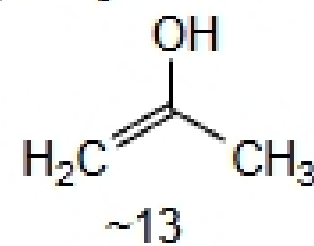
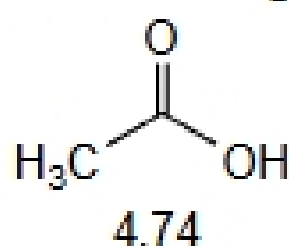
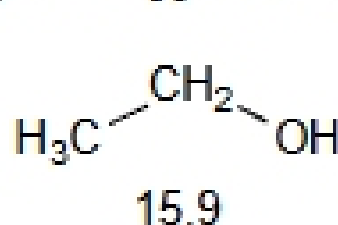


1. (3 minutes) Give approximate pK_a values for the following compounds (no explanations required):



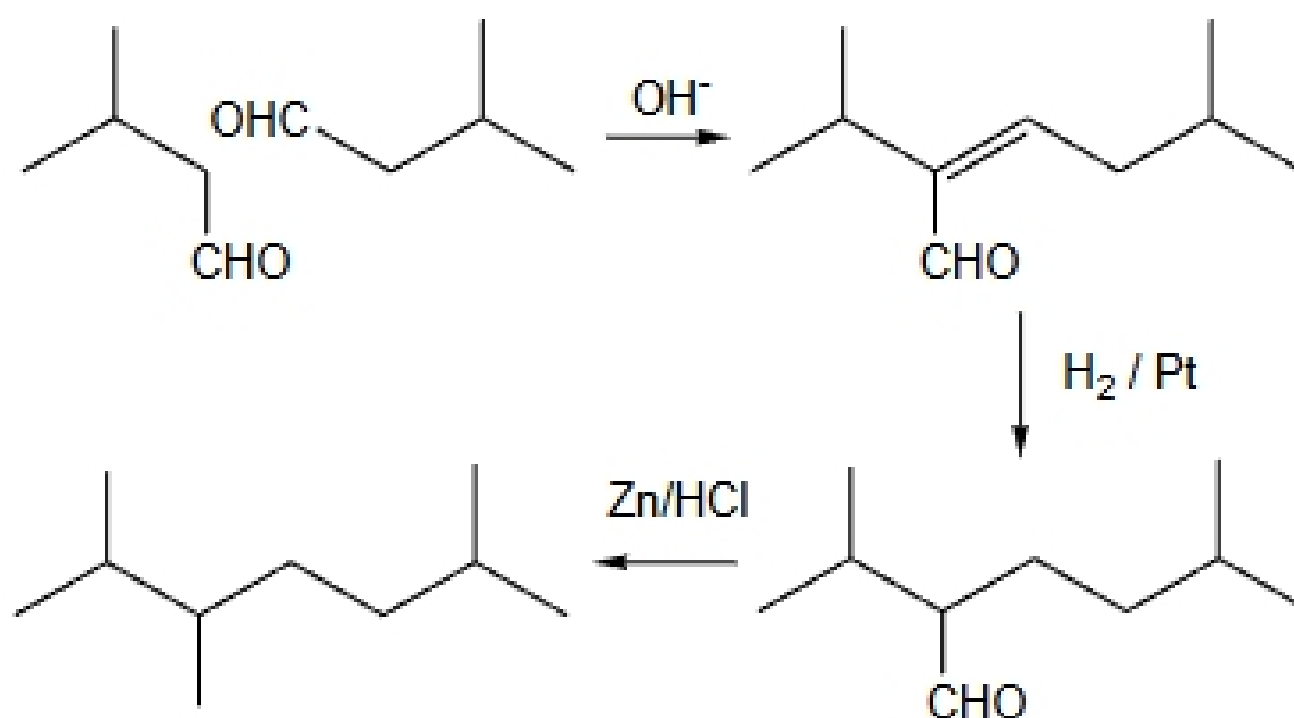
[2 points for each within ± 1 unit; 1 point for each within ± 2 units. Note that 19 is the pK_a of acetone. The enol here is less stable than acetone, thus more acidic in giving the same anion. Clearly the acidity of an enol should fall between those of an alcohol and a carboxylic acid.]

2. (3 minutes) What lesson about the design of a synthesis is taught by the practical preparation of $(\text{CH}_3)_3\text{C}-\text{NH}-\text{NH}_2$?

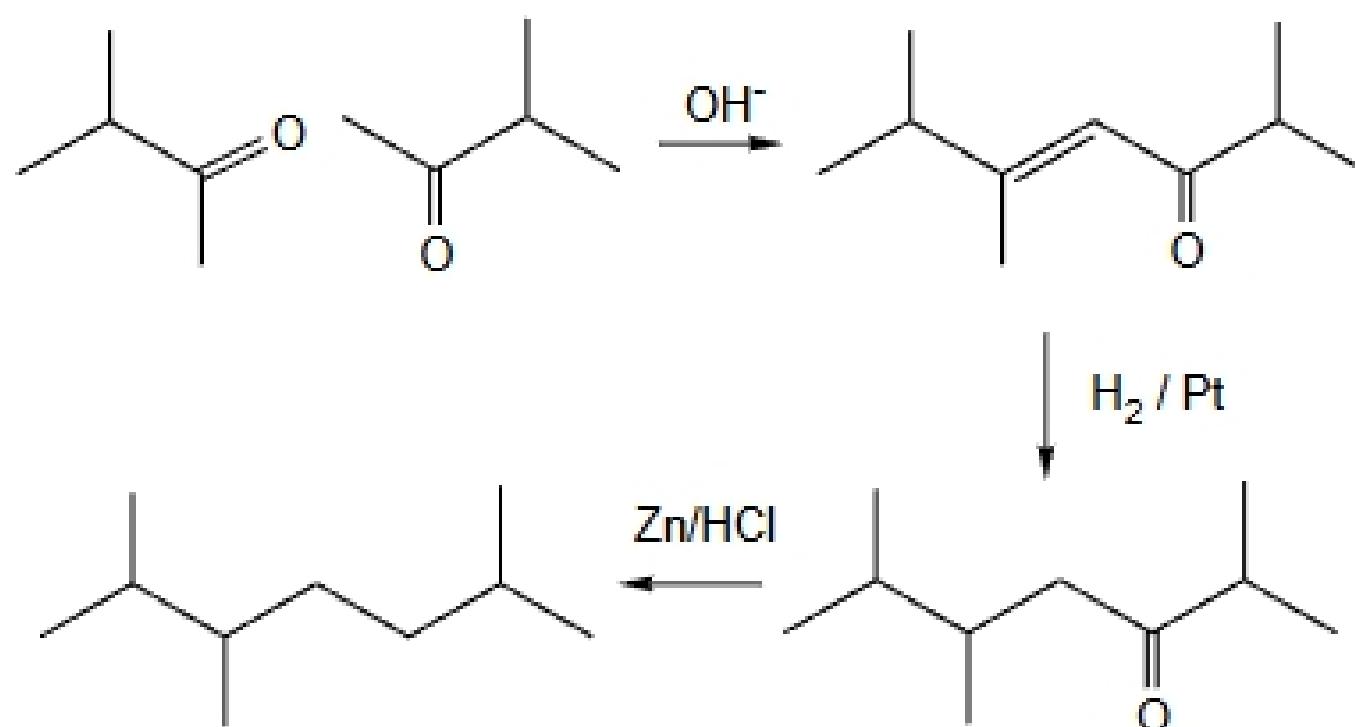
The main lesson is that even a reaction that gives very low yield ($t\text{-BuCl} + \text{H}_2\text{NNH}_2$ gives only 5% S_N2) can still be quite practical, if the starting materials are cheap and the desired product is easily purified (the predominant product is a gas, and the desired hydrochloride salt is easily purified by crystallization). *The method recommended in the chemical literature was expensive and cumbersome with many steps, several of them low-yield, just to avoid the admittedly low-yield S_N2 reaction.*

3. (6 minutes) Show a sequence of reagents and intermediate products that would allow preparation of the following 10-carbon alkane in good yield. You may use any reagents you wish, but **all carbons must come from a single 5-carbon compound**. No mechanisms or curved arrows are necessary, just reagents and intermediates.

[This is problem 6:2f, from the assigned set. It also appeared on a previous exam. Note the bold-face restriction that both 5-carbon units come from the same molecule, suggesting aldol.]



There are many other schemes for reducing the two double bonds. One could also begin the aldol-dehydration sequence with methyl isopropyl ketone:



4. (8 minutes) One reaction in Woodward's synthesis of cortisone involved acid-catalyzed conversion of a keto acid to an enol lactone. Add necessary atoms, bonds, and arrows to the following structures to show every step involved in this conversion. **Draw only one curved arrow in each structure.** You will probably not need all of the structures.

Three possibilities are shown below. As we'll see in Ch. 19, it is slightly easier to protonate the carbonyl of an acid than of a ketone, but it is not obvious which mechanism is best, and probably all contribute to some extent. Isotopic labeling with ^{18}O might allow some distinctions, if independent loss of ^{18}O is not too rapid. At any rate, a correct answer should show a reasonable sequence involving low-energy cationic intermediates. Direct protonation of the OH group of COOH and loss of water to generate the cation $\text{R}-\text{C}=\text{O}^+$ can occur, but only when the normal Fischer protonation of the $\text{C}=\text{O}$ group cannot lead to product (as we'll see shortly). Many papers ignored the instruction to draw one curved arrow in each structure.

I. Initial protonation and ultimate loss of acid oxygen:

keto acid

