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OMS-2-Supported Cu Hydroxide-Catalyzed Benzoxazoles Synthesis from Catechols and Amines via Domino Oxidation Process at Room Temperature

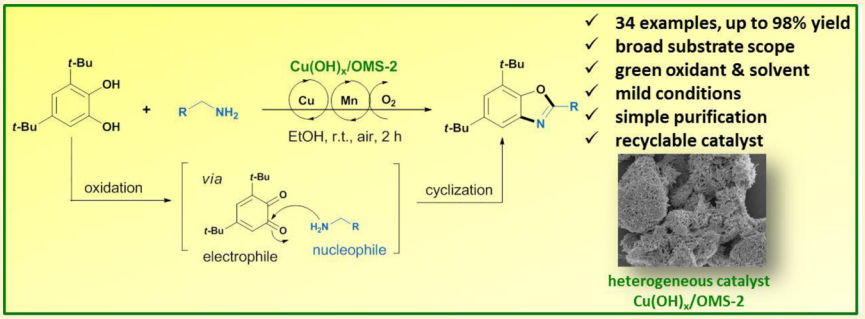
Xu Meng,[†] Yanmin Wang,[†] Yuanguang Wang,[†] Baohua Chen,[‡] Zhenqiang Jing,[§] Gexin Chen,[†] and Peiqing Zhao*[,†]

[†]State Key Laboratory for Oxo Synthesis and Selective Oxidation, Suzhou Research Institute of LICP, Lanzhou Institute of Chemical Physics (LICP), Chinese Academy of Sciences, Lanzhou 730000, P. R. China

[‡]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China

[§]Suzhou Institute of Nano-Tech and Nano-Bionic (SINANO), Chinese Academy of Sciences, Suzhou 215123, P. R. China

Supporting Information



ABSTRACT: In the presence of manganese oxide octahedral molecular sieve (OMS-2) supported copper hydroxide $Cu(OH)_x$/OMS-2, aerobic synthesis of benzoxazoles from catechols and amines via domino oxidation/cyclization at room temperature is achieved. This heterogeneous benzoxazoles synthesis initiated by the efficient oxidation of catechols over $Cu(OH)_x$/OMS-2 tolerates a variety of substrates, especially amines containing sensitive groups (hydroxyl, cyano, amino, vinyl, ethynyl, ester, and even acetyl groups) and heterocycles, which affords functionalized benzoxazoles in good to excellent yields by employing low catalyst loading (2 mol % Cu). The characterization and plausible catalytic mechanism of $Cu(OH)_x$/OMS-2 are described. The notable features of our catalytic protocol such as the use of air as the benign oxidant and EtOH as the solvent, mild conditions, ease of product separation, being scalable up to the gram level, and superior reusability of catalyst (up to 10 cycles) make it more practical and environmentally friendly for organic synthesis.

INTRODUCTION

The oxidation process plays a crucial role in organic synthesis from academic and industrial points of view, particularly selective oxidative catalysis by the use of green oxidants such as O_2 and H_2O_2.[1,2] To realize such green oxidations under mild conditions, considerable effort has been made to design efficient catalytic systems inspired by naturally occurring redox-active metalloenzymes such as copper-containing amine oxidases (CuAOs).[3] For example, Largeron's group reported an iminoquinone/Cu-like cocatalytic system for the oxidative synthesis of imines under mild conditions, which showed that iminoquinone was a redox organocatalyst, and copper salt transferred electrons to terminal oxidant air.[4] Similarly, Sthal with co-workers performed various biomimetic oxidations by the use of *o*-quinones as redox catalysts and O_2 as oxidant under ambient conditions with assistance of transition metals.[5] On the other hand, Kobayashi and Doris with their coworkers respectively developed a series of heterogeneous cooperative catalytic systems using noble metal nanoclusters or nanoparticles as catalysts, catechols as cocatalysts, and O_2 as the terminal oxidant for the oxidations under mild conditions.[6] By contrast, heterogeneous systems are more advantageous than homogeneous counterparts because of easy separation and recyclability of catalysts. As a result, there is an incentive to design a bioinspired heterogeneous redox catalytic process using non-noble metals able to synthesize value-added organic products under mild conditions.

Recently, we reported a series of mixed valent manganese oxide octahedral molecular sieve (OMS-2)[7] supported copper catalysts for the oxidative synthesis of heterocycles using air as the oxidant through a multistep redox process (Scheme 1).[8,9] From the perspective of redox potential, electrons of an oxidative reaction can quickly transfer from the substrate to the oxidant under a low-energy barrier path that is formed by the synergistic interaction between copper and OMS-2.[10] This kind

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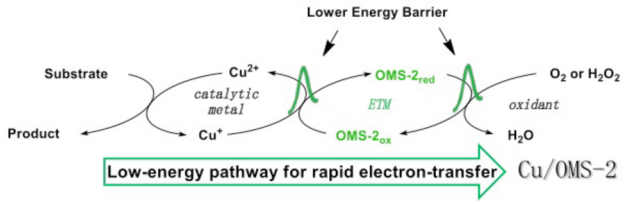
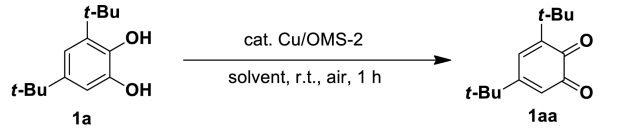
Scheme 1. Multistep Electron-Transfer Process over Cu/OMS-2 Catalyst



of synergistic catalytic system enhances the catalytic efficiency, decreases the catalyst loading, enables air to be a terminal oxidant and, more importantly, makes oxidations occur under mild conditions. Interestingly, we quite recently discovered that OMS-2-supported Cu-based catalysts were highly active in the oxidation of catechol **1a** via a double-electron transfer process at room temperature using air as the oxidant (Scheme 2).[11]

Scheme 2. Cu/OMS-2-Catalyzed Oxidation of Catechol 1a



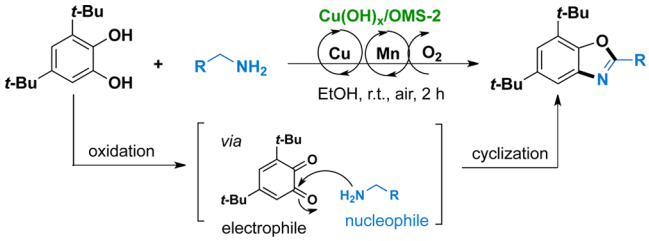
CuO/OMS-2 in DCM:	95% yield, 100% conversion
CuO/OMS-2 in EtOH:	92% yield, 100% conversion
$Cu(OH)_x$/OMS-2 in EtOH:	**>98% yield, 100% conversion**
$Cu(OH)_2$ in EtOH:	18% yield, 30% conversion
OMS-2 in EtOH:	<5% yield, <10% conversion
no catalyst in EtOH:	N.R.

$Cu(OH)_x$/OMS-2 (Cu: 2 mol %) demonstrated a synergistic effect in ethanol under mild conditions, and *o*-quinone **1aa** was obtained in nearly quantitative yield from electron-rich catechol **1a** that is a general cofactor in CuAOs.[3a,5] We therefore envisaged that using a suitable nucleophile to seize the active *o*-quinone in situ generated from catechol for further oxidative reaction in one-pot manner via a domino process. With this strategy, amine would be able to react with *o*-quinone in situ generated to form 2-substituted benzoxazole via a domino oxidation/cyclization process over $Cu(OH)_x$/OMS-2 under mild conditions using air as the terminal oxidant.

Benzoxazoles as structural motifs in natural products are frequently used as building blocks for pharmaceuticals and organic materials.[12] Condensation of 2-amino-phenols with carboxylic acid derivatives followed by annulation under acidic conditions is the traditional method for the synthesis of benzoxazoles.[13] Recently, Ru-based catalysts were applied in the oxidation of alcohols and amines via hydrogen transfer, and their oxidative products can subsequently react with 2-amino-phenols to offer benzoxazoles.[14] Inspired by metalloenzymes, Bäckvall and coworkers developed a biomimetic electron-transfer process for the synthesis of benzoxazoles using quinone/Co-salen as ETMs at 120 °C.[9e] In terms of heterogeneous catalysis, Kobayashi's group reported supported nano-Pt-catalyzed oxidative cyclization of phenolic imines to realize 2-substituted benzoxazoles with assistance of base.[15]

Herein, we describe an efficient $Cu(OH)_x$/OMS-2-catalyzed synthesis of 2-substituted benzoxazoles from catechols and amines via domino oxidation/cyclization process using ambient air as the oxidant at room temperature (Scheme 3). The heterogeneous catalyst demonstrates favorable synergistic interaction between copper hydroxide and OMS-2, which promotes the reaction through a multistep redox process.

