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DIRECT SYNTHESIS OF PROTECTED THIOLS BY TRIBUTYLSTANNYL GROUP

Yoshio UENO,* Mamoru NOZOMI, and Makoto OKAWARA
Research Laboratory of Resources Utilization, Tokyo Institute of
Technology, Nagatsuta, Midoriku, Yokohama 227

Organic thiocyanates react with tributyltin hydride under homolytic conditions to give thiostannanes ($Bu_3Sn{-}SR$), which are air-stable and high boiling protected forms of the parent thiols.

Thiols are the most fundamental compounds as starting materials for numerous organosulfur compounds, and are also of biological importance. Various preparative methods for thiols starting from organic halides are well known.[1] Thiols are, however, generally air-sensitive and also possess unpleasant odor. Especially, volatile thiols such as methanethiol (bp.6°C) are troublesome to handle.[2] Therefore, it is desirable to prepare directly the protected forms of thiols from organic halides, and high boiling carriers of volatile thiols.

Formation of relatively strong bond between silicon atom and oxygen atom enables organosilyl groups to be effective protecting groups for alcohols.[3] Sulfur can be expected to combine more strongly with organostannyl groups rather than organosilyl ones. With this object in view, we investigated the general preparative method for thiostannanes starting from organic halides. We found that organothiocyanates, readily accessible from organic halides, reacted with tributyltin hydride under mild conditions to give thiostannanes in good yiels.[4]

$$\mathrm{RSCN} \xrightarrow[\text{AIBN, 60°, 2h}]{\mathrm{Bu_3SnH}} \mathrm{Bu_3Sn{-}SR}$$

The reaction was carried out simply in neat conditions under nitrogen atmosphere either in presence or absence of azobisisobutyronitrile (AIBN). Distillation of the mixture afforded the thiostannanes, which were air-stable[5] and high boiling compounds. The latter property highly reduced the unpleasant odor of the parent thiols. The results are summarized in Table 1.

Table 1. Preparation of Thiostannanes from Organothiocyanates[6,a]

Thiocyanates	Thiostannanes	Yield (%)	Bp (°C/mmHg)	NMR(CCl_4) δ
MeSCN	Bu_3SnSMe	86	97-98 /0.15	2.0(s,3H),0.77-1.8(m,27H)
EtSCN	Bu_3SnSEt	90	110-112 /1	2.49(q,2H),0.67-1.76(m, 30H)
BuSCN	Bu_3SnSBu	99	108-110 /0.1	2.46(t,2H),0.73-1.86(m, 34H)
$CH_3(CH_2)_7SCN$	$Bu_3SnS(CH_2)_7CH_3$	99	134-136 /0.25	2.44(t,2H),0.73-1.73(m, 42H)
$NCS(CH_2)_3SCN$	$Bu_3SnS(CH_2)_3SSnBu_3$	98	205-210 /0.05	2.61(t,4H),0.73-1.97(m, 56H)
$CH_3COS(CH_2)_3SCN$	$Bu_3SnS(CH_2)_3SCOCH_3$	92	144/0.07	0.77-2.0(m,29H),2.3(s, 3H),2.58(t,2H),3.0(t,2H)

[a] RSCN: Bu_3SnH = 1:1 , $NCS(CH_2)_3SCN$: Bu_3SnH = 1:2

The last entry in Table 1 shows that the thiolacetate group is completely inert towards tributyltin hydride.

Considering the availability of the starting organothiocyanates from organic halides, or by the reaction of thiocyanogen or related species with olefins or aromatic compounds,[7] the present method provides an attractive entry to the preparation of various type of thiostannanes.

Most typical procedures for the preparation of thiols hitherto used are alkaline or acid hydrolysis of S-alkylthiouronium salts or xanthates. In contrast to these methods, the present one can be carried out under neutral conditions and in the absence of water.[8] Moreover, volatile thiols such as methane- or ethanethiols are easily handled as high boiling precursors (vide infra). If desired, facile hydrolysis of thiostannanes to alkali metal thiolates is also possible.[9]

Next, we examined the one-pot conversion of organothiocyanates to thiolesters without isolation of the intermediate thiostannanes.

$$\mathrm{RSCN} \xrightarrow[\text{2)R'COCl, CHCl}_3\text{,rt, 5 min}]{\text{1)Bu}_3\text{SnH}} \mathrm{RSCOR'}$$

Organothiocyanates were treated with tributyltin hydride followed by an acid chloride in chloroform at room temperature for 5 min to give the corresponding thiolesters in good yield.[10] The results are summarized in Table 2.

