REDUCTION OF ORGANOSULFUR COMPOUNDS

1982

HIDEO TOGO

REDUCTION OF ORGANOSULFUR COMPOUNDS

HIDEO TOGO

THE DEPARTMENT OF CHEMISTRY,
THE UNIVERSITY OF TSUKUBA

1982, Dec. 12

CONTENTS

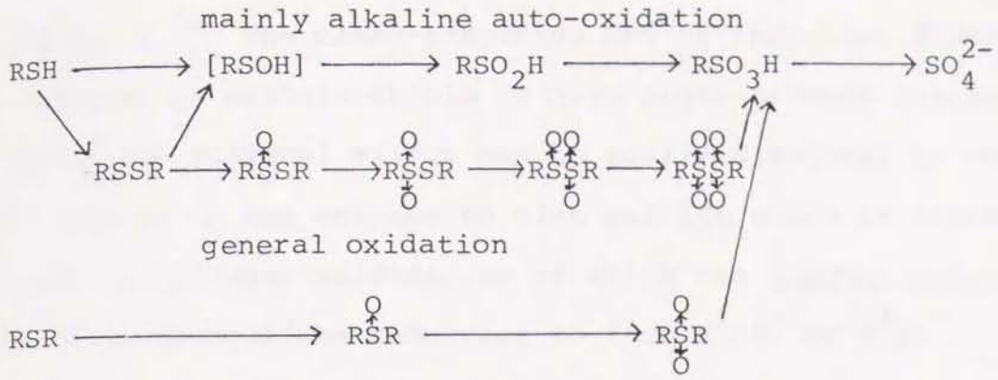
Introduction

General Introduction

When we look at the chemical phenomena of the various reactions on sulfur atom, we notice that substitution, oxidation, and reduction reactions are very important. Among them, substitution reaction has been studied in rather extensively and systematically from 1950's;particularly, the stereochemical research by Oae, Johnson, Cram, Andersen, Montanari, and Mikolajczyk et al, the stereo-electronic effect on reaction rate, the mechanism and product analyses of the cleavage reactions of S-S, S-O, S-N bonds by use of ^{18}O tracer by Kice, Kobayashi, Fava, and Oae et al, have led to understand considerably the whole nature of nucleophilic substitution reaction on the sulfur atom.[1)]

Meanwhile, a systematic study on the oxidation have been carried out extensively by Oae et al for these several years, and the main features of the oxidation have been reviewed in detail.[2,3,4)] Perhaps, these studies on oxidation may become quite important as a chemical reaction but obviously be more important in connection with biochemical oxidation of sulfur compounds with enzymes including metabolism. If we assume that the oxidation is opposite of reduction, we could understand the nature of reduction, as we understand the oxidation reaction more in detail. But the reduction reaction is not so simple. The reduction reaction of organosulfur compounds is quite important not only in organic syntheses but also in biochemical transformation, but up to date, no systematic investigation has evolved except isolated several individual studies. The oxidation of thiols and disulfides has been known to proceed

successively via the following pathways as shown in Scheme 1.



[]: isolation is impossible

Scheme 1.

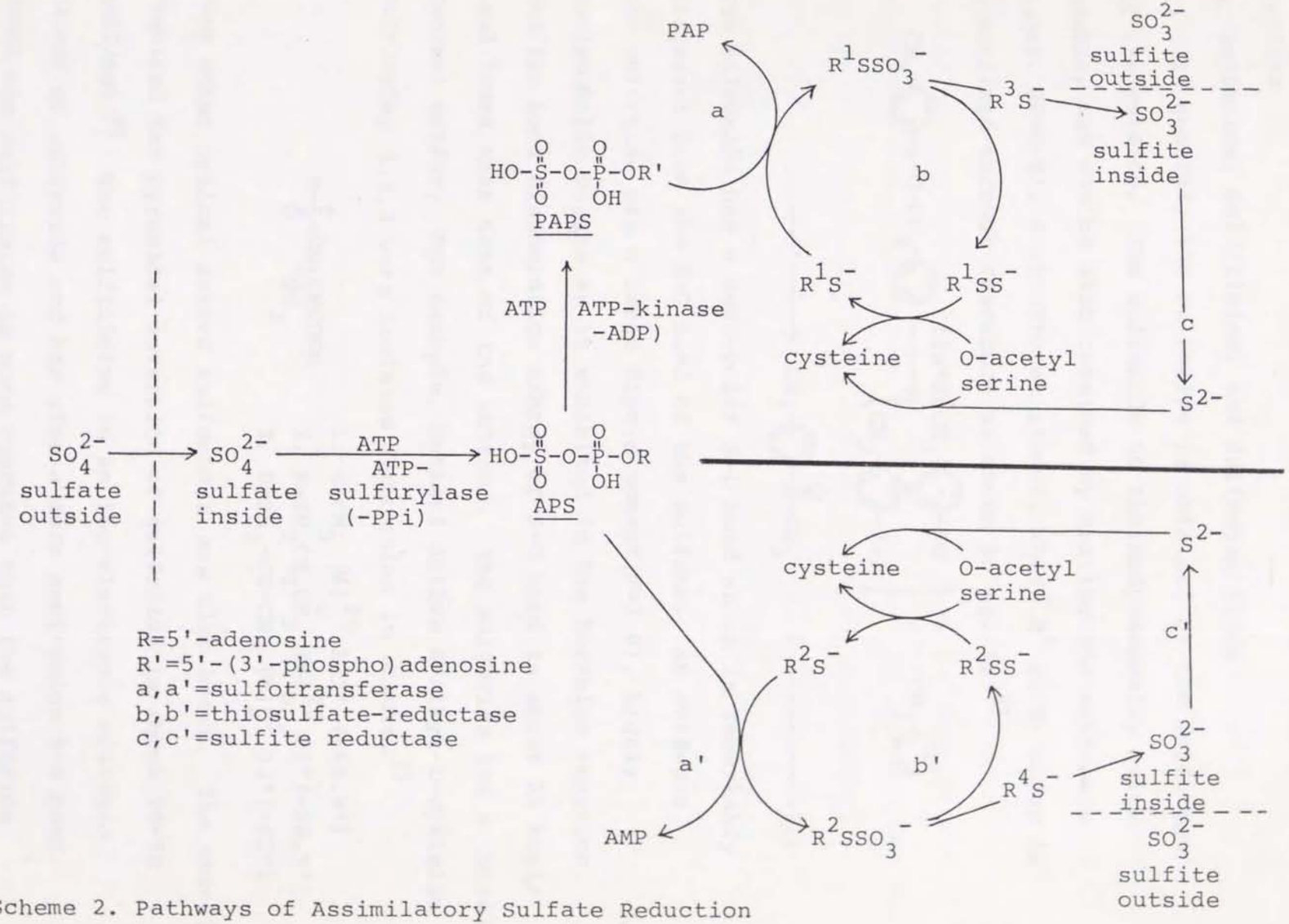
The reduction of oxidized sulfur compounds would follow the opposite path to this Scheme 1; namely the reduction would proceed from right to left side. However the individual steps in the reduction reaction have not been studied in detail except that of sulfoxide. In general oxidized organosulfur compounds of low states such as sulfoxide, disulfide, sulfinic acid are known to be readily reduced, while those of the high oxidation states such as sulfuric acid, sulfonic acid, sulfone, and disulfone are difficult to be reduced. The higher the oxidative state of the sulfur compound, the more difficult it becomes to oxidize the central sulfur. Therefore it is relatively easy to isolate or detect the individual reaction intermediates in the oxidation usually. However, it is not easy to isolate the individual reaction intermediates in the reduction reaction, since the compounds of the lower oxidative states are so readily reduced.

Meanwhile, many plants, fungi, microorganisms are known to take in sulfate which is at the highest oxidative state and difficult to be reduced, into their bodies by forming

APS or PAPS, mixed-anhydrides, each of which has an electrophilic central sulfur, using ATP(Adenosine Triphosphate) as shown in Scheme 2.[5] The mixed-anhydride APS or PAPS thus formed was reduced by protein-thiols to give protein-bound thiosulfates of which the sulfenyl sulfur can be easily displaced by other thiol groups in the enzymes to give sulfite which is ultimately reduced to hydrogen sulfide, or of which the sulfur group is reduced by thiosulfate reductase to form R^1SS^- or R^2SS^-.

---My target is the followings. The research of the reduction of high oxidative state sulfur compounds has not been studied, meanwhile, in nature, many plants, fungi, and microorganisms reduce sulfate, which is in the highest oxidative state among sulfur compounds, to sulfide which is the source of sulfur-containing amino-acids in their assimilatory metabolisms. In this process there are two important key steps. The first one is the formation of P-O-S linkage which sulfur is activated, and in the second step, protein-thiol plays a very important role as a reducing agent. Therefore, from chemical and biological points of view, I tried to use thiol or thiol analogous as a reducing agent in the reduction of many oxidative sulfur compounds in order to examine the reducing ability of thiol function, and to mimic the biological reduction method(for key steps) to the reduction of high oxidative sulfur compounds, and finally to find a successful simple chemical model reaction for the assimilatory reduction of inorganic sulfate and sulfonic acid------.

At first, I will introduce the individual researchs for the reduction of oxidative organosulfur compounds hitherto studied for a long time in the past in Outline, then I will mention the results of my research works.

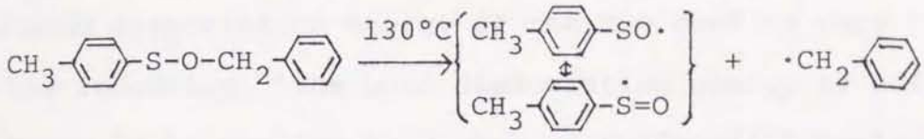


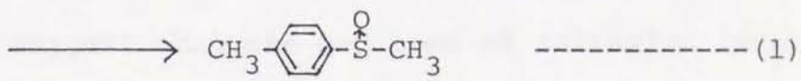
Scheme 2. Pathways of Assimilatory Sulfate Reduction

Outline

1. Sulfoxide, Sulfilimine, and Sulfonium Ylide

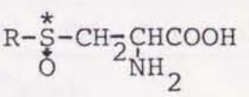
In general, the sulfoxide is obtained by the oxidation of the sulfide. The sulfoxide is thermodynamically quite stable, and can be also obtained by heating the sulfenate ester, RS-O-R', a structural isomer, where R^+ or R· group is stabilized through resonance as shown in eq. 1).[6]





----------(1)

The sulfoxide has a semi-polar S-O bond which is remarkably different from the S-O bond of the sulfone. As evidence, the sulfoxide has a large dipole moment(μ=3.0), highly nucleophilic oxygen as is exhibited in the Kornblum reaction, and the bond dissociation energy of S-O bond is about 25 kcal/mol lower than that of the sulfone. The sulfoxide has a chiral central sulfur. For example, optical active S-alkyl-L-cysteine sulfoxides 1,2,3 were isolated from onion in nature.[7]



1. R=CH_3 $[\alpha]_D^{25}$ 121° (-94.8°)
2. R=$CH_2CH_2CH_3$ $[\alpha]_D^{25}$ 25°(-30.9°)
3. R=CH_2-CH=CH_3 $[\alpha]_D^{25}$ 93°(-65°)

Many other optical active sulfoxides are also known. The energy required for pyramidal inversion of sulfoxide is about 20~30 kcal/mol.[8] The sulfilimine is an iso-electronic nitrogen isomer of sulfoxide and has also a more semi-polar S-N bond. Hence the sulfilimine is more reactive than the sulfoxide generally. Optical active sulfilimines can also be synthesized because of its pyramidal structure. For example, optical

active Ar-$\overset{*}{\underset{\downarrow}{\underset{NTs}{S}}}$-$CH_3$ is stable at room temperature, but easily racemizes over 80°C.[9] The sulfonium ylide has also a pyramidal structure. The relative ratio of the rates of thermodynamic racemization, pyramidal inversion, of these three coordinated sulfur compounds is in the following oder; sulfoxide: 1, sulfilimine: 10^6, and sulfonium ylide: 10^{14}. Since the reduction of the sulfoxide involves the cleavage of S-O bond, the bond dissociation energy of the S-O bond is very important in the reduction. The bond dissociation energy of sulfoxide is known to be smaller than that of sulfone(115 kcal/mol). This alone may suggest that the S-O bond of sulfoxide is semi-polar and of single bond character, while that of the sulfone has a double bond character. Because of the weaker S-O bond, the sulfoxide can be considerable easily reduced.[10]

Table 1. The Bond Dissociation Energy of Sulfoxide[11]

	S-O(kcal/mol)
$(CH_3)_2S\rightarrow O$	86.6
$(CH_3CH_2)_2S\rightarrow O$	88.7
$(C_6H_5)_2S\rightarrow O$	89.3
$H_2S\rightarrow O$	[71]

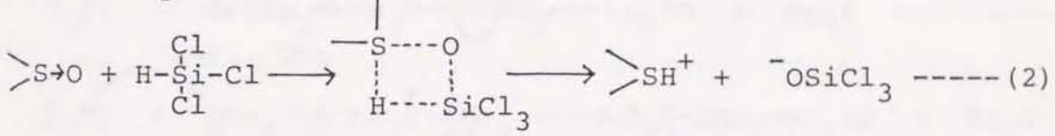
Table 2. The Force Constant of S-X Bond

$>S\rightarrow O$	7.0×10^5 dyne/cm
$>S\rightarrow NR$	4.4×10^5 dyne/cm

The bond dissociation energy of S-N bond in sulfilimine is not known, however the force constant can be calculated from the absorption of IR spectra as listed in Table 2. These data reveal that the bond energy of sulfilimine is smaller than that of sulfoxide.

1-i Hydride Reduction

Sulfoxide can be easily reduced by treatment with various aluminium hydride agents such as $LiAlH_4$.[12] One attractive example is a partial asymmetric reduction of racemic sulfoxide with optical active $LiAlH_{4-n}(OR^*)_n$ [R*=(+)-quinidine]. Thus the recovered sulfoxide was found to retain 0.2~2.7% optical activity.[13] No boron hydride agent can reduce the sulfoxide except B_2H_6, but the sulfonium compound can be reduced not only with $NaBH_4$[14] but also $NaBH_3CN$[15] which is a weak reducing agent. Both free sulfilimine and the N-tosylsulfilimine can be reduced easily by $LiAlH_4$,[16] but not with $NaBH_4$. The sulfoxide can be reduced under milder conditions by these hydride agents in the presence of Lewis acid like $TiCl_4$[17] or $Co(II)Cl_2$.[18] Since silicone has a strong oxygen affinity, Cl_3SiH[19] can also reduce the sulfoxide via the mechanism as shown in eq. 2.



$$\rangle S\rightarrow O + H\text{-}SiCl_3 \longrightarrow \rangle SH^+ + {}^-OSiCl_3 \quad \text{-----(2)}$$

1-ii Carbene

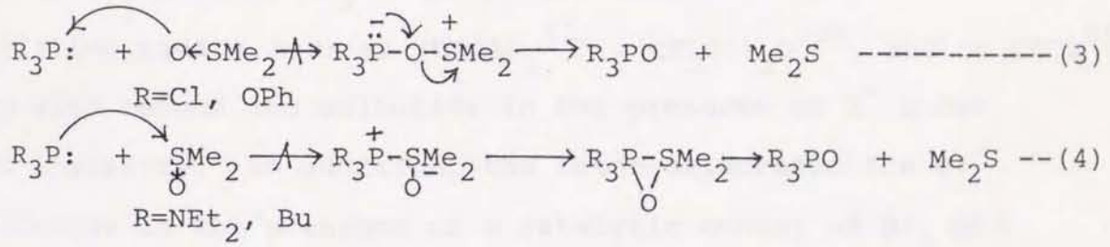
Sulfoxide can be deoxygenated by carbene species which is electron deficient. This was shown by Oda[20] and also Dilanjan[21] ; the reactivity of sulfoxide decreases in the following order, $(t\text{-}Bu)_2S\rightarrow O > (i\text{-}Pr)_2S\rightarrow O > Ph_2S\rightarrow O > Me_2S\rightarrow O$.[22] The sterically hindered sulfoxide can be reduced more readily. Both sulfilimine and N-tosylsulfilimine can be reduced under mild conditions. The reaction proceeds undoubtedly by the attack of carbene on the nitrogen of sulfilimine in a similar manner as in the reaction of sulfoxide. Therefore free sulfilimine can be reduced more easily than the N-tosylsulfilimine.[16]

1-iii Metal

Though Al-Hg[23] desulfinylizes the sulfoxide, following other transition metal complexes, $Fe(CO)_5$[24], $Mo(CO)_6$[25], $MoCl_3/Zn$[26], VCl_2[26], $K_3W_2Cl_9$[27], $(NH_4)_4Mo_2Cl_8.NH_4Cl$[27], $Cs_3Mo_2Cl_8H$[27], K_3MoCl_6[27], $TiCl_3$[28], $TiCl_4/Zn$[29], $SnCl_2$[30], and $Rh(III)/H_2$[31] can also reduce the sulfoxide to the sulfide in high yields under inert atmosphere. As an interesting example, the sulfoxide can be reduced by Grignard reagents[32,33], in particular the Grignard reagent reduces vinyl sulfoxides to the corresponding vinyl sulfides without isomerization in the presence of Cu(I).[33]

I-iv Tricoordinated Phosphorus Compounds

The mechanism of the reduction of the sulfoxide with tricoordinated phosphorus compound, PR_3, changes from that of eq. 3 to that of eq. 4 as the change of the R group[34,36].



Ph_3P is a weak reducing agent, but the reaction is accelerated by addition of Lewis acid.[35] $P(OR)_3$ cannot reduce the sulfoxide since it isomerizes to $R\text{-}P(O)(OR)_2$ upon heating, while $P(OSiMe_3)_3$ can opperate as a strong reducing agent because of the high thermal stability.[37] Other systems, Ph_3P/CCl_4[38], 2-chloro-1,3,2-benzodioxaphosphole[39], 2-phenoxy-1,3,2-benzodioxaphosphole[40], $P(NEt_2)_3/I_2/NaI$[41], $Ph_3P/I_2/NaI$[42], and P_2I_4[43] can also reduce the sulfoxide readily. All these reactions proceed via nucleophilic attack of oxygen of sulfoxide on the phosphorus atom.

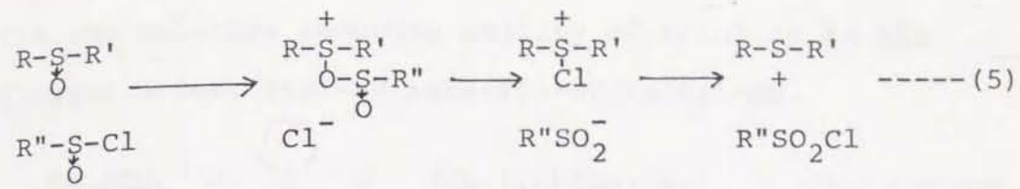
I-v Halide

As is well known, optical active sulfoxides readily undergo racemization in the reaction with acids. In the reaction of sulfoxides with hydrogen halides HX(HI, HBr, HCl), the reduction takes place faster than the racemization especially in the case of HI. However, HCl or HBr only gives rise to racemization but not reduction.[44,45] The rate of the reaction, V, can be expressed as $V=k[\text{sulfoxide}]^1[HI]^2$ [46,48] and is effected much by steric bulkiness of substituent.[47]

The rate of reduction of cyclic sulfoxides by HI depends on $\Delta S^{\neq}$.[49] For example, 4 or 5-membered cyclic sulfoxide can be reduced more easily than 6 or 7-membered cyclic sulfoxide. The sulfoxide cannot be reduced by I^- alone, but the reaction requires H^+. Me_3SiCl/I^- [50], or Me_3SiI[51] can reduce sulfoxide, because Me_3Si^+ plays the same role as H^+. Acylating agents such as $(COCl)_2$[52], $(CF_3CO)_2O$[53], and CH_3COCl[54] can also reduce the sulfoxide in the presence of I^- under 0°C instantly. In addition, the inter-oxidoreduction of sulfoxide in the presence of a catalytic amount of Br_2 or HBr is known. This reaction of sulfoxide is composed of bromination of α-H, reduction by HBr, and the Kornblum reaction.[55]

I-vi Sulfur Compounds

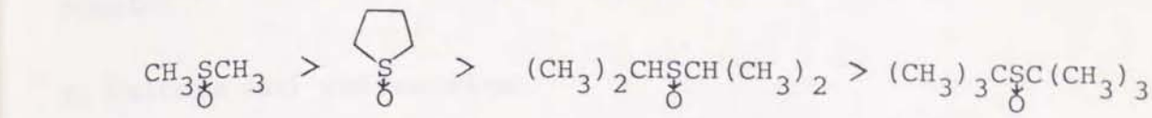
The Kornblum reaction is a reduction of sulfoxide, but is limited only to DMSO.[56] The reduction of sulfoxide with CH_3SOCl, or $O_2NC_6H_4SOCl$ is interesting and known to proceed by the following Scheme.[57]



-----(5)

Acetyl chloride can also reduce sulfoxides or sulfilimines under mild conditions by similar pathway.[58] Though the reduction of sulfoxide with $I_2/SO_2/Py$[59] or $Na_2S_2O_5$[60] is very convenient, the reaction mechanism is not known. While it is known in detail that the reduction by $NaHSO_3$ proceeds by the nucleophilic attack of SO_3^{2-} on the sulfur of the sulfoxide.[61] Diphosphorus pentasulfide, which is usually used as a thianating agent, can also reduce the sulfoxide.[62] The reaction proceeds by the nucleophilic attack of oxygen of the sulfoxide on the phosphorus atom via a transition state which involves both the leaving and attacking groups at apical positions.[63] Sulfilimine and N-tosyl sulfilimine can be also reduced by a similar reaction pathway.[64] Phosphorus thiobromide $SPBr_3$ has a stronger reducing ability than diphosphorus pentasulfide, though $SPCl_3$ has no reducing ability.[65] In these reactions, the driving force of these reductions is the formation of P=O linkage which has a larger (about 10 kcal/mol) bond energy than that of P=S linkage. Although elemental sulfur has no reducing ability, the sulfoxide can be reduced by elemental sulfur. The reduction proceeds by S-O cleavage of the sulfoxide by thiyl radicals.[66] Thiols are known to be oxidized by DMSO[67]; thus thiols are good reducing agents. Actually, cysteamine or glutathione are important biological reducing agents. Sulfoxides and sulfilimines can be reduced to sulfides by various kinds of thiols[68,69], the relative reactivity is as shown below[70],

while the relative reducing ability of thiol is in the following order, aryl-SH >aralkyl-SH >alkyl-SH.



In this reaction, both the acidity of thiol and the basicity of sulfoxide are very important because the addition of both base[71] and acid[72] accelerates this reduction. Therefore, highly acidic $R\overset{S}{\overset{\|}{C}}-SH$(pKa=2.5)[73], $(RO)_2\overset{S}{\overset{\|}{P}}-SH$(pKa=1.8)[74,77] can reduce sulfoxide, N-tosylsulfilimine, or sulfonium ylide very rapidly. Since the selenol is in the similar family of compound and is more acidic, it can reduce sulfoxides or sulfilimines readily.[75,76] $[(CH_3)_3Si]_2S$ [82] can also reduce sulfoxides and sulfilimines because $(CH_3)_3Si^+$ is a synthon of H^+. Though H_2S[79], thiol[80], and CH_3SCH_3[81] are mild reducing agents, the reduction is accelerated remarkably by the presence of $(CF_3CO)_2O$ which is a strong acylating agent. The reduction of N-tosyl sulfilimine with elemental sulfur or diaryl disulfide is an interesting example, the reaction proceeds by a radical mechanism.[83] As another interesting method, sulfinic acid, i.e. CH_3SO_2H, or p-$CH_3C_6H_4SO_2H$ can also reduce sulfoxide, N-tosyl sulfilimine to the sulfide easily.[84,85,86]

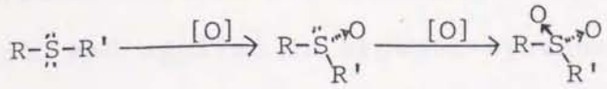
I-vii Others

Though a few examples of reduction of sulfoxides and sulfilimines by hydrogenation are known[87,88] this method generally can not be used because of the catalytic poisoning of divalent sulfur compounds. Singlet oxygen, produced in-situ, undergoes photochemical deoxygenation[89], however reduction is limited only to a certain sulfoxide. N-Tosylsulfilimines and free sulfilimines can be reduced by CN^- [90], also t-$BuSNO_2$ and p-$TolSO_2NO$[91] which are powerful nitrosating agents,

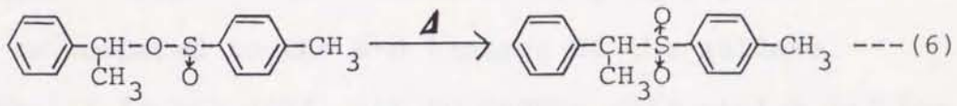
respectively. The electrolytic reduction has not been well studied.[92)]

2. Sulfone and Sulfoximine

Sulfones which can be obtained by oxidation of sulfides and sulfoxides are the most stable compounds among oxidized organosulfur compounds.



For example, even upon refluxing at its boiling point 379°C, diphenyl sulfone does not decompose. The facile isomerization of the benzylic or allylic sulfinate ester to the sulfone also stems from this unusual stability of the sulfone.



---(6)

The S-O linkage of the sulfone, which is structually tetrahedral, has a highly double bond character, therefore the oxygen terminals of the sulfone are poor nucleophiles and does not react with organic halide RX. Actually, the bond length of S-O linkage in dimethyl sulfone is 1.42Å which is considerably shorter than that of S-O bond of $(F_5S\text{-}O\rightarrow)_2$, 1.66Å, due mainly to the double bond character. The bond dissociation energy of S-O linkage(Table) is very large as compared with those of the sulfoxide or the phosphine oxide of which P-O bond energy is about 105 kcal/mol and is believed to have a considerably high bond energy. Since the C-S bond dissociation energy of sulfone is remarkably small, the reductive cleavage of C-S bond takes place readily in various

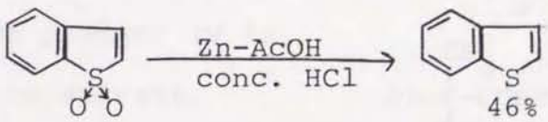
Table. The Bond Dissociation Energy of Sulfone(kcal/mol)[93]

Sulfone	$CH_3SO_2CH_3$	$CH_3CH_2SO_2CH_2CH_3$	$C_6H_5SO_2C_6H_5$
S-O	112	112	113
C-S	68	68	70

reactions. Therefore, the reactions in which the SO_2 function of sulfone is directly involved are rather limited, however, the reaction involving active α-methylene group have been studied and applied in organic syntheses. In general, the sulfone is very inert and it is very difficult to be reduced by a mixture of metal and acid, phosphorus pentachloride, phosphorus, phosphine, Ph_3SnH, R_3SiH, B_2H_6, and $AlCl_3$-$NaBH_4$. Meanwhile, sulfoximine which is prepared by the reaction of sulfoxide and Chloramine-T and is analogous to the sulfone, is not symmetrical and has a considerably semi-polar S-N linkage as compared to the S-O linkage of the sulfone. Therefore, it is not difficult to reduce sulfoximine and the reduction product is sulfoxide but not sulfilimine.

2-i Transition Metal and Acid

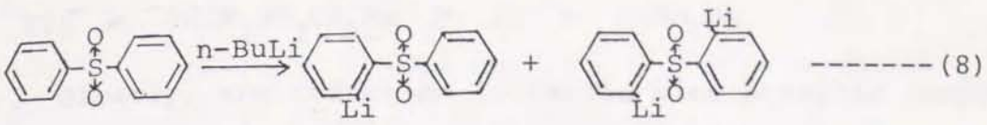
The conjugated sulfone as shown in eq. 7 is the only sulfone which can be reduced by Zn-HCl system.[94]



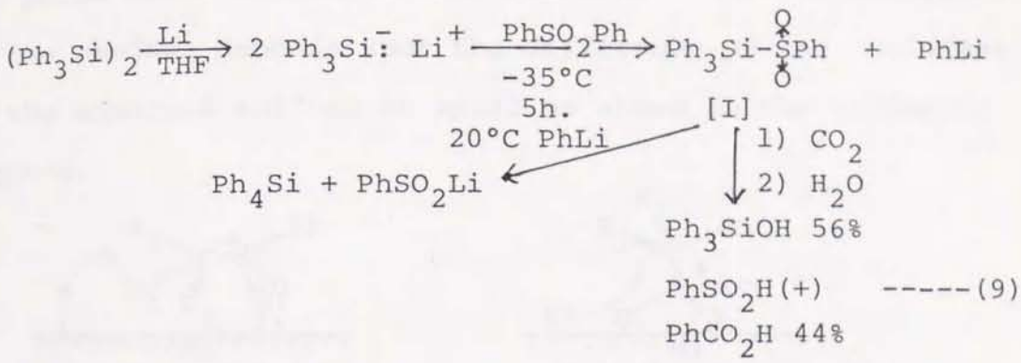
----------(7)

2-ii Carbanion, Silylanion[95]

Generally, a strong base, such as carbanion, abstracts the α-proton of alkyl sulfone and *o*-hydrogen of diaryl sulfone, respectively. While, triphenylsilyl anion attacks the central sulfur atom of diphenyl sulfone to form lithium benzenesulfinate via an intermediate[I].

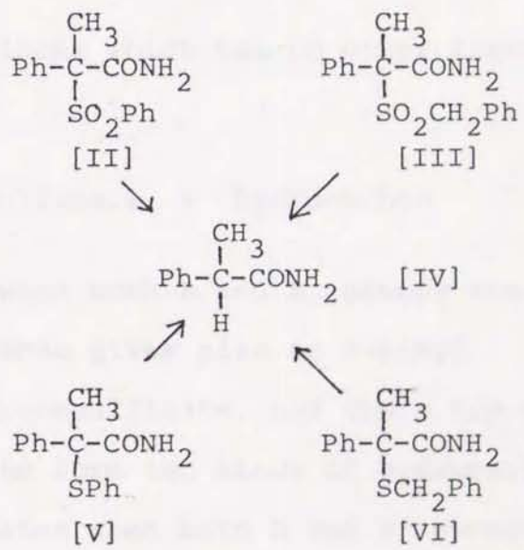


-------(8)



2-iii Metal(Na, Al, Ni, Al-Hg)

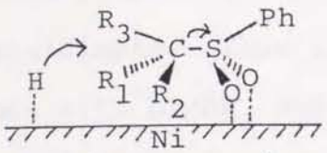
The sulfone which has a carboxy or carbonyl group at α-position easily gives rise to reductive cleavage of C-S bond by metal to give a hydrocarbon and the sulfinate.[96] For example, the reductive cleavage products of the following sulfone with Raney-Ni[97] vary with the structure of the sulfone and solvent used. So, the reductive cleavage product of II is the inversion product in ethanol but the retention product IV in acetone as solvent, respectively. The product in the reduction of III is



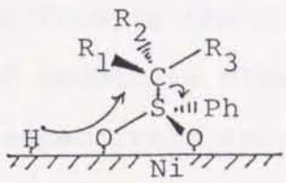
of retention IV both in ethanol and acetone as solvents. However, stereoselectivity is not high. While, the reductive cleavage compounds IV from the sulfides V, VI are racemic. The relative reactivity of reductive cleavage is in the following

III > $PhCH_2SO_2CH_2Ph$ > II > $PhSO_2Ph$

order. Clearly, the reduction is facile with benzylic compounds and polar media accelerate the reaction. The stereoselectivity of the product depends upon the difference of the conformation of the absorbed sulfone on metal as shown in the following figures.



Walden Inversion



Retention

Analogous Na-Hg also gives rise to the reductive cleavage.[98] This treatment has been applied to organic syntheses.

$$RCH(SO_2Ph)(CO_2CH_3) \xrightarrow[CH_3OH,\ Na_2HPO_4,\ 0°C,\ 1h]{6\%\ Na\text{-}Hg} RCHCO_2CH_3 \quad 60\text{-}90\% \quad \text{----------(10)}$$

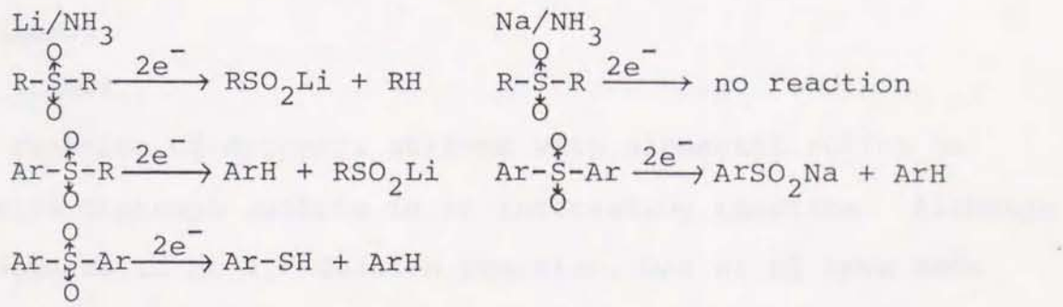
The reductive cleavage of sulfone which has no other functional group is the following.[99]

$$R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}\text{-}R' \xrightarrow[EtOH,\ 4h]{6\%\ Na\text{-}Hg} \text{sulfinate} + \text{hydrocarbon}$$

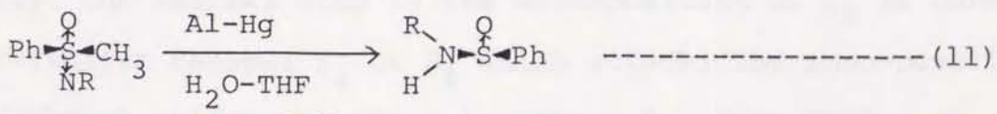
The reaction does not occur when both R and R' groups are alkyl groups. Alkyl aryl sulfone gives rise to S-alkyl reductive cleavage to form arenesulfinate, and there are two possible cleavage positions to form two kinds of hydrocarbons and two kinds of arenesulfinates when both R and R' groups are aryl groups.

In the case of Birch reduction(Li, Na/NH_3)[100], the mode of reductive cleavage and the reactivity are different. Namely, dialkyl sulfones can be reduced and the site of reductive cleavage of the alkyl aryl sulfone is opposite. Moreover,

once arenesulfinate is formed in the reaction of diaryl sulfone, it is readily reduced further to the corresponding arenethiol with this system. Probably, since the Li-O linkage of lithium arenesulfinate produced has a considerable covalent bond character, it may be reduced to arenethiol. Actually, in the reaction with the Na/NH_3 system, the reductive cleavage product of the diaryl sulfone is the sodium arenesulfinate. Thus the mode of reductive cleavage of the sulfone with Li/NH_3 and Na/NH_3 respectively are summarized as in the following.



Sulfoximines(VII~IX) also give rise to the reductive cleavage of the C-S bond to form the sulfinamide(X, XI) with the Al-Hg system. But, oxysulfonium salt, XII, which is the N-alkylation compound, can give the normal reduction product, XIII which is the retention product in the reduction with this system.[101]

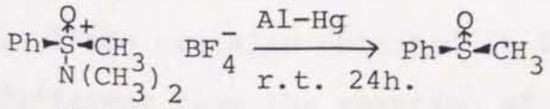


(11)

VII R=CH_3 X R=CH_3

VIII R=H XI R=H

IX R=p-$CH_3C_6H_4SO_2$



(12)

XII XIII

2-iv Electrode Reduction[102)]

The sulfone also gives rise to the reductive cleavage of C-S bond in the electrode reduction to form the sulfinate and hydrocarbon.

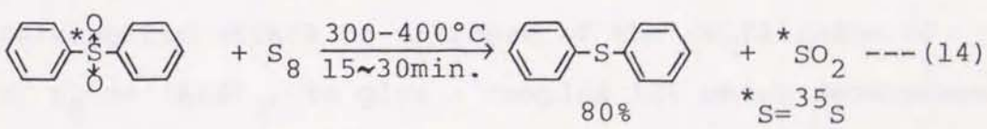
$$2[N(CH_3)_4]^+ + 2e^- + nHg \xrightarrow[0.5h]{CH_3OH,\ 5°C} 2[N(CH_3)_4]Hg_n\text{=TMA}$$

$$RSO_2R' + 2\ TMA + H^+ \longrightarrow RSO_2^- + R'H + 2\ TMA^+ \quad \text{----(13)}$$

Sulfones bearing halogens give dehalogenated reductive cleavage products. The mode of reductive cleavage and the reactivity are quite similar to that with metal(Na, Al)-amalgam.

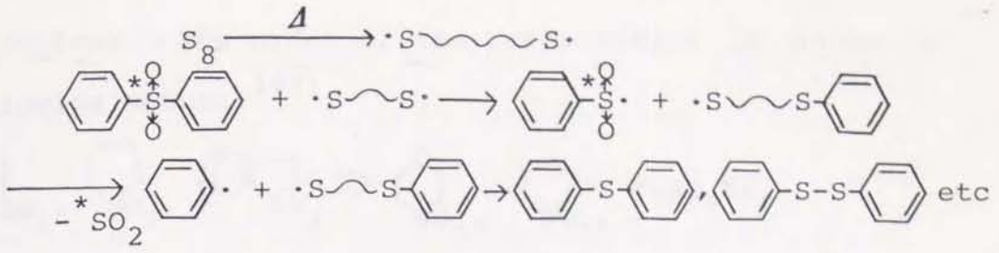
2-v Sulfur

The reaction of diphenyl sulfone with elemental sulfur to to give diphenyl sulfide is an interesting reaction. Although it appears to be a reduction reaction, Oae et al have made clear that this reaction was not a reduction reaction by carrying out a tracer experiment with diphenyl sulfone labeled with ^{35}S as shown in eq. 14.[103)]



---(14)

Namely, the initial step is the decomposition of S_8 to form a polysulfur radical S_3 or S_4 which attacks the ipso-position of diphenyl sulfone as shown in Scheme 3. Once $PhSO_2\cdot$ is formed, this can be readily decomposed to Ph· and SO_2 gas. Thus diphenyl sulfide is formed by the reaction of Ph· and benzenethiyl radical. Diphenyl disulfide and diphenyl polysulfide are also obtained in this reaction. This reaction is different from the reaction of diphenyl sulfoxide and

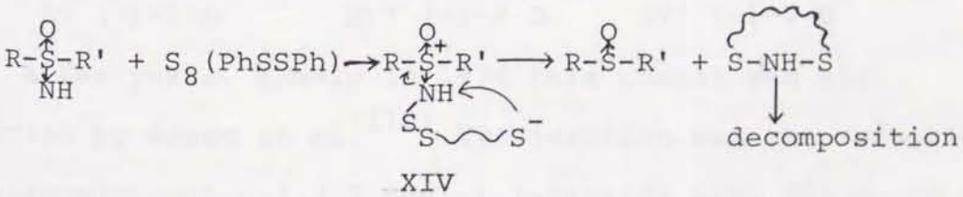


Scheme 3.

elemental sulfur which is essentially a reduction involving the S-O bond cleavage. In the reaction of dibenzyl sulfone with elemental sulfur,[104]

$$PhCH_2\overset{O}{\underset{O}{S}}CH_2Ph \xrightarrow[250°C,\ 7h.\ (\text{conversion } 70\%)]{S_8} H_2S\ (32\%) + PhCH{=}CHPh\ (68\%) + H_2O\ (\text{trace}) \quad --(15)$$

dibenzyl sulfide was not obtained. The products are shown in eq. 15 and are formed via the abstraction of α-hydrogen of the sulfone by polysulfur radical, $\cdot S_n \cdot$, subsequent rearrangement and elimination reaction. Meanwhile, the sulfoximine is reduced to the sulfoxide in a good yield by elemental sulfur.[105] Moreover, the deimination reaction proceeds with completely retention of configuration.[106] The reaction proceeds via the nucleophilic attack of nitrogen of the sulfilimine to sulfur, S_8 or $(ArS)_2$, to give a complex XIV which decomposes to the sulfoxide as shown in Scheme 4.



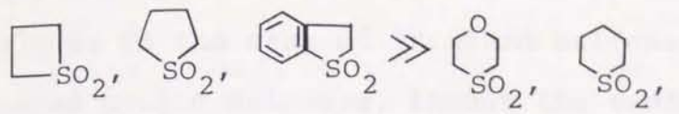
XIV

Scheme 4.

2-vi Aluminium Hydride

The reduction of the sulfone with $LiAlH_4$ has been studied in detail. The reactivity remarkably depends upon the structure

of the sulfone. The order of the reactivities is shown in the following manner.[107]

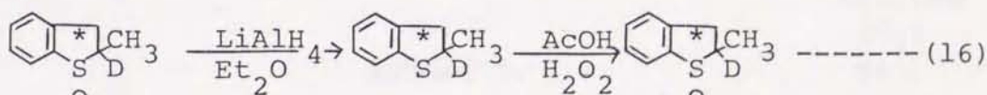


$PhSO_2Et$,

$n\text{-}BuSO_2Bu\text{-}n$, $PhSO_2Ph \gg t\text{-}BuSO_2Bu\text{-}t$

Namely, the strained sulfone, i.e. 4- or 5-membered cyclic sulfone, can be readily reduced.[108] The reactivity and the bond strength of O-S bond is well correlated. While, highly steric-hindered di-t-butyl sulfone which has no α-hydrogen atom can not ne reduced.

In 1970, Cram reported that the reduction of optically active 5-membered cyclic sulfone which has deuterium in α-position, XV, with $LiAlH_4$ gave the corresponding optical active sulfide, XVI which retained the configuration of α-carbon. Upon oxidation the sulfide gave the starting material XV'.[109] Thus the results suggest that hydride species of $LiAlH_4$ directly attacks the central sulfur atom of the sulfone.

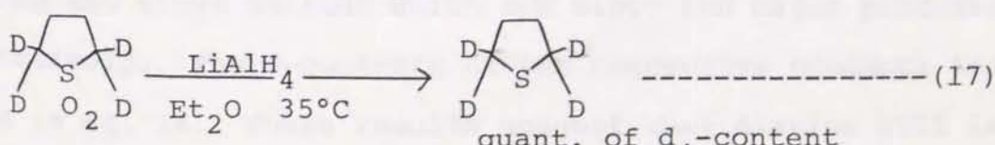


(16)

$[\alpha]_{540}^{25}$ -13.3 $[\alpha]_{540}^{25}$ +87.0 $[\alpha]_{540}^{25}$ -13.23

XV (-)-2-D XVI (+)-2-D XV' (-)-2-D

After a few years, namely in 1974 this result was also supported by Weber et al.[110] The reaction was the reduction of thiacyclopentane-2,2,5,5-d_4-1,1-dioxide with $LiAlH_4$ to give thiacyclopentane-2,2,5,5-d_4.

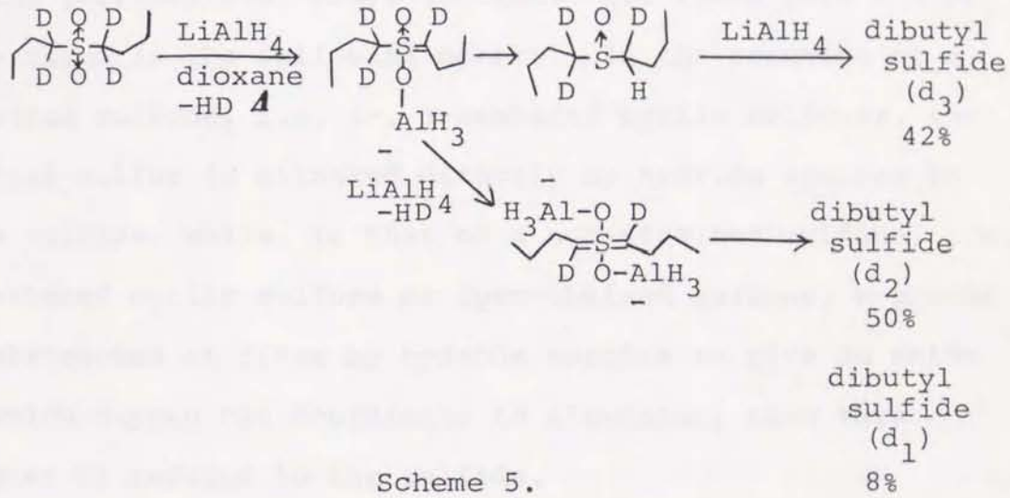


(17)

quant. of d_4-content

In the reduction of open-chained sulfones or a non-strained 6-membered cyclic sulfone, reduction does not proceed easily as in the case of strained sulfones, i.e. 4-, 5-membered cyclic sulfones, though the evolution of hydrogen gas can be detected.

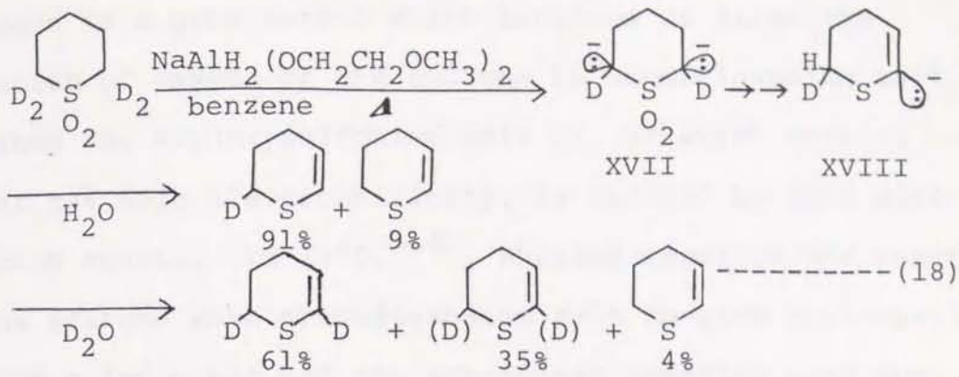
When $\alpha,\alpha,\alpha',\alpha'$-$d_4$-dibutyl sulfone was used in this system, Weber et al obtained the mixture of d_2- and d_3-dibutyl sulfides but not d_4-dibutyl sulfide.[110] So, the initial step is the abstraction of α-proton of the sulfone by hydride species as shown in Scheme 5.



Scheme 5.

In the reaction of the 6-membered cyclic sulfone with $NaAlH_2(OCH_2CH_2OCH_3)_2$, hydrogen gas also evolves and the α-deuterated sulfone is recovered when D_2O was added to this reaction mixture.[111] Upon refluxing the mixture of $\alpha,\alpha,\alpha',\alpha'$-$d_4$-thiacyclohexane-1,1-dioxide and $NaAlH_2(OCH_2CH_2OCH_3)_2$,[110] the reaction product was the mixture of the corresponding sulfide and vinyl sulfide which are minor and major products respectively. The d-contents of the respective products are shown in eq. 18. These results suggest that dianion XVII is the first intermediate, while XVIII is the final intermediate.

Though Bordwell et al[107] obtained the thiacyclohexane in the reduction of thiacyclohexane-1,1-dioxide with $LiAlH_4$,

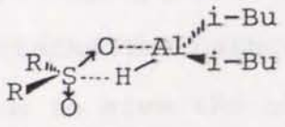


XVII XVIII

----------(18)

there is a possibility that it was formed by further reduction of the intermediate, vinyl sulfide. All these data can be summarized in the following manner. In the reaction of a strained sulfone, i.e. 4-, 5-membered cyclic sulfones, the central sulfur is attacked directly by hydride species to give sulfide, while, in that of a non-strained sulfone, i.e. 6-membered cyclic sulfone or open-chained sulfone, α-proton is abstracted at first by hydride species to give an anion of which oxygen can coordinate to aluminium, then this complex is reduced to the sulfide.

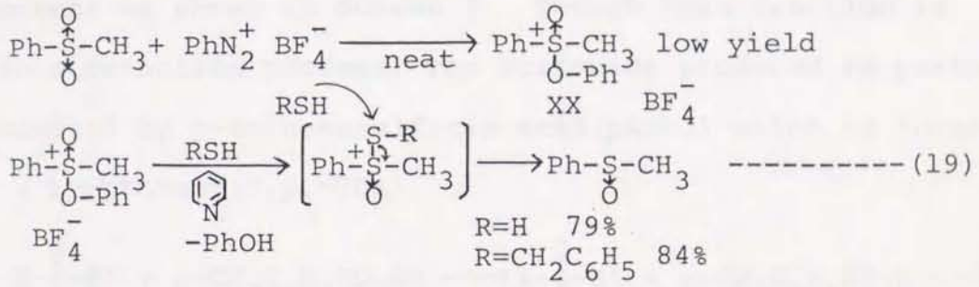
Di-iso-butyl aluminium hydride, $(i\text{-}Bu)_2AlH$, can also reduce various kinds of sulfones to sulfides.[112,113] The reactivity of $(i\text{-}Bu)_2AlH$ is similar to that with $LiAlH_4$. Though no detailed study has been reported, the reaction is presumed to proceed via a cyclic transition state as shown in XIX, because the aluminium atom of $(i\text{-}Bu)_2AlH$ functions as a Lewis acid.



XIX

2-vii Arenediazonium/Reducing Agent

The reduction of sulfonyl group with arenediazonium compound is a good method which involves at first the arylation of oxygen of the sulfone by arenediazonium salt, and then the aryloxysulfonium salt XX, of which central sulfur has high electrophilicity, is reduced by some mild reducing agents. In 1970,[114], Whiting reported the reaction of the sulfone with arenediazonium salt to give aryloxysulfonium salt in a low yield and the subsequent reaction with some nucleophiles. Oishi et al[115] could obtain the sulfoxide from XX by addition of thiols in good yields.



once such an aryloxysulfonium salt XX is formed, the sulfoxide is the product not the sulfide in the subsequent reaction with the mild reducing agent. However, it is difficult to obtain aryloxysulfoniums in moderate yields, because there is no good solvent which can be used for the preparation of aryloxysulfonium salt due to the very strong electrophilicity of the diazonium salt. Meanwhile, the melting point of the sulfone is usually rather high. Therefore, the yield of aryloxysulfonium salt is low(10~30%) since the reaction is a solid phase reaction. If alkoxysulfonium salt is used, the nucleophile usually attacks the carbon of O-C bond but not the central sulfur atom to give the original sulfone, the starting material. When p-$ClC_6H_4N_2^+BF_4^-$ is used instead

of $C_6H_5N_2^+BF_4^-$, the yield of the aryloxysulfonium salt increases to 40~60%. Aryloxysulfonium salt can also be reduced to the sulfoxide by $NaBH_4$.[116]

2-viii Nitroso Agents

The sulfoximine can be deiminated by $NaNO_2$[117] or $NO^+PF_6^-$[118] to give the sulfoxide in a good yield. The stereochemistry is retention. This deimination reaction can be carried out in non-aqueous media when p-toluenesulfonylnitrite, $p\text{-}CH_3C_6H_4SO_2NO$, instead of the previous agents, is used.[119] The N-substituted sulfoximine, $R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{NR''}{\downarrow}}{S}}\text{-}R'$ or $R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{NTs}{\downarrow}}{S}}\text{-}R'$, cannot be deiminated because nitrosation is difficult. The reaction proceeds as shown in Scheme 7. Though this reaction is also a retention process, the sulfoxide produced is partially racemized by p-toluenesulfinic acid(pKa=2) which is formed as a by-product(o.p.~70%).

$$R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{NH}{\downarrow}}{S}}\text{-}R' + p\text{-}CH_3C_6H_4SO_2NO \longrightarrow R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{NO}{\downarrow}}{S}}\text{-}R' + p\text{-}CH_3C_6H_4SO_2H \longrightarrow$$

$$(p\text{-}CH_3C_6H_4SO_2)_2NOH + (p\text{-}CH_3C_6H_4SO_2)_2N\text{-}OSO_2C_6H_4CH_3\text{-}p +$$

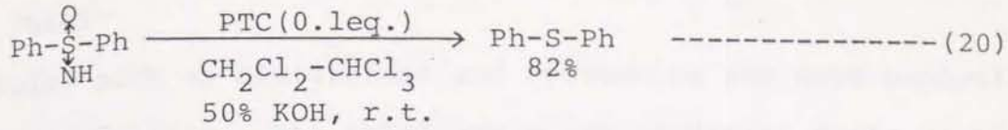
$$N_2O + R\text{-}\underset{\underset{O}{\downarrow}}{S}\text{-}R'$$

Scheme 7.

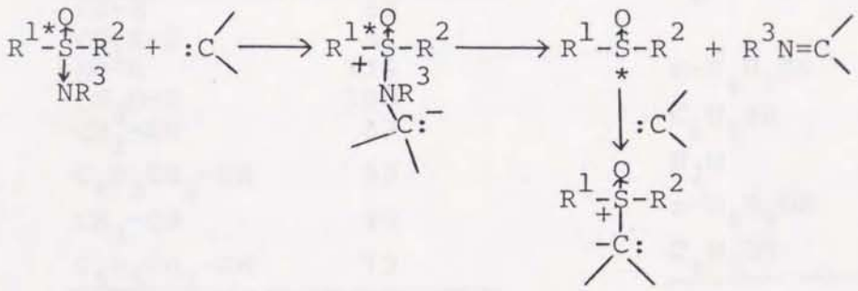
The racemization does not occur when t-butyl thionitrate, $t\text{-}BuSNO_2$, instead of p-toluenesulfonylnitrite is used, since there is no generation of acid species.[119]

2-iv Carbene

Though the sulfone does not react with carbene, the sulfoximine can be reduced to the sulfide by carbene via the sulfoxide.[120]



The reduction of the sulfoximine with dimethyl diazomalonate (DDT) mainly gives the oxosulfonium ylide in the presence of a catalytic amount of Cu-salt. The sulfoxide is the intermediate and the oxosulfonium ylide is formed by the reaction between the sulfoxide and Cu-carbenoid(or carbene).[121] The reaction mechanism is shown in Scheme 8. The initial step is the nucleophilic attack of imino-nitrogen of the sulfoximine on carbene, followed by decomposition to the sulfoxide and the imine derivative. Therefore, this deimination is also a retention process.



Scheme 8.

3. Thiol

Thiols, such as glutathione and cysteamine are good biological reducing agents. The thiol has a low oxidative state of -2, and moreover the reduction by hydrogenation or decomposition in the presence of Ni or Al-Hg etc gives rise to the reductive cleavage of C-S bond to yield alkane or alkene. These procedures have been summarized in many good reviews[122] and already have been applied to organic syntheses and petrochemical industries. Thiols are quite acidic and also possess nucleophilicity. The bond dissociation energy and pKa constant are listed in Tables.

Table. The Bond Dissociation[123] Energies of S-H, O-H, C-S, and C-O(kcal/mol)

HS-H	89
CH_3S-H	89
HO-H	116
CH_3O-H	100
CH_3-SH	67
$C_6H_5CH_2$-SH	53
CH_3-OH	90
$C_6H_5CH_2$-OH	73

Table. The pKa Constant Data[123] of Thiol and Alcohol

H_2S	pK_1 7.24
	pK_2 14.92
n-C_4H_9SH	pKa 11.51
C_6H_5SH	pKa 7.47(8.3)
H_2O	pKa 14
n-C_4H_9OH	pKa 16
C_6H_5OH	pKa 9.95

As shown in these Tables, the bond dissociation energies of both S-H and C-S bonds are small as compared with those of both H-O and C-O bonds, while thiols have considerably low pKa values. The pKa values of selenols are even smaller and highly polarzable.[125] Since the thiol has a considerably large nucleophilicity, thiophilicity, it can function as a mild reducing agent. Both dithiophosphoric acids and

Table. pKa Constant for[124] Substituted Benzene-thiol at 25°C

X	X-⟨⟩-SH
p-OH	8.30
p-CH_3	8.03
p-CH_3O	7.99
H	7.76
p-Cl	6.96
p-NO_2	5.11
p-CH_3SO_2	5.57

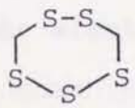
dithiocarboxylic acids have remarkably low pKa values because of the high stabilities of their conjugate beses.

Table. pKa Constants of Dithiophosphoric Acid, Dithiophosphinic Acids and Dithiocarboxylic Acids at 25°C [123]

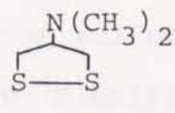
$(CH_3O)_2P(S)-SH$	1.55	$(C_2H_5)_2P(S)-SH$	1.71
$(C_6H_5O)_2P(S)-SH$	1.81	$(C_6H_5)_2P(S)-SH$	1.75
$CH_3C(S)-SH$	2.55	$CH_3C(O)-SH$	3.33
$H_2NC(S)-SH$	2.95	$C_6H_5C(O)-SH$	2.48

4. Disulfide

There are many kinds of disulfides or polysulfides in nature, for example as in the following.



Lenthionine



nereistoxine

$CH_2=CH-CH_2-S-S-CH_2-CH=CH_2$

allyin

The bond dissociation energy of S-S bond is considerable large as compared with that of the O-O bond because of 3d orbital resonance between the polysulfide linkage.

Table. The Bond Dissociation Energy of S-S bond[126] (kcal/mol)

HS-SH	66	$C_6H_5S-SCH_3$	65
CH_3S-SCH_3	74	C_6H_5S-SH	61
$C_6H_5S-SC_6H_5$	55		

The disulfide receives the nucleophilic attack on the sulfur atom as in the case of peroxide.

$$RS-SR + :Nu^- \longrightarrow RS^- + RSNu \qquad \text{----------(21)}$$

In many reductions of disulfide, the reactions proceed via the S_N2 pathway as shown in eq. 21. While, the reduction with electrode, flavine, and NADH may proceed via a single electron transfer pathway.

4-i $LiAlH_4$

The reduction of the disulfide with $LiAlH_4$ occurs readily to give the corresponding thiol and hydrogen gas in quantitative yields.[127]

$$2\ RSSR + LiAlH_4 \xrightarrow[Et_2O]{\Delta} 2\ H_2\uparrow + LiAl(SR)_4 \xrightarrow{H_2O} 4\ RSH \quad \text{--(22)}$$

100% quant.

The reaction markedly depends on the structure of the disulfide, since this reaction is a typical S_N2 reaction.

n-RSSR-n, ArSSAr, $ArCH_2SSCH_2Ar$ $>$ n-RSSR'-t $\gg$ t-R'SSR'-t

Diaryl disulfides can be reduced faster than dialkyl disulfides,[128] since the electron density of sulfur atom in diaryl disulfides is less than that of dialkyl disulfides because of the electron delocalization to aromatic ring while ArS^- ion is more stable than RS^- ion. The reactivities of disulfides with many kinds of aluminium hydrides are summarized in Table.

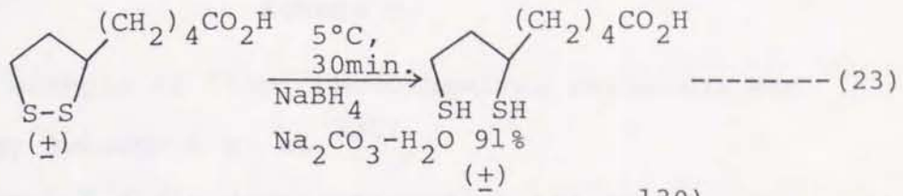
Table. Reaction of Disulfide with excess Aluminium Hydride Derivatives in THF at 0°C

	compound	Hydride Evol. Used	Reduction	Time(h)
AlH_3	n-BuSSBu-n	0.6	1.3	24
	PhSSPh	0.92	1.09	0.25
$LiAlH_4$	n-BuSSBu-n	0.98	1.01	1.0
	PhSSPh	1.02	1.0	0.5
$LiAlH(OCH_3)_3$	n-BuSSBu-n	1.02	0.98	0.5
	PhSSPh	1.05	1.16	0.5
$LiAlH(OBu\text{-}t)_3$	n-BuSSBu-n	0.13	0.04	24
	PhSSPh	1.03	0.96	6.0

As shown in Table, AlH_3, $LiAlH_4$, $LiAlH(OCH_3)_3$ can readily reduce disulfide to thiol, while the reaction with $LiAlH(OBu\text{-}t)_3$ take a longer time because of its steric hindrance. B_2H_6 can not reduce disulfide, but $NaBH_4$ can reduce only diaryl disulfide in which the aromatic ring is substituted by an electron-withdrawing group. As an exceptional example of the reduction

of dialkyl disulfides with $NaBH_4$, there is the reduction of 5-membered cyclic disulfides which are very easily reduced to the dithiols and then oxidized to the disulfides.[129)]

For example, optical active lipoic acid can be readily reduced to optical active dithioloctanoic acid(eq. 23).

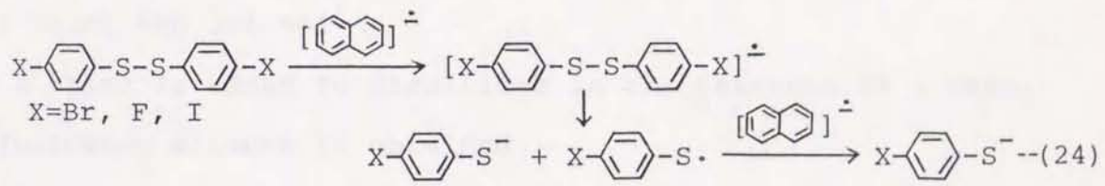


--------(23)

$NaBH_4$-$AlCl_3$ system can also reduce disulfides,[130)] but probably many kinds of active species, i.e. $Al(BH_4)_3$, BH_3, AlH_3 etc function as reducing agents.

4-ii e^-, hv, or Metal

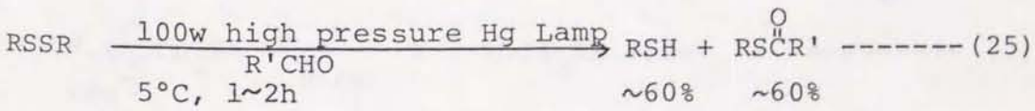
Only diaryl disulfides can be reduced to arenethiols in high yields by [naphthalene]$^{\cdot-}Na^+$ via SET process.[131)]



--(24)

A few examples of reduction of cystine, lipoic acid, glutathione disulfide with Na-Sn/HCl[132)] and Zn/HCl[133)] are also known.

