

Name \_\_\_\_\_

PHAR 332 SPRING 2006  
FUNDAMENTALS OF DRUG ACTION II  
EXAM 4 - FINAL EXAM

To preserve privacy and to help identify your exam  
WRITE YOUR NAME ON THE **SECOND PAGE** also.  
You may also wish to write your name on the rest of the pages of the exam.

**DIRECTIONS**

Sit in the assigned seat. This is a two-hour exam, worth 240 points. The exam is closed-book; no aids are permitted. Answer all questions completely and accurately. In the multiple choice questions, indicate your answer by circling the letter of the correct response. Draw chemical structures clearly and complete them to the degree necessary to clearly indicate your answer; you may use abbreviated structures where they are appropriate, but use care in abbreviating your structures. In the essay questions, use good English; your score will reflect your use of proper English as well as the scientific content of your answer. The exam has 13 (thirteen) pages; check your exam to make sure it is complete.

***Warning! Cheating on an exam may result in failing the exam, dismissal from the course, and/or other penalties!***

We reserve the right to photocopy your exam for our files.

Name \_\_\_\_\_

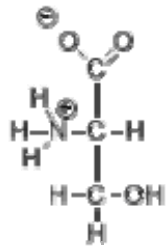
<u>PROBLEM</u>	<u>SCORE/POSSIBLE</u>	
I	_____/ 20	Dr. Woodbury
II	_____/ 10	Dr. Woodbury
III	_____/ 30	Dr. Woodbury (60 points total)
IV	_____/ 25	Dr. Bolton
V	_____/ 23	Dr. Bolton
VI	_____/ 28	Dr. Bolton
VII	_____/ 18	Dr. Bolton
VIII	_____/ 40	Dr. Bolton
IX	_____/ 21	Dr. Bolton
X	_____/ 25	Dr. Bolton (180 points total)
<b>TOTAL</b>	_____/ 240	
BONUS	_____/02	

Name \_\_\_\_\_

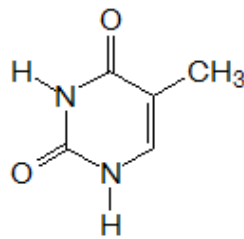
I. (20 pts total; 5 pts each) Fill in the blanks with the appropriate word, phrase, or abbreviation.

1. In the biosynthesis of L-serine, the amino group comes from the amino acid \_\_\_\_\_ through the action of an amino transferase.
2. The two major pathways for biosynthesis of nucleotides are *de novo*, and \_\_\_\_\_.
3. In treating certain cancers, the compound \_\_\_\_\_ is used to form a “suicide” substrate (inhibitor) of thymidylate synthase.
4. Lesch-Nyhan syndrome results from the absence of activity of the enzyme \_\_\_\_\_.

