CALIFORNIA STATE SCIENCE FAIR
2014 PROJECT SUMMARY

Name(s)
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Project Number
34329

Project Title
Palladium-Catalyzed Direct Arylation of Amino Acids

Abstract

Objectives/Goals
The goal of this research is to modify proteins through direct arylation, a method used for coupling aromatic molecules through transition-metal catalyzed C-H activation. The coupling is between a brominated aromatic ring and a non-functionalized arene. This method is typically used for the polymerization of semi-random polymers. However, due to its ability to create C-C bonds, my hypothesis is that this method can be used on modifying biological molecules. Proteins are broken down into amino acids, which have the same basic structure with varying functional groups. Although these R-groups differ, they all contain C-H bonds, lending themselves to direct arylation. By taking an amino acid, different prefunctionalized substrates can be added to it.

Methods/Materials
The two amino acids that I chose were histidine and tryptophan because their R-groups resemble the molecules 1-butylimidazole and indole, respectively. These smaller molecules acted as model systems for the entire amino acid. Bromotoluene was a simple arene that was added to the imidazole and indole as it would be added to the functional group on the amino acid. A typical catalytic system was used, which included palladium acetate, neodecanoic acid, and potassium carbonate in the solvent N,N-dimethylacetamide (DMA). The reaction was optimized, varying conditions and adding ligands to help reactivity. These reactions were then analyzed using a Gas Chromatography Mass Spectrometer (GCMS), which uses the molecules various characteristics, such as the point at which they vaporize, to separate and analyze them.

Results
There was increased coupling between the 1-butylimidazole and bromotoluene in the presence of bis(diphenylphoshino)ferrocene, or dppf. The indole did respond slightly to some transition metals, like copper, that may have acted like co-catalysts. However, due to its acidic NH group, the hydrogen on the indole was not easily activated, so there was little coupling observed. Further data is being collected.

Conclusions/Discussion
I did not reach the step of direct arylation on actual amino acids, but the model system for histidine adds more creditability and possibility to my hypothesis. There still needs to be some issues solved with the acidic NH group on the indole to move onto tryptophan. However, this coupling expands the possibilities for protein labeling, for the delivery and development of pharmaceuticals, and for protein synthesis.

Summary Statement
My project looks into applying direct arylation to biological compounds for the purposes of modifying amino acids that can then be used for labeling and forming new proteins.

Help Received
used lab equipment and chemicals from California Lutheran University under the supervision of Dr. John Tannaci