*Kirk-Othmer Encyclopedia of Chemical Technology.*

# SULFOXIDES

Sulfoxides are compounds that contain a sulfinyl group covalently bonded at the sulfur atom to two carbon atoms. They have the general formula RS(O)R′, ArS(O)Ar′, and ArS(O)R, where Ar and Ar′ = aryl. Sulfoxides represent an intermediate oxidation level between sulfides and sulfones. The naturally occurring sulfoxides often are accompanied by the corresponding sulfides or sulfones. The only commercially important sulfoxide is the simplest member, dimethyl sulfoxide [67-68-5] (DMSO) or sulfinylbismethane.

Sulfoxides occur widely in small concentrations in plant and animal tissues, eg, allyl vinyl sulfoxide [81898-53-5] in garlic oil and 2,2′-sulfinylbisethanol [3085-45-8] as fatty esters in the adrenal cortex (1, 2). Homologous methylsulfinylalkyl isothiocyanates, which are represented by the formula $CH_3SO(CH_2)_nNCS$, where $n = 3$ [37791-20-1], 4 [4478-93-7], 5 [646-23-1], 8 [75272-81-0], 9 [39036-83-4], or 10 [39036-84-5], have been isolated from a number of mustard oils in which they occur as glucosides (3). Two methylsulfinyl amino acids have also been reported: methionine sulfoxide [454-41-1] from cockroaches and the sulfoxide of *S*-methylcysteine, 3-(methylsulfinyl)alanine [4740-94-7]. The latter is the dominant sulfur-containing amino acid in turnips and may account in part for their characteristic odor (4).

Dimethyl sulfoxide occurs widely at levels of $\leq 3$ ppm. It has been isolated from spearmint oil, corn, barley, malt, alfalfa, beets, cabbage, cucumbers, oats, onion, Swiss chard, tomatoes, raspberries, beer, coffee, milk, and tea (5). It is a common constituent of natural waters, and it occurs in seawater in the zone of light penetration where it may represent a product of algal metabolism (6). Its occurrence in rainwater may result from oxidation of atmospheric dimethyl sulfide, which occurs as part of the natural transfer of sulfur of biological origin (7, 8).

## 1. Properties

For the most part, sulfoxides are crystalline, colorless substances, although the lower aliphatic sulfoxides melt at relatively low temperatures (Table 1). The lower aliphatic sulfoxides are water soluble, but as a class the sulfoxides are not soluble in water. They are soluble in dilute acids and a few are soluble in alkaline solution. They dissolve to a variable extent in organic solvents, depending on associated functional groups. Because of the very polar sulfoxide group, they generally are high boiling and when distillable require reduced pressure. DMSO is a colorless liquid and its properties are listed in Table 2. Dimethyl sulfoxide generally undergoes typical sulfoxide reactions. It is used herein as an illustrative example.

### 1.1. Thermal Stability

Dimethyl sulfoxide decomposes slowly at 189°C to a mixture of products that includes methanethiol, formaldehyde, water, bis(methylthio)methane, dimethyl disulfide, dimethyl sulfone, and dimethyl sulfide. The decomposition is accelerated by acids, glycols, or amides (30). This product mixture suggests a sequence in which DMSO initially undergoes a Pummerer reaction to give (methylthio)methanol, which is labile and reacts according to

**Table 1. Melting and Boiling Points of Sulfoxides**

| Name | CAS Registry Number | Formula | Mp, °C | Bp, °C | Ref. |
|---|---|---|---|---|---|
| sulfinylbismethane | [67-68-5] | $(CH_3)_2SO$ | 18.55 | 189.0 | 9 |
| 1,1′-sulfinylbisethane | [70-29-1] | $(C_2H_5)_2SO$ | 15 | 88–90[a] | 10 |
| 1,1′-sulfinylbispropane | [4253-91-2] | $(n\text{-}C_3H_7)_2SO$ | 18 | | 10 |
| 1,1′-sulfinylbisbutane | [2168-93-6] | $(n\text{-}C_4H_9)_2SO$ | 32 | | 11 |
| 1,1′-sulfinylbis(2-chlo-roethane) | [5819-08-9] | $(ClCH_2CH_2)_2SO$ | 110.2 | | 12 |
| 1,1′-sulfinylbisbenzene | [945-51-7] | $(C_6H_5)_2SO$ | 70.5 | 340 dec[b] | 13 |
| methylsulfinylbenzene | [1193-82-4] | $C_6H_5S(O)CH_3$ | 30–30.5 | 139–140 | (14, 15) |
| phenylmethylsulfinyl-benzene | [833-82-9] | $C_6H_5S(O)CH_2C_6H_5$ | 125.5 | | 16 |
| 1,1′-sulfinylbis(methyl-enebenzene) | [621-08-9] | $(C_6H_5CH_2)_2SO$ | 135 | | 17 |

[a] At 2.0 kPa (15 mm Hg).
[b] Slowly.

