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The Synthesis of Solid Supported Palladium Nanoparticles: Effective Catalysts for Batch and Continuous Cross Coupling Reactions

Kendra W. Brinkley
Virginia Commonwealth University

The Synthesis of Solid Supported Palladium Nanoparticles: Effective Catalysts for Batch and Continuous Cross Coupling Reactions

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By Kendra W. Brinkley

Advisor: Dr. B.F. Gupton

Research Professor and Chair, Department of Chemical and Life Science Engineering

Virginia Commonwealth University

Richmond, VA

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This is to certify that the dissertation prepared by Kendra W. Brinkley entitled *The Synthesis of Solid Supported Palladium Nanoparticles: Effective Catalysts for Batch and Continuous Cross Coupling Reactions* has been approved by her committee as satisfactory completion of dissertation requirement for degree of Doctor of Philosophy in Chemical and Life Science Engineering.

Dr. B.F. Gupton; School of Engineering, College of Humanities and Sciences, Dissertation Advisor

---

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List of Abbreviations

1.	EnPd	Encapsulated Palladium Catalyst
2.	B.M.- MWNT	Ball Milled Multi-walled Carbon Nanotubes
3.	B.M.- SWNT	Ball Milled Single-walled Carbon Nanotubes
4.	M.P. MWNT	Mortar and Pestle Synthesized Palladium Multi-walled Carbon Nanotubes
5.	M.P. SWNT	Mortar and Pestle Synthesis Palladium Single-walled Carbon Nanotubes
6.	M.P.-BN	Mortar and Pestle Synthesized Palladium Boron Nitride Catalyst
7.	Micro-G	Microwave Synthesized Palladium Graphene Catalyst
8.	(MWNT)$_M$	Multi-walled Carbon Nanotube Supported Palladium Nanoparticles: Synthesized using the Balled Milled Mechanical Method
9.	(MWNT)$_T$	Multi-walled Carbon Nanotube Supported Palladium Nanoparticles: Synthesized using the Balled Milled Thermal Method
10.	(SWNT)$_M$	Single-walled Carbon Nanotube Supported Palladium Nanoparticles: Synthesized using the Balled Milled Mechanical Method
11.	(SWNT)$_T$	Single-walled Carbon Nanotube Supported Palladium Nanoparticles: Synthesized using the Balled Milled Thermal

	Method
12. Pd/G	Lab Synthesized Graphene Supported Palladium Nanoparticles Using Microwave Assisted Technique

List of Abbreviations

13. Pd/Gc	Commercially Bought Graphene Supported Palladium Synthesized Using Continuous Microwave Assisted Technique Nanoparticles
14. DOE	Design of Experiments
15. GC-MS	Gas Chromatography-Mass Spectrometry
16. TEM	Transmission Electron Microscopy
17. SEM	Scanning Electron Microscopy
18. XPS	X-Ray Photon Spectroscopy
19. XRD	X-Ray Diffraction
20. Pd	Palladium

Abstract

Catalysis is one of the pillars of the chemical industry. While the use of catalyst is typically recognized in the automobile industry, their impact is more widespread as; catalysts are used in the synthesis of 80% of the US commercial chemicals. Despite the improved selectivity provided by catalyst, process inefficiencies still threaten the sustainability of a number of synthesis methods, especially in the pharmaceutical industry. Recyclable solid supported catalysts offer a unique opportunity to address these inefficiencies. Such systems coupled with continuous synthesis techniques, have the potential to significantly reduce the waste to desired product ratio (E-factor) of the production techniques. This research focuses developing sustainable processes to synthesize organic molecules by using continuous synthesis methods. In doing so, solid supported metal catalyst systems were identified, developed, and implemented to assist in the formation of carbon-carbon bonds. Newly developed systems, which utilized metal nanoparticles, showed reactivity and recyclability, comparable to commercially available catalyst.

Nanoparticles are emerging as useful materials in a wide variety of applications including catalysis. These applications include pharmaceutical processes by which complex and useful organic molecules can be prepared. As such, an effective and scalable synthesis method is required for the preparation of nanoparticle catalysts with significant control of the particle size, uniform dispersion, and even distribution of nanoparticles when deposited on the surface of a solid support. This project describes the production of palladium nanoparticles on a variety of solid supports and the evaluation of these nanoparticles for cross coupling reactions.

This report highlights novel synthesis techniques used in the formation of palladium nanoparticles using traditional batch reactions. The procedures developed for the batch formation of palladium nanoparticles on different solid supports, such as graphene and carbon nanotubes,

are initially described. The major drawbacks of these methods are discussed, including limited scalability, variation of nanoparticle characteristics from batch to batch, and technical challenges associated with efficient heating of samples.

Furthermore, the necessary conditions and critical parameters to convert the batch synthesis of solid supported palladium nanoparticles to a continuous flow process are presented. This strategy not only alleviates the challenges associated with the robust preparation of the material and the limitations of scalability, but also showcases a new continuous reactor capable of efficient and direct heating of the reaction mixture under microwave irradiation. This strategy was further used in the synthesis of zinc oxide nanoparticles. Particles synthesized using this strategy as well as traditional synthesis methods, were evaluated in the context industrially relevant applications.

Chapter 1

Introduction/Background: Solid Supported Catalysts and Their Role in Cross Coupling Chemistry

1.1 Background and Project Significance

Catalysis is the hidden gem in environmental and chemical industries. While the use of catalysts is most commonly known in automotive catalytic converters, they are routinely used in other applications including gasoline, automobile lubrication and its additives, and the synthesis of fine chemicals. It is estimated that 85% of all US products include at least one catalytic step in the synthesis.[1] The economic impact on the US GDP, an aggregate measure of production equal to the sum of the gross values added of all resident, institutional units engaged in production, cannot be understated as catalytic processes constitute 20%.[2] In addition to their economic impact, catalysts play a critical role in developing sustainable and environmentally friendly processes. The 50 highest-produced chemicals by volume in the US correlate with a substantial carbon footprint via the emission of carbon dioxide and other harmful gases into the earth's atmosphere. Currently 30 of these processes have employed catalysts to reduce the emissions released and waste generated.[3]

Despite catalysis emerging in the forefront of developing sustainable, efficient processes, industries still struggle to successfully develop such processes, as evident in their E-factors (Figure 1-1). The E-factor, one of the most straightforward and useful green chemistry metrics, is defined as kilograms of waste produced per kilograms of product.[4] While catalysts have proven to assist in product selectivity, future advancements in process efficiency may be achieved by developing immobilized catalysts for use in continuous production methods. Over half of all chemicals produced are still made using traditional batch reactions, yet continuous reactions offer unique advantages including intensified mixing, smaller volume to heating ratio, and safer operating conditions.[5] The highly reproducible nature and therefore the robust application of continuous processes in the production of commodity chemicals has led to an increased interest in developing such technologies for fine and specialty chemical production.[6]

Figure 1-1[4]

Industry Segment	Product Tonnage	E-factor (kg waste/kg product)
Oil Refining	10^6–10^8	< 0.1
Bulk Chemicals	10^4–10^6	<1-5
Fine Chemicals	10^2–10^4	5-50
Pharmaceuticals	10–10^3	25-100

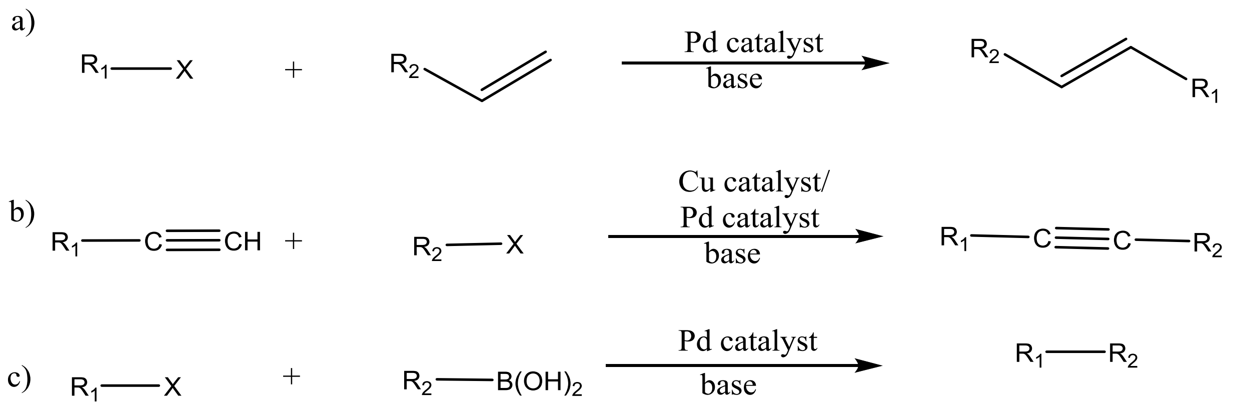
E factors in the chemical industry

In 2012, the pharmaceutical industry spent 49.6 billion dollars on research and development expenditures alone, in part aimed at finding more cost-effective synthetic processes in an effort to reduce the e-factor for this sector of the chemical industry.[7] Despite this statistic, there are myriad opportunities for generics manufacturers, contractors, and those in academia to innovate within the realm of process development for pharmaceuticals and other specialty chemicals. The focus of this research project seeks to address one strategic element of process development. Specifically, it was hypothesized that the development of solid supported catalyst systems would provide significant advantages for cross coupling reactions, a key reaction category in the pharmaceutical industry, in both batch and continuous operations. Furthermore, implementation of such systems in the continuous production of organic compounds is expected to increase the production and purity of the desired product, as solid supported catalysts can be recovered for recycling and product isolation is greatly simplified.

1.2 Carbon-Carbon Cross Coupling Reactions

While there are a number of reactions used for synthesizing complex molecules in the pharmaceutical industry, some of the most powerful are cross coupling reactions that form a new carbon-carbon bond, such as the Heck, Sonogashira, and Suzuki reactions (Figure 1-2).[8] The Heck reaction was developed by Tsutomu Mizoroki and Richard F. Heck. This reaction is conducted between an aryl halide or vinyl halide and an activated alkene, proceeding in the presence of a palladium catalyst and a base. It has been cited for its excellent trans-selectivity, but often requires harsh reaction conditions.[9] In contrast, the Sonogashira reaction, developed by Kenkichi Sonogashira, Yasuo Tohda, and Nobue Hagihar, is conducted between a terminal alkyne and an aryl or vinyl halide. This reaction proceeds under relatively mild reaction conditions using two metal catalysts, palladium and copper. Lastly, the Suzuki-Miyaura reaction requires the mildest condition of the three. Developed by Akira Suzuki and Norio Miyaura, it is often used in the synthesis of biphenyls and polystyrenes. The reaction takes place between an aryl halide and a boronic acid in the presence of a base and a palladium catalyst.[5,10] In 2010 Heck, Sonogashira, and Suzuki shared the Nobel Prize in Chemistry for their contributions to the field.

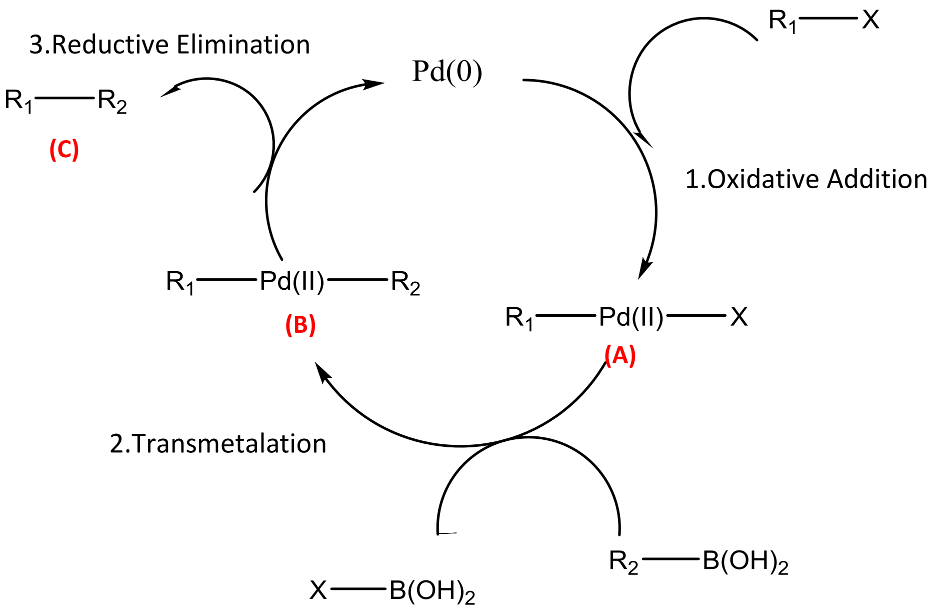
Figure 1-2



a- General schematic for Heck reaction b- General schematic for Sonogashira reaction c- General schematic for Suzuki reaction.

Though there are differences in the substrate requirements for each reaction, these three cross coupling reactions can be described using a generalized catalytic cycle of palladium which they all employ. A typical palladium catalytic cycle is described as a three step process - oxidative addition, transmeltalation, and reductive elimination (Figure 1-3). This research focuses only on the Suzuki coupling reaction because of its ease in preparation and characterization, and the low cost of its reactants.

Figure 1-3



A general schematic for the palladium catalytic cycle.

During oxidative addition, the palladium (0) catalyst is oxidized to an active palladium (II) species while inserting into the aryl halide bond to form the first reaction intermediate (**A**). This insertion is typically the rate determining step for a Suzuki reaction. During the transmeltalation step of the Suzuki reaction, the organoboron species is activated by a base, followed by metal exchange with palladium and resulting in the second reaction intermediate (**B**). During the last step, the product is eliminated and palladium (0) is regenerated.[5,11,8] Like many other metal catalysts, palladium is typically coupled to ligands to provide extra stability. One example of a common system used is palladium acetate with a phosphine ligand.

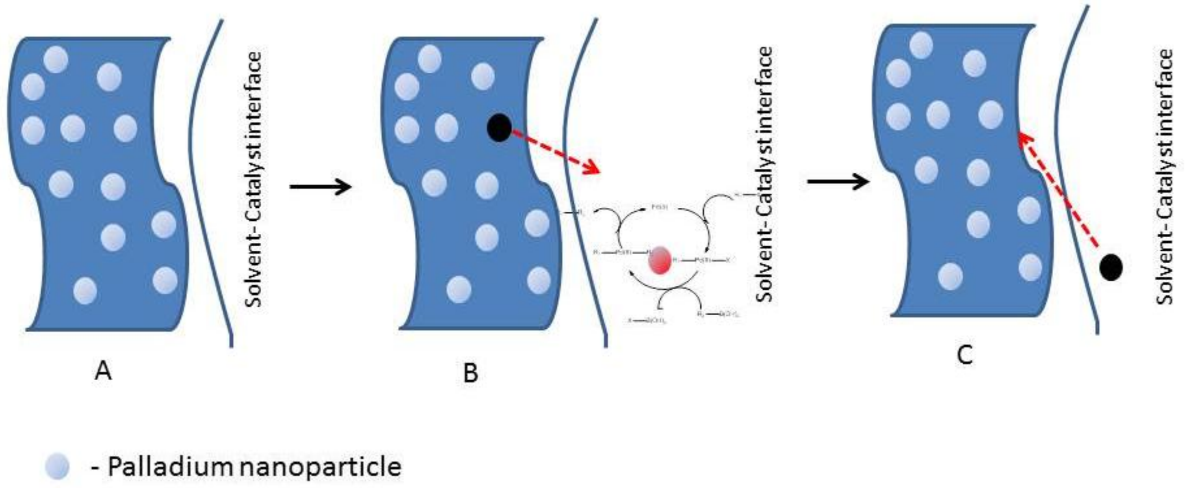
1.3 Homogeneous vs. Heterogeneous Catalyst Systems

Catalyst systems such as palladium acetate are often characterized by their high conversion to the desired product, but these catalysts can be difficult to remove from the final product solution because of their solubility in the reaction medium. Catalysts are often divided into two classes - homogeneous and heterogeneous. A homogeneous catalyst is a catalyst in the same physical phase (usually liquid) as the reaction solvent and substrates, while a heterogeneous catalyst (usually solid) is in a different physical phase than the solvent and the substrates.[12] From a reactivity perspective, a homogeneous catalyst offers a significant advantage over a heterogeneous catalyst because mass transfer effects are essentially negligible.[13]

It has been well established in reaction kinetics that rate of a solid catalyst reaction is dependent on the rate of diffusion for the boundary layer, rate of adsorption, reaction on the surface, and the rate of desorption.[14] The rates of diffusion, adsorption, and desorption are negligible when using a homogenous catalyst. For solid catalysts, active sites may be located in the bulk or inner parts of the solid particle. This makes the rate of reaction also dependent on the thickness of the particle, which is often difficult not only to measure but also to control and tends to result in slower reactions. Despite the mass transfer difficulties, a well-developed heterogeneous catalyst can prove more advantageous than a homogeneous catalyst because of its potential to be easily recovered, decreasing the overall cost and effort put into purification of the final product. Additionally, the potential to reuse the catalyst often makes solid supported catalysts the more economically efficient choice.

1.4 Proposed Catalytic Mechanism for Solid Support Catalysts

Figure 1-4



Proposed leaching and redeposition method of metal catalyst on a solid support

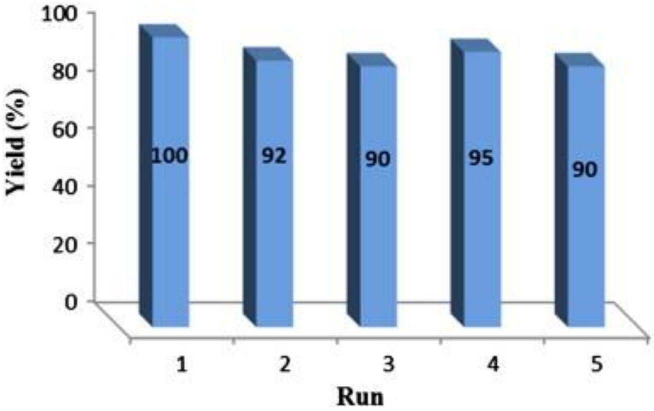
One proposed mechanism for a solid palladium catalyst suggests a leaching and redisposition process shown in Figure 1-4[15]. In this proposed mechanism, the catalyst starts as solid supported palladium (0) nanoparticles **(panel A)**. As the palladium is oxidized to palladium (II), it detaches from the surface and is solubilized in the solvent system **(panel B).** The palladium species then completes the catalytic cycle and regenerates the palladium (0) species that redeposits onto the surface of the support **(panel C).**[**11**]

This mechanism highlights the importance of understanding the interaction between the solid support and the palladium particles. Two standard reactions can be conducted to test this theory: hot filtration and the "three phase" test. In hot filtration method, a small portion of the reaction mixture is extracted and filtered halfway through the reaction. The filtrate is introduced to new reagents to test for catalytic activity. Activity suggests there is reactive palladium within the solution. It should be noted that leaching and redeposition may occur before the filtration is completed, thus other evidence of heterogeneity is often used in conjunction with this test[16]. The three phase test utilizes the reactivity of the intermediates. An aryl halide is immobilized and added to a vessel with the other reagents and the solid-phase catalyst. After the reaction has been incubated for an allotted time, the immobilized substrate is separated, cleaved from its support, and analyzed.[11] Some have referred to catalysts that can convert the aryl halide substrate to product during this test as semi-heterogeneous, suggesting that during the catalytic process the catalyst alternates between being in solution and out of solution (supported) to complete the catalytic cycle.

1.5 Recent Developments in Supported Palladium Catalysts

A number of materials have been used in the development of solid supports for palladium and other transition metals; the following section provides an overview of the state of this art. Besides minimizing conversion during the three phase test and the hot filtration test, ideal solid supports typically possess large surface area (increasing the surface to volume ratio), are chemically inert under the reaction conditions, and provide thermal and mechanical stability. Polymers are one type of support that has been utilized in a variety of ways. Webb and coworkers reported the development of a polymeric styrene divinylbenzene support for palladium particles through a two-step mix and heat synthesis.[13] The synthesized catalyst was used in a coupling reaction between iodobenzene and phenylboronic acid in a DMF and water solvent system. At 100 ^{o}C, complete conversion to the biphenyl product was observed in 12 hours. The catalyst was also recycled 4 times without a loss in conversion; however, it did not give consistent conversion or trend from each run (Figure1-5).

Figure 1-5



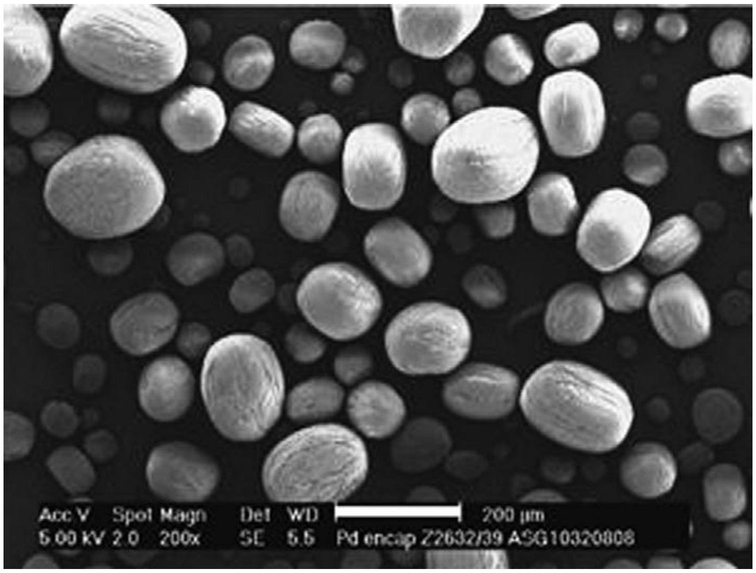
Recycling study, Suzuki–Miyaura cross-coupling reaction of iodobenzene with phenylboronic acid using the polymeric styrene divinylbenzene supported palladium (0.5 mol%).

The extended period of time required for the catalyst to reach complete conversion suggests that this catalyst was unable to complete the catalytic cycle quickly, likely due to mass transfer limitations because of the polymer thickness. Thus, it is expected to exhibit a low turnover frequency (mol of product per mol of catalyst per unit time). High turnover frequencies are indicative of a catalyst that is able to complete its cycle quickly, which is an advantageous feature for catalysts used in continuous processes. Thus this particular system is likely to be impractical for commercial applications.

Other researchers have encapsulated the palladium catalyst using polymer materials.[17] In one case, a polystyrene, tetrakis triphenylphosphine palladium (0), and cyclohexane mixture was heated and cooled, resulting in an enveloped palladium core.[14] The encapsulated system was able to drive a Suzuki coupling reaction to completion in 6 hours under reflux conditions in the presence of an external phosphine ligand and 20 mol% catalyst. To use this type of catalyst for large scale manufacturing would also prove costly because of the amount of catalyst required, as well as the need for an additional ligand for stability.

In 2002, Dr. Steven Ley and coworkers were able to introduce an improved encapsulated system with a microencapsulated palladium acetate species.[15] Specifically, the palladium catalyst was encapsulated in a polyurea framework system created by the hydrolytic polycondensation of multi-functional oligo-arylisocyanates (Figure 1-6).[18] This particular catalyst worked well in alcohols at lower temperatures. At increased temperatures and in solvent systems such as dimethylformamide (DMF) and dimethylacetamide (DMA), significant swelling was observed and as well as leaching of palladium. In a Suzuki reaction, 0.25 mol% of the catalyst was used and yielded 99% product conversion in 30 minutes, a significant improvement seen for polymer systems. When palladium content in the product solution was tested, less than 10 ppm were found without recrystallization of the final product. This material is now produced by Reaxa for commercial use.

