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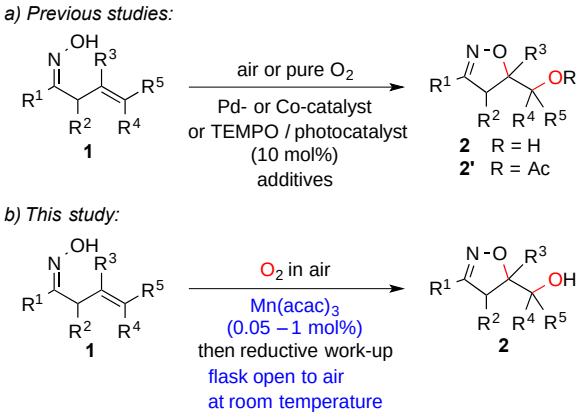
Manganese-promoted oxidative cyclisation of unsaturated oximes using molecular oxygen in air under ambient conditions

Daisuke Yamamoto,[a] Takuto Oguro,[a] Yuuki Tashiro,[a] Masayuki Soga,[a] Kazuhito Miyashita,[a] Yoshiaki Aso,[a] and Kazuishi Makino*[a]

Abstract: A highly efficient manganese-promoted oxidative cyclisation of unsaturated oximes to afford the corresponding 4,5-dihydroisoxazoline alcohols was developed. A very low loading (generally 0.1–0.2 mol%) of $Mn(acac)_3$ promoted the oxidative cyclisation through the direct incorporation of molecular oxygen present in air (open flask) at room temperature.

Introduction

Molecular oxygen is recognized as an ideal oxidant because it is abundantly available, inexpensive and environmentally benign.[1] In this context, transition metal-catalysed and metal-free oxidative difunctionalisation of unactivated carbon–carbon double bonds for directly incorporating molecular oxygen into substrates has emerged as an attractive and powerful strategy for efficient assembly of new bonds.[2-12] Recently, a few novel approaches have been reported for the construction of the 4,5-dihydroisoxazoline alcohols, which are an important class of compounds found in several biologically active agents[13] and versatile intermediates in organic synthesis,[14] by the oxidative cyclisation of β,γ-unsaturated oximes using molecular oxygen (Scheme 1). In 2010, Loh *et al.* demonstrated the use of 10 mol% palladium complex-promoted 4,5-dihydroisoxazoline formation from β,γ-unsaturated oximes to yield a mixture of 4,5-dihydroisoxazoline alcohol and its acetate ester in the presence of acetic acid.[15] Yu *et al*. reported a 10 mol% cobalt (II) complex in the presence of *tert*-butyl hydroperoxide acting as a catalyst to afford 4,5-dihydroisoxazoline alcohols under a pure molecular oxygen atmosphere.[16] Very recently, Chen *et al*. reported a organophotocatalytic reaction to provide 4,5-dihydroisoxazoline alcohols using 9-metsityl-10-methyl-acridinium perchlorate (5 mol%) and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 10 mol%) under O_2 atmosphere.[17] While these pioneering works provided new methods for the construction of 4,5-dihydroisoxazolines from unsaturated oximes through the incorporation an oxygen atom from gaseous dioxygen into carbon–carbon double bonds, there still remain challenges in terms of yield, substrate scope, functional group tolerance and environmentally friendly conditions. In particular, highly active and robust catalysts capable of directly incorporating molecular oxygen present in air into organic substrates without cooling or heating are in high demand. In the course of our studies on manganese-promoted oxidative reactions using molecular oxygen,[18] we report herein a highly efficient manganese-promoted oxidative cyclisation of unsaturated oximes to provide 4,5-dihydroisoxazolines using molecular oxygen present in air (open flask) at room temperature.



