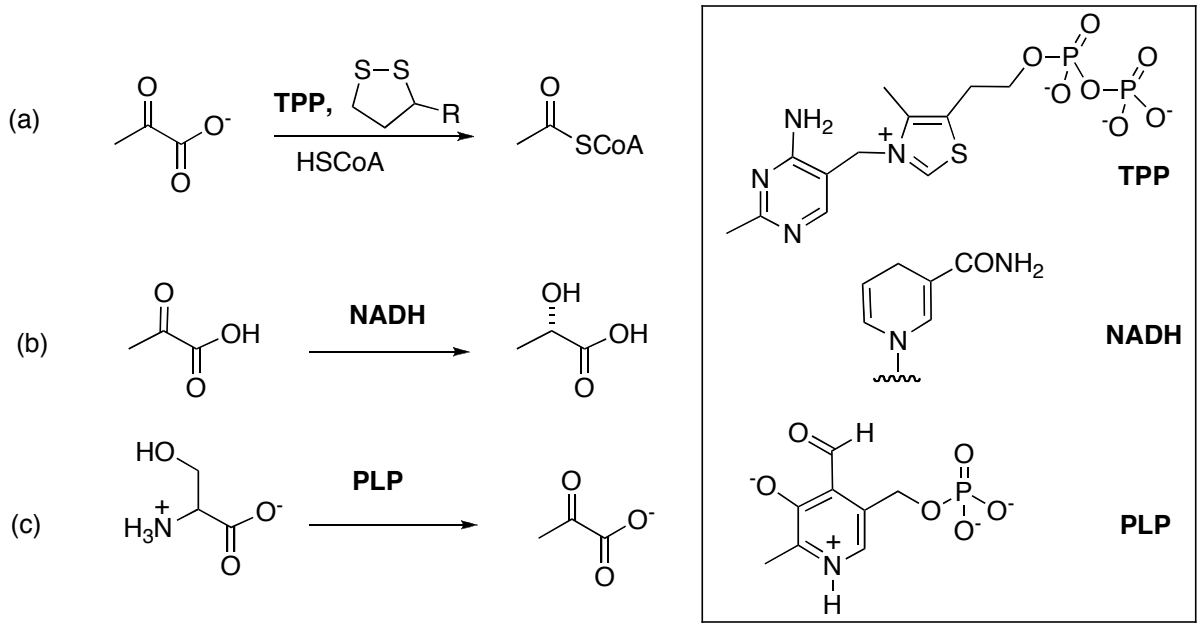
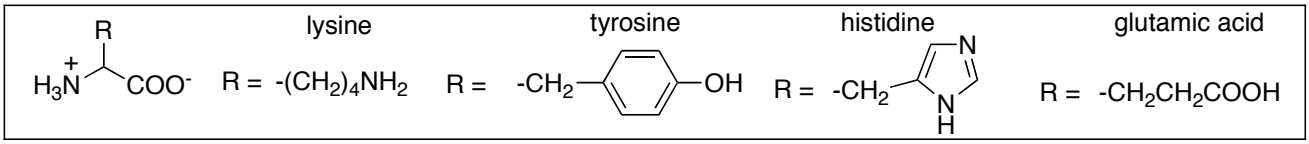
4. Biological chemistry. Answer ***both*** **Parts A and B.**

Part A. Suggest reaction mechanisms and explain as fully as possible ***two*** of the following.

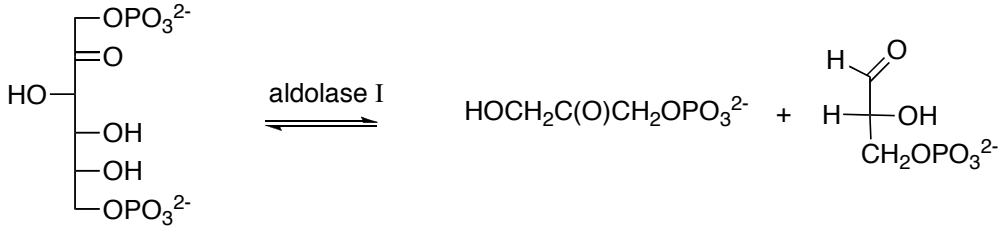


[2 × 5]

Part B. Answer ***two*** questions below.

