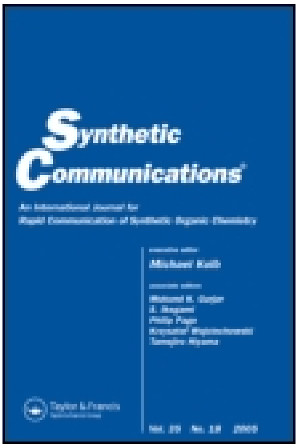

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Transformation of Amines to Oximes Using Heterogeneous Nanocrystalline Titanium(IV) Oxide as a Green Catalyst

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TRANSFORMATION OF AMINES TO OXIMES USING HETEROGENEOUS NANOCRYSTALLINE TITANIUM(IV) OXIDE AS A GREEN CATALYST

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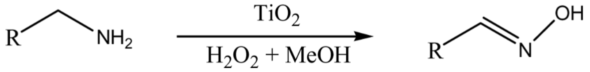
GRAPHICAL ABSTRACT



Abstract *The oxidation of amines into corresponding oximes has been described using heterogeneous nanocrystalline titanium(IV) oxide as catalyst and H_2O_2 as oxidizing agent in quantitative yields. Both aromatics and aliphatic amines undergo oxidation. Besides this, nanocrystalline TiO_2 was recovered and used for further reactions. Hence our present protocol is economical and clean and uses green reagent, solvent, and catalyst.*

Keywords Green chemistry; nanoparticles; oxidation; oxime

INTRODUCTION

Sustainable development can be defined as the ability to meet the needs of the current generation while preserving the ability of future generations to meet their needs. Green chemistry is one way to achieve it. Several ways are known through which a reaction can be said to be clean and green. Industry favors catalytic processes induced by green heterogeneous catalysts over homogeneous processes in view of ease of handling, simple workup, and regenerability.[1,2]

Titanium dioxide is a prominent heterogeneous material for various kinds of industrial applications, for example, in the selective reduction of NO_x in stationary sources, organic synthesis, photovoltaic devices, and sensors.[3–6] Despite this, researchers have not yet explored catalytic activity of nanocrystalline titanium(IV) oxide.

Oximes were successfully transformed into amides, amines, hydroxylamines, and hydroxylamine-O-ether.[7–9] Besides this, they are good synthons for heterocyclic compounds, for example, 1,3-oxazoles, thiazoles, and diazoles.[10]

Recently, oximes and their derivatives have drawn attention in medicinal research because of their significant bioactivity. Some molecules containing oxime

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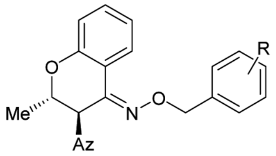
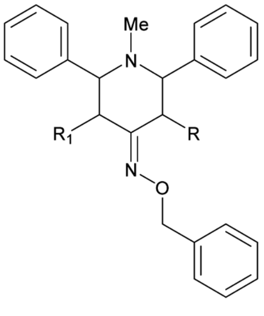
moieties are given here. All these applications make oximes very important synthetic intermediate.[11]



Azolyl-2-methylcromanone oxime ether



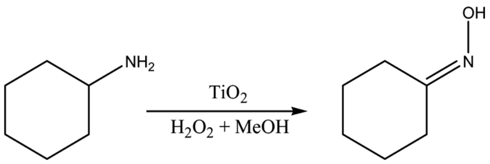
Piperidine-4-one oxime ether

Therefore, synthetic organic chemists are interested in facilitation of oxime synthesis. Many alternative methods exist for the synthesis of oximes,[12–15] but all these methods are obsolete and accompanied by serious drawbacks and limitations, for example, use of toxic reagent,[16] poor selectivity,[17] and rigorous reaction conditions with poor yield.[18] However, aerobic oxidative transformations of amines are very limited. These are not effective for a variety of amines[19] and are not eco-friendly.[20] There is a strong need for methods that involve direct conversion of amines into oximes under sustainable reaction conditions. In continuation of our progressive program toward the development of green and sustainable synthetic methods[21–23] for organic synthesis and the role of transition-metal catalysts in such syntheses,[24,25] we report a novel and efficient method for the oxidation of amines into oximes using nanocrystalline titanium(IV) oxide as green catalyst.

