Preparation and characterization of radical-coated nanoparticles

Aisha Abdulwahab Alsaleh

University of Windsor

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Preparation and characterization of radical-coated nanoparticles

by

Aisha Abdulwahab Alsaleh

A Dissertation
Submitted to the Faculty of Graduate Studies through the Department of Chemistry and Biochemistry in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy at the University of Windsor

Windsor, Ontario, Canada

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Aisha Abdulwahab Alsaleh

APPROVED BY:

_____________________________
M. Workentin, External Examiner
Western University

_____________________________
D. Northwood
Department of Mechanical, Automotive and Materials Engineering

_____________________________
S. Loeb
Department of Chemistry and Biochemistry

_____________________________
T. Carmichael
Department of Chemistry and Biochemistry

_____________________________
J. Rawson, Advisor
Department of Chemistry and Biochemistry

October 9, 2018
DECLARATION OF ORIGINALITY

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ABSTRACT

The topic of this dissertation is the surface modification and functionalization of inorganic nanoparticles with free radicals. These particles have a diameter up to ca. 15 nm and consist of an inorganic core with an organic surface coating comprising open shell organic TEMPO radicals.

Chapter 1 describes synthetic methods for the preparation of gold nanoparticles (AuNPs) and introduces the range of analytical methods for nanoparticle characterization. A survey of previous work on radical-coated nanoparticles is presented and the objectives of the current studies are outlined, highlighting the range of different bonding strategies for attaching the TEMPO radical to the AuNP surface.

Chapter 2 describes the synthesis and characterization of citrate-coated AuNPs of 18 nm diameter. Treatment of these citrate-stabilized AuNPs with a water-soluble TEMPO radical [WS-TEMPO]Br led to aggregation at high [WS-TEMPO]Br concentrations identified by a long wavelength absorption but is suppressed at low concentration (10^{-4} M). Treatment with [WS-TEMPO]Br unexpectedly led to bromide/citrate exchange on the AuNP surface which was determined by IR spectroscopy and EDS. EPR studies on the resultant 14 nm nanoparticles reveal low concentrations of WS-TEMPO on the surface and these particles appear stable up to 345 K.

Chapter 3 describes a one-pot reaction to covalently bond TEMPO radicals to the AuNP surface via an Au-S bond generated from TEMPO-thioacetate precursors or
via a TEMPO-disulfide derivative. IR spectroscopy was used to identify cleavage of the thioacetate bond to generate a thiolate-bound TEMPO radical. TEM images reveal spherical AuNPs of ca. 3 nm diameter with EPR studies revealing high coverage of TEMPO radicals on the nanoparticle surface. Variable temperature UV/vis and EPR spectroscopies show that the effect of heat on these radical-coated AuNPs appears sensitive to the length of the alkyl chain. Thus, heat can variously lead to either an increase or decrease in AuNP size on heating.

Chapter 4 examines the use of non-covalent, hydrophobic, dispersion driven interactions to tether TEMPO radicals to the AuNP. N-Octyl thiolate-coated AuNPs were prepared and treated with n-C₈H₁₇-O-TEMPO to afford 18 nm diameter nanoparticles. EPR studies reveal only low coverage of TEMPO radical on the surface. Preliminary studies showed that these radical-coated AuNPs could be used in the thermal polymerization of styrene, suggesting that free-radical moderation of the polymerization process is operative.

Chapter 5 examines the synthesis of a more complex core topology, comprising a superparamagnetic iron core and gold outer shell of 9 nm diameter. This was then coated using a covalent S-bound thiolate-TEMPO surface. Unlike the S-bonded AuNPs described in Chapter 3, surface coating with TEMPO radicals is low. This system was confirmed by IR, EDX, PXRD, UV-vis and EPR spectroscopy.

Chapter 6 summarises the findings of the current studies and reviews potential areas for future exploitation.
To all the people in my life who touch my heart
ACKNOWLEDGEMENTS

This thesis would not be possible without the support of my supervisor Dr. Jeremy M. Rawson. Without his encouragement, guidance all the time, support, trust and understanding, any accomplishment would not have been possible.

I would like also to extend my deepest appreciation and gratitude to my committee members Dr. Derek Northwood, Dr. Stephen Loeb, Dr Tricia Carmichael and Dr. Mark Workentin for their important comments, insights, and questions.

My gratitude is extended to my group members, the Rawsome group, I appreciate their help, questions, information and transparency during my research. Special thanks to Dr. Elodie Heyer and Nadia Stephaniuk for their kind support in this research.

I would also like to thank, from the bottom of my heart, my family for being my best people in the world: my great parents, my beloved kids Wasan and Fares, my brother and my sisters, particularly my dearest sister, Safa, who stands by me when things get bleak. All my honors are for my family. I am also grateful to my friends especially Dhuha who has been continuously supporting me through our friendship.

Furthermore, I deeply appreciate and thank Marlene Bezaire for her help, kindness and generosity since my first day in Windsor, Sharon Lachie at Great Lakes Institute for Environmental Research (GLIER) at University of Windsor for helping me out with SEM measurements and I thank Dr. Richard Gardiner and Karen
Nygard at Biotron at University of Western Ontario for helping and training me using TEM.

Finally, I am so grateful to the King Abdullah scholarship program supported by the Saudi Government for scholarship and funding received and the Faculty of Chemistry and Biochemistry at the University of Windsor for making it possible for me to study here. This work was also supported by the funding from The Canada Research Chairs program CFI and ORF for an infrastructure grant (J.M.R.).
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Chapter 1: Literature review
1.1 Introduction

The rapid and increasingly amplified developments in nanotechnology in recent decades has resulted in the emergence of a number of diverse nanostructures with their own unique and novel properties.\(^1\) The nanostructures which can be assembled is large in terms of size, composition, complexity and degree of functionalization.\(^2,3,4\) They include materials such as single-walled and multi-walled nanotubes (NTs) as well as nanoparticles (NPs) (Figure 1.1) whose size and aspect ratio and composition can all be tailored for specific applications.\(^5,6,7,8\) Some of these structures have shown great promise in the field of biotechnology including quantum dots (QD),\(^9,10\) magnetic nanoparticles,\(^11,12,13\) polymeric particles,\(^14,15\) metallic nanoparticles,\(^14,16\) and carbon-based nanostructures.\(^17,18\) Among these structures, quantum dots have many suitable properties which make them suitable for biological labelling and as fluorescent markers (Fig 1.2).\(^19,20\) Magnetic nanoparticles have a number of uses including cell sorting, MRI, magnetic hyperthermia therapy and drug delivery.\(^11,21,22\) Drug delivery has also been achieved with the assistance of lipid and polymeric nanoparticles which have been used as molecular capsules for targeted drug delivery. Drug delivery by nanoparticles has a number of advantages including safety, increased solubility, increased efficiency, and enhanced permeability and retention in the tissue.\(^23\) Carbon tubes have also shown great use in designing medical devices such as endoscopes as well as in photothermal therapy and drug delivery.\(^24\)
Figure 1.1 Different types of nanoparticles (NPs).

Figure 1.2 Absorption of various sizes of Quantum Dots (QDs). Reproduced from Ref.32 with permission from The Royal Society of Chemistry
Amongst these, gold nanoparticles (AuNPs) have attracted attention due to (i) the chemically inert nature of gold; (ii) their ease of synthesis and; (iii) their optical properties which are strongly dependent upon their shape, size, composition and encapsulation.\textsuperscript{25,26,27} AuNPs are formed as colloidal gold which is a sol or colloidal suspension of nanoparticles in a liquid.\textsuperscript{27} The colour of the sol is usually red or bluish-purple depending upon the particle size.\textsuperscript{27} These gold nanoparticles have attracted the interest of many researchers due to their optical and electronic properties and ready surface functionalization which can make useful in molecular recognition.\textsuperscript{27} They have been explored across a large number of applications such as microscopy, electronics and as biomarkers.\textsuperscript{26,28,30,31,32}

Gold nanoparticles has become a favored nanomaterial because of their optical properties, localized surface plasmon resonance (LSPR), stability and their chemical functionality.\textsuperscript{33} The well-established chemistry of AuNPs, coupled with their chemically robust (inert) nature, makes them particularly well suited as an entry point to explore new aspects of nanoparticle chemistry and the following sections of this introduction highlight synthetic and physical aspects of AuNPs.

\section*{1.2 Synthesis of Gold Nanoparticles}

The synthesis of monolayer-protected (surface-protected) AuNPs have been reported in many studies. The surface monolayers play an important role in the NP stability and control the tendency of the AuNPs to aggregate. A number of synthetic methods have been reported and have proved fundamental starting points for introducing chemical functionality to AuNPs.\textsuperscript{34} Brust \textit{et al.}\textsuperscript{35} described a simple
method for the synthesis of gold nanoparticles protected by alkanethiols which were soluble in organic, non-polar media. After that Murray et al. explored the possibilities for surface modification through ligand exchange of surface alkanethiols with another thiol ligand.\textsuperscript{36} Another important method by Turkevich produced water soluble AuNPs particles.\textsuperscript{37} Both Brust-Schiffrin and Turkevich methods are widely implemented due to their ability to generate monodisperse AuNPs and are both described here.

1.2.1 Turkevich Method

This method was described by J. Turkevich in 1951 and later refined by G. Frens in the 1970s.\textsuperscript{38} However, the synthesis was initially reported Hauser and Lynn in 1940.\textsuperscript{39} This method is considered the simplest method for the preparation of spherical, monodisperse AuNPs with diameters in the range 10-20 nm in water.\textsuperscript{40} This experimental method is advantageous because the synthetic approach is cheap, easy functionalization due to the weak bonding of the citrate anion on the surface and robust producing well-defined AuNPs under a variety of conditions.\textsuperscript{41}

The Turkevich method involves the reduction of tetrachloroauric acid (HAuCl\(_4\)) in hot aqueous solution with sodium citrate solution. The citrate anions not only act as reducing agents but also serve as a surface capping agent. The former aspect leads to formation of colloidal gold while the surface coating of citrate terminates the AuNP growth and prevents aggregation.\textsuperscript{42} The mechanism (Scheme 1.1) involves the oxidation of citrate (1) to acetone dicarboxylate (2). The by-product (2) is very important for the growth of nanoparticles through formation of Au\(^+\).
complexes (3). The soft Au\(^+\) ion undergoes disproportionation in aqueous solution resulting in elemental gold and regenerating Au\(^{3+}\) ions. These Au atoms then become the center of nucleation and more Au\(^+\) ions are reduced around them. In the latter stages of AuNP growth, citrate acts as a capping agent, stabilizing the positive charge on the AuNP via an electrostatic attraction.

![Scheme 1.1 Key mechanistic steps associated with the Turkevich method.](image-url)
The size of the nanoparticles can be controlled by adjusting the amount of sodium citrate used with the average diameter of the resultant AuNPs inversely related to the amount of citrate used. For NPs the surface:volume ratio is very high in relation to the bulk material. Thus by decreasing the concentration of sodium citrate there are fewer surface-stabilizing anions present and this favors formation of larger AuNPs upon aggregation.\(^\text{27}\) The weak bonding between hard citrate anions and the softer gold nanoparticle surface makes the particles well-suited for further functionalization but rather unstable upon drying so large-scale manufacturing cannot be achieved.

### 1.2.2 Brust-Schiffrin method

This method was developed in the 1990s by Brust and Schiffrin,\(^\text{43}\) who were investigating Faraday’s two-phase (organic/aqueous) fabrication of gold nanoparticles.\(^\text{44}\) The process is similarly based upon reduction of tetrachloroaurate anions but permits the production of gold nanoparticles which are soluble in organic media (Scheme 1.2). The reaction involves initial transfer of gold ions from the aqueous phase to toluene using tetraoctyl ammonium bromine (TOAB) to generate a toluene-soluble inverse micelle which encapsulates AuCl\(_4^–\) anions. Reduction with thiol, RSH, affords a reduced inverse micelle with Au(I) which undergoes reduction with NaBH\(_4\) (aq) to form an Au(0) NP core. Finally, reaction with the thiol leads to Au-S bond formation on the NP surface, affording the thiolate-coated AuNP.\(^\text{45}\) This method produces stable, readily isolable thiolate-protected gold nanoparticles in the 1 – 10 nm diameter range which are soluble on organic media.
Scheme 1.2 Mechanistic steps associated with the Brust-Schiffrin method.

This method can be modified by optimizing the conditions such as ratio of thiol ligands to gold salt, solvent concentration and different gold precursor molecules (such as using AuCl$_3$ instead of AuCl$_4$). In general, larger thiol:gold ratios result in smaller average core sizes, e.g. Schaaff et al. used a thiol:gold ratio of 3:1, resulting in a smaller NP core size (below 2 nm).

1.2.3 Ligand exchange

As mentioned earlier the first ligand exchange study was done by Murray and co-workers. Initial ligands on as-prepared gold nanoparticles can be substituted by more strongly binding ligands which can be used to improve the stability, solubility and provide new functionality to gold nanoparticles. Gold is a soft transition metal and so forms particularly strong bonds to softer donor ligands such as thiolate, selenolate and phosphine ligands inter alia. The core-shell bonding in citrate-coated gold nanoparticles produced by the Turkevich method is therefore susceptible to ligand loss and aggregate irreversibly. These citrate-stabilized AuNPs readily react with ligands that bond more strongly to the gold surface such as mercaptoacetic acid (MAA), mercaptopropionic acid (MPA) or
mercaptoundecanoic acid (MUA). These modified nanoparticles can be precipitated, isolated and even exploited in further reaction chemistry.\textsuperscript{50}

The ligand exchange can also be achieved with gold nanoparticles synthesis by Brust two phase method. However, given the stability of gold-sulfur bonds (\textit{Au-S} bond energy 184.1 kJ.mol\textsuperscript{-1})\textsuperscript{51} and significant hydrophobic, dispersion-driven forces between alkyl groups then ligand exchange is slow at ambient temperature.\textsuperscript{52} Nevertheless, Brust's method can be modified and the initial alkanethiol ligand can be substituted by a variety of other functionalized molecules such as thiol-containing peptides.\textsuperscript{53,52} Typically the new ligand should have a much stronger binding affinity to the gold surface in order to provide a thermodynamic preference for replacement of the original ligand.\textsuperscript{54} Conversely ligands with similar or poorer binding affinities to gold will tend to have little thermodynamic stabilization and incomplete substitution is likely to occur.

1.3 Size dependent optical and electronic properties

AuNPs are established methods to color glass since ancient times and exemplified by the famous Lycurgus cup in the 4\textsuperscript{th} century (Figure 1.3). The Lycurgus cup exhibits different colors depending on the incident light and Faraday explained this phenomenon as result of the presence of very small gold colloids (now known to be AuNPs).\textsuperscript{44,55}
Since then many studies have aimed to understand the photo-physical properties of these AuNPs, focusing on their large surface area, optic and electronic properties and reactivity. These properties are strongly dependent on their size and shape and conferred by the interaction of light with conduction electrons. When AuNPs are irradiated with light, then this drives an oscillation in the electron cloud of the metal. The collective oscillation of the free electrons in the conduction band cause charge separation known as a surface plasmon oscillation (Figure 1.4). However, at a specific frequency the oscillation amplitude reaches a maximum and the induced absorption of the incident light gives rise to a surface plasmon resonance (SPR). The SPR phenomenon has been studied theoretically by Mie who showed that the SPR band strongly depends on the electron density on the particle surface which is a function of the metal type, particle size, shape, structure, composition and the dielectric constant of the surrounding medium. Spherical AuNPs exhibit one SPR band in the visible region.

Figure 1.3 Photograph of the Lycurgus Cup with different color. (Image courtesy of the British Museum)
around 520 nm giving rise to a characteristic red color. When the AuNP’s size decreases, the electrons become more confined within the particle, leading to a shift of the SPR toward shorter wavelengths. The SPR is also sensitive to the geometry of AuNPs. While spherical AuNPs are isotropic and lead to a single absorption, changing the geometry from spherical to rod-like drives an anisotropy in the system. This is typically reflected in two SPR bands known as the longitudinal (the vis-NIR region) and transverse (vis region) SPR bands.

For semiconductor NPs, a similar absorption band is observed but the shift in absorption now correlated to the size of the band gap which itself is particle size dependent (Figure 1.5).

Figure 1.4 Surface plasmon resonance due to the interaction of the electrons in the conduction band with light (Reproduced from Ref.42 with permission from The Royal Society of Chemistry).
Chapter 1: Literature Review

Figure 1.5 The size dependency of the band gap between conduction band (CB) and valence band (VB) for semiconductor NPs.

Figure 1.6 Gold nanoparticles – absorption of various sizes and shapes. Reproduced from Ref.32 with permission from The Royal Society of Chemistry.

