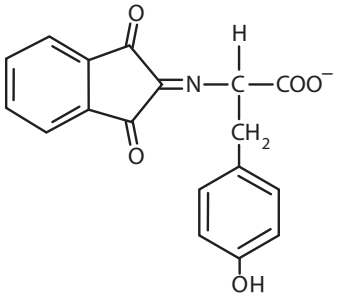
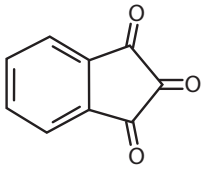
Aldehydes & Ketones Practice Items

1. The substance ninhydrin is a tool of quantitative analysis. The reaction of two equivalents of ninhydrin with an α-amino acid produces both CO_2 and the intensely colored Ruheman's purple. Reaction with the first equivalent of ninhydrin produces a ketamine such as is depicted in the figure below.



Which figure below represents the structure of ninhydrin?

A.



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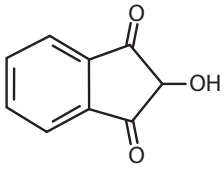

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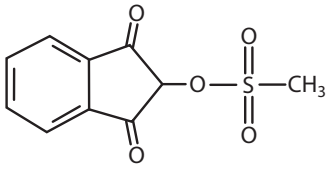

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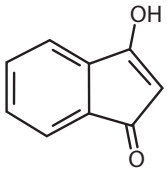
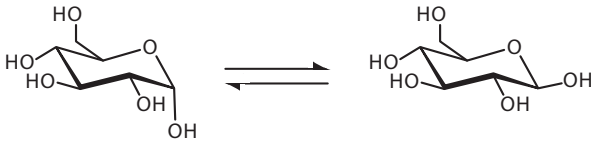
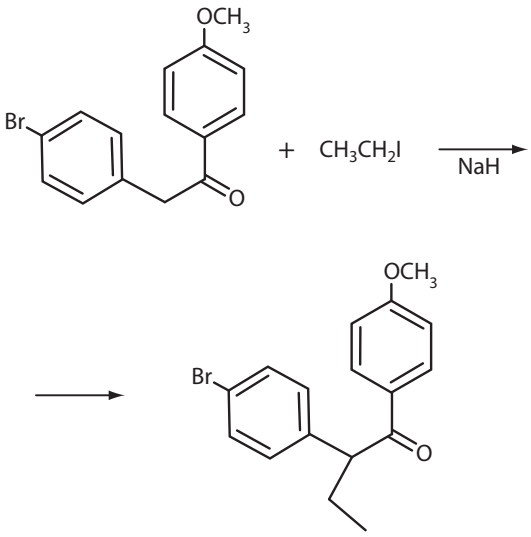


2. Which of the following choices best describes the pathway of interconversion of α-glucopyranose and β-glucopyranose?



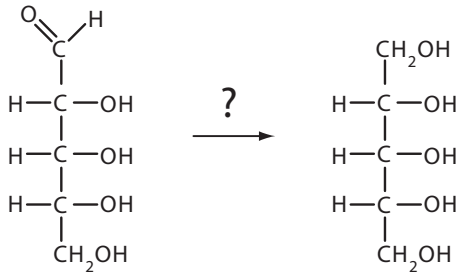
A. tautomerization
B. ring flipping
C. hemiacetal formation
D. aldol cleavage

3. The figure below shows a step in the benchtop synthesis of tamoxifen, a medication used to treat hormone-receptor positive early and metastatic breast cancers. What is the mechanism of this reaction?



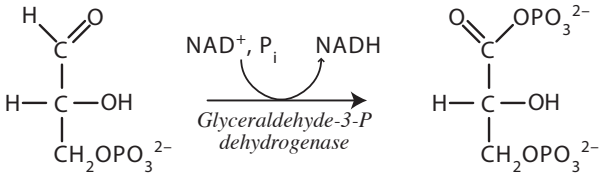
A. SN2 substitution
B. cyanohydrin formation
C. aldol addition
D. nucleophilic acyl substitution

4. Which reagent could be used to carry out the conversion of D-ribose to D-ribitol?



A. FAD
B. $NaBH_4$
C. KOH
D. PCC

5. In one of the reactions of the glycolytic pathway, glyceraldeyde-3-phosphate is oxidized by NAD^+ to form 1,3-bisphosphoglycerate in a reaction catalyzed by the enzyme glyceraldehyde-3-phosphate dehydrogenase.

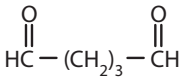


What change has occurred to the oxidation state of the aldehyde carbon of glyceraldeyde-3-phosphate as a result of this reaction?

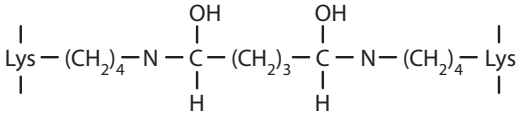
A. +1 → +2
B. +1 → +3
C. +2 → +3
D. +2 → +4

6. A method for quaternary structure analysis, which is especially useful for oligomeric proteins that decompose easily, employs cross-linking agents.

