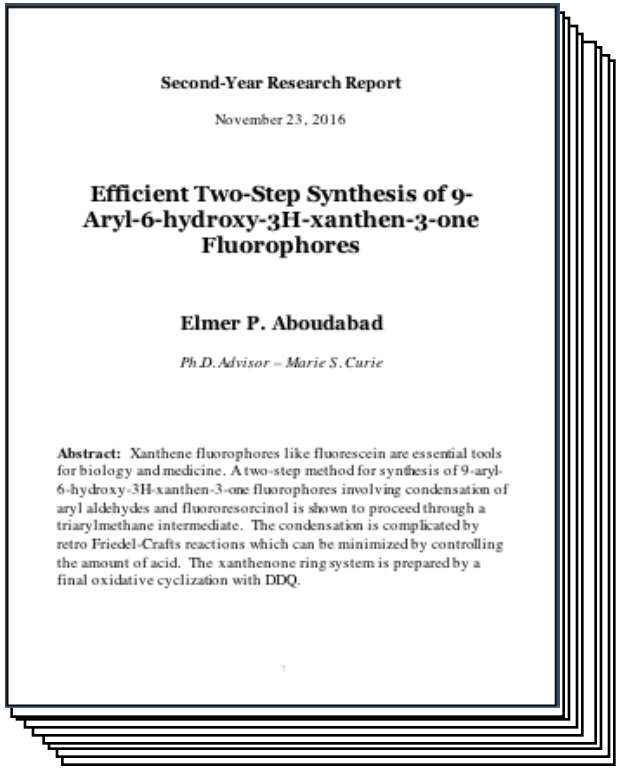
Written Research Reports

The Second-Year Report



Second-Year Research Report

November 23, 2016

Efficient Two-Step Synthesis of 9-Aryl-6-hydroxy-3H-xanthen-3-one Fluorophores

Elmer P. Aboudabad

Ph.D. Advisor – Marie S. Curie

Abstract: Xanthene fluorophores like fluorescein are essential tools for biology and medicine. A two-step method for synthesis of 9-aryl-6-hydroxy-3H-xanthen-3-one fluorophores involving condensation of aryl aldehydes and fluororesorcinol is shown to proceed through a triarylmethane intermediate. The condensation is complicated by retro Friedel-Crafts reactions which can be minimized by controlling the amount of acid. The xanthenone ring system is prepared by a final oxidative cyclization with DDQ.

Due: Wednesday, noon, Nov. 27, 2019
(Just before Thanksgiving break)

Six Basic Requirements for a Ph.D. in Chemistry

http://www.chem.uci.edu/

1. Completion of a minimum of seven approved courses with maintenance of an average grade of B or better.
2. **Completion of a second-year Written Examination.**
3. Completion of an Oral Examination for *Advancement to Candidacy*.
4. Completion of the teaching requirement (four quarters).
5. Completion of six quarters in residence at UCI.
6. Submission of an acceptable doctoral dissertation.

Year 1
- Fall
- Winter
- Spring

} **Courses**

- Summer

Year 2
- Fall ⬅ **Y2R**
- Winter
- Spring ⬅ **Orals**
- Summer

Years 3-

GOAL OF THE 2ND-YEAR WRITTEN EXAMINATION

https://www.chem.uci.edu/graduate/current-students

PREPARE PUBLICATION-READY MANUSCRIPTS

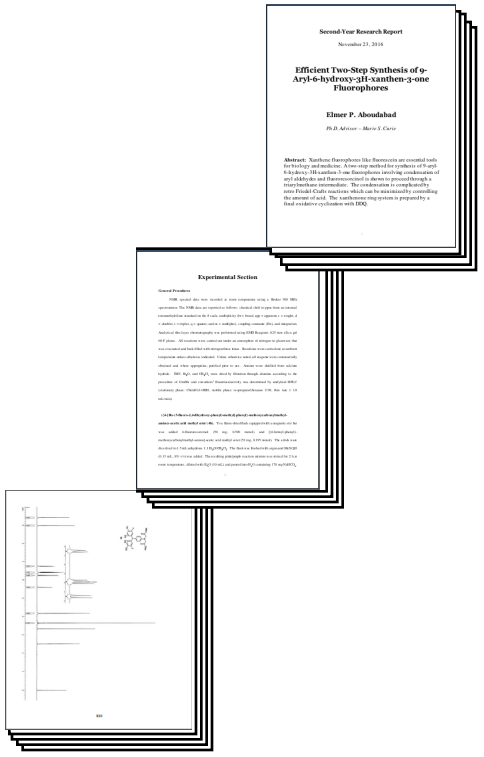
Organization of the Research Report

Second-Year Report and Orals

Generally, you will compile:

1. Descriptive Title + Abstract
2. **Introduction**
3. **a. Results** and **b. Discussion** (combined or separate)
4. **Conclusions and Future Work**
5. Scholarly References
6. Experimental Section
7. Supporting Information

≤10 pages



What are we looking for in a Second-Year Report?

