

University of Canterbury

Mid Year Examination and Test Period 2007

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

Time Allowed: 2 HOURS

Number of pages: TEN

Answer **ALL** questions

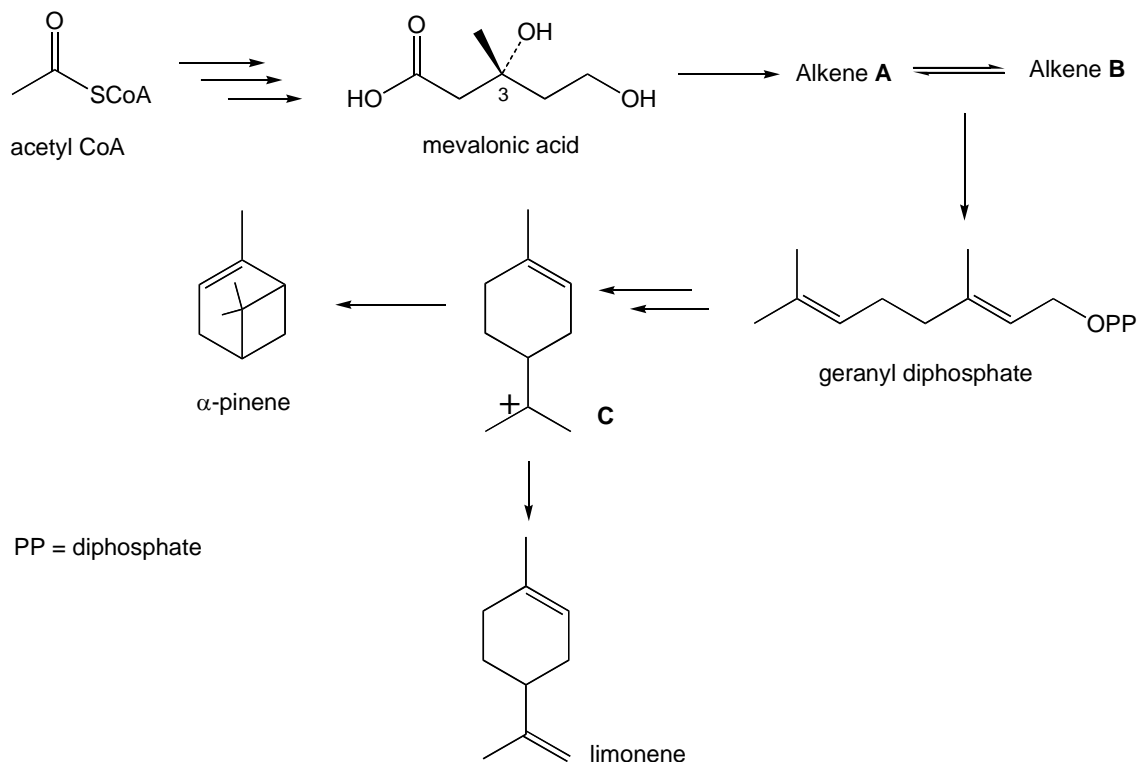
Total marks = 120

You should allocate about 1 minute
per mark

TURN OVER

1. (14 marks)

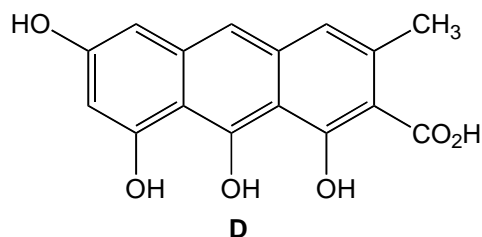
In the mevalonate biosynthetic pathway to terpenes, acetyl CoA is converted to mevalonic acid and hence to geranyl diphosphate, as shown in the scheme below.