Glutaraldehyde is a bifunctional reactent that reacts to covalently crosslink two Lys residues.



Which of the following structures below represents the cross-links formed by treatment of a multi-subunit protein with glutaraldehyde?

A.


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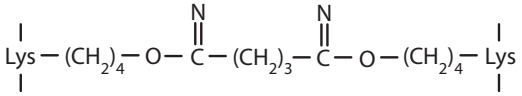

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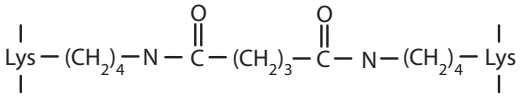
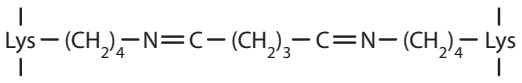
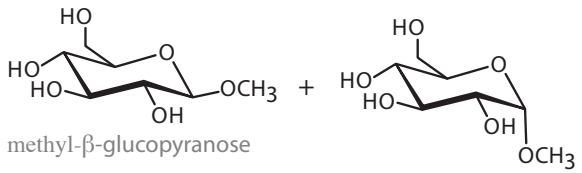


D.


7. Under conditions of acid catalysis, glucose reacts with methanol to form a mixture of glucoside anomers.



methyl-β-glucopyranose

methyl-α-glucopyranose

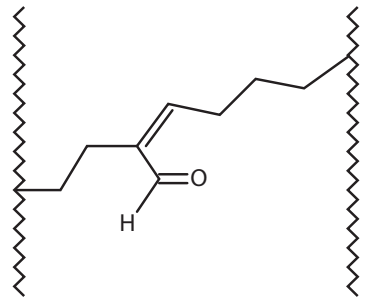
Because normal glucose crystalizes as the α form, a solution of the pure α anomer of glucose can be obtained upon dissolving crystalized glucose in water. Excess methanol was introduced under acidic conditions to a pure solution of the α anomer of glucose and the reaction completed prior to to any signficant mutarotation having occurred. In other words, only the α form and not the β form of the glucose reagent was available to react. The rate of glucaside formation at normal temperatures is several orders of magnitude faster than mutarotation of glucose. The optical activity of the solution was measured upon completion of synthesis of the methyl glucoside. The optical activity measurement obtained was most likely consistent with which of the following solutions?

A. pure methyl-α-glucopyranose
B. pure methyl-β-glucopyranose
C. a mixture of the α and β forms with a greater concentration of the β form
D. a racemic mixture

8. To elongate the carbon chain of an aldose, the Kilani-Fisher synthesis utilizes a particular reagent to form a new carbon-carbon bond. What is that reagent?

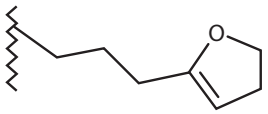
A. sodium cyanide
B. dihydroxyacetone
C. sodium amalgum
D. methyl amine

9. Subsequent to its export to the extracellular compartment by a fibroblast, tropocollagen is assembled into collagen fibrils via cross-linking. The figure below depicts a crosslink between two modified amino acid side chains in side-by-side tropocollagen helices.



Which of the following depictions represents one of the modified side chains prior to the formation of the cross-link?

A.



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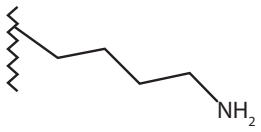

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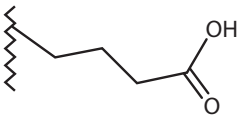
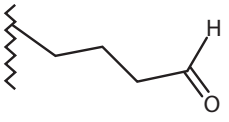
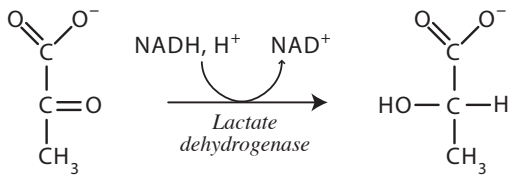


D.



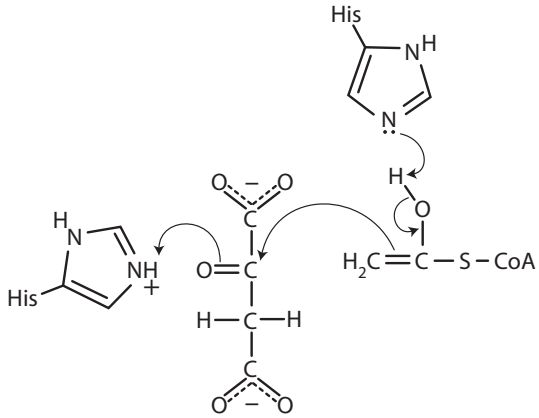
10. In the process of fermentation, pyruvate is reduced by NADH to form lactate in a reaction catalyzed by the enzyme lactate dehydrogenase.



What change has occurreed to the oxidation state of the carbonyl carbon of pyruvate as a result of this reaction?

