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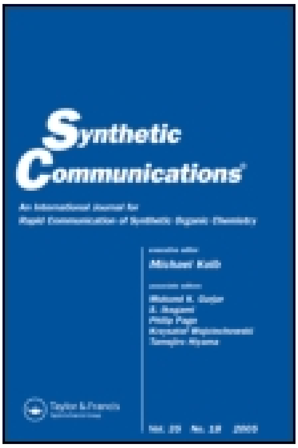

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Efficient Mo(VI)-Catalyzed Hydration of Nitrile with Acetaldoxime

Xiaoyun Ma [a] , Ying He [a] & Ming Lu [a]

[a] Chemical Engineering College , Nanjing University of Science and Technology , Nanjing , China

Published online: 27 Dec 2013.

To cite this article: Xiaoyun Ma , Ying He & Ming Lu (2014) Efficient Mo(VI)-Catalyzed Hydration of Nitrile with Acetaldoxime, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 44:4, 474-480, DOI: 10.1080/00397911.2013.806668

To link to this article: http://dx.doi.org/10.1080/00397911.2013.806668

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Synthetic Communications®, 44: 474–480, 2014
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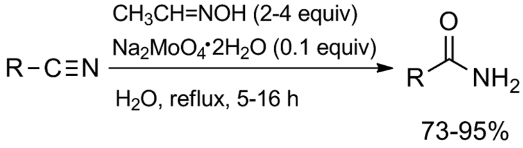
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2013.806668

EFFICIENT Mo(VI)-CATALYZED HYDRATION OF NITRILE WITH ACETALDOXIME

Xiaoyun Ma, Ying He, and Ming Lu
Chemical Engineering College, Nanjing University of Science and Technology, Nanjing, China

GRAPHICAL ABSTRACT



Abstract *A method for the selective hydration of nitrile to amide by employing commercially available acetaldoxime and inexpensive oxometallate such as molybdate, vanadate, and tungstate in environmentally friendly water is described. Under this protocol, nitriles including aromatic nitriles, heterocyclic nitriles, and aliphatic nitriles were converted into the corresponding amides in good to excellent yields.*

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Keywords Acetaldoxime; amide; hydration; nitrile; sodium molybdate(VI) dihydrate

INTRODUCTION

Hydration of nitriles to the corresponding amides is an important transformation from both academic and industrial points of view.[1] Classically the reaction was carried out in the presence of a strong acid or base catalyst, methods which usually cause overhydrolysis of the amides into the corresponding carboxylic acids, a faster reaction specially under basic conditions.[2] To overcome the limitation, several protocols using enzymes,[3] hydroxylamine derivatives,[4] heterogeneous catalysts,[5] and homogeneous catalysts based on transition metals such as rhodium,[6] ruthenium,[7] palladium,[8] cobalt,[9] molybdenum,[10] platinum,[11] and gold[12] have been developed for selective conversion of nitriles to amides. In addition, the hydration of nitriles promoted by the combination of oxime and metal compounds, such as $RhCl(PPh_3)_3$,[13] $Pd(OAc)_2$,[14] and $InCl_3$[15] etc. have also been reported. Recently, the study on efficient, cheaper, and environmentally friendly

Received December 18, 2012.

Address correspondence to Ming Lu, Chemical Engineering College, Nanjing University of Science and Technology, Nanjing 210094, China. E-mail: lumingnjust@163.com

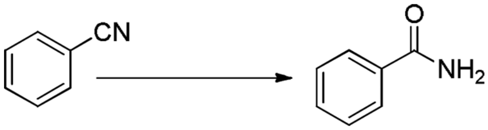
catalysts for functional group transformation has become a research hotspot.[16] During our recent studies of conversion of nitrile to amide, we disclosed an efficient method for the preparation of amides from nitriles by employing acetaldoxime and bivalent metal salt such as copper oxide (CuO) and nickel(II) chloride hexahydrate ($NiCl_2 \cdot 6H_2O$) in water.[17] Under this protocol, nitriles were selectively converted to amides in excellent yields, and nitriles having electron-withdrawing groups could be converted into the corresponding amides in good to excellent yields at room temperature. Heterocyclic nitriles with a lone heteroatom pair positioned ortho to the nitrile group could be hydrated at refluxing temperature in the absence of acetaldoxime. In the continuation of our study on inexpensive catalysts for the hydration of nitriles, we found that some oxometallates also showed good catalytic activity for hydration of various nitriles.