Scheme 3. $Cu(OH)_x$/OMS-2-Catalyzed Synthesis of Benzoxazoels Initiated by Catechol Oxidations



RESULTS AND DISCUSSION

$Cu(OH)_x$/OMS-2 was prepared by impregnation−precipitation in water via the treatment of NaOH solution using $CuCl_2$ as the precursor. X-ray diffraction (XRD) showed that the diffraction peaks of $Cu(OH)_x$/OMS-2 with increased crystallite size were the same as that of OMS-2, and no peaks of copper species were observed (Figure S1, see Supporting Information), which means that copper was highly dispersed on OMS-2 and the catalyst was typical cryptomelane material (JCPDS no. 29-1020).[7b] Then, electron microscopy (SEM and TEM) was employed to characterize the morphology of the catalyst. It is worth noting that the morphology of $Cu(OH)_x$/OMS-2 was significantly different from that of support OMS-2 and even CuO/OMS-2 catalyst. $Cu(OH)_x$/OMS-2 was aggregated in a micrometer-sized sphere with decreased BET surface area, while OMS-2 or CuO/OMS-2 both had a typical nanorod morphology (Figure 1). Similarly, TEM images illustrate

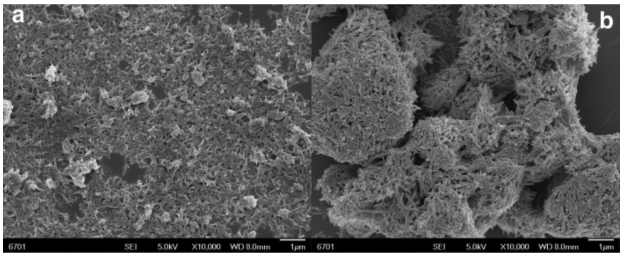


Figure 1. SEM images of OMS-2 (a) and $Cu(OH)_x$/OMS-2 (b).

aggregated, more uniform, and longer nanorod morphology of $Cu(OH)_x$/OMS-2 compared with highly dispersed and broken nanorod morphology of OMS-2 (Figure 2). The lattice vibrational behavior of $Cu(OH)_x$/OMS-2 was studied by FTIR, and the results show it had representative Mn−O lattice

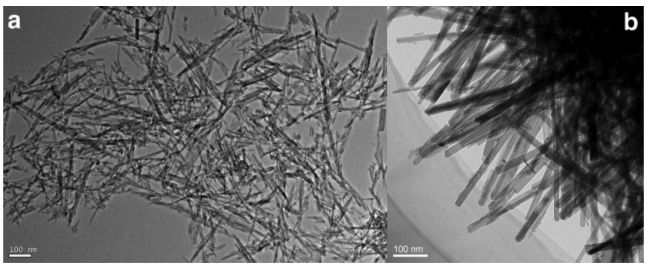


Figure 2. TEM images of OMS-2 (a) and $Cu(OH)_x$/OMS-2 (b).

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vibration modes in MnO_6 octahedra (Figure 3).[16] More importantly, the supported copper hydroxide catalyst possessed

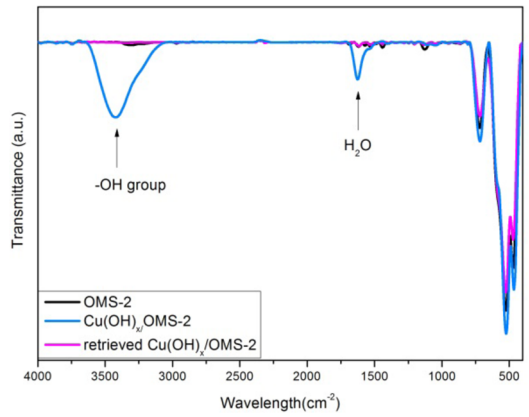


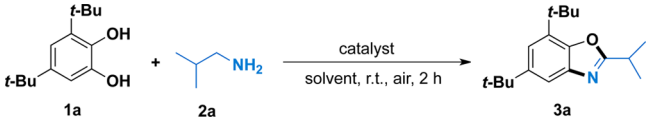
Figure 3. FTIR of OMS-2, fresh $Cu(OH)_x$/OMS-2, and retrieved $Cu(OH)_x$/OMS-2.

large amount of water in tunnels of OMS-2 (1627 cm^{-2}) and hydroxyl group on the surface of catalyst (3425 cm^{-2}).[17] More results of catalyst characterization are included in the Supporting Information.

After investigating distinctive physical properties of $Cu(OH)_x$/OMS-2, the one-pot domino oxidative synthesis of 2-substituted benzoxazole from catechol **1a** and *i*-butylamine **2a** was studied by the use of different catalysts and solvents at room temperature (Table 1). When CuO/OMS-2 (20 mg, Cu: 1.3 wt %) and $Cu(OH)_x$/OMS-2 (20 mg, Cu: 1.48 wt %) were employed in dichloromethane and ethanol respectively, excellent yields of desired product were observed (Table 1, entries 1 and 2). Specifically, $Cu(OH)_x$/OMS-2 led to nearly quantitative yield of benzoxazole **3a** in EtOH, which made the purification process very simple. Without column chromatographic isolation, 95% yield of **3a** was obtained by filtration of solid catalyst followed by removal of EtOH and excess *i*-butylamine under reduced pressure. More importantly, EtOH is a nontoxic and environmentally friendly solvent compared with DCM and other organic solvents. Control experiments show that both copper species and support material were indispensable for the reaction, although catalytic amounts of $Cu(OH)_2$ demonstrated catalytic activity to some extent (Table 1, entries 3 and 4). However, a physical mixture of $Cu(OH)_2$ and OMS-2 did not show fruitful results, which means highly dispersed copper species on OMS-2 might be crucial for the catalysis (Table 1, entry 5). Subsequently, reaction time was examined, and the results indicate that decreased time was unfavorable for the reaction (Table 1, entry 6). The yield of the product decreased if less $Cu(OH)_x$/OMS-2 was used (Table 1, entry 7). Then, different atmospheres were investigated. When the reaction was carried out under O_2, a low yield of benzoxazole **3a** was observed because catechol **1a** decomposed to pigment melanin slightly under strong oxidative conditions (Table 1, entry 8).[18] On the other hand, the reaction proceeded with difficultly under N_2, which means air was the terminal oxidant, and 9% yield of the product might be a result of the supported $Cu(OH)_x$ reoxidized by OMS-2 (Table 1, entry 9). H_2O was deleterious to the reaction, while the reaction did not proceed at all under solvent-free conditions (Table 1, entries 10 and 11). Commercial copper catalysts were used in place of supported catalysts in EtOH at room temperature, and the results illustrate that supported copper exhibited superior behavior compared with that of CuBr and unsupported CuO, and even high catalyst loading (10 mol %) was employed (Table 1, entries 1, 2, 12, and 13). As a result of the optimization, we concluded that the best reaction conditions for synthesis of 2-substituted benzoxazole **3a** in ethanol involve the use of $Cu(OH)_x$/OMS-2 under air at room temperature.

