

Synthesis of Functional Nanomaterials Using Green Chemistry

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Abstract: Green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products. The 12 principles of green chemistry have now been applied to the design of a wide range of chemical products and processes with the aims of minimizing chemical hazards to health and the environment, reducing waste and preventing pollution. Application of these principles has reduced the use of hazardous reagents and solvents, improved the material and energy efficiency of chemical processes and enhanced the design of products for end of life. Employing these principle nanosciences will facilitate the production and processing of inherently safer nanomaterials and nanostructured devices

Key words: Nanomaterials • Green chemistry • Minimizing • Chemical hazards • Health and environment

INTRODUCTION

During recent years, scientists have tried to initiate and develop techniques for synthesizing and characterizing many new materials with at least one dimension on the nanoscale, including nanoparticles, nanolayers and nanotubes [1]. The method to design and synthesise (or fabrication) of nanoscale materials with controlled properties is a significant and ongoing challenge within nanoscience and nanotechnology.

Nanotechnology is progressing very first in the twenty first century. It is still largely in the "discovery phase" wherein new materials are being synthesized (using any means available) on small scales (IOOs of milligrams or less) for testing specific physical properties. Typically, during this phase of development of a new technology area, researchers have focused mainly on identifying new properties and applications. As a result, the examination of any unintended properties of the material (e.g. environmental or health hazards) or concerns about hazards or efficiencies of the production process is often deferred. Given the anticipated wide application and distribution of these materials in

commerce, consideration of the materials design, processes and applications that minimize hazard and waste will be essential as nanoscience discoveries transition to commercialized products of nanotechnology.

Green chemistry is a new concept. It is indeed a new arena of research with unlimited future prospects. The nature of engineered nanomaterials and their proposed uses provides compelling reasons for the implementation of green chemistry in the development of the new materials and applications. The technology is early in development and expected to be widely applied and distributed. These materials are expected to (i) exhibit new size based properties (both beneficial and detrimental) that are intermediate between molecular and particulate, (ii) incorporate a wide range of elemental and material compositions, including organics, inorganic and hybrid structures and (iii) possess a high degree of surface functionality. Assessment of the potential toxicological and environmental effects of nanoscale materials before they are accepted as mature technologies presents an opportunity to minimize putative negative consequences [2] from the outset and ultimately lead to the design of higher performance materials. Understanding the

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structure-function relationships that relate specifically to nanomaterials could lead to new "design rules" for producing benign, high-performance nanoscale substances.

Recently green chemistry has been employed successfully in the preparation of highly functionalized products (e.g. pharmaceuticals) that have a strong analogy to the functionalized nanomaterials proposed for a range of future applications, one would expect successful application of this approach for these nascent materials. Application of green chemistry to nanoscience should also prove beneficial in developing production level commercial scale materials. The development of high-precision, low-waste methods of nanomanufacturing will be crucial to commercialization. In addition to providing enhanced research and development strategies, green chemistry offers an opportunity to improve public perception of nanoscience, as this approach is relatively easy to explain and can be used to convey a responsible attitude toward the development of this new technology. For these reasons, green chemistry can play a prominent role in guiding the development of nanotechnology to provide the maximum benefit of these products for society and the environment.

In the present program we wish to explore the application of green chemistry principles to the field of nanoscience. We first define *green nanoscience* [3] and offer examples of the ways in which green chemistry has been, or can be, applied to the design of greener products, processes and applications. Because the vast majority of the research in this area has, thus far, involved developing greener approaches and processes, this review will focus on nanosynthesis. We further focus the review on those methods that involve wet-chemical approaches to the production, functionalization, purification and assembly of nanoparticle building blocks. The bulk of the materials covered within the review are ligand-functionalized inorganic nanoparticles, due to the fact that these have been the most prevalent in the literature to date. Throughout the review, we strive to examine how the application of green chemistry principles to nanoscience can guide technological progress within this emerging field. Because this is an emerging area of technology, we identify future research needs and directions throughout the review.

A survey of literature reveals that a number of outstanding reviews on the synthesis and assembly of functionalized nanoparticles have already been published [4-7]. This review does not intend to provide

comprehensive coverage of these topics but rather will focus instead on the aspects of these processes that are most relevant to green chemistry. However, publications in nanoscience that identify the environmentally benign aspects of the work are just starting to appear, so we have attempted to identify and highlight the examples from the literature that illustrate greener nanosynthesis concepts and techniques and that help inform the reader of research needs within this emerging field.

Green Nanoscience: *Green chemistry* may be defined as "the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products" [8]. The 12 principles of green chemistry summarized in Figure 1.1) have now been applied to the design of a wide range of chemical products and processes with the aims of minimizing chemical hazards to health and the environment, reducing waste and preventing pollution. Application of these principles has reduced the use of hazardous reagents and solvents, improved the material and energy efficiency of chemical processes and enhanced the design of products for end of life. Employing these principle nanosciences will facilitate the production and processing of inherently safer nanomaterials and nanostructured devices.

Further, *green nanoscience/nanotechnology* involves the application of green chemistry principles to the design of nanoscale products, the development of nanomaterial production methods and the application of nanomaterials [3]. The approach aims to develop an understanding of the properties of nanomaterials, including those related to toxicity and ecotoxicity and to design nanoscale materials that can be incorporated into high performance products that pose little hazard to human health or the environment. It strives to discover synthesis/production methods that eliminate the need for harmful reagents and enhance the efficiency of these methods, while providing the necessary volume of pure material in an economically viable manner. It also provides proactive design schemes to ensure that the nanomaterials produced are inherently safer by assessing the biological and ecological hazards in tandem with design. Finally, it seeks applications of nanoscience that maximize societal benefit while minimizing impact on the ecosystem. In this way, green nanoscience guides materials development, processing and application design throughout the life cycle, starting with raw material selection through end-of-life.

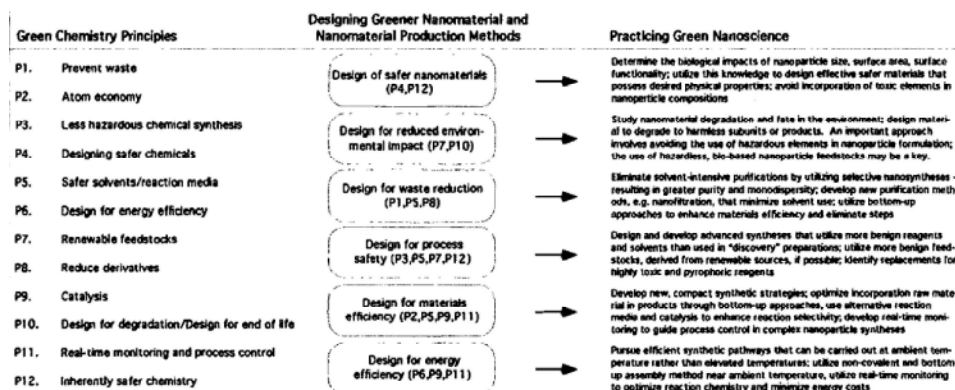


Fig. 1.1: Translating the 12 green chemistry principles for application in the practice of green nanoscience.