equations 1–3. Disproportionation (eq. 4) also occurs to a small extent:

$$CH_3SCH_2OH \rightleftharpoons CH_3SH + HCHO \qquad (1)$$

$$2\ CH_3SH + HCHO \rightleftharpoons CH_3SCH_2SCH_3 + H_2O \qquad (2)$$

$$2\ CH_3SH + (CH_3)_2\,SO \longrightarrow CH_3SSCH_3 + CH_3SCH_3 + H_2O \qquad (3)$$

$$2\ (CH_3)_2\,SO \longrightarrow CH_3SO_2CH_3 + CH_3SCH_3 \qquad (4)$$

### 1.2. Oxidation

Sulfoxides are readily converted to sulfones, usually in high yield, by a number of strong oxidizing agents, eg, potassium permanganate, hypochlorites, hydrogen peroxide, ozone, selenium dioxide, or hot nitric acid (31). Side reactions producing sulfonic acids sometimes occur during oxidation with nitric acid. Treatment of DMSO under strongly alkaline conditions with either sodium hypochlorite or hypobromite results in oxidation accompanied by halogenation; the hexahalodimethyl sulfone forms in high yield (eq. 5) (32):

$$CH_3SOCH_3 + 6\ NaOCl + 0.5\ O_2 \longrightarrow CCl_3SO_3CCl_3 + 6\ NaOH \qquad (5)$$

The moderate resistance of DMSO to oxidation permits it to be used as a solvent for oxidations with lead tetraacetate or the 2-nitropropane anion (33, 34). Dichromate oxidation and permanganate oxidation have been used for quantitative determination of DMSO (35, 36).

### 1.3. Reduction

Dimethyl sulfoxide is reduced to dimethyl sulfide by a number of strong reducing agents, including aluminum hydrides, hydriodic acid, diborane, thiols, phosphine derivatives, and zinc in sulfuric acid (31). Quantitative

**Table 2. Properties of Dimethyl Sulfoxide**

| Property | | | Value | | Ref. |
|---|---|---|---|---|---|
| boiling point, °C | | | 189.0 | | 9 |
| conductivity, at 20°C, S/cm | | | $3 \times 10^{-8}$ | | 9 |
| dielectric constant, at 25°C, 10 MHz | | | 46.7 | | 18 |
| dipole moment, C·m[a] | | | $1.4 \times 10^{-29}$ | | 9 |
| entropy of fusion, J/(mol·K)[b] | | | 45.12 | | 19 |
| free energy of formation gas, $C_{graph}$, $S_2(g)$, at 25°C, kJ/mol[b] | | | 115.7 | | 20 |
| freezing point, °C | | | 18.55 | | 9 |
| heat capacity, J/(mol·K)[b] | | | | | |
| liquid at 25°C | | | 153.2 | | 19 |
| ideal gas, ($T$, K), $C_p$ | | | $6.94 + 5.6 \times 10^{-2}\ T$<br>$-0.227 \times 10^{-4}\ T^2$ | | 20 |
| heat of formation liquid, $C_{graph}$, $S_{rhomb}$, at 18°C, kJ/mol[b] | | | −199.6 | | 21 |
| heat of fusion, kJ/mol[b] | | | 13.5 | | 22 |
| heat of vaporization, at 70°C, kJ/mol[b] | | | 47.3 | | 23 |
| molal fp constant, °C/(mol·kg) | | | 4.07 | | 24 |
| p$K_a$ | | | 35.1 | | 25 |
| p$K_{BH^+}$ (aq sulfuric acid) | | | −2.7 | | 26 |
| refractive index, $n^{25}{}_D$ | | | 1.4768 | | 27 |
| flash point, open cup, °C | | | 95 | | 23 |
| autoignition temperature in air, °C | | | 300–302 | | 23 |
| flammability limits in air, vol % | | | | | |
| lower, 100°C | | | 3–3.5 | | 23 |
| upper, 180°C | | | 42–63 | | 23 |
| | 25°C | 35°C | 45°C | 100°C | |
| vapor pressure, kPa[c] | 0.080 | 0.159 | 0.303 | 4.0 | (23, 28) |
| density, g/cm$^3$ | 1.0955 | 1.0855 | 1.0757 | | 29 |
| viscosity, mPa·s(=cP) | 1.996 | 1.654 | 1.396 | 0.68 | 29 |

[a] To convert C·m to debye, divide by $3.336 \times 10^{-30}$.
[b] To convert J to cal, divide by 4.184.
[c] To convert kPa to mm Hg, multiply by 7.5.

procedures for determining DMSO have been based on its reduction by stannous chloride in hydrochloric acid, titanium trichloride in dilute hydrochloric acid, or sodium borohydride reduction followed by gas–liquid chromatography for low levels in aqueous systems (6, 37, 38). However, DMSO is sufficiently resistant to reduction to function as a solvent for polarography from a $+0.3$ V anode potential to a $-2.8$ V cathode potential, both being relative to a calomel electrode, with ammonium perchlorate electrolyte (39).