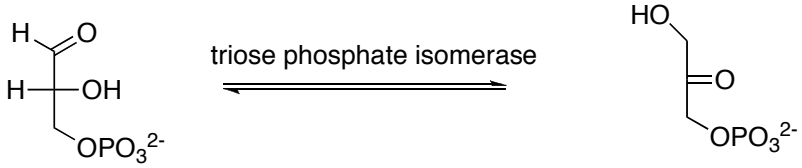


(a) Provide a reaction mechanism for this aldolase I catalysed reaction below (aldolase I features a key lysine and tyrosine residue within the active site).



(b) Suggest a suitable metabolic pathway for orsellinic acid using acetyl S Coenzyme A as the starting building block. Suggest why nature has opted for thioester chemistry in these transformations.

(c) Provide a reaction mechanism for the following transformation. Triose phosphate isomerase features a key histidine and glutamic acid residue within the active site.



[2 × 5]

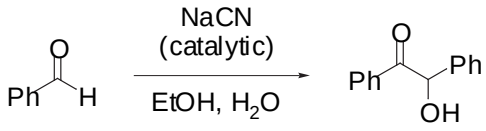
5. Answer ***all*** **Parts A, B and C**.

Part A.
Explain and exemplify what is meant by the term "***umpolung***" in organic chemistry.

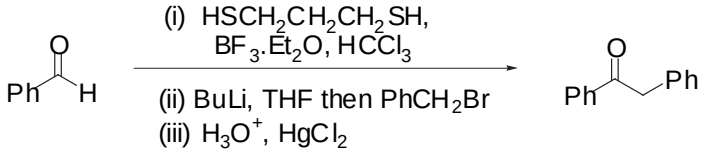
[2]

Part B
Explain the chemistry for ***both*** of the following reactions, referring to the concept of "umpolung", and providing detailed mechanisms.

(a)



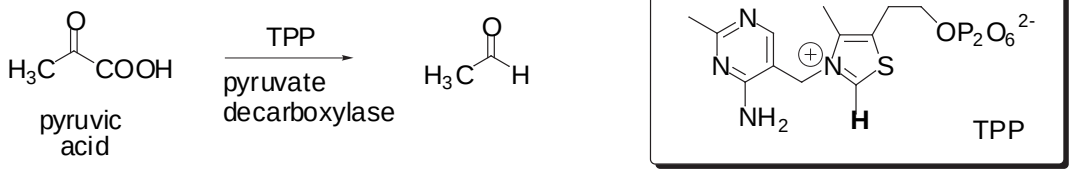
(b)



[2 x 4]

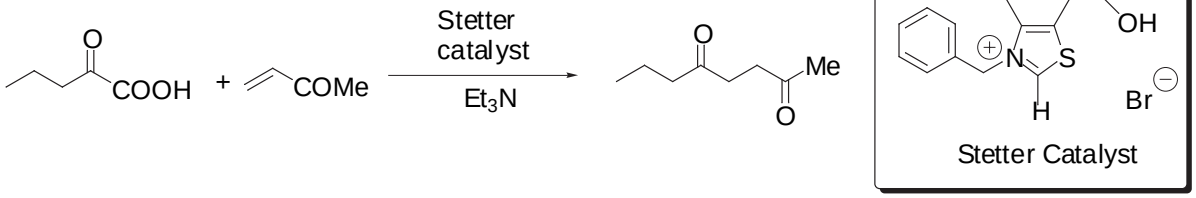
Part C

(a) An example of "umpolung" in Nature can be found in the coenzyme thiamine pyrophosphate (TPP) mediated decarboxylation of pyruvic acid, as shown below. Explain how TPP mediates the conversion of pyruvic acid into acetaldehyde. (HINT: The proton indicated in **bold** is readily exchanged for deuterium under $NaOD/D_2O$ conditions).



[5]

(b) Give a mechanism for the following reaction. Why can this sequence be described as "***biomimetic***"?



[5]

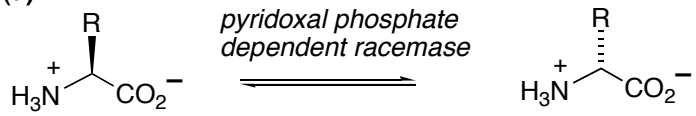
8. Answer **BOTH** Part **A** and Part **B.**

Part A.

