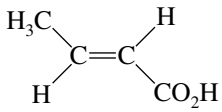
CHAPTER 19

CARBOXYLIC ACIDS

SOLUTIONS TO TEXT PROBLEMS

19.1 (*b*) The four carbon atoms of crotonic acid form a continuous chain. Because there is a double bond between C-2 and C-3, crotonic acid is one of the stereoisomers of 2-butenoic acid. The stereochemistry of the double bond is *E*.

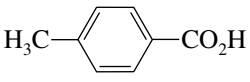


(*E*)-2-Butenoic acid
(crotonic acid)

(*c*) Oxalic acid is a dicarboxylic acid that contains two carbons. It is **ethanedioic acid.**

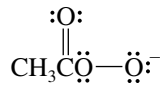
Ethanedioic acid
(oxalic acid)

(*d*) The name given to $C_6H_5CO_2H$ is benzoic acid. Because it has a methyl group at the para position, the compound shown is ***p*-methylbenzoic acid,** or **4-methylbenzoic acid.**



p-Methylbenzoic acid or
4-methylbenzoic acid
(*p*-toluic acid)

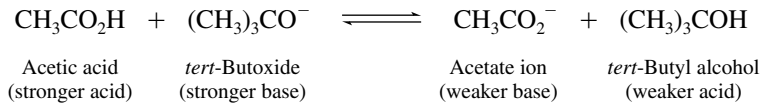
19.2 Ionization of peroxy acids such as peroxyacetic acid yields an anion that cannot be stabilized by resonance in the same way that acetate can.



Delocalization of negative charge into carbonyl group is not possible in peroxyacetate ion.

19.3 Recall from Chapter 4 (text Section 4.6) that an acid–base equilibrium favors formation of the weaker acid and base. Also remember that the weaker acid forms the stronger conjugate base, and vice versa.

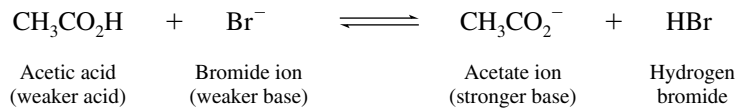
(*b*) The acid–base reaction between acetic acid and *tert*-butoxide ion is represented by the equation



CH_3CO_2H	$(CH_3)_3CO^-$		$CH_3CO_2^-$	$(CH_3)_3COH$
Acetic acid (stronger acid)	*tert*-Butoxide (stronger base)		Acetate ion (weaker base)	*tert*-Butyl alcohol (weaker acid)

Alcohols are weaker acids than carboxylic acids; the equilibrium lies to the right.

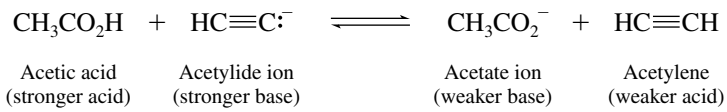
(*c*) Bromide ion is the conjugate base of hydrogen bromide, a strong acid.



CH_3CO_2H	Br^-		$CH_3CO_2^-$	HBr
Acetic acid (weaker acid)	Bromide ion (weaker base)		Acetate ion (stronger base)	Hydrogen bromide (stronger acid)

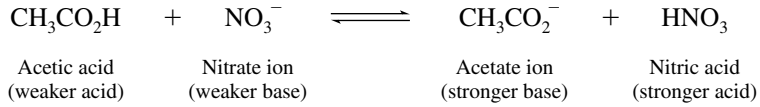
In this case, the position of equilibrium favors the starting materials, because acetic acid is a weaker acid than hydrogen bromide.

(*d*) Acetylide ion is a rather strong base, and acetylene, with a K_a of 10^{-26}, is a much weaker acid than acetic acid. The position of equilibrium favors the formation of products.



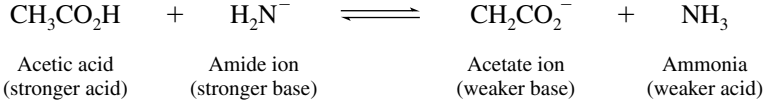
CH_3CO_2H	$HC{\equiv}C:^-$		$CH_3CO_2^-$	$HC{\equiv}CH$
Acetic acid (stronger acid)	Acetylide ion (stronger base)		Acetate ion (weaker base)	Acetylene (weaker acid)

(*e*) Nitrate ion is a very weak base; it is the conjugate base of the strong acid nitric acid. The position of equilibrium lies to the left.



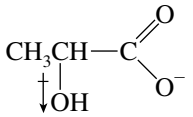
CH_3CO_2H	NO_3^-		$CH_3CO_2^-$	HNO_3
Acetic acid (weaker acid)	Nitrate ion (weaker base)		Acetate ion (stronger base)	Nitric acid (stronger acid)

(*f*) Amide ion is a very strong base; it is the conjugate base of ammonia, $pK_a = 36$. The position of equilibrium lies to the right.



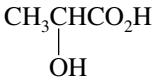
CH_3CO_2H	H_2N^-		$CH_2CO_2^-$	NH_3
Acetic acid (stronger acid)	Amide ion (stronger base)		Acetate ion (weaker base)	Ammonia (weaker acid)

19.4 (*b*) Propanoic acid is similar to acetic acid in its acidity. A hydroxyl group at C-2 is electron-withdrawing and stabilizes the carboxylate ion of lactic acid by a combination of inductive and field effects.



Hydroxyl group stabilizes
negative charge by attracting electrons.

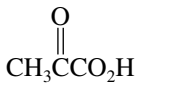
Lactic acid is more acidic than propanoic acid. The measured ionization constants are



Lactic acid
K_a 1.4×10^{-4}
(pK_a 3.8)

Propanoic acid
K_a 1.3×10^{-5}
(pK_a 4.9)

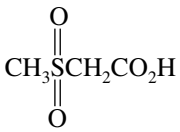
(*c*) A carbonyl group is more strongly electron-withdrawing than a carbon–carbon double bond. Pyruvic acid is a stronger acid than acrylic acid.



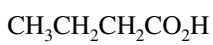
Pyruvic acid
K_a 5.1×10^{-4}
(pK_a 3.3)

Acrylic acid
K_a 5.5×10^{-5}
(pK_a 4.3)

(*d*) Viewing the two compounds as substituted derivatives of acetic acid, RCH_2CO_2H, we judge  to be strongly electron-withdrawing and acid-strengthening, whereas an ethyl group has only a small effect.



Methanesulfonylacetic acid
K_a 4.3×10^{-3}
(pK_a 2.4)



Butanoic acid
K_a 1.5×10^{-5}
(pK_a 4.7)

19.5 The compound can only be a carboxylic acid; no other class containing only carbon, hydrogen, and oxygen is more acidic. A reasonable choice is $HC{\equiv}CCO_2H$; C-2 is *sp*-hybridized and therefore rather electron-withdrawing and acid-strengthening. This is borne out by its measured ionization constant K_a, which is 1.4×10^{-2} (pK_a 1.8).

19.6 For carbonic acid, the "true K_1" is given by

$$\text{True } K_1 = \frac{[H^+][HCO_3^-]}{[H_2CO_3]}$$

The "observed K" is given by the expression

$$4.3 \times 10^{-7} = \frac{[H^+][HCO_3^-]}{[CO_2]}$$

which can be rearranged to

$$[H^+][HCO_3^-] = (4.3 \times 10^{-7})[CO_2]$$

and therefore

$$\text{True } K_1 = \frac{(4.3 \times 10^{-7})[CO_2]}{[H_2CO_3]}$$

$$= \frac{(4.3 \times 10^{-7})(99.7)}{0.3}$$

$$= 1.4 \times 10^{-4}$$

Thus, when corrected for the small degree to which carbon dioxide is hydrated, it can be seen that carbonic acid is actually a stronger acid than acetic acid. Carboxylic acids dissolve in sodium bicarbonate solution because the equilibrium that leads to carbon dioxide formation is favorable, not because carboxylic acids are stronger acids than carbonic acid.

19.7 (*b*) 2-Chloroethanol has been converted to 3-hydroxypropanoic acid by way of the corresponding nitrile.

$$\underset{\text{2-Chloroethanol}}{HOCH_2CH_2Cl} \xrightarrow[H_2O]{NaCN} \underset{\text{2-Cyanoethanol}}{HOCH_2CH_2CN} \xrightarrow[\text{heat}]{H_3O^+} \underset{\text{3-Hydroxypropanoic acid}}{HOCH_2CH_2CO_2H}$$

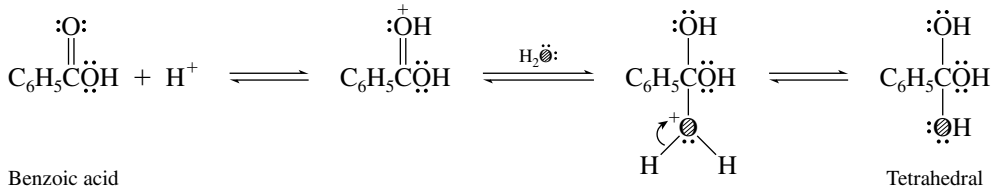
The presence of the hydroxyl group in 2-chloroethanol precludes the preparation of a Grignard reagent from this material, and so any attempt at the preparation of 3-hydroxypropanoic acid via the Grignard reagent of 2-chloroethanol is certain to fail.

(*c*) Grignard reagents can be prepared from tertiary halides and react in the expected manner with carbon dioxide. The procedure shown is entirely satisfactory.

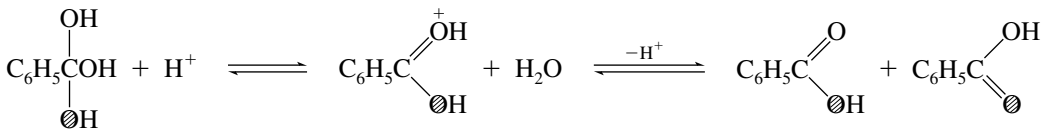
$$\underset{\textit{tert}\text{-Butyl chloride}}{(CH_3)_3CCl} \xrightarrow[\text{diethyl ether}]{Mg} \underset{\textit{tert}\text{-Butylmagnesium chloride}}{(CH_3)_3CMgCl} \xrightarrow[2.\ H_3O^+]{1.\ CO_2} \underset{\text{2,2-Dimethylpropanoic acid (61–70\%)}}{(CH_3)_3CCO_2H}$$

Preparation by way of the nitrile will not be feasible. Rather than react with sodium cyanide by substitution, *tert*-butyl chloride will undergo elimination exclusively. The S_N2 reaction with cyanide ion is limited to primary and secondary alkyl halides.

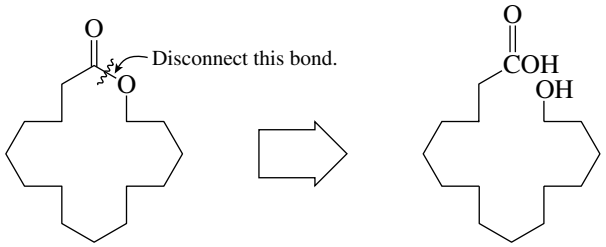
19.8 Incorporation of ^{18}O into benzoic acid proceeds by a mechanism analogous to that of esterification. The nucleophile that adds to the protonated form of benzoic acid is ^{18}O-enriched water (the ^{18}O atom is represented by the shaded letter ⓪ in the following equations).



The three hydroxyl groups of the tetrahedral intermediate are equivalent except that one of them is labeled with ^{18}O. Any one of these three hydroxyl groups may be lost in the dehydration step; when the hydroxyl group that is lost is unlabeled, an ^{18}O label is retained in the benzoic acid.

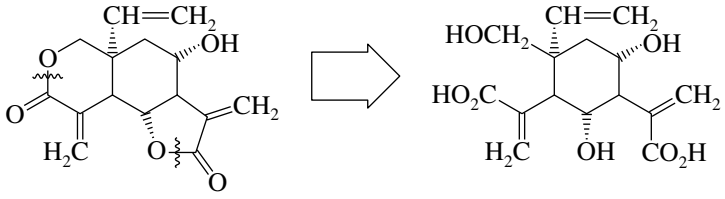


19.9 (*b*) The 16-membered ring of 15-pentadecanolide is formed from 15-hydroxypentadecanoic acid.



