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**PAPER**

# Nickel-catalyzed C–H direct amination of benzoxazoles with secondary amines†

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In this article, a facile, efficient and practical method for Ni-catalyzed direct C–H amination of benzoxazole with secondary amines has been developed. This procedure requires $Ni(OAc)_2{\cdot}4H_2O$ as catalyst, TBHP as oxidant and acid as the additive. A variety of substituted benzoxazol-2-amines were synthesized in moderate to good yields.

## Introduction

The $sp^2$ C–N bond reaction is of great interest in organic synthesis. Traditionally, methods include nucleophilic substitution,[1] the Cu-catalyzed Ullmann and Goldberg C–N couplings[2] and the Pd-catalyzed Buchwald–Hartwig reaction.[3] 2-Aminooxazoles are widely employed in biological, pharmaceutical and material sciences.[4] Thus, the synthesis of 2-aminooxazoles has reached more and more attention in recent years. While, for the above methods, they often require pre-installation of reactive functional groups[5] (*e.g.*, aryl iodides, bromides, chlorides, triflates and sulfonates) and high temperature as well as the use of expensive ligands (for Ullmann and Buchwald–Hartwig reaction). To further improve the efficiency, an immense effort has been made to develop efficient strategies for the construction of C–N bond.[6–8] Transition-metal-catalyzed C–H direct amination of azoles have been described recently, a wide range of metal catalysts, including Ag,[9] Mn,[5] Co,[5] Fe,[10] Cu,[11] Sc,[12] have been exploited with varying degrees of success (Scheme 1, route A). Another route to synthesize 2-aminooxazoles is the metal-free version of the C–H direct amination[13] (Scheme 1, route B). Nickel catalysts have recently been developed for cross coupling of C–X (X = O, N, *etc.*).[6,14] Often, the use of expensive $Ni(cod)_2$ [cod = 1,5-cyclooctadiene] and toxic $P(Cy)_3$ ligand limit the scope of the Ni-catalyzed reaction. The advantage of using other Ni sources as a catalyst is apparent, as they are often ready available and inexpensive. Our laboratory focuses on the C–X bond construction. Recently, we successfully developed a milder Cu-catalytic protocol for azole amination under acid conditions. Herein, we report a cheap and easily available Ni-catalyzed C–H direct amination of azoles.

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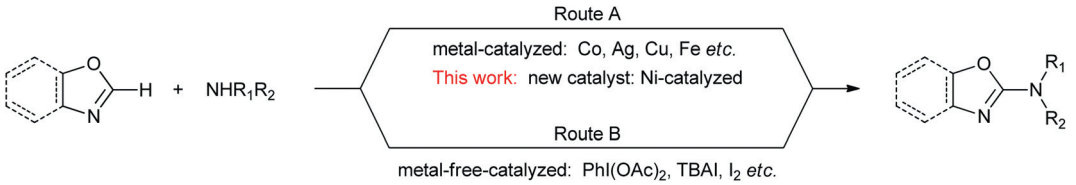
## Results and discussion

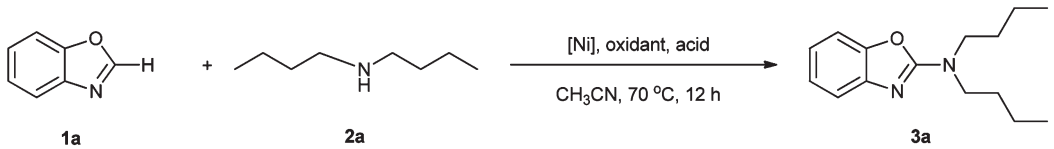
Our laboratory has already reported the direct copper-catalyzed C–H amination of benzoxazoles with oxygen as oxidant,[11f] and so we were eager to develop a new approach and expand the substrate scope. We started our study by examining the conversion of benzoxazole into 2-dibutylamine benzoxazole as shown in Table 1. The use of 20 mol% $Ni(OAc)_2{\cdot}4H_2O$ in $CH_3CN$ at 70 °C under an oxygen atmosphere in acid conditions produced the desired product in 7% yield after 12 h and no dimer of benzoxazole was observed. A satisfactory result was obtained when $O_2$ was replaced by TBHP as the oxidant (82% yield, Table 1, entries 2–3). Using propanoic acid, the yield was enhanced to 89% yield (Table 1, entry 4). We subsequently tested other oxidants and acids, the results demonstrated that TBHP was the best choice as the oxidant and *p*-anisic acid provided comparable results (see ESI†). Other nickel sources, including $NiCl_2{\cdot}6H_2O$, $Ni(acac)_2$, $Ni(NO_3)_2{\cdot}6H_2O$, $Ni(ClO_4)_2$ were also tested, but only $NiCl_2{\cdot}6H_2O$ gave comparable yield (see ESI†). In addition, in the absence of oxidant, catalyst or acid, the reaction proceeded unsuccessfully. The catalyst loading could be decreased to 5 mol % and still provided good yield without increasing the reaction temperature. With further optimization of reaction conditions, the best result was obtained using the $Ni(OAc)_2{\cdot}H_2O$ (0.05 equiv.)/TBHP (3 equiv.) system in acid conditions at 70 °C after 12 h (Table 1, entry 14).

