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FULL PAPER

Selective Aerobic Oxidation of Alcohols with NO_3^- Activated Nitroxyl Radical/Manganese Catalyst System

Kalle Lagerblom, Juha Keskiväli, Arno Parviainen, Jere Mannisto and Timo Repo*[a]

Abstract: Homogeneous $Mn(NO_3)_2$/2,2,6,6-tetramethylpiperidin-1-yl)oxyl/2-picolinic acid catalyst system has been found highly active and versatile for the selective aerobic oxidation of alcohols (2,2,6,6-tetramethylpiperidin-1-yl)oxyl = TEMPO, 2-picolinic acid = PyCOOH). The catalytic method enables near quantitative conversion of various primary alcohols to the respective aldehydes using a very simple reaction setup and workup. This study presents findings on the catalyst stability and mechanisms of deactivation. The results show that NO_3^- plays a crucial catalytic role in the reaction as a source of oxygen activating NO_x species. Yet, disproportionation of NO_3^- to the volatile NO_2 during the reaction leads to catalyst deactivation under open air conditions. Catalyst deactivation through this route can be overcome by adding a catalytic amount of nitrate salt, for example $NaNO_3$ into the reaction. This stabilizes the $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst and enables oxidation of various primary alcohols to the respective aldehydes using low catalyst loadings under ambient conditions. Secondary alcohols can be oxidized with a modified catalyst utilizing sterically accessible nitroxyl radical 9-azabicyclo[3.3.1]nonane *N*-oxyl (ABNO) instead of TEMPO. At the end of the alcohol oxidation, pure carbonyl products and reusable catalyst can be recovered simply by extracting with organic solvent and dilute aqueous acid, followed by evaporation of both phases.

Introduction

The selective oxidation of alcohols to carbonyl compounds is one of the most used transformations in organic chemistry.[1] Traditionally, this reaction is performed using stoichiometric oxidants, such as CrO_3,[2,3] MnO_2,[4,5] hypervalent iodine[6,7] or activated DMSO.[8–10] These reagents are all costly and their use in industrial-scale reactions result in large quantities of hazardous waste. Cost efficient and environmentally benign catalytic approaches employing O_2[11–16] or NaOCl[17–21] as oxidant have lately received great attention to ease the environmental and economic burden of alcohol oxidation. Especially aerobic oxidation has gained prominence due to its advantages, such as abundance of O_2 in the atmosphere and water as the only byproduct. The selective oxidation of alcohols to the respective carbonyl compounds using O_2 as the terminal oxidant has been demonstrated using catalysts based on noble metals, such as Pd,[22–25] Ru,[26–29] and Au.[30–34] However, industrial-scale processes utilizing aerobic oxidation reactions have been limited due to restricted substrate scopes,[35,36] frequent use of halogenated solvents[37–41] and safety concerns related to use of flammable reagents and solvents under high pressures of O_2.[42] On the other hand, when selecting oxidation methods for small scale synthesis in laboratory, practical aspects are most often emphasized.[43,44] In this respect, it is not surprising that simple traditional uncatalyzed reactions are often preferred over the catalytic aerobic reactions, averting complex catalyst syntheses and laborious use of special equipment, such as autoclaves and O_2 cylinders.[26,45–50] Accordingly, there is a high demand for aerobic alcohol oxidation methods that utilize commonly used chemicals as catalysts, provide sufficient reactivity under low pressures of dilute O_2:N_2 mixtures and have broad substrate scopes.

In the search of new aerobic oxidation methods for alcohols, promising results have been obtained with the combined use of nitroxyl radicals, such as (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and first-row transition metals, such as Cu and Fe.[51–58] Recently, we reported that a highly active alcohol oxidation catalyst can be easily prepared by combining TEMPO with $Mn(NO_3)_2$ and 2-picolinic acid (PyCOOH) *in situ*.[59] This catalyst system is straightforward and practical to use and it enables selective conversion of various primary alcohols incorporating aliphatic, allylic, benzylic and heteroaromatic structures to the respective aldehydes under ambient air at room temperature. Also, secondary alcohols are amenable to oxidation to ketones by simply replacing TEMPO with sterically more accessible 9-azabicyclo[3.3.1]nonane *N*-oxyl (ABNO). The oxidized products can be isolated simply via extraction using organic solvents and the reaction has shown to be tolerant with alcohols containing various types of functionalities. Despite of these benefits, the above Mn-catalyst exhibits the following limitations: catalytic activity is low and high catalyst loadings have to be utilized to achieve complete substrate conversion (4-7.5 mol% of $Mn(NO_3)_2$, TEMPO and PyCOOH); catalyst stability has not been studied and recycling protocol has not been developed for the catalyst.

