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An Iron and Copper System Catalyzed C–H Arylation of Azoles with Arylboronic Acids

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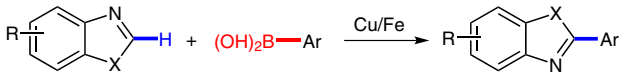

X = O, S
R = 5-Cl, 5-NO_2
Ar = Ph, 4-MeC_6H_4, 3,5-$Me_2C_6H_3$, 3-$MeOC_6H_4$, 4-NCC_6H_4, 4-$F_3CC_6H_4$, 2-naphthyl, 9-phenanthryl, 5-pyrimidyl, 8-quinolyl

up to 92% yield

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Abstract An efficient, environmentally friendly, and economical new method for arylation reactions of azoles with arylboronic acids via copper–iron-catalyzed C–H and C–B bond activation has been developed. The protocol tolerates a series of functional groups, such as methoxy, nitro, cyano, chloro, and trifluoromethyl groups.

Key words environmentally friendly, copper and iron, C–H activation, azoles, arylboronic acids

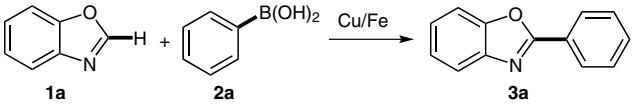
Azoles are an important class of structures in natural products and pharmaceuticals and they have shown a wide range of biological activity, such as antitumor, antiviral, and antimicrobial activity.[1] Hence interest in the development of the synthesis of azole compounds has continued.

The traditional methods for the synthesis of aryl-substituted azole compounds consist of cyclization of functional groups containing the heteroatom[2] and cross-coupling of 2-chloro-1,3-benzoxazoles or 2-chloro-1,3-benzothiazoles with arylboronic acids.[3] Among these methods, the palladium-catalyzed Suzuki–Miyaura reaction is one of the most powerful and convenient methods for the synthesis of aryl-substituted azole compounds.[4] In recent year, direct C–H bond functionalization has