In this article, the catalytic activity of various oxometallate such as molybdate, vanadate, and tungstate for hydration of nitriles has been investigated. Sodium molybdate showed the greatest catalytic activity and it was used as catalyst for hydration of various nitriles.

RESULTS AND DISCUSSION

As shown in Table 1, we found that all the metal salts displayed catalytic properties in the hydration of benzonitrile to benzamide with the aid of acetaldoxime. Use of sodium molybdate(VI) dihydrate ($Na_2MoO_4 \cdot 2H_2O$) alone at room temperature resulted in no product (Table 1, entry 1) and a trace amount of benzamide was detected after 24 h at reflux temperature (Table 1, entry 2). No benzamide was obtained in the presence of $Na_2MoO_4 \cdot 2H_2O$ and acetaldoxime at room temperature (Table 1, entry 3); however, benzamide was obtained in 76% yield when the temperature was raised to reflux (Table 1, entry 4). Therefore, we concluded that the reaction temperature had a significantly effect on the reaction rate and the product yield.

Table 1. Screen of reaction conditions[a]



Entry	Conditions	Yield (%)[b]
1	$Na_2MoO_4 \cdot 2H_2O$ (0.1 equiv), H_2O, rt, 24 h	0
2	$Na_2MoO_4 \cdot 2H_2O$ (0.1 equiv), H_2O, reflux, 24 h	Trace
3	$Na_2MoO_4 \cdot 2H_2O$ (0.1 equiv), acetaldoxime (1.0 equiv), H_2O, rt, 24 h	0
4	$Na_2MoO_4 \cdot 2H_2O$ (0.1 equiv), acetaldoxime (1.0 equiv), H_2O, reflux, 24 h	76
5	$NaVO_3 \cdot 2H_2O$ (0.1 equiv), acetaldoxime (1.0 equiv), H_2O, reflux, 24 h	70
6	$Na_2WO_4 \cdot 2H_2O$ (0.1 equiv), acetaldoxime (1.0 equiv), H_2O, reflux, 24 h	38
7	$Na_3PO_4 \cdot 12WO_3 \cdot 18H_2O$ (0.1 equiv), acetaldoxime (1.0 equiv), H_2O, reflux, 24 h	13
8	$Na_2MoO_4 \cdot 2H_2O$ (0.1 equiv), acetaldoxime (3.0 equiv), H_2O, reflux, 12 h	90

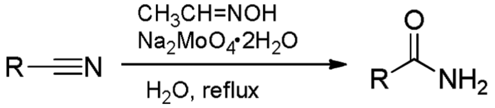
[a] Reaction conditions: benzonitrile (2 mmol), H_2O (10 mL).
[b] Isolated yield.

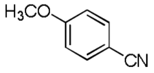
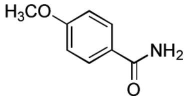
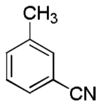
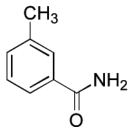
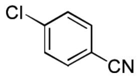
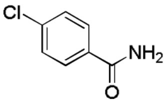
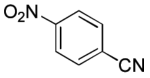
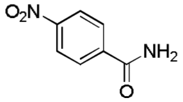
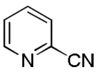
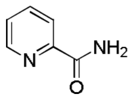
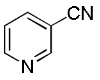
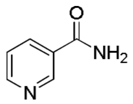
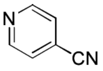
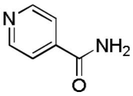
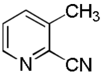
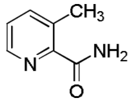
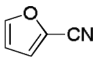
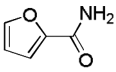
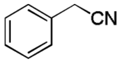
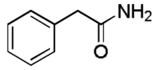
Sodium metavanadate(V) dihydrate ($NaVO_3 \cdot 2H_2O$) exhibited a low catalytic activity as compared to $Na_2MoO_4 \cdot 2H_2O$ (Table 1, entry 5). In the cases of sodium tungstate(VI) dihydrate ($Na_2WO_4 \cdot 2H_2O$) and sodium phosphotungstate octadecahydrate ($Na_3PO_4 \cdot 12WO_3 \cdot 18H_2O$), benzamide was obtained in poor yield (Table 1, entries 6 and 7). When we increased the amounts of acetaldoxime to 3 equiv, the reaction time was reduced from 24 h to 12 h and the yield was increased (Table 1, entry 8). It should be noted that no benzoic acid was detected in the reaction mixture at high temperatures.

