FULL PAPER DOI: 10.1002/adsc.202001521

Advanced Synthesis & Catalysis

[3+1+1] Annulation Reaction of Benzo-1,2-Quinones, Aldehydes and Hydroxylamine Hydrochloride: Access to Benzoxazoles with Inorganic Nitrogen Source

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Manuscript received: December 6, 2020; Revised manuscript received: February 17, 2021;
Version of record online: March 9, 2021

Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.202001521

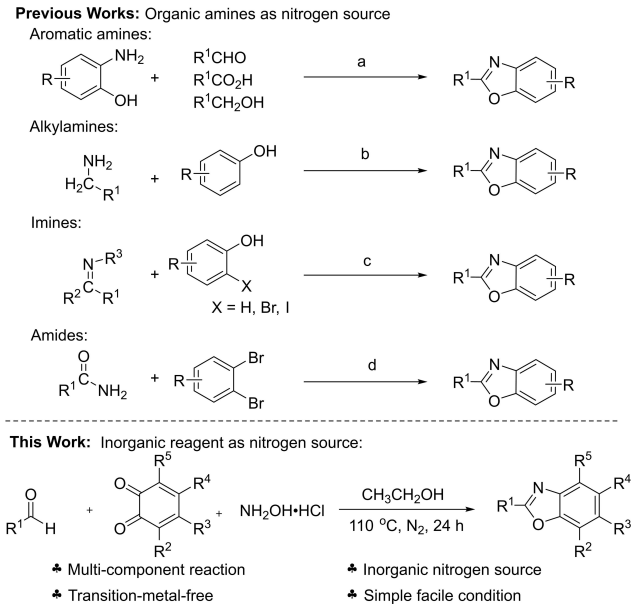
Abstract: A synthesis of benzoxazoles with an inorganic nitrogen source is reported. By employing large-tonnage industrial feedstock inorganic hydroxylamine hydrochloride as the nitrogen source, its [3+1+1] annulation reaction with benzo-1,2-quinones and aldehydes delivers various useful benzoxazoles in high yields. Preliminary mechanistic studies prove that the quinone oxime rather than the aldehyde oxime is the reaction intermediate.

Keywords: multi-component reaction; benzoxazoles; inorganic nitrogen source; annulation

Introduction

Benzoxazole skeletons are extraordinarily valuable structures existed in multidisciplinary fields, such as natural products, materials, pharmaceuticals, and biologically active molecules.[1–2] Therefore, the development of efficient methods for the construction of benzoxazoles becomes a more and more important research topic in synthetic chemistry.[3–8] According to nitrogen source for the construction of the benzoxazole rings, these well documented methods could be classified into four types: 1) condensation of 2-hydroxyanilines with carbonyl-containing substrates (Scheme 1, a),[3] 2) transition-metal-catalyzed annulation reaction of alkyl amines with phenol derivatives (Scheme 1, b),[4] 3) tandem cyclization reactions of imines with phenol and their analogues (Scheme 1, c),[5] and 4) intermolecular coupling reactions of amides with 1,2-dihalogenated aromatic compounds (Scheme 1, d).[6] Despite of this progress, however, these reported synthetic methods generally require the organic amine compounds as the nitrogen source to construct the benzoxazole ring. However, the method for the construction of these useful compounds with an inorganic amino source has not been reported.

Hydroxylamine hydrochloride is a well-known inorganic reagent. As an inexpensive and abundant industry feedstock in the areas of chemistry and



Scheme 1. Nitrogen Source in the Synthesis of Benzoxazoles.

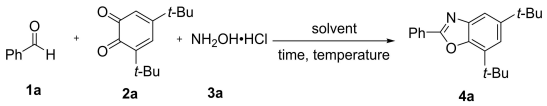
chemical industry, it has been used to construct various high value-added *N*-heterocycles.[9] To the best of our knowledge, the utilizatioin of hydroxylamine hydrochloride as the inorganic nitrogen source for the synthesis of benzoxazoles has not been reported. Benzo-1,2-quinones, as a class of stable and readily available raw materials, have been employed as oxidants in many oxidative transformations,[10] and served as fundamental building blocks inmaterial science,[11] ligand design,[12] catalyst engineering,[13] and the construction of complexmolecules.[14] As our recent interest for the construction of heterocyclic compounds with benzo-1,2-quinones,[15] we herein describe a highly chemoselective [3 + 1 + 1] annulation of benzo-1,2-quinones, aldehydes and hydroxylamine hydrochloride for the direct synthesis of benzoxazoles under transition-metal-free conditions. This protocol features operationally simple, a broad substrate scope, high yields, valuable functional group tolerance, and gram-scalable.

Results and Discussion

We commenced our exploration with optimization studies by screening the reaction parameters of aldehyde **1a**, benzo-1,2-quinone **2a** and hydroxylamine hydrochloride **3a**. The desired product **4a** was detected by NMR in 22% yield, when CH_3CN was used as the solvent at 110 °C under N_2 for 12 h (Table 1, entry 1). Then different types of solvents were screened. Nonprotic polar solvent such as DMSO, DMF, DMA, and NMP could afford the desired product **4a** in reasonable yields (entries 2–5), while nonprotic nonpolar solvent seemed to be fatal to this transformation, because only trace amount of product **4a** was detected under these conditions (entries 6–8). Gratifyingly, a protic polar solvent of CH_3CH_2OH improved the yield of **4a** to 65% (entry 9). Moreover, changing the reaction temperature in either direction eroded the yield of **4a** slightly (entries 10–11). Prolonging the reaction time to 24 h, the NMR yield of **4a** was further enhanced to 73% (entries 12–13).

With the established reaction conditions in hand (Table 1, entry 13), the scope of the aldehydes was explored firstly for this cyclization reaction, and the results were summarized in Table 2. In general, a series of aldehydes with both electron-donating and electron-withdrawing substituents at the *para*-, *meta*-, and *ortho*- position of the phenyl ring has no influence on the conversion, the corresponding products **4a**–**w** were isolated in highly yields. Functional groups such as alkoxy, methylthio, amino, halo, nitro, cyano and trifluoromethyl groups were well tolerated under this reaction system, providing ample potential for further synthetic utilities. Moreover, the structure of **4s** was unambiguously confirmed by single-crystal X-ray crystallography.[16] 1-Naphthaldehyde and 2-naphthaldehyde gave the corresponding products **4x** and **4y** in 60% and 62% yields, respectively. Different heteroaromatic aldehydes such as pyridyl, thienyl, and furanyl aldehydes were well tolerated, and the desired products **4z**–**4ac** were obtained in moderate to good yields. Cinnamaldehyde was also found to be good substrate

Table 1. Optimization of the reaction conditions.[a]

