Diabetes is a complex disease, involving (among other things) high levels of glucose in the bloodstream. This is a problem because this glucose can react with other biomolecules, interfering with normal biological processes.

One way in which free blood glucose causes problems is by forming an imine with free primary amino groups (RNH₂) on proteins, such as hemoglobin. (Glycolated hemoglobin is also called A1c, and is a primary measure of history of free glucose in the blood.)

1. (3) Write in the box the imine product formed when acyclic glucose reacts with the RNH₂ of hemoglobin.

2. (3) The mechanism for the reaction involved in question 1 involves which of the following? Circle all that apply.
   - Tetrahedral adduct
   - Proton transfer
   - Nucleophilic attack at C=O
   - Enolate

3. (8) Fructose is another sugar that might react with hemoglobin to form an imine. Is the fructose/hemoglobin reaction faster or slower than the glucose/hemoglobin reaction? For each part below circle "faster than" or "slower than", as appropriate, then complete the sentence by adding no more than ten words in each case. The reasons for parts (a) and (b) should be very different.

   (a) The fructose/hemoglobin reaction is faster than / slower than the glucose/hemoglobin reaction because...

   (b) The fructose/hemoglobin reaction is faster than / slower than the glucose/hemoglobin reaction because...
4. (6) In the bloodstream, glucose spends most of its time as glucopyranose (i.e. its cyclic form). Write the mechanism for this acid-catalyzed version of this process as illustrated here.

5. (4) Consider the rate of the glucose to glucopyranose conversion in question 4 in the absence of H$_3$O$^+$. Complete the following statement by circling "faster" or "slower" as appropriate, and then add **no more than ten words**. Be very specific.

   The reaction of question 4 is faster / slower in the absence of H$_3$O$^+$ because...

6. (4) In lecture we learned that NADH is a coenzyme that reacts with oxaloacetate to produce malate:

   (a) Why does the ketone carbonyl react instead of the carboxylate groups? Circle one or more reasons:

   - Steric effects
   - Magnitude of $\delta^+ C=O$
   - Resonance
   - Changes in aromaticity
   - Leaving group

   (b) In this reaction the oxaloacetate is (circle one or more): Oxidized Reduced Neither
7. (3) Walter Dieckmann discovered the Dieckmann reaction, which is similar to the Claisen condensation. Write in the box the product of the following Dieckmann reaction:

![Dieckmann reaction diagram]

Questions 8 and 9 refer to the following Claisen reaction, which is somewhat similar to the Claisen condensation:

![Claisen reaction diagram]

8. (2) In the box above, write the structure of the missing reactant for this reaction.

9. (10) Write the mechanism for the ester hydrolysis portion of the reaction using the following abbreviations:

![Ester hydrolysis mechanism diagram]
10. (9) Write the major reaction product in the box. In the space below write the mechanism showing the formation of this major product.

Mechanism:

11. (1) Write the name of the halogen-containing functional group of question 10: _______________________

12. (1) In the box draw a thioester having exactly five carbon atoms (plus any number of atoms of other elements):

13. (4) Rank the rate of hydrolysis of the functional groups listed below by writing the one that hydrolyzes fastest in the 'fastest' blank, second fastest in the second blank, etc. If there is a tie, write more than one functional group in each blank. Leave unused columns blank. Functional group choices: Amide, anhydride, ester, thioester.

____________________ > ____________________ > ____________________ > ____________________

Fastest                                                                                                                          Slowest

14. (4) Of the two reactions shown below, write the product of the faster reaction in the box.

15. (4) Write the reaction mechanism for the product you drew in question 14.
16. (4) Of the two reactions shown below, write the product of the faster reaction in the box.

\[
\begin{array}{c}
\text{H}_3\text{C} \quad \text{O} \\
\text{OCH}_3
\end{array}
\xrightarrow{1. \text{CH}_3\text{MgBr}}
\begin{array}{c}
\text{H}_3\text{C} \\
\text{N(\text{CH}_3)_2}
\end{array}
\xrightarrow{2. \text{H}_2\text{O}^-}
\begin{array}{c}
\text{H}_3\text{O}^+ \\
\text{or}
\end{array}
\xrightarrow{2. \text{H}_2\text{O}^-}
\begin{array}{c}
\text{H}_3\text{C} \quad \text{O} \\
\text{OCH}_3
\end{array}
\]

17. (8) Write the reaction mechanism for the product you drew in question 16.

18. (2) Consider the pK_a data shown below, then circle the most likely pK_a value for molecule A.

\[
\begin{array}{c}
\text{O} \quad \text{O} \\
\text{O}
\end{array}
\quad pK_a \quad 9
\]
\[
\begin{array}{c}
\text{O} \\
\text{pK}_a \quad 19
\end{array}
\]
\[
\begin{array}{c}
\text{O} \\
\text{OCH}_3
\end{array}
\quad pK_a \quad 25
\]
\[
\begin{array}{c}
\text{H}_2\text{CO} \quad \text{O} \\
\text{OCH}_3
\end{array}
\quad \text{Molecule A}
\]

The pK_a of molecule A is...

Less than 9  Very close to 9  Between 9 and 19  Very close to 19
Between 19 and 25  Very close to 25  More than 25

19. (7) Write the major product of the following reaction in the box. In the space below write the mechanism that produces this major product.

\[
\begin{array}{c}
\text{O} \quad \text{O} \\
\text{1. LDA}
\end{array}
\xrightarrow{\text{1. LDA}}
\begin{array}{c}
\text{O} \\
\text{2. PhCH}_2\text{Br}
\end{array}
\]

**Mechanism:**

20. (1) In question 19, LDA is an abbreviation that stands for... *Spelling counts.*

L____________________  D____________________  A____________________
21. (12) Complete each of the following reactions by writing the major organic product(s) in the boxes. If two or more products are formed in roughly equal amounts, write all of these products. If no reaction occurs, write “NR” in the product box. Assume the reactants above and below the arrow are present in excess. Do not provide any mechanism details.

(a) \[
\text{[Diagram]} \quad \text{KOH} \quad \text{H}_2\text{O} \]

(b) \[
\text{[Diagram]} \quad 1. \text{LiAlH}_4 \quad 2. \text{H}_3\text{O}^+ \]

(c) \[
\text{[Diagram]} \quad \text{NH}_3 \]

(d) \[
\text{[Diagram]} \quad 1. \text{Na}^+ \quad \text{?} \quad \text{C} \equiv \text{C} \quad \text{CH}_3 \quad 2. \text{H}_3\text{O}^+ \]

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