

Chapter 20 – Carboxylic Acids and Nitriles

Chapter Outline

- I. General information about carboxylic acids and nitriles (Sections 20.1 – 20.4).
- A. Naming carboxylic acids (Section 20.1).
1. Noncyclic carboxylic acids are named by replacing the *-e* of the corresponding alkane by *-oic acid*.
 2. Compounds that have a carboxylic acid bonded to a ring are named by using the suffix *-carboxylic acid*.
 3. Many carboxylic acids have historical, nonsystematic names.
- B. Naming nitriles.
1. Simple nitriles are named by adding *-nitrile* to the alkane name.
The nitrile carbon is C1.
 2. More complex nitriles are named as derivatives of carboxylic acids by replacing *-oic acid* by *-onitrile* or by replacing *-carboxylic acid* by *-carbonitrile*.
The nitrile carbon is bonded to C1.
- C. Structure and properties of carboxylic acids (Section 20.2).
1. The carbonyl group of carboxylic acids is sp^2 -hybridized and planar.
 2. Carboxylic acids are strongly associated because of hydrogen bonding, and their boiling points are elevated.
- D. Carboxylic acid acidity (Sections 20.2 – 20.4).
1. Dissociation of carboxylic acids (Section 20.2).
 - a. Carboxylic acids react with bases to form salts that are water-soluble.
 - b. Carboxylic acids dissociate slightly in dilute aqueous solution to give H_3O^+ and carboxylate anions.
The K_a values for carboxylic acids are near 10^{-5} , making them weaker than mineral acids but stronger than alcohols.
 - c. The relative strength of carboxylic acids is due to resonance stabilization of the carboxylate anion.
 - i. Both carbon–oxygen bonds of carboxylate anions are the same length.
 - ii. The bond length is intermediate between single and double bonds.
 2. Biological acids: the Henderson–Hasselbalch equation (Section 20.3)
 - a. The pH of biological fluids (7.3) determines the ratio of dissociated to nondissociated forms of carboxylic acids.
 - b. This ratio can be calculated by using the Henderson–Hasselbalch equation.
$$\log \frac{[A^-]}{[HA]} = pH - pK_a$$
 - c. At physiological pH, carboxylic acids are almost completely dissociated.
2. Substituent effects on acidity (Section 20.4).
- a. Carboxylic acids differ in acid strength.
 - i. Electron-withdrawing groups stabilize carboxylate anions and increase acidity.
 - ii. Electron-donating groups decrease acidity.
 - b. These inductive effects decrease with increasing distance from the carboxyl group.
 - c. Substituent effects in substituted benzoic acids.
 - i. Groups that are deactivating in electrophilic aromatic substitution reactions increase the acidity of substituted benzoic acids.
 - ii. The acidity of benzoic acids can be used to predict electrophilic reactivity.

II. Carboxylic acids (Sections 20.5 – 20.6).

A. Preparation of carboxylic acids (Section 20.5).

1. Methods already studied.
 - a. Oxidation of substituted alkylbenzenes.
 - b. Oxidative cleavage of alkenes and alkynes.
 - c. Oxidation of primary alcohols and aldehydes.
2. Nitrile hydrolysis.
 - a. Nitriles can be hydrolyzed by strong aqueous acids or bases to yield carboxylic acids.
 - b. The sequence nitrile formation \rightarrow nitrile hydrolysis can be used to prepare a carboxylic acid from a halide.
 - c. This method is generally limited to compounds that can undergo S_N2 reactions.
3. Carboxylation of Grignard reagents.
 - a. A Grignard reagent can be treated with CO_2 and protonated to form a carboxylic acid.
 - b. This method is limited to compounds that don't have other functional groups that interfere with Grignard reagent formation.

B. Reactions of carboxylic acids (Section 20.6).

1. Carboxylic acids may undergo reactions typical of alcohols and ketones.
2. Other types of reactions of carboxylic acids:
 - a. Alpha substitution.
 - b. Decarboxylation.
 - c. Nucleophilic acyl substitution.
 - d. Reduction.

III. Chemistry of nitriles (Section 20.7).

A. Preparation of nitriles.

1. Nitriles can be prepared by S_N2 reaction of ^-CN with a primary alkyl halide.
2. They can also be prepared by $SOCl_2$ dehydration of primary amides.

B. Reactions of nitriles.

1. Nitriles can react with nucleophiles via sp^2 -hybridized imine intermediates.
2. Hydrolysis.

Aqueous base hydrolyzes nitriles to carboxylates, plus an amine/ammonia.

 - a. The reaction involves formation of a hydroxy imine that isomerizes to an amide, which is further hydrolyzed.
 - b. Milder conditions allow isolation of the amide.
3. Reduction.

$LiAlH_4$ reduces nitriles to primary amines.
4. Reaction with Grignard reagents.

Reaction of a nitrile with Grignard reagents yields a ketone.

IV. Spectroscopy of carboxylic acids and nitriles (Section 20.8).

A. Infrared spectroscopy.

1. The O–H absorption occurs at $2500\text{--}3300\text{ cm}^{-1}$ and is easy to identify.
2. The C=O absorption occurs at $1710\text{--}1760\text{ cm}^{-1}$.

The position of this absorption depends on whether the acid is free (1760 cm^{-1}) or associated (1710 cm^{-1}).
3. Nitriles have an intense absorption at 2250 cm^{-1} that readily identifies them.

B. NMR spectroscopy.

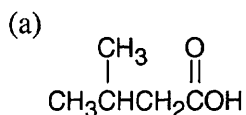
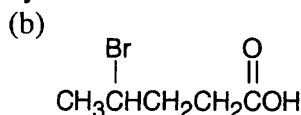
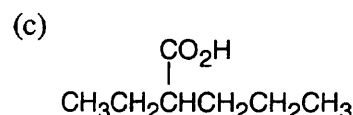
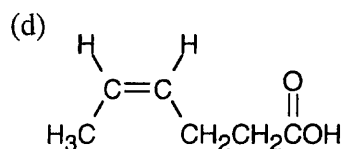
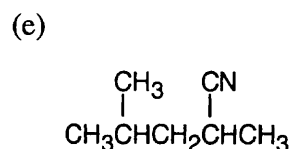
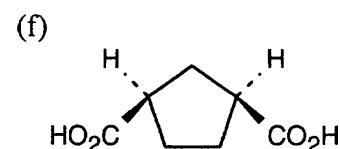
1. ^{13}C NMR spectroscopy.
 - a. Carboxylic acids absorb between $165\text{--}185\text{ }\delta$.
 - b. Saturated acids absorb downfield from α,β -unsaturated acids.
2. 1H NMR spectroscopy.

The carboxylic acid proton absorbs at around $12\text{ }\delta$.

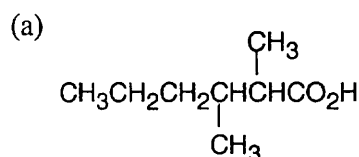
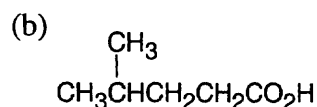
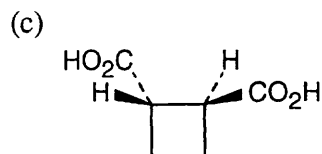
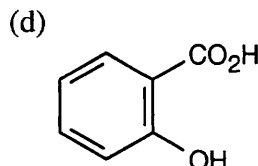
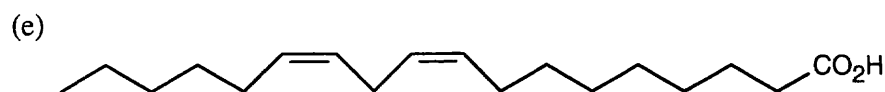
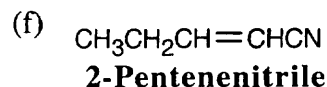
Solutions to Problems

20.1 Carboxylic acids are named by replacing *-e* of the corresponding alkane with *-oic acid*. The carboxylic acid carbon is C1.

When $\text{-CO}_2\text{H}$ is a substituent of a ring, the suffix *-carboxylic acid* is used; the carboxyl carbon is not numbered in this system.

**3-Methylbutanoic acid****4-Bromopentanoic acid****2-Ethylpentanoic acid****(Z)-4-Hexenoic acid****2,4-Dimethylpentanenitrile****cis-1,3-Cyclopentane-dicarboxylic acid**

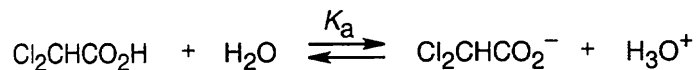
20.2

**2,3-Dimethylhexanoic acid****4-Methylpentanoic acid****trans-1,2-Cyclobutane-dicarboxylic acid****o-Hydroxybenzoic acid****(9Z,12Z)-9,12-Octadecadienoic acid**

20.3 Naphthalene is insoluble in water and benzoic acid is only slightly soluble. The *salt* of benzoic acid is very soluble in water, however, and we can take advantage of this solubility in separating naphthalene from benzoic acid.

Dissolve the mixture in an organic solvent, and extract with a dilute aqueous solution of sodium hydroxide or sodium bicarbonate, which will neutralize benzoic acid. Naphthalene will remain in the organic layer, and all the benzoic acid, now converted to the benzoate salt, will be in the aqueous layer. To recover benzoic acid, remove the aqueous layer, acidify it with dilute mineral acid, and extract with an organic solvent.

