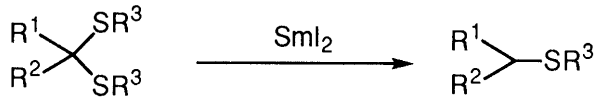
# REDUCTION OF DITHIOACETALS WITH $SmI_2$ IN BENZENE–HMPA

Munetaka KUNISHIMA,* Daisuke NAKATA, Kazuhito HIOKI, and Shohei TANI*
*Faculty of Pharmaceutical Sciences, Kobe Gakuin University, Nishi-ku, Kobe 651-2180, Japan.*

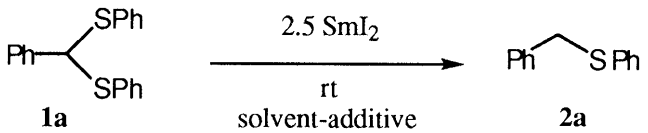
Partial reduction of dithioacetals to the corresponding sulfides was effected by samarium iodide in the presence of either *t*-BuOH or acetic acid in benzene–HMPA. An α-sulfenyl anion was shown to be involved.
**KEY WORDS** samarium iodide; dithioacetals; sulfides; reduction

Over the past two decades, a wide range of organic functional groups has been shown to be reduced with samarium iodide ($SmI_2$).[1] Reductions of sulfur-containing functional groups, deoxygenation of sulfoxides and sulfones,[2] reductive elimination of sulfenyl or sulfinyl groups at the α-position of a carbonyl group,[3] desulfonylation of various sulfones,[3,4] and desulfurization or reduction of isothiocyanates have been reported.[5] Reduction of ketene dithioacetals with an alkoxycarbonyl group in the α-position with $SmI_2$ was shown to proceed stereoselectively to give vinyl samarium species.[6] However, there is no report, to our knowledge, on the reduction of simple dithioacetals with $SmI_2$. Here, we report the first example of the reduction of dithioacetals to sulfides with $SmI_2$ in benzene–HMPA.




As shown in Table 1, reaction of **1a** with $SmI_2$ (2.5 eq) in benzene containing 5% hexamethylphosphoric triamide (HMPA) gave the corresponding sulfide (**2a**), albeit in low yield, along with a significant amount of recovered **1a**.[7,8] A similar result was observed in the reaction conducted in THF or acetonitrile. Interestingly, both the yield and reaction rate increased dramatically with the addition of *t*-BuOH (2.0 eq) to the benzene–HMPA system. The yield of **2a** was also improved in THF by addition of the alcohol, whereas the reaction was completely suppressed in acetonitrile. The results of the synthesis of sulfides by the partial reduction of dithioacetals under the conditions of benzene–HMPA containing a variety of additives including *t*-BuOH are summarized in Table 2.[9] The reactions were allowed to continue until either

**Table 1. Attempts to Reduce Dithioacetal with $SmI_2$**



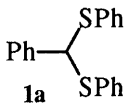
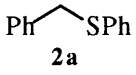
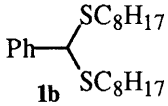
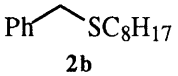
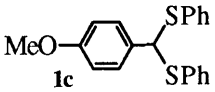
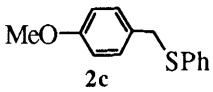
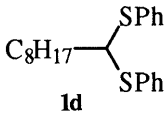
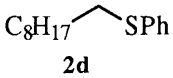
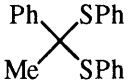
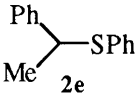
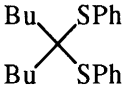
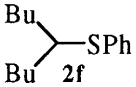

**1a** **2a**

| Run | Solvent | Additive | Time | Yield |
|---|---|---|---|---|
| 1 | Benzene-HMPA | None | 72 h | 17% |
| 2 | THF-HMPA | None | 42 h | 28% |
| 3[a)] | $CH_3CN$-HMPA | None | 2 h | 15% |
| 4 | Benzene-HMPA | *t*-BuOH | 45 min | 85% |
| 5 | THF-HMPA | *t*-BuOH | 26 h | 69% |
| 6[a)] | $CH_3CN$-HMPA | *t*-BuOH | 1 h | 0% |

*a*) 5 eq of $SmI_2$ was used.

* To whom correspondence should be addressed.