Using the optimized conditions, we next explored the scope and generality of the procedure. Various linear and cyclic secondary amines such as dibutylamine, dipropylamine, diethylamine, piperidine, 4-methylpiperidine could be used efficiently in our procedure. The desired products **3a–3h** were obtained in 68–78% yields. Unsymmetrical *N*-methylbenzylamine gave the desired product **3i** in 67% yield. Furthermore we could synthesize **3j** in 67% yield starting from unsymmetrical and bulky *N*-methyl-2-chlorobenzylamine. In addition to simple dialkylamines, synthetically more useful diallylamines were tolerated (65% yield, Scheme 2, **3k**), which was obtained in 20% GC




**Scheme 1** C–H direct amination methods.

**Table 1** Optimization of reaction conditions[a]




**1a** **2a** **3a**

| Entry | [Ni] (equiv.) | Oxidant (equiv.) | Acid (equiv.) | Yield[b] (%) |
|---|---|---|---|---|
| 1 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | $O_2$, | AcOH (2) | 7 |
| 2 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | AcOH (1.2) | 82 |
| 3 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | AcOH (1.2) | 82[c] |
| 4 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | $C_2H_5COOH$ (1.2) | 89[c] |
| 5 | — | TBHP (1.2) | $C_2H_5COOH$ (1.2) | 25[c] |
| 6 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | — | $C_2H_5COOH$ (1 2) | 5[c] |
| 7 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | — | 45[c] |
| 8 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | $C_2H_5COOH$ (1.2) | 87[d] |
| 9 | $Ni(OAc)_2{\cdot}4H_2O$ (0.2) | TBHP (1.2) | $C_2H_5COOH$ (1.2) | 87 |
| 10 | $Ni(OAc)_2{\cdot}4H_2O$ (0.05) | TBHP (1.2) | $C_2H_5COOH$ (1.2) | 85 |
| 11 | $Ni(OAc)_2{\cdot}4H_2O$ (0 02) | TBHP (1.2) | $C_2$ $H_5COOH$ (1.2) | 74 |
| 12 | $Ni(OAc)_2{\cdot}4H_2O$ (0 05) | TBHP (1.5) | $C_2H_5COOH$ (1.2) | 89 |
| 13 | $Ni(OAc)_2{\cdot}4H_2O$ (0.05) | TBHP (2) | $C_2H_5COOH$ (1.2) | 95 |
| 14 | $Ni(OAc)_2{\cdot}4H_2O$ (0.05) | TBHP (3) | $C_2H_5COOH$ (1.2) | 96 (68)[e] |

[a] Reaction conditions. Benzoxazole (0.5 mmol), amine (0.6 mmol), $Ni(OAc)_2{\cdot}4H_2O$, oxidant acid under air. $CH_3CN$ (2 ml), 70 °C, 12 h. [b] GC yield. [c] Under $O_2$. [d] Under Ar. [e] Isolated yield in parenthesis.



yield in our previous $Cu(OAc)_2{\cdot}H_2O/O_2$ catalytic system. In addition, we were pleased to find that with $Ni(OAc)_2{\cdot}4H_2O$/TBHP catalytic system an aryl secondary amine *N*-methylaniline could produce the desired product **3l** in 35% yield.

