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N-Heterocyclic Carbene (NHC)-Catalyzed One-Pot Aerobic Oxidative Synthesis of 2-Substituted Benzo[*d*]oxazoles, Benzo[*d*]thiazoles and 1,2-Disubstituted Benzo[*d*]imidazoles

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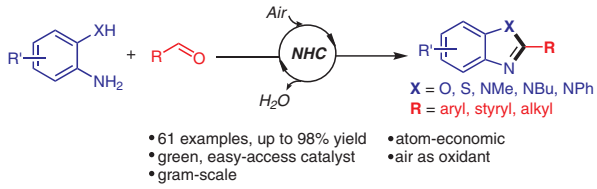

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Abstract N-Heterocyclic carbene (NHC), generated in situ from easily available N-heterocyclic imidazolium salt with air as terminal oxidant, has successfully been utilized as a cheap and efficient catalyst for one-pot aerobic oxidative synthesis of 2-arylbenzo[*d*]oxazoles, 2-substituted benzo[*d*]thiazoles, and 1,2-disubstituted benzo[*d*]imidazoles.

Key words N-heterocyclic carbene, organocatalysis, aerobic oxidation, cyclization, benzazoles

Five-membered heterocyclic rings, such as benzoxazoles, benzothiazoles, and benzimidazoles are versatile building blocks in biologically and therapeutically active compounds, natural products, and functional materials, etc.[1] For example, telmisartan is a well-known angiotensin-receptor blocker used for the treatment of essential hypertension.[2] Pittsburgh compound B is a positron emission tomography (PET) imaging agent for Alzheimers disease,[3] which has entered the stages of clinical trials. In photoredox field, 2-arylbenzo[*d*]oxazole- or 2-aryl benzo[*d*]thiazole-fused iridium/rhodium complexes could function as both the Lewis acid catalyst and the photocatalyst for asymmetric transformations (Figure 1).[4]

Mainly, the synthetic protocol for benzo[*d*]oxazoles, -thiazoles and -imidazoles could be classified into two methods. First, various transition-metal-catalyzed cross-coupling between benzo[*d*]oxazole, -thiazole, -imidazole and expensive/toxic organometallic regents[5] or intramolecular *ortho*-arylation of *o*-haloanilides;[6] second, *ortho*-aminophenol/benzenethiol/aniline coupling with aryl carboxylic acid or analogues,[7] aryl aldehydes,[8] or benzyl alcohols.[9] In

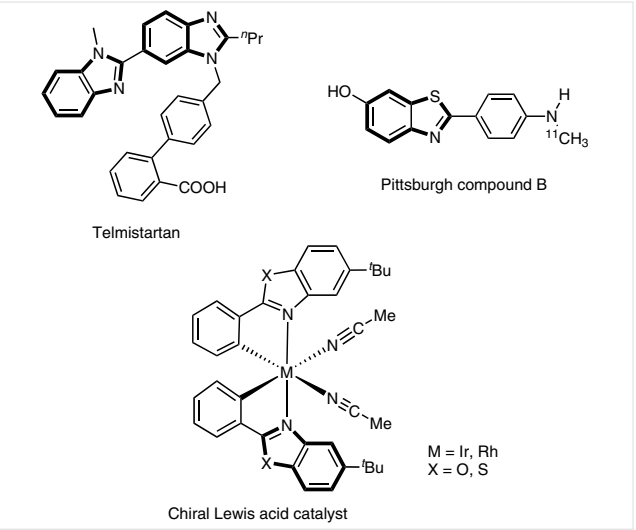


Figure 1 Molecules containing benzazole motif

the last few years, aerobic oxidative cyclization between *ortho*-aminophenol/benzenethiol/aniline and aryl aldehydes with the molecular oxygen/air as the terminal oxidant have frequently been studied. Activated carbon,[10] metal nanoparticles,[11] metal salts,[12] aminoxyl radical 4-methoxy-TEMPO,[13] and cyanide[14] could work as catalysts in the aerobic oxidative cyclization process. However, relatively high catalyst loadings or toxic catalysts are required as well as the scopes and types of substrates are limited in some case. Recently, water as 'ambiphilic catalyst' was applied in the process for the synthesis of various 2-arylbenzazoles;[15] however, the substrates were limited to aromatic aldehydes. Hence, an efficient and versatile catalyst was still needed.

N-Heterocyclic carbene (NHC) is an important class of organocatalyst in the field of umpolung reaction towards aromatic aldehydes,[16] which has been discovered to be a good alternative to the toxic cyanides and utilized in the benzoin condensation. More recently, NHC organocatalyst utilizing oxidant or even molecular oxygen have been applied in various cascade reactions starting with aryl aldehydes.[17]

Inspired from our group's previous studies on NHC[18] and 2-arylbenzo[*d*]oxazoles,[19] we speculated that NHC could be utilized in the aerobic oxidative synthesis of 2-arylbenzo[*d*]oxazole from 2-aminophenol derivatives and benzaldehydes. Herein, we report a one-pot aerobic oxidative synthesis of 2-arylbenzo[*d*]oxazoles, 2-substituted benzo[*d*]thiazoles, and 1,2-disubstituted benzo[*d*]imidazoles with in situ generated NHC from easy-available *N*-heterocyclic imidazolium salts.