RESULTS AND DISCUSSION

To evaluate the catalytic activity of TiO_2 nanoparticles, initially a reaction was performed involving 0.01 mol of cyclohexamine and 0.04 mol of H_2O_2. Only 20% yield of the desired product was obtained. After that same reaction was performed using TiO_2 nanoparticles, the yield of the product reached 80%. This proves the high catalytic activity of nanocrystalline titanium(IV) oxide (Scheme 1).

Next, we investigated the efficiency of TiO_2 nanoparticles over other catalysts. The catalytic abilities of various catalysts are summarized in Table 1.



Scheme 1. Oxidation of cyclohexylamine to cyclopentanone oxime.

Table 1. Conversion of amine into oxime using different catalysts[a]

Entry	Catalyst	Conversion of oxime (%)	Selectivity of oxime (%)
1	SiO_2/H_2O_2	42	70
2	ZrO_2/H_2O_2	51	60
3	Al_2O_3/H_2O_2	40	67
4	$Ti(OiPr)_4$	55	75
5	$Ti(Oacac)_2$	54	76
6	Nb_2O_5/H_2O_2	40	70
7	TiO_2/H_2O_2	84	92

[a] Reaction conditions: benylamine (1 mmol), hydrogen peroxide (4 mmol), and 10 mol% catalyst; MeOH; temperature 60 °C.

The increased catalytic activity of nano-TiO_2 over the commercially available bulk TiO_2 and other nano-oxides may be attributed to the higher surface area for nano-TiO_2. This is thought to be due to morphological differences. Whereas larger crystallites have only a small percentage of reactive sites on the surface, smaller crystallites possess a much higher surface concentration of such sites [shown in powder x-ray diffraction (XRD) pattern] crystal corners, edges, or ion vacancies.[26] See Fig. 1.

Besides this, we had screened the solvent for this oxidation reaction to get maximum yield of the product. Among the solvent screened, MeOH gave the maximum yield of the product. All results are depicted in Table 2.

It was important to check the chemoselectivity of the reaction; we took a mixture of cyclohexamine and cyclohexanol. Under similar conditions, we obtained cyclohexanoxime as a sole product. The alcoholic group of other reactant did not give oxidized product. Then we explored the generativity and scope of the nano-TiO_2-catalyzed reaction; arrays of structurally divergent amines were tested. From NMR spectra, it was evident that amines underwent oxidation and gave maximum yield of product.

The literature suggested that superoxide species O_2^- over metal oxide and zeolitic systems usually acts as the active species in radical reactions.[27] This highly active species immediately reacted with substituted hydroxylamine and formed its free radical, which easily converted into the product (Scheme 2, Table 3).

For practical applications of heterogeneous systems, the lifetime of the catalyst and its level of reusability are very important factors. The catalyst was also recycled after accomplishment of the reaction. Here we have recycled the catalyst four times. Results are summarized in Table 4.