The surface coating of AuNPs is also an important factor. Since the SPR depends on the surrounding medium, this effect allows plasmonic NPs to be used as efficient molecular sensors\textsuperscript{33} since changes to the local refractive index around the
particles result in different SPR wavelengths.\textsuperscript{33} The SPR offers a series of advantages including rapid analysis, detection, and the possibility to determine kinetic and thermodynamic parameters of interacting partners without the requirement of tagging one of the two partners. The excited electrons from SPR can relax in two different ways:

1. Radiative emission in which light is emitted as SPR scattering when the energy of emitted light is the same as the energy of the incident radiation.
2. Non-radiative emission in which absorbed energy is transferred to the NPs in the form of thermal energy and then on to the surrounding medium.\textsuperscript{63,64,65}

1.4 Gold nanoclusters (AuNCs)

AuNPs smaller than 3 nm in diameter may exhibit unique definite formulae, placing them in between conventional metal-ligand complexes and plasmonic nanoparticles and can be described as gold nanoclusters (AuNCs). The energy levels of electrons in nanocluster are discrete to multiple absorption bands due to the strong quantum size effects as well as the extremely high surface-to-volume ratio (Figure 1.7).\textsuperscript{66,67} Their physico-chemical and optical properties can be enhanced, offering these AuNCs great potential for applications such as catalysis, energy conversion, biology, biomedicine and chemical sensors.\textsuperscript{67,68,69,70,71,72} AuNCs are essentially inorganic–organic hybrid molecular compounds represented by well-defined organometallic formula $\text{Au}_n(\text{SR})_m$ with a specific mass (kDa) allowing the total structures (core plus surface) to be determined by single crystal X-ray crystallography.\textsuperscript{68,73}
Intense work has been made in the last few years to generate a library of stable sizes holding stable stoichiometries and monodisperse gold thiolate NCs (Figure 1.8). In 1990s the Whetten group identified several masses (∼5, ∼8, 14–15, 22–23, 28–29 kDa) of gold thiolate NCs but at that time the control over atomic precision and molecular purity was still challenging. Since then extensive work continued until 2004 where Tsukuda group identified water soluble glutathione-protected AuNCs including Au_{15}(SG)_{13}, Au_{18}(SG)_{14}, Au_{22}(SG)_{16}, Au_{22}(SG)_{17}, Au_{25}(SG)_{18}, Au_{29}(SG)_{20}, Au_{33}(SG)_{22}, and Au_{39}(SG)_{24} and thiolate-protected AuNCs Au_{25}(SR)_{18} using electrophoretic isolation and electrospray mass spectrometric. Subsequently Jin and coworkers successfully established a size-focused methodology, one-pot-for-one-size synthesis of Au_{n}(SR)_{m} NCs without the need for electrophoretic or chromatographic isolation. Among all the NCs, Au_{25}(SR)_{18} received the most extensive attention due to its high stability. Theoretical computational studies and single-crystal X-ray crystallography
analyses indicate that the structure of Au\textsubscript{25}(SR)\textsubscript{18} NCs exhibited an icosahedral (I\textsubscript{h}) Au\textsubscript{13} core, covered by 6 stable dimeric (-RS-Au-RS-Au-RS-) units sometimes described as ‘staples’.\textsuperscript{79} The icosahedral core contrasts with the known reported \textit{fcc} structure for elemental gold. Notably other AuNCs do reflect face-centered cubic, hexagonal-close-packed (\textit{hcp}) and body-centered-cubic (\textit{bcc}) structures.\textsuperscript{80} The core structures essentially comprise Au(0) whereas the surface ‘staples’ contain near linear S-Au-S units in which the Au atoms are formally gold(I) and are no longer directly tied into the core structure. These crystallographic studies provide some insight into the composition of larger AuNPs.

![Diagram of crystal structures](image.png)

Figure 1.8 Non-crystallographic (I\textsubscript{h}) and crystallographically determined structures of AuNCs. (Reproduced from Ref.81 with permission from The Royal Society of Chemistry).

1.5 Gold Coated Iron Oxide Nanoparticles

Magnetic nanoparticles have attracted great interest over the past decades due to their unique nano-size properties compared with bulk materials.\textsuperscript{82,83} Conventional magnetic materials are capable of storing bits of magnetic data because of the orientation of spins within a macroscopic region known as a domain (typically 10^{-4}
– $10^{-6}$ m in diameter). While the alignment of electrons within a domain can be considered coparallel, electron alignment in neighbouring domains need not be coparallel. Energy is stored in these domain wall boundaries and an applied field is required to align the electrons in different domains.\textsuperscript{84} The applied field necessary to align all domains in the same direction is known as a coercive field and the energy stored in the domain walls is proportional to the area enclosed within the hysteresis loop (Figure 1.9). When the particle size drops below that of a single domain then a superparamagnetic response is observed where each particle can be considered as a single magnetic domain.\textsuperscript{85} The magnetic response is similar to a hysteresis loop but with zero coercive field since all the spins within the sub-domain particle move cooperatively to align with the applied field, leading to an S-shaped or superparamagnetic response.

Figure 1.9 (left) Magnetization vs field plots for a paramagnet (solid line) and a diamagnetic materials (dashed line); (right) magnetization vs field plots for a ferromagnet (black line) and a superparamagnet (red line).
Superparamagnetism gives rise to many potential applications including cancer therapy\textsuperscript{86}, biomedicines\textsuperscript{87}, drug delivery\textsuperscript{88}, biosensors\textsuperscript{89}, molecule detection\textsuperscript{90}, immobilisation of enzymes\textsuperscript{91}, catalysts\textsuperscript{92}, adsorbents\textsuperscript{93}, high-density magnetic storage media\textsuperscript{94} and nanodielectrics\textsuperscript{95}. Like gold nanoparticles, magnetic nanoparticles tend to aggregate due to the increase in the magnetic interaction in competition with repulsive forces due to the electric double layer and their tendency to aggregate limits their application.\textsuperscript{96} However, the aggregation can be controlled with appropriate surface chemistry.

1.6 Radical Functionalization of Nanoparticles

1.6.1 The nature of free radicals

In the majority of organic compounds, electrons tend to form electron pairs either as lone pairs, core electrons or electron pairs in bond formation. Radicals are atoms or molecules with one (or more) unpaired electrons. In many cases radicals are extremely reactive with very short half lives and will typically react via dimerization, H-atom abstraction, addition to a conjugated system etc.\textsuperscript{97} However, stable families of radicals are known which can have much longer lifetimes or are chemically stable at ambient temperature. These radicals are typically stabilized through a combination of electronic stabilization (delocalized via $\pi$ conjugation and/or use of electronegative atoms to lower the orbital energies) and steric protection.\textsuperscript{98} The simplest two systems comprise dioxygen, O\textsubscript{2}, which is a diradical, and nitric oxide, NO. In both cases the unpaired electron is delocalized in a $\pi^*$
orbital. In O\(_2\) the two unpaired electrons are in degenerate \(\pi^*\) orbitals which are mutually orthogonal.

### 1.6.2 Nitroxide Radicals

NO itself provides the basis for a family of stable organic radicals known as nitroxides, \(R_2\)NO. Electronically, \(R_2\)NO can be considered comparable with ketones \(R_2\)C=O with N replacing C and the additional electron therefore being located in the singly occupied molecular orbital (SOMO) which is an antibonding \(\pi^*\) orbital. For the \(\pi\) system the more electronegative atom (O) is lower lying and contributes more to the \(\pi\) bonding MO whereas the more electropositive atom (N) contributes more to the \(\pi^*\) MO (Scheme 1.3) This \(\pi\) stabilization can also be considered as two resonance forms (Scheme 1.3). The absence of an \(\alpha\)-hydrogen atom suppresses disproportionation to form a nitrone and hydroxylamine (Scheme 1.4 top)\(^{99}\) while the steric bulk of the alkyl substituents coupled with weak O-O bonds (145 kJ.mol\(^{-1}\)) and/or ring strain suppresses dimerization (Scheme 1.4 bottom)\(^{100}\).

![Scheme 1.3](image_url) 

Scheme 1.3 (left) Singly occupied molecular orbital (SOMO) of the TEMPO radical; (right) resonance forms for TEMPO.
The first reported nitroxide radical was Fremy’s salt, \( \text{K}_2[(\text{SO}_3)_2\text{NO}] \) which was synthesized by Edmond Fremy in 1845,\textsuperscript{101} but at that time the concept of the free radical had not yet been discovered. The emergence of radical chemistry commenced in 1900, when Gomberg inadvertently discovered the triphenyl methyl radical, \( \text{Ph}_3\text{C•} \) which he described as an example of trivalent carbon.\textsuperscript{102} After this discovery, Piloty and Schwerind\textsuperscript{103} synthesized a heterocyclic compound as the derivative of a four-valent nitrogen named porphyrexide and considered the first nitroxide radical. Since then the chemistry of nitroxides has developed rapidly and a variety of nitroxides derivatives have been reported with a range of applications such as radical inhibitors,\textsuperscript{104} oxidizing agents,\textsuperscript{105,106} spin labels,\textsuperscript{107} and polymerisation mediators.\textsuperscript{108} One of the most widely used nitroxide radicals is 2,2,6,6-tetramethyl piperidine-N-oxyl (TEMPO) and a range of TEMPO derivatives are known which are functionalized at the 4-position of the piperidine ring and are commercially available (Figure 1.10). The most powerful motivation for development of TEMPO and its derivatives is the successful application in surface modification processes as well as important industrial developments such as highly...
selective oxidation catalysts to produce pharmaceuticals, flavors, fragrances, agrochemicals and a variety of other specialty chemicals. However, TEMPO is considered expensive ($80-100 per Kg) and recycling potentially time consuming. From this perspective, immobilization of TEMPO on a surface enables an alternative easy separation and is strongly preferred not only from an economic, but also environmental perspective. This has led to many efforts to develop TEMPO-modified surfaces for applications in catalysis and pharmaceuticals.

![TEMPO and its derivatives](image)

Figure 1.10 TEMPO and its derivatives.

1.7 TEMPO-immobilized onto inorganic nanoparticles

TEMPO and its derivatives immobilized onto the surface of nanomaterials have been studied over the last 20 years. Among all the numerous nanomaterials, inorganic nanoparticles have been actively explored due to their applications as oxidation catalysts for alcohols, diols and sugar, sensor and polymerization. These TEMPO-coated NPs can be broken down into TEMPO coated on metal NPs and TEMPO coated on metal-oxide NPs.
1.7.1 TEMPO immobilized onto metal NPs

Metal nanoparticles have attracted scientists for over a century because of their large surface area. However, the inherent tendency for self-aggregation has led scientists to focus on surface modification of these NPs with diverse functional groups. This has focused on incorporation of highly stable functionality and dispersibility. A number of AuNPs and silver nanoparticles (AgNPs) functionalized with TEMPO have been reported and showed promising applications in biology and chemistry.\textsuperscript{113,114} TEMPO-modified gold nanoparticles were first reported by Templeton and co-workers\textsuperscript{115} in 1998 via amide and ester coupling reaction between amino-TEMPO and ω-functionalized monolayer-protected gold cluster molecules (MPCs) as a new kind of polyfunctionalized material. Subsequently multifunctional electrodes have been developed based on AuNPs coated with thiol-terminated TEMPO via electrochemical polymerization.\textsuperscript{116} In 2002, Ionita et al.\textsuperscript{117} studied the ligand exchange reaction of a diradical disulfide with butanethiol protected gold nanoparticles (Figure 1.11). Their EPR study revealed that the two branches of the disulfide did not adsorb on the gold nanoparticles surface close to each other. Their proposed rationale was the heterolytic cleavage of the Au-SR bond to afford a reactive site on the Au surface followed by disulfide scrambling in solution with R’S’SR’ to generate R’S⁻ which can then diffuse back onto the gold surface. On repeating this process, the second R’S⁻ ligand need not coordinate adjacent to the first R’S⁻ group.
Subsequently the same research group used ligand exchange reactions between AuNPs (average diameter ca. 2.2 nm) coated with varying carbon chain length alkanethiols and disulfide modified nitroxides (Figure 1.12, 1, 2 and 3). They investigated the dynamics of surface-attached nitroxide radicals at different distances from the nanoparticle surface which showed that when the chain length of the nitroxides was shorter than the chain length of the surrounding alkanethiol protected gold nanoparticles the motion of the spin labels were hindered and vice versa. A protocol for the synthesis of AuNPs with high nitroxide coverage were suggested in the same paper. The idea was based on a ligand exchange reaction between gold nanoparticles coated with weakly bonded triphenylphosphine and diradical disulfide. Another ligand exchange reaction was done by Megiel and co-workers (Figure 1.12, 4) using disulfide diradicals with n-butane-thiol and n-dodecanethiol protected gold nanoparticles. They obtained gold nanoparticles which were used in sandwich-like structures using gold electrode substrate. This electrode was applied in electrocatalytic oxidation of benzyl alcohol to...
benzaldehyde. The catalytic efficiency of the prepared electrode was enhanced compared to a simple TEMPO-SH electrode. The same group developed a new one pot synthesis reaction to increase TEMPO grafting density based in reverse micelles of tetraoctylammonium ions using 4. These AuNPs comprised a multi-layer structure of TEMPO ligands and tetraoctylammonium bromide ions which adsorbed weakly on the gold surface. They argued that the high nitroxide coverage was achieved due to the elimination of the ligand exchange reaction.\textsuperscript{121} Lloveras \textit{et al.}\textsuperscript{122} reported a one pot phase procedure using thiol, phosphine and triamine surface-stabilized AuNPs, followed by a ligand exchange reaction with bis-nitroxide-diradicals (Figure 1.12, 1). Initial particles were very small based on the plasmon band, but particle size could be increased through heat treatment in the solid state.

\[
\text{O} \quad \text{N} \quad \text{O} \quad \text{N} \\
\text{H} \quad \text{N} \quad \text{O} \quad \text{S} \\
\text{S} \quad \\n\text{(1)}
\]

\[
\text{O} \quad \text{N} \quad \text{O} \\
\text{H} \quad \text{N} \quad \text{(CH2)10} \quad \text{S} \quad \text{(CH2)10} \quad \text{NH} \\
\text{(2)}
\]

\[
\text{O} \quad \text{N} \quad \text{O} \\
\text{(3)}
\]

\[
\text{O} \quad \text{N} \quad \text{O} \\
\text{(4)}
\]

Figure 1.12 TEMPO derivatives have been used in previous literature.
1.7.2 TEMPO immobilized on metal oxide

The first synthesis of magnetic nanoparticles functionalized by TEMPO was reported in 2008 by Schatz et al. The TEMPO-functionalized, graphene-coated ferromagnetic cobalt nanoparticles were utilized as a heterogeneous oxidation catalyst for primary and secondary alcohols. The immobilization of TEMPO on iron oxide (Fe₃O₄) superparamagnetic nanoparticles (ca. 11.7 nm) was prepared by Tucker-Schwartz and Garrell and used as catalysts for the selective oxidation of a wide range of primary and secondary alcohols to aldehydes, ketones or lactones. In this approach, Fe₃O₄ NPs were first synthesized by a co-precipitation method, followed by surface modification with 3-azidopropylphosphonic acid (Scheme 1.5, 5) and then performing a ‘click’ reaction with 4-propargyloxy-TEMPO using copper(I) catalysed 6. (Scheme 1.5) Due to the paramagnetic properties of TEMPO and the superparamagnetic properties of the magnetic nanoparticle core, the preparation of spin-labeled Fe₃O₄ attracted interest in biomedical applications and drug delivery.

Scheme 1.5 Synthesis of TEMPO-coated iron oxide nanoparticles.
1.8 TEMPO as a polymerisation mediator

Nitro oxide derivatives have been widely used in polymerization processes.\textsuperscript{112} TEMPO coated NPs with silicon oxide,\textsuperscript{126} magnetite,\textsuperscript{127} 128 129 titanium,\textsuperscript{130} quantum dots\textsuperscript{131} and gold nanoparticle cores,\textsuperscript{132} provide them with many favorable properties such as increased stability and dispersibility of nanoparticles in both organic solvents and in polymer matrices. Recently, Megiel and co-workers\textsuperscript{120} prepared polystyrene polymer brushes on gold and silver surfaces based on Nitroxide Mediated Radical Polymerization (NMRP). The preparation process involves injection of TEMPO-coated nanoparticles into a TEMPOL-mediated styrene polymerization system.\textsuperscript{108} Afterwards, a new method for the synthesis of polystyrene grafted AgNPs was also reported by the same group and exhibited antibacterial activity against pathogenic bacteria. The high grafting density of the nitroxide radicals attached to the silver surface are capable of recombining with polymer macroradicals and therefore form covalent bonds.\textsuperscript{133} Polymerization was also achieved from TEMPO-immobilized magnetic nanoparticles. Poly (styrene-co-maleic anhydride) copolymer brushes have also been prepared on the surface of Fe\textsubscript{3}O\textsubscript{4} magnetite nanoparticles.\textsuperscript{134}

1.9 Development of TEMPO-coated gold nanoparticles in this thesis

Many essential chemical and optical properties of AuNPs appear sensitive to the nature of the ligand and the gold core and the exploitation of ligand chemistry of AuNPs and their self-assembly properties is still challenging. Previous work on
TEMPO-coated NPs (sections 1.7 and 1.8) has revealed a diversity of applications but approaches to modulate the coverage of TEMPO is desirable. The objective of the current studies was to (i) investigate different approaches to bind TEMPO radicals to the AuNP surface using a diversity of covalent and non-covalent (ionic and dispersion) interactions; (ii) to investigate the extent of surface coverage using these different approaches and (iii) probe the thermal stability of the radical-coated AuNPs produced.

