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OMS-2/H_2O_2/Dimethyl Carbonate: an Environmentally-Friendly Heterogeneous Catalytic System for Oxidative Synthesis of Benzoxazoles at Room Temperature

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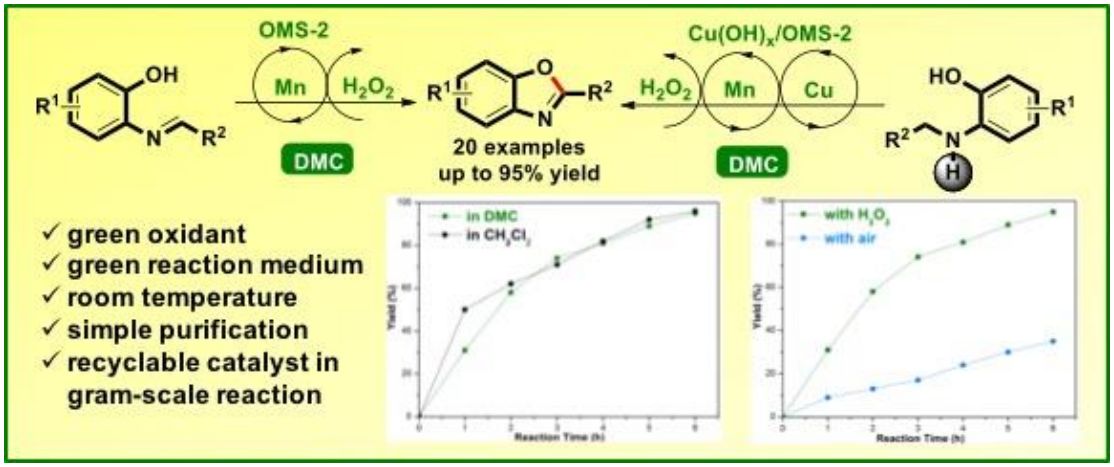


ABSTRACT: Manganese octahedral molecular sieve (OMS-2) was found to be an efficient and recyclable heterogeneous catalyst for the oxidative synthesis of benzoxazoles in gram-scale from phenolic imines at room temperature. H_2O_2 and bio-based reagent dimethyl carbonate (DMC) were successfully employed as the environmentally-friendly oxidant and solvent respectively in OMS-2-catalysted redox reaction for the first time. Benzoxazoles could also be obtained from N-substituted 2-aminophenols via $Cu(OH)_x$/OMS-2-catalyzed sequential oxidative transformation at elevated temperature.

KEYWORDS: heterogeneous catalysis; catalytic oxidation; benzoxazole; green synthesis

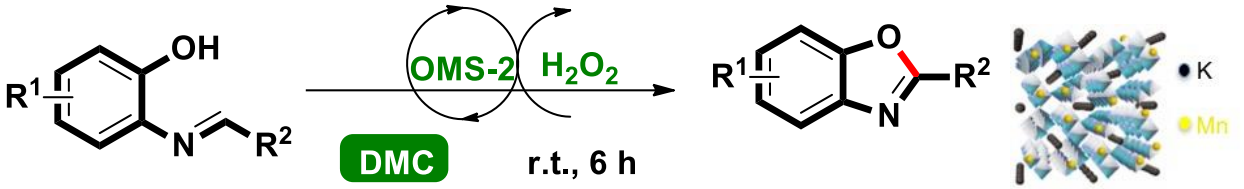
INTRODUCTION

Benzoxazole and its derivatives are frequently found as structure motifs in biologically active natural products and used as building blocks in pharmaceuticals and organic materials,[1] therefore, they are of great importance. Traditional methodologies of obtaining benzoxazoles are through the condensation of 2-aminophenols with carboxylic-acid derivatives followed by cyclization under either acidic or harsh reaction conditions.[2] In recent years, several innovative catalytic oxidative systems have emerged.[3] For example, Bäckvall`s group developed an alternative Ru-catalyzed biomimetic aerobic system towards the preparation of benzoxazoles from amines and 2-aminophenols using air as the terminal oxidant.[4] More recently, our group reported a heterogeneous $Cu(OH)_x$/OMS-2-catalyzed the oxidative synthesis of benzoxazoles between catechols and amines via quick electron-transfer under a low-energy pathway.[5] Nevertheless, one of the most general and facile pathways for the synthesis of benzoxazoles is the oxidative cyclization of phenolic imines generated in situ from the condensation of aldehydes and 2-aminophenols using various stoichiometric amount of strong oxidants.[6] Catalytic oxidative methods have been developed by the use of transition metals, TEMPO and NaCN.[7] Due to the ease in separation, recovery and recycling of catalysts, heterogeneous catalytic processes based on the aerobic cyclization of phenolic imines have also been realized in recent years. Recyclable Cu-based nanoparticles, Co-based nanocomposite, ZnO nanoparticles, active carbon, molecular sieve and polymer-incarcerated Pt nanoclusters have been found to be efficient heterogeneous catalysts associated with oxygen.[8] However, in the aforementioned cases, base additives, elevated reaction temperatures or toxic catalyst and reaction solvents were employed to achieve satisfied catalytic performance. From the perspective of sustainable industrial chemistry, it is desirable to develop an environmentally-safe catalytic system that consists of recyclable catalyst, green oxidant, non-toxic solvent and mild reaction conditions.

