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2,6-Dicarboxypyridinium chlorochromate: a mild, efficient, and selective reagent for oxidative deprotection of oximes to carbonyl compounds

Rahman Hosseinzadeh,* Mahmood Tajbakhsh* and Mohammad Yazdani Niaki

Department of Chemistry, Mazandaran University, Babolsar, Iran

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Abstract—The use of 2,6-dicarboxypyridinium chlorochromate (2,6-DCPCC) as a new, rapid, efficient, and selective reagent for the oxidative deprotection of oximes to their corresponding carbonyl compounds in acetonitrile at ambient temperature is described.

Nitrogen derivatives of aldehydes and ketones such as oximes are highly crystalline compounds. They constitute a very efficient method for the isolation, purification, and characterization of carbonyl compounds.[1] Oximes not only serve as protecting groups for carbonyl compounds[2] but also have other uses such as the preparation of nitriles,[3] amides via Beckmann rearrangement,[4] or to activate the carbonyl group.[5] In addition, oximes can be prepared from non-carbonyl compounds[6a–c] and, therefore, regeneration of carbonyl compounds from their oximes is an important reaction.

Some of the methods reported earlier for deoximation of carbonyl compounds consist of oxidative[7] or reductive methods,[8] using for example, trimethylsilyl chlorochromate,[9] titanium silicalite-1,[10] dimethyl dioxirane,[11] *t*-butylhydroperoxide,[12] *o*-iodoxybenzoic acid (IBX),[13] manganese triacetate,[14] ammonium persulphate-silica,[15] Dess–Martin periodinane,[16] quinolinium fluorochromate,[17] peroxymonosulfate on silica gel,[18] 3-carboxypyridinium chlorochromate,[19] etc. Some of these reagents suffer from one or other disadvantages such as long reaction times, difficulties in isolation of products, expense and also the potential to cause explosions by excessive heating during preparation.[7a,13,14,16a] Moreover, many of the methods cited in the literature describe the deoximation of aldoximes, which give low yields of aldehydes as the liberated aldehydes are overoxidized.[8a,20] In this paper we wish to report 2,6-dicarboxypyridinium chlorochromate (2,6-DCPCC) as a new, rapid and efficient reagent for the oxidative deprotection of oximes to their carbonyl compounds at room temperature.

This reagent is easily and cheaply prepared by the reaction of pyridine 2,6-dicarboxylic acid with chromium trioxide in 6N hydrochloric acid. 2,6-DCPCC is soluble in polar solvents such as acetonitrile and acetone, slightly soluble in THF, chloroform and dichloromethane and insoluble in benzene, *n*-hexane and carbon tetrachloride. This oxidant is stable and can be stored for months without losing its activity. The pH of the 0.01 M aqueous solution of this compound is 2.3, which is less acidic than that reported for the 3-carboxypyridinium chlorochromate (2.02)[19] and pyridinium chlorochromate (1.75).[21] The chromium content of the reagent was determined by atomic absorption and the experimental and calculated results are in a very good agreement.

The results illustrated in Table 1 indicate that the reaction is successful for a variety of aliphatic and aromatic oximes (Scheme 1).

It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of the aldehydes to their carboxylic acid was not observed. Interestingly, α,β-unsaturated oximes underwent deoximation very efficiently without rearrangement of the C=C bond and the reaction is essentially chemoselective. Furthermore, functional groups such as hydroxy and methoxy were inert to this reagent and no by-product formation was observed (Table 1). Deprotec-

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* Corresponding authors. E-mail: rahman@umz.ac.ir

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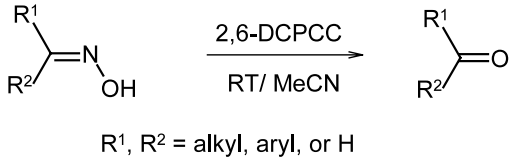
Table 1. Oxidative deprotection of oximes using 2,6-DCPCC

