

***O*-Xylylenebis(Triphenylphosphonium) Dichlorochromate: a Selective and Efficient Reagent for Oxidation of Alcohols, Trimethylsilyl Ethers and Thiols**

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Abstract: Alcohols, trimethylsilyl ethers and thiols were efficiently converted to their corresponding carbonyl and disulfides compounds using *o*-xylylenebis (triphenylphosphonium) dichlorochromate (XTPPDCC). This reagent can selectively oxidize thiols to disulfides in the presence of alcohols and trimethylsilyl ethers in acetonitrile at room temperature.

Key words: *O*-Xylylenebis(triphenylphosphonium) Dichlorochromate • Alcohols • Trimethylsilyl ethers • Thiols • Disulfides

INTRODUCTION

The oxidation of organic compounds under mild conditions has found valuable applications in modern organic synthesis. The oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones is a fundamental area that is encountered at all levels of organic synthesis. Disulfides are one of the most important classes of organic sulfur compounds, possessing noteworthy reactivity in biochemistry and as key intermediates in wide variety of organic synthetic routes. In recent years significant improvements have been achieved by the use of new oxidizing agents, examples being: silica-supported 1,1,3,3-tetramethylguanidine/Br₂ complex [1], melamine hydrogen peroxide (MHP) [2], K₂S₂O₈ [3], bis-(2,4,6-trimethylpyridinium) dichromate (BTMPDC) [4], (PhCH₂PPh₃)⁺Br⁻ [5], TEMPO-linked metalloporphyrins [6], NaIO₄/TEMPO/NaBr [7]. Unfortunately, many of the reagents mentioned in the literature suffer from at least one of the following disadvantages: cost of preparation, hygroscopicity, photosensitivity, instability, lack of selectivity and tedious work-up procedure [5-8].

In connection with our ongoing work on the application of selective oxidation of organic compounds [9-21], we report here the oxidation of structurally different alcohols, trimethylsilyl ethers and thiols using *o*-xylylenebis (triphenylphosphonium) dichlorochromate

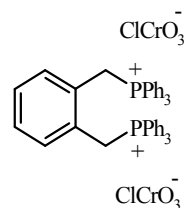


Fig. 1: *O*-xylylenebis (triphenylphosphonium) dichlorochromate

in acetonitrile at reflux conditions. *o*-xylylenebis (triphenylphosphonium) dichlorochromate (XTPPDCC, Figure 1) as an oxidant can overcome most of the above-mentioned disadvantages for the oxidation of organic compounds.

Experimental: All the alcohols were purchased from Fluka and Merck. The reactions were monitored by TLC using silica gel plates. The products were purified by flash column chromatography on silica gel (Merck; 230-400 mesh) and were identified by comparison of their IR and ¹H NMR spectra and physical data with those of authentic samples. ¹H NMR spectra were measured at 90 MHz with a JEOL JNM-EX 90 spectrometer with tetramethylsilane as an internal reference and DMSO-d₆ as solvent. IR spectra were recorded with a Pye-unicam SP 1100 spectrophotometer. Elemental analyses were performed on a LECO 250 instrument.

Preparation of *O*-Xylylenebis(Triphenylphosphonium)

Dichlorochromate (XTPPDCC): To a solution of *o*-xylylenebis (triphenylphosphonium chloride) (5 mmol, 3.49 g) in water (25 ml) was added a solution of CrO_3 (10 mmol, 0.99 g) in HCl 6 N (15 ml) under stirring at room temperature until an orange precipitate was formed. After 30 min stirring, the mixture was filtered, washed with water (2×15 ml) and dried at room temperature (4.27 g, 95% Yield). m.p: 185°C to a light brown material; ^1H NMR (DMSO): δ 4.5 (d, 4H, CH_2), 6.85-7.98 (m, 34H, arom. H). IR (KBr) $\nu(\text{cm}^{-1})$: 3053, 2096, 1900, 1586, 1495, 1484, 1437, 1115, 954, 937, 787, 746, 696; Elemental analysis: Calculated C, 62.56; H, 4.53, Found: C, 62.50; H, 4.48.

