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PCC-Promoted Dehydration of Aldoximes: A Convenient Access to Aromatic, Heteroaromatic, and Aliphatic Nitriles

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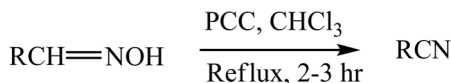
PCC-PROMOTED DEHYDRATION OF ALDOXIMES: A CONVENIENT ACCESS TO AROMATIC, HETEROAROMATIC, AND ALIPHATIC NITRILES

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GRAPHICAL ABSTRACT



R = aryl, heteroaryl, alkyl

Abstract A simple and convenient procedure for the synthesis of nitriles by dehydration of aldoximes using a PCC (pyridiniumchlorochromate) has been developed. A variety of aromatic, heteroaromatic, and aliphatic aldoximes are converted.

Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications[®] for the full spectral details.

Keywords Aldoxime; carbonyl group; dehydration; nitrile; oxidizing agent; PCC

INTRODUCTION

Organic nitriles are very important in organic synthesis as they are versatile intermediates in the synthesis of amines, carboxylic acids, esters, and ketones, which are useful raw materials for pharmaceuticals, agrochemicals, and dyes.^[1] The cyano moiety is also present in numerous bioactive molecules.^[2] The classical method for the synthesis of alkyl cyanide involves nucleophilic substitution of an alkyl halide with metal cyanides,^[1] whereas aromatic nitriles are produced by the Sandmeyer reaction and ammoxidation.^[3] However, these methods are associated with the use of NaCN/KCN/metal cyanides, which are in general highly poisonous, and heavy-metal cyanides such as zinc cyanide, which leave residues of heavy-metal salts.

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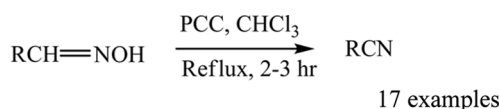
This is not desirable in the context of a clean environment. Dehydration of aldoximes to nitriles is one of the cleanest routes, avoiding inorganic cyanides. Many methods have been developed for this transformation and some of the recently reported procedures involve $\text{Pd}(\text{OAc})_2/\text{PPh}_3$ in CH_3CN ,^[4] benzotriazole phosphonium-hexafluorophosphate derivative 1,8-diaza bicyclo[5.4.0]undec-7-ene (DBU)/in CH_2Cl_2 ,^[5] *N*-chlorosuccinimide/pyridine in CH_3CN ,^[6] dimethyl formamide (DMF) at 135 °C,^[7] tungsten–tin mixed hydroxide in *o*-xylene at 149 °C,^[8] diethylchlorophosphate in toluene,^[9] molecular sieves under flash vacuum pyrolysis,^[10] $\text{ZnO}/\text{CH}_3\text{COCl}$,^[11] chlorosulfonic acid in toluene,^[12] dimethylthiocarbonate/ Et_3N in dioxane,^[13] diethylchlorophosphite in CHCl_3 ,^[14] zeolite under microwave irradiation,^[15] $\text{AlCl}_3 \cdot 6\text{H}_2\text{O}/\text{KI}/\text{H}_2\text{O}/\text{CH}_3\text{CN}$,^[16] Preyssler's anion $[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$,^[17,18] Burgess reagent, and thionyl chloride as dehydrating agents. Among these, only a few are catalytic, and most of them use stoichiometric amounts of reagents. In general, all these procedures are satisfactory; however, a majority of them are restricted to the reactions of aromatic aldoximes. The aliphatic aldoximes are addressed by a few methods.^[19]

Moreover, many of them involve expensive and toxic chemicals and require long reaction times. Thus, alternative procedures with more general applicability, considerably faster reaction, and easy workup conditions are still in demand.

RESULTS AND DISCUSSION

Pyridiniumchlorochromate (PCC) is a mild oxidizing reagent, a readily available, stable reagent commonly used for the oxidation of alcohols to aldehydes or ketones in organic synthesis,^[20–25] and it has not been studied and utilized as a reagent for the preparation of nitriles from aldoximes. Hence, this scenario has prompted us to envisage an alternative strategy for the dehydration of aldoximes keeping in view the following significant aspects: (1) use of commercially available stable PCC reagent, (2) short reaction time leading to overall efficiency, (3) tolerance of broad functional groups. We studied this unique transformation reaction in more detail. Herein, we report for the first time a general procedure for the dehydration of aldoximes to nitriles in the presence of PCC (Scheme 1).

