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DIMETHYL SULFOXIDE OXIDATIONS

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CONTENTS

I. INTRODUCTION

Dimethyl sulfoxide, first prepared in 1866 (85), has until recently held eminence in chemistry as a solvent of some importance but has not been considered a reactant. Since the time that dimethyl sulfoxide was first employed as an oxidizing agent (48), the knowledge concerning the variety of compounds that can be oxidized by dimethyl sulfoxide has grown considerably. Mild conditions, uncomplicated work-ups, and high yields with which most oxidations can be effected have elevated this technique into prominence.

Recent publications have considered dimethyl sulfoxide oxidations to some extent (23, 29, 45, 84), but to date no comprehensive review exists. In the following review only reactions in which dimethyl sulfoxide is clearly the oxidizing agent have been included. The literature has been surveyed through May 1966.

A. TOXICITY

Caution: Although pure dimethyl sulfoxide is not considered toxic, solutions of inorganic salts or organic compounds in dimethyl sulfoxide are potentially dangerous because of the high penetrating power of dimethyl sulfoxide and its ability to transport some substances across skin membranes (10, 16, 54a). DMSO reacts violently with a wide variety of acyl halides and related compounds (17a).

B. PURIFICATION

The drying of dimethyl sulfoxide with magnesium perchlorate has resulted in an explosion (19). Although not normally a purification technique, treatment of dimethyl sulfoxide with sodium hydride in large batches has also resulted in explosions (18). Satisfactory purity can be obtained by distillation under reduced pressure from calcium hydride followed by storage over Linde molecular sieves, Type 4A. No account of difficulties resulting from this method of purification and drying has been published.

The nomenclature of the compounds listed in the review is according to *Chemical Abstracts*, even if the author of the paper has preferred a different one.

The following abbreviations are commonly employed in the literature and will be used consistently throughout the remainder of this review: DMSO, dimethyl sulfoxide; DMS, dimethyl sulfide; DCC, dicyclohexylcarbodiimide.

II. General Considerations

A. DMSO. Structure and Reactivity

The physical properties of DMSO are well described in the literature (23, 46). Dimethyl sulfoxide is a colorless, odorless, and very hygroscopic liquid (bp 189°, mp 19.5°) with a slightly bitter taste. The structure of DMSO is usually represented by the following resonance hybrid

$$\underset{\text{I}}{(CH_3)_2S{=}O} \longleftrightarrow \underset{\text{II}}{(CH_3)_2\overset{+}{S}{-}\overline{O}}$$

Resonance structure I owes its existence to the ability of the 3d orbitals of sulfur to accommodate an additional electron pair, in this case the p electrons of the oxygen (20). Although there is still debate over which hybrid best represents the structure of DMSO, or sulfoxides in general, it seems certain that the sulfur–oxygen bond can be justly characterized as being semipolar (78).

The oxidizing capacity of DMSO is somewhat dependent on its ability to act as a nucleophile. Its basicity is slightly greater than that of water (54a), and its nucleophilicity has been estimated to exceed that of ethanol toward alkyl sulfonate esters (90).

B. DMSO as an Oxidizing Agent

Although the evidence is not yet conclusive in every case, there is a strong indication that most of the DMSO oxidations involve the same dimethylalkoxysulfonium salt intermediate III which subsequently reacts with a base to give the observed carbonyl product and DMS. The intimate details of this step will be considered in the discussions of the various methods of DMSO oxidation along with the pertinent evidence for the mechanism. It has been demonstrated that dimethylmethoxysulfonium fluoroborate, $[(CH_3)_2S{-}OCH_3]^{\oplus}BF_4^{\ominus}$, reacts in the presence of base to form formaldehyde (39, 40) and in addition will undergo rapid alkoxide exchange, with inversion of configuration at sulfur (38, 39, 41) in the presence of sodium ethoxide and sodium isopropoxide with subsequent formation of acetylaldehyde and acetone, respectively (39, 40).

There are two routes by which a substrate may be converted into the dimethylalkoxysulfonium salt intermediate III, and the route is determined by the structure of the substrate. These two routes are illustrated in general fashion below. The first pathway involves reaction of DMSO with an intermediate "activating"

Pathway A

$$(CH_3)_2S{=}O + E \longrightarrow (CH_3)_2\overset{+}{S}{-}O{-}E + R{-}\underset{\displaystyle OH}{\underset{|}{CH}}{-}R$$

Pathway B

$$(CH_3)_2S{=}O + R{-}\underset{\displaystyle X}{\underset{|}{CH}}{-}R \longrightarrow \underset{\displaystyle III}{(CH_3)_2{-}\overset{+}{S}{-}O{-}\underset{\displaystyle R}{\underset{|}{CH}}} \xrightarrow{\text{base}} CH_3{-}S{-}CH_3 + \underset{\displaystyle R}{\underset{|}{\overset{\displaystyle R}{\overset{|}{C}}}}{=}O$$

electrophilic species, E (the nature of E is considered in the discussions of the individual methods), which is subsequently displaced by the substrate to be oxidized, usually an alcohol, to form III.

The second pathway involves a leaving group X (X = Cl, Br, I or sulfonate) being displaced by DMSO acting as a nucleophile and resulting directly in the dimethylalkoxysulfonium salt III. Although it has not been verified by experiment, it is generally assumed that this step proceeds by way of a bimolecular nucleophilic displacement by the oxygen of DMSO (34, 36, 42, 68). It is also possible that both bimolecular and unimolecular processes are operative depending on the substrate (37), or that a "merged substitution–elimination reaction" of the type that has been proposed for *t*-butyl cyclohexane-4-*p*-toluenesulfonate is occurring in some cases (102). The question of oxygen *vs.* sulfur displacement of X has been considered (44, 90) and in most cases the product from oxygen attack, III, is formed by kinetic control with the sulfur displacement product, an alkyldimethylsulfoxonium salt, $[R(CH_3)_2S{-}O]^+ X^-$, becoming important only after long reaction times (90). The considerations of the individual oxidations which follow are divided into three groups: those which proceed through pathway A, those which proceed through pathway B, and miscellaneous cases which are not clear as to mechanism.

III. DMSO + DCC Method

A. General

This method of oxidation is generally referred to as the "Pfitzner–Moffatt" technique, after its originators (75–77). The reaction involves addition of an alcohol substrate to a solution of DCC in DMSO with phosphoric acid or pyridinium trifluoroacetate present as a proton source which results in reaction conditions near neutrality. Dimethyl sulfoxide concentration may vary from 10 to 100% of the total solvent with an inert solvent like benzene making up the remainder. Dimethyl sulfoxide and DCC have been successfully replaced by tetramethylene sulfoxide and isopropyl carbodiimide. The oxidation technique is applicable to primary or secondary alcohol groups in an almost

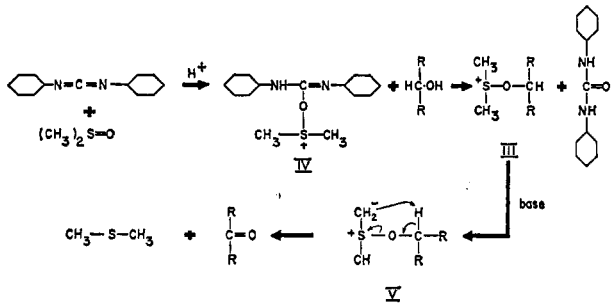


Figure 1.

unlimited variety of compounds including alkaloids, steroids, carbohydrates, and other complex substances. Steric effects are not important except in highly hindered sytems where oxidation of the less hindered alcohol will predominate. Tosylates, tertiary alcohols, olefins, and amines are unaffected by the conditions of the reaction.

