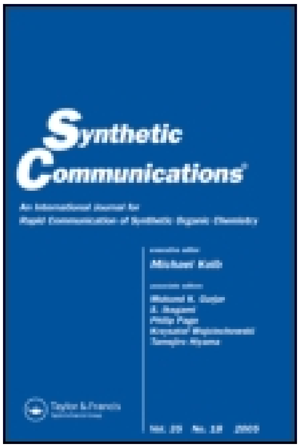
This article was downloaded by: [University of North Dakota]
On: 09 October 2013, At: 15:09
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

Silica Chromate as a Novel Oxidizing Agent for the Oxidation of 1,4-Dihydropyridines

Mohammad Ali Zolfigol [a] , Peyman Salehi [b] , Arash Ghorbani-Choghamarani [c] , Maliheh Safaiee [a] & Mozhgan Shahamirian [a]

[a] Faculty of Chemistry , Bu-Ali Sina University , Hamadan, Iran

[b] Department of Chemistry , Medicinal Plants and Drugs Research Institute, Shahid Beheshti University , Evin, Tehran, Iran

[c] Department of Chemistry, Faculty of Science , Ilam University , Ilam, Iran

Published online: 30 Jun 2007.

To cite this article: Mohammad Ali Zolfigol , Peyman Salehi , Arash Ghorbani-Choghamarani , Maliheh Safaiee & Mozhgan Shahamirian (2007) Silica Chromate as a Novel Oxidizing Agent for the Oxidation of 1,4-Dihydropyridines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 37:11, 1817-1823, DOI: 10.1080/00397910701316276

To link to this article: http://dx.doi.org/10.1080/00397910701316276

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

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. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

Synthetic Communications®, 37: 1817–1823, 2007
Copyright © Taylor & Francis Group, LLC
ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701316276

Silica Chromate as a Novel Oxidizing Agent for the Oxidation of 1,4-Dihydropyridines

Mohammad Ali Zolfigol
Faculty of Chemistry, Bu-Ali Sina University, Hamadan, Iran

Peyman Salehi
Department of Chemistry, Medicinal Plants and Drugs Research Institute,
Shahid Beheshti University, Evin, Tehran, Iran

Arash Ghorbani-Choghamarani
Department of Chemistry, Faculty of Science, Ilam University, Ilam, Iran

Maliheh Safaiee and Mozhgan Shahamirian
Faculty of Chemistry, Bu-Ali Sina University, Hamadan, Iran

Abstract: Silica chromate easily converts 1,4-dihydropyridines to their corresponding pyridines in the presence of $NaHSO_4 \cdot H_2O$ and wet SiO_2 in dichloromethane at room temperature in good to excellent yields.

Keywords: 1,4-dihydropyridines, $NaHSO_4$, oxidation, pyridines, silica chromate, sodium hydrogen sulfate

Hantzsch 1,4-dihydropyridines, a class of model compounds of nicotine amid adenine dinucleotide (NADH) coenzyme, have been extensively studied in view of the biological pertinence of these compounds to the NADH redox process.[1,2] They process neuroprotective, platet anti-aggregration, and anti-diabetic activities.[3] Some representative, such as nifedipine, niguldipine, nicardipine, and amlodipine, are widely used for treatment of hypertension.[4]

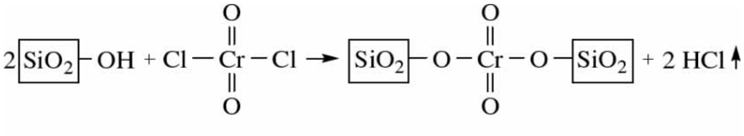
Received in the U.K. November 23, 2005

Address correspondence to Mohammad Ali Zolfigol, Faculty of Chemistry, Bu-Ali Sina University, P.O.Box 6517838483, Hamadan, Iran. E-mail: zolfi@basu.ac.ir

