1 Background and Introduction

1.1 Functional Nanomaterials

The term nanomaterial is widely used in materials science, and it encompasses a wide range of substances from organic and polymer materials\textsuperscript{1-3} to inorganic materials. The drive to develop novel materials, coupled with the invention of new technology that enables the detailed study of nanometer scale materials, has helped fuel the recent upsurge in nanomaterials research. To a synthetic chemist, the term “nano” may seem redundant and superfluous, since synthetic chemists have been synthesizing molecules, which are technically on the nanometer scale, for over a century. Recently, however, scientists have begun to define the area of nano research, and it can involve contributions from synthetic and inorganic chemistry and materials and polymer science. The ability to create these new materials requires expertise from each of these areas, and it is this necessity that has spurred the movement of scientists from traditional backgrounds into the multidisciplinary field of “nano-science”. It is the collaboration of scientists from many different backgrounds that has led to the development of new materials for applications in drug delivery,\textsuperscript{4-6} electronics,\textsuperscript{7,8} and even diagnostic medicine, to name a few (Figure 1-1). The work that will be described in this thesis will demonstrate the effectiveness of
such collaboration to develop new functional nanomaterials, and will outline research done at the interfaces of materials science, polymer science, and synthetic chemistry.

**Figure 1-1.** Illustration of a multidisciplinary approach to functional nanomaterials for applications in diagnostic medicine, drug delivery, and electronics.
1.2 Nanocrystals

Nanocrystals represent a class of crystalline inorganic materials defined by their dimensions, which, by general standards, must include at least one dimension that is 100 nm or less. One of the reasons that nanocrystals are so interesting to study is the fact that they can have unique properties which are dependent upon size. Typically these effects are observed at sizes less than 20 nm. Perhaps the best example of this phenomenon is the unique optical and electrical properties that are exhibited by semiconducting nanocrystals, or “quantum dots.” These nanocrystals are usually between 2 and 10 nm in size, and their properties enable tunable light emission simply by altering the size of the nanocrystals (Figure 1-2). As semiconducting nanocrystals become smaller and smaller, they begin to exhibit distinctive properties that are not possessed by the bulk, and not possessed by the single molecule, but rather some size in between. This result is directly related to the band gap of the semiconducting material, and is attributed to quantum confinement effects. As the particles become smaller and smaller, the band gap becomes larger, resulting in a blue shift in the fluorescence of the nanocrystals versus their macrocrystalline counterparts when they are excited by light.
Semiconducting nanocrystals are a special class of nanocrystals that undergo a change in optical and electrical properties with decreasing size, but all nanocrystals have the advantage of a large surface-to-volume ratio, which can often lead to an increase in reactivity of a particular metal or metal oxide nanocrystal. There are many processes that can be governed by the reactive sites on the surface of metal nanocrystals, two of the most common of which are hetero- and homogeneous catalysis. The two most widely used industrial catalysts in the United States are polymerization catalysts and oxidative catalysts. The development of new catalysts that can make these processes more efficient is essential to the progress of certain industries, including the manufacture of many plastics, paints, detergents, and cosmetics. Many industrial oxidation processes use toxic reagents, chlorine and organic peroxides, to carry out the oxidation of hydrocarbons. The former can lead to extremely
toxic byproducts, and the latter are very expensive, leaving the process uneconomical.\textsuperscript{18} It would indeed be beneficial to be able to directly activate molecular oxygen to facilitate hydrocarbon oxidation, however this might seem highly improbable given that the bonding energy for molecular oxygen is 498 kJ/mol.\textsuperscript{19} However, Hughes and coworkers recently found a way to use gold nanocrystals to activate oxygen under very mild conditions.\textsuperscript{20} It might seem counterintuitive that gold would be used to oxidize anything, given that it is considered a noble metal and relatively inert, however, gold is yet another example of a material that exhibits unique chemical reactivity on the nanometer scale. It was both surprising and ground-breaking when Haruta and coworkers initially found that gold nanocrystals could catalyze the oxidation of CO at low temperature (-77 °C).\textsuperscript{21} This increase in reactivity of gold is still not completely understood, but researchers are continuously developing new applications for these unique nanocrystals. Since this discovery, scientists have developed other nanocrystalline materials that display high reactivity towards catalytic oxidation.\textsuperscript{18,22,23} Nanocrystals have begun to replace bulk metal oxides for many of these applications, since the increased surface-to-volume ratio renders a more active catalyst, thus lowering the catalyst loading necessary for many processes.\textsuperscript{24} The ability to reproducibly and efficiently synthesize nanocrystals has revolutionized the field of catalysis.\textsuperscript{9}
Metal oxide nanocrystals are yet another class of nanocrystals that have recently commanded a great deal of attention. Similarly to gold nanocrystals, some metal oxides, such as copper oxides, have been used in the oxidation of CO to CO₂. Magnetic metal oxide nanocrystals, particularly γ-Fe₂O₃ and Fe₃O₄, have also drawn interest due to their application in a variety of areas including magnetic storage, magnetic drug delivery, and as magnetic resonance imaging (MRI) contrast agents. A third class of metal oxide nanocrystals that warrant investigation are the ceramic nanocrystals, such as titanium dioxide (TiO₂). TiO₂ nanocrystals have applications in electronics, photocatalysis, pigments, and even cosmetics. In the following chapters, both magnetic iron oxide nanocrystals (γ-Fe₂O₃) and ceramic nanocrystals (TiO₂) will be described in greater detail. In this report the functionalization of both types of nanocrystals, and the exploitation of their properties for applications will be described in detail.

The development of new synthetic methods for making nanocrystals has allowed for the expansion of techniques to functionalize them. Many researchers have been interested in functionalizing nanocrystals with polymeric materials for various applications like drug delivery and molecular electronics, to name a couple. Such applications can sometimes require the synthesis of very well-defined polymers with narrow molecular weight ranges. It is therefore important to consider new methods of polymer synthesis that can provide
polymers with the desired properties. There are several widely used polymerization techniques that allow for this control over polymer architecture, and they are classified as “living” polymerization due to the controlled nature under which they take place. Living polymerization has enabled the development of many new materials, and it has become an invaluable technique for making polymers.

1.3 Living Radical Polymerization

“Living” polymerization was a term first coined by Szwarc as being a chain growth process by which no termination or chain transfer occurs (transfer of one radical chain to another), thus the molecules “live” for a period of time. In a living system, radical propagation and reversible termination happen at a much faster rate than irreversible termination. This kind of process allows for control over end-functionality, as well as block copolymer synthesis through the consecutive addition of different monomers. One of the limitations of living radical polymerization (LRP) is that there is no control over the molecular weight (MW) or molecular weight distribution, also called polydispersity (PD), of the subsequent polymers. “Controlled” polymerization is a term that was used to describe a process in which there is control over the MW and PD of the growing polymer, but in which chain transfer and termination occur. The terminology
of these kinds of processes has been debated, and no universal vocabulary has been accepted.\textsuperscript{35,36} The definition of LRP has been relaxed, however, and has been used to describe any polymerization, including free-radical polymerization, in which there is low PD and linear chain growth, which occur more readily when irreversible termination is kept to a minimum.\textsuperscript{37} For the purpose of this thesis, the term living radical polymerization (LRP) will be used to describe processes that differ from standard radical polymerization by the above criteria.

An important feature of LRP is the equilibrium between active and a dormant species (Scheme 1-1).\textsuperscript{38} This equilibrium allows for the steady growth of polymer chains while keeping the concentration of radicals in solution very low, thus preventing termination.\textsuperscript{37} The PD of a polymer is defined below (eq. 1-1), where $M_w$ is the weight average of the polymer, and $M_n$ is the number average. Ideally, the PD should be 1, however it is usually true that $M_w > M_n$. A respectable PD is often considered anything less than 1.5.

$$PD = \frac{M_w}{M_n}$$  \hspace{1cm} eq. 1-1

The kinetics of LRP should produce a linear plot of $\ln([M]_0/[M])$ vs. time if the reaction is first-order with respect to monomer concentration, where $[M]_0$ is the initial monomer concentration and $[M]$ is the actual monomer concentration.\textsuperscript{37,39,40} There should also be a linear increase of MW as the reaction progresses. The MW, or degree of polymerization (DP$_n$), should depend upon
the ratio of monomer concentration, \([M]\), to initiator concentration, \([I_0]\), (eq. 1-2), and deviations from this value can be caused by chain transfer (lower MW than expected) or inefficient initiation (higher MW than expected).\(^{37}\)

\[
DP_n = \Delta[M]/[I_0]
\]

\text{eq. 1-2}

\[\sim P_n^-X \quad \overset{(+Y)}{\underset{k_{da}}{\rightleftharpoons}} \quad \sim P_n^+ \quad + \quad X(-Y)^+ \]

\text{Scheme 1-1.} Representation of the exchange between active and inactive polymer species.

As previously stated, one important component of a LRP is the presence of an active and a dormant species. This allows for a slow, steady growth of the polymer chain. The majority of LRP systems can be summarized by the reaction sequence in Scheme 1-1 above, where \(P_n^-X\) is the dormant polymer species, \(Y\) is an additive that may or may not be used during the polymerization, and \(M\) is the monomer. One of the main advantages of LRP over conventional free radical polymerization is that chain termination is kept to a minimum during the polymerization. The kinetics of LRP are governed by the rates of activation and deactivation, \(k_a\) and \(k_{da}\) respectively, the rates of termination and chain transfer, \(k_t\) and \(k_{tr}\) respectively, and the rate of chain propagation, \(k_p\). The PD and the preservation of end-functionality can be affected by both \(k_t\) and \(k_{tr}\).\(^{37}\) As a
general trend, the PD increases and polymer chains lose their end-functionality as the conversion increases. It is important to note that the loss of end-functionality on polymer chains is much more significant at high conversion, thus it is not ideal to allow 100% conversion of monomer if end-functionality is to be preserved.\textsuperscript{41}

The control over PD and MW, and the preservation of functional end-groups are a product of the fact that chain transfer and termination occur minimally during polymerization, which a results of the Persistent Radical Effect (PRE).\textsuperscript{42} If $k_a$ is sufficiently small, the concentration of propagating radical, $P_n\cdot$, is also small, so there can be little termination occurring (Scheme 1-1). In addition, $P_n\cdot$ can only be present for a short period of time before it will recombine with the persistent radical, $X-(Y)\cdot$. $X-(Y)\cdot$ is called a persistent radical because it does not self-terminate or propagate, rather it persists until it recombines with the propagating radical. Even though $P_n\cdot$ and $X-(Y)\cdot$ are initially formed in equal amounts, as termination occurs, the relative concentration of persistent radical increases. Over time, the persistent radical concentration becomes so high that termination becomes less and less likely to occur, due to the occurrence of the reverse reaction of $P_n\cdot$ with $X-(Y)\cdot$ to form the dormant species. The PRE thus allows for the stepwise incorporation of monomer into the polymer chain, and thus minimizes the termination and transfer reactions.\textsuperscript{42}
There are three specific classes of LRP that are the most efficient controlled methods of polymerization, and they allow for control over polymer end-functionality, yield low PD polymers, and allow control over MW. The three classes are atom transfer radical polymerization (ATRP), nitroxide mediated polymerization (NMP), and reversible addition-fragmentation transfer (RAFT) polymerization (Scheme 1-2). Each varies slightly from the rest by its mechanism, as well as the types of monomers and initiators that can be used. NMP relies upon a unimolecular initiation, whereas ATRP involves activation/catalysis by some transition metal species (e.g. Ru, Cu, Fe, Pd) via a redox cycle. RAFT involves the use of a transfer agent, typically a dithioester, to facilitate polymerization. In both NMP and ATRP, the rate of polymerization is dependent upon the concentration of the persistent radical species, \( X \cdot \) or \( X-Y \cdot \) respectively. In the case of RAFT, there is no persistent radical, and the kinetics are different than for NMP or ATRP.
Scheme 1-2. General scheme of the mechanism for nitroxide mediated polymerization (1), atom transfer radical polymerization (2), and reversible addition-fragmentation transfer polymerization (3).

Each type of LRP has its own specific kinetics, which govern the degree of polymerization, PD, and MW. When selecting a type of LRP to use, one must take into account a variety of factors: the range of monomers that can be used, the conditions under which the polymerization is carried out, the type of transferable group employed, and the additives that might be used. Both ATRP and RAFT require the use of a catalyst and a radical source, respectively, whereas NMP can be carried out in the absence of any additives. NMP usually requires elevated temperatures (> 120 °C) when using 2,2,6,6-tetramethyl-1-
piperidinyloxy (TEMPO) radical, whereas ATRP and RAFT usually proceed at lower temperatures (20-120 °C). RAFT allows for the use of the widest range of monomers, while ATRP provides the means to build block copolymers that would otherwise be unavailable, and NMP enables polymerization in the absence of any metals. Clearly, there are advantages and disadvantages to each method, and many factors need to be considered before selecting one method over the others. Regardless of the choice of polymerization technique, the recent advances in LRP undoubtedly have enabled the development of new materials, most notably functional materials, with a variety of applications.

With the advancement of all of the LRP reactions, new materials can be designed with novel properties. It is reasonable to imagine that with the progress being made in polymer science and nanocrystal research that the two might somehow fit together. These new materials incorporate the properties of both polymers and nanocrystals, and the improvement of synthetic methods for both has lead to an entirely new field of research whereby the nanocrystal surface can be functionalized with polymers, also called polymer brushes.

1.4 Polymer Brushes

For as long as scientists have studied surfaces there has been a desire to understand surface properties with the ultimate ambition of being able to control
surface properties, and to rationally design surface/interface functionality. For decades, researchers have been interested using polymer coatings to customize surface properties like wettability, adhesion, biocompatibility, and corrosion. As the field expanded, the term “polymer brush” began to be used to describe an array of polymer chains that are affixed by one end to a surface.\textsuperscript{44,45} These systems are likened to brushes because the polymer chains stretch away from the surface to prevent overlap with the neighboring chains (Figure 1-3). The model for polymer brushes is a general one, and can be used to study polymer chains attached to a solid substrate, a liquid-liquid interface, a liquid-air interface, or an interface between a polymer melt and a solution of polymer chains.

![Polymer Adsorption and Polymer Brush Formation](image)

**Figure 1-3.** Polymer brush formation (right) from a random coil polymer (left). As the polymer molecule adsorbs to the surface, the untethered end moves away from the surface in order to minimize stearic interactions with neighboring polymer molecules.

