

Chapter 10 Alcohols, Phenols, and Ethers

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Problems

Answers

Of the elements to compose organic compounds, oxygen is widely distributed and excels all other elements in this regard except carbon and hydrogen. Many molecules occurring in nature contain oxygen in their functional groups. It is quite understandable since our earth is covered with air and get wet with water.

In organic compounds, oxygen can exist both in sp^3 hybridized and sp^2 hybridized states. In this chapter, compounds containing sp^3 hybridized oxygen atoms will be treated. These are roughly classified into two groups, *i.e.*, one with hydroxy groups and others with ether bonds. The former is further classified into two groups, alcohols in which hydroxy groups are bonded with aliphatic hydrocarbon moieties, and phenols in which hydroxy groups are bonded with aromatic hydrocarbon moieties.

Though having the same hydroxy group, the properties of alcohols and phenols are considerably different, and it will be appropriate to treat them separately.

10.1 Properties and nomenclature of alcohols, phenols, and ethers

(a) Alcohols

(1) Properties and types of alcohols

Compounds in which hydrogen atom(s) is replaced by hydroxy group(s) (-OH) are named alcohols. Because of hydrophilic property of hydroxy group, alcohols with small molecular weight are readily soluble in water. As the molecular weight increases, the hydrophobic effect of hydrocarbon moieties will become more important, and alcohols are less soluble in water and more soluble in organic solvents.

The boiling and melting points of alcohols are considerably higher than these of alkanes with much the same molecular weight. For instance, the melting and boiling points of ethanol (M = 46) are -115 °C and 78 °C, respectively, while these of propane (M = 44) are -188 °C and -42 °C, respectively. Much the same is true for phenols.

This is because alcohols and phenols associate themselves *via* the intermolecular hydrogen bond (Figure 10.1). The bond energy of a hydrogen bond is *ca.* 20 kJ mol⁻¹ and only about 1/20 of that of typical O-H bond (4000 kJ mol⁻¹). However, the energy required in melting or vaporization of alcohols and phenols is larger than that of hydrocarbon due to breaking of the hydrogen bond. This is the reason for higher melting and boiling points of alcohols.

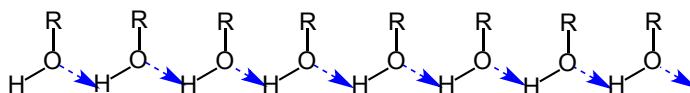


Figure 10.1 Hydrogen bond of alcohol

Some alcohols, which have two hydroxy groups, are called “diol”, and those with three hydroxy groups are called “triol”. Alcohols with several hydroxy groups are “polyol”. Alcohols are classified into three groups, primary, secondary, and tertiary, depending on the substitution state of the carbon atom to which the hydroxy group is bonded.

(2) Nomenclature of alcohols

Similar with halides, alcohols can be named based on both substitutive and radicofunctional nomenclatures. In substitutive names, the end of alkanes “ane” is changed to “ol”. In radicofunctional names, the name of the functional group and alcohol are combined. Do not mix, however, two methods.

[Example] CH₃CH(OH)CH₃

2-propanol (substitutive)

isopropyl alcohol (radicofunctional)

isopropanol (error; mixed use)

[Example] C₆H₅CH₂OH

phenylmethanol (substitutive)

benzyl alcohol (radicofunctional)

Exercise 10.1 Naming of alcohols

- (1) Give names to the compounds below.
- (a) $(\text{CH}_3)_2\text{C}(\text{OH})\text{CH}_3$
 (b) $\text{CH}_3\text{CH}(\text{OH})\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$
- (2) Draw the structural formulas of the compounds below.
- (a) 3-hexanol
 (b) 3-bromo-2-butanol

Answer

- (1) (a) 2-methyl-2-propanol
 (b) 1,4-pentanediol
- (2) (a) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}_3$
 (b) $\text{CH}_3\text{CHBrCH}(\text{OH})\text{CH}_3$

In Table 10.1, representative alcohols are summarized.

Table 10.1 Representative alcohols*

| name | simple structural formula | m.p. (°C) | b.p. (°C) |
|--|---|-----------|--------------------|
| methanol (methyl alcohol) | CH_3OH | -97.78 | 64.65 |
| ethanol (ethyl alcohol) | $\text{CH}_3\text{CH}_2\text{OH}$ | -114.5 | 78.32 |
| 1-propanol (<i>n</i> -propyl alcohol) | $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ | -126.5 | 97.15 |
| 2-propanol (isopropyl alcohol) | $(\text{CH}_3)_2\text{CHOH}$ | -89.5 | 82.4 |
| 1-butanol (<i>n</i> -butyl alcohol) | $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ | -89.53 | 117.25 |
| 2-butanol (<i>s</i> -butyl alcohol) | $\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}_3$ | -114.7 | 98.5 ¹⁾ |
| 2-methyl-1-propanol (isobutyl alcohol) | $(\text{CH}_3)_2\text{CHCH}_2\text{OH}$ | -108 | 108 |
| 2-methyl-2-propanol (<i>t</i> -butyl alcohol) | $(\text{CH}_3)_3\text{COH}$ | 25.6 | 82.50 |
| 1,2-ethanediol (ethylene glycol**) | $\text{HOCH}_2\text{CH}_2\text{OH}$ | -12.6 | 197.85 |
| 1,2,3-propanetriol (glycerin**) | $\text{HOCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$ | 17.8 | 154 ²⁾ |
| phenylmethanol (benzyl alcohol) | $\text{C}_6\text{H}_5\text{CH}_2\text{OH}$ | -15.5 | 205.41 |

* substitutive name (radicofunctional name) **common name

¹⁾ 740 mmHg ²⁾ 5 mmHg

(b) Phenols**(1) Properties and types of phenols**

Phenols are aromatic compounds which possess hydroxy group(s) directly bonded to the aromatic ring. Some phenols have two or more than two hydroxy groups.

Phenols are weakly acidic, and dissolve in water to some extent. The solubility in organic solvents is generally large. Phenols are liquids or solids at standard temperature, and many of them have strong smell. Phenols have sterilizing power. Phenol has, in particular, long been used as a disinfectant or a sterilizer.

(2) Nomenclature of phenols

Because a small amount of phenol is contained in coal, it was once named carbolic acid. Its old Japanese name was “acid of coal”. From the 19th century, a variety of phenols were produced by dry distillation of coal, including cresol, hydroquinone, *etc.*, and those are called by common

names (see Table 10.2). Most of them are allowed to use.