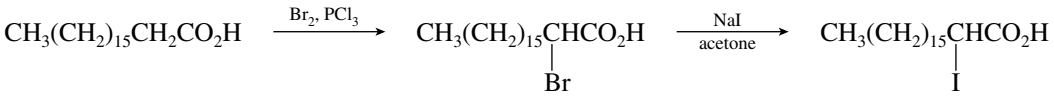
15-Pentadecanolide 15-Hydroxypentadecanoic acid

(*c*) Vernolepin has two lactone rings, which can be related to two hydroxy acid combinations.



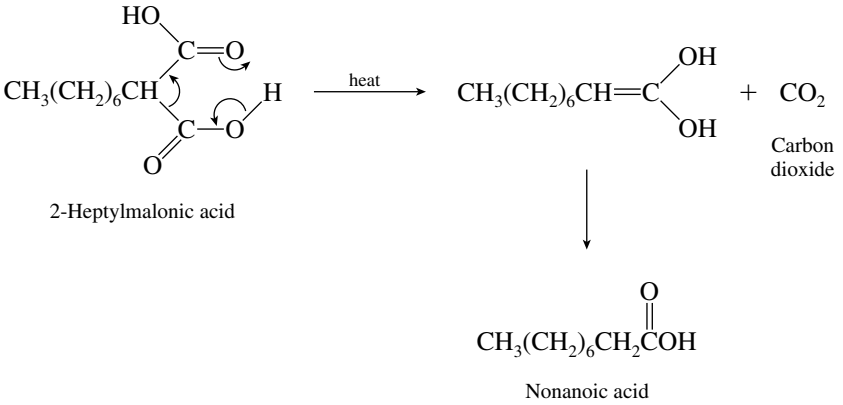
Be sure to keep the relative stereochemistry unchanged. Remember, the carbon–oxygen bond of an alcohol remains intact when the alcohol reacts with a carboxylic acid to give an ester.

19.10 Alkyl chlorides and bromides undergo nucleophilic substitution when treated with sodium iodide in acetone (Section 8.1). A reasonable approach is to brominate octadecanoic acid at its α-carbon atom, then replace the bromine substituent with iodine by nucleophilic substitution.



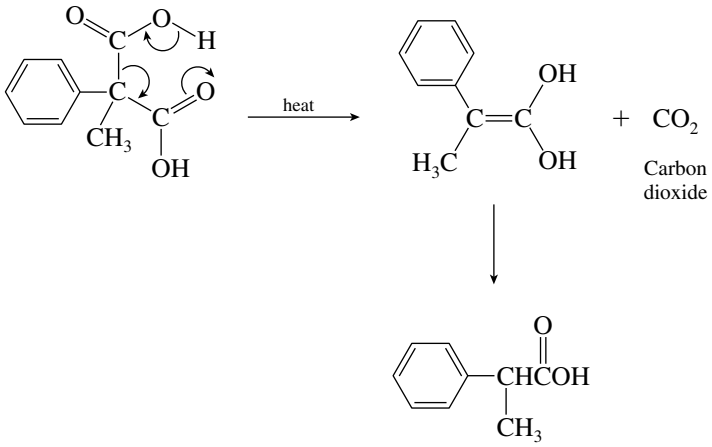
Octadecanoic acid 2-Bromooctadecanoic acid 2-Iodooctadecanoic acid

19.11 (*b*) The starting material is a derivative of malonic acid. It undergoes efficient thermal decarboxylation in the manner shown.



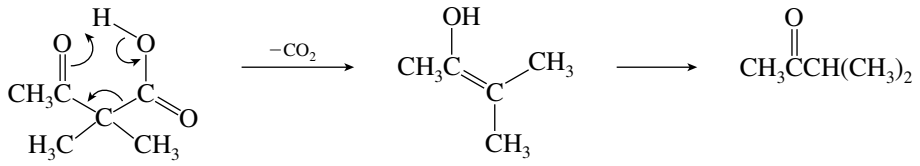
2-Heptylmalonic acid Carbon dioxide Nonanoic acid

(*c*) The phenyl and methyl substituents attached to C-2 of malonic acid play no role in the decarboxylation process.



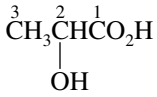
2-Phenylpropanoic acid

19.12 (*b*) The thermal decarboxylation of β-keto acids resembles that of substituted malonic acids. The structure of 2,2-dimethylacetoacetic acid and the equation representing its decarboxylation were given in the text. The overall process involves the bonding changes shown.



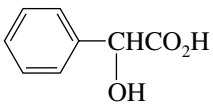
2,2-Dimethylacetoacetic acid | Enol form of 3-methyl-2-butanone | 3-Methyl-2-butanone

19.13 (*a*) Lactic acid (2-hydroxypropanoic acid) is a three-carbon carboxylic acid that bears a hydroxyl group at C-2.



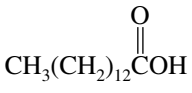
2-Hydroxypropanoic acid

(*b*) The parent name **ethanoic acid** tells us that the chain that includes the carboxylic acid function contains only two carbons. A hydroxyl group and a phenyl substituent are present at C-2.



2-Hydroxy-2-phenylethanoic acid
(mandelic acid)

(*c*) The parent alkane is **tetradecane,** which has an unbranched chain of 14 carbons. The terminal methyl group is transformed to a carboxyl function in tetradecanoic acid.

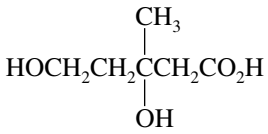


Tetradecanoic acid
(myristic acid)

(*d*) Undecane is the unbranched alkane with 11 carbon atoms, undecanoic acid is the corresponding carboxylic acid, and **undecenoic acid** is an 11-carbon carboxylic acid that contains a double bond. Because the carbon chain is numbered beginning with the carboxyl group, 10-undecenoic acid has its double bond at the opposite end of the chain from the carboxyl group.

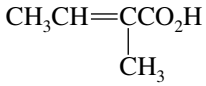
10-Undecenoic acid
(undecylenic acid)

(*e*) Mevalonic acid has a five-carbon chain with hydroxyl groups at C-3 and C-5, along with a methyl group at C-3.



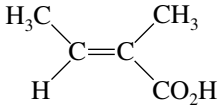
3,5-Dihydroxy-3-methylpentanoic acid
(mevalonic acid)

(*f*) The constitution represented by the systematic name 2-methyl-2-butenoic acid gives rise to two stereoisomers.

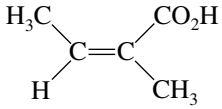


2-Methyl-2-butenoic acid

Tiglic acid is the *E* isomer, and the *Z* isomer is known as **angelic acid.** The higher ranked substituents, methyl and carboxyl, are placed on opposite sides of the double bond in tiglic acid and on the same side in angelic acid.

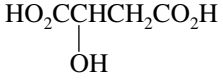


(*E*)-2-Methyl-2-butenoic
acid (tiglic acid)



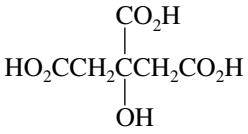
(*Z*)-2-Methyl-2-butenoic acid
(angelic acid)

(*g*) Butanedioic acid is a four-carbon chain in which both terminal carbons are carboxylic acid groups. Malic acid has a hydroxyl group at C-2.



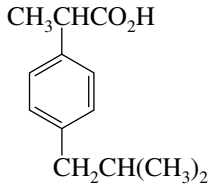
2-Hydroxybutanedioic acid
(malic acid)

(*h*) Each of the carbon atoms of propane bears a carboxyl group as a substituent in 1,2,3-propanetricarboxylic acid. In citric acid C-2 also bears a hydroxyl group.



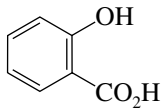
2-Hydroxy-1,2,3-propanetricarboxylic acid
(citric acid)

(*i*) There is an aryl substituent at C-2 of propanoic acid in ibuprofen. This aryl substituent is a benzene ring bearing an isobutyl group at the para position.



2-(*p*-Isobutylphenyl)-propanoic acid

(*j*) Benzenecarboxylic acid is the systematic name for benzoic acid. **Salicylic acid** is a derivative of benzoic acid bearing a hydroxyl group at the position ortho to the carboxyl.



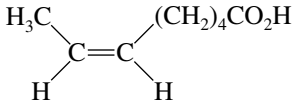
o-Hydroxybenzenecarboxylic acid (salicylic acid)

19.14 (*a*) The carboxylic acid contains a linear chain of eight carbon atoms. The parent alkane is **octane,** and so the systematic name of $CH_3(CH_2)_6CO_2H$ is **octanoic acid.**

(*b*) The compound shown is the potassium salt of octanoic acid. It is **potassium octanoate.**

(*c*) The presence of a double bond in $CH_2{=}CH(CH_2)_5CO_2H$ is indicated by the ending *-enoic acid.* Numbering of the chain begins with the carboxylic acid, and so the double bond is between C-7 and C-8. The compound is **7-octenoic acid.**

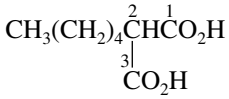
(*d*) Stereochemistry is systematically described by the *E–Z* notation. Here, the double bond between C-6 and C-7 in octenoic acid has the *Z* configuration; the higher ranked substituents are on the same side.



(*Z*)-6-Octenoic acid

(*e*) A dicarboxylic acid is named as a **dioic acid.** The carboxyl functions are the terminal carbons of an eight-carbon chain; $HO_2C(CH_2)_6CO_2H$ is **octanedioic acid.** It is not necessary to identify the carboxylic acid locations by number because they can only be at the ends of the chain when the *-dioic acid* name is used.

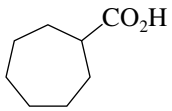
(*f*) Pick the longest continuous chain that includes both carboxyl groups and name the compound as a *-dioic acid.* This chain contains only three carbons and bears a pentyl group as a substituent at C-2. It is not necessary to specify the position of the pentyl group, because it can only be attached to C-2.



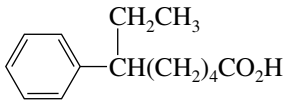
Pentylpropanedioic acid

Malonic acid is an acceptable synonym for propanedioic acid; this compound may also be named **pentylmalonic acid.**

(*g*) A carboxylic acid function is attached as a substituent on a seven-membered ring. The compound is **cycloheptanecarboxylic acid.**



(*h*) The aromatic ring is named as a substituent attached to the eight-carbon carboxylic acid. Numbering of the chain begins with the carboxyl group.



6-Phenyloctanoic acid

19.15 (*a*) Carboxylic acids are the most acidic class of organic compounds containing only the elements C, H, and O. The order of decreasing acidity is

		K_a	pK_a
Acetic acid	CH_3CO_2H	1.8×10^{-5}	4.7
Ethanol	CH_3CH_2OH	10^{-16}	16
Ethane	CH_3CH_3	$\approx 10^{-46}$	≈46

(*b*) Here again, the carboxylic acid is the strongest acid and the hydrocarbon the weakest:

		K_a	pK_a
Benzoic acid	$C_6H_5CO_2H$	6.7×10^{-5}	4.2
Benzyl alcohol	$C_6H_5CH_2OH$	10^{-16}–10^{-18}	16–18
Benzene	C_6H_6	$\approx 10^{-43}$	≈43

(*c*) Propanedioic acid is a stronger acid than propanoic acid because the electron-withdrawing effect of one carboxyl group enhances the ionization of the other. Propanedial is a 1,3-dicarbonyl compound that yields a stabilized enolate; it is more acidic than 1,3-propanediol.

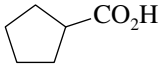
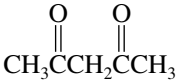
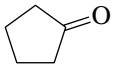
		K_a	pK_a
Propanedioic acid	$HO_2CCH_2CO_2H$	1.4×10^{-3}	2.9
Propanoic acid	$CH_3CH_2CO_2H$	1.3×10^{-5}	4.9
Propanedial	$O{=}CHCH_2CH{=}O$	$\approx 10^{-9}$	≈9
1,3-Propanediol	$HOCH_2CH_2CH_2OH$	$\approx 10^{-16}$	≈16

(*d*) Trifluoromethanesulfonic acid is by far the strongest acid in the group. It is structurally related to sulfuric acid, but its three fluorine substituents make it much stronger. Fluorine substituents

increase the acidity of carboxylic acids and alcohols relative to their nonfluorinated analogs, but not enough to make fluorinated alcohols as acidic as carboxylic acids.

