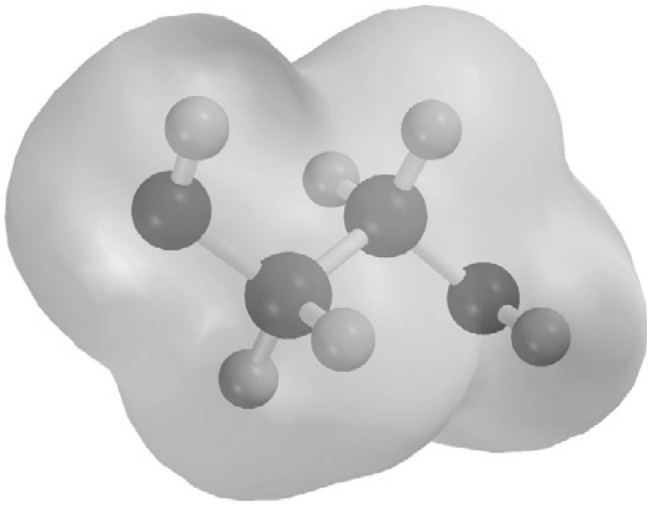
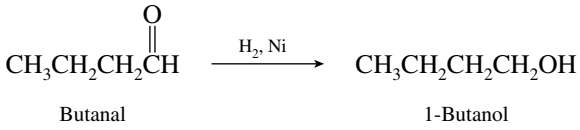


CHAPTER 15

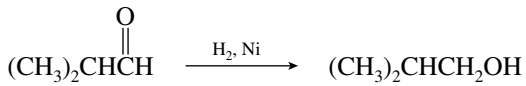
ALCOHOLS, DIOLS, AND THIOLS

SOLUTIONS TO TEXT PROBLEMS

15.1 The two primary alcohols, 1-butanol and 2-methyl-1-propanol, can be prepared by hydrogenation of the corresponding aldehydes.

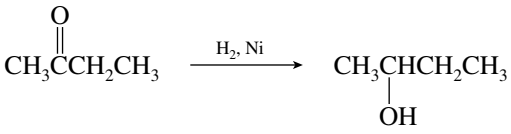


Butanal — 1-Butanol



2-Methylpropanal — 2-Methyl-1-propanol

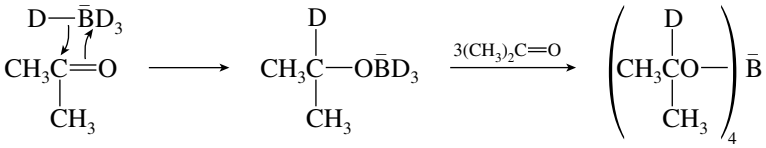
The secondary alcohol 2-butanol arises by hydrogenation of a ketone.



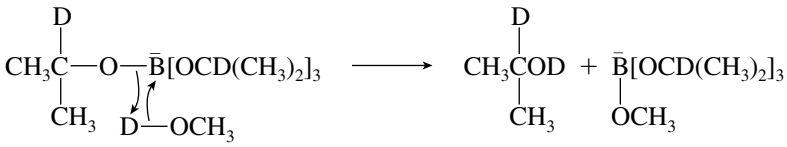
2-Butanone — 2-Butanol

Tertiary alcohols such as 2-methyl-2-propanol, $(CH_3)_3COH$, cannot be prepared by hydrogenation of a carbonyl compound.

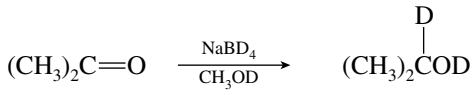
15.2 (*b*) A deuterium atom is transferred from $NaBD_4$ to the carbonyl group of acetone.



On reaction with CH_3OD, deuterium is transferred from the alcohol to the oxygen of $[(CH_3)_2CDO]_4\bar{B}$.

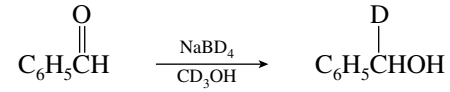


Overall:



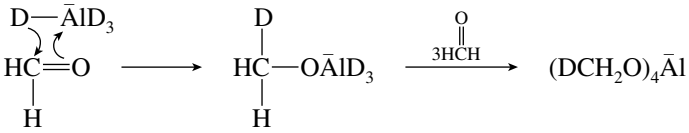
Acetone — 2-Propanol-2-d-*O*-d

(*c*) In this case $NaBD_4$ serves as a deuterium donor to carbon, and CD_3OH is a proton (not deuterium) donor to oxygen.

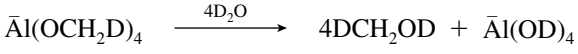


Benzaldehyde — Benzyl alcohol-1-d

(*d*) Lithium aluminum deuteride is a deuterium donor to the carbonyl carbon of formaldehyde.

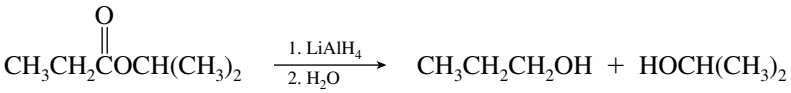


On hydrolysis with D_2O, the oxygen–aluminum bond is cleaved and DCH_2OD is formed.



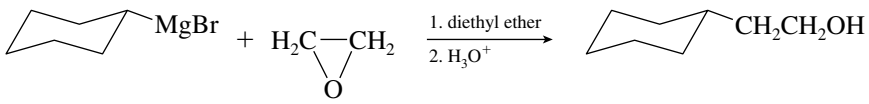
Methanol-d-*O*-d

15.3 The acyl portion of the ester gives a primary alcohol on reduction. The alkyl group bonded to oxygen may be primary, secondary, or tertiary and gives the corresponding alcohol.



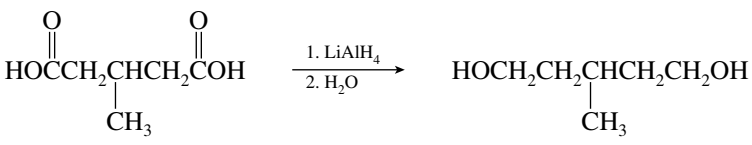
Isopropyl propanoate — 1-Propanol — 2-Propanol

15.4 (*b*) Reaction with ethylene oxide results in the addition of a $—CH_2CH_2OH$ unit to the Grignard reagent. Cyclohexylmagnesium bromide (or chloride) is the appropriate reagent.



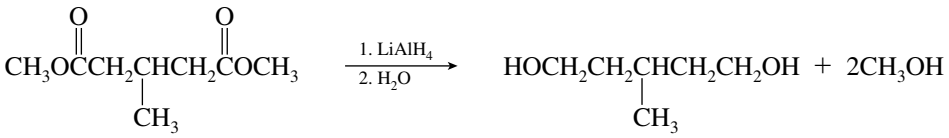
Cyclohexylmagnesium bromide — Ethylene oxide — 2-Cyclohexylethanol

15.5 Lithium aluminum hydride is the appropriate reagent for reducing carboxylic acids or esters to alcohols.



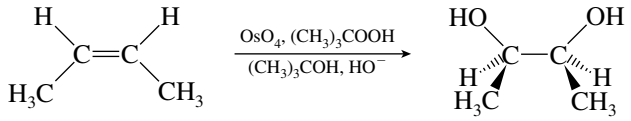
3-Methyl-1,5-pentanedioic acid — 3-Methyl-1,5-pentanediol

Any alkyl group may be attached to the oxygen of the ester function. In the following example, it is a methyl group.



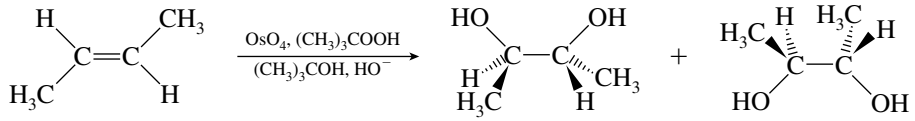
Dimethyl 3-methyl-1,5-pentanedioate — 3-Methyl-1,5-pentanediol — Methanol

15.6 Hydroxylation of alkenes using osmium tetraoxide is a syn addition of hydroxyl groups to the double bond. *cis*-2-Butene yields the meso diol.



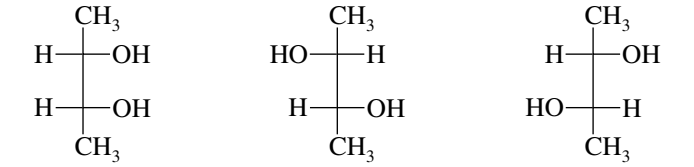
cis-2-Butene — *meso*-2,3-Butanediol

trans-2-Butene yields a racemic mixture of the two enantiomeric forms of the chiral diol.



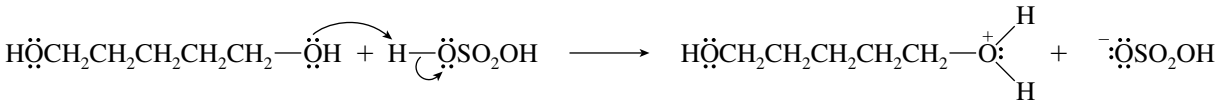
trans-2-Butene — (2*R*,3*R*)-2,3-Butanediol — (2*S*,3*S*)-2,3-Butanediol

The Fischer projection formulas of the three stereoisomers are



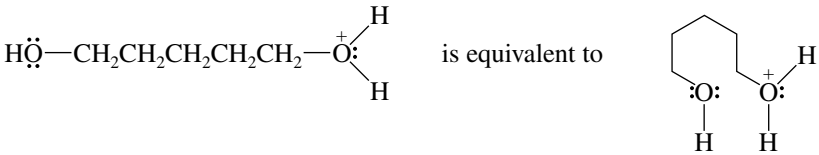
meso-2,3-Butanediol — (2*R*,3*R*)-2,3-Butanediol — (2*S*,3*S*)-2,3-Butanediol

15.7 The first step is proton transfer to 1,5-pentanediol to form the corresponding alkyloxonium ion.



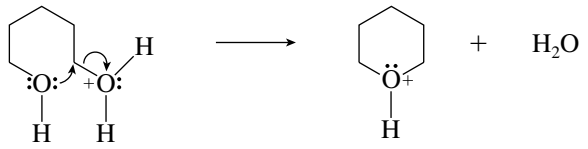
1,5-Pentanediol — Sulfuric acid — Conjugate acid of 1,5-pentanediol — Hydrogen sulfate

Rewriting the alkyloxonium ion gives



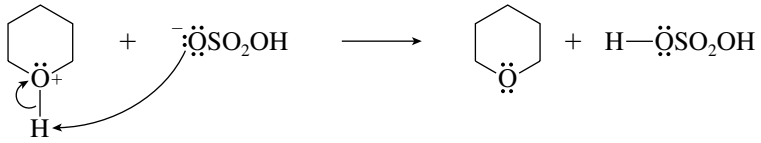
is equivalent to

The oxonium ion undergoes cyclization by intramolecular nucleophilic attack of its alcohol function on the carbon that bears the leaving group.



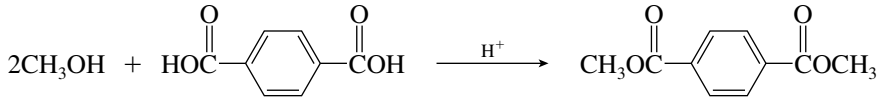
Conjugate acid of 1,5-pentanediol | Conjugate acid of oxane | Water

Loss of a proton gives oxane.



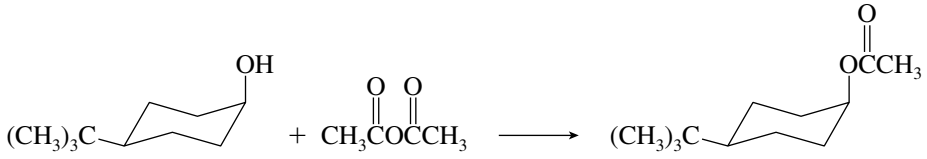
Conjugate acid of oxane | Hydrogen sulfate | Oxane | Sulfuric acid

15.8 (*b*) The relationship of the molecular formula of the ester ($C_{10}H_{10}O_4$) to that of the starting dicarboxylic acid ($C_8H_6O_4$) indicates that the diacid reacted with 2 moles of methanol to form a diester.



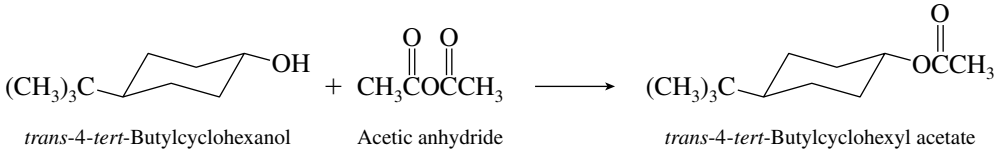
Methanol | 1,4-Benzenedicarboxylic acid | Dimethyl 1,4-benzenedicarboxylate

15.9 While neither *cis*- nor *trans*-4-*tert*-butylcyclohexanol is a chiral molecule, the stereochemical course of their reactions with acetic anhydride becomes evident when the relative stereochemistry of the ester function is examined for each case. The cis alcohol yields the cis acetate.



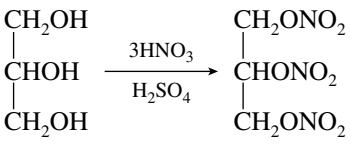
cis-4-*tert*-Butylcyclohexanol | Acetic anhydride | *cis*-4-*tert*-Butylcyclohexyl acetate

The trans alcohol yields the trans acetate.



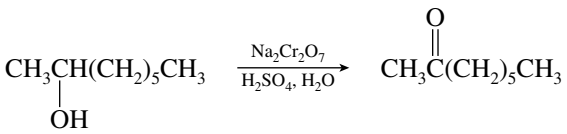
trans-4-*tert*-Butylcyclohexanol | Acetic anhydride | *trans*-4-*tert*-Butylcyclohexyl acetate

15.10 Glycerol has three hydroxyl groups, each of which is converted to a nitrate ester function in nitroglycerin.



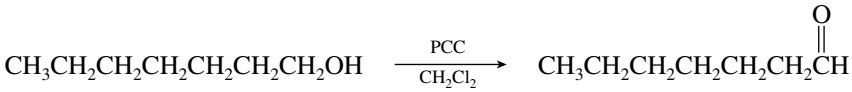
Glycerol | Nitroglycerin

15.11 (*b*) The substrate is a secondary alcohol and so gives a ketone on oxidation with sodium dichromate. 2-Octanone has been prepared in 92–96% yield under these reaction conditions.