Subsequently, the scope of heterocycles was expanded to test the generality of this synthetic protocol and the results are summarized in Scheme 3. Various types of benzoxazoles were readily employed and afforded the desired products **3a**, **3d**, **4a–4f** in moderate to good yields. Here a significant difference was observed in the amounts of propanoic acid between 5-*tert*-butylbenzoxazole and other benzoxazoles. In contrast to the high efficiency of benzoxazole or benzoxazoles bearing substituents such as methyl and chloro at 5-position in 5 equiv. propanoic acid condition, 5-*tert*-butylbenzoxazole reacted more smoothly in 1.2 equiv. acid than in 5 equiv. acid conditions (Scheme 3, **4a**, **4d–4f**). It was also observed that electron-withdrawing groups attached at the 5-position of benzoxazole resulted in lower conversion than benzoxazoles bearing electron-donating groups, 5-chlorobenzoxazole yielded the desired products **4b**, **4c** in 57%, 31% yield (5 equiv. acid conditions) and 43%, 26% yield (1.2 equiv. acid conditions) respectively. Notably, moderate yield was obtained even in the case of bulky 5-*tert*-butylbenzoxazole with bulky *N*-methyl-2-chlorobenzylamine. In contrast to benzoxazole, benzothiazole and benzimidazole didn't yield the desired product.

Although the exact reaction mechanism still remains unclear, the reaction may proceed in a similar way to Co-catalyzed amination reported by Chang: (I) protonation of benzoxazole, (II) nucleophilic addition of amines, (III) oxidation provides the desired product. Ongoing work seeks to uncover the detailed mechanism and expand the reaction scope in the Ni-catalyzed direct amination of heterocycles.

## Conclusion

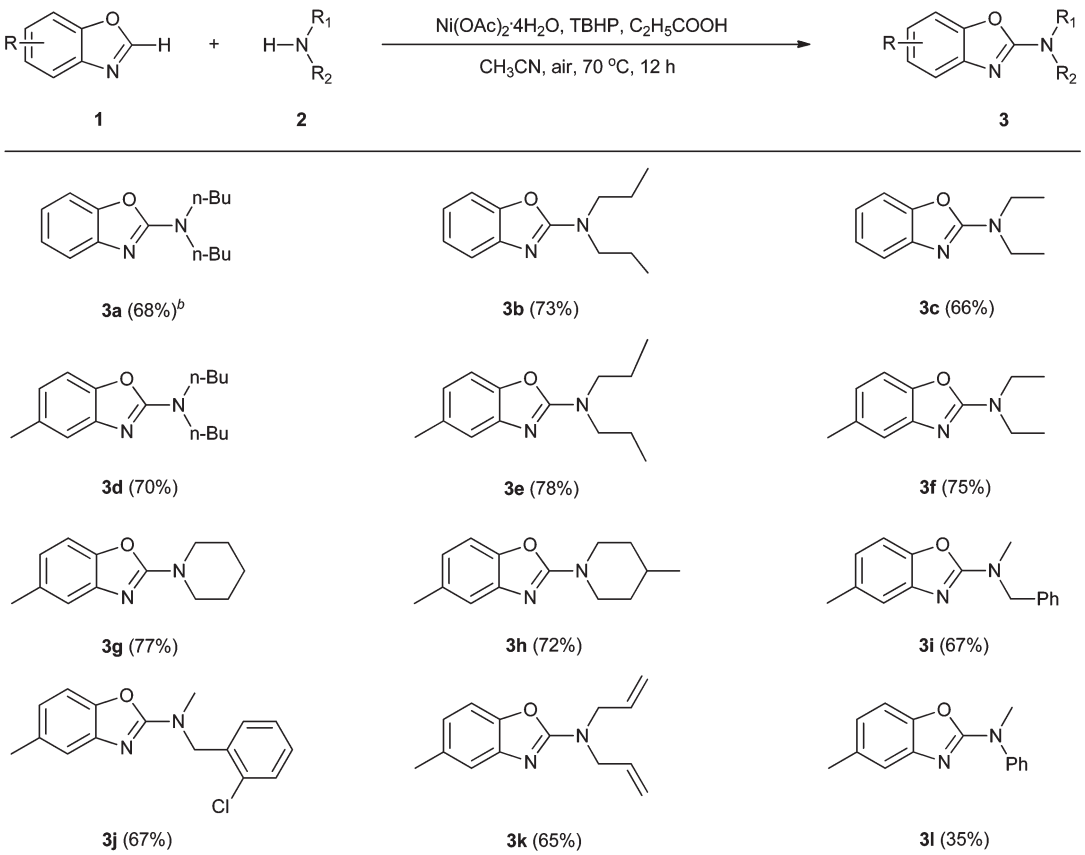
In conclusion, an efficient nickel-catalyzed C–H functionalization approach providing regioselective formation of C–N bonds through C–H direct amination of benzoxazoles has been developed. Moderate to good results were achieved for a series of substrates including arylamine. The new methods require inexpensive reagents, such as $Ni(OAc)_2{\cdot}4H_2O$ or $NiCl_2{\cdot}6H_2O$, TBHP, propanoic acid or acetic acid under air, which is anticipated to be a useful and complementary tool for the synthesis of 2-aminobenzoxazoles.