		K_a	pK_a
Trifluoromethanesulfonic acid	CF_3SO_2OH	10^6	−6
Trifluoroacetic acid	CF_3CO_2H	5.9×10^{-1}	0.2
Acetic acid	CH_3CO_2H	1.8×10^{-5}	4.7
2,2,2-Trifluoroethanol	CF_3CH_2OH	4.2×10^{-13}	12.4
Ethanol	CH_3CH_2OH	$\approx 10^{-16}$	≈16

(*e*) The order of decreasing acidity is carboxylic acid > β-diketone > ketone > hydrocarbon.

		K_a	pK_a
Cyclopentanecarboxylic acid		1×10^{-5}	5.0
2,4-Pentanedione		10^{-9}	9
Cyclopentanone		10^{-20}	20
Cyclopentene		10^{-45}	45

19.16 (*a*) A trifluoromethyl group is strongly electron-withdrawing and acid-strengthening. Its ability to attract electrons from the carboxylate ion decreases as its distance down the chain increases. 3,3,3-Trifluoropropanoic acid is a stronger acid than 4,4,4-trifluorobutanoic acid.

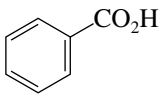
$CF_3CH_2CO_2H$	$CF_3CH_2CH_2CO_2H$
3,3,3-Trifluoropropanoic acid	4,4,4-Trifluorobutanoic acid
K_a 9.6×10^{-4}	K_a 6.9×10^{-5}
(pK_a 3.0)	(pK_a 4.2)

(*b*) The carbon that bears the carboxyl group in 2-butynoic acid is *sp*-hybridized and is, therefore, more electron-withdrawing than the sp^3-hybridized α carbon of butanoic acid. The anion of 2-butynoic acid is therefore stabilized better than the anion of butanoic acid, and 2-butynoic acid is a stronger acid.

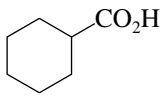
$CH_3C{\equiv}CCO_2H$	$CH_3CH_2CH_2CO_2H$
2-Butynoic acid	Butanoic acid
K_a 2.5×10^{-3}	K_a 1.5×10^{-5}
(pK_a 2.6)	(pK_a 4.8)

(*c*) Cyclohexanecarboxylic acid is a typical aliphatic carboxylic acid and is expected to be similar to acetic acid in acidity. The greater electronegativity of the sp^2-hybridized carbon

attached to the carboxyl group in benzoic acid stabilizes benzoate anion better than the corresponding sp^3-hybridized carbon stabilizes cyclohexanecarboxylate. Benzoic acid is a stronger acid.

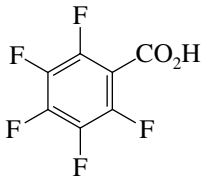


Benzoic acid
K_a 6.7×10^{-5}
(pK_a 4.2)

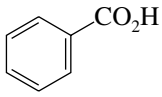


Cyclohexanecarboxylic acid
K_a 1.2×10^{-5}
(pK_a 4.9)

(*d*) Its five fluorine substituents make the pentafluorophenyl group more electron-withdrawing than an unsubstituted phenyl group. Thus, pentafluorobenzoic acid is a stronger acid than benzoic acid.

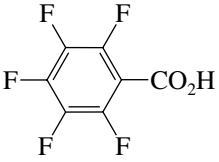


Pentafluorobenzoic acid
K_a 4.1×10^{-4}
(pK_a 3.4)

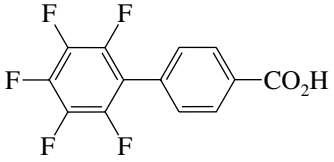


Benzoic acid
K_a 6.7×10^{-5}
(pK_a 4.2)

(*e*) The pentafluorophenyl substituent is electron-withdrawing and increases the acidity of a carboxyl group to which it is attached. Its electron-withdrawing effect decreases with distance. Pentafluorobenzoic acid is a stronger acid than *p*-(pentafluorophenyl)benzoic acid.

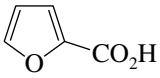


Pentafluorobenzoic acid
K_a 4.1×10^{-4}
(pK_a 3.4)

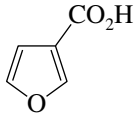


p-(Pentafluorophenyl)benzoic acid
(K_a not measured in water; comparable with benzoic acid in acidity)

(*f*) The oxygen of the ring exercises an acidifying effect on the carboxyl group. This effect is largest when the oxygen is attached directly to the carbon that bears the carboxyl group. Furan-2-carboxylic acid is thus a stronger acid than furan-3-carboxylic acid.



Furan-2-carboxylic acid
K_a 6.9×10^{-4}
(pK_a 3.2)



Furan-3-carboxylic acid
K_a 1.1×10^{-4}
(pK_a 3.9)

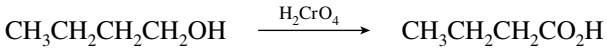
(*g*) Furan-2-carboxylic acid has an oxygen attached to the carbon that bears the carboxyl group, whereas pyrrole-2-carboxylic acid has a nitrogen in that position. Oxygen is more

electronegative than nitrogen and so stabilizes the carboxylate anion better. Furan-2-carboxylic acid is a stronger acid than pyrrole-2-carboxylic acid.

Furan-2-carboxylic acid
K_a 6.9×10^{-4}
(pK_a 3.2)

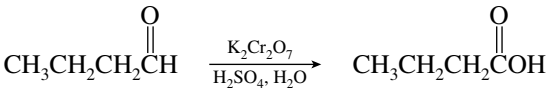
Pyrrole-3-carboxylic acid
K_a 3.5×10^{-5}
(pK_a 4.4)

19.17 (*a*) The conversion of 1-butanol to butanoic acid is simply the oxidation of a primary alcohol to a carboxylic acid. Chromic acid is a suitable oxidizing agent.



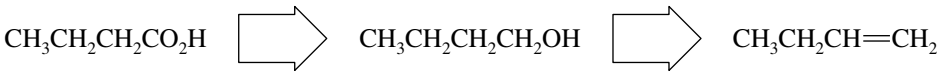
1-Butanol — Butanoic acid

(*b*) Aldehydes may be oxidized to carboxylic acids by any of the oxidizing agents that convert primary alcohols to carboxylic acids.

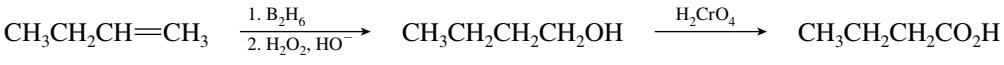


Butanal — Butanoic acid

(*c*) The starting material has the same number of carbon atoms as does butanoic acid, and so all that is required is a series of functional group transformations. Carboxylic acids may be obtained by oxidation of the corresponding primary alcohol. The alcohol is available from the designated starting material, 1-butene.

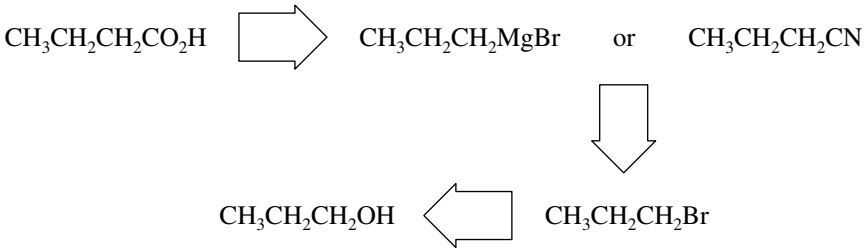


Hydroboration–oxidation of 1-butene yields 1-butanol, which can then be oxidized to butanoic acid as in part (*a*).

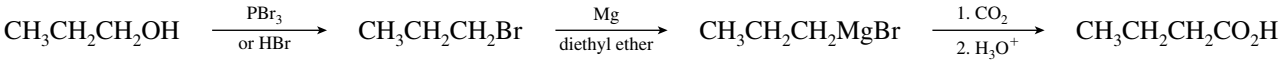


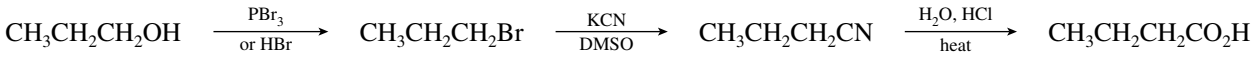
1-Butene — 1-Butanol — Butanoic acid

(*d*) Converting 1-propanol to butanoic acid requires the carbon chain to be extended by one atom. Both methods for achieving this conversion, carboxylation of a Grignard reagent and formation and hydrolysis of a nitrile, begin with alkyl halides. Alkyl halides in turn are prepared from alcohols.

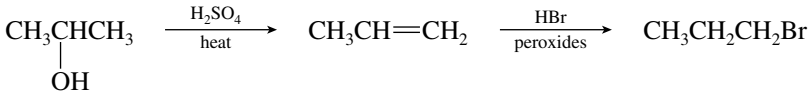


Either of the two following procedures is satisfactory:



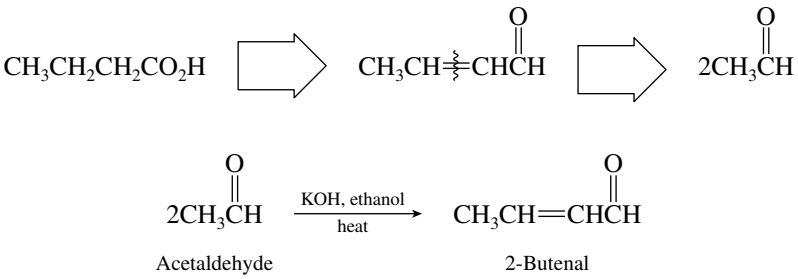


(*e*) Dehydration of 2-propanol to propene followed by free-radical addition of hydrogen bromide affords 1-bromopropane.

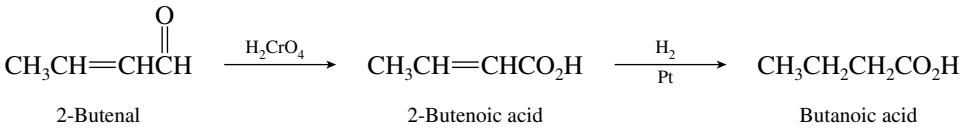


Once 1-bromopropane has been prepared it is converted to butanoic acid as in part (*d*).

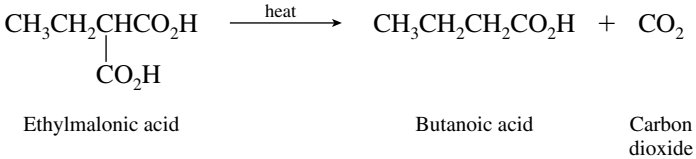
(*f*) The carbon skeleton of butanoic acid may be assembled by an aldol condensation of acetaldehyde.



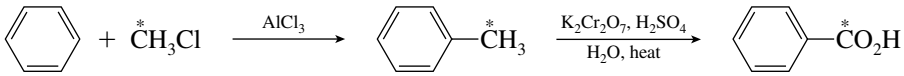
Oxidation of the aldehyde followed by hydrogenation of the double bond yields butanoic acid.



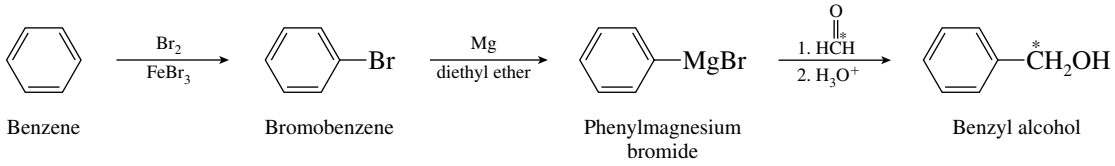
(*g*) Ethylmalonic acid belongs to the class of substituted malonic acids that undergo ready thermal decarboxylation. Decarboxylation yields butanoic acid.



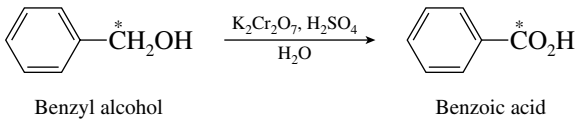
19.18 (*a*) The Friedel–Crafts alkylation of benzene by methyl chloride can be used to prepare ^{14}C-labeled toluene (C* = ^{14}C). Once prepared, toluene could be oxidized to benzoic acid.