Herein, we report a markedly improved catalyst system, that enables the selective aerobic oxidation of alcohols using low loading of $Mn(NO_3)_2$ and TEMPO. We also report a highly practical recycling protocol for the catalyst along with our intriguing findings on catalyst stability and mechanisms of deactivation.

Results and Discussion

Initial studies

The study was initiated by investigating the effect of catalyst loading on oxidation of 5-hydroxymethyl furfural (**1a**, HMF) to 2,6-diformylfuran (**2a**, DFF) with $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst.

[a] K. Lagerblom, J. Keskiväli, Dr. A. Parviainen, J. Mannisto and Prof. Dr. T. Repo
Department of Chemistry
Faculty of Science
A. I. Virtasen aukio 1, 00014 University of Helsinki
P.O. Box 55
Finland
E-mail: timo.repo@helsinki.fi

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HMF was chosen as a model substrate because it is readily available through dehydration of biomass-based hexoses, and the target compound, DFF, is a versatile platform chemical having numerous potential applications in the industry.[60–63] For example, DFF can be used as a starting material in the synthesis of resins, binders, sealants, organic conductors and fungicides.[64–68] HMF oxidations were conducted using 1, 2, 3 and 10 mol% catalyst loadings under ambient conditions and progression of each reaction was followed for 180 minutes with off-line GC analysis (Figure 1). With 1 mol% catalyst loading, the oxidation of HMF started rapidly, affording DFF in 8% yield after the first 5 minutes. However, the reaction rate decreased sharply after the first 10 minutes, presumably due to catalyst deactivation and only 15% DFF yield was achieved during the 180 min observation period. The experiment conducted with 2 mol% catalyst loading resulted in faster initial HMF oxidation and slower catalyst deactivation, resulting in 46% DFF yield after 180 min. The use of larger catalyst loadings improved the conversion of HMF to DFF even further. With 3 mol% of catalyst, full conversion of HMF and DFF yield of 95% was recorded after 40 min. When the highest catalyst loading of 10 mol% was used, the reaction was even faster. It consumed all of the HMF in 20 min and resulted in 95% DFF yield.

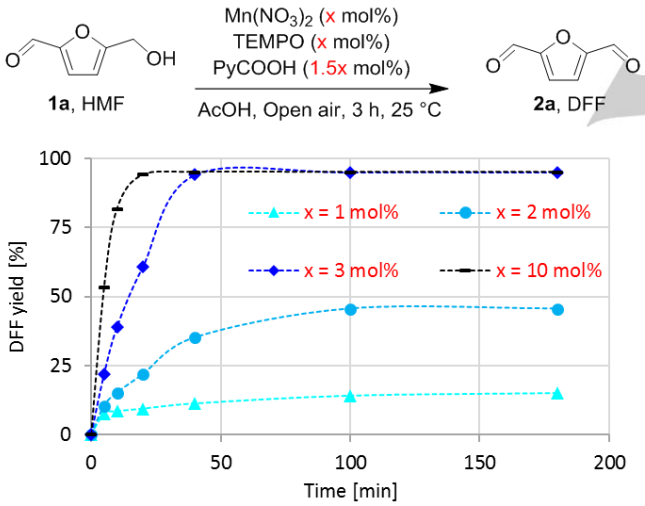


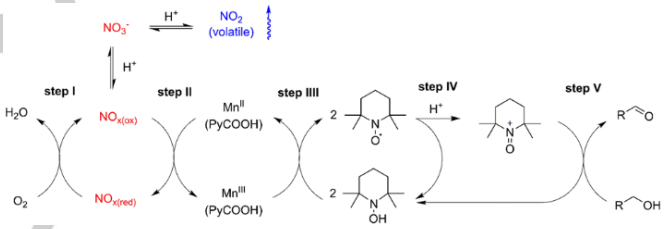
Figure 1. The effect of $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst loading on the aerobic oxidation of HMF to DFF.

