CHEM 109 HW Assignments

Lecture	Assignment
1	McMurry & Begley (M&B) Chapter 1 #1-6 – PDF posted on 8M Website: acrochem.sites.ucsc.edu
2	M&B Chapter 1 # 7, 8, 16, Discussion Worksheet #1
3	M&B Chapter 1 # 12 part (1), 14 part (2); print out or open blank lecture 3 notes and fill in the mechanisms
4	M&B Chapter 1 # 9, 10, 13, 15
5 & 5'	M&B Chapter 1 # 11, 12, 14 Draw the ionic species for full pH range (1-14) for acidic & basic amino acids. *No posted key for L4 HW. Check your solutions with your TA in office hours or discussion
6	Lecture 6 HW on page HW-2 of this document (next page)
7	See p. HW-3
8	See p. HW-4-5
9	See p. HW-6
10	Print out a blank Lecture 10 and re-do without looking at your notes. It's ok to use different amino acid residues, as long as they're reasonable (still an acid or base). No key posted for this HW (bring this up in discussion and refer to your notes / webcast).
11	See p. HW-7-8
12	See p. HW-8-9
13	See p. HW-10-11
14	See p. HW-12-13
15	See p. HW-13
16	Carry out the 9 starred mechanisms from the Lecture 16 notes (see also HW-14-16) using acids (H^+) and bases (:B) – not for credit, but for exam prep!

*HW is not checked for credit. HW should be completed as soon as possible after lecture, but to keep you on track, plan on having your HW done by Monday of the following week. Monday dates are given in the table for clarity. Expect a quiz to be given each week directly from the previous week's lectures.

Lecture 6 Homework – updated 4/22

Learn those amino acids! Please find the template on the 109 acrochem site to **redraw each amino acid along with its full name and three-letter & single-letter abbreviation.**

Extra Credit: re-draw all the amino acids with names and abbreviations three times. Submit on Canvas for 3 extra points ©

Biological Mechanisms: Assume that the reactions are taking place at physiological pH (7.4). Take that into account when determining charges and proton movement. Use acids (H^+) and bases (:B) freely when needed.

1. On page L6-3 of your notes, we covered the biosynthesis of asparagine from aspartate. The biosynthesis of glutamine from glutamate is strikingly similar! Show the **mechanisms for each of the three steps in the synthesis of glutamine from glutamate:** (1) hydrolysis of glutamine, (2) phosphate transfer with ATP, and (3) amide formation. The ammonia needed to make glutamine does actually come from the hydrolysis of glutamine. It is not uncommon for the degradation products of metabolic intermediates to be used to make the same molecule again!



2. The final phase in the biosynthesis of proline is the reductive amination of glutamate 5-semialdehyde. Without looking at your notes, draw the arrow-pushing mechanism for both steps. Check your mechanism with what your notes.



3. Go through your lecture 6 notes and make a list of the different types of mechanisms using terms in the mechanism review from lectures 1-4.

4. Explain the difference between glutamate and glutamic acid. Do the same for aspartate and aspartic acid. When is each name more appropriate?

NOTE: You are NOT expected to memorize the schemes in the notes and HW for the exams! You are expected to be able to work through the mechanisms given the starting materials, intermediates, products, and/or reaction names. This is more about understanding reactions than memorizing the complex reaction schemes.

Lecture 7 HW

1. (Klein 3rd Ed. 22.21) **Draw the structure of each of the following peptides at pH 7.4** with the N-terminus on the left and C-terminus on the right. Include stereochemistry.

(a) Leu-Ala-Gly (b) Cys-Asp-Ala-Gly

(c) Met-Lys-His-Tyr-Ser-Phe-Val

2. (McMurry 8th Ed. 26.38 + more) **Draw the structure of each of the following peptides at pH 7.4** with the N-terminus on the left and C-terminus on the right. Include stereochemistry.

(a) C-H-E-M
 (b) P-E-P-T-I-D-E
 (c) C-A-I-T-L-I-N
 (d) Draw your peptide! There are 20 common amino acids and 26 letters of the alphabet so you should be able to get most of your name ©

3. Re-draw the following peptides across the full pH range (0-14). There should be at least 3 different ionic forms. The pH ranges should be based on the pKa₁ of the C terminal amino acid, pKa₂ of the N-terminal amino acid, and all pKa_R values for acidic / basic side chains. Use this information to **determine the pI for each peptide**.

(a) Cys-Asp-Ala-Gly (b) C-H-E-M

4. (McMurry 8th Ed. 26.38 + more)Which of the following amino acids are more likely to be found on the **outside of a globular protein and which on the inside**? Assume pH of 7.4 (physiological pH). Explain your choice.