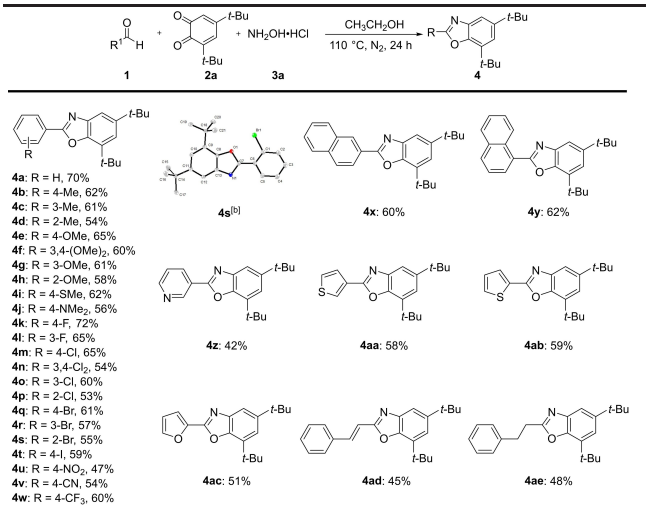


1a 2a 3a 4a

Entry	Solvent	Time (h)	Temp (°C)	Yield of **4a** (%)[b]
1	CH_3CN	12	110	22
2	DMSO	12	110	25
3	DMF	12	110	45
4	DMA	12	110	45
5	NMP	12	110	10
6	DCE	12	110	trace
7	THF	12	110	trace
8	toluene	12	110	trace
9	CH_3CH_2OH	12	110	65
10	CH_3CH_2OH	12	100	53
11	CH_3CH_2OH	12	120	60
12	CH_3CH_2OH	18	110	70
13	**CH_3CH_2OH**	**24**	**110**	**73(70)**

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.2 mmol), **3a** (0.4 mmol), solvent (2.0 mL) under N_2 for 12 h.
[b] Determined by ^1H NMR using $BrCH_2CH_2Br$ as the internal standard. The value in parentheses is the isolated yield.

Table 2. Substrate Scope of Aldehydes.[a]



[a] Reaction conditions: **1** (0.4 mmol), **2a** (0.2 mmol), **3a** (0.4 mmol), CH_3CH_2OH (2.0 mL), 110 °C, N_2, 24 h. Isolated yield.
[b] ORTEP representation with 50% probability thermal ellipsoids of a crystal structure of **4s**.

to give product **4 ad** in 45% yield. In addition, aliphatic 3-phenylpropanal also delivered the desired product **4 ae** in acceptable yield.

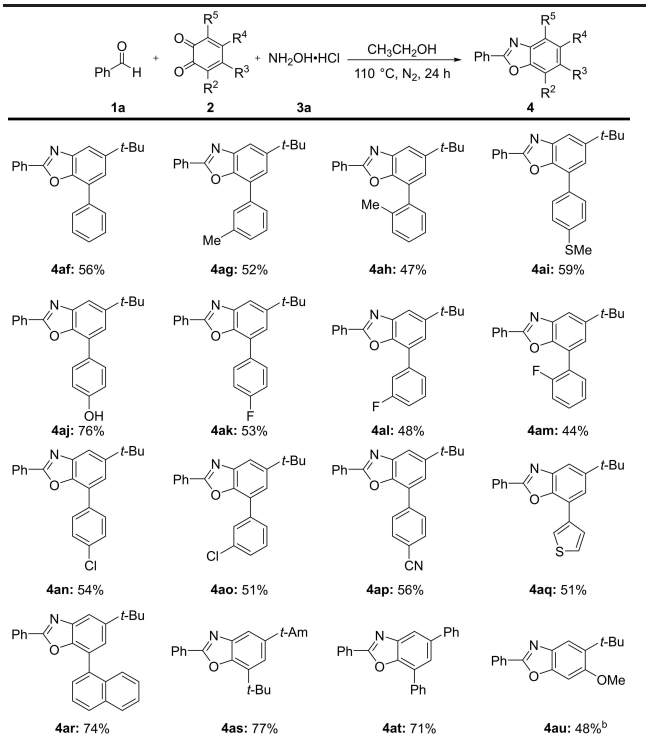
To further define the generality of our method, the substrate scope was extended to different benzo-1,2-quinones (Table 3). Pleasingly, diverse *di*-substituted benzo-1,2-quinones derivatives could undergo reaction smoothly with **1 a** and **3 a** to give the corresponding products in moderate to good isolated yields. Benzo-1,2-quinones with both electron-donating substitutents such as methyl, and methylthio groups, and electron-withdrawing substitutents such as fluoro, chloro, and cyano groups, were well tolerated, the obtained products **4 af**–**4 au** might be beneficial for further coupling reactions. It is worth mentioning that unprotected hydroxyl group could also be tolerated under the standard reaction conditions, delivering the desired product **4 aj** in 76% yield. Heteroaromatic benzo-1,2-quinones also afforded product **4 aq** in 51% yield.

To demonstrate the potential utility of this reaction, a 5 mmol scale reaction was performed under the standard reaction to give product **4 a** in 60% yield (Scheme 2).

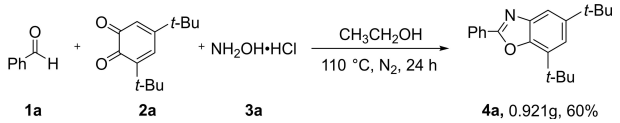
A series of mechanistic experiments were performed to further clarify the reaction pathway as shown in Scheme 3. Quinone oxime **5** was synthesized, which could give the desired product **4 a** in 88% yield under the standard reaction conditions (Scheme 3, eq 1), however the aldehyde oxime **6** could not afford the desired product **4 a** under the standard reaction conditions (Scheme 3, eq 2). These results indicated that the quinone oxime **5** rather than aldehyde oxime **6** was the reaction intermediate. 3,5-Di-*tert*-butylbenzene-1,2-diol **7** was used instead of 3,5-Di-*tert*-butyl-*o*-benzoquinone **2 a**, product **4 a** was detected in $<2\%$ yield, which also ruled out compound **7** as an intermediate in this reaction (Scheme 3, eq 3). Importantly, the oxidation of 3,5-di-*tert*-butylbenzene-1,2-diol **7** to 3,5-di-*tert*-butyl-*o*-benzoquinone **2 a** was difficult under this copper-free reaction system,[4c] because only a trace amount of **4 a** was detected (Scheme 3, eq 4). It is noted that when air instead of N_2 was tested, the corresponding product **4 a** was obtained in 26% yield (Scheme 3, eq 5).