General Procedure for Oxidation of Alcohols and Trimethylsilyl Ethers and Coupling of Thiols:

In a round-bottomed flask (25 ml), equipped with a reflux condenser and a magnetic stirrer, a solution of substrate (1 mmol) and *o*-xylylenebis (triphenylphosphonium) dichlorochromate (0.5 mmol, 0.44 g for thiols and 1 mmol, 0.89 g for alcohols and trimethylsilyl ethers) in acetonitrile was added and stirred for 2-80 min at refluxed temperature (7-15 min at room temperature for thiols). The reaction was monitored by TLC (EtOAc/*n*-Hexane 10:90). The reaction mixture was cooled to room temperature and the solid was then separated through a short pad of silica gel and washed with acetonitrile (5 ml). The solvent was evaporated to afford pure corresponding product. If necessary, the crude product was purified by column chromatography on silica gel using a mixture of ethyl acetate and *n*-hexane as eluent (10:90).

RESULTS AND DISCUSSION

O-Xylylenebis(triphenylphosphonium) dichlorochromate was readily prepared in high yield by adding a solution of CrO_3 in HCl (6 N) into a stirring solution of *o*-xylylenebis (triphenylphosphonium chloride) in water and continued to stir for 30 min at room temperature. Filtration and drying the precipitate produced an orange powder (Scheme 1). The chromium

Table 1: Oxidation of benzylalcohol in different solvents with XTPPDCC^a

Entry	Solvent	Time (min)	Yield (%)
1	CH_3CN	15	97
2	CHCl_3	60	65
3	CH_2Cl_2	60	50
4	<i>n</i> - C_6H_{14}	60	30
5	THF	60	45

^aReactions were carried out at reflux condition using substrate/oxidant molar ratio (1:1)

^bYields refer to isolated products

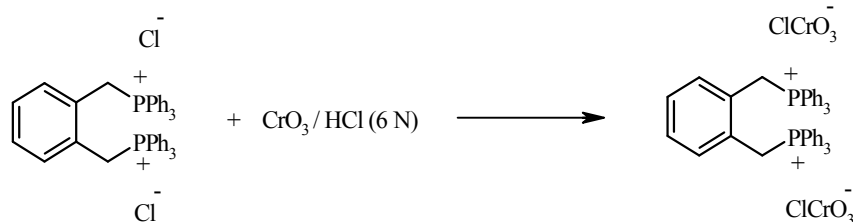
content of the reagent was determined by atomic absorption. Elemental analyses (C, H, N) were also performed and the experimental and calculated results were in very good agreement with the proposed structure.

This compound is non-hygroscopic and can be stored in a polyethylene bag for long periods without decomposition. It is soluble in polar solvents such as acetonitrile and *N,N* dimethylformamide and slightly soluble in THF, chloroform and dichloromethane and insoluble in benzene, *n*-hexane and carbon tetrachloride.

The effect of solvent on the oxidation reaction was evaluated by carrying out the oxidation in different solvents. Oxidation of benzyl alcohol with *o*-xylylenebis (triphenylphosphonium) dichlorochromate was carried out in acetonitrile, chloroform, dichloromethane, *n*-hexane and tetrahydrofuran at reflux temperature. The results are presented in Table 1.


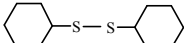
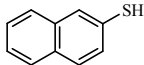
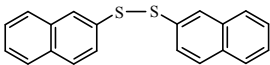
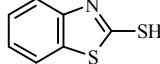
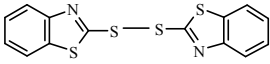
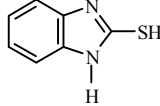
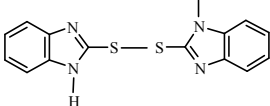
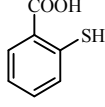
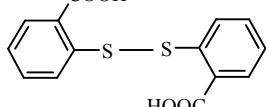
As indicated in Table 1, a 1:1 molar ratio of benzyl alcohol and *o*-xylylenebis (triphenylphosphonium) dichlorochromate in acetonitrile gave excellent yield of benzaldehyde (entry 1). The effect of temperature on this reaction was also studied by carrying out the oxidation of benzyl alcohol at lower temperatures, but, much longer reaction time was necessary to achieve complete conversion to benzaldehyde.

