



Development of a New Method for the Alkynogenic Fragmentation of 5-Pyrazolone Derivatives

Aldyn F. Landas and Dr. Martin A. Walker

Department of Chemistry, State University of New York at Potsdam

Introduction

The research currently underway in our laboratory focuses on synthetic procedures for preparing alkynes from 5-pyrazolone derivatives. It has been known for some time that 5-pyrazolone derivatives can be made to decompose to 2-alkynoic esters and acids by a number of methods (Thallium(III) Nitrate, Iodosobenzene, Dehydrohalogenation, and Lead(IV) Acetate). These syntheses all proceed through an unstable diazacyclopentadienone intermediate which is opened to form the alkyne on solvolysis. It has also been observed that the oxidation of 3-pyrazolidinones with mercury(II) oxide produced alkenes on fragmentation. We believe that the diazacyclopentadienone intermediate may be persuaded to fragment into the stable gases, carbon monoxide and nitrogen, without solvolysis and produce useful alkyne derivatives.

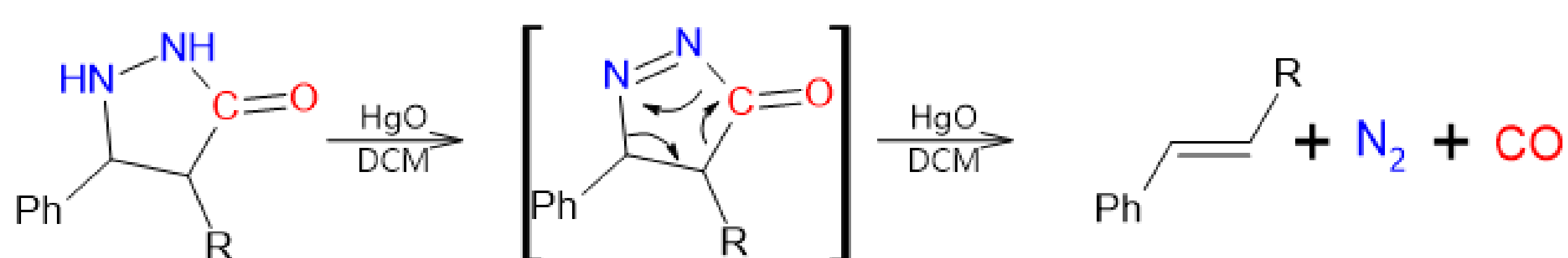


Figure 1. Fragmentation of 3-pyrazolidinones to alkenes

Project Goal

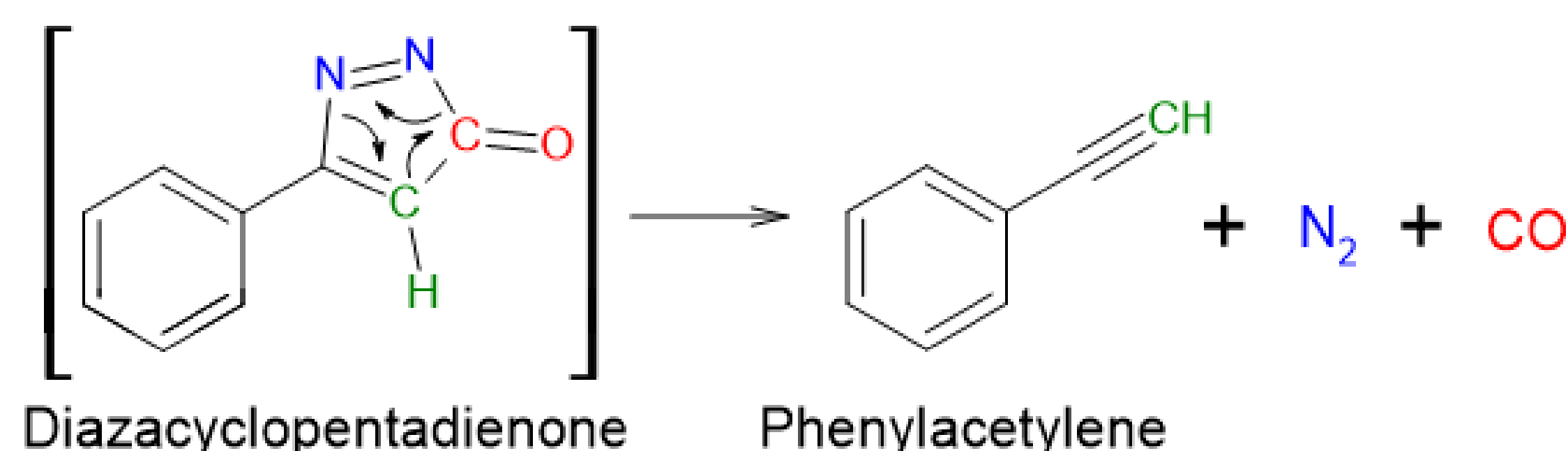
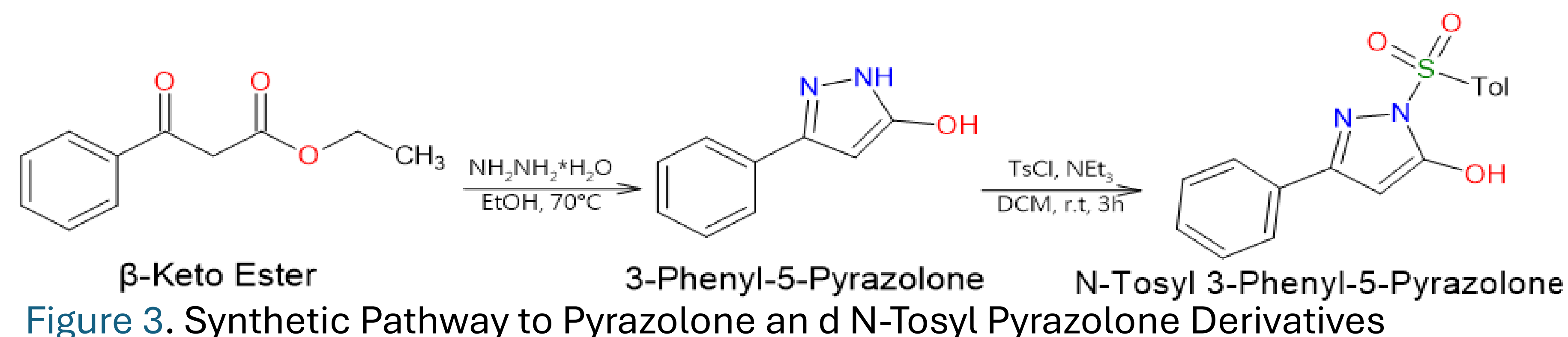


Figure 2. Final step in the proposed synthesis of phenylacetylene from 3-phenyl-5-pyrazolone

The formation of diatomic nitrogen and carbon monoxide provide a very good driving force for reactions, due to their high stability. The form of the diazacyclopentadienone is very unstable, as it is antiaromatic, and should readily decompose to form an alkyne. In this project, we intended to synthesize phenylacetylene by the fragmentation of N-tosyl 3-phenyl-5-pyrazolone. Phenylacetylene appeared to be a good target molecule because it would be stable enough to isolate, should it be formed.

