Kirk-Othmer Encyclopedia of Chemical Technology.

THIOLS

The chemistry of organic sulfur compounds is very rich and organosulfur compounds are incorporated into many molecules. Thiols, or mercaptans as they were originally called, are essential as feedstocks in the manufacture of many types of rubber (qv) and plastics (qv). They are utilized as intermediates in agricultural chemicals, pharmaceuticals (qv), in flavors and fragrances, and as animal feed supplements. Many reviews have been undertaken on the chemistry of the thiols, regarding both their preparation and their reactions (1–7).

1. Nomenclature

Thiols are still commonly named as mercaptans, although the proper nomenclature is that established by the International Union of Pure and Applied Chemists (IUPAC). A listing of the IUPAC name, common name, and structure, is shown in Table 1.

2. Occurrence

Cysteine [52-90-4] is a thiol-bearing amino acid which is readily isolated from the hydrolysis of protein. There are only small amounts of cysteine and its disulfide, cystine, in living tissue (7). Glutathione [70-18-8] contains a mercaptomethyl group, $HSCH_{2-}$, and is a commonly found tripeptide in plants and animals. Coenzyme A [85-61-0] is another naturally occurring thiol that plays a central role in the synthesis and degradation of fatty acids.

Methanethiol has been found in sewer gases (8, 9) and is thought to be produced by the bacterial degradation of methionine. Methanethiol, 1-butanethiol, and 2-methyl-1-propanethiol are produced by the bacterial degradation of blue-green algae. Some yeasts produce ethanethiol, 2-propanethiol is produced by actively growing *Microcystis flosaquae* (10). Methanethiol, ethanethiol, 1-propanethiol, 2-propanethiol, 2-methyl-1-propanethiol, 2-methyl-2-propanethiol, and 1-butanethiol are found in the environment near domestic animal pens (11).

Skunks excrete 1-butanethiol and 2-methyl-1-butanethiol [1878-18-8] as a natural defense mechanism (12). Methanethiol is found in cheese, milk, coffee, and oysters (13–16). It is also found in the kurrin fruit, which is endemic to Southeast Asia.

3. Physical Properties

The physical characteristic of thiols that most distinguishes them is their odor. Thiols have been used since the late 1800s as malodorants in combustible gases. In the 1930s the U.S. Bureau of Mines published a series of reports regarding the intensity of odors of warning agents that put this practice on a scientific basis (17).

Table 1. Nomenclature of Thiols

IUPAC name	Common name	Structure
methanethiol	methyl mercaptan	CH_3SH
ethanethiol	ethyl mercaptan	CH_3CH_2SH
2-propanethiol	isopropyl mercaptan	$CH_3CH(SH)CH_3$
2-butanethiol	*sec*-butyl mercaptan	$CH_3CH(SH)CH_2CH_3$
1-butanethiol	*n*-butyl mercaptan	$CH_3CH_2CH_2CH_2SH$
2-methyl-2-propanethiol	*t*-butyl mercaptan	$(CH_3)_3CSH$
2,4,4-trimethyl-2-pentanethiol	*tert*-octyl mercaptan	$(CH_3)_2C(SH)CH_2C(CH_3)_3$
cyclohexanethiol	cyclohexyl mercaptan	$C_6H_{11}SH$
benzenethiol	thiophenol	C_6H_5SH
α-toluenethiol	benzyl mercaptan	$C_6H_5CH_2SH$

There have been innumerable studies since that time regarding the odor intensity of thiols, primarily about their role in the odorization of natural gas and propane gas. All of the definitive studies on thiol threshold odor levels have been brought together and normalized to give a standardized odor scale (18). Even the heavier mercaptans have a significant odor, particularly when heated.

Thiols range over the gamut of physical properties. Most of the important thiols are liquids, however methanethiol is a gas, and 1-hexadecanethiol and 1-octadecanethiol are waxy solids. Tables 2 and 3 list a variety of physical properties for the more important thiols.

The heat capacities and entropies of organic compounds, including many thiols, have been compiled (19, 20). The thermochemistry of thiols and other organosulfur compounds has been extensively reviewed (21).

4. Preparation of Thiols

Thiols can be prepared by a variety of methods. The most-utilized of these synthetic methods for tertiary and secondary thiols is acid-catalyzed synthesis; for normal and secondary thiols, the most-utilized methods are free-radical-initiated, alcohol substitution, or halide substitution; for mercaptoalcohols, the most-utilized method is oxirane addition; and for mercaptoacids and mercaptonitriles, the most-utilized methods are Michael-type additions.