Dimethyl sulfoxide is reduced to dimethyl sulfide in a variety of organic reactions which entail initial attachment of an electrophilic activating reagent to the oxygen atom of DMSO to give **1** as shown in equation **6**. This is followed by displacement of the oxygen-containing groups from the sulfur by a nucleophile and leads to a sulfonium intermediate **2** (eq. **7**), which usually reacts further to give the following products (40):

$$(CH_3)_2SO + \text{electrophile} \longrightarrow (CH_3)_2\overset{+}{S}O\text{-electrophile} \qquad (6)$$

**(1)**

$$\text{nucleophile} + (CH_3)_2\overset{+}{S}O\text{-electrophile} \longrightarrow \text{nucleophile-}\overset{+}{S}(CH_3)_2 + (O\text{-electrophile})^- \qquad (7)$$

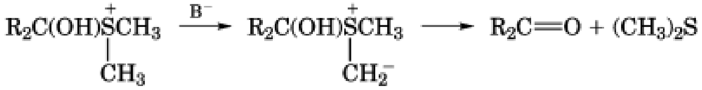
**(2)**

Compounds, eg, phenacyl halides, benzyl halides, alkyl iodides, or alkyl esters of sulfonic acids, react with DMSO at 100–120°C to give aldehydes (qv) and ketones (qv) in 50–85% yields (eq. 8) (41):

$$C_6H_5CH_2Cl + (CH_3)_2SO \longrightarrow \left[C_6H_5CH_2OS(CH_3)_2\right]^+ Cl^- \longrightarrow CH_3SCH_3 + HCl + C_6H_5CHO \qquad (8)$$

By a suitable choice of activating reagents, primary and secondary alcohols can be selectively oxidized to carbonyl compounds in good yields at room temperatures. Typical activating reagents are acetic anhydride, sulfur trioxide–pyridine, dicyclohexyl carbodiimide, and phosphorus pentoxide (40).

In the alcohol oxidations, the sulfonium intermediate (**2**, nucleophile = $R_2C(OH)$) loses a proton and dimethyl sulfide to give the carbonyl compound (42). The most common mechanism for the decomposition of **2** is attack by a mild base to remove a proton from one of the methyl groups. Subsequent cyclic collapse leads to the carbonyl compound and dimethyl sulfide (eq. **9**):



$$\underset{\substack{|\\CH_3}}{R_2C(OH)\overset{+}{S}CH_3} \xrightarrow{B^-} \underset{\substack{|\\CH_2^-}}{R_2C(OH)\overset{+}{S}CH_3} \longrightarrow R_2C{=}O + (CH_3)_2S \qquad (9)$$

(**2**)

Because of the mild reaction conditions and the reaction path, these oxidations are very selective and often are used to oxidize hydroxyl groups in molecules containing sensitive groups that would also react with the common oxidizing agents.

### 1.4. Carbon–Sulfur Cleavage

The carbon–sulfur bond of DMSO is broken in a number of reactions. Attempts to form the DMSO anion by the reaction of DMSO with sodium result in cleavage accompanied by methane evolution (eqs. **10** and **11**) (43):

$$CH_3\overset{\overset{O}{\|}}{S}CH_3 + 2\,Na^0 \longrightarrow CH_3SONa + CH_3Na \qquad (10)$$

$$CH_3Na + CH_3\overset{\overset{O}{\|}}{S}CH_3 \longrightarrow CH_4 + CH_3\overset{\overset{O}{\|}}{S}CH_2Na \qquad (11)$$

Sulfoxides containing $\beta$-hydrogen atoms, eg, di-*t*-butylsulfoxide [2211-92-9], react with strongly basic systems, eg, potassium *t*-butoxide, in DMSO by sulfenic acid elimination to produce olefins (eq.12) (44):

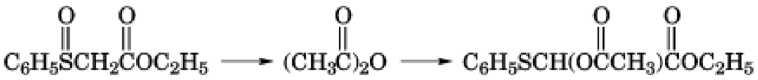
$$[(CH_3)_3C]_2SO \xrightarrow[DMSO]{t-C_4H_9OK} (CH_3)_2C{=}CH_2 + (CH_3)_3CSOH \qquad (12)$$

In other cases, sulfenic acid elimination can involve $\gamma$-hydrogen atoms with the formation of cyclopropane derivatives. $\gamma$-Elimination is favored when DMSO is the reaction solvent. An example involving 1-methylsulfinyl-2-ethyl-3-phenyl propane [14198-15-3] is shown in equation **13** (45):

(13)

### 1.5. Pummerer Reactions

Acetic anhydride at 70°C converts ethyl phenylsulfinylacetate [54882-04-1] **3** to the $\alpha$-acetoxy sulfide **4** in 70% yield (eq. **14**) (46):

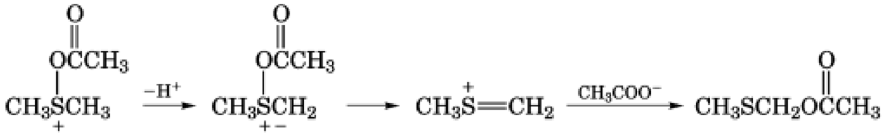


$$C_6H_5\overset{O}{\overset{\|}{S}}CH_2\overset{O}{\overset{\|}{C}}OC_2H_5 \longrightarrow (CH_3\overset{O}{\overset{\|}{C}})_2O \longrightarrow C_6H_5SCH(O\overset{O}{\overset{\|}{C}}CH_3)\overset{O}{\overset{\|}{C}}OC_2H_5 \qquad (14)$$

(**3**) (**4**)

The reaction is quite general and usually results in 75–90% yields (47). All reactions in which a sulfoxide containing at least one $\alpha$-hydrogen is reduced to the sulfide and also oxidized at the $\alpha$-carbon are referred to as Pummerer reactions (48).

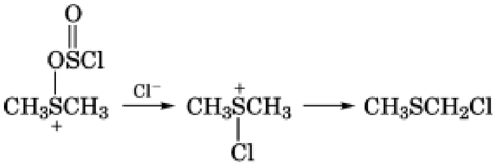
The initiating step in these reactions is the attachment of a group to the sulfoxide oxygen to produce an activated intermediate **5**. Suitable groups are proton, acyl, alkyl, or almost any of the groups that also initiate the oxidations of alcohols with DMSO (40, 48). In a reaction, eg, the one between DMSO and acetic anhydride, the second step is removal of a proton from an $\alpha$-carbon to give an ylide **6**. Release of an acetate ion generates the sulfur-stabilized carbonium ion **7**, and the addition of acetate ion to the carbonium ion **7** results in the product (eq. **15**):



$$CH_3\overset{O\overset{O}{\overset{\|}{C}}CH_3}{\overset{|}{\underset{+}{S}}}CH_3 \xrightarrow{-H^+} CH_3\overset{O\overset{O}{\overset{\|}{C}}CH_3}{\overset{|}{\underset{+}{S}}}\underset{-}{C}H_2 \longrightarrow CH_3\overset{+}{S}{=}CH_2 \xrightarrow{CH_3COO^-} CH_3SCH_2O\overset{O}{\overset{\|}{C}}CH_3 \qquad (15)$$

(**5**) (**6**) (**7**)

Both inorganic and organic acid chlorides react vigorously with DMSO to give $\alpha$-chloromethyl methyl sulfide **9** when conditions are sufficiently controlled. In these reactions, a chloride ion displacement of the oxygen-containing group from the initial activated intermediate gives the labile chlorodimethylsulfonium ion **8**. This sulfonium salt follows the reaction pattern shown for the acetoxydimethylsulfonium ion **5** to give the product **9**. The sequence involving thionyl chloride is shown in equation **16**:



$$CH_3\overset{O\overset{O}{\overset{\|}{S}}Cl}{\overset{|}{\underset{+}{S}}}CH_3 \xrightarrow{Cl^-} CH_3\underset{\underset{Cl}{|}}{\overset{+}{S}}CH_3 \longrightarrow CH_3SCH_2Cl \qquad (16)$$

(**8**) (**9**)

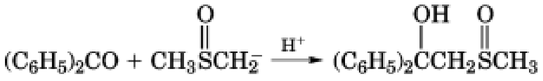
When DMSO is mixed with concentrated hydrochloric acid, protonated DMSO is in equilibrium with the chlorodimethylsulfonium ion. Pummerer reactions and subsequent reaction of the initial products give a complex mixture of products including formaldehyde, bis(methylthio)methane, methanethiol, dimethyl disulfide, dimethyl sulfide, and others.

### 1.6. Methylsulfinyl Carbanion

The activating influence of the sulfinyl group on $\alpha$-hydrogens, considerably less than that of a carbonyl group, is nonetheless sufficient to result in a p$K_a$ of 35.1 for DMSO. Consequently, strong bases, eg, sodium hydride or sodium amide, react with DMSO producing solutions of methylsulfinyl carbanion [15590-23-5], known as the dimsyl ion, which are synthetically useful (49). The solutions also provide a strongly basic reagent for generating other carbanions. The dimsyl ion shows the expected nucleophilicity of carbanions and serves as a source of methylsulfinylmethyl groups (49). Thus, with alkyl halides or sulfonate esters, sulfoxides are obtained (eq. **17**), carbonyl compounds yield $\beta$-hydroxysulfoxides (eq. **18**), and esters give $\beta$-ketosulfoxides (eq. **19**) (49):

$$n\text{-}C_4H_9Br + CH_3\overset{\overset{O}{\|}}{S}CH_2^- \longrightarrow C_5H_{11}\overset{\overset{O}{\|}}{S}CH_3 + Br^- \qquad (17)$$

*[1561-74-6]*



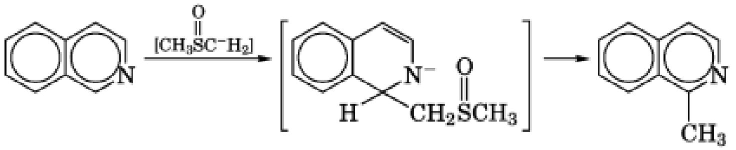
$$(C_6H_5)_2CO + CH_3\overset{\overset{O}{\|}}{S}CH_2^- \xrightarrow{H^+} (C_6H_5)_2\overset{\overset{OH}{|}}{C}CH_2\overset{\overset{O}{\|}}{S}CH_3 \qquad (18)$$

*[2863-39-0]*

$$C_6H_5\overset{\overset{O}{\|}}{C}OC_2H_5 + CH_3\overset{\overset{O}{\|}}{S}CH_2^- \longrightarrow C_6H_5\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{O}{\|}}{S}CH_3 + C_2H_5O^- \qquad (19)$$

*[2813-22-1]*

The dimsyl ion also adds to carbon–carbon double bonds, and if the mixture is heated for several hours, methanesulfenate is eliminated. The overall result is methylation, and for compounds such as quinoline or isoquinoline (eq. **20**), yields are nearly quantitative (50). The reaction sequence for isoquinoline to 1-methylisoquinoline is as follows:



(20)

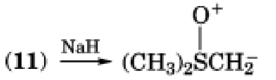
Care is required in running these reactions because the decomposition of the intermediate sulfoxide and of dimsyl sodium during the heating in the strongly alkaline system is exothermic and also produces a precipitate which can interfere with heat removal. Explosions have occurred (51).

### 1.7. Methoxydimethylsulfonium and Trimethylsulfoxonium Salts

Alkylating agents react with DMSO at the oxygen. For example, methyl iodide gives methoxydimethylsulfonium iodide **10** as the initial product. The alkoxysulfonium salts are quite reactive and, upon continued heating, either decompose to give carbonyl compounds or rearrange to the more stable trimethylsulfoxonium salts, eg, **11** (eq. **21**) (52):

$$(CH_3)_2SO + CH_3I \longrightarrow \underset{(\mathbf{10})}{[(CH_3)_2SOCH_3]^+I^-} \longrightarrow \underset{(\mathbf{11})}{[(CH_3)_3SO]^+I^-} \qquad (21)$$

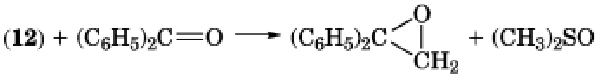
Trimethylsulfoxonium iodide **11** is of interest because treatment with sodium hydride or dimsyl sodium produces dimethylsulfoxonium methylide [5367-24-8] **12** (eq. **22**), which is an excellent reagent for introducing a methylene group into a variety of structures (53):



$$(\mathbf{11}) \xrightarrow{NaH} (CH_3)_2\overset{\overset{O^+}{|}}{S}CH_2^- \qquad (22)$$

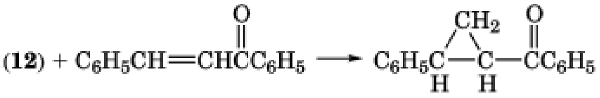
(**12**)

Many aldehydes and ketones react with **12** to give better than 75% yields of epoxides (eq. **23**):



(23)

In similar reactions, **12** with carbon–carbon double bonds that are conjugated with carbonyl groups gives cyclopropane derivatives (eq. **24**) (48):



(24)

### 1.8. Complexes

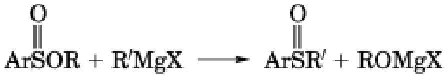
The sulfoxides have a high (ca 4) dipole moment, which is characteristic of the sulfinyl group, and a basicity about the same as that of alcohols. They are strong hydrogen-bond acceptors. They would be expected, therefore, to solvate ions with electrophilic character, and a large number of DMSO complexes of metal ions have been reported (54). The bonding to the metal is through the oxygen except for platinum(II), palladium(II), and rhodium(II) complexes where metal–sulfur bonds occur. The strength of the solvates is commonly about the same as that of the corresponding hydrate, and exchange of ligands is readily accomplished.

The strong tendency of the DMSO oxygen to act as a hydrogen-bond acceptor leads also to a number of organic complexes. Chloroform forms both 1:1 and 1:2 complexes (55). Pyrrole and phenol give 1:1 complexes (56, 57). In solutions of monosaccharides in DMSO, the anomer with cis hydroxyls on the first and second carbons is stabilized (58). Complexes with organic molecules that do not involve hydrogen bonding also occur, eg, the 1:1 complex of DMSO and 4-chlorobenzonitrile and other nitriles (59, 60). Strong 1:1 complexes form with nitrogen tetroxide and sulfur trioxide (61, 62). Charge-transfer complexes occur with cyanogen iodide, tetracyanoethylene, and oxygen (63–65).

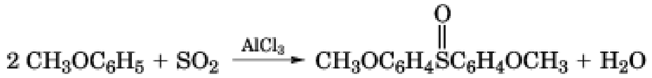
## 2. Synthesis and Manufacture

The sulfoxides are most frequently synthesized by oxidation of the sulfides (66, 67). A broad group of oxidizing agents can be used and, because the oxidation to the sulfoxide is considerably more rapid than further oxidation to the sulfone, a proper choice of reagent quantity and conditions leads to high sulfoxide yields; eg, hydrogen peroxide in stoichiometric amounts can give 75–90% sulfoxide yields (68). Nitrogen tetroxide in a solvent, eg, carbon tetrachloride at temperatures below ca 0°C, selectively gives the sulfoxide in yields of up to 95% (69). Oxidations using sodium metaperiodate in aqueous or water–methanol solutions at ice-bath temperatures give high sulfoxide yields without sulfone formation (70). Oxidation using tertiary amine–bromine complexes in aqueous acetic acid gives yields above 70% and has been suggested as a convenient procedure for preparing $^{18}$O-labeled sulfoxides when $H_2{}^{18}O$–acetic acid is used as the reaction solvent (71). There are a number of sulfoxide synthesis procedures in which the appropriate fragments are joined to give the product.

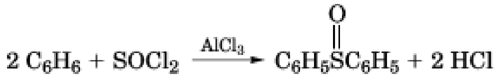
$$\mathrm{RO\overset{\overset{O}{\|}}{S}OR + 2\,R'MgX \longrightarrow R'\overset{\overset{O}{\|}}{S}R' + 2\,ROMgX} \quad (25)$$



$$\mathrm{Ar\overset{\overset{O}{\|}}{S}OR + R'MgX \longrightarrow Ar\overset{\overset{O}{\|}}{S}R' + ROMgX} \quad (26)$$



$$\mathrm{2\,CH_3OC_6H_5 + SO_2 \xrightarrow{AlCl_3} CH_3OC_6H_4\overset{\overset{O}{\|}}{S}C_6H_4OCH_3 + H_2O} \quad (27)$$



$$\mathrm{2\,C_6H_6 + SOCl_2 \xrightarrow{AlCl_3} C_6H_5\overset{\overset{O}{\|}}{S}C_6H_5 + 2\,HCl} \quad (28)$$

The reaction of Grignard reagents with sulfite esters gives 40–70% yields (eq. **25**), and with arylsulfinate esters the yields are ca 55% (eq. **26**) (72). Optically active sulfoxides are synthesized in good yield from the reaction of optically active sulfinate esters using Grignard reagents (73). Sulfoxides are obtained in greater than 50% yield by alkylating sulfenates with alkyl bromides (74). Diaryl sulfoxides are also obtained by Friedel-Crafts syntheses, eg, the reaction of anisole with sulfur dioxide and aluminum chloride to obtain 40% bis(4-methoxyphenyl) sulfoxide [1774-36-3] (eq. **27**) or the reaction of benzene and thionyl chloride and aluminum chloride to obtain 51% diphenyl sulfoxide [945-57-7] (eq. **28**) (75). A comprehensive review of procedures for synthesizing sulfoxides is available (76).

### 2.1. Dimethyl Sulfoxide

Dimethyl sulfoxide is manufactured from dimethyl sulfide (DMS), which is obtained either by processing spent liquors from the kraft pulping process or by the reaction of methanol or dimethyl ether with hydrogen sulfide. In the kraft pulping process, the spent liquors are normally concentrated to ca 50% solids and burned to recover inorganic chemicals and heat values (see Pulp). The lignin in the liquor contains aromatic methoxyl groups, which are cleaved by sulfide ions to produce dimethyl sulfide when the concentrated liquor is processed in a reactor at 200–250°C (77). The synthesis of dimethyl sulfide from methanol and hydrogen sulfide is accomplished by a vapor-phase reaction over a catalyst at above 300°C.

Dimethyl sulfide has been oxidized to DMSO by several procedures. In pilot-plant quantities, the oxidation was accomplished with nitric acid, but this route has been supplanted by oxidation with nitrogen dioxide or oxygen containing minor amounts of nitrogen dioxide. The oxidation using nitrogen dioxide is diagrammed in Figure 1 (78). Dimethyl sulfide is oxidized with a DMSO solution of nitrogen dioxide in a reactor at 40–50°C. The reactor contents pass into a zone at 100°C where excess dimethyl sulfide is sparged from the crude DMSO with nitrogen; the crude DMSO is then neutralized and distilled. The flow of nitrogen dioxide into the reactor is kept insufficient to oxidize all of the dimethyl sulfide so that all the nitrogen dioxide is converted to nitric oxide, which is quite insoluble in DMSO and escapes in the exit-gas stream. The gas stream passes through a heat exchanger for condensation of some of the dimethyl sulfide which is recycled to the reactor. The gases

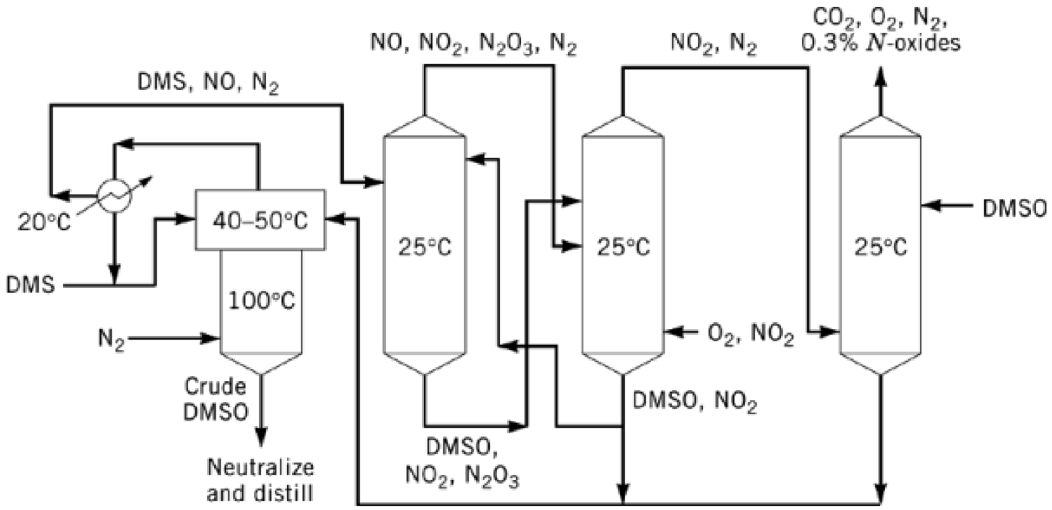


**Fig. 1.** Dimethyl sulfoxide manufacture with nitrogen tetroxide.

**Table 3. Analysis of Industrial Dimethyl Sulfoxide**

| Properties | Analysis |
|---|---|
| DMSO assay, wt % | 99.9 |
| water content, wt % | 0.1 |
| color | water-white |
| other impurities | negligible |
| nonvolatiles | negligible |

then are conducted to a second reactor where an excess of nitrogen dioxide converts all of the remaining sulfide to the sulfoxide. The gases from this reactor contain substantially no organic matter and are oxidized with oxygen in a third reactor to regenerate the nitrogen dioxide. The gases finally pass through a DMSO scrubber for removal of nitrogen dioxide before venting to the atmosphere.

Processes involving oxygen and nitrogen oxides as catalysts have been operated commercially using either vapor- or liquid-phase reactors. The vapor-phase reactors require particularly close control because of the wide explosive limit of dimethyl sulfide in oxygen (1–83.5 vol %); plants in operation use liquid-phase reactions. Figure 2 is a schematic diagram for the liquid-phase process. The product stream from the reactor is neutralized with aqueous caustic and is vacuum-evaporated, and the DMSO is dried in a distillation column to obtain the product.

Dimethyl sulfoxide is produced in commercial quantities in the United States by Crown Zellerbach Corporation. A typical analysis of industrial DMSO is given in Table 3 (23).

## 3. Health and Safety Factors

Dimethyl sulfoxide is a relatively stable solvent of low toxicity. The LD$_{50}$ for single-dose oral administration to rats is ca 17,400–28,300 mg/kg. Dimethyl sulfoxide by itself presents less hazard than many chemicals and solvents commonly used in industry. However, DMSO can penetrate the skin and may carry with it certain chemicals with which it is combined under certain conditions. Normal protective measures should be followed

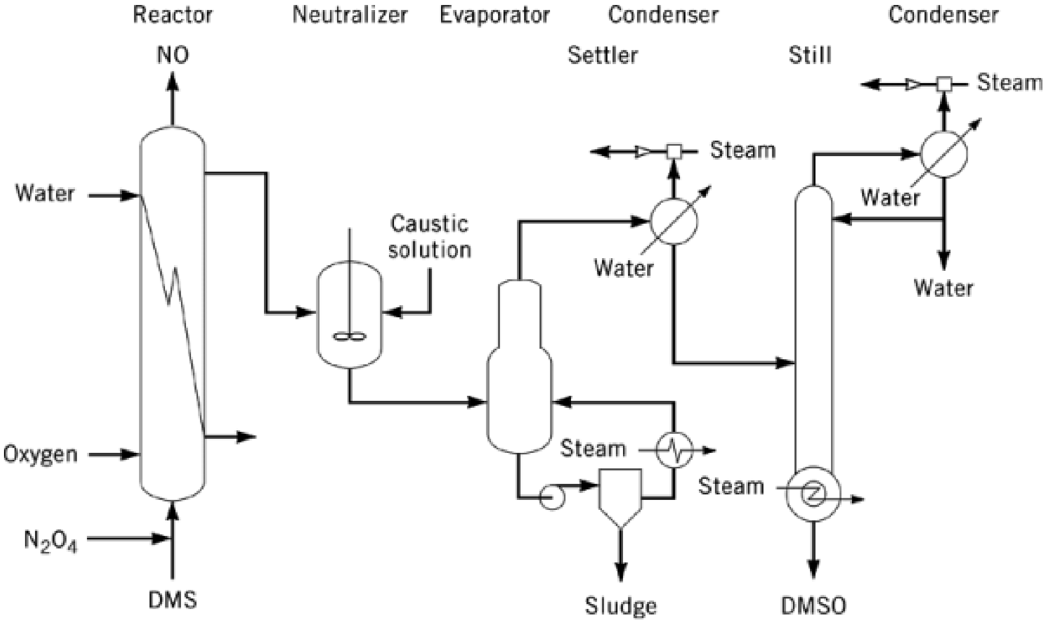


**Fig. 2.** Dimethyl sulfoxide manufacture with oxygen.

in the laboratory. If large quantities are handled where splashing and accidental contact may occur, protective clothing is recommended including suitable gloves and eye protectants. Butyl rubber gloves are more suitable than other types of material in terms of resisting penetration by DMSO solutions (79).

Dimethyl sulfoxide has received considerable attention as a useful agent in medicine (80, 81). Compositions containing it are marketed in Germany and Austria as prescription items for analgesic uses. In the United States in 1981, the possible efficacy of DMSO as a drug was examined under jurisdiction of the FDA, but this agency has not released DMSO for drug use by humans other than for a painful bladder condition called interstitial cystitis. In veterinary medicine, DMSO is used for horses and dogs as a topical application to reduce swelling resulting from injury or trauma (see Veterinary drugs).