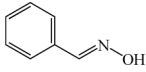

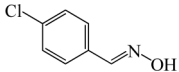
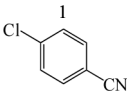
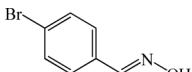
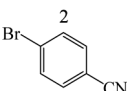
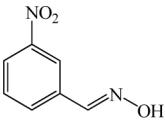
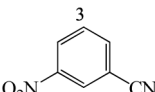
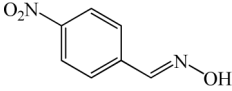
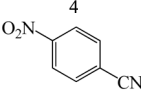
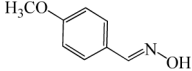
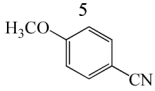
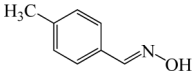
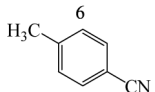
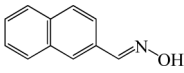
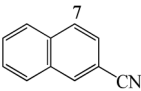
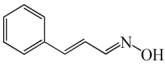
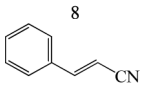
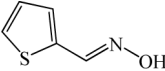

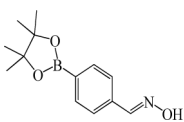
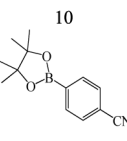
A preliminary examination using benzaldoxime as a model showed that PCC effectively mediated its conversion into benzonitrile. When a CHCl_3 solution of benzaldoxime (1.0 equiv) and PCC (1.1 equiv) was stirred at reflux, the starting material was consumed in 2 h, as indicated by thin-layer chromatography (TLC). In addition, it is interesting to note that aliphatic, aromatic, and heteroaromaticoximes bearing various functionalities such as chloro, bromo, nitro, methyl methoxy, boronate, olefins, amine, and benzyl oxy carbonyl groups survived the reaction and provided good yields of corresponding nitriles. The results are presented in Table 1. A plausible mechanism of nitrile synthesis is outlined in Scheme 2.



R = aryl, heteroaryl, alkyl

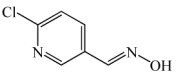
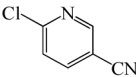
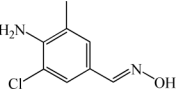
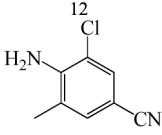
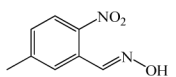
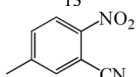
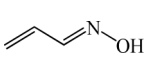
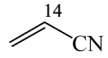
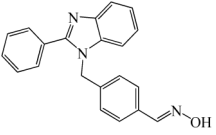
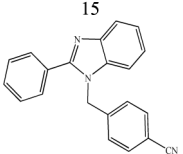
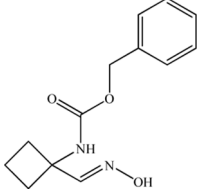
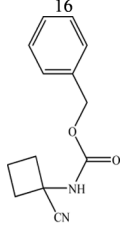
Scheme 1. Dehydration of aldoximes to nitriles.

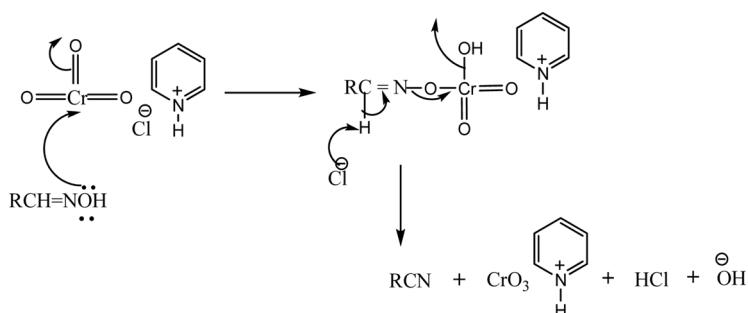
Table 1. Structure of the synthesized compounds, reaction time, and yield

Entry	Aldoximes	Time (h)	Product	Yield (%)	Ref.
1		2		86	4d
2		3		85	—
3		3		82	4e
4		2.5		79	4a
5		2.5		80	4e
6		3		85	4e
7		3		86	4e
8		2		90	4a
9		3		85	4a
10		2.5		82	4d
11		2.5		86	5

(Continued)

Table 1. Continued

Entry	Aldoximes	Time (h)	Product	Yield (%)	Ref.
12		3		88	5
13		2.5		80	—
14		3		79	—
15		2		81	6
16		2.5		86	—
17		2.5		83	—



Scheme 2. Plausible mechanism of nitrile synthesis.