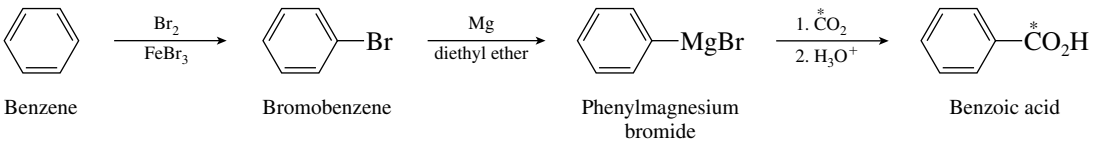
(*b*) Formaldehyde can serve as a one-carbon source if it is attacked by the Grignard reagent derived from bromobenzene.



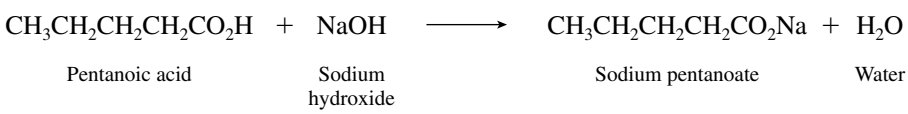
This sequence yields ^{14}C-labeled benzyl alcohol, which can be oxidized to ^{14}C-labeled benzoic acid.



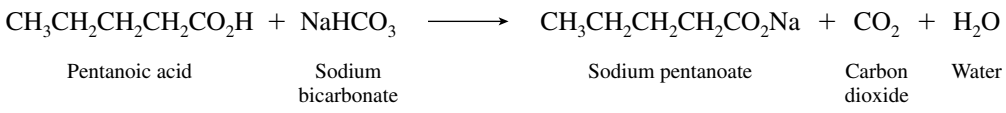
(*c*) A direct route to ^{14}C-labeled benzoic acid utilizes a Grignard synthesis employing ^{14}C-labeled carbon dioxide.



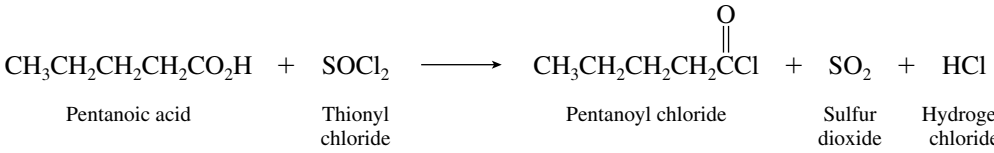
19.19 (*a*) An acid–base reaction takes place when pentanoic acid is combined with sodium hydroxide.



(*b*) Carboxylic acids react with sodium bicarbonate to give carbonic acid, which dissociates to carbon dioxide and water, so that the actual reaction that takes place is

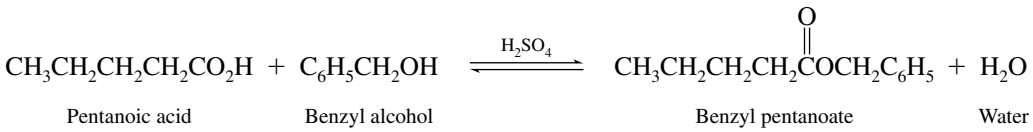


(*c*) Thionyl chloride is a reagent that converts carboxylic acids to the corresponding acyl chlorides.

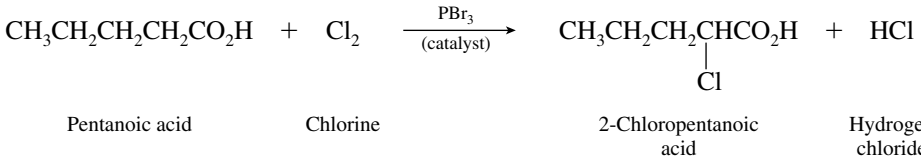


(*d*) Phosphorus tribromide is used to convert carboxylic acids to their acyl bromides.

(*e*) Carboxylic acids react with alcohols in the presence of acid catalysts to give esters.

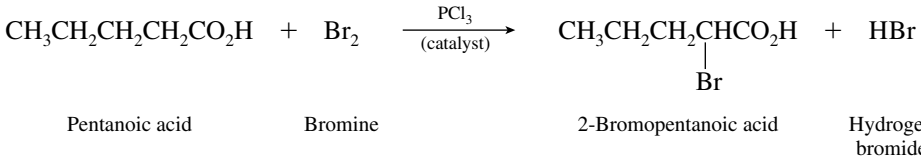


(*f*) Chlorine is introduced at the α-carbon atom of a carboxylic acid. The reaction is catalyzed by a small amount of phosphorus or a phosphorus trihalide and is called the Hell–Volhard–Zelinsky reaction.

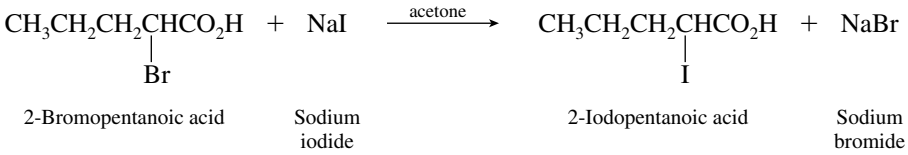


The α-halo substituent is derived from the halogen used, not from the phosphorus trihalide.

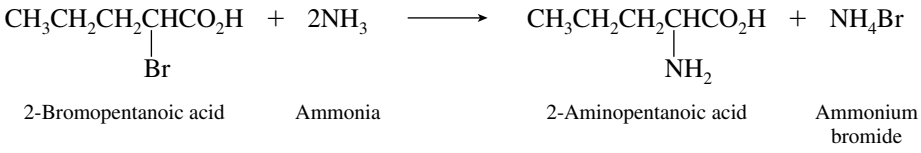
(*g*) In the case, bromine is introduced at the α carbon.



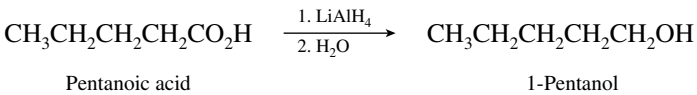
(*h*) α-Halo carboxylic acids are reactive substrates in nucleophilic substitution. Iodide acts as a nucleophile to displace bromide from 2-bromopentanoic acid.



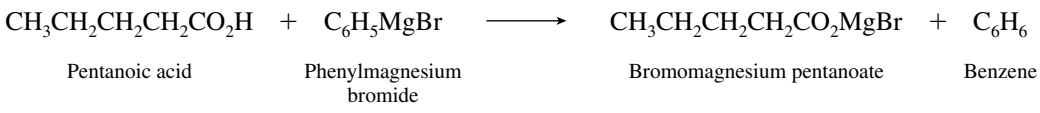
(*i*) Aqueous ammonia converts α-halo acids to α-amino acids.



(*j*) Lithium aluminum hydride is a powerful reducing agent and reduces carboxylic acids to primary alcohols.

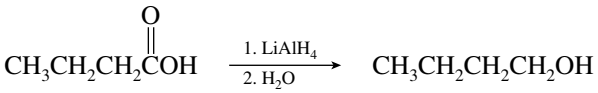


(*k*) Phenylmagnesium bromide acts as a base to abstract the carboxylic acid proton.



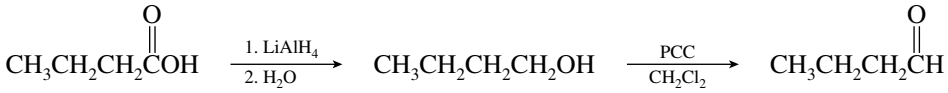
Grignard reagents are not compatible with carboxylic acids; proton transfer converts the Grignard reagent to the corresponding hydrocarbon.

19.20 (*a*) Conversion of butanoic acid to 1-butanol is a reduction and requires lithium aluminum hydride as the reducing agent.



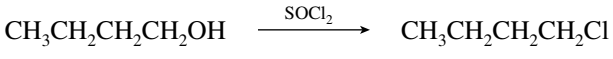
Butanoic acid 1-Butanol

(*b*) Carboxylic acids cannot be reduced directly to aldehydes. The following two-step procedure may be used:



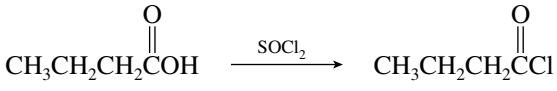
Butanoic acid 1-Butanol Butanal

(*c*) Remember that alkyl halides are usually prepared from alcohols. 1-Butanol is therefore needed in order to prepare 1-chlorobutane.



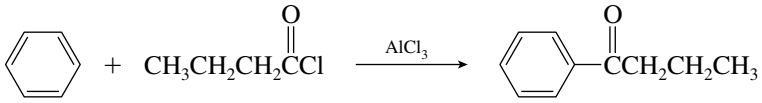
1-Butanol [from part (*a*)] 1-Chlorobutane

(*d*) Carboxylic acids are converted to their corresponding acyl chlorides with thionyl chloride.



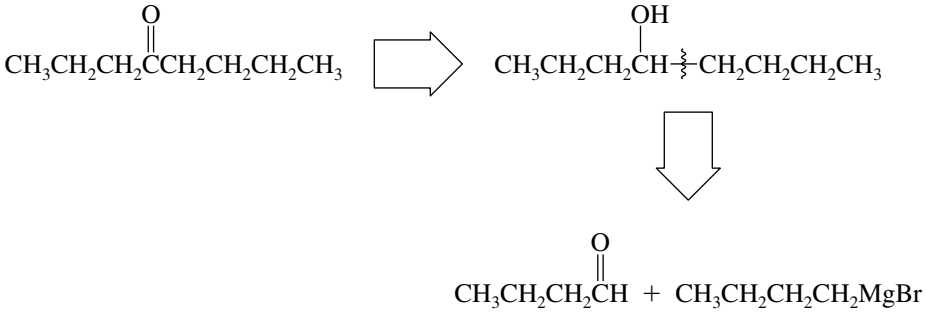
Butanoic acid Butanoyl chloride

(*e*) Aromatic ketones are frequently prepared by Friedel–Crafts acylation of the appropriate acyl chloride and benzene. Butanoyl chloride, prepared in part (*d*), can be used to acylate benzene in a Friedel–Crafts reaction.



Benzene Butanoyl chloride Phenyl propyl ketone

(*f*) The preparation of 4-octanone using compounds derived from butanoic acid may be seen by using disconnections in a retrosynthetic analysis.



The reaction scheme which may be used is

$$CH_3CH_2CH_2CH_2Cl \xrightarrow{Mg} CH_3CH_2CH_2CH_2MgCl$$

1-Chlorobutane [from part (*c*)] — Butylmagnesium chloride

$$CH_3CH_2CH_2CH_2MgCl + CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}H \xrightarrow[2.\ H_3O^+]{1.\ \text{diethyl ether}} CH_3CH_2CH_2\underset{\underset{OH}{|}}{C}HCH_2CH_2CH_2CH_3$$

Butylmagnesium chloride — Butanal [from part (*b*)] — 4-Octanol

$$\text{4-Octanol} \xrightarrow{H_2CrO_4} CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2CH_3$$

4-Octanone

(*g*) Carboxylic acids are halogenated at their α-carbon atom by the Hell–Volhard–Zelinsky reaction.

$$CH_3CH_2CH_2CO_2H \xrightarrow[Br_2]{P} CH_3CH_2\underset{\underset{Br}{|}}{C}HCO_2H$$

Butanoic acid — 2-Bromobutanoic acid

A catalytic amount of PCl_3 may be used in place of phosphorus in the reaction.

