Reactants and Substrates

1. Define reactant and substrate. Where do you find these in a chemical reaction equation?

2. Which of the following is more nucleophilic?
   
   a. \( \text{OH} \) vs. \( \text{O} \)

   b. \( \text{NH}_2 \) vs. \( \text{NH}_2 \)

   c. \( \text{OH} \) vs. \( \text{NH}_2 \)

   d. \( \text{O} \) vs. \( \text{O} \)

3. For the following molecules, identify any nucleophilic sites. If you select more than one site, which do you expect is more nucleophilic? Explain your reasoning.

4. What are steric effects? What is steric hindrance?

5. Identify and draw the structure for each reactant in the situations below.
   
   a. The combustion of propane in the presence of oxygen producing carbon dioxide and water.

   b. The decomposition of hydrogen peroxide into water and oxygen gas.

   c. The synthesis of aspirin from acetic anhydride and salicylic acid.
6. Lactose intolerance is the inability of a person to digest lactose, a sugar found in milk. Lactase is an enzyme that breaks down lactose into glucose and galactose. Would lactose be considered a reactant, substrate, neither, or both? Explain.

What is needed to balance the reaction?

Reagents

7. Define reagent. Where are reagents indicated in a chemical reaction equation? How do reagents differ from reactants?

8. A wide variety of reagents are used to perform reductions in organic synthesis due to the fact that different reagents affect different functional groups. For this reason, it is very important to choose a proper reducing agent to achieve the desired transformation in a synthesis.

a. What functional groups can the following reagents be used to reduce?

i. \(\text{NaBH}_4\)

ii. Lithium aluminum hydride

iii. \(\text{H}_2, \text{Pd}\)

b. Which reagent would you use to perform the following transformations of epothilone C, a natural product with anticancer activity?

9. When performing an elimination reaction, the base used can play a role in the product that is formed. In the case of the example below, the use of tert-butoxide results in the formation of 1-hexene preferentially, while the use of methoxide results in preferential formation of 2-hexene. Draw a mechanism for each elimination reaction. Provide an explanation for the difference in preference depending on the reagent used. (J. Am. Chem. Soc. 1967, 91, 1376)
10. Describe what you expect would generally happen with the following types of reagents:

a. alkylating agent
b. fluorinating agent
c. dehydrating agent
d. oxidizing agent
e. reducing agent

11. Reagents are used to oxidize as well as to reduce organic compounds. For each reaction below, identify the reagent and determine if it oxidized or reduced the substrate.

12. The petroleum industry uses alkylation to produce high-octane components of gasoline. This is often done using isobutene and a strong acid catalyst such as sulfuric acid. For each of the reactions below, assign the terms reactant, reagent, and substrate. Identify what part of the product is from isobutene and the new carbon-carbon bond formed. (Alkylation is an important source for octane in gasoline. U.S. Energy Information Administration. Eia.gov)

13. Define product. Where are products indicated in a chemical reaction equation?

14. What is a kinetic product? What is a thermodynamic product? Draw energy diagrams showing both types of products of a reaction.
15. Complete the following mechanism by filling in any missing products or curved arrows.

16. What is the difference between a transition state and an intermediate? Would either of these be considered products?

17. Draw a reaction diagram with only one transition state. Draw a reaction diagram with one intermediate. Label each diagram with reactant, transition state, intermediate, and product.

18. Some reactions are performed in order to determine what functional groups are present in the starting material or to get an idea of the possible structure. For each set of reactions below, determine a possible structure for the reactant and products.

\[ \text{C}_4\text{H}_8\text{O} \xrightarrow{\text{LiAlH}_4} \text{C}_4\text{H}_{10}\text{O} \]
\[ \text{H}_2, \text{Pt} \xrightarrow{} \text{No reaction} \]

\[ \text{C}_5\text{H}_{10}\text{O}_2 \xrightarrow{\text{LiAlH}_4} \text{C}_2\text{H}_4\text{O} + \text{C}_3\text{H}_6\text{O} \]
\[ \text{LiBH}_4 \xrightarrow{} \text{No reaction} \]

**Reaction Conditions**

19. Name three examples of variables that could be considered reaction conditions?

20. While \( S_{\text{N}2} \) reactions are typically more favorable in polar aprotic solvents, the use of polar protic solvents can result in \( S_{\text{N}2} \) reactions as well. What variables in your reaction could you alter to achieve an \( S_{\text{N}2} \) substitution reaction in a polar protic solvent? How would you change these conditions?

21. In green organic chemistry, the focus is development of more environmentally friendly processes of preparation of organic compounds. One way that this can be achieved is through the minimal use of organic solvents. In the following reaction, an aldol condensation results in the formation of the product along with water. Would you expect the use of water as the solvent to increase or decrease the yield of the product? If the product is insoluble in water, does this change? (J. Chem. Educ. 2007, 84, 475-476)
22. When performing an aldol addition, reaction conditions can dictate whether a kinetic or thermodynamic enolate forms. An example of this is shown below (kinetic top, thermodynamic bottom). (J. Am. Chem. Soc. 1974, 96, 5944)

![Reaction Scheme](image)

a. Which product is lower in energy?

b. Why is a larger base used to form the kinetic enolate?

c. Given the following reactant and desired product, which enolate should be formed?

![Reactant and Product](image)

23. Explain whether it would be better to alter one condition at a time or change multiple conditions when trying to find the best set of conditions for a reaction. How would you determine which set of reaction conditions were best?