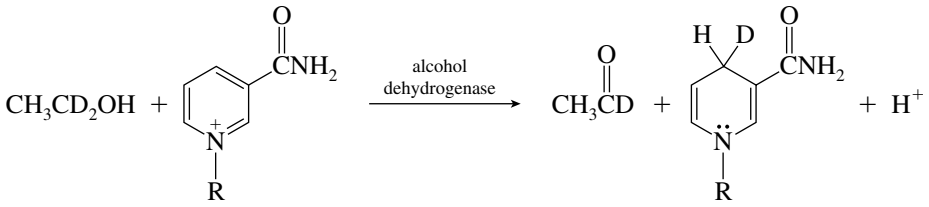
2-Octanol 2-Octanone

(*c*) The alcohol is primary, and so oxidation can produce either an aldehyde or a carboxylic acid, depending on the reaction conditions. Here the oxidation is carried out under anhydrous conditions using pyridinium chlorochromate (PCC), and the product is the corresponding aldehyde.



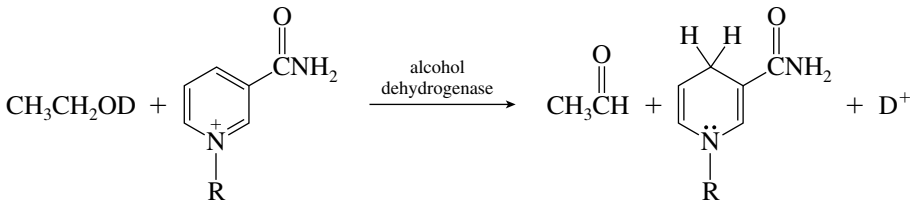
1-Heptanol Heptanal

15.12 (*b*) Biological oxidation of CH_3CD_2OH leads to loss of one of the C-1 deuterium atoms to NAD^+. The dihydropyridine ring of the reduced form of the coenzyme will bear a single deuterium.



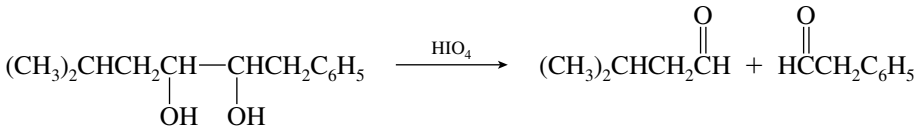
1,1-Dideuterio-ethanol NAD^+ 1-Deuterio-ethanal NADD

(*c*) The deuterium atom of CH_3CH_2OD is lost as D^+. The reduced form of the coenzyme contains no deuterium.



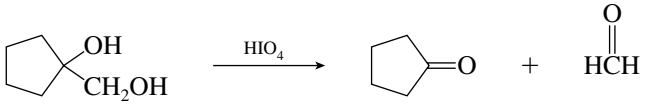
Ethanol-*O*-d NAD^+ Ethanal NADH

15.13 (*b*) Oxidation of the carbon–oxygen bonds to carbonyl groups accompanies their cleavage.



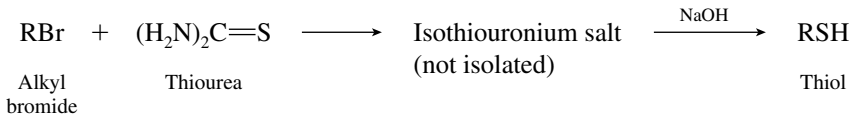
1-Phenyl-5-methyl-2,3-hexanediol 3-Methylbutanal 2-Phenylethanal

(*c*) The CH_2OH group is cleaved from the ring as formaldehyde to leave cyclopentanone.

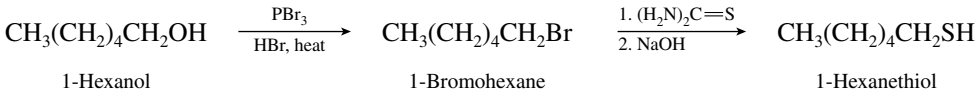


1-(Hydroxymethyl)-cyclopentanol Cyclopentanone Formaldehyde

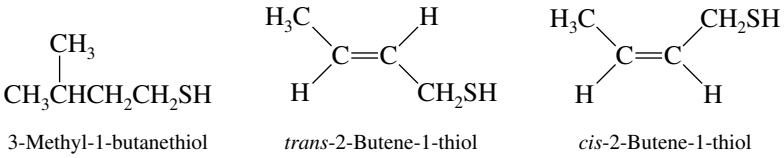
15.14 Thiols may be prepared from the corresponding alkyl halide by reaction with thiourea followed by treatment of the isothiouronium salt with base.



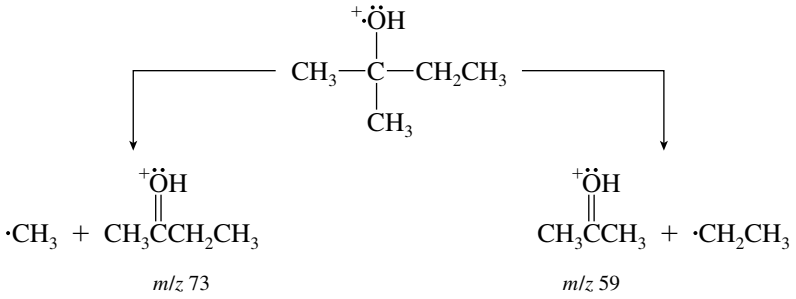
Thus, an acceptable synthesis of 1-hexanethiol from 1-hexanol would be



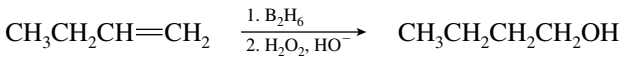
15.15 The three main components of "essence of skunk" are



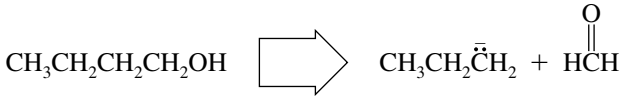
15.16 The molecular weight of 2-methyl-2-butanol is 88. A peak in its mass spectrum at m/z 70 corresponds to loss of water from the molecular ion. The peaks at m/z 73 and m/z 59 represent stable cations corresponding to the cleavages shown in the equation.



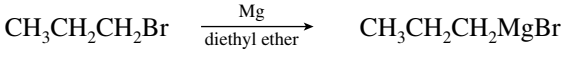
15.17 (*a*) The appropriate alkene for the preparation of 1-butanol by a hydroboration–oxidation sequence is 1-butene. Remember, hydroboration–oxidation leads to hydration of alkenes with a regioselectivity opposite to that seen in acid-catalyzed hydration.

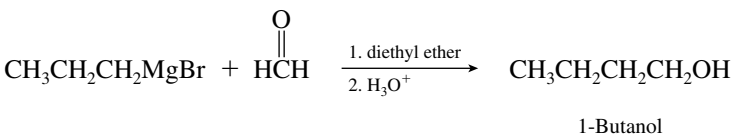


(*b*) 1-Butanol can be prepared by reaction of a Grignard reagent with formaldehyde.

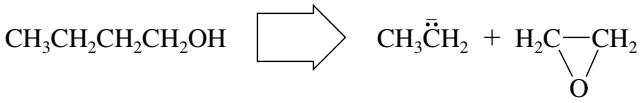


An appropriate Grignard reagent is propylmagnesium bromide.

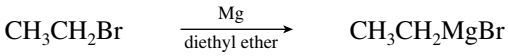




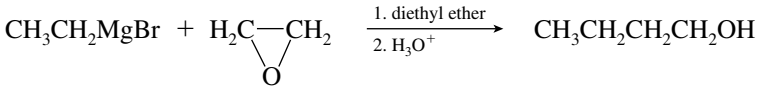
(*c*) Alternatively, 1-butanol may be prepared by the reaction of a Grignard reagent with ethylene oxide.



In this case, ethylmagnesium bromide would be used.

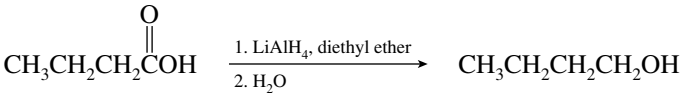


Ethyl bromide — Ethylmagnesium bromide



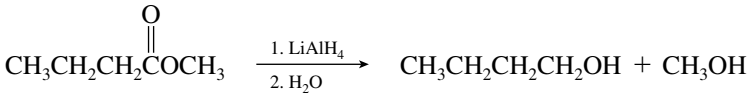
Ethylene oxide — 1-Butanol

(*d*) Primary alcohols may be prepared by reduction of the carboxylic acid having the same number of carbons. Among the reagents we have discussed, the only one that is effective in the reduction of carboxylic acids is lithium aluminum hydride. The four-carbon carboxylic acid butanoic acid is the proper substrate.



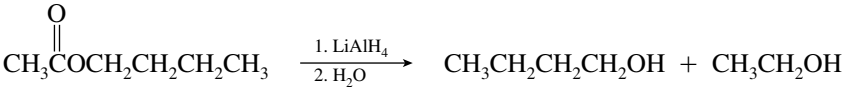
Butanoic acid — 1-Butanol

(*e*) Reduction of esters can be accomplished using lithium aluminum hydride. The correct methyl ester is methyl butanoate.



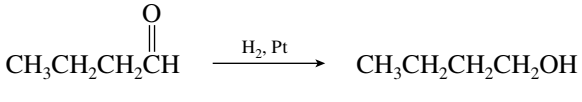
Methyl butanoate — 1-Butanol — Methanol

(*f*) A butyl ester such as butyl acetate may be reduced with lithium aluminum hydride to prepare 1-butanol.



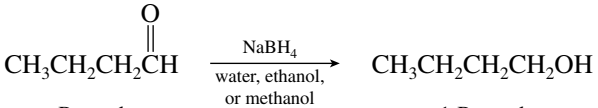
Butyl acetate — 1-Butanol — Ethanol

(*g*) Because 1-butanol is a primary alcohol having four carbons, butanal must be the aldehyde that is hydrogenated. Suitable catalysts are nickel, palladium, platinum, and ruthenium.



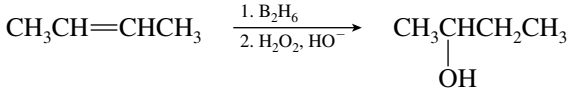
Butanal — 1-Butanol

(*h*) Sodium borohydride reduces aldehydes and ketones efficiently. It does not reduce carboxylic acids, and its reaction with esters is too slow to be of synthetic value.



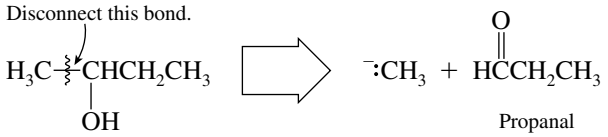
Butanal — 1-Butanol

15.18 (*a*) Both (*Z*)- and (*E*)-2-butene yield 2-butanol on hydroboration–oxidation.

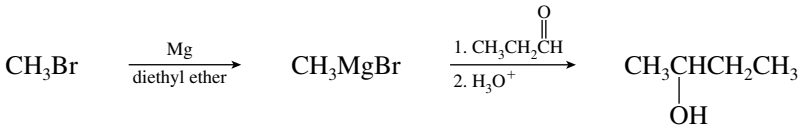


(*Z*)- or (*E*)-2-butene — 2-Butanol

(*b*) Disconnection of one of the bonds to the carbon that bears the hydroxyl group reveals a feasible route using a Grignard reagent and propanal.

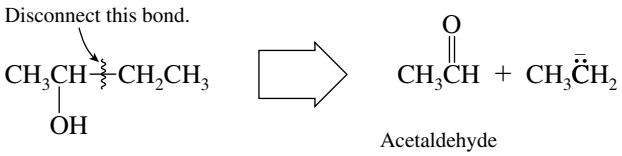


The synthetic sequence is

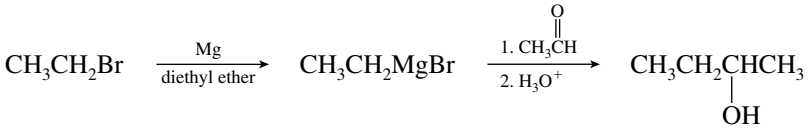


Methyl bromide — Methylmagnesium bromide — 2-Butanol

(*c*) Another disconnection is related to a synthetic route using a Grignard reagent and acetaldehyde.

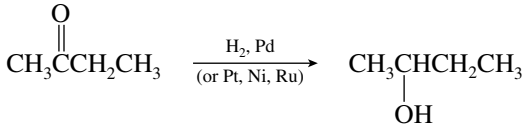


Acetaldehyde

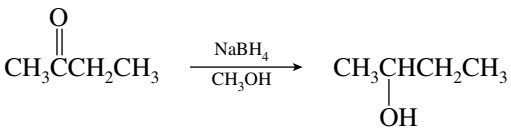


Ethyl bromide — Ethylmagnesium bromide — 2-Butanol

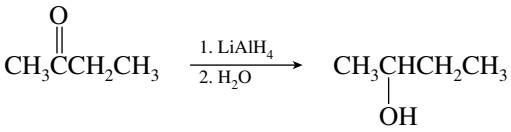
(*d–f*) Because 2-butanol is a secondary alcohol, it can be prepared by reduction of a ketone having the same carbon skeleton, in this case 2-butanone. All three reducing agents indicated in the equations are satisfactory.



2-Butanone — 2-Butanol

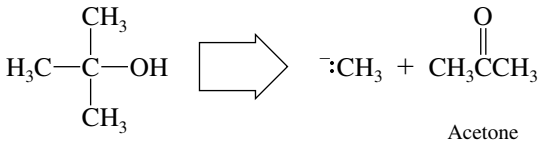


2-Butanone — 2-Butanol

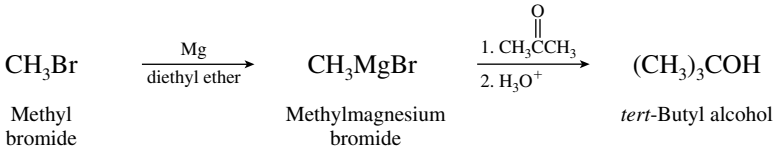


2-Butanone — 2-Butanol

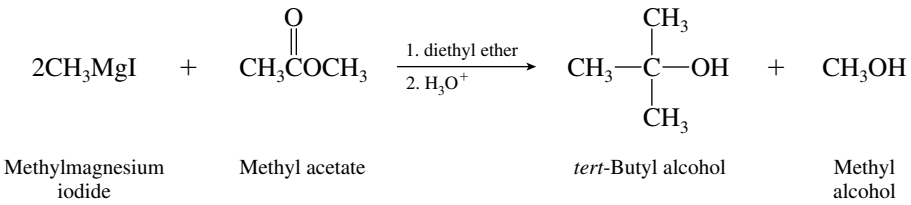
15.19 (*a*) All the carbon–carbon disconnections are equivalent.



