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A GENERAL, HIGH-YIELD PREPARATION OF THIOSULFINATE ESTERS USING ORGANOTIN PRECURSORS[1a]

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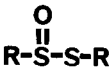
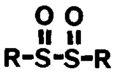
ABSTRACT: A variety of thiosulfinate esters are produced in >90% isolated yield by the reaction of organotin thiolates with sulfinyl chlorides.

Thiosulfinate esters (1) have been the subject of numerous, recent investigations. Among others, mechanistic studies[2] have been prominent involving such questions as which sulfur is attacked by nucleophiles. Block[3] has carefully examined this class as to their specific modes of decomposition while Freeman[4] Oae [5], Kice [6] and Gilbert[7] have recently studied thiosulfinates as precursors to the elusive α-disulfoxides (2). In addition, Baldwin[8] has demonstrated that thiosulfinates are effective precursors to thioaldehydes.



$\mathrm{R{-}\overset{O}{\overset{\|}{S}}{-}S{-}R}$

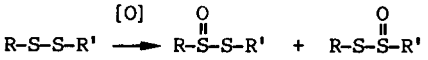
1



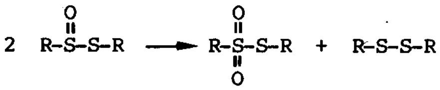
$\mathrm{R{-}\overset{O}{\overset{\|}{S}}{-}\overset{O}{\overset{\|}{S}}{-}R}$

2

In most of these instances, the preparation of the requisite starting materials involves a careful oxidation of the corresponding symmetrical disulfide. In disulfides where the two sulfur atoms are in similar environments, this preparative technique is not useful,in that a mixture of closely related thiosulfinates are produced (eq. 1). Another problem involves ready disproportionation of 1 to thiosulfonate and disulfide (eq. 2).

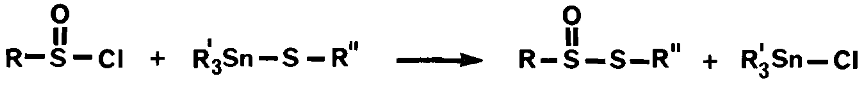


$$\mathrm{R{-}S{-}S{-}R'} \xrightarrow{[O]} \mathrm{R{-}\overset{O}{\overset{\|}{S}}{-}S{-}R'} + \mathrm{R{-}S{-}\overset{O}{\overset{\|}{S}}{-}R'} \qquad \text{eq. 1}$$



$$2\ \mathrm{R{-}\overset{O}{\overset{\|}{S}}{-}S{-}R} \longrightarrow \mathrm{R{-}\underset{O}{\underset{\|}{\overset{O}{\overset{\|}{S}}}}{-}S{-}R} + \mathrm{R{-}S{-}S{-}R} \qquad \text{eq. 2}$$

We wish to report a general method for the synthesis of 1 which is rapid, efficient and proceeds in excellent (> 90%) isolated yield. The product thiosulfinates (1) are produced by the reaction of readily-prepared sulfinyl chlorides (3)[9] with organotin mercaptides (4)[10] for 3-5 min. from -10° C to room temperature (Table I). The neutral and mild reaction conditions make possible the detection of thermally-unstable derivatives such as $CH_3SOSCH_2C_6H_5$, 1b and $C_6H_5SOSCH_2C_6H_5$, 1k. Even highly-hindered thiosulfinates such as 1d can be prepared in high yield (95%). Where silicon is substituted for tin, heat is required for the reaction to proceed and while thiosulfinates are initially formed, they undergo disproportionation at these elevated temperatures. The isolation of 1 from the reaction mixture was achieved by a combination of the Jacobus method[12] and silica-gel column chromatography.



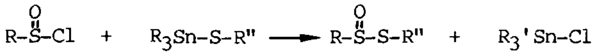
$$R-\overset{O}{\overset{\|}{S}}-Cl + R'_3Sn-S-R'' \longrightarrow R-\overset{O}{\overset{\|}{S}}-S-R'' + R'_3Sn-Cl$$

3 4 1

A typical procedure for the synthesis of 1 is given as follows. To a solution of 4 (1.15 mmol) in 5.0 ml of $CHCl_3$, a solution of sulfinyl chloride 3 (1.15 mmol) in 2.0 ml of $CHCl_3$ was added dropwise (-10°C or room temperature). The mixture was stirred at that temperature for 10 min. After evaporation of solvent, the oily product was dissolved in 2 ml of ether and 4 ml of a saturated aqueous KF solution was added. The mixture was vigorously stirred for 10 min (0° or room temperature); the white precipitate (R_3SnF) was collected. After dilution with 2 ml of ether, the organic layer was separated and dried over anhydrous Na_2SO_4; removal of solvent gave the product. The final purification was completed by silica-gel column chromatography using CH_2Cl_2 as eluent.

Except for 1b and 1k which were relatively unstable at room temperature, the isolated yields of 1 were excellent. In the case of 1b and 1k the yield was high but their disproportionation could be conveniently followed by pmr spectroscopy. In sum, this oxidative coupling procedure appears to be the most general and effective for the construction of this class of compound.

TABLE



$$\mathrm{R\text{-}\overset{O}{\overset{\|}{S}}\text{-}Cl} + \mathrm{R_3Sn\text{-}S\text{-}R''} \longrightarrow \mathrm{R\text{-}\overset{O}{\overset{\|}{S}}\text{-}S\text{-}R''} + \mathrm{R_3'Sn\text{-}Cl}$$

5 4 1

Thiosulfinate			Reaction	Conditions	
R R''	R'	No.	Temp (^{o}C)	Time (min)	Yield (%)
$\mathrm{CH_3\overset{O}{\overset{\|}{S}}\text{-}SBut}$	nBu	a	RT	3	95
$\mathrm{CH_3\overset{O}{\overset{\|}{S}}\text{-}SBz}$	nBu	b	-10	5	(>90)[a]
$\mathrm{CH_3\overset{O}{\overset{\|}{S}}\text{-}SC_6H_5}$	nBu	c	-10	5	89
$\mathrm{tBu\overset{O}{\overset{\|}{S}}\text{-}SBut}$	nBu	d	RT	5	95
	Me		RT	5	95
$\mathrm{tBu\overset{O}{\overset{\|}{S}}\text{-}SBz}$	nBu	e	-10	5	90
$\mathrm{tBu\overset{O}{\overset{\|}{S}}\text{-}SC_6H_5}$	nBu	f	-10	5	93
$\mathrm{Bz\overset{O}{\overset{\|}{S}}\text{-}SBut}$	nBu	g	RT	3	90
	Me		RT	3	93
$\mathrm{Bz\overset{O}{\overset{\|}{S}}\text{-}SBz}$	nBu	h	-10	5	94
$\mathrm{Bz\overset{O}{\overset{\|}{S}}\text{-}SC_6H_5}$	nBu	i	-10	5	90
$\mathrm{C_6H_5\overset{O}{\overset{\|}{S}}\text{-}SBut}$	nBu	j	RT	3	92
	Me		RT	3	93
$\mathrm{C_6H_5\overset{O}{\overset{\|}{S}}\text{-}SBz}$	nBu	k	-10	5	(>90)[b]
$\mathrm{C_6H_5\overset{O}{\overset{\|}{S}}\text{-}SC_6H_5}$	nBu	l	-10	5	95

a) Isolated yields; each ester was homogeneous on tlc.
b) Estimated by pmr spectroscopy.

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