Entry	Substrate	*t* (min)	Product[a]	Yield (%)[b]
1	PhCH=NOH	8	PhCHO	94
2	4-MeC_6H_4CH=NOH	12	4-MeC_6H_4CHO	92
3	2-$MeOC_6H_4CH$=NOH	10	2-$MeOC_6H_4CHO$	92
4	2-HOC_6H_4CH=NOH	9	2-HOC_6H_4CHO	94
5	4-$NO_2C_6H_4CH$=NOH	20	4-$NO_2C_6H_4CHO$	92
6	4-BrC_6H_4CH=NOH	14	4-BrC_6H_4CHO	90
7	$C_6H_5C(CH_3)$=NOH	9	$C_6H_5COCH_3$	95
8	$(Ph)_2C$=NOH	8	$(Ph)_2CO$	94
9	4-$ClC_6H_4C(CH_3)$=NOH	14	4-$ClC_6H_4COCH_3$	89
10	3,4-$(MeO)_2C_6H_3C(Me)$=NOH	17	3,4-$(MeO)_2C_6H_3COCH_3$	87
11	4-$PhC_6H_4C(CH_3)$=NOH	12	4-$PhC_6H_4COCH_3$	92
12	$PhCOC(CH_3)$=NOH	19	$PhCOCOCH_3$	88
13	$(PhC=NOH)_2$	9	$(PhCO)_2$	89
14	PhCH(OH)C(Ph)=NOH	22	PhCH(OH)COPh	90
15	$CH_3COC(CH_3)$=NOH	30	$CH_3COCOCH_3$	86
16	PhCH=CHCH=NOH	20	PhCH=CHCHO	80
17	Cyclohexanone oxime	30	Cyclohexanone	84
18	Camphor oxime	35	Camphor	82

[a] All the products were identified by comparing IR, NMR and TLC with those of authentic samples.
[b] Yield refers to isolated product.



Scheme 1.

tion of aliphatic oximes normally requires longer reaction times (entries 15–18).

Another noteworthy advantage of the reagent is the exclusive oxidation of oximes irrespective of the presence of semicarbazones or phenylhydrazones. When mixtures of equimolar amounts of 2-methoxybenzaldehyde oxime and 2-methoxybenzaldehyde semicarbazone or 2-methoxybenzaldehyde phenylhydrazone were treated with 2,6-DCPCC, only the oxime was selectively oxidized to the corresponding carbonyl compound and the semicarbazone or phenylhydrazone remained unchanged (Scheme 2).

Oxidation of semicarbazones or phenylhydrazones with 2,6-DCPCC requires a higher molar ratio of oxidant, much longer reaction times, reflux temperature in acetonitrile, and gives low yields.

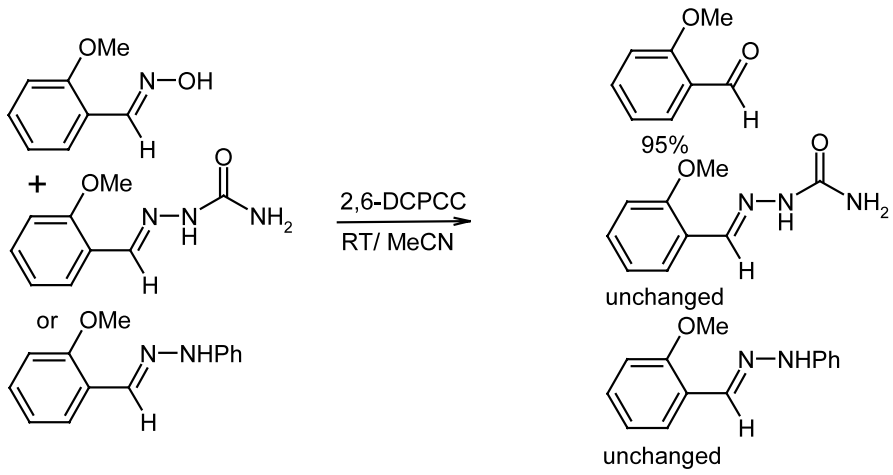
This reagent has been used for oxidative deprotection of various oximes to the corresponding carbonyl compounds in acetonitrile at room temperature and is superior to previously reported methods in terms of yields, molar ratio, and shorter reaction times. The advantage of using this reagent over related compounds as the oxidative deprotecting reagent is illustrated in Table 2. We consider that our procedure represents a useful addition to the array of deoximation reactions. The oxidizing activity of this reagent is under further investigation.