In recent years, manganese octahedral molecular sieves (OMS-2) composed of 2 × 2 edge- and corner-shared MnO_6 octahedral chains (Scheme 1) have gained importance because of its superior properties, such as unique microporous tunnel structure, large surface areas, semi-conductivity and oxygen reduction ability.[9] More importantly, the co-existence of various oxidation states of Mn in OMS-2 is critical for electron transfer in a redox process. As a result, OMS-2 has been applied as heterogeneous redox catalyst in various oxidations, including CO oxidation,[10a,10b] water oxidation,[10c] epoxidation,[10d] oxidation of alcohols/sulfides,[10e,10f] oxidative C-C/N formation,[11] aerobic cyanation/amidation.[12] Although previously reported OMS-2-catalyzed oxidations have demonstrated merits of sustainable chemistry, green oxidant H_2O_2 and solvent are not successfully used to establish a cleaner synthetic system yet to date. H_2O_2 is relatively easy to handle and also only produces H_2O as the by-product in aerobic oxidations, while the H_2O in commercial H_2O_2 sometimes limits its scope of applications in organic synthesis because water is not compatible with the entire system. On the other hand, it is well known that the major waste generated in organic synthesis results from the use of solvents that are usually produced from fossil resources. To avoid using toxic solvents, water or bio-based solvents become alternatives. Among these, dimethyl carbonate (DMC), as a biomass-derived reagent, has been considered a benign solvent because it is nontoxic and biodegradable and can be produced from CO_2.[13]

In continuation of our research toward sustainable catalysis,[14] herein, we describe an environmentally-friendly protocol for aerobic oxidative cyclization of phenolic imines into benzoxazoles using OMS-2 as the catalyst (Scheme 1). The absence of additives and the use of bio-based DMC as reaction media under very mild reaction conditions by using H_2O_2 as the terminal oxidant are advantages of this approach. More importantly, OMS-2 can be reused many

times in gram-scale synthesis without the loss of catalytic activity, which makes this catalytic system more practical and competitive with previous processes. This study is meant to be an important step towards enriching the content of OMS-2-catalyzed oxidations due to achieving the clean synthesis in larger scale.



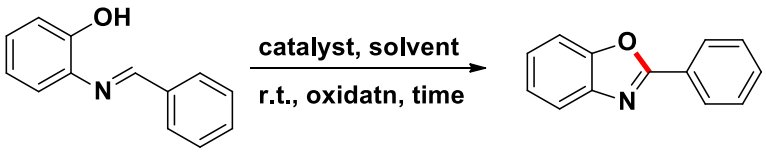
Scheme 1. Clean Synthesis of Benzoxazoles Under OMS-2/H_2O_2/DMC System

RESULTS AND DISCUSSION

Initially, a screening was performed at room temperature to optimize the catalyst, oxidant and solvent through the cyclization of phenolic imine **1a** (Table 1). Using ethanol as the solvent, OMS-2-supported copper catalyst (20 mg, Cu: 1.48 wt.%) provided benzoxazole **2a** in good yields under aerobic conditions, although oxygen could accelerate the reaction (Table 1, entries 1 and 2). Interestingly, it was found that an additional transition metal was not necessary in the catalysis and OMS-2 was able to catalyze the cyclization of **1a** into **2a** in around 85% yield with some yellow pigment using air as the terminal oxidant under very mild conditions. Moreover, O_2 did not show superior oxidizing ability compared with air under OMS-2-catalysis in EtOH when the reaction was run for 12 h (Table 1, entries 3 and 4). To further better the reaction, several OMS-2 materials, including OMS-2 prepared via different methods and ion-exchanged ones, with different properties were tested, and the results were unfruitful (Table 1, entries 5-8). Moreover, amorphous manganese oxide (AMO) and α-MnO_2 did not lead to higher yields (Table 1, entries 9 and 10). After that, we paid our attention to using more environmentally-friendly

reagent as the reaction media. Delightedly, EtOH was successfully replaced by biomass-derived reagent DMC in the reaction, and 78% yield was obtained in the presence of air at room temperature (Table 1, entry 11). More importantly, we found that H_2O_2 could be a highly efficient oxidant for the aerobic cyclization in DMC under mild conditions, and the water in commercial H_2O_2 did not make the reaction sluggish (Table 1, entry 12). Furthermore, the reaction time could be decreased to 6 h with full conversion of raw**,** which led to a 95% yield of benzoxazole **2a** without yellow pigment (Table 1, entry 13). Due to the high conversion and yield and the absence of pigment under OMS-2/H_2O_2/DMC system, the isolation and purification of desired product become very simple. Without column chromatographic isolation, 95% yield of pure **2a** was readily obtained by filtration of solid catalyst followed by removal of DMC under reduced pressure (For NMR spectrum of crude product, Fig. S1 and S2, in SI). However, the reaction did not proceed at all when EtOH or water was used as the reaction solvent in the presence of H_2O_2 (Table 1, entry 12). Similarly, the reaction did not occur without catalyst no matter what oxidant was used (Table 1, entries 14 and 15). Finally, more experiments demonstrated that the low catalyst loading (5 mol%) and N_2 atmosphere was deleterious for the reaction and decreased reaction time also slashed the yield of **2a** (Table 1, entries 16 and 17).