Chapter 2 describes the first studies into the use of electrostatic interactions to bind radicals to nanoparticles using commercially available cationic TEMPO derivatives (7). Chapter 3 reinvestigates the use of covalent interactions to generate AuNPs capped with thiolate-TEMPO ligands (8).135,136 These studies implement thioacetate precursors as a novel, efficient, approach to the one-pot generation of TEMPO-coated AuNPs with high radical coverage and compared to the generation of AuNPs prepared from the disulfide diradical (DISS) (9). Chapter 4 implements dispersion forces for the first time to bind TEMPO radicals to AuNPs through the use of TEMPO-O-C₈ radicals (10) and octanethiol stabilized AuNPs.

In Chapter 5 the synthetic methodology developed in Chapter 3 is exploited to attach TEMPO ligands 8 to superparamagnetic gold-coated iron oxide NPs. This is compared to a previous study in which iron oxide NPs were coated directly with TEMPO ligands bound to the Fe₃O₄ surface via a phosphate ligand.98
1.10 Methods for detection and characterization

Characterization of nanoparticles requires a diversity of approaches to gain information about the nanoparticle's properties such as particle size, shape, geometry, composition, size distribution or even the environment around the nanoparticles. Knowing these measurements are important in term of stability, toxicity.¹³⁷ These measurements can be classified as detection and characterization. Detection merely determines the presence of nanoparticles and their coatings, while characterization provide more details on the physical and chemical properties such size and shape, reactivity, aggregation and/or chemical composition. This section reviews the characterization methods used in this work.
1.10.1 Stability

UV-Visible (or UV-Vis) spectroscopy is one of the common methods for characterization of nanoparticles.\textsuperscript{138} This method is based on excitation of the sample with UV/visible radiation and measuring the sample absorbance as function of wavelength. Gold nanoparticles are plasmonic and exhibit a surface plasmon resonance (SPR) and optical properties arise from the oscillation of electrons at the metal-dielectric interface, leading to a characteristic absorption band. The position and intensity of this band strongly depends on the size, shape, coating and refractive index of the surrounding medium.\textsuperscript{139} Which make this technique a valuable tool for identifying, characterizing, and studying these materials.

The size dependence of plasmonic nanoparticles can be explained through the quantum confinement effect.\textsuperscript{140} The presence and position of this SPR band provides a tool to confirm the presence and stability of NPs over time.\textsuperscript{141} When nanoparticles aggregate the size will increase and the plasmonic band will shift to higher wavelength (Figure 1.14).
Any changes around the particles such as different coating, solvent, nanoparticles separation distance can also have a great influence on the local refractive index and therefore the position of the plasmon band. The position of plasmon band will increase with increasing the refractive index according to Mie scattering theory. However, in many studies the SPR position has been characterized in term of a responsiveness equation

$$\Delta \lambda_{\text{peak}} = m \eta$$

Eq. 1.1
where $\Delta \lambda_{\text{peak}}$ is the shift in the SPR peak position, $\eta$ is the refractive index of the medium, and $m$ is the responsiveness of the nanoparticle. A plot of the SPR peak position versus refractive index of the surrounding medium is often a straight line and called a response function.\textsuperscript{143} The bandwidth of the plasmon peak is also sensitive to the form of the AuNP. Smaller particles frequently have broader spectra than larger particles due to increasing in surface to volume ratio as result the oscillating electrons possess a higher probability of being scattered at the particle surface. This enhanced scattering reduces the lifetime of the oscillation and hence increases its spectral width (Figure 1.15).\textsuperscript{144}

Figure 1.15 SPR band of AuNPs as a function of AuNP size.
1.10.2 Determination of nanoparticle size and chemical composition

Particle size is one of most basic measurements to characterize nanoparticles. Transmission and scanning electron microscopy (TEM) and (SEM), respectively have been used in this work to give direct evidence about a single particle size and shape in the solid phase. Both techniques use an electron beam to create an image. In TEM the electron beam passes through the sample and interacts with the electron density in the sample, offering valuable information on the inner structure of the sample. While the beam in SEM is reflected towards a detector, providing information on the sample’s surface and its composition. Moreover, the resolution that can be achieved from TEM is higher than SEM which is very important to determine the size distribution of nanoparticles. The size distribution of nanoparticles in this thesis were determined based measurements of 100+ individual particles and the frequency determined for each particle size. The mean was determined from the weighted average of these data and the standard deviation is quoted as the sample standard deviation defined as:

$$s = \frac{\sqrt{\sum_{i=1}^{n}(x_i-\bar{x})^2}}{n-1}$$  \hspace{1cm} Eq. 1.2

Where $n$ is the number of data points, $x_i$ each of the values of the data and $\bar{x}$ the mean of the $x_i$.

The size distribution of particles in solution can be measured using dynamic light scattering (DLS). DLS measures the light scattered from the laser that passes through a sample. The modulation of the scattered light intensity as a function of time is analyzed, and the hydrodynamic particle size can be determined. DLS is
used to determine the true state of particles in media. Since it is a solution technique, we should be careful to consider the tendency of particles to agglomerate in solution. Both the surface charge and functional groups present may play a central role in preserving the nanoparticles monodisperse nature. As a consequence of agglomeration, the size distribution obtained from DLS data might differ from TEM images.

TEM and SEM are also equipped with Energy dispersive X-ray spectroscopy (EDS or EDX). EDX is an analytical technique used to investigate the elemental distribution. When an electron beam interacts with the sample, electrons are ionized from core orbitals of atoms within the sample. Higher energy electrons then relax to fill these vacancies and emit X-rays during this process. Since the orbital energies of each element are different, the energies of the emitted x-rays are diagnostic of the elements present.

Figure 1.16 EDX principle (Image courtesy of AZoM)
Powder X-ray diffraction (PXRD) is another technique to characterize materials including nanoparticles. In PRXD, the diffraction pattern is measured as diffracted X-ray intensity as a function of detector angle, $2\theta$. Every material has its own unique diffraction pattern based on the crystallographic unit cell parameters which define the position in $2\theta$ and unit cell contents which define relative intensities. The powder profile provides a diagnostic fingerprint for the nature of the nanoparticle core and can be identified using a database.

1.10.3 Analysis of nanoparticle surface coating

While SEM and TEM provide direct images of the NP size, characterization of the NP surface relies on more conventional chemical techniques.

Fourier-transform infrared spectroscopy (FTIR) has been used to characterize the surface groups attached to the surface of the nanoparticle with high accuracy and reproducibility. It has the capability to determine functional groups based on their vibrational stretching modes and molecular symmetry. It has also been extended to the study of nano-scale materials for evaluating the functional groups adsorbed within NPs. IR spectroscopy measures the absorption of light due to bond stretching or bending (vibration), different types of bond absorb at different energies therefore different frequencies. However, the vibration should be an IR active mode which means it should have a change in dipole moment during this process.
1.10.4 Free Radical Characterization

Electron paramagnetic resonance (EPR) has been used extensively in this thesis as a probe of the free radical environment. Similar to other techniques the EPR depends on the absorption of electromagnetic radiation.\(^{151}\) An organic radical typically has one unpaired electron and has \(S = \frac{1}{2}\). This gives rise to two possible microstates; \(m_s = \pm \frac{1}{2}\) corresponding to ‘spin up’ and ‘spin down’.\(^{152}\) In the absence of a magnetic field the two possible spin orientations are degenerate but in the presence of an external ‘applied’ magnetic field the unpaired electron interacts with the magnetic field \(B_0\) and the degeneracy of the two spin states \((m_s = \pm \frac{1}{2})\) are lifted according to:

\[
E(m_s) = g\beta B_0 m_s \tag{Eq. 1.3}
\]

The application of a magnetic field is known as the Zeeman effect, and the energy difference \((\Delta E)\) between the two \(m_s\) two states can be readily shown to be:\(^{153}\)

\[
\Delta E = g\beta B_0 \tag{Eq. 1.4}
\]

In the EPR experiment we apply a microwave frequency, \(\nu\) (ca 9.5 GHz) and sweep the applied field \(B_0\) to find the resonance condition where \(h\nu = g\beta B_0\) which corresponds to flipping of the electron spin. Knowing the operating frequency and the resonant magnetic field \(B_0\) we can determine the g-factor, \(g\) from the expression:

\[
g = \frac{h\nu}{\beta B_0} \tag{Eq. 1.5}
\]
The g factor is somewhat akin to the chemical shift in NMR spectroscopy and for organic radicals is typically close to the free electron value \( (g_e = 2.0023192778) \). Deviations from \( g_e \) arise from the presence of spin-orbit coupling between the ground state and excited states of the complex.

So far we have neglected the presence of nuclei with non-zero nuclear spins. The nuclear spin is defined by the quantum number \( I \) (which is integer or half-integer). The nuclear spin also interacts with the electron spin leading to hyperfine coupling. Coupling to \( n \) equivalent nuclei, each with spin \( I \) splits the original signal into \( 2nI + 1 \) lines.

Both the magnitude of g and the hyperfine coupling constant \( (a) \) are typically diagnostic of a particular family of radicals. The coupling patterns expected for some common values of \( n \) and \( I \) are presented in Figures 1.17 and 1.18. For example the TEMPO radical has the unpaired electron delocalized between N (\(^{14}\)N has \( I = 1 \) and is ~100% abundant) and O (\(^{16}\)O ~ 100% abundant but has \( I = 0 \)). Thus there is no coupling to O (\( I = 0 \)) but we do observe coupling to \(^{14}\)N (\( I = 1 \)) giving rise to \( 2nI + 1 = (2)(1)(1) + 1 = 3 \) lines (Figure 1.17, \( I = 1 \)).
An additional factor which should be taken into account in the context of this thesis is the effect of spin-spin interactions between radicals. This can be intramolecular or intermolecular. Each unpaired electron has a dipole moment, \( \mu \). The strength of the dipole-dipole interaction is given by:
\[ E = -\frac{\mu_1 \mu_2}{4\pi|d^2|} \]

Thus as the distance \( d \) between radicals increases then the energy of the dipole-dipole interaction drops off rapidly. At low concentrations the mean distance between particles is large and hence the dipole-dipole interaction is negligible. At high concentration (small \( d \)) then dipole-dipole interactions become significant and this can lead to dipolar broadening of the EPR spectra which can ultimately ‘wash out’ the anticipated hyperfine coupling and lead to broad singlets in the EPR spectrum (Figure 1.19).

Figure 1.19 intra-molecular spin-spin interaction in TEMPO radical.
Chapter 1: Literature Review

A useful experiment to undertake in the presence of dipolar broadening is to undertake dilution studies. If dipolar broadening arises from intermolecular dipole-dipole interactions then dilution should lead to sharper, better resolved lines (Figure 1.20). Conversely if dipolar broadening is of intramolecular origin then dilution would have no effect (apart from decreasing the total signal intensity) since the radical-radical distance for an intramolecular process is unaffected (Figure 1.21).154
Figure 1.20 Dilution effect in inter-molecular exchange coupling system
1.11 Outline of this thesis

This thesis explores the synthesis and characterization of three families of AuNPs coated with TEMPO radicals. In Chapter 2 electrostatic interactions between cationic TEMPO derivatives and an AuNP with an anionic surface is described. In Chapter 3 the radicals are bound to the AuNP surface using covalent interactions, whereas in Chapter 4 dispersion forces are used to bind radicals onto the AuNP surface. In each Chapter the NPs are fully characterized in terms of both the NP size but also the nature of the surface coating. The stability of the AuNPs are established through VT UV/vis and VT-EPR studies and radical-radical interactions have been explored through EPR spectroscopy. In Chapter 4 the use
of these TEMPO-coated AuNPs is explored as mediators with respect to polymerization of styrene. In Chapter 5 work towards multi-layer systems is described in which a superparamagnetic iron oxide core has a layer of gold and an additional layer of TEMPO is applied to the gold surface.

1.12 Objectives

The objectives of this research are to:

1) prepare TEMPO-coated gold nanoparticles
2) investigate different types of interaction between the gold core and the TEMPO radical (covalent, electrostatic, dispersion)
3) examine methods to control the extent of coverage with TEMPO
4) examine both intramolecular and intermolecular magnetic communication between TEMPO radicals
5) examine the properties of TEMPO-coated gold nanoparticles with respect to free radical polymerization where TEMPO radicals are known to act as mediators.\textsuperscript{111,112}
1.13 References

Chapter 1: Literature Review

Chapter 1: Literature Review


Chapter 1: Literature Review

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Chapter 2: Synthesis and Self-Assembly of TEMPO Bromide-Capped Gold Nanoparticles
2.1 Introduction

Metal nanoparticles have been extensively studied due to their intermediate size regime, bridging the space between the molecular and macroscopic regimes. This brings a series of unique properties to these particles such as quantum size effects, which have a direct influence on their optical, electronic and magnetic properties.\(^1\) These properties can be tuned by the size and geometry of the nanoparticles as well as the surface chemistry which can affect solubility, self-assembly, aggregation and dispersion.\(^2\) These nanoparticles serve as fundamental building blocks for many applications in biology, chemistry and medicine.\(^3\) The emergence of size/shape sensitive response has led to increasing research efforts to control the preparation of these nanoscale blocks to ensure reproducible periodicity in the size and shape distribution of the nanoparticles through tuning of the surface ligands employed to stabilize the nanoparticles.\(^4\)

The stability and facile preparation of gold nanoparticles have made them some of the most extensively studied nanoparticles to date whose chemistry is relatively well understood.\(^4b,c,5\) The soft nature of the gold NP core makes it particularly attractive for capping with thiol groups (RSH) or other related soft donors such as phosphines.\(^6,7,8\) For thiols, the aurophilic nature of the ligand (Au-S bond energy is around 184.1 kJ.mol\(^{-1}\))\(^9\) leads to high stability and gold NPs can remain stable in solution and/or solid form for at least 1 year without decomposition. The R group can be modified to provide good solubility in a range of polar or non-polar media which can be suitable in wide range of applications including templates for building superstructures and formation of polymers.\(^6\)
Both the charge and chemical properties (e.g. hydrophilicity) of the surface are important to determine the thermal stability and the chemical reactivity of the gold NP. Therefore, the development of well-controlled but tunable self-assembly properties of gold nanoparticles is required. The self assembly of the gold nanoparticles depend on the kind of chemical bond between the gold core and the ligand. Thiol-capped gold nanoparticles have been synthesized in one step, two-phase reactions. Nanoparticles can also be post-synthetically modified via ligand exchange reactions with another thiol ligand. Both the self-assembly and post-synthetic modification approaches involve formation of chemical bonds between the thiols and the gold surface, either during formation or in an Au-S bond cleavage/formation process as part of a substitution reaction.

Post-synthetic modification of NPs is a convenient strategy as it permits the outer surface of the NP to be modified while potentially retaining the (mono)disperse size characteristics of the pre-formed NP core. The robust nature of the Au-S interaction can lead to slow kinetics for thiol exchange reactions. While increasing the temperature can increase the ligand exchange rate, such elevated temperatures can also lead to changes in AuNP core size distribution. This has led many groups to develop alternative systems in which ligand exchange on the AuNP surface is more facile and may permit the study of gold nanoparticles with different functional groups. In particular the use of charged NP surfaces in which additional shells can be electrostatically coated on the surface has attracted attention. Notably coating AuNPs with tetraalkyl ammonium groups (Figure
2.1) affords tunable electrostatic, ion-dipole as well as dispersion forces at the nanoparticle surface.\textsuperscript{21}

Figure 2.1 Schematic of an $R_4N^+$ surface-coated nanoparticle [Copyright © 1998, American Chemical Society]\textsuperscript{21}

Studies have demonstrated non-covalent approaches to bonding $R_4N^+$ groups to AuNP surfaces through either two-phase procedures or in reverse microemulsions.\textsuperscript{19,22,23} In this context citrate-stabilized AuNPs provide a potentially versatile starting material. The citrate surface is negatively charged and provides a suitable building block from which to develop electrostatically driven surface coatings. In the simplest approach reaction of an anionic citrate-capped AuNP with $[R_4N]Br$ has been employed to provide a surface coating of long chain $R_4N^+$ cations ($TTAB = [nC_{14}H_{29}NMe_3]Br$) on the citrate-coated AuNP.\textsuperscript{24} However, the hydrophobic nature of these tetra-alkyl ammonium-coated gold nanoparticles tends to lead to aggregation in aqueous solution.\textsuperscript{20} Chen and co-workers\textsuperscript{24} studied the hydrophobic effect of quaternary ammonium surfactants using citrate-stabilized gold nanoparticles and confirmed that hydrophobic interactions are the
main driving force behind nanoparticle aggregation. Lim and coworkers\textsuperscript{25} have successfully converted the surface charge from negative to positive via electrostatic interaction between anionic citrate and cationic head group in CTAB (CTAB = cetyltrimethylammonium bromide) via two possible models; a) formation of a bilayer of CTAB on the citrate-capped gold nanoparticles or b) formation of a micelle. This study successfully converted the surface charge from negative to positive via electrostatic interactions. A study by Robin \textit{et al.}\textsuperscript{26} reacted anionic, citrate-capped, AuNPs with thiol ligands bearing quaternary ammonium groups. Rather than generating an electrostatic interaction between the thiol-containing ammonium group and the citrate-stabilized AuNP, the surface-bound citrate was displaced by thiol, leading to an ammonium group covalently bound via the thiol group to the gold surface. These studies clearly reveal the subtle interplay between developing multilayer electrostatically bound NPs and the potential for surface substitution at the AuNP surface.