## Experimental

### Typical experimental procedure

A dried Schlenk test tube containing a magnetic stirring bar was charged under air with benzoxazole (0.5 mmol), amine



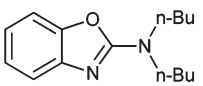

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Ni(OAc)_2{\cdot}4H_2O$ (5 mol%), TBHP (3 equiv) $C_2H_5COOH$ (1.2 equiv), $CH_3CN$ (2 ml), 70 °C, 12 h. [b] isolated yield.

**Scheme 2** Nickel-catalyzed C–H amination of benzoxazole and 5-methylbenzoxazole with amines.[a]



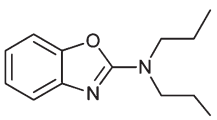
(0.6 mmol), $Ni(OAc)_2{\cdot}4H_2O$ (5 mol%), $C_2H_5CO_2H$ (1.2 or 5 equiv.), TBHP (70% solution in water, 3 equiv.), $CH_3CN$ (2 mL). Then the tube was sealed and the mixture was treated at 70 °C for 12 h. The resulting mixture was allowed to cool to room temperature and washed with a saturated solution of $NaHCO_3$, extracted with ethyl acetate for three times. The combined organic layers were dried with $Na_2SO_4$ and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel with EtOAc–petroleum (1 : 1–1 : 30) to provide the desired product.

***N*,*N*-Dibutylbenzoxazol-2-amine (3a)[11f]**



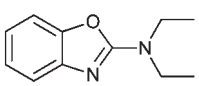
Light yellow liquid; Yield 68%; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.96 (t, $J$ = 7.2 Hz, 6H), 1.34–1.43 (m, 4H), 1.62–1.70 (m, 4H), 3.51 (m, 4H), 6.97 (m, 1H), 7.13 (t, $J$ = 8.0 Hz, 1H), 7.23 (d, $J$ = 8.0 Hz, 1H), 7.34 (d, $J$ = 8.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 14.1, 20.2, 30.3, 48.5, 108.6, 115.9, 120.0, 123.9, 143.8, 148.9, 162.8; GC-MS (EI) $m/z$ = 246 $[M]^+$.