II. (10 pts total; 5 pts each) Name the compounds correctly. Correct abbreviations are acceptable.



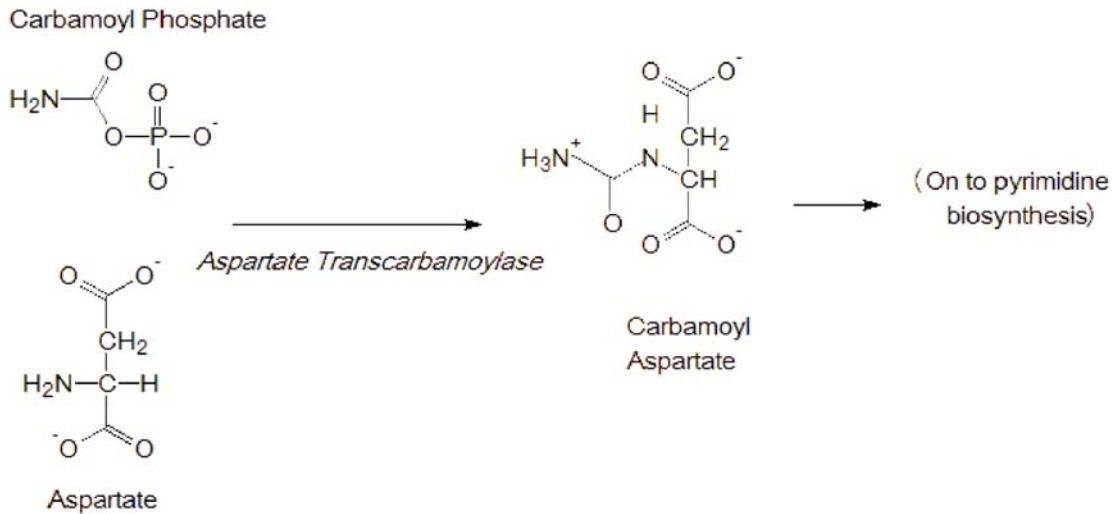
1. \_\_\_\_\_



2. \_\_\_\_\_

III. (30 pts total; 15 pts each) Short answers, please - one or two paragraphs at most.

1. The committed step in pyrimidine biosynthesis is catalyzed by the enzyme aspartate transcarbamoylase. This enzyme is inhibited by high levels of UMP (uridyl monophosphate; uridylate). Explain why this pattern of inhibition is a good metabolic strategy.



2. Explain why tyrosine would be considered an essential amino acid for a person with classical phenylketonuria (PKU) who is on a diet restricted in phenylalanine.

**DRUG METABOLISM AND CHEMICAL TOXICOLOGY - Dr. Bolton**

IV. (25 pts total; 5 pts each) Answer the questions on drug metabolism and chemical toxicology below.

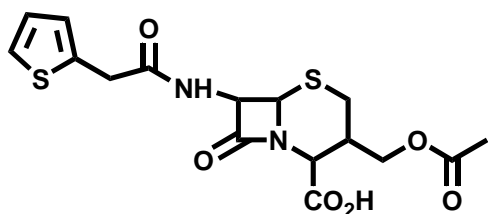
1) (5 pts) Mercapturic acid derivatives in phase II metabolism can result from reactions of:

(circle the correct answer)

- a. glutathione conjugates.
- b. glucuronide conjugates.
- c. glycine conjugates.
- d. glutamate conjugates.
- e. sulfate conjugates.

2) (5 pts) The major pathway for the biotransformation of the following compound is by hydrolysis.

Clearly identify the site which would be most susceptible to hydrolysis.



3) (5 pts) Which of the following metabolic reactions is NOT a **Phase I reaction**?

(circle the correct answer)

- a. Oxidation
- b. Conjugation
- c. Hydrolysis
- d. Reduction

4) (5 pts) Which of the following ARE NOT **Phase-I enzymes**?

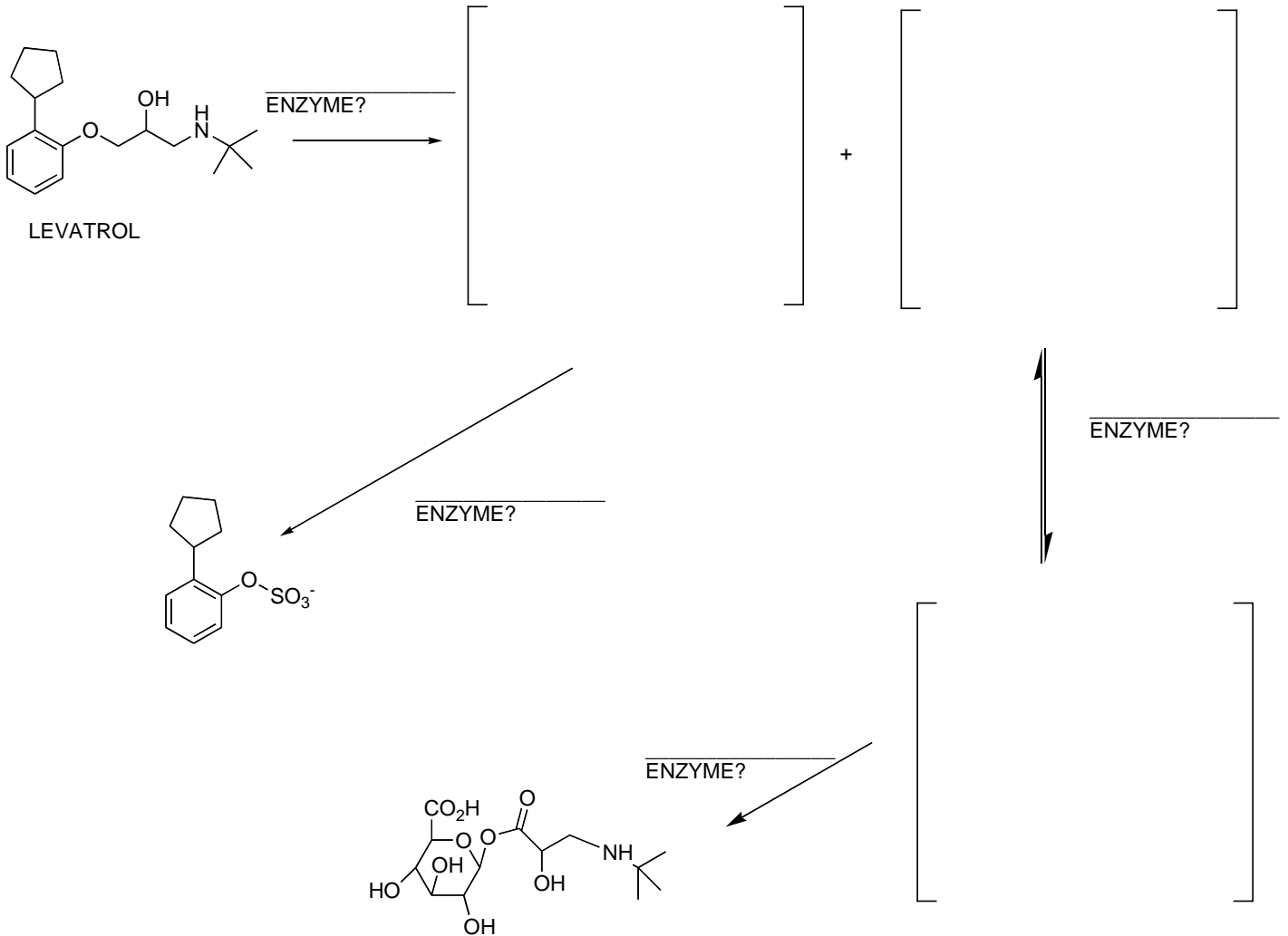
(circle the correct answer)