**Table 2. Reduction of Dithioacetals in Benzene–HMPA–Additive**[a]

| Run | Dithioacetals | Sulfide | Additive | Conditions | Yield (%)[b] | Recovery (%) |
|---|---|---|---|---|---|---|
| 1 |  **1a** |  **2a** | *t*-BuOH (2 eq) | rt, 45 min | 85 (85) | 0 |
| 2 | | | AcOH (2 eq) | rt, 96 h | 49 (92) | 47 |
| 3 |  **1b** |  **2b** | *t*-BuOH (2 eq) | rt, 29 h | 59 | –[e] |
| 4 | | | AcOH (2 eq) | rt, 24 h | 57 (76) | 25[d] |
| 5 |  **1c** |  **2c** | *t*-BuOH (2 eq) | rt, 1 h | 83 (99) | 16[c,d] |
| 6 |  **1d** |  **2d** | *t*-BuOH (2 eq) | rt, 96 h | 61 (75) | 19[c] |
| 7 | | | *t*-BuOH (2 eq) | 40°, 44 h | 23 (52) | 56[c] |
| 8 | | | None | 50°, 74 h | 59 (79) | 26[c] |
| 9 | | | None | Reflux, 24 h | 39 (45) | 14[c] |
| 10 | | | iso-PrOH (2 eq) | rt, 96 h | 38 (75) | 49[c] |
| 11 | | | EtOH (2 eq) | rt, 96 h | 47 (76) | 38[c] |
| 12 | | | $SnCl_4$ (1 eq) | rt, 10 min | 0 | 100 |
| 13 | | | $AlCl_3$ (2 eq) | rt, 67 h | 23 (96) | 76 |
| 14 | | | CuI (1 eq) | rt, 69 h | 5 (100) | 95 |
| 15 | | | TsOH (1.2 eq) | rt, 3 h | 0 | 100 |
| 16 | | | AcOH (2 eq) | rt, 96 h | 80 (88) | 9[c] |
| 17 |  **1e** |  **2e** | *t*-BuOH (2 eq) | rt, 1 h | 65 | –[e] |
| 18 | | | AcOH (2 eq) | rt, 5 min | 71 (79)[c,d] | 10[c,d] |
| 19 |  **1f** |  **2f** | *t*-BuOH (2 eq) | rt, 73 h | 69 (95)[c,d] | 27[c,d] |

*a*) All reactions were performed with 5 eq of $SmI_2$ in benzene–HMPA except for Run 1 where 2.5 eq of $SmI_2$ was used. For the standard procedure, see text. *b*) Isolated yield unless noted otherwise; yields in parentheses are based on conversion of **1**. *c*) Isolated as a mixture of PhSSPh. Yield was determined by $^1$H NMR. *d*) Isolated as a mixture of **1** and **2**. Yield was determined by $^1$H NMR. *e*) Yield was not determined. rt, room temperature.

disappearance of the purple color of $SmI_2$ or the starting material was no longer detectable on tlc. With *t*-BuOH as an additive, the reduction proceeded in moderate to good yield. While the reduction of dithioacetals derived from aromatic aldehydes or ketones proceeded relatively fast (Runs 1, 3, 5, 17), dithioacetals of aliphatic carbonyl compounds required a longer reaction time (Runs 6, 19). A cyclic dithioacetal, 2-phenyl-1,3-dithiane, was not subject to reduction under these conditions.

In order to accelerate the reduction of **1d**, which was found to be reduced slowly, the reaction was performed at 40°C (Run 7). However, the yield of **2d** decreased with the increasing recovery of **1d**, probably due to promoting the reaction of the alcohol with $SmI_2$. When the reaction was carried out without the alcohol at a higher temperature, the yield was not improved in spite of consumption of **1d** (Runs 8, 9).[10] Several additives were examined (Runs 10–16). With both ethanol and

isopropyl alcohol, **2d** was afforded in a yield lower than that with *t*-BuOH (Runs 6, 10, 11). Although some Lewis acids and *p*-toluenesulfonic acid (TsOH) were found to be ineffective for the reduction, AcOH was shown to be comparable to *t*-BuOH. The results for the reaction with AcOH are also summarized in Table 2 (Runs 2, 4, 16, 18).

When the reduction of **1a** with $SmI_2$ was conducted using *t*-BuOD followed by quenching with $D_2O$, 96% deuterium was incorporated at the benzylic position of **2a**.[11] This result indicates the generation of an α-sulfenyl anion resulting from reductive cleavage of a carbon–sulfur bond of dithioacetals.

