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| <b>REPORT DOCUMENTATION PAGE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                   |                                | Form Approved OMB NO. 0704-0188                          |                                                           |                                       |
| <p>The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA, 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.</p> <p>PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.</p> |                   |                                |                                                          |                                                           |                                       |
| 1. REPORT DATE (DD-MM-YYYY)<br>16-05-2015                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                   | 2. REPORT TYPE<br>Final Report |                                                          | 3. DATES COVERED (From - To)<br>17-Feb-2014 - 17-Feb-2015 |                                       |
| 4. TITLE AND SUBTITLE<br>Final Report: Purchase of Microwave Reactors for Implementation of Small-scale Microwave-accelerated Organic Chemistry Laboratory Program in Undergraduate Curriculum and Synthetic Chemistry Research at HU                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                   |                                | 5a. CONTRACT NUMBER<br>W911NF-14-1-0095                  |                                                           |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 5b. GRANT NUMBER                                         |                                                           |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 5c. PROGRAM ELEMENT NUMBER<br>206022                     |                                                           |                                       |
| 6. AUTHORS<br>Bump, Charles, Ghebreyessus, Kesete, Ndip, EdmundM., Nwokogu, Godson C., Waddell, Michelle K.,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                   |                                | 5d. PROJECT NUMBER                                       |                                                           |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 5e. TASK NUMBER                                          |                                                           |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 5f. WORK UNIT NUMBER                                     |                                                           |                                       |
| 7. PERFORMING ORGANIZATION NAMES AND ADDRESSES<br>Hampton University<br>100 E. Queen Street<br><br>Hampton, VA 23668 -0108                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                   |                                | 8. PERFORMING ORGANIZATION REPORT NUMBER                 |                                                           |                                       |
| 9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS (ES)<br>U.S. Army Research Office<br>P.O. Box 12211<br>Research Triangle Park, NC 27709-2211                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                   |                                | 10. SPONSOR/MONITOR'S ACRONYM(S)<br>ARO                  |                                                           |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 11. SPONSOR/MONITOR'S REPORT NUMBER(S)<br>64759-CH-REP.1 |                                                           |                                       |
| 12. DISTRIBUTION AVAILABILITY STATEMENT<br>Approved for Public Release; Distribution Unlimited                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |                                |                                                          |                                                           |                                       |
| 13. SUPPLEMENTARY NOTES<br>The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other documentation.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                |                                                          |                                                           |                                       |
| 14. ABSTRACT<br>The selection and purchase of microwave systems from two vendors and supporting equipment from other vendors have been completed. In order to house all the microwave reactor systems in one room to be designated as a microwave laboratory facility, an old laboratory space is being remodeled to suit the new purpose. The remodeling will be completed soon and the microwave systems will be installed and functional by the fall of 2015. During the project year, microwave assisted activities were carried out using the one pre-existing CEM Discover microwave reactor in the department. With this one reactor, and while waiting for the installation of the new microwave                                                                                                                                                                                                                          |                   |                                |                                                          |                                                           |                                       |
| 15. SUBJECT TERMS<br>Microwave laboratory facility, Undergraduate organic chemistry laboratory, Implementation/Development of microwave reaction procedures, Microwave-assisted organic reactions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                   |                                |                                                          |                                                           |                                       |
| 16. SECURITY CLASSIFICATION OF:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                | 17. LIMITATION OF ABSTRACT                               | 15. NUMBER OF PAGES                                       | 19a. NAME OF RESPONSIBLE PERSON       |
| a. REPORT<br>UU                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | b. ABSTRACT<br>UU | c. THIS PAGE<br>UU             |                                                          |                                                           | Godson Nwokogu                        |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                   |                                |                                                          |                                                           | 19b. TELEPHONE NUMBER<br>757-727-5276 |



## Report Title

Final Report: Purchase of Microwave Reactors for Implementation of Small-scale Microwave-accelerated Organic Chemistry Laboratory Program in Undergraduate Curriculum and Synthetic Chemistry Research at HU

### ABSTRACT

The selection and purchase of microwave systems from two vendors and supporting equipment from other vendors have been completed. In order to house all the microwave reactor systems in one room to be designated as a microwave laboratory facility, an old laboratory space is being remodeled to suit the new purpose. The remodeling will be completed soon and the microwave systems will be installed and functional by the fall of 2015. During the project year, microwave assisted activities were carried out using the one pre-existing CEM Discover microwave reactor in the department. With this one reactor, and while waiting for the installation of the new microwave systems, we have (a) implemented a few microwave procedures in our undergraduate organic chemistry laboratory courses, (b) developed some microwave procedures that are ready to implement in the next academic year, (c) been developing new microwave procedures that will be ready for implementation in the near future. Two research projects have investigated some synthetic reactions using microwave assisted heating. It is enthusiastically anticipated that more work will be accomplished both in teaching and research when the eight new microwave reactors become operational in the fall of 2015.

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**Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:**

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**TOTAL:**

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Number of Manuscripts:

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TOTAL:

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Patents Submitted

Patents Awarded

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for the Department of Defense ..... 0.00

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NAME

**Total Number:**

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### **Names of personnel receiving PHDs**

NAME

**Total Number:**

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### **Names of other research staff**

NAME

PERCENT SUPPORTED

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**Scientific Progress**

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SEE ATTACHMENTS

## **FINAL PROGRESS REPORT**

### **FORWORD:**

In the proposal, we projected to accomplish the following tasks during the program year:

1. Select, purchase and install the microwave reactors and enabling accessories that are necessary for the implementation of the Small-scale Microwave-assisted Organic Laboratory (SMOL) model in undergraduate labs and synthetic research.
2. Select from the chemical literature, a number of reactions commonly run in undergraduate organic laboratory courses either already run with or without microwave technology.
3. Start to test and evaluate, in our undergraduate organic laboratory courses, microwave procedures already verified by our team of organic chemistry laboratory instructors
4. Optimization of a choice of reported microwave procedures and establishment of microwave procedures for reactions that up till now, have been carried out with classical energy sources and analogs that have not been subjected to known reaction by microwave technology.
5. Broaden the use of microwave technology in the research projects of students and faculty.

This report is a summary of the progress made towards achieving each of the five objectives during the project year.



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**STATEMENT OF THE PROBLEM STUDIED:**

The technical goal of this project is to employ microwave technology to enhance and better exploit the existing laboratory infrastructure in all undergraduate organic chemistry laboratory courses and also to modernize bench-top infrastructure for research in chemical syntheses in the chemistry department at Hampton University. The short reaction times of microwave-accelerated reactions will free up time for students to experience other aspects of laboratory learning experience such as computational prediction/explanation of reaction outcomes and spectroscopic characterization of products within the same laboratory period. The cleaner reaction will allow for reduced consumption of resources and generation of wastes. The broader impact of the project is the production of STEM graduates who will be skilled in the use of modern technology in the practice of chemistry both in graduate school and industry. Another broad impact of the project is the development of a student-tested compendium of microwave-accelerated reactions optimized and standardized for undergraduate laboratory courses which will be diverse enough to serve as resource for any chemistry program wishing to transition from conventional to microwave-assisted heating in the undergraduate laboratory.

## **SUMMARY OF THE MOST IMPORTANT RESULTS:**

### **1. Establishment of a Microwave Reactor Laboratory( Drs. Bump, Ghebreyessus, Ndip, Nwokogu and Waddell and Other Faculty and Staff).**

#### **(A) Choice of Vendors:**

Three vendors of microwave instruments, CEM, Anton Paar and Biotage were invited to acquaint the project personnel, technical staff and any faculty interested in the use of microwave reactors, on their microwave systems and suitability to our needs. Both CEM and Anton Paar sent sales and applications representatives to make presentations to our group in March and April of 2014. Both three vendors provided quotations but eventually we selected products from CEM and Anton Paar because their systems matched our requirements.

#### **(B) Purchase of Microwave Equipment and Supporting Components:**

Five (5) Discover SP unimode microwave reactors, a CoolMate microwave cooling device and two (2) 24-slot MARS multi-mode microwave reactors and accessories were ordered from CEM. One Monomode 300 microwave reactor that can operate at up to 500°C using quartz reaction tubes was ordered from Anton Paar. Components for each microwave reactor system which are manufactured by other companies, such as reactor control and data processing computer, air compressor for temperature control and compressed air filters were also ordered. These included six of each component. All the ordered equipment and components were received by the beginning of the fall of 2014.

#### **(C) Identification and Establishment of a Microwave Laboratory Facility at Hampton University:**

We initially considered having the uni-mode reactors on tables that can be rolled from one lab to another as needed and the multi-mode reactors to be installed in the undergraduate laboratory. But the undergraduate laboratory did not have adequate power supply and space/hoods. The Department decided that it would be better to have all the microwave reactor systems installed in one location within the Department which will serve as a Microwave-assisted Laboratory Facility. This arrangement would be similar to other instrumentation laboratories in the Department where one can run an experiment and then process the experimental data at another location or instrument so that somebody else can use the same instrument. The laboratory must also be located adjacent to our regular spacious undergraduate organic chemistry lab so that students can set up microwave reactions in the microwave laboratory and when the reaction is over, then walk their reaction tubes a short distance into the regular laboratory for work-up. This arrangement would allow student laboratory classes and researchers to use the microwave reactors without interfering with each other or limiting access to the reactors for each type of user. The room that met all of the above conditions was another adjacent regular laboratory space that needed to be remodeled by removing some items and installing other items in order to fit this new intended use. A schematic (Appendix B) for remodeling this room showing what needed to be installed (suitable power outlets, network connections, openings on walls to vent vapors to the outside) was presented to the administration for action. Work on the remodeling has been going on since the fall of 2014 and currently, what remains to have the

room ready for installation of the instruments is the drilling of holes for venting vapors from the two MARS multi-mode reactors to the outside. Once this last step is completed, the vendors will be requested to schedule the installation of the microwaves and training for our faculty and graduate students on the running of the different types of microwave reactors. We anticipate that this final phase of the set-up of the microwave laboratory facility will be completed before the beginning of fall 2015.

## **2. Literature Survey of Reactions for Optimization and/or Adaptation for Microwave Procedure for Undergraduate Laboratory (Drs. Bump, Ndip, Nwokogu and Waddell).**

The Journal of Chemical Education (JCE) is a great source for reactions that have been successfully run with microwave technology as well as reactions run by conventional methods only as undergraduate laboratory activities. Using the search term “microwave”, a long list of experiments reported in the journal over the last few years was obtained (Appendix C). These reported procedures were not identified as optimized, i.e. it is not indicated whether the microwave reaction conditions used for the reactions represent the lowest irradiation power, lowest hold temperature and shortest hold time for the reported result or if the reported result is the best yield and the cleanest product. We also identified reported examples of reactions that have been run by classical heating in undergraduate laboratory exercises for which the microwave procedure can be developed and optimized. These two groups of reported reactions contain both the types of reactions found in current laboratory text books and the new reactions made possible for undergraduate laboratory by the use of microwave technology. From the identified list we have made a short list of procedures to optimize and those classical procedures to adapt and optimize for microwave heating. They include the following reactions for optimization and/or development of microwave procedures:

- (a) Electrophilic aromatic substitution,<sup>1</sup> (b) Knoevenagel condensation<sup>2</sup> (c) Etherification,<sup>3</sup> (d) Elimination,<sup>4</sup> (e) Suzuki reaction,<sup>5</sup> (f) Diels-Alder cycloadditions,<sup>6</sup> and a two-step esterification scheme used in one of the P.I.’s current research projects.

And the following reactions that have reported microwave procedures which will be subjected to optimization efforts:

- (a) Electrophilic aromatic substitution,<sup>7</sup> (b) Reduction,<sup>8</sup> (c) Esterification,<sup>9</sup> (d) Diels-Alder cycloaddition, Wittig reaction and Williamson etherification.<sup>10</sup>

In some cases, we will develop the best procedure for analogs of the substrates reported. We will continue in the future of this project, to monitor the literature for new and/or better examples of experiments as our laboratory courses transition from the current mostly cook-book to the future mostly inquiry-based and project-based undergraduate laboratory activities.

## **3. Testing and Implementation of Selected Microwave Procedures in the Sophomore and Other Organic Laboratory Courses (Drs. Bump, Ndip, Nwokogu and Waddell).**

Since the reactor systems have not yet been installed and readied for use, their exploitation as planned in the proposal has not been realized for the project year. However, we have continued to use the one available CEM Discover reactor for the sophomore (Che 301 and Che 302) laboratory activities during the 2014-2015 project year. Table I (Appendix A) summarizes microwave-assisted reactions

that were run in the undergraduate organic chemistry laboratory courses during the 2014 – 2015 academic year. The table also includes the Fischer esterification procedure which uses a published procedure. All microwave experiments run by undergraduate students were run in the safest mode using the pressure device. The capping of the reaction tube, its placement into the microwave cavity, the placement of the pressure device and retrieval of reaction tube after reaction is over were supervised by the instructor for the laboratory section.

