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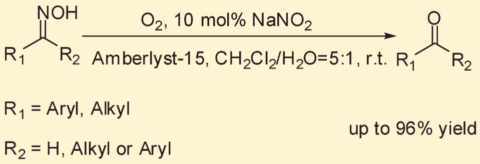
Sodium Nitrite Catalyzed Aerobic Oxidative Deoximation under Mild Conditions

Guofu Zhang, Xin Wen, Yong Wang, Weimin Mo,* and Chengrong Ding*

College of Chemical Engineering and Materials Science, Zhejiang University of Technology, Hangzhou 310014, People's Republic of China

Supporting Information

ABSTRACT: A mild, simple process for the effective deoximation of a wide range of ketoximes and aldoximes has been developed, which utilizes available $NaNO_2$ as the catalyst and molecular oxygen as the green oxidant. Notably Amberlyst-15, which acts as the initiator of $NaNO_2$, can be reused without regeneration. This environmentally benign protocol could provide a valuable synthetic method for practical applications.



In the past two decades, the use of molecular oxygen as terminal oxidant has received great attention for both economic and environmental benefits. Many efforts have been focused on the efficient activation of oxygen for the oxidation of alcohols,[1] oxyhalogenation of arenes and ketones,[2] oxidative coupling,[3] and so on. To efficiently activate the oxygen, various transition metals and transition-metal complexes have been employed.[4] One major drawback of these protocols is the utilization of expensive metals such as Pd, Ru, Pt, and Au or complex ligands, which extremely limit their practical application.

Recently Liang and co-workers have developed a sodium nitrite ($NaNO_2$)/O_2 system, which is a highly efficient transition-metal-free protocol for aerobic oxidation reactions such as oxidation of alcohols,[5] oxybromination of arenes and ketones,[6] and oxidative degradation of environmental pollutants.[7] Encouraged by its excellent performance, we are greatly interested in expanding its application to the deoximation reaction. Oximes not only act as a kind of synthetic precursor of corresponding carbonyl compounds[8] but also serve as a powerful strategy to protect the carbonyl group. Although there are many methods for deoximation,[9] a few examples involving aerobic oxidative deoximation reactions have been reported.[10] Groves et al. have presented the first example of synthetic iron porphyrin mediated oxidation of oximes by molecular oxygen, which utilized a stoichiometric amount of hydroxoiron(III) porphyrin and a high oxygen pressure.[10a] Wu et al. have developed a novel system for aerobic oxidative deoximation photosensitized by a platinum(II) terpyridyl acetylide complex.[10c] Recently, Garcia et al. used gold supported on nanoparticulated ceria (Au/CeO_2) as a catalyst for the aerobic oxidation of oximes to the corresponding carbonyl compounds in the presence of 5 bar of oxygen, and good to excellent yields have been achieved under related conditions.[10d]

Obviously, there still exists a great demand for innovative catalytic aerobic oxidative deoximation reaction systems using inexpensive and easily available catalysts under mild conditions. Herein we wish to report a simple, mild, and efficient protocol for the deoximation of ketoximes and aldoximes which utilizes $NaNO_2$ as the catalyst and O_2 as the green oxidant under mild conditions.

To optimize the experimental conditions, we began our explorations with 4-chloroacetophenone oxime as a model substrate. The results were listed in Table 1. First we tested the effect of the solvent, which played an important role in the $NaNO_2/O_2$ catalytic reaction system in our previous research.[6] During the screening of solvents, we found that when using CH_3CN/H_2O as a mixed solvent, the desired product was obtained in 76% yield in the presence of $NaNO_2$ and Amberlyst-15 at room temperature for 1 h (Table 1, entry 1). However, when the reaction was carried out in CH_2Cl_2/H_2O (5/1, v/v), the yield was sharply increased to 86% (Table 1, entry 7). Other solvents such as $MeOH/H_2O$, $EtOH/H_2O$, dioxane/H_2O, $EtOAc/H_2O$, and THF/H_2O were much less effective for this transformation (Table 1, entries 2−6). Encouraged by the good preliminary results, we further optimized the amounts of Amberlyst-15 and $NaNO_2$. The results revealed that when the amount of Amberlyst-15 was less than 0.100 g, lower yields were obtained even with prolonged reaction time (Table 1, entries 9−11). When the amount of $NaNO_2$ was reduced from 50 mol % to 10 mol %, however, it was interesting to find that an excellent yield of the desired product was obtained after 5 h (95%, Table 1, entry 14). This observation might be ascribed to the suppression of unidentified byproducts, which might result from the reaction of the "NO_2" active species and the hydroxyl group of the oxime. Moreover, the presence of Amberlyst-15, $NaNO_2$, and O_2 was proven to be crucial for this transformation (Table 1, entries 12, 16, and 17).