A. –2 → 0
B. –2 → –1
C. +2 → +1
D. +2 → 0

11. What reaction is occuring in this step of the citrate synthase mechanism?



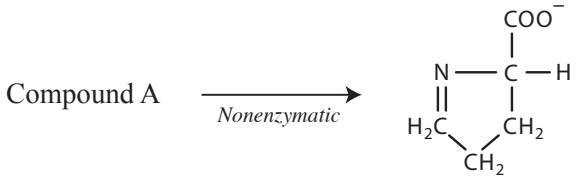
A. Michael addition
B. Claisen condensation
C. Aldol addition
D. Hydrolysis of a thioester

12. Fill in the blank to complete the following analogy:

An enol is to a ketone as an enamine is to a(n) _____.

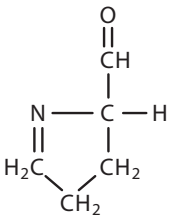
A. amine
B. amide
C. nitrile
D. Schiff base

13. A step in the biosynthesis of proline involves the non-enzymatic comversion of Compound A into 1-pyrroline-5-carboxylic acid.

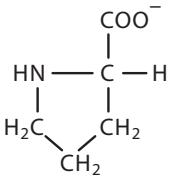


Which of the following is Compound A?

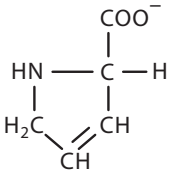
A.



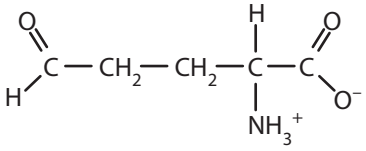
B.



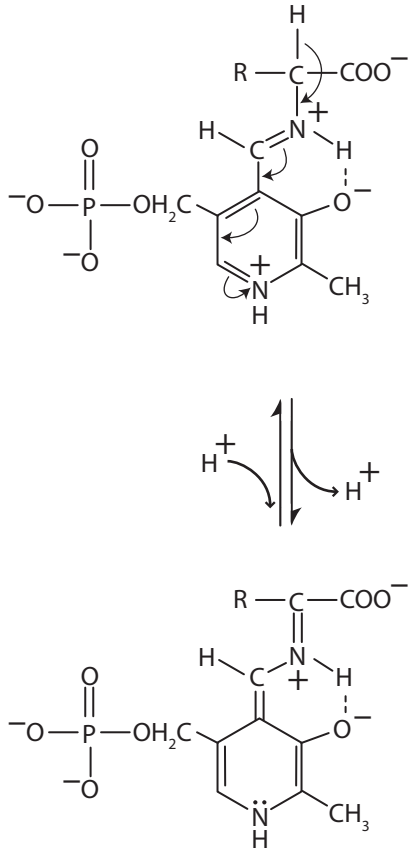
C.



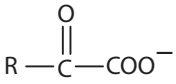
D.

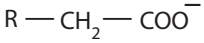


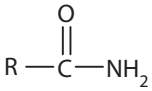
14. The figure below depicts a step in the transminase mechanism. Loss of a proton occurs in this step from the PLP-amino acid Schiff base, leading to formation of a resonance stabilized ketimine intermediate.

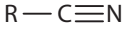


The mechanism then proceeds with subsequent hydrolysis of the ketamine intermediate. Which of the following is a product of the subsequent hydrolysis of the ketamine intermediate?

A. 

B. 

C. 

D. 

15. Which of the following reaction mechanisms involves an enolate or enol intermediate?

I. decarboxylation of acetoacetate
II. pyruvate kinase
III. enoyl CoA hydratase
IV. triose phosphate isomerase

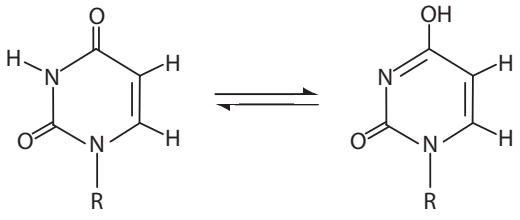
A. I and II
B. II and IV
C. I, II, and III
D. I, II, III and IV

16. The liberation of cyanide serves as a defense mechanism against herbivores and microbial attack in plants. The activity of which of the following enzymes corresponds to this phenotype?

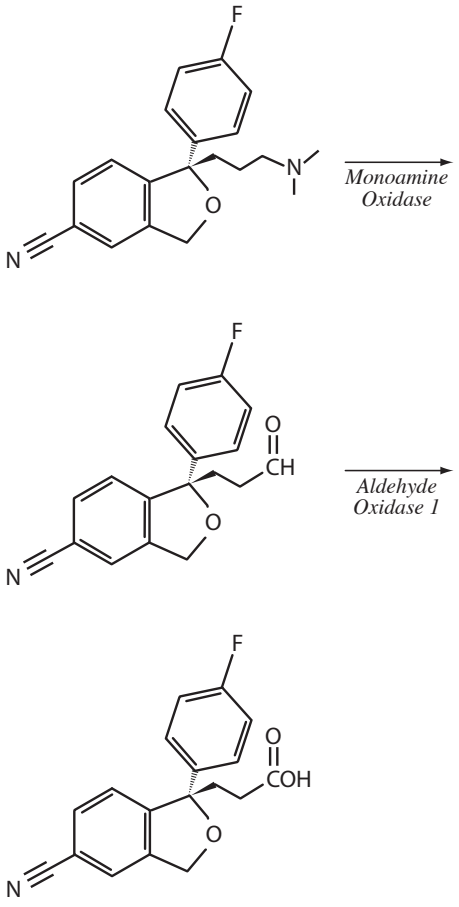
A. hydroxynitrile lyase
B. transaminase
C. hydroxylamine oxidoreductase
D. fatty acylamidase

