DO NOT BEGIN THE EXAM OR TURN THE PAGE UNTIL INSTRUCTED TO DO SO.
In the meantime, please read the instructions below.

In each of the following problems, use your knowledge of organic chemistry conventions to answer the questions in the proper manner. **Be sure to read each question carefully.** You have 2.5 hours to complete this exam. Point distributions are given throughout the exam so you can use your time wisely. **Skip page 7 or 8 and draw a large “X” through that page.**

Keep your eyes on your own paper. Electronic devices of any kind are not allowed, including cell phones and calculators. Any student found using any of said devices, or found examining another student’s exam, will be promptly removed from the exam room and at minimum will receive a zero on this exam. Such an incident may also be considered a form of academic dishonesty and reported to the UCSC Judiciary Affairs Committee.
1. Functional Groups & Acid-Base

(a) (30 points) Provide the name of each functional group in the box below each molecule.

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</tbody>
</table>

(b) (10 points) Circle all of the basic nitrogens in nicotine and risperidinone. For each compound, put a star (*) next to the N that you would predict to be the most basic. Hint: the pKa of the conjugate acid of pyridine is significantly lower than that of alkyl amines.

(c) (10 points) The pKa of purine (8.9) is significantly lower than a secondary alkyl amine such as diethylamine (pKa 35). Draw the conjugate base of each and briefly explain this large difference in acidity in ten words or less.
2. Nucleic Acids

(a) (20 points) Consider the structures of the nucleobases below. Indicate each atom that has the potential to serve as an H-bond donor (D) or H-bond acceptor (A). Circle the atoms that participate in G-C and A-T base pairing.

(b) (10 points) Draw the nucleoside of adenine and nucleotide of thymine as DNA monomers.

(c) (10 points) Draw the A-T dinucleotide in DNA form. You may abbreviate the nucleobase portions of the structure as “A” and “T.”
3. Medicinal Chemistry

(a) (10 points) Indicate whether cephalaxin and penicillin G are more likely to be absorbed through the membranes in stomach lining (pH 2) or intestinal walls (pH 8). The structures provided show the dominant ionic form under physiological conditions (pH 7.4).

Circle one:
Stomach
Intestines

Cephalaxin
(a cephalosporin)

Penicillin G

(b) (20 points) Identify the pharmacophore common in the following antiviral agents. Omit double bonds.

Vidarabine

Famciclovir

Ganciclovir

Acyclovir

Pharmacophore
4. Medicinal Chemistry - Absorption

Table 1. Solubility Potential

<table>
<thead>
<tr>
<th>Functional Group</th>
<th>Solubility Potential (in a polyfunctional molecule)</th>
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<tbody>
<tr>
<td>Alcohol</td>
<td>3-4 carbons</td>
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<tr>
<td>Phenol</td>
<td>3-4 carbons</td>
</tr>
<tr>
<td>Amine</td>
<td>3 carbons</td>
</tr>
<tr>
<td>Carboxylic acid</td>
<td>3 carbons</td>
</tr>
<tr>
<td>Ester</td>
<td>3 carbons</td>
</tr>
<tr>
<td>Amide</td>
<td>2-3 carbons</td>
</tr>
<tr>
<td>Ether</td>
<td>2 carbons</td>
</tr>
<tr>
<td>Aldehyde</td>
<td>2 carbons</td>
</tr>
<tr>
<td>Ketone</td>
<td>2 carbons</td>
</tr>
<tr>
<td>Urea</td>
<td>2 carbons</td>
</tr>
<tr>
<td>Charged groups</td>
<td>20-30 carbons</td>
</tr>
<tr>
<td>(N+: ammonium salts; O#: carboxylates, phenolates, sulfates; N#: sulfonamides)</td>
<td></td>
</tr>
</tbody>
</table>

(a) (10 points) Use the solubility potential table to determine whether Oxycodone and Iriomoteolide-1a are water-soluble. Circle your answer.

(b) (30 points) Circle and name the two functional groups on valium that contribute to its solubility potential (see Table 1 above). Calculate the solubility potential of valium and report whether it is soluble or not as shown. Explain in 10 words or less why/how valium can be soluble in the extracellular fluid and the cytoplasm (aqueous conditions at roughly neutral pH), but still passes through the non-polar cell membrane.
5. The Morphine Page!

(a) (10 points) Draw the structure of (S)-N-Methylcoclaurine, the product of two successive reactions with S-adenosyl methionine (SAM) with the heteroatoms in bold on (S)-Norcoclaure. 

(b) (10 points) Draw the structure of salutaridinol, the product of the reaction of salutaridine with NADPH.

(c) (10 points) Add the arrows to complete the mechanism in the biosynthesis thebaine. Use an acid (H⁺) or base (:B) if necessary.
Biosynthesis of $\beta$–Lactam Antibiotics

**Amoxicillin**, a common antibiotic, is biosynthesized from three amino acids. A tripeptide is formed and the side chains react to give the bicyclic ring structure shown below.

(a) (5 points) **Circle the three separate portions** of the molecule that are derived from **two common amino acids and one uncommon amino acid**.

![Amoxicillin](image)

(b) (5 points) What are the names of the two common amino acids circled in part (a)?

_______________________ & __________________________

(c) (20 points) Connect those three amino acids to **draw the corresponding tripeptide** (if all else fails, at least draw a simple tripeptide!).

**Tripeptide pre-cursor to amoxicillin (include stereochemistry):**
Morphine Biosynthesis

The first cyclization reaction in the biosynthesis of morphine involves the coupling of tyrosine derivatives dopamine and \( p \)-hydroxyphenylacetaldehyde. These two react to form an iminium intermediate. Subsequent electrophilic aromatic substitution facilitates cyclization, producing (S)-Norcoclaurine.

Use the materials below along with appropriate amino acid residues as acids and bases to show the full arrow-pushing mechanism of the reactions below within the enzyme active site. Each reaction requires at least one intermediate. No stabilizing factors such as H-bonds are necessary.

(a) (15 points) Redraw the reactants (no arrows to or from the structures provided) in the space provided. You may abbreviate parts of structures not directly involved in the mechanism.

(b) (15 points) Begin the arrow pushing on the iminium provided and continue the mechanism in the space below. You may abbreviate parts of structures not directly involved in the mechanism.

CHOOSE EITHER PAGE 7 OR 8. DRAW A LARGE “X” OVER THE PAGE TO SKIP.
Lipid Biosynthesis
The first step in the mevalonate pathway is a Claisen condensation to yield acetoacetyl CoA:

1. The acetyl group is first bound to the enzyme by a nucleophilic acyl substitution reaction with the thiol group of a cysteine residue.
2. Formation of an enolate ion from a second molecule of Acetyl CoA is followed by Claisen condensation to yield the product.

Draw the product after both steps in the boxes provided. Use the appropriate amino acid residues as acids and bases to show the full arrow-pushing mechanisms for each step. Amino acids must start in the natural physiological state and recycled through the pathway. Each mechanism requires at least one intermediate. Stabilizing factors such as H-bonds are not necessary.

Redraw the components – please do not draw any arrows to or from the structures provided!
Have a great summer!