A Novel Catalyst System, Trimethylsilyl Chloride and Indium(III) Chloride, as an Efficient Catalyst in the Sulfide Synthesis

Teruaki MUKAIYAMA, Takashi OHNO, Takashi NISHIMURA, Jeong Sik HAN, and Shū KOBAYASHI
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

(Received April 12, 1991)

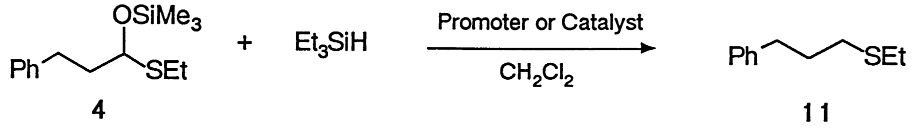
O-Trimethylsilyl monothioacetals, which are generally difficult to activate under acidic conditions due to their rapid disproportionation, smoothly react with triethylsilane in the presence of a novel catalyst system, trimethylsilyl chloride and indium(III) chloride, to afford the corresponding sulfides in good to high yields. One pot synthesis of sulfides from aldehydes is also attained in high yields by successive treatments of aldehydes with trimethylsilyl alkyl (aryl) sulfides and triethylsilane in the presence of the above catalyst system under extremely mild conditions.

Utilities of acetals are widely extended during last few decades, not only as protective groups but also as electrophiles in various coupling reactions, especially carbon–carbon bond forming reactions.[1] *O*-trimethylsilyl monothioacetals are also useful intermediates as masked carbonyl compounds, however, activations of these compounds in the reaction with some nucleophiles are generally difficult because of their readiness to disproportionate under acidic conditions, and hitherto only a few examples of the reactions of *O*-trimethylsilyl monothioacetals with nucleophiles were reported.[2]

A novel method for the preparation of sulfides from carbonyl and related compounds, reduction of *O*-trimethylsilyl monothioacetals, was prelimirarily reported in the previous communication.[3] In this paper, we would like to describe on a novel catalyst system, trimethyisilyl chloride (TMSCl) and indium(III) chloride ($InCl_3$), which effectively catalyzes the reaction of *O*-trimethylsilyl monothioacetals with triethylsilane. Further, one pot synthesis of sulfides just starting from aldehydes using trimethylsilyl alkyl(aryl) sulfide and triethylsilane in the presence of the above catalyst system is described in detail.

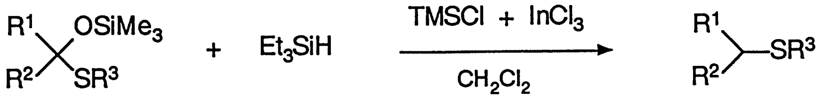
Synthesis of Sulfides from *O*-Trimethylsilyl Monothioacetals. An Efficient Activation of *O*-Trimethylsilyl Monothioacetals Using TMSCl and $InCl_3$ as a Catalyst. In the first place, the reaction of 1-ethylthio-1-trimethyisiloxy-3-phenylpropane (**4**) with triethylsilane was chosen as a model and several reaction conditions were examined. When a typical Lewis acid such as $TiCl_4$, $SnCl_4$, BF_3OEt_2 or $ZnCl_2$ etc. was employed, no desired product was obtained after examination of several reaction conditions such as solvent, reaction temperature, amount of promoter, etc (Table 1, Entries 1—3). In these reactions, disproportionation of **4** took place quite readily to result in the formation of dithioacetal, an undesirable by-product. Trimethylsilyl triflate (TMSOTf) or trimethylsilyl iodide (TMSI), which was reported to be an effective catalyst in the reaction of ethylthio(phenyl)trimethylsiloxymethane (**1**) or 1-ethylthio-1-trimethylsiloxycyclohexane with trimethylsilane,[4] did not work well in the case when Et_3SiH was employed as a reducing reagent (Table 1, Entries 4 and 5). These results indicated that, under these reaction conditions of employing the above mentioned Lewis acids, the reaction systems were so acidic that the disproportionation proceeded faster than the desired reduction did. Therefore, milder reaction conditions were supposed to be necessary to accomplish this reaction. We have recently developed quite efficient catalyst system, TMSCl–$SnCl_2$[5] or TrCl–$SnCl_2$,[6] in the aldol or Michael reactions of silyl enol ethers with aldehydes or α,β-unsaturated ketones. These catalysts consist of a neutral molecule and a weak Lewis acid and effectively lead to the completion of the reactions under mild conditions. Bearing in mind these catalyst sys-

