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Microwave Assisted Synthesis of Tri-substituted Pyridazine Exploration

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3,4,6-Trisubtituted Pyridazine Derivatives as Drug Candidates for Cancer Treatments

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Introduction

Triphenylpyridazine derivatives are known to exhibit anti-cancer properties. The purpose of this project is to synthesize 3,4,6-tri-substituted pyridazine derivatives using microwave energy. Microwave assisted organic synthesis (MAOS) of the biologically active pyridazine compounds using solvent-free methods will help shorten reaction times and produce high, efficient yields. Given that the heat and length of the reaction can change the identity of the product, the reaction mixture will be tested under variable conditions in order to determine what product that specific parameters can yield. Various methodologies will be applied for synthesizing different pyridazine derivatives. After synthesis, testing of the anticancer properties of 3,4,6-triphenylpyridazine will be carried out at Augusta University. Various catalysts, reaction times, and temperatures will be explored to study the scope of the reactions.

Methodology

To synthesize the tri-substituted pyridazine derivatives, hydrazine will be added to a 4,6-diketone and a 4,6-ketoacid, and will be allowed to react under basic conditions with an alkali metal catalyst, such as potassium hydroxide impregnated alumina. The mixture will be allowed to react under variable temperature and reaction time while being subject to microwave energy.

Reactions

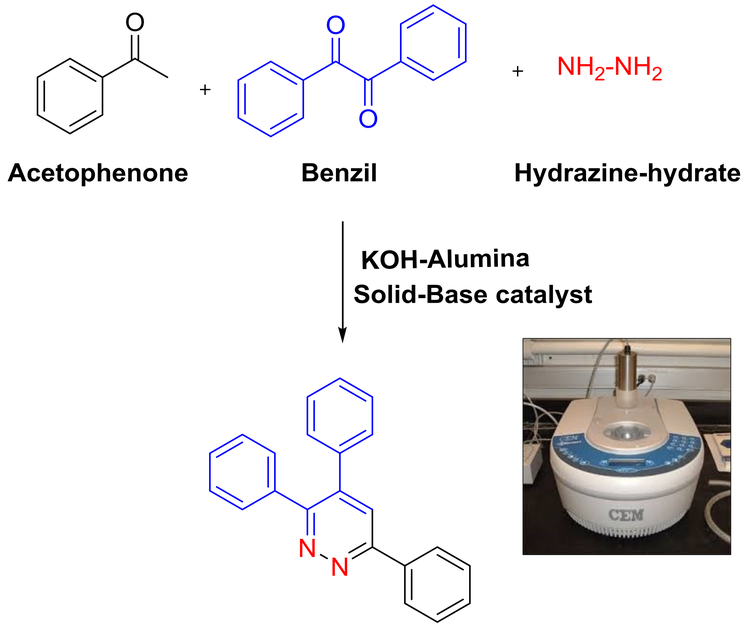


Figure 1. Multicomponent organic reaction for the microwave-assisted solvent-free synthesis of 3,4,6-trisubtituted pyridazine derivatives. The CEM discover microwave reactor is shown in the inset.

Table

Results and Discussion

Following the completion of the first reaction, the product was analyzed using gas chromatography and mass spectroscopy, and was found to lack the presence of reacted acetophenone.

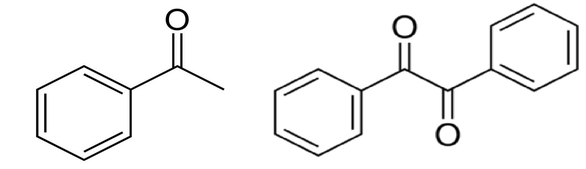
The second reaction, following characterization, was shown to possess all of the major reacting components, but with mixture of products. Future directions include utilizing the initial results and focussing on time and temperature to give the maximum yield of our desired product. Our analysis will also reveal the exact identity of the products, and the methodologies will be archived for future reference.

References

1. Mecadon H, Myrboh B. *"Potassium Hydroxide Impregnated Alumina (KOH-Alumina) as a Recyclable Catalyst for the Solvent-Free Multicomponent Synthesis of Highly Functionalized Substituted Pyridazines and/or Substituted Pyridazin-3(2H)-ones under Microwave Irradiation."* ISRN Organic Chemistry, Vol. 2011: p1-7.
2. Sukata K. *"Selective Alpha-monoalkylation of Phenylacetonitrile Using Akali Metal Hydroxide Impregnated on Alumina."* The Chemical Society of Japan, Vol. 56: p3306-3307.
3. *www.cem.com*

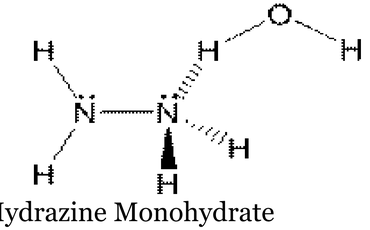
Acknowledgements

1. *Department of Chemistry, Georgia Southern University.*
2. *College of Science and Mathematics, Georgia Southern University .*



Acetophenone

Benzil



Hydrazine Monohydrate

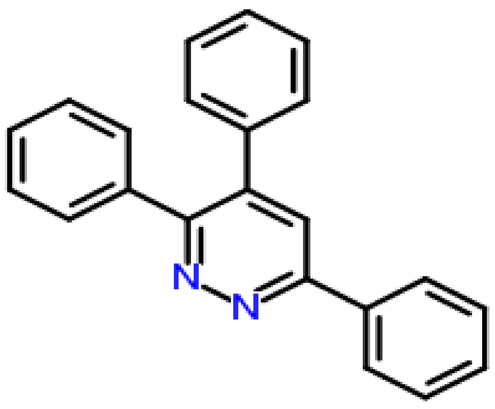


Figure 2. Target compound, 3,4,6-triphenylpyridazine, known to have anti-cancer properties.