Carboxylic Acids and Derivatives

Reading:

1. J .H. Jones, "Chemistry of the Carbonyl Group", OUP Primer No. 47
2. "Chemistry of the Carbonyl Group" Stuart Warren
3. Lecture Notes.

All the major texts - March, Carey and Sundberg, Norman and Coxon, McMurray etc. have decent sections on this subject as well.

Notes

1a) Chemistry of the Carbonyl Group. Preparation and reactions of acyl chlorides, anhydrides, amides, hydrazides from acids.

b) Oxidation and reduction, Cover alcohols, aldehydes/ketones and acid derivatives; understand reagents and mechanisms where appropriate for the interconversion of these species by oxidation and reduction. Relative ease of reduction of carbonyl compounds by $LiAlH_4$ and $NaBH_4$; reduction of carboxylic acids, esters, amides etc. Bayer-Villiger oxidation of ketones. Anodic oxidation of carboxylate ions [Kolbe electrolysis]. Also revise what you know about the oxidation of C=C with peracid, permanganate, osmium tetraoxide, oxone etc.

c) Synthesis of carboxylic acids from other simple precursors. Particularly note routes via the carboxylation of anions and oxidation of olefins, alcohols and aldehydes. Learn to look at nitriles as masked acids by hydrolysis, etc.

2. Addition - elimination at acyl carbon Basic reactivity sequence:- RCOCl > RCHO > R_2CO > RCO_2R > $RCONR_2$.
Why is this reactivity sequence observed? Consider the electronic impact of the substituent attached to the carbonyl carbon.

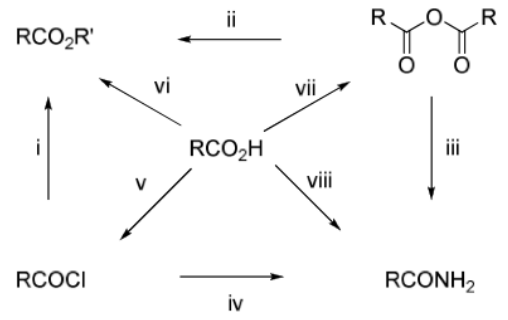
3. Ester Hydrolysis
Review the mechanisms for ester hydrolysis; Maskill, OUP Primer No 81, Ch.4 is good. (March has an extensive section on this topic). Look for evidence for acyl or alkyl cleavage. Evidence for involvement of a tetrahedral intermediate in ester hydrolysis. Irreversibility of base catalysed hydrolysis.

Then do the following:
1. Summary: Carboxylic acid esterification and ester hydrolysis: Mechanisms and evidence, stereochemistry, rates, etc. Max = 4 sides.

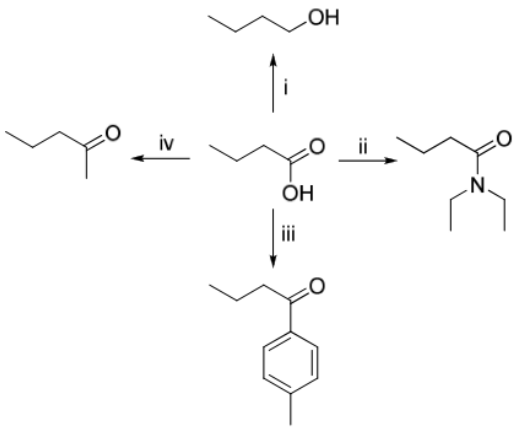
2. Problems on Esters, acids and derivatives.

1. Suggest reagents, conditions and give mechanisms (where appropriate) for the interconversion of the derivatives below.

a)



b)



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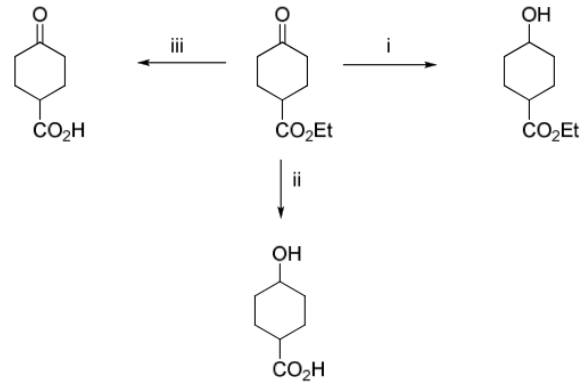

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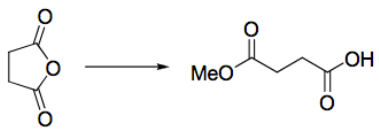
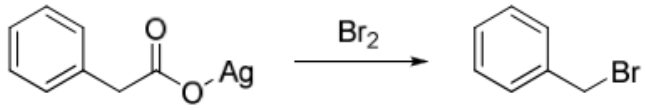
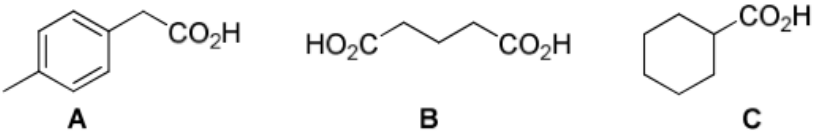


2a) Explain the reactivity difference and mechanisms for the decarboxylation reactions shown below.

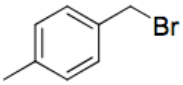
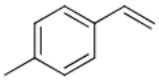
b) Give a mechanism for the Hunsdieker decarboxylation reactions below.

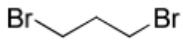


3. Provide routes to the following (more than one step may be required in each case).



A B C

a) To A from  and from 

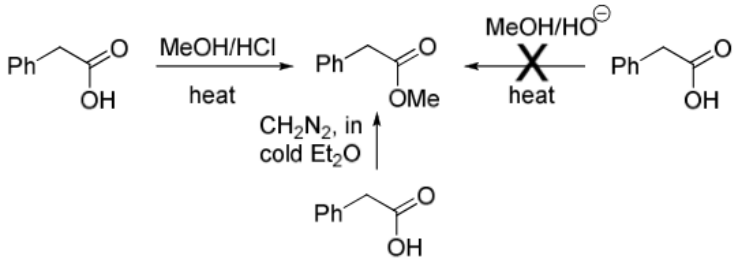
b) To B from  and from 

c) To C from whatever you feel appropriate.

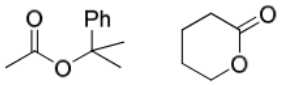
4. Explain the following, giving mechanisms:

a)

b)

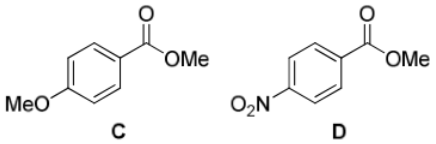


5a) Give mechanisms for the following ester hydrolyses:



A B

b) Substituent effects can make a large difference to the reactivity of esters; explain why C and D are hydrolysed at similar rates in acid but vastly dissimilar ones in base.



C D

c) When the chiral ester PhCH(Me)COOEt is hydrolysed by NaOH in aqueous ethanol, the resulting acid is extensively racemised. Explain.

d) When ethyl acetate [MeCOOEt] is partially hydrolysed by NaOH in $H_2{}^{18}O$, the unchanged ester is found to have incorporated a significant amount of labelled oxygen. When phenyl acetate [MeCOOPh] is used, no labelled oxygen is incorporated. Explain these results.

Now check your answers:
http://paton.chem.ox.ac.uk/teaching/files/Y1_carboxyclicacids_Notes.pdf