Hantzsch 1,4-dihydropyridines are easily prepared from the Hantzsch reaction or its modifications.[5–8] In recent years, it was found that drugs such as nifedipine and niguldipine undergo redox processes due to the catalysis of cytochrome P-450 in the liver during their metabolism.[9] Therefore, the oxidation of 1,4-dihydropyridines has attracted considerable attention. Several oxidation reagents have been reported for the oxidation of 1,4-dihydropyridines, such as isoxazolones,[1a] SeO_2,[3] lead (IV) tetraacetate,[4] $FeCl_3/KMnO_4$,[9] triazolinediones,[10] ferric or cupric nitrates on a solid support (clayfen or claycop), ceric ammonium nitrate, clay-supported cupric nitrate accompanied by ultrasound-promotion NO gas,[11] Pd/C,[12] O_2/activated carbon,[13] manganese dioxide or DDQ, nitric oxide, bismuth nitrate pentahydrate, pyridinum chloro chromate (PCC), tetrakis-pyridine cobalt(II) dicromate (TPCD), nicotinium dichromate,[14] the N_2O_4 complex of 18-crown-6,[15] *S*-nitrosogluthathione, diphenylpicrylhydrazyl and benzoyl peroxide as free-radical oxidizing agents, $KMnO_4$, CrO_3, HNO_3, HNO_2, *tert*-butylhydroperoxide, silica-gel-supported ferric nitrate (silfen), N_2O_3, $MCl_x/NaNO_2$/wet SiO_2 and silica chloride/$NaNO_2$ wet SiO_2,[16] photochemical and voltammetric oxidation,[17] $H_2O_2/Co(OAc)_2$,[18] $NaHSO_4/Na_2Cr_2O_7$/wet SiO_2,[19] peroxydisulfate-cobalt(II),[20] $Zr(NO_3)_4$,[21] hypervalent iodine reagents,[22] Co(II)-catalyzed auto oxidation,[23] inorganic acidic salts and sodium nitrite or nitrate,[24–28] I_2-MeOH and I_2-ultrasound,[29] $KBrO_3/MCl_n$,[30] $(n\text{-Bu})_4IO_4$/[Mn(TPP)Cl],[31] and heteropolyacid/$NaNO_2$/wet SiO_2.[32]

Our goal in undertaking this line of work was twofold: (i) to overcome the limitations and drawbacks of the reported methods such as tedious workup, acidic media, and safety problems, and moreover (ii) to develop a high-yielding conversion of 1,4-dihydropyridines to their corresponding pyridines by using a novel synthetic silica-based oxidant.

In continuation of our studies on the synthesis of new inorganic silica-based resins,[33] we found that silica gel reacts with dichloro chromium oxide to give silica chromate (**I**). It is interesting to note that the reaction is easy and clean without any workup procedure because HCl gas is evolved from the reaction vessel immediately (Scheme 1).[34] Here, we report a simple, cheap, and mild method for the effective oxidation of 1,4-dihydropyridines using silica chromate **I** in the presence of $NaHSO_4 \cdot H_2O$ and wet SiO_2 in dichloromethane at room temperature.

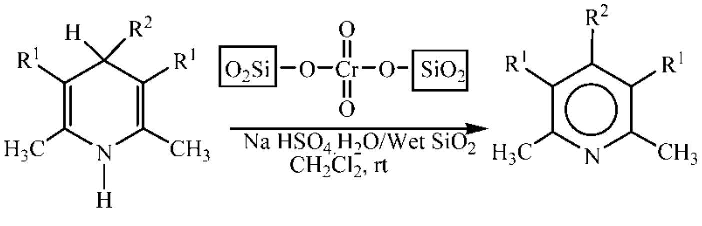


$$2\,\boxed{SiO_2}\!-OH + Cl-\overset{\displaystyle O}{\overset{\|}{\underset{\underset{\displaystyle O}{\|}}{Cr}}}-Cl \rightarrow \boxed{SiO_2}\!-O-\overset{\displaystyle O}{\overset{\|}{\underset{\underset{\displaystyle O}{\|}}{Cr}}}-O-\boxed{SiO_2} + 2\,HCl\uparrow$$

I

Scheme 1.