When the substitutive name of systematic nomenclature is used, phenols are treated as the derivatives of arenes, and hence the hydroxy group is represented by the suffix “-ol”.

[Example] C_6H_5OH

phenol (common name; allowed to use)

benzeneol (substitutive name)

[Example] $o\text{-}C_6H_4(OH)_2$

catechol (common name; allowed to use)

benzene-1,2-diol (substitutive name)

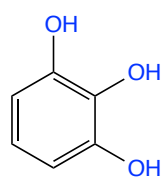
Metal salts of phenols are named “phenoxides”.

[Example] C_6H_5ONa

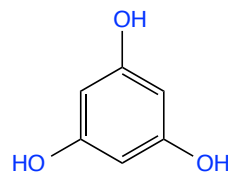
sodium phenoxide

Exercise 10.2 Nomenclature of phenols

Give the substitutive names of the following trivalent phenols.



(a) pyrogallol



(b) phloroglucinol

Answer

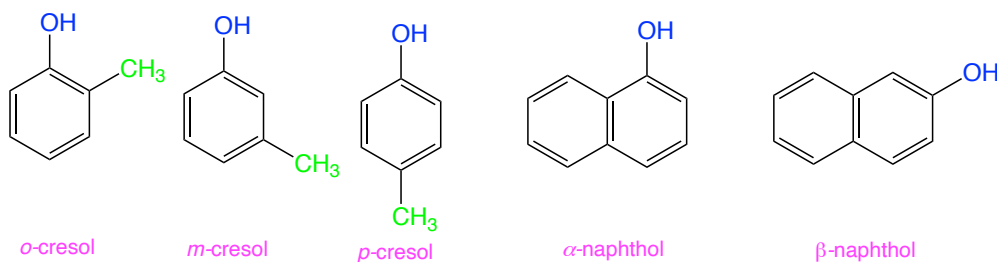
(a) benzene-1,2,3-triol

(b) benzene-1,3,5-triol

Table 10.2 Representative phenols*

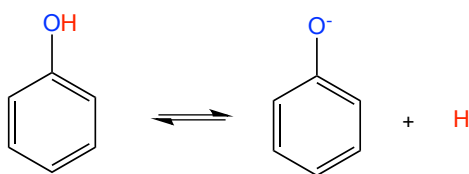
| name | simplified structural formula | m.p. (°C) | b.p. (°C) | pKa |
|------------------------------------|---------------------------------------|-----------|--------------------|-------|
| phenol | C_6H_5OH | 40.95 | 181.75 | 9.82 |
| <i>o</i> -cresol | $C_6H_4(OH)(CH_3)(1,2\text{-})$ | 31 | 191 | 10.28 |
| <i>m</i> -cresol | $C_6H_4(OH)(CH_3)(1,3\text{-})$ | 11.9 | 202.7 | 10.09 |
| <i>p</i> -cresol | $C_6H_4(OH)(CH_3)(1,4\text{-})$ | 34.7 | 201.9 | 10.26 |
| <i>o</i> -nitrophenol | $C_6H_4(OH)(NO_2)(1,2\text{-})$ | 45.8 | 96.4 ¹⁾ | 7.23 |
| <i>m</i> -nitrophenol | $C_6H_4(OH)(NO_2)(1,3\text{-})$ | 97.6 | 194 ²⁾ | 8.40 |
| <i>p</i> -nitrophenol | $C_6H_4(OH)(NO_2)(1,4\text{-})$ | 114.9 | 186 ³⁾ | 7.15 |
| 2,4-dinitrophenol | $C_6H_4(OH)(NO_2)_2(1,2,4\text{-})$ | 114 | - | 4.11 |
| 2,4,6-trinitrophenol (picric acid) | $C_6H_4(OH)(NO_2)_3(1,2,4,6\text{-})$ | 122.5 | 255 ⁴⁾ | 0.29 |
| 1-naphthol (α -naphthol) | $1\text{-}C_{10}H_7OH$ | 96 | 288 | 9.14 |
| 2-naphthol (β -naphthol) | $2\text{-}C_{10}H_7OH$ | 122 | 296 | 9.31 |

* common name ¹⁾ 10 mmHg ²⁾ 70 mmHg ³⁾ 18.7 mmHg ⁴⁾ 50 mmHg



(3) Acidity of phenols

Phenol itself dissolves in water to some extent, and its aqueous solution is slightly acidic but its acidity is too weak to be positive to litmus paper and other test papers ($pK_a = 9.82$ (25 C°)).



One of the unshared electron pairs of negatively charged oxygen atom of the phenoxide ion generated by the electronic dissociation of phenol flows into the C-O bond. Pushed by the flow, the π electrons of C=C bond move into *o*-carbon. As a result, a resonance structure (B) which possesses negative charge on *o*-carbon is formed, and the phenoxide is stabilized (Figure 10.2).

By a similar migration of electron, the resonance formula (B) with negative charge on α -carbon atom is obtained. In this way, the phenoxide ion is stabilized by four resonance formulas including the one with negative charge on *o*-carbon atom. This is the reason why phenol is weakly acidic. No such resonance stabilization is involved with alkoxide ions obtained from alcohol.

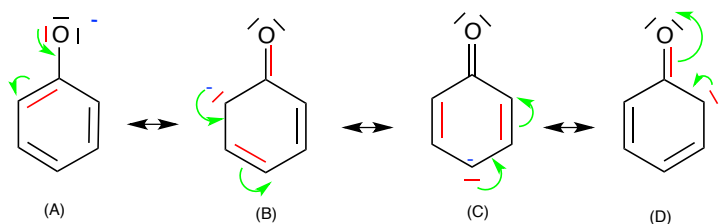


Figure 10.2 Resonance structure of phenol

(4) Acidity of substituted phenols

If the acidity of phenol can be explained by the above mechanism, the variation of acidity of substituted phenols caused by substituents can easily be predicted. Thus, if an electron-withdrawing group is on either *o*- or *p*-position, the acidity will be enhanced by the delocalization of electron on oxygen atom. If an electron-donating group is on either *o*- or *p*-position, the acidity will be reduced by the delocalization of electron on oxygen atom.

pK_a values in Table 10.2 indicate that the effect of an electron-donating methyl group is not clear, but the effect of electron-withdrawing nitro group is very clear. If a nitro group is introduced to a position conjugating with the hydroxy group, the acidity will be enhanced.