Table 1. Effect of Promoter or Catalyst



Entry	Promoter or Catalyst (mol%)	Temp/°C	Yield/%
1	$TiCl_4$ (100)	−78→0	0
2	BF_3OEt_2 (100)	−78→0	0
3	$SnCl_4$ (20)	−78→0	0
4	TMSOTf (20)	0	0
5	TMSI (20)	0	0
6	TMSCl (50)+$SnCl_2$ (20)	R.T.	0
7	TMSCl (50)+$InCl_3$ (20)	R.T.	68

Table 2. Synthesis of Sulfides from *O*-Trimethylsilyl Monothioacetals



Entry	*O*-Trimethylsylilyl monothioacetal				Temp/°C	Product	Yield/%
	R^1	R^2	R^3				
1	Ph	H	Et	(**1**)	R.T.	**8**	83
2	Ph	H	^{i}Pr	(**2**)	0→R.T.	**9**	88
3	Ph	H	Ph	(**3**)	R.T.	**10**	77
4	$Ph(CH_2)_2$	H	Et	(**4**)	R.T.	**11**	68
5	$CH_3(CH_2)_7$	H	Et	(**5**)	R.T.	**12**	70
6	Ph	Me	Et	(**6**)	R.T.	**13**	97
7	$-(CH_2)_5-$		Et	(**7**)	0→R.T.	**14**	96

tems, we employed TMSCl-$SnCl_2$ as a catalyst in the present reaction. While **1** smoothly reacts with Et_3SiH at rt in the presence of 10 mol% each of TMSCl and $SnCl_2$ give the corresponding sulfide in 63% yield, no desired reduction product was obtained in the reaction of **4** with Et_3SiH (Table 1, Entry 6). We further searched for novel catalyst systems, and after screening several weak Lewis acids other than $SnCl_2$, $InCl_3$ was found to be very effective and the desired sulfide was obtained in 68% yield when a novel catalyst system, TMSCl-$InCl_3$, was employed (Table 1, Entry 7). It should be noted that neither TMSCl nor $InCl_3$ alone is effective in the present reaction and the reaction proceeds only when TMSCl and $InCl_3$ are combined.

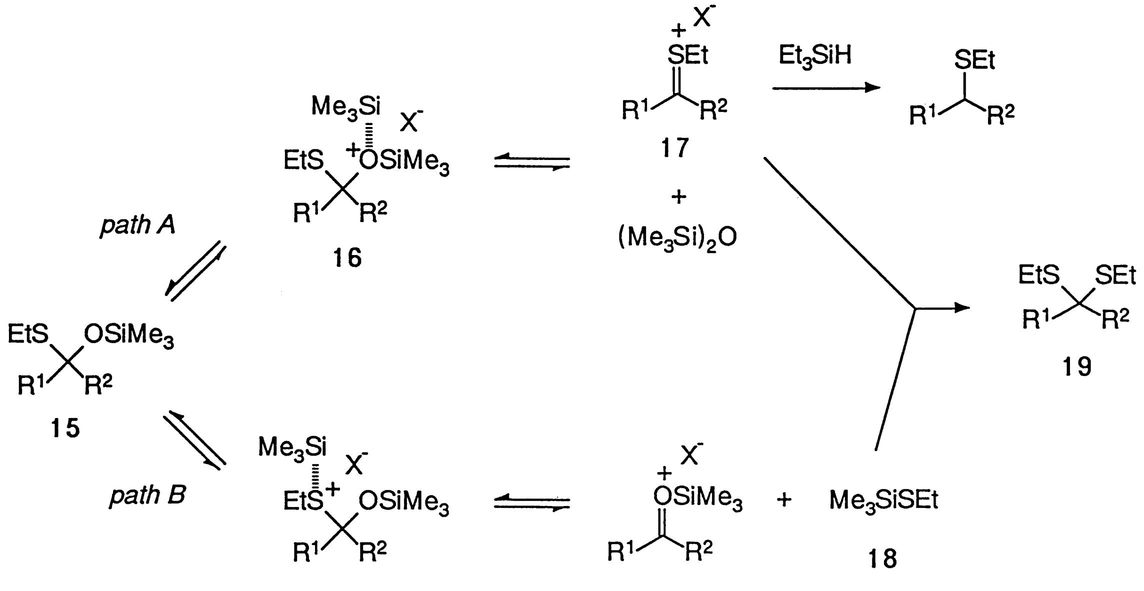
Several examples of the present reaction of *O*-trimethylsilyl monothioacetals with triethylsilane are demonstrated in Table 2. In every case, the desired sulfides are obtained in good to high yields.