4.1. Acid-Catalyzed Synthesis

The acid-catalyzed reaction of alkenes with hydrogen sulfide to prepare thiols can be accomplished using a strong acid (sulfuric or phosphoric acid) catalyst. Thiols can also be prepared continuously over a variety of solid acid catalysts, such as zeolites, sulfonic acid-containing resin catalysts, or aluminas (22). The continuous process is utilized commercially to manufacture the more important thiols (23, 24). The acid-catalyzed reaction is commonly classed as a Markownikoff addition. Examples of two important industrial processes are 2-methyl-2-propanethiol and 2-propanethiol, given in equations 1 and 2, respectively.

$$(CH_3)_2\,C{=}CH_2 + H_2S \longrightarrow (CH_3)_3\,CSH \qquad (1)$$

$$CH_3CH{=}CH_2 + H_2S \longrightarrow (CH_3)_2CH(SH) \qquad (2)$$

Table 2. Properties of Thiols

Compound	CAS Registry Number	Molecular weight	Melting point, K	Boiling point, K
methanethiol	[74-93-1]	48.11	150.18	279.11
ethanethiol	[75-08-1]	62.14	125.26	308.15
2-mercaptoethanol	[60-24-2]	78.14	200.00	430.90
1,2-ethanedithiol	[540-63-6]	94.20	231.95	419.20
mercaptoacetic acid	[68-11-1]	92.12	256.65	493.00
1-propanethiol	[107-03-9]	76.16	159.95	340.87
2-propanethiol	[75-33-2]	76.16	142.61	325.71
3-mercaptopropionic acid	[107-96-0]	106.15	290.65	501.00
1-butanethiol	[109-79-5]	90.19	157.46	371.61
2-butanethiol	[513-53-1]	90.19	133.02	358.13
2-methyl-1-propanethiol	[513-44-0]	90.19	128.31	361.64
2-methyl-2-propanethiol	[75-66-1]	90.19	274.26	337.37
2,2′-oxybisethanethiol	[2150-02-9]	138.26	193.15	490.15
1-pentanethiol	[110-66-7]	104.22	197.45	399.79
cyclohexanethiol	[1569-69-3]	116.23	189.64	431.95
1-hexanethiol	[111-31-9]	118.24	192.62	425.81
benzenethiol	[108-98-5]	110.18	258.26	442.29
1-heptanethiol	[1639-09-4]	132.27	229.92	450.09
α-toluenethiol	[100-53-8]	124.21	243.95	472.03
1-octanethiol	[111-88-6]	146.30	223.95	472.19
2,4,4-trimethyl-2-pentanethiol	[141-59-3]	146.30	199.00	428.65
1-nonanethiol	[1455-21-6]	160.32	253.05	492.95
1-decanethiol	[143-10-2]	174.35	247.56	512.35
1-undecanethiol	[5332-52-5]	188.38	270.15	530.55
1-dodecanethiol	[112-55-0]	202.40	265.15	547.75
tert-dodecanethiol[a]	[25103-58-6]	202.40		515.65
1-hexadecanethiol	[2917-25-2]	258	291–293	$396–401_{0.07}$[b]
1-octadecanethiol	[2885-00-9]	286	301	$461_{0.1}$[b]

[a] *tert*-Dodecanethiol is a mixture of isomers.

[b] Subscripted value represents pressure in kPa at which boiling point was taken. To convert kPa to mm Hg, multiply by 7.5.

These reactions tend to give few by-products. The main by-product in each case is the sulfide, RSR, which amounts to less than 3–5% of the thiols produced. Some of the sulfides produced have applications, although they tend to be much smaller-volume requirements than the amounts produced. The sulfides can be incinerated for disposal, assuming that the incineration facility can handle high sulfur feedstocks.

4.2. Free-Radical-Initiated Synthesis

Free-radical-initiated reactions of hydrogen sulfide to alkenes are commonly utilized to prepare primary thiols. These reactions, where uv light is used to initiate the formation of hydrosulfuryl (HS) radicals, are utilized to prepare thousands of metric tons of thiols per year. The same reaction can be performed using a radical initiator, but is not as readily controlled as the uv-initiated reaction. These types of reactions are considered to be anti-Markownikoff addition reactions.