Table 1. Optimization of The Oxidative Cyclization of Phenolic Imine **1a**[a]



1a **2a**

Entry	Catalyst	Oxidant	Solvent	Time [h]	Yield [%][b]
1	$Cu(OH)_x$/OMS-2	air	EtOH	12	75
2	$Cu(OH)_x$/OMS-2	O_2	EtOH	6	79
3	OMS-2	air	EtOH	12	87
4	OMS-2	O_2	EtOH	6	77 (85[c])

5	OMS-2-Urea	air	EtOH	12	72
6	OMS-2- H_2O_2	air	EtOH	12	75
7	Ce-OMS-2	air	EtOH	12	53
8	Cr-OMS-2	air	EtOH	12	85
9	AMO	air	EtOH	12	71
10	α-MnO_2	air	EtOH	12	65
11	OMS-2	air	DMC	12	78
12	OMS-2	H_2O_2	DMC	12	92 (0[d])
13	OMS-2	H_2O_2	DMC	6	95
14	-	air	DMC	6	0
15	-	H_2O_2	DMC	6	Trace
16	OMS-2	H_2O_2	DMC	6	70[e] (65[f])
17	OMS-2	H_2O_2	DMC	3	75

[a] Reaction conditions: **1a** (0.2 mmol), catalyst (20 mg), solvent (1 mL), room temperature, H_2O_2 (50 uL) was used in entries 12, 13 and 15-17.

[b] Isolated yields.

[c] For 12 h.

[d] Using EtOH or H_2O replace DMC as the solvent.

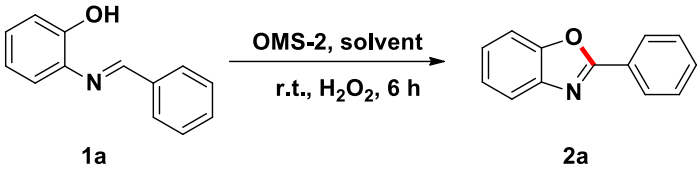
[e] 10 mg of OMS-2 was used.

[f] Under N_2.

After initially establishing a clean synthetic system by the combination of H_2O_2 and DMC, more biomass-derived reagents were examined as reaction solvents in the synthesis of benzoxazole **1a** from **2a** (Table 2). Firstly, polyethylene glycol (PEG) and glycerol were not compatible with H_2O_2 in the reaction and phenolic imine **1a** did not convert at all (Table 2, entries 1-3). Other biomass-based reagents, like 2-Me-THF, ethyl lactate and γ-valerolactone, could work with OMS-2/H_2O_2 to offer benzoxazole **2a** with yields ranging from 42% to 76% under mild conditions (Table 2, entries 4-6). After that, other alkyl or cyclic carbonates that have been applied in C-H functionalization reactions[13] were investigated in our system. The results

showed that diethyl carbonate (DEC) acted as reaction media very well, while cyclic ethylene carbonate also successfully worked with OMS-2/H_2O_2 to give **2a** in slightly low yield of 82% (Table 2, entries 7 and 8). As a result of the optimization process, we concluded that the best reaction conditions for the cyclization of phenolic imines involve the use of OMS-2/H_2O_2/DMC system.

Table 2. Investigation of Bio-Derived Reagents as Reaction Media[a]



1a 2a

Entry	Solvent	Isolated yield [%]
1	PEG-200	N.R.
2	PEG-400	N.R.
3	glycerol	N.R.
4	2-Me-THF	42
5	ethyl lactate	48
6	γ-valerolactone	76
7	DEC	90
8	Ethylene carbonate	82

[a] Reaction conditions: **1a** (0.2 mmol), OMS-2 (20 mg, 10 mol%), H_2O_2 (50 uL), solvent (1 mL), room temperature, 6 h.

According the optimization, it was found that air was also a quite efficient green oxidant for the cyclization of **1a** in DMC (Table 1, entry 11). The reaction profiles for OMS-2-catalyzed cyclization of **1a** to **2a** in DMC at room temperature with air or H_2O_2 as the oxidant were carefully monitored (Figure 1). The results showed that H_2O_2 could accelerate the reaction significantly and offered full conversion of **1a** and 95% yield of **2a** in 6 h (Figure 1, left). In air, the reaction provided nearly 40% conversion and 35% yield under the standard conditions. So, in our catalytic system, H_2O_2 was superior and favorable environmentally-friendly oxidant. As we

known, previously reported oxidative cyclizations of phenolic imines were generally performed in polar and aprotic solvents, such as CH_2Cl_2, toluene and EtOAc, or alcohol.[6-8] When we used CH_2Cl_2 as the solvent under the present conditions, the reaction proceeded faster in initial stage and led to full conversion and excellent yield in 6 h (Figure 1, right). Comparatively, the reaction in DMC proceeded slightly slow in initial stage, but eventually showed very similar kinetic profile like it was run in CH_2Cl_2. So, it was proved that DMC was a suitable alternative reaction media for the aerobic cyclization of phenolic imine.

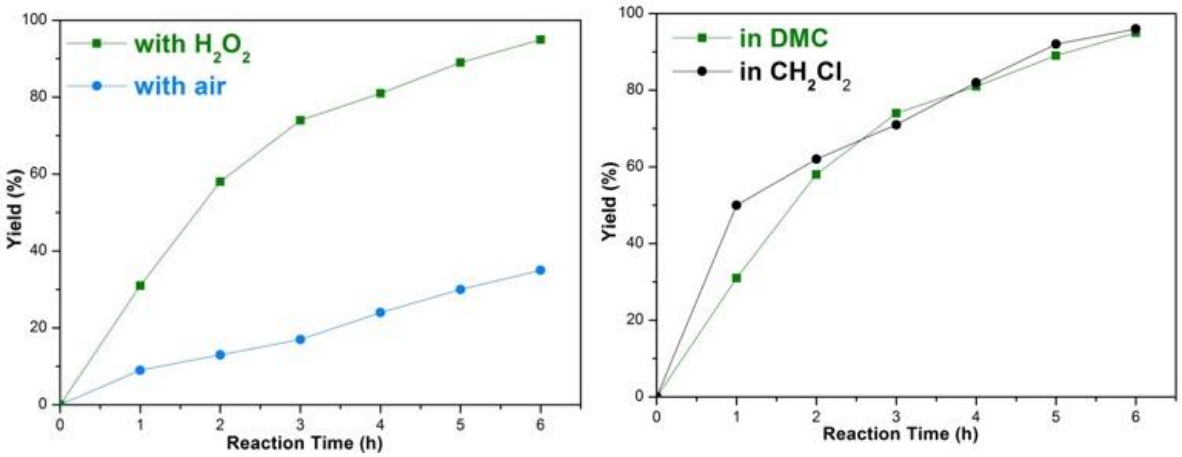
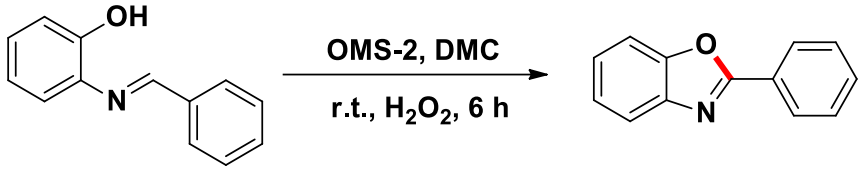


