Chemistry 415
Advanced Synthesis Laboratory
Spring 2017
Room 236, Chemistry

Instructors

Prof. Mitch Smith, Rm 406, 353-1071, smithmil@msu.edu
Please contact Prof. Smith with any general questions related to the class.

Dr. Chrysoula Vasileiou, Rm 538B, 353-0506, vassilio@msu.edu
Lab Coordinator. Please contact Dr. Vasileiou with any questions regarding the labs.

Teaching Assistants:
Sara Adelman (adelman7@chemistry.msu.edu)
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Class Website

http://www2.chemistry.msu.edu/courses/cem415/index2011CEM415.html
Any class announcements and copies of any given class notes and module notes, as well as other useful links, will be found on this website.

Class Description

CEM415 is a capstone course that focuses on advanced synthetic organic and inorganic chemistry. During this class you are expected to work in pairs to complete the synthesis of a variety or organic and inorganic compounds. In addition, all products and their synthetic intermediates must be fully characterized using advanced spectroscopic methods that include NMR, electronic absorption and emission spectroscopy and FT-IR. Student credit hours for the course are allocated entirely to laboratory time.

Course Schedule

Three sections of this course will be taught this semester:

Section 1: Tue, Thu 8:00 – 11:50 am	TA: Yu-Ling
Section 2: Mon, Wed 12:40 – 4:30 pm	TA: Ryan
Section 3: Tue, Thu 12:40 – 4:30 pm	TA: Sara

Office Hours

Office hours with the instructors or the TAs can be set up by email or during class periods.

Honors Options

If you wish to receive credit for an Honors Option, you must email Prof. Smith during the first two weeks of class to discuss the assignment.

Modules

During the semester you will complete 7 modules (see List of Modules below). Some of the modules require only one lab period but most of them require multiple lab periods. A description of each module will be available to you (either by email or through the web page) ahead of time so you get enough time to prepare for the lab. Proper lab preparation includes reading through the experiment, writing down the prelab experimental details in your notebook (see below) and familiarize yourself with the chemistry related to the module.

Notebooks

You will be required to purchase a laboratory notebook with duplicate pages. All notes related to the laboratory should be recorded in your laboratory notebook. This includes the prelab, all experimental details, (e.g., volumes used, amounts weighted out, etc.) drawings or photographs of experimental setups, and all observations must be recorded while experiments are performed. An article describing how to keep a proper notebook and an example of an actual lab book page are attached at the end of this syllabus. **Although you are completing the experiments in pairs, each of you need to keep your own lab notebook.**

The TAs will grade prelabs within 15 minutes of the beginning of class. You will not receive credit for the prelab if you arrive after this period. If your prelab is incomplete, you will not be permitted to perform the laboratory. **If you show up unexcused more than 30 minutes late, you may not be allowed to start the lab**.

If you plan to do experiments in two different modules, prepare prelabs for each on separate notebook pages. When each module is complete, remove the related pages from your lab notebook, attach copies of all relevant spectra you have recorded, and give them to your TA along with your module report.
At the end of each module, you must give your products (in appropriately labeled vials) to your TA.

Module Reports

After each module is completed and all the appropriate spectra of your compounds have been recorded and analyzed, you will have to write an official module report to describe your results and discuss the chemistry behind each module. Your report should be written according to the given template (See attached template) and should contain:

i) Your notebook pages;
ii) A write up of your experimental procedure;
iii) Copies of all the recorded and analyzed spectra (you will need to completely analyze your spectra, i.e. assign the peaks and/or correlate them to your structures);
iv) Discussion of your observations and results;
v) Complete answers to the questions at the end of each modules.

The reports must be typed and should look professional. Any structures and/or schemes included should be drawn using Chemdraw or a similar computer program. 50% of your overall grade is based on the module reports.

Although you are completing the experiments in pairs, each of you need to submit your own module report.

Due Dates: Reports must be submitted to your TA a week after each module is completed. 25 points will be automatically deducted for each period that a report is late.