There are two types of interactions that can govern polymer brush formation on a surface: physisorption and chemisorption. Physisorption is a...
physical attraction between the polymer chains and the surface, whereas, chemisorption requires the formation of a covalent bond between the surface and the polymer brushes. Chemisorption can either occur through grafting-to or grafting-from the surface (Figure 1-4). Grafting-to requires a functional end group on a polymer chain that can undergo some sort of reaction with surface groups on the substrate. One of the disadvantages of this method is the inherently low grafting density (total number of polymer chains per unit area) of polymer chains. As more polymer chains react with the surface, it becomes harder for new chains to reach the surface to react. This limits the total number of chains that can be grafted to the surface. Grafting-from overcomes this impediment because the polymer chain grows from the surface, so the only stearic interaction is between neighboring polymer chains as they grow away from the surface. Also called surface initiated polymerization (SIP), grafting-from requires the covalent attachment of a small molecule initiator to the substrate, which allows for polymerization directly from the substrate surface. Because there is no diffusion barrier for the small molecule initiators, higher grafting densities may be achieved.
There have been many advances in applications for both grafting-to and SIP from solid surfaces, and recently, a great deal of research has been focused on applying both methods to nanocrystal surfaces. The development of new methods for attaching polymers to surfaces is important to the progress of the field. Through the use of a handful of exceedingly high yielding, selective, and mild chemical reactions, it would be possible to build up surfaces very quickly and easily. This concept is exemplified through the use of “click” reactions, which will be described in the following section.
1.5 Click Chemistry

“Click” chemistry is a term coined by Sharpless and coworkers that describes a synthetic approach relying on very simple building blocks that can be used in a range of chemical systems.\textsuperscript{39} There are very specific criteria in order for a reaction to be classified as click; that is, the reaction must be “modular, wide in scope, give very high yields, generate only inoffensive byproducts that can be removed by nonchromatographic methods, and be stereospecific.” The process must also “include simple reaction conditions, readily available starting materials...no solvent or a solvent that is benign or easily removed, and simple product isolation.”\textsuperscript{47}

There are a number of reactions which can be classified as click by these guidelines, and recent research has focused on making these methods more widely applicable. There are three types of click reactions that are considered the most useful: nucleophilic ring-opening reactions, cycloaddition reactions, and protecting group reactions.\textsuperscript{47} The best click reactions are considered to be those that are fusion reactions, that is to say, those reactions in which the combined chemical formulas of the reactants is the same as the product. Scheme 1-3 shows examples of each of the three classes of click reactions. The $S_{N}2$ ring-opening reactions that are highlighted as click (A in Scheme 1-3) are usually those involving three-membered rings, due to the fact that the competing elimination
processes are highly disfavored, thus making the reactions very high yielding. The archetypical click cycloaddition reaction is the Huisgen 1,3-dipolar cycloaddition reaction involving a terminal alkyne and a terminal azide (B in Scheme 1-3). The fact that organic azides are stable to the vast majority of other functional groups also makes this type of reaction very special. The last click category involves protecting group reactions (C in Scheme 1-3). The argument is that the acetal protecting group, for example, should not be considered a protecting group at all, but should be thought of as a heterocycle for synthetic chemistry. In each case, the reactions are selective, high yielding, and stereospecific, thus adhering to the classification of click chemistry.  

\[ \text{Scheme 1-3. Examples of (A) ring opening, (B) cycloaddition, and (C) protecting group click reactions.} \]

The click chemistry philosophy of taking a few reactions and using them to assemble new materials is an attractive one. Perhaps this is why in recent
years so many scientists from backgrounds in biology, materials science, and chemistry have begun to use these reactions. As touched upon earlier, the 1,3-dipolar cycloaddition reaction of azides with alkynes is the click reaction that stands out among the others as being particularly useful in a variety of applications. This reaction is the embodiment of click, and it has been utilized across several disciplines. This reaction will be described in greater detail in chapter 3, and we will demonstrate the utility of the azide-alkyne cycloaddition reaction for the functionalization of nanocrystals.

1.6 Research Objective

In previous sections the importance of nanocrystals for various applications was discussed. Recently, O’Brien and coworkers developed a reliable synthesis for magnetic iron oxide nanocrystals (MIONs),\textsuperscript{40} with the goal of utilizing the nanocrystals for contrast enhancement agents in Magnetic Resonance Imaging (MRI). In order to develop nanocrystal systems that can be used in vivo for MRI applications, the nanocrystals must first be transformed into something that is biocompatible. This was accomplished by utilizing the physical interactions of various phospholipids with the oleic acid stabilized nanocrystals, which makes the MIOns both water soluble and biocompatible.\textsuperscript{49,50}
The resulting nanocrystals can then be conjugated to antibodies for targeted MRI enhancement (Figure 1-5).

![Schematic representation of phospholipid coated magnetic iron oxide nanocrystals (MIONs).](image)

**Figure 1-5.** Schematic representation of phospholipid coated magnetic iron oxide nanocrystals (MIONs). The phospholipids make the MIONs water soluble, while the bioconjugation allows for targeted delivery of the MIONs.

One of the disadvantages of the phospholipids stabilized MIONs is that the phospholipids are simply physisorbed to the nanocrystal surface, and over time they may desorb from the surface, leading to nanocrystal aggregation. It can also be difficult to fine tune nanocrystal concentration within the phospholipids coating, since many nanocrystals can cluster together within the phospholipids membranes. This strategy is also only specific to a handful of phospholipids, thus limiting its applicability to other systems. The limitations of this system motivated us to attempt to develop a parallel method for nanocrystal functionalization that might be more universal in nature.
Our goal was to develop a general method for nanocrystal functionalization, which would enable us to covalently attach any molecule of our choice to the nanocrystal core. In this report, we demonstrate a strategy for the synthesis of surface functionalized metal oxide nanocrystals through the design of versatile ligands, whose structures include the following features: (1) a robust anchor that can bind generally to a variety of metal oxide surfaces; (2) tailored surface groups that act as spacers or branches from the metal oxide surface and (3) a general method for covalently attaching a functional perimeter to the spacers through efficient and high yielding chemical transformations (Figure 1-6). Ligands which possess the flexibility and synthetic generality of features 1–3 possess the characteristic of "universal" ligands which allow the construction of a broad range of functionalities for the periphery of nanocrystals with good yields and synthetic facility.⁵¹
Figure 1-6. Nanocrystal cores functionalized with universal ligands. The ligands are anchored to the surface and have a tailored spacer with a functional periphery (red spheres) that can undergo reactions with the complementary functionalized molecules.

In the design of functional ligands for nanocrystal surfaces, one must consider both the binding properties as well as the stability of the ligand, and, importantly, prevention of nanocrystal aggregation. It has been established that organo-phosphates as well as carboxylates bind strongly to the surface of metal oxides.\textsuperscript{52-61} For our studies we chose ligands containing either a phosphonic acid group or a carboxylic acid group at one terminus, to serve as anchors which can bind strongly to the surface of the $\gamma$-Fe$_2$O$_3$, and either an azide or alkyne group at the other terminus, providing orthogonal functionality for further chemical modification of the nanocrystal-ligand complex surface. Because organo-
phosphates and carboxylates bind well to most metal oxides, this method also
has the potential of applying to a range of metal oxide surfaces.

In many practical applications, nanocrystal cores must be provided with
surface ligands which both prevent aggregation and also provide a handle that
conveniently allows functionalization of the final periphery of the system. The
harsh conditions generally required for nanocrystal preparation severely limit
the use of functionalized ligands during the synthesis. As a result, a common
method of functionalizing the nanocrystal surface involves stripping off non-
functional ligands used for synthesis and then redispersing the particles with
functionalized ligands.\textsuperscript{51} We have developed a reliable method for this type of
ligand exchange, the details of which will be described in the following chapter.

1.7 Summary

The convergence of traditional scientific disciplines into a contemporary
theme of scientific research requires a contemporary ideology. A
multidisciplinary approach to materials engineering is essential to the
continuation of technological advances. The following chapters demonstrate the
benefits of this type of multidisciplinary research. By blurring the lines between
synthetic chemistry and polymer and materials science, new and interesting
materials with novel applications can be made.
In this thesis, the design of click functional ligands for metal oxide nanocrystals will be described. The characterization of the resultant nanocrystals will be carried out, and the properties will be investigated. Once the success of the click functionalization is determined, the nanocrystals will be carried on to a Cu-catalyzed azide-alkyne cycloaddition (CuAAC) reaction. Both γ-Fe₂O₃ and TiO₂ nanocrystals will be functionalized in this way, demonstrating the scope of this methodology. Both small molecules and polymer materials will be utilized for the nanocrystal functionalization, combining organic, materials, and polymer chemistry. The TiO₂ nanocrystals will then be used to fabricate dielectric devices for potential application in the field of large area, flexible electronics. The functionalization and characterization of these systems will be described in great detail in the following chapters.
1.8 References


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2 Design, Synthesis, and Surface Characterization of “Universal” Ligands for Iron Oxide Nanocrystals

2.1 Background and Introduction

Nanocrystals exhibit unique properties when compared to their bulk counterparts, a fact that makes them prime candidates for a variety of commercial applications. In order to expand the use of nanocrystals in commercial applications, the ability to functionalize them in a straightforward, uncomplicated manor must first be achieved. The goal of the research outlined in this thesis is to develop a simple methodology for nanocrystal functionalization that could be generalized to any type metal oxide surface, nanocrystal or bulk. This concept involves the use of a “universal” ligand, which in the case of nanocrystal functionalization would both stabilize the nanocrystals against aggregation and provide a handle for further functionalization. In this chapter, the concept of the universal ligand for functionalization of $\gamma$-Fe$_2$O$_3$ nanocrystals will be described in detail (Figure 2-1).
2.1.1 Magnetic Nanocrystals

Magnetic nanomaterials have attracted a great deal of attention from scientists due to their potential applications in various fields. Recent advances have included using magnetic nanocrystals as cellular delivery carriers,\(^1\) drug delivery vehicles,\(^2,3\) magnetic storage media,\(^4\) Magnetic Resonance Imaging (MRI) contrast agents,\(^5,8\) and even as a magnetically recoverable chiral catalysts.\(^9\) There are several different types of magnetic materials. A ferromagnetic material is one in which all of the magnetic ions contribute to the overall magnetic moment of the species, meaning that there is a net magnetic moment in the absence of a magnetic field. Ferrimagnetic materials have magnetic ions that are randomly aligned, but the net magnetic moment is positive, so spontaneous magnetization still occurs. There are numerous ferromagnetic materials, however most of them have a Curie temperature \((T_c)\), the temperature above which the material loses its ferromagnetic character, too low to make them useful in practical applications. Iron has a higher saturation magnetism \((M_0)\) at room temperature than any other magnetic compound, and the \(T_c\) is 1043 K,\(^10\) however elemental iron is so reactive toward oxygen that it readily oxidizes to one of various forms of iron oxide. This
is not a problem for many applications, as iron oxides can still exhibit ferro- and ferrimagnetic properties.

There are two major forms of magnetic iron oxide: magnetite and maghemite, Fe₃O₄ and γ-Fe₂O₃ respectively. Magnetite and maghemite are isostructural and have a spinal crystal structure. Maghemite has a cubic unit cell which contains 32 O²⁻ ions, 21 1/3 Fe³⁺ ions and 2 1/3 vacancies (Figure 2-2). Bulk maghemite is ferrimagnetic at room temperature (273 K), however at sizes below approximately 20 nm it becomes superparamagnetic. Superparamagnetic nanocrystals differ from ferro- and ferrimagnetic materials in that the crystals are comprised of a single magnetic domain, rather than multiple magnetic domains. This means that each particle has a fixed magnetic moment that can only change in direction; thus, as a result of the cancellation of moments by particles with opposite magnetic dipoles, the net moment of a solution of such particles is zero. One benefit of superparamagnetic nanocrystals is that they require a relatively low field in order to reorient the spins into a material with a net magnetic moment. Once the magnetic field is removed, the nanocrystals demagnetize without the aid of external energy. These magnetic properties are size, temperature, and even shape dependent, and they are in part why recent research has focused so heavily on this area.
Iron oxide nanocrystals can be synthesized by a variety of methods including the thermal decomposition of iron pentacarbonyl ([Fe(CO)$_5$]),$^{11-13}$ sonochemical decomposition of [Fe(CO)$_5$],$^{14}$, as well as the decomposition of various other iron precursors.$^{15}$ One of the inherent difficulties in the sonochemical synthesis is control over size of the nanocrystals. Recently, highly reliable methods of nanocrystals synthesis have been described in the literature, which yield monodisperse nanocrystals and allow for control over nanocrystals size.$^{16}$ The method that will be highlighted in this chapter is that which uses the decomposition of [Fe(CO)$_5$] in the presence of oleic acid as a ligand.$^{13}$
2.1.2 Surface Ligands for Nanocrystals

Various types of surface ligands (also referred to as surfactants) can be used in the stabilization of nanocrystals. For the purpose of consistency, the term surface ligand will be used exclusively in this report. One of the biggest challenges in selecting an appropriate ligand is predicting whether or not it will prevent aggregation of the nanocrystals. In the initial studies of the decomposition of iron pentacarbonyl, polymers were used as the ligands.\textsuperscript{11} It was not until later that small molecule organics began being used in this way. Fatty acids are some of the most widely used surface ligands, and are beyond doubt some of the most studied systems.\textsuperscript{4} There are several commonly used functional groups that readily bind to the surface of metal oxides in general: carboxylates,\textsuperscript{13} phosphates\textsuperscript{17} and phosphonates\textsuperscript{18}, silanes,\textsuperscript{19} and catechols.\textsuperscript{20} While each of these functionalities has been incorporated into ligands for iron oxides, to our knowledge there has been no systematic study comparing the relative binding strengths of the entire spectrum of ligands.

Researchers are often interested in studying the surface ligands on nanocrystals; both the structure of surface ligands and the nature of the binding are important questions to be answered. Metal oxides in general have three types of surface groups that are capable of interacting with ligands: O\textsuperscript{−} and O\textsuperscript{2−} anions, metal cations, and O-H groups. This makes the issue of defining surface
interactions complicated, as there can be a variety of interactions within a single sample. There are also two types of surface adsorption that can take place on any surface: chemisorption and physisorption. As the names indicate, chemisorption takes place when there is a covalent bond formed between the surface ligand and the surface, whereas physisorption is simply a physical interaction/adsorption of the ligand to the surface. When describing chemisorption of surface ligands to metal oxides there are several different modes of binding that are proposed in the literature for both carboxylic acids and phosphates (Figure 2-3). The complication arises in the fact that any and all of these mechanisms of chemisorption can occur in a single sample, as well as some physisorption of surface ligands.

![Figure 2-3. Possible modes of binding for (A) carboxylates and (B) phosphates on the surface of metal oxide nanocrystals (M). Not drawn to scale.](image)

Perhaps the most common technique for studying the nature of adsorption of surface ligands on metal oxide nanocrystals and bulk surfaces is
Fourier Transform Infrared Spectroscopy (FTIR). Because metal oxides have been used for decades as catalysts there has been great interest in determining the mechanism of adsorption of various species on the surface of metal oxide bulk materials.\textsuperscript{24,25} FTIR has been used to study this process since it is a well understood and it is a non-destructive spectroscopic technique. One of the drawbacks of using FTIR to study metal oxide surfaces is the fact that there are discrepancies among data reported by different authors. Varying the sample preparation and experimental procedure can have a large effect on the FTIR obtained for the same metal oxides.\textsuperscript{25}

Iron oxide in particular has been studied extensively by FTIR. Since fatty acids were some of the first surface ligands used to stabilize nanocrystals, the adsorption of these species on iron oxide nanocrystals has been well studied. Typically, when a fatty acid is adsorbed to the iron oxide surface it chemisorbs as a carboxylate. Kreller and coworkers have studied the adsorption of both carboxylates and phosphates on the surface of iron oxide nanocrystals and iron oxide bulk surfaces.\textsuperscript{26,27}

Many researchers in recent years have been interested in the binding strength of various ligands. Thermogravimetric Analysis (TGA) is a technique commonly used to determine the strength of binding. As the sample of nanocrystals is heated there is a weight loss associated with the decomposition
temperature of each component of the sample. Those molecules which bind more strongly to the surface of the nanocrystals decompose/desorb at higher temperature than those that bind weakly and simply boil off. TGA can also be used to determine the surface coverage of ligands on nanocrystals by comparing the total change in mass as a result of ligand desorption to the mass of the inorganic core that remains. Elemental Analysis can also be used to determine surface coverage through analysis of the % composition of various elements, and this measurement can be compared with that derived from TGA data.

