Topics in Synthetic Organic Chemistry
CHM 6227, Fall Semester 2020

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When:

- *Classes/Lecture*: Thursdays, Period 5 – 6, 11:45 AM – 1:40 PM
- *Exams:* None.
- *Final Exam:* None.
- *Office Hours:* Mondays from 9:30 am – 10:10 am; Tuesdays from 9:30 am – 10:10 am

Zoom information:

https://ufl.zoom.us/j/97450999416?pwd=S2FSV2h6WTUwVEVQWFhxa09MN0J4UT09
Meeting ID: 974 5099 9416
Passcode: Provided *via* email and on *e*Learning

Course Description:

Course Objective: Synthesis of complex organic molecules, with emphasis on recent developments in approaches and methods.

Course Content: In this flipped classroom, there will be two types of class periods:

Student Organized Class Periods (1 hr 55 mins): students will choose a topic of interest to modern synthetic organic chemistry and develop a *mini*-course on the subject. **Every student will develop one mini-course.** The mini-course will consist of:

(a) *a short take-home assignment* distributed to the class the Sunday *before* the lecture, which will be completed by the other students and due to AG *via* eLearning by the start of the class period.
(b) *a 30 – 35 minute student-presented* lecture on a sub-topic of the student's choosing.
(c) *a 40 – 50 minute* guest lecture from an expert in the field.

AG Organized Class Periods (1 hr 55 mins): There are more class periods than students. Thus, AG will develop the take-home assignment and lecture for the days that students have not been assigned.

The goal is to teach students how to design questions, content, and media that will probe and aid understanding on a modern subject matter.

Teaching Philosophy: The course will be primary lecture, problem solving, and Q & A.

Attendance: Attendance is required.

Required Texts: None. For this course, we will be directly be using the *review* and *primary literature*. Review and primary literature will be freely available to all students on the UF network: https://it.ufl.edu/ict/documentation/network-infrastructure/vpn/

***Grading*:**

<u>Grading</u>*: Students will be graded on three criteria*

- Your presentation – *35% of grade*
- Your take-home assignment – *35% of grade*
- Completing colleague's take-home assignments – *15% of grade*
- Attendance – *15% of grade*

***Specifics*:**

The presentation:

The topics chosen are ***broad research areas*!** Even though I have singled out 6 - 8 papers for you to focus on, this is still *too much* content for a 30-minute presentation. You need to read these papers closely and identify a significant sub-topic that will make for a compelling/informative/educational lecture. It should be cohesive but manageable for the time frame.

- You do not have to talk about all papers.
- You can find other papers that might better fit your targeted narrative.
- While designing a presentation around your sub-topic, think about questions such as the following to address in your lecture:
  - What is the theme of your presentation?
  - What is the take-away message?
  - What is the historical context?
  - What are the most important underlying chemical principles within your sub-topic?
  - What are the important mechanistic principles and understanding that are essential to your sub-topic?
- 2 – 3 weeks prior to your presentation, we will have an individual meeting to discuss what "sub-topic" you plan to present on. Make sure you have read the papers and have begun to formulate the sub-topic. ***The student will reach out to AG to schedule a ~30 minute meeting.*** *Please be prepared to address some of the following:*
  - *What is your sub-topic for your presentation?*
  - *Is the material concise enough for a 35 minute presentation?*
  - *What do you want to your colleagues to learn from your seminar?*
  - *What is the theme and questions you specifically want to address through your presentation?*
  - *What is the outline for your presentation?*
  - *What might be on your "take-home assignment" (vide infra)?*

The take-home assignment:

Once you specifically know what you plan to lecture on, you will prepare a short take home assignment to complement your lecture that that will highlight a key concept that is essential to the understanding of your presentation. For example, a key mechanism, arrow pushing, or pieces of background information. The take home assignment should take a student whom has looked over the primary literature on your topic ~20 minutes to complete. Your completed homework assignment is due to AG the Sunday before your presentation. AG will post the assignment to eLearning that Monday.