(a) Valine (b) Aspartic Acid (c) Phenylalanine (d) Lysine

<u>5. Design an enzyme active site</u> for each reaction in the synthesis of glutamine from glutamate (Lecture 6, HW #1) using the following steps. Remember enzymes will perform reactions in the least number of steps possible. There are many correct ways of designing this active site, have fun with it!

(a) Re-draw the first step in the first mechanism from L6-HW #1 – glutamine + H_2O with arrows, H⁺ and :B. Don't include the intermediate yet.

(b) Replace each H⁺ and :B with appropriate **amino acid residues (3-letter abbreviation connected to acidic or basic group).** Note these are the side chains within the enzyme, not loose amino acids!

(c) Add at least **two stabilizing factors** to each substrate (in this case glutamine and water) to hold them in place within the active site. Examples are below, take your pick!

- *ion dipole interactions:* your favorite essential mineral (Cu+, Zn+, Mg²⁺) to stabilize any negatively charged atoms

- *Hydrogen-bonding*: show the coordination of any O-H or N-H bonds in the substrate to the peptide backbone or appropriate amino acid residues.

- *Hydrophobic interactions:* any non-polar regions of the substrates will be surrounded by hydrophobic side chains (use 3-letter abbreviations)

(d) Draw a squiggly bubble around your creation to signify the rest of the protein chain – that's your first active site design! Share on IG and tag me @acrochemist or make a TikTok :P

(d) Draw the reaction intermediate (result of the 1st step of the glutamine + H₂O reaction) and repeat steps (b) and (c) to make the active site for that step. Repeat with the remaining reactions.
 Lecture 8 HW - CARBOHYDRATE ACTIVITY

A. Draw an example or define the following terms on a separate sheet <u>while you complete Part B.</u> Include formulas or structures, where appropriate.

Carbohydrate	Triose	Hemiacetal
Monosaccharide	Tetrose	Anomeric Carbon
Disaccharide	Pentose	Anomers
Trisaccharide	Hexose	Epimers
Polysaccharide	Penultimate Carbon	Furanose
Aldose	D-Monosaccharide	Pyranose
Ketose	L-Monosaccharide	Glycosidic Bond

B. Structural Conventions

- 1. Draw one example of each of the following types of monosaccharides (there may be several correct answers) and indicate the number of possible stereoisomers (while keeping the same D/L configuration).
 - a. D-Aldotriose
 - b. L-Ketotetrose
 - c. L-Aldopentose
 - d. D-Ketohexose
 - e. L-Aldohexose
- 2. Draw Fischer projections of the following:
 - a. The C2 epimer of D-Glucose
 - b. The C3 epimer of D-Glucose
 - c. The C4 epimer of D-Glucose

#3-6. Use the following templates when drawing sugars in Haworth projections and chair conformations.



- 3. Draw Haworth projections for the following (consult Fig 25.3 of McMurry; memorize the structure of D-Glucose for the second exam). What is the relationship between a & b; between a & c?
 - a. α -D-Allopyranose
 - b. β -D-Altropyranose
 - c. α -D-Glucopyranose
 - d. β -D-Mannopyranose
 - e. *α*-D-Gulopyranose
 - f. β -D-Idopyranose
 - g. α -D-Galactopyranose
 - h. β -D-Talopyranose
- 4. Draw the chair conformations for the monosaccharides in problem 4.

- 1. There are at least eight common ways for two glucose units to be linked together to form eight different disaccharides. Show the mechanism for the linking of D-glucose units to make a disaccharide with loss of water. Use any glycosidic linkage or try a few!
- 2. Draw the Haworth projection for β -D-idopyranosyl-(1→6)- α -D-allopyranoside, disaccharide formed between D-ldose and D-Allose linked by a β -1,6-glycosidic bond (consult Fig 25.3 of McMurry).
- 3. Draw the Haworth projection for milk sugar (lactose).

 β -D-galactopyranosyl-(1 \rightarrow 4)- β -D-glucopyranoside - disaccharide formed from D-galactose and D-glucose linked by a β -1,4-glycosidic bond (consult Fig 25.3 of McMurry).

4. Draw the Haworth projection for table sugar (sucrose).

 α -D-glucopyranosyl-(1→2)-β-D-fructofuranoside – disaccharide formed between D-glucose and D-fructose by a α -1,2-glycosidic bond (consult Fig 25.3 of McMurry and the structure below).

HO О. 2 HO HO OH OH

β-D-fructofuranose

5. Show the mechanism for the hydrolysis (addition of water) to a disaccharide into two D-monosaccharides.

Lectures 9 & 10 HW - use amino acid residues as acids and bases.