Although it is important to determine the modes of binding and the properties of surface ligands on metal nanocrystals, it is also important to determine if the binding of these ligands in any way influences or alters the crystal structure of the inorganic core. The most common methods of studying the inorganic core of the nanocrystal are Transmission Electron Microscopy (TEM) and X-ray Diffraction (XRD). TEM allows one to visualize the inorganic core, enabling the determination of the size and shape of the nanocrystals. XRD simply provides information about the crystallinity and size of the nanocrystals, as well as the oxidation state of metal atoms.28 Another technique that is commonly employed for surface studies of nanocrystals is X-ray Photoelectron Spectroscopy (XPS). In XPS, the sample is bombarded with x-rays while the kinetic energy (KE) of the electrons that escape the surface (1-10 nm in depth) is
measured. From the KE of the electrons that are ejected, it is possible to
determine the atoms they came from, and what environment those atoms are in
(chemical structure), which can give information about both the inorganic core of
the nanocrystals as well as the organic ligands. One downfall of this technique is
that it can be difficult to use for the study of nanocrystals due to the high
vacuum under which the experiments are run, which can cause the nanocrystals
to be pulled off of the sample to damage the detector.

The following sections will describe the ligand exchange process used to
functionalize $\gamma$-Fe$_2$O$_3$ nanocrystals. The success of the ligand exchange
procedure was determined through examination of FTIR spectra, TEM
micrographs, and TGA experiments. The resultant nanocrystals were stabilized
against aggregation in solution, and the dispersion of the nanocrystals was
dependent upon the ligand solubility. The ease of this procedure will be
demonstrated, and subsequent chemical modification of the nanocrystals will be
outlined in the next chapter.
2.2 Experimental Methods

2.2.1 Synthesis of Maghemite Nanocrystals (Fe₂O₃-OA)

γ-Fe₂O₃ nanocrystals were synthesized by modification of a previously published method. Oleic acid (9.5 mmol) and trioctylamine (32.1 mmol) were added to an oven-dried flask (150 °C) under N₂. The mixture was heated to 180 °C with stirring for 1 hour. Fe(CO)₅ (3.1 mmol) was then added and the mixture was heated to 350 °C for 1 hour. Dehydrated trimethylamine N-oxide (9.3 mmol) was then added to the reaction vessel and heating at 350 °C was continued for 2 additional hours. The reaction mixture was allowed to cool to room temperature, at which time the mixture was dispersed in CHCl₃. The resultant nanocrystals were precipitated by addition of MeOH (to cloud point) to the solution. The mixture was centrifuged and the precipitate was collected and dispersed in CHCl₃. The supernatant was further washed with MeOH until no more nanocrystals precipitate out of solution.

2.2.2 Synthesis of 2-bromo-2-methyl-propionic acid 2-hydroxy-ethyl ester (2)

\[
\text{HO} - \text{O} - \text{O} - \text{Br}
\]

Anhydrous ethylene glycol (225 mL, 4.1 mol) was added to a 500 mL 2-neck round bottom flask that had been flame-dried under vacuum and purged with 3 times with argon. The flask was equipped with a magnetic stir bar and
rubber septum. The flask was then cooled to 0 °C in an ice bath. Slowly, α-bromoisobutyryl bromide (20 mL, 161.8 mmol) was added drop-wise to the stirring ethylene glycol. The reaction stirred at 0 °C for 3 h. The reaction was quenched with 100 mL H₂O and extracted with CHCl₃ (3 x 100 mL). The combined organic extracts were dried over MgSO₄, filtered, and the CHCl₃ was removed by a rotary evaporator. The subsequent liquid was purified by distillation (85 °C, 30 mTorr) to yield a viscous, clear, colorless liquid (30.4 g, 89%). ¹H NMR (300 MHz, CDCl₃): δ 4.41 (t, 2H, J = 3.5 Hz), 3.87 (t, 2H, J = 3.3 Hz), 3.21 (s, 1H), 1.95 (s, 6H); ¹³C NMR (300 MHz, CDCl₃): δ 171.80, 67.16, 60.31, 55.72, 30.49.

2.2.3 Synthesis of 2-azido-2-methyl-propionic acid 2-hydroxy-ethyl ester (3)

![Chemical structure](image)

2 (2.0 g, 9.48 mmol) was dissolved in anhydrous DMF (15 mL) in a 2-neck round bottom flask that had been flame-dried and purged with argon 3 times. The flask was equipped with a magnetic stir bar and rubber septum. NaN₃ (677 mg, 10.42 mmol) was then added to the stirring solution. The reaction stirred at ambient temperature (21 °C) for 20 h. The reaction was quenched with H₂O (20 mL) and extracted with CHCl₃ (3 x 20 mL). The combined organic extracts were filtered over MgSO₄ and the solvent was removed by a rotary evaporator. The
resultant liquid was dried *en vacuo* overnight to remove additional DMF. This yielded a clear, colorless liquid (1.51 g, 94%) that required no further purification. 

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 4.25 (t, 2H, $J = 4.8$ Hz), 3.81 (t, 2H, $J = 4.8$ Hz), 2.68 (s, 1H), 1.46 (s, 1H); $^{13}$C NMR (300 MHz, CDCl$_3$): $\delta$ 172.55, 66.55 62.70, 59.72, 23.68.

### 2.2.4 Synthesis of azide ligand (4)

![Chemical Structure](image)

3 (1.00 g, 5.77 mmol) was dissolved in anhydrous THF (2 mL) in a flame-dried pear-shaped flask that was purged 3 times with argon. In a flame-dried round bottom flask, POCl$_3$ (0.6 mL, 6.35 mmol) was dissolved in 15 mL THF under Ar. The flask was equipped with a magnetic stir bar and rubber septum. Anhydrous tri-ethylamine (0.9 mL, 6.35 mmol) was added, the mixture was then cooled to 0 °C with an ice bath. Slowly the ester was added drop-wise to the cooled solution. The mixture became cloudy and white upon addition. The reaction mixture was allowed to warm to ambient temperature (21 °C) as the ice melted. Let stir for an additional 3 hr. The reaction became light yellow and clear. Quenched the reaction with H$_2$O (10 mL). Checked pH to ensure it was < 2. The mixture was extracted with CHCl$_3$ (3 x 15 mL). The combined organic extracts were filtered over MgSO$_4$ and the solvent was removed from the product.
using a rotary evaporator. The resultant liquid was dried for several hours under vacuum (10 mTorr) to remove excess solvent. This yielded a light amber, highly viscous, clear liquid (0.80 g, 55%). No further purification was done. $^1$H NMR (300 MHz, CDCl$_3$): δ 10.21 (br, 2H), 4.41 (br, 2H), 4.33 (br, 2H), 1.51 (s, 6H); $^{31}$P NMR (300 MHz, CDCl$_3$): δ 0.68. FTIR (cm$^{-1}$): 3700-2500 (br), 2114 (vs), 1742 (s), 1469 (m), 1252 (s), 1148 (s), 1075 (s), 1024 (s).

2.2.5 **General procedure for stripping oleic acid from γ-Fe$_2$O$_3$ nanocrystals**

EtOH (10 mL) was added to a solution of oleic acid coated maghemite nanocrystals (Fe$_2$O$_3$-OA) that were dispersed in CHCl$_3$ (5 mL). The solution became cloudy upon addition of EtOH. The mixture was then centrifuged, and the precipitated particles were collected. An additional 5 mL of EtOH was added to the solid particles and the solution was sonicated for 15 min. The solution was then centrifuged and the precipitated particles were collected. The particles were washed an additional 2x with EtOH and sonicated. The resultant nanocrystals were no longer dispersible in CHCl$_3$.

2.2.6 **Procedure for synthesizing Fe$_2$O$_3$-azide (5)**
A 1:1 weight ratio of 4:Fe$_2$O$_3$ nanocrystals was added to a centrifuge tube. Approximately 5 mL of CHCl$_3$ was added to the particles. The resultant mixture was then sonicated for 30 min. until the particles appeared dispersed. Hexane was then added to the solution of particles until the mixture became cloudy. This was done to remove excess 4 that was not attached to the surface of the particles. The mixture was then centrifuged, and the precipitate was collected, while the supernatant was discarded. The precipitated particles were then redispersed in CHCl$_3$. The particles were no longer soluble in hexanes and other non-polar solvents. FTIR (cm$^{-1}$): 3500-2500 (br), 2115 (vs), 1742 (s), 1468 (m), 1252 (s), 1148 (s), 1074 (s), 991 (s).

Scheme 2-1. General scheme for the synthesis of azide functional iron oxide nanocrystals (Fe$_2$O$_3$-azide).
2.2.7 Procedure for attaching 5-hexynoic acid to the surface of maghemite nanocrystals (Fe₂O₃-alkyne)

A 1:1 weight ratio of 5-hexynoic acid:Fe₂O₃ nanocrystals was added to a centrifuge tube. Approximately 5 mL of hexanes was added to the particles. The resultant mixture was then sonicated for 60 min. until the particles appeared dispersed. Ethanol was then added to the solution of particles until the mixture became cloudy. This was done to remove excess 5-hexynoic acid that was not attached to the surface of the particles. The mixture was then centrifuged, and the precipitate was collected, while the supernatant was discarded. The precipitated particles were then redispersed in hexanes.

2.3 Results and Discussion

2.3.1 TEM Characterization

Maghemite nanocrystals were synthesized by decomposition of Fe(CO)₅, as stated in the experimental methods. The subsequent nanocrystals (Fe₂O₃-OA) were relatively monodispersed (<5% rms) and varied in size from 10-15 nm from one batch to another. XRD and XPS were performed on these samples by other researchers, and the results were previously published.²⁹⁻³¹ It was determined
that the nanocrystals were $\gamma$-Fe$_2$O$_3$ and that the oleic acid was chemi- and physisorbed to the surface. The size was estimated within the limits of accuracy for transmission electron microscopy (TEM) (Figure 2-4). The nanocrystals are spherical in shape, and they do not appear to form aggregates.

![Image](image.png)

**Figure 2-4.** Transmission electron micrograph of Fe$_2$O$_3$ nanocrystals synthesized from Fe(CO)$_5$.

As stated previously, two types of ligands were used to modify the surface of maghemite nanocrystals. The 5-hexyloic acid ligand was purchased from Sigma-Aldrich and used without further modification or purification, while the azide ligand was synthesized from commercially available starting materials (Scheme 2-1). Once the ligand exchange was carried out, the nanocrystals were dispersed in solvents that were dictated by the properties of the new ligands. For example, the nanocrystals that were stabilized with the hexyloic acid were dispersible in nonpolar solvents such as hexanes, whereas the nanocrystals
stabilized with the phosphate ligand were dispersible in slightly more polar solvents such as THF and chloroform. As seen in the TEM images (Figure 2-5), both the Fe₃O₅-azide, A, and the Fe₃O₅-alkyne, B, retained their core size and did not form aggregates upon ligand exchange.

Figure 2-5. Transmission electron micrographs of (A) Fe₃O₅-azide and (B) Fe₃O₅-alkyne. Scale bar is 50 nm.

2.3.2 TGA Analysis

It has previously been demonstrated that when oleic acid is used as a surface ligand in the synthesis of Fe₃O₅ nanocrystals it binds relatively strongly to the surface of the nanocrystals by both physisorption and chemisorption.¹³,³¹,³² This phenomenon has been extensively studied. For the purposes of this study, the FTIR spectra and TGA data for Fe₃O₅-OA have been included for comparison purposes only.

Thermogravimetric analysis (TGA) was used to gain insight into the nature of the surface binding of the various ligands on Fe₃O₅ nanocrystals. A
TGA instrument is comprised of an analytical balance and a furnace. A typical experiment involves heating a sample while monitoring the loss in mass. TGA generally gives quantitative information on the amount (mass) of organics on the nanocrystals, and qualitative information on the nature of surface adsorption.

Figure 2-6 shows the TGA data for Fe$_2$O$_3$-OA. Plot A is a thermogram which shows the percent mass of the sample as a function of temperature. The mass loss is attributed to the decomposition/desorption of various molecules that are adsorbed on the nanocrystals. When the derivative of the thermogram is plotted as a function of temperature the result is a plot that displays the decomposition/desorption temperature for each surface ligand. In some cases, the presence of multiple desorption temperatures for one sample is interpreted as an indication of the relative binding strength of each adsorbed species. That is to say, the stronger a molecule adsorbs to the surface, the higher the desorption temperature. Another theory to explain the presence of multiple decomposition/desorption temperatures is that there can be multiple types of bonding that occur between the ligand and the nanocrystal surface. The two desorption signals in plot B (large peak at $\sim$220 °C and small peak at $\sim$ 275 °C) are attributed to the fact that both physisorption and chemisorption occur, thus there are two stages of desorption as expected.
Figure 2-6. (A) TGA thermogram of Fe$_2$O$_3$-OA and (B) derivative thermogram for Fe$_2$O$_3$-OA.

The TGA data for Fe$_2$O$_3$-OA can then be compared to that for Fe$_2$O$_3$-azide and Fe$_2$O$_3$-alkyne (Figure 2-7). In the derivative plot for Fe$_2$O$_3$-azide there are two broad peaks at ~ 200 °C and 400 °C, which are attributed to the surface desorption of the phosphate ligand (4 in Scheme 2-1). It is possible that the azide ligand is both physisorbed and chemisorbed to the surface of the nanocrystals, or that there are two modes of chemisorption (see Figure 2-3), one of which may be stronger than the other. The 5-hexynoic acid ligand also shows a small peak at ~ 200 °C and another, larger peak at ~450 °C (the loss at ~ 100 °C is attributed to residual solvent present in the sample). The normal boiling point of the acid is 224-225 °C. This two-step desorption phenomena has been documented for similar systems,$^{18}$ thus this is not a surprising finding. It is hypothesized that the
bimodal desorption occurs because of a mixture of chemisorption and physisorption of the ligands on the surface of the γ-Fe₂O₃ nanocrystals.

![Graphs A and B](image)

**Figure 2-7.** Plot of dm/dT vs. temperature for (A) Fe₂O₃-azide and (B) Fe₂O₃-alkyne. Each signal indicates the temperature at which the ligands desorb from the nanocrystal surface.

### 2.3.3 Fourier Transform Infrared Spectroscopy

Fourier Transform Infrared Spectroscopy (FTIR) was used to study the surface functionality of the nanocrystals, and to verify a successful ligand exchange. For the azide ligand, there are three important regions to examine (Figure 2-7). The first is the signal at 2115 cm⁻¹ which is due to the azide stretching frequency, indicating that this functionality remained in tact. The second signal, at 1742 cm⁻¹, is due to the carbonyl stretching of the ester moiety. The last region of importance is between 1000-1250 cm⁻¹, and these signals are due to the phosphate stretches. There are multiple peaks in this region as a
result of the fact that there are multiple P-O bonds which absorb different frequencies of radiation. Because there are so many signals in the region from 1000-1250 cm\(^{-1}\), it is difficult to determine from the FTIR if there is a change in the P-O stretching frequencies that would result from chemisorption to the surface of the nanocrystals, thus the mode of binding is difficult to determine from this data. However, the fact that all of the functionality remains intact, combined with the information obtained from the TGA data and TEM data, it is clear that the phosphate-azide ligands adsorb relatively strongly to the surface of the nanocrystals, and that they stabilize the nanocrystals against aggregation.
Figure 2-7. FTIR spectrum comparing the free azide ligand (bottom) and Fe$_2$O$_3$-azide (top).

