

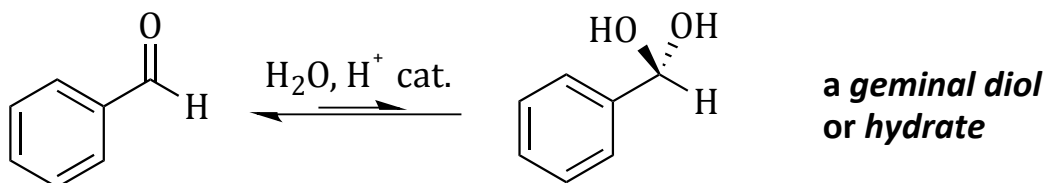
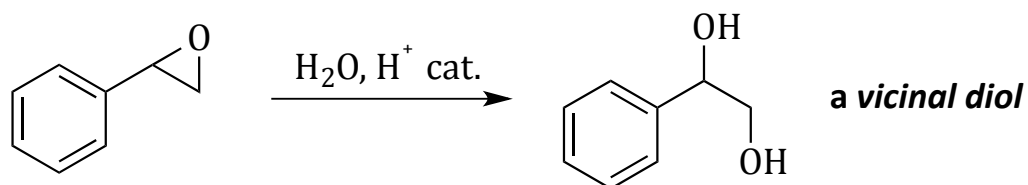
Reversible Addition to Carbonyls: pH-Dependence

Hydride reducing agents and organometallic reagents are both examples of *excellent*, strong nucleophiles. What happens if we treat a carbonyl compound with a *weaker* nucleophile?

Acid catalysts make an *electrophile* more *electrophilic*;
base catalysts make a *nucleophile* more *nucleophilic*.

Reversible Addition to Carbonyls: Acidic Conditions

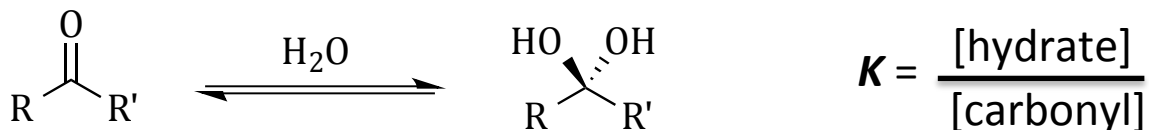
Provide complete curved-arrow mechanisms for the following reactions:



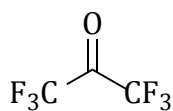
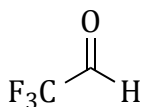
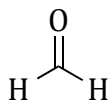
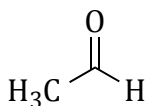
Why is the hydration of an aldehyde or ketone *reversible*?

Reversible Addition to Carbonyls: Hydration Equilibria

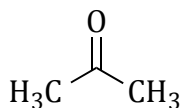
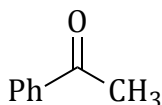
Explain the observed ranking of equilibrium constants for carbonyl hydration:



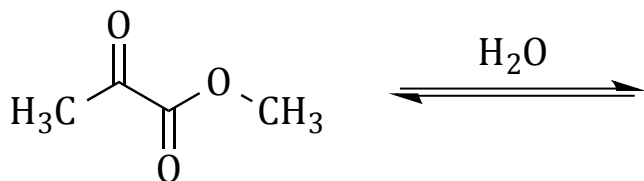
Carbonyl compound	relative K
<chem>FC(F)(F)C(=O)C(F)(F)F</chem>	1×10^6
<chem>FC(F)(F)C=O</chem>	3×10^4
<chem>C=O</chem>	2×10^3
<chem>CC=O</chem>	1
<chem>CC(=O)C</chem>	1×10^{-3}
<chem>CC(=O)c1ccccc1</chem>	9×10^{-6}


 1×10^6

 3×10^4

 2×10^3


1

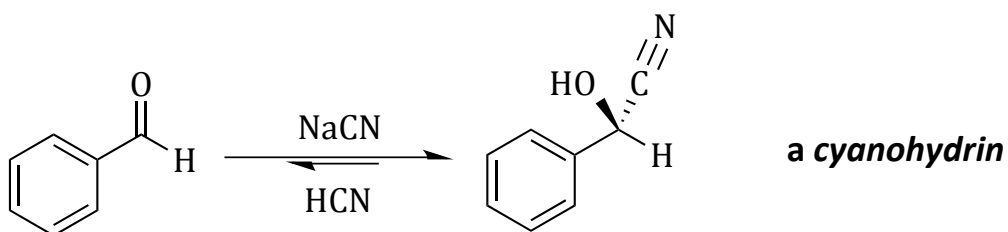
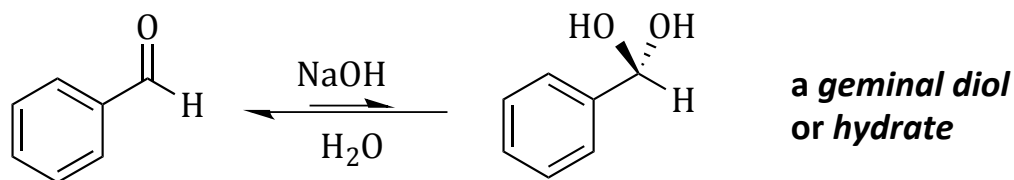
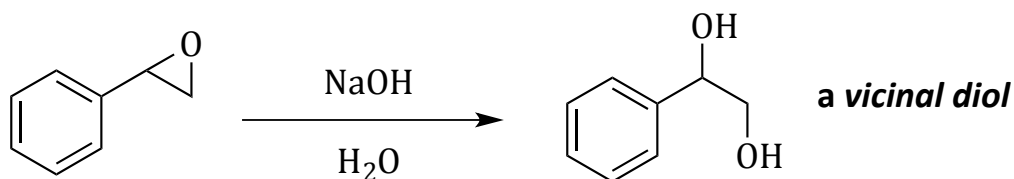

 1×10^{-3}

 9×10^{-6}

The following compound has two carbonyl groups. Which one will become hydrated under aqueous conditions? Explain why $K_{\text{rel}} = 0.8$, i.e. significantly larger than for most unsubstituted ketones such as acetone (above).



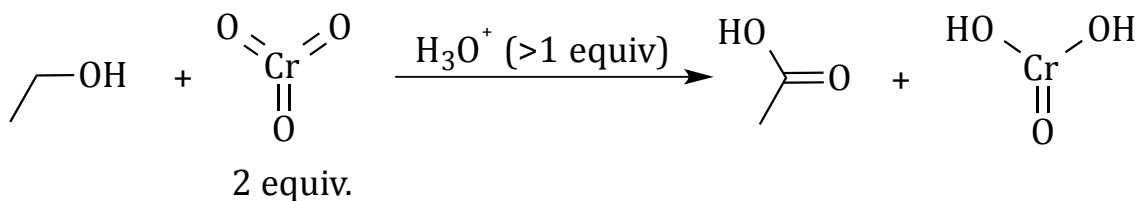
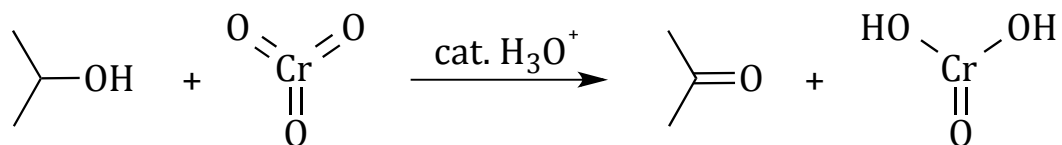
Reversible Addition to Carbonyls: Basic Conditions

Provide complete curved-arrow mechanisms for the following reactions:



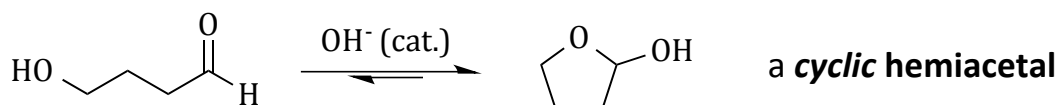
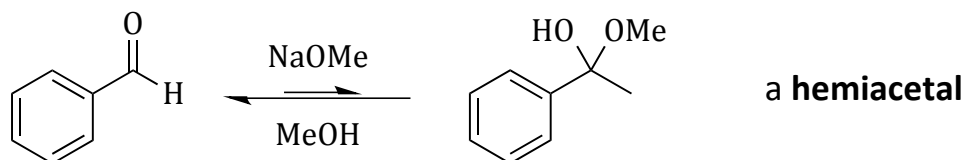
Going Backward: Oxidation of Alcohols

Provide curved-arrow mechanisms for each of the following oxidation reactions.



Reversible Addition to Carbonyls: Hemiacetals

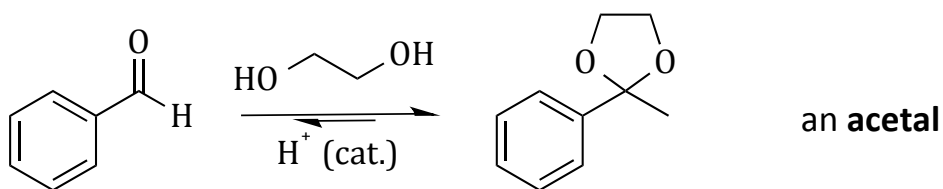
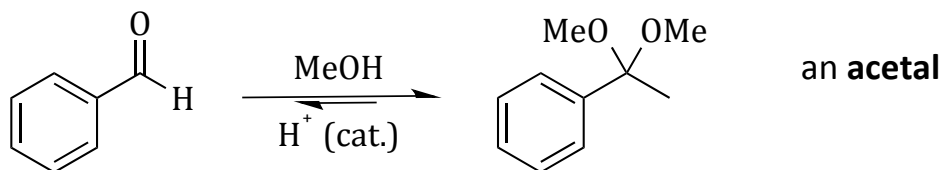
Provide a complete curved-arrow mechanism for each of the following reactions:



Monosaccharides (glucose, fructose, etc.) all exist naturally as hemiacetals; we'll discuss more later...

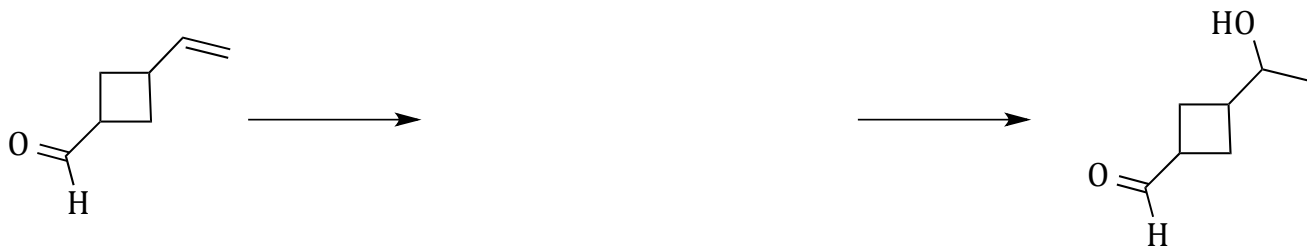
Reversible Addition to Carbonyls: Acetals

Provide a complete curved-arrow mechanism for each of the following reactions:



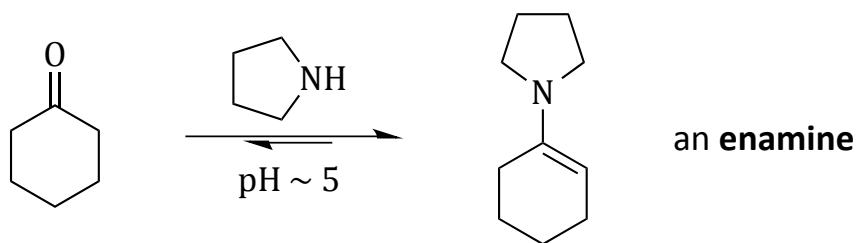
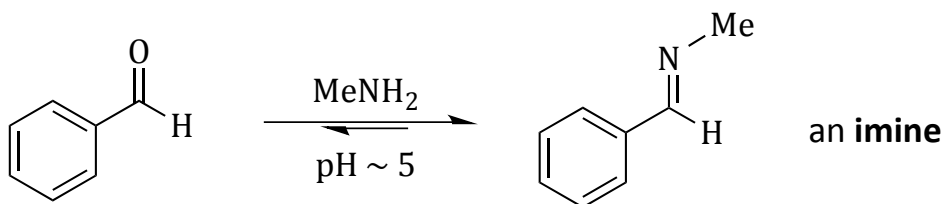
Reversible Addition to Carbonyls: Acetals as Protecting Groups

How would you carry out the following synthetic transformations?



Reversible Addition to Carbonyls: Imines, Iminium Ions, and Enamines

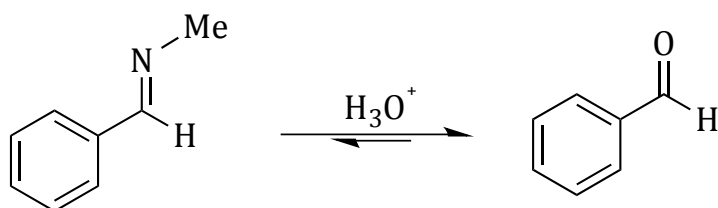
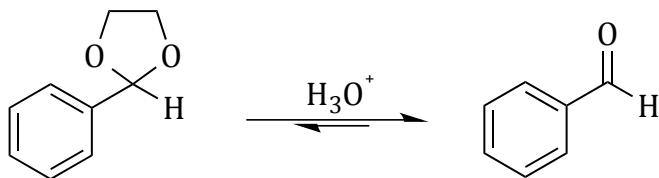
Provide a complete curved-arrow mechanism for each of the following reactions.



Why pH 5?

Reversible Addition to Carbonyls: Hydrolysis of Acetals, Iminium Ions, & Enamines

The hydrolysis of acetals & imines is simply the reverse of their formation! Provide a complete curved-arrow mechanism for each of the following reactions.

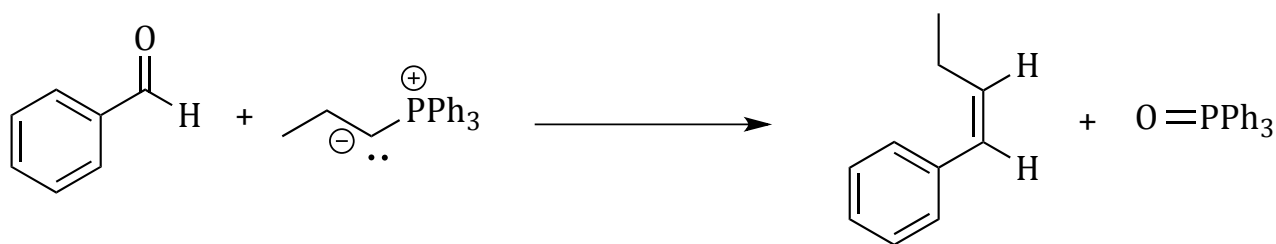


The Wittig Reaction: Synthesizing Alkenes from Carbonyls

The Wittig reaction is a remarkably useful synthesis of alkenes. First, an alkyl halide is used to form a **phosphonium ylide**. Provide a curved-arrow mechanism.



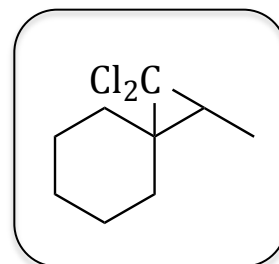
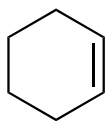
Then the phosphonium ylide is added to an aldehyde or ketone to yield a new carbon-carbon **double** bond! Provide a mechanism.



** The Wittig reaction tends to give *cis* alkenes when there is a choice. **

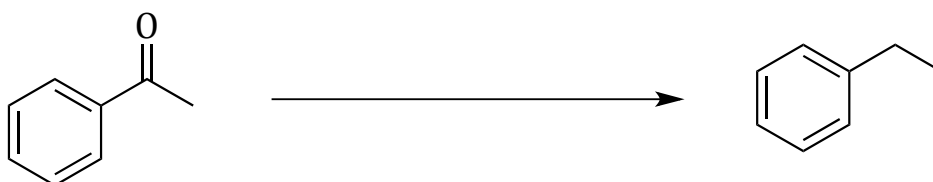
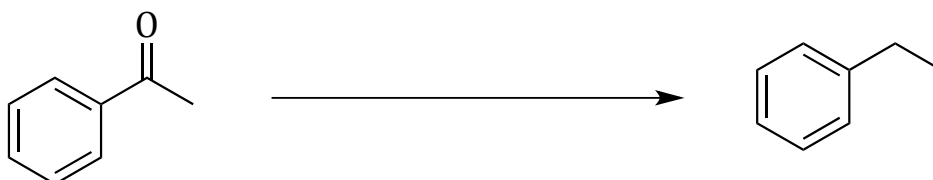
The Wittig Reaction in Synthesis

How would you carry out the following transformation?



“Removing” a Carbonyl Group from Aldehydes & Ketones

What reagents could you use to carry out the following transformations?



**** The Wolff-Kishner & Clemmensen reactions only work on
carbonyl groups at the ketone oxidation level! ****