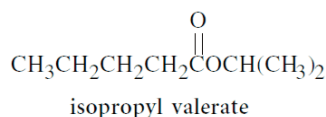


Chapter 21

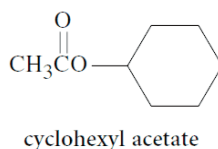
The Chemistry of Carboxylic Acid Derivatives

Solutions to In-Text Problems

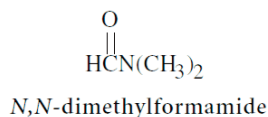
21.1 (b)



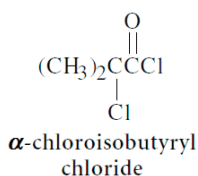
(d)



(e)

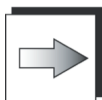


(h)

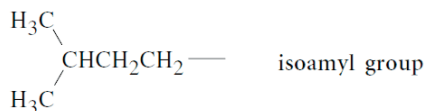


21.2

- (a) butanenitrile (common: butyronitrile)
(c) isopentyl 3-methylbutanoate (*common*: isoamyl isovalerate)

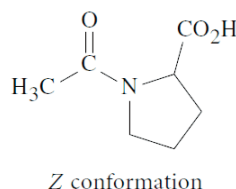
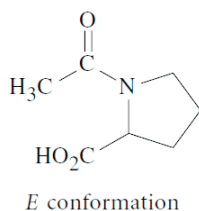


The *isoamyl* group is the same as an isopentyl or 3-methylbutyl group:

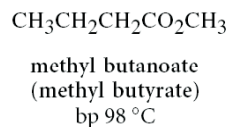
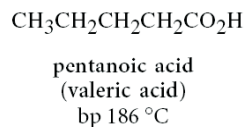


(d) *N,N*-dimethylbenzamide

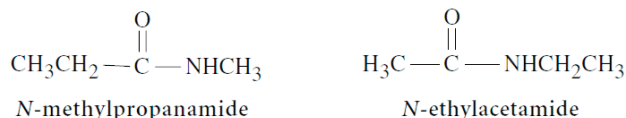
21.3 The *E* and *Z* conformations of *N*-acetylproline:



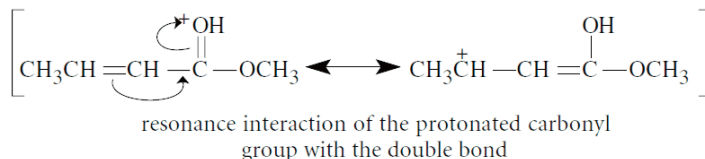
21.5 As shown by the data above the problem, a carboxylic acid has a higher boiling point than an ester because it can both donate and accept hydrogen bonds within its liquid state; hydrogen bonding does not occur in the ester. Consequently, pentanoic acid (valeric acid) has a higher boiling point than methyl butanoate. Here are the actual data:



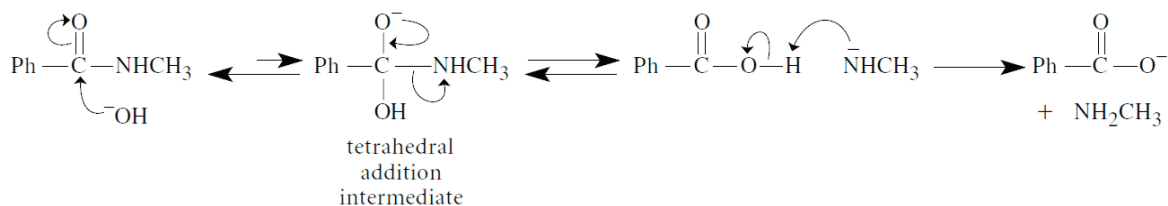
- 21.7 (a) The carbonyl absorption of the ester occurs at higher frequency, and only the carboxylic acid has the characteristic strong, broad O—H stretching absorption in 2400–3600 cm^{-1} region.
- (d) In *N*-methylpropanamide, the *N*-methyl group is a doublet at about δ 3. *N*-Ethylacetamide has no doublet resonances. In *N*-methylpropanamide, the α -protons are a quartet near δ 2.5. In *N*-ethylacetamide, the α -protons are a singlet at δ 2. The NMR spectrum of *N*-methylpropanamide has no singlets.



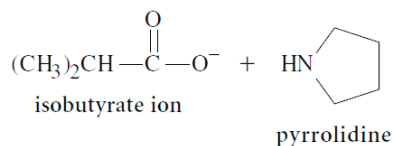
- 21.9 (a) The first ester is more basic because its conjugate acid is stabilized not only by resonance interaction with the ester oxygen, but also by resonance interaction with the double bond; that is, the conjugate acid of the first ester has one more important resonance structure than the conjugate acid of the second. (See Problem 19.14(b), text p. 906, and its solution for a similar situation.)



- 21.10 (b) The mechanism of the base-promoted hydrolysis of *N*-methylbenzamide is essentially a saponification mechanism analogous to that shown for esters in Eq. 21.9a–b, text p. 1005.