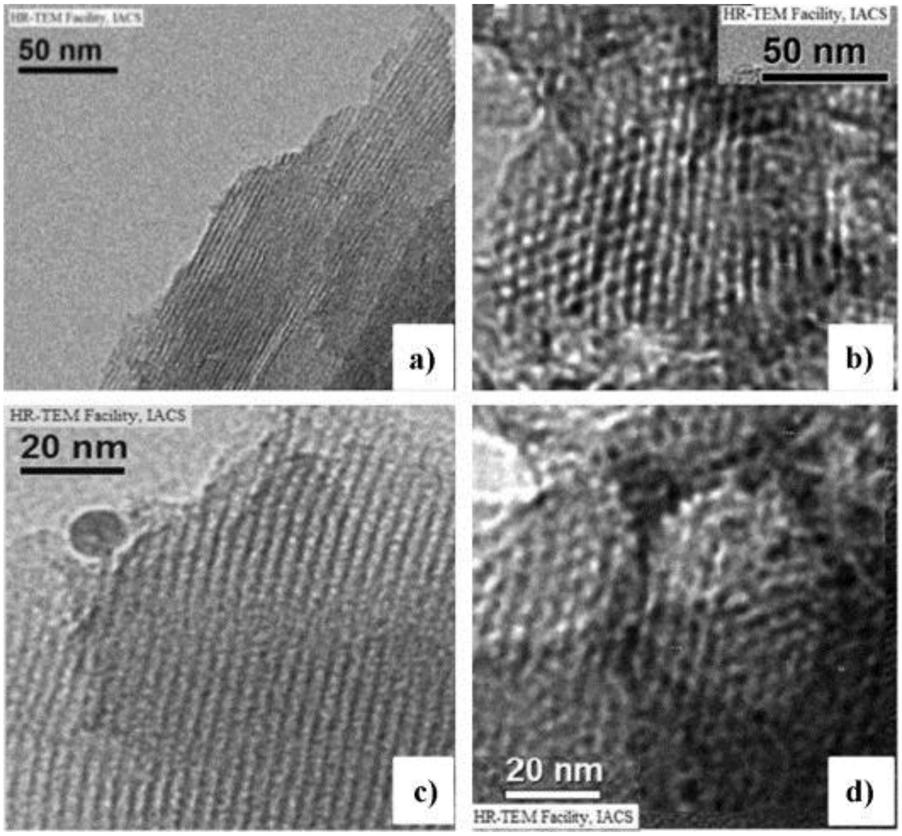
Figure 1-6



SEM image of Encapsulated Palladium Catalyst

Silica has also been used as a support for metal catalysts, and palladium on silica in particular has been widely studied as viable catalyst for the Suzuki cross coupling reaction. It has been reported that metals attached to SiO_2 have enhanced catalytic activity and selectivity in not only the Suzuki coupling reaction but a number of other chemical reactions.[16] In 2014, Das and co-workers developed a Pd-Schiff-base anchored mesoporous silica catalyst (Figure 1-7). The Schiff base is composed of o-vanillin and 3-[2-aminoethylamino)propyl]trimethoxysilane that was chemically anchored onto MCM-41.[16]

Figure 1-7[19]

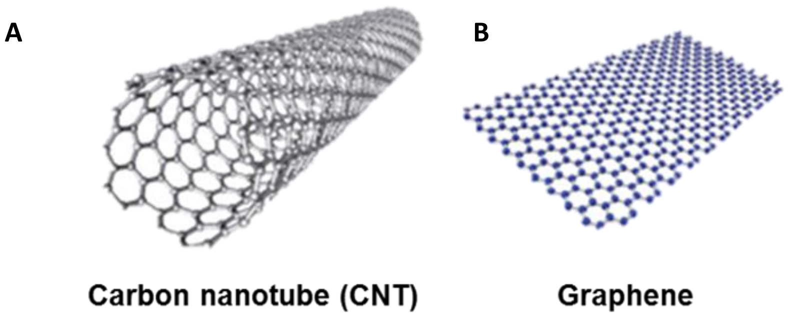


TEM images of mesoporous silica –palladium particles

These mesoporous silica supports were decorated with palladium particles with diameters of less than 20 nm; these Pd nanoparticles were found to be embedded in the channels of the silica complex. At 60 ^{o}C and with only 0.011 mol% palladium present, this silica palladium complex was able to reach complete conversion in a Suzuki coupling reaction of bromobenzene and phenylboronic acid in 50 minutes. Additionally, four recycles were completed before a decrease in reactivity was observed.

Despite the high conversion of Ley's and Das's solid supported systems, all required moderate reaction times that may prove troublesome in the conversion to continuous coupling reactions. Supports that help increase the reaction rate have emerged with the development of carbon-based materials such as graphene and graphene derivatives.

Figure 1-8[20]



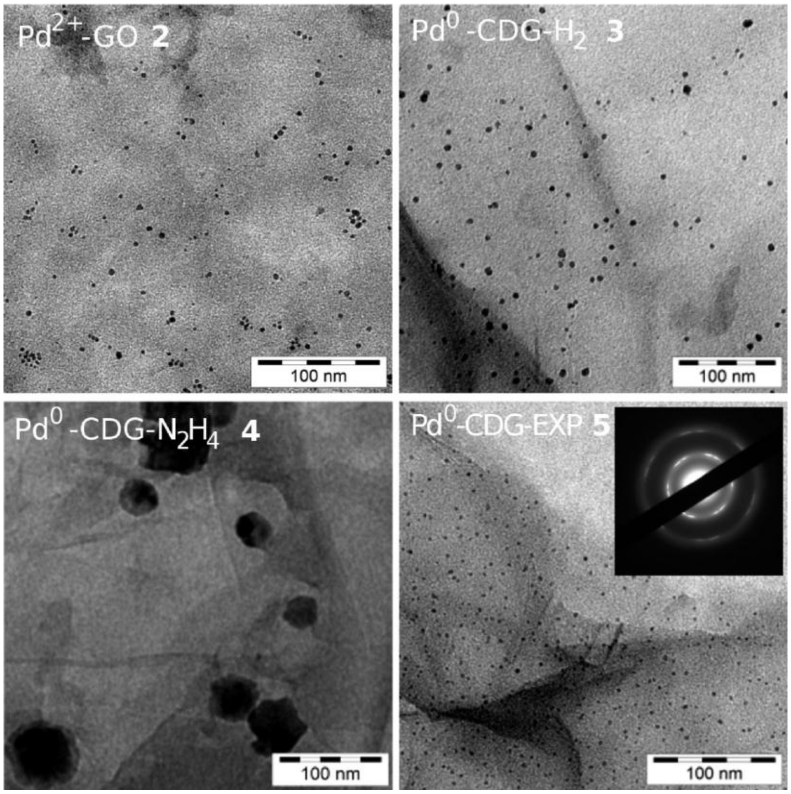
Panel A: A cylindrical 3-dimensional honey comb shaped lattice (carbon nanotube).

Panel B: A dimensional mono-layer honeycomb shaped lattice (graphene sheet)

Graphene can be described as a 2-dimensional mono-layered surface packed into a honeycomb shaped lattice (**Figure 1-8**). It was first produced and analyzed in a laboratory setting in 2003.[21] This material has been cited for its excellent thermal and mechanical strength, and it is currently being used in the electronics industry to make semi-conductors. Reduction of graphite oxide, a crystalline form of carbon that has been chemically modified using oxidizers,[22] using hydrazine was one of the earliest methods used to generate uniform sheets of graphene.[23] Since then, graphene has been produced through vapor deposition and the use of lasers.[20] Carbon nanotubes, which are 3-dimensional derivatives of graphene, also have been used in electronics for their excellent strength and electronic properties.

Several researchers who have used these organized carbon frameworks as solid supports for catalysts have observed excellent activity. Scheuermann and coworkers reported the formation of chemically reduced graphene supported palladium nanoparticles (Figure 1-9) using various reducing agents.[24] While all methods resulted in formation of supported palladium nanoparticles, the graphene oxide and hydrazine-reduced graphene samples showed the most promise. The lack of reactivity in other samples was attributed to the elongated structures of the palladium particles, which lack uniformity, and to the graphite still present in the catalytic system.

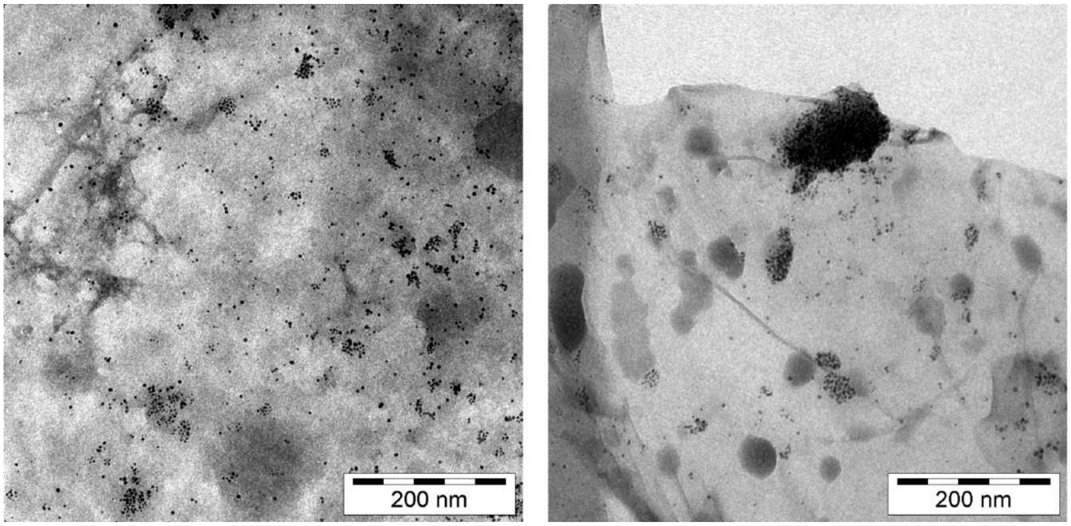
Figure 1-9



TEM images of Pd nanoparticles supported on graphite oxide and chemically reduced graphene

The graphite oxide supported palladium (**2**, Figure 1-9) and graphene supported Pd generated by the hydrazine reduction method (4) had an average particle diameters of 4 and 7 nm respectively. After evaluation of reactivity in a Suzuki coupling reaction, the turnover number for the hydrazine reduced catalyst system (4) was found to be 6700 and turnover frequency was found to be 39000 h^{-1}. Complete conversion was observed after only 30 minutes, and analysis of their product solution showed less than 1 ppm palladium present. The recyclability of the catalyst was also evaluated. Although the catalyst exhibited excellent activity, it could only be recycled twice before a significant decrease in reactivity occurred. The spent catalyst was imaged using TEM (Figure 1- 10), which showed significant agglomeration of the palladium nanoparticles on the surface of the support. The evidence of agglomeration on each of the spent catalysts and the low palladium content in the product solutions strengthens the argument for the leaching –redeposition process proposed for solid catalyst particles. Studies focusing on carbon nanotubes as supports have also been reported.[25] These systems display high catalytic activity as well, but also show limited recyclability in the Suzuki coupling reaction.

Figure 1-10

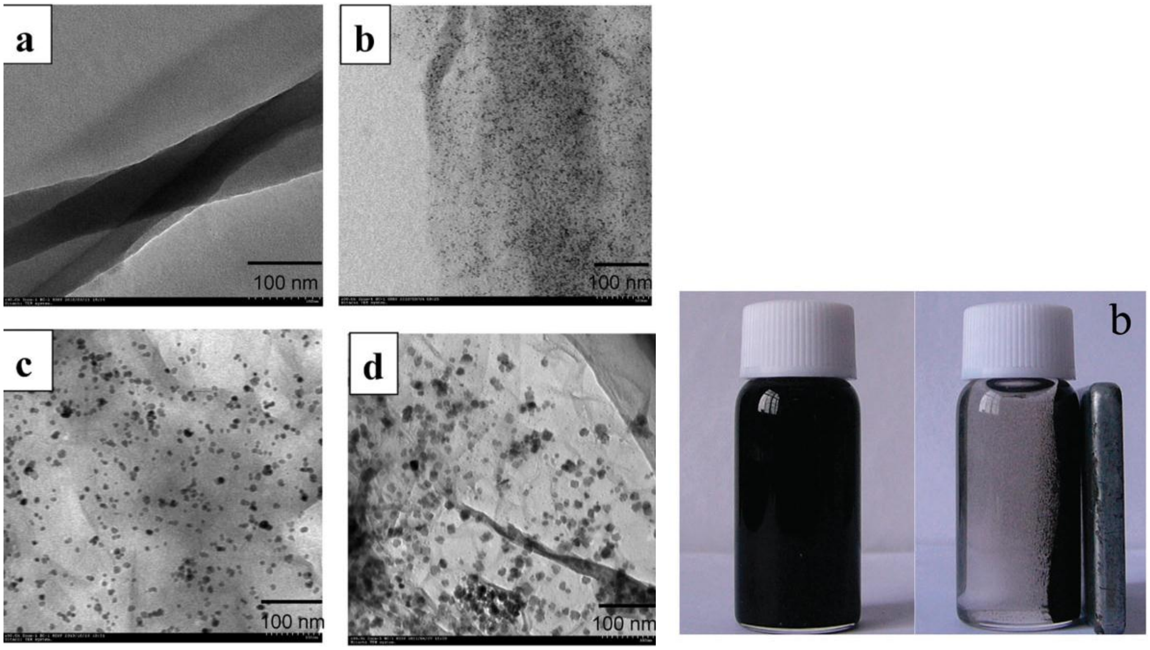


TEM images of graphene oxide supported (left panel) and chemically reduced graphene supported (right panel) palladium particles after a Suzuki coupling reaction.

New studies have been dedicated to enhancing the already excellent properties of organized carbon frameworks by doping or surface modification, or even by producing magnetic particles. Researchers believe that doping graphene sheets with nitrogen or boron may assist in building a tighter interface between catalyst and support. Nitrogen-doped graphene sheets have been used as a support for palladium and palladium oxide nanoclusters formed by a chemical reduction procedure.[26] When tested in a Suzuki reaction, this catalyst system gave complete conversion to the biphenyl product after one hour at 80 ^{o}C. Moreover, this catalyst could be recycled 4 times before a decrease in yield was observed. Ongoing work is being conducted to further evaluate the effects of nitrogen atoms.

A magnetic palladium-iron oxide-graphene species was recently reported by Hu and coworkers.[24] After 30 minutes at 100 ^{o}C, complete conversion to a biphenyl product was observed when testing this catalyst with a typical Suzuki reaction. Furthermore, the magnetic properties of this catalyst facilitated recovery: it only took 5 minutes to re-isolate the catalyst from the reaction solution using a simple magnet.

Figure 1- 11[27]



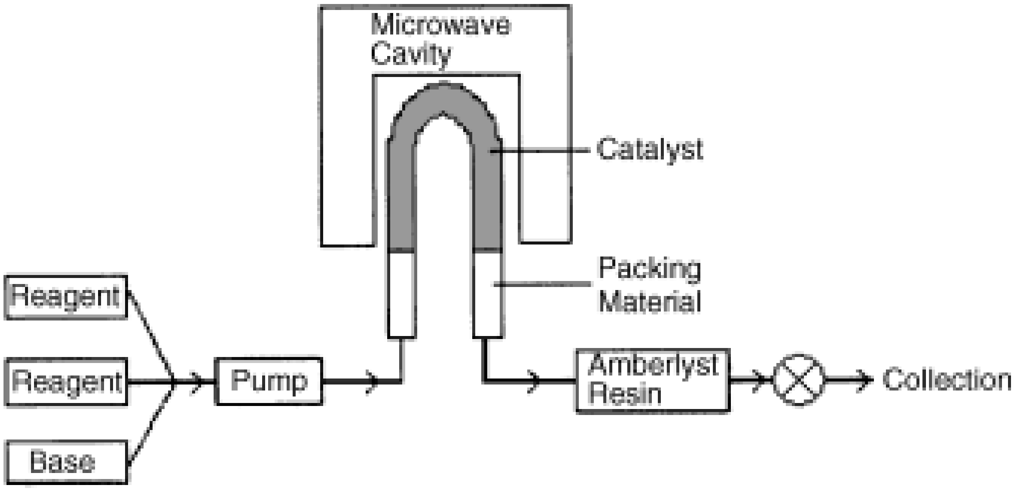
Graphene Supported Magnetic Palladium-Iron Nanoparticles

Elazab and coworkers also recently reported a graphene supported palladium iron oxide nanoparticle with magnetic properties and an excellent recyclability profile.[25] The turnover number and frequency for this catalyst are 9250 and 111,000 h^{-1} respectively.[28] Advancements and continued research in solid support development have made continuous coupling reactions an increasingly attractive option for academia and industrial settings, but there is still room for improvement in catalyst development and application.

1.6 Continuous Reactors and Their Role in Cross Coupling Reactions

The previously mentioned microencapsulated palladium acetate catalyst developed by Ley and co-workers was used in a continuous coupling reaction with a supercritical fluid solvent system. The catalyst was loaded into a microreactor as a packed bed. 4-Methylbiphenyl was produced by feeding 4-methylphenylboronic acid and iodobenzene at 0.2 mL/min over the packed bed at 70 ^{o}C of conventional heating.[29] Complete conversion was observed under these conditions. When flow rates were increased or the temperature was lowered, a dramatic decrease in product conversion was evident.

Figure 1-12[26]

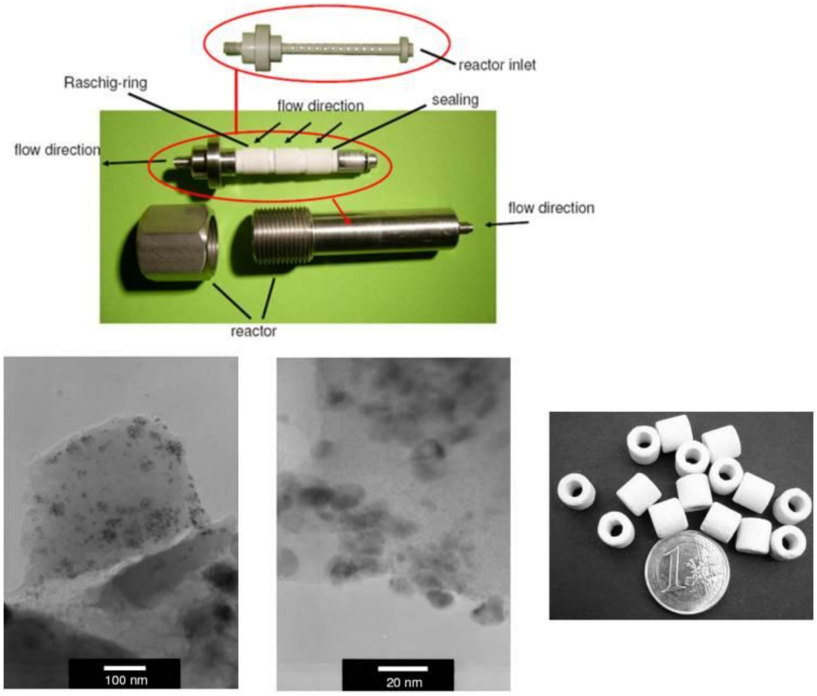


Microwave Assisted Continuous Reactor

The Ley group also used the packed bed reactor model to demonstrate the use of this encapsulated palladium catalyst with microwave heating.[26] In this case, a U-shaped glass tube was packed with 190 mg of the encapsulated palladium catalyst and placed in a microwave cavity (Figure 1-12). The reactants were fed at 0.1 mL/min over the bed using syringe pumps, then through an Amberlyst resin before being collected for further analysis.[26] Again, complete conversion was observed. It should be noted that microwave heating can dramatically increase the rate of reaction as the metal particles absorb such energy readily.

Monolithic flow reactors have also been used to conduct continuous coupling reactions. These reactors have polymer cells connected to the reactor where the metal catalysts are immobilized. This type of reactor was used by Kirschning for a continuous Suzuki reaction (Figure 1-13).[30] Reactants were fed to the reactor at flow rates between 0.1 mL/min and 1 mL/min. The continuous coupling of 4′-bromoacetophenone and phenylboronic acid was optimized at 85% conversion to the biphenyl product at 95 °C using conventional heating methods. Recyclability of the catalyst was also evaluated. The catalyst was used 10 times, but consistent conversions were not obtained. The lack of reliability in the recycling of this catalyst makes it an unrealistic option for commercial use. Leaching of the palladium catalyst was found to be 0.7 ppm for each run.

Figure 1-13[27]



Monolithic Flow Reactor

Development of solid supports for palladium catalysts has advanced to the point where the potential for industrial application of these systems is becoming apparent. This field of research is poised to transform the technology used to synthesize complex structures such as pharmaceuticals and other fine chemicals. This research project sought to exploit solid support systems and continuous technology to develop a catalyst system that readily goes through a cross-coupling catalytic cycle with high turnover number and frequencies, exhibits low leaching with a reaction system, and is compatible with multiple substrates. Furthermore this project aimed to use the developed catalyst in a continuous coupling reaction by employing of modern continuous reactors.

CHAPTER 2

Identifying a Viable Solid Support System and Deposition Technique for Palladium Nanoparticles

2.1 Background and Significance

The development of solid supported palladium nanoparticles has gained considerable attention due to their potential use in pharmaceutical synthesis, drug delivery, imaging, polymer development, and catalysis.[2] Researchers in catalysis have become increasingly interested in supported nanoparticles because of the enhanced reactivity afforded by increased active sites and because of ease in purification seen in initial studies.[2, 3] However, evaluating support systems for such particles has proven to not be a trivial task. An efficient catalyst support must be inert in the reaction mixture, supply a large surface area where particles may reside, offer great thermal and mechanical strength, and allow an optimum number of active sites to be available.[3] Silica, activated carbon, layered clay, and organic polymers have been used as supports for transition metal nanoparticles and a number of different transition metals[7,13,31]. Despite high conversions and yields observed using such catalyst systems, many have complex synthetic methods, require a significant amount of thermal energy within chemical reactions, and are not reusable over multiple reactions.[7] Recently, carbon-based materials, specifically graphene and carbon nanotubes have piqued significant interest in the electronics industry and in the field of catalysis due to their thermal and mechanical stability.[32,33]

Despite their appeal to multiple industries, the synthesis of both carbon nanotubes and graphene is complex and costly. Synthetic approaches may include the use of lasers, vapor deposition, and liquid phase exfoliation, amongst others. A number of studies have shown that various conformations of silicon, and boron nitride may offer similar mechanical and thermal stabilities to those of graphene and its derivatives.[34]

This project focuses on evaluating a variety of solid supported palladium nanoparticles. The aims for the initial studies were to identify both a viable option for a solid support system and a deposition technique to anchor the particle on the chosen support. An ideal deposition technique would decorate the surface of the support evenly with uniform metal palladium nanoparticles as well as be environmentally friendly. In addition to meeting these criteria, the support system should readily facilitate the detachment and redeposition of the palladium nanoparticles. Previous studies have suggested that the active species in the palladium cycle transfers into the liquid phase and completes the catalytic cycle.[11] The solid support system for the palladium nanoparticles would allow the palladium species to go into the reaction solution freely and successfully redeposit on the surface without deactivation.

Both graphene and carbon nanotubes have been used in the electronics industry because they readily allow the free transfer of energy. For this reason, these were the first materials investigated as possible solid support systems. Despite their established advantages, manufacturing remains expensive due to their complex synthesis techniques. Modeling studies have suggested that with the correct treatment, silica and boron nitride may exhibit the same electrical and mechanical properties as graphene and carbon nanotubes. Therefore, for economic reasons, silica and boron nitride were investigated as alternative solid supports. In this chapter, various particle deposition techniques are described. The resulting palladium–support complexes were then evaluated for catalytic activity in subsequent Suzuki cross coupling reactions. These preliminary studies were used to guide catalyst system choices for more in depth studies.

2.2 Methods

2.2.1 Deposition Techniques for Decorating Solid Supports with Palladium Nanoparticles

Two techniques to deposit palladium on solid supports, the mortar/pestle method and the ball-mill method, were developed in collaboration with Dr. Yi Lin at the NASA Langley research facilities. Both of these methods proved to be unique, and neither employed the use of a solvent, which greatly streamlined purification of final products. A third deposition method, microwave synthesis, was originally developed by Dr. El-Shall's research group in the Department of Chemistry at Virginia Commonwealth University, and unlike the two previous methods, employed a solvent to facilitate the reaction.

2.2.2 Materials

Multi-walled carbon nanotubes, MWNT, (outer diameter 6-9 nm, length of 5 µm, over 95% carbon), single walled nanotubes, SWNT, (diameter 0.7- 1.1 nm, over 90% carbon), palladium (II) acetate (98% reagent grade), palladium (II) nitrate solution (10 wt% in 10 wt% nitric acid), boron nitride powder, and silica nanopowder were obtained from Sigma. Graphene was supplied by the University of Kentucky chemical engineering laboratories.

2.2.3 Manual -Mortal Pestle Method:

To prepare solid supported Pd-nanoparticles with 10 wt% Pd loading, 100 mg of the solid support was mixed with solid palladium (II) acetate (22 mg) using a mortar and pestle until a homogenous mixture was obtained. The mixture was then divided into two glass vials, each containing equal mass. The first container was stored at room temperature for further analysis. The second glass vial was covered with aluminum foil with small holes to provide ventilation to the vessel. The vial and its content were heated in a nitrogen oven (Blue M Electric A-5245-Q Inert Gas oven) to 350 ^{0}C over 1 hour and held at a constant temperature for 3 hours. The resulting solid was collected for further analysis.

2.2.4 Ball Mill Method:

To prepare solid supported Pd-nanoparticles (10 wt%) using a ball mill mixer, 500 mg of the carbon support was loaded in a 45 ml zirconia grinding vial and 110 mg of palladium (II) acetate was loaded in the same vial. Two 12.77 mm diameter zirconia balls were also placed in the vial before sealing. The sealed vial was mechanically shaken using a 8000 M Spex Mixer/ Mill. The contents in the mixer were shaken back and forth 5.9 cm and side to side 2.5 cm for a specified time at 115 volts (1060 cycles/minute). The mixture was then divided into two glass vials (each containing equal mass). The first container was stored at room temperature for further analysis. The second glass vial was heated in a nitrogen oven (Blue M Electric A-5245-Q Inert Gas oven) to 350 C over 1 hour and held at a constant temperature for 3 hours. The resulting solid was collected for further analysis.