During the oxidation of HMF with the highest, 10 mol% catalyst amount, orange gas was detected in the headspace of the reaction. This suggested the presence of NO_2, which is known to from NO_3^- under the acidic reaction conditions, according to equation (1).[69] To identify the gas, it was trapped into an alkaline water solution, where the NO_2 would disproportionate to NO_3^- and NO_2^- anions according to equation (2).[70,71] From this solution, the presence of NO_3^- and NO_2^- was investigated by classical qualitative analysis using diphenylamine and permanganate tests, respectively (See SI for details).[72,73] Both tests turned out positive, confirming that NO_3^- and NO_2^- were present in the alkaline aqueous solution and that the orange gas over the reaction was indeed NO_2. In this light, it seems plausible that acid induced conversion of NO_3^- to NO_2 and evaporation of the later might contribute to the rapid catalyst deactivation, clearly observed during the HMF oxidations with the low 1 and 2 mol% catalyst loadings above.

$$4\ HNO_3 \rightleftharpoons 4\ NO_2 + 2\ H_2O + O_2 \quad (1)$$

$$2\ NO_2 + H_2O \rightleftharpoons HNO_3 + HNO_2 \quad (2)$$

According to current mechanistic understanding, the presence of NO_3^- is crucially important in the $Mn(NO_3)_2$/TEMPO/PyCOOH-catalyzed aerobic alcohol oxidation (Scheme 1).[59] It acts as a source of oxygen activating NO_x species, which oxidizes Mn^{II} to Mn^{III} (Scheme 1, steps I & II). Accordingly, if NO_3^- concentration is reduced, the reaction slows down as oxidation of Mn^{II} to Mn^{III} is impeded. As a consequence, oxidation of hydroxylamine TEMPOH back to TEMPO by Mn^{III} is hindered (step III). This, in turn, leads to depletion of TEMPO, which forms the active oxidant $TEMPO^+$ and TEMPOH through acid induced disproportionation (Step IV). Eventually, alcohol oxidation cannot occur (step V), as all $TEMPO^+$ has been reduced to TEMPOH through reaction with alcohol.



Scheme 1. Proposed mechanism for the aerobic oxidation of alcohols with $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst system, wherein the crucial role of NO_3^- is illustrated with red color together with NO_2 evaporation in blue color.

The effect of added NO_3^- on the catalytic activity was studied by oxidizing HMF with 1, 2, 3 and 10 mol% catalyst loadings in the presence of $NaNO_3$ (2 mol%) (Figure 2). Evidently, the presence of added $NaNO_3$ had a positive effect on catalytic activity. The significance of added $NaNO_3$ was especially clear in the reactions performed using 1 mol% and 2 mol% catalyst loadings, as the catalyst lifetime was now significantly increased from the initial experiments performed without $NaNO_3$. At the end of the reactions performed with 1 and 2 mol% catalyst loadings, DFF yields of 65% and 95% were recorded, respectively. In comparison, the use of same catalyst amounts resulted in only 15% and 46% DFF yields when $NaNO_3$ additive was not included in the reaction. The presence of $NaNO_3$ had less prominent effect on reaction outcome with higher catalyst loadings (3 and 10 mol%) as sufficient NO_3^- concentration was already achieved in the initial experiments conducted without added $NaNO_3$.

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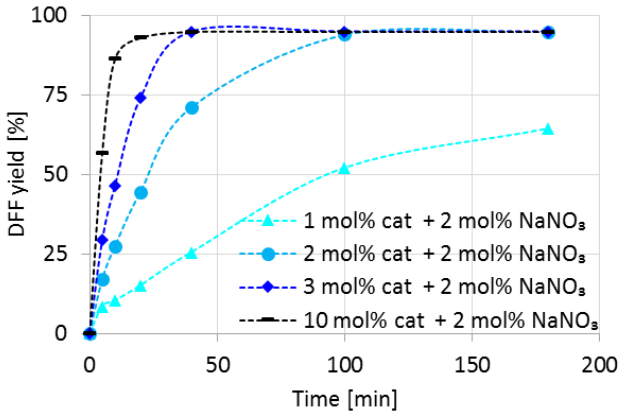


Figure 2. $NaNO_3$ enhanced aerobic oxidation of HMF to DFF with $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst.