***N*,*N*-Dipropylbenzoxazol-2-amine (3b)[11d]**

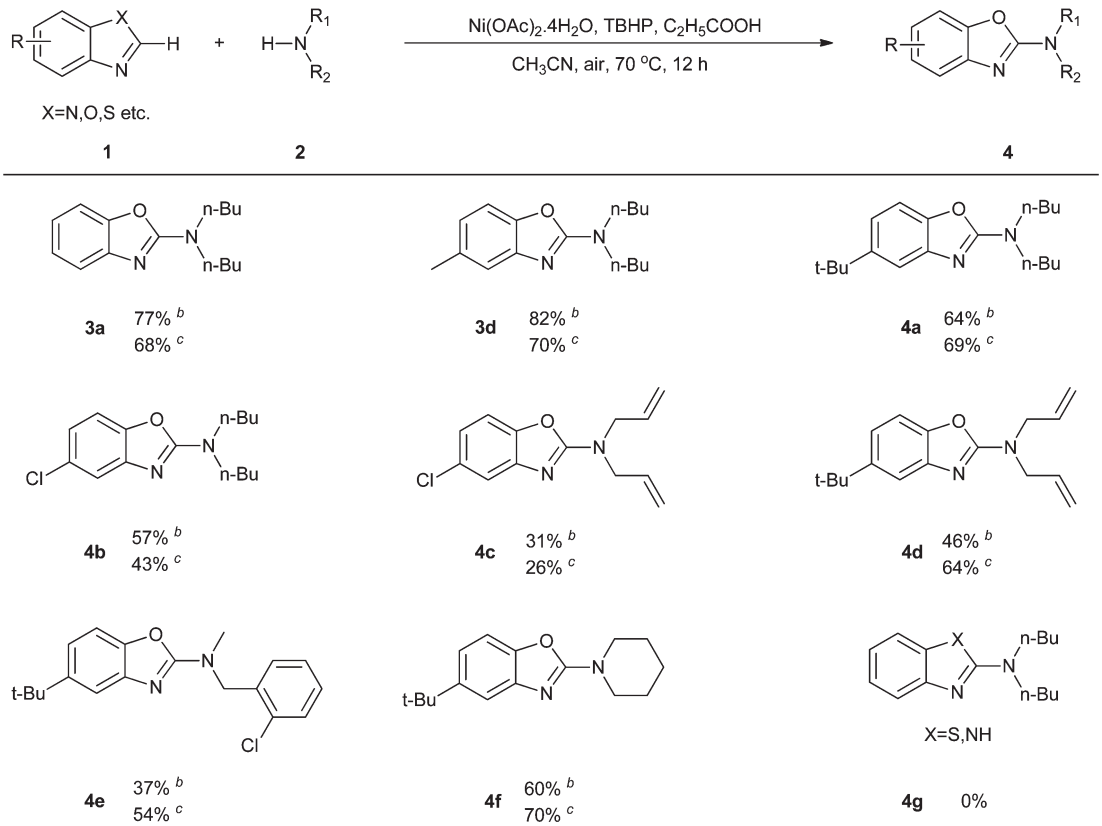


Light yellow liquid; Yield 73%; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.96 (t, $J$ = 7.2 Hz, 6H), 1.66–1.76 (m, 4H), 3.48 (t, $J$ = 7.6 Hz, 4H), 6.95–6.99 (m, 1H), 7.11–7.15 (m, 1H), 7.23 (d, $J$ = 8.0 Hz, 1H), 7.35 (d, $J$ = 7.6 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 11.3, 21.4, 50.5, 108.6, 115.9, 120.0, 123.9, 143.8, 148.9, 162.8; GC-MS (EI) $m/z$ = 218 $[M]^+$.

***N*,*N*-Diethylbenzoxazol-2-amine (3c)[11f]**



Colorless liquid; Yield 66%; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 1.29 (t, $J$ = 7.2 Hz, 6H), 3.57–3.62 (q, $J$ = 7.2, 4H), 6.96–7.00 (m, 1H), 7.12–7.16 (m, 1H), 7.24 (d, $J$ = 8.0 Hz, 1H), 7.36 (d, $J$ = 8.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 13.6,



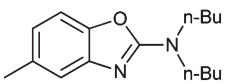

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Ni(OAc)_2.4H_2O$ (5 mol%), TBHP, $CH_3CN$ (2 ml), 70 °C, 12 h. [b] $C_2H_5COOH$ (5 equiv). [c] $C_2H_5COOH$ (1.2 equiv).

**Scheme 3** Ni-catalyzed C–H amination of benzoxazoles.[a]



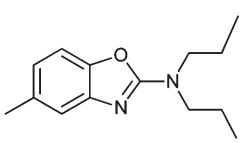
43.1, 108.7, 115.9, 120.1, 124.0, 143.5, 148.9, 162.2; GC – MS (EI) $m/z$ = 190 $[M]^+$.

