Alcohols and Phenols

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13

Alcohols and Phenols

DID YOU EVER WONDER…

what causes the hangover associated with drinking alcohol and whether anything can be done to prevent a hangover?

Veisalgia, the medical term for a hangover, refers to the unpleasant physiological effects that result from drinking too much alcohol. These effects include headache, nausea, vomiting, fatigue, and a heightened sensitivity to light and noise. Hangovers are caused by a multitude of factors. These factors include (but are not limited to) dehydration caused by the stimulation of urine production, the loss of vitamin B, and the production of acetaldehyde in the body. Acetaldehyde is a product of the oxidation of ethanol. Oxidation is just one of the many reactions that alcohols undergo. In this chapter, we will learn about alcohols and their reactions. Then, we will revisit the topic of acetaldehyde production in the body, and we will see if anything can be done to prevent a hangover.

DO YOU REMEMBER?

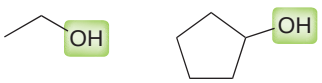
Before you go on, be sure you understand the following topics.
If necessary, review the suggested sections to prepare for this chapter.

- Brønsted-Lowry Acidity (Sections 3.3-3.4)
- Mechanisms and Curved Arrows (Sections 6.8-6.11)
- E2 and E1 Reactions (Sections 8.6-8.11)
- Designating the Configuration of a Chirality Center (Section 5.3)
- S_N2 and S_N1 Reactions (Sections 7.4-7.8)

Visit www.wileyplus.com to check your understanding and for valuable practice.

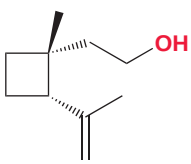
13.1 Structure and Properties of Alcohols

Alcohols are compounds that possess a **hydroxyl group** (OH) and are characterized by names ending in "ol":

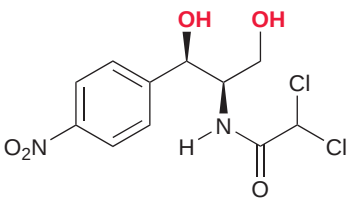


Ethanol **Cyclopentanol**

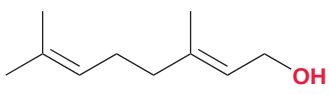
A vast number of naturally occurring compounds contain the hydroxyl group. Here are just a few examples.



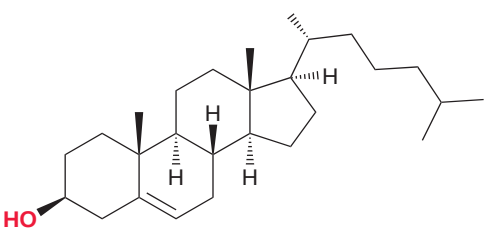
Grandisol
The sex pheromone of the male boll weevil



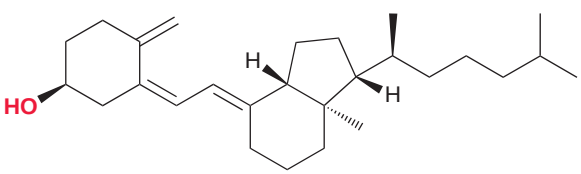
Chloramphenicol
An antibiotic isolated from the *Streptomyces venezuelae* bacterium. Potent against typhoid fever



Geraniol
Isolated from roses and geraniums. Used in perfumes

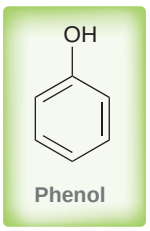


Cholesterol
Plays a vital role in the biosynthesis of many steroids

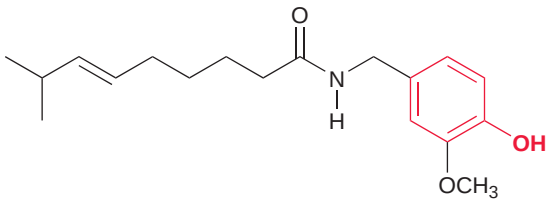


Cholecalciferol (vitamin D_3)
Regulates calcium levels and helps to form and maintain strong bones

