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NEW SELECTIVE OXIDATION OF UNSYMMETRICAL THIOLSULFINATES TO THE CORRESPONDING THIOLSULFONATES WITH SODIUM METAPERIODATE

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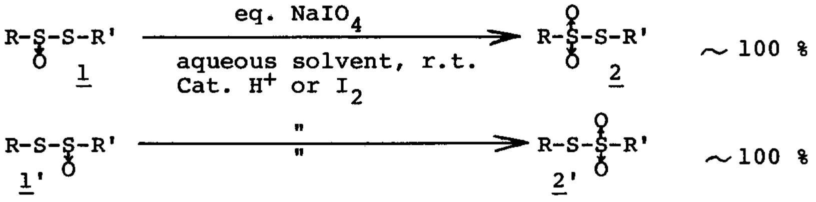
We have recently reported that oxidations of unsymmetrical thiolsulfinates with peroxy acid1) or dinitrogen tetraoxide2) afforded the corresponding symmetrical thiolsulfonates which were undoubtedly derived by the cleavage of sulfur-sulfur bond. We now have found that both aryl- and alkyl unsymmetrical thiolsulfinates are oxidized selectively with sodium metaperiodate in aqueous media to the corresponding unsymmetrical thiolsulfonates quantitatively. The oxidation was accelerated by addition of a catalytic amount of inorganic or organic acid as well as iodine3) (Table II).

Since thiolsulfinates are generally unstable and known to disproportionate readily to the corresponding disulfides and thiolsulfonates4), only a sporadic studies on the oxidation of thiolsulfinate have been carried out1)2)5) and showed that all these oxidations involve the cleavage of sulfur-sulfur bond and gave the corresponding thiolsulfonates.

However, surprisingly, with an equimolar amount of $NaIO_4$ all these unsymmetrical thiolsulfinates were selectively oxidized to the corresponding unsymmetrical thiolsulfonates in aqueous solvent such as water-dioxan, acetonitrile or acetic acid under mild conditions(ca. 25°), with no apparent cleavage of sulfur-sulfur bond.



$$\underset{\underline{1}}{R\text{-}\underset{O}{S}\text{-}S\text{-}R'} \xrightarrow[\text{aqueous solvent, r.t.; Cat. } H^+ \text{ or } I_2]{\text{eq. } NaIO_4} \underset{\underline{2}}{R\text{-}\overset{O}{\underset{O}{S}}\text{-}S\text{-}R'} \quad \sim 100\ \%$$

$$\underset{\underline{1}'}{R\text{-}S\text{-}\underset{O}{S}\text{-}R'} \xrightarrow[\text{"}]{\text{"}} \underset{\underline{2}'}{R\text{-}S\text{-}\overset{O}{\underset{O}{S}}\text{-}R'} \quad \sim 100\ \%$$

	R	R'		R	R'		R	R'
1a	Ph	p-Tol	1e	Ph	Bu	1h	Ph	Ph
1b	p-Tol	Ph	1f	Bu	Ph	1i	p-Tol	Me
1c	Ph	Me	1g	Me		1j	p-ClC_6H_4	Me
1d	Me	Ph						

Unsymmetrical thiolsulfonates have been generally synthesized by treatment of corresponding sulfinic acids with some sulfenyl chlorides6) or with certain thionitrites7). Yields are quite substantial, however, these procedures form some side products such as symmetrical disulfides. Our new method has overcome the side reaction and markedly increased the yield of unsymmetrical thiolsulfonates.

A typical experimental procedure is the following.

A solution of sodium metaperiodate(257 mg, 1.2 mmole) in 2.0 ml of water was added to the thiolsulfinate8) (1)(1.0 mmole) in dioxan(3.5 ml), into which a few drops of conc. hydrochloric or trifluoroacetic acid was added. Immediately the solution turned to light yellow. After stirring for ca.30 min. at 25° until the solution usually changed to dark brown9), the reaction mixture was poured into water and extracted three times with chloroform(100 ml) and then washed with aqueous sodium thiosulfate solution(sat. 10 ml) and water. When chloroform was removed the residue was the highly pure thiolsulfonate: GC, LLC and NMR showed only one component. New products were identified by compairing their IR and NMR spectra with those of authentic samples prepared by other methods6). The results thus obtained were summarized in Table I and II.