- (a) Assign the configuration (*R* or *S*) of C-3 in mevalonic acid. (2 marks)
- (b) Give structures for **A** and **B**. (4 marks)
- (c) Give mechanisms for the following:-
- Coupling of **A** and **B** to form geranyl pyrophosphate (2 marks)
 - Cyclisation of geranyl pyrophosphate to **C** (2 marks)
 - Conversion of **C** to α -pinene and limonene (4 marks)

2. (8 marks)

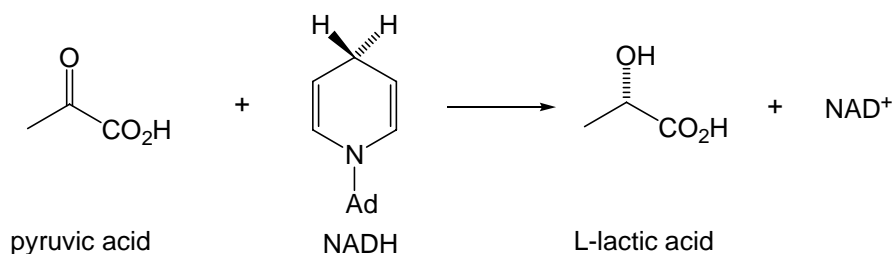
The aromatic compound **D** is derived from a polyketide biosynthetic pathway



- (a) Give the structure of the enzyme (PKS) bound polyketide chain and give mechanisms to illustrate how cyclisation occurs to give **D**
- (b) Which carbon atoms in **D** would be labelled if the organism producing **D** was fed sodium [2-¹³C] acetate?

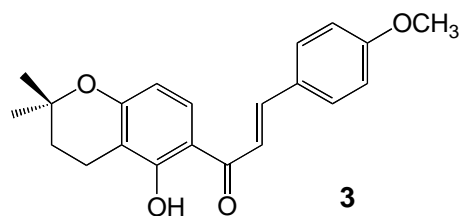
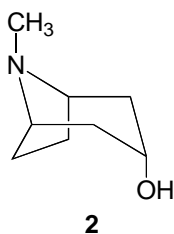
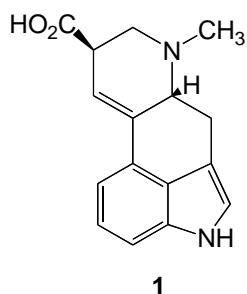
3. (8 marks)

The enzyme catalysed reduction of pyruvic acid to L-lactic acid is shown below.



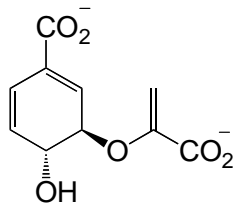
- (a) Label the pro-*R* and pro-*S* hydrogens of NADH
- (b) Give a mechanism for the reduction of pyruvic acid and the structure of NAD⁺
- (c) Does attack of hydride occur on the *Re* or *Si* face of the ketone to give L-lactic acid?

4. (a) Suggest biosynthetic origins for compounds **1**, **2** and **3** below. (6 marks)
- (b) What isotopically-labeled precursors could be used to test your biogenetic hypotheses as to the origins of each of these compounds? (6 marks)

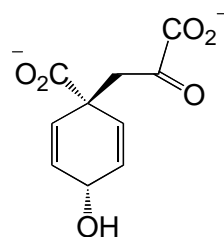


5. (3 marks)

One of the most remarkable reactions in secondary metabolism is the conversion of chorismic acid to prephenic acid. How does this transformation proceed? Why is it considered a remarkable reaction?



Chorismic acid



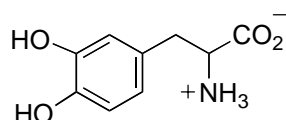
Prephenic acid

6. (15 marks)