In summary, the short reaction period, simple workup, good yield, broad substrate scope in tolerating various functional groups, and straightforward approach should be of further interest in synthetic chemistry.

EXPERIMENTAL

Representative Experimental Procedure for Dehydration of Aldoximes: Conversion of Benzaldoxime to Benzonitrile (Table 1, Entry 1)

A mixture of benzaldoxime (121 mg, 1 mmol) and PCC (237 mg, 1.1 mmol) in CHCl_3 was heated to reflux for 2 h (monitored by TLC). After the reaction was over, the black reaction mixture was filtered through a Celite pad and washed with EtOAc. Evaporation of the solvent left the crude product, which was purified by column chromatography over silica gel (hexane/EtOAc, 95:5) to afford pure benzonitrile (89 mg, 86%). The infrared (IR) and ^1H and ^{13}C NMR data of this compound are in good agreement with the reported data.^[4d]

Compounds **1–12** and **15** are known and were identified by comparison of their spectroscopic data (IR, ^1H NMR, and ^{13}C NMR) with those reported (see references in Table 1). Compounds **13**, **14**, **16**, and **17** were characterized by their spectroscopic data, which are in agreement with the proposed structures.

Representative spectroscopic characterization data (IR, ^1H NMR, and ^{13}C NMR) for the compounds are provided (compounds **13**, **14**, **16**, and **17**).

4-Amino-3-chloro-5-methylbenzonitrile (**13**)

The general protocol was used for cyclization; 0.35 g of **13** was isolated as off-white solid; mp: 128–130 °C; ^1H NMR (CDCl_3 , 400 MHz) δ : 7.42 (1H, s, Ar-H), 7.22 (1H, s, Ar-H), 4.5 (2H, br s, $-\text{NH}_2$), 2.19 (3H, s, $-\text{CH}_3$); δ_{C} (100.6 MHz, CDCl_3), 145.4, 132.2, 130.9, 123.1, 118.9, 118.2, 100.2, 17.6; IR ν_{max} (KBr, cm^{-1}): 3391, 2932, 2235, 1509, 1350, 803, 775; MS (ESI) $[\text{M} + 1]^+$: 165.2.

5-Methyl-2-nitrobenzonitrile (**14**)

The general protocol was used for cyclization; 0.21 g of **14** was isolated as pale yellow solid; mp: 108–111 °C; ^1H NMR (CDCl_3 , 400 MHz) δ : 8.02–8.0 (1H, d, $J = 8.4$ Hz, Ar-H), 7.67–7.64 (2H, m, Ar-H), 2.6 (3H, s, $-\text{CH}_3$); δ_{C} (100.6 MHz, CDCl_3), 152.3, 136.5, 134.6, 130.7, 125.2, 116.8, 116.7, 19.9; IR ν_{max} (KBr, cm^{-1}): 2942, 2228, 1605, 1455, 833, 793; MS (ESI) $[\text{M} + \text{Na}]^+$: 185.1, $[\text{M} + \text{K}]^+$: 203.1.

4-((2-Phenyl-1H-benzoimidazol-1-yl)methyl)benzonitrile (**16**)

The general protocol was used for cyclization; 0.56 g of **16** was isolated as pale yellow solid; mp: 119–121 °C; ^1H NMR (CDCl_3 , 400 MHz) δ : 7.94–7.92 (1H, d, $J = 8.0$ Hz, Ar-H), 7.76–7.64 (4H, m, Ar-H), 7.54–7.48 (3H, m, Ar-H), 7.41–7.37 (1H, m, Ar-H), 7.36–7.30 (1H, m, Ar-H), 7.26–7.24 (2H, d, $J = 8.4$ Hz, Ar-H), 7.21–7.19 (1H, d, $J = 8.0$ Hz, Ar-H), 5.55 (2H, s, $-\text{CH}_2$); δ_{C} (100.6 MHz, CDCl_3), 154, 143, 141.6, 135.6, 132.9, 132.5, 130.2, 129.6, 129.1, 126.7, 123.4, 123.1, 120.2,

118.2, 112, 110, 48; IR ν max (KBr, cm^{-1}): 2926, 2229, 1559, 1460, 829, 745; MS (ESI) $[\text{M} + 1]^+$: 310.1.