(c) Ethers

(1) Structure and property of ethers

The general structural formula of ethers is R-O-R. That is, two hydrocarbon groups are bonded to an oxygen atom. The largest characteristic property of ethers, liquid ether in particular, is a superior solubility to organic compounds. Diethyl ether easily dissolves many organic compounds. Diethyl ether is often used to extract organic compounds from aqueous solution. Diethyl ether is a little soluble in water, but the dissolved water can easily be removed from diethyl ether by some desiccants.

The boiling point of diethyl ether is very much lower than alcohols with much the same molecular weight. The reason is that in ethers no hydrogen bonding is involved. The low boiling point of diethyl ether is advantageous as a solvent to be used for extraction, but it is highly inflammable, and care should be taken to handle in the laboratory.

(2) Nomenclature of ethers

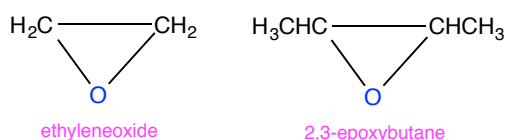
The general formula of ethers is R-O-R'. When substitutive system is employed, they are named as derivatives of hydrocarbon RH of higher priority. When radicofunctional nomenclature is employed, ethers are named as derivatives of radicofunctional name "ether". Frequently used ethers are often named after radicofunctional system.

[Example] $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$
 ethoxyethane (substitutive name)
 diethyl ether (radicofunctional name)

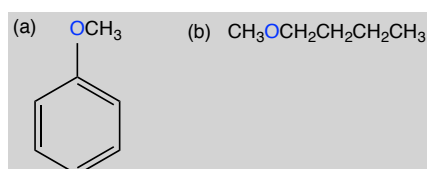
[Example] $\text{CH}_3\text{OCH}=\text{CH}_2$
 methoxyethylene (substitutive name)
 methyl vinyl ether (radicofunctional name)

The partial structure made from an oxygen atom attached to two connected carbon atoms is named by prefix "epoxy". However, the parent structure is frequently referred to "epoxide".

[Example]

**Exercise 10.3** Naming of ethers

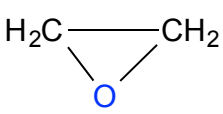
Name the following compounds.

**Answer**

- (a) methoxybenzene (substitutive name), methyl phenyl ether (radicofunctional name), anisole (common name; very popular)
 (b) 1-methoxybutane (substitutive name), butyl methyl ether (radicofunctional name)

In Table 10.3, some examples of ethers are given.

Table 10.3 Representative ethers*

| name | simple structure | m.p. (°C) | b.p. (°C) |
|--------------------------------|---|-----------|-----------|
| dimethyl ether | CH ₃ OCH ₃ | -141.50 | -24.82 |
| ethyl methyl ether | CH ₃ OCH ₂ CH ₃ | — | 6.6 |
| diethyl ether | CH ₃ CH ₂ OCH ₂ CH ₃ | -116.3 | 34.48 |
| dibutyl ether | (CH ₃ CH ₂ CH ₂ CH ₂) ₂ O | -95.35 | 141.97 |
| methyl phenyl ether (anisole)* | C ₆ H ₅ OCH ₃ | -37.5 | 153.85 |
| ethyl phenyl ether (phenetol)* | C ₆ H ₅ OCH ₂ CH ₃ | -29.5 | 170.0 |
| diphenyl ether | C ₆ H ₅ OC ₆ H ₅ | 26.90 | 259.0 |
| epoxyethane (ethylene oxide) |  | -112 | 10.73 |

* common name

10.2 Structure and reactions of alcohols

(a) Structure of alcohols

The states of the hybridization orbitals of carbon atoms largely influence the shape of compounds, and similarly the states of the hybridization orbitals of atoms constituting functional groups largely influence the shape of compounds.

The electron configuration of oxygen atoms in the ground state is $1s^2 2s^2 2p_x^2 2p_y^1 2p_z^1$. If four atomic orbitals, $2s$, $2p_x$, $2p_y$, and $2p_z$, are hybridized, four sp^3 hybridized orbitals with the same energy are generated (Figure 10.3). Four orbitals stretch to the directions of four vertices from the center of tetrahedron. Two out of four hybridization orbitals possess unshared electron pairs.

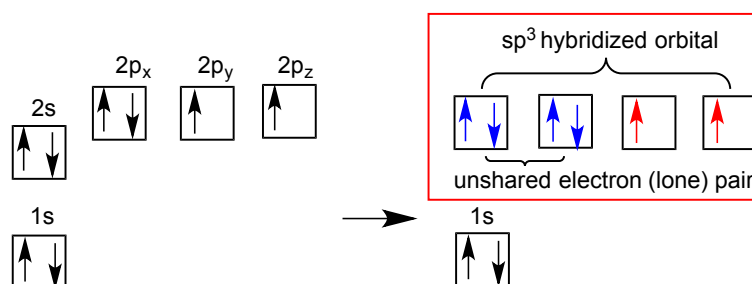


Figure 10.3 Atomic orbitals of oxygen atom

In water molecules, the remaining two sp^3 hybridized orbitals overlap with $1s$ orbitals of hydrogen atoms. In Figure 10.4 the structure of water molecule represented by the overlaps of atomic orbitals is given.

Different from methane, the bond angle (104.5°) made by two O—H bonds is a little smaller than tetrahedral angle. The structure of water is the basis of the structures of alcohols and ethers.

When one hydrogen atom of water molecule is replaced by a hydrocarbon residue, an alcohol or a phenol is formed. When two hydrogen atoms of water molecules are replaced by hydrocarbon residues, an ether is formed.

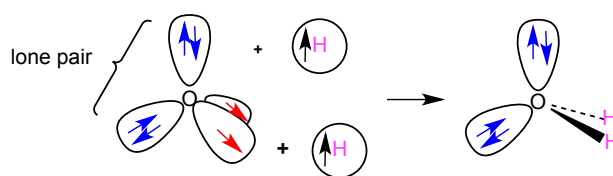


Figure 10. 4 Structure of water

(b) Polarity of alcohols

The oxygen atom of the hydroxy group, the functional group of alcohols, has a large electronegativity. Because of this, polarization of electric charge takes place. It can be assumed that the negative charge δ^- locates on the oxygen atom of hydroxy group, and the positive δ^+ locates on the hydrogen atom of hydroxy group (Figure 10.5). This polarization is the driving force of the reactivity of alcohols.

The structure (A) of Figure 10.5 shows the possibility that alcohols dissociate and behave as an acid. Since the degree of dissociation is extremely small (Ch. 3.1(c)), alcohols are generally regarded neutral.