TEMPO and its derivatives have found industrial applications in the production of medicines and other speciality chemicals e.g. catalysts in organic synthesis, oxidation of alcohols, polymerization.\textsuperscript{27,28,29,30} TEMPO coated gold nanoparticles were first reported in 2001 and have been studied extensively in recent years.\textsuperscript{31} All of these studies involved derivatives in which a strong covalent interaction was achieved between the gold NP core and a thiol-functionalized TEMPO. In this Chapter the synthesis and characterization of AuNPs electrostatically coated with TEMPO radicals is described from the reaction of citrate-stabilized AuNPs with the water-soluble TEMPO derivative WS-TEMPO (Scheme 2.1). The new AuNPs are
characterized and unexpectedly reveal a citrate/bromide exchange at the gold surface with an outer surface coating of WS-TEMPO.

Scheme 2.1 The structure of the water-soluble (WS) TEMPO derivative, WS-TEMPO (2,2,6,6-Tetramethyl-4-[1-oxo-6-(triethylammonio)hexylamino]-1-piperidinyloxy bromide).

2.2 Experimental

HAuCl$_4$.3H$_2$O, trisodium citrate, WS-TEMPO, THF and DMF were used as received. All aqueous solutions were prepared with Milli-Q ultrapure grade (resistivity $18.2 \text{ M}\Omega \text{ cm}^{-1}$). IR spectra were recorded on a Bruker alpha FTIR spectrometer. UV–Vis spectra were recorded on Agilent1103A. TEM images were obtained using a Philips CM10 at Biotron (University of Western Ontario). Samples were prepared on a formvar/carbon film grid on which a drop of the diluted nanoparticle solution was deposited and evaporated at room temperature. EPR spectra were recorded on a Bruker EMXplus EPR spectrometer. EPR simulations were undertaken using Winsim.$^{32}$ SEM images were obtained with FEI Quanta Environmental Scanning Electron Microscope (ESEM) with an EDAX Octane SDD detector at GLIER (University of Windsor) with the assistance of Sharon Lackie.
2.2.1 Synthesis of citrate-capped AuNPs

Citrate-stabilized gold nanoparticles were synthesized following Turkevich’s method. In a typical procedure, an aqueous solution of HAuCl₄·3H₂O (1.1 × 10⁻³ M, 100 mL) was brought to reflux. Reduction was then initiated by addition of freshly prepared aqueous trisodium citrate solution (10.0 mL, 38.8 mM). The mixture was vigorously stirred using a Teflon-coated magnetic bar under constant heat (90 °C) for 20 min. The mixture was then removed from the heat and stirring continued for a further 10 min. The resultant AuNPs were separated by centrifugation and re-dispersed into water to remove residual reagents in solution.

2.2.2 Synthesis of AuNPs coated by WS-TEMPO

WS-TEMPO was prepared in 4 different concentrations ranging from 10⁻¹ to 10⁻⁴ M in H₂O/DMF (1:4). 10 mL of each concentration were added to 3 mL of a solution of citrate stabilized AuNPs (prepared as outlined in section 2.2.1) under vigorous stirring on an ice bath for 2 hours. The resultant solutions were purified by precipitation on addition of H₂O and the supernatant was removed by pipette. The samples were more stable if maintained in DMF but could be isolated and dried under vacuum and later resuspended in DMF without significant aggregation.

2.3 Results and Discussion

2.3.1 AuNP characterization

The most routine protocol to synthesise citrate-stabilized AuNPs is the Turkevich method which is based upon the reduction of gold (III) chloride or chloroauric acid,
HAuCl₄, with trisodium citrate. In this reaction sodium citrate is used as both the reductant and capping agent. The mechanistic details of this process are described in Chapter 1 (Scheme 1.1). The UV/vis spectrum of these citrate-capped gold nanoparticles (Figure 2.2) shows a typical surface plasmon resonance band with λ<sub>max</sub> = 525 nm. Humbert <i>et al.</i> synthesized gold nanoparticles in the range of 20 nm diameter which revealed a λ<sub>max</sub> at 525 nm. TEM images (Figure 2.3) reveal monodisperse, spherical gold nanoparticles with a narrow particle size distribution of 17.8 nm diameter (standard deviation = 3.6 nm) (Figure 2.3) in good agreement with the UV/vis data.

Figure 2.2  UV/vis spectra of citrate-stabilized AuNP recorded in H₂O.
Initial addition of WS-TEMPO to these citrate-stabilized gold nanoparticles in aqueous media led to a marked change in absorption and formation of a dark
solution (Figure 2.4). The UV-vis spectroscopy revealed a decrease in the plasmon band at 525 nm and the emergence of a red-shifted band at 680 nm. While it is possible that the charged nature of the ammonium group of the WS-TEMPO may cause changes to the surface charge of AuNP and its zeta-potential, ammonium salts are well-known as aggregation agents for AuNPs. Microscopy studies (Figure 2.5) revealed that the addition of WS-TEMPO to the citrate-stabilized Au NPs led to formation of a black precipitate, consistent with aggregation.

![UV-vis spectrum](image)

Figure 2.4 The effect of adding WS-TEMPO to an aqueous solution of citrate-stabilized gold NPs, emergence of a new low energy.
Chapter 2: Synthesis and Self-Assembly of TEMPO Bromide-Capped Gold Nanoparticles

2.3.2 Effect of WS-TEMPO concentration and solvent

Use of a DMF/H₂O mixture 4:1 (v/v %) rather than pure water was subsequently used as reaction medium to inhibit aggregation since DMF is better able to solvate organics while stabilizing charged species. In addition, an ice bath was used to maintain a constant temperature throughout the process. When WS-TEMPO solutions (concentrations ranging from 10⁻¹ to 10⁻⁴ M) were added to a solution of citrate-capped AuNPs, a concentration dependent response was observed. Addition of a large amount of WS-TEMPO expectedly resulted in aggregation of AuNPs but when the concentration of added WS-TEMPO was decreased monodisperse nanoparticles were obtained. Figure 2.6 (top) displays the changes in color of AuNP solutions upon addition of WS-TEMPO. The well-dispersed AuNPs exhibit a bright red color due to the localized surface plasmon resonance.
(LSPR). As aggregation occurs, multiple interactions between the AuNP surface plasmons shift the LSPR band to a longer wavelength region, resulting in a dark blue color. The TEM image (Figure 2.7) of the gold nanoparticles obtained using a $10^{-4}$ M solution of WS-TEMPO (T-AuNPs) revealed formation of monodisperse gold nanoparticles with an average particle size of 14(2) nm in diameter.

![Image of gold nanoparticles with varying concentrations of WS-TEMPO](image)

![Absorbance spectra of WS-TEMPO solutions](image)

Figure 2.6 (bottom) Emergence of long wavelength absorption upon increasing the WS-TEMPO concentration; (top) change in color of the AuNP on addition of WS-TEMPO from red (left) through purple (centre) to dark blue (right)
Figure 2.7 (top) TEM images of well defined monodisperse WS-TEMPO AuNPs; (bottom) size distribution of WS-TEMPO AuNPs. The dashed line corresponds to the sample normal distribution with mean = 14.1 and standard deviation = 2.4 nm.
Addition of excess H\textsubscript{2}O led to precipitation of these AuNPs which could be washed and dried under vacuum. The resultant material obtained was then re-dissolved in THF for further characterization. The UV/vis spectra of these nanoparticles (Figure 2.8 (purple)) shows a broadening of the plasmon band consistent with plasmon coupling, which results from two or more plasmonic particles approaching each other to a distance less than the diameter of one of the nanoparticles where the resonance for these particles hybridize resulting in red shifting of the spectral peak. However, when the solution was sonicated for ca. 10 minutes, the solution afforded a narrow plasmon band (Figure 2.8) confirming the reversible nature of this process.

![Figure 2.8 Effect of sonication time on the plasmon band of WS-TEMPO-AuNPs.](image)
2.3.3 Characterization of surface coating

As outlined in the introduction, use of \([R_4N]Br\) salts typically leads to a cationic layer electrostatically bound on the citrate-stabilized AuNP. Replacement of \(R_4N^+\) by WS-TEMPO was anticipated to follow similar chemistry, affording an outer coat of TEMPO radicals on the negatively charged citrate-coated AuNPs. The IR spectra of the citrate-stabilized AuNPs before and after adding WS-TEMPO are shown in Figure 2.9. The IR spectrum of the initial citrate capped gold nanoparticles shows characteristic \(\nu_{C=O}\) bands diagnostic of the carbonyl groups of the citrate anion at 1585 and 1395 cm\(^{-1}\). The IR spectrum of the AuNPs generated after addition of WS-TEMPO (Figure 2.9) confirmed the presence of WS-TEMPO on the gold surface with the characteristic \(\nu_{\text{CH}_2}, \nu_{\text{CH}_3}, \nu_{C=O}\) and \(\nu_{\text{NH}}\) vibrations comparable to those of pure WS-TEMPO. Conversely the vibrational frequencies associated with the citrate anion disappeared from the IR spectrum of the AuNPs formed after treatment with WS-TEMPO and the IR spectrum closely resembles that of WS-TEMPO.
Figure 2.9 IR spectra of (top) TEMPO-coated AuNPs (T-AuNPs) (middle) citrate-stabilized AuNPs; (bottom) WS-TEMPO

Energy dispersive X-ray spectrum (EDS) of the WS-TEMPO coated AuNPs (Figure 2.10) clearly reveal high concentrations of Au (peaks at 2.16, 9.71 and 11.43 keV) as well as characteristic peaks of bromine (1.48, 11.36 and 11.90 keV). The absence of citrate (IR) and presence of bromide (EDS) points to an initial anion exchange on the AuNP surface, while the IR data suggest the presence of WS-TEMPO. This is consistent with displacement of the oxophilic citrate by softer bromide anions on the AuNP surface and then a further coating of WS-TEMPO on the surface. (Scheme 2.2).
Figure 2.10 EDS spectrum of WS-TEMPO-coated bromide-stabilized AuNPs

Scheme 2.2 Schematic of the structure of the WS-TEMPO-coated, bromide-stabilized AuNP

### 2.3.4 Thermal stability

These nanoparticles were studied by variable-temperature UV/vis spectroscopy (Figure 2.11). The spectra were recorded from 295 K to 345 K and showed no significant change except for the minor changes in plasmon intensity known to
occur upon heating. After cooling to room temp the original spectrum was obtained indicating the thermally robust nature of these particles.

Figure 2.11 Temperature (in)dependence of the plasmon band for the WS-TEMPO-coated bromide-stabilized AuNPs.

2.3.5 Radical characterization

The room temperature X-band EPR spectrum of WS-TEMPO in DMF (Figure 2.11) reveals a classical 1:1:1 triplet due to coupling to $^{14}\text{N}$ ($I = 1$) characteristic of the nitroxide radical. The g-factor and hyperfine coupling ($a_N$) were 2.0054 and 16.0 G respectfully. A similar triplet spectrum was observed for the AuNPs in solvent ($g = 2.0063$, $a_N = 15.5$ G). The absence of significant line broadening suggests that the
TEMPO radicals are magnetically well isolated, indicating a low coverage of the ligand on the gold surface.

Figure 2.12 Room temperature X-band EPR spectra of (left) WS-TEMPO and (right) WS-TEMPO coated AuNPs

2.4 Conclusions

When citrate-coated AuNPs were treated with WS-TEMPO in pure aqueous solution, aggregation was initially observed but could be suppressed at lower concentrations using a water:DMF mixture to afford well-defined 14 nm AuNPs. IR and EDS studies revealed that rather than forming the expected Au:citrate:WS-TEMPO multishell structure a ligand exchange process occurred on the Au surface in which hard citrate anions were displaced by softer aurophilic bromide ions generating a Au:Br:WS-TEMPO structure. The presence of WS-TEMPO was reflected in the IR data but EPR studies revealed low concentrations of radical on the AuNP surface. These AuNPs are stable to 345 K in solution.
2.5 References


Chapter 2: Synthesis and Self-Assembly of TEMPO Bromide-Capped Gold Nanoparticles

Chapter 3: An efficient one-pot synthesis of high coverage TEMPO-coated gold nanoparticles
3.1 Introduction

Nanomaterials have attracted considerable interest in the last few decades as they span the boundary between the molecular and macroscopic regimes. The physical properties of such nanoparticles can be tuned by the composition and size of the nanoparticles (NP), their geometry and the nature of the coating on the nanoparticle surface. These NPs have been examined for a plethora of applications in electronic, biomedical and optical fields. Among their intrinsic properties in relation to the size of these materials, one can highlight their semiconducting properties, the surface plasmon resonance in metallic nanoparticles and the superparamagnetic nature of sub-domain size magnetic nanoparticles.

More recently radical coated metal nanoparticles have started to be explored and TEMPO radicals have been successfully coated on to a range of NP cores such as magnetite, titanium oxide, gold and quantum dots. Promising applications in nanomedicine, sensors, catalysis and polymerisation have been reported to date. Swiech and co-workers showed that a gold electrode modified with TEMPO-coated AuNPs exhibited an enhanced activity when compared to a traditional coated Au monolayer for electrocatalytic oxidation applications. Work by Du et al. implemented nitrone radicals on gold nanoparticles (AuNPs) as a highly sensitive spin trap to detect free radicals with chemical, biochemical and biomedical applications. In other areas, nitroxide radicals have been widely used in polymerization systems and have been
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successfully achieved from different TEMPO-coated NPs such as magnetite,\textsuperscript{4,5,6} titanium,\textsuperscript{10} quantum dots\textsuperscript{12} and gold nanoparticles.\textsuperscript{8}

Other studies have focused on making organic radical polymers as battery materials.\textsuperscript{19} Elegant synthetic work by Rajca,\textsuperscript{20} Bushby,\textsuperscript{21} Veciana\textsuperscript{22} and others\textsuperscript{23} has focused on developing poly(radical) oligomers and dendrimers with high spin ground states generated through exchange coupling via a $\pi$-conjugated backbone.\textsuperscript{24} These studies provide a synthetic tour de force but are ultimately challenging due to steric issues which can lead to breakdown in the $\pi$-conjugated pathway essential for efficient exchange coupling. In this context we were interested to develop an alternative strategy to develop poly(radical) systems through the use of NPs as templates for the self-organization of paramagnetic radicals. Pioneering work by Chechik had shown that substitution of thiol-protected AuNPs with a TEMPO diradical disulfide occurred to form AuNPs with low concentrations of surface radical which were not located adjacent to each other.\textsuperscript{11e}

Work by Vidal-Gancedo and co-workers similarly described the synthesis of TEMPO-modified AuNPs through a multi-step synthesis in which AuNPs were substituted via ligand exchange using a very large excess of TEMPO-disulfide ($\sim$ 1:100);\textsuperscript{25} Under ambient conditions nBuS-functionalized and Ph$_3$P-coated AuNPs underwent substitution to form small NPs ($\sim$ 2nm diameter) with low and intermediate coverage respectively. Only after heat treatment of these AuNPs in the presence of [(C$_8$H$_{17}$)$_4$N]Br, followed by purification by GPC, were larger AuNPs (up to 5.6 nm mean diameter) with high radical coverage obtained.\textsuperscript{25} Access to a simple route to well-defined AuNPs displaying high radical coverage therefore
remains a challenge in this field. In this Chapter, we describe the facile and direct synthesis of AuNPs (~ 3 nm) with high coverage of TEMPO ligands covalently linked via a sulfur-Au bond.