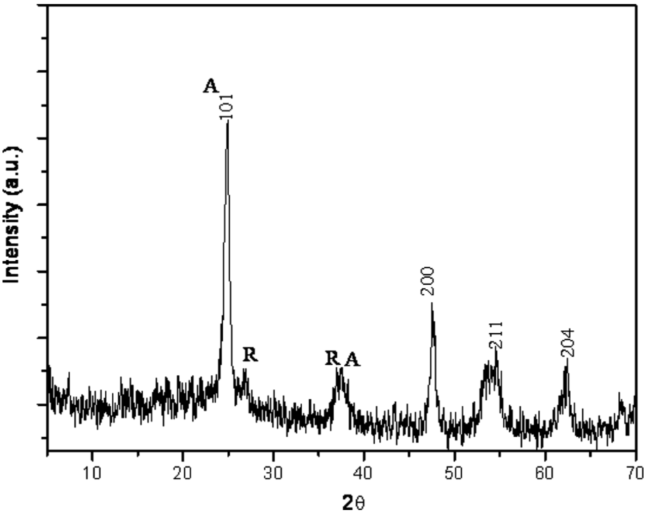


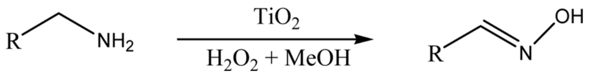
Figure 1. Powder XRD pattern of nanocrystalline titanium(IV) oxide.

Table 2. Screening of solvent for oxidation reaction[a]

Entry	Solvent	Yield (%)[b]
1	MeOH	84
2	EtOH	75
3	CH_3CN	60
4	THF	50
5	Benzene	52
6	Toluene	53

[a] Reaction conditions: benzylamine (1 mmol), hydrogen peroxide (4 mmol), and 10 mol% nanoTiO_2 (50 ± 2) nm; solvent; temperature 60 °C.
[b] Isolated yields.

It was further confirmed by TEM technique. Both fresh and recovered catalysts were observed under TEM to understand the shape and size of the particles. As shown in Fig. 2a, the fresh nanoparticles have size range of 20–50 nm with well-defined shapes. Figure 2b shows the TEM image of the used catalyst after four recycles. Interestingly, it was observed that the shape and size of the particles remain unchanged even after recycling. This shows that the morphology of the catalyst remains the same even after recycling. Besides this, XRD patterns of the fresh and used nano-TiO_2 do not differ in the range $2\theta = 0$–$70°$, which also confirms that the structure and morphology of the catalyst remain the same during the course of the reaction.



Scheme 2. Oxidation of amine to oxime.

Table 3. Nanocrystalline titanium(IV) oxide–catalyzed oxidation of amines into oxime[a]

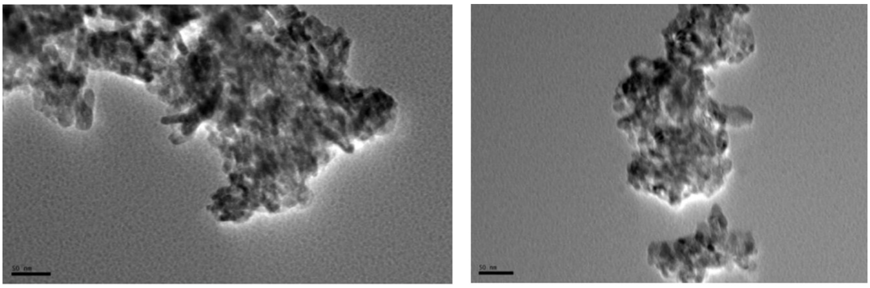
Entry	Alcohols	Products	Time (h)	Yield (%)[b]
1	Benzylamine	Benzaldehyde oxime	6	84
2	*p*-Chlorobenzylamine	*p*-Chlorobenzaldehyde oxime	7	81
3	*o*-Nitrobenzylamine	*o*-Nitro benzaldehyde oxime	8	80
4	Cyclopentylamine	Cyclopentanone oxime	7	82
5	*n*-Pentylamine	Pentanal oxime	8	78
6	*n*-Butylamine	Butanal oxime	6	74
7	Cyclohexylamine	Cyclohexanone oxime	8	82
8	*n*-Hexylamine	Hexanal oxime	10	78

[a] Reaction conditions: benzylamine (1 mmol), hydrogen peroxide (4 mmol), and 10 mol% nanoTiO_2 (50 ± 2) nm; MeOH; temperature 60 °C.
[b] Isolated yields.

Table 4. Recyclability studies of nano-TiO_2 oxidation reaction[a]

Run	Time	Yield (%)[b]
1	6	84
2	7	83
3	7	83
4	8	82

[a] Reaction conditions: benzylamine (1 mmol), hydrogen peroxide (4 mmol), and 10 mol% nanoTiO_2 (50 ± 2) nm; MeOH; temperature 60 °C.
[b] Isolated yields.