To test our hypothesis, the aerobic oxidative cyclization was attempted between 2-amino-4-methylphenol (**1a**) and benzaldehyde (**2a**) catalyzed by in situ generated NHC from imidazolium salts (10 mol%) with K_2CO_3 (50 mol%) (Table 1). Initially, three imidazolium salts with different steric hindered substitutions (Figure 2, NHC precursors **A**, **B**, **C**) were tested as catalysts. To our delight, **B** and **C** could smoothly afford the desired products in 64% and 79% yield, respectively, while **A** showed no catalytic activity for this transformation (Table 1, entries 1–3), which could result from its steric hindered substitution. To consolidate this hypothesis and improve the product yield, N-heterocyclic imidazolium salts **D–I** bearing less steric substitutions were utilized as catalysts (entries 4–9). All these imidazolium salts could afford the product in moderate to good yields. Imidazolium salts with different counter anions slightly affected this catalytic process, and the decrease of the catalytic activity was observed in the series $I^- > PF_6^- > Br^- > Cl^-$ (entries 5–8). Probably, it would result from the counter-anion effect on the imidazolium salts' stability and solubility.[20] Additionally, two benzo[*d*]imidazolium salts **J** and **K**, whose in situ generated carbene were more stable under basic condition,[21] were also tested as NHC precursor and moderate NMR yields were obtained by using NaOH as a stronger base (entries 10, 11). Although the reaction using **I** was complete in 6 hours and high conversion and 83% yield were obtained, considering that the preparation of **I** involved the use of highly toxic iodomethane, **G** was chosen as the NHC precursor for further reaction optimization. Decreasing the amount of base to 25 mol% led to an increased NMR yield of up to 95% (entry 12, 90% isolated yield), while further reducing the base amount, no better conversion was achieved even under prolonged reaction time (entries

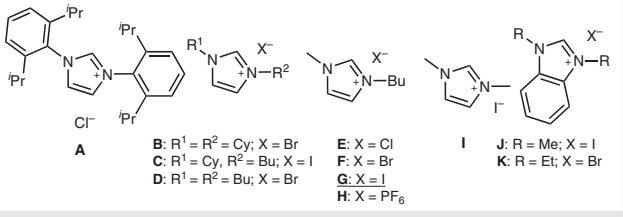
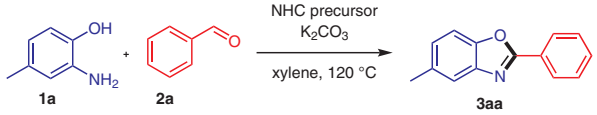
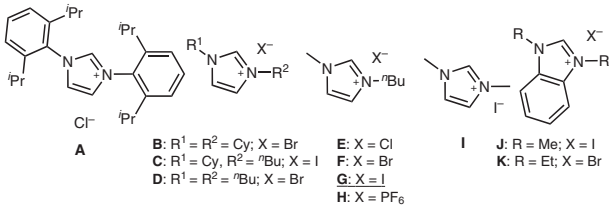


Figure 2 NHC precursors

Table 1 Optimization of Reaction Conditions[a]



Entry	NHC Precursor	Time (h)	Base (equiv)	Yield (%)[b]
1	**A**	16	0.5	trace
2	**B**	16	0.5	64
3	**C**	16	0.5	79 (75)[c]
4	**D**	10	0.5	73
5	**E**	10	0.5	61
6	**F**	10	0.5	73
7	**G**	10	0.5	82
8	**H**	10	0.5	78
9	**I**	6	0.5	83
10	**J**	10	0.1	63[d]
11	**K**	10	0.1	64[d]
12	**G**	**10**	**0.25**	**95 (90)[c]**
13	**G**	12	0.15	74
14	**G**	24	0.15	81
15	–	12	0.5	trace[e]
16	**G**	24	0.5	trace[f]
17	**G**	12	–	trace[g]
18	**G**	12	0.25	48[h]
19	**G**	12	0.25	20[i]
20	**G**	12	0.25	80[j]