This synthesis method can be utilized by any alkene or alkyne, but steric hindrance on internal double bonds can cause these reactions to be quite slow. Conjugated dienes and aromatic alkenes are not suited for the ultraviolet light-initiated process. The use of other free-radical initiators is required in free-radical-initiated reactions involving these species.

Table 3. Physical Properties of Thiols

Compound	Flash point, K	Lower flammability limit, %	Heat of formation,[a] kJ/mol[b]	Gibbs heat of formation,[a] kJ/mol
methanethiol	217	3.9	−22.9	−9.80
ethanethiol	225	2.8	−46.3	−4.81
2-mercaptoethanol	340.15	2.3	−197	−134
1,2-ethanedithiol	317.15	1.9	−9.70	26.7
mercaptoacetic acid	398	3.1	−394	−344
1-propanethiol	253.15	1.8	−67.5	2.58
2-propanethiol	238.15	1.8	−75.9	2.18
3-mercaptopropionic acid	366.15	2.2	−406	−344
1-butanethiol	274.82	1.4	−87.8	11.4
2-butanethiol	250.15	1.4	−96.6	5.12
2-methyl-1-propanethiol	264.15	1.4	−96.9	5.98
2-methyl-2-propanethiol	<253	1.4	−109	1.01
2,2′-oxybis(ethanethiol)	371.15	1.3	−173, 000	−59, 900
1-pentanethiol	291	1.2	−110	18.0
cyclohexanethiol	316.15	1.1	−96.0	36.7
1-hexanethiol	293.15	1	−129	27.6
benzenethiol	346.15	1.2	112	148
1-heptanethiol	319.15	0.9	−150	36.2
α-toluenethiol	343.15	1.1	93.3	163
1-octanethiol	341.15	0.8	−170	44.6
2,4,4-trimethyl-2-pentanethiol	304	0.8	−202	31.1
1-nonanethiol	351.15	0.7	−191	52.8
1-decanethiol	371.15	0.6	−211	61.7
1-undecanethiol	382	0.6	−233	69.0
1-dodecanethiol	360.15	0.5	−253	77.2
tert-dodecanethiol	363.15	0.6	−273	68.2

[a] To gaseous product.

[b] To convert kJ to kcal, divide by 4.814.

Examples of thiols prepared using this type of technology are 2-methyl-1-propanethiol, 1-butanethiol, and 2-butanethiol, in equations 3–5, respectively.

$$\mathrm{(CH_3)_2\,C{=}CH_2 + H_2S \longrightarrow (CH_3)\,CHCH_2SH} \tag{3}$$

$$\mathrm{CH_3CH_2CH{=}CH_2 + H_2S \longrightarrow CH_3CH_2CH_2CH_2SH} \tag{4}$$

$$\mathrm{CH_3CH{=}CHCH_3 + H_2S \longrightarrow CH_3CH\,(SH)\,CH_2CH_3} \tag{5}$$

The main by-products of this synthesis type are sulfides and the isomer resulting from the Markownikoff addition to the alkene. For example, in the synthesis of 1-butanethiol (eq. 4), 5-thianonane, $C_4H_9SC_4H_9$, and 2-butanethiol are produced as by-products. The 2-butanethiol has uses as a herbicide intermediate and a gas odorant blend component and is further processed. The 5-thianonane is incinerated or reprocessed for fuel value. Sulfides account for up to 10% of the thiols produced. Another 2–5% is the Markownikoff addition product.

Table 4. Toxicological Studies of Thiols[a]

Species	Route[b]	Concentration, mg/kg	LD_{50}, mg/kg[c]
Methanethiol			
mice	respiratory (4)	1200–2200	1664^d
Ethanethiol			
rat	respiratory (4)	2600–5125	4870^d (1) 4420^d (15) d
rat	respiratory (0.25)	27,000–38,000	
rat	oral	210–3360	1034 (15) d
rat	intraperitoneal	105–1680	450 mg/kg
mice	respiratory (4)	2600–4812	2770^d
Propanethiol			
rat	respiratory (4)	3050–11260	7300^d
rat	oral	1327–3344	2360
rat	intraperitoneal	209–1672	1028
Butanethiol 0.0pt7,498.65906pt			
mice	respiratory (4)	3050–11260	4950^d (24) 4010^d (15) d
rat	oral	1039–3344	2475 (1) 4020 (15) d
rat	intraperitoneal	209–672	2475 (1) 1500 (15) d
t-Butanethiol			
rat	respiratory (4)		$97^{d,e}$
rat	oral		8.4^f
rabbit	dermal		20.8^f
Dodecanethiol			
mice	intragastric		4225

[a] Refs. (56, 58).
[b] Value in parentheses is exposure time in hours.
[c] Value in parentheses is time in days.
[d] Value is LC_{50}.
[e] Value is in mg/L.
[f] Value is in g/kg.

4.3. Alcohol Substitution

In the early period of normal thiol production, the normal alcohols were utilized as feedstocks. The use of a strong acid catalyst results in the formation of a significant amount of secondary thiol, along with other isomers resulting from skeletal isomerization of the starting material. This process has largely been replaced by uv-initiation because of the higher relative cost of alcohol vs alkene feedstock.

Methanethiol (eq. 6) and cyclohexanethiol (eq. 7) are the only commercially important thiols prepared using alcohol substitution. In most cases, when the alcohol is utilized, less control over the substitution patterns is obtained. Only one isomer is obtainable in the case of methanol and cyclohexanol.

$$CH_3OH + H_2S \longrightarrow CH_3SH + H_2O \qquad (6)$$

$$C_6H_{11}OH + H_2S \longrightarrow C_6H_{11}SH + H_2O \qquad (7)$$

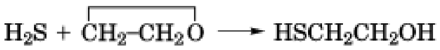
The main by-product of this type of reaction is the sulfide. For the synthesis of methanethiol (eq. 6), the main by-product is 2-thiapropane, CH_3SCH_3. This material has a variety of uses and is further processed.

4.4. Oxirane Ring Opening

Mercaptoalcohols are prepared by the reaction of hydrogen sulfide and a suitable oxirane. This reaction is readily extendable to many oxiranes, but in general, there are only three oxiranes that are readily available: oxirane (ethylene oxide), 1-methyloxirane (propylene oxide), and α-chloromethyloxirane (epichlorhydrin). Epichlorhydrin is too corrosive and the resulting thiol is too unstable for general use. The oxiranes made from long-chain normal alkenes (C_{10}–C_{18}) also work in this type of reaction. There are, however, no known applications utilizing the mercaptoalcohols prepared from the higher alkyl oxiranes of this type.

The oxirane ring-opening reaction requires the presence of a basic catalyst. An acidic catalyst also works, but the polymerization of the oxirane limits its usefulness. In the case of 2-mercaptoethanol (eq. **8**), the product has been found to be autocatalytic, ie, the product is a catalyst for the reaction.

These reactions are extremely exothermic and there is also the potential of initiating oxirane self-polymerization, which is an extremely exothermic reaction. In general, these reactions are run by adding oxirane to a large excess of thiol for heat control purposes and to minimize the multiple addition of oxirane to the resulting mercaptoalcohol. 2-Mercaptoethanol (eq. **8**) is the only product prepared in large scale using this technology, although 2-mercapto-1-propanol can also be prepared in this manner (eq. **9**):



$$H_2S + CH_2\text{–}CH_2O \longrightarrow HSCH_2CH_2OH \qquad (8)$$

$$H_2S + CH_3CH\text{–}CH_2O \longrightarrow HOCH_2CH(SH)CH_3 \qquad (9)$$

The by-products of these reactions are sulfides. The sulfide formed in the synthesis of 2-mercaptoethanol, 3-thia-1,5-pentanediol (thiodiglycol), has a variety of uses ranging from lubricant additive intermediates to textile finishing.

4.5. Michael-Type Additions

Michael additions are generally used to prepare methyl 3-mercaptopropionate (eq. 10) and mercaptopropionitrile (eq. 11) by the reaction of methyl acrylate or acrylonitrile and hydrogen sulfide using a basic catalyst. This reaction proceeds as shown:

$$CH_2{=}CHCOOCH_3 + H_2S \longrightarrow HSCH_2CH_2COOCH_3 \qquad (10)$$

$$CH_2{=}CHCN + H_2S \longrightarrow HSCH_2CH_2CN \qquad (11)$$

The catalyst for this type of reaction is generally an amine. These reactions are quite exothermic, and the selection of the amine plays an important role in the rate of the reaction as well as in the amount of heat generated. The processes utilized to make these types of products are either batch or continuous (25–27).

The main by-products of this type of process are sulfides and disulfides. The disulfides are formed by the inclusion of an oxidizing agent (generally oxygen) that may be present in the reaction mixture or upon purification. Some of the sulfides formed in this fashion are useful as intermediates for the production of antioxidants. Other mercaptopropionates can be made in similar fashion, if the alkyl acrylate is available.

4.6. Halide Displacement

Halide displacement is a method used to prepare thiols that are not readily available by normal means. It requires a two-phase, water–organic system, that can be quite corrosive. Normally, this type of reaction, a classic S_N2 type, is undertaken in Hastelloy or glass-lined reactors. The syntheses of the two most important thiols prepared using this technology, α-toluenethiol and 1,2-ethanedithiol, are shown in equations 12 and 13, respectively.

$$C_6H_5CH_2Cl + NaHS \longrightarrow C_6H_5CH_2SH + NaCl \qquad (12)$$

$$ClCH_2CH_2Cl + 2\ NaHS \longrightarrow HSCH_2CH_2SH + 2\ NaCl \qquad (13)$$

The main by-products of this type of reaction are sulfides. By exercising careful control of stoichiometry, these can be minimized quite readily. By-products are disposed of by incineration or by reprocessing for fuel value.

4.7. Esterification and Transesterification to Produce Alkyl Mercaptopropionates

The other methods used to produce many of the alkyl mercaptopropionates are either transesterification of methyl 3-mercaptopropionate or esterification of 3-mercaptopropionic acid. The process to obtain 3-mercaptopropionic acid is shown in equation 14. A transesterification is shown in equation 15 and an esterification in equation 16, both to the n-butyl 3-mercaptopropionate.

$$HSCH_2CH_2CN + H_2O \longrightarrow HSCH_2CH_2COOH + NH_3 \qquad (14)$$

$$HSCH_2CH_2COOCH_3 + C_4H_9OH \longrightarrow HSCH_2CH_2COOC_4H_9 + CH_3OH \qquad (15)$$

$$HSCH_2CH_2COOH + C_4H_9OH \longrightarrow HSCH_2CH_2COOC_4H_9 + H_2O \qquad (16)$$

These reactions, catalyzed using sulfuric acid or a titanate ester, tend to be free of by-products.

4.8. Arenethiols

Most of the chemistry described for alkanethiols is not applicable to benzenethiols and other arenethiols. The synthesis of benzenethiol is best carried out by reduction of the benzene sulfonyl chloride (eq. 17). Other methods for synthesizing arenethiols are discussed at greater length in the literature (28).

$$C_6H_5SO_2Cl + 3\ H_2 \longrightarrow C_6H_5SH + 2\ H_2O + HCl \qquad (17)$$

5. Reactions of Thiols

5.1. Oxidation

Disulfides are prepared commercially by two types of reactions. The first is an oxidation reaction utilizing the thiol and a suitable oxidant as in equation 18 for 2,2,5,5-tetramethyl-3,4-dithiahexane. The most common oxidants are chlorine, oxygen (29), elemental sulfur, or hydrogen peroxide. Carbon tetrachloride (30) has also been used. This type of reaction is extremely exothermic. Some thiols, notably tertiary thiols and long-chain thiols, are resistant to oxidation, primarily because of steric hindrance or poor solubility of the oxidant in the thiol. This type of process is used in the preparation of symmetric disulfides, RSSR. The second type of reaction is the reaction of a sulfenyl halide with a thiol (eq. 19). This process is used to prepare unsymmetric disulfides, RSSR′ such as 4,4-dimethyl-2,3-dithiahexane. Other methods may be found in the literature (28).

$$2\ (CH_3)_3\,CSH + 1/2\ O_2 \longrightarrow (CH_3)_3\,CSSC\,(CH_3)_3 + H_2O \qquad (18)$$

$$(CH_3)_3\,CSH + Cl_2 \longrightarrow (CH_3)_3\,CSCl + HCl$$

$$(CH_3)_3CSCl + CH_3SH \longrightarrow (CH_3)_3CSSCH_3 + HCl \qquad (19)$$

When oxygen is used as the oxidant, a basic catalyst is required for the lighter thiols (31) and a transition metal co-catalyst may be required for the heavier thiols (32). Oxidation using sulfur as the oxidant requires a basic catalyst.