1. Satisfactory **research progress**
   - Fully characterized products
   - Yields for many, many reactions
   - Purified proteins or peptides
   - Developed and validated new assays

2. A written document that **communicates effectively**

Scholarly Background

- Why is the project important to society?
- What was done in the past?
- What is the gap in technology/knowledge that needs to be filled?

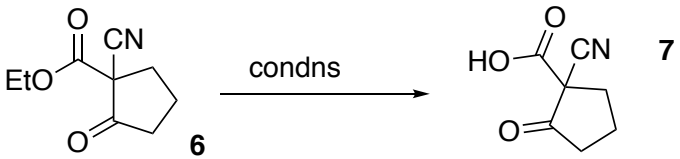
Research

- What obstacles did you overcome?
- If you worked with someone else, which accomplishments are yours?
- Future goals

About Research Progress on the Second-Year Report

- I can not overemphasize the importance of making **significant research progress**.
- A well written report **identifies challenges** you faced - unstable compounds, poor protein expression, low transformation efficiencies, difficulties in purification, assay (ir-reproducibility).
- **Faculty understand the difference between lack of effort and challenging projects.**

this doesn't demonstrate thinking



conditions	yield 7
1 M HCl, 100 °C	0%
6 M HCl, 100 °C	0%
0.1 M H_2SO_4, 100 °C	0%
0.05 eq. p-TsOH, 100 °C	0%
1 M KOH/EtOH, 25 °C	0%
C. ligrea lipase, phosphate buffer, 25 °C	0% (S.M.)
0.1 M acetic acid, H_2O/dioxane, 25 °C	0% (S.M.)
0.1 M acetic acid, H_2O/dioxane, 100 °C	0%

Explain WHY it didn't work:

- Identify the side-products.
- Look up reactivity of similar functional groups.

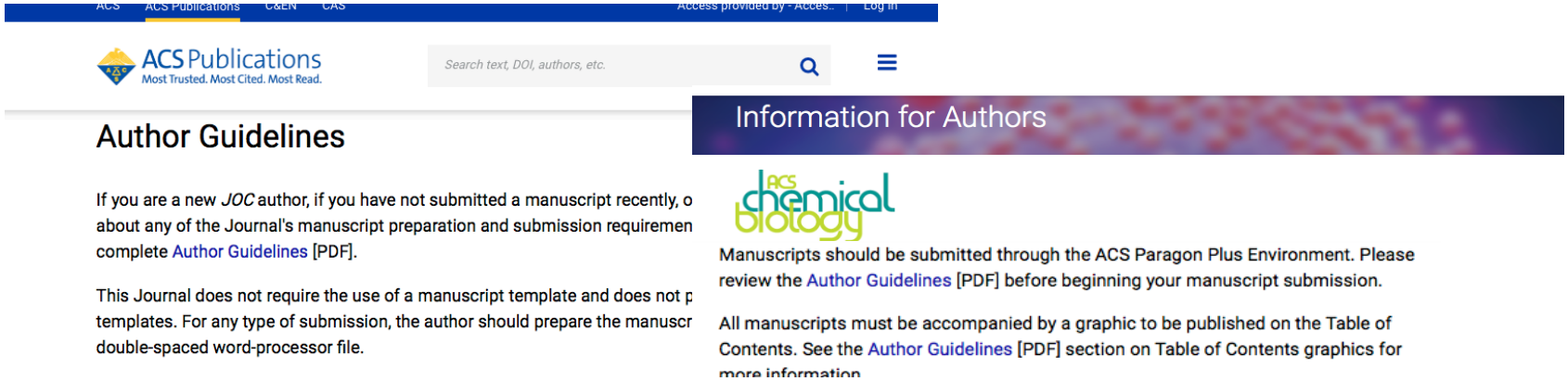
Experimental and Characterization Data

1. **Follow the standards of the community**

See: "Author Guidelines."

- *The Journal of Organic Chemistry*
- *ACS Chemical Biology*

http://pubsapp.acs.org/paragonplus/submission/joceah/joceah_authguide.pdf?



2. **Follow the standards of your research group**

- See *perfected* research reports from senior students.
- See published papers from your group
- See dissertations from your group

Experimental and Characterization Data

I. WHAT YOU GOT (e.g., ... 36.2 mg of diene **43** (3:1 *E*/*Z*) as a yellowish solid.)

A. Yield. Significant figures should match measured reagents.

1. Isolated mass
2. Spectroscopic/chromatographic peak ratios versus an internal standard

B. Stereoisomeric ratios

(e.g., (±)-2-hydroxybut-3-ene, 4:1 *E*/*Z*, 95:5 *syn/anti*, 74% ee)

C. Physical state (for solids, include a m.p.)

D. R_f and eluant system

II. EVIDENCE FOR IDENTITY AND PURITY (*J. Org. Chem.* Dec, 2018)

http://pubsapp.acs.org/paragonplus/submission/joceah/joceah_authguide.pdf?