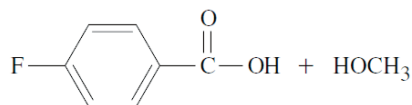
- 21.11 (a) The hydrolysis products consist of the conjugate base of the carboxylic acid and an amine:



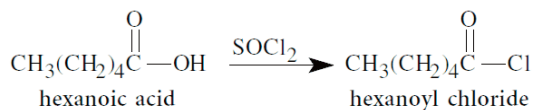
- 21.12 *Resonance effects:* The application of the resonance effect for predicting the relative rates of acid-catalyzed ester and amide hydrolyses is exactly the same as it is for the corresponding base-promoted hydrolyses. (See Eq. 21.26, text p. 1013, and Eq. 21.28, text p. 1014, and the discussion on text pp. 1012–1014.)

Leaving-group basicities: In the acid-catalyzed hydrolysis of an ester, the leaving group is an alcohol; in the acid-catalyzed hydrolysis of an amide, the leaving group is ammonia or an amine. Alcohols are much weaker bases (conjugate-acid $\text{p}K_{\text{a}} = -2$ to -3) than amines or ammonia (conjugate-acid $\text{p}K_{\text{a}} = 9$ –10). Because weaker bases are better leaving groups, esters should hydrolyze more rapidly, and they do.

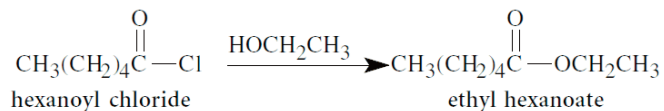
- 21.14 (b) This is an ordinary ester saponification followed by acidification.



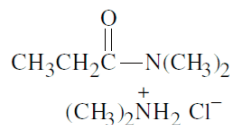
- 21.15 First, prepare the acid chloride from hexanoic acid:



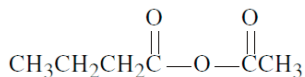
- (a) To prepare the ester, allow the acid chloride to react with ethanol:



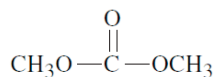
21.16 (a)



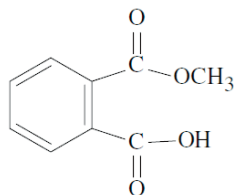
(d)



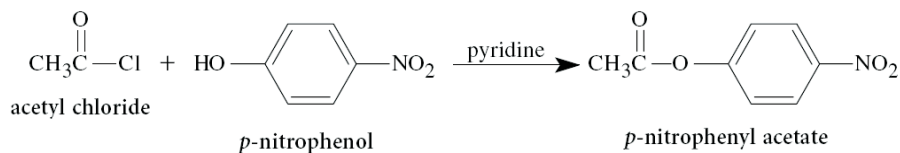
(f)



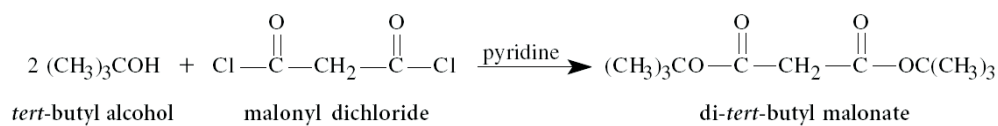
(h)



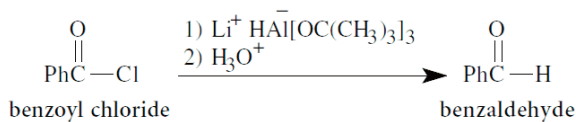
21.18 (b)



(d)

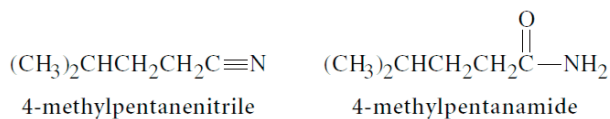


21.19 (a) Carry out one of the reductions in Sec. 21.9D, text p. 1027:

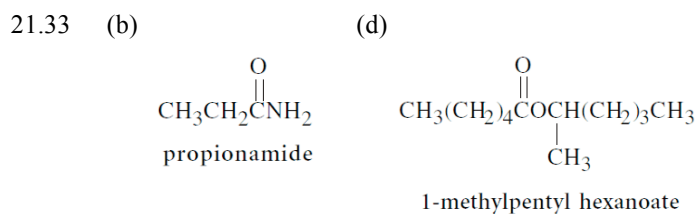
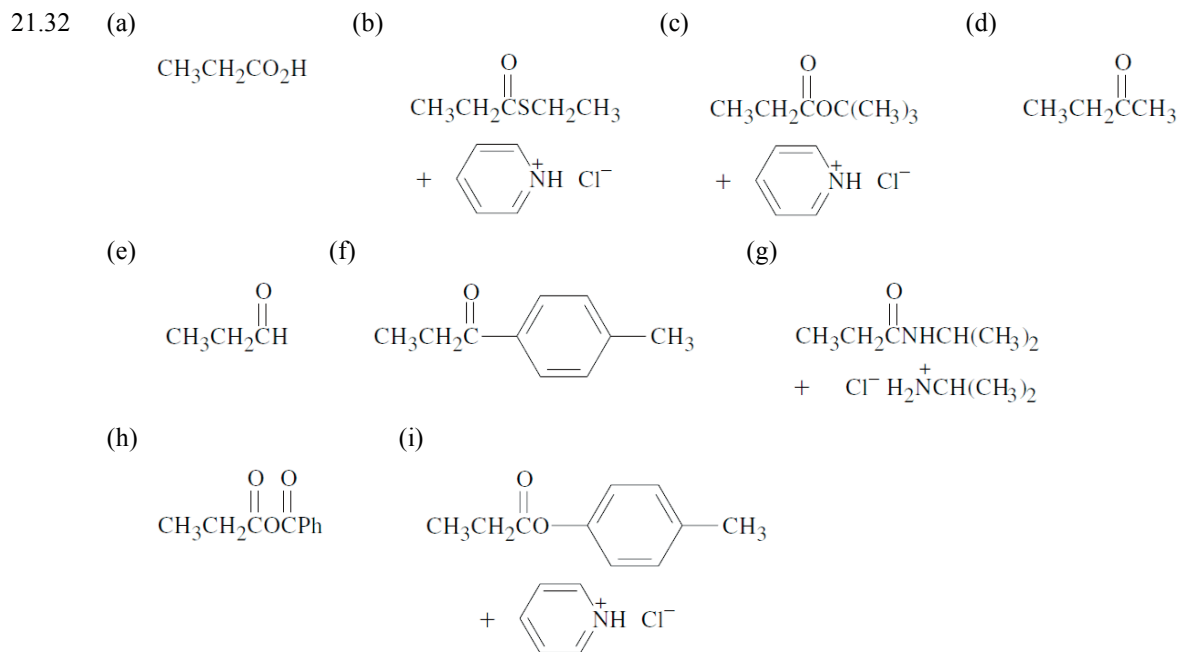