3.2 Experimental Section

All chemicals and solvents were purchased from Sigma-Aldrich or Oakwood Chemical and used as received. Water was Milli-Q ultrapure grade (resistivity 18.2 MΩ cm$^{-1}$). EPR spectra were recorded on a Bruker EMXplus EPR spectrometer equipped with a variable temperature control unit. EPR simulations were undertaken using Winsim$^{26}$ to extract the relative intensities of exchange broadened (broad singlet) and ‘isolated’ TEMPO radicals (1:1:1 triplet). Synthesis of thioacetate-functionalized TEMPO derivatives 1 and 2 (Figure 3.1) as well as the disulfide DISS (Figure 3.1) followed established literature protocols and were performed by Dr. Elodie Heyer.$^{27,28}$

Figure 3.1 (top) Thioacetate capped TEMPO ligands 1 and 2 used in the syntheses of the targeted spin labelled AuNPs; (bottom) TEMPO-functionalized disulfide, DISS.
3.2.1 Synthesis of Gold Nanoparticles Capped with TEMPO-C₈-thio-ligand

AuNPs were prepared according to a modified Brust-Schiffrin procedure.²⁹ Different w/w ratios of gold:nitroxide radicals were tested from 4:1 to 1:4. A ratio of Au:S = 1:4 gave the highest radical surface coverage and showed a slight excess of the ligand, which was removed by washing at the end of the AuNP synthesis. Specific details are presented here for the Au:S = 1:4 ratio:

In a typical procedure, a freshly prepared solution of [(nC₈H₁₇)₄N]Br (TOAB, 12.0 mL, 0.1 M in toluene) was added to an aqueous HAuCl₄ solution (19.6 mL, 0.03 M, 0.5 mmol) with vigorous stirring until the aqueous phase appeared clear and the organic phase was deep red. 0.8 g of thioacetate-functionalized TEMPO (1 or 2) was added to the organic phase. After 20 min of stirring, a freshly prepared solution of NaBH₄(aq) (0.2 g in 15 mL, 5.3 mmol) was added slowly under vigorous stirring and then continued for a further 2 h. The aqueous layer was separated and additional toluene (30 mL) added to the organic layer, followed by sonication for 1 min. A black precipitate was obtained after 1 h at rt and this was repeatedly washed with toluene (3 × 20 mL) until the solvent washings remained colorless. The precipitate was then dried in vacuo and characterized by IR, UV/vis, EPR, DLS and TEM.

3.2.1 Synthesis of Gold Nanoparticles Capped with DISS

A w/w ratios of Au:S = 1:2 were prepared according to a modified Brust-Schiffrin procedure.²⁹ In a typical procedure, a freshly prepared solution of [(nC₈H₁₇)₄N]Br
(TOAB, 12.0 mL, 0.1 M in toluene) was added to an aqueous HAuCl₄ solution (19.6 mL, 0.03 M, 0.5 mmol) with vigorous stirring until the aqueous phase appeared clear and the organic phase was deep red. 0.4 g of DISS was added to the organic phase. After 20 min of stirring, a freshly prepared solution of NaBH₄(aq) (0.2 g in 15 mL, 5.3 mmol) was added slowly under vigorous stirring and then continued for a further 2 h. The aqueous layer was separated and additional toluene (30 mL) added to the organic layer, followed by sonication for 1 min. A black precipitate was obtained after 1 h at rt and this was repeatedly washed with toluene (3 × 20 mL) until the solvent washings remained colorless. The precipitate was then dried in vacuo and characterized by IR, UV/vis, EPR, DLS and TEM.

3.3 Results and Discussion

3.3.1 Nanoparticle Synthesis

Previous approaches to generate gold nanoparticles (AuNPs) with high coverage of TEMPO radicals in a one-pot reaction from reduction of HAuCl₄ in the presence of disulfide proved unsuccessful. The previous route to high coverage TEMPO-coated AuNPs involved ligand exchange on pre-formed AuNPs, in which disulfides displaced either phosphine or thiolate ligands. The latter required a 1:100 ratio of Au:disulfide making nanoparticle preparation chemically inefficient in terms of TEMPO. Another group had previously reported the synthesis of AuNPs with high TEMPO coverage using a disulfide diradical (DISS). However, under the conditions employed we were unable to reproduce these results in agreement with a previous report (but see section 3.3.4).
TEMPO-labeled AuNPs were synthesized (Scheme 3.1) by reduction of HAuCl₄ in the presence of 1 or 2 using an Au:S ratio in the range from 1:4 to 1:0.25 (w/w %) to study the effect of the ratio on the grafting density of TEMPO on gold surface. The AuNP analysis which follows is based on the 1:4 w/w ratio studies which provided the highest level of radical coverage (vide infra). The gold NPs are hereafter labelled AuNPs₁ and AuNPs₂ when coated with short-chain TEMPO derivative 1 and longer chain TEMPO derivative 2 respectively.

Scheme 3.1 Preparation of AuNPs from thioacetates 1 and 2.

### 3.3.2 Nanoparticle Characterization

The initial core size of the AuNPs formed was estimated through an examination of the plasmon band in the UV/vis spectra coupled with particle size measurements determined by TEM. UV-visible spectroscopy measurements on both AuNP₁ and AuNP₂ were performed at room temperature in DMF. These revealed a well-resolved plasmon absorption band with λ_max ~ 513 nm for AuNPs₁ and AuNPs₂ (Figure 3.2). These should be compared with previous reports on 3 nm diameter nanoparticles which reveal a plasmon band in the vicinity of 514 nm.³⁰ The shape and particle size distribution of the nanoparticles were determined by TEM and
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revealed spherical AuNP core sizes of 3 nm for both AuNPs\textsubscript{1} and AuNPs\textsubscript{2} (Figure 3.3).

![Figure 3.2 UV-Vis spectra of AuNPs\textsubscript{1} and AuNPs\textsubscript{2}](image)

In order to probe the AuNP surface coating we employed a combination of IR and EPR spectroscopy. The labelling of the AuNP surface with thiol was readily monitored using IR spectroscopy. Starting materials 1 and 2 revealed two distinct $\nu_{C=O}$ stretches in the IR spectrum around 1691 and 1732 cm\textsuperscript{-1} associated with the thioacetate and carboxylate groups respectively (Figures 3.4 and 3.5). Formation of the TEMPO-coated AuNP occurs via breakdown of the thioacetate to form a thiolate ligand and this is associated with the corresponding disappearance of the thioacetate group in the IR spectrum (at 1691 cm\textsuperscript{-1}) for both AuNPs\textsubscript{1} and AuNPs\textsubscript{2} (Figure 3.4).
Figure 3.3 (top) TEM image of AuNPs₁ and AuNPs₂ (bottom); (right) particle size distribution for AuNPs₁ (top, diameter = 3.0(9) nm) and AuNPs₂ (bottom, diameter = 3.3(8) nm). The dotted lines represent the fit to a normal distribution function.
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Figure 3.4 (top) IR spectra of thioacetate-functionalized TEMPO radicals n=2 (right) and n=5 (left); (bottom) AuNPs1 (right) and AuNPs1 (left).

Figure 3.5 (left) Carbonyl region of the IR spectrum of 1 (top) and AuNP1 (bottom); (right) Carbonyl region of the IR spectrum of 2 (top) and AuNP2 (bottom).

In order to probe the loading of the radical on the AuNP surface, a series of EPR studies were undertaken. Simple TEMPO derivatives typically display a 1:1:1 triplet due to coupling of the unpaired electron to the unique $^{14}$N nucleus ($I = 1$). Indeed
dilute solutions of the parent TEMPO-based radicals 1 and 2 both reveal 1:1:1 triplets (Figure 3.6 (top)). When these radicals are attached to AuNPs in low concentration hyperfine coupling is still observed although the slow rotational times for these larger particles can lead to a decrease in intensity of the high field resonance.\(^{31}\) Dipolar interactions between radicals depend on \(1/d^3\) and at higher surface concentrations the EPR spectra broaden to form singlets. The EPR spectra of AuNPs\(_1\) and AuNPs\(_2\) reveal a composite spectrum, comprising a well-resolved 1:1:1 triplet superimposed on a broader singlet (\(\Delta H_{pp} = 15.62\) G and 15.55 G for AuNPs\(_1\) and AuNPs\(_2\) respectively (Figure 3.6 (bottom))). The broad singlet is diagnostic of high coverage of radicals on the AuNP surface.

\(\text{Figure 3.6 (bottom-right) X-band EPR spectrum of AuNPs}_2\) (in DMF) generated using a 4:1 S:Au ratio (1% 1:1:1 triplet, \(g = 2.0064\), \(a_N = 15.7\) G; 99.0% broad singlet \(g = 2.0064\), \(LW = 11.9\) G); (bottom-left) X-band EPR spectrum of AuNPs\(_1\) (in DMF) generated using a 4:1 S:Au ratio (1.3% 1:1:1 triplet, \(g = 2.0064\), \(a_N = 15.6\) G; 98.7% broad singlet \(g = 2.0064\), \(LW = 11.2\) G); (top-right) X-band EPR spectrum of 5 (\(g = 2.0064\), \(a_N = 12.6\) G); (top-left) X-band EPR spectrum of 2 (\(g = 2.0064\), \(a_N = 15.0\) G) in DMF.
Additional washing of the sample to remove any ‘free’ spin label (1 or 2) showed no change in the EPR spectrum indicating the 1:1:1 triplet is associated with a small percentage of $S = 1/2$ spins which appear not to exhibit exchange broadening. This suggests more than one type of chemical environment on the AuNP surface. Notably close-packing of TEMPO radicals on a Au(111) surface gives similar line broadening effects. Conversely the curvature associated with edges and or smaller nanoparticles may lead to larger radical-radical separation and may afford at least one explanation for the persistent low intensity 1:1:1 triplet component observed in the experimental spectra. Additional dilution experiments revealed no significant change in spectral profile indicating that the line broadening is intramolecular in nature and not due to AuNP aggregation (Figure 3.7). Based on the essentially concentration independent nature of the EPR and the absence of change in the

![Figure 3.7 EPR spectra of AuNPs2 upon dilution, highlighting the absence of intermolecular exchange.](image)
UV/vis and EPR upon sonication, the EPR response is most likely intramolecular in nature. Simulation of the EPR spectra was used to quantify the percentage of line-broadened spins on the surface (Figures 3.8 and 3.9) for both AuNPs₁ and AuNPs₂. The exact percentage of the line-broadened component was sensitive to both the TEMPO radical used (1 or 2) and particularly the Au:S ratio (Figure 3.10). Higher thioacetate: gold ratios favored greater surface coverage. For both AuNPs₁ and AuNPs₂ the percentage of the spectrum associated with dipolar broadening was in excess of 98% when using an Au:S ratio of 1:4. Both thioacetate ligands showed similar trends in binding, although the longer chain system 2 showed a slightly higher contribution from dipolar exchange.
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Figure 3.9 Experimental and simulated EPR spectra of AuNPs$_2$ with different S:Au ratios

Figure 3.10 Percent composition of the broad singlet component of the EPR spectra as a function of S:Au ratio for thioacetate starting materials 1 and 2.
Dynamic light scattering (DLS) experiments (Figure 3.11) were additionally used to estimate the size distribution of the particles in DMF solution. For AuNPs$_2$ a maximum in the size distribution was observed around 5 nm consistent with the core size estimates from UV/vis spectroscopy and TEM.

![Figure 3.11 DLS measurements of AuNPs2 in DMF.](image)

### 3.3.3 Thermal stability

Previous work on the most closely related TEMPO-coated AuNP reveals growth of the AuNP core upon heating in the solid state with [((C$_8$H$_{17}$)$_4$N]Br (TOAB) and more TEMPO-functionalized ligand at 130 °C.$^{32}$ A recent study by Shimpi et al.$^{32}$ applied Ostwald ripening theory$^{33}$ to grow nanocrystals (NCs) in which surface etching of the NC and redeposition on existing NCs led to an increase in size and narrowing of their size distribution, although both the binding strength of the thiol and the temperature were found to play an important role in determining the final
NC size. In order to probe the thermal stability of AuNPs₁ and AuNPs₂ variable temperature UV/vis studies (295 – 380 K) were undertaken. These resulted in a decrease in the intensity of the plasmon band on warming but without significant broadening of the plasmon band and a slight increase in the absorption maximum to longer wavelength for AuNPs₁ and decrease in the absorption maximum to shorter wavelength for AuNPs₂ (Figure 3.12). The plasmon band intensity or position is very sensitive to the size and particle shapes as well as the optical and electronic properties of the medium and are affected by four factors: nanoparticle aggregation, change in solvent refractive index, solvent volume and metal resistance.⁴⁴,⁴⁵,⁴⁶,⁴⁷ While it is clear that these NPs appear stable up to 360 K, the small changes in the UV/vis data pointed towards subtle changes in the AuNPs at temperatures above 360 K. In order to probe these spectroscopic changes we undertook TEM images before and after heat treatment for both AuNPs₁ and AuNPs₂ (Figure 3.13). For AuNPs₁ the nanoparticles clearly grow from 3 nm to 9 nm in size (Figure 3.14). Conversely heat treatment of AuNPs₂ reveals a smaller size and narrower size distribution after heat treatment when compared to the pristine sample.
Figure 3.12 Temperature dependence of the UV/vis spectra of AuNPs1 (top) and AuNPs2 (bottom) in the range 295 – 380 K.
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Figure 3.13 TEM images before and after heating of AuNP1 (top) and AuNPs2 (bottom).

Figure 3.14 Size distributions for (left) AuNP1 before and after heating and (right) AuNPs2 before and after heating. The average particle diameter for AuNP1 post heat treatment was 9(1) nm whereas it was 2.2(4) nm for AuNPs2. The dashed lines reflect fitted normal distribution functions.
Variable temperature EPR studies on AuNPs\textsubscript{1} and AuNPs\textsubscript{2} samples were undertaken in DMF from 295 to 420 K (Figures 3.15) and their simulated spectra are shown in Figure 3.16 and 3.17. These spectra clearly reveal a small relative increase in the broad singlet associated with high concentrations of radicals on the AuNP surface and an overall reduction in isolated TEMPO radicals. Simulation of each spectrum shows that the relative increase in the broad singlet increases from 97.8\% at 295 K to 98.0 \% at 350 K for AuNPs\textsubscript{1} and from 99.0 \% at 295 K to 99.6\% at 350 K for AuNPs\textsubscript{2}. However, these percentage drop to 93.6 \% and 92.0 \% at 410 K for AuNPs\textsubscript{1} and AuNPs\textsubscript{2} respectively. (Figure 3.18) This could be due to migration of the isolated radicals on the surface to a preferred site and/or some redistribution of particle shape/size.

Figure 3.15 X-band VT-EPR studies of AuNPs\textsubscript{1} (right) and AuNPs\textsubscript{2} (left).
Figure 3.16 Experimental and simulated VT-EPR spectra of AuNPs$_1$
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Figure 3.17 Experimental and simulated VT-EPR spectra of AuNPs$_2$. 
In order to probe the abrupt change in the EPR spectrum on heating, a series of heat/cool cycles were undertaken. For both AuNP$_1$ and AuNP$_2$ samples were heated in THF to dryness (bp of THF = 339 K) and the nanoparticle residue washed with toluene to remove any free TEMPO ligand. The sample was then redissolved in THF and the EPR spectra recollected at ambient temperature. The EPR spectra of the toluene washings revealed three equidistant narrow lines, typical for free ligand, whereas the redissolved nanoparticles still revealed a combination of broad
singlet and narrow 1:1:1 triplet. Simulation of each spectrum after 1, 2 and 3 heating cycles revealed that the relative broad singlet was reasonably constant, around 98% for AuNPs₁ and AuNPs₂ (Figure 3.19). These data are consistent with degradation of the surface and a change in nanoparticle size upon heating, in agreement with the UV/vis and TEM data described previously.

![Experimental and simulated EPR spectra of heating cycle of AuNPs₁ (top); and AuNPs₂ (bottom).](image)

**Figure 3.19** Experimental and simulated EPR spectra of heating cycle of AuNPs₁ (top); and AuNPs₂ (bottom).

**Table 3.1 Broad singlet area percentages.**

<table>
<thead>
<tr>
<th>Heating cycle</th>
<th>1ˢᵗ heating</th>
<th>2ⁿᵈ heating</th>
<th>3ʳᵈ heating</th>
</tr>
</thead>
<tbody>
<tr>
<td>AuNPs₁</td>
<td>98.6 %</td>
<td>98.5 %</td>
<td>98.2 %</td>
</tr>
<tr>
<td>AuNPs₂</td>
<td>98.7 %</td>
<td>98.6 %</td>
<td>98.0 %</td>
</tr>
</tbody>
</table>
3.3.4 Effect of different sulfur containing functional group

Previous approaches to synthesis gold nanoparticles (AuNPs) with high coverage of TEMPO radicals in a one-pot reaction using disulfide diradical (DISS) (Figure 3.1) proved unsuccessful due to breakdown of the TEMPO under the reducing conditions employed.\textsuperscript{31} Nevertheless their studies indicated that DISS could successfully be employed in a post-synthetic modification to generate high coverage TEMPO-coated AuNPs via ligand exchange of phosphine or thiolate stabilized AuNPs with DISS.\textsuperscript{31} However, the latter required a 1:100 ratio of Au:disulfide making nanoparticle preparation chemically inefficient in terms of TEMPO.