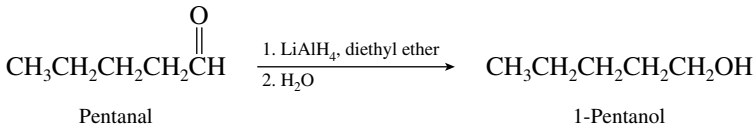
The synthesis via a Grignard reagent and acetone is

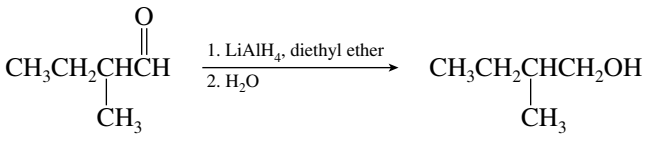


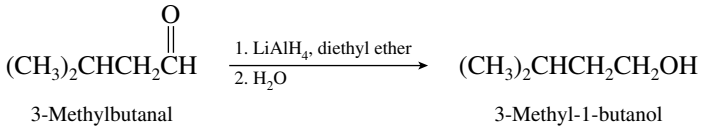
(*b*) An alternative route to *tert*-butyl alcohol is addition of a Grignard reagent to an ester. Esters react with *2 moles* of Grignard reagent. Thus, *tert*-butyl alcohol may be formed by reacting methyl acetate with 2 moles of methylmagnesium iodide. Methyl alcohol is formed as a by-product of the reaction.

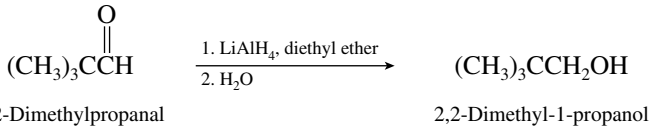


15.20 (*a*) All of the primary alcohols having the molecular formula $C_5H_{12}O$ may be prepared by reduction of aldehydes. The appropriate equations are

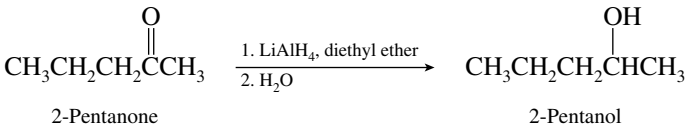




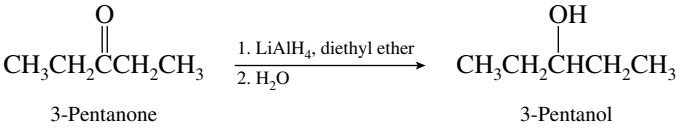




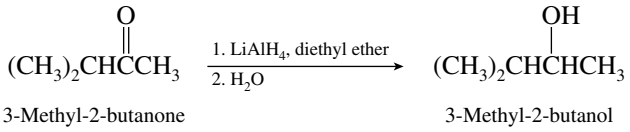
(*b*) The secondary alcohols having the molecular formula $C_5H_{12}O$ may be prepared by reduction of ketones.



2-Pentanone 2-Pentanol

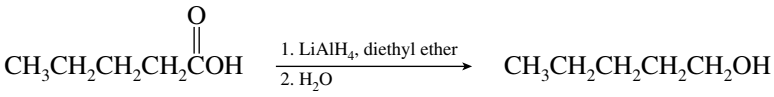


3-Pentanone 3-Pentanol



3-Methyl-2-butanone 3-Methyl-2-butanol

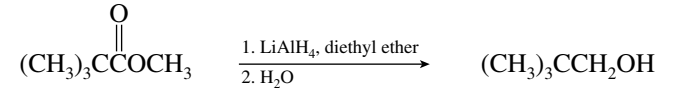
(*c*) As with the reduction of aldehydes in part (*a*), reduction of carboxylic acids yields primary alcohols. For example, 1-pentanol may be prepared by reduction of pentanoic acid.



Pentanoic acid 1-Pentanol

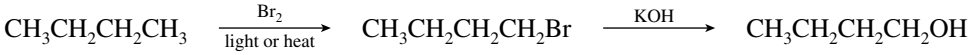
The remaining primary alcohols, 2-methyl-1-butanol, 3-methyl-1-butanol, and 2,2-dimethyl-1-propanol, may be prepared in the same way.

(*d*) As with carboxylic acids, esters may be reduced using lithium aluminum hydride to give primary alcohols. For example, 2,2-dimethyl-1-propanol may be prepared by reduction of methyl 2,2-dimethylpropanoate.



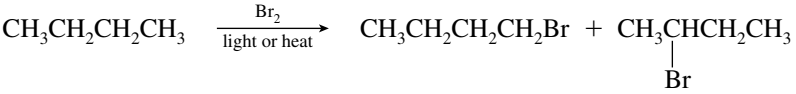
Methyl 2,2-dimethylpropanoate 2,2-Dimethyl-1-propanol

15.21 (*a*) The suggested synthesis



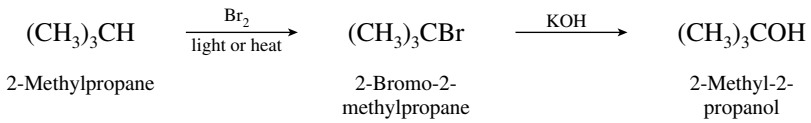
Butane 1-Bromobutane 1-Butanol

is a poor one because bromination of butane yields a mixture of 1-bromobutane and 2-bromobutane, 2-bromobutane being the major product.



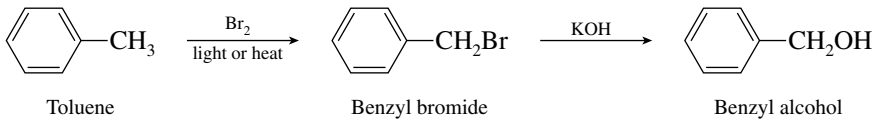
Butane 1-Bromobutane (minor product) 2-Bromobutane (major product)

(*b*) The suggested synthesis



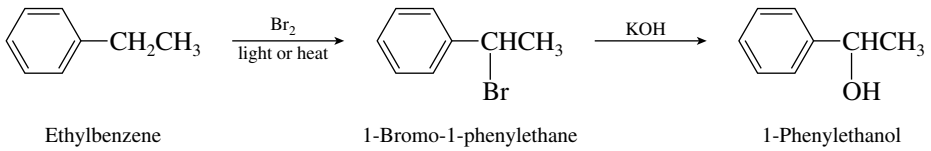
will fail because the reaction of 2-bromo-2-methylpropane with potassium hydroxide will proceed by elimination rather than by substitution. The first step in the process, selective bromination of 2-methylpropane to 2-bromo-2-methylpropane, is satisfactory because bromination is selective for substitution of tertiary hydrogens in the presence of secondary and primary ones.

(*c*) Benzyl alcohol, unlike 1-butanol and 2-methyl-2-propanol, can be prepared effectively by this method.



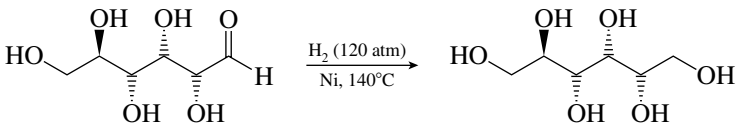
Free-radical bromination of toluene is selective for the benzylic position. Benzyl bromide cannot undergo elimination, and so nucleophilic substitution of bromide by hydroxide will work well.

(*d*) The desired transformation

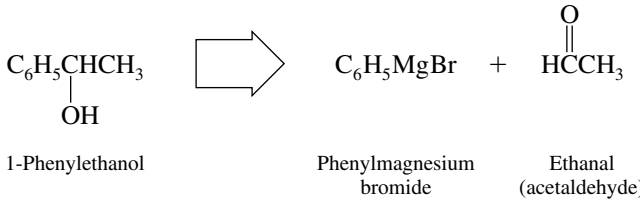


fails because it produces more than one enantiomer. The reactant ethylbenzene is achiral and although its bromination will be highly regioselective for the benzylic position, the product will be a racemic mixture of (*R*) and (*S*)-1-bromo-1-phenylethane. The alcohol produced by hydrolysis will also be racemic. Furthermore, the hydrolysis step will give mostly styrene by an E2 elimination, rather than 1-phenylethanol by nucleophilic substitution.

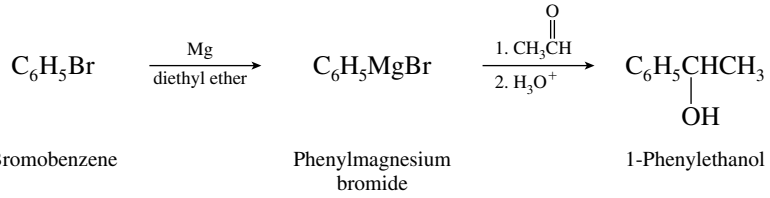
15.22 Glucose contains five hydroxyl groups and an aldehyde functional group. Its hydrogenation will not affect the hydroxyl groups but will reduce the aldehyde to a primary alcohol.



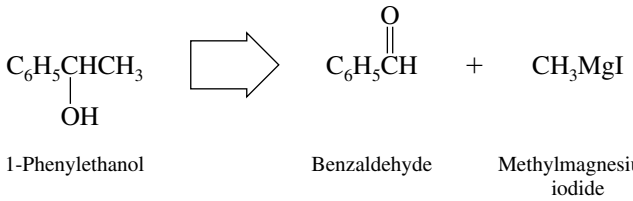
15.23 (*a*) 1-Phenylethanol is a secondary alcohol and so can be prepared by the reaction of a Grignard reagent with an aldehyde. One combination is phenylmagnesium bromide and ethanal (acetaldehyde).



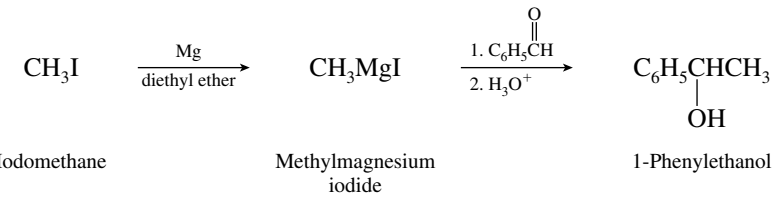
Grignard reagents—phenylmagnesium bromide in this case—are always prepared by reaction of magnesium metal and the corresponding halide. Starting with bromobenzene, a suitable synthesis is described by the sequence



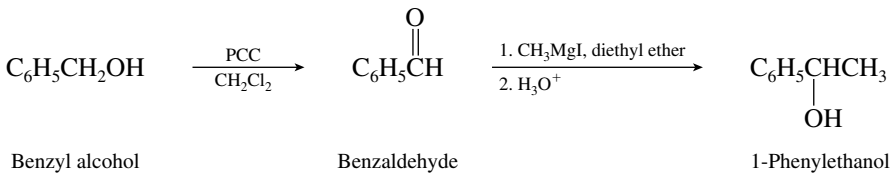
(*b*) An alternative disconnection of 1-phenylethanol reveals a second route using benzaldehyde and a methyl Grignard reagent.



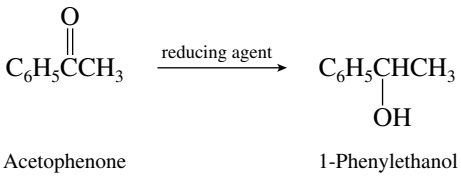
Equations representing this approach are



(*c*) Aldehydes are, in general, obtainable by oxidation of the corresponding primary alcohol. By recognizing that benzaldehyde can be obtained by oxidation of benzyl alcohol with PCC, we write



(*d*) The conversion of acetophenone to 1-phenylethanol is a reduction.



Any of a number of reducing agents could be used. These include

1. $NaBH_4$, CH_3OH
2. $LiAlH_4$ in diethyl ether, then H_2O
3. H_2 and a Pt, Pd, Ni, or Ru catalyst

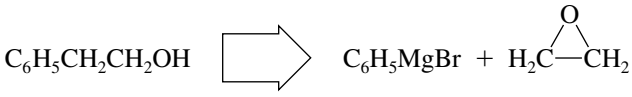
(*e*) Benzene can be employed as the ultimate starting material in a synthesis of 1-phenylethanol. Friedel–Crafts acylation of benzene gives acetophenone, which can then be reduced as in part (*d*).

Benzene Acetyl chloride Acetophenone

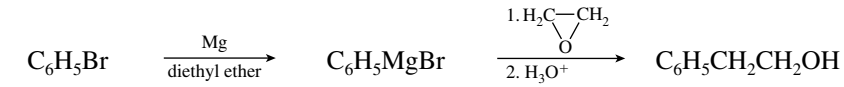
Acetic anhydride (CH_3COCCH_3, with two O) can be used in place of acetyl chloride.

15.24 2-Phenylethanol is an ingredient in many perfumes, to which it imparts a rose-like fragrance. Numerous methods have been employed for its synthesis.

(*a*) As a primary alcohol having two more carbon atoms than bromobenzene, it can be formed by reaction of a Grignard reagent, phenylmagnesium bromide, with ethylene oxide.

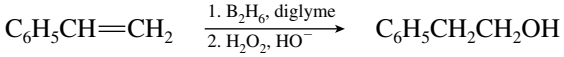


The desired reaction sequence is therefore



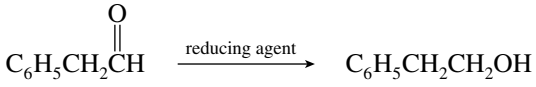
Bromobenzene Phenylmagnesium bromide 2-Phenylethanol

(*b*) Hydration of sytrene with a regioselectivity contrary to that of Markovnikov's rule is required. This is accomplished readily by hydroboration–oxidation.



Styrene 2-Phenylethanol

(*c*) Reduction of aldehydes yields primary alcohols.

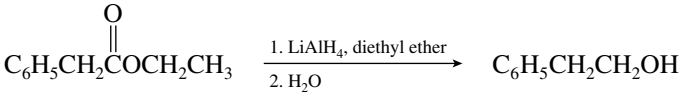


2-Phenylethanal 2-Phenylethanol

Among the reducing agents that could be (and have been) used are

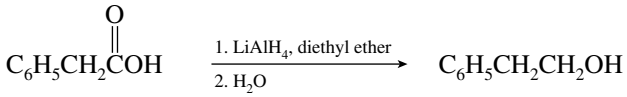
1. $NaBH_4$, CH_3OH
2. $LiAlH_4$ in diethyl ether, then H_2O
3. H_2 and a Pt, Pd, Ni, or Ru catalyst

(*d*) Esters are readily reduced to primary alcohols with lithium aluminum hydride.



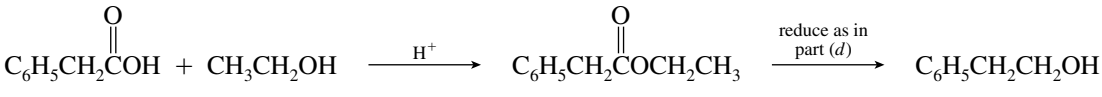
Ethyl 2-phenylethanoate 2-Phenylethanol

(*e*) The only reagent that is suitable for the direct reduction of carboxylic acids to primary alcohols is lithium aluminum hydride.