Concerning the structure of the novel catalyst system, we assumed the following equilibrium and the generation of the cationic species shown in Chart 1 similar to that in the case of TMSCl-$SnCl_2$ or TrCl-$SnCl_2$. The most important point is preferential activation of trimethylsiloxy group (Scheme 1, path A) to ethylthio group (path B) using TMSCl-$InCl_3$ catalyst system, which depends on stronger affinity of silicon atom toward oxygen atom than toward sulfur atom.9) When path A and path B proceed parallelly in the case of using other Lewis acid catalysts such as $TiCl_4$, BF_3OEt_2, $SnCl_4$, etc., a dithioacetal **19** is mainly formed by the reaction of the intermediate **16** (or **17**) with ethylthiotrimethylsilane **18**, which is more reactive than Et_3SiH. It is also notable that $InCl_3$ is a quite mild Lewis acid and do not participate in the direct activation of **15**.

$$\overset{\delta+}{Me_3SiCl}\cdots\cdots\overset{\delta-}{InCl_3}$$

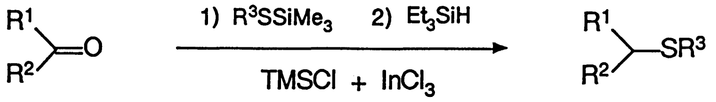
Chart 1.

Thus, a novel catalyst system, TMSCl-$InCl_3$, effectively catalyzes the reaction of *O*-trimethylsilyl monothioacetals with triethylsilane. It should be noted that



Scheme 1.

Table 3. One Pot Synthesis of Sulfides from Aldehydes



Entry	R^1	R^2	R^3	Temp/°C	Product	Yield/%
1	Ph	H	Et	−23→R.T.	**8**	87
2	Ph	H	^{i}Pr	0→R.T.	**9**	83
3	Ph	H	Ph	0→R.T.	**10**	82
4	$Ph(CH_2)_2$	H	Et	0→R.T.	**11**	81
5	$CH_3(CH_2)_7$	H	Et	R.T.	**12**	78
6	Ph	Me	Et	−78→R.T.	**13**	98
7	$-(CH_2)_5-$		Et	0→R.T.	**14**	93

the undesirable disproportionation of *O*-trimethylsilyl monothioacetal is restricted and effective activation of this mixed acetal in the reaction with Et_3SiH is realized by employing the novel catalyst system under extremely mild reaction conditions.

One-Pot Snythesis of Sulfides from Aldehydes. *O*-trimethylsilyl monothioacetals used in the first section are prepared by the reaction of aldehydes with trimethylsilyl alkyl(aryl) sulfide in the presence of a catalytic amount of TMSOTf or ZnI_2 and imidazole.[2] If this reaction is catalyzed by TMSCl–$InCl_3$, one pot synthesis of sulfides will be successfully achieved; namely aldehydes react with trimethylsilyl alkyl(aryl) sulfide under the influence of TMSCl and $InCl_3$ to generate *O*-trimethylsilyl monothioacetals in situ, which are readily reduced by Et_3SiH to afford the corresponding sulfides.

According to this hypothesis, benzaldehyde was successively treated with trimethylsilyl alkyl(aryl) sulfide and Et_3SiH in the presence of a catalytic amount of TMSCl–$InCl_3$. The reaction smoothly proceeded to give the corresponding sulfide in 87% yield. Similarly, other aldehydes and ketones can be converted to the corresponding sulfides in high yields according to the present procedure (Table 3). It is noteworthy that the yields of the sulfides by this one pot synthesis consisting of two successive reactions are improved in most cases compared with those of the reaction of *O*-trimethylsilyl monothioacetals with Et_3SiH.

Though several methods for the preparation of sulfides have been reported, one pot synthesis from aldehydes is rare.[8] The present reaction provides a convenient route to sulfides from aldehydes under extremely mild reaction conditions. Current work to develop other useful synthetic reactions employing this novel catalyst system is now in progress.

Experimental

IR spectra were recorded on Horiba FT-300 infrared spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-1100, R-1200, or JEOL JNR-EX270L spectrometer, and tetramethylsilane (TMS) served as internal standard. Column chromatography was performed on Silica gel 60 (Merck) or Wakogel B5F. All reactions were carried out under argon atmosphere in dried glassware.