Here, we followed our experimental protocol adapting to a modified Brust-Schiffrin procedure\textsuperscript{29} to coat AuNPs with DISS. This method affords high coverage of TEMPO radical on gold surface using simple steps and fewer product and solvents and most importantly we do not observe hydrolysis of the ester linker. TEMPO-labeled AuNPs were synthesized by reduction of HAuCl\textsubscript{4} in the presence of DISS using an Au:S ratio (1:2) (w/w %). The TEMPO-coated AuNPs prepared by this route are hereafter labelled AuNPs\textsubscript{3} when prepared from DISS and directly compared to AuNPs\textsubscript{1} with short-chain TEMPO derivative 1 which should exhibit the same structure (Scheme 3.2).
Scheme 3.2 Preparation of AuNPs\textsubscript{3} from DISS (AuNPs\textsubscript{3}).

The labelling of the AuNP surface with thiol was readily monitored using IR spectroscopy. Thioacetate 1 revealed two distinct $\nu_{C=O}$ stretches in the IR spectrum around 1691 and 1732 cm\textsuperscript{-1} (as described previously, Figure 3.4) whereas DISS exhibited a single peak around 1732 cm\textsuperscript{-1} associated with $\nu_{C=O}$ stretch of the carboxylate group (Figure 3.20). The IR spectra of both AuNPs\textsubscript{1} and AuNPs\textsubscript{3} appeared almost identical consistent with formation of similar structures.

![Figure 3.20 IR spectra of AuNPs\textsubscript{1} (top) and AuNPs\textsubscript{3} (bottom).](image)

Simple TEMPO derivatives typically display a 1:1:1 triplet but for diradicals more complex spectra are observed due to exchange coupling and manifested in the...
observation of additional features between the three features of the classical 1:1:1 triplet. The exact position and intensity of these features depends on the strength of the exchange coupling (J) in relation to the magnitude of the hyperfine coupling (aN) (Figure 3.20 (left)).

When DISS is attached to the AuNP, cleavage of the S-S bond breaks the diradical down and a simpler triplet hyperfine coupling is observed, along with a broader singlet arising from dipolar interactions, analogous to AuNPs1. Thus the EPR spectrum of AuNPs3 reveals a composite spectrum, comprising a well-resolved 1:1:1 triplet superimposed on a broader singlet (ΔHpp = 15.4 G) (Figure 3.21 (centre)). The broad singlet is diagnostic of high coverage of radicals on the AuNP surface.

Figure 3.21 (left) X-band EPR spectrum of DISS (g = 2.0060, aN = 9.0 G, J = 20.0 G); (centre) X-band EPR spectrum of AuNPs3 (in DMF) generated using a 4:1 S:Au ratio (1.2% 1:1:1 triplet, g = 2.0064, aN = 15.4 G; 98.8% broad singlet g = 2.0064, LW = 11.6 G); (right) X-band EPR spectrum of AuNPs1 (in DMF) generated using a 4:1 S:Au ratio (1.3% 1:1:1 triplet, g = 2.0064, aN = 15.6 G; 98.7% broad singlet g = 2.0064, LW = 11.2 G).
UV-visible spectroscopy measurements on AuNPs$_3$ were performed at room temperature in DMF (Figure 3.22). The bandwidth of the plasmon peak was broad indicating smaller particles.$^{38}$ The shape and particle size distribution of the nanoparticles were determined by TEM (Figure 3.23 and 3.24) and revealed spherical AuNP core sizes of $1.55 \pm 0.22$ nm for AuNPs$_3$ consistent with the UV/vis data (Figure 3.22). The TEMPO-thioacetate 1 affords significantly larger particles (3.0(9) nm diameter) than DISS. Previous work has shown that the efficiency of monolayer formation on gold surfaces is sensitive to the thiolate source (thiol, thioacetate vs disulfide).$^{39}$

*Figure 3.22 UV-Vis spectra of AuNP$_1$ and AuNPs$_3$.***
3.4 Conclusions

We have described a convenient one-pot synthesis for the self-assembly of thermally robust TEMPO-coated AuNPs with high surface coating of radicals of ca. 3 nm core diameter. The grafting density increases with increase S/Au ratio.
Examining the temperature dependence of the EPR spectra give further confirmation of the thermodynamic behavior the plasmon absorption in which heating the sample will cause drastic changes to the nanoparticle size, resulting in either smaller nanoparticle (AuNPs₂) or larger nanoparticles (AuNPs₁). Use of TEMPO-thioacetate led to nanoparticles with larger sizes (3 nm) compared to nanoparticles produced using DISS.
3.5 References


Chapter 3: An efficient one-pot synthesis of high coverage TEMPO-coated gold nanoparticles


Chapter 4: TEMPO coated AuNPs supported through non-covalent hydrophobic interactions
4.1 Introduction

The preparation and properties of gold nanoparticles have been the subject of intense research over the past two decades due to their unique size and shape dependent physical properties arising from quantum confinement effects. This has led to a wide range of applications in the fields of optics, data storage, electronics and sensors. For many applications surface functionalization of the nanoparticles is desirable to develop flexible nanoparticles with controlled surface chemistry. In fact, the surface chemistry of nanoparticles plays an important role to control the structure of nanoparticle arrays through charge interactions, van der Waals forces, hydrogen bonding, etc. For example, a quasi-honeycomb hexagonal close packing was formed through two adjacent nanoparticles functionalized with carboxylic acid groups to induce hydrogen bonding. Recently, many studies have focused on fabricating gold nanoparticles surface-stabilized by alkyl chains due to their thermal stability. The alkyl chain surface of these nanoparticles are hydrophobic and chemically inert, preventing further chemical functionalization. The interdigitation of alkyl chains through weak van der Waals forces affords weak mechanical and thermal stability, reducing their ability to partake in many applications. Many efforts have focused on enhancing the chemical, thermal and mechanical stability by incorporating these nanocrystals within inorganic thin film matrices such as silica or titania, encapsulating them inside sol-gel matrices or using mesoporous materials as templates. However, the host materials typically generate less ordered structures, less control over particle size and loading or/and less control of interparticle spacing. This is...
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particularly problematic when searching for reproducible data or collective physical properties and limits their use especially in solid state devices and bio-applications.\textsuperscript{4,8,9,24} Recent advances in the formation of nanocrystal arrays have been made using nanocrystal-based micelles as building blocks.\textsuperscript{5,25,26} These demonstrated the formation of highly ordered nanoparticles arrays in both inorganic or organic frameworks. The flexible surface chemistry of these micelles causes them to be engaged in many applications such as phase transfer of hydrophilic nanoparticles from the aqueous phase into organic solvents or, conversely, passage of hydrophobic nanoparticles into the aqueous phase.\textsuperscript{27} In addition to phase transfer, these micelles can be applied to lipids in which the NP coating protects the native inorganic environment of the nanoparticle core when attached to the lipid, suppressing nanoparticle oxidation. Another approach utilizes a secondary layer on top of the initial NP surface coating through use of an amphiphilic ligand or polymer. In the former case additional layers are chemically adsorbed to the hydrophobic ligand surface of alkyl-coated NPs and stabilized through hydrophobic, dispersion-driven van der Waals forces.\textsuperscript{27} In the latter case surface polymer grafting onto the nanoparticles can be achieved via non-covalent interactions in which the nanoparticles are wrapped in polymer, maintaining the electronic properties of these nanoparticles.\textsuperscript{28,29,30,31} However, this can limit the variety of polymers available in relation to covalent attachment which has been achieved with a variety of polymers such as poly(ethylene glycol) (PEG),\textsuperscript{32} polyetherimides,\textsuperscript{33} dendritic polymers\textsuperscript{34,35} and more.\textsuperscript{36,37,38} Many approaches have been made to control polymerisation on nanoparticle surfaces through modulation
of the molecular weight, polymer architecture, chain structure and length and end group functionality by using nitroxide mediated radical polymerisation (NMRP), atom transfer radical polymerization (ATRP) and reversible addition–fragmentation chain transfer (RAFT). Several studies have focused on the synthesis of AuNPs grafted with polystyrene using NMRP technique by covalent attachment of radicals to the AuNP surface using a thiol group (RSH). However, many physicochemical interactions determine the ultimate fate of nanoparticles and we are still far from having a detailed knowledge of these interactions and the relationships between nanoparticles’ structure and activity. The investigation presented here focuses on understanding the nature of capping ligands in the collective mechanical response of nanoparticles by obtaining gold nanoparticles stabilized by bilayer non-covalent coating of octanothiol and TEMP-O-C₈ (Figure 4.1) as primary and secondary layers respectively. In particular we aim to understand the extent of surface coating of the TEMPO radical and whether the TEMPO radicals are clustered (forming regions of high density of radicals) or more monodisperse across the NP surface. The advantage of the surfactant encapsulation technique is that the interdigitated bilayer involves no chemical reactions and, therefore, would not change the physical properties (optical, aggregation, electronic, etc.) of the original NCs. Critical aspects such as TEMPO concentration, thermal stability and polymerisation were optimized to ensure the orientation and the stability.
4.2 Experimental Section

All chemicals and solvents were purchased from Sigma-Aldrich or Oakwood Chemical and used as received. Water was Milli-Q ultrapure grade (resistivity 18.2 MΩ cm\(^{-1}\)). IR spectra were recorded on a Bruker alpha FTIR spectrometer. UV–Vis spectra were recorded on an Agilent 1103A. TEM images were obtained using a Philips CM10 with a formvar/carbon film grid on which a drop of the diluted nanoparticle solution was deposited and evaporated at room temperature. EPR spectra were recorded on a Bruker EMXplus EPR spectrometer. Samples were sealed in quartz capillaries. EPR simulations were undertaken using Winsim\(^{47}\) to extract the relative intensities, line shape and line width.

4.2.1 Synthesis of gold nanoparticles capped with alkanethiol ligand (AuNPs)

AuNPs were prepared according to a Brust-Schiffrin procedure.\(^{48}\) In a typical procedure, a freshly prepared solution of \(\left[\left(\text{n}C_8\text{H}_{17}\right)_4\text{N}\right]\text{Br}\) (TOAB, 80.0 mL, 0.05 M) in toluene was added to an aqueous HAuCl\(_4\) solution (30 mL, 0.03 M, 0.9 mmol) with vigorous stirring until the aqueous phase appeared clear and the organic phase was deep red. Octanothiol (0.17 g, 1.16 mmol) was added to the organic
phase and stirred for 20 min. After 20 min of stirring, a freshly prepared aqueous solution of NaBH$_4$(aq) (0.37 g in 25 mL, 10 mmol) was added slowly with vigorous stirring and stirring maintained for 3 h. The organic layer was separated and evaporated to 10 mL on a rotary evaporator and then mixed with 400 mL of EtOH to remove any excess unreacted thiol. The black precipitate was dried in vacuo and characterized by IR, UV/vis, EPR and TEM.

### 4.2.2 Synthesis of TEMPO-encapsulated AuNPs (AuNPs$^4$)

AuNPs$^4$ were prepared by the addition of TEMPO-O-C$_8$ (0.17 g, 0.59 mmol) to a toluene solution of AuNPs (prepared as above; 2 mL of a 1:1 w/w % solution). The mixture was stirred for 24 h, 48 h, 72 h and 96 h. The same procedure was repeated for various TEMPO-O-C$_8$ concentrations (10$^{-1}$ M, 10$^{-2}$ M, 10$^{-3}$ M and 10$^{-4}$ M). EtOH (20 mL) was added to the final product to remove ‘free’ TEMPO. The upper phase was removed using a pipet and the black precipitated was collected and dried under vacuum.

### 4.2.3 Synthesis of polystyrene grafted to AuNPs$^4$

AuNPs$^4$ (37.5 mg) was mixed with styrene (3.36 g, 32 mmol) and then degassed using three freeze-pump-thaw cycles. The mixture was then stirred at 120 ℉ under argon for 24 h. The product was purified by three cycles of dissolving in THF and precipitating from methanol.
4.3 Results and Discussion

4.3.1 Synthesis

Octanethiol-coated AuNPs were synthesized by reduction of HAuCl₄ in the presence of alkanethiol using the literature method (Chapter 1, Scheme 1.2). Subsequent surface modification of AuNPs with TEMPO was undertaken in one step by mixing AuNPs with TEMPO-O-C₈ in toluene with vigorous stirring. This allowed the hydrophobic van der Waals interactions between the primary octanethiol coating of the stabilizing ligand AuNP surface and the secondary alkane from the secondary alkane from TEMPO. This was anticipated to afford a thermodynamically driven interdigitated bilayer structure (Scheme 4.1)

![Scheme 4.1 Schematic representing the hydrophobic dispersion-driven interaction between TEMPO-O-C₈ and AuNPs₄.](image)
4.3.2 Nanoparticle Characterization

The initial core size of the AuNPs formed was determined through examination of the plasmon band in the UV/vis spectra coupled with TEM. UV-visible spectroscopy measurements were performed at room temperature in toluene (Figure 4.2). These revealed a well-resolved plasmon absorption band with $\lambda_{\text{max}} \sim 515$ nm. The shape and particle size distribution of the initially prepared octanothiol-coated (AuNPs) nanoparticles were determined by TEM and revealed spherical AuNP core sizes of 2.8(8) nm. The surface plasmon peak is in perfect agreement with previous studies.\(^49,50,51\) After adding a TEMPO coating (AuNPs\(_4\)), TEM measurements showed no change in core size indicating the blue-shift in the plasmon band by 2.7(4) nm is likely a result of increasing the refractive index of the surrounding medium (Figure 4.3 and 4.3).\(^52\) Alternatively Su et al.\(^53\) found an exponential decay of the particle resonance red shift with increasing particle distance for gold nanoparticles. Similar results were observed by Rooney et al.\(^54\) who added dielectric organic coatings on hemispherical particles with specific surface-to-surface separations (metal-to-metal for uncoated particles or dielectric-to dielectric for coated particles). They described experimental and theoretical studies of the dependence of the optical plasmon resonance spectrum on optical cluster formation due to the coating of a dimer of nanoparticles by an organic layer.
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Figure 4.2 Surface plasmon resonance of AuNPs and AuNPs₄.

Figure 4.3 TEM image of AuNPs (left) and AuNPs₄ (right).
In order to probe the AuNP surface coating we employed a combination of IR and EPR spectroscopy. The labelling of the AuNPs surface with octanothiol was readily monitored using IR spectroscopy where the CH$_2$ vibrations are observed at 2920 cm$^{-1}$ (asymmetric stretch) and 2851 cm$^{-1}$ (symmetric stretch). The CH$_3$ stretching
mode associated with the terminal methyl group is also observed near 2959 cm\(^{-1}\). The band around 1067 cm\(^{-1}\) was identified as a C-H out-of-plane bending \(^{55}\) whereas the bands at 1256 cm\(^{-1}\) and 1234 cm\(^{-1}\) represent C-H in-plane bending. For AuNPs\(_4\), additional surface coating with TEMPO is reflected in a band at 1356 cm\(^{-1}\) (N-O stretching vibration) \(^{56}\) and bands at 1101 cm\(^{-1}\) and 1018 cm\(^{-1}\) attributed to C-O. A band at 1361 cm\(^{-1}\) is assigned to the C-H methyl rock of the piperidine ring. (Figure 4.4)

![IR spectra](image)

*Figure 4.5 IR spectra of TEMPO-O-C\(_8\) (top) AuNPs\(_4\) (centre) and AuNPs (bottom).*

In order to probe the loading of the radical on the AuNP surface we undertook a series of EPR studies. (Figure 4.6) Simple TEMPO derivatives typically display a
1:1:1 triplet due to coupling of the unpaired electron to the unique $^{14}$N nucleus ($I = 1$) under dilute conditions but broad singlets in high concentration due to dipolar broadening (see Chapter 3). Dilute solutions of the AuNPs$_4$ reveal well-resolved 1:1:1 triplet ($a_N = 15.35$ G) comparable to the parent TEMPO-O-C$_8$ ($a_N = 15.20$ G, Fig. 4.3). However, the linewidths are somewhat broader in AuNPs$_4$ (2.33 G) when compared to TEMPO-O-C$_8$ (0.92 G). This suggests the presence of slightly higher local concentrations of radicals on the AuNPs$_4$ surface where broadening of the spectra through dipolar interactions between radicals depends on $1/d^3$.