A good range of dihydropyridines (**1**) was subjected to the oxidation reaction in the presence of silica chromate **I**, $NaHSO_4 \cdot H_2O$, and wet SiO_2 (50% *w*/*w*) in dichloromethane (Scheme 2). The oxidation reactions were performed under mild and completely heterogeneous conditions at room temperature and took place with good to excellent yields. The reaction was mild and the workup was straightforward, requiring simple filtration of the silica-based reagents. Highly pure pyridine derivatives **2** could be obtained by passing the filtrate through a short pad of silica gel and evaporation of the solvent. The results and reaction conditions are give in Table 1. The



1 **2**

Scheme 2.

1,2	R^1	R^2
a	COOEt	H
b	COOEt	Me
c	COOEt	Et
d	COOEt	*n*-Pr
e	COOEt	Ph
f	COOEt	2-Thienyl
g	COOEt	2-Furyl
h	COOEt	$3\text{-}NO_2\text{-}C_6H_4\text{-}$
i	COOEt	$4\text{-}NO_2\text{-}C_6H_4\text{-}$
j	COOEt	$4\text{-Br-}C_6H_4\text{-}$
k	COOMe	Me
l	COOMe	Et
m	COOMe	*n*-Pr
n	COOMe	Ph
o	COOMe	2-Thienyl
p	COOMe	2-Furyl
q	COOMe	$3\text{-}NO_2\text{-}C_6H_4\text{-}$
r	COOMe	$4\text{-}NO_2\text{-}C_6H_4\text{-}$
s	COOMe	$2\text{-Br-}C_6H_4\text{-}$
t	COOMe	$4\text{-Br-}C_6H_4\text{-}$

Table 1. Oxidation of 1,4-dihydropyridines (1) to their corresponding pyridine derivatives (2) with a combination of silica chromate (I), $NaHSO_4 \cdot H_2O$ (II), and wet SiO_2 (50% w/w) in dichloromethane at room temperature

Entry	Substrate	Product	Reagents/substrate[a] I	Reagents/substrate[a] II	Time (min)	Yield[b] (%)
1	**1a**	**2a**	1.05	7	20	76
2	**1b**	**2b**	1.125	7.5	35	98
3	**1c**	**2c**	1.05	7	50	97
4	**1d**	**2d**	1.05	7	35	85
5	**1e**	**2e**	1.125	7.5	150	88
6	**1f**	**2f**	1.2	8	75	97
7	**1g**	**2g**	1.2	8	100	95
8	**1h**	**2h**	1.2	8	65	91
9	**1i**	**2i**	1.2	8	60	98
10	**1j**	**2j**	1.05	7	50	89
11	**1k**	**2k**	1.125	7.5	45	80
12	**1l**	**2l**	1.05	7	40	83
13	**1m**	**2m**	1.05	7	75	91
14	**1n**	**2n**	1.125	7.5	125	90
15	**1o**	**2o**	1.2	8	90	83
16	**1p**	**2p**	1.2	8	60	91
17	**1q**	**2q**	1.2	8	100	94
18	**1r**	**2r**	1.2	8	105	92
19	**1s**	**2s**	1.05	7	50	85
20	**1t**	**2t**	1.05	7	120	91

[a] Wet SiO_2:substrate (0.3 g:1 mmol); I and II refer to gram of the silica chromate and mmol of $NaHSO_4 \cdot H_2O$ respectively.

[b] Isolated yields.

pyridine derivatives were characterized by comparison of their spectral (IR, ^1H NMR) and physical data with the authentic samples (Table 1).

