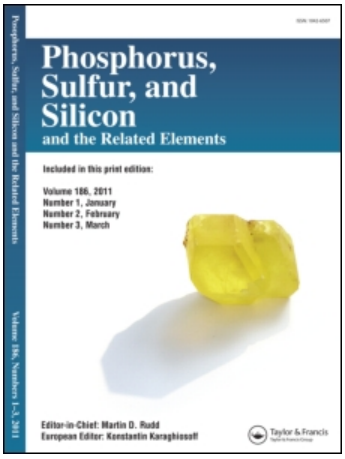

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Chemoselective Deprotection of Thioacetals/Thioketals Using HIO_3 in the Presence of Wet SiO_2 Under Mild Solvent-Free Conditions

Moslem M. Lakouraj[a]; Mahmood Tajbakhsh[a]; Farhad Shirini[b]; Mohammad V. Asady Tamami[b]
[a] Department of Chemistry, University of Mazandaran, Babolsar, Iran [b] Department of Chemistry, Guilan University, Rasht, Iran

To cite this Article Lakouraj, Moslem M. , Tajbakhsh, Mahmood , Shirini, Farhad and Tamami, Mohammad V. Asady(2005) 'Chemoselective Deprotection of Thioacetals/Thioketals Using HIO_3 in the Presence of Wet SiO_2 Under Mild Solvent-Free Conditions', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 11, 2423 — 2429
To link to this Article: DOI: 10.1080/104265090921146
URL: http://dx.doi.org/10.1080/104265090921146

Phosphorus, Sulfur, and Silicon, 180:2423–2429, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090921146

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Chemoselective Deprotection of Thioacetals/Thioketals Using HIO_3 in the Presence of Wet SiO_2 Under Mild Solvent-Free Conditions

Moslem M. Lakouraj
Mahmood Tajbakhsh
Department of Chemistry, University of Mazandaran, Babolsar, Iran

Farhad Shirini
Department of Chemistry, Guilan University, Rasht, Iran

Mohammad V. Asady Tamami
Department of Chemistry, University of Mazandaran, Babolsar, Iran

HIO_3 in the presence of wet SiO_2 is highly efficient and a mild reagent for selective deprotection of a variety of thioacetals/thioketals to the corresponding parent carbonyl compounds at room temperature and under solvent-free conditions.

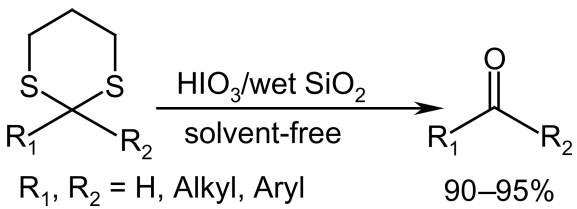
Keywords Carbonyl compounds; deprotection; HIO_3/wetSiO_2; solvent-free; thioacetals/thioketals

Carbonyl compounds often are protected as thioacetals and thioketals in organic synthesis,[1] particularly in multistep natural product synthesis,[2] due to their stability in both acidic and basic conditions. Several procedures are available in the literature for preparation of thioacetals and thioketals,[3] but their deprotection to the parent carbonyl compounds is not always an easy process. Many of the deprotection reactions require strong acidic[4] or oxidizing conditions using corrosive or toxic reagents.[5]

In addition, some chemical methods often require the use of heavy metal reagents such as Hg^{2+}, Ag^{+}, Tl^{3+}, Cd^{2+}, and Se^{4+}, which are inherently toxic and/or expensive to use.[6] In view of economical, practical, and recent environmental demands, there is a need for a simple, less

Received August 24, 2004; accepted October 26, 2004.
We are thankful to the Mazandaran University Research Council for their partial support of this work.
Address correspondence to Moslem M. Lakouraj, University of Mazandaran, Department of Chemistry, Faculty of Science, Babolsar 47415, Iran. E-mail: Lakouraj@umz.ac.ir

expensive, and safer method for deprotection of thioacetals and thioketals. On the other hand, recently, there has been an increasing interest in reactions that proceed in the absence of solvents due to their reduced pollution, low costs, and simplicity in process and handling.[7] More recently, we have introduced HIO_3 as a mild, inexpensive, and efficient reagent for the coupling of thiols and convenient regeneration of carbonyls from oximes and hydrazones.[8] We, herein, explored the utility of this reagent for selective deprotection of thioacetals and thioketals in the presence of wet SiO_2 under solvent-free condition (Scheme 1). This reagent is readily prepared by adding HIO_3 to wet SiO_2, which is stable and could be stored for months without any activity lost at room temperature. This easily handled reagent allows the conversion of thioacetals and thioketals to the corresponding carbonyl compounds under mild conditions.



