CHEM 4000A: Synthesis Assignment
5 + 10 + 5 + 9 + 6 = 35
Due by midnight on Friday, April March 29th, 2022
PLEASE TYPE THE TEXT PORTIONS OF THIS ASSIGNMENT.
STRUCTURES, ETC. MAY BE HAND DRAWN.

Preamble
In addition to considering the overall yield of a synthesis, attention is now also being paid to how green it is. This particularly true for syntheses performed on industrial scales since greener syntheses are often cheaper for a variety of reasons including the cost of waste treatment and disposal. The 12 principles of green chemistry were originally published in a book by Paul Anastas and John Warner entitled "Green Chemistry: Theory and Practice". They are summarized and converted into a convenient mnemonic in an article by Samantha Yang, Richard Smith and Martyn Poliakoff entitled "Principles of green chemistry: PRODUCTIVELY"[1].

Assignment
Choose one of the syntheses in Chapter 11 of your text.[2] Don't choose the syntheses corresponding to Schemes 11.11, 11.12, 11.26 or 11.27 as the original papers corresponding to those syntheses will be difficult to access in a timely fashion.
Given the concerns about Coronavirus and how that may affect access to campus in the upcoming weeks, I am waiving my usual requirement that everyone drop by my office to sign up for a different synthesis. That said, these are INDIVIDUAL assignments. If you want to work with another student to find green reactions that accomplish specific tasks (e.g. greener ways to oxidize an alcohol to a ketone), you must be working on DIFFERENT syntheses.

1. Introduce your synthesis by identifying the key challenges in making your target molecule. Include the structure of your target molecule in this section! *This section does not address how the challenges were met; it answers "why is this molecule hard/interesting/important to make".* **[5]**
2. Summarize your synthesis by presenting it in retrosynthetic form to show the key disconnections used by the originator of the synthesis. (Don't include every single step of the synthesis! Focus on the key steps in which major things are accomplished – attaching two large pieces, forming rings, setting chirality centers, etc.) Remember that retrosynthesis is the "thinking backward" part of chemistry. Try to put yourself in the shoes of the originator of the synthesis, breaking a complex molecule into more manageable pieces. You are showing me that you can tell the difference between the "big steps" of a synthesis and the set-up and/or clean-up steps. A complete answer will include verbal explanation as well as the diagram(s). **[10]**
3. Evaluate your synthesis in terms of how green it is. How well does it live up to the 12 principles of green chemistry? **[5]**
4. Identify three steps which could be performed in a greener way. Explain why each is less green than it could be, and suggest how you would change each to make it greener. Note that you must include three *different* changes. If you can improve upon a reagent used in multiple steps, that's great, but it's only one improvement. *While all of these syntheses are classics from a chemistry standpoint, most of them were developed long before we started thinking about green chemistry. This is <u>not</u> a request to "be better than the experts".* **[9]**

Properly citing references will be worth 1 mark, and presentation/writing style will be worth 5 marks. I am not looking for poetry, but I am looking for clarity.

To get an idea of the sort of thinking I'm looking for in parts 3 and 4, I highly recommend reading "The development of an environmentally benign synthesis of sildenafil citrate (Viagra™) and its assessment by Green Chemistry metrics" by Peter Dunn, Stephen Galvin and Kevni Hettenbach[3].

While I'm not setting a formal word/page limit for this assignment, please be reasonable. I don't see how it would be possible to answer the questions properly in 2-3 pages (including diagrams). On the other hand, it would take me a very long time to read and evaluate 16 novels, each on a different synthesis. I suspect that 5-10 pages (including diagrams) is a reasonable length.

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[1] Green Chem., 2005, 7, 761–762. http://pubs.rsc.org/en/content/articlepdf/2005/gc/b513020b
(need to be on campus or logged in as U. of L. library user to use direct link)
[2] R.W. Hoffmann *Elements of Synthesis Planning*, Springer-Verlag Berlin Heidelberg, 2009
[3] Green Chem., 2004, 6, 43–48 http://pubs.rsc.org/en/content/articlepdf/2004/gc/b312329d
(need to be on campus or logged in as U. of L. library user to use direct link)