17. The interconversion shown below between the lactam and lactim forms of uracil is a type of

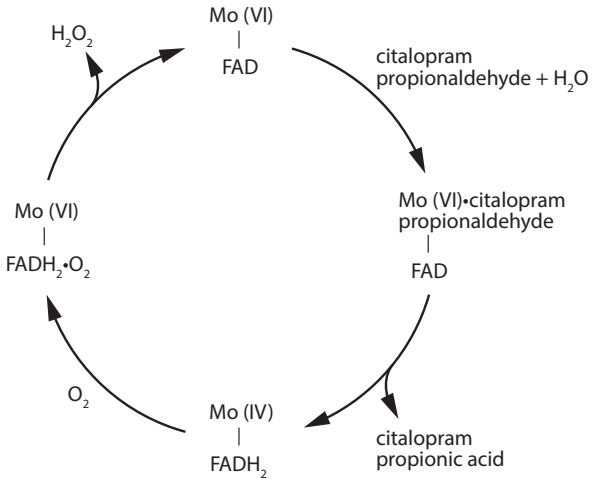
A. mutarotation
B. epimerization
C. tautomerization
D. resonance



18. One of the pathways in the liver for the metabolism of the drug citalopram involves the activity of the enzymes monoamine oxidase and aldehyde oxidase.



The figure below shows the catalytic cycle of aldehyde oxidase.



Which of the following is a true description of the net aldehyde oxidase reaction in the metabolism of citalopram?

A. a transfer of two electrons from molecular oxygen to citalopram propionaldehyde

B. a transfer of four electrons from citalopram propionaldehyde to molybdenum and FAD

C. a transfer of two electrons from citalopram propionate to molecular oxygen

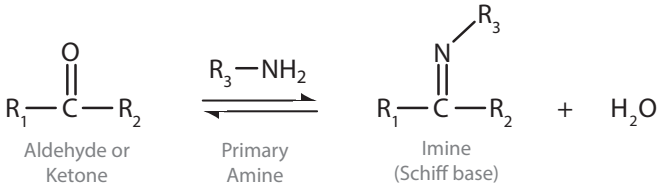
D. a transfer of two electrons from citalopram propionaldehyde to molecular oxygen

Aldehydes & Ketones

Answers and Explanations

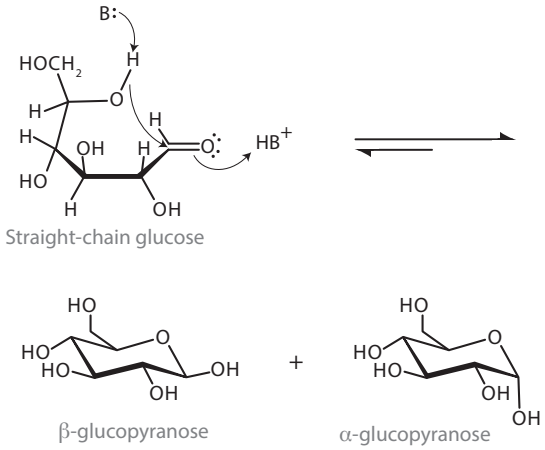
1. A

The reaction which has occurred is imine formation. The amino acid tyrosine has reacted with the ninhydrin reagent through nucleophilic addition of its α-amine group of the to the carbonyl group of the ninhydrin. Imine formation proceeds first with nucleophlic addition to form a tetrahedral intermediate followed by dehydration to form the imine.



2. C

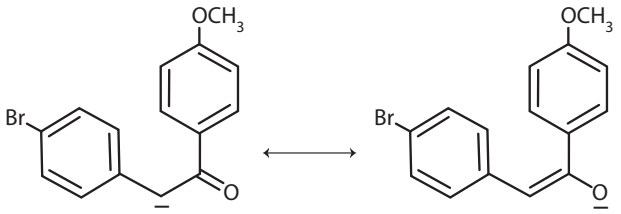
Glucose ring formation is an example of the hemiacetal phase of acetal formation in which an equivalent of alcohol forms a tetrahedral intermediate with an aldehyde.



The intercoversion of the α and β anomeric forms of glucopyranose occurs through the straight chain, ring opening by hemiacetal formation in reverse, and followed by closure to form the hemiacetal now inverted at C1.

3. A

Sodium hydride base converts the reagent into a resonance stabilized enolate anion.



The negatively charged carbon depicted in one of the resonance forms of the enolate anion is nucleophilic. The reaction proceeds via SN2 substitution.