Upon discovering the positive effect of $NaNO_3$ addition on catalyst performance, other additives containing nitrate and nitrite anions were studied as the catalyst activators. For this purpose, a series of HMF oxidations was conducted with 1 mol% loading of $Mn(NO_3)_2$/TEMPO/PyCOOH in the presence of 2 mol% of selected nitrate and nitrite sources (Figure 3). The control reaction, performed in the absence of additives, resulted in 16% HMF conversion and 15% DFF yield. Over three-fold increase in reactivity was achieved with the nitrate additives, resulting in 68%-70 HMF conversions and 65-67% DFF yields. Also addition on nitrite salts clearly activated the catalyst, although resulting in slightly lower 57-61% HMF conversions and 54%- 58% DFF yields than obtained with nitrate additives. To see if the presence of Na^+ cation affects reactivity, addition of CH_3COONa was tried, but it had little effect on the reaction outcome, leading to 21% HMF conversion and 19% DFF yield. These results indicate that the presence of nitrates and nitrites in the reaction has a beneficial effect on catalyst activity, nitrates being superior to nitrites, while the counter cation of the salt has no notable effect.

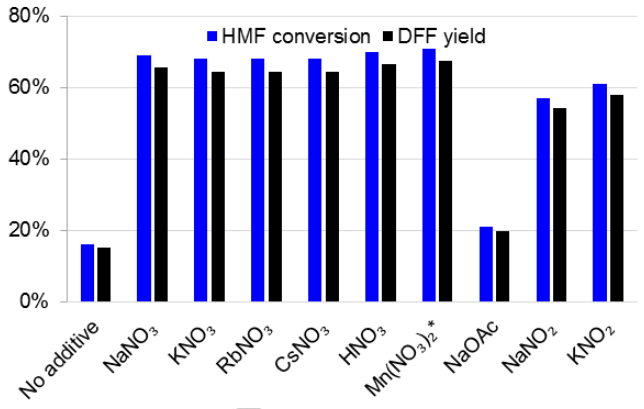


Figure 3. The effect of different nitrates and nitrites (2 mol%) to catalytic oxidation of HMF with $Mn(NO_3)_2$/TEMPO/PyCOOH (1/1.5/1 mol%) catalyst under ambient conditions. Reaction time 3h. * 1 mol% of $Mn(NO_3)_2$

To study the effect of nitrate amount on catalyst activity, a series of HMF oxidations was conducted with 1 mol% of $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst and varied amount (0-15 mol%) of $NaNO_3$ and HNO_3 (Figure 4). The results revealed that, the DFF yields were steadily increased from 15% to ≥95% when loading of $NaNO_3$ was increased from 0 mol% to 4 mol% or higher. At the same time, HMF conversions were increased from 16% to >99% (SI Figure S1). Interestingly, addition of HNO_3 resulted in similar catalyst activation with small amounts (1-4 mol%), but decreasing DFF yields were recorded with higher HNO_3 amounts (≥6 mol%) due to decreasing substrate conversion. Evidently, excessive acidity of the reaction solution hampers the catalytic activity. Presumably, the loss of catalytic activity is caused by accelerated conversion of NO_3^- to volatile NO_2 under highly acidic conditions, according to equation (1).[69] The increased proton concentration might also alter the coordination sphere of the redox active Mn-center, leading to reduced activity.[59] According to these results, a neutral nitrate source, such as $NaNO_3$, should be preferred over HNO_3 to enhance catalytic performance.