- a. Cytochrome P450
- b. Sulfotransferase
- c. Epoxide hydrolase
- d. Alcohol dehydrogenase
- e. Quinone reductase

5) (5 pts) The metabolically-based interaction between alcohol (ethanol) and acetaminophen is based on: (circle the correct answer)

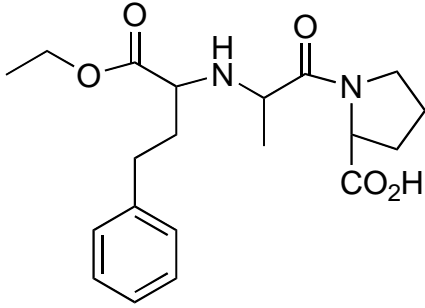
- a. Ethanol-based induction of a P-450 isoform responsible for the metabolism of acetaminophen.
- b. Ethanol-based inhibition of a P-450 isoform responsible for the metabolism of acetaminophen.
- c. Acetaminophen-based induction of a P-450 isoform responsible for the metabolism of ethanol.
- d. Acetaminophen-based inhibition of a P-450 isoform responsible for the metabolism of ethanol.

V. (23 pts) Levatol is a synthetic b-receptor antagonist used to treat arterial hypertension. It could be metabolized as shown below. Give the enzymes catalyzing each reaction and draw the structures of the intermediate metabolites.



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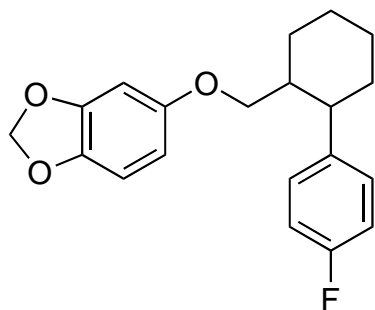
VI. (28 pts.) The structure of enalapril (ACE inhibitor used to treat hypertension) is shown below. Give three different phase I metabolites of enalapril (Hint there is at least 6 different phase I metabolites). Name the enzymes catalyzing each reaction. Make sure you do not repeat the same metabolic pathway on a different part of the molecule. Show how one of your metabolites could be metabolized in a phase II reaction and name the enzyme catalyzing the reaction.