The acidity of alcohols is considerably larger than that of hydrocarbons, but a little weaker than that of water.

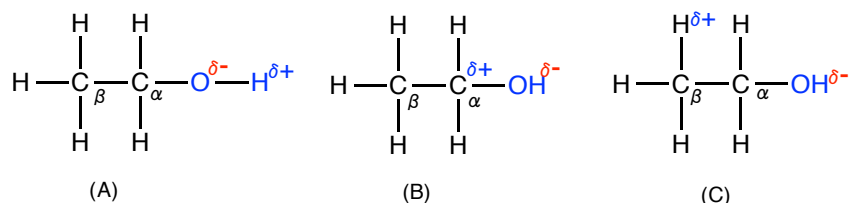
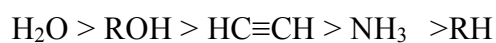


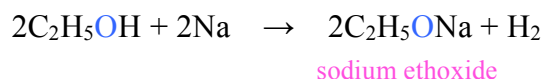
Figure 10.5 Polarization of ethanol

Point: Order of strength of acidity

(This point was already discussed. Just for confirmation)



Alcohols react with such alkali metals as sodium and potassium to yield hydrogen and alkoxides. Alkoxides are strong bases and at the same time nucleophiles.

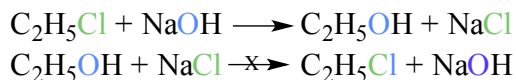


(c) Nucleophilic substitution

The polarization structure (B) of ethanol given in Figure 10.5 indicates that alcohols are susceptible to S_N type (nucleophilic substitution) reactions as halides do. The polarization structure (C) indicates that alcohols are also susceptible to E type (nucleophilic elimination) reactions. Hydroxide ions are strong nucleophiles, but poor leaving groups. As a result, when

alcohols react with nucleophilic reagents, substitution reactions do not necessarily take place.

For instance, ethyl chloride reacts with sodium hydroxide to give ethanol, but the reverse reaction does not take place. These are understandable if the strength of nucleophilic reagents and leaving ability of leaving groups are taken into consideration.



OH^- ion is a strong nucleophile and a poor leaving group. Cl^- ion is, when compared with OH^- a weaker nucleophile and the leaving ability is larger.

(d) Acid-catalyzed nucleophilic substitution

Under an acidic condition, nucleophilic substitutions readily occur with alcohols. The reason is as follows. As mentioned before, a hydroxy group is a strong nucleophile but a poor leaving group. Under an acidic condition, however, a proton coordinates with the oxygen atom of the hydroxy group. In protonated alcohols, the leaving group is not a hydroxy group, but water, which is much easy to leave. Hence an elimination readily takes place. One example of this situation is the formation of *t*-butyl chloride from the reaction between *t*-butyl alcohol and conc. hydrochloric acid by $\text{S}_{\text{N}}1$ mechanism.

The 1st stage of the reaction (1) is the formation of an oxonium-type intermediate formed by the coordination of proton with the oxygen atom (Figure 10.6).

The 2nd stage (2) is the elimination of water to give a carbocation. The carbon atom will become sp^2 hybridized so that the overcrowding is reduced.

The 3rd stage (3) is the bonding of carbocation with chloride ion to yield *t*-butyl chloride. In this reaction, the reactivity of *t*-butyl alcohol is very high and the reaction takes place by just mixing them at room temperature. It must be added that, as mentioned before, eliminations as well as substitutions take place.

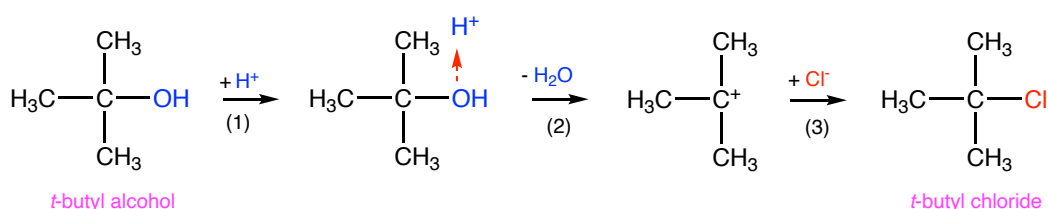


Figure 10.6 Acid-catalyzed nucleophilic substitution of *t*-butyl alcohol

Though acid-catalyzed nucleophilic substitutions take place with primary and secondary alcohols, their reactivity is considerably lower, and heating is required. Under such conditions $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ occur simultaneously.



When alkyl halides are to be synthesized, thionyl chloride SOCl_2 , which is a strong reagent, should be used instead of hydrogen chloride HCl .

Preparation of diethyl ether from ethanol under the acid-catalyzed condition (under the

presence of concentrated sulfuric acid at 140 °C) is a kind of acid-catalyzed nucleophilic substitution.

The 1st stage (1) of the reaction is the addition of a proton to alcohol to enhance the reactivity of ethanol.

The 2nd stage (2) is the attack of the second alcohol to the carbocation center of the 1st alcohol.

The 3rd stage (3) is the removal of water molecule.

The 4th stage (4) is the removal of proton (Figure 10.7).

The figure is prepared in stepwise manner so that the details of the reaction would be clear. Since ethanol is a primary alcohol, the reaction proceeds by S_N2 mechanism.

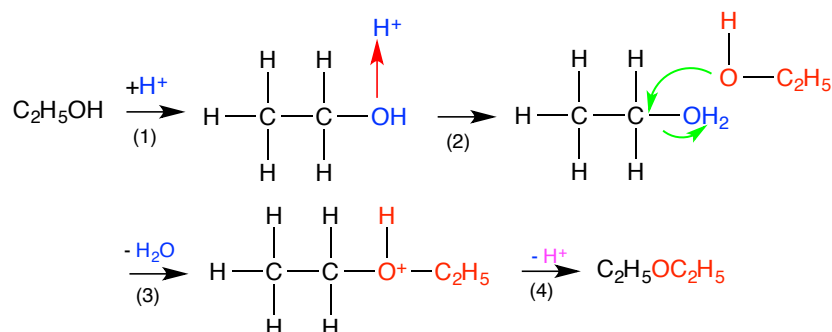


Figure 10.7 Formation of diethyl ether from ethanol.

The formation of ethers by dehydration of alcohols is practically important, but this reaction can form only symmetrical ether R-O-R. For the formation of asymmetric ether R-O-R', the Williamson synthesis (Ch. 9.3) must be used.