Gas-phase oxidation of thiols has been discussed in some depth (33). This review mainly emphasizes atmospheric processes, but a section on nitrogen oxides and thiols appears to be broadly applicable. The atmospheric oxidation chemistry of thiols is quite different from that of alcohols.

Thiols can be utilized to prepare polysulfides such as 2,2,6,6-tetramethyl-3,4,5-trithiaheptane. These are prepared (eq. 20) using sulfur as the only oxidant (34, 35).

$$2\ (CH_3)_3\,CSH + 1/4\ S_8 \longrightarrow (CH_3)_3\,CSSSC\,(CH_3)_3 + H_2S \qquad (20)$$

Alkyl sulfonic acids are prepared by the oxidation of thiols (36, 37). This reaction is not quite as simple as would initially appear, because the reaction does not readily go to completion. The use of strong oxidants can result in the complete oxidation of the thiol to carbon dioxide, water, and sulfur dioxide.

5.2. Formation of Sulfides

Thiols react readily with alkenes under the same types of conditions used to manufacture thiols. In this way, dialkyl sulfides and mixed alkyl sulfides can be produced. Sulfides are a principal by-product of thiol production. Mixed sulfides can be formed by the reaction of the thiol using a suitable starting material, as shown in equations 21, 22, and 23. Vinyl sulfides can be produced by the reaction of alkynes with thiols (38).

$$RSH + R'CH{=}CH_2 \longrightarrow RSCH_2CH_2R' \qquad (21)$$

$$RSH + R'Cl + NaOH \longrightarrow RSR' \qquad (22)$$

$$RSH + CH_2CH_2O \longrightarrow RSCH_2CH_2OH \qquad (23)$$

Mixed sulfides are prepared in the flavor industry by the reaction of thiols, zinc oxide, and a bromoalkane (39). Some of these mixed sulfides are constituents of allium, asafetida, coffee, and meat flavors. A representative reaction is represented in equation 24.

$$RSH + ZnO + R'Br \longrightarrow RSR' + ZnBr_2 \qquad (24)$$

5.3. Reactions with Aldehydes and Ketones

Thiols react with carbonyl compounds to form dithioacetals and thioacetals. The dithioacetals have been utilized as protecting groups for carbonyl compounds. They generally require stringent conditions to remove the blocking groups. The thioacetals are not overly stable. At least two thioacetals, 2,2,2-trichloro-1-thioethylethanol (40) and 1-dodecanethiomethanol (41), are stable.

This type of chemistry also functions for hydroxyketones and aldehydes. The process using 1,2-ethanedithiol or 2-mercaptoethanol results in cyclic structures (eq. 25). The 1,3-ditholenes ($X = S$) and 1,3-thioxalanes ($X = O$) resulting from these reactions have been shown to be of interest commercially.

$$RCH(OH)COR' + HXCH_2CH_2SH \longrightarrow RC{=}C(R')SCH_2CH_2X + 2\,H_2O \qquad (25)$$

A wide variety of products can be obtained by thioalkylation (42). The reactants are usually an aldehyde, a thiol, and either a phenol, a sulfone, an amine, or a heterocyclic compound. Phenols primarily react with formaldehyde in a process known as thiomethylation (eq. 26). Other types of reactions are depicted in equations 27 and 28.

$$C_6H_5OH + CH_2O + RSH \longrightarrow RSCH_2C_6H_4OH \qquad (26)$$

$$C_6H_5SO_2CH_2C_6H_5 + RSH + CH_2O \longrightarrow C_6H_5SO_2CH(SR)C_6H_5 \qquad (27)$$

$$CH_3NH_2HCl + C_6H_5CH_2SH + CH_2O \longrightarrow CH_3NHCH_2SCH_2C_6H_5HCl \qquad (28)$$

5.4. Decomposition of Thiols

Thiols decompose by two principal paths (r43– r45). These are the carbon–sulfur bond homolysis and the unimolecular decomposition to alkene and hydrogen sulfide. For methanethiol, the only available route is homolysis, as in reaction 29. For ethanethiol, the favored route is formation of ethylene and hydrogen sulfide via the unimolecular process, as in reaction 30.

$$CH_3SH \longrightarrow CH_3 + HS\cdot \qquad (29)$$

$$C_2H_5SH \longrightarrow C_2H_4 + H_2S \qquad (30)$$

The preferred route depends upon the availability of a hydrogen atom in the beta-position to the thiol group. In other words, α-toluenethiol (in toluene) decomposes to give 1,2-diphenylethane and hydrogen sulfide, via the homolytic route, whereas 2-methyl-2-propanethiol decomposes to give 2-methyl-1-propene and hydrogen sulfide.