Table I Acid Catalyzed Oxidation of Unsymmetrical Thiolsulfinates with $NaIO_4$ at Room Temperature.

Exp.No.	Substrate	Solvent	Catalyst	Reaction Time [h]	Products	Yield [%].
1 1a	$Ph\underset{O}{S}STol\text{-}p$	$CH_3CN\text{-}H_2O$	conc.HCl	<1.0	$Ph\underset{OO}{S}STol\text{-}p$	quant.^{*1}
2 1b	$PhS\underset{O}{S}Tol\text{-}p$	$CH_3CN\text{-}H_2O$	conc.HCl	<1.0	$PhS\underset{OO}{S}Tol\text{-}p$	quant.^{*1}
3 1c	$Ph\underset{O}{S}SMe$	dioxan-H_2O	CF_3COOH	<2.0	$Ph\underset{OO}{S}SMe$	quant.^{*1}
4 1d	$PhS\underset{O}{S}Me$	dioxan-H_2O	no	8.0	$PhS\underset{OO}{S}Me$	98^{*2}
5 1e	$Ph\underset{O}{S}SBu$	dioxan-H_2O	conc.HCl	0.5	$Ph\underset{OO}{S}SBu$	95^{*2}
6 1f	$PhS\underset{O}{S}Bu$	dioxan-H_2O	conc.HCl	0.5	$PhS\underset{OO}{S}Bu$	95^{*2}
7 1g	$\langle H\rangle S\underset{O}{S}Me$	dioxan-H_2O	conc.HCl	0.5	$\langle H\rangle S\underset{OO}{S}Me$	90^{*3}
8 1h	$Ph\underset{O}{S}SPh$	dioxan-H_2O	no	26.0	$Ph\underset{OO}{S}SPh$	quant.^{*1}
9 1i	$p\text{-}Tol\underset{O}{S}SMe$	$CD_3CO_2D\text{-}D_2O$	no	0.5	$p\text{-}Tol\underset{OO}{S}SMe$	quant.^{*1,*4}
10 1j	$p\text{-}ClC_6H_4\underset{O}{S}SMe$	$CD_3CO_2D\text{-}D_2O$	no	0.5	$p\text{-}ClC_6H_4\underset{OO}{S}SMe$	quant.^{*1,*4}

*1) No other product was observed in GC and NMR.
*2) Isolated yield.
*3) The yield was determined by GC and NMR.
*4) The reaction was carried out in NMR sample tube; substrate: 0.1 mmole.

Yields of the unsymmetrical thiolsulfonates are nearly quantitative regardless of the substituent. With other methods methyl benzenethiolsulfinate1) and p-chlorophenyl benzenethiolsulfinate4) are suggested to be oxidized at first to "α-disulfoxide"1)4), which are so unstable, and collapse to yield the corresponding symmetrical thiolsulfonates by the cleavage of sulfur-sulfur bond. However, our new procedure oxidizes only the sulfinyl sulfur atom of methyl benzenethiolsulfinate 1c and phenyl methanethiolsulfinate 1d and did not give any symmetrical thiolsulfonates. Apparently the oxidation with $NaIO_4$ is the first case of the selective oxidation of the electrophilic sulfinyl sulfur atom instead of the electron-rich sulfenyl sulfur atom.

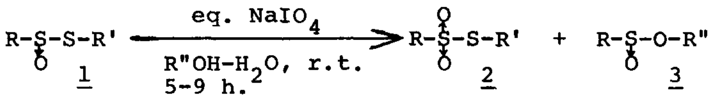
Table II Effects of Catalysts and Solvents in The Reaction of 1c with $NaIO_4$ at ca. 25°

Exp.No.	Solvent	Catalyst	Reaction Time[h]	Yield[%].[*5]
11	dioxan-H_2O	no	6.0	92[*4]
12	CH_3CN-H_2O	no	5.0	98
13	CH_3COCH_3-H_2O	no	27.0	*1
14	CH_3COOH-H_2O	no[*6]	0.5	95
15	dioxan-H_2O	CF_3COOH	2.0	quant.[*2,*3]
16	dioxan-H_2O	conc.HCl	1.0	93
17	dioxan-H_2O	CH_3COOH	6.0	90
18	CH_3COCH_3-H_2O	I_2	3.0	quant.[*3]

*1) Starting material was recovered in 30-40 %.
*2) Same data in Table I.
*3) No other product was observed in GC and NMR.
*4) The yield was determined by GC and NMR.
*5) Product was $PhS(O)_2SMe$: methyl benzenethiolsulfonate.
*6) $CH_3COOH/H_2O=7/4$(v/v).