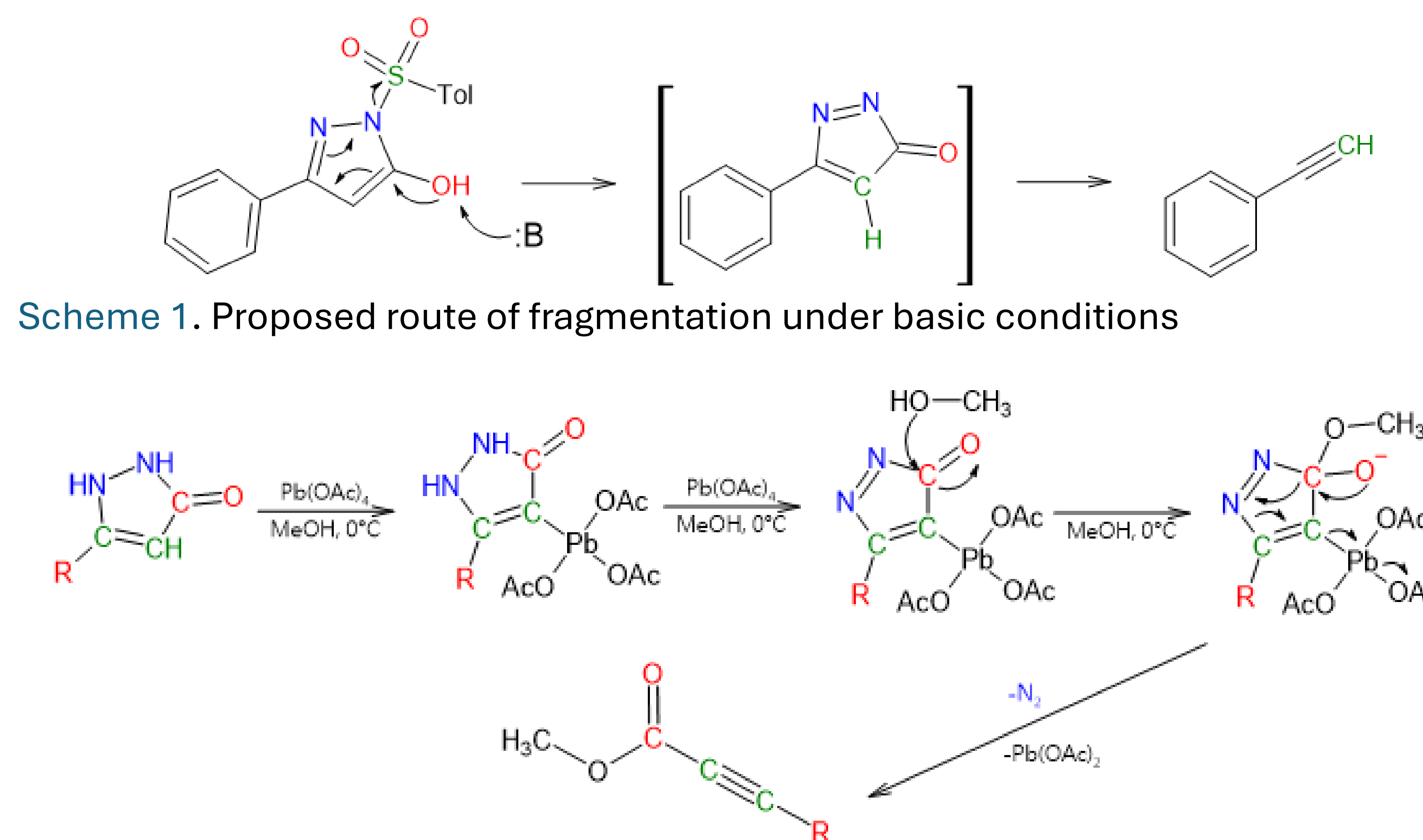
Syntheses



Pyrazolone derivatives are readily prepared from the action of Hydrazine Hydrate on β -Keto Esters in alcoholic solvent. We were able to achieve a ~60% yield of 3-phenyl-5-pyrazolone in our laboratory reliably. Tosylation of 3-phenyl-5-pyrazolone is achieved by the action of TsCl (1 mol eq.) on the pyrazolone in DCM at room temperature for 3 hours. Neutralize, then remove solvent *in vacuo*.

Our Approach

One of the most famous alkynogenic fragmentations is the Eschenmoser fragmentation. This reaction fragments an α,β -epoxy tosylhydrazone into p-toluenesulfinate and N_2 while producing an alkyne. We believe that this could be applied to 5-pyrazolone derivatives to produce the diazacyclopentadienone intermediate which would subsequently decompose to the alkyne. If the reaction proceeds under basic conditions, it may follow Scheme 1.



Scheme 2. Synthesis of 2-alkynoic esters with lead tetraacetate. The first step is electrophilic addition of lead tetraacetate to the C4 position, followed by oxidation with a second equivalent, then solvolysis with methanol⁹. The synthesis from thallium follows this same mechanism. It is additionally driven by the fact that Pb(II) and Tl(I) are more stable than Pb(IV) and Tl(III).

Results

Ultimately, we were unsuccessful in achieving our goal of synthesizing phenylacetylene by this method. Reaction of the N-Tosyl Pyrazolone with base typically yielded back starting material, or nothing at all. We believe this to be due to the possible resonance stabilization within the ring. Since coming to this conclusion, we have shifted our focus to using other oxidative methods to produce the diazacyclopentadienone intermediate. We have turned to using silver(I) oxide as a possible oxidant, as it is less toxic than lead and thallium, but it shares similar properties and has previously shown oxidize hydrazine bonds to diazo compounds. We are also looking into applying lead tetraacetate because, although it is toxic, it is less dangerous than thallium and has been used to do this chemistry before. With proper handling, storage, and disposal the risk associated is minimal. Another potential route which this project has opened, is the direct synthesis of 2-alkynoic esters by dehydrohalogenation of 4,4-dihalo-5-pyrazolone derivatives.

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