Figure 1. Reaction profiles for the OMS-2-catalyzed cyclization of **1a** to **2a** in DMC for 6 h at room temperature with different oxidant (left). Reaction profiles for the OMS-2-catalyzed cyclization of **1a** to **2a** using H_2O_2 as the oxidant for 6 h at room temperature in different reaction medium (right).

To verify whether the observed catalysis was truly caused by OMS-2 or leached Mn species from it, the hot filtration experiment of phenolic imine **1a** in DMC under the standard conditions was performed (For experimental details, see SI). After the reaction proceeded for 1 h, OMS-2 was removed by filtration from DMC, and product **2a** was observed in around 32% NMR yield. Meanwhile, the filtrate was kept stirring without adding fresh catalyst for further 5 h, and no

more benzoxazole **2a** was detected (Figure S6, in SI). ICP-AES was employed to analyze the filtrate, which shows manganese species were hardly observed in filtrate. These facts indicated manganese did not leach from OMS-2 and the observed catalysis was truly heterogeneous. Next, the recyclability of OMS-2 was tested in gram-scale synthesis of benzoxazole **2a** to show the practicality of this catalytic system (Table 3). Firstly, we delightedly found that the reaction could proceed smoothly in gram-scale by the use of 1 g of OMS-2 and 10 mmol of raw at room temperature and the product was obtained in 1.97 g (96% yield). After the reaction, the catalyst was readily recycled by filtration, washing and drying at 120 °C for overnight. The results of BET, XRD and TEM analysis showed that OMS-2 was highly stable in structure and morphology (Figures S3-S5, in SI). Under gram-scale conditions, the catalyst was employed in 7 successive runs without any loss of activity.

Table 3. Recycling of OMS-2 in Gram-Scale Reaction[a]



1a **2a**

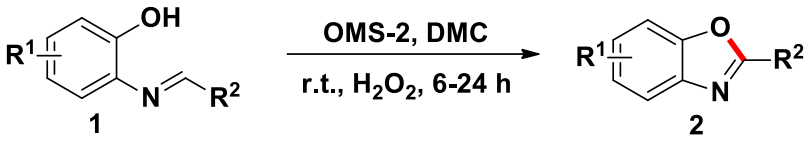
Cycle	1	2	3	4	5	6	7
Yield [%]	96	96	95	94	96	95	95

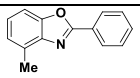
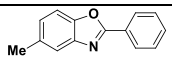
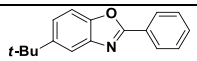
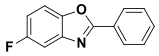
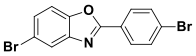
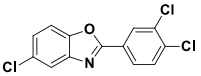
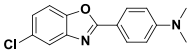
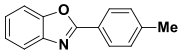
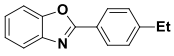
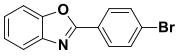
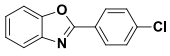
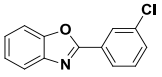
[a] Reaction conditions: **1a** (10 mmol, 1.97 g), OMS-2 (1 g), DMC (50 mL), H_2O_2 (2.5 mL), r.t., 6 h, isolated yields.

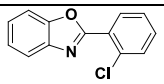
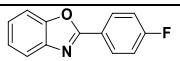
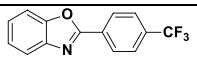
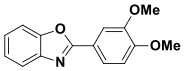
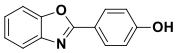
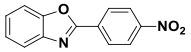
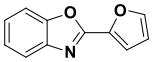
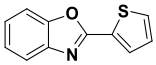
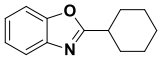
With the optimized conditions in hand, the substrate scope of the oxidative cyclization was investigated. As show in Table 4, OMS-2/H_2O_2/DMC system could tolerate a lot of substrates with functional groups. Phenolic imines derived from the condensation of substituted 2-amino

phenols and benzaldehydes were readily converted into corresponding 2-subustituted benzoxazoles in excellent yields under the presence conditions, although some substrates, such as **1h**, **1r** and **1t**, had to react for prolonging time in order to realize full conversion. It is worth mentioning that hydroxyl group (**2r**) was tolerated in the reaction very well and multi-halogen-substituted benzoxazoles (**2f** and **2g**) were also isolated in excellent yields. Moreover, heterocyclic phenolic imines participated into the reactions successfully resulting into high yields of benzoxazoles (**2s** and **2t**). In addition, phenolic imine generated from alkyl aldehyde and 2-amino phenol was oxidized to benzoxazole **2u** in 96% yield with the help of base to ensure full conversion. Unfortunately, sensitive group nitro-substituted phenolic imine could not react under the standard conditions and it was recovered after the reaction.