5.5. Photolysis of Thiols

Thiols undergo photolytic reactions (46–48). These reactions proceed as shown in equations 31 and 32. A secondary mechanistic pathway is also observed. This is shown in equations 33 and 34.

$$CH_3SH + h\nu \longrightarrow CH_3S + H\cdot \qquad (31)$$

$$CH_3SH + H\cdot \longrightarrow CH_3S + H_2 \qquad (32)$$

$$CH_3SH + h\nu \longrightarrow CH_3 + HS\cdot \qquad (33)$$

$$CH_3SH + CH_3\cdot \longrightarrow CH_4 + CH_3S\cdot \qquad (34)$$

A review of the role of thiols as electron donors in photoinduced electron-transfer reactions has been compiled (49).

5.6. Thiol–Disulfide Interchange Reactions

The interchange between thiols and disulfides has been reviewed (50). This reaction is base-catalyzed. It involves the nucleophilic attack of a thiolate ion on a disulfide. This is shown in equations 35, 36, and 37.

$$RSH \rightleftharpoons RS^- + H^+ \qquad (35)$$

$$RS^- + R'SSR' \rightleftharpoons RSSR' + R'S^- \qquad (36)$$

$$H^+ + R'S^- \rightleftharpoons R'SH \qquad (37)$$

The effect of pH and the pK_a of the thiol has been discussed. This reaction is not of great synthetic interest, primarily because it yields a mixture of products, but it is of commercial consequence. It is also applicable in polysulfide synthesis, where the presence of small amounts of thiols can cause significant problems for the stability of the polysulfide (51). A similar reaction between thiols and sulfides has also been described (52). In this instance, the process is heterogenous and acid-catalyzed.

5.7. Metal Ion-Promoted Reactions of Thiols

Metal ion-promoted reactions of thiols have been reviewed (53). The bulk of the coverage concerns metal ion promoted aspects of sulfur chemistry. The main topics of interest are the formation of sulfenamides, sulfides, and disulfides using metal-mediated reactions.

6. Applications of Alkanethiols

The principal impetus behind the synthesis of thiols came from the need to produce synthetic rubber in the early 1940s. These rubbers, styrene–butadiene rubbers (SBRs), were produced by many companies at that time. Originally, 1-dodecanethiol was utilized, but the most important thiol became *tert*-dodecanethiol, which was made from propylene tetramer, using an acid-catalyzed process (54, 55).

In rubber production, the thiol acts as a chain transfer agent, in which it functions as a hydrogen atom donor to one rubber chain, effectively finishing chain growth for that polymer chain. The sulfur-based radical then either terminates with another radical species or initiates another chain. The thiol is used up in this process. The length of the rubber polymer chain is a function of the thiol concentration. The higher the concentration, the shorter the rubber chain; and the softer the rubber. An array of thiols have subsequently been utilized in the production of many different polymers. Some of these applications are as follow:

Thiol	Polymer
1-dodecanethiol	polybutadiene–acrylonitrile (PBAN)
	neoprene
	nitrile
	acrylic resins
tert-dodecanethiol	SBR
	SBR latex
	polyacrylates
	polymethacrylates
	nitrile rubber
	ABS
	SB latex
	expandable polystyrene
2-mercaptoethanol	PVC
	polyacrylates
	polymethacrylates
alkyl mercaptopropionates	polyacrylates
	polymethacrylates

In general, rubber manufacturers balance thiol reactivity and odor. The structure of the thiol plays a significant role in its ability to be transported within the polymer matrix, particularly in emulsion polymerizations, ie, mixed water–monomer emulsion. The odor of light thiols is generally too strong for most rubber manufacturers, as it is generally hard to remove residual odors from polymers.