25. Pressure and temperature are important conditions to consider for some reactions, such as the Haber-Bosch Process used to produce ammonia. Why would pressure be important for this reaction but not for the reaction between acetic acid and sodium hydroxide? Would increasing the temperature favor the forward (exothermic) or reverse (endothermic) reaction for the Haber-Bosch Process?

\[
\ce{N_2(g) + 3 H_2(g) \rightarrow 2 NH_3(g)}
\]

26. Determine the overall yield for the selected steps from the convergent synthesis of hemibrevetoxin B, a marine neurotoxin. If you were able to find reaction conditions that would improve the percent yield of the second step to \(89\%\) and the third step to \(95\%\), how would the overall yield improve? (J. Am. Chem. Soc. 2002, DOI: 10.1021/ja029225v)

<table>
<thead>
<tr>
<th>Step</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>\ce{AcO}</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>\ce{AcO}</td>
<td>83%</td>
</tr>
<tr>
<td>3</td>
<td>\ce{Ph}</td>
<td>93%</td>
</tr>
<tr>
<td>4</td>
<td>\ce{OH}</td>
<td></td>
</tr>
</tbody>
</table>

27. Define catalyst. Is a catalyst consumed in a reaction? What is the catalyst's role in a reaction?

28. Draw a mechanism for the following reaction. Is there a catalyst present? If so, what is acting as a catalyst?

\[
\text{PhCO}^- + \text{HCl, Water} \rightarrow \text{PhCOOH}
\]
29. 2,4-dinitrophenylhydrazine, or Brady's reagent, is used to test compounds for the presence of an aldehyde or ketone functional group. The 2,4-dinitrophenylhydrazine reacts with the aldehyde or ketone group of the compound, in the presence of an acid catalyst, to form an insoluble dinitrophenylhydrazine. You perform Brady's test using both concentrated hydrochloric acid and acetic acid. For the hydrochloric acid, you observe immediate formation of the hydrazone, but do not see formation of the hydrazone for the acetic acid. After 15 minutes, you begin to see formation of the hydrazone. Why does the acid used result in differing rates of reaction? (*J. Chem. Educ. 1959, 36, 575*)

30. Does the presence of a catalyst have an effect on the change in free energy of a reaction?

31. What is the difference between a heterogeneous catalyst and a homogeneous catalyst?

32. Carbonic anhydrase catalyzes the reaction from carbonic acid to carbon dioxide and water in the lungs, where there the carbon dioxide concentration is low. Carbonic anhydrase is also present in other tissues; in the tissues with high concentrations of carbon dioxide, would you expect the enzyme to catalyze the decomposition of carbonic acid?

33. Catalase is an important enzyme for protecting cells from damage from reactive oxygen species by catalyzing the decomposition of hydrogen peroxide into water and oxygen. The uncatalyzed decomposition is thermodynamically favorable, but it is slow enough that hydrogen peroxide is fairly stable at room temperature and can be bought at grocery stores. It has many uses; it is often used for cleaning wounds, and in microbiology it can aid in identifying catalase-positive bacteria. What causes the bubbling observed when it is applied to a wound? Why would this not be observed if it was applied to uncut skin? What would be the observable difference between catalase-positive and catalase-negative bacteria when it comes into contact with hydrogen peroxide?

**The Role of Energy**

34. Estimate \(\Delta H\) for the following reactions. Are they exothermic or endothermic? Is the entropy, \(\Delta S\), positive, negative, or approximately zero for these reactions? Identify any reactions that you expect to be spontaneous at any temperature.

   a. 
   \[
   \begin{array}{c}
   \text{Cl} \\
   \text{Cl}
   \end{array} 
   \xrightarrow{H^+} 
   \begin{array}{c}
   \text{OH} \\
   \text{OH}
   \end{array} 
   \]

   b. 
   \[
   \begin{array}{c}
   \text{C} \\
   \text{C}
   \end{array} 
   \xrightarrow{H^+} 
   \begin{array}{c}
   \text{C} \\
   \text{C}
   \end{array} 
   \]

   c. 
   \[
   \begin{array}{c}
   \text{O} \\
   \text{O}
   \end{array} 
   \xrightarrow{H^+} 
   \begin{array}{c}
   \text{O} \\
   \text{O}
   \end{array} 
   \]

35. Determine whether the reactants, products, or neither are favored in the following equilibrium reactions.
a. A reaction with $K_{\text{eq}} = 3$

b. A reaction with $K_{\text{eq}} = 0.5$

c. A reaction with $\Delta G = 0$

d. An endothermic reaction with negative entropy

e. An exothermic reaction with positive entropy

36. In the following equilibrium, will more products form at a higher or lower temperature? Explain why this occurs.

\[ \text{CO} \rightleftharpoons \text{OH} \stackrel{H_2O^+}{\longrightarrow} \text{HO} \]

37. One method used to reduce alkenes and alkynes to alkanes is a combination of palladium and hydrogen gas. If one wants to reduce an alkyn to an alkene, one cannot use this system, but must use a modified (poisoned) version of the palladium catalyst so that the reaction stops at the alkene.

a. What is the enthalpy for the reduction of 2-butyne to 2-butenef?

b. What is the enthalpy for the reduction of 2-buten to 2-butane?

c. Explain why the normal palladium-catalyzed reduction does not stop at the alkene, but continues to the alkane.

38. Define enthalpy, entropy, Gibb's free energy, exothermic, endothermic, exergonic, and endergonic.

39. What are the units for a reaction rate? What are the units for the rate constant of a first order, second order, and third order reaction?

40. Is this reaction spontaneous at room temperature ($\sim 21^\circ\text{C}$)? Above what temperature would this reaction become spontaneous? $\Delta S = +120 \text{J/mol} \cdot \text{K}$

41. Use the Hammond Postulate to determine which of the structures is a better representation of the transition state for the exothermic reaction. Use this information to predict the transition state for the endothermic reaction. What generalization can you make about the transition state for an exothermic reaction and an endothermic reaction with only one transition state?