4. B

The reducing agents $NaBH_4$ or $LiAlH_4$ transform an aldehyde or a ketone into an alcohol. The reduced form of an aldehyde is a primary alcohol.

5. B

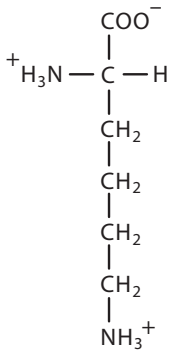
When you have the structural formula of an organic compound, assign oxidation numbers by deciding which atom has 'control' of the electrons in the bonds. Control goes to the more electronegative atom.

Each of the electrons carbon brought to the double bond in the carbonyl bond to oxygen in G3P is assigned to oxygen. Those are under oxygen's control. They are oxygen's property in the oxidation-reduction accountig system. However, that carbon has also 'gained' the one electron that hydrogen brought to its bond to the carbon. The carbon in the aldehyde at the start, in other words, is in the position of having lost two and having gained one, so the oxidation state of the aldehyde carbon in glyceraldehyde-3-phosphate is +1. Remember henceforth that the oxidation state of a carbonyl carbon in an aldeyde is +1.

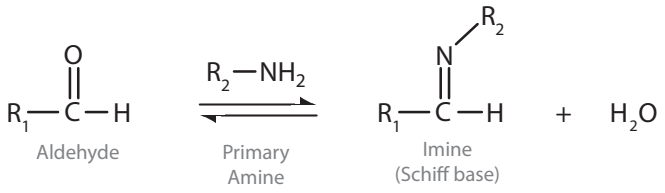
After the reaction, the carbon will now have three electrons invested in bonds to oxygen (a double bond and a single bond), so its oxidation state in 1,3-bisphosphoglycerate has become +3. It has been oxidized by NAD^+ in a two electron transfer. These two electrons are now the property of NADH. Remember that the oxidation state of a carbon in a carboxylic acid (or carboxylic acid derivative, here a phosphate anhydride) is +3.

6. D

The amino acid lysine possesses a primary amine side-chain.

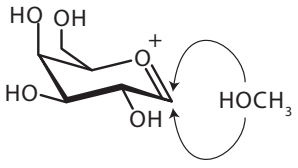


A primary amine reacts with an aldehyde to form an amine.



7. C

The ring form of glucose is a hemiacetal (See question 2 explanation). The methyl glucoside formed in this reaction is an acetal. Formation of an acetal from a hemiacetal proceeds through nucleophlic attack of an alcohol upon an oxonium cation intermediate. Because the attack can occur from either plane of the ring, a mixture of α and β forms is obtained.

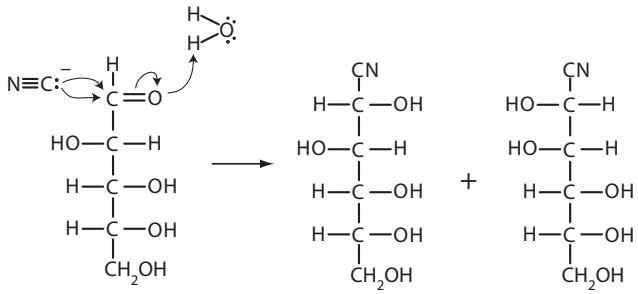


Because the β form possesses lower free energy, it will form predominatly. Even if the two forms occurred at equal concentration, however, the choice could not be 'D' because the solution would not be racemic. The α and β forms are not enantiomers. They are diasteriomers and a solution with equal concentrations of the two would still show optical activity.

8. A

The first step in Kilani-Fischer synthesis is to react the starting sugar with aqueous cyanide. The cyanide undergoes nucleophilic addition to the carbonyl group of the sugar forming a cyanohydrin. Cyanohydrin formation is an important tool of organic synthesis because it can form a new carbon-carbon bond.

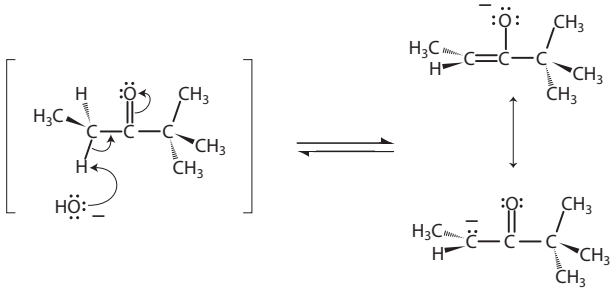
While sugars tend to exist mainly as cyclic hemiacetal, they are always in chemical equilibrium with their open-chain aldehyde or ketone forms, and in the case of these aldoses it is that aldehyde form that reacts in this synthesis.



Note that because the cyanide can add to either plane of the trigonal planar carbonyl group, the cyanohydrin resulting from this addition consists of a mixture of two diastereomers. The stereochemistry of all the previously present chiral carbons is preserved.