In order to evaluate the general applicability of this method we have treated benzylic, allylic and aliphatic alcohols, trimethylsilyl ethers and thiols with *o*-xylylenebis(triphenylphosphonium) dichlorochromate in refluxing acetonitrile (room temperature for thiols) and results are shown in Table 2.



Scheme 1:

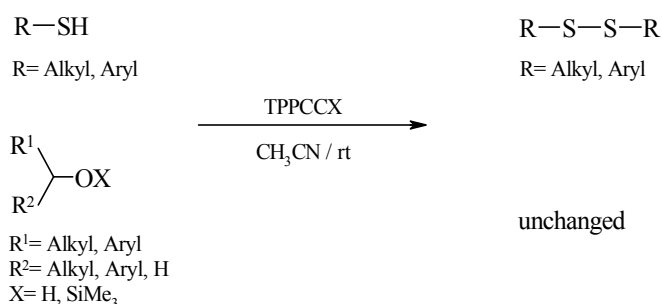
Table 2: Oxidation of Alcohols and Trimethylsilyl Ethers to Carbonyl Compounds and Conversion of thiols to disulfides with XTPDCC^a

Entry	Substrate	Product	Time (min)	Yield (%) ^b
1	C ₆ H ₅ CH ₂ OH	C ₆ H ₅ CHO	10	96
2	<i>m</i> -MeOC ₆ H ₄ CH ₂ OH	<i>m</i> -MeOC ₆ H ₄ CHO	15	92
3	<i>p</i> -MeOC ₆ H ₄ CH ₂ OH	<i>p</i> -MeOC ₆ H ₄ CHO	10	89
4	<i>o</i> -MeC ₆ H ₄ CH ₂ OH	<i>o</i> -MeC ₆ H ₄ CHO	12	95
5	<i>o</i> -ClC ₆ H ₄ CH ₂ OH	<i>o</i> -ClC ₆ H ₄ CHO	5	93
6	<i>p</i> -ClC ₆ H ₄ CH ₂ OH	<i>p</i> -ClC ₆ H ₄ CHO	15	97
7	<i>o</i> -BrC ₆ H ₄ CH ₂ OH	<i>o</i> -BrC ₆ H ₄ CHO	7	92
8	<i>p</i> -BrC ₆ H ₄ CH ₂ OH	<i>p</i> -BrC ₆ H ₄ CHO	17	90
9	<i>o</i> -NO ₂ C ₆ H ₄ CH ₂ OH	<i>o</i> -NO ₂ C ₆ H ₄ CHO	30	85
10	<i>m</i> -NO ₂ C ₆ H ₄ CH ₂ OH	<i>m</i> -NO ₂ C ₆ H ₄ CHO	17	88
11	C ₆ H ₅ CH(OH)CH ₃	C ₆ H ₅ COCH ₃	3	95
12	C ₆ H ₅ CH(OH)CH ₂ CH ₃	C ₆ H ₅ COCH ₂ CH ₃	3	92
13	C ₆ H ₅ CH(OH)COC ₆ H ₅	C ₆ H ₅ COCOC ₆ H ₅	25	90
14	(C ₆ H ₅) ₂ CHOH	(C ₆ H ₅) ₂ CO	5	91
15	C ₆ H ₅ CH=CHCH ₂ OH	C ₆ H ₅ CH=CHCHO	35	89
16	C ₆ H ₅ CH ₂ CH ₂ OH	C ₆ H ₅ CH ₂ CHO	60	85
17	CH ₃ (CH ₂) ₅ CH ₂ OH	CH ₃ (CH ₂) ₅ CHO	70	78
18	CH ₃ (CH ₂) ₆ CH ₂ OH	CH ₃ (CH ₂) ₆ CHO	70	81
19	Cyclohexanol	Cyclohexanone	60	80
20	C ₆ H ₅ CH ₂ OSiMe ₃	C ₆ H ₅ CHO	2	92
21	(C ₆ H ₅) ₂ CHOSiMe ₃	(C ₆ H ₅) ₂ CO	5	94
22	<i>p</i> -ClC ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -ClC ₆ H ₄ CHO	3	90
23	<i>o</i> -ClC ₆ H ₄ CH ₂ OSiMe ₃	<i>o</i> -ClC ₆ H ₄ CHO	3	90
24	<i>p</i> -BrC ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -BrC ₆ H ₄ CHO	5	93
25	<i>p</i> -NO ₂ C ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -NO ₂ C ₆ H ₄ CHO	80	65
26	C ₆ H ₅ CH=CHCH ₂ OSiMe ₃	C ₆ H ₅ CH=CHCHO	17	84
27	C ₆ H ₅ CH(OSiMe ₃)COC ₆ H ₅	C ₆ H ₅ COCOC ₆ H ₅	7	95
28	C ₆ H ₅ CH ₂ CH ₂ OSiMe ₃	C ₆ H ₅ CH ₂ CHO	30	80
29	CH ₃ (CH ₂) ₅ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₅ CHO	50	83
30	CH ₃ (CH ₂) ₆ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₆ CHO	40	80
31	C ₆ H ₅ SH	C ₆ H ₅ SSC ₆ H ₅	7	92
32	<i>p</i> -MeC ₆ H ₄ SH	<i>p</i> -MeC ₆ H ₄ SSC ₆ H ₄ Me- <i>p</i>	10	94
33	<i>p</i> -ClC ₆ H ₄ SH	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i>	8	96
34	<i>p</i> -BrC ₆ H ₄ SH	<i>p</i> -BrC ₆ H ₄ SSC ₆ H ₄ Br- <i>p</i>	10	89
35	C ₆ H ₅ CH ₂ SH	C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅	7	96
36	CH ₃ (CH ₂) ₃ CH ₂ SH	CH ₃ (CH ₂) ₃ CH ₂ SSCH ₂ (CH ₂) ₃ CH ₃	12	90
37	CH ₃ (CH ₂) ₆ CH ₂ SH	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃	12	90
38	HOOCCH ₂ SH	HOOCCH ₂ SSCH ₂ COOH	10	87
39	HOCH ₂ CH ₂ SH	HOCH ₂ CH ₂ SSCH ₂ CH ₂ OH	7	92
40			10	86
41			8	90
42			15	40
43			12	94
44			12	85

