

NaHSO₄.H₂O promoted oxidative deprotection of trimethylsilyl, tetrahydropyranyl and methoxymethyl ethers with HIO₃

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Abstract

Different types of trimethylsilyl, tetrahydropyranyl and methoxymethyl ethers are efficiently converted to their corresponding aldehydes and ketones with HIO₃ in the presence of NaHSO₄.H₂O. All reactions were performed in moistured CH₃CN in good to high yields.

Keywords: Oxidative deprotection, trimethylsilyl ethers, tetrahydropyranyl ethers, methoxymethyl ethers, HIO₃

Introduction

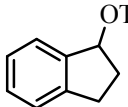
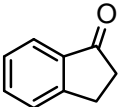
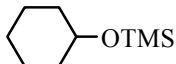
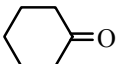
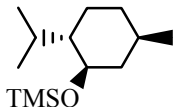
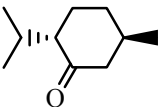
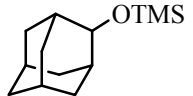
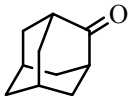
Aldehydes and ketones represent an important class of products and intermediates in the fine chemicals and specialities.¹ The oxidation of trimethylsilyl and tetrahydropyranyl ethers is an important transformation in organic synthesis, and several methods have been explored to accomplish such a conversion.²⁻⁹ Some of these methods involve the use of expensive reagents, long reaction times, low yields of the products and tedious work-up. Therefore, introduction of new methods and reagents for such functional group transformation is still in demand.

Application of solid acids in organic transformations have a very important role, because solid acids have many advantages such as simplicity in handling, decrease reactor and plant corrosion problems, and more environmentally safe disposal. Also wastes and by-products can be minimized or avoided by developing cleaner synthesis routes.¹⁰ During the last decade, the use of metal hydrogen sulfates have attracted the attention of many organic chemists. The stability and cheapness of most of these compounds, high yields of the products and relatively short reaction times are important advantages of these reagents.

To the best of our knowledge, there are only three reports in the literature related to the preparation of carbonyl compounds *via* the oxidation of alcohols by using HIO₃,¹¹⁻¹³ but there is not any report about the oxidation of trimethylsilyl and tetrahydropyranyl ethers using this reagent.

In continuation of our studies on the application of metal hydrogen sulfates in the promotion of organic reactions¹⁴⁻¹⁸ and also using HIO₃ in organic transformations,^{12, 13, 19-21} we have found that HIO₃ in the presence of NaHSO₄.H₂O is able to oxidize TMS and THP ethers to their corresponding carbonyl compounds under mild reaction conditions. Herein we wish to report an efficient, simple and cheap method for the oxidation of the above mentioned substrates to aldehydes and ketones using HIO₃ / NaHSO₄.H₂O reagent system in moistured CH₃CN. All reactions were performed under mild conditions in good to high yields (Scheme 1).

Table 1. Oxidative deprotection of trimethylsilyl ethers^a

Entry	Substrate	Product	Time (h)	Yield (%) ^b
1	2-ClC ₆ H ₄ CH ₂ OTMS	2-ClC ₆ H ₄ CHO	0.33	90
2	4-ClC ₆ H ₄ CH ₂ OTMS	4-ClC ₆ H ₄ CHO	0.17	92
3	2-BrC ₆ H ₄ CH ₂ OTMS	2-BrC ₆ H ₄ CHO	0.67	90
4	4-BrC ₆ H ₄ CH ₂ OTMS	4-BrC ₆ H ₄ CHO	0.17	93
5	3-NO ₂ C ₆ H ₄ CH ₂ OTMS	3-NO ₂ C ₆ H ₄ CHO	4	90
6	4-NO ₂ C ₆ H ₄ CH ₂ OTMS	4-NO ₂ C ₆ H ₄ CHO	4.7	85
7			5.5	90
8	Ph ₂ CHOTMS	Ph ₂ O	3	90
9	PhCH(OTMS)COPh	PhCOCOPh	2	82
10	PhCH=CHCH ₂ OTMS	PhCH=CHCHO	2.5	85
11	PhCH ₂ CH ₂ OTMS	PhCH ₂ CHO	5	70
12	PhCH(Me)CH ₂ OTMS	PhCH(Me)CHO	3.3	85
13			4.7	87
14			1.7	90
15			3	89

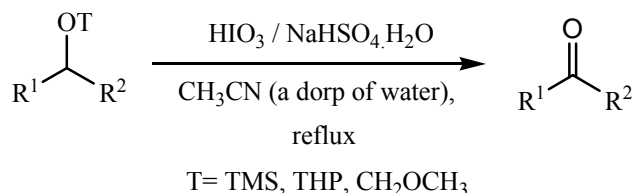
^a Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy.