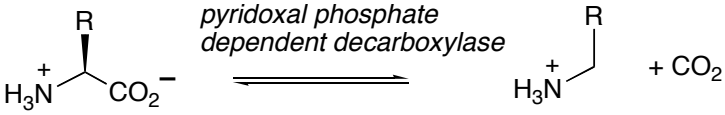
Enzymes that employ the cofactor **pyridoxal phosphate** are important in the metabolism of alpha-amino acids. Outline mechanisms for the pyridoxal phosphate mediated decarboxylation and racemisation of an amino acid, as shown below. You are not required to give descriptions of the active sites of the enzymes.

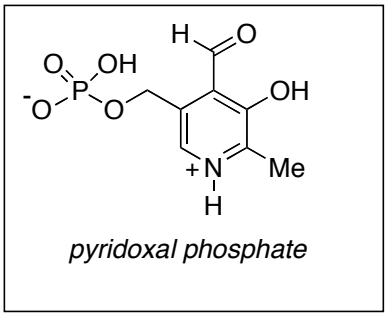
[2 x 4]

(a)



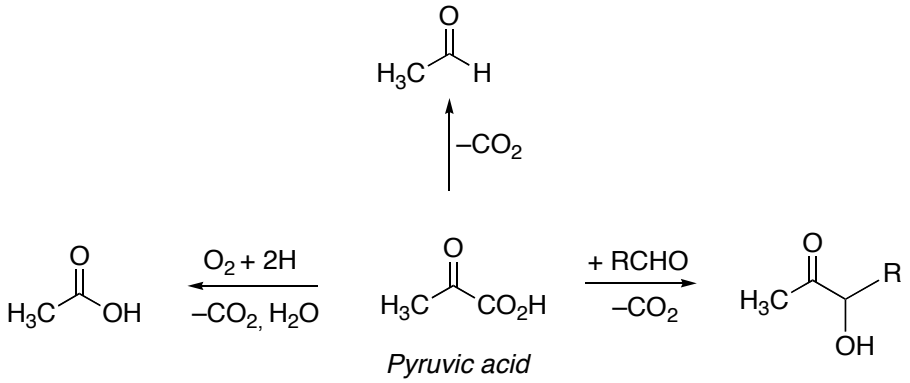
(b)



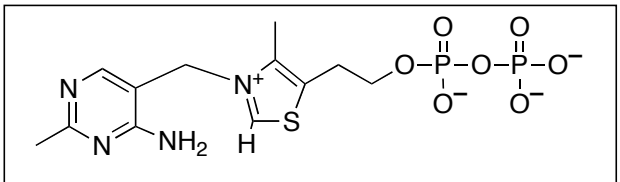


Part B

(b) The decarboxylation of pyruvic acid is catalysed by various thiamine diphosphate dependent enzymes to yield a variety of products including acetaldehyde, alpha-hydroxyacetyl compounds, and acetic acid as shown in the scheme. Outline mechanisms for each of these reactions. You are not required to give descriptions of the active sites of the enzymes. **[3 x 4]**