A. Evidence for IDENTITY (chemical structure and stereochemistry)

1. ^{1}H NMR and ^{13}C NMR

http://pubsapp.acs.org/paragonplus/submission/acs_nmr_guidelines.pdf?

2. HRMS or Elemental Analysis to support molecular formula
3. IR absorptions of distinctive functional groups (C=O), O-H, sp C-H, et

Experimental and Characterization Data

II. EVIDENCE FOR IDENTITY AND PURITY (*J. Org. Chem.* Dec, 2018)

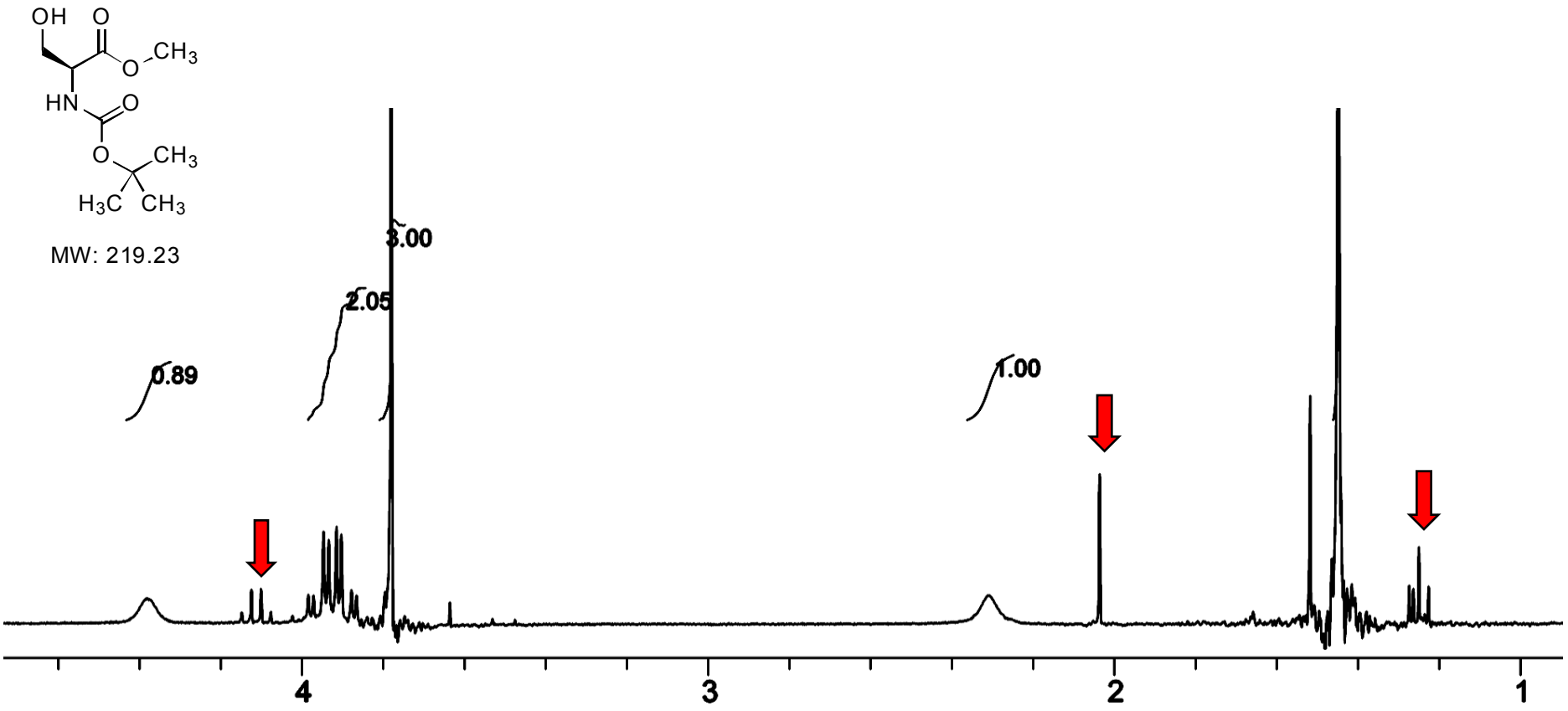
B. Degree of and Evidence of PURITY

The *Journal of Organic Chemistry* requires "that the purity level that has been attained be faithfully documented. When new or known synthesized compounds are the study materials for physical measurements or bioassays, a purity level of at least 95% needs to be documented."

