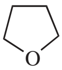
ETHERS

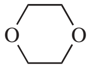
1. Introduction

Ethers are compounds of the general formula $\mathrm{Ar{-}O{-}Ar'}$, $\mathrm{Ar{-}O{-}R}$, and $\mathrm{R{-}O{-}R'}$ where Ar is an aryl group and R is an alkyl group. If the two R or Ar groups are identical, the compound is a symmetrical ether. Examples of symmetrical ethers are (di)methyl ether, CH_3OCH_3, and (di)phenyl ether, $C_6H_5OC_6H_5$; examples of unsymmetrical ethers are methyl ethyl ether, $CH_3OCH_2CH_3$, and methyl *tert*-butyl ether, $CH_3OC(CH_3)_3$. Cyclic ethers are variously designated. Three-membered ring cyclic ethers are olefin oxides, eg, ethylene oxide (**1**) (qv), 1,2-propylene oxide (qv), and 1,2-butylene oxide (see GLYCOLS). This ether group is also known as an epoxy group or oxirane. When the ring containing the ether is larger, the ethers are usually classified as oxygen heterocyclics such as tetrahydrofuran (THF) (**2**), or *p*-dioxane (**3**).

(**1**)



(**2**)



(**3**)

Simple ethers derive their name from the two groups attached to the oxygen followed by the word ether, eg, diethyl ether, $CH_3CH_2OCH_2CH_3$. For symmetrical ethers the “di” prefix is often omitted. If one group has no simple name, the compound may be named as an alkoxy derivative, eg, 2-ethoxyethanol, $CH_3CH_2OCH_2CH_2OH$.

Diethyl ether [60-29-7] is one of the more important members of the ether family. It is a colorless, very volatile, highly flammable liquid with a sweet, pungent odor and burning taste. As a commercial product it is available in several grades; it is used in chemical manufacture, as a solvent, extractant, or reaction medium, and as a general anesthetic.

MTBE was first commercially produced in Italy in 1973 for use as an octane enhancer in gasoline. U.S. production of MTBE started in 1979 after Atlantic Richfield Co. (ARCO) was granted a waiver by the U.S. Environmental Protection Agency (EPA) that allowed MTBE to be blended up to 7 vol% in U.S. unleaded gasoline. The use of other aliphatic ethers was allowed when the U.S. EPA issued its “substantially similar” definition for unleaded gasoline specifications in 1981. Under this definition, any aliphatic ether or ether mixture could be blended in unleaded gasoline as long as the total oxygen contribution from the ethers does not exceed 2.0% oxygen by weight in the gasoline. This allowed MTBE to be blended up to approximately 11 vol% in gasoline.

MTBE production grew during the 1980s as lead-based octane enhancers were being phased out of gasoline. In August 1988, U.S. EPA granted a waiver requested by Sun Refining and Marketing Co. that allowed the use of MTBE up to 15 vol%, which is approximately equal to 2.7 wt% oxygen in gasoline. This oxygen limit was extended to all aliphatic ethers in gasoline in 1990 when the U.S. EPA raised the oxygen in the “substantially similar” definition to 2.7 wt% oxygen.

In November 1990, the U.S. government again revised the Clean Air Act (CAA). One of the new requirements was for gasolines sold in ambient air quality nonattainment areas of the United States to contain a minimum amount of oxygen. For the 39 metropolitan areas that exceed the federal standard for carbon monoxide, the gasoline would have to contain at least 2.7 wt% oxygen for at least four winter months beginning November 1992. This represents nearly 30% of the U.S. gasoline market.

Starting in January 1995, the nine metropolitan areas with the most severe ozone problem must sell a “reformulated” gasoline all year long. These nine cities represent approximately 20% of the U.S. gasoline market. In addition to many other very restrictive specifications, this gasoline must also contain at least 2.0 wt% oxygen. Other metropolitan areas exceeding the federal ozone standard are also allowed to choose the program when sufficient capacity exists to make the reformulated gasoline.

In 1999, Governor Gray Davis of California announced a ban on MTBE as an oxygenate in gasoline after trace amounts were found in drinking water. The phase out decision was postponed to January 2004. Ethanol has been used as a replacement oxygenate. It is possible that the 2% mandated requirement for oxygen may be eliminated (1).

Except for the special case of the epoxides, THF represents the largest use of a heterocyclic ether. Its consumption is also much larger than that of ethyl ether. Unlike the dialkyl ethers, THF is totally miscible in water at ambient conditions. Its cyclic structure also allows it to be more reactive than the dialkyl ethers. More than half of the THF produced is used as an intermediate in making other chemicals or elastomers.

2. Physical Properties

In general, ethers are neutral, pleasant-smelling compounds that have little or no solubility in water, but are easily soluble in organic liquids (2). Their boiling points approximate those of hydrocarbons having comparable molecular weights and geometries. Table 1 gives the basic physical properties for many of the ethers. More detailed physical properties for the ethers most commonly used as solvents are listed in Table 2.

3. Chemical Properties

Most ethers, particularly dialkyl ethers, are comparatively unreactive compounds because the carbon-oxygen bond is not readily cleaved. For this reason, ethers are frequently employed as inert solvents in organic synthesis. However, within the ether family, the cyclic ethers are more reactive, the most reactive being the olefin oxides or epoxides. Epoxides are generally used as intermediates for producing other small molecules or polymers (see EPOXY RESINS; POLYETHERS). Ethers do react with exceptionally powerful basic reagents, particularly certain alkali metal alkyls, to give cleavage products (7). Ethers react with less powerful bases to give the same cleavage products, but only under the forcing conditions of high temperature and pressure.

$$CH_3Na + CH_3CH_2OCH_2CH_3 \longrightarrow CH_4 + CH_2{=\!=}CH_2 + CH_3CH_2ONa$$

The ether linkage can also be cleaved by strong acids, generally at high temperatures (6):

$$(CH_3)_2CHOCH(CH_3)_2 + 2\,HBr \xrightarrow{140^\circ C} 2(CH_3)_2CHBr + H_2O$$

$$C_6H_5OCH_3 + HI \xrightarrow{130^\circ C} C_6H_5OH + CH_3I$$

Other acids that have been used for this cleavage arephosphoric acid, pyridine hydrochloride, boron tribromide, trifluoroacetic acid, and nitric acid. Acid cleavage of aryl alkyl ethers always gives phenol because the aromatic carbon–oxygen bond is much stronger than the aliphatic carbon–oxygen bond. Unsymmetrical aliphatic ethers usually yield a mixture of alkyl halides and alcohols when cleaved by halogen containing acids.

Most ethers are potentially hazardous chemicals because, in the presence of atmospheric oxygen, a radical-chain process can occur, resulting in the formation of peroxides that are unstable, explosion-prone compounds (8). The reaction may be generalized in terms of the following steps involving initiation, propagation, and termination.

Table 1. **Physical Properties of Some Representative Ethers**

Systematic name	Common name	CAS Registry number	Bp,^{a} °C	d_4^{20b}	n_{D}^{20}
		Saturated			
symmetrical					
methyl ether		[115-10-6]	−23.7	1.617^{c}	
2-methoxyethyl ether		[111-96-6]	162	0.9451	1.4097
ethyl ether		[60-29-7]	34.5	0.7146	1.3527
1-chloroethyl ether		[986-48-7]	116−117	1.1060^{25}	1.4185^{25}
n-propyl ether		[111-43-3]	90.5	0.7360	1.3809
isopropyl ether		[108-20-3]	68.5	0.7257	1.3682
n-butyl ether		[142-96-1]	142.0	0.7704	1.3981
sec-butyl ether		[6863-58-7]	122.0	0.7590^{25}	1.3931
isobutyl ether		[628-55-7]	123.0	0.7612^{15}	
tert-butyl ether		[6163-66-2]	108.0	0.7622^{15}	1.3946
n-amyl ether		[693-65-2]	188.0	0.7849	1.4119
isoamyl ether		[544-01-4]	173.0	0.7777	1.4085
sec-amyl ether		[56762-00-6]	161.0	0.7830	1.4058
n-hexyl ether		[112-58-3]	223_{102}	0.7936	1.4204
n-heptyl ether		[629-64-1]	258.5_{102}	0.8008	1.4275
n-octyl ether		[629-82-3]	286−287	0.8063	1.4327
unsymmetrical					
methyl *n*-propyl ether		[557-17-5]	38.9	0.738	1.3579
methyl isopropyl ether		[598-53-8]	32.5_{104}	0.7237^{15}	1.3576
methyl *n*-butyl ether		[628-28-4]	70.5	0.7443	1.3736
methyl isobutyl ether		[625-44-5]	$105{-}106_{96}$	0.7549	1.3852^{25}
methyl *tert*-butyl ether	MTBE	[1634-04-4]	55.1	0.7406	1.3690
methyl *tert*-amyl ether	TAME	[994-05-8]	85−86	0.770	1.3896
ethyl isopropyl ether		[625-54-7]	53.5	0.7211	1.3624
ethyl *n*-butyl ether		[628-81-9]	91.5	0.7490	1.3818
ethyl *tert*-butyl ether	ETBE	[637-92-3]	72−73	0.742	1.3756
ethyl *n*-amyl ether		[17952-11-3]	118.0	0.7622	1.3927
ethyl *tert*-amyl ether		[919-94-8]	101	0.7657	1.3912
isopropyl *tert*-butyl ether		[17348-59-3]	87.6	0.7365^{25}	1.3799
2-ethoxyethanol	cellosolve	[110-80-5]	135	0.931^{20}	1.406^{25}
2-(2-ethoxy) ethoxyethanol ether	carbitol	[111-90-0]	196	0.9855^{25}	1.4273

		Unsaturated			
vinyl ether		[109-93-3]	28–31	0.767^{25}	
vinyl methyl ether		[107-25-5]	5–6	0.7511	
vinyl ethyl ether		[109-92-2]	35.0	0.7533	1.3739^{25}
vinyl *n*-butyl ether		[111-34-2]	93.5	0.7735^{25}	1.3997^{25}
allyl ether		[557-40-4]	95.0	0.8053	1.4163
bis(2-methallyl) ether		[628-56-8]	105.4	0.8627	1.4206
allyl ethyl ether		[557-31-3]	67.6	0.765	1.3881
allyl glycidyl ether		[106-92-3]	$75.0_{6.7}$		1.4310^{30}
ethynyl ethyl ether		[927-80-0]	49.0	0.8001	1.3796
ethynyl butyl ether		[3329-56-4]	104.0	0.8078^{25}	1.4033^{25}
		Cyclic			
ethylene oxide	oxirane	[75-21-8]	$13.5_{99.4}$	0.8824^{10}	1.3597^{7}
1,2-propylene oxide	methyloxirane	[75-56-9]	34.3	0.8590^{10}	1.3670
1,3-propylene oxide	oxetane	[503-30-0]	47.8	0.8930^{25}	1.3961
tetrahydrofuran	oxolane	[109-99-9]	64.5	0.8892	1.4050
furan	oxole	[110-00-9]	31.36	0.9514	1.4214^{2}
tetrahydropyran	oxane	[142-68-7]	88	0.8810	1.4200
1,4-dioxane		[123-91-1]	101_{100}	1.0337	1.4224
		Aromatic			
methyl phenyl ether		[100-66-3]	153.8	0.9954	1.5179
4-methoxytoluene		[104-93-8]	176.5	0.9689	1.5124
ethyl phenyl ether		[103-73-1]	172	0.9792	1.5076
1-methoxy-4-*trans*-propenylbenzene	*trans*-anethole	[4180-23-8]	253 21^{d}	0.9882	1.5615
1-methoxy-4-allylbenzenephenyl	estragole	[140-67-0]	215	0.9645	1.5230
		[101-84-8]	258 28^{d}	1.0863	1.5780
2-methoxyphenol	guaiacol	[90-05-1]	205.5	1.1287	1.5385
1,2-dimethoxy-benzene	veratrole	[91-16-7]	206.7 $22–23^{d}$	1.084	1.5385
1,4-dimethoxy-benzene		[150-78-7]	212.6 $58–60^{d}$	1.0526^{55}_{55}	
2-methoxy-4-allylphenol	4-allylguaiacol	[97-53-0]	255	1.0664	1.5410
1,2-dimethoxy-4-allylbenzene	4-allylveratrole	[93-15-2]	248	1.055	1.532
1-allyl-3,4-methylenedioxy-benzene	safrole	[94-59-7]	234.5	1.0950	1.5383
1-propenyl-3,4-methylene- dioxy-benzene	isosafrole	[93-16-3]	252	1.1224	1.5782

Table 1 (*Continued*)

Systematic name	Common name	CAS Registry number	Bp,[a] °C	d_4^{20b}	n_D^{20}
2-methoxy-4-*cis*-propenyl-phenol	*cis*-isoeugenol	[5912-86-7]	$134_{1.7}$	1.0851	1.5700
2-methoxy-4-*trans*-propenyl-phenol	*trans*-isoeugenol	[5932-68-3]	$141_{1.6}$	1.0852	1.5782
1-benzyloxy-2-methoxy-4-*trans*-propenylbenzene	benzyl isoeugenol	[120-11-6]	58[d]		
butyrated hydroxyanisole (BHA), a mixture of: 2-*tert*-butyl-4-methoxy-phenol and 3-*tert*-butyl-4-methoxyphenol		[25013-16-3,55949-47-8] [121-00-6][88-32-4]	$264–270_{98}$ 48–55[d]		

[a] At 101.3 kPa unless otherwise noted by subscript in kPa; to convert kPa to mm Hg, multiply by 7.5.

[b] Unless otherwise noted as superscript, °C.

[c] Specific gravity (air).

[d] Melting point.

Table 2. **Typical Physical and Chemical Properties of Commonly Used Ethers**[a]

Property	Ethyl	MTBE	THF	Isopropyl	*n*-Butyl
chemical formula	$C_4H_{10}O$	$C_5H_{12}O$	C_4H_8O	$C_6H_{14}O$	$C_8H_{18}O$
molecular weight	74.12	88.15	72.10	102.17	139.22
boiling point at 101.3 kPa,[b] °C	34.5	55.0	66.0	68.4	142.0
vapor pressure at 20°C, kPa[b]	56	27	17	16	0.67
evaporation rate[c]	11.8	8.5	5.7	8.0	0.66
viscosity at 20°C, mPa · s(= cP)	0.23	0.35	0.48	0.38	0.65
surface tension in air, 25°C, mN/m (= dyn/cm)	17.0	18.3	26.4	32.0	22.9
dipole moment, 25–50°C, C · m[d]	4.3×10^{-30}	4.7×10^{-30}	5.3×10^{-30}	4.7×10^{-30}	4×10^{-30}
Hilderbrand solubility parameter	7.4	7.4	9.1	7.1	7.7
water solubility, wt%, 20°C[e]					
ether in water	6.9	4.8	inf.	1.07	0.03
water in ether	1.3	1.4	inf.	0.53	0.19
flash point	−40	−30	−17	−13	25
autoignition temp, °C	160	426	321	440	185
flammability limits in air, vol%					
lower	1.9	1.6	1.8	1.0	0.9
higher	48.0	8.4	11.8	21.0	8.5
reactivity with hydroxyl radical[f]	13.6	3.2	17.8		27.8

[a] Ref. 3.

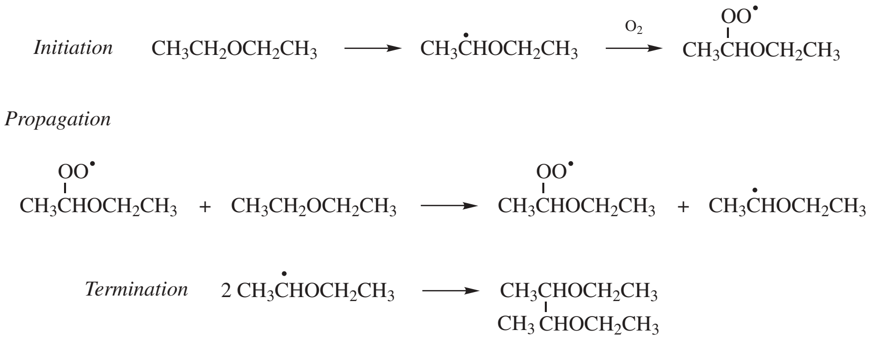
[b] To convert kPa to mm Hg, multiply by 7.5.

[c] *n*-Butylacetate = 1.

[d] To convert CC · m to debyes, multiply by 3×10^{29}.

[e] Ref. 4.

[f] k_{OH} (298 K), 10^{12} $cm^3 \cdot mol^{-1}sec^{-1}$; Refs. 5 and 6.



Initiation $CH_3CH_2OCH_2CH_3 \longrightarrow CH_3\dot{C}HOCH_2CH_3 \xrightarrow{O_2} CH_3\overset{OO^{\bullet}}{C}HOCH_2CH_3$

Propagation

$$CH_3\overset{OO^{\bullet}}{C}HOCH_2CH_3 + CH_3CH_2OCH_2CH_3 \longrightarrow CH_3\overset{OO^{\bullet}}{C}HOCH_2CH_3 + CH_3\dot{C}HOCH_2CH_3$$

Termination $2\,CH_3\dot{C}HOCH_2CH_3 \longrightarrow \begin{array}{l} CH_3CHOCH_2CH_3 \\ CH_3\,CHOCH_2CH_3 \end{array}$

The nature of the initiation step, which may occur in a variety of ways, is not known in all cases. Commonly used ethers such as ethyl ether, isopropyl ether, tetrahydrofuran, and *p*-dioxane are particularly prone to form explosive peroxides on prolonged storage and exposure to air and light (see PEROXIDES AND PEROXY COMPOUNDS,ORGANIC), and should contain antioxidants (qv) to prevent their buildup. One of the exceptions to the peroxide forming tendency of ethers is methyl *tert*-alkyl ethers such as methyl *tert*-butyl ether[1634-04-4] (MTBE) and *tert*-amyl methyl ether[994-05-8] (TAME). Both have shown little tendency if any to form peroxides (3,9).

Table 3. **Typical Gasoline-Related Properties for Ethers Used in Gasoline**[a]

Property	MTBE	ETBE	TAME
research octane number (RON)	118	119	112
motor octane number (MON)	102	104	99
(RON + MON)/2	110	111	105.5
boiling point			
°F	131	161	187
°C	55	72	86
Reid vapor pressure, kPa[b]	55	28	7
oxygen, wt%	18.2	15.7	15.7

[a] Ref. 12.

[b] To convert kPa to psi, multiply by 0.145.

Ethers are weakly basic and are converted to unstable oxonium salts by strong acids such as sulfuric acid, perchloric acid, and hydrobromic acid; relatively stable complexes are formed between ethers and Lewis acids such as boron trifluoride, aluminum chloride, and Grignard reagents (qv) (10):

$$CH_3OCH_3 + CH_3BF_4 \longrightarrow (CH_3)_3O^+BF_4^-$$

Like other aromatic compounds, aromatic ethers can undergo substitution in the aromatic ring with electrophilic reagents, eg, nitration, halogenation, and sulfonation. They also undergo Friedel-Crafts (qv) alkylation and acylation.

Allyl phenyl ethers rearrange cleanly at high temperatures, producing *o*-allyl phenols or *p*-allylphenols if both ortho positions are blocked. This reaction is called the Claisen rearrangement (11).

4. Fuel Properties

In addition to MTBE, two other ethers commonly used as fuel additives are *tert*-amyl methyl ether (TAME) and ethyl *tert*-butyl ether[637-92-3] (ETBE). There are a number of properties that are important in gasoline blending (see GASOLINE AND OTHER MOTOR FUELS) (Table 3).

5. Manufacture

5.1. General.

The most versatile method of preparing ethers is the Williamson ether synthesis, particularly in the preparation of unsymmetrical alkyl ethers (13,14). The reaction of sodium alcoholates with halogen derivatives of hydrocarbons gives the ethers:

$$RX + NaOR' \longrightarrow ROR' + NaX$$

Dialkyl sulfates can replace the halogen derivatives, and this modification is especially useful for the preparation of phenolic ethers:

$$(RO)_2SO_2 + C_6H_5ONa \longrightarrow C_6H_5OR + ROSO_3Na$$

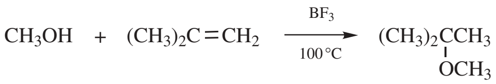
Aromatic halides do not react easily with phenoxide ions to produce diaryl ethers unless the aromatic halide is substituted with one or more electron-withdrawing groups, eg, nitro or carboxyl groups. The Ullmann reaction uses finely divided copper or copper salts to catalyze the reaction of phenoxides with aromatic halides to give diaryl ethers.

Alcohols can be dehydrated with strong acid catalysts and high reaction temperatures to produce ethers. This method is particularly useful for the preparation of symmetrical lower alkyl ethers, such as ethyl ether.

$$2\,CH_3CH_2OH \xrightarrow[H_2SO_4]{140^\circ C} CH_3CH_2OCH_2CH_3 + H_2O$$

The reaction gives poor yields of ethers with secondary and tertiary alcohols; dehydration to form the corresponding olefin is a more favorable reaction. The reaction fails for the production of diaryl ethers from phenols.

Alkyl tertiary alkyl ethers can be prepared by the addition of an alcohol or phenol to a tertiary olefin under acid catalysis (Reycler reaction); sulfuric acid, phosphoric acid, hydrochloric acid, and boron trifluoride have all been used as catalysts:



$$CH_3OH + (CH_3)_2C{=}CH_2 \xrightarrow[100\,^\circ C]{BF_3} (CH_3)_2\underset{\displaystyle OCH_3}{\underset{|}{C}}CH_3$$

Commercially, sulfonic acid ion-exchange resins are used in fixed-bed reactors to make these tertiary alkyl ethers (15). Since the reaction is very selective to tertiary olefins and also reversible, a two-step procedure is also used to recover commercially pure tertiary olefins from mixed olefin process streams. The corresponding tertiary alkyl ether is produced in the olefin mixture and then easily separated from the unreacted olefins by simple fractionation. The reaction is then reversed in a second step to make a commercially pure tertiary olefin, usually isobutylene or isoamylene.

Ether production from the reaction of monohydric alcohols with linear olefins has also been demonstrated under more severe conditions using a zeolite-type catalyst system (16). However, it has not been commercialized as yet.

5.2. Commercially Important Ethers. *Ethyl Ether.* Much of the diethyl ether manufactured is obtained as a by-product when ethanol (qv) is produced by the vapor-phase hydration of ethylene (qv) over a supported phosphoric acid catalyst. Such a process has the flexibility to adjust to some extent the relative amounts of ethanol and diethyl ether produced in order to meet existing market demands. Diethyl ether can be prepared directly to greater than 95% yield by the vapor-phase dehydration of ethanol in a fixed-bed reactor using an alumina catalyst (17).

Methyl tert-Butyl Ether. MTBE is easily made by the selective reaction of isobutylene and methanol over an acidic ion-exchange resin catalyst, in the liquid phase and at temperatures below 100°C. To be economically competitive, MTBE's use as an octane enhancer in gasoline has been dependent on low cost isobutylene. There are a number of possible isobutylene sources for making MTBE (see BUTYLENES). During the 1980s, much of the MTBE was made with isobutylene contained in mixed butanes/butylenes process streams that was produced from petrochemical olefin plants or refinery fluid catalytic crackers. MTBE plant sizes from these feedstock sources are limited by the amount of by-product isobutylene produced in these operations, and are usually in the range of one to six thousand barrels per day (40 to 250 t/yr). Larger amounts of isobutylene for MTBE can be made from butanes by first isomerizing the normal butanes to isobutane, and then dehydrogenating to isobutylene. This is a much more capital intensive process, and therefore the plant sizes in the United States are usually at least 500,000 t/yr to be economically competitive. Even at this size, it is still a relatively higher cost source of MTBE than that made from by-product isobutylene in ethylene plants or refineries.

Tetrahydrofuran. Almost all the THF in the United States is currently produced by the acid-catalyzed dehydration of 1,4-butanediol. Du Pont claimed a new low cost process for producing THF from n-butane (18–20). This process transport-bed oxidizes n-butane to crude maleic anhydride, then follows with a hydrogen reduction of aqueous maleic acid to THF (18).

5.3. Other Ethers. *n-Butyl Ether.* n-Butyl ether is prepared by dehydration of n-butyl alcohol by sulfuric acid or by catalytic dehydration over ferric chloride, copper sulfate, silica, or alumina at high temperatures.

Isopropyl Ether. Isopropyl ether is manufactured by the dehydration of isopropyl alcohol with sulfuric acid. It is obtained in large quantities as a by-product in the manufacture of isopropyl alcohol from propylene by the sulfuric acid process, very similar to the production of ethyl ether from ethylene. Isopropyl ether is of moderate importance as an industrial solvent, since its boiling point lies between that of ethyl ether and acetone.

Tertiary-Amyl Methyl Ether. Like MTBE, TAME is produced by the simple reaction of methanol and isoamylenes (2-methyl-1-butene and 2-methyl-2-butene).

Ethyl tertiary-Butyl Ether. Similar to methanol in the MTBE reaction, ethanol can react with isobutylene to produce ETBE. Which alcohol is used to make the ether is highly dependent on the relative cost of the alcohols. To make ethanol more economically competitive with methanol, the federal tax credit for biomass-based ethanol used in fuel also applies to ethanol used to make ETBE in the United States (21).

Vinyl Ether. Vinyl ether is manufactured by the pyrolytic dehydrochlorination of 1,1′-dichloroethyl ether.

2-Methoxyphenol. This ether is prepared by methylating 1,2-dihydroxybenzene.

Butylated Hydroxyanisole. 2- and 3-*tert*-Butyl-4-methoxyphenol (butylated hydroxyanisole (BHA)) is prepared from 4-methoxyphenol and *tert*-butyl alcohol over silica or alumina at 150°C or from hydroquinone and *tert*-butyl alcohol or isobutene, using an acid catalyst and then methylating.

6. Shipment

6.1. Handling. The handling of ethyl ether is hazardous because of its highly flammable properties. Not only is it highly volatile, but it is also has a low autoignition temperature and, as a nonconductor, can generate static electrical charges that may result in ignition or vapor explosion. The area in which ethyl ether is handled should be considered a Class 3 hazardous location as defined by the National Electrical Code (22). All tools used in making connections or repairs should be of the nonsparking type. All possible care should be taken in loading and unloading tank cars. The tank cars should be properly spotted, and the usual caution signs and derails placed in position. Before any connection is made, the tank car should be grounded and bonded. Tank cars should always be unloaded through dome connections rather than through bottom outlets, eg, a pressure-type LPG tank car. A positive suction-type pump or natural gas can be used to remove the ethr from the tank car. In no event should air pressure be used.

Special containers have been developed for anesthetic either to prevent deterioration before use. Their effectiveness as stabilizers usually depends on the presence of a lower oxide of a metal having more than one oxidation state. Thus the sides and the bottoms of tin-plate containers are electroplated with copper, which contains a small amount of cuprious oxide. Stannous oxide is also used in the linings for the containers. Instead of using special containers, iron wire or certain other metals and alloys or organic compounds have been added to other to stablize it.

6.2. Peroxide Formation. Except for the methyl *tert*-alkyl ethers, most ethers tend to absorb and react with oxygen from the air to form unstable peroxides that may detonate with extreme violence when concentrated by evaporation or distillation, when combined with other compounds that give a detonable mixture, or when disturbed by heat, shock, or friction. Appreciable quantities of crystalline solids have been observed as gross evidence for the formation of peroxides, and peroxides may form a viscous liquid in the bottom of ether-filled containers. If viscous liquids or crystalline solids are observed in ethers, no further tests for the detection of peroxides are recommended. Several chemical and physical methods for detecting and estimating peroxide concentrations have been described. Most of the qualitative tests for peroxides are readily performed and strongly recommended when any doubt is present (23).

Isopropyl ether very readily forms hazardous peroxides and hydroperoxides, much more so than other ethers.

7. Economic Aspects

In January 2003, U.S. capacity of methyl-*tert*-butyl ether (MTBE) was 259,190 barrels/day. Demand in 2001 was 282,000 barrels/day. Demand equals production plus imports minus exports. In 2001, 90,000 barrels/day were imported and 20,000 barrels/day were exported. It is estimated in 2005 demand will be 203,000 barrels/day.

In 1999, California announced that it would ban MTBE as an oxygenate after trace amounts were found in the drinking water. MTBE found its way into the drinking water from underground gasoline storage tanks that were leaking. The decision to ban MTBE was postponed until January 2004 because of the fear of rising gasoline process. Some refineries have already switched to ethanol as an oxygenate. For these reasons, growth for MTBE through 2005 is estimated at negative 7.9% (1).

Tetrahydrofuran's major use is as a monomer in the production of polytetramethylene ether glycol (PTMEG). PTMEG is a component in the prodution of stretch fibers and high-performance copolyester–polyether elastomers. U.S. consumption grew at a rate of 5.7%/yr from 1989 to 1999. Growth is projected at a rate of 5.6%/yr through 2005. Expected consumption for 2005 is 145×10^3 (24).

The Western European market is expected to grow at the rate of 6.8%/yr through 2005. Market is estimated at 75×10^3 t. Japan consumption is expected to grow at a rate of 8–9%/yr to about 54×10^3 t through 2005. Most of the tetrahydrofuran consumed in Japan goes into the production or PTMEG (24).

8. Specifications

Ethyl ether is commercially available in the following grades: USP anesthesia, absolute (ACS) industrial, solvent (conc), and synthetic. Specifications vary, depending on the consumer and use. In many instances, the ether has to meet a specific test written into the specification, eg, it may be important that the ether is completely anhydrous or free from alcohol and aldehyde.

The technical concentrated ether contains very small amounts of alcolhol, water, aldehydes, peroxides, and other impurities (Table 4). The more refined grades, such as anesthetic ether, are obtained from technical ether by redistillation and dehydration followed by alkali or charcoal treatment.

Ethyl ether is classified by the ICC as a flammable liquid. As such it must be packed in ICC specification containers when shipped by rail, water, or highway; all ICC regulations regarding loading, handling, and labeling must be followed. Each container of ethyl ether must carry an identifying label or

Table 4. **Specifications for Various Grades of Ethyl Ether**

Specification	Technical refined	ACS, absolute	USP XIX[a]
color, max	water-white	water-white	colorless
d_{25}^{25}	0.710–0.713	0.7079	0.713–0.716
acidity as acetic acid, wt%	0.0025	0.0010	passes test[b]
peroxides, max wt%	passes text[c]	0.0001	passes test[c]
aldehydes, max wt%	passes test[d]	0.0005	passes test[d]
alcohol, max %	0.5 vol%	0.05 wt%	
nonvolatile matter, max wt%	0.002	0.0010	0.003
water, max wt%	0.3	0.0100	
odor	nonresidual	passes test[e]	passes test[e]
net container contents, kg[f]			
19-L (5-gal) drum	13.6	13.6	13.6
208-L (55-gal) drum	147	147	147

[a] For use in anesthesia; the USP (22) also recognizes slightly less pure grades: ethyl oxide (solvent ether), ether abs, and reagent-grade ether.

[b] Free acid, requiring no more than 0.4 mL of 0.02 *N* sodium hydroxide for 25 mL of ethyl ether.

[c] No color with potassium iodide reagent; USP test.

[d] No turbidity with alkaline mercuric chloride–potassium iodide reagent; USP test.

[e] No foreign odor when last traces of ether evaporate from odorless absorbent paper; USP test.

[f] The tech-grade can also be shipped in 103 W insulated tank cars of 15.1-m^3 (4000-gal), 22.7-m^3 (6000-gal), 30.3-m^3 (8000-gal), and 37.9-m^3 (10,000-gal) capacity.

stencil. Tank cars and boxcars, either carload or less than carload, must bear the ICC dangerous placard. Each drum or each box with inside containers must bear the ICC red label for flammable liquids.

For fuel-grade MTBE, the typical specification of merchant product is 95 wt% minimum purity in the United States and 98% minimum in Europe. The maximums for impurities are usually 0.5 wt% for methanol, and 0.15 wt% for water. To maintain quality, fuel-grade MTBE is normally stored in fixed-roof tanks, to keep rain water out, with internal floaters, to minimize vapor losses.

Besides its use in gasoline, a high purity refined grade (99.9% min) of MTBE is produced for other industrial uses.The general industry specifications are a minimum purity of 99.9 wt%. Maximum impurities are 300 ppm water and 150 ppm of the hydroperoxide of THF. Like most ethers, it is prone to forming peroxides on storage, and therefore is usually sold containing an antioxidant such as BHT.

9. Analytical Methods

Most of the analytical and testing methods used for ethyl ether are conventional laboratory methods. Ethyl ether that is to be used for anesthetic purposes or in processes that involve heating or distillation must be peroxide-free, and should pass the USP standard test with potassium iodide. This test detects approximately 0.001% peroxide as hydrogen peroxide.

10. Health and Safety Factors

Although ethers are not particularly hazardous, their use involves risks of fire, toxic effects, and several unexpected reactions.

10.1. Flammability. Since almost all ethers burn in air, an assessment of their potential hazards depends on flash points and ignition temperatures. The flash point of a liquid is the lowest temperature at which vapors are given off in sufficient quantities for the vapor–air mixture above the surface of the liquid to propagate a flame away from the source of ignition. In other words, an explosive vapor–air mixture can form whenever a liquid is used or stored in an open container at a temperature above its flash point. Table 2 includes the flash points of several common ethers.

The ignition temperature is the minimum temperature required to initiate or cause self-sustained combustion. Table 2 also lists ignition temperatures of several common ethers. Attention is directed to the particularly low ignition temperature of ethyl ether, especially with reference to some common ignition sources such as a lighted cigarette (732°C) or a pressurized (0.7 MPa or 100 psi) steam line (180°C).

If an ethyl ether fire occurs, carbon dioxide, carbon tetrachloride, and dry chemical fire extinguishers meeting National Fire Prevention Association Code 1 and 2 requirements may be used successfully (25). Water may also be effectively applied (see Plant safety). Hose streams played into open tanks of burning ethyl ether serve only to scatter the liquid and spread the fire. However, ether fires may be extinguished by a high pressure water spray that cools the burning surface and smothers the fire. Automatic sprinklers and deluge systems are also effective.

10.2. Toxicity. The effect of ethers owing to ingestion, skin contact, or inhalation may range from drowsiness and lack of coordination to serious injury or death. Ethers are reported to have a low order of toxicity when ingested, although 30–60 mL may be fatal when swallowed (26), and a case of fatal poisoning owing to ingestion of a large quantity of 2-methoxyethanol has been recorded (27).

Prolonged or repeated contacts of ethers with skin cause tissue defatting and dehydration leading to dermatitis. Some compounds penetrate the skin in harmful amounts. 1,4-Dioxane and 1-allyl-3,4-methylenedioxybenzene (safrole) have been listed as Category I carcinogens by OSHA. Category I carcinogens are confirmed cancer-causing agents based on human data, or based on tests in two mammalian species, or in one species if the tests have been replicated.

Inhalation is the most common means by which ethers enter the body. The effects of various ethers may include narcosis, irritation of the nose, throat, and mucous membranes, and chronic or acute poisoning. In general, ethers are central nervous system depressants, eg, ethyl ether and vinyl ether are used as general anesthetics.

The toxicity of ethyl ether is low and its greatest hazards in industry are fire and explosion. The vapor is absorbed almost instantly from the lungs and very promptly from the intestinal tract. It undergoes no chemical change in the body. Prevention and control of health hazards associated with the handling of ethyl ether depend primarily on prevention of exposure to toxic atmospheric concentrations and scrupulous precautions to prevent explosion and fire.

A concentration of 35,000 ppm in air produces unconsciousness in 30–40 minutes. This concentration also constitutes a serious fire and explosion hazard, and should not be permitted to exist under any circumstance. Any person exposed to ethyl ether vapor of any appreciable concentration should be promptly removed from the area. Recovery from exposure to sublethal concentrations is rapid and generally complete. Except in emergencies, and then only with appropriate protective equipment, no one should enter an area containing ether vapor until the concentration has been found safe by measurement with a combustible-gas indicator.

Airborne exposure limits for ethyl ether OSHA PEL and ACGIH threshhold limit are both 400 ppm (TWA) (28).

11. Uses

Alkyl ethers are used for organic reactions and extractions, as plasticizers, as vehicles for other products, as anesthetics (qv), and octane (and oxygen) enhancers in gasoline. Most ethers have very low solubility in water, but dissolve most organic compounds, and therefore have found wide application in paint and varnish removers; as high boiling solvents for gums, resins, and waxes; in lubricating oils (see LUBRICATION); as an extraction solvent in the fragrance industry; and as an inert reaction medium in the pharmaceutical industry. The vapors of certain ethers are toxic to insects and are useful as agricultural insecticides (see INSECT CONTROL TECHNOLOGY) and industrial fumigants. Except for those used in gasoline, the lower mol wt technical-grade ethers are the least expensive and most commonly used in industry.

Aryl ethers have distinctive, pleasant odors and flavors which make them valuable to the perfume (qv) and flavor industries (see FLAVORS). Because of their heat stability, they are useful as heat-transfer fluids (see HEAT-EXCHANGE TECHNOLOGY). Other aryl ethers are useful as food preservatives and antioxidants (see FOOD ADDITIVES).

11.1. Ethyl Ether. Ethyl ether [60-29-7] has a wide range of uses in the chemical industry. It is a good solvent or extractant for fats, waxes, oils, perfumes, resins, dyes, gums, and alkaloids. When mixed with ethanol, ethyl ether becomes an excellent solvent for cellulose nitrate in the manufacture of guncotton (see EXPLOSIVES AND PROPELLANTS), collodion solutions (see MEMBRANE TECHNOLOGY), and pyroxylin plastics (see CELLULOSE ESTERS). Another important use is an extractant for acetic acid as well as other organic acids, eg, in the cellulose acetate and plastic industries to recover acetic acid from dilute aqueous systems. Ethyl ether is also used as a denaturant in several denaturant alcohol formulas. It has been used as a starting fuel for diesel engines and as an entrainer for dehydration of ethanol and isopropyl alcohol. It may be used as an anhydrous, inert reaction medium for the Grignard and Wurtz-Fittig reactions. Ethyl ether is used as a general anesthetic in surgery.

11.2. Methyl-*tert*-Butyl Ether. MTBE and related ethers are used to add octane to gasoline. This comprises 99.5% of use. It also adds oxygen to the gasoline, which allows for more efficient combustion, and therefore less carbon monoxide and unburned hydrocarbon in the exhaust emissions (12,21). The remaining 0.5% is used as a chemical intermediate and solvent.

A refined grade of MTBE is used in the solvents and pharmaceutical industries. The main advantage over other ethers is its uniquely stable structural framework that contains no secondary or tertiary hydrogen atoms, which makes it very resistive to oxidation and peroxide formation. In addition, its higher autoignition temperature and narrower flammability range also make it relatively safer to use compared to other ethers (see Table 3).

The refined grade's fastest growing use is as a commercial extraction solvent and reaction medium. Other uses are as a solvent for radical-free copolymerization of maleic anhydride and an alkyl vinyl ether, and as a solvent for the polymerization of butadiene and isoprene using lithium alkyls as catalyst. Other laboratory applications include use as a solvent for Grignard reagents, and also for phase-transfer catalysts.

One other unique use of MTBE is a medical procedure for the removal of gallstones. This alternative to gallbladder surgery was developed at the Mayo Clinic, and takes advantage of MTBE's capability to quickly dissolve cholesterol. A small incision is used to inject a small amount of MTBE directly into the gallbladder, and the gallstone can then be removed in solution form (29).

11.3. Tetrahydrofuran. A major portion of the U.S. production is used to make poly(tetramethylene ether glycol) [25190-06-1] (PTMEG), also known as poly-THF, which is used in the production of urethane elastomers, polyurethane fibers (ether-based spandex), and copolyester–ether elastomers. PTMEG is also the fastest growing use (see POLYETHERS, TETRAHYDROFURAN). The remaining production is used as a solvent for the manufacture of poly(vinyl chloride) cements and coating, precision magnetic tape, and a reaction solvent in the production of pharmaceuticals.

11.4. Other Ethers. *n*-Butyl ether is an important solvent for Grignard reagents and other reactions that require an anhydrous, inert medium. It is also an excellent extracting agent for use with aqueous systems owing to its very low water-solubility.

Isopropyl ether forms hazardous peroxides and hydroperoxides, but this tendency can be controlled with commercial antioxidants. It is being promoted as another possible ether to be used in gasoline (30).

tert-Amyl methyl ether (TAME) is used in gasoline blending and as a feedstock to make high purity isomylene. Its use in octane blending has not grown rapidly because of less favorable economics (TAME's lower octane number). However, it is possible that the need for gasoline with lower vapor pressure and that contain oxygen may prove favorable for TAME.

Vinyl ether is used as a general inhalation anesthetic for procedures of short duration. Approximately 4% ethanol is added to the vinyl ether used as an anesthetic to reduce ice formation in the masks used for administration. Die attach adhesives with vinyl ether and urea functionality for use in microelectronics have been described (31).

2-Methoxyphenol is used as an antioxidant for fats, oils, and vitamins. It is effective at levels of 10–100 ppm.

Butyrated hydroxyanisole (BHA) is used as an antioxidant in foods such as butter, lard, other fats, meats, cereals, baked goods, candies, and beer. Its antioxidant properties are not lost during cooking so that flour, fats, and other BHA-stabilized ingredients may be used to produce stablized products.

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