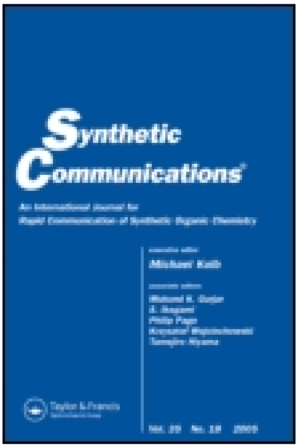
This article was downloaded by: [Dalhousie University]
On: 06 May 2013, At: 08:37
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

2,6-Dicarboxypyridinium Fluorochromate-Promoted Oxidation of Alkyl-Arenes into Carbonyl Compounds Under Nonaqueous and Aprotic Conditions

Yaghoub Sarrafi [a] , Mahmood Tajbakhsh [a] , Rahman Hosseinzadeh [a] , Marzieh Sadatshahabi [a] & Kamal Alimohammadi [a]
[a] Faculty of Chemistry, Mazandaran University, Babolsar, Iran
Accepted author version posted online: 10 Aug 2011.Published online: 01 Nov 2011.

To cite this article: Yaghoub Sarrafi , Mahmood Tajbakhsh , Rahman Hosseinzadeh , Marzieh Sadatshahabi & Kamal Alimohammadi (2012): 2,6-Dicarboxypyridinium Fluorochromate-Promoted Oxidation of Alkyl-Arenes into Carbonyl Compounds Under Nonaqueous and Aprotic Conditions, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 42:5, 678-685

To link to this article: http://dx.doi.org/10.1080/00397911.2010.529228

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Downloaded by [Dalhousie University] at 08:37 06 May 2013

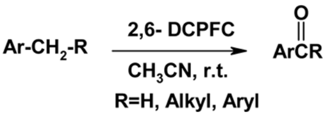
Synthetic Communications®, 42: 678–685, 2012
Copyright © Taylor & Francis Group, LLC
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2010.529228

Downloaded by [Dalhousie University] at 08:37 06 May 2013

2,6-DICARBOXYPYRIDINIUM FLUOROCHROMATE–PROMOTED OXIDATION OF ALKYL-ARENES INTO CARBONYL COMPOUNDS UNDER NONAQUEOUS AND APROTIC CONDITIONS

**Yaghoub Sarrafi, Mahmood Tajbakhsh,
Rahman Hosseinzadeh, Marzieh Sadatshahabi, and
Kamal Alimohammadi**
Faculty of Chemistry, Mazandaran University, Babolsar, Iran

GRAPHICAL ABSTRACT



$$\text{Ar-CH}_2\text{-R} \xrightarrow[\text{CH}_3\text{CN, r.t.}]{\text{2,6- DCPFC}} \text{Ar}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{R}$$

R=H, Alkyl, Aryl

Abstract *Benzylic C-H oxidation of a wide variety of alkyl- and cycloalkyl arenes employing 2,6-dicarboxypyridinium fluorochromate under mild reaction conditions is described. The corresponding carbonyl compounds are obtained in good to excellent yields.*

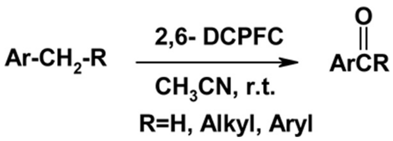
Keywords Alkyl-arenes; carbonyl compounds; 2,6-dicarboxypyridinium fluorochromate; oxidation

INTRODUCTION

The introduction of carbonyl functionality at the benzylic position from the corresponding alkyl-arenes is an important transformation in organic synthesis,[1] because the carbonyl compounds can serve as valuable building blocks in the manufacture of special chemicals in pharmaceutical and agrochemical industries. In addition, aryl ketones are integral parts of various natural products.[2] In the past few years, many methods have been devised for introducing a carbonyl moiety at the benzylic position,[3] for example, pyridinium chlorochromate (PCC),[4] Gif reagent/picolinic acid,[5] $RuCl_2$ $(PPh_3)_3$-t-BuOOH,[6] $[Rh_2(cap)_4]$,[7] mesoporous CrMCM-41 molecular sieves,[8] 3,6-bis(triphenylphosphonium) cyclohexene peroxodisulfate,[9] and in situ–generated Bi(0) as catalyst along with *tert*-butyl hydroperoxide and picolinic acid.[10] Although all of these methods are effective, some of them have drawbacks such as lengthy workup procedures, harsh reaction conditions,[10]

Received April 25, 2010.