21.20 (a) $\text{PhCH}_2\text{CH}_2\text{NH}_2$

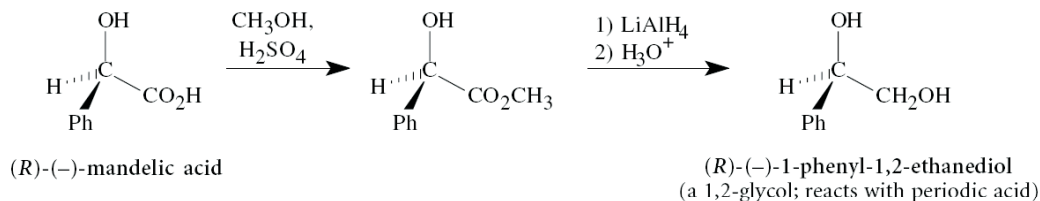
21.21 Among the compounds that would give $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ as the result of LiAlH_4 reduction are the following:



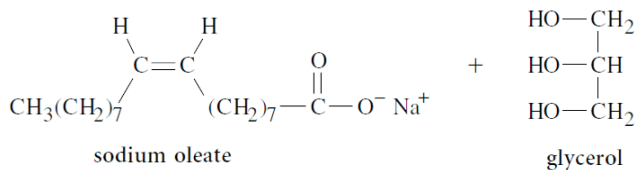
Solutions to Additional Problems



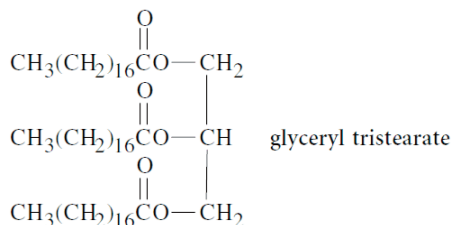
21.35 The product is (*R*)-(-)-1-phenyl-1,2-ethanediol. Notice that the asymmetric carbon is unaffected by these transformations.



21.38 (a) In aqueous base the ester groups are saponified to give glycerol (1,2,3-propanetriol) and three equivalents of sodium oleate, the sodium salt of oleic acid.

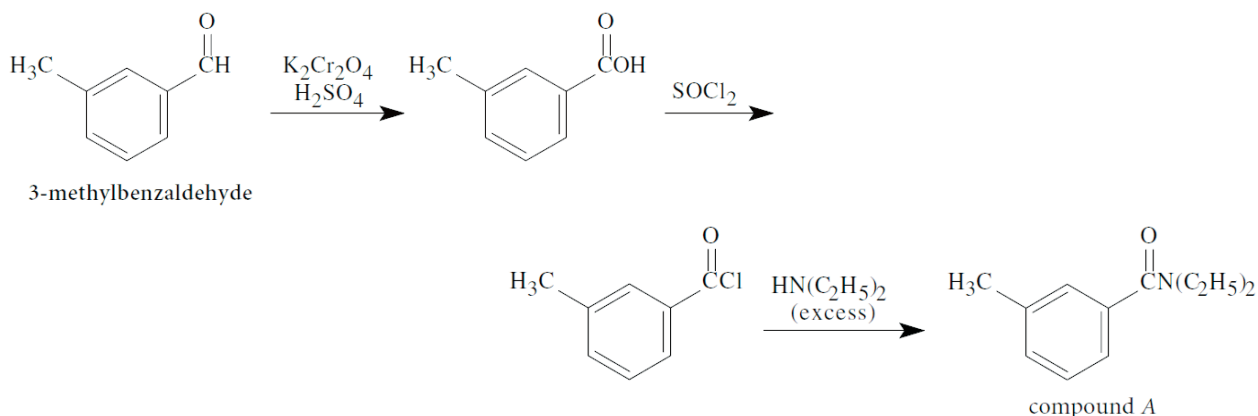


(b) The structure of glyceryl tristearate:

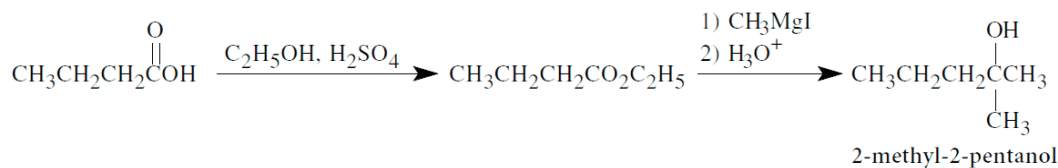


Because unsaturated fats are oils and saturated fats are solids, glyceryl trioleate is a liquid, whereas the product of hydrogenation is a solid. In fact, glyceryl trioleate is a major component of olive oil, whereas glyceryl tristearate is a major component of lard.