In Che 301 during the fall of 2014, we introduced a microwave procedure for the *cis-to-trans*-isomerization of maleic acid starting with maleic anhydride. Students also ran the reaction by traditional heating in the same laboratory period and were required to compare the two methods in terms of ease of set up, amount of materials used, the time of reaction, the initial cleanliness of the product and percent yield as a required component of their laboratory report on the activity. Students obtained melting points of their products and the starting anhydride and used these values to infer whether the expected product was obtained as well as the purity of the products obtained by classical and microwave methods. In Che 302 during the spring 2015 semester, Diels-Alder cycloaddition between 1,3-cyclohexadiene and N-phenylmaleimide was carried out by both refluxing on a sand bath and by microwave heating. Student reports included comparison of the two methods according to the criteria given before ( see Appendix D for some student responses). Students also used  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the starting materials and the products to evaluate purity of the products. Fischer esterification was also carried out by a reported microwave-accelerated procedure. Laboratory work groups were assigned different alcohols which produced a potpourri of fruity smells in the laboratory during this activity. Each product of this exercise was subjected to both IR and NMR spectroscopy which were to be interpreted to determine purity and functional group of the product. The laboratory reports were richer in content because they had more product characterization data and interpretation of the data.

The microwave activities led us to recognize that some re-tooling will be required for the small scale microwave reactions because use of regular sized glassware leads to high loss and low yield relative to the actual amount of product. We intend to restock the laboratory lockers with smaller glassware, filter funnels etc in order to reduce loss during product isolation and purification. We may also use an alcohol solvent for the Diels-Alder reaction since the low microwave absorption efficiency of ethyl acetate used in the original report would require a higher microwave power to attain any required temperature in a short time. For example, at 20 watts, a temperature of 80°C can be reached in less than 2 min in ethanol but in more than 5 min in ethyl acetate. We currently use a power of 30 watts to achieve the less than 2 min temperature ramp time in ethyl acetate.

We expect more time to be freed for computational exercises, spectroscopic characterization and data analyses during the laboratory period when the six uni-mode and two multi-mode reactors become operational so that all students or work groups in a laboratory section can run their reactions simultaneously rather than one after another.

#### **(4) Development of Microwave Procedures with New Substrates (Dr. Nwokogu)**

##### ***(A) Other Diels-Alder Cycloaddition Reactions***

In order to broaden the variety of Diels-Alder cycloaddition reactants for microwave-assisted organic laboratory activities, we have developed microwave procedures for all combinations of two dienes (1,3-cyclohexadiene and cyclopentadiene) and two dienophiles (maleic anhydride and N-Phenylmaleimide) that we have previously run using classical heating. To generate cyclopentadiene for our classical procedure, the first part of the experiment is the thermal cracking of dicyclopentadiene in hot paraffin oil to collect 6 – 10mL of cyclopentadiene. Then, the cyclopentadiene is reacted with the dienophile in another set-up. We have developed a one-pot microwave procedure in which the thermal cracking occurs in the presence of the dienophile (Scheme I, Appendix A). At the temperature of the reaction, dicyclopentadiene is liquid and serves also as solvent to dissolve the dienophile. Table II summarizes the combinations of diene and dienophile pairs and the reaction conditions for each new combination of reactants. Specific details of each procedure are in the procedure described for each reaction in the Appendix E.

In the cycloadditions with cyclohexadiene, only one stereoisomer was observed in the NMR spectra of the crude product with each dienophile, even when some of the reactions were run at the higher temperature of 160°C. Also, only one stereoisomer was observed by NMR spectral analysis of the crude products in the cycloaddition between cyclopentadiene and N-phenylmaleimide, probably due to the stacking effect of the phenyl ring which will favor the endo transition state. On the other hand, cycloaddition of cyclopentadiene with maleic anhydride gave two stereo-isomers which are observed in the NMR ( $^1\text{H}$  and  $^{13}\text{C}$ ) spectra of the crude product. At reaction temperatures lower than 200°C, the endo product is the major isomer. The amount of the exo-product increased as reaction temperature increased and at 200°C, a 1:1 ratio of isomers was observed by NMR spectra. The exo-product is more soluble and the endo-product can be isolated in pure form even from the 1:1 mixture by recrystallization. Details of the isomer isolation, type of spectroscopic and melting point data for each experiment are included in the experimental procedure for each reaction (Appendix E).  $^1\text{H}$ ,  $^{13}\text{C}$ , DEPT-135, COSY and HETCOR NMR spectra of products were consistent with structures of the expected products.

Apart from providing options for Diels-Alder reactions than can be selected for microwave-assisted cycloaddition reactions, the temperature effect on isomer ratios in the case of cyclopentadiene/maleic anhydride cycloaddition can be adopted as a project-based or inquiry-based activity for second semester organic and/or intermediate organic chemistry laboratory courses.

The microwave-assisted isomerization of maleic anhydride reported under the “Testing and Implementation -----” subheading and Table I (Appendix A) is also a microwave procedure we developed and implemented in our organic chemistry laboratory course material during this project year.

##### ***(B) Other Esterification Reactions***

We also are developing microwave-assisted reaction procedures which will be the materials for the transition from cook-book to project-based/ inquiry-based activities in second semester (Che 302) and

intermediate (Che 407) laboratory courses. These activities will be multi-step (2 – 3) step synthetic schemes that will also involve 2 - 3 common operations such as distillations, chromatographic separations and product characterization using spectroscopic and other methods.

Currently, we are developing a two-step scheme for the synthesis of esters that will require distillation and/or column chromatography to obtain a pure sample for analysis. Emphasis will be on producing enough pure product for data acquisition and analyses but not on percent isolated yield. The rationale for accepting this limitation is that esters are usually volatile and sustain a lot of loss during distillations and evaporative purification steps. Working on a small scale (1- 2g of product) imposes this limitation if we are to be realistic with our expectations of student work and results. Each such activity is planned to provide a multi-week or month series of activities that will combine a 2-3 step reaction scheme, 2 – 3 laboratory operations beyond initial work-up of the reaction and the identification of the structure of an unknown compound that is the result of the sequence of the activities by spectroscopy. Such a sequence of activities better illustrates to students the connection between chemical syntheses (constructing new compounds from simpler compounds), isolation of reaction products (purification of reaction products), data generation and data analysis on the products (determination of the structure of the product). Our laboratory schedule, up till now, includes the above aspects of laboratory learning but with different and unrelated substances. As such, students regard them as unrelated exercises and fail to recognize the link between them.

We are developing for the above purpose, the microwave-assisted, two-step synthesis of high boiling point esters. The first step is the microwave conversion of a benzoic acid or a carboxylic acid with an aromatic ring in its structure to the corresponding acid chloride using thionyl chloride. In the second step, the acid chloride is treated with a choice of low-boiling point ( bp < 110°C) alcohol with microwave irradiation to complete the ester synthesis. We have found that isolation of the product ester is possible when the boiling point of the alcohol and the chlorosulfite of the alcohol are much lower than the bp of the aromatic ester. In these instances, pure ester can be obtained by either vacuum distillation of the crude, column chromatography or chromatography followed by vacuum distillation of the crude. Details of the procedures for the syntheses and purification of n-propyl phenylacetate (Appendix E-6), n-propyl salicylate and isopropyl salicylate (Appendix E-7) are included as example procedures of this activity. They will be deployed in the future when the procedures have been reliably established and refined for implementation in undergraduate laboratory activities. Tables III and IV (Appendix A) summarize the procedures and list other alcohols that can be used similarly with the described procedures. Other aryl carboxylic acids can be included with a few more low-boiling alcohols to develop a large library of such esters. Copies of spectra of the prepared esters included in the Appendix E are proof of the purity of the products that can be achieved with the described procedures. We found it difficult to isolate the ester of the higher boiling alcohol isoamyl alcohol (bp = 130°C) from the excess alcohol and the corresponding chlorosulfite in satisfactory purity for structure identification. The use of base in the reaction of the alcohol with the acid chloride complicated the purification process. Absence of base did not affect the reaction. Working either in a hood or directing the produced HCl<sub>(g)</sub> into NaOH<sub>(aq)</sub> during each reaction step sufficiently addresses the hazard of the small amount of HCl gas generated in the reaction.



When this activity is implemented in a laboratory course, students or student groups will be assigned unknown acids and alcohols to synthesize unknown ester. Either distillation and/or chromatography will be used to obtain enough pure ester for structure determination using spectroscopy and the other types of data that can be acquired when the unknown is at hand. Students will also be given the molecular formula of their unknown ester product.

#### **4. Microwave Use in Intermediate Organic Chemistry (Che 407) Laboratory and Research.**

##### **(A) Che 407 Laboratory (Dr. Nwokogu).**

The usual microwave-assisted activities (cracking of trioxane derivatives into aldehydes, allylic halogenation and Arbuzov reactions) were carried out during the project year in Che 407 laboratory experiments. We expect that more activities in Che 407 laboratory will be implemented when the six new reactors are installed and operational.

##### **(B) Research (Drs. Nwokogu and Waddell).**

#### **Synthesis of *tert*-Butyl 5-Aryl-(2E, 4E)-2,4-Pentadienoate – An Advanced Precursor for Derivatives of Resveratrol (Dr. Godson C. Nwokogu):**

In this project, microwave irradiation has been used for both the allylic bromination of *tert*-butyl crotonate and the Arbuzov phosphonation of the resulting 4-bromocrotonate esters (Scheme III, Appendix A). Condensation of this phosphonate ester with substituted aryl aldehydes by the Haworth, Wadsworth and Emmons reaction should lead to the desired *tert*-butyl pentadienolate ester.

#### **Fabrication of Magnetic Iron Nanoparticles for Oil Spill Remediation by Facile Microwave Process (Dr. Michelle K. Waddell and Breyinn Loftin)**

The goal of this research project is to synthesize unique iron magnetic nanoparticles as a green chemistry method for the removal of organic pollutants such as oil contaminants in water.

A two-step synthesis of iron magnetic nanoparticles is being investigated (Appendix A; Scheme IV). In the first step, precursor iron(III) chloride nanoparticles were prepared in aqueous media using various amounts of capping agents (see Appendix A, Table V) and ionic surfactants (lecithin or tetrabutylammonium iodide). The capping agents and surfactants served: (1) to protect the easily oxidized iron center, (2) to assist in micelle formation of the nanoparticles, and (3) to form emulsions with organic contaminants in aqueous media. In the second step, which requires microwave irradiation, hydrazine reduces some of the  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$ . Then  $\text{Fe}^{2+}$  reacts with  $\text{O}_2$  and hydroxyl ions to form  $\gamma\text{-FeOOH}$  which reacts with the capping agents and surfactants to form the nanoparticles. Initial studies in the summer of 2014 indicated that lecithin produced better results in forming nanoparticles. Therefore, the current microwave studies use lecithin as the ionic surfactant.

UV-Vis spectroscopy was used to primarily characterize the iron nanoparticle because literature indicates that iron nanoparticles absorb between 400-600nm. In each trial, the UV-Vis of the precursor and the irradiated precursor were obtained for comparison. Trials 1, 2 and 3 (Table V) in which the amounts of the tannic acid capping agent was varied, showed weak absorption band between  $\lambda_{\text{max}} = 353 - 393\text{nm}$ , all of which are outside the expected absorption region for iron nanoparticles (see Appendix A, Figure I for UV of Trial #2). The absence of the expected absorption between 400 – 600nm means that nanoparticles were not formed in these trials. However, varying the ratio of tannic acid to lecithin (Trial

5) produced a promising evidence of formation of iron nanoparticles. In the UV-Vis spectrum of the irradiated precursor of this trial, there was a strong absorption at  $\lambda_{\text{max}} = 557 \text{ nm}$  with a maximum absorbance of about 2.5 (Appendix A, Figure 2) which was not observed in the UV-Vis spectrum of the precursor. The large peak within the 400-600nm region for nanoparticles with a high absorbance is evidence of the presence of nanoparticles. Additional indication of the presence of nanoparticles was the appearance of the solution of the microwave product. The solution was a deep purple color unlike the black or rust color precipitates from the other reactions. The presence of precipitate was noticed, but the overall composition of the product was a solution. Further characterization methods such as scanning electron microscopy (SEM) would be applied to confirm the presence, size and morphology of these nanoparticles.

The microwaved precursor in Trial 4 with Bisphenol A carbonate did not show any absorption either close to or above the 400nm region. Increasing the irradiation times for all the trials did not appear to affect the results.