^b Isolated yields.

Yields and reaction times are shown in Tables 1 and 2. Using this method benzylic TMS and THP ethers, including electron donating and withdrawing groups are converted to their corresponding carbonyl compounds in good to high yields. Aliphatic TMS and THP ethers are also efficiently oxidized to their corresponding aldehydes and ketones under the same reaction conditions. In all cases, no over-oxidation products were observed.

The methoxymethylation is also used for the protection of alcoholic hydroxyl groups. Although a number of methods are available for deprotection of methoxymethyl ethers to the parent alcohols,^{22, 23} but, to the best of our knowledge and *in spite* of TMS and THP ethers, there is only one report for the direct oxidation of these type of ethers to their corresponding carbonyl compounds.²⁴ Our investigation clarified that HIO₃ in the presence of NaHSO₄·H₂O can also be used for the oxidation of various methoxymethyl ethers to the aldehydes and ketones mostly in quantitative yields as well as TMS and THP ethers (Scheme 1, Table 3).

It is important to note that the progress of the reaction is extremely depends on the presence of NaHSO₄·H₂O in the reaction mixture, so that in the absence of this reagent, the starting material remains intact during the course of the reaction. This observation suggests the important role of sodium hydrogen sulfate monohydrate in the promotion of the oxidation reactions. On the other hand when the reaction is carried out in dry CH₃CN the reaction time became very long. This result clarifies that the presence of water is essential for such processes.



Scheme 1

A plausible mechanism for the oxidation reactions is shown in Scheme 2.

Table 2. Oxidative deprotection of tetrahydropyranyl ethers ^a

1	2-ClC ₆ H ₄ CH ₂ OTHP	2-ClC ₆ H ₄ CHO	1.3	92
2	4-ClC ₆ H ₄ CH ₂ OTHP	4-ClC ₆ H ₄ CHO	0.9	89
3	2-BrC ₆ H ₄ CH ₂ OTHP	2-BrC ₆ H ₄ CHO	1	85
4	4-BrC ₆ H ₄ CH ₂ OTHP	4-BrC ₆ H ₄ CHO	0.8	90
5	4-NO ₂ C ₆ H ₄ CH ₂ OTHP	4-NO ₂ C ₆ H ₄ CHO	3.1	90
6	2-MeC ₆ H ₄ CH ₂ OTHP	2-MeC ₆ H ₄ CHO	0.75	95
7	4-PhCH ₂ OC ₆ H ₄ CH ₂ OTHP	4-PhCH ₂ OC ₆ H ₄ CHO	2.2	85
8			6.3	82
9	PhCH(OTHP)Ph	Ph ₂ O	0.6	90
10	PhCOCH(OTHP)Ph	PhCOCOPh	5.7	85
11	PhCH ₂ CH ₂ OTHP	PhCH ₂ CHO	3	85
12	PhCH ₂ CH ₂ CH ₂ OTHP	PhCH ₂ CH ₂ CHO	4.25	82
13	PhCH(Me)CH ₂ OTHP	PhCH(Me)CHO	3.5	85
14	PhCH ₂ CH(OTHP)Me	PhCH ₂ COMe	4.7	90
15			2	90
16			3.5	87

^a Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy.

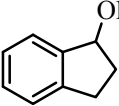
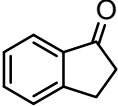
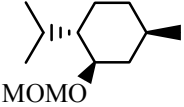
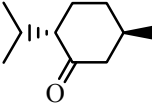
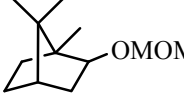
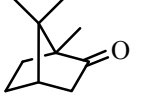
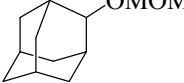
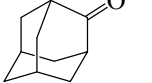
^b Isolated yields.

In conclusion, in this study we have developed a mild, efficient and simple method for the oxidative deprotection of trimethylsilyl, tetrahydropyranyl and methoxymethyl ethers. In addition, the low cost and availability of the reagents, easy and clean work-up, and high yields are other advantages of the present method.