As a photochemical reduction, the following example was reported by Tagagi et al.[134)]



-------(25)

This reaction requires aldehydes not ketones, and has a induction period. Therefore, a radical initiator such as AIBN accelerates this reaction. Both aromatic aldehyde and diaryl disulfide decrease the yield of products. Based on these results, the following reaction mechanism via radical

process, Scheme 9, may be proposed.

$$\text{initiator} \xrightarrow{\Delta} \text{In}\cdot$$
$$(\text{ or } \text{RCHO} \xrightarrow{h\nu} \text{R}\cdot + \cdot\text{CHO})$$
$$\text{In}\cdot(\text{or R}\cdot) + \text{RCHO} \longrightarrow \text{InH(or RH)} + \text{R}\dot{\text{C}}\text{O}$$
$$\text{In}\cdot(\text{or R}\cdot) + \text{R'SSR'} \longrightarrow \text{In-SR'(or RSR')} + \text{R'S}\cdot$$
$$\text{R}\dot{\text{C}}\text{O} + \text{R'SSR'} \longrightarrow \text{RCOSR'} + \text{R'S}\cdot$$
$$\text{R'S}\cdot + \text{R'CHO} \longrightarrow \text{R'SH} + \text{R}\dot{\text{C}}\text{O}$$

Scheme 9.

A similar example of other photochemical reduction was reported by Swanepoel et al.[135]

BNAH(1-benzyl-1,4-dihydronicotinamide) can also reduce only diaryl disulfides in the presence of a radical initiator or by photolysis.[136]

The reduction with Ph_3SnH is limited only to diaryl disulfides because of the facile reductive cleavage of C-S bond in the case of dialkyl disulfides.[137]

4-iii Thiol and Selenol

When a thiol is added to disulfides in the presence of a base, the following mixture is obtained.

$$\text{RSSR} + 2\ \text{R'SH} \rightleftharpoons \text{RSSR'} + \text{RSH} + \text{R'SH} \rightleftharpoons \text{R'SSR'} + 2\ \text{RSH} \quad \text{--(26)}$$

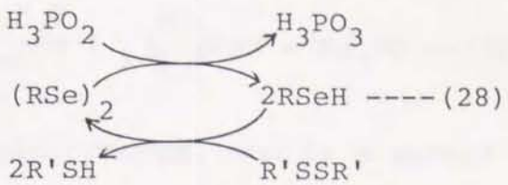
Meanwhile, NaSH or $Na_2S_2O_4$ can also reduce disulfides to thiols.[138] Though H_2Se is a deadly poison, it has a low pKa and a strong reducing ability as compared with H_2S.[139]

$$\text{PhCH}_2\text{S}\overset{\curvearrowright}{\underset{\text{HSe}^-}{\text{S}}}\text{CH}_2\text{Ph} \xrightarrow[\text{EtOH}]{} 2\ \text{PhCH}_2\text{SH} + \text{Se} \quad \text{----------(27)}$$

The active species is HSe^- or Se^{2-} not H_2Se. Since this reaction proceeds via S_N2 process as shown in eq. 27, t-BuSSBu-t cannot be reduced. The reduction of disulfide with hypophosphorus acid(H_3PO_2) in the presence of catalytic amount of diselenide(alkyl or aryl) is very convenient,[140] because

diselenide is not as poisonous as selenol(eq 28).

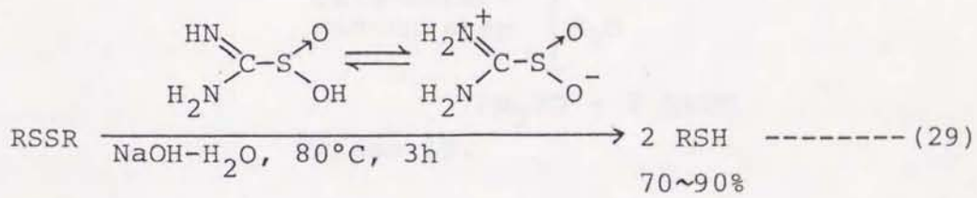
Though the reaction of disulfides with thiols gives a reaction mixture (eq. 26), the reaction of disulfides with the selenols gives only the mixture of thiols and the diselenides, because of the low pKa value of the selenols. Bunte salt can be also reduced by HSe^-.[141] The main product is the disulfide and the thiol when the molar ratio of $HSe^-/RSSO_3^-$ is ≦1 and ≧1.6 respectively.



----(28)

4-iv Formamidinesulfinic Acid

The reduction of disulfides with formamidinesulfinic acid is known.[142]



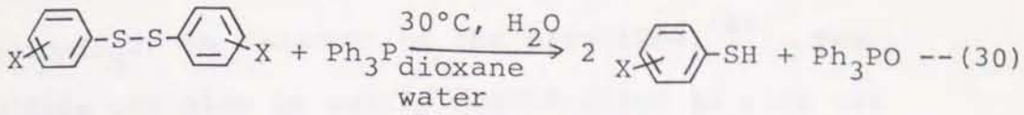
--------(29)

This reagent can also reduce sulfoxides or sulfilimines. Probably, the reaction may proceed via the nucleophilic attack of the sulfur atom of formamidinesulfinic acid on the sulfur atom of disulfides.

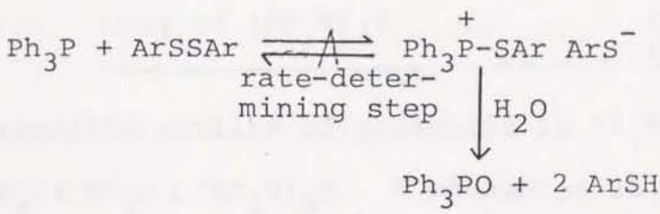
4-v Trivalent Phosphorus Compounds

The reduction of disulfide with Ph_3P[143] or Bu_3P[144] requires water while the molar ratio of disulfide/phosphine is usually one. Since Bu_3P is a stronger reducing agent than Ph_3P, it can reduce easily both aliphatic and aromatic disulfides, while the reduction of dialkyl disulfides with Ph_3P is slow. The mechanism of the reaction which was studied by Overman

et al is shown in Scheme 10.

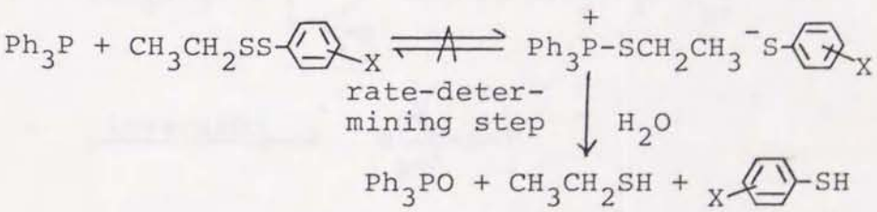


This reaction proceeds via an ionic process, and is a second order reaction, first order each with both disulfide and phosphine, respectively.[145] The increase of polarity of solvent accelerates the rate of this reaction. The mechanism involving the nucleophilic attack of Ph_3P on the S-S bond to afford the phosphonium intermediate has been suggested on the basis of the sensitivity of the reaction to the solvent ionizing power(the slope of the plot of k_{obsd} vs. Y is 0.89) and also to the electronic effect of substituent(ρ=2.94).



Scheme 10.

Meanwhile, in the reduction of alkyl aryl disulfide, RSSAr, with Ph_3P,[146] the intermediate is a $Ph_3\overset{+}{P}$-SR ArS^- ion which thiolate anion is more stable than in $Ph_3\overset{+}{P}$-SAr RS^-, as the substituent effect of aromatic ring(ρ=1.76) reveals.



Scheme 11.

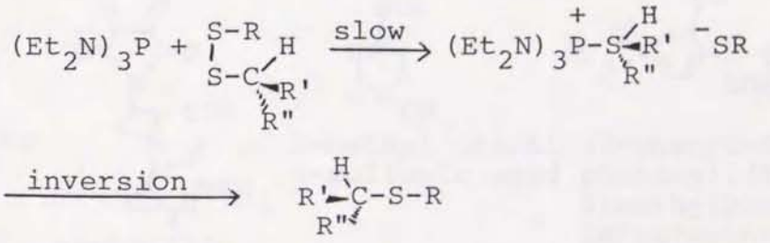
The electron-withdrawing group, X, accelerates the reactivity of dialkyl disulfide, $(XCH_2S)_2$, in the reduction of dialkyl disulfide with Ph_3P.[147] Therefore, the plot of log k vs. pKa of XCH_2SH gives a good linearity. The disulfide can be

desulfurized by phosphine under an usually drastic condition in the absence of water, and the reaction leads to net inversion(S_N2) on α-carbon of the disulfide.[148] The trisulfide can also be easily desulfurized to give the corresponding disulfide by phosphine. Usually, the desulfurized sulfur is the middle sulfur in the trisulfide, but it can change as the phosphine used is changed. The desulfurization study with ^{35}S labeled dibenzyl trisulfide has been reported as shown below(eq. 31).[149]

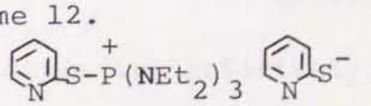
$$R_3P + PhCH_2S\overset{*}{S}-S-CH_2Ph \longrightarrow R_3P\overset{(*)}{S} + PhCH_2S-\overset{(*)}{S}CH_2Ph \quad --(31)$$

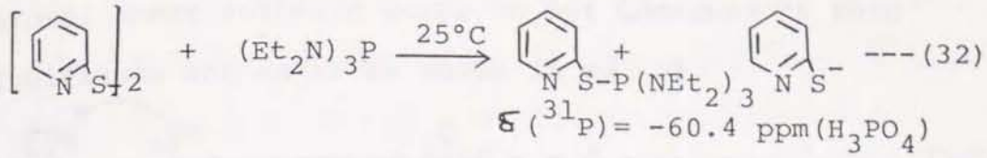
desulfurization	
case of Ph_3P	central sulfur ~90%
case of Bu_3P	central sulfur ~75%
	the sulfur bonded to carbon ~25%
case of $(Et_2N)_3P$	the sulfur bonded to carbon ~96%

The nucleophilic ability of phosphine is in the following order, $Ph_3P < Bu_3P < (Et_2N)_3P$. A phosphine which has a stronger nucleophilicity can desulfurize more readily the sulfur bonded to carbon of the trisulfide. Actually, $(Et_2N)_3P$ is a very strong nucleophile, and can desulfurize even the disulfide easily to give sulfide,[150] via inversion process at α-carbon.[151]



Scheme 12.

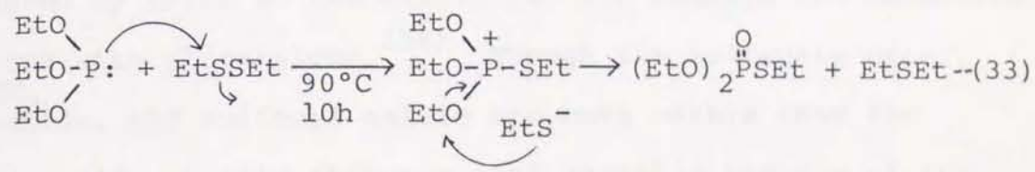
Phosphonium intermediate ion,  can be detected by ^{31}P-NMR in the reaction of 2,2'-dipyridyl disulfide and $P(NEt_2)_3$.



$\delta(^{31}P) = -60.4$ ppm (H_3PO_4)

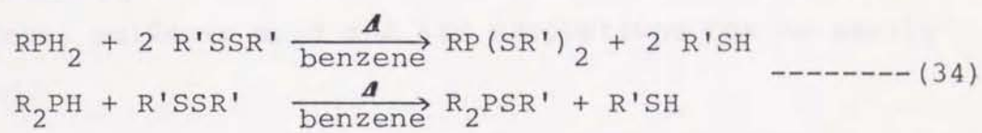
---(32)

When phosphite is used instead of phosphine, the Arbuzov reaction takes place.[152] The driving force of this reaction is the formation of P=O bond which has dissociation energy of 105 kcal/mol.



---(33)

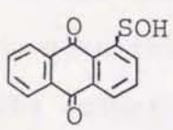
Finally, primary, and secondary phosphines can also reduce the disulfide.[153]



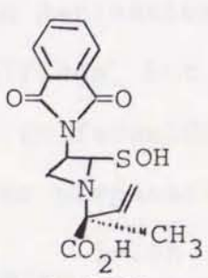
--------(34)

5 Sulfenic Acid and its Derivatives

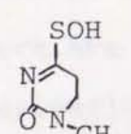
It is difficult to isolate the sulfenic acid, because the sulfenic acid is unstable, and readily decompose to the thiolsulfinate and water. However a few following stable sulfenic acids are known.[154]



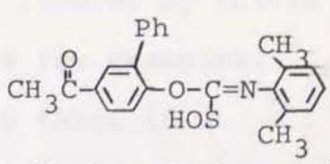
1-anthraquinone sulfenic acid



penicillin sulfenic acid



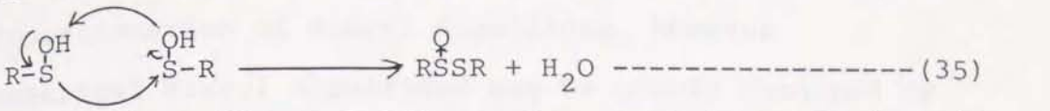
1-methyl uracil 4-sulfenic acid



(2-phenyl-4-acetyl-phenoxy)[(2,6-dimethylphenyl) imine]methane-sulfenic acid

The reason why these sulfenic acids are relatively stable is that they all have electron-withdrawing groups on the sulfur atom and OH group can form intramolecular hydrogen bonding.

Therefore, these sulfenic acids do not condense to form thiolsulfinate and water as shown in eq. 35.



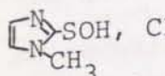
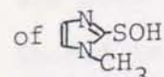
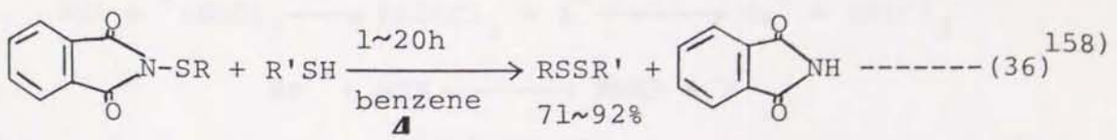
Other sulfenic acids, t-BuSOH, various protein sulfenic acids,  , CH_3SOH (pyrolysis of $CH_3\overset{O}{\overset{\uparrow}{S}}SCH_3$),[155] can be also detected at low temperatures or even trapped. The sulfenic acid can be reduced by thiol to the disulfide, for example the reduction of  with glutathione.[156] Though the sulfenate ester, sulfenamide, and sulfenyl halide are more stable than the sulfenic acid, usually they are also unstable because of the low bond dissociation energies of S-X bond in RS-X.[157] Therefore, sulfenic acid and its derivatives can be easily reduced.

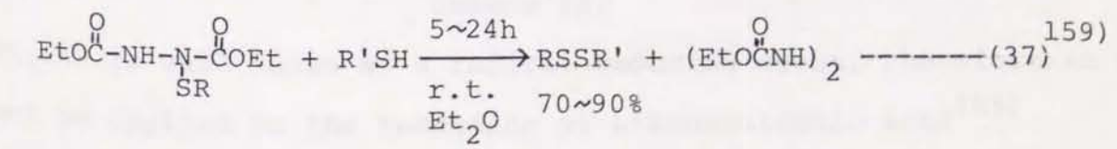
Table. The Bond Dissociation Energy of S-X in RSX(kcal/mol)

CH_3S-Cl	70
PhS-Cl	31
CH_3S-NO	25
PhS-N=NPh	29

5-i Thiols

The sulfenic acid derivatives can be easily reduced by thiols to give the disulfides, but there are only a few examples. The reduction of sulfenamide derivative with thiol is a good procedure for preparation of unsymmetrical disulfides.





The preparation of unsymmetrical diaryl disulfides by the former reaction(eq. 36) is difficult because of concomitant disproportionation of diaryl disulfides, however unsymmetrical diaryl disulfides may be nicely obtained by the latter method(eq. 37). The sulfenyl thiocyanate can also be reduced by thiols.[160] Though it has two kinds of sulfurs, thiols attack the sulfur bonded to α-carbon because thiols are soft nucleophiles, and can attack the sulfur bonded to α-carbon; this sulfur atom is soft as compared with the sulfur bonded to cyano group, and SCN^- is a good leaving group. The sulfenic acid, RSOH, also receive the nucleophilic attack of $:Nu^-$ on the sulfur atom to form RSNu.

5-ii Electrode Reduction

Sulfenic acid derivatives, RSX, can be reduced by electrode reduction to the corresponding thiol and HX.[161, 162]

5-iii R_3SiH, Cl_3SiH, and Ph_3SnH

The reduction with Cl_3SiH/Pr_3N or Et_3SiH/CF_3CO_2H system is also known.[163, 164] From the result that this former reaction requires the amine, $Cl_3Si:^-$ is probably an active species.

$$2\ PhSCl \xrightarrow[20°C,\ 4h]{Pr_3N/Cl_3SiH} \underset{53\%}{PhSSPh}$$

$$2\ PhSOCH_3 \xrightarrow["]{"} \underset{88\%}{PhSSPh}$$

The reaction mechanism is shown in Scheme 13.

$$RSX + {}^-:SiCl_3 \longrightarrow RSSiCl_3 + X^- \longrightarrow RS^- + XSiCl_3$$

$$RS^- + RSX \longrightarrow RSSR + X^-$$

Scheme 13.

Ph_3SnH is well known as a radical reducing agent, therefore it can not be applied to the reduction of alkanesulfenic acid[165] derivatives because of the occurrence of C-S bond reductive

cleavage.

$$PhSCl \xrightarrow{Ph_3SnH} \underset{78\%}{Ph_3SnCl} + H_2 + \underset{60\%}{Ph_3SnSPh} \quad \text{---------(38)}$$

Once Ph_3SnSPh is formed, it gives easily PhSH by alkaline-hydrolysis. $NaBH_4$, $LiAlH_4$, phosphine and Me_3SiI[166] can also readily reduce the sulfenic acid derivatives to the thiols or disulfides.

6. Sulfinic Acid and its Derivatives

The sulfinic acid is a considerably strong organic acid and its pKa value is very small as compared to that of the carboxylic acid. The pKa values of aromatic and aliphatic sulfinic acids are about 1.2 and 2.2 respectively.[167] The sulfinic acid is thermodynamically not so stable, and easily disproportionates to give the thiolsulfonate, water and sulfonic acid.[168] The addition of acid species

$$3\ RSO_2H \longrightarrow RSO_2SR + RSO_3H + H_2O \quad \text{----------(39)}$$

accelerates this disproportionation. The detailed study on the disproportionation mechanism has been carried out by Kice[169] as shown in Scheme 14.

$$2\ ArSO_2H \rightleftharpoons Ar\overset{O}{\overset{\uparrow}{S}}-\overset{O}{\overset{\uparrow}{S}}Ar + H_2O$$

$$Ar\overset{O}{\overset{\uparrow}{S}}-\overset{O}{\overset{\downarrow}{S}}Ar \xrightarrow[\text{slow}]{} ArS-O-\overset{O}{\overset{\downarrow}{S}}Ar \xrightarrow[\text{fast}]{ArSO_2H} ArS-\overset{O}{\overset{\downarrow}{S}}Ar + ArSO_3H$$

Scheme 14.

Addition of a strong acid increases the concentration of the sulfinylsulfone intermediate.

6-i Trivalent Phosphorus Compounds

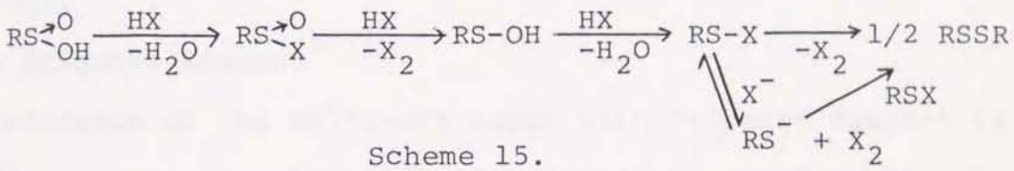
Arenesulfinic acids but not alkanesulfinic acids can be reduced by ethyl hypophosphite[170] to the corresponding disulfides.

$$ArSO_2Na \xrightarrow[DMSO,\ r.t.\ over\ night]{EtO\overset{O}{\overset{\|}{P}}H_2} 1/2\ ArSSAr \quad (50\sim60\%) \qquad \text{----------(40)}$$

Though it has been postulated that the sulfinylsulfone, the thiolsulfonate, and the thiolsulfinate have been considered to be the intermediates, there is no evidence to suppert it.

6-ii HX[171], $(CH_3)_3SiI$[172]

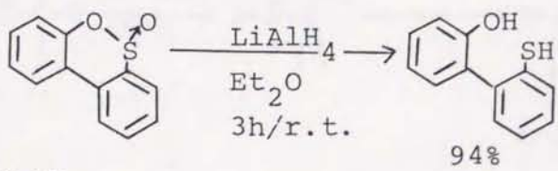
Many sulfinic acids can be easily reduced by HBr or HI via the reaction pathways as shown in Scheme 15.



Scheme 15.

6-iii $LiAlH_4$

Though the sulfinic acid can be reduced by $LiAlH_4$ evolving hydrogen gas, the initial product is the sulfinate. This reaction requires heating. Sulfinate esters can be readily reduced to the thiols.[173]



94%

6-iv NH_2NH_2

Hydrazine can also reduce the sulfinate ester or the sulfinyl halide but not the sulfinic acid to the disulfide evolving hydrogen gas.[174]

$$4\ RSO_2R' + 3\ N_2H_4.H_2O \xrightarrow{r.t.} 2\ RSSR + 4\ R'OH + 3\ N_2 \quad \text{--(42)}$$

$$4\ RSOCl + 7\ N_2H_4 \xrightarrow{r.t.} 2\ RSSR + 3\ N_2 + 4\ N_2H_5Cl + 4\ H_2 \text{--(42)}$$

The reaction probably proceeds via the formation of the sulfinylhydrazine, and the sulfenic acid.

6-v $HSiCl_3/Pr_3N$[175)]

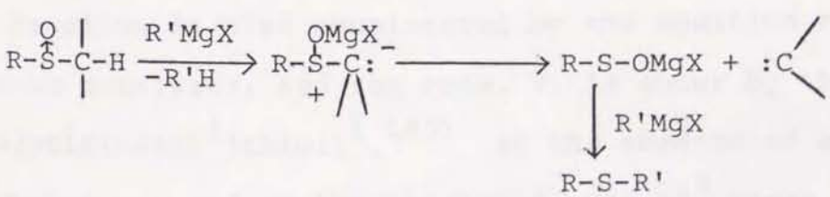
Though the detail mechanism is not known, the sulfinate ester or the sulfinyl halide can be readily reduced by $HSiCl_3$ in the presence of amine. The reaction probably proceeds by the nucleophilic substitution of $Cl_3Si:^-$ on the sulfur of the sulfinic acid derivative.

6-vi Na[176)]

Metallic sodium can reduce sulfinic acids to thiols, however even arenesulfinic acids give rise to the C-S reductive cleavage.

6-vii Grignard Reagent[177)]

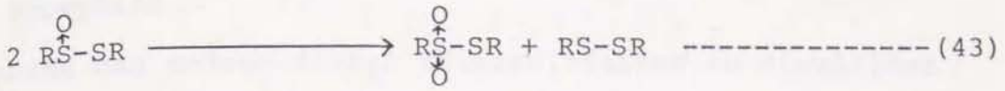
The reduction of the sulfinate ester with Grignard reagent is a method to prepare the sulfoxide, in particular for the preparation of optical active sulfoxides. But as the amount of Grignard reagent increases in this reaction, a further reaction occurs to give the sulfide. Probably the reaction proceeds via the following pathway.



Scheme 16.

7. Thiolsulfinate

Thiolsulfinates are relatively unstable and decompose to the following products.[178)]



This disproportionation is accelerated by acids or nucleophiles and its mechanism has been studied by Kice in detail.[179] In nature, however there are many thiolsulfinates.[180, 181, 182]

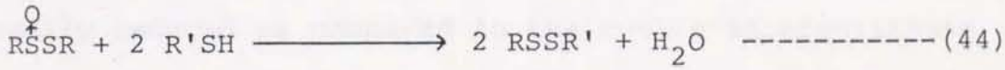
Table.

	$CH_3\overset{O}{\overset{\uparrow}{S}}SCH_3$	$Ph\overset{O}{\overset{\uparrow}{S}}SPh$	$[Ph\overset{OO}{\overset{\uparrow\uparrow}{S}}SPh]$ (kcal/mol)[183]
S-S	46	(36)	<16
S-O	-	83	83

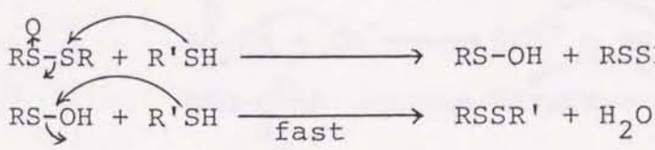
The bond dissociation energies of S-SO bonds are listed in Table.

7-i Thiol

Thiolsulfinates can be reduced to disulfides by treatment with thiols.



The following reaction Scheme has been suggested.[184] The intermediate, RSOH, has not been detected.



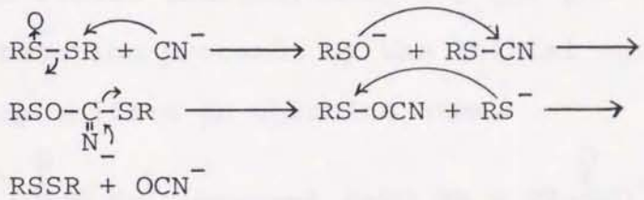
Scheme 17.

This reaction is also accelerated by the addition of acids or bases as catalysts, and the rate, V, is shown by the $V=k[\text{thiolsulfinate}]^1[\text{thiol}]^1$.[185] In the absence of any catalyst, thiophenol can reduce the thiolsulfinate 10^3 times faster than n-butanethiol.

Cystine-S-oxide which is a sulfur containing amino-acid is also reduced.[186] Meanwhile, the reduction with H_2S and HSO_3^- gives the corresponding trisulfide and disulfide respectively.[187]

7-ii Phosphine[188)]

Phosphine can reduce diaryl thiolsulfinates to disulfides exothermically, while the reaction of dialkyl thiolsulfinates is not so fast. The reason is that the electron density on the sulfur atoms of the diaryl thiolsulfinate is less than that of the dialkyl thiolsulfinate. The initial step is the nucleophilic attack of phosphine on the sulfenyl sulfur, because of the good leaving ability of the sulfenate ion. Therefore, Ph_3As, which is a family compound of Ph_3P and a very weak nucleophile, reduces even the diaryl thiolsulfinate slowly, while the dialkyl thiolsulfinate cannot be reduced. As an interesting example, the reduction of the thiolsulfinate with CN^- was reported.[189)] The open-chained thiolsulfinate is readily reduced as compared to the cyclic thiolsulfinate. The reaction proceeds via the initial nucleophilic attack of CN^- on the sulfenyl sulfur as shown in Scheme 18.



Scheme 18.

8. Sulfonic Acid Derivatives

Sulfonyl halides, sulfonate esters, sulfonamides, sulfonic anhydrides, and thiolsulfonates are sulfonic acid derivatives. Among these derivatives, there are many examples of the reductions of sulfonyl halides and thiolsulfonates because of their comparatively labile character.

8-i Na_2SO_3

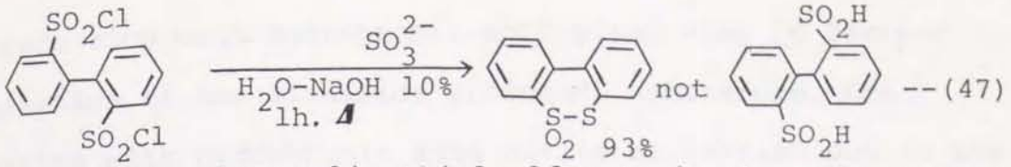
Sodium sulfite can easily reduce sulfonyl halides, sulfonic anhydrides to give the corresponding sulfinic acids. Particularly, the reduction of both arene- and alkanesulfonyl chlorides with sodium sulfite is a good method to prepare the corresponding sulfinic acids in good yields.[190]

$$ArSO_2X \xrightarrow[H_2O,\ 70°C,\ 5h]{Na_2SO_3} ArSO_2Na \quad (X=F,\ Cl;\ >80\%) \qquad \text{-----(45)}$$

Though both sulfonyl bromides and iodides can also be reduced, they are not so stable thermodynamically and photochemically. Probably this reaction proceeds by the initial nucleophilic attack of sodium sulfite on chlorine atom.

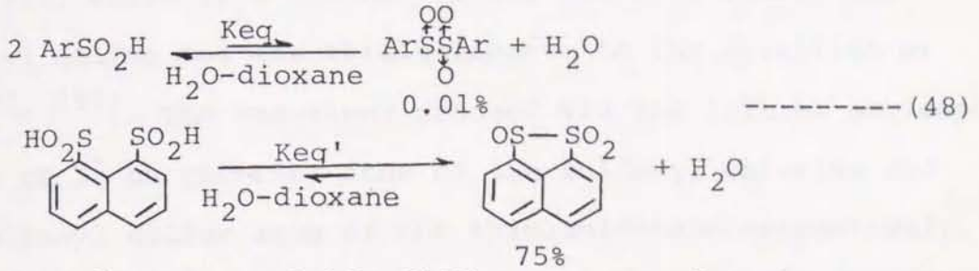
$$ArS(=O)_2\text{-}Cl + :S(=O)(=O)\text{-}O^-Na^+ \longrightarrow ArSO_2Na + Cl\text{-}S(=O)_2\text{-}O^-Na^+ \xrightarrow{H_2O} HCl + NaHSO_4 \qquad \text{-----(46)}$$

The reduction of the sulfonic anhydride with sodium sulfite gives an equimolar mixture of the sulfinic acid and the sulfonic acid.[191] As an interesting example,[192] the cyclic thiolsulfonate in the reduction of bis(sulfonyl chloride) compound with sodium sulfite is obtained as shown below.



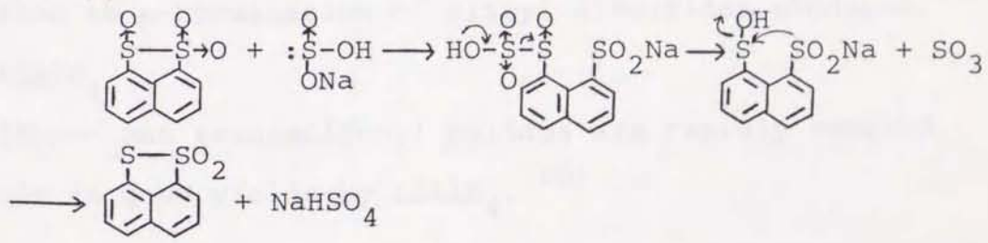
--(47)

The reason why the cyclic thiolsulfonate is the main product is the following. Both the sulfinic acid and the sulfinylsulfone are in an equilibrium(eq. 48), but both equilibrium constants,



---------(48)

Keq and Keq' are remarkably different. Namely, the concentrations of sulfinylsulfone in the former is 0.01% while that of the latter is 75% respectively. After the reduction of the sulfonyl chloride with sodium sulfite, the reaction mixture is usually acidified by HCl- or H_2SO_4-water solution. In this step, the cyclic sulfinylsulfone derived from bis(sulfinic acid) is formed, and reduced by excess sodium sulfite to the cyclic thiolsulfonate through the process shown in Scheme 19.



Scheme 19.

8-ii HX

Various kinds of sulfonyl halides can be reduced exothermically by commercial 55~57% hydriodic acid to disulfides.[193] A mixture of red phosphorus and iodine in acetic acid can also reduce the sulfonyl chloride to the thiol.[194] Meanwhile,

the reduction with hydrobromic acid gives rise to further bromination of the disulfide produced. Therefore, the reduction with hydrobromic acid has to be carried out in the presence of trapping agent of bromine produced such as aniline.[195]

$(CH_3)_3SiI$, which is a synthon of HI, can also reduce the sulfonyl halide and the thiolsulfonate to the disulfide at r.t.[196, 197] The reactions proceed via the initial nucleophilic attack of I^- on chlorine atom of the sulfonyl chloride and the sulfenyl sulfur atom of the thiolsulfonate respectively. BI_3 and BBr_3 are Lewis acids and hence can reduce the sulfonyl halide in the presence of KI to the corresponding disulfide.[198] The reactivities of both the reagents and the substartes are

$$BI_3,\ BBr_3/KI > BCl_3/KI > BF_3/KI, \text{ and } ArSO_2Cl > ArSO_2F$$

respectively. This reactivity of substrate suggests that nucleophile I^- attacks the halogen atom at first. BI_3 can also reduce alkyl sulfonate esters to disulfides. The reduction of arenesulfonic anhydrides with hydrogen bromide gives rise to p-bromination of diaryl disulfides produced.[199]

8-iii $LiAlH_4$

Both alkane- and arenesulfonyl halides are rapidly reduced to thiols in good yields by $LiAlH_4$.[200]

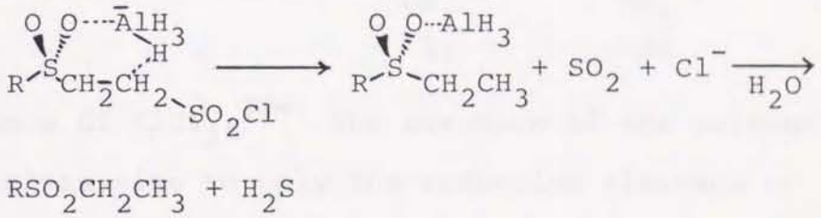
$$2\ \underset{(Ar)}{RSO_2Cl} + 3\ LiAlH_4 \xrightarrow[\text{ether}]{} LiAlCl_2(SR)_2 + 6\ H_2 + 2\ LiAlO_2 \quad \cdots(49)$$

Evidence to support that the sulfinic acid(sulfinate) is one of the intermediates is the following. When either the reaction was carried out at low temperature, or the molar-ratio of $LiAlH_4/RSO_2Cl$ decreased, the sulfinate is obtained in 80~90% yield. Therefore, the main reduction product depends on the

reaction condition. Whereas reduction of the sulfonyl chloride which has a sulfonyl group in β-position gives rise to an unusual reaction.[201]

$$\underset{(Ar)}{R\text{-}SO_2\text{-}CH_2CH_2\text{-}SO_2Cl} \xrightarrow[\substack{1h,\\ LiAlH_4}]{THF} \underset{(Ar)}{R\text{-}SO_2\text{-}CH_2CH_3}\ _{80\sim90\%} \quad \text{----------(50)}$$

$RSO_2CH_2CH_2SH$ or $RSO_2CH{=}CH_2$ is not an intermediate. The reaction proceeds via direct nucleophilic attack of hydride on α-carbon at the 6-membered cyclic transition state as shown in Scheme 20.



$$RSO_2CH_2CH_3 + H_2S$$

Scheme 20.

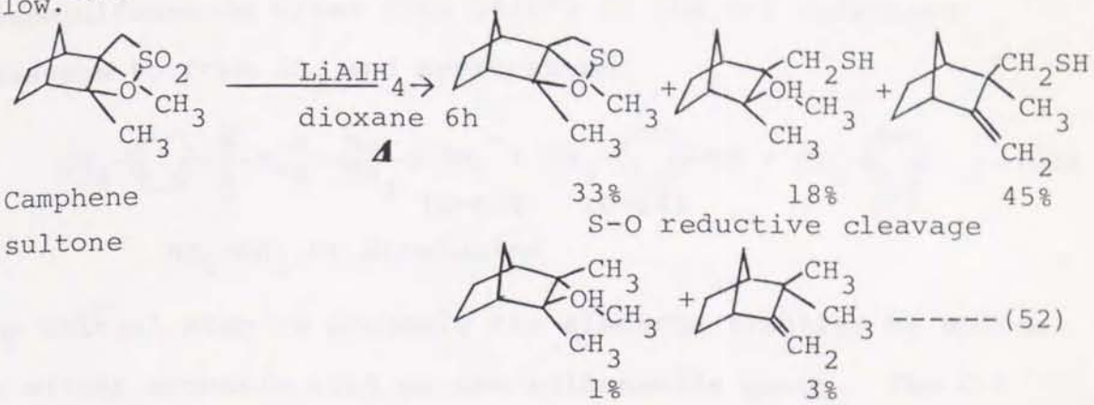
The sulfonic anhydride can also be reduced by $LiAlH_4$ via formation of the sulfinate.[202] Both non-N-substituted and mono-N-substituted sulfonamides cannot be reduced by $LiAlH_4$ because proton abstraction by hydride gives very inert sulfonamide N-lithium salts. While, N, N-disubstituted sulfonamides can be reduced under drastic conditions.[202, 203]

$$PhSO_2\text{-}N\begin{matrix}Et\\Et\end{matrix} \xrightarrow[\substack{THF,\\ 7\ days}]{LiAlH_4} \underset{57\%}{PhSO_2Li} + \underset{10\%}{PhSH} + HNEt_2 \quad \text{----(51)}$$

Therefore, sulfonamide is the most inert compound among sulfonic acid derivatives.

The reaction of alkyl sulfonate ester with $LiAlH_4$ gives rise to the O-C reductive cleavage by hydride attack to form hydrocarbon and lithium sulfonate,[204] due to the high leaving ability of the sulfonate group. Meanwhile, in the reaction

of the 5-membered cyclic sultone, which is a comparative strained compound, with $LiAlH_4$, reductive cleavage of both the S-O and O-C bonds may occur to give many products as shown below.[205]

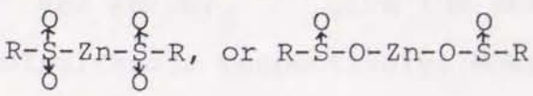


------(52)

In the presence of $AlCl_3$,[206] the reaction of the sultone with $LiAlH_4$ gives rise to only the reductive cleavage of C-S bond.

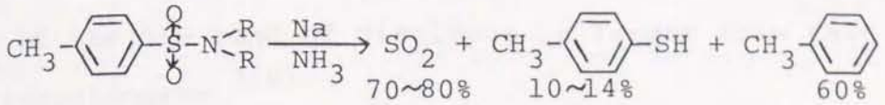
8-iv Metal

A $Zn/HCl(H_2SO_4)$ system can reduce the sulfonyl halide to the thiol. The sulfinic acid is one of the intermediates in this reduction because it can be isolated.[207, 210] A $SnCl_2/HCl$,[208] or Sn/HCl[209] system can also reduce the sulfonyl halide to the thiol in a good yield. In the reduction of ^{18}O-labeled arenesulfonyl chloride, $ArS(^{18}O)_2Cl$, with Zn/NaOH,[211] Oae et al isolated $[ArS(^{18}O)_2]_2Zn$ which was stable in water and retained ^{18}O-content completely. The following structures have been postulated. The reduction of the sulfonyl halide, RSO_2Cl, with Fe also gives the similar intermediate, $(RSO_2)_2Fe$.[212]



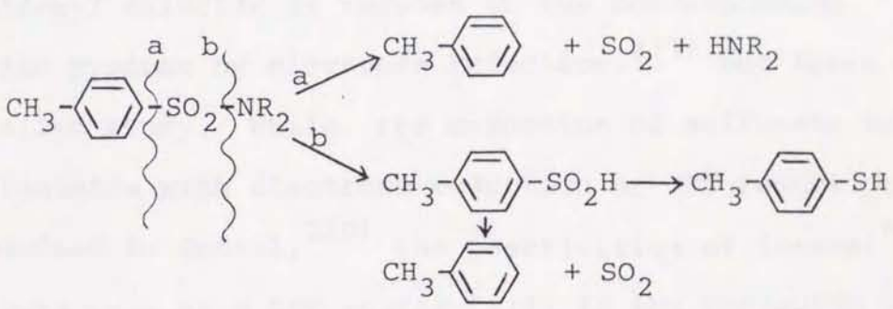
Sodium, Na, can reduce the cyclic thiolsulfonate to the disodium salt of mercaptosulfinic acid in liquid ammonia.[213]

Therefore, the reaction of thiolsulfonate with Na is considered to give a mixture of sodium thiolate and sodium sulfinate. In the reaction of the sulfonamide with Na,[214] even arenesulfonamide gives rise mainly to the C-S reductive cleavage to form SO_2 and hydrocarbon.



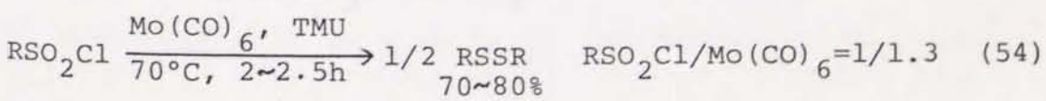
NR_2=NH_2 or DL-alamine

The initial step is probably the electron transfer by sodium to either aromatic ring or the sulfonamide group. The C-S reductive cleavage occurs in the former case, and the S-N reductive cleavage occurs in the latter case as the side-reaction as shown below.



Scheme 21.

The reactions of various sulfonamides with alkaline metal, Li, Na, and K also give the mixtures of hydrocarbon, SO_2, and amine,[215] whereas the reductive cleavage of the O-S bond occurs mainly in sulfonate esters,[215] but there is no detail study on it. The reduction of the sulfonyl chloride with $Mo(CO)_6$,[216] and $Fe(CO)_5$[217] give the corresponding disulfide and the thiolsulfonate respectively, however the mechanism is not known at all.

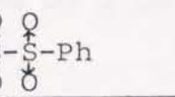
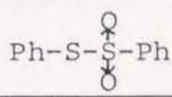


$$RSO_2Cl \xrightarrow[60\sim65°C,\ 12\sim15\ min]{Fe(CO)_5,\ TMU} 1/2\ RSO_2SR \quad (40\sim70\%) \qquad ----(55)$$

TMU=tetramethylurea $RSO_2Cl/Fe(CO)_5$=1/1.2

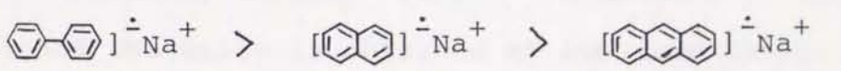
In this latter reaction, Alper et al proposed that the disulfone produced via the further coupling of sulfut-iron complex is the intermediate, but it is doubtful because the dissociation energy of the S-O bond of disulfone is larger than that of the thiolsulfonate.[218]

Table. Bond Dissociation Energy(kcal/mol)

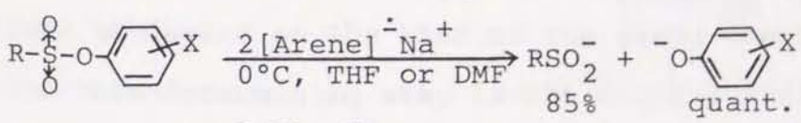
		
S-O	122	115
S-S	41	-

8-v Electrode Reduction or SET

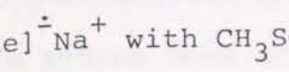
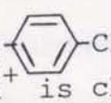
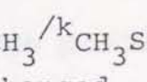
The sulfonyl chloride is reduced to the corresponding reduction product by electrode reduction,[219] but there is no detailed study. While, the reduction of sulfonate ester or sulfonamide with electrode reduction or SET reduction has been studied in detail,[220] the reactivities of $[Arene]^{\cdot-}Na^+$ which were used as a SET source falls in the following order.

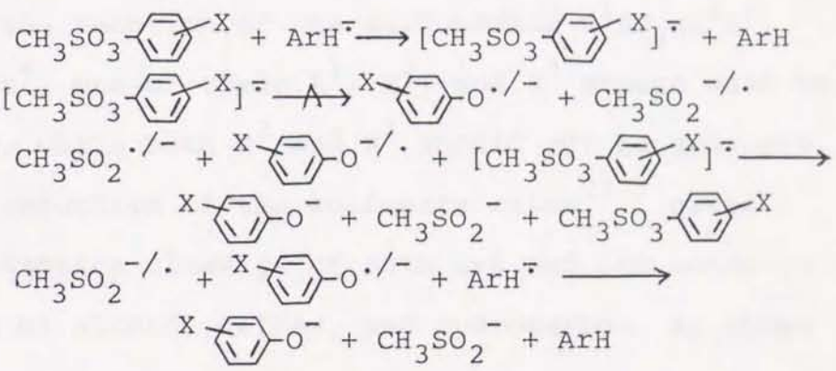


Treatment of aryl alkanesulfonates with any of the widely used anion radical, $[Arene]^{\cdot-}Na^+$, results in the rapid disappearance of the anion radical and formations of the aryloxides and the alkanesulfinate ions are quantitative.



R=Et, Me
X=H, CH_3, Cl, CH_3O

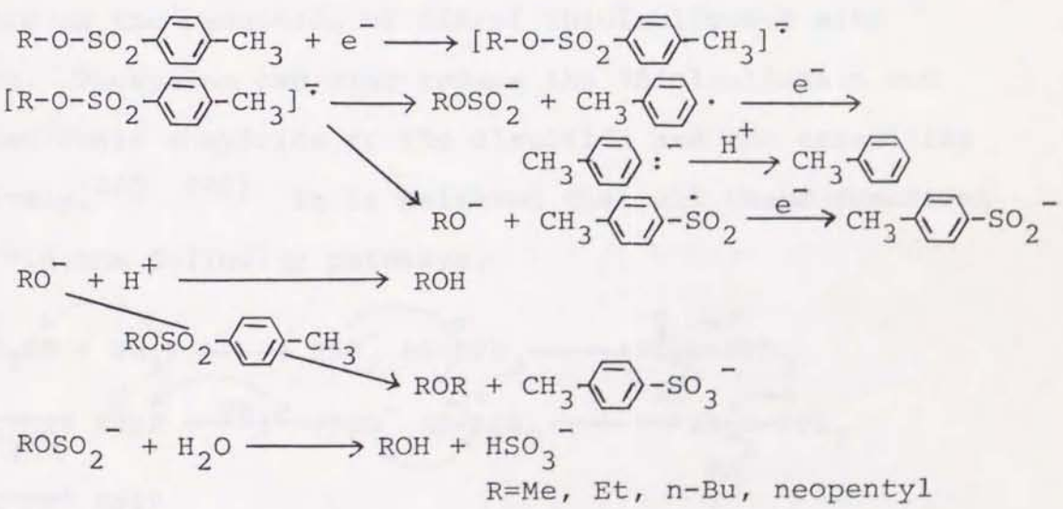
Rates of disappearance were found to be clearly first order each in both the anion radical and the sulfonate ester and a large substituent effect(ρ=6.0) was observed in the reaction of [Arene]$^{\cdot-}$Na^{+} with  . Moreover, the rate ratio of $k_{CH_3SO_3}$  $CH_3/k_{CH_3SO_3}$  is constant even when the [Arene]$^{\cdot-}$Na^{+} is changed. Therefore, the initial SET step is not rate-determining step. The mechanism is considered to involve the initial rapid electron transfer from the donor to the sulfonate ester, followed by a considerably slower cleavage as shown in Scheme 22.



Scheme 22.

In the cleavage of the sulfonamide of secondary amine with arene anion radical, [Arene]$^{\cdot-}$ Na^{+},[221] a mixture of the sulfinate and the amide is obtained at low temperature, however the cleavage of both C-S and S-N bonds occurs at room temperature. Upon competitive reactions, the rate, V, was found to be expressed by the equation of V=k[(Arene)$^{\cdot-}$Na^{+}] [sulfonamide] while the rate ratio of $k_{PhSO_2N^{Et}_{Ph}}/k_{p\text{-}TolSO_2N^{Et}_{Ph}}$ was found to depend on the kind of the arene compound. Thus the rate-determining step is the initial electron transfer from the arenide ion to the sulfonamide. At room temperature, once the arenesulfinate is formed, the subsequent much slower

reduction converts it to the arene hydrocarbon and a mixture of the thiosulfate, sulfite, and sulfide salts. The reaction of the non-N-substituted sulfonamide, i.e. RSO_2NH_2, $ArSO_2NH_2$ with this system does not occur, while the yield of the reductive cleavage product in the reaction of mono-N-substituted sulfonamide, i.e. RSO_2NHAr, $ArSO_2NHAr'$, is low because of facile proton abstraction of their sulfonamides by amide ion produced to form the inert salts, RSO_2NAr^-, $ArSO_2NAr'^-$. In general, RSO_2NH_2, RSO_2NHR', and $RSO_2NR'R''$(R, R', R"=alkyl group) does not give rise to the reductive cleavage reaction. Therefore, in the reaction of the sulfonamide $R^1SO_2NR^2R^3$, with $[Arene]^{\cdot-}Na^+$, one of these R^1, R^2, and R^3 groups must be aromatic group, while both R^2 and R^3 should not be hydrogen. The electrode reduction of the sulfonate ester[222] gives rise to the reductice cleavage of both C-S and S-O bonds to form a mixture of alcohol, ether, and hydrocarbon, as shown in the following pathway.



Scheme 23.

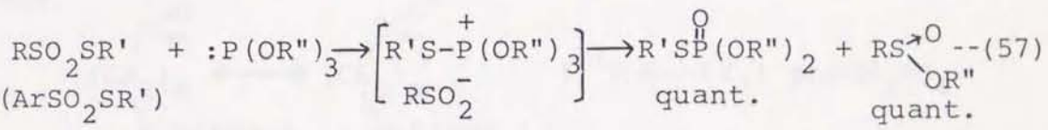
p-Toluenesulfinate can also be detected by UV and the amount of the ether produced(S_N2 process) decreases in the following order; $CH_3- > CH_3CH_2- > CH_3(CH_2)_3- \gg (CH_3)_3CCH_2-$

The electrode reduction of the sulfonamide gives a mixture of the amine and the sulfinate[223] in a good yield.

The initial electron transfer is the rate-determining step. Non-, and mono-N-substituted sulfonamides consume only one electron to give a mixture of the amine, the sulfinate, and sodium sulfonamide, $ArSO_2NR^-Na^+$, in 50% yields respectively due to proton abstraction of $ArSO_2NHR$ by amide ion produced

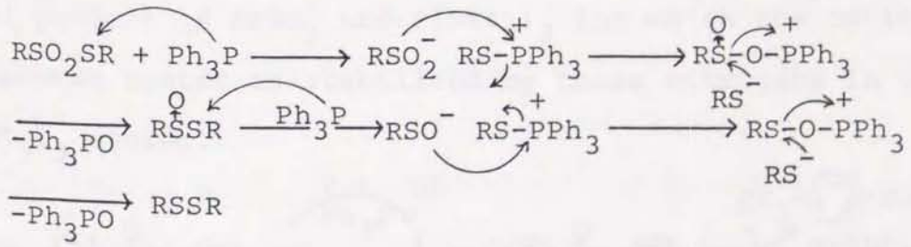
8-vi Three Coordinated Phosphorus Compounds

The reaction of the thiolsulfonate with phosphite[224] gives rise to the Arbuzov reaction similar to the reaction of disulfide and phosphite.



RSO_2SR' ($ArSO_2SR'$) + $:P(OR")_3$ → $[R'S-\overset{+}{P}(OR")_3\ RSO_2^-]$ → $R'S\overset{O}{\overset{\|}{P}}(OR")_2$ (quant.) + $RS\overset{O}{\diagdown}_{OR"}$ (quant.) --(57)

The corresponding disulfide can be obtained in a moderate yield only in the reduction of diaryl thiolsulfonate with phosphite. Phosphine can also reduce the thiolsulfonate and the thiosulfonic anhydride to the disulfide and the trisulfide respectively.[225, 226] It is believed that all these reactions proceed via the following pathways.



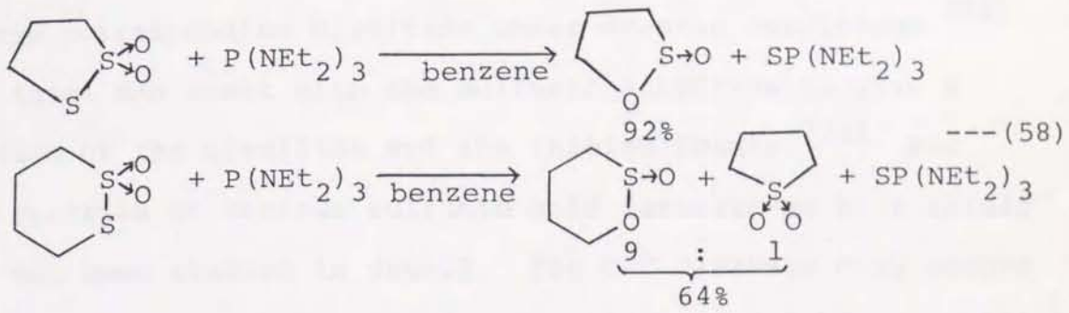
$RSO_2SR + Ph_3P \longrightarrow RSO_2^- \ RS\text{-}\overset{+}{P}Ph_3 \longrightarrow RS\overset{O}{\overset{\|}{S}}\text{-}O\text{-}\overset{+}{P}Ph_3$

$\xrightarrow{-Ph_3PO} RS\overset{O}{\overset{\|}{S}}SR \xrightarrow{Ph_3P} RSO^- \ RS\text{-}\overset{+}{P}Ph_3 \longrightarrow RS\overset{RS^-}{\underset{}{S}}\text{-}O\text{-}\overset{+}{P}Ph_3$

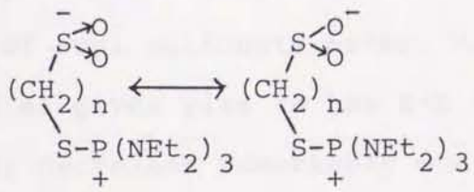
$\xrightarrow{-Ph_3PO} RSSR$

Scheme 24.

phosphorus atom attacks the sulfenyl sulfur. The reaction of thiolsulfonate with tris(diethylamino)phosphine which is one of the strongest nucleophiles among the phosphine derivatives has been studied by Harpp et al.[227] Usually, the product is a mixture of the sulfone and the sulfinate ester. In the case of the cyclic thiolsulfonate, the formation of the sulfone depends on the size of ring.



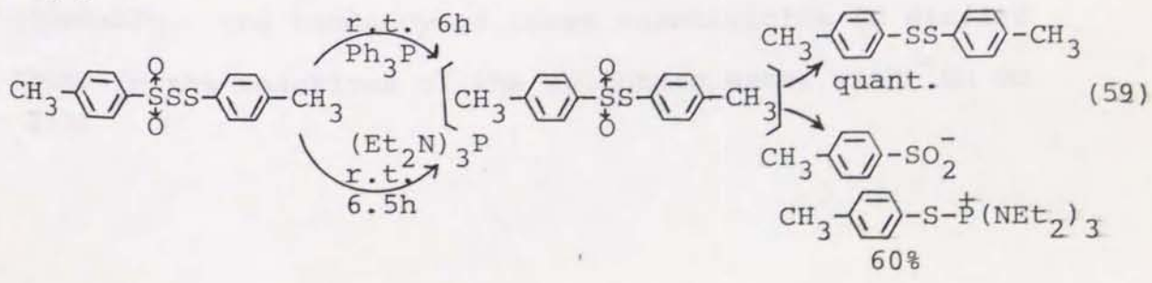
The intermediate, the phosphonium salt can be detected by ^{31}P-NMR.



(^{31}P) δ=-62.1 ppm(H_3PO_4)

The formation of sulfone increases remarkably in the reaction of open-chained thiolsulfonate.[228]

The difference of Ph_3P and $P(NEt_2)_3$ is remarkable in the reaction with $ArSO_2SAr$ as shown in eq. 59. Namely, the disulfide is the final product in the Ph_3P system, while the final product is $ArSO_2^-$ $ArS\text{-}\overset{+}{P}(NEt_2)_3$ ion which the cationic phosphorus center is stabilized by three nitrogens in the $P(NEt_2)_3$ system.

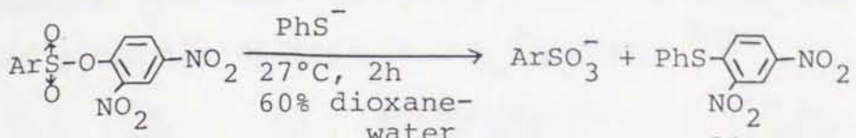


(59)

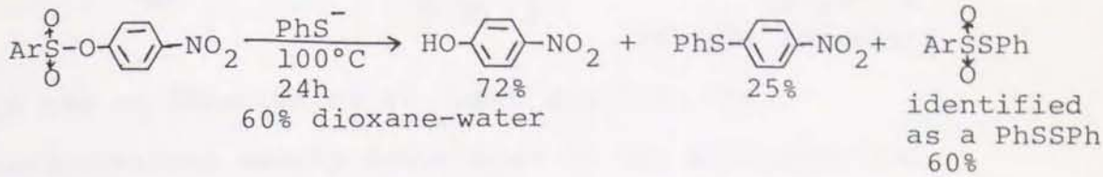
Both alkane- and arenesulfonyl chlorides can be reduced by phosphine or phosphite, but no detail study has been carried out.

8-vii Thiol

The sulfonyl chloride can be reduced by thiols to a mixture of the sulfinate and the disulfide in the presence of bases.[229] In the absence of base, the sulfonyl chloride can be reduced to the corresponding disulfide under drastic conditions.[230] The thiol can react with the sulfonic anhydride to give a mixture of the disulfide and the thiolsulfonate.[231] But the reaction of various sulfonic acid derivatives with thiols has not been studied in detail. The O-C cleavage only occurs in the reaction of alkyl sulfonate ester and thiol(nucleophile) in a S_N2 process, while, there is a possibility that the reaction of aryl sulfonate ester, RSO_3Ar, $ArSO_3Ar'$ with nucleophiles gives rise to the S-O cleavage, though the reactivity decreases remarkably where the central sulfur is considerably sterically-hindered. The substitution of an electron-withdrawing group on the aromatic ring accelerates the reaction, but the cleavage of S-O and O-C bonds may occur. The following experiment was reported by Bunnett et al.[232] Dinitro substituted compound accelerates the reactivity but results in the cleavage of C-O bond, meanwhile, though the reactivity of the mono-nitro substituted compound is low, the reaction gives rise to the cleavage of S-O bond considerably. The tendency of these reactivities is similar to those in the reactions of the sulfonate ester with ^-OH or RO^-.[233]

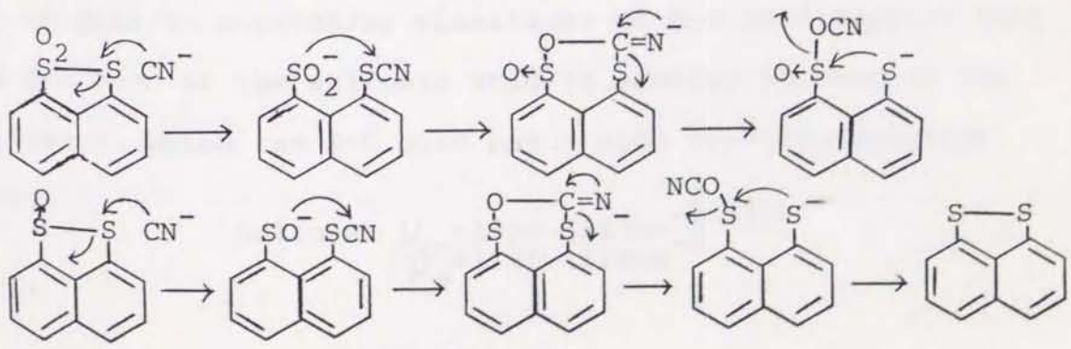


---(60)



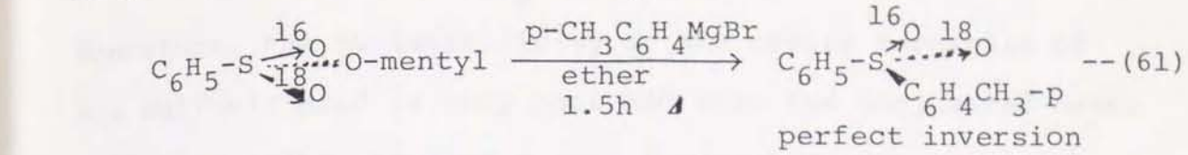
The cleavage of both C-O and S-O bonds occurs at the ratio of 1 to 1 in the reaction of 2-(p-toluenesulfonoxy)lepidine with thiophenolate.[234]

The sulfonamide cannot be reduced by the thiol at all. The reaction of the thiolsulfonate with the thiol to form the sulfinic acid was also studied,[235] and the detailed mechanism has been proposed by Kice et al.[236] The reducing ability of the aromatic thiol is about ~10^3 times higher than that of the aliphatic thiol in this system. This result suggests that the active species of the reduction of the thiolsulfonate is the thiolate. Therefore, Na_2S can reduce the sulfonyl chloride to the sulfinate in a good yield.[237] As an interesting example, CN^- can reduce the thiolsulfonate to the corresponding disulfide,[238] and in particular the open-chained thiolsulfonate is reduced more readily. The reaction proceeds via the initial nucleophilic attack of CN^- on the sulfenyl sulfur as shown in Scheme 25.



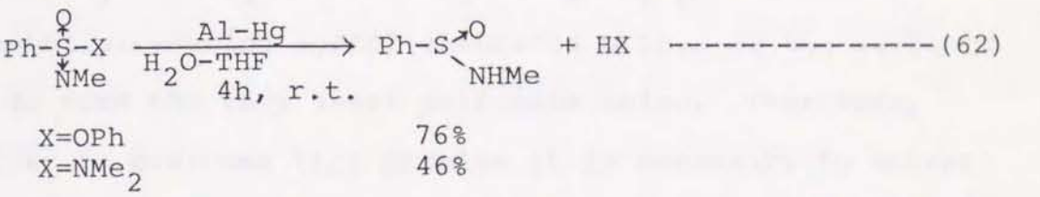
Scheme 25.