2.2.5 Microwave Synthesis

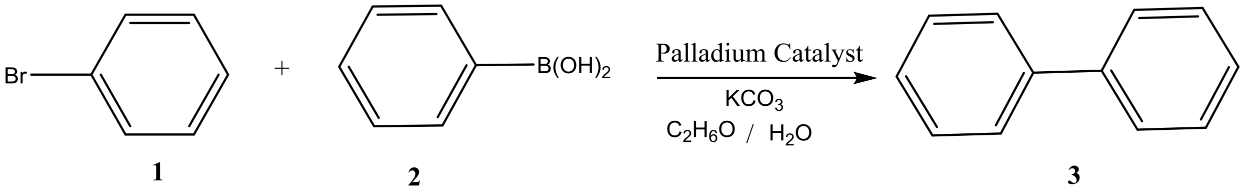
Solid support (0.1 g) was sonicated in deionized water (400 mL) until a homogenous suspension was obtained. Palladium nitrate (210 μL) was added to the suspension. This homogenous mixture was then placed in a Emerson conventional kitchen microwave where 100 μL of hydrazine hydrate (10 wt.% in 10 wt.% HNO_3, 99.999%) was added. The solution was immediately microwaved on full power (1000W) in 30-s cycles (on for 10 s, off and stirring for 20 s) for a total reaction time of 60 s. The resulting black solution was centrifuged in an Eppendorf 5804 centrifuge at 5000 rpm for 20 minutes and excess water was decanted from the reaction vessel. The mud-like substance was dried under vacuum until black flakes were obtained.

2.3 Characterization of Solid Supported Nanoparticles

2.3.1 Catalytic Activity in a Suzuki Cross Coupling Reaction

Each sample was first evaluated for their catalytic activity in a Suzuki cross coupling reaction. In a typical reaction, bromobenzene (**1,** 50 mg, 0.032 mmols, 1 eq.) is combined with a phenylboronic acid (**2**, 47 mg, 0.384mmol, 1.2 eq.), potassium carbonate (133mg, 0.96 mmol, 3 eq.), and a solid supported palladium catalyst in a 1:1 volume ethanol and water solvent mixture. The reaction mixture is heated using microwave irradiation for an allotted time. An aliquot of the solution is placed in 1 ml of acetonitrile and evaluated for the biphenyl product using gas chromatography-mass spectrometry (GC-MS). The Suzuki reaction used is shown in Scheme 2-1.

Scheme 2-1



Suzuki reaction used to evaluate catalyst activity levels

2.4 Results and Discussion

Five different solid supports were used for each deposition technique resulting in 15 samples in total. Each was first evaluated in the prescribed Suzuki reaction in a batch microwave reactor for 10 minutes at 150 ^{0}C with 3 mol% catalyst loading. Testing the reactivity was the first analysis because it is the fastest way to identify a procedure that may potentially be optimized.

As a standard of comparison, commercially available palladium on activated carbon was also evaluated under the same conditions. Upon GC-MS analysis the commercially available palladium on carbon had full conversion to the biphenyl product under these reaction conditions.

Table 2-1

Ball milled Samples Percent Conversion		
1	Multi-walled Carbon Nanotubes	100
2	Single-walled Carbon Nanotubes	100
3	Graphene	62
4	Boron Nitride	50
5	Silica	42
Mortar and Pestle Samples Percent Conversion		
6	Multi-walled Carbon Nanotubes	93
7	Single-walled Carbon Nanotubes	90
8	Graphene	98
9	Boron Nitride	100
10	Silica	88
Microwaved Samples Percent Conversion		
11	Multi-walled Carbon Nanotubes	35
12	Single-walled Carbon Nanotubes	20
13	Graphene	100
14	Boron Nitride	10
15	Silica	N/A

Reaction Temperature: 150 ^{o}C, Reaction time: 10 minutes, Catalyst loading 3 mol%

For the initial studies an acceptable catalyst was defined as one whose GC-MS product conversion was 95% or greater. It is believed that with other advantages of solid supported catalysts – namely the possible recyclability and decreased product contamination - the slight difference in the product conversion for the commercially available catalyst will become negligible. As shown in Table 2-1,seven samples were able to satisfy these conditions - samples 1, 2, 6,7,8,9 and 13. These catalysts were taken on for further characterization.

Fresh samples of each of these catalysts were further evaluated in a Suzuki reaction with reduced energy from microwave irradiation and a reduced reaction time. The temperature on the CEM microwave was set to 80 ^{o}C for five minutes with a 3 mol% catalyst loading. Table 2 shows the GC-MS product conversions from the synthesized catalysts. For these sets of experiments, a good catalyst was defined as a catalyst for which the GC-MS product conversion was 90% or greater. As before, palladium on activated carbon was also evaluated under the same conditions, and it yielded a 95% conversion upon GC-MS analysis.

Table 2-2

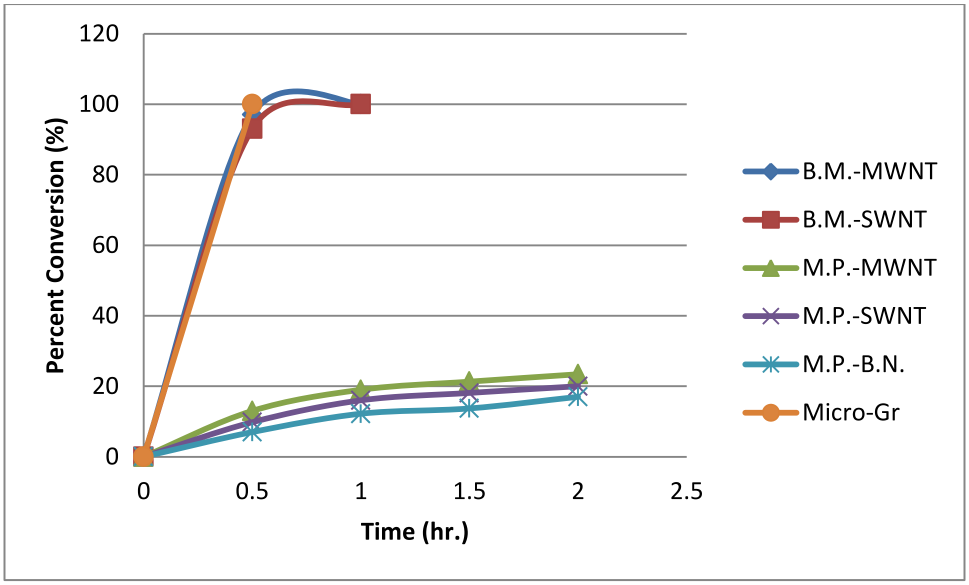
Ball milled Samples Percent Conversion		
1	Multi-walled Carbon Nanotubes	100
2	Single-walled Carbon Nanotubes	100
Mortar and Pestle Samples Percent Conversion		
6	Multi-walled Carbon Nanotubes	93
7	Single-walled Carbon Nanotubes	93
8	Graphene	97
9	Boron Nitride	90
Microwaved Samples Percent Conversion		
13	Graphene	100

Reaction Time: 5 min. Reaction Temperature: 80 ^{o}C, Catalyst loading 3 mol %

The slight difference in the conversion of the commercially available catalyst and the synthesized catalysts will become negligible if the desired catalyst is recyclable and displays little to no product contamination by metal leaching. Because no catalyst was eliminated from this round of experiments, the catalyst loading was significantly reduced (to 0.5 mol%) and the reaction temperature and time were set to 80 ^{o}C and 10 minutes. All samples achieved 90% and above percent conversion to the desired product under these conditions.

In order to determine the most promising catalyst system, a final test for reactivity was conducted at room temperature with only 0.5 mol % catalyst loading. Each sample was mixed in a microwave test tube and placed on a stir plate. Aliquots were taken for GC-MS analysis from each reaction every 30 minutes until product conversion reached completion or the reaction showed minimal change in conversion through 3 separate aliquots. Graph 2-1 shows the results from these experiments.

Graph 2-1



B.M.-MWNT-Balled milled multi-walled tubes, B.M-SWNT-Balled milled single-walled nanotubes, M.P.-MWNT-Mortar Pestle multi-walled nanotubes, M.P.-SWNT- Mortar pestle single-walled nanotubes, M.P.-B.N.- Mortar Pestle Bronon Nitride, Micro-Gr- grapheme catalyst loading: 0.5 mol%, reaction temperature: room temp.

Unlike the results from microwave irradiation reactions, none of the catalysts synthesized using the mortar pestle method exhibited conversion over 50%. However, both the multi-walled and single-walled supported nanoparticles that were ball milled and the graphene supported particles that were microwaved exhibited high conversion after only 30 minutes. It should be noted that commercially available palladium on activated carbon only reached 38% conversion after 2 hours. The low catalyst loading and reduced thermal energy requirements indicate that the ball-milled and microwave-generated catalyst systems evaluated here are highly reactive and are good candidates to use in continuous reactions where the reaction must take place quickly and efficiently. From these results, it was concluded that these three catalysts would be the main focal point for continued synthesis and evaluation.

Despite the discontinued use of the samples evaluated during reactivity testing some explanation of their failure may be offered. All of the silica samples, regardless of the deposition technique, exhibited significant swelling after the reaction had been completed. For this reason, the silica systems would have been eliminated as solid support candidates even if product conversion had been higher. It should also be noted that in these instances product conversion evaluation was limited to the small amount of solvent that had not been absorbed by the silica support.

The ball milled deposition technique only worked for the supports that are 3-dimensional in nature, namely the carbon nanotubes. All other samples, including the graphene surface, can be considered 2-dimensional. It may be speculated that because the main driving force in this deposition method is a mechanical force, the surface must have some depth for particle growth. There are two stages to nanoparticle synthesis: nucleation and growth. The 3-dimensional surface assists in providing a nucleation site for the particles since strong physical contact is needed when no solvent is present. TEM images of the graphene sample decorated using the ball milled deposition method further support this argument, as barely any visible particles are seen (Figure 2-1). Moreover, XPS analysis of the ball milled graphene sample indicated that the dominant palladium species remained in the palladium oxide and salt oxidation states, suggesting that the palladium precursor failed to decompose and transform into palladium metal.

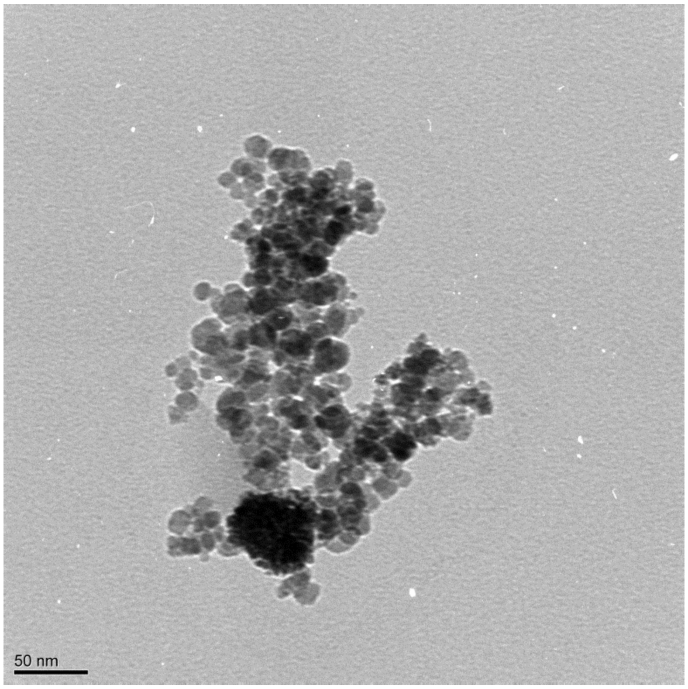
Figure 2-1

TEM/SEM image of ball milled graphene surface with only a small amount of palladium nanoparticles visible.

The same explanation may be valid for the mortar and pestle method. Furthermore, the mortar and pestle method's lack of success with the 3-dimensional surfaces may additionally be due to variable and inconsistent mechanical force applied when mixing because of a researcher's physical strength rather automated force as in the ball milled method.

The microwave assisted synthesis, which required the use of a solvent, proved to have its own difficulties as well. Boron nitride has only limited solubility in water. While other solvents were considered, including ethanol, diglyme, and benzene, their feasibility at this time is unknown and further investigation is needed to draw conclusions about their future use. The boron nitride constantly needed to be re-suspended, even after ultra-sonication treatment. This observation may suggest that the mixture used to synthesize the catalyst was not truly homogeneous in this case. Thus, instead of the boron nitride acting as a nucleation site for particle growth, the palladium species adhered to other palladium particles and grew into large agglomerates unbound to the boron surface. This theory was confirmed by TEM images shown in Figure 2-2.

Figure 2-2



TEM image of microwave assisted boron nitride "supported" nanoparticles. Palladium nanoparticles have formed agglomerates and are not found on any support system.

2.5 Conclusion

Two deposition techniques (ball mill and microwave assisted synthesis) have been identified as possible methods for manufacturing solid supported palladium nanoparticles. The ball mill method is unique, as it does not use a solvent and has no excess waste. Also, large quantities of catalyst may be made in a single pass when using this method. Lastly, this method is environmentally friendly as excess waste is not produced. While this method is environmentally friendly, it is limited to 3-dimensional substrates (single-walled and multi-walled carbon nanotubes), as a strong physical contact is needed to effectively decompose and deposit palladium metal on the surface.

The microwave assisted deposition method is a facile way to produce catalyst that employs the use of a non-toxic and environmentally benign solvent, water. This particular method is dependent on a substrate’s ability to evenly disperse in the solvent system, which limited success during this study to only the graphene support. Also, by using microwave energy this catalyst synthesis is completed at a much faster rate than conventional heating techniques may have afforded.

In summary, three types of support systems (multi-walled nanotube, single- walled nanotubes, and graphene) were identified that effectively facilitate the rapid completion of the palladium cycle in a Suzuki cross coupling, reaching complete conversion in 30 minutes at room temperature in 0.5 mol% catalyst loading. One of two different deposition techniques were required to achieve this high level of catalytic activity; the choice was dependent on the physical characteristics of the carbon-based support in question. Subsequent chapters will focus on the in-depth analysis of these three catalyst systems.

Chapter 3

Comparative Study of Ball Milled Multi-Walled and Single-Walled Nanotubes Supported Palladium Nanoparticles: A Viable Catalyst for Suzuki Cross Coupling Reactions

3.1 Introduction/ Background Information

In the previous chapter three different supports and two deposition techniques were identified as viable options to synthesize solid supported palladium nanoparticles, ball milled MWNT and SWNT, and microwave synthesized graphene. This chapter focuses on comparing the ball milled MWNT and SWNTs. Carbon nanotubes are a type of fullerene that may be divided into two classes, single walled and multi-walled nanotubes.[35, 36] Single walled nanotubes are characterized by their single sheet of hexagonal carbon rings wrapped into a cylindrical column. Single walled nanotubes are extremely difficult to synthesize and are typically made on very small scales by chemical vapor deposition or carbon arc discharge/electric arc technique.[37] Their complex synthesis techniques make them costly to obtain, with a cost of approximately $750 per gram in 2013 for high purity single walled carbon nanotubes.[34]

Multi-walled carbon nanotubes may be described as multiple sheets of hexagonal wrapped in cylindrical columns with a defined center. [22-25] Like single-walled nanotubes, the multi-walled analogs may be synthesized using laser ablation, chemical vapor deposition, or carbon arc discharge.[38] Comparative studies evaluating the mechanical, thermal and electrical properties of the two classes of structures have cited the multi-walled nanotubes' extra layers as the source of its superior thermal and mechanical stability when compared to single-walled carbon nanotubes.[39] Despite their differences, both classes of carbon nanotubes showed enhanced abilities when compared to other commercially available support materials. Researchers are now evaluating multiple uses, semiconductors, catalyst supports, hydrogen storage vessels, for carbon nanotubes particularly as support systems.

An extensive comparative study was conducted on both the single-walled and multi-walled ball milled systems to gain a better understanding of the effects of ball milling and the differences between the multi-walled and single walled systems and evaluate if any of these samples are candidates for continuous Suzuki cross coupling reactions. This work was done in collaboration with Dr. Yi Lin and Dr. John Connell at NASA Langley research facilities, and with Dr. Ali Siamaki at Virginia Commonwealth University Chemical and Life Science Engineering department.[40] The carbon nanotube supported Pd catalysts were also evaluated for their reactivity in continuous cross coupling reactions.

3.2.1 Materials and Methods

To prepare solid supported Pd nanoparticles (10 wt%) using a ball mill mixer, 500 mg of the carbon nanotube support were loaded in a 45 ml zirconia grinding vial. 106 mg of palladium (II) acetate were loaded in the same vial. Two 12.77 mm diameter zirconia balls are also placed in the vial before sealing. The sealed vial was mechanically shaken using an 8000 M Spex Mixer/ Mill for 30 minutes. The contents in the mixer were shaken back and forth (5.9 cm) and side to side (2.5 cm) for a specified time at 115 volts (1060 cycles/minute). The mixture was then divided into two glass vials (each containing equal mass). The first container was stored at room temperature for further analysis. This approach is referred to as the mechanical route. The second glass vial was heated in a nitrogen oven (Blue M Electric A-5245-Q Inert Gas oven) to 350 C over 1 hour and held at a constant temperature for 3 hours. The resulting solid was collected for further analysis. These samples were said to follow the thermal route.

3.2.2 Characterization of Palladium Carbon Nanotube Samples

TEM images were obtained using a JOEL JEM-1230 electron microscope operated at 120 kV. The microscope is equipped with Gatan UltraScan software and CCD camera (4000SP 4K x 4K). TEM samples were prepared by adding one droplet of suspended sample in methanol on a Formvar carbon-carbon, 300 mesh copper grid, obtained from Ted Pella, and allowed to evaporate in air at room temperature. X-ray photoelectron spectroscopy (XPS) was performed on a Thermo Fisher Scientific ESCALAB 250 using a monochromatic Al KR X-ray. Dry samples were mounted to a sample holder using two way carbon tape and indium foil.

3.2.3 Procedure for Batch Suzuki Reactions

Batch cross-coupling reactions were performed in a CEM Discover microwave reactor operating at a maximum output power of 250 W. Bromobenzene (50 mg, 0.32 mmol, 1 eq.) was dissolved in a 4 mL mixture of H_2O/EtOH (1:1) and placed in a 10 mL microwave tube. Phenylboronic acid (47 mg, 0.38 mmol, 1.2 eq.) and potassium carbonate (133 mg, 0.96 mmol, 3 eq.) were added to the same tube. Pd/nanotubes (5 mg, 2 mol% based on Pd content) was then added, and the tube was sealed and heated under microwave irradiation (250 W, 2.45 MHz) at 80 ^{o}C for 10 minutes. Reaction conversions were determined using an Agilent 6890 gas chromatograph (GC) equipped with an Agilent 5973 mass selective detector.

3.2.4 Procedure for Suzuki Recycling Studies

All recycling studies were carried out by Dr. Ali Siamaki. Bromobenzene (50 mg, 0.32 mmol, 1 eq.) and phenylboronic acid (47 mg, 0.384 mmol, 1.2 eq.) were dissolved in 4 mL of H_2O:EtOH (1:1) and placed in a 10 mL microwave tube. Potassium carbonate (133 mg, 0.96 mmol, 3 eq.) was added to the mixture along with Pd/nanotubes(3 mg, 3.2 μmol, 1 mol%). The tube was sealed and heated at 80 ºC for 10 minutes under microwave irradiation (250 W, 2.45 MHz), and the progress of the reaction was monitored by the GC-MS analysis. Upon the completion of the reaction period, the mixture was diluted with 10 mL of ethanol and shaken. The entire mixture was centrifuged and the solvent above the Pd/nanotube was completely decanted. The washing and centrifugation were repeated for two additional times to ensure the removal of the organic products from the surface of the catalyst. The Pd/nanotube was then reused for the subsequent reaction adding fresh reagents to the tube. This procedure was applied for every recycling experiment and the percent conversion to the products was determined by means of GC-MS spectroscopy.

3.2.5 Procedure for Continuous Suzuki Reaction

4-Bromobenzaldehyde (**1b**, 625 mg, 3.37 mmol, 1 eq.) was dissolved in 100 mL of H_2O/EtOH/THF (1:1:1) and placed in a 150 mL flask. Phenylboronic acid (**2b**, 494 mg, 4.05 mmol, 1.2 eq.) and potassium carbonate (1400 mg, 10.1 mmol, 3 eq.) were added to the same flask. For the preparation of the catalyst cartridge, Pd/carbon nanotube (100 mg) was suspended in deionized water and loaded with a syringe into a stainless steel cartridge (70 x 4 mm) fitted with a porous metal frit and an 8 µm membrane at one end. The catalyst bed was established by filtering off the water by applying vacuum to the base of the cartridge. The other end of the cartridge was then sealed with a 8 µm membrane and placed in the cartridge holder on the X-cube. Solvent was pumped through the apparatus and the temperature was changed to the set point in 5 ^{o}C increments to equilibrate the system. Once the desired temperature was reached, the reagent solution was fed into the X-cube at a flow rate of 0.2 mL/min. Samples were collected in 30 minute increments and analyzed by GC-MS as previously described

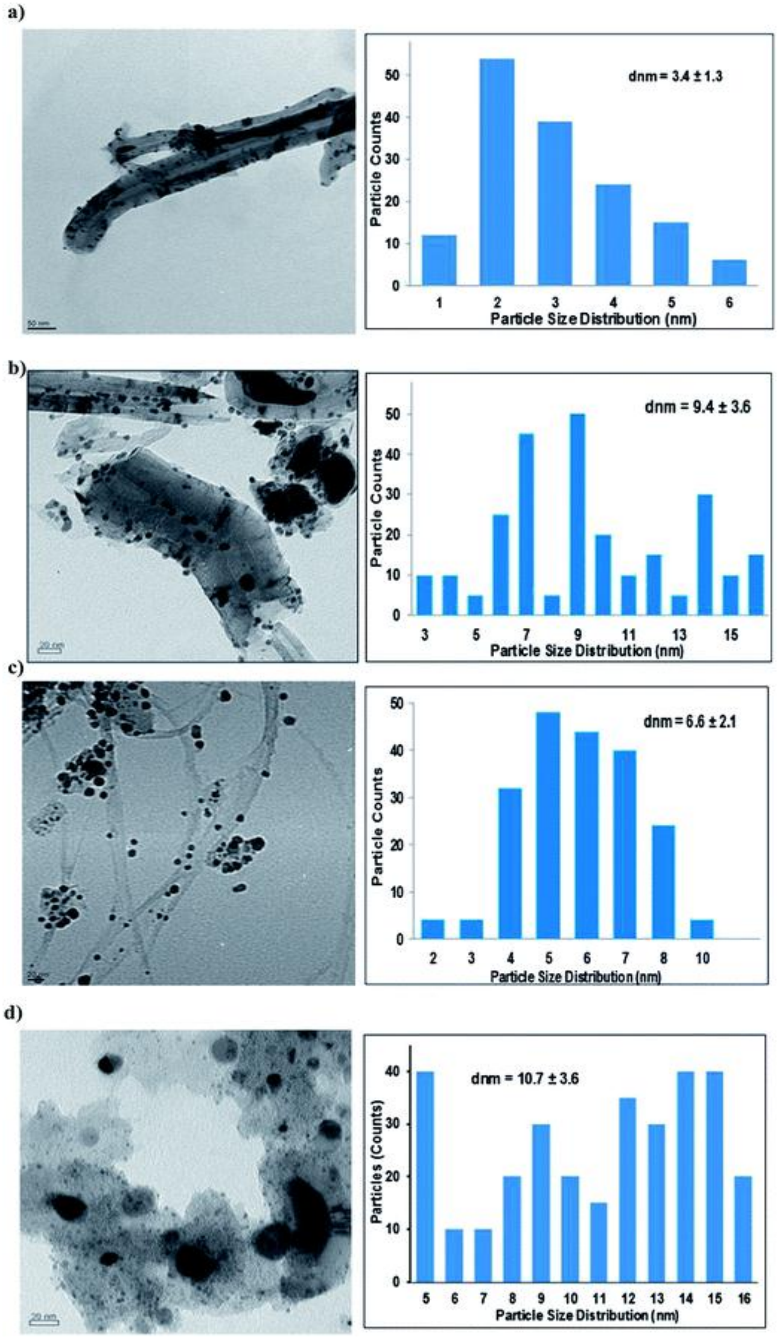
3.3 Results and Discussion

3.3.1 Thermal Effects on Particle Formation

Four samples of solid supported palladium catalysts were obtained using the ball mill deposition methods follow two treatment routes mechanical and thermal treatment. The samples are referred to as the following: thermally treated multi-walled nanotubes $(Pd/MWNT)_T$, thermally treated single-walled nano tubes$(Pd/SWNT)_T$, mechanically treated multi-walled tubes

(Pd/MWNT)$_{M,}$ and mechanically treated single -walled nanotube (Pd/SWNT)$_{M.}$ The two routes had clearly definable trends in particle formation.

