Topic 7

Presentations

7.1 Day 1 (1-6)

3/11:

- Nate's presentation.
  - Figure out what IC_{50} means, and why nanomolar (including single-digit) is good!
  - Explain bio terms (but I'm already planning this).
    - Make sure I have oncometabolite definition right!
  - Make sure all mechanistic/synthetic details are right and explainable (but I'm already planning this).
    - "You should be able to right a mechanism for any reaction you're going to present" - Steve.
    - "If you're in a job interview, you have to be able to have some answer if someone asks how the reaction goes."
    - "Sometimes I know and sometimes I don't, and then I have to look up a bunch of papers. And then sometimes I can figure it out and sometimes I can't, but at least I have something to say then." Sweet!
- Steve to Dennis: "All of these presentations should have been downloaded ahead of time."
- Frank's (Harvard) presentation.
  - Vadadustat.
  - "Slow down, breathe, and don't read from the slide."
  - "You gonna walk us through that scheme? Because otherwise, it's useless."
    - Make sure I explain all figures, including crystal structures!! Learn the hydrogen bonds.
  - Make sure I can explain ambiguous selectivity, too!!
  - HBr works to hydrolyze *activated* (e.g., phenyl) methyl ethers (and can do nitrile hydrolysis at the same time).
    - Explain selectivity for chloro S_NAr on *s*-triazene vs. *ortho*-pyridine.
    - More activated/under more mild conditions. Look up typical conditions for pyridine S_NAr and look to differentiate temperature, acid, etc. from the used conditions.
- Minh's presentation.
  - Voydeya.
  - Appreciating structural/retrosynthetic challenges is probably a good idea!
  - Make sure I know what the biuret test is (a protein test — like the functional group tests Steve discussed that day — that does not contain biuret, but gives a positive result to the peptide-like bonds in biuret).

  - Check timing: Make sure I get everything in in 10 minutes, and don't linger on the bio!
  - Sleep well both of the next two nights!

- Alexander's presentation.

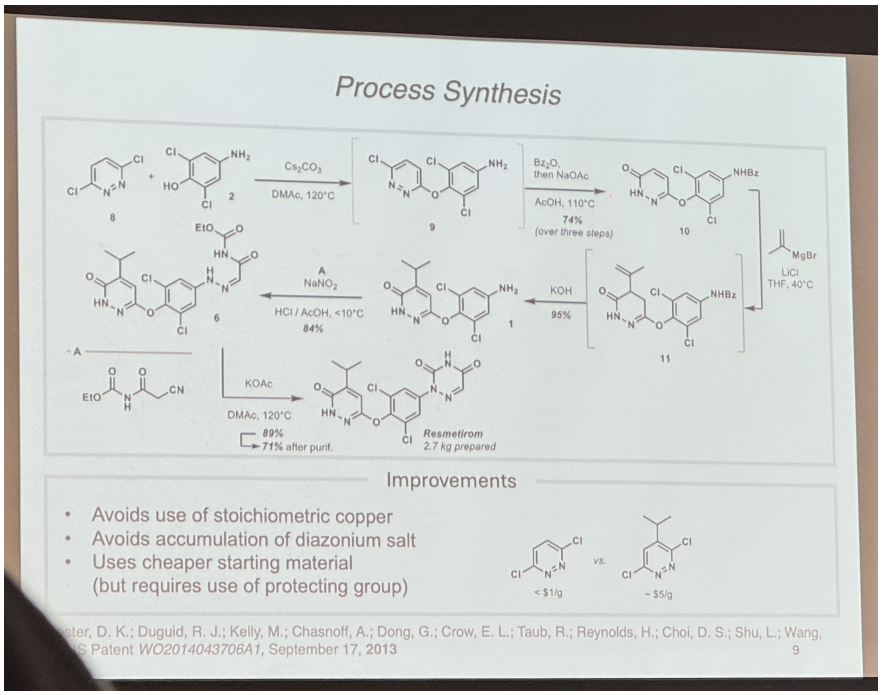

Figure 7.1: Alexander Müller's graphic design.

  - Resmetirom.
  - Electron-rich arenes easily oxidize in the body, leading to redox cycling. Causes safety/toxidity issues.
    - Good discussion of design principles; keep doing the same!
  - Good retrosynthesis, followed by synthesis.
  - Dives into mechanisms of key steps.
  - Good graphic design: Boxes. Very clean and clear. Citations in light grey at bottom left.
  - Numbering chemicals and compounds is a good idea.
  - Explaining selectivity is definitely needed!

- Angel's presentation.

