + 3.98$</td>
<td>0.999</td>
<td>4.45E-04</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>$y = -1.51E-03x + 3.99$</td>
<td>0.987</td>
<td>1.51E-03</td>
<td>353</td>
</tr>
<tr>
<td><strong>P(8_{50-co-9S_{50}})</strong></td>
<td>50</td>
<td>$y = 7.70E-04x + 2.50$</td>
<td>0.901</td>
<td>7.70E-04</td>
<td>323</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>$y = 1.31E-03x + 2.45$</td>
<td>0.950</td>
<td>3.41E-03</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>$y = 2.31E-03x + 2.45$</td>
<td>0.768</td>
<td>2.31E-04</td>
<td>343</td>
</tr>
</tbody>
</table>
Table 4.5: Least squares calculation of helix inversion barriers.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Least squares fit</th>
<th>$R^2$</th>
<th>Inversion Barrier (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P8</td>
<td>$y = -10.2x + 28.3$</td>
<td>0.999</td>
<td>20 +/- 1</td>
</tr>
<tr>
<td>P(8_{90-co-9S_{10}})</td>
<td>$y = -9.41x + 19.2$</td>
<td>1.00</td>
<td>19 +/- 1</td>
</tr>
<tr>
<td>P(8_{80-co-9S_{20}})</td>
<td>$y = -8.74x + 20.3$</td>
<td>1.00</td>
<td>17 +/- 2</td>
</tr>
<tr>
<td>P(8_{70-co-9S_{30}})</td>
<td>$y = -7.38x + 14.5$</td>
<td>1.00</td>
<td>15 +/- 2</td>
</tr>
<tr>
<td>P(8_{50-co-9S_{50}})</td>
<td>$y = -6.07x + 11.6$</td>
<td>0.999</td>
<td>12 +/- 2</td>
</tr>
</tbody>
</table>