Table 4. Scope of The Reactions for The Synthesis of Benzoxazoles[a]



 **2b**, 94%	 **2c**, 91%	 **2d**, 97%
 **2e**, 95%	 **2f**, 92%	 **2g**, 95%
 **2h**, 80%[b]	 **2i**, 97%	 **2j**, 97%
 **2k**, 88%	 **2l**, 90%	 **2m**, 92%

 **2n**, 96%	 **2o**, 95%	 **2p**, 96%
 **2q**, 82%	 **2r**, 95%[c]	 N. R.
 **2s**, 96%	 **2t**, 95%[d]	 **2u**, 96%[e]

[a] Reaction conditions: phenolic imine (0.2 mmol), OMS-2 (20 mg, 10 mol%), DMC (1 mL), H_2O_2 (50 uL) r.t., 6-12 h, isolated yields.

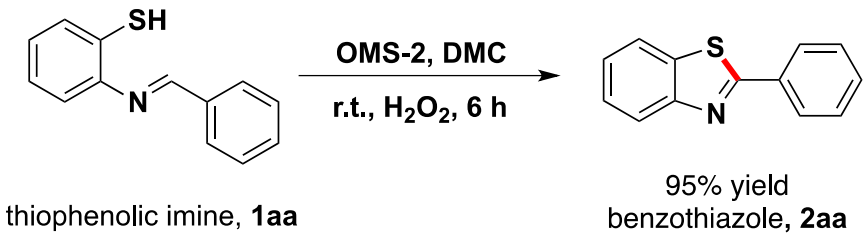
[b] For 20 h.

[c] For 12 h.

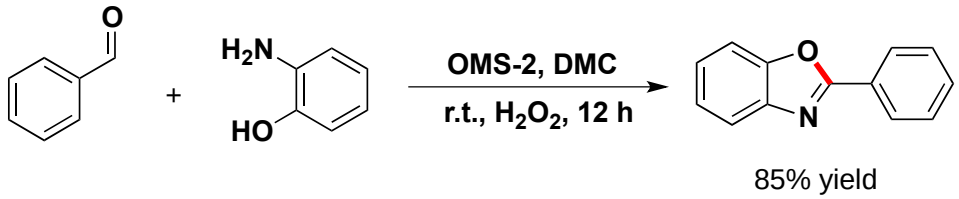
[d] For 24 h.

[e] Reaction conditions: phenolic imine (0.2 mmol), OMS-2 (20 mg, 10 mol%), H_2O_2 (100 uL), K_2CO_3 (0.2 mmol), DMC (1 mL), r.t., 12 h, isolated yield.

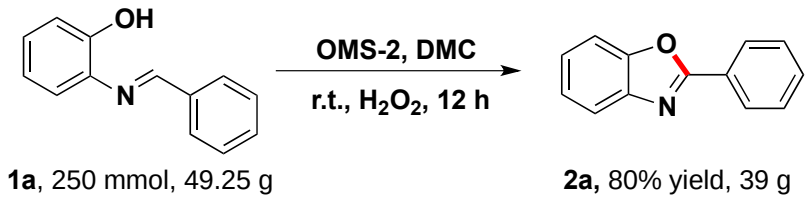
To assess the versatility of the present catalytic system, we turned our attention to the oxidative cyclization of thiophenolic imine **1aa**. The corresponding product benzothiazole **2aa** was obtained in excellent yield without any changes in the standard conditions, which indicated OMS-2 was not poisoned by sulphur (Scheme 2). Afterwards, we examined the catalytic system in one-pot synthesis of benzaxazole from aldehyde and 2-aminophenol (Scheme 3). Under mild reaction conditions, benzoxazole **2a** was successfully synthesized directly from benzaldehyde and 2-amino phenol via the in-situ generated phenolic imine with good yield. Then, a multigram-scale synthesis of benzoxazole **2a** was performed to demonstrate the reaction is also feasible for process, and the reaction gave us a satisfactory yield of 80% (Scheme 4).



Scheme 2. The oxidative synthesis of benzothiazole from thiophenolic imine. Reaction conditions: **1aa** (0.2 mmol), OMS-2 (20 mg, 10 mol%), H_2O_2 (50 uL), DMC (1 mL), r.t., 6 h, isolated yield.

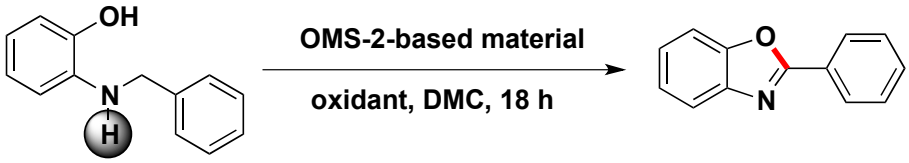


Scheme 3. The one-pot synthesis of benzoxazole **2aa** from benzaldehyde and 2-amino phenol. Reaction conditions: benzaldehyde (0.2 mmol), 2-amino phenol (0.24 mmol), OMS-2 (20 mg, 10 mol%), DMC (1 mL), H_2O_2 (50 uL), r.t., 12 h, isolated yield.



Scheme 4. The multigram-scale synthesis of benzoxazole via OMS-2/H_2O_2/DMC system. Reaction conditions: phenolic imine **1a** (250 mmol, 49.25 g), OMS-2 (25 g, 10 mol%), DMC (1.25 L), H_2O_2 (70 mL), r.t., 12 h, isolated yield.