4.6 Mannose, a component of dietary glycoproteins, is metabolized by an initial phosphorylation and isomerization to fructose 6-phosphate. Propose a mechanism for the isomerization.



4.7 Plants, but not animals, are able to synthesize glucose from acetyl CoA by a pathway that begins with the *glyoxalate cycle*. One of the steps in the cycle is the conversion of isocitrate to glyoxalate plus succinate, a process catalyzed by isocitrate lyase. Propose a mechanism for the reaction.



4.8 Galactose, a constituent of the disaccharide lactose found in dairy products, is metabolized by a pathway that includes the epimerization of UDP-galactose to UDP-glucose, where UDP = uridylyl diphosphate. The epimerase enzyme uses NAD⁺ as cofactor. Propose a mechanism for the reaction.



. 9

4.9 Propose a mechanism for the conversion of 6-phosphogluconate to 2-keto-3-dcoxy-6-phosphogluconate, a step in the Entner–Doudcroff bacterial pathway for glucose catabolism.



Lecture 11 HW – Read all instructions carefully before attempting! Refer to Lecture 10 notes to learn reactivity patterns in these new cofactors.

1. Show the mechanism for Step 4 of the citric acid cycle, conversion of α -ketoglutarate into succinyl CoA. The reaction involves...

- (1) an initial nucleophilic addition reaction to *a*-ketoglutarate by TPP ylid,
- (2) decarboxylation,
- (3) reaction with **lipoamide**,
- (4) elimination of **TPP ylid**, and finally
- (5) a transesterification of the dihydrolipoamide thioester with coenzyme A.

Use the structures below to complete this transformation, plus amino acid residues as acids and bases where appropriate.



2. Show the mechanism for Step 7 of the reductive pentose phosphate (RPP) pathway. This is a transketolase-catalyzed reaction that involves...

- (1) an initial nucleophilic addition reaction to fructose-6-phosphate by TPP ylid,
- (2) C-C cleavage to release erythrose-4-phosphate,
- (3) nucleophilic addition of the TPP adduct to glyceraldehyde-3-phosphate, and
- (4) elimination of **TPP ylid** with release of **xylulose-5-phosphate**.

Use the structures below and descriptions above to complete this transformation, plus amino acid residues as acids and bases where appropriate.



Lecture 11 HW (cont'd)

3. Show the mechanism for Step 10 of the reductive pentose phosphate (RPP) pathway. This is a transketolase-catalyzed reaction that involves...

- (1) an initial nucleophilic addition reaction to seduheptulose-7-phosphate by TPP ylid,
- (2) C-C cleavage to release ribose-5-phosphate,
- (3) nucleophilic addition of the TPP adduct to glyceraldehyde-3-phosphate, and
- (4) elimination of **TPP ylid** with release of **xylulose-5-phosphate**.

Use the structures below and descriptions above to complete this transformation, plus amino acid residues as acids and bases where appropriate. Number. Your. Carbons.



Lecture 12 HW

1. Refer to the *mevalonate pathway* in your notes or the textbook when determining the final positions of the **carbon-14** labeled carbon atoms from **Acetyl CoA** into **IPP**, **DMAPP**, **GPP**, and **Limonene**. You are you not expected to memorize the pathways, but given the outline of the process, you should be able to follow a labeled atom. Indicate the positions with a star (*).



Lecture 12 HW (cont'd)

2. The biosynthesis of terpenes often involves complex skeletal rearrangements, including hydride and methyl shifts. Add the arrows to complete the mechanism for the synthesis of **trichodiene** from **FPP**. Note that the last step requires base involvement, similar to the second step of an E1 mechanism.



3. Propose a mechanistic pathway for the synthesis of **borneol** from **GPP** and **water**. The first step should be to carefully number the carbons in the starting material to align with the product. You will find a somewhat similar addition of water to alkenes in your lecture 1 notes!



Lectures 13 Homework Set – Heterocycles & Nucleotides

1. Build the Nucleosides and Nucleotides. You are responsible for knowing how to build RNA and DNA bases in their nucleoside & nucleotide form, given the structures of the nucleobases. You are expected to know the structure of ribose, 2-deoxyribose, and of course a phosphate.