(*h*) Dehydrohalogenation of 2-bromobutanoic acid gives 2-butenoic acid.

$$CH_3CH_2\underset{\underset{Br}{|}}{C}HCO_2H \xrightarrow[2.\ H^+]{1.\ KOC(CH_3)_3,\ DMSO} CH_3CH{=}CHCO_2H$$

2-Bromobutanoic acid — 2-Butenoic acid

19.21 (*a*) The compound to be prepared is **glycine,** an α-amino acid. The amino functional group can be introduced by a nucleophilic substitution reaction on an α-halo acid, which is available by way of the Hell–Volhard–Zelinsky reaction.

$$CH_3CO_2H \xrightarrow[P]{Br_2} BrCH_2CO_2H \xrightarrow{NH_3,\ H_2O} H_2NCH_2CO_2H$$

Acetic acid — Bromoacetic acid — Aminoacetic acid (glycine)

(*b*) Phenoxyacetic acid is used as a fungicide. It can be prepared by a nucleophilic substitution using sodium phenoxide and bromoacetic acid.

$$BrCH_2CO_2H \xrightarrow[2.\ H^+]{1.\ C_6H_5ONa} C_6H_5OCH_2CO_2H + NaCl$$

Bromoacetic acid — Phenoxyacetic acid

(*c*) Cyanide ion is a good nucleophile and will displace bromide from bromoacetic acid.

$$\underset{\text{Bromoacetic acid [from part (a)]}}{BrCH_2CO_2H} \xrightarrow[Na_2CO_3,\ H_2O]{NaCN} \underset{\text{Sodium cyanoacetate}}{NCCH_2CO_2Na} \xrightarrow{H^+} \underset{\text{Cyanoacetic acid}}{NCCH_2CO_2H}$$

(*d*) Cyanoacetic acid, prepared as in part (*c*), serves as a convenient precursor to malonic acid. Hydrolysis of the nitrile substituent converts it to a carboxyl group.

$$\underset{\text{Cyanoacetic acid}}{NCCH_2CO_2H} \xrightarrow[\text{heat}]{H_2O,\ H^+} \underset{\text{Malonic acid}}{HO_2CCH_2CO_2H}$$

(*e*) Iodoacetic acid is not prepared directly from acetic acid but is derived by nucleophilic substitution of iodide in bromoacetic acid.

$$\underset{\text{Bromoacetic acid}}{BrCH_2CO_2H} \xrightarrow[\text{acetone}]{NaI} \underset{\text{Iodoacetic acid}}{ICH_2CO_2H}$$

(*f*) Two transformations need to be accomplished, α bromination and esterification. The correct sequence is bromination followed by esterification.

$$\underset{\text{Acetic acid}}{CH_3CO_2H} \xrightarrow[P]{Br_2} \underset{\text{Bromoacetic acid}}{BrCH_2CO_2H} \xrightarrow[H^+]{CH_3CH_2OH} \underset{\text{Ethyl bromoacetate}}{BrCH_2CO_2CH_2CH_3}$$

Reversing the order of steps is not appropriate. It must be the carboxylic acid that is subjected to halogenation because the Hell–Volhard–Zelinsky reaction is a reaction of carboxylic acids, not esters.

(*g*) The compound shown is an ylide. It can be prepared from ethyl bromoacetate as shown

$$\underset{\text{Ethyl bromoacetate}}{BrCH_2CO_2CH_2CH_3} + \underset{\text{Triphenylphosphine}}{(C_6H_5)_3P} \longrightarrow (C_6H_5)_3\overset{+}{P}CH_2CO_2CH_2CH_3\ Br^-$$

$$\downarrow NaOCH_2CH_3$$

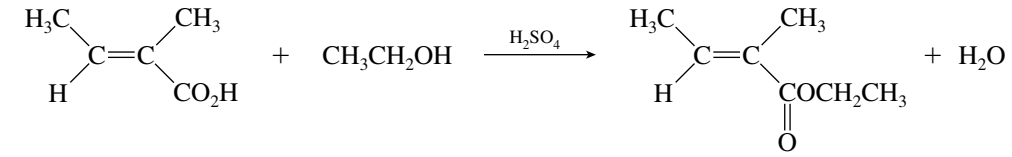
$$\underset{\text{Ylide}}{(C_6H_5)_3\overset{+}{P}-\bar{\ddot{C}}HCO_2CH_2CH_3}$$

The first step is a nucleophilic substitution of bromide by triphenylphosphine. Treatment of the derived triphenylphosphonium salt with base removes the relatively acidic α proton, forming the ylide. (For a review of ylide formation, refer to Section 17.12.)

(*h*) Reaction of the ylide formed in part (*g*) with benzaldehyde gives the desired alkene by a Wittig reaction.

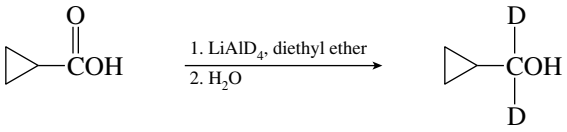
$$\underset{\text{Ylide from part (g)}}{(C_6H_5)_3\overset{+}{P}-\bar{\ddot{C}}HCO_2CH_2CH_3} + \underset{\text{Benzaldehyde}}{C_6H_5CH{=}O} \longrightarrow \underset{\text{Ethyl cinnamate}}{C_6H_5CH{=}CHCO_2CH_2CH_3} + \underset{\text{Triphenylphosphine oxide}}{(C_6H_5)_3\overset{+}{P}-\bar{O}}$$

19.22 (*a*) Carboxylic acids are converted to ethyl esters when they are allowed to stand in ethanol in the presence of an acid catalyst.



(*E*)-2-Methyl-2-butenoic acid — Ethanol — Ethyl (*E*)-2-methyl-2-butenoate (74–80%) — Water

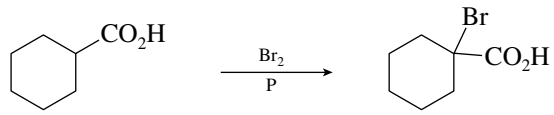
(*b*) Lithium aluminum hydride, $LiAlH_4$, reduces carboxylic acids to primary alcohols. When $LiAlD_4$ is used, deuterium is transferred to the carbonyl carbon.



Cyclopropanecarboxylic acid — 1-Cyclopropyl-1,1-dideuteriomethanol (75%)

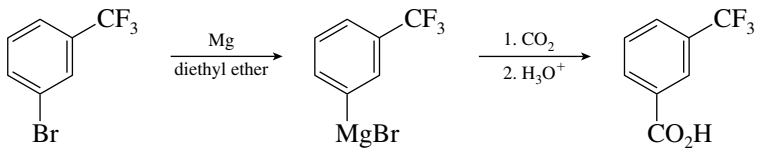
Notice that deuterium is bonded only to carbon. The hydroxyl proton is derived from water, not from the reducing agent.

(*c*) In the presence of a catalytic amount of phosphorus, bromine reacts with carboxylic acids to yield the corresponding α-bromo derivative.



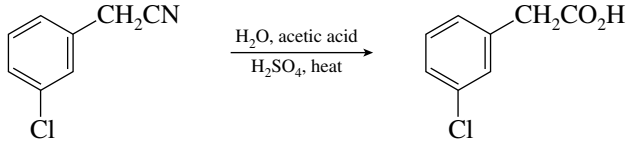
Cyclohexanecarboxylic acid — 1-Bromocyclohexanecarboxylic acid (96%)

(*d*) Alkyl fluorides are not readily converted to Grignard reagents, and so it is the bromine substituent that is attacked by magnesium.



m-Bromo(trifluoromethyl)-benzene — *m*-(Trifluoromethyl)-benzoic acid

(*e*) Cyano substituents are hydrolyzed to carboxyl groups in the presence of acid catalysts.



m-Chlorobenzyl cyanide — *m*-Chlorophenylacetic acid (61%)

(*f*) The carboxylic acid function plays no part in this reaction; free-radical addition of hydrogen bromide to the carbon–carbon double bond occurs.

$$\underset{\text{10-Undecenoic acid}}{H_2C{=}CH(CH_2)_8CO_2H} \xrightarrow[\text{benzoyl peroxide}]{HBr} \underset{\substack{\text{11-Bromoundecanoic acid}\\(66\text{–}70\%)}}{BrCH_2CH_2(CH_2)_8CO_2H}$$

Recall that hydrogen bromide adds to alkenes in the presence of peroxides with a regioselectivity opposite to that of Markovnikov's rule.

19.23 (*a*) The desired product and the starting material have the same carbon skeleton, and so all that is required is a series of functional group transformations. Recall that, as seen in Problem 19.17, a carboxylic acid may be prepared by oxidation of the corresponding primary alcohol. The needed alcohol is available from the appropriate alkene.

$$\underset{\substack{\textit{tert}\text{-Butyl}\\\text{alcohol}}}{(CH_3)_3COH} \xrightarrow[\text{heat}]{H^+} \underset{\text{2-Methylpropene}}{(CH_3)_2C{=}CH_2} \xrightarrow[2.\ H_2O_2,\ HO^-]{1.\ B_2H_6} \underset{\text{2-Methyl-1-propanol}}{(CH_3)_2CHCH_2OH} \xrightarrow[H_2SO_4,\ H_2O]{K_2Cr_2O_7} \underset{\text{2-Methylpropanoic acid}}{(CH_3)_2CHCO_2H}$$

(*b*) The target molecule contains one more carbon than the starting material, and so a carbon–carbon bond-forming step is indicated. Two approaches are reasonable; one proceeds by way of nitrile formation and hydrolysis, the other by carboxylation of a Grignard reagent. In either case the key intermediate is 1-bromo-2-methylpropane.

$$\underset{\text{3-Methylbutanoic acid}}{(CH_3)_2CHCH_2CO_2H} \Longrightarrow \underset{\substack{\text{1-Bromo-2-}\\\text{methylpropane}}}{(CH_3)_2CHCH_2Br}$$

The desired alkyl bromide may be prepared by free-radical addition of hydrogen bromide to 2-methylpropene.

$$\underset{\substack{\textit{tert}\text{-Butyl}\\\text{alcohol}}}{(CH_3)_3COH} \xrightarrow[\text{heat}]{H^+} \underset{\text{2-Methylpropene}}{(CH_3)_2C{=}CH_2} \xrightarrow[\text{peroxides}]{HBr} \underset{\substack{\text{1-Bromo-2-}\\\text{methylpropane}}}{(CH_3)_2CHCH_2Br}$$

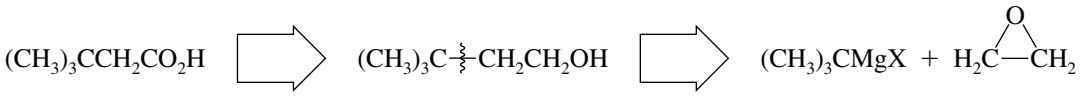
Another route to the alkyl bromide utilizes the alcohol prepared in part (*a*).

$$\underset{\text{2-Methyl-1-propanol}}{(CH_3)_2CHCH_2OH} \xrightarrow[\text{or HBr}]{PBr_3} \underset{\substack{\text{1-Bromo-2-}\\\text{methylpropane}}}{(CH_3)_2CHCH_2Br}$$

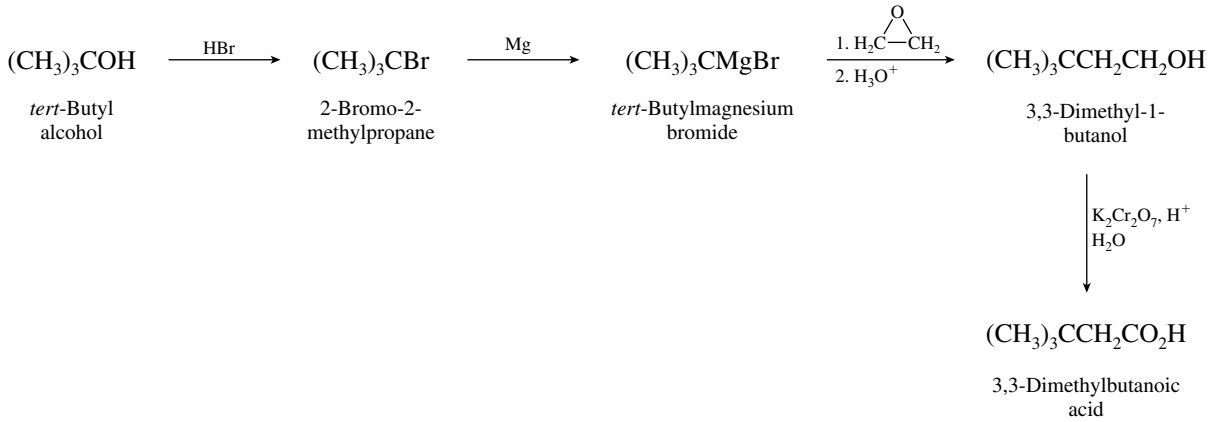
Conversion of the alkyl bromide to the desired acid is then carried out as follows:

$$\underset{\substack{\text{1-Bromo-2-methylpropane}}}{(CH_3)_2CHCH_2Br} \begin{cases} \xrightarrow{KCN} (CH_3)_2CHCH_2CN \xrightarrow[\text{heat}]{H_2O,\ H^+} \underset{\text{3-Methylbutanoic acid}}{(CH_3)_2CHCH_2CO_2H} \\ \xrightarrow[\text{diethyl ether}]{Mg} (CH_3)_2CHCH_2MgBr \xrightarrow[2.\ H_3O^+]{1.\ CO_2} \underset{\text{3-Methylbutanoic acid}}{(CH_3)_2CHCH_2CO_2H} \end{cases}$$

(*c*) Examining the target molecule reveals that it contains two more carbon atoms than the indicated starting material, suggesting use of ethylene oxide in a two-carbon chain-extension process.