Furthermore, compared with aldehyde oxime **6** the kinetic dynamic analysis showed that quinone oxime **5** was generated more efficiently by the condensation of benzo-1,2-quinone **2 a** and hydroxylamine hydrochloride **3 a** under our standard reaction con-

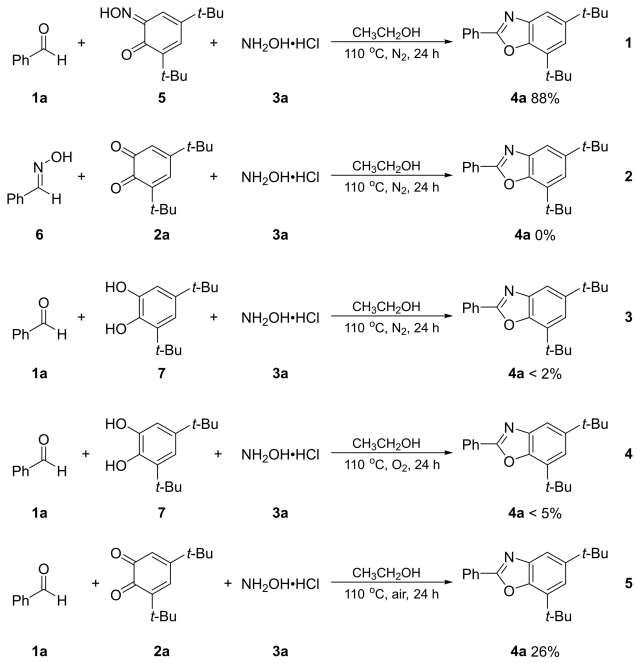
Table 3. Substrate Scope of Benzo-1,2-quinones.[a]



[a] Reaction conditions: **1 a** (0.4 mmol), **2** (0.2 mmol), **3 a** (0.4 mmol), CH_3CH_2OH (2.0 mL), 110 °C, N_2, 24 h. Isolated yield.
[b] CH_3OH as solvent.



Scheme 2. Gram-Scale Synthesis.



Scheme 3. Control Experiments.

ditions (Figure 1). Significantly, the structure of intermediate **5** was also characterized by X-ray diffraction analysis.[16]

Based on above investigations and previous reports,[3–14] we tentatively proposed the reaction mechanism in Scheme 4. Initially, the condensation of the hydroxylamine hydrochloride **3a** with benzo-1,2-quinone **2a** gave the quinone oxime intermediate **5**, which reacted with **1a** to form intermediate **A**. The subsequent intramolecular cyclization of **A** afforded intermediate **B**,[4b] which then gave the desired product **4a** by dehydration.

Conclusion

In summary, we have developed a novel strategy to synthesize benzoxazoles through a [3+1+1] annulation protocol of benzo-1,2-quinones, aldehydes and hydroxylamine hydrochloride. Remarkably, useful benzoxazoles could be directly synthesized with an inorganic amino source. This protocol features operationally simple, a broad substrate scope, high yields, valuable functional group tolerance, and gram-scalable. Further explorations of hydroxylamine hydrochloride to construct nitrogen-containing heterocycles are in progress in our laboratory.

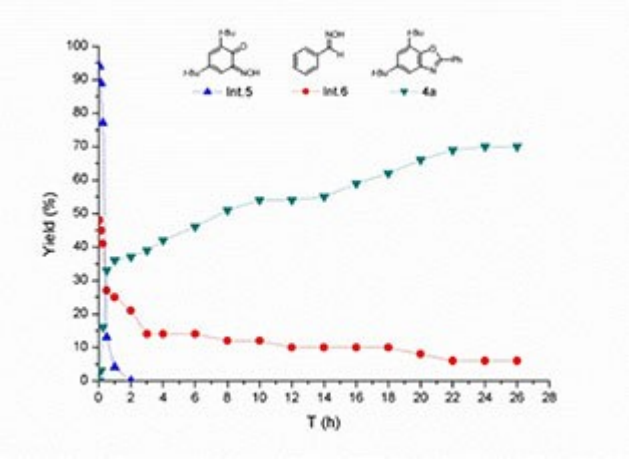
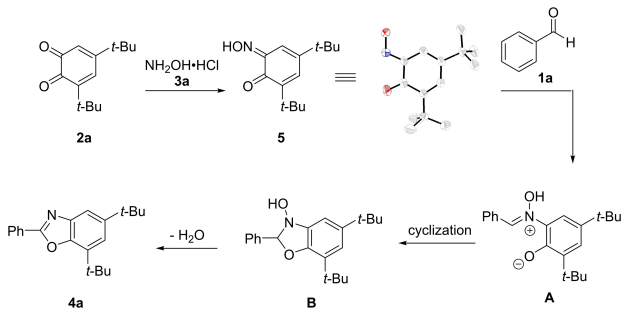


Figure 1. Diagram of Yields with Time Variation.



Scheme 4. Proposed mechanism.

Experimental Section

General Procedure for the Synthesis of Benzoxazoles 4

A 25 mL oven-dried Schlenk tube equipped with a magnetic stirring bar, aldehydes **1** (0.4 mmol), benzo-1,2-quinonnes **2** (0.2 mmol), $NH_2OH{\cdot}HCl$ **3a** (0.4 mmol), and CH_3CH_2OH (2.0 mL) was vigorously stirred at 110 °C for 24 h under N_2. Then the mixture was cooled to room temperature, added water (15 mL), extracted with EtOAc (15 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Further purification by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) provided the product **4**.

Procedure for the Synthesis of Benzoxazole 4a on a Preparative Scale

A 250 mL oven-dried round-bottom flask equipped with a magnetic stirring bar, aldehydes **1a** (10.0 mmol), benzo-1,2-quinonnes **2a** (5.0 mmol), $NH_2OH{\cdot}HCl$ **3a** (10.0 mmol), and CH_3CH_2OH (50.0 mL) was vigorously stirred at 110 °C for 24 h under N_2. Then the mixture was cooled to room temperature, added water (150 mL), extracted with EtOAc (150 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Further purification by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) provided the product **4a** in 60% yield (0.921 g).

5,7-Di-*tert*-butyl-2-phenylbenzo[*d*]oxazole (4a). 43.1 mg, 70% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 4.0 Hz, 2H), 7.67 (s, 1H), 7.53 (s, 3H), 7.32 (s, 1H), 1.57 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 147.8, 146.9, 142.2, 133.7, 131.2, 128.9, 127.6, 127.4, 119.6, 114.2, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2955, 1558, 1471, 1379, 1179, 1056 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{25}NO$ + H, 308.2009; found, 308.2012.