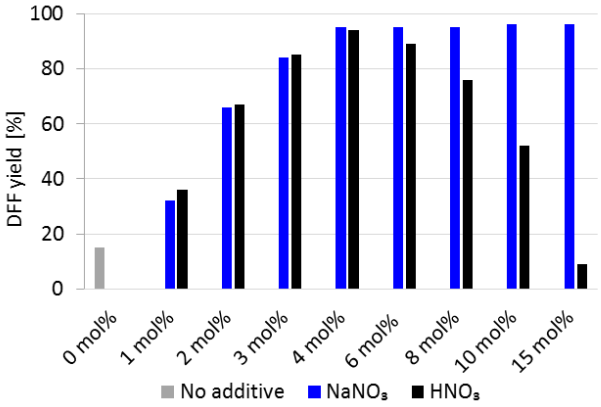


Figure 4. The effect of $NaNO_3$ and HNO_3 amount on DFF yield obtained through aerobic oxidation of HMF with $Mn(NO_3)_2$/TEMPO/PyCOOH (1/1.5/1 mol%) catalyst under ambient conditions. Reaction time 3 h.

Reaction scope

Earlier, we demonstrated that $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst can be used for oxidation of wide variety of primary alcohols.[59] However, the method required using high loadings of $Mn(NO_3)_2$, TEMPO and PyCOOH, (4-7.5 mol% each) to achieve complete alcohol conversions. Based on the mechanistic insights obtained from the HMF oxidation experiments presented herein, it seemed plausible that oxidation of various primary alcohols could be achieved using significantly lower amount of $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst if $NaNO_3$ was added into the reaction to stabilize the catalyst. To test this hypothesis, a series of oxidation experiments with different substrates was conducted (Table 1). Heteroaromatic (**1b**), benzylic, (**1c**, **1d**) aliphatic (**1e**, **1f**) and allylic (**1g**, **1h**) primary alcohols were all smoothly converted to the respective aldehydes (**2b**-**2h**) using just 2 mol% of $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst in the presence of 6 mol%

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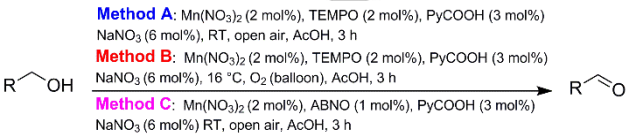
of $NaNO_3$, under ambient conditions (Table 1, method A). Over 99% conversion was achieved with all of the above substrates within 4 h, after which, pure aldehydes **2b**-**2e**, **2g** and **2h** could be recovered from the reaction solution by simple extraction with ether and water, followed by evaporation of the organic phase. Flash column chromatography was only conducted to purify **2f**.

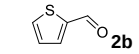
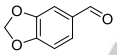
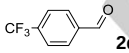
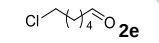
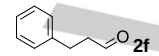
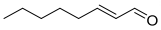
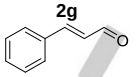
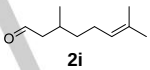
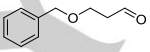
As oxidation of substrates bearing unconjugated C-C double bonds, benzylic ethers and C-C triple bonds with $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst results in side reactions at room temperature, oxidation of citronellol (**1i**), 3-benzyloxy-1-propanol (**1j**) and 3-phenyl-2-propyn-1-ol (**1k**) was conducted at 16 °C using balloon of O_2 over the reaction (Table 1, method B).[59] Under these conditions, 79-83% substrate conversions were achieved and aldehydes **2i**-**2k** could be recovered in 71-76% yields.

Previous studies have showed that secondary alcohols are oxidized sluggishly with TEMPO-based catalysts.[51,18] The unsatisfactory performance of these catalysts with secondary alcohols has been attributed to steric crowding around the alcohol α-hydrogen, which impedes the rate-determining hydride abstraction by sterically hindered oxoammonium ions like $TEMPO^+$.[16,57] Oxidation rates of secondary alcohols are generally increased notably when sterically less hindered nitroxyl radicals, such as such as ABNO are used as catalyst, instead of TEMPO.[74] Accordingly, oxidation of diphenyl methanol (**1l**), 2-octanol (**1m**) and borneol (**1n**) was conducted using $NaNO_3$ enhanced $Mn(NO_3)_2$/ABNO/PyCOOH catalyst system under ambient conditions (Table 1, Method C). This resulted in >99% alcohol conversions and ketones **2l**-**2n** could be isolated in excellent 94-98% yields by straightforward extraction with ether and water, followed by evaporation of the organic phase.