20.4



$$K_a = \frac{[\text{Cl}_2\text{CHCO}_2^-][\text{H}_3\text{O}^+]}{[\text{Cl}_2\text{CHCO}_2\text{H}]} = 3.32 \times 10^{-2}$$

	<i>Initial molarity</i>	<i>Molarity after dissociation</i>
$\text{Cl}_2\text{CHCO}_2\text{H}$	0.10 M	$0.10 \text{ M} - y$
$\text{Cl}_2\text{CHCO}_2^-$	0	y
H_3O^+	0	y

$$K_a = \frac{y \cdot y}{0.10 - y} = 3.32 \times 10^{-2}$$

Using the quadratic formula to solve for y , we find that $y = 0.0434$

$$\text{Percent dissociation} = \frac{0.0434}{0.1000} \times 100\% = 43.4\%$$

20.5

(a)

$$\log \frac{[\text{A}^-]}{[\text{HA}]} = \text{pH} - \text{p}K_a = 4.50 - 3.83 = 0.67$$

$$\frac{[\text{A}^-]}{[\text{HA}]} = \text{antilog}(0.67) = 4.68: [\text{A}^-] = 4.68 [\text{HA}]$$

$$[\text{HA}] + [\text{A}^-] = 100\%$$

$$[\text{HA}] + 4.68 [\text{HA}] = 5.68 [\text{HA}] = 100\%$$

$$[\text{HA}] = 100\% \div 5.68 = 18\%$$

$$[\text{A}^-] = 100\% - 18\% = 82\%$$

82% of 0.0010 M glycolic acid is dissociated at pH = 4.50

(b)

$$\log \frac{[\text{A}^-]}{[\text{HA}]} = \text{pH} - \text{p}K_a = 5.30 - 4.87 = 0.43$$

$$\frac{[\text{A}^-]}{[\text{HA}]} = \text{antilog}(0.43) = 2.69: [\text{A}^-] = 2.69 [\text{HA}]$$

$$[\text{HA}] + [\text{A}^-] = 100\%$$

$$[\text{HA}] + 2.69 [\text{HA}] = 3.69 [\text{HA}] = 100\%$$

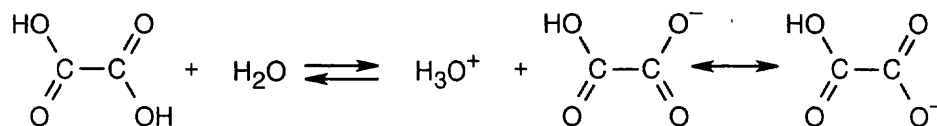
$$[\text{HA}] = 100\% \div 3.69 = 27\%$$

$$[\text{A}^-] = 100\% - 27\% = 73\%$$

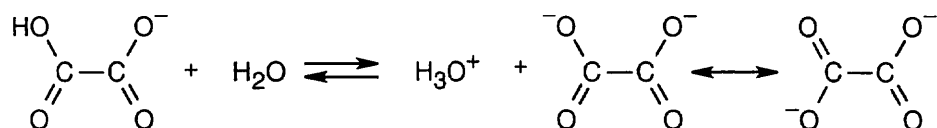
73% of 0.0020 M propanoic acid is dissociated at pH = 5.30.

20.6 You would expect lactic acid to be a stronger acid because the electron-withdrawing inductive effect of the hydroxyl group can stabilize the lactate anion.

20.7



The $\text{p}K_1$ of oxalic acid is lower than that of a monocarboxylic acid because the carboxylate anion is stabilized both by resonance and by the electron-withdrawing inductive effect of the nearby second carboxylic acid group.



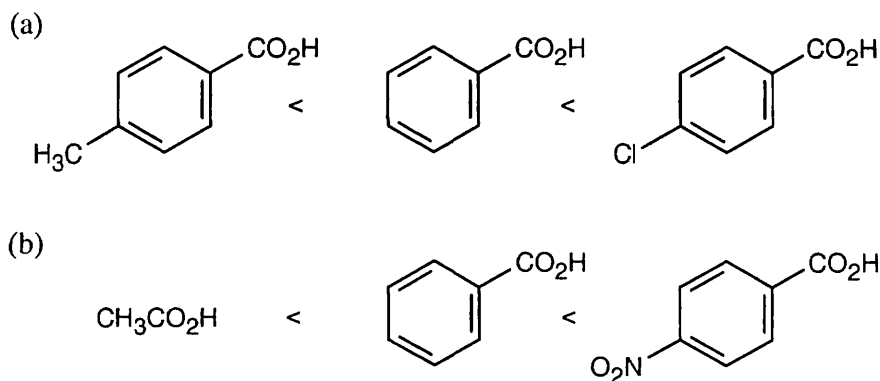
The $\text{p}K_2$ of oxalic acid is higher than $\text{p}K_1$ because an electrostatic repulsion between the two adjacent negative charges destabilizes the dianion.

20.8 A $\text{p}K_a$ of 4.45 indicates that *p*-cyclopropylbenzoic acid is a weaker acid than benzoic acid. This, in turn, indicates that a cyclopropyl group must be electron-donating. Since electron-donating groups increase reactivity in electrophilic substitution reactions, *p*-cyclopropylbenzene should be more reactive than benzene toward electrophilic bromination.

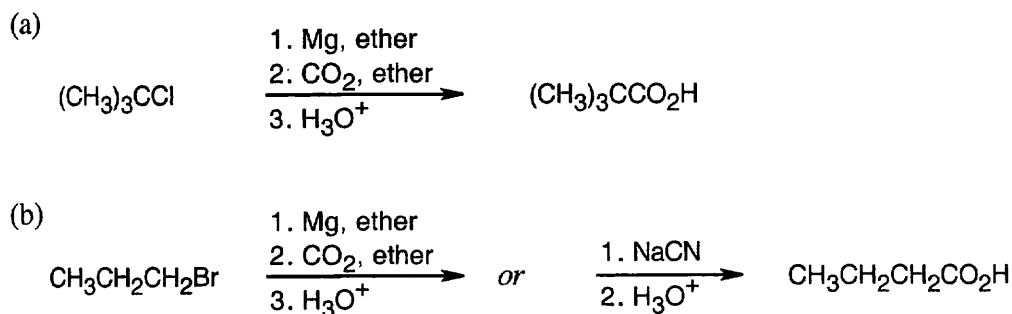
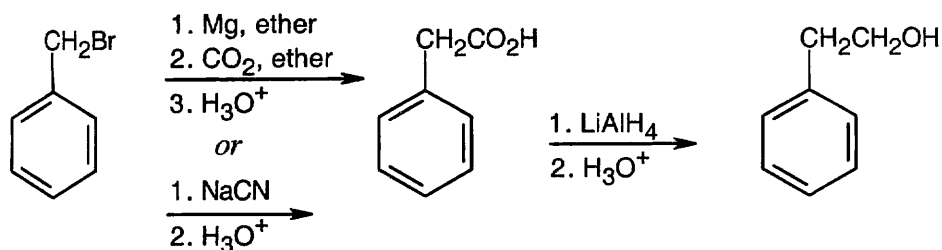
20.9 Strategy: Remember that electron-withdrawing groups increase carboxylic acid acidity, and electron donating groups decrease carboxylic acid acidity. Benzoic acid is more acidic than acetic acid.

Solution:

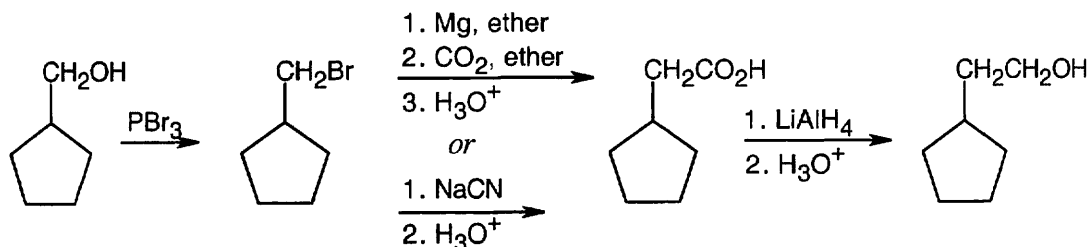
Least acidic $\xrightarrow{\hspace{2cm}}$ *Most acidic*



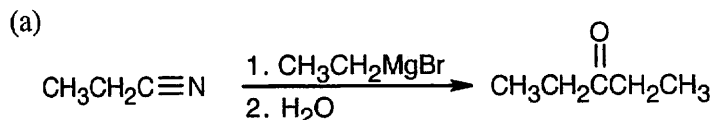
20.10 In part (a), Grignard carboxylation must be used because the starting materials can't undergo S_N2 reactions. In (b), either method can be used.

**20.11**

The alcohol product can be formed by reduction of a carboxylic acid with LiAlH_4 . The carboxylic acid can be synthesized either by Grignard carboxylation or by nitrile hydrolysis. The product can also be formed by a Grignard reaction between benzyl bromide and formaldehyde.

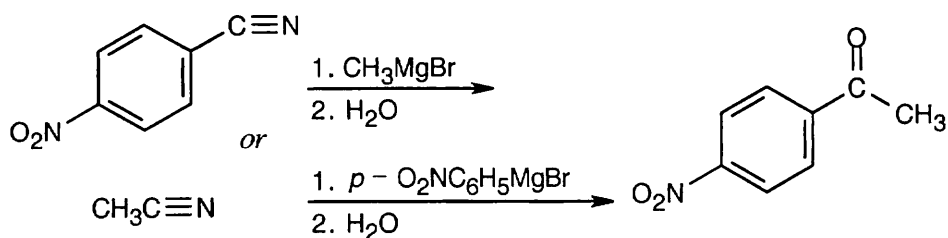
20.12

After treating the initial alcohol with PBr_3 , the same steps as used in the previous problem can be followed. A Grignard reaction between the cycloalkylmagnesium bromide and formaldehyde also yields the desired product.

20.13

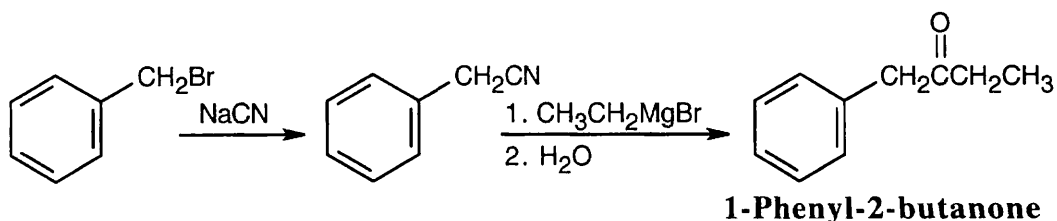
This symmetrical ketone can be synthesized by a Grignard reaction between propanenitrile and ethylmagnesium bromide.

(b)



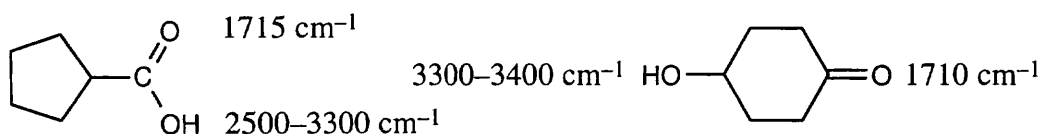
p-Nitroacetophenone can be synthesized by either of two Grignard routes.

