

A New Entry for the Deprotection of Monothioacetals and Dithioacetals: Silver Nitrite - Iodine System

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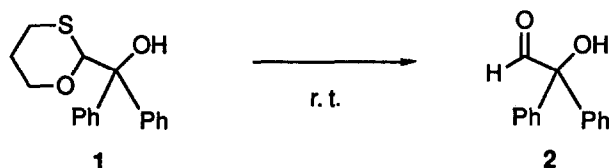
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Abstract: A new reagent system (silver nitrite-iodine) was developed for demonothioacetalization and dedithioacetalization reactions. The reaction using this reagent afforded the parent carbonyl compound in excellent yield under mild conditions.

1,3-Oxathiane is a versatile conjunctive reagent for the carbon-carbon bond formation reaction as an acyl anion equivalent¹. A landmark was established by Eliel² and Utimoto³ groups that a chiral 1,3-oxathiane could be used in the enantioselective synthesis of α -hydroxyaldehyde. Compared to many deprotective methods⁴ of 1,3-dithiolanes and 1,3-dithianes, a few methods are known for 1,3-oxathiolanes or 1,3-oxathianes. Deprotection of 1,3-oxathiolanes or 1,3-oxathianes using Raney nickel needs harsh reaction conditions and is contaminated with by-products in some cases because of its radical process.⁵ Hydrolysis by mineral acids requires the drastic conditions to give the ketones in moderate yields.⁶ Reactions using isoamyl nitrite⁷ or chloramine-T⁸ afford the parent carbonyl compound under mild reaction conditions, but isolated examples of simple 1,3-oxathiolanes are documented. The Corey's method (NCS-AgNO₃)⁹ was applied to deprotection of 2-hydroxyalkyl-1,3-oxathianes in moderate yields of desired α -hydroxyaldehydes (62-65 %).^{2a, 2c} The use of conventional mercuric chloride for the deprotection of the same type of 1,3-oxathiane gave the corresponding aldehyde in 54 % yield.^{2d} These facts prompted us to develop more effective reagent for the deprotection of monothioacetals. We envisioned that iodo cation would have more stronger affinity (soft acidity) to sulfur atom than chloro cation in the Corey's system, and furthermore, iodo cation could be generated from iodine assisted by silver cation. Here we describe the development of new reagent system for deprotection of monothioacetals as well as dithioacetals.

We found that silver nitrite-iodine¹⁰ system was effective for the desired transformation.¹¹ Although several aqueous solvents could be used, THF was the solvent of choice to give benzophenone from 2,2-diphenyl-1,3-dithiane in quantitative yield. The comparison of this reagent system to the known methods is shown in Table 1. Isoamyl nitrite and silver nitrate-NCS caused the desired reaction in moderate yields.

Table 1. Comparison of Deprotective Reagents on 2-(Diphenylhydroxymethyl)-1,3-Oxathiane

Reagent	Molar. eq.	Solvent	Time (h)	Yield (%)
<i>iso</i> -Amyl Nitrite	1	CH ₂ Cl ₂ , H ₂ O	20	49
AgNO ₃ - NCS (1 : 1)	2	aq. CH ₃ CN	2	75
AgNO ₂ - I ₂ (1 : 0.5)	1.2	aq. THF	5	92
AgClO ₄ - I ₂ (1 : 1)	1.2	aq. THF	10 min.	94

Silver nitrite-iodine and silver perchlorate-iodine systems were excellent. Especially in silver perchlorate-iodine system the reaction proceeded quickly, however, possibility of explosion is suspected in a large scale so that we recommend silver nitrite-iodine system.

Results of demonothioacetalization and dedithioacetalization reactions using the new reagent system were summarized in Table 2. Yields of deprotective reactions were generally high. The deprotection of aromatic aldehydes or ketones proceeded smoothly than those of aliphatic aldehydes or ketones. The reactions proceeded in almost same reaction times on 1,3-oxathiolane 4 and 1,3-oxathiane 7. Ester and lactone in 5 remained intact, for which six equivalents of the reagents were used. A chiral 1,3-oxathiolane 6 was converted into (-)-menthone without loss of optical purity. The low yield in 14 is presumably due to the rearrangement of norkaurane skeleton.

In the deprotective reaction of 1, use of iodine, silver iodide, silver nitrite, or silver perchlorate alone gave no desired product but a complex mixture. The combination of silver salt and iodine was essential. These facts indicate that a possible mechanism of this reaction is the oxidation of sulfur with iodo cation as illustrated in the Scheme.

In summary we developed a new reagent system (silver nitrite-iodine) for the deprotection of monothioacetals and dithioacetals. The yields using this system were excellent in general. Particularly the yield of 2-hydroxy-2,2-diphenylethanal (2) using new reagent system was best among the other known methods so far. Work-up of the reaction mixture and purification of the product are very easy, because both of the reagents are inorganic materials so that no contamination of organic materials from the reagents occurs.

