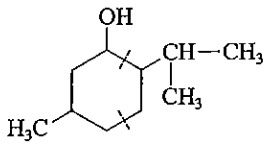
2. The alcohol $CH_3—CH_2—CH_2—CH_2—OH$ is classified as a
   a. 1° alcohol
   b. 2° alcohol
   c. 3° alcohol
   d. no correct response

Answers: 1. c; 2. a

CHEMICAL CONNECTIONS

Menthol: A Useful Naturally Occurring Terpene Alcohol

Menthol is a naturally occurring terpene (Section 13-7) alcohol with a pleasant, minty odor. Its IUPAC name is 2-isopropyl-5-methylcyclohexanol.



In the pure state, menthol is a white crystalline solid with a melting point of 41°C to 43°C. Menthol occurs naturally in peppermint oil. As is the case with many natural products, the demand for menthol exceeds its supply from natural sources. Methods now exist for the synthetic production of menthol.

Topical application of menthol to the skin causes a refreshing, cooling sensation followed by a slight burning-and-prickling sensation. Its mode of action is that of a *differential* anesthetic. It stimulates the receptor cells in the skin that normally respond to cold to give a sensation of coolness that is unrelated to body temperature. (This cooling sensation is particularly noticeable in the respiratory tract when low concentrations of menthol are inhaled.) At the same time as cooling is perceived, menthol can depress the nerves for pain reception.

Menthol's mode of action is opposite that of capsaicin (Section 17-14), the natural product responsible for the "spiciness" of hot peppers. Capsaicin stimulates heat sensors without causing an actual change in body temperature.

Numerous products contain menthol.

- Throat sprays and lozenges containing menthol temporarily soothe inflamed mucous surfaces of the nose and throat. Lozenges contain 2–20 milligrams of menthol per wafer.
- Cough drops and cigarettes of the "mentholated" type use menthol for its counterirritant effect.
- Pre-electric shave preparations and aftershave lotions often contain menthol. A concentration of only 0.1% (m/v) gives ample cooling to allay the irritation of a "close" shave.
- Many dermatologic preparations contain menthol as an anti-pruritic (anti-itching agent).
- Chest-rub preparations containing menthol include BENGAY [7% (m/v)] and Mentholatum [6% (m/v)].
- Mint flavoring agents used in chewing gum and candies contain menthol as an ingredient. Several toothpastes and mouthwashes also contain menthol as a flavoring agent.

Many kinds of cough drops contain menthol as a counterirritant.

14-9 Chemical Reactions of Alcohols

LEARNING FOCUS

Be aware of reaction conditions and products formed for each of the following alcohol reactions: combustion, dehydration, condensation, oxidation, and halogenation.

Of the many chemical reactions that alcohols undergo, five will be considered in this section: (1) combustion, (2) dehydration, (3) condensation, (4) oxidation, and (5) halogenation.

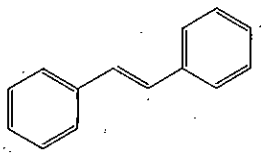
CHEMICAL CONNECTIONS 14B

Red Wine and Resveratrol

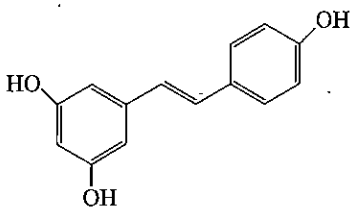
The "French Paradox" is a name associated with a study indicating that people in France were less likely to die of heart attacks than people living in the United States, despite both groups having similar high levels of saturated fats in their diets. A proposed explanation for this "paradox" was the idea that regular moderate consumption of red wine with meals (a common French, but not American, tradition) provides some type of added protection from cardiovascular disease.

This idea that red wine consumption has cardiovascular health benefits has spawned numerous investigational studies concerning what compounds might be present in red wine that produce such benefits. From such studies, one particular compound whose presence in red wine was discovered in 1992 has garnered much attention. It is the compound resveratrol.

Resveratrol (pronounced "ress-ver-a-trole") is an antioxidant compound produced by some plants, including grapes, to protect themselves against environmental stresses such as fungal diseases and sun damage. It is a polyphenol derivative of the aromatic hydrocarbon stilbene.



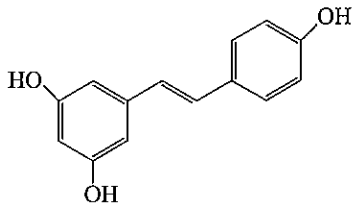
Stilbene



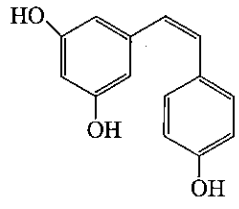
Resveratrol

Because of the double bond present in the carbon chain connecting the two benzene (phenol) centers, *cis*- and *trans*- isomers exist for both stilbene and resveratrol. It is the *trans*- isomer of resveratrol that is produced in plants.

Resveratrol is found in grapes, grape juice, berries of the *vaccinum* species (which includes blueberries and cranberries), and peanuts. Grapes contain the highest levels of resveratrol, where it is concentrated in the skin of the grapes. Red wines contain more resveratrol than white wines because red wine is fermented with grape skins, allowing the wine to absorb the resveratrol, whereas white wine is fermented after the grape skins have been removed. On an ounce-for-ounce basis, peanuts have levels of resveratrol about half those in red wine. Blueberries and cranberries contain much smaller amounts of the substance.



trans-Resveratrol



cis-Resveratrol

Almost all research conducted to date on resveratrol has been done on animals and not humans. Research involving mice given resveratrol shows a positive correlation with reduced risk of inflammation and blood clotting, as well as a protective effect against obesity and diabetes. Of importance, the dose of resveratrol used in the mice studies would be equivalent to people consuming more than 100 bottles of wine a day. Resveratrol administration has also increased the life spans of yeast, worms, fruit flies, fish, and mice that were fed a high-calorie diet. Whether such effects would be observed in humans is not yet known.

Resveratrol supplements are now available in the United States. Their source varies from extracts of the plant kojo-kon to red wine extracts and red grape extracts. The effectiveness and safety of the supplements is not well established. It is known that throat lozenges are the most effective way of administering resveratrol to humans. About 70% of an orally given resveratrol dose is absorbed; however, oral bioavailability is low because the absorbed resveratrol is rapidly metabolized in the intestine and liver. The oral availability of resveratrol from wine has been found to be no higher than that from a pill.

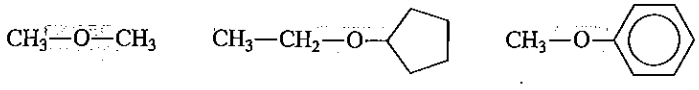
Resveratrol concentration levels found in the human body as the result of moderate drinking of red wine do not appear to be sufficiently high to explain the observations associated with the "French Paradox."

14-14 Structural Characteristics of Ethers

LEARNING FOCUS

Characterize ethers in terms of general structural properties and functional group identity.

An **ether** *is an organic compound in which an oxygen atom is bonded to two carbon atoms by single bonds.* In an ether, the carbon atoms that are attached to the oxygen atom can be part of alkyl, cycloalkyl, or aryl groups. Examples of ethers include



CHEMICAL CONNECTIONS

Ethers as General Anesthetics

For many people, the word *ether* evokes thoughts of hospital operating rooms and anesthesia. This response derives from the *former* large-scale use of diethyl ether as a general anesthetic. In 1846, the Boston dentist William Morton was the first to demonstrate publicly the use of diethyl ether as a surgical anesthetic.

In many ways, diethyl ether is an ideal general anesthetic. It is relatively easy to administer, it is readily made in pure form, and it causes excellent muscle relaxation. There is less danger of an overdose with diethyl ether than with almost any other anesthetic because there is a large gap between the effective level for anesthesia and the lethal dose.

Despite these ideal properties, diethyl ether is rarely used today because of two drawbacks: (1) It causes nausea and irritation of the respiratory passages and (2) it is a highly flammable substance, forming explosive mixtures with air, which can be set off by a spark.

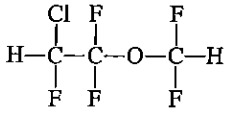
Dennis Drenner/Aurora Photos/Alamy

Preparing to administer an anesthetic to a child.

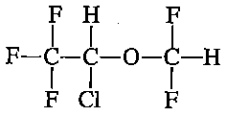
By the 1930s, non-ether anesthetics had been developed that solved the problems of nausea and irritation. They also, however, were extremely flammable compounds. The simple hydrocarbon cyclopropane was the most widely used of these newer compounds.

It was not until the late 1950s and early 1960s that nonflammable general anesthetics became available. Anesthetic nonflammability was achieved by incorporating halogen atoms into anesthetic molecules. Three of the most used of these "halogenated" anesthetics were enflurane, isoflurane, and halothane.

Enflurane and isoflurane, which are constitutional isomers, are hexahalogenated ethers.



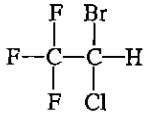
Enflurane



Isoflurane

With these compounds, induction of anesthesia can be achieved in less than 10 minutes with an inhaled concentration of 3% in oxygen.

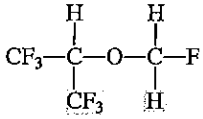
Halothane, which is potent at relatively low doses and whose effects wear off quickly, is a pentahalogenated alkane derivative rather than an ether.



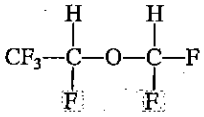
Halothane

It is the only inhalation anesthetic that contains a bromine atom.

Phase-out of the use of the preceding three compounds began in the late 1980s and early 1990s. They have largely been replaced by a "second generation" of similar halogenated ethers with even better anesthetic properties. In general, these new compounds have more fluorine atoms and fewer chlorine atoms. Two of the most prominent of these second-generation anesthetic agents now in use are sevoflurane and desflurane.



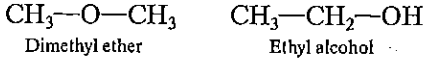
Sevoflurane



Desflurane

Functional Group Isomerism

Ethers and alcohols with the same number of carbon atoms and the same degree of saturation have the same molecular formula. The simplest manifestation of this phenomenon involves dimethyl ether, the C_2 ether, and ethyl alcohol, the C_2 alcohol. Both have the molecular formula C_2H_6O.



Dimethyl ether

Ethyl alcohol

CHEMICAL CONNECTIONS 14-D

Garlic and Onions: Odiferous Medicinal Plants

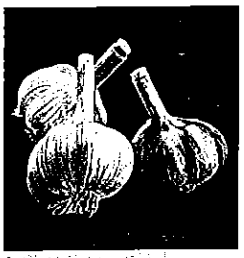
Garlic and onions, which botanically belong to the same plant genus, are vegetables known for the bad breath—and perspiration odors—associated with their consumption. These effects are caused by organic sulfur-containing compounds, produced when garlic and onions are cut, that reach the lungs and sweat glands via the bloodstream. The total sulfur content of garlic and onions amounts to about one percent of their dry weight.

Less well known about garlic and onions are the numerous studies showing that these same "bad breath" sulfur-containing compounds are health-promoting substances that have the capacity to prevent or at least ameliorate a host of ailments in humans and animals. The list of beneficial effects associated with garlic use is longer than that for any other medicinal plant. Only onions come close to having the same kind of efficacy. Garlic has been shown to function as an antibacterial, antiviral, antifungal, antiprotozal, and antiparasitic agent. In the area of heart and circulatory problems, garlic contains vasodilative compounds that improve blood fluidity and reduce platelet aggregation. The health-promoting role of onions has not been explored as thoroughly as that of garlic, but the studies undertaken so far seem to confirm that onions are second only to garlic in their "healing powers."

Whole garlic bulbs and whole onions that remain undisturbed and intact do not contain any strongly odiferous compounds and display virtually no physiological activity. The act of cutting or crushing these vegetables causes a cascade of reactions to occur in damaged plant cells. Exposure to oxygen in the air is an important facet of these reactions. More than one hundred sulfur-containing organic compounds are formed in garlic, and a similar number are probably produced in the less-studied onion. Many of the compounds so produced are common to both garlic and onions. The compounds associated with garlic ingestion that contribute to bad breath include allyl methyl sulfide, allyl methyl disulfide, diallyl sulfide, and diallyl disulfide. Their structures are given in the accompanying table.

Not all of the strongly odiferous compounds associated with garlic and onions elicit negative responses from the human olfactory system. For example, the smell of fried onions is considered a pleasant odor by most people. Compounds contributing to the "fried onion smell" include methyl propyl disulfide, methyl propyl trisulfide, allyl propyl disulfide, and dipropyl trisulfide. Structures for these compounds are also given in the accompanying table.

In addition to physiologically active sulfur compounds, garlic and onions also contain a variety of other healthful ingredients. Among these are the B vitamins thiamine and riboflavin and vitamin C. Almost all of the trace elements are also present, including manganese, iron, phosphorus, selenium, and chromium. The actual amount of a given trace element depends on the soil in which the garlic or onion was grown.



Getty Images

Garlic Breath

$CH_2=CH-CH_2-S-CH_3$
Allyl methyl sulfide

$CH_2=CH-CH_2-S-S-CH_3$
Allyl methyl disulfide

$CH_2=CH-CH_2-S-CH_2-CH=CH_2$
Diallyl sulfide

$CH_2=CH-CH_2-S-S-CH_2-CH=CH_2$
Diallyl disulfide

Getty Images

Fried Onions

$CH_3-S-S-CH_2-CH_2-CH_3$
Methyl propyl disulfide

$CH_3-S-S-S-CH_2-CH_2-CH_3$
Methyl propyl trisulfide

$CH_2=CH-CH_2-S-S-CH_2-CH_2-CH_3$
Allyl propyl disulfide

$CH_3-CH_2-CH_2-S-S-S-CH_2-CH_2-CH_3$
Dipropyl trisulfide

Sulfides and disulfides contribute heavily to the odors of "garlic breath" and "fried onions." "Garlic breath" odorants are primarily sulfides, whereas the smell, usually considered pleasant, of fried onions is heavily influenced by the presence of disulfides. The focus on relevancy feature Chemical Connections 14-D—Garlic and Onions: Odiferous Medicinal Plants—further considers studies about garlic and onions, plants which belong to the same plant genus.

Chemistry at a Glance—Alcohols, Thiols, Ethers, and Thioethers—contrasts the four major types of compounds considered in this chapter—alcohols, thiols, ethers, and thioethers—in terms of structure, hydrogen-bonding characteristics, and nomenclature.