Figure 3-1

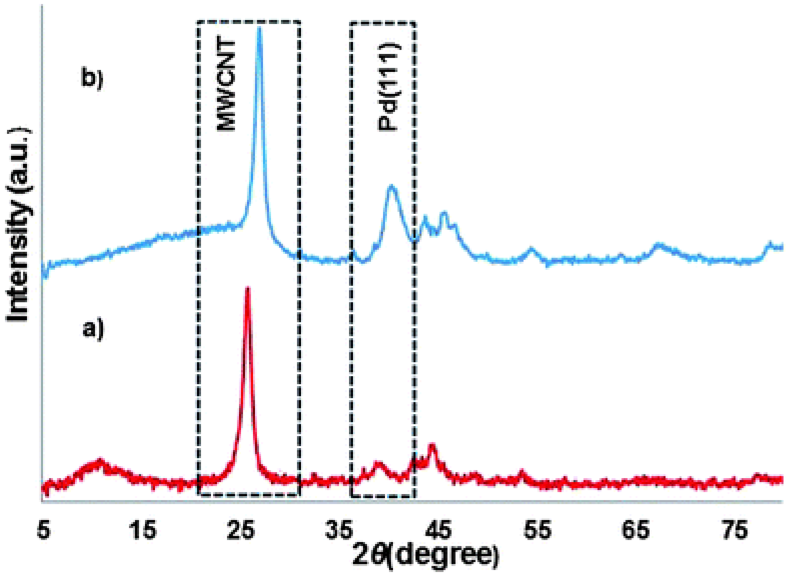


TEM images of Pd/MWCNT and Pd/SWCNT nanoparticles (a) (Pd/MWCNT)$_M$ (b) (Pd/MWCNT)$_T$ (c) (Pd/SWCNT)$_M$ (d) (Pd/SWCNT)$_T$.

When examining the palladium nanoparticles formed on the MWNT surface by TEM, samples that were only mechanically treated exhibited much smaller particles than those that were thermally treated, with average diameters of 3.4 nm +/- 1.3 vs. 9.4nm +/- 3.6 respectively. Though the SWNT samples followed the same patterns, particles on these surfaces were overall larger for both deposition routes when compared to MWNT, averaging 6.6 +/- 2.1 nm and 10.7 +/- 3.6 nm respectively. Nanoparticles were formed by the decomposition of palladium salt into palladium metal along with side products such as CO, $CO_{2,}$ water, and acetic acid. The decomposition was triggered by mechanical energy and further promoted by thermal energy, with no other reducing agent required. It is believed that during thermal treatment of the samples, Ostwald ripening simultaneously occurs. Ostwald ripening is a thermodynamically favorable process that occurs because large particles are energetically more stable.[41] During this process large particles are formed when smaller particles redeposit themselves on larger particle forming larger particles.[27, 38] This process accounts for the larger particle sizes observed on both of the thermally treated samples. The general increase in particle diameter on the SWNT also suggests that Ostwald ripening is more likely to occur in this system even without thermal treatment. This phenomenon may be due to the decreased surface area on the single walled carbon nanotubes for the nucleation and subsequent growth of the particle to occur. Lastly, it should be noted that SWNT were almost indistinguishable after ball-milling treatment; their characteristic structural features were unrecognizable in TEM images. The amorphotized nanotubes were further hidden by impurities within the SWNT, as MWNT were seen by TEM. Nevertheless, palladium was deposited on the surface of the nanotubes. The extent of this deposition was examined by inductively coupled plasma mass spectroscopy (ICP-MS), which revealed that the with a 10 wt%

target the $(MWNT)_{M}$, $(MWNT)_{T}$, $(SWNT)_{M}$, and $(SWNT)_{T}$ were loaded with 8.5 wt%, 7.3 wt%, 7.3 wt%, and 7.0 wt% Pd respectively.

Figure 3-2

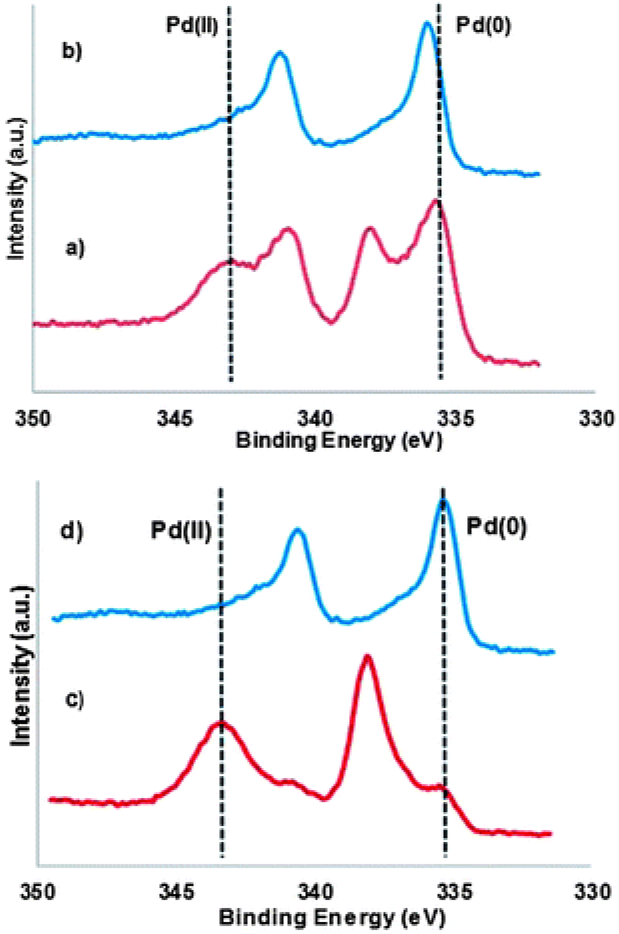


X-Ray Diffraction Patterns

The palladium presence was also confirmed by X-ray diffraction patterns shown in figure 3-2. The peaks at 2*θ*, 26° were assigned to the signature graphitic layered structure, the (002) peak of MWCNTs in $(Pd/MWCNT)_{M}$ and $(Pd/MWCNT)_{T}$, respectively (Figure 3-2a and 3-2b). The typical XRD patterns of Pd(0) are observed in the $(Pd/MWCNT)_{T}$ spectrum in Figure 3-2b. Palladium metal exhibits a four peaks consistent with the (111) d-spacing of the atom, that corresponds with 40.1^{o}. $(Pd/MWCNT)_{M}$ sample palladium peaks were less discernible by XRD.

This is likely due to the decreased salt to metal conversion that this sample experienced. The extent of palladium reduction was further examined by X-ray photonelectron spectroscopy (XPS).

Figure 3-3

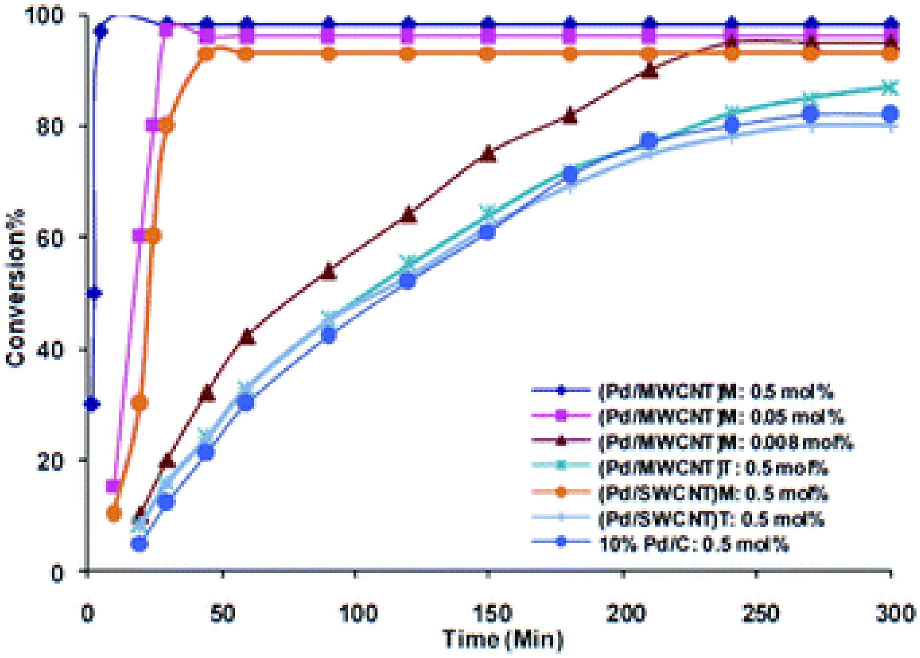


XPS spectra of a. (Pd/MWNT)$_M$ b. (Pd/MWNT)$_T$ c. (Pd/SWNT)$_M$ and d.(Pd/SWNT)$_T$

XPS is a technique used to examine the surface chemistry (first 10 nm) of a material. In these experiments it was used to evaluate the chemical state and chemical composition of the atoms on the surface. It measures the kinetic energy and intensity of excited electrons. Palladium (0) metal exhibits doublet peaks at binding energies of 335.3 eV and 340.6 eV, resulting from the magnetic spin of the palladium core electrons. Deconvolution of the XPS spectrum of the $(MWCNT)_M$ indicates the presence of Pd(0) with corresponding peaks at 335.8 and 341.0 eV, but also another palladium species, Pd(II), at binding energies of 338.1 and 343.3 eV, in a ratio of 52% to 48% respectively. The $(MWCNT)_T$ spectrum shows Pd(0) metal (90%) as the dominant palladium species with doublet peaks at 336.0 and 341.4 eV, indicating decomposition more complete conversion of palladium acetate into Pd metal under the thermal conditions. As previously stated, the high decomposition of the palladium salt precursor to palladium metal is likely responsible for the increase in particle diameter observed. Following the same general trend, XPS spectra of $(Pd/SWCNT)_M$ show measured binding energies of at 338.2 and 343.6 eV corresponding to Pd(II) as the dominant palladium species (74%). The thermally treated SWNT sample $(SWNT)_T$ showed increased decomposition of the salt precursor with peaks at at 335.4 and 340.7 eV, indicating that Pd(0) is the dominant species in this sample.

3.3.2 Catalytic Activity

Figure 3-4



Catalytic Activity at room temperature and varying concentrations

Dr. Siamaki tested the catalytic activity of each sample using a Suzuki coupling reaction of bromobenzene and phenylboronic acid at room temperature with varying catalyst concentrations. At 0.5 mol% loading, the $(Pd/MWCNT)_M$ nanoparticles showed complete conversion (100%) to the biphenyl product within 5 minutes at room temperature. However under the same conditions the $(Pd/MWCNT)_T$ sample was only able to achieve 78% conversion after 6 hours to the desired biphenyl product. Similarly, the $(Pd/SWCNT)_M$ achieved 95% conversion after 30 minutes, and the $(Pd/SWCNT)_T$ reaction only proceeded with 75% conversion after 5 hours. $(Pd/MWCNT)_M$ samples were the most catalytically active in a Suzuki cross coupling reaction at room temperature. The reactivity of the (Pd/MWCNT)$_M$ was further tested by decreasing the catalyst loading to 0.05 mol% and 0.008 mol% at room temperature. At 0.05 mol%, the catalyst system was still able achieve 98% conversion to the desired product in 30 minutes and 100% conversion in 3 hours. At 0.008 mol% the catalyst was able to convert 98% in 3 hours. Turnover number and frequency were calculated for this particular sample and were found to be 7250 and 217500h^{-1} respectively. These values are more than reported values of other solid supported palladium catalyst. The superior catalytic ability may be attributed to the evenly distributed small particles. The MWNT's electron rich surface may also play a role in enhancing the reaction rate.

Literature has suggested that solid supported palladium undergoes a release and redeposition onto the support during the catalytic cycle.[12] To test this theory with the carbon nanotube catalyst systems, two experiments were designed in order to learn more about the possible mechanism: recycling studies and ICP-MS evaluation of the product solution. During the recycling studies (Table 3-1), the (MWNT)$_M$ again showed superior activity; this catalyst was recycled 8 times before a significant decrease in product conversion was observed in a coupling reaction between iodobenzene and phenylboronic acid.

Table 3-1

Run	**Percent Conversion** [a] **$(Pd/MWNT)_M$**	**Percent Conversion** [b] **$(Pd/MWNT)_M$**	**Percent Conversion** [a] **$(Pd/SWNT)_M$**	**Percent Conversion** [b] **$(Pd/SWNT)_M$**
1	100	100	100	100
2	100	100	100	100
3	100	100	98	100
4	100	100	78	100
5	85	100	60	100
6	60	100	45	100
7	42	100	-	100
8	-	100	-	100
9	-	100	-	62
10	-	70	-	48
11	-	52	-	-

a Bromobenzene, $(Pd/MWCNT)_M$ or $(Pd/SWCNT)_M$, *b* Iodobenzene and $(Pd/MWCNT)_M$ or $(Pd/SWCNT)_M$ Conversions were determined by GC-MS.

A fresh Suzuki reaction using bromobenzene and phenylboronic acid with 0.05 mol% catalyst loading was prepared. The mixture was heated in the CEM microwave at 80 ^{o}C for 10 minutes.

The product solution was hot filtered over celite and analyzed using ICP-MS. Only 200 ppb of palladium were found in the final product solution. New bromobenzene and phenylboronic acid were introduced to the filtered product solution and heated again with irradiation at 80 ^{o}C for 10 minutes. No additional product conversion was observed. This evidence suggests a strong interaction between the palladium nanoparticles and MWNTs, and indicates that if the release and redeposition mechanistic proposal is accurate, then the redeposition of Pd nanoparticles onto the carbon nanotubes is favorable and efficient since it is readily reused. Both solvent investigations and modeling studies are underway to understand the fundamental components of the metal-surface interaction and the catalytic mechanism.

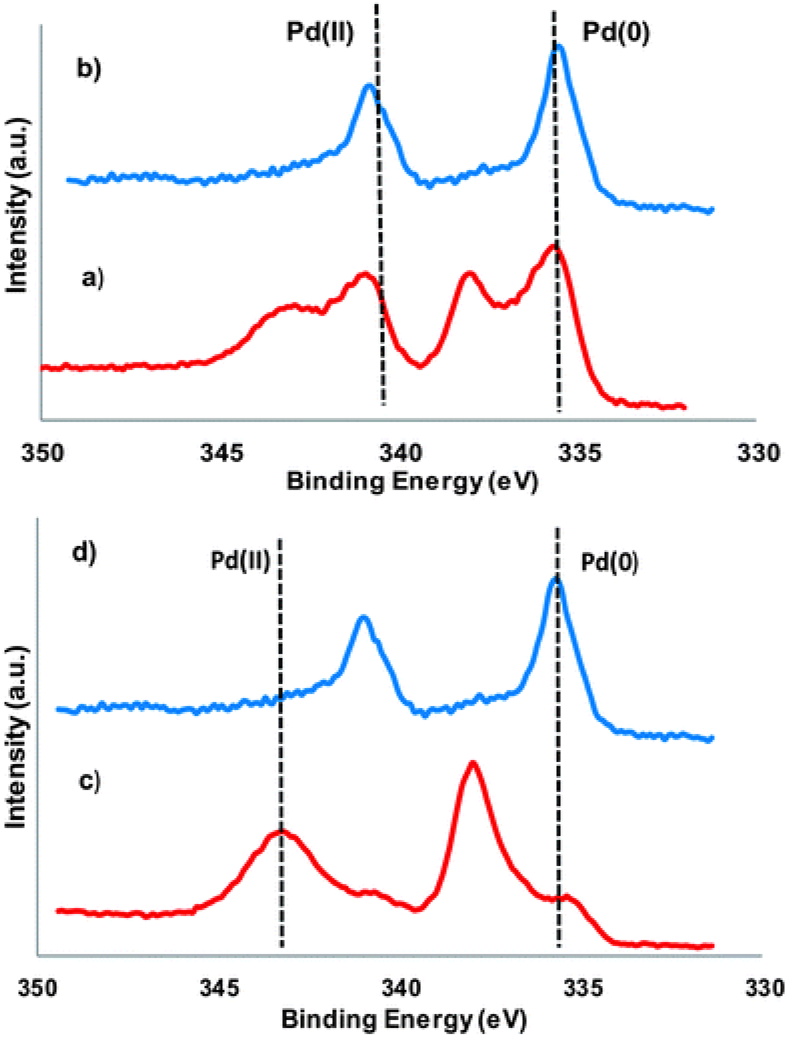
Table 3-2

	(Pd/MWNT)$_M$	**(Pd/MWNT)$_T$**	**(Pd/SWNT)$_M$**	**(Pd/SWNT)$_T$**
Particle Diameter (nm)	**3.4 +/- 1.3**	**9.4 +/- 3.6**	**6.6 +/- 2.1**	**10.7 +/- 3.6**
Pd (0) Content (%)	**52**	**90**	**74**	**100**

Summary of Physical Characteristics of Synthesized Catalyst

. The data initially suggest that while diameter size is an important contributor to reactivity in a Suzuki reaction, the palladium content is a smaller factor as the mechanically treated (Pd/MWNT)$_M$ exhibited the best conversion. Yet, results up to this point gave little indication on why the system was recyclable or the mode of deactivation for the catalyst. To understand this phenomenon, surface characterization of each recycled catalyst was conducted using both XPS (Figure 3-5) and TEM (Figure 3-6).

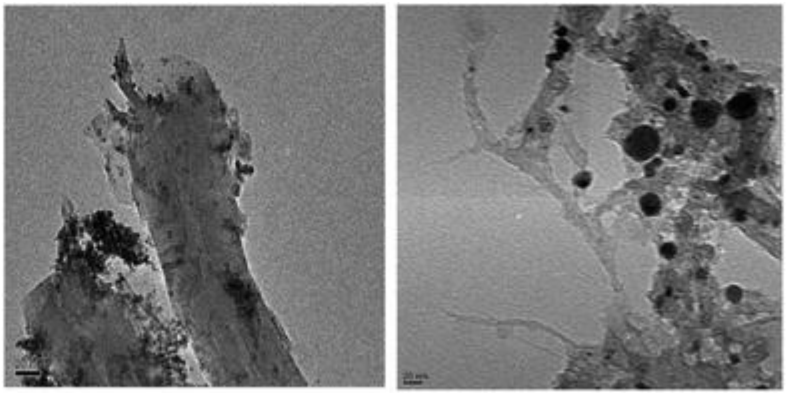
Figure 3-5



XPS Spectra a- Before Suzuki reaction $(Pd/MWNT)_M$ b- After Suzuki reaction $(Pd/MWNT)_M$ c- Before Suzuki reaction $(Pd/SWNT)_M$ d- After Suzuki reaction $(Pd/SWNT)_M$

The XPS spectrum for both the $(Pd/SWNT)_M$ and the $(Pd/MWNT)_M$ showed that Pd(0) was formed during the reaction as seen by the disappearance of Pd(II) peaks. This is most likely facilitated by a protic solvent under basic conditions, which may act as a reducing agent. Another plausible theory is the microwave heating. Carbon nanotubes are often described as great conductors of electrical current and absorbent materials. Microwave energy during the Suzuki reaction may have been absorbed by the support and transferred to the nanoparticle, resulting in decomposition of the Pd(II) species. If the microwave treatment acts similarly to thermal treatment, we anticipated that we also would see the formation of larger particles. Another possible mode of deactivation could be leaching of palladium in the solution. Further characterization of recycled catalysts and reaction mixtures was pursued in order to address the potential for Pd agglomeration and/or leaching to play a role in catalyst deactivation.

Figure 3-6



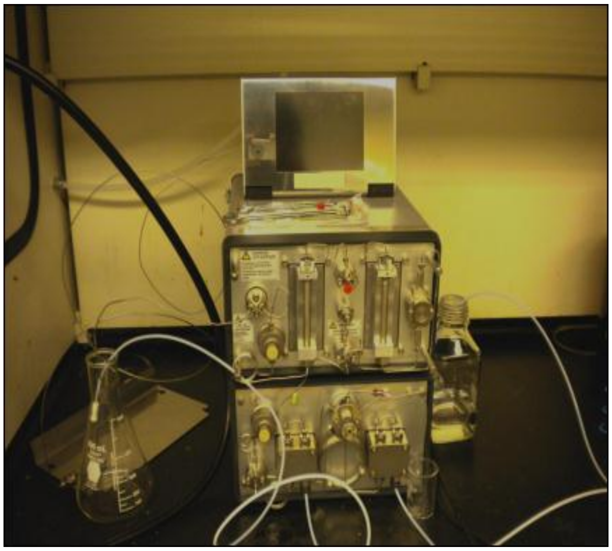
Significant agglomeration of (a) (Pd/MWCNT)$_M$ after the 6th run (b) (Pd/SWCNT)$_M$after the 5th run.

As suspected, TEM analysis of recycled catalysts (Figure 17) indicated significant agglomeration of particles on both the single walled and multi-walled nanotubes. This factor could contribute to the deactivation of the catalyst. ICP-MS was also conducted on the filtered reaction mixture to verify that palladium leaching could not be a major contributor to the deactivation of the catalyst. The concentration for palladium in the reaction mixture for mechanically treated $(Pd/MWNT)_M$ and SWNT was found to be 150 and 350 ppb respectively. These data eliminate leaching as a major factor in the deactivation of the catalyst. Therefore we concluded that the primary mode of deactivation was the decreased dispersion of uniform particles, and the corresponding decreased availability of reaction sites because of agglomeration.

3.4.1 Continuous Cross Coupling Reactions.

There have been many proven advantages to the use of continuous methods to synthesize complex molecules, including but not limited to increased mixing, smaller volume to heating ratio, user friendly. However, when converting a traditional batch synthesis into a continuous process, a number of design features must be considered, such tubing size& material, type of pump, reactor volume. Such features may affect the type of solvent used, operating flow rates, and solubility of the reactant.

Figure 3-7



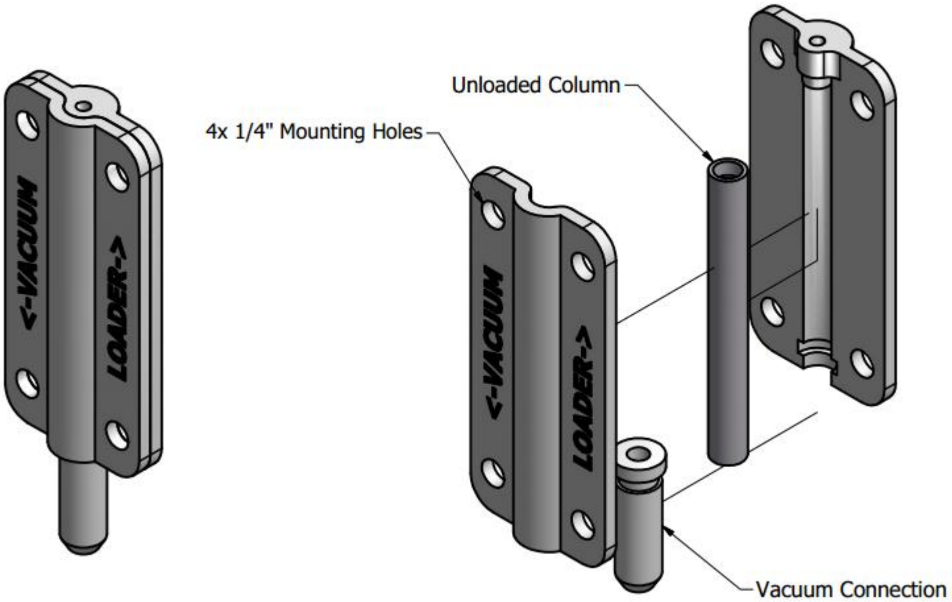
X-Cube Continuous Reactor

All continuous reactions were carried out in the X-Cube continuous reaction system shown in Figure 3-7.This system is equipped with two piston pumps that allows the user to pump two reagent streams simultaneously. It also features two cartridge holders mounted on heating blocks where packed beds of catalyst may be placed to facilitate a reaction. The system may be plumbed so that the reaction mixture may pass through either both or just one column with 3 mm tubing. Finally, the system has an internal computer that regulates temperature (max 200 C), pressure (max 100 bar) and flow rate of each of the pumps. Typically, commercially available catalysts are used with this system, manufactured by Thalesnano in pre-packed cartridges through their high vacuum system. However a packing system was designed and assembled so that users could evaluate catalysts developed in house.

3.4.2 Packing Cartridges

Commercially available Thalesnano cartridges are packed using a high vacuum system. At VCU, we created a system using this model as an example. First, a cartridge loader was designed. The three part system is shown in Figure 3-8.

Figure 3-8



Cartridge Loader

To use the system, slurry of the desired catalyst and water are placed in a plastic syringe. The slurry is then placed in the unloaded cartridge that is only sealed at the bottom. The cartridge is placed on the vacuum connection, and a two sided holder is fitted around the cartridge and sealed using four screws. The whole apparatus is then placed in a sealed filtering flask with a vacuum line connected. The system was put under vacuum for one hour to ensure that no excess liquid is present and the catalyst is packed tightly. Once unloaded from the apparatus, the top of the cartridge is sealed using a filter, o-ring, and plastic cap, and then pressed using a bench press. The cartridge is then ready for use.