In addition, the reaction of the sulfonate ester and Grignard reagent gives the sulfone in a S_N2 process.[239]



--(61)

Though the sulfonamide is an inert species, the sulfonylhydrazine easily decomposes to the sulfinate and nitrogen in the presence of base.[240] The reductive cleavage of the following sulfonic acid derivative with Al-Hg was also reported.[241]



(62)

X=OPh 76%
X=NMe_2 46%

9. Sulfonic Acid

The sulfonic acid is a strong organic acid and the acidity is comparable to that of hydrochloric acid or nitric acid, but the correct pKa value has not been measured because of its remarkably low pKa value. The bond lengths of benzenesulfonate salt by X-ray analysis is shown in Table.[242]

	C-C	C-S	S-O(Å)
$(PhSO_3)_2Mg.6H_2O$	1.40	1.90	1.42
$(PhSO_3)_2Zn.6H_2O$	1.40	1.82	1.39

The IR data on stretching vibrations of S-O bond suggest that the S-O bond of the sulfonic acid is similar to that of the sulfone in which the S-O bond has a high bond dissociation energy.

Sulfone ν_{as}=1350~1310cm^{-1} [243]
ν_s=1160~1120cm^{-1}

Sulfoxide ν_s=1060~1040cm^{-1}

Sulfonic Acid ν_{as}=~1345cm^{-1}, ν_s=~1155cm^{-1}

Therefore, the nucleophilicity of the oxygen terminals of the sulfonic acid is very poor and even the conjugated base, sulfonate anion, is also a poor nucleophilicity.

Up to present, the reduction of sulfonic acid has not been achieved. Only in 1980, Oae et al reported the first example of direct reduction. Sulfonic acids, sulfonate salts can not be reduced by usual reduction systems, i.e. $LiAlH_4$, AlH_3, Cl_3SiH, Ph_3SnH, Ph_3P, HI, $AlCl_3$-$NaBH_4$, B_2H_6 etc, because the nucleophile(reducing agent) abstracts proton of the sulfonic acid to form the very inert sulfonate anion. Therefore, in order to overcome this problem it is necessary to convert the OH group of the sulfonic acid to other group, X(halogen), NR_2, OR, OSO_2R, etc at first, and then the reduction of these sulfonic acid derivatives with some reducing agents has been carried out.

9-i $LiAlH_4$[244)]

The sulfonic acid cannot be reduced at all by $LiAlH_4$ in refluxing n-Bu_2O for 3 days, only lithium sulfonate is formed.

9-ii XSO_3H(X=Cl, F), PCl_5, $SOCl_2$

The conversion of the sulfonic acid to the sulfonyl halide by XSO_3H(X=Cl, F)[245)], PCl_5, $SOCl_2$[246)] is not a reduction. But once this halide is formed, the sulfonyl halide can be reduced easily to the corresponding reduction product.

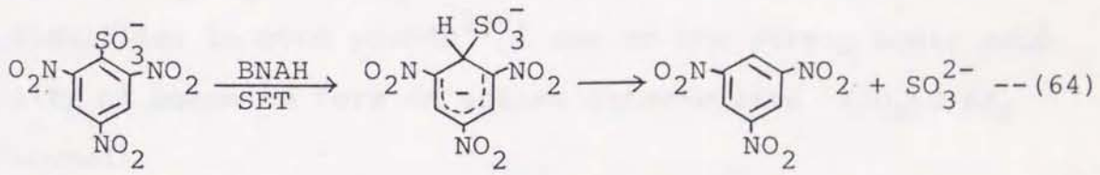
$$RSO_3H \xrightarrow{Py} RSO_3^- PyH^+ \xrightarrow[50\sim60°C,\ 2h.]{PCl_5\ or\ SOCl_2} RSO_2Cl \xleftarrow[60\sim70°C]{ClSO_3H,\ 6h.} RSO_3Na \quad --(63)$$

9-iii Ni-Al[247)]

No correct bond dissociation energy of C-S bond of the sulfonic acid is known. However since that of the sulfone is 70 and 68 kcal/mol in $ArSO_2Ar$ and RSO_2R respectively,[248)] the bond dissociation energy of C-S bond of sulfonic acid is considered to be pretty close to that of the sulfone. Therefore, even the reaction of the arenesulfonic acid with Ni-Al gives rise to the reductive cleavage of C-S bond to form hydrocarbon as in the case of the sulfone.

9-iv Electrode or SET Reduction

The reductive cleavage of C-S bond occurs in the reaction of arenesulfonic acids in the electrode reduction to form hydrocarbon and the sulfite.[249)] In a recent interesting study, the following cleavage of C-S bond with N-benzyl-1,4-dihydronicotinamide(BNAH) which is a NADH model was reported by Ohno et al.[250)]



--(64)

The driving force of this reaction would be the steric strain between SO_3^- group and NO_2 group. A similar study was also done by Shinkai[251)] by use of 1,8-naphthalene disulfonates.

9-v $(CF_3CO)_2O/Bu_4NI$[252)], $BX_3(BI_3, BBr_3/KI)$[253)]

The first example of the direct reduction was carried out by Oae et al using a mixture of $(CF_3CO)_2O$ and Bu_4NI under mild conditions. Though a large amounts of $(CF_3CO)_2O$ and Bu_4NI have to be used, it is very significant since the reaction made a first break through in the direct reduction of

sulfonic acids to thiols and disulfides in-situ.

$$\underset{1}{ArSO_3H} + \underset{20}{(CF_3CO)_2O} + \underset{20}{Bu_4NI} \xrightarrow[16\sim23h,\ CH_2Cl_2]{r.t.} CF_3\overset{O}{\overset{\|}{C}}SAr + ArSH \quad \text{high yield} \qquad \text{-----(65)}$$

This reaction produces considerable amounts of the corresponding thiolsulfonates in the case of alkanesulfonic acids. This reaction is believed to proceed via the following Scheme.

$$RSO_3H + (CF_3CO)_2O \longrightarrow \underset{CF_3CO_2H}{\overset{O}{\overset{\|}{RS}}(O)-O-\overset{O}{\overset{\|}{C}}CF_3} \xrightarrow[CF_3CO_2^-]{I^-} RSO_2I \xrightarrow[I_2]{I^-} RSO_2^-$$

$$\xrightarrow[CF_3CO_2^-]{(CF_3CO)_2O} \overset{O}{\overset{\|}{RS}}(O)-O-\overset{O}{\overset{\|}{C}}CF_3 \xrightarrow[CF_3CO_2^-]{I^-} \overset{O}{\overset{\|}{RS}}-I \xrightarrow[I_2]{I^-} RSO^- \xrightarrow[CF_3CO_2^-]{(CF_3CO)_2O}$$

$$RS-O-\overset{O}{\overset{\|}{C}}CF_3 \xrightarrow[CF_3CO_2^-]{I^-} RSI \xrightarrow{I^-} RS^- + I_2$$

Scheme 26.

A system, BX_3(BI_3 or BBr_3/I^-) can also reduce sulfonic acids to disulfides in good yields[253] due to the strong Lewis acid ability of boron to form an active intermediate, RSO_2-O-BX_2 (proposed).

$$\underset{(R)}{ArSO_3H} \xrightarrow[ClCH_2CH_2Cl,\ 80°C,\ 16h.]{BX_3} \underset{(RSSR)}{1/2ArSSAr} \quad \text{80~98\%} \qquad \text{----------(66)}$$

$$RSO_3H/KI/BBr_3/Bu_4NI = 10/100/50/cat$$

10. Sulfuric Acid

Sulfuric acid has the highest oxidative state, +6, which ranks with SF_6, among all the sulfur compounds, and has very low pKa value, though the correct value has not measured. The bond dissociation energy and bond length are shown in Table.[254]

	$HO-\overset{O}{\overset{\uparrow}{\underset{\downarrow}{S}}}-OH$	$MeO-\overset{O}{\overset{\uparrow}{\underset{\downarrow}{S}}}-OMe$	$Cl-\overset{O}{\overset{\uparrow}{\underset{\downarrow}{S}}}-Cl$ (kcal/mol)
S-O	110	108	95
S-OH(Cl)	88	-	63

$$HO-\overset{O}{\overset{\uparrow}{\underset{\downarrow}{S}}}-OH \quad \begin{matrix} O \rightarrow 1.42\sim1.43\ \text{Å} \\ O \rightarrow 1.52\sim1.55\ \text{Å} \end{matrix}$$

The bond dissociation energy of S-O bond of sulfuric acid would be about 100 kcal/mol since these four oxygens are equivalent. It is difficult to reduce sulfuric acid due to facile abstraction of proton from sulfuric acid by any nucleophile to form an inert sulfate. Therefore no nucleophile can approach the central sulfur. While, dialkyl sulfate is also a strong alkylation agent to form sulfate anion in the reaction with nucleophiles. Though the reduction of sulfuric acid has been studied, particularly in inorganic chemistry, the reduction in this case is mainly by thermal decomposition,[255] with active-C,[256] hydrogenation in the presence of metal,[257] and radiation.[258] Meanwhile, many plants, fungi, microorganisms take in sulfate in their bodies and reduce sulfate under mild conditions to sulfide which is the source of the sulfur-containing amino-acids (assimilatory metabolism). In this reduction pathway, there are two key steps. The first step is the formation of APS or PAPS which has a $-O-\overset{O}{\overset{\|}{\underset{O^-}{P}}}-O-\overset{O}{\overset{\uparrow}{\underset{\downarrow}{S}}}-O-^-$ linkage in the reaction of sulfate with ATP. The second step is the reduction by a protein-thiol to form sulfite.

Finally, SO_2, SO_3^{2-} which is considered to be as an intermediate in the reduction of sulfuric acid with some reducing agents is easily reduced.[259] However, the important and

interesting study in organic and biochemistry is the reduction of SO_2 with thiols.[260] The reaction proceeds in the presence of amine.

$$4\ EtSH + SO_2 \xrightarrow[\text{r.t.}\ 3\ \text{days}]{\text{amine}} \underset{72\%}{EtSSEt} + \underset{28\%}{EtSSSEt} \quad \text{----------(67)}$$

The central sulfur of the trisulfide is probably derived from SO_2. The reaction would proceed via the following pathway.

$$SO_2 + RSH \longrightarrow RS\overset{\overset{\downarrow}{O}}{S}\text{-}OH \xrightarrow[-H_2O]{RSH} RS\overset{\overset{\downarrow}{O}}{S}SR \xrightarrow{RSH} RSSOH + RSSR$$

$$RSSOH \xrightarrow{RSH} RSSSR$$

Scheme 27.

References

1) Shigeru Oae,"Organic Sulfur Chemistry—Reaction mechanism—", Chap. 4, Kagaku Dojin.
2) S. Oae and T. Takata, "Chemistry", Vol. 34, 756, 891, 961 (1980).
3) S. Oae, "Kagaku no Ryoiki", 34, 344, 445(1980).
4) Shigeru Oae, "Organic Sulfur Chemistry—Reaction Mechanism—", Chap. 5, Kagaku Dojin.
5) M.L.-S.Tsang, J.A.Schiff, J. Bacterial., 125, 923(1976). A.B.Roy, P.A.Trudinger,"The Biochemistry of Inorganic Compounds of Sulfur".
6) E.Miller, D.R.Rayner, K.Mislow, J. Amer. Chem. Soc., 88, 3139(1966).
7) Shigeru Oae,"The Chemistry of Organic Sulfur Compounds", page 208, Kagaku Dojin.
8) D.R.Rayner, E.G.Miller, P.B.Bicket, A.J.Gordon, K.Mislow, J. Amer. Chem. Soc., 88, 3138(1966).
9) Shigeru Oae,"Organic Sulfur Chemistry—Reaction Mechanism—", Chap. 7, Kagaku Dojin.
10) J. Drabowicz, T. Numata, S. Oae, Org. Prep. and Proced. Int., 9, 63(1977).
11) S.W.Benson, Chem. Review, 78, 23(1978).
12) H.C.Brown, P.Heim, N.M.Yoon, J. Amer. Chem. Soc., 92, 1637(1970). H.C.Brown, N.M.Yoon, ibid., 88, 1464(1966). H.C.Brown, P.M.Weissman, ibid., 87, 5614(1965). H.C.Brown, P.M.Weissman, N.M.Yoon, ibid., 88, 1458(1966). A.G.Anastassion, J.C.Wetzel, B.Y-H. Chao, ibid., 97, 1124(1975).
13) M.Mikolajczyk, J.Drabowicz, Phosphorus and Sulfur., 301(1976).
14) C.R.Johnson, W.G.Phillips, J. Org. Chem., 32, 3233(1967).
15) H.D.Durst, J.W.Zubrick, G.R.Kieczykowski, Tet. Lett., 1777(1974).
16) N.Furukawa, K.Hoshino, S.Oae, unpublished data.
17) J.Drabowicz, M.Mikolajczyk, Synthesis, 527(1976).
18) D.W.Chasar, J. Org. Chem., 36, 613(1971).
19) T.H.Chan, A.Melnyk, D.N.Harpp, Tet. Lett., 201(1969). T.H.Chan, A.Melnyk, J. Amer. Chem. Soc., 92, 3718(1970).
20) R.Oda, M.Mieno, Y.Hayashi, Tet. Lett., 2363(1967).
21) H.S.Dilanjan, W.P.Weber, Tet. Lett., 1969(1978).
22) J.C.Dyer, S.A.Evans, Jr, J. Org. Chem., 45, 5350(1980).
23) E.J.Corey, M.Chaykovsky, J. Amer. Chem. Soc., 86, 1639(1964).
24) H.Alper, E.C.H.Keung, Tet. Lett., 53(1970).
25) H.Alper, G.Wall, Chem. Commun., 263(1976). T.-L.Ho, Synth. Commun., 7, 321(1977).
26) G.A.Olah, G.K.S.Rakash, T.-L.Ho, Synthesis, 810(1976).
27) R.G.Nuzzo, H.J.Simon, J.S.Filippo, Jr, J. Org. Chem., 42, 568 (1977).
28) D.J.Abbott, S.Colonna, C.J.M.Stirling, J. Chem. Soc., I, 492(1976). D.J.Abbott, Chem. Commun., 471(1971).
29) J.Drabowicz, M.Mikolajczyk, Synthesis, 138(1978).
30) T.-L.Ho, C.M.Wong, Synthesis, 206(1973).
31) B.R.James, F.T.T.Ng, G.L.Rempel, Can. J. Chem., 47, 4520(1969).
32) D.Manya, A.Sekera, P.Pumpf, Tetrahedron, 26, 467(1970).
33) G.H.Posner, P.W.Tang, J. Org. Chem., 43, 4131(1978).
34) E.H.Amonoo-neizer, S.K.Ray, R.A.Shaw, B.C.Smith, J. Chem. Soc., 4296(1965).
35) H.H.Szmant, O.Cox, J. Org. Chem., 31, 1595(1966).
36) S.Oae, A.Nakanishi, S.Kozuka, Tetrahedron, 28, 549(1972).
37) M.Sekine, H.Yamagata, T.Hata, Tet. Lett., 375(1979).
38) J.P.A.Castrillon, H.H.Szmant, J. Org. Chem., 30, 1338(1965).
39) D.W.Chasar, T.M.Pratt, Synthesis, 262(1976).
40) M.Drenx, Y.Leroux, P. Savignac, Synthesis, 506(1974).

41) G.A.Olah, B.G.B.Gupta, S.C.Narang, J. Org. Chem., 43, 4503 (1978).
42) G.A.Olah, B.G.B.Gupta, S.C.Narang, Synthesis, 137(1980).
43) H.Suzuki, N.Sato, A.Osuka, Chem. Lett., 143(1980).
44) D.Landini, F.Montanari, J. Chem. Soc. Chem. Comm., 86(1968).
45) E.N.Karaulova, G.D.Galpern, Zhur. Obshchri. Klrim., 29, 3033(1959).
D.W.Chasar, J.P.Shockcor, Phosphorus and Sulfur, 187(1980).
46) D.Landini, F.Montanari, H.Hogeveen, G.Macoagnani, Tet. Lett., 2691(1964).
47) G.Modena, G.Scorrano, D.Landini, F.Montanari, Tet. Lett., 3309(1966).
48) R.A.Strecker, K.K.Anderson, J. Org. Chem., 33, 2234(1968).
49) S.Tamagaki, M.Mizuno, H.Yoshida, H.Hirata, S.Oae , Bull. Chem. Soc. Jpn., 44, 2456(1971).
50) G.A.Olah, S.C.Narang, B.G.B.Gupta, R.Melhotra, Synthesis, 61(1979).
51) G.A.Olah, B.G.B.Gupta, S.C.Narang, Synthesis, 583(1979).
52) G.A.Olah, R.Malhotra, S.C.Narang, Synthesis, 58(1979).
53) J.Drabowicz, S.Oae, Synthesis, 404(1977).
54) A.Allenmark, Acta. Chem. Scand., 20, 910(1966).
55) T.Aida, N.Furukawa, S.Oae, Tet. Lett., 3853(1973).
T.Aida, T.Akasaka, N.Furukawa, S.Oae, Bull. Chem. Soc. Jpn., 49, 1117(1976).
56) N.Kornblum, W.J.Jones, G.J.Anderson, J. Amer. Chem. Soc., 81, 4113(1959).
N.Kornblum, J.W.Powers, G.J.Anderson, W.J.Jones, H.O.Larson, O.Levand, W.M.Weaver, J. Amer. Chem. Soc., 79, 6562(1957).
W.W.Epstein, F.W.Sweat, Chem. Review, 67, 247(1967).
57) T.Numata, K.Ikura, Y.Shimao, S.Oae, Org. Prep. and Proced. Int., 8, 119(1976).
58) T.Numata, S.Oae, Chem. and Ind. 277(1973).
59) M.Nojima, T.Nagata, N.Tokura, Bull. Chem. Soc. Jpn., 48, 1343 (1975).
60) G.A.Russell, E.T.Sabourin, J. Org. Chem., 34, 2336(1969).
61) C.R.Johnson,C.C.Bacon, J.J.Rigan, J. Org. Chem., 37, 919 (1972).
62) I.W.J.Still, Phosphorus and Sulfur, 293(1979).
I.W.J.Still, S.K.Hasan, K.Turnbull, Can. J. Chem., 56, 1423 (1978).
I.W.J.Still, S.K.Hasan, K.Turnbull, Synthesis, 468(1977).
63) K.Sakaki, S.Oae, Chem. Lett., 1003(1977).
64) I.W.J.Still, K.Turnbull, Synthesis, 541(1978).
I.W.J.Still, Phosphorus and Sulfur, 293(1979).
65) I.W.J.Still, R.N.Reed, K.Turnbull, Tet. Lett., 1481(1979).
66) S.Oae, S.Kawamura, Bull. Chem. Soc. Jpn., 36, 163(1963).
W.Tagaki, S.Kiso, S.Oae, Bull. Chem. Soc. Jpn., 38, 414 (1965).
S.Kiso, S.Oae, Bull. Chem. Soc. Jpn., 40, 1722(1967).
67) C.N.Yiannias, J.V.Karabinos, J. Org. Chem., 28, 3246(1963).
68) K.Balenovic, N.Bregant, Chem. Ind., 1577(1964).
69) G.Guanti, C.Dell'Erba, G.Gaiani, Phosphorus and Sulfur, 179(1976).
70) T.J.Wallace, J. Amer. Chem. Soc., 86, 2018(1964).
71) T.J.Wallace, J.J.Mahon, J.Org. Chem., 30, 1502(1965).
72) O.G.Lowe, J. Org. Chem., 40, 2096(1975).
73) S.Oae, T.Yagihara, T.Okabe, Tetrahedron, 28, 3203(1972).
74) S.Oae, A.Nakanishi, N.Tsujimoto, Tetrahedron, 28, 2981 (1972).

75) S.Oae, K.Fujimori, H.Yoshimoto, unpublished data.
76) D.L.J.Clive, W.A.Kiel, S.M.Menchen, C.K.Wong., J. Chem. Soc. Chem. Com., 657(1977).
77) M.Mikolajczyk, M.Para, Chem. Commun., 1192(1969).
78) T. Numata, H.Togo, S.Oae, Chem. Lett., 329(1979).
79) J.Drabowicz, S.Oae, Synthesis, 767(1977).
80) Y.Hiraki, M.Kamiya, R.Tanikaga, N.Ono , A.Kaji, Bull. Chem. Soc. Jpn., 50, 440(1977).
81) R.Tanikaga, K.Nakayama, K.Tanaka, A.Kaji, Chem. Lett., 395(1977).
82) H.S.Dilanjan.Soysa, W.P.Weber, Tet. Lett., 235(1978).
83) S.Oae, K.Tsujihara, N.Furukawa, Bull. Chem. Soc. Jpn., 45, 2856(1972).
84) J.Drabowicz, M.Mikolajczyk, Synthesis, 542(1978).
85) G.Borgogno, S.Colonna, R.Fornwsior, Synthesis, 529(1975).
86) T.Numata, T.Nagata, S.Oae, unpublished data.
87) K.Ogura, M.Yamashita, G.Tsuchihashi, Synthesis, 383(1975).
88) R.L.Letsinger, C.W.Kammeyer, J. Amer. Chem. Soc., 73, 4476(1951).
89) G.M.Gurria, G.H.Posner, J. Org. Chem., 38, 2419(1973).
90) S.Oae, T.Aida, K.Tsujihara, N.Furukawa, Tet. Lett., 1145(1971).
91) S.Oae, K.Iida, T.Takata, Tet. Lett., 573(1981).
S.Oae, K.Iida, T.Takata, Phosphorus and Sulfur, 12, 103 (1981).
92) Y.Tsuchiya, Japan, No. 22, 7722(1954).
93) S.W.Benson, Chem. Review, 78, 23(1978).
94) F.G.Bordwell, W.H.Mckellin, J. Amer. Chem. Soc., 73, 2251 (1951).
95) D.Wittenberg, T.C.Wv, H.Gilmann, J. Org. Chem., 23, 1898 (1958).
96) E.J.Corey, M.Chaykovsky, J. Amer. Chem. Soc., 86, 1639 (1964).
97) R.A.Grimm, W.A.Bonner, J. Org. Chem., 32, 3470(1967).
98) B.M.Trost, H.C.Arndt, P.E.Strege, T.R.Verhoever, Tet. Lett., 3477(1976).
99) R.E.Dabby, J.Kenyon, R.F.Mason, J. Chem. Soc., 4881(1952).
100) W.E.Truce, D.P.Tate, D.N.Burdge, J. Amer. Chem. Soc., 82, 2872(1960).
101) C.W.Schrock, C.R.Johnson, J. Amer. Chem. Soc., 93, 5305 (1971).
102) L.Horner, H.Neumann, Chem. Ber., 98, 1715(1965).
103) S.Oae, S.Kawamura, Bull. Chem. Soc. Jpn., 36, 163(1963).
104) W.Tagaki, S.Kiso, S.Oae, Bull. Chem. Soc. Jpn., 38, 414(1965).
105) S.Oae, Y.Tsuchida, K.Tsujihara, N.Furukawa, Bull. Chem. Soc. Jpn., 45, 2856(1972).
106) S.Oae, Y.Tsuchida, N.Furukawa, Bull. Chem. Soc. Jpn., 46, 648(1973).
107) F.G.Bordwell, W.H.Mckellin, J. Amer. Chem. Soc., 73, 2251 (1951).
108) L.A.Paquette, R.E.Wingard, Jr, J.C.Philips, G.L.Thonpson, L.K.Read, J.Clardy, J. Amer. Chem. Soc., 93, 4508(1971).
L.A.Paquette, R.W.Houser, J. Amer. Chem. Soc., 93, 4522 (1971).
109) T.A.Whitney, D.J.Cram, J. Org. Chem., 35, 3964(1970).
110) W.P.Weber, P.Stromquist, T.I.Ito, Tet. Lett., 2595(1974).
111) L.Bateman, J.I.Cunnen, J.Ford, J. Chem. Soc., 1539(1957).

112) A.Krubiner, H.Lucus, Can. J. Chem., 51, 1419(1973).
113) A.G.Anastassion, J.C.Wetzel, B.Y-H.Chao, J. Amer. Chem. Soc., 97, 1124(1975).
114) G.R.Chalkley, D.J.Snodin, G.Stevens, M.C.Whiting, J. Chem. Soc., C, 682(1970).
115) M.Shimagaki, H.Tsuchiya, Y.Ban, T.Oishi, Tet. Lett., 3435 (1978).
116) I.W.J.Still, S.Szilagyi, Synth. Commun., 9, 923(1979).
117) T.R.Williams, A.Nudelman, R.E.Booms, D.J.Cram., J. Amer. Chem. Soc., 94, 4684(1972).
118) D.R.Rayner, D.M.Schriltz, J.Day, D.J.Cram., J. Amer. Chem. Soc., 90, 2721(1968).
D.J.Cram, J.Day, D.R.Rayner, D.M.Schriltz, D.J.Duchamp, D.C.Garwood, J. Amer. Chem. Soc., 92, 7369(1970).
119) S.Oae, K.Iida, T.Takata, Tet. Lett., 22, 573(1981).
120) N.Furukawa, K.Hoshino, S.Oae, unpublished data.
121) N.Furukawa, F.Takahashi, T.Yoshimura, S.Oae, Tetrahedron, 35, 317(1979).
122) N.Kharasch, C.Y.Meyers,"The Chemistry of Organic Compounds" Vol. 2, 35(1966). Pergamon Press.
R.Mozingo, D.E.Wolf, S.A.Harris, K.Folkers, J. Amer. Chem. Soc., 65, 1013(1943).
J.Bougault, E.Cattelain, P.Chabrier, Bull. Soc. Chim. France, 7, 781(1940).
123) Shigeru Oae," The Chemistry of Organic Sulfur Compounds", Vol. 1. Kagaku Dojin.
124) G.Schwarzenbach, H.A.Egli, Helv. Chim. Acta., 17, 1176 (1934).
F.G.Bordwell, H.M.Anderson, J. Amer. Chem. Soc., 75, 6019 (1953).
125) K. Fujimori, C.Higuchi, S.Oae, unpublished data.
126) S.W.Benson, Chem. Review, 78, 23(1978).
127) R.C.Arnold, A.P.Lien, R.M.Alm, J. Amer. Chem. Soc., 72, 731(1950).
128) H.C.Brown, P.M.Weissman, N.M.Yoon, J. Amer. Chem. Soc., 88, 1458(1966).
H.C.Brown, P.M.Weissman, ibid., 87, 5614(1965).
H.C.Brown, N.M.Yoon, ibid., 88, 1464(1966).
129) I.C.Gunsalus, L.S.Barton, W.Gruber, J. Amer. Chem. Soc., 78, 1763(1956).
130) H.C.Brown, B.C.S.Rao, ibid., 78, 2582(1956).
131) C.A. 61, 1799c.
132) S.Rolski, R.Dobrzanska, Acta. Polon. Pharm., 19, 523(1962).
133) I.C.Gunsalus, L.S.Barton, W.Gruber, J. Amer. Chem. Soc., 78, 1763(1956).
134) M.Tagagi, S.Goto, M.Tazaki, T.Matsuda, Bull. Chem. Soc. Jpn., 53, 1982(1980).
135) O.A.Swanepoel, J.S.African. Chem. Inst., 16, 48(1963).
136) S.Oae, T.Nagata, T.Yoshimura, K.Fujimori, Tet. Lett., in press.
137) M.Pang, E.I.Becker, J. Org. Chem., 29, 1948(1964).
138) C.A. 52, 14670b.
C.A. 53, 13094a.
A.Burawoy, C.Turner, J. Chem. Soc., 469(1950).
139) T.S.Woods, D.L.Klayman, J. Org. Chem., 39, 3716(1974).
140) W.H.H.Günther, ibid., 31, 1202(1966).
141) T.S.Woods, D.L.Klayman, ibid., 39, 3716(1974).

142) G. Borgogno, S. Colonna, R. Fornasier, Synthesis, 529(1975).
143) R.E. Humphrey, J.M. Hawkins, Anal. Chem., 36, 1813(1964).
144) R.E. Humphrey, J.L. Potter, Anal. Chem., 37, 165(1965).
145) L.E. Overman, D. Matzinger, E.M. O'Connor, J.D. Overmannn, J. Am. Chem. Soc., 96, 6081(1974).
146) L.E. Overmann, S.T. Petty,J. Org. Chem., 40, 2779(1975).
147) L.E. Overmann,E.M. O'Connor, J. Am. Chem. Soc., 98, 771 (1976).
148) S. Safe, A. Taylor, Chem. Commun., 1466(1969).
149) D.N. Harpp, D.K. Ash, Chem. Commun., 811(1970).
150) D.N. Harpp, J.G. Gleason, J. Am. Chem. Soc., 90, 4181(1968).
151) D.N. Harpp, J.G. Gleason, ibid., 93, 2437(1971).
152) H.I. Jacobson, R.G. Harvey, E.V. Jensen, ibid., 77, 6064(1955). R.S. Davidson, J. Chem. Soc., C, 2131(1967).
153) M. Grayson, C.E. Farley, J. Org. Chem., 32, 236(1967).
154) F.A. Davis, R.H. Jenkins, Jr, S.O.A. Rizvi, S.G. Yocklovich, J. Org. Chem., 46, 3467(1981).
155) S. Oae,"Organic Sulfur Chemistry－Mechanism－ " Kagaku Dojin
156) L.L. Poulson, R.M. Hyslop, D.M. Zieglar,"Archives of Biochemistry and Biophysics" 198, 78(1979).
157) S.W. Benson, Chem. Reviews, 78, 23(1978).
158) D.N. Harpp, D.K. Ash, T.G. Back, J.G. Gleason, B.A. Orwig, W.F. Horn, Tet. Lett., 3551(1970).
159) T. Mukaiyama, K. Takahashi, Tet. Lett., 5907(1968).
160) R.G. Hiskey, F.I. Carroll, R.M. Babb, J.O. Bledsol, R.T. Puckett, B.W. Roberts, J. Org. Chem., 26, 1152(1961).
161) B.J. Lindberg, Acta. Chem. Scand., 24, 1110(1970).
162) L. Horner, M. Vogt, Phosphorus and Sulfur, 287(1979).
163) T.H. Chan, J.P. Montillier, W.F. Horn, D.N. Harpp, J. Am. Chem. Soc., 92, 7224(1970).
164) Z.V. Todres, S.P. Avagyan, Phosphorus and Sulfur, 223(1978).
165) M. Pang, E.I. Becker, J. Org. Chem., 29, 1948(1964).
166) G.A. Olah, S.C. Narang, L.D. Field, G.F. Salem, J. Org. Chem., 45, 4792(1980).
167) R.K. Burkhard, D.E. Sellers, F. Decou, J.L. Lambert, J. Org. Chem., 24, 767(1959).
C.J.M. Stirling, Int. J. Sulfur Chem., B, 6, 278(1971).
P. Rumph, J. Sadet, Bull. Soc. Chim. France., 447(1958).
168) R. Otto, Ann., 145, 13, 317(1868).
L. Horner, O.H. Basedow, Justus. Liebigs. Ann.Chem., 612, 108 (1958).
169) J.L. Kice, J. Org. Chem., 28, 1162(1963).
170) H.W. Pinnick, M.A. Reynolds, R.T. Mcdonald, Jr., W.D. Brewster, J. Org. Chem., 45, 930(1980).
171) A. Burawoy, C. Turner, J. Chem. Soc., 469(1950).
172) G.A. Olah, S.C. Narang, L.D. Field, G.F. Salem, J. Org. Chem., 45, 4792(1980).
173) G. Hanson, D.S. Kemp, J. Org. Chem., 46, 5441(1981).
174) M. Kobayashi, A. Yamamoto, Bull. Chem. Soc. Jpn., 39, 2736 (1966).
175) T.H. Chan, J.P. Montillier, W.F. Horn, D.N. Harpp, J. Am. Chem. Soc., 92, 7224(1970).
176) J. Kovacs, U.R. Ghatak, J. Org. Chem., 31, 119(1966).
177) D.N. Harpp, S.M. Vines, J.P. Montillier, T.H. Chan, J. Org. Chem., 41, 3987(1976).
178) D. Barnard, J. Chem. Soc., 4675(1957).

179) J.L. Kice, J. Am. Chem. Soc., 95, 109(1973).
180) S. Oae, G. Tsukamoto, Chemistry(Japan), 26, 50(1971).
181) C.J. Cavallito, J.H. Bailey, J. Am. Chem. Soc., 66, 1950 (1944).
182) W.E. Savige, J. Eager, J.A. Maclaren, C.M. Roxburgh, Tet. Lett., 3289(1964).
J.L. Kice, G.B. Large, Tet. Lett., 3537(1965).
183) E. Block, L. O'Connor, J. Am. Chem. Soc., 96, 3929(1974).
M.M. Chan, J.L. Kice, J. Am. Chem. Soc., 98, 7711(1977).
S.W. Benson, Chem. Reviews, 78, 23(1978).
184) L.D. Small, J.H. Baily, C.J. Cavallito, J. Am. Chem. Soc., 69, 3565(1949).
185) J.L. Kice, J. Org. Chem. 33, 1940(1968).
186) M. Wälti, D.B. Hope, J. Chem. Soc., c, 2326(1971).
187) N. Kharasch, C.Y. Meyers,"The Chemistry of Organic Sulfur Compounds", Vol. 2, Chap. 15, Pergamon Press(1966).
188) J.F. Carson, F.F. Wong, J. Org. Chem., 26, 1467(1961).
189) S. Tamagaki, H. Hirota, S. Oae, Bull. Chem. Soc. Jpn., 47, 2075(1974).
190) S. Smiles, C.M. Bere, Org. Synth., Coll. Vol. 1, 7(1941).
M. Kulka, J. Am. Chem. Soc., 72, 1215(1950).
191) L. Field, J. Am. Chem. Soc., 74, 394(1952).
192) H.J. Barber, S. Smiles, J. Chem. Soc., 1141(1928).
W.L.F. Armarege, E.E. Tumer., ibid., 3668(1956).
M.M. Chau, J.L. Kice., 42, 3265(1977).
193) W.A. Sheppard, Org. Synth., Coll. Vol. 5, 843(1970).
L. Bauer, J. Cymermann, J. Chem. Soc., 3434(1949).
194) W. Wagner, Chem. Ber., 99, 375(1966).
195) D. Klamann, G. Hofbauer, Monatsh., 83, 1489(1952).
196) G.A. Olah, S.C. Narang, L.D. Field, G.F. Saln., J. Org. Chem., 45, 4792(1980).
197) C. Ferreri, R. Caputo, Tet. Lett., 23, 2391(1982).
198) G.A. Olah, S.C. Narang, L.D. Field, R. Karpeles, J. Org. Chem., 46, 2408(1981).
199) L.D. Field, J. Am. Chem. Soc., 74, 394(1952).
200) C.S. Marvel, P.D. Caeser, J. Am. Chem. Soc., 72, 1033(1950).
L. Field, F.A. Grunwald, J. Org. Chem., 16, 946(1951).
201) H.O. Fong, W.R. Hardstaff, D.G. Kay, R.F. Langler, R.H. Morse, D.N. Sandoval, Can. J. Chem., 57, 1206(1979).
202) C.S. Marvel, P.D. Caeser, J. Am. Chem. Soc., 72, 1033(1950).
L. Field, F.A. Grunwald, J. Org. Chem., 16, 946(1951).
203) D. Klamann, Monatsh. Chem., 84, 651(1953).
204) R.A. Appleton, J.C. Fairlie, R. Mccrindle, Chem. Commun., 690(1967).
E.L. Allred, S. Winstein, J. Am. Chem. Soc., 89, 4008 (1967).
W. Krans, C. Chassin, Tet. Lett., 1443(1970).
Y. Fujimoto, T. Tatsuno, Tet. Lett., 3325(1976).
L.J. Dolby, D.R. Rosencrantz, J. Org. Chem., 28, 1888(1963).
205) J. Wolinsky, R.L. Marhenke, J. Org. Chem., 40, 1766(1975).
J. Wolinsky, D.R. Dimmel, T.W. Gibson, J. Org. Chem., 32, 2087(1967).
206) J. Wolinsky, R.L. Marhenke, E.J. Eustace, J. Org. Chem. 38, 1428(1973).
M.B. Smith, J. Wolinsky, J. Org. Chem., 46, 101(1981).
207) C.A., 51, 1125a.

C. Hansch, W.A. Blondon, J. Am. Chem. Soc., 70, 1562(1948).
R. Adams, C. S. Marvel, Org. Synth.., Coll. Vol. 1, 504 (1956).
H. Gilman, S. Broadbent, J. Am. Chem. Soc., 69, 2053(1947).
E. Vinkler, F. Klivengi, Acta. Chim. Acad. Sci. Hung., 1, 319(1951), 5, 159(1954).
208) C.A., 44, 8380c.
H.F. Wilson, D.S. Tarbell, J. Am. Chem. Soc., 72, 5200 (1950).
C.G. Overberger, H. Biletch, F.W. Orttung, J. Org. Chem. 24, 289(1959).
209) S. Mirata, The University of Yamaguchi, College of Engineering paper, 12, 138(1961).
210) C.S. Marvel, P.D. Caeser, J. Am. Chem. Soc., 73, 1097(1951).
211) N. Kunieda, K. Sakai, S. Oae, Bull. Chem. Soc. Jpn., 41, 3015(1968).
212) C.A, 49, 10369d.
213) L. Field, V. Eswarakrishnan, J. Org. Chem., 46, 2025(1981).
214) J. Kovacs, U.R. Ghatak, J. Org. Chem., 31, 119(1966).
215) T. Cuving, M. Larcheveque, J. Organomet. Chem., 64, 315 (1974).
216) H. Alper, Angew. Chem., 81, 706(1969).
217) H. Alper, Tet. Lett., 1239(1969).
218) S.W. Benson, Chem. Reviews, 78, 23(1978).
219) C.A., 51, 14447g.
S. Takagi, T. Suzuki, K. Imaeda, J. Pharm. Soc. Jpn., 69, 358(1949).
N. Urabe, K. Yasukochi, electrochemistry, 25, 17(1957).
220) J.C. Carnahan, Jr, W.D. Closson, J.R. Ganson, D.A. Juckett, K.S. Ouaal, J. Am. Chem. Soc., 98, 2526(1976).
221) W.D. Closson, S. Ji, S. Schulenberg, J. Am. Chem. Soc., 92, 650(1950).
K.S. Quaal, S. Ji, Y.H. Kim, W.D. Closson, J.A. Zubieta, J. Org. Chem., 43, 1311(1978).
222) P. Yousefzadeh, C.K. Mann, J. Org. Chem., 33, 2716(1968).
223) A.J. Verbiscar, B. Witkop, J. Org. Chem., 35, 1924(1970).
P.T. Cottrell, C.K. Mann, J. Am. Chem. Soc., 93, 3579(1971).
224) J. Michalski, T. Modro, J. Wieczohowski,J. Chem. Soc., 1665 (1960).
225) S. Hayashi, M. Furukawa, J. Yamamoto, K. Hamamura, Chem. Pharm. Bull., 15, 1310(1967).
226) J.L. Kice, K. Krowicki, J. Org. Chem., 46, 4894(1981).
227) D.N. Harpp, J.G. Gleason, Tet. Lett., 1447(1969).
228) D.N. Harpp, J.G. Gleason, D.K. Ash, J. Org. Chem., 36, 322 (1971).
229) L. Field, R.B. Barke, J. Org. Chem., 34, 36(1969).
230) D. Cipris, D. Pouli, Synth. Commun., 207(1979).
231) L. Field, J. Am. Chem. Soc., 74, 394(1952).
232) J.F. Bunnett, J.Y. Bassett, Jr, J. Org. Chem., 27, 2345(1962).
J.F. Bunnett, J.Y. Bassett, Jr, J. Am. Chem. Soc., 81, 2104(1959).
233) S. Oae, R. Kiritani, Bull. Chem. Soc. Jpn., 39, 611(1966).
S. Oae, R. Kiritani, W. Tagaki, Bull. Chem. Soc. Jpn., 39, 1961(1966).
234) J.F. Bunnett, J.Y. Bassett, Jr, J. Org. Chem., 27, 1887(1962).
235) E. Vinkler, F. Klivenyi, Acta. Chim. Acad. Sci. Hung., 4, 271(1954).

L. Field, H. Härle, T.C. Owxy, A. Ferretti, J. Org. Chem., 29, 1632(1964).
L. Field, P.M. Giles, Jr, J. Org. Chem., 36, 309(1971).
236) J.L. Kice, J. Am. Chem. Soc., 96, 8015(1974).
237) V.V. Kozlov, D.D. Smolin, Zhur. Obshchei. Khim., 19, 740 (1949).
238) S. Tamagaki, H. Hirota, S. Oae, Bull. Chem. Soc. Jpn., 47, 2075(1974).
239) M.A. Sabol, K.K. Anderson, J. Am. Chem. Soc., 91, 3603(1969).
240) L. Caglioti, Tetrahedron, 22, 487(1966).
241) C.W. Schrock, C.R. Johnson, J. Am. Chem.Soc., 93, 5305 (1971).
242) S. Oae,"The Chemistry of Organosulfur Compounds" Vol. 2, 404, Kagaku Do-jin.
243) K. Nakanishi, P.H. Solomon, and N. Furutachi,"Infrared Absorption Spectroscopy" Nankodo
244) L.D. Dolby, D.R. Rosencrantz, J. Org. Chem., 28, 1888(1963).
245) M. Kulka, J. Am. Chem. Soc., 72, 1215(1950).
246) A. Barco, S. Benetti, G.P. Pollini, R. Taddia, Synthesis, 877(1974).
H. Grarboyes, A.R. Day, J. Am. Chem. Soc., 79, 6421(1957).
247) E. Schwenk, D. Papa, B. Whitman, H. Ginsberg, J. Org. Chem., 9, 1(1943).
248) S.W. Benson, Chem. Reviews, 78, 23(1978).
249) A.I.A. Khodair, A. Swelin, F. El-Sheikh, Inst. J. Sulfur Chem., B, 6, 213(1971).
250) A. Ohno, H. Yamamoto, S. Oka, Tet. Lett., 4061(1979).
251) S. Shinkai, H. Kuroda, Y. Kusano, O. Manabe, A. Ito, Tet. Lett., 22, 3201(1981).
252) T. Numata, H. Awano, S. Oae, Tet. Lett., 21, 1235(1980).
253) G.A. Olah, S.C. Narang, L.D. Field, R. Karpeles, J. Org. Chem., 46, 2408(1981).
254) S.W. Benson, Chem. Reviews, 78, 23(1978).
255) C.A., 50, 11869i.
256) C.A., 55, 7769c.
C.A., 55, 13978i.
C.A., 54, 8508c.
C.A., 54, 18149b.
257) C.A., 55, 14150b.
G. Pannetier, J.L. Abegg, Bull. Soc. Chim. France., 186(1961).
F. Habashi, S.A. Mikkail, K. Vo. Van, Can. J. Chem., 54, 3646(1976).
A. Katagiri, K. Watanabe, S. Yoshizawa, Bull. Chem. Soc. Jpn., 54, 1(1981).
A. Katagiri, K. Watanabe, S. Yoshizawa, Bull. Chem. Soc. Jpn., 54, 5(1981).
A.J. Hegedus, K. Fukker, Z. Anory. U. Allgem. Chem., 284, 20(1956).
258) C.J. Hochanadel, J.A. Ghormley, T.J. Sworski, J. Am. Chem. Soc., 77, 3215(1955).
259) F. Feher, E. Schliep, H. Weber, Z. Elektrochem., 57, 916 (1953).
C.A., 55, 11166i.
C.A., 56, 6900f.
C.A., 54, 15861d.
C.A., 41, 3932c.

G.L. Klyanina, A.I. Shlygin, Zh. Fiz. Khim., 36, 1849(1962).
F.B. Shakhlakhtinski, A.I. Gulieu, Azerb. Khim. Zh., 123(1962).
A.A. Fotiev, Zh. Prikl. Khim., 35, 2402(1962).
N. Konopik, F. Holzinger, Monatsh., 85, 140(1954).
A.R. Vasudeva Murthy, Proc. Indian. Acad. Sci., 37A, 11(1953). 37A, 17(1953).
260) F. Akiyama, J. Chem. Soc., I, 1046(1978).

Chapter 1.

The Reduction of Sulfonic Acid Derivatives to the Corresponding Sulfinic Acids with Thiols

Abstract

Sulfonic acid derivatives, such as sulfonic anhydrides and sulfonyl halides, can be easily reduced to the corresponding sulfinates with either sodium thiolates or thiophenol/pyridine. Meanwhile in the reaction of sulfonic acid derivatives with butanethiol/pyridine system, butanethiolsulfonates were obtained as reaction intermediates. In fact, these thiolsulfonates were also reduced to the sulfinates with sodium thiolates or thiophenol/pyridine system, though in the reaction with the butanethiol/pyridine system, the reduction of thiolsulfonates proceeded very slowly. The sulfonate ester which is the most inert species among these derivatives was not reduced, however, in the reaction with sodium thiolate system, the sulfonate ester is reduced eventually to the sulfinate under drastic conditions.

Introduction

Organic sulfonic acids are generally very inert toward any nucleophilic or even electrophilic reagent, and hence it is very difficult to reduce sulfonic acids with common reducing agents. On the other hand, the reductive cleavage of C-S bond occurs in electrolytic reduction of the sulfonic acids because of the low bond dissociation energy of C-S bond as compared with that of S-O bond(S=O 110 kcal/mol, C-S 70 kcal/mol).[1] Thus, it is necessary to convert the sulfonic acids to the sulfonic acid derivatives such as sulfonic anhydride, sulfonyl halide, sulfonate ester, and thiolsulfonate in order to activate the central sulfur atom of the sulfonic acids to be ready for the reduction. The reductions of the sulfonyl chlorides to the corresponding thiols with Zn-HCl,[2] $SnCl_2$-HCl,[3] or $NaBH_4$-$AlCl_3$,[4] and of the sultone with $LiAlH_4$, $LiAlH_4$-$AlCl_3$[5] have hitherto been reported, however in the reduction with strong reducing agents, it is impossible to isolate any reduction intermediate such as sulfinic acid. As to the reduction of sulfonyl derivatives to sulfinic acids, the γ-ray radiolysis, electrolysis of the sulfonyl chloride,[6] the reactions of sulfonyl chloride with thiol[7], and that of thiolsulfonate with thiol[8] and CN^- [9,10] etc have been reported.

$$RSO_2Cl \xrightarrow[\text{or } 2e^-]{\gamma\text{-ray}} RSO_2\cdot \longrightarrow RSO_2H \quad \text{----------(1)}$$

$$RSO_2Cl + 2\ R'S^- \longrightarrow RSO_2^- + R'SSR' \quad \text{----------(2)}$$

$$RSO_2SR' + :Nu^- \longrightarrow RSO_2^- + R'SNu\ (:Nu^- = R'S^-,\ CN^-,\ \text{or}\ OH^-) \quad \text{--(3)}$$

Since thiols are mild reducing agents and some thiols such as glutathione and cysteamine are good biological reducing agents,

the reduction of many sulfonic acid derivatives to the corresponding sulfinic acids has been investigated in detail.

Results and Discussion

a) Sulfonic Anhydride:

$$(RSO_2)_2O + 2\ R'SNa \xrightarrow{Ar} RSO_2Na + R'SSR' + RSO_3Na \quad ---(4)$$

The reaction of sulfonic anhydrides with sodium thiolate is exothermic, and is completed in five minutes to give equimolar mixtures of sulfinic acids and disulfides. It is difficult to isolate sodium sulfinate formed, while the sulfinic acid formed upon acidification disproportionates readily to the following products.[11-16]

$$3\ RSO_2H \longrightarrow RSO_2SR + RSO_3H + H_2O \quad ----------(5)$$

Therefore it is desirable to trap the sulfinate by the conversion to the stable sulfone by treatment with methyl iodide or benzyl chloride, or to convert the sulfinic acid to methyl sulfinate upon treating with diazomethane. A mixture of pyridine/thiol instead of sodium thiolate can reduce the sulfonyl halide to the sulfinate, but in this case, the reaction depends on the kind of the thiol. The thiols which have low pKa values like thiophenol(pKa=7) have good reducing abilities as compared with butanethiol(pKa=11). Thus the result suggests that the active species in this reaction is thiolate anion. Since the thiolsulfonate was obtained in this reaction of sulfonic derivatives with butanethiol, the thiolsulfonate is the intermediate in this reaction (Table 1).

b) Sulfonyl Chloride:

As both arene- and alkanesulfonyl bromides and sulfonyl

iodides are generally unstable to light or even heating, only the reduction of sulfonyl chlorides has been studied. As in the case of the sulfonic anhydride, the sulfonyl chloride was easily reduced to the sulfinate and the disulfide in the reaction with sodium thiolate or thiol/pyridine system.

$$RSO_2Cl + 2\ R'SNa \xrightarrow[EtOH]{Ar} RSO_2Na + R'SSR' + NaCl \quad \text{------(6)}$$

c) Thiolsulfonate:

Since thiolsulfonate was obtained in the reaction of the sulfonic anhydride with butanethiol/pyridine system, the thiolsulfonate is considered to be the reaction intermediate in the reaction of the sulfonic acid derivatives with the thiols to the sulfinic acids. In fact, the thiolsulfonate was easily reduced to the sulfinate with sodium thiolate or thiophenol/pyridine system, while, in the reaction with butanethiol/pyridine system, the thiolsulfonate was reduced very slowly under refluxing condition.

d) Sulfonate Ester:

The sulfonate esters are rather inert sulfonic acid derivatives as compared to the former three derivatives, however nucleophiles may attack both the central sulfur and the α-carbon; especially alkyl esters are strong alkylating agents. Therefore, the reduction is limited only to the aryl sulfonate esters in which the α-carbon is an aromatic SP^2 carbon. However generally, aryl sulfonate esters can not be reduced readily by the thiophenol/pyridine system alone, but could be reduced by sodium thiolate under rather drastic conditions.

Table 1. Reduction of Sulfonic Anhydride and Sulfonyl Chloride with Thiol/Py or Sodium Thiolate System[a)]

$$R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}\text{-}X + 2\ R'SH/Py \text{ or } 2\ R'SNa \xrightarrow{\text{under Ar}} RSO_2H + R'SSR' + Py.HX \text{ or } NaX$$

R-	-X	Reagent	Solvent	Condition	RSO_2H(%)	R'SSR'(%)
Me-	$-OSO_2Me$	PhSNa	EtOH	r.t. 5 min	41	93
p-Tol-	$-OSO_2$Tol-p	n-BuSNa	EtOH	r.t. 5 min	84	85
Ph-	-Cl	PhSNa	EtOH	r.t. 5 min	89	90
Ph-	-Cl	$NaS(CH_2)_3SNa$	EtOH	0°C 5 min	98	100(polymer)
Me-	-Cl	PhSNa	EtOH	0°C 5 min	47	98
Me-	-Cl	$NaS(CH_2)_3SNa$	EtOH	0°C 5 min	38	100(polymer)
Me-	$-OSO_2Me$	PhSH/Py	CH_3CN	r.t. 5 min	65	78
Ph-	-Cl	PhSH/Py	CH_3CN	r.t. 5 min	86	100

a)[Sulfonic Anhydride or Sulfonyl Chloride]/[Thiol or Thiolate]=1/2.1

$$(CH_3SO_2)_2O \xrightarrow[\text{r.t. 90 min}]{\text{n-BuSH/Py}} \underset{47\%}{CH_3SO_2SBu\text{-}n}$$

$$p\text{-}TolSO_2OPh \xrightarrow[\text{ether}]{\text{n-BuSNa 55h. reflux}} \underset{34\%}{p\text{-}TolSO_2H} + \underset{58\%}{(n\text{-}BuS)_2}$$

Table 2. Reduction of Thiolsulfonate with Thiol/Py or Sodium Thiolate System[a)]

$$RSO_2SR' + \underset{\text{or R'SNa}}{\text{R'SH/Py}} \xrightarrow{\text{under Ar}} RSO_2H + R'SSR'$$

RSO_2SR'	Reagent	Solvent	Condition	RSO_2H(%)[b)]	R'SSR'(%)
p-$TolSO_2S$Bu-n	n-BuSNa	EtOH	r.t. 5 min	90	96
$MeSO_2S$Bu-n	n-BuSNa	EtOH	r.t. 10 min	63	87
$MeSO_2S$Ph	PhSH/Py	CH_3CN	r.t. 10 min	69	100
$MeSO_2S$Bu-n	n-BuSH/Py	CH_3CN	reflux 4h	trace	-

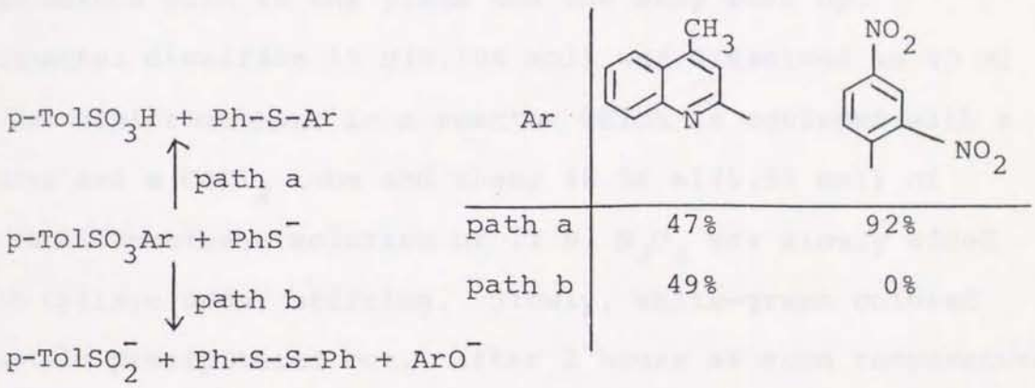
a) [Thiolsulfonate]/[Thiol or Thiolate]=1/1.1

b) The yield of sulfinic acid was determined as sulfinic acid derivatives by the following reactions

$$RSO_2Na + R'X \xrightarrow[\text{r.t., over night}]{\text{EtOH-}H_2O} R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}\text{-}R'$$

$$RSO_2H + CH_2N_2 \xrightarrow[\text{ether, 0°C, 30 min}]{} R\text{-}S(=O)OCH_3$$

Since aryl arenesulfonates possess an activated central sulfur atoms, I attempted to reduce p-nitrophenyl arenesulfonate; however we could not get any favorable result. Meanwhile, in 1962 Bunnett et al reported that the reaction of 2,4-dinitrophenyl p-toluenesulfonate[17,18] or 2-p-toluenesulfonoxy lepidine[19] bearing electron-withdrawing substituents with thiols or amines gave rise to both C-O and O-S bond cleavage to afford a mixture of the corresponding sulfonic acid(path a, no reduction) and the sulfinic acid(path b, reduction), but in the former case, the formation of sulfonic acid was the main path.



Ar		
path a	47%	92%
path b	49%	0%

Experimental

General: Benzenesulfonyl chloride, methanesulfonyl chloride, thiophenol, butanethiol, 1,3-propanedithiol, diphenyl disulfide, and dibutyl disulfide were obtained from Wako Chemicals. Co.

The Preparation of Sulfonic Anhydride

Sulfonic anhydrides were prepared either by treating the disulfides with N_2O_4 [20] or by the reaction of sulfonic acids with P_2O_5 [21] in moderate yields. Recently, Michals reported an excellent reaction to afford sulfonic anhydride by treatment of sulfonic acid with succinyl dichloride. This is the best method both in the yield and the easy work up.

a)Dimethyl disulfide 10 g(0.106 mol) was dissolved in 20 ml of tetrachloromethane in a reactor which is equipped with a cooler and a $CaCl_2$ tube and then, 48.56 ml(0.53 mol) of tetrachloromethane solution of 11 N. N_2O_4 was slowly added with cylinge under stirring. Slowly, white-green colored crystals precipitated out. After 2 hours at room temperature, temperature was elevated at 40°C and the mixture was stirred for 2 hours. After the reaction, solvent was evaporated and the residue was recrystallized with ether to obtain methanesulfonic anhydride in 85% yield.

$(CH_3SO_2)_2O$ yield 85% mp=68-69.5°C(lit,[20] 69.5-70.5°C)

IR(KBr) 750cm^{-1}(s) 1380cm^{-1}(s) 1180cm^{-1}(s)

NMR($CDCl_3$) 3.4ppm(s)

This method cannot be applied to diaryl disulfide since the yield of sulfonic anhydride was very poor.

A mixture of 30 g of P_2O_5 and 10 g of silica-gel was added to a reactor equipped with a $CaCl_2$ tube. Then a mixture of 20.1 g of p-toluenesulfonic acid and 3 g of glass wool was added into this mixture under stirring. The mixture was kept standing for 9 hours at 120-130°C under occasional stirring. As the reaction proceeded, the mixture became a completely homogeneous brown colored liquid. After this reaction, 42 ml of dichloromethane was added and the solution was decanted 3 times. This dichloromethane solution was evaporated and the residue was recrystallized with a mixed solvent of benzene and ether.

$(CH_3-C_6H_4-SO_2)_2O$ yield 10%

mp=131-133°C(lit,[20] 129-130°C)

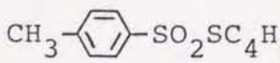
IR(KBr) 1400cm^{-1}(s) 1175cm^{-1}(s) 1200cm^{-1}(s) 730cm^{-1}(s)

b) Succinyl dichloride 1032 mg(6.6 mmol) and 1269 mg(13.2 mmol) of methanesulfonic acid were added into a reactor which was equipped with a $CaCl_2$ tube. Soon, hydrogen chloride gas was generated to give a mixed-anhydride. The mixture was kept standing for 2 hours at 60°C under stirring. After this reaction, dry ether was added and the solution was decanted a few times. Succinic anhydride was obtained from this residue in 73-84% yield. Sulfonic anhydride was obtained from this ether solution in 90% yield. p-Toluenesulfonic anhydride was also obtained similarly by this procedure in 87% yield.

The Preparation of Thiolsulfonate

Dibutyl disulfide was placed in a reactor which was equipped with a $CaCl_2$ tube and while the reaction was cooled at -10°C

to -20°C, chlorine gas was introduced into this reactor, maintaining this temperature. The color of the reacting solution soon changed to red which is the color of the sulfenyl chloride. After the reaction, the solvent was evaporated and the residue was distilled to give butanesulfenyl chloride. After 415 mg(3.33 mmol) of butanesulfenyl chloride was dissolved into tetrachloromethane under cooling at 0°C, a mixture of 315 mg(4 mmol) of pyridine and tetrachloromethane were slowly added into the reaction mixture to obtain a precipitation. Then a mixture of 519 mg(3.33 mmol) of p-toluenesulfinic acid and tetrachloromethane was slowly added to this mixture while maintaining the temperature. After the addition, the reaction mixture was kept standing for 30 min, and then the reaction mixture was poured into benzene, which was then washed with water, dried over $MgSO_4$. The thiolsulfonate obtained was purified with column chromatography(silica-gel, eluent: benzene/hexane=1/1)



yield 98%

NMR($CDCl_3$) 0.9ppm(m, 3H)
1.5ppm(m, 4H)
7.25ppm(d, 2H)
2.55ppm(s, 3H)
7.7ppm(d, 2H)
2.9ppm(t, 2H)

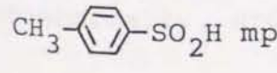
TLC(eluent:benzene) R_f=0.5

IR(KBr) 810cm^{-1}(m)
1080cm^{-1}(m) 1140cm^{-1}(s)
1320cm^{-1}(s)

Found: C; 54.17,H; 6.64

Calcd for $C_{11}H_{16}O_2S_2$: C; 54.06, H; 6.59

p-Toluenesulfinic acid was obtained by acidification of the commercial sample of sodium p-toluenesulfinate.



mp=84-85°C (lit,[23] 84-85°C)

Methanesulfinic acid was obtained by the following method. A mixture of 5 g(53 mmol) of dimethyl disulfide and 10.8 g (106 mmol) of acetic anhydride was placed in a reactor which was equipped with a $CaCl_2$ tube under cooling at -10°C to -20°C. Into this solution, chlorine gas was introduced maintaining the same temperature. Color of the solution changed to yellow, red and finally green-yellow. After the reaction, solvent was evaporated and the residue was distilled to afford methanesulfinyl chloride.[24)]
A mixture of 1 g(10 mmol) of methanesulfinyl chloride and tetrachloromethane was slowly added to a cooled etheral water solution(0°C). After the mixture was stirred for 0.5 hour, the reaction mixture was acidified further and extracted with ether to afford methanesulfinic acid. Various thiolsulfonates were synthesized by the same procedure as in the case of p-$TolSO_2SBu$-n.

$CH_3SO_2SC_4H_9$-n yield 78% NMR($CDCl_3$) 0.95ppm(m 3H), 1.6ppm(m 4H)
3.2ppm(t 2H), 3.4ppm(s 3H)

IR(NaCl) 1320cm^{-1}(s), 1135cm^{-1}(s)

Found: C;35.89, H;7.29
Calcd for $C_5H_{12}S_2O_2$: C;35.68, H;7.18

$CH_3SO_2SC_6H_5$ mp=82-83°C(lit,[25)] 85-86.5°C)

The Reaction of Sulfonic Acid Derivatives with Sodium Thiolates

Metal sodium 137 mg(5.95 mmol) was dissolved into 20-30 ml of dry ethanol under argon atmosphere and then 6.23 mmol of a thiol was added to prepare the sodium thiolate. As soon as 2.83 mmol of the sulfonic anhydride or the sulfonyl chloride was slowly added into this mixture, the reaction proceeded exothermically, and the starting material was no longer

present after 5 min. The mixture was poured into water and washed with chloroform, then the solution was dried over $MgSO_4$. Upon evaporation of solvent, a mixture of the disulfide and a small amount of thiol were obtained. Disulfides were identifical to the commercial samples. Meanwhile after the water solution containing sodium sulfinate was concentrated to about 3-5 ml solution which was mixed with ethanol(EtOH/H_2O=1/1=v/v). Into this solution 14.15 mmol of methyl iodide was added and the mixture was stirred over night. After the reaction, the reaction mixture was poured into benzene which was then washed with 0.5 N. $Na_2S_2O_3$ solution, water, dried over $MgSO_4$, and evaporated to give the sulfone.