On the basis of these results, we can conclude that using $Na_2MoO_4 \cdot 2H_2O$ and acetaldoxime at refluxing temperature is the optimality conditions for nitrile hydration. This protocol of hydration was subsequently applied to various aromatic nitriles, aliphatic nitriles, and heterocyclic nitriles. As shown in Table 2, various nitriles including aromatic nitriles having electron-donating or electron-withdrawing substituents (Table 2, entries 1–4), heterocyclic nitriles (Table 2, entries 5–9), and aliphatic nitriles (Table 2, entries 10–12) were converted into the corresponding amides in good to excellent yields. Substrates bearing electron-donating groups (Table 2, entries 1 and 2) renders the nitrile carbon less electrophilic to nucleophilic attack by acetaldoxime and exhibited relatively lower conversions. In addition, 4 mol equiv of acetaldoxime was used in these cases. In contrast, the hydration of nitriles with an electron-withdrawing group proceeded more effectively (Table 2, entries 3–7 and 9). For example, nicotinonitrile was converted to the corresponding amide with complete conversion after a relatively short reaction time of 5 h and 2 mol equiv of acetaldoxime was used in this case. It is worth noting that the nitrile hydration was affected by steric factors. By-products are generated in the hydartion of nitriles bearing a group positioned ortho to the nitrile group. For example, compared with isonicotinamide, the yield of picolinamide is relatively lower due to a lone pair at the ortho position (Table 2, entry 5). Similarly, 3-methylpicolinonitrile showed low reactivity due to the methyl group at the ortho position (Table 2, entry 8). In addition, the water solubility of the nitriles also affect the hydration reaction and the hydration of poorly water-soluble nitriles required a long reaction time. For example, the hydration of isonicotinonitrile proceeded fast compared with the hydration of 4-nitrobenzonitrile (Table 2, entries 4 and 7). In the case of aliphatic nitriles the hydration process was similar to aromatic nitriles; aliphatic nitriles (Table 2, entries 10–12) were smoothly hydrated to give the corresponding amides in good yields under the employed reaction conditions.

Nitrile with strong electron-withdrawing substituent can be hydrated at room temperature. As shown in Scheme 1, isonicotinonitrile was converted into isonicotinamide in the presence of $Na_2MoO_4 \cdot 2H_2O$ and acetaldoxime. Actually, the hydration of isonicotinonitrile to isonicotinamide did not proceed at all with either $Na_2MoO_4 \cdot 2H_2O$ or acetaldoxime taken alone at room temperature. Therefore, we are certain that $Na_2MoO_4 \cdot 2H_2O$ is a catalyst in this case. Noteworthy, the oxometalates are readily prone to hydrolysis in aqueous solution under the high-temperature condition and form their poly-condensed types called polyoxometalates according to the literature.[18] Under our protocol for the hydraton of various nitriles, the reactions were carried out in water at high temperature, so we thought that the polyoxometalate generated and acted as a catalyst in the reaction. According to our previous metal-catalyzed hydration papers[17] and other literature,[13–15]

Table 2. Hydration of various nitriles using $Na_2MoO_4 \cdot 2H_2O$ and acetaldoxime[a]