Nucleobase	Nucleoside (DNA)	Nucleotide (RNA)
$ \begin{array}{c} NH_2 \\ N \\ N \\ N \\ N \\ N \\ H \\ Adenine \end{array} $		
$ \begin{array}{c} $		
NH ₂ N N O H Cytosine		
O NH NH NH O H Thymine		X
O NH NH O H Uracil	X	

Lecture 13 HW Continued

2. Use the structures of the nucleobases and practice drawing the H-bonding patterns in DNA base pairing.

3. Look up the structures of the following pharmaceuticals online used in common-brand medicines (trade names and conditions they are used for in parenthesis). Rewrite them, and circle and name any heterocyclic substructure present in them. We are not looking for the actual IUPAC name of the pharmaceutical, just the name of the heterocycles present in them (such as pyridine, piperidine, etc.). *This is more for application of material to everyday life. You will not need to memorize the structures and names of heterocycles for the exam.*

- a) Loratadine (Claritin; allergies)
- b) Rosuvastatin (Crestor; hypercholesterolemia)
- c) Atorvastatin (Lipitor; hypercholesterolemia)
- d) Cimetidine (Tagamet; heartburn)
- e) Ciprofloxacin (Cipro; antibiotic)
- f) Tioconazole (Vagistat-1; antifungal)
- 4. Check the structures of the heterocycles mentioned below and explain why...

a) Pyrrole (pK_a = 17.5) is more acidic than pyrrolidine (pK_a \approx 35)

- b) The conjugate acid of pyrrole ($pK_a = 0.4$) is more acidic than the conjugate acid of pyrrolidine ($pK_a = 11.3$)
- c) Pyrimidine (pK_a conj. acid = 1.3) is less basic than pyridine (pK_a conj. acid = 5.25)
- d) Pyridine ($pK_a \text{ conj. acid} = 5.25$) is less basic than piperidine ($pK_a \text{ conj. acid} = 11.2$)
- e) N7 in purine (pK_a conj. acid = 2.4) is less basic than N3 in imidazole (pK_a conj. acid = 6.95)
- f) H on purine's N9 ($pK_a = 8.9$) is more acidic than H on imidazole's N1 ($pK_a = 14.2$)
- g) Imidazole (pK_a conj. acid = 6.95) is more basic than pyrimidine (pK_a conj. acid = 1.3)

5. Consider Risperidone, a drug used to treat schizophrenia and bipolar disorder, shown below; pK_a (B⁺H) = 7.91. Circle the most basic nitrogen and 'X' out any non-basic nitrogens.



Lecture 14 HW

1. Propose a mechanism for the deamination of cytosine catalyzed by acid. I hope you've realized by now that <u>you're not expected to memorize each new mechanism</u>! Instead, you should be gaining an understanding of reasonable electron flow to lead to the observed product. With this, you can predict the mechanism of almost any reaction, regardless of whether you've seen it before! That being said, parts of this mechanism should be familiar!



2. One of the drawbacks of eating nitrite-cured meats is potential for nucleobase mutation, although at low concentration the risk is low. Everything in moderation! Several intermediates are given for such a mutation. Propose reasonable mechanisms for each step, using **:B** and **H**⁺ for bases and acids, respectively. This is a more involved version of problem #2.



3. Draw the full structures of the ribonucleotides A & G, then draw the mechanism for the reaction between the two, leading to the formation of the A-G dinucleotide. Include the pentacoordinate phosphate intermediate. It is definitely OK to abbreviate the nucleobases in the intermediate and product!

4. Show the mechanism for the hydrolysis (cleavage) of the A-G dinucleotide.

5. Associate each one of the following terms with one of the three phases: pharmaceutical, pharmacokinetic, pharmacodynamic

- (a) absorption
- (b) dosage form
- (c) receptor
- (d) metabolism
- (e) binding site
- (f) elimination
- (g) excipient
- (h) oral administration

6. Classify each method of drug administration as enteral or parenteral:

- (a) Inhalation
- (b) Subcutaneous
- (c) Rectal
- (d) Intravenous
- (e) Oral
- (f) Topical
- (g) Intramuscular
- (h) Sublingual

7. Consider the following local anesthetic agents and find the pharmacophore.



8. Consider the following local anesthetic agents and find the pharmacophore.



9. Calculate the therapeutic index of a drug that produces a toxic effect in 50% of the test population at a dose of 85 mg/kg and has a therapeutic effect in 50% of the test population at a dose of 100 μ g/kg. Is this a better drug than a similar one with a therapeutic index of 100? Justify your answer.

Lecture 15 HW

1. Look up the structures of the following drugs and predict if they are soluble in water. If not, what could you do to increase its solubility? Does pH affect the solubility potential?

- (a) Ropivacaine (see previous page)
- (b) Mephophenobarbital (or mephobarbital)
- (c) Indomethacin

2. Propose a structure for the active metabolite of Famciclovir, an antiviral agent. In other words, which bonds are likely to be hydrolyzed and what would be the resultant structure?



3. Calculate the solubility potential of Penicillin G and Isopenicillin N using the solubility potential table from lecture 16.



Lecture 16 HW – Carry out the 9 starred mechanisms from the Lecture 16 notes (copied below) using acids (H^+) and bases (:B).