According to the initial optimization, it is notable that the combination of copper and OMS-2 had a superior effect on the reaction. To further investigate this heterogeneous catalytic system, other supported catalysts were examined under the standard conditions (Table 2). Because metal hydroxide is hard

Table 1. Optimization of the Reaction between Catechol and Amine[a]

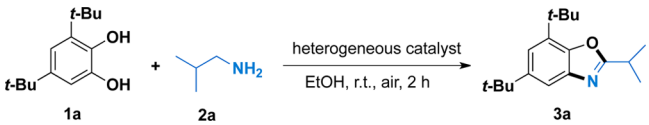


1a 2a 3a

entry	catalyst	solvent	yield (%)[b]
1	CuO/OMS-2	DCM	90
2	$Cu(OH)_x$/OMS-2	EtOH	>98 (95)
3	OMS-2	EtOH	trace
4	$Cu(OH)_2$ (2 mol %)	EtOH	15
5[c]	$Cu(OH)_2$ + OMS-2	EtOH	18
6[d]	$Cu(OH)_x$/OMS-2	EtOH	75
7[e]	$Cu(OH)_x$/OMS-2	EtOH	67
8[f]	$Cu(OH)_x$/OMS-2	EtOH	87
9[g]	$Cu(OH)_x$/OMS-2	EtOH	9
10	$Cu(OH)_x$/OMS-2	H_2O	18
11[h]	$Cu(OH)_x$/OMS-2		0
12	CuBr (2 mol %)	EtOH	5
13	CuO (10 mol %)	EtOH	0

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst (20 mg), solvent (1 mL), room temperature, 2 h, under air. [b]NMR yield using CH_2Br_2 an internal standard; yield is given in parentheses. [c]$Cu(OH)_2$ (2 mol %) and OMS-2 (20 mg) were used. [d]For 1 h. [e]Five milligrams of $Cu(OH)_x$/OMS-2 was used. [f]Under 1 atm O_2. [g]Under N_2. [h]One milliliter of **2a** was used.

Table 2. Investigation of Heterogeneous Catalysts[a]



1a 2a 3a

entry	catalyst	yield (%)[b]
1	CuO/OMS-2	93
2	CuO/Al–Ti	33
3	CuO/nano-TiO_2	trace
4	CuO/nano-Al_2O_3	trace
5[c]	Cu–Mn spinel oxide	0
6	CuO_x-MnO_x/nano-TiO_2	0
7	CuO_x-MnO_x/Al–Ti	0
8	CuO/Mn_3O_4	60
9	CuO/amorphous MnO_2	69

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst (20 mg, theoretical loading of supported metal is 1.5 wt %), EtOH (1 mL), room temperature, 2 h, under air. [b]NMR yield using CH_2Br_2 an internal standard; yield is given in parentheses. [c]Cu–Mn spinel oxide in molecular weight ratio of 1:0.25.

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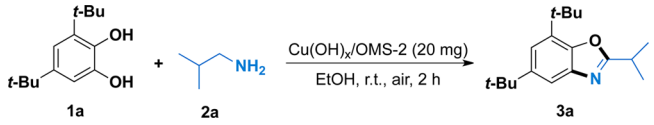
Table 3. Recycling of $Cu(OH)_x$/OMS-2[a]



cycle	1	2	3	4	5	6	7	8	9	10
yield (%)	95	96 (80[b])	94	95	92	93	95	94	94	92

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), $Cu(OH)_x$/OMS-2 (20 mg), EtOH (1 mL), rt, 2 h, under air. [b]The retrieved catalyst without NaOH treatment was used directly.

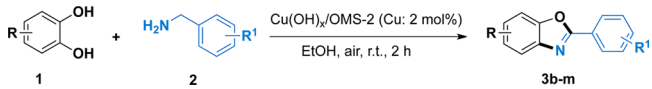
to prepare for some metals, we used catalysts containing metal oxide (CuO_x or MnO_x) for the comparison. First, CuO/OMS-2 also showed high catalytic activity in EtOH for the reaction, although it provided lower yield of product than did $Cu(OH)_x$/OMS-2 (Table 2, entry1). When Al−Ti was used as support, a 33% yield of **3a** was obtained. However, nano-TiO_2 and -Al_2O_3 supported CuO did not show any catalytic activity under the standard conditions (Table 2, entries 3 and 4). Next, we used Cu−Mn spinel oxide in the absence of any supports in the reaction, but the result was frustrating (Table 2, entry 5). Then, we prepared supported CuO_x−MnO_x catalyst by means of wet impregnation using nano-TiO_2 and Al−Ti as supports, respectively. However, this kind of bimetallic catalyst was intrinsically inactive for the oxidation and did not result in cooperative effect, which means catalytic mechanism of OMS-2-supported copper catalyst is different from that of supported Cu−Mn bimetallic catalysts. Eventually, we made supported CuO catalysts using other manganese oxides such as Mn_3O_4 and amorphous MnO_2 instead of OMS-2 as supports, and they offered desired products in moderate yields (Table 2, entries 8 and 9). The results indicate Mn-based support is critical for the catalytic system probably because they are easy to be reoxidized by oxygen under mild conditions, while manganese oxide with the feature of mixed valence is an important role in the catalytic system and improves the catalytic activity significantly.

To verify whether the catalysis was derived from $Cu(OH)_x$/OMS-2 or leached copper species in solution, the reaction between catechol **1a** and *i*-butylamine **2a** catalyzed by $Cu(OH)_x$/OMS-2 under present conditions was performed. After the reaction carried out for 30 min, the catalyst was removed by filtration from the reaction solution, and the NMR yield of desired product was approximately 68%. Meanwhile, the filtrate was kept reacting without addition of fresh $Cu(OH)_x$/OMS-2 for further 2 h, and no more product **3a** was detected (Figure S7, see Supporting Information). The filtrate was analyzed by ICP-AES, which shows copper and manganese species were both hardly detected in filtrate. These observations prove that copper and manganese did not leach from the solid catalyst, and the observed catalysis was genuinely heterogeneous.

On the basis of above research, the recyclability of $Cu(OH)_x$/OMS-2 was studied. Generally, the catalyst was easily separated from the reaction solution by filtration at the end of each run. The retrieved $Cu(OH)_x$/OMS-2 was washed by water and EtOH and reused after drying in a vacuum oven at 50 °C overnight. Although the retrieved catalyst maintained the morphology and structure of cryptomelane very well (Figures S2−S4, see Supporting Information), it resulted in a decreased yield of product by 80% (Table 3). After analysis of retrieved catalyst by FTIR, it was found that the catalyst lost the hydroxyl group on the surface and water in the tunnel of OMS-2 (Figure 3), which likely caused a low efficiency of the catalytic system. To our delight, the catalytic activity of retrieved $Cu(OH)_x$/OMS-2 could be regenerated by the treatment of NaOH solution (for detailed procedure and characterization of regenerated catalyst, see Supporting Information). The recycling experiments show that the regenerated catalyst could be reused at least 9 times without loss of catalytic activity and provided **3a** in excellent yields (Table 3).

Next, with the optimized reaction conditions in hand, we investigated the substrate scope of the domino oxidation by the use of substituted benzylamines (Table 4). In general,

Table 4. Scope of Reactions between Catechols and Aryl Benzylamines[a]



entry	R	R^1	yield (%)
1	3,5-di-*t*-Bu	H	88
2	3,5-di-*t*-Bu	4-Br	96
3	3,5-di-*t*-Bu	4-Cl	95
4	3,5-di-*t*-Bu	4-F	82
5	3,5-di-*t*-Bu	4-CF_3	80
6	3,5-di-*t*-Bu	4-OH	86
7	3,5-di-*t*-Bu	4-CN	63
8	3,5-di-*t*-Bu	2-NH_2	95
9	3,5-di-*t*-Bu	3-NH_2	70
10	4-Me	H	91
11	4-*t*-Bu	H	97
12	3-Me	H	93

[a]Reaction conditions: **1** (0.2 mmol), **2** (0.24 mmol), $Cu(OH)_x$/OMS-2 (20 mg), EtOH (1 mL), rt, 2 h, under air.

benzylamines with electron-withdrawing and electron-donating groups all reacted with catechol **1a** smoothly and offered desired benzoxazoles in very good yields. Moreover, benzylamines with quite sensitive groups such as hydroxyl, cyano, and amino groups participated in the reactions very well, and good to excellent yields of products were obtained under mild conditions (Table 4, entries 6−9). On the other hand, more electron-rich catechols were successfully tolerated in the domino oxidations, and corresponding products were obtained in excellent yields (Table 4, entries 10−12). Notably, the homogeneous $CuBr_2$ catalytic system gave only amino group-functionalized benzoxazoles other than desired ones.[21] Unfortunately, electron-neutral and -poor catechols were not applicable because they were hardly oxidized to corresponding *o*-quinones under the present conditions.