### *N,N*-Dibutyl-5-methylbenzoxazol-2-amine (3d)



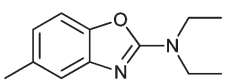
White solid; Yield 70%; M.p. 58–60 °C; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.95 (t, $J$ = 7.2 Hz, 6H), 1.33–1.42 (m, 4H), 1.61–1.69 (m, 4H), 2.38 (s, 3H), 3.49 (t, $J$ = 7.6 Hz, 4H), 6.77 (d, $J$ = 8.0 Hz, 1H), 7.09 (d, $J$ = 8.0 Hz, 1H), 7.15 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 14.1, 20.2, 21.7, 30.3, 48.4, 107.9, 116.4, 120.6, 133.5, 144.0, 147.0, 163.0; GC-MS (EI) $m/z$ = 260 $[M]^+$.

### 5-Methyl-*N,N*-dipropylbenzoxazol-2-amine (3e)



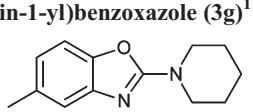
White solid; Yield 78%; M.p. 38–40 °C; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.96 (t, $J$ = 7.2 Hz, 6H), 1.66–1.75 (m, 4H), 2.38 (s, 3H), 3.46 (t, $J$ = 7.2 Hz, 4H), 6.77 (d, $J$ = 8.0 Hz, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 7.15 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 11.3, 21.4, 50.5, 108.7, 115.9, 120.0, 123.9, 143.8, 148.9, 162.8; HRESI-MS ($m/z$): Calculated for $C_{14}H_{21}N_2O$ $[M + H]^+$ 233.1654, found $[M + H]^+$: 233.1657.

### *N,N*-Diethyl-5-methylbenzoxazol-2-amine (3f)[11f]



Colorless liquid; Yield 75%; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 1.27 (t, $J$ = 7.2 Hz, 6H), 2.38 (s, 3H), 3.57 (q, $J$ = 7.2 Hz, 4H), 6.78 (d, $J$ = 8.0 Hz, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 7.15 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 13.7, 21.7, 43.1, 108.0, 116.4, 120.7, 133.6, 143.9, 147.1, 162.5; GC-MS (EI) $m/z$ = 204 $[M]^+$.

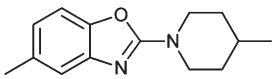
### 5-Methyl-2-(piperidin-1-yl)benzoxazole (3g)[11a]



White solid; Yield 77%; M.p. 97–98 °C; Prepared as shown in the general experimental procedure. $^1H$ NMR ($CDCl_3$,

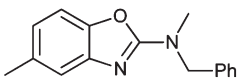
400 MHz) $\delta$ (ppm): 1.669 (s, 6H), 2.38 (s, 3H), 3.64 (s, 4H), 6.79 (d, $J$ = 8.0 Hz, 1H), 7.09 (d, $J$ = 8.0 Hz, 1H), 7.14 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 24.2, 25.4, 46.7, 108.0, 116.6, 121.1, 133.6, 143.6, 147.0, 162.8; GC-MS (EI) $m/z$ = 216 $[M]^+$.

**5-Methyl-2-(4-methylpiperidin-1-yl)benzoxazole (3h)**



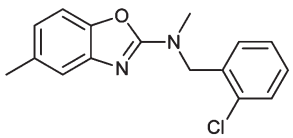
White solid; Yield 72%; M.p. 63–65 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.98 (d, $J$ = 6.4 Hz, 3H), 1.22–1.32 (m, 2H), 1.61–1.64 (m, 1H), 1.74 (d, $J$ = 13.2 Hz, 2H), 2.38 (s, 3H), 3.01–3.08 (m, 2H), 4.25 (d, $J$ = 12.8 Hz, 2H), 6.79 (d, $J$ = 8.0 Hz, 1H), 7.09 (d, $J$ = 8.0 Hz, 1H), 7.14 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 22.0, 30.8, 33.6, 46.2, 108.0, 116.6, 121.1, 133.6, 143.6, 147.0, 162.8; HRESI-MS ($m/z$): Calculated for $C_{14}H_{19}N_2O$ $[M + H]^+$ 231.1497, found $[M + H]^+$: 231.1496.

***N*-Benzyl-*N*,5-dimethylbenzoxazol-2-amine (3i)[11f]**



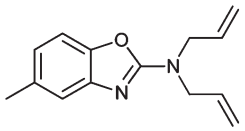
White solid; Yield 67%; M.p. 50–51 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 2.40 (s, 3H), 3.11 (s, 3H), 4.74 (s, 2H), 6.81 (d, $J$ = 8.0 Hz, 1H), 7.13 (d, $J$ = 8.0 Hz, 1H), 7.18 (s, 1H), 7.28–7.35 (m, 5H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 35.3, 54.0, 108.3, 116.7, 121.2, 127.9, 127.9, 128.9, 133.8, 136.7, 143.8, 147.3, 163.3; GC-MS (EI) $m/z$ = 252 $[M]^+$.