Finally, more challenging staring substrate N-substituted 2-aminophenol **3a** was used for the synthesis of benzoxazole **2a** via a sequential oxidative process (Scheme 5).[15] At the first place, it was found that the standard catalytic system could not give desired product with green oxidants even at elevated reaction temperature, because OMS-2 could not catalyze the oxidative dehydrogenation of C-N bond. Then, the introduction of a transition metal in the OMS-2 showed an obvious fruitful effect in the conversion. In the presence of O_2 or H_2O_2, OMS-2-supported copper catalyst made the reaction proceed under heating conditions probably via a multi-electron redox cycle we proposed previously.[5] The yield of benzoxazole **2a** could reach to 70% yield when using H_2O_2 as the oxidant in DMC through the efficient oxidative dehydrogenation of C-N bond of **3a** and following aerobic cyclization, which provides a potential of applying the sustainable Cu-OMS-2/H_2O_2/DMC synthetic system in other oxidative dehydrogenation reactions for the synthesis of valuable organic molecules.[16]



3a **2a**

OMS-2 (20 mg, 10 mol%), H_2O_2 or O_2, r.t.- 60 ^oC	trace
$Cu(OH)_x$/OMS-2 (40 mg, Cu: 4 mol%), H_2O_2 or O_2, r.t.	trace
$Cu(OH)_x$/OMS-2 (40 mg, Cu: 4 mol%), O_2, 80 ^oC	55% yield
$Cu(OH)_x$/OMS-2 (40 mg, Cu: 4 mol%), H_2O_2, 80 ^oC	70% yiled

Scheme 5. The sequential reaction for the synthesis of benzoxazole **2a** from **3a** (2 mmol) via oxidative dehydrogenation and cyclization.

CONCLUSION

In conclusion, we have developed an environmentally-safe reaction condition by the use of OMS-2 as heterogeneous catalyst, H_2O_2 as oxidant and DMC as reaction medium for the oxidative synthesis of 2-substituted benzoxazoles and 2-phenyl benzothiazole at room temperature. Moreover, via introducing transition metal, $Cu(OH)_x$/OMS-2 can catalyze benzoxazole synthesis from N-substituted 2-aminophenol through oxidative dehydrogenation of C-N bond followed by oxidative cyclization. The use of environmentally-friendly reagents, mild reaction conditions, and catalyst reusability in gram-scale synthesis and easy isolation of products make this scalable catalytic methodology practical and potential for industrial application, which will prompt us to develop other sustainable chemical transformation processes.

EXPERIMENTAL SECTION

General. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Metal salts were commercially available and were used directly. H_2O_2 (35 wt.% in water) purchased from Sigma-Aldrich was used in this work and DMC (CAS NO. 616-38-6, ReagentPlus®, 99%) was purchased from Sigma-Aldrich with a mark of Greener Alternative Product. All reactions were performed in vials or flasks capped under air. AMO (amorphous manganese oxide) and *a*-MnO_2 were prepared according previous report. Flash chromatography was carried out with Merck silica gel 60 (200-300 mesh) when column chromatographic isolation is necessary. Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection.

Preparation of OMS-2. 5.89 g of $KMnO_4$ in 100 mL of deionized water was added to a solution of 8.8 g of $MnSO_4 \cdot H_2O$ in 30 mL of deionized water and 3 mL concentrated HNO_3. The solution

was refluxed at 100 °C for 24 h, and the product was filtered, washed, and dried at 120 °C for 8 h. Finally, the OMS-2 was calcined in a muffle furnace at 350 °C for 2 h. Then, the black powder OMS-2 was obtained.

General procedure for OMS-2-catlayzed 2-substituted benzoxazoles synthesis. OMS-2 (20 mg, 10 mol%), phenolic imine (0.2 mmol), H_2O_2 (50 uL) and DMC (1 mL) were added to a vial with a bar. The mixture was stirred at ambient temperature for 6 h. Then, the mixture was diluted with ethyl acetate and filtered. The filtrate was removed under reduced pressure to get the crude product or pure product for some cases, and the crude product was further purified by silica gel chromatography (petroleum/ethyl acetate = 40/1 as eluent) to yield corresponding product if it is necessary.

Procedure for $Cu(OH)_x$/OMS-2-catlayzed 2-phenyl benzoxazole synthesis from N-substituted 2-aminophenol 3a. $Cu(OH)_x$/OMS-2 (40 mg, Cu: 4 mol%), **3a** (0.2 mmol), H_2O_2 (50 uL) and DMC (1 mL) were added to a vial with a bar. The mixture was stirred at 80 °C for 18 h. Then, the mixture was diluted with ethyl acetate and filtered. The filtrate was removed under reduced pressure to get the crude product, and the crude product was purified by silica gel chromatography (petroleum/ethyl acetate = 40/1 as eluent) to yield pure **2a**.

Synthesis of benzoxazole 2a in gram-scale. OMS-2 (1 g, 10 mol%), phenolic imine **1a** (10 mmol, 1.97 g), H_2O_2 (2.5 mL) and DMC (50 mL) were added to a 250 mL flask with a bar. The mixture was stirred at ambient temperature for 6 h. Then, the mixture was filtered to remove the catalyst, and remove the solvent under reduced pressure to yield corresponding product **2a** in almost 96% yield directly.