(a) (b)

Figure 2. (a) TEM images of fresh nanoparticles; (b) TEM images of recycled nanoparticles.

CONCLUSION

To conclude, we have shown that nano-TiO_2 is a highly active reusable catalyst for the conversion of amines to oximes. Thus, nano-TiO_2 with its well-defined shape and size (10–20 nm) and higher specific surface area shows greater activity than other catalysts. Use of nontoxic reagent, catalyst, and good yield of product within a short reaction time make present protocol useful in organic synthesis.

EXPERIMENTAL

The materials procured from Sigma-Aldrich and Merck were used without further purification. Infrared (IR) spectra were obtained on Perkin-Elmer Fourier transform (FT)–IR spectrometer (Spectrum 2000) using potassium bromide pellets or as liquid films between two sodium chloride pellets. Mass spectra were recorded in a, turnover frequency (TOF)–mass spectrometer, model no. KC455. ^{1}H NMR spectra were recorded on a Bruker Spectrospin (400 MHz). All NMR samples were run in $CDCl_3$, and chemical shifts are expressed as parts per million (ppm) relative to internal Me_4Si.

TiO_2 (10 mol%) was added to the mixture of benzyl amine (0.01 mmol) and H_2O_2 (0.04 mmol) in MeOH (8 ml). This reaction mixture was refluxed with stirring for 6 h. Reaction was continuously monitored by thin-layer chromatography (TLC). After accomplishment of reaction as indicated by TLC, the crude mixture was filtered to get TiO_2 nanopowder. Filtrate was removed in a vacuum at room temperature. Obtained solid product was purified by column chromatography using 80:20 ethyl acetate and hexane.

Spectral Data

Benzaldehyde oxime. IR ν_{max} (KBr) 3355 cm^{-1} (OH of oxime), 1660 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 8.39 (1H, br, OH), 8.12 (1H, s), 7.76–7.79 (1H, $J = 8.12$ Hz, dd, φ), 7.56–7.57 (1H, 8.12 Hz, dd, φ), 7.22–7.35 (3H, m, φ). m/z (GC-MS, HRMS): 121.05 (M$^+$).

***p*-Chlorobenzaldehyde oxime.** IR ν_{max} (KBr) 3321 cm^{-1} (OH of oxime), 1654 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 8.26 (s, br, OH), 8.12 (1H, s), 7.6 (2H, $J = 8.10$, d, φ), 7.3 (2H, $J = 8.10$, d, φ). m/z (GC-MS, HRMS): 155.01 (M$^+$).

***o*-Nitrobenzaldehyde oxime.** IR ν_{max} (KBr) 3390 cm^{-1} (OH of oxime), 1670 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): 8.94 (1H, s), 8.35 (s, br, OH), 8.06–8.08 (1H, $J_1 = 8$ Hz, $J_2 = 1.2$ Hz, dd, φ), 7.90–7.92 (1H, $J_1 = 8$ Hz, $J_2 = 1.2$ Hz, dd, φ), 7.62–7.68 (1H, m, φ), 7.54–7.59 (1H, m, φ). m/z (GC-MS, HRMS): 166.03 (M$^+$).

Cyclohexanone oxime. IR ν_{max}(KBr) 3294 cm^{-1}(OH of oxime), 1666 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 6.54 (OH, br), 2.32 (2H, $J = 8$ Hz, t), 2.03 (2H, $J = 8$ Hz, d), 1.55–1.74 (6H, m). m/z (GC-MS, HRMS): 113.08 (M$^+$).

Hexanal oxime. IR ν_{max} (KBr) 3256 cm^{-1} (OH of oxime), 1640 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 7.90 (1H, s, br), 7.72 (1H, s), 2.90 and 2.01 (2 m, altogether 4H at C_2 and one of allylic position of both isomer are in 3:1), 1.20–1.43 (6H, m), 0.79–0.83 (3H, m). m/z (GC-MS, HRMS): 115.12 (M$^+$).