The application of silica-gel-supported chromium trioxide in the aromatization of 1,4-dihydropyridines has already been reported.[35] To the best of our knowledge, silica chromate is the first example of silica-chromium-based oxidant with covalent linkages (silica vulcanized with CrO_2 linkages).[34] Thus, we hoped that the silica chromate **I** would be superior to the previously reported chromium-based oxidants[36–41] because (i) toxic chromium cations could be collected from the reaction mixture easily, (ii) workup is very simple and pure products are obtained solely by filtration and removing of solvent, and (iii) there is no need for any chelating agents such as pyridine in pyridinium chlorochromate (PCC).[41] Moreover, in older procedures, isolation of the oxidation products from reaction mixture and chelating agents such as pyridine in PCC was difficult.[36,41]

In conclusion, the low cost and the availability of the reagents, easy and clean workup, and high yields make this method attractive for chemists. We believe that the present methodology could be an important addition to the existing methodologies.

EXPERIMENTAL

General

Chemicals were purchased from Fluka, Merck, and Aldrich chemical companies. The pyridine derivatives were characterized by comparison of their spectral (IR, ^1H NMR) and physical data with those of the authentic samples.[1,33] All Hantzsch 1,4-dihydropyridines were easily prepared by our recent published procedure.[5]

Preparation of Silica Chromate

A 500-mL suction flask was equipped with a constant-pressure dropping funnel containing dichloro chromium oxide (23.2 g, 0.15 mol) and gas inlet tube for conducting HCl gas over an adsorbing solution (i.e., water). Silica gel (100 g) was charged into the flask. Dichloro chromium oxide was added dropwise over a period of 20 min at room temperature. HCl gas evolved from the reaction vessel immediately (Scheme 1). After the addition was complete, the mixture was shaken for 90 min. A brown solid (silica chromate) was obtained quantitatively.[34]

General Procedure for the Oxidation of 1,4-Dihydropyridines

A suspension of compound **1**, silica chromate, and wet SiO_2 [(50% w/w)] in CH_2Cl_2 (10 mL) was stirred at room temperature for a specific time (molar ratio of reagents and needed reactions times indicated in Table 1). The progress of the reaction was monitored by thin-layer chromatography (TLC). After disappearing the spot of starting material **1** on TLC, the reaction mixture was filtered off. The residue was washed with CH_2Cl_2 (2×10 mL). Anhydrous Na_2SO_4 (1 g) was added to the filtrate and filtered off after 20 min. Dichloromethane was removed, and product **2** was obtained.

ACKNOWLEDGMENT

Financial support of this work by the Management and Programming Organization of Iran (award of the selection by ESI) and Research Affair, Bu-Ali Sina University, Hamadan, Iran, is gratefully acknowledged.