Since dithioacetals can be easily prepared from ketones or aldehydes,[12] the present reaction appears to be a useful procedure for conversion of carbonyl compounds into sulfides under mild and nonbasic conditions.[13]

For a typical procedure: a solution of **1a** (100 mg, 0.32 mmol) in benzene (1 ml) was added to a solution of $SmI_2$ (19.3 ml of 0.042 mol/l in benzene–HMPA, 0.81 mmol) under a $N_2$ atmosphere, followed by addition of *t*-BuOH (48.1 mg, 0.64 mmol) in 1 ml benzene. After stirring for 45 min at room temperature, the mixture was poured into saturated $NaHCO_3$ and extracted with ether. The organic layer was dried and concentrated to give a crude mixture, which was purified by silica gel column chromatography (hexane).

**References and Notes**


1) For recent reviews on $SmI_2$, see: *a)* Molander G. A., *Org. React.*, **46**, 211-367 (1994); *b)* Molander G. A., Harris, C. R., *Chem Rev.*, **96**, 307-338 (1996).
2) Girard P., Namy J. L., Kagan H. B., *J. Am. Chem. Soc.*, **102**, 2693-2698 (1980); Handa Y., Inanaga J., Yamaguchi M., *J. Chem. Soc., Chem. Commun.*, **1989**, 298-299.
3) Molander G. A., Hahn G., *J. Org. Chem.*, **51**, 1135-1138 (1986); Arai Y., Matsui M., Koizumi T., *J. Chem. Soc., Perkin Trans. 1*, **1990**, 1233-1234.
4) Kende A. S., Mendoza J. S., *Tetrahedron Lett.*, **31**, 7105-7108 (1990); Künzer H., Stahnke M., Sauer G., Wiechert R., *Tetrahedron Lett.*, **32**, 1949-1952 (1991); Trost B. M., Neilsen J. B., Hoogsteen K., *J. Am. Chem. Soc.*, **114**, 5432-5434 (1992); Pouilly P., Chénedé A., Mallet J.-M., Sinaÿ P., *Tetrahedron Lett.*, **33**, 8065-8068 (1992); Ihara M., Suzuki S., Taniguchi T., Tokunaga Y., Fukumoto K., *Synlett*, **1994**, 859-860; Urban D., Skrydstrup T., Riche C., Chiaroni A., Beau J.-M., *Chem. Commun.*, **1996**, 1883-1884.
5) Liu Y.-S., Bei M.-Z., Zhou Z.-H., Takai K., Fujiwara Y., *Chem. Lett.*, **1992**, 1143-1144; Park H. S., Lee I. S., Kim Y. H., *Chem. Commun.*, **1996**, 1805-1806.
6) Hojo M., Harada H., Yoshizawa J., Hosomi A., *J. Org. Chem.*, **58**, 6541-6542 (1993).
7) CAUTION: Since both benzene and HMPA are potent carcinogens, care should be taken in their use.
8) For the synthesis and reactions of $SmI_2$ in the benzene–HMPA system, see: Kunishima M., Hioki K., Ohara T., Tani S., *J. Chem. Soc., Chem. Commun.*, **1992**, 219-220; Kunishima M., Hioki K., Kato A., Tani S., *Tetrahedron Lett.*, **35**, 7253-7254 (1994); Kunishima M., Hioki K., Kono K., Sakuma T., Tani S., *Chem. Pharm. Bull.*, **42**, 2190-2192 (1994); Kunishima M., Hioki K., Kono K., Kato A., Tani S., *J. Org. Chem.*, **62**, 7542-7543 (1997); Ref. 1*a*).
9) Although 2 eq of $SmI_2$ should be mechanistically sufficient for the reaction, an excess of $SmI_2$ (2.5 or 5.0 eq) was actually used because $SmI_2$ gradually decomposed during a long period of reaction probably due to contamination with air.
10) Since **2d** was found to undergo slow reduction with $SmI_2$ under similar reaction conditions, the low yields of **2d** can be attributed to further reduction.
11) Determined by proton NMR.
12) Greene T. W., Wuts P. G. M., "Protective Groups in Organic Synthesis," 2nd ed., John Wiley & Sons, Inc., New York, 1991, pp. 198-207.
13) For conversion of dithioacetals into sulfides, see: Krief A., Kenda B., Barbeaux P., *Tetrahedron Lett.*, **32**, 2509-2512 (1991); Ikehira H., Tanimoto S., Oida T., *J. Chem. Soc., Perkin Trans. 1*, **1984**, 1223-1226; Kikugawa Y., *J. Chem. Soc., Perkin Trans. 1*, **1984**, 609-610; Cohen T., Daniewski W. M., Weisenfeld R. B., *Tetrahedron Lett.*, **1978**, 4665-4668.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