The mechanism illustrated in Figure 1 was proposed (1, 76, 77) and later proved by O^{18}-and deuterium-labeling studies (25). The first step involves activation of the DMSO by reaction with DCC (this is the E referred to earlier) in an acid-catalyzed process to give an intermediate IV. Formation of IV by nucleophilic attack of DMSO is consistent with the chemistry of carbodiimides (47). Attack on intermediate IV by an alcohol substrate results in dimethylalkoxysulfonium salt III and N,N′-dicyclohexylurea. The preceeding sequence was established by using O^{18}-labeled DMSO and noting that all the O^{18} ended up in the N,N′-dicyclohexylurea and not in the carbonyl compound which would be required if the alternate mechanism of the alcohol first attacking DCC followed by reaction with DMSO were the correct route (25).

Formation of V by reaction of III with a base followed by an intramolecular hydrogen transfer to give the observed carbonyl product plus DMS was proved by means of deuterium-labeling studies. A deuterium label on the carbon of the substrate bearing the hydroxyl was found in the DMS isolated from the reaction—a fact consistent only with the ylid, intramolecular hydrogen-transfer pathway (25).

The proposed mechanism requires not only acid catalysis but base catalysis as well, which is consistent with the observation that the reaction fails when a strong mineral acid (HCl, H_2SO_4, or $HClO_4$) is used in place of phosphoric acid or pyridinium trifluoroacetate (76). The above observation is presumably due to the inability of an ylid intermediate to form in the absence of a strong enough base and the rapid depletion of DCC by an alternate reaction in the presence of a strong acid (47). The intermediacy of ylid V has been further substantiated by use of a tritium-labeled alcohol substrate rather than a deuterium one and recovery of CH_3–S–CH_2T (93). In these experiments a small (less than 5%) but real quantity of tritium was detected in the N,N′-dicyclohexylurea which could only have resulted from direct abstraction of the proton from intermediate III without intervention of the ylid intermediate V.

Varying, but usually small quantities of the side product VI, R_2–CHO–CH_2SCH_3, have been reported in some instances (43, 77). A thorough discussion of this product is presented in a later section.

Thiols have not been studied extensively but generally are not oxidized by this method (77). It is possible that the high nucleophilicity of the thiol allows it to compete successfully with DMSO for DCC which would have the effect of removing both substrate and DCC from further reaction. Although this is not in complete agreement with the experimental facts (77), the reaction of thiols with carbodiimides to give stable products has been established (17, 47). Data for this type of oxidation are given in Table I.

B. THE OXIDATION OF NUCLEOTIDES AND NUCLEOSIDES

Treatment of nucleotides possessing a free 3′-hydroxyl group with DMSO and DCC results in cleavage of the glycosidic as well as the 5′-phosphate bond (75, 76). The glycosidic bond of the corresponding nucleoside (3′-hydroxyl present) is cleaved in the presence of DMSO, DCC, and anhydrous phosphoric acid (76). If the 3′-hydroxyl is absent (3-dehydro) or blocked (3′-O-acetyl), the 5′ position of the nucleoside is oxidized to the 5′-aldehyde. In nucleotides with a blocked 3′-hydroxyl, oxidation or cleavage does not take place but starting material and dinucleotide pyrophosphates are recovered (76).

Oxidation of the 5′ position is of importance, since other oxidative techniques on the carbohydrate moiety lead exclusively or in part to the 5′ acid (64).

Oxidative cleavage is reported to proceed by oxidation of the 3′-hydroxyl, followed by spontaneous β elimination of the heterocyclic base and 5′-phosphate, if one is present (76) This proposal is based upon little experimental evidence, but repeated attempts at oxidation of 3′-hydroxyl groups in deoxynucleosides and deoxynucleotides have led to glycosidic cleavage without any detectable carbonyl intermediates being recovered (76). The data are listed separately in Table I.

C. OXIDATION OF CARBOHYDRATES

Application of this oxidation technique to carbohydrates will result in the oxidation of most free hydroxyl groups to the corresponding carbonyl compound (5–7, 24).

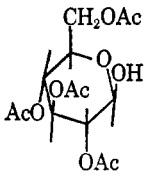
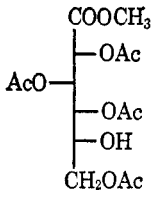
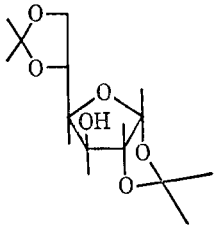
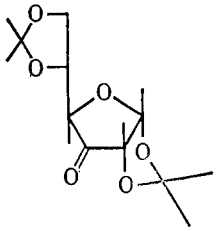
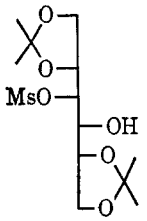
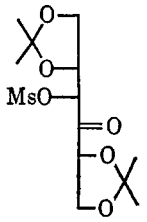
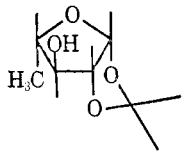
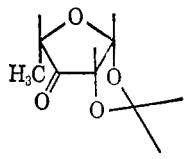
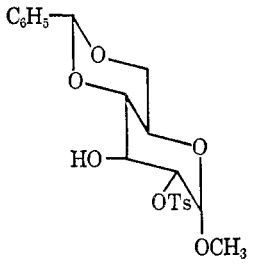
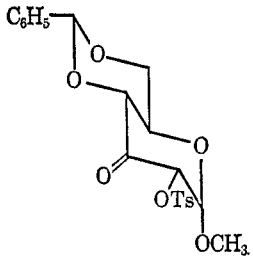
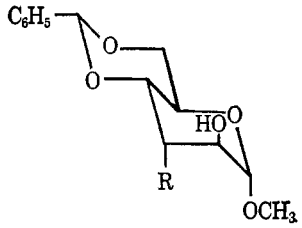
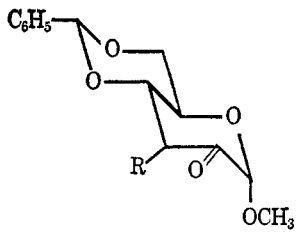
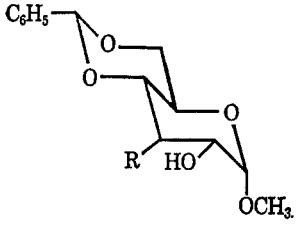
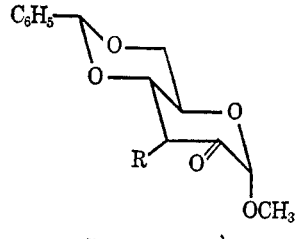
The extremely mild conditions and high yields give this method great potential in carbohydrate oxidations. While sulfonate esters are capable of undergoing oxidation and elimination in DMSO, these groups remain

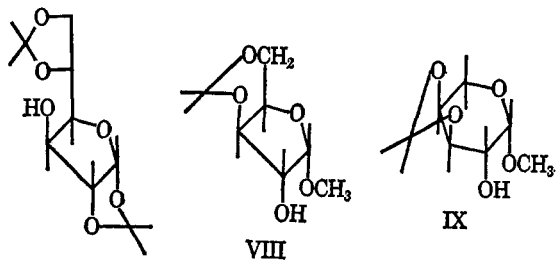
relatively inert under these reaction conditions (7), but may undergo epimerization to a more stable conformation, *i.e.*, from an axial to equatorial position (5). This method has been shown to fail in the attempted oxidation of several carbohydrates which have hydroxyl groups flanked by acetal and/or ether moieties (7). Thus VII, VIII, and IX remain resistant to oxidation by DMSO and DCC mixtures (7).

