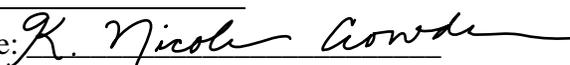


UNIVERSITY OF MARY WASHINGTON UNDERGRADUATE RESEARCH GRANT PROGRESS REPORT

Project Title: The Use of Click Chemistry for the Creation of a Universal Platform for Metal Oxide Functionalization

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Eric Johnson	2014	3.53	3.60

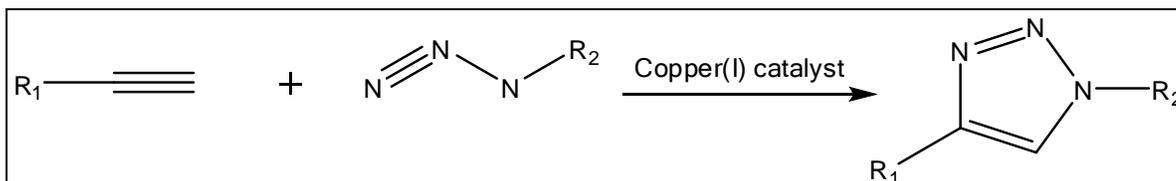
Project Summary:

Purpose of Research

Since its proposal in 2001 by Sharpless, *et al.*, click chemistry has exploded across chemical research.¹ Click chemistry is given this nickname due to the modular nature of the reactants and the rapid, irreversible nature of the reaction, like the snapping of a seat belt. Click reactions have added benefits for undergraduate research in that the solvents are benign, the byproducts are limited so product isolation is simplified and yields are high, and the reactions are insensitive to air and water. The copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) is a classic example of click chemistry, where the product is a 1,2,3-triazole ring with 1,4-disubstituted regiochemistry (see Figure 1).²⁻⁵ The modular nature of this reaction comes into play with the two R groups seen in the figure; these R groups can be varied to yield a wide array of products. This click reaction has been used in fields as varied as polymer synthesis, biotherapeutics, drug discovery, and nanomaterials.^{2,6}

In the decade since its discovery, click research has turned to modifying surfaces with groups that terminate in either the azide or the alkyne as a means of bringing this modular reaction to surface modification techniques.^{2,7-8} This research project aims to continue in this vein but working with a new type of surface, metal oxides. Although some work has been done with metal oxide nanoparticles,⁸ this project will concentrate on the bulk metal surfaces of titanium and copper. These metal oxide surfaces can be derivatized with organic compounds containing phosphonic acid functional groups as a covalently bound phosphonate monolayer.⁹⁻¹¹ If the terminus of this compound is an azide, then CuAAC would be possible with any alkyne containing compound, yielding a universal platform for metal oxide surface functionalization.

Figure 1: Triazole Formation via Copper(I)-Catalyzed Azide-Alkyne Cycloaddition



Project Goals

1. Synthesize various compounds containing both a phosphonic acid and an azide functional group.
2. Modify metal oxide surfaces with these synthesized compounds and conduct CuAAC reactions.

Progress to Date

The work of this fall semester has focused on various synthetic routes to the desired compounds containing a phosphonic acid and an azide functional group. Click reactions have also been undertaken. Work on both goals will continue in the spring semester.

During this research, three synthetic routes have been used in an attempt to create a compound that can be used with click chemistry to functionalize a metal oxide surface.

Route 1 used α -bromoisobutyryl bromide which reacted with anhydrous ethylene glycol in order to form 2-bromo-2-methyl-propionic acid 2-hydroxy-ethyl ester (**1**). This was then reacted with anhydrous dimethylformamide (DMF) and sodium azide (NaN_3) to yield 2-azido-2-methyl-propionic acid 2-hydroxy-ethyl ester (**2**). This product was next reacted with anhydrous tetrahydrofuran (THF), anhydrous triethylamine, and phosphorous oxychloride (POCl_3) to yield 2-azido-2-methyl-propionic acid 2-phosphonoxy-ethyl ester (**3**).

A click reaction was then performed on (**3**) using two different methods. One used copper sulfate pentahydrate, ascorbic acid sodium salt, dimethylsulfoxide (DMSO) and 5-chloro-pentyne, while the other substituted a t-butanol and water mixture for DMSO to yield the triazole (**4**) by way of a copper catalyzed Huisgen 1,3-dipolar cycloaddition. A tethering by aggregation and growth (TBAG) deposition was also done using (**3**) to attach the molecule to a copper plate, creating a surface-bound triazole compound (**5**).

The latter of the previous click reactions was then attempted on (**2**) in order to produce a different triazole compound (**6**).

Route 2 began by using 1,12-dibromododecane and triethyl phosphite in a reflux in order to produce diethyl (12-bromododecyl) phosphonate (**7**) by way of a Michaelis-Arbuzov reaction. Next, (**7**) was used in two different reactions. One reaction combined (**7**) with DMF and sodium azide to synthesize diethyl (12-azidododecyl) phosphonate (**8**), while the other deprotected (**7**) by using trimethylsilyl bromide (TMSBr) and methanol and then precipitating it with hydrochloric acid (HCl) to yield 12-bromododecyl phosphonic acid (**9**). (**8**) was deprotected using TMSBr in an anhydrous acetonitrile solvent and then methanol was added to give 12-azidododecyl phosphonic acid (**10**).

Route 3 started off using diethyl 2-bromoethyl phosphonate and deprotecting it with TMSBr in acetonitrile and then combining it with methanol to produce 2-bromoethyl phosphonic acid (**11**). The diethyl 2-bromoethyl phosphonate was also used in combination with acetone and sodium azide to produce diethyl 2-azidoethyl phosphonate (**12**). (**12**) was then deprotected using TMSBr in acetonitrile and methanol to yield 2-azidoethyl phosphonic acid (**13**).

A full report on this research, including spectra of compounds synthesized (as required for CHEM 491) is available upon request.

Budget

The budget proposed at the beginning of the fall semester was for funding for the full academic year of 2011-2012. To date, approximately \$171 has been spent of the \$590 awarded. This has been to cover the registration fees and travel for Eric to present at the Mid-Atlantic Regional Conference of Undergraduate Scholarship and the South-Eastern Regional Meeting of the American Chemical Society. Unfortunately, a late order on last year's undergraduate research grant has also been covered using this year's funds. Expenses for registration for Eric to present at the VA Section of the American Chemical Society meeting in April 2012 in Charlottesville, VA, will be incurred during the spring semester. We also anticipate purchasing other research materials and supplies during the spring semester as needed for the project.

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