20.14



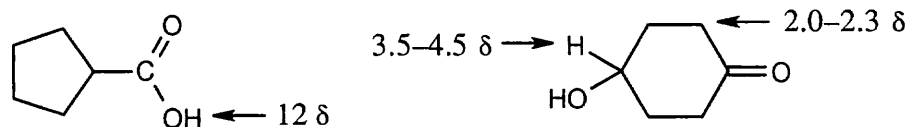
Once you realize that the product results from a Grignard reaction with a nitrile, this synthesis is easy.

20.15



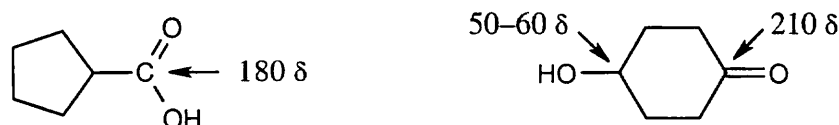
The positions of the carbonyl absorptions are too similar to be useful. The --OH absorptions, however, are sufficiently different for distinguishing between the compounds; the broad band of the carboxylic acid hydroxyl group is especially noticeable.

20.16 ^1H NMR:



The distinctive peak at $12\text{ }\delta$ serves to identify the carboxylic acid. For the hydroxyketone, the absorption of the hydrogen on the oxygen-bearing carbon ($3.5\text{--}4.5\text{ }\delta$) is significant. The position of absorption of the hydroxyl hydrogen is unpredictable, but addition of D_2O to the sample can be used to identify this peak.

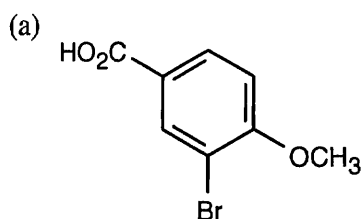
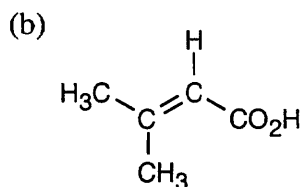
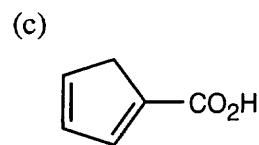
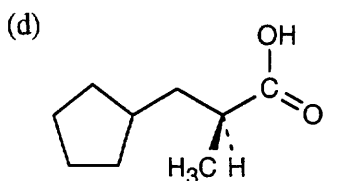
^{13}C NMR:



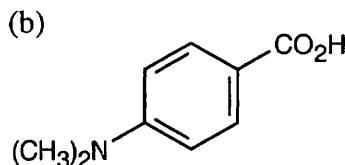
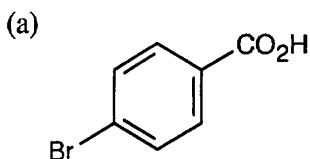
The positions of the carbonyl carbon absorptions can be used to distinguish between these two compounds. The hydroxyketone also shows an absorption in the range $50\text{--}60\text{ }\delta$ due to the hydroxyl group carbon.

Visualizing Chemistry

20.17

**3-Bromo-4-methoxybenzoic acid****3-Methyl-2-butenoic acid****1,3-Cyclopentadiene-carboxylic acid****(S)-3-Cyclopentyl-2-methylpropanoic acid**

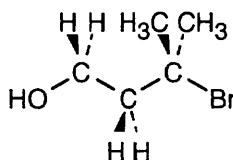
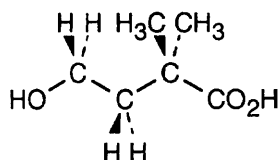
20.18



(a) *p*-Bromobenzoic acid is more acidic than benzoic acid because the electron-withdrawing bromine stabilizes the carboxylate anion.

(b) This *p*-substituted aminobenzoic acid is less acidic than benzoic acid because the electron-donating group destabilizes the carboxylate anion.

20.19

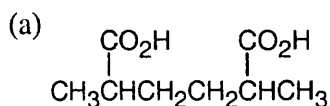
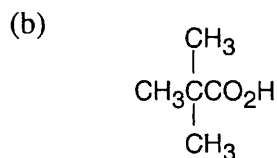
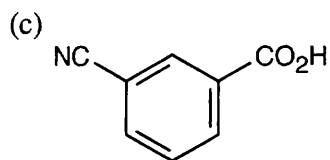
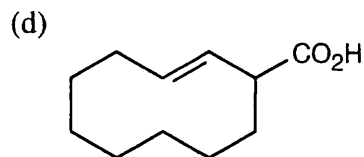
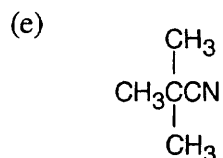
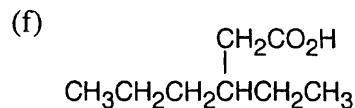
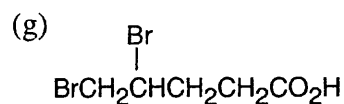
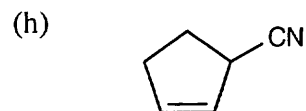


Nitrile hydrolysis can't be used to synthesize the above carboxylic acid because the tertiary halide precursor (shown on the right) doesn't undergo S_N2 substitution with cyanide. Grignard carboxylation also can't be used because the acidic hydroxyl hydrogen interferes with formation of the Grignard reagent. If the hydroxyl group is protected, however, Grignard carboxylation can take place.

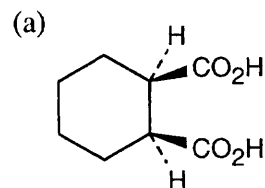
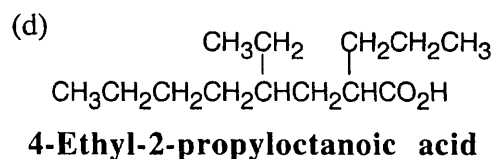
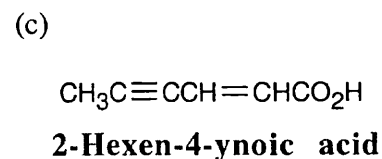
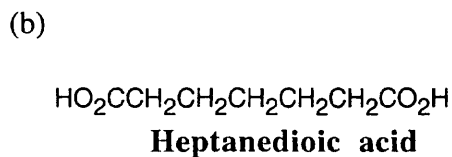
20.20 The electrostatic potential maps show that the aromatic ring of anisole is more electron-rich than the aromatic ring of thioanisole, indicating that the methoxyl group is more strongly electron-donating than the methylthio group. Since electron-donating groups decrease acidity, *p*-(methylthio)benzoic acid is likely to be a stronger acid than *p*-methoxybenzoic acid.

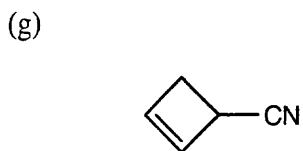
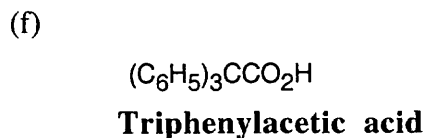
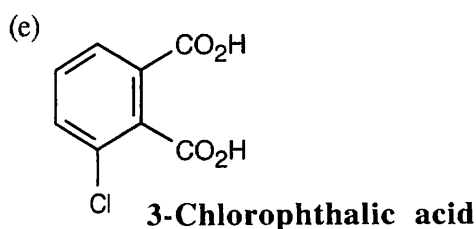
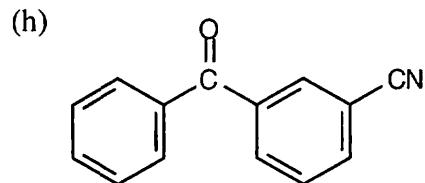
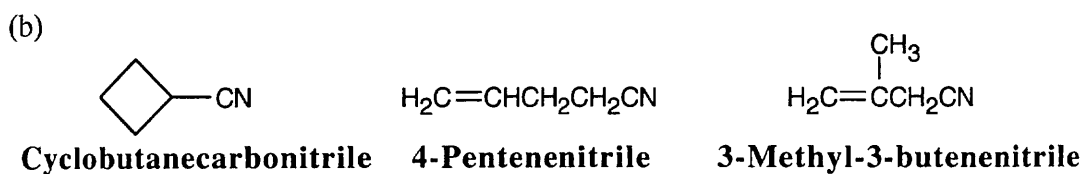
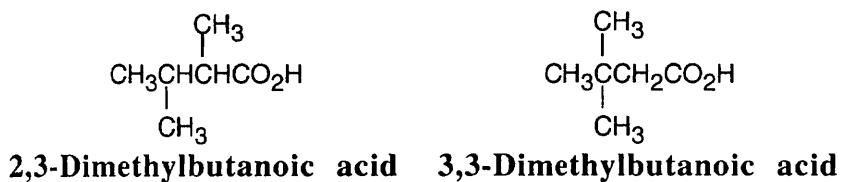
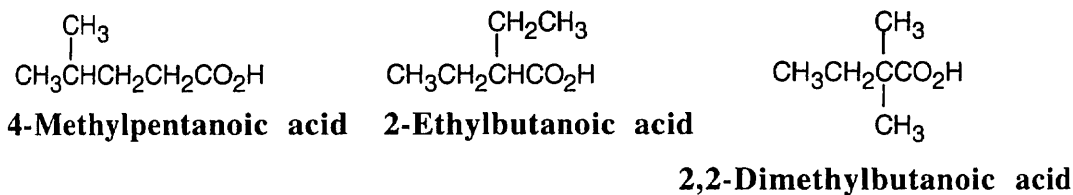
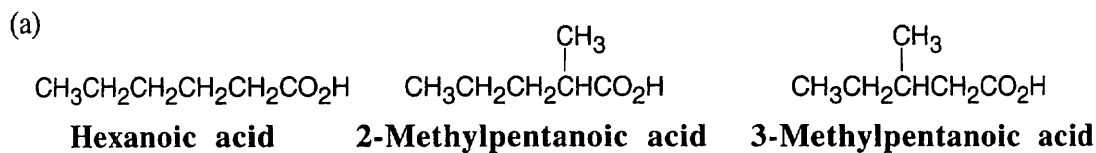
Additional Problems

20.21

**2,5-Dimethylhexanedioic acid****2,2-Dimethylpropanoic acid*****m*-Cyanobenzoic acid*****E*-2-Cyclodecenecarboxylic acid****2,2-Dimethylpropanenitrile****3-Ethylhexanoic acid****4,5-Dibromopentanoic acid****2-Cyclopentenecarbonitrile**

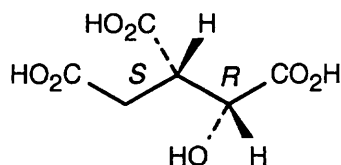
20.22

***cis*-1,2-Cyclohexane-dicarboxylic acid**

**2-Cyclobutenecarbonitrile*****m*-Benzoylbenzonitrile****20.23**

Other nitriles with the formula $\text{C}_5\text{H}_7\text{N}$ can also be drawn.