5,7-Di-*tert*-butyl-2-(*p*-tolyl)benzo[*d*]oxazole (4b). 39.8 mg, 62% yield; yellow soild, mp: 90–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.6 Hz, 2H), 7.67 (s, 1H), 7.32–7.34 (m, 3H), 2.44 (s, 3H), 1.57 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 147.6, 146.8, 142.3, 141.6, 133.6, 129.6, 127.4, 124.8, 119.3, 114.1, 35.0, 34.5, 31.8, 30.0, 21.6; IR (KBr): 2958, 1589, 1472, 1387, 1182, 1067 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{27}NO$ + H, 322.2165; found, 322.2167.

5,7-Di-*tert*-butyl-2-(*m*-tolyl)benzo[*d*]oxazole (4c). 39.2 mg, 61% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.09 (m, 2H), 7.67 (s, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.32–7.35 (m, 2H), 2.47 (s, 3H), 1.57 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 147.7, 146.9, 142.3, 138.7, 133.7, 132.0, 128.8, 127.9, 127.4, 124.5, 119.5, 114.1, 35.1, 34.5, 31.8, 30.0, 21.4; IR (KBr): 2957, 1558, 1472, 1384, 1171, 1069 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{27}NO$ + H, 322.2165; found, 322.2163.

5,7-Di-*tert*-butyl-2-(*o*-tolyl)benzo[*d*]oxazole (4 d). 34.7 mg, 54% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.6 Hz, 1H), 7.71 (s, 1H), 7.33–7.42 (m, 4H), 2.83 (s, 3H), 1.56 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 147.6, 146.6, 142.1, 138.4, 133.7, 131.7, 130.7, 130.0, 126.6, 126.1, 119.5, 114.3, 35.1, 34.4, 31.9, 30.0, 22.3; IR (KBr): 2955, 1681, 1554, 1470, 1383, 1041 cm^{-1}; HRMS (ESI, m/z): $[M+Na]^+$ Calcd. for $C_{22}H_{27}NO+Na$, 344.1985; found, 344.1986.

5,7-Di-*tert*-butyl-2-(4-methoxyphenyl)benzo[*d*]oxazole (4 e). 43.8 mg, 65% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.4 Hz, 2H), 7.63 (s, 1H), 7.28 (s, 1H), 7.04 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 162.1, 147.6, 146.8, 142.2, 133.5, 131.6, 129.2, 120.0, 119.1, 114.3, 113.9, 55.4, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2957, 1607, 1492, 1256, 1172, 1038 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{27}NO_2+H$, 338.2115; found, 338.2114.

5,7-Di-*tert*-butyl-2-(3,4-dimethoxyphenyl)benzo[*d*]oxazole (4 f). 44.0 mg, 60% yield; white soild, mp: 101–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 1H), 7.80 (s, 1H), 7.64 (s, 1H), 7.29 (s, 1H), 6.99 (d, J = 8.0 Hz, 1H), 4.02 (s, 3H), 3.96 (s, 3H), 1.55 (s, 9H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 151.8, 149.3, 147.7, 146.8, 142.2, 133.5, 120.8, 120.1, 119.2, 113.8, 111.0, 110.0, 56.1, 56.0, 35.1, 34.4, 31.8, 30.0; IR (KBr): 2953, 1601, 1495, 1262, 1147, 1025 cm^{-1}; HRMS (ESI,m/z): $[M+H]^+$ Calcd. for $C_{23}H_{29}O_3+H$, 368.2220; found, 368.2223.

5,7-Di-*tert*-butyl-2-(3-methoxyphenyl)benzo[*d*]oxazole (4 g). 41.1 mg, 61% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.81 (s, 1H), 7.67 (s, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.32 (s, 1H), 7.08 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 1.56 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 159.9, 147.8, 146.9, 142.1, 133.8, 130.0, 128.6, 119.9, 119.7, 117.7, 114.2, 112.1, 55.5, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2954, 1565, 1470, 1309, 1231, 1048 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{27}NO_2+H$, 338.2115; found, 388.2118.

5,7-Di-*tert*-butyl-2-(2-methoxyphenyl)benzo[*d*]oxazole (4 h). 39.1 mg, 58% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.0 Hz, 1H), 7.71 (s, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.07–7.12 (m, 2H), 4.01 (s, 3H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.5, 147.4, 146.5, 142.1, 133.5, 132.4, 131.0, 120.7, 119.2, 116.6, 114.4, 112.1, 56.1, 35.1, 34.4, 31.8, 29.9; IR (KBr): 2954, 1594, 1471, 1258, 1036 cm^{-1}; HRMS (ESI, m/z): $[M+Na]^+$ Calcd. for $C_{22}H_{27}NO_2+Na$, 360.1934; found, 360.1932.

5,7-Di-*tert*-butyl-2-(4-(methylthio)phenyl)benzo[*d*]oxazole (4 i). 43.8 mg, 62% yield; yellow soild, mp: 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.0 Hz, 2H), 7.65 (s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.31 (s, 1H), 2.54 (s, 3H), 1.56 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 147.7, 146.8, 143.2, 142.3, 133.6, 127.6, 125.8, 123.8, 119.4, 114.0, 35.0, 34.4, 31.8, 30.0, 15.1; IR (KBr): 2956, 1598, 1477, 1394, 1182, 1085 cm^{-1}; HRMS (ESI, m/z): $[M+Na]^+$ Calcd. for $C_{22}H_{27}NOS+Na$, 376.1706; found, 376.1708.

4-(5,7-Di-*tert*-butylbenzo[*d*]oxazol-2-yl)-*N*,*N*-Dimethylaniline (4 j). 39.2 mg, 56% yield; yellow solid, mp: 142–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.11 (s, 1H), 7.61 (s, 1H), 7.24 (s, 1H), 6.80 (s, 1H), 6.78 (s, 1H), 3.06 (s, 6H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 152.2, 147.3, 146.6, 142.5, 133.2, 128.9, 118.4, 114.7, 113.5, 111.6, 40.1, 35.0, 34.4, 31.9, 30.0; IR (KBr): 2955, 1609, 1508, 1360, 1179, 1065 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{30}N_2O+H$, 351.2431; found, 351.2433.

5,7-Di-*tert*-butyl-2-(4-fluorophenyl)benzo[*d*]oxazole (4 k). 46.8 mg, 72% yield; orange solid, mp: 98–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.27 (m, 2H), 7.65 (s, 1H), 7.32 (s, 1H), 7.20–7.32 (m, 2H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (d, $^{1}J_{C\text{-}F}$ = 250.8 Hz), 161.6, 147.9, 146.9, 142.2, 133.7, 129.6 (d, $^{3}J_{C\text{-}F}$ = 8.8 Hz), 123.8 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 119.6, 116.1 (d, $^{2}J_{C\text{-}F}$ = 22.0 Hz), 114.2, 35.1, 34.5, 31.8, 30.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.0 (s, 1F); IR (KBr): 2957, 1601, 1489, 1306, 1062 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}FNO+H$, 326.1915; found, 326.1914.