Figure 4.6 EPR spectra of TEMPO-O-C$_8$ ($g = 2.0055$, $a_N = 15.20$ G, $\Delta H_{pp} = 0.92$ G) and AuNPs$_4$ ($g = 2.0064$, $a_N = 15.35$ G, $\Delta H_{pp} = 2.33$ G).

### 4.3.3 Influence of TEMPO on AuNPs$_4$ spectral properties

In solution, radical motion (translation and rotation) of radicals modulates both the Heisenberg spin exchange (HSE) and dipole-dipole interactions between them.
and this is manifested in changes to the EPR line shape. The line shape of AuNPs was studied in detail as a function of concentration and reveal subtle changes in linewidth. During the experiments different concentrations of TEMPO-O-C₈ (10⁻¹ M, 10⁻², 10⁻³ M and 10⁻⁴ M) were added to AuNPs, the mixtures were then purified with EtOH to remove any excess TEMPO-O-C₈.

As a benchmark for these studies it should be noted that dilute solutions of pure TEMPO-O-C₈ exhibited linewidths less than 1.0 Gₚₚ (Fig. 4.6). In addition, well-resolved EPR spectra tend to generate a Lorentzian lineshape whereas the presence of unresolved coupling or dipolar broadening generates a more Gaussian lineshape. Both the linewidth and the percentage Lorentzian vs Gaussian line shape can be extracted from spectral simulation. (Figure 4.7) Even at very low concentration (less than ~ 10⁻⁴ M) the EPR spectra of AuNPs reveal linewidths greater than 3.0 G, substantially greater than those observed for free TEMPO-O-C₈ indicating that (i) the TEMPO-O-C₈ is bound on the AuNPs surface rather than being free in solution and (ii) the relative concentration of TEMPO-O-C₈ on the surface is higher than free TEMPO-O-C₈ in solution. This linewidth continues to increase up to 5.0 G at 10⁻¹ M, consistent with dipolar broadening.
Figure 4.7 (left) X-band EPR concentration dependence studies of AuNPs in toluene; (right) relative line shape and line width of the EPR spectrum as a function of TEMPO concentration.

The effects of TEMPO concentration on the EPR spectra agree well with the corresponding UV/vis spectra (Figure 4.8). The peak wavelength $\lambda_{\text{max}}$ changed from 513 to 507 nm as a function of concentration (Figure 4.8).

Figure 4.8 (left) Concentration dependence of the UV/vis spectra of AuNPs; (right) Concentration dependence of the peak wavelength $\lambda_{\text{max}}$. 

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The concentration dependence of both the UV/vis and EPR reflect the same behaviour; increasing the concentration of TEMPO added to solution of AuNPs resulted in an increase in EPR bandwidth and a decrease in the $\lambda_{\text{max}}$ of absorption peak. These variations indicate that TEMPO radicals bind to AuNPs surface. Since there is no chemical reaction, the size of the nanoparticles core will not change. Therefore, the decrease in wavelength will be as result of increasing in TEMPO loaded on gold surface which will increase the particle - particles distance.\textsuperscript{54,55}

4.3.4 Influence of temperature on AuNPs\textsubscript{4}

The mobility of the TEMPO chain in AuNPs\textsubscript{4} is directly reflected in the line-shape of the EPR spectrum.\textsuperscript{57} In a highly mobile region, TEMPO radicals afford sharp EPR transitions, whereas a site with low mobility gives broad peaks. Therefore, any changes in the line width can be used to differentiate between surface bound TEMPO (broad) and free TEMPO (sharp) in solution. Variable temperature EPR studies on AuNPs\textsubscript{4} (295 – 410 K) reveal that as the temperature increases, a small increase in linewidth occurs up to 350 K, whereupon a sudden decrease in linewidth is observed (Figure 4.9). The initial increase in linewidth is unexpected as increased rotational motion of the nanoparticles on warming should lead to narrowing of the lines and it is possible that the increased linewidth can be attributed to migration of the radicals on the AuNP surface potentially giving rise to increased dipolar interactions. Conversely above 350 K the decrease in the linewidth to less than 1.0 G_{pp} is consistent with diffusion of the radicals from the AuNP surface affording free TEMPO-O-C\textsubscript{8} in solution.
Variable temperature UV/vis studies revealed that the AuNPs obtained in this fashion were stable up to 350 K with no sign of decomposition or aggregation (Figure 4.10).

Figure 4.9 (left) X-band VT-EPR studies of AuNPs$_4$ in toluene; (right) linewidth of the EPR spectrum in the range 295 – 410 K.

Figure 4.10 Temperature dependence of the UV/vis spectra of AuNPs$_4$ in the range 298 – 340 K.
4.3.5 Polymerization of styrene using AuNPs as nitroxide mediator

The TEMPO radical is considered as a stable π radical so will not act as a free radical initiator but will act as a moderator. In the absence of a radical initiator styrene will undergo a thermal self-initiation at elevated temperatures through radical generation (Scheme 4.2). The thermal self-initiation of styrene has been studied by Mayo. During the thermal polymerisation of styrene, two radicals are formed; \( R_1 \) and \( R_2 \) (Scheme 4.2). Of these the less hindered derivative \( R_2 \) is believed to be the active agent in the polymerization process. The role of the TEMPO radical is to moderate the amount of living styrene radicals through a reversible bond forming reaction at the end of the growing polymer.

We hypothesized that the introduction of AuNPs into the polymerisation system should moderate the polymerization process as the growing polymer may combine with TEMPO radicals attached to the nanoparticle surface. In addition, it should permit some confirmation of the binding orientation of the TEMPO radical on the AuNP surface. Specifically, if the TEMPO is bound with the TEMPO radical oriented \( \text{exo} \) to the AuNP then catalytic activity is to be expected whereas if the TEMPO radical is embedded within the nanoparticle interior then AuNPs is likely to be unreactive in binding the growing polymer. To probe this, a sample of styrene was heated in the presence of AuNPs at 120 °C to initiate polymerization. It is recognised that thermal studies on AuNPs at this temperature indicate the commencement of some degree of diffusion of TEMPO radicals from the AuNP surface (Figure 4.9). After polymerization the AuNPs were separated by
dissolution in THF, followed by precipitation in MeOH. EPR signal was not observed after polymerizing with styrene as result of NO-C bond formation.

Scheme 4.2 Thermally initiated polymerization following Mayo mechanism. (Adapted from references. 60 and 61)
The SEM and TEM images of PS-AuNPs reveal a clear contrast between the interior (TEM) and the shell (SEM) (Figure 4.11). The polystyrene grafted to AuNPs cannot be observed under TEM due to the low contrast between the carbon-coated grid used during the measurements and the polymer chains, as well as the large contrast compared to the AuNPs (Figure 4.11 (top)). The TEM image provides similar particle sizes (Figure 4.12) for the AuNP core before and after treatment with styrene (2.7(4) nm and 3.6(3) nm respectively).

SEM studies on pure PS reveals it often exhibits a spheroidal nanoparticle geometry. In the current system, the SEM images reveal a globular texture to the polymer but reflects some aggregation rather than formation of discrete microspheres. In the interactive 3D surface plot used to visualize the TEM image (Figure 4.11(bottom)), the image luminance reflects the height of the plot. While the bright core is easily distinguishable, the depth of the image is consistent with a polymer coating of comparable magnitude to the features observed by SEM.
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Figure 4.11 (top left) SEM image of PS-AuNPs₄, (top right) TEM image of PS-AuNPs₄ and (bottom) the interactive 3D surface plot.

Figure 4.12 Size distribution of PS-AuNPs₄ core based on TEM image (mean particle size = 3.6(3) nm).
An EDS study was carried out to map the sample composition in different locations. Figure 4.13 illustrates the EDS for AuNPs prior to treatment with styrene and highlights the presence of Au and S above 2 keV consistent with the thiolate-coated AuNP with N and O evident at lower energy consistent with the TEMPO functional group.

EDS studies on a sample after reaction with styrene are presented in Figure 4.14. The top spectrum reflects a background EDS spectrum taken in a region away from material. This reveals predominantly features associated with the substrate (Al/Si) and just trace C content (ca. 0.27 keV). Conversely the lower image taken within the particles clearly reveal high concentrations of C (peaks at 0.27 keV), Au (peaks at 2.13 and 9.7 keV) as well as characteristic peaks of S (peaks at 0.11, 2.2 and 2.4 keV), N (peaks at 0.4 keV) and O (peaks at 0.53 keV).

Figure 4.13 Energy dispersive x ray (EDX) elemental analysis of AuNPs.
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Figure 4.14 Energy dispersive x ray (EDX) elemental analysis of PS-AuNPs4 (bottom) for EDS spot 1 (top) for EDS spot 3.

The solution UV-Vis spectrum of PS-AuNPs4 in toluene shows no signs of aggregation (Figure 4.15) but the spectrum is shifted from 518 nm to 530 nm with broadening of the plasmon band. During the self-assembly of PS-AuNPs4, collapsed PS chains on the surface of AuNPs domains and pull AuNPs together and encapsulate of AuNPs4 within the polymer, resulting in a distance reduction between nanoparticles with a red-shift of the plasmon band while simultaneously preventing aggregation.53,54,62
Figure 4.15 Comparison of the UV/vis spectra of AuNPs4 and PS-AuNPs4.

The IR spectrum of PS-AuNPs4 is shown in Figure 4.16 and is dominated by features associated with polystyrene, viz. a methylene bending absorption at 1467 cm⁻¹, benzylic C-H stretching frequency at 3024 cm⁻¹ and C-C bond of the aromatic ring at 1740 cm⁻¹. Furthermore, the band around 1365 cm⁻¹ attributed to nitroxide radical disappear which give us further conformation of successful polymerization. We have not observed any EPR signal due to formation of the covalent C-ON bond between nanoparticles and polymer chain.
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4.4 Conclusion

These studies provide a non-covalent dispersion-driven approach to grafting of radicals onto AuNP surfaces. The resultant AuNPs₄ nanoparticles of ca 2.7(4) nm diameter with low radical surface coating appear thermally stable up to 350 K and have been characterized by EPR, IR, UV/vis, SEM and TEM. Initial studies of their function in the polymerisation of styrene reveals a quenching of the TEMPO EPR spectrum and formation of a surface coating of PS on AuNPs₄ indicative of binding of the growing styrene polymer to surface TEMPO. Further studies are required to determine the molecular weight and poly-dispersity in order to compare the results of these studies with previous work.
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4.5 References

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Chapter 5: Synthesis and characterization of TEMPO radical-coated iron oxide core/gold shell nanoparticles
5.1 Introduction

Magnetism is the physical study of the effect of an applied magnetic field (H) on the magnetization (M) of the sample. For chemists we are familiar with diamagnetism and paramagnetism.\(^1\) A diamagnetic material with no unpaired electrons has \(\frac{dM}{dH} < 0\) and the gradient \(\frac{dM}{dH}\) per mole of materials is given by the diamagnetic susceptibility, \(\chi_d\). For materials with unpaired electrons then \(\frac{dM}{dH} > 0\) and the gradient \(\frac{dM}{dH}\) in a small to medium sized applied fields is constant and given by the paramagnetic susceptibility, \(\chi_p\). Eventually in large applied fields all the unpaired electrons are perfectly aligned with the applied field and the magnetization saturates \((M_{\text{sat}} = gS)\) (Figure 5.1).

![Diagram of magnetization vs field plots for paramagnetic (solid line) and diamagnetic materials (dashed line); (right) magnetization vs field plots for a ferromagnet (black line) and a superparamagnet (red line).](image)

If the unpaired electrons in a bulk solid are allowed to communicate with each other then long range magnetic order may occur.\(^2\) A variety of types of long range order can be observed including ferromagnetism (all spins align coparallel) and ferrimagnetism (some ‘spin up’ and some ‘spin down’ electrons but more ‘spin up’ moments than ‘spin down’
also leading to a net magnetic moment). Metals such as Co, Fe and Ni exhibit ferromagnetism. Many oxides such as Fe_2O_3 and Fe_3O_4 exhibit ferrimagnetism. The onset of long range magnetic order occurs below a critical temperature known as the Curie temperature, T_C. Within the magnetically ordered regime there are macroscopic regions of spin alignment known as domains (usually of micron size). These domains are typically randomly oriented, and energy is stored in the domain wall boundaries between domains of different spin orientations. An applied magnetic field known as the coercive field (H_co) is required to reorient domains to align coparallel with the applied field (H). Once aligned with the applied field a large magnetization is observed. Such magnetically ordered materials exhibit a hysteresis loop (Figure 5.1) where the area enclosed within the hysteresis loop is related to the energy stored in the domain walls. Magnetic nanoparticles are of interest because the particle size (nanometers) is smaller than the domain size (microns). Thus there is efficient alignment of the electrons within the nanoparticle but no domain wall and so no coercive field. Such magnetic nanoparticles exhibit a very rapid alignment of the magnetic moment with the applied field (Figure 5.1) which is much more rapid than a conventional paramagnet. Such behaviour is known as superparamagnetism. These magnetic nanoparticles have attracted great interest over the last few decades due to the unique properties associated with the nano-size domain which are intermediate between the molecular domain and bulk materials. Each magnetic nanoparticle can be considered as a single magnetic domain. This gives rise to many potential applications including cancer therapy, biomedicines, drug delivery, biosensors, molecule detection, immobilisation of enzymes, catalysts, adsorbents, high-density magnetic storage media and nanodielectrics. Like gold nanoparticles, uncoated magnetic nanoparticles tend to aggregate in solution. However, aggregation can be suppressed with appropriate surface chemistry and such surface-
coated ferromagnetic nanoparticles suspended in an appropriate solvent are often referred to as ferrofluids. \(^{18}\)

Alternatively, another inert layer such as \(\text{SiO}_2\) or a polymer has been used to protect magnetic nanoparticle cores such as \(\text{Fe}_2\text{O}_3\) and Co. \(^{19}\) Noble metals have also been used to fabrication magnetic nanoparticles, resulting in more complex hybrid nanostructures such as iron oxide cores with a gold metal shell. The core-shell nanostructures have increased rapidly after Halas and co-workers \(^{20}\) reported a study in the synthesize and characterization of \(\text{SiO}_2@\text{Au}\) but challenges still remain in different aspects. Gold has become a favored coating material because of its optical properties, localized surface plasmon resonance (LSPR) and its chemical functionality. \(^{21}\) Simultaneously the inert nature of the gold coating can prevent the oxidation of iron oxide and aggregation. \(^{22}\) A variety of functional groups with a high affinity for gold, such as amino (-NH\(_2\)) or thiol (-SH) groups have been used to functionalize the gold shell. \(^{20,23}\)

Nitroxide radicals became well known as spin probes for many applications to gain useful information about molecular mobility, \(^{24}\) spin-spin interactions between radicals and spin-spin interactions between radicals and other species possessing a magnetic moment. \(^{25}\) These interactions give a fundamental understanding of spin relaxation. Recently, there has been interest in TEMPO-functionalized superparamagnetic nanoparticles due to the potential catalytic use of TEMPO, coupled with the superparamagnetism properties enabling the rapid separation and quantitative recycling of the nanoparticles. \(^{26}\) To date there are few studies of TEMPO immobilized on magnetic nanoparticles. \(^{27}\)

In this paper we present a detailed study of the synthesis, characterization, and self-assembly of TEMPO modified gold-coated iron nanoparticles and study the nature of spin-spin interactions in these nanoparticles.
5.2 Experimental

Cetyltrimethylammonium bromide (CTAB), sodium borohydride (NaBH₄), ferrous sulfate heptahydrate (FeSO₄), 1-butanol, chloroform, methanol, octane, toluene and HCl were used without further purification. Distilled water was used throughout. All liquid starting materials were degassed with argon for 2h prior to the experiment. The syntheses of the thioacetate-functionalized TEMPO derivatives 1 and 2 followed established literature protocols and were undertaken by Dr. Elodie Heyer.²⁸,²⁹

5.2.1 Synthesis of gold coated iron oxide nanoparticles (Fe@Au)

Gold coated iron oxide nanoparticles were formed using an adaptation of the previously reported microemulsion method.³⁰ A solution containing FeSO₄·7H₂O (0.33 g) dissolved in water (2.4 mL), CTAB (6.0 g), 1-butanol (6.3 mL) and n-octane (21.5 mL) was mixed under argon with a solution containing NaBH₄ (0.9 g) dissolved in water (2.4 mL), CTAB (6.0 g), 1-butanol (6.25 mL) and n-octane (21.5 mL). After 1 h, the color of the mixture changed from pale green to black, consistent with formation of iron nanoparticles. A solution containing HAuCl₄ (83.25 mg) in water (1.8 mL), CTAB (3.0 g), 1-butanol (6.25 mL) and n-octane (21.45 mL) and a further solution containing NaBH₄ (0.11 g) in water (1.8 mL), CTAB (3.0 g), 1-butanol (6.25 mL) and n-octane (21.5 mL) were then added to the iron nanoparticle solution and stirred for a further 2 hours. The final solution was centrifuged to remove remaining surfactants and then washed with methanol (3 × 20 mL). The black nanoparticles were dried in vacuo.