Address correspondence to Yaghoub Sarrafi, Faculty of Chemistry, Mazandaran University, Babolsar, Iran. E-mail: ysarrafi@umz.ac.ir



Scheme 1.

and requirements for absolutely dry and inert media.[6] Thus, there is still a need to develop an operationally simple, mild, and useful method.

Herein, we report a convenient method for the oxidation of benzylic hydrocarbons to the corresponding carbonyl compounds using 2,6-dicarboxypyridinium fluorochromate (2,6-DCPFC) at room temperature (Scheme 1).

RESULTS AND DISCUSSION

The use of chromium(VI) reagents having quaternary ammonium ions as effective oxidizing agents has been reported in organic transformations.[11] Recently we have noticed that the 2,6-dicarboxypyridinium moiety in chromium(VI) reagents is very effective in the oxidation of alcohols, silyl and tetrahydropyrane (THP) ethers,[12a] oxidative deprotection of oximes, phenylhydrazones, and semicarbazones to carbonyl compounds,[12b,c] deprotection of thioacetals and 1,1-diacetates,[13] oxidation of thiols to disulfides and sulfides to sulfoxides,[14] deprotection of trimethylsilyl ethers to their parent aldehydes,[15] and oxidation of alcohols, phenols, and hydroquinones.[16] As a part of our ongoing program to develop new oxidation methods, we have used 2,6-DCPFC in the oxidation of benzylic hydrocarbons.

2,6-DCPFC is easily prepared by treatment of aqueous solution of CrO_3 and HF with pyridine 2,6-dicarboxylic acid. It is a stable yellowish solid that can be stored for months without losing its activity.

In this study, oxidation of different alkyl arenes to the corresponding carbonyl compounds was investigated. To gain some preliminary information on this synthetically useful reaction, ethyl benzene was chosen as a model substrate. When a mixture of 1:1 mol ratio of oxidant to ethyl benzene was stirred in different solvents (Table 1), after only 7 min was an almost quantitative yield of acetophenone obtained in acetonitrile (Table 1, entry 3). As shown in Table 1, this reaction in other solvents gave

Table 1. Oxidation of ethyl benzene to acetophenone with 2,6-DCPFC in different solvents at room temperature

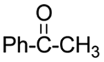
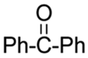
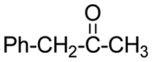
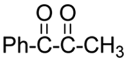
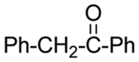
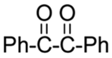
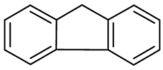
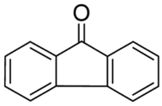
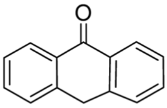
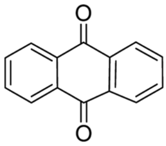
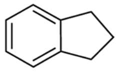
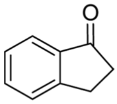
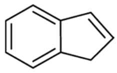
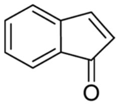
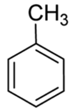
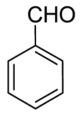
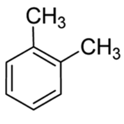
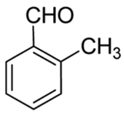
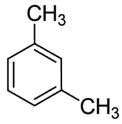
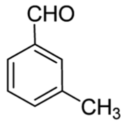
Entry	Solvent	Time (min)	Yield (%)^a
1	CH_2Cl_2	90	70
2	C_6H_6	120	40
3	CH_3CN	7	99
4	THF	40	60
5	$CHCl_3$	90	50
6	DMF	90	70
7	DMAC	90	30
8	Acetone	90	60

^{a}Isolated yield.

