

University of Canterbury

End of Year Examinations 2005

Prescription Number(s):	CHEM 325 BCHM 302
Paper Title:	Biological Chemistry

Time Allowed: **THREE HOURS**

Number of pages: **EIGHT**

Answer **FIVE** questions.

This paper is in **THREE** sections.
At least **ONE** question must be
answered from **EACH** section.

All questions are of equal value.

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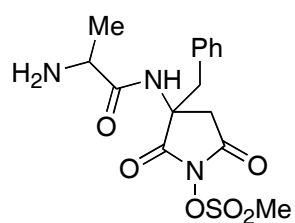
SECTION A

(Answer **AT LEAST ONE** question from this section)

- Provide a detailed mechanism for the Bergman cycloaromatisation of an enediyne to give a 1,4-benzenoid diradical.
 - Provide a detailed mechanism by which a 1,4-benzenoid diradical is able to cleave DNA. Include a brief reference to the structure of DNA in your answer.
 - Provide a detailed biological mechanism of action for the naturally occurring enediyne, **A**, below. Consider all aspects of the mechanism and refer to your answers to (a) and (b) above as appropriate.
 - Compare the 'trigger' component of **A** with an Fmoc amino acid protecting group. Consider aspects of deactivation and removal.

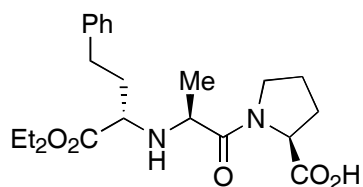


2. (a) For each of the **two** inhibitors below, propose a detailed mechanism of inhibition for the specified target enzyme.



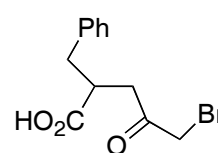
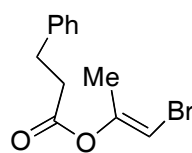
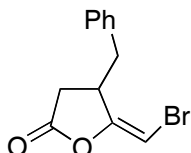
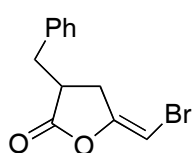
Target Enzyme

α -chymotrypsin



angiotensin-converting enzyme

- (b) For each of the following **four** compounds explain, with reasons, whether or not you would expect it to be a mechanism-based inhibitor of α -chymotrypsin?



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SECTION B

(Answer **AT LEAST ONE** question from this section)

3. Use the Michaelis-Menten description of enzyme-catalyzed reactions to exemplify and briefly explain each of the following aspects of (bio)chemical kinetics:
- (a) complex mechanism;
 - (b) elementary step;
 - (c) rate-determining step;
 - (d) catalyst;
 - (e) intermediate;
 - (f) species (or population) balance equation;
 - (g) steady-state approximation;
 - (h) (differential) rate law;
 - (i) linear least-squares fitting;
 - (j) non-linear least-squares fitting.

4. (a) (6 marks)

By studying the kinetics of an enzyme-catalyzed reaction, the values of the parameters R_{\max} (so-called ‘maximum rate’), k_2 (‘catalytic constant’ or ‘turnover number’) and K_M (‘Michaelis constant’) can be obtained.

- (i) Give the definition of each of the parameters R_{\max} , k_2 and K_M .
- (ii) Explain why it is of interest to know the value of each of R_{\max} , k_2 and K_M .

(b) (14 marks)

The following statement is from a textbook on *Fundamentals of Enzyme Kinetics*:

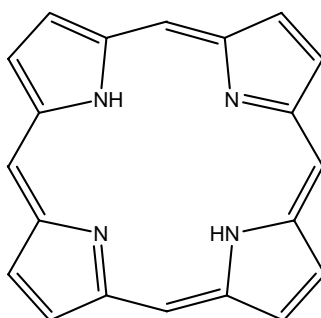
“The two limiting cases of inhibition are competitive and uncompetitive inhibition; pure non-competitive inhibition is simply a special case of mixed inhibition in which the two inhibition constants are equal.”

- (i) Briefly outline the four mechanisms of inhibitor action (competitive, uncompetitive, non-competitive and mixed) referred to above.
- (ii) Explain how kinetic studies show that “the two limiting cases of inhibition are competitive and uncompetitive inhibition”.
- (iii) Explain how kinetic studies show that “pure non-competitive inhibition is simply a special case of mixed inhibition”.
- (iv) What are “the two inhibition constants” that are referred to in the above statement?

SECTION C

(Answer **AT LEAST ONE** question from this section)

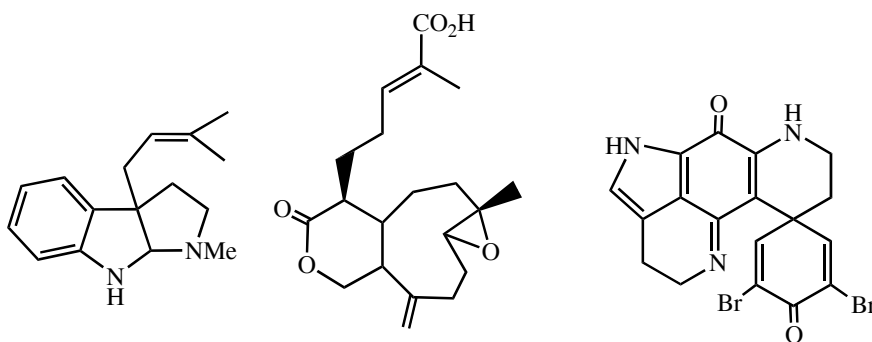
5. Porphyrin (shown below) and its substituted derivatives are excellent ligands that are used in a wide range of biological systems.



- (a) Explain why they are such good ligands.
- (b) Why is this kind of ligand an excellent choice for use in the active site of many electron-transport proteins?
- (c) Discuss whether or not porphyrin ligands could be used as siderophores.
- (d) Outline how model compounds can be used to validate mechanistic proposals for the reactions catalysed by hydrolytic enzymes, such as carboxypeptidase.
6. Describe, in detail, the different ways in which a lead structure can be identified and developed into a potential pharmaceutical. Give detailed examples to illustrate your answer and discuss the key technical aspects of any methodology that you propose.

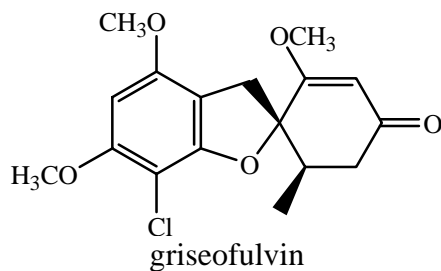
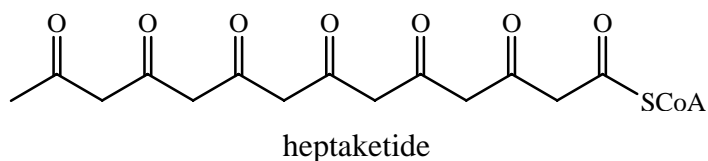
7. (a) (12 marks)

What are the biosynthetic origins of **each** of the following compounds. For each compound indicate (delineate) the “building blocks” of each structure and other features relevant to the biosynthetic origins of the compound (*ie* isoprene and polyketide chains, shikimic acid, the starter unit, SAM, O atoms lost, *etc.*).
[Note that some compounds could be of “mixed” biosynthetic origin.]



(b) (8 marks)

Griseofulvin is of polyketide origin and is formed from a heptaketide unit. This polyketide chain can be folded in more than one way to produce griseofulvin. Draw two **alternative** folding patterns for the polyketide chain that would fit the observed structure and functionality of griseofulvin.



END OF PAPER

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