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Organotin-Mediated Preparation of Monothioacetals

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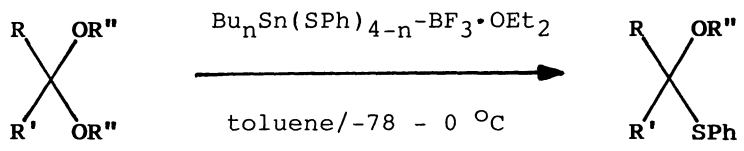
Monothioacetals are obtained by treating the corresponding acetals with organotin thiophenoxides in the presence of $BF_3 \cdot OEt_2$. The reaction proceeds under mild conditions to provide the desired compounds with high selectivity.

Monothioacetals **1** are synthetically useful reagents[1] and the most convenient route to **1** is the transformation of acetals **2** with thiols. However, the transacetalization occasionally suffers from low yields and contamination of the dithioacetals **3** [$RR'C(SR")_2$].[1a,2] More recently, diethylaluminum thiophenoxide proved to be effective to this end.[1a,3]

In the studies on the applications of methoxy(phenylthio)methane as a one-carbon homologation reagent we disclosed unique reactivities and synthetic utilities of the resulting monothioacetals.[4] In order to develop their further versatilities, we required a wider variety of monothioacetals. Based on experiences of organotin-mediated functional group modifications,[5] we have found that organotin thiophenoxides do effect the conversion of acetals into the corresponding monothioacetals in an extremely selective manner.



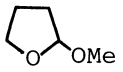
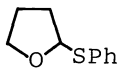
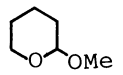
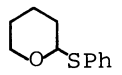
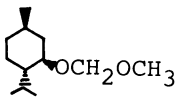
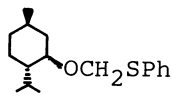
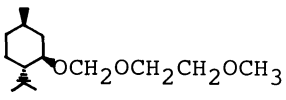
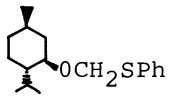
2 **1**

The following procedure is representative. To a toluene solution (5 ml) of nonanal diethylacetal (216 mg, 1 mmol) and Bu_3SnSPh (**4**) (439 mg, 1.1 mmol) was added $BF_3 \cdot OEt_2$ (1.0 M toluene solution, 1 ml, 1 mmol) at -20 °C. After the solution was stirred for 1 h, GLC analysis indicated the formation of the corresponding monothioacetal in 100% yield. No dithioacetal was detected. To the reaction mixture were added pyridine (0.24 ml, 3 mmol) and 1 M NaOH solution(1 ml). The mixture was extracted with ether and the organic layer was washed with 1 M NaOH and H_2O, dried (Na_2SO_4), and concentrated. The residue was subjected to column chromatography on silica gel (4:1 hexane-benzene) to give 1-ethoxy-1-phenylthiononane (239 mg, 85%).

The results are summarized in Table 1. No appreciable dithioacetals **3** were formed except in the case of entry 2. As an organotin compound, $Bu_2Sn(SPh)_2$ (**5**) proved to be effective as well. The employment of $BF_3 \cdot OEt_2$ was crucial since the yields and the selectivities for **1** over **3** were lowered when Lewis acids such as $SnCl_4$, $TiCl_4$, $AlCl_3$, $ZnBr_2$, SnI_2, and BCl_3 were used. Toluene was the best solvent and hexane served as a cosolvent in some cases.[6] Use of dichloromethane, ether, and acetonitrile gave less satisfactory results. Acetals of aliphatic aldehydes (entries 1-5), acyclic and cyclic ketones[7] (entries 6 and 7), an aromatic aldehyde (entry 8), and an α,β-acetylenic aldehyde (entry 9) were employable. The reaction proceeded quantitatively with cyclic ethers having an α-alkoxy substituent (entries 10 and 11). Of special interest is that methoxymethyl (MOM) and (2-methoxyethoxy)methyl (MEM) ethers (entries 12-14) are successfully converted into the corresponding phenylthiomethyl ethers. No other products were isolated. To the best of our knowledge, the only precedented successful transformation is that by Morton et al.[8] who utilized the two-step procedure, i.e. reaction with dimethylboron bromide followed by treatment of the resulting bromomethyl ethers with thiols in the presence of diisopropylethylamine.

In summary, employment of organotin thiophenoxides dramatically suppress the formation of dithioacetals. This is ascribed to the decreased nucleophilicity of the phenylthio group of the highly covalent Sn-S(Ph) bond. Furthermore, the present method seems to be synthetically promising on account of the chemical inertness of organotin compounds compared with organoaluminums.