REFERENCES

1. (a) Han, B.; Liu, Q.; Liu, Z.; Mu, R.; Zhang, W.; Liu, Z. L.; Yu, W. *Synlett* **2005**, 2333; (b) Liu, Z. G.; Han, B.; Liu, Q.; Zhang, W.; Yang, L.; Liu, Z. L.; Yu, W. *Synlett* **2005**, 1579.
2. (a) Simon, C.; Constantieux, T.; Rodriguez, J. *Eur. J. Org. Chem.* **2004**, 4957; (b) Tewari, N.; Dwivedi, N.; Tripathi, R. P. *Tetrahedron Lett.* **2004**, *45*, 9011.
3. Cai, X.; Yang, H.; Zhang, G. *Can. J. Chem.* **2005**, *83*, 273.
4. Litvic, M.; Cepanec, I.; Filipan, M.; Kos, K.; Bartolincic, A.; Druskovic, V.; Tibi, M. M.; Vinkovic, V. *Heterocycles* **2005**, *65*, 23.
5. Zolfigol, M. A.; Safaiee, M. *Synlett* **2004**, 827.
6. Chari, M. A.; Syamasundar, K. *Catal. Commun.* **2005**, *6*, 624.
7. Ji, S. J.; Jiang, Z. Q.; Lu, J.; Loh, T. P. *Synlett* **2004**, 831.
8. Sabitha, G.; Reddy, G. S. K. K.; Reddy, C. S.; Yadav, J. S. *Tetrahedron Lett.* **2003**, *44*, 4129.
9. Xia, J. J.; Wang, G. W. *Synthesis* **2005**, 2379.
10. Zolfigol, M. A.; Ghorbani Choghamarani, A.; Shahamirian, M.; Safaiee, M.; Mohammadpoor-Baltork, I.; Mallakpour, S.; Abdollahi-Alibeik, M. *Tetrahedron Lett.* **2005**, *46*, 5581.
11. Itoh, T.; Nagata, K.; Matsuya, Y.; Miyazaki, M.; Ohsawa, A. *J. Org. Chem.* **1997**, *62*, 3582, and references cited therein.
12. Nakamichi, N.; Kawashita, Y.; Hayashi, M. *Org. Lett.* **2002**, *4*, 3955.
13. Nakamichi, N.; Kawashita, Y.; Hayashi, M. *Synthesis* **2004**, 1015.
14. Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R.; Sobhani, S. *Synth. Commun.* **2000**, *30*, 1661, and references cited therein.
15. Zolfigol, M. A.; Zebarjadian, M. H.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R.; Shamsipur, M. *Synth. Commun.* **2001**, *31*, 929.
16. (a) Zolfigol, M. A.; Ghorbani Choghamarani, A.; Dialameh, S.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R. *J. Chem. Res-S.* **2003**, 18, and references cited therein; (b) Zolfigol, M. A.; Shirin, F.; Ghorbani Choghamarani, A.; Mohammadpoor-Baltork, I. *Phosphorus. Sulfur.* **2003**, *178*, 1709, and references cited therein.
17. (a) Memarian, H. R.; Sadeghi, M.; Aliyan, H. *Indian J. Chem.* **1998**, *37B*, 219; (b) Arguello, J.; Nunez-Vergara, L. J.; Sturm, J. C.; Squella, J. A. *Electrochim. Acta* **2004**, *49*, 4989.
18. Hashemi, M. M.; Ahmadibeni, Y.; Ghafuri, H. *Monatsh. Chem.* **2003**, *134*, 107.
19. Zolfigol, M. A.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Ghorbani Choghamarani, A.; Taqian-Nasab, A. *Asian J. Chem.* **2001**, *13*, 887.
20. Anniyappan, M.; Muralidharan, D.; Perumal, P. T. *Tetrahedron* **2002**, *58*, 5069.
21. Sabitha, G.; Kumar Reddy, G. S. K.; Reddy, C. S.; Fatima, N.; Yadav, J. S. *Synthesis* **2003**, 1267.
22. Lee, J. W.; Ko, K. Y. *B. Kor. Chem. Soc.* **2004**, *25*, 19.
23. Chavan, S. P.; Kharul, R. K.; Kalkote, U. R.; Shivakumar, I. *Synth. Commun.* **2003**, *38*, 1333.
24. Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Memarian, H. R.; Mohammadpoor-Baltork, I. *J. Chem. Res-S.* **2000**, 167.
25. Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Memarian, H. R.; Mohammadpoor-Baltork, I. *Synth. Commun.* **2000**, *30*, 2945.
26. Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Mohammadpoor-Baltork, I; Memarian, H. R. *Synth. Commun.* **2000**, *30*, 3919.