For further investigation of reaction scope, aromatic heterocycles were suitable substrates and corresponding heteroatom-containing benzoxazoles were obtained in excellent yields (Table 5, **4a**−**4c**). Afterward, amines substituted by

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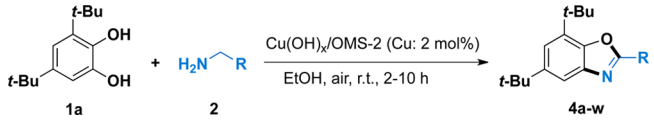
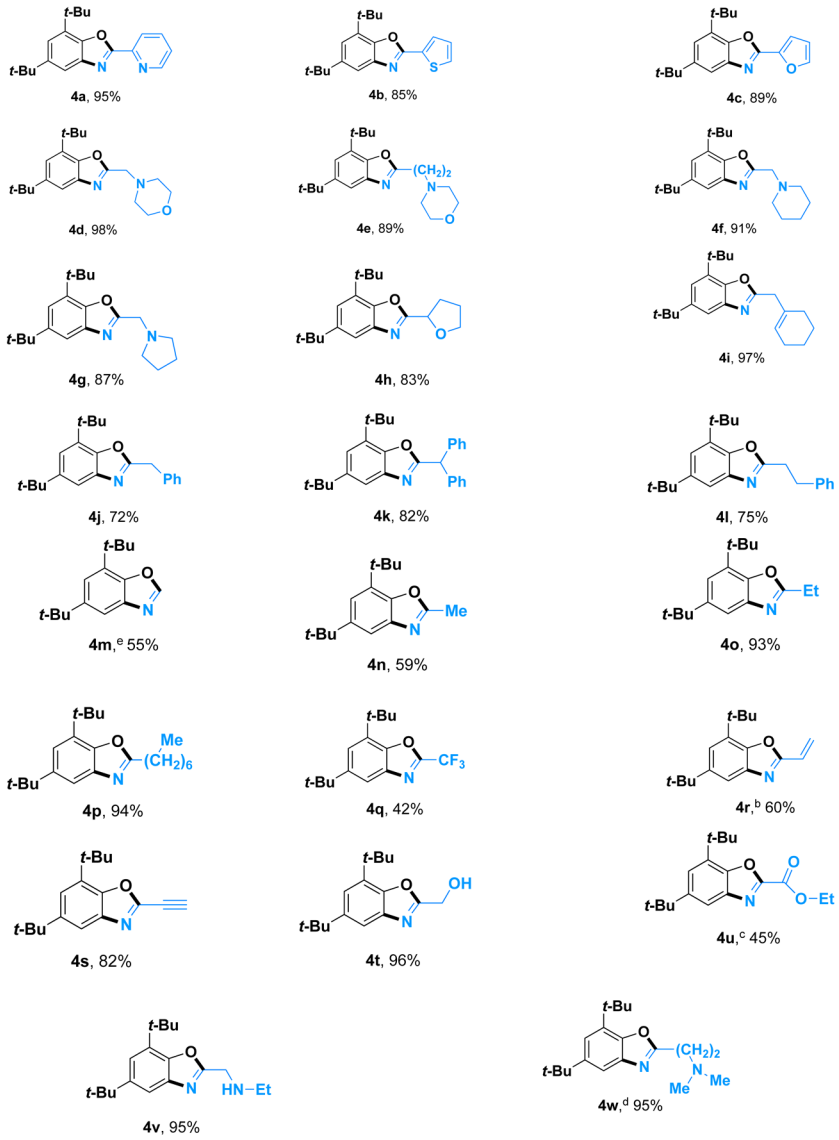
Table 5. Scope of the Reactions between Catechol 1a and Substituted Amines[a]





[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.24 mmol), $Cu(OH)_x$/OMS-2 (20 mg), EtOH (1 mL), rt, 2 h, under air, yields. [b]For 4 h. [c]For 6 h. [d]For 10 h. [e]Ammonia (0.48 mmol) was used, and the reaction was run at 40 °C for 20 h.

aliphatic heterocycles such as morpholine, pyrrolidine, piperidine, and tetrahydrofuran reacted with **1a** fruitfully, while amines with unsaturated compounds such as 2-(1-cyclohexenyl)ethylamine and phenethylamine gave corresponding products in good yields as well (Table 5, **4d**–**4l**). Simple linear alkyl amines, even trifluoroethylamine, were successful reaction partners, although longer reaction time was needed in the case of ammonia (Table 5, **4m**–**4q**). 2-Vinylbenzoxazole and 2-ethynylbenzoxazole were synthesized in good yields from **1a** and allylamine or propargylamine, and they can be used raw for further organic transformations (Table 5, **4r** and **4s**). Eventually, aliphatic amines with various sensitive groups were tolerated in the domino oxidation, and benzoxazoles with hydroxyl, ester, and secondary or tertiary amino groups were isolated in excellent yields (Table 5, **4t**–**4w**).

Encouraged by the good tolerance of the heterogeneous catalytic system, *p*-xylylenediamine **2aa** was employed in the reaction for the synthesis of dicyclized product. Interestingly, expected dicyclized symmetric 1,4-bis(benzoxazol-2-yl)benzene **5a** was isolated; meanwhile, 4-(benzoxazol-2-yl)benzaldehyde **5b** was observed in the reaction through a competitive reaction (Scheme 4). The results indicate that $Cu(OH)_x$/OMS-2 was bifunctional because it not only catalyzed the regular oxidative synthesis of dibenzoxazole **5a** but also hydrolyzed intermediate **3aa** into **5b**.[19] This transformation can produce synthetically useful formyl group-functionalized benzoxazoles from simple substrates in one pot, which was not observed previously.

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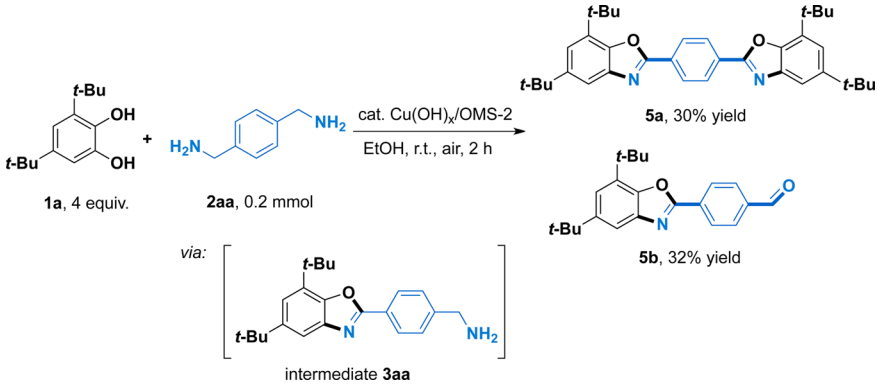
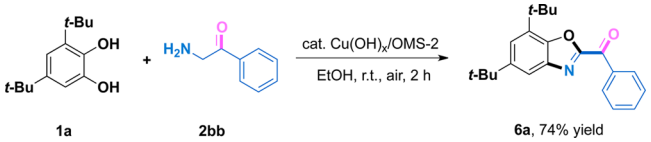
Scheme 4. Domino Oxidation between Catechol 1a and *p*-Xylylenediamine 2aa[a]



[a]Reaction conditions: **1a** (0.8 mmol), **2aa** (0.2 mmol), $Cu(OH)_x$/OMS-2 (20 mg), EtOH (1 mL), rt, air, 2 h.

To make our catalytic system more attractive, more challenging substrate 2-aminoacetophenone **2bb** was employed to react with catechol **1a** (Scheme 5). Delightedly, the desired

Scheme 5. Domino Oxidation between Catechol 1a and 2-Aminoacetophenone 2bb[a]

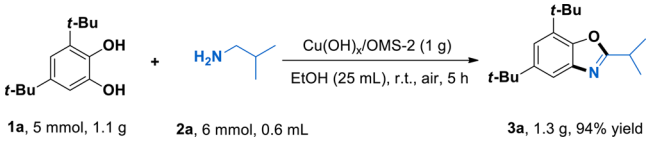


[a]Reaction conditions: **1a** (0.2 mmol), **2bb** (0.24 mmol), $Cu(OH)_x$/OMS-2 (20 mg), EtOH (1 mL), rt, air, 2 h.

diheteroaryl ketone **6a** was isolated in 74% yield at room temperature using air as terminal oxidant, while homogeneous catalysts such as $CuBr_2$, $Cu(OAc)_2$, and CuI cannot provide desired product due to quick decomposition of **2bb** in these systems. Diheteroaryl ketones are generally synthesized by noble metal-catalyzed carbonylation with CO.[20] Take into account safety and price issues, the recyclable $Cu(OH)_x$/OMS-2/air system for the synthesis of diheteroaryl ketones is more favorable and greener.