In order to see how significant impact addition of $NaNO_3$ has on the catalyst activity, oxidation of alcohols **1b**-**1n** was also conducted in the absence of $NaNO_3$ (Table 1). On average, this resulted in 59% lower substrate conversion and 60% lower product yield compared to the results obtained in the presence of $NaNO_3$. When $NaNO_3$ was used to stabilize the catalyst, alcohol oxidations generally reached >99% conversion and formation of side products was negligible. However, with few substrates (**1e**, **1f** and **1k**) the reaction halted before 99% alcohol conversion was reached. Gratifyingly, these reactions could be restarted by adding another 6 mol% batch of $NaNO_3$ after initial stalling of the reaction. This method for re-activating the catalyst is worth noting if one uses the catalyst systems described herein for alcohol oxidation and the reaction stops progressing prior complete substrate conversion is achieved.

Table 1. Substrate scope of the aerobic oxidation of alcohols.[a]



Product	Method	With $NaNO_3$		Without $NaNO_3$	
		Conv. %[b]	Isol. Yield%	Conv. %[b]	Isol. Yield%
 **2b**	A	>99	94	22	14
 **2c**	A	>99	98	31	25
 **2d**	A	>99	98	69	63
 **2e**	A[c]	>99	92	36	30
 **2f**	A[c]	>99	90	34	27
 **2g**	A	>99	93	14	8
 **2h**	A	>99	94	71	65
 **2i**	B	83	75	23	16
 **2j**	B	83	76	32	23
 **2k**	B[c]	79	71	12	5
 **2l**	C	>99	98	75	69
 **2m**	C	>99	94	32	26
 **2n**	C	>99	96	35	28

[a] Conditions: substrate (2 mmol), AcOH (4 ml), 800 rpm stirring, open test tube. [b] Conversion determined using GC-FID with acetophenone as internal standard. [c] 12 mol% $NaNO_3$.

Catalyst recycling

Recyclability of $Mn(NO_3)_2$/TEMPO/PyCOOH/$NaNO_3$ catalyst was examined by using benzyl alcohol (**1o**) oxidation as a model reaction. It turned out, that the catalyst could be easily recycled by the following extractive treatment: upon completion of the alcohol oxidation, the reaction solution was extracted with diethyl ether and 1 M HCl, in order to dissolve benzaldehyde (**2o**) into the organic phase and the catalyst into the aqueous phase. The catalyst was recovered from the aqueous phase by evaporation *in vacuo*. A subsequent run was started by dissolving the recovered solid catalyst, fresh $NaNO_3$ and a new batch of **1o** into glacial AcOH. By following this procedure, the catalyst was used successfully for five consecutive **1o** oxidations (Figure 5). After the fifth use, substrate conversion of 80 % was still recorded, showing that the catalyst is recyclable with minor decrease in

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activity. In contrast, if fresh $NaNO_3$ was not added between subsequent uses of the catalyst, alcohol conversion declined sharply already after the first use, resulting in only 4% conversion during the second run (SI Figure S2). These observations further support the mechanistic insight about NO_3^- loss as the main route for catalyst deactivation that can be easily overcome by adding a catalytic amount of $NaNO_3$ into the reaction.

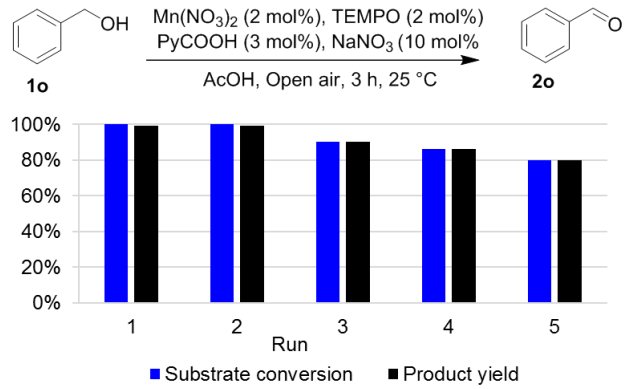


Figure 5. Oxidation of benzyl alcohol to benzaldehyde with recycled $Mn(NO_3)_2$/PyCOOH/TEMPO/$NaNO_3$ catalyst.