Scheme 1. Aerobic oxidative cyclisation of β,γ-unsaturated oximes

Results and Discussion

Our initial investigations began with the screening of various metal complexes for the oxidative cyclisation reaction of β,γ-unsaturated oxime **1a** in MeOH in air. Among them, using 1 mol% of $Mn(acac)_3$ provided the desired 4,5-dihydroisoxazoline alcohol **2a** incorporating an oxygen atom present in air in 80% yield at room temperature after treatment with a saturated aqueous sodium thiosulfate solution (Table 1, entry 1). The corresponding peroxide derived from **1a** was obtained without a reductive work-up.[19] This result clearly indicates that this manganese-promoted 4,5-dihydroisoxazoline formation does not proceed through an epoxidation of carbon–carbon double bond. On the other hand, other metal acetylacetonate complexes such as $Co(acac)_3$, $Fe(acac)_3$, $Ti(acac)_3$, $MoO_2(acac)_2$, and $Ni(acac)_2$, were completely ineffective at 1 mol%, and 1 mol% of $Cu(acac)_2$ gave poor yield in the same conditions (entries 2–7). The solvent screening indicated that the use of alcohols such as MeOH and EtOH were suitable for this reaction (entries 1 and 8), while C_6H_6, CH_2Cl_2 and CH_3CN furnished 4,5-dihydroisoxazoline **2a** in poor yield (entries 9–11). Encouraged by these initial findings, we examined the possibility of further decreasing the loading of $Mn(acac)_3$ in air at room temperature. The yield was at a similar level with 0.5 mol% of $Mn(acac)_3$ (entry 12), whereas a significant deterioration of yield was observed after reducing the $Mn(acac)_3$ loading to 0.1 mol% (entry 13). To our delight, we found that higher substrate concentration improved the yield and reaction rate (entries 14–17). At a starting substrate concentration of 2.0 M in MeOH, 0.1 mol% of $Mn(acac)_3$ worked effectively to afford 4,5-dihydroisoxazoline **2a** in 87% yield (entry 15). This protocol could be applied to the gram-scale synthesis of 4,5-dihydroisoxazoline **2a** using a 0.1 mol% $Mn(acac)_3$ in high yield in air at room temperature (entry 16). Moreover, using only 0.05 mol% $Mn(acac)_3$ promoted the oxidative cyclisation of unsaturated oximes carried out at room temperature for 72 h

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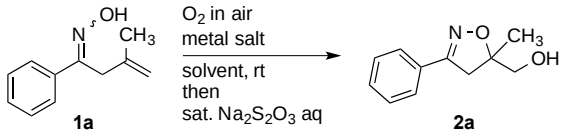
(61% yield) at a higher concentration (4.0 M in MeOH), directly incorporating molecular oxygen present in air (entry 17).

Table 1. Optimisation of the transition metal-promoted 4,5-dihydroisoxazoline formation through the incorporation of molecular oxygen present in air[a]

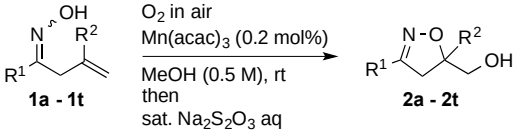


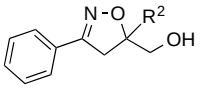
Entry	Metal salt (mol%)	Solvent (M)	Time (h)	Yield (%)
1	$Mn(acac)_3$ (1)	MeOH (0.1)	0.25	80
2	$Co(acac)_3$ (1)	MeOH (0.1)	24	N.R.[b]
3	$Fe(acac)_3$ (1)	MeOH (0.1)	24	N.R.[b]
4	$Ti(acac)_3$ (1)	MeOH (0.1)	24	N.R.[b]
5	$MoO_2(acac)_2$ (1)	MeOH (0.1)	24	N.R.[b]
6	$Ni(acac)_2$ (1)	MeOH (0.1)	24	N.R.[b]
7	$Cu(acac)_2$ (1)	MeOH (0.1)	24	< 10
8	$Mn(acac)_3$ (1)	EtOH (0.1)	0.25	73
9	$Mn(acac)_3$ (1)	C_6H_6 (0.1)	4	34
10	$Mn(acac)_3$ (1)	CH_2Cl_2 (0.1)	24	33
11	$Mn(acac)_3$ (1)	CH_3CN (0.1)	2	42
12	$Mn(acac)_3$ (0.5)	MeOH (0.1)	0.25	73
13	$Mn(acac)_3$ (0.1)	MeOH (0.1)	24	Trace
14	$Mn(acac)_3$ (0.2)	MeOH (0.5)	4	81
15	$Mn(acac)_3$ (0.1)	MeOH (2.0)	24	87
16[c]	$Mn(acac)_3$ (0.1)	MeOH (2.0)	24	81
17	$Mn(acac)_3$ (0.05)	MeOH (4.0)	72	61