$CH_3SO_2CH_3$ NMR($CDCl_3$) 3.0ppm(s) mp=108-109°C(lit,[26] 109°C)

$CH_3SO_2CH_2C_6H_5$ NMR(CCl_4) 2.54ppm(s 3H) 4.1ppm(s 2H) 7.3ppm(s 5H) mp=124-125°C(lit,[26] 127°C)

$C_6H_5SO_2CH_3$ NMR($CDCl_3$) 3.0ppm(s 3H) 7.54ppm(m 3H) 7.86ppm(m 2H) mp=87-88°C(lit,[26] 88°C)

p-$CH_3C_6H_4SO_2CH_3$ NMR($CDCl_3$) 2.45ppm(s 3H) 3.0ppm(s 3H) 7.28ppm(d 2H) 7.75ppm(d 2H) mp=84-85°C(lit,[27] 87°C)

The Reaction of Thiolsulfonate with Sodium Thiolate

After 49.5 mg(2.15 mmol) of metal sodium was dissolved into 50 ml of dry ethanol, 203 mg(2.25 mmol) of butanethiol was added to this solution. As soon as 500 mg(2.05 mmol) of S-butyl p-toluenethiosulfonate was slowly added to this mixture, the thiolsulfonate was consumed completely after 5 min. After this reaction, the reaction mixture was poured into water which was then washed with chloroform. This organic solution was dried over $MgSO_4$ and then upon evaporation of solvent dibutyl disulfide was obtained in 90% yield.

The water solution was treated with the same method in the case of sulfonic anhydride or sulfonyl chloride to give the corresponding sulfone.

The Reaction of Sulfonic Acid Derivatives with Thiol/Pyridine

After 2.83 mmol of the sulfonic anhydride or the sulfonyl chloride was dissolved into 20-30 ml of dry acetonitrile under argon atmosphere, 6.23 mmol of thiophenol and 6.23 mmol of pyridine were added to this mixture in this order. After 5 or 10 min, the starting material was completely consumed. After the reaction, the mixture was treated with the same procedure as in the case of sodium thiolate.

The Preparation of Phenyl p-Toluenesulfonate

In a reactor, 31.47 mmol of p-toluenesulfonyl chloride and 94.41 mmol of phenol were dissolved in a mixture of 10 ml of benzene and 10 ml of acetonitrile and the whole mixture was stirred. Then, 157 mmol of pyridine was added to this mixture. After 30 min, the starting sulfonyl chloride was no longer present upon analysis with TLC. The solution was poured into benzene, washed with water for 3 times, and dried over $MgSO_4$. The sulfonate ester was recrystallized to obtain pure sample in 50-60% yield.

$p\text{-}CH_3C_6H_4SO_3C_6H_5$ mp=92-93°C(lit,[28] 93°C)

Phenyl p-toluenesulfonate ester could not be easily reduced because of its rather low reactivity, however under refluxing in ether for 55 hours in the presence of excess sodium thiolate not thiol/pyridine, p-toluenesulfinate was obtained in 34% yield.

References

1) S.W.Benson, Chem. Review., 78, 23(1978).
2) P.P.Caeser,"Organic Syntheses", Coll. Vol. IV, 695(1963).
3) C.S.Marvel, P.D.Caeser, J. Amer. Chem. Soc., 73, 1097(1951).
4) H.C.Brown, B.C.S.Rao, ibid., 78, 2582(1956).
5) H.C.Brown, P.M.Weissman, ibid., 87, 5614(1965).
6) S.G.Mairanovski, M.B.Heiman, Dokl. Akad. Nauk. SSSR., 79, 85(1951).
7) C.J.Miller, S.Smiles, J. Chem. Soc., 224(1925).
8) F.Ostermayer, P.S.Tarbell, J. Amer. Chem. Soc., 82, 3752 (1960).
9) S.Smiles, P.T.Gibson, J. Chem. Soc., 176(1924).
10) G.Leandri, A.Tundo, Ann. Chim., 44, 255(1954).
11) C.Pauly, R.Otto, Ber., 10, 2182(1877).
12) J.L.Kice, K.W.Bowers, J. Amer. Chem. Soc., 84, 605(1962).
13) E.H.Beck, H.Berlinger, K.G.Kottenhahn, Angew. Chem., 70 268(1958).
14) P.Allen, L.Reich, J. Phys. Chem., 64, 1928(1960).
15) C.M.Bere, S.Smiles, J. Chem. Soc., 125, 2359(1924).
16) J.von.Braun, K.Weissbach, Ber., 63, 2837(1930).
17) J.F.Bunnett, J.Y.Bassett, J. Amer. Chem. Soc., 81, 2014 (1959).
18) J.F.Bunnett, J.Y.Bassett, J. Org. Chem., 27, 1887(1962).
19) J.F.Bunnett, J.Y.Bassett, ibid., 27, 2345(1962).
20) N.Kunieda, S.Oae, Bull. Chem. Soc. Jpn., 41, 233(1968).
21) Organic Syntheses, 4, 940.
22) M.H.Karger, Y.Mazur, J. Org. Chem., 36, 528(1971).
23) R.K.Burkhard, D.E.Sellers, F.Decov, J.L.Lambert, J. Amer. Chem. Soc., 72, 1215(1950).
24) I.B.Douglass, D.R.Poole, J. Org. Chem., 22, 536(1957).
25) T.Takata, Y.H.Kim, S.Oae, Bull. Chem. Soc. Jpn., 54, 1443 (1981).
26) C.M.Sutter,"The Organic Chemistry of Sulfur", J.Wiley and Sons, Inc., 683(1964).
27) L.Katz, L.S.Karger, W.Schroeder, M.S.Cohen, J. Org. Chem., 18, 1380(1953).
28) H.Gilmann, N.J.Beaber, C.H.Myers, J. Amer. Chem. Soc., 47, 2047(1925).

Chapter 2.

Reaction of Sulfinic Acid and Thiol

Abstract

Sulfinic acid reacts with thiol to give two kinds of disulfides and only one kind of thiolsulfonate. The reaction proceeds via the formation of sulfinylsulfone and thiolsulfinate. In the presence of trimethylsilyl chloride, however the reaction gave disulfides as the only products, since the reactive intermediate is corresponding sulfinyl chloride.

Introduction

Sulfinic acid is a considerably strong acid and the pKa values of arene- and alkanesulfinic acids are about 1.2 and 2.2, respectively.[1] Sulfinic acids are not very stable thermodynamically, easily disproportionate to give thiolsulfonates, sulfonic acids and water.[2] Horner and Basedow have shown that the disproportionation of benzenesulfinic acid is represented by the following equation.

$$3\ PhSO_2H \longrightarrow PhSO_3H + PhSO_2SPh + H_2O \quad \text{--------(1)}$$

Addition of acid species accelerates this disproportionation. Reduction of the sulfinic acid has been relatively little studied. Electrolytic,[3] lithium aluminium hydride,[4] ethyl hypophosphite,[5] HI(HBr),[6] or Me_3SiI[7] reduction gives the corresponding disulfide, while there is a reductive transformation of sulfinic acid to thiocyanate by treatment with diethyl phosphorocyanidate.[8] Thiols are mild reducing agents to reduce such organosulfur compounds as sulfoxide,[9] sulfinic acid,[10] thiolsulfinate,[11, 12] thiolsulfonate,[12] and sulfonyl chloride.[13]

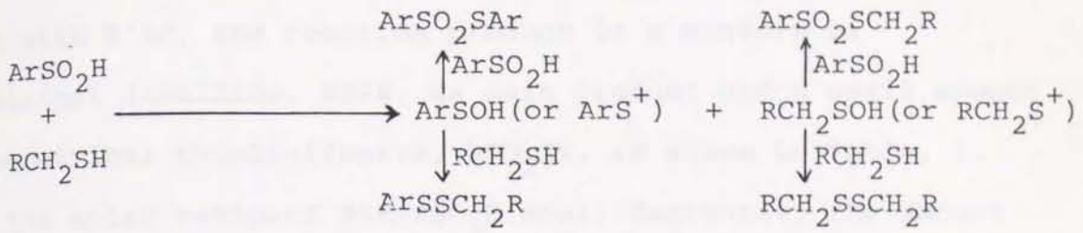
However, the reaction of sulfinic acid and thiol has not been studied. Therefore we have studied the reaction of sulfinic acid with thiol.

Kice et al reported earlier the reaction of sulfinic acid and dialkyl sulfide to form two kinds of thiolsulfonates and aldehyde as shown by eq, (2).

$$ArSO_2H + RCH_2SCH_2R \xrightarrow[AcOH-H_2O-H_2SO_4]{70\,^\circ C} ArSO_2SAr + ArSO_2SCH_2R + RCHO \quad \text{--(2)}$$

As a blank experiment in this study, they have studied the

reaction of p-toluenesulfinic acid and butanethiol to give the mixture of p-$TolSO_2STol$-p, p-$TolSO_2SBu$-n, p-TolSSBu-n, and n-BuSSBu-n, and have suggested that the reaction proceeded via the following Scheme.



Namely, in the initial stage, treatment of $ArSO_2H$ with RCH_2SH leads to the sulfenic acids, ArSOH and RCH_2SOH by multi-steps, and these intermediates then react rapidly with either sulfinic acid or thiol.[14] However they did not study the reaction pathways in detail and the suggested reaction pathway is quite ambiguous.

Results and Discussion

The reactions of sulfinic acids and thiols were carried out in refluxing methylene chloride under argon atmosphere. When both groups, R and R' are identical in the reaction of RSO_2H with R'SH, the reaction product is a mixture of symmetrical disulfide, RSSR, as main product and a small amount of symmetrical thiolsulfonate, RSO_2SR, as shown in Table. 1. When the molar ratio of RSH/RSO_2H(mmol) decreases, the amount of the by-product, thiolsulfonate, increases.

Table. 1. Reaction of Sulfinic Acid and Thiol I.[a)]

$$RSO_2H + 3\ RSH \xrightarrow[\text{reflux in } CH_2Cl_2]{Ar} 2\ RSSR + 2\ H_2O$$

R-	[RSH]/[RSO_2H]	Time (h)	RSSR (%)	RSO_2SR (%)	Recovered (%)
CH_3O- 	5	19	70	0	30
CH_3- 	5	19	73	0	4.3
CH_3- 	3	44	88	12	not determined
	5	19	70	0	0
Cl- 	5	19	100	0	0
n-Butyl-	5	20	37	15	6.4
n-Butyl-	5	25	35	25	5.2
n-Pentyl-	5	20	17	15.3	24
n-Pentyl-	5	25	38	21.4	10.5

a) Yields were calculated based on RSO_2H.

Table. 2. Reaction of Sulfinic Acid with Thiol II.

$$RSO_2H + 3R'SH \xrightarrow[\text{reflux in } CH_2Cl_2]{Ar} RSSR'^{a)} + R'SSR' + 2\ H_2O$$

R-	R'-	[R'SH]/[RSO_2H]	Time (h)	RSSR'[b] (%)	R'SSR'[b] (%)	RSO_2SR (%)	RSO_2SR' (%)
CH_3-C$_6$H$_4$-	C$_6$H$_5$-	5	19	70	80	0	0
CH_3-C$_6$H$_4$-	Cl-C$_6$H$_4$-	5	19	78	100	0	2.1
CH_3-C$_6$H$_4$-	n-Butyl-	5	19	74	56.2	trace	9
CH_3-C$_6$H$_4$-	n-Butyl-	3	41	81.3	76.1	0	17
C$_6$H$_5$-	CH_3-C$_6$H$_4$-	5	19	64	64	0	14
Cl-C$_6$H$_4$-	CH_3-C$_6$H$_4$-	5	19	80	88	0	7.7
n-Butyl-[c]	C$_6$H$_5$-	5	20	24	25	trace	not determined
n-Pentyl-[d]	C$_6$H$_5$-	5	27	42.3	45	0	0

a) Disproportionation of unsymmetrical disulfide was found to be negligible under these reaction conditions. b) Determined by NMR measurement. c), d) Starting sulfinic acids were recovered in 20% and 27%, respectively.

Generally, when both R and R' groups in sulfinic acid and thiol respectively are aromatic groups, sulfinic acid can be readily reduced and the main product is disulfide alone, whereas, when those groups in sulfinic acid and thiol are aliphatic, the reaction is slow and a considerable amount of thiolsulfonate is formed.

While, when both groups of R and R' are different, the reaction product is a mixture of two kinds of disulfides(major) and a small amount of unsymmetrical thiolsulfonate as shown in Table 2. The data in this Table reveals that arenethiol which has an electron-withdrawing substituent can reduce sulfinic acid to corresponding disulfide more readily than that which has an electron-donating group.

Meanwhile, an arenesulfinic acid which has an electron-withdrawing substituent can be reduced faster than that which has an electron-donating group. Another important feature is that, when the molar ratio of $R'SH/RSO_2H$ decreases, the formation of unsymmetrical thiolsulfonate, RSO_2SR', increases. This process is obviously a result of multi-step reactions, and would involve a few intermediates, such sulfinylsulfone, thiolsulfonate, and thiolsulfinate during the reaction.

$$2\ ArSO_2H \underset{60\%}{\overset{Keq}{\rightleftharpoons}} \underset{\sim 0.01\%}{ArS(=O)SAr} + H_2O \qquad \text{----------(3)}$$

(H_2O-dioxane)

Kice et al[15] have reported that the sulfinylsulfone and sulfinic acid is in an equilibrium. Therefore, the reaction of sulfinylsulfone and thiol has been examined.

The reaction was carried out at r.t. in methylene chloride as shown in Table 3. In the reaction of di-p-tolyl

sulfinylsulfone and thiophenol, formations of two kinds of disulfides, i.e. PhSSPh and p-TolSSPh in high yields, and a small amount of one kind of unsymmetrical thiolsulfonate, p-$TolSO_2SPh$, have been observed.

Table 3. Reaction of Sulfinylsulfone and Thiol[a)]

$RS(O)SR$	R'SH	$[RS(O)SR]/[R'SH]$	Time (h)	RSSR' (%)	R'SSR' (%)	RSO_2SR (%)	RSO_2SR' (%)
p-TolS(O)STol-p	p-TolSH	1/5	2	50(R=R')-		23	-
p-TolS(O)STol-p	PhSH	1/5	2	74	78	trace	32

a) These reactions were carried out in CH_2Cl_2 at room temperature.

These results are very similar to the those of the reaction of p-toluenesulfinic acid and thiophenol shown in Table 2. Why the yield of thiolsulfonate, RSO_2SR', is very low in the reaction of sulfinic acid, RSO_2H, and thiol, R'SH? The reason may be that, under our conditions(reflux in CH_2Cl_2, 19 h), thiolsulfonate would be reduced by thiol to a mixture of disulfide and sulfinic acid. Therefore, thiolsulfonate formed in the reaction of thiol with sulfinylsulfone produced in-situ from sulfinic acid, would be reduced further by thiol to disulfide and sulfinic acid

Table 4. Reaction of Thiolsulfonate with Thiol[a)]

$RSO_2SR(R')$	R'SH	$\frac{[R'SH]}{[RSO_2SR(R')]}$	RSO_2H (%)	RSSR (%)	RSSR' (%)	R'SSR' (%)	$RSO_2SR(R')$ (%)
p-$TolSO_2STol$-p	PhSH	5/1[b)]	69	0	88.3	22.4	0
p-$TolSO_2SPh$	PhSH	5/1[b)]	51.3	trace	trace	97	0
$PhSO_2SPh$	PhSH	5/1[b)]	not determined	-	90(R=R')-		0

a) These reactions were carried out in CH_2Cl_2 reflux condition for 19 hours.

Kice et al reported already that the rate-determining step of the disproportionation of sulfinic acid is the formation of sulfenic-sulfonic anhydride from sulfinylsulfone.[16)]

$$ArSO_2H \rightleftharpoons ArS(O)SAr + H_2O$$

$$ArS(O)SAr \xrightarrow{slow} ArS\text{-}O\text{-}S(O)Ar \xrightarrow[fast]{ArSO_2H} ArSO_3H + ArSO_2SAr \quad --(4)$$

All these results listed in Table 2, 3, 4 together with this disproportionation mechanism, may suggest that sulfinylsulfone is one key intermediate in the reaction of sulfinic acid and thiol.

Then, why unsymmetrical thiolsulfonate, RSO_2SR', is formed in the reaction of sulfinic acid, RSO_2H, and thiol, R'SH? We may postulate a second intermediate i.e. thiolsulfinate, since thiolsulfinate is readily reduced by thiol.[11, 12)]

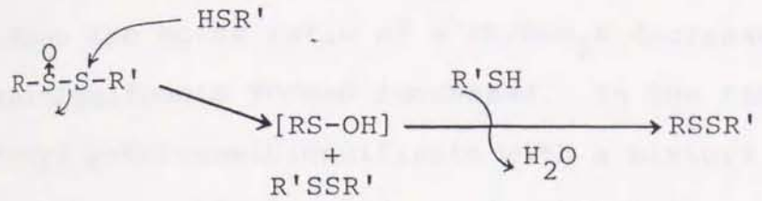
Probably the initial reaction product of either sulfinic acid or sulfinylsulfone with thiol is thiolsulfinate and water, or thiolsulfinate and sulfinic acid respectively. Under our reaction conditions, thiolsulfinate was found to be very readily reduced to disulfide alone.

S-Phenyl p-toluenethiosulfinate which is presumed to be formed in the reaction of p-toluenesulfinic acid and thiophenol, can be reduced to PhSSPh and PhSSTol-p alone by thiophenol. The reaction obviously proceeds via nucleophilic attack of thiol on the sulfenyl sulfur of thiolsulfinate.

Table 5. Reaction of Thiolsulfinate with Thiol[a)]

$RS(O)SR'$[a)]	R'SH	$\frac{[RS(O)SR']}{[R'SH]}$	Time (h)	RSSR' (%)	R'SSR' (%)	RSO_2SR (%)	RSO_2SR' (%)
p-TolS(O)STol-p	p-TolSH	$\frac{1}{3}$	7	99(R=R')	-	0	-
p-TolS(O)SPh	PhSH	(R≠R') $\frac{1}{3}$	3.5	95	106	0	0

a) These reactions were carried out in CH_2Cl_2 at room temperature.

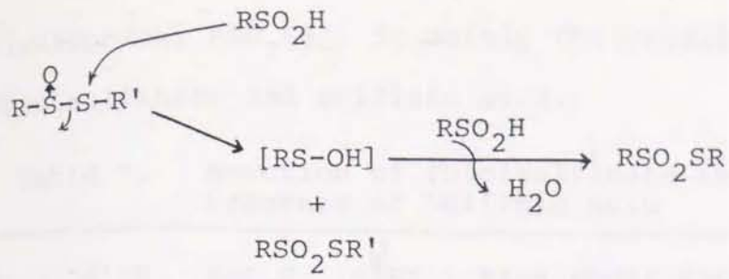


Meanwhile, thiolsulfinate was found to react with sulfinic acid to give mainly thiolsulfonate alone more readily than thiol since the reaction is acid-catalyzed and sulfinic acid is stronger acid than thiol. The reaction of S-phenyl p-toluenethiosulfinate with p-toluenesulfinic acid, and also a similar reaction of p-toluenesulfinic acid and thiophenol, gave the two kinds of thiolsulfonates, $p\text{-TolSO}_2\text{STol-p}$ and $p\text{-TolSO}_2\text{SPh}$ alone. Therefore in the reaction of sulfinic acid and thiol, thiolsulfinate once formed in-situ, is believed to react immediately with both thiol and sulfinic acid.

Table 6. Reaction of Thiolsulfinate with Sulfinic Acid[a)]

$RS(O)SR'$	RSO_2H	$\frac{[RS(O)SR']}{[RSO_2H]}$	Time (h)	RSSR (%)	RSSR' (%)	R'SSR' (%)	RSO_2SR (%)	RSO_2SR' (%)
p-TolS(O)STol-p	p-$TolSO_2H$	$\frac{1}{3}$	1	-	4(R=R')	-	98	-
p-TolS(O)SPh		(R≠R') $\frac{1}{3}$	1	2.5	4.1	trace	77	96

a) These reaction were carried out in CH_2Cl_2 at room temperature.



Therefore we have carried out the reaction of thiolsulfinate and thiol in the presence of sulfinic acid as shown in Table 7. When the molar ratio of $R'SH/RSO_2H$ decreased, the amount of thiolsulfonate formed increased. In the reaction of S-phenyl p-toluenethiosulfinate with a mixture of thiophenol and p-toluenesulfinic acid, as in the similar reaction of p-toluenesulfinic acid and thiophenol, we obtained two kinds of disulfides, i.e. p-TolSSPh and PhSSPh, and only one kind of unsymmetrical thiolsulfonate, $p\text{-TolSO}_2\text{SPh}$. From all these separate experiments, i.e. the reactions of sulfinylsulfone, thiolsulfonate, and thiolsulfinate with thiol or sulfinic acid, we may safely conclude the following multi-step pathways. The initial formation of sulfinylsulfone from sulfinic acid is an equilibrium state but this equilibrium constant is rather small as Kice et al proposed. Once sulfinylsulfone is formed, this can react with thiol very readily to give a mixture of thiolsulfinate and sulfinic acid. Thiolsulfinate can also react readily with thiol or sulfinic acid. When it reacts with thiol, disulfide is formed, while when it reacts with sulfinic acid, the product is thiolsulfonate. Therefore when the molar ratio of $R'SH/RSO_2H$ is large, the amount of disulfide formed increases. The rate-determining step in the reaction of sulfinic acid and thiol is the formation of sulfinylsulfone, and the formation of unsymmetrical

thiolsulfonate, RSO_2SR', is mainly the result of the reaction of thiolsulfinate and sulfinic acid.

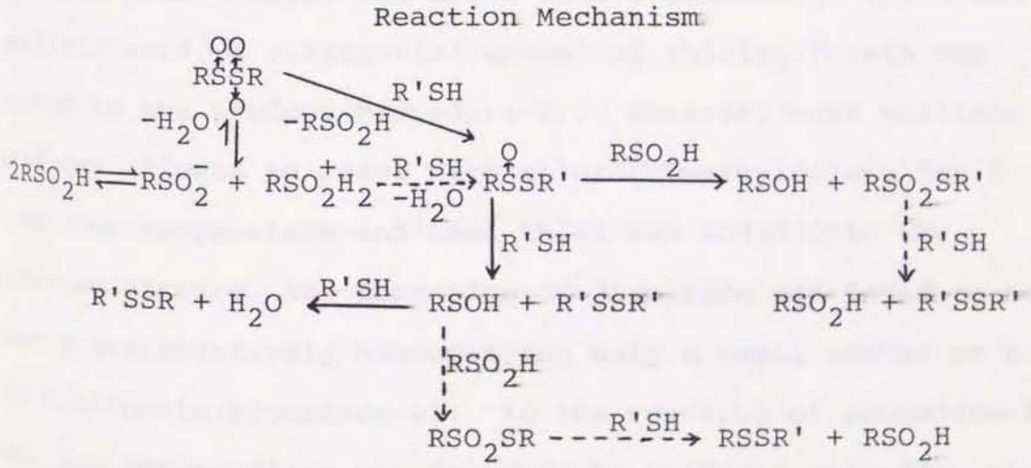
Table 7. Reaction of Thiolsulfinate and Thiol in the Presence of Sulfinic Acid

$R\overset{O}{\overset{\uparrow}{S}}SR'$	R'SH	RSO_2H	$\frac{[R\overset{O}{\overset{\uparrow}{S}}SR']}{[R'SH]}\frac{}{[RSO_2H]}$	Time (h)	RSSR' (%)	R'SSR' (%)	RSO_2SR (%)	RSO_2SR' (%)
p-Tol$\overset{O}{\overset{\uparrow}{S}}$STol-p	p-TolSH	p-TolSO_2H	1/4/1	5	62(R=R')-		40	-
p-Tol$\overset{O}{\overset{\uparrow}{S}}$STol-p	p-TolSH	p-TolSO_2H	1/2/2	5	51(R=R')-		49	-
p-Tol$\overset{O}{\overset{\uparrow}{S}}$SPh	PhSH(R≠R')	p-TolSO_2H	1/5.8/1	3	88(R≠R')	52	2.5	54.4

These reactions were carried out in CH_2Cl_2 at room temperature.

In this reaction shceme, the block lines are the main reaction path and the dotted lines are the minor reaction path, while the formation of sulfinylsulfone is the rate-determining step. Although we could not detect or isolate any of the intermediates, such as sulfinylsulfone, thiolsulfinate, and sulfenic acid because of the high reactivities of these intermediates with nucleophiles such as thiol, all these intermediates have been shown to give the same products as in the reaction of sulfinic acid and thiol.

Reaction Mechanism



II. Facile Reduction of Sulfinic Acid to Disulfide with Thiol and Chlorotrimethylsilane

We have found recently that sulfoxides can be reduced to the corresponding sulfides upon treatment with thiols in the presence of chlorotrimethylsilane. Apparently silylation of sulfinyl oxygen activated the sulfur atom to be susceptible to the nucleophilic attack of thiol. This thiol/chlorotrimethylsilane system has also been found to be effective in the reduction of sulfinic acid, the reaction shown by eq. 1 being completed within an hour at room temperature.

$$RSO_2H + 3\ R'SH + 4\ (CH_3)_3SiCl \longrightarrow RSSR' + R'SSR' + 2[(CH_3)_3Si]_2O + 4\ HCl \quad \text{--------(1)}$$

This reduction procedure can be applied to all kinds of sulfinic acids including alkanesulfinic acids, sterically hindered ones and those bearing electron-donating substituents, most of which are difficult to be reduced by common procedures to the corresponding disulfides quantitatively. Depending on the sequence of mixing of the reactants, the reaction products were found to be somewhat changed. Namely, when chlorotrimethylsilane was added into a mixture of thiol and sulfinic acid, a substantial amount of thiolsulfonate was formed as the product(Procedure-1). However, when sulfinic acid was allowed to react with chlorotrimethylsilane for 1 h at room temperature and then thiol was added into the reaction mixture, the formation of disulfide was found to be nearly quantitatively accompanying only a small amount or no thiolsulfonate(Procedure-2). In the reaction of procedure-2, the key intermediate was found to be sulfinyl chloride, since

treatment of a mixture of p-toluenesulfinic acid and chlorotrimethylsilane for 30 min in $CHCl_3$ gave quantitatively p-toluenesulfinyl chloride(eq. 2), which upon treatment with p-toluenethiol(eq. 3) at room temperature yielded di-p-tolyl disulfide quantitatively.

$$p\text{-TolSO}_2\text{H} + 2\ (CH_3)_3SiCl \xrightarrow[CHCl_3]{\text{r.t.}} p\text{-TolSOCl} + [(CH_3)_3Si]_2O \quad \text{--(2)}$$
$$30\ \text{min}$$

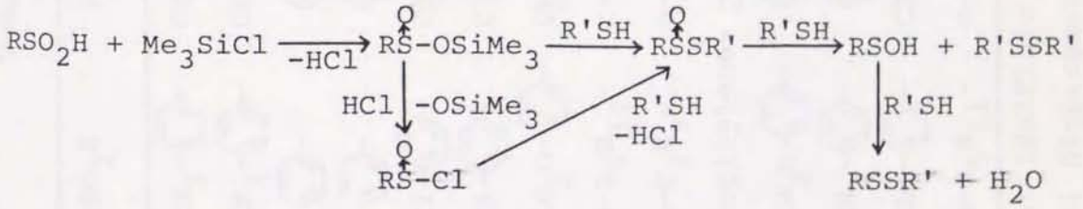
$$p\text{-TolSOCl} + 3\ p\text{-TolSH} \xrightarrow[CHCl_3]{\text{r.t.}} 2\ (p\text{-TolS})_2 + H_2O + HCl \quad \text{-----(3)}$$
$$15\ \text{min}$$

Trimethylsilyl sulfinate is expected to be formed at initial reactions in both procedures. In order to examine the behavior of trimethylsilyl sulfinate toward thiol, a trimethylsilyl sulfinate was prepared by treating silver p-toluenesulfinate with chlorotrimethylsilane and then treated with benzenethiol. A mixture of two disulfides and two thiolsulfonates were obtained as shown in eq. 4.

$$p\text{-TolS}\overset{\nearrow O}{\underset{\searrow OSi(CH_3)_3}{}} + PhSH \xrightarrow[CHCl_3]{\text{r.t. 15 min}} \underset{6.3\%}{p\text{-TolSSPh}} + \underset{4\%}{PhSSPh} +$$
$$\underset{1.9\%}{p\text{-TolSO}_2\text{STol-p}} + \underset{4\%}{p\text{-TolSO}_2\text{SPh}} \quad \text{------(4)}$$

The yields are calculated based on the amount of starting silver p-toluenesulfinate. The low yields of the products would be due to the recovery of a large amount of p-toluenesulfinic acid. Trimethylsilyl p-toluenesulfinate was so sensitive to moisture that most of trimethylsilyl p-toluenesulfinate was hydrolyzed to give starting p-toluenesulfinic acid upon exposure tc moisture during the filtration of silver chloride before the treatment with benzenethiol. The results shown in eqs. 2-4 suggest clearly that the thiolsulfonate is formed by the reaction of benzenethiol with trimethylsilyl

p-toluenesulfinate which is presumed to be formed in the reduction of sulfinic acid with thiol/chlorotrimethylsilane system. All these observations suggest the following mechanism for the reduction of sulfinic acids with a mixture of thiol/chlorotrimethylsilane. The control experiment of the reaction between the thiolsulfinate which is presumed to be one of key intermediates in the reaction of the sulfinic acid with a mixture of thiol/chlorotrimethylsilane, and the thiol gave only the disulfide, but no thiolsulfonate. The different products distributions between the two procedures(1 and 2) depend on whether thiol is present or not when trimethylsilyl sulfinate is formed by the reaction of sulfinic acid with chlorotrimethylsilane. In the procedure-2, most trimethylsilyl sulfinate reacts with chloride anion to give sulfinyl chloride prior to the addition of thiol and eventually affords disulfide nearly quantitatively by the reaction with thiol. On the other hand, since thiol is already present in the reaction system when trimethylsilyl sulfinate is formed in the procedure-1, a substantial amount of thiolsulfonate is formed by the reaction between thiol and trimethylsilyl sulfinate.



When the ratio of R'SH/RSO_2H decreases, the formation of thiolsulfonate increases as shown in Table.

Table. Reaction of Sulfinic Acid with Thiol/Chlorotrimethylsilane at Room Temperature in $CHCl_3$

RSO_2H	R'SH	$\frac{[R'SH]}{[RSO_2H]}$ [a]	Time (h)	RSSR' (%)	R'SSR' (%)	RSO_2SR (%)	RSO_2SR' (%)
CH_3-C$_6$H$_4$-	CH_3-C$_6$H$_4$-	5	0.5[b]	89	-	-	8
CH_3-C$_6$H$_4$-	CH_3-C$_6$H$_4$-	5	1+0.5[c]	99	-	-	1
C$_6$H$_5$-	C$_6$H$_5$-	5	0.5[b]	80	-	-	13
C$_6$H$_5$-	C$_6$H$_5$-	5	1+0.5[c]	95.4	-	-	4.7
Cl-C$_6$H$_4$-	Cl-C$_6$H$_4$-	5	0.5[b]	85	-	-	7
Cl-C$_6$H$_4$-	Cl-C$_6$H$_4$-	5	1+0.5[c]	100	-	-	0
CH_3O-C$_6$H$_4$-	CH_3O-C$_6$H$_4$-	5	0.5[b]	80.4	-	-	6
n-C_5H_{11}-	n-C_5H_{11}-	5	1[b]	92	-	-	0
n-C_4H_9-	n-C_4H_9-	5	1[b]	89	-	-	0
mesitylene-	mesitylene-	5	1[b]	98	-	-	0
CH_3O-C$_6$H$_4$-	C$_6$H$_5$-	5	0.5[b]	59[d]	88	0	6
CH_3-C$_6$H$_4$-	C$_6$H$_5$-	5	1+0.5[c]	87	100	0	0
CH_3-C$_6$H$_4$-	CH_3-C$_6$H$_4$-	3.1	0.5[b]	68	-	-	8.2
n-C_5H_{11}-	n-C_5H_{11}-	3.1	1.0[b]	84	-	-	12.4

a) [Sulfinic Acid]/[Me_3SiCl]=1/5. b) Procedure-1. c) Procedure-2.

d) Disproportionation product [(p-$CH_3OC_6H_4S)_2$] was also obtained in 11% yield.

Experimental

Materials. Following thiols and disulfides, i.e. thiophenol, butanethiol, p-toluenethiol, p-methoxybenzenethiol, p-chlorobenzenethiol, and pentanethiol, diphenyl disulfide, dibutyl disulfide, and dipentyl disulfide, and sodium benzenesulfinate, sodium p-toluenesulfinate, and chlorotrimethylsilane were all obtained from Wako Chemicals Co.

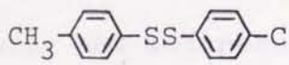
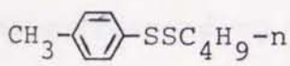
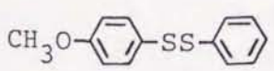
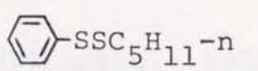
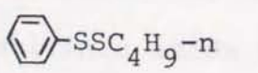
Apparatus. All melting points were measured by Yanako instrument, IR spectra were taken on Hitachi-215 spectrometer, NMR spectra of the compounds were taken with a Hitachi Perkin-Elmer R-20 spectrometer, and GAS chromatograph was taken with Hitachi 163 using OV-1 1 m glass column or SE-30 1 m glass column.

Preparation of Disulfides. To a benzene solution(150 ml) of thiol(0.05 mol) and pyridine(0.055 mol) was added dropwise iodine(0.025 mol) dissolved in benzene(50 ml). When the color of the solution changed to brown by excess iodine, the addition was stopped. The reaction mixture was washed with 5% HCl solution, $Na_2S_2O_3$ solution, and then dried over $MgSO_4$. After evaporation of benzene, the residual disulfide was purified by recrystallization usually from hexane. Yields were nearly quantitatively.

$(p\text{-}CH_3C_6H_4S)_2$ m.p.=44~45°C(lit,[17] 46°C)
$(p\text{-}ClC_6H_4S)_2$ m.p.=70~71°C(lit,[18] 73°C)
$[2,4,6\text{-}(CH_3)_3C_6H_2S]_2$ m.p.=124~125°C(lit,[19] 125°C)
$(p\text{-}CH_3OC_6H_4S)_2$ m.p.=35~36°c, b.p.=205°C/4 mmHg (lit,[20] 41~43°C)

Other symmetrical disulfides were commercial products. Unsymmetrical disulfides were prepared by the following procedure, according to the reported method.[21]

23.45 mmol of a sulfenyl chloride was dissolved in dry benzene or tetrachloromethane and cooled at 0°C. After 23.45x1.1 mmol of pyridine dissolved in dry benzene or tetrachloromethane was added to this mixture slowly, 23.45 mmol of a chosen thiol dissolved in dry benzene or tetrachloromethane was slowly added. After the addition of thiol, cooling bath was removed and the reaction mixture was stirred until the temperature reached room temperature. The resulting reaction mixture was transfered into a separatory funel, and washed with water, dilute HCl, and water again. The organic layer was dried over $MgSO_4$. After evaporation, this disulfide was chromatographed with column with a mixture of benzene and hexane(v/v=1/1) as an eluent. Complete purification of unsymmetrical disulfide is very difficult. A tiny or a small amount of symmetrical disulfide was detected by GLC.

	CCl_4 solvent	2.27ppm(s 3H) 7.3ppm(m 8H)
	CCl_4 solvent	7.03ppm(d 2H) 7.35ppm(d 2H) 0.9ppm(m 3H) 2.3ppm(s 3H) 1.1~1.9ppm(m 4H) 2.7ppm(t 2H)
	CCl_4 solvent	3.63ppm(s 3H) 6.7ppm(d 2H) 7.0~7.6ppm(m 7H)
	CCl_4 solvent	1.1~1.8ppm(m 6H) 0.9ppm(m 3H) 2.65ppm(t 2H) 7.1~7.6ppm(m 5H)
	CCl_4 solvent	0.9ppm(m 3H) 1.1~1.8ppm(m 4H) 2.66ppm(t 2H) 7.1~7.6ppm(m 5H)

Sulfinic Acids. p-Toluenesulfinic acid and benzenesulfinic acid were obtained by acidification of the corresponding sodium arenesulfinates which were obtained as commercial samples.

The white precipitates were recrystallized from water yielding the corresponding arenesulfinic acids.

$C_6H_5SO_2H$ m.p.=78~80°C(lit,[22] 81.5~83°C)
p-$CH_3C_6H_4SO_2H$ m.p.=84~85°C(lit,[22] 84~85°C)

Five g(0.0237 mol) of p-chlorobenzenesulfonyl chloride and 18 g(0.0237x3 mol) of sodium sulfite were added into 100 ml of water. The reaction mixture was kept at a temperature ranging 70~80°C for 5 hours. Then, this water solution was washed with chloroform twice, and acidified with excess conc. HCl solution, cooled and filtered. The white precipitate was recrystallized from water yielding p-chlorobenzenesulfinic acid in 79% yield. p-Methoxybenzenesulfinic acid was also obtained from p-methoxybenzenesulfonyl chloride by the same procedure.

p-$ClC_6H_4SO_2H$ m.p.=95~97°C(lit,[22] 98~99°C)
p-$CH_3OC_6H_4SO_2H$ m.p.=97°C (lit,[23] 97~98°C)

Pentane- and butanesulfinic acids were obtained by hydrolyses of the corresponding sulfinyl chlorides.

Alkanesulfinic acids were detected as 2,4-dinitrophenyl sulfones by treatment with 2,4-dinitrophenylchlorobenzene.

n-C_5H_{11}-SO_2-$C_6H_3(NO_2)_2$-2,4 m.p.=84°C(lit,[24] 83°C)
TLC($CHCl_3$) R_f=0.5
n-C_4H_9-SO_2-$C_6H_3(NO_2)_2$-2,4 m.p.=92°C (lit,[24] 92°C)

Thiolsulfonate. Sulfenyl chloride was prepared by treating thiol or disulfide with gaseous chlorine in CCl_4 at 0°C. Free sulfinic acids other than those which were obtained by acidification of commercial sodium sulfinates with conc. HCl were synthesized by hydrolyses of the corresponding sulfinyl chlorides. To a dry CCl_4 solution(150 ml) of a sulfenyl chloride(0.03 mol) which was freshly prepared and was made free from chlorine under reduced pressure was added dropwise into

dry pyridine(0.033 mol) at a temperature lower than 0°C and then slightly white precipitate of pyridinium salt of the sulfenyl chloride was formed. A solution containing free sulfinic acid(0.03 mol) in dry CCl_4 or ether(50 ml) was added to this solution at a temperature lower than 0°C. Then a new precipitate was formed gradually as the addition proceeded. After stirring the reaction mixture containing the white salt for 30 min and subsequent warming to room temperature, the reaction mixture was washed with 5% HCl solution and then water. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. From the residue, the thiolsulfonate was obtained in 80~90% yield and recrystallized from ethanol or benzene.

$C_6H_5SO_2SC_6H_5$ m.p.=44~45°C(lit,[25] 44~45°C)

$p\text{-}CH_3C_6H_4SO_2SC_6H_4CH_3\text{-}p$ m.p.=72~74°C(lit,[26] 76°C)

$p\text{-}ClC_6H_4SO_2SC_6H_4Cl\text{-}p$ m.p.=136~138°C(lit,[27] 134~136°C)

$C_6H_5SO_2SC_6H_4CH_3\text{-}p$ NMR(CCl_4) δ=2.4ppm(3H s)
7.05~7.25ppm(4H m)
7.35~7.65ppm(5H m)
m.p.=52°C(lit,[28] 54°C)

$p\text{-}CH_3C_6H_4SO_2SC_6H_5$ NMR(CCl_4) δ=2.42ppm(3H s)
7.0~7.5ppm(9H m)
m.p.=78~80°C(lit,[28] 78°C)

$p\text{-}ClC_6H_4SO_2SC_6H_4CH_3\text{-}p$ NMR(CCl_4) δ=2.42ppm(3H s)
7.13~7.3ppm(4H m)
7.35~7.5ppm(4H m)
m.p.=129~131°C(lit,[29] 129~131°C)

$p\text{-}CH_3C_6H_4SO_2SC_6H_4Cl\text{-}p$ NMR(CCl_4) 2.45ppm(3H m)
7.1~7.6ppm(8H m)
m.p.=87~88°C(lit,[30] 87~88°C)

$p\text{-}CH_3OC_6H_4SO_2SC_6H_5$ NMR(CCl_4) δ=3.85ppm(3H s)
6.8ppm(d 2H J=9Hz)
7.42ppm(d 2H J=9Hz)
7.36ppm(5H s)
m.p.=55~57°C (lit,[31] 54~55°C

In the preparation of symmetrical thiolsulfonate, 19.4 mmol of disulfide was dissolved in 10 ml of acetic acid at 0°C,

then, 19.42x2.5 mmol of hydrogen peroxide was slowly added to this mixture. Temperature was raised to r.t. and the mixture was stirred for 24 hours. Then this reaction mixture was poured into benzene and neutralized by Na_2CO_3, washed with $Na_2S_2O_3$, water, and dried over $MgSO_4$. After evaporation of solvent, the residue was chromatographed with column(eluent:benzene) to give thiolsulfonate in 50% yield.

$n\text{-}C_5H_{11}\text{-}SO_2S\text{-}C_5H_{11}\text{-}n$ oil TLC(benzene) R_f=0.5

elem. anal.

	C	H
obsed.	50.49	9.34
calcd.	50.38	9.30

IR(NaCl) 1120(s) 1320(s), 1460cm^{-1}(s)

NMR(CCl_4) 0.7~2.2ppm(m 18H) 2.9~3.4ppm(m 4H)

$p\text{-}CH_3C_6H_4SO_2SC_4H_9\text{-}n$ TLC(benzene) R_f=0.5

elem. anal.

	C	H
obsed.	54.17	6.64
calcd.	54.06	6.59

IR(KBr) 810(m) 1080(m) 1140(s) 1320cm^{-1}(s)

NMR($CDCl_3$) δ=0.9ppm(m 3H) 2.55ppm (s 3H) 1.5ppm(4H m) 2.9ppm(2H t) 7.25ppm(d 2H) 7.7ppm(d 2H)

$n\text{-}C_4H_9SO_2SC_4H_9\text{-}n$ TLC(benzene) R_f=0.4 oil

elem. anal.

	C	H
obsed.	45.81	8.71
calcd.	45.68	8.62

IR(NaCl) 1127, 1323, 1465, 2950, 2930, 2870cm^{-1}

Preparation of Thiolsulfinate. Both symmetrical and unsymmetrical thiolsulfinate were prepared by known methods with a rather little modification. Namely, addition of thiol into a desired, distilled sulfinyl chloride in the presence of pyridine in CCl_4 under cooling at a temperature lower than 0°C, gave rise to the formation of thiolsulfinate(80~90% yield).

The thiolsulfinate after purification by column chromatography or recrystallization, was identical with that of reported upon examination of m.p.

$p\text{-}CH_3C_6H_4\overset{O}{\overset{\uparrow}{S}}SC_6H_4CH_3\text{-}p$ TLC(benzene) R_f=0.2
NMR(CCl_4) 2.4ppm(3H s), 2.42ppm(3H s)
6.95~7.6ppm(m 8H)
IR(KBr) 800, 1480, 1060, 1580, 1090cm^{-1}
m.p.=87°C(lit,[32] 87.5°C)

$p\text{-}CH_3C_6H_4\overset{O}{\overset{\uparrow}{S}}SC_6H_5$ NMR(CCl_4) 2.43ppm(3H s) 7.1~7.6ppm(9H m)
IR(KBr) 800, 1065, 750, 1090, 693, 1440
1465, 1590cm^{-1}
m.p.=82°C(lit,[33] 83~84°C)

The Reaction of Sulfinic Acid and Thiol. p-Toluenethiol 1192 mg(1.923x5 mmol) dissolved in 5 ml of CH_2Cl_2 was added to 300 mg(1.923 mmol) of p-toluenesulfinic acid. The reaction was carried out under argon atmosphere for 19 hours in refluxing condition.(bath temp. 50°C). Then the reaction mixture was poured into benzene which was washed with 0.1N. $NaHCO_3$ for 3 times. The organic layer was dried over $MgSO_4$ and evaporated (in this reaction, thiolsulfonate was not obtained). The product was chromatographed with column using benzene to give the mixture of p-toluenethiol and di-p-tolyl disulfide. The yield of di-p-tolyl disulfide was determined by NMR.

$p\text{-}CH_3C_6H_4SSC_6H_4CH_3\text{-}p$ 689 mg(2.9 mmol) 73%
$p\text{-}CH_3C_6H_4SH$ 321 mg(2.6 mmol)

Disulfide was identical with the authentic disulfide in both GLC and NMR. The water layer obtained was washed with $CHCl_3$ for 3 times. Then into the solution conc. HCl solution was added and the mixture was extracted with $CHCl_3$ or ether, dried over $MgSO_4$, evaporated to give 4.3% of starting p-toluenesulfinic acid.

Reaction of Thiolsulfinate and Thiol in the Presence of Sulfinic Acid. p-Toluenesulfinic acid 148 mg(0.948 mmol) and 600 mg(0.948x5.76 mmol) of thiophenol were dissolved in 3 ml of CH_2Cl_2 under argon atmosphere and then the 235 mg(0.948 mmol) of S-phenyl p-toluenethiosulfinate dissolved in 2 ml of CH_2Cl_2 was added. The reaction was carried out at r.t. After 3 hours, the starting thiolsulfinate was not present. The reaction mixture was evaporated and chromatographed through silica-gel column using a mixture of benzene and hexane(v/v=1/1). The first fraction was a mixture of PhSH, p-TolSSPh and PhSSPh, and the second fraction was a mixture of p-TolSO_2SPh and p-TolSO_2STol-p. Yields of these products were determined by NMR. These products were identified by comparison with authentic disulfides and thiolsulfonates.

$p\text{-}CH_3C_6H_4SSC_6H_5$ 88%, $C_6H_5SSC_6H_5$ 52%, $p\text{-}CH_3C_6H_4SO_2SC_6H_4CH_3\text{-}p$ 2.5%

$p\text{-}CH_3C_6H_4SO_2SC_6H_5$ 54.4%

The mixtures obtained in other separate experiments were also treated by the same procedure.

Reaction of Sulfinic Acid and Thiol in the Presence of Chlorotrimethylsilane.

Procedure-1. p-Chlorobenzenethiol 1390 mg(1.923x5 mmol) which was dissolved in 5 ml of $CHCl_3$ was added into a reactor containing 340 mg(1.923 mmol) of p-chlorobenzenesulfinic acid by a micro-cylinge. Then, 1 ml of chlorotrimethylsilane(ca.5eq) was added to a mixture by a micro-cylinge. The reaction was carried out at r.t. for 30 min under argon atmosphere. Then, the reaction mixture was evaporated and chromatographed through column(silica-gel) using a mixture of benzene and hexane(v/v=1/1) to give a mixture of p-chlorobenzenethiol

and di-p-chlorophenyl disulfide(fraction-1) and 43 mg of S-p-chlorophenyl p-chlorobenzenethiosulfonate(7%). The yield of di-p-chlorophenyl disulfide was determined by NMR(85%).

Procedure-2. p-Chlorobenzenesulfinic acid, 340 mg(1.923 mmol) was dissolved in 3 ml of chloroform and then 1254 mg(1.923x6 mmol) of chlorotrimethylsilane was added into the solution. The mixture was kept standing under stirring for 1 hour in argon atmosphere. After 1 hour, 1390 mg(1.923x5 mmol) of p-chlorobenzenethiol which was dissolved in 3 ml of chloroform was added to the reactor and an exothermal reaction occurred. After 30 min, the reaction mixture was evaporated and treated in the same procedure as in the procedure-1.

$p\text{-}ClC_6H_4SSC_6H_4Cl\text{-}p$ 100%

Isolation of p-Toluenesulfinyl Chloride. p-Toluenesulfinic acid 300 mg(1.923 mmol) was dissolved in 3 ml of chloroform under argon atmosphere, then 1254 mg(1.923x6 mmol) of chlorotrimethylsilane was added to this solution and the mixture was kept standing for 1 hour with stirring. After the reaction, the mixture was evaporated to give p-toluenesulfinyl chloride in 100% yield. IR(NaCl) 750(s), 815(s), 920(s), 1155(s)cm^{-1}

NMR(CCl_4) 2.45ppm(3H s) 7.35ppm(2H d) 7.75ppm(2H d)

The authentic sulfinyl chloride was obtained by treating di-p-tolyl disulfide with chlorine in acetic anhydride in 91 % yield. 91°C/3 mmHg (lit,[34] 113~115°C/3.5 mmHg)

Preparation of Trimethylsilyl p-Toluenesulfinate. $p\text{-}CH_3C_6H_4SO_2Ag$ 500 mg(1.902 mmol) was dissolved in 5 ml of chloroform and then, 206 mg(1.902 mmol) of chlorotrimethylsilane was added to this solution. Immediately white precipitate, AgCl appeared.

This solution was filtered under dry nitrogen and evaporated to give the silyl ester in a quantitative yield. This ester was very sensitive to moisture.

NMR(CCl_4) δ=0.26ppm(s 7.1H) 2.4ppm(s 3H) 7.27ppm(d 2H)
7.55ppm(d 2H)

References

1) F.G. Bordwell, H.M. Anderson, J. Am. Chem. Soc., 75, 6019 (1953).

R.K. Burkhard, D.E. Sellers, F. Decou, J.L. Lambert, J. Org. Chem., 24, 767(1959).

P. Rumph, J. Sadet, Bull. Soc. Chim. France., 447(1958).

2) L. Horner, O.H. Basedow, J. Liebigs, Ann. Chem., 612, 108 (1958).

C.M.J. Stirling, Int. J. Sulfur. Chem., B, 6, 279(1971).

J.L. Kice, D.C. Hampton, A. Fitzgerald, J. Org. Chem., 30, 882(1965).

J.L. Kice, N.E. Pawlowski, J. Org. Chem. 28, 1162(1963).

J.L. Kice, K.W. Bowers, J. Am. Chem. Soc., 84, 605(1962).

3) S. Takagi, T. Suzuki, K. Imaeda, J. Pharm. Soc. Jpn., 69, 358(1979).

4) J. Starting, H.J. Backer, Rec. Trav. Chim. Pays-Bas., 69, 638 (1950).

5) H.W. Pinnick, M.A. Reynolds, R.T. Mcdonald, Jr, W.D. Drewster, J. Org. Chem., 45, 930(1980).

6) A. Burawoy, C. Turner, J. Chem. Soc., 469(1950).

7) J.A. Olah, S.C. Narang, L.D. Field, G.F. Salen, J. Org. Chem., 45, 4792(1980).

8) S. Harusawa, T. Shioiri, Tet. Lett., 23, 447(1982).

9) S. Oae, A. Nakanishi, N. Tsujimoto, Tetrahedron, 28, 2981 (1972).

T.J. Wallace, J.J. Nahon, J. Org. Chem., 30, 1502(1965).

T.J. Wallace, J. Am. Chem. Soc., 86, 2018(1964).

T. Numata, H. Togo, S. Oae, Chem. Lett., 329(1979).

10) S. Oae, H. Togo, T. Numata, K. Fujimori, Chem. Lett., 1193 (1980).

11) J.L. Kice, B.G. Large, J. Org. Chem., 33, 1940(1968).

12) J.L. Kice, T.E. Rogers, J. Am. Chem. Soc., 96, 8015(1974).

13) D. Cipris, D. Pouli, Synth. Commun., 9, 207(1979).

14) J.L. Kice, E.H. Morkved, J. Am. Chem. Soc., 85, 3472(1963).

15) M.M. Chau, J.L. Kice, J. Org. Chem., 42, 3265(1977).

16) J.L. Kice, K.W. Bowers, J. Am. Chem. Soc., 84, 605(1962).

J.L. Kice, G. Guaraldi, C.G. Venier, J. Org. Chem., 31, 3561 (1966).

17) L. Field, J. Am. Chem. Soc., 74, 394(1954).
18) M.B. Sprk, J.L. Cameron, N. Kharasch, J. Am. Chem. Soc., 75, 4907(1953).
19) H.J. Backer, E. Westerhuis, Rec. Trav. Chim., 71, 1065, 1071(1952).
20) C. Ferreri, R. Caputo, Tet. Lett., 23, 2391(1982).
21) H. Bredereck, A. Wagner, H. Beck, R.-J. Klein, Chem. Ber., 93, 2739(1960).
22) R.K. Burkhard, D.E. Sellers, F. Decov, J.L. Lambert, J. Am. Chem. Soc., 72, 1215(1950).
23) S. Oae, O. Yamada, T. Maeda, Bull. Chem. Soc. Jpn., 47, 166 (1974).
24) R.W. Bost, J.O. Turner, R.D. Norton, J. Am. Chem. Soc., 54, 1985(1932).
25) S. Oae, R. Nomura, Y. Toshikawa, W. Tagaki, Bull. Chem. Soc. Jpn., 42, 2903(1969).
26) R. Otto, J. Lowenthal, A.V. Gruber, Ann., 149, 101(1969).
27) G. Polumbo, R. Caputo, Synthesis, 888(1981).
28) S. Oae, R. Nomura, Y. Yoshikawa, W. Tagaki, Bull. Chem. Soc., Jpn., 42, 2903(1969).
29) S. Oae, T. Takata, and Y.H. Kim, Tetrahedron, 37, 37(1981).
30) S. Oae, T. Takata, and Y.H. Kim, Tetrahedron, 37, 37(1981).
31) S. Oae, R. Nomura, Y. Yoshikawa, W. Tagaki, Bull. Chem. Soc. Jpn., 42, 2903(1969).
32) J.L. Kice, C.G. Venier , L. Heasley, J. Am. Chem. Soc., 89, 3557(1967).
33) S. Oae, Y. Yoshikawa, W. Tagaki, Bull. Chem. Soc. Jpn., 42, 2899(1969).
34) K. Kurzer, Org. Synth., Coll. Vol., IV, 937(1964).

Chapter 3

Reduction of Sulfonic Acids and Related Organosulfur Compounds with Triphenylphosphine-Iodine System. I.

Abstract

Arenesulfonic acids, its sodium salts, and alkyl arenesulfonates can be reduced readily to the corresponding arenethiols quantitatively with a mixture of triphenylphosphine and a catalytic amount of iodine, while alkanesulfonic acids, sulfinic acids, thiols, disulfides, thiolsulfonates, sulfonates are also readily reduced to the corresponding thiols similarly. Upon treatment with triphenylphosphine and excess iodine, however, these aliphatic sulfur compounds are converted eventually to the corresponding alkyl iodide. The relative reactivities of these sulfonyl derivatives toward triphenylphosphine-iodine are the following.

Aromatic series: $ArSO_3Ar'$, $ArSO_3CH_2C(CH_3)_3 \ll ArSO_2SO_2Ar < ArSO_3H < ArSO_3^- HNBu_3^+ (PyH^+) < ArSO_3R < ArSO_2H < ArSO_2Cl$, $ArSO_2SAr'$.

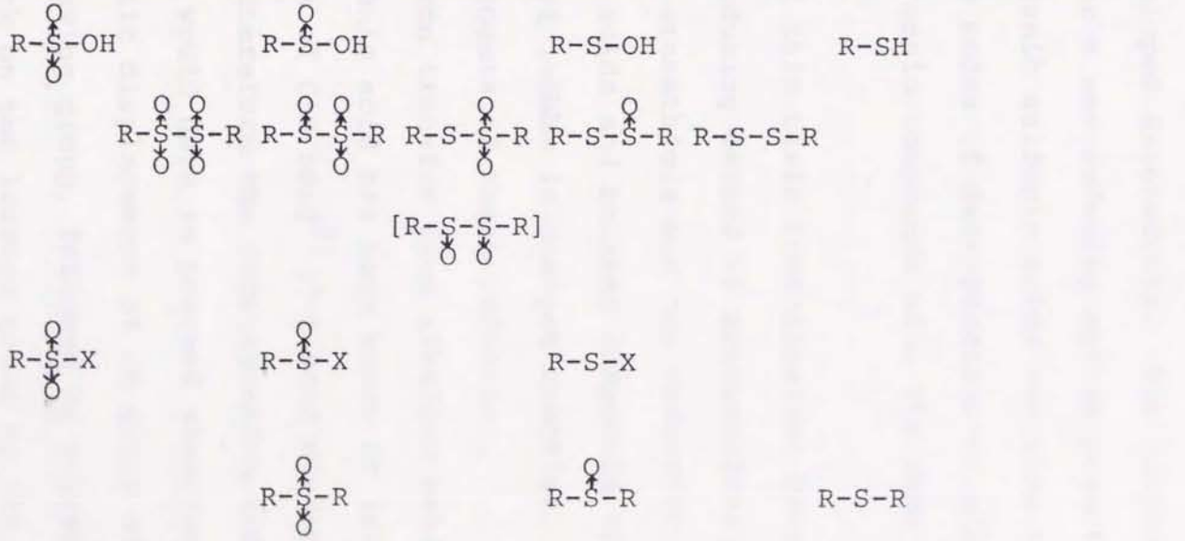
Aliphatic series: $RSO_3R' < RSH < RSO_3H < RSSR$, $RSO_2H < RSO_3^- HNBu_3^+ < RSH/Bu_3N < RSO_2Cl$, RSO_2SR, $RSO_2^- HNBu_3^+$. In these reactions, the arenesulfonic acids bearing electron-donating substituents can be reduced more readily than the ones having electron-withdrawing substituents.

Introduction

Organosulfur compounds can have several oxidative states, and the systematic representation of those compounds is given in "Oxidoreduction Table of Organosulfur Compounds" in which various sulfur compounds are arranged in order of the decrease of oxidation state from left to right side.[1] Sulfur atom in sulfonic acids is in the highest oxidation state. Since the disulfone is formally a dehydrated condensation product between the sulfonic acid and the sulfinic acid, it is placed at the position between these two compounds in the Table. The sulfinylsulfone occupies the same position as the sulfinic acid, since the sulfinylsulfone is formed by dehydration of the sulfinic acid. While the thiolsulfonate and the α-disulfoxide are also placed in the same position, the thiolsulfinate and the disulfide are assigned as the different oxidation states as shown in Table.

Among these compounds, the sulfonic acid is exceptionally stable and inert to most reducing agents hitherto known, and no good method has been found to reduce sulfonic acids. Reduction of other oxidized sulfur compounds can be found in numerous literatures most of which are, however, on rather fragmentary works done only for synthetic interests. Thus no systematic investigation on the reduction of these organic compounds has been carried out. Meanwhile, sulfonation of hydrocarbons has been a very important industrial process and one convenient method to introduce sulfur functional group into organic compounds. However, sulfonic acids are so stable toward any reducing agents that there has been no known method

Oxidoreduction Table for Organosulfur Compounds



←high oxidation state of sulfur ———

X: Halogens, NRR', OR.

to reduce sulfonic acids to organic sulfur compounds of lower oxidation state. Sulfonic acids are so widely used generally and also in organic syntheses, and hence a good method to reduce sulfonic acids has long been invoked, since synthetic chemistry using organosulfur compounds has recently been developed extensively. The Purpose of this work is to discover a new reducing system powerful enough to reduce even organic sulfonic acids and also to investigate systematically the modes of deoxygenation of all these common oxidized organic compounds with the same reducing agent.

The fruits of this basic investigation have provided us a convenient reducing method of arenesulfonic acids to the corresponding arenethiols and the reductive conversion of alkanesulfonic acids and related compounds to the corresponding alkyl iodides in one-pot reaction. This chapter gives detailed accounts of these reduction.

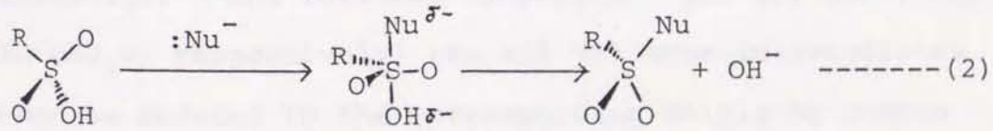
Direct electron transfer from alkaline metal and related compounds to sulfonic acid has been known to lead mainly to reductive cleavage of C-S bond[2] (C-S bond dissociation energy: ~70kcal/mol[3]). Therefore the deoxygenative reduction of the sulfonic acid would have to proceed stepwise via the initial nucleophilic displacement of OH group of the sulfonic acid by a good leaving group, followed by subsequent nucleophile as shown in eq. 1.

$$R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}\text{-}OH + :Nu^- \xrightarrow[-OH^-]{} R\text{-}\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}\text{-}Nu \xrightarrow{:Nu^-} RSO_2^- + Nu\text{-}Nu \quad \text{-----(I)}$$

However, unfortunately such nucleophilic substitution of OH^- group of the sulfonic acid does not readily proceed. Following are some of the reasons why the sulfonic acid is so inert toward common reducing agents.

1) The sulfonic acid is so a strong acid that it gives away proton to the nucleophilic reducing agent which upon protonation becomes no longer effective nucleophiles, while the deprotonated sulfonate anion possesses negatively charged three oxygen atoms which repel even strong nucleophiles to approach the central sulfur atom.

2) The reactivities of sulfonic acids and its derivatives in nucleophilic displacements would be somewhat reduced since there would be unfavorable lone pair-lone pair repulsion between the nucleophile and two very electronegative oxygens at equatrial positions at the transition state of the trigonal bipyramid. The sulfinic acid and its derivatives, having only one polarized oxygen atom on the sulfur, is more reactive in the nucleophilic displacement.



-------(2)

3) The poor leaving ability of OH group may also be partly responsible for the low reactivity of sulfonic acid toward nucleophile.