Application Green Chemistry Principles to Nanoscience:

Nanoparticles and other nanomaterials that exhibit size-dependent properties are already finding application in products ranging from consumer healthcare goods to highperformance composites [9]. In addition, a growing number of applications of nanoscience/nanotechnology are being developed that promise environmental benefit, including new catalysts for environmental remediation, [10] cheap and efficient photovoltaics [11] thermoelectric materials for cooling without refrigerants, [12] lightweight (and thus energy-conserving) nanocomposite materials for vehicles, [13] miniaturized devices that reduce material consumption and sensors that eliminate the need for (often) wasteful wet chemical analyses. Nanoscale sensors can [14] also offer faster response times and lower detection limits, making on-site, real-time detection possible. New manufacturing strategies that are additive, rather than subtractive, such as functional group directed processes involving self-assembly, can reduce energy requirements and waste generation. The use of self-assembly methods also enables materials disassembly, incorporating a potential design for end-of-life. To realize new nanotechnologies that pose little harm to human health or the environment and to develop technologies that can be used to improve or protect the environment, it is desirable to design and use greener nanomaterials and develop greener nanoproduction methods.

Nearly all of the principles of green chemistry can be readily applied to the design of nanoscale products, the development of nanosynthesis methods and the application of nanomaterials (Figure 1.1). In nearly every case, several of the principles can be applied simultaneously to drive the best design or solution. We will first discuss how the principles *guide* the design

and application of nanoscale materials. Next, we describe how the principles *apply* to design, application and production of nanoscale materials. *Principles of Greener Nanomaterial Design*. Three of the 12 principles (as shown in Figure 1.1) relate directly to nanomaterial design and the application of these materials as

The principles are listed, in abbreviated form, along with the general approaches to designing greener nanomaterials and nanomaterial production methods and specific examples of how these approaches are being implemented in green nanoscience. Within the figure PX, where X =1-12, indicates the applicable green chemistry principle.

Nanodevices. These are Principle 4 (Designing Safer Chemicals), Principle 10 (Design for Degradation/Design for End of Life) and Principle 12 (Inherent Safety). Application of Principle 4 to product design involves considering the structural features of the nanomaterial (i.e. the size, shape, composition and surface chemistry) that dictate its health hazards (e.g. toxicity) as well as its physical properties. In order to routinely implement this design approach, improved understanding of the structure/activity relationships for nanomaterials is needed. The rich structural diversity of nanomaterials provides significant opportunities to tune and optimize the physical and toxicological properties.

Although a significant body of research exists on environmental and health effects of ultrafine particles, there is still a lack of toxicological data regarding the effects of engineered nanomaterials both on human health and the environment. Ultrafine particle data show that materials such as silicates, asbestos fibers and to a lesser extent, carbon black and titanium dioxide, can cause oxidative stress, induce pulmonary inflammation, trigger the release of cytokines and induce signal transduction

pathways.^{15,16} "Nanoparticles" represent intentionally engineered products below 100 nm in diameter with carefully controlled sizes, shapes and surface chemistries. The unusual properties of nanoparticles (e.g. chemical, optical, or electronic) could lead to adverse biological effects that may be unique compared to larger compositions of the same material. Variations in particle size [10-19] and surface chemistry ^{15,18} can affect the degree of toxicity. For example, nanoparticles may generate free radicals that can adversely affect biological molecules. Significant differences may exist between toxicity of nanoparticles and larger particles of the same chemical composition [2], ²⁰ For instance, smaller nanoparticles are more likely to enter the circulatory system and travel throughout the body, lodging in distal organs [15-16].

Methods developed to analyze the toxicity of ultrafine particles may provide a starting point for determining toxicity of engineered nanoparticles and comparisons can be made in terms of methods of injury (e.g. oxidative stress, inflammatory responses, signal transduction pathways, etc). Traditional testing and screening strategies may be employed initially, leading to novel detection methods that account for the unique properties of nanoparticles. These include in vitro cellular assays [17-22] and biochemical analyses which probe the generation of reactive oxygen species and effects on enzymatic pathways. Using in vitro assays, route of nanoparticle entry can be determined as well as biochemical effects (such as protein interactions, DNA damage, gene expression changes, or generation of reactive oxygen species). Genomics and proteomics can track oxidative stress, induction of signal transduction pathways and apoptosis. Since susceptibility factors vary across a given population based on individual genetic makeup, risk assessment evaluation should accompany information provided by various assays and screens. In vivo studies are essential for identifying potential target organs, travel routes of nanoparticles within the body or other phenotypic changes. Such studies could lead to reliable methods for tracking and quantifying nanoparticles in cells and whole animals [23]. Additionally, dose-response relationships, calculated using a variety of metrics including mass, number of nanoparticles and surface area, provide a means of normalizing information gathered from individual toxicology studies. As an example, one study analyzed the cellular uptake of citrate stabilized gold nanoparticles and found acute effects on cell proliferation, motility and

morphology. Unfortunately, only high concentrations were examined, so no definitive conclusions could be drawn on the toxicity of these nanoparticles [21], exemplifying how dose-response studies are critical to accurate evaluation of nanoparticles.

One has to become serious in experimental design and analysis of engineered nanoparticles, since variations in structure and purity can lead to altered toxicity. Drastically different methods may be used to produce similar products, but variations in methodology and reaction route often lead to differences in yields, purity and side products. For example, carbon nanotubes are routinely mass-produced by at least four unique methods, leading to compositionally diverse products [20-24]. Thus, engineered nanoparticles should be well characterized, with known size and/or distribution, surface area, shape, solubility, purity, surface chemistry, physical (e.g. crystal structure), electronic or optical properties. Well-characterized nanomaterials are essential to accurate assessments of biological and ecological impacts.

Principle 10 focuses on design related to the environmental impacts of nanomaterials. The approach is to design materials that rapidly degrade in the environment, producing innocuous degradation products. In order to implement Principle 10, further understanding of the fate and transport of designed nanomaterials in the environment will be needed. Long-term effects of nanoparticles in the air, soil and water are also important considerations in relation to human health because persistence in the environment is directly proportional to the amount of nanoparticles in use [19, 25]. Environmental impacts of nanoparticles are usually considered in terms of toxicity or exposure⁹ but information garnered from the biological studies described above would complement our understanding of the corresponding environmental implications. For example, bioaccumulation in aquatic and terrestrial organisms will aid in developing models for environmental insult, as well as studies from whole animal analyses and in vitro experiments. Taxonomic and genetic susceptibility are also important considerations. Since chronic exposures often impact the environment in assessing ecological risk, long-term studies analyzing a range of sub-lethal doses should be included. Preliminary studies of the toxicological effects of engineered nanoparticles on *Daphnia magna* have been inconclusive [26, 27], highlighting the present need for carefully designed assessments.

As stated above principle 12 addresses the inherent safety of the material being used. For example, the high

surface area and increased reactivity of nanoparticles may lead to explosions and fires in large-scale production, yet when incorporated into macroscale structures, the same material is less likely to be released into the workplace or environment. Taken together, Principles 4, 10 and 12 provide a robust framework for designing nanomaterials with reduced health, environmental or safety concerns.

Green Nanomaterial Production Principle: It is very wellknown that green chemistry provides a number of advantages in process development and manufacturing as well as product design. Many preparations of the building blocks of nanotechnology involve hazardous chemicals, low material conversions, high energy requirements and difficult, wasteful purifications; thus, there are multiple opportunities to develop greener processes for the manufacture of these materials.