***N*-(2-Chlorobenzyl)-*N*,5-dimethylbenzoxazol-2-amine (3j)**



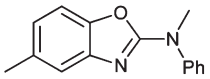
White solid; Yield 67%; M.p. 69–70 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 2.40 (s, 3H), 3.19 (s, 3H), 4.88 (s, 2H), 6.82 (d, $J$ = 8.0 Hz, 1H), 7.12 (d, $J$ = 8.0 Hz, 1H), 7.19 (s, 1H), 7.21–7.28 (m, 3H), 7.39–7.41 (m, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 35.9, 51.5, 108.3, 116.8, 121.3, 127.3, 128.5, 129.0, 130.0, 133.6, 133.8, 134.2, 143.7, 147.4, 163.2; HRESI-MS ($m/z$): Calculated for $C_{16}H_{15}N_2ONaCl$ $[M + Na]^+$ 309.0771, found $[M + Na]^+$: 309.0776.

***N*,*N*-Diallyl-5-methylbenzoxazol-2-amine (3k)[5]**



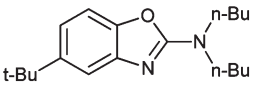
Yellow liquid; Yield 65%; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 2.39 (s, 3H), 4.14 (d, $J$ = 5.6 Hz, 4H), 5.21–5.26 (m, 4H), 5.83–5.92 (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 50.0, 108.2, 116.7, 118.0, 121.2, 132.8, 133.7, 143.6, 147.2, 162.6; GC-MS (EI) $m/z$ = 228 $[M]^+$.

***N*,5-Dimethyl-*N*-phenylbenzoxazol-2-amine (3l)**



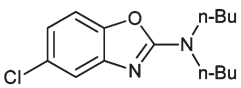
Yellow crystal; Yield 35%; M.p. 55–56 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 2.40 (s, 3H), 3.62 (s, 3H), 6.84 (d, $J$ = 8.0 Hz, 1H), 7.10 (d, $J$ = 8.0 Hz, 1H), 7.23–7.25 (m, 2H), 7.42 (s, 4H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 21.7, 39.2, 108.5, 117.2, 122.0, 124.6, 126.1, 129.4, 133.9, 143.1, 143.2, 147.1, 161.6; HRESI-MS ($m/z$): Calculated for $C_{15}H_{15}N_2O$ $[M + H]^+$ 239.1184, found $[M + H]^+$: 239.1189.

***5-tert*-Butyl-*N*,*N*-dibutylbenzoxazol-2-amine (4a)[11f]**



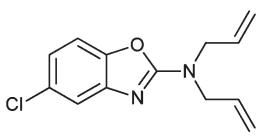
Light yellow liquid; Yield 64% (5 equiv. acid), 69% (1.2 equiv. acid); Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.95 (t, $J$ = 7.2 Hz, 6H), 1.34–1.40 (m, 13H), 1.61–1.69 (m, 4H), 3.49 (t, $J$ = 7.6 Hz, 4H), 7.01 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 7.14 (d, $J$ = 8.4 Hz, 1H), 7.43 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 14.0, 20.1, 30.3, 32.0, 35.0, 48.5, 107.6, 113.1, 117.1, 143.6, 146.8, 147.3, 163.0; GC-MS (EI) $m/z$ = 302 $[M]^+$.

***N*,*N*-Dibutyl-5-chlorobenzoxazol-2-amine (4b)[11f]**



White solid; Yield 57% (5 equiv. acid), 43% (1.2 equiv. acid); M.p. 60–61 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 0.96 (t, $J$ = 7.2 Hz, 6H), 1.33–1.43 (m, 4H), 1.61–1.69 (m, 4H), 3.49 (t, $J$ = 7.6 Hz, 4H), 6.92 (dd, $J$ = 8.4 Hz, 2 Hz, 1H), 7.12 (d, $J$ = 8.4 Hz, 1H), 7.29 (d, $J$ = 2 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 14.0, 20.1, 30.2, 48.6, 109.0, 116.0, 119.8, 129.2, 145.3, 147.5, 163.6; GC-MS (EI) $m/z$ = 280 $[M]^+$.