[a] Reaction conditions: **1a** (0.300 mmol), metal salt (0.05 – 1 mol%), O_2 (flask open to air), rt. [b] N.R. = no reaction. [c] The reaction was carried out using **1a** (1.00 g, 5.71 mmol).

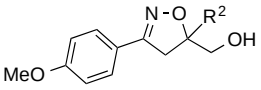
With the optimal reaction conditions, we explored the scope of this manganese-promoted reaction to various unsaturated oximes (Table 2). Considering the solubility of each solid oxime, the reaction was carried out in 0.5 M MeOH solution using 0.2 mol% of $Mn(acac)_3$. Generally, the reactions of oximes with 1,1-disubstituted and monosubstituted alkenes proceed effectively to afford the oxygenated products **2a** and **2b** in 81% and 93% yield, respectively. The oximes bearing electron-donating (*p*-OMe) or electron-withdrawing (*p*-CN) substituents on the aryl ring furnished the desired 4,5-dihydroisoxazoline (**2c**–**2f**) in high yield. Additionally, more hindered substrates, α- and β-naphthyl oximes, also reacted with molecular oxygen in air at room temperature to afford the corresponding products (**2g**–**2j**) in 71%–82% yield. Heteroaromatic substrates such as the 2-thienyl oximes **1k** and **1l** were suitable for the oxidative cyclisation. On the other hand, the oxidative cyclisation of 2-furanyl oximes **1m** and **1n** proceeded in good to moderate yield. Alkyl-substituted oximes were also viable substrates for this reaction. The highly hindered *tert*-butyl oximes **1q** and **1r** as well as the primary alkyl oximes **1o** and **1p** afforded the corresponding 4,5-dihydroisoxazoline **2o**–**2r** in high yield. The *tert*-butyldimethylsilyl and *tert*-butoxycarbonyl groups were tolerated under the reaction conditions (**2s** and **2t**).

Table 2. Substrate scope of the manganese-promoted 4,5-dihydroisoxazoline formation through the incorporation of molecular oxygen present in air

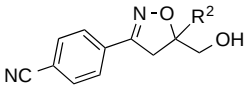




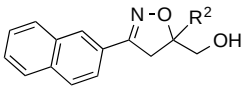
2a $R^2 = CH_3$ 4 h, 81%
2b $R^2 = H$ 4 h, 93%



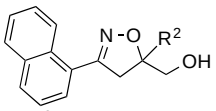
2c $R^2 = CH_3$ 24 h, 80%
2d $R^2 = H$ 5 h, 82%



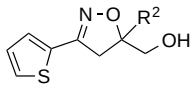
2e $R^2 = CH_3$ 24 h, 88%
2f $R^2 = H$ 5 h, 80%



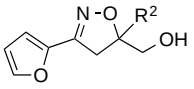
2g $R^2 = CH_3$ 24 h, 82%
2h $R^2 = H$ 4 h, 81%



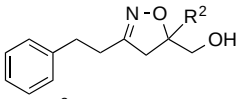
2i $R^2 = CH_3$ 28 h, 71%
2j $R^2 = H$ 48 h, 82%



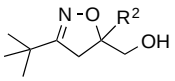
2k $R^2 = CH_3$ 6 h, 89%
2l $R^2 = H$ 2 h, 92%