1. **^{1}H NMR spectrum with all peaks integrated** (0-10 ppm)
2. **Combustion Analysis** (%C, %H, %N)
3. **Narrow melting point range** when matching known solids

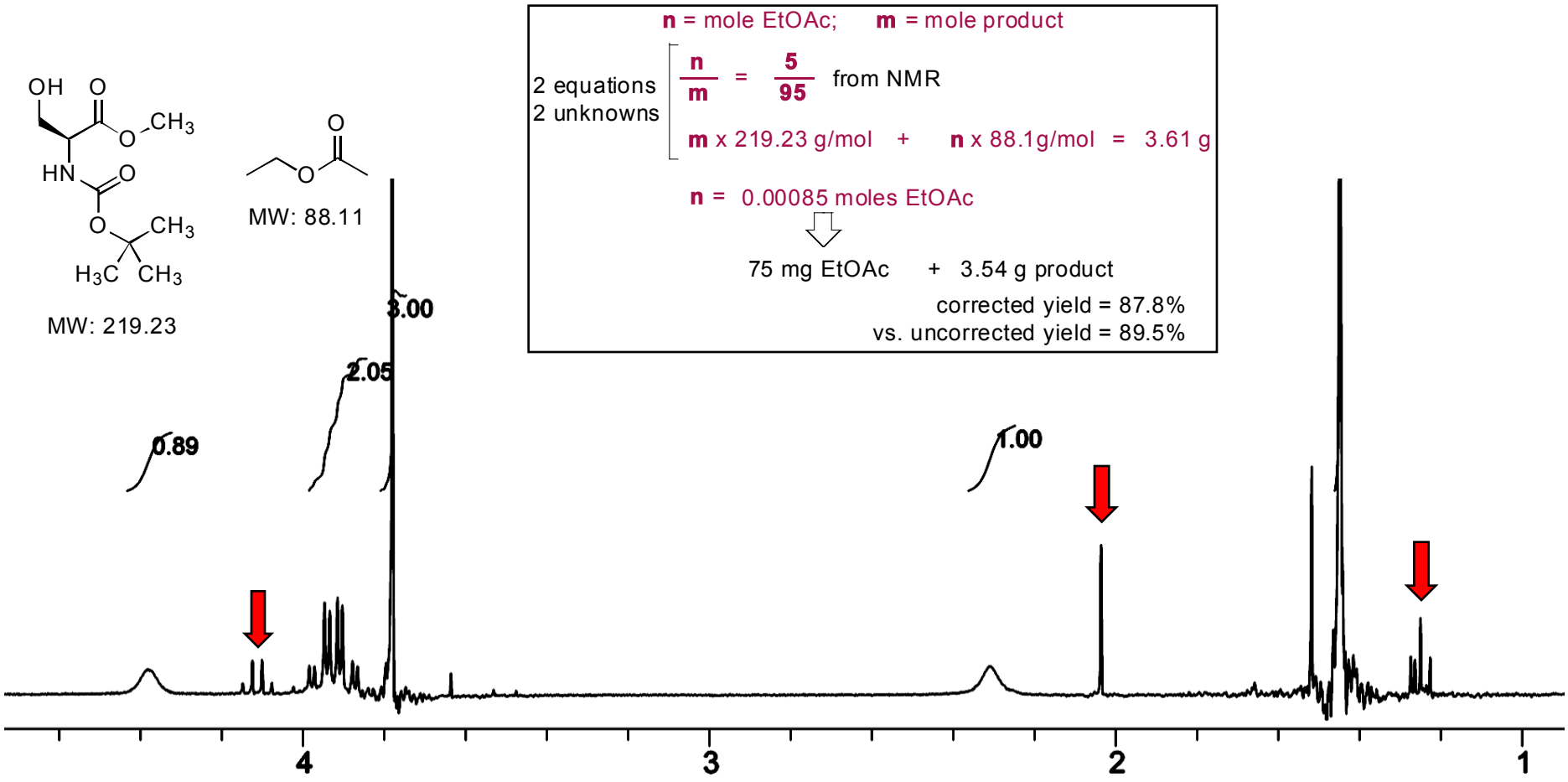
Selective Analysis of ^{1}H NMR Spectra?

20.24 mmol) in DCM (60 mL) was stand overnight. After the solvent removal, the residue was purified with gel column chromatograph (EtOAc/petrol ether, 1:5), and the compound **25** (3.61 g, 90%) was obtained as pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.45 (s, 9H), 2.31 (br, 1H), 3.79 (s, 3H), 3.85-4.00 (m, 2H), 4.39 (br, 1H), 5.45 (br, 1H).