5,7-Di-*tert*-butyl-2-(3-fluorophenyl)benzo[*d*]oxazole (4 l). 42.3 mg, 65% yield; orange solid, mp: 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 1H), 7.99 (d, J = 9.6 Hz, 1H), 7.72 (s, 1H), 7.53–7.59 (m, 1H), 7.39 (s, 1H), 7.28–7.32 (m, 1H), 1.61 (s, 9H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, $^{1}J_{C\text{-}F}$ = 245.3 Hz), 161.2, 148.1,147.0, 142.0, 133.9, 130.6 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 129.5 (d, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 123.1 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 120.1, 118.2 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 114.3, 114.3 (d, $^{2}J_{C\text{-}F}$ = 23.8 Hz), 35.1, 34.5, 31.8, 30.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −111.9 (s, 1F); IR (KBr): 2958, 1568, 1471, 1204, 1063 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}FNO+H$, 326.1915; found, 326.1917.

5,7-Di-*tert*-butyl-2-(4-chlorophenyl)benzo[*d*]oxazole (4 m). 44.3 mg, 65% yield; yellow solid, mp: 114–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 2H), 7.66 (s, 1H), 7.50 (d, J = 7.6 Hz, 2H), 7.33 (s, 1H), 1.56 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 148.0, 146.9, 142.2, 137.4, 133.8, 129.2, 128.6, 126.0, 119.8, 114.3, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2957, 1590, 1476, 1386, 1180, 1079 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}ClNO+H$, 342.1619; found, 342.1618.

5,7-Di-*tert*-butyl-2-(3,4-dichlorophenyl)benzo[*d*]oxazole (4 n). 40.5 mg, 54% yield; orange solid, mp: 133–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.65 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.35 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 148.2, 147.0, 142.1, 135.5, 133.9, 133.4, 131.0, 129.0, 127.4, 126.3, 120.3, 114.4, 35.1, 34.5, 31.8, 30.1; IR (KBr): 2955, 1553, 1465, 1377, 1253, 1063 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{23}Cl_2NO+H$, 376.1229; found, 376.1226.

5,7-Di-*tert*-butyl-2-(3-chlorophenyl)benzo[*d*]oxazole (4 o). 40.9 mg, 60% yield; yellow solid, mp: 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.14 (d, J = 7.2 Hz, 1H), 7.66 (s, 1H), 7.44–7.50 (m, 2H), 7.34 (s, 1H), 1.56 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1 148.1, 147.0, 142.1, 135.0, 133.9, 131.1, 130.2, 129.3, 127.3, 125.4, 120.0, 114.4, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2957, 1557, 1469, 1304, 1184, 1070 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}ClNO+H$, 342.1619; found, 342.1619.

5,7-Di-*tert*-butyl-2-(2-chlorophenyl)benzo[*d*]oxazole (4p). 36.1 mg, 53% yield; red solid, mp: 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 1H), 7.73 (s, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.42–7.44 (m, 2H), 7.36 (s, 1H), 1.55 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 147.9, 147.0, 141.7, 134.0, 133.3, 131.8, 131.7, 131.4, 126.9, 126.6, 120.0, 114.5, 35.1, 34.4, 31.8, 29.9; IR (KBr): 2954, 1563, 1464, 1249, 1187, 1034 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}ClNO+H$, 342.1619; found, 342.1624.

2-(4-Bromophenyl)-5,7-Di-*tert*-butylbenzo[*d*]oxazole (4q). 46.8 mg, 61% yield; red solid, mp: 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.0 Hz, 2H), 7.65–7.67 (m, 3H), 7.33 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 148.0, 147.0, 142.2, 133.8, 132.2, 128.8, 126.5, 125.8, 119.9, 114.3, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2955, 1573, 1485, 1387, 1181, 1062 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}BrNO+H$, 386.1114; found, 386.1112.

2-(3-Bromophenyl)-5,7-Di-*tert*-butylbenzo[*d*]oxazole (4r). 43.9 mg, 57% yield; yellow solid, mp: 101–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.19 (d, J = 7.6 Hz, 1H), 7.63–7.67 (m, 2H), 7.35–7.41 (m, 2H), 1.56 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 147.0, 142.1, 134.0, 133.9, 130.4, 130.2, 129.4, 125.9, 123.0, 120.0, 114.3, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2959, 1554, 1470, 1395, 1184, 1067 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}BrNO+H$, 386.1114; found, 386.1119.

2-(2-Bromophenyl)-5,7-Di-*tert*-butylbenzo[*d*]oxazole (4s). 42.3 mg, 55% yield; red solid, mp: 159–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.34–7.37 (m, 2H), 1.56 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 147.9, 147.0, 141.8, 134.6, 134.1, 132.2, 131.7, 128.8, 127.4, 121.6, 119.9, 114.5, 35.1, 34.4, 31.8, 30.0; IR (KBr): 2956, 1563, 1463, 1312, 1185, 1025 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}BrNO+H$, 386.1114; found, 386.1116.

5,7-Di-*tert*-butyl-2-(4-iodophenyl)benzo[*d*]oxazole (4t). 51.1 mg, 59% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.98 (m, 2H), 7.86–7.88 (m, 2H), 7.66 (s, 1H), 7.33 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 148.0, 146.9, 142.1, 138.1, 133.8, 128.8, 127.0, 119.9, 114.3, 97.9, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2957, 1573, 1485, 1387, 1181, 1062 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}INO+H$, 434.0975; found, 434.0978.

5,7-Di-*tert*-butyl-2-(4-nitrophenyl)benzo[*d*]oxazole (4u). 33.0 mg, 47% yield; orange solid, mp: 195–196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36–8.42 (m, 4H), 7.68 (s, 1H), 7.39 (s, 1H), 1.56 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 149.1, 148.5, 147.3, 142.2, 134.1, 133.1, 128.1, 124.2, 120.9, 114.7, 35.1, 34.5, 31.7, 30.0; IR (KBr): 2955, 1623, 1532, 1344, 1206, 1076 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{24}N_2O_3+H$, 353.1860; found, 353.1867.

4-(5,7-Di-*tert*-butylbenzo[*d*]oxazol-2-yl)benzonitrile (4v). 35.9 mg, 54% yield; green solid, mp: 122–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 7.6 Hz, 2H), 7.67 (s, 1H), 7.37 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 148.4, 147.1, 142.1, 134.0, 132.7, 131.4, 127.7, 120.7, 118.2, 114.6, 114.3, 35.1, 34.5, 31.7, 30.0; IR (KBr): 2959, 1565, 1480, 1384, 1192, 1066 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{24}N_2O+H$, 333.1961; found, 333.1969.