Exercise 10.4 Synthesis of ether

An attempt was made to synthesize methyl propyl ether $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_3$ from methanol CH_3OH and propanol $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ by heating a mixture of them. Compounds other than the objects were, however, obtained. Draw the structures of these ethers.

Answer

The following ethers will be obtained together with the object ether.
dimethyl ether (CH_3OCH_3), dipropyl ether ($\text{CH}_3\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_3$)

(e) Eliminations

When *t*-butyl alcohol reacts with concentrated sulfuric acid, a carbocation intermediate is firstly formed as is the case with concentrated hydrochloric acid. This intermediate is dehydrated to give an alkene by E1 mechanism (Figure 10.8). The reason why an elimination, rather than a substitution, takes place in this case is that there is no appropriate nucleophile.

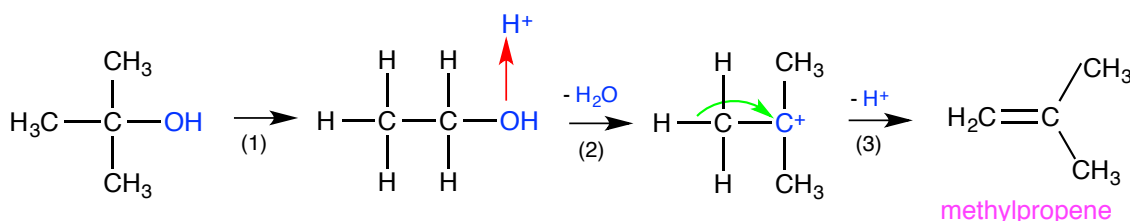


Figure 10.8 Acid-catalyzed elimination of *t*-butyl alcohol

An elimination readily takes place for tertiary alcohols but heating is required for primary and secondary alcohols. The reaction proceeds by E2 type with *trans*-elimination mechanism.

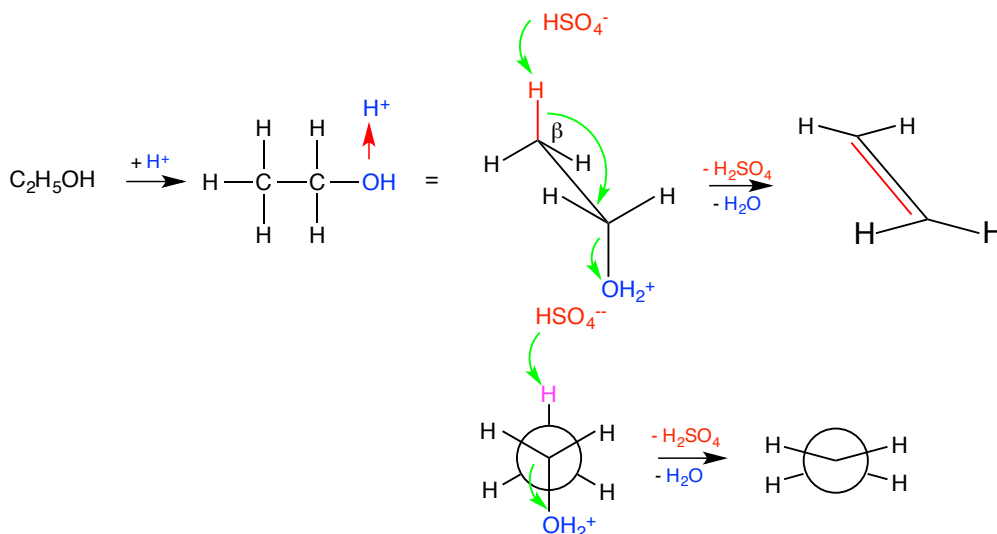
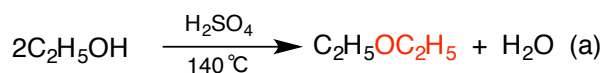
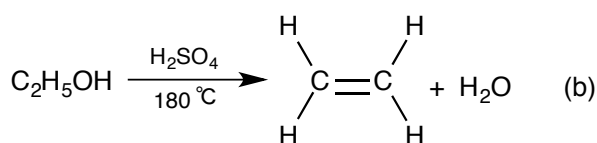


Figure 10.9 Acid-catalyzed elimination of ethanol

It was already mentioned that when a mixture of ethanol and concentrate sulfuric acid is heated at $140\text{ }^\circ\text{C}$, diethyl ether is obtained by S_N type intermolecular dehydration (Figure 10.10 (a)). On the other hand, when the mixture is heated at $180\text{ }^\circ\text{C}$, E type intermolecular dehydration will occur and ethylene is formed (Figure 10.10 (b)).



(intermolecular dehydration; S_N type reaction)



(intramolecular dehydration; E type reaction)

Figure 10.10 Substitution and elimination of ethanol

The orientation of the elimination is the same with the elimination of hydrogen halides from haloalkanes. It is expected that the orientation will follow the Saitzeff rule (Ch. 9.3(d)), and indeed this is the case (Figure 10.11).

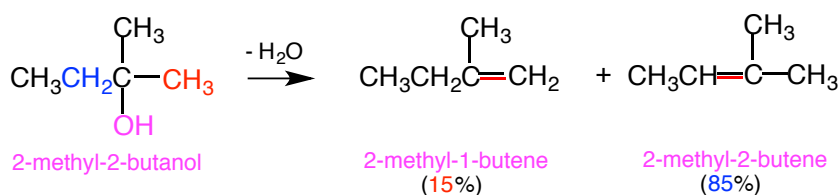


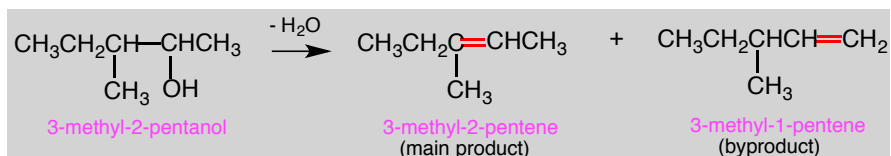
Figure 10.11 Orientation of elimination

Exercise 10.5 Orientation of elimination

Predict the structure of the main product of dehydration of 3-methyl-2-pentanol.

Answer

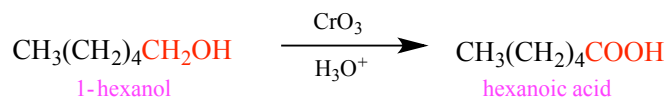
Following the Saitzeff rule, the main product is the more branched one.