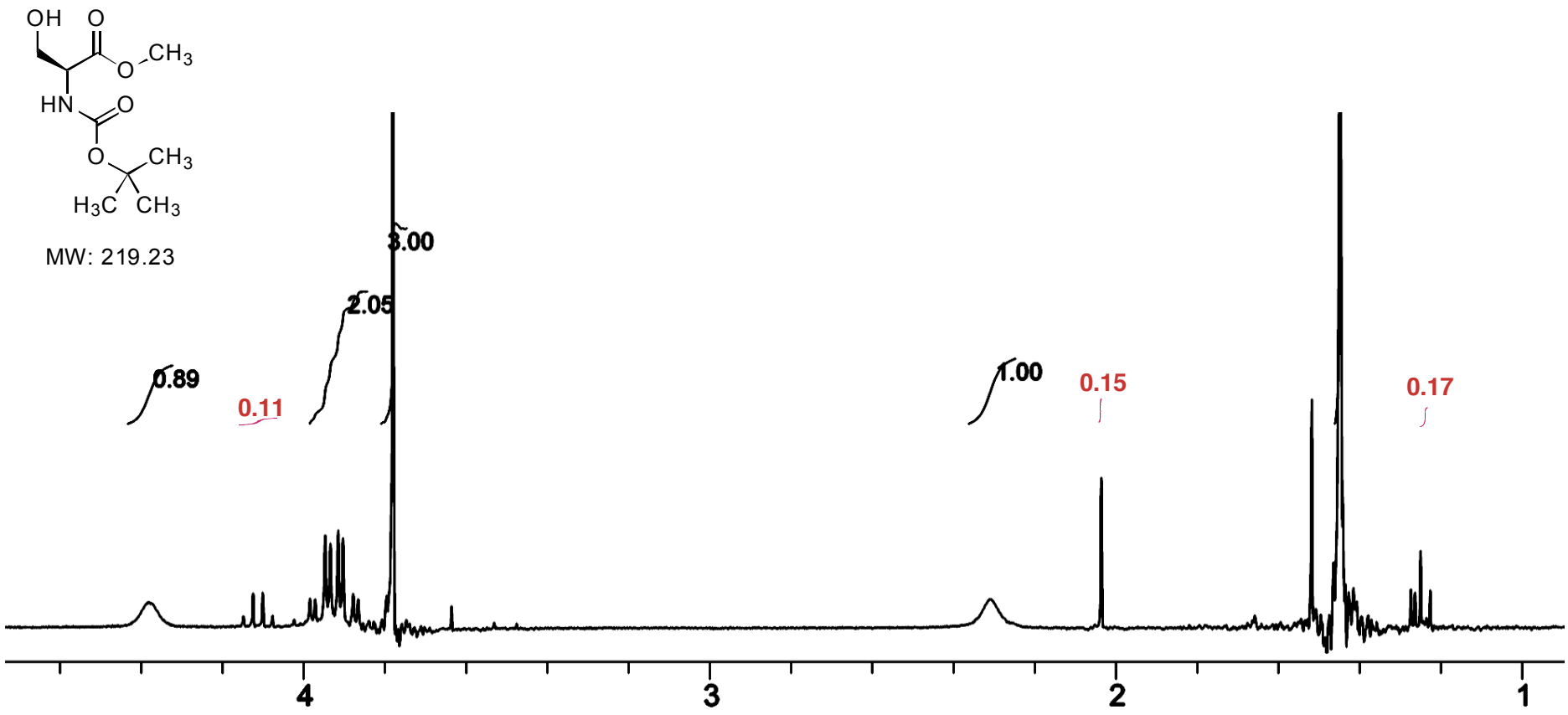
Algebra: Derive Wt% from NMR Mole Ratios

20.24 mmol) in DCM (60 mL) was stand overnight. After the solvent removal, the residue was purified with gel column chromatograph (EtOAc/petrol ether, 1:5), and the compound **25** (3.61 g, 90%) was obtained as pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.45 (s, 9H), 2.31 (br, 1H), 3.79 (s, 3H), 3.85-4.00 (m, 2H), 4.39 (br, 1H), 5.45 (br, 1H).



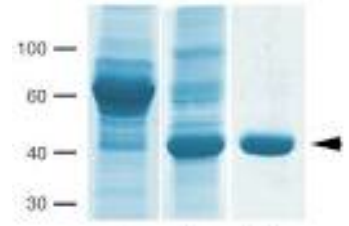
An Accurate Honest Description

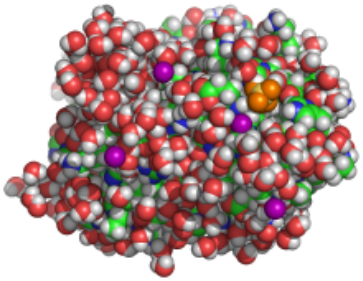
Alternative writeup: …After the solvent removal, the residue was purified with gel column chromatography (EtOAc/petrol ether, 1:5). After evaporation of solvent, compound **25** was obtained as a pale yellow oil (3.61 g) containing a small amount (5 mol%, 2.1 wt% by ^{1}H NMR) of ethyl acetate (88% yield of **25**).