All *other registered* students will complete the assignments, which is due to AG *via* eLearning before the start of each class period. Student's should use the assigned primary literature and any other resources as a guide to complete the assignment. Assignments should be handwritten on paper, converted to PDF, and uploaded onto eLearning.
Weekly Topics and Associated Primary Literature:

Sept. 3rd: Introduction to the class
Sept. 10th: Enantioselective and enantiospecific cross-coupling

Lecture 1: Enantioselective Cross-Coupling (Alex Grenning)

(1) Potter, B.; Edelstein, E. K.; Morken, J. P. Modular, Catalytic Enantioselective Construction of Quaternary Carbon Stereocenters by Sequential Cross-Coupling Reactions. *Org. Lett.* **2016**, *18* (13), 3286–3289. https://doi.org/10.1021/acs.orglett.6b01580.
(2) Jiao, Z.; Chee, K. W.; Zhou, J. "Steve". Palladium-Catalyzed Asymmetric α-Arylation of Alkylnitriles. *J. Am. Chem. Soc.* **2016**, *138* (50), 16240–16243. https://doi.org/10.1021/jacs.6b11610.
(3) Eno, M. S.; Lu, A.; Morken, J. P. Nickel-Catalyzed Asymmetric Kumada Cross-Coupling of Symmetric Cyclic Sulfates. *J. Am. Chem. Soc.* **2016**, *138* (25), 7824–7827. https://doi.org/10.1021/jacs.6b03384.
(4) Guduguntla, S.; Hornillos, V.; Tessier, R.; Fananas-Mastral, M.; Feringa, B. L. Chiral Diarylmethanes via Copper-Catalyzed Asymmetric Allylic Arylation with Organolithium Compounds. *Org. Lett.* **2016**, *18* (2), 252–255. https://doi.org/10.1021/acs.orglett.5b03396.
(5) Suzuki, N.; Hofstra, J. L.; Poremba, K. E.; Reisman, S. E. Nickel-Catalyzed Enantioselective Cross-Coupling of N-Hydroxyphthalimide Esters with Vinyl Bromides. *Org. Lett.* **2017**, *19* (8), 2150–2153. https://doi.org/10.1021/acs.orglett.7b00793.
(6) Huang, W.; Wan, X.; Shen, Q. Enantioselective Construction of Trifluoromethoxylated Stereogenic Centers by a Nickel-Catalyzed Asymmetric Suzuki-Miyaura Coupling of Secondary Benzyl Bromides. *Angew. Chemie, Int. Ed.* **2017**, *56* (39), 11986–11989. https://doi.org/10.1002/anie.201706868.
(7) Poremba, K. E.; Kadunce, N. T.; Suzuki, N.; Cherney, A. H.; Reisman, S. E. Nickel-Catalyzed Asymmetric Reductive Cross-Coupling To Access 1,1-Diarylalkanes. *J. Am. Chem. Soc.* **2017**, *139* (16), 5684–5687. https://doi.org/10.1021/jacs.7b01705.
(8) Cui, X.-Y.; Ge, Y.; Tan, S. M.; Jiang, H.; Tan, D.; Lu, Y.; Lee, R.; Tan, C.-H. (Guanidine)Copper Complex-Catalyzed Enantioselective Dynamic Kinetic Allylic Alkynylation under Biphasic Condition. *J. Am. Chem. Soc.* **2018**, *140* (27), 8448–8455. https://doi.org/10.1021/jacs.7b12806.

Lecture 2: Prof. Mark Biscoe, City University of New York. Topic: Enantiospecific Cross-Coupling

Sept. 17th: Catalytic Intermolecular Alkene Functionalization

Lecture 1: Intermolecular alkene functionalization: Heck-like-, free radical-, and directed pathways. (Alex Grenning)

(1) Sun, X.; Li, X.; Song, S.; Zhu, Y.; Liang, Y.-F.; Jiao, N. Mn-Catalyzed Highly Efficient Aerobic Oxidative Hydroxyazidation of Olefins: A Direct Approach to β-Azido Alcohols. *J. Am. Chem. Soc.* **2015**, *137* (18), 6059–6066. https://doi.org/10.1021/jacs.5b02347.
(2) Yuan, Y.-A.; Lu, D.-F.; Chen, Y.-R.; Xu, H. Iron-Catalyzed Direct Diazidation for a Broad Range of Olefins. *Angew. Chemie Int. Ed.* **2016**, *55* (2), 534–538. https://doi.org/10.1002/anie.201507550.

(3) Tang, X.; Studer, A. Alkene 1,2-Difunctionalization by Radical Alkenyl Migration. *Angew. Chemie, Int. Ed.* **2018**, *57* (3), 814–817. https://doi.org/10.1002/anie.201710397.

(4) Liu, Z.; Zeng, T.; Yang, K. S.; Engle, K. M. β,γ-Vicinal Dicarbofunctionalization of Alkenyl Carbonyl Compounds via Directed Nucleopalladation. *J. Am. Chem. Soc.* **2016**, *138* (46), 15122–15125. https://doi.org/10.1021/jacs.6b09170.

(5) Wu, X.; Lin, H.-C.; Li, M.-L.; Li, L.-L.; Han, Z.-Y.; Gong, L.-Z. Enantioselective 1,2-Difunctionalization of Dienes Enabled by Chiral Palladium Complex-Catalyzed Cascade Arylation/Allylic Alkylation Reaction. *J. Am. Chem. Soc.* **2015**, *137* (42), 13476–13479. https://doi.org/10.1021/jacs.5b08734.