TABLE I
DIMETHYL SULFOXIDE OXIDATION OF ALCOHOLS

Substrate	Product(s)	Method	Yield, %	Ref
1-Butanol	Butyraldehyde	Chloroformate (collidine)	65	9
1-Hexanol	Hexanal	Chloroformate (collidine)	68	9
1-Octanol	Octanal	DCC	100	77
Isobutyl alcohol	Isobutyraldehyde	Chloroformate (collidine)	70	9
1,4-Butanediol	1,4-Butanedione	Chloroformate (collidine)	80	9
Neopentyl alcohol	Pivaldehyde	Chloroformate (collidine)	57	9
2-Butanol	2-Butanone	Chloroformate (collidine)	78	9
(−)-Menthol	Menthone	Chloroformate (collidine)	26	9
Citronellol	Citronellal	Chloroformate (collidine)	46	9
Cinnamyl alcohol	Cinnamaldehyde	O_2	60	95
3-Phenyl-1-propanol	3-Phenyl-1-propanal	O_2	26	95
	1-Phenyl-2-propanone	O_2	25	95
1-Phenyl-2-propanol	1-Phenyl-1-propene		36	
Benzyl alcohol	Benzaldehyde	O_2	80	95
o-Nitrobenzyl alcohol	*o*-Nitrobenzaldehyde	O_2	27	95
m-Nitrobenzyl alcohol	*m*-Nitrobenzaldehyde	O_2	63	95
p-Nitrobenzyl alcohol	*p*-Nitrobenzaldehyde	O_2	77	95
p-Nitrobenzyl alcohol	*p*-Nitrobenzaldehyde	Ac_2O	75	1
	p-Nitrobenzyl acetate		25	
p-Nitrobenzyl alcohol	*p*-Nitrobenzaldehyde	DCC	92	77
o-Chlorobenzyl alcohol	*o*-Chlorobenzaldehyde	O_2	78	95
p-Chlorobenzyl alcohol	*p*-Chlorobenzaldehyde	O_2	86	95
p-Chlorobenzyl alcohol	*p*-Chlorobenzaldehyde	DCC	100	77
p-Methoxybenzyl alcohol	*p*-Methoxybenzaldehyde	O_2	8.8	95
	p,p'-Dimethoxybibenzyl	O_2	85	95
p-Methylbenzyl alcohol	*p*-Methylbenzaldehyde	O_2	85	95
Cholestanol	3-Cholestanone	Chloroformate (collidine)	20	9
Cholestanol	3-Cholestanone	DCC	80	77
Cholesterol	Δ^5-3-Cholestenone	DCC	66	77
24-Hydroxycholane	24-Cholanal	DCC	94	77
Testosterone	Δ^4-Androstene-3,17-dione	DCC	92	77
Testosterone	Δ^4-Androstene-3,17-dione	Ac_2O	34	1
11α-Hydroxyprogesterone	11-Oxoprogesterone	Ac_2O	13	1
11α-Hydroxyprogesterone	11-Oxoprogesterone	DCC	99	77
11β-Hydroxyprogesterone	11-Oxoprogesterone	DCC	0	77
11β-Hydroxy-21-acetoxyhydrocortisone	Cortisone acetate	Ac_2O	53	1
3β-Hydroxy-Δ^5-androsten-17-one	Δ^5-Androstene-3,17-dione	DCC	90	77
19-Hydroxy-3β-acetoxy-Δ^5-androsten-17-one	3β-Acetoxy-17-oxo-Δ^5-androsten-19-al	DCC	53	77
19-Hydroxy-Δ^4-androstene-3,17-dione	3,17-Oxo-Δ^4-androsten-19-al	DCC	82	77
(α or β)-Yohimbine	Yohimbinone	Ac_2O	80–85	1, 2
Methyl reserpate	Methyl ketoreserpate	Ac_2O	33	1
Ajmaline	Ajmalidine	Ac_2O	...	1
Aspidospermine	Aspidospermone	DCC	...	14
Spegazzinidine dimethyl ether	3-Dehydrospegazzinidine dimethyl ether	DCC	83	77
(±)-Dihydroxyepiibogamine	Hydroxyketoepiibogamine	DCC	50	15
1,2-O-Isopropylidene-5,6-anhydro-D-glucose	1,2-O-Isopropylidene-D-glucohexodialdose	BF_3		32
3'-O-Acetylthymidine	3'-O-Acetylthymidine-5'-aldehyde	DCC	90	75
2',3'-O-Isopropylideneuridine	2',3'-O-Isopropylideneuridine-5'-aldehyde	DCC		75
2',3'-O-Isopropylideneadenosine	2',3'-O-Isopropylideneadenosine-5'-aldehyde	DCC		75
Thymidine 5'-phosphate	Thymine	DCC		75
5'-O-Acetylthymidine	Thymine	DCC		75
p^1,p^2-Dithymidine pyrophosphate	Thymine	DCC		75

TABLE I (*Continued*)

Substrate	Product(s)	Method	Yield, %	Ref
		P_4O_{10} MeOH	25	72
		P_4O_{10}	65	72
		Ac_2O	60	91
		DCC	74	7
		DCC		24
		DCC	80	7
 R=NH-CO-C_6H_5	 R=NH-CO-C_6H_5	DCC	86	5
 R=$NHCOC_6H_5$	 R=$NHCOC_6H_5$	DCC	96	5



VII VIII IX

VII is oxidized in good yield by DMSO–Ac_2O or DMSO–P_4O_{10} (72, 91), perhaps because of less steric requirements of the oxidation intermediate in the latter methods.

The carbohydrates which have been oxidized by this method are listed in Table I.

IV. Acetic Anhydride Method

This method, which is similar to the Pfitzner–Moffatt technique, utilizes DMSO and acetic anhydride mixtures to oxidize primary and secondary alcohols to the corresponding carbonyl compound (1, 2). Acetic anhydride is the "E" of pathway A which activates the DMSO for reaction with the alcohol to form the dimethylalkoxysulfonium salt intermediate III. Acetic anhydride can be replaced by benzoic anhydride (presumably other anhydrides would work as well) and tetramethylene sulfoxide can replace DMSO.

The reaction of DMSO and organic acid anhydrides has been well studied (33, 40, 70, 74a, 79) and intermediate X (Figure 2), which results from nucleophilic attack of DMSO at one carbonyl of the acetic anhydride, is generally accepted as the product of the first step of the reaction. Intermediate X may undergo one of two reactions (1). One sequence involves attack by the alcohol substrate to form dimethylalkoxysulfonium salt III and give a carbonyl product *via* an intramolecular hydrogen transfer (93). A second pathway requires elimination of acetate to give a sulfonium ylid XI which can also react with the alcohol substrate to yield the side product VI (1). The major route to the carbonyl product proceeds through ylid intermediate V which has been established by labeling studies similar to those described in the previous section (93).

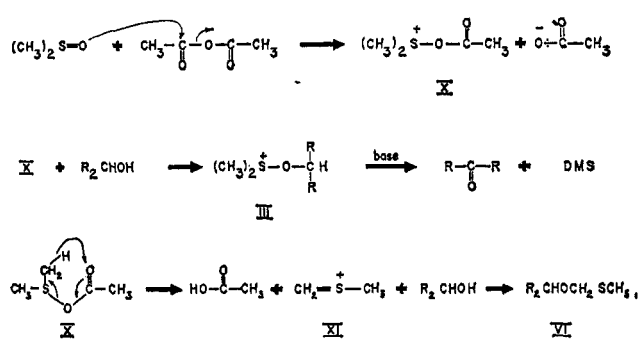


Figure 2.

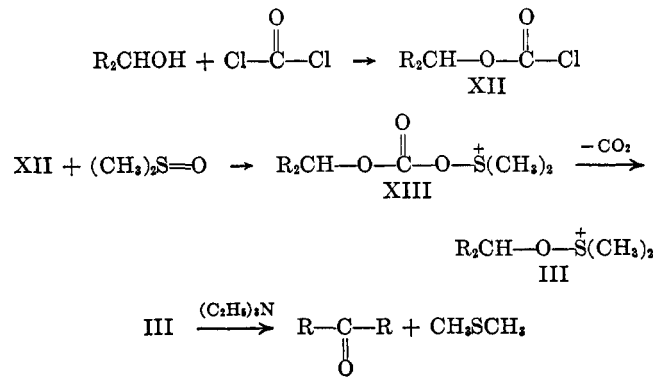
It appears that this method of oxidation will be of limited utility for oxidation of many unhindered primary and secondary alcohols, in light of the higher yields obtained with the Pfitzner–Moffatt technique. Formation of acetates (1, 93) as well as increased amounts of methylthiomethyl ether VI as side products are also distinct disadvantages. This method appears to be superior to the DMSO–DCC method in hindered systems. More hindered axial alcohol groups of steroids are oxidized in higher yields than the corresponding equatorial epimers (1) contrary to the Pfitzner–Moffatt technique. It may be that the difference in the selectivity of the two methods is due to the difference in size between the DMSO–DCC intermediate and X. The data for this method are given in Table I.

V. Phosphorus Pentoxide Method

Phosphorus pentoxide and DMSO have been used for a limited number of carbohydrate oxidations (72). No mechanistic details have been elaborated, but in light of previous mechanisms phosphorus pentoxide (P_4O_{10}), which is an anhydride, probably acts as an E group to activate the DMSO resulting in oxidation *via* pathway A. This oxidation method like DMSO–Ac_2O, will probably be capable of oxidizing some carbohydrates which remain inert to the Pfitzner–Moffatt technique (7, 72). The formation of methylthiomethyl ether IV as a side product has been reported in this oxidation (73), which is consistent with oxidation *via* pathway A. Since there is a limited amount of data available (Table I), it is difficult to assess the utility of this method.

VI. Chloroformate Method

Another approach to the oxidation of alcohols involves conversion of the alcohol to the chloroformate XII which will react with DMSO at room temperature or below in the presence of a base like triethylamine, to give the corresponding aldehyde or ketone (9). The chloroformate XII has two purposes in the reaction. It first acts as the E group to activate the DMSO giving salt XIII, and second as the source of the alcohol sub-



strate which by necessity is in near proximity to the activated DMSO. Intermediate XIII collapses giving carbon dioxide and the dimethylalkoxysulfonium salt intermediate III which, in the presence of the base triethylamine, is converted, likely *via* ylid V, into the observed products. Addition of DMSO and triethylamine together to the chloroformate results in no carbonyl compound being formed, indicating an intermediate such as XIII. Data for this method are given in Table I.

VII. Oxidation of Halides and Tosylates

In the previous sections, DMSO oxidations involving pathway A were considered. The following discussion will consider oxidations proceeding by pathway B, *i.e.*, formation of the dimethylalkoxysulfonium salt III by direct nucleophilic displacement of a leaving group by DMSO. Applications of this technique to α-halo esters (Br, Cl, I) or acids (34), phenacyl halides (48, 59), benzyl halides (49, 68), primary sulfonates (49, 60, 68), primary iodides (37), and a limited number of secondary halides (35, 67, 92) and secondary tosylates (36, 42, 83) have been successful in a preparative sense. Oxidation never proceeds past the carbonyl, and other functional groups remain generally inert. In contrast to *n*-alkyl iodides and tosylates, chlorides and bromides are not oxidized in yields large enough to be of preparative significance, but these compounds may be converted *in situ* to the corresponding tosylate and oxidized without prior purification (49). In the oxidation of secondary sulfonates (36, 42) and halides (35, 67) elimination becomes a competing (35, 36, 42, 67) and often the major reaction (65, 66), particularly when the reaction is carried out in the absence of a suitable base, *e.g.*, collidine (42). In cases where elimination is structurally prohibited, as with diphenylmethyl chloride, oxidation will occur in good yield (68). Factors affecting oxidation and elimination will be considered later.

The oxidations are facilitated by adding halide or tosylate to an excess of DMSO with an acid acceptor present, usually sodium bicarbonate or collidine. The nonalkaline hydrogen bromide scavenger 1,2-epoxy-3-phenoxypropane has also been employed (34). In the absence of base many activated halides are capable of being oxidized but in lower yields (42) while secondary tosylates react in DMSO, in the absence of base, to form mainly olefins (65, 66). The reactions of DMSO with halides and tosylates are similar to those of tertiary amine oxides with alkyl halides since the salts formed are also capable of forming aldehydes and ketones in basic media (34). The role of the base is probably twofold. In reacting with HX formed during a halide oxidation the base decreases the possible side reactions shown in the following equations (34).

$$(CH_3)_2S{=}O + 2HX \rightarrow CH_3SCH_3 + X_2 + H_2O$$

$$CH_3SCH_3 + BrCH_2\underset{\underset{O}{\|}}{C}R \rightarrow [(CH_3)_2\overset{+}{S}CH_2\underset{\underset{O}{\|}}{C}R]Br^-$$

$$CH_3SCH_3 + [(CH_3)_2\overset{+}{S}CH_2\underset{\underset{O}{\|}}{C}R]Br^- \rightarrow (CH_3)_3S^+Br^- + CH_3SCH_2\underset{\underset{O}{\|}}{C}{-}R$$

The second role of base is that of promoting proton abstraction in the actual oxidation step. It has been established that secondary alkyl tosylates are primarily oxidized *via* dimethylalkoxysulfonium salt intermediates like III and ylid V to the carbonyl compound in the same manner as was discussed in earlier sections (93). In light of the above, and the fact that pathway A oxidations proceed from ylid V by means of an intramolecular hydrogen-transfer step to the final products, it is attractive to suggest the same route for halide oxidations. A direct proton abstraction pathway rather than ylid formation must be considered for situations where acid strengthening groups are α to the halide, for example, α-halo ketones and esters. In these cases it may be that both mechanisms are operative.

The notable absence in the literature of any reports of the formation of the side product methylthiomethyl ether VI in pathway B oxidations (34–37, 42, 67) and their common occurrence in pathway A oxidations (1, 73, 77) have an important bearing on the mechanism of formation of VI. Two suggestions have been made to account for VI. One proposal involves rearrangement of dimethylalkoxysulfonium salt III to give VI directly (77). This proposal is inconsistent with the fact that VI has never been reported in pathway B oxidations. These pathway B, or displacement, oxidations have been shown to involve the same dimethylalkoxysulfonium intermediate III as the pathway A oxidations (93). Therefore the absence of methylthiomethyl ether VI in the pathway B oxidations can be taken as evidence against its formation proceeding from the common intermediate. The other proposal suggests the formation of sulfonium ylid XI, $CH_2{=}S^+{-}CH_3$ (1, 76), which can react with an alcohol substrate but not with a tosylate or halide to give VI, which is consistent with the observed data.

A survey of the yields and temperatures necessary to effect oxidation of the analogous substrates from the data in Tables II and III indicates that in most cases the reactivity toward oxidation follows the order $TsO^- > I^- > Br^- > Cl^-$ which is in support of an initial S$_N$2 process. Considerable evidence favoring a S$_N$2 DMSO attack based upon steric considerations of reactivity toward steroid sulfonate esters has also been presented (42). Some substrates, for example, $(C_6H_5)_2$-CH–X (X = Cl, OTs), certainly react by an initial S$_N$1 process (37).

TABLE II
DIMETHYL SULFOXIDE OXIDATION OF HALIDES

Substrate	Product(s)	Method	Yield, %	Ref
Methyl iodide	Trimethylsulfoxonium iodide			51
Heptyl chloride[a]	Heptanal	$NaHCO_3$	71	49
Heptyl bromide[a]	Heptanal	$NaHCO_3$	74	49
Heptyl iodide[a]	Heptanal	$NaHCO_3$	70	49
Octyl iodide	Octanal	Na_2CO_3	74	37
Dodecyl iodide	Dodecaldehyde	Glyme	44	37
2-Iodooctane	2-Octanone	MgO	32	37
1-Iodo-7-octene	7-Octenal	$NaHCO_3$	83	37
1-Iodo-7-octyne	7-Octynal	$NaHCO_3$	70	37
p-Bromobenzyl bromide[a]	*p*-Bromobenzaldehyde	$NaHCO_3$	76	49
p-Methylbenzyl bromide[a]	*p*-Methylbenzaldehyde	$NaHCO_3$	65	49
p-Methylbenzyl bromide	*p*-Methylbenzaldehyde	$NaHCO_3$	63	68
p-Nitrobenzyl bromide[a]	*p*-Nitrobenzaldehyde	$NaHCO_3$	76	49
p-Nitrobenzyl bromide	*p*-Nitrobenzaldehyde	$NaHCO_3$	48	48
Benzyl chloride	Benzaldehyde	$NaHCO_3$	58	68
Diphenylchloromethane	Benzophenone	$NaHCO_3$	44	68
6-Iodohexan-1-ol	6-Hydroxyhexanal	$NaHCO_3$	62	37
8-Iodo-2-octanone	2-Octanon-8-al	$NaHCO_3$	25	37
Phenacyl bromide	Phenylglyoxal		71	48
p-Bromophenacyl bromide	*p*-Bromophenylglyoxal		84	48
p-Chlorophenacyl bromide	*p*-Chlorophenylglyoxal		69	48
p-Phenylphenacyl bromide	*p*-Phenylphenylglyoxal		85	48
α-Bromobenzylphenone	Benzyl		95	48
Chloroacetic acid	Glyoxylic acid			34
Ethyl bromoacetate	Ethyl glyoxylate	1,2-Epoxy-3-phenoxypropane	70	34
Iodoacetic acid	Glyoxylic acid			34
Methyl chloroacetate	Methyl glyoxylate			34
Ethyl chloroacetate	Ethyl glyoxylate			34
Ethyl α-bromopropionate	Ethyl pyruvate			34
Diethyl bromomalonate	Diethyl mesoxalate			34
2α-Bromo-5α-cholestan-3-one	2-Oxo-3-hydroxy-5α-cholest-3-ene	$NaHCO_3$	60	67
	3-Oxo-5α-cholest-1-ene		12	
	2α-Hydroxy-5α-cholestan-3-one		15	
2,2-Dibromo-5α-cholestan-3-one	3-Oxo-2-bromo-5α-cholest-1-ene	$NaHCO_3$	50	67
3β-Acetoxy-6β-bromo-5α-cholestan-7-one	3β-Acetoxy-7-oxo-cholest-5-ene	$NaHCO_3$	73	35
	Cholesta-3,5-dien-7-one		12	
3β-Bromo-5α-cholestane	5α-Cholestan-3-one	Collidine	55	42
	5α-Cholest-2-ene		27	
Methyl 4β-bromo-3-keto-5β-cholanate	Methyl 3,4-dioxo-5β-cholanate	$NaHCO_3$	25	35
	Methyl 3-ketochol-4-enate		28	
7α-Bromo-3β-acetoxy-5α-cholestan-6-one	3β-Acetoxy-6-hydroxycholest-5-en-7-one	$NaHCO_3$, N_2	55	35
2,3-Bis(bromomethyl)quinoxaline	*dl*-1,2-Dibromo-1,2-bis(3-methyl-2-quinoxalyl)ethane	1,2-Epoxy-3-phenoxypropane	11	63
2,3-Bis(iodomethyl)quinoxaline	*dl*-1,2-Diiodo-1,2-bis(3-methyl-2-quinoxalyl)ethane	1,2-Epoxy-3-phenoxypropane	20	63
Benzoyl chloride	Benzoyl chloride		49	3, 82
	Benzoic acid		49	11
Benzenesulfonyl chloride	Benzenesulfonic acid		48	69
	Benzenesulfonyl chloride		49	
Triphenylphosphine	Triphenylphosphine oxide			82
Diphenylcholorophosphine	Diphenylphosphonic acid		94	3, 82
Phenyldichlorophosphine	Phenylphosphoric acid		75	3, 82
Diphenylphosphorus oxychloride	Diphenylphosphoric acid		48	3
Hexachlorocylotriphosphazatriene	Trimetaphosphimate			82
Cyanuric chloride	Cyanuric acid		84	3, 81, 82
Thionyl chloride	Sulfur dioxide, Chloromethyl methyl sulfide		~92	11
Trichlorophosphine	Phosphoric acid		96	3
BCl_3	$CH_3—S(=O)—CH_2Cl$ (B)		97	53
$SiCl_4$	SiO_2, chloromethyl methyl sulfide		100	53

TABLE II (*Continued*)

Substrate	Product(s)	Method	Yield, %	Ref
$NbCl_5$	$NbOCl_3 \cdot 2DMSO$, Chloromethyl methyl sulfide			22
$NbBr_5$	$NbOBr_3 \cdot 2DMSO$, Chloromethyl methyl sulfide			22
$TaCl_5$	$TaOCl_3 \cdot 2DMSO$ Chloromethyl methyl sulfide			22
$TaBr_5$	$TaOBr_3 \cdot 2DMSO$ Chloromethyl methyl sulfide			22
$MoCl_5$	$MoOCl_3 \cdot 2DMSO$			33a
	$MoO_2Cl_2 \cdot 2DMSO$			33a
VCl_3	$VOCl_2 \cdot 3DMSO$			33b

[a] Converted to tosylate with AgOTs.