5,7-Di-*tert*-butyl-2-(4-(trifluoromethyl)phenyl)benzo[*d*]oxazole (4w). 45.0 mg, 60% yield; yellow solid, mp: 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.80 (m, 2H), 7.66–7.68 (m, 2H), 6.83 (s, 1H), 6.82 (s, 1H), 2.01 (s, 3H), 1.43 (s, 9H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 148.2, 147.1, 142.1, 134.0, 132.7 (q, $^2J_{C\text{-}F}$ = 32.3 Hz), 130.8, 127.6, 125.9 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 123.8 (q, $^4J_{C\text{-}F}$ = 270.7 Hz), 120.3, 114.5, 35.1, 34.5, 31.7, 30.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 3F); IR (KBr): 2960, 1562, 1478, 1322, 1139, 1072 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{24}F_3NO+H$, 376.1883; found, 376.1879.

5,7-Di-*tert*-butyl-2-(naphthalen-2-yl)benzo[*d*]oxazole (4x). 42.8 mg, 60% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.34 (d, J = 8.8 Hz, 1H), 7.97–8.03 (m, 2H), 7.89–7.90 (m, 1H), 7.73 (s, 1H), 7.56–7.58 (m, 2H), 7.36 (s, 1H), 1.63 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 147.8, 147.1, 142.4, 134.6, 133.7, 133.0, 128.9, 128.7, 127.9, 127.6, 127.6, 126.8, 124.8, 123.9, 119.6, 114.2, 35.1, 34.5, 31.8, 30.1; IR (KBr): 2956, 1558, 1471, 1375, 1180, 1060 cm^{-1}; HRMS (ESI, m/z): $[M+Na]^+$ Calcd. for $C_{25}H_{27}NO+Na$, 380.1985; found, 380.1980.

5,7-Di-*tert*-butyl-2-(naphthalen-1-yl)benzo[*d*]oxazole (4y). 44.2 mg, 62% yield; white solid, mp: 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.79 (s, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.58–7.65 (m, 2H), 7.38 (s, 1H), 1.60 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 147.8, 146.4, 142.4, 134.0, 133.7, 132.0, 130.7, 129.1, 128.6, 127.8, 126.4, 126.3, 125.0, 124.0, 119.8, 114.5, 35.1, 34.5, 31.9, 30.1; IR (KBr): 2955, 1546, 1469, 1382, 1195, 1114 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{25}H_{27}NO+H$, 358.2165; found, 358.2161.

5,7-Di-*tert*-butyl-2-(pyridin-3-yl)benzo[*d*]oxazole (4z). 25.9 mg, 42% yield; orange solid, mp: 100–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 8.75 (s, 1H), 8.50 (d, J = 8.0 Hz, 1H), 7.67 (s, 1H), 7.45–7.48 (m, 1H), 7.35 (s, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 151.7, 148.5, 148.2, 147.0, 142.0, 134.5, 133.9, 123.7, 120.2, 114.4, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2959, 1587, 1472, 1193, 1076, 1019 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{20}H_{24}N_2O+H$, 309.1961; found, 309.1958.

5,7-Di-*tert*-butyl-2-(thiophen-3-yl)benzo[*d*]oxazole (4aa). 36.3 mg, 58% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.80 (d, J = 4.8 Hz, 1H), 7.64 (s, 1H), 7.45 (s, 1H), 7.30 (s, 1H), 1.54 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 147.8, 146.5, 142.0, 133.6, 129.6, 127.4, 126.9, 126.6, 119.5, 114.1, 35.1, 34.5, 31.8, 30.0; IR (KBr): 2958, 1585, 1477, 1388, 1275, 1071 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{23}NOS+H$, 314.1573; found, 314.1576.

5,7-Di-*tert*-butyl-2-(thiophen-2-yl)benzo[*d*]oxazole (4ab). 37.0 mg, 59% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 3.6 Hz, 1H), 7.62 (s, 1H), 7.53 (d, J = 5.2 Hz, 1H), 7.30 (s, 1H), 7.18 (t, J = 4.4 Hz, 1H), 1.54 (s, 9H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 147.9, 146.6, 142.1,

133.6, 130.1, 129.7, 129.4, 128.1, 119.6, 114.0, 35.1, 34.4, 31.8, 30.0; IR (KBr): 2956, 1580, 1480, 1384, 1226, 1042 cm^{-1}; HRMS (ESI, m/z): $[M+Na]^+$ Calcd. for $C_{19}H_{23}NOS+Na$, 336.1393; found, 336.1391.

5,7-Di-*tert*-butyl-2-(furan-2-yl)benzo[*d*]oxazole (4 ac). 30.3 mg, 51% yield; black oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.62 (s, 1H), 7.30 (s, 1H), 7.24 (s, 1H), 6.60 (s, 1H), 1.53 (s, 9H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 148.0, 146.3, 145.3, 143.0, 141.8, 133.7, 119.7, 114.3, 113.5, 112.0, 35.0, 34.4, 31.8, 30.0; IR (KBr): 2956, 1535, 1381, 1300, 1082, 1004 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{19}H_{23}NO_2+H$, 298.1802; found, 298.1804.

(E)-5,7-Di-*tert*-butyl-2-Styrylbenzo[*d*]oxazole (4 ad). 30.0 mg, 45% yield; yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, $J=16.0$ Hz, 1H), 7.60–7.63 (m, 3H), 7.37–7.44 (m, 3H), 7.31 (s, 1H), 7.11 (d, $J=16.4$ Hz, 1H), 1.55 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 146.6, 142.4, 138.5, 135.3, 133.5, 129.5, 128.9, 127.5, 119.7, 114.4, 114.1, 35.0, 34.4, 31.8, 30.0; IR (KBr): 2954, 1636, 1540, 1465, 1368, 1160 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{28}NO+H$, 334.2165; found, 334.2169.

5,7-Di-*tert*-butyl-2-Phenethylbenzo[*d*]oxazole (4 ae). 32.2 mg, 48% yield; yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.27–7.29 (m, 5H), 7.24 (s, 1H), 3.22–3.26 (m, 4H), 1.45 (s, 9H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 147.0, 141.3, 140.2, 133.6, 128.6, 128.3, 126.4, 119.0, 113.8, 35.0, 34.4, 33.0, 31.9, 30.4, 30.0; IR (KBr): 2953, 1578, 1472, 1380, 1146, 1011 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{29}NO+H$, 336.2322; found, 336.2321.

5-(*tert*-butyl)-2,7-Diphenylbenzo[*d*]oxazole (4 af). 36.6 mg, 56% yield; orange solid, mp: 102–103 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.18–8.20 (m, 2H), 7.97–7.99 (m, 2H), 7.77 (s, 1H), 7.57–7.65 (m, 6H), 7.45–4.48 (m, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 148.9, 146.3, 142.8, 135.7, 132.3, 129.7, 129.5, 128.6, 128.5, 127.7, 127.0, 123.9, 122.2, 116.0, 35.3, 32.0; IR (KBr): 2959, 1556, 1478, 1393, 1331, 1203, 1057 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}NO+H$, 328.1696; found, 328.1692.