3.4.3 Solubility Studies

The pumps and the small tubing used in the X-cube system require all solutions pumped into the system to be soluble. Therefore, solubility studies on substrate/solvent combinations were conducted. An ideal solvent system would not only be able to solubilize all solid reactants but would also maintain the high conversion obtained in the original solvent system.

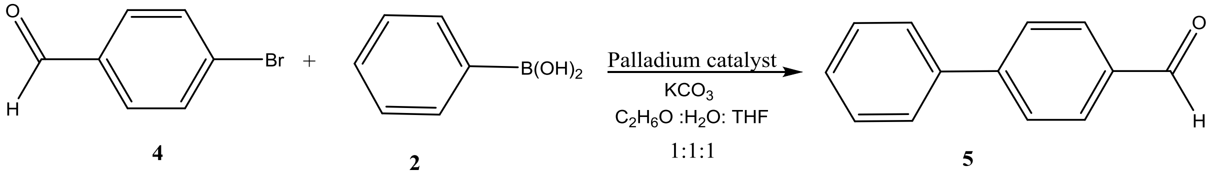
Table 3-3

Solvents	
1	THF
2	Ethanol
3	H_2O
4	DMF
5	Propanol
__Boronic Acids	
1	Methylthio Phenyl-
2	1- dimethyl aminobenzo
3	4- amino carbonyl phenyl-
4	4-methyl phenyl
5	3,4- methylenedioxy
6	phenyl-
Aryl Halides	
1	4-bromonitrobenze
2	4-bromobenzonitril
3	Bromobenzealdehyde
4	1-bromoanisole
5	Bromobenze
Bases	
1	Potassium carbonate

Solvents and substrates examined for continuous coupling reactions

Table 3-3 list the solvents, boronic acids, and aryl halides that were the focus of this inquiry. Interestingly combination that did not include water experienced lower conversion despite the solubility of the substrates. It is speculated that the water and particle interface is behaving as a double layer. At this interface an electric charge is distributed across the surface which assist in the stabilization of the palladium particle. As These experiments determined that using a bromobenzaldehyde and phenyl boronic acid in a 1:1:1 Ethanol:Water:THF solvent mixture successfully solubilized all reactants without compromising conversion to the final product (Scheme 3-1).

Scheme 3-1



Suzuki Cross Coupling Reaction used for Continuous Reactions

Recycling experiments and concentration studies were repeated to test catalytic activity within this system in a batch regime. Bromobenzaldehyde was loaded into a 10 ml glass reaction vial. Phenyl boronic acidand potassium carbonate were loaded into the same vessel, along with 0.05 mol% Pd/(MWNT)$_M$ catalyst. Each run was heated to 80 ^{o}C in the CEM microwave reactorfor 10 minutes and evaluated using GC-MS. Complete conversion (100%) was observed using the $(MWNT)_M$ in this particular solvent system. Additionally the catalyst was recycled 5 times before a significant loss in product conversion (54% shown in table 3-4) was observed.

Table 3-4

Run	Percent Conversion $(MWNT)_M$
1	100
2	100
3	100
4	100
5	83
6	54

Percent conversion in recycling studies in the coupling of Bromobenzenaldehyde and phenyl boronic acid

3.4.4 $(MWNT)_M$ reactivity in a Continuous Coupling Reaction

Upon using the previously described packing method, we found that the water being vacuumed out of the system had turned a slight dark brown/ red color. This color change is usually attributed to a palladium species within the solution. We also noticed a black solid in the effluent.   Despite the apparent color change in the water, the packed catalyst was evaluated in the X-cube reactor system. After flowing the reactant mixture through the system, leaching of the

$(MWNT)_M$ into the final product was confirmed, which ultimately compromises the utility of this system. In hopes of alleviating the leaching of the catalyst, the original 8 micron filters at the ends of the catalyst cartiridge were replaced with 2 micron filters. No visible leaching was observed of the catalyst into the product after using the 2 micron filters upon repeating the continuous coupling reaction. However, a system pressure spike was observed, which triggered the X-cube regulation systems and shut down the pumps. We concluded that we would be unable to use the $(Pd/MWNT)_M$ within this continuous system without substantial effort to overcome these problems.

Figure 3-9

Uniqsis Flow reactor and omnifit catalyst cartridge holder

The Uniqsis flow system is an alternative continuous reactor that was evaluated for cross coupling reactions using $(Pd/MWNT)_M$ (Figure 3-9). In this system, an Omnifit column is used to hold packed catalyst. It is held in place using two mechanical forces acting as press on the catalyst to create the packed bed, instead of relying on the packed bed created by the vacuum system. The packed Omnifit column is placed on a heating block and heated to the desired temperature. It should be noted that with this system, a higher volume of catalyst must be used to generate an adequate packed bed. $(Pd/MWNT)_M$ (300mg) was loaded into the Omnifit column to test the catalyst on the Uniqsis system. Upon flowing the reactant mixture through the system, a color change occurred and was observed in product mixture, again indicating leaching. GC-MS analysis of the product mixture revealed that only a 20% conversion was achieved under these conditions. The color change and low product conversion may be attributed to the high initial palladium (II) content of the multi-walled catalyst. In a batch reaction, the reaction mixture is able to reach a state of equilibrium, allowing generation of palladium (0) in situ. In a continuous reaction, equilibrium is never achieved. Palladium is apparently unable to go through the complete catalytic cycle while remaining in constant contact with the support surface; thus, it can be washed away in the product stream. From this preliminarily data it was concluded that despite the superior catalytic activity of the multi-walled catalyst systems, they are not acceptable catalyst systems for continuous cross coupling reactions.

3.5 Conclusion

Four samples were successfully synthesized used the ball milled deposition method, $(Pd/MWNT)_{M,}$ $(Pd/MWNT)_{T,}$ $(Pd/SWNT)_{M,}$ $(Pd/SWNT)_T$. TEM analysis revealed that samples that were thermally treated exhibited larger particles, attributed to the simultaneous formation of new particles and Ostwald ripening. Thermal treatment further facilitated the decomposition of the palladium salt precursor to palladium metal which was evident from the increase palladium (0) content on each of the thermally treated samples. Each sample was tested in a batch coupling reaction using 0.05 mol% catalyst loading. In batch, the $(MWNT)_M$ exhibited superior catalytic activity, with a higher turnover number (7250) and turnover frequency ($217500h^{-1}$) than had been previously been reported for a solid supported catalyst. These same catalysts were also reused 7 times before a decrease in reactivity was observed. Despite the excellent catalytic activity observed in batch the $(MWNT)_M$ sample could not be used in a continuous coupling reaction because of system design constraints. Currently other applications for these catalyst are being explored.

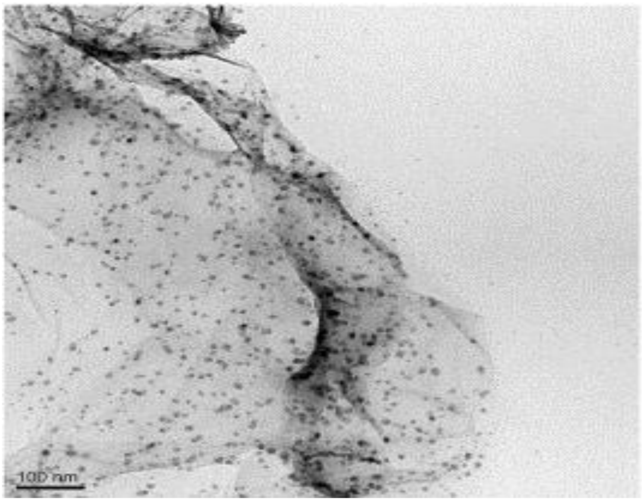
Chapter 4

Analysis of Graphene Supported Nanoparticles

4.1 Previous Work: Optimization of Graphene Supported Palladium Nanoparticles for Application in a Batch Suzuki Cross Coupling Reaction

Dr. Elshall's research lab at Virginia Commonwealth University (VCU) in collaboration with Dr. Siamaki and Dr. Gupton, in the department of Chemistry and Chemical and Life Science Engineering at VCU, were the first to develop and optimize graphene supported palladium nanoparticles using the microwave assisted deposition method.[37]

Figure 4-1[42]



Microwave Assisted Synthesized Grapheme Supported Pd Nanoparticles

The catalyst showed remarkable catalytic activity for a Suzuki cross coupling reaction, which was attributed to the small particle diameter (7-9nm) and complete decomposition of the palladium salt precursor (100%) to palladium metal, and was able to reach complete conversion in a Suzuki reaction in less than 30 minutes.[37] The catalyst was readily recycled, 8 times, before significant loss in activity was observed. Like the Pd/MWNT catalyst, the nanoparticles supported by graphene had minimal leaching into the product solution (300 ppb) and had turnover frequency that had not been seen by commercially available solid supported catalyst, 108,000 h^{-1}. The fast reaction times, great recyclability, and low leaching, shown in batch cross coupling reactions was used as reason to evaluate the same catalyst in a continuous coupling reaction.

4.2.1 Materials and Methods

Graphite powder (99.999%, 200 mesh) was purchased from Alfa Aesar. Palladium nitrate (10 wt% in 10 wt% HNO_3 99.99%) and hydrazine hydrate were obtained from Sigma Aldrich. Aryl bromides, aryl substituted boronic acids, and potassium carbonate were also obtained from Sigma Aldrich and used as received. Graphite oxide was obtained using Hummers method that was previously described in section 2.2.

4.2.2 Synthesis of Palladium Graphene (Pd/G) Catalyst

Graphite oxide (0.1 g) was sonicated in deionized water (400 mL) until a homogenous suspension was obtained. Palladium nitrate (210 μL) was added to the homogenous mixture, and agitated using a magnetic stir plate.. The homogenous mixture was then placed in a Emerson conventional kitchen microwave where 100 μL of hydrazine hydrate solution (25% in H_2O) was added. The solution was immediately microwaved on full power (1000 W) in 30-second cycles (on for 10 s, off and stirring for 20 s) for a total reaction time of 60 seconds. The resulting black solution was centrifuged in an Eppendorf 5804 centrifuge at 5000 rpm for 20 minutes and dried under vacuum until black flakes obtained.

4.2.3 Characterization Palladium Graphene (Pd/G) Catalyst

TEM images were obtained using a JOEL JEM-1230 electron microscope operated at 120 kV. The microscope is equipped with Gatan UltraScan software and CCD camera (4000SP 4K x 4K). TEM samples were prepared by adding one droplet of suspended sample in methanol on a Formvar carbon-carbon, 300 mesh copper grid, obtained from Ted Pella, and allowed to evaporate in air at room temperature. X-ray photoelectron spectroscopy (XPS) was performed on a Thermo Fisher Scientific ESCALAB 250 using a monochromatic Al KR X-ray. Dry samples were mounted to a sample holder using two way carbon tape and indium foil.

4.2.4 General Procedure for Solvent/ Reactivity Studies

The solvent study was used from the MWNT studies. Several different solvents were chosen. 2ml of a selected solvent were taken and placed into a test tube. Bromobenezene (50 mg) was added to the test tube. The solution was stirred for one minute. The solubility was recorded and the same procedure was repeated with phenyl boronic acid (47 mg). If the solvent successfully solubilized both reactants it was tested in combination with another

4.2.5 General Procedure for Continuous Suzuki Cross Coupling Reaction

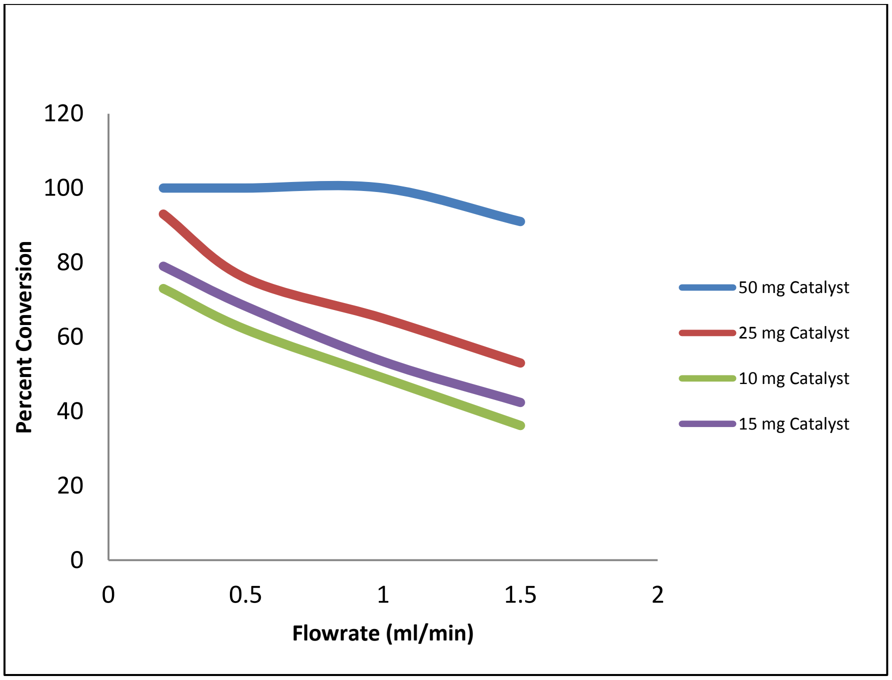
4-Bromobenzaldehyde (**d**, 625 mg, 3.37 mmol, 1 eq.) was dissolved in 100 mL of H_2O/EtOH/THF (1:1:1) and placed in a 150 mL flask. Phenylboronic acid (**b**, 494 mg, 4.05 mmol, 1.2 eq.) and potassium carbonate (1400 mg, 10.1 mmol, 3 eq.) were added to the same flask. Catalyst Cartridge was prepared by suspending 100 mg of Pd/G in deionized water and loaded into a stainless steel cartridge (70 x 4 mm) fitted with a porous metal frit and a 8 µm membrane at one end using a 5 mL syringe. The catalyst bed was established by, applying vacuum to the base of the cartridge to dispose of excess water. The other end of the cartridge was then sealed with an 8 µm membrane and placed in the cartridge holder on the X-cube. Solvent was pumped through the apparatus and the temperature was changed to the set point in by increasing in 5 ^{o}C increments to equilibrate the system. Once the desired temperature was reached, the reactant solution was fed into the X-cube at a designated flow rate. Samples were collected in 30 minute increments and analyzed by GC-MS.

4.3 Results and Discussion

4.3.1 Reactivity in Continuous Coupling Reactions

The objective of the initial experiments was to evaluate the optimal catalyst loading in which to conduct subsequent reactions. The coupling of bromobenzealdehyde and phenyl boronic acid in a water ethanol THF (1:1:1 vol) solvent system was used. Four different cartridges were packed with varying amounts of the Pd-graphene catalyst, 10 mg, 15 mg, 25mg and 50 mg. Fresh reagents were fed to each cartridge at the flow rates of 0.5 ml/min, 1 ml/min, and 1.5 ml/min. Product solutions were collected for 10 minutes at each flow rate. The temperature was held constant at 100 ^{o}C for all experiments.

Graph 4-1

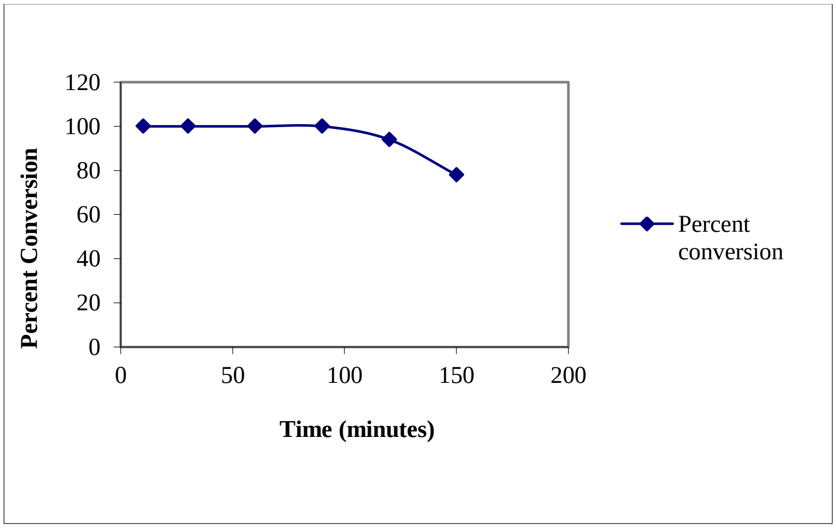


Effects of Catalyst loading and Flow rate on product conversion in a Suzuki Coupling reaction

Only at a catalyst loading of 50 mg (Pd/G catalyst) was complete conversion observed in a Suzuki coupling reaction. However, at 50 mg catalyst loading, if the flow rate exceeded 1 ml/min a decrease in product conversion was observed (< 95%). It should be noted that at 25mg catalyst loading a product conversion of 97% was observed at a flow rate of 0.5 ml/min. However, in this instance higher cahigher flow rates give higher throughput therefore the higher ccatalyst loading proves to be more advantegous. It should also be noted as the temperature was decreased; a decrease in product conversion was observed for all catalyst loadings. To directly compare the batch process to the continuous the moles of product produced per mole of catalyst was calculated. To accurately evaluate this value for the continuous reaction the point of deactivation, a significant drop in product conversion <90%, was identified, by conducted an extended Suzuki reaction.

To carry out the extended study, a new cartridge was packed with 50 mg of the palladium graphene (Pd/G) catalyst using the laboratory packing system. Collection vessels were exchanged for new vessel every 10 minutes; however only samples at the half hour time points were analyzed using GC-MS analysis. If a dramatic change in product conversion was seen intermediate time points were also evaluated.

Graph 4-2

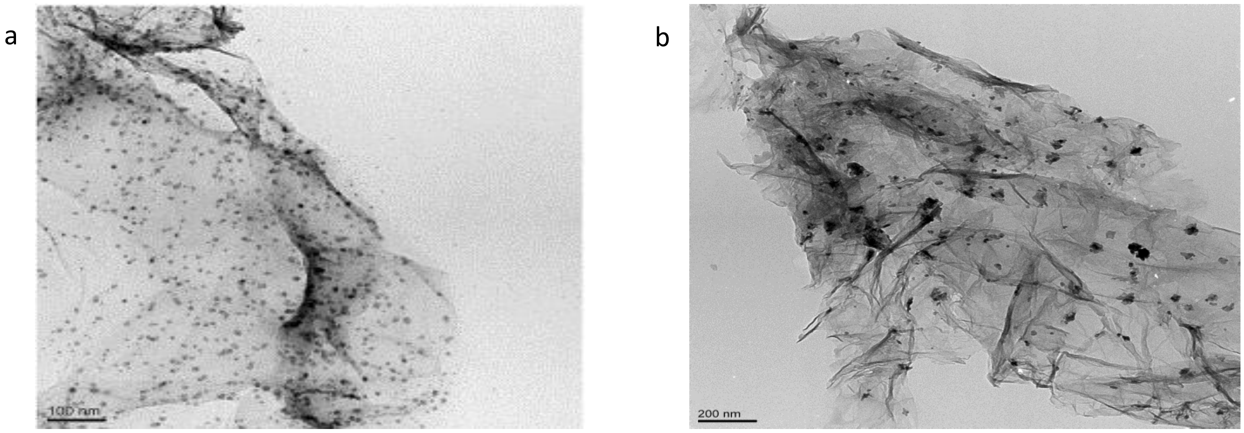


Catalyst Life Experiments Reaction Temp: 100 ^{o} C, Catalyst loading 50 mg

At constant a temperature (100 ^{o}C) and flow rate (1mL/min) complete conversion was observed for two and a half hours until the conversion decreased to79%, by GC-MS analysis. At three and a half hours the product conversion was observed to be 52%. After which the reaction was discontinued. The mole of product produced per mole of catalyst was calculated for a reaction that ended at 2.5, was found to be 89.9. The results from the recycling study were considered when evaluating the moles of product per mole of catalyst ratio for the batch reaction and were found to be 110. Though the continuous reaction production ratio was found to be slightly less than that of the batch it may be argued that it is comparable because of the advantages that a continuous reaction may offer, including safe operation conditions, small heat to volume ratio. During the continuous reaction, purification of reaction vessels was not needed and the researcher only needed one stock solution of reagent. However, after every recycle run the researcher made new solutions and cleaned the reaction vessels repeatedly. Despite this argument researchers still sought to narrow the gap in the ratio moles of product produced and moles of catalyst used in the continuous and batch Suzuki reactions. This goal may be achieved by increasing the concentration of the continuous stock solution. A number of studies were needed to complete this study however the reproduction and scale up of the synthesized catalyst (Pd/Gr) stifled continued studies.

As previously mention the microwaved assisted deposition method was optimized to produce 110 mg of product for each reaction. Typically after reaction, due to purification losses only 60- 80 mg of actual catalyst was retained. This ultimately meant only one continuous reaction may be carried out for each batch of catalyst that was synthesized. The synthesis was scaled to yield 300 mg of material at a given time. However, upon scaling the synthesis method the material obtained had different physical and catalytic characteristics, Figure 4-2 The palladium size increased to 15-30 nm and the formation of palladium agglomerates was evident when examined by TEM.

Figure 4-2



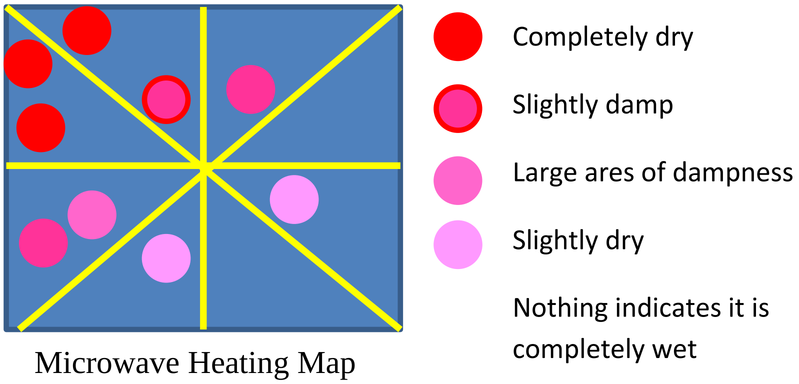
TEM image of graphene support palladium nanoparticles a- Previous synthesized palladium on grapheme catalyst b- Palladium on graphene scaled synthesis

The synthesis reaction for Pd/G was repeated at the original scale. A decrease in catalytic was observed as it was not readily recyclable. Batch to batch variability is often cited as a drawback of batch processes[29]. The variability in the synthesis of Pd/G catalyst was evaluated by synthesizing 10 discrete samples at the small scale (110 mg) level. Only the reactivity of the samples was tested as it gave the quickest characterization of each sample. Of the 10 reactions only 4 exhibited the same reactivity to one another and none exhibited the same reactivity as the catalyst that was previously tested. Several synthesis conditions could have contributed the variability in the synthesis method, including uniformity of heating, drying time, user error. Each of the fore mentioned conditions were evaluated to draw further conclusions.

4.3.2 Uniformity in heating

The use of a conventional kitchen microwave is typically uncommon in a laboratory setting. One reason is that it is difficult to map and measure how much energy is actually delivered to the reaction system. To ensure that the same microwave energy is delivered to the system mapping of the microwave was conducted. The spinning disk was taken out of the microwave and was replaced with a stationary piece of cardboard. The card board was divided into 8 sections by drawing on the cardboard. The card board was wetted and the microwave was heated for 2minute.

Figure 4-3



Microwave Heating Map

In each section there were vary degrees of dryness. These areas are noted in Figure 4-3. The intense red circle was the driest area on the cardboard. The decrease in intensity signifies and area that exhibited awetter surface. It seemed that the back of the microwave received more energy as it was the driest area. It should be noted that even in areas of dryness there were varying degrees of dryness in the given section. Originally samples were placed in the microwave and spun on the rotating disk. Thus only a portion of the reaction mixture was exposed to microwave energy at a given time, making the actual reaction time (time the solution is exposed to heating) less than what the researcher had intended. For future experiments the reaction vessel was placed in the areas of the most intense heating. It was suggested that the reaction time be increased to compensate for the uneven microwave energy dispersed to the reaction mixture. Though this mapping method is qualitative and thus very subjective analysis of heating within the microwave it will provide some uniformity between users and batches of Pd/G synthesized.