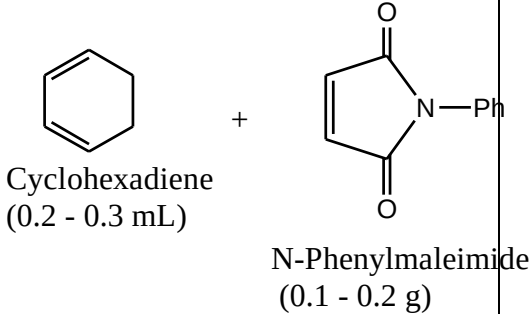
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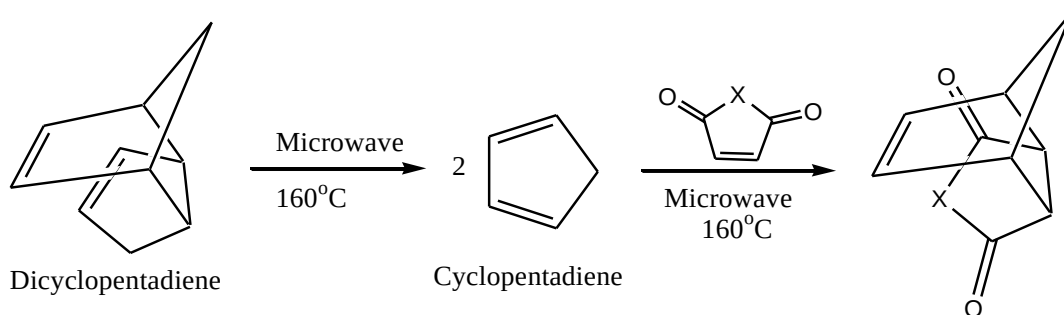
1. Gregoriy A. Sereda and Vikul B. Rajpara, A Green Alternative to Aluminum Chloride Alkylation of Xylene, *Journal of Chemical Education*, **2007**, 84(4), 692 - 693
2. Marcos Carolli Rezende, Francisco Jara and Moises Dominguez, Evaluating the Internal Charge-Transfer in Benzyldiene Derivatives of N,N-Dimethylbarbituric Acid, *Journal of Chemical Education*, **2006**, 83(6), 937 – 939; Ryan G. Stabile and Andrew P. Dicks, Two-Step Semi-Microscale Preparation of a Cinnamate Ester Sunscreen Analog, *Journal of Chemical Education*, **2004**, 81(10), 1488 – 1491.
3. Ryan G. Stabile and Andrew P. Dicks, Semi-Microscale Williamson Ether Synthesis and Simultaneous Isolation of an Expectorant from Cough Tablets, *Journal of Chemical Education*, **2003**, 80(3), 313 – 315; John J. Esteb, John R. Magers, LuAnne McNulty, Paul Morgan, Anne M. Wilson, A Simple SN2 Reaction for the Undergraduate Organic Laboratory, *Journal of Chemical Education*, **2009**, 86(7), 850 – 852
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5. Evangelos Aktoudianakis, Elton Chan, Amanda R. Edward, Isabel Jarosz, Vicki Lee, Leo Mui, Sonya S. Thatipamala, and Andrew P. Dicks, “Greening Up” the Suzuki Reaction, *Journal of Chemical Education*, **2008**, 85(4), 555 – 557; Christopher S. Callam and Todd L. Lowary, Suzuki Cross-Coupling Reactions: Synthesis of Unsymmetrical Biaryls in the Organic Laboratory, *Journal of Chemical Education*, **2001**, 78(7), 947 – 948.
6. Marsha R. Baar and Kristin Wustholz, Diels–Alder Synthesis of endo-*cis*-N-Phenylbicyclo[2.2.2]oct-5-en-2,3-dicarboximide, *Journal of Chemical Education* **2005** 82 (9), 1393
7. Urvashi Yadav, Hemant Mande, and Prasanna Ghalsasi, Nitration of Phenols Using Cu(NO<sub>3</sub>)<sub>2</sub>: Green Chemistry Laboratory Experiment, *Journal of Chemical Education* **2012** 89 (2), 268-270
8. Lori L. White and Kevin W. Kittredge, A Microwave-Assisted Reduction of Cyclohexanone Using Solid-State-Supported Sodium Borohydride, *Journal of Chemical Education* **2005** 82 (7), 1055
9. Aaron M. Hartel and James M. Hanna Jr., Preparation of Oil of Wintergreen from Commercial Aspirin Tablets. A Microscale Experiment Highlighting Acyl Substitutions, *Journal of Chemical Education* **2009** 86 (4), 475 - 476
10. Marsha R. Baar, Danielle Falcone, and Christopher Gordon, Microwave-Enhanced Organic Syntheses for the Undergraduate Laboratory: Diels–Alder Cycloaddition, Wittig Reaction, and Williamson Ether Synthesis, *Journal of Chemical Education*, **2010**, 87 (1), 84-86.

## APPENDICES

### Appendix A

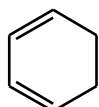
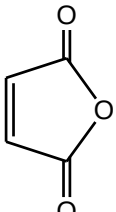
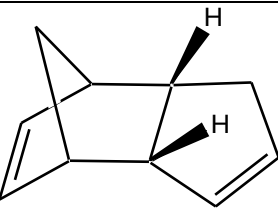
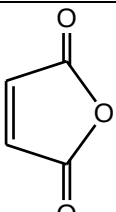
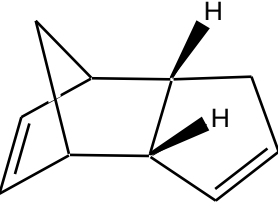
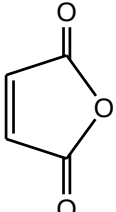
Table 1: Reactions Carried out by Microwave and by Classical Heating for Comparison During the 2014-2015 Organic Undergraduate Laboratory Course

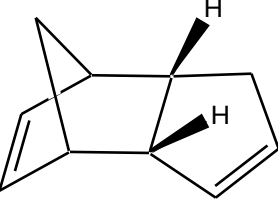
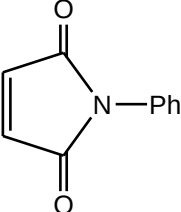
| Reaction                     | Solvent(Amount)                           | Reactants(Amount)                                                                                                                                          | Hold Temp/Time            | Other Data                                         | Method               |
|------------------------------|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|----------------------------------------------------|----------------------|
| Isomerization of Maleic Acid | 24%(V/V) HCl <sub>(aq)</sub> (0.5 mL)     | Maleic Anhydride (0.1 – 0.2 g)                                                                                                                             | 100°C/2 min               | Mp, IR Spectrum if possible for solids             | Microwave (20 Watts) |
| Same reaction                | 24%(V/V) HCl <sub>(aq)</sub> (10 - 20 mL) | Maleic Anhydride (1 – 2 g)                                                                                                                                 | 100°C/30 min              | Mp, IR Spectrum if possible for solids             | Sand bath heating    |
| Diels-Alder Cycloaddition    | Ethyl acetate (1 mL)                      |  <p>Cyclohexadiene (0.2 - 0.3 mL) + N-Phenylmaleimide (0.1 - 0.2 g)</p> | 90°C/2 min                | Mp, <sup>1</sup> H and <sup>13</sup> C NMR spectra | Microwave (30 Watts) |
| Same reaction                | Ethyl acetate (15 mL)                     | Cyclohexadiene (0.6 mL); N-Phenylmaleimide (1.0 g)                                                                                                         | 90°C (1 h)                | Mp, <sup>1</sup> H and <sup>13</sup> C NMR spectra | Sand bath Heating    |
| Fischer Esterification       | Neat                                      | Glacial acetic acid (4 mL) and Various aliphatic alcohols – Isobutyl, benzyl, n-octyl, isopentyl (1 mL)                                                    | 110 – 130°C (10 – 15 min) | IR, <sup>1</sup> H and <sup>13</sup> C NMR spectra | Microwave (20 Watts) |

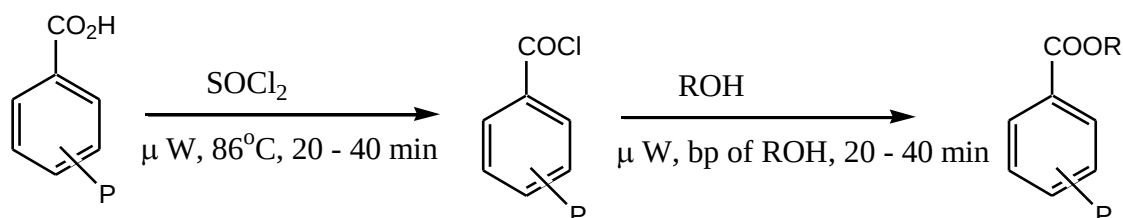


Scheme I: One-pot generation of cyclopentadiene and cycloaddition to Activated Cyclic Dienophiles

Table II: Summary of New Diels-Alder Cycloaddition Procedures:

| Diene                                                                                                    | Dienophile                                                                                              | Hold Temp/Time | Stereo-isomers             | Power     | Type of Data Acquired                                                                                     |
|----------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------|----------------------------|-----------|-----------------------------------------------------------------------------------------------------------|
| <br>Cyclohexadiene      | <br>Maleic Anhydride  | 90°C/2 min     | Endo only                  | 30 watts  | Mp: 143 – 5°C<br><sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR                               |
| <br>Dicyclopentadiene | <br>Maleic Anhydride | 160°C/3 min    | Endo(major)+<br>Exo(minor) | 100 watts | For isolated endo-product:<br>Mp: 160 – 1°C<br><sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR |
| <br>Dicyclopentadiene | <br>Maleic Anhydride | 200°C/5 min    | Endo:Exo = 1 : 1           | 100 watts | Same as above                                                                                             |

|                                                                                   |                                                                                   |             |           |           |                                                                               |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------|-----------|-----------|-------------------------------------------------------------------------------|
|  |  | 160°C/3 min | Endo only | 100 watts | Mp: 139 – 141°C<br><sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR |
| Dicyclopentadiene                                                                 | N-Phenylmaleimide                                                                 |             |           |           |                                                                               |



Scheme II: Two-Step Microwave-assisted Synthetic Scheme for Esters: P = OH, Cl etc; R = 1<sup>o</sup>, 2<sup>o</sup> Alkyl groups

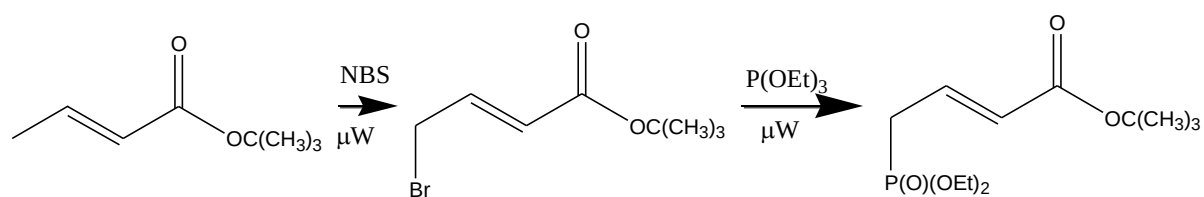
Table III: Some Data on the Two-step Microwave-assisted Syntheses of Alkyl Esters of Salicylic Acid

| Alkyl Group, R | Hold Time for Formation of Acid Halide | Hold Temp(°C) & ( Time) for Reaction with ROH | Distillation Parameters for Vacuum Distillation | Microwave Power for Chlorination & (Reaction with Alcohol) | Spectral Data for Purity and Structure Confirmation                                                     |
|----------------|----------------------------------------|-----------------------------------------------|-------------------------------------------------|------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| n-Propyl       | 40 min                                 | 100(40)                                       | 1.4 - 3 Torr, 140 - 160°C pot temp.             | 20(20)                                                     | <sup>1</sup> H NMR for Acid Halide, <sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR of Ester |
| 2-Propyl       | 40 min                                 | 90(40)                                        | 1.3Torr (Forerun)                               | 20(20)                                                     | <sup>1</sup> H NMR for Acid Halide, <sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR of Ester |
| 1-Butyl        |                                        |                                               |                                                 |                                                            |                                                                                                         |
| Isobutyl       |                                        |                                               |                                                 |                                                            |                                                                                                         |

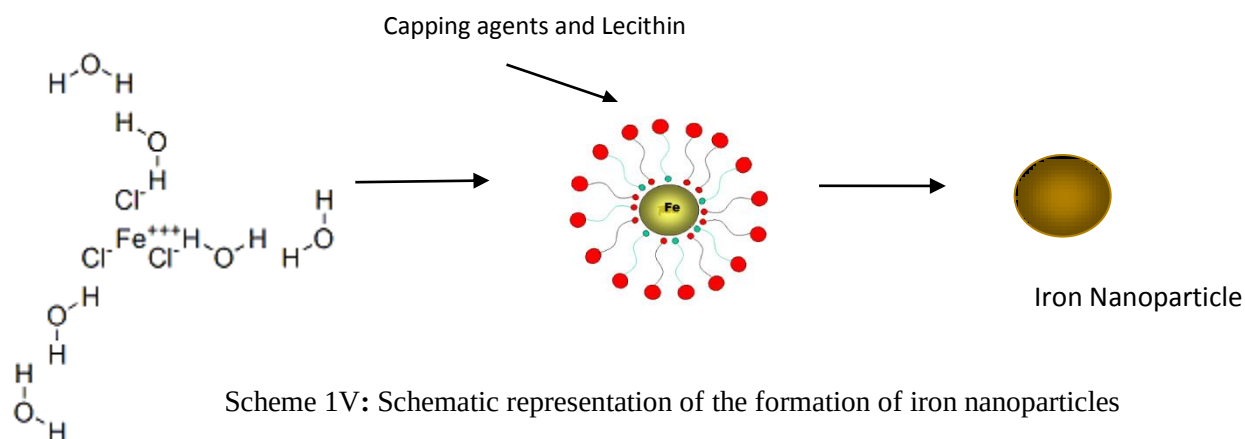
Table IV: Data on the Two-step Microwave-assisted Syntheses of Alkyl Esters of Phenylacetic Acid

| Alkyl Group, R | Hold Time for Formation of | Hold Temp(°C) & ( Time) for | Distillation Parameters for | Microwave Power for | Spectral Data for Purity and |
|----------------|----------------------------|-----------------------------|-----------------------------|---------------------|------------------------------|
|----------------|----------------------------|-----------------------------|-----------------------------|---------------------|------------------------------|

|          | Acid Halide | Reaction with ROH | Vacuum Distillation                                           | Chlorination & (reaction with Alcohol) in watts | Structure Confirmation                                                                                  |
|----------|-------------|-------------------|---------------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| n-Propyl | 20 min      | 100(30)           | 1.4 Torr, 140°C<br>pot temp, fore-run Temp<br>Range = 70-85°C | 20(20)                                          | <sup>1</sup> H NMR for Acid Halide, <sup>1</sup> H, <sup>13</sup> C, DEPT-135, COSY and HETCOR of Ester |
| 2-Propyl |             |                   |                                                               |                                                 |                                                                                                         |
| 1-Butyl  |             |                   |                                                               |                                                 |                                                                                                         |
| Isobutyl |             |                   |                                                               |                                                 |                                                                                                         |