The FTIR spectrum of the alkyne ligand also has three regions to consider (Figure 2-8). At 2118 cm$^{-1}$ there is a very weak signal due to the C-C triple bond.$^{34}$ The alkyne C-H absorbance shows up as a signal at 3298 cm$^{-1}$. At 1709 cm$^{-1}$ there is a signal due to the carbonyl stretch of the carboxylic acid moiety. The fact that the IR spectrum for the free ligand is nearly identical to the spectrum for the Fe$_2$O$_3$-alkyne suggests that the ligand is merely physisorbed to the surface of the nanocrystals. This conclusion is also supported by the TGA data, which shows two distinct temperatures for desorption, with the lower temperature being
attributed to physisorption. Although this interaction appears to be a physical one, it is still strong enough to prevent aggregation of the nanocrystals (as evidenced by TEM micrographs), and the alkyne functionality is still present.

Figure 2-8. FTIR spectra of free 5-hexynoic acid (top) and Fe$_2$O$_3$-alkyne (bottom).

2.4 Determination of Surface Coverage

It is important not only to determine the structure of surface ligands on nanocrystals, but also how much ligand is on the nanocrystals. The TGA data (shown above) not only gives information about the binding strength of both the
azide and alkyne ligands, but also allows us to calculate an estimated surface coverage of ligand on the nanocrystals. Through the use of TEM, it is possible to obtain an approximate diameter for the nanocrystal core. Once the diameter of the nanocrystals was estimated, the surface area (SA) was calculated using a spherical model for the nanocrystals.\textsuperscript{33} For a batch of 12 nm $\gamma$-Fe$_2$O$_3$ nanocrystals, the surface area (SA) was calculated to be 452 nm$^2$ per particle. The following equations were used to determine the surface coverage (number of ligands per unit area) of the functionalized nanocrystals, where $\delta$ is the graft density, $\Delta w$ is the % weight loss, $M_{\text{group}}$ is the mass of the functional group, $\chi$ is the number of ligands/nm$^2$, $A_N$ is Avogadro’s number, and $S$ is the specific surface area of the nanocrystal core:\textsuperscript{33}

\begin{align*}
\delta &= \frac{\Delta w}{M_{\text{group}}} \quad \text{eq. 2-1} \\
\chi &= \frac{\delta A_N}{S} \quad \text{eq. 2-2}
\end{align*}

Using equation 2-1, the graft density of functional ligands on the nanocrystals was estimated, and the values are found in Table 2-1. These grafting densities are reasonable compared to experimental values obtained by other researchers, ranging anywhere from 0.7-3.1 ligands/nm$^2$.\textsuperscript{33,35} It is important to note that when one considers the grafting density of ligands on spherical nanocrystals the curvature of the nanocrystals will have a greater effect on the
surface coverage for small diameter nanocrystals. Thus, the number of ligands per particle should change not only due to increasing surface area for larger nanocrystals, but also for increasing curvature.

**Table 2-1.** Grafting density of various ligands on the surface of Fe₂O₃ nanocrystals.

<table>
<thead>
<tr>
<th></th>
<th>Diameter (nm)</th>
<th>δ (mol/g)</th>
<th>χ (ligands/nm²)</th>
<th>Ligands/particle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe₂O₃-OA</td>
<td>12</td>
<td>1.9 x 10⁻³</td>
<td>5.6</td>
<td>2.5 x 10⁻⁴</td>
</tr>
<tr>
<td>Fe₂O₃-alkyne</td>
<td>12</td>
<td>1.6 x 10⁻³</td>
<td>5.1</td>
<td>2.3 x 10⁻⁴</td>
</tr>
<tr>
<td>Fe₂O₃-azide</td>
<td>12</td>
<td>3.2 x 10⁻⁴</td>
<td>1.0</td>
<td>4.6 x 10⁻²</td>
</tr>
</tbody>
</table>

In order to understand what this data means, the estimated surface coverage of must be calculated based upon two models: one where the ligands are upright and stretching away from the surface of the nanocrystal, and one where the ligands are lying down on the surface. For each ligand, the surface area that it occupies can be estimated by treating it as a cylinder. Given the bond lengths and angles of the head group that is attached to the surface, the radius of the head group can be determined using basic trigonometry (Table 2-2). By treating the head group as a circle (area = πr²), the surface area occupied by a carboxylic acid head group was found to be 1.2 x 10⁻² nm², which would facilitate
the attachment of ~37,000 ligands per nanocrystal ($\chi = 83$ ligands/nm$^2$). In order to calculate the surface coverage based upon the model where the ligands are lying down on the surface, a cylindrical model must be used for a ligand (surface area = $2\pi rh + 2\pi r^2$). From these assumptions it was estimated that if the ligands are lying down on the surface there would be ~1600 ligands per nanocrystal, or 3 ligands/nm$^2$.

The same analysis can be performed on the phosphate ligand using the same assumptions. The surface area occupied by the phosphate head group was calculated, and it was determined that the maximum surface coverage would be ~14,000 ligands/nanocrystal (32 ligands/nm$^2$). The surface coverage estimated for ligands that are lying down on the surface was ~1400 ligands/nanocrystal (3 ligands/nm$^2$).

Table 2-2. Estimated range of surface coverage for different ligands on a 12 nm $\gamma$-Fe$_2$O$_3$ nanocrystals. The low value is based upon a model where the ligand is lying down on the surface, and the high value is based upon a model where the ligands are stretching out away from the surface.\(^\text{10}\)

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Bond</th>
<th>Distance (Å)</th>
<th>Bond Angle (Degrees)</th>
<th>Estimated $\chi$ (# lig./nm$^2$)</th>
<th>Estimated # of ligands/particle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C-O$_a$</td>
<td>1.214</td>
<td>$&lt;$ OCO 122.8</td>
<td>3–83</td>
<td>1,600–37,000</td>
</tr>
<tr>
<td></td>
<td>C-O$_b$</td>
<td>1.364</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O$_a$-O$_b$</td>
<td>1.240</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>P-O$_b$,c</td>
<td>1.571</td>
<td>$&lt;$ O$_a$PO$_b$ 101.5</td>
<td>3–32</td>
<td>1,400–14,000</td>
</tr>
<tr>
<td></td>
<td>O$_b$-O$_c$</td>
<td>1.987</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
When the estimated surface coverage values are compared to the experimental values, some conclusions can be drawn. First, it makes sense that for the phosphonate ligand there are fewer ligands/nm² because the head group occupies more surface area. This piece of evidence is in agreement with the experimental results. The experimental data also falls reasonably well into the range of values estimated. Considering that the experimental results are also consistent with other literature reports, we feel confident that our results are reliable.

2.5 Conclusions

We have successfully functionalized the surface of γ-Fe₂O₃ nanocrystals with both alkyne- and azide-functional ligands. The resultant nanocrystals were well dispersed, and the metal core of the nanocrystals did not change in shape or size upon ligand exchange, as indicated by TEM images. The functionality of the nanocrystals was confirmed by FTIR spectroscopy, as both the azide and alkyne moieties were in tact. The surface coverage of the nanocrystals was estimated by analyzing both the TEM images of the nanocrystal core and the TGA data. It was estimated that for 12 nm diameter nanocrystals, the Fe₂O₃-alkyne had approximately 5 ligands/nm² and the Fe₂O₃-azide had approximately 1
ligands/nm². On the basis of experimental results of other researchers, these values were found to be reasonable for these types of surfaces.¹³

Not only was the ligand exchange process successful, but the solubility and dispersibility of the subsequent nanocrystals was solely dependent upon that of the surface ligands. Although the type of surface adsorption (chemisorption vs. physisorption) is not clearly indicated by the experimental results, the binding is clearly strong enough to stabilize the nanocrystals against aggregation for long periods of time. In conclusion, we have demonstrated a straight-forward, simple method of ligand exchange for iron oxide nanocrystals. The versatility of this methodology will be demonstrated in subsequent chapters.
2.6 References


3 Using “Click” Chemistry to Functionalize the Surface of Iron Oxide Nanocrystals

3.1 Background and Introduction

The ligand exchange of γ-Fe₂O₃ nanocrystals was discussed in previous sections, and here the reaction of these nanocrystals with click functional molecules will be described as a general route to the rational design of nanocrystal systems. The “universal” nature of this approach will also be demonstrated with its use for the covalent attachment of both small molecule and polymer groups (Scheme 3-1).

Scheme 3-1. General scheme for functionalizing the surface of iron oxide nanocrystals.
3.1.1 Copper-catalyzed Azide-alkyne Cycloaddition Reaction

As stated in chapter 1, there are several classes of organic reactions that have been around for decades, but have only recently been classified as click reactions. Among them is the Huisgen 1,3-dipolar cycloaddition reaction of an azide with an alkyne.\(^1\) Although this reaction has been known and employed for decades, it wasn’t until more recently that the scope and versatility of this reaction have begun to be fully understood. More recently, this synthetic tool has become widely used in the fields of materials and polymer science,\(^2\) synthetic chemistry,\(^15,16\) and even biology.\(^17\) With the development of the copper catalyzed version of this reaction, termed the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction by Sharpless and coworkers,\(^26,27\) came the widespread use of this methodology. The relatively mild conditions under which the CuAAC reaction proceeds (at low temperature [23–60 °C] and in the presence of air and water), opened up a plethora of opportunities for using this chemistry. The CuAAC is considered an exemplary click reaction, and thus has been employed in many practical applications. One of the highlights of this chemical transformation is that it is orthogonal to most other chemical reactions. That is to say, azides and alkynes react primarily with each other, thus pesky side reactions rarely, if ever, occur. This fact is in part what makes this
methodology so attractive for use in biological systems, as the functional groups do not interact with most biological molecules.

The mechanism of the CuAAC reaction is not completely understood, but several proposed mechanisms have been published to date. The first purported mechanism involves the formation of a copper(I) acetylide complex (Figure 3-1), a complex that is well preceded. The surprising finding, as evidenced by DFT calculations, was that the concerted [2 + 3] cycloaddition reaction (B-direct) is disfavored by about 15 kcal/mol when compared to the stepwise process involving a six-membered cyclic intermediate containing copper, indicating that no direct cycloaddition is likely to occur.\textsuperscript{30}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig3-1.png}
\caption{Proposed catalytic cycle for the Cu-catalyzed azide-alkyne cycloaddition reaction.}
\end{figure}
A more thorough investigation into the mechanism of this reaction has been done more recently. Based upon kinetics studies, DFT calculations, and the results from experiments involving a known multinuclear Cu-acetylide compound, a modified catalytic cycle was proposed (Figure 3-2). What is interesting about this mechanistic investigation is that it suggests not only the involvement of a multinuclear Cu-complex, but also the complexation of a completely formed triazole ring with a Cu-acetylide. Studies involving reaction of multi-azido functionalized compounds imply that this proposal is quite plausible.

Figure 3-2. Proposed catalytic cycle for the ligand-free CuAAC reaction involving a multinuclear Cu-acetylide complex.
Due to the ease of carrying out a CuAAC reaction, as well as the mild conditions under which the reaction takes place, researchers have been utilizing it more and more in recent years, despite many researchers’ fear of using azide compounds for safety reasons. The fact that this reaction is also a very high yielding one makes it particularly applicable to surface modifications, where it is often difficult to quantify the extent of reaction at the surface. Recent examples of such endeavors include the modification of silica,\textsuperscript{32,33} gold,\textsuperscript{3,34} and even carbon nanotubes.\textsuperscript{35} Herein, the use of the CuAAC reaction to functionalize the surface of $\gamma$-Fe$_2$O$_3$ nanocrystals will be demonstrated.

### 3.1.2 Atom Transfer Radical Polymerization

As mentioned in chapter 1, new methods for generating functional nanomaterials are becoming more and more important. Materials such as inorganic nanoparticle-polymer core-shell materials are gaining much attention from researchers, and it has become even more critical to develop better methods for polymer synthesis. Living radical polymerization (LRP) was described in detail in chapter 1. Atom transfer radical polymerization (ATRP) is a specific type of LRP, which is catalyzed by a metal complex through a redox cycle.\textsuperscript{36} The general mechanism of this process is depicted in Scheme 3-2, where R is the polymer, M$^{cnt}$/Ligand is the metal complex, and X is a transfer group.
Scheme 3-2. General mechanism for ATRP. \( k_a \) is the rate of activation, \( k_{da} \) is the rate of deactivation, \( k_p \) is the rate of propagation, and \( k_t \) and \( k_{tr} \) are the rates of termination and transfer respectively.

One of the advantages of ATRP over other LRP methods is that it can be used with a large variety of monomers, where other methods of LRP can be limited in the types of monomers that can be used. Some of the monomers commonly used in ATRP include styrenes, acrylates, methacrylates, acrylamides, methacrylamides, and acrylonitrile.\(^{36}\) An additional benefit of ATRP is that there are more ATRP initiators available than initiators for any other LRP method. Because functional initiators are so readily available for ATRP, it is possible to incorporate end-group functionality into the polymer, which is another characteristic that makes ATRP so seductive.

As mentioned earlier, ATRP involves a transition metal catalyst which facilitates polymerization through a redox cycle, whereby the oxidized metal readily reacts with the growing polymer chain to form a dormant species (Scheme 3-2). Although various metals have been utilized in ATRP (Mo, Cr, Re, Ru, Fe, Pd, and Ni), the most widely used and least expensive is Cu.\(^{36}\) Not only
is the metal important, but the type of ligand also greatly effects the efficiency of the reaction and the polydispersity of the resulting polymers.\textsuperscript{36}

The fact the ATRP produces well-defined polymers with end functionality was in part why this method was chosen for the synthesis of the polymers for the studies in this report.

3.2 Experimental Methods

3.2.1 Synthesis of $\alpha$-acetylene-poly(tert-butyl acrylate) (PtBA-alkyne)

\[
\text{CuBr (168 mg, 1.17 mmol) and 2-propynyl 2-bromo-2-methylpropanoate}\textsuperscript{37} (240 mg, 1.17 mmol) were added to a clean, dry round bottom flask, which was subsequently evacuated for 15 min. and back-filled with argon. Freshly distilled tert-butyl acrylate (11.4 g, 88.9 mmol) was added via a degassed syringe followed by degassed toluene (5.7 mL), and PMDETA (1.95 g, 11.7 mmol). The reaction flask was immediately submerged in liquid N\textsubscript{2} until frozen, evacuated for 15 min., removed from liquid N\textsubscript{2}, and backfilled with argon. When the mixture thawed completely, the flask was submerged in a 70 °C oil bath and stirred for 12 hrs. under argon atmosphere. After this time, the reaction flask was opened to air, frozen in liquid N\textsubscript{2}, thawed and diluted with tetrahydrofuran (20 mL). This solution was passed through a column of neutral alumina, concentrated on a}
rotary evaporator, precipitated in a 10:1 volume of 50-50 methanol-water:toluene three times, dissolved in diethyl ether, dried over MgSO₄, filtered, concentrated on a rotary evaporator, and dried in vacuo for 2 d to yield compound ω-acetylene-poly(tert-butyl acrylate) (Mₙ(NMR): 11,100 Da) as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 4.64 (s, 2 H), 2.23 (br, 85 H), 1.82 (br, 49 H), 1.43 (br, 765 H), 1.16 (s, 6 H); ¹³C NMR (400 MHz, CDCl₃): δ 174.5, 80.60, 74.83, 52.20, 42.09, 37.52, 35.93, 28.19; FTIR (cm⁻¹) 2978, 2933, 1727, 1479, 1456, 1392, 1366, 1256, 1148, 845; THF-SEC: Mₙ = 11,650, PDI = 1.19.