20.24

**(2R,3S)-3-Carboxy-2-hydroxypentanedioic acid**

20.25

Less acidic \longrightarrow *More acidic*

- (a) $\text{CH}_3\text{CO}_2\text{H} < \text{HCO}_2\text{H} < \text{HO}_2\text{C}-\text{CO}_2\text{H}$
 Acetic acid Formic acid Oxalic acid
- (b) *p*-Bromobenzoic acid < *p*-Nitrobenzoic acid < 2,4-Dinitrobenzoic acid
 (weakly electron-withdrawing substituent) (strongly electron-withdrawing substituent) (two strongly electron-withdrawing substituents)
- (c) $\text{FCH}_2\text{CH}_2\text{CO}_2\text{H} < \text{ICH}_2\text{CO}_2\text{H} < \text{FCH}_2\text{CO}_2\text{H}$

In (c), the strongest acid has the most electronegative atom next to the carboxylic acid group. The next strongest acid has a somewhat less electronegative atom next to the carboxylic acid group. The weakest acid has an electronegative atom two carbons away from the carboxylic acid group.

20.26 Remember that the conjugate base of a weak acid is a strong base. In other words, the stronger the acid, the weaker the base derived from that acid.

Less basic \longrightarrow *More basic*

- (a) $\text{Mg}(\text{OAc})_2 < \text{Mg}(\text{OH})_2 < \text{H}_3\text{C}^- \text{MgBr}^+$

Acetic acid is a much stronger acid than water, which is a much, much stronger acid than methane. The order of base strength is just the reverse.

- (b) Sodium *p*-nitrobenzoate < Sodium benzoate < $\text{HC}\equiv\text{C}^- \text{Na}^+$

p-Nitrobenzoic acid is stronger than benzoic acid, which is much stronger than acetylene.

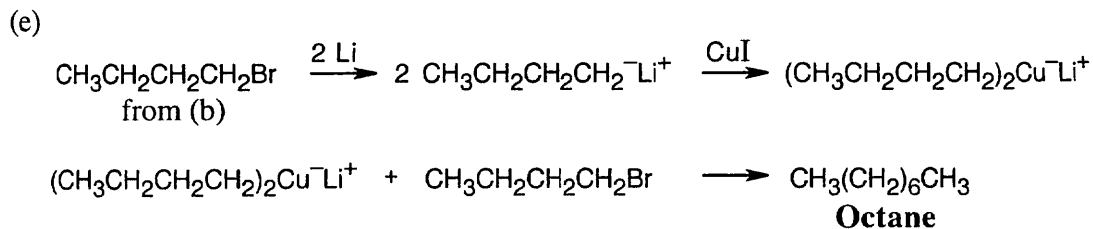
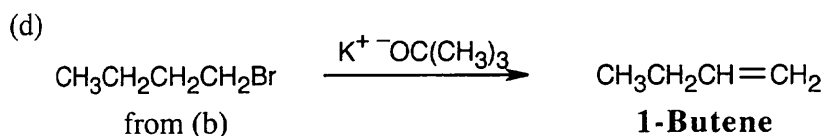
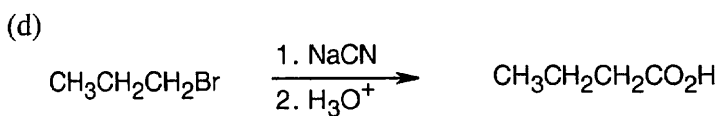
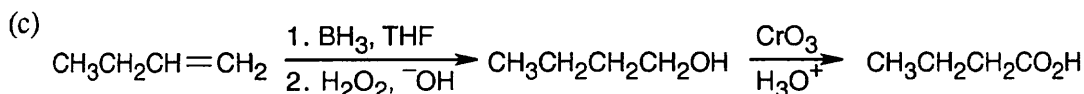
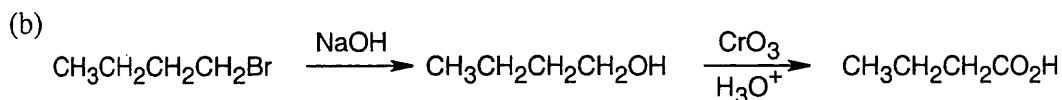
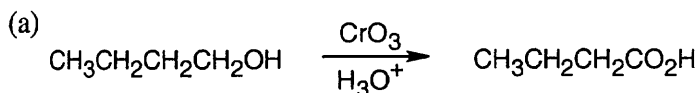
- (c) $\text{HCO}_2^- \text{Li}^+ < \text{HO}^- \text{Li}^+ < \text{CH}_3\text{CH}_2\text{O}^- \text{Li}^+$

LiOH and $\text{LiOCH}_2\text{CH}_3$ are very similar in basicity.

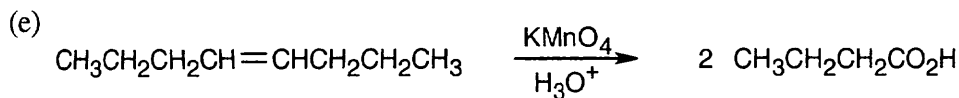
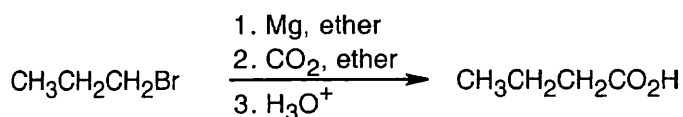
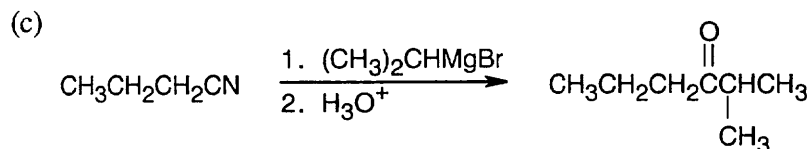
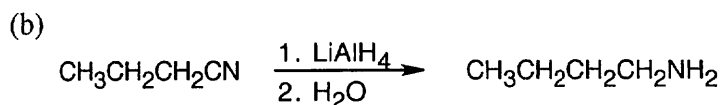
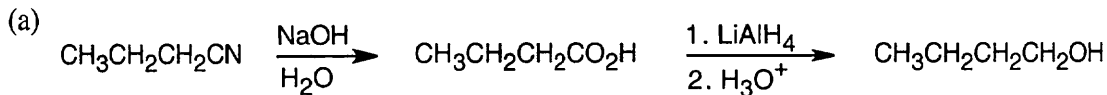
20.27

- (a) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H} \xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{LiAlH}_4} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$
1-Butanol
- (b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \xrightarrow{\text{PBr}_3} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$
 from (a) **1-Bromobutane**
- (c) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} \xrightarrow[2. \text{H}_3\text{O}^+]{1. \text{NaCN}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$
 from (b) **Pentanoic acid**

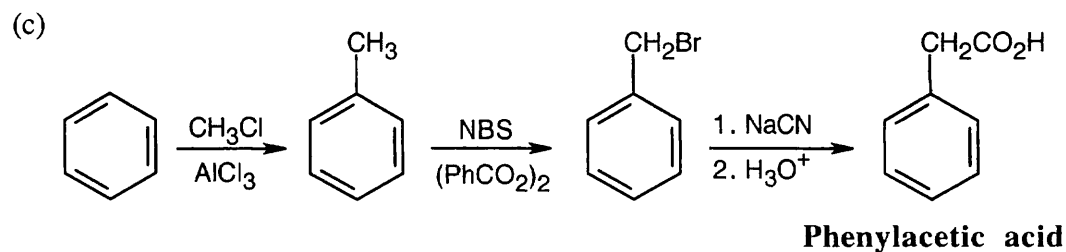
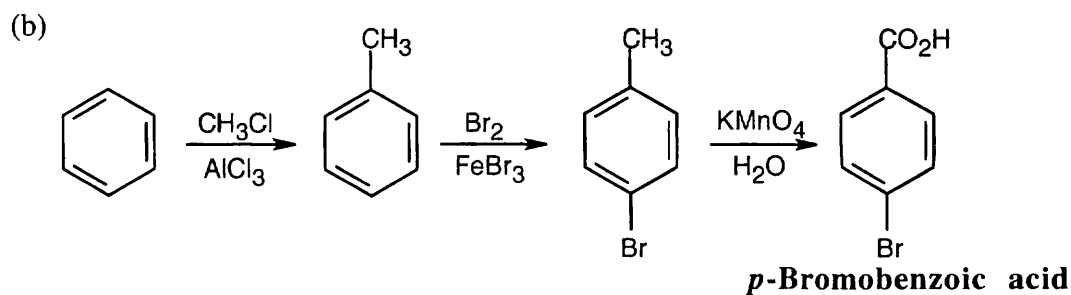
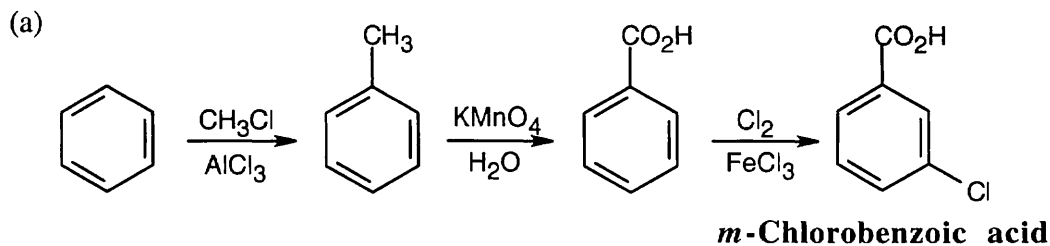
Grignard carboxylation can also be used.

**20.28**

or

**20.29**

20.30



Alternatively, benzyl bromide can be converted to a Grignard reagent, poured over CO_2 , and the resulting mixture can be treated with aqueous acid.