Experimental Section

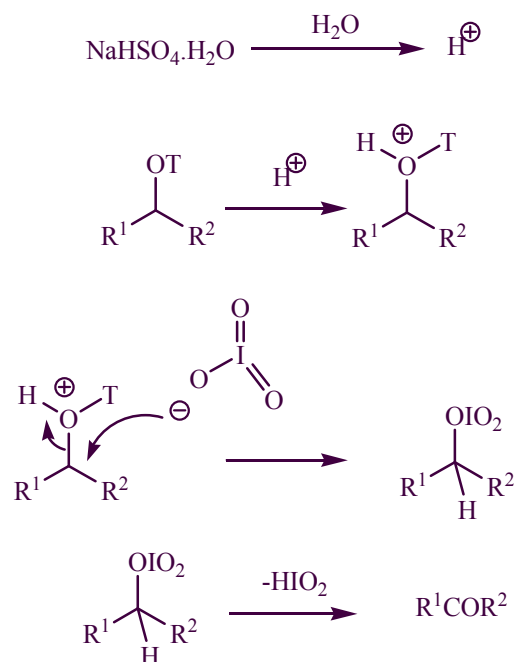
General Procedures. Trimethylsilyl, tetrahydropyranyl and methoxymethyl ethers were prepared according to the literature procedures.^{16, 17, 25-27} All oxidation products are known compounds; they are identified by comparison of their physical data, IR and NMR spectra with those of authentic samples. Yields refer to isolated products or their 2,4-dinitrophenylhydrazones.

Table 3. Oxidative deprotection of methoxymethyl ethers (MOM-ethers).^a

Entry	Substrate	Product	Time (h)	Yield (%) ^b
1	PhCH ₂ OMOM	PhCHO	1.7	92
2	2-BrC ₆ H ₄ CH ₂ OMOM	2-BrC ₆ H ₄ CHO	1.7	90
3	2-ClC ₆ H ₄ CH ₂ OMOM	2-ClC ₆ H ₄ CHO	2.5	95
4	4-ClC ₆ H ₄ CH ₂ OMOM	4-ClC ₆ H ₄ CHO	0.5	92
5	4-NO ₂ C ₆ H ₄ CH ₂ OMOM	4-NO ₂ C ₆ H ₄ CHO	3.25	87
6	2-MeC ₆ H ₄ CH ₂ OMOM	2-MeC ₆ H ₄ CHO	1.5	90
7			1.6	85
8	Ph ₂ CHOMOM	Ph ₂ CO	1.2	92
9	PhCH=CHCH ₂ OMOM	PhCH=CHCHO	1.1	85
10	PhCH(Me)CH ₂ OMOM	PhCH(Me)CHO	3.25	90
11			2.2	90
12			1.8	92
13			1.3	89

^a Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy.

^b Isolated yields.

**Scheme 2****General Procedure**

To a solution of the substrate (1 mmol) in CH_3CN (3 mL), which is moistured with a drop of water, were added HIO_3 (1.5 mmol, 0.264 g) and $\text{NaHSO}_4 \cdot \text{H}_2\text{O}$ (0.25 mmol, 0.035 g) and refluxed for the appropriate time (Tables 1 and 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid residue was washed with CH_3CN (5 mL). The solvent was evaporated and the residue was triturated with H_2O (10 mL). The product was extracted with diethyl ether (3×5 mL) the combined organic solution was dried over MgSO_4 and filtered. Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding carbonyl compounds in good to high yields.²⁸

Acknowledgements

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28. Spectra and physical data of some of the products:
Benzaldehyde: Colourless liquid; IR (neat): $\nu=1700\text{ cm}^{-1}$; $^1\text{H NMR}$ (300 MHz, CDCl_3 , ppm): $\delta=7.48\text{-}7.52$ (m, 2H), $7.60\text{-}7.65$ (m, 1H), $7.85\text{-}7.90$ (m, 2H), 9.95 (s, 1H).
4-Chlorobenzaldehyde: White solid; mp= $45\text{-}46\text{ }^\circ\text{C}$; IR (KBr): IR (neat): $\nu=1703\text{ cm}^{-1}$;

^1H NMR (300 MHz, CDCl_3 , ppm): δ = 7.55 (d, J = 7.8 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H), 9.95 (s, 1H).

Phenylacetaldehyde: Colourless liquid; IR (neat): ν = 1710 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3 , ppm): δ = 3.25 (d, J = 2 Hz, 2H), 7.05-7.10 (m, 2H), 7.25- 7.30 (m, 3H), 9.75 (t, J = 2 Hz, 1H).

Cyclohexanone: Colourless liquid; IR (neat): ν = 1700 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3 , ppm): δ = 1.70- 1.78 (m, 2H), 1.85- 1.92 (m, 4H), 2.40 (t, J = 6.8 Hz, 4H).