Characterization of New Biological Substances
Identity and Homogeneity

- **Identity** = the sequence of an oligonucleotide, gene, or protein
- **Homogeneity** = usually means only one type of biooligomer
  Biologists rarely account for water content, buffer molecules, or ions. An enzyme might be considered "pure" even if contaminated with DNA, as long as they don't affect the biological activity.





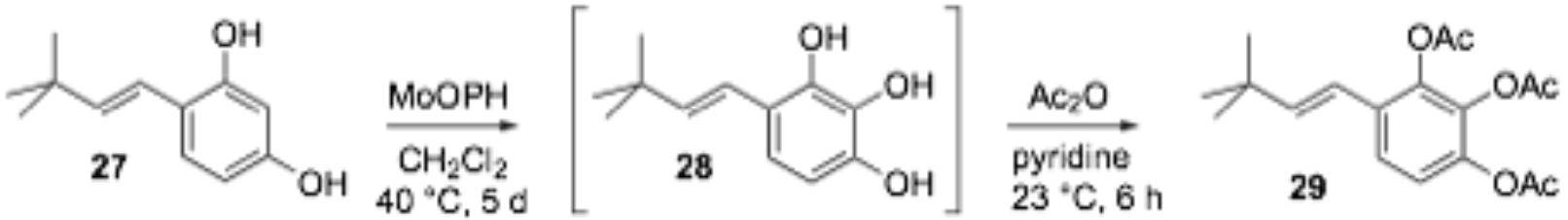
- ***ACS Chemical Biology***: "Provide evidence to firmly establish both the identity and the purity of new substances. The criteria vary according to substance categories but may include **electrophoretic**, **chromatographic**, **spectrometric,** spectroscopic, crystallographic, or other analytical methods. Supply **sequencing** or **functional data** for all biological constructs, such as fusion proteins, plasmids, etc."

Exceptions to Standard Characterization

Consult with your advisor in these situations.

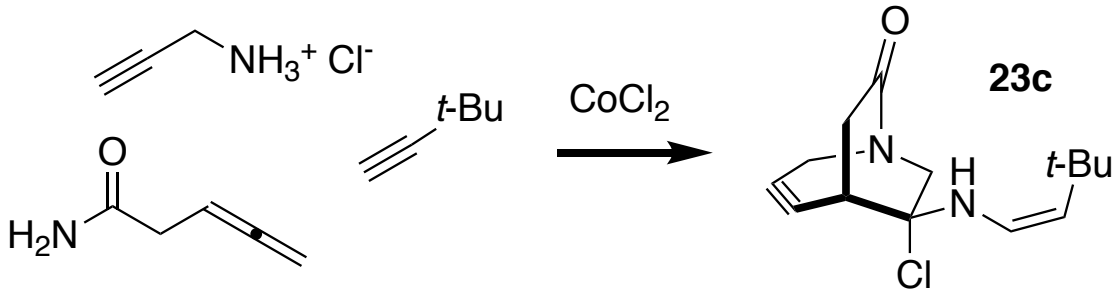
- **Sensitive (unstable) compounds**

  Explain their reactivity (thermal ring-opening, oxygen autoxidation, acid-sensitivity). Estimate the final level of purity and offer convincing evidence of the chemical structure. You can convert it to a stable, characterizable derivative.



- **Unexpected chemical structures**:

  Require more detailed characterization.