Finally, attempts to realize the synthesis of benzoxazole **3a** on a gram-scale were carried out. The gram-scale reaction led to 94% yield of desired product without using column purification, which illustrates our heterogeneous catalytic system is practical and can be a potential option for industrial application (Scheme 6).

Scheme 6. Gram-Scale Reaction



To gain insight into the catalytic mechanism of the domino oxidation, some control experiments were performed. First of all, *o*-quinone **1aa** produced from oxidation of catechol **1a** was directly used as starting material to react with *i*-butylamine **2a**, and product **3a** was isolated in nearly quantitative yield (Scheme 7a). Further, it was found that benzoxazole **3a** could be obtained even without $Cu(OH)_x$/OMS-2 in a low yield by use of **1aa** as the raw directly, while unoxidized intermediate **3à** was not detected no matter whether the catalyst was used (Scheme 7a). Then, another possible intermediate **7a** gave desired product 2-phenylbenzoxazole **7b** smoothly under $Cu(OH)_x$/OMS-2/O_2 system at room temperature (Scheme 7b). These observations indicate that amine was able to react with *o*-quinone in situ generated from catechol via nucleophilic addition/dehydration/tautomerization to give intermediate substituted 2-(benzylideneamino)phenol, which is further transferred to benzoxazole through oxidative cyclization. On the other hand, Yiǹs group reported homogeneous $CuBr_2$ catalyzed the synthesis of benzoxazoles from catechols and amines, which shows amine is a necessity for the copper-catalyzed oxidation of catechol, and the entire reaction proceeds via a synergistic catalysis between catechol and amine.[21] However, in our catalytic system, the homocoupling of amine **2b** did not occur in the presence of different amounts of catechol or *o*-quinone, which means catechol in our system did not play a role as cofactor (Scheme 7c). Furthermore, we used GC−MS to analyze the reaction mixture of catechol **1a** and 3-phenylpropylamine **2l**, and there is no corresponding aldehyde formed in the reaction under our catalytic system (Figure S8, see the Supporting Information). More importantly, catechol **1a** could be oxidized efficiently by $Cu(OH)_x$/OMS-2 without the involvement of amine at all (Scheme 2). These experimental facts indicate that the competitive oxidation and synergistic effect between catechol and amine did not exist in our catalytic system; however, the synergistic effect from $Cu(OH)_x$/OMS-2 played a vital role for the catalysis. As a consequence, amines can quickly trap the in situ generated *o*-quinone species to perform further transformation.

CONCLUSION

In summary, we developed the combination of heterogeneous catalyst $Cu(OH)_x$/OMS-2 and ambient air as an effective system for the aerobic oxidative synthesis of 2-substituted benzoxazoles from catechols and amines under mild conditions. The domino reaction initiated by the oxidation of catechols proceeds through oxidation/cyclization in a one-pot manner and tolerates a great number of substrates. The use of air as the terminal oxidant, mild reaction conditions, and catalyst reusability and easy isolation of the products make the catalytic protocol practical and environmentally friendly. Mechanistic studies suggest that copper hydroxide and OMS-2 work cooperatively to facilitate the electron transfer process of the domino oxidation. This catalytic system should be useful for

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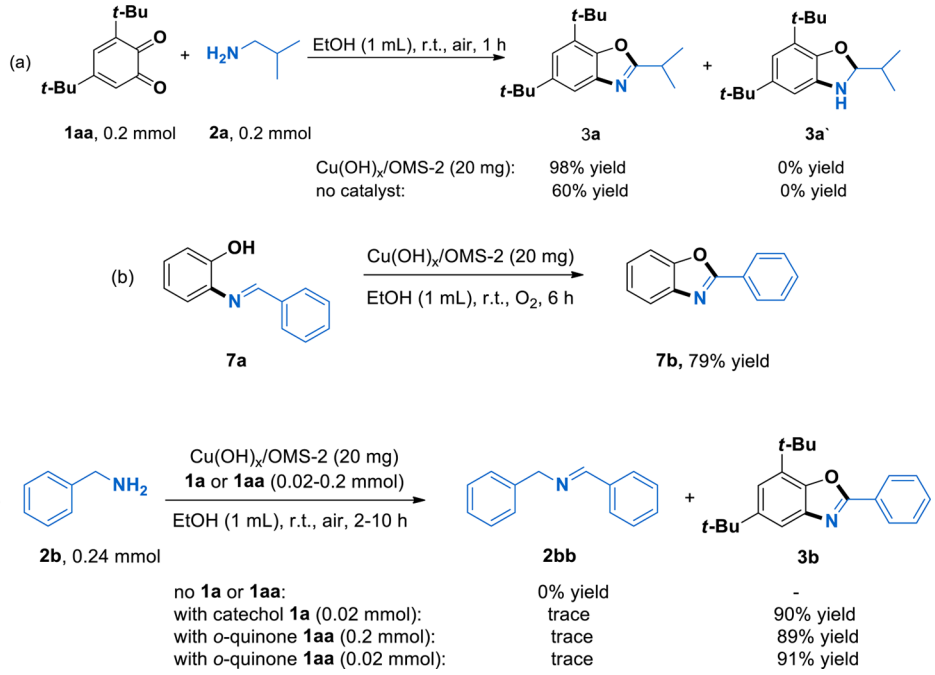
Scheme 7. Control Experiments a−c



other organic transformations involving other nucleophiles as the reaction partners.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Metal salts were commercially available and used directly. All experiments were carried out under air. Flash chromatography was carried out with Merck silica gel 60 (200−300 mesh). Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection. ^{1}H NMR and ^{13}C NMR (400 and 100 MHz respectively) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm using TMS as internal standard, and spin−spin coupling constants (J) are given in Hz. The electron ionization (EI) method was used as the ionization method for the HRMS measurement, and the mass analyzer type is TOF for EI. GC−MS spectra were recorded on a Shimadzu GCMS-QP2010 equipped with an InertCap-5 capillary column at an ionization voltage of 70 eV. All supported catalysts are synthesized by wet impregnation in deionized water, and $Cu(OH)_x$/OMS-2 was made by deposition−precipitation in water. The crystal phase and composition were determined by powder X-ray diffraction using a X-Pert PRO X-ray diffractometer with Cu Kα radiation in the 2θ range of 10−90°. Infrared spectra of the materials were recorded on calcined powders dispersed in KBr (2 mg sample in 300 mg KBr) using a PerkinElmer One FTIR spectrometer with a resolution of 4 cm^{-1} operating in the range 500−2000 cm^{-1} with 4 scans per spectrum. The morphologies of the samples were characterized by a TF20 transmission electron microscope and SM-5600LV or Quanta 250 FEG scanning electron microscope. Nitrogen adsorption−desorption measurements were performed at 76 K using an ASAP 2020 M analyzer utilizing the BET model for the calculation of specific surface areas. The reducibility of the catalysts was measured by the hydrogen temperature-programmed reduction (H2-TPR) technique. Fifty milligrams of OMS-2 and $Cu(OH)_x$/OMS-2 were placed in a quartz reactor that was connected to a TPR apparatus, and the reactor was heated from rt to 550 °C with a heating rate of 10 °C/min. The reducing atmosphere was the mixture of H_2 and N_2 with a total flow rate of 30 mL/min, and the amount of H_2 uptake during the reduction was measured by a TCD. The XPS measurements were performed on a Kratos AXIS Ultra DLD high performance electron spectrometer using a nonmonochromatized Al Kα excitation source (hv = 1486.6 eV). Binding energies were calibrated by using the contaminant carbon (C 1s = 284.6 eV).

Preparation of OMS-2. $KMnO_4$ (5.89 g, 37 mmol) in 100 mL of deionized water was added to a solution of $MnSO_4$−H_2O (8.8 g, 52 mmol) 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 dry OMS-2 was calcined in a muffle furnace at 350 °C for 2 h. Then, the black powder OMS-2 was obtained.