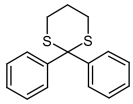
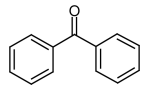
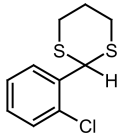
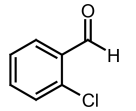
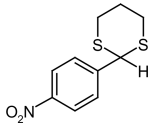
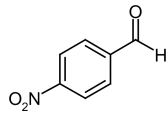
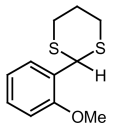
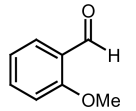
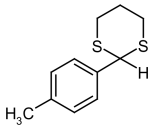
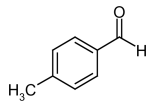
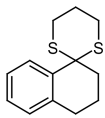
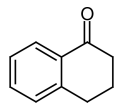
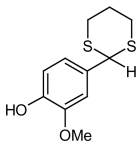
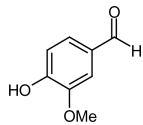
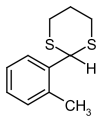
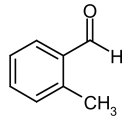
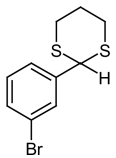
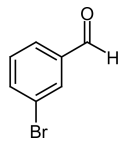
SCHEME 1

RESULTS AND DISCUSSION

As shown in Table I, a wide variety of thioacetals and thioketals are easily deprotected to the corresponding carbonyl compounds in high yields. The deprotection of 2,2-diphenyl-1,3-dithiane as the model compound was examined under solvent-free conditions at room temperature. The optimum ratio of thioacetals and thioketals to reagent (1:1) is found to be ideal for complete conversion of thioacetals and thioketals to aldehydes and ketones. By using this reagent, a variety of alkyl aryl, dialkyl, and diaryl thioacetals and thioketals were transformed to their corresponding aldehydes and ketones.

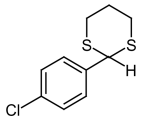
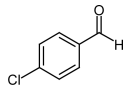
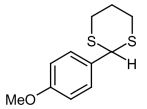
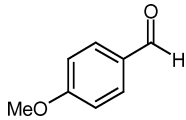
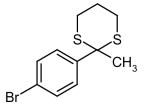
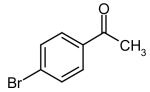
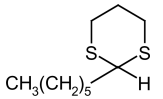
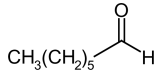
As evident from the results in Table I, most reactions proceed immediately and give excellent yields of products (entries 1, 2, 4–13). Electron-withdrawing groups such as NO_2 on the aromatic ring decrease the reaction rate (entry 3). We have also carried out this reaction in solvents such as dichloromethane, n-hexane, acetonitrile, and diethyl ether; the results show that the reaction proceeds more slowly and the yields are less than satisfactory even after hours.

TABLE I Deprotection of Thioacetals/Thioketals With HIO_3/Wet SiO_2 Under Solvent-Free Conditions[a]

Entry	Substrat	Products	Time (sec)	[b]yields (%)	m.p. or b.p. (°C) Found	m.p. or b.p. (°C) Reported[12]
1			50	95	48–50	48.5–49
2			75	93	212–213	212–214
3			520	90	104.5–106	106
4			50	94	34–36.5	35–37
5			55	93	105–106	106.10
6			25	92	—	113–116/6 mm
7			130	90	81.5–83	81–83
8			60	92	196–198	196–199
9			45	94	227.5–230	228–230

(Continued on next page)

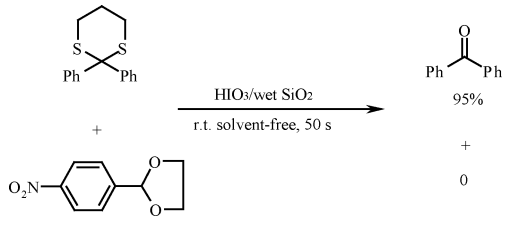
TABLE I Deprotection of Thioacetals/Thioketals With HIO_3/Wet SiO_2 Under Solvent-Free Conditions[a] *(Continued)*

Entry	Substrat	Products	Time (sec)	[b]yields (%)	m.p. or b.p. (°C) Found	m.p. or b.p. (°C) Reported[12]
10			30	90	46–47	47
11			47	93	247–248	248
12			40	93	59–61	59–60
13			25	94	153–155	153

[a]Reactions are carried out at room temperature using substrate/reagent (1:1) molar ratio.