9. D

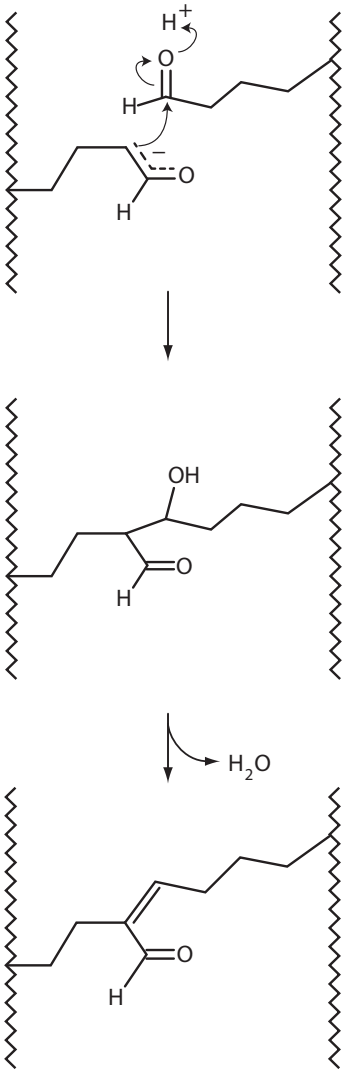
Keto-enol tautomerism can occur with carbonyl compounds if the carbon adjacent to the carbonyl, the α carbon, possesses a hydrogen. Such α hydrogens are acidic. The conjugate base formed is resonance stabilized. Keto-enol tautomerism is an important factor in the reactivity of aldehydes and ketones.



One of the MCAT's favorite reactions is aldol addition, in which the enolate form of one aldehyde or ketone acts as a nucleophile to attack the carbonyl carbon of another (or another equivalent of the same aldehyde or ketone).

The cross-link in collagen depicted in the problem has formed between two *alllysine* residues. Allysine is an aldehyde derivative of lysine produced by the action of the enzyme lysyl oxidase.

The reaction below would be termed aldol condensation. Aldol condensation is aldol addition followed by a dehydration step. An aldol condensation product is an α,β unsaturated carbonyl compound.



To be able to work backwards from an aldol addition product or an aldol condensation product to determine the original carbonyl compounds involved in forming the product is an important figure of merit for the MCAT. The key is locating the original α carbon in the product (it will be adjacent to a carbonyl group) and the original carbonyl carbon, which will either possess a hydroxyl group, in the case of aldol addition, or be on the far side of a double bond in the case of the full aldol condensation.

10. D

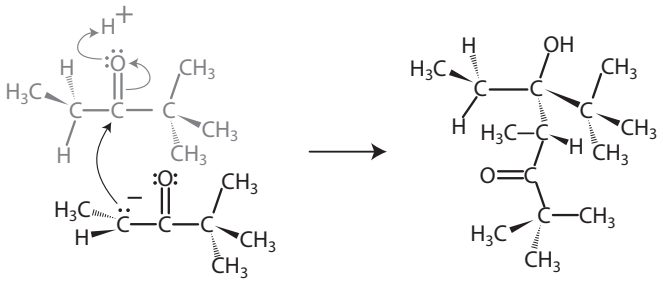
When you have the structural formula of an organic compound, assign oxidation numbers by deciding which atom has 'control' of the electrons in the bonds. Control goes to the more electronegative atom.

Each of the electrons carbon brought to the double bond in the carbonyl bond to oxygen in pyruvate is assigned to oxygen. Those are under oxygen's control. They are oxygen's property in the oxidation-reduction accountig system. The C2 carbon of pyruvate at the start, in other words, is in the position of having lost two electrons, so the oxidation state at the start is +2. Remember henceforth that the oxidation state of a carbonyl carbon in an ketone is +2.

After the reaction, the carbon will now have one electron invested in a bond to oxygen, so it loses that one, but it also has a bond to hydrogen, so it gains an electron there, the electron hydrogen brought to that bond. The carbon's oxidation state in lactate is therefore 0. It has been reduced by NADH in a two electron transfer.

11. C

In aldol addition, the enolate of one carbonyl compound nucleophilically attacks the carbonyl of another.



In the step of the citrate synthase mechanism shown in the problem, the enolate ester of acetyl CoA is acting as a nucleophile to attach to the carbonyl group of oxaloacetate.

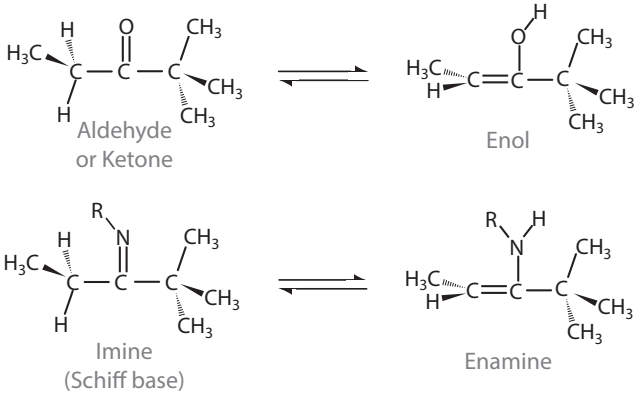
12. D

Two substances with the same molecular formula but different connectivities in their structural formulas are called constitutional isomers. Tautomers are constitutional isomers which readily interconvert.

As long as it possesses an α hydrogen, a ketone will interconvert with its enol tautomer. This means that some of the enol form will be present in aqueous solution, as well as the enolate intermediate in the conversion (in neutral to

basic conditions). Keto-enol tautomerism opens aldehydes and ketones up to a whole dimension of reactivity.

Similarly, an imine possessing an α hydrogen will be interconverting with its enamine tautomer, which opens up imines to a dimension of reactivity.

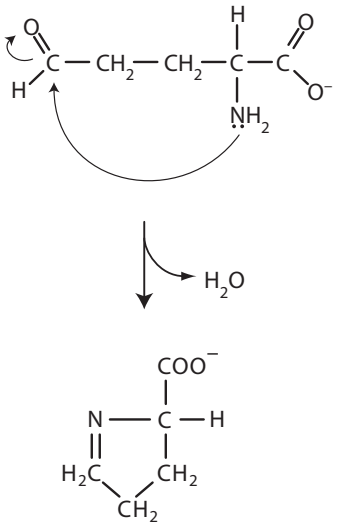


In biochemistry imines (the subset possessing an 'R' group on the nitrogen) are referred to as Schiff bases. In other words, what an organic chemist would call it an imine (or a ketimine), a biochemist calls a Shiff base.

Imine-enamine tautomerism is at least as important to biochemistry as keto-enol tautomerism, and keto-enol tautomerism is important!

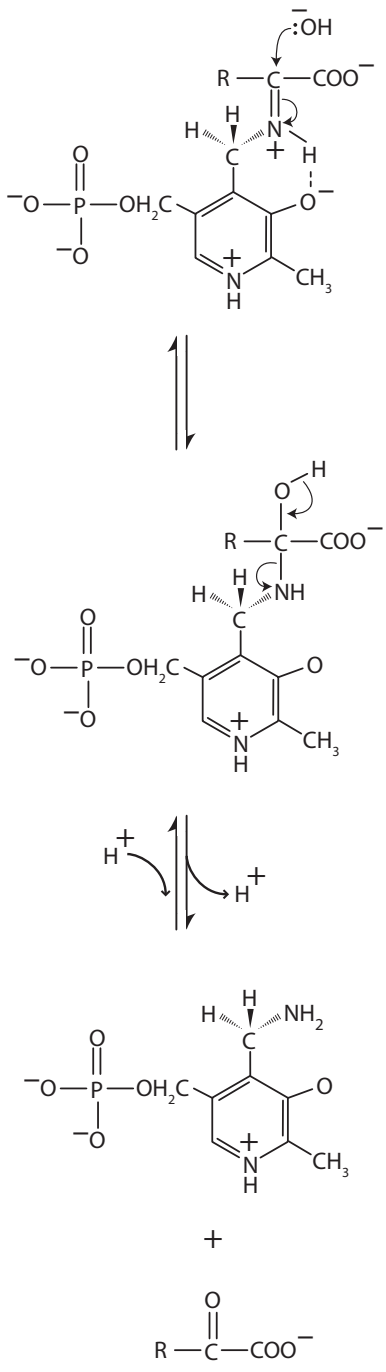
13. D

The intermediate which converts nonenzymatically into 1-pyrroline-5-carboxylic acid in proline biosynthesis is glutamate-5-semialdehyde. The reaction that occurs is an intramolecular imine formation.



14. A

Hydrolysis of an imine is simply imine formation in reverse.



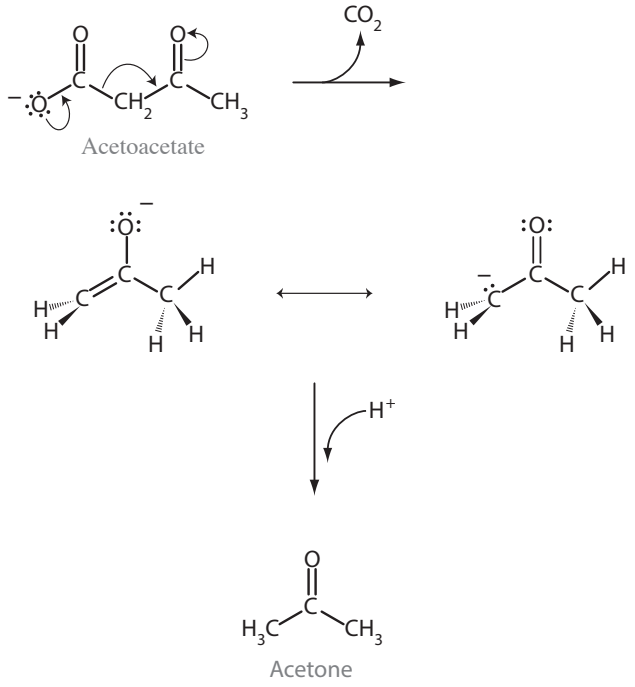
Transaminase interconverts α-amino acids and α-keto acids. Examples the transaminase reaction include the interconversion of alanine and pyruvate, aspartate and oxaloacetate and glutamate and α-ketoglutarate. Transaminase is an key enzyme in amino acid breakdown and synthesis, the malate aspartate shuttle, and the urea cycle.

15. D

It is an important point to emphasize in biochemistry that many biochemical processes are facilitated because their occurance coincides with formation of a resonance stabilized enolate anion.

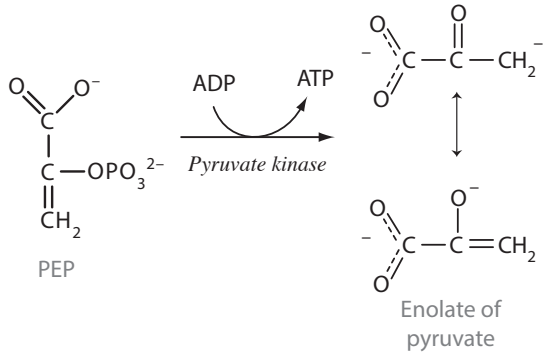
Decarboxylation of acetoacetate:

The ketone body acetoacetate undergoes a steady rate of nonenzymatic decarboxylation forming acetone in the blood. Acetoacetate is a β-keto acid. β-keto acids lose CO_2 very easily because the reaction passes through a resonance stabilized enolate anion.



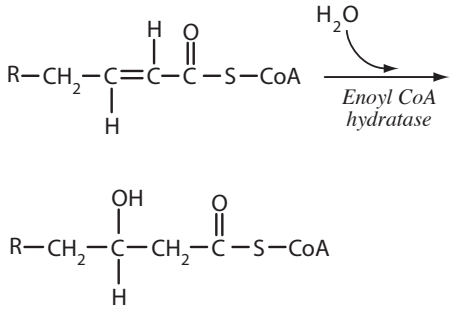
Pyruvate kinase:

One of the driving factors behind the phosphoryl transfer potential of phosphoenolpyruvate (PEP) is that transfer of the phosphoryl group onto ADP leaves behind an enolate anion.

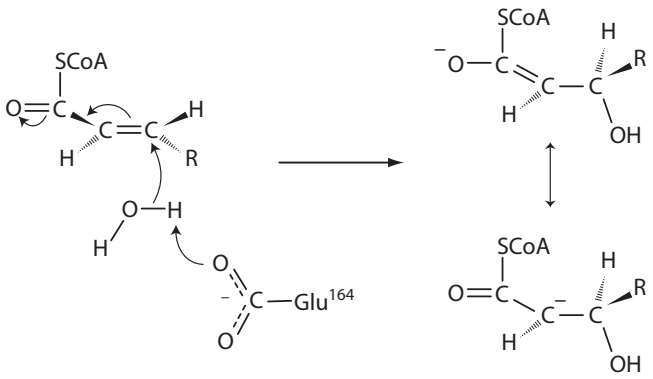


Enoyl CoA hydratase:

Enoyl CoA hydratase is a step in the pathway for the oxidation of fatty acids.

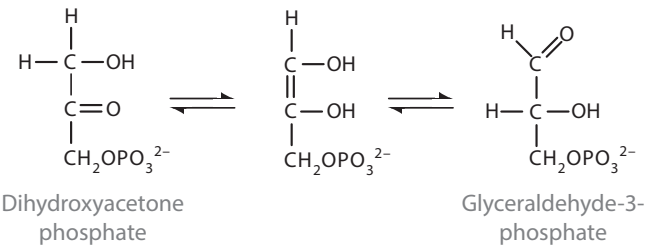


The reaction is a Michael addition. Although Michael addition is not on the list of MCAT reactions, from the AAMC section bank, knowledge of Michael addition does appear to be figure of merit for the exam. In Michael addition, a nucleophile attacks the β carbon of an α,β unsaturated carbonyl compound. Nucleophiles attack the β carbon because the addition leads to an enolate intermediate as in the enoyl CoA hydratase mechanism:



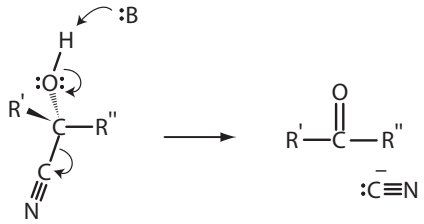
Triose phosphate isomerase:

In glycolysis (and gluconeogenesis) triose phosphate isomerase interconverts dihydroxyacetone phosphate and glyceraldehyde-3-phosphate. The enol of both is an intermediate in the interconversion.



16. A

Hydroxynitriles are more often referred to as cyanohydrins. In cyanohydrin formation, cyanohydrins are produced through the reversible nucleophilic addition of cyanide anion (CN–) to an aldehyde or ketone. Reasoning function from its name, hydroxynitrile lyase is the only plausible choice among those given which could liberate cyanide. The enzyme catalyzes the reverse reaction.



17. C

Constitutional isomers are two molecules with the same molecular formula but different connectivity. Constitutional isomers that can interconvert in a rapid equilibrium are tautomers. The lactam and lactim forms of uracil are tautomers. The interconversion would be a tautomerization.