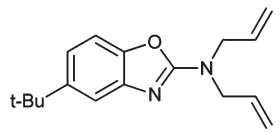
***N*,*N*-Diallyl-5-chlorobenzoxazol-2-amine (4c)**



Colorless liquid; Yield 31% (5 equiv acid), 26% (1.2 equiv acid); Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 4.15 (d, $J$ = 5.6 Hz, 4H), 5.23–5.27 (m, 4H), 5.82–5.92 (m, 2H), 6.96 (dd, $J$ = 8.4 Hz, 2 Hz, 1H), 7.14 (d, $J$ = 8.4 Hz, 1H), 7.32 (d, $J$ = 2.0 Hz, 1H);

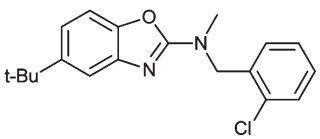
$^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 50.2, 109.4, 116.4, 118.4, 120.4, 129.5, 132.4, 144.8, 147.7, 163.3; HRESI-MS (*m*/*z*): Calculated for $C_{13}H_{13}N_2ONaCl$ $[M + Na]^+$ 271.0614, found $[M + Na]^+$: 271.0613.

**N,N-Diallyl-5-*tert*-butylbenzoxazol-2-amine (4d)**



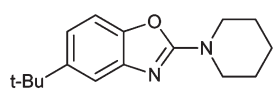

Colorless liquid; Yield 46% (5 equiv acid), 64% (1.2 equiv acid); Prepared as shown in general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 1.34 (s, 9H), 4.15 (d, $J$ = 5.6 Hz, 4H), 5.21–5.26 (m, 4H), 5.83–5.91 (m, 2H), 7.05 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 7.17 (d, $J$ = 8.4 Hz, 1H), 7.45 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 32.0, 35.0, 50.1, 108.0, 113.5, 117.7, 118.0, 132.8, 143.3, 147.1, 147.5, 162.7; HRESI-MS (*m*/*z*): Calculated for $C_{17}H_{22}N_2ONa$ $[M + Na]^+$ 293.1630, found $[M + Na]^+$: 293.1634.

**5-*tert*-Butyl-*N*-(2-chlorobenzyl)-*N*-methylbenzoxazol-2-amine (4e)**




Yellow solid; Yield 37% (5 equiv. acid), 54% (1.2 equiv. acid); M.p. 89–92 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 1.35 (s, 1H), 3.20 (s, 3H), 4.88 (s, 2H), 7.07 (dd, $J$ = 8.4 Hz, 2 Hz, 1H), 7.17 (d, $J$ = 8.4 Hz, 1H), 7.21–7.26 (m, 3H), 7.39–7.41 (m, 1H), 7.46 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 32.0, 35.0, 36.0, 51.5, 108.0, 113.6, 117.8, 127.3, 128.5, 129.0, 130.0, 133.6, 134.2, 143.3, 147.2, 147.7, 163.2; HRESI-MS (*m*/*z*): Calculated for $C_{19}H_{22}N_2OCl$ $[M + H]^+$ 329.1421, found $[M + H]^+$: 329.1427.

**5-*tert*-Butyl-2-(piperidin-1-yl)benzoxazole (4f)**




White acicular crystal; Yield 60% (5 equiv. acid), 70% (1.2 equiv. acid); M.p. 84–87 °C; Prepared as shown in the general experimental procedure. $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ (ppm): 1.34 (s, 9H), 1.67 (s, 6H), 3.64 (s, 4H), 7.03 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 7.14 (d, $J$ = 8.4 Hz, 1H), 7.42 (d, $J$ = 1.6 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ (ppm): 24.2, 25.4, 32.0, 35.0, 46.8, 107.7, 113.3, 117.5, 143.2, 146.8, 147.4, 162.8; HRESI-MS (*m*/*z*): Calculated for $C_{16}H_{23}N_2O$ $[M + H]^+$ 259.1810, found $[M + H]^+$: 259.1815.



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