TABLE III
DIMETHYL SULFOXIDE OXIDATION OF SULFONATES

Substrate	Product(s)	Method	Yield, %	Ref
n-Propyl tosylate	Propionaldehyde	$NaHCO_3$		68
n-Pentyl tosylate	Valeraldehyde	$NaHCO_3$	20	68
n-Hexyl tosylate	Capraldehyde	$NaHCO_3$		68
Octyl tosylate	Octanal	$NaHCO_3$	78	49
Neopentyl tosylate	Starting material	$NaHCO_3$	100	49
Oleyl tosylate	Oleyaldehyde	$NaHCO_3$	64	60
Elaidyl tosylate	Elaidaldehyde	$NaHCO_3$	72	60
1,3-Diphenoxy-2-propyltosylate	1,3-Diphenoxy-2-propanone	$NaHCO_3$	90	4
p-Methylbenzyl tosylate	*p*-Methylbenzaldehyde	$NaHCO_3$	74	49
p-Bromobenzyl tosylate	*p*-Bromobenzaldehyde	$NaHCO_3$	65	49
p-Nitrobenzyl tosylate	*p*-Nitrobenzaldehyde	$NaHCO_3$	84	49
5α-Cholestan-3β-yl-tosylate	5α-Cholestan-3-one	Collidine	64	42
	Δ^2-Cholestene		26	
	5α-Cholestan-3α-ol		10	
5-α-Cholestan-3β-yl tosylate	5α-Cholestan-3-one	NaOAc	20	36
	Δ^2-Cholestene		32	
	5α-Cholestane-3β-yl tosylate		48	
Cholesterol-3β-yl tosylate	5α-Cholestan-6-one	NaOAc	51	36
	Cholest-4-en-3-one		12	
	$\Delta^{3,5}$-Cholestadiene cholesterol		7	
	Cholesterol		9	
5α-Cholestan-7β-yl tosylate	5α-Cholestan-7-one	Collidine	76	42
	5α-Cholestan-7-ene		23	
5α-Cholestan-3-β-yl methanesulfonate	5α-Cholestan-3-one	Collidine	42	42
	5α-Cholestan-2-ene		10	
5α-Cholestan-7β-yl methanesulfonate	5α-Cholestan-7-one	Collidine	64	42
	5α-Cholestan-7-ene		10	
Methyl reserpate *p*-bromobenzenesulfonate	Methyl ketoreserpate	Triethylamine	60	83
Yohimbine-*o*-tosylate	Yohimbinone	Tri-*n*-propylamine	38	2
β-Yohimbine-*o*-tosylate	Yohimbinone	Tri-*n*-propylamine	25	2

As was noted earlier, in the oxidation of secondary halides and tosylates, elimination usually predominates. There are a limited number of cases known where the oxidation could be of synthetic utility and these compounds are listed in Table III.

Several attempts have been made to differentiate the mechanisms leading to oxidation and elimination (35, 36, 42, 67). The proposal that a common intermediate (*i.e.*, the dimethylalkoxysulfonium salt) proceeds to ketone and olefin has been made (36); however, this is not completely consistent with other experimental results. It has been demonstrated that axial halides or tosylates will give more elimination than the corresponding equatorial isomers (35, 42, 67). If SN2 attack is assumed to be correct, an axial halide or tosylate would be displaced by DMSO and result in the formation of an equatorial dimethylalkoxysulfonium salt, which should undergo elimination less readily than the axial intermediate formed by SN2 reaction of DMSO with an equatorial halide or tosylate (35). It appears that elimination and oxidation does not involve the common dimethylalkoxysulfonium intermediate. It should also be noted that tosylate eliminations carried out in DMSO do not appear to proceed by

a *trans*-diaxial mechanism (35). The data for halides are given in Table II and for sulfonates in Table III.

VIII. Oxidation of Thiols

Thiols (RSH, $ArCH_2SH$, ArSH) can be oxidized to disulfides (R–S–S–R, etc.) by DMSO (96–99, 101) (see Table IV). Oxidation of 1,4-butane- and 1,3-propanedithiol resulted in the formation of 1,3-dithianes (98). Success of the oxidation of dithiols depends on slow addition to an excess of DMSO to avoid polymerization. Despite this method an attempt to oxidize 1,2-ethanedithiol resulted in polymer formation (98). Other sulfoxides have been used but DMSO and tetramethylene sulfoxide remain the most satisfactory in this oxidation (98). Reactivity depends upon the acidity of the thiol (ArSH > $ArCH_2SH$ > RCH_2SH) (98). Aromatic thiols are oxidized spontaneously at room temperatures (97), whereas higher temperatures are required for oxidation of aliphatic thiols (101).

The mechanism proposed for this reaction (99) is analogous to that of the reaction of sulfoxides with hydrogen iodide (50, 52). Intermediate XIV is formed by nucleophilic attack at the sulfur of the protonated sulfoxide. Attempts to isolate or detect the presence of this intermediate by nmr failed (99). Formation of intermediate XIV has been suggested as the rate-limiting step. Reaction of intermediate XIV with another molecule of thiol leads to the formation of disulfide XV. The last step (XIV → XV) conceivably involves attack of thiol anion on intermediate XIV, in a manner similar to that predicted for the reaction of I^- in the sulfoxide oxidation of hydrogen iodide (52). The previous mechanistic proposals have analogy in the reaction of trimethylsulfoxonium iodide XVI with thiols to form the corresponding methyl aryl sulfides XVII (100).

$$(CH_3)_2S{=}O + R{-}SH \rightleftharpoons R{-}S^- + (CH_3)_2\overset{+}{S}{-}OH \rightleftharpoons$$

$$(CH_3)_2\overset{OH}{\overset{|}{S}}{-}S{-}R$$

XIV

$$XIV + R{-}SH \rightleftharpoons R{-}S{-}S{-}R + DMS + H_2O$$

XV

$$[(CH_3)_3S{-}O]^+I^- + ArSH \rightarrow [(CH_3)_3S{-}O]^+\bar{S}{-}Ar + HI$$

XVI

$$[(CH_3)_3S{-}O]^+\bar{S}{-}Ar \rightarrow ArSCH_3 + (CH_3)_2S{=}O$$

XVII

IX. Miscellaneous Oxidations

A. Diazonium Method

Benzaldehydes have been obtained by diazotization of benzylamines in DMSO (86). Intermediate formation of a carbonium ion XVIII is a reasonable prediction (86). Reaction of this carbonium ion with DMSO would result in the formation of aldehyde presumably *via* the dimethylalkoxysulfonium salt XIX.

$$p\text{-}R{-}C_6H_4CH_2{-}NH_2 \xrightarrow{HNO_2} p\text{-}R{-}C_6H_4CH_2^+$$

XVIII

$$XVIII + (CH_3)_2S{=}O \rightarrow p\text{-}R{-}C_6H_4{-}CH_2{-}O{-}\overset{+}{S}(CH_3)_2$$

XIX

$$XIX \rightarrow p\text{-}R{-}C_6H_4{-}CHO + CH_3SCH_3$$

B. Oxidation of Sulfides

The aliphatic sulfides, di-*n*-propyl and di-*n*-butyl sulfides, have been shown to undergo oxygen exchange with DMSO forming di-*n*-propyl and di-*n*-butyl sulfoxides in yields of 59 and 55%, respectively (87). Al-