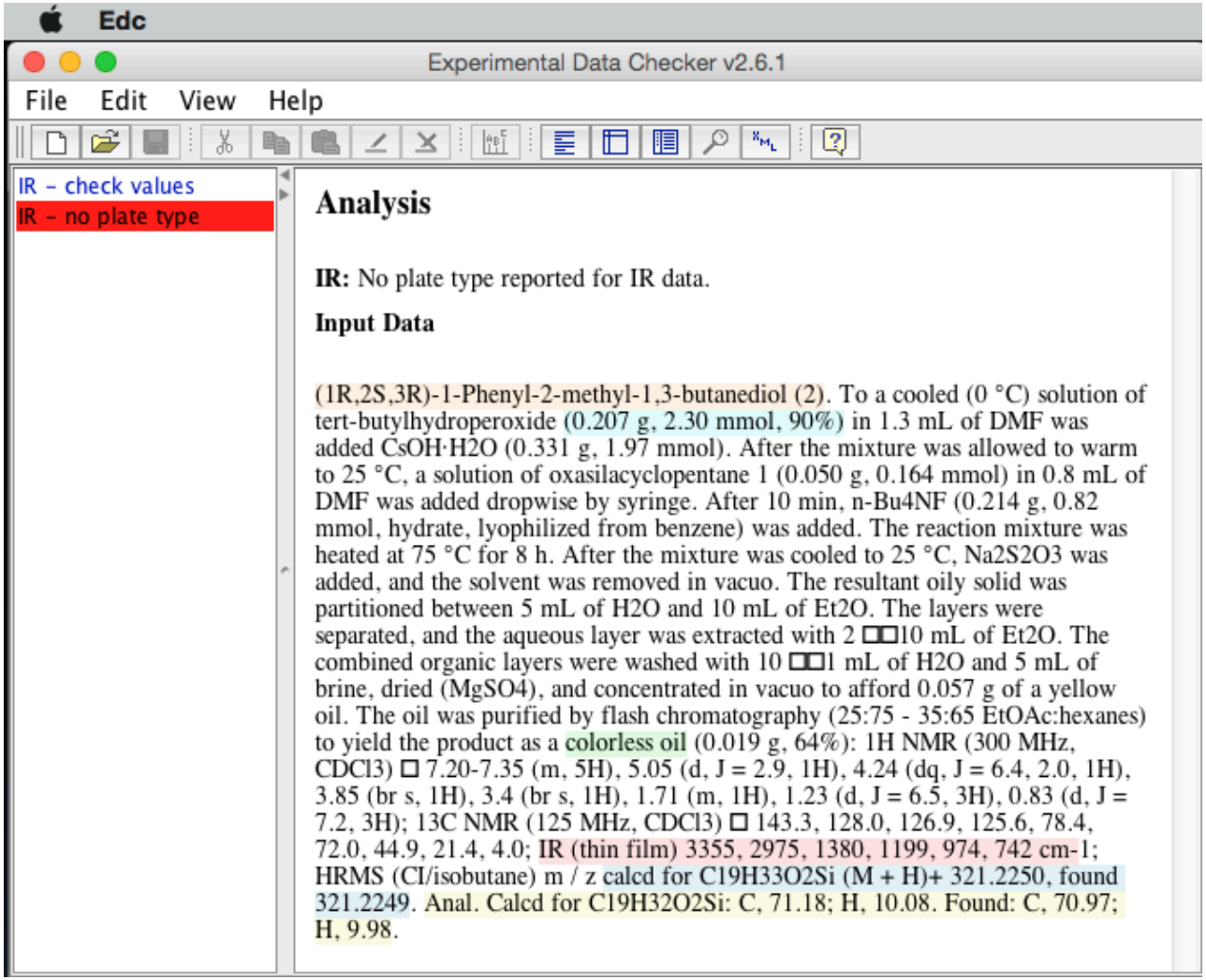


Evaluation Criteria for the Second-Year Research Report

Your report should be perfect.

- The spelling should be perfect.
- The grammar should be perfect.
- The references should be perfect with perfect formatting, perfect spelling, and perfect scholarship.
- The layout should be perfect.
  - Consistent fonts
  - Consistent structure drawing settings
  - Consistent orientation of chemical structures
- Drawings should appear professional
  - Key features should be clearly labeled
  - Easily readable font sizes should be chosen
- Writing or figures from other sources should be clearly referenced.

Java-Based Experimental Data Checker



OnLine Version at:
http://www-jmg.ch.cam.ac.uk/tools/magnus/checker.html

S. E. Adams, J. M. Goodman, R. J. Kidd, A. D. McNaught, P. Murray-Rust, F. R. Norton, J. A. Townsend and C. A. Waudby
Org. Biomol. Chem. 2004, **2**, 3067-3070.

Advice For Preparation

1. Read a perfected report and a from a senior student and look at some completed Ph.D. theses from your group.
2. Talk about the report with a senior lab member and your advisor
3. Get help. **Have senior students and your advisor read over it.**
4. Consult the UCI Department of Chemistry web page on Graduate Advising Information.