20.31 (a) $K_a = 8.4 \times 10^{-4}$ for lactic acid
 $\text{p}K_a = -\log(8.4 \times 10^{-4}) = 3.08$

(b) $K_a = 5.6 \times 10^{-6}$ for acrylic acid
 $\text{p}K_a = -\log(5.6 \times 10^{-6}) = 5.25$

20.32 (a) $\text{p}K_a = 3.14$ for citric acid
 $K_a = 10^{-3.14} = 7.2 \times 10^{-4}$

(b) $\text{p}K_a = 2.98$ for tartaric acid
 $K_a = 10^{-2.98} = 1.0 \times 10^{-3}$

20.33

$$\log \frac{[A^-]}{[HA]} = \text{pH} - \text{pK}_a = 3.00 - 3.42 = -0.42$$

$$\frac{[A^-]}{[HA]} = \text{antilog}(-0.42) = 0.38 : [A^-] = 0.38 [HA]$$

$$[HA] + 0.38 [HA] = 1.38 [HA] = 100\%$$

$$[HA] = 100\% \div 1.38 = 72\%$$

$$[A^-] = 100\% - 72\% = 28\%$$

At pH = 3.00, thioglycolic acid is 28% dissociated.

20.34

$$\log \frac{[A^-]}{[HA]} = \text{pH} - \text{pK}_a = 6.00 - 5.61 = 0.39$$

$$\frac{[A^-]}{[HA]} = \text{antilog}(0.39) = 2.45 : [A^-] = 2.45 [HA]$$

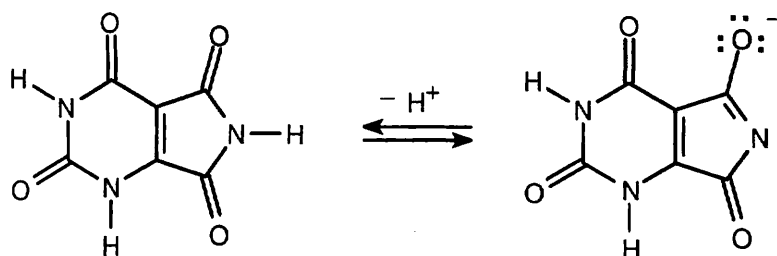
$$[HA] + 2.45 [HA] = 3.45 [HA] = 100\%$$

$$[HA] = 100\% \div 3.45 = 29\%$$

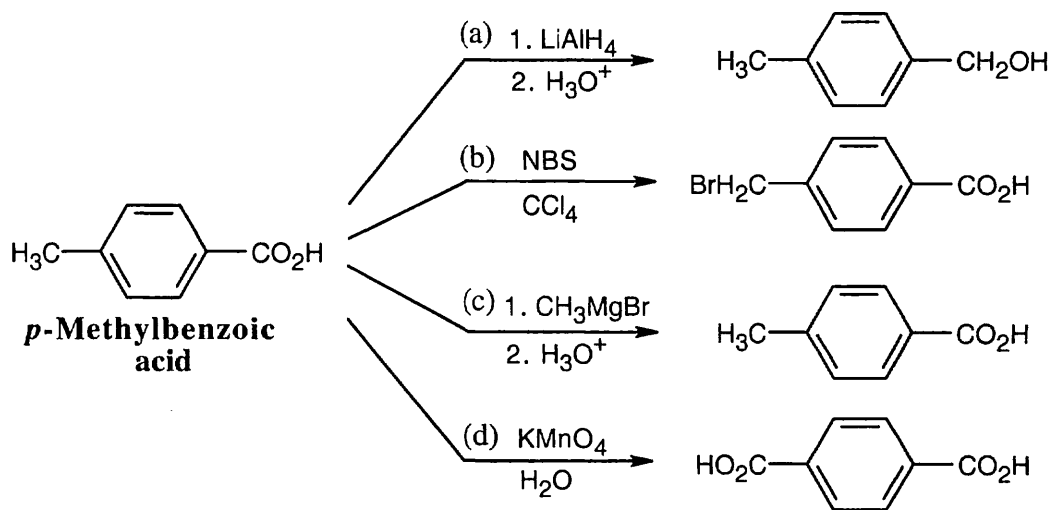
$$[A^-] = 100\% - 29\% = 71\%$$

At pH = 6.00, uric acid is 71% dissociated.

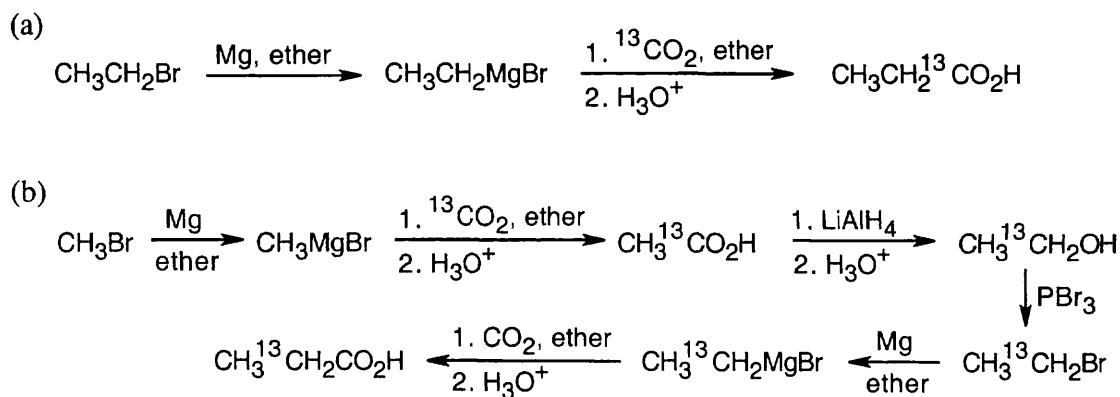
Uric acid is acidic because the anion formed by dissociation of any of the three hydrogens is stabilized by resonance. An example of a resonance form:



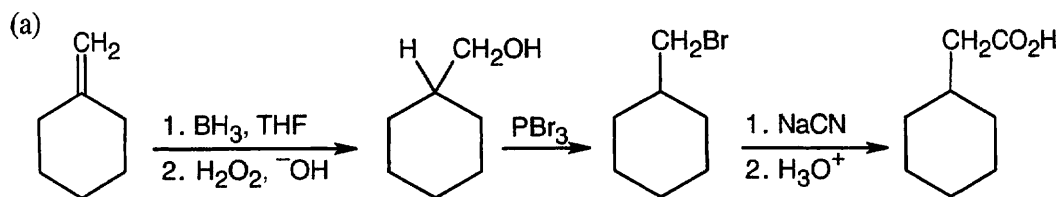
20.35 Inductive effects of functional groups are transmitted through σ bonds. For oxalic acid, the electron-withdrawing inductive effect of one carboxylate group decreases the acidity of the remaining carboxylate group. However, as the length of the carbon chain increases, the effect of one functional group on another decreases. In this example, the influence of the second carboxylate group on the ionization of the first is barely felt by succinic and adipic acids.

20.36

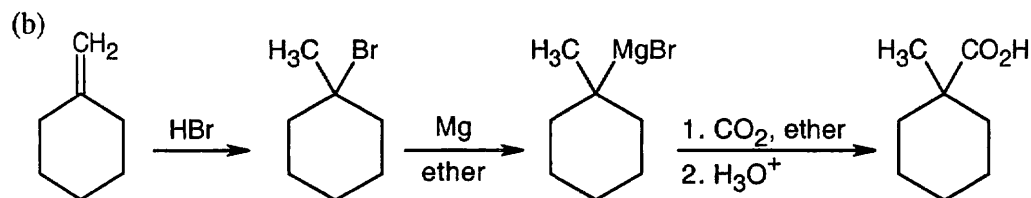
In (c), the acidic proton reacts with the Grignard reagent to form methane.

20.37

20.38



Grignard carboxylation can also be used to form the carboxylic acid.



Only Grignard carboxylation can be used because ^-CN brings about elimination of the tertiary bromide to form a double bond.

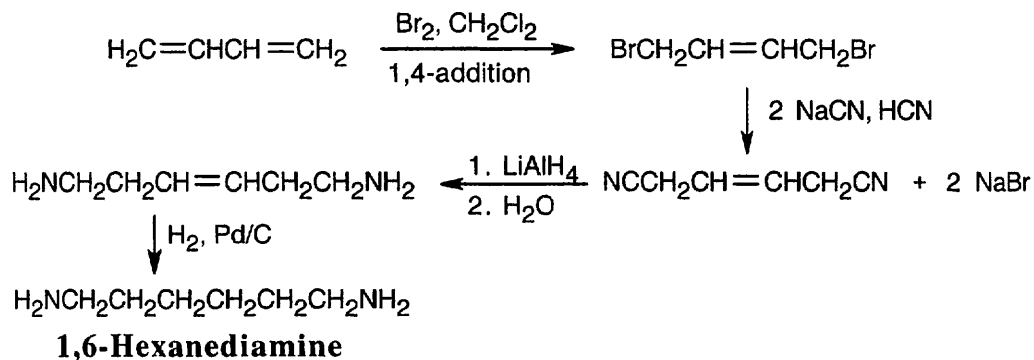
20.39 (a) Grignard carboxylation can't be used to prepare the carboxylic acid because of the acidic hydroxyl group. Use nitrile hydrolysis.

(b) Either method produces the carboxylic acid. Grignard carboxylation is a better reaction for preparing a carboxylic acid from a secondary bromide. Nitrile hydrolysis produces an optically active carboxylic acid from an optically active bromide.

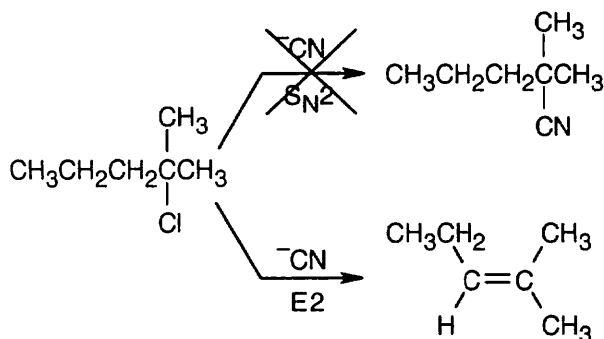
(c) Neither method of acid synthesis yields the desired product. Any Grignard reagent formed will react with the carbonyl functional group present in the starting material. Reaction with cyanide occurs at the carbonyl functional group, producing a cyanohydrin, as well as at halogen. However, if the ketone is first protected by forming an acetal, either method can be used.