^aReactions were carried out in acetonitrile (at reflux temperature for alcohol and trimethylsilyl ethers and at room temperature for thiols). Substrates/oxidant molar ratio for alcohol and trimethylsilyl ethers (1:1), for thiols (1:0.5)^bYields refer to pure isolated products

Table 3: The selective coupling of thiols to disulfids in the presence of alcohols or trimethylsilyl ethers in acetonitrile at room temperature

Entry	Substrates	Products	Time (min)	Yield(%) ^a
1	<i>p</i> -ClC ₆ H ₄ SH Cyclohexanol	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i> Cyclohexanone	8	90-
2	C ₆ H ₅ CH ₂ SH C ₆ H ₅ CH ₂ OH	C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅ C ₆ H ₅ CHO	7	94-
3	CH ₃ (CH ₂) ₆ CH ₂ SH <i>p</i> -ClC ₆ H ₄ CH ₂ OH	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃ <i>p</i> -ClC ₆ H ₄ CHO	14	91-
4	<i>p</i> -ClC ₆ H ₄ SH (C ₆ H ₅) ₂ CHOSiMe ₃	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i> (C ₆ H ₅) ₂ CO	7	95-
5	C ₆ H ₅ CH ₂ SH C ₆ H ₅ CH ₂ OSiMe ₃	C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅ C ₆ H ₅ CHO	7	89-
6	CH ₃ (CH ₂) ₆ CH ₂ SH CH ₃ (CH ₂) ₅ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃ CH ₃ (CH ₂) ₅ CHO	12	91-

^aYield refers to pure isolated products or GC

Scheme 2:

It is evident from Table 2, that aromatic substrates, including benzylic alcohols as well as, trimethylsilyl ethers and thiols were rapidly converted to the corresponding carbonyl compounds and disulfides in excellent yields under the reaction conditions, whereas aliphatic compounds needed longer reaction time.

