

Fe(NO₃)₃·9H₂O / Fe(HSO₄)₃ : An efficient reagent system for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers in the absence of solvent

Farhad Shirini,^{a*} Mohammad A. Zolfigol,^b and Abdol-Reza Abri^a

^aDepartment of Chemistry, College of Science, University of Guilan, Rasht, zip 41335, I. R. Iran

Fax: +98 131 3220066

^bCollege of Chemistry, Bu-Ali Sina University, Hamadan zip code 65174, I. R. Iran

E-mail: shirini@guilan.ac.ir

Abstract

A mild and efficient method for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers with Fe(NO₃)₃·9H₂O in the presence of Fe(HSO₄)₃ in the absence of solvent at room temperature is reported.

Keywords: Oxidative deprotection, trimethylsilyl ethers, tetrahydropyranyl ethers, Fe(HSO₄)₃, Fe(NO₃)₃·9H₂O

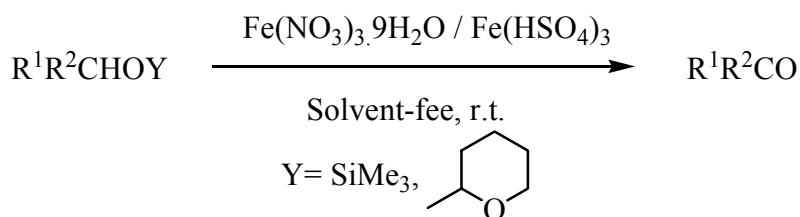
Introduction

Trimethylsilylation and tetrahydropyranylation are important reactions widely used for the protection of alcoholic hydroxyl group during a multi-step organic synthesis.^{1,2} Direct oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to their corresponding carbonyl compounds are of value to synthetic organic chemists and, in recent years, have attracted much attentions. The available methods have been extensively reviewed,³ and some representative reagents are: Jones reagent,⁴ NBS,⁵ aqueous acid,⁶ tetrabutylammonium fluoride,⁷ wet alumina supported chromium (VI) oxide,⁸ cobalt and manganese salts of *p*-aminobenzoic acid supported on silica gel,⁹ benzyltriphenylphosphonium chlorate,¹⁰ (NO₃)₃CeBrO₃,¹¹ [(NO₃)₃Ce]₃·H₂IO₆,¹² silica chromate,¹³ SiF₄-MeCN¹⁴ and K₂S₂O₈ in the presence of [bmim]Br.¹⁵ However, the disadvantages, such as long reaction times, low yields of the products, the requirement for the acidic and aqueous conditions, unavailability of the reagents, tedious work-up and, in most cases, inapplicability in the oxidation of the both type of the above mentioned substrates, clearly identifies a need to introduce new methods for such functional group transformations.

In 1999, Heravi and coworkers¹⁶ reported that montmorillonite supported $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ can be used for the oxidative deprotection of tetrahydropyranyl ethers under microwave irradiation. Although, the yields of the obtained carbonyl compounds using this method are relatively high, the need to proceed under microwave, and the use of equimolar amounts of the reagents to substrate and also 1 g of montmorillonite K-10 during the course of each reaction, can be regarded as limitations of this method.

Results and Discussion

In continuation of our ongoing research program directed towards the development of the applications of hydrogen sulfate salts in organic reactions,¹⁷⁻¹⁹ we have found that $\text{Fe}(\text{HSO}_4)_3$ ²⁰ is efficiently able to promote the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers with $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ in the absence of solvent at room temperature in good to high yields (Scheme 1).



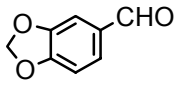
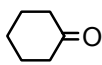
Scheme 1

Yields and reaction times are tabulated in Table 1. Benzylic trimethylsilyl and tetrahydropyranyl ethers, including electron-donating and -withdrawing groups are oxidized to their corresponding aldehydes and ketones in high yields (Table 1). Substrates containing the ethereal linkages are efficiently converted to their corresponding carbonyl compounds without cleavage of carbon-oxygen bond (Table 1, entries 10-12). This method is also very effective for the oxidation of aliphatic trimethylsilyl and tetrahydropyranyl ethers (Table 1, entries 15-18). The method is not useful for the oxidation of allylic substrates (Table 1, entry 19). Over-oxidation of the products to their carboxylic acids or esters was not observed using this method.