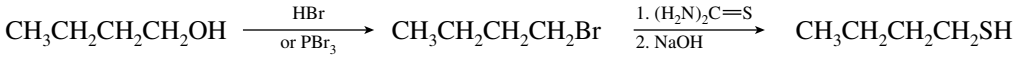
2-Phenylethanoic acid — 2-Phenylethanol

Alternatively, the carboxylic acid could be esterified with ethanol and the resulting ethyl 2-phenylethanoate reduced.



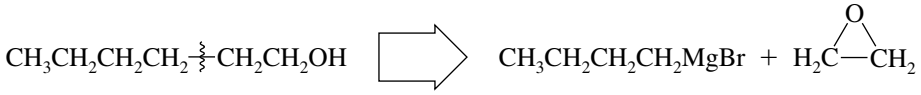
2-Phenylethanoic acid — Ethanol — Ethyl 2-phenylethanoate — 2-Phenylethanol

15.25 (*a*) Thiols are made from alkyl halides by reaction with thiourea, followed by hydrolysis of the isothiouronium salt in base. The first step must therefore be a conversion of the alcohol to an alkyl bromide.

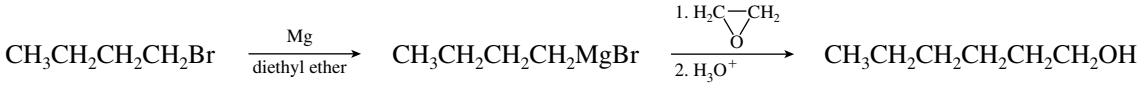


1-Butanol — 1-Bromobutane — 1-Butanethiol

(*b*) To obtain 1-hexanol from alcohols having four carbons or fewer, a two-carbon chain extension must be carried out. This suggests reaction of a Grignard reagent with ethylene oxide. The retrosynthetic path for this approach is

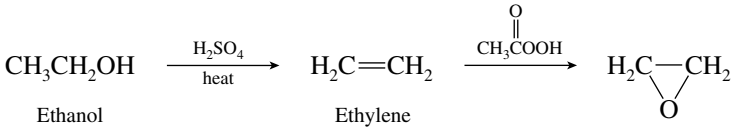


The reaction sequence therefore becomes



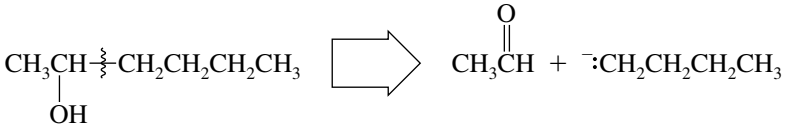
1-Bromobutane from part (*a*) — Butylmagnesium bromide — 1-Hexanol

Given the constraints of the problem, we prepare ethylene oxide by the sequence



Ethanol — Ethylene

(*c*) The target molecule 2-hexanol may be mentally disconnected as shown to a four-carbon unit and a two-carbon unit.



The alternative disconnection to $^{-}{:}CH_3$ and $HC(=O)CH_2CH_2CH_2CH_3$ reveals a plausible approach to 2-hexanol but is inconsistent with the requirement of the problem that limits starting materials to four carbons or fewer. The five-carbon aldehyde would have to be prepared first, making for a lengthy overall synthetic scheme.

An appropriate synthesis based on alcohols as starting materials is

$$\underset{\text{Ethanol}}{CH_3CH_2OH} \xrightarrow[CH_2Cl]{PCC} \underset{\text{Ethanal}}{CH_3CH(=O)}$$

$$\underset{\text{Butylmagnesium bromide from part } (b)}{CH_3CH_2CH_2CH_2MgBr} + \underset{\text{Ethanal}}{CH_3CH(=O)} \xrightarrow[2.\ H_3O^+]{1.\ \text{diethyl ether}} \underset{\text{2-Hexanol}}{CH_3CH(OH)CH_2CH_2CH_2CH_3}$$

(*d*) Hexanal may be obtained from 1-hexanol [prepared in part (*b*)] by oxidation in dichloromethane using pyridinium chlorochromate (PCC) or pyridinium dichromate (PDC).

$$\underset{\text{1-Hexanol from part } (b)}{CH_3(CH_2)_4CH_2OH} \xrightarrow[CH_2Cl_2]{\text{PCC or PDC}} \underset{\text{Hexanal}}{CH_3(CH_2)_4CH(=O)}$$

(*e*) Oxidation of 2-hexanol from part (*c*) yields 2-hexanone.

$$\underset{\text{2-Hexanol}}{CH_3CH(OH)CH_2CH_2CH_2CH_3} \xrightarrow[H_2SO_4,\ H_2O]{Na_2Cr_2O_7} \underset{\text{2-Hexanone}}{CH_3C(=O)CH_2CH_2CH_2CH_3}$$

PCC or PDC can also be used for this transformation.

(*f*) Oxidation of 1-hexanol with chromic acid (sodium or potassium dichromate in aqueous sulfuric acid) yields hexanoic acid. Use of PDC or PCC in dichloromethane is not acceptable because those reagents yield aldehydes on reaction with primary alcohols.

$$\underset{\text{1-Hexanol from part } (b)}{CH_3(CH_2)_4CH_2OH} \xrightarrow[H_2SO_4,\ H_2O]{K_2Cr_2O_7} \underset{\text{Hexanoic acid}}{CH_3(CH_2)_4CO_2H}$$

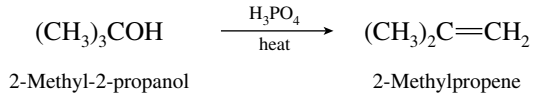
(*g*) Fischer esterification of hexanoic acid with ethanol produces ethyl hexanoate.

$$\underset{\text{Hexanoic acid from part } (f)}{CH_3(CH_2)_4CO_2H} + \underset{\text{Ethanol}}{CH_3CH_2OH} \xrightarrow{H^+} \underset{\text{Ethyl hexanoate}}{CH_3(CH_2)_4C(=O)OCH_2CH_3}$$

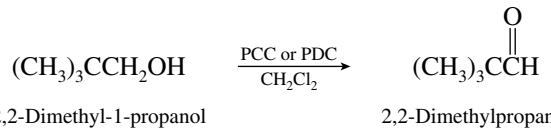
(*h*) Vicinal diols are normally prepared by hydroxylation of alkenes with osmium tetraoxide and *tert*-butyl hydroperoxide.

$$\underset{\text{2-Methylpropene}}{(CH_3)_2C{=}CH_2} \xrightarrow[(CH_3)_3COH,\ HO^-\ (CH_3)_3COH]{OsO_4} \underset{\text{2-Methyl-1,2-propanediol}}{(CH_3)_2C(OH)CH_2OH}$$

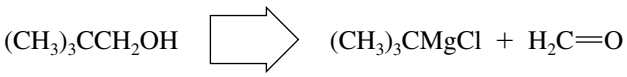
The required alkene is available by dehydration of 2-methyl-2-propanol.

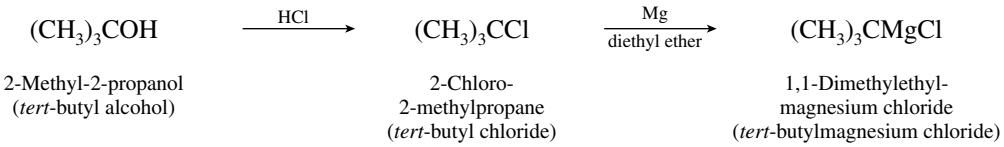


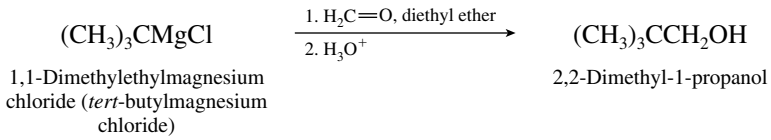
(*i*) The desired aldehyde can be prepared by oxidation of the corresponding primary alcohol with PCC or PDC.



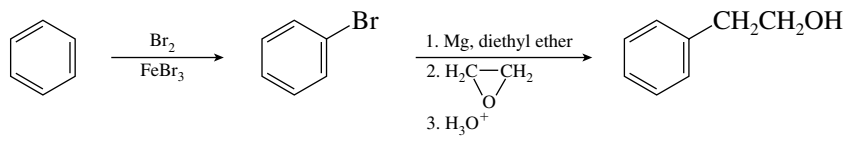
The necessary alcohol is available through reaction of a *tert*-butyl Grignard reagent with formaldehyde, as shown by the disconnection

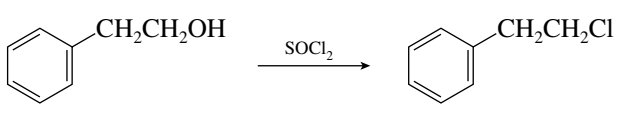






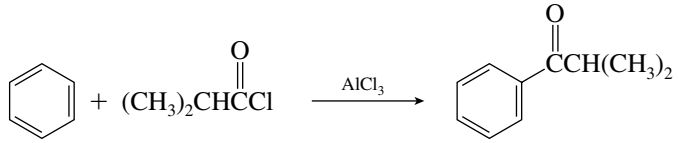
15.26 (*a*) The simplest route to this primary chloride from benzene is through the corresponding alcohol. The first step is the two-carbon chain extension used in Problem 15.24*a*.





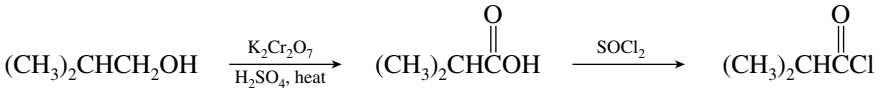
The preparation of ethylene oxide is shown in Problem 15.25*b*.

(*b*) A Friedel–Crafts acylation is the best approach to the target ketone.



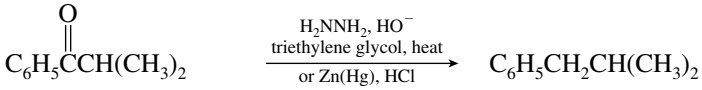
Benzene — 2-Methylpropanoyl chloride — 2-Methyl-1-phenyl-1-propanone

Because carboxylic acid chlorides are prepared from the corresponding acids, we write



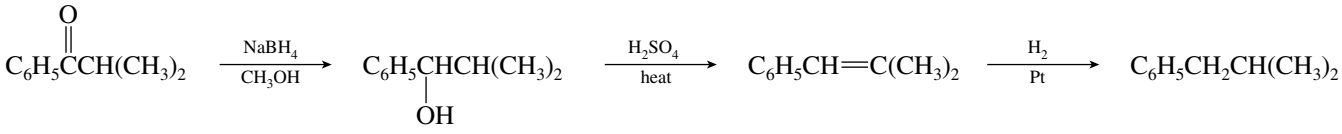
2-Methyl-1-propanol — 2-Methylpropanoic acid — 2-Methylpropanoyl chloride

(*c*) Wolff–Kishner or Clemmensen reduction of the ketone just prepared in part (*b*) affords isobutylbenzene.



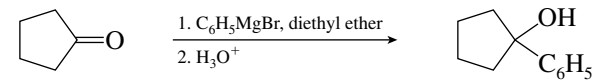
2-Methyl-1-phenyl-1-propanone — Isobutylbenzene

A less direct approach requires three steps:



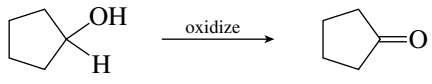
2-Methyl-1-phenyl-1-propanone — 2-Methyl-1-phenyl-1-propanol — 2-Methyl-1-phenylpropene — Isobutylbenzene

15.27 (*a*) Because 1-phenylcyclopentanol is a tertiary alcohol, a likely synthesis would involve reaction of a ketone and a Grignard reagent. Thus, a reasonable last step is treatment of cyclopentanone with phenylmagnesium bromide.



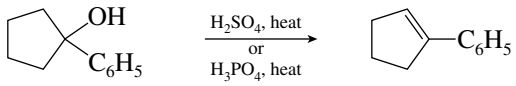
Cyclopentanone — 1-Phenylcyclopentanol

Cyclopentanone is prepared by oxidation of cyclopentanol. Any one of a number of oxidizing agents would be suitable. These include PDC or PCC in CH_2Cl_2 or chromic acid (H_2CrO_4) generated from $Na_2Cr_2O_7$ in aqueous sulfuric acid.



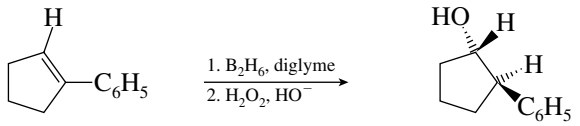
Cyclopentanol — Cyclopentanone

(*b*) Acid-catalyzed dehydration of 1-phenylcyclopentanol gives 1-phenylcyclopentene.



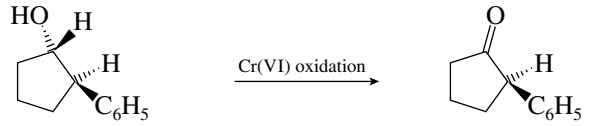
1-Phenylcyclopentanol — 1-Phenylcyclopentene

(*c*) Hydroboration–oxidation of 1-phenylcyclopentene gives *trans*-2-phenylcyclopentanol. The elements of water (H and OH) are added across the double bond opposite to Markovnikov's rule and syn to each other.



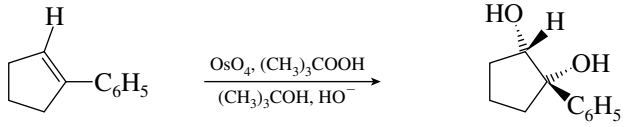
1-Phenylcyclopentene — *trans*-2-Phenylcyclopentanol

(*d*) Oxidation of *trans*-2-phenylcyclopentanol converts this secondary alcohol to the desired ketone. Any of the Cr(VI)-derived oxidizing agents mentioned in part (*a*) for oxidation of cyclopentanol to cyclopentanone is satisfactory.



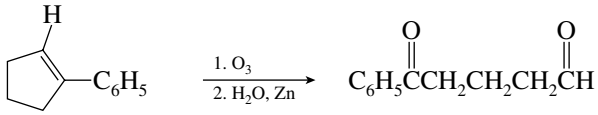
trans-2-Phenylcyclopentanol — 2-Phenylcyclopentanone

(*e*) The standard procedure for preparing *cis*-1,2-diols is by hydroxylation of alkenes with osmium tetraoxide.