(d) Since the hydroxyl proton interferes with formation of the Grignard reagent, nitrile hydrolysis must be used to form the carboxylic acid.

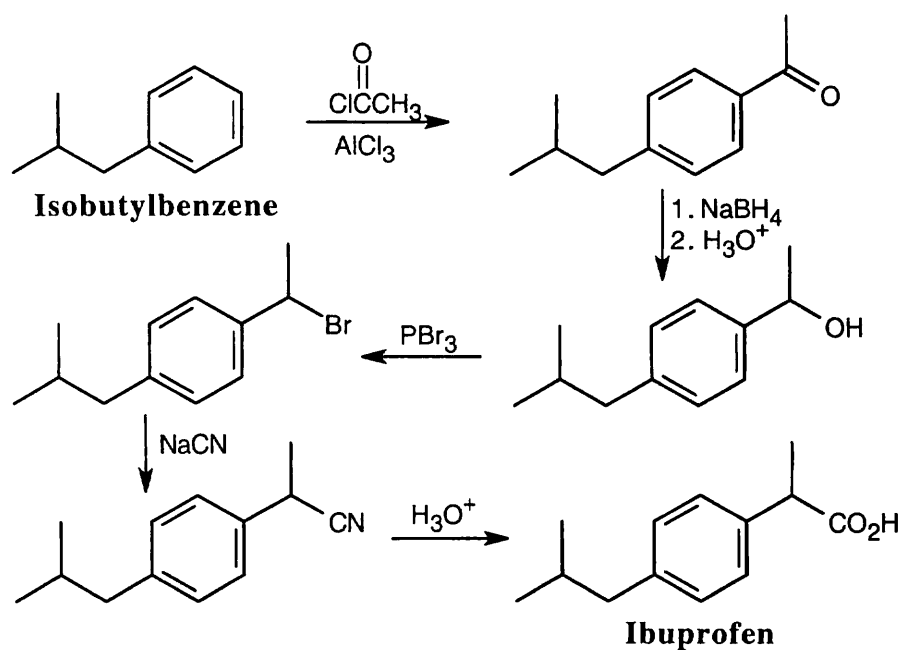
20.40



20.41 2-Chloro-2-methylpentane is a tertiary alkyl halide and ^-CN is a base. Instead of the desired $\text{S}_{\text{N}}2$ reaction of cyanide with a halide, E2 elimination occurs and yields 2-methyl-2-pentene.



20.42

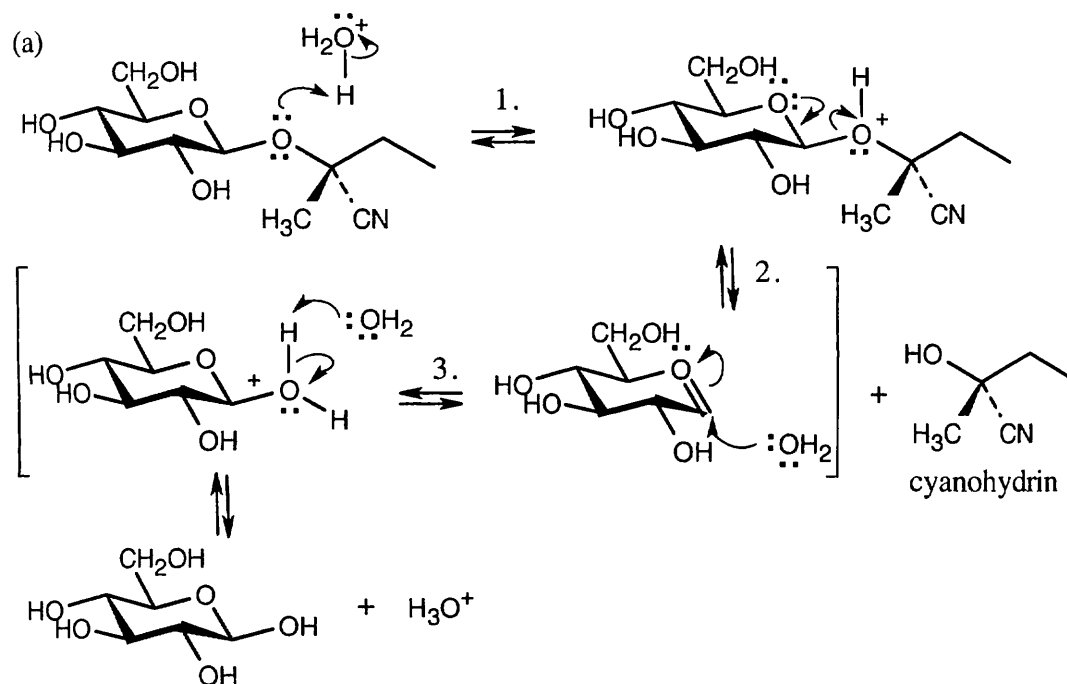


20.43 (a) Use CO_2 instead of NaCN to form the carboxylic acid, or eliminate Mg from this reaction scheme and form the acid by nitrile hydrolysis.

(b) Reduction of a carboxylic acid with LiAlH_4 yields an alcohol, not an alkyl group.

(c) Acidic hydrolysis of the nitrile will also dehydrate the tertiary alcohol. Use basic hydrolysis to form the carboxylic acid.

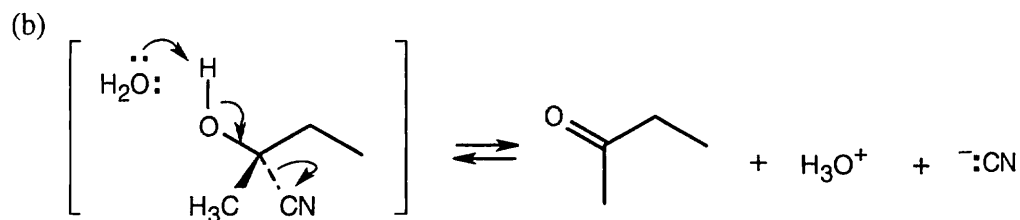
20.44



Step 1: Protonation of acetal oxygen.

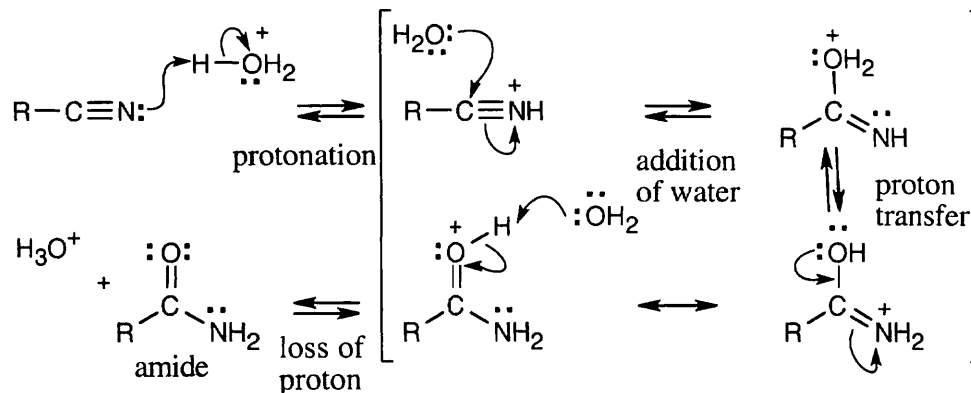
Step 2: Loss of cyanohydrin.

Step 3: Addition of water, followed by deprotonation.

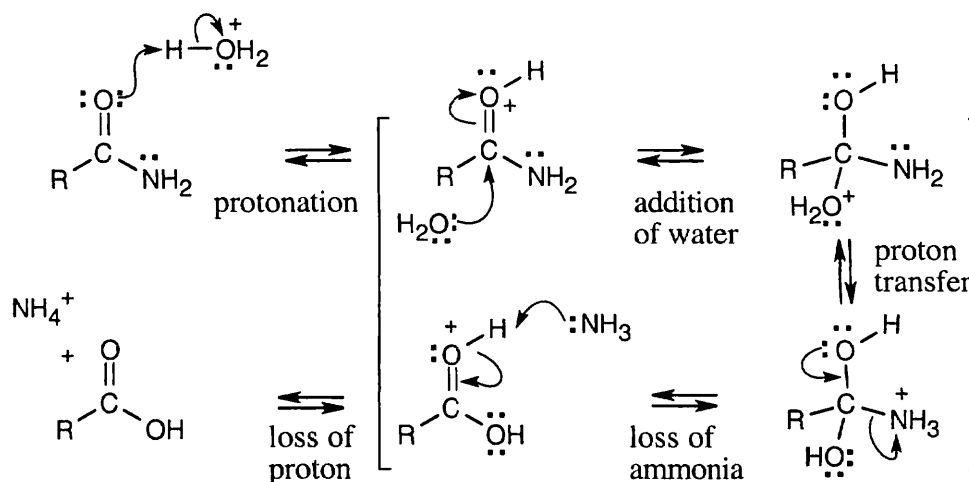


Deprotonation of the cyanohydrin hydroxyl group is followed by loss of CN^- , forming 2-butanone.

20.45

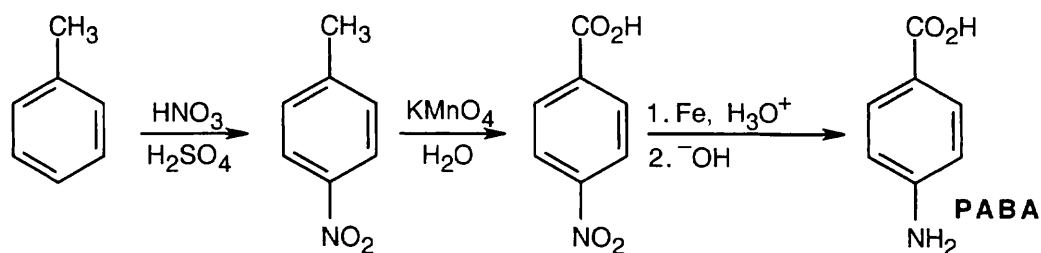


The first equivalent of water adds to a nitrile to produce an amide.



