Chem 227 / Library Research / Organic Synthesis

Dr. Rusay / Spring 2006

Planning is a critical component of any endeavor including scientific research and organic synthesis. A thorough examination of the published literature is necessary to develop a strategic and efficient approach to any experiment including the syntheses of organic molecules. Electronic search tools are most valuable in surveying the scientific literature. They can provide summaries and lead to an enormous body of published experimental data. Evaluating and communicating the results of a literature search in a concise well written form are essential requirements and highly important skills.

See the course Web calendar for scheduled assignment due dates.

PART I: Calibrated Peer Review (CPR) writing assignment

Design and Development of Drugs
http://cpr.molsci.ucla.edu/

- You are to read an article from the *Journal of Chemical Education* about organic synthesis and the history of many drugs and medicines,
  K.C. Nicolaou, et. al., JChemEd, 75, 1226-1258, (1998); See Course Assignments Webpage for pdf files.
- Learn about the way that one drug (aspirin) was discovered and how chemists contributed to its improvement.
- Learn to identify new synthetic methods necessary in drug synthesis and future drug development.
- Learn about a widely used approach to the rapid development of new chemical compounds using "Combinatorial Synthesis" and how "chemical libraries" (in a non-traditional sense) are used.
- Write an essay explaining how aspirin was developed, the methods chemists currently use to develop new and better drugs, which can be applied to any area including nano-materials, and the future of organic synthesis.

PART II: Research Paper

You are to select a compound, *eg. thienamycin*, [General Class, *antibiotics*]. See the accompanying list for some possibilities. Everyone will have a different individual compound. You are to identify and report your target compound and its general class to Dr. R. on or before **March 24th**. The compound does not have to come from the accompanying list, but you must have your selection approved before you begin your research.

> You are to: 1) develop a short but detailed profile of the general class of compounds, their uses and their value to society, 2) find available physical and spectroscopic data on the compound. Minimal data should include: m.p or b.p., IR and/ or ^{1}H NMR (^{13}C NMR if available.), and 3) find one or more primary literature references for a synthesis of the selected compound. Your synthesis must contain a minimum of five reactions. Three of the five reactions **must** be reactions that are found in the *Bruice* textbook. You are to name the type of reaction (eg. *oxidation*) and provide a citation for the reaction from the textbook: *chapter, section and page number*. The reagents do not need to match textbook examples exactly but the general reaction does, *eg. Reduction: ketone to a secondary alcohol, 18.5, pg. 743.*
>
> The accompanying list includes a number of compounds for your consideration,

BEWARE: The compounds included in the list may or may not lend themselves to easily finding the required information. Some are patented, proprietary compounds which have a much smaller body of published information, and limited availability of the patents themselves.

The Internet, DVC library and the UC Berkeley Chemistry libraries will provide you with the necessary resources for literature searches and/or access to primary literature sources. Three lab sessions plus additional out of class time will be budgeted for the entire project. Your attendance will be required at a UC Berkeley Chemistry Library presentation on Monday March 27th either at 10:00 AM or 1:30 PM. Failure to attend a session will result in a 20% reduction in your grade. (Details to follow.) Cal's Chemistry librarian, Mary Ann Mahoney, will introduce you to several most useful search tools and resources. Mary Ann commented that she would work backwards; first seeing what is available in the literature for a compound before selecting one. You may want to adopt this approach after perusing the literature for your chosen sompound. You may change your compound after seeing what is or is not available, but you may do this only once and only on March 27th/ 28th after consulting with Dr. R.

Your report is to be type-written with a complete bibliography (5 references minimum: Web URLs are acceptable, but there must be at least one primary journal reference). The report is to include a narrative section of at least one type-written page and no more than three pages, double spaced, on the general class of compounds uses and their importance, plus the specific compound's origin, history and significance within the class. The report is to include a table of physical and spectroscopic data for the specific compound and a separate section with a detailed synthetic reaction scheme that includes digitally drawn structures and reagents. In the event that you do not find a single reference for the synthesis, which includes a sufficient number of reactions, you may use multiple references that offer different synthetic approaches to the same compound or to its intermediates in order to satisfy the minima. The synthetic scheme(s) can be abbreviated (compressed) if there are more than five reaction steps (drawings of all steps do not need to be included). You are to use a chemical drawing program such as ISIS/Draw, which is free to students and faculty (See course Web site for download link) or it can be used directly on the PS 110 computers. (Freehand or stenciled drawings are unacceptable.)