To illustrate the efficiency of the proposed method, we have compared some of the results with some of those reported in the literature (Table 2),⁸⁻¹⁰ which demonstrates its significant superiority.

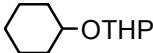
In conclusion, in this study we have developed a mild, efficient and high-yielding method for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers in the absence of solvent. In addition, the stability of the reagents, high reaction rates and easy and clean work-up are worthy advantages of the present method.

Table 1. Oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers in the absence of solvent^{a,b}

Entry	Product	Trimethylsilyl ethers		Tetrahydropyranyl ethers		m.p. (°C) or b.p. (°C) / kPa	
		Time/min	Yield/% ^c	Time/min	Yield/% ^c	Found	Reported
1	C ₆ H ₅ CHO	2	95	2	90	180-181/101	179/101 ²¹
2	2-BrC ₆ H ₄ CHO	2	90	3	87	226-228/101	228-230/101 ²¹
3	2-ClC ₆ H ₄ CHO	2	90	2	90	209/101	208/101 ²¹
4	4-ClC ₆ H ₄ CHO	3	95	2	95	44-46	46 ²¹
5	2-NO ₂ C ₆ H ₄ CHO	10	85	3	85	39-41	41-43 ²¹
6	3-NO ₂ C ₆ H ₄ CHO	10	90	3	88	57-59	58 ²¹
7	4-NO ₂ C ₆ H ₄ CHO	9	87	3	90	103-105	106 ²¹
8	2-MeC ₆ H ₄ CHO	2	90	2	91	196-198/101	198-200/101 ²¹
9	4-MeOC ₆ H ₄ CHO	2	90	3	85	248-250	247-249/101 ²¹
10	4-PhCH ₂ OC ₆ H ₄ CHO	3	80	2	90	68-70	70-72 ²¹
11		4	80	2	92	80-82	83-84 ²²
12	PhCOMe	2	85	3	85	199-201/101	202/101 ²¹
13	PhCOPh	2	92	2	90	50-52	47-49 ²¹
14	PhCH ₂ CH ₂ CHO	3	85	2	90	220-222/101	222-224/101 ²¹
15	PhCH(Me)CHO	2	87	2	85	57-59	60 ²¹
16	PhCH ₂ COMe	3	85	2	90	217-219/101	214-216/101 ²³
17		5	90	3	90	155-157/101	156/101 ²¹
18	PhCH=CHCO	3	^c	3	^c	—	—

^a Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy. ^b Yields are based on isolated products. ^c Mixture of unidentified products.

Table 2. Comparison of some of the results obtained by our method (I), with some of those reported by benzyltriphenyl-phosphonium chlorate (II),¹⁰ Co and Mn salts / O₂ system (III),⁹ and wet alumina supported chromium (VI) oxide (IV)⁸

Entry	Substrate	Time (min) / Yield (%)			
		(I)	(II)	(III)	(IV)
1	PhCH ₂ OTMS	2 / 95	15 / 100	12 (h) / 90	10 / 93
2	Ph ₂ CHOTMS	2 / 92	18 / 95	8.5 (h) / 96	10 / 92
3	 OTHP	3 / 90	—	—	25 / 83
4	4-ClC ₆ H ₄ CH ₂ OTHP	2 / 95	60 / 100	—	—
5	2-NO ₂ C ₆ H ₄ CH ₂ OTHP	3 / 85	10 (h) / 50	—	—

Experimental Section

General Procedures. Chemicals were purchased from Fluka, Merck and Aldrich Chemical Companies. Yields refer to isolated products. Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy. The purity determination of the substrates and reaction monitoring were accompanied by TLC on silica gel polygram SILG/ UV 254 plates.

General method. A mixture of the substrate (1 mmol) substrate, 0.101 g Fe(NO₃)₃·9 H₂O (0.25 mmol) and 0.087 g Fe(HSO₄)₃ (0.25 mmol) was ground in a mortar with a pestle for the specified time (Table 1). The progress of the reaction was monitored by TLC or GC. After completion of the reaction, the mixture was diluted with CH₂Cl₂ (10 mL) and filtered to remove the solids. The solid residue was washed with CH₂Cl₂ (5 mL). Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding carbonyl compounds in good to high yields.²⁴

Acknowledgements

We are thankful to the University of Guilan Research Council for the partial support of this work.