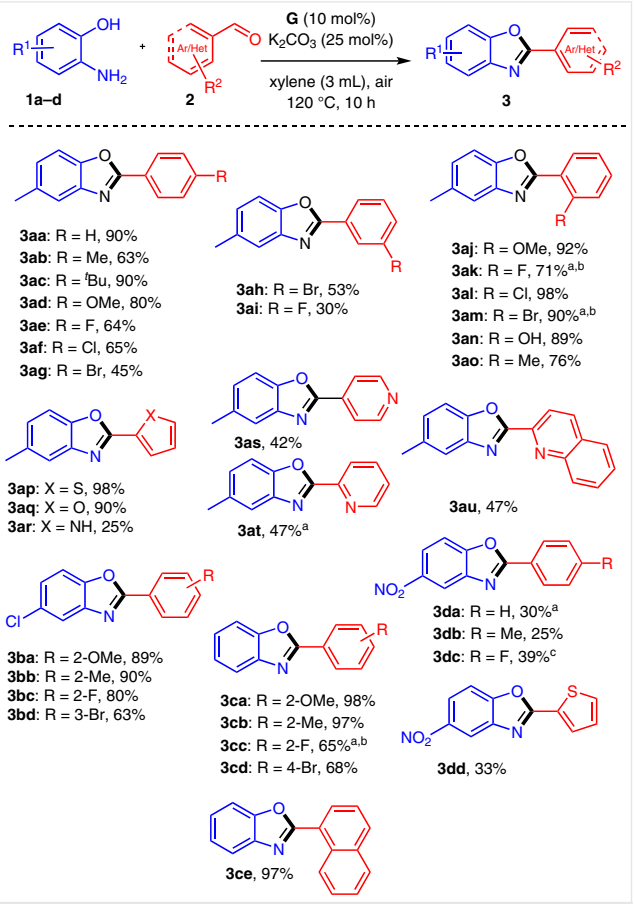


[a] Unless otherwise noted, the reactions were carried on a 1 mmol scale between 2-amino-4-methylphenol and benzaldehyde in a 15 × 150 mm tube in xylene (3 mL, mixture of *o*-, *m*-, and *p*-xylene) in the presence of NHC precursor (10 mol%) and K_2CO_3 at 120 °C.
[b] Yield observed by ^1H NMR spectroscopy.
[c] Isolated yield.
[d] NHC Precursor (5 mol%), 10 mol% NaOH as base, O_2.
[e] Without **G**.
[f] Under N_2 atomsphere.
[g] Without base.
[h] DMF as solvent.
[i] EtOH as solvent, 70 °C.
[j] Toluene as solvent.

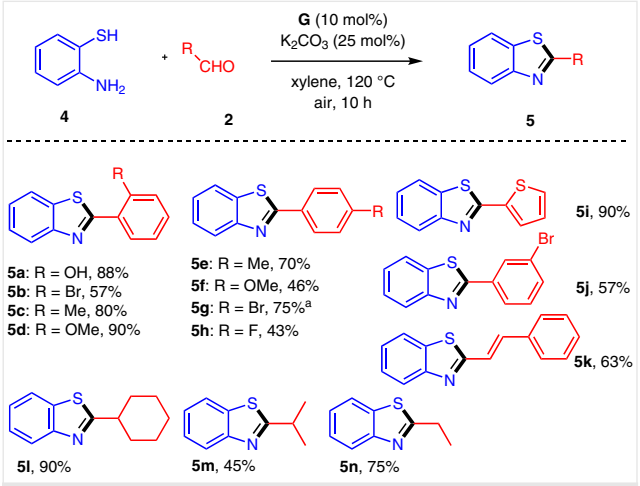
13, 14). Control experiments show that N-heterocyclic imidazolium salt, air, and base were indispensable (entries 15–17). When DMF, ethanol, and toluene were used as solvent instead of xylene, no better yield was noticed and nonpolar aromatic solvent toluene was found to be more effective than polar solvents (DMF or ethanol) under the same reaction conditions (entries 18–20). Notably, no benzoin condensation product was observed in the reaction.[17,22]

With the optimal conditions in hand (Table 1, entry 12), the scope and limitation of the reaction were examined (Scheme 1). First, a wide range of aromatic aldehydes with 2-amino-4-methylphenol (**1a**) were found to be compatible, delivering the corresponding 2-substituted benzo[*d*]oxazoles in good to excellent yields. Aromatic aldehydes with electron-withdrawing or -donating substituents at the *ortho*-position **3aj–ao** generated the target products in good to excellent yields, which may be due to the benefit of *ortho*-substituted group in this oxidative cyclization process. With substituents at the *para*- or *meta*-position, the yields decrease slightly. Second, aromatic aldehydes with heterocyclic rings were also tested. To our delight, the reaction showed good tolerance to thiophene-2-carbaldehyde and furan-2-carbaldehyde affording **3ap** and **3aq**, respectively. More importantly, aromatic aldehydes containing nitrogen atoms, for example, pyrrolyl, pyridinyl, and quinolinyl could also give the corresponding products **3ar–au** in moderate yields. Furthermore, among the different *ortho*-aminophenol derivatives, chloro-substituted and unsubstituted *ortho*-aminophenols afforded the related products **3ba–bd** and **3ca–ce**, respectively, in good yields; 4-nitro-2-aminophenol could also give the desired products **3da–dd**. Under the optimized conditions, the strategy was not feasible for the synthesis of 2-alkylbenzoxazoles or 2-aryloxazolines from the corresponding nonaromatic fragment. In addition, we noticed that when 2-fluorobenzaldehyde was used, small amount of dibenz[*b*,*f*]-1,4-oxazepines **3ak′**, **3bc′**, and **3cc′** were generated via intermolecular cyclization besides the aerobic oxidative products (see Supporting Information).[23]