However, the sulfonic acid can be made more reactive by replacing hydrogen by a suitable electron-withdrawing Y group to form RSO_2-OY. Indeed, nucleophilic displacement of OH group on the sulfur atom of sulfonic acid has to be rather difficult, while once RSO_2-OY is formed, nucleophilic

displacement of OY group in RSO_2OY proceeds rather readily. Chlorination of sulfonic acids with PCl_5[4] or $SOCl_2$[5] is a good example(eqs. 3 and 4) of transformation of RSO_2OY species. Obviously the formation of very stable phosphorus oxychloride or SO_2 is the driving force of the reaction.

$$RSO_3H + PCl_5 \xrightarrow[-H^+]{} RSO_2\text{-}O\text{-}PCl_4 \xrightarrow[-Cl^-]{} RSO_2Cl + OPCl_3 \quad ---(3)$$

$$RSO_3H + SOCl_2 \xrightarrow[-H^+]{} RSO_2\text{-}O\text{-}SOCl \xrightarrow[-Cl^-]{} RSO_2Cl + SO_2 + HCl \quad --(4)$$

Thus, the key step of the reduction of the sulfonic acid represented by eq. 5 is the activation of leaving OH group by the introduction of Y group on the sulfonyl oxygen, while Y should be an electron-withdrawing group and hence ^-OY ought to be an excellent leaving group in the subsequent nucleophilic displacement. Once the intermediate (1) is formed, subsequent reactions are quite facile.

$$RSO_3H + XY \xrightarrow[-HX]{} \underset{(1)}{RSO_2\text{-}O\text{-}Y} \xrightarrow{:Nu^-} RSO_2Nu + {}^-OY \quad --------(5)$$

For example, sulfonyl chloride,[6] sulfonamide,[7] sulfonate,[8] thiolsulfonate,[9] and sulfonic anhydride[10] (Nu=Cl, NRR', OR, SR, and OSO_2R, respectively) are all (1) type intermediates which can be reduced to the corresponding thiols by common reducing agents. Thus, the success of the reduction of the sulfonic acid depends entirely upon a choice of XY and Nu^- to promote the reaction in eq. 5. The first example of one-pot reduction of sulfonic acids to thiols was recently reported from this laboratory, by using $(CF_3CO)_2O/Bu_4N^+I^-$, $X=CF_3CO_2^-$, $Y=CF_3CO$, $Nu^-=I^-$ shown in eq. 5. This method is the first break through in the direct deoxygenative reduction of sulfonic acids, however, it not only requires a large

excess of expensive reagents but also affords a mixture of reduction products, i.e. thiols and thioltrifluoroacetates.[11] More recently, G.A. Olah et al reported the reduction of sulfonic acids to the corresponding disulfides with BX_3(X=Cl, Br, I)/KI.[12] This chapter deals with another facile and quantitative deoxygenative reduction of sulfonic acid and its derivatives by a new reducing system, i.e. triphenylphosphine-iodine system. Although triphenylphosphine is known to be a relatively strong reducing agent, it does not react directly with sulfonic acids. Triphenylphosphine has a strong oxygen affinity and hence if Ph_3P^+ group is introduced as Y in eq. 5, even a weak nucleophile may attack the sulfonyl sulfur atom because of the excellent leaving ability of the triphenylphosphine oxide. Meanwhile, the mixture of triphenylphosphine with halogen[13] and that of triphenylphosphine and disulfide[14] respectively are known to give phosphonium salts. Several reactions are known to utilize such phosphonium salts e.g. the conversion of alcohol and phenol derivatives to the corresponding halides by treatment with phosphine and halogen,[15] the desulfurization of disulfides to the corresponding sulfides with phosphine,[14, 16~18] the condensation of carboxylic acids and alcohols or amines to the corresponding esters or amides by treatment of phosphine and diaryl disulfide,[19~22] diselenide,[23] or halogen and the conversion of alcohols to sulfides with phosphine and disulfides.[24] Thus a mixture of triphenylphosphine and a catalytic amount of iodine was our choice system for the reduction, eq. 5, where not only

RSO_2-OY(Y=Ph_3P^+) is easily generated from the reaction between the reagent and the sulfonic acid but also iodide is a relatively strong reducing agent enough to reduce the sulfonyl derivatives.[10, 11, 25)]

Results and Discussion

The Reduction of Arenesulfonic Acids, its Sodium Salts, and Alkyl Arenesulfonates with Triphenylphosphine and Iodine.[26]

Triphenylphosphine is known to react with iodine to afford iodotriphenylphosphonium iodide[13, 27] which would behave as a halogenating agent of sulfonic acids like phosphorus pentachloride(eq. 3), while hydrogen iodide formed may act as a reducing agent. Based on this assumption the reaction between sulfonic acids and Ph_3P/I_2 was initiated, while the successful conversion of alcohols and thiols into the corresponding halides with halotriphenylphosphonium halide also prompted us to work on this reduction. As soon as triphenylphosphine was dissolved into a benzene solution, iodine color disappeared immediately giving a pale yellow solution of iodotriphenylphosphonium iodide. Upon treatment of p-toluenesulfonic acid with this reagent in refluxing benzene, the expected reduction of the sulfonic acid proceeded smoothly and p-toluenethiol was obtained nearly quantitatively. Even when the amount of iodine was reduced, the yield of the thiol was not reduced but reaction required a prolonged period to complete, suggesting that iodine acts as the catalyst of the reduction of the sulfonic acid with triphenylphosphine. Thus, the whole reaction between arenesulfonic acids and triphenylphosphine in the presence of iodine can be expressed as eq. 6.

$$Ar\text{-}SO_3H + 3\ Ph_3P \xrightarrow{I_2} Ar\text{-}SH + 3\ Ph_3PO \quad \text{----------(6)}$$

Since the reagent readily reacts with water, eventually affording triphenylphosphine oxide and hydrogen iodide, the sulfonic acid was carefully dehydrated by azeotropic distillation with benzene just before subjecting to the reduction in refluxing benzene. The results are summarized in Table 1. Neither triphenylphosphine alone nor iodide anion reacts with the arenesulfonic acid at all. The initial reaction is undoubtedly the reaction of the arenesulfonic acid with iodotriphenylphosphonium iodide to generate the arenesulfonyloxytriphenylphosphonium iodide as an incipient intermediate which receives subsequently nucleophilic attack of gegen ion, I^-, at the sulfonyl sulfur atom to form the arenesulfonyl iodide as shown in eqs. 7~9.

$$Ph_3P + I_2 \rightleftharpoons Ph_3\overset{+}{P}\text{-}I\ I^- \qquad \text{----------(7)}$$

$$ArSO_3H + Ph_3\overset{+}{P}\text{-}I\ I^- \rightleftharpoons ArSO_3^-\ Ph_3\overset{+}{P}\text{-}I + HI \qquad \text{--------(8)}$$

$$ArSO_3^-\ Ph_3\overset{+}{P}\text{-}I \rightleftharpoons ArSO_2\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- \qquad \text{----------(8')}$$

$$ArSO_2\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- \longrightarrow ArSO_2I + Ph_3PO \qquad \text{----------(9)}$$

$$ArSO_2I + HI \longrightarrow ArSO_2H + I_2 \qquad \text{----------(10)}$$

$$ArSO_2H + Ph_3\overset{+}{P}\text{-}I\ I^- \longrightarrow ArSO\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- + HI \qquad \text{---------(11)}$$

$$ArSO\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- \longrightarrow ArSOI + Ph_3PO \qquad \text{----------(12)}$$

$$ArSOI + HI \longrightarrow ArSOH + I_2 \qquad \text{----------(13)}$$

$$ArSOH + Ph_3\overset{+}{P}\text{-}I\ I^- \longrightarrow ArS\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- + HI \qquad \text{----------(14)}$$

$$ArS\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- \longrightarrow ArSI + Ph_3PO \qquad \text{----------(15)}$$

$$ArSI + Ph_3\overset{+}{P}\text{-}I\ I^- \longrightarrow ArS\text{-}\overset{+}{P}Ph_3\ I^- \qquad \text{----------(16)}$$

$$ArS\text{-}\overset{+}{P}Ph_3\ I^- + HI \longrightarrow ArSH + Ph_3\overset{+}{P}\text{-}I\ I^- \qquad \text{----------(17)}$$

Table 1. The Reaction of Arenesulfonic Acids with Triphenylphosphine/Iodine in Benzene under Reflux Condition

$ArSO_3H$	$ArSO_3H/I_2/Ph_3P$	Time (h)	Products[a]	
			ArSH(%, GLC)	Ph_3PO(%)
p-$CH_3C_6H_4SO_3H$	2/1/10	2.5	89	(128)[b]
p-$ClC_6H_4SO_3H$	2/1/10	4.0	98	(95)[b]
$C_6H_5SO_3H$	2/1/10	2.0	90	(116)[b]
β-$C_{10}H_7SO_3H$	2/1/10	2.0	85(67)[b]	-
p-$CH_3C_6H_4SO_3H$	2/0.2/8	5.5	88	-
	2/0/10	2.5	0	0
	2/1/10(Bu_3P)	2.0	33	-
	2/1(Br_2)/10	3.0	13	-
β-$C_{10}H_7SO_3H$	2/1/8/2(Bu_3N)[c]	0.5	70	-
p-$CH_3C_6H_4SO_3H$	2/1/8/2(Bu_3N)[c]	0.5	95	-

a) Yields of products were calculated based on the stoichiometry as shown in eq. 6. b) Isolated yield. c) Amine was added into this system.

$$ArSO_2I + Ph_3P \longrightarrow ArSO_2^- \overset{+}{P}h_3P\text{-}I \longrightarrow ArSO\text{-}O\text{-}\overset{+}{P}Ph_3\ I^-$$
$$\longrightarrow ArSOI + Ph_3PO \quad \text{----------(18)}$$
$$ArSOI + Ph_3P \longrightarrow ArSO^- \overset{+}{P}h_3P\text{-}I \longrightarrow ArS\text{-}O\text{-}\overset{+}{P}Ph_3\ I^-$$
$$\longrightarrow ArSI + Ph_3PO \quad \text{----------(19)}$$

The arenesulfonyl halide is known to be reduced with hydrogen iodide[28] to afford the diaryl disulfide, and also can be reduced by triphenylphosphine alone to give a mixture of the diaryl disulfide and the arenethiol.[29] Thus two paths are conceivable for the reduction of the arenesulfonyl iodide. One path involves the initial nucleophilic attack of iodide anion of the arenesulfonyl iodide to afford iodine and the sulfinic acid which is eventually reduced to the diaryl disulfide via the arenesulfenic acid by the same reaction cycles through which the arenesulfonic acid is converted to the arenesulfonyl iodide as shown in eqs. 7~9. Another conceivable process involves nucleophilic attack of triphenylphosphine on the arenesulfonyl iodide to result in the formation of the same reaction intermediate, the arenesulfinyloxytriphenylphosphonium iodide obtained in the former path, as shown in eqs. 18 and 19. In order to clarify which nucleophilic reagent, iodide anion or triphenylphosphine initiated the reduction of the arenesulfonyl iodide, the sulfonyl iodide was treated with either triphenylphosphine alone or hydriodic acid respectively. However, since the reduction was found to proceed in the both systems readily, it could not be conclude which process predominates over the order. Probably both processes are participating concurrently. The extremely fast reduction of the arenesulfonyl iodide is clearly by the fact that no probable intermediate can be

detected during the reactions of the arenesulfonic acid with Ph_3P/I_2 system, since the initial conversion of sulfonic acid to the sulfonyl iodide is undoubtedly the slowest step of this multi-step reduction of the sulfonic acid to the thiol. One interesting observation is that the reduction is accelerated considerably by the presence of such an amine as tributylamine(Table 1), which can readily dissociate the arenesulfonic acid to the corresponding nucleophilic anion to facilitate the reduction. The effect of aromatic substituent observed in the reduction of the arenesulfonic acid also indicates that the sulfonic acid bearing an electron-donating substituent was found to be reduced more readily than the one having an electron-withdrawing substituent as shown in Fig. 1, therefore eq. 8' should be the rate-determining step.

Though arenesulfinic acid can be reduced very slowly with triphenylphosphine alone, the addition of iodine accelerates this reduction remarkably to give the corresponding arenethiol quantitatively(Table 2). While sodium arenesulfinate cannot be reduced almost alone with triphenylphosphine, the triphenylphosphine/iodine system can reduce it easily to the arenethiol and diaryl disulfide even in the absence of any phase transfer catalyst.

The arenesulfonyl chloride and the diaryl thiolsulfonate can be readily reduced with triphenylphosphine alone, or better with the mixture of triphenylphosphine and iodine (Table 3).

Fig. 1. Reaction of $ArSO_3H$ with Ph_3P/I_2 in Benzene at 72°C to 73°C.

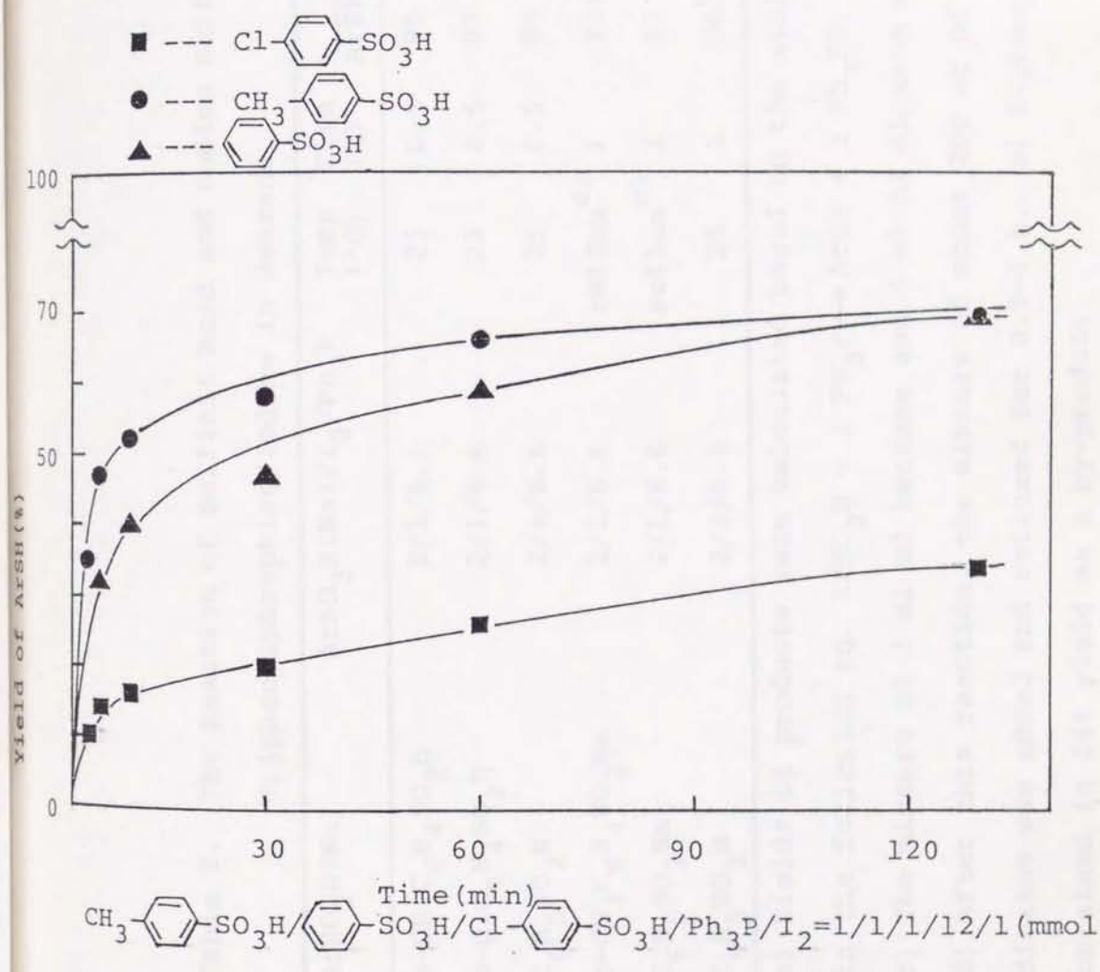


Table 2. The Reaction of Sulfinic Acid and Sodium Sulfinate with Triphenylphosphine/Iodine in Benzene

$ArSO_2H(Na)$	$ArSO_2H(Na)/I_2/Ph_3P$	Temp (°C)	Time (h)	Products[a] ArSH(%, GLC)	Ph_3PO(%)
p-$CH_3C_6H_4SO_2H$	2/1/6.6	25	0.5	95	(118)[b]
p-$ClC_6H_4SO_2H$	2/1/6.6	25	0.5	87	-
$C_6H_5SO_2H$	2/1/6.6	25	0.5	90	(111)[b]
p-$CH_3C_6H_4SO_2Na$	2/1/6.6	reflux[c]	2	92(88)[b]	- d)
$C_6H_5SO_2Na$	2/1/6.6	reflux[c]	2	87	- d)
$C_6H_5SO_2H$	2/0/6.6	25	2	50[e]	-

a) Yields of products were calculated based on the stoichiometry as shown in the following eq. $ArSO_2H + 2\ Ph_3P \longrightarrow ArSH + 2\ Ph_3PO$. b) Isolated Yield. c) The mixture of 3 ml of benzene and 5 ml of dioxane was used as a solvent. d) After this reaction, the mixture of about 200 mg of water and 1 ml of dioxane was added and refluxed for 0.5~1 h. e) Diphenyl disulfide was obtained in 24% yield as a by-product.

Table 3. The Reaction of $ArSO_2X$ with Triphenylphosphine/Iodine in Benzene[a)]

$ArSO_2X$	$ArSO_2X/I_2/Ph_3P$	Temp (°C)	Time (min)	ArSH (%)[b)]
$p\text{-}ClC_6H_4SO_2Cl$	2/1/8	25	30	100
$p\text{-}CH_3C_6H_4SO_2Cl$	2/0/8	25	30	92
$C_6H_5SO_2SC_6H_5$	1/1/4	25	10	89
$C_6H_5SO_2SC_6H_5$	1/0/4	25	10-15	83

a) After this reaction, the mixture of about 200 mg of water and 1 ml of dioxane was added and refluxed for 0.5~1.0 h. b) GLC yield (20% OV-1, 1 m glass column).

Alkyl arenesulfonates were found to react smoothly with Ph_3P/I_2 in benzene forming alkyl iodides and diaryl disulfides. The disulfides were converted ultimately to the arenethiols[30] upon treatment with triphenylphosphine and water(Table 4).

$$2\ ArS(=O)_2\text{-}O\text{-}R + 6\ Ph_3P + I_2 \xrightarrow{I_2} (ArS)_2 + 2\ RI + 6\ Ph_3PO \quad \text{--(20)}$$

$$(ArS)_2 + Ph_3P + H_2O \longrightarrow 2\ ArSH + Ph_3PO \quad \text{----------(21)}$$

On the other hand, both aryl arenesulfonates and neopentyl arenesulfonates were found to be quite inert in this reducing system even under prolonged reaction times as shown in Table 4, suggesting that the reaction eq.(20) is initiated by the nucleophilic displacement(S_N2) at the alkyl carbon with iodide anion to form the alkyl iodides and arenesulfonate anions which is further reduced to arenethiols by Ph_3P/I_2, while aryl arenesulfonates, neopentyl arenesulfonates resist the nucleophilic attack of iodide anion and no reaction appears to start even after a prolonged treatment with Ph_3P/I_2. Interestingly, however, pentyl benzenesulfonate, an alkyl arenesulfonate, reacted readily with tetrabutylammonium iodide in benzene affording tetrabutylammonium benzenesulfonate and pentyl iodide, however, under similar condition phenyl p-toluenesulfonate did not react with tetrabutylammonium iodide.

$$C_6H_5SO_3CH_2(CH_2)_3CH_3 + Bu_4N^+I^- \xrightarrow[\text{benzene reflux}]{\text{10 min}} C_6H_5SO_3^-\ Bu_4N^+ + \underset{100\%}{CH_3(CH_2)_4I} \quad \text{---(22)}$$

$$p\text{-}CH_3C_6H_4SO_3C_6H_5 + Bu_4N^+I^- \xrightarrow[\text{benzene reflux}]{\text{15 min}} \text{no reaction} \quad \text{----------(23)}$$

Table 4. The Reaction of Arenesulfonate Esters with Triphenylphosphine/ Iodine in Benzene under Argon Atmosphere

$ArSO_3R(Ar')$	$ArSO_3R(Ar')/I_2/Ph_3P$	Time Reflux	Products[a] ArSH(%)	RI(%)
$p\text{-}CH_3C_6H_4SO_3CH_2C(CH_3)_3$	2/1.5/8	5 h	no reaction[b]	
$p\text{-}CH_3C_6H_4SO_3C_6H_5$	2/1/10	45 h	no reaction[c]	
$C_6H_5SO_3CH_2CH_3$	2/1.5/8	10 min	88	-
$p\text{-}CH_3C_6H_4SO_3(CH_2)_4CH_3$	2/1.5/8	10 min	95	90
$C_6H_5SO_3(CH_2)_4CH_3$	2/1.5/8	10 min	90	96
$C_6H_5SO_3CH_2CH_3$	2/0/10	2 h	no reaction	

a) Yields of products were calculated based on the stoichiometry as shown in the eqs. 20 and 21. After this reaction, the mixture of about 200 mg of water and 1 ml of dioxane was added and refluxed for 0.5~1 h. b) Starting material was recovered in 85% yield. c) Starting material was recovered in 86% yield.

When bromine was used instead of iodine as the catalyst of the reduction of p-toluenesulfonic acid with triphenylphosphine, the yield of the thiol was found to be low(Table 1). Although tributylphosphine is a much stronger reducing agent, only 33% of p-toluenethiol was obtained together with unidentified side products upon treatment of the sulfonic acid with Bu_3P/I_2.

Phosphorus trichloride or phosphorus acid gave only small amounts of diaryl disulfides and arenethiols upon treatment of sulfonic acids in the presence of iodine.

Inspection of data in Table 1 and 4 reveals that the reduction of arenesulfonic acids takes place much more slowly than alkyl arenesulfonates. This may mean that arenesulfonate anions are more reactive than arenesulfonic acids in the reducing system, Ph_3P/I_2, because the treatment of alkyl arenesulfonates with iodide involves the nucleophilic attack of iodide ion on alkyl group and eventually gives arenesulfonate anions as primary intermediates. Similarly tertiary amine was already found to accelerate the reduction of arenesulfonic acids with Ph_3P/I_2. All these observations, i.e. the higher reactivity of arenesulfonic acid bearing an electron-donating substituent in the reduction, the acceleration of the reduction by addition of amine, and the facile rate of reduction of arenesulfonate esters, suggest clearly that the rate-determining step is the nucleophilic substitution of the sulfonate anion, which is a gegen anion, on the central phosphorus atom of iodotriphenylphosphonium cation to form

arenesulfonyloxytriphenylphosphinium iodide which has a P-O-S bond linkage(eq. 8').

Sodium arenesulfonate did not react with Ph_3P/I_2 in benzene at all because of its insolubility, however, it was smoothly reduced to the thiol in the presence of such a phase transfer catalyst as 18-crown-6. The rate of the reaction was found to depend on the amount of the phase transfer catalyst(Table 5). Thus, this reducing method is quite useful, since sulfonic acids are usually available in the form of sodium salt in industry. However, p-aminobenzenesulfonic acid, arenesulfonamides, and sulfones were not reduced by our system even at high temperatures and under prolonged heating in any solvent. Unsuccessful reduction of p-aminobenzenesulfonic acid and arenesulfonamide is believed to be due to the insolubility of the compounds in solvents such as benzene, acetonitrile, and dioxane, we used.

Finally, since triphenylphosphine/tetrachloromethane system was known to produce phosphonium salt,[31] arenesulfonic acids were treated with this Ph_3P/CCl_4 system. Actually, the corresponding diaryl disulfides were obtained, but yields were usually only 40% to 50%[arenesulfonic acid/Ph_3P=2/8(mmol)] when the reduction was carried out in the mixture of 1 ml of tetrachloromethane and 5 ml of benzene under reflux conditions for 1.5 hours.

Table 5. The Reaction of Sodium Arenesulfonate with Ph_3P/I_2/18-Crown-6 in Benzene under Argon Atmosphere[a)]

$ArSO_3Na$	$ArSO_3Na/I_2/Ph_3P$/18-Crown-6	Time(h) reflux	ArSH(%)[b)]
p-$CH_3C_6H_4SO_3Na$	2/1/10/0[d)]	24	trace
	2/2/10/1	5	51(50)[c)]
	2/2/10/1	31	85
$C_6H_5SO_3Na$	2/2/10/1	35	83
β-$C_{10}H_7SO_3Na$	2/2/10/1	24	67(50)[c)]
	2/2/10/1	36	96(93)[c)]
p-$CH_3C_6H_4SO_3Na$	2/2/8/0.02	79	80
2,4-$(CH_3)_2C_6H_3SO_3Na$	2/2/10/0.5	41	(63)[c)]
α-$C_{10}H_7SO_3Na$	2/2/10/0.5	35	70

a) Yields of products were calculated based on the stoichiometry as shown in the following eq. 2 $ArSO_3Na$ + 7 Ph_3P $\xrightarrow[2)\ H_2O]{1)\ I_2}$ 2 ArSH + 7 Ph_3PO. After this reaction, the mixture of about 200 mg of water and 2 ml of dioxane was added, and refluxed for 0.5~1 h. b) GLC yield(OV-1 20%, 1 m glass column). c) Isolated yield. d) The mixture of 3 ml of benzene and 5 ml of dioxane was used as a solvent.

The Reductive Conversion of Alkanesulfonic Acids, Sulfinic Acids, Thiols, Disulfides, Thiolsulfonates, and Sulfonates to the Corresponding Alkyl Iodides with Triphenylphosphine/Iodine.[32]

When this reducing system was applied for the reduction of pentanesulfonic acid, pentanethiol, the expected product, was not obtained, but pentyl iodide was the sole product obtained, when one equimolar amount of iodine was used.

$$RSO_3H + 4\ Ph_4P + I_2 \longrightarrow RI + 3\ Ph_3PO + Ph_3PS + HI \quad ---(24)$$

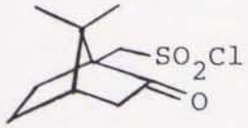
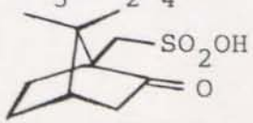
Pentanesulfonic acid is considered to be reduced at first to dipentyl disulfide or pentanethiol as in the case of arenesulfonic acids. The subsequent multi-step reaction of either the disulfide or the thiol with Ph_3P/I_2 would afford eventually the iodide. In separate experiments, both pentanethiol and dipentyl disulfide were found to be converted to pentyl iodides quantitatively upon treatment with Ph_3P/I_2.

$$RSSR + Ph_3P + \overset{+}{Ph_3P}\text{-}I\ I^- \longrightarrow 2\ R\text{-}S\text{-}\overset{+}{P}Ph_3I^- \longrightarrow 2\ RI + 2\ Ph_3PS \quad ----(25)$$

$$RSH + \overset{+}{Ph_3P}\text{-}I\ I^- \longrightarrow R\text{-}S\text{-}\overset{+}{P}Ph_3\ I^- + HI \longrightarrow RI + Ph_3PS \quad --------(26)$$

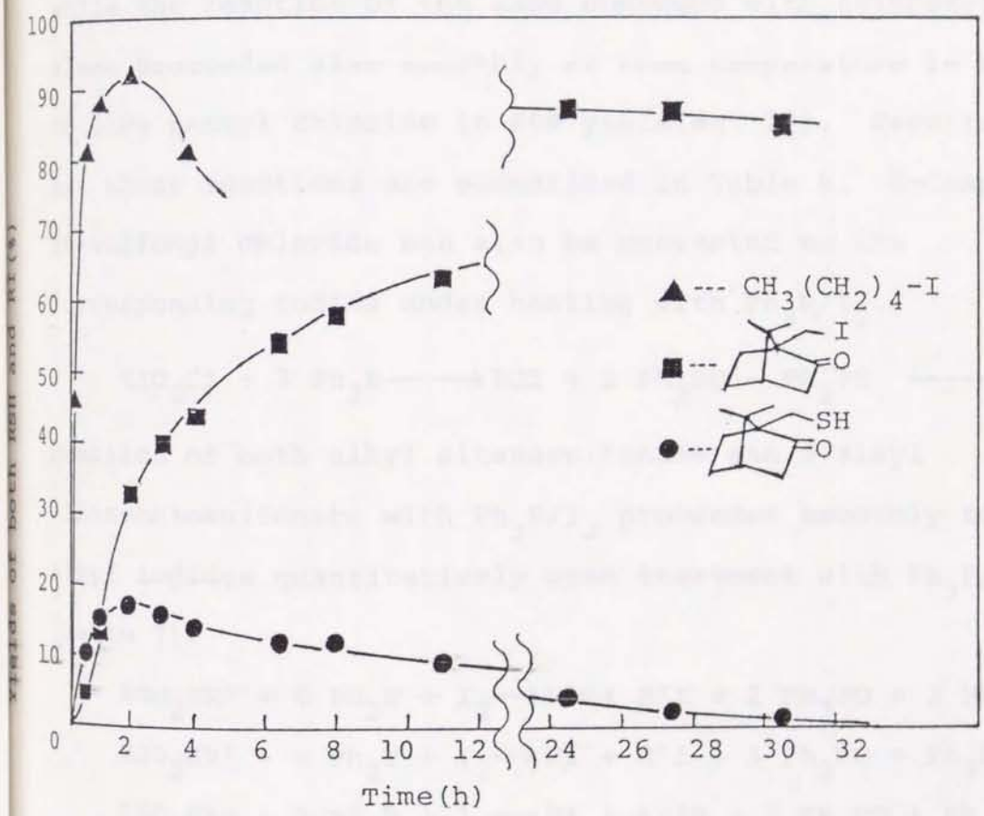
It is worthy to note that even sterically-hindered d-camphor-10-sulfonic acid was successfully converted to the corresponding optically active d-camphor-10-yl iodide. The formation of the corresponding thiol as the intermediate is shown in Fig. 2. Although pentanethiol was not detected in the direct conversion of pentanesulfonic acid to pentyl iodide in the reduction with Ph_3P/I_2, since unsterically-hindered pentanethiol is so reactive, d-camphor-10-thiol was actually isolated in a maximum yield of about 15% in the conversion of

Table 6. Reaction of Aliphatic Sulfur Compounds with Triphenylphosphine/Iodine in Benzene under Nitrogen Atmosphere

Substrate	Substrate/I_2/Ph_3P/amine	Temp (°C)	Time	Yield of RI(%)[a]
$CH_3(CH_2)_4SO_3H$	2/3/10/0	25	26 h	81
	2/3/10/0	reflux	0.5 h	63
$CH_3(CH_2)_4SO_2H$	2/1/6.6/0	25	0.5 h	71[b]
	2/3/6.6/0	25	2 h	95
$CH_3(CH_2)_7SO_2H$	2/3/6.6/0	25	2 h	85
$CH_3(CH_2)_7SO_2Cl$	2/3/8/0	25	10 min	75[c]
	2/0/8/0	25	20 min	80 [$CH_3(CH_2)_7Cl$]
	2/4/8/0	reflux	8 h	(87)[d]
$CH_3(CH_2)_7SH$	2/3/3/0	reflux	1 h	98
$CH_3(CH_2)_4SH$	2/2/2.5/0	reflux	1.5 h	90
$CH_3(CH_2)_4SO_3Na$	2/3/8[e]	reflux	26 h	40
$CH_3(CH_2)_4SO_3H$	2/3/10/2(Bu_3N)[f]	25	25 min	79
$CH_3(CH_2)_4SO_2H$	2/3/6.6/2(Bu_3N)	25	10 min	100
$CH_3(CH_2)_7SH$	2/3/3/2(Pyridine)	25	20 min	88
$CH_3(CH_2)_4SH$	2/3/3/2(Bu_3N)	25	20 min	100
	2/6/10/0	reflux	9 h	87(67)[d]

a) GLC yield(20% OV-1, 1 m glass column). b) Pentanethiol was obtained as by-product(10% yield). c) Chlorooctane was obtained as by-product(12% yield). d) Isolated yield. e) 18-Crown-6 was used as a phase transfer catalyst. f) The mixture of benzene and acetonitrile was used as a solvent.

Fig. 2. Reaction of RSO_3H with Ph_3P/I_2 in Benzene under Reflux Condition.
(d-Camphor-10-sulfonic Acid and Pentanesulfonic Acid)



$RSO_3H/Ph_3P/I_2$=2/10/4 (mmol)

d-camphor-10-sulfonic acid to d-camphor-10-yl iodide with Ph_3P/I_2. Since the d-camphor-10-thiol has neopentyl structure, further desulfurization(S_N2) reaction is rather slow. Therefore, we can detect d-camphor-10-thiol during the reductive conversion of d-camphor-10-sulfonic acid to the corresponding iodide. Pentanesulfinic acid reacted more readily with Ph_3P/I_2 than pentanesulfonic acid, however both affording pentyl iodide. Pentanesulfonyl chloride gave a mixture of pentyl iodide(major) and pentyl chloride(minor), while the reaction of the same compound with triphenylphosphine alone proceeded also smoothly at room temperature in benzene to give pentyl chloride in 80% yield(eq. 27). Results of all these reactions are summarized in Table 6. d-Camphor-10-sulfonyl chloride can also be converted to the corresponding iodide under heating with Ph_3P/I_2.

$$RSO_2Cl + 3\ Ph_3P \longrightarrow RCl + 2\ Ph_3PO + Ph_3PS \quad \text{-------(27)}$$

Reaction of both alkyl alkanesulfonate and S-alkyl alkanethiosulfonate with Ph_3P/I_2 proceeded smoothly to give alkyl iodides quantitatively upon treatment with Ph_3P/I_2 (Table 7).

$$RSO_2SR' + 4\ Ph_3P + I_2 \longrightarrow RI + R'I + 2\ Ph_3PO + 2\ Ph_3PS \quad \text{--(28)}$$

$$RSO_2OR' + 4\ Ph_3P + I_2 \longrightarrow RI + R'I + 3\ Ph_3PO + Ph_3PS \quad \text{----(29)}$$

$$RSO_2SAr + 3\ Ph_3P + I_2 \longrightarrow RI + ArSH + 2\ Ph_3PO + Ph_3PS \quad \text{---(30)}$$

Nucleophilic substitution on alkyl group, R', by iodide ion is undoubtedly involved in the initial step of the reaction of the sulfonate(eq. 29), while there are two possible paths to initiate the reaction of S-alkyl alkanethiosulfonate(eq. 28), i.e. nucleophilic substitution on the sulfenyl sulfur and

Table 7. Reaction of Aliphatic Sulfur Compounds with Triphenylphosphine/Iodine in Benzene under Nitrogen Atmosphere

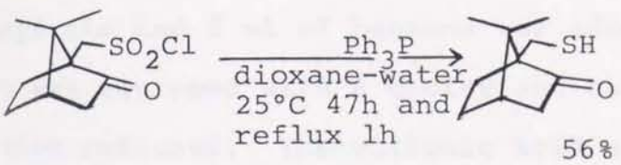
Substrate R^1- R^2-	Substrate/I_2/Ph_3P	Temp(°C)	Time	Products(%)[a] R^1I	R^2I
$CH_3(CH_2)_7SO_2O(CH_2)_4CH_3$	2/7/11	reflux	5 h	95	95
$CH_3(CH_2)_4SO_2S(CH_2)_4CH_3$	1/2.5/5	25	10 min		200(R^1=R^2)
$CH_3(CH_2)_7SO_2S(CH_2)_7CH_3$	1/2.5/5	25	10-15 min		184(R^1=R^2)
$CH_3(CH_2)_4SS(CH_2)_4CH_3$	1/2/3	25	90 min		200(R^1=R^2)
$CH_3(CH_2)_7SS(CH_2)_7CH_3$	1/2/3	25	120 min		200(R^1=R^2)
$CH_3(CH_2)_4SO_2SC_6H_5$	1/2.5/5	25	10 min	92	c)

a) GLC yields(20% OV-1, 1 m glass column). b) The mixture of benzene and dichloromethane was used as a solvent. c) After this reaction, the mixture of 0.5 ml of water and 2.5 ml of dioxane was added. Benzenethiol was obtained in 89% yield.

that on alkyl carbon, the S-aryl alkanethiosulfonate reacts with Ph_3P/I_2 quite readily to form the alkyl iodide and the arenethiol. This reaction should also be initiated by the nucleophilic displacement on the sulfenyl sulfur of the substrate with either triphenylphosphine or iodide anion. However, since the reaction of both S-alkyl alkanethiosulfonate and S-aryl alkanethiosulfonate with Ph_3P/I_2 proceed much more readily than the reaction of alkyl alkanesulfonate under the same conditions, the reactions of the former two thiolsulfonates are undoubtedly initiated by nucleophilic substitution on the divalent sulfur. Both iodide anion and triphenylphosphine being just as strong nucleophiles for divalent sulfur, it is hard to conclude which nucleophile plays an important key role in initiating of the reaction. The rate-determining step of the reaction of alkanethiols, sulfinic acids, and sulfonic acids are presumed to be the nucleophilic attack of conjugate bases of these oxidized organosulfur compounds on the phosphorus atom of iodotriphenylphosphonium ion[33, 34] as discussed in the former section which deals with the reduction of arenesulfonic acids. In accordance with this assumption, these reactions were markedly accelerated by the presence of amine(Table 6) while the reduction of the other aprotic derivatives were not affected by the addition of base. These reactions are quite useful in conversion of alkanesulfonic acids, thiolsulfonates, sulfonates, disulfides, thiols, and sulfonyl chlorides to the corresponding alkyl iodides quantitatively under mild conditions in one flask.

Finally, various alkanesulfonyl chlorides were converted to the corresponding iodides by Ph_3P/I_2 system, while they could be converted to the corresponding chlorides with Ph_3P alone. But, in an interesting and useful reaction, the corresponding thiols can be obtained in the reduction of alkanesulfonyl chlorides with Ph_3P/H_2O system as shown in the following.

$$CH_3(CH_2)_7SO_2Cl \xrightarrow[\text{dioxane-water}\ 25°C\ 24h\ \text{and reflux}\ 1h]{Ph_3P} CH_3(CH_2)_7SH \quad 75\%$$



56%

RSO_2Cl/Ph_3P=1/4(mmol), dioxane/water=4/1(ml)

Experimental

Conversion of Sodium Sulfonate to the Corresponding Sulfonic Acid. The cation exchange resin which was converted to the protonated form by flowing 1N. HCl water solution packed in a column [Dowex 50w-x8 mesh H-form, Muromachi Kagaku Co.] was used.

GLC. 20% OV-1 1 m glass column, Hitachi-163 gas chromatograph was used.

Reduction of Arenesulfonic Acid with Ph_3P/I_2 System. A mixture of 380 mg(2 mmol) of p-toluenesulfonic acid monohydrate and 5 ml of benzene was added into a reactor which was equipped with a cooler and calcium chloride tube and then refluxed. The sulfonic acid was carefully dehydrated to completely dry prior to the reaction by way of azeotropic distillation with benzene. After 2620 mg(10 mmol) of triphenylphosphine was added to this dried sulfonic acid, the reactor was equipped with another dry cooler and a argon or nitrogen balloon, and substituted with this inert gas with a vacuum pump for 30 minutes to 20 minutes at room temperature. Then, 5 ml of dry benzene and 254 mg(1 mmol) of iodine were added into this mixture and the whole mixture was stirred and refluxed(bath temperature 90-100°C) for 2.5 hours. The reaction was followed by GLC. After the reaction was complete, a mixture of 3 ml of dioxane and 3 ml of water was added to this reaction mixture which was refluxed for 1~0.5 hour to decompose the small excess of triphenylphosphine-iodine complex to triphenylphosphine oxide and hydrogen iodide. The solution was poured into benzene and washed with water

for three times. This benzene solution was dried over $MgSO_4$. p-Toluenethiol was obtained by GLC in 89% yield. After the benzene solution was evaporated, the residue was separated with silica-gel column chromatography(Kieselgel-60, 70-230 mesh, MERCK, eluent:$CHCl_3$). A mixture of p-toluenethiol and a small excess of triphenylphosphine was obtained from fraction-1, and 2133 mg(128%) of triphenylphosphine oxide was obtained from fraction-2. Fraction-1 was separated further with silica-gel column chromatography(eluent:benzene/hexane=1/5=v/v) to give p-toluenethiol(R_f=0.5) in 54% yield. This was identical with commercially available authentic compound. The low yield of p-toluenethiol isolated as compared with that of GLC yield is believed to be due to the high volatility of the thiol. Ph_3PO m.p.=154~155°C(lit,[35] 154~157°C)

Reduction of Arenesulfonic Acid with Ph_3P/I_2/Amine System.

To a carefully dehydrated 380 mg(2 mmol) of p-toluenesulfonic acid, 2100 mg(8 mmol) of triphenylphosphine was added and the reactor was equipped with another dry cooler and an argon or nitrogen balloon, and substituted with this inert gas with a vacuum pump for 30 to 20 minutes at room temperature. Then, after 5 ml of dry benzene and 254 mg(1 mmol) of iodine were added to this mixture, 371 mg(2 mmol) of tributylamine was finally added to this mixture. This reaction mixture was stirred and refluxed for 20 minutes, following the reaction by GLC. Then a mixture of 3 ml of water and 3 ml of dioxane was added to this reaction mixture which was refluxed for 5 minutes. p-Toluenethiol was obtained in 95% yield by GLC.

Reduction of Sodium Arenesulfonate with Ph_3P/I_2/18-Crown-6 System. After 460 mg(2 mmol) of sodium β-naphthalenesulfonate was dissolved in 5 ml of benzene, the mixture was refluxed and dehydrated to nearly completely dry by the same method. Triphenylphosphine 2620 mg(10 mmol) and 264 mg(1 mmol) of 18-crown-6 were added to this sodium salt. The reactor was equipped with another dry cooler and argon or nitrogen balloon, and substituted with this inert gas with a vacuum pump. Then, 5 ml of dry benzene and 508 mg of iodine were added to this mixture which was stirred and refluxed for 36 hours. After the reaction, a mixture of β-naphthalenethiol and di-β-naphthyl disulfide were detected by GLC. Di-β-naphthyl disulfide was converted to the β-naphthalenethiol by addition of a mixture of 200 mg of water and 2 ml of dioxane and then the reaction mixture was refluxed for 1 hour. The reaction mixture was then treated in a similar way as in the case of arenesulfonic acids. β-Naphthalenethiol was obtained in 95% yield and isolated in 93.4% yield, however the amount of triphenylphosphine oxide was not determined.

Competition Reduction of p-Substituted Benzenesulfonic Acids with Ph_3P/I_2 System. A mixture of 190.2 mg(1 mmol) of p-toluenesulfonic acid, 176 mg(1 mmol) of benzenesulfonic acid, and 192.5 mg(1 mmol) of p-chlorobenzenesulfonic acid was dissolved in 5 ml of benzene in a reactor which was equipped with a cooler and a $CaCl_2$ tube and the whole mixture was refluxed. All these sulfonic acids were dehydrated nearly completely dry prior to the reaction by way of azeotropic distillation with benzene. After 3144 mg(12 mmol) of

triphenylphosphine and 154 mg(1 mmol) of biphenyl(standard compound) were added to this dry sulfonic acids, the reactor was equipped with another dry cooler and a nitrogen balloon, and substituted with this inert gas. Then, 254 mg(1 mmol) of iodine and 6 ml of dry benzene were added to this mixture which was then stirred at 72~73°C. A small portion(0.1 ml) of reaction mixture was picked up by a micro-cylinge and quenched with a mixture of water-dioxane-benzene(v=1/1/2) every fixed time interval(3, 5, 10, 30, 60, and 120 min from the initial time, respectively). The yields of three thiols obtained in every case, were determined by calibration curve with GLC.

Reduction of Arenesulfonate Ester with Ph_3P/I_2 System.

Pentyl p-toluenesulfonate 484 mg(2 mmol) and 2100 mg(8 mmol) of triphenylphosphine were added into a reactor which was equipped with a dry cooler and an argon or nitrogen balloon and substituted with dry inert gas with a vacuum pump. Then, 5 ml of dry benzene and 381 mg(1 mmol) of iodine were added into this mixture which was refluxed and stirred for 10 minutes. The starting ester was no longer present by this time upon analysis with GLC and TLC(silica-gel R_f=0.3 eluent:benzene), and p-toluenethiol, di-p-tolyl disulfide, and pentyl iodide were resulted. After the reaction, a mixture of 200 mg of water and 1 ml of dioxane was added into the mixture which was then refluxed for 30 minutes to convert the disulfide to the corresponding thiol completely. The yield of the reaction products were determined by GLC(20% OV-1). p-Toluenethiol 95%. Pentyl Iodide 90%.

Authentic pentyl iodide was obtained by the following reaction. A mixture of 2 g(22.7 mmol) of pentyl alcohol, 5950 mg(22.7 mmol) of triphenylphosphine and 5670 mg(22.7 mmol) of iodine was dissolved in dry 20 ml of ether. Then the mixture was refluxed for 5 hours under nitrogen atmosphere, and poured into benzene which solution was washed with water for 3 times, and dried over $MgSO_4$. The solution was evaporated and distilled to give pentyl iodide in a high yield. Pentyl Iodide b.p.=157°C/760 mmHg(lit,[36] 157°C/760 mmHg).

Synthesis of p-Toluenesulfonyl Iodide. Sodium p-toluenesulfinate dihydrate 2140 mg(10 mmol) was dissolved in 10 ml of water while 2540 mg(10 mmol) of iodine was dissolved in 10 ml of benzene and both solutions were mixed under 0°C for 0.5 hour with stirring. Then the reaction mixture was poured into benzene which solution was washed with water for three times and dried over $MgSO_4$. p-Toluenesulfonyl iodide was recrystallized from a mixture of hexane and benzene. Rock-crystals of m.p.=85~86°C (decomposition) were obtained(lit,[37] 84~85°C).

Reductive Conversion of d-Camphor-10-sulfonic Acid with Ph_3P/I_2 System. The reaction is carried out under dry nitrogen atmosphere in a two-necked flask with a reflux condenser. To 8 ml of dry benzene solution of a mixture of d-camphor-10-sulfonic acid, 464 mg(2 mmol), and triphenylphosphine 2620 mg(10 mmol), was added solid iodine 1524 mg(6 mmol) at room temperature. Then the mixture was refluxed for 9 hours in nitrogen atmosphere. Benzene was added to the resultant mixture which was then washed with

water. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was then subjected to column chromatography on silica gel(eluent:benzene) in order to separate triphenylphosphine sulfide[R_f=0.5, yield 60%, m.p.= 162~163°C(lit,[38] 162~164°C)], d-camphor-10-yl iodide(R_f=0.4), and triphenylphosphine oxide[R_f=0.1, yield 90%, m.p.=154~155°C (lit,[35] 154~157°C)]. d-Camphor-10-yl Iodide 488 mg, 87%(GLC) and isolated in 67% yield: m.p.=71°C; $[\alpha]_D^{25}$ -20.6(c=1, $CHCl_3$); IR(KBr) 1735(C=O), 1375, and 1390cm^{-1}; NMR(CCl_4) δ=0.9(3H, s), 1.1(3H, s), 3.05(1H, d, J=10.5Hz), 3.35(1H, d, J=10.5Hz), and 1.0~2.4(7H, m); Found: C, 43.29; H, 5.38; I, 45.75. Calcd for $C_{10}H_{15}OI$: C, 43.18; H, 5.43; I, 45.62.

The Reductive Conversion of Alkanesulfonate Ester with Ph_3P/I_2 System. Pentyl octanesulfonate 529 mg(2 mmol) and 2882 mg(11 mmol) of triphenylphosphine were added to a reactor which was equipped with a dry condenser and a nitrogen balloon and substituted with dry inert gas with a vacuum pump. Then, 8 ml of dry benzene and 1778 mg(7 mmol) of iodine were added to this mixture which was refluxed and stirred for 5 hours. The starting ester readily absent by this time upon GLC and TLC analysis and pentyl iodide, octyl iodide, triphenylphosphine oxide and triphenylphosphine sulfide were resulted. After the reaction, a mixture of 200 mg of water and 1 ml of dioxane was added into the mixture. The yields of reaction products were determined by GLC.

Octyl Iodide 95%. Pentyl Iodide 95%.

Octyl iodide was synthesized by the same method as in the case of pentyl iodide in a high yield. Octyl Iodide b.p.=110°C/23 mmHg(lit,[39] 226°C/760 mmHg).

The Preparation of d-Camphor-10-thiol. d-Camphor-10-sulfonic acid 10 g(42 mmol) was dissolved in 15 ml of chloroform and then 18 g(86 mmol) of phosphorus pentachloride was added slowly. After this mixture was refluxed for 2 hours, it was poured into chloroform which was then washed with water for 4 times, dried over $MgSO_4$ and evaporated to give d-camphor-10-sulfonyl chloride in 69% yield. m.p.=65~67°C(lit,[40] 67~68°C). d-Camphor-10-sulfonyl chloride 3000 mg(12 mmol) and 12576 mg(48 mmol) of triphenylphosphine were dissolved in the mixture of 40 ml of dioxane and 10 ml of water and the whole mixture was stirred for 47 hours at room temperature and refluxed for 1 hour. After the reaction, the mixture was separated through silica-gel column chromatography using benzene as eluent to give d-camphor-10-thiol in 56% yield. m.p.=65~66°C; TLC(eluent:benzene) R_f=0.2~0.3; IR(KBr) 1375, 1385, 1730(C=O), and 2560cm^{-1}(SH); NMR(CCl_4) δ=0.95(3H, s), 1.05(3H, s), 1.2~2.6(8H, m), 2.73(1H, d, J=6Hz), and 2.95(1H, d, J=6Hz); Found: C, 65.24; H, 8.72; S, 17.24. Calcd for $C_{10}H_{16}OS$: C, 65.17; H, 8.75; S, 17.40.

Monitoring the Reaction of Alkanesulfonic Acid with Ph_3P/I_2. d-Camphor-10-sulfonic acid 464 mg(2 mmol), 2620 mg(10 mmol) of triphenylphosphine, and 308 mg(2 mmol) of biphenyl(standard) were dissolved in 10 ml of dry benzene, into which 1016 mg(4 mmol) of iodine was then added and the solution was refluxed under nitrogen atmosphere. At fixed time intervals, 0.1 ml of the reaction mixture was picked up by micro-cylinge and quenched with a mixture of water and benzene(v/v=1/1). The yields of the thiol and iodide obtained in every case were

determined by calibration curve with GLC(SE-30). In the case of pentanesulfonic acid, the corresponding thiol was not present in every sample under this condition.

Preparation of Thiolsulfonate. Arenesulfenyl chloride was prepared by treating a thiol or a disulfide with gaseous Cl_2 in CCl_4 at 0°C. Free sulfinic acids other than those which were obtained by acidification of commercial sodium arenesulfinates with conc. HCl, were synthesized by hydrolyses of the corresponding sulfinyl chlorides. To a dry CCl_4 solution(150 ml) of a sulfenyl chloride(0.03 mol) which was freshly prepared and was made free from Cl_2 under reduced pressure, was added dropwise into dry pyridine(0.033 mol) at lower than 0°C and then slightly white precipitate of pyridinium salt of the sulfenyl chloride formed. A solution containing a free sulfinic acid(0.03 mol) in dry CCl_4 or ether(50 ml) was added to that solution at a temperature lower than 0°C. Then a new precipitate was formed gradually as the addition proceeded. After stirring the reaction mixture containing the white salt for 30 min and subsequent warming to room temperature, the reaction mixture was washed with 5% HCl solution and then water. The organic layer was dried over $CaCl_2$ and then solvent was evaporated. From the residue, the thiolsulfonate was obtained in 80~90% yield and recrystallized from ethanol.

S-Phenyl Benzenethiosulfonate m.p.=44~45°C(lit,[41] 44~45°C).

S-p-Tolyl p-Toluenethiosulfonate m.p.=72~74°C(lit,[42] 76°C).

Preparation of Sulfonate Ester. In a reactor, 31.47 mmol of sulfonyl chloride and 94.41 mmol of alcohol were dissolved

in the mixture of 10 ml of benzene and 10 ml of acetonitrile and the whole mixture was stirred. Then, 157.25 mmol of pyridine was added to this mixture. After 30 minutes, the starting arenesulfonyl chloride was found no longer present upon analysis with TLC(R_f=0.5, eluent:benzene). Meanwhile, in the case of alkanesulfonyl chloride, the reaction was carried out for 12 hours at room temperature. Then, the solution was poured into benzene which solvent was washed with water for three times, and dried over $MgSO_4$. The sulfonate ester obtained was distilled or recrystallized with benzene to give the pure sulfonate. The yield of the sulfonate is usually 50~60%.

Phenyl p-Toluenesulfonate m.p.=92~93°C(lit,[43] 93°C).

Neopentyl p-Toluenesulfonate m.p.=46~47°C(lit,[44] 48°C).

Pentyl p-Toluenesulfonate b.p.=167~168°C/3 mmHg(lit,[46] 169~170 °C/3 mmHg).

Pentyl Benzenesulfonate b.p.=138~140°C/1 mmHg(lit,[45] 136~138 °C/1 mmHg).

Pentyl Octanesulfonate TLC(eluent:benzene) R_f=0.4~0.5; IR(NaCl) 1340(SO) and 1160cm^{-1}(SO); NMR(CCl_4) δ=4.1(2H, t, J=6Hz), 3.0(2H, t, J=6.7Hz), and 2.1~0.7ppm(24H, m); Found: C, 59.13; H, 10.55; S, 11.94. Calcd for $C_{13}H_{28}SO_3$: C, 59.05; H, 10.67; S, 12.12.

Preparation of Sulfinic Acid. p-Chlorobenzenesulfonyl chloride 5 g(23.7 mmol) and 18 g(71.1 mmol) of sodium sulfite sevenhydrate were added into 100 ml of water. The reaction mixture was kept at a temperature ranging 70~80°C for five hours. After the reaction, this water solution was washed with chloroform twice, acidified with excess conc. HCl solution, cooled and filtered. The white precipitate was recrystallized

from water yielding p-chlorobenzenesulfinic acid in a high yield(79%). p-Chlorobenzenesulfinic Acid m.p.=95~97°C(lit,[47] 98~99°C). Octanesulfinic acid can be also obtained from octanesulfonyl chloride by the same procedure. $CH_3(CH_2)_7SO_2CH_3$ m.p.=62~63°C(lit,[48] 62°C, octanesulfinic acid was converted to the octyl methyl sulfone by the reaction with methyl iodide, 57%)

p-Toluenesulfinic acid and benzenesulfinic acid were obtained by acidification of the corresponding sodium arenesulfinates which were obtained as commercial samples. The white precipitates were recrystallized from water yielding the corresponding arenesulfinic acids.

Benzenesulfinic Acid m.p.=78~80°C(lit,[47] 81.5~83°C).

p-Toluenesulfinic Acid m.p.=84~85°C(lit,[47] 84~85°C).

Preparation of Dialkyl Thiolsulfonate. To the mixture of 19.42 mmol of dialkyl disulfide and 10 ml of acetic acid, 5.5 g, 35%(48.55 mmol) of hydrogen peroxide was slowly added, under stirring at 0°C. Then reaction mixture was warmed up to room temperature and stirred for over night, then poured into benzene solution which was neutralized with Na_2CO_3 solution, washed with $Na_2S_2O_3$ solution and water for twice respectively, and dried over $MgSO_4$. The thiolsulfonate was purified by through a separative silica-gel column chromatography using benzene as eluent.

S-Pentyl Pentanethiosulfonate TLC(eluent:benzene) R_f=0.5; IR(NaCl) 1120(SO) and 1320cm^{-1}(SO); NMR(CCl_4) δ=0.7~2.2 (18H, m), 2.9~3.4(4H, m); Found: C, 50.49; H, 9.34. Calcd for $C_{10}H_{22}O_2S_2$: C, 50.38; H, 9.30.

S-Octyl Octanethiosulfonate TLC(eluent:benzene) R_f=0.5;

IR(NaCl) 1120(SO) and 1320cm^{-1}(SO); NMR(CCl_4) τ=0.7~2.2(30H, m), 2.9~3.4(4H, m); Found: C, 59.77; H, 10.68. Calcd for $C_{16}H_{34}O_2S_2$: C, 59.57; H, 10.62.

Preparation of Pentanesulfinic Acid. Dipentyl disulfide, 11.54 g(0.056 mol) and 11.44 g(0.112 mol) of acetic anhydride were placed in a flask which was equipped with a gas inlet tube and a gas outlet tube, attached to a calcium chloride tube, cooled by dry ice until the internal temperature has cooled down to -20°C to -10°C. Chlorine was passed into the well-stirred mixture maintaining the temperature. The progress of the reaction can be followed by color change, from yellow, raddish and green finally. After the reaction, the excess chlorine was evaporated and the mixture was distilled to give pentanesulfinyl chloride, in 77% yield (77~78°C/8 mmHg). Five ml of tetrachloromethane dissolving pentanesulfinyl chloride 2000 mg(12.94 mmol) was added into a mixture of 2250 mg(28.47 mmol) of pyridine, 10 ml of ether and 5 ml of water under 0°C, and then white precipitate of pyridinium chloride was obtained instantly. The reaction mixture was poured into water and the solution was washed with ether for three times, acidified with conc. HCl solution, extracted with ether. The ether extract was dried over $MgSO_4$ and evaporation of solvent gave pentanesulfinic acid in a quantitative yield. $CH_3(CH_2)_4SO_2C_6H_3(NO_2)_2$-2,4 m.p.=84°C (lit,[49] 83°C, pentanesulfinic acid was converted to the pentyl 2,4-dinitrophenyl sulfone by the reaction with 2,4-dinitrochlorobenzene).

S-Phenyl Pentanethiosulfonate. Benzenesulfenyl chloride was prepared by treating the thiol with gaseous chlorine in tetrachloromethane at 0°C(45~52°C/4 mmHg, red color, 81%). To a dry tetrachloromethane solution(150 ml) of benzenesulfenyl chloride(0.03 mol) was added dropwise dry pyridine(0.033 mol) at 0°C and then sightly white precipitate of pyridinium salt of sulfenyl chloride formed. A solution containing free pentanesulfinic acid(0.03 mol) in dry tetrachloromethane was added to that solution at 0°C. Then, new precipitate was formed gradually as the addition proceeded. After stirring the reaction mixture containing the white salt for 30 minutes and subsequent warming to room temperature, the reaction mixture was washed with dilute HCl solution and then water. The organic layer was dried over $MgSO_4$ and solvent was evaporated. From the residue, the S-phenyl pentanethiosulfonate was obtained in a high yield. TLC(eluent:benzene) R_f=0.4; IR(NaCl) 1120(SO) and 1320cm^{-1} (SO); NMR(CCl_4) δ=0.7~2.2(9H, m), 2.9~3.3(2H, t, J=7.5Hz), 7.2~7.7(5H, m); Found: C, 54.07; H, 6.58. Calcd for $C_{11}H_{16}S_2O_2$: C, 54.06; H, 6.59.

Other Compounds.

α-Naphthalenethiol 160~165°C/35 mmHg(lit,[50] 142~142.5/7 mmHg, 85~88°C/0.27 mmHg). NMR(CCl_4) δ=3.4(1H, s), 7.05~8.30(7H, m).

2,4-Dimethylbenzene-1-thiol 74~76°C/4 mmHg(lit,[51] 80.5°C/9 mmHg, 93°C/12 mmHg). NMR(CCl_4) δ=2.2(6H, s), 2.9(1H, s). 6.5~7.0(4H, m).

References

1) Oxidation of Organic Sulfur Compounds — Mainly Thiols and the Compounds Having Sulfur-Sulfur Linkage(Japanese). S. Oae and T. Takata, Chemistry(Japan), 34(10), 756, 891, and 961(1979).

2) A.I.A. Khodair, A. Swelim, F. El-Sheikh, Inst. J. Sulfur Chem., B, 6, 213(1971).
E. Schwenk, D. Papa, B. Whitman, H. Ginsberg, J. Org. Chem., 9, 1(1944).

3) S.W. Benson, Chem. Rev., 78, 23(1978).

4) R. Adams and C.S. Marvels, Org. Synth., 1, 83(1941).
J. Burdon, I. Farazmand, and J.C. Tatlow, J. Chem. Soc., (1957), 2574.
C.M. Suter, J. Am. Chem. Soc., 53, 1112(1931).
P.D. Bartlett, L.H. Knox, Org. Synth., 5, 196(1973).

5) A. Barco, S. Benetti, G.P. Pollini, and R. Taddia, Synthesis, (1974), 877.
H.H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, Helv. Chim. Acta., 42, 1653(1959).

6) R. Adams and C.S. Marvel, Org. Synth., Coll. Vol. 1, 504(1956).
O. Litvay, E. Riesz, and L. Landau, Chem. Ber., 62, 1863(1929).
W.A. Sheppard, Org. Synth., 40, 80(1960).
J.I.G. Cadogan, Quart.Rev.(London)., 16, 223(1962).
D. Cipris and D. Pouli, Synth. Commun., 9, 207(1979).
H. Alper, Angew. Chem., Int.Ed. Engl., 8, 677(1969).
S. Smiles and C.M. Bere. Org. Synth., Coll. Vol. 1, 7(1941).
S. Krishna and H. Singh, J. Am.Chem. Soc., 50, 792(1928).
M. Kulka, J. Am. Chem. Soc., 72, 1216(1950).
P.D. Caeser, Org. Synth., Coll. Vol. 5, 685(1963).
T.H. Chan, J.P. Montillier, W.F. van Horn, and D.N. Harpp, J. Am. Chem. Soc., 92, 7224(1970).

7) C.S. Marvel and P.D. Caeser, J. Am. Chem. Soc.,73,1097(1951).
D. Klamann, Monatsh. Chem., 84, 651(1953).
E. Fisher, Chem. Ber., 48, 93(1915).
T. Cuving and M. Larchevegue, J. Organomet. Chem., 64, 315 (1974)

8) A. Zobacova, V. Hermankova, and J. Jary, Collect Czech. Chem. Commun., 42, 2540(1977).

J. Wolinsky, R.L. Marhenke, and E.J. Eustace, J. Org. Chem., 38, 1428(1973).

9) J. Strating and H.J. Baker, Recl. Trav. Chim. Pays-Bas., 69, 638(1950).
S. Hayashi, M. Furukawa, J. Yamamoto, and K. Hamamura, Chem. Pharm. Bull., 15, 1310(1967).

10) T. Numata, H. Togo, and S. Oae, Chapter 1.

11) T. Numata, H. Awano, and S. Oae, Tet. Lett., 21, 1235(1980).