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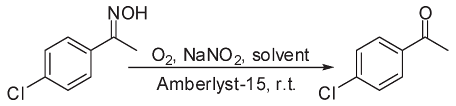
Table 1. $NaNO_2$-Catalyzed Deoximation with Amberlyst-15 and Molecular Oxygen under Different Reaction Conditions[a]



entry	solvent	amt of Amberlyst-15 (g)	amt of $NaNO_2$ (mol %)	time (h)	yield[b] (%)
1	CH_3CN/H_2O	0.200	50	1	76
2	$MeOH/H_2O$	0.200	50	1	20
3	$EtOH/H_2O$	0.200	50	1	16
4	dioxane/H_2O	0.200	50	1	18
5	CH_3COOEt/H_2O	0.200	50	1	25
6	THF/H_2O	0.200	50	1	10
7	CH_2Cl_2/H_2O	0.200	50	1	86
8	CH_2Cl_2/H_2O	0.100	50	1	85
9	CH_2Cl_2/H_2O	0.050	50	5	70
10	CH_2Cl_2/H_2O	0.025	50	6	55
11	CH_2Cl_2/H_2O	0.012	50	9	50
12	CH_2Cl_2/H_2O		50	10	10
13	CH_2Cl_2/H_2O	0.100	20	3	91
14	**CH_2Cl_2/H_2O**	**0.100**	**10**	**5**	**95**
15	CH_2Cl_2/H_2O	0.100	5	9	91
16	CH_2Cl_2/H_2O	0.100		15	12
17[c]	CH_2Cl_2/H_2O	0.100	10	5	9

[a] Reaction conditions: 4-chloroacetophenone oxime (1.0 mmol), solvent (5/1, 6.0 mL), 25 °C, under 1 atm of O_2. [b] Isolated yield. [c] Ar was used instead of O_2.

Under the optimized conditions: 1 mmol of substrate, 10 mol % of $NaNO_2$ as the catalyst, and 0.100 g of Amberlyst-15 in CH_2Cl_2/H_2O (5/1, 6.0 mL) at 25 °C under 1 atm of O_2 (Table 1, entry 14), we next explored the scope of this methodology to different ketoximes and aldoximes, and the results were summarized in Table 2. It was gratifying to observe that all substrates tested could afford the desired products in moderate to excellent yields under the standard reaction conditions. Generally, the oxidative deoximation reaction was influenced by the electronic properties of the substituents on the arene ring. The ketoximes bearing electron-withdrawing groups (such as Cl, Br, Ph, NO_2) on the arene ring could easily be converted to the corresponding ketones with 91−95% yields (Table 2, entries 1−4). It was also important to note that when the amount of $NaNO_2$ was reduced to 5 mol %, comparable yields could still be obtained. However, for oximes with electron-donating groups on the arene ring, a certain percentage of a byproduct was generated and only moderate yields were obtained (Table 2, entries 7 and 8). Interestingly, for the sterically hindered benzophenone oxime and 1-tetralone oxime, excellent yields of the desired products could also be achieved (Table 2, entries 9 and 10). Similarly, cyclic ketoximes could undergo a smooth reaction to give the corresponding ketones in high yields (Table 2, entries 10−12). It was surprising that, when aldoximes were subjected to the standard conditions, only moderate conversions and yields were obtained with longer reaction time (Table 2, entries 13−16). These results might indicate that the aldoximes are more stable than ketoximes under the reaction conditions.

A significant advantage of this mild protocol was the reuse of Amberlyst-15. The recycling experiments were examined for the deoximation of 4-chloroacetophenone oxime under standard conditions. The results were displayed in Scheme 1. After the reaction, the Amberlyst-15 was easily recovered by filtration and then washing with CH_2Cl_2, deionized water, and acetone, and eventually drying under vacuum for the next cycle. We were pleased to observe that the reaction did take place with simply treated Amberlyst-15, and a satisfactory yield was also obtained even after six cycles, although the reaction time was prolonged slightly. This impressive recyclability may be partially attributable to the little or no consumption of Amberlyst-15 at all during each cycle.

