Review of Spirocycles and an Organic Chemistry Textbook

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Introduction

Many complex molecules found in natural products and pharmaceutical industries rely on their unique of spirocyclic structure to function properly in various environments. Of particular interest to researchers is how to optimize the synthesis of such compounds through cascade processes. This procedure utilizes a one-pot method that minimizes waste and saves time during synthesis.

The other project that made significant progress this past summer involved creating a textbook of practice problems on the reactions learned in organic chemistry courses. This way, students can enhance their learning experience by testing their skills with real reactions.

Methods

With the help of a team from CSU San Marcos, the scientific database SciFinder® was used to conduct literature searches and collect real data from published experiments focusing on the formation of spirocyclic compounds. Then, individual articles were written to summarize the authors' findings and the data included was sorted into categories, such as the type of reaction that was run and the conditions used to synthesize spirocyclic products.

A similar process was taken to write the supplementary organic chemistry textbook. Articles from SciFinder® provided conditions for specific reactions, a mechanism was drawn with the software ChemDraw, and all relevant information for the reaction was put in its respective chapter corresponding that found in L. G. Wade's textbook.

Name: Kayla Klussman

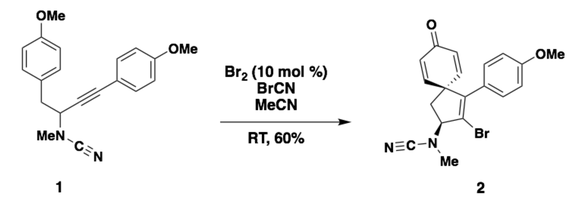
Reference: Singh, R.; Spears, J.; Dalipe, A.; Yousufuddin, M.; Lovely, C. *Tetrahedron Letters* **2016**, *57*, 3096 - 3099. DOI:10.1016/j.tetlet.2016.05.104.

Title: Dearomatizing spirocyclization reactions of alkynyl cyanamides

Key words: Cyanogen bromide, cyclohexadienone, *Leucetta* alkaloids, total synthesis, electrophile-induced
Reactions: dearomative spirocyclization, cyanation

Methodology: When propargylic cyanamides undergo electrophile-induced dearomatizing spirocyclization, cyclohexadienone derivatives are produced. Here, a one-pot spirocyclization-*N*-cyanation reaction has been discovered, which leads directly to the spiro fused derivative.

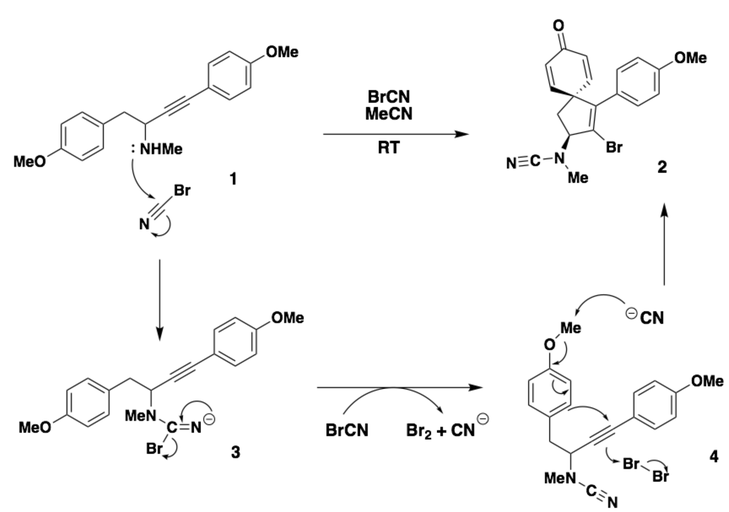
General Reaction Scheme:



Scope and limitations:
- Using HBr as an additive in place of Br_2 reduced the yield significantly to 35% and created a byproduct
- No reaction occurs in the absence of an additive
- Cyanamide is a competent substrate in the electrophile-initiated dearomatizing spirocyclization with halogens, sulfur, and selenium but not with cyanogen bromide

Stereochemical Explanation: It was found that bromine was formed *in situ* under non-basic conditions which triggers the spirocyclization.

Mechanism:



Applications: The cyclohexadienone products may be key intermediates in the construction of imidazole-containing alkaloids belonging to the *Leucetta* family.

Summary: An electrophile-induced dearomatizing spirocyclization produced cyclohexadienone derivatives that may serve as intermediates in developing *Leucetta* alkaloids. In this process, bromine is formed under nonbasic conditions and spurs spirocyclization. Consequently, it was found that using Br_2 as an additive was more effective in this process than HBr.

Figures 1-2 (left). A sample entry from the review of spirocyclic compounds

Results

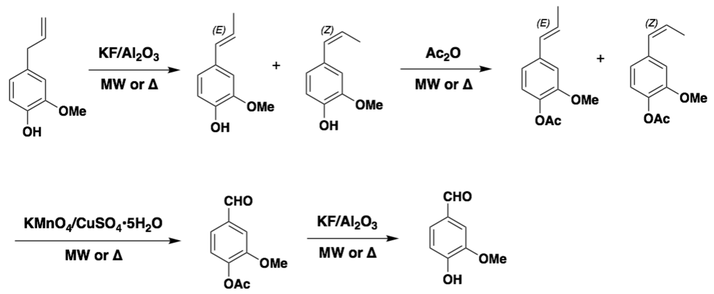
In total, roughly 200 articles gathered from SciFinder® were analyzed for the spirocyclic compound analysis. Summaries for these articles were sorted into categories based upon their similarities, focusing on domino-like reactions. In total, all the summaries were combined into a review on the synthesis of spirocyclic compounds involving cascade processes that will assist the academic world in understanding the formation and behavior spirocycles in various environments. Currently, the review is in the final stages of editing and will then be submitted to the European Journal of Chemistry for publication.

The creation of a textbook consisting of multiple practical uses of common reactions in organic chemistry will enable students to easily look up a reaction, practice writing the mechanism from reactants to products, and see novel methods in which the reactions they are studying have been utilized in research. Thus far, problems for the first semester of organic chemistry has been written and is being refined for publication.

2. Reference: Thi Luu, T.; To Lam, T.; Le, T.; Duus, F. *Molecules* **2009**, *14*, 3411 - 3424

Title: Fast and green microwave-assisted conversion of essential oil allylbenzenes into the corresponding aldehydes via alkene isomerization and subsequent potassium permanganate promoted oxidative alkene group cleavage

Scheme:



Applications:
- Conversion of eugenol into vanillin under solvent-free conditions
- Considered a green reaction since it is solvent-free

Additional:
a) Intermediate in total synthesis

b) Both the *E* and *Z* isomers are formed during the reaction sequence, but the final product does not have distinct stereochemistry

Figure 3 (above). A sample entry from the organic chemistry practice problem textbook

References

- SciFinder® https://scifinder.cas.org/
- Wade, L. G. *Organic Chemistry*, 8th ed; Pearson Education: Illinois, 2013.

Acknowledgments

- Dr. Jesus Cordova Guerrero
- CLU OURCS Program
- Dr. Robert Iafe, Emily Lyon, and Amanda Melanese from CSU San Marcos who collaborated with us on the spirocycle review
- My fellow research team members