After examining the scope of the synthesis of 2-substituted benzo[*d*]oxazoles, we turned our attention to apply this catalytic system to construct 2-substituted benzo[*d*]thiazoles (Scheme 2). Different aromatic aldehydes including *ortho*-, *para*-, and *meta*-substituted aromatic aldehyde were successfully fused with the 2-aminobenzenethiol affording the 2-arylbenzo[*d*]thiazoles. These results suggest that electron-donating functional groups have a positive effect on the reaction conversion, while electron-withdrawing ones revealed a slight negative effect (**5a–j**). Additionally, cinnamaldehyde could also successfully afford **5k** in moderate yield under the optimized conditions. More importantly, alkyl aldehydes demonstrated good compatibility in this catalytic system, which afforded the corresponding 2-alkylbenzo[*d*]thiazoles **5l–n** in excellent yields. The apparent success with respect to 2-arylbenzo[*d*]oxaz-



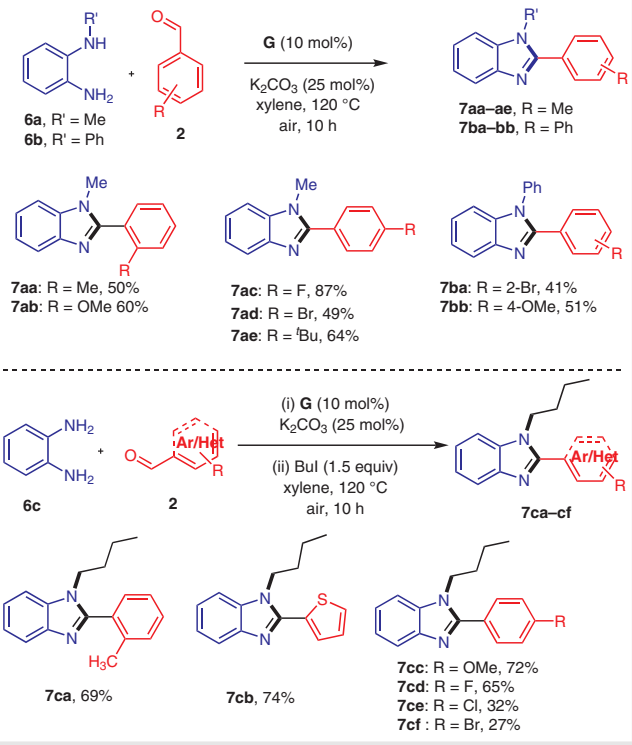
Scheme 1 Aerobic oxidative synthesis of 2-arylbenzo[*d*]oxazoles. *Reagents and conditions*: **1** (1 mmol), **2** (1 mmol), xylene (3 mL), K_2CO_3 (25 mol%), **G** (10 mol%), 120 °C, 10 h, air. Isolated yields are given. [a] 5 mmol scale; [b] **K** (5 mol%), NaOH (10 mol%), O_2; [c] 3 mmol scale.



Scheme 2 Aerobic oxidative synthesis of 2-substituted benzo[*d*]thiazoles. Reactions conditions given in Table1 entry 12 were used. [a] NHC **I** instead of **G** was used.

oles may benefit from the sulfur atom possessing more electrons, and thus a stronger driving force for dehydrogenative aromatization.[24]

After the successful scope of constructing 2-arylbenzo[*d*]oxazoles and 2-substituted benzo[*d*]thiazoles, we tried to expand the catalytic system to the oxidative synthesis of 2-substituted benzo[*d*]imidazoles.[25] However, under the optimized conditions, attempts to synthesize 2-arylbenzo[*d*]imidazoles from *o*-phenylenediamine with aryl aldehydes were unsuccessful. According to previous reports, one molecule of *o*-phenylenediamine was prone to condense with two molecules of benzaldehyde, then isomerized to *N*-benzyl-2-arylimidazo[*d*]imidazoles.[26] Thus, we speculated that monoalkylated *o*-phenylenediamine instead of *o*-phenylenediamine might promote the one-pot synthesis of 1,2-disubstituted benzo[*d*]imidazoles (Scheme 3), which own broad-spectrum biological activities and synthesis challenge.[27] Two commercial N^1-substituted *o*-diaminobenzenes [N^1-methylbenzene-1,2-diamine (**6a**); N^1-phenylbenzene-1,2-diamine, (**6b**)] were then tried as starting materials. To our delight, aerobic oxidative products **7aa–ae**, **ba**, **bb** were formed in good isolated yields. After these successes, we wondered whether the in situ alkylation of *o*-diaminobenzene could furnish the target aerobic oxidative products, so we tried 1-iodobutane as alkylation reagent.[28] When 1.5 equivalents of 1-iodobutane were introduced into the catalytic system, 1,2-disubstituted benzo[*d*]imidazoles **7ca–cf** were successfully obtained in a one-pot three-component synthesis approach (Scheme 3).