Policy Regarding Academic Dishonesty

Academic dishonesty of any kind will not be tolerated in this course. Please see the following website for information regarding Michigan State University's policy on academic dishonesty:

https://www.msu.edu/~ombud/academic-integrity/index.html

Supplemental Texts

- *Inorganic Chemistry*, Gary L. Miessler, Donald A. Tarr) Prentice Hall: Englewood Cliffs, NJ; 1991 (QD151.2 .M54 1991). This is a good text for undergraduate inorganic chemistry.
- Online E-textbook "Introduction to Organic Chemistry" by Prof. William Reusch. You can also use your current text from CEM 351 and 352.
- *Physical Methods*, 2nd ed., Russell S. Drago (RSD), Saunders: Fort Worth; 1992 (QD 453.2.D7). This book is particularly useful for the spectroscopic aspects of the course.

Attendance Policy

Attendance is mandatory. *If you will be absent for observance of a religious holiday, participation in a field trip, rehearsal, or performance, or an athletic competition, you must notify your instructor in advance and schedule to make up the missed period during another section of the course within one week of the absence.*

This is a relatively open lab since after some time into the semester different people will be at different stages of the same or even different modules, depending on everybody's progress. That means that you have to come to the lab prepared and have an exact plan for the lab period. The TAs are there to help you but you will need to organize your steps and manage your time for each module.

Considering that during the semester you might have to repeat several steps of some modules, repeated absences might lead to incomplete experiments which in turn will directly reflect on your final grade (loss of points).

Safety

Lab safety is largely a matter of using good common sense. Some experiments will require the use of vacuum lines and compressed gasses in addition to the organic solvents and chemicals typical of a synthetic lab. **Approved eye protection must be worn at all times. You will be denied admission to the lab if you do not have goggles**. **Closed toe shoes must be worn in the laboratory.** In addition, gloves and a lab coat are useful for protecting your hands and clothes. We will provide special instructions during lectures to ensure safe use of specialized equipment. **If you have any questions about how to perform an experiment safely, ask you lab instructor first.** (See attached Lab Safety rules for more details)

Laboratory Equipment

In pairs, you will receive a drawer containing supplies for the course. During check in you must notify the TAs of any missing supplies and he/she will assist you in replacing them at no cost.

At the end of the course, you must check out with your TA. You will be responsible for any replacement costs for any missing items.

Glassware must be clean when returned at the checkout. Students who fail to do so will lose 100 pts.

Grading

- Each module is worth 100 pts total, that will be weighted as follows:

- Laboratory Notebooks	20 pts
- Laboratory Performance (Technique, Completion of Experiments, Safety, Housekeeping)	10 pts
- Module Reports	70 pts

- 1st NMR spectrum and structure elucidation is worth 20 pts.

- Your overall grade for the class will be out of 720 pts, and will follow the scale below:

Total Points	Percent	Grade	Total Points	Percent	Grade
648	90	*4.0*	360	50	*2.0*
576	80	*3.5*	324	45	*1.5*
504	70	*3.0*	288	40	*1.0*
432	60	*2.5*	<288	<40	*0.0*

Tentative List of Modules

Module 1: Silicon Polymers: Preparations of Bouncing Putty (Silly Putty)

Module 2: Nanochemistry: Synthesis and Properties of Cadmium Selenide Quantum Dot Nanoparticles

Module 3: Grubbs' Inspired Ruthenium Catalysts for Olefin Metathesis, Nobel Prize Winning Chemistry

Module 4: Synthesis of *cis*- and *trans*- Diaminedichloroplatinum(II)

Module 5: Cobaloximes: Models of Vitamin B_{12}A Demonstration of "Umpolung" in the Reactivity of an Organometallic Complex

Module 6: Methyl Migration to Coordinated CO

Module 7: Iridium Catalyzed Functionalization of C-H Bonds

If anything changes regarding these modules, i.e. order that they need to be performed or anything else, you will be notified by email ahead of time.

Throughout the semester, make sure you pay attention to emails with the subject: CEM415

ACS Diagnostic of Undergraduate Chemistry Knowledge (DUCK) Test

The Department of Chemistry mandates for all the Chemistry BS majors to take a test in order to assess chemical learning and understanding. This test, known as the DUCK (Diagnostic of Undergraduate Chemistry Knowledge) test, is one of the American Chemical Society standard tests, designed for the end of an undergraduate curriculum. As the capstone for the Chemistry BS program, CEM 415 was chosen for administration of the ACS-DUCK since it requires students to use what they have learned in previous courses. The ACS-DUCK test is just another way to look at how students use what they have learned previously.

