12-4-2019

Determination of Optimal Mild Organic Solvents of PdNPs for Carbon-Carbon Coupling Reactions

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Determination of Optimal Mild Organic Solvents for Synthesis of PdNPs for Carbon-Carbon Coupling Reactions

An Honors Thesis submitted in partial fulfillment of the requirements for Honors in *Chemistry and Biochemistry.*

By
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Under the mentorship of *Dr. Beverly Penland*

ABSTRACT

The synthesis of nanoparticles is an increasingly popular field of interest. The application of nanoparticles is especially popular in the field of nanocatalysts. Metal nanoparticles (NPs) are favorable for catalysis because of the large surface area to volume ratio, which allows them to catalyze a variety of reactions using lesser amounts of active material. As the field of nanoparticle research expands, efforts are being made to create more sustainable approaches to the synthesis of these particles. This research sought to translate the benefits of peptide-based synthesis to organic solvents and use less toxic organic solvents for carbon-carbon coupling reactions, like Heck coupling with new peptide-based nanocatalysts. Using less toxic organic solvents, PdNPs were synthesized in ethanol, with the use of peptides to mediate the NP formation. The PdNPs were characterized by UV-Vis, hydrodynamic size, and SEM-TED analysis. The effectiveness of these nanoparticles as catalysts was examined through the use of carbon-carbon coupling reactions with aryl halides to yield biphenyl products. The catalytic studies were conducted in matching solvent concentrations as the NP synthesis at room temperature and pressure at a catalyst loading of 0.05 mol%. The results of the carbon-carbon coupling utilizing the PdNPs were quantified using NMR and GC-MS.

Thesis Mentor:_____

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Honors Director:_____

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November 2019
Department Chemistry and Biochemistry
University Honors Program
Georgia Southern University

Acknowledgements

I would first like to thank my research mentor Dr. Beverly Briggs Penland for her guidance during my research. Over the past two years in her research lab, I have grown my skills as a scientist and a student. I am grateful for the opportunity to exercise my passion for sustainability and science in her research lab.

I would also like to thank my fellow students in the Penland research group. They have provided me with support and camaraderie in and outside of the lab.

I would like to thank the Department of Chemistry and Biochemistry. The faculty and staff have given me the knowledge and resources that have helped me complete my thesis and degree program.

Additionally, I would like to thank the Georgia Southern University Honors Program for encouraging academic research and inquiry and for motivating me to become a student researcher.

Finally, I would like to acknowledge my friends and family for their continued support.

Introduction

Nanoparticles, due to their large surface area to volume ratio, can be effective catalysts in various reactions. The synthesis of these nanoparticles can be performed in many ways. In this study, peptides, specifically the Pd4 peptide (TSNAVHPTLRHL), was used to mediate the formation of palladium nanoparticles (PdNPs). The use of peptides is a biomimetic method of nanoparticle synthesis that is beneficial due to the specificity of biomolecules as well as the ability to use them in biological systems.[2] Biomimetic synthetic methods are also environmentally-friendly, and a goal of this research was to translate this benefit to organic solvents. This study focused on the synthesis of PdNPs in organic solvents and their possible catalytic use. These PdNPs have previously been synthesized in water and has been shown to be effective catalysts in the Suzuki coupling reaction.[1] The mild organic solvent used to test the effectiveness and formation of the nanoparticles was ethanol (EtOH). PdNPs were synthesized in various concentrations of ethanol with various Pd^{2+} solutions. The PdNPs were then used as catalysts in the Suzuki reaction to form biphenyl carboxylic acid.

Pd4 Peptide

The Pd4 peptide (TSNAVHPTLRHL) is a hydrophilic peptide that is composed of 12 amino acids. Previous studies have shown that this peptide is effective in mediating the formation of PdNPs in water.[2] Based on modeling

studies, there is evidence that the histidine residues at the 6 and 11 positions of the peptide coordinate to the fcc Pd facet and stabilize the Pd nanoparticles. These spherical, homogenous nanoparticles have an average diameter of 1.9 nm (Figure 1b and c). In this study, the Pd4 peptide was used to mediate the formation of palladium nanoparticles (PdNPs). These PdNPs have previously been synthesized in aqueous conditions.