Scheme 3 Aerobic oxidative synthesis of N-substituted-2-arylbenzo[*d*]imidazoles. Reactions were carried out on a 1 mmol scale; isolated yields are shown.

Furthermore, to demonstrate the practicability of this method, the preparation of 2-arylbenzo[*d*]oxazoles **3ad**, **3ac**, **3am**, and 2-arylbenzo[*d*]thiazole (**5i**) were tried on a gram-scale (Figure 3). The desired aerobic oxidative synthesis was proved to be effective with elongated time and/or changing to oxygen atmosphere.

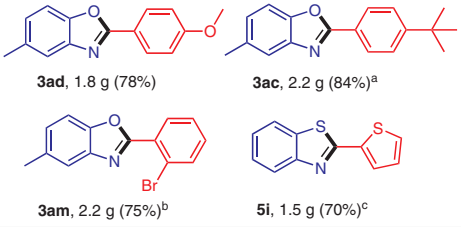
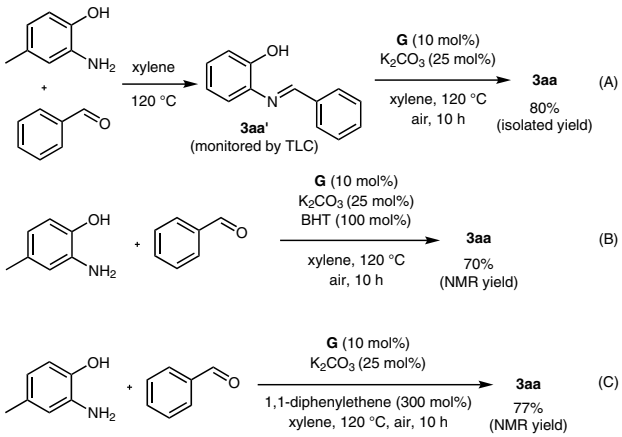


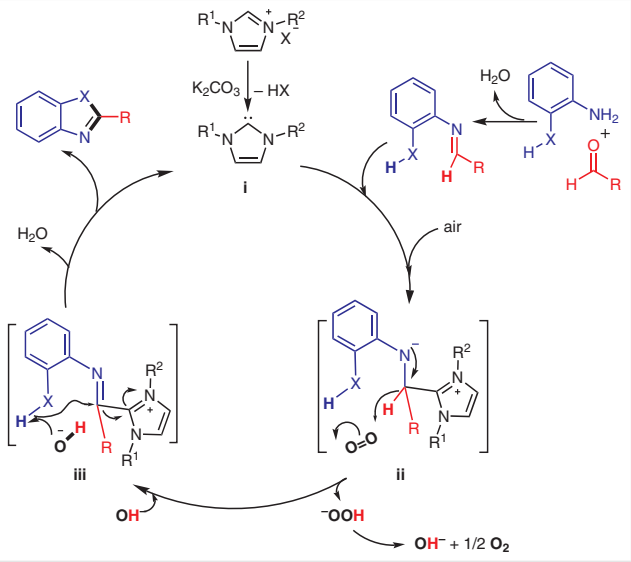
Figure 3 Gram-scale reactions. Reactions were conducted in a 50 mL tube on a 10 mmol scale, xylene (30 mL), K_2CO_3 (25 mol%), **G** (10 mol%), 120 °C, 48 h, air; isolated yield are shown. [a] Under O_2 atmosphere, 6 h; [b] **K** (5 mol%), NaOH (10 mol%), O_2; [c] NHC **I** was used instead of **G**.

Several experiments were carried out to have an insight into the reaction mechanism (Scheme 4). We found that the condensation product **3aa′** between **1a** and benzaldehyde was smoothly converted into **3aa** in quantitative yield (Scheme 4, A), which demonstrated the Schiff base phenol might be one intermediate in the catalytic cycle. Additionally, the aerobic oxidative process from imine **3aa′** to target product **3aa** was thought to involve free radical species.[13a,29] To test the presence of a radical intermediate, two radical-trapping experiments were performed. Both 2,6-di-*tert*-butyl-4-methylphenol (BHT) and 1,1-diphenylethene were employed in the optimal conditions and the desired products were obtained in 70% and 77% yield (Scheme 4, B, C), which indicated that this transformation is unlikely to involve a radical intermediate.[30]