American Chemical Society
Division of Chemical Education Examinations Institute

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Diagnostic of Undergraduate Chemistry Knowledge - 2013

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Stock Code	Title	Questions	Time
DUCK13	Diagnostic of Undergraduate Chemistry Knowledge - 2013 - Exam designed for the end of an undergraduate curriculum.	60	120

The Diagnostic of Undergraduate Chemistry Knowledge (DUCK) exam is designed to be taken at or near the end of a four-year undergraduate curriculum. All items on the exam are part of scenarios that require knowledge from more than one traditional area of chemistry, so students are less likely to segment their knowledge into such areas and be successful on this exam.

During the DUCK test students will demonstrate **chemical understanding** through the:

a. Use of appropriate models and representations to describe, explain, and predict the **structure and properties** (chemical and physical) of molecular systems. In applying models to explain and predict chemical reactivity and physical behavior, students will make explicit connections between structure at the atomic and molecular level and macroscopic properties observed and studied in laboratory experiments.
b. Application of quantitative reasoning, concepts from physics, and mathematics through differential equations to explain and evaluate the roles of **energy, entropy, equilibrium, and dynamics** in determining the outcomes of chemical and physical processes.

As part of the CEM415 class, we will administer the DUCK test some time in April (the exact day and time will be announced later on in the semester).

<u>Remember: Taking this test IS MANDATORY!</u> If you do not take the test, 50 points will be deducted from your overall points earned for the class. If you do attend and take the test, you can earn up to 50 bonus points for the class, depending on your performance in the test. The scale for the bonus points is as follows:
> 80% (48/60 correct answers): 50 bonus points
70–80% (42-47 correct answers): 40 bonus points
60–70% (36-41 correct answers): 30 bonus points
50–60% (30-35 correct answers): 20 bonus points
<50% (29 correct answers or lower): 10 bonus points

If you have any questions about the ACS-DUCK test, please contact the instructors for the class.

SAFETY REGULATIONS

1. DRESS CODE

Firm footwear is required
(NO sandals, NO open-toed shoes)

Long pants that cover the entire leg must be worn at all times (NO shorts, NO skirts)

Safety Goggles must
ALWAYS be worn in the lab

The dress code will be strictly enforced!

2. SAFETY EQUIPMENT

Every student MUST do all they can to prevent accidents in their own work and they must be prepared for accidents by knowing in advance what emergency aids are available.

The laboratory is equipped with several type of safety equipment and it is essential that you become familiar with the location and the operation of these tools.

- ***a.*** Emergency Shower: There is an emergency shower located on the hallway. It is for use when corrosive liquids have spilled over large areas of clothes and skin, or when clothing is on fire.

- ***b.*** Eye Wash Stations: The laboratory is equipped with eye wash stations. These stations dispense water and provide thorough irrigation of the eyes and face in the event a person is splashed with an irritating chemical. The contaminated body part should be rinsed for a minimum of 15 minutes.

- ***c.*** Fire Extinguisher: The fire extinguisher is located outside the laboratory. Know its location and how to operate it. It is very effective for fires involving organic liquids and electrical fires. If a fire extinguisher is used it must be given to the laboratory coordinator for recharging. Small fires in test tubes, beakers etc can usually be smothered by covering with a watch glass.

In any case, REPORT any accident to your instructor immediately

3. ***Absolutely NO EATING or DRINKING is permitted in the lab.***

4. ***Waste Disposal***

Please place the waste materials in the appropriate containers. If you are unsure, make sure you ASK your instructor .

For this lab you should expect to have both Inorganic and Organic waste, placed separately in different containers inside the last fumehood.

Broken glassware belongs in the BROKEN GLASS bucket

Sharp objects (syringes, needles, razor blades) belong in the SHARPS container.