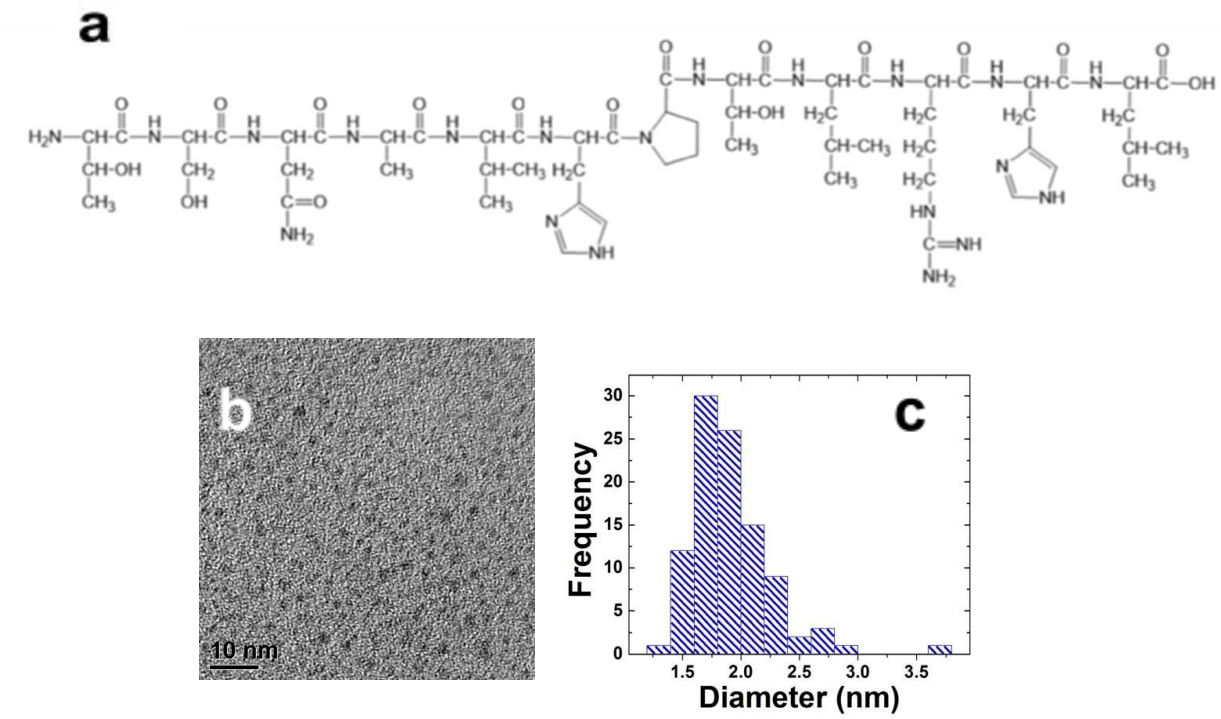

Figure 1. a) structure of Pd4 peptide with amino acid sequence TSNAVHPTLRHL.b) SEM-TED image of PdNPs synthesized in water showing an average diameter of 1.9 ± 0.4 nm. c) average size distribution of PdNPs in water. [2]

S2 Peptide

The S2 peptide (AFILPTG) is a hydrophobic peptide that is composed of seven nonpolar amino acids. Previous studies have shown that the neutral, hydrophobic amino acids exhibit Van der Waals interactions with silica nanoparticles.[4] This particular peptide could potentially exhibit the same Van der Waals interactions with PdNPs. The hydrophobicity may also be favorable in organic solvents. While ethanol is a polar solvent, the future of this research includes testing the catalytic ability of PdNPs in other organic solvents, including nonpolar solvents.

Methods

A total 2.00 mL of nanoparticle solution was prepared for each peptide; each solvent system was tested in triplicate. Varying amounts of the solvent, based on the Pd^{2+}: peptide concentration were added to a glass vial. Then 40 µL of 10 mg/mL peptide stock solution were added to the vial and stirred. The peptide stock solutions were prepared with 1.0 mg of the peptide in 100 µL of solvent. The peptide solution remained in the freezer until use. Before the addition of the peptide stock, it was allowed to reach room temperature

Following the addition of the peptide solution, 0.1 M Pd^{2+} solution was added to the vial. The Pd^{2+} solution was prepared with 11.23 mg of palladium (II) acetate ($Pd(OAc)_2$) and 500 µL of acetone.