Table IV
Dimethyl Sulfoxide Oxidation of Thiols

Substrate	Product(s)	Yield, %	Ref
1-Butanethiol	Di-*n*-butyl disulfide	86	96
1-Dodecanethiol	Di-*n*-dodecane disulfide	72	97, 98, 101
1-Hexadecanethiol	Di-*n*-hexadecane disulfide	84	97, 98
1-Octadecanethiol	Di-*n*-octadecane disulfide	72	98
1,3-Propanedithiol	1,2-Dithiacyclopentane	70	98
1,4-Butanedithiol	1,2-Dithiacyclohexane	89	98
2-Mercaptoacetic acid	Dithiodiglycolic acid	92	96
3-Mercaptopropionic acid	3,3′-Dithiodipropionic acid	93.8	96
2-Diethylaminoethanethiol hydrochloride	2,2′-Diethylamine diethyl disulfide hydrochloride	91.4	96
α-Toluenethiol	Dibenzyl disulfide	96.5	96–98, 101
p-Chloro-α-toluenethiol	Di-*p*-chlorobenzyl disulfide	96.8	96
p-Bromo-α-toluenethiol	Di-*p*-bromobenzyl disulfide	95	96
Benzenethiol	Diphenyl disulfide	94.5	96, 97
p-Chlorobenzenethiol	Di-*p*-chlorophenyl disulfide	96.5	96–98
o-Aminobenzenethiol	Di-*o*-aminophenyl disulfide	80	96
p-Methylbenzenethiol	Di-*p*-methylphenyl disulfide	70	96
o-Methylbenzenethiol	Di-*o*-methylphenyl disulfide		99
Pentachlorobenzenethiol	Dipentachlorophenyl disulfide	80	96
2-Naphthalenethiol	Di-2-naphthal disulfide	98	98

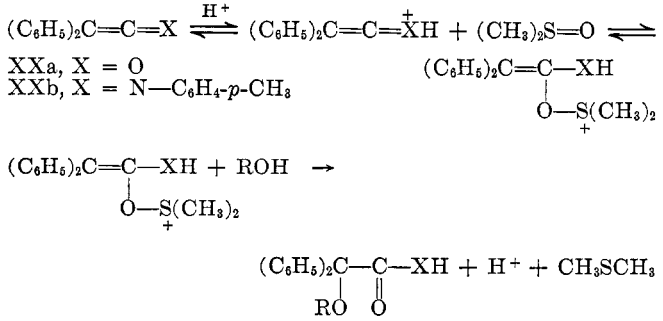
TABLE V
MISCELLANEOUS OXIDATIONS WITH DIMETHYL SULFOXIDE

Substrate	Product(s)	Method	Yield, %	Ref
Benzylamine	Benzaldehyde	Nitrous acid	82	86
p-Methylbenzylamine	*p*-Methylbenzaldehyde	Nitrous acid	60	86
p-Methoxybenzylamine	*p*-Methoxybenzaldehyde	Nitrous acid	65	86
Di-*t*-butyl sulfide	Di-*t*-butyl sulfoxide			87
Di-*n*-propyl sulfide	Di-*n*-propyl sulfoxide		59	87
Di-*n*-butyl sulfide	Di-*n*-butyl sulfoxide		55	87
Diphenylketene-N-*p*-tolylimine	N-(*p*-Tolyl)-α-hydroxydiphenylacetamide	Aqueous acid	91.5	57
Diphenylketene-N-*p*-tolylimine	N-(*p*-Tolyl)-α-methoxydiphenylacetamide	Methanol Aqueous acid	70	57
Diphenylketene-N-*p*-tolylimine	N-(*p*-Tolyl)-diphenylacetamide	Anhydrous acid	66	57
Diphenylketene	Benzilic acid	Aqueous acid	88	57
1,1-Diphenylsila-2-cyclohexanol	1,1-Diphenylsila-2-cyclohexanone	DCC	70	12
2,5-Dimethyl-*o*-quinol acetate	3-Hydroxy-4-methylbenzaldehyde	$NaHCO_3$	58	56
2,3,5-Trimethyl-*o*-quinol acetate	2-Hydroxy-3,4-dimethylbenzaldehyde	$NaHCO_3$	48	56
2,3,5,6-Tetramethyl-*o*-quinol acetate	3-Hydroxy-2,4,5-trimethylbenzaldehyde	$NaHCO_3$	45	56
Methyl 9,10-epoxy-(*cis* or *trans*)-octadecanoate	Methyl 9-hydroxy-10-keto octadecanoate, or -10-hydroxy-9-keto-	BF_3	65	13
Cyclohexene oxide	2-Hydroxycyclohexanone	BF_3	76	21
Cyclohexene oxide	2-Hydroxycyclohexanone	O_2	65	95a
2β,3β-Epoxy-5α-cholestane	3β-Hydroxy-5α-cholestan-3-one	BF_3	55	21
	5α-Cholestane-2,3-dione		11	
	5α-Cholestane-2β,3α-diol		10	
2α,3α-Epoxy-5α-cholestane	3β-Hydroxy-5α-cholestan-2-one	BF_3, dioxane	45	21
	5α-Cholestane-2,3-dione		19	
	5α-Cholestane-2β,3α-diol		19	
Styrene oxide	Phenacyl alcohol	BF_3	57	21
Styrene oxide	Phenacyl alcohol	O_2	92	95a
1,2-Epoxyoctane	1-Hydroxy-2-octanone	O_2	72	95a
Methyldiphenylsilane	Methyldiphenylsilanol Bis(methyldiphenyl)siloxane			74
Diborane	B_2O_3			61
Sodium	Na_2O			71
Potassium	K_2O			71

though this method circumvents the formation of sulfones in the preparation of sulfoxides from sulfides, a more recent technique utilizing *t*-butyl hypochlorite will surpass this method for laboratory preparation of sulfoxides (88).

C. OXIDATION OF KETENES AND RELATED COMPOUNDS

Oxidation of keteneimine (XXb) and a ketene (XXa) by DMSO has been demonstrated (57) to occur as indicated, but the generality of this reaction is not yet known. Acid catalysis is required. The following mechanism has been proposed to account for the observed products (57). There is an obvious similarity between these reactions and the initial acid-catalyzed reaction of DMSO with DCC.



D. AIR OXIDATION OF ALCOHOLS

A variety of benzyl alcohols have been successfully oxidized by refluxing in DMSO while passing a stream of air through the reaction mixture (95). In the absence of air the reaction failed. Dimethyl sulfide was obtained in 60–65% yield along with the aldehyde, establishing DMSO as the oxidant. A free-radical mechanism is indicated from the fact that oxidation proceeds, though in lower yield, in the presence of *t*-butyl peroxide (0.001 *M*) under oxygen-free conditions.

Benzylic and tertiary alcohols undergo elimination by refluxing in DMSO under a nitrogen atmosphere (94). Some evidence indicates that these dehydrations involve intermediate formation of a carbonium ion. Although the oxidation mechanism remains obscure, a carbonium ion intermediate is possible. This is congruent with the general increased yields observed with *p*-nitro- and *p*-chloro-substituted benzylic alcohols (95).