5-(*tert*-butyl)-2-Phenyl-7-(*m*-tolyl)benzo[*d*]oxazole (4 ag). 35.5 mg, 52% yield; red oil; ^1H NMR (400 MHz, DMSO-d_6) δ 8.17–8.19 (m, 2H), 7.76–7.78 (m, 3H), 7.61–7.64 (m, 4H), 7.44–7.48 (t, $J=7.6$ Hz, 1H), 7.27 (d, $J=7.6$ Hz, 1H), 2.45 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 148.8, 146.3, 142.8, 138.7, 135.7, 132.3, 129.8, 129.3, 129.2, 129.0, 127.7, 127.0, 125.7, 124.0, 122.2, 115.9, 35.3, 32.0, 21.6; IR (KBr): 2957, 1557, 1475, 1383, 1192, 1054 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{23}NO+H$, 342.1852; found, 342.1850.

5-(*tert*-butyl)-2-Phenyl-7-(*o*-tolyl)benzo[*d*]oxazole (4 ah). 32.1 mg, 47% yield; red oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, $J=7.2$ Hz, 2H), 7.83 (s, 1H), 7.44–7.50 (m, 4H), 7.36–7.39 (m, 4H), 2.33 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 148.2, 146.5, 141.8, 136.6, 136.2, 131.4, 130.4, 130.4, 128.8, 128.1, 127.6, 127.2, 125.9, 124.5, 124.5, 115.4, 35.0, 31.8, 20.4; IR (KBr): 2959, 1555, 1475, 1390, 1331, 1204, 1052 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{23}NO+H$, 342.1852; found, 342.1853.

5-(*tert*-butyl)-7-(4-(methylthio)phenyl)-2-Phenylbenzo[*d*]oxazole (4 ai). 44.0 mg, 59% yield; yellow solid, mp: 115–116 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.21 (d, $J=6.8$ Hz, 2H), 7.95 (d, $J=7.6$ Hz, 2H), 7.76 (s, 1H), 7.62–7.66 (m, 4H), 7.47 (d, $J=8.0$ Hz, 2H), 2.56 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 148.9, 146.1, 142.8, 139.0, 132.4, 132.0, 129.8, 128.9, 127.7, 127.0, 126.7, 123.3, 121.7, 115.8, 35.3, 32.0, 15.0; IR (KBr): 2956, 1556, 1480, 1330, 1201, 1057 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{23}NOS+H$, 374.1573; found, 374.1571.

4-(5-(*tert*-butyl)-2-Phenylbenzo[*d*]oxazol-7-yl)phenol (4 aj). 41.8 mg, 61% yield; colorless solid, mp: 245–246 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 1H), 8.21 (d, $J=4.8$ Hz, 2H), 7.83 (d, $J=8.0$ Hz, 2H), 7.70 (s, 1H), 7.59–7.64 (m, 4H), 6.98 (d, $J=8.0$ Hz, 2H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9, 158.1, 148.8, 146.0, 142.7, 132.3, 129.8, 129.7, 127.7, 127.1, 126.3, 124.0, 121.4, 116.3, 114.9, 35.3, 32.0.; IR (KBr): 2962, 1743, 1612, 1462, 1376, 1242, 1049 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{21}NO_2+H$, 344.1645; found, 344.1640.

5-(*tert*-butyl)-7-(4-fluorophenyl)-2-Phenylbenzo[*d*]oxazole (4 ak). 36.6 mg, 53% yield; colorless solid, mp: 130–131 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28–8.31 (m, 2H), 7.90–7.94 (m, 2H), 7.83 (d, $J=1.6$ Hz, 1H), 7.55–7.57 (m, 4H), 7.28–7.30 (m, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 162.6 (d, $^1J_{C\text{-}F}=246.3$ Hz), 148.7, 146.2, 142.7, 131.5 (d, $^4J_{C\text{-}F}=3.1$ Hz), 129.9 (d, $^3J_{C\text{-}F}=8.1$ Hz), 129.8, 128.9, 127.6, 127.1, 123.1, 121.9, 115.8 (d, $^2J_{C\text{-}F}=21.4$ Hz), 115.7, 35.1, 31.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.0 (s, 1F); IR (KBr): 2958, 1557, 1476, 1331, 1225, 1053 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}FNO+H$, 346.1599; found, 346.1602.

5-(*tert*-butyl)-7-(3-fluorophenyl)-2-Phenylbenzo[*d*]oxazole (4 al). 33.1 mg, 48% yield; gray solid, mp: 83–84 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.18 (d, $J=7.2$ Hz, 2H), 7.78–7.85 (m, 3H), 7.68 (s, 1H), 7.59–7.64 (m, 4H), 7.29 (t, $J=8.4$ Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.1, 163.0 (d, $^1J_{C\text{-}F}=241.9$ Hz), 148.9, 146.2, 142.8, 138.0 (d, $^3J_{C\text{-}F}=8.2$ Hz) 132.3, 131.4 (d, $^3J_{C\text{-}F}=8.5$ Hz), 129.7, 127.7, 126.9, 124.6 (d, $^4J_{C\text{-}F}=2.8$ Hz), 122.5, 122.3, 116.6, 115.4 (d, $^2J_{C\text{-}F}=20.6$ Hz), 115.1 (d, $^2J_{C\text{-}F}=22.4$ Hz), 35.3, 31.9; ^{19}F NMR (376 MHz, DMSO-d_6) δ −112.4 (s, 1F); IR (KBr): 2957, 1570, 1474, 1388, 1207, 1056 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}FNO+H$, 346.1599; found, 346.1602.

5-(*tert*-butyl)-7-(2-fluorophenyl)-2-Phenylbenzo[*d*]oxazole (4 am). 30.4 mg, 44% yield; colorless oil; ^1H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, $J=7.6$ Hz, 2H), 7.85 (s, 1H), 7.77 (t, $J=7.6$ Hz, 1H), 7.54–7.61 (m, 5H), 7.39–7.46 (m, 2H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 159.8 (d, $^1J_{C\text{-}F}=246.0$ Hz) 148.6, 146.5, 142.3, 132.4, 131.9 (d, $^3J_{C\text{-}F}=3.2$ Hz), 131.0 (d, $^3J_{C\text{-}F}=8.2$ Hz), 129.8, 127.6, 126.9, 125.5 (d, $^4J_{C\text{-}F}=3.6$ Hz), 123.5 (d, $^2J_{C\text{-}F}=14.7$ Hz), 116.7, 116.6 (d, $^2J_{C\text{-}F}=21.9$ Hz), 35.3, 31.9; ^{19}F NMR (376 MHz, DMSO-d_6) δ −114.8 (s, 1F); IR (KBr): 2957, 1559, 1477, 1395, 1216, 1052 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}FNO+H$, 346.1597; found, 346.1602.

