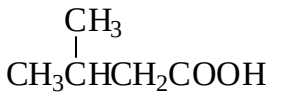
Chem 226 — Problem Set #10 —
"Fundamentals of Organic Chemistry," 4th edition, John McMurry.

Chapter 10

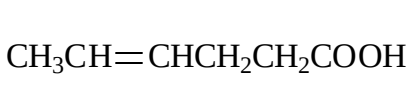
1. Give IUPAC names for compounds (a) - (e).

(a) 

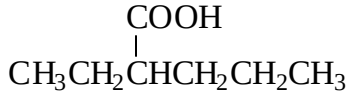
3-methylbutanoic acid

(b) 

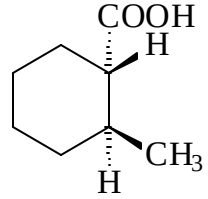
4-bromopentanoic acid

(c) 

4-hexenoic acid

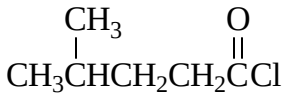
(d) 

2-ethylpentanoic acid

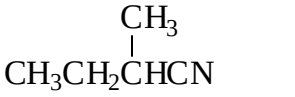
(e) 

(1S,2S)-2-methylcyclohexanecarboxylic acid

2. Give IUPAC names for the following structures.

(a) 

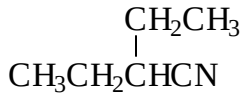
5-methylpentanoyl chloride

(b) 

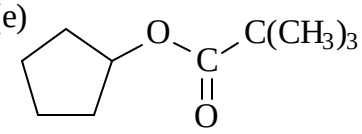
2-methylbutanenitrile

(c) 

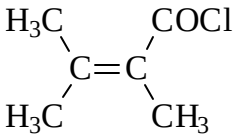
4-pentenamide

(d) 

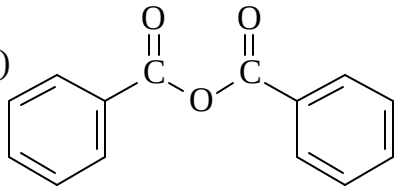
2-ethylbutanenitrile

(e) 

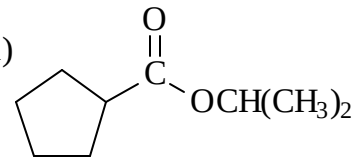
cyclopentyl 2,2-dimethylpropanoate

(f) 

2,3-dimethylbutanoyl chloride

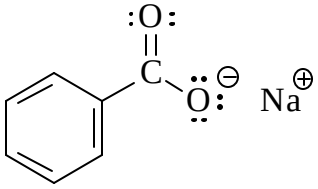
(g) 

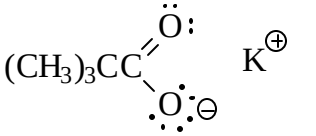
benzoic anhydride

(h) 

isopropyl cyclopentanecarboxylate

5. Draw structures for the products of the following reactions.

(a) benzoic acid + $NaOCH_3$ ⟶  + $HOCH_3$

(b) $(CH_3)_3CCOOH$ + KOH ⟶  + H_2O

6. Rank the following compounds in order of increasing acidity: sulfuric acid, methanol, phenol, *p*-nitrophenol, acetic acid.

Sulfuric acid is a very strong acid. Carboxylic acids are usually stronger acids than phenols and phenols are stronger acids than alcohols. Electron withdrawing groups, like nitro, will increase the acidity of phenols and carboxylic acids because they stabilize the phenoxide and carboxylate anions that are produced as the acid gives up its proton.