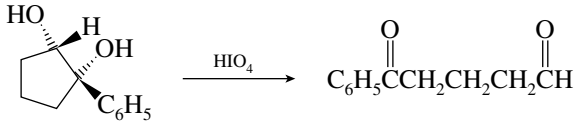
1-Phenylcyclopentene — 1-Phenyl-*cis*-1,2-cyclopentanediol

(*f*) The desired compound is available either by ozonolysis of 1-phenylcyclopentene:



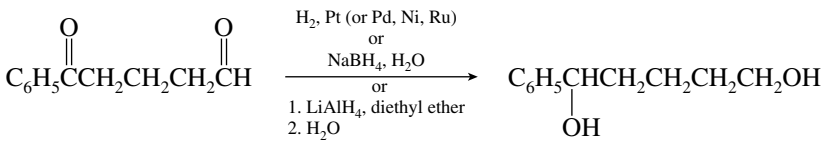
1-Phenylcyclopentene — 5-Oxo-1-phenyl-1-pentanone

or by periodic acid cleavage of the diol in part (*e*):



1-Phenyl-*cis*-1,2-cyclopentanediol — 5-Oxo-1-phenyl-1-pentanone

(*g*) Reduction of both carbonyl groups in the product of part (*f*) gives the desired diol.



5-Oxo-1-phenyl-1-pentanone — 1-Phenyl-1,5-pentanediol

15.28 (*a*, *b*) Primary alcohols react in two different ways on being heated with acid catalysts: they can condense to form dialkyl ethers or undergo dehydration to yield alkenes. Ether formation is favored at lower temperature, and alkene formation is favored at higher temperature.

$$\underset{\text{1-Propanol}}{2CH_3CH_2CH_2OH} \xrightarrow[140^\circ C]{H_2SO_4} \underset{\text{Dipropyl ether}}{CH_3CH_2CH_2OCH_2CH_2CH_3} + \underset{\text{Water}}{H_2O}$$

$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} \xrightarrow[200^\circ C]{H_2SO_4} \underset{\text{Propene}}{CH_3CH{=}CH_2} + \underset{\text{Water}}{H_2O}$$

(*c*) Nitrate esters are formed by the reaction of alcohols with nitric acid in the presence of a sulfuric acid catalyst.

$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} + \underset{\text{Nitric acid}}{HONO_2} \xrightarrow{H_2SO_4(cat)} \underset{\text{Propyl nitrate}}{CH_3CH_2CH_2ONO_2} + \underset{\text{Water}}{H_2O}$$

(*d*) Pyridinium chlorochromate (PCC) oxidizes primary alcohols to aldehydes.

$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} \xrightarrow[CH_2Cl_2]{PCC} \underset{\text{Propanal}}{CH_3CH_2\overset{\overset{O}{\|}}{C}H}$$

(*e*) Potassium dichromate in aqueous sulfuric acid oxidizes primary alcohols to carboxylic acids.

$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} \xrightarrow[\substack{H_2SO_4,\ H_2O\\ \text{heat}}]{K_2Cr_2O_7} \underset{\text{Propanoic acid}}{CH_3CH_2\overset{\overset{O}{\|}}{C}OH}$$

(*f*) Amide ion, a strong base, abstracts a proton from 1-propanol to form ammonia and 1-propanolate ion. This is an acid–base reaction.

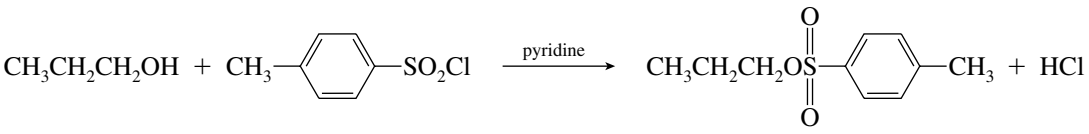
$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} + \underset{\text{Sodium amide}}{NaNH_2} \longrightarrow \underset{\text{Sodium 1-propanolate}}{CH_3CH_2CH_2ONa} + \underset{\text{Ammonia}}{NH_3}$$

(*g*) With acetic acid and in the presence of an acid catalyst, 1-propanol is converted to its acetate ester.

$$\underset{\text{1-Propanol}}{CH_3CH_2CH_2OH} + \underset{\text{Acetic acid}}{CH_3\overset{\overset{O}{\|}}{C}OH} \underset{}{\overset{HCl}{\rightleftharpoons}} \underset{\text{Propyl acetate}}{CH_3\overset{\overset{O}{\|}}{C}OCH_2CH_2CH_3} + \underset{\text{Water}}{H_2O}$$

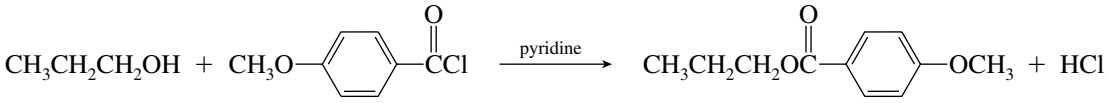
This is an equilibrium process that slightly favors products.

(*h*) Alcohols react with *p*-toluenesulfonyl chloride to give *p*-toluenesulfonate esters.



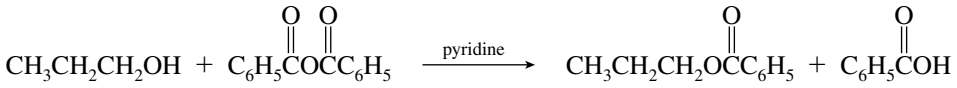
1-Propanol *p*-Toluenesulfonyl chloride Propyl *p*-toluenesulfonate

(*i*) Acyl chlorides convert alcohols to esters.



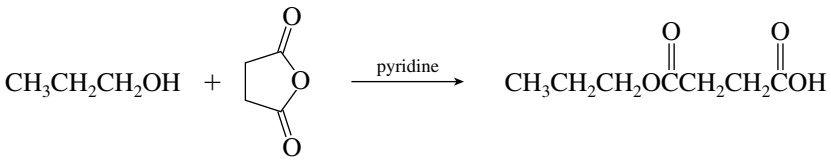
1-Propanol — *p*-Methoxybenzoyl chloride — Propyl *p*-methoxybenzoate

(*j*) The reagent is benzoic anhydride. Carboxylic acid anhydrides react with alcohols to give esters.



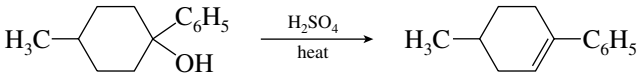
1-Propanol — Benzoic anhydride — Propyl benzoate — Benzoic acid

(*k*) The reagent is succinic anhydride, a cyclic anhydride. Esterification occurs, but in this case the resulting ester and carboxylic acid functions remain part of the same molecule.



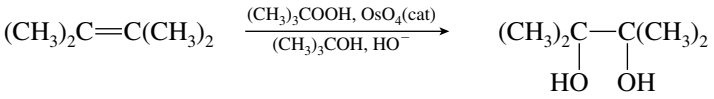
1-Propanol — Succinic anhydride — Hydrogen propyl succinate

15.29 (*a*) On being heated in the presence of sulfuric acid, tertiary alcohols undergo elimination.



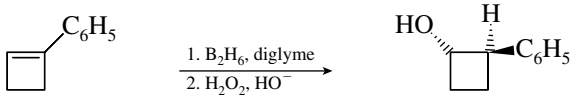
4-Methyl-1-phenylcyclohexanol — 4-Methyl-1-phenylcyclohexene (81%)

(*b*) The combination of reagents specified converts alkenes to vicinal diols.



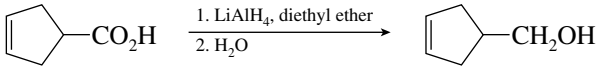
2,3-Dimethyl-2-butene — 2,3-Dimethyl-2,3-butanediol (72%)

(*c*) Hydroboration–oxidation of the double bond takes place with a regioselectivity that is opposite to Markovnikov's rule. The elements of water are added in a stereospecific syn fashion.



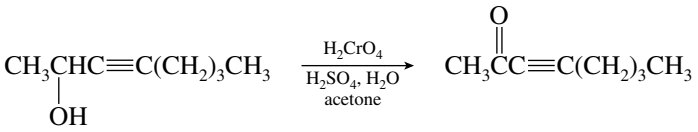
1-Phenylcyclobutene — *trans*-2-Phenylcyclobutanol (82%)

(*d*) Lithium aluminum hydride reduces carboxylic acids to primary alcohols, but does not reduce carbon–carbon double bonds.



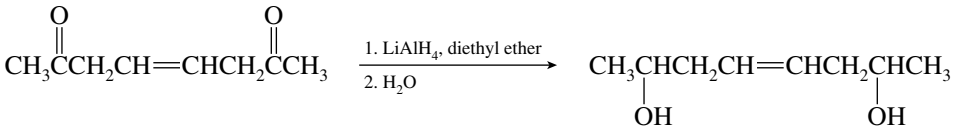
Cyclopentene-4-carboxylic acid — (3-Cyclopentenyl)-methanol

(*e*) Chromic acid oxidizes the secondary alcohol to the corresponding ketone but does not affect the triple bond.



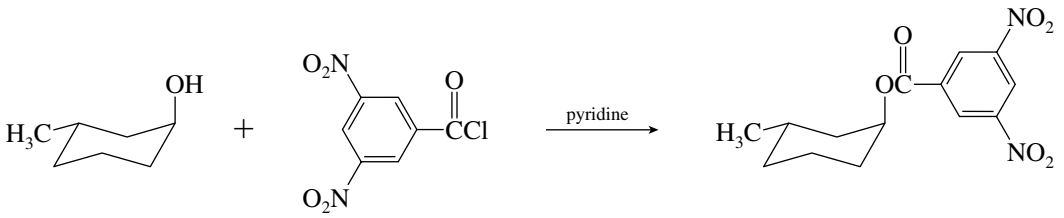
3-Octyn-2-ol — 3-Octyn-2-one (80%)

(*f*) Lithium aluminum hydride reduces carbonyl groups efficiently but does not normally react with double bonds.



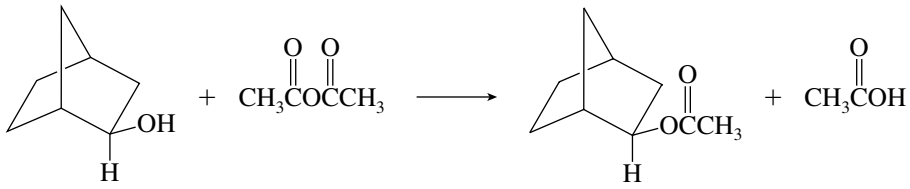
4-Octen-2,7-dione — 4-Octen-2,7-diol (75%)

(*g*) Alcohols react with acyl chlorides to yield esters. The O—H bond is broken in this reaction; the C—O bond of the alcohol remains intact on ester formation.



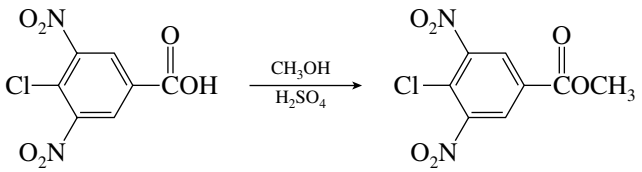
trans-3-Methylcyclohexanol — 3,5-Dinitrobenzoyl chloride — *trans*-3-Methylcyclohexyl-3,5-dinitrobenzoate (74%)

(*h*) Carboxylic acid anhydrides react with alcohols to give esters. Here, too, the spatial orientation of the C—O bond remains intact.



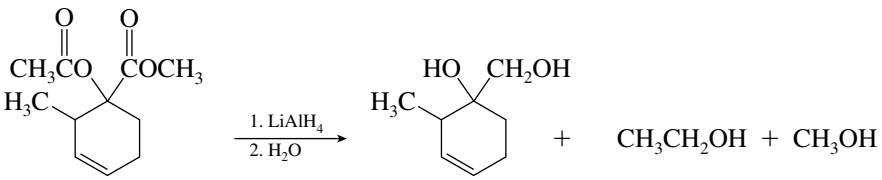
exo-Bicyclo[2.2.1]-heptan-2-ol — Acetic anhydride — *exo*-Bicyclo[2.2.1]hept-2-yl acetate (90%) — Acetic acid

(*i*) The substrate is a carboxylic acid and undergoes Fischer esterification with methanol.



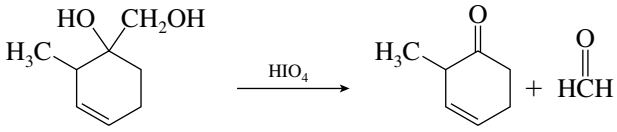
4-Chloro-3,5-dinitrobenzoic acid — Methyl 4-chloro-3,5-dinitrobenzoate (96%)

(*j*) Both ester functions are cleaved by reduction with lithium aluminum hydride. The product is a diol.



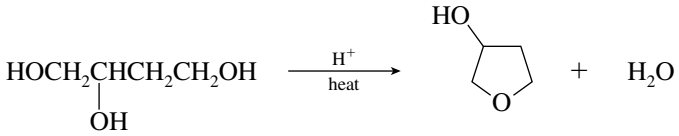
(96%)

(*k*) Treatment of the diol obtained in part (*j*) with periodic acid brings about its cleavage to two carbonyl compounds.



(74%)

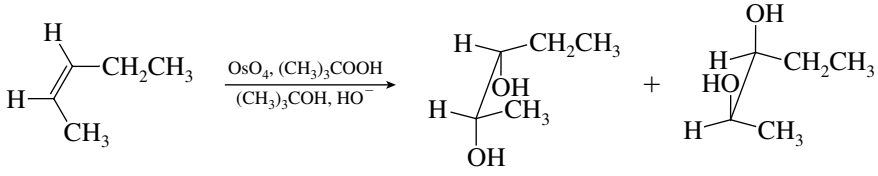
15.30 Only the hydroxyl groups on C-1 and C-4 can be involved, since only these two can lead to a five-membered cyclic ether.



1,2,4-Butanetriol — 3-Hydroxyoxolane ($C_4H_8O_2$)

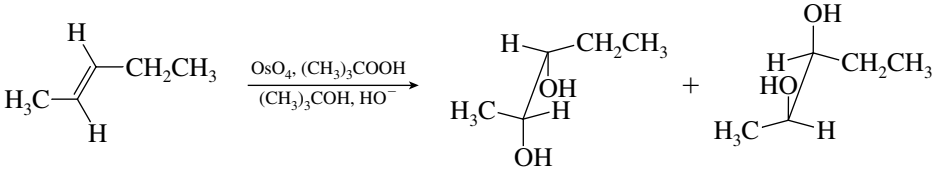
Any other combination of hydroxyl groups would lead to a strained three-membered or four-membered ring and is unfavorable under conditions of acid catalysis.

15.31 Hydroxylation of alkenes with osmium tetraoxide is a syn addition. A racemic mixture of the 2*R*,3*S* and 2*S*,3*R* stereoisomers is formed from *cis*-2-pentene.



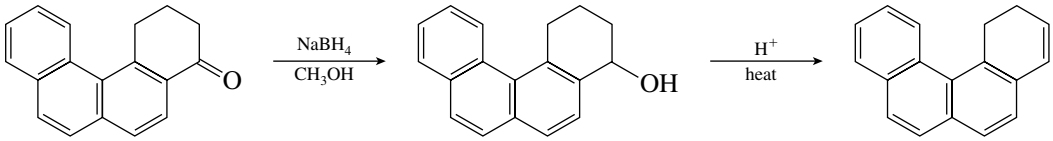
cis-2-Pentene — 2*S*,3*R*-2,3-Pentanediol — 2*R*,3*S*-2,3-Pentanediol

trans-2-Pentene gives a racemic mixture of the 2*R*,3*R* and 2*S*,3*S* stereoisomers.