Indium(III) chloride ($InCl_3$) was purchased from Soekawa Rika Co., Ltd., and was used without further purification. Trimethylsilyl chloride (TMSCl) was distilled before use and was stored as 0.25 M (1 M=1 mol dm^{-3}) dichloromethane solution.

O-trimethylsilyl monothioacetals **1**—**3** and **7** were prepared from the corresponding aldehydes according to the literature.[2] Similarly, other *O*-trimethylsilyl monothioacetals **4** and **5** were synthesized. In the synthesis of **6**, zinc(II) iodide (ZnI_2) was used instead of trimethylsilyl trifluoromethanesulfonate (TMSOTf).

1-Ethylthio-1-trimethylsiloxy-3-phenylpropane (4). Bp 86—89 °C (0.2 mmHg, 1 mmHg=133.322 Pa); IR (neat) 1100, 840 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.13 (s, 9H), 1.24 (t, 3H, J=7.2 Hz), 1.82—2.25 (m, 2H), 2.29—2.89 (m,4H), 4.73 (t, 1H, J=6.0 Hz), 7.13—7.33 (m, 5H). Found: C, 62.42; H, 9.11; S, 11.67%. Calcd for $C_{14}H_{24}OSSi$: C, 62.63; H, 9.01; S, 11.94%.

1-Ethylthio-1-trimethylsiloxynonane (5). Bp 76—77 °C (0.15 mmHg); IR (neat) 2960, 1250, 1090, 870 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.14 (s, 9H), 0.84—1.94 (m, 20H), 2.54 (q, 2H, J=6.0 Hz), 4.67 (t, 1H, J=6.0 Hz). Found: C, 60.50; H, 11.93; S, 11.38%. Calcd for $C_{14}H_{32}OSSi$: C, 60.80; H, 11.66; S, 11.59%.

1-Ethylthio-1-phenyl-1-trimethylsiloxyethane (6). Bp 73—75 °C (0.50 mmHg); IR (neat) 1140, 850 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.25 (s, 9H), 0.99 (t, 3H, J=6.6 Hz), 1.84 (s, 3H), 2.16 (t, 2H, J=6.6 Hz), 6.80—7.30 (m, 5H). Found: C, 61.21; H, 8.88; S, 12.02%. Calcd for $C_{13}H_{22}OSSi$: C, 61.36; H, 8.71; S, 12.60%.

A Typical Procedure for the Synthesis of Sulfides from *O*-Trimethylsilyl monothioacetal. A typical procedure is described for the reaction of 1-ethylthio-1-phenyl-1-trimethylsiloxyethane (**2**) with Et_3SiH; to a suspension of $InCl_3$ (0.056 mmol) in dichloromethane (1 ml) was added 0.25 M (1 M=1 mol dm^{-3}) dichloromethane solution of TMSCl (0. 14 mmol), and the reaction mixture was stirred for 30 min at room temperature. Then **2** (0.28 mmol) in dichloromethane (1 ml) and triethylsilane (0.34 mmol) in dichloromethane (1 ml) was successively added and the reaction mixture was further stirred for 5 h at room temperature. Then aqueous sodium hydrogen carbonate was added at 0 °C and the aqueous layer was extracted with dichloromethane. The organic layer was washed with brine and dried over $MgSO_4$. After the removal of the solvents under reduced pressure, benzyl ethyl sulfide (**8**)[4] was isolated by thin layer chromatography on silica gel (83% yield). IR (neat) 2950, 1450, 700 cm^{-1}; ^{1}H NMR

($CDCl_3$) δ=1.22 (t, 3H, J=7.3 Hz), 2.43 (q, 2H, J=7.3 Hz), 3.71 (s, 2H), 7.21—7.38 (m, 5H).

A Typical Procedure of the One Pot Synthesis of Sulfides from Aldehydes. A typical procedure is described for the one pot synthesis of benzyl ethyl sulfide (**8**) from benzaldehyde; to a suspension of $InCl_3$ (0.071 mmol) in dichloromethane was added 0.25 M dichloromethane solution of TMSCl (0.17 mmol) and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was cooled down to −23 °C, and benzaldehyde (0.35 mmol) in dichloromethane (1 ml), ethylthiotrimethylsilane (**18**, 0.42 mmol) in dichloromethane (1 ml) and Et_3SiH (0.42 mmol) in dichloromethane (1 ml) were successively added. The mixture was further stirred for 5 h at room temperature, then aqueous sodium hydrogen carbonate was added at 0 °C and the aqueous layer was extracted with dichloromethane. The organic layer was washed with brine and dried over $MgSO_4$. After the removal of the solvents under reduced pressure, benzyl ethyl sulfide (**8**) was isolated by thin layer chromatography on silica gel (87% yield).

