Betty A. and Donald J Baumann Family Scholarship Fund Application Form

1. Name

   Brianna Callahan

2. Chemistry Faculty Research Director

   Dr. Hulce

3. Research proposed (Please copy proposal into the box below this section. It will expand to include all text. The proposal is not to exceed 500 words and is not to exceed 2 pages. A summary of work already completed should also be included, if appropriate.)

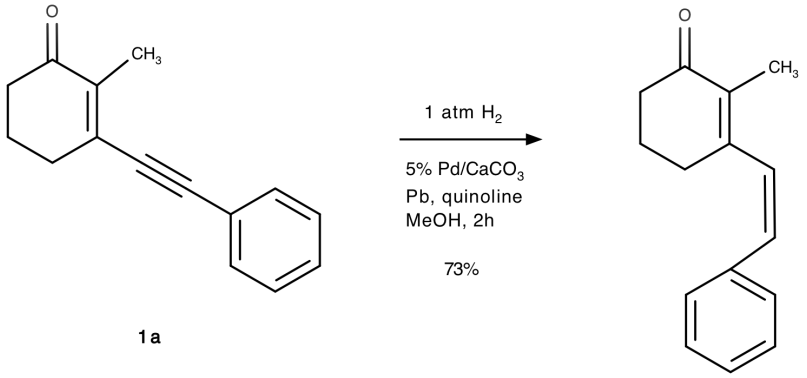
Stereoselective Syntheses and Reduction of 3-Alkenyl-2-cycloalkenones

I. Introduction

Through a Lindlar semihydrogenation, 2-methyl-[(Z)-2-phenylethenyl]-2-cyclohexenone can be synthesized from 2-methyl-3-(phenylethynyl)-2-cyclohexenone by selective reduction of the exocyclic alkyne. The (E)-isomer, 2-methyl-[(E)-2-phenylethenyl]-2-cyclohexenone, can be synthesized through a substitution reaction using [(E)-2-lithiumvinyl]benzene and 3-isobutoxy-2-methyl-2-cyclohexen-1-one. Through a reduction reaction with sodium bis(20methoxyethoxy)aluminum hydride (Red-Al), we hypothesize that both the (Z)- and (E)-isomers will yield the stereoselective product (1S*,2S*,Z)-2-methyleydohexanol-3-(2-phenylethylidenyl) based on previous similar mechanistic studies that yielded primarily the (Z)-isomer.

II. Background

Thus far, the exocyclic alkyne starting compound, 2-methyl-3-(phenylethynyl)-2-cyclohexenone (**1a**), was synthesized from 3-isobutoxy-2-methyl-2-cyclohexenone using ethylmagnesium bromide and phenylethyne in THF.[1] From this starting compound, 2-methyl-[(Z)-2-phenylethenyl]-2-cyclohexenone (**1b**) was synthesized through a Lindlar reaction to semihydrogenate the exocyclic alkyne.[2] We reduced compound **1a** using 1 atm H_2, 5% $Pd/CaCO_3$ (Lindlar catalyst), and quinoline in CH_3OH solution. The reaction was optimized by monitoring the progress of the alkyne reduction using TLC. After 2 hours of the reaction, we obtained a 73% yield of our desired (Z)-isomer product, **1b**. The compound **1b** was isolated using flash column chromatography and characterized by GC/MS, IR spectroscopy, ^{13}C NMR and ^{1}H NMR. Now, we are in the process of characterizing the other minor products formed from the reaction using the same methods.