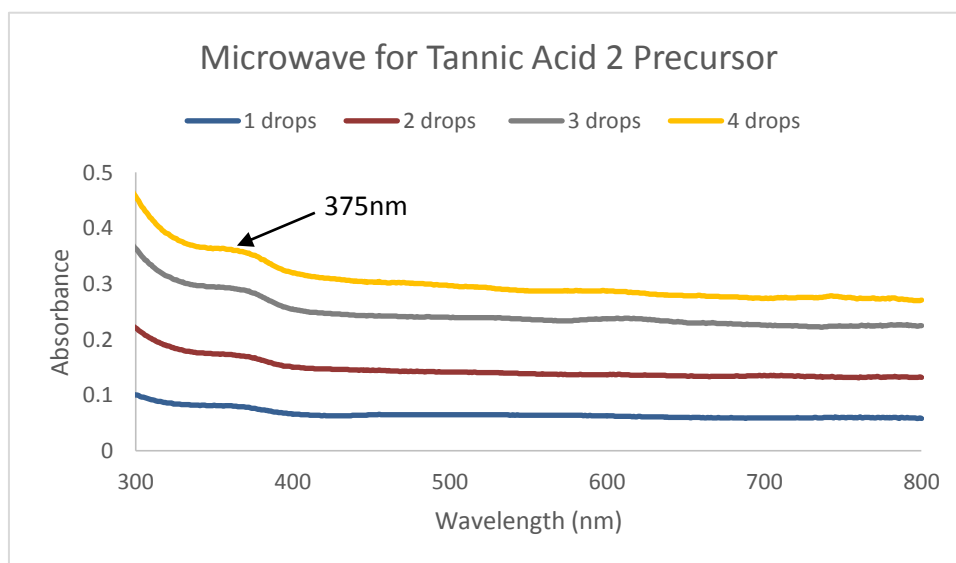
Scheme III: Microwave-assisted Synthesis of the Phosponate Ester of t-Butyl Crotonate



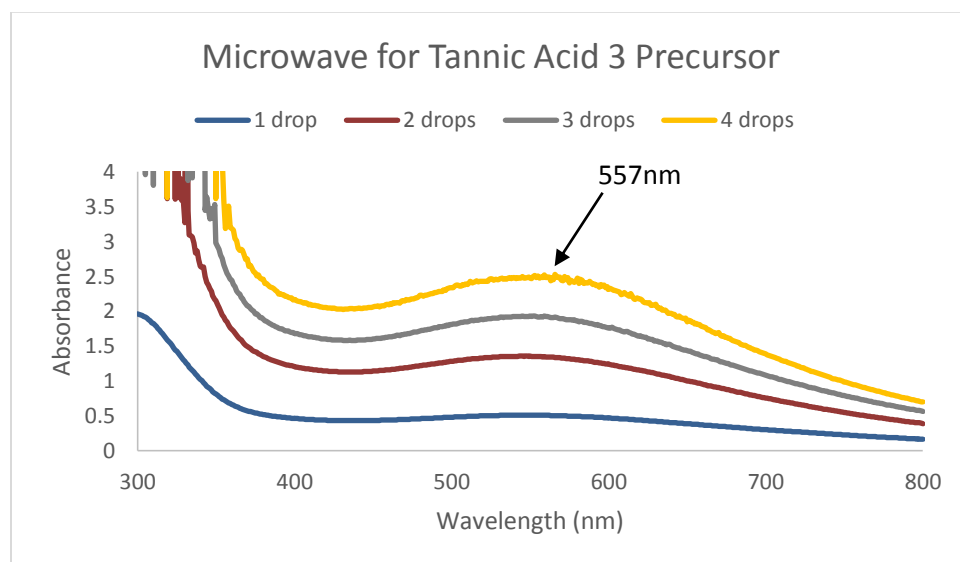
Scheme IV: Schematic representation of the formation of iron nanoparticles

Table V: Amounts of Substances Used in Trials for Preparation of the Precursor Nanoparticles

| Precursor Trial | Capping Agent              | Amount of Capping Agent | $FeCl_3$ Solution, 0.5M (mL) | HCl Solution, 0.04M (mL) | Lecithin (mg) |
|-----------------|----------------------------|-------------------------|------------------------------|--------------------------|---------------|
| 1               | Tea Extract                | 1.98 mL                 | 1.975                        | 1.95                     | 0.025g        |
| 2               | Tannic Acid I              | 0.22g                   | 1.975                        | 1.95                     | 0.025g        |
| 3               | Tannic Acid II             | 1.12 g                  | 1.975                        | 1.95                     | 0.025g        |
| 4               | Pol(Bisphenol A Carbonate) | 5.94 g                  | 1.975                        | 1.95                     | 0.1g          |
| 5               | Tannic Acid III            | 0.22 g                  | 1.975                        | 1.95                     | 0.1g          |

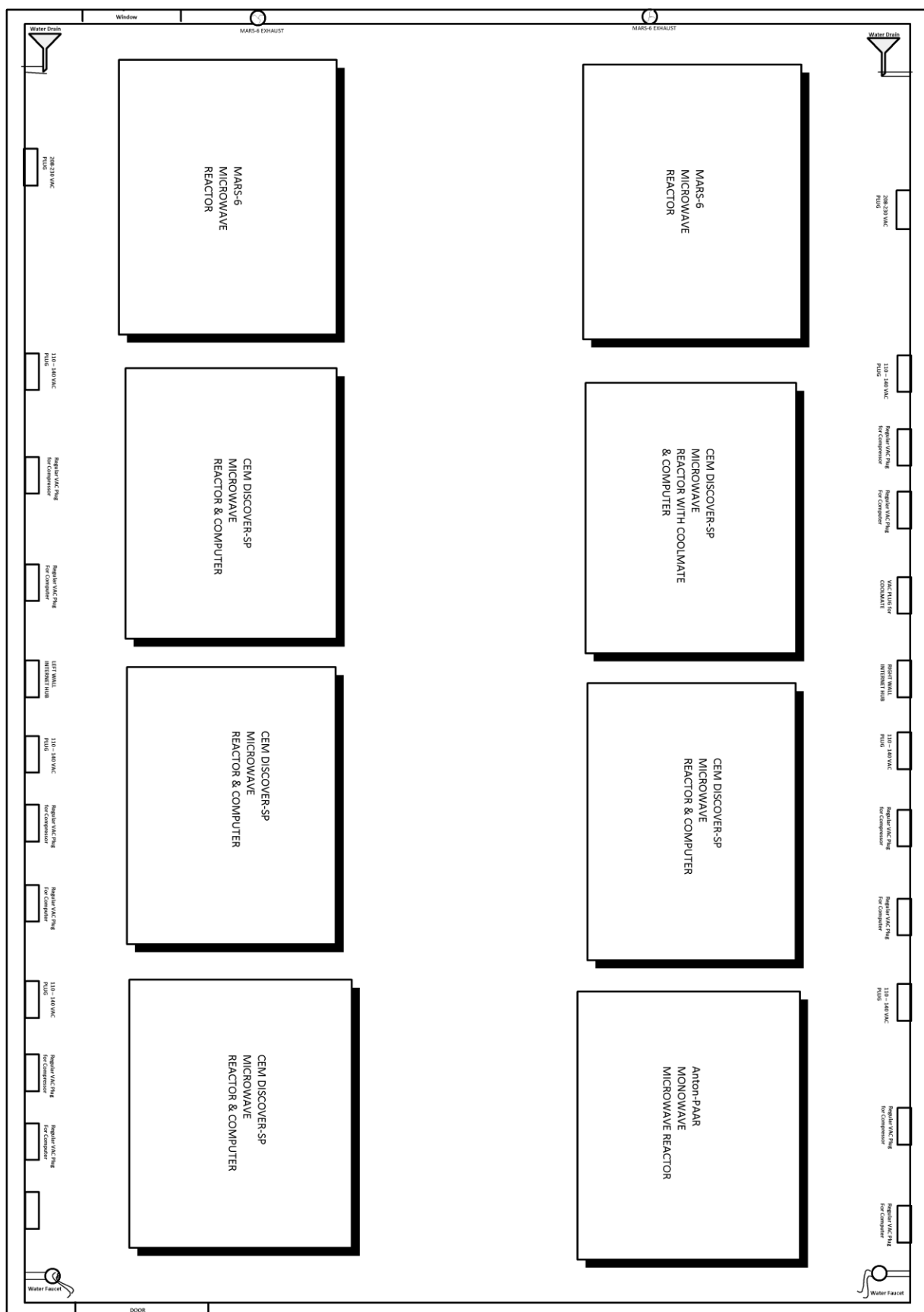


**Figure 1.** UV-Vis of microwave trial 8 after 30 minutes. The precursor used for this trial was the tannic acid 2. There was a very slight peak at 375nm that sharpened as the concentration increased.



**Figure 2.** UV-Vis of microwave trial 15 after 30 minutes. The precursor used for this trial was the tannic acid 3 reaction mixture. Here, there was a large peak at 557nm with a maximum absorbance of about 2.5





## Appendix C

### 1. Microwave-Assisted Heterocyclic Chemistry

William F. Coleman

*Journal of Chemical Education* **2006** 83 (4), 621

### 2. Microwave Assisted Wolff-Kishner Reduction Reaction

Eric Parquet and Qun Lin

*Journal of Chemical Education* **1997** 74 (10), 1225

### 3. Fries Rearrangement Accelerated by Microwave Radiation in the Undergraduate Organic Laboratory

Inder R. Trehan, Jasvinder S. Brar, Ajay K. Arora, and Goverdhan L. Kad

*Journal of Chemical Education* **1997** 74 (3), 324

### 4. Reactions accelerated by microwave radiation in the undergraduate organic laboratory

Shamsher S. Bari, Ajay K. Bose, Ashok G. Chaudhary, Maghar S. Manhas, Vegesna S. Raju, and Ernest W. Robb

*Journal of Chemical Education* **1992** 69 (11), 938

### 5. Microwave Irradiation Reactions: Synthesis of Analgesic Drugs

Gholam A. Mirafzal and Jolene M Summer

*Journal of Chemical Education* **2000** 77 (3), 356

### 6. Microwave-Mediated Synthesis of Lophine: Developing a Mechanism To Explain a Product

R. David Crouch, Jessica L. Howard, Jennifer L. Zile, and Kathryn H. Barker

*Journal of Chemical Education* **2006** 83 (11), 1658

### 7. A Greener Approach to Aspirin Synthesis Using Microwave Irradiation

Ingrid Montes, David Sanabria, Marilyn García, Joaudimir Castro, and Johanna Fajardo

*Journal of Chemical Education* **2006** 83 (4), 628

**8. Microwave-Enhanced Organic Syntheses for the Undergraduate Laboratory: Diels–Alder Cycloaddition, Wittig Reaction, and Williamson Ether Synthesis**

Marsha R. Baar, Danielle Falcone, and Christopher Gordon

*Journal of Chemical Education* **2010** 87 (1), 84-86

**9. Microwave Microscale Organic Experiments**

Fernando G. Braga

*Journal of Chemical Education* **1996** 73 (5), A104

**10. A Microwave-Assisted Friedel–Crafts Acylation of Toluene with Anhydrides**

Fehmi Damkaci, Michelle Dallas, and Megan Wagner

*Journal of Chemical Education* **2013** 90 (3), 390-392

**11. Simple Microwave-Assisted Claisen and Dieckmann Condensation Experiments for the Undergraduate Organic Chemistry Laboratory**