27. Zolfigol, M. A.; Shirin, F.; Ghorbani Choghamarani, A.; Mohammadpoor-Baltork, I. *Green Chem.* **2002**, *4*, 562.
28. Zolfigol, M. A.; Kiany-Borazjani, M.; Sadeghi, M. M.; Mohammadpoor-Baltork, I.; Memarian, H. R. *Synth. Commun.* **2000**, *30*, 551.
29. (a) Yadav, J. S.; Reddy, B. V. S.; Sabitha, G.; Reddy, G. S. K. K. *Synthesis* **2000**, 1532; (b) Zeynizadeh, B.; Dilmaghani, K. A.; Roozijoy, A. *J. Chin. Chem. Soc.* **2005**, *52*, 1001.
30. (a) Zeynizadeh, B.; Dilmaghani, K. A.; Roozijoy, A. *J. Chem. Res. Synop.* **2005**, 675; (b) Zeynizadeh, B.; Dilmaghani, K. A.; Roozijoy, A. *Synth. Commun.* **2005**, *35*, 557.
31. Nasr-Esfahani, M.; Moghadam, M.; Tangestaninejad, S.; Mirkhani, V. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3276.
32. (a) Niknam, K.; Zolfigol, M. A.; Razavian, S. M.; Mohammadpoor-Baltork, I. *Heterocycles* **2005**, *65*, 657; (b) Zolfigol, M. A.; Bagherzadeh, M.; Niknam, K.; shirini, F.; Mohammadpoor-Baltork, I.; Ghorbani-Choghamarani, A.; Baghbanzadeh, M. *J. Iran. Chem. Soc.* **2006**, *3*, 73; (c) Karami, B.; Montazerozohori, M.; Habibi, M. H.; Zolfigol, M. A. *Heterocycl. Commun.* **2006**, *11*, 513; (d) Nikname, K.; Zolfigol, M. A.; Razavian, S. M.; Mohammadpoor-Baltork, I. *J. Heterocycl. Chem.* **2006**, *65*, 199.
33. (a) Zolfigol, M. A. *Tetrahedron* **2001**, *57*, 9509; (b) Zolfigol, M. A.; Madrakian, T.; Ghaemi, E.; Afkhami, A.; Azizian, S.; Afshar, S. *Green Chem.* **2002**, *4*, 611; (c) Zolfigol, M. A.; Shirini, F.; Zamani, K.; Ghofrani, E.; Ebrahimi, S. *Phosphorus Sulfur* **2004**, *179*, 2177; (d) Madrakian, T.; Zolfigol, M. A.; Afkhami, A.; Afshar, S. *Asian J. Chem.* **2005**, *17*, 1941; (e) Bamoniri, A.; Zolfigol, M. A.; Mohammadpoor-Baltork, I.; Mirjalili, B. F. *J. Iran. Chem. Soc.* **2006**, *3*, 85.
34. Zolfigol, M. A.; Shirini, F.; Mohammadpoor-Baltork, I.; Ghorbani-Choghamarani, A.; Hajjami, M.; Sedaghat, A. M. *Mendeleev Commun.* **2005**, *15*, 113.
35. Khadilkar, B.; Jaisinghani, H.; Khare, A. *Indian. J. Chem.* **1998**, *37B*, 817.
36. Salehi, P.; Firouzabadi, H.; Farrokhi, A.; Gholizadeh, M. *Synthesis* **2001**, 2273.
37. Mahjoub, A. R.; Ghammami, S.; Kassaee, Z. *Tetrahedron Lett.* **2003**, *44*, 4555.
38. (a) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Zarei, A. *B. Kor. Chem. Soc.* **2003**, *24*, 400; (b) Shirini, F.; Zolfigol, M. A.; Khaleghi, M. *B. Kor. Chem. Soc.* **2003**, *24*, 1021; (c) Shirini, F.; Zolfigol, M. A.; Mallakpour, B.; Mallakpour, S. E.; Hajipour, A. R. *Aust. J. Chem.* **2001**, *54*, 405.
39. Yamato, T.; Shinoda, N. *J. Chem. Res-S* **2002**, 400.
40. Bressette, A. R.; Glover IV, L. C. *Synlett* **2004**, 738.
41. Fernandes, R. A. *Synlett* **2003**, 741.