McKensie Mason

Dr. Harper

Project Advisor: Dr. Serra

HON 498 Research Project Proposal

Working Title: Quantum Mechanical Investigations of the Aldol Condensation Transition State

The aldol reaction is a carbonyl condensation reaction which involves the combination of two carbonyl compounds through α-substitution and nucleophilic addition steps to form a β-hydroxy carbonyl product (McMurry 905). The aldol reaction is a useful tool in organic synthesis, and is a reaction I have been working with experimentally under the guidance of Dr. Theunis van Aardt in the synthesis of *trans*-pterocarpans.

The mechanism of the aldol reaction is proposed to be as follows in Figure 1 (McMurry 905, Myers) between two different carbonyl compounds with only one containing an α-hydrogen. The carbonyl containing the α-hydrogen is transformed by a base, in this case LDA (lithium diisopropylamide) into an enolate ion, which then acts as a nucleophilic donor to the electrophilic carbonyl on the second carbonyl compound, in this case an aldehyde. The reaction is believed to contain a transition state in which the oxygen atoms are attracted to the positively charged lithium ion and arrange into an energetically favorable chair-like six-membered ring which dictates the stereochemistry of the product (Myers).

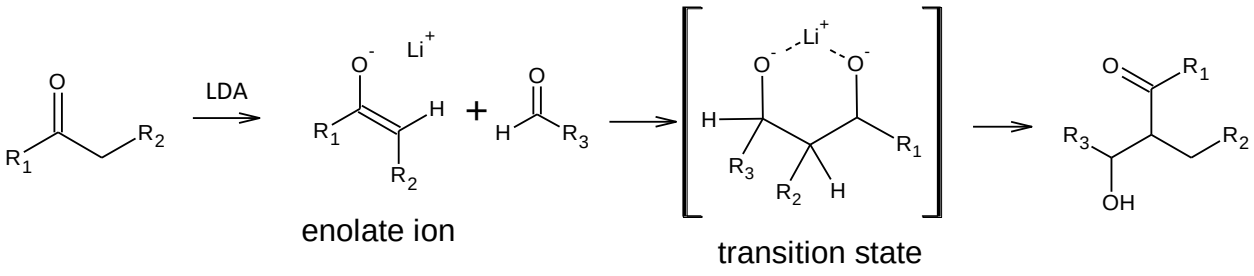

Figure 1 The aldol reaction mechanism

Transition state geometries are important in determining the structure of a reaction's product, but are difficult to verify because they are impossible to obtain experimentally. Therefore, computational methods such as molecular modeling are useful to predict and verify transition state geometries.

For my Honors 498 Senior Honors Project I will utilize Spartan 14 molecular modeling software to model the transition state of the aldol reaction in order to better understand and verify the mechanism of the reaction. The molecules used will be the specific compounds used in my experimental research in the synthesis of *trans*-pterocarpans. This project will involve broadening my knowledge and skill in using Spartan 14 software as a modeling tool as well as developing a method to model the transition state within the program. My background research will involve selecting the best level of theory and basis sets for the software to perform its calculations as well as research into similar projects in the field. Objectives of the project will be to calculate an energy profile of the transition state and perform a geometry optimization in order to verify that the proposed geometry would be the most likely to occur. I will discuss the results in a final report following the typical style and guidelines of an academic paper in the field.

My project advisor will be Dr. Jon Serra. The time period for this project will be the Spring 2016 semester and the proposed timeline is as follows:

January

- Background research on existing work and the aldol reaction
- Research and select theory and basis sets
- Familiarize with Spartan 14 software
- Begin developing experimental methods

February

- Develop experimental methods
- Implement computational experiment

March

- Continue and finish with calculations
- Interpret results of experiment and begin writing final paper

April

- Finalize paper
- Prepare and present final project results

Preliminary Literature Cited

McMurry, John. *Organic Chemisty. 8th ed*. Belmont: Brooks/Cole Cengage Learning, 2012. Print.

Myers, *Stereoselective, Directed Aldol Reaction.* Web. 22 January 2016.