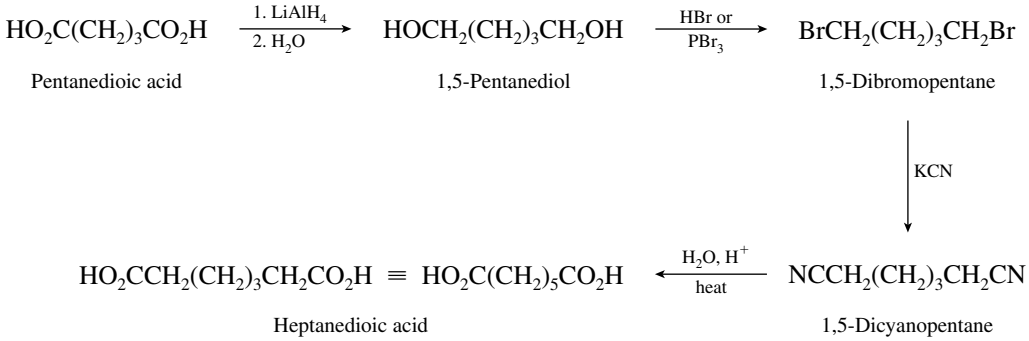


This suggests the following sequence of steps:

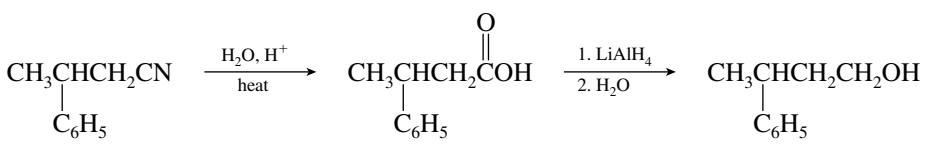


(*d*) This synthesis requires extending a carbon chain by two carbon atoms. One way to form dicarboxylic acids is by hydrolysis of dinitriles.

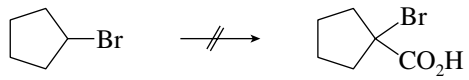
This suggests the following sequence of steps:



(*e*) The desired alcohol cannot be prepared directly from the nitrile. It is available, however, by lithium aluminum hydride reduction of the carboxylic acid obtained by hydrolysis of the nitrile.

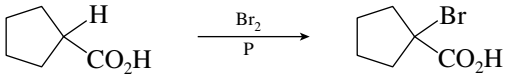


(*f*) In spite of the structural similarity between the starting material and the desired product, a one-step transformation cannot be achieved.



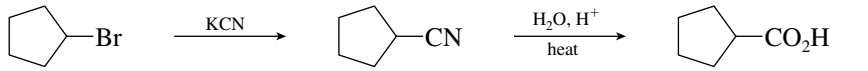
Cyclopentyl bromide — 1-Bromocyclopentane-carboxylic acid

Instead, recall that α-bromo acids are prepared from carboxylic acids by the Hell–Volhard–Zelinsky reaction:

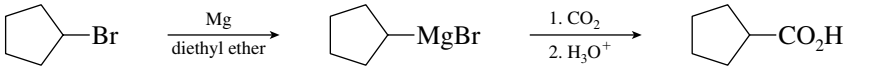


Cyclopentane-carboxylic acid — 1-Bromocyclopentane-carboxylic acid

The problem now simplifies to one of preparing cyclopentanecarboxylic acid from cyclopentyl bromide. Two routes are possible:



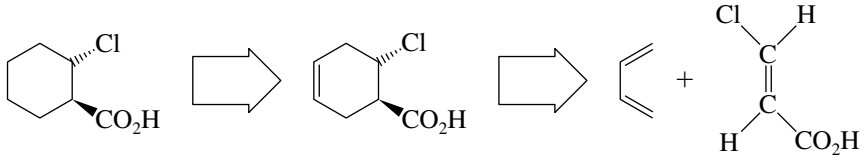
Cyclopentyl bromide — Cyclopentyl cyanide — Cyclopentanecarboxylic acid

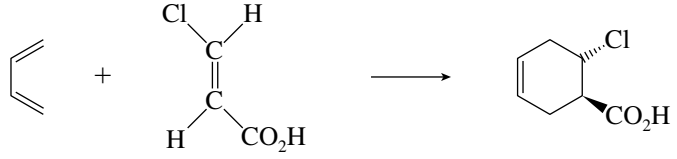


Cyclopentyl bromide — Cyclopentylmagnesium bromide — Cyclopentanecarboxylic acid

The Grignard route is better; it is a "one-pot" transformation. Converting the secondary bromide to a nitrile will be accompanied by elimination, and the procedure requires two separate operations.

(*g*) In this case the halogen substituent is present at the β carbon rather than the α carbon atom of the carboxylic acid. The starting material, a β-chloro unsaturated acid, can lead to the desired carbon skeleton by a Diels–Alder reaction.

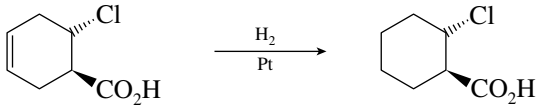




1,3-Butadiene — (*E*)-3-Chloropropenoic acid — *trans*-2-Chloro-4-cyclohexenecarboxylic acid

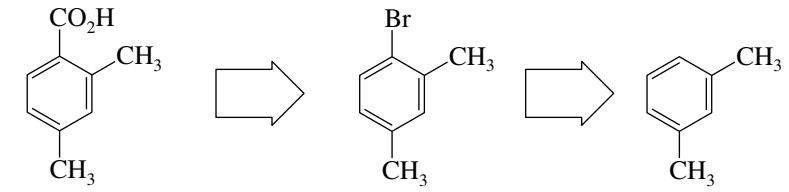
The required trans stereochemistry is a consequence of the stereospecificity of the Diels–Alder reaction.

Hydrogenation of the double bond of the Diels–Alder adduct gives the required product.



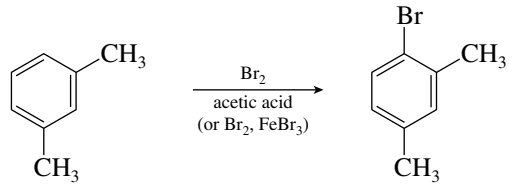
trans-2-Chloro-4-cyclohexenecarboxylic acid — *trans*-2-Chlorocyclohexanecarboxylic acid

(*h*) The target molecule is related to the starting material by the retrosynthesis



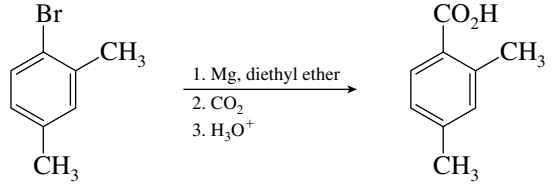
2,4-Dimethylbenzoic acid — *m*-Xylene

The necessary bromine substituent can be introduced by electrophilic substitution in the activated aromatic ring of *m*-xylene.



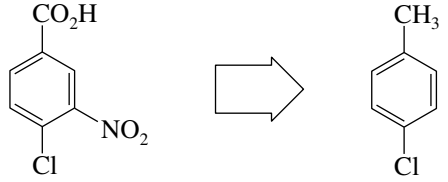
m-Xylene — 1-Bromo-2,4-dimethylbenzene

The aryl bromide cannot be converted to a carboxylic acid by way of the corresponding nitrile, because aryl bromides are not reactive toward nucleophilic substitution. The Grignard route is necessary.



1-Bromo-2,4-dimethylbenzene — 2,4-Dimethylbenzoic acid

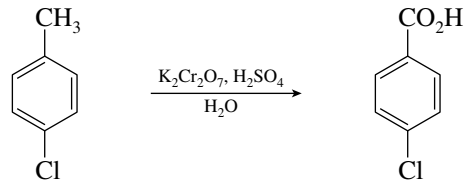
(*i*) The relationship of the target molecule to the starting material



4-Chloro-3-nitrobenzoic acid — *p*-Chlorotoluene

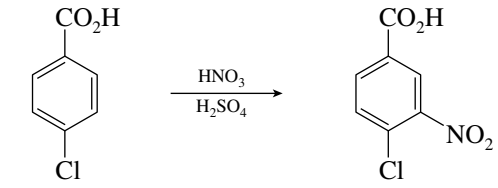
requires that there be two synthetic operations: oxidation of the methyl group and nitration of the ring. The orientation of the nitro group requires that nitration must follow oxidation of the

methyl group of the starting material



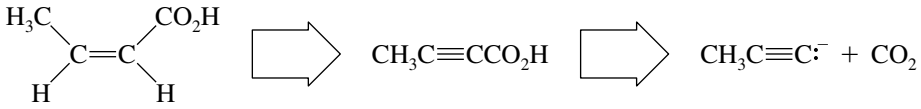
p-Chlorotoluene — *p*-Chlorobenzoic acid

Nitration of *p*-chlorobenzoic acid gives the desired product, because the directing effects of the chlorine (ortho, para) and the carboxyl (meta) groups reinforce each other.

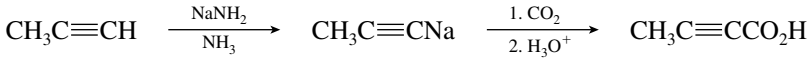


p-Chlorobenzoic acid — 4-Chloro-3-nitrobenzoic acid

(*j*) The desired synthetic route becomes apparent when it is recognized that the *Z* alkene stereoisomer may be obtained from an alkyne, which, in turn, is available by carboxylation of the anion derived from the starting material.

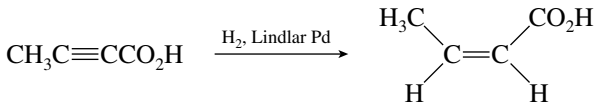


The desired reaction sequence is



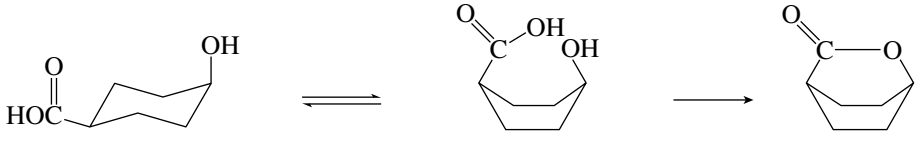
Propyne — Propynylsodium — 2-Butynoic acid

Hydrogenation of the carbon–carbon triple bond of 2-butynoic acid over the Lindlar catalyst converts this compound to the *Z* isomer of 2-butenoic acid.



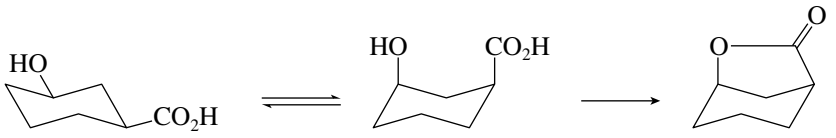
2-Butynoic acid — (*Z*)-2-Butenoic acid

19.24 (*a*) Only the cis stereoisomer of 4-hydroxycyclohexanecarboxylic acid is capable of forming a lactone, as can be seen in the following drawings or with a molecular model. The most stable conformation of the starting hydroxy acid is a chair conformation; however, in the lactone, the cyclohexane ring adopts a boat conformation.



cis-4-Hydroxycyclohexane carboxylic acid (chair conformation) — *cis*-4-Hydroxycyclohexane carboxylic acid (boat conformation) — Lactone

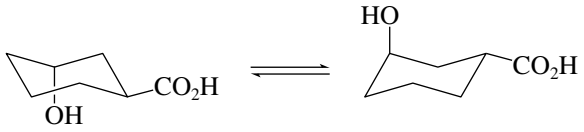
(*b*) As in part (*a*), lactone formation is possible only when the hydroxyl and carboxyl groups are cis.



cis-3-Hydroxycyclohexanecarboxylic acid — Lactone

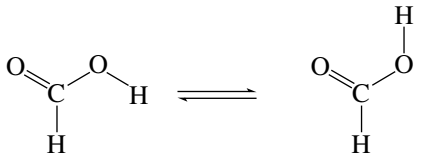
Although the most stable conformation of *cis*-3-hydroxycyclohexanecarboxylic acid has both substituents equatorial and is unable to close to a lactone, the diaxial orientation is accessible and is capable of lactone formation.