This oxidation was accelerated by addition of a few drops of hydrochloric or trifluoroacetic acid as well as iodine[10)]. A similar catalytic action with iodine was noticed in the oxidation of dithiane S-monoxides to the corresponding thiolsulfonates by Field and Kim[3)]. Addition of a small amount of acetic acid did not accelerate the oxidation, however the oxidation was dramatically accelerated when acetic acid was used as solvent(Exp.No. 14 and 17). The best solvent appears to be dioxan-water or acetonitrile-water, whichever has higher solubility of the substrate.

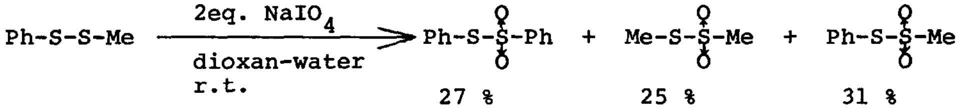
When alcohols such as ethanol, iso-propanol and tert-butanol were used as solvents, a small amounts of the corresponding sulfinates were obtained in the expense of the thiolsulfonates, as shown below.



$$R\text{-}\underset{O}{S}\text{-}S\text{-}R' \xrightarrow[\text{R"OH-}H_2O,\ \text{r.t.}\ 5\text{-}9\ \text{h.}]{\text{eq. }NaIO_4} R\text{-}\overset{O}{\underset{O}{S}}\text{-}S\text{-}R' + R\text{-}\underset{O}{S}\text{-}O\text{-}R''$$

1c(R=Ph, R'=Me) , R"=	Et	42 % (44 %)	39 % (47 %)	(): H^+ Catalyze within 1 h.
	^{i}Pr	67	27	
	^{t}Bu	82	7	
1d(R=Me, R'=Ph) , R"=	Et	78	3	

When, however, an unsymmetrical disulfide, e.g. methyl phenyl disulfide was oxidized with two equimolar amount of $NaIO_4$ under the same condition, the following two symmetrical thiolsulfonates were obtained as major products which are undoubtedly derived by the cleavage of sulfur-sulfur bond as shown below.



$$\text{Ph-S-S-Me} \xrightarrow[\text{dioxan-water, r.t.}]{\text{2eq. NaIO}_4} \underset{27\ \%}{\text{Ph-S-}\overset{O}{\underset{O}{S}}\text{-Ph}} + \underset{25\ \%}{\text{Me-S-}\overset{O}{\underset{O}{S}}\text{-Me}} + \underset{31\ \%}{\text{Ph-S-}\overset{O}{\underset{O}{S}}\text{-Me}}$$

The oxidation of the disulfide is probably initiated by the electrophilic attack of oxygen of the periodate on the two sulfur atoms. On the other hand, the selective oxidation of the thiolsulfinate appears to proceed by the nucleophilic attack of the periodate on the sulfinyl sulfur atom to form the corresponding thiolsulfonate. Further study on the mechanism will be reported.

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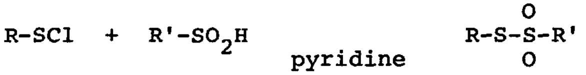
6) This method is very popular today;



$$\text{R-SCl} + \text{R'-SO}_2\text{H} \quad \underset{\text{pyridine}}{} \quad \text{R-S-}\overset{O}{\underset{O}{S}}\text{-R'}$$

7) S.Oae, Y.H.Kim, D.Fukushima and T.Takata, Chemistry Letters, 1977, 893.
8) Symmetrical or unsymmetrical thiolsulfinates were prepared, according to Backer's method, by the reaction of the sulfinyl chloride with thiols in the presence of tert-amine such as pyridine. H.J.Backer and H.Kloostziel, Rec. Trav., 73, 129(1954).
9) Without acid as a catalyst or a solvent, color of iodine appeared only at the end of the oxidation, whereas with acid the solution was colored from the beginning by iodine generated in the reaction.
10) Even the mineral acid and iodine, when used only in a trace amount , did not catalyze the oxidation.