https://www.chem.uci.edu/Graduate-Advising

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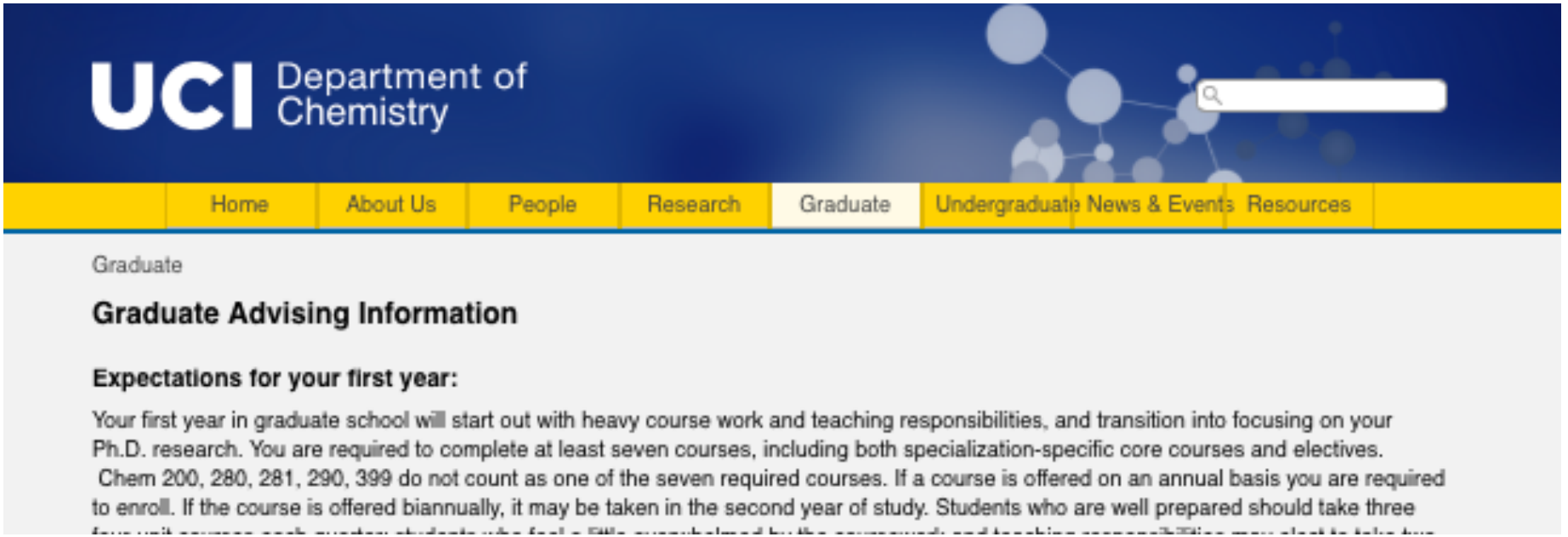

Blah, blah blah…

Advising Handouts by Research Area

Chemical Biology (Prof. David Van Vranken) and Organic Synthesis (Prof. Chris Vanderwal)

- UCI Organic/Inorganic/Chem Bio Pre-advising Handout
- 2nd-Year Research Report
- Advancement to Candidacy Examination (Orals)

posted down here

Inorganic Chemistry (Prof. Bill Evans)

- UCI Organic/Inorganic/Chem Bio Pre-advising Handout
- 2nd-Year Research Report

Who Reviews the Second-Year Report?

- The second-year report is assigned for review by **two faculty referees**, much like a manuscript or grant application.
- Your Ph.D. advisor does not review your report.
- Each faculty member reviews 2-4 reports, depending on the number of reports to be reviewed.
- Faculty meet to discuss their reviews, identify weak and strong students, and determine the outcome.

Evaluation Criteria for the Second Year Report

1. **Research Progress**

   Is student making satisfactory progress in their research?

2. **Clarity of presentation**

   a. **Introduction**: Have the problem and the current state of knowledge been clearly defined?

   b. **Results**: Are results clearly presented? Did you distinguish your accomplishments from those of coworkers?

   c. **Discussion**: Are the conclusions supported by the data?

   d. **Future Goals**: Is there a plan to circumvent problems or capitalize on key findings?

   e. **Experimental Procedures**: Are compounds characterized with respect to identity and purity? Details are important. Format is important.

   f. **Literature Cited**: Is literature cited generously? Are correct formats employed?

   g. **Supporting Information**: Are the data accurately and clearly portrayed?

How is the Second-Year Report Reviewed?

Two faculty members will be assigned the report as primary readers.

Second-Year Written Examination in Organic Chemistry

2013

Student:_____

The outcome of this exam is based on an assessment of research progress as well as the quality and accuracy of the written report. These factors are considered independently, and satisfactory completion of both components is required to receive a "Pass." A "Rewrite required" rating will require that a revised version of the document be deemed satisfactory before the exam has been formally passed.

Research Progress: Satisfactory ❑ Marginal Progress ❑ Unsatisfactory ❑

Reviewer's Comments:

Written Report: Accept without revision ❑ Accept with minor revision ❑

Accept after major revision ❑ Unsatisfactory ❑

Reviewer's Comments:

Outcomes of the Second-Year Written Report / Exam

1. Pass
2. Deferred for written, pass upon rewrite/approval
3. Research progress needs to accelerate, but acceptable
4. Fail