E. OXIDATION OF INORGANIC HALIDES

While most inorganic halides form coordination compounds with DMSO (23), several halides have been shown to undergo oxidation (3, 22, 53, 54, 80, 82). Other sulfoxides also form complexes which are generally more stable than those of DMSO. Stability of the DMSO metal complex is somewhat dependent on the polarizability of the metal halogen bond and in the case where the bond is highly polarizable, a 1,3 shift of a halogen is predicted (3, 53).

$$(CH_3)_2S{=}O + M(X)_n \rightarrow [(CH_3)_2S{-}O{-}M(X)_{n-1}]^+X^- \rightarrow$$
$$\text{XXI}$$

$$O{=}M(X)_{n-2} + [(CH_3)_2\overset{+}{S}{-}X]X^- \rightarrow CH_3SCH_2X + HX$$
$$\text{XXII} \qquad \text{XXIII} \qquad \text{XXIV}$$

Oxidation is proposed to proceed by SN2 attack by oxygen of DMSO at the electron-deficient metal, resulting in formation of intermediate XXI (53). XXI can decompose by a 1,3-halide shift forming the reaction products XXII and XXIV. The 1,3 shift leading to formation of intermediate XXIII is supported by the fact that when X = Br^- the more stable $[(CH_3)_2SBr]^+Br^-$ is isolatable (22). An ylid intermediate and intramolecular halide shift would also explain the formation of the chloromethyl methyl sulfide XXIV (3). The oxidation of sulfuryl chloride to sulfur dioxide by a sulfoxide seems to support such a postulate, and a mechanism to account for the observed reaction products has been proposed (11).

$$p\text{-}CH_3OC_6H_4{-}\overset{O}{\overset{\|}{S}}{-}CH_3 + SOCl_2 \rightarrow$$

$$[p\text{-}CH_3OC_6H_4{-}\overset{CH_3}{\overset{+}{S}}{-}O{-}\overset{O}{\overset{\|}{S}}{-}Cl]Cl^-$$
$$\text{XXV}$$

$$\text{XXV} \rightarrow [p\text{-}CH_3OC_6H_4{-}\overset{Cl}{\overset{+}{S}}{-}CH_3]^+Cl^- + SO_2 \xrightarrow{-HCl}$$

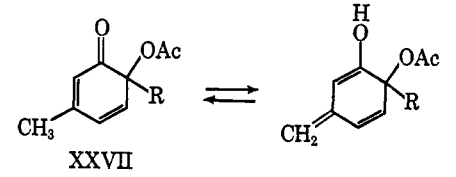
$$p\text{-}CH_3OC_6H_4{-}\overset{Cl}{\overset{+}{S}}{-}\bar{C}H_2 \rightarrow p\text{-}CH_3OC_6H_4{-}S{-}CH_2Cl$$
$$\text{XXVI} \qquad\qquad \text{XXVII}$$

Chloromethyl *p*-methoxyphenyl sulfide (XXVII) is recovered, and no sulfide is found with chloro substitution on the activated aromatic ring. This product could result from the ylid intermediate XXVI (3).

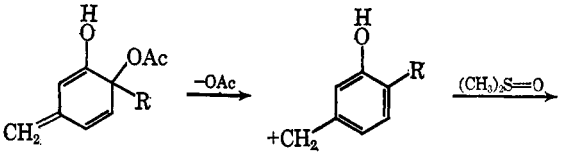
These oxidations are not limited to the replacement of one halogen as is evident from the list of reactions. The great utility of these reactions is not in the resultant metal, but in the synthesis of monohalogenated sulfides.

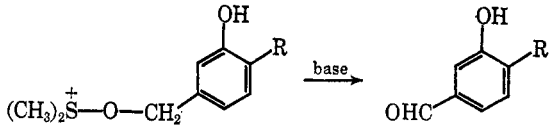
F. OXIDATION OF QUINOL ACETATES

Quinol acetates XXVIII have been shown to be selectively oxidized to substituted *m*-hydroxybenzaldehydes by DMSO and a base, *e.g.*, $NaHCO_3$ (55, 56). The reaction appears to be general for these compounds and is selective for oxidation of alkyl groups in the three position with respect to the phenol hydroxyl group. Other alkyl substituents remain inert. Quinol acetates XXVIII are readily prepared from the proper substituted phenol by reaction with lead tetraacetate. The proposed mechanism for these oxidations is (56)

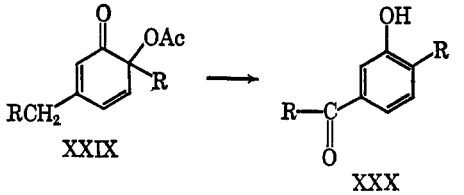


XXVII

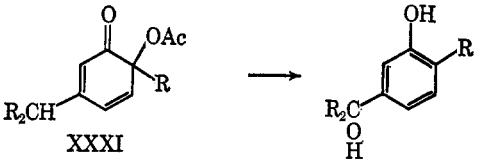




If the carbon attached to the aromatic ring is secondary XXIX, a ketone is formed, XXX, although in lower yield. A tertiary carbon substituted at the 3 position (XXXI) will be oxidized to an alcohol.



XXIX XXX



XXXI

G. OXIDATIVE HALOGENATION

Sulfoxides in general will oxidize hydrogen bromide and hydrogen iodide *via* an acid-catalyzed reaction to give Br_2 and I_2, respectively (46, 52).

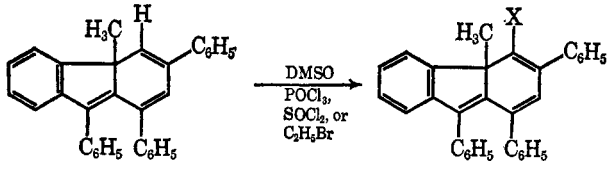
$$(CH_3)_2S{=}O + HX \rightarrow CH_3{-}S{-}CH_3 + X_2 + H_2O$$

Therefore DMSO in the presence of hydrogen halides is capable of effecting halogenations (31). This technique afforded a superior method for bromination of 2-aminofluorenone (XXXII) to 2-amino-3-bromofluorenone (XXXIII) (27). In the presence of ethyl bromide and DMSO, phenol reacted to give a mixture of brominated phenols, ethyl ether, ethyl phenyl ether, and unreacted phenol (89). When a primary or secondary alkyl or benzyl halide, instead of hydrogen halide, is used as a bromine source, both bromination

and N-alkylation take place in the presence of an amine (26, 28). Use of *t*-butyl bromide results in amine bromination only.

XXXII XXXIII

The bromination of 4a-methyl-1,3,9-triphenyl-4aH-fluorene (XXXIV) was carried out with DMSO and ethyl bromide (62). Chlorinations of this same compound (XXXIV) were effected with thionyl chloride or phosphorus oxychloride with the oxidant DMSO in yields of *ca.* 90% (62).



XXXIV X = Cl, Br

Previous proposals of intermediates in the reaction of DMSO with phosphorus oxychloride, thionyl chloride, I_2, and Br_2 (11, 30, 62) implicates XXXV as the reactive intermediate effecting these halogenations.

$$[(CH_3)_2\overset{+}{S}\text{—}X]X^-$$

XXXV, X = Cl^-, Br^-, I^-

There does not appear to be any greater degree of selectivity in this method of halogenation than that observed in direct halide addition. It should be mentioned, however, that the use of DMSO and alkyl bromides, and presumably iodides, results in a near-neutral media for halogenations.

H. OXIDATION OF EPOXIDES

Epoxides can be oxidized by DMSO in two different fashions. In the presence of boron trifluoride etherate and DMSO epoxides are converted into α-hydroxy ketones (13, 21). Results of a limited number of studies indicate that a mixture of two possible products will be obtained and the predominant compound will depend upon the relative steric hindrance to attack by DMSO. In spite of the fact that boron trifluoride will react with epoxides in the absence of DMSO, it seems likely that the DMSO is activated by the boron trifluoride, acting as an E group. Boron trifluoride is known to form a 1:1 complex with DMSO (54, 58). If the above is true, the reaction would fit into a pathway A classification.

The second method of oxidation required a stream of air to be bubbled through a solution of the epoxide in DMSO (95a). In a limited number of cases good yields have been obtained by this means. Oxygen is not consumed during the reaction and DMS is formed establishing DMSO as the oxidant (95a). The reaction does not occur when air is absent but if *t*-butyl hydroperoxide is present the reaction proceeds but in lower yield indicating the likelihood of a free radical rather than ionic mechanism (8).

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