Javier E. Horta

*Journal of Chemical Education* **2011** 88 (7), 1014-1015

**12. Microwave-Assisted Heterocyclic Chemistry for Undergraduate Organic Laboratory**

Robert Musiol, Bozena Tyman-Szram, and Jaroslaw Polanski

*Journal of Chemical Education* **2006** 83 (4), 632

**13. Triboluminescent Crystals from the Microwave Oven**

David M. Wilhite and Bruce W. Baldwin

*Journal of Chemical Education* **2002** 79 (11), 1344

**14. A Microwave-Assisted Reduction of Cyclohexanone Using Solid-State-Supported Sodium Borohydride**

Lori L. White and Kevin W. Kittredge

*Journal of Chemical Education* **2005** 82 (7), 1055

**15. Microwave-Assisted Organic Synthesis in the Organic Teaching Lab: A Simple, Greener Wittig Reaction**

Eric Martin and Cynthia Kellen-Yuen

*Journal of Chemical Education* **2007** 84 (12), 2004

**16. Microwave-Assisted Synthesis of N-Phenylsuccinimide**

Thomas A. Shell, Jennifer R. Shell, Kathleen A. Poole, and Thomas F. Guetzloff

*Journal of Chemical Education* **2011** 88 (10), 1439-1441

**17. Microwave Synthesis of a Fluorescent Ruby Powder**

Géraldine Leyral, Laurent Bernaud, Alain Manteghetti, and Jean-Sébastien Filhol

*Journal of Chemical Education* **2013** 90 (10), 1380-1383

**18. Microwave-Assisted Carbonyl Chemistry for the Undergraduate Laboratory**

C. Oliver Kappe and S. Shaun Murphree

*Journal of Chemical Education* **2009** 86 (2), 227

**19. Microwave-Assisted Synthesis of a Natural Insecticide on Basic Montmorillonite K10 Clay. Green Chemistry in the Undergraduate Organic Laboratory**

Matthew R. Dintzner, Paul R. Wucka, and Thomas W. Lyons

*Journal of Chemical Education* **2006** 83 (2), 270

**20. Microwave Synthesis of a Long-Lasting Phosphor**

David Zitoun, Laurent Bernaud, Alain Manteghetti, and Jean-Sébastien Filhol

*Journal of Chemical Education* **2009** 86 (1), 72

**21. Triboluminescent Crystals from the Microwave Oven. In California, N-Acetylanthranilic Acid and Anthranilic Acid Are Controlled Substances—Have You Been Using Them Illegally?**

Arnold L. Rheingold

*Journal of Chemical Education* **2004** 81 (8), 1121

**22. Triboluminescent Crystals from the Microwave Oven. What Is the Proper Regulation of Controlled Substances at Educational Institutions? (the author replies)**

Bruce Baldwin

*Journal of Chemical Education* **2004** 81 (8), 1121

**23. Microwave-Assisted Hydantoins Synthesis on Solid Support**

Thibault Coursindel, Jean Martinez, and Isabelle Parrot

*Journal of Chemical Education* **2010** 87 (6), 640-642

**24. Microwave-Induced Chain Transfer Polymerization of a Stimuli-Responsive Polymer and Determination of Its Critical Solution Temperature**

R. Freitag and F. Fischer

*Journal of Chemical Education* **2006** 83 (3), 447

**25. Microwave Synthesis of Tetraphenylcyclopentadienone and Dimethyl Tetraphenylphthalate**

John W. Elder

*Journal of Chemical Education* **1994** 71 (6), A142

**26. A Knoevenagel Initiated Annulation Reaction Using Room Temperature or Microwave Conditions**

A. Gilbert Cook

*Journal of Chemical Education* **2007** 84 (9), 1477

**27. Novel Preparation of a Tetraaza Macrocyclic: An Advanced Inorganic Chemistry Laboratory**

Jerry W. Hayes II, Cynthia J. Taylor, and Richard P. Hotz

*Journal of Chemical Education* **1996** 73

*Journal of Chemical Education* **2000** 77 (11), 1486

**28. Solventless and One-Pot Synthesis of Cu(II) Phthalocyanine Complex: A Green Chemistry Experiment**

R. K. Sharma, Chetna Sharma, and Indu Tucker Sidhwani

*Journal of Chemical Education* **2011** 88 (1), 86-87

**29. Acylation of Ferrocene: A Greener Approach**

Kurt R. Birdwhistell, Andy Nguyen, Eric J. Ramos, and Robert Kobelja

*Journal of Chemical Education* **2008** 85 (2), 261

**30. Nitration of Phenols Using Cu(NO<sub>3</sub>)<sub>2</sub>: Green Chemistry Laboratory Experiment**

Urvashi Yadav, Hemant Mande, and Prasanna Ghalsasi

*Journal of Chemical Education* **2012** 89 (2), 268-270

**31. Preparation of Oil of Wintergreen from Commercial Aspirin Tablets. A Microscale Experiment Highlighting Acyl Substitutions**

Aaron M. Hartel and James M. Hanna Jr.

*Journal of Chemical Education* **2009** 86 (4), 475

**32. Diels–Alder Cycloadditions: A MORE Experiment in the Organic Laboratory Including A Diene Identification Exercise Involving NMR Spectroscopy and Molecular Modeling**

Roosevelt Shaw, Ashika Severin, Miguel Balfour, and Columbus Nettles

*Journal of Chemical Education* **2005** 82 (4), 625

**33. Synthesis and Characterization of Self-Assembled Liquid Crystals: p-Alkoxybenzoic Acids**

Jana Jensen, Stephan C. Grundy, Stacey Lowery Bretz, and C. Scott Hartley

*Journal of Chemical Education* **2011** 88 (8), 1133-1136

**34. Reaction of Morpholine with t-Butyl Acetoacetate: A Study in Kinetic vs Thermodynamic Control, Product Identification, and Molecular Modeling**

A. Gilbert Cook and Pamela K. Kreeger

*Journal of Chemical Education* **2000** 77 (1), 90

**35. Synthesis of Well-Defined Copper N-Heterocyclic Carbene Complexes and Their Use as Catalysts for a “Click Reaction”: A Multistep Experiment That Emphasizes the Role of Catalysis in Green Chemistry**

Elon A. Ison and Ana Ison

*Journal of Chemical Education* **2012** 89 (12), 1575-1577

**36. The Baylis-Hillman Reaction: Synthesizing a Compound and Explaining Its Formation**

R. David Crouch and Todd D. Nelson

*Journal of Chemical Education* **1995** 72 (1), A6

**37. Chemoselective Reactions of Citral: Green Syntheses of Natural Perfumes for the Undergraduate Organic Laboratory**

Anna D. Cunningham, Eun Y. Ham, and David A. Vosburg

*Journal of Chemical Education* **2011** 88 (3), 322-324

**38. Synthesis and Testing of Molecules of Medical Interest**

William F. Coleman

*Journal of Chemical Education* **2010** 87 (6), 654-655

**39. Rapid and Stereoselective Conversion of a trans-Cinnamic Acid to a beta-Bromostyrene**

Thomas A. Evans

*Journal of Chemical Education* **2006** 8

**40. "Greening Up" the Suzuki Reaction**

Evangelos Aktoudianakis, Elton Chan, Amanda R. Edward, Isabel Jarosz, Vicki Lee, Leo Mui, Sonya S. Thatipamala, and Andrew P. Dicks

*Journal of Chemical Education* **2008** 85 (4), 555

**41. Designing and Incorporating Green Chemistry Courses at a Liberal Arts College To Increase Students' Awareness and Interdisciplinary Collaborative Work**

Renuka Manchanayakage

*Journal of Chemical Education* **2013** 90 (9), 1167-1171

**42. Diels–Alder Synthesis of endo-cis-N-Phenylbicyclo[2.2.2]oct-5-en-2,3-dicarboximide**

Marsha R. Baar and Kristin Wustholz

*Journal of Chemical Education* **2005** 82 (9), 1393

**43. Rapid Multistep Synthesis of a Bioactive Peptidomimetic Oligomer for the Undergraduate Laboratory**

Yeliz Utku, Abhinav Rohatgi, Barney Yoo, Kent Kirshenbaum, Ronald N. Zuckermann, and Nicola L. Pohl

*Journal of Chemical Education* **2010** 87 (6), 637-639

**44. Benzodiazepine Synthesis and Rapid Toxicity Assay**

James T. Fletcher and Grit Boriraj

*Journal of Chemical Education* **2010** 87 (6), 631-633

**45. A Safer and Convenient Synthesis of Sulfathiazole for Undergraduate Organic and Medicinal Chemistry Classes**

Jeff Boyle, Sandra Otty, and Vijayalekshmi Sarojini

*Journal of Chemical Education* **2012** 89 (1), 141-143

**46. Polymer Nanocomposition Approach to Advanced Materials**

Christopher O. Oriakhi

*Journal of Chemical Education* **2000** 77 (9), 1138

**47. Demonstration of a Runaway Exothermic Reaction: Diels–Alder Reaction of (2E,4E)-2,4-Hexadien-1-ol and Maleic Anhydride**

Brendon A. Parsons and Veljko Dragojlovic

*Journal of Chemical Education* **2011** 88 (11), 1553-1557



**48. The Petasis Reaction: Microscale Synthesis of a Tertiary Amine Antifungal Analog**

Katherine J. Koroluk, Derek A. Jackson, and Andrew P. Dicks

*Journal of Chemical Education* **2012** 89 (6), 796-798

**49. Exploring the Stereochemistry of the Wittig Reaction: The Unexpected Influence of a Nominal Spectator Ion**

John Hanson, Bill Dasher, Eric Scharrer, and Tim Hoyt

*Journal of Chemical Education* **2010** 87 (9), 971-974

**50. Visually Following the Hydrogenation of Curcumin to Tetrahydrocurcumin in a Natural Product Experiment That Enhances Student Understanding of NMR Spectroscopy**

Carl E. Wagner, Pamela A. Marshall, Thomas M. Cahill, and Zeynab Mohamed

*Journal of Chemical Education* **2013** 90 (7), 930-933

**51. Isolation and Analysis of Essential Oils from Spices**

Stephen K. O'Shea, Daniel D. Von Riesen, and Lauren L. Rossi

*Journal of Chemical Education* **2012** 89 (5), 665-668

**52. "Click" and Olefin Metathesis Chemistry in Water at Room Temperature Enabled by Biodegradable Micelles**

Bruce H. Lipshutz, Zarko Bošković, Christopher S. Crowe, Victoria K. Davis, Hannah C. Whittemore, David A. Vosburg, and Anna G. Wenzel

*Journal of Chemical Education* **2013** 90 (11), 1514-1517

**53. Green Carbonyl Condensation Reactions Demonstrating Solvent and Organocatalyst Recyclability**

Jason M. Stacey, Andrew P. Dicks, Aaron A. Goodwin, Brittney M. Rush, and Manisha Nigam

*Journal of Chemical Education* **2013** 90 (8), 1067-1070

**54. New Nanotech from an Ancient Material: Chemistry Demonstrations Involving Carbon-Based Soot**

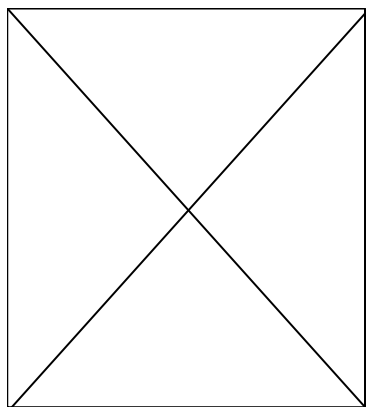
Dean J. Campbell, Mark J. Andrews, and Keith J. Stevenson

*Journal of Chemical Education* **2012** 89 (10), 1280-1287

**55. A Two-Step Synthesis of the Laundry Detergent Perfume Additive  $\beta$ -Citronellyl Tosylate**

Cheryl M. Mascarenhas

*Journal of Chemical Education* **2013** 90 (9), 1231-1234



## APPENDIX D

#1 2015 Spring

100mL round bottom flask containing the maleimide solution. The mixture was heated to reflux for one hour. At the end of the reflux period the reaction mixture was first cooled to room temperature and then to 0°C in an ice bath. The product was collected by suction filtration and allowed to dry until the next lab period. The mass of the dry product was weighed and recorded as 1.01g

$\frac{1.5}{2}$

### Microwave Assisted:

0.13g of N-phenylmaleimide was weighed and added to the microwave reaction tube. Using a 1mL calibrated pipette, 0.5mL of ethyl acetate was added to the reaction tube and stirred until the maleimide was completely dissolved. With the reaction tube containing the solution in the hood, another calibrated pipette was used to add 0.25mL of 1,3-cyclohexadiene into the reaction tube. The plastic cap was attached securely to seal the reaction tube. The reaction vessel was then set up in the microwave reactor and irradiated for two minutes using the following reaction conditions using the control application, Synergy.exe, on the control computer.

|                                                  |          |
|--------------------------------------------------|----------|
| Reaction Temperature (Hold Temperature)          | 100°C    |
| Reaction Time (Hold Time at 100°C)               | 2 min    |
| Pressure Device Release Temperature on Cool Down | 50°C     |
| Microwave Power                                  | 20 watts |
| Maximum Pressure                                 | 300 psi  |

After the reaction was retrieved from the microwave reactor, the reaction tube was allowed to sit for a few minutes to allow supernatant liquid to clarify and for the solid to compact. The cap was then removed and the excess ethyl acetate and 1,3-cyclohexadiene was decanted into the designated container in the hood. Two mL of hexane was added to the solid residue in the tube. The suspension was stirred with a glass rod to disperse the solid product in the hexane. The suspension was filtered using suction filtration and left on the aspirator to dry. The mass of the product was weight and recorded as 0.04g.

$\frac{2}{2}$

It was observed that the final product was not completely white in the microwave method of the reaction, which could point to unreacted N-phenylmaleimide. This could mean that either there was excess N-phenylmaleimide or the reaction was not complete, leading to a smaller than normal yield.