Synthesis of benzoxazole 2a in multigram-scale. OMS-2 (25 g, 10 mol%), phenolic imine **1a** (250 mmol, 49.25 g) and DMC (1.25 L) were added to a 2 L reaction flask with a bar under air and the reaction flask was capped. H_2O_2 (70 mL) was added dropwise in the reaction mixture via a constant pressure dropping funnel within 2 h. After that, the reaction was allowed to vigorously stir at room temperature for 12 h. Then, the mixture was filtered to remove the catalyst, and remove the solvent under reduced pressure to yield corresponding product **2a** by flash chromatography on silica gel in almost 80% yield.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

The authors declare no competing financial interest.

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SUPPORTING INFORMATION

Experimental information, characterization of catalyst, hot filtration experiments and copies of ^{1}H and ^{13}C NMR for all products.

REFERENCES

(1) (a) Viirre, R. D.; Evindar, G.; Batey, R. A. *J. Org. Chem*. **2008**, *73*, 3452-3459. (b) Boyd, G. V. *Science of Synthesis: Houben-W*eyl *Methods of Molecular Transformation*, Category 2, Vol. 11, Product Class 13 (Benzoxazoles and Other Annulated Oxazoles) (Ed. Schaumann, E.), Thieme, Stuttgart, **2002**, pp 481-492.

(2) (a) Stephens, F. F.; Bower, J. D. *J. Chem. Soc*. **1949**, 2971-2972. (b) Hein, D. W.; Alheim, R. J.; Leavitt, J. J. *J. Am. Chem. Soc*. **1957**, *79*, 427-429.

(3) (a) Blacker, A. J.; Farah, M. M.; Hall, M. I.; Marsden, S. P.; Saidi, O.; Williams, J. M. J. *Org. Lett.* **2009**, *11*, 2039-2042. (b) Altenhoff, G.; Glorius, F. *Adv. Synth. Catal*. **2004**, *346*, 1661-1664. (c) Chen, X.; Ji, F.; Zhao, Y.; Liu, Y.; Zhou, Y.; Chen, T.; Yin, S.-F. *Adv. Synth. Catal*. **2015**, *357*, 2924-2930. (d) Zhang, W.; Zeng, Q.; Zhang, X.; Tian, Y.; Yue, Y.; Guo, Y.; Wang, Z. *J. Org. Chem*. **2011**, *76*, 4741-4745. (e) Liu, L.; Qian, L.-W.; Wu, S.; Dong, J.; Xu, Q.; Zhou, Y.; Yin, S.-F. *Org. Lett.* **2017**, *19*, 2849-2852. (f) Xu, D.; Wang, W.; Miao, C.; Zhang, Q.; Xia, C.; Sun, W. *Green Chem*. **2013**, *15*, 2975-2980. (g) Lamani, M.; Prabhu, K. R. *J. Org. Chem*. **2011**, *76*, 7938-7944. (h) Li, Y.; Xie, Y.; Zhang, R.; Jin,

K.; Wang, X.; Duan, C. *J. Org. Chem*. **2011**, *76*, 5444-5449. (i) Ueda, S.; Nagasawa, H. *Angew. Chem. Int. Ed*. **2008**, *47*, 6411-6413. (j) Koleda, O.; Broese, T.; Noetzel, J.; Roemelt, M.; Suna, E.; Francke, R. *J. Org. Chem*. **2017**, DOI: 10.1021/acs.joc.7b01686.

(4) Endo, Y.; Bäckvall, J.-E. *Chem. Eur. J.* **2012**, *18*, 13609-13613.

(5) Meng, X.; Wang, Y.; Wang, Y.; Chen, B.; Jing, Z.; Chen, Zhao, P. *J. Org. Chem.* **2017**, *82*, 6922-6931.

(6) (a) Varma, R. S.; Saini, R. K.; Prakash, O. *Tetrahedron Lett*. **1997**, *38*, 2621-2622. (b) Chang, J.; Zhao, K.; Pan, S. *Tetrahedron Lett*. **2002**, *43*, 951-954. (c) Praveen, C.; Kumar, K. H.; Muralidharan, D. P.; Perumal, T. *Tetrahedron* **2008**, *64*, 2369-2374. (d) Chen, F.; Shen, C.; Yang, D. *Tetrahedron Lett*. **2011**, *52*, 2128-2131.

(7) (a) Chen, W.-H.; Pang, Y. *Tetrahedron Lett.* **2009**, *50*, 6680-6683. (b) Chen, Y.-X.; Qian, L.-F.; Zhang, W.; Han, B. *Angew. Chem. Int. Ed*. **2008**, *47*, 9330-9333. (c) Cao, K.; Tu, Y.; Zhang, F. *Sci. China Chem*. **2010**, *53*, 130-134. (d) Cho, Y. H.; Lee, C.-Y.; Ha, D.-C.; Cheon, C.-H. *Adv. Synth. Catal*. **2012**, *354*, 2992-2996. (e) Cho, Y. H.; Lee, C.-Y.; Cheon, C.-H. *Tetrahedron* **2013**, *69*, 6565-6573.

(8) (a) Yoo, W.-J.; Yuan, H.; Miyamura, H.; Hobayashi, S. *Adv. Synth. Catal*. **2011**, *353*, 3085-3089. (b) Yang, D.; Zhu, X.; Wei, W.; Sun, N.; Yuan, L.; Jiang, M.; You, J.; Wang, H. *RSC Adv*. **2014**, 4, 17832-17839. (c) Reddy, P. L.; Arundhathi, R.; Triphthi, M.; Rawat, D. S. *RSC Adv*. **2016**, *6*, 53596-53601. (d) Kidwai, M.; Bansal, V.; Saxena, A.; Aerry, S.; Mozumdar, S. *Tetrahedron Lett.* **2006**, *47*, 8049-8053. (e) He, J.; Lin, F.; Yang, X.; Wang, D.; Tan, X.; Zhang, S. *Org. Process Res. Dev.* **2016**, *20*, 1093-1096. (f) Banerjee, S.; Payra,

S.; Saha, A.; Sereda, G. *Tetrahedron Lett*. **2014**, *55*, 5515-5520. (g) Kawashita, Y.; Nakamichi, N.; Kawabata, H.; Hayashi, M. *Org. Lett*. **2003**, *5*, 3713-3715. (h) Chang, W.; Sun, Y.; Huang, Y. *Hetero. Chem*. **2017**, *28*, 21360-21372.