It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over oxidation of the resulting aldehydes is not observed under the reaction conditions. α,β -Unsaturated derivatives are oxidized very efficiently without affecting the olefinic bond and the reaction is essentially chemoselective (Table 2, entries 15, 26). Furthermore, functional groups such as methoxy, nitro and alkyl groups were also inert to this reagent and no byproduct formation was observed (Table 2).

Aliphatic and aromatic thiols are easily oxidized to their corresponding disulfides with XTPPDCC at room temperature in excellent yield (Table 2, entries 32-44).

It is interesting to mention that XTPPDCC can selectively oxidize thiols to disulfides in the presence of alcohols or trimethylsilyl ethers in acetonitrile at room temperature (Scheme 2). When an equimolar mixture of thiol and alcohol or trimethylsilyl ether was treated with

XTPPDCC, only the thiol was oxidized, while the alcohol or trimethylsilyl ether remained unaffected (Table 3).

CONCLUSION

In summary, we have developed a convenient and efficient method for oxidation of structurally different alcohols and trimethylsilyl ethers to the corresponding carbonyl compounds and coupling of thiols to disulfides. Our new method has significant advantages such as selective procedure, high yields and mild reaction conditions.

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REFERENCES

1. Shaabani, A., E. Farhangi and A. Rahmati, 2010. An Efficient and Selective Oxidation of Sulfides and Thiols with Silica-Supported 1,1,3,3-Tetramethylguanidine/Br₂ Complex. Phosphorus, Sulfur Silicon Relat. Elem., 185: 463-468.