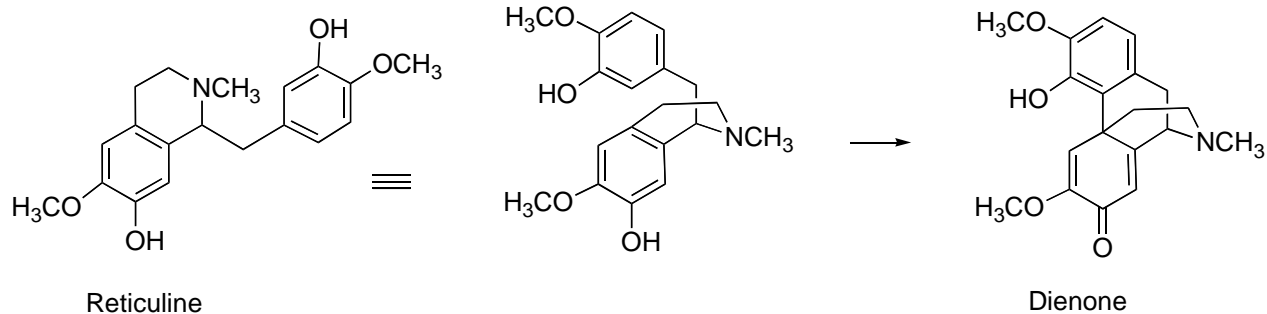
Answer **EITHER** (a) **OR** (b).**Either**

(a) Transamination and decarboxylation are frequently encountered reactions in biosynthesis. Pyridoxal phosphate is the co-factor for each reaction.

(i) What are the products from transamination and decarboxylation reactions on DOPA?



DOPA (dihydroxy-phenylalanine)

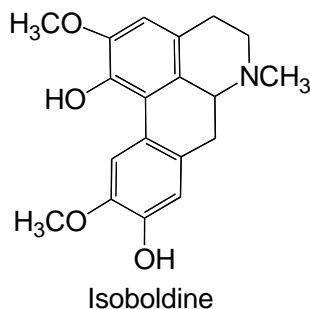
(ii) Reticuline is a precursor of morphine. Identify the products of transamination and decarboxylation reactions on DOPA **within** the reticuline structure.

Reticuline

Dienone

(iii) Show how reticuline can be converted to the dienone.

(iv) Reticuline can also be converted to isoboldine. Suggest how isoboldine can be formed.



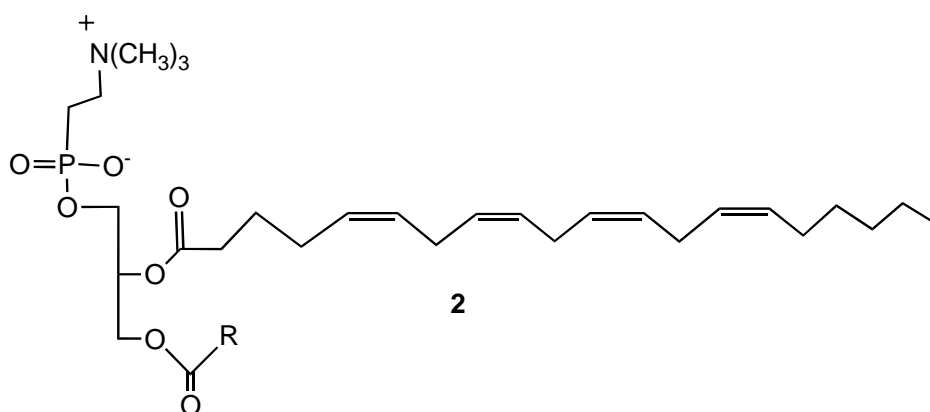
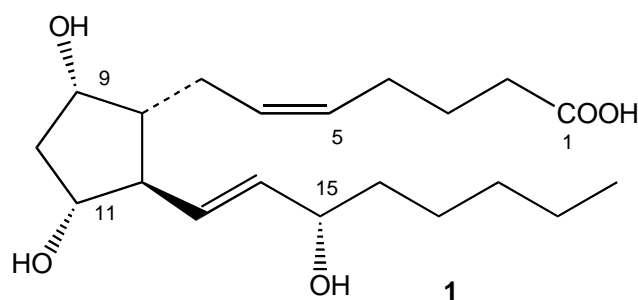
Isoboldine

Question 6 continued on following page

*Question 6 continued***OR**

(b) Arachidonic acid is the biosynthetic precursor for the prostaglandins.

- (i) Outline the steps in the biosynthesis of PGF_{2α} **1** from lecithin **2**.
- (ii) If ¹⁸O₂ were used in a biosynthetic experiment what positions in PGF_{2α} would be labelled?
- (iii) What are the differing roles ascribed to COX-1 and COX-2?
- (iv) What are the supposed attributes of COXIBs over NSAIDs?