Scheme 4 Control experiments

Finally, on the basis of the above results and related NHC-catalyzed aerobic reaction,[17] a tentative mechanism is proposed for 2-arylbenzo[*d*]oxazoles as shown in Scheme 5. N-Heterocyclic carbene **i** is first generated in situ by deprotonation of the N-heterocyclic imidazolium salt in the presence of K_2CO_3, which plays a role of cyanide, and undergoes a nucleophilic addition to imine C=N bond,[14] forming the intermediate **ii**. Then the aldehyde proton (red font) is transferred to molecular oxygen,[22] which forms the intermediate **iii** and HOO^-. HOO^- decomposes to hydroxide ion and O_2 under basic solution. Driven by the aromatization force and the deprotonation of HX, nucleophilic attack from the anion X^- forms the aerobic oxidative product with concomitant regeneration of the NHC catalyst.[17o] Meanwhile, hydroxide ion traps the proton, forming the by-product, water.[31]



Scheme 5 Proposed mechanism for 2-arylbenzo[*d*]oxazoles

In summary, N-heterocyclic carbene, generated in situ from an easily available N-heterocyclic imidazolium salt was discovered to be an efficient catalyst for one-pot aerobic oxidative synthesis of 2-arylbenzo[*d*]oxazoles, 2-substituted benzo[*d*]thiazoles as well as 1,2-disubstituted benzo[*d*]imidazoles. The strategy presents high efficiency, atom economy, and good tolerance over broad scopes of substrates. Both catalyst and oxidant are environment-friendly and easily accessible. The gram-scale preparation demonstrates that this method is practical. Initial mechanistic studies demonstrated that the process does not involve free radicals. Meanwhile, the extension of this catalytic system for the preparation of other useful heterocyclic compounds is in progress in our laboratory.

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All commercially available compounds were purchased and used without purification. Reaction temperatures are reported as the temperature of the bath surrounding the reaction vessel, unless otherwise stated. Toluene, xylenes (mixture of *o*-, *m*-, and *p*-xylene), DMF, CH_2Cl_2, and EtOH were purchased from commercial vendors and used without purification.

Analytical TLC was performed on GF 254 plates. Flash chromatography was performed on silica gel (200–300 mesh) by standard technical eluting with solvents as indicated. ^1H and ^{13}C NMR spectra were recorded at 295 K in $CDCl_3$ or DMSO-d_6. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_H = 7.26, δ_C = 77.16; CD_3OD: δ_H = 3.31, δ_C = 49.00; DMSO-d_6: δ_H = 2.50, δ_C = 39.52). For ^{19}F NMR, chemical shifts refer to an external calibration using $CFCl_3$ (δ = 0.00). Data for ^1H NMR are reported as follows: chemical shift, multiplicity (standard abbreviations), coupling constants (*J*) in Hz, and integration. Mass spectrometric data were obtained using ESI (electrospray ionization, Q-Tof, positive ion) mode, and GC-MS (electron impact ionization). All FT-IR spectra of solids were recorded as KBr pellets. Melting points of the reported values are tested in capillary auxiliary.

2-Arylbenzo[*d*]oxazoles 3 and 2-Substituted Benzo[*d*]thiazoles 5; General Procedure A

A 15 × 150 mm glass tube was charged with *o*-aminophenol (**1**)/benzenethiol (**4**) (1 mmol) and the corresponding aldehyde (1 mmol), xylenes (3 mL), K_2CO_3 (34 mg, 0.25 mmol), and NHC precursor **G** (26 mg, 0.1 mmol). The glass tube containing the mixture was lowered into a pre-heated oil bath, and the mixture was stirred vigorously for 10 h under air atmosphere. After completion of the reaction, the mixture was diluted with EtOAc, and filtered. The organic solution was concentrated under vacuum, and the residue was purified by silica gel column chromatography, which afforded the corresponding oxidative cyclization product.

N-Substituted 2-Arylbenzo[*d*]imidazoles 7; General Procedures B and C

Procedure B (for **7aa–ae**): A 15 × 150 mm glass tube was charged with **6a** (195 mg, 1 mmol; salts with two molecules of HCl) and Et_3N (212 mg, 2.1 mmol). The mixture was stirred at 120 °C by immersing the glass tube in a preheated oil-bath for 0.5 h, then the corresponding aromatic aldehyde (1 mmol), NHC precursor **G** (10 mol%), and K_2CO_3 (25 mol%) were added sequentially. The resulting mixture was stirred at 120 °C using a preheated oil bath for an additional 10 h. After completion of the reaction, the solution was transferred into a 25 mL round-bottomed flask, and concentrated under reduced pressure. The residue was purified by flash silica column chromatography, which afforded the targeted product.

Procedure C (for **7ba–bb**): A 15 × 150 mm tube was charged with **6b** (184 mg, 1 mmol), the corresponding aromatic aldehyde (1 mmol), NHC precursor **G** (10 mol%), and K_2CO_3 (25 mol%). The mixture was stirred at 120 °C by immersing the glass tube in a preheated oil bath for 10 h. After completion of the reaction, the solution was transferred into a 25 mL round-bottomed flask, and concentrated under reduced pressure. The residue was purified by flash silica column chromatography, which afforded the targeted product.

Details of all imidazolium salts and products are given in the Supporting Information. Analytical and spectroscopic data for some selected compounds are given below.

2-(3-Fluorophenyl)-5-methylbenzo[*d*]oxazole (3ai)[32a]

Following general procedure A on a 1 mmol scale, **3ai** was obtained as a white solid; yield: 154 mg (30%); mp 83–85 °C; R_f = 0.3 (PE/EtOAc 50:1).

FT-IR (KBr): 3074, 3016, 2968, 2930, 1559, 1469, 1264, 1210, 874, 806 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.7 Hz, 1 H), 7.94 (d, *J* = 9.4 Hz, 1 H), 7.57 (s, 1 H), 7.54–7.41 (m, 2 H), 7.31–7.15 (m, 2 H), 2.50 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.8 (d, *J* = 246.8 Hz), 161.8, 149.0, 142.1, 134.6, 130.5 (d, *J* = 8.1 Hz), 129.3 (d, *J* = 8.6 Hz), 126.6, 123.2 (d, *J* = 2.6 Hz), 120.1, 118.3 (d, *J* = 21.3 Hz), 114.4 (d, *J* = 24.0 Hz), 110.0, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –111.90 (td, *J* = 8.9, 5.8 Hz).

MS: *m*/*z* (%) = 227 (100), 226 (38), 78 (38).

5-Methyl-2-(quinolin-2-yl)benzo[*d*]oxazole (3au)

Following general procedure A on a 1 mmol scale, **3au** was obtained as a grey solid; yield: 101 mg (47%); mp 141–143 °C; R_f = 0.3 (PE/EtOAc 15:1).

FT-IR (KBr): 3443, 3051, 2920, 2856, 1594, 1542, 1503, 1350, 1339, 1314, 1075, 959, 835, 796, 762, 594 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.42 (t, *J* = 11.7 Hz, 1 H), 8.34 (t, *J* = 6.8 Hz, 1 H), 8.31 (d, *J* = 8.6 Hz, 1 H), 7.85 (t, *J* = 9.5 Hz, 1 H), 7.79 (t, *J* = 7.6 Hz, 1 H), 7.69–7.52 (m, 3 H), 7.24 (d, *J* = 8.3 Hz, 1 H), 2.50 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.6, 149.5, 148.0, 146.0, 142.0, 137.1, 134.9, 130.3, 130.2, 128.6, 128.0, 127.6, 127.5, 120.5, 120.2, 110.8, 21.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{13}N_2O$: 261.1028; found: 261.1022.

5-Nitro-2-(thiophen-2-yl)benzo[*d*]oxazole (3dd)[32b]

Following general procedure A on a 1 mmol scale, after completion of the reaction finished, the solution was concentrated under reduced pressure, and the residue was recrystallized from PE/EtOAc (10:1), which afforded **3dd** as a red colored solid; yield: 81 mg (33%); mp 182–183 °C; R_f = 0.4 (PE/EtOAc 10:1).

FT-IR (KBr): 3109, 3080, 1620, 1527, 1348, 1264, 995, 809, 745, 720, 691 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 8.56 (d, *J* = 1.8 Hz, 1 H), 8.29 (dd, *J* = 8.9, 2.0 Hz, 1 H), 8.04 (dd, *J* = 10.3, 4.0 Hz, 2 H), 7.98 (d, *J* = 8.9 Hz, 1 H), 7.33 (t, *J* = 4.3 Hz, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 161.7, 154.1, 145.5, 142.3, 133.9, 132.4, 129.6, 127.8, 121.7, 115.7, 111.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_7N_2O_3S$: 247.0177; found: 247.0172.

2-Cyclohexylbenzo[*d*]thiazole (5l)[32c]

Following general procedure A on a 1 mmol scale, **5l** was obtained as a colorless oil; yield: 160 mg (90%); R_f = 0.35 (PE/EtOAc 100:1).

FT-IR (neat): 3429, 3071, 2926, 2851, 1514, 1448, 1436, 1313, 1244, 1146, 1124, 1094, 1014, 992, 757, 728 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.0 Hz, 1 H), 7.81 (dd, *J* = 7.9, 0.4 Hz, 1 H), 7.48–7.36 (m, 1 H), 7.29 (dt, *J* = 12.5, 2.7 Hz, 1 H), 3.08 (tt, *J* = 11.7, 3.6 Hz, 1 H), 2.19 (dd, *J* = 13.3, 2.1 Hz, 2 H), 1.93–1.80 (m, 2 H), 1.79–1.70 (m, 1 H), 1.62 (qt, *J* = 12.2, 6.1 Hz, 2 H), 1.51–1.35 (m, 2 H), 1.35–1.23 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.5, 153.1, 134.5, 125.8, 124.5, 122.5, 121.5, 43.4, 33.4, 26.0, 25.8.