Preparation of $Cu(OH)_x$/OMS-2. Support OMS-2 (2 g, 2.7 mmol) was added to a 100 mL round-bottom flask. A solution of $CuCl_2$ (0.085 g, 0.6 mmol) in deionized water (60 mL) was added to OMS-2. Then, the mixture was stirred for 1 h at room temperature, and the pH was quickly adjusted to 12 by the addition of an aqueous solution of NaOH (1.0 M). After that, the above solution was stirred for 24 h at room temperature. Then, the solid in the solution was filtered, washed with 1 L of water, and dried in oven at 50 °C overnight. Eventually, the dried black solid was dried in vacuo oven at 50 °C for another 10 h to afford about 2 g $Cu(OH)_x$/OMS-2 catalyst. The black powder $Cu(OH)_x$/OMS-2 (1.5 wt % theoretical loading, actual loading is 1.48 wt %) was characterized by ICP-AES, BET, XRD, FTIR, TEM, SEM, H_2-TPR, and XPS techniques.

General Procedure for $Cu(OH)_x$/OMS-2 2-Substituted Benzoxazoles Synthesis. $Cu(OH)_x$/OMS-2 (20 mg, 2 mol % for Cu), catechol (0.2 mmol), amine (0.24 mmol), and EtOH (1 mL) were added to a vial with a bar. The mixture was stirred at ambient temperature for 2 h under air. 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 chromatography (petroleum/ethyl acetate = 40/1 as eluent) to yield corresponding product if it is necessary.

General Procedure for Catalyst Regeneration. Once the reaction was finished, the mixture was diluted with 10 mL of EtOH. The solid catalyst was filtered via filter paper and washed by water and EtOH. Then, the retrieved catalyst was stirred in 1 M NaOH solution for 2 h at room temperature. After that, the catalyst was filtered, washed with 1 L water, and dried in oven at 50 °C overnight. Then, the dried catalyst was further dried in vacuo oven at 50 °C for another 10 h to afford about regenerated $Cu(OH)_x$/OMS-2 catalyst for the next run. This procedure was repeated every cycle, and the yield of the

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reaction was determined by ^{1}H NMR using Br_2CH_2 as internal standard.

5,7-Di-tert-butyl-2-isopropylbenzo[d]oxazole (**3a**).[21] Brown liquid, yield 95%, 51 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.16 (s, 1H), 3.24−3.09 (m, 1H), 1.40 (s, 9H), 1.37 (s, 6H), 1.29 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 170.6, 147.1, 146.9, 141.3, 133.4, 118.6, 113.8, 34.9, 34.3, 31.8, 29.9, 28.8, 20.3.

5,7-Di-tert-butyl-2-phenylbenzo[d]oxazole (**3b**).[21] Yellow liquid, yield 88%, 54 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 2H), 7.68 (s, 1H), 7.53 (s, 3H), 7.32 (s, 1H), 1.57 (s, 9H), 1.41 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 162.4, 147.8, 146.9, 142.3, 133.7, 131.2, 128.9, 127.5, 127.4, 119.6, 114.2, 35.1, 34.5, 31.9, 30.1.

2-(4-Bromophenyl)-5,7-di-tert-butylbenzo[d]oxazole (**3c**).[21] Colorless liquid, yield 96%, 73 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.8 Hz, 2H), 7.66 (d, J = 7.5 Hz, 3H), 7.33 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 161.6, 147.9, 146.9, 142.2, 133.8, 132.2, 128.8, 126.5, 125.8, 119.9, 114.3, 35.1, 34.5, 31.9, 30.1.

5,7-Di-tert-butyl-2-(4-chlorophenyl)benzo[d]oxazole (**3d**).[21] Pale yellow liquid, yield 95%, 65 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.0 Hz, 2H), 7.65 (s, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.32 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 161.5, 147.9, 146.9, 142.1, 137.3, 133.7, 129.2, 128.6, 125.9, 119.8, 114.2, 35.1, 34.5, 31.8, 29.9.

5,7-Di-tert-butyl-2-(4-fluorophenyl)benzo[d]oxazole (**3e**).[21] Colorless liquid, yield 82%, 53 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, J = 8.8, 5.3 Hz, 2H), 7.65 (d, J = 1.8 Hz, 1H), 7.32 (d, J = 1.8 Hz, 1H), 7.21 (t, J = 8.6 Hz, 2H), 1.56 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 165.9, 163.3, 161.6, 147.8, 146.9, 142.2, 133.7, 129.6, 129.5, 123.9, 123.8, 119.6, 116.2, 116.1, 114.1, 35.1, 34.5, 31.8, 30.1.

5,7-Di-tert-butyl-2-(4-(trifluoromethyl)phenyl)benzo[d]oxazole (**3f**).[21] Colorless liquid, yield 80%, 60 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, J = 7.3 Hz, 2H), 7.80 (d, J = 7.4 Hz, 2H), 7.69 (s, 1H), 7.37 (s, 1H), 1.57 (s, 9H), 1.41 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 160.9, 148.2, 147.1, 142.1, 133.9, 132.8, 132.5, 130.7, 127.8, 127.6, 125.9, 125.8, 125.1, 122.4, 120.3, 114.5, 35.1, 34.5, 31.8, 29.9.

4-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)phenol (**3g**).[21] Colorless liquid, yield 86%, 55 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.08 (d, J = 8.0 Hz, 2H), 7.58 (s, 1H), 7.30 (s, 1H), 7.00 (d, J = 7.9 Hz, 2H), 1.55 (s, 9H), 1.36 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 163.2, 160.4, 148.1, 146.4, 141.1, 133.7, 129.6, 119.4, 118.2, 116.4, 113.2, 35.1, 34.4, 31.8, 29.9.

4-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)benzonitrile (**3h**). Colorless liquid, yield 63%, 41 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 1.8 Hz, 1H), 7.37 (d, J = 1.8 Hz, 1H), 1.55 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 160.3, 148.4, 147.1, 142.1, 134.0, 132.6, 131.4, 127.7, 120.7, 118.2, 114.6, 114.3, 35.1, 34.5, 31.7, 29.9. HRMS (EI): calcd for $C_{22}H_{24}N_2O$: 332.1976; found: 332.1998.

2-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)aniline (**3i**). Colorless liquid, yield 95%, 61 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 7.2 Hz, 1H), 7.65 (d, J = 1.7 Hz, 1H), 7.38−7.25 (m, 2H), 6.89−6.77 (m, 2H), 6.24 (s, 2H), 1.61 (s, 9H), 1.45 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 171.1, 162.5, 147.6, 147.3, 145.2, 141.9, 133.3, 131.9, 128.5, 119.1, 116.6, 116.1, 113.6, 108.9, 35.0, 34.4, 31.8, 29.9. HRMS (EI): calcd for $C_{21}H_{26}N_2O$: 322.2048; found: 322.2076.

3-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)aniline (**3j**). Colorless liquid, yield 70%, 45 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67−7.62 (m, 2H), 7.59−7.56 (m, 1H), 7.33−7.27 (m, 2H), 6.83 (ddd, J = 8.0, 2.4, 0.9 Hz, 1H), 3.88 (s, 2H), 1.55 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 162.7, 147.6, 146.8, 146.8, 142.2, 133.6, 129.8, 128.3, 119.4, 117.9, 117.7, 114.1, 113.5, 35.0, 34.4, 31.8, 29.9. HRMS (EI): calcd for $C_{21}H_{26}N_2O$: 322.2048; found: 322.2076.

5-Methyl-2-phenylbenzo[d]oxazole (**3k**).[15a] White solid, yield 91%, 38 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 6.6, 2.8 Hz, 2H), 7.55 (d, J = 7.0 Hz, 1H), 7.54−7.49 (m, 3H), 7.45 (d, J = 8.3 Hz, 1H), 7.15 (d, J = 8.3 Hz, 1H), 2.48 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 163.0, 148.9, 142.2, 134.3, 131.3, 128.8, 127.5, 127.2, 126.2, 119.8, 109.9, 21.5.

5-(tert-Butyl)-2-phenylbenzo[d]oxazole (**3l**).[15a] White solid, yield 97%, 48 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 6.6, 2.9 Hz, 2H), 7.72 (d, J = 1.5 Hz, 1H), 7.45−7.38 (m, 4H), 7.31 (dd, J = 8.6, 1.7 Hz, 1H), 1.30 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 163.0, 148.6, 148.0, 141.9, 131.2, 128.8, 127.4, 127.2, 122.8, 116.4, 109.6, 34.8, 31.7.