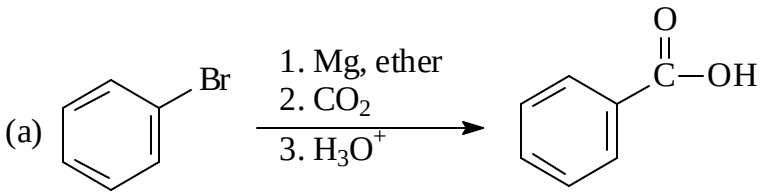
methanol < phenol < *p*-nitrophenol < acetic acid < sulfuric acid

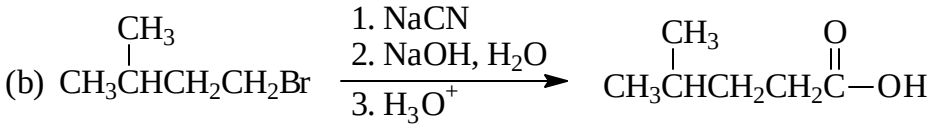
7. Rank the following compounds in order of increasing acidity.
(a) CH_3CH_2COOH, $BrCH_2COOH$, $BrCH_2CH_2COOH$
(b) benzoic acid, ethanol, *p*-cyanobenzoic acid

(a) $CH_3CH_2COOH < BrCH_2CH_2COOH < BrCH_2COOH$
(b) ethanol < benzoic acid < p-cyanobenzoic acid

In (a) the issue is that bromine is more electronegative than carbon; hence 3-bromopropanoic acid and bromoacetic acid are more acidic than propanoic acid. Since the bromine is closer to the carboxyl group in bromoacetic acid than it is in 3-bromopropanoic acid it has a greater effect in the bromoacetic acid.

8. Predict the products of the following reactions.

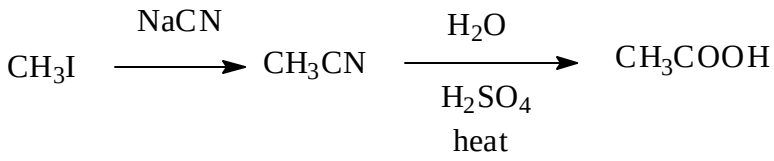




Carboxylation of Grignard reagents and hydrolysis of nitriles are common ways of preparing carboxylic acids. Note that the products each have one more carbon than the starting materials. In (a) CO_2 provides the additional carbon; in (b) it is the CN^- group.

9. Show the steps in the conversion of iodomethane to acetic acid by the nitrile hydrolysis route. Would a similar route work for the conversion of iodobenzene to benzoic acid? Explain.

I thought the question a little ambiguous in terms of how much is wanted with regard to the "steps in the conversion." Does he want the synthetic steps, or all of the steps in the mechanisms of the two synthetic steps? To find out, I looked in the Solutions Manual written by Susan McMurry, the author's wife. She provides the synthetic steps, so this is surely what he meant. **(**



The first step here is a nucleophilic substitution. In this case it is S_N2, since the site of attack is a methyl group. This first step would not be possible for iodobenzene. Aryl halides do not undergo S_N2 reactions for steric reasons and do not undergo S_N1 reactions for electronic reasons (phenyl carbocations are quite unstable).

11. Which compound in each of the following sets is more reactive in nucleophilic acyl substitution reactions?

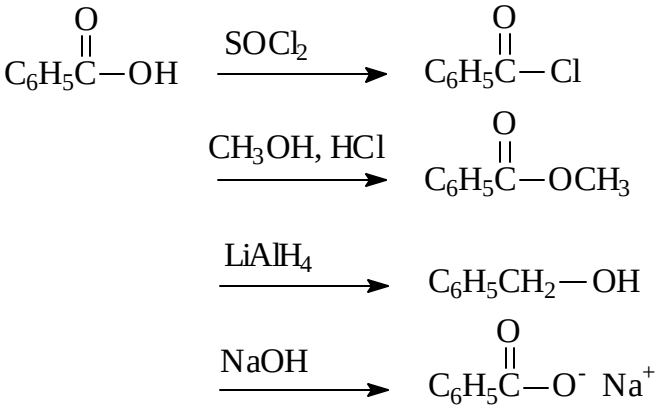
(a) $\boxed{CH_3COCl}$ or CH_3COOCH_3 (b) $(CH_3)_2CHCONH_2$ or $\boxed{CH_3CH_2COOCH_3}$

(c) CH_3COOCH_3 or $\boxed{CH_3COOCOCH_3}$ (d) $\boxed{CH_3COOCH_3}$ or CH_3CHO

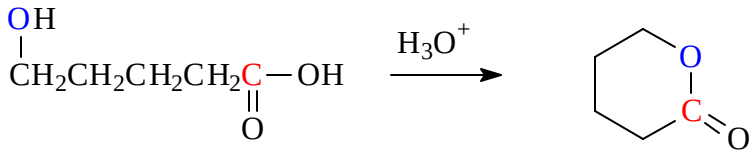
The answers are boxed. (a) Acid chlorides are more reactive than esters. This is because Cl is more electronegative than O. A more complete explanation is available in the fine print of the Carboxylic Acid Derivatives lecture notes. (b) Esters are more reactive than amides in these reactions. Also, the amide is more sterically hindered than the ester. (c) Acid anhydrides are more reactive than esters in these reactions. (d) Aldehydes undergo nucleophilic addition, not substitution.

13. What products would you obtain by treating benzoic acid with the following reagents? Formulate the reactions.

(a) $SOCl_2$, (b) CH_3OH, HCl, (c) $LiAlH_4$, (d) NaOH

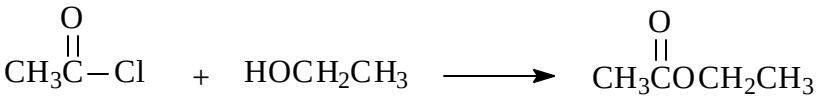


15. If 5-hydroxypentanoic acid is treated with an acid catalyst, an intramolecular esterification reaction occurs. What is the structure of the product?

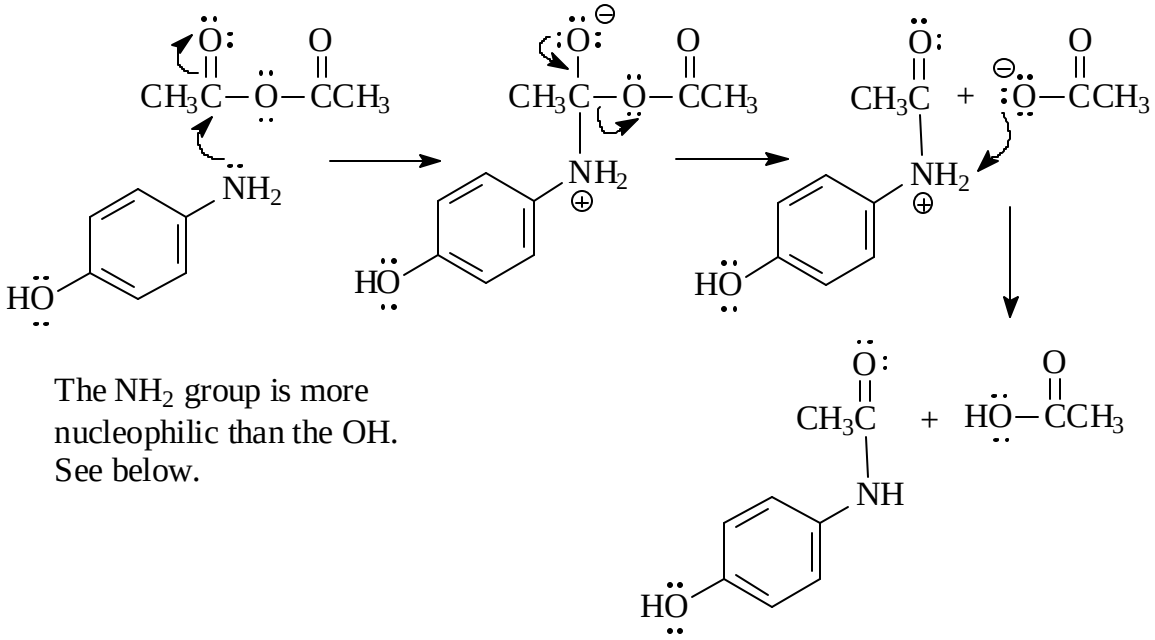


When an ester is formed from an alcohol functional group and a carboxylic acid group that are in the same molecule, a ring forms. These ester rings are called lactones.

16. How could you prepare the following esters using the reaction of a acid chloride with an alcohol?
(b) $CH_3COOCH_2CH_3$



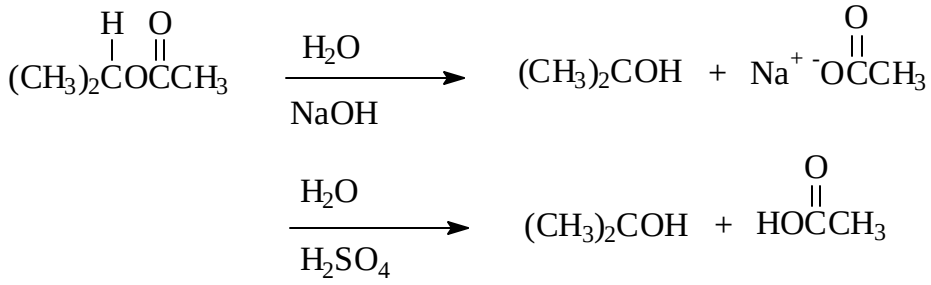
19. Write the steps in the mechanism of the reaction between *p*-hydroxyaniline and acetic anhydride to prepare acetaminophen.



The NH_2 group is more nucleophilic than the OH. See below.

With *p*-hydroxyaniline the question arises as to which of the two substituent groups is more nucleophilic. The oxygen is more electronegative than the nitrogen, so we might expect it to hold its electrons more tightly and, hence, be less nucleophilic. On the other hand, the oxygen has two unshared pairs of electrons, while the nitrogen has only one. It might be worth noting that in water phenol acts as an acid, not a base. On the other hand, amines, like ammonia from which they are derived, are bases in aqueous solution. Bases are nucleophiles. Acids are electrophiles. So, we might expect the NH_2 group to be more nucleophilic than OH.

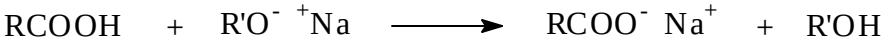
21. Show the products of hydrolysis of the following esters.
(a) isopropyl acetate



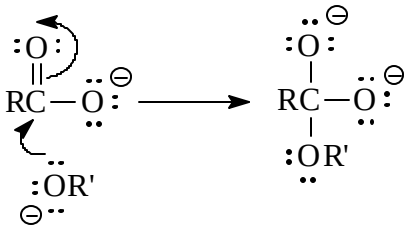
If the hydrolysis is done under basic conditions (NaOH) the products will be the alcohol and the salt of the carboxylic acid. On the other hand, if the reaction is carried out under acidic conditions (reverse of Fisher esterification) the products will be the alcohol and the carboxylic acid. If the reaction is carried out under basic conditions the salt of the carboxylic acid can be converted to the acid by adding a stronger acid. Hydrochloric and sulfuric acids are commonly used for this purpose.

22. Why do you suppose saponification of esters is not reversible? In other words, why doesn't treatment of a carboxylic acid with an alkoxide ion give an ester?

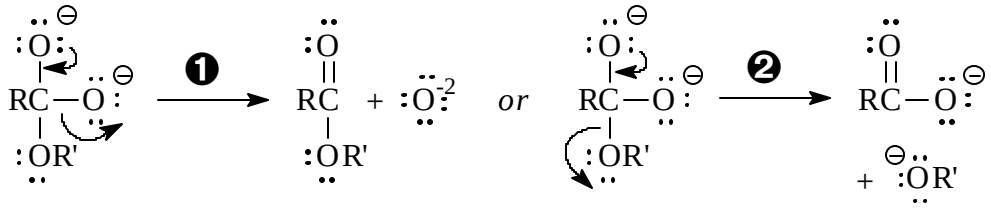
If a carboxylic acid is treated with alkoxide ion, a strong base, it will be deprotonated.



This happens very quickly. Assuming that another mole of alkoxide ion is available (the first mole is used up deprotonating the acid) let's see what happens if it attacks the carboxylate anion. This is shown to the right. Forming a dianion is possible although the proximity of the two negative charges is likely to not be very favorable.

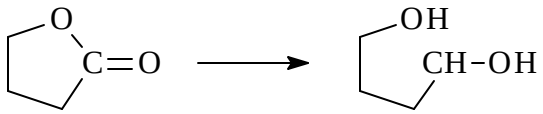


What can the dianion do? Basically (pardon the pun), two things could happen.



Which is more likely, route ❶ or route ❷ ? Route ❶ produces O^{-2}, which is not a stable anion. Even if it were stable enough to form, it would have to be a very powerful nucleophile. Owing to this, route ❶ would be reversible and the tetrahedral dianion on the left would be reformed. Route ❷ , on the other hand leads back to alkoxide and carboxylate anions. This is much more likely since the products here are reasonable ones. So we can conclude that, although alkoxide anion may possibly attack the carboxylate anion, the bottom line is that the carboxylate anion and alkoxide anion would reform, making the reaction unproductive.

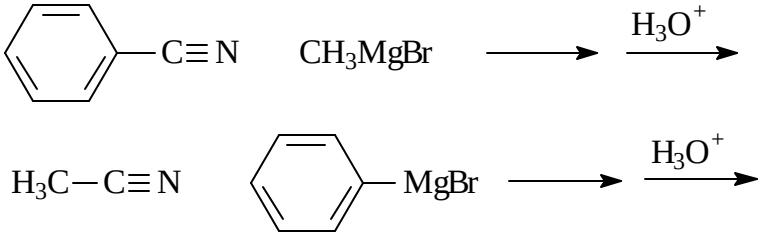
24. What product would you expect from the reaction of a cyclic ester such a butyrolactone with $LiAlH_4$?



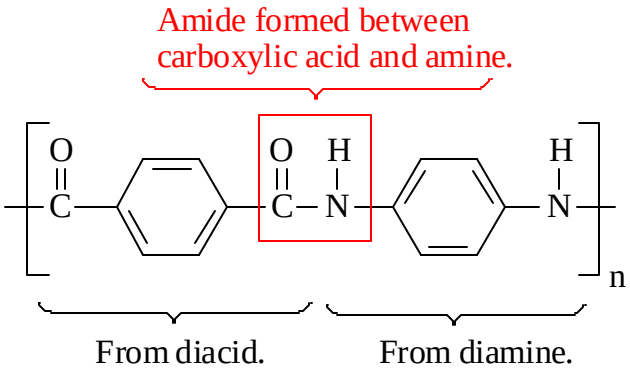
Lactones are reduced by lithium aluminum hydride in the same way that other esters are. The carbonyl group becomes an alcohol as does the "OR" group of the ester. So, a diol is produced whereas in other esters two separate alcohol molecules are produced.

28. What nitrile would you react with what Grignard reagent to prepare the following ketones?
(c) acetophenone (methyl phenyl ketone)

A ketone has two R groups attached to a carbonyl carbon. If we look at the generic reaction between Grignard reagents and nitriles in McMurry, we can see that one of these R groups comes from the Grignard reagent and the other comes from the nitrile. Furthermore, the carbon in the nitrile group becomes the carbonyl carbon of the ketone. Knowing this we can come up with two possible routes.



30. Kevlar, a nylon polymer used in bulletproof vests, is made by reaction of 1,4-benzenedicarboxylic acid with 1,4-benzenediamine. Show the structure of Kevlar.



34. Acetic acid boils at 118° C, but its ethyl ester boils at 77° C. Why is the boiling point of the acid so much higher, even though it has a lower molecular weight?

The acid is an associated liquid. That is to say, molecules of the acid hydrogen bond to each other in the liquid. This hydrogen bonding has to be completely or at least partially broken down for the acetic acid to boil. This requires thermal energy, hence the high temperature for the boiling point. Ethyl acetate is not an associated liquid. Hydrogen bonds do not have to be broken for it to boil.

The molecular weight argument is a bit of a red herring here. When acetic acid boils, some of the molecules go into the vapor phase as hydrogen bonded dimers. The molecular weight of one of these dimers is greater than that of ethyl acetate.

37. The following reactivity order has been found for the saponification of alkyl acetates by aqueous NaOH: $CH_3COOCH_3 > CH_3COOCH_2CH_3 > CH_3COOCH(CH_3)_2 > CH_3COOC(CH_3)_3$
How can you explain this reactivity order?

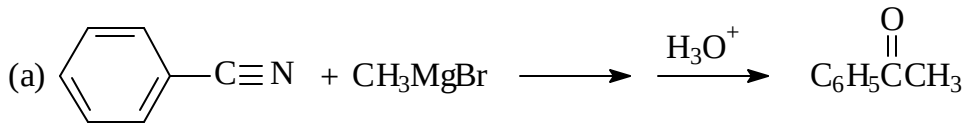
The slow step in the mechanism of saponification is the attack by hydroxide ion on the carbonyl carbon of the ester, causing it to become tetrahedral. Crowding increases in this region of the molecule as the bond angles of the carbon go from ~120o to ~109o. Bulky groups accentuate this effect; this is a steric effect.

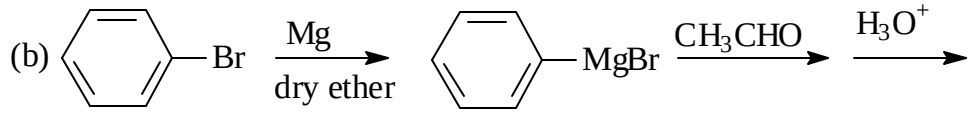
41. Rank the following compounds in order of their reactivity toward nucleophilic acyl substitution.
(a) CH_3COOCH_3, (b) CH_3COCl, (c) CH_3CONH_2, (d) $CH_3CO_2COCH_3$

Most reactive first: (b) > (d) > (a) > (c). Reactivity order: acid chlorides > anhydrides > esters > amides.

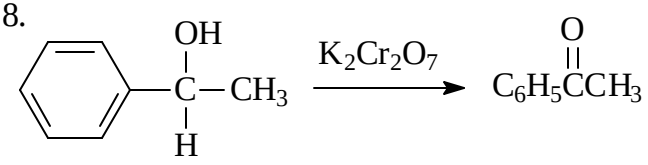
42. How can you prepare acetophenone from the following starting materials? (More than one step may be required.)

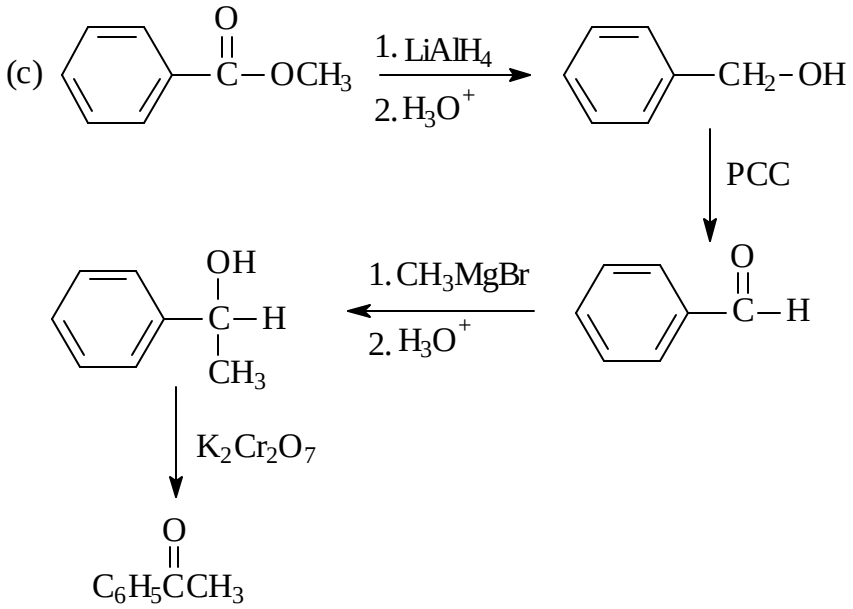
(a) benzonitrile, (b) bromobenzene, (c) methyl benzoate, (d) benzene

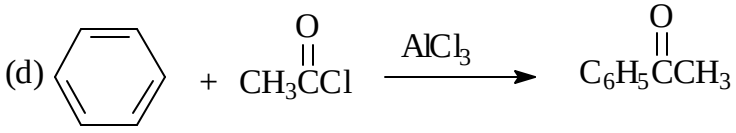




Also see question #28.



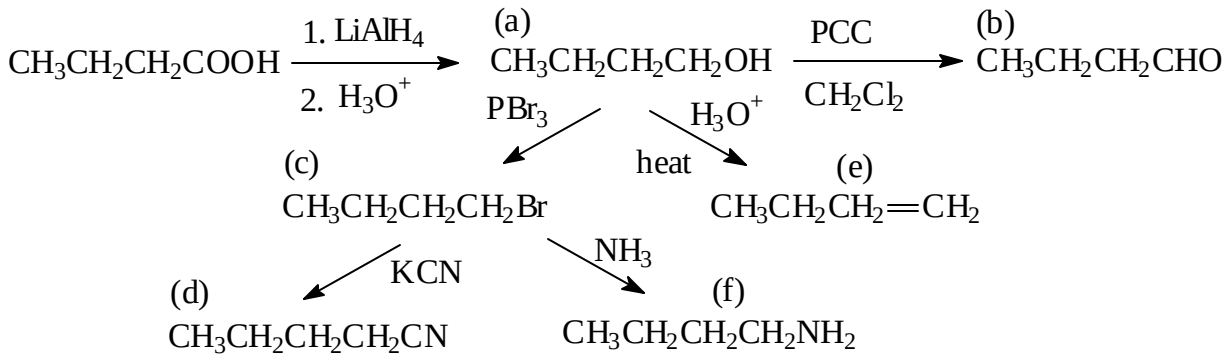




Solutions (a) and (d) are pretty straightforward. Either you know the reactions or you don't. Solutions (b) and (c) are more complex since several steps are involved. In cases like these, where a one or two step sequence does not leap to mind, the trick is to work backwards from the product and forward from the reactant at the same time. You might approach (c) in this way, for example:
1. How can I make a ketone like acetophenone?
Ketones can be made by oxidation of secondary alcohols. I can make acetophenone by oxidation of 1-phenylethanol.
2. How can I make 1-phenylethanol?
There are several ways to make alcohols. Maybe a Grignard synthesis would be appropriate. In this case I would need to react benzaldehyde with methyl magnesium bromide or phenyl magnesium bromide with acetaldehyde. Can I get to benzaldehyde from methyl benzoate. Possibly. Can I get to bromobenzene (to make phenyl magnesium bromide) from methyl benzoate? No. I don't know any reaction that will replace a carbon attached to a benzene ring with bromine.
3. To get to benzaldehyde from methyl benzoate I can reduce the ester to benzyl alcohol (phenylmethanol) and then oxidize this primary alcohol to an aldehyde.

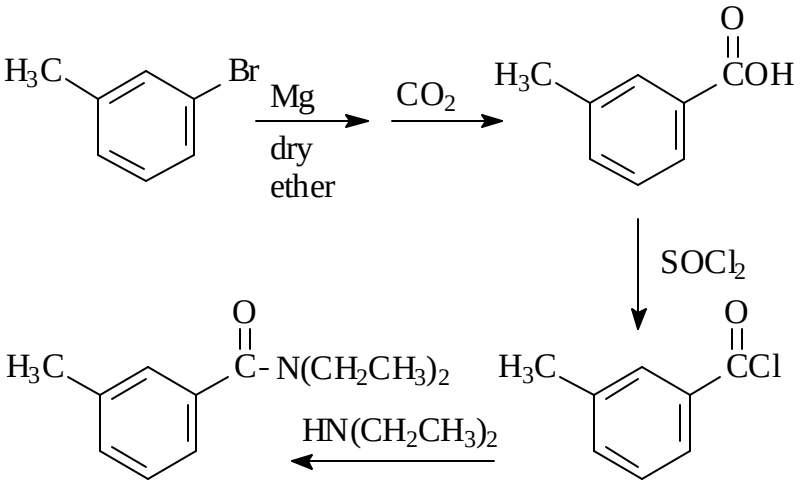
43. How might you prepare the following products from butanoic acid? (More than one step may be required.)

(a) 1-butanol, (b) butanal, (c) 1-bromobutane, (d) pentanenitrile, (e) 1-butene, (f) butylamine



Other solutions are possible. If in doubt, ask.

61. N,N-Diethyl-*m*-toluamide (DEET) is the active ingredient in many insect repellents. How might you synthesize DEET from *m*-bromotoluene?



The trick here is replacing the bromine on the aromatic ring with a carbon. A Grignard reaction will do this. You could elect to react the Grignard with carbon dioxide, as above, or with formaldehyde to give the alcohol which could then be oxidized to the carboxylic acid.