Downloaded by [Dalhousie University] at 08:37 06 May 2013

Downloaded by [Dalhousie University] at 08:37 06 May 2013

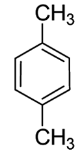
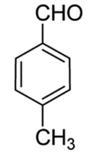
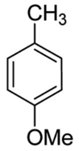
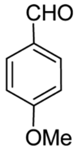
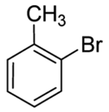
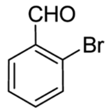
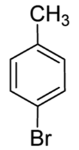
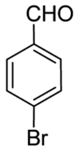
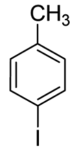
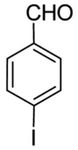
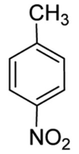
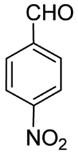
Table 2. Oxidation of alkyl-arenes to carbonyl compounds using 2,6-DCPFC in CH_3CN at room temperature

					Mp or Bp (°C)	
Entry	Substrate	Product[a]	Time (min)	Yield[b] (%)	Observed	Reported[17]
1	**Ph-CH$_2$CH$_3$**	 $\mathrm{Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3}$	7	99, 97[c]	18–20	20[17a]
2	**Ph-CH$_2$Ph**	 $\mathrm{Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}Ph}$	10	92	47–48	49[17a]
3	 $\mathrm{Ph\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3}$	 $\mathrm{Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3}$	60	82	104–105	103–105[17a]
4	 $\mathrm{Ph\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}Ph}$	 $\mathrm{Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}Ph}$	55	95	94–95	95[17a]
5			60	98	81–83	83[17a]
6			55	97	283–285	285[17a]
7			15	89	41–43	42[17b]
8			65	88	38–40	38–41[17a]
9			15	76	175–177	178[17a]
10			20	70	198–200	200[17a]
11			20	75	198–200	199[17a]

(*Continued*)

Downloaded by [Dalhousie University] at 08:37 06 May 2013

Table 2. Continued

Entry	Substrate	Product[a]	Time (min)	Yield[b] (%)	Mp or Bp (°C)	
					Observed	Reported[17]
12			15	80	202–203	204[17a]
13			25	80	247–250	248[17a]
14			60	20	228–232	230[17a]
15			60	25	66	67[17a]
16			60	50	76–77	78[17a]
17			120	Trace		106[17a]

[a] All of the products were characterized by comparison of their spectral and physical data with authentic samples.

[b] Yields refer to isolated products.

[c] The reaction was carried out with 10 mmol of substrates.

less yield of the products in longer reaction time (Table 1, entries 1, 2, and 4–8). An interesting feature of this procedure is that the reaction could be followed visually. Completion of the reaction was recognized when the color of the reaction mixture changed from yellowish to dark green.

To show the generality and applicability of this method, a variety of benzylic substrates were oxidized under the optimal reaction conditions, and the results are presented in Table 2.

Downloaded by [Dalhousie University] at 08:37 06 May 2013

As shown in Table 2, when conducting the oxidation of ethyl benzene on a 10-mmol scale, nearly the same yield of acetophenone as in small-scale reaction was obtained (Table 2, entry 1). Similarly, diphenyl methane gave 92% yield of benzophenone after 10 min (Table 2, entry 2). Oxidation of benzyl methyl ketone and benzyl phenyl ketone to afford the corresponding dicarbonyl compounds takes a longer reaction time (Table 2, enteries 3 and 4). Under the same reaction conditions, fluorene, anthrone, indan, and indene gave fluorenone, anthraquinone, 1-indanone, and 2-indene-1-one respectively in good yields (Table 2, entries 5–8). Indan, after only 15 min, selectively gave a good yield of its mono-oxidized product (Table 2, entry 7).

2,6-DCPFC can also act as an efficient reagent for the oxidation of methyl benzenes to the corresponding aldehydes. When toluene was treated with 2,6-DCPFC at room temperature, after about 15 min 76% of benzaldehyde together with a small amount of benzoic acid formed (Table 2, entry 9). Similarly, xylenes converted selectively to their tolualdehyde derivatives in good yields together with a small amount of the corresponding toluic acids (Table 2, entries 10–12). *p*-Methoxytoluene also gave good yield of *p*-methoxybenzaldehyde after 25 min (Table 2, entry 13). However, alkyl arenes with electron-withdrawing groups proceeded to the corresponding aldehydes in poor yields and long reaction time (Table 2, entries 14–17). For example, *o*-bromotoluene or *p*-nitrotoluene even after 60 and 120 min gave 20% *o*-bromobenzaldehyde and a trace amount of *p*-nitrobenzaldehyde, respectively. Increasing the amount of reagent and reaction temperature did not improve the yield of the corresponding aldehydes but led to the formation of the corresponding acid in poor yields.

