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ACTIVATION AND SYNTHETIC APPLICATIONS OF THIOSTANNANES. EFFICIENT CONVERSION OF THIOLS INTO DISULFIDES

Tsuneo Sato, Junzo Otera,* and Hitosi Nozaki
Department of Applied Chemistry, Okayama University of Science
Ridai-cho, Okayama 700, Japan

Summary: Various kinds of thiols are converted into the corresponding disulfides under mild conditions with the aid of alkoxystannane-ferric chloride.

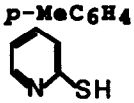
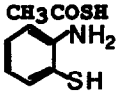
Oxidation of thiols to disulfides is important from both synthetic and biochemical points of view and accordingly numerous studies have appeared.[1] We report here a thiostannane methodology applicable to a wide spectrum of thiols. Thiostannanes found a limited number of synthetic applications on account of thermal as well as chemical stabilities of the Sn-S bond.[2] We disclosed recently that the Sn-S bond can be activated in the presence of Lewis acids and thus thiostannanes served as mild thioalkoxylation reagents.[3] Extension of the relevant study has led us to find that ferric chloride effects cleavage of the Sn-S bond: an equimolar mixture of phenylthiotributyltin and anhydrous ferric chloride (**3**) was stirred in acetonitrile at room temperature. After 1 h, diphenyl disulfide and Bu_3SnCl were obtained in 92% and 100% yields, respectively (eq 1).[4,5] Since exposure of organotin alkoxides to thiols readily provides the corresponding thioalkoxides,[6] the next goal was the one-pot conversion of thiols into disulfides (eq 2). An acetonitrile solution (3 ml) of 2-methyl-2-propanethiol (1 mmol), Bu_3SnOMe (**2**) (1 mmol), and **3** (1 mmol) was stirred at room temperature for 2 h. GLC analysis of the reaction mixture showed 100% yield of di-*t*-butyl disulfide and 98% yield of Bu_3SnCl. Column chromatography provided the disulfide in 84% yield. The results with other thiols are summarized in Table 1.

$$Bu_3SnSPh + \underset{\mathbf{3}}{FeCl_3} \xrightarrow[CH_3CN]{} 1/2\,PhSSPh + Bu_3SnCl \quad (1)$$

$$\underset{\mathbf{1}}{RSH} + \underset{\mathbf{2}}{Bu_3SnOMe} \xrightarrow[CH_3CN]{\mathbf{3}} 1/2\ RSSR + Bu_3SnCl \quad (2)$$

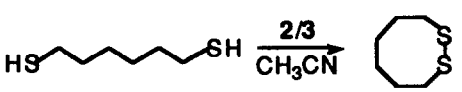
Following comments are worthy of note. In addition to primary and secondary alkanethiols, tertiary derivatives are equally employable. Facile formation of di-*t*-alkyl disulfides is remarkable since only three successful examples with 2-methyl-2-propanethiol have been known thus far.[7] Aryl mercaptans also give satisfactory results. Various functional groups remain intact under the present reaction conditions. Of particular significance is that no oxidation takes place on amino groups which were found not to be tolerable in many occasions.[8]

Table 1. Conversion of Thiols 1 into Disulfide with the Aid of Bu_3SnOMe (2) and $FeCl_3$ (3). [a]

1	reaction time/h	yield/%[b]
n-$C_6H_{13}SH$	2	83 (100)
$MePrCHSH$	2	92 (100)
$cyclo$-$C_6H_{11}SH$	2	95 (100)
Me_3CSH	2	84 (100)
$EtMe_2CSH$	2	82 (81)
Ph_3CSH	12	96
$PhSH$	2	99 (100)
p-MeC_6H_4SH	2	86
	2	(95)
$HOCH_2CH_2SH$	3	84
CH_3COSH	3	80
	4	89
$MeOCOCHCH_2SH$ $NHCOMe$	6	97

a) Reaction conditions: 1:2:3 = 1:1:1, CH_3CN, room temperature.
b) Isolated yields. GLC yields are given in parentheses.

Cyclization of α,ω-alkane dithiols has received much attention.[4,5,9] Amongst 1,6-hexanedithiol most difficultly affords the eight-membered cyclic monomer in 30% yield with $FeCl_3 \cdot 6H_2O/CH_3COOH$[5a] and 37% yield with $Bu_3SnS(CH_2)_6SSnBu_3/I_2$.[4] Our method provided 50% yield of the monomer (eq 3).



(3)

Table 2 summarizes the results on screening of organotin compounds. The crucial role played by these compounds is evident from the control experiment which gave only 10% yield of the desired product. Organotin alkoxides are superior to the oxides due to more susceptibility of the former to thioalkoxylation. An alkoxysilane is not effective, a quite reasonable result on the basis of strong affinity of silicon towards oxygen.

Table 2. Screening of Organotin Reagents (OR).[a]

$$t\text{-BuSH} + \text{OR} \xrightarrow{3} 1/2\ (t\text{-BuS})_2$$

OR (equiv)	yield/%[b]
---	10
Bu_3SnOMe (1.0)	100
$Bu_2Sn(OEt)_2$ (0.5)	100
$Bu_3SnOSnBu_3$ (1.0)	73
Bu_2SnO (0.5)	78
Me_3SiOMe (1.0)	17

a) In CH_3CN, room temperature, 2 h. b) Based on GLC.

Table 3. Screening of Iron Salts (IS).[a]

$$t\text{-BuSH}\ (1\ \text{mmol}) + 2\ (1\ \text{mmol}) + \text{IS} \longrightarrow 1/2(t\text{-BuS})_2$$

IS (mmol)	yield/%[b]
$FeCl_3$ (0.1)	8
(0.4)	53
(0.7)	75
(1.0)	100
$FeCl_2 \cdot 4H_2O$ (1.0)	12
$Fe(acac)_3$ (1.0)	1
$K_3Fe(CN)_6$ (1.0)	0
Fe_2O_3 (1.0)	0

a) In CH_3CN, room temperature, 2 h. b) Based on GLC.

Unique activity of **3** as compared with other iron salts is seen from Table 3. The reason is not clear at present. One equivalent of **3** is necessary for completion of the reaction, suggestive of reduction from Fe (III) to Fe (II) as a pivotal step. Free radical mechanism, however, is not plausible since the reaction in the presence of 1-hexene did not provide the corresponding sulfide which was expected to arise if a thiyl radical had been generated.[10]

In summary, thiostannanes are nice protected thiols due to the long shelf-life and little odorousness. Facile conversion of these compounds into disulfides, therefore, is of considerable synthetic value. Yet more intriguing is the one-pot oxidation of thiols by making use of the thiophilicity of alkoxystannanes. The mildness and versatility of this process no doubt meet a variety of synthetic demands.

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