Another area in which sulfur compounds have long found use is in the area of agricultural chemicals. Many of these materials had been produced by the manufacturer of the agricultural chemicals, but difficulties in containing odor and the use of hydrogen sulfide in heavily populated areas again pushed toward specialization by several companies. A list of agricultural chemicals, and the thiol that is used or has been used in production, follows:

Thiol	Agricultural chemical
ethanethiol	butylate
	cycloate
	demeton
	disulfoton
	oxydemeton-methyl
	oxydeprofos
	dipropetryn
	EPTC
	molinate
	phenothiol
	phorate
	sethoxydim
1-propanethiol	ethoprop
	pebulate
	profenophos
	prothiophos
	sulprofox
	vernolate
1-butanethiol	DEF
	merphos
	terbufos
1-octanethiol	MGK R-874
	pyridate
2-mercaptoethanol	Vitavax
1,2-ethanedithiol	Harvade
α-toluenethiol	IBP
	tiocarbazil
	Londax
methyl 3-mercaptopropionate	Kathon

Over the years, a diverse group of products made use of the rather unique chemistry of organosulfur chemicals. These include the following:

Thiol	Application
methanethiol	DL-methionine
ethanethiol	propane odorant
2-methyl-2-propanethiol	natural gas odorant components
1-octanethiol	water repellants
cyclohexanethiol	prevulcanization inhibitor
2-propanethiol	flocculent
	natural gas odorant component
tert-nonanethiol	polysulfides for oil additives
tert-dodecanethiol	polysulfides for oil additives
	surfactants
2-mercaptoethanol	PVC stabilizers
	solvent for acrylic fibers

Organosulfur chemicals serve a diverse group of industries. In these applications ways have been found to control the odor of the thiols, thus utilizing these compounds effectively in a wide range of products.

7. Toxicology and Handling

The toxicology and procedures for handling thiols used in gas odorants have been reviewed (56), as have thiols as a whole (57). A partial listing of toxicological results is shown in Table 4.

A listing of known TLV values and odor thresholds for a variety of thiols is given in Table 5.

Table 5. Odor Threshold Levels and Threshold Limit Values (TLV)

Thiol	Odor threshold,[a] ppb	TLV,[b] ppm
methanethiol	1.05	0.5
ethanethiol	1.07	0.5
1,2-ethanedithiol	19.50	
1-propanethiol	1.26	
2-propanethiol	0.35	
2-propene-1-thiol	0.40	
1-butanethiol	1.41	0.5
2-butanethiol	0.18	0.5
2-butene-1-thiol	0.13	
2-methyl-1-propanethiol	1.12	0.5
2-methyl-2-propanethiol	0.33	0.5
1-pentanethiol	0.12	0.5
2-methyl-1-butanethiol	0.26	
2-methyl-2-butanethiol	0.72	
benzenethiol	0.31	0.1
4-methylbenzenethiol	1.70	
α-toluenethiol	1.58	
1-dodecanethiol	0.25	
2-methyl-1-undecanethiol	190.55	

[a] Ref. 18.
[b] Refs. 59 and 60.

Thiol spills are handled in the same manner that all chemical spills are handled, with the added requirement that the odor be eliminated as rapidly as possible. In general, the leak should be stopped, the spill should be contained, and then the odor should be reduced. The odor can be reduced by spraying the spill area with sodium hypochlorite (3% solution), calcium hypochlorite solution (3%), or hydrogen peroxide (3–10% solution). The use of higher concentrations of oxidant gives strongly exothermic reactions, which increase the amount of thiol in the vapor, as well as pose a safety hazard. The application of an adsorbent prior to addition of the oxidant can be quite helpful and add to the ease of cleanup.

Thiols interact readily with many rubber-containing materials. For this reason, care should be taken in the selection of gasket and hose materials. Teflon, Kel-F, Viton, or other suitable fluoroelastomers function as gasket materials. Viton is suitable for hoses. Carbon steel is useful for many thiols, although some thiols become very discolored when carbon steel is utilized. In these cases, the use of stainless steel is very desirable. Isolation from air and water also minimizes color formation. 2-Mercaptoethanol and 1,2-ethanedithiol should be stored in stainless steel (61).

Thiols are shipped in every conceivable container size. Drums and cans can be of carbon steel for most thiols, provided color is not a determining factor. Truck, rail, and isocontainer shipments should be set up to utilize a vapor return line from the tank to the shipping container. This substantially minimizes the amount of odor that escapes. Phillips Petroleum Company and Atochem North America can supply further information regarding the handling and properties of many thiols.

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