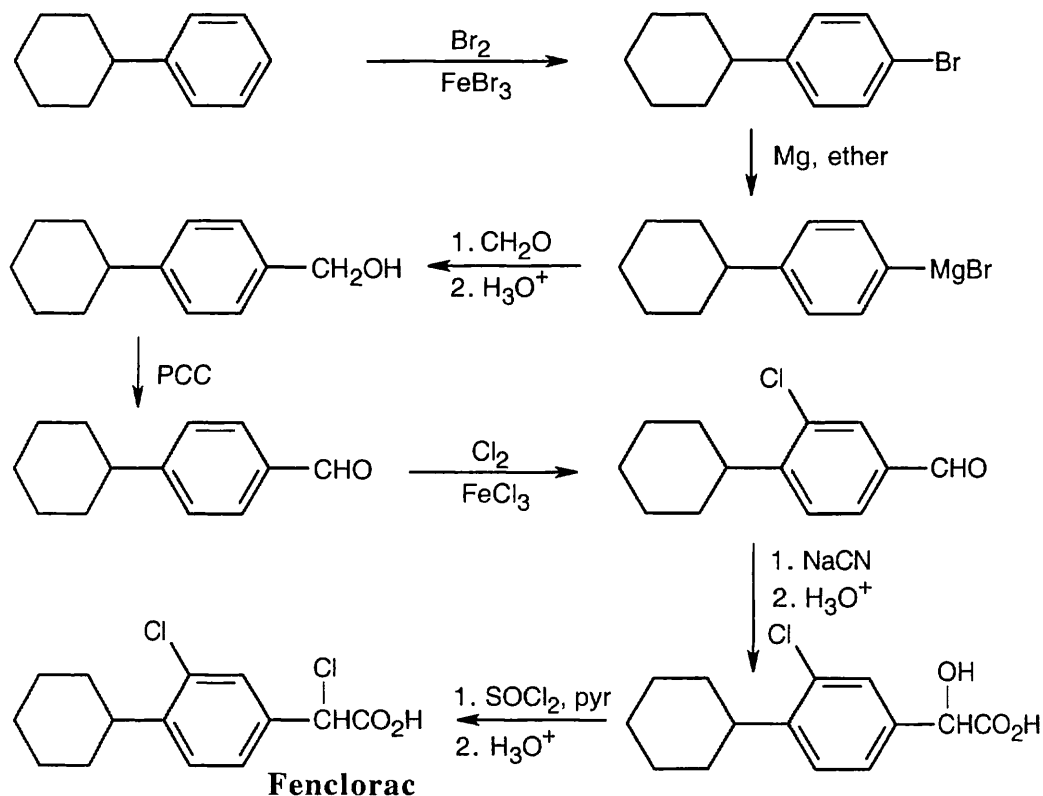
The second equivalent of water adds to the amide to yield a carboxylic acid, plus ammonium ion.

20.46



Notice that the order of the reactions is very important. If toluene is oxidized first, the nitro group will be introduced in the meta position. If the nitro group is reduced first, oxidation to the carboxylic acid will reoxidize the $-\text{NH}_2$ group.

20.47



Other routes to this compound are possible. The illustrated route was chosen because it introduced the potential benzylic functional group and the potential carboxylic acid in one step. Notice that the aldehyde functional group and the cyclohexyl group both serve to direct the aromatic chlorination to the correct position. Also, reaction of the hydroxy acid with SOCl_2 converts $-\text{OH}$ to $-\text{Cl}$ and $-\text{CO}_2\text{H}$ to $-\text{COCl}$. Treatment with H_3O^+ regenerates the carboxylic acid.

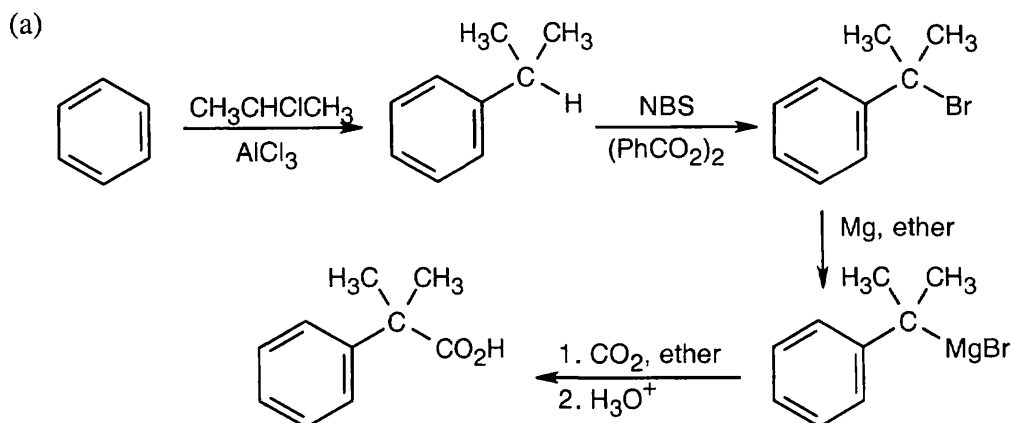
20.48

Substituent	pK_a	Acidity	*E.A.S. reactivity
$-\text{PCl}_2$	3.59	Most acidic	Least reactive (most deactivating)
$-\text{OSO}_2\text{CH}_3$	3.84		
$-\text{CH}=\text{CHCN}$	4.03		
$-\text{HgCH}_3$	4.10		
$-\text{H}$	4.19		
$-\text{Si}(\text{CH}_3)_3$	4.27	Least acidic	Most reactive (least deactivating)

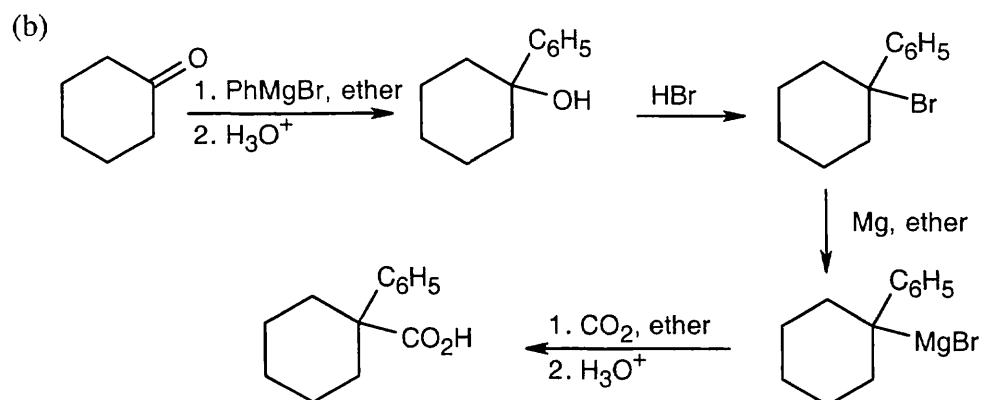
*Electrophilic aromatic substitution

Recall from Section 20.4 that substituents that increase acidity also decrease reactivity in electrophilic aromatic substitution reactions. Of the above substituents, only $-\text{Si}(\text{CH}_3)_3$ is an activator.

20.49

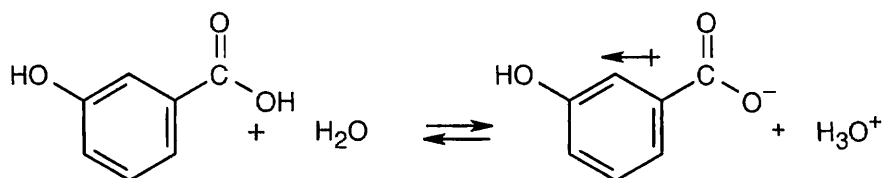


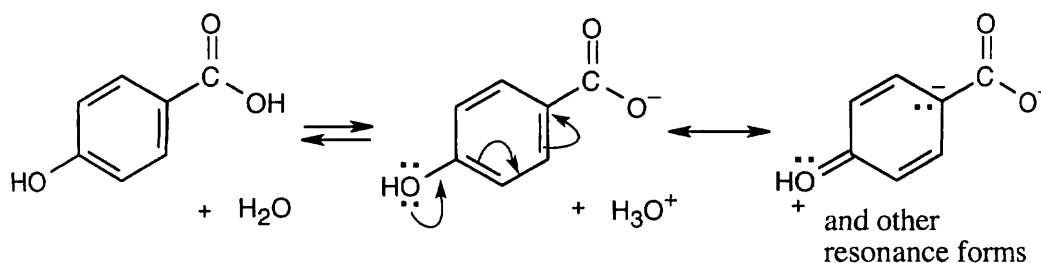
Again, other routes to this compound are possible. The above route was chosen because it has relatively few steps and because the Grignard reagent can be prepared without competing reactions. Notice that nitrile hydrolysis is not a possible route to this compound because the halide precursor is tertiary and doesn't undergo $\text{S}_{\text{N}}2$ substitution.



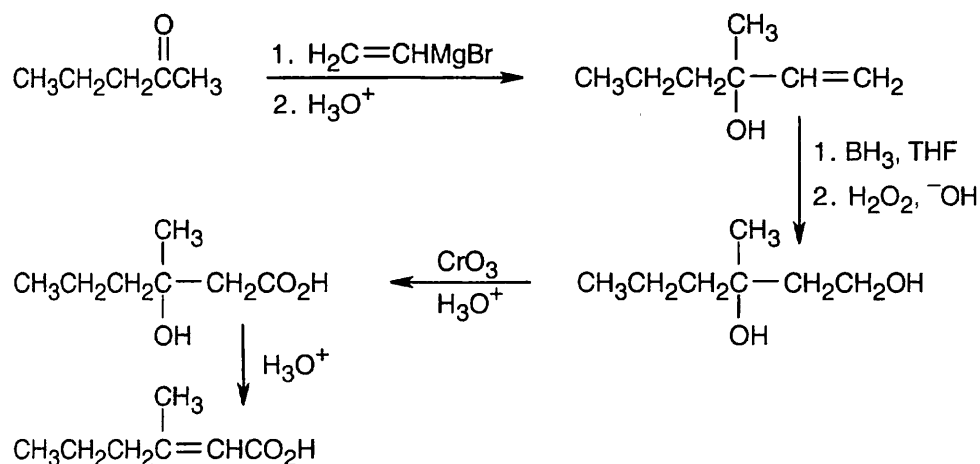
The product results from two Grignard reactions. As in (a), nitrile hydrolysis is not a route to this compound.