(9) For reviews of OMS-2, see: (a) Brock, S. L.; Duan, N.; Tian, Z. R.; Giraldo, O.; Zhou, H.; Suib, S. L. *Chem. Mater*. **1998**, *10*, 2619-2628. (b) Suib, S. L. Acc. Chem. Res. 2008, 41, 479-487. (c) Suib, S. L. *J. Mater. Chem*. **2008**, *18*, 1623-1631.

(10) (a) Xia, G. G.; Yin, Y. G.; Willis, W. S.; Wang, J. Y.; Suib, S. L. *J. Catal.* **1999**, *185*, 91-105. (b) Liu, X.-S.; Jin, Z.-N.; Lu, J.-Q.; Wang, X.-X.; Luo, M.-F. *Chem. Eng. J*. **2010**, *162*, 151-157. (c) Pokhrel, R.; Goetz, M. K.; Shaner, S. E.; Wu, X.; Stahl, S. S. *J. Am. Chem. Soc*. **2015**, *137*, 8384-8387. (d) Ghosh, R.; Shen, X.; Billegas, J. C.; Ding, Y.; Malinger, K.; Suib, S. L. *J. Phys. Chem. B* **2006**, *110*, 7592-7599. (e) Son, Y.-C.; Makwana, V. D.; Howell, A. R.; Suib, S. L. *Angew. Chem. Int. Ed*. **2001**, *40*, 4280-4283. (f) Uematsu, T.; Miyamoto, Y.; Ogasawara, Y.; Suzuki, K.; Yamaguchi, K.; Mizuno, N. *Catal. Sci. Technol.* **2016**, *6*, 222-233.

(11) (a) Sarmah, B.; Srivastava, R.; Manjunathan, P.; Shanbhag, G. V. *ACS Sustainable Chem. Eng*. **2015**, *3*, 2933-2943. (b) Wang, M.; Ma, J.; Yu, M.; Zhang, Z.; Wang, F. *Catal. Sci. Technol*. **2016**, *6*, 1940-1945. (c) Meng, X.; Zhang, J.; Chen, G.; Chen, B.; Zhao, P. *Catal. Commun*. **2015**, *69*, 239-242. (d) Jin, X.; Yamaguchi, K.; Mizuno, N. *RSC Adv*. **2014**, *4*, 34712-34715.

(12) (a) Yamaguchi, K.; Kobayashi, H.; Wang, Y.; Oishi, T.; Ogasawara, Y.; Mizuno, N. *Catal. Sci. Technol*. **2013**, *3*, 318-327. (b) Yamaguchi, K.; Wang, Y.; Mizuno, N. *ChemCatChem* **2013**, *5*, 2835-2838. (c) Wang, Y.; Yamaguchi, K.; Mizuno, N. *Angew. Chem. Int. Ed*.

2012, *51*, 7250-7253. (d) Yamaguchi, K.; Kobayashi, H.; Oishi, T.; Mizuno, N. *Angew. Chem. Int. Ed*. **2012**, *51*, 544-547.

(13) For reviews and selective papers on applications of bio-based solvents, see: (a) Santoro, S.; Ferlin, F.; Luciani, L.; Ackermann, L.; Vaccaro, L. *Green Chem*. **2017**, *19*, 1601-1612. (b) Parker, H. L.; Sherwood, J.; Hunt, A. J.; Clark, J. H. *ACS Sustainable Chem. Eng.* **2014**, *2*, 1739-1742. (c) Chikhi, S.; Djebbai, S.; Soulé, J-F.; Doucet, H. *Chem. Asian J*. **2016**, *11*, 2443-2452. (d) Ferlin, F.; Santoro, S.; Ackermann, L.; Vaccaro, L. *Green Chem*. **2017**, *19*, 2510-2514. (e) Gu, Y.; Jérõme, F. *Chem. Soc. Rev*. **2013**, *42*, 9550-9570.

(14) (a) Meng, X.; Yu, C.; Chen, G.; Zhao, P. *Catal. Sci. Technol*. **2015**, *5*, 372-379. (b) Meng, X.; Zhang, J.; Chen, B.; Jiang, Z.; Zhao, P. *Catal. Sci. Technol.* **2016**, *6*, 890-896. (c) Meng, X.; Bi, X.; Wang, Y.; Chen, G.; Chen, B.; Jing, Z.; Zhao, P. *Catal. Commun*. **2017**, *89*, 34-39.

(15) Yoo, W.-J.; Yuan, H.; Miyamura, H.; Kobayashi, S. *Can. J. Chem.* **2012**, *90*, 306-313.

(16) For selective examples on oxidative dehydrogenation of organic compounds under heterogeneous systems, see: (a) Mullick, K.; Biswas, S.; Angeles-Boza, A. M.; Suib, S. L. *Chem. Commun*. **2017**, *53*, 2256-2259. (b) Cui, X.; Li, Y.; Bachmann, S.; Scalone, M.; Surkus, A.-E.; Junge, K.; Topf, C.; Beller, M. *J. Am. Chem. Soc*. **2015**, *137*, 10652-10658.