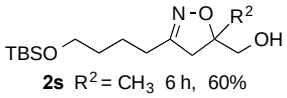
2m $R^2 = CH_3$ 48 h, 44%
2n $R^2 = H$ 48 h, 59%
(Recovered **1n**: 13%)



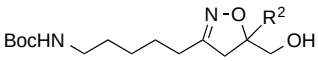
2o $R^2 = CH_3$ 24 h, 82%
2p $R^2 = H$ 28 h, 82%



2q $R^2 = CH_3$ 2 h, 88%
2r $R^2 = H$ 24 h, 74%



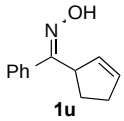
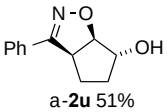
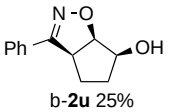
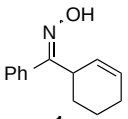
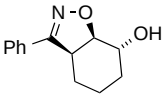
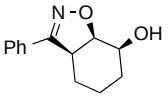
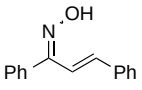
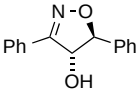
2s $R^2 = CH_3$ 6 h, 60%



2t $R^2 = CH_3$ 8 h, 75%

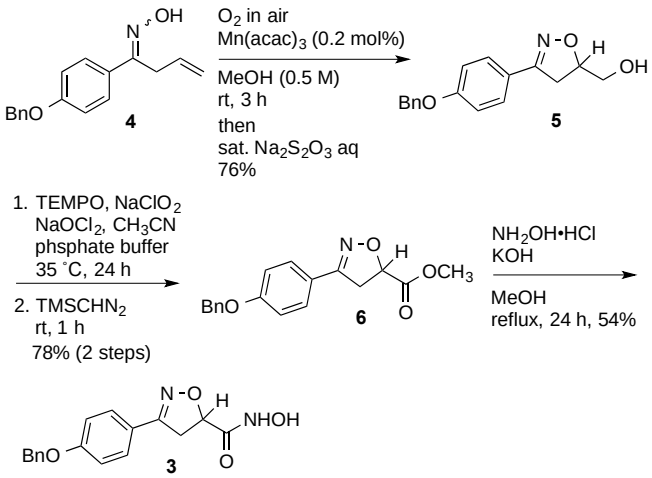
Subsequently, to assess the potential for diastereocontrol in the aerobic cyclisation process, we examined a number of different substrates (Table 3). The oxime **1u** with the cyclopentenyl group and **1v** with the cyclohexenyl group afforded *cis*-fused products as a 2:1 diastereomeric mixture (entries 1 and 2).[20] The α,β-unsaturated substrate **1w** was also viable for the aerobic cyclisation. The addition of molecular oxygen exclusively occurred from the opposite direction of the phenyl group via a 5-endo-trig cyclisation to afford a single diastereomer **2w** in 57% yield.

Table 3. Manganese-promoted diastereoselective oxidative cyclisation of unsaturated oximes through the incorporation of molecular oxygen from air

Entry	Oxime	Products	
1[a]	 **1u**	 a-**2u** 51%	 b-**2u** 25%
2[a]	 **1v**	 a-**2v** 54%	 b-**2v** 26%
3[b]	 **1w**	 **2w** 57% (single diastereomer)	

[a] $Mn(acac)_3$ (0.2 mol%), O_2 (flask open to air), MeOH (0.5 M), rt, 2 h. [b] $Mn(acac)_3$ (0.5 mol%), O_2 (flask open to air), MeOH (1.0 M), rt, 24 h.