12) G.A. Olah, S.C. Narang, L.D. Field, and R. Karpeles, J. Org. Chem., 46, 2408(1981).

13) A.D. Beveridge, G.S. Harris, and F. Inglis, J. Chem. Soc., Perkin Trans I, (1966), 520.
L. Horner and H. Nickel, Ann. Chim.(Paris), 597, 20(1955).

14) D.N. Harpp and J.G. Gleason, J. Am. Chem. Soc., 93, 2437 (1971).

15) G.A. Wiley, R.L. Hershkowitz, B.M. Rein, and B.C. Chung, J. Am. Chem. Soc., 86, 964(1964).
G.A. Wiley, B.M. Rein, and R.L. Hershkowitz, Tet. Lett., (1964), 2509.
R. Michinek and W. Liittke, Synthesis, (1975), 255.

16) D.N. Harpp and J.G. Gleason, J. Org. Chem., 35, 3259(1970).
D.N. Harpp, J.G. Gleason, and J.P. Snyder, J. Am. Chem. Soc., 90, 4181(1968).

17) I.L. Knunyants, Dokl. Chem., 224, 521(1975).

18) D.N. Harpp and J.G. Gleason, J. Org. Chem., 36, 73(1971).

19) S. Kobayashi, T. Iimori, T. Izawa, and M. Ohno, J. Am. Chem. Soc., 103, 2406(1981).
R. Matsueda, H. Maruyama, M. Ueki, and T. Mukaiyama, Bull. Chem. Soc. Jpn., 44, 1373(1971).

20) T. Endo, S. Ikenaga, and T. Mukaiyama, Bull. Chem. Soc. Jpn., 43, 2632(1970).

21) T. Mukaiyama, K. Goto, R. Matsueda, and M. Ueki, Tet. Lett., (1970), 5293.

22) T. Mukaiyama, H. Maruyama, M. Ueki, and R. Matsueda, Bull. Chem. Soc. Jpn., 44, 1373(1971).
E.J. Corey and D.J. Brunelle, Tet. Lett., (1976), 3409.
T. Mukaiyama, M. Ueki, H. Maruyama, and R. Matsueda, J. Am. Chem. Soc., 90, 4490(1968).
H. Takaku and Y. Shimada, Chem. Lett., (1975), 873.

23) T. Mukaiyama and M. Hashimoto, J. Am. Chem. Soc., 94, 8528 (1972).
H. Takaku, T. Konishi, and H. Hata, Chem. Lett., (1977), 655.
24) I. Nakagawa and T. Hata, Tet. Lett., (1975), 1409.
25) L. Bauer and J. Cymermann, J. Chem. Soc., (1949), 3434.
26) K. Fujimori, H. Togo, and S. Oae, Tet. Lett., 21, 4921(1980).
27) L. Horner and H. Winkler, Tet. Lett., (1964), 455.
K. Issleib and W. Seidel, Z. Anorg. Allg. Chem., 288, 201 (1956).
28) W.A. Sheppard, Org. Synth., Coll. Vol., 5, 844(1973).
L. Bauer and L. Cymermann, J. Chem. Soc., (1949), 3434.
D. Klamann and G. Hofbauer, Monatsh. Chem., 83, 1489(1952).
29) G.M. Kosolapoff and L. Maier,"Organic Phosphorus Compounds", Wiley-Interscience, (1972).
30) L.E. Overman and E.M. O'Connor, J. Am. Chem. Soc., 98, 771(1976).
31) M. Suda and A. Fukushima, Tet. Lett., 22, 757(1981).
P. Hogge and G. Richardson, J. Chem. Soc., Chem. Commun., 622(1975).
R. Appel and R.K. Kleinstuck, Chem. Ber., 107, 5(1974).
S. Yamada and Y. Takeuchi, Tet. Lett., (1971), 3595.
B. Castro and R. Dormoy, Bull. Soc. Chim. Fr., 3034(1971).
R. Appel, R. Kleinstuck, K.-D. Ziekn, Chem. Ber., 104, 1335 (1971).
32) S. Oae and H. Togo, Synthesis, (1981), 371.
33) G.A. Wiley, R.L. Hershkowitz, B.M. Rein, and B.C. Chung, J. Am. Chem. Soc., 86, 964(1964).
34) G.A. Wiley, B.M. Rein and R.L. Hershkowitz, Tet. Lett., (1964), 2509.
35) Authentic sample was obtained from Wako Chemical Co.
36) I. Simon, Bull. Soc. Chim. Belg., 38, 2519(1929).
Beilstein, E. II. 1, 98(1920-1929).
37) L.M. Litvinenko, V.A. Dadali, V.A. Sovelova, and T.I. Krichevtsova, Zh. Obshch. Khim., 34, 3730(1964).
C.A., 62, 6420(1965).
38) Authentic sample was obtained from Wako Chemical Co.
39) A.I. Vogel, J. Chem. Soc., (1943), 636.

40) S. Smiles and J. Stewart, Org. Synth., Coll. Vol. 5, 196 (1973).
41) S. Oae, R. Nomura, Y. Yoshikawa, and W. Tagaki, Bull. Chem. Soc. Jpn., 42, 2903(1969).
42) R. Otto, J. Lowenthal, and A.V. Gruber, Ann. Chim.(Paris), 149, 101(1869).
43) H. Gilmann, N.J. Beaber, and C.H. Myers, J. Am. Chem. Soc., 47, 2047(1925).
44) P. Yousefzadeh and C.K. Mann, J. Org. Chem., 33, 2716(1968).
45) B.L. Emling, J. Am. Chem. Soc., 74, 4702(1952).
46) H. Gilmann, N.J. Beaber J. Am. Chem. Soc., 47, 518(1925).
47) R.K. Burkhard, D.E. Sellers, F. Decou, and J.L. Lambert, J. Org. Chem., 24, 767(1959).
48) D. Jerchel, L. Dippelhofen, D. Renner, Chem. Ber., 87, 947 (1954).
49) R.W. Bost, J.O. Turner. R.D. Norton, J. Am. Chem. Soc., 54, 1985(1932).
50) I.N. Tits-Skvortsova, S.Y. Levina, H.I. Levova, and T.A. Danilova, J. Gen. Chem.(USSR), 22, 135(1952).
H.C. Godt and R.E. Wann, J. Org. Chem., 26, 4047(1961).
51) H.C. Godt and R.E. Wann, J. Org. Chem., 26, 4047(1961).
J.H. Uhlenbroek and M. Slagt, Recl. Trav. Chim. Pays-Bas., 80, 1057(1961).

Reduction of Sulfonic Acids with Triphenylphosphine-Diaryl Disulfide System. II.

Abstract

Diaryl disulfides are effective catalysts to reduce arenesulfonic acids with triphenylphosphine to the corresponding arenethiols in good yields, while, alkanesulfonic acids are transformed into the corresponding alkyl aryl sulfide. In these reactions, the arenesulfonic acids bearing electron-donating substituents can be reduced more readily than the ones having electron-withdrawing substituents, while diaryl disulfides with electron-withdrawing substituents are more effective catalyst than the electron rich diaryl disulfide.

Introduction

The first example of one pot reduction of sulfonic acids to thiols was recently reported from this laboratory, by using $(CF_3CO)_2O/Bu_4NI$. This method is the first break through in the direct deoxygenative reduction of sulfonic acids, however, it not only requires a large excess of expensive reagents but also affords a mixture of reduction products, i.e. thiols and thioltrifluoroacetates.[1] More recently, G.A. Olah et al reported the reduction of sulfonic acids to the corresponding disulfides with BX_3(X=Cl, Br, I)/KI.[2] And in the previous paper, we reported another facile and quantitative deoxygenative reduction of sulfonic acids and its derivatives by a new reducing system, i.e. triphenylphosphine-iodine system.[3] This chapter deals with a facile and attractive reduction of sulfonic acids with triphenylphosphine-diaryl disulfide system. Although triphenylphosphine is known to be a relatively strong reducing agent, it does not react directly with sulfonic acids. Meanwhile, the mixture of triphenylphosphine with halogen[4] and that of triphenylphosphine with disulfide[5] respectively are known to give phosphonium salts. Several reactions are known to utilize such phosphonium salts e.g. the conversion of alcohol and phenol derivatives to the corresponding halides by treatment with phosphine and halogen,[6] the desulfurization of disulfides to the corresponding sulfides with phosphine,[7] the condensation of carboxylic acids and alcohols or amines to the corresponding esters or amides by treatment of phosphine and diaryl disulfide[8] or diselenide,[9] and the conversion of alcohols to sulfides

with phosphine and disulfides.[10] Thus a mixture of triphenylphosphine and a catalytic amount of diaryl disulfide or diaryl diselenide was our choice system for the reduction of sulfonic acids.

Results and Discussion

The Reduction of Arenesulfonic Acids and Alkanesulfonic Acids to the Corresponding Arenethiols and Alkyl Aryl Sulfide with Triphenylphosphine and Diaryl Disulfide.

Arenesulfenyltriphenylphosphonium arenethiolate is known to be formed upon treatment of diaryl disulfide with triphenylphosphine and has been utilized for the synthetic organic chemistry, e.g. syntheses of alkyl aryl sulfides, peptide synthesis, etc. This reagent can also reduce arenesulfonic acids. Reducing ability of the reagent appears to depend on the choice of disulfide used for the preparation of the reagent. Some disulfides showed the same activity as iodine, while others were found to be much weaker reducing catalysts than iodine.[3] In this reducing system, the amount of disulfide did not affect the yield (Table 2) of the reduction but changed the time to complete the reaction, suggesting that the disulfide acts as a catalyst. GLC analysis after the completion of reaction showed two kinds of thiols and three kinds of disulfides. These disulfides were then heated with enough amounts of triphenylphosphine and water, to be reduced to the thiols of which the yields were determined by GLC or isolation(eq. 1).

$$ArSO_3H + (3+1/2)\ Ph_3P + 1/2\ (Ar'S)_2 \xrightarrow[2)\ H_2O]{1)\ \text{reflux in benzene}} ArSH + Ar'SH + (3+1/2)\ Ph_3PO \qquad \text{-------(1)}$$

The reaction is considered to be resulted by the following consecutive multi-steps of reactions(eqs. 2~7) as postulated in the reaction of triphenylphosphine/iodine system.

Table 1. Reaction of Sulfonic Acid with Triphenylphosphine/Diaryl Disulfide in Benzene under Nitrogen Atmosphere[a)]

$ArSO_3H$	$ArSO_3H/Ph_3P/(Ar'S)_2$	$(Ar'S)_2$	Time(h) Reflux	Products(%) ArSH b)	Ar'SH b)	Ph_3PO
$2,4\text{-}(CH_3)_2C_6H_3SO_3H$	2/8/1	$(p\text{-}ClC_6H_4S)_2$	21	(60)[c)]	(76)[c)]	-
$p\text{-}CH_3C_6H_4SO_3H$	2/10/1	$(p\text{-}ClC_6H_4S)_2$	24	75(60)[c)]	100(90)[c)]	-
$C_6H_5SO_3H$	2/10/1	$(p\text{-}ClC_6H_4S)_2$	24.5	90	94	-
$p\text{-}ClC_6H_4SO_3H$	2/8/1	$(p\text{-}ClC_6H_4S)_2$	24	26	100	-
$2,4\text{-}(CH_3)_2C_6H_3SO_3H$	2/8/1	$(p\text{-}CH_3C_6H_4S)_2$	28	46(42)[c)]	(78)[c)]	-
$p\text{-}CH_3C_6H_4SO_3H$	2/8/1	$(p\text{-}CH_3C_6H_4S)_2$	23.5	90(90)[c)]	100	90
$C_6H_5SO_3H$	2/8/1	$(p\text{-}CH_3C_6H_4S)_2$	36	14	85	-
$p\text{-}ClC_6H_4SO_3H$	2/8/1	$(p\text{-}CH_3C_6H_4S)_2$	22	trace	100	-
$p\text{-}CH_3C_6H_4SO_3H$	2/8/1		24	63	-	-
$p\text{-}CH_3C_6H_4SO_3H$	1/4/0.5	$(C_6H_5Se)_2$	24	29	-	-
$p\text{-}ClC_6H_4SO_3H$	2/14(Bu_3P)/1.5	$(p\text{-}CH_3C_6H_4S)_2$	18	no reaction		
$p\text{-}CH_3C_6H_4SO_3H$	2/8/1/0.2(Bu_4NI)	$(p\text{-}ClC_6H_4S)_2$	2	91	100	-
$CH_3CH_2SO_3H$	2/11/3	$(p\text{-}ClC_6H_4S)_2$	29	no reaction		

a) After this reaction, the mixture of 300 mg of water and 2 ml of dioxane was added and refluxed for 0.5~1.0 h. b) GLC yield(20% OV-1, 1 m glass column). c) Isolated yield.

Table 2. Reaction of Sulfonic Acid with Triphenylphosphine/Diaryl Disulfide in Benzene under Nitrogen Atmosphere[a)]

$ArSO_3H$	$ArSO_3H/Ph_3P/(Ar'S)_2$	$(Ar'S)_2$	Time(h) Reflux	Products(%) ArSH b)	Ar'SH b)	Ph_3PO
$2,4\text{-}(CH_3)_2C_6H_3SO_3H$	2/8/1		2	(92)[c)]	-	(88)[c)]
$p\text{-}CH_3C_6H_4SO_3H$	2/8/1		2	87(73)[c)]	-	-
$\beta\text{-}C_{10}H_7SO_3H$	2/8/1		4	(76)[c)]	-	-
$p\text{-}ClC_6H_4SO_3H$	2/8/1		4	60(53)[c)]	-	(65)[c)]
$C_6H_5SO_3H$	2/8/1		2	85	-	(76)[c)]
$p\text{-}CH_3C_6H_4SO_3H$	2/8/0.2		5	(73)[c)]	-	-
$p\text{-}CH_3C_6H_4SO_3H$	$2/8(Bu_3P)/1$		4	(26)[c)]	-	-
$CH_3(CH_2)_4SO_3H$	2/10/2		3.5(room temperature)		60[$CH_3(CH_2)_4$-] d)	
$C_6H_5SO_3H$	$2/9/1/2(Bu_3N)$		2	18	-	-
$\beta\text{-}C_{10}H_7SO_3H$	2/8/1		32	trace	-	-
$p\text{-}CH_3C_6H_4SO_3H$	2/8/1		3	75(60)[c)]	(100)[c)]	(75)[c)]
$C_6H_5SO_3H$	2/8/1		5	68	-	-
$2,4\text{-}(CH_3)_2C_6H_3SO_3H$	2/8/1		5	(66)[c)]	(97)[c)]	(61)[c)]
$p\text{-}ClC_6H_4SO_3H$	2/8/1		25	trace	-	-

a) After this reaction, the mixture of 300 mg of water and 2 ml of dioxane was added and refluxed for 0.5~1.0 h. b) GLC yield(20% OV-1, 1 m glass column). c) Isolated Yield. d) Pentyl pyridyl sulfide was obtained, and Ph_3PS was also obtained in 83% isolated yield.

$$Ar'SSAr' + Ph_3P \rightleftharpoons Ar'S\text{-}\overset{+}{P}Ph_3\ Ar'S^- \quad \text{---------(2)}$$

$$ArSO_3H + Ar'S\text{-}\overset{+}{P}Ph_3\ Ar'S^- \overset{K_3}{\rightleftharpoons} ArSO_3^-\ Ar'S\text{-}\overset{+}{P}Ph_3 + Ar'SH \quad \text{--(3)}$$

$$ArSO_3^-\ Ar'S\text{-}\overset{+}{P}Ph_3 \overset{K_4}{\rightleftharpoons} ArSO_2\text{-}O\text{-}\overset{+}{P}Ph_3\ Ar'S^- \quad \text{--------(4)}$$

$$ArSO_2\text{-}O\text{-}\overset{+}{P}Ph_3\ Ar'S^- \longrightarrow ArSO_2SAr' + Ph_3PO \quad \text{---------(5)}$$

$$ArSO_2SAr' + 2\ Ph_3P \longrightarrow 1/3(ArSSAr + ArSSAr' + Ar'SSAr') + 2\ Ph_3PO \quad \text{----------(6)}$$

$$ArSSAr + ArSSAr' + Ar'SSAr' + 3\ Ph_3P + 3\ H_2O \longrightarrow 3\ ArSH + 3\ Ar'SH + 3\ Ph_3PO \quad \text{-------(7)}$$

The reaction of alkanesulfonic acid such as n-pentanesulfonic acid with triphenylphosphine/bis(2-pyridyl) disulfide gave the alkyl pyridyl sulfide.

$$CH_3(CH_2)_4SO_3H + (PyS)_2 + 4\ Ph_3P \longrightarrow CH_3(CH_2)_4\text{-}S\text{-}Py + 3\ Ph_3PO + Ph_3PS + PySH \quad \text{---(8)}$$

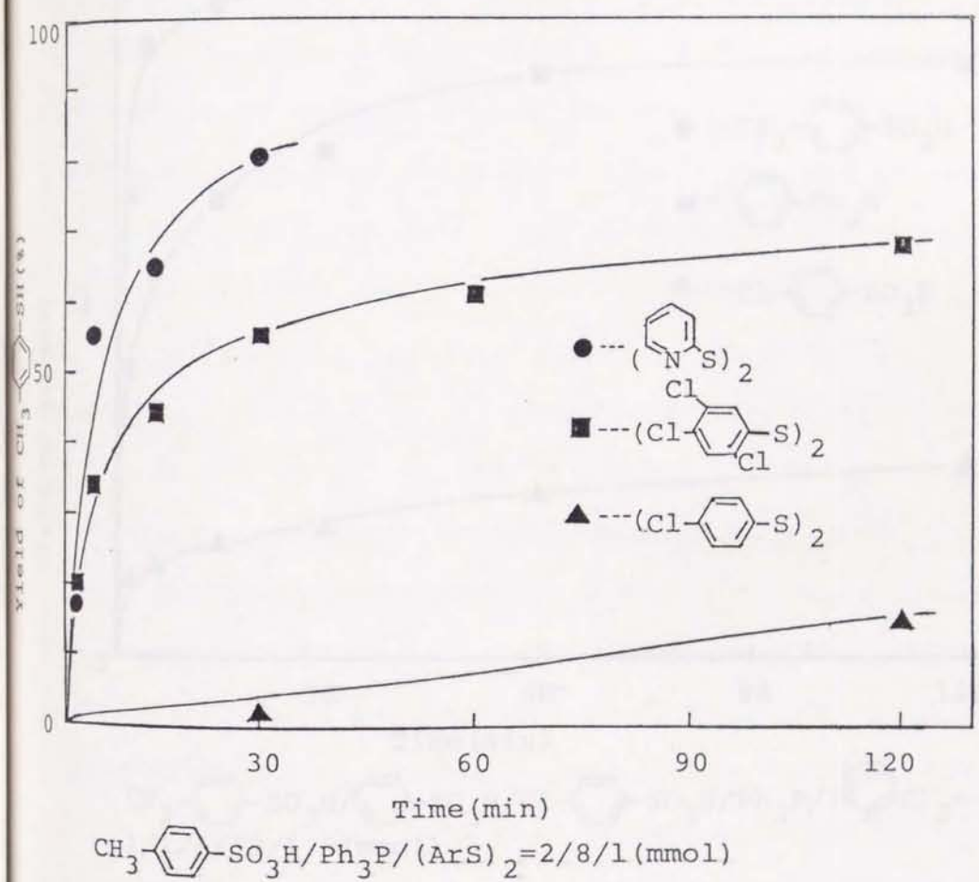
When dialkyl disulfide, such as lipoic acid or dibutyl disulfide was used, the following known desulfurization reaction took place rather than the expected reduction to the thiol.[11]

$$RSSR + Ph_3P \longrightarrow RSR + Ph_3PS \quad \text{---------(9)}$$

Thus, diaryl disulfides had to be used for this purpose. Inspection of the data in Tables 1, 2, and Fig. 1 reveals that the diaryl disulfide which bears a stronger electron-withdrawing aryl group is a better catalyst in the reduction of sulfonic acids with triphenylphosphine; e.g. unsubstituted diphenyl disulfide exhibits only trivial catalytic activity, however, the catalytic ability of bis(2,4,5-trichlorophenyl) disulfide is nearly as strong as that of iodine.[3]

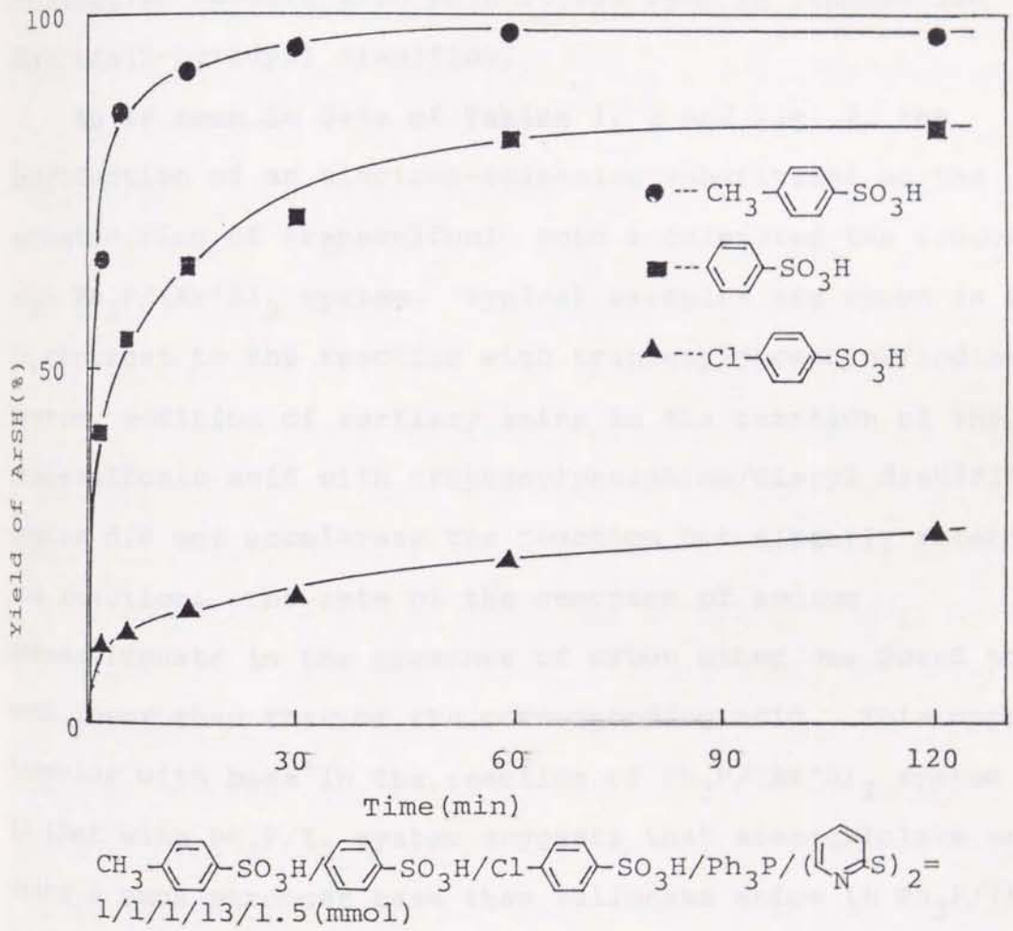
Bis(2-pyridyl) disulfide was found to be the best among

Fig. 1. Reaction of CH_3-⬡-SO_3H with $Ph_3P/(ArS)_2$ in Benzene under Reflux Condition.



CH_3-⬡-$SO_3H/Ph_3P/(ArS)_2$=2/8/1(mmol)

Fig. 2. Reaction of $ArSO_3H$ with $Ph_3P/(\text{pyridyl-2-S})_2$ in Benzene at 75°C.



CH_3-C_6H_4-SO_3H/C_6H_5-SO_3H/Cl-C_6H_4-SO_3H/Ph_3P/$(\text{pyridyl-2-S})_2$=
1/1/1/13/1.5(mmol)

several disulfides tested(Tables 1 and 2), while 1,8-dithiaacenaphthene was not a good catalyst, probably due to the unfavorable equilibrium(eq. 2) because of its extraordinarily high stability of the steric arrangement, or due to the formation of a very stable phosphorane intermediate by the reaction between triphenylphosphine and 1,8-dithiaacenaphthene. Diphenyl diselenide indicated only a weak catalytic activity. The use of tributylphosphine instead of triphenylphosphine led to sluggish results even when it was used in conbination with bis(2-pyridyl) disulfide.

As is seen in data of Tables 1, 2 and Fig. 2, the introduction of an electron-releasing substituent on the aromatic ring of arenesulfonic acid accelerates the reduction with $Ph_3P/(Ar'S)_2$ system. Typical examples are shown in Fig. 2. In contrast to the reaction with triphenylphosphine/iodine system, addition of tertiary amine in the reaction of the arenesulfonic acid with triphenylphosphine/diaryl disulfide system did not accelerate the reaction but slightly retarded the reaction. The rate of the reaction of sodium arenesulfonate in the presence of crown ether was found to be much lower than that of the corresponding acid. This opposite behavior with base in the reaction of $Ph_3P/(Ar'S)_2$ system to that with Ph_3P/I_2 system suggests that arenethiolate anion being a much stronger base than sulfonate anion in $Ph_3P/(Ar'S)_2$ system, K_3 is quite large and hence a higher concentration of the sulfonate anion can be maintained, however K_4 is very small. Whereas in the case of Ph_3P/I_2 system, since hydrogen iodide would be a strong acid comparable to the sulfonic acid

$$ArSO_3H + Ph_3\overset{+}{P}\text{-}I\ I^- \overset{K_{10}}{\rightleftharpoons} ArSO_3^- \ Ph_3\overset{+}{P}\text{-}I\ I^- + HI \quad \text{----(10)}$$

$$ArSO_3^- \ Ph_3\overset{+}{P}\text{-}I\ I^- \overset{K_{11}}{\rightleftharpoons} ArSO_2\text{-}O\text{-}\overset{+}{P}Ph_3\ I^- \quad \text{---------(11)}$$

in a aprotic solvent, K_{10} would not be sufficiently large enough to maintain a high concentration of the sulfonate anion in the absence of any base catalyst, however, K_{11} is larger than K_4.[3] These observations would suggest the rate-determining step involves the nucleophilic substitution on the phosphorus atom of the arenesulfenyltriphenylphosphonium ion by the sulfonate anion. This hypothesis is also in accordance with the observation that the electron-withdrawing groups in diaryl disulfide catalysts and electron-donating aryl group in arenesulfonic acids accelerate the reaction as shown in Figs. 1 and 2; i.e. the better leaving ability of $Ar'S^-$ and the stronger nucleophilicity of $ArSO_3^-$ facilitate the reaction eqs. 2 and 4. If the following elemental reaction eq. 5 is the rate-determining step of this reaction, the observed electronic demand should be opposite, since the nucleophilicity of $Ar'S^-$ increases with the decrease of electronegativity of Ar' group and any electron-withdrawing substituent on Ar group should accelerate the nucleophilic displacement on the sulfonyl sulfur. The retardation of the rate of the reaction eq. 3 by addition of base can be rationalized in terms of the our postulate that the rate-determining step is the reaction shown by eq. 4. If the reaction eq. 5 would be the rate-determining step, the addition of base ought to accelerate the reaction, since the base ionizes the thiol, generating the thiolate anion which is a much stronger nucleophile than the thiol, toward the sulfonyl sulfur. Once the thiolsulfonate is formed, this

can be very easily reduced by either triphenylphosphine[3] or thiol.

Alkyl arenesulfonate, sodium arenesulfonate, and tetraethylammonium benzenesulfonate could not be reduced to the corresponding thiols even with triphenylphosphine/dipyridyl disulfide which was the best catalyst.

Experimental

Synthesis of 1,2-Dithiaacenaphthene. According to the method of Zweig and Hoffmann, commercial 8-aminonaphthalene-1-sulfonic acid(60 g, 0.27 mol) was mixed with water to form a paste, which was then suspended in a beaker containing 200 ml of water. After 50 ml of concentrated H_2SO_4 was added into the beaker, a sufficient amount of ice was added to make up the solution to 80 ml. A solution of sodium nitrite(30 g, 0.43 mol) in 100 ml of water was added with vigorous stirring over 30 min, keeping the temperature of the mixture at about -10°C. After stirring the mixture for additional 1.5 hours at -10°C to -15°C, solid diazonium salts was filtered, washed with 100 ml of ice water, and treated with aqueous Na_2S_2 at 0°C to -10°C. The foamy mass was allowed to stand at room temperature for 3 hours, neutralized by addition of conc. HCl solution and then boiled. The hot reaction mixture was filterated. The crude disulfide precipitated out from the cooled filtrated was collected. Saturation of the filtrate with NaCl gave additional crops. The total yield of the dried product was 47 g. This material was treated with PCl_5(30 g, 0.14 mol). Immediately an exothermic reaction occurred and the solid mixture turned to a paste. When the reaction did not start, 200 ml of benzene was added and the mixture was heated under reflux for 1 hour. The reaction mixture was allowed to stand at room temperature for 5 hours. After filtration, the product was extracted with benzene until the extract became almost clear, the extract was washed with water, dried over $MgSO_4$, and concentrated to give a yellow residue, which was taken up with hot methanol,

treated with charcoal and crystallized to give the thiolsulfonate in yellow needles(5 g, 8.3% based on 1-amino-8-naphthalenesulfonic acid). m.p.=147.5~149°C(lit,[12] 148~149°C). To a solution of the thiolsulfonate(3.48 g, 15.7 mmol) in 30 ml of dry benzene was added a suspension of $LiAlH_4$(0.89 g) in 30 ml of dry ether at room temperature under argon atmosphere. An exothermic reaction occurred and the mixture was kept stirring at room temperature overnight. Ten ml of 10% NaOH solution was added to decompose excess hydride, followed by addition of dilute HCl solution to acidify. The mixture was extracted with benzene. The organic layer was dried over $MgSO_4$, evaporated under vacuum pump to afford yellow crystals of naphthalene-1,8-dithiol(2.7 g, 86%). NMR($CDCl_3$) δ=4.11(2H, s), 7.0~7.8ppm(6H, m).

1,2-dithiaacenaphthene was obtained quantitatively by autoxidation of the dithiol(84%). The product was recrystallized from ethanol. m.p.=116~117°C(lit,[12] 116°C).

Preparation of Disulfide. Disulfides which are not commercially available were synthesized by a known method.[13] To a benzene solution(150 ml) of thiol(0.05 mol) and pyridine(0.055 mol) was added dropwise iodine(0.025 mol) dissolved in benzene(50 ml). When the color of the solution changed to brown by excess iodine, the addition was stopped. The reaction mixture was washed with water, 5% HCl solution, $Na_2S_2O_3$ solution, and then water, and the organic layer was dried over $MgSO_4$. After evaporation of benzene, the residual disulfide was purified by recrystallization usually from hexane. Yields were nearly quantitative.

Di-p-Tolyl Disulfide m.p.=44~45°C(lit,[14] 46°C).

Di-p-Chlorophenyl Disulfide m.p.=70~71°C(lit,[15] 73°C).

The Competation Reduction of p-Substituted Benzenesulfonic Acids with $Ph_3P/(PyS)_2$ System. A mixture of 190.2 mg(1 mmol) of p-toluenesulfonic acid, 176 mg(1 mmol) of benzenesulfonic acid, and 192.5 mg(1 mmol) of p-chlorobenzenesulfonic acid was dissolved in 5 ml of benzene, and the mixture was refluxed in a reactor which was equipped with a condenser and a calcium chloride tube. These sulfonic acids were dehydrated to nearly completely dry prior to the reaction by way of azeotropic distillation with benzene. After 3406 mg(13 mmol) of triphenylphosphine and 154 mg(1 mmol) of biphenyl were added to these sulfonic acids, this reactor was equipped with another dry condenser and a nitrogen balloon and then substituted with this inert gas with a vacuum pump. Then, 330 mg(1.5 mmol) of dipyridyl disulfide which was dissolved in dry 5 ml of benzene was added into the mixture which was stirred in 75°C. A small portion, 0.1 ml of the reaction mixture was picked up by micro-cylinge and quenched with a mixture of water-dioxane-benzene(v=1/1/2) at every fixed time(2, 6, 15, 30, 60, and 120 minutes from reaction initial time respectively). The yields of three thiols obtained by this method were determined by calibration curve with GLC(SE-30, standard: biphenyl).

The Relative Catalytic Effects of Various $(Ar'S)_2$ Catalysts in the Reduction of p-Toluenesulfonic acid with $Ph_3P/(Ar'S)_2$ System. p-Toluenesulfonic acid monohydrate 381 mg(2 mmol) was dissolved in 5 ml of benzene, refluxed, and dehydrated

to nearly completely dry by the same procedure. After 2100 mg(8 mmol) of triphenylphosphine and 300 mg(2 mmol) of biphenyl were added to this dried sulfonic acid, this reactor was equipped with another dry cooler and a nitrogen balloon, and was substituted with this inert gas with a vacuum pump. Then, 3 ml of dry benzene was added to this mixture and 1 mmol of diaryl disulfide(di-2-pyridyl disulfide, bis(2,4,5-trichlorophenyl) disulfide, or di-p-chlorophenyl disulfide) which was dissolved in 5 ml of dry benzene was added to this mixture(total benzene 8 ml) and the whole mixture was stirred, and refluxed(bath temperature 112°C). A small portion, 0.1 ml, of reaction mixture was picked up by a micro-cylinge and quenched with a mixture of water-dioxane-benzene(v=1/1/2) at fixed intervals. The yields of thiols obtained by this procedure were determined by calibration curve with GLC(SE-30, standard:biphenyl).

Reductive Conversion of Alkanesulfonic Acid with $Ph_3P/(PyS)_2$ System. Pentanesulfonic acid, 304 mg(2 mmol) which was made completely dry by a vacuum pump and 2620 mg(10 mmol) of triphenylphosphine were added into a reactor which was equipped with a dry condenser and a nitrogen balloon. Then, 440 mg(2 mmol) of di-2-pyridyl disulfide which was dissolved in 5 ml of dry benzene was added to this mixture which was then stirred for 3.5 hours at room temperature. The reaction was monitored by GLC. After the reaction, the yields of triphenylphosphine sulfide, 2-pyridyl pentyl sulfide were determined by GLC(SE-30).

2-Pyridyl Pentyl Sulfide 60% IR(NaCl) 750, 1120, 1400 1440, 1570cm^{-1}. GC-MS:m/e=181.

TLC(benzene) R_f=0.4
b.p.=104~106°C/5.5 mmHg

Found: C, 66.33; H, 8.35; N, 7.77

Calcd for $C_{10}H_{15}NS$: C, 66.25; H, 8.33; N, 7.72

NMR(CCl_4) δ=8.3(m, 1H), 6.7~7.5(m, 3H)
0.9(t, 3H, J=6Hz), 1.1~2.0(m, 6H)
3.15ppm(t, 2H, J=6Hz)

Triphenylphosphine Sulfide 83%

The yield of triphenylphosphine oxide was determined through a separative silica-gel column chromatography with benzene as eluent(85%).

Preparation of Diphenyl Diselenide. A three-necked round bottom flask is fitted with a reflux condenser, a mechanical stirrer, a dropping funnel, and a gas inlet tube(in draft hood) and swept with dry nitrogen. Phenylmagnesium bromide was then prepared in the flask by the usual procedure from 7.85 g(0.05 mol) of bromobenzene, 1.2 g(0.05 gram atom) of magnesium, and 50 ml of dry ether. The dropping funnel is then replaced by an addition flask containing 3.8 g(0.048 gram atom) of dry powdered black selenium. The solution was warmed sufficiently to bring about gentle refluxing, and selenium was then added gradually. Stirring was continued for 0.5 hour. The contents of the flask are poured into ice, and HCl solution is then added. The aqueous layer was extracted with ether, and dried over calcium chloride. Ether was removed and selenophenol was obtained in a high yield.[16] Diphenyl diselenide was obtained quantitatively by autoxidation of selenophenol. The product was recrystallized from hexane. Diphenyl diselenide m.p.=57~58°C (lit,[17] 61~63°C).

References

1) T. Numata, H. Awano, and S. Oae, Tetrahedron Lett., 21, 1235(1980).
2) G.A. Olah, S.C. Narang, L.D. Field, and R. Karpeles, J. Org. Chem., 46, 2408(1981).
3) S. Oae and H. Togo, Bull. Chem. Soc. Jpn., in contribution.
4) A.D. Beveridge, G.S. Harris, and F. Inglis, J. Chem. Soc., Perkin Trans II, (1966), 520.
L. Horner and H. Nickel, Ann. Chim(Paris), 597, 20(1955).
5) D.N. Harpp, J.G. Gleason, J. Am. Chem. Soc., 93, 2437(1971).
6) G.A. Wiley, R.L. Hershkowitz, B.M. Rein, and B.C. Chung, J. Am. Chem. Soc., 86, 964(1964).
G.A. Wiley, B.M. Rein, and R.L. Hershkowitz, Tetrahedron Lett., (1964), 2509.
R. Michinek and W. Liittke, Synthesis, (1975), 255.
7) D.N. Harpp and J.G. Gleason, J. Org. Chem., 35, 3259(1970).
D.N. Harpp, J.G. Gleason, and J.P. Snyder, J. Am. Chem. Soc., 90, 4181(1968).
I.L. Knunyants, Dolk. Chem., 224, 521(1975).
D.N. Harpp and J.G. Gleason, J. Org. Chem., 36, 73(1971).
D.N. Harpp and J.G. Gleason, J. Am. Chem. Soc., 93, 2437(1971).
8) S. Kobayashi, T. Iimori, T. Izawa, and M. Ohno, J. Am. Chem. Soc., 103, 2406(1981).
R. Matsueda, H. Maruyama, M. Ueki, and T. Mukaiyama, Bull. Chem. Soc. Jpn., 44, 1373(1971).
T. Endo, S. Ikenaga, and T. Mukaiyama, Bull. Chem. Soc. Jpn., 43, 2632(1970).
T. Mukaiyama, K. Goto, R. Matsueda, and T. Ueki, Tetrahedron Lett., (1970), 5293.
E.J. Corey and D.J. Brunelle, Tetrahedron Lett., (1976), 3409.
T. Mukaiyama, M. Ueki, H. Maruyama, and R. Matsueda, J. Am. Chem. Soc., 90, 4490(1968).
T. Takaku and Y. Shimada, Chem. Lett., (1975), 873.
T. Mukaiyama and M. Hashimoto, J. Am. Chem. Soc., 94, 8528 (1972).
9) H. Takaku, T. Konishi, and H. Hata, Chem. Lett., (1977), 655.
10) I. Nakagawa and T. Hata, Tetrahedron Lett., (1975), 1409.
11) D.N. Harpp, J.G. Gleason, and J.P. Snyder, J. Am. Chem. Soc., 90, 4181(1968).
D.N. Harpp and J.G. Gleason, J. Org. Chem., 36, 73(1971).
12) A. Zweig and A.K. Hoffmann, J. Org. Chem., 30, 3997(1965).
13) D.T. McAllen, T.V. Cullum, R.A. Dean, and F.A. Fidler, J. Am. Chem. Soc., 73, 3629(1951).
14) L. Field, J. Am. Chem. Soc., 74, 394(1954).
15) M.B. Sprk, J.L. Cameron, and N. Kharasch, J. Am. Chem. Soc., 75, 4907(1953).
16) E.C. Horning, Org. Synth., Coll. Vol. 3, 771(1965).
17) Aldrich Chemical Co.

Chapter 4.

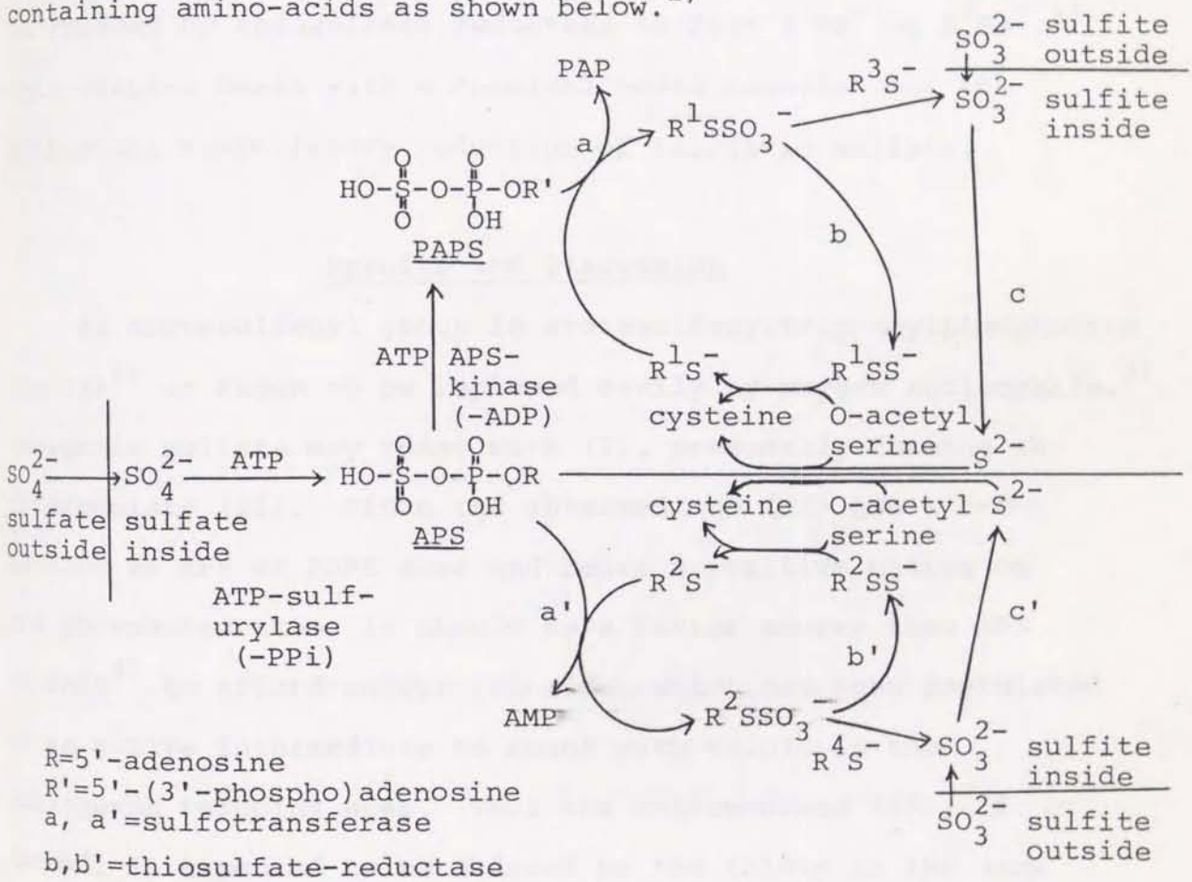
Biomimetic Reduction of Sulfuric Acid

Abstract

Inorganic sulfate was reduced by treatment with either arenesulfenyltriphenylphosphonium arenethiolate or iodotriphenylphosphonium iodide to triphenylphosphine sulfide via formation of hydrogen sulfide. The reaction of sulfate to sulfide is considered to proceed via the course which resembles the biological reaction path involved in the assimilatory metabolism of inorganic sulfate in microorganisms.

Introduction

Inorganic sulfate which has the highest oxidative state of sulfur atom is one of the most inert species toward any reducing agent among the naturally occurring sulfur compounds, hence the reduction of inorganic sulfate by any chemical method under mild conditions has been considered to be rather difficult. Meanwhile, many plants, fungi, and microorganisms are known to reduce inorganic sulfate in their assimilatory metabolisms which eventually convert sulfate to some sulfur-containing amino-acids as shown below.[1)]



R=5'-adenosine
R'=5'-(3'-phospho)adenosine
a, a'=sulfotransferase
b,b'=thiosulfate-reductase
c,c'=sulfite-reductase

Fig. Pathways of Assimilatory Sulfate Reduction

The biological reduction of sulfate to sulfide is consisted of the following two key steps, i.e. conversion of sulfate to the mixed-anhydride, APS or PAPS, to activate sulfate to be ready for the subsequent second reaction, and the subsequent nucleophilic attack of protein-thiol on the sulfur atom of APS or PAPS to generate protein bound thiosulfate of which the sulfenyl sulfur can be easily displaced by other thiol group in the enzyme to give sulfite which is ultimately reduced to hydrogen sulfide, or of which the sulfonyl group is reduced by thiosulfate reductase to form R^1SS^- or R^2SS^-.[1] This chapter deals with a chemical model reaction for the biological assimilatory reduction of inorganic sulfate.

Results and Discussion

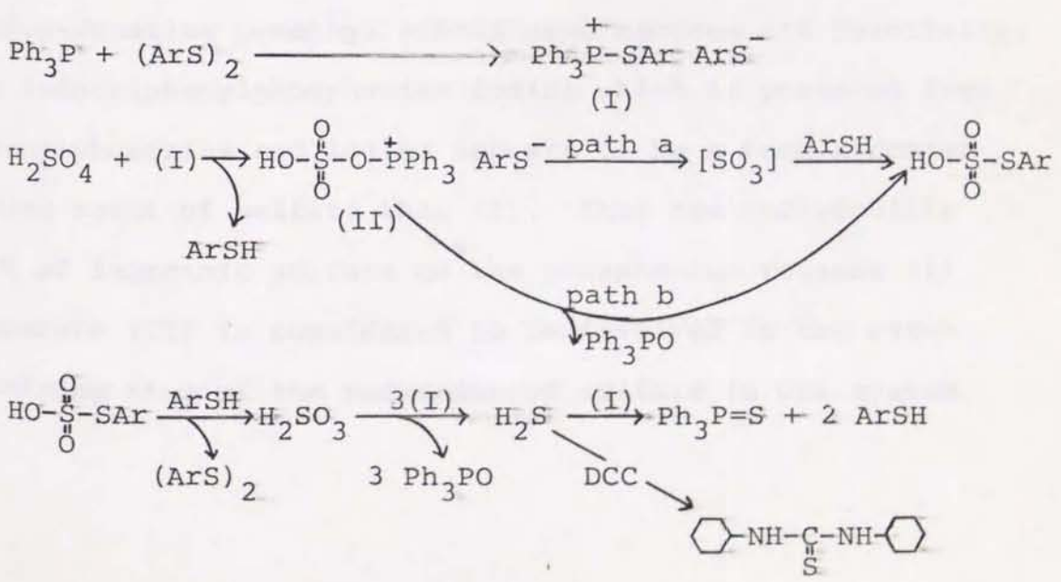
As arenesulfenyl group in arenesulfenyltriphenylphosphonium ion (I)[2] is known to be replaced easily by oxygen nucleophile,[3] inorganic sulfate may react with (I), presumably forming an intermediate (II). Since the intermediate (II) has a P-O-S bonding as APS or PAPS does and bears a positive charge on the phosphorus atom, it should be a better source than APS or PAPS[4] to afford sulfur trioxide, which has been postulated as an active intermediate to react with thiols in the subsequent reducing step. Thus the intermediate (II), if formed, is expected to be reduced by the thiols in the same manner as APS or PAPS which is reduced by the thiol groups in APS- or PAPS-sulfotransferase. Indeed, inorganic sulfate is successfully reduced by this system to afford triphenylphosphine sulfide as the final product. As the control experiment revealed that hydrogen sulfide reacted with (I) to form triphenylphosphine

sulfide and arenethiol, hydrogen sulfide once formed from inorganic sulfate is considered to be converted to triphenylphosphine sulfide upon encountering with (I) in

$$H_2SO_4 + 5\ Ph_3P + X_2 \longrightarrow Ph_3P{=}S + 4\ Ph_3P{=}O + 2\ HX \quad --(1)$$

our reducing system. In fact hydrogen sulfide can be isolated as dicyclohexyl thiourea in the trapping experiment with dicyclohexyl carbodiimide(DCC); namely when nitrogen gas was bubbled into the reaction mixture and the exhausted gas was introduced into a benzene solution of DCC(0.99 M), dicyclohexyl thiourea was obtained, though in a low yield. Undoubtedly most of hydrogen sulfide is readily consumed in the facile reaction with compound(I).

Two paths (a and b) are conceivable for the reaction of (II) with thiols. While path b may be unfavorable due to the stereoelectronic repulsion between the nucleophile, i.e. arenethiolate anion and negative oxygen poles of bulky sulfate group of (II) at the transition state of the S_N2 reaction on the sulfur atom of (II), path a would be quite likely



since hydrogen bound to the oxygen atom of (II) is extremely acidic while the formation of triphenylphosphine oxide must be a big driving force. Thus the 1,2-elimination reaction of (II) to form arenethiol, sulfur trioxide and triphenylphosphine oxide (path a) should take place quite readily.[4] Sulfur trioxide thus formed may react arenethiol to afford thiosulfate which is subsequently reduced with the thiol giving sulfite.[5,6] Sulfite ion is reduced further with this system to hydrogen sulfide. Meanwhile, Tagaki and Eiki,[8] and Benkovic and Hevey[7] showed independently that nucleophilic substitution of phenylphosphosulfate(PPS), an APS or PAPS model compound, by OH^- proceeded sluggishly, however, hydrolysis of PPS took place readily in an acidic medium or in the presence of some metal ions in an aprotic solvent.[8] These results also suggest an elimination-addition mechanism involving formation of sulfur trioxide in the facile acid- or metal- catalyzed reaction. In the light of all these observations, path a is more favorable than path b. In keeping with this conceivable mechanism, an introduction of electronegative substituent on aryl group in (I) increases the reactivity of (I), and electron-donating p-methyl substituent reduces its reactivity, while iodotriphenylphosphonium iodide which is prepared from triphenylphosphine and iodine appears to be a much stronger reducing agent of sulfate than (I). Thus the nucleophilic attack of inorganic sulfate on the phosphonium reagent (I) to generate (II) is considered to be involved in the rate-determining step of the reduction of sulfate in our system.

Table. Reduction of Sulfuric Acid and Sulfate with $Ph_3\overset{+}{P}-X\ X^-$ in Benzene[a)]

X_2	$H_2SO_4/Ph_3P/X_2$ (mmol)	Temp. °C	Time hr	Product Yields (%)[b)] Ph_3PS	H_2S c)	HX
$(p\text{-}ClC_6H_4S)_2$	d) 0/14.3/7	140	5	0	-	g)
"	d) 2/14.3/7	"	4	77	-	90
"	d) 2/14.3/7	"	10	99	-	92
"	h,d) 3/11/9	reflux[e)]	7	7	trace	g)
$(C_6H_5S)_2$	d) 2/14.3/7	140	10	60	-	g)
$(p\text{-}CH_3C_6H_4S)_2$	d) 2/14.3/7	"	10	45	-	85
$(C_6H_5Se)_2$	2/14.3/7.8	135-137	13	79	-	90[f)]
I_2	2/14.3/6.1	reflux	3	91	-	g)
"	h) 3/15.8/8	r.t.	3	18	4	g)
"	h) 3/15.8/8	40-45	3	89	2.5	g)
"	i) 2/14.3/6.1	reflux	4	61	-	g)

a) Sulfuric acid was dissolved in 6 ml of benzene. b) Yields were calculated based on sulfuric acid according to stoichiometry, as shown in eq. 1. c) Hydrogen sulfide was isolated as dicyclohexylthiourea by treatment with dicyclohexylcarbodiimide. d) After this reaction, a mixture of 500 mg of H_2O and 3 ml of dioxane were added and the mixture was refluxed for 0.5 h. e) p-Xylene was used as solvent. f) Isolated as diphenyl diselenide. g) Not determined. h) 20 ml of benzene was used. i) $[(n\text{-}Bu_3NH)]_2SO_4$ as sulfate was used.

Experimental

Material: Iodine, triphenylphosphine, sulfuric acid, tributylamine, diphenyl disulfide are all from Wako Chemicals Co.

The Reduction of Sulfuric Acid with Ph_3P/I_2 System: Triphenylphosphine 3741 mg(14.28 mmol) was dissolved in the mixture of 200 mg(1.98 mmol) of sulfuric acid(97%) and 15 ml of dry benzene into which 1554 mg(6.14 mmol) of iodine was then added. The mixture was stirred and refluxed for 3 hours under nitrogen atmosphere. After the reaction, the odor of hydrogen sulfide was not detected. The reaction mixture was poured into benzene which was then washed with water, dried over $MgSO_4$. Triphenylphosphine sulfide was separated and purified with column chromatography using benzene as eluent in 91% yield.

$Ph_3P{=}S$ (R_f=0.5 eluent:benzene) IR(KBr) 1090cm^{-1}(s)

mp=162-163°C(lit,[9] 162-164°C)

Similar procedure and work-up were used in the reduction of sulfuric acid with $Ph_3P/(ArS)_2$ system. As a blank experiment, dry hydrogen sulfide was introduced into a mixture of 576 mg (2 mmol) of triphenylphosphine and 574 mg(2 mmol) of di-p-chlorophenyl disulfide were dissolved into 10 ml of dry benzene at room temperature. After 8 hours, the mixture was poured into benzene, which was then washed with water, and dried over $MgSO_4$. Triphenylphosphine sulfide was purified with column chromatography and obtained in 90% yield, while di-p-chlorophenyl disulfide was converted to p-chlorobenzenethiol with H_2O/Ph_3P for experimental convenience. The yield of p-chlorobenzenethiol was 89%.

Hydrogen Sulfide Trapping in the Reduction of Sulfuric Acid with Ph_3P/I_2 System:

Reactor A.

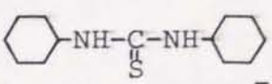
Sulfuric acid(97%) 300 mg(2.97 mmol) and 4150 mg(15.84 mmol) of triphenylphosphine were dissolved in 20 ml of dry benzene, into which 2011 mg(7.92 mmol) of iodine was then added.

Reactor B.

Dicyclohexylcarbodiimide(DCC) 2042 mg(9.9 mmol) was dissolved in 10 ml of dry benzene in a flask which was equipped with a empty balloon.

Reactor B was jointed to Reactor A with a glass tube. The mixture in Reactor A was stirred for 3 hours at r.t. under slow flow of nitrogen gas, while the mixture in Reactor B was also stirred at r.t. under nitrogen. Then hydrogen sulfide was introduced into the Reactor B. After the reaction, 10 ml of water was added into A and the mixture was poured into benzene which was then washed with water for 3 times, dried over $MgSO_4$, filterated and evaporated. The mixture was separated with column chromatography using benzene as eluent. Reactor A $Ph_3P=S$ 18%

Meanwhile, 10 ml of water was added into the Reactor B to quench any excess of DCC to urea and the mixture was kept standing for a few hours. The mixture was poured into chloroform which was then washed with water, dried over $MgSO_4$, and evaporated. The residue was separated through silica-gel column(MERCK 70-230 mesh) with chloroform.

Reactor B  26mg 4%

IR(KBr) 3275cm^{-1}(s) 1540cm^{-1}(s)

$1490cm^{-1}$(m) $1220cm^{-1}$(m)

R_f=0.3-0.4($CHCl_3$) m.p.=182-184°C

(lit,[10] 182-182.5°C)

Di-p-tolyl disulfide, di-p-chlorophenyl disulfide, and diphenyl diselenide were synthesized by known methods.

$p\text{-}CH_3C_6H_4SSC_6H_4CH_3\text{-}p$ m.p.=44-45°C(lit,[11] 46°C)

$p\text{-}ClC_6H_4SSC_6H_4Cl\text{-}p$ m.p.=70-71°C(lit,[12] 73°C)

$C_6H_5SeSeC_6H_5$ m.p.=57-58°C(lit,[13] 61-63°C)

References

1) M.L.-S.Tsang and J.A.Schiff, J. Bacteriol., 125, 923(1976).
A.B.Roy and P.A.Trudinger,"The Biochemistry of Inorganic Compounds of Sulfur", Chap.10, Cambridge University Press (1970).

2) D.N.Harpp and J.G.Gleason, J. Amer. Chem. Soc., 93, 2437(1971).

3) T.Mukaiyama and M.Hashimoto, J. Amer. Chem. Soc., 94, 8528 (1972).
H.Takaku and Y.Shimada, Chem. Lett., 1975, 873.
I.Nakagawa and T.Hata, Tet. Lett., 1975, 1409.
L.E.Overman and E.M.O'Connor, J. Amer. Chem. Soc., 98, 771 (1976).
K.Fujimori, H.Togo and S.Oae, Tet. Lett., 21, 4921(1980).

4) Even monoaryl sulfate and Bunte salt hydrolyzed by A-1 mechanism in acidic media.
J.L.Kice, J.M.Anderson, and N.E.Pawlowski, J. Amer. Chem. Soc., 88, 5245(1966).

5) Since metal ion-catalyzed hydrolysis of phenylphosphosulfate, a model compound of APS or PAPS, proceeds through A-1 mechanism via sulfur trioxide intermediate while the nucleophilicity of thiol toward sulfonyl sulfur(*) is relatively weak, the reaction of APS or PAPS with the dithiol enzyme in the presence of metal ion is also presumed to involve the formation of sulfur trioxide as the intermediate.
(*)J.L.Kice"Nucleophilic Substitution at Different Oxidative States of Sulfur".

6) T.W.Szczepkowski, Nature(London)., 182, 934(1958).

7) S.J.Benkovic and R.C.Hevey, J. Amer. Chem. Soc., 92, 4971 (1970).

8) W.Tagaki, T.Eiki, and I.Tanaka, Bull. Chem. Soc. Jpn., 44, 1139(1971).
W.Tagaki and T.Eiki, Advances in Chemistry Series, No. 191, 409(1980).

9) Authentic sample was obtained from Wako Chemicals Co.

10) D.Martin, W.Mucke, Monatsber. Dent. Akad. Wiss. Berlin, 6(5), 362(1964).

11) L.Field, J. Amer. Chem. Soc., 74, 394(1954).

12) M.B.Sprk, J.L.Cameron, N.Kharasch, J. Amer. Chem. Soc., 75, 4907(1953).

13) Authentic sample was obtained from Wako Chemicals Co.

Chapter 5.

Reduction of Sulfonic Acids, Sodium Sulfonates and Sulfonate Esters to Corresponding Disulfides with Polyphosphoric Derivatives, Potassium Iodide and Tetrabutylammonium Iodide System.

Abstract

Sulfonic acids, sodium sulfonates, and alkyl sulfonate esters were readily reduced to the corresponding disulfides in moderate yields upon treatment with a mixture of polyphosphoric derivative and iodide. In these reactions, formation of mixed-anhydrides which have a P-O-S linkage is the key step, and subsequent attack of iodide on the sulfur atom gives corresponding sulfonyl iodide which are reduced further exothermally to the disulfides with hydrogen iodide. Actually, p-toluenesulfonyl chloride was isolated in the reaction of p-toluenesulfonic acid and polyphosphoric derivatives with chloride ion. The competitive reduction of various aromatic sulfonic acids reveal that an aromatic sulfonic acid bearing an electron-donating p-substituent is more readily reduced to the disulfide than that which has an electron-withdrawing p-substituent.

Introduction

The reduction of organic sulfonic acid which is in the highest oxidative state among all organosulfur compounds is one of the most challenging problems in organosulfur chemistry. Sulfonic acids, however, can be reduced in multi-step processes through initial conversion of sulfonic acids to the corresponding sulfonyl derivatives, i.e. sulfonyl halide,[1] sulfonic anhydride,[2] sulfonate ester,[3] and sulfonamide[4] and subsequent reduction of these derivatives with reducing agents to the corresponding thiols or thiol derivatives. Recently, there have appeared three procedures which can reduce sulfonic acid directly to the corresponding disulfide or thiol in one pot process.[5~7] Each of these three procedures is epochal, and quite useful, since a one pot process reduction of various sulfonic acids and its derivatives to thiols or disulfides can be achieved, however, there reactions are rather expensive, since the reagents used in these procedures, i.e. $(CF_3CO)_2O/(n\text{-}Bu)_4NI$,[5] Ph_3P/I_2(catalyst),[6] $Ph_3P/(ArS)_2$(catalyst),[8] and BX_3(X=Cl, Br, I)/KI[7] systems are either in large excess or by no means cheap. Another facile procedure to reduce both arene- and alkanesulfonic acids to the corresponding disulfides as the sole products has been found by us who used cheap reagents, such as polyphosphoric acid(PPA), ethyl polyphosphate(PPE), tetraphosphorus decaoxide(P_4O_{10}) and iodide ion, in an organic phase. This chapter gives a full account of the direct reduction of sulfonic acids.

Results and Discussion

Arene- and alkanesulfonic acids used in this investigation are listed in Table 1,2, and 3, while sulfonate esters are summarized in Table 4. The condensing reagents used were tetraphosphorus decaoxide, polyphosphoric acid, and ethyl polyphosphate,[9] while acetonitrile and sulfolane are the choice solvents in the reduction with P_4O_{10}/I^- and PPA/I^- systems respectively because of the solubility of polyphosphoric derivatives, whereas acetonitrile, sulfolane, and chloroform were the choice solvents in the reduction with PPE/I^- system. Of the three systems, the reduction with P_4O_{10}/I^- or PPE/I^- gives the corresponding disulfides in higher yields than that with PPA/I^- system in the presence of $(n\text{-}Bu)_4NI$, whereas, in the absence of $(n\text{-}Bu)_4NI$ the yields of the disulfides are more satisfactory in the reduction with PPA/I^- than those with the former systems.

It is worthy to note that d-camphor-10-sulfonic acid, which is a highly sterically hindered alkanesulfonic acid, was also reduced to the corresponding disulfide in a high yield, though the reaction was substantially slow. In these reactions, the sulfonyl iodide is considered to be the key intermediate which is stepwisely reduced further very readily to the corresponding sulfinyl and sulfenyl iodides which are eventually reduced to the symmetrical disulfide[10] as shown in Scheme. Indeed, p-toluenesulfonyl chloride was obtained in 48% and 28% yields respectively when potassium chloride which has no reducing ability at all and tetraethylammonium chloride were added into the mixture of either P_4O_{10} or PPE

Table 1. Reduction of Sulfonic Acids to Disulfides Using the Tetraphosphorus Decaoxide/Potassium Iodide/Tetrabutylammonium Iodide System in CH_3CN

Sulfonic Acid	Amounts(mmol) of Reagents Used[a] $RSO_3H/P_4O_{10}/KI/Bu_4NI$	Reaction Conditions Temp(°C)/Time(h)	Yield of Disulfide[b] (%)
	6.0/33.8/30.0/1.5	Reflux/14	57
	6.0/42.2/36.2/1.5	Reflux/24	40
	6.0/42.2/36.2/1.5	Reflux/14	55
	6.0/42.2/36.2/1.5	Reflux/34	60
	6.0/33.8/30.0/0	Reflux/14	33[c]

a) The molecular weight of P_4O_{10} was taken as 142. b) Yield of isolated product.

c) Small amount of thiolsulfonate was obtained as by-product.

