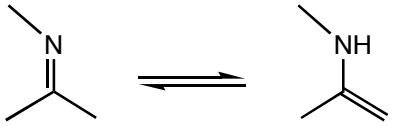
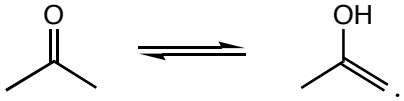
Additional Problems for Catalysis:

1. Which of the following acids could give specific or general catalysis in the following reaction (the pKa of the conjugate acid of an amine is 4.5): HCl, picric acid, acetic acid, ammonium ion, and phenol.



2. For the following enolization of acetone:

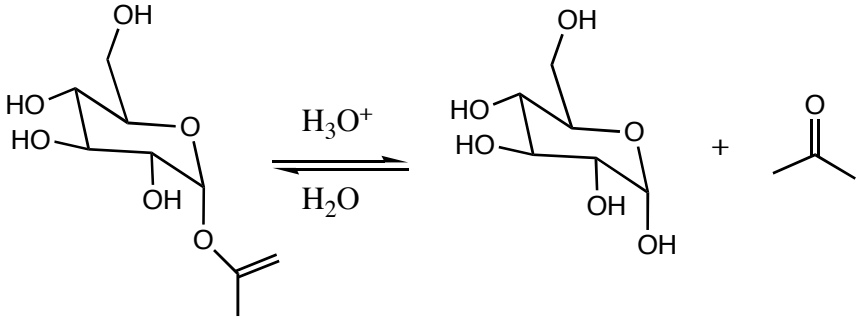


   a.) Write a specific-acid-catalyzed mechanism
   b.) Write a general acid-catalyzed mechanism
   c.) Write a specific base-catalyzed mechanism
   d.) Write a general base-catalyzed mechanism

3. The enolization of acetone shown above was also found to have the following rate term: rate = k_{ab}[HA][B][acetone]. Experiments revealed that for this term, there were two isotope effects and two different Bronsted relationships described below:
   a.) when the reaction is run in D_2O, the k_{ab} is one-half the k_{ab}in H_2O. In other words, k_{H2O}/k_{D2O} is near 2 for the various acids (note that any acidic hydrogen atom on an acid in D_2O will become deuterated)
   b.) If one deuterates the methyl protons of acetone, an isotope effect of k_H/k_D=5.8 is found
   c.) An α value of 0.2 and a β value of 0.88 were found for this third-order term.

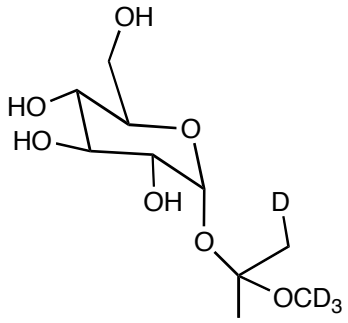
   Write a mechanism for this enolization that is consistent with all these data. Explain each piece of data and how it is consistent with the mechanism you wrote.

4. For the following reaction:



The following data were collected to elucidate the rate-determining step.

a.) Electrophilic addition of $DOCD_3$ catalyzed with $D_2O^+CD_3$ resulted in the following product and no incorporation of deuterium could be found in the starting material:



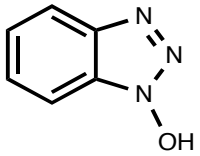
b.) Similarly, when the hydrolysis was performed in D_2O, no deuterium was incorporated into the starting material, and only one atom of deuterium was found in the acetone produced.

c.) An isotope effect of $k_H/k_D = 3.06$ was found when the reaction was catalyzed by H_3O^+ or D_3O^+

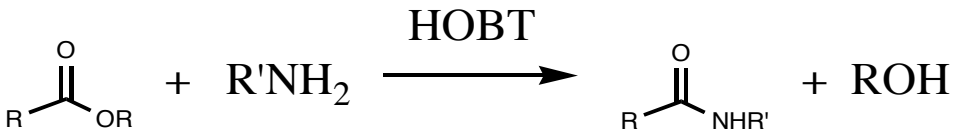
d.) An α value of 0.637 was found for this reaction

Do these four experiments support general acid or specific acid catalysis? Explain how each of these four pieces of data supports your conclusion as to the type of catalysis by which this reaction proceeds.

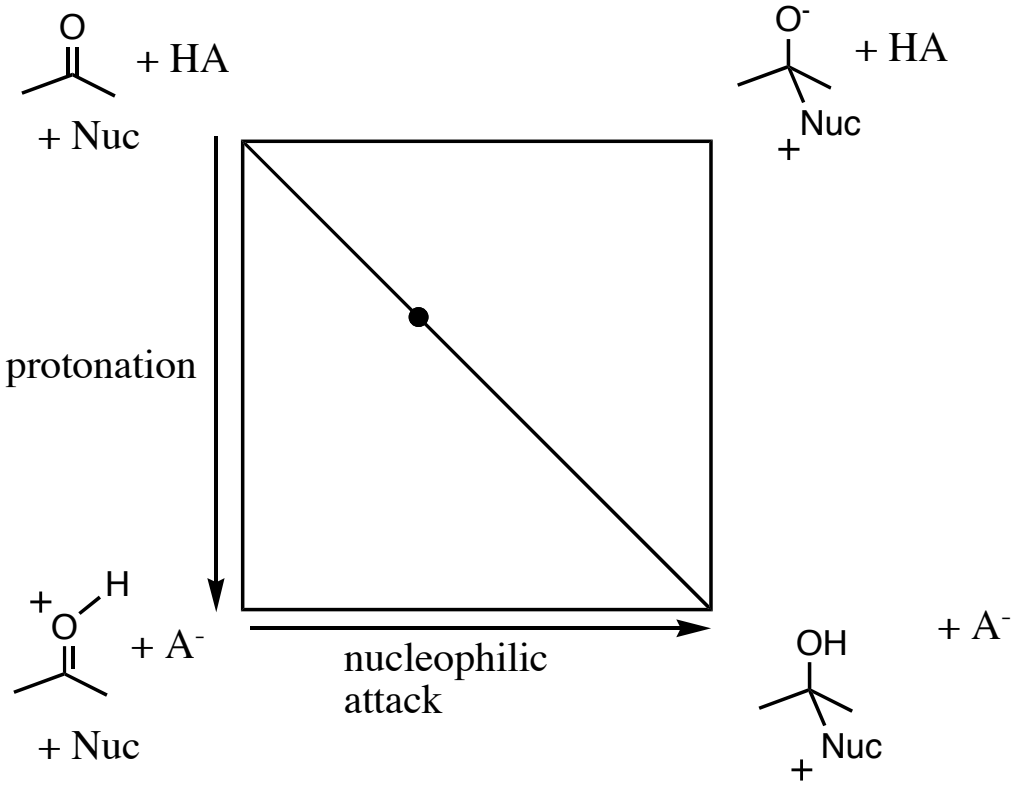
5. The compound N-hydroxybenzotriazole (HOBT) is often added to increase the rate of reaction of an ester with an amine to form an amide. What is the role of HOBT?



HOBT



6. On the More-O'Ferrall plot below for nucleophilic addition to a carbonyl, what happens to the transition state in terms of the extent of nucleophilic attack and the extent of protonation (α value) as the acid HA becomes stronger? Draw the position of the new transition state on the diagram.


O
+ HA
+ Nuc
O-
+ HA
Nuc
+
protonation
+
O
H
+ A-
+ Nuc
nucleophilic
attack
OH
+ A-
Nuc
+