**(f) Oxidation**

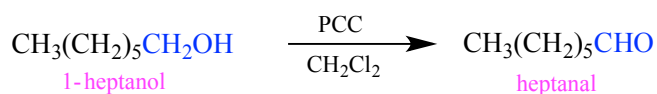
Oxidations are one of the most important reactions of alcohols. The structures of oxidation products depend on the structure of alcohols. Primary alcohols are oxidized to carboxylic acid *via* aldehydes, and secondary alcohols to ketones, but tertiary alcohols are somewhat difficult to oxidize.

Commonly used oxidizing agents contain Cr(VI) or Mn(VII). Chromium trioxide (CrO_3), sodium dichromate $\text{Na}_2\text{Cr}_2\text{O}_7$ acidified with sulfuric acid, and potassium permanganate KMnO_4 are representative oxidizing agents.

Oxidation of primary alcohols by chromium trioxide or sodium dichromate acidified with sulfuric acid does not stop at the stage of aldehydes and proceeds to the stage of carboxylic acids

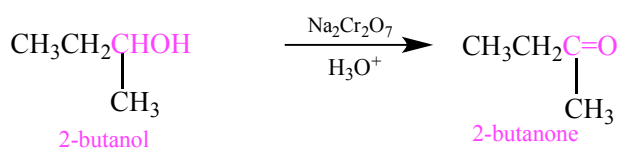


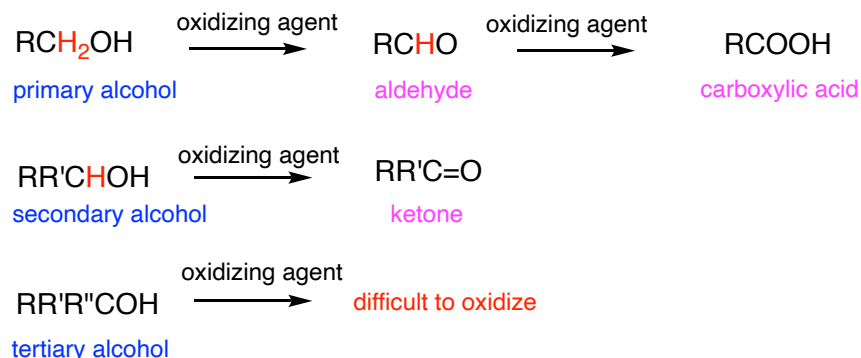
It is necessary to use milder oxidizing agent if the oxidation should be stopped at the stage of aldehydes. Pyridinium chlorochromate $\text{C}_5\text{H}_6\text{NCr}_3\text{Cl}$ (PCC) is one of such oxidizing agents.



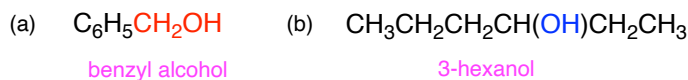
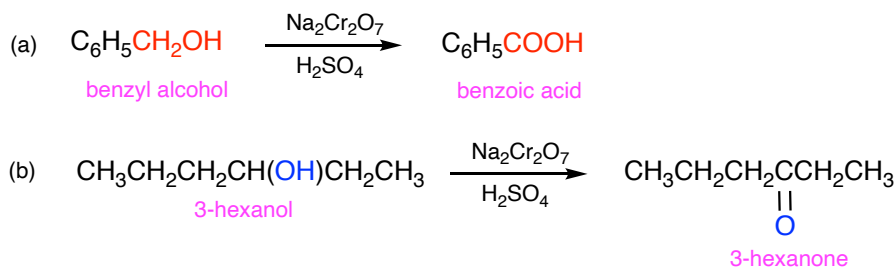
The yields of these oxidation reactions are generally good.

For the oxidation of secondary alcohols to ketones, sodium dichromate acidified with sulfuric acid is employed.



Point: Oxidation of alcohols**Exercise 10.6** Oxidation of alcohols

Predict the products of the following oxidation of alcohols by sodium permanganate acidified with sulfuric acid.

**Answer****10.3 Reaction of phenols****(a) Electrophilic substitution**

In Figure 10.2, it was shown that the negative charge on oxygen atom of phenoxide ion flows into the *o*- and *p*-carbon atoms of the benzene ring with the aid of resonance. This type of resonance structures associated with phenoxide ions is also possible for phenols themselves, and in fact for the benzene ring of phenol, resonance structure with negative charges on *o*- and *p*-carbon atoms are possible (Figure 10.12).

This type of resonance structure is much the same with that considered for haloarenes. In terms of the substituent effect, the hydroxy group of phenol exerts -*R* effect and activate the benzene ring to show *o*, *p*-directing effect.

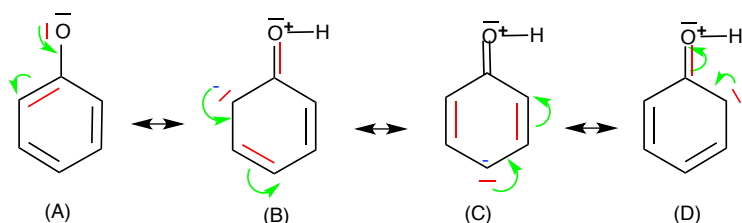


Figure 10.12 Resonance structures of phenol

An oxygen atom is, however, electronegative, and shows $+I$ effect to behave as an electron withdrawing group ($+I$). As a result, the benzene ring is deactivated.

In fact, the nitration of phenol proceeds at $20\text{ }^{\circ}\text{C}$, showing that nitration of phenol is easier than that of benzene (Figure 10.13). Thus, the benzene ring is activated by a hydroxy group. Thus, the hydroxy group is an activating group for electrophilic substitution.

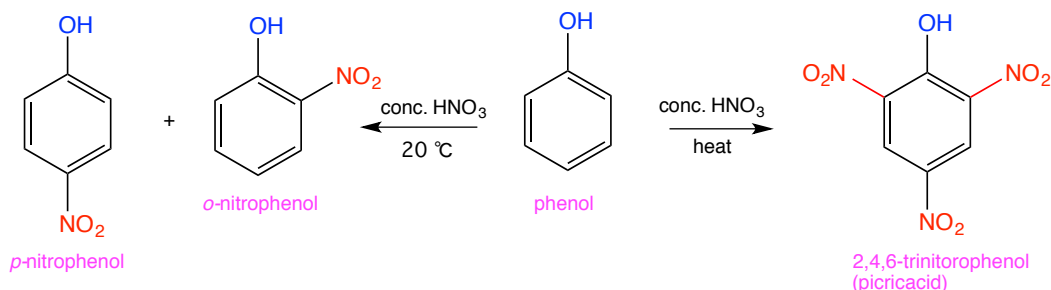


Figure 10.13 Nitration of phenol

As for the orientation, *o*- and *p*-nitrophenol were obtained to indicate the reaction is *o*- and *p*-directing. Nitration with concentrated nitric acid afforded 2,4,6-trinitrophenol (picric acid)

Point: Nitration of phenol

The hydroxy group is an activating group. The increase of electron density of benzene ring due to the R effect of oxygen atom is larger than the decrease of electron density of benzene ring due to the I effect of oxygen atom.