  - Ceftobiprole: Staph antibiotic.
  - Starts with retrosynthetic analysis of moieties.
  - Gives a total nitrogen count; I could/should, too!
  - Gives a discovery timeline.
  - Know the mutations.
  - Drawing out arrow-pushing mechanisms is not inappropriate.
  - Make changes clear in large molecules moving from one to the next with colored bonds, as Steve does! Otherwise, you just get lost as to what's changing...

- On Thursday, we'll start at 9:00 instead of 9:05.
- Kwanwoo's presentation.

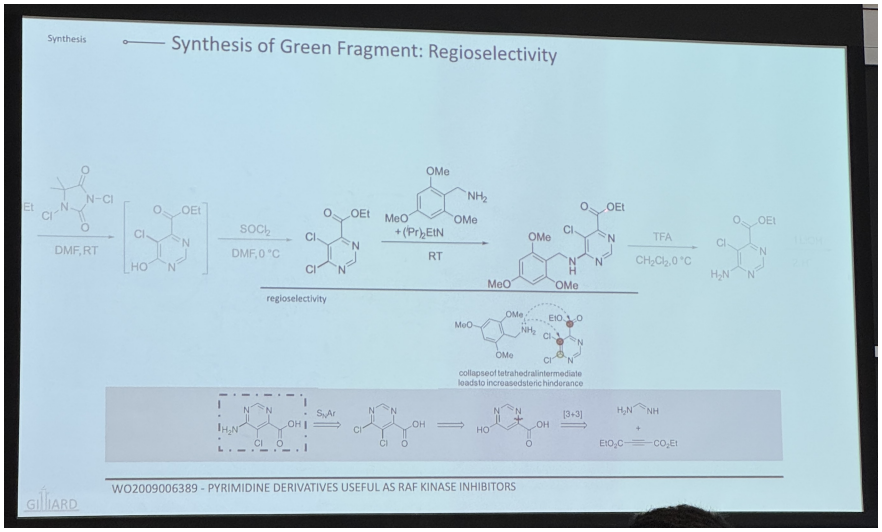

Figure 7.2: Kwanwoo Park's graphic design.

  - Ojemda.
  - Also uses MIT/Gilliard slide template!
  - Also discussing a glioma; could give him a shoutout in my presentation!
  - Slides are too cluttered and he's reading off the slides.
  - Good retrosynthetic analysis. Color-codes fragments (using pastel-colored boxes might be better, then keeping them on each slide).
  - Points out Hantzsch; I should make a fuss about names as well.
  - Know the names of functional groups! Know the carbon numbering in my molecule.
  - Graphic design.
    - Mechanism in pop-up box is a good approach.
    - Keeping the general scheme at the bottom of each slide, being progressively highlighted, as you move through bigger synthetic details up top.
    - Chemoselectivity with circles in popup box.
  - Know reagent names, and functional group names.

7.2 Day 2 (7-14)

3/13:
- Jasmin's presentation.
  - Xolremdi.
  - Also does limitations of ok med chem synthesis!
  - Does retrosynthetic analysis separately from forward synthesis; would have been a good idea, as Christine suggested.
  - Uses a table beneath a larger, marked up scheme to show screened conditions for one reaction.
  - "Silica gel pad" means filtration, not chromatography, which is why they can get away with it.
  - Catalytic KI and bulky base can do Finkelstein-type chloride/iodide exchange *in situ* before S_N2 displacement with the other reaction.

- Yifan's presentation.

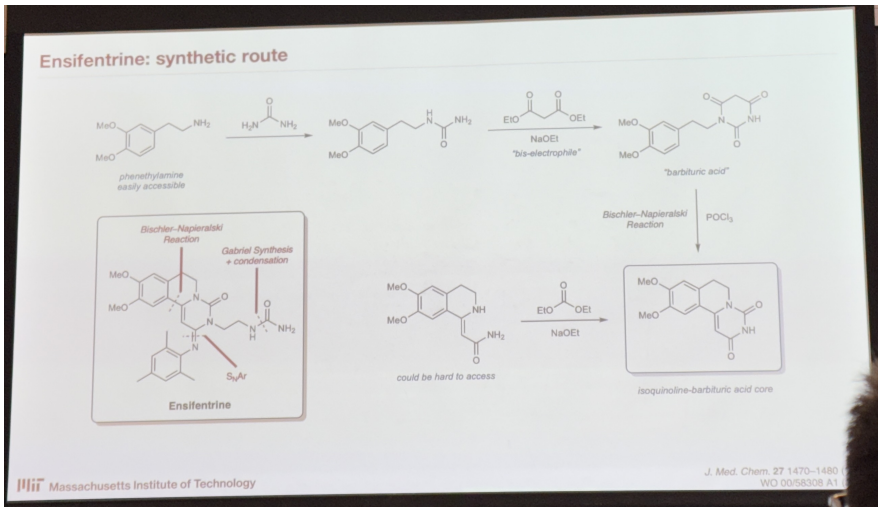

Figure 7.3: Yifan's graphic design.