Preparation of 2,6-DCPCC

To a solution of 10 g chromium trioxide (0.1 mol) in 18 ml hydrochloric acid (0.11 mol), 16.7 g pyridine-2,6-dicarboxylic acid (0.1 mol) was added over 5 min at −5°C. The resulting solution was stirred at −5°C for 2 h by which time a yellow-orange solid precipitated. The crystals were collected on a sintered glass funnel and dried in vacuum, yield 24.5 g, 90% (Cr% calcd 17.13%, found 17.03%).

General procedure for the regeneration of carbonyl compounds from oximes

To a solution of oxime (2 mmol) in acetonitrile (20 ml), 2,6-DCPCC (4 mmol) was added and the mixture was stirred at room temperature. The progress of the reaction was followed by TLC or GC. The reaction mixture was filtered and the solid material was washed with acetonitrile (20 ml). Purification of the crude products using a silica-gel plate or silica-gel column (eluent: CCl_4/Et_2O) afforded pure carbonyl compounds in 80–94% yields.



Scheme 2.

Table 2. Deprotection of oximes by 2,6-DCPCC in comparison with other reagents

Substrate	Reagent	Ratio of reagent:substrate	Time	Temp.	Yield (%)	Ref.
PhCH=NOH	2,6-DCPCC[a]	2:1	8 min	rt	94	–
$PhC(CH_3)$=NOH	2,6-DCPCC[a]	2:1	9 min	rt	95	–
PhCH=NOH	3-CPCC[b]	2:1	1 h	reflux CH_2Cl_2	85	19
$PhC(CH_3)$=NOH	3-CPCC[b]	2:1	1 h	reflux CH_2Cl_2	90	19
$PhC(CH_3)$=NOH	QFC[c]	3:1	4–6 h	reflux CH_3CN	87	22
PhCH=NOH	TEACC[d]	–	2 h	rt	56	23
PhCH=NOH	MCC[e]/SiO_2	1.5:1	0.5 h	40°C	86	24
PhCH=NOH	PFC[f]/H_2O_2	4:1	20 min	rt	74	25
$PhC(CH_3)$=NOH	PFC[f]/H_2O_2	4:1	4 h	rt	92	25
$PhC(CH_3)$=NOH	QDC[g]	2:1	1.25 h	reflux CH_3CN	98	26

[a] 2,6-Dicarboxypyridinium chlorochromate.
[b] 3-Carboxypyridinium chlorochromate.
[c] Quinolinium fluorochromate.
[d] Triethylammonium chlorochromate.
[e] Methylammonium chlorochromate.
[f] Pyridinium fluorochromate.
[g] Quinolinium dichromate.