Benzyl-1-cyanocyclobutylcarbamate (**17**)

The general protocol was used for cyclization; 0.192 g of **17** was isolated as pale yellow solid; mp: 99–101 °C; ^1H NMR (DMSO-d_6 , 400 MHz) δ : 8.4 (1H, br s, -NH), 7.36–7.29 (5H, m, Ar-H), 5.07 (2H, s, -CH₂), 2.55–2.48 (2H, m, -CH₂), 2.34–2.27 (2H, m, -CH₂), 1.99–1.95 (2H, m, -CH₂); δ_{C} (100.6 MHz, DMSO-d_6), 154.4, 136.3, 128.3, 128.2, 127.9, 121.5, 65.8, 47.3, 32.8, 15.4; IR ν max (KBr, cm^{-1}): 2912, 2232, 1649, 1362, 803; MS (ESI) $[\text{M} + 1]^+$: 230.1, $[\text{M} + \text{Na}]^+$: 253.1.

SUPPORTING INFORMATION

Compound characterization data and copies of ^1H NMR and ^{13}C NMR for compounds (see Table 1; **13**, **14**, **16**, and **17**) described in Scheme 1 can be found via the Supplementary Content section of this article's webpage.

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REFERENCES

1. (a) Fatiadi, A. J. In *Preparation and Synthetic Applications of Cyano Compounds*; S. Patai and Z. Rappaport (Eds.); Wiley: New York, 1983; (b) Miller, J. S.; Manson, J. L. Designer magnets containing cyanides and nitriles. *Acc. Chem. Res.* **2001**, *34*, 563–570; (c) Magnus, P.; Scott, D. A.; Fielding, M. R. Direct conversion of α,β -unsaturated nitriles into cyanohydrins using $\text{Mn}(\text{dpm})_3$ catalyst, dioxygen, and phenylsilane. *Tetrahedron Lett.* **2001**, *42*, 4127–4129.
2. Romero, M.; Renard, P.; Caignard, D. H.; Atassi, G.; Solans, X.; Constans, P.; Bailly, C.; Pujol, M. D. Synthesis and structure–activity relationships of new benzodioxinic lactones as potential anticancer drugs. *J. Med. Chem.* **2007**, *50*, 294–307.
3. (a) Ellis, G. P.; Romney-Alexander, T. M. Cyanation of aromatic halides. *Chem. Rev.* **1987**, *87*, 779–794; (b) Raja, R.; Adams, R. D.; Blom, D. A.; Pearl, W. C.; Gianotti Jr., E.; Thomas, J. M. A new catalytic liquid-phase ammoxidation approach towards the preparation of niacin (vitamin B3). *Langmuir* **2009**, *25*, 7200–7204.
4. Kim, H. S.; Kim, S. H.; Kim, J. N. Highly efficient Pd-catalyzed synthesis of nitriles from aldoximes. *Tetrahedron Lett.* **2009**, *50*, 1717–1719.
5. Singh, M. K.; Lakshman, M. K. A simple synthesis of nitriles from aldoximes. *J. Org. Chem.* **2009**, *74*, 3079–3084.
6. Guema, M.; Golebiewski, W. M. Convenient conversion of aldoximes into nitriles with N-chlorosuccinimide and pyridin. *Synthesis* **2008**, 1997–1999.
7. Supsana, P.; Liaskopoulos, T.; Tsoungas, P. G.; Varvounis, G. DMF-catalysed thermal dehydration of aldoximes: A convenient access to functionalized aliphatic and aromatic nitrile. *Synlett.* **2007**, 2671–2674.