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VII. (18 pts total)

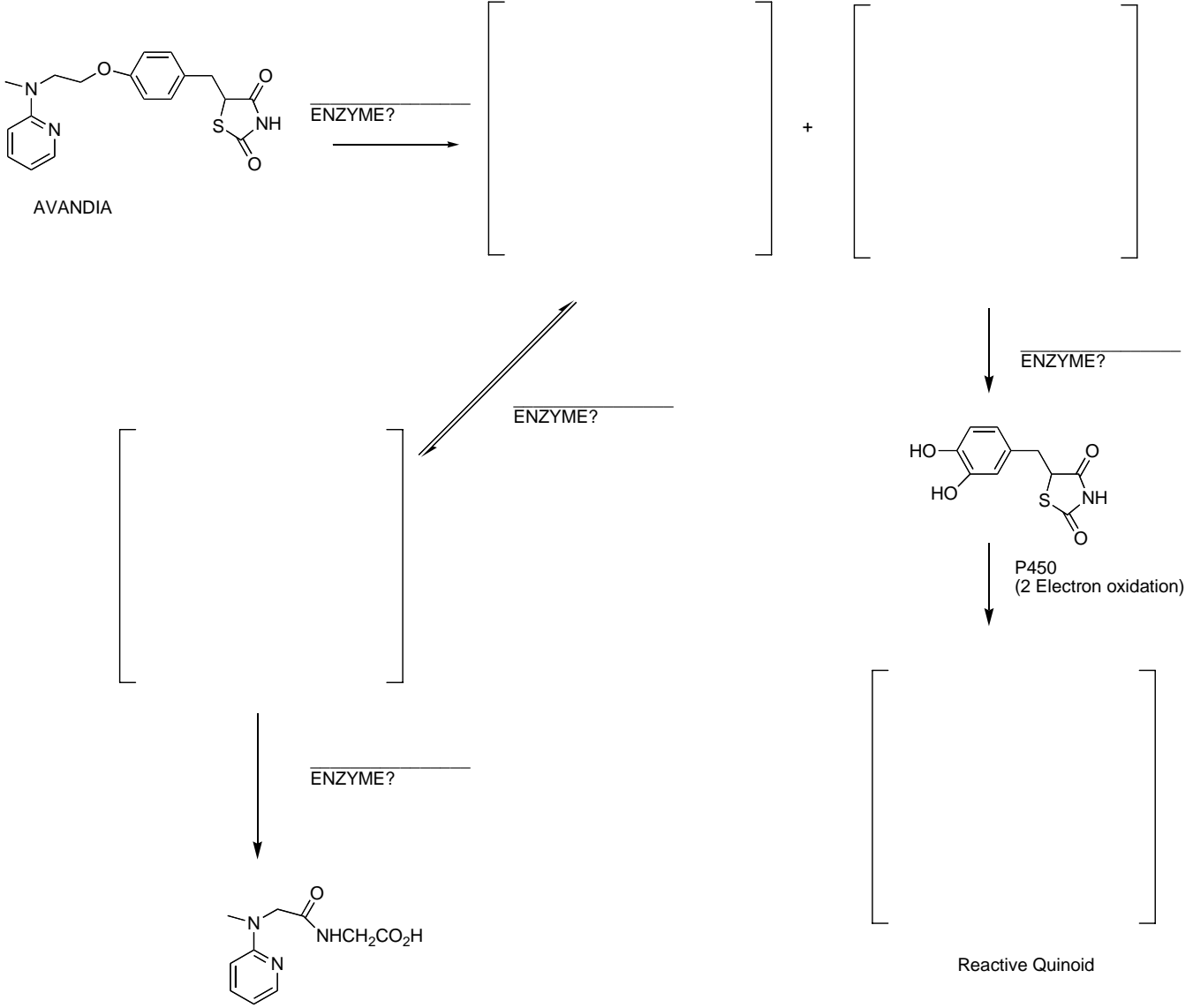
a. (6 pts) Paxil (paroxetine) can be metabolized by P450 to a phenol. Circle the ring which would be hydroxylated and briefly explain why.