Some progress toward greener nanosynthesis has already been made. For example, a more efficient and less hazardous synthesis of metal nanoparticles has been developed, producing greater amounts of particles, in less time, under milder conditions, while using less hazardous reagents than the traditional preparation [28]. Metal nanoparticles have been synthesized using intact organisms, such as living plants and in microorganisms.²⁹ Microreactors have been used to synthesize nanoparticles in a rapid, continuous process, resulting in reduced waste, improved energy efficiency and increased control of product properties. In each of these processes, green chemistry principles have provided strategies for the development of synthetic methods that are more efficient, reduce waste and have improved health and environmental impacts.

In future, green nanosynthesis will certainly be an iterative process. As greener methods are developed to provide the nanomaterials needed for testing or applications, the demand for enhanced, or more precise, surface chemistry will often lead to new synthetic methods that require use of materials that are less green. Thus, another round of innovation will be required to meet the material needs while reducing hazards and environmental impact. Reducing the biological and ecological hazards can only be met through tandem testing during the 'discovery' synthesis phase. At each stage of iteration, compromises may arise; thus, metrics will have to be developed to assess the relative greenness of the competing alternatives. As green nanoscience becomes more developed, more benign discovery phase syntheses will be constructed in the first iteration.

One subset of these principles, *Prevent Waste* (P1), *Safer Solvents/Alternative Reaction Media* (PS) and *Reduce Derivatives* (P8), aims to reduce waste by designing methods that minimize the number of processing steps and the amount of ancillary material (solvents, processing aids) used to carry out those steps. An illustrative example involves the fabrication of nanoscale features on a substrate such as a silicon wafer. The traditional strategy for producing these structures is a top-down approach that creates features through a lithographic process involving a significant number of deposition, patterning, etching and cleaning steps that, in effect, remove material to produce nanoscale structures. This method employs many materials processing and cleaning steps that contribute to the waste stream. The vast majority of the materials used do not end up in the product, therefore resulting in low materials utilization. Alternative greener approaches include additive or bottom-up processes, employing self-assembly reactions or "direct" write deposition to generate and interconnect the structures. Such alternatives eliminate many processing steps, thus minimizing material and solvent use.

Solvent use is of particular concern in the purification and size selection of nanomaterials. Current methods for purification of nanoparticle samples involve washing or extraction to remove impurities. This process typically requires liters of solvent per gram of nanoparticles and is not usually effective in removal of all the impurities. Size selection is essentially a form of purification that consumes solvents in extraction, fractional crystallization, or chromatographic methods used to separate the different sizes. Development of methods to reduce solvent use in purification and size selection remain essential areas of research in nanoscience.

Another subset of the principles (*Atom Economy* (P2), *Catalysis* (P9) and *Realtime Monitoring* (P11)) aims to maximize materials efficiency, i.e. optimizing conversion of raw materials into desired products by enhancing reaction selectivity and yields. The concept of atom economy (P2) readily applies to wet-chemical nanomaterial preparations in the same fashion as for other synthetic transformations. However, the concept also applies to the fabrication of extended nanoscale structures that use bottom-up approaches such as self-assembly of molecules or nanoscale subunits into more complex structures. Because these approaches incorporate more of the raw materials in the product than corresponding top-down methods, they have higher atom economy.

At the molecular level, catalysis (P9) can enhance materials conversion by enhancing the selectivity of reactions, thereby preventing the channeling of raw material into by-products. The development of highly selective transformations that can be carried out in the presence of diverse, sensitive functionality is a continuing challenge in nanoscience as it is in molecular reaction chemistry. Real-time monitoring (PU) of the production and transformation of nanomaterials, though in its infancy, will be one of the keys to enhancing materials conversion in the future.

Four of the principles, *Less Hazardous Reagents* (P3), *Safer Solvents/Alternative Reaction Media* (PS), *Renewable Feedstocks* (P7) and *Inherent Safety* (P12), can be employed to enhance the process safety or reduce the hazards associated with a process. Many of the "discovery phase" preparations of nanomaterials utilize hazardous reagents (P3, P12) or solvents (PS). There are already a few examples that illustrate the application and benefits of applying these principles to enhance process safety by developing alternatives for toxic and/or inherently hazardous reagents and replacing or reducing the use of hazardous solvents. This is a rich area for investigation as the demand for larger volumes of nanomaterials increases and new methods for nanomaterial synthesis are developed. In some cases, the use of benign feedstocks derived from renewable sources (P7) may prove a successful strategy for enhancing safety in nanomaterial production.

The last subset of the principles involves enhancing energy efficiency and includes *Design for energy efficiency* (P6), *Catalysis* (P9) and *Real-time Monitoring* (PU). Assembly reactions occur under mild conditions with a wide range of suitable materials and synthetic methods to choose from. Bottom-up assembly of nanodevices greatly reduces the number of processing steps, the chances of particle contamination and reliance on cleanrooms, all contributing to energy savings. In the event that higher reaction temperatures are needed, as is currently the case for a number of nanoparticle preparations, the development of specific catalysts may be a useful strategy. Given the complexity of many nanoparticle preparation reactions (requiring simultaneous control of composition, dispersity, shape and functionality), in most cases careful in situ monitoring of reaction conditions and progress (PII) will lead to energy savings as well as improved product characteristics.

This discussion thus far provides an overview of the broad applicability of the green chemistry principles to nanoscience. Each of the 12 principles provides guidance in the design of safer nanomaterials and greener production of these materials. The bulk of this review will describe the current status and on-going challenges for greener synthesis and production of nanomaterials within the context of these defining principles.

Toward Greener Synthetic Methods for Functionalized Metal Nanoparticles:

In recent years many synthesis of nanoparticles, in an effort to produce structures that have specific form and function relevant to a given application. The preparation of functionalized nanoparticles within a green context poses interrelated challenges in terms of maintaining product integrity (such as structure, shape and size dispersity, functionality, purity and stability) while employing greener methods whenever possible. For example, control over particle size and dispersity may reduce purification requirements by eliminating the need for extensive separations, while the ability to control surface functionalization, intended to enhance particle stability, dictate surface chemistry, solubility and the degree of particle interactions (Figure 1.2) helps to better define the safety and reactivity of nanoparticles. Nanosynthesis methods are being refined such that they are convenient and scalable, whether it involves the direct synthesis of a functionalized material or the preparation of a versatile precursor particle whose surface properties can be easily modified to meet the demands of a given application.⁵ While a tremendous body of knowledge related to nanosynthesis currently exists, the need for more advanced materials and techniques may bring nanosynthesis back to the discovery phase. Thus, we are presented with a unique opportunity to utilize green chemistry principles while acknowledging existing information, rather than simply retrofitting existing methods to meet greener standards. To illustrate the status of green nanosynthesis as well as describe the challenges presented by the application of green chemistry to the field of nanoscience, we review the synthesis of noble metal nanomaterials, beginning first with citrate reductions of metal ions, followed by direct synthesis of ligand stabilized materials. Seeded growth approaches are discussed next, as they relate to both spherical and anisotropic particles. Emerging technologies in green nanosynthesis are discussed, followed by sections describing modifications to nanomaterials that

