CHEMISTRY LETTERS, pp. 2239-2242, 1990.

# An Effective Activation of O-Trimethylsilyl Monothioacetal under Extremely Mild Conditions Using a Novel Catalyst System, Trimethylsilyl Chloride and Indium(III) Chloride

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

A novel catalyst system, trimethylsilyl chloride and indium(III) chloride, effectively catalyzes the reaction of O-trimethylsilyl monothioacetals with triethylsilane and silylated carbon nucleophiles, respectively, to afford the corresponding sulfide derivatives in good to high yields.

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 are generally difficult because of their readiness of disproportionation under acidic conditions, and hitherto only a few examples of the reactions of O-trimethylsilyl monothioacetals with nucleophiles were reported.$^{2)}$

In the course of our investigations to develop new preparative method for thiols from carbonyl compounds, reduction of O-trimethylsilyl monothioacetals was investigated.$^{3)}$ In this communication, we would like to describe a novel catalyst system, *trimethylsilyl chloride (TMSCl) and indium(III) chloride* (*$InCl_3$*), which effectively catalyzes the reaction of O-trimethylsilyl monothioacetals with triethylsilane ($Et_3SiH$) and some silylated carbon nucleophiles.

In the first place, the reaction of 1-ethylthio-1-trimethylsiloxy-3-phenylpropane (**1**) 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 even after examination of reaction conditions as solvent, reaction temperature, amount of promoter, etc. (Table 1, entries 1-3). Under these conditions disproportionation took place quite readily to form the corresponding dithioacetal, which resisted the desired reduction reaction. Trimethylsilyl triflate (TMSOTf) or trimethylsilyl iodide (TMSI), which was reported to be an effective catalyst in the reaction of ethylthio(phenyl)-trimethylsiloxymethane (**2**) or 1-ethylthio-1-trimethylsiloxycyclohexane with trimethylsilane,$^{4)}$ did not work well when more stable $Et_3SiH$ was used in the same reaction (Table 1, entries 4 and 5). These results indicated that, under these reaction conditions of employing the above Lewis acids, the reaction systems were so acidic that the disproportionation proceeded faster than the desired reduction. 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 and Michael reactions of silyl enol ethers with aldehydes and α, β-unsaturated ketones. These catalysts, consisting of a neutral molecule and a weak Lewis acid, smoothly promote the reactions under mild conditions. The catalyst, TMSCl-$SnCl_2$, was not effective in the present reaction (Table 1, entry 6),[7)] however, after screening several weak Lewis acids other than $SnCl_2$, ***Indium(III) chloride*** was found to be very effective. The desired sulfide was obtained in 68% yield when a novel catalyst system, ***TMSCl-InCl$_3$***, was employed (Table 1, entry 7).

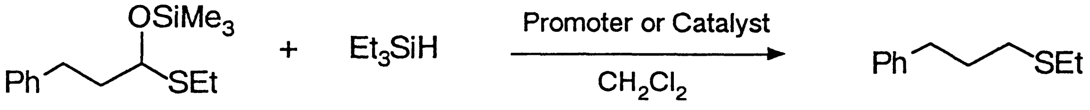


Table 1. Effect of Promoter or Catalyst

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

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

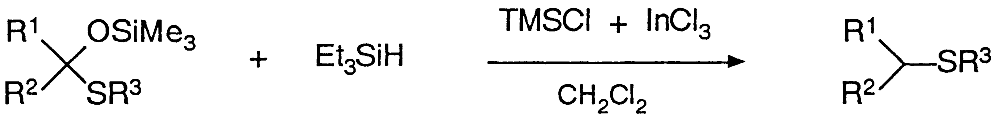
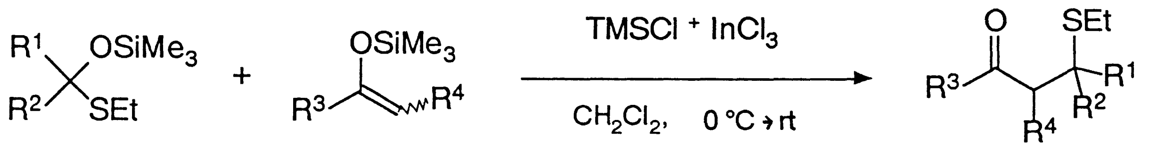


