

N₂O₄/SiO₂ System as an Efficient Reagent for Rapid and Chemoselective Conversion of Trimethylsilyl Ethers to the Parent Alcohols under Nonaqueous Conditions

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(Received 3 May 2007, Accepted 23 June 2007)

N₂O₄ was easily impregnated on silica gel to give a stable heterogeneous reagent N₂O₄/SiO₂ (**I**). Chemoselective deprotection of trimethylsilyl ethers to the corresponding alcohols was achieved in the presence of **I** in CH₂Cl₂ in excellent yields. The stability, easy preparation and high selectivity of the reagent make this method as a useful procedure for the selective deprotection of TMS ethers at room temperature.

Keywords: Dinitrogen tetroxide, Silica gel, Deprotection, Trimethylsilyl ethers, Tetrahydropyranyl ethers, Alcohols

INTRODUCTION

Dinitrogen tetroxide and its complexes have found wide applications in organic transformations [1]. Apart from difficulties in handling the poisonous and corrosive dinitrogen tetroxide, a serious disadvantage of utilizing gaseous N₂O₄ in organic reactions, for example, its high reactivity which usually causes undesired side reactions. In order to overcome the above mentioned limitations, some reports have been published on the use of N₂O₄ complexes of organic [2], polymeric [3] and inorganic compounds [4] as useful reagents in organic reactions.

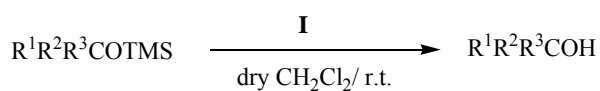
The transformation of alcohols to the corresponding trimethylsilyl ethers (TMS ethers) is a very common way to protect hydroxyl group [5]. There are various methods for regeneration of the parent hydroxy group from the silyl ethers by the use of aqueous HF [6], KF-crown ether [7], BF₃.Et₂O [8], *N*-bromo succinimide [9], CF₃SO₃SiMe₃ [10], NH₄F [11], SiF₄ [12], aqueous acids [13], (*n*-Bu)₄NF (TBAF) [14], K₂CO₃

[15], polymer supported π -acid [16], Lewis acids [17], K₅CoW₁₂O₄₀.3H₂O [18], and neutral alumina [19]. Fluoride ion is very basic, especially under anhydrous conditions, and cannot be used for base-sensitive molecules [20]. Other procedures are not acceptable for acid-sensitive systems and also a few methods are employed under nonaqueous conditions. Consequently, the development of alternative methods of deprotection under nonaqueous and neutral conditions would be desirable.

As a part of our ongoing program on silica supported reagents [21], and dinitrogen tetroxide applications [1] as well as development of eco-friendly methodologies, we undertook the study on the application of (N₂O₄/SiO₂) **I** as a safe, cheap, and heterogeneous reagent. Firouzabadi *et al.* have reported that dinitrogen tetroxide can only convert TMS ethers to the parent alcohols [22]. Nishiguchi and Okamoto could oxidize ethers to the corresponding aldehydes or ketones in the presence of silicagel in carbon tetrachloride at room temperature or reflux conditions under atmosphere of excess NO₂ [23].

Herein we wish to report SiO₂ impregnated with N₂O₄ as

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$\text{R}^1, \text{R}^2, \text{R}^3 = \text{Aryl, Alkyl, H}$

Scheme 1

an efficient agent for the fast deprotection of TMS ethers to the corresponding alcohols (Scheme 1).

EXPERIMENTAL

General

Materials were purchased from Merk, Fluka and Aldrich. TMS ethers [25] and THP ethers [26] were synthesized in the based of previous reported procedure. All products were characterized by the comparison of their spectral data (¹H NMR and IR spectroscopy) and physical properties with those of authentic samples.

Preparation of N₂O₄

To the solution of fuming 100% HNO₃ (82 ml) and 98% H₂SO₄ (30 ml) was added arsenic oxide (100 g). By heating the reaction mixture, N₂O₄ was produced and collected in salt ice-bath receiver [27].

Preparation of Silica-Supported N₂O₄

To a suspension of silica gel (mesh 60, 5 g) in dry dichloromethane (10 ml) at 0 °C was added 4 ml of liquid N₂O₄ while the mixture was gently stirred. After 1 h, bubbling of N₂ gas was performed through the solution in order to extrude the excess of NO₂ and then the solvent was evaporated under reduced pressure to give **I** (9 g) as a white powder. The reagent could be stored in the refrigerator for several months without losing its weight or activity.

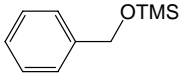
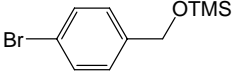
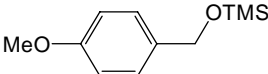
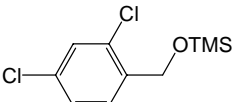
General Procedure for the Preparation of Alcohols from TMS Ethers

To a solution of trimethylsilyl ether (1 mmol) and CH₂Cl₂ (5 ml), **I** (225-300 mg) was added and the mixture was stirred for the appropriate time at room temperature (Table 1). After completion of reaction, the mixture was filtered and evaporation of the solvent on a rotary evaporator afforded a residue, which was passed through a short pad of silica gel using a mixture of ethyl acetate and *n*-hexane as eluent to afford the highly pure alcohol.