Neither conformation of *trans*-3-hydroxycyclohexanecarboxylic acid has the substituents close enough to each other to form an unstrained lactone.



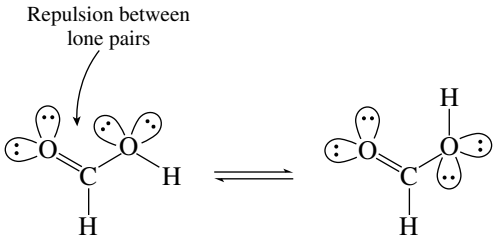
trans-3-Hydroxycyclohexanecarboxylic acid: lactone formation impossible

19.25 (*a*) The most stable conformation of formic acid is the one that has both hydrogens anti.



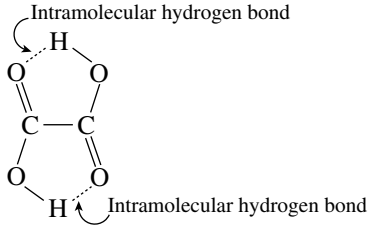
Syn: less stable conformation of formic acid — Anti: more stable conformation of formic acid

A plausible explanation is that the syn conformation is destabilized by lone-pair repulsions.

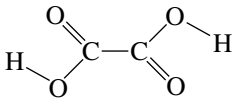


Syn — Anti

(*b*) A dipole moment of zero can mean that the molecule has a center of symmetry. One structure that satisfies this requirement is characterized by intramolecular hydrogen bonding between the two carboxyl groups and an anti relationship between the two carbonyls.

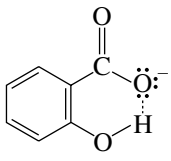


Another possibility is the following structure; it also has a center of symmetry and an anti relationship between the two carbonyls.

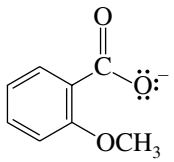


Other centrosymmetric structures can be drawn; these have the two hydrogen atoms out of the plane of the carboxyl groups, however, and are less likely to occur, in view of the known planarity of carboxyl groups. Structures in which the carbonyl groups are syn to each other do not have a center of symmetry.

(*c*) The anion formed on dissociation of *o*-hydroxybenzoic acid can be stabilized by an intramolecular hydrogen bond.

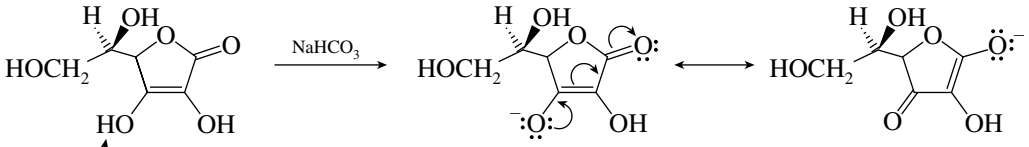


o-Hydroxybenzoate ion (stabilized by hydrogen bonding)

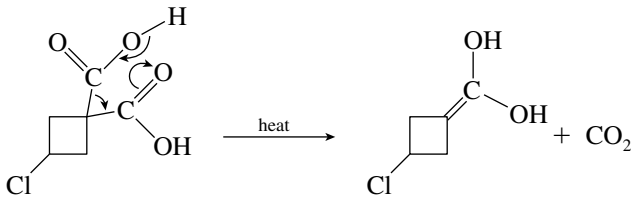


o-Methoxybenzoate ion (hydrogen bonding is not possible)

(*d*) Ascorbic acid is relatively acidic because ionization of its enolic hydroxyl at C-3 gives an anion that is stabilized by resonance in much the same way as a carboxylate ion; the negative charge is shared by two oxygens.

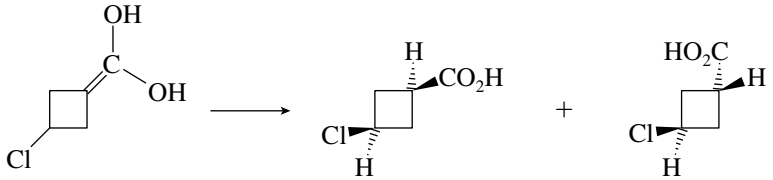


19.26 Dicarboxylic acids in which both carboxyl groups are attached to the same carbon undergo ready thermal decarboxylation to produce the enol form of an acid.



Compound A

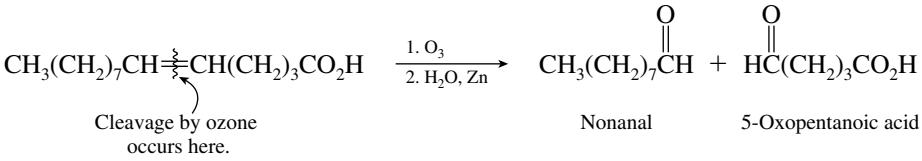
This enol yields a mixture of *cis*- and *trans*-3-chlorocyclobutanecarboxylic acid. The two products are stereoisomers.



cis-3-Chlorocyclobutane-carboxylic acid

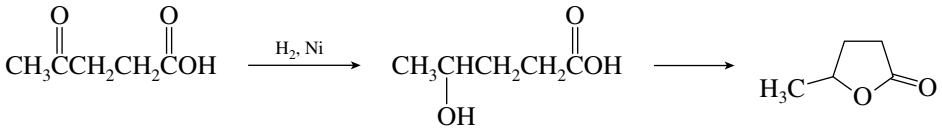
trans-3-Chlorocyclobutane-carboxylic acid

19.27 Examination of the molecular formula $C_{14}H_{26}O_2$ reveals that the compound has an index of hydrogen deficiency of 2. Because we are told that the compound is a carboxylic acid, one of these elements of unsaturation must be a carbon–oxygen double bond. The other must be a carbon–carbon double bond because the compound undergoes cleavage on ozonolysis. Examining the products of ozonolysis serves to locate the position of the double bond.

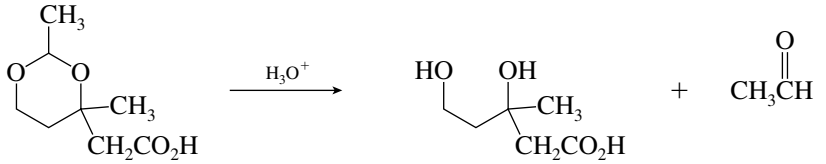


The starting acid must be 5-tetradecenoic acid. The stereochemistry of the double bond is not revealed by these experiments.

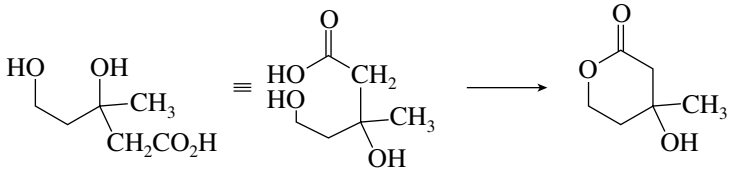
19.28 Hydrogenation of the starting material is expected to result in reduction of the ketone carbonyl while leaving the carboxyl group unaffected. Because the isolated product lacks a carboxyl group, however, that group must react in some way. The most reasonable reaction is intramolecular esterification to form a γ-lactone.



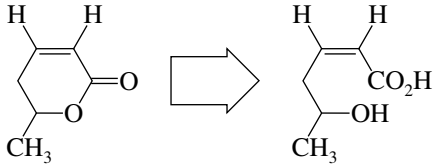
19.29 Compound A is a cyclic acetal and undergoes hydrolysis in aqueous acid to produce acetaldehyde, along with a dihydroxy carboxylic acid.



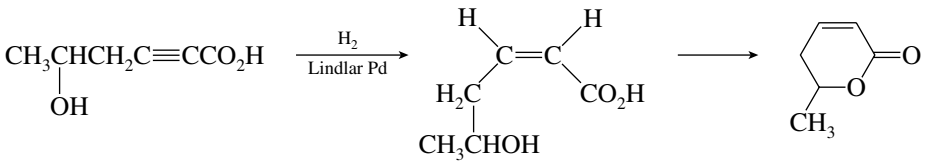
The dihydroxy acid that is formed in this step cyclizes to the δ-lactone mevalonolactone.



19.30 Compound A is a δ-lactone. To determine its precursor, disconnect the ester linkage to a hydroxy acid.

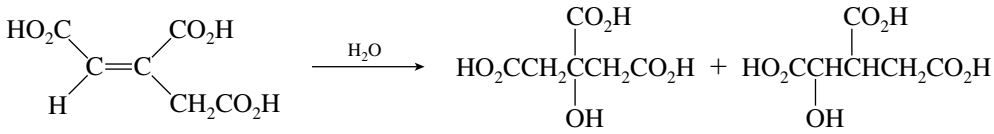


The precursor has the same carbon skeleton as the designated starting material. All that is necessary is to hydrogenate the double bond of the alkynoic acid to the cis alkene. This can be done by using the Lindlar catalyst. Cyclization of the hydroxy acid to the lactone is spontaneous.

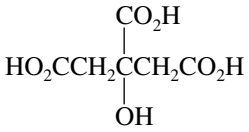


5-Hydroxy-2-hexynoic acid | (Not isolated) | Compound A

19.31 Hydration of the double bond can occur in two different directions:

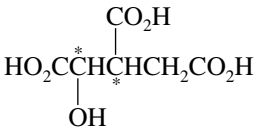


(*a*) The achiral isomer is citric acid.



Citric acid has no stereogenic centers.

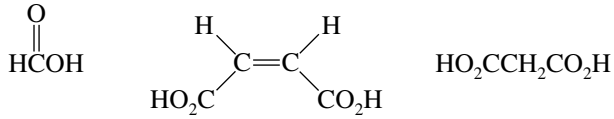
(*b*) The other isomer, isocitric acid, has two stereogenic centers (marked with an asterisk*). Isocitric acid has the constitution



Isocitric acid

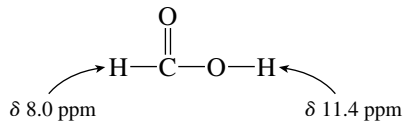
With two stereogenic centers, there are 2^2, or four, stereoisomers represented by this constitution. The one that is actually formed in this enzyme-catalyzed reaction is the 2*R*,3*S* isomer.

19.32 Carboxylic acid protons give signals in the range δ 10–12 ppm. A signal in this region suggests the presence of a carboxyl group but tells little about its environment. Thus, in assigning structures to compounds A, B, and C, the most useful data are the chemical shifts of the protons other than the carboxyl protons. Compare the three structures:



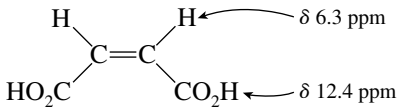
Formic acid | Maleic acid | Malonic acid

The proton that is diagnostic of structure in formic acid is bonded to a carbonyl group; it is an aldehyde proton. Typical chemical shifts of aldehyde protons are 8–10 ppm, and therefore formic acid is compound C.



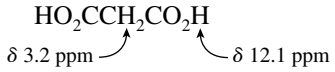
Compound C

The critical signal in maleic acid is that of the vinyl protons, which normally is found in the range δ 5–7 ppm. Maleic acid is compound B.



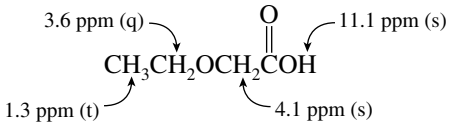
Compound B

Compound A is malonic acid. Here we have a methylene group bearing two carbonyl substituents. These methylene protons are more shielded than the aldehyde proton of formic acid or the vinyl protons of maleic acid.