To show the advantages and drawbacks of this method, we compared oxidation of diphenylmethane to benzophenone with some other oxidants reported in the literature in Table 3. As shown in this table, oxidation with 2,6-DCPFC is

Table 3. Oxidation of diphenylmethane to benzophenone by 2,6-DCPFC in comparison with some other reagents

Entry	Reagent	Conditions	Time	Yield (%)	Reference
1	2,6-DCPFC	CH_3CN, rt	10 min	92	—
2	2,6-DCPFC	Solid phase	1 h	14	—
3	$HBr–H_2O_2$	CH_2Cl_2, rt	12 h	91	3b
4	CrO_3-H_5IO_6	CH_3CN, rt	1 h	99	3c
5	Cr-PILCP[a] - t-BuOOH	CH_2Cl_2, rt, N_2 atm	44 h	90	3d
6	PDC[b] -t-BuOOH	Substrate–t-BuOOH–PDC = 1:4:4, benzene, rt	14 h	76	3e
7	$Rh_2(cap)_4$[c] - t-BuOOH	K_2CO_3, CH_2Cl_2, rt	16 h	55	7
8	Mesoporous CrMCM-41, Molecular Sieves, H_2O_2 (50%)	Methanol, 80 °C	12 h	53.8	8
9	t-BuOOH, Catalyst Bi(0), Picolinic Acid	Pyridine–AcOH (9:1), 100 °C	16 h	95	—

[a] Cr-PILCP: chromium-pillared clay catalyst.

[b] PDC: pyridinium dichromate.

[c] $Rh_2(cap)_4$: dirhodium caprolactamate.

superior to other methods in terms of yields, easier isolation of the products, milder reaction conditions, and shorter reaction time.

CONCLUSION

In conclusion, oxidation of benzylic C-H in arenes to their carbonyl compounds can be effectively performed with 2,6-DCPFC under mild reaction conditions. Selective oxidation, simple procedure, easy reaction workup, efficiency, good yields, and short reaction time are the advantages of this method that make this reagent a useful addition to the category of oxidants for benzylic substrates.

EXPERIMENTAL

All the chemicals were purchased from Merck. The reactions were monitored by thin-layer chromatography (TLC) using silica-gel plates, and the products were purified by flash column chromatography on silica gel (Merck, 230–400 mesh) and were identified by comparison of their spectra (^{1}H NMR and FT-IR) and physical data with those of the authentic samples. ^{1}H NMR spectra were recorded with Brucker DRX500 Avance (400-MHz) spectrometers, using $CDCl_3$ as solvent. IR spectra were recorded on a Pye-Unicam SP 1100 spectrophotometer.

Preparation of 2,6-Dicarboxypyridinium Fluorochromate (2,6-DCPFC)

To a solution of CrO_3 (2.00 g, 0.02 mol) in 1.0 cm^3 water in a polyethylene beaker, 40% HF (1.5 cm^3, 0.03 mol) was added with stirring. An orange-red solution was obtained. The reaction mixture was then cooled in an ice bath ($-5\,°C$), and pyridine 2,6-dicarboxylic acid (3.342 g, 0.02 mol) was added portionwise. The orange crystalline compound formed that was then filtered under vacuum using a polyethylene funnel, washed with petroleum ether ($3 \times 10\,cm^3$), rapidly dried in a vacuum desicator, and finally stored in a polyethylene bag. The yield of 2,6-DCPFC was found to be 92% (5.28 g).[12c]

General Procedure for the Oxidation of Benzylic Hydrocarbons

In a round-bottomed flask (50 ml) equipped with a magnetic stirrer, a mixture of the substrate (1 mmol) in CH_3CN (5 cm^3) and 2,6-DCPFC (1 mmol) was placed. The reaction mixture was stirred at room temperature for the specified time (Table 2). The progress of the reaction was monitored by TLC or visually. After the reaction was completed, the mixture was filtered, and the solid material was washed with diethyl ether ($2 \times 10\,cm^3$). The combined filtrate was evaporated under reduced pressure to afford pure carbonyl compound. If necessary, the product was further purified on a silica-gel plate or silica-gel column with appropriate eluent.