Conclusions

This study shows that NO_3^- plays a crucial catalytic in the $Mn(NO_3)_2$/TEMPO/PyCOOH-catalyzed aerobic alcohol oxidation reaction as a source of oxygen activating NO_x species. However, disproportionation of NO_3^- to the volatile NO_2 during the reaction leads to catalyst deactivation under open air conditions. Catalyst deactivation can be overcome by adding a catalytic amount of nitrate salt, for example $NaNO_3$ into the reaction. This stabilizes the $Mn(NO_3)_2$/TEMPO/PyCOOH catalyst and enables highly selective and near quantitative oxidation of various primary alcohols to the respective aldehydes within few hours under ambient air. The system is also suitable for oxidation of secondary alcohols when catalytic TEMPO is replaced with sterically less hindered nitroxyl radical ABNO. At the end of the alcohol oxidation, pure carbonyl products and reusable catalyst can be separated and recovered simply by extracting with organic solvent and dilute acid, followed by evaporation of both phases.

Experimental Section

General Information

All the chemicals used during the work were acquired from commercial sources and used as received. ^1H and ^{13}C NMR spectra were recorded on Varian 300 MHz spectrometer. The chemical shifts are reported in parts per million (δ) relative to TMS (0 ppm). The peak patterns are indicated as follows: s (singlet), d (doublet), t (triplet) q (quartet); dd (doublet of doublets), dt (doublet of triplets), m (multiplet). *J*-coupling values are reported in Hertz (Hz). Determination of DFF yields during catalyst optimization studies were performed on Agilent 6890N GC system equipped with FID detector using calibration curves with acetophenone as internal standard. Flash column chromatography was performed using 60 Å pore size silica gel.

Oxidation of HMF to DFF for catalyst optimization studies

Oxidation of HMF to DFF presented in figures 1-3 were performed as follows. First, the catalyst solution was prepared by adding a desired amount of $Mn(NO_3)_2 \cdot 4\,H_2O$, 2-picolinic acid, TEMPO, $NaNO_3$ and glacial AcOH (2 mL), in this order, to a 30 mL test tube equipped with a magnetic stirring bar. The resulting solution was stirred in open air for 5 minutes and HMF (126.1 mg, 1.0 mmol) was then added. The mixture was stirred (800 rpm) at room temperature for desired time, after which the reaction was quenched by adding EtOAc (10 ml).

Conversion and yield determination with GC-FID

Conversions and yields presented Figures 1-3, as well as conversions in Table 1 were determined as follows. Upon completion, the reaction was quenched by adding EtOAc (10 ml). The mixture was then poured into volumetric flask, internal standard (acetophenone, 200 µL) was added and the solution was diluted to 100 mL with EtOAc. A sample for GC-analysis was prepared by filtrating an aliquot of 1.5mL of the solution through a layer of silica gel (1 cm thick). The yields and conversions were determined using GC-FID with calibration curves, (see SI for examples). The reported HMF conversions and DFF yields are average values obtained by performing two parallel reactions and taking two parallel samples from both reactions.

Procedures for alcohol oxidation (Table 1)

Method A for oxidation of primary alcohols 1b-1h: $Mn(NO_3)_2 \cdot 4\,H_2O$ (10.0 mg 0.04 mmol), 2-picolinic acid (7.4 mg 0.06 mmol), TEMPO (6.3 mg, 0.04 mmol), $NaNO_3$ (10.2 mg, 0.12mmol) and glacial AcOH (4 mL) were added, in this order, to a 30 mL test tube equipped with a magnetic stirring bar. The resulting solution was stirred in open air for 5 minutes and the desired alcohol (2 mmol) was then added. Stirring (800 rpm) was continued at room temperature until the reaction was completed (monitored by TLC). Upon completion, the reaction solution was diluted with diethyl ether (20 mL), followed by washing with water (3×10 mL) to remove the catalyst. Aqueous phases were combined and extracted with diethyl ether (1×10 ml). Organic phases were then combined, dried with $MgSO_4$ and evaporated *in vacuo* to afford carbonyl products. No further purification was performed for **2b**-**2e**, **2g** and **2h**. Flash column chromatography was used to purify **2f**.