A Typical Procedure: A suspension of silver nitrite (28 mg, 0.18 mmol) and iodine (23 mg, 0.09 mmol) in aqueous THF (1.0 mL) was stirred for 0.5 h at room temperature. 2-(Diphenylhydroxymethyl)-1,3-oxathiane (1) (45 mg, 0.15 mmol) was added and the resulting mixture was stirred for additional 5 h. A dilute sodium thiosulfate solution was added to the mixture at 0 °C, followed by

extraction with dichloromethane, washing with brine, drying (MgSO_4), concentration *in vacuo*. Preparative TLC on silica gel afforded 2-hydroxy-2,2-diphenylethanal (2) (31 mg, 92 %).

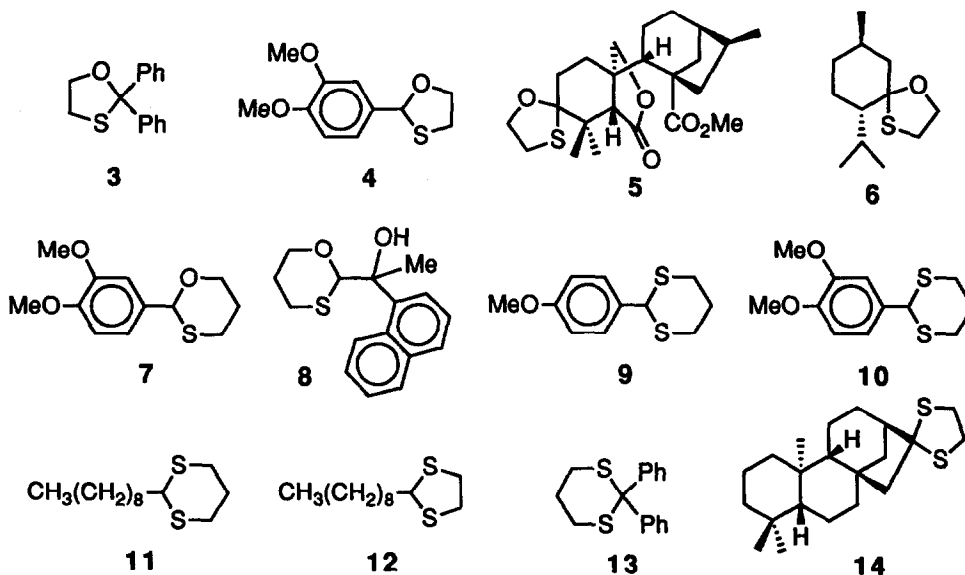
Table 2. Demonithioacetalization and Dedithioacetalization^{a)}

Run	Substrate	Silver Salt (equiv.)	Iodine equiv.	Time, h	Yield of Carbonyl Compound, % ^{b)}
1	3	$\text{AgNO}_2(2.0)$	1.0	0.5	96
2	4	$\text{AgNO}_2(2.4)$	1.2	5	83
3	5	$\text{AgNO}_2(6.0)$	3.0	3	84
4	6	$\text{AgNO}_2(2.4)$	1.2	2	57(67) ^{c)}
5	7	$\text{AgNO}_2(2.4)$	1.2	5	94
6	8	$\text{AgNO}_2(2.4)$	1.2	1	61
7	9	$\text{AgNO}_2(2.4)$	1.2	20 min	89
8	9	$\text{AgClO}_4(2.4)$	1.2	5 min	95
9	10	$\text{AgNO}_2(2.4)$	1.2	1.5	100
10	11	$\text{AgNO}_2(1.2)$	0.6	6	88
11	12	$\text{AgNO}_2(2.4)$	2.4	2.5	73
12	13	$\text{AgNO}_2(1.2)$	0.6	0.5	99
13	14	$\text{AgNO}_2(1.2)$	0.6	43	47
14	14	$\text{AgClO}_4(2.4)$	1.2	5 min	53

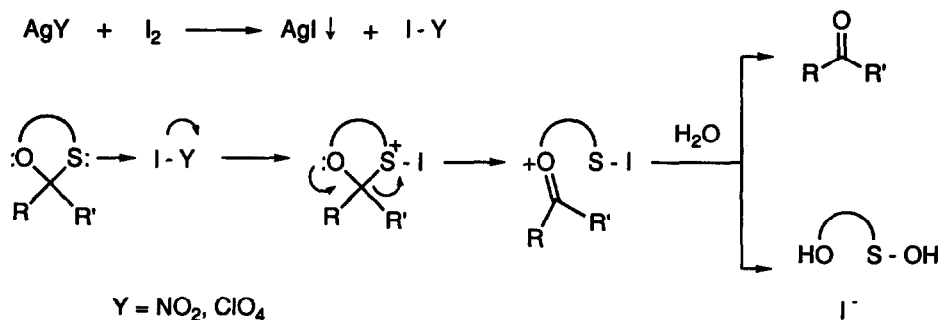
a) The reactions were done in THF at room temperature.

b) Isolated yields.

c) Calculated from NMR spectroscopy based on the internal standard.



Scheme. Possible Mechanism for Deprotection



ACKNOWLEDGMENT

Partial financial support of this research by the Ministry of Education, Science and Culture, Japan (No. 04671317 to M. N.) is gratefully acknowledged.

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(Received in Japan 17 March 1993)