20.50 As we have seen throughout this book, the influence of substituents on reactions can be due to inductive effects or to resonance effects. For *m*-hydroxybenzoic acid, the negative charge of the carboxylate anion is stabilized by the electron-withdrawing *inductive* effect of $-\text{OH}$, making this isomer more acidic. For *p*-hydroxybenzoic acid, the negative charge of the anion is destabilized by the electron-donating *resonance* effect of $-\text{OH}$ that acts over the π electron system of the ring but is not important for *m*-substituents.





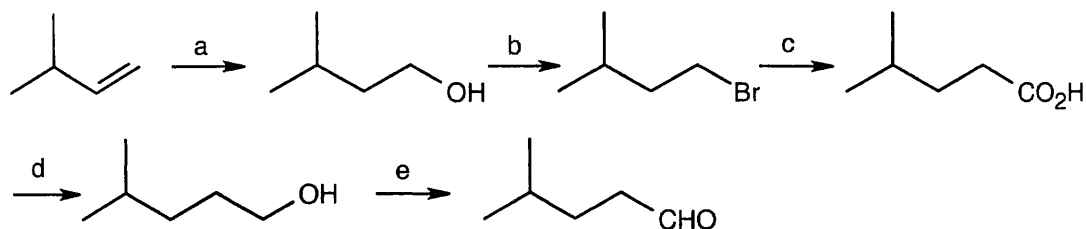
20.51



3-Methyl-2-hexenoic acid

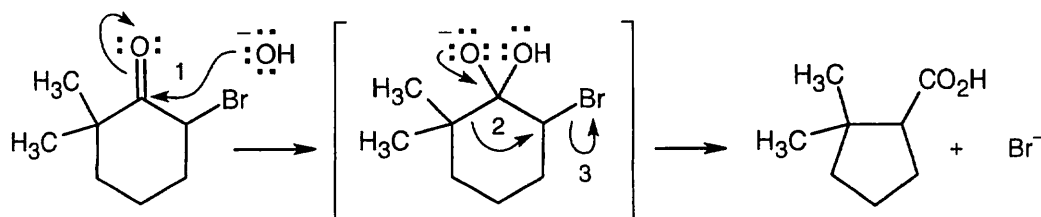
As in all of these more complex syntheses, other routes to the target compound are possible. This route was chosen because the Grignard reaction introduces a double bond without removing functionality at carbon 3. Dehydration occurs in the desired direction to produce a double bond conjugated with the carboxylic acid carbonyl group.

20.52



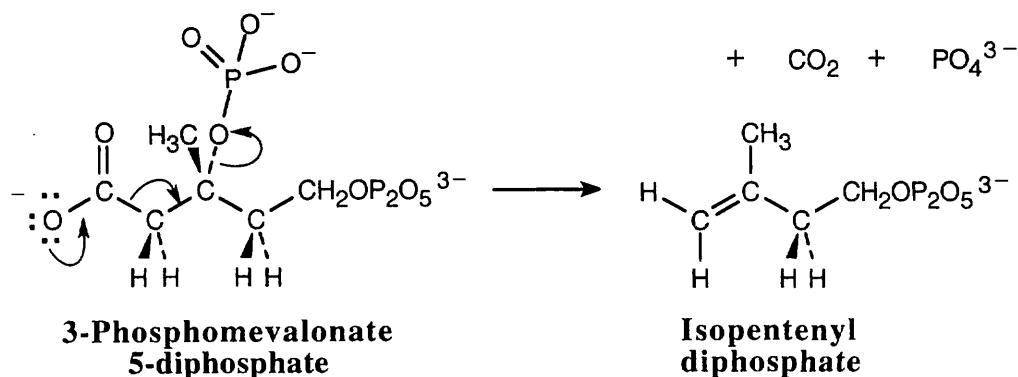
(a) BH_3 , THF, then H_2O_2 , OH^- ; (b) PBr_3 ; (c) Mg , then CO_2 , then H_3O^+ (or CN^- , then H_3O^+); (d) LiAlH_4 , then H_3O^+ ; (e) PCC

20.53



Nucleophilic addition (1), alkyl shift (2), and displacement of bromide (3) lead to the observed product.

20.54

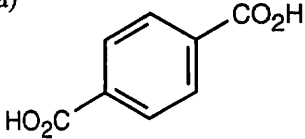
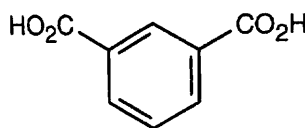


20.55 The peak at 1.08 δ is due to a *tert*-butyl group, and the peak at 11.2 δ is due to a carboxylic acid group. The compound is 3,3-dimethylbutanoic acid, $(\text{CH}_3)_3\text{CCH}_2\text{CO}_2\text{H}$.

20.56 Either ^{13}C NMR or ^1H NMR can be used to distinguish among these three isomeric carboxylic acids.

Compound	Number of ^{13}C NMR absorptions	Number of ^1H NMR absorptions	Splitting of ^1H NMR signals
$\text{CH}_3(\text{CH}_2)_3\text{CO}_2\text{H}$	5	5	1 triplet, peak area 3, 1.0 δ 1 triplet, peak area 2, 2.4 δ 2 multiplets, peak area 4, 1.5 δ 1 singlet, peak area 1, 12.0 δ
$(\text{CH}_3)_2\text{CHCH}_2\text{CO}_2\text{H}$	4	4	1 doublet, peak area 6, 1.0 δ 1 doublet, peak area 2, 2.4 δ 1 multiplet, peak area 1, 1.6 δ 1 singlet, peak area 1, 12.0 δ
$(\text{CH}_3)_3\text{CCO}_2\text{H}$	3	2	1 singlet, peak area 9, 1.3 δ 1 singlet, peak area 1, 12.1 δ

20.57 In all of these pairs, different numbers of peaks occur in the spectra of each isomer.
 (a), (b) Use either ^1H NMR or ^{13}C NMR to distinguish between the isomers.

Compound	Number of ^{13}C NMR absorptions	Number of ^1H NMR absorptions
(a)		
	3	2
	5	4
(b)		
$\text{HO}_2\text{CCH}_2\text{CH}_2\text{CO}_2\text{H}$	2	2
$\text{CH}_3\text{CH}(\text{CO}_2\text{H})_2$	3	3

(c) Use ^1H NMR to distinguish between these two compounds. The carboxylic acid proton of $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ absorbs near 12 δ , and the aldehyde proton of $\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CHO}$ absorbs near 10 δ and is split into a triplet.

(d) Cyclopentanecarboxylic acid shows four absorptions in both its ^1H NMR and ^{13}C NMR spectra. $(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{CO}_2\text{H}$ shows six absorptions in its ^{13}C NMR and five in its ^1H NMR spectrum; one of the ^1H NMR signals occurs in the vinylic region (4.5 – 6.5 δ) of the spectrum. The ^{13}C NMR spectrum of the unsaturated acid also shows two absorptions in the C=C bond region (100–150 δ).

20.58 The compound has one degree of unsaturation, consistent with the carboxylic acid absorption seen in the IR spectrum.

	a = 1.3 δ
a b c d	b = 3.7 δ
$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CO}_2\text{H}$	c = 4.1 δ
	d = 11.1 δ

20.59 A compound with the formula $\text{C}_4\text{H}_7\text{N}$ has two degrees of unsaturation. The IR absorption at 2250 cm^{-1} identifies this compound as a nitrile.

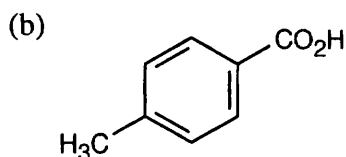
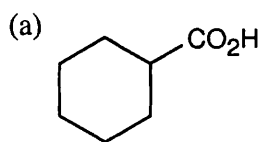
a b c	a = 1.1 δ
$\text{CH}_3\text{CH}_2\text{CH}_2\text{C}\equiv\text{N}$	b = 1.7 δ
	c = 2.3 δ

- 20.60** Both compounds contain four different kinds of protons (the $\text{H}_2\text{C}=\text{CH}$ protons are nonequivalent). The carboxylic acid proton absorptions are easy to identify; the other three absorptions in each spectrum are more complex.

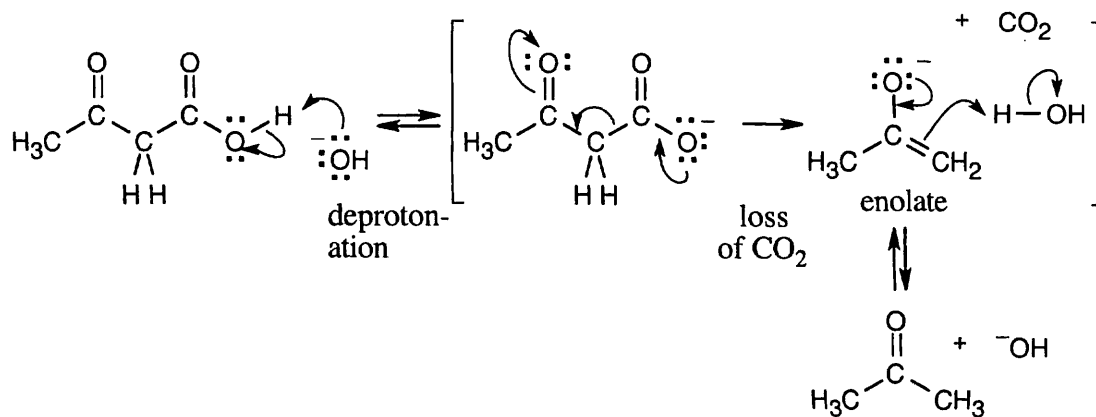
It is possible to assign the spectra by studying the methyl group absorptions. The methyl group peak of crotonic acid is split into a doublet by the geminal ($\text{CH}_3\text{CH}=\text{CH}$) proton, while the methyl group absorption of methacrylic acid is a singlet. The first spectrum (a) is that of crotonic acid, and the second spectrum (b) is that of methacrylic acid.

- 20.61** (a) From the formula, we know that the compound has 2 degrees of unsaturation, one of which is due to the carboxylic acid group that absorbs at $183.0\ \delta$. The ^{13}C NMR spectrum also shows that no other sp^2 carbons are present in the sample and indicates that the other degree of unsaturation is due to a ring, which is shown to be a cyclohexane ring by symmetry and by the types of carbons in the structure.

(b) The compound has 5 degrees of unsaturation, and is a methyl-substituted benzoic acid. The symmetry shown by the aromatic absorptions identifies the compound as *p*-methylbenzoic acid.



20.62



This reaction proceeds because of the loss of CO_2 and the stability of the enolate anion.