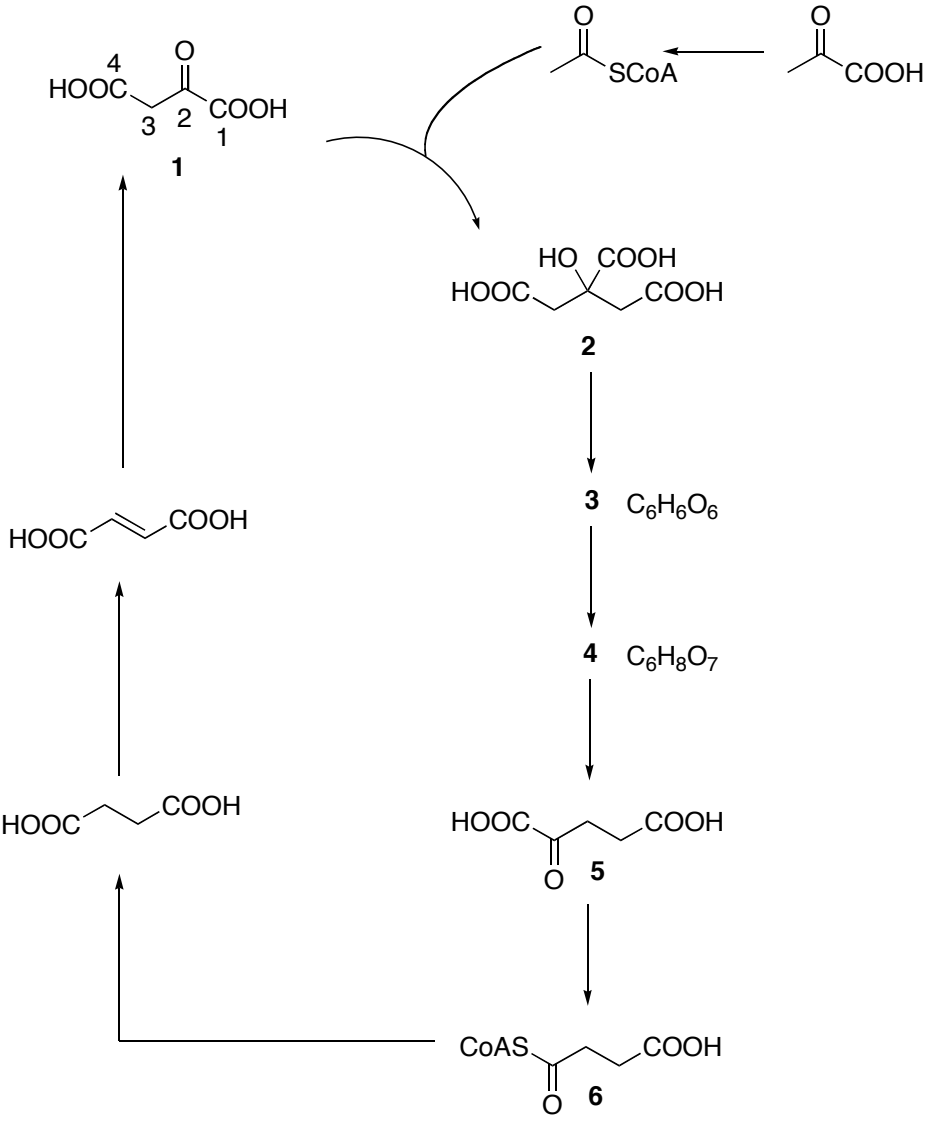


Pyruvic acid



Thiamine diphosphate, THDP

2. The Citric Acid Cycle (CAC) is central to metabolism. Examine the CAC scheme and answer **ALL** of the questions below.



Part A.

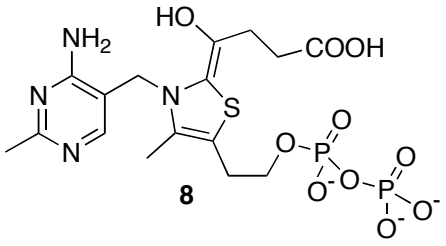
(i) Give structures for intermediates **3** and **4**. **[2]**

(ii) Give a mechanism for the formation of **4** from its isomer **2** via **3**. **[4]**

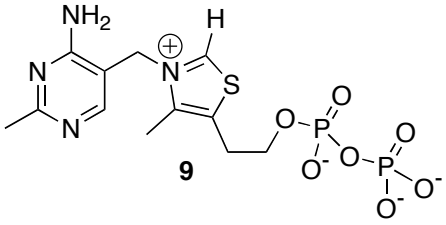
(iii) Outline a mechanism for the formation of **5** from **4**. **[4]**

(iv) By considering your answers above explain why when oxaloacetate **1** containing a ^{14}C radiolabel at C-4 is introduced to the CAC all the radioactive label remains in **5**. **[2]**

Part B.



8



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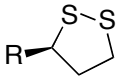
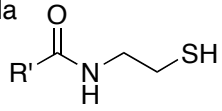


10

N.B. You can consider CoA–SH to be of the general formula



in your answers

The conversion of **5** to **6** involves TPP **9**, Umpolung chemistry, the formation of intermediate **8** and reaction with a co-factor of general formula **10**. Give a mechanism.

[8]

END OF QUESTION

Turn over