University of Canterbury

End of Year Examinations 2007

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

Time Allowed:	TWO HOURS
Number of pages:	SIX

This paper is divided into TWO sections.

Answer **TWO** questions from each section.

All questions are of equal value.

TURN OVER

SECTION A

(Answer **TWO** questions from this section.)

1. (a) Outline the ways that a metal ion can promote the hydrolysis of an ester or amide.

   (b) Many metalloenzymes that catalyse hydrolytic reactions employ a Zn^{2+} ion at the active site. Discuss the factors that make Zn^{2+} a good choice for this role.

   (c) Discuss the possibility that more than one metal ion could contribute to the structure and activity of an enzyme active site.

2. The selective binding and release of metal ions is critical to many living organisms. Discuss the means by which such selectivity can be achieved, making use of examples (both naturally occurring and synthetic) in which Na^{+}, K^{+} and Fe^{3+} ions are transported.

3. (a) Metal ions are used in biology in both enzyme systems (e.g. hydrolytic enzymes) and transport systems (e.g. electron transport, oxygen transport). Comment on the properties that would be desirable for a metal ion in each kind of system and then use this as a basis on which to identify possible or likely metal ions for each kind of system.

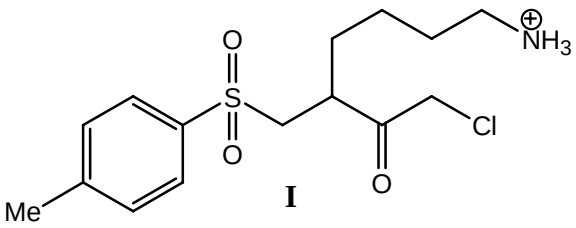
   (b) Outline some of the ways in which model compounds can help us understand the chemistry that is occurring in bioinorganic systems. Give examples.

SECTION B

(Answer **TWO** questions from this section.)

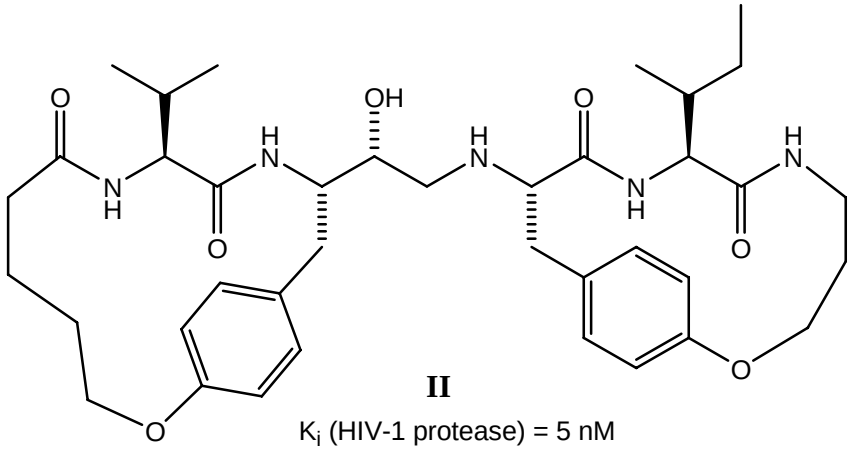
4. Give a critical account of the interaction of proteases with substrates and inhibitors. Your account should cover more than one class of protease and incorporate a wide range of specific examples. You should discuss natural and synthetic substrates and inhibitors. You should also include detailed explanations of the following observations (a) and (b):

(a) Compound **I** is a selective irreversible inhibitor of trypsin;



I

(b) Compound **II** is a selective tight-binding inhibitor of HIV protease.