4.3.3 Drying Study

In the original synthesis of Pd/G catalyst drying took place after washing and decanting water from the reaction vessel. Depending on the amount of water left in the vessel drying could be extended longer than a day. A drying study was conducted over a week period of time. 7 separate reactions were used completed using the original reaction conditions (100 mg of graphite oxide, 400 ml of water, 60 sec reaction time, 1000 W reaction power, 100 µL of Hydrazine, and 210µL of palladium (II) nitrate). After the reaction was completed half was placed in a separate vessel and centrifuged as previously described with only 50 mL left after the final washing. The other half was directly placed into the drying oven without washing. The Pd (0) content was evaluated for each sample. Table 4-1 records the Pd (0) content for each sample

Table 4-1

		Days dried	Pd (0) Content (%)
A	Washed	1	-
	Unwashed	1	-
B	Washed	2	-
	Unwashed	2	-
C	Washed	3	-
	Unwashed	3	-
D*	Washed	4	85
	Unwashed	4	84
E*	Washed	5	82
	Unwashed	5	89
F	Washed	6	83
	Unwashed	6	93
G	Washed	7	82
	Unwashed	7	98

*Samples obtained were slightly damp but dry enough to analyze

The effect of drying time on Pd (0) content

Among the reactions samples that were unwashed the Pd (0) content increased as the drying time increased. This indicates that the reduction of the palladium precursor, palladium nitrate, is not complete when it removed from the microwave oven. Instead reduction is further induced by time and drying at 70 ^{o}C in the drying oven. The washed samples did not follow the same trend and were virtually the same value despite the drying time, however no samples reached complete conversion to Pd(0). Washed sample D exhibited a higher Pd(0) content than other washed samples , 85, 82 and 83 respectively. This increase in Pd (0) content may be attributed residual hydrazine on the in solution. Samples dried 3 days or less, samples A- C, could not be evaluated because they were not completely dry and product was still suspend in solution despite being washed or unwashed and would not be able to be used as a catalyst. Samples D and E were also slightly damp and unlikely to be used in their current state as catalyst. It should be noted that after the reaction mixture is removed from the microwave it is no longer a homogeneous suspension but rather solid agglomerations suspended throughout the solution. Therefore there is no way to accurately get the same concentration of solid catalyst in the washed and unwashed samples. Despite the uncertainty in concentration clear trends are seen in the samples collected. It was speculated that an increase in hydrazine content during the synthesis of Pd/G catalyst would increase the Pd(0) content to 100% as was observed by the original catalyst sample.

4.3.4 Design of Experiments Optimization

The last major area of uncertainty is in the graphite oxide source. Graphite oxide is synthesized in the lab. Though oxidation of the graphite powder (starting material for synthesis of graphite oxide) is readily checked by X-ray Diffraction, techniques to quantify the extent of oxidation or differentiate between epoxy oxygen atoms and carboxyl oxygen atoms are still being developed. Each time graphite oxide is synthesized there will be some variation from the previous batch. The alternative is to obtain commercially available graphite oxide where variability in oxidation, may be reduced because of a more standardized method in production. The suggested modification in the catalyst synthesis caused a re-evaluation of the synthesis process parameters. To gain a better understanding of these parameters a design of experiment (DOE) was constructed. A DOE is a systematic method to evaluate parameters and their interactions within a given process on a particular output variable. A two level DOE was designed to identify evaluate these parameters and there effects on catalyst reactivity

Table 4-2

	Reaction Time (min)	***Reaction Power (W)***	***Hydrazine Content(mL)***
Lower Limit (-1)	.5	750	.1
Upper Limit (1)	2	1000	3
Midpoint	1.5	850	1.5

Boundary conditions for DOE

Specifically, the effects of reaction time, hydrazine content, and reaction power were evaluated upper and lower limits for each parameter are given in table 4-2. The concentration was held constant throughout the reaction (.5mg/mL). The concentration was increased from its original value to decrease the waste being produced, and to decrease the drying time needed even though each sample was allowed to dry for 1 week during initial studies. Eight experiments were generated by the DOE (Table **4-3**).

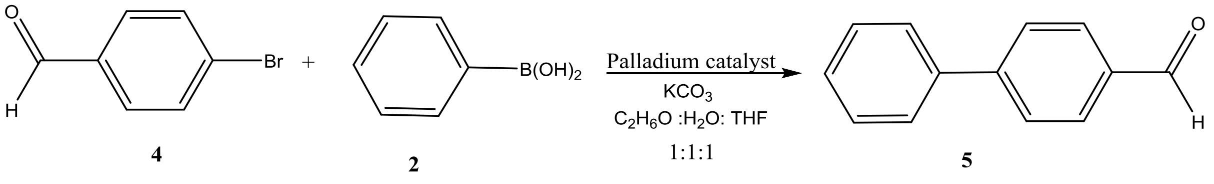
Table 4-3

	Reaction Time (min)	*Reaction Power (W)*	*Hydrazine Content(mL)*
1	.5	750	.1
2	2	750	.1
3	.5	1000	.1
4	2	1000	.1
5	.5	750	3
6	2	750	3
7	.5	1000	3
8	2	1000	3

Experiments Generated by the 2-level DOE

The reactivity in a Suzuki coupling reaction , coupling of bromobenzealdehyde and phenyl boronic acid, and evaluated for each sample generated by the 2-level DOE. One midpoint was repeated 5 times to test reproducibility of the synthesis method. Reaction conditions for the Suzuki coupling reaction were as follows; reaction temperature 80 ^{o} C , reaction time10 minutes, catalyst loading 1 mol% catalyst (Scheme 4-1).

Scheme 4-1



Suzuki Cross Coupling Reaction for Continuous Reactions

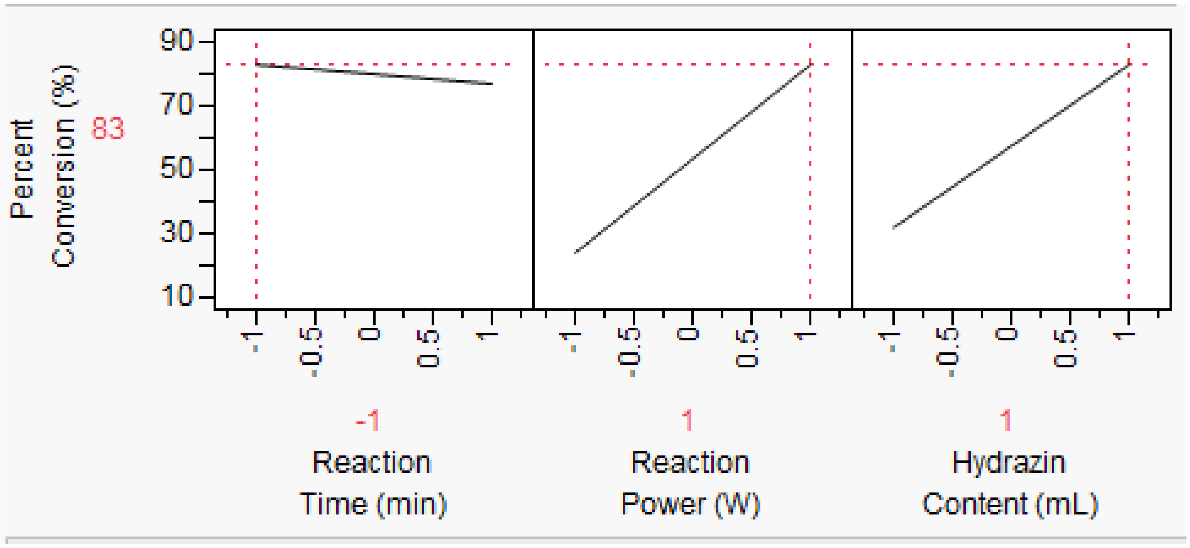
It was noted that of trials from the midpoint value exhibited the same reactivity in the coupling reaction 4 out of 5 times. The one outlier was completed in an older version of the conventional microwave and may be attributed the change in reaction microwave. JMP software was used to analysis the collected data. A least squares model was used to fit the percent conversion at the reaction conditions specified in table 4-4. The coefficient of determination (R^2) value found using this model was 1. This value is an indication that this model is a good fit for the experimental data collected. The rate of change for each main parameter is given graphically. The graph that exhibits the largest change is usually indicative of the parameter that is the most significant effect in the dependent variable (percent conversion). Figure 25 shows the graphical representation of the main effect parameters. These profiles also may be used to predict the effect on percent conversion each parameter has when changed.

Table 4-4

	Reaction Time (min)	***Reaction Power (W)***	***Hydrazine Content(mL)***	***Percent Conversion (%)***
1	.5	750	.1	17
2	2	750	.1	30
3	.5	1000	.1	32
4	2	1000	.1	53
5	.5	750	3	24
6	2	750	3	44
7	.5	1000	3	83
8	2	1000	3	77

Percent Conversion in the Suzuki Cross Coupling Reaction of Bromobenzenaldhye and phenyl boronic acid

Figure 4-4



Main Parameters/Effects Prediction Profile

The rate of change for each parameter and interaction may also be given mathematically.

Equation 4-1 was obtained to further help predict percent conversions.

Equation 4-1

$$Y= 45 + (16.25*X_1)+(12*X_2)-(6.75*X_3)+(6*X_4)-(4.25*X_5)-(2.5*X_6)-(2.25*X_7)$$

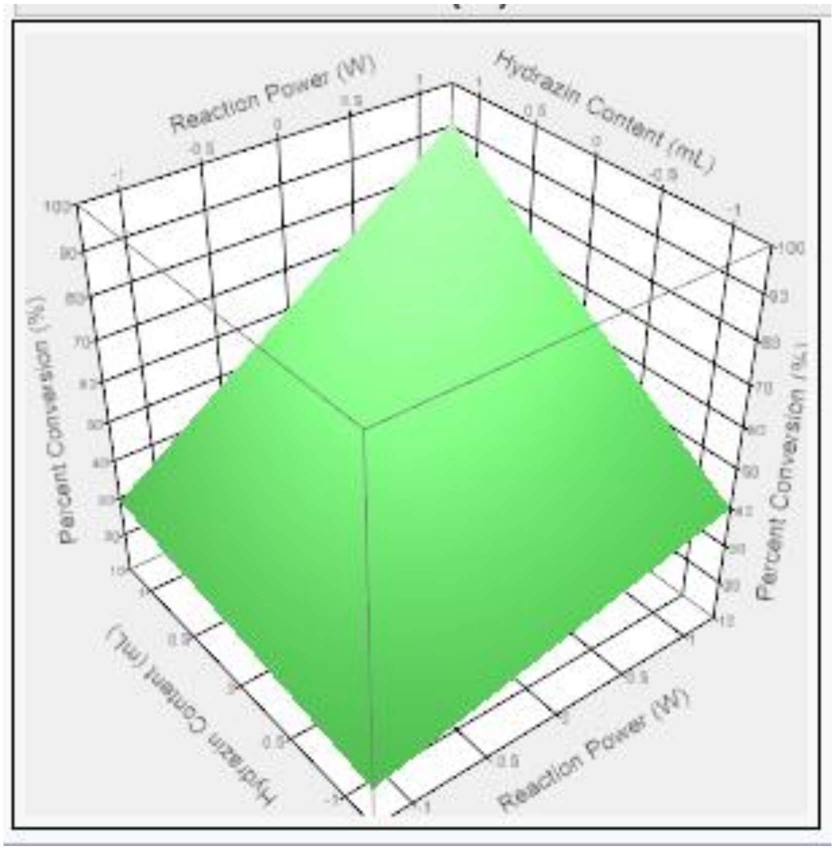
Where Y is percent conversion and X_i are as follows

i	
1	Reaction Power (W)
2	Hydrazine Content (mL)
4	Reaction Power (W)* Hydrazine Content (mL)
5	Reaction Time (min)
8	Reaction Power (W)* Reaction Time (min)* Hydrazine Content (mL)
11	Reaction Time (min)* Hydrazine Content (mL)
12	Reaction Time (min) * Reaction Power (W)

The coefficient for each Xi value is the slope (rate of change) of that particular parameter.

From the equation and main effects profile the most significant parameter was concluded to be the reaction power. The most significant interaction between Pd/G synthesis reaction parameters was concluded to be between power and hydrazine content. Equation 1 was optimized using solver in excel. The optimal synthesis conditions were as follows; Reaction power 1000 W, hydrazine content of 3 mL and Reaction time of 1.5 minutes. This is further confirmed when examining the surface plot of percent conversion with reaction power and hydrazine content as the variables. It's noted that the percent conversion optimal area is when both the hydrazine content and reaction power is maximized. Pd/Gcatalyst was synthesized using the "optimal" reaction conditions, and yielded 64 mg of product. TEM analysis of this catalyst showed the formation of palladium particles on the surface of graphene (figure 4-6)

Figure 4-5

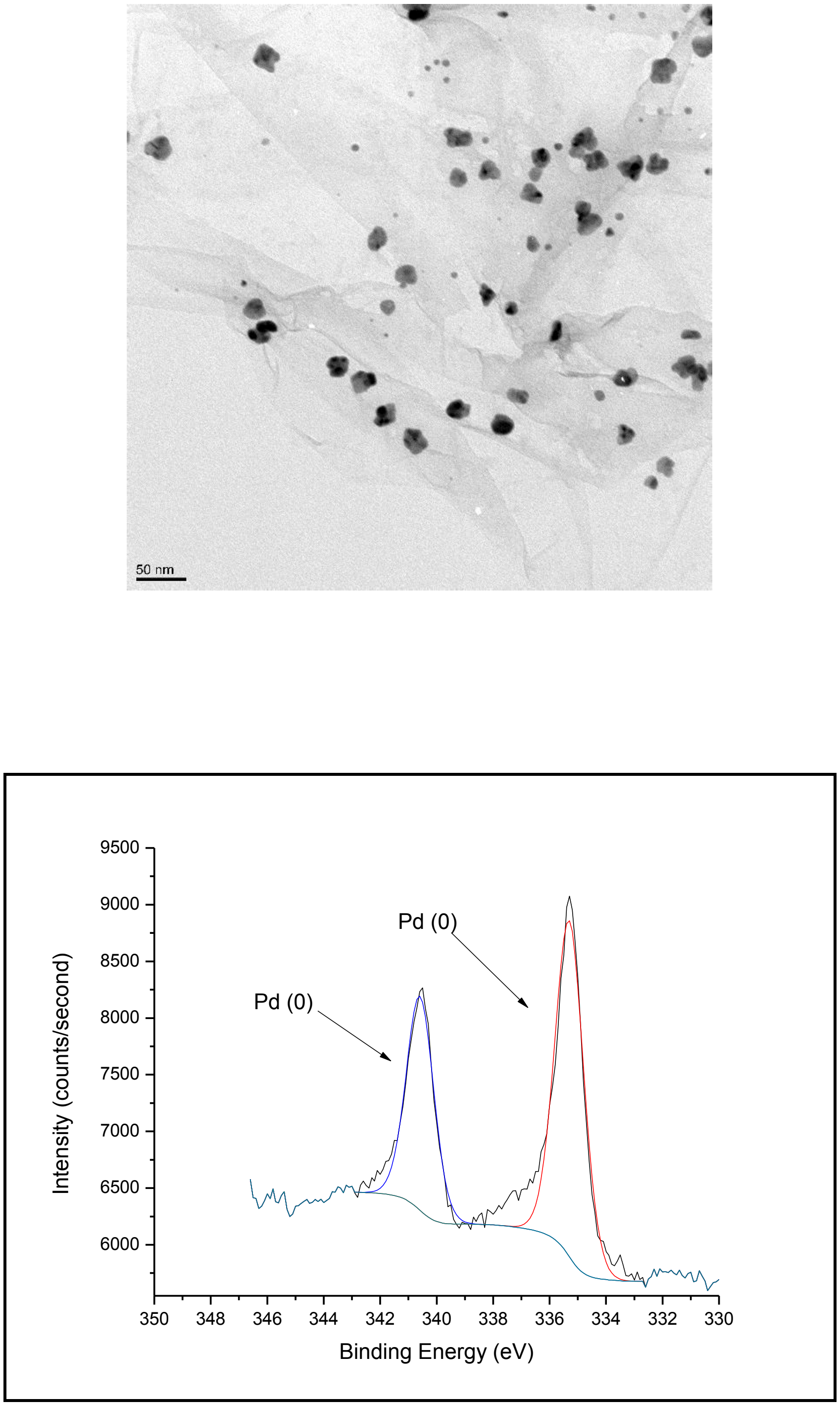


Surface plot describing the effect of reaction power and hydrazine content on percent conversion

Figure 4-6

a)

b)



(a)TEM image, (b) XPS spectra of Graphene supported Pd synthesized y optimal reaction conditions predicted by a 2- Level DOE.

The average particle diameter was 10.2 +/- 1.6 nm, and complete conversion of the palladium precursor to Pd (0). Though the particle diameter is larger than observed in the original catalyst they were still evaluated in the Suzuki cross coupling reaction. At 80 ^{o}C, at 10 minutes with 1 mol % catalyst loading 100 % conversion was observed. A second Suzuki reaction was completed at room temperature with 0.5 mol % catalyst loading (Graph 4-2). After 1 hour the reaction reached complete conversion. However, the catalyst was only recycled twice before a decrease in reactivity was observed. This decrease in reactivity is likely due to the increased particle diameter, which consequently gives fewer reactive sites. The 2-level DOE successfully predicted the percent conversion of a single Suzuki reaction. However to gain a complete understanding of the parameter effects multiple y values must be considered, particle diameter, Pd(0) content, and reactivity at various catalyst loadings.

4.4 Conclusion:

The microwave assisted deposition method successfully decorated graphene sheets with palladium nanoparticles that are reactive in both batch and continuous Suzuki cross coupling reactions. However due to work-up loses this method is typically only 60-80% efficient. Variability is also observed due to uneven heating, drying time, and graphite oxide sources. Though these challenges have successfully been identified and improved replication of the original activity has yet to be seen. A 2- level DOE was used to gain a better understanding of process parameters which contribute to a catalyst product conversion in a Suzuki coupling reaction. An eight experiment DOE was completed and concluded that the reaction microwave power and the interaction between the power and hydrazine content were the most important factors in this deposition method. Despite the promise that this deposition shows low product yields and uneven heating (with heating being one of the mostimportant factors), continuing to optimize this particular system would prove to be inefficient. Instead It was hypothesized that synthesizing graphene supported palladium nanoparticles continuously will improve the heating mechanism, reproducibility and scalability of this deposition method.

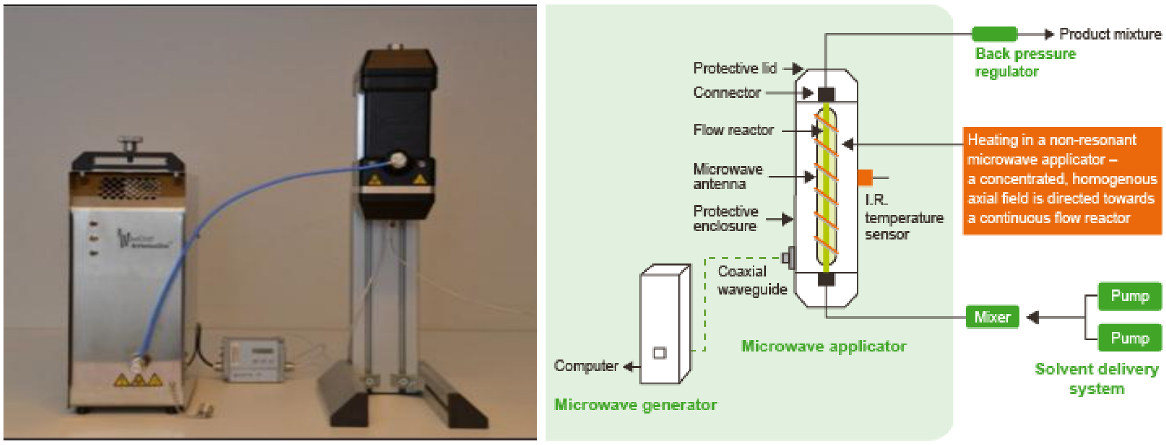
Chapter 5

Continuous Synthesis of Graphene Supported Palladium Nanoparticles

5.1 Introduction: Continuous Synthesis of Graphene Supported Nanoparticles

Thus far the developments of continuous processes have been limited to the synthesis of complex molecules/ organic compounds. However, it was hypothesized that the advantages of continuous processes, increased product quality, reduced waste production, and safer operation conditions, may expand further than just the synthesis of complex molecules or organic compounds, but also to catalyst and their support systems. Furthermore, it was hypothesized that using a continuous method to generate graphene supported palladium nanoparticles, would create a scalable, tunable, and more reliable synthesis process. A DOE was used to evaluate the process parameters in order to adopt a continuous process for other particle synthesis.

Figure 5-1



Arrhenius One Wave Craft Continuous Microwave reactor

There have been multiple reports of gold, silica, zinc, and many other nanoparticles in micro reactor chips. However, there have been no reports on the continuous synthesis of nanoparticles on solid supports. To develop this synthesis technique the Arrenhius One Wave

Craft continuous reactor was used. Arrhenius One uses microwave and cell phone technology to provide instantaneous microwave radiation uniformly across a glass reactor in the deviice's interior. The temperature is controlled using an infrared (IR) sensor that is able to give real time feedback to the units process control system, which adjusts the microwave radiation frequencies. Initial studies sought to synthesize graphene supported palladium nanoparticles. These solid supported particles, specifically graphene supported palladium nanoparticles, were evaluated in both batch and continuous Suzuki reactions.[43]

5.2 Materials and Methods

5.2.1 Materials

Graphite powder (99.999%, 200 mesh) was purchased from Alfa Aesar. Palladium nitrate (10 wt% in 10 wt% HNO_3 99.99%) and hydrazine hydrate were obtained from Sigma Aldrich. Aryl bromides, aryl substituted boronic acids, and potassium carbonate were also obtained from Sigma Aldrich and used as received. Graphite oxide was obtained using Hummers method that was previously described. Graphite oxide was also obtained from the graphene super market in the powder form. The second source of graphene was used as a standard of comparison.

5.2.2 Synthesis of Palladium Graphene (Pd/G) Catalyst

A two level DOE was used to determine which experiments should be conducted to synthesize graphene supported palladium nanoparticles and gain a better understanding of the systems process parameters. The reaction temperature,flow rate, and hydrazine were the parameters selected to investigate. Upper and lower limits of the parameters are shown in table 5-1.

Table 5-1

	Reaction Temperature (C)	Reaction Flow rate (mL/min)	Hydrazine Concentration (mL N_2H_4/ mL H_2O)
Lower Limit (-1)	80	2	.2
Upper Limit (+1)	100	4	.5

Upper and Lower limits for the2-level DOE investigation

Graphene oxide (0.09 g) was sonicated in deionized water (200 ml) until a homogenous suspension was obtained. Palladium nitrate (194 μL, 0.094 mmol) was added to the homogenous mixture and mixed with a magnetic stirrer for an hour. In a separate vessel, a 2 M hydrazine hydrate solution was prepared and agitated with a magnetic stirrer. Using a calibrated peristaltic pump, the two solutions were fed at equal rates into an ArrheniusOne Wavecraft continuous microwave reactor operating at a designated temperature and flow rate. The resulting solution was placed in a drying oven at 70 ^{o}C for several hours to give a fine black powder that was used for further analysis.

5.2.3 Characterization Palladium Graphene (Pd/G) Catalyst

TEM images were obtained using a JOEL JEM-1230 electron microscope operated at 120 kV. The microscope is equipped with Gatan UltraScan software and CCD camera (4000SP 4K x 4K). TEM samples were prepared by adding one droplet of suspended sample in methanol on a Formvar carbon-carbon, 300 mesh copper grid, obtained from Ted Pella, and allowed to evaporate in air at room temperature. X-ray photoelectron spectroscopy (XPS) was performed on a Thermo Fisher Scientific ESCALAB 250 using a monochromatic Al KR X-ray. Dry samples were mounted to a sample holder using two way carbon tape and indium foil.

5.2.4 General Procedure for Batch Suzuki Reaction

Batch cross-coupling reactions were performed in a CEM Discover microwave operating at a maximum output power of 250 W. Bromobenzene (**1a**, 43 mg, 0.27 mmol, 1 eq.) was dissolved in a 4 mL mixture of H_2O/EtOH (1:1) and placed in a 10 mL microwave tube. Phenyl boronic acid (**2a**, 40 mg, 0.33 mmol, 1.2 eq.) and potassium carbonate (113.5 mg, 0.82 mmol, 3 eq.) were added to the same tube. Pd/G catalyst (5 mg, 2 mol% based on Pd content) was then added, and the tube was sealed and heated under microwave irradiation (250 W, 2.45 MHz) at 80^{o}C for 10 minutes. Reaction conversions were determined using an Agilent 6890 gas chromatograph (GC) equipped with an Agilent 5973 mass selective detector. All compounds were compared to authentic standards.

5.2.5 General Procedure for Suzuki Recycling Studies

All recycling studies were carried out by Dr. Ali Siamanki. Bromobenzene (**1a**, 50 mg, 0.32 mmol) and phenyl boronic acid (**2a**, 47 mg, 0.384 mmol, 1.2 eq.) were dissolved in 4 mL of H_2O:EtOH (1:1) and placed in a 10 mL microwave tube. To this were added potassium carbonate (133 mg, 0.96 mmol, 3 eq.), and Pd/G nanoparticles (3 mg, 3.2 μmol, 1 mol%). The tube was sealed and heated at 80 ºC for 10 minutes under microwave irradiation (250 W, 2.45 MHz), and the progress of the reaction was monitored by the GC-MS analysis. Upon the completion of the reaction period, the mixture was diluted with 10 mL of ethanol and shaken. The entire mixture was centrifuged and the solvent above the Pd/G nanoparticles was completely decanted. The washing and centrifugation were repeated for two additional times to ensure the removal of the organic products from the surface of the catalyst. The Pd/G catalyst was then reused for the subsequent reaction adding fresh reagents to the tube. This procedure was applied for every recycling experiment and the percent conversion to the products was determined by means of GC-MS spectroscopy.