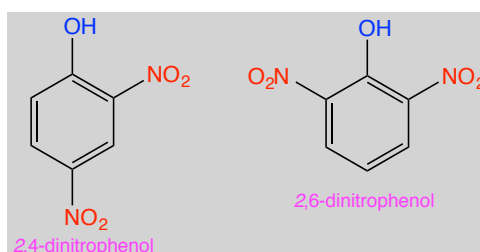
The hydroxy group is *o*, *p*-directing one.

Exercise 10.7 Nitration of phenol

Suppose nitration of phenol to picric acid proceeds step by step, from mononitration, and dinitration, to trinitration. Draw the structures of intermediate dinitrophenols.

Answer

Since the hydroxy group is *o*, *p*-directing, 2,4- and 2,6-dinitrophenols will be obtained from *o*-nitrophenol. From *p*-nitrophenol, only 2,4-dinitrophenol will be obtained.



When carbon dioxide is passed through an alkaline solution of phenol at high temperature and pressure, and then acidified, salicylic acid (2-hydroxybenzoic acid) is obtained (Figure 10.14). This is the long-known Kolbe-Schmitt reaction, and an electrophilic substitution to phenols. Here carbon dioxide behaves as an electrophilic reagent. 反応操作ですので受動態にしました。

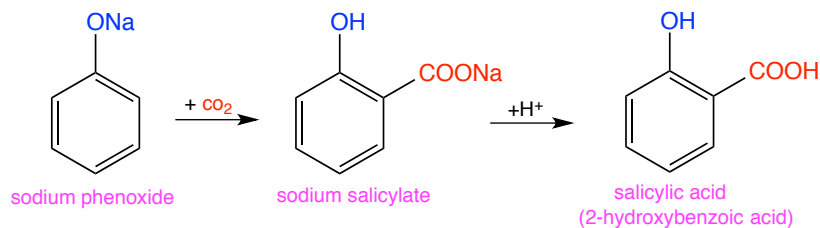
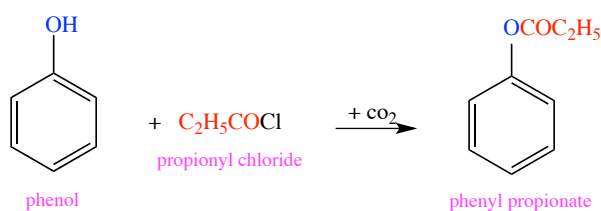


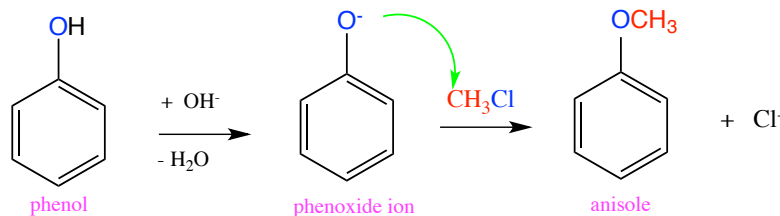
Figure 10.14 Kolbe-Schmitt reaction

(b) Reaction of hydroxy group

Sometimes phenols react in a similar manner with alcohols since both have the same functional group, a hydroxy group. For instance, phenols readily react with carboxylic acid to give esters.

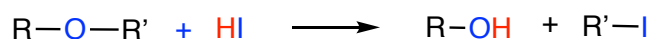


Under a basic condition, the reaction between phenols and alkyl halides affords phenol ethers. This reaction is an electrophilic substitution. This is a nucleophilic substitution in which the phenoxide ion formed from phenol attacks alkyl halides.

**10.4 Reaction of ethers****(a) Nucleophilic substitution**

The reactivity of ethers is considerably lower than that of alcohols and phenols. Ethers do not react with alkali metals and do not react with strong acids and bases unless heated. Ethers are also stable to oxidizing agents.

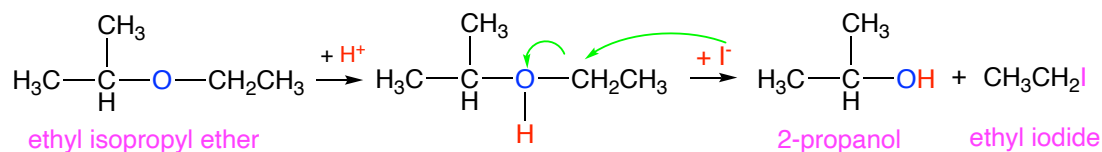
Dialkyl ethers react, however, with hydroiodic acid and hydrobromic acid to be cleaved to give alcohols and alkyl halides.



The reaction proceeds by either S_N1 or S_N2 depending on the structure of ethers.

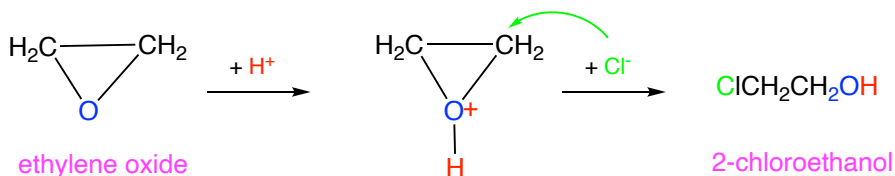
The reaction between ethyl isopropyl ether and hydroiodic acid is explained as an example. Firstly, proton coordinates with ether oxygen. The iodide ion makes a nucleophilic attack on slightly positively charged carbon atom. As a result, the alcohol is eliminated. In the case of asymmetric ethers, a problem arises: which carbon will be attacked by the iodide ion?

What takes place is shown in the following equation. The oxygen atom remains bonded to the more crowded alkyl group, while the iodide ion approaches less crowded carbon atom and the substitution takes place.