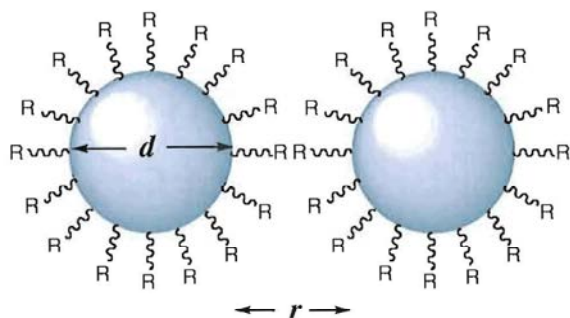


Fig. 1.2: Key properties of nanomaterials. The overall size (d) and shape of the particle dictates optical and electronic properties. A stabilizing shell composed of either covalently bound ligands (depicted above) or associated ions provides stability and solubility. Pendant functional groups define reactivity, while the length of the ligand shell determines the minimum interparticle spacing (r).

serve not only to impart new functionality, but also allow manipulation of the materials at the nanoscale. Not all of the practices and methods described would be characterized as "green." Indeed, many classic benchmark methods are described with the intent of providing a historical context for the implementation of green chemistry within nanoscience, while more recent reports offer incremental improvements to traditional practices, addressing process challenges including reducing agent selection, avoiding surfactants, solvent choice and improving yields, size distribution and purity. It is by this gradual mechanism that the development of new methods to meet greener standards will occur: without compromise to the overall quality of the nanomaterial products, through continuous effort and revision, rather than as a single revolutionary event.

Direct synthesis of nanoparticles occurs under conditions where the nanoparticles nucleate and grow, usually by the reduction of metal ions. Nanoparticles are often synthesized in the presence of a ligand or a stabilizer that can bind to the surface of the newly formed particle, offering stability and imparting well-defined surface chemistry. Excess ligands may be used to arrest further particle growth, thus offering increased control over nanoparticle size and polydispersity. It is critical that the ligand does not interfere with particle development in an undesirable manner (i.e. by preventing reduction of the metal ion precursor, or inducing the formation of

misshaped particles). Typical ligands include phosphines, thiols and amines, which may be organic or water soluble, depending on the pendant functionality.

Citrate Reductions: The reduction of gold salts by citrate anions was pioneered by Turkevich over half a century ago, yielding nearly monodisperse, water soluble gold clusters with diameters ranging from 7-100 nm^{1,32}. Although the synthesis predates green chemistry principles by several decades, it is a rather benign procedure, as the reagents pose little hazard, the preparation does not rely on organic solvents and few (if any) undesirable side products are generated in the course of the reaction. Revered for its simplicity, requiring only a gold salt (hydrogen tetrachloroaurate, HAuCl_4), trisodium citrate and water, it remains one of the most reliable methods of creating large gold nanoparticles. Upon addition to a refluxing solution of HAuCl_4 , citrate plays the dual role of reductant and stabilizer, reducing Au(III) to colloidal gold clusters, where virtually all of the gold starting material is converted to product, demonstrating excellent atom economy. Excess citrate stabilizes the particles by forming a complex multilayered assembly of anions having various oxidation states, lending an overall negative charge to the surface, imparting repulsive forces to prevent aggregation. The stability of colloidal and nanoparticle solutions is attributed to the collective effects of van der Waals interactions, electrostatics and steric forces (Figure 1.3).¹³ However, these solutions are very sensitive to changes in pH, ionic strength of the medium and the presence of other organic materials, thus complicating efforts to modify the surface chemistry by standard ligand exchange techniques.

Citrate has proven to be a useful reagent in the synthesis of silver nanomaterials, in addition to gold. Pillai and Kamat investigated the role of citrate ions in the synthesis of spherical and anisotropic silver nanoparticles. Citrate reduction of gold ions leads to the formation of spherical particles, but the analogous reaction with silver ions (Figure 1.4) can yield large silver particles 60-200 nm having a wide range of morphologies, depending upon the reaction conditions, due to citrate's additional role as a complexing agent. The formation of citrate-silver complexes influences crystal growth and even facilitates photochemical reactions that convert spherical silver nanocrystals to triangular nanoprisms. Molar ratios of reagents that produce silver crystals in the size range of 50-100 nm produce much smaller nanocrystals

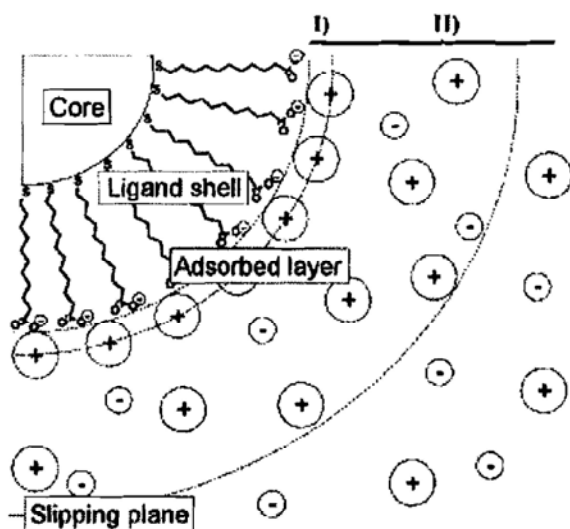


Fig. 1.3: The electric double layer of nanoparticles in solution. The tightly bound Stern layer (or adsorbed layer) prevents aggregation by maintaining interparticle repulsion, while a graduated diffuse layer of ions provides compatibility between the dissolved nanomaterials and their solvent environment. (reproduced with permission from Laaksonen, T., Ahonen, P., Johans, C. Kontturi, K. Chern. Phys. Chem. 2006, 7, 2143, Figure 1. Copyright 2006 Wiley Publishing).

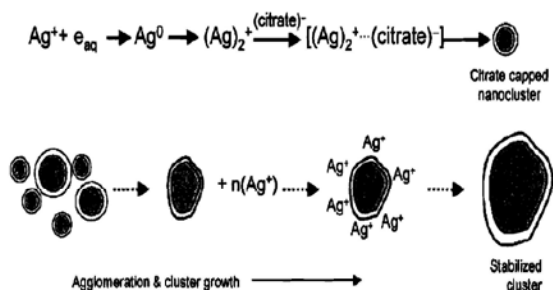


Fig. 1.4: Large silver nanoparticles prepared by the citrate reduction route. Excess silver ions permit fusion of smaller particles into a large, stable cluster. Analogous reactions with citrate stabilized gold nanoparticles have been shown to yield higher ordered structures, such as nanowires, from smaller "building block" particles. (reprinted with permission from Pillai, Z. S.; Kamat, P. V. J. Phys. Chem. B 2004, 108, 945, Scheme 1. Copyright 2004 American Chemical Society.)

(5-20 nm) if a different reducing agent is used, such as sodium borohydride, suggesting that citrate reductions have a unique reaction mechanism. Studies comparing the impact of various concentrations of citrate ions in reactions where the molar amount of silver ion is held constant demonstrate that excess citrate ions dramatically slow the growth of silver nanoparticles. A series of pulse radiolysis experiments demonstrated that citrate ions complex with Ag^2+ dimers in the early stages of the reaction, hindering seed formation while promoting slow growth of large nanocrystals. These results contrast sharply with the citrate reduction of gold ions, where increased molar ratios of citrate lead to smaller nanoparticles [29-34].

Despite the benign nature of the citrate method, the need for greater stability and precise control over surface chemistry has driven researchers to explore alternative syntheses which may better suit these goals, but cannot match the green merits of the citrate route. Later sections in the review will highlight methods which preserve or improve upon green aspects of the synthesis of more complex materials and recent efforts to control the surface chemistry of citrate stabilized gold nanoparticles will be discussed.