### Comparison of Methods

| Item                    | Traditional                                         | Microwave                                                        |
|-------------------------|-----------------------------------------------------|------------------------------------------------------------------|
| Amount of Material Used | Large amount of reagents                            | Very small amount of reagents                                    |
| Ease of Setup           | More tedious                                        | Not difficult, very little setup                                 |
| Purity of Product       | Product was white, but not very crystalline         | Although not completely white, this product was more crystalline |
| Time of Reaction        | Very time consuming (1+ hours)                      | Very fast reaction time (2mins)                                  |
| Equipment               | Extensive equipment, boiling setup, multiple flasks | Computer and microwave reactor and tube                          |

$\frac{1}{1}$

# 2

Table for Comparison of Methods :

| Item                     | Classical                                                                  | Microwave                            | Conclusion                                                                                             |
|--------------------------|----------------------------------------------------------------------------|--------------------------------------|--------------------------------------------------------------------------------------------------------|
| Amount of materials used | More amounts of the reagents used                                          | Used <u>less amounts</u> of reagents | It takes smaller amounts of materials used for the microwave method than the classical                 |
| Ease of set up           | Took a long time to set up everything                                      | Only took <u>less than 2 minutes</u> | It was easier to conduct the microwave method                                                          |
| Purity of product        | White crystals with some brown spots                                       | <u>White crystals</u>                | The crystals formed by the microwave method produced a purer/cleaner product than the classical method |
| Time of reaction         | One hour                                                                   | 5 minutes                            | The microwave method was a faster process than the classical method                                    |
| Equipment                | Beakers, Erlenmeyer Flask, pipette, round bottom flask, graduated cylinder | Microwave, tube, pipette             | Microwave method required less equipment than the classical method                                     |

**Conclusion:**

In this experiment the sole purpose was to perform a Diels-Alder reaction using maleic anhydride and cyclopentadiene to separate the adduct in the formation of pure crystals. We aimed to get the crystals as pure as possible. However, we observed that the final product was not completely white in the microwave method of the reaction, which could point to unreacted N-phenylmaleimide. This may have meant that either there was excess N-phenylmaleimide or the reaction was not complete. This may have caused a small yield. With that being said it was observed that the traditional method gave a more pure product as the substance appeared to be white. The traditional process was the better process to use because there was a 97 percent yield in the traditional and only a 37 percent yield in the microwave. This data tells us that a more pure product was obtained using the traditional method.

# 3

- Pressure Device Release Temperature on Cool Down: 50°C
- Microwave Power 30 Watts
- Maximum Pressure 300 psi

When the microwave reached the hold time it was allowed to cool down to below 50°C before the pressure device was released and the tube was obtained. After cooling the reaction was allowed to rest so that the supernatant liquid would clarify and the solid would compact. Once this occurred the cap was removed and the ethyl acetate and excess cyclohexadiene was decanted. The suspension then underwent suction filtration and afterwards the solid product was allowed to dry. Once dried the product was weighed and the mass was recorded.

Table for comparison of methods:

| Item                    | Classical                                                           | Microwave                                                                       | Conclusion                                                                                                    |
|-------------------------|---------------------------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| Amount of Material used | 1.00g                                                               | 0.13g                                                                           | More material was needed to run classical versus Microwave                                                    |
| Ease of setup           | Many different parts to assemble.                                   | Easy to set up, just required entering information into the microwave computer. | Microwave was easier to set up                                                                                |
| Purity of Product       | Slightly tinged yellow so was not completely pure                   | Not entirely white partially yellow so not completely pure                      | Both had some impurities. According to observations one was not significantly more pure than the other method |
| Time of Reaction        | Longer than 1 hour                                                  | 2minutes                                                                        | Microwave was much faster reaction                                                                            |
| Equipment               | Thermowell, calibrated pipet, boilerezer, fume hood, various flasks | Microwave reaction vessel                                                       | Microwave reaction method uses less equipment                                                                 |

Theoretical yield:

Classical:

$$1.09 \text{ g} = 0.005 \text{ moles} * \frac{1}{1} * \frac{243 \text{ g}}{\text{mole}} = \frac{1.09}{1.215} = .8971 \text{ g}$$

Microwave:

$$0.04 \text{ g} = 7.5 * 10^{-4} \text{ moles} * \frac{1}{1} * \frac{243 \text{ g}}{\text{mole}} = \frac{0.04}{.18225} = .2194 \text{ g}$$

Percent Yield:

Classical:

$$\frac{1.09}{.8971} = 1.215 * 100\% = 121.5\%$$

Microwave:

$$\frac{0.04}{.2194} * 100\% = 18.23\%$$

Conclusion:

The microwave isomerization method is the best method to complete the Diel's Alder reaction because it requires less equipment, is much faster, uses less material, is easier to set up and produces better results in regards to the purity of the compound. The classical method produced more product than originally started with so compound was definitely not pure. It is also safer than the Classical method. The reaction for the microwave method is heated and occurs in a microwave that contains a pressurized system that keeps the contents inside of the tube until temperature is lowered and the tube is cool enough to touch. Whereas the classical method is heated in the fume hood of the Thermowell, and when the time is completed must be allowed to sit until cool and the scientist has to judge and or use a thermometer in order to determine whether or not the flask is too hot to grasp or not.

# 4

filtered and allowed to dry over night. 0.8 grams of product was obtained. The product was then used to perform an H-NMR and a  $^{13}\text{C}$ MR.

#### Microwave Method:

0.13 g of N-phenylmaleimide was added into the microwave tube with 0.5 mL ethyl acetate. 0.3mL of 1,3, cyclohexadiene was dissolved into the solution. It was placed in to the microwave with the parameters of 90°C, 2 minutes reaction time, 50°C cool down temperature, 30 watts power and 300 psi. 0.13g of product was obtained.

#### Percent Yield

$$\frac{\text{actual}}{\text{theoretical}} \times 100 = \% \text{ yield}$$

#### Classical Method

$$\text{Classical Theoretical: } 5.78 \times 10^{-3} \text{ mol LR} * \left(\frac{1 \text{ mol}}{1 \text{ mol}}\right) \left(\frac{178.0 \text{ g}}{1 \text{ mol}}\right) = 1.03 \text{ g}$$

$$\frac{0.80 \text{ g}}{1.03 \text{ g}} \times 100 = 77.70\%$$

#### Microwave method

$$\text{Microwave Theoretical: } 7.51 \times 10^{-4} \text{ mol LR} * \left(\frac{1 \text{ mol}}{1 \text{ mol}}\right) \left(\frac{173.0 \text{ g}}{1 \text{ mol}}\right) = 0.1301 \text{ g}$$

$$\frac{0.13 \text{ g}}{0.1301 \text{ g}} \times 100 = 99.92\%$$

Table for Comparison of Methods

| Item              | Classical                             | Microwave                        | Conclusion                                       |
|-------------------|---------------------------------------|----------------------------------|--------------------------------------------------|
| Amount used       | 1 g                                   | .13g                             | Less was needed for microwave method.            |
| Ease of Set up    | Medium                                | Easy                             | It was easier to set up the microwave            |
| Purity of Product | Clumpy with some yellow impurities    | Fine, powdery with no impurities | The microwave was a cleaner product.             |
| Time of reaction  | 1 hour                                | 2 min                            | The microwave was quicker                        |
| Equipment         | Glassware (flask, condenser) and bath | Reaction tube, magnetic tube     | There was less bulky equipment for the microwave |

Conclusion: The microwave method was cleaner, produce a purer product and had a higher percent yield then the classical method. Therefore, it is concluded that the microwave method is the most effective method to perform this experiment.

#5

$$\frac{0.00578 \text{ mol Product } 253 \text{ g product}}{1 \text{ mol product}} = 1.46 \text{ g} \quad \checkmark$$

Amount of Product formed in microwave procedure: (0.000693mol, 0.175g product) mol endo-cis-N-phenylbicyclo[2.2.2]oct-5-en-2,3-dicarboximide

$$\frac{0.000693 \text{ mol N - phenylmaleimide}}{1 \text{ mol N - phenylmaleimide}} \frac{1 \text{ mol product}}{1 \text{ mol product}}$$

$$\frac{0.000693 \text{ mol Product } 253 \text{ g product}}{1 \text{ mol product}} = 0.175 \text{ g} \quad \checkmark$$

### Percent yield

Classical: 1g/1.46g = 68.49% yield. ✓

Microwave: 0.12g/0.175g = 68.57% yield. ✓

### Table of Comparison

|                          | Classical                                                                              | Microwave                                                                | Conclusion                                                                                  |
|--------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| Amount of Materials Used | 1 g                                                                                    | 0.12g                                                                    | Classical requires more material; Microwave preferred to save product                       |
| Ease of Setup            | Tedious measurements, Simple mixtures, Medium difficulty setting up condenser          | Tedious measurements, Simple mixtures, <u>Easy set up</u>                | <u>Microwave set up preferred</u>                                                           |
| Purity of Product        | Pale grey in color, Long thin filaments                                                | Short Filaments, grey in color                                           | Classical product preferred                                                                 |
| Time of Reaction         | 1 hour                                                                                 | <u>2-5 min</u>                                                           | Microwave preferred for time's sake                                                         |
| Equipment                | Round bottom flask, Erlenmeyer flask, Filtration equipment, reflux condenser apparatus | Microwave reaction tube, Microwave reactor, suction filtration equipment | Either method preferred due to similar amounts of equipment; Classical preferred for budget |

### Conclusion

The microwave and classical both gave a product yield of about 68%. The microwave set up over all was faster and easier. However, the classical gave a cleaner product. I would go with the classical method based on the fact that I can make more product at once, and obtain a cleaner product.



# 6

Percent yield for Classical Method:  $\frac{1.02 \text{ grams}}{1.30 \text{ grams}} * 100\% = 78.46\%$  Percent yield for Microwave

Method:  $\frac{0.05 \text{ grams}}{0.17 \text{ grams}} * 100\% = 29.41\%$

Table for Comparison of Methods:

|           | Amount of Material used | Ease of Setup  | Purity of Product                                        | Time of Reaction                      | Equipment                                                                          | Conclusion                                                  |
|-----------|-------------------------|----------------|----------------------------------------------------------|---------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------|
| Classical | Less material was used  | More difficult | Product seemed pure but not as pure as microwave results | Took much longer (1 hour)             | Simple lab equipment but takes much longer time to heat and carry out the reaction | This method was longer, however, obtained more product.     |
| Microwave | More material was used  | Very simple    | Product seemed more pure based on color                  | Very short (no longer than 5 minutes) | Very expensive equipment but much faster and efficient                             | This method was much faster, however, obtained less product |

1  
1

#7

Comparison Table

| Item                     | Classical                                                                  | Microwave                     | Conclusion                                                                                             |
|--------------------------|----------------------------------------------------------------------------|-------------------------------|--------------------------------------------------------------------------------------------------------|
| Amount of materials used | Used more amounts of the reagents                                          | Used less amounts of reagents | It takes smaller amounts of materials used for the microwave method than the classical                 |
| Ease of set up           | Took a while to set up everything                                          | Only took less than 2 minutes | It was easier to conduct the microwave method                                                          |
| Purity of product        | White crystals with some brown spots                                       | White crystals                | The crystals formed by the microwave method produced a purer/cleaner product than the classical method |
| Time of reaction         | One hour                                                                   | 5 minutes                     | The microwave method was a faster process than the classical method                                    |
| Equipment                | Beakers, Erlenmeyer Flask, pipette, round bottom flask, graduated cylinder | Microwave, tube, pipette      | Microwave method required less equipment than the classical method                                     |

$$\frac{\text{actual}}{\text{theoretical}} \times 100 = \%$$

#### Classical Method

$$\text{Classical Theoretical: } 5.78 \times 10^{-3} \text{ mol LR} * \frac{1 \text{ mol Prod}}{1 \text{ mol LR}} * \frac{178.0 \text{ g Prod}}{1 \text{ mol Prod}} = 1.03 \text{ g}$$

$$\frac{0.80 \text{ g}}{1.03 \text{ g}} \times 100 = 77.70\%$$

#### Microwave method

$$\text{Microwave Theoretical: } 7.51 \times 10^{-4} \text{ mol LR} * \frac{1 \text{ mol Prod}}{1 \text{ mol LR}} * \frac{173.0 \text{ g Prod}}{1 \text{ mol Prod}} = 0.1301 \text{ g}$$

$$\frac{0.13 \text{ g}}{0.1301 \text{ g}} \times 100 = 99.92\%$$

#### Comparison of Methods:

|                          | <u>Classical</u>                                     | <u>Microwave</u>                                                |
|--------------------------|------------------------------------------------------|-----------------------------------------------------------------|
| <b>Amount used</b>       | 1.0 g N-phenylmaleimide<br>0.6 mL 1,3-cyclohexadiene | <del>2.0</del> g N-phenylmaleimide<br>0.3 mL 1,3-cyclohexadiene |
| <b>Ease of set up</b>    | More complicated                                     | Simpler                                                         |
| <b>Purity of product</b> | Clumpy, powdery, a few yellow specs of impurities    | Finer, powdery, less yellow specs of impurities                 |
| <b>Time of reaction</b>  | 1 hour                                               | 2 minutes                                                       |
| <b>Equipment</b>         | Glassware (flasks, condenser), sand bath             | Reaction tube, magnetic stirrer                                 |

The classical method had a longer synthesis period as well as the set up time. On the other hand, the microwave method was quicker, had a simpler set up, produced a cleaner product, and did not require as much observational skills compared to the classical method. The classical method produced a greater amount of product compared to the microwave method, but that is due to the greater amount of reactants used. The classical method produced 0.8 g of product while the microwave produced 0.13 g. Concerning the percent yield, a reaction will never yield 100% due to other side reactions and human error. However, the microwave method seemed to produce an extremely high percent yield, almost 100%. The microwave method produced 99.92% while the

## APPENDIX E

Microwave Procedures Already Implemented, Ready for Implementation and Under Development and Optimization for Small-scale Microwave-accelerated Organic Laboratory Program at Hampton University.