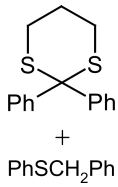
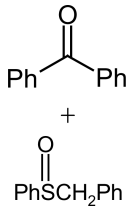
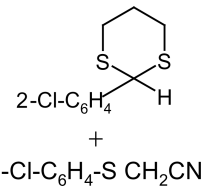
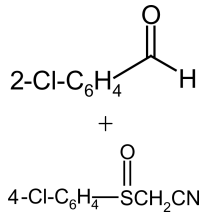
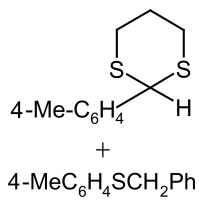
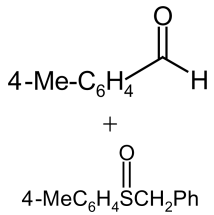
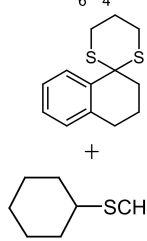
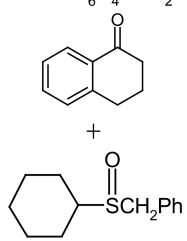
[b]Yields of isolated pure products.

We also have investigated the selective deprotection of thioacetals and thioketals in the presence of sulfides, acetals, and ketals. When one equimolar amount of a thioacetal or a thioketal is mixed with one equivalent of HIO_3/wet SiO_2, only thioketal or thioacetal is transformed to its carbonyl compound and the sulfide remained intact (Table II, entries 1–4). Similarly, when 2,2-diphenyl-1,3-dithiane in the presence of acetal and ketal was treated with HIO_3/wet SiO_2, only benzophenone was formed and the acetal or ketal remained unchanged (Schemes 2 and 3).

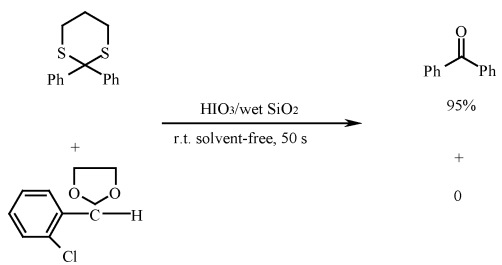


SCHEME 2

TABLE II The Competitive Reactions Between Deprotection of the Thioacetals and Thioketals, with Oxidation of Sulfides to Sulfoxides Using HIO_3/Wet SiO_2 Under Solvent-Free Condition[a]

Entry	Substrate	Products	Time (s)	Yields (%)
1			50	95 + 0
2			75	93 + 0
3			55	93 + 0
4			25	92 + 0

[a]Reactions are carried out at room temperature using substrate/reagent (1:1) molar ratio.



SCHEME 3

TABLE III Comparison of Our Method With Some of Those Methods Reported in the Literature for Deprotection of 2,2-diphenyl-1,3- dithiane(thioketal)[13]

Entry	Reagent/(Molar Ratio of Substrate/Reagent)	Condition	Yield (%)/ Time (min)
1	$PhCH_2Ph_3PHSO_5/BiCl_3$ (1:2)	CH_3CN, reflux[13a]	95/180
2	$Fe(NO_3)_3$/Montmorillonite K.10 (1:1)	Hexane, 50°C[13b]	98/10
3	IBX/ß-CD, (1:1)	H_2O, r.t.[13c]	88/240
4	TT, (1:0.5)	DMSO, r.t.[13d]	96/150
5	$NaNO_2$, (1:1)	$AcCl/H_2O$, 0–5°C CH_2Cl_2[13e]	90/45
6	**HIO_3/wet SiO_2(1:1)**	**Solvent-free, r.t.**	95/0.83

Deprotection of acetals and ketals need longer reaction time and give a low yield of the corresponding carbonyl compound.

In order to show the advantages of the method, we have compared the results of deprotection of 2,2-diphenyl-1,3-dithiane(thioketal) with some of those reported in the literature (Table III). As indicated in Table III, our method is very simple and gives excellent yields of products immediately after mixing the starting materials together.

In conclusion, We have introduced a new application for HIO_3 in the presence of wet SiO_2. A high yield of the products, the absence of the toxic waste disposal, short reaction times, mild reaction conditions, and selectivity of the method make this protocol an alternative to the existing methods.

EXPERIMENT

Chemicals were purchased from Merck, Fluka, and Aldrich Chemical companies. The carbonyl derivatives were prepared from the corresponding carbonyl compounds and 1,3-propanedithiol according to the reported procedures.[9] Products were separated and purified by different chromatographic techniques and were characterized by comparison of their spectral (IR, ^{1}H-NMR, and TLC) and physical data (m.p. and b.p.) with those of authentic samples.[10–12]

General Procedure

To a mixture of HIO_3, (0.176 g. 1 mmol) and wet SiO_2 [(SiO_2/H_2O; 20% ww), 0.08 g], was added thioacetal or thioketal (1 mmol). The resulting mixture was mixed throughly at room temperature for the

specified time (Table I). The reaction was monitored by TLC. After completion of the reaction, dichloromethane or diethyl ether (5 mL) and sodium thiosulfate solution were added to the mixture and the resultant mixture was filtered after 15 min. Anhydrous Na_2SO_4 was added to the filtrate and filtered. Evaporation of the solvent gave the corresponding aldehydes and ketones.

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