**TURN OVER**

7. (30 marks)

Answer any **THREE** of the following **four** parts (a) – (d).

(a) The Michaelis-Menten equation for the rate of an enzyme-catalyzed reaction is:

$$v = \frac{k_{\text{cat}}[E]_0[S]}{K_M + [S]}$$

- (i) Define the five variables, v , k_{cat} , $[E]_0$, $[S]$ and K_M in this equation and provide common units for these variables.
 - (ii) Explain why K_M alone is not a sufficient measure of the ability of a compound to act as a substrate for an enzyme. Which parameter (or combination of parameters) is used to best describe the **effective reactivity** of substrate for a particular enzyme?
- (b) Various **assumptions** are made in deriving the Michaelis-Menten equation, including:
- the steady state approximation;
 - No back reaction occurs;
 - $[S] \sim [S]_0$.

Discuss these assumptions and **explain** their role in the derivation of the Michaelis-Menten equation.

(c) An inhibitor is a substance that changes the rate of an enzyme-catalyzed reaction. Types of inhibiting action include ‘competitive inhibition’ and ‘uncompetitive inhibition’.

- (i) **Briefly outline** these two mechanisms of inhibitor action.
- (ii) If the mechanism of inhibitor action is purely **competitive**, then the following rate expression holds, where V_{max} , K_M and K_I are kinetic constants:

$$v = \frac{V_{\text{max}}[S]}{K_M \left(1 + \frac{[I]}{K_I} \right) + [S]}$$

Using your mechanism for competitive inhibition from part (i), **show** how this rate expression is derived.

Question 7 continued on following page

Question 7 continued

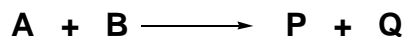
- (d) Kinetic data for enzyme-catalyzed reactions are often displayed in a linear form. Two common linear plots are the **Lineweaver-Burk** plot and the **Eadie-Hofstee** plot. **Show** how these plots are constructed, and **explain** which of these plots is more likely to give an accurate representation of the kinetic data.

Question 8 is on following page

8. (30 marks)

(a) (8 marks)

For the following two-substrate, two-product reaction:

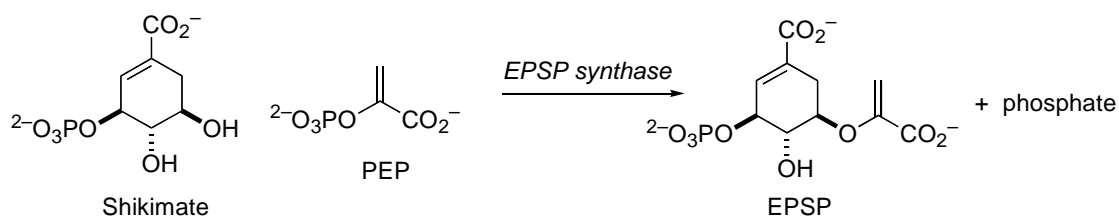


Outline the following two kinetic mechanisms and **explain briefly** how these mechanisms can be distinguished by kinetic measurements:

- (i) ordered sequential; and
- (ii) ping-pong.

(b) (10 marks)

EPSP synthase catalyses the formation of EPSP from shikimate and phosphoenol pyruvate (PEP).



Describe the mechanism of this transformation and use it to **explain** which of the two kinetic mechanisms given in part (a) above most closely resembles the EPSP synthase mechanism.

(c) (12 marks)

Answer **ONE** of the following **two** parts.

- (i) Most enzymatic reactions involve the use of **general acid** and **general base** catalysis. Briefly **describe** what general acid and general base catalysis is, and, using **examples**, illustrate how it can be used to provide catalysis in enzyme reactions.
- (ii) Type I dehydroquinase catalyses the reversible dehydration of dehydroquinone to give dehydroshikimate. Describe how the enzyme catalyses this reaction, and contrast the enzymatic reaction and the non-enzyme catalyzed reaction.

END OF PAPER