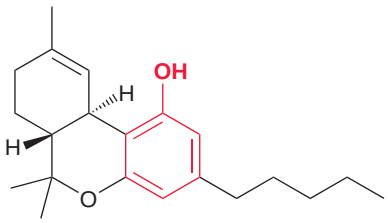
Phenol is a special kind of alcohol. It is comprised of a hydroxyl group attached directly to a phenyl ring. Substituted phenols are extremely common in nature and exhibit a wide variety of properties and functions, as seen in the following examples.



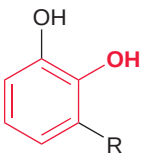
Phenol



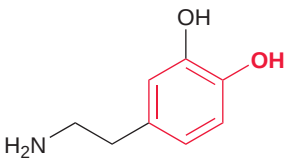
Capsaicin
The compound responsible for the spicy hot flavor of chili peppers



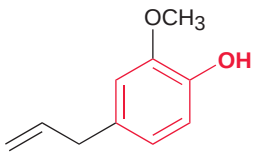
Tetrahydrocannabinol (THC)
The psychoactive drug found in marijuana (cannabis)



Urushiols
Present in the leaves of poison ivy and poison oak. Cause skin irritation



Dopamine
A neurotransmitter that is deficient in Parkinson's disease



Eugenol
Isolated from cloves and used in perfumes and as a flavor additive

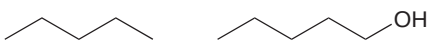
Nomenclature

Recall that four discrete steps are required to name alkanes, alkenes, and alkynes.

1. Identify and name the parent.
2. Identify and name the substituents.
3. Assign a locant to each substituent.
4. Assemble the substituents alphabetically.

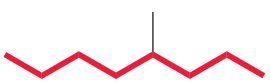
Alcohols are named using the same four steps and applying the following rules.

- When naming the parent, replace the suffix "e" with "ol" to indicate the presence of a hydroxyl group:



Pentane **Pentanol**

- When choosing the parent of an alcohol, identify the longest chain that includes the carbon atom connected to the hydroxyl group.

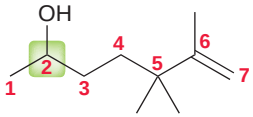


Parent = octane

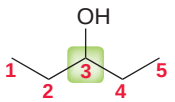
Parent = hexanol

- When numbering the parent chain of an alcohol, the hydroxyl group should receive the lowest number possible, despite the presence of alkyl substituents or π bonds.

Correct **Incorrect**

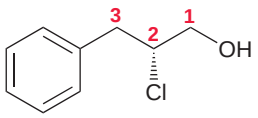


- The position of the hydroxyl group is indicated using a locant. The IUPAC rules published in 1979 dictate that this locant be placed immediately before the parent, while the IUPAC recommendations released in 1993 and 2004 allow for the locant to be placed before the suffix "ol." Both names are acceptable IUPAC names.



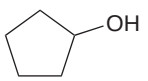
3-Pentanol
or
Pentan-3-ol

- When a chirality center is present, the configuration must be indicated at the beginning of the name; for example:

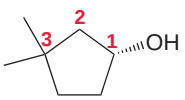


(*R*)-2-Chloro-3-phenyl-1-propanol

- Cyclic alcohols are numbered starting at the position bearing the hydroxyl group, so there is no need to indicate the position of the hydroxyl group; it is understood to be at C–1.



Cyclopentanol

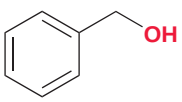


(*R*)-3,3-Dimethylcyclopentanol

IUPAC nomenclature recognizes the common names of many alcohols, such as the following three examples:

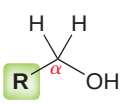
Isopropyl alcohol
(2-propanol)

tert-Butyl alcohol
(2-methyl-2-propanol)

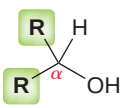


Benzyl alcohol
(phenylmethanol)

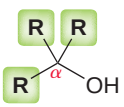
Alcohols are also designated as primary, secondary, or tertiary, depending on the number of alkyl groups attached directly to the alpha (α) position (the carbon atom bearing the hydroxyl group).



Primary

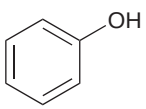


Secondary

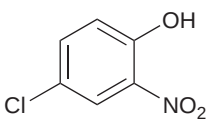


Tertiary

The word "phenol" is used to describe a specific compound (hydroxybenzene) but is also used as the parent name when substituents are attached.



Phenol



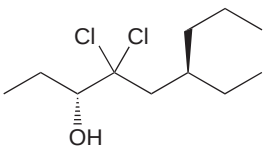
4-Chloro-2-nitrophenol

SKILLBUILDER

13.1 NAMING AN ALCOHOL

LEARN the skill

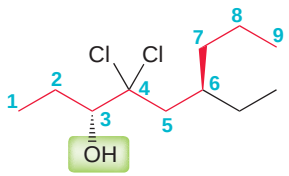
Assign an IUPAC name for the following alcohol.



SOLUTION

Begin by identifying and naming the parent. Choose the longest chain that includes the carbon atom connected to the hydroxyl group, and then number the chain to give the hydroxyl group the lowest number possible.

STEP 1 Identify and name the parent.

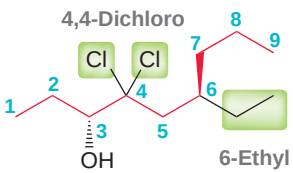


3-Nonanol

Then identify the substituents and assign locants.

STEPS 2 AND 3 Identify the substituents and assign locants.

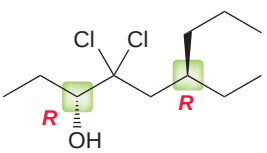
STEP 4 Assemble the substituents alphabetically.



Next, assemble the substituents alphabetically: 4,4-Dichloro-6-ethyl-3-nonanol

Before concluding, we must always check to see if there are any chirality centers This compound has two chirality centers. Using the skills from Section 5.3, we can assign the *R* configuration to both chirality centers.

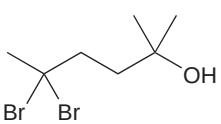
STEP 5 Assign the configuration of any chirality center.

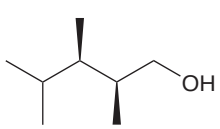


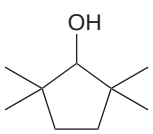
Therefore, the complete name is (3*R*,6*R*)-4,4-Dichloro-6-ethyl-3-nonanol.

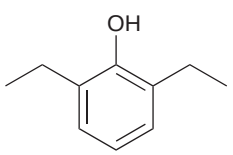
PRACTICE the skill

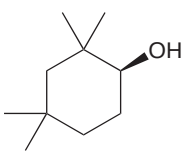
13.1 Provide an IUPAC name for each of the following alcohols:

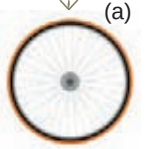
(a) 

(b) 

(c) 

(d) 

(e) 



APPLY the skill

13.2 Draw the structure of each of the following compounds:

(a) (*R*)-3,3-Dibromocyclohexanol (b) (*S*)-2,3-Dimethyl-3-pentanol

(c) (1*S*,2*S*,4*R*)-Bicyclo[2.2.1]heptan-2-ol

need more **PRACTICE?** **Try Problems 13.30–13.31a-d,f, 13.32**

Commercially Important Alcohols

Methanol (CH_3OH) is the simplest alcohol. It is toxic, and ingestion can cause blindness and death, even in small quantities. Methanol can be obtained from heating wood in the absence of air and has therefore been called "wood alcohol." Industrially, methanol is prepared by the reaction between carbon dioxide (CO_2) and hydrogen gas (H_2) in the presence of suitable catalysts. Each year, the United States produces approximately 2 billion gallons of methanol, which is used as a solvent and as a precursor in the production of other commercially important compounds.

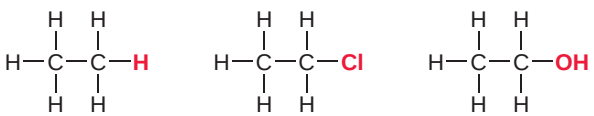
Methanol can also be used as a fuel to power combustion engines. In the second lap of the 1964 Indianapolis 500, a bad accident involving seven cars resulted in a large fire that claimed the lives of two drivers. That accident prompted the decision that all race cars switch from gasoline-powered engines to methanol-powered engines, because methanol fires produce no smoke and are more easily extinguished. In 2006, the Indianapolis 500 switched the choice of fuels for the race cars again, replacing methanol with ethanol.

Ethanol (CH_3CH_2OH), also called grain alcohol, is obtained from the fermentation of grains or fruits, a process that has been widely used for thousands of years. Industrially, ethanol is prepared via the acid-catalyzed hydration of ethylene. Each year, the United States produces approximately 5 billion gallons of ethanol, used as a solvent and as a precursor for the production of other commercially important compounds. Ethanol that is suitable for drinking is highly taxed by most governments. To avoid these taxes, industrial-grade ethanol is contaminated with small quantities of toxic compounds (such as methanol) that render the mixture unfit for human consumption. The resulting solution is called "denatured alcohol."

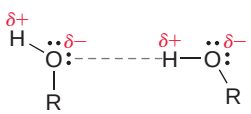
Isopropanol, also called rubbing alcohol, is prepared industrially via the acid-catalyzed hydration of propylene. Isopropanol has antibacterial properties and is used as a local antiseptic. Sterilizing pads typically contain a solution of isopropanol in water. Isopropanol is also used as an industrial solvent and as a gasoline additive.

Physical Properties of Alcohols

The physical properties of alcohols are quite different from the physical properties of alkanes or alkyl halides. For example, compare the boiling points for ethane, chloroethane, and ethanol.



The boiling point of ethanol is much higher than the other two compounds as a result of the hydrogen-bonding interactions that occur between molecules of ethanol.



These interactions are fairly strong intermolecular forces, and they are also critical in understanding how alcohols interact with water. For example, methanol is **miscible** with water, which means that methanol can be mixed with water in any proportion (they will never separate into two layers like a mixture of water and oil). However, not all alcohols are miscible with water. To understand why, we must realize that every alcohol has two regions. The **hydrophobic** region does *not* interact well with water, while the **hydrophilic** region *does* interact with water via hydrogen bonding. Figure 13.1 shows the hydrophobic and hydrophilic regions of methanol and octanol. In the case of methanol, the hydrophobic end of the molecule is fairly small. This

FIGURE 13.1
The hydrophobic and hydrophilic regions of methanol and octanol.

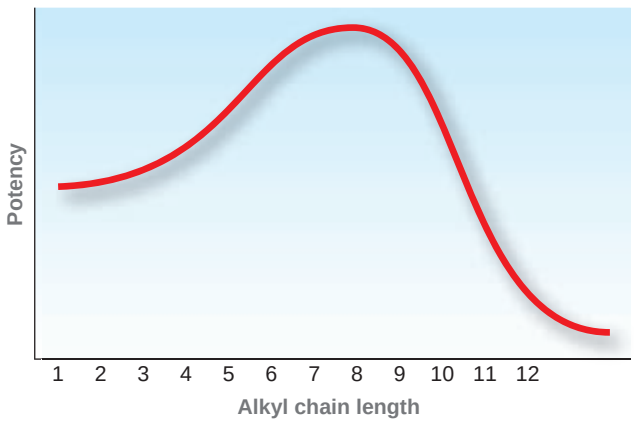
is true even of ethanol and propanol, but it is not true of butanol. The hydrophobic end of the butanol molecule is large enough to prevent miscibility. Water can still be mixed with butanol, but not in all proportions. In other words, butanol is considered to be soluble in water, rather than miscible. The term **soluble** means that only a certain volume of butanol will dissolve in a specified amount of water at room temperature.

As the size of the hydrophobic region increases, solubility in water decreases. For example, octanol exhibits extremely low solubility in water at room temperature. Alcohols with more than eight carbon atoms, such as nonanol and decanol, are considered to be insoluble in water.

MEDICALLYSPEAKING

Chain Length as a Factor in Drug Design

Primary alcohols (methanol, ethanol, propanol, butanol, etc.) exhibit antibacterial properties. Research indicates that the antibacterial potency of primary alcohols increases with increasing molecular weight, and this trend continues up to an alkyl chain length of eight carbon atoms (octanol). Beyond eight carbon atoms, the potency decreases. That is, nonanol is less potent than octanol, and dodecanol (12 carbon atoms) has very little potency.



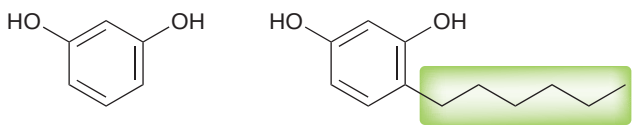
Two trends explain the observations:

- An alcohol with a larger alkyl chain (hydrophobic region) exhibits a greater ability to penetrate microbial membranes, which are composed of molecules with hydrophobic regions. According to this trend, potency should continue to increase with increased alkyl chain length, even beyond eight carbon atoms.
- A compound with a larger alkyl chain exhibits lower solubility in water, decreasing its ability to be transported through aqueous media. This trend explains why the potency of alcohols decreases steeply as the alkyl chain becomes larger than eight carbon atoms. A larger alcohol simply cannot reach its destination and therefore has low potency.

The balance between these two trends is achieved for octanol, which has the highest antibacterial potency of the primary alcohols.

Studies also show that chain branching decreases the ability of an alcohol to penetrate cell membranes. Accordingly, isopropanol is actually less potent as an antibacterial agent than *n*-propanol. Nevertheless, isopropanol (rubbing alcohol) is used because it is less expensive to produce than *n*-propanol, and the difference in antibacterial potency does not justify the added expense of production.

Many other antibacterial agents are specifically designed with alkyl chains that enable them to penetrate cell membranes. The design of these agents is optimized by carefully striking the right balance between the two trends previously discussed. Various chain lengths are tested to determine optimal potency. In most cases, the optimal chain length is found to be between five and nine carbon atoms. Consider, for example, the structure of resorcinol.

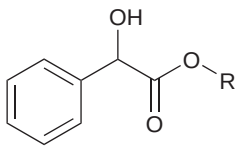


Resorcinol Hexylresorcinol

Resorcinol is a weak antiseptic (antimicrobial agent) used in the treatment of skin conditions such as eczema and psoriasis. Placing an alkyl chain on the ring increases its potency as an antiseptic. Studies indicate that the optimal potency is achieved with a six-carbon chain length. Hexylresorcinol exhibits bactericidal and fungicidal properties and is used in many throat lozenges.

CONCEPTUAL CHECKPOINT

13.3 Mandelate esters exhibit spasmolytic activity (they act as muscle relaxants). The nature of the alkyl group (R) greatly affects potency. Research indicates that the optimal potency is achieved when R is a nine-carbon chain (a nonyl group). Explain why nonyl mandelate is more potent than either octyl mandelate or decyl mandelate.



Mandelate esters
(R = alkyl chain)