5-(*tert*-butyl)-7-(4-chlorophenyl)-2-Phenylbenzo[*d*]oxazole (4 an). 39.0 mg, 54% yield; yellow solid, mp: 115–116 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25–8.27 (m, 2H), 7.81–7.86 (m,

3H), 7.52–7.56 (m, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 148.8, 146.2, 142.8, 134.6, 133.9, 131.5, 129.4, 129.0, 128.9, 127.6, 127.1, 122.8, 121.8, 116.1, 35.1, 31.8; IR (KBr): 2958, 1557, 1482, 1379, 1203, 1092 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}ClNO+H$, 362.1306; found, 362.1304.

5-(*tert*-butyl)-7-(3-chlorophenyl)-2-Phenylbenzo[*d*]oxazole (4 ao). 36.8 mg, 51% yield; yellow oil; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17–8.19 (m, 2H), 8.02 (s, 1H), 7.98 (d, J= 7.6 Hz, 1H), 7.81 (s, 1H), 7.70 (s, 1H), 7.60–7.64 (m, 4H), 7.52–7.54 (m, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.1, 149.0, 146.2, 142.8, 137.8, 134.2, 132.4, 131.3, 129.8, 128.5, 128.1, 127.7, 127.3, 126.9, 122.4, 116.7, 35.4, 31.9; IR (KBr): 2956, 1559, 1473, 1382, 1204, 1059 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{23}H_{20}ClNO+H$, 362.1306; found, 362.1303.

4-(5-(*tert*-butyl)-2-Phenylbenzo[*d*]oxazol-7-yl)benzonitrile (4 ap). 39.4 mg, 56% yield; yellow solid, mp: 148–149 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (d, J=7.2 Hz, 4H), 8.03 (d, J=8.0 Hz, 2H), 7.85 (s, 1H), 7.74 (s, 1H), 7.62–7.63 (m, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.2, 149.1, 146.3, 143.0, 140.2, 133.3, 132.5, 129.7, 129.3, 127.8, 126.8, 122.5, 122.0, 119.2, 117.4, 111.1, 35.4, 31.9; IR (KBr): 2957, 2227, 1608, 1474, 1205, 1052 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{24}H_{20}N_2O+H$, 353.1648; found, 353.1650.

5-(*tert*-butyl)-2-Phenyl-7-(thiophen-3-yl)benzo[*d*]oxazole (4 aq). 34.1 mg, 51% yield; orange solid, mp: 98–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.30 (m, 2H), 7.98 (s, 1H), 7.74–7.75 (m, 2H), 7.67 (s, 1H), 7.55 (s, 3H), 7.50–7.51 (m, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 148.5, 145.9, 142.6, 136.5, 131.5, 128.9, 127.6, 127.2, 126.6, 126.0, 123.0, 120.9, 118.9, 115.4, 35.0, 31.8; IR (KBr): 2957, 1556, 1476, 1201, 1056 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{21}H_{19}NOS+H$, 334.1260; found, 334.1256.

5-(*tert*-butyl)-7-(naphthalen-1-yl)-2-phenylbenzo[*d*]oxazole (4 ar). 56.0 mg, 74% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (m, 2H), 7.98 (d, J=8.0 Hz, 2H), 7.91 (d, J= 1.6 Hz, 1H), 7.83 (d, J=8.4 Hz, 1H), 7.61–7.69 (m, 2H), 7.53–7.57 (m, 2H), 7.41–7.47 (m, 4H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 148.3, 147.1, 142.1, 134.4, 133.8, 131.6, 131.4, 128.8, 128.5, 128.4, 127.8, 127.6, 127.1, 126.2, 126.0, 125.9, 125.4, 125.2, 123.3, 115.7, 35.1, 31.8; IR (KBr): 2954, 1556, 1475, 1201, 1057 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{27}H_{23}NO+H$, 378.1852; found, 378.846.

7-(*tert*-butyl)-5-(*tert*-pentyl)-2-phenylbenzo[*d*]oxazole (4 as). 49.2 mg, 77% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (m, 2H), 7.68 (s, 1H), 7.58–7.60 (m, 3H), 7.31–7.38 (m, 1H), 1.78 (q, J=7.2 Hz, 2H), 1.62 (s, 9H), 1.43–1.47 (m, 6H), 0.78 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 146.0, 142.3, 133.6, 131.1, 128.8, 127.5, 127.4, 120.1, 115.0, 38.3, 37.2, 34.4, 31.8, 30.1, 30.0, 28.9, 9.2; IR (KBr): 2960, 1557, 1473, 1178, 1063 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{22}H_{27}NO+H$, 322.2165; found, 322.2160.

2,5,7-triphenylbenzo[*d*]oxazole (4 at). 49.4 mg, 71% yield; white solid, mp: 195–196 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09–8.11 (m, 2H), 7.77 (s, 1H), 7.59–7.61 (m, 2H), 7.26–7.27 (m, 4H), 7.16–7.18 (m, 2H), 7.10–7.12 (m, 2H), 7.00–7.02 (m, 2H), 6.87–6.89 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.7, 141.9, 141.2, 139.6, 138.9, 137.2, 134.9, 132.6, 132.1, 130.8, 130.7, 130.3, 129.8, 128.4, 128.1, 127.8, 127.8, 127.7, 126.8, 126.8, 125.2, 120.3; IR (KBr): 3050, 2922, 1421, 1046, 697 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{25}H_{17}NO+H$, 348.1383; found, 348.1382.

5-(*tert*-butyl)-6-methoxy-2-phenylbenzo[*d*]oxazole (4 au). 27.0 mg, 48% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21–8.23 (m, 2H), 7.72 (s, 1H), 7.50–7.52 (m, 3H), 7.11 (s, 1H), 3.93 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 157.7, 149.8, 136.7, 134.5, 131.1, 128.9, 127.3, 127.2, 117.1, 94.1, 55.6, 35.3, 29.9; IR (KBr): 2931, 1625, 1459, 1319, 1048 cm^{-1}; HRMS (ESI, m/z): $[M+H]^+$ Calcd. for $C_{18}H_{19}NO_2+H$, 282.1489; found, 282.1484.

Acknowledgements

The authors thank the National Program on Key Research Project (2016YFA0602900), and the Fundamental Research Funds for the Central Universities (2019PY05) for financial support.

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[16] CCDC 2021608 (**4s**) and 2022337 (**5**) contain the supplementary crystallographic data. These data can also be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.a-c.uk/data_request/cif.