5.2.6 General Procedure for Continuous Suzuki Reaction

4-Bromobenzaldehyde (**1b**, 625 mg, 3.37 mmol, 1 eq.) was dissolved in 100 mL of H_2O/EtOH/THF (1:1:1) and placed in a 150 mL flask. Phenylboronic acid (**2b**, 494 mg, 4.05 mmol, 1.2 eq.) and potassium carbonate (1400 mg, 10.1 mmol, 3 eq.) were added to the same flask. For the preparation of the catalyst cartridge, Pd/G (100 mg) was suspended in deionized water and loaded with a syringe into a stainless steel cartridge (70 x 4 mm) fitted with a porous metal frit and a 8 µm membrane at one end. The catalyst bed was established by filtering off the water by applying vacuum to the base of the cartridge. The other end of the cartridge was then sealed with an 8 µm membrane and placed in the cartridge holder on the X-cube. Solvent was pumped through the apparatus and the temperature was changed to the set point in 5 ^{o}C increments to equilibrate the system. Once the desired temperature was reached, the reagent solution was fed into the X-cube at a flow rate of 0.2 mL/min. Samples were collected in 30 minute increments and analyzed by GC-MS as previously described

5.3 Results and Discussion

5.3.1 Evaluation of Design of Experiments (DOE)

Table 5-2

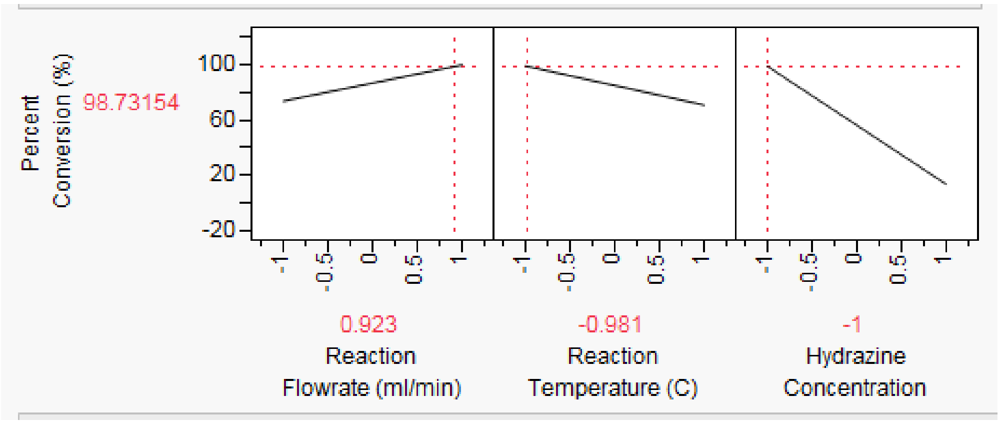
	Reaction Flow rate (ml/min)	Reaction Temperature (C)	Hydrazine Concentration (mL N_2H_4/ mL H_2O)	Percent Conversion (%)
1	2	80	0.2	74
2	4	80	0.2	100
3	2	100	0.2	42
4	4	100	0.2	72
5	2	80	0.5	5
6	4	80	0.5	14
7	2	100	0.5	0
8	4	100	0.5	0

Continuously synthesized graphene supported palladium nanoparticles percent conversion in Suzuki cross coupling

Eight samples were obtained from a 2-Level DOE. Each sample was examined a using the prescribed procedure for a batch Suzuki Cross coupling reaction. The percent conversion was evaluated and report in Table 5-2. Conditions to achieve 100% product conversion in a Suzuki Cross Coupling Reaction was achieved in the eighth experiment conducted using the DOE method. JMP analytical software was used to evaluate the process parameter effect on the percent conversion to product. Evaluation of the main effects parameter predictor profiles indicated that (Figure 5-2) hydrazine concentration is the most significant process parameter.

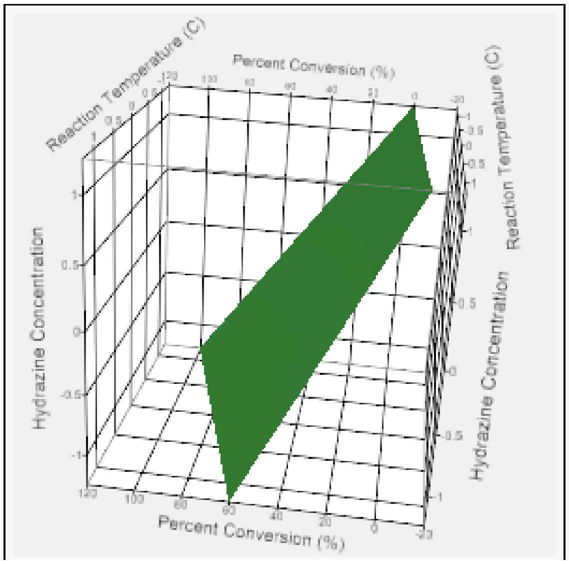
Figure 5-2

a)



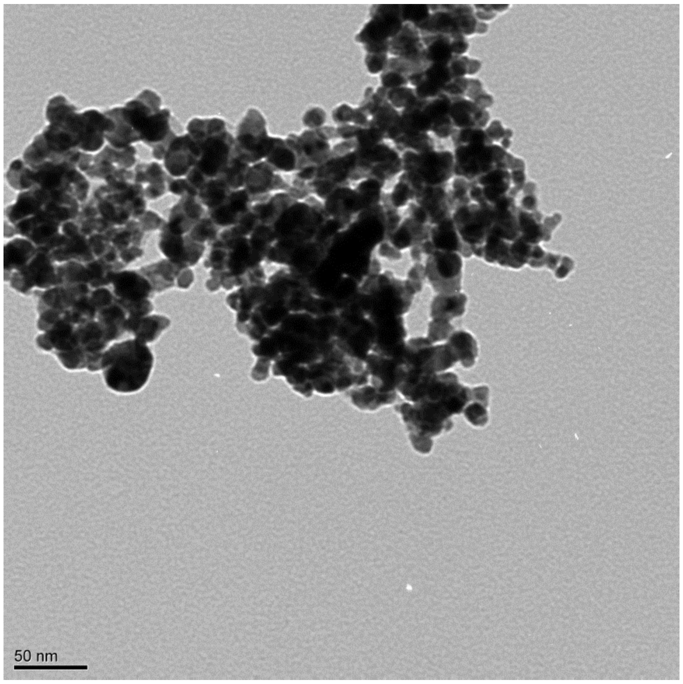
2-LEVEL DOE Main Parameter Profile Predictor

b)



The reagents flow rate is the second most significant parameter within the continuous system. The optimal area of operation is at a low hydrazine concentration and a high flow. As previously stated the Wave Craft continuous reactor offers a more uniformed heating profile, because of a smaller volume to heating ratio and a complete coverage of the reactors perimeter. The improved heating almost instantaneously induces the growth of nanoparticle and over saturation of hydrazine may cause particle to form agglomerates away from the graphene surface. This theory was quantified by looking at the TEM image of those samples synthesized at high concentrations of hydrazine.

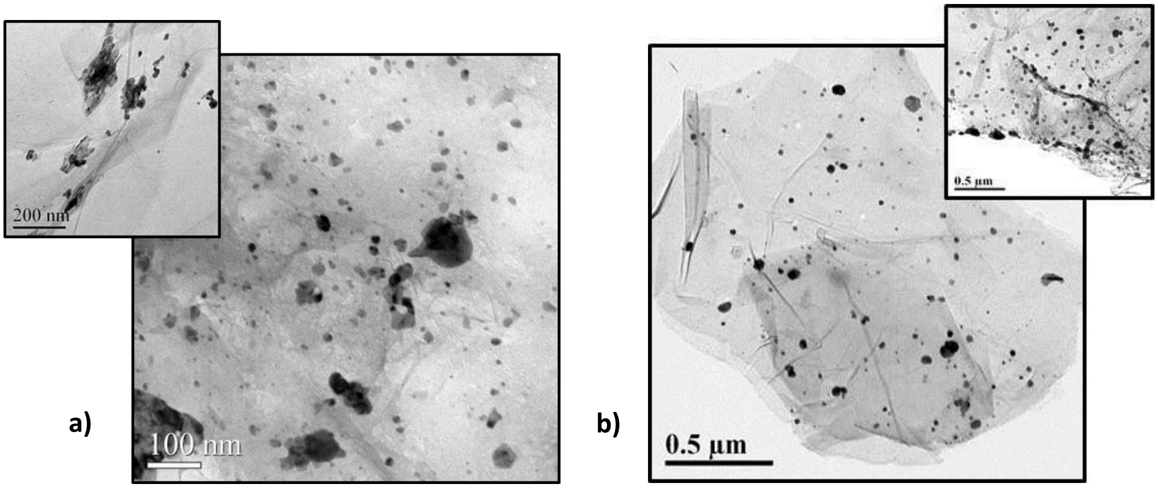
Figure 5-3



Palladium nanoparticles synthesized continuously at 4 ml/min, at 80 ^{o}C, at with a .5ml/ml H_2O hydrazine concentration

Sample 6 was synthesized with a flow rate of 4 ml/min , at 80 ^{o}C, at with a .5ml hydrazine per mL of water concentration, and evaluated to test this theory. TEM images of these samples showed evidence that particles formed away from the graphene surface resulting in palladium agglomerates. In subsequent reactions using the ArrheniusOne Wavecraft microwave flow reactor, graphene supported palladium nanoparticles were prepared by the reductive deposition of palladium (II) nitrate onto graphene sheet using both graphite oxide made in the lab and commercially available as a graphene precusor. To distinguish between the two samples those supported with commercially available graphite oxide will be referred to as Pd/Gc. The particles supported on the graphite oxide synthesized in the lab will be referred to Pd/G. The resulting Pd/G exhibited a narrow particle size distribution with an average particle diameter of 9.37 nm (Figure 5-4 a). Palladium agglomerates were observed, mainly along the edges and creases of the graphene sheets. The Pd/Gc sample also had small particles averaging 9.42 nm in diameter with large agglomerates (Figure 5-4 b). The localization of the agglomerates is likely due to an increased concentration of defect sites within these areas.

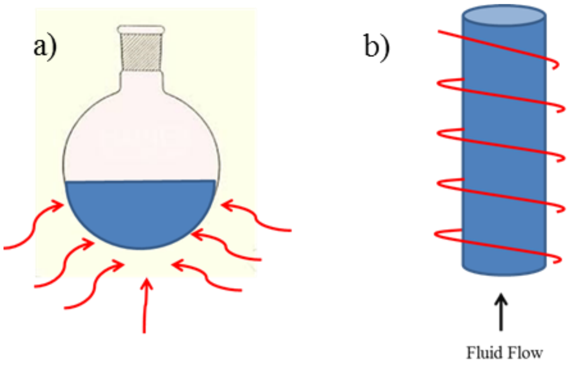
Figure 5-4



TEM images of Pd/G catalyst produced using a continuous microwave reactor. Inset shows creases along graphene sheets where palladium agglomerations tend to form.

The narrow size distribution and palladium content may be attributed to the increased control of heating. In traditional heating techniques the energy source has to heat the reaction vessel, and then transfer that energy to a bulk solution (Figure 5-4a).The rate at which the solution is heated depends on the reaction vessel material and the volume of the solution being heated, which often creating a heating gradient within the sample. In contrast, the efficiency of microwave heating depends on the ability of a reaction mixture to absorb microwave radiation, which can be optimized by careful selection of the solvent system. The potential for heating gradients is further reduced with an increased number of points of contact with the heating source, thus reducing the possibility of localized hotspots within the system.[44] As shown in figure 5-5b, the coil that delivers microwave irradiation to the reaction solution, covers the glass reactors surface making for more efficient and uniform energy transfer.

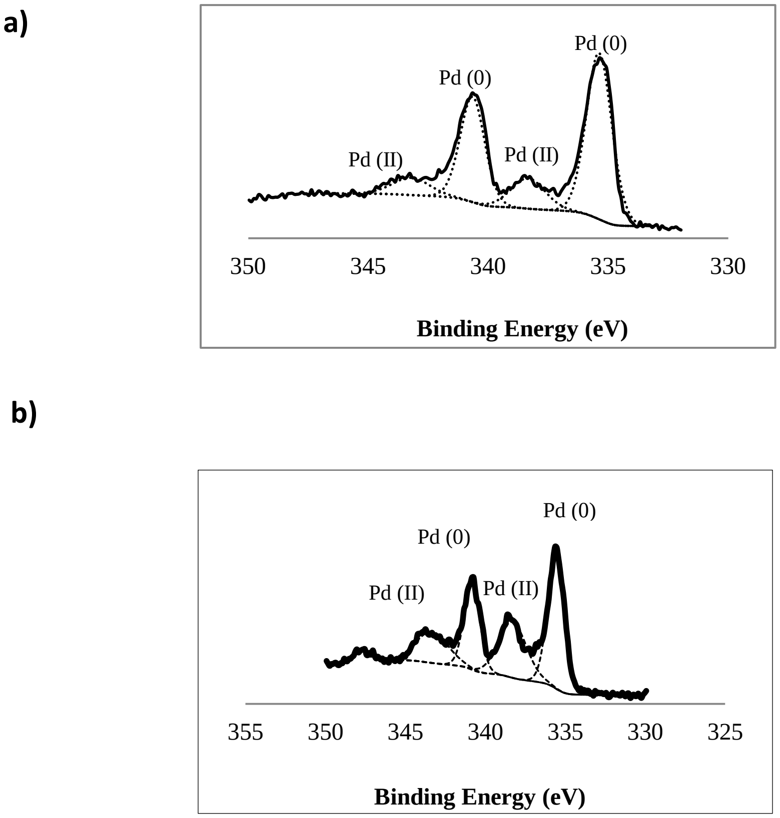
Figure 5-5



a) Traditional heating used in batch reactions, b) Improved energy transfer in a continuous reactor

The continuous-flow microwave assisted synthesis of Pd/G, using lab synthesized graphite oxide, produced a catalyst with a high concentration of Pd(0), the active redox species required to initiate Pd-catalyzed cross-coupling reactions. Analysis of the XPS spectra (Figure 5-4 a) indicated a Pd(0) content of 80 %, with the remaining 20 % as palladium (II). Observed binding energies were 335 eV and 341 eV for palladium (0) and 339 eV and 344 eV for palladium (II) for the Pd/G samples. However, the Pd/Gc Palladium (0) concentration decreased by 20 % resulting in only 60 % Palladium (0) on the surface and 40% palladium (II) (Figure 5-4 b). Binding energies were observed at 338 eV and 343 eV. The high concentration of palladium (II) in the Pd/Gc sample may become problematic when using these samples in in a continuous cross coupling reaction. Palladium (II) more readily goes in solution than the palladium (0) counterpart thus increasing the risk of contamination in the final product. There have been reports of the generation of palladium (0) insitu in a batch reaction when the reaction is in a state of equilibrium. However, in a continuous reaction a state of equilibrium never is reached and thus the palladium content may be wash away in the product stream. For these reasons evaluation of the Pd/Gc samples were limited to continuous coupling reactions, consistency of various lots and catalyst loading studies.

Figure 5-6



XPS spectra of unused catalyst. _______ Raw data; ……….. Fitted Spectrum a-Lab Synthesized G (Pd/G) b- Commercially available G(Pd/Gc)

Eight discrete lots of Pd/G, and four discrete lots of Pd/Gc were generated. Samples were picked randomlyand characterized to test the reproducibility of the synthesis approach. All samples exhibited similar size distribution of the palladium nanoparticles and formation of agglomerations around the creases and edges of the graphene sheets. Moreover, all lots were consistent with respect to palladium (0) content, suggesting that a continuous microwave-assisted approach to the synthesis of Pd/G provides reliable access to this useful ligand-free catalyst system.

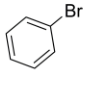
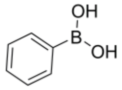
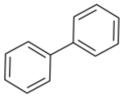
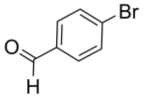
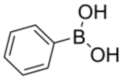
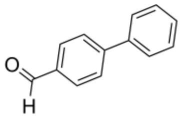
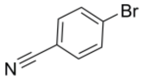
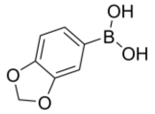
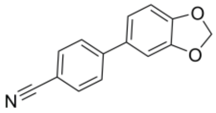
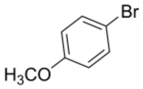
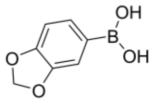
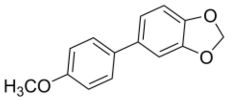
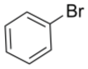
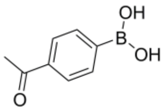
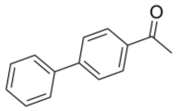
5.3.2 Catalytic Activity of Pd/G and Pd/Gc in Traditional "Batch" Suzuki-Miyaura Cross-Coupling Reactions

The initial catalytic activity of Pd/G and Pd/Gc prepared using the continuous synthesis method was evaluated for the Suzuki-Miyaura cross-coupling reaction between bromobenzene (**1a**) and phenylboronic acid (**2a**) in microwave-assisted batch reactions. The catalyst loading was varied between 0.5 mol% and 5 mol % to determine optimum catalyst loading. Using the Pd/G sample full conversion was observed by GC-MS at 1 mol% catalyst loading for this reaction; however, below this level a decrease in conversion was evident when evaluating the Pd/G sample. The Pd/Gc sample was also varied between 5 mol % and .5 mol% catalyst loading, and was successfully used at .5 mol % loading without a decrease in product conversion. However below this threshold a decrease in product conversion was observed. However, it is unclear whether palladium (0) or palladium (II) on the surface is catalyzing the coupling reaction. Because Pd/Gc sample is mainly comprised of Pd (II), a readily soluble species of palladium and not good for continuous reactions, further evaluation of these catalyst were terminated.

5.3.3 Diversity and Recycling Studies of Pd/Gc in Traditional "Batch" Suzuki-Miyaura Cross-Coupling Reactions

A variety of functionalized aryl bromides (**1**) and phenylboronic acids (**2**) were then used to evaluate catalyst versatility in Suzuki cross-coupling reactions (Table 1). For these batch reactions, substrates were combined with Pd/G and potassium carbonate in a H_2O/EtOH solvent system and heated to 80 °C for 10 minutes in a CEM microwave. The Pd/G catalyst exhibited good to excellent conversion in Suzuki reactions with both electron-withdrawing and electron-donating functional groups.

Table 5-3

Entry	Aryl Halide	Boronic Acid	Product	Percent Conversion
1	 **1a**	 **2a**	 **3**	100
2	 **1b**	 **2a**	 **4**	100
3	 **1c**	 **2b**	 **5**	94
4	 **1d**	 **2b**	 **6**	95
5	 **1a**	 **2c**	 **7**	65

Suzuki reactions completed under traditional batch conditions.[1] Aryl halide (0.3 mmol), boronic acid (0.32 mmol), K_2CO_3 (0.9 mmol), and Pd/G catalyst (5 mol%) were combined in 4 ml of H_2O: EtOH (1: 1) and irradiated at 80 ^oC for 10 minutes.

We then tested eight separate lots of continuously-produced Pd/G with the first two Suzuki- Miyaura cross-coupling reactions in order to determine the lot-to-lot variability in catalytic activity (Table 5-4). We examined two different aryl halide substrates and all eight catalyst lots gave essentially equivalent yields under the same reaction conditions. The reproducible physical characteristics and catalytic activity of continuously-produced Pd/G may also be attributed to the uniform application of microwave irradiation.

Table 5-4

Pd/G	**Conversion (%)**[1] **1a + 2a**[2]	**Conversion (%)**[1] **1b + 2a**[2]
Lot 1	100	100
Lot 2	100	99
Lot 3	100	100
Lot 4	100	100
Lot 5	100	97
Lot 6	100	97
Lot 7	100	100
Lot 8	100	99

Lot-to-lot consistency of Pd/G activity in two Suzuki-Miyaura reactions.

[1] Conversions determined by GC-MS. [2] Reaction conditions as listed in Table 5-1.

The recyclability of the Pd/G sample, was then evaluated using the Suzuki-Miyaura reaction between bromobenzene and phenylboronic acid. The solid-supported catalyst was isolated from microwave-assisted batch reactions by filtration, washed, and re-used in subsequent reactions with fresh substrates and reagents. High conversions were recorded for the first three rounds of reactions (Table 5-5), indicating that Pd/G may be a good candidate for continuous applications. Upon examination of the reaction filtrate, we observed 347 ppm Pd in solution indicating minimal loss of catalyst to the reaction mixture.

Table 5-5.

Run	**Conversion (%)**[1] **1a + 2a**[2]
1	100
2	100
3	95
4	77

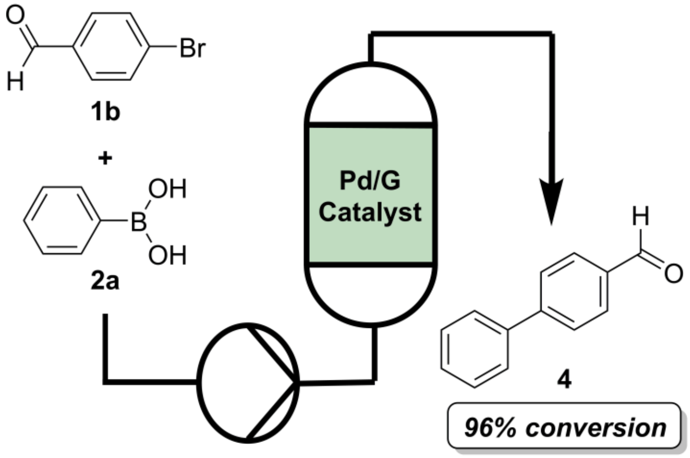
Recyclability of Pd/G in Suzuki-Miyaura reactions

[1] Conversions determined by GC-MS. [2] Reaction conditions as listed in Table5- 1.

5.3.4 Suzuki-Miyaura Cross-Coupling Reactions Executed Under Continuous Flow Conditions

With a reliable and scalable preparation of Pd/G in hand, we sought to highlight the combined benefits of solid-supported catalysts and flow synthesis by applying our catalyst to a continuous Suzuki-Miyaura cross-coupling system. The reaction between 4-bromobenzaldehyde (**1b**) and phenylboronic acid (**2a**) provided the best solubility profile to demonstrate the application of our catalyst in flow (Figure 5-6). A small amount (100 mg) of the Pd/G or Pd/ Gc catalyst synthesized under continuous flow conditions was loaded into a catalyst cartridge using the procedure previously described. The catalyst cartridge was then equilibrated to 135 °C on a Thalesnano X-Cube flow reactor. Reactants were dissolved in a H_2O/EtOH/THF (1:1:1) solvent mixture and fed into the packed bed at a flow rate of 0.2 mL/min, resulting in a contact time of less than 5 minutes. Using these conditions, the Suzuki reaction proceeded with a conversion of 96% for the Pd/G sample but yielded only 23% for the Pd/Gc. The product was collected in 30 minute increments for 2 hours without a reduction in product conversion.

Figure 5-7



Process Flow Diagram for a Continuous Suzuki Reaction

One of the major concerns in translating the Pd/G catalyzed Suzuki-Miyaura reaction from batch to continuous operations is the potential for rapid catalyst deactivation due to metal leaching under non-equilibrium (continuous) conditions. Accordingly, the palladium content of the continuous Suzuki-Miyaura reaction product stream was evaluated using inductively coupled plasma mass spectrometry (ICP-MS). The solution from the experiments conducted with the Pd/G sample contained only 357 ppb of palladium, suggesting that graphene is a reliable and robust support for palladium nanoparticles. However, the solution that was collected from experiments using Pd/Gc contained more than 700 ppm of palladium, which suggest that the commercially graphite oxide was not successfully reduced to a reliable source of graphene to support the palladium particles. Furthermore, the palladium leaching offered some insight of the delicate relationship between the palladium particles and the graphene support system. Low palladium suggests a strong interaction between the nanoparticles and the graphene support system while high palladium content suggests a superficial physical reaction between nanoparticles and the support.

5.4 Conclusion

In conclusion, we have developed a highly efficient method for the preparation of Pd nanoparticles supported on graphene by the continuous microwave-assisted chemical reduction of an aqueous mixture of palladium nitrate and dispersed graphite oxide sheets. Despite the success we have seen with the graphite oxide made in the laboratory setting the commercial available graphite oxide should less favorable results. This particular graphite source was not a good support system for the palladium particles, which was evident in product leaching. Furthermore this method was unable to produce uniform graphene sheets and seemed to exhibit characteristics of stacked layers (graphite). Further analysis is needed to optimize this procedure using the commercially available graphite oxide.

This process serves as a convenient and scalable method for accessing multi-gram quantities of this material. Furthermore, this procedure is capable of delivering a catalyst of consistent and reproducible physical and catalytic properties and serves as the first flow-based method for producing a solid-supported palladium catalyst. We were also able to demonstrate that these catalysts can be employed in continuous Suzuki-Miyaura cross-coupling reactions under ligand-free conditions in an environmentally friendly solvent system with minimal catalyst leaching/deactivation over an extended period of time.