4-Methyl-2-phenylbenzo[d]oxazole (**3m**).[15a] White solid, yield 93%, 39 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 6.6, 3.0 Hz, 2H), 7.49−7.37 (m, 3H), 7.30 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 7.7 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 2.59 (s, 3H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 162.2, 150.4, 141.3, 131.2, 130.5, 128.8, 128.7, 128.7, 127.5, 127.3, 124.9, 124.6, 107.8, 16.5.

5,7-Di-tert-butyl-2-(pyridin-2-yl)benzo[d]oxazole (**4a**).[21] Colorless liquid, yield 95%, 58 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (dd, J = 4.7, 0.7 Hz, 1H), 8.28 (d, J = 7.9 Hz, 1H), 7.86 (td, J = 7.8, 1.7 Hz, 1H), 7.69 (d, J = 1.9 Hz, 1H), 7.41 (ddd, J = 7.6, 4.8, 1.1 Hz, 1H), 7.36 (d, J = 1.8 Hz, 1H), 1.56 (s, 9H), 1.40 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 161.1, 150.4, 148.0, 147.3, 146.4, 142.1, 136.8, 134.1, 125.1, 123.1, 120.4, 114.7, 35.1, 34.5, 31.8, 30.1.

5,7-Di-tert-butyl-2-(thiophen-2-yl)benzo[d]oxazole (**4b**).[21] Colorless liquid, yield 85%, 53 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.54 (s, 1H), 7.44 (s, 1H), 7.21 (s, 1H), 7.09 (s, 1H), 1.45 (s, 9H), 1.30 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 158.4, 147.8, 146.5, 142.1, 133.5, 130.1, 129.7, 129.3, 128.1, 119.5, 114.0, 35.0, 34.4, 31.8, 29.9.

5,7-Di-tert-butyl-2-(furan-2-yl)benzo[d]oxazole (**4c**).[21] Colorless liquid, yield 89%, 52 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 15.4 Hz, 2H), 7.27−7.09 (m, 2H), 6.53 (s, 1H), 1.45 (s, 9H), 1.31 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 154.8, 147.9, 146.3, 145.3, 142.9, 141.8, 133.7, 119.6, 114.3, 113.5, 112.1, 35.0, 34.4, 31.8, 29.9.

5,7-Di-tert-butyl-2-(morpholinomethyl)benzo[d]oxazole (**4d**). Pale yellow oil, yield 98%, 64 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.28 (d, J = 1.5 Hz, 1H), 3.88 (s, 2H), 3.76−3.70 (m, 4H), 2.67 (d, J = 4.1 Hz, 4H), 1.48 (s, 9H), 1.36 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 162.1, 147.5, 141.2, 133.7, 119.3, 114.1, 66.8, 55.3, 53.0, 34.9, 34.3, 31.8, 29.9. HRMS (EI): calcd for $C_{20}H_{30}N_2O_2$: 330.2223; found: 330.2248.

5,7-Di-tert-butyl-2-(2-morpholinoethyl)benzo[d]oxazole (**4e**). Brown liquid, yield 89%, 61 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 1.6 Hz, 1H), 7.25 (d, J = 1.6 Hz, 1H), 3.73−3.68 (m, 4H), 3.13 (t, J = 7.4 Hz, 2H), 2.93 (t, J = 7.4 Hz, 2H), 2.54 (s, 4H), 1.47 (s, 9H), 1.36 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 164.8, 147.2, 146.9, 141.4, 133.5, 118.8, 113.7, 66.87, 55.6, 53.4, 34.9, 34.4, 31.8, 29.9, 26.5. HRMS (EI): calcd for $C_{21}H_{32}N_2O_2$: 344.2554; found: 344.2532.

5,7-Di-tert-butyl-2-(piperidin-1-ylmethyl)benzo[d]oxazole (**4f**). Brown liquid, yield 91%, 59 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.27 (d, J = 1.6 Hz, 1H), 3.90 (s, 2H), 2.60 (s, 4H), 1.62 (dt, J = 11.0, 5.6 Hz, 4H), 1.48 (s, 9H), 1.43−1.34 (m, 11H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 162.8, 147.3, 146.9, 141.3, 133.7, 119.1, 114.1, 55.65, 53.8, 34.9, 34.4, 31.8, 29.9, 25.9, 23.9. HRMS (EI): calcd for $C_{21}H_{32}N_2O$: 328.2509; found: 322.2526.

5,7-Di-tert-butyl-2-(pyrrolidin-1-ylmethyl)benzo[d]oxazole (**4g**). Yellow oil, yield 87%, 54 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 1.8 Hz, 1H), 7.29 (d, J = 1.8 Hz, 1H), 4.03 (s, 2H), 2.77 (s, 4H), 1.84 (dt, J = 6.4, 3.1 Hz, 4H), 1.50 (s, 9H), 1.39 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 171.1, 163.2, 147.3, 146.9, 141.3, 133.6, 119.1, 114.1, 60.4, 53.7, 51.9, 34.9, 34.4, 31.8, 29.9. HRMS (EI): calcd for $C_{20}H_{30}N_2O$: 314.2446; found: 322.2471.

5,7-Di-tert-butyl-2-(tetrahydrofuran-2-yl)benzo[d]oxazole (**4h**). Pale green liquid, yield 83%, 50 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.20 (s, 1H), 5.15 (s, 1H), 4.05 (d, J = 6.2 Hz, 1H), 3.95 (s, 1H), 2.31 (d, J = 6.6 Hz, 2H), 2.12 (s, 1H), 1.98 (s, 2H), 1.40 (s, 9H), 1.29 (s, 9H). $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$): δ 165.8, 147.5, 147.1, 140.9, 133.8, 119.4, 114.3, 73.8, 69.2, 34.9, 34.4, 31.8, 30.8, 29.9, 29.7. HRMS (EI): calcd for $C_{19}H_{27}NO_2$: 301.2009; found: 301.2031.

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*5,7-Di-tert-butyl-2-(cyclohex-1-en-1-ylmethyl)benzo[d]oxazole (**4i**).* Colorless liquid, yield 97%, 63 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.29 (s, 1H), 5.72 (s, 1H), 3.61 (s, 2H), 2.09 (d, J = 4.0 Hz, 4H), 1.68 (d, J = 3.9 Hz, 2H), 1.61 (d, J = 4.5 Hz, 2H), 1.52 (s, 9H), 1.42 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 164.9, 147.0, 141.6, 133.4, 132.0, 125.4, 118.7, 113.8, 37.6, 34.9, 34.3, 31.8, 29.8, 28.3, 25.3, 22.7, 21.9. HRMS (EI): calcd for $C_{22}H_{31}NO$: 325.2498; found: 325.2466.

*2-Benzyl-5,7-di-tert-butylbenzo[d]oxazole (**4j**).*[21] Brown liquid, yield 72%, 46 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.38 (s, 2H), 7.32 (s, 2H), 7.24 (s, 2H), 4.26 (s, 2H), 1.44 (s, 9H), 1.35 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 164.6, 147.2, 141.5, 135.2, 133.5, 128.8, 128.6, 127.1, 118.9, 113.9, 35.3, 34.9, 34.3, 31.7, 29.8.

*2-Benzhydryl-5,7-di-tert-butylbenzo[d]oxazole (**4k**).* Pale yellow liquid, yield 82%, 65 mg. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 8H), 7.06 (m, 4H), 5.68 (s, 1H), 1.33 (s, 9H), 1.28 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.9, 147.3, 141.3, 139.6, 133.7, 128.7, 128.5, 128.3, 127.2, 119.1, 114.3, 51.5, 35.0, 34.3, 31.7, 29.8. HRMS (EI): calcd for $C_{28}H_{31}NO$: 397.2424; found: 972.2431.

*5,7-Di-tert-butyl-2-phenethylbenzo[d]oxazole (**4l**).*[21] Brown liquid, yield 75%, 50 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 1.9 Hz, 1H), 7.34−7.25 (m, 5H), 7.25−7.19 (m, 1H), 3.26 (dd, J = 8.1, 4.4 Hz, 4H), 1.48 (s, 9H), 1.40 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 165.5, 147.1, 146.9, 141.4, 140.1, 133.4, 128.5, 128.2, 126.3, 118.7, 113.7, 34.9, 34.3, 32.9, 31.8, 30.3, 29.8.