Direct Synthesis of Ligand Stabilized Nanoparticles:

A wide range of materials can be generated by reducing metal ions in the presence of a capping agent, providing libraries of diverse materials useful for determining structure/function relationships essential to understanding potential health and environmental impacts, aside from creating materials for targeted applications. The direct preparation of ligand-stabilized nanoparticles provides a simple route to functionalized materials, usually in a single-step, one pot procedure, imparting stability and chemical functionality to the nanoparticle products, often without the need for further modification. Current research challenges are focused on modifying solvents, reaction conditions and reagents to access a target material, but one should not overlook the opportunity to incorporate greener methods by giving equal consideration to more benign reaction conditions (i.e. choosing safer solvents, avoiding biphasic conditions and eliminating toxic surfactants), overall yield and atom economy and environmental fate of new nanoproducts. Additional attention towards controlling average size, dispersity and purity can further drive processing in a greener direction. The following sections

describe the preparation of nanomaterials capped by various classes of ligands, including thiol, amines and phosphines, highlighting green improvements that have emerged in recent years. Subsequent discussions will address the synthesis of more complex materials and emerging methods towards greener nanosynthesis.

Thiol Stabilized Nanoparticles: The number of direct syntheses of thiol-stabilized nanoparticles has expanded in recent years since Brust reported the preparation of dodecanethiol-stabilized nanoparticles in 1994. The Brust synthesis provides ready access to functionalized nanomaterials with properties analogous to those of large molecules, as they are stable under ambient conditions and can exist in solvent free forms, in contrast to the less robust citrate based materials. In this reaction a gold salt (hydrogen tetrachloroaurate) is reduced by sodium borohydride in the presence of a capping agent, yielding particles having average core diameters in the range of 2-8 nm. This reaction was first developed within a biphasic context, taking advantage of phase transfer compounds to shuttle ionic reagents to an organic phase where particle nucleation, growth and passivation occur. Subsequent variations of this procedure demonstrated the full scope of this reaction, substituting a wide range of thiols and varying the ratio of reagents in order to control the average diameter of the products. More recently, reports of water-soluble nanoparticles prepared in this manner have further extended the utility of this procedure and it remains the simplest direct synthesis of functionalized nanoparticles. The greatest limitation of the Brust prep is that the stabilizing thiolligands must be compatible with all of the reagents, including NaBH_4 and the phase transfer catalysts (if used for a biphasic preparation of organic soluble particles), thus sidestepping adverse influences on the reaction chemistry. For example, the thiols must not be subject to any unwanted reduction of other functional groups that may be present on the ligand and the thiol cannot interact with the phase transfer catalyst in such a way that leads to persistent reagent contamination, or products that are inseparable from the reaction mixture. To this end, Brust-type reactions have been performed in other solvents such as water and THF, permitting a single-phase synthesis of organic soluble gold nanoparticles while eliminating the need for phase transfer reagents.

Here, we will describe modifications to this classic method of synthesizing monolayer protected clusters,

noting refinements offered from Brust and others. Emphasis has been placed on modifications in either design or process that represent improvements within the context of green nanosynthesis, by improving size control and dispersity, utilizing safer solvents, or avoiding surfactants by adapting reactions for a single phase context. Methods that enhance monodispersity are inherently greener, since solvent consumption due to size separation efforts is avoided. Biphasic methods requiring phase transfer reagents are valued for obtaining high quality materials with narrow size distributions, while greener, single phase methods sometimes fail to yield products of equal merit, underscoring the need for continued research efforts within this highly developed class of nanosynthesis.

In 2000, Chen and Murray et al. addressed specific issues of particle growth and monodispersity issues in the preparation of hexanethiol protected gold nanoparticles, monitoring size evolution of the clusters over the course of 125 hrs. Core diameters reached a maximum of 3.0 nm at 60 hrs and particle growth occurs only if the nanoparticles remain in situ, while toluene solutions of isolated, purified nanoparticles are stable in solution for extended periods [36]. A stable AU_{38} compound was isolated by a slightly different method, using a reduced temperature adaptation of the Brust synthesis where the biphasic reduction of HAuCl_4 was carried out at 0 °C in the presence of a phenylethanethiol passivating ligand. Reduced reaction temperatures impact nanoparticle growth without significantly slowing nucleation and passivation events, thus leading to a product enriched in smaller particles [38]. Jiminez and Murray et al. detailed the synthesis of a AU_{38} compound having narrow size dispersity. By either reducing the reaction temperature to -78°C, or by running the reaction at ice temperature with a hyperexcess (300 fold, relative to Au) of thiol, nanoparticle growth is arrested, enriching the products with AU_{38} clusters. The above cases highlight the importance of controlling competing particle nucleation and growth processes in order to limit the size dispersity of nanosynthesis products.

Larger (5-8 nm) gold clusters can be prepared in biphasic water/toluene systems [38]. Brust explored a range of biocompatible moieties by using derivatives of thioalkylated polyethylene glycol ligands to impart water soluble ligand shells to 5-8 nm TOAB (tetraoctylammonium bromide) stabilized particles. To access more versatile surface chemistries, a range of

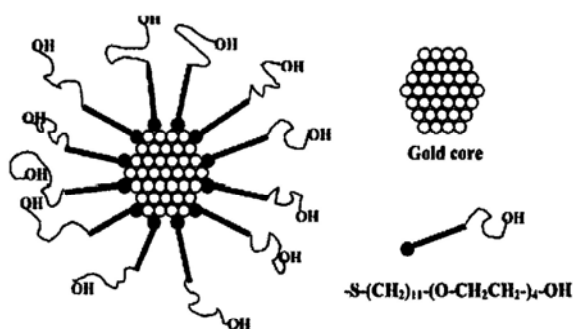


Fig. 1.5: Tetraethylene glycol tenninates a CII alkylthioligand, which offers the combined advantages of water solubility with the high surface coverage characteristic of an alkylthiol capping ligand

target ligands featuring carboxylate, amino and monohydroxy pendant groups (attached to the terminus of the polyethylene glycol portion of the ligand) were prepared for use in ligand exchange reactions [39]. Although the ligands used in these reactions present biocompatible moieties, special care must be taken to ensure that all traces of TOAB are removed from the system prior to use in biological applications.

To generate nanomaterials featuring biocompatible surfaces, Kanaras and Brust used a thioalkylated ligand (monohydroxy (1-mercaptoundec-11-yl) tetraethylene glycol) to introduce a stable, neutral, water soluble functionality to gold nanoparticles by both ligand exchange and direct synthesis routes (Figure 1.5) This work was inspired by Foos' report of water soluble gold nanoparticles capped with short chain thiolated polyethylene glycol ligands that were capable of place exchange reactions and the work of Murray, whom demonstrated the synthesis of gold clusters in the presence of thiolated PEG. By successfully incorporating water soluble functional groups, these reports inspired researchers to consider new ligands, solvents and reaction conditions that permit synthesis within a single phase context.