RESULTS AND DISCUSSION

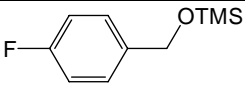
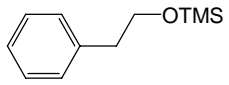
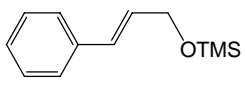
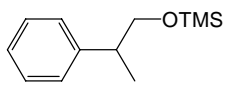
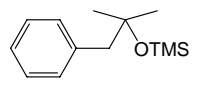
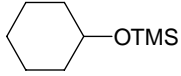
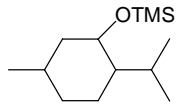
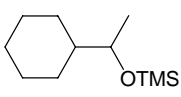
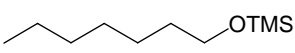
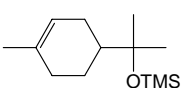
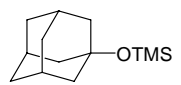
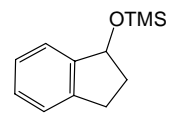
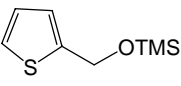
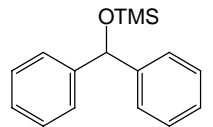
In this work we used SiO₂ impregnated with N₂O₄ as an efficient agent for the fast deprotection of TMS ethers to the corresponding alcohols as shown in Scheme 1. TMS benzyl

Table 1. Conversion of TMS Ethers to the Corresponding Alcohols in the Presence of N₂O₄/SiO₂ System at Room Temperature

Entry	Substrate	Subst. (mmol)/ Reagent (mg)	Time (min)	Yield (%) ^a
1		1/225 1/225 ^b	c 24 h	95 0
2		1/225	c	93
3		1/225	c	75
4		1/225	4	93

N₂O₄/SiO₂ System as an Efficient Reagent

Table 1. Continued

5		1/225	c	92
6		1/225	c	95
7		1/1.5	c	70
8		1/225	c	96
9		1/300	20	95
10		1/225	5	quant. ^d
11		1/225	10	quant. ^d
12		1/225	15	quant. ^d
13		1/225	10	quant. ^d
14		1/300	25	quant. ^d
15		1/300	30	90
16		1/225	c	75
17		1/225	c	78
18		1/225	5	90

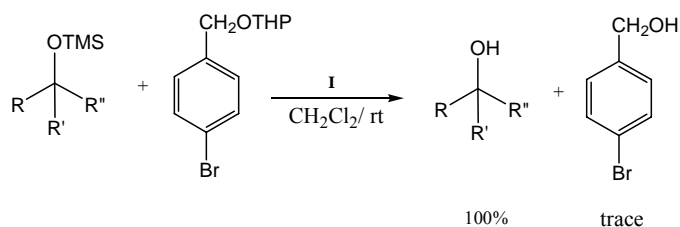
^aIsolated yields. ^bIn this case SiO₂ was used as a catalyst. c = Immediately. ^dDetected by GC.

ether was immediately converted to benzyl alcohol using **I** in CH_2Cl_2 at room temperature. In order to establish the generality and applicability of this method, various TMS ethers such as primary, secondary, tertiary, allylic, benzylic and alkylic were proceeded rapidly in good to excellent yields (Table 1). We also found that trimethylsilyl benzyl ether was not deprotected in the presence of SiO_2 in 24 h (Table 1, entry 1). It is notable that the mentioned amounts of the reagent presented in Table 1 is needed for completion of the reaction. Iranpoor and co-workers have successfully investigated

selective oxidation of TMS ethers to the carbonyl compound with charcoal/ N_2O_4 in the presence of tetrahydropyranyl ethers [24]. Therefore, we studied the deprotection of (4-bromobenzyl), benzhydryl and 1-phenyl-, 2-methyl- and 2-propyl-TMS ethers in the presence of (4-bromobenzyl) THP ether with **I**. Surprisingly, the substrates bearing *O*-THP group gives no or low yields of the corresponding alcohols, while TMS ethers were converted completely to the parent alcohols. The results are given in Table 2.

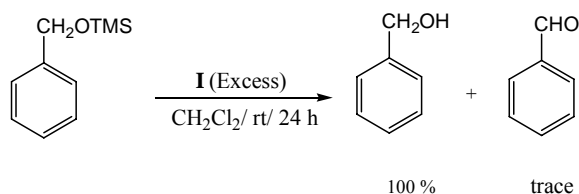
Although N_2O_4 has been used as an oxidizing agent, its

Table 2. Comparative Reaction Between TMS and THP Ethers in the Presence of $\text{N}_2\text{O}_4/\text{SiO}_2$ System at Room Temperature in CH_2Cl_2 ^a



Entry	Substrate	TMS ether (mmol)/THP ether (mmol)/Reagent (mg)	Time (min)
1		1/1/300	10
2		1/1/300	25
3		1/1/300	40

^aDetected by GC.



Scheme 2

mixture with SiO₂ has a lower oxidizing ability so that a little carbonyl compound can be produced as a by product in the course of reactions (Table 1, entries 3,7,16 and 17). In the control experiment, were trimethylsilyl benzyl ether was stirred with an excess amount of **I** in CH₂Cl₂ overnight, only benzyl alcohol was produced (Scheme 2). Although we experienced no difficulties in handling this reagent, care should always be exercised when handling reagents containing N₂O₄.

In conclusion, in this study we have introduced a new reagent for the chemoselective deprotection of different TMS ethers under nonaqueous and heterogeneous conditions. The stability, easy preparation and high selectivity of the reagent make this method as a useful procedure for the selective deprotection of TMS ethers at room temperature.

ACKNOWLEDGMENTS

Financial support for this work, as a joint project, by the Research Councils of Bu-Ali Sina University (Hamedan) and Esfahan University, Iran is gratefully acknowledged.

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