After the Pd^{2+} solution was added, the vial was mixed once again. The sample was allowed to complex on the benchtop for twenty-five minutes. Following the twenty-five

minutes, the reductant was added. The reductant was 0.1 M hydrazine monohydrate (N_2H_4) in ethanol.The sample was allowed to reduce for approximately 1 hour before being used in Suzuki coupling reaction.

S2 Peptide Group

With the addition of the S2 group on the N and C terminus of Pd4 the concentration of Pd^{2+}: peptide was lowered. The original Pd4 PdNPs had a 1:4 Pd: peptide ratio. With PdNPs formed with S2Pd4 and Pd4S2, the concentration was lowered to a 0.1:1, 0.2:1. 0.3:1 and 0.4:1 Pd^{2+}:peptide ratio. A 10 mg/mL peptide stock solution was made in the desired solvent. The total volume of the PdNP remained at 2.00 mL. The amount of solvent varied based on the concentration. 40 uL of peptide solution were added to the solution. Various amounts of Pd^{2+} were added to the solution. Following 25 minutes of complexation, varying amounts of the reductant, N_2H_4 were added at a 4x molar excess to the Pd^{2+} concentration.. All nanoparticle solutions were initially monitored for 24 hours to verify stability. After the initial check, the nanoparticles could be used after one hour of reduction.

Suzuki Coupling of Palladium Nanoparticles

The Suzuki coupling reaction was performed in 0.1M, 0.5M and 0.75M triethylamine solution following a previously published protocol.[1] In a small round bottom flask or glass vial., ethanol and triethylamine are added.. Then 124 mg (0.5 mmol) of 4-iodobenzoic acid were added to the flask and mixed. 73 mg (0.6 mmol) of phenyl boronic acid were added to the flask. Finally, the PdNP was added at 0.05 mol %

to the flask. The reaction was checked for solubility at each step. A stir bar was added to the flask and the flask was stirred between 300-400 rpm for approximately 24 hours. Following the 24 hours, the reaction was quenched by pouring the reaction mixture in an Erlenmeyer flask containing 50 mL of 5% HCl solution.

Suzuki Extractions

The quenched solutions were added to a separatory funnel and washed three times with 30 mL of ethyl ether. The aqueous layer was disposed of and the ether layers were collected in a 200 mL round bottom flask. The collected ether layers were washed with an additional 20 mL of saturated sodium chloride solution (NaCl). The aqueous layers were once again disposed of. The ether layers were collected in the empty Erlenmeyer flask. A scoopula full of anhydrous sodium sulfate (Na_2SO_4) were added to the ether and the flask was mixed until particles of Na_2SO_4 were mobile. 75 mg of tert-butyl phenol were added to the round-bottom flask as an internal standard. The ether layer was added to the round bottom flask following the addition of tert-butyl phenol. The ether was dried on the rotary evaporator for approximately fifteen minutes.The dried product was stored and tested for H-NMR and GC-MS.

Characterization of PdNP and Suzuki Products

The PdNPs were characterized by UV-Vis from 900-200 nm. The hydrodynamic size and zeta potential of the particles were also analyzed on the Zetasizer. The extracted product of the Suzuki coupling was characterized by ^{1}H NMR and GC-MS.

Data

Palladium nanoparticle synthesis was attempted with various peptides, precursors, reductants, and solvents. N_2H_4 at a concentration of 0.1 M in ethanol was determined to be the best reductant for PdNPs formed in ethanol. While sodium borohydride ($NaBH_4$) was used to for the Pd4 PdNP in aqueous conditions, N_2H_4 showed better reduction on the UV-Vis (Figure 1) with a sharp peak at approximately 250 nm. In comparison, PdNPs made with Pd4 under the same conditions show a broad region from 300-400 nm. The change in the spectrum of the complex of Pd4S2 versus the reduced when compared to very little change of the Pd4 spectra suggests that the reduction is better using the peptide with a hydrophobic region in the new ethanol solvent.