See: *http://chemconnections.llnl.gov/organic/Chem227/227assign06.html* for a collection of past papers, which are examples of varying quality (A, B, C). You can judge for yourself which paper is which.

Two copies of the report are to be submitted by **5:00PM** on **April 10th. Late reports will not be accepted**. One or more reports, which are considered to be of the highest quality, will be selected for electronic publication with the author's consent and approval. Electronic file copies will be required for Web publication. They will be linked from WEB-sters' Organic Chemistry, *http://chemconnections.llnl.gov/organic/Websters/*, which has had over 2,000,000 hits since its inception in the fall of 1997.

To begin your research, see *http://www.liv.ac.uk/Chemistry/Links/* and *http://www.chemdex.org/* also, refer to the Web links under *Information & Search Tools* which follows the list of compounds.

COMPLETED ASSIGNMENT DUE April 10th.

Compound	*General Class*
abrusoside E	sweeteners
acyclovir	antivirals / AIDs
adriamycin	anticancer / antineoplastic agents
aflatoxins	toxic fungal metabolites
albuterol	bronchodilators
amphotericin B	antibiotics
avenaciolide	antifungals
betulinic Acid	anticancer / antineoplastic agents
brevitoxin	marine natual products
bufenolide	vasodilators / antihypertensives
calciferol	vitamin / rodenticide
campherenone	aromas and fragrances
camptothecin	anticancer / antineoplastic agents
chlorpheniramine	antihistaminics
cognex	alzheimers drugs
cortisone	steroids / hormones
dendrobine	convulsants
depudecin	anticancer / antineoplastic agents
epothilone A	anticancer / antineoplastic agents
estrone	steroids / hormones
ethacrynic acid	diuretics
fumagillin	anti- fungals
grandisol (boll weevil)	pheromones
grass hopper ketone	allochemicals (defensive)
illudin S	anticancer / antineoplastic agents
juvenile hormone/methoprene	insect hormones
lactitol	laxatives
lovastatin	antihypercholesterolemics
lufenuron	ectoparasitic agent
lysergic acid/lysergide/LSD	psychoactive active agents
mifepristone	abortifacients
mitomycins	anticancer / antineoplastic agents
monensin	antibiotics
morphine	narcotic analgesics
muscone	aromas and fragrances
nootketone	aromas and fragrances
norepinephrine	adrenergic agents
occidentalol	aromas and fragrances
patchouli alcohol	aromas and fragrances
penicillin / cephalosporins	antibiotics
periplanone B	prostaglandins
porphyrins/ porphobilogen	photodynamic light therapy
progestrone	steroids / hormones
prostaglandin E2/PGE2	prostaglandins
prozac	antidepressants
pyrethrins/pyrethroids	insecticides
quinine	antimalarials
raloxifene	anticancer / antineoplastic agents
rapamycin	immuno-suppressants
resperpine	antihypertensives
ropivacaine	anesthetics
saxitoxin	marine natural products
squalene/ squalestatin S1	antibiotics
stevioside	sweeteners
strychnine	natural product poisons

Compound	*General Class*
tamoxifen	anticancer / antineoplastic agents
tertatolol	antihypertensives
testosterone	steroids / hormones
tetrahydrocannabinols	psychoactive active agents
thienamycin	antibiotics
triketones	herbicides
vamicamide	anticholinergics
vincristine/vinblastine	anticancer / antineoplastic agents
vitamin B	vitamins
warfarin	anticoagulants

Information & Search Tools:

DVC Library
http://www.dvc.edu/library/
UCB Chemistry Library
http://www.lib.berkeley.edu/CHEM/
UCB Pathfinder
http://sunsite2.berkeley.edu:8000/
ERIC: Educational Resources Information Center
http://www.eric.ed.gov/

Some other compounds to consider: atisine, disparlure, milbemycin, sinensal, cedrene, longifolene, vermiculine, seychellene, emodin, eleuthrin, occidentalol, methyl jasmonate, gephyrotoxin, eremophilone, chyrosophanol, acoradiene, griseofulvin, mesembrine, trachelanthamidine, lycopodine, daphniphyllium alkaloids, juvabione, pupukeanone, yohimbine