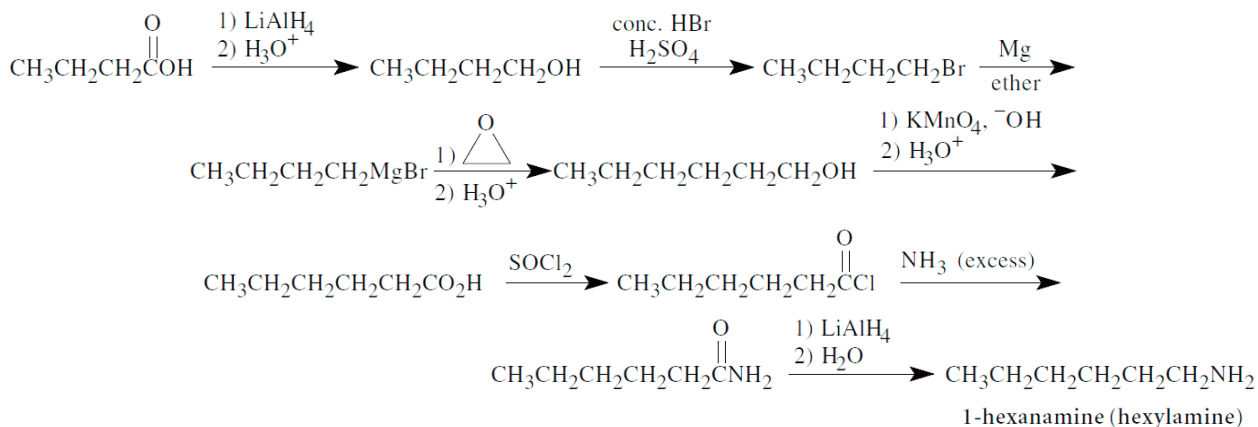
21.39 (a)



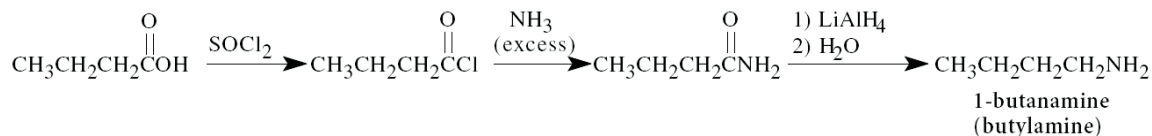
21.40 (b)



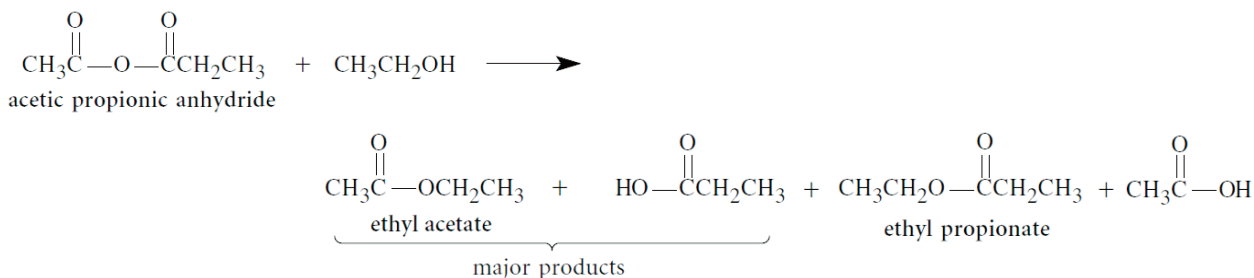
(d)



(f)

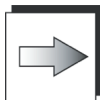


- 21.42 Because the two carbonyl groups of the anhydride are not equivalent, two different products are possible; each corresponds to reaction with the ethanol at a different carbonyl group. Because ethyl propionate has a higher molecular mass than ethyl acetate, ethyl propionate should have the higher boiling point. Since it is given that the ester with the lower boiling point is formed in greater amount, then ethyl acetate is the major product.



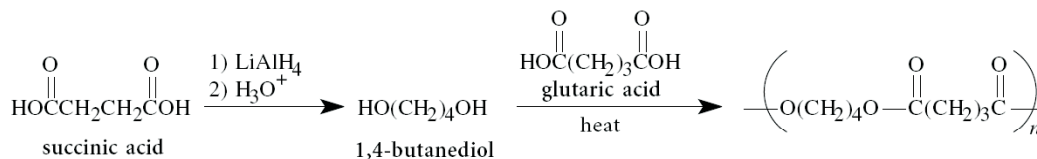
- 21.43 Carboxylate salts are less reactive than esters in nucleophilic acyl substitution reactions for two reasons. First, resonance stabilization of carboxylate salts is particularly important because carboxylates have two identical, important resonance structures; see Eq. 20.4 on text p. 957. Resonance stabilization of esters is less important because one resonance structure separates charge; see the structures in Eq. 21.28, text p. 1014. Because resonance stabilization reduces reactivity, carboxylates are less reactive than esters.