MS: *m*/*z* (%) = 217 (12), 162 (100), 149 (95).

2-Isopropylbenzo[*d*]thiazole (5m)[32d]

Following general procedure A on a 1 mmol scale, **5m** was obtained as a colorless oil; yield: 80 mg (45%); R_f = 0.3 (PE/EtOAc 100:1).

FT-IR (neat): 3436, 2966, 2936, 2869, 1518, 1456, 1437, 1094, 1037, 1013, 758, 729 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 7.9 Hz, 1 H), 7.84 (dd, *J* = 8.0, 0.5 Hz, 1 H), 7.49–7.38 (m, 1 H), 7.38–7.29 (m, 1 H), 3.43 (hept, *J* = 6.9 Hz, 1 H), 1.49 (d, *J* = 6.9 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.6, 153.1, 134.7, 125.8, 124.5, 122.6, 121.5, 34.1, 22.9

MS: *m*/*z* (%) = 177 (32), 162 (100).

2-Ethylbenzo[*d*]thiazole (5n)[32d]

Following general procedure A on a 1 mmol scale, **5n** was obtained as a colorless oil; yield: 123 mg (75%); R_f = 0.2 (PE/EtOAc 100:1).

FT-IR (neat): 3443, 2973, 2934, 2879, 1522, 1455, 1436, 1310, 1066, 947, 759, 729 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.0 Hz, 1 H), 7.83 (dd, *J* = 8.0, 0.5 Hz, 1 H), 7.44 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1 H), 7.37–7.29 (m, 1 H), 3.19–3.06 (m, 2 H), 1.47 (dd, *J* = 9.9, 5.3 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5, 153.2, 135.0, 125.8, 124.6, 122.5, 121.5, 27.8, 13.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{10}NS$: 164.0534; found: 164.0528.

2-[4-(*tert*-Butyl)phenyl]-1-methyl-1*H*-benzo[*d*]imidazole (7ae)[32e]

Following general procedure B, **7ae** was obtained as a white solid; yield: 170 mg (64%); R_f = 0.3 (PE/EtOAc 10:1); mp 152–154 °C.

FT-IR (KBr): 3051, 2965, 2943, 2901, 2862, 1610, 1485, 1472, 1460, 1434, 1386, 1328, 835, 733, 604 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 3.2 Hz, 1 H), 7.72 (d, *J* = 6.8 Hz, 2 H), 7.53 (t, *J* = 15.2 Hz, 2 H), 7.35 (d, *J* = 21.4 Hz, 3 H), 3.92–3.70 (m, 3 H), 1.40 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.9, 152.9, 142.9, 136.6, 129.1, 127.2, 125.6, 122.6, 122.3, 119.7, 109.5, 34.8, 31.6, 31.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}N_2$: 265.1705; found: 265.1699.

2-(2-Bromophenyl)-1-phenyl-1*H*-benzo[*d*]imidazole (7ba)[32f]

Following general procedure C, **7ba** was obtained as a yellow solid; yield: 145 mg (41%); mp 178–180 °C; mp 178–180 °C; R_f = 0.2 (PE/EtOAc 10:1).

FT-IR (KBr): 3064, 3013, 1597, 1495, 1452, 1426, 1383, 1323, 771, 758, 741, 728, 697 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.6 Hz, 1 H), 7.55 (d, *J* = 7.9 Hz, 1 H), 7.47 (d, *J* = 6.7 Hz, 1 H), 7.43–7.22 (m, 11 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.6, 142.8, 135.9, 135.7, 132.8, 132.5, 132.4, 131.1, 129.4, 128.1, 127.0, 126.7, 123.7, 123.6, 123.0, 120.3, 110.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{14}BrN_2$: 349.0340 (100.0%), 351.0320 (97.3%); found: 349.0335 (100.0%), 351.0315 (97.3%).

2-(4-Methoxyphenyl)-1-phenyl-1*H*-benzo[*d*]imidazole (7bb)

Following general procedure C, **7bb** was obtained as a white solid; yield: 154 mg (51%); mp 136–138 °C; R_f = 0.3 (PE/EtOAc 10:2).

FT-IR (KBr): 3055, 3039, 2991, 2939, 2834, 1609, 1494, 14833, 1451, 1381, 1324, 1250, 1172, 1062, 831, 749, 699, 604 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 1 H), 7.57–7.46 (m, 5 H), 7.33 (d, *J* = 7.5 Hz, 3 H), 7.28–7.22 (m, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 3.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.5, 152.4, 143.0, 137.2, 130.9, 129.8, 128.5, 127.5, 123.0, 122.8, 122.3, 119.5, 113.7, 110.2, 55.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{17}N_2O$: 301.1341; found: 301.1348.

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Supporting Information

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