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References

1. Shriner, R. L.; Fuson, R. C.; Curtin, D. H.; Morril, T. C. *The Systematic Identification of Organic Compounds*; 6th ed.; Wiley: New York, 1980.
2. Green, T. G.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 2nd ed.; Wiley: New York, 1991; pp. 172–223.
3. Sampath Kumar, H. M.; Mohanty, P. K.; Suresh Kumar, M.; Yadav, J. S. *Synth. Commun.* **1997**, *27*, 1327 and references cited therein.
4. (a) Donaruma, L. G.; Heldt, W. Z. *Org. React.* **1960**, *11*, 1; (b) Bosch, A. L.; Cruz, P.; Diez-Barra, E.; Loupy, A.; Langa, F. *Synlett* **1995**, 1259.
5. Kabalka, G. W.; Pace, R. D.; Wadgaonkar, P. P. *Synth. Commun.* **1990**, *20*, 2453.
6. (a) Barton, D. H. R.; Beaton, J. M. *J. Am. Chem. Soc.* **1961**, *83*, 4083; (b) Kadzayanskas, N. S.; Zefirov, N. S. *Russ. Chem. Rev. (Engl. Trans.)* **1968**, *37*, 543; (c) Williams, D. L. H. *Nitrosation*; Cambridge University Press: Cambridge, 1988; pp. 1–43.
7. (a) Barton, D. H. R.; Lester, D. J.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1977**, 445; (b) Bandgar, B. P.; Shaikh, S. I.; Iyer, S. *Synth. Commun.* **1996**, *26*, 1163; (c) Boruah, A.; Baruah, B.; Prajapati, D.; Sandhu, J. S. *Synlett* **1997**, 1251.
8. (a) Drabowicz, J. *Synthesis* **1980**, 125; (b) Corey, E. J.; Hopkins, P. B.; Kim, S.; Nambiar, K. P.; Falck, J. R. *J. Am. Chem. Soc.* **1979**, *110*, 71.
9. Aizpurua, J. M.; Palomo, C. *Tetrahedron Lett.* **1983**, *24*, 4367.
10. Joseph, R.; Sudalai, A.; Ravindranathan, T. *Tetrahedron Lett.* **1994**, *35*, 5493.
11. Olah, G. A.; Liao, Q.; Lee, C. S.; Suryaprakash, G. K. *Synlett* **1993**, 427.
12. Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Sendalai, A. *Tetrahedron Lett.* **1997**, *38*, 653.

13. Bose, D. S.; Srinivas, P. *Synlett* **1998**, 977.
14. Ayhan, H. D.; Tanyeli, B. A. *Tetrahedron Lett*. **1997**, *38*, 7267.
15. Varma, R. S.; Meshram, H. M. *Tetrahedron Lett*. **1997**, *38*, 5427.
16. (a) Bose, D. S.; Venkat Narsaiah, A. *Synth. Commun*. **1999**, *29*, 937; (b) Chaudhari, S. S.; Akamanchi, K. G. *Tetrahedron Lett*. **1998**, *39*, 3209.
17. Subhas, B.; Naresaiah, V. *Synth. Commun*. **2000**, *30*, 1153.
18. Subhas, B.; Venkat Narsaiah, A.; Lakshminarayana, V. *Synth. Commun*. **2000**, *30*, 3121.
19. Mohmmadpoor Baltork, I.; Pouranshirvani, S. *Synth. Commun*. **1996**, *26*, 1.
20. (a) Matoney, J. R.; Lyle, R. E.; Scavedra, J. F.; Lyle, G. C. *Synthesis* **1978**, 212; (b) Aizpurua, J. M.; Juaristi, M.; Lecea, B.; Paloma, C. *Tetrahedron* **1985**, *41*, 2903.
21. Corey, E. J.; Sugges, J. W. *Tetrahedron Lett*. **1975**, *15*, 2647.
22. Bose, D. S.; Narasaiah, A. V. *Synth. Commun*. **2000**, *30*, 1153.
23. Rao, C. G.; Radhakrishan, A. S.; Singh, B. B.; Bhatnagar, S. P. *Synthesis* **1983**, 808.
24. Zhang, G.-S.; Chai, B. *Synth. Commun*. **2000**, *30*, 2507.
25. Ganguly, N. C.; Sukai, A. K.; De, S.; De, P. *Synth. Commun*. **2001**, *31*, 1607.
26. Sadeghi, M. M.; Baltork, I. M.; Azarm, M.; Mazidi, M. R. *Synth. Commun*. **2001**, *31*, 435.