5. ***Laboratory Rules***

a. NO student may work in the laboratory unless an instructor is present.
b. NO student may perform an unauthorized experiment.
c. NEVER leave an experiment in progress unattended.
d. Any chemical that produces toxic vapors MUST be used in a fumehood.
e. Wipe-up spilled chemicals and bottle “rings” immediately.
f. NEVER handle or poor flammable liquids near an open flame.
g. REPORT any accident to the instructor immediately.
h. BEWARE if burns from forgotten still-lit burners and hot glassware.
i. Keep ALL sinks clean.
j. Before you leave the lab, MAKE SURE the hood, work area and sink are clean and tidy.
k. OVERALL, if you are unsure about any directions, ASK your instructor.
l. Finally, NEVER HURRY when performing experiments. Safety always has the highest priority.

Report Template

(an interactive .docx template will be posted on the web and also e-mailed to you the first week of class)

All module reports should follow this template.

Experiment Name | 2014

Your Name

Section X

Experimental Methods

Observations and Results

Questions

Signature

X______________________________

Keeping a Laboratory Notebook

Anne Eisenberg
Department of Humanities, Polytechnic Institute of New York, Brooklyn, NY 11201

Le Monnier, the eighteenth-century astronomer, observed Uranus twelve times, but decided that it was a fixed star, not a planet. The great discovery fell to Herschel, who identified Uranus correctly in 1781. Historians have since decided Le Monnier's mistake was due at least in part to his habit of writing measurements on scraps of paper—including a paper bag originally containing hair powder (*1*).

The keeping of good records is essential in a laboratory: a second example is provided by the case of Daniel Drawbaugh v. Alexander Graham Bell. Bell filed a patent application for the telephone in 1875; Drawbaugh sued, claiming the invention for his own and producing at court witnesses who testified he had discussed a crude telephone with them. But this personal testimony did not convince the Supreme Court, which rejected Drawbaugh's claims largely on the basis of his inability to produce a single properly dated piece of paper describing the invention (*2*).

A third, contemporary instance of the importance of laboratory notebooks is provided by the case of Gordon Gould, who as a young physicist filed an application for a basic laser patent in 1959. Gould failed to get the patent, which was awarded instead in 1960 to Charles Townes and Arthur Schawlow. Gould went to court, claiming he was the true inventor. His challenge was based in part on his research notebook which showed, among other items, a sketch, a statement of the main idea, and a derivation of the acronym LASER—Light Amplification by Stimulated Emission of Radiation (*3*).

In October 1977, after a series of litigated oppositions, Gould was granted a patent for optically pumped laser amplifiers. The world market has been estimated at between 100 million and 200 million dollars.

As these examples suggest, well-kept notebooks are valuable documents. They provide complete, accurate records of ongoing work. In the event of litigation or contests for patent rights, they are submitted as evidence. They serve the important role of corroboration should the researcher or inventor have to prove origin or substantiate statements and conclusions. They are valuable documents to validate a company's claims to funds spent for research, particularly in support of tax deductions.

The uses of laboratory notebooks are not limited to legal issues. They are vehicles for organizing and focusing the thinking of the writer, as well as being receptacles for detailed procedural information that might not be available in highly compressed journal articles. Finally, they may serve not only the researcher or inventor but also the public. If properly maintained, they are a record of success and failure, a safeguard against error and carelessness in such important areas as the testing of drugs and chemicals.

General Rules for Notebook Format

The notebook should reflect a daily record of work. It is best to make entries explaining the results expected from each stage of the investigation. Entries should be in chronological order, and so thorough and comprehensive that they can be understood by the corroborating witnesses. Each page should be signed by the inventor or researcher below the last entry, and by one or preferably two witnesses. Full names should be used and the signatures dated.

Of course, each company has its own style of notebooks, its own way of keeping records. Any new employee may need to alter habits to conform to the practices of a particular laboratory. However, there are general guidelines that one can follow. These are as follows:

1. Use a *bound* notebook, if possible.
2. If a loose leaf notebook is preferred, the pages should be numbered in advance and a record kept of the numbered pages given to each laboratory worker. The point is to rebut any inference that a worker may have inserted a page at a later date (*4*).
3. Do not remove any pages, or any part of a page. Pages missing from a notebook will seriously weaken a case in the Patent Office, or in cases that go to court for litigation.
4. Record all entries directly and legibly in solvent-resistant black ink.
5. Define the problem or objective concisely. Make entries consistently as the work is performed.
6. All original work, including simple arithmetical calculations, should be performed in the notebook. If you make a mistake, recalculate—**do not erase.**
7. Never use correction fluid or paste-overs of any kind. If you decide to correct an error, place a single line through the mistake, sign and date the correction, and give a reason for the error. Take care the underlying type can still be read. However, even the practice of drawing a line through numbers entered in error is discouraged in many companies. Instead, workers are asked simply to make a new entry, correcting the error when possible.
8. Do not leave blank spaces on any page. Instead, either draw diagonal lines or a cross through any portion of the page you don't use.
9. Date and sign what you have written on the day of entry. In addition, have each notebook page read, signed, and dated by a qualified witness—someone who is not directly involved in the work performed, but who understands the purpose of the experiment and the results obtained.
10. Extra materials such as graphs and charts should be inserted, signed, and witnessed in the same way as other entries.
11. All apparatus should be identified. Schematic sketches should be included.
12. Head each entry with a title. If you are continuing on the next page, say so at the bottom of the page before you continue.

These rules have received a popular formulation as, "Record it. Date it. Sign it. Have it witnessed." They have also been stated formally in many documents, among them the important "Good Laboratory Practice" (GLP) regulations of the Food and Drug Administration (*5*).

> All data generated during the conduct of a nonclinical laboratory study, except those that are generated by direct computer output, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change.

Have It Witnessed

Many questions arise regarding the provision, "Have it witnessed." To many people, it is not clear that the inventor or co-inventor cannot under any circumstances serve as witnesses. Nor can a nearby office worker, notary public, or technician, solely because they happen to be conveniently at hand at the moment one needs a witness. Instead, witnesses must be those with the technical competence to understand the details of the subject matter. Further, they should be able to read and understand the entries without receiving any oral instructions from the inventor. Finally, the witness must be an adult, preferably over 21, and preferably one who has actually witnessed the work performed.

The witnesses should sign their full names below a statement to the following effect: Disclosed to and understood by me this ___day of _____, 19___.

The role of the witness may be crucial in cases of Interference Proceedings. These proceedings occur when two applications are filed in the United States Patent and Trademark Office disclosing similar inventions, and the Patent and Trademark Office acts to determine which of the inventors is entitled to the patent. There have been instances in Interference Proceedings where the inventor's own testimony, supported by thorough sets of notebooks unquestionably prepared and dated, did not alone serve to establish date of conception and reduction to practice of the invention. In these cases, the witnesses' backgrounds became crucial. It was necessary for the witnesses to have understood all the entries; *merely witnessing them on the date did not in and of itself suffice* in a contest where the other claimant also had properly substantiated testimony. "The point is that a witness is called upon to substantiate the facts and nature of the work performed at the date that the person signed as a witness, and not merely the fact that an entry was made by the inventor on that date" (*6*).

Conception and Due Diligence

Patent law places emphasis on "date of conception," "due diligence," and "reduction to practice." In terms of a notebook, this means the following:

1. Get the idea into the notebook as quickly as possible. If it is written down after some delay, relate the date and place of conception of the idea and the circumstances that stimulated the idea.

2. In this initial record, stress the newness, why the idea is novel. If you make notes on scrap paper at home or at work, the original of the notes should be preserved, but the contents transcribed into the permanent notebook as soon as possible. The dates are important in two ways: they may help refresh a recollection, and they may help substantiate a claim in the event of a subsequent dispute.

3. Continue to record every instance when you return to the idea so there is ample evidence of "due diligence," of not setting aside the idea.

Notebooks are particularly important in establishing due diligence. New York patent attorney Philip Furgang relates cases where an inventor who is first to have the idea and first to reduce it to practice still loses the patent for lack of properly signed, dated, and witnessed records demonstrating due diligence. Thus, inventor Smith may have the idea first, enter it properly in her notebook, and then set about reducing it to practice for two years. However, she is busy during these two years and keeps the notebook poorly: not a single entry after the one establishing the date of conception is properly witnessed. Then a second person, inventor Jones, has the same idea. He reduces it to practice and files his patent just before Smith. Between contesting inventors, the burden of providing who is entitled to the patent falls on the inventor *last* to file. Thus, in this instance the burden was on Smith to prove her right to the patent. She went to court, and there was no question of witnesses who could testify to origin; clearly Smith was first. Unfortunately, however, she could not prove due diligence because she did not have witnessed, signed notebook entries for the period in question, and thus Jones won the interference (*7*).

