Reactivity at alpha-carbon III

1. Complete the following synthesis scheme with the missing products, reagents and relevant reaction conditions. Make sure to know the mechanism of the reactions.

a)
$$E1O_{2}C CO_{2}E1 H_{3}O^{+} HO_{2}C HO CN A HO_{2}C HO C$$

Favorably oriented hydroxy group attacs the carboxylic acid and spontaneously forms the 6-membered lactone (cyclic ester)

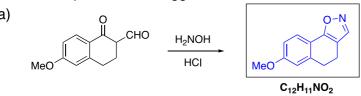
Step 1 and 2:

Step 3:

Make sure you know the mechanism of enamine formation!

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2. Provide the product and suggest the mechanism for the following reactions.



MeO

C)
$$\begin{array}{c} O \\ AcOH, H_2O \\ \hline \\ C_{11}H_{14}O_2 \end{array}$$

.....

Note:

3. Propose a synthesis of pentanoic acid using diethyl malonate as starting material. Clearly state any other reagents needed and provide the reaction mechanism.

4. In class, we learned how to make furans via Paal Knorr synthesis. Another way of synthesising substituted furans is using 1,3-dicarbonyls and α -chloroketones under basic conditions. They can further react with electrophiles. Provide the products of the following reactions and include the mechanisms.

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1st step: alternative

2nd step:

- α -Substitution is favoured over β -substitution more resonance forms for intermediate, so the charge is less localized
- Some β-substitution is usually observed (depends on the other substituents)

Regioselectivity: See more in Clayden, 2nd Edition, Chapter 29, p. 733

 α -substitution

$$X = O \text{ (furan)}$$
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β-substitution

$$X = O \text{ (furan)}$$
NH (pyrrole)

5. Provide the product and a mechanism accounting for its formation. (Hint: FeCl₃ acts as a Lewis Acid)

Aromatisation in the final step is irreversible and drives the reaction

6. Dihydropyridine can be synthesised using a multi-component organic reaction between an aldehyde such as formaldehyde, 2 equivalents of a β -keto ester (e.g. ethyl acetoacetate) and a nitrogen donor such as ammonium acetate. Provide the product and include the mechanism.

7. Complete the following synthesis scheme with the missing intermediates / products, reagents and relevant reaction conditions. Mechanisms are not required.