3.2.2 Procedure for copper(I) catalyzed azide-alkyne cycloaddition³¹ of Fe₂O₃-azide (1)

In a round bottom flask (rbf) in air, Fe₂O₃-azide (30 mg, 0.103 mmol of azide at the surface) was dissolved in 5 mL of 4:1 DMSO:H₂O. To this mixture was added 5-chloro-pentyne (13 μL, 0.124 mmol), followed by CuSO₄·5H₂O (3.1 mg, 0.008 mmol) and sodium ascorbate (4.1 mg, 0.0206 mmol). The reaction mixture stirred in air at room temperature for 24 h. Added CHCl₃ (1 mL), acetone (1 mL), and ethanol (1 mL) to the mixture. The mixture was then centrifuged, and the precipitated particles were collected and characterized. The particles were soluble in MeOH and CHCl₃, but not less polar solvents, and they were not soluble in H₂O. In order to obtain a ¹H NMR spectrum of the particles,
the solution had to be extremely dilute. TEM images were taken of the resultant particles.

3.2.3 Procedure for copper(I) catalyzed azide-alkyne cycloaddition of Fe2O3-alkyne (2)

In a rbf in air, Fe2O3-alkyne (232 mg, 2.07 mmol of 5-hexynoic acid at the surface) was dissolved in 5 mL of 4:1 DMSO:H2O. To this mixture was added benzyl azide (276 mg, 2.07 mmol), CuSO4·5H2O (62 mg, 0.25 mmol), and sodium ascorbate (81 mg, 0.41 mmol) and the reaction stirred overnight at RT in air. Added H2O to precipitate particles and centrifuged. Collected the precipitate and dispersed in a mixture of CHCl3:EtOH (8:2). In order to obtain a 1H NMR spectrum of the particles, the solution had to be extremely dilute. TEM images were taken of the resultant particles.

3.2.4 Procedure for copper(I) catalyzed azide-alkyne cycloaddition of Fe2O3-azide with PtBA-alkyne (Fe2O3-PtBA)

Fe2O3-azide (64 mg, 0.22 mmol) was dissolved in 4 mL DMSO in a rbf in air, then 1 mL of H2O was added. PtBA-alkyne (2.4 g, 0.241 mmol) was then added, followed by the addition of 35 mL of 4:1 DMSO:H2O. CuSO4·5H2O (6.7 mg, 0.027 mmol), sodium ascorbate (8.7 mg, 0.044 mmol), and BIPY (5.4 mg, 0.034 mmol) were then added and the mixture was heated to 60°C in air for 36h. Stopped reaction and added CHCl3 and saturated solution of NH4Cl. Extracted
three times with CHCl₃ and washed organic extracts with NH₄Cl solution to remove excess copper. Concentrated the sample by rotary evaporator, then washed particles with 10:1 MeOH:H₂O to precipitate particles and remove excess unbound polymer. The solution was centrifuged, and the precipitated particles were collected (brown in color) and redispersed in THF.

Scheme 3-3. Synthetic scheme for the copper-catalyzed azide-alkyne Cycloaddition (CuAAC) reaction of Fe₂O₃ nanocrystals with various substrates.
3.3 Results and Discussion

3.3.1 TEM Characterization

TEM micrographs were taken of the nanocrystals after they had undergone reaction with various substrates. It is important to note that the nanocrystal core did not change in shape or size upon reaction, thus indicating that the CuAAC reaction does not affect the nanocrystal core (Figure 3-3). The other significant finding was that the nanocrystals did not aggregate upon reaction. The solubility of the nanocrystals was governed by the physical properties of the ligands, so the nanocrystals became dispersible in a new set of solvents after reaction, but they were still dispersed.

![TEM micrographs of (A) Fe₂O₃-azide after CuAAC with 5-chlorohexyne and (B) Fe₂O₃-alkyne after CuAAC with benzyl azide. Scale bars are 100 nm.](image)

Figure 3-3. TEM micrographs of (A) Fe₂O₃-azide after CuAAC with 5-chlorohexyne and (B) Fe₂O₃-alkyne after CuAAC with benzyl azide. Scale bars are 100 nm.

The Fe₂O₃-P⁵BA did not form aggregates during or after the CuAAC reaction had taken place. As seen in the TEM image, the nanocrystals still
retained their size and shape (Figure 3-4). Comparing the TEM image from the Fe$_2$O$_3$-OA to the Fe$_2$O$_3$-PBA (A and B respectively in Figure 3-2), this point becomes obvious. It is clear from these images that the ligand periphery effectively stabilizes the nanocrystals against aggregation, which is one of the more difficult challenges of working with nanocrystal systems.

![Figure 3-4. TEM micrographs of (A) Fe$_2$O$_3$-azide (scale bar is 50 nm) and (B) Fe$_2$O$_3$-PBA (scale bar is 100 nm).](image)

3.3.2 FTIR Characterization

As mentioned in previous chapters, Fourier-Transform Infrared Spectroscopy (FTIR) is a useful tool in determining the success of nanocrystal functionalization.$^{\text{38-40}}$ In this work, FTIR was used to monitor the CuAAC reaction progress, and to verify the reaction of the azide and alkyne moieties. This is a standard method of characterization, as the alkyne and azide stretches have very characteristic peaks in the IR, the disappearance of which can be
monitored as the reaction progresses.\textsuperscript{34,35} Based upon the estimated surface coverage from the previous chapter, a 1:1 molar ratio of azide to alkyne was allowed to react in both the case of Fe\textsubscript{2}O\textsubscript{3}-azide and Fe\textsubscript{2}O\textsubscript{3}-alkyne.

In the reaction of Fe\textsubscript{2}O\textsubscript{3}-azide with 5-chlorohexyne, the FTIR signal due to the azide stretching frequency (2115 cm\textsuperscript{-1}) was monitored in relation to the signal due to the carbonyl moiety (1742 cm\textsuperscript{-1}) (Figure 3-5). The peak area of the signal at 1742 cm\textsuperscript{-1} was compared to the peak area of the signal at 2115 cm\textsuperscript{-1}, and the results are summarized in Table 3-1.
Figure 3-5. FTIR spectra of Fe$_2$O$_3$-azide (top) and the Fe$_2$O$_3$-azide nanocrystals that have been subjected to CuAAC reaction conditions (bottom).

Table 3-1. Comparison of the FTIR peak areas of the signals due to the azide stretching and the carbonyl stretching of the Fe$_2$O$_3$-azide before and after the CuAAC reaction with benzyl azide.

<table>
<thead>
<tr>
<th></th>
<th>N$_3$ Signal (2115 cm$^{-1}$)</th>
<th>C=O Signal (1742 cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative Peak Area</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before CuAAC</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Relative Peak Area</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After CuAAC</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
Before the CuAAC reaction occurred, the peak area of the signal at 2115 cm\(^{-1}\) was double that of the signal at 1742 cm\(^{-1}\). However, once the reaction took place, the peak area of the signal at 1742 cm\(^{-1}\) became 3 times that of the signal at 2115 cm\(^{-1}\). Although FTIR is not a quantitative method for determining reaction yield, the data does indicate that some of the azide has been consumed during the reaction. It is also important to note that the signal due to the phosphate functionality at the surface of the nanocrystals is also still present (1075 cm\(^{-1}\)), which is interpreted as meaning that the ligand is still attached to the nanocrystals. This signal is due to the stretching of the various P-O bonds in the ligand. Although it appears that some of the azide has reacted, there is still a signal at 2115 cm\(^{-1}\) due to this stretch, signifying that the reaction did not go to completion. The incomplete reaction could be the result of inaccuracy in estimating the surface coverage of the azide ligand on the Fe\(_2\)O\(_3\) nanocrystals, or could be due to a change in the reactivity of the ligand once it attaches to the surface of the nanocrystals. The evidence does suggest, however, that the reaction has taken place to some extent.

Control reactions were also run, and the FTIR spectra of the control reactions were compared to those for the click reactions. It is evident from Figure 3-6 that the FTIR spectrum of the control reaction of free phosphate ligand with 5-chlorohexyne very closely resembles that for the Fe\(_2\)O\(_3\)-azide reaction with
5-chloropentyne. The reaction conditions for the control were identical, with the difference being the absence of $\gamma$-Fe$_2$O$_3$ nanocrystals in the control. It also appears from the FTIR that the control reaction did not proceed to 100% completion either.

![FTIR spectra of Fe$_2$O$_3$-azide (top), control reaction of free azide ligand with 5-chlorohexyne (middle), and Fe$_2$O$_3$-azide-click product (bottom).](image)

**Figure 3-6.** FTIR spectra of Fe$_2$O$_3$-azide (top), control reaction of free azide ligand with 5-chlorohexyne (middle), and Fe$_2$O$_3$-azide-click product (bottom).

The reaction of Fe$_2$O$_3$-alkyne was also followed by FTIR. One complication of studying this reaction is that the IR signal due to the alkyne
moiety is very weak to start, so monitoring its disappearance is more difficult than monitoring the disappearance of an azide signal. Although this can be a challenge, it was possible to monitor the disappearance of the signals (3298 cm\(^{-1}\) and 2118 cm\(^{-1}\)) due to the alkyne (Figure 3-7). It is also apparent that there is no azide signal remaining, indicating that there is no unreacted benzyl azide left in the mixture. When considering the IR spectrum for the control reaction of benzyl azide with hexynoic acid, it appears to very closely match that for the Fe:O\(_2\)-alkyne cycloaddition reaction with benzyl azide. This evidence supports the conclusion that the CuAAC reaction of the Fe:O\(_2\)-alkyne was successful.
Figure 3-7. FTIR spectra of Fe$_2$O$_3$-alkyne-click reaction with benzyl azide (top), Fe$_2$O$_3$-alkyne (middle), and the control reaction of free hexynoic acid with benzyl azide (bottom). Inset is the region from 2200 cm$^{-1}$ to 1600 cm$^{-1}$ which focuses on the signals due to the carbonyl C=O stretch and the alkyne C-C stretch.

The reaction of Fe$2$O$3$-azide with poly(tert-butyl acrylate) (PtBA) was also monitored by FTIR (Figure 3-8). There are several signals of significance in this spectrum. The first is the signal due to the azide moiety (2115 cm$^{-1}$) that completely disappears in the spectrum that was taken after the CuAAC reaction, indicating that there is no unreacted azide present. There is also a signal at 1055 cm$^{-1}$ that is present in the spectrum of Fe$2$O$3$-PtBA, but is not present in the spectrum of pure PtBA. This peak is attributed to P-O-R asymmetric stretching.
from the phosphate ligand. This evidence supports the conclusion that the CuAAC reaction was successful in covalently attaching PtBA to the surface of the nanocrystals. The last thing to note is that the rest of the spectrum for Fe2O3-PtBA is in agreement with the spectrum for pure PtBA, which confirms the presence of PtBA on the nanocrystal surface.

**Figure 3-8.** FTIR spectra of Fe2O3-azide (top), Fe2O3-azide that has undergone CuAAC with alkyne functional PtBA (middle) and PtBA (bottom).
3.3.3 Characterization of Surface Reaction by NMR

Nuclear Magnetic Resonance (NMR) has been used as a tool to study the surface and dynamics of nanocrystal systems.\textsuperscript{41-44} Some of the most studied nanocrystal systems are semiconducting nanocrystals. Both solid state and solution state NMR have been used to study the surface ligands of these nanocrystals. An advantage of these systems over the $\gamma$-Fe$\textsubscript{2}$O$\textsubscript{3}$ system is that they are diamagnetic nanocrystals, whereas the iron is paramagnetic. Paramagnetic atoms in general pose a problem in NMR, as they can cause severe broadening of peaks due to a reduction in the $T_2$ relaxation time (transverse, or spin-spin relaxation time).\textsuperscript{45} It was perhaps for this reason that NMR spectrometry was not a primary tool for examining the binding of ligands on paramagnetic nanocrystals like Fe$\textsubscript{3}$O$\textsubscript{4}$ and $\gamma$-Fe$\textsubscript{2}$O$\textsubscript{3}$. In a recent report, however, it was established that in the specific case of oleic acid capped $\gamma$-Fe$\textsubscript{2}$O$\textsubscript{3}$, NMR can be used to investigate these nanocrystals.\textsuperscript{40} It was surprising to the authors that no peak broadening occurred in the spectra, and very detailed analysis could be done.

Although it is not completely understood how we are able to obtain detailed NMR spectra, we were able to use the spectra we obtained in conjunction with the evidence we obtained from the FTIR to make conclusions about the success of the CuAAC reaction on $\gamma$-Fe$\textsubscript{2}$O$\textsubscript{3}$ nanocrystals.
At high concentrations of Fe$_3$O$_3$-azide-click and Fe$_3$O$_3$-alkyne-click, there is significant broadening of the NMR signals, however at low concentrations (< .5 mg/mL) the signals become much sharper. The purpose of the NMR study was primarily to determine if indeed the triazole formation took place in order to further confirm that the CuAAC reaction had taken place. Because there is a proton on the triazole ring that produces a signal from approximately 7-8 ppm in the $^1$H NMR, where no other signals should appear in this case, it is fairly straightforward to confirm the presence of this moiety.\textsuperscript{46} Although there is still a discernable NMR spectrum for the iron oxide nanocrystals, there is still some line broadening, which is attributed to the paramagnetic nature of the nanocrystals.

The $^1$H NMR spectrum for the control CuAAC reaction of benzyl azide was compared with that for the Fe$_3$O$_3$-alkyne reaction with benzyl azide (Figure 3-9). Although there is some broadening in the spectrum for the Fe$_3$O$_3$-alkyne-click (top), and there is no defined signal splitting, the spectra line up very well. There is some difference in the chemical shift of several of the peaks, but this is attributed to the effect of the paramagnetic iron nanocrystals. The most notable finding is that there is a signal at ~ 7.8 ppm due to the proton signal from the triazole moiety. This seems to confirm what the FTIR spectra indicated, which is that the CuAAC reaction was successful.
Figure 3-9. $^1$H NMR spectra of $\text{Fe}_2\text{O}_3$-alkyne-click product (top) and the control reaction of hexynoic acid with benzyl azide (bottom). NMR experiments were run in MeOD.

It was also possible to compare the NMR for the control reaction of the free phosphate ligand with 5-chloropentyne with the NMR for the $\text{Fe}_2\text{O}_3$-azide-click product (Figure 3-10). The spectrum for $\text{Fe}_2\text{O}_3$-azide-click clearly has more broadening than that for the $\text{Fe}_2\text{O}_3$-alkyne-click, which could be an effect of the concentration of the solution. There is also a more significant change in the
chemical shift for many of the peaks. This could also be an effect of the nature of the ligand binding on the surface of the γ-Fe$_2$O$_3$ nanocrystals. It has been shown that chemisorbed ligands are more affected (have a greater change in $T_1$ and $T_2$) by the nanocrystals than are physisorbed ligands.$^{41-44}$ These changes in chemical shift could be due to some complication arising from the ligand binding.

