Chemistry 41c Final Review Sheet – Spring Quarter 2013

The take-home final exam questions will focus primarily on 41c material covered in class, but material from earlier quarters and other chapters is certainly fair game. To prepare for the exam, you should re-familiarize yourself with 41c review sheets from earlier chapters, as well as the general layout of Loudon's book and associated class notes. The exam has been written as a four hour exercise.

You will be allowed to only use the following when working the final exam: a calculator, molecular models, Loudon's text & solutions manual, and any class notes associated with 41a-c.

Chapter 26 topics covered in class:

1. The basis of the DL nomenclature for amino acids (aa's). Review this and the (+/-), *d*/*l*, and R/S convention one last time.

2. Acid/base behavior of amino acids and the isoelectric point, pI.

3. Racemic syntheses of aa's. Gabriel or ammonia-based syntheses starting from α-halo acids, made from the HVZ reaction. Malonate approaches to aa synthesis. Be able to use a Strecker aa synthesis and demonstrate a mechanistic understanding of the reaction.

4. Be aware of at least two methods for resolving racemic mixtures of aa's. One way is to react a racemic mixture with a chiral compound to make separable diastereomers. The other way is to use an N-acetylated racemate and an acylase enzyme to selectively de-acetylate one enantiomer.

5. Determining the primary sequence of polypeptides. Complete acid hydrolysis of a peptide to the constituent amino acids and their quantitation via ion-exchange chromatography as assisted by ninhydrin visualization or AQC derivatization via the AQC-NHS ester. Partial hydrolysis using acid or enzymes such as trypsin or chymotrypsin. Edman and Sanger terminal residue analysis. Complete sequence analysis via MS-MS.

6. Activation of the aa carboxyl group for amide bond formation. The dicyclohexylcarbodiimide (DCC) method as a prototype carbodiimide coupling mechanism. Be familiar with other coupling reagents (DIC, EDC, and HBTU) and how their use varies with reaction/work-up conditions. Know why HOBT is used as a peptide coupling additive and the nature of the active ester formed when it is used (an intermediate not unlike the NHS ester mentioned in #5). Understand why some aa side chains need to be protected during peptide coupling reactions.

7. Solution phase peptide synthesis. Utility of the "Boc" protecting group: conditions for its deprotection. Be able to explain, mechanistically, why these groups can be cleaved with TFA and without any amide or ester bond cleavage.

8. Application of the olefin metathesis reaction to construct peptides with constrained architectures, such as helices, and their potential use as peptide therapeutics.

9. Solid-phase peptide synthesis. Be cognizant of the time advantage, relative to solution-phase chemistry, as well as the stoichiometry differences between the two approaches. Be able to outline the steps in the synthesis of a small peptide using the solid-phase approach using acid-labile resin linker chemistry. Understand why Fmoc (a base-labile group) is the N-protecting group of choice in an application like this, understand and how it can be removed with a base such as piperidine.