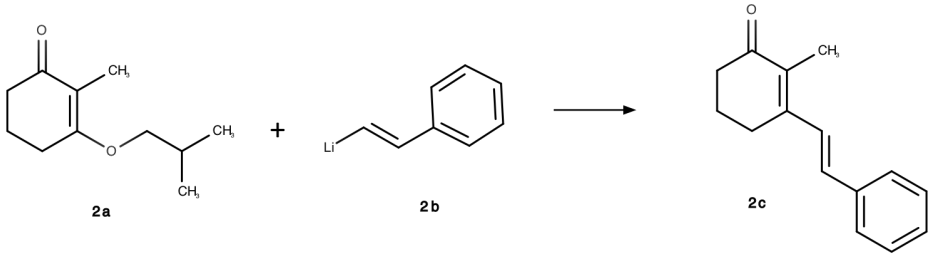


1a 1b

III. Experimental Design and Methods

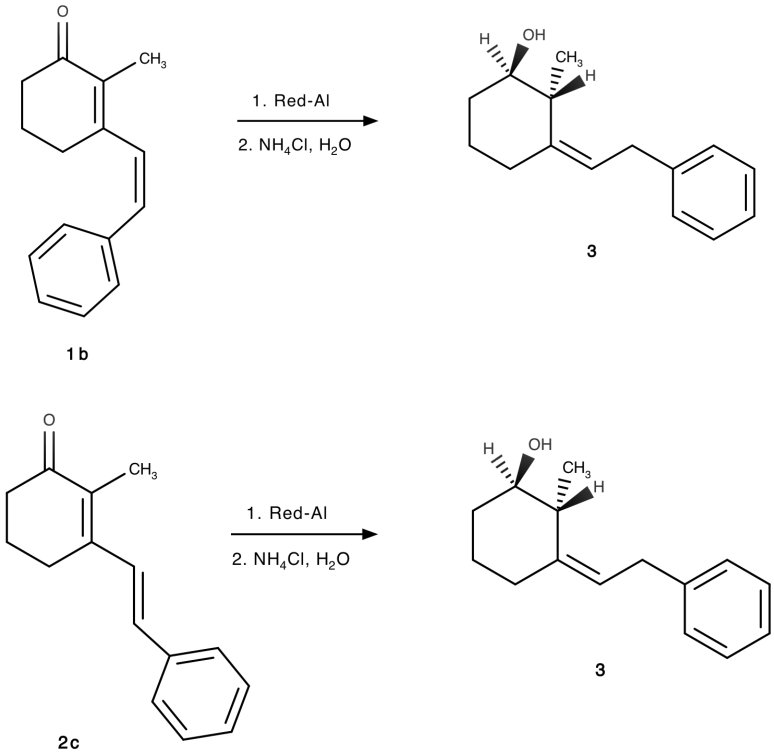
A. Synthesis of 2-methyl-[(E)-2-phenylethenyl]-2-cyclohexenone

The starting material for the synthesis of 2-methyl-[(E)-2-phenylethenyl]-2-cyclohexenone (**2c**) will be prepared through a substitution reaction using [(E)-2-lithiumvinyl]benzene (**2a**) and 3-isobutoxy-2-methyl-2-cyclohexen-1-one (**2b**).[3,4] We will optimize this reaction for sufficient yield. Our compound will be isolated and characterized using the same techniques used for the synthesis of compound **1b**.



B. Reduction of 2-methyl-[(E)-2-phenylethenyl]-2-cyclohexenone and 2-methyl-[(Z)-2-phenylethenyl]-2-cyclohexenone Isomers

Next, we will reduce our (E)- and (Z)-isomers, compounds **1b** and **2c**, respectively, using Red-Al and NH_4Cl with H_2O to quench the reaction. We anticipate that we will obtain (1S*,2S*,Z)-2-methyleydohexanol-3-(2-phenylethylidenyl) (**3**) from this reduction reaction for both isomers, based on knowledge of the stereoselectivity demonstrated in previous mechanistic studies of the reaction.[2] Finally, we will characterize the product of each reaction specifically using ^1H-^1H Nuclear Overhauser Effect Spectroscopy (NOESY NMR) to investigate the stereochemical outcomes of the products from the reduction of both **1b** and **2c**.



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[1] Gubbels, M. A.; Hulce, M.; Kum, J. M.; Urick, A. K.; Villa, E. M. *Tetrahedron* **2016**, *72*(40), 6052–6063.

[2] Hulce, M.; Callahan, B. L. "Stereoselective Syntheses of Allenols and Alkenols by 1,2-, 1,4-Double Hydride Reductions of 3-Alkynyl- and 3-Alkenyl-2-cycloalkenones." Midwest Regional Meeting of The American Chemical Society, Lawrence, KS, 2017, 181.

[3] Cheng, M.; Hulce, M. *Journal of Organic Chemistry* **1990**, 55, 964-975.

[4] Müller, D.; Alexakis, A. *Chemistry - A European Journal* **2013**, *19*(45), 15226–15239.

4. Plans for presentation of research results (conference, publication, seminar, etc.)

   I plan to present my research at St. Albert's Day and the Nebraska Academy of Sciences Annual Meeting. If possible, another publication for future work will be written.

5. Post-graduate plans (job market, graduate school, medical school, etc.)

   I will attend graduate school for chemistry, intending to study organic chemistry or physical organic chemistry. In the future, I plan to pursue a career in organic chemistry research.

Applicant signature	Chemistry research director's signature