In further research, the gram-scale application of this methodology was also studied and 4-chloroacetophenone oxime was taken as a representative substrate. When the amount of the substrate was increased from 1 mmol (0.169 g) to 50 mmol (8.450 g) and the amount of $NaNO_2$ and Amberlyst-15 were reduced correspondingly, to our delight, the desired product was isolated in 92−95% yields (Table 3). The success of the reactions suggested that this aerobic oxidative deoximation method could provide a valuable and convenient tool for practical application in the laboratory.

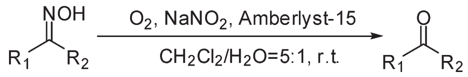
Taking these observations into account, we propose a plausible mechanism for this transition-metal-free catalytic oxidative deoximation in Scheme 2. First, the sodium nitrite ($NaNO_2$) reacts with Amberlyst-15 in CH_2Cl_2/H_2O to release nitric oxide (NO), which is immediately oxidized by oxygen to form nitrogen dioxide (NO_2). Then the highly active species NO_2 reacts with C=N double bonds of the oxime **a** to produce the intermediate **b**. This intermediate **b** can subsequently form **c** through a proton transfer process, which is then attacked by NO_2 to give the active material **d**. Subsequent hydrolysis of **d** generates the carbonyl compound as well as HNO_2, HNO_3, and NH_2OH. The HNO_2 is unstable and releases NO, meanwhile the oxidative HNO_3 and reductive NH_2OH can also interact to generate NO. They can both be reoxidized to NO_2 by oxygen and continue the catalytic cycle.

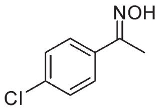
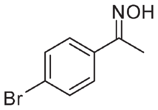
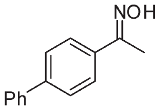
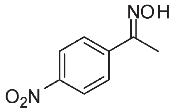
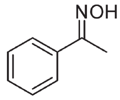
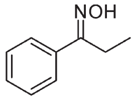
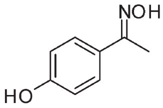
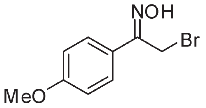
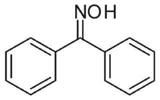
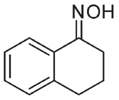
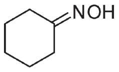
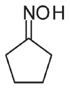
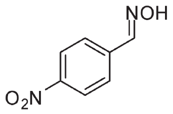
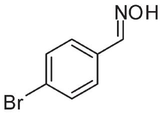
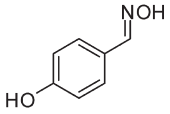
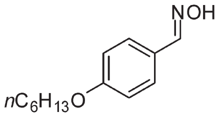
In conclusion, we have developed an efficient, mild, and easily handled system using $NaNO_2$ as the catalyst, molecular oxygen as the terminal oxidant, and Amberlyst-15 as a recyclable initiator for oxidative cleavage of oximes to the corresponding carbonyl compounds. As far as we know, the protocol presented here represents the first example of aerobic oxidative deoximation to carbonyl compounds using catalytic amounts of $NaNO_2$. A plausible mechanism is also proposed in this paper. The use of O_2 as an economical terminal oxidant and $NaNO_2$ as the catalyst make this practical transformation attractive in both laboratory and industrial applications.

■ EXPERIMENTAL SECTION

General Experimental Procedure for Deoximation to the Corresponding Carbonyl Compounds. Oximes (1.0 mmol), Amberlyst-15 (0.100 g), and CH_2Cl_2/H_2O (5/1, 6.0 mL) were introduced into an 80 mL Schlenk flask equipped with a magnetic stirrer, and the flask was purged several times with oxygen (balloon filled). Then the sodium nitrite (0.1 mmol, 0.007 g) was added and the system was immediately sealed. The reaction mixture was stirred at 25 °C for several hours. After the reaction, Amberlyst-15 was separated from the reaction mixture by filtration and the filtrate was

Table 2. Deoximation of Keto- and Aldoximes to Carbonyl Compounds Catalyzed by $NaNO_2$ Using O_2 as the Oxidant under Mild Conditions[a]



entry	substrate	$NaNO_2$ (mol%)	time (h)	yield[b,c] (%)
1		10(5)	5(9)	95(91)
2		10(5)	3(7)	94(93)
3		10(5)	4(7)	92(90)
4		10(5)	3(6.5)	91(90)
5		10(5)	9(12)	85(77)
6		10(5)	9(13)	82(74)
7		10	6.5	54
8		10	6	52
9		10(5)	0.5(1)	96(95)
10		10(5)	1.5(3)	92(89)
11		10	6	82
12		10	7	79
13		10	12	60[d]
14		10	13	47[d]
15		10	13	40[d]
16		10	14	38[d]

[a] Reaction conditions: oxime (1.0 mmol), Amberlyst-15 (0.100 g), CH_2Cl_2/H_2O (5/1, 6.0 mL), 25 °C, under 1 atm of O_2. [b] Isolated yield. [c] Values in parentheses are the isolated yields when 5 mol % $NaNO_2$ was used. [d] Incomplete conversion of the starting material.