In a University Setting

If the notebook is kept with an eye to the preparation of a scientific paper, there should be statements on the purpose of each experiment and a summary of conclusions. Under no circumstances should the researcher succumb to the desire to keep notes on the backs of memos or other odd bits of paper.

Usually the first 10 or 20 pages of the research notebook is left blank, with the formal log commencing afterwards. These blank pages are used for a table of contents maintained each day or after a series of similar experiments is completed. The table of contents is a simple step that saves a great deal of time later when the search begins for a piece of information. In some research laboratories, the director and staff prepare an annual report based on the notebooks, with each person responsible for abstracting different major headings from the notebooks.

The notebook is not the spot for polished writing: data should be entered in primary form. In one laboratory, for instance, a worker had the habit of performing all the calculations separately and then entering only results. This made it difficult to detect error that was the result of digits transposed during calculation. Instead, be as detailed as possible so that someone else can duplicate what you've done by reading your account. This means putting in the contradictions, the unpromising experiments, the failures. If there is a conflict, enter a description of it rather than omitting it. The negative results may be important for another worker at another time.

Literature Cited

(1) Wilson, Jr., E. Bright, "An Introduction to Scientific Research," McGraw-Hill Inc., New York, **1952**.

(2) Furgang, Philip, "Memorandum, Rules for Keeping Invention Records," 437 Madison Avenue, New York, NY.

(3) *Laser Focus*, Vol. 13, No. 12, p. 14; *New York Times*, **2,** 5 (17 July 1979); **34,** 1 (21 July 1979).

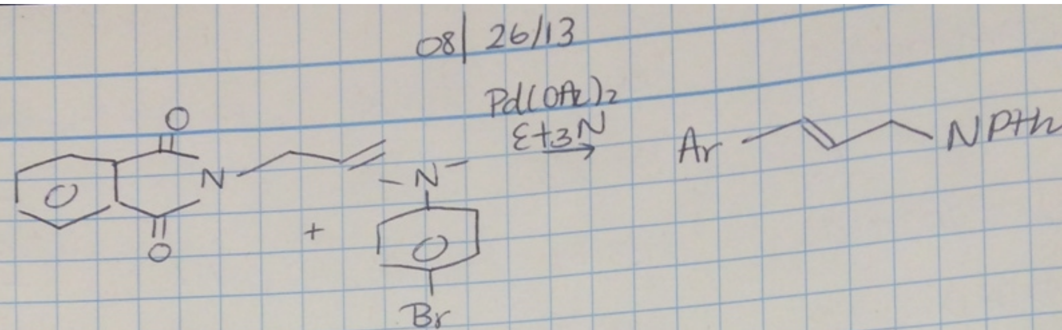
(4) 1976 Patent Institute. "A Continuing Seminar of New Developments in Law and Practice," College of Business Administration, Fairleigh Dickinson University, Madison, NJ.

(5) "Good Laboratory Practice Regulations, Nonclinical Laboratory Studies," *Federal Register*, Vol. 43, No. 247, 22 December 1979, 58.185.

(6) 1976 Patent Institute, p. 131.

(7) Furgang, p. 3.

08/26/13



	compound	MW	equiv	mmol	wt/vol	d
	4-bromo-N,N-dimethylaniline	200.08	1.0	1.0	200.08 mg	–
	N-allylphthalimide (es.02.156.ac)	187.19	1.03	1.03	193mg	–
in12B	$Pd(OAc)_2$	224.5	0.01	0.01	2.5mg	–
S20B	tri-o-tolyl phosphine	304.37	0.02	0.02	6 mg	–
	Et_3N	101.19	2.0	2.0	1mL	0.726

start time 9:45 pm

The aryl bromide, N-allyl phathalimide were placed in a RBF. This was then flushed with nitrogen. Anhydrous triethylamine was then added, followed by palladium acetate and tri-o-tolyl phosphine. The mixture was heated to reflux.

8/27/13 1:10pm Remove from heat. 20 mL DCM and DI water were added. The mixture was then extracted with 20 mL x3 DCM. The combined organics were washed with water and then brine. Take crude NMR.

Ref: Methods of reducing virulence in bacteria