To demonstrate the utility of this manganese-promoted aerobic cyclisation, we applied our method to the synthesis of the hydroxamic acid **3**, which is a promising antitrypanosomal agent for the management of Chagas disease (Scheme 2).[13d] The β,γ-unsaturated oxime **4** was treated with 0.2 mol% $Mn(acac)_3$ in MeOH (0.5 M) in air to afford 4,5-dihydroisoxazline alcohol **5** in 76% yield. The transformation to the methyl ester **6** was attained in 78% yield by oxidation with sodium hypochlorite–sodium chlorite in the presence of TEMPO[21] followed by esterification with trimethylsilyl diazomethane. Finally, the desired hydroxamic acid **3** was obtained in 54% yield by a reaction with hydroxyl amine.



Scheme 2. Synthesis of the antitrypanosomal agent **3**

In conclusion, we have developed a manganese-promoted oxidative cyclisation reaction to provide 4,5-dihydroisoxazoline alcohols. All manipulations in this reaction could be carried out in air without cooling, heating or high pressure conditions. Notably, a very low loading of $Mn(acac)_3$ promoted the oxidative cyclisation through the direct incorporation of molecular oxygen from air (pure oxygen is not required) without any other additives. In addition of the conventional 4,5-dihydroisoxazolines synthesis by nitrile oxide cycloaddition,[14] this highly efficient manganese-promoted oxidative cyclisation reaction utilizing molecular oxygen in air as a sole oxidant provides another approach to produce 4,5-dihydroisoxazolines in terms of the desirable features such as simple operation, a wide substrate scope, functional tolerance, and mild and environmentally benign conditions. Further mechanistic investigations of the manganese-promoted unactivated alkene difunctionalisation reactions incorporating molecular oxygen and development of an asymmetric version is currently ongoing in our laboratory.

Experimental Section

Gram-scale synthesis of 4,5-dihydroisoxazoline alcohol 2a using manganese-promoted oxidative cyclisation

To a stirred solution of β,γ-unsaturated oxime **1a** (1.00 g, 5.71 mmol) in MeOH (2.9 mL) at room temperature was added $Mn(acac)_3$ (2.0 mg, 5.7 μmol, 0.10 mol%) and the mixture was stirred for 24 h at room temperature under air (open flask). The reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$ (3.0 mL) and the mixture was stirred for 30 min at room temperature. The resulting mixture was extracted with EtOAc (3 x 3.0 mL). The combined organic layers were washed with brine (1 x 3.0 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The obtained crude material was purified by column chromatography (silica gel, hexane : ethyl acetate = 2 : 1 to 1 : 1) to give **2a** (889.0 mg, 4.65 mmol, 81%).

Acknowledgements

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Keywords: dihydroisoxazoline • manganese • aerobic cyclisation • molecular oxygen • environmentally benign

[1] For selected reviews of oxidation reactions with molecular oxygen, see: a) T. Mukaiyama, T. Yamada, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 17–35; b) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329–2363; c) J. Piera, J.-E. Bäckvall, *Angew. Chem. Int. Ed.* **2008**, *47*, 3506–3523; d) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem. Int. Ed.* **2011**, *50*, 11062-11087; e) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381–3430.

[2] For transition metal-promoted aerobic dioxygenation of carbon–carbon double bonds using NHPI, HOBt, NHS, or hydroxamic acids, see: a) S. Ozaki, T. Hamaguchi, K. Tsuchida, Y. Kimata, M. Masui, *J. Chem. Soc. Perkin Trans. 2* **1989**, 951-956; b) R. Bag, D. Sar, T. Punniyamurthy, *Org. Lett.* **2015**, *17*, 2010–2013; c) A. A. Andia, M. R. Miner, K. A. Woerpel, *Org. Lett.* **2015**, *17*, 2704–2707; d) Q. Lu, Z. Liu, Y. Luo, G. Zhang, Z. Huang, H. Wang, C. Liu, J. T. Miller, A. Lei, *Org. Lett.* **2015**, *17*, 3402–3405; e) Q. Lu, P. Peng, Y. Luo, Y. Zhao, M. Zhou, A. Lei, *Chem. Eur. J.* **2015**, *21*, 18580–18583; f) X.-F. Xia, S.-L. Zhu, Z. Gu, H. Wang, W. Li, X. Liu and Y.-M. Liang, *J. Org. Chem.*, 2015, **80**, 5572–

5580; g) J.-Z. Zhang, Y. Tang, *Adv. Synth. Catal.* **2016**, *358*, 752–764; h) M. R. Miner, K. A. Woerpel, *Eur. J. Org. Chem.* **2016**, 1860–1866; i) R. Bag, D. Sar, T. Punniyamurthy, *Org. Biomol. Chem.* **2016**, *14*, 3246–3255.