Development of a single phase adaptation of the Brust method of nanoparticle synthesis was motivated by a desire to eliminate issues posed by the use of phase transfer reagents, including cytotoxicity and the potential for persistent contamination. In the course of such developments, many of the single-phase procedures became much greener as well, sometimes eliminating organic solvents, improving atom economy and using

milder reaction conditions. Quite often the products are benign enough for use in biological applications, especially in the case of certain aqueous procedures. Most single phase adaptations of the Brust method yield products with larger average diameters and size distributions than those produced by the original biphasic procedure, which poses a challenge to researchers targeting smaller functionalized nanoparticles prepared by greener routes. It is believed that variations in product morphology may be attributed to the difference in the ordering of the capping agent in highly polar aqueous environments. Thus, possible solutions may include the use of capping agents that present additional order to aqueous phases (such as those containing hydrogen-bonding moieties) or the substitution of somewhat less polar solvents in lieu of water. The following section highlights some examples of cleaner, more efficient single phase Brust-type syntheses of metal nanoparticles, concluding with some reports of alternative procedures that are likely to open up a new area of innovation in nanosynthesis.

In 1999, Murray et al. reported water-soluble clusters with an average diameter of 1.8 nm, synthesized in single aqueous phase using a method adapted from Brust, where HAuCl_4 was reduced by NaBH_4 in the presence of tiopronin (N-2-mercaptopropionylglycine). This report focused on the viability of these water soluble nanoparticles as precursors for both ligand exchange and post-synthetic modification via amide coupling reactions [40]. In the same year, Chen and Kimura reported the synthesis of nanoparticles ranging in size from 1.0 to 3.4 nm by NaBH_4 reduction of HAuCl_4 in the presence of mercaptosuccinic acid, using methanol as a solvent. Although size evolution of the nanoparticle products in solution became apparent over time, the dried nanoparticle powders were stable and completely redispersible in water. Such nanoparticles could be used to construct various nanostructures by taking advantage of hydrogen bonding or electrostatic interactions controlled by the pendant carboxylate groups [41].

In 2003 a single-phase nanoparticle procedure was developed Pengo, using ligands having common features to those used in the biphasic synthesis of Brust and Twigg. Water soluble nanoparticles with core sizes ranging from 1.5 to 4.2 nm were synthesized in a single water/methanol phase, using an amphiphilic thiol featuring a hydrophobic mercaptoheptane portion and a hydrophilic triethylene glycol monomethyl ether unit

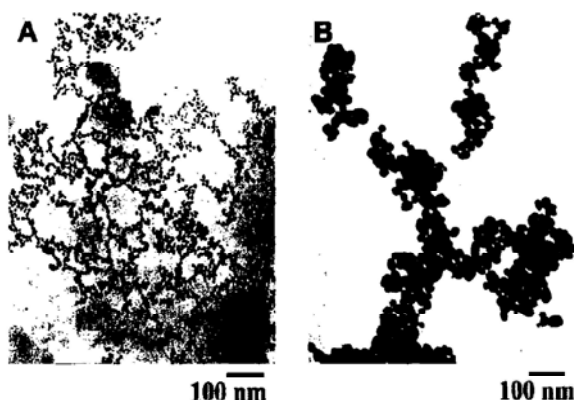


Fig. 1.6: Lysine capped gold nanoparticles feature inherently pH-sensitive pendant groups, which may be manipulated to control the degree of interparticle interaction. (Left) Particles at pH = 3. (Right) Particles at pH = 10. (Reprinted with permission from Selvakannan, P. R.; Mandai, S.; Phadtare, S.; Pasricha, R.; Sastry, M., *Langmuir* 2003,19,3545, Figure 5. Copyright 2003 American Chemical Society.)

linked together by a central secondary amide. The rate of NaBH_4 addition impacted the average core size and monodispersity, especially if the ratio of gold to thiol was high. The rate of Au reduction corresponds to the initial borohydride concentration: if a reducing agent is added rapidly, small nanoparticles form rapidly and sequester much of the thiols, leaving little capping agent to stabilize (and arrest the growth of) larger nanoparticles [42]. Such issues are not encountered in the traditional biphasic Brust synthesis, since the rate of NaBH_4 addition is controlled by the phase transfer process at the interface.

A unique approach to water soluble nanoparticles was presented Selvakannan, where aqueous HAuCl_4 is reduced by NaBH_4 in the absence of any potentially toxic stabilizers or phase transfer reagents, yielding 6.5 nm bare gold clusters [43]. The amino acid lysine was added to the solution as a capping agent, rather than a thiol. NMR studies suggest that lysine binds to the bare gold clusters via the α -amino group, leading to [28] reversible pH dependent properties attributed to the pendant carboxyl and amino moieties, agglomerating at pH = 10 and redispersing at lower pH values. TEM images of these structures are shown in Figure 1.6.

Fabris designed thiolated ligands with a various numbers of peptide moieties for use in aqueous Brust procedures, finding that capping agents with greater

degrees on conformational constraint (imparted by hydrogen bonding interactions amongst the peptides) yield smaller nanoparticles, reconciling the difference in core sizes provided by biphasic and single phase methods [44]. Beyond offering more control over the average core size of the products, the presence of hydrogen-bonding peptides increases the overall stability of the particles, evidenced by resistance to cyanide etching [45]. Conformational constraint appears to be key to the trend reported by Fabris, where Higashi discovered an opposing trend: that increased numbers of helical peptide moieties within a thiol capping agent lead to larger particles [46]. However, in Higashi's case, the peptides of neighboring thiols on a nanoparticle probably do not strongly interact with each other (as in Fabris' study) due to their particular conformational arrangement.

In 2004, Rowe and Matzger reported a single-phase synthesis of gold nanoparticles in tetrahydrofuran using metal-to ligand ratios similar to those of the Brust route, yielding products indistinguishable from the biphasic Brust method. While the methods described in this report aren't particularly green, the importance of eliminating phase transfer reagents was highlighted during evaluation of the products. Since small nanoparticles are often synthesized with electrical applications in mind, it is imperative that unnecessary ionic species are removed from the products. The materials obtained by this route were compared to those of the Brust method and it was found that the charge transport properties of the Brust products were dominated by ionic conduction, overshadowing the tunneling-based behaviors expected of gold nanoparticles [47].

Besides eliminating issues of contamination associated with biphasic reactions, single phase procedures can provide a facile route to synthesizing water soluble nanoparticles that can act as useful, modifiable precursor materials for use in biologically relevant applications.. For example, Latham and Williams recently developed a unique ligand, trifluoroethyl ester-polyethylene glycol-thiol, which may be used for direct synthesis, ligand exchange and post-synthetic modification approaches to functionalized nanomaterials (Figure 1.7).

Direct synthesis of gold clusters via the modified Brust route leads to particles having average core diameters of 3-4 nm. Ligands used in direct synthesis may be modified via the trifluoroethyl ester moiety prior to particle formation, which reacts with amines to form

Scheme 1. General Routes for Use of TFEE-PEG-SH for the Functionalization of Nanoparticles^a

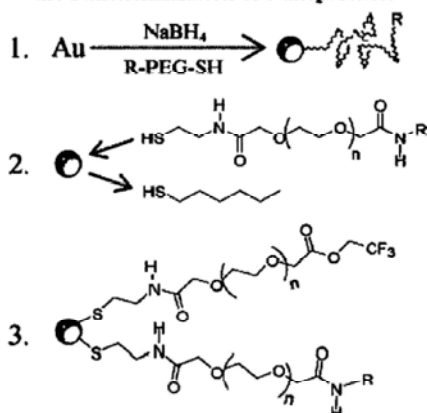


Fig. 1.7: The versatile trifluoroethylester-PEG-thiol ligand may serve multiple roles, acting as (1) a capping agent for direct synthesis, (2) an incoming ligand for place exchange reactions on preformed particles, and (3) an ideal candidate for post-synthesis coupling reactions, due to the labile CF₃ protecting group. (Reprinted with permission from Latham, A. H.; Williams, M. E. *Langmuir* 2006J 22, 4319, Scheme 1. Copyright 2006 American Chemical Society).

amides in the absence of coupling agents, or it may be hydrolyzed in water to yield a pendant carboxylic acid. Coupling reactions of the ligand with primary amines prior to its use in direct synthesis afford a diverse range of pendant functionalities, including butane, pyridine, amino and biotin. The ligands are capable of participating in exchange reactions with alkanethiol-protected particles. The trifluoroethylester group remains intact after direct synthesis of nanoparticles or after a ligand exchange reaction (if anhydrous conditions are maintained), offering multiple opportunities to introduce other functional groups or small biomolecules to the surface of the nanoparticle. This ligand has also been used to impart similar chemistries to FePt nanoparticles, which are gaining prominence^[48] as MRI imaging agents.