### Appendix E-1. Procedure for Microwave-assisted Synthesis of *endo-cis*-N-Phenylbicyclo[2.2.2]oct-5-en-2,3-dicarboximide

If already not in the 10 mL microwave reaction tube provided, drop the micro-magnetic bar into the tube. Weigh and add 0.10g - 0.15g of N-phenylmaleimide into the microwave reaction tube. Using a 1 mL calibrated plastic pipette, add 0.5 mL of ethyl acetate to the reaction tube and stir on the magnetic stirrer until the maleimide is completely dissolved. Using another calibrated plastic pipette, obtain no less than 0.2 mL but no more than .25 mL of 1,3-cyclohexadiene and squirt this into the solution in the reaction tube. Attach the plastic cap securely to seal the reaction tube.

The reaction vessel is then set up in the microwave reactor and irradiated for 2 min using the following reaction conditions which will be entered using the reaction control application on the control computer.

|                                                  |          |
|--------------------------------------------------|----------|
| Reaction Temperature (Hold Temperature)          | 90°C     |
| Reaction Time (Hold Time at 100°C)               | 2 min    |
| Pressure Device Release Temperature on Cool Down | 50°C     |
| Microwave Power                                  | 30 watts |
| Maximum Pressure                                 | 300 psi  |

Before microwave irradiation begins, a pressure device is placed at the top of the reactor cavity and automatically engaged to protect against explosion. Then, there will be a temperature “ramp up” time when the reaction mixture is heated by microwave radiation to the set reaction temperature. The temperature will be maintained at the reaction temperature for the set “hold time” with intermittent puffs of compressed air from a compressor. After the “hold time” is counted down to zero, then the compressed air pump turns on (noisily) and runs continuously to “ramp down” i.e. cool down the reaction to 50°C. When the reaction temperature has been lowered to 50 °C, the pressure device will become disengaged for retrieval of the reaction tube.

After the reaction is retrieved from the microwave reactor, leave the reaction tube a few minutes with the cap on for the supernatant liquid to clarify and the solid to compact. Then remove the cap and **decant the ethyl acetate and excess cyclohexadiene into a designated container in the hood.** Add 2 mL of hexane to the solid residue in the tube. Stir the suspension with either a spatula or glass rod to disperse the solid product in the hexane. Suction-filter the suspension. If

necessary, use additional 2 mL portions of hexane to transfer more of the product from the reaction tube on to the filter paper. Leave the solid product on the aspirator to dry. Weigh and record the mass of the dry product. Record also the color and consistency of this product for comparison with the product from heating on a sand bath.

The product can be recrystallized with ethyl acetate.

**After you have retrieved your product, rinse the reaction tube and the micro-bar with 1 – 2 mL of methylene chloride and return the tube, micro-bar and the plastic cap to your instructor. DO NOT LOSE THE MICROBAR! Discard the methylene chloride rinse into the chlorinated waste bottle.**

After you have prepared an NMR sample of your product and carried out any other product characterization (e.g. melting point or IR spectroscopy), the remainder of your product should be handed over to your instructor. **Your product is not a waste. DO NOT DISCARD IT AS WASTE!**

**Notes:**

1. Only one stereoisomer is observed in the  $^1\text{H}$  NMR spectrum of the crude product.
2. The melting point of the recrystallized product is 204 – 206°C with a Thomas Hoover Melting Point apparatus and 206°C with DSC.
3. Thiele tube and paraffin oil may be used also.

**Appendix E-2. Microwave Procedure for Isomerization of Maleic Acid**

Into a 10mL microwave reaction tube with a micro-magnetic bar, weigh from 0.1 – 0.2 g of maleic anhydride. To this solid, using a 1 mL calibrated pipette, add 0.5 mL of 24% (V/V) aqueous hydrochloric acid. Snap the pressure cap on to the reaction tube and place the tube into the microwave cavity. Place the pressure device into its position over the top of the reaction tube. Using the pressure mode, program the reaction conditions as follows:

Power: 20 watts; Hold temperature: 100°C Hold time: 2 min

Pressure: 200 psi

After the parameters have been entered, click the “Play” button. The pressure device will be engaged and temperature ramp up will begin. After the hold time at 100°C, cool down to < 50°C and release of the pressure device, retrieve the reaction tube from the microwave. Add 1 mL of ice-cold water into the tube. Use a glass rod or spatula to stir the white cake with the cold water. Pour the suspension on to a suction filtration set-up. Use an additional 1 mL of cold water to transfer much of the solid on the sides of the reaction tube onto the filtration set-up. Leave the aspirator on to air-dry the solid.

Weigh the solid white product and record its mass in your lab notebook. Using a Thiele tube and capillary tubes, determine and compare the melting point of the product with the melting point of maleic anhydride (54°C) and maleic acid (142°C). If your solid does not melt even at 200°C, then it cannot be unreacted maleic anhydride or un-isomerized maleic acid. It will not be necessary to continue heating after 200°C.

The dilute aq. HCl waste generated goes down the drain. Return used hot oil and Thiele tube to their appropriate locations in the lab. Hand in the remainder of your product to your instructor for storage.

*Note for Instructors:*

1. Any amount between 0.10 – 0.15 g or between 0.20 – 0.25 g should work with the given volumes of reagent, solvent and time of reaction.
2. Temperature ramp up to 100 °C and cool down to 50°C take less than 2 min. Total time on the microwave reactor should be less than 4 min.
3. Yield varies from ~ 60% for 0.1 g to 80% for 0.2 g of maleic anhydride and will vary depending on how much cold water is used in rinsing the suction-filtered solid.

**Appendix E-3. Procedure for Microwave-assisted Diels-Alder Cycloaddition of 1,3-Cyclohexadiene and Maleic Anhydride**

If already not in the 10 mL microwave reaction tube provided, drop the micro-magnetic bar into the tube. Weigh 0.3535g of maleic anhydride into the microwave reaction tube. Using a 1 mL calibrated plastic pipette, add 0.5 mL of ethyl acetate to the reaction tube. After taring the reaction tube, use another calibrated plastic pipette, to add 0.5156g of 1,3-cyclohexadiene into the reaction tube. Attach the plastic cap securely to seal the reaction tube.

The reaction vessel is then set up in the microwave reactor and irradiated for 2 min using the following reaction conditions which will be entered using the reaction control application on the control computer.

|                                                  |          |
|--------------------------------------------------|----------|
| Reaction Temperature (Hold Temperature)          | 90°C     |
| Reaction Time (Hold Time at 100°C)               | 2 min    |
| Pressure Device Release Temperature on Cool Down | 50°C     |
| Microwave Power                                  | 30 watts |
| Maximum Pressure                                 | 50 psi   |

Before microwave irradiation begins, a pressure device is placed at the top of the reactor cavity and automatically engaged to protect against explosion. Then, there will be a temperature “ramp up” time when the reaction mixture is heated by microwave radiation to the set reaction

temperature. The temperature will be maintained at the reaction temperature for the set “hold time” with intermittent puffs of compressed air from a compressor. After the “hold time” is counted down to zero, then the compressed air pump turns on (noisily) and runs continuously to “ramp down” i.e. cool down the reaction to 50°C. When the reaction temperature has been lowered to 50 °C, the pressure device will become disengaged for retrieval of the reaction tube.

After the reaction is retrieved from the microwave reactor, cool the reaction tube for a few minutes in an ice-water bath with the cap on. The homogeneous reaction solution forms a white cake with the solid product and the small liquid reaction medium. Then remove the cap and add 2 mL of cold hexane to the solid residue in the tube. Stir the suspension with either a spatula or glass rod to disperse the solid product in the hexane/ethyl acetate/xs cyclohexadiene liquid mixture. Leave the reaction tube a few minutes, with the cap on, for the supernatant liquid to clarify and the solid to compact. Then remove the cap and **decant the hexane, ethyl acetate and excess cyclohexadiene into a designated container in the hood.** Add 1 mL of cold hexane to the reaction tube. Stir vigorously and pour on to a suction-filtration set-up before the suspension settles. If necessary, use additional 1 mL portions of hexane to transfer more of the product from the reaction tube on to the filter paper. Leave the solid product on the aspirator to dry. Weigh and record the mass of the dry product. Check if some product dissolved in the reaction liquids and the initial 2 mL of cold hexane by rotary evaporation of the decanted liquid mixture.

**After you have retrieved your product, rinse the reaction tube and the micro-bar with 1 – 2 mL of methylene chloride and return the tube, micro-bar and the plastic cap to your instructor. DO NOT LOSE THE MICROBAR! Discard the methylene chloride rinse into the chlorinated waste bottle.**

After you have prepared an NMR sample of your product and carried out any other product characterization (e.g. melting point or IR spectroscopy), the remainder of your product should be handed over to your instructor. **Your product is not a waste. DO NOT DISCARD IT AS WASTE!**

Record also in your laboratory notebook the following information: Crude Mass of Product =

Crude % Yield:

Stereoisomers found in  $^1\text{H}$  NMR spectrum

Purification : Recrystallization – Solvent

Mp. Instrumentation: Thomas Hoover

Thiele Tube

Types of NMR Spectra obtained

**Notes:**

1. No solid residue is obtained when the cold hexane extract is rotary-evaporated off.
2. The cold hexane triturated solid product gives good enough NMR spectra for product characterization but additional purification can be achieved by dissolving in minimal  $\text{CH}_2\text{Cl}_2$  and then adding hexane until solution is cloudy, then leaving to develop crystals.
3. When this reaction was run at  $90^\circ\text{C}$ , the crude yield was 93% and only one stereoisomer was observed.
4. When the reaction was run at  $160^\circ\text{C}$  (100 watts, 2 min), the crude yield was 98% and still only one isomer was observed by  $^1\text{H}$  NMR spectroscopy of the crude.
5. The product obtained at  $90^\circ\text{C}$  had a melting point of  $124\text{--}6^\circ\text{C}$  on a Thomas Hoover Melting Point apparatus. On the differential scanning calorimeter (DSC), it showed a weak endotherm at  $110^\circ\text{C}$  and a strong one at  $143^\circ\text{C}$ . After cooling and reheating, only the endotherm at  $143^\circ\text{C}$  was observed.
6. The product obtained at  $160^\circ\text{C}$  had a melting point of  $143\text{--}5^\circ\text{C}$  on a Thomas Hoover Melting Point apparatus. On the DSC, it showed a strong endotherm at  $145^\circ\text{C}$  which remained the same after cooling and reheating to melt.

**Appendix E-4. Cycloaddition Reaction of Cyclopentadiene with N-Phenylmaleimide**

In this microwave-assisted Diels-Alder cycloaddition reaction, dicyclopentadiene is cracked in-situ and the resulting cyclopentadiene then reacts with the N-phenylmaleimide. Excess dicyclopentadiene serves both as source of diene and as solvent for the reaction. Unreacted dicyclopentadiene and cyclopentadiene are easily removed during work-up as hexane solution in the digestion step.

0.4049g ( 2.34 mmol) of N-phenylmaleimide is placed in a 10 mL reaction tube containing a magnetic microbar. 0.8170g (6.19 mmol) of dicyclopentadiene was added on top of the N-phenylmaleimide so that as temperature rises, dicyclopentadiene melts, suffuses the solid N-phenylmaleimide and dissolves it at the reaction temperature. The plastic cap is securely attached and the reaction tube is placed in the microwave reactor and irradiated under the following set conditions:

power = 100 watts,

reaction temperature =  $160^\circ\text{C}$ ,

hold time = 3 min,

maximum pressure = 300 psi.

After the reaction tube is released by the pressure device (release temperature set at  $50^\circ\text{C}$ ), the reaction tube is retrieved from the reactor. The reaction mixture is now a homogeneous solution. This viscous solution is either left to cool further in air or in ice-water bath. The reaction mixture becomes a white cake as the reaction product crystallizes out of the unreacted



bicyclopentadiene/cyclopentadiene. The content of the reaction tube is digested by adding 1 mL of cold hexane, using either a glass rod or spatula to break up the solid material. A fine white suspension results which is suction-filtered. The reaction tube is rinsed two more times, each time with 1 mL of cold hexane, and the suspension poured on to the Buchner funnel to get as much of the product as possible transferred from the tube into the funnel. The white solid is left on the running aspirator to dry. The crude product is weighed and an NMR sample is prepared in deuterated chloroform for the acquisition of  $^1\text{H}$  NMR spectrum which will be used to determine whether diastereomers are formed and in what ratio. The remaining product is triturated with 2 mL of boiling hexane and the suspension is filtered while hot to remove the impurities.  $^1\text{H}$  NMR of the air-dried solid,  $^{13}\text{C}$ , DEPT-135, COSY and HETCOR spectra which will be used to match signals to protons and carbons in the structure of the endo diastereomer. Recrystallization, if necessary, for purer product can be effected by dissolving in minimum  $\text{CH}_2\text{Cl}_2$  and then adding hexane until solution becomes cloudy and leaving to crystallize.