Chapter 6

Continuous Synthesis of Zinc Oxide: A Viable Option for Automotive Oil Additive

6.1 Introduction: Automotive Oil Additives

While the focus of this research has been on the synthesis of solid supported nanoparticles to use in the continuous synthesis of organic molecules, the use of continuous technology may be expanded to other applications in the synthesis of nanoparticles. In collaboration with Afton chemical company such technology was used in efforts to make nanoparticles that may serve as automobile oil additives.

As the sources of oil continues to be depleted those in the automotive industry are looking for technologies not only to fuel new cars but increase the efficiency of existing cars. The US government has set regulations that by 2016 cars will have a standard of 35.5 miles per gallon (MPG).[45, 30] Europe, Japan, and China, are also seeking to improve fuel efficiency to an average of 35 MPG by 2015.[29,46] One technique to increase fuel efficiency is to decrease the friction and frictional losses within the car engine. An average economy car requires a significant amount of energy from its fuel to run correctly including roughly 70% of its effiency in the engine due to combustion, radiation, thermal heat, etc, 5% parasitic loses, and 17% to power the wheels.[47]

There are a number of frictional properties that contribute to fuel efficiency loses, including high temperature high shear viscosity, thin film friction, film thickness, and boundary friction coefficient.[48] When testing the efficiency of a fuel or oil, companies first look at the boundary friction coefficient[31], thus this guided the focus of recent inquiries. Friction may be defined as the force that resists free movement of two solid surfaces/boundaries. The boundary friction coefficient is a dimensionless measurement of the ratio of friction and the pressure pushing the two surfaces together. When lubricant is added to moving surfaces, a thin film is formed that allows the boundaries to move freely[49]. Friction modifiers such as glycerol monooleate have been used to create the film needed to reduce friction[33,]. Effective modifiers should be oil soluble, and uniform in size and shape[50]. While a number of nanoparticles have been explored as oil additives, cerium and zinc oxide nanoparticles show the most promise, with zinc oxide particles as the more practical because of cost and availability[33,51]. Despite the unique advantages of nanoparticles as oil additives, their use has been limited because of availability. It was hypothesized that the synthesis of ZnO particles may be scaled up without compromising particles ability to reduce friction, using a continuous synthesis method. A two level design of experiments was carried out to identify the critical parameters in the synthesis method.

6.2 Materials and Methods

6.2.1 Materials

Zinc nitrate (98% reagent grade), sodium hydroxide pellets (reagent > 97%), olelic acid (99%), and oleyamine (98%) were obtained from Sigma Aldrich. 2-propanol (99.5%) was purchased from Fisher Scientific. Analysis of DOE data was conducted using JMP software.

6.2.2 Batch Synthesis of ZnO nanoparticles

50 ml of a 0.2 molar stock solution of zinc nitrate in 2- propanol was prepared in a glass storage vial. In a separate storage vial 50 ml of a 0.4 molar stock solution of sodium hydroxide in 2-propanol was prepared. 2 ml of both stock solutions were placed in a 10 ml reaction vessel with a magnetic stir bar. The vial was sealed and placed in in the CEM microwave at a temperature set point and time designated by the DOE. The reaction solution was then centrifuged in an Eppendorf 5804 centrifuge at 5000 rpm for 30 minutes. Excess propanol was decanted. The recovered solid was resuspended and centrifuged for two additional cycles. Following the last cycle the solid product were rinsed with acetone and dried in a drying oven at 70 ^{o}C.

6.2.3 General Procedure Continuous Synthesis of ZnO Nanoparticles

One liter of a 0.2 molar stock solution of zinc nitrate in 2- propanol was prepared in a glass storage vial. In a separate storage vial 1 liter of a 0.4 molar stock solution of sodium hydroxide in 2-propanol was prepared. Both stock solutions were simultaneously fed to the Arrenhius One Wavecraft reactor using Chemtrix alternating syringe pumps, flow rates and reaction temperatures were predetermined using a DOE. Collection vessels were changed after 10 ml of product solution were collected, and conditions were changed when 50 ml of solution was collected. The reaction solution was then centrifuged in an Eppendorf 5804 centrifuge at 5000 rpm for 30 minutes. Excess propanol was decanted. The recovered solid was resuspended and centrifuged for two additional cycles. The solid particles were rinsed with acetone and dried in a drying oven at 70 ^{o}C.

6.2.4 General Procedure of Batch Synthesis of Coated ZnO Nanoparticles

Oleic acid (3.6 mL.011 mols), and oleyamine (3.75 mL.011 mol) were added to a 25 ml round bottom flask and heated to 120 ^{o} C using an oil bath to remove any excess water. Zinc nitrate (0.133g, 0.7mmol) was added to the flask, and held at 120 ^{o} C for an hour. The mixture was then placed in a conventional microwave oven at full power (1000 watts) for 10 minutes. The resulting mixture was allowed to dry overnight in an oven at 75 ^{o}C.

6.2.5 Conditions and Experiments for DOE

Two level DOE was created for both the continuous and synthesis of ZnO nanoparticles. A low, high, and midpoint were selected for each parameter. The experiments were carried out randomly, with the midpoint repeated 3 times to test reproducibility. Each sample was evaluated using high frequency reciprocating rig (HFRR) testing, at Afton chemicals. The data collected was evaluated using a regression model in JMP software. Tables 16 show the parameters for the batch and continuous reactions. In the continuous process reaction time is defined as the time in which the liquid solution is in the microwave cavity, flow rates of the reaction solution were adjusted accordingly

Table 6-1

a)

Batch Reaction Parameters		
	Temperature (^{o} C)	Reaction Time (minutes)
Low Level (-1)	80	5
High Level (+1)	100	10
Midpoint	90	7.5

b)

Continuous Reaction Parameters		
	Temperature (^{o} C)	Reaction Time
Low Level (-1)	80	5
High Level (+1)	100	10
Midpoint	90	7.5

2-Level DOE boundary conditions for batch and continuous synthesis of ZnO nanoparticles

6.2.6 General Procedure for High Frequency Reciprocating Rig Testing

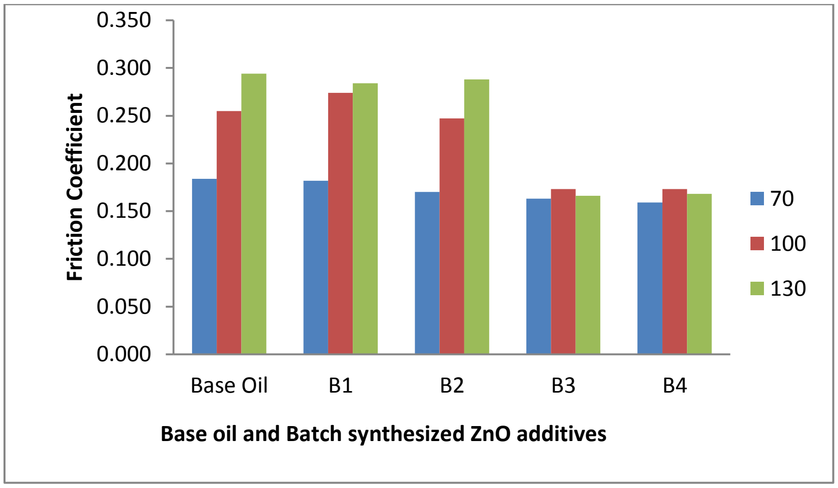
Base engine oil, Yubase 6, was obtained by Afton chemicals (3.98g). Synthesized nanoparticles (0.02g, 0.5 wt%) were added to the base oil. The mixture was then loaded in a steel disk of the PCS High frequency reciprocating rig. A standard load (4N) was applied to the steel ball and disk. The ball was mechanically moved at a speed of 3mm/s and a frequency of 20 Hz for 3 minutes. The friction coefficient was tested at 70 ^{o}C, 100 ^{o}C and 130 ^{o}C.

6.3 Results and Discussion

6.3.1 Batch Synthesized ZnO Nanoparticles

ZnO nanoparticles were successful synthesized using the batch microwaved synthesis. When added in a base oil system, representative of automotive oil, it was noted that none of the tested samples were soluble within the oil. Despite the insolubility of each sample all samples were successful in reducing the friction coefficient.

Figure 6-1



Changes in Friction Coefficient

Friction Coefficient of 0.5 wt% batch synthesized ZnO nanoparticles additives, Synthesis conditions- B1(temp-80 ^{o}C, reaction time- 5 min.), B2(temp-100 ^{o}C, reaction time- 5 min.), B3(temp-80 ^{o}C, reaction time- 10 min.), B4(temp-100 ^{o}C, reaction time- 100 min.).

At 70 ^{o}C all samples slightly decreased the friction coefficient. During HFRR testing at this temperature the base oil had a base oil of approximately 0.184. Sample B1(synthesized at 80 ^{o} C for 5 minutes) was the least effective additive and only reduced the oil by 1.1 %. The most effect additive, B4 synthesized at 100 ^{o} C for 10 minutes, was able to reduce this friction by 13.6%. The sample synthesized at 80 ^{o}C for the same amount of time (B3) only differed slightly and was able to decrease friction by 11.4%

Table 6-2

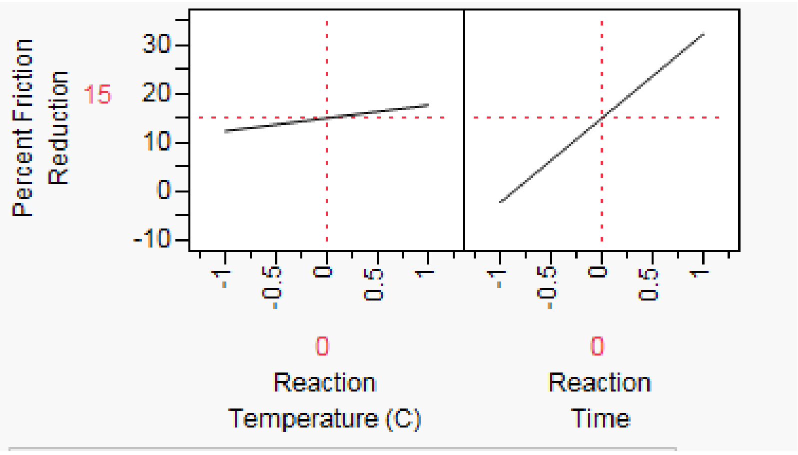
	70	***100***	***130***
B1	1.1	-7.5	3.4
B2	7.6	3.1	2.0
B3	11.4	32.2	43.5
B4	13.6	32.2	42.9
Midpoint (100)	23.6	21.9	24.3

Percent reduction of friction coefficient for batch synthesized ZnO nanoparticles

At higher testing temperatures samples B3 and B4 proved to be superior additives. While the base oil additive had a friction coefficient of 0.255 samples B3 and B4 were both able to reduce the coefficient by 32.2%. At 130 ^{o}C sample B3 was able to reduce friction slightly more B4, 43.5% and 42.9% respectively. It is hypothesized that higher temperature the percent reduction will converge to a single value. This was proposed because of the lack of solubility of the nanoparticles. Literature suggests that nanoparticles are able to form a uniformed layer that moving objects are able to move freely along[31]. Insoluble particles will not form a complete uniform layer within oil, and possibly have areas where no particles may be found, thus reducing the effectiveness of the particles. Additional test were not conducted to test this hypothesis but will be included in future work. Data obtained at 100 ^{o} C was used to make a model and predict the contribution to friction percent reduction from each of the process parameters.

Data was analyzed using JMP model fit software. During the analysis the following parameters and interactions were evaluated during modeling; the reaction time, temperature and the interaction between time and temperature, the interaction time has with itself and the interaction temperature has with itself. The linear model suggested that time is the most significant parameter. The interactions of time with itself and temperature with itself may be ignored as they have no effect on the output values. The coefficient of determination (R^2) is 1 indicating this model is a perfect match for the data collected.

Figure 6-2



Parameter Profile Predictors: Batch ZnO

Figure 34 shows the linear fitted lines of the two process parameters. The slope of the line shows the rate of change within that particular parameter. Time changes at a faster rate which is confirmation that the reaction time provides a significant contribution to the percent friction reduction. Equation 6-1 was obtained using this model to predict the percent reduction when given synthesis temperature and time.

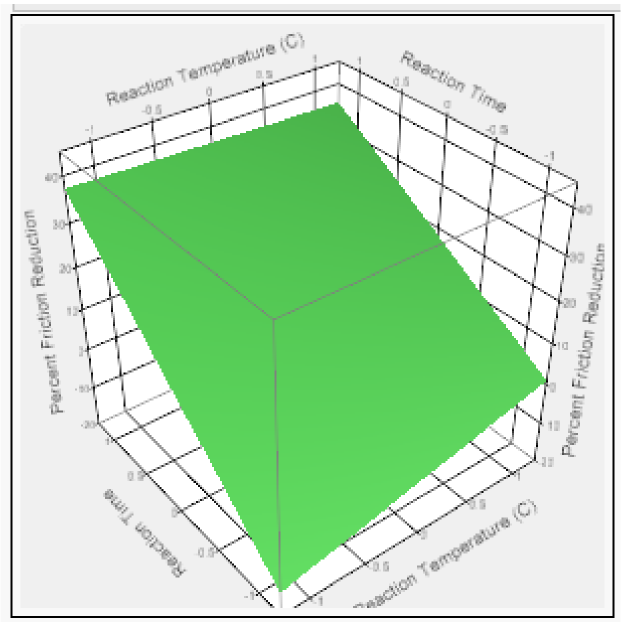
Equation 6-1

$$\mathbf{Y = 15+ 2.65*(X1) +17.2*(X2)- 2.65*(X3)}$$

Y- Predicted Percent friction reduction , X1-reaction temperature X2- reaction time, X3- Interaction between time and temperature

The surface plot of the optimal reaction condition suggest that as the time of synthesis reaction is increased or extended the percent friction reduction will also increase. This may be attributed to an increase in particles formed during the reaction.

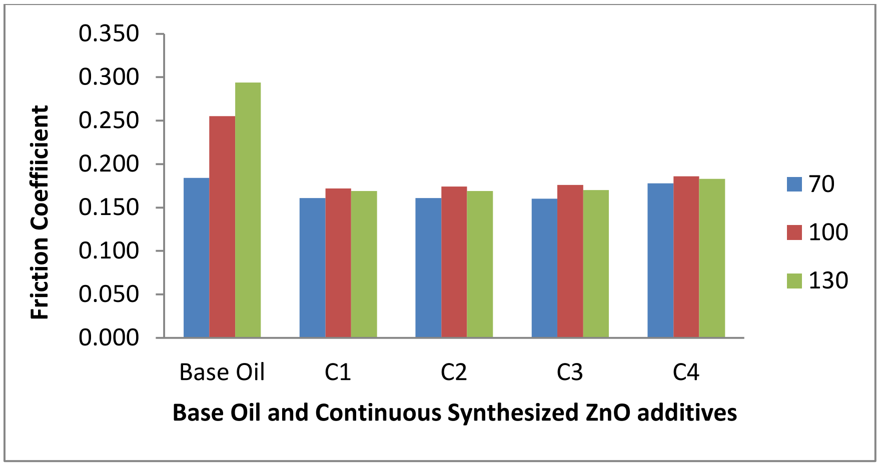
Figure 6-3



Surface Plot of Optimal Operation Conditions for Batch Synthesized ZnO Nanoparticles

6.3.2 Continuous Synthesis of ZnO nanoparticles

Figure 6-4



Friction coefficient of base oil and ZnO nanoparticles synthesized continuously

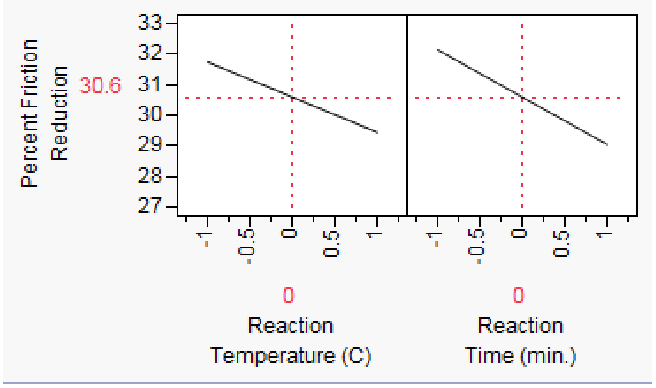
Four samples were produced using the continuous synthesis method. All were evaluated using the HFRR testing. As seen with the ZnO nanoparticles made in batch none of the new samples were soluble in the base oil obtained by Afton. All samples made continuously, effectively reduced the friction coefficient. Unlike the samples made by the batch synthesis there are only slight differences in the friction coefficients at the various temperatures tested despite the temperature or reaction time (flow rate) in which they were synthesized. Sample C4 (100 ^{o} C, 10 minutes) deviated the most from the other three samples. These conditions must be reproduced in order to draw any conclusions to the cause of the deviation. It should be noted that the deviation between the three midpoint values was only .24. This indicates that the particles made using this method are highly reproducible and there is virtually no batch to batch variability in this particular set of experiments. Regression data was also obtained for these sets of experiment the percent reduction at 100 ° C was used.

Table 6-3

	70	*100*	*130*
C1	12.5	32.5	42.5
C2	12.5	31.8	42.5
C3	13.0	31.0	42.2
C4	3.3	27.1	37.8
midpoint (100)	25.4	25.1	25.7

Percent Friction Reduction of Continuous Synthesized Oil Additives

Figure 6-5



Main Parameters Prediction Profiles

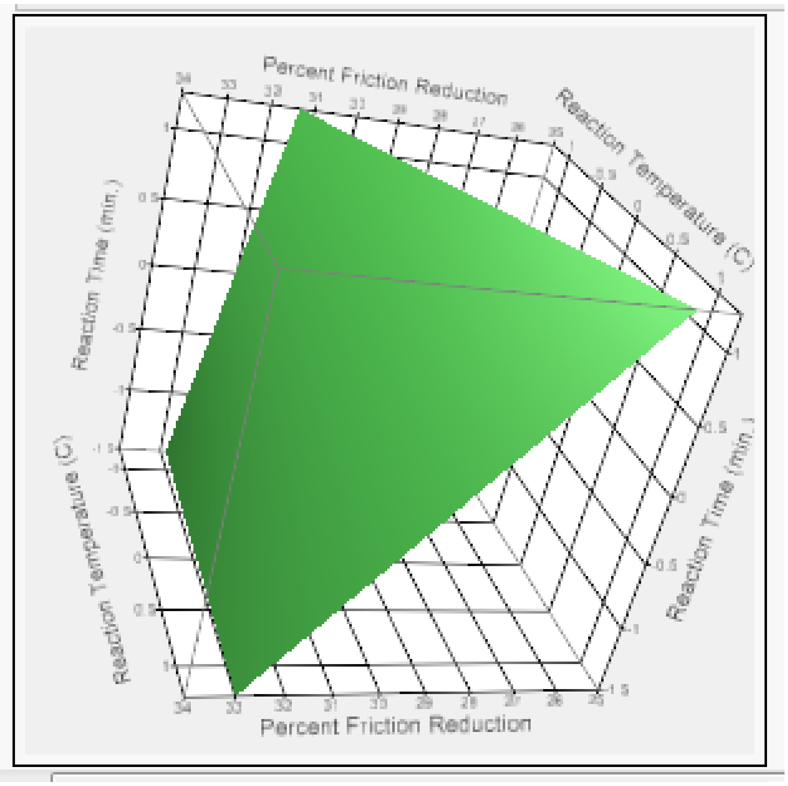
When examining the parameters prediction profile there only seemed to be slight difference in the slope of the lines, indicating there is a parameter that has more significance over the other however it is minimal. This theory was confirmed when looking at the mathematical model for this data (Equation 6-2).

Equation 6-2

$$\mathbf{Y = 30.6 + 1.15* (X1) + 1.55 * (X2) - 0.8 * (X3)}$$

Where Y - predicted percent friction reduction, X1-reaction temperature X2- reaction time, X3-Interaction between time and temperature

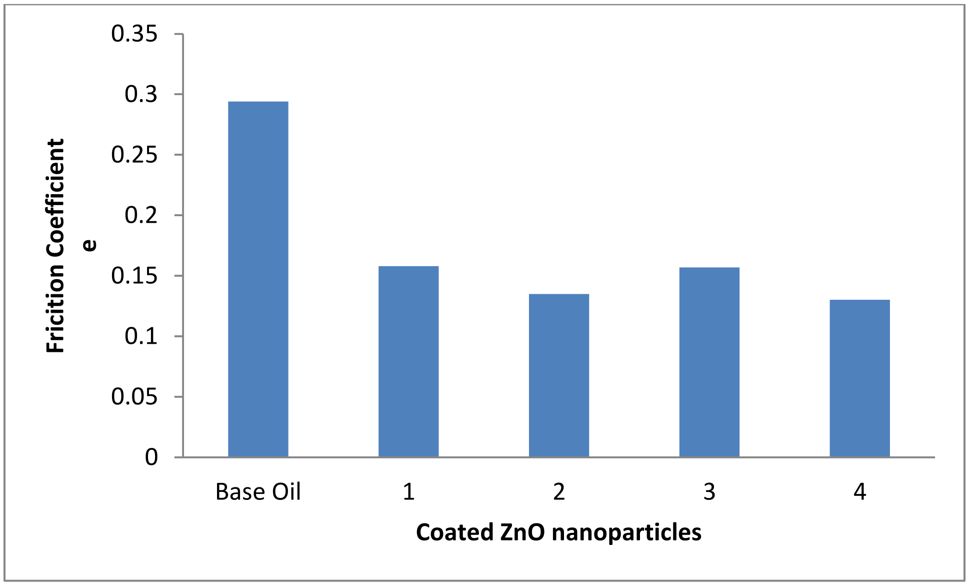
Figure 6-6



Surface Profile Plot of Predicted Percent Friction Reduction

Where change in reaction time is slightly greater than the temperature, which indicates it is slightly more significant. The surface plot of this data indicates the optimal conditions for the continuous reaction occurs when both the temperature and time are at their maximums (Figure 6-6) Though a well fitted model was developed for this data it is speculated that the effects of these parameters were not captured based on the boundary conditions. In Future studies the distance between the upper and lower limits of each parameter will be increased, so previous findings may be accepted or rejected. When the two sample sets were compared to one another those synthesized using the continuous method were able to reduce the friction coefficient more those synthesized in batch. Conclusions about the process parameters are reserved until DOE experiments are repeated. However the continuous method exhibited less variation between batches, which is evident through the standard deviation between the batch and continuous midpoint trials, 1, and 0.24 respectively. The initial hypothesis was accepted ZnO nanoparticles were successfully made and effectively reduced the friction coefficient using a continuous synthesis method.

Figure 6-7



Friction coefficient in Base oil 6 with 0.5 wt% additive loading at 130 °C

As previously stated none of the samples were soluble in the base oil obtained by the Afton chemical company. Coated cerium oxide nanoparticles have been synthesized by Dr. Elshall's research group. During this study the produce was applied to coat zinc oxide nanoparticles. Four samples of coated zinc oxide nanoparticles were successfully produced using the prescribed reaction conditions, and evaluated in HFRR test at 130 ° C (Figure 6-6). Only one temperature was tested because this temperature is more representative of conditions in an automobile. At this temperature the base oil had a friction coefficient of 0.294. All samples were able to reduce the friction coefficient of Base oil 6 (Figure 6-7). Samples 2 and 4, both synthesized at 100 °C, exhibited the greatest reduction in friction, 54.1 % and 55.8% respectively (table 6-4). Though significant reduction in friction was observed the surfactants used the coat the particles may reduce friction. At these same conditions oleic acid is able to reduce friction by

59% and oleamine by 54%. The reduction in friction seen in the particles may be attributed to the coating and not the particles themselves. It is recommended that future studies develop a method to quantify the thickness of the particle coating and conduct a DOE with 2 output values, percent friction reduction and coating thickness.

Table 6-4

	Synthesis Temperature ©	Synthesis Time (min)	Percent Friction Reduction (%)
1	80	5	46.3
2	100	5	54.1
3	80	10	46.6
4	100	10	55.8

Coated ZnO nanoparticles synthesis conditions and percent friction reduction

6.4 Conclusion

ZnO nanoparticles were successfully synthesized using both a batch and continuous method. For the batch process samples whose reaction time were longer exhibited higher reductions in friction, B3- and B4. JMP analysis of the process revealed that time was the most significant parameter when reaction time and temperature were considered. When the same parameters were considered for the continuous method time was slightly more significant than temperature. This was evident as the percent reduction only changed slightly as the synthesis parameters were changed. However, a greater reduction in friction was observed at all conditions among the continuous samples. Further conclusions were reserved as a broader range in DOE boundary limits must be chosen. Despite the too narrow range the continuous method was highly reproducible as the standard deviation between the batches was found to be only 0.24. Neither the batch nor the continuous synthesized ZnO samples were soluble in the base oil, thus coated ZnO oxide particles were synthesized. When the coated zinc oxide particles were tested by HFFR a decrease in the friction coefficient was observed. The reduction in the friction coefficient maybe attributed to the coating and not the particles themselves. A DOE studying the effects of coating thickness and friction reduction should be considered.

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