PdNPs were formed using three different peptides: Pd4, S2Pd4, and Pd4S2. TEM images were taken of PdNPs made with all three peptides. The images are shown in Figure 3. The average diameter of these PdNPs are shown in Table 1.

The hydrodynamic size averages of the PdNPs varied. With increasing Pd:peptide concentration, there was a trend of increasing hydrodynamic size (Figure 5). The zeta potential, however, had averages among all PdNPs of approximately 29.6 mV (Figure 6).

PdNPs using Pd4S2 and S2Pd4 peptides were used as a catalyst in Suzuki coupling reactions. The Suzuki yields are shown in Figure 7. The yields of all peptide PdNPs showed varying yields with high standard deviations. With

Pd4S2 PdNPs, there were better yields with the higher base concentrations of 0.75M Et_3N. There was no such trend among S2Pd4 PdNPs. The amount of error in the yields may be due to a decrease in catalytic ability of PdNPs in ethanol.

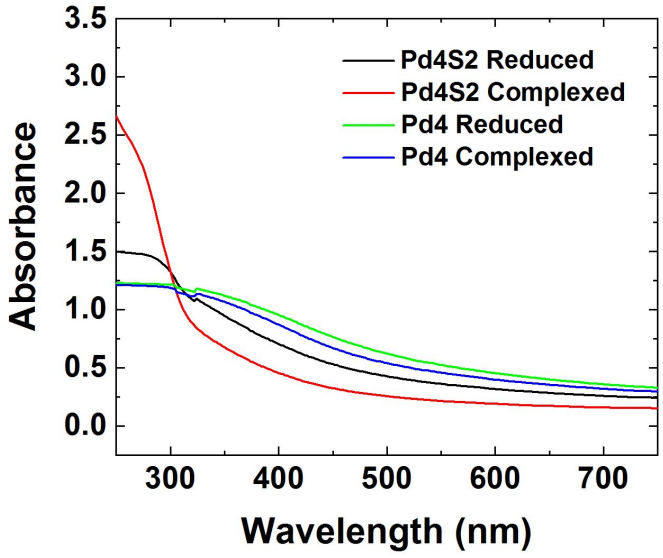

Figure 2. UV-Visible spectrum of PdNPs formed with Pd4 and Pd4S2 peptides. All PdNPs were made in ethanol and reduced with 0.1M N_2H_4.

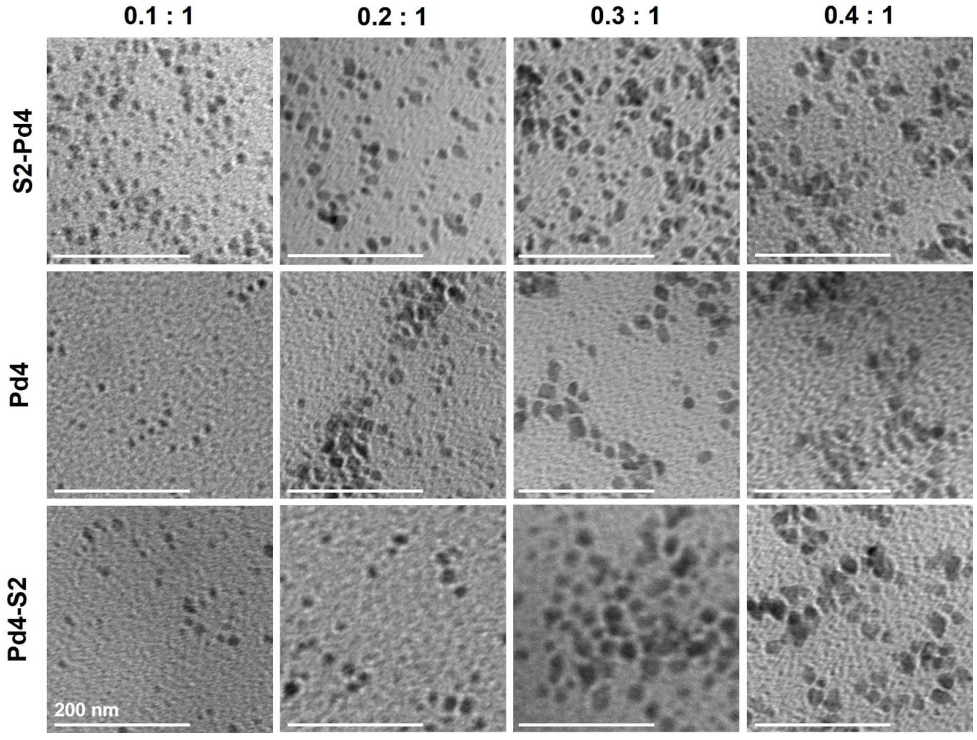

Figure 3. TEM images of S2Pd4, Pd4, and Pd4S2 PdNPs formed in ethanol with N_2H_4 at various Pd:peptide concentrations.