[3] For metal-free aerobic dioxygenation of carbon–carbon double bonds using hydroxamic acids, see: a) V. A. Schmidt, E. J. Alexanian, *Angew. Chem. Int. Ed.* **2010**, *49*, 4491–4494; b) B. C. Giglio, V. A. Schmidt, E. J. Alexanian, *J. Am. Chem. Soc.* **2011**, *133*, 13320–13322; c) V. A. Schmidt, E. J. Alexanian, *Chem. Sci.* **2012**, *3*, 1672–1674.

[4] For metal-free aerobic dioxygenation of carbon–carbon double bonds of 2-norbornene using NHPI, see: Y. Ishii, *J. Mol. Catal. A: Chemical* **1997**, *117*, 123–137.

[5] For aerobic oxytrifluoromethylation of carbon–carbon double bonds, see: a) C.-P. Zhang, Z.-L. Wang, Q.-Y. Chen, C.-T. Zhang, Y.-C. Gu, J.-C. Xiao, *Chem. Commun.* **2011**, *47*, 6632–6634; b) A. Deb, S. Manna, A. Modak, T. Patra, S. Maity, D. Maiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 9747–9750; c) Y. Yang, Y. Liu, Y. Jiang, Y. Zhang, D. Vicic, *J. Org. Chem.* **2015**, *80*, 6639–6648; d) C. Liu, Q. Lu, Z. Huang, J. Zhang, F. Liao, P. Peng, A. Lei, *Org. Lett*. **2015**, *17*, 6034–6037.

[6] For aerobic oxy-2,2,2-trifluoroethylation of carbon–carbon double bonds, see: L. Li, M. Huang, C. Liu, J.-C. Xiao, Q.-Y. Chen, Y. Guo, Z.-G. Zhao, *Org. Lett.* **2015**, *17*, 4714–4717.

[7] For aerobic oxysulfonylation of carbon–carbon double bonds, see: a) Q. Lu, J. Zhang, F. Wei, Y. Qi, H. Wang, Z. Liu, A. Lei, *Angew. Chem. Int. Ed.* **2013**, *52*, 7156–7159; b) W. Wei, C. Liu, D. Yang, J. Wen, J. You, Y. Suo, H. Wang, *Chem. Commun.* **2013**, *49*, 10239–10241.

[8] For aerobic oxysulfoxidation of carbon–carbon double bonds, see: T. Keshari, V. K. Yadav, V. P. Srivastava, L. D. S. Yadav, *Green Chem.* **2014**, *16*, 3986–3992.

[9] For aerobic oxysulfurisation of carbon–carbon double bonds, see: S.-F. Zhou, X. Pan, Z.-H. Zhou, A. Shoberu, J.-P. Zou, *J. Org. Chem*. **2015**, *80*, 3682–3687.

[10] For aerobic oxyphosphorylation of carbon–carbon double bonds, see: W. Wei, J.-X. Ji, *Angew. Chem. Int. Ed*. **2011**, *50*, 9097–9099.

[11] For aerobic oxyazidation of carbon–carbon double bonds, see: X. Sun, X. Li, S. Song, Y. Zhu, Y.-F. Liang, N. Jiao, *J. Am. Chem. Soc.* **2015**, *137*, 6059-6066.