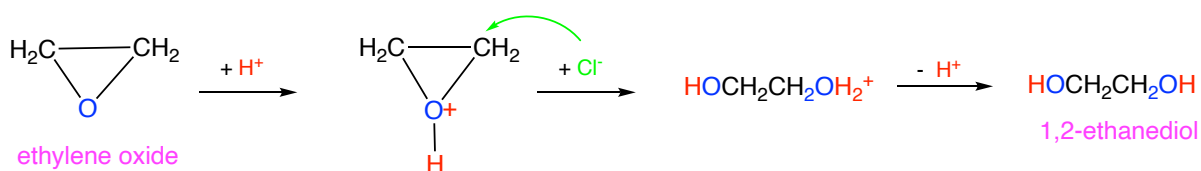


(b) Reaction of epoxides

Compounds with epoxy bonds (Ch. 10.1(c)) are named “epoxides”. The simplest one, ethylene oxide, is a three-membered cyclic compound and is ready to open the ring by the reaction with an acid. The reaction with hydrochloric acid gives 2-chloroethanol. The reaction is an acid-catalyzed nucleophilic substitution. Since the leaving group is a part of the ring, the reaction may be regarded as ring-opening rather than elimination.

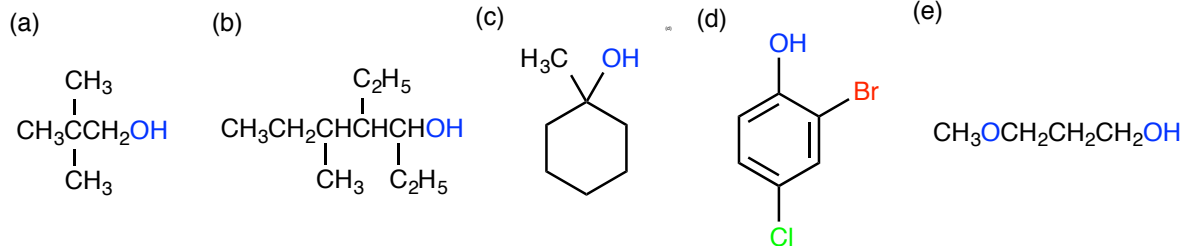


When the concentration of acid is low, the nucleophilic reagent is water, and at the last stage of the reaction, proton is eliminated to give 1,2-ethanediol (ethylene glycol). This diol is used as the antifreeze solution for radiators of automobiles.



Problems**10.1**

Give names for the following compounds.

**10.2**

Draw the structures of the following compounds.

- 4-methyl-2-pentanol
- 3,6-dichlorooctanol
- 2-cyclohexenol
- 2,3,5-trimethylphenol
- ethyl 2-cyclohexenyl ether

10.3

Draw the structures of all possible products obtained by the dehydration of each of the following compounds and give names of all of them. Point out the main product.

- 2-butanol
- 2-methylcyclohexanol
- 2-methyl-3-hexanol

10.4

Explain the chemical (non-spectroscopic) method to distinguish the following pair of compounds.

- t*-butyl alcohol and *s*-butyl alcohol
- allyl alcohol and *n*-propyl alcohol
- 3-methyl-1-butanol and 2-methyl-1-butanol
- p*-cresol and benzyl alcohol

10.5

Of *p*-chlorophenol and *p*-nitrophenol, which one is stronger as an acid?

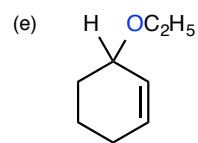
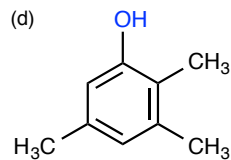
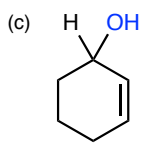
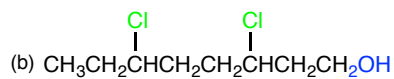
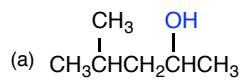
10.6


When 4-chloro-1-butanol reacts with a strong base such as sodium hydride (NaH), a cyclic ether, tetrahydrofuran (THF) is obtained.

- Draw the reaction formula.
- Explain the course of the reaction.

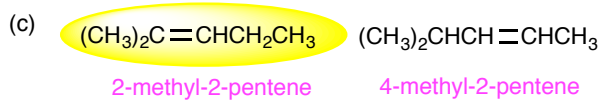
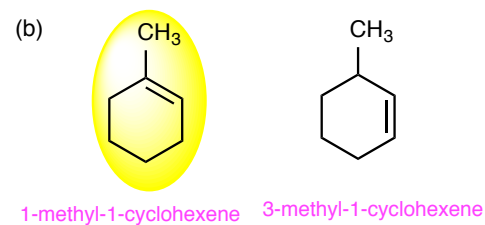
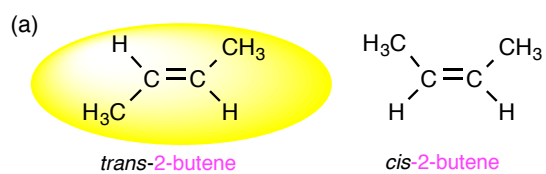
Answers**10.1**

- (a) 2,2-dimethyl-1-propanol
 (b) 4-ethyl-5-methyl-3-heptanol
 (c) 1-methyl-1-cyclohexanol
 (d) 2-bromo-4-chlorophenol
 (e) 3-methoxy-1-propanol

10.2

10.3 The main products are marked with .

ピリオドの位置を右端に動かしました。



 main product

10.4

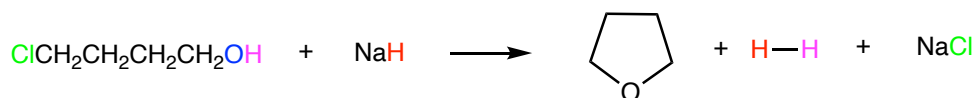
- (a) *t*-Butyl alcohol reacts with concentrated hydrochloric acid to afford *t*-butyl chloride. Such a reaction does not occur with *s*-butyl alcohol.
- (b) Any reaction that can detect a double bond can be applied to allyl alcohol.
- (c) By dehydration, these compounds are changed into alkenes. Then the alkenes are decomposed by oxidation. Analysis of decomposed products will determine the structure of the original compounds.
- (d) *p*-Cresol is weakly acidic but benzyl alcohol is neutral.

10.5

Though the chlorine atom is *o*-, *p*-directing, it does not increase the reactivity of the benzene ring.

10.6

(1)



(2) This reaction is a kind of Williamson reaction. The reaction between the alcohol and NaH yields alkoxide R₂ONa, which attacks the carbon atom to which hydrogen atom is bonded (an intramolecular reaction). Hydrogen molecule H₂ is formed from H⁻ of NaH and H⁺ of hydroxy group.