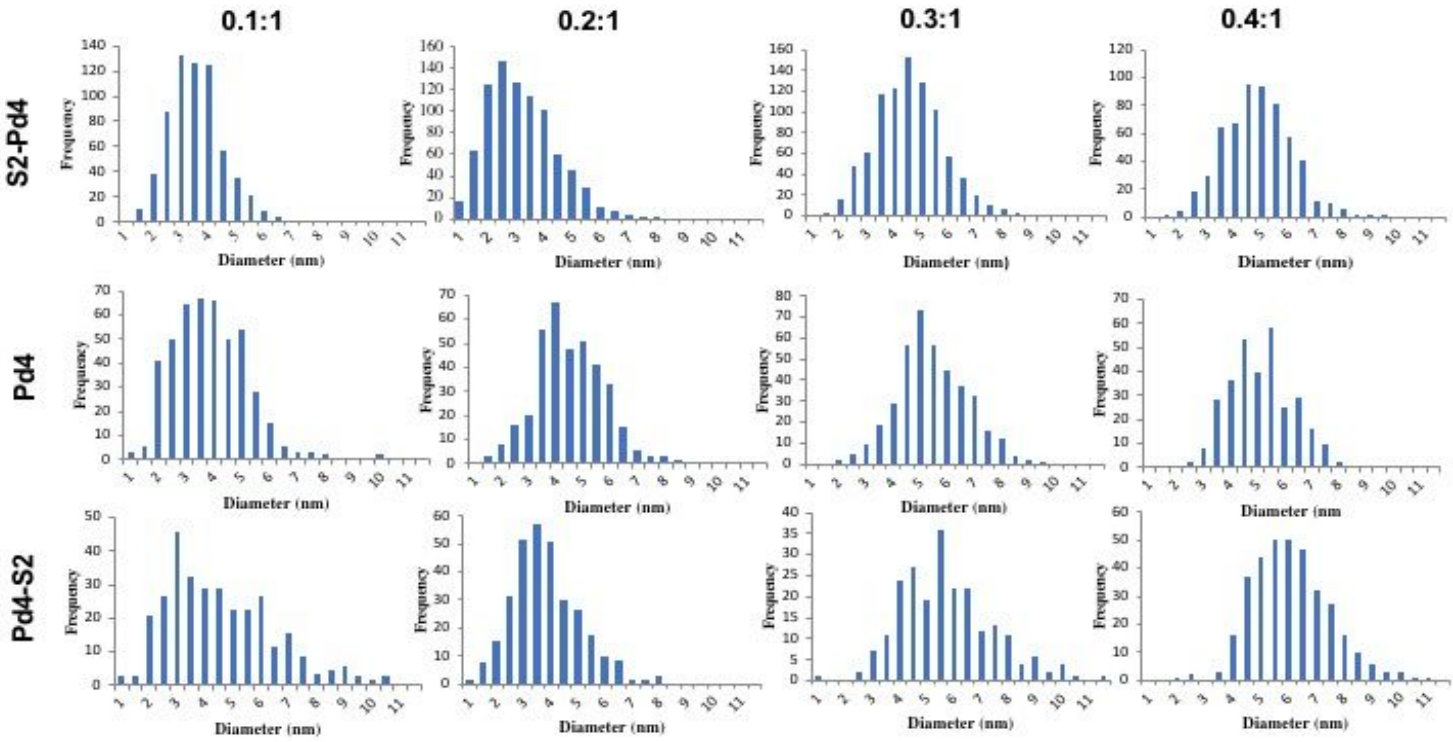

Figure 4. Diameters of PdNPs measured from TEM images in Figure 3. Images were measured using Image J.