Record also in your laboratory notebook the following information:

Mass and % Yield of Product for the crude and each purification stage

Number of stereoisomers found in  $^1\text{H}$  NMR spectrum

Purification : Recrystallization – Solvent for each purification stage

Mp. Instrumentation:            Thomas Hoover                            Thiele Tube

Types of NMR spectra obtained for the pure product

**Notes:**

1. Digestion of product with cold hexane gave a crude product as a white powder. The hexane filtrate showed, on evaporation of the solvent, only an oil of cyclopentadiene/dicyclopentadiene and no solids. This implies that no product adduct was removed by the trituration process.  $^1\text{H}$  NMR spectrum of this crude showed small impurities from the dicyclopentadiene.
2. Only one stereoisomer is found in the NMR spectra of the crude product with traces of impurities from dicyclopentadiene.
3.  $^1\text{H}$  NMR spectrum of the cold hexane digestion crude product showed only one diastereomer. Crude yield after cold digestion with hexane is up to 96%. Hot hexane digestion to remove trace impurities reduces the percent yield.
4. Trituration of the crude product with boiling hexane, filtering while hot and leaving to dry gave a solid whose  $^1\text{H}$  NMR spectrum showed reduced intensity of the impurity signals observed in the first crude.  $^1\text{H}$  NMR spectrum of the solid that recrystallized from the hexane solution showed a clean product.

5. Recrystallization to obtain a purer product results in additional loss of product and therefore, even lower percent yield.
6. Recrystallization of the impure solid from trituration with hot hexane can be achieved by dissolving in minimal cold  $\text{CH}_2\text{Cl}_2$  and then adding hexane dropwise until the  $\text{CH}_2\text{Cl}_2$  solution turned cloudy. Resulting crystals showed no trace of impurities.
7.  $^1\text{H}$ ,  $^{13}\text{C}$ , DEPT-135, COSY and HETCOR spectra will be used to assign chemical shifts and match signals to nuclei.
8. Melting point of the pure endo isomer was found to be 139-141°C (crystals from hot hexane extract) on a Thomas Hoover melting point apparatus and 142°C using differential scanning calorimeter (DSC). Paraffin oil in a Thiele tube can also be used.

#### **Appendix E-5. Cycloaddition Reaction of Cyclopentadiene with Maleic Anhydride**

In this microwave-assisted Diels-Alder cycloaddition reaction, dicyclopentadiene is cracked *in-situ* and the resulting cyclopentadiene then reacts with the maleic anhydride. Excess dicyclopentadiene is used so as to serve both as source of diene and as solvent for the reaction. Unreacted dicyclopentadiene and cyclopentadiene are easily removed during work-up as hexane solution in the digestion step.

0.4918g ( 5.02 mmol) of maleic anhydride is placed in a 10 mL reaction tube containing a magnetic microbar. 0.8563g (6.49 mmol) of dicyclopentadiene was added on top of the maleic anhydride so that as temperature rises, it melts, suffuses the solid maleic anhydride and serves to dissolve it at the reaction temperature. The plastic cap is securely attached and the reaction tube is placed in the microwave reactor and irradiated under the following set conditions:

Power = 100 watts,

Reaction temperature = 160 °C,

Hold time = 3 min,

Maximum pressure = 300 psi.

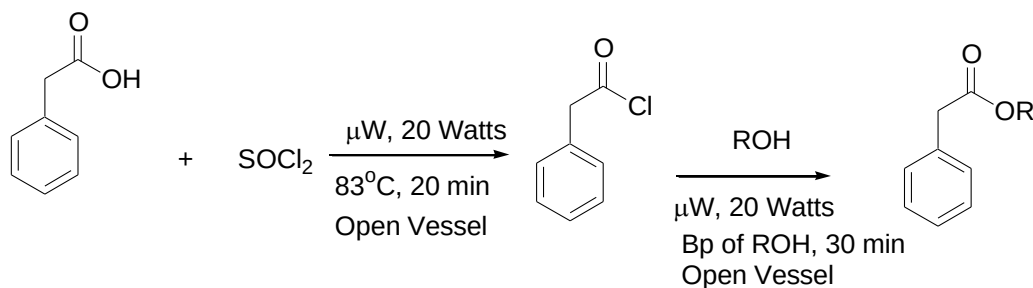
After the reaction tube is released by the pressure device (release temperature set at 50°C), the reaction tube is retrieved from the reactor. The reaction mixture is now a transparent glass. The content of the reaction tube is digested by adding 3 mL of boiling hexane, using either a glass rod or spatula to break up the glassy material. A fine white suspension results which is suction-filtered while hot. The white solid is left on the running aspirator to dry. The product is weighed and an NMR sample is prepared in deuterated chloroform for the acquisition of  $^1\text{H}$ ,  $^{13}\text{C}$ , DEPT-135, COSY and HETCOR spectra to determine (a) diastereomer ratio and (b) assign structure of the various diastereomers. Recrystallization gives a substance that contains the major diastereomer only. Its NMR spectra is used in assigning structure to the major and minor diastereomer by comparison with the spectra of the mixture.

To obtain the actual diastereomer ratio from the reaction, the glassy reaction mixture should be triturated with cold hexane which will not dissolve out any one of the stereoisomers.  $^1\text{H}$  NMR signals for each diastereomer are easily identified from this crude and some peaks are well separated to serve as basis for determining the mole ratio of diastereomers. Crude yield after cold digestion with hexane is up to 98%. Hot hexane digestion to remove trace impurities reduces the yield and recrystallization to obtain the major stereoisomer results in even lower % yield.

**Notes:**

1. The hexane filtrate showed, on evaporation of the solvent, no solids. This implies that no product adduct was removed by the trituration process.  $^1\text{H}$  NMR spectrum of this crude was clean enough for determination of isomer ratio.
2. Trituration of the crude product with boiling hexane, filtering while hot and leaving to dry gave a solid that had lost much of the impurity peaks observed in the first crude. The ratio of the major to the minor isomer has, however increased indicating that the minor isomer is either as equally soluble or more soluble than the major isomer in hot hexane.  $^1\text{H}$  NMR spectrum of the solid that recrystallized from the hexane solution showed a clean 1:1 mixture of both isomers.
3. Recrystallization of the clean mixture by dissolving in minimal cold  $\text{CH}_2\text{Cl}_2$  and then adding hexane dropwise until the  $\text{CH}_2\text{Cl}_2$  solution turned cloudy gave crystals that had just trace of the minor isomer.  $^{13}\text{C}$  NMR showed no additional low peaks for the minor isomer.  $^1\text{H}$ ,  $^{13}\text{C}$ , DEPT-135, COSY and HETCOR spectra were used to assign chemical shifts and match signals to nuclei. Then by subtraction from the  $^{13}\text{C}$  of the 1:1 mixture, the signals for the minor isomer were matched also to corresponding  $^1\text{H}$  and  $^{13}\text{C}$  in its structure.
4. Melting point of the pure endo isomer was found to be 160-161°C on a Thomas Hoover melting point apparatus. Paraffin oil in a Thiele tube can also be used.
5. Running the reaction at 200°C led to ~ 1:1 mixture of endo:exo stereoisomers with the exo slightly more than the endo. At 160°C, the endo is greater than five times more abundant than the exo.
6. The major product can be obtained pure by recrystallizing the crude with  $\text{CH}_2\text{Cl}_2$ /hexane mixture.

## Appendix E-6. Microwave-Assisted Two-step Synthesis of Alkyl 2-Phenylacetate

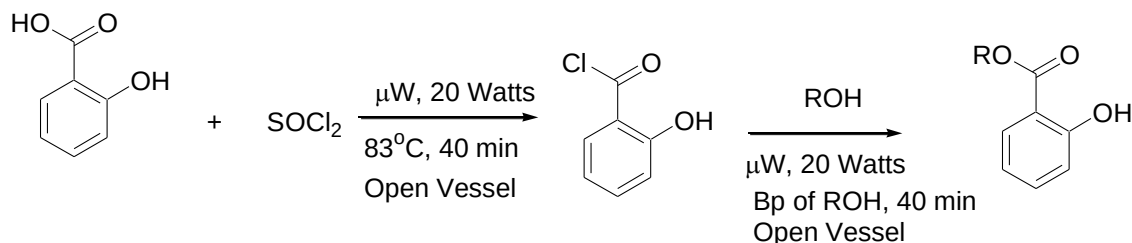


A 50 mL single neck round bottom flask containing a micro-stir bar is charged with 1.0135g (7.452 mmol) of phenylacetic acid. In a fume hood, 1 mL of thionyl chloride was added to the flask using a calibrated 1.0 mL plastic pipette. The reaction flask was placed into the reactor cavity. Adaptors for open vessel mode were attached, followed by a reflux condenser. The condenser was topped with an adaptor that conducts gaseous HCl generated for absorption into an aqueous base solution in the fume hood. Reaction parameters for the reaction were set: power = 20 watts, hold temperature =  $83^\circ\text{C}$ , hold time = 20 min, stirring rate = low. The acid dissolved in the thionyl chloride at room temperature and remained a transparent colorless liquid after the reaction and cooling back to room temperature.  $^1\text{H}$  NMR spectrum of the reaction mixture showed complete conversion of the acid to the acid halide by the absence of the acidic proton, downfield shift of the benzylic protons relative to their chemical shift in the acid and also, by a slight separation of the ortho from the meta / para proton signals for the aromatic protons in the halide which is not observed in the free acid.

To the acid chloride was added, drop-wise, 1.25 mL of 1-propanol in the fume hood. Then, the reaction set-up was reassembled. The reaction parameters are: power = 20 watts, hold temperature =  $100^\circ\text{C}$ , hold time = 30 min and stirring rate – low. After the reaction was over,  $^1\text{H}$  NMR spectrum of the reaction mixture showed completion of reaction. In addition to the product, product(s) from the reaction of the excess  $\text{SOCl}_2$  and the alcohol were also present. These products were effectively removed by vacuum distillation.

$^1\text{H}$  NMR spectrum of the residue left after collecting the fore-run indicated a pure ester devoid of the sulfur components of the original product mixture.

## Appendix E-7. Microwave-Assisted Two-step Synthesis of Alkyl Salicylates



A 50 mL single neck round bottom flask containing a micro-stir bar is charged with 1.0152g (7.349 mmol) of salicylic acid. In a fume hood, 2.25 mL of thionyl chloride was added to the flask using a calibrated 1.0 mL plastic pipette. The reaction flask was placed into the reactor cavity. Adaptors for open vessel mode were attached, followed by a reflux condenser. The condenser was topped with an adaptor that conducts gaseous HCl generated for absorption into an aqueous base solution in the fume hood. Reaction parameters for the reaction were set: power = 20 watts, hold temperature =  $83^\circ\text{C}$ , hold time = 40 min, stirring rate = low. The acid did not dissolve in the thionyl chloride at room temperature but a transparent colorless liquid was obtained after the reaction and cooling back to room temperature.  $^1\text{H}$  NMR spectrum of the reaction mixture showed complete conversion of the acid to the acid halide by the absence of the acidic proton at 10.67 ppm, downfield shift of the aromatic protons in the halide when compared with their positions in the free acid.

To the acid chloride is added, drop-wise, 4.6 mL of 1-propanol in the fume hood. Then, the reaction set-up was reassembled. This time, the reaction parameters are: power = 20 watts, hold temperature = boiling point of the alcohol used – in this case,  $100^\circ\text{C}$ , hold time = 40 min and stirring rate – low. After the reaction is over,  $^1\text{H}$  NMR spectrum of the reaction mixture showed complete conversion of the acid chloride. In addition to the expected ester product, product(s)\* from the reaction of the excess  $\text{SOCl}_2$  with the alcohol were also present. These products were effectively removed by vacuum distillation. Purified product was characterized using IR, NMR and UV spectroscopy.

In the vacuum distillation at 1.4 – 3 Torr, the fraction collected from  $52 - 100^\circ\text{C}$  contained some ester but mostly the chlorosulfite and other sulfur-containing compounds as pot temperature rose to  $160^\circ\text{C}$ .  $^1\text{H}$  NMR spectrum of the residue left after collecting the fore-run indicated a pure ester devoid of the sulfur components of the original product mixture.

In the case of 2-propanol, the quantities were 1.0131g of salicylic acid, 2.25 mL of  $\text{SOCl}_2$ , and 4.7 mL of 2-propanol. Distillation parameters were 1.4 Torr, pot temperature rose to  $140^\circ\text{C}$  and fore-run was collected from  $70 - 85^\circ\text{C}$ , leaving a residue that was pure ester.