References

- Greene, T. W.; Wuts, P. G. M., *Protective Groups in Organic Synthesis*, 2nd Edn, Wiley: New York, 1991.
- Smith, M. B., *Organic Synthesis*, McGraw-Hill: New York, 1994.

3. Muzart, J. *Synthesis* **1993**, 11.
4. Paquette, L. A.; Lin, H. S.; Gunn, B. P.; Coghlan, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 5818.
5. Battone, R. J.; Dixon, N. J.; Taylor, R. J. K. *Synthesis* **1980**, 234.
6. Newton, R.F.; Reynolds, D. P.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, 3981.
7. Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
8. Heravi, M. M.; Ajami, D.; Tabar-Heydar, K. *Monatsh. Chem.* **1999**, *130*, 337.
9. Hashemi, M. M.; Ahmadibeni, Y. *Monatsh. Chem.* **2003**, *134*, 411.
10. Hajipour, A. R.; Mallakpour, S. E.; Mohammadpoor-Baltork, I.; Malakoutikhah, M. *Tetrahedron* **2002**, *58*, 134.
11. Shirini, F.; Esm-Hosseini, M.; Hejazi, Z. *Synth. Commun.* **2005**, *35*, 2913.
12. Firouzabadi, H.; Shirini, F. *Synth. Commun.* **1996**, *26*, 423.
13. Zolfigol, M. M.; Shirini, F.; Mohammadpoor-Baltork, I.; Ghorbani Choghamarani, A.; Hajjami, M.; Sedaghat, A. M. *Mendeleev Commun.* **2005**, 113.
14. Corey, E. J.; Yi, K. K. *Tetrahedron Lett.* **1992**, *33*, 2289.
15. Hajipour, A. R.; Mostafavi, M.; Ruoho, A. E. *Catal. Commun.* **2007**, *8*, 1825.
16. Heravi, M. M.; Ajami, D.; Mojtahedi, M. M.; Ghassemzadeh, M. *Tetrahedron Lett.* **1999**, *40*, 561.
17. Shirini, F.; Zolfigol, M. A.; Mallakpour, B.; Mallakpour, S. E.; Hajipour, A. R.; Mohammadpoor-Baltork, I. *Tetrahedron Lett.* **2002**, *43*, 1555.
18. Shirini, F.; Zolfigol, M. A.; Abedini, M. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1982.
19. Shirini, F.; Zolfigol, M. M.; Safari, A. *J. Chem. Res.(S)* **2006**, 154.
20. Shirini, F.; Zolfigol, M. A.; Abri, A. R. *Chinese Chem. Lett.* **2007**, 803.
21. *Merck Chemical Reagents*, Wolfgang Baden, Merck K Ga A: Darmstadt, 2002.
22. Lei, M.; Hu, R. J.; Wang, Y.G. *Tetrahedron* **2006**, *62*, 8928.
23. Fluka Catalogue, *Handbook of Fine Chemicals*, 1997-1998.
24. Selected spectral data:
 - 4-Chlorobenzaldehyde.** ^1H NMR (CDCl_3) δ : 7.55 (d, $J=7.8$ Hz, 2H), 7.85 (d, $J=7.8$ Hz, 2H), 9.95 (s, 1H).
 - 4-Nitrobenzaldehyde.** ^1H NMR (CDCl_3) δ : 8.10 (d, $J=8.6$ Hz, 2H), 8.40 (d, $J=8.6$ Hz, 2H), 9.90 (s, 1H).
 - 4-Methoxybenzaldehyde.** ^1H NMR (CDCl_3) δ : 3.85 (s, 3H), 7.00 (d, J 8.2 Hz, 2H), 7.85 (d, J 8.2 Hz, 2H), 9.80 (s, 1H).
 - 3,4-Methylenedioxybenzaldehyde.** ^1H NMR (CDCl_3) δ : 6.00 (s, 2H), 6.95-7.35 (m, 3H), 9.82 (s, 1H).
 - Cyclohexanone.** ^1H NMR (CDCl_3) δ : 1.70-1.78 (m, 2H), 1.85-1.92 (m, 4H), 2.4 (t, J 6.8 Hz, 4H).