ACKNOWLEDGMENT

Financial support of this work from the Research Council of Mazandaran University is gratefully acknowledged.

Downloaded by [Dalhousie University] at 08:37 06 May 2013

REFERENCES

1. (a) Warren, S. *Organic Synthesis: The Disconnection Approach*; John Wiley and Sons: Singapore, 2004; p. 57, 201, and 330; (b) Ghosh, S.; Banik, B. K.; Ghatak, U. R. An expeditious synthesis of 1,2,3,4-tetrahydro-1,1-dimethylphenanthrenes. *J. Chem. Soc., Perkin Trans. 1.* **1991**, 3195–3197.
2. Compere, D.; Marazano, C.; Das, B. C. An enantioselective access to lobelia alkaloids. *J. Org. Chem.* **1999**, *64*, 4528–4532.
3. (a) Larock, R. C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; VCH: New York, 1989; p. 591; (b) Khan, A. T.; Parvin, T.; Choudhury, L. H.; Ghosh, S. A simple synthetic protocol for oxidation of alkyl arenes into ketones using a combination of HBr–H_2O_2. *Tetrahedron Lett.* **2007**, *48*, 2271–2274; (c) Yamazaki, S. Chromium(VI) oxide–catalyzed benzylic oxidation with periodic acid. *Org. Lett.* **1999**, *1*, 2129–2132; (d) Choudary, B. M.; Prasad, A. D.; Bhuma, V.; Swapna, V. Chromium-pillared clay as a catalyst for benzylic oxidation and oxidative deprotection of benzyl ethers and benzylamines: A simple and convenient procedure. *J. Org. Chem.* **1992**, *57*, 5841–5844; (e) Chidambaram, N.; Chandrasekaran, S. *tert*-Butyl hydroperoxide-pyridinium dichromate: A convenient reagent system for allylic and benzylic oxidations. *J. Org. Chem.* **1987**, *52*, 5048–5051.
4. Hosseinzadeh, R.; Tajbakhsh, M.; Vahedi, H. Selective oxidation of methylarenes with pyridinium chlorochromate. *Synlett* **2005**, 2769–2770.
5. Kim, S. S.; Sar, S.; Tamrakar, P. Gif chemistry for oxidation of activated methylenes to ketones. *Bull. Korean Chem. Soc.* **2002**, *23*, 937–938.
6. Murahashi, S. I.; Komiya, N.; Oda, Y.; Kuwabara, T.; Naota, T. Ruthenium-catalyzed oxidation of alkanes with *tert*-butyl hydroperoxide and peracetic acid. *J. Org. Chem.* **2000**, *65*, 9186–9193.
7. Catino, A. J.; Nichols, J. M.; Choi, H.; Gottipamula, S.; Doyle, M. P. Benzylic oxidation catalyzed by dirhodium(II, III) caprolactamate. *Org. Lett.* **2005**, *23*, 5167–5170.
8. Mohapatra, S. K.; Selvam, P. A highly selective, heterogeneous route to enones from allylic and benzylic compounds over mesoporous CrMCM-41 molecular sieves. *J. Catal.* **2007**, *249*, 394–396.
9. Badri, R.; Soleymani, M. 3,6-Bis(triphenylphosphonium) cyclohexene peroxodisulfate as an efficient and mild oxidizing agent for conversion of alkylbenzenes to corresponding carbonyl compounds. *Synth. Commun.* **2002**, *32*, 2385–2389.
10. Bonvin, Y.; Callens, E.; Larrosa, I.; Henderson, D. A.; Oldham, J.; Burton, A. J.; Barrett, A. G. M. Bismuth-catalyzed benzylic oxidations with *tert*-butyl hydroperoxide. *Org. Lett.* **2005**, *21*, 4549–4552.
11. (a) Patel, S.; Mishra, B. K. Chromium(VI) oxidants having quaternary ammonium ions: Studies on synthetic applications and oxidation kinetics. *Tetrahedron* **2007**, *63*, 4367–4406; (b) Tajbakhsh, M.; Mohammadpoor-Baltork, I.; Alimohammadi, K. An efficient and selective solid state oxidation of thiols to disulfides with quinolinium fluorochromate on silica gel. *Monatsh Chem.* **2003**, *134*, 1571–1575; (c) Tajbakhsh, M.; Alimohammadi, K.; Ramzanian Lehmali, F.; Barghamadi, M.; Shakeri, A. Quinolinium fluorochromate: An efficient and convenient reagent for oxidative cleavage of thioacetals to their parent carbonyl compounds. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 2587–2591.
12. (a) Tajbakhsh, M.; Hosseinzadeh, R.; Yazdani-Niaki, M. Synthesis and application of 2,6-dicarboxypyridinium chlorochromate as a new oxidizing reagent for alcohols, silyl ethers, and THP ethers under mild and non-aqueous conditions. *J. Chem. Res., Synop.* **2002**, 508–510; (b) Tajbakhsh, M.; Hosseinzadeh, R.; Yazdani-Niaki, M. 2,6-Dicarboxypyridinium chlorochromate: A mild, efficient, and selective reagent for oxidative deprotection of oximes to carbonyl compounds. *Tetrahedron Lett.* **2002**, *43*, 9413–9415; (c)