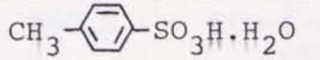
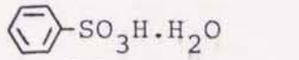
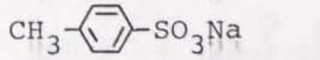
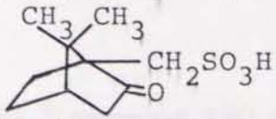
Table 2. Reduction of Sulfonic Acids to Disulfides Using the Polyphosphoric Acid/Potassium Iodide/Tetrabutylammonium Iodide System in Sulfolane

Sulfonic Acid	Amounts (mmol) of Reagent Used[a] RSO_3H/PPA/KI/Bu_4NI	Reaction Conditions Temp (°C)/Time (h)	Yield of Disulfide[b] (%)
CH_3-C$_6$H$_4$-$SO_3H.H_2O$	6.0/48.0/48.0/1.5	95~100/8	65
	6.0/48.0/48.0/0	95~100/8	75
Cl-C$_6$H$_4$-SO_3H	6.0/48.0/60.0/1.5	95~100/10	47
	6.0/48.0/48.0/0	95~100/8	58
CH_3-C$_6$H$_3$(CH_3)-SO_3H	6.0/48.0/48.0/1.5	95~100/8	68
	6.0/48.0/48.0/0	95~100/8	70
CH_3-C$_6$H$_4$-SO_3Na	6.0/48.0/48.0/1.5	95~100/23	58
	6.0/48.0/48.0/0	95~100/21	55 c)
$CH_3(CH_2)_7SO_3H.H_2O$	6.0/48.0/48.0/1.5	80/5	66

a) The molecular weight of PPA was taken as 338. b) Yield of isolated product.

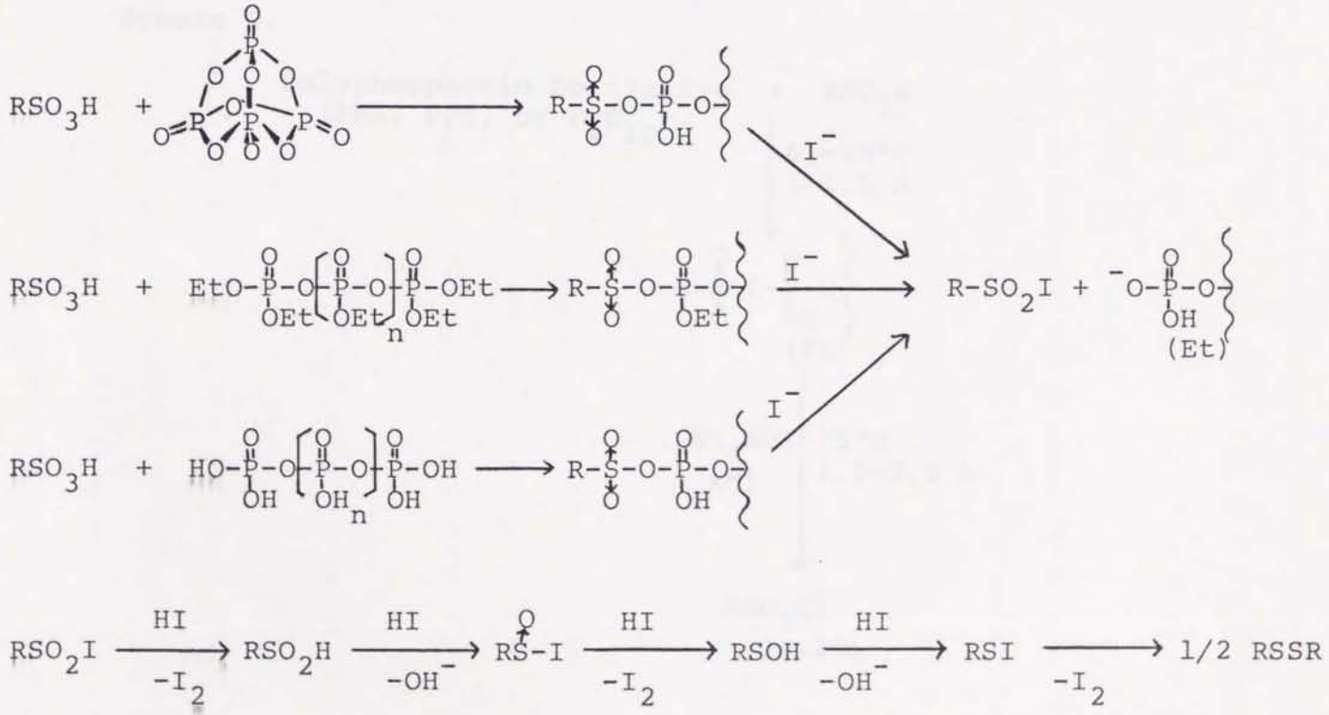
c) Small amount of thiolsulfonate was obtained as by-product.

Table 3. Reduction of Sulfonic Acids to Disulfides Using the Ethyl Polyphosphate/ Potassium Iodide/Tetrabutylammonium Iodide System in Chloroform

Sulfonic Acid	Amounts (mmol) of Reagents Used RSO_3H/PPE/KI/Bu_4NI a)	Reaction Conditions Temp (°C)/Time (h)	Yield of Disulfide b) (%)
	6.0/35.6/48.0/1.5	Reflux/1.5	60
	6.0/35.6/48.0/0	Reflux/2	12
	6.0/47.4/48.0/1.5	Reflux/2	43
	6.0/35.6/48.0/1.5	Reflux/6	43
$CH_3(CH_2)_7SO_3H.H_2O$	6.0/47.4/48.0/1.5	Reflux/2	47
	6.0/47.4/48.0/1.5	Reflux/5	74

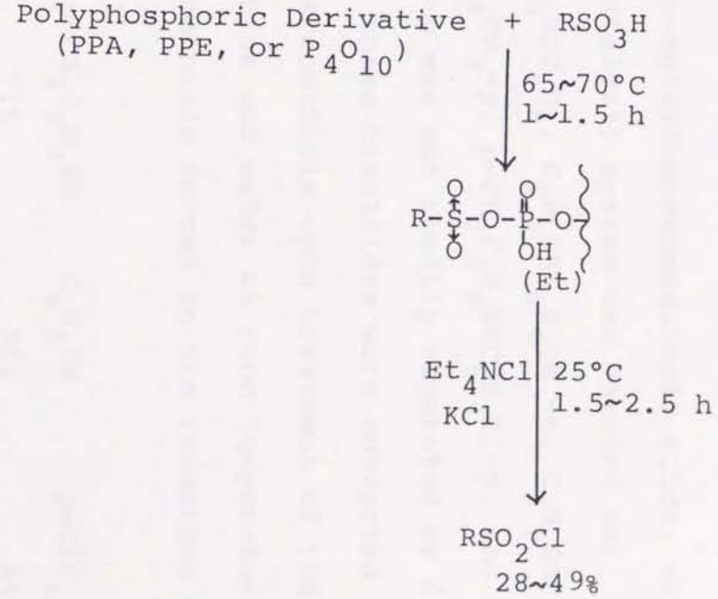
a) The molecular weight of PPE was taken as 500. b) Yield of isolated product.

Scheme 1.



(189)

Scheme 2.


Polyphosphoric Derivative
(PPA, PPE, or P_4O_{10})
+ RSO_3H
65~70°C
1~1.5 h
R-S-O-P-O
OH
(Et)
Et_4NCl
KCl
25°C
1.5~2.5 h
RSO_2Cl
28~49%

and p-toluenesulfonic acid in acetonitrile.

Meanwhile, p-toluenesulfonyl iodide, which was prepared from the reaction of sodium p-toluenesulfinate and iodine in a mixture of benzene and water, was found to be reduced exothermally to the corresponding disulfide with hydriodic acid in a high yield in dioxane.

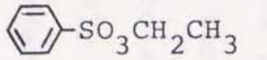
Competitive reduction of an equimolar mixture of p-substituted benzenesulfonic acids, i.e. p-chlorobenzene-benzene-, and p-methylbenzenesulfonic acids, with the PPA/KI/$(n\text{-}Bu)_4NI$(catalyst) system was carried out. Since the mixture of $C_6H_5SSC_6H_5$, $C_6H_5SSC_6H_4CH_3$-p, $C_6H_5SSC_6H_4Cl$-p, p-$CH_3C_6H_4SSC_6H_4CH_3$-p, p-$CH_3C_6H_4SSC_6H_4Cl$-p, and p-$ClC_6H_4SSC_6H_4Cl$-p was not readily separated or determined, the mixture of these disulfides were converted to the corresponding arenethiols upon treatment of the mixture of triphenylphosphine and water at room temperature. Thus amounts of arenethiols formed in the reduction were estimated as shown below.

p-$CH_3C_6H_4SH$	C_6H_5SH	p-ClC_6H_4SH
71%	60%	34%

These data reveal clearly that, in the reduction of p-substituted benzenesulfonic acids, benzenesulfonic acid bearing an electron-donating substituent such as methyl group is more readily reduced than that has an electron-withdrawing group. Apparently, the rate-determining step is the formation of a P-O-S mixed anhydride which is formed by nucleophilic attack of sulfonic acid on the polyphosphoric derivative.

These reduction procedures were found to be applied for the reduction of sulfonate ester(Table 4). Alkyl arene- and alkanesulfonates were found to react with these systems under similar conditions to give corresponding alkyl iodides and disulfides. On the other hand, phenyl p-toluenesulfonate, an aryl arenesulfonate was found to be quite inert under the same treatment with these reducing systems even under much harder conditions. These observations suggest that the initial step is the S_N2 attack of iodide on the α-carbon of alkyl sulfonates to form the alkyl iodides and sulfonate anions which are then reduced further to the corresponding disulfide in the reaction with the polyphosphoric derivative/ iodide system. In the case of phenyl p-toluenesulfonate, an aryl arenesulfonate, the initial nucleophilic attack of iodide on aromatic ipso carbon is so sluggish that the reduction does not proceed. Alkyl iodide was usually obtained quantitatively after about 15 minutes in this reaction, however the yield of the corresponding disulfide was very poor in the early stage of the reaction. Thus, the initial S_N2 reaction by the attack of iodide on the alkyl group is quite fast, however, the reduction of sulfonate anion produced is relatively slow. Actually, pentyl benzenesulfonate was found to react readily with tetrabutylammonium iodide in benzene to afford tetrabutylammonium benzenesulfonate and pentyl iodide, however phenyl p-toluenesulfonate was not found to react with tetrabutylammonium iodide at all.

Table 4. Reduction of Sulfonate Esters with Polyphosphoric Derivative/ Potassium Iodide/Tetrabutylammonium Iodide

Sulfonate Ester RSO_3R'	Polyphosphoric Derivative	Reaction Conditions Solvent/Temp(°C)/Time(h)	Products(%) RSSR	R'I
	PPA a)	Sulfolane/93/7	no reaction[c]	
	PPA b)	Sulfolane/93/8	50	d)
	P_4O_{10} b)	Acetonitrile/Reflux/33	70	d)
	PPA b)	Sulfolane/93/12	54	89[e]
$CH_3(CH_2)_7SO_3(CH_2)_4CH_3$	PPA b)	Sulfolane/100/7	45	81[e]

a,b) Amounts(mmol) of reagents used of sulfonate ester/polyphosphoric derivative/potassium iodide/tetrabutylammonium iodide: a=2/16/16/0; b= 2/16/16/0.2. c) Starting material was recovered in 91% yield. d) Not determined. e) The yield was after 15 minutes.

Experimental

Materials: PPA, potassium iodide, tetraphosphorus decaoxide, p-toluenesulfonic acid, sodium p-toluenesulfonate, potassium chloride, sodium benzenesulfonate, sodium 2,4-dimethylbenzenesulfonate, p-toluenesulfonyl chloride, and d-camphor-10-sulfonic acid were all from Wako Chemicals Co. Tetrabutylammonium iodide, p-chlorobenzenesulfonic acid, benzenesulfonic acid, sodium octanesulfonate, tetraethylammonium chloride and ethyl benzenesulfonate were from Tokyo Kasei Co.

Conversion of Sodium Sulfonate to the Corresponding Sulfonic Acid: The cation exchange resin which was converted to the protonated form by flowing 1N. HCl water solution with column(Dowex, 50w-x8, 200~400 mesh H-form, Muromachi Kagaku Co.) was used to convert sodium sulfonate to the corresponding sulfonic acid.

Preparation of Ethyl Polyphosphate: Ethyl polyphosphate, PPE, was prepared according to the known method.[9] Tetraphosphorus decaoxide, 150 g, was added into a solution of 300 ml of dry ether and 150 ml of dry chloroform. The mixture was refluxed for 4 days under nitrogen(bath temperature 50°C). As the reaction proceeded, the crystalline P_4O_{10} faded away eventually affording a homogeneous liquid. After completion of the reaction, PPE liquid was decanted in dry box. The solution was evaporated to a colorless syrup. The residue was dried by a vacuum pump for 36 hours at 40°C. A colorless syrupy(hard) ester which is very sensitive to

moisture, was obtained.

General Procedure for the Reduction of Sulfonic Acid to the Corresponding Disulfide: Potassium iodide, 8 g(48 mmol) and tetrabutylammonium iodide 583 mg(1.5 mmol) were added into a mixture of PPE 24g(48 mmol) and d-camphor-10-sulfonic acid 1.39 g(6 mmol). Then, into this mixture, 20 ml of dry chloroform was added. The whole mixture was stirred and refluxed for 5 hours under nitrogen atmosphere. Then 10 ml of water was added to this mixture and the mixture was refluxed for 1 hour. The reaction mixture was poured into benzene(100 ml), and washed with water for 3 times. The benzene solution was washed with 0.5 M. sodium thiosulfate solution and dried over $MgSO_4$. The solvent was evaporated and the crude product, i.e. the disulfide was chromatographed on a silica-gel column with benzene(R_f=0.2, eluent:benzene). Removal of the solvent afforded bis(d-camph-10-yl) disulfide as a colorless crystalline in 74% yield(817 mg).
m.p.=236~238°C; $[\alpha]_D^{25}$ -103.66°(c=1, $CHCl_3$); IR(KBr) 1730cm^{-1} (C=O); NMR($CDCl_3$) δ=0.90(3H, s), 1.05(3H, s), 2.75(1H, d, J=13.5Hz), 3.20(1H, d, J=13.5Hz), 2.5~1.1(7H, m); Found: C, 65.33; H, 8.25; S, 17.27%. Calcd for $C_{20}H_{30}S_2O_2$: C, 65.53; H, 8.24; S, 17.49%.
Reductions of other sulfonic acids to the corresponding disulfides with the polyphosphoric derivative/iodide system were conducted by the same procedure.
di-p-tolyl disulfide m.p.=44~45°C (lit,[11] 46°C)
di-p-chlorophenyl disulfide m.p.=70~71°C (lit,[12] 73°C)
bis(2,4-dimethylphenyl) disulfide b.p.=180~186°C/2~2.5 mmHg

IR(NaCl) 540 and 800cm^{-1}; NMR(CCl_4)δ=2.24(3H,s), 2.33(3H,s), 3.4~2.6 (3H, m); Found: C, 69.69; H, 6.65; S, 23.58%. Calcd for $C_{16}H_{18}S_2$: C, 70.02; H, 6.61; S, 23.36%.

Dioctyl disulfide and diphenyl disulfide were identical to the authentic commercial samples.

Trapping Experiment of Sulfonyl Function:

Tetraphosphorus decaoxide, 1600 mg(11.27 mmol) and 381 mg (2 mmol) of p-toluenesulfonic acid were dissolved in 5 ml of dry acetonitrile and the reaction mixture was heated(60~65°C) for 1.5 hours under nitrogen. Then, 33 mg(0.2 mmol) of tetraethylammonium chloride, 746 mg(10 mmol) of potassium chloride and 5 ml of dry acetonitrile were added to this reaction mixture at 0°C and the mixture was kept standing for 3 hours at room temperature. Then, the mixture was poured into 100 ml of benzene and the benzene solution was washed with water for three times, and then dried over $MgSO_4$. When the solvent was evaporated, p-toluenesulfonyl chloride was obtained in 48% yield(GLC); the isolated yield was 43%. The sulfonyl chloride was identical to the authentic sample of p-toluenesulfonyl chloride both in GLC and TLC. In the reduction with the PPE system, PPE, 6 g and 381 mg(2 mmol) of p-toluenesulfonic acid were dissolved in 5 ml of dry acetonitrile and the mixture was heated for 1 hour at about 70°C under nitrogen. Then, at 0°C 33 mg of tetraethylammonium chloride and 746 mg(10 mmol) of potassium chloride were added to the reaction mixture which was kept standing for 2.5 hours at room temperature. After the reaction, a similar treatment as that with P_4O_{10}, gave p-toluenesulfonyl chloride in 28% yield(GLC).

Synthesis of p-Toluenesulfonyl Iodide: Sodium p-toluenesulfinate dihydrate 2.14 g(10 mmol) and 2.54 g(10 mmol) of iodine were dissolved in a mixture of 10 ml of benzene and 10 ml of water and the mixture was stirred for 30 minutes at 0°C. Then, the mixture was poured into benzene and the benzene solution was washed with water for 3 times as quickly as possible, dried over $MgSO_4$, recrystallized from a mixture of benzene and hexane, and sealed with aluminium foil. p-Toluenesulfonyl iodide was obtained nearly quantitatively. m.p.=85~86°C decomposition (lit,[13] 84~85°C)

Reduction of p-Toluenesulfonyl Iodide with Hydriodic Acid to Di-p-Tolyl Disulfide: p-Toluenesulfonyl iodide 300 mg(1.06 mmol) was dissolved in 3 ml of dioxane and then 4 ml of hydriodic acid(57%) was slowly added to this mixture at room temperature. An exothermic reaction occurred affording di-p-tolyl disulfide. After 1 hour the mixture was poured into benzene and the benzene solution was washed with water for two times, 0.5N. $Na_2S_2O_3$ solution, dried over $MgSO_4$. Only di-p-tolyl disulfide was obtained in 79% yield(GLC).

Competitive Reaction of Arenesulfonic Acids with PPA/KI/Bu_4NI (catalyst): p-Toluenesulfonic acid 190.2 mg(1 mmol), 176 mg (1 mmol) of benzenesulfonic acid, and 192.2 mg(1 mmol) of p-chlorobenzenesulfonic acid were dissolved in 10 ml of sulfolane, then 8100 mg of PPA, 3984 mg(24 mmol) of potassium iodide, 184 mg(0.5 mmol) of tetrabutylammonium iodide and 154 mg(1 mmol) of biphenyl were added to this mixture and the whole mixture was stirred(95~100°C) for 4 hours. The reaction was followed by GLC. After the reaction, 5 ml

of water was added into the mixture which was then heated for 0.5 hour. The solution was poured into benzene and the benzene solution was washed with water for 3 times, then with 0.5N. solution of $Na_2S_2O_3$ and dried over $MgSO_4$. The solution was found to contain only the mixture of disulfides, i.e. $C_6H_5SSC_6H_5$, $C_6H_5SSC_6H_4CH_3$-p, $C_6H_5SSC_6H_4Cl$-p, p-$CH_3C_6H_4SSC_6H_4CH_3$-p, p-$CH_3C_6H_4SSC_6H_4Cl$-p, and p-$ClC_6H_4SSC_6H_4Cl$-p which are converted to the corresponding thiols by treating with a mixture of triphenylphosphine or tributylphosphoine(2 mmol) and water in a mixed solvent of benzene and dioxane over night at room temperature. The yields of the mixture of three thiols were determined with GLC. p-Toluenethiol, 71%; Benzenethiol, 60%; p-Chlorobenzenethiol, 34%.

In the reduction with the P_4O_{10} system, a mixture of three different of p-substituted benzenesulfonic acids each with 1 mmol were dissolved in 20 ml of dry acetonitrile, and then 3000 mg(21 mmol) of P_4O_{10}, 3984 mg(24 mmol) of potassium iodide, and 184 mg(0.5 mmol) of tetrabutylammonium iodide were added to this mixture which was then refluxed for 7 hours. After the reaction, a similar work-up procedure afforded a mixture of three p-substituted benzenethiols. The yields of these thiols were determined by GLC(SE-30, I m glass column) to be the following. p-Toluenethiol, 50%; Benzenethiol, 50%; p-Chlorobenzenethiol, 26%.

Preparation of Sulfonate Esters: In a reactor, 31.47 mmol of a certain sulfonyl chloride and 94.41 mmol of a choice alcohol, were dissolved in the mixture of 10 ml of benzene and 10 ml of acetonitrile and the whole mixture was stirred.

Then, 157.25 mmol of pyridine was added to this mixture. After 0.5 hour, the starting sulfonyl chloride was no longer present upon analysis with TLC(R_f=0.5, eluent:benzene). In the reaction of alkanesulfonyl chlorides, it usually took about 12 hours to complete at room temperature. Then, the solution was poured into benzene and washed with water for three times, dried over $MgSO_4$. Sulfonates obtained were either distilled or recrystallized from hexane to give pure sulfonates. The yields of sulfonates are usually 50~60%.

Pentyl Benzenesulfonate 138~140°C/1 mmHg (lit,[14] 136~138°C /1 mmHg)

Pentyl p-Toluenesulfonate 167~168°C/3 mmHg(lit,[15] 169~170°C /3 mmHg)

Phenyl p-Toluenesulfonate m.p.=92~93°C(lit,[17] 93°C)

Pentyl Octanesulfonate TLC(eluent:benzene) R_f=0.4~0.5;
IR(NaCl) 1340(SO_2), 1160(SO_2)cm^{-1};
NMR(CCl_4)δ=4.1(2H, t, J=6Hz),
3.0(2H, t, J=6.7Hz),
2.1~0.7(24H, m)
Found: C, 59.13; H, 10.55; S, 11.94
Calcd for $C_{13}H_{28}O_3S$: C, 59.05; H, 10.67; S, 12.12.

Reduction of Sulfonate Ester with Polyphosphoric Derivative/ Potassium Iodide/Tetrabutylammonium Iodide System:

PPA 5408 mg(16 mmol), 2656 mg(16 mmol) of potassium iodide, and 484 mg(2 mmol) of pentyl p-toluenesulfonate were dissolved in 10 ml of sulfolane, and then 74 mg(0.2 mmol) of tetrabutylammonium iodide and 308 mg(2 mmol) of biphenyl (standard material) were added to this mixture, which was then heated(~93°C) with stirring under nitrogen. After 15 minutes, the starting ester was found to have disappeared upon GLC analysis and pentyl iodide was formed in 89% yield upon determination with GLC, but the yield of disulfide was still very poor during this period. After 12 hours, 10 ml of water

was added to this mixture and heated for 0.5 hour. The mixture was poured into benzene which was then washed with water for three times, again with 0.5N. $Na_2S_2O_3$ solution and dried over $MgSO_4$. Thus, di-p-tolyl disulfide was obtained in 54% yield(GLC), and the yield of pentyl iodide was found to remain unchanged as compared with that, estimated after 15 minutes.

Pentyl Iodide 157°C/760 mmHg(lit,[16] 157°C/760 mmHg)

References

1) W.A. Sheppard, Org. Synth., 40, 80(1960).
D. Cipris and D. Pouli, Synth. Commun., 9, 207(1979).
H. Alper, Angew. Chem., Int. Ed. Engl., 8, 677(1969).
2) T. Numata, H. Togo, and S. Oae, Chapter 1.
3) A. Zobacova, V. Hermankova, and J. Jary, Collect. Czech. Chem. Commun., 42, 2540(1977).
4) C.M. Marvel and P.D. Caeser, J. Am. Chem. Soc., 73, 1097 (1951).
T. Cuving and M. Larcheveque, J. Organomet. Chem., 64, 315 (1977).
5) T. Numata, H. Awano, and S. Oae, Tet. Lett., 21, 1235(1980).
6) K. Fujimori, H. Togo, and S. Oae, Tet. Lett., 21, 4921(1980).
S. Oae and H. Togo, Synthesis,(1981), 371.
7) G.A. Olah, S.C. Narang, L.D. Field, and R. Karpeles, J. Org. Chem., 46, 2408(1981).
8) S. Oae and H. Togo, Bull. Chem. Soc. Jpn., in contribution.
9) M.P. Cava, M.V. Lakshmikantham, and M.J. Mitchell, J. Org. Chem., 34, 2665(1969).
10) W.A. Sheppard, Org. Synth., Coll. Vol. 5, 844(1973).
11) L. Field, J. Am. Chem. Soc., 74, 394(1952).
12) J.L. Sparke, J.L. Cameron, and N. Kharasch, J. Am. Chem. Soc., 75, 4907(1953).
13) L.M. Litvinenko, V.A. Dadai, V.A. Savelova, and T.I. Krichevtsoba, Zh. Obshch. Khim., 34, 3730(1964).
14) B.L. Emling, J. Am. Chem. Soc., 74, 4702(1952).
15) H. Gilman and N.J. Beaber, J. Am. Chem. Soc., 47, 518(1925).
16) I. Simon, Bull. Soc. Chim. Belg., 38, 2519(1929).
17) H. Gilmann, N.J. Beaber, and C.H. Myers, J. Am. Chem. Soc., 47, 2047(1925).

Chapter 6.

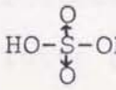
Biomimetic Reduction of Sulfuric Acid

Abstract

Sulfuric acid, sodium sulfate were readily reduced to elemental sulfur and hydrogen sulfide upon treatment with a mixture of polyphosphoric derivatives(PPE, PPA, and P_4O_{10}), which can form mixed-anhydrides having P-O-S linkage, and iodide or thiol. Sulfur dioxide, which is undoubtedly one of important intermediates, was trapped by p-tolyl lithium to afford p-toluenesulfinic acid which was converted to p-tolyl methyl sulfone upon treatment with methyl iodide, though the yield was low. Sulfur trioxide, which has been postulated as the key intermediate in the biological reduction of inorganic sulfate, was also trapped by mesitylene to give mesitylenesulfonic acid in a high yield. The reduction of sulfate to elemental sulfur and hydrogen sulfide is considered to proceed through the course which resembles the biological reaction path involved in the assimilatory metabolism of inorganic sulfate in microorganisms and plants.

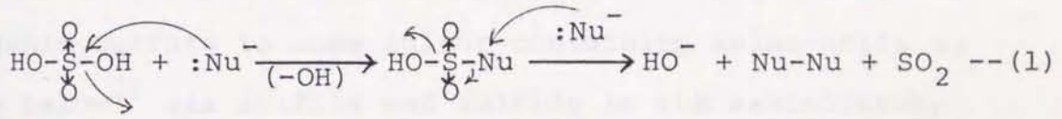
Introduction

Inorganic sulfate which is in the highest oxidative state of sulfur atom is one of the most inert species toward any reducing agent among the naturally occurring sulfur compounds, and hence clean reduction of inorganic sulfate by any chemical means under mild conditions has been considered to be most difficult.



S→O 110 kcal/mol 1.42~1.43Å[1)]
S-OH 88 kcal/mol 1.52~1.55Å

The deoxygenative reduction of sulfuric acid may proceed stepwise via an initial nucleophilic displacement of OH group of sulfuric acid by a leaving group, followed by subsequent nucleophilic attack on the leaving group by a second nucleophile as shown in eq. 1).



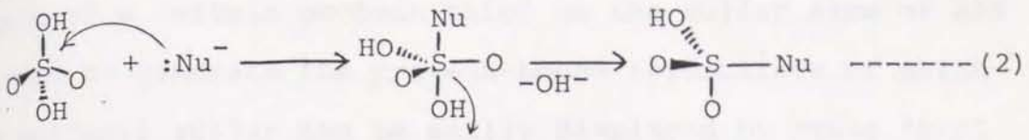
--(1)

However, such a simple nucleophilic replacement of OH group of sulfuric acid does not seem to proceed readily, due mainly to the following few reasons.

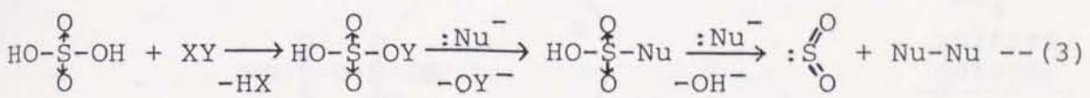
a) Sulfuric acid is a very strong acid which can turn to sulfate dianion by supplying two protons to the attacking nucleophiles that eventually lose the nucleophilic reducing ability due to the protonation to the lone electron pair of nucleophile. Sulfate dianion, bearing two negative charge, may also no longer readily receive nucleophilic attack at this central sulfur atom due to the charge repulsion.

b) Even undissociated sulfuric acid would resist the nucleophilic attack, due to the steric hindrance and electronic repulsion by four oxygen atoms bound to the central sulfur,

while three electronegative oxygens must be placed in the unfavorable equatorial position in the transition state of the substitution as shown in eq. 2).

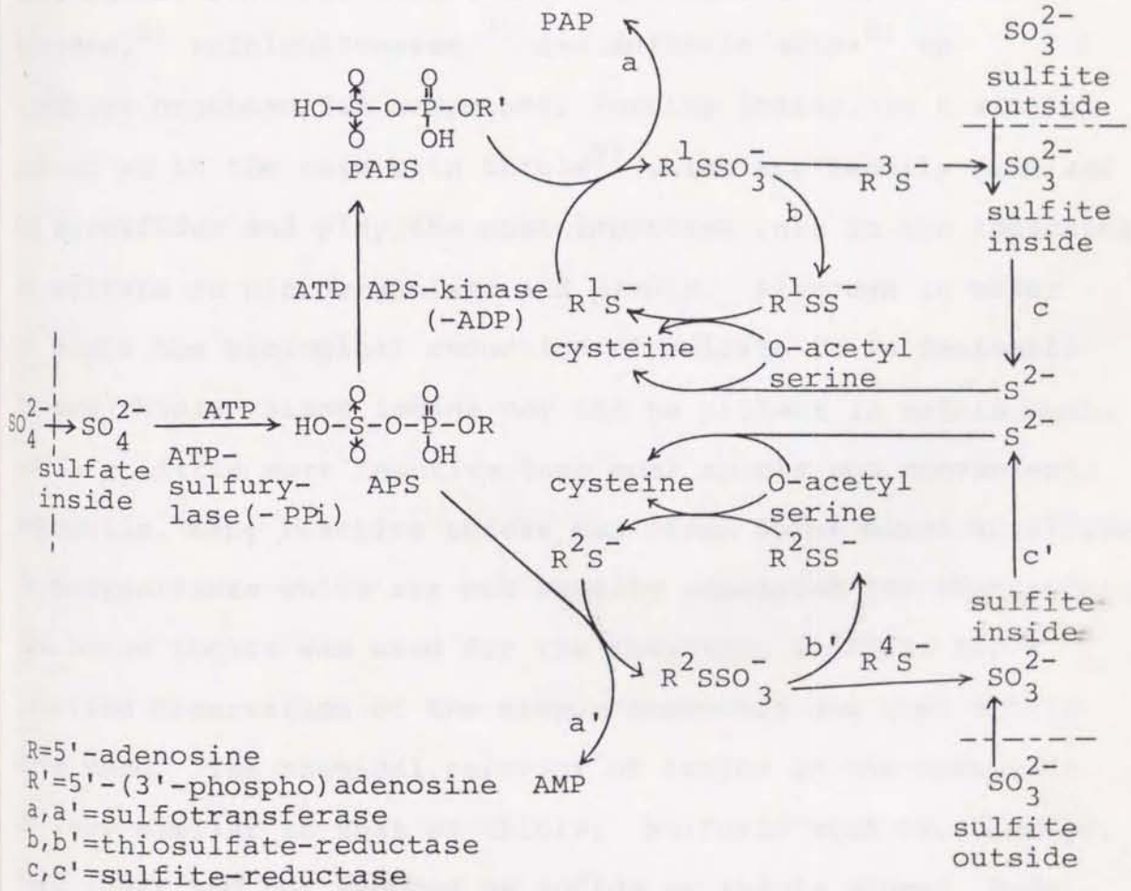


c) The leaving ability of OH group is rather poor in most nucleophilic substitution reactions. Therefore, it would be necessary to substitute proton by some other electron-withdrawing group by treatment with some condensing reagent XY to activate the central sulfur to receive nucleophilic attack as shown in eq. 3).



Meanwhile, many plants, microorganisms are known to reduce inorganic sulfate to some sulfur-containing amino-acids as shown below[2] via sulfite and sulfide in the assimilatory metabolisms.

The biological reduction of sulfate is consisted of the following two key steps, i.e. conversion of sulfate to a mixed-anhydride, APS or PAPS, to activate sulfate, and the subsequent nucleophilic attack of a certain protein thiol on the sulfur atom of APS or PAPS to generate the protein-bound thiosulfate of which the sulfenyl sulfur can be easily displaced by other thiol group in the enzyme to give sulfite which is ultimately reduced to hydrogen sulfide, or of which the sulfonyl group is reduced by thiosulfate reductase to form R^1SS^- or R^2SS^-. This chapter describes first successful chemical model reactions for the assimilatory biological reduction of inorganic sulfate.

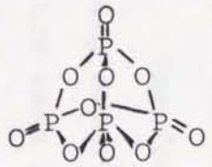


Results and Discussion

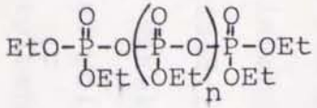
Since the essential part of ATP which takes part in the biological reduction of sulfate is the triphosphate linkage, polyphosphoric acid(PPA), ethyl polyphosphate(PPE),[3] and tetraphosphorus decaoxide are considered to be used as ATP model compounds. When sulfuric acid was added to either one of these polyphosphoric derivatives, we observed mild evolution of heat, probably due to the formation of $-\overset{O}{\overset{\|}{P}}-O-\overset{O}{\overset{\|}{S}}-O-$ bond, which is a mixed anhydride. Iodide is known to be a facile reducing agent which can reduce oxidized organosulfur derivatives such as sulfoxides,[4] sulfinic acids,[5] sulfonyl halides,[6] thiolsulfonates,[7] and sulfonic acids[8] to divalent organosulfur compounds, forming iodine, in a similar manner as in the case with thiols[9] which are readily oxidized to disulfides and play the most important role in the reduction of sulfate in microorganisms and plants. Although in order to mimic the biological reduction of sulfate it is desirable to use thiols since iodide may not be present in nature while it is a little more reactive than most thiols and convenient. Meanwhile, many reactive thiols can often forms mixed disulfides or polysulfides which are not readily separated for characterization, and hence iodide was used for the reduction at first for a detailed observation of the simple reduction and then thiols were used. The chemical behavior of iodide in the reduction is very similar to that of thiols. Sulfuric acid is, however, very inert and not reduced by iodide or thiols alone. Only in the presence of such condensing agents as polyphosphoric derivatives, sulfate was reduced to sulfide with either iodide or thiols. The solvent used for the reactions with PPA and

P_4O_{10} were dried sulfolane and acetonitrile respectively, since both solvents can readily dissolve these polyphosphoric derivatives, however, other polar aprotic solvents can also be used in the reaction with PPE because of its high solubility in these solvents. The results obtained in reduction of sulfuric acid are shown in Table. The products were elemental sulfur and hydrogen sulfide. Under acidic conditions, thiol group(i.e. hydrogen sulfide) and polysulfide(i.e. elemental sulfur) are in an equilibrium as shown in eq.4)(generally, thiol is oxidized by iodine in the presence of a base, e.g. pyridine or amine). Therefore the reduction products obtained were a mixture of hydrogen sulfide and elemental sulfur. The rather low yields of the reduction products are mainly due to the difficulty of purification and isolation of these products from the reaction mixture. In the absence of $Bu_4N^+I^-$, the yields of the reduction products were markedly decreased. In the runs 1,2,3,4, and 5, the reduction of sulfate was carried out in one flask(A), whereas, in the runs a,b, and c, while the reduction was carried out in flask(A), nitrogen gas was introduced into flask(A) to drive out evolving hydrogen sulfide into flask(B) which contained a dry benzene solution of DCC that can trap hydrogen sulfide to afford the thiourea derivative. Generally, when iodide ion was added into a mixture of sulfuric acid and any one of the polyphosphoric derivatives, the formation of hydrogen sulfide gas was easily detected.

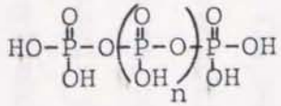
$$H\text{-}S\text{-}H \underset{I_2 \quad HI}{\overset{I_2 \quad HI}{\rightleftharpoons}} H\text{-}S\text{-}S\text{-}H \underset{I_2 \quad HI}{\overset{I_2 \quad HI}{\rightleftharpoons}} \underset{I_2 \quad HI}{\overset{I_2 \quad HI}{\rightleftharpoons}} H\text{-}S\text{-}(S)_n\text{-}S\text{-}H \underset{I_2 \quad HI}{\overset{I_2 \quad HI}{\rightleftharpoons}} S_8 \quad \text{--(4)}$$



P_4O_{10}



PPE



PPA

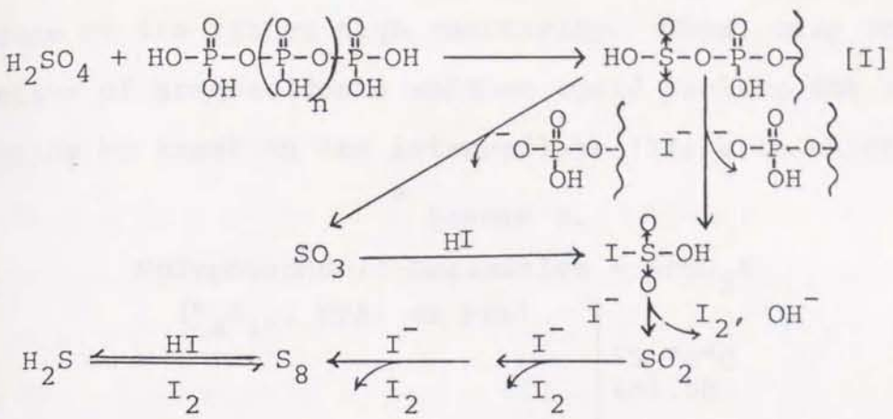
Table. The Reduction of Sulfuric Acid and Sulfate

$$H_2SO_4(M_2SO_4) \xrightarrow[(-I_2)]{KI,\ Bu_4NI(cat)} S_8 \text{ and } H_2S^{a)}$$

polyphosphoric derivative	solvent	condition	time (h)	yields (%) (A) S_8	(B)[a] S_8	(B)[a] H_2S
1. P_4O_{10}	acetonitrile	42~45°C	10	17		-
2. PPE	chloroform	r.t.	7	4~10		-
3. PPA	sulfolane	75°C	8	58		-
4.[b] "	"	"	17	15		-
5.[c] "	"	70~73°C	7	40~44		-
a. PPE	acetonitrile	r.t.	5	23	0	trace
b. PPA	sulfolane	75°C	4	42	trace	15
c.[b] "	"	"	8	10	0	trace
6.[d] "	"	"	8	0		-

a) Hydrogen sulfide was isolated as dicyclohexylthiourea in the trapping experiment with DCC. When N_2 gas was bubbled into the reaction mixture(A) and the exhausted gas was introduced into a benzene solution of DCC(B). b) Na_2SO_4 was used. c) $(Bu_3NEt)_2SO_4$ was used. d) No presence of H_2SO_4.

Both elemental sulfur and the thiourea can be readily identified by comparison with the authentic samples(TLC, mp).

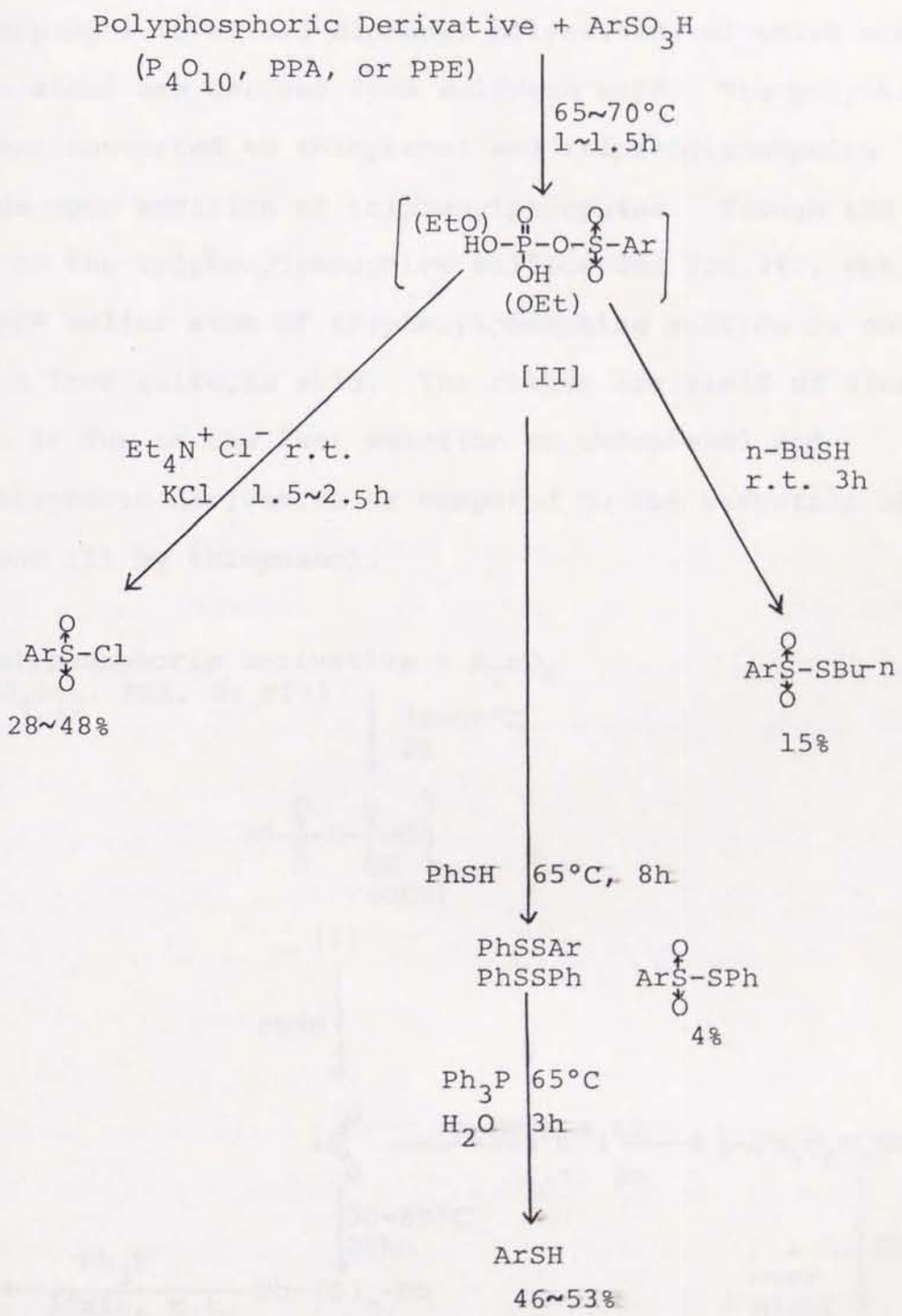


Scheme 1.

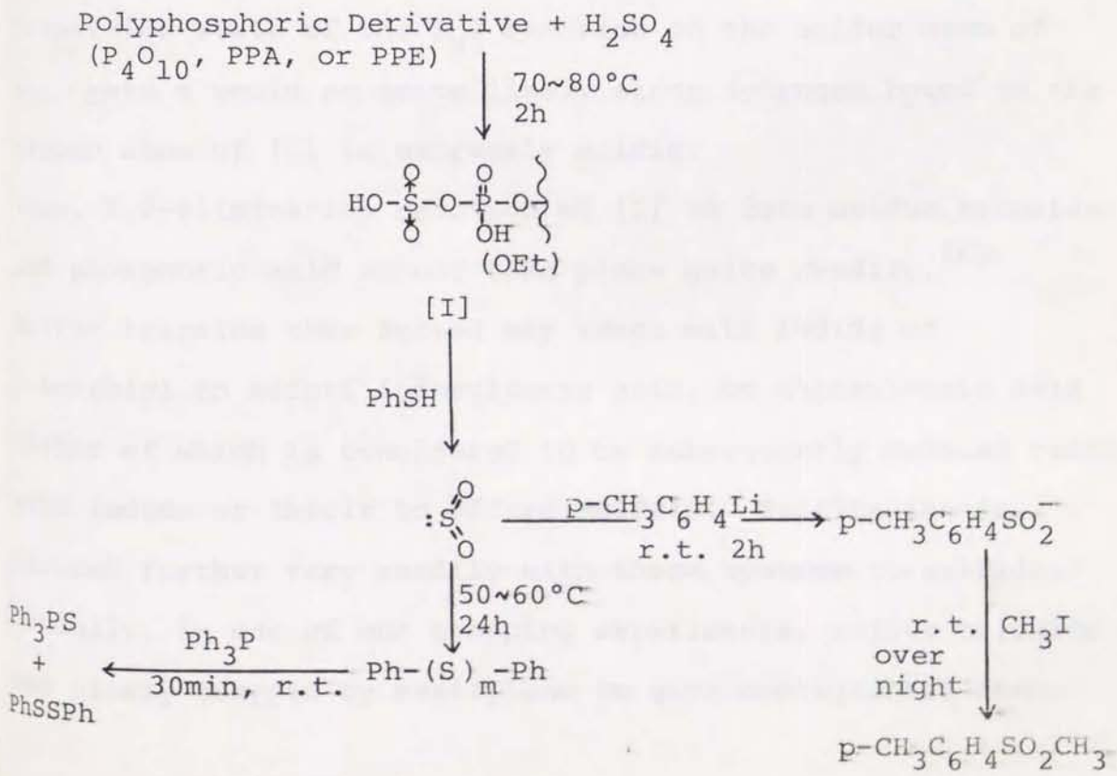
Inspection of the data in the Table, reveals that PPA is the best model substrate for ATP, and gave sulfur and hydrogen sulfide in the highest yields. The rather low yields of reduction species in the reaction with either P_4O_{10} or PPE is believed to be due to the subsequent reaction between hydrogen sulfide formed and P_4O_{10}, which is a strong proton acceptor, or PPE which is an effective alkylating agent. The postulated mechanism is shown in Scheme 1. In this Scheme, [I] is believed to be the key intermediate, in the presence of excess polyphosphoric derivative. Sulfite is also one of the intermediates, which is eventually reduced to elemental sulfur in a high yield in the reaction with a mixture of PPA and KI under similar conditions. The formation of intermediate [I] may be supported by a trapping experiment described in the reduction of sulfonic acid with the same system.[16] Namely, when chloride ion was added in the reaction mixture of polyphosphoric derivative and p-toluenesulfonic acid, p-toluenesulfonyl chloride was obtained as shown in Scheme 2.

However, isolation of chlorosulfonic acid in the reaction of the intermediate [I] with chloride anion was not achieved because of its rather high reactivity. Thus, only in the reaction of arenesulfonic acid we could isolate the sulfonyl chloride by treating the intermediate [II] with chloride.

Scheme 2.



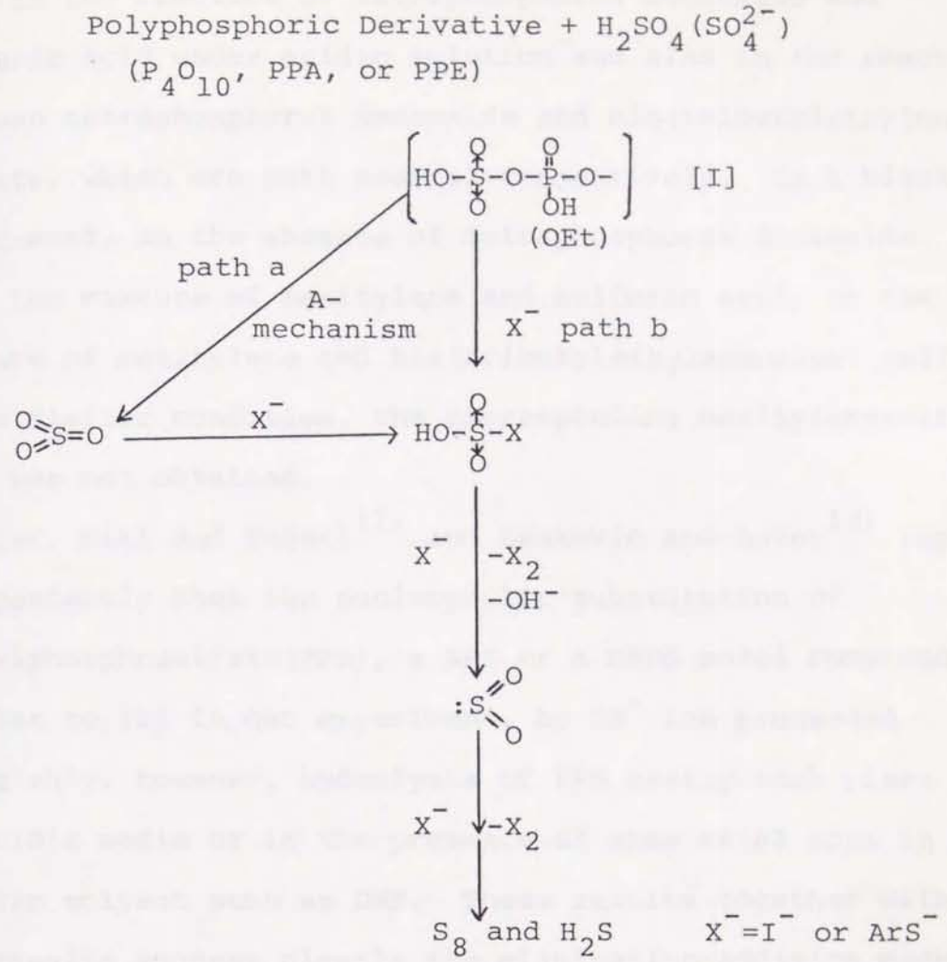
Sulfur dioxide is also an intermediate, however, since it is so readily reduced by hydrogen iodide that it is difficult to trap SO_2 when iodide ion is used as the reducing agent. Instead of using iodide, excess thiophenol can be added as the reducing agent into the mixture of polyphosphoric derivative and sulfuric acid. Thus, sulfuric acid was reduced by thiophenol to afford diphenyl polysulfide of which middle sulfur atoms are derived from sulfuric acid. The polysulfide was then converted to thiophenol and triphenylphosphine sulfide upon addition of triphenylphosphine. Though the yield of the triphenylphosphine sulfide was low(2%), the combined sulfur atom of triphenylphosphine sulfide is obviously derived from sulfuric acid. The rather low yield of divalent sulfur is due to the fast reaction of thiophenol and polyphosphoric derivative as compared to the reduction of compound [I] by thiophenol.



Scheme 3.

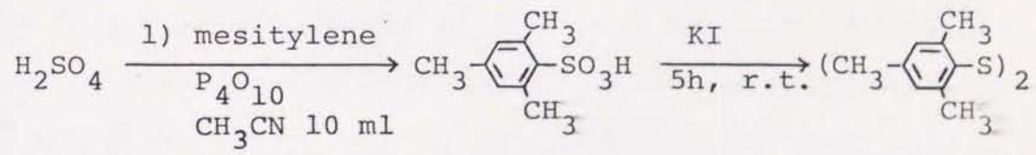
Since thiophenol is a mild reducing agent as compared to hydrogen iodide, sulfur dioxide was successfully trapped by p-tolyl lithium, when SO_2 gas formed was driven out into an ether solution of p-tolyl lithium to afford p-toluenesulfinic acid which was then converted to the sulfone by treating with methyl iodide, though the yield of the sulfone was poor(~1%). Although the yields of the reduction products are not high, the successful reduction of sulfuric acid and sulfate to sulfides in this biomimetic reduction with polyphosphoric derivatives with iodide or thiols, and the trapping of sulfur dioxide under mild conditions would be the first reported experiment which can successfully mimic the biological assimilatory sulfate reduction. In the reduction, two paths (a and b) are conceivable for the reaction of compound[I] with nucleophile(I^-, PhSH). While path b may be unfavorable due to the stereo-electronic repulsion between the nucleophile and negative oxygen poles of bulky sulfate group of [I] at the transition state of the S_N2 reaction on the sulfur atom of [I], path a would be quite likely since hydrogen bound to the oxygen atom of [I] is extremely acidic.

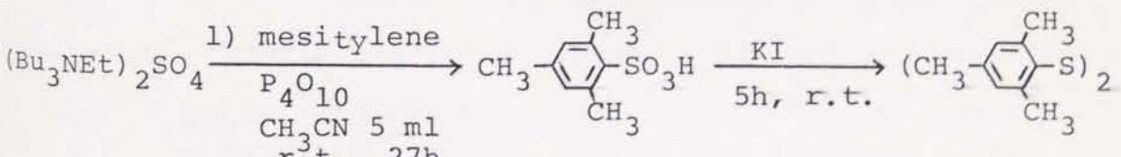
Thus, 1,2-elimination reaction of [I] to form sulfur trioxide and phosphoric acid should take place quite readily.[10] Sulfur trioxide thus formed may react with iodide or arenethiol to afford iodosulfonic acid, or thiosulfuric acid either of which is considered to be subsequently reduced readily with iodide or thiols to afford sulfite. Sulfite ion is reduced further very readily with these systems to sulfide. Actually, in one of our trapping experiments, sulfur trioxide was nicely trapped by mesitylene to give mesitylenesulfonic



Scheme 4.

Sulfur Trioxide Trapping with Mesitylene





acid in the reaction of tetraphosphorus decaoxide and sulfuric acid under acidic solution and also in the reaction between tetraphosphorus decaoxide and bis(tributylethylammonium) sulfate, which are both neutral respectively. In a blank experiment, in the absence of tetraphosphorus decaoxide, i.e. the mixture of mesitylene and sulfuric acid, or the mixture of mesitylene and bis(tributylethylammonium) sulfate under similar condition, the corresponding mesitylenesulfonic acid was not obtained.

Earlier, Eiki and Tagaki[11] and Benkovic and hevey[12] reported independently that the nucleophilic substitution of phenylphosphosulfate(PPS), a APS or a PAPS model compound, similar to [I] in our experiment, by OH^- ion proceeded sluggishly, however, hydrolysis of PPS easily took place in acidic media or in the presence of some metal ions in aprotic solvent such as DMF. These results together with our results suggest clearly the elimination-addition mechanism involving the formation of sulfur trioxide in the acidic media(path a) as shown in Scheme 4.

Experimental

Materials: PPA, potassium iodide, mesitylene, sulfuric acid, tributylamine, diethylsulfate, tetraphosphorus decaoxide, and dicyclohexyl carbodiimide are all from Wako Chemical Co., tetrabutylammonium iodide was from Tokyo Kasei Co., and sodium sulfite was obtained from Kanto Kagaku Co.

Ethyl Polyphosphate Ester: Ethyl polyphosphate ester was prepared by a known method.[13] Tetraphosphorus decaoxide, 150 g, was added into a solution of 300 ml of dry ether and 150 ml of dry chloroform. The mixture was refluxed for 4 days under N_2(bath temp. 50°C). As the reaction proceeded, the crystalline P_4O_{10} faded away to give a homogeneous liquid. After completion of this reaction, the liquid phase was decanted into a flask in a dry box. Then the solution was evaporated to a colorless syrup. The residue was then dried by vacuum pump for 36 hours at 40°C. A colorless syrupy(hard) ester which is very sensitive to moisture, was obtained

PPE NMR($CDCl_3$) 1.9~1.5ppm(m, 2H), 4.2~5.0ppm(m, 3H)

Reduction of Sulfuric Acid with PPA/KI/Bu_4NI(cat) System to Sulfide: Polyphosphoric acid, 10 g(2.97x10 mmol, M.W.=338) and 4.93 g(2.97x10 mmol) of potassium iodide were added into 6 ml of dry sulfolane. Then, 300 mg(2.97 mmol) of sulfuric acid(97%) was added into this mixture, into which finally 184 mg(0.5 mmol) of tetrabutylammonium iodide was added. The reaction was carried out for 8 hours at 75°C with stirring under nitrogen atmosphere. The odor of hydrogen sulfide was clearly detected. After the reaction, 10 ml of water was added and the mixture was heated under similar conditions for 0.5 hour in order to hydrolyze excess PPA. The reaction mixture was poured into benzene which

solution was washed with water for 3 times, dried over $MgSO_4$, filterated and the filtrate was evaporated. The residue was subjected to TLC(MERCK, silica-gel type-60), separated with benzene to exclude iodine, then 55 mg of sulfur was obtained and identified by comparison with the authentic sulfur (TLC R_f=0.7, eluent:benzene) m.p.=112-114°C(lit,[14] 115°C). After recrystallization with a mixture of benzene and hexane. the yield of sulfur was 58%.

Hydrogen Sulfide Trapping in PPA/KI/Bu_4NI(cat) System:

Reactor A.

PPA 10~8 g and 4.93 g(2.97x10 mmol) of potassium iodide were added into 6 ml of dry sulfolane. Then, 300 mg of sulfuric acid was added and finally 184 mg(0.5 mmol) of tetrabutylammonium iodide was added into this mixture.

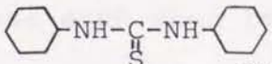
Reactor B.

Dicyclohexyl carbodiimide 1836 mg(2.97x3 mmol) was dissolved in 10 ml of dry benzene in a flask which was equipped with a empty balloon.

Reactor B was jointed to Reactor A with a glass tube. The content in Reactor A was stirred and heated for 4 hours at 75°C under slow flowing of nitrogen gas. While the reaction mixture in Reactor B was stirred at room temperature, nitrogen and hydrogen sulfide were introduced into the Reactor B. After the reaction, 10 ml of water was added to the Reactor A and the mixture was heated under similar conditions for one hour. The reaction mixture in Reactor A was poured into benzene and washed with water for 3 times, dried over $MgSO_4$, filterated and evaporated. The residue was separated by TLC with benzene to give sulfur. From the Reactor A, 40 mg of

sulfur was obtained. Reactor A: S_8 yield 42%

Then 10 ml of water was added into the Reactor B to quench any excess of DCC to urea and the mixture was kept standing for a few hours. The mixture was poured into benzene which solution was washed with water, dried over $MgSO_4$, and benzene was evaporated. The residue was separated through silica-gel column(MERCK 70~230 mesh) with chloroform.

Reactor B  103 mg yield 15%

TLC R_f=0.3~0.4(eluent:$CHCl_3$)

IR(KBr) 1540cm^{-1} 3275cm^{-1}
1490cm^{-1} 1220cm^{-1}

m.p.=182~184°C(lit, 182~182.5°C[15])

(DCC is known to react with hydrogen sulfide under room temperature) Thiourea obtained in our system was identical to the authentic sample(IR, m.p., and TLC). A similar procedure with similar molar ratio was used in the reduction of sodium sulfate in PPA system.

Reduction of Sulfuric Acid with P_4O_{10}/KI/Bu_4NI(cat) System:

Tetraphosphorus decaoxide 2100 mg(2.97x5 mmol) and 4930 mg (2.97x10 mmol) of potassium iodide were added into 6 ml of dry acetonitrile. In this mixture, 300 mg(2.97 mmol) of sulfuric acid and 184 mg(0.5 mmol) of tetrabutylammonium iodide were added. The mixture was stirred and heated for 10 hours at 42~45°C under nitrogen atmosphere. Then, 10 ml of water was added into the reaction mixture to destroy excess P_4O_{10}. The reaction mixture was treated similarly as in the case of PPA system. Elemental sulfur, 16 mg, was obtained.

S_8 yield 17%

Reduction of Sulfuric Acid with PPE/KI/Bu_4NI(cat) System: potassium iodide 4930 mg(2.97x10 mmol) and 184 mg(0.5 mmol) of tetrabutylammonium iodide were added into 10 ml of dry chloroform, then 300 mg(2.97 mmol) of sulfuric acid was added into the mixture and finally 10 g of PPE was added into the mixture. The reaction was carried out for 7 hours at room temperature under nitrogen atmosphere. The yield of sulfide did not increase even when temperature was raised. Then, 10 ml of water was added and the mixture was treated similarly as in the case with PPA system. Elemental sulfur was obtained in 4~10% yield.

Trapping of Sulfur Trioxide in P_4O_{10}/KI/Bu_4NI(cat) System by Mesitylene: Tetraphosphorus decaoxide, 2100 mg(2.97x5 mmol), was added into 6 ml of dry acetonitrile into which 2 ml of mesitylene was then added. The mixture was cooled down to 0°C and 300 mg(2.97 mmol) of sulfuric acid was added into this mixture. The mixture was stirred for one hour at room temperature(0°C→r.t.) under nitrogen atmosphere. Then, 4930 mg(2.97x10 mmol) of potassium iodide, 184 mg(0.5 mmol) of tetrabutylammonium iodide and 4 ml of dry acetonitrile were added into this reaction mixture which was stirred for 5 hours at room temperature under nitrogen. (Since the isolation of mesitylenesulfonic acid is difficult in our system, the sulfonic acid was reduced to the disulfide with P_4O_{10}/KI system under mild condition. Thus, mesitylenesulfonic acid was converted to dimesityl disulfide.[16]) After the reaction, 10 ml of water was added and the mixture was stirred for one hour. The reaction mixture was poured into benzene which

solution was washed with water for 3 times, 0.5N. of $Na_2S_2O_3$ water solution once, again with water and dried over $MgSO_4$. Dimesityl disulfide, which was derived from mesitylenesulfonic acid, was obtained in ca. 50% yield by GLC(OV-1, 1m glass column). Authentic dimesityl disulfide was obtained by reducing mesitylenesulfonyl chloride with $LiAlH_4$ in dry ether for one hour(0°C→r.t.) to mesitylenethiol which was oxidized further to dimesityl disulfide with iodine and pyridine at room temperature in 81% yield. m.p.=124~125°C(lit,[17] 125°C)

Trapping of Sulfur Trioxide: Bis(tributylethylammonium) sulfate 588 mg(1.12 mmol) was dissolved in dry 5 ml of acetonitrile and 2 ml of mesitylene was added to this mixture. Then, 1200 mg(1.12x7.54 mmol) of tetraphosphorus decaoxide was added and the whole mixture was stirred for 27 hours at room temperature under nitrogen atmosphere. Potassium iodide, 1860 mg(1.12x10 mmol), was added into this mixture, into which 5 ml of acetonitrile was added and the whole mixture was stirred for 5 hours at room temperature.

