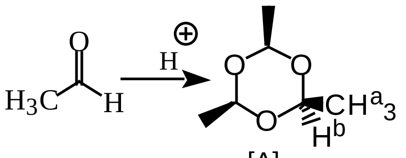
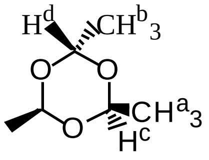
Chemistry 304B Spring, 1999 KEY TO Problem Set 6

1. Consider the following data for the major product, **A**, from the following reaction. Note that a minor amount of another isomer is also detected, **B**, which shows the same mass spec and IR properties, but the NMR data are different. [Hint: a carbonyl oxygen can be a nucleophile, even if a very weak one]



[A]

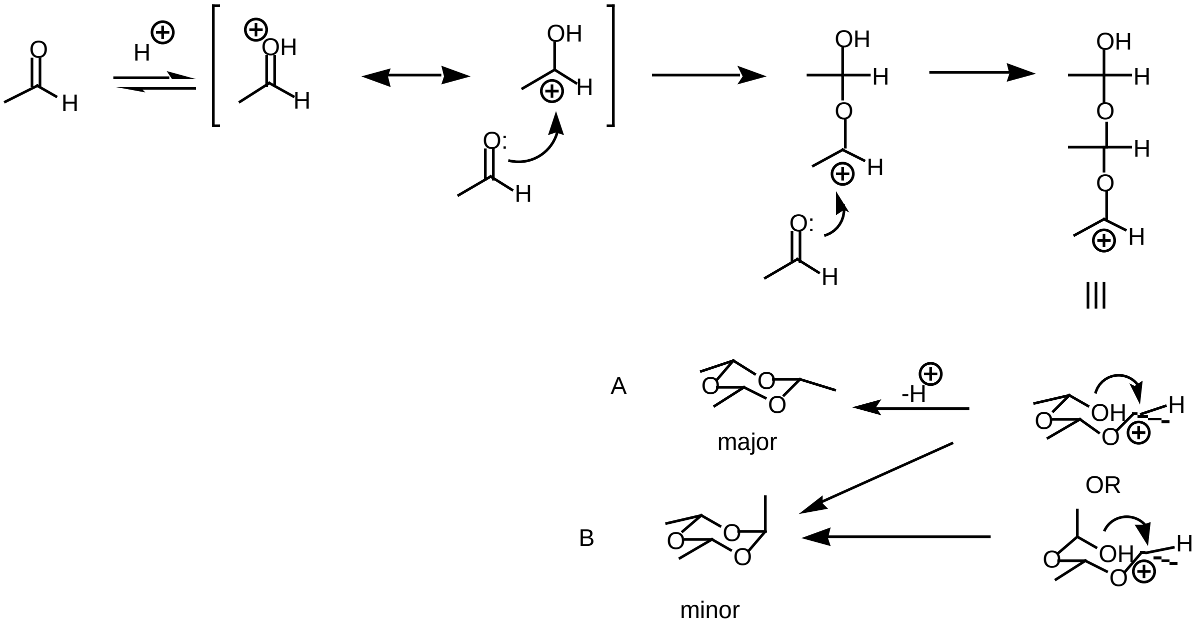
IR: no significant peaks in region **No C=O**
1600-4000 cm^{-1} except for C-H stretch
^{1}H NMR: δ 1.1 ($3H^a$, doublet, J=7 Hz), 4.8 ($1H^b$, quartet, J=7)
^{13}C NMR: two signals 20.0 (C^a) and 100 ppm (C^b)
Mass spec: parent ion at 132 mass units (daltons) **$C_6H_{12}O_3$**



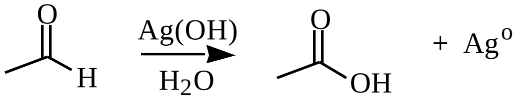
^{1}H NMR: d 1.1 ($6H^a$, doublet, J=7 Hz), 1.21 ($3H^b$, doublet, J=7Hz), 4.8 ($2H^c$, quartet, J=7), 4.95 ($1H^d$, quartet)
^{13}C NMR: four signals 20.0 (C^a), 20.5 (C^b), 98 (C^c) and 100 ppm (C^d)

[B]

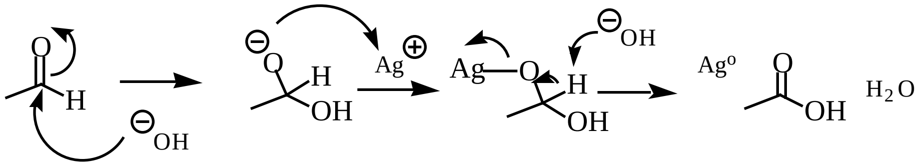
Draw the most likely structures for **A** and **B**, and explain how your structures are consistent with the spectral data. Write a careful mechanism for the formation of **A.** YOU SHOULD WRITE A THOROUGH ANALYSIS OF THE NMR DATA, INCLUDING THE COUPLING CONSTANTS AND CHEMICAL SHIFTS POSITION BASED ON TABLES OF GENERIC CHEMICAL SHIFTS.



2. We discussed in class the oxidative metabolism of ethanol to acetic acid with two enzyme-catalyzed steps. The formation of acetaldehyde follows our general mechanism for oxidation of alcohols to aldehydes, but what about the conversion of acetaldehyde to acetic acid?

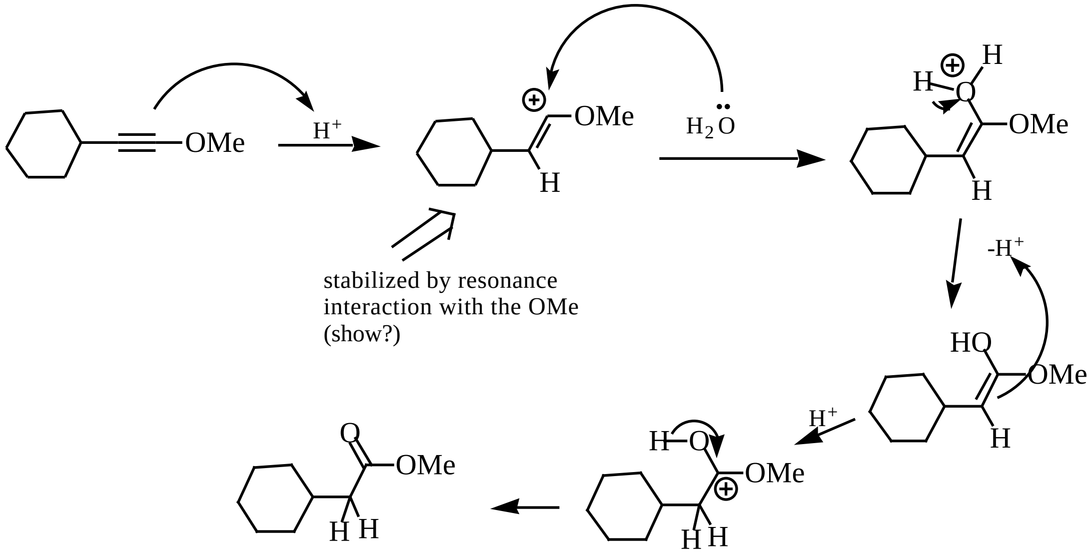


In fact, this conversion is typically slow with conventional oxidizing agents unless water or another weak nucleophile (pyridine) is present in the solution. A standard mixture to carry out this process is silver hydroxide in basic aqueous solution. The products are the acid and silver metal, as a mirror on the flask, which indicates that reaction has occurred. Propose a mechanism which takes into account the presence of hydroxide anion and produces silver metal. [Hint: the oxidation mechanism operates on alcohols. What is the likely reaction between hydroxide anion and the aldehyde?]



The point in oxidation is to replace the H on an OH with a species which can favorably accept electrons (electronegative atom, metal in positive oxidation state). The trick here is to see that the aldehyde can become a special sort of alcohol in base, the hydrated version. This then can be oxidized like any alcohol. The second trick is seeing that Ag^+ can serve as the repository for an electron, giving Ag metal.

3. Write a stepwise mechanism to rationalize the following conversion:

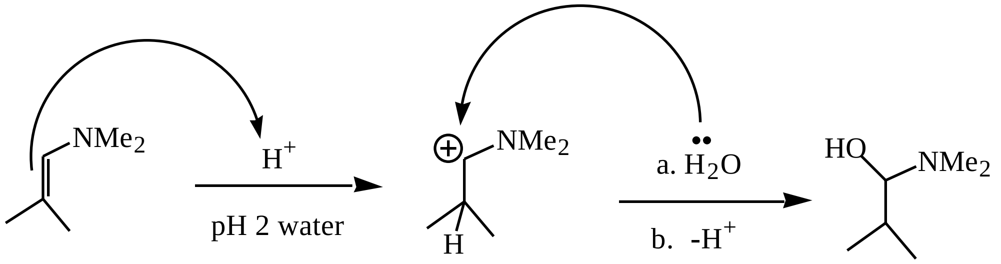


stabilized by resonance
interaction with the OMe
(show?)

This is an example of the protonation of an electron rich pi bond, made electron rich by the presence of an alkoxy group. In the first case, it is an alkyne, and in the second stage, an alkene. But the driving force and selectivity is the same, dominated by the formation of a carbocation stabilized by resonance interaction with the alkoxy oxygen.

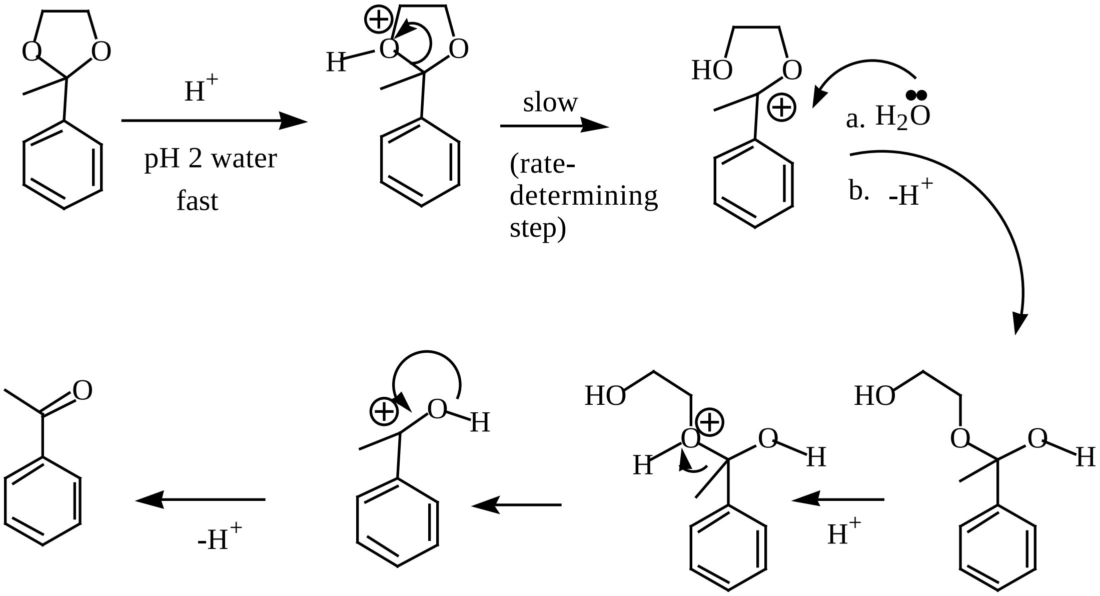
4. Choose which of the following reactions would be faster and write the product of that reaction. Explain your choice.

A.



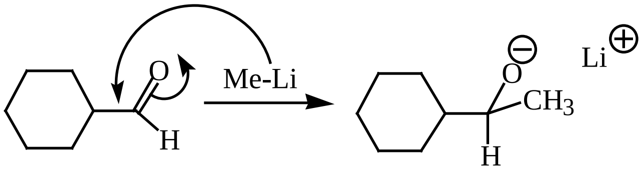
faster since goes through more stable carbocation (N is less electronegative and thererfore bear a positive charge better through resonance donation of the electron pair)

B.



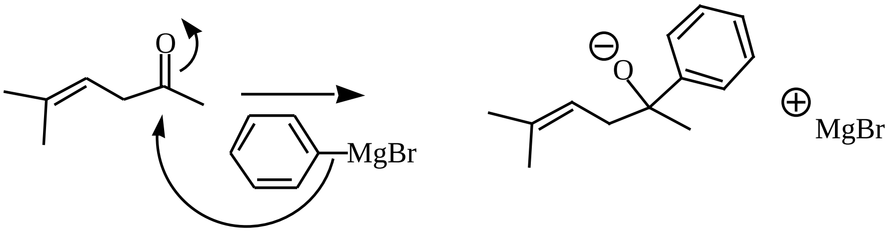
The point here is that in acid, all of the oxygens CAN be protonated, and such protonation can lead to further reaction. Often protonation at O just leads backwards or nowhere; your job is to see which protonation leads onward to the product in the shortest way and involving the "best" (lowest energy, most stable) intermediates. The first high energy intermediate here is the carbocation from ionization of the ketal, and it is made more favorable by resonance stabililization with the phenyl group (show resonance structures for complete answer). Generally, protonation of O or N cannot be the rate-determining steps; the barrier to such protonation is always very low.

C.



Aldehyde is more reactive then a ketone because the carbonyl group in a ketone is more stabilized and more hindered.

D.



Mg is more electropositive, therefore the nucleophile is more reactive, more electron-rich.

4. Write a stepwise mechanism to rationalize the following conversion.