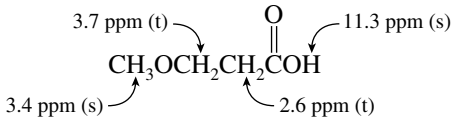


Compound A

19.33 Compounds A and B both exhibit ^{1}H NMR absorptions in the region δ 11–12 ppm characteristic of carboxylic acids. The formula $C_4H_8O_3$ suggests an index of hydrogen deficiency of 1, accounted for by the carbonyl of the carboxyl group. Compound A has the triplet–quartet splitting indicative of an ethyl group, and compound B has two triplets, suggesting —CH_2CH_2—.

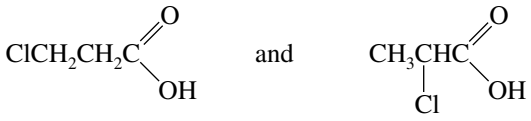


Compound A



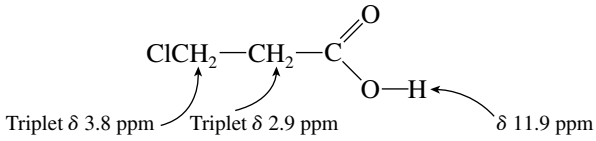
Compound B

19.34 (*a*) The formula of compound A ($C_3H_5ClO_2$) has an index of hydrogen deficiency of 1—the carboxyl group. Only two structures are possible:



3-Chloropropanoic acid and 2-Chloropropanoic acid

Compound A is determined to be 3-chloropropanoic acid on the basis of its ^{1}H NMR spectrum, which shows two triplets at δ 2.9 and δ 3.8 ppm.

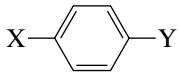


Compound A

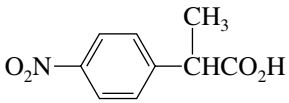
Compound A cannot be 2-chloropropanoic acid, because that compound's ^{1}H NMR spectrum would show a three-proton doublet for the methyl group and a one-proton quartet for the methine proton.

(*b*) The formula of compound B ($C_9H_9NO_4$) corresponds to an index of hydrogen deficiency of 6. The presence of an aromatic ring, as evidenced by the ^{1}H NMR absorptions at δ 7.5 and

8.2 ppm, accounts for four of the unsaturations. The appearance of the aromatic protons as a pair of doublets with a total area of 4 suggests a *para*-disubstituted ring.



That compound B is a carboxylic acid is evidenced by the singlet (area = 1) at δ 12.1 ppm. The remaining ^{1}H NMR signals—a quartet at δ 3.9 ppm (1H) and a doublet at δ 1.6 ppm (3H)—suggest the fragment CH—CH_3. All that remains of the molecular formula is —NO_2. Combining this information identifies compound B as 2-(4-nitrophenyl)propanoic acid.

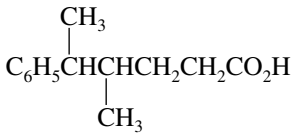


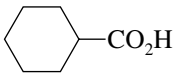
2-(4-Nitrophenyl)propanoic acid
(compound B)

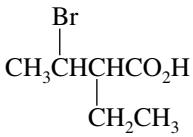
SELF-TEST

PART A

A-1. Provide an acceptable IUPAC name for each of the following:

(*a*) 

(*b*) 

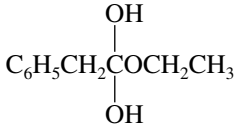
(*c*) 

A-2. Both of the following compounds may be converted into 4-phenylbutanoic acid by one or more reaction steps. Give the reagents and conditions necessary to carry out these conversions.

$C_6H_5CH_2CH_2CH(CO_2H)_2$ $C_6H_5CH_2CH_2CH_2Br$

(Two methods)

A-3. The species whose structure is shown is an intermediate in an esterification reaction. Write the complete, balanced equation for this process.

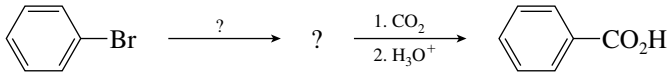


A-4. Give the correct structures for compounds A through C in the following reactions:

(*a*) $(CH_3)_2CHCH_2CH_2CO_2H \xrightarrow[P]{Br_2} A \xrightarrow[acetone]{KI} B$

(*b*) $C \xrightarrow{heat} C_6H_5\overset{O}{\overset{\|}{C}}CH(CH_3)_2 + CO_2$

A-5. Give the missing reagent(s) and the missing compound in each of the following:

(*a*) 

(*b*) $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH \xrightarrow{?} ? \xrightarrow[CH_2Cl_2]{PCC} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$

(*c*) $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH \xrightarrow{?} ? \xrightarrow{NaSCH_3} CH_3CH_2\underset{SCH_3}{\overset{O}{\overset{\|}{C}}}COH$

(*d*) $CH_3CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow[HCl]{NaCN} ? \xrightarrow{?} CH_3CH_2\underset{OH}{\overset{O}{\overset{\|}{C}}}COH$

A-6. Identify the carboxylic acid ($C_4H_7BrO_2$) having the ^1H NMR spectrum consisting of

δ 1.1 ppm, 3H (triplet)
δ 2.0 ppm, 2H (pentet)
δ 4.2 ppm, 1H (triplet)
δ 12.1 ppm, 1H (singlet)

A-7. Draw the structure of the tetrahedral intermediate in the esterification of formic acid with 1-butanol.

A-8. Write a mechanism for the esterification reaction shown.

$$CH_3\overset{O}{\overset{\|}{C}}OH + CH_3OH \xrightarrow{H^+} CH_3CO_2CH_3 + H_2O$$

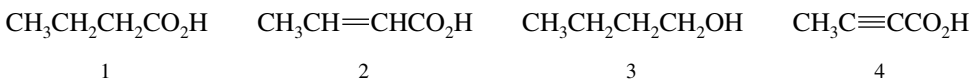
PART B

B-1. Which of the following is a correct IUPAC name for the compound shown?

$$(CH_3CH_2)_2\underset{CO_2H}{\overset{|}{C}}CH_2CH(CH_2CH_3)_2$$

(*a*) 1,1,3-Triethylhexanoic acid
(*b*) 2,2,4-Triethylhexanoic acid
(*c*) 3,5-Diethyl-3-heptylcarboxylic acid
(*d*) 3,5,5-Triethyl-6-hexanoic acid

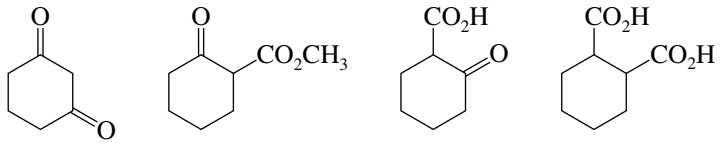
B-2. Rank the following substances in order of decreasing acid strength (strongest → weakest):



1 2 3 4

(*a*) 4 > 2 > 1 > 3
(*b*) 1 > 2 > 4 > 3
(*c*) 3 > 1 > 2 > 4
(*d*) 2 > 4 > 1 > 3

B-3. Which of the following compounds will undergo decarboxylation on heating?

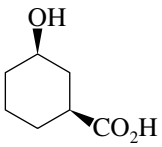


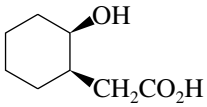
1 2 3 4

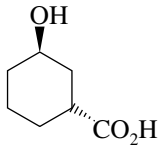
(*a*) 2 and 3
(*b*) 3 and 4
(*c*) 3 only
(*d*) 1 and 4

B-4. Which of the following is *least* likely to form a lactone?

(*a*) 

(*c*) 

(*b*) 

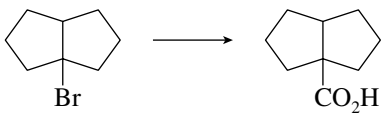
(*d*) 

B-5. Compare the two methods shown for the preparation of carboxylic acids:

Method 1:

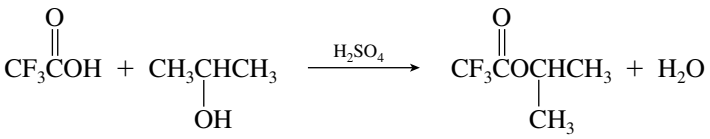
Method 2:

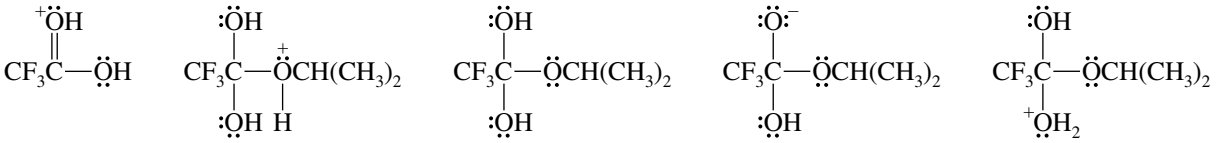
Which one of the following statements correctly describes this conversion?



(*a*) Both method 1 and method 2 are appropriate for carrying out this conversion.
(*b*) Neither method 1 nor method 2 is appropriate for carrying out this conversion.
(*c*) Method 1 will work well, but method 2 is not appropriate.
(*d*) Method 2 will work well, but method 1 is not appropriate.

B-6. Which one of the following is *not* an intermediate in the generally accepted mechanism for the reaction shown?

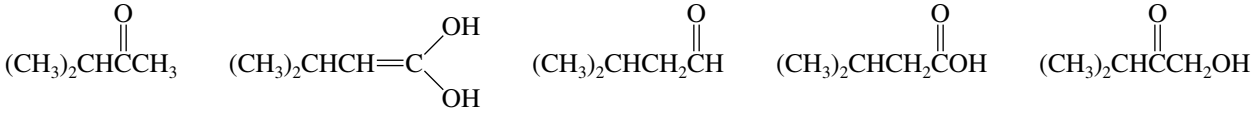




(*a*) (*b*) (*c*) (*d*) (*e*)

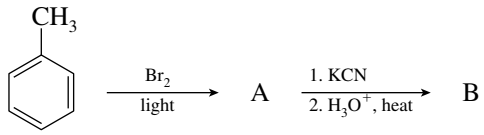
B-7. Identify compound C in the following sequence:

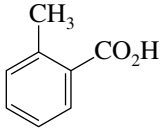
$(CH_3)_2CHCH_2C{\equiv}N \xrightarrow[\text{heat}]{HCl,\ H_2O}$ compound A $\xrightarrow[2.\ H_2O]{1.\ LiAlH_4}$ compound B $\xrightarrow[CH_2Cl_2]{PCC}$ compound C

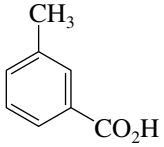


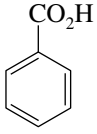
(*a*) (*b*) (*c*) (*d*) (*e*)

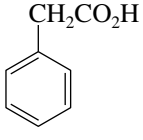
B-8. What is the final product (B) of this sequence?



(*a*)  + para

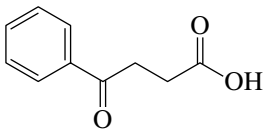
(*b*) 

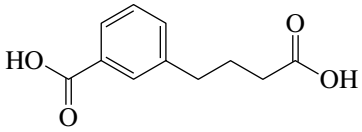
(*c*) 

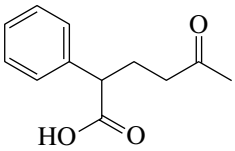
(*d*) 

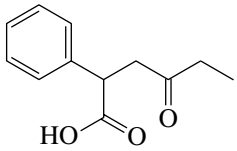
(*e*) None of these

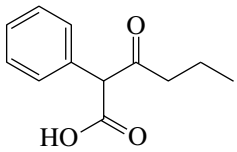
B-9. Which one of the following undergoes decarboxylation (loses carbon dioxide) most readily on being heated?

(*a*) 

(*b*) 

(*c*) 

(*d*) 

(*e*) 

B-10. Which of the compounds in the previous problem yields a δ-lactone on being reduced with sodium borohydride?

B-11. What is compound Z?

$$CH_3CH_2CH_2Br \xrightarrow{NaCN} X \xrightarrow[heat]{H_3O^+} Y \xrightarrow[H^+]{CH_3CH_2OH} Z$$

(*a*) $CH_3CH{=}CHC(=O)OH$

(*b*) $CH_3CH_2CH_2CH(OCH_2CH_3)_2$

(*c*) $CH_3CH_2CH(OCH_2CH_3)C{\equiv}N$

(*d*) $CH_3CH_2CH_2CH{=}NOCH_2CH_3$

(*e*) $CH_3CH_2CH_2C(=O)OCH_2CH_3$