II

K_i (HIV-1 protease) = 5 nM

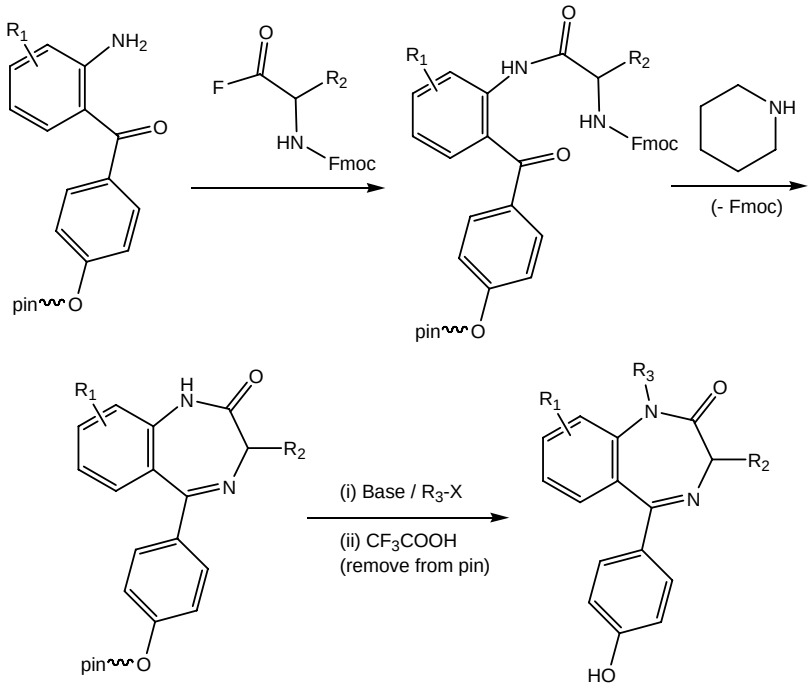
5. A review by Professor Peter Schultz (*Acc. Chem. Res.* **1996,** *29,* 164-170) started with the following introduction:

> "Nature has produced a remarkable array of molecules that perform the complex processes of living organisms, from the immune response and catalysis to signal transduction and gene regulation. However, in contrast to chemists who typically synthesize and characterize a single molecule at a time, Nature draws upon a vast combinatorial library of precursor molecules and screens them for desired properties. Perhaps the most notable example of this strategy is the immune system, which is capable of generating tremendous molecular diversity via gene rearrangements and somatic mutation and screening this diversity for high-affinity, selective receptors to foreign antigens. This natural example of the power of combinatorial processes has inspired chemists and biochemists alike to apply this strategy to other problems, ranging from catalysis and drug discovery to materials science."

Give a critical account of combinatorial chemistry and the way its development relates to an understanding of the way in which the immune system accomplishes efficient molecular recognition. Incorporate a wide range of specific examples. In your essay you should include a discussion of **one** of the following examples (a) and (b).

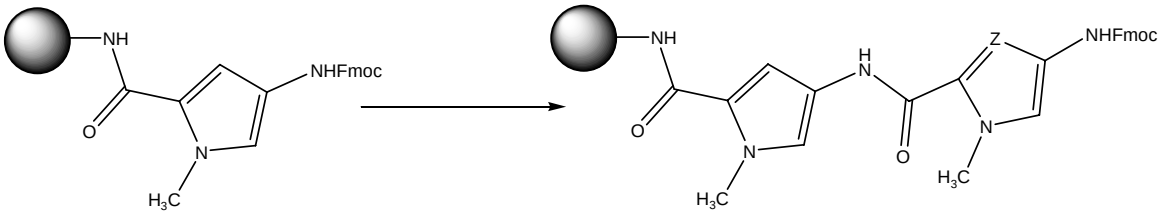
(a) Solid phase synthesis of oligopeptides on 8 x 12 arrays of polyethylene pins has been successfully used for antibody epitope mapping.

(b) Pin-based combinatorial libraries of benzodiazepines have been prepared to identify potential drug targets using chemistry described in the following scheme.



6. (a) Many treatments for cancer are based on the binding of small molecules to DNA. Give a critical account of the interaction of small molecules with DNA. Illustrate your essay with a wide range of specific examples.

(b) Explain the methodology by which specific sequences of DNA can be recognized by small molecules and oligomers. In your answer, include an explanation for the fact that the synthesis of polyamides containing *N*-methylimidazole (Z = N) and *N*-methylpyrrole (Z = CH) units (as outlined below) is a powerful tool for sequence-specific recognition of DNA.



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