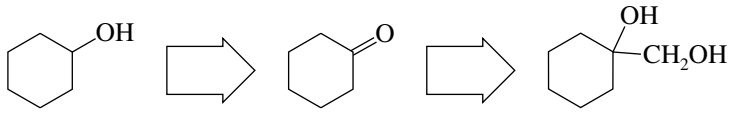
trans-2-Pentene — 2*R*,3*R*-2,3-Pentanediol — 2*S*,3*S*-2,3-Pentanediol

15.32 (*a*) The task of converting a ketone to an alkene requires first the reduction of the ketone to an alcohol and then dehydration. In practice the two-step transformation has been carried out in 54% yield by treating the ketone with sodium borohydride and then heating the resulting alcohol with *p*-toluenesulfonic acid.

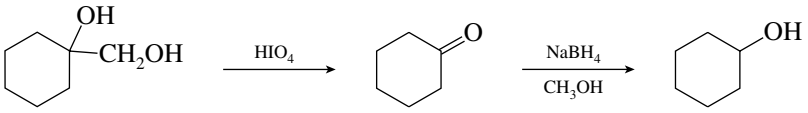


Of course, sodium borohydride may be replaced by other suitable reducing agents, and *p*-toluenesulfonic acid is not the only acid that could be used in the dehydration step.

(*b*) This problem and the next one illustrate the value of reasoning backward. The desired product, cyclohexanol, can be prepared cleanly from cyclohexanone.

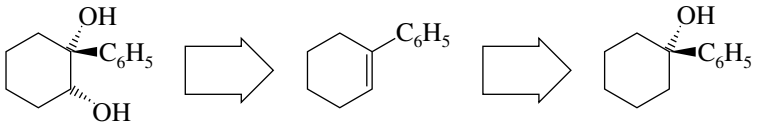


Once cyclohexanone is recognized to be a key intermediate, the synthetic pathway becomes apparent—what is needed is a method to convert the indicated starting material to cyclohexanone. The reagent ideally suited to this task is periodic acid. The synthetic sequence to be followed is therefore

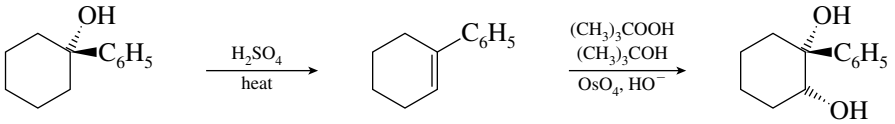


1-(Hydroxymethyl)-cyclohexanol — Cyclohexanone — Cyclohexanol

(*c*) No direct method allows a second hydroxyl group to be introduced at C-2 of 1-phenylcyclohexanol in a single step. We recognize the product as a vicinal diol and recall that such compounds are available by hydroxylation of alkenes.



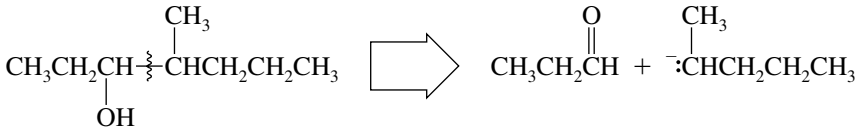
This tells us that we must first dehydrate the tertiary alcohol, then hydroxylate the resulting alkene.



1-Phenylcyclohexanol — 1-Phenylcyclohexene — 1-Phenyl-*cis*-1,2-cyclohexanediol

The syn stereoselectivity of the hydroxylation step ensures that the product will have its hydroxyl groups cis, as the problem requires.

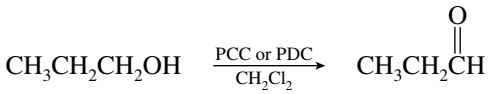
15.33 Because the target molecule is an eight-carbon secondary alcohol and the problem restricts our choices of starting materials to alcohols of five carbons or fewer, we are led to consider building up the carbon chain by a Grignard reaction.



4-Methyl-3-heptanol

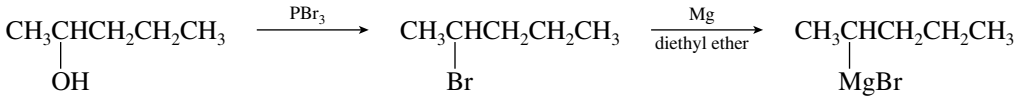
The disconnection shown leads to a three-carbon aldehyde and a five-carbon Grignard reagent. Starting with the corresponding alcohols, the following synthetic scheme seems reasonable.

First, propanal is prepared.



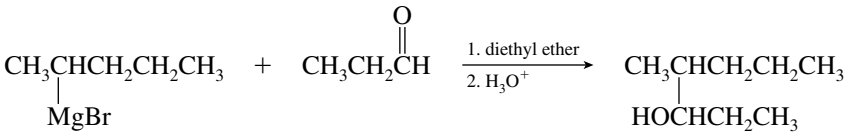
1-Propanol Propanal

After converting 2-pentanol to its bromo derivative, a solution of the Grignard reagent is prepared.



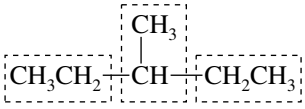
2-Pentanol 2-Bromopentane 1-Methylbutylmagnesium bromide

Reaction of the Grignard reagent with the aldehyde yields the desired 4-methyl-3-heptanol.



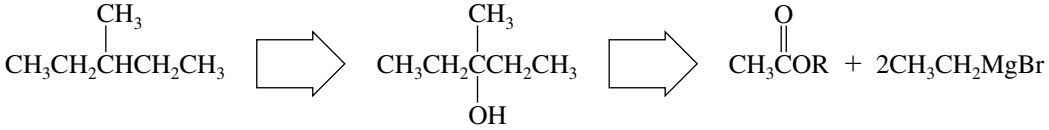
1-Methylbutylmagnesium bromide Propanal 4-Methyl-3-heptanol

15.34 Our target molecule is void of functionality and so requires us to focus attention on the carbon skeleton. Notice that it can be considered to arise from three ethyl groups.

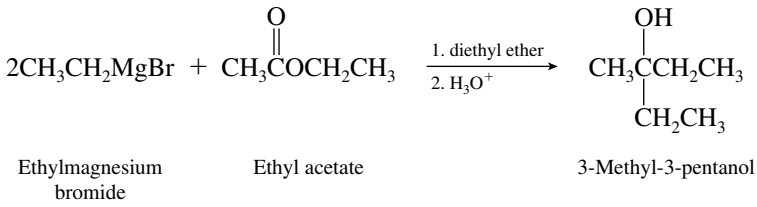


3-Methylpentane

Considering the problem retrosynthetically, we can see that a key intermediate having the carbon skeleton of the desired product is 3-methyl-3-pentanol. This becomes apparent from the fact that alkanes may be prepared from alkenes, which in turn are available from alcohols. The desired alcohol may be prepared from reaction of an acetate ester with a Grignard reagent, ethylmagnesium bromide.

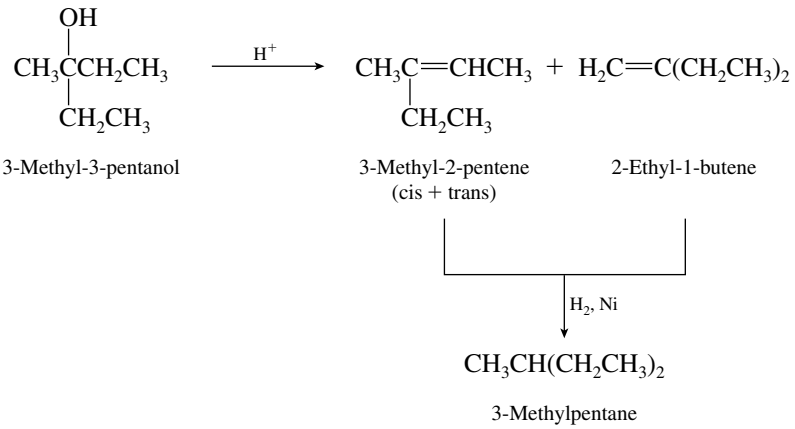


The carbon skeleton can be assembled in one step by the reaction of ethylmagnesium bromide and ethyl acetate.



Ethylmagnesium bromide — Ethyl acetate — 3-Methyl-3-pentanol

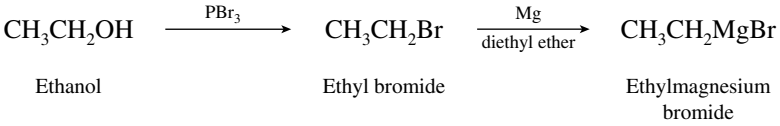
The resulting tertiary alcohol is converted to the desired hydrocarbon by acid-catalyzed dehydration and catalytic hydrogenation of the resulting mixture of alkenes.



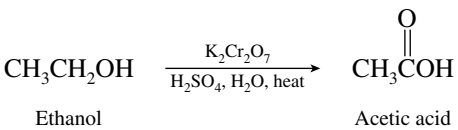
3-Methyl-3-pentanol — 3-Methyl-2-pentene (cis + trans) — 2-Ethyl-1-butene

3-Methylpentane

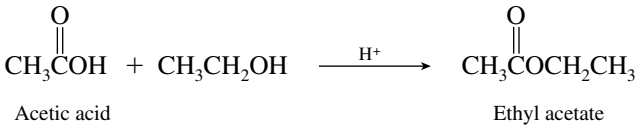
Because the problem requires that ethanol be the ultimate starting material, we need to show the preparation of the ethylmagnesium bromide and ethyl acetate used in constructing the carbon skeleton.



Ethanol — Ethyl bromide — Ethylmagnesium bromide

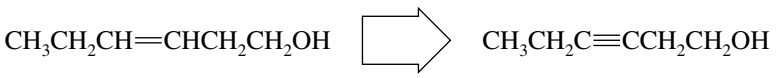


Ethanol — Acetic acid

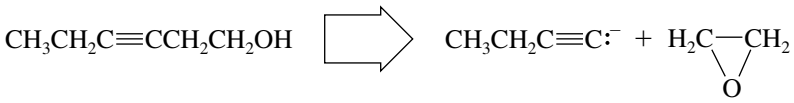


Acetic acid — Ethyl acetate

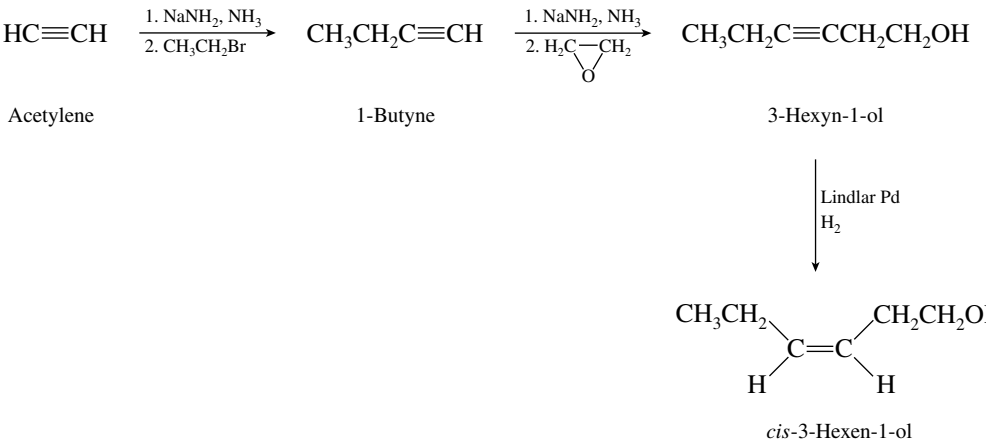
15.35 (*a*) Retrosynthetically, we can see that the cis carbon–carbon double bond is available by hydrogenation of the corresponding alkyne over the Lindlar catalyst.



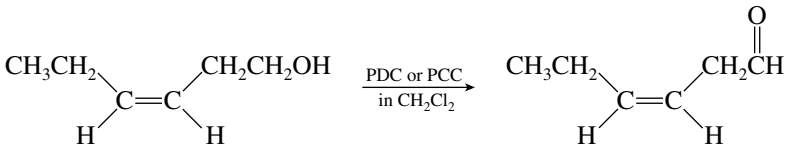
The $—CH_2CH_2OH$ unit can be appended to an alkynide anion by reaction with ethylene oxide.



The alkynide anion is derived from 1-butyne by alkylation of acetylene. This analysis suggests the following synthetic sequence:

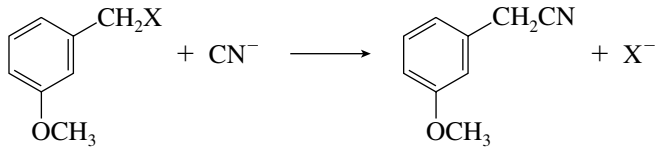


(*b*) The compound cited is the aldehyde derived by oxidation of the primary alcohol in part (*a*). Oxidize the alcohol with PDC or PCC in CH_2Cl_2.



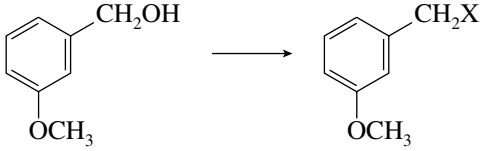
15.36 Even though we are given the structure of the starting material, it is still better to reason backward from the target molecule rather than forward from the starting material.

The desired product contains a cyano (—CN) group. The only method we have seen so far for introducing such a function into a molecule is by nucleophilic substitution. The last step in the synthesis must therefore be



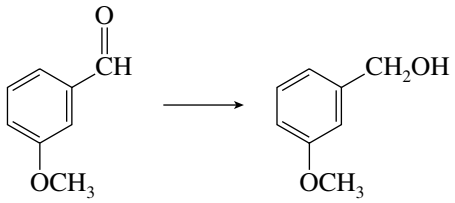
This step should work very well, since the substrate is a primary benzylic halide, cannot undergo elimination, and is very reactive in S_N2 reactions.

The primary benzylic halide can be prepared from the corresponding alcohol by any of a number of methods.



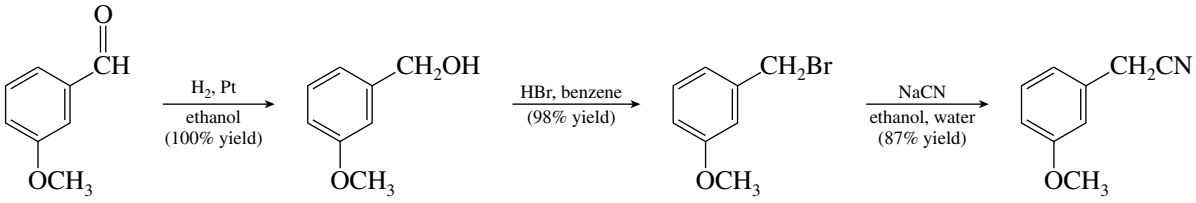
Suitable reagents include HBr, PBr_3, or $SOCl_2$.