Downloaded by [Dalhousie University] at 08:37 06 May 2013

Tajbakhsh, M.; Hosseinzadeh, R.; Ramzanian Lehmali, F.; Sadatshahabi, M. 2,6-Dicarboxyopyridinium fluorochromate: A mild and efficient reagent for oxidative deprotection of oximes, phenylhydrazones to their corresponding carbonyl compounds under solvent-free conditions. *J. Chin. Chem. Soc.* **2005**, *52*, 1005–1009.

13. Hosseinzadeh, R.; Tajbakhsh, M.; Shakoori, A. R.; Yazdani-Niaki, M. 2,6-Dicarboxypyridinium chlorochromate: An efficient and selective reagent for the mild deprotection of acetals, thioacetals, and 1,1-diacetates to carbonyl compounds. *Monatsh Chem.* **2004**, *135*, 1243–1249.
14. (a) Tajbakhsh, M.; Hosseinzadeh, R.; Shakoori, A. R. 2,6-Dicarboxypyridinium chlorochromate: An efficient and selective reagent for the oxidation of thiols to disulfides and sulfides to sulfoxides. *Tetrahedron Lett.* **2004**, *45*,1889–1893; (b) Tajbakhsh, M.; Mohammadpoor Baltork, I.; Ramzanian Lehmali, F. Quinulinium fluorochromate $C_9H_7NHCrO_3F$: An efficient and convenient reagent for the oxidative deprotection of trimethylsilyl ethers in nonaqueous conditions. *Phosphorus, Sulfur Silicon Relat. Elem.* **2003**, *178*, 2617–2620; (c) Tajbakhsh, M.; Khazaei, A.; Shabani Mahalli, M.; Ghorbani Vaghi, R. N,N-Dibromobenzenesulfonamide as a reagent for oxidative cleavage of oximes to their parent carbonyl compounds under non-aqueous and aprotic conditions. *J. Chem. Res., Synop.* **2004**, 141–142; (d) Tajbakhsh, M.; Lakouraj, M. M.; Fadavi, A. Allyltriphenylphosphonium peroxodisulfate $(CH_2{=}CHCH_2PPh_3)_2S_2O_8$: An efficient and convenient reagent for the oxidation of alcohols, silyl, and THP ethers under nonaqueous conditions. *Synth. Commun.* **2004**, *34*, 1173–1181.
15. Tajbakhsh, M.; Hosseinzadeh, R.; Sadatshahabi, M. 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.* **2005**, *180*, 2279–2283.
16. Tajbakhsh, M.; Hosseinzadeh, R.; Sadatshahabi, M. Synthesis and application of 2,6-dicarboxypyridinium fluorochromate as a new solid phase oxidant. *Synth. Commun.* **2005**, *35*, 1547–1554.
17. (a) Furniss, B. S.; Manaford, A. J.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 4th Ed.; 1978; p. 1192, 1196; (b) Shriner, R. L.; Hermann, C. K. F.; Morrill, T. C.; Curtin, D. Y.; Fuson, R. C. *The Systematic Identification of Organic Compounds*; Wiley: New York, 2004; p. 652.

Downloaded by [Dalhousie University] at 08:37 06 May 2013