*5,7-Di-tert-butylbenzo[d]oxazole (**4m**).*[21] Colorless liquid, yield 55%, 25 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.65 (s, 1H), 7.34 (s, 1H), 1.49 (s, 9H), 1.39 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 147.7, 134.1, 119.8, 114.6, 35.0, 34.4, 31.8, 29.8.

*5,7-Di-tert-butyl-2-methylbenzo[d]oxazole (**4n**).*[21] Brown liquid, yield 59%, 28 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.16 (s, 1H), 2.56 (s, 3H), 1.39 (s, 9H), 1.29 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 163.2, 147.1, 141.7, 133.3, 118.6, 113.6, 34.9, 34.3, 31.8, 29.9, 14.6.

*5,7-Di-tert-butyl-2-ethylbenzo[d]oxazole (**4o**).*[21] Colorless crystal, yield 93%, 48 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.24 (s, 1H), 2.96 (q, J = 7.6 Hz, 2H), 1.47 (s, 9H), 1.45 (s, 3H), 1.37 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 147.0, 141.4, 133.3, 118.6, 113.6, 34.9, 34.3, 31.8, 29.8, 22.1, 11.0.

*5,7-Di-tert-butyl-2-heptylbenzo[d]oxazole (**4p**).*[21] Brown liquid, yield 94%, 62 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (s, 1H), 7.16 (s, 1H), 2.84 (s, 2H), 1.80 (s, 2H), 1.39 (s, 9H), 1.29 (s, 9H), 1.21 (s, 7H), 0.80 (s, 3H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 166.7, 147.0, 146.9, 141.4, 133.3, 118.5, 113.7, 34.9, 34.3, 31.8, 31.6, 29.8, 29.6, 29.0, 28.8, 28.6, 26.9, 22.5, 14.0.

*5,7-Di-tert-butyl-2-(trifluoromethyl)benzo[d]oxazole (**4q**).*[21] Brown liquid, yield 42%, 25 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.47 (s, 1H), 1.50 (s, 9H), 1.39 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 149.3, 147.0, 139.7, 134.9, 122.2, 115.6, 35.1, 34.5, 31.6, 29.7.

*5,7-Di-tert-butyl-2-vinylbenzo[d]oxazole (**4r**).*[21] Colorless liquid, yield 60%, 30 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.29 (s, 1H), 6.76 (dd, J = 17.1, 11.2 Hz, 1H), 6.44 (d, J = 17.5 Hz, 1H), 5.82 (d, J = 10.7 Hz, 1H), 1.50 (s, 9H), 1.37 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 161.5, 147.6, 141.9, 133.6, 124.4, 124.3, 124.1, 119.8, 114.2, 35.0, 34.3, 31.7, 29.9.

*5,7-Di-tert-butyl-2-ethynylbenzo[d]oxazole (**4s**).*[21] Brown liquid, yield 82%, 41 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.37 (s, 1H), 3.36 (s, 1H), 1.48 (s, 9H), 1.37 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 155.9, 148.4, 147.0, 140.7, 134.0, 121.2, 114.6, 81.0, 72.1, 35.0, 34.4, 31.7, 29.8.

*(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)methanol (**4t**).*[21] Colorless liquid, yield 96%, 50 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.20 (s, 1H), 5.26 (s, 1H), 4.89 (s, 2H), 1.37 (s, 9H), 1.28 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 168.6, 147.7, 146.9, 140.6, 133.9, 119.5, 113.7, 57.7, 35.0, 34.3, 31.7, 29.8.

*Ethyl 5,7-Di-tert-butylbenzo[d]oxazole-2-carboxylate (**4u**).*[21] Colorless liquid, yield 45%, 27 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.45 (s, 1H), 4.54 (s, 2H), 1.51 (s, 13H), 1.38 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 156.7, 149.0, 140.9, 134.9, 122.5, 115.7, 62.9, 35.1, 34.5, 31.7, 29.9, 14.2.

*N-((5,7-Di-tert-butylbenzo[d]oxazol-2-yl)methyl)ethanamine (**4v**).*[21] Colorless liquid, yield 95%, 54 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.19 (s, 1H), 4.02 (s, 2H), 2.70 (d, J = 6.0 Hz, 2H), 1.40 (s, 9H), 1.29 (s, 9H), 1.08 (s, 3H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 147.1, 146.8, 143.9, 140.9, 133.6, 133.4, 118.9, 113.7, 34.7, 34.1, 31.5, 31.3, 29.6, 29.5, 14.9.

*2-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)-N,N-dimethylethanamine (**4w**).*[21] Colorless liquid, yield 95%, 57 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.25 (s, 1H), 3.12 (s, 2H), 2.89 (s, 2H), 2.33 (s, 6H), 1.49 (s, 9H), 1.38 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 164.9, 147.1, 147.0, 141.5, 133.5, 118.8, 113.8, 56.41, 45.2, 35.0, 34.3, 31.8, 29.9, 27.3.

*1,4-Bis(5,7-di-tert-butylbenzo[d]oxazol-2-yl)benzene (**5a**).* White solid, yield 30%, 32 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 4H), 7.69 (s, 2H), 7.35 (s, 2H), 1.58 (s, 18H), 1.41 (s, 18H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 161.5, 148.0, 147.0, 142.2, 133.8, 129.6, 127.8, 120.0, 114.3, 35.1, 34.5, 31.8, 30.0. HRMS (EI): calcd for $C_{36}H_{44}N_2O_2$: 536.3471; found: 536.3480.

*4-(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)benzaldehyde (**5b**).* White solid, yield 32%, 21 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.11 (s, 1H), 8.41 (d, J = 7.3 Hz, 2H), 8.04 (d, J = 7.3 Hz, 2H), 7.68 (s, 1H), 7.36 (s, 1H), 1.56 (s, 9H), 1.40 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 191.5, 161.0, 159.3, 148.2, 142.2, 137.7, 133.9, 132.6, 130.1, 127.8, 120.4, 114.5, 35.1, 34.5, 31.7, 30.0. HRMS (EI): calcd for $C_{22}H_{25}NO_2$: 335.1965; found: 335.1958.

*(5,7-Di-tert-butylbenzo[d]oxazol-2-yl)(phenyl)methanone (**6a**).*[20] White solid, yield 74%, 49 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 7.3 Hz, 2H), 7.79 (d, J = 1.8 Hz, 1H), 7.68 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.7 Hz, 2H), 7.50 (d, J = 1.8 Hz, 1H), 1.55 (s, 9H), 1.41 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 180.6, 149.0, 146.9, 141.1, 135.4, 135.1, 134.0, 130.9, 128.5, 122.9, 116.0, 35.2, 34.6, 31.7, 29.9.

*3,5-Di-tert-butylcyclohexa-3,5-diene-1,2-dione (**1aa**).*[21] Colorless liquid, yield 98%, 43 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.91 (s, 1H), 6.18 (s, 1H), 1.24 (s, 9H), 1.20 (s, 9H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 181.0, 179.9, 163.2, 149.8, 133.4, 121.9, 35.9, 35.3, 29.1, 27.7.

*(E)-2-(Benzylideneamino)phenol (**7a**).*[15a] Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (s, 1H), 7.97−7.89 (m, 2H), 7.54−7.45 (m, 3H), 7.34−7.26 (m, 2H), 7.21 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.92 (t, J = 7.6 Hz, 1H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 157.0, 152.2, 135.7, 135.3, 131.6, 128.9, 128.8, 128.8, 120.0, 115.8, 114.9.

*2-Phenylbenzo[d]oxazole (**7b**).*[15a] Colorless solid, yield 79%, 31 mg. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38−8.24 (m, 2H), 7.83 (dd, J = 5.3, 3.7 Hz, 1H), 7.67−7.54 (m, 4H), 7.44−7.37 (m, 2H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$): δ 162.9, 150.6, 142.0, 131.5, 128.8, 127.6, 127.0, 125.0, 124.5, 119.9, 110.6.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01119.

Characterization of catalysts, hot filtration experiment, and copies of NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: zhaopq@licp.cas.cn.

ORCID

Xu Meng: 0000-0002-4131-3383

Notes

The authors declare no competing financial interest.

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