Table 1. Average diameters of PdNPs with standard deviations. Diameters were determined with measurements from TED images from Figure 3.

	Pd4-S2	Pd4	S2Pd4
0.1:1	4.3±1.9 nm	3.6±1.2 nm	3.3±0.9 nm
0.2:1	3.6±1.2 nm	4.2±1.2 nm	2.9±1.2 nm
0.3:1	5.5±1.7 nm	5.5±1.7 nm	4.3±1.3 nm
0.4:1	5.8±1.4 nm	5.2±1.3 nm	4.6±1.2 nm

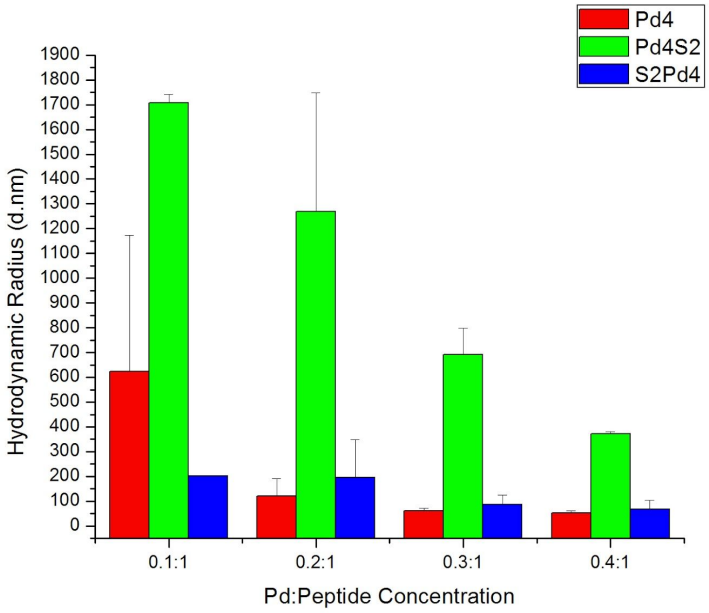

Figure 5. The hydrodynamic radius of PdNPs made with Pd4, Pd4S2 and S2Pd4 peptides. All were measured with Malvern Zetasizer.

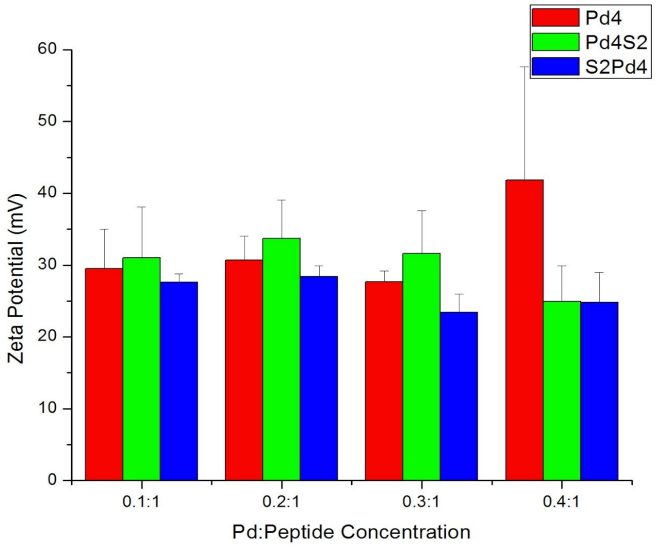

Figure 6. Zeta potential of PdNPs in ethanol with various peptides (Pd4,Pd4S2,

and S2Pd4). Zeta potential among all had a similar charge, with the average being approximately 29.6 mV. All were measured with Malvern Zetasizer.

