Understanding the Suzuki-Miyaura (SM) Reaction via WebMO calculations

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Slide 1:

Hello, my name is Alexis Paskach. I am a junior at Illinois College studying biochemistry. This summer and fall semester, Dr. Jocelyn Lanorio and I worked together in collaboration with Dr. Clayton Spencer's WebMO to better understand the Suzuki-Miyaura reaction using WebMO calculations due to the COVID-19 pandemic.

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The Suzuki-Miyaura or SM coupling is a metal-catalyzed carbon to carbon bond reaction between an organoboron and organohalide under basic conditions as shown in the image below. These types of reactions are generally catalyzed by the expensive palladium metal.

This reaction is commonly used in the synthesis of pharmaceuticals, polymers, and agrochemicals.

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This image on the left shows the entire mechanism of the Suzuki-Miyaura cross-coupling reaction. However, in the research we administered, we addressed the key factors in the first step as shown on the right. The oxidative addition step.

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After reviewing various literatures over the SM reaction, we realized that most studies focused on trying different reactants, optimizing reaction conditions, and investigating different metal catalysts such as use of the more abundant and benign nickel.

Very few studied the individual mechanistic steps.Therefore, we have used WebMO to obtain properties of the reactants and products of the reactions.

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Our objectives included obtaining the chemical properties of the reactants and the products (such as the change in heat of the reaction value that determines the reactions spontaneity (informing us if we need to input energy or if the reaction will occur naturally) and bond-dissociation energy (BDE)) which is a measure of the bond strength between two atoms. In my case, I am looking at homolytic bond cleavage or the bond breaking and giving one electron each to the two atoms involved in the bonding.

We are also examining the characterization elements (including IR, NMR, and UV-Vis), and determining the factor or factors affecting the 1st step in the mechanism of SM reaction which

imply finding the best halogen to proceed the oxidative addition between the few halogens listed and the most ideal sterics of the products.

Calculating the BDE will aid me in examining why organobromides are commonly used organohalides instead of a cheaper and easier to handle organochlorides considering bromides are generally corrosive.

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The specific reactions we had studied are shown.

These are the reactions that I wanted to base my calculations on since in previous years, there were a couple of students who investigated the use of nickel complexes as catalysts at Illinois College. This calculation project will have many aspects that will be significant to the experimental side of those projects.

The images were created using ChemSketch. However, all calculations were done through the web-based interface program called WebMO. The WebMO software itself was fairly basic and easy to navigate. We used different theories, calculations, and basis sets to get the results desired.

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As a result of our calculations, we obtained the heat of the reactions calculated by using the formula shown which equals out to be roughly 1.725×10^6 kcal/mol for both reactions. This tells us that the reactions are endothermic and need a catalyst and heating to follow through with the reactions.

The chart below shows the BDE in respect to the different halides along with the different bond lengths. The BDE demonstrates the strength of a bond. This is essential to our research in finding the best leaving group for the organohalide or the easiest to attach to the Pd catalyst.

This chart informs us that the weakest therefore the most ideal leaving group is 5-bromopyrimidine due to it having the weakest bond as well as the longest.

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These next few charts display the physical characteristics of the first SM reaction's product. This IR spectrum shows the functional groups in the molecule.

Slide 9:
This chart gives us the intensity and number of hydrogens in the product.

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This table shows the chemical shift of the carbons as other atoms like oxygen are added.

Slide 11:
UV-Vis charts determine if conjugation is present in organic compounds or a confirmation of product formation. If there was no conjugation, there would be no peak.

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The final calculation obtained was the dihedral angles of the product before and after adding methyl groups to observe the ideal sterics desired for the synthesis of various products used in our lives. The angles and the matching images make it evident that the flattest form (being the original) is the key piece.

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The same results were reported for the second SM reaction we studied.

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1. Chemical properties such as heats of formation, heat of reaction, and BDE can be successfully obtained using the WebMO program

2. Characterization can be done by WebMO calculations and is a great way to confirm product's properties for newer reactant combinations

3. The carbon-bromide bond is more reactive toward oxidative addition than the carbon-fluorine bond due to the small BDE value of organobromide and thus the coupling product will form via the carbon-bromide bond.

4. The molecule changes from flat to 3D shape once substituents are added to the phenyl ring. This has potentially useful applications such as knowing what reactants to use to attain the desired shape for activity (example: lock and key concept in medicine / enzyme active site)

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Considering we had only investigated the first part of the mechanism of the Suzuki-Miyaura cross-coupling, possible future research could include examining the other parts of the whole mechanism.

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I would like to acknowledge these individuals and organizations for their aid in my research.