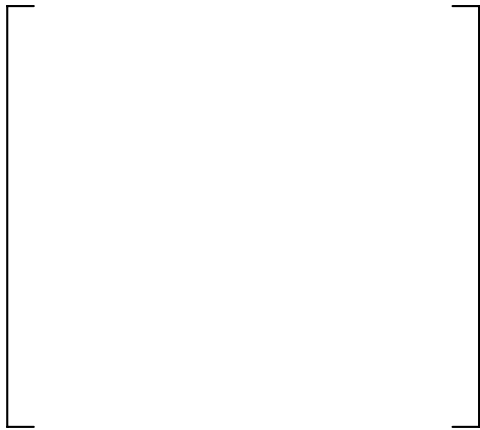
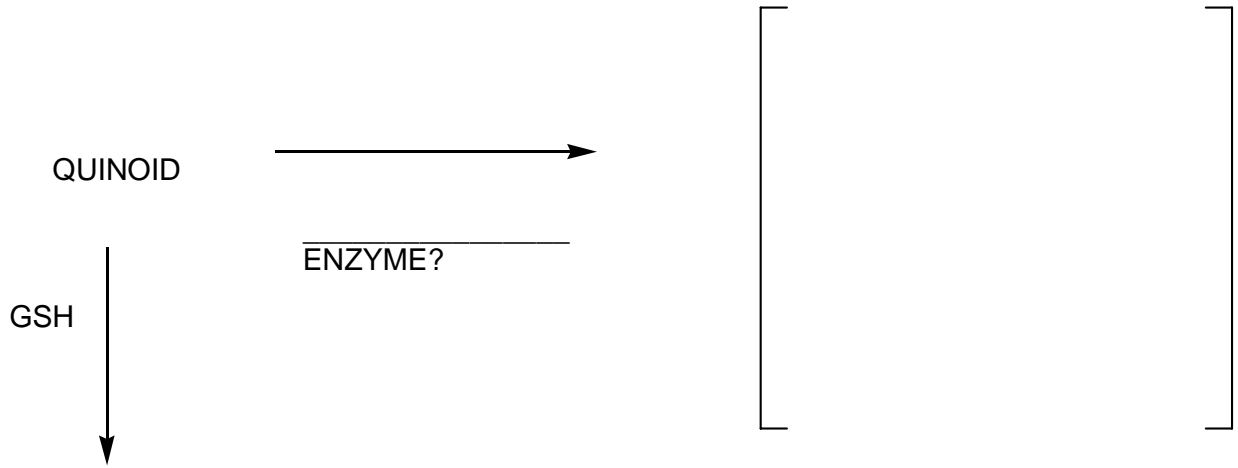
b. Show conjugation of your phenol metabolite with sulfate and name the enzyme catalyzing the reaction (12 pts)

VIII. (40 pts total)

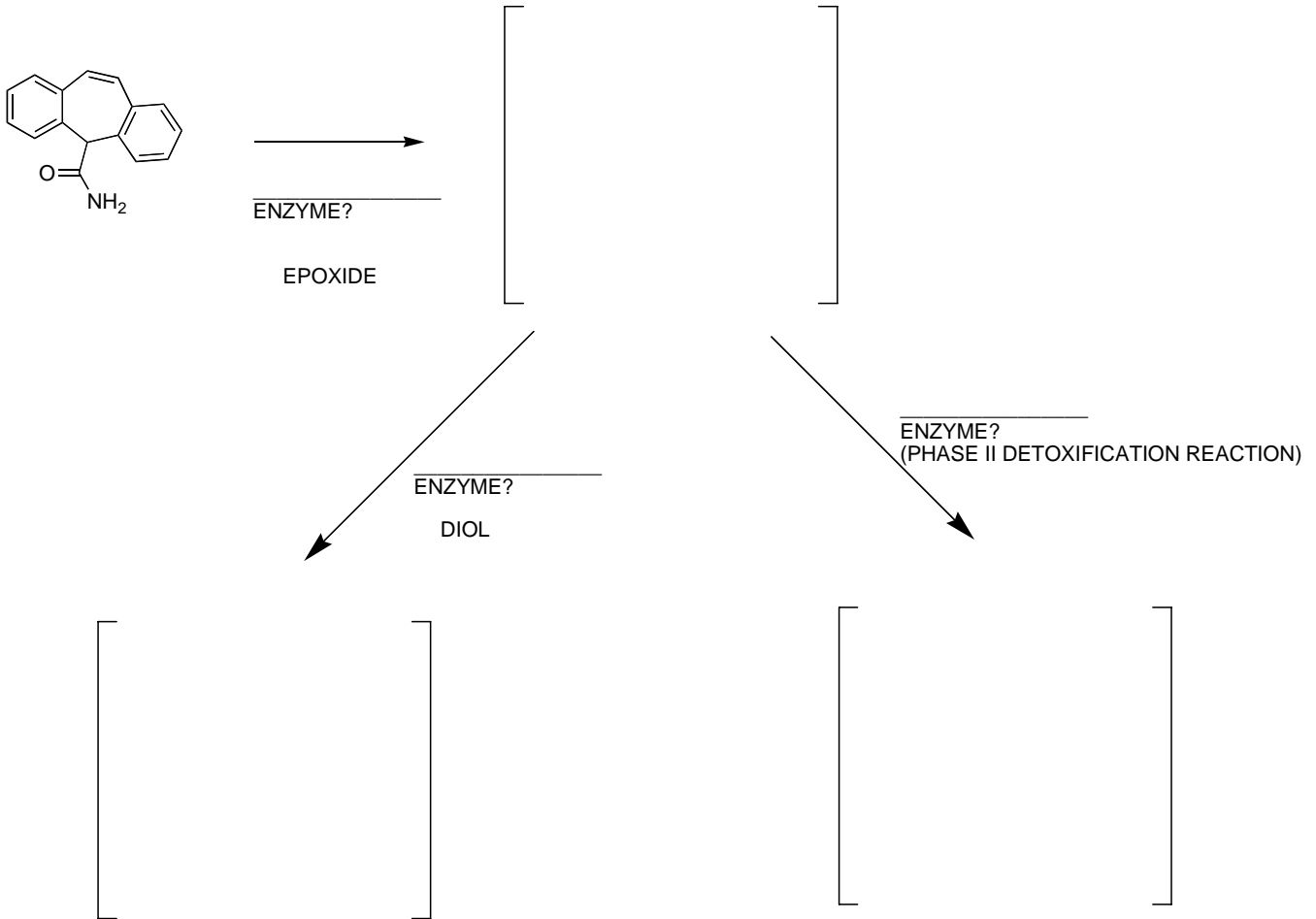
a. (28 pts) Avandia could be metabolized by the pathway outlined below. Give the intermediate metabolites and provide names for the enzymes involved in each transformation.



VIII b) (12 pts) The reactive quinoid in (VIII a) could be detoxified by an enzyme catalyzed reaction or by direct reaction with GSH. Show the reaction products and name the enzyme involved.



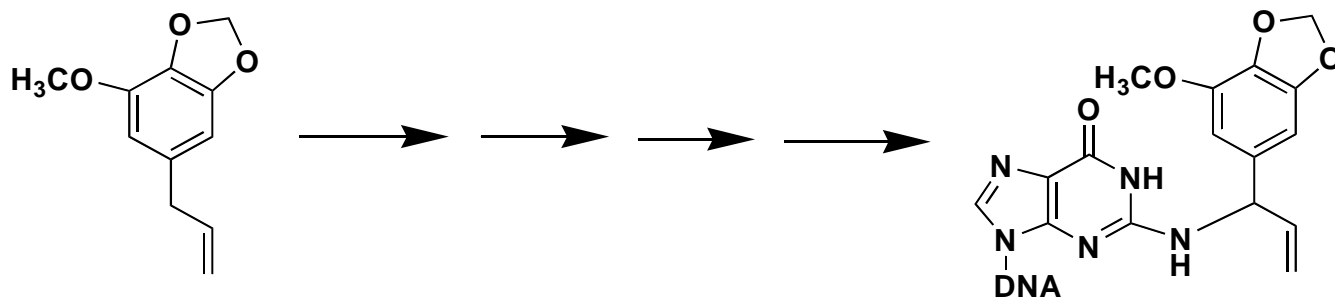
IX. (21 pts) Carbamazepine can be metabolized by the EPOXIDE/DIOL pathway. Give the structures of the metabolites and name the enzymes catalyzing the reactions. The epoxide can be detoxified by a phase II reaction. Give the structure of the phase II metabolite and name the enzyme catalyzing the reaction.



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- X. (25 pts) Myristicin is a component of nutmeg. It could be metabolized to a reactive intermediate which could alkylate DNA as shown below. Give the enzymes catalyzing each reaction and show the intermediate metabolites. Hint. There are three intermediates and only the first two steps are enzyme catalyzed.

Name the ultimate toxin (i.e. type of reactive intermediate): \_\_\_\_\_.



### BONUS POINT QUESTIONS

Each is worth ONE bonus point. Be sure you have finished with the other parts of the exam before attempting these questions.

A. Tetrahydrofolic acid (THF) is composed of three distinct parts: the amino acid glutamate, the benzoic acid derivative PABA, and a third component composed of a fused conjugated heterocyclic structure. What is the name of this third structural component?

B. In humans, cysteine is considered nonessential only if the diet contains adequate amounts of methionine. Explain why.