Scheme 1. Reuse of Amberlyst-15 for Deoximation of 4-Chloroacetophenone Oxime

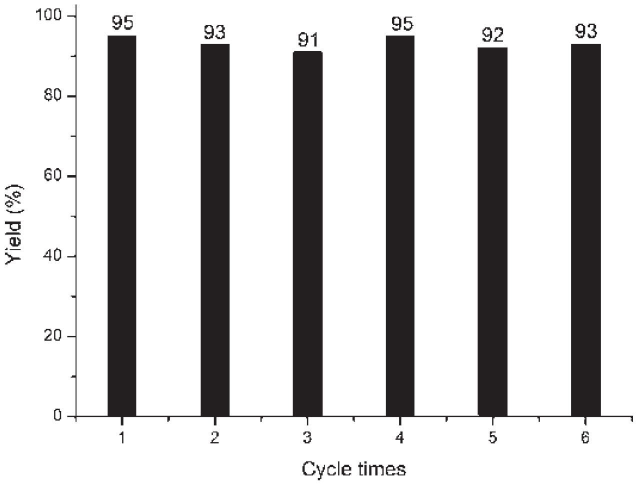


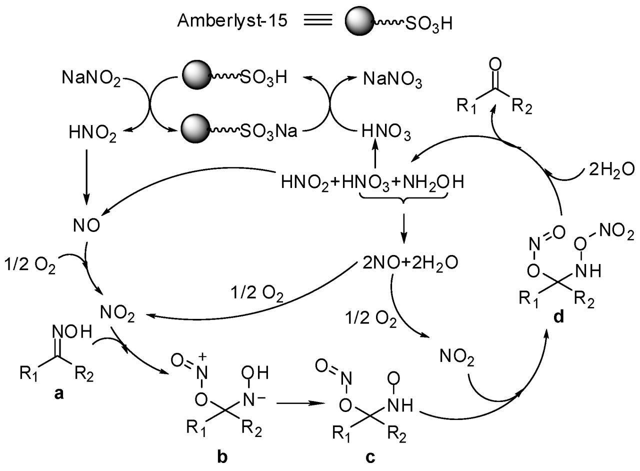
Table 3. Gram-Scale Test for Deoximation of 4-Chloroacetophenone Oxime[a]

entry	substrate (mmol)	amt of Amberlyst-15 (g)	amt of $NaNO_2$ (mol %)	time (h)	yield[b] (%)
1	1	0.100	10	5	95
2	5	0.100	10	7	93
3	10	0.200	5	12	92
4	50	1.000	3	30	92

[a] Reaction conditions: 4-chloroacetophenone oxime, Amberlyst-15, $NaNO_2$, CH_2Cl_2/H_2O (5/1, v/v), 25 °C, under 1 atm of O_2 (oxygen ball). [b] Isolated yield.

extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, and then the solvent was removed under reduced pressure. The residue was further purified by column chromatography on silica gel (300−400 mesh) with hexane and ethyl acetate (for ketoximes, 10/1; for aldoximes, 5/1) to give the corresponding carbonyl compounds.

Scheme 2. Possible Mechanism for Aerobic Oxidative Deoximation Catalyzed by $NaNO_2$



■ ASSOCIATED CONTENT

Supporting Information. Text and figures giving experimental procedures and characterization data, including ^1H and ^{13}C NMR spectral data and melting points for solid compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mowm@zjut.edu.cn (W.M.); dingcr2004@yahoo.com.cn (C.D.).

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(8) One particular case is the commercial synthesis of carvone, which is an essential oil used in the fragrance industry. See: (a) *The Chemistry of Essential Oils: An Introduction for Aromatherapists, Beauticians, Retailers and Students*; Williams, D. G., Ed.; Micelles Press: Dorset, U.K., 2008. For oximes obtained from the hydrogenation of nitroalkanes, see: (b) Corma, A.; Serna, P.; García, H. *J. Am. Chem. Soc.* **2007**, *129*, 6358. (c) Serna, P.; López-Haro, M.; Calvino, J. J.; Corma, A. *J. Catal.* **2009**, *263*, 328.

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