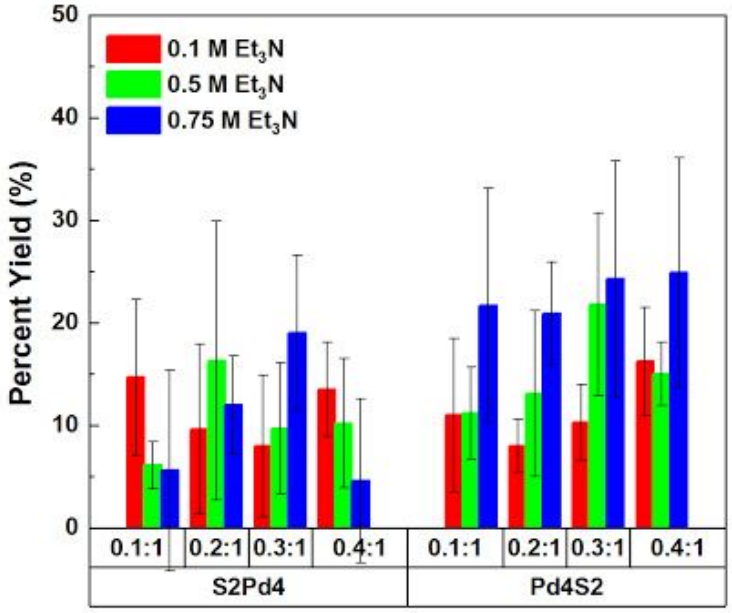

Figure 7. Yields of Suzuki coupling reactions in various base concentrations of 0.1M, 0.5 M, and 0.75M Et_3N. PdNPs used were formed in ethanol and with the two peptides: S2Pd4 and Pd4S2 at various Pd: peptide concentrations. Results were quantified using NMR.

Future Work

Future work for this research includes testing the catalytic ability of PdNPs made with the S2Pd4S2 peptide. The addition of the hydrophobic S2 group on both the C and the N terminus of the peptide could possibly make a difference in the formation of nanoparticles in organic solvents.

Ethanol was the solvent primarily used in this research, however, another direction for the future of this research is the formation of the PdNPs

and catalytic reactions in other organic solvents. Particularly, solvents such as dimethylformamide (DMF), dimethylsulfoxide (DMSO), and xylenes will be explored. DMF is a standard solvent in many carbon-carbon coupling reactions as it has the ability to dissolve a lot of materials due to the polar aprotic nature. DMF also has a high boiling point, making it ideal for reactions that need higher temperatures.[5] However, DMF is classified as toxic. As such, DMSO is not toxic and has the same polar aprotic and high boiling point properties.[6] So DMSO will be explored as an alternative. Finally, xylenes represent a nonpolar solvent, which is necessary for considering a full range of reaction materials that may need dissolved.

References

1. Briggs, B.; Knecht, M.; Pekarek, R. Examination of Transmetalation Pathways and Effects in Aqueous Suzuki Coupling Using Biomimetic Pd Nanocatalysts. *J. Phys. Chem. C* **2014**, *118,* 18543-18553.
2. Briggs, B.; Knecht, M. Nanotechnology Meets Biology: Peptide-based Methods for the Fabrication of Functional Materials. *J. Phys. Chem. Lett.* **2012***, 3,* 405-418. Nano 2009
3. Pacardo, D.B.; Sethi, M.; Jones, S.E.; Naik, R.R.; and Knecht, M.R. Biomimetic Synthesis of Pd Nanocatalysts for the Stille Coupling Reaction. *ACS Nano*, **2009**, *3*, 1288-1296.
4. Puddu, V.; Perry, C. Peptide Adsorption on Silica Nanoparticles: Evidence of Hydrophobic Interactions. *ACS Nano*, **2012**, *6,* 6356-6363.
5. *N,N-Dimethylformamide*; MSDS No. A0338 [Online]; Fischer Scientific: Fair Lawn NJ, Sept 03, 2009 .https://www.fishersci.com/msdsproxy%3FproductName%3DD1314%26productDescription%3DDIMETHYLFORMAMIDE%2BSPECTRA%2B4L%26catNo%3DD131-4%26vendorId%3DVN00033897%26storeId%3D10652 (accessed Oct 31, 2019).
6. *Dimethyl sulfoxide*; MSDS No. 67-68-5 [Online]; Fischer Scientific: Fair Lawn NJ, Jan 23,2009.https://www.fishersci.com/msdsproxy%3FproductName%3DD1314%26productDescription%3DDIMETHYLFORMAMIDE%2BSPECTRA%2B4L%26c

atNo%3DD131-4%26vendorId%3DVN00033897%26storeId%3D10652

(accessed Oct 31, 2019).