Method B for oxidation of primary alcohols 1i-1k $Mn(NO_3)_2 \cdot 4\,H_2O$ (10.0 mg 0.04 mmol), 2-picolinic acid (7.4 mg 0.06 mmol), TEMPO (6.3 mg, 0.04 mmol), $NaNO_3$ (10.2 mg, 0.12mmol) and glacial AcOH (4 mL) were added, in this order, to a 30 mL test tube equipped with a magnetic stirring bar. The resulting solution was stirred in open air for 5 minutes and cooled down to 16 °C using water bath fitted with immersion cooler. The desired alcohol (2 mmol) was added and an O_2-filled balloon was mounted on top of the reaction. The mixture was stirred (800 rpm) at 16 °C until the reaction was completed (monitored by TLC). Upon completion, the reaction solution was diluted with diethyl ether (20 mL), followed by washing with water (3×10 mL) to remove the catalyst. Aqueous phases were combined and extracted with diethyl ether (1×10 ml). Organic phases were then combined, dried with $MgSO_4$ and evaporated *in vacuo* to afford crude **2i**-**2k**. Flash column chromatography was used to purify the products**.**

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Method C for oxidation of secondary alcohols 1l-1n: $Mn(NO_3)_2 \cdot 4\,H_2O$ (10.0 mg 0.04 mmol), 2-picolinic acid (7.4 mg 0.06 mmol), ABNO (2.8 mg, 0.02 mmol), $NaNO_3$ (10.2 mg, 0.12mmol) and glacial AcOH (4 mL) were added, in this order, to a 30 mL test tube equipped with a magnetic stirring bar. The resulting solution was stirred in open air for 5 minutes and the desired alcohol (2 mmol) was then added. Stirring (800 rpm) was continued at room temperature until the reaction was completed (monitored by TLC). Upon completion, the reaction solution was diluted with diethyl ether (20 mL), followed by washing with water (3×10 mL) to remove the catalyst. Aqueous phases were combined and extracted with diethyl ether (1×10 ml). Organic phases were then combined, dried with $MgSO_4$ and evaporated *in vacuo* to afford ketones **2l-2n**. No further purification was required.

Catalyst recycling

Oxidation of benzyl alcohol for catalyst recycling experiments was conducted according to the following protocol: $Mn(NO_3)_2 \cdot 4\,H_2O$ (50.2 mg 0.2 mmol), 2-picolinic acid (36.9 mg 0.3 mmol), TEMPO (31.3 mg, 0.2 mmol), $NaNO_3$ (51.0 mg, 0.6 mmol) and AcOH (20 mL) were added, in this order, to a 50 mL round bottom flask equipped with a magnetic stirring bar. The formed catalyst solution was stirred for five minutes and benzyl alcohol (1.04 mL, 10 mmol) was then added. Stirring (800 rpm) was continued at room temperature for 4 h. After completion, the reaction solution was transferred into a separatory funnel, followed by the addition of diethyl ether (20 mL). The ether solution was then extracted three times with 1M HCl (20 ml, 10 ml, 10 ml) to transfer the catalyst into aqueous phase. The aqueous phases were combined, washed with diethyl ether (10 ml) and evaporated *in vacuo* to afford the recovered catalyst as dark green solid. Prior to subsequent run, fresh $NaNO_3$ (85.0 mg, 1.0 mmol) and glacial AcOH (20 ml) were added on top of the catalyst and the formed mixture was stirred for 5 min. New reaction was then initiated by adding benzyl alcohol (1.04 ml, 10 mmol). **Note:** the recycled catalyst should be dried under oil pump vacuum until the color changes from yellow to dark green. The use of wet catalyst leads to hampered reactivity.

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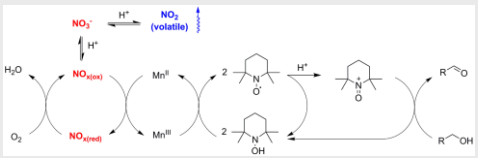
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Aerobic oxidation of alcohols with homogenous Mn/nitroxyl radical-based catalyst is investigated. The study presents findings on catalyst stability and its deactivation mechanisms as well as shows that catalyst deactivation can be overcome by adding small amount of nitrate ions into the reaction. The nitrate stabilized catalyst enables straightforward, highly practical and selective oxidation of various alcohols to aldehydes and ketones under mild conditions.

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