[12] For autoxidative 4,5-dihydroisoxazoline ring formation via nitrooxylation of carbon–carbon double bonds using stoichiometric amounts of *tert*-butyl nitrite, see: X.-W. Zhang, Z.-F. Xiao, Y.-J. Zhuang, M.-M. Wang, Y.-B. Kang, *Adv. Synth. Catal*. **2016**, *358*, 1942–1945.

[13] For selected examples of biologically active compounds containing a 4,5-dihydroisoxazoline ring, see: a) Y. Okamoto, M. Ojika, S. Kato, Y. Sakagami, *Tetrahedron* **2000**, *56*, 5813–5818; b) S. Castellano, D. Kuck, M. Viviano, J. Yoo, F. López-Vallejo, P. Conti, L. Tamborini, A. Pinto, J. L. Medina-Franco, G. Sbardella, *J. Med. Chem.* **2011**, *54*, 7663–7677; c) N. C. Patel, J. Schwarz, X. J. Hou, D. J. Hoover, L. Xie, A. J. Fliri, R. J. Gallaschun, J. T. Lazzaro, D. K. Bryce, W. E. Hoffmann, A. N. Hanks, D. McGinnis, E. S. Marr, J. L. Gazard, M. Hajós, R. J. Scialis, R. S. Hurst, C. L. Shaffer, J. Pandit, C. J. O'Donnell, *J. Med. Chem.* **2013**, *56*, 9180–9191; d) G. C. Rodrigues, D. F. Feijó, M. T. Bozza, P. Pan, D. Vullo, S. Parkkila, C. T. Supuran, C. Capasso, A. P. Aguiar, A. B. Vermelho, *J. Med. Chem*. **2014**, *57*, 298–308.

[14] For selected reviews, see: a) N. Nishikawa, *Method and applications of cycloaddition reactions in organic syntheses*, A John Wiley & Sons, Inc., **2014**; b) H. Feuer, *Nitrile oxides, nitrones, and nitronates in organic synthesis: novel strategies in synthesis*, A John Wiley & Sons, Inc., **2008**; c) A. I. Kotyatkina, V. N. Zhabinsky, V. A. Khripach, *Russ. Chem. Rev*. **2000**, *70*, 641–653; d) A. P. Kozikowski, *Acc. Chem. Res*. **1984**, *17*, 410-416.

[15] M.-K. Zhu, J.-F. Zhao, T-P. Loh, *J. Am. Chem. Soc.* **2010**, *132*, 6284–6285.

[16] W. Li, P. Jia, B. Han, D. Li, W. Yu, *Tetrahedron* **2013**, *69*, 3274–3280.

[17] X.-Q. Hu, J. Chen, J.-R. Chen, D.-M. Yan, W.-J. Xiao, *Chem. Eur. J.* **2016**, DOI: 10.1002/chem.201602597.

[18] D. Yamamoto, M. Soga, H. Ansai, K. Makino, *Org. Chem. Front.* **2016**, DOI: 10.1039/C6QO00318D.

[19] The physical and spectral data of the corresponding peroxide are presented in the supporting information.

[20] The relative stereochemistries **2u** and **2v** were determined by ROEY experiments, see the supporting information.

[21] M. Zhao, J. Li, E. Mano, Z. Song, D. M. Tschaen, E. J. J. Grabowski, P. J. Reider, *J. Org. Chem*. **1999**, *64*, 2564–2566.

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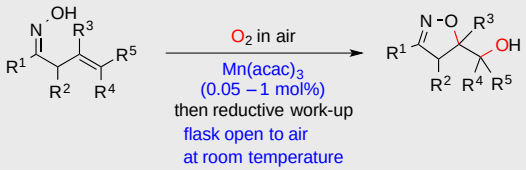

A very low loading of $Mn(acac)_3$ promoted the oxidative cyclisation of β,γ-unsaturated oximes through the direct incorporation of molecular oxygen present in air (open flask) at room temperature.

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Manganese-promoted oxidative cyclisation of unsaturated oximes using molecular oxygen in air under ambient conditions