5.2.2 Functionalization of Fe@Au NPs with TEMPO

Fe@Au NPs coated with thioacetate-functionalized TEMPO (n = 2) (T3-Fe@Au NPs) and TEMPO (n = 5) (T6-Fe@Au NPs) were prepared as follows:
Fe@AuNPs (9 mg) and thioacetate-functionalized TEMPO (40 mg) were dissolved in toluene (5 mL) with stirring and degassed by bubbling with N₂. Then an aqueous solution of NaBH₄ (9.2 mg) was added drop-wise into the mixture and stirred for 24 h. The organic layer was collected and dried under vacuum. Finally, EtOH (5 mL) was added to the powder follow by sonication and the mixture left to precipitate and the precipitate filtered and dried under vacuum. This last step was repeated 3 times.

5.3 Results and Discussion

5.3.1 Nanoparticle synthesis

The iron-core nanoparticles were synthesized using a microemulsion method and then coated with gold by reduction using NaBH₄, following the literature procedure (Scheme 5.1). These Fe@Au nanoparticles were then treated with the thioacetate-functionalized TEMPO (n= 2, n = 5) (Scheme 5.2). These TEMPO-coated nanoparticles are hereafter referred to as T3-Fe@Au and T6-Fe@Au respectively where the T refers to TEMPO and the 3 and 6 refer to the number of atoms in the link between the gold surface and the -C(=O)-O-TEMPO fragment.

Scheme 5.1 Synthese of Au coated Fe₂O₃ nanoparticles (Fe@Au NPs).
5.3.2 Nanoparticle characterization

The UV/vis spectra of Fe@Au NPs, T3-Fe@Au NPs and T6-Fe@Au NPs are presented in Figure 5.2. Fe@Au NPs shows an absorption band around 580 nm due to the surface plasmon resonance band of the gold,\textsuperscript{31} confirming the presence of the gold coating on the iron oxide particles. The long wavelength ‘tail’ associated with Fe@Au NPs is a result of an increasing thickness of the gold shell.\textsuperscript{32} However, after surface modification with TEMPO the plasmon band was much less pronounced and observed to shift to lower wavelength (ca. 550 nm) for both T3-Fe@Au and T6-Fe@Au. The shifting in the plasmon band is attributed to a reduction in the gold shell thickness during the final coating process. This was confirmed by TEM studies (\textit{vide infra}) and in agreement with previous studies.\textsuperscript{33}
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Figure 5.2 UV/vis spectra of Fe@Au NPs, T3-Fe@Au NPs and T6-Fe@Au NPs in EtOH.

The TEM images of Fe@Au, T3-Fe@Au and T6-Fe@Au NPs are presented in Figure 5.3. The shape of Fe@Au NPs was spherical, and the particles appear monodisperse which is a clear evidence that capping iron oxide with gold will reduce its tendency for aggregation.\textsuperscript{30a} The average size of the obtained Fe@Au NPs was 9.0(2.6) nm and have a narrow size distribution which is common to the microemulsion method.\textsuperscript{4} Subsequent coating with TEMPO led to a small reduction in particle size in agreement with the UV/vis data. The average size of T3-Fe@Au NPs and T6-Fe@Au NPs determined from TEM data (Figure 5.3) were found to be 7.7(1.1) and 7.0 (1.3) nm (Figure 5.4).
Figure 5.3 TEM image of Fe@Au (top); T3-Fe@Au NPs (left) and T6-Fe@Au NPs (right)
While the Fe@Au core of the NPs is well resolved, details of the core-shell structure of these nanoparticles could not be resolved due to the high electronic density of gold compared to iron oxide.\(^{34}\) Pairing TEM images with other techniques such as PXRD and EDX is a complementary approach to characterize these particles.\(^{35}\)

The PXRD spectrum of Fe@Au NPs is shown in Figure 5.5. The peaks at \(2\theta = 38.00^\circ, 44.36^\circ, 64.33^\circ, 77.54^\circ\) and \(82.00^\circ\) correspond to those expected for diffraction from Au (which adopts a cubic \textit{fcc} structure). However, the resolution failed to discriminate this from the iron pattern which is largely coincident with the gold PXRD profile. Nevertheless,
the positions and relative intensities of the diffraction peaks for Fe@Au NPs agree with those reported previously.\textsuperscript{36} Previous studies suggested that modification of the surface structure had little effect on the PXRD pattern and so PXRD measurements on T3-Fe@Au and T6-Fe@Au were not performed.\textsuperscript{37} Instead the NP surface was examined using EDX analysis.

![XRD patterns of Fe@Au NPs](image)

**Figure 5.5 XRD patterns of Fe@Au NPs**

### 5.3.3 Surface coating characterization

The EDX spectra of T3-Fe@Au NPs and T6-Fe@Au NPs are shown in Figure 5.6 with the characteristic peaks of Fe, O and Au confirming the presence of the iron oxide and gold core/shell structure. The EDX spectra also showed characteristic peaks for C, N, S and O which are diagnostic of the TEMPO radical, indicating successful surface modification with TEMPO.
Figure 5.6 EDX spectra of T3-Fe@Au NPs (top) and T6-Fe@Au NPs (bottom).

FTIR analysis were also used to confirm the surface modification of TEMPO onto Fe@Au NPs (Figure 5.7). FTIR spectra of T3-Fe@Au NPs and T6-Fe@Au NPs shows peaks at 2924 cm\(^{-1}\) attributed to the CH\(_2\) vibrations (asymmetric stretch) and 2850 cm\(^{-1}\) (symmetric stretch). The CH\(_3\) stretching mode associated with the terminal methyl groups of the tetramethyl piperidine ring is also observed near 2956 cm\(^{-1}\). The band around 1069 cm\(^{-1}\) was identified as a C-H out-of-plane bend \(^{38}\) as well as C-H in-plane bending modes (1261 and 1271 cm\(^{-1}\)). In additional surface coating with TEMPO is reflected in a band at 1375 cm\(^{-1}\) (N-O stretching vibration)\(^{39}\) and bands at 1116 cm\(^{-1}\) and 1020 cm\(^{-1}\) were attributed to C-O. While a band at 1456 cm\(^{-1}\) is assigned to the C-H methyl rock of the piperidine ring. It should be noted that the band at 1732 cm\(^{-1}\) attributed to the stretching vibration of C=O.
in the ester group of the functionalized TEMPO is retained whereas the peak at 1687 cm$^{-1}$ belonging to the C=O stretching band in thioacetate disappears confirming the successful surface coating of the Fe@Au NPs via cleavage of the thioacetate group (compare Figure 5.7 for the thioacetate-TEMPO starting materials with Figure 5.8 for Fe@Au, T3-Fe@Au and T6-Fe@Au).

Figure 5.7 Reference spectra of thioacetate-TEMPO n=2 (top) and n=5 (bottom).
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Figure 5.8 IR spectra of Fe@Au NPs (top) T3-Fe@Au NPs (centre) and T6-Fe@Au NPs (bottom)

The EPR spectrum of a solution of Fe@Au NPs (Figure 5.9) consists of two lines at $g = 4.1915$ and at $g = 2.1092$ consistent with previous reports. Surface-modification of Fe@Au generated an additional sharp 1:1:1 triplet signal ($g$-value = 2.0035) for both T3-Fe@Au NPs and T6-Fe@Au NPs, confirming that the TEMPO radical was adsorbed on the surface albeit in low concentrations (lack of line broadening). These spectra are comparable to those observed by Dobosz et al. who coated iron(II,III) oxide NPs with 3-chloropropyl trimethoxysilane and then 4-amino-TEMPO.
5.3.4 Influence of temperature

Variable temperature UV/vis studies on T3-Fe@Au NPs and T6-Fe@Au revealed that the NPs obtained were stable up to 365 K with no sign of decomposition or aggregation (Figure 5.10).
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Figure 5.10 Temperature dependence of the UV/vis spectra of T3-Fe@Au NPs (right) and T6-Fe@Au NPs (left) in the range 298 – 365 K.

We have shown before (Chapter 3 and 4), that the concentration of the TEMPO chain in AuNPs is directly reflected in the line-shape of the EPR spectrum. In a highly mobile region with low concentrations of TEMPO radicals sharp EPR transitions are observed. Conversely sites with high radical concentrations afford broad peaks. Therefore, any changes in the line width can be used to study the surface coating. Variable temperature EPR studies on T3-Fe@Au NPs (295 – 440 K) (Figure 5.11) reveal that as the temperature increases, a decrease in the signal intensity and a change in spectra shape occurs. In particular spectra at and above 350 K reveal low intensity features between the 1:1:1 triplet which can be attributed to a spin-spin interaction. After cooling the sample to room temperature, the spectrum (black) returned to the classical 1:1:1 triplet indicating that this effect is reversible. For T6-Fe@Au NPs (Figure 5.12), more complex behaviour was observed. Not only is there a marked increase in linewidth and decrease in spectral
intensity but clear additional features became evident to low field and high field of the original triplet. On cooling the sample to room temperature these new features were retained suggesting that the process is irreversible, but the origin of the additional features is currently unclear.

Figure 5.11 Variable temperature EPR of T3-Fe@AuNPs (top) full spectrum (range from 500G-5000G); (bottom) expansion of the spectrum in the range 3320G-3390G.
Figure 5.12 Variable temperature EPR of T6-Fe@Au NPs (top) full spectrum (from 500G to 5000G); (bottom) expansion of the spectrum in the range 3200G-3500G.

5.4 Conclusions

These studies provide a covalent approach to grafting of radicals onto Fe@Au NP surfaces with two different chain lengths. Both the T3-Fe@Au (7.7(1.1) nm diameter) and T6-Fe@Au (7.0(1.3) nm diameter) NPs reveal a low surface coating of radicals at room temperature. The obtained NPs appear thermally stable up to 365 K. However, TEMPO radical adsorbed onto these nanomaterials are sensitive to temperature changes and the T3-Fe@Au NPs shows thermally-driven spin-spin interactions at high temperature and a more complex irreversible response for T6-Fe@Au NPs after heating the sample up to 440 K.
5.5 References

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Chapter 6: Conclusions and Future Work
6.1 Conclusions

The overall goal of this work (Section 1.12 of Chapter 1) was to develop spin labelled-NPs via different types of intermolecular interactions; covalent, electrostatic and dispersion. With these in hand their relative thermal stabilities could be explored, and the extent of surface coating examined through EPR spectroscopy.

In Chapter 2 an electrostatic approach was employed to bind the water soluble WS-TEMPO cation to the surface of citrate-stabilized AuNPs. UV/vis studies indicated a tendency for AuNP aggregation at high concentration but well-defined 14 nm diameter spherical AuNPs were prepared working under dilute conditions (10^{-4} M). Unexpectedly the AuNPs formed also underwent bromide citrate exchange forming an Au/Br/WS-TEMPO core structure which was confirmed by IR and EDS studies. Similar behaviour has been observed just once previously in AuNP surface chemistry in which citrate was displaced by softer iodide ions.\(^1\) EPR studies revealed low concentrations of radical on the AuNP surface and were found to be stable to 345 K in solution.

Chapter 3 described a convenient one-pot synthesis for the self-assembly of thermally robust TEMPO-coated 3 nm diameter AuNPs via covalent Au-S bonds using thioacetate-based TEMPO derivatives as precursors. This improves upon previous methods\(^2\) where particle sizes were very small and solid state heat treatment was required to generate high-coverage AuNPs or via surface substitution which led to low concentrations unless a large excess of thiol (100:1) was employed. The radical grafting density was high (in excess of 95% dipolar...
broadened) at S/Au ratios in excess of 1:1. The thermal behaviour of the two derivatives unexpectedly revealed two different types of behaviour; using the short chain TEMPO derivative, TEMPO-O(C=O)CH2CH2S-, an increase in particle size was found upon heating leading to average 9 nm particle size whereas the longer chain TEMPO derivative, TEMPO-O(C=O)(CH2)5S-, led to a decrease in particle size upon heating (mean diameter 2.2 nm). Approaches using the disulfide (TEMPO-O(C=O)CH2CH2S)2 also led to high-coverage AuNPs but of a smaller size (2 nm diameter) compared to the thioacetate approach (1.5 nm diameter).

Chapter 4 investigated a non-covalent dispersion-driven approach to grafting of radicals onto AuNP surfaces using alkyl functionalized TEMPO derivatives coated onto pre-formed alkyl-thiolate-coated AuNPs. The resultant nanoparticles (2.7 nm diameter) afforded low radical surface coverage but appeared thermally stable up to 350 K. To confirm that the TEMPO ‘head group’ was on the periphery of the AuNP, initial studies examined their function in styrene polymerisation. This showed tethering of polystyrene around the AuNP which became encapsulated, indicative of its binding function during the free-radical polymerization of polystyrene.

Chapter 5 applied the robust covalent approach to grafting of TEMPO radicals onto AuNP surfaces developed in Chapter 3 to coat a dual core Fe@Au NP (9 nm diameter). This would permit a comparison of through-space electron-electron interactions between the superparamagnetic iron core and the surface TEMPO radical. Unexpectedly, coating with both shorter chain and longer chain thioacetate-functionalized TEMPO derivatives led to slightly smaller AuNPs with
low surface coating of radicals. The obtained NPs appear thermally stable up to 365 K. The short-chain TEMPO derivative shows subtle changes in its EPR spectrum suggesting some form of reversible spin-spin interaction upon heating whereas an irreversible exchange coupling was observed for the longer chain TEMPO derivative. Similar behaviour has been observed previously in which the high field peak of EPR spectra of TEMPO in an aqueous solution changes at higher temperature (above 308 K), while the low field and the centre peaks remain unaffected.3

6.2 Future Work

This thesis has explored different methods to produce gold nanoparticles in the 3 – 15 nm regime with either high or low surface coatings of TEMPO radicals. These particles appear robust at room temperature but degrade at elevated temperatures in solution.

In Chapter 2 the coating of TEMPO onto citrate-coated AuNPs was accompanied by citrate/bromide exchange. This unexpected exchange is likely driven by the strength of the soft gold-bromide interaction. There is significant scope here to pursue other coatings through similar exchange reactions using sulfide, selenide, iodide ions etc. In this context, recent work by Perera et al.4 has used SERS to show that iodide enhances thiol desorption from the Au surface. The change in the surface coating of the AuNP will likely adjust the efficiency of binding of other substrates to the surface.

Chapter 3 revealed very high coatings of TEMPO radicals on AuNPs, leading to exchange broadening of the EPR spectra in solution. To probe the nature of the
electron-electron interactions further magnetic measurements are scheduled. These, combined with the AuNP core size, will give an estimate of the average number of radicals covering the surface. In the solid state both intramolecular exchange on the surface of the AuNP is possible as well as intermolecular exchange between adjacent AuNPs. In an inert matrix e.g. dispersed in polymethylmethacrylate (PMMA) or polystyrene (PS) then intermolecular exchange can be ‘switched off’. The magnetic measurements will also provide information on the strength and nature (ferromagnetic or antiferromagnetic) of the magnetic exchange. Chapter 5 commenced an approach to develop radicals coated onto Fe/Au core NPs in which the distance between the superparamagnetic Fe core and the surface radicals can be modified through changes to the thickness of the Au coating or length of the thiolate chain. To date only low surface coverage of radicals has been achieved and further experimental work to modify the reaction conditions is required. In this context we would point to the sensitivity in using disulfide precursors as appropriate starting materials discussed in Chapter 3 where subtle changes in reaction conditions can lead to high coverage.

Radical coated gold nanoparticles have a diversity of applications. In Chapter 4 the use of radicals as mediators in the polymerization of styrene was briefly explored. This thesis has developed a range of AuNPs of different sizes with high and low radical surface coverage. A more systematic study of the size and level of radical coverage could be applied to the polymerization of styrene (or other free-radical polymerization processes). In particular a more complete analysis of the polystyrene produced should be probed through a determination of the average
molecular weight and poly-dispersity index (PDI). The difference in thermal behaviour of the TEMPO-coated AuNPs with short and long chain alkyl groups was unexpected and merits further study. A more extensive range of TEMPO-functionalized alkyl thiolates could be employed with a greater range of chain lengths to see how the behaviour changes as a function of chain length. In addition, the thiolate coating on the AuNP core could also be systematically modified to explore such variations in response.
6.3 References

APPENDICES

Order detail ID: 71504429
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VITA AUCTORIS

NAME: Aisha Abdulwahab Alsaleh

PLACE OF BIRTH: Saudi Arabia

YEAR OF BIRTH: 1987

EDUCATION: 10th high school, Dammam, Saudi Arabia, 2005

King Faisal University (KFU), B.Sc., Dammam, Saudi Arabia, 2009

University of Windsor, M.Sc., Windsor, ON, 2013