Table 2. Thiolesters from Thiocyanates[6]

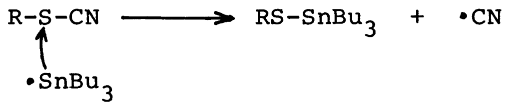
	Thiocyanates	Thiolesters	Yield (%)	Mp or bp (°C)
1	MeSCN	$p\text{-}NO_2C_6H_4COSMe$	100	62
2	EtSCN	$p\text{-}NO_2C_6H_4COSEt$	100	90-92
3	BuSCN	CH_3COSBu	61	70-75/3 mmHg
4	$CH_3(CH_2)_7SCN$	$p\text{-}NO_2C_6H_4COS(CH_2)_7CH_3$	98	140-145/0.1 mmHg
5	$NCS(CH_2)_3SCN$	$p\text{-}NO_2C_6H_4COS(CH_2)_3SCOC_6H_4NO_2\text{-}p$	95	118.5-119.5

Entries 1 and 2 in Table 2 represent the typical examples of thiostannane as a high boiling carrier.

Limitations of our method, however, were observed in the case of phenacylthiocyanate or banzylthiocyanate, in which acetophenone or toluene was obtained in 94 and 70% yields, respectively.

$$\mathrm{PhCOCH_2SCN} \xrightarrow[\text{PhH, rt, 6 h}]{\text{Bu}_3\text{SnH}} \mathrm{PhCOCH_3} \qquad 94\%$$

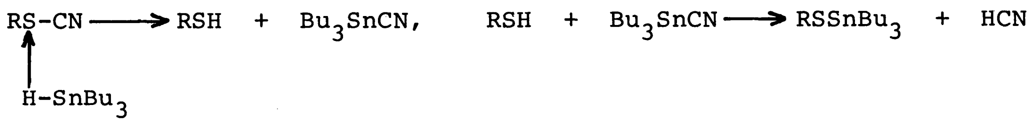
The present reduction may proceed via homolytic process, which is supported by the acceleration effect of AIBN as a radical initiator.[11,12]



$$\underset{\overset{\uparrow}{\bullet\mathrm{SnBu_3}}}{\mathrm{R\text{-}S\text{-}CN}} \longrightarrow \mathrm{RS\text{-}SnBu_3} + \bullet\mathrm{CN}$$

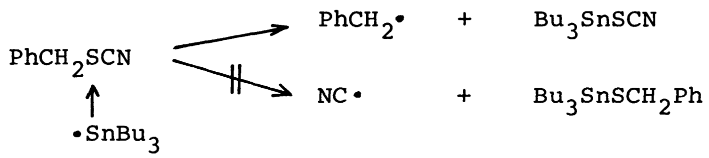
$$\bullet\mathrm{CN} + \mathrm{Bu_3SnH} \longrightarrow \mathrm{Bu_3Sn}\bullet + \mathrm{HCN}$$

Ionic mechanism is also possible involving hydride transfer.



$$\underset{\overset{\uparrow}{\mathrm{H\text{-}SnBu_3}}}{\mathrm{RS\text{-}CN}} \longrightarrow \mathrm{RSH} + \mathrm{Bu_3SnCN}, \qquad \mathrm{RSH} + \mathrm{Bu_3SnCN} \longrightarrow \mathrm{RSSnBu_3} + \mathrm{HCN}$$

However, quantitative formation of methyl p-nitrothiolbenzoate from methylthiocyanate suggests the above scheme involving volatile methanethiol is unlikely.[13] In the case of phenacyl or banzylthiocyanates, relatively stable phenacyl or benzyl radical may split exclusively.



$$PhCH_2\cdot + Bu_3SnH \longrightarrow PhCH_3 + Bu_3Sn\cdot$$

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6) All new compounds obtained here had satisfactory spectral and analytical data.

7) R. G. Guy, "The chemistry of cyanates and their thio derivatives", part 2, S. Patai, Ed., John Wiley, New York, 1977, Chapter 18.

8) For the reduction of organothiocyanates with $LiAlH_4$ or $NaBH_4$, see, R. K. Olsen and H. Snyder, J. Org. Chem., 30, 184 (1965); G. L. O'Connor and H. R. Nace, J. Am. Chem. Soc., 75, 2118 (1953).

9) H. Schumann and M. Schmidt, Chem. Ber., 96, 3017 (1963).

10) D. N. Harpp, T. Aida, and T. H. Chan, Tetrahedron Lett., 2853 (1979). For sulfide preparations from thiostannanes, see, P. L. Clarke and J. L. Wardell, J. Chem. Soc., Dalton Trans., 190 (1974).

11) When the similar reaction was carried out using n-butylthiocyanate in the absence of AIBN, the final product, butyl thiolacetate was obtained in 15% yield.

12) The reaction of toluenesulfenic acid ethyl ester with trimethyltin hydride has been reported to proceed via S_H2 mechanism. W. P. Neumann and J. Schwindt, Chem. Ber., 108, 1346 (1975).

13) Volatile MeSH could not be trapped with Bu_3SnH in the following reaction.

$$CH_2{=}CHCH_2SCOSMe + Bu_3SnH \longrightarrow Bu_3SnCH_2CH{=}CH_2 + MeSH\uparrow + COS\uparrow$$

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