Other spectral data are presented below.

Benzyl 2-Propyl Sulfide (9). IR (neat) 2950, 1450, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.25 (d, 6H, J=6.6 Hz), 2.72—2.84 (m, 1H), 3.74 (s, 2H), 7.19—7.34 (m, 5H). Found: C, 72.23; H, 8.65; S, 19.43%. Calcd for $C_{10}H_{14}S$: C, 72.23; H, 8.49; S, 19.28%.

Benzyl Phenyl Sulfide (10).[8] IR (neat) 1450, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.10 (s, 2H), 7.15—6.31 (m, 10H).

Ethyl 3-Phenylpropyl Sulfide (11). IR (neat) 2900, 1450, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.24 (t, 3H, J=7.3 Hz), 1.85—1.96 (m, 2H), 2.49—2.57 (m, 4H), 2.72 (t, 2H, J=7.7 Hz), 7.15—7.31 (m, 5H). Found: C, 72.80; H, 8.92; S, 17.70%. Calcd for $C_{11}H_{16}S$: C, 73.27; H, 8.94; S, 17.78%.

Ethyl Nonyl Sulfide (12). IR (neat) 2920 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.70—1.82 (m, 20H), 2.14—2.65 (m, 4H). Found: C, 70.19; H, 13.01; S, 16.75%. Calcd for $C_{11}H_{24}S$: C, 70.14; H, 12.84; S, 17.02%.

Ethyl 1-Phenylethyl Sulfide (13).[9] IR (neat) 2970, 700 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.10 (t, 3H, J=7.2 Hz), 1.48 (d, 3H, J=7.8 Hz), 2.22 (q, 2H, J=8.4 Hz), 3.86 (q, 1H, J=8.4 Hz), 7.00—7.35 (m, 5H).

Ethyl Cyclohexyl Sulfide (14).[4] IR (neat) 2930 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.03—2.13 (m, 13H), 2.25—2.80 (m, 3H).

The present research is partially supported by Grant-in Aids for Scientific Research on Priority Areas (Multiplex Organic Systems) from Ministry of Education, Science and Culture.

References

1) T. Mukaiyama and M. Murakami, *Synthesis,* **1987**, 1043; T. Mukaiyama, K. Wariishi, M. Furuya, and S. Kobayashi, *Chem. Lett.,* **1989**, 1277.

2) M. B. Sassaman, G. K. S. Prakash, and G. A. Olah, *Synthesis,* **1990**, 104, and references cited therein.

3) T. Mukaiyama, T. Ohno, T. Nishimura, J. S. Han, and S. Kobayashi, *Chem. Lett.,* **1990**, 2239.

4) M. B. Sassaman, G. K. S. Prakash, and G. A. Olah, *Tetrahedron,* **44**, 3771 (1988).

5) N. Iwasawa and T. Mukaiyama, *Chem. Lett.,* **1987**, 463; T. Mukaiyama, K. Wariishi, Y. Saito, M. Hayashi, and S. Kobayashi, *Chem. Lett.,* **1988**, 1101.

6) T. Mukaiyama, S. Kobayashi, M. Tamura, and Y. Sagawa, *Chem. Lett.,* **1987**, 491; T. Mukaiyama, H. Sugumi, H. Uchiro, and S. Kobayashi, *Chem. Lett.,* **1988**, 1291.

7) Trityl salts are efficient activators of dithioacetals. M. Ohshima, M. Murakami, and T. Mukaiyama, *Chem. Lett.,* **1985**, 1871; **1986**, 1593.

8) R. S. Glass reported conversion of aldehydes into sulfides using a trimethyisilyl alkyl sulfide and "mixed hydride" (lithium aluminum hydride and aluminum chloride in 1 : 3.3—4.0 molar ratio). R. S. Glass, *Synth. Commun.,* **6**, 47 (1976).

9) T. Mukaiyama, T. Izawa, K. Saigo, and H. Takei, *Chem. Lett.,* **1973**, 355.