At this point, all discussion has been focused on gold nanoparticles, but further insight can be derived from similar treatments of platinum, lending greater understanding to the preparation of other noble metal materials. For example, Yang and Too et al. described the multiple roles of NaBH₄ in nanosynthesis, demonstrating its additional capability as a stabilizing agent. Platinum nanoparticles were synthesized in the aqueous phase by

NaBH₄ reduction of a Pt(IV) precursor. The authors proposed that excess BH₄⁻ anions hinder transfer to the organic phase by acting as stabilizing agents that hinder the binding of alkanethiols. To confirm this hypothesis, platinum nanoparticles were prepared with a four fold stoichiometric excess of NaBH₄ and indeed could not be transferred to an alkanethiol/toluene solution unless concentrated HCl was added to the platinum sol in order to accelerate the decomposition of BH₄⁻ anions. In light of these results, the authors modified their procedure such that the platinum nanoparticles could be transferred to the organic phase immediately upon formation, without the use of a phase transfer reagent, resulting in nanoparticles with an average core size of 2.6 ± 0.4

Like other methods of preparing gold nanomaterials, weaker reducing agents may be substituted for sodium borohydride. Eklund and Cliffel prepared organic and watersoluble platinum nanoparticles for use as catalytic reagents. Organic soluble particles were synthesized by reducing HAuCl₄ with lithium triethylborohydride (LiTEBH) in the presence of alkanethiols suspended in THF. Aqueous platinum nanoparticles were prepared in an analogous manner with water soluble thiols, substituting NaBH₄ for LiTEBH and using water as a solvent.⁵⁰ Most recently, the microwave-assisted preparation of platinum nanoparticles catalysts was reported, using only aqueous sugar solutions as a support medium. In this procedure, numerous green challenges were met, including the elimination of organic solvents, surfactants and strong reducing agents, while demonstrating excellent atom economy.⁵¹

The Brust method of nanoparticle synthesis can be used to generate aminestabilized nanoparticles by simply substituting an appropriate amine for the thiol. Such particles may provide a route to larger (5-15 nm) materials capable of participating in ligand exchange reactions, since amines are more labile ligands than thiols.

Amine stabilized particles were first prepared by Leff using a method analogous to that of Brust, substituting a primary amine for alkanethiol. Larger nanoparticles having diameters up to 7 nm can be accessed by this method, although dispersity broadens at the upper limit of the size range. If harsh reducing agents (Le. NaBH₄) are replaced by weaker reagents, or completely omitted from the procedure, even larger noble metal nanoparticles may be obtained, as primary amines are strong enough reducing agents to nucleate and grow particles. Iana and Peng further extended the Brust analogy, synthesizing

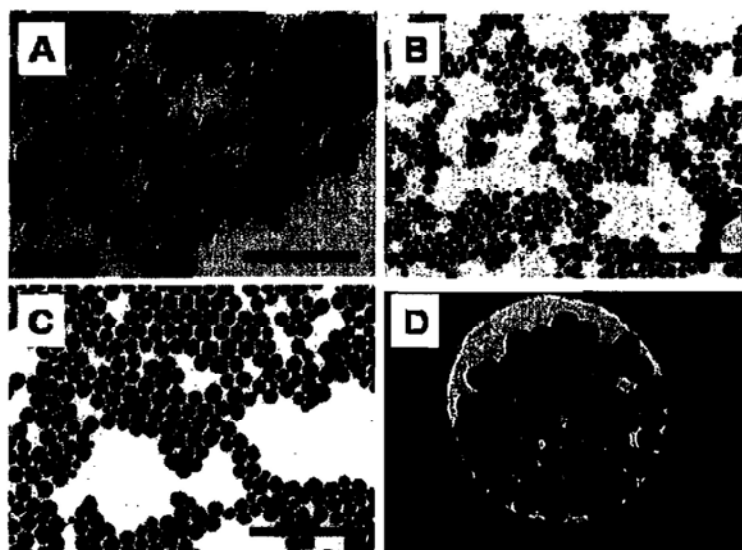


Fig. 1.8: Nanoparticles prepared by refluxing gold or silver precursors with oleylamine. (A) 21 nm gold, (B) 9 nm Ag, (C) 12 nm Ag, and (D) 32 nm Ag. Scale bars indicate 100 nm. (Reprinted with permission from Hiramatsu, H.; Osterloh, F. E., *Chem. Mater.* 2004~ 16, 2509, Figure 1. Copyright 2004 American Chemical Society.)

noble metal nanoparticles in a single organic phase from $AuCl_3$ (or another organic soluble metal cation), tetrabutylammonium borohydride (TBAB) and either fatty acids or aliphatic amines. Organic soluble particles between 1.5 and 7.0 nm were obtained without the use of surfactants, depending on the amount of capping agent used [48-52].

Hiramatsu and Osterloh found that borohydride reducing agents are unnecessary for the synthesis of nanomaterials in larger size regimes. Gold and silver amine stabilized particles with core diameter ranges of 6-21 nm for gold and 8-32 nm (Figure 1.8) for silver were synthesized in a simple scalable preparation where either $HAuCl_4$ or silver acetate were refluxed with oleylamine in an organic solvent. Other reducing agents are not necessary, since amines are capable of reducing gold, forming nitriles upon further oxidation. In the case of gold, core size was controlled by regulating the gold to amine ratio, although it is acknowledged that samples with good monodispersity (less than 10%) were achieved only if a minimum of 65 equivalents of amine (relative to gold) were used. Silver nanoparticles were formed by refluxing silver acetate with oleylamine in a variety of organic solvents. The particle size is determined primarily by the reflux temperature associated with each solvent: hexanes (bp: 69°C) yield 8.5 nm particles, while the use of toluene (bp: 110°C) and 1,2-dichlorobenzene (bp: 181°C) results in

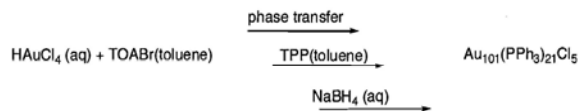
12.7 and 32.3 nm particles, respectively [53].