(6) Wang, F.; Wang, D.; Wan, X.; Wu, L.; Chen, P.; Liu, G. Enantioselective Copper-Catalyzed Intermolecular Cyanotrifluoromethylation of Alkenes via Radical Process. *J. Am. Chem. Soc.* **2016**, *138* (48), 15547–15550. https://doi.org/10.1021/jacs.6b10468.

(7) Chen, B.; Cao, P.; Yin, X.; Liao, Y.; Jiang, L.; Ye, J.; Wang, M.; Liao, J. Modular Synthesis of Enantioenriched 1,1,2-Triarylethanes by an Enantioselective Arylboration and Cross-Coupling Sequence. *ACS Catal.* **2017**, *7* (4), 2425–2429. https://doi.org/10.1021/acscatal.7b00300.

Lecture 2: Prof. Kami Hull, University of Texas. Topic: New Catalytic Methods for alkene functionalization [Note: This seminar will be at 4:00 PM as part of the Organic Division Seminar Series].

Sept. 24th: Parallel Chemistry
Oct. 1st: Decarboxylative Chemistry: photochemistry and polar decarboxylation

Lecture 1: "photocatalytic decarboxylative transformations." (Presenter: Alex Grenning)

(1) Griffin, J. D.; Zeller, M. A.; Nicewicz, D. A. Hydrodecarboxylation of Carboxylic and Malonic Acid Derivatives via Organic Photoredox Catalysis: Substrate Scope and Mechanistic Insight. *J. Am. Chem. Soc.* **2015**, *137* (35), 11340–11348. https://doi.org/10.1021/jacs.5b07770.

(2) Beatty, J. W.; Douglas, J. J.; Cole, K. P.; Stephenson, C. R. J. A Scalable and Operationally Simple Radical Trifluoromethylation. *Nat. Commun.* **2015**, *6*, 7919pp. https://doi.org/10.1038/ncomms8919.

(3) Zuo, Z.; Cong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. Enantioselective Decarboxylative Arylation of α-Amino Acids via the Merger of Photoredox and Nickel Catalysis. *J. Am. Chem. Soc.* **2016**, *138* (6), 1832–1835. https://doi.org/10.1021/jacs.5b13211.

(4) Li, C.; Wang, J.; Barton, L. M.; Yu, S.; Tian, M.; Peters, D. S.; Kumar, M.; Yu, A. W.; Johnson, K. A.; Chatterjee, A. K.; Yan, M.; Baran, P. S. Decarboxylative Borylation. *Science (80-.).* **2017**, *356* (6342), eaam7355. https://doi.org/10.1126/science.aam7355.

(5) Proctor, R. S. J.; Davis, H. J.; Phipps, R. J. Catalytic Enantioselective Minisci-Type Addition to Heteroarenes. *Science (80-.).* **2018**, *360* (6387), 419 LP – 422. https://doi.org/10.1126/science.aar6376.

(6) Sun, X.; Chen, J.; Ritter, T. Catalytic Dehydrogenative Decarboxyolefination of Carboxylic Acids. *Nat. Chem.* **2018**, *10* (12), 1229–1233. https://doi.org/10.1038/s41557-018-0142-4.

(7) Cartwright, K. C.; Tunge, J. A. Organophotoredox/Palladium Dual Catalytic Decarboxylative Csp3–Csp3 Coupling of Carboxylic Acids and π-Electrophiles. *Chem. Sci.* **2020**, *11* (31), 8167–8175. https://doi.org/10.1039/D0SC02609C.

Lecture 2: Prof. Rylan Lundgren: "Polar decarboxylative transformations."

Oct 8th and onward: Materials for these lectures will be made available at a later date.

Other Policies:

Accommodations for Students with Disabilities:

Students requesting classroom accommodation must first register with the Dean of Students Office. The Dean of Students Office will provide documentation to the student who must then provide this documentation to the instructor when requesting accommodation

UF Honor Code:

The UF Student Honor Code (see http://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/ for details):

We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment."

Honor Code violations include copying on an exam (or helping another student to copy) and/or turning in an exam for regrading that has been changed since it was graded by the instructor.

Any student found responsible for an academic honesty violation in this course will forfeit any applicable exam drop policy and be recommended sanctions consistent with the offense.

Classroom Etiquette:

Cell phone or other small electronic device use of any sort is strictly prohibited in the lecture hall at all times.

Evaluations:

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at https://evaluations.ufl.edu. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at https://evaluations.ufl.edu/results/