Table 2. Synthesis of Sulfides

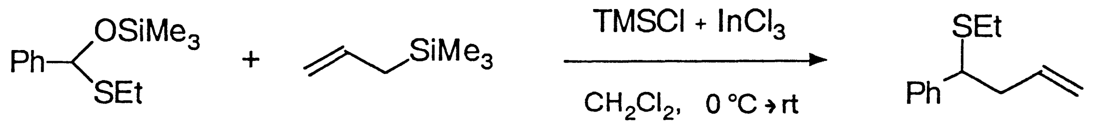
| Entry | $R^1$ | $R^2$ | $R^3$ | Temp/ °C | Yield/% |
|---|---|---|---|---|---|
| 1 | Ph | H | Et | rt | 83 |
| 2 | Ph | H | $^{i}Pr$ | 0 → rt | 88 |
| 3 | Ph | H | Ph | rt | 77 |
| 4 | $Ph(CH_2)_2$ | H | Et | rt | 68 |
| 5 | $CH_3(CH_2)_7$ | H | Et | rt | 70 |
| 6 | Ph | Me | Et | rt | 97 |
| 7 | $-(CH_2)_5-$ | | Et | 0 → rt | 96 |

A typical experimental procedure is described for the reaction of 1-ethylthio-1-phenyl-1-trimethylsiloxyethane (**2**) with triethylsilane; to a suspension of $InCl_3$ (0.056 mmol) in dichloromethane (1 ml) was added 0.25 M dichloromethane solution of TMSCl (0.14 mmol), and the reaction mixture was stirred for 30 min at rt. 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 rt. After usual work up, ethyl benzyl sulfide was obtained in 83% yield.

This novel catalyst system, TMSCl-$InCl_3$, is also successfully employed in the important carbon-carbon bond forming reactions. Silyl enol ethers or allyltrimethylsilane smoothly react with O-trimethylsilyl monothioacetals to afford the corresponding sulfide derivatives, versatile intermediates in organic synthesis,$^{8)}$ in fairly good yields.



| | |
|---|---|
| $R^1$=Ph, $R^2$=H, $R^3$=Ph, $R^4$=Me | 83% yield |
| $R^1$=Ph, $R^2$=H, $R^3$=$R^4$=-$(CH_2)_4$- | 70% yield |
| $R^1$=Ph, $R^2$=H, $R^3$=SEt, $R^4$=H | 63% yield |
| $R^1$=$R^2$=-$(CH_2)_4$-, $R^3$=Ph, $R^4$=Me | 45% yield |



60% yield

Though the precise structure of TMSCl-$InCl_3$ is not yet clear, we assumed the generation of the cationic species shown below similar to the cases of TMSCl-$SnCl_2$ and TrCl-$SnCl_2$. It is pointed out that, in the present reductions, neither TMSCl nor $InCl_3$ is effective and the reactions proceed only when TMSCl and $InCl_3$ are combined.

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

undesirable disproportionation of O-trimethylsilyl monoacetal is restrained and effective activation of this mixed acetal is effectively promoted by employing the novel catalyst system under extremely mild reaction conditions.

Further investigations toward direct synthesis of thiols from aldehydes as well as to develop novel synthetic reactions using this novel catalyst system, are now in progress.

The present research is partly supported by Grant-in-Aids for Scientific Research No. 01649008 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) R. S. Glass reported conversion of aldehydes into sulfides using a alkylthiosilane 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).

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, *ibid.*, **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, *ibid.*, **1988**, 1291.

7) In the presence of 10 mol% each of TMSCl and $SnCl_2$, **2** smoothly reacts with $Et_3SiH$ at rt to give the corresponding sulfide in 63% yield.

8) M. T. Reetz and A. Giannis, *Synth. Commun.*, **11**, 315 (1981); B. M. Trost and E. Murayama, *J. Am. Chem. Soc.*, **103**, 6529 (1981); M. Ohshima, M. Murakami, and T. Mukaiyama, *Chem. Lett.*, **1985**, 1871; **1986**, 1593.

( Received October 1, 1990 )