Aslam and Dravid et al. reported a similar method of generating water-soluble gold nanoparticles that eliminates harsh reducing agents and organic solvents, while demonstrating greatly improved atom economy. $HAuCl_4$ is reduced by oleylamine in water, creating nanoparticles that are water soluble despite the apparent mismatch in polarity between the solvent and the stabilizing ligand. Gold is used in excess over the amine, perhaps leading to products with mixed ligand shells whose stability is bolstered by chloride complexes. The products of this reaction have core sizes of 9.5 to 75 nm and the greatest monodispersity is achieved for particles at the lower end of the size range, where a 10: 1 ratio of gold:amine is used. Lesser amounts of amines lead to particles with very wide polydispersities [54].

Phosphine Stabilized Nanoparticles: The Brust method of nanoparticle synthesis is a valuable technique for preparing thiol-stabilized nanoparticles, where functional groups are limited only by the compatibility of thiols. However, the identification of a unique set of reaction conditions is often required for the preparation of each functionalized target and it is often difficult to access smaller nanomaterials by this route. An approach pioneered in our laboratories involves producing a nanoparticle precursor having a temporary stabilizing

ligand shell, amenable to ligand exchange reactions with an incoming molecule that has the desired chemical functionality. By optimizing the preparation of a common precursor (synthon) one can generate libraries of diverse nanoparticles that bear pendant functional groups, thus introducing the desired chemical functionality to the surface of the particle. Although this procedure requires two steps and employs triphenylphosphine as temporary stabilizing group, this synthon approach has permitted greater control of nanoparticle size, dispersity and functionality. The tradeoff made is the use of an additional step to avoid the inefficiencies and waste generating purification steps inherent in developing a specific preparation for each direct synthesis. While somewhat unstable, as-synthesized triphenylphosphine stabilized nanoparticles are valued for their ready participation in ligand exchange reactions (which will be discussed in later sections of this review covering nanoparticle functionalization and exchange reactions). The earliest reported syntheses of such particles by Schmid provided the benchmark method for preparing high quality small gold nanoparticles [55-57]. $\text{AuCl}(\text{PPh}_3)$ is prepared from HAuCl_4 , suspended in warm benzene and reduced by a stream of diborane gas, presenting significant health and explosion hazards. Despite the hazards involved, this method remained the most reliable large-scale preparation of phosphine stabilized gold nanoparticles for nearly two decades.

In 1997, Hutchison et al. presented a convenient, safer and scalable synthesis (Scheme 1.1) that yields high-quality 1.4 nm triphenylphosphine stabilized gold nanoparticles through a much greener route that eliminates the use of diborane gas (>40 L diborane/g nanoparticle) and benzene (>1000g benzene/g nanoparticle). This biphasic synthesis involves the use of a phase transfer reagent (TOAB) to facilitate the transfer of chloroaurate ions from an aqueous solution to an organic phase (toluene) containing triphenylphosphine. Reduction is carried out using aqueous NaBH_4 delivered to the organic phase via complexation with TOAB. There is still opportunity to further green this preparation. Substitutions of NaBH_4 for diborane and toluene for benzene are clearly beneficial, however, it would be preferable to avoid using TOAB and find a yet greener solvent. In addition the purification of these particles still requires solvent washes. If membrane filtration methods suitable for use with organic solvents could be developed to replaced solvent washes as the purification step, the preparation could be made even less wasteful.



Scheme 1.1: Biphasic synthesis of 1.4 nm gold nanoparticles stabilized by triphenylphosphine.

The triphenylphosphine stabilized nanoparticles may be stored as a powder under cold, dry conditions until they are needed for ligand exchange reactions [58]. Besides being greener and safer, this synthesis also features a great improvement in yield, providing 500 mg of purified nanoparticles from one gram of HAuCl_4 , compared to 150 mg of product from Schmid's method. The products of both preparations yield nanoparticles of equal core diameter, monodispersity and reactivity. The nanoparticles from Hutchison's prep have been functionalized by a wide range of ligands through ligand exchange reactions, yielding a diverse library of functional nano "building blocks" ideal for use in the bottom up assembly of new nanostructures, all from a versatile gold nanoparticle precursor.

Seeded Growth and Shape Control of Nanoparticles:

In the pursuit of nanoscale materials featuring optical properties, nanoparticles having core diameters exceeding 5 nm can be grown from smaller seed particles through the epitaxial addition of metal atoms. Delivered to the surface of the seed particle in a partially reduced form, supplemental amounts of a metal salt can be reduced in a surface catalyzed reaction with a mild reducing agent, transforming a solution of small particles to larger colloids. Whether the goal is to grow large spherical particles or nanorods, the use of well-defined seeds is critical to obtaining products with narrow size dispersity. Other reagents such as surfactants may be present as a component of the nanoparticle growth solution, acting in the capacity of a directing agent that promotes the formation of anisotropic materials, or simply as surface passivants and stabilizing agents. Growth of such materials from monodisperse seeds allows the researcher to employ milder reaction conditions for the synthesis of materials and the wide range of weaker reducing agents capable of reducing metal ions in a growth solution offers increased possibilities for designing greener syntheses. Larger nanomaterials are especially valued for their optical properties, useful for surface enhanced Raman scattering, imaging, sensing and waveguiding applications, where the optical absorption arising from the surface plasmons (Figure 1.9) of noble metal materials is key.

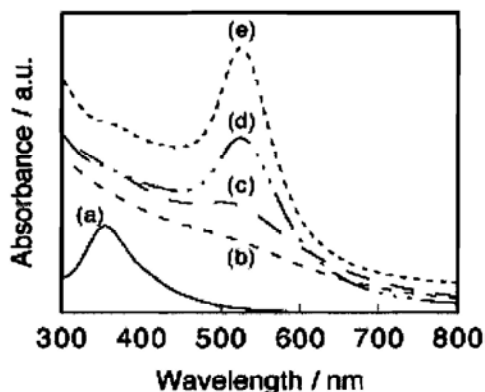


Fig. 1.9: UV-Vis absorption spectra of gold nanoparticles corresponding to (a) 1.5 nm (b) 3.4 nm (c) 5.4 nm (d) 6.8 nm and (e) 8.7 nm. Absorptions due to interactions with surface plasmons feature extinction coefficients that increase with particle size, making particles with average diameters > 8 nm appropriate for optical applications. (Reprinted with permission from Shimizu, T.; Teranishi, T.; Hasegawa, S.; Miyake, M. J. Phys. Chem B. 2003, 107, 2719, Figure 1. Copyright 2003 American Chemical Society.)

CONCLUSION

The synthesis of larger spherical nanoparticles from smaller seed materials is reviewed, as is the formation of anisotropic nanorod materials. (A complete analysis of seeded growth methods is beyond the scope of this review, but an excellent review of gold nanorods was recently offered by Perez-Juste and coworkers.⁴) A special focus has been placed on studies intended to elucidate the individual roles of nanoparticle seeds, reducing agents and additives, with respect to their impact on the morphology of the final products. The information garnered from these studies has ultimately contributed to a better understanding of the surface chemistry of these materials, which should in turn lead to targeted functionalization methods that will enable their utility in solution-based sensing applications and beyond. Next, shape controlled methods that provide access to more exotic materials are discussed, followed by selective etching techniques (see section 2.3.4) which can be used to give new life to nanomaterials by transforming their shape. Gaining access to larger particles through growth techniques provides a secondary use for small gold clusters (which serve as seeds), while etching techniques can be especially helpful for transforming larger spherical and rodlike structures back to smaller particles. Ultimately,

the application of these recycling measures prolongs the useful lifetime of a nanomaterial, reducing the amount of products entering the wastestream.

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