***n*-Pentanal oxime.** IR ν_{max} (KBr) 3245 cm^{-1} (OH of oxime). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 7.97 (1H, s, br), 7.74 (1H, s), 2.93 and 2.01 (2 m, altogether 4H at C_2 and one of allylic position of both isomer are in 3:1), 1.22–1.43 (4H, m), 0.84–0.85 (3H, m). m/z (GC-MS, HRMS): 100.82 (M$^+$).

Cyclopentanone oxime. IR ν_{max} (KBr) 3298 cm^{-1} (OH of oxime), 1660 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 8.20 (s, br, OH), 2.42 (2H, t), 2.10 (2H, t). m/z (GC-MS, HRMS): 99.06 (M^+).

***n*-Butanal oxime.** IR ν_{max} (KBr) 3250 cm^{-1} (OH of oxime), 1648 cm^{-1} (C=N). ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ 7.90 (s, OH, br), 7.70 (1H, s), 2.90 and 2.01 (2 m, altogether 4H at C_2 and one of allylic position of both isomer are in 3:1), 0.87–1.43 (6H, m). m/z (GC-MS, HRMS): 87.10 (M^+).

REFERENCES

1. Choudary, B. M.; Mulukutla, R. S.; Klabunde, K. J. Benzylation of aromatic compounds with different crystallites of MgO. *J. Am. Chem. Soc.* **2003**, *125*, 2020–2021.
2. Choudary, B. M.; Kantam, M. L.; Ranganath, K. V. S.; Mahender, K.; Sreedhar, B. Bifunctional nanocrystalline MgO for chiral epoxy ketones via claisen-schmidt condensation–asymmetric epoxidation reactions. *J. Am. Chem. Soc.* **2004**, *126*, 3396–3397.
3. Bosh, H.; Janssen, F. Formation and control of nitrogen oxides. *Catat. Today* **1988**, *2*, 369.
4. Forzatti, P. Enviromental catalysis for stationary applications. *Catal. Today* **2000**, *62*, 51–65.
5. Hoffman, M. R.; Martin, S. T.; Choi, W. D.; Wahneman, W. Environmental applications of semiconductor photocatalysis. *Chem. Rev.* **1995**, *95*, 69–96.
6. Maldoti, A.; Molinari, A.; Amadeni, R. Photocatalysis with organized systems for the oxofunctionalization of hydrocarbons by O_2. *Chem. Inform. Rev.* **2002**, *102*, 3811–3836.
7. Frutos, R. P.; Spero, D. M. Synthesis of protected, chiral α,α-disubstituted α-amino acids via a Beckmann rearrangement. *Tetrahedron Lett.* **1998**, *39*, 2475–2478.
8. Sasatani, S.; Miyazak, T.; Maruoka, K.; Yamamoto, H. Diisobutylaluminum hydride: A novel reagent for the reduction of oximes. *Tetrahedron Lett.* **1983**, *24*, 4711–4712.
9. Negi, S.; Matsukura, M.; Mizuno, M.; Miyake, K. Synthesis of (2R)-1-(4-cholro-2-pyridyl)-2-(2-pyridyl) ethylamine: A selective oxime reduction and crystallization–induced asymmetric transformation. *Synthesis* **1996**, 991–996.
10. Bougrin, K.; Loupy, A.; Souaoui, M. Trois nouvelles voies de synthèse des dérivés 1,3-azoliques sous micro-ondes. *Tetrahedron* **1998**, *54*, 8055–8064.
11. Ramalingan, C.; Park, Y. T.; Kabilan, S. Stereochemistry and antimicrobial evaluation of substituted piperidin-4-one oxime ethers. *Eur. J. Med. Chem.* **2006**, *41*, 683–696.
12. Hanson, J. R. Application of chromium salt in preparative organic chemistry. *Synthesis* **1974**, 1–8.
13. Barton, D. H. R.; Fernandez, I.; Richard, C. S.; Zard, S. A mild procedure for the reduction of nitro compounds to oximes. *Tetrahedron* **1987**, *43*, 551–558.
14. Albanese, D.; Landini, D.; Penso, M. Reduction of allylic nitro compounds to oximes with carbon disulfide under solid–liquid phase-transfer catalyst conditions. *Synthesis* **1990**, 333–336.
15. Kizil, M.; Murphy, J. A. A new free radical route to oximes using alkyl halides, hexabutylditin, and readily available nitrite esters. *Tetrahedron* **1997**, *53*, 16847–16858.
16. Hwu, J. R.; Tseng, W. N.; Patel, H. V.; Wong, F. F.; Horng, D. N.; Liaw, B. R.; Lin, L. C. Mono-deoxygenation of nitroalkanes, nitrones, and heterocyclic *N*-oxides by hexamethyldisilane through 1,2-elimination: Concept of "counterattack reagent." *J. Org. Chem.* **1999**, *64*, 2211–2218.
17. Reddy, J. S.; Sayari, A. Oxidation of primary amines over vanadium silicalite molecular sieve, VS-1. *Catal. Lett.* **1994**, *28*, 263.