The second and major reason that carboxylate salts are less reactive is that they contain no leaving group. The oxygen anion of the carboxylate, in order to serve as a leaving group, would have to depart as an oxide ion, O_2^- . This very basic leaving group is unprecedented in the usual reactions of organic chemistry.

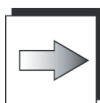
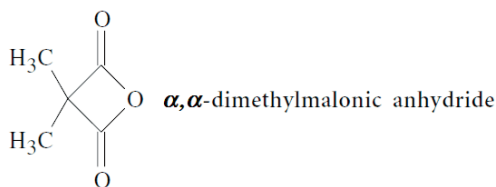


Reactions such as LiAlH_4 reduction that occur on carboxylate salts might at first glance appear to involve oxide ions as leaving groups. In such reactions, however, the “oxygen anion” is bonded to another species that allows the oxygen to serve as a leaving group. (See the details in Further Exploration 20.4 on p. 479 of the Study Guide and Solutions Manual.)

- 21.45 (b) The preparation of this polyester requires heating 1,4-butanediol with glutaric acid.
(Alternatively, the di-acid chloride of glutaric acid could be mixed with 1,4-butanediol.)



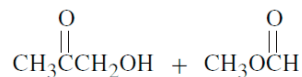
- 21.47 The high-frequency IR absorption and the reaction with water to give a dicarboxylic acid suggest that this compound is the anhydride of α,α -dimethylmalonic acid. The formation of a half ester in the reaction with methanol also supports the hypothesis that this compound is an anhydride.



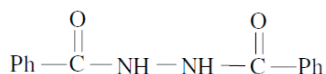
In most cases cyclic anhydrides show two carbonyl stretching absorptions. Can you think of a reason why this particular anhydride shows only one? (*Hint:* See Study Problem 12.2 on text p. 551.) Is the missing carbonyl absorption at lower or higher frequency than the one that is observed at 1820 cm^{-1} ? (*Hint:* See Table 21.3, text p. 996, and extrapolate from the absorptions of six- and five-membered cyclic anhydrides.)

- 21.50 (a) This is a reprise of Problem 10.59 on text pp. 480–481, which is answered on p. 209 of the Study Guide and Solutions Manual. The very weak acid HCN is not significantly dissociated. Consequently, the solution is insufficiently acidic to effect protonation of the —OH group of the alcohol. This protonation is necessary to convert this group into a good leaving group. Furthermore, there is virtually no cyanide ion ($\text{C}\equiv\text{N}^-$) present, and hence virtually no nucleophile to displace the —OH group.
- (b) First of all, an excess of an alcohol is generally required to drive acid-catalyzed esterification to completion. However, even if some of the adipic acid is converted into its ester, there is no reason why this monoester would not be essentially as reactive as adipic acid itself, and the reaction mixture would ultimately contain a mixture of adipic acid, its monomethyl ester, and its dimethyl ester. The yield of the desired monoester would be poor, and it would have to be separated from both the di-ester and the unreacted adipic acid.
- (c) There is no reason why acetic acid should form an anhydride only with benzoic acid, and vice-versa; substantial amounts of acetic anhydride and benzoic anhydride should also be obtained. If all the reactions were totally random, the desired unsymmetrical anhydride would be formed in a maximum of 50% yield.
- (d) The hydroxide ion reacts *much* more rapidly with the O—H proton of the phenol than it does with the ester. (See Study Guide Link 20.1 on p. 473 of the Study Guide and Solutions Manual for a discussion of this point.) Consequently, the one equivalent of hydroxide is consumed by this reaction, and no base is left to saponify the ester.
- (e) Several functional groups in the β -lactam molecule are more reactive toward acid hydrolysis than the amide indicated. Because esters are more reactive than amides, the acetate ester will undoubtedly also hydrolyze under the reaction conditions. The β -lactam ring itself is an amide, and because hydrolysis of this amide relieves substantial ring strain, this amide should also hydrolyze more rapidly. Once the β -lactam hydrolyzes, the resulting enamine also should hydrolyze readily in acid, and the N—C—S linkage is also unstable toward hydrolysis in the same sense that an acetal is unstable. With so many faster competing processes, Klutz has no hope for a selective reaction.

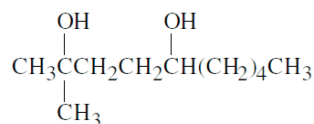
- 21.52 (b) Transesterification of the formate ester occurs.



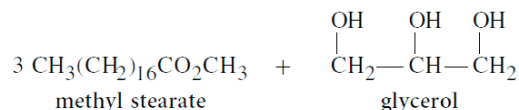
- (d) Both amino groups are acylated by the excess of the acid chloride.



- (g) The Grignard reactions of lactones are much like those of esters, except that the alcohol displaced by the nucleophilic acyl substitution reaction remains as part of the same molecule.