Figure 3-10. $^1$H NMR spectra of Fe$_2$O$_3$-azide-click (top) and the control reaction of the free azide ligand with 5-chlorohexyne (bottom). Inset is a magnified image of the signal from the triazole proton. NMR experiments were done in MeOD.
NMR was useful in confirming the covalent attachment of small molecules to the surface of the nanocrystals, and it was also used to determine the success of the covalent attachment of ω-acetylene-poly(tert-butyl acrylate) (PBA-alkyne) to the surface of the nanocrystals (Figure 3-11). NMR signals for polymeric materials are typically much broader than the monomers that comprise them due to molecular weight distribution and loss of mobility, so the signals in the 1H NMR spectrum of Fe₃O₅-PBA were expected to be broad with no line-splitting. The important finding, however, was the presence of the signal due to the triazole proton at ~ 7.8 ppm. It was expected that this signal would be very weak, as the concentration of the triazole compared to the polymer backbone is very low. The presence of the signal from the triazole proton, coupled with the fact that the rest of the spectrum matches that for the PBA-alkyne, supports the conclusion that the triazole ring was formed, and the PBA was covalently attached to the nanocrystal core.
3.4 Conclusions

The ligand exchange on γ-Fe₃O₃ nanocrystals was performed with two types of ligands: (1) phosphonic acid-azide and (2) carboxylic acid-alkyne. The resultant particles were submitted to CuAAC reactions with organic substrates, the products of which were well-dispersed in a range of solvents, a property
which is dependent upon the ligand of choice. These results establish a "universal ligand" approach for the surface functionalization of \( \gamma \)-Fe\(_2\)O\(_3\) nanoparticles and demonstrate that the nanoparticles can be dispersed in a variety of media by control of the ligand. Not only is this method applicable to iron oxide nanoparticles, but it is also presumably applicable to any other metal oxide surface (nanocrystal or bulk).
3.5 References


4 Polymer Coated Nanocrystals for Flexible Electronics Applications

4.1 Background and Introduction

The universal ligand concept was described and demonstrated in the previous chapters, with the goal of the methodology being to make the synthesis and functionalization of inorganic nanocrystals so straightforward that researchers could build libraries of functional materials for various applications. With the success of the Cu-catalyzed azide-alkyne cycloaddition (CuAAC) reaction on the γ-Fe₂O₃ system (Chapter 3), the aim was to demonstrate the universal nature of this new system by applying it to other metal oxide nanocrystals. The following sections will discuss the synthesis of click functional ligands for titanium dioxide (TiO₂) nanocrystals, and the subsequent functionalization of the nanocrystals with polymers through use of the CuAAC reaction. The resultant materials were then used to fabricated capacitors and thin film transistors (TFTs) for applications in large area flexible electronics (Figure 4-1).
Organic electronics, most notably organic thin film transistors (OTFTs), have recently taken center stage in research to develop low voltage, flexible, and inexpensive technology.\(^1\) An OTFT is simply a specific type of field effect transistor (FET). An OTFT works as a capacitor with one plate acting as a conducting channel between two contacts, the source and drain electrodes. The density of charge carriers in the channel is controlled by the voltage that is applied to the gate electrode (the other plate of the capacitor). OTFTs are comprised of four major components: a gate electrode, a dielectric layer, an active semiconducting layer, and source and drain electrodes (see Figure 4-1).\(^2\) TFTs act as on/off switches. That is to say, when \([V_C - V_T] = 0\), where \(V_C = \text{gate}\)
voltage and $V_T$ = threshold voltage (gate voltage necessary to make the channel conductance equal to the entire semiconductor), there is negligible current between the drain and source ($I_{DS}$), and the device is off (see eq. 4-1). When $[V_G - V_T] \neq 0$, the device turns on and charges begin to accumulate at the semiconductor/dielectric interface, causing a current to flow between the source and drain.\(^2\) The composition and deposition of each layer is critical to the overall device performance.

When developing semiconducting materials for OTFTs, it is important to consider the carrier mobility ($\mu$) of the material. Most OTFTs utilize p-type semiconductor materials, which means that as a negative voltage is applied to the gate, holes (positive charges) form and are attracted to, or accumulate at, the dielectric/semiconductor interface (Figure 4-2).\(^3\) This process forms an accumulation layer, also called a channel. One of the most widely used organic semiconductors is pentacene, due to its relatively high $\mu$ when compared to other materials and its environmental stability, and it is often used as a benchmark when developing new organic semiconducting materials.\(^{1,4}\)
The dielectric constant (K) of a material is a measure of its polarizability as a function of an applied electric field. As the electric field is applied, the charges within the dielectric reorient. It is usually desirable to have a high capacitance material for the dielectric because the higher the capacitance, the lower the threshold voltage ($V_T$), the voltage necessary to turn a transistor “on”, and the lower the operating voltage, which ultimately allow for a lower gate voltage ($V_G$). Equation 4-1 demonstrates this concept, showing that the same current gains ($I_{DS}$) can be obtained with a lower operating voltage simply by increasing the capacitance ($C_i$) of the dielectric material (W and L in eq. 4-1 are the TFT channel width and length respectively). The insulator capacitance of a material per unit area can be calculated by using equation 4-2 ($\varepsilon_0$ is the vacuum permittivity, k is the dielectric constant, and d is the insulator thickness). That is to say, a lower
voltage is necessary to operate a device when the dielectric layer has a higher capacitance.

\[ I_{DS} = \frac{W}{2L} \mu C_i \left[ V_G - V_T \right]^2 \]  
\[ C_i = \varepsilon_0 \frac{k}{d} \]

Table 4-1 shows literature values for various dielectric materials. Early OTFTs involved the use of SiO$_2$ as the dielectric material, since its performance and processing were well established in the electronics industry. SiO$_2$ is still commonly employed as a benchmark for the measurement of new insulating materials.\(^1\) The dielectric constants for some commonly used polymeric insulators are also included in Table 4-1.
Table 4-1. Dielectric constants (K) for some common dielectric materials.

<table>
<thead>
<tr>
<th>Dielectric</th>
<th>Dielectric Constant (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO$_2$</td>
<td>4</td>
</tr>
<tr>
<td>Al$_2$O$_3$</td>
<td>9</td>
</tr>
<tr>
<td>Ta$_2$O$_5$</td>
<td>30</td>
</tr>
<tr>
<td>TiO$_2$: rutile$^5$</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>anatase</td>
</tr>
<tr>
<td></td>
<td>31</td>
</tr>
<tr>
<td>BaTiO$_3$</td>
<td>300</td>
</tr>
<tr>
<td>SrTiO$_3$</td>
<td>150</td>
</tr>
<tr>
<td>Polystyrene$^7$</td>
<td>2.6</td>
</tr>
<tr>
<td>Poly(methyl methacrylate)$^7$</td>
<td>3.5</td>
</tr>
<tr>
<td>Poly(vinyl alcohol)$^8$</td>
<td>10</td>
</tr>
</tbody>
</table>

The deposition of the dielectric layer on the gate is an important parameter to control in order to get a reasonable device performance. It is essential to ensure complete coverage of the gate in order to prevent leakage currents, which is a loss of charge from the dielectric layer through defects.$^2$ The dielectric/semiconductor interface is also an important parameter to control. The quality of this interface is essential, as surface roughness, interface polarity, and impurities can all lead to poor performance (low $\mu$).$^9$ In organic semiconductors, true conduction bands never form, thus limiting the motion of the electrons.
Rather than having a delocalized conduction band through which the charges can move, the charges “hop” between localized states. It is hypothesized that this is the reason that the morphology of the semiconductor and the semiconductor/dielectric interface are so critical. Regardless of the cause, it is apparent that surface roughness, in particular, can greatly reduce the mobility of the semiconducting material, which limits the performance of the TFT.

When developing large area electronics, such as displays, one of the considerations that must be made is the cost of commercial production of these components. The development of solution processing for the patterning of TFTs, and the replacement of more expensive inorganic materials with less expensive organic materials should lead to a more cost effective method of manufacturing these electronic devices. Although silicon-based transistors are far more efficient than some of their organic counterparts, the high efficiency is not necessarily important for device performance. The performance of OTFTs is still good enough that they can begin to replace their crystalline silicon equivalent, allowing for a much more cost effective, and flexible, material.

OTFT technology is still a relatively new area of research. Scientists continue to strive to understand the factors that influence device performance, while at the same time they are testing new materials that can improve the device performance and processibility. Researchers are primarily focusing on
new materials for the semiconducting and dielectric layers, however overall TFT design is still important. As listed in Table 4-1, there are numerous high K materials that could be used for dielectrics, and the following sections will describe the potential for titanium dioxide (TiO₂), and specifically TiO₂ nanocrystals, as dielectric materials for TFTs.

4.1.2 Titanium Dioxide

Titanium dioxide (TiO₂) is one of the most widely used transition metal oxides. There are three crystal forms of TiO₂: anatase, rutile, and brookite (Figure 4-3). Anatase has a tetragonal structure with an elongated unit cell on the c axis, brookite has an orthorhombic structure, and rutile has a tetragonal structure. Rutile is the most thermodynamically stable form of TiO₂, though anatase is kinetically stable. On the nanometer scale, however, there is a size below which it appears that anatase is the more thermodynamically stable phase. This is yet another example of how on the nanometer scale materials can exhibit unique properties. When developing new synthetic procedures for TiO₂ nanocrystals it is important to try to control the crystal phase of the material, since the properties for which it is desired can change considerably. This is demonstrated in the dielectric constant values for anatase (K ≈ 31) and rutile (K ≈ 86) shown in Table 4-1. Recently, a great deal of research has focused on studying the unique
properties of TiO$_2$ on the nanometer scale, as well as developing new synthetic methods for making the nanocrystals.

![Figure 4-3. Crystal lattice structures for (A) anatase, (B) brookite, and (C) rutile TiO$_2$. Titanium atoms are blue, and oxygen atoms are red.](image)

TiO$_2$ nanocrystals have applications in electronics,$^{6,14}$ photocatalysis, pigments,$^{12}$ and even cosmetics.$^{15}$ As the size of the TiO$_2$ crystals are scaled down to the nanometer scale there is an increase in the chemical reactivity, as well as an increase in photochemical reactivity, with a potential decrease in the scattering of light.$^{16}$ There are several methods for synthesizing TiO$_2$ nanocrystals. Currently, the most common methods of preparation include sol-gel,$^{17-19}$ surfactant mediated,$^{20}$ and hydrothermal methods.$^{21,22}$ Sol-gel methods usually involve the hydrolysis of some starting material in order to yield a suspension of colloidal particles (sol), followed by gel formation, where the gel is comprised of aggregated sol particles. Sol-gel procedures usually involve a metal alkoxide starting material, and they generally proceed at relatively low temperature. One problem with this method is that it almost always requires post-synthetic calcinations, which can present a practical problem in the commercial production.
of these materials for various applications. Surfactant mediated methods, as the name implies, involve the use of surfactants to stabilize the nanocrystal during synthesis. Hydrothermal methods involve the hydrolysis of metal alkoxides and halides through oxygen donation from water.\textsuperscript{23}

Some of the problems with these synthetic methods is that they can often lead to random morphologies of nanocrystals, with little control over the crystal phase, and the products can also be very insoluble in most solvent systems.\textsuperscript{24} Calcination of the products to form crystalline materials can also be a problem in practical applications where high temperature is can lead to processing challenges. Recent advances in surfactant mediated hydrolysis of titanium alkoxides has lead to the reproducible, relatively low temperature synthesis of anatase TiO\textsubscript{2} nanocrystals.\textsuperscript{6,24} The nanocrystals that will be described in the following sections were synthesized by the surfactant mediated method. The specific property of the TiO\textsubscript{2} nanocrystals that was desired was the relatively high dielectric constant, which makes it a prime candidate for TFT technology.

\subsection*{4.2 Research Objective}

With the development of new technologies and chemical transformations, the world of materials science has blossomed. The push for new, higher
performance materials has become even greater. It was under this pressure that the goal of making novel nanocrystal-polymer composites was born.

As discussed in the introduction to this chapter, OTFTs are important for the development of new devices for electronics applications. Much of the recent efforts in the area of OTFTs and flexible electronics has focused on the improvement of the semiconductor layer of the TFT devices (see Figure 4-1).4 However, as described previously (Equation 4-1), it is also possible to improve the device performance by manipulating the dielectric layer. Thus, some researchers have focused on the development of new materials for the dielectric layer of TFTs.1,3,8,11 Some of the recent efforts to increase the capacitance of the dielectric materials have included the loading of polymer materials with inorganic oxide nanocrystals,25-27 or synthesizing inorganic oxides in the presence of polymeric materials.28 The benefit of loading polymeric materials (low K) with inorganic nanocrystals (high K) is that the polymer lends its flexibility and ability for solution processing to the material, while the nanocrystals give the material a higher dielectric constant. One of the drawbacks of the methods described above is that they produce materials that are not easily processed, or that are so poorly defined that they do not respond well to thermal or mechanical stress.

Previous work by Maliakal and coworkers at Bell Laboratories, Alcatel-Lucent demonstrated the utility of covalent functionalization of anatase TiO2
nanocrystals with polystyrene, which was then used as the dielectric layer for TFTs. The advantage of this method over other methods of loading polymer materials with ceramic nanocrystals is that this material is pseudo-homogeneous, so no phase separation of the nanocrystals occurs as it might with these other methods. This property is due to the fact that the polymer is covalently linked to the nanocrystals (Scheme 4-1).

Scheme 4-1. Covalent attachment of polystyrene to the surface of TiO₂ nanocrystals by the grafting-to method with a phosphonate anchor.

One of the disadvantages of this method is that in order to covalently attach a polymer to the nanocrystal surface it must first be functionalized with a phosphonate end group. That is to say, if ATRP is used to synthesize the polymer, a phosphonate initiator must be employed. This could pose a problem if the polymer in question is reactive toward a phosphonate group, or if the ATRP of a particular monomer does not proceed efficiently with a phosphonate
initiator. Another general consideration when functionalizing nanocrystals is the potential for particle aggregation. If the TiO$_2$ nanocrystals, capped with oleic acid, are not soluble/dispersible in the same solvent as the polymer, then aggregation of the nanocrystals nearly always results during polymer grafting. Once aggregation occurs, it is difficult, if not impossible, to re-disperse the nanocrystals in solution. Nanocrystal aggregation is perhaps one of the biggest problems surrounding the use of these materials in commercial applications.

One way to overcome the complication of nanocrystal aggregation is to develop a new ligand that can exchange with the oleic acid to stabilize the nanocrystals. In theory, the new ligand would not only be soluble in the same solvents as the oleic acid, but also in a variety of other solvents as well. The concept of a universal ligand, as described in detail in chapter 2, is one that is adaptable to this system (Figure 4-4). As discussed in chapter 1, the universal ligand would dictate nanocrystal dispersibility, and would also allow for further functionalization of the nanocrystals through a straightforward, efficient chemical transformation.$^{31}$ The additional advantage of the universal ligand, beyond the fact that it would stabilize the nanoparticles for months of shelf-life, is that it would allow for the covalent attachment of a library of polymers that are available using ATRP. By utilizing the CuAAC reaction, and an alkyne functional ligand, any polymer with an azide terminus should react to covalently
attach to the nanocystal surface. An additional benefit of this process is the selective nature of the azide-alkyne cycloaddition reaction, which would prevent any unwanted side reactions from occurring.\textsuperscript{32}

![Diagram of TiO\textsubscript{2} nanocrystals functionalized with alkyne ligands](image)

**Figure 4-4.** Schematic representation of TiO\textsubscript{2} nanocrystals functionalized with alkyne ligands (left), which can undergo reaction with azide functional polymers to form polymer brushes on the nanocystal surface.

The proceeding chapter will outline the synthesis and characterization of alkyne functionalized TiO\textsubscript{2} nanocrystals (TiO\textsubscript{2}-alkyne), which can then be reacted with azide functional polymers to produce inorganic-polymer core-shell nanoparticles. The utility of these nanoparticle systems will be demonstrated through the fabrication of prototypical capacitors and TFT devices. It has been shown that these materials exhibit modest performance as insulating materials for TFTs. It has also been shown that the TiO\textsubscript{2}-alkyne nanocrystals are stabilized against aggregation, and that the dispersibility of the nanocrystals is governed by the functional ligand.
4.3 Experimental Methods

4.3.1 Synthesis of 12-Bromo-dodec-1-yne (1)

\[
\begin{align*}
\text{Br} \\
8
\end{align*}
\]

In oven-dried glassware under N\(_2\), 1,10-dibromodecane (15 g, 50.1 mmol) was dissolved in 20 mL anhydrous DMF. Sodium acetylide (14.7 g, 18% wt. in xylene) was added drop-wise to the reaction mixture. The mixture was then heated to 70 °C and stirred under N\(_2\) for 4h. A light precipitate formed upon reaction. An equal volume of water was added to the mixture, and the precipitate dissolved. The mixture was extracted 3x with CHCl\(_3\) and the combined organic extracts were washed 5x to remove DMF. The organics were dried with MgSO\(_4\), filtered, and the solvent was removed by rotary evaporator. The resultant crude mixture was carried on to the next step of the synthesis.

Synthesis of Dodec-11-ynyl-phosphonic acid diethyl ester (2)

\[
\begin{align*}
\text{P} \\
\text{OEt} \\
\text{OEt}
\end{align*}
\]

In oven-dried glassware under N\(_2\), 12-bromo-dodec-1-yne (12.3 g, 50.1 mmol) was added to triethyl phosphite (21.8 mL, 125.25 mmol). The mixture was heated to 150 C and stirred for 17h. The mixture was allowed to cool to RT, and the excess triethyl phosphite was removed under vacuum. The material was
purified via column chromatography with 40% ethyl acetate, 1-% Et₂O, and hexanes as the eluent. A light yellow liquid was isolated (1.8 g, 18% overall). \(^1\)H NMR (360 MHz, CDCl₃): \(\delta\) 4.16-3.99 (m, 4H), 2.19-2.14 (m, 2H), 1.92 (t, 1H, \(J = 2.7\) Hz), 1.79-1.48 (m, 24H). \(^1^3\)C NMR (360 MHz, CDCl₃): \(\delta\) 84.30, 67.85, 61.02, 30.35, 30.17, 29.09, 28.99, 28.74, 28.4, 28.18, 26.17, 24.62, 18.08, 16.21. \(^3^1\)P NMR (360 MHz, CDCl₃): \(\delta\) 32.51; FTIR (cm\(^{-1}\)) 3311 (m), 2984 (s), 2930 (vs), 2856 (s), 2117 (vw), 1465 (m), 1392 (m), 1246 (s), 1164 (m), 1059 (vs), 1031 (vs), 963 (s), 754 (s). FAB HRMS calcd. for C₁₆H₃₁O₃P [M+H]⁺ 303.40, found 303.32.

4.3.2 Synthesis of \(\omega\)-bromo-poly(tert-butyl acrylate)

The tert-butyl acrylate (tBA) was passed through an alumina column prior to reaction in order to remove inhibitor. The tBA (17.0 mL, 117.03 mmol), PMDETA (0.27 mL, 1.29 mmol), and acetone (4mL) was added to a dry round bottom flask (rbf). The mixture was degassed by bubbling with N\(_2\) for 45 min. CuBr (168 mg, 1.17 mmol) and ethyl \(\alpha\)-bromoisobutyrate (0.35 mL, 2.34 mmol) were added to the mixture under N\(_2\) and the vessel was placed in a 60 C oil bath. The reaction stirred for 28h. The mixture was opened to air and diluted with acetone. The solution was passed through a column of alumina to remove the copper. The solvent was removed on a rotary evaporator, and the resultant viscous material was analyzed. \(^1\)H NMR (360 MHz, CDCl₃): \(\delta\) 4.12 (br), 3.72 (br), 2.26 (br), 1.84 (br), 1.46 (br), 1.27 (br), 1.14 (br); GPC: \(M_n = 6483\), PDI= 1.05.
4.3.3 Synthesis of ω-bromo-poly(styrene)

Styrene was passed through an alumina column prior to use to remove inhibitor. Styrene (27 mL, 234 mmol) and PMDETA (0.97 mL, 4.68 mmol) were added to a dry rbf. The mixture was degassed by bubbling with N₂ for 45 min. CuBr (671 mg, 4,68 mmol) and ethyl α-bromoisobutyrate (0.7 mL, 4.68 mmol) were added to the mixture under N₂. The reaction vessel was place in a 100 C oil bath and allowed to stir for 20h. Dissolved the polymer in CH₂Cl₂ and passed through a column of alumina to remove the residual copper. Solvent was removed by rotary evaporator. ¹H NMR (360 MHz, CDCl₃): δ 7.08 (br), 6.58 (br), 3.63 (br), 1.84 (br), 1.51 (br); GPC: Mₙ = 8093, PDI = 1.18.

4.3.4 Synthesis of ω-azido-polymers

Polymer (4.68 mmol) was dissolved in 60 mL of DMF under N₂. Sodium azide (5.62 mmol) was added and the mixture was heated to 60 C in an oil bath for 48h. Dissolved the polymer in CHCl₃ and washed with H₂O and dried over MgSO₄ and filtered. Solvent was removed by a rotary evaporator. The resultant polymers (Figure 4-5) were characterized by both ¹H NMR and FTIR.
**Figure 4-5.** Structure of azide-functional polystyrene (PS-N$_3$) and azide functional poly-(tert-butyl acrylate) (PBA-N$_3$).

**PBA:**

$^1$H NMR (360M MHz, CDCl$_3$): $\delta$ 4.11 (br), 3.74 (br), 2.23 (br), 1.83 (br), 1.44 (br); FTIR (cm$^{-1}$): 2978, 2934, 2110, 1729, 1479, 1457, 1393, 1368, 1257, 1150, 846. THF-SEC: M$_n$ = 6483, PDI = 1.05.

**PS-N$_3$:**

$^1$H NMR (360 MHz, CDCl$_3$): $\delta$ 7.08 (br), 6.58 (br), 3.74 (br), 1.85 (br), 1.43 (br); FTIR (cm$^{-1}$): 3059, 3025, 2922, 2849, 2090, 1724, 1600, 1493, 1452, 1384, 1180, 1142, 1075, 1028, 760, 698. THF-SEC: M$_n$ = 8513, PDI = 1.18.

4.3.5 **Ligand exchange reaction to yield TiO$_2$-alkyne**

TiO$_2$ nanoparticles (TiO$_2$-OA) were prepared by a previously published method, with oleic acid as the surface ligand.$^6$ The number of surface groups was estimated using a rod model for the nanoparticle surface area calculation. The oleic acid coated particles (660 mg, 1.58 mmol) were added to a dry rbf under N$_2$ and dispersed in 15 mL of chlorobenzene. Dodec-11-ynyl-phosphonic acid diethyl ester was then added, and the resultant mixture was heated to 100$^\circ$C.
for 48h. A transparent yellow solution resulted. MeOH was added to the solution to precipitate the particles. The mixture was then centrifuged. The precipitate was collected and the supernatant was discarded. MeOH was then added to the precipitate and the mixture was sonicated, then centrifuged. The supernatant was discarded and the precipitate was washed in this manner two more times to remove oleic acid and unbound ligand. The resultant particles were dispersible in CHCl₃, CH₂Cl₂, chlorobenzene, and toluene. FTIR (cm⁻¹): 3314, 3003, 2925, 2854, 2119, 1628, 1526, 1432, 1261, 1098, 1039.

Scheme 4-2. General Scheme for the synthesis of alkyne functional TiO₂ nanoparticles.

4.3.6 General Procedure for CuAAC Reaction

TiO₂-alkyne (500 mg of wet slurry, approximately 250 mg dry particles) was added to a dry round bottom flask and anhydrous toluene (3 mL) was added to disperse the nanoparticles. The resulting solution was light yellow. Anhydrous DMF (2 mL) was then added to the solution, followed by the addition of CuBr (13 mg, 0.09 mmol), and polymer (0.009 mmol azide). The
resultant mixture was bubbled with Ar for 30 min. After bubbling with Ar, freshly distilled PMDETA (19 μL, 0.09 mmol) was added to the reaction, and the flask was placed in a 100 °C oil bath. Upon addition of the PMDETA the lt. yellow solution turned bright blue. As the reaction stirred, the color turned a dark blue-green color. The reaction was monitored by FTIR and was allowed to stir at 100 °C for 48h.

\[
\begin{align*}
\text{TiO}_2\text{-alkyne} & \quad \text{PS-N}_3 \\
\text{CuBr/PMDETA} & \quad \text{P'tBA-N}_3 \\
\text{TiO}_2\text{-PS} & \quad \text{TiO}_2\text{-P'tBA}
\end{align*}
\]

Scheme 4-3. General scheme for preparing polystyrene (TiO$_2$-PS) and poly(tert-butyl acrylate) (TiO$_2$-P’BA) functional TiO$_2$ nanoparticles.

### 4.3.7 FET Device Fabrication

In order to measure the dielectric constant (K) and the thin film transistor (TFT) performance of using these new TiO$_2$-polymer materials, both capacitors and TFTs had to be fabricated (Figure 4-6). Top contact geometry was used. The gate material was indium tin oxide (ITO) which was deposited on glass. This was purchased from Aldrich. The ITO-glass was prepared by polishing with celite to diminish surface roughness. It was then washed with acetone, followed
by washing with methanol, and then finally washing with water. The ITO-glass was then dried under N₂ flow, and was ready for deposition. A 10% wt/volume solution of the TiO₂-polymer in chlorobenzene was then filtered through a 500 μm syringe filter onto the ITO-glass. The resulting glass was then spin coated at 1000 rpm for 45 s using a Headway Research spin coater, and was then placed in an oven at 100 °C for 1 h. For the capacitors, gold electrodes were evaporated through a shadow mask directly onto the TiO₂-polymer layer (0.0855 mm² area circles at a thickness of 100 nm). For the TFTs, pentacene was first evaporated onto the TiO₂-polymer layer at a rate of 0.3-0.4 Å/s to a thickness of 50 nm, then the gold top electrodes were evaporated in the same way as for the capacitors (bars, 3 mm x 0.32 mm, W/L = 9.4, thickness = 100 nm). All evaporations were done using an Edwards Auto 306 Vacuum Coater. Thin film characterization was performed using a probe station and HP 4155A Semiconductor Parameter Analyzer. Capacitance measurements were made using an HP 4284A LCR meter.

**Figure 4-6** Representation of device fabrication for a dielectric device (left) and a field effect transistor (FET) with pentacene as the semiconductor (right). In both cases, gold top electrodes were deposited.
4.4 Results and Discussion

4.4.1 Fourier Transform Infrared Spectroscopy

As stated in previous chapters, Fourier Transform Infrared Spectroscopy (FTIR) can be a useful tool in determining the binding mechanism of surface ligands on nanocrystals. In order to confirm the success of the ligand exchange process, FTIR was used to compare the IR absorbance for TiO$_2$-OA to that of TiO$_2$-alkyne (Figure 4-7). There are several regions to consider when examining the FTIR spectra. At 2118 cm$^{-1}$ there is a signal due to the C-C triple bond stretch, at 3312 cm$^{-1}$ there is a signal due to the C-H stretch on the acetylene group, and at 1040 cm$^{-1}$ there is a signal due to the antisymmetric phosphonate P-O-R stretch. It is clear from these spectra that although some ligand exchange did take place, not all of the oleic acid was replaced, as evidenced by the two peaks due to the carboxylate stretches are still present (1527 cm$^{-1}$ and 1457 cm$^{-1}$).$^{34}$
It is also possible to compare the FTIR spectrum free (unbound) alkyne ligand to the spectrum for the TiO$_2$-alkyne (Figure 4-8). It is clear from examining the spectra that for the most part all of the characteristic peaks for the alkyne ligand are still present. It is important to note that the signals due to the C-C triple bond and the acetylene C-H bond stretches are unchanged (2118 cm$^{-1}$ and 3312 cm$^{-1}$ respectively). Perhaps the most significant change in the two spectra is the nearly complete loss of the signal at 1247 cm$^{-1}$, where the signal due to the P=O stretch is present in the unbound ligand. This result is consistent with other
reports of TiO2-phosphonate complexes in which the phosphonate is bound to the surface through all three P-O bonds, and there is delocalization of electrons. These spectra support the conclusion that the ligand exchange was successful.

![Figure 4-8](image)

**Figure 4-8.** FTIR spectra of free alkyne ligand (top) and TiO2-alkyne (bottom). Inset is the region between 2135 cm\(^{-1}\) and 2100 cm\(^{-1}\) showing signal due to the C-C triple bond stretch.

Once the adsorption of the alkyne ligand was verified, the TiO2-alkyne nanoparticles were subjected to CuAAC conditions, described in the experimental methods. The reaction of the nanoparticles with PS-N\(_3\) and P\(^\text{BA}\)-N\(_3\) was monitored using FTIR. In the reaction of TiO2-alkyne with PS-N\(_3\), the
disappearance of the signal due to the azide moiety (2111 cm$^{-1}$) could be unambiguously monitored as the reaction progressed (Figure 4-9). Because there is an excess of alkyne with respect to azide end groups on the polymer, it was expected that upon complete reaction of the polymer, there should still be alkyne remaining. This hypothesis was confirmed by the presence of a signal at 2118 cm$^{-1}$ and a signal at 3312 cm$^{-1}$, which are due to the stretching frequency of the C-C triple bond and the acetylene C-H bond respectively. With the disappearance of the signal due to the azide, and the preservation of all other characteristic signals due to PS, it was concluded that the CuAAC reaction was successful.
The TiO₂-PBA reaction was also monitored by FTIR (Figure 4-10). Although there was some overlapping of the peaks for the acetylene C-H absorbance and the N₃ absorbance, due to the TiO₂-alkyne and PBA-N₃ respectively, it was possible to deduce from the FTIR that reaction has taken place. The initial spectrum taken at t = 0h (top in Fig. 4-5) shows a very broad peak from approximately 2119 cm⁻¹ to 2110 cm⁻¹. The inset spectra in the figure clearly show that as the reaction progresses, this broad peak becomes much sharper, and the peak maximum shifts. This shift is attributed to reaction of the
azide end group on the polymer. As in the case of the TiO$_2$-PS, there was excess alkyne on the TiO$_2$, so the residual peak is due to the alkyne, as expected. A view of the entire spectrum shows that while the azide signal has disappeared, the characteristic peaks from P$_3$BA remain. There is also a signal due to the C=O bond which at 1728 cm$^{-1}$ that is still present, indicating that the triazole formation was successful, and the polymer is covalently attached to the TiO$_2$ nanoparticles.

**Figure 4-10.** FTIR spectra of TiO$_2$-P$_3$BA at $t=0$h (top) and $t=48$h (bottom). Inset is the region from 2160-2060 cm$^{-1}$ for the spectra of TiO$_2$-alkyne, P$_3$BA-N$_3$, and TiO$_2$-P$_3$BA at $t=0$ and $t=24$, which shows the loss of the signal due to the N$_3$ absorbance.
4.4.2 TEM Characterization

The TiO$_2$ nanocrystals (TiO$_2$-OA) used in this study were provided by Dr. Ashok Maliakal at Bell Laboratories, Alcatel-Lucent, and were synthesized by a previously published method.$^6$ The TiO$_2$-OA was then submitted to a ligand exchange process with a phosphonate ligand (2 in Scheme 4-1) to yield alkyne functional TiO$_2$ (TiO$_2$-alkyne). Transmission Electron Microscopy (TEM) was then used to study the core size and shape of the TiO$_2$-alkyne, and to determine if any aggregation occurred during ligand exchange. The result was a relatively monodispersed sample of TiO$_2$-alkyne nanorods, which did not aggregate. The dimensions of the nanorods were determined to be approximately 50 x 10 nm within the limits of accuracy for TEM (Figure 4-11).
Once the nanoparticles were successfully functionalized with alkyne, they were subjected to Cu-catalyzed azide-alkyne Cycloaddition reaction conditions with both PS-N\(_3\) and P'BA-N\(_3\). The subsequent nanoparticles, TiO\(_2\)-PS and TiO\(_2\)-P'BA respectively, were studied by TEM (Figure 4-12). The TiO\(_2\)-PS, A, retained their size and shape, and they had not formed aggregates. The TiO\(_2\)-P'BA nanoparticles also appear to be dispersed, with the nanoparticle core retaining its size and shape.
Figure 4-12. TEM micrographs of TiO$_2$ nanoparticles functionalized with (A) polystyrene (TiO$_2$-PS) and (B) poly(tert-butyl acrylate) (TiO$_2$-PBA). Scale bars are 50 nm.

4.4.3 TGA Analysis

Thermogravimetric analysis (TGA) was also carried out on both the TiO$_2$-OA and the TiO$_2$-alkyne in order to examine the binding strength of the new ligand, and also to determine the grafting density of the ligand. First, TGA was done on a sample of TiO$_2$-alkyne to determine the mass loss, and also to determine the temperature at which the alkyne ligand desorbs from the surface (Figure 4-13). From the graph of $\text{dm/dT}$ vs. $T$, it was determined that the alkyne ligand desorbs from the surface of the TiO$_2$ nanocrystals at 454 °C, which is a relatively high temperature. This data indicates that the alkyne ligand is bound very strongly to the surface of the TiO$_2$ nanocrystals, which is consistent with literature reports.$^{35}$
Figure 4-13. TGA analysis of TiO$_2$-alkyne. (A) is the thermogram showing mass loss vs. temperature. (B) is the derivative of the thermogram, which shows the temperature at which the ligand decomposes or desorbs from the surface.

It is also possible to compare the binding strength of the alkyne ligand with oleic acid (OA), the ligand that is typically used to stabilize the nanocrystals during synthesis. Figure 4-14 shows the graphs of dm/dT vs. T for both TiO$_2$-OA and TiO$_2$-alkyne. As the graphs indicate, the OA desorbs from the nanocrystal surface at approximately 427 °C, whereas the alkyne ligand desorbs approximately 30 °C higher, at 454 °C. This data supports the conclusion that the phosphonate group on the alkyne ligand binds more strongly to the nanocrystal surface than does the carboxylate group on the OA. This is not a surprising finding given that the ligand exchange process works readily in the presence of OA, which indicates that the OA must be a more labile ligand.
Figure 4-14. Graphs of $\frac{dm}{dT}$ vs. temperature for (A) TiO$_2$-OA and (B) TiO$_2$-alkyne. The graphs indicate the temperature at which each of the ligands desorbs from the surface.

As discussed in chapter 2, not only can we glean information about the binding strength of ligands from TGA, but we can also determine the grafting density of ligands on the surface of the nanocrystals. Based upon the size and shape of the nanocrystals, as estimated from the TEM micrographs, the surface area of the nanocrystals was determined using the formula for a cylinder. From this value, the grafting density of the ligands on the surface was determined using equations 2-1 and 2-1. The results are summarized in Table 4-2. It is estimated that for the OA ligand, there are $\sim 7$ ligands/nm$^2$, whereas for the phosphonate ligand there are $\sim 5$ ligands/nm$^2$. This seems reasonable since the phosphonate ligand can be bound through three oxygen atoms, and the surface area that one phosphonate head group occupies is greater than that for OA. These values are also reasonable when compared to other values for similar systems reported in the literature.$^{36,37}$
Table 4-2. Estimation of the grafting density of oleic acid and alkyne ligand on the TiO₂ nanocrystal surface.

<table>
<thead>
<tr>
<th></th>
<th>δ (mol/g)</th>
<th>χ (# ligands/nm²)</th>
<th># Ligands/particle</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO₂-OA</td>
<td>7.6 x 10⁻³</td>
<td>7.4</td>
<td>6.9 x 10³</td>
</tr>
<tr>
<td>TiO₂-alkyne</td>
<td>5.6 x 10⁻³</td>
<td>5.4</td>
<td>5.1 x 10³</td>
</tr>
</tbody>
</table>

4.4.4 Dielectric Measurements

Prototypical Thin Film Transistors (TFTs) and capacitors were fabricated using the TiO₂-polymer materials as the dielectric layer, as described in Section 4.3.8. First, the capacitance for the TiO₂-polymer layers was measured, and the K values were calculated from the capacitance. Figure 4-15 shows the experimental values obtained for capacitors with TiO₂-PS as the insulating material. The K values are in a range between the value for pure PS (K ≈ 2.6) that for pure anatase TiO₂ (K ≈ 31). Using a parallel model for capacitors (eqn. 4-3, where $K_{\text{eff}}$ is the effective dielectric constant, $v_1$ and $v_2$ are the volume fraction of each of the two components, and $K_1$ and $K_2$ are the dielectric constants of each of the two components), the effective K of the “composite” material was calculated as a function of volume fraction of TiO₂ (B in Figure 4-15). When the experimental results were compared to the model, they agreed with the model for ~15% loading of TiO₂. This is a reasonable approximation because the experimental loading was 20% by volume of TiO₂. The parallel model is therefore a reasonable
model for these types of devices, and the K values obtained experimental are in reasonable agreement with the model. The experimental values are also consistent with other literature reports for polymer nanocomposites comprised of TiO$_2$ nanoparticles embedded in a PS matrix (K ≈ 3.5).$^{6,38}$

![Figure 4-15. (A) Experimental values for dielectric constant (K) vs. frequency for TiO$_2$-PS capacitors, and (B) experimental results (dashed line) for K compared to theoretical values (red) as a function of volume fraction of TiO$_2$ for TiO$_2$-PS capacitors. A parallel model for capacitors was used.](image)

$$K_{\text{eff}} = v_1K_1 + v_2K_2 \quad \text{eq. 4-3}$$

TFT devices were also fabricated using TiO$_2$-PS as the dielectric layer, and the source-drain current ($I_{sd}$) was measured as a function of the gate voltage ($V_g$) for the devices (Figure 4-16). The mobility of the TFTs was calculated from these measurements, and it was found to be 0.05 cm$^2$/Vs. This is an order of magnitude lower than the mobility of the TFT devices developed by Maliakal
and coworkers, however it is still a reasonable mobility and leaves room for optimization.

Figure 4-16. (A) Dielectric constant values (K) at various frequencies for TiO$_2$-PS devices and (B) TFT measurements of source-drain current ($I_{sd}$) vs. gate voltage ($V_g$) for TiO$_2$-PS devices. $\mu$ is the mobility.

The capacitors that were initially fabricated from TiO$_2$-PBA were very leaky, meaning that there was a gradual discharge of the capacitor (leakage current), which is generally caused by impurities in the dielectric film. This leakage was attributed to both the thickness of the films, which was actually quite thin (0.05-0.08 $\mu$m), and to nanoparticle aggregates that were believed to have formed. The difference in device performance between the TiO$_2$-PS and the TiO$_2$-PBA was thought to be a result of the different solubility of the polymers, as well as the different post-reaction work-up. It was hypothesized that the initial introduction of water into the TiO$_2$-PBA reaction somehow caused some
particle aggregation to occur, which was exhibited through poor device performance. At this point, it was important to develop a work-up procedure that did not involve the use of water, and to somehow deposit thicker films onto the ITO-glass.

Since the work-up of the TiO$_2$-PBA nanoparticles was a problem, the work-up was skipped altogether. Once the CuAAC reaction was determined to be complete, the solution was deposited on the ITO substrate and the capacitance was measured. It was thought that the minimal amount of Cu that was present from the CuAAC reaction would not have a large effect on the device performance, and this was found to be the case. The films in this case were drop-cast instead of spin-cast, and they were much thicker (2.2 – 2.5 μm) and there was very little leakage (Figure 4-17). Using a parallel model for capacitors as before, the $K_{\text{eff}}$ was calculated for the composite material as a function of volume fraction of TiO$_2$, which was then compared with the experimental values (B in Figure 4-17). Using this model, it is estimated that there is ~18% TiO$_2$ in the films. This is in line with the experimental results, in which a loading of 20% TiO$_2$ was used.
Figure 4-17. (A) Experimental values for dielectric constant (K) vs. frequency for capacitors with TiO$_2$PBA as the dielectric layer, and (B) experimental results for K (dashed line) compared to theoretical values (red line) for K as calculated using a parallel capacitor model.

For both the TiO$_2$-PS and TiO$_2$-PBA, capacitors were made in which the nanocrystal-polymer material was used as the dielectric layer. They performed with modest dielectric values and minimal leakage. These devices leave room for optimization, yet they demonstrate the utility of the universal ligand concept for functionalizing the nanocrystals for applications in flexible electronics.

4.5 Conclusions

It has been demonstrated that using the universal ligand concept, TiO$_2$ nanocrystals could be functionalized through a ligand exchange process, and the resultant nanocrystals were stabilized against aggregation. The “click” functional nanocrystals were then further functionalized through the utilization of the Cu-catalyzed azide-alkyne cycloaddition (CuAAC) reaction with click functional polymers.
The CuAAC reaction was successfully used to graft ω-azido polymers to the surface of TiO₂ nanocrystals. The resulting nanocrystals were used to manufacture prototypical capacitors and TFT devices, where the nanoparticles were employed as the dielectric layer. The TiO₂-PS caps showed an effective \( K = 6.6 \pm 0.5 \), and the TFT device, with pentacene as the semiconductor and TiO₂-PS as the insulator, showed \( \mu = 0.05 \text{ cm}^2/\text{Vs} \), which is an order of magnitude lower than that for the parent system defined by Maliakal et al.\(^6\) The K values for TiO₂-PS dielectrics was in line with the parallel capacitor model, where the value was in between that of pure PS and that of pure anatase TiO₂ (\( K \approx 2.6 \) and 31 respectively). The TiO₂-PtBA caps show a slightly higher effective \( K = 7.6-9.4 \), which is expected since the K for pure PtBA is \( \sim 3.5 \).\(^7\) This value is also in agreement with the parallel capacitor model.

4.6 Summary and Outlook

Although the initial goals of the research outlined in this thesis were completed (nanocrystals were successfully functionalized with “universal” ligands, and the CuAAC reaction was used to further derivatize the nanocrystals), there are several questions that arose during the completion of the research which remain unanswered. This section will outline those areas which
the author feels are most critical to the understanding of functional nanocrystal systems.

The first issue that is unresolved is that of the binding of various ligands to the surface of different metal oxide nanocrystals. When comparing the TGA data for the Fe₂O₃-alkyne and Fe₂O₃-azide (Figure 2-7) to the TGA for TiO₂-alkyne (Figure 4-14) there are distinct differences. The TGA for the Fe₂O₃ complexes seem to indicate almost complete physisorption of the ligands on the nanocrystal surface, whereas the TiO₂-alkyne appears to be completely chemisorbed to the surface. The FTIR data for these complexes also seem to support these conclusions (Figures 2-7, 2-8, and 4-8). It is unclear why this occurs, but this may be a result of the inherent differences between the two surfaces, or the differences between the ligand exchange reactions (sonochemical for the Fe₂O₃ and thermal for the TiO₂), or the difference in the types of anchors used for each ligand (carboxylic acid, phosphonic acid, or phosphonate). This is a question that is worth delving into by carrying out a comprehensive study of various ligands for different metal oxide nanocrystals. It would be beneficial to compare the binding strengths of carboxylates, phosphates, phosphonates, and perhaps even catechols. This would be an enormous benefit to the scientific community, as we have not found an example of a comprehensive study of ligand adsorption in the literature to date.
Another area that would warrant attention is studying the nature of polymer interactions with the surface. Although the surface coverage of ligands on the nanocrystals was estimated based upon TGA, the surface coverage of the polymer (and thus the percent conversion of reactants to products) was never definitively determined. This is an important parameter to determine for various applications. Perhaps through the use of FTIR (to study the peak area of azide/alkyne moieties) and elemental analysis this could be determined more clearly.

Another area involving the polymer functionalized nanocrystals is the field of water soluble nanocrystals. As an offshoot of the research involving Fe₃O₃-P'BA and the TiO₂-P'BA would be to convert the P'BA to PAA in order to make the particles water soluble (Figure 4-18). This research would be relevant for a number of applications involving green chemistry where the use of water as a solvent is imperative.

Figure 4-18. Illustration of the conversion of P'BA coated nanocrystals to PAA coated nanocrystals in order to make the particles water soluble.
Although we were able to carry out grafting-to in order to attach polymers to the nanocrystal surfaces, we were never successful in carrying out surface initiated polymerization (SIP) from the nanocrystals. One of the difficulties in accomplishing this task was that when the sonochemical ligand exchange was carried out, the Br end group on the ATRP initiator was destroyed. This challenge could be avoided by either thermally carrying out the ligand exchange, or by using a universal click ligand to attach an ATRP initiator (Figure 4-19). It would, however, be interesting to compare the grafting density of polymer-coated nanocrystals synthesized by SIP to those synthesize by grafting-to.

**Figure 4-19.** General scheme for the functionalization of nanocrystals with ATRP initiators.

A final area that was not studied in detail was the phase separation of polymer coated nanocrystals in a polymer matrix. It is important to understand
the factors that influence the phase separation of nanocrystals for a variety of applications. It is crucial to determine the molecular weight that is required of both the polymer that is attached to the nanocrystals as well as the matrix polymer in order to prevent phase separation.

There are a number of questions that have been raised given the results of the research that has been carried out thus far. This section outlines those areas that would be most critical to gaining a more comprehensive understanding of functional nanocrystal systems.
4.7 References