Bis(tributylethylammonium) sulfate obviously plays the role of phase transfer catalyst. Then, 10 ml of water was added at 0°C into the mixture which was stirred for 1 h at room temperature. The mixture was poured into benzene and washed with water for 3 times, with 0.5N. of $Na_2S_2O_3$ water solution once, again with water once and dried over $MgSO_4$. Dimesityl disulfide was obtained in 37% yield(GLC, SE-30 1m glass column). In a separate experiment, bis(tributylethylammonium) sulfate was treated in acetonitrile without P_4O_{10} in the presence of mesitylene. However, no dimesityl disulfide was formed.

The Preparation of Bis(tributylethylammonium) Sulfate:

Diethyl sulfate,1247 mg(8 mmol) and 4500 mg(24.3 mmol) of tributylamine were dissolved in 6 ml of methylene chloride or chloroform and the mixture was refluxed for 2 days under nitrogen atmosphere. Disappearance of diethyl sulfate was followed by TLC(silica-gel Et_2SO_4 R_f=0.4 eluent:benzene). After this reaction, the solvent was evaporated and then, excess of tributylamine was excluded in vacuo at 50°C. White crystals were obtained in a high yield(quant.). This ammonium salt is neutral and very soluble in most all solvents(i.e. H_2O, alcohol, benzene, and ether) except hexane.

$(Bu_3NEt)_2SO_4$ IR(KBr) 2930cm^{-1} 2850cm^{-1} 1490cm^{-1} 1460cm^{-1} 1380cm^{-1} 1210~1250cm^{-1} 1020cm^{-1}

The Trapping of Sulfonyl Group in $ArSO_3H/P_4O_{10}$/KCl System:

Tetraphosphorus decaoxide, 1600 mg(11.27 mmol), was added into 5 ml of dry acetonitrile, into which 381 mg(2 mmol) of p-toluenesulfonic acid was added. The mixture was heated and stirred for 1.5 hours at 60~65°C under nitrogen atmosphere. Then, 33 mg(0.2 mmol) of tetraethylammonium chloride, 746 mg (10 mmol) of potassium chloride were added into the reaction mixture at 0°C and the mixture was stirred for 3 hours at room temperature. After the reaction, the mixture was poured into benzene and washed with water for 3 times, then dried over $MgSO_4$. p-Toluenesulfonyl chloride was obtained in 48% yield(GLC)(isolated yield: 43%), and identified by comparison with the commercial compound(R_f=0.7, eluent:benzene). In the reaction with PPE, (PPE=6 g, p-$CH_3C_6H_4SO_3H.H_2O$=381 mg), the yield of p-toluenesulfonyl chloride was 28% under similar conditions.

The Reduction of $ArSO_3H$ to ArSH with PPA/Ar'SH System:

PPA, 6 g, and 381 mg of p-toluenesulfonic acid were added into 5 ml of dry sulfolane, which was stirred and heated for 1.5 hours at 90°C under nitrogen atmosphere(the initial step). Then, 2 ml of thiophenol was added to this mixture, and the reaction mixture was kept at 90°C for 3 hours(the latter step). After the reaction, 10 ml of water was added, the mixture was poured into benzene which solution was washed with water for 3 times, dried over $MgSO_4$. A mixture of diphenyl disulfide and phenyl tolyl disulfide was obtained. Ditolyl disulfide was not formed. S-Phenyl p-toluenethiosulfonate was also not formed. The mixture was purified by column chromatography through silica-gel(eluent:benzene/hexane=1/1=v/v), and the disulfides obtained were converted to the corresponding thiols by the addition of a mixture of Ph_3P/H_2O/dioxane. The yield of p-toluenethiol was 53% (GLC). In the reduction with PPE(PPE=7 g, $p\text{-}CH_3C_6H_4SO_3H.H_2O$= 381 mg), both the initial step and the latter step required 1.5 hours/65°C and 8 hours/65°C respectively. The reaction mixture was then treated similarly and gave nearly the similar result. p-toluenethiol 46%(GLC)

S-phenyl p-toluenethiosulfonate 4% m.p.=78~80°C (lit,[18] 78°C)

S-butyl p-toluenethiosulfonate

TLC(eluent:benzene) R_f=0.5

elem. anal.	C	H
obsd.	54.17	6.64
calcd.	54.06	6.59

IR(KBr) 810cm^{-1} 1080cm^{-1} 1140cm^{-1} 1320cm^{-1}

NMR($CDCl_3$) =0.9ppm(m, 3H) 1.5ppm(m, 4H) 7.25ppm(d, 2H) 7.7ppm(d, 2H) 2.55ppm(s, 3H) 2.9ppm(t, 2H)

Trapping of SO_2 by p-Tolyl Lithium:

Reactor A(step 1)

A mixture of 10 g of PPE and 800 mg(8 mmol) of sulfuric acid was heated and stirred at 80°C for one hour under nitrogen atmosphere(neat).

Reactor B(step 2)

Lithium, 280 mg(40 mmol), was added into 5 ml of dry ether into which 5 ml of dry ether solution containing 5100 mg(30 mmol) of p-bromotoluene was added.[19] The mixture was stirred for a few hours under nitrogen atmosphere.

step 3

Recator A and B were jointed by a glass tube. Thiophenol, 3 ml, was added into the Reactor A at room temperature. Then the solutions in the Reactors A and B were stirred for 2 hours at room temperature under nitrogen atmosphere. After the reaction, the reaction mixture in Reactor B was poured into water and washed with benzene for 3 times. The water was evaporated, the solution was concentrated, and excess methyl iodide was added into the mixture which was stirred for over night(H_2O/EtOH=1/1=v/v). p-Tolyl methyl sulfone 11.4 mg was obtained(~1%). TLC(eluent:$CHCl_3$) R_f=0.5

In the case of PPA,

step 1.(PPA=10 g, H_2SO_4=840 mg neat) 2 hours/70~80°C

step 2.(Li=280 mg, p-$CH_3C_6H_4Br$=5130 mg, Et_2O=15 ml) a few hours/r.t.

step 3. The mixture of 2 ml of thiophenol and 6 ml of sulfolane were added to Reactor A and stirred for 2 hours at r.t.

The similar procedure and reaction condition were used.

p-tolyl methyl sulfone 10 mg m.p.=84~85°C(lit,[21] 87°C)

The Reduction of Sulfuric Acid by Thiophenol in PPA:

A mixture of PPA 10 g and 800 mg of sulfuric acid(neat) was heated under stirring for 2 hours at 80°C in nitrogen atmosphere. Then, 5 ml of thiophenol was added into this mixture which was stirred for 24 hours at 50~60°C. After the reaction, 10 ml of water was added and the mixture was poured into benzene, which solution was washed with water for three times, and dried over $MgSO_4$. Triphenylphosphine 786 mg(3 mmol) was then added to this benzene solution, and then 46 mg(3 mmol) of triphenylphosphine sulfide was obtained. Triphenylphosphine sulfide was not obtained at all in the reaction of triphenylphosphine and diphenyl disulfide or thiophenol. Sulfur(S_8) and diaryl polysulfide are known to be desulfulized by triphenylphosphine to give only triphenylphosphine sulfide, triphenylphosphine sulfide and arenethiol, respectively.

$Ph_3P=S$ TLC R_f=0.5(eluent:benzene)
m.p.=162~163°C(lit,[20] 162~164°C)

References

1) S.W. Benson, Chem. Reviews., 78, 23(1978).

2) M.L.-S. Tsang, J.A. Schiff, J. Bacteriol, 125, 923(1976).
A.B.Roy and P.A. Trudinger,"The Biochemistry of Inorganic Compounds of Sulfur", Chap. 10, Cambridge University Press (1970).

3) M.P. Cava, M.V. Lakshmikantham, M.J. Mitchell, J. Org. Chem. 34, 2665(1969).

4) D. Landini and F. Montanari, Tet. Lett., 2691(1964).
J.Drabowicz and S. Oae, Synthesis, 404(1977).
G.A. Olah, S.C.Narang, B.G.B. Gupta, and R. Malhotra, Synthesis, 61(1979).

5) K. Fries, H. Koch, and H. Stukenbrock, Ann., 468, 177(1929).
K. Fries and G. Schürmann, Ber., 47, 1195(1914).

6) G.A. Olah, S.C. Narang, L.D. Field, and G.F. Salem, J. Org. Chem., 45, 4792(1980).
W.A. Scheppard,"Org. Syntheses", Coll. Voll. 5, 843(1970).

7,8) G.A. Olah, S.C. Narang, L.D. Field, and R. Karpeles, J. Org. Chem., 46, 2408(1981).
T. Numata, H. Awano, S. Oae, Tet. Lett., 21, 1235(1980).
K. Fujimori, H. Togo, and S. Oae, Tet. Lett, 21, 4921(1980).
S. Oae and H. Togo, Synthesis, 152(1982).

9) S. Oae, H. Togo, T. Numata, K. Fujimori, Chem. Lett., 1193 (1980).
S. Oae, H. Togo, Bull. Chem. Soc. Jpn., in contribution.
D. Cipris, D. Pouli, Synth. Commun., 9, 207(1979).
T. Numata, H. Togo, and S. Oae, Chem. Lett., 329(1979).
T.J. Wallace, J.J. Mahon, J. Org. Chem., 30, 1502(1965).
S. Oae, H. Togo, Bull. Chem. Soc. Jpn., in contribution.

10) Monoaryl sulfate and Bunte salt hydrized by A-1 mechanism in acidic media.
J.L. Kice, J.M. Anderson, N.E. Pawlowski, J. Amer. Chem. Soc., 88, 5245(1966).
J.L. Kice and J.M. Anderson, J. Amer. Chem. Soc., 88, 5242 (1966).

11) W. Tagaki, T. Eiki, I. Tanaka, Bull. Chem. Soc. Jpn., 44, 1139(1971).
W. Tagaki and T. Eiki,"Advances in Chemistry Series", No. 191, 409(1980).
T. Eiki, W. Tagaki, Chem. Lett., 1465(1981).

12) S.J. Benkovic and R.C. Hevey, J. Amer. Chem. Soc., 92, 4971(1970).
13) M.P. Cava, M.V. Lakshmikantham, M.J. Mitchell, J. Org. Chem., 34, 2665(1969).
14) The MERCK Index, ninth editions paga 8762. published by MERCK Co.
15) D. Martin, W. Mucke, Monatsber. Dent. Akad. Wiss. Berlin., 6(5), 362(1964).
16) S. Oae and H. Togo, Synthesis, 152(1982).
17) H.J. Backer, E. Westerhuis, Rec. Trav. Chim., 71, 1065, 1071(1952).
18) Y. Yoshikawa, W. Tagaki, R. Nomura, and S. Oae, Bull. Chem. Soc. Jpn., 42, 2903(1969).
19) W.E. Truce and J.F. Lyons, J. Amer. Chem. Soc., 73, 126 (1951).
20) Authentic sample was obtained from Wako Chemicals Co.
21) R. Uehara, Bull. Chem. Soc. Jpn., 32, 1082(1959).

Chapter 7.

Reduction of Sulfonic Acids with Phosphorus Pentasulfide

Abstract

Arene- and alkanesulfonic acids were easily reduced to the corresponding polysulfide $R-(S)_n-R$ (n=2.9~3.3) by treatment with phosphorus pentasulfide. In this reaction, the formation of both P-O-S bond and P-S-H bond is considered to be involved in the key step of the reduction.

Introduction

Both arene- and alkanesulfonic acids are known to be so inert that they cannot be reduced directly by ordinary procedures; for example sulfonic acids are unchanged with $LiAlH_4$ in refluxing Bu_2O for 3 days.[1] However, we[2] have recently shown a few facile and convenient one-pot reduction procedures of sulfonic acids to thiols or disulfides in excellent yields. A similar reduction was found by Olah et al.[3] In these reduction, iodide ion is the reducing agent which is oxidized eventually to iodine. Reduction of both arenesulfonic acids and sulfuric acid was found to be carried out successfully by treating these acids with a mixture of phosphorus pentaoxide, polyphosphoric acid, or ethyl polyphosphate(PPE) and arenethiols. The initial step of this reduction is obviously the formation of $RSO_2\text{-}O\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O^-}{|}}{P}}\text{-}O\text{-}$ bond which is attacked nucleophilically on sulfur atom by thiol group.[4] Phosphorus pentasulfide is a sulfur analog of phosphorus pentaoxide and is considered to be attacked similarly by sulfonic acids at central phosphorus atom, generating an addition complex which possesses a thiol function, which can function as a reducing agent like iodide ion. Indeed, phosphorus pentasulfide has been found to be a good reducing agent to convert both arene- and alkanesulfonic acids to the corresponding polysulfides.

Results and Discussion

One big advantage of phosphorus pentasulfide as a new reducing agent is that it can reduce sulfonic acids to the corresponding polysulfides in good yields without any additional reagent. The reduction results in a mixture of mainly disulfide, trisulfide, tetrasulfide, as summarized in Table. The driving force of the reduction of the sulfonic acid with phosphorus pentasulfide is the formation of P-O or P=O bond which has a higher bond energy than that of P-S or P=S bond. Meanwhile, the thiol group combined to five-coordinate phosphorus, such as $(EtO)_2P(S)SH$ which is highly acidic(pKa 1.5~2.0)[5] and known to be a good reducing agent, to reduce readily many organosulfur compounds[6] such as sulfoxides,[6a] sulfinic acids,[6b] and thiolsulfonates.[6c] Even phosphorus pentasulfide alone is known to reduce sulfoxides to corresponding sulfides.[7] In the reduction of the sulfonic acid with phosphorus pentasulfide, one of oxygen atoms of the sulfonic acid would attack the central phosphorus atom of phosphorus pentasulfide to give an intermediate [I], an mixed-anhydride, which has a P-O-S bond, and a $-\overset{\overset{\|}{P}}{|}-S-H$ group which would be a strong acid similar to $(EtO)_2P(S)SH$, a powerful reducing agent.

Inspection of data in the Table reveals that the sulfinic acid is also reduced readily to the polysulfide. Thus, the plausible reaction pathway is shown in the Schme. Actually, the thiol function can be generated noticeably upon hydrolysis. For this reduction, sulfolane seems to be the best solvent among polar aprotic solvent because of the high solubilities of sulfonic acids and the moderate solubility of phosphorus pentasulfide in this solvent. The number of

sulfur atoms in the polysulfides obtained is in the range of 2.9~3.3, based upon the elemental analysis. These polysulfides can be reduced readily to the corresponding thiols by treatment with either $LiAlH_4$ or $NaBH_4$ and thus the yields of the products were determined. Based on the competitive reductions of three different sulfonic acids, the arenesulfonic acid which has an electron-donating substituent was found to be more reactive than the that which has an electron-withdrawing substituent, in keeping with the tendency of the reactivities of arenesulfonic acids in the reduction with other reducing systems with phosphorus compounds.[13] Non-acidic p-toluenesulfonamide, which cannot activate the phosphorus pentasulfide by protonation for nucleophilic attack of sulfonamide, is not readily reduced. While, sulfonate ester was also not be reduced very readily under the same condition since the initial reaction with P_2S_5 would not generate $P\text{-}S^-$ or P-SH function which can act as a reducing agent.

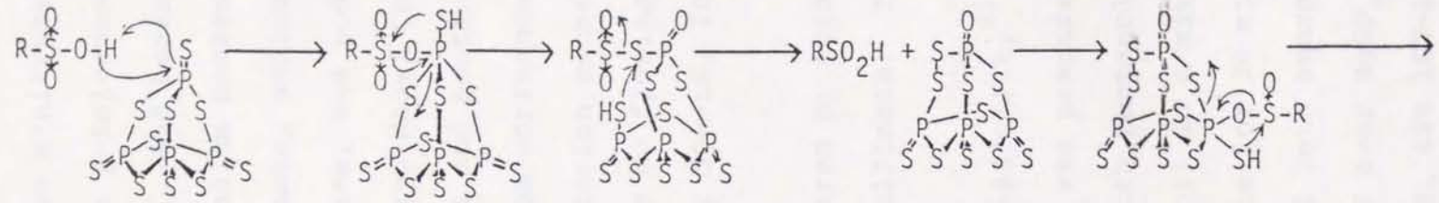
Table. Reduction of Sulfonic Acids with Phosphorus Pentasulfide in Sulfolane

$$RSO_3H \xrightarrow{P_2S_5} 1/2\ R\text{-}(S)_n\text{-}R \xrightarrow{LiAlH_4 \text{ or } NaBH_4} R\text{-}SH$$

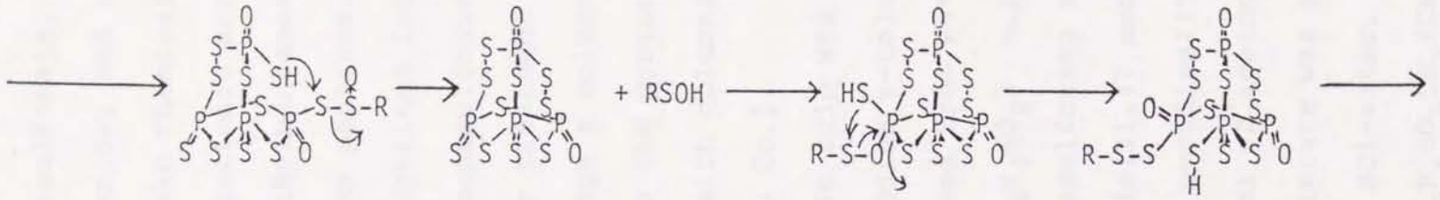
Substrate	Substrate/P_2S_5	Time (h) 90~100°C	Polysulfide (%)	Reducing Agent e)	Thiol (%) b)
$p\text{-}CH_3C_6H_4SO_3H$	a)	24	-	$LiAlH_4$	93
$C_6H_5SO_3H$	a)	24	-	$LiAlH_4$	91
$p\text{-}ClC_6H_4SO_3H$	a)	24	-	$LiAlH_4$	77
$p\text{-}CH_3C_6H_4SO_3H.H_2O$	2/9	23	$p\text{-}CH_3C_6H_4\text{-}(S)_n\text{-}C_6H_4CH_3\text{-}p$ n=3.30~3.35 d) (86) c)	$LiAlH_4$	68(68) c)
$p\text{-}CH_3C_6H_4SO_3Na$	2/9	24	$p\text{-}CH_3C_6H_4\text{-}(S)_n\text{-}C_6H_4CH_3\text{-}p$ n=2.91~2.92 d) (73) c)	$LiAlH_4$	67
$C_6H_5SO_3Na.H_2O$	2/9	24	-	$LiAlH_4$	62
$2,4\text{-}(CH_3)_2C_6H_3SO_3H$	2/9	24	-	$LiAlH_4$	(62) c)
$\beta\text{-}C_{10}H_7SO_3Na$	2/9	25	-	$LiAlH_4$	57
$CH_3(CH_2)_4SO_3H$	1.9/11.3	24	-	$LiAlH_4$	63 f)
$m\text{-}O_2N\text{-}C_6H_4SO_3Na$	4/18	24	$m\text{-}O_2NC_6H_4\text{-}(S)_n\text{-}C_6H_4NO_2\text{-}m$ n=2.9~3.1 d)	$NaBH_4$	(74) c)
$CH_3(CH_2)_{11}SO_3^-\ H_2N{=}\overset{+}{C}(NH_2)\text{-}SCH_2C_6H_5$	1.2/9	24	-	$LiAlH_4$	71
$p\text{-}CH_3C_6H_4SO_2NH_2$	2/10.3	60	-	$LiAlH_4$	5 g)
$p\text{-}CH_3C_6H_4SO_3CH_2(CH_2)_3CH_3$	2/9	27	-	$LiAlH_4$	16 h)
$p\text{-}CH_3C_6H_4SO_2H$	2/6	14	-	$LiAlH_4$	70

a) In this competition reaction, a mixture of p-$CH_3C_6H_4SO_3H$/$C_6H_5SO_3H$/p-$ClC_6H_4SO_3H$=2/2/2(mmol) was carefully dehydrated by azeotropic distillation with benzene, and was placed in 15 ml of sulfolane containing P_2S_5(27 mmol). b) Overall yield ($RSO_3H \longrightarrow RSH$), GC(SE-30, or OV-1, 1m glass column). c) Isolated yield. d) The number of sulfur atoms in the molecule was estimated from the elemental analysis. e) The reductions of polysulfides with $LiAlH_4$ and $NaBH_4$ were carried out in ether(30 min) and ether-ethanol(3 h) at room temperature respectively. f) In the hydrolysis of phosphoric derivatives, a mixture of 14% of pentanethiol and dipentyl polysulfide was obtained. g) Starting material was not recovered. h) Starting material was obtained in 26% yield.

The Reaction Pathway of Sulfonic Acid and Phosphorus Pentasulfide



[I]



$$\longrightarrow \frac{1}{2}\ \text{R-(S)}_n\text{-R} + \text{Phosphoric Derivatives} \xrightarrow{H_2O} \frac{1}{2}\ \text{R-(S)}_n\text{-R} + \underset{\text{trace}}{\text{RSH}} + S_8 + H_2S + H_3PO_4$$

Scheme

Experimental

Materials: Phosphorus pentasulfide, p-toluenesulfonic acid, sodium p-toluenesulfonate, sodium m-nitrobenzenesulfonate, p-toluenesulfonamide, and sodium p-toluenesulfinate were obtained from Wako Chemicals Co., and benzenesulfonic acid, p-chlorobenzenesulfonic acid, sodium benzenesulfonate, sodium 2,4-dimethylbenzenesulfonate, sodium β-naphthalenesulfonate, sodium pentanesulfonate, and sodium dodecanesulfonate were obtained from Tokyo Kasei Chemicals Co. 2,4-Dimethylbenzenesulfonic acid and pentanesulfonic acid were obtained by treatment of the corresponding sodium sulfonates through a column of cation exchange resin which was converted to the proton form by flowing 1N. HCl dist. water solution with column[Dowex 50w-x8, 200~400mesh H-form, Muromachi Kagaku Co.].

p-Toluenesulfinic acid was prepared by acidification of the corresponding sodium p-toluenesulfinate. The white precipitate was recrystallized from water.

$p\text{-}CH_3C_6H_4SO_2H$ m.p.=84-85°C(lit,[9] 84-85°C)

Pentyl p-toluenesulfonate ester was prepared by treating the sulfonyl chloride(31.47 mmol) with pentanol(94.41 mmol) in the presence of pyridine(157 mmol) in a mixture of 10 ml of benzene and 10 ml of acetonitrile for 30 min. After this reaction, the mixture was poured into benzene which solution was washed with HCl-water, dried over $MgSO_4$, and distilled.

$p\text{-}CH_3C_6H_4SO_3CH_2(CH_2)_3CH_3$ 48% 167-168°C/3 mmHg (lit,[10] 169-170°C/ 3 mmHg)

S-Benzylisothioronium dodecanesulfonate was prepared by treatment of sodium dodecanesulfonate with S-benzylisothioronium

chloride in acetonitrile. This salt was recrystallized from acetonitrile.

$n\text{-}C_{12}H_{25}SO_3^- \overset{+}{H_2}N{=}\underset{\underset{NH_2}{|}}{C}\text{-}S\text{-}CH_2C_6H_5$

elem. anal.	C	H	N
obsd.	57.92	8.67	6.71
calcd.	57.65	8.70	6.72

IR(KBr) 3600~2850cm^{-1}, 1660cm^{-1} 1680cm^{-1} 1465cm^{-1} 1220cm^{-1} 1200cm^{-1} 1190cm^{-1} 1160cm^{-1} 1125cm^{-1} 1100cm^{-1} 1080cm^{-1} 1040cm^{-1}

General Procedure: A mixture of 902 mg(4 mmol) of sodium m-nitrobenzenesulfonate and 4000 mg(18 mmol) of phosphorus pentasulfide was dissolved in 10 ml of dry sulfolane. The mixture was heated at about 90°C for 24 hours with stirring. Then, 5 ml of water was added into the mixture which was heated for 0.5 hour to hydrolyze phosphoric derivatives to afford the polysulfide, hydrogen sulfide, sulfur, and phosphoric acid.[8] The mixture was poured into benzene or ether, which was then washed with water for 2,3 times, dried over $MgSO_4$, and evaporated. The mixture was extracted with a mixture of benzene and hexane(V/V=1/1), and chromatographed through a silica-gel column with a mixture of benzene and hexane(v/v=1/1) to obtain the polysulfide[R_f=0.25~0.30, IR (NaCl) 1345cm^{-1}, 1520cm^{-1}, n=2.9~3.1]. In the reduction of other sulfonic acids, hexane was used for extraction and column chromatography, except sulfur, sulfolane, etc. Then 430 mg of di(m-nitrophenyl) polysulfide(a part of obtained polysulfide) was dissolved in a mixture of Et_2O-EtOH into which 200 mg of $NaBH_4$ was slowly added at room temperature. After 3 hours, the mixture was poured into ether and acidified, then washed with water, before drying over $MgSO_4$. From the ether extract,

275 mg of m-nitrobenzenethiol was obtained in 74% yield[IR(NaCl) 1520cm^{-1}, 1345cm^{-1}, 2560cm^{-1}, b.p.=100-103°C/4 mmHg]. m-Nitrobenzenethiol was identified by the oxidation to the corresponding disulfide. m-Nitrobenzenethiol 275 mg(1.774 mmol) and 225 mg(1.774/2 mmol) of iodine were dissolved in chloroform, and then 140 mg(1.774 mmol) of pyridine was slowly added to this mixture at r.t. After 15 min, the mixture was poured into chloroform and washed with dilute HCl solution, water, and dried over $MgSO_4$. After evaporation, the crystals was obtained and recrystallized with benzene.

$m\text{-}O_2NC_6H_4SSC_6H_4NO_2\text{-}m$ m.p.=81-82°C(lit,[12] 79-81°C)

Other thiols were identified by comparison with authentic commercial thiols.

$2,4\text{-}(CH_3)_2C_6H_3SH$ b.p.=83-85°C/5 mmHg 62%(isolated yield) (lit,[11] 93°C/12 mmHg)

Polysulfide: From the reaction of sodium p-toluenesulfonate and phosphorus pentasulfide;

$p\text{-}CH_3C_6H_4\text{-}(S)_n\text{-}C_6H_4CH_3\text{-}p$ IR(NaCl)

74% yield
n=2.91~2.92

485cm^{-1} 505cm^{-1} 805cm^{-1}
750cm^{-1} 1490cm^{-1}
2850~3100cm^{-1}

elem. anal.	C	H	S
obsd.	60.97	5.09	33.84

total=99.9%

From the reaction of p-toluenesulfonic acid monohydrate and phosphorus pentasulfide;

$p\text{-}CH_3C_6H_4\text{-}(S)_n\text{-}C_6H_4CH_3\text{-}p$ IR(NaCl)

86% yield
n=3.30~3.35

2850-3100cm^{-1} 1490cm^{-1}
805cm^{-1} 485cm^{-1} 502cm^{-1}

elem. anal.	C	H	S
obsd.	58.18	4.87	37.10

total=100.15%

NMR(CCl_4) δ=2.3ppm(s 3H)
6.8~7.05ppm(m 2H)
7.05~7.4ppm(m 2H)

From the reaction of sodium m-nitrobenzenesulfonate and phosphorus pentasulfide;

$m\text{-}O_2NC_6H_4\text{-}(S)_n\text{-}C_6H_4NO_2\text{-}m$ IR(NaCl) $1345cm^{-1}$ $1520cm^{-1}$

n=2.9~3.1 NMR(CCl_4) =7.0~8.1ppm(m)

elem. anal.	C	H	N
obsd.	42.50	2.36	8.14

References and note

1) L.D.Dolby and D.R.Rosencrantz, J. Org. Chem., 28, 1888(1963).

2) a) T.Numata, H.Awano, and S.Oae, Tet. Lett., 21, 1235(1980).
b) S.Oae and H.Togo, Synthesis, (1981), 371.
c) K.Fujimori, H.Togo, and S.Oae, Tet. Lett., 21, 4921(1980).
d) S.Oae and H.Togo, Synthesis, (1982), 152.

3) G.A.Olah, S.C.Narang, L.D.Field, and R.Karpeles, J. Org. Chem., 46, 2408(1981).

4) PPA 6 g and 381 mg of p-toluenesulfonic acid were added into 5 ml of dry sulfolane, which was stirred and heated for 1.5 hours at 90°C under nitrogen atmosphere. Then, 2 ml of thiophenol was added to this mixture, and the reaction mixture was kept at 90°C for 3 hours. After this reaction, the mixture was purified by column silica-gel chromatography (eluent:benzene/hexane=1/1). The mixture of diphenyl disulfide and phenyl tolyl disulfide was obtained. The disulfides obtained were converted to the corresponding thiols by addition of a mixture of Ph_3P/H_2O/dioxane. The yield of p-toluenethiol was 53%. In the reduction with PPE, 46% of p-toluenethiol and 4% of S-phenyl p-toluenethiosulfonate were obtained.

5) S.Oae, "The Chemistry of Organosulfur Compounds" Kagaku Do-jin.

6) a) S.Oae, A.Nakanishi, and N.Tsujimoto, Tetrahedron, 28, 2981(1972).
T.J.Wallace and J.J.Mahn,J. Org. Chem., 30, 1502(1965).
T.J.Wallace, J. Amer. Chem. Soc., 86, 2018(1964).
T.Numata, H.Togo, and S.Oae, Chem. Lett., (1979), 329.
b) S.Oae, H.Togo, T.Numata, and K.Fujimori, Chem. Lett., (1980), 1193.
c) S.Oae and H.Togo, unpublished data(Chapter 1).

7) I.W.J.Still, Phosphorus and Sulfur, (1979), 293.
I.W.J.Still, S.K.Hasan, and K.Turnbull, Can. J. Chem., 56, 1423(1978).
I.W.J.Still, S.K.Hasan, and K.Turnbull, Synthesis, (1977), 468.

8) J.C.Bailar, H.J.Emeleus, R.Nyholm, and A.F.Trotman-Dickenson, "Comprehensive Inorganic Chemistry" Vol. 2, 448, Pergman Press.

9) R.K.Burkhard, D.E.Sellers, F.Decov, and J.L.Lambert, J. Amer. Chem. Soc., 72, 1215(1950).
10) H.Gilman, N.J.Beaber, J. Amer. Chem. Soc., 47, 518(1925). J.H.Uhlenbroek and M.Slagt, Rec. Trav. Chim., 80, 1057(1961).
11) H.C.Godt, Jr, R.E.Wann, J. Org. Chem., 26, 4047(1961). J.H.Uhlenbroek and M.Slagt, Rec. Trav. Chim., 80, 1057(1961).
12) Aldrich Chemicals Co.
13) S.Oae and H.Togo, Bull. Chem. Soc. Jpn., in contribution. K.Fujimori, H.Togo, and S.Oae, Tet. Lett., 21, 4921(1980). S.Oae and H.Togo, Synthesis, (1982), 152.

Chapter 8.

The Reduction of Sulfoxides and Sulfimides with Thiol/ Trimethylsilyl Chloride System

Abstract

Sulfoxides and sulfimides are slowly deoxygenated by treatment with thiosilane, $PhSSiMe_3$, while deoxygenation of sulfoxides with the thiosilane proceeds smoothly in the presence of a catalytic amount of tetrabutylammonium bromide. For a preparative purpose, a mixed system of thiol and trimethylsilyl chloride can be used successfully for both deoxygenation of sulfoxides and deimination of sulfimides.

Introduction

Sulfoxides are known to be rather reactive compounds among various organosulfur compounds. The bond energy of S-O linkage in sulfoxides is about 7×10^5 dyn/cm(87~89 kcal/mol), smaller than that of sulfone(9.5×10^5 dyn/cm, 112 kcal/mol), while, the S-O bond of sulfoxide is semi-polar and is longer than that of sulfone. Thus, many facile procedures for reduction of sulfoxide have been reported, among those are treatment with HX,[1~8] phosphine derivative,[9~12] silyl derivative,[13~16] sodium sulfite,[17, 18] elemental sulfur,[19, 20] transition metal complex,[21~23] hydride complex,[24~27] contact hydrogenation,[28] thionyl chloride,[29] and photoreduction.[30] Though the reduction of sulfoxides with thiol which is our target was already reported by T.J. Wallace,[31~33] and Lowe,[34] both methods need somewhat high temperatures, and longer times, while the reaction is mostly limited to that of DMSO which

$$2\ RSH + DMSO \xrightarrow{160°C,\ 10h} \underset{70\%}{RSSR} + DMS + H_2O \quad (R=alkyl)$$

$$2\ ArSH + DMSO \xrightarrow{r.t.\ 24h} \underset{70\sim90\%}{ArSSAr} + DMS + H_2O$$

has a unique character. In 1972, Oae et al [35, 36] reported the reduction of sulfoxides with dithiophosphoric acid and dithioacetic acid, which have very low pKa values, i.e. 1.5~2, under very mild conditions.

$$\overset{O}{\uparrow}\!RSR' + 2(R''O)_2PSSH \text{ or } CH_3CS_2H \xrightarrow{r.t.\ neat\ 25\ min} \underset{quant.}{RSR'} + \underset{or\ (CH_3CS)_2S_2}{[(R''O)_2PS]_2S_2} + H_2O$$

$$\overset{NTs}{\uparrow}\!RSR' + 2(R''O)_2PSSH \text{ or } CH_3CS_2H \xrightarrow{r.t.\ neat\ 25\ min} \underset{quant.}{RSR'} + \underset{or\ (CH_3CS)_2S_2}{[(R''O)_2PS]_2S_2} + TsNH_2$$

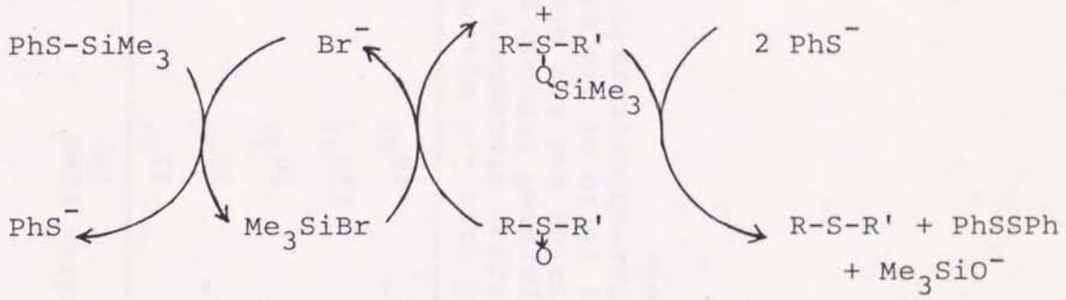
Another way to achieve facile reduction of ordinary sulfoxides or sulfimides by treatment with ordinary thiols is to activate the central sulfur atom of the sulfoxide or the sulfimide by silylation with such reagents as $RSSiMe_3$, Me_3SiCl at the initial stage of the reduction. Meanwhile, treatment of carbonyl compounds with thiosilane, $RSSiMe_3$, was reported to give O-trimethylsilyl hemithioacetals via an initial O-silylation and subsequent nucleophilic addition of the thiolate.[37] Thus, the thiosilane is considered to be a composite of a good oxygenophilic silyl group and a strong nucleophilic thiolate group, and should be able to reduce sulfoxide or sulfimide, since reduction of sulfoxides with sulfhydryl compounds is known to proceed through an initial protonation of sulfinyl oxygen and subsequent nucleophilic attack of thiolate on oxysulfonium sulfur atom.[38] Indeed, various sulfoxides and sulfimides have been found to be reduced to sulfides by treatment with the thiosilane. This chapter describes these reductions.

Results and Discussion

When alkyl phenyl sulfoxide was treated with about two equivalent amounts of phenylthiotrimethylsilane at room temperature under argon atmosphere, deoxygenation of the sulfoxide was found to take place slowly(eq.1), while upon addition of a catalytic amount of $Bu_4N^+I^-$ (1/10 equivalent of the sulfoxide) to this system, the

$$Ph\text{-}\underset{\underset{O}{|}}{S}\text{-}R + 2\ PhSSiMe_3 \longrightarrow Ph\text{-}S\text{-}R + PhSSPh + (Me_3Si)_2O \quad ---(1)$$

deoxygenation with the thiosilane took place smoothly. Apparently bromide ion acts as a catalyst for heterolysis of the S-Si bond of the thiosilane, resulting in the facile O-silylation of the sulfinyl oxygen atom as shown in the following figure.



These results are listed in Table 1.

Table 1. Reduction of Sulfoxide with $PhSSiMe_3$ [a]

R-S(O)-R' R-	-R'	Additive	Time (h)	Products (isolated yield, %) [b] R-S-R'	PhSSPh	R-S(O)-R' (recovered)
$PhCH_2$-	$PhCH_2$-	-	31 [c]	30	32	58
$PhCH_2$-	$PhCH_2$-	$Bu_4N^+Br^-$	31 [c]	78	70	15
Ph-	Et-	-	50 [d]	17	15	67
Ph-	Et-	-	120 [d]	42	56	44
Ph-	Et-	$Bu_4N^+Br^-$	48 [d]	69	66	8

a) Sulfoxide was treated with 2.3 equivalent amounts of the thiosilane at room temperature under argon atmosphere. b) Work-up method is following: reaction mixture was separated through column chromatography affording the recovered starting sulfoxide and the mixture of the sulfide and diphenyl disulfide, and the molar ratio of the mixture was determined by NMR measurement. c) Dry ether-chloroform(v/v=1/1) was used as solvent. d) Dry ether was used as solvent.

In order to promote the facile O-silylation of sulfinyl oxygen, we applied a trimethylsilyl chloride/thiol system, and found that deoxygenation of the sulfoxide took place quite smoothly in a high yield(eq. 2).

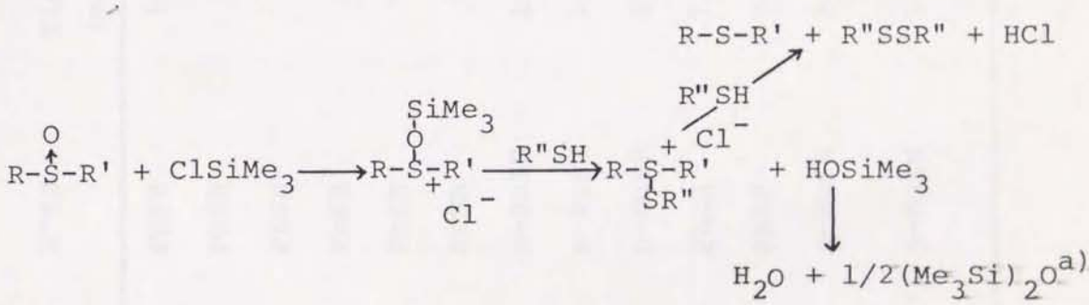
$$R\text{-}\overset{\overset{O}{\downarrow}}{S}\text{-}R' + 2\ R''SH + Me_3SiCl \longrightarrow R\text{-}S\text{-}R' + R''SSR'' + 1/2\ (Me_3Si)_2O \quad \text{---(2)}$$

Dialkyl, alkyl aryl, and dibenzyl sulfoxides and ω-(p-tolylsulfinyl) acetophenone were reduced nicely within 15 min, while benzyl phenyl, diphenyl and o-substituted diaryl sulfoxides were found to be reduced substantially slowly, mainly due to the lower basicities of these sulfinyl oxygens and the steric bulkiness of these substrates.

Reactivity

$$R\text{-}\overset{\overset{O}{\uparrow}}{S}\text{-}R' > R\text{-}\overset{\overset{O}{\uparrow}}{S}\text{-}Ar > \triangleright\text{-}\overset{\overset{O}{\uparrow}}{S}\text{-}Ar > Ar\text{-}\overset{\overset{O}{\uparrow}}{S}\text{-}Ar'$$

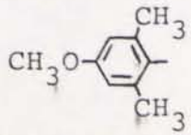
A plausible pathway is shown in Scheme 1.



a) $(Me_3Si)_2O$ was determined by GLC in 47% yield.

Scheme 1.

Table 2. Reduction of Sulfoxide with Thiol/Me_3SiCl System at Room Temperature

R-S(=O)-R' R-	R'-	R"SH	Time (min)	Products (isolated yield, %) R-S-R'	R"SSR"
Ph-	Et-	PhSH	10	96	100
Ph-	Me-	PhSH	5	100	100
n-Bu-	n-Bu-	PhSH	5	90	100
s-Bu-	Me-	PhSH	5	70	100
$PhCH_2$-	Me-	PhSH	5	80	98
$PhCH_2$-	$PhCH_2$-	PhSH	5[a]	(100)[b]	(100)[b]
$PhCH_2$-	$PhCH_2$-	n-BuSH	15[a]	73	83
p-Tol-	$PhCCH_2$- (O)	n-PrSH	15	90	52
$PhCH_2$-	Ph-	n-BuSH	60	82	100
$PhCH_2$-	Ph-	PhSH	70	(92)[b]	(100)[b]
Ph-		PhSH	90	76	78
Ph-	Ph-	n-BuSH	36 h[a]	98	94
	(R=R')	n-BuSH	78 h[a]	7[c]	7

a) The reaction was carried out in chloroform.
b) The sulfide and diphenyl disulfide cannot be separated by vacuum distillation, and the yields were estimated by NMR measurements of these mixtures.
c) The starting sulfoxide was recovered in 93% yield.

This reducing system(thiol/Me_3SiCl) can also be applied for the reduction of sulfimides,[39] and the corresponding sulfide, disulfide and p-tosylamide were obtained in good yields as shown in Table 3.

$$R\text{-}\underset{\underset{N\text{-}Ts}{|}}{S}\text{-}R' + 2\ R''SH \xrightarrow{Me_3SiCl} R\text{-}S\text{-}R' + R''SSR'' + TsNH_2 \quad ---(3)$$

Although deoxygenation of sulfoxides after activation of O-silylation with Me_3SiI(or Me_3SiBr)[40] and $(Me_3Si)_2S$[41] has recently been reported, the deoxygenation is always accompanied with substantial side reactions(i.e. halogenation or degradation) espicially with sulfoxides each having an activated methylene group, such as dibenzyl sulfoxide and ω-methylsulfinylacetophenone. Thus, we believe our system to be more convenient for preparative purposes than those with other reagents which are not commonly available.

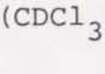
Table 3. Reduction of Sulfimides with Thiol/Me_3SiCl System[a)]

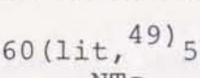
R-S(NTs)-R' R	R'	R"SH	Time (h)	Products (isolated yield, %)[b)] R-S-R'	R"SSR"	$TsNH_2$
n-Bu-	n-Bu-	PhSH	6	91	90	100
Ph-	Me-	PhSH	1.5	96	100	83
Ph-	Me-	PhSH	1.5[c)]	73	70	90
$PhCH_2$-	Me-	PhSH	9	72	80	72
p-Tol-	Et-	PhSH	20	72	94	75
p-Tol-	p-Tol-	n-BuSH	60	83	93	79
$-(CH_2)_5-$		PhSH	8	(82)[d)]	81	80

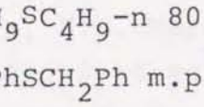
a) Reaction was carried out in chloroform at room temperature under argon atmosphere. b) Work-up method is following: tosylamide precipitated was filtered off and the filtrate was analyzed according to a similar manner in the case of sulfoxide. c) This experiment was carried out in the presence of an equimolar amount of Me_3SiCl. d) Yield was determined by GLC analysis.

Experimental

Typical Experimental Procedure. After treatment of a certain sulfoxide(3~4 mmol) with two equivalent amounts of benzenethiol (or alkanethiol) in 5 ml of dry ether at room temperature under argon atmosphere until the starting sulfoxide disappeared upon monitoring with TLC test, the reaction mixture was hydrolyzed with aqueous sodium bicarbonate solution. (before hydrolyzing, $Me_3SiOSiMe_3$ was found to be formed in 47% yield upon determination by GLC analysis of the reaction mixture of dimethyl sulfoxide, PhSH(2 eq.) and Me_3SiCl(1.1 eq). Then the mixture was extracted with chloroform and the resulting dried chloroform solution was evaporated under reduced pressure to give a mixture of the corresponding sulfide and disulfide, which were found to be formed nearly in a quantitative yield upon measurement with NMR. The sulfide and disulfide formed were easily separated by vacuum distillation.

Materials. Authentic disulfides were commercial samples. Sulfoxides were synthesized by oxidation of the corresponding sulfides with hydrogen peroxide in acetic acid at 0°C~r.t. The sulfoxides obtained in 60~90% were purified by column chromatography, eluting with chloroform and then recrystallized or distilled. $Ph\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}Ph$ m.p.=70~71°C(lit,[42] 71°C), $PhCH_2\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}Ph$ m.p.=121~122°C(lit,[42] 123°C), $PhCH_2\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}CH_2Ph$ m.p.=136~137°C(lit,[42] 133°C), $n\text{-}C_4H_9\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}C_4H_9\text{-}n$ 120°C/1.2 mmHg(lit,[43] 120/1.2 mmHg), $Ph\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}CH_3$ 110°C/1~2 mmHg(lit,[44] 84°C/0.25 mmHg), $CH_3\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}C_4H_9\text{-}s$ 93°C/10 mmHg(lit,[45] 93°C/10 mmHg), $Ph\text{-}\overset{O}{\overset{\uparrow}{S}}\text{-}C_2H_5$ 102°C/2 mmHg(lit,[46] 102°C/2 mmHg), $Ph\text{-}\overset{O}{\overset{\uparrow}{S}}$  ($CDCl_3$)δ=0.5~1.4(4H m), 1.9~2.4(1H m), 7.3~7.8ppm(5H m).[47]

All the N-tosylsulfonylsulfilimines were prepared from the corresponding sulfides and chloramine T.[48] $n\text{-}C_4H_9\text{-}\overset{\overset{NTs}{\uparrow}}{S}\text{-}C_4H_9\text{-}n$ m.p.=59~60(lit,[49] 59~60°C),  m.p.=148~149°C(lit,[49] 148~149°C), $Ph\text{-}\overset{\overset{NTs}{\uparrow}}{S}\text{-}CH_3$ m.p.=129~130°C(lit,[49] 129~130°C), $p\text{-}CH_3C_6H_4\text{-}\overset{\overset{NTs}{\uparrow}}{S}\text{-}C_2H_5$ m.p.=89~90°C(lit,[50] 89~90°C).

All the sulfides were identified with authentic samples which were obtained from commercial sulfides or praparation from thiolate and alkyl halide. $PhSCH_3$ 85~86°C/13 mmHg[51], $PhSC_2H_5$ 52~53°C/1 mmHg[51], $n\text{-}C_4H_9SC_4H_9\text{-}n$ 80°C/20 mmHg[51],  141~142°C/760 mmHg[52], $PhSCH_2Ph$ m.p.=44°C[53], $PhSC_2H_5$ 220~1°C/760 mmHg[54], $p\text{-}CH_3C_6H_4SCH_2\overset{\overset{O}{\|}}{C}Ph$ m.p.=37°C[55], $CH_3SC_4H_9\text{-}s$ 111~112°C /760 mmHg[56]

Preparation of $PhSSiMe_3$. Thiophenol 5 g was dissolved in dry ether in a reactor equipped with a cooler and nitrogen balloon. Then into the reactor 32.7 ml(1.1eq) of n-butyl lithium hexane solution was dropped slowly. Finally 6 g of trimethylsilyl chloride was added into the mixture which was refluxed for 12 hours. After the reaction, the reaction mixture was filtered under N_2, evaporated and distilled to give the thiosilane in a good yield. $PhSSiMe_3$ 100~110°C/30 mmHg cololess liquid(lit,[57] 72~74°C/3 mmHg)

References and Note

1) D. Landini, F. Montanari, H. Hogevein, G. Maccagnari, Tet. Lett., (1964), 2691.
2) H. Bretschweide, W. Klotzer, Monatsh Chem., 81, 589(1950).
3) W.E. Savige, J.A. Machasen,"Organic Sulfur Compounds".
4) S. Tamagaki, M. Mizuno, H. Yoshida, H. Hirota, S. Oae, Bull. Chem. Soc. Jpn., 44, 2456(1971).
5) T. Aida, N. Furukawa, S. Oae, Tet. Lett., (1973), 3853.
6) G.A. Olah, B.G. Balaram Gupta, S.C. Narang, Synthesis, (1978), 137.
7) J. Drabowicz, S. Oae, Synthesis, (1977), 404.
8) G.A. Olah, R. Malhotra, S.C. Narang, Synthesis, (1979), 58.
9) D.W. Chasar, T.M. Pratt, Synthesis, (1976), 262.
10) I.W.J. Still, S.K. Hasan, K. Turnbull, Synthesis, (1977), 468.
11) I.W.J. Still, J.N. Reed, K. Turnbull, Tet. Lett, (1979), 1481.
12) K.S. Ray, R.A. Shaw, B.C. Smith, Nature, 196, 372(1962).
13) T.H. Chan, A. Melnyk, J. Am. Chem. Soc., 92, 3718(1970).
14) T.H. Chan, A. Melnyk, D.N. Harpp, Tetrahedron, (1969), 201.
15) H.S. Dilanjan Soysa, W.H. Weber, Tet. Lett., (1978), 235.
16) G.A. Olah, B.G. Balaram Gupta, S.C. Narang, Synthesis, (1977) 583.
17) C.R. Johnson, C.C. Bacon, J.J. Rigan, J. Org. Chem. 37, 919(1972).
18) F. Michael, H. Schmitz, Chem. Ber., 72, 992(1939).
19) S. Oae, S. Kawamura, Bull. Chem. Soc. Jpn., 36, 163(1963).
20) W. Tagaki, S. Kiso, S. Oae, ibid., 38, 414(1965).
21) H. Alper, E.C.H. Keung, Tet. Lett., (1970), 53.
22) B.R. James, F.T.T. Ng, G.L. Rempel, Can. J. Chem., 47, 4521(1969).
23) G.A. Olah, G.K.S. Prakash, T-L. Ho, Synthesis, (1976), 810.
24) D.W. Chasar, J. Org. Chem., 36, 613(1971).
25) H.C. Brown, J. Am. Chem. Soc., 75, 255(1953).
26) H.C. Brown, J. Org. Chem., 35, 1900(1970).
27) J. Drabowicz, M.Mikolajczyk, Synthesis, (1976), 527.
28) K. Ogura, M. Yamashita, G. Tsuchihashi, Synthesis, (1975), 385.
29) N.P. Volynski, Neftekhimiya, 1, 473(1961).
30) G.M. Gurria, G.H. Posner, J. Org. Chem., 38, 2419(1973).
31) T.J. Wallace, J.J. Mahon, ibid., 30, 1502(1965).
32) T.J. Wallace, J.J. Mahon, J. Am. Chem. Soc., 86, 4099(1964).
33) T.J. Wallace, ibid., 86, 2018(1964).

34) O.G. Lowe, J. Org. Chem., 40, 2096(1975).
35) S. Oae, A. Nakanishi, N. Tsujimoto, Tetrahedron, 28, 2981(1972).
36) S. Oae, T. Yagihara, T. Okabe, ibid., 28, 3203(1972).
37) D.A. Evans, L.K. Truesdale, K.G. Grimm, S.L. Nesbitt, J. Am. Chem. Soc., 99, 5009(1977).
38) J. Drabowicz, T. Numata, S. Oae, Org. Prep. Proced., Int., 9, 63(1977).
39) Sulfimide was found to be reduced with benzenethiol alone, though substantially slowly: PhSMe was reduced in 78% yield at room temperature for 24 h, while $(CH_2)_5$ with NTs SNTs was reduced partially during a long reaction time(51%, 3 days).
40) G.A. Olah, B.G. Balaram Gupta, S.C. Narang, Synthesis, (1977), 583.
41) H.S. Dilanjan Soyas, W.P. Webwe, Tet. Lett., (1978), 235.
42) N. Kunieda, K. Sakai, S. Oae, Bull. Chem. Soc. Jpn., 42, 1090 (1969).
43) S. Kise, S. Oae, ibid., 40, 1722(1967).
44) S. Kise, S. Oae, ibid., 43, 1426(1970).
45) S. Tamagaki, M. Mizuno, H. Yoshida, S. Oae, ibid., 44, 2456 (1971).
46) S. Oae, A. Nakanishi, S. Kozuka, Tetrahedron, 28, 155(1972).
47) T. Masuda, T. Numata, N. Furukawa, S. Oae, J. Chem. Soc., Perkin II, 1302 (1978).
48) K. Tsujihara, N. Furukawa, K. Oae, S. Oae, Bull. Chem. Soc. Jpn., 42, 2631(1969).
49) K. Tsujihara, N. Furukawa, S. Oae, ibid., 43, 2153(1970).
50) K. Tsujihara, N. Furukawa, S. Oae, Tetrahedron, 27, 4921(1971).
51) J. Drabowicz, S. Oae, Synthesis, (1977), 405.
52) S. Tamagaki, M. Mizuno, H. Yoshida, H. Hirota, S. Oae, Bull. Chem. Soc. Jpn., 44, 2456(1971).
53) H. Hepworth, H.W. Claphan, J. Chem. Soc., (1921), 119, 1188.
54) R. Otto, Ber., 13, 1272(1880).
55) H. Gilman, W.B. King, J. Am. Chem. Soc., 47, 1136(1925).
56) S. Tamagaki, M. Mizuno, H. Yoshida, S. Oae, Bull. Chem. Soc. Jpn., 44, 2456(1971).
57) D.N. Harpp, B.T. Friedlander, C. Larsen, K. Stelion, A. Stockton, J. Org. Chem., 43, 3481(1978).

LIST OF PUBLICATIONS

1) Facile Reduction of Sulfoxides and Sulfimides with Thiol/Trimethylsilyl Chloride System
T. Numata, H. Togo, and S. Oae, Chem. Lett., (1979), 329.

2) Facile Reduction of Sulfinic Acid to Disulfide with Thiol and Chlorotrimethylsilane
S. Oae, H. Togo, T. Numata, and K. Fujimori, Chem. Lett., (1980), 1193.

3) Iodine Catalyzed Reduction of Arenesulfonic Acid to the Arenethiol with Triphenylphosphine
K. Fujimori, H. Togo, and S. Oae, Tet. Lett., 21, 4921(1980).

4) Facile Conversion of Aliphatic Sulfonic Acids, Sulfinic Acids, Thiols, Sulfonates, Thiolsulfonates, and Disulfides to the Corresponding Alkyl Iodides by Triphenylphosphine/Iodine.
S. Oae and H. Togo, Synthesis, (1981), 371.

5) Biomimetic Reduction of Sulfuric Acid
S. Oae and H. Togo, Chem. Lett., (1981), 1387.

6) Facile Reduction of Sulfonic Acids and Sodium Sulfonates to the Corresponding Disulfides with Polyphosphoric Derivatives/Potassium Iodide/Tetrabutylammonium Iodide System
S. Oae and H. Togo, Synthesis, (1982), 152.

7) Reduction of Sulfonic Acids with Phosphorus Pentasulfide
S. Oae and H. Togo, Tet. Lett., 23, 4701(1982).

8) Reduction of Sulfonic Acids and Related Organosulfur Compounds with Triphenylphosphine-Iodine System. I.
S. Oae and H. Togo, Bull. Chem. Soc. Jpn., in contribution.

9) Reduction of Sulfonic Acids with Triphenylphosphine-Diaryl Disulfide System. II.
S. Oae and H. Togo, Bull. Chem. Soc. Jpn., in contribution.
10) Reduction of Sulfonic Acids, Sodium Sulfonates and Sulfonate Esters to the Corresponding Disulfides with Polyphosphoric Derivatives, Potassium Iodide and Tetrabutylammonium Iodide System. III.
S. Oae and H. Togo, Bull. Chem. Soc. Jpn., in contribution.
11) Reaction of Sulfinic Acid and Thiol
S. Oae and H. Togo, in preparation.

Review

1) Reduction of Sulfur Compounds——Mainly Organosulfur Compounds(Japanese)———— .
S. Oae and H. Togo,
Chemistry(Japan),

part I. Vol. 37(11), 812 - 818,(1982).
The Reduction of Sulfoxides, Sulfilimines, and Sulfonium Ylides.
part II. Vol. 37(12), 909 - 917,(1982).
The Reduction of Sulfones and Sulfoximines.
part III. Vol. 38(1), in press(1983).
The Reduction of Thiols, Disulfides, Sulfenic Acids and its Derivatives, Sulfinic Acids and its Derivatives, and Thiolsulfinates.
part IV. Vol. 38(2), in press(1983).
The Reduction of Sulfonic Acid Derivatives.
part V. Vol. 38(3), in press(1983).
The Reduction of Sulfonic Acids and Sulfuric Acid.

ACKNOWLEDGEMENT

The author wishes to thank Professor Oae for constant guidance, and many helpful discussion and suggestions throughout the course of this study.

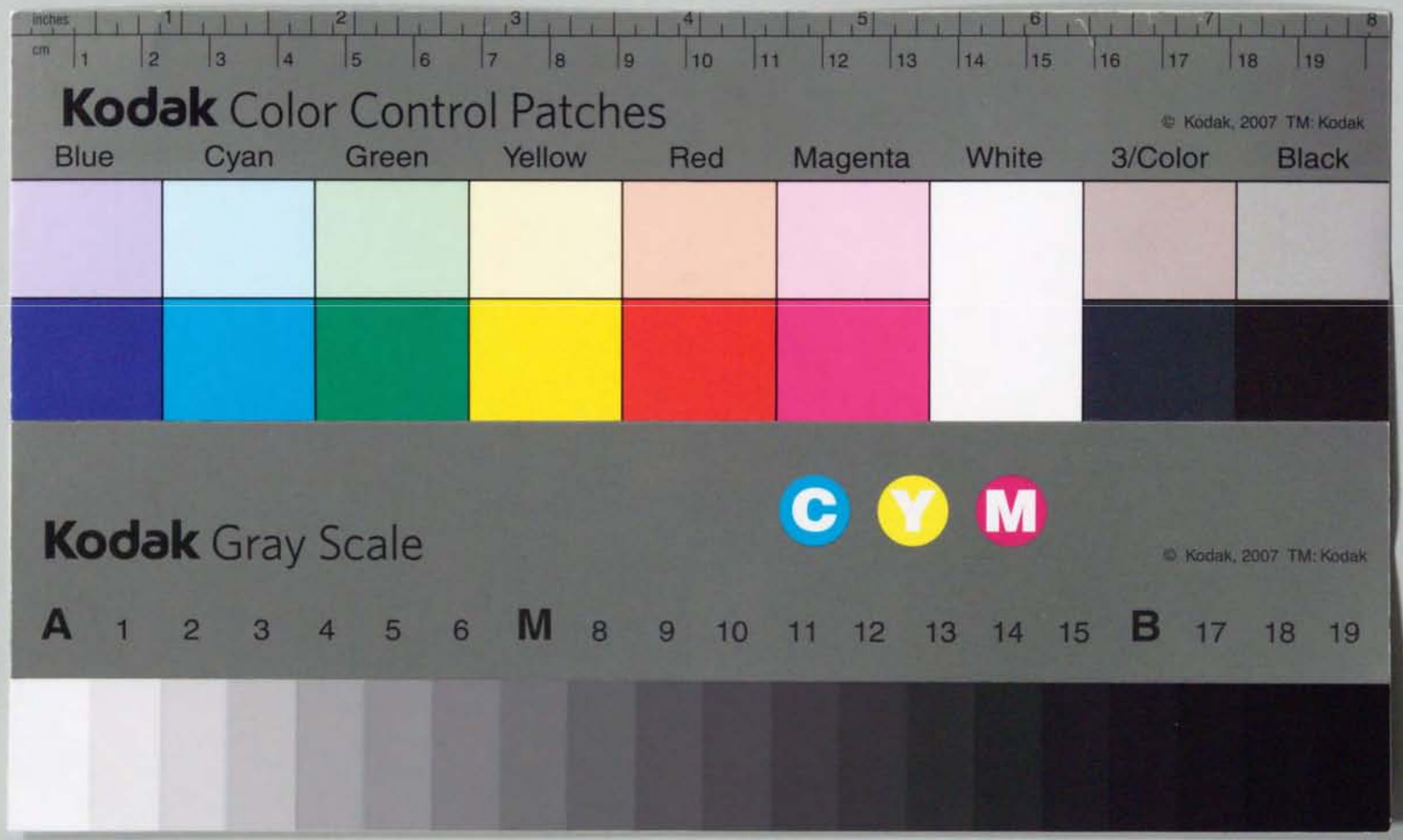
The author also would like to thank Dr. Ken Fujimori for wonderful suggestions throughout this study.

The author would like to thank Associate Professor Furukawa and Dr. Tatsuo Numata for their advices and encouragement.

Acknowledegement is also due to many O.B., especially Dr. Toshikazu Takata, Dr. Osamu Itoh, and Dr. Yoshihito Watanabe, and his friends of Professor Oae's research group for various advices and encouragement.

Hideo Togo

1982 Dec. 12


inches
cm
Kodak Color Control Patches
© Kodak, 2007 TM: Kodak
Blue
Cyan
Green
Yellow
Red
Magenta
White
3/Color
Black
Kodak Gray Scale
C
Y
M
© Kodak, 2007 TM: Kodak
A 1 2 3 4 5 6 M 8 9 10 11 12 13 14 15 B 17 18 19