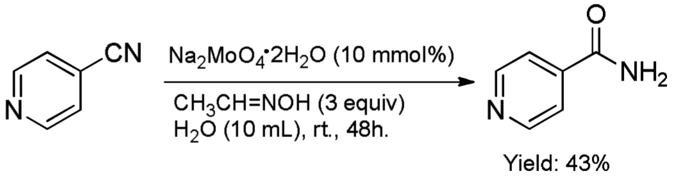
Entry	Nitrile	Amide	Time (h)	Yield (%)[b]
1			16	73[c]
2			16	83[c]
3			12	91
4			12	92
5			5	87[d]
6			5	95[d]
7			5	95[d]
8			16	77[c]
9			5	86[d]
10			12	89
11	$CH_3(CH_2)_{10}CN$	$CH_3(CH_2)_{10}CONH_2$	12	88
12	$CH_3(CH_2)_6CN$	$CH_3(CH_2)_6CONH_2$	12	87

[a] Reaction conditions: nitrile (2 mmol), acetaldoxime (6 mmol), $Na_2MoO_4 \cdot 2H_2O$ (0.2 mmol), H_2O (10 mL), reflux.

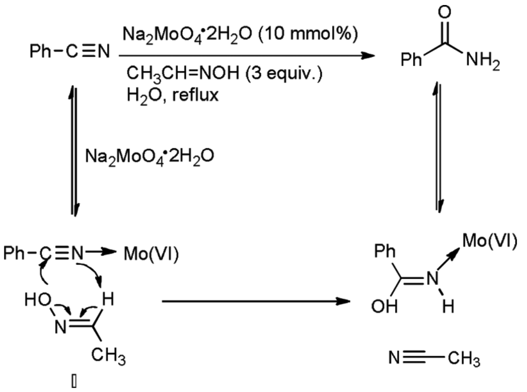
[b] Isolated yield.

[c] 8 mmol acetaldoxime was used.

[d] 4 mmol acetaldoxime was used.



Scheme 1. Hydration of isonicotinonitrile at room temperature.



Scheme 2. Proposed mechanism of nitrile hydration via molybdenum catalyst and acetaldoxime.

the nucleophilic addition of acetaldoxime to nitrile can be carried out only when coordination of nitrile to the metal catalyst and the catalytic effect of catalyst is attributed to the coordination of nitrile to metal catalyst. In this article, we thought that coordination of nitrile to molybdenum (VI) results in an enhanced electrophilicity of the nitrile carbon, whether $Na_2MoO_4 \cdot 2H_2O$ or polyoxomolybdate. So both $Na_2MoO_4 \cdot 2H_2O$ and polyoxomolybdates can act as catalyst in the hydration of nitriles. We thought that the reaction mechanism for nitrile hydration is likely to be similar to the mechanism reported in the literatures.[13–15,17,19] As shown in Scheme 2, initially, coordination of benzonitrile to molybdenum(VI) results in an enhanced electrophilicity of the nitrile carbon, then the nucleophilic addition of acetaldoxime yields the intermediate I, and the following disruption of the intermediate I into benzamide and acetonitrile proceeds in a concerted manner.

CONCLUSIONS

In conclusion, we disclosed a method for the hydration of nitrile to amide using commercially available acetaldoxime and inexpensive oxometallate such as molybdate, vanadate, and tungstate in water. The catalytic activities of these oxometallates were investigated, and molybdate showed the greatest catalytic activity. Sodium molybdate(VI) dihydrate was used as a catalyst for the hydration of various nitriles and nitriles including aromatic nitriles, heterocyclic nitriles, and aliphatic nitriles were converted into the corresponding amides in good to excellent yields.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary apparatus and were uncorrected. ^{1}H NMR spectra were recorded on Bruker DPX-400 or DPX-500 spectrometer. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates. Yields refer to the isolated yields of the products after purification by silica-gel column chromatography (300 mesh). All starting chemicals are commercially available. All the amide products are known compounds and they were characterized by melting point and ^{1}H NMR spectra.

To a 25 mL round-bottom flask equipped with magnetic stirrer were added nitrile (2 mmol), acetaldoxime (6 mmol), sodium molybdate(VI) dihydrate (0.2 mmol), and H_2O (10 mL). The mixture was heated to reflux for 5–16 h. After cooling to room temperature, the solution was directly evaporated to dryness and the residue was purified by column chromatography on silica gel (ethyl acetate/n-hexane) to give the corresponding amide.

ACKNOWLEDGMENT

Financial support from the National Natural Science Foundation of China-NSAF (Grant No. 11076017) is gratefully acknowledged.

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