Now we only need to prepare the primary alcohol from the given starting aldehyde, which is accomplished by reduction.



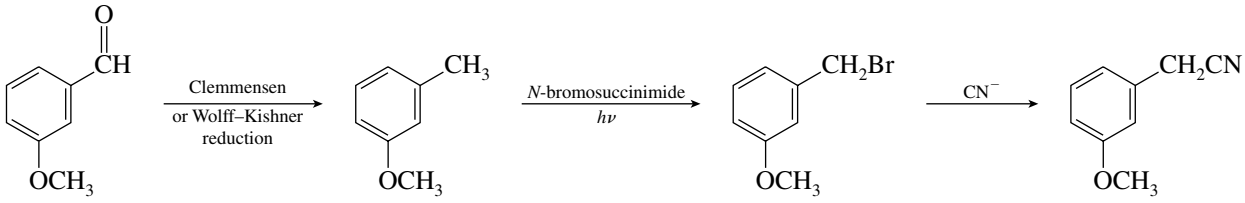
Reduction can be achieved by catalytic hydrogenation, with lithium aluminum hydride, or with sodium borohydride.

The actual sequence of reactions as carried out is as shown.



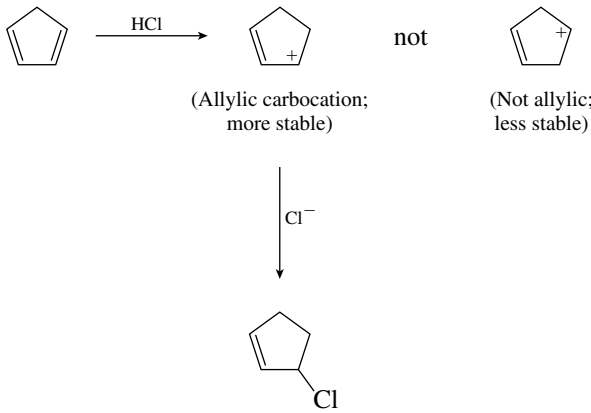
m-Methoxybenzaldehyde | *m*-Methoxybenzyl alcohol | *m*-Methoxybenzyl bromide | *m*-Methoxybenzyl cyanide

Another three-step synthesis, which is reasonable but does not involve an alcohol as an intermediate, is



m-Methoxybenzaldehyde | *m*-Methoxytoluene | *m*-Methoxybenzyl bromide | *m*-Methoxybenzyl cyanide

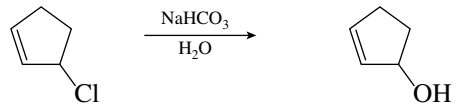
15.37 (*a*) Addition of hydrogen chloride to cyclopentadiene takes place by way of the most stable carbocation. In this case it is an allylic carbocation.



(Allylic carbocation; more stable) | (Not allylic; less stable)

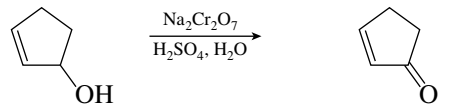
3-Chlorocyclopentene (80–90%)
(Compound A)

Hydrolysis of 3-chlorocyclopentene gives the corresponding alcohol. Sodium bicarbonate in water is a weakly basic solvolysis medium.



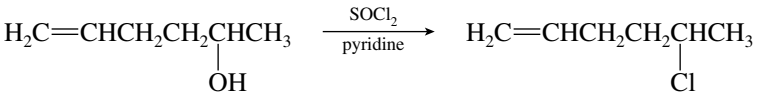
Compound A — 2-Cyclopenten-1-ol (88%) (compound B)

Oxidation of compound B (a secondary alcohol) gives the ketone 2-cyclopenten-1-one.



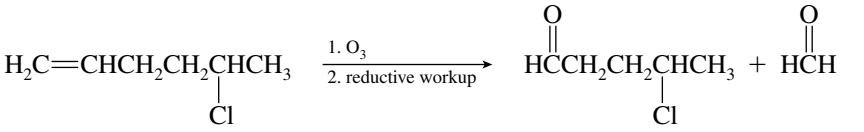
Compound B — 2-Cyclopenten-1-one (60–68%) (compound C)

(*b*) Thionyl chloride converts alcohols to alkyl chlorides.



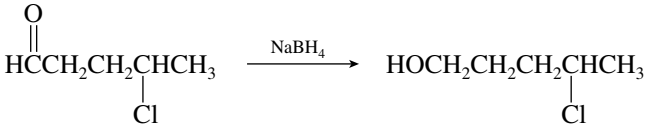
5-Hexen-2-ol — 5-Chloro-1-hexene (compound D)

Ozonolysis cleaves the carbon–carbon double bond.



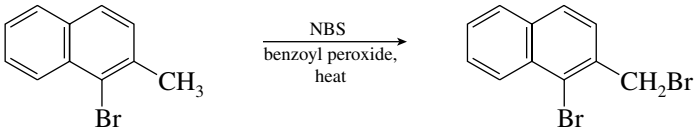
Compound D — 4-Chloropentanal (compound E) + Formaldehyde

Reduction of compound E yields the corresponding alcohol.



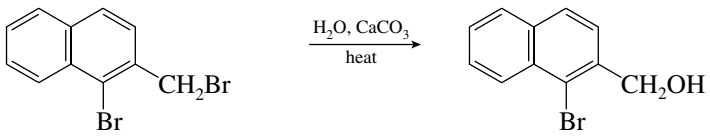
4-Chloropentanal — 4-Chloro-1-pentanol (compound F)

(*c*) *N*-Bromosuccinimide is a reagent designed to accomplish benzylic bromination.



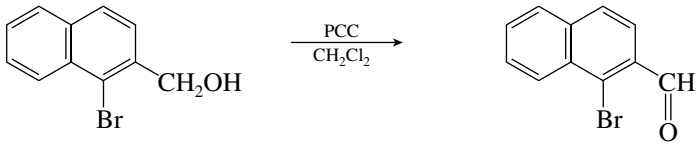
1-Bromo-2-methylnaphthalene — 1-Bromo-2-(bromomethyl)naphthalene (compound G)

Hydrolysis of the benzylic bromide gives the corresponding benzylic alcohol. The bromine that is directly attached to the naphthalene ring does not react under these conditions.



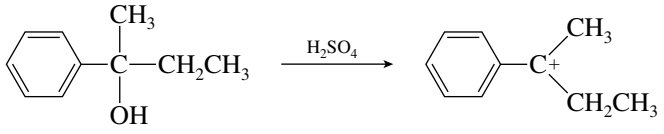
1-Bromo-2-(bromomethyl)naphthalene — (1-Bromo-2-naphthyl)methanol (compound H)

Oxidation of the primary alcohol with PCC gives the aldehyde.



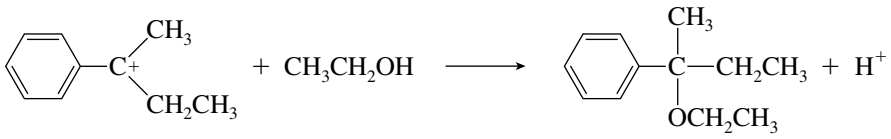
(1-Bromo-2-naphthyl)methanol — 1-Bromonaphthalene-2-carboxaldehyde (compound I)

15.38 The alcohol is tertiary and benzylic and yields a relatively stable carbocation.



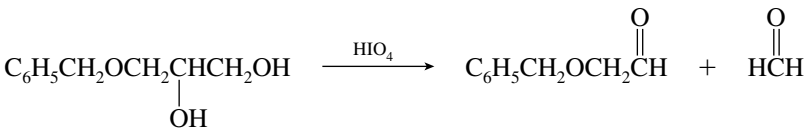
2-Phenyl-2-butanol — 1-Methyl-1-phenylpropyl cation

The alcohol is chiral, but the carbocation is not. Thus, irrespective of which enantiomer of 2-phenyl-2-butanol is used, the same carbocation is formed. The carbocation reacts with ethanol to give an optically inactive mixture containing equal quantities of enantiomers (racemic).

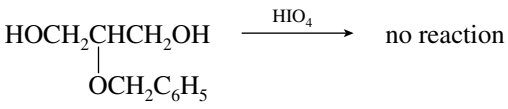


1-Methyl-1-phenylpropyl cation — Ethanol — 2-Ethoxy-2-phenylbutane (50% *R*, 50% *S*)

15.39 The difference between the two ethers is that 1-*O*-benzylglycerol contains a vicinal diol function, but 2-*O*-benzylglycerol does not. Periodic acid will react with 1-*O*-benzylglycerol but not with 2-*O*-benzylglycerol.

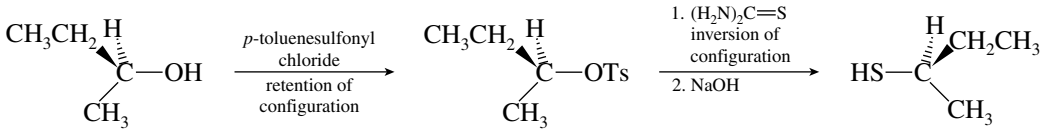


1-*O*-Benzylglycerol — 2-Benzyloxyethanal — Formaldehyde



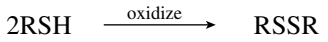
2-*O*-Benzylglycerol

15.40 The formation of an alkanethiol by reaction of an alkyl halide or alkyl *p*-toluenesulfonate with thiourea occurs with inversion of configuration in the step in which the carbon–sulfur bond is formed. Thus, the formation of (*R*)-2-butanethiol requires (*S*)-*sec*-butyl *p*-toluenesulfonate, which then reacts with thiourea by an S_N2 pathway. The *p*-toluenesulfonate is formed from the corresponding alcohol by a reaction that does not involve any of the bonds to the stereogenic center. Therefore, begin with (*S*)-2-butanol.



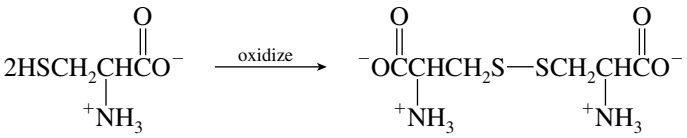
(*S*)-2-Butanol — (*S*)-*sec*-Butyl *p*-toluenesulfonate — (*R*)-2-Butanethiol

15.41 (*a*) Cysteine contains an —SH group and is a thiol. Oxidation of thiols gives rise to disulfides.



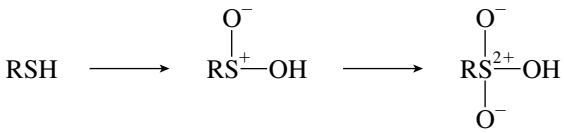
Thiol — Disulfide

Biological oxidation of cysteine gives the disulfide cystine.



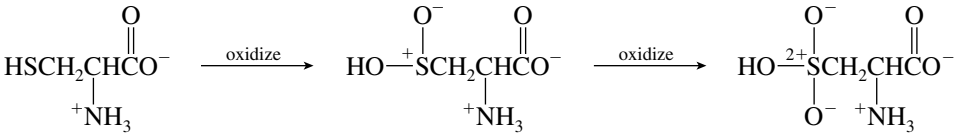
Cysteine — Cystine

(*b*) Oxidation of a thiol yields a series of acids, including a sulfinic acid and a sulfonic acid.



Thiol — Sulfinic acid — Sulfonic acid

Biological oxidation of cysteine can yield, in addition to the disulfide cystine, cysteine sulfinic acid and the sulfonic acid cysteic acid.

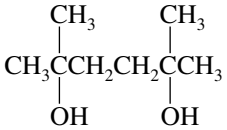


Cysteine — Cysteine sulfinic acid ($C_3H_7NO_4S$) — Cysteic acid ($C_3H_7NO_5S$)

15.42 The ratio of carbon to hydrogen in the molecular formula is C_nH_{2n+2} ($C_8H_{18}O_2$), and so the compound has no double bonds or rings. The compound cannot be a vicinal diol, because it does not react with periodic acid.

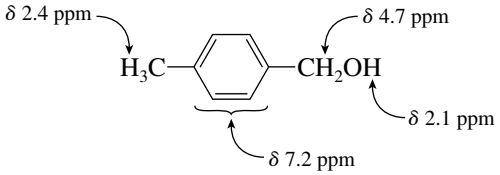
The NMR spectrum is rather simple as all peaks are singlets. The 12-proton singlet at δ 1.2 ppm must correspond to four equivalent methyl groups and the four-proton singlet at δ 1.6 ppm to two equivalent methylene groups. No nonequivalent protons can be vicinal, because no splitting is observed. The two-proton singlet at δ 2.0 ppm is due to the hydroxyl protons of the diol.

The compound is 2,5-dimethyl-2,5-hexanediol.

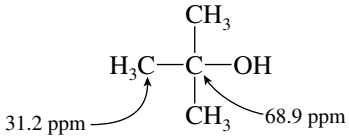


15.43 The molecular formula of compound A ($C_8H_{10}O$) corresponds to an index of hydrogen deficiency of 4. The 4 hydrogen signal at δ 7.2 ppm in the ^{1}H NMR spectrum suggests these unsaturations are due to a disubstituted benzene ring. That the ring is para-substituted is supported by the symmetry of the signal; it is a pair of doublets, not a quartet.

The broad signal (1H) at δ 2.1 ppm undergoes rapid exchange with D_2O, indicating it is the proton of the hydroxyl group of an alcohol. As the remaining signals are singlets, with areas of 2H and 3H, respectively, compound A can be identified as 4-methylbenzyl alcohol.

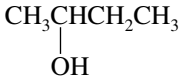


15.44 (*a*) This compound has only two different types of carbons. One type of carbon comes at low field and is most likely a carbon bonded to oxygen and three other equivalent carbons. The spectrum leads to the conclusion that this compound is *tert*-butyl alcohol.

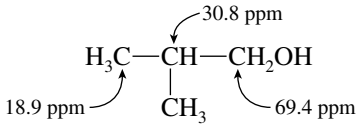


(*b*) Four different types of carbons occur in this compound. The only $C_4H_{10}O$ isomers that have four nonequivalent carbons are $CH_3CH_2CH_2CH_2OH$, $CH_3CHCH_2CH_3$ (OH), and $CH_3OCH_2CH_2CH_3$.

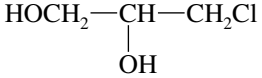
The lowest field signal, the one at 69.2 ppm from the carbon that bears the oxygen substituent, is a methine (CH). The compound is therefore 2-butanol.



(*c*) This compound has two equivalent CH_3 groups, as indicated by the signal at 18.9 ppm. Its lowest field carbon is a CH_2, and so the group —CH_2O must be present. The compound is 2-methyl-1-propanol.