18. Kaszonyi, A.; Cvengrosoova, Z.; Hronec, M. Oxidation of cyclohexylamine by air to its oxime. *J. Mol. Catal. A* **2000**, *160*, 393–402.
19. Joseph, R.; Ravindranathan, T.; Sudalai, A. Selective catalytic oxidation of benzylic and allylic amines to oximes with H_2O_2 over TS-1. *Tetrahedron Lett.* **1995**, *36*, 1903–1904.
20. Suzuki, K.; Watanabe, T.; Shun-Ichi, M. Aerobic oxidation of primary amines to oximes catalyzed by DPPH and WO_3/Al_2O_3. *Angew. Chem. Int. Ed.* **2008**, *47*, 2079–2081.
21. Kidwai, M.; Poddar, R.; Diwaniyan, S.; Kuhad, R. C. Laccase from basidiomycetous fungus catalyzes the synthesis of substituted 5-deaza-10-oxaflavins via a domino reaction. *Adv. Synth. Catal.* **2009**, *351*, 589–595.
22. Kidwai, M.; Poddar, R. Transesterification of chromenes employing immobilized lipase in ionic liquids. *Catal. Lett.* **2008**, *124*, 311–317.
23. Kidwai, M.; Jain, A.; Poddar, R.; Bhardwaj, S. Bis[(L)prolinato-N,O]Zn in acetic acid–water: A novel catalytic system for the synthesis of β-amino carbonyls via Mannich reaction at room temperature. *Appl. Organomet. Chem.* **2011**, *25*, 335–340.
24. Kidwai, M.; Bhardwaj, S.; Mishra, N. K.; Bansal, V.; Kumar, A.; Mozumdar, S. A novel method for the synthesis of β-enaminones using Cu nanoparticles as catalyst. *Catal. Commun.* **2009**, *10*, 1514–1517.
25. Kidwai, M.; Jain, A.; Bhardwaj, S. 1,4-Addition of terminal alkynes to conjugated enones in water using green catalyst bis[(l)proliato-N,O]Zn—An environmentally benign protocol. *Catal. Lett.* **2011**, *141*, 183–190.
26. Lee, H.; Park, Y. H.; Kok, H. Role of water in the photocatalytic degradation of trichloroethylene vapor on TiO_2 films. *Langmuir* **2000**, *16*, 7289–7293.
27. Zhao, Q.; Bao, X.-H.; Wang, Y.; Lin, L.-W.; Guo, X.-W.; Wang, X.-S. Studies on superoxide O_2^- species on the interaction of TS-1 zeolite with H_2O_2. *J. Mol. Catal. A: Chem.* **2000**, *157*, 265–268.