  - Emphasizing first-in-class and novel mechanisms of action may be a good idea.
  - Graphic design: Disconnections labeled with reactions in a popup box!
  - Finkelstein again: NaI, K_2CO_3, and 2-butanone (like W. S. Johnson!).

- Yuzhe's presentation.
  - Deyryxikutubub.
  - Talks about mental health effects of having a disease, too!
  - Numbering compounds with different numbers for different protecting groups (variables), as papers often do!

- My presentation.
  - C–F–O bonds aren't really a thing; it's more of an interaction.
  - We did actually talk about *s*-triazines in class (oops); Steve made fun of the name.
  - TFA, $HC(OMe)_3$ is a common drying agent, an alternative to a Dean-Stark apparatus.
    - Both things I put up are plausible, but drying is more common.
  - Steve points out that Cyanamid was acquired by another company, then bought by Pfizer (like everything else).

- Jordan Bench's presentation.
  - Lazertinib.
  - Steve points out a number of things in the reactions that would be hard to tell from patents.
    - Formate is for transfer hydrogenation.
  - Patent authors use patent generics a lot, because otherwise people will make a slight improvement, repatent, and sell more cheaply.
  - You have to do a certain number of the examples in the patent in order to justify it, but not all of them.

- Georgia's presentation.

  - Miplyffa.
  - Rare disease (only 300 people in the US), so test cases to justify the approval were only on 4-5 people.
  - Process synthesis at 50 g scale, but maybe that makes sense with the small number of people affected.

- Elizabeth's presentation.

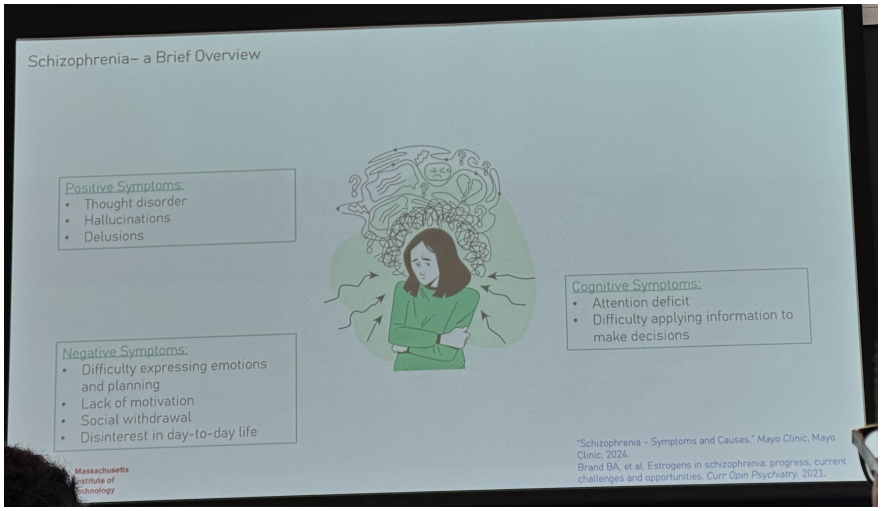

Figure 7.4: Elizabeth's graphic design.

  - Cobenfy: Combination drug of xanomeline and trospium chloride.
  - Graphic design: Boxes around an image to identify different aspects. Hard lines, good font, and color are all useful, though the color is a bit light and hard to read...
  - TMSCN is an alternate nucleophilic cyanide equivalent to KCN.
  - Thiadiazole synthesis from S_2Cl_2, and a nitrile/amine. Mechanistically pretty complicated, per Steve.

- Eva Bayer's (Harvard) presentation.

  - Has radioactive ^{18}F.
  - Higher image resolution (for PET) among competitors. Goes *very specifically* to mitochondria.
  - Good that a precursor was approved in pesticides, because it flushes out of humans super quickly, so no long-term toxicity. But hangs around long enough for imaging.
  - Time really matters in the synthesis (it's 110 minutes, 35% yield) because the ^{18}F decays so rapidly!
  - You basically need a cyclotron on site to produce this stuff and get it into a patient ASAP.