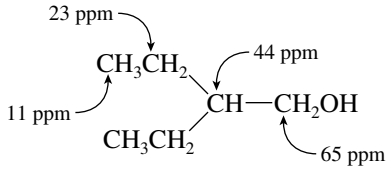


15.45 The compound has only three carbons, none of which is a CH_3 group. Two of the carbon signals arise from CH_2 groups; the other corresponds to a CH group. The only structure consistent with the observed data is that of 3-chloro-1,2-propanediol.



The structure $HOCH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2OH$ cannot be correct. It would exhibit only two peaks in its ^{13}C NMR spectrum, because the two terminal carbons are equivalent to each other.

15.46 The observation of a peak at *m/z* 31 in the mass spectrum of the compound suggests the presence of a primary alcohol. This fragment is most likely $H_2C{=}\overset{+}{O}H$. On the basis of this fact and the appearance of four different carbons in the ^{13}C NMR spectrum, the compound is 2-ethyl-1-butanol.

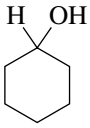


15.47–15.49 Solutions to molecular modeling exercises are not provided in this *Study Guide and Solutions Manual*. You should use *Learning By Modeling* for these exercises.

SELF-TEST

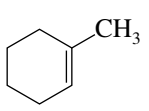
PART A

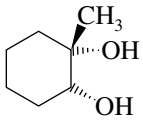
A-1. For each of the following reactions give the structure of the missing reactant or reagent.

(*a*) ? $\xrightarrow[2.\ H_2O]{1.\ LiAlH_4}$ 

(*b*) ? + $2CH_3CH_2MgBr$ $\xrightarrow[2.\ H_3O^+]{1.\ \text{diethyl ether}}$ $C_6H_5\overset{\displaystyle OH}{\underset{|}{C}}(CH_2CH_3)_2$ + CH_3CH_2OH

(*c*) $C_6H_5CH_2\overset{\displaystyle CH_3}{\underset{|}{C}}{=}CH_2$ $\xrightarrow{?}$ $C_6H_5CH_2\overset{\displaystyle CH_3}{\underset{|}{C}}HCH_2OH$

(*d*) 

$\xrightarrow{?}$ 

(*e*) $C_6H_5CH_2Br$ $\xrightarrow[2.\ NaOH]{1.\ ?}$ $C_6H_5CH_2SH$

A-2. For the following reactions of 2-phenylethanol, $C_6H_5CH_2CH_2OH$, give the correct reagent or product(s) omitted from the equation.

(*a*) $C_6H_5CH_2CH_2OH$ $\xrightarrow[CH_2Cl_2]{PCC}$?

(*b*) $C_6H_5CH_2CH_2OH$ $\xrightarrow{?}$ $CH_3CO_2CH_2CH_2$ 

(*c*) $C_6H_5CH_2CH_2OH$ (2 mol) $\xrightarrow[\text{heat}]{H^+}$ H_2O + ?

(*d*) $C_6H_5CH_2CH_2OH$ $\xrightarrow{?}$ $C_6H_5CH_2CO_2H$

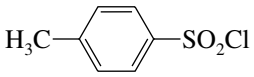
A-3. Write the structure of the major organic product formed in the reaction of 2-propanol with each of the following reagents:

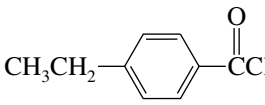
(*a*) Sodium amide ($NaNH_2$)

(*b*) Potassium dichromate ($K_2Cr_2O_7$) in aqueous sulfuric acid, heat

(*c*) PDC in dichloromethane

(*d*) Acetic acid ($CH_3\overset{\overset{O}{\|}}{C}OH$) in the presence of dissolved hydrogen chloride

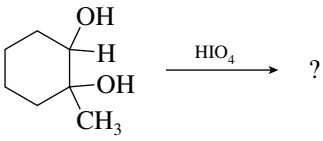
(*e*)  in the presence of pyridine

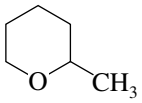
(*f*)  in the presence of pyridine

(*g*)  in the presence of pyridine

A-4. Outline two synthetic schemes for the preparation of 3-methyl-1-butanol using different Grignard reagents.

A-5. Give the structure of the reactant, reagent, or product omitted from each of the following. Show stereochemistry where important.

(*a*) 

(*b*) ? (a diol) $\xrightarrow[\text{heat}]{H^+}$ 

(*c*) ? $\xrightarrow[(CH_3)_3COH,\ HO^-]{OsO_4,\ (CH_3)_3COOH}$ 2,3-butanediol (chiral diastereomer)

A-6. Give the reagents necessary to carry out each of the following transformations:

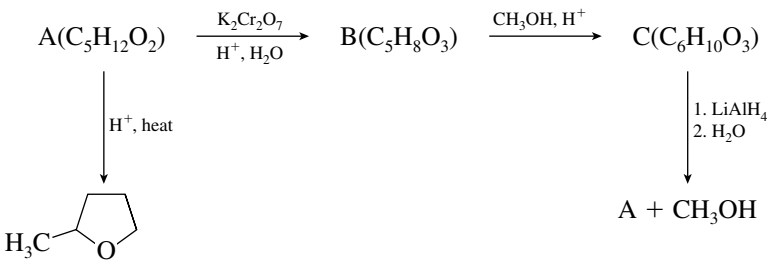
(*a*) Conversion of benzyl alcohol ($C_6H_5CH_2OH$) to benzaldehyde ($C_6H_5CH{=}O$)

(*b*) Conversion of benzyl alcohol to benzoic acid ($C_6H_5CO_2H$)

(*c*) Conversion of $H_2C{=}CHCH_2CH_2CO_2H$ to $H_2C{=}CHCH_2CH_2CH_2OH$

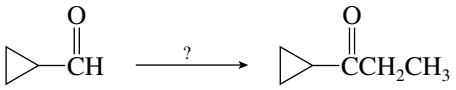
(*d*) Conversion of cyclohexene to *cis*-1,2-cyclohexanediol

A-7. Provide structures for compounds A to C in the following reaction scheme:



A-8. Using any necessary organic or inorganic reagents, outline a scheme for each of the following conversions.

(*a*) $(CH_3)_2C{=}CHCH_3 \xrightarrow{?} (CH_3)_2CHC(=O)CH_3$

(*b*) 

(*c*) $C_6H_5CH_3 \xrightarrow{?} C_6H_5CH_2CH_2CO_2CH_2CH_3$

PART B

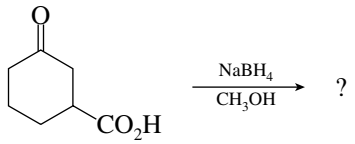
B-1. Ethanethiol (CH_3CH_2SH) is a gas at room temperature, but ethanol is a liquid. The reason for this is

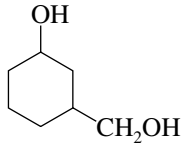
(*a*) The C—S—H bonds in ethanethiol are linear.
(*b*) The C—O—H bonds in ethanol are linear.
(*c*) Ethanol has a lower molecular weight.
(*d*) Ethanethiol has a higher boiling point.
(*e*) Ethanethiol is less polar.

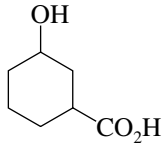
B-2. Which of the following would yield a secondary alcohol after the indicated reaction, followed by hydrolysis if necessary?

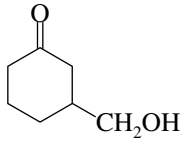
(*a*) $LiAlH_4$ + a ketone
(*b*) CH_3CH_2MgBr + an aldehyde
(*c*) 2-Butene + aqueous H_2SO_4
(*d*) All of these

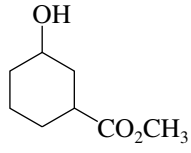
B-3. What is the major product of the following reaction?



(*a*) 

(*c*) 

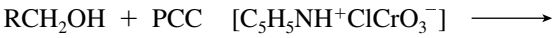
(*b*) 

(*d*) 

B-4. Which of the esters shown, after reduction with $LiAlH_4$ and aqueous workup, will yield two molecules of only a single alcohol?

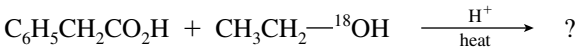
(*a*) $CH_3CH_2CO_2CH_2CH_3$
(*b*) $C_6H_5CO_2C_6H_5$
(*c*) $C_6H_5CO_2CH_2C_6H_5$
(*d*) None of these

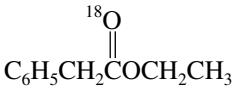
B-5. For the following reaction, select the statement that best describes the situation.

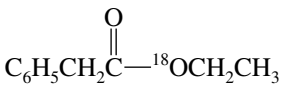


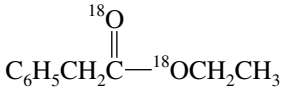
(*a*) The alcohol is oxidized to an acid, and the Cr(VI) is reduced.
(*b*) The alcohol is oxidized to an aldehyde, and the Cr(VI) is reduced.
(*c*) The alcohol is reduced to an aldehyde, and the Cr(III) is oxidized.
(*d*) The alcohol is oxidized to a ketone, and the Cr(VI) is reduced.

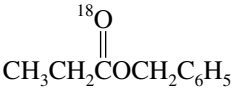
B-6. What is the product from the following esterification?



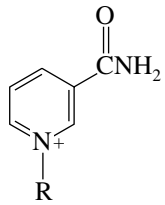
(*a*) 

(*b*) 

(*c*) 

(*d*) 

B-7. The following substance acts as a coenzyme in which of the following biological reactions?



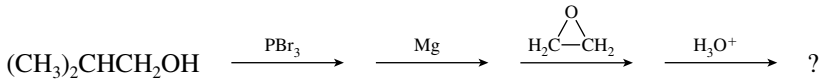
(R = adenine dinucleotide)

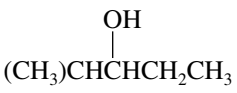
(*a*) Alcohol oxidation
(*b*) Ketone reduction
(*c*) Aldehyde reduction
(*d*) None of these

B-8. Which of the following alcohols gives the best yield of dialkyl ether on being heated with a trace of sulfuric acid?

(*a*) 1-Pentanol
(*b*) 2-Pentanol
(*c*) Cyclopentanol
(*d*) 2-Methyl-2-butanol

B-9. What is the major organic product of the following sequence of reactions?



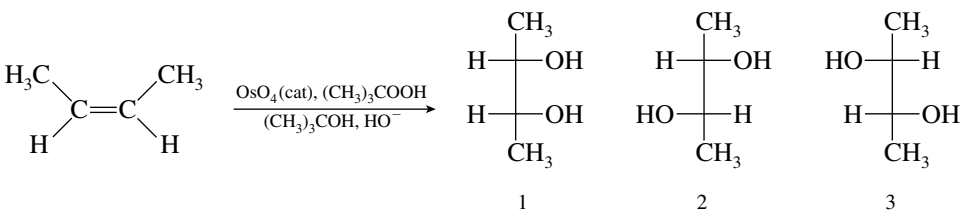
(*a*) 

(*b*) 

(*c*) $(CH_3)_2CHCH_2CH_2OH$

(*d*) $(CH_3)_2CHCH_2CH_2CH_2OH$

B-10. What is the product of the following reaction?

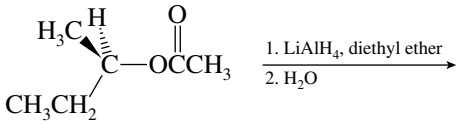


1 2 3

(*a*) Only 1
(*b*) Only 2
(*c*) Only 3
(*d*) A 1:1 mixture of 2 and 3.
(*e*) A 1:1:1 mixture of 1, 2, and 3.

B-11. Which reaction is the best method for preparing (*R*)-2-butanol?

(*a*) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_3 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4,\ \text{diethyl ether}}$

(*b*) 

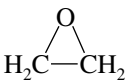
$\xrightarrow[2.\ H_2O]{1.\ LiAlH_4,\ \text{diethyl ether}}$

(*c*) $CH_3CH_2\overset{\overset{O}{\|}}{C}H \xrightarrow[2.\ H_3O^+]{1.\ CH_3MgBr,\ \text{diethyl ether}}$

(*d*) $CH_3\overset{\overset{O}{\|}}{C}H \xrightarrow[2.\ H_3O^+]{1.\ CH_3CH_2Li,\ \text{diethyl ether}}$

(*e*) None of these would be effective.

B-12. An organic compound B is formed by the reaction of ethylmagnesium iodide (CH_3CH_2MgI) with a substance A, followed by treatment with dilute aqueous acid. Compound B does *not* react with PCC or PDC in dichloromethane. Which of the following is a possible candidate for A?

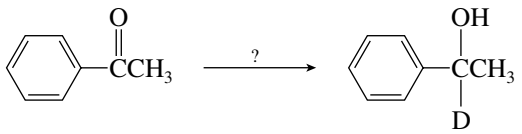
(*a*) $CH_3\overset{\overset{O}{\|}}{C}H$
(*b*) $H_2C{=}O$
(*c*) 

(*d*) $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_3$
(*e*) None of these

B-13. Which alcohol of molecular formula $C_5H_{12}O$ has the fewest signals in its ^{13}C NMR spectrum?

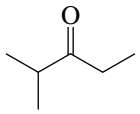
(*a*) 1-Pentanol
(*b*) 2-Pentanol
(*c*) 2-Methyl-2-butanol
(*d*) 3-Methyl-2-butanol
(*e*) 2,2-Dimethyl-1-propanol

B-14. Which of the following reagents would carry out the following transformation? (D = ^2H, the mass-2 isotope of hydrogen)



(*a*) $NaBD_4$ in CH_3OH
(*b*) $NaBD_4$ in CH_3OD
(*c*) $LiAlH_4$, then D_2O
(*d*) $LiAlD_4$, then D_2O
(*e*) $NaBH_4$ in CH_3OD

B-15. Which sequence of steps describes the best synthesis of 2-methyl-3-pentanone?



2-Methyl-3-pentanone

(*a*) 1. 1-Propanol + $(CH_3)_2CHMgBr$, diethyl ether
2. H_3O^+
3. PDC, CH_2Cl_2

(*b*) 1. 1-Propanol + $Na_2Cr_2O_7$, H_2SO_4, H_2O, heat
2. $SOCl_2$
3. $(CH_3)_2CHCl$, $AlCl_3$

(*c*) 1. 1-Propanol + PCC, CH_2Cl_2
2. $(CH_3)_2CHLi$, diethyl ether
3. H_3O^+
4. $Na_2Cr_2O_7$, H_2SO_4, H_2O, heat

(*d*) 1. 2-Propanol + $Na_2Cr_2O_7$, H_2SO_4, H_2O, heat
2. $CH_3CH_2CH_2Li$, diethyl ether
3. H_3O^+
4. PCC, CH_2Cl_2