Table 1. Organotin-mediated conversion of acetals **2** into monothioacetals **1**[a)]

Entry	**2**	Organotin compd[b)]	Reaction temp/°C	time/h	**1**	Yield/%[c)]
1	n-$C_8H_{17}CH(OMe)_2$	**4** (1.1)	-20	1	n-$C_8H_{17}CH(OMe)(SPh)$	100
2	n-$C_8H_{17}CH(OMe)_2$	**5** (0.55)	-78	4	n-$C_8H_{17}CH(OMe)(SPh)$	91(76)[d)]
3	n-$C_8H_{17}CH(OEt)_2$	**4** (1.1)	-20	1	n-$C_8H_{17}CH(OEt)(SPh)$	100(85)
4	cyclo-$C_6H_{11}CH(OMe)_2$	**4** (1.3)	-20	1	cyclo-$C_6H_{11}CH(OMe)(SPh)$	99(70)
5	n-$C_8H_{17}C(CH_3)_2CH(OMe)_2$	**4** (1.1)	-20	1	n-$C_8H_{17}C(CH_3)_2CH(OMe)(SPh)$	100
6	n-$C_6H_{13}C(OMe)_2CH_3$	**4** (1.1)	-78	1[e)]	n-$C_6H_{13}C(OMe)(SPh)CH_3$	85[f)]
7	$\overline{(CH_2)_5C(OMe)_2}$	**4** (1.1)	-78	1[g)]	$\overline{(CH_2)_5C(OMe)(SPh)}$	69[f)]
8	$C_6H_5CH(OMe)_2$	**4** (1.1)	-78	1[e)]	$C_6H_5CH(OMe)(SPh)$	100
9	n-$C_6H_{13}C{\equiv}CCH(OMe)_2$	**5** (0.6)	-50--30	5	n-$C_6H_{13}C{\equiv}CCH(OMe)(SPh)$	96(73)
10		**4** (1.1)	-78	2		100
11		**4** (1.1)	-20	1		100(100)
12	n-$C_{11}H_{23}CH_2OCH_2OCH_3$	**4** (1.1)	0	4	n-$C_{11}H_{23}CH_2OCH_2SPh$	69
13		**4** (1.1)	0	4		80(64)
14		**4** (1.1)	0	4		77

a) All reactions were carried out with 1 mmol of **2** in the presence of 1.0 equiv. of $BF_3 \cdot OEt_2$.

b) The amount of employed organotin compounds (mmol) is shown in the parentheses.

c) Based on GLC analysis. Isolated yields are indicated in the parentheses.

d) A small amount of the dithioacetal was contaminated (**1**/3 = 93:7).

e) A mixture of toluene-hexane (3:2 in volume) served as a solvent.

f) Based on NMR spectra.

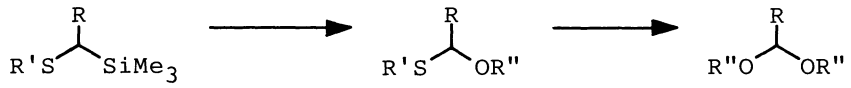
g) $BF_3 \cdot OEt_2$ (0.5 equiv.) was utilzed.

References

1) a) Y. Masaki, Y. Serizawa, and K. Kaji, Chem. Lett., 1985, 1933, and references cited therein; b) E. Block and M. Aslam, J. Am. Chem. Soc., 107, 6729 (1985); c) M. Ohwa and E. L. Eliel, Chem. Lett., 1987, 41; d) T. Kametani, K. Kawamura, and T. Honda, J. Am. Chem. Soc., 109, 3010 (1987).

2) We also confirmed the analogous results: treatment of benzaldehyde dimethylacetal with 1.1 equiv. of thiophenol in the presence of $BF_3 \cdot OEt_2$ (1.0 equiv.) in toluene provided monothioacetal (62%), dithioacetal (3%), and unchanged acetal (33%) after 2 h.

3) It has been reported that electrolysis of **6** (R = phenyl) in an alcohol solvent (R"OH) affords the corresponding monothioacetal: T. Koizumi, T. Fuchigami, and T. Nonaka, Chem. Lett., 1987, 1095. However, acetals **7** are the products on the electrolysis of **6** (R = alkyl) although the monothioacetals are formed as intermediates: J. Yoshida and S. Isoe, Chem. Lett., 1987, 631.



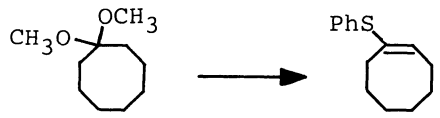
6 **7**

4) J. Otera, Synthesis, in press.

5) For the most recent study, see J. Otera and H. Nozaki, Tetrahedron Lett., 27, 5743 (1986).

6) Unless hexane had been added in entries 6 and 8, dithioacetals were formed to some extent (<5%).

7) Under the same reaction conditions, cyclooctanone dimethylacetal afforded 1-phenylthio-1-cyclooctene in 66% yield.



8) H. E. Morton and Y. Guindon, J. Org. Chem., 50, 5379 (1985).

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