2. Chehardoli, G. and M.A. Zolfigol, 2010. Melamine Hydrogen Peroxide (MHP): Novel and Efficient Reagent for the Chemo- and Homoselective and Transition Metal-Free Oxidation of Thiols and Sulfides. *Phosphorus, Sulfur Silicon Relat. Elem.*, 185: 193-203.
3. Hajipour, A.R., M. Mostafavi and A.E. Ruoho, 2009. Oxidation of Thiols Using $K_2S_2O_8$ in Ionic Liquid. *Phosphorus, Sulfur Silicon Relat. Elem.*, 184: 1920-1923.
4. Shiri, L. and A. Ghorbani-Choghamarani, 2009. Chemoselective Oxidation of Benzylic Alcohols and Hydroquinones with bis-(2,4,6-Trimethylpyridinium) Dichromate (BTMPDC) as an Efficient and New Oxidizing Agent. *Phosphorus, Sulfur Silicon Relat. Elem.*, 184: 492-498.
5. Shirini, F., G.H. Imanzadeh, A.R. Mousazadeh, I. Mohammadpoor-Baltork, A.R. Aliakbar and M. Abedini, 2010. $(PhCH_2PPh_3)^+Br_3^-$: A Versatile Reagent for the Preparation, Deprotection and Oxidation of Trimethylsilyl Ethers. *Phosphorus, Sulfur Silicon Relat. Elem.*, 185: 641-646.
6. Huang, J.Y., S.J. Li and Y.G. Wang, 2006. TEMPO-linked metalloporphyrins as efficient catalysts for selective oxidation of alcohols and sulfides. *Tetrahedron Lett.*, 47: 5637-5640.
7. Lei, M., R.J. Hu and Y.G. Wang, 2006. Mild and selective oxidation of alcohols to aldehydes and ketones using $NaIO_4$ /TEMPO/ $NaBr$ system under acidic conditions. *Tetrahedron*, 62: 8928-8932.
8. Ay, K., E. Ay, N. Yenil and L. Yuceer, 2009. Synthesis and characterization of 2'-oxopropylene derivatives of chloraloses. *World Appl. Sci. J.*, 6(5): 880-885.
9. Alinezhad, H., M. Tajbakhsh and R. Soleimani, 2009. Selective oxidation of benzylic and allylic alcohols with $NaOCl$ /silica gel system. *J. Iran. Chem. Soc.*, 6: 288-292.
10. Lakouraj, M.M., M. Tajbakhsh, F. Ramzanian-Lehmali and K. Ghodrati, 2008. Ionene supported peroxodisulfates: Polymeric reagents for the oxidative deprotection of TMS and THP ethers and oxidative cleavage of the C=N bond in water. *Monatshefte Fur Chemie*, 139: 537-541.
11. Ghasemnejad-Bosra, H., M. Tajbakhsh, F. Ramzanian-Lehmali, M. Shabani-Mahali and M.A. Khalilzadeh, 2008. A mild and efficient method for oxidative deprotection of trimethylsilyl ethers to the corresponding carbonyl compounds using $[PhCH_2NMe_2Ph]_2S_2O_8$. *Phosphorus, Sulfur Silicon Relat. Elem.*, 183: 1496-1500.
12. Lakouraj, M.M., M. Tajbakhsh and F. Ramzanian-Lehmali, 2008. α -Naphthyltriphenyl phosphonium peroxodisulfate: A selective and regenerable reagent for oxidation of organic compounds. *Phosphorus, Sulfur Silicon Relat. Elem.*, 183: 1388-1395.
13. Geran-Urimi, A., H. Alinezhad and M. Tajbakhsh, 2008. Oxidation of alcohols and hydroquinones to carbonyl compounds using cetyltrimethylammonium peroxodisulfate as a new, selective and regenerable oxidant. *Acta Chim. Slov.*, 55: 481-485.
14. Norouzi, M., M. Tajbakhsh, H. Alinezhad and A. Geran-Urimi, 2008. Deprotection of oximes, phenylhydrazones, semicarbazones and thiosemicarbazones to the corresponding carbonyl compounds using cetyltrimethylammonium peroxodisulfate as a new and selective oxidizing agent. *J. Chin. Chem. Soc.*, 55: 508-511.
15. Tajbakhsh, M., M.M. Lakouraj and F. Ramzanian-Lehmali, 2006. $\{-N^+(CH_3)_2CH_2CH_2N^+[(CH_3)_2](CH_2)_4-\}_n S_2O_8^{2-}$: A selective and recyclable reagent for oxidation of alcohols and hydroquinones in water. *Synlett*, pp: 1724-1728.
16. Hosseinzadeh, R., M. Tajbakhsh, F. Ramzanian-Lehmali and M. Sadatshahabi, 2005. 2,6-Dicarboxypyridinium fluorochromate: A mild and efficient reagent for oxidative deprotection of trimethylsilyl ethers to their corresponding carbonyl compounds. *Phosphorus, Sulfur Silicon Relat. Elem.*, 180: 2279-2283.
17. Tajbakhsh, M., M.M. Lakouraj, M.H. Gholami and F. Ramzanian-Lehmali, 2004. Caro's acid supported on silica gel, Part VIII: An efficient and selective reagent for conversion of phenylhydrazones and semicarbazones to the corresponding carbonyl compounds. *Phosphorus, Sulfur and Silicon*, 179: 1731-1736.
18. Tajbakhsh, M., I. Mohamadpoor-Baltork and F. Ramzanian-Lehmali, 2003. Benzyltriphenylphosphoniumperoxodisulfate: An efficient and convenient reagent for the oxidative cleavage of phenylhydrazones, paranitrophenylhydrazones and semicarbazones to their parent carbonyl compounds. *Phosphorus, Sulfur and Silicon*, 178: 2621-2625.
19. Tajbakhsh, M., I. Mohamadpoor-Baltork and F. Ramzanian-Lehmali, 2003. Quinolinium fluorochromate as a reagent for selective oxidative cleavage of oximes and phenylhydrazones to their parent carbonyl compounds under non-aqueous and aprotic conditions. *J. Chem. Res.*, (S): 710-711.

20. Tajbakhsh, M., I. Mohamadpoor-Baltork and F. Ramzanian-Lehmali, 2003. Quinolinium fluorochromate: An efficient and convenient reagent for the oxidative deprotection of trimethylsilyl ethers in non-aqueous conditions. *Phosphorus, Sulfur and Silicon*, 178: 2617-2620.
21. Tajbakhsh, M., I. Mohamadpoor-Baltork and F. Ramzanian-Lehmali, 2001. Benzyltriphenylphosphonium peroxodisulfate: A mild and inexpensive reagent for selective oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals under non-aqueous and aprotic conditions. *J. Chem. Res., (S)*: 185-187.