8. Yamaguchi, K.; Fujiwara, H.; Ogasawara, Y.; Kotani, M.; Mizuno, N. A tungsten–tin mixed hydroxide as an efficient heterogeneous catalyst for dehydration of aldoximes to nitriles. *Angew. Chem., Int. Ed.* **2007**, *46*, 3922–3925.
9. Sardarian, A. R.; Shahsavari-Fard, Z.; Shahsavari, H. R.; Ebrahimi, Z. Efficient Beckmann rearrangement and dehydration of oximes via phosphonate intermediates. *Tetrahedron Lett.* **2007**, *48*, 2639–2643.
10. Campbell, J. A.; McDougald, G.; McNab, H.; Rees, L. V. C.; Tyas, R. G. Laboratory-scale synthesis of nitriles by catalysed dehydration of amides and oximes under flash vacuum pyrolysis (FVP) conditions. *Synthesis* **2007**, 3179–3184.
11. Sarvari, M. H. ZnO/CH₃COCl: A new and highly efficient catalyst for dehydration of aldoximes into nitriles under solvent-free condition. *Synthesis* **2005**, 787–790.
12. Li, D.; Shi, F.; Guo, S.; Deng, Y. Highly efficient Beckmann rearrangement and dehydration of oximes. *Tetrahedron Lett.* **2005**, *46*, 671–674.
13. Khan, T. A.; Peruncheralathan, S.; Ila, H.; Junjappa, H. S,S-Dimethyl dithiocarbonate: A useful reagent for efficient conversion of aldoximes to nitrile. *Synlett.* **2004**, 2019–2021.
14. Jie, Z.; Rammoorthy, V.; Fischer, B. Diethyl chlorophosphite: A versatile reagent. *J. Org. Chem.* **2002**, *67*, 711–719.
15. Heqedues, A.; Cwik, A.; Hell, Z.; Horvath, Z.; Esek, A.; Uzsoki, M. Microwave-assisted conversion of oximes into nitriles in the presence of a zeolite. *Green Chem.* **2002**, *4*, 618–620.
16. Boruah, M.; Konwar, D. AlCl₃·6H₂O/KI/H₂O/CH₃CN: A new alternate system for dehydration of oximes and amides in hydrated media. *J. Org. Chem.* **2002**, *67*, 7138–7139.
17. Heravi, M. M.; Sadjadi, S.; Hekmatshoar, R.; Oskooie, H. A.; Bamoharram, F. F. Dehydration of oximes to nitriles catalyzed by a green heteropolyacid catalyst: Preyssler's anion, [NaP₅W₃₀O₁₁₀]¹⁴⁻. *Chin. J. Chem.* **2009**, *27*, 607–609.
18. Jose, B.; Sulatha, M. S.; Pillai, P. M.; Prathapan, S. A new method for the generation of nitriles from aldoximes. *Synth. Commun.* **2000**, *30*, 1509–1514.
19. Chaudhari, S. S.; Akananchi, K. G. Thionyl chloride–benzotriazole: An efficient system for transformation of aldoximes to nitriles. *Synth. Commun.* **1999**, *29*, 1741–1756.
20. Arumugam, S.; Verkade, J. G. P(CH₃NCH₂CH₂)₃N: A nonionic superbases for efficient dehydrohalogenation. *J. Org. Chem.* **1997**, *62*, 4827–4828.
21. Augustine, K.; Rajendra, N. A.; Balakrishna, K. R.; Chandrakantha, B. Propylphosphonic anhydride (T3P[®]): A remarkably efficient reagent for the one-pot transformation of aromatic, heteroaromatic, and aliphatic aldehydes to nitriles. *Synlett.* **2009**, *20*, 3378–3382.
22. Corey, E. J.; Ensley, H. E.; Suggs, W. J. Convenient synthesis of (S)–(–)-pulegone from (–)-citronellol. *J. Org. Chem.* **1976**, *41*(2), 380–381.
23. Hollenberg, D. H.; Klien, R. S.; Fox, J. J. Pyridiniumchlorochromate for the oxidation of carbohydrates. *Carbohydr. Res.* **1978**, *67*, 491–494.
24. (a) Piancatelli, G.; Scettri, A.; Auria, M. D. The oxidation of furan derivatives with pyridiniumchlorochromate: A novel synthesis of 6-hydroxy-2h-pyran-3(6H)-ones. *Tetrahedron Lett.* **1977**, *18*, 2199–2200; (b) Piancatelli, G.; Scettri, A.; Auria, M. D. Pyridiniumchlorochromate in the organic synthesis: A convenient oxidation of 5-bromo-2-furan-derivatives to γ -hydroxybutenolides. *Tetrahedron Lett.* **1979**, *20*, 1507–1508.
25. Corey, E. J.; Suggs, W. J. Pyridiniumchlorochromate: An efficient reagent for oxidation of primary and secondary alcohols to carbonyl compounds. *Tetrahedron Lett.* **1975**, *16*, 2647–2650.