Sulfanilamide is an antibiotic that exerts its antibiotic effect by reacting with dihydropteridine diphosphate as shown below. The product of this reaction inhibits an enzyme necessary for bacterial folic acid synthesis and subsequent growth.

Questions 1–4 refer to diphosphate ion, a leaving group in a wide range of biological reactions.

1. (3) Using no more than twenty words, write a precise yet concise definition for “leaving group.”

2. (2) Complete this statement by writing "excellent", "moderate", "special circumstances", or "never" in the blank.
   Diphosphate ion is most likely in the ______________________________ remaining group category.

3. (4) List two distinctly different molecular structure features of diphosphate ion that influenced your thinking in question 2.
   Feature #1 (fifteen words or less):

   Feature #2 (fifteen words or less):

   O
   O
   O
   O
   O
   OH
   OH
   OH
   OH
   OH

   Diphosphate ion
4. (3) By adding, subtracting, or changing into another element *no more than three atoms*, rewrite the structure of diphosphate ion (in the box) to make it an *obviously worse* leaving group. Include all lone pairs and formal charges.

Questions 5–9 refer to the reaction of dihydropteridine diphosphate with sulfanilamide shown on the previous page. For these questions you may abbreviate dihydropteridine diphosphate as RCH$_2$–O–phos.

5. (2) Complete this statement by writing "substitution", "addition", "elimination", "oxidation", or "reduction" in the blank. This reaction is an example of a(n) __________________________ reaction.

6. (6) Write an S$_N$2 mechanism for the reaction of RCH$_2$–O–phos with sulfanilamide. In the first step label the nucleophile as ‘nuc’ and electrophile as ‘elec’

7. (6) Write an S$_N$1 mechanism for the reaction of RCH$_2$–O–phos with sulfanilamide.

8. (6) Complete this statement by adding *no more than thirty words (be very specific)*: This reaction probably occurs by the S$_N$2 mechanism and not the S$_N$1 mechanism because...
9. (8) *Using thirty words or less*, briefly explain why the sulfanilamide reacts at the aniline nitrogen atom instead of the sulfonamide nitrogen atom. *Hint: The answer lies in the reaction mechanism, not in the drug effects or biological effects.*

![Reaction Diagram]

When sulfanilamide was commonly used as a drug, it was necessary to produce many thousands of kilograms per year. Questions 10–17 refer to this industrial synthesis.

10. (7) One important reaction in this synthesis is the conversion of acetaldehyde into acetyl chloride (as shown here). Write a mechanism for this reaction.

\[
\text{H}_3\text{C} = \text{H} \xrightarrow{\text{Cl}_2, \text{heat}} \text{H}_3\text{C} - \text{Cl} + \text{HCl}
\]

Acetaldehyde \hspace{1cm} Acetyl chloride

The next step is the reaction of aniline with acetyl chloride to produce acetanilide:

\[
\text{PhNH}_2 + \text{H}_3\text{C} = \text{Cl} \rightarrow \text{H}_3\text{C} - \text{N} - \text{H} + \text{PhNH}_3^+ + \text{HCl}
\]

Aniline \hspace{1cm} Acetanilide

Present in excess

11. (3) Finish this statement by adding *no more than twenty words*: The most important reason this reaction occurs at the nitrogen atom instead of the benzene ring is...

12. (6) Write a mechanism for this reaction.
13. (6) By adding no more than twenty words in each case, complete these descriptions two *distinctly different aspects of molecular structure* that account for the high reactivity of acetyl chloride, as compared to many other carbonyl-containing carbonyl molecules.

Molecular structure factor #1 (*twenty words or less*): Acetyl chloride is more reactive than many other carbonyl-containing molecules because acetyl chloride...

Molecular structure factor #2 (*twenty words or less*): Acetyl chloride is more reactive than many other carbonyl-containing molecules because acetyl chloride...

14. (2) Complete the following statement by writing "faster", "slower", or "equal" in the blank: When trifluoroacetyl chloride (CF\(_3\)COCl) is used instead of acetyl chloride (CH\(_3\)COCl) in the reaction on the previous page, the reaction rate is ______________________________.

Questions 15–17 refer to the next step in the synthesis of sulfanilamide, in which acetanilide is reacted with sulfur trioxide in concentrated (anhydrous) sulfuric acid to produce a sulfonic acid (ArSO\(_3\)H).

15. (2) Finish this sentence *by adding no more than ten words*: Sulfur trioxide is an electrophile because...

16. (6) Write a mechanism for this reaction.
17. (8) Using **thirty words or less**, briefly explain how the *molecular structure of the arenium ion* causes the reaction to produce more of the para sulfonic acid isomer than the meta sulfonic acid isomer. Your answer may include pictures, but **must include** a written description (in words).

18. (12) For the following reaction:

\[
\text{Molecule } A \xrightarrow{\text{aq. } H_2SO_4} \text{Molecule } B + \text{Molecule } C + \text{Molecule } D
\]

(a) Write the letter (B, C, or D) of the product produced in the **least amount**:  

(b) Write a mechanism showing the formation of the two products you **did not list** in part (a).
19. (8) In each box write the reactants needed to carry out this reaction sequence:

Work space. Nothing below this line will be graded.