## 4. Uses of Dimethyl Sulfoxide

### 4.1. Polymerization and Spinning Solvent

Dimethyl sulfoxide is used as a solvent for the polymerization of acrylonitrile and other vinyl monomers, eg, methyl methacrylate and styrene (82, 83). The low incidence of transfer from the growing chain to DMSO leads to high molecular weights. Copolymerization reactions of acrylonitrile with other vinyl monomers are also run in DMSO. Monomer mixtures of acrylonitrile, styrene, vinylidene chloride, methallylsulfonic acid, styrenesulfonic acid, etc, are polymerized in DMSO–water (84). In some cases, the fibers are spun from the reaction solutions into DMSO–water baths.

Dimethyl sulfoxide can also be used as a reaction solvent for other polymerizations. Ethylene oxide is rapidly and completely polymerized in DMSO (85). Diisocyanates and polyols or polyamines dissolve and react in DMSO to form solutions of polyurethanes (86) (see Solvents, industrial).

### 4.2. Solvent for Displacement Reactions

As the most polar of the common aprotic solvents, DMSO is a favored solvent for displacement reactions because of its high dielectric constant and because anions are less solvated in it (87). Rates for these reactions are sometimes a thousand times faster in DMSO than in alcohols. Suitable nucleophiles include acetylide ion, alkoxide ion, hydroxide ion, azide ion, carbanions, carboxylate ions, cyanide ion, halide ions, mercaptide ions, phenoxide ions, nitrite ions, and thiocyanate ions (31). Rates of displacement by amides or amines are also greater in DMSO than in alcohol or aqueous solutions. Dimethyl sulfoxide is used as the reaction solvent in the manufacture of high performance, polyaryl ether polymers by reaction of bis(4,4′-chlorophenyl) sulfone with the disodium salts of dihydroxyphenols, eg, bisphenol A or 4,4′-sulfonylbisphenol (88). These and related reactions are made more economical by efficient recycling of DMSO (89). Nucleophilic displacement of activated aromatic nitro groups with aryloxy anion in DMSO is a versatile and useful reaction for the synthesis of aromatic ethers and polyethers (90).

### 4.3. Solvent for Base-Catalyzed Reactions

The ability of hydroxide or alkoxide ions to remove protons is enhanced by DMSO instead of water or alcohols (91). The equilibrium change is also accompanied by a rate increase of $10^5$ or more (92). Thus, reactions in which proton removal is rate-determining are favorably accomplished in DMSO. These include olefin isomerizations, elimination reactions to produce olefins, racemizations, and H–D exchange reactions.

### 4.4. Extraction Solvent

Dimethyl sulfoxide is immiscible with alkanes but is a good solvent for most unsaturated and polar compounds. Thus, it can be used to separate olefins from paraffins (93). It is used in the Institute Français du Pétrole (IFP) process for extracting aromatic hydrocarbons from refinery streams (94). It is also used in the analytical procedure for determining polynuclear hydrocarbons in food additives (qv) of petroleum origin (95).

### 4.5. Solvent for Electrolytic Reactions

Dimethyl sulfoxide has been widely used as a solvent for polarographic studies and a more negative cathode potential can be used in it than in water. In DMSO, cations can be successfully reduced to metals that react with water. Thus, the following metals have been electrodeposited from their salts in DMSO: cerium, actinides, iron, nickel, cobalt, and manganese as amorphous deposits; zinc, cadmium, tin, and bismuth as crystalline deposits; and chromium, silver, lead, copper, and titanium (96–103). Generally, no metal less noble than zinc can be deposited from DMSO.

### 4.6. Cellulose Solvent

Although DMSO by itself does not dissolve cellulose, the following binary and ternary systems are cellulose solvents: DMSO–methylamine, DMSO–sulfur trioxide, DMSO–carbon disulfide–amine, DMSO– ammonia–sodamide, DMSO–dinitrogen tetroxide, DMSO–paraformaldehyde, and DMSO–sulfur dioxide–ammonia (104, 105). At least a ratio of three moles of active agent per mole of glucose unit is necessary for complete dissolution (104). Although only 80% of cellulose (qv) dissolves in DMSO–methylamine under cold anhydrous conditions, DMSO–dinitrogen tetroxide is a better solvent, particularly when a small quantity of water is added (106). Most of these systems can be used to produce cellulose fibers. The DMSO–paraformaldehyde system does not degrade cellulose, and it can form solutions containing up to 10 wt % cellulose (107). It is believed that a methylolcellulose compound forms and is stable for extended periods of storage at ambient conditions (107).

Regenerated cellulose articles, eg, films and fibers, can be prepared by contacting the DMSO–paraformaldehyde solutions with methanol and water (107, 108).

### 4.7. Pesticide Solvent

The majority of organic fungicides, insecticides, and herbicides (qv) are soluble in DMSO, including such difficult-to-solvate materials as the substituted ureas and carbamates (see Fungicides, agricultural; Insect control technology; Pesticides). Dimethyl sulfoxide forms cosolvent systems of enhanced solubility properties with many solvents (109).

### 4.8. Clean-Up Solvent

Dimethyl sulfoxide is used to remove urethane polymers and other difficult-to-solvate materials from processing equipment.

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