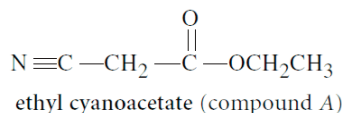


- (i) Lithium aluminum hydride reacts with acid chlorides in the same way that it reacts with esters, only faster. The product is $(\text{CH}_3)_3\text{CCH}_2\text{OH}$ (2,2-dimethyl-1-propanol).
- (k) Transesterification occurs to give three equivalents of methyl stearate and one of glycerol.

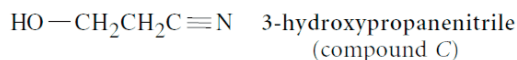


- 21.54 (a) The odd molecular mass indicates the presence of an odd number of nitrogens, and the hydroxamate test and the IR carbonyl absorption at 1733 cm^{-1} indicate the presence of an ester. The IR absorption at 2237 cm^{-1} indicates a nitrile. The triplet–quartet pattern in the NMR spectrum clearly indicates that compound *B* is an

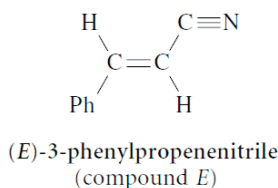
ethyl ester. Subtracting the masses of all the atoms accounted for leaves 14 mass units, the mass of a CH_2 group. Compound *A* is ethyl cyanoacetate.



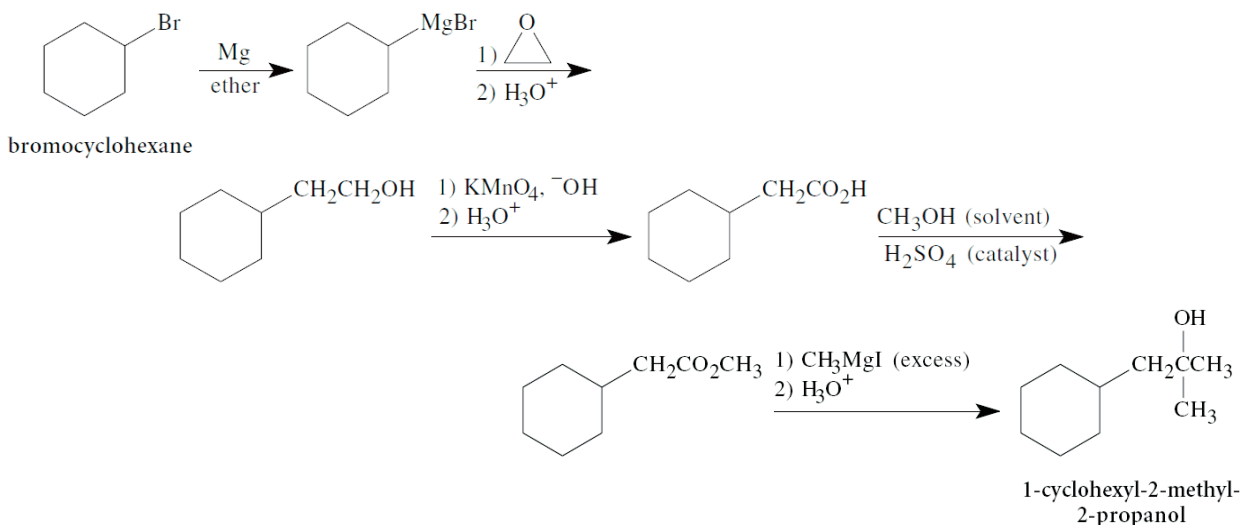
- (c) The odd molecular mass indicates the presence of nitrogen. The IR spectrum indicates the presence of both a nitrile and an alcohol. The broad, D_2O -exchangeable resonance at δ 3.4 in the NMR spectrum confirms the presence of an $\text{O}-\text{H}$ group, and the pair of triplets indicates a $-\text{CH}_2\text{CH}_2-$ group. Compound *C* is 3-hydroxypropanenitrile (β -hydroxypropionitrile).



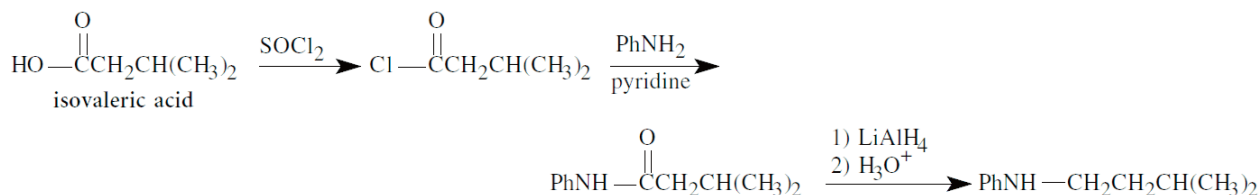
- (e) The mass spectrum shows an odd mass, which indicates the presence of nitrogen. The IR spectrum could indicate the presence of a nitrile, although, if so, the $\text{C} \equiv \text{N}$ absorption is about 50 cm^{-1} lower in frequency than the $\text{C} \equiv \text{N}$ absorption of an ordinary nitrile. The IR spectrum also indicates a trans alkene. The UV spectrum indicates extensive conjugation. This shift of the nitrile IR absorption is similar to that observed with conjugated carbonyl groups, and it suggests that the nitrile group is conjugated with the double bond. The NMR shows resonances for 7 protons. The large splitting in the resonances at δ 5.85 and δ 7.35 confirms the presence of the trans alkene. Evidently, the apparent singlet at δ 7.4 corresponds to five protons, that is, to a monosubstituted benzene ring. Compound *E* is (*E*)-3-phenylpropenenitrile.



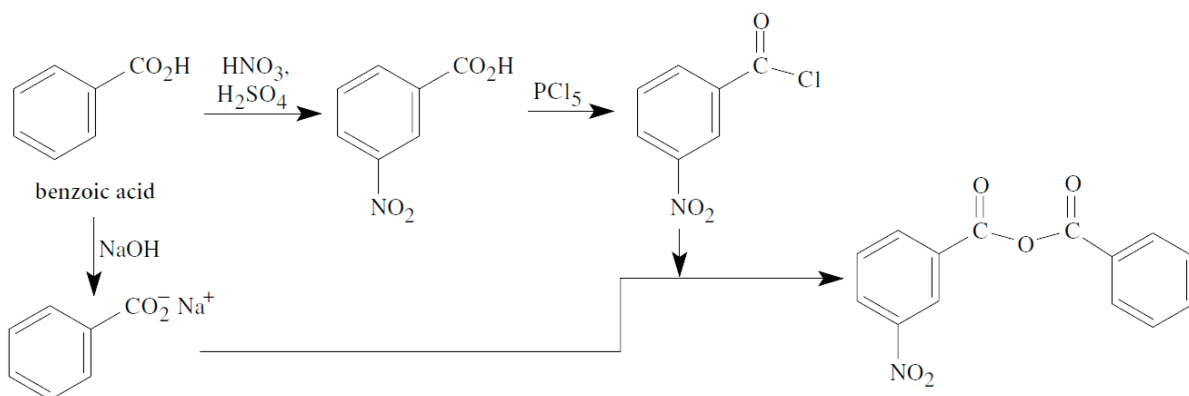
21.55 (b)



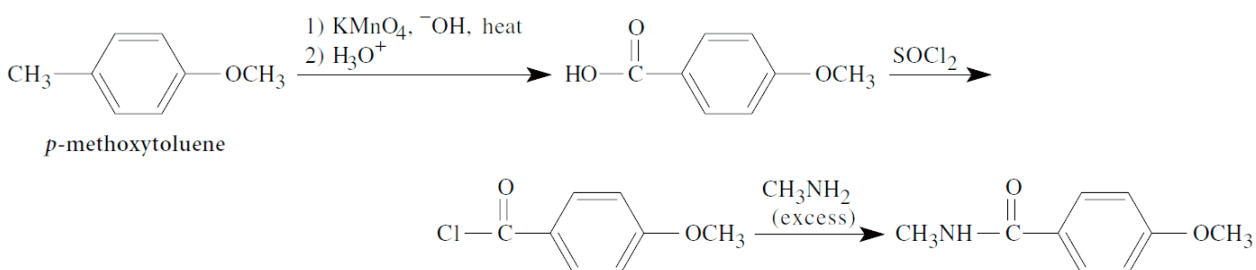
(d)



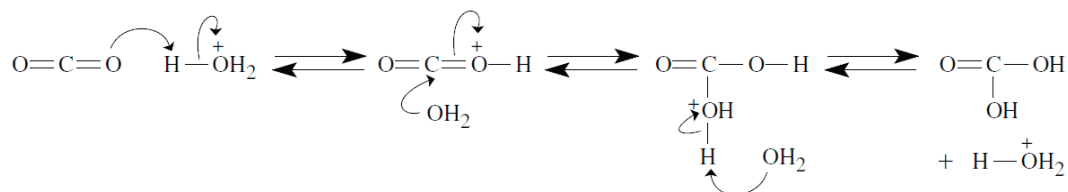
(g)



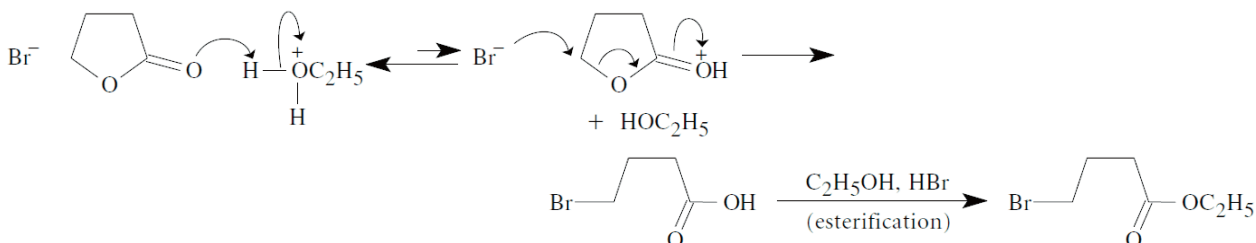
(i)



- 21.56 (a) The reversible hydration of carbon dioxide to carbonic acid is an acid-catalyzed addition of water that is mechanistically identical to the hydration of aldehydes and ketones shown in Eq. 19.18a–b, text pp. 909–910.

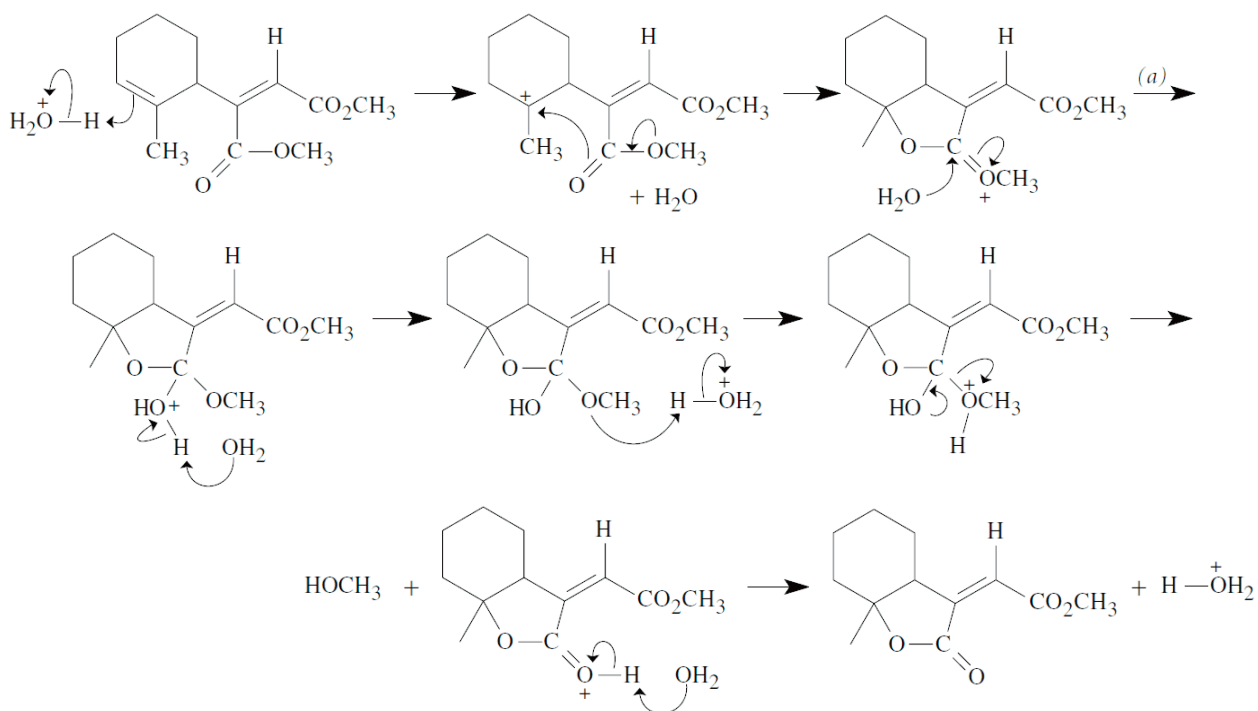


- (c) Protonation of the carbonyl oxygen produces a good leaving group which is displaced by bromide ion. The carboxy group is then esterified by the usual mechanism (Eqs. 20.18a–c, text pp. 966–7).

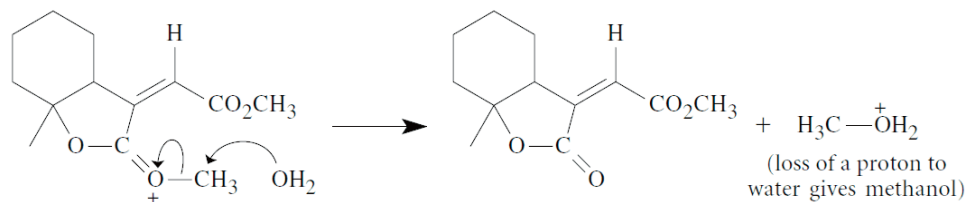


An alternative reasonable mechanism involves transesterification of the lactone by ethanol to give a hydroxy ester, followed by conversion of the alcohol to a bromide by an acid-catalyzed $\text{S}_{\text{N}}2$ reaction. (See Eqs. 10.11a–b, text p. 441.) However, it is likely that the mechanism shown above is the correct one, because the equilibrium between lactone and hydroxy ester is likely to strongly favor the lactone, and because a protonated carboxy group is an excellent leaving group.

- (e) Protonation of the ring double bond gives a tertiary carbocation that reacts with the carbonyl oxygen of the ester to give the lactone.

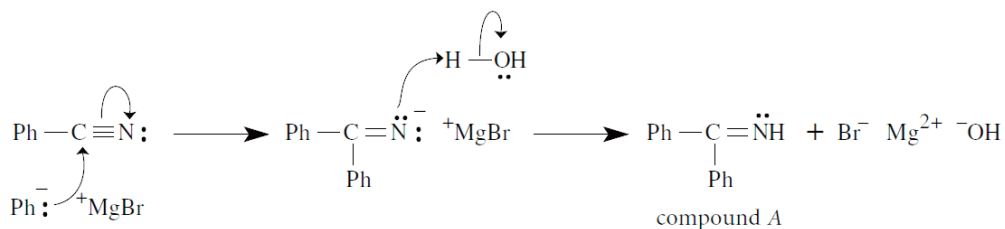


As an alternative to step (a) and the subsequent steps in the foregoing mechanism, water could react with the methyl group:



How might carrying out the reaction in ^{18}O -water enable one to distinguish between these two mechanisms?

- 21.57 Addition of the Grignard reagent to the carbon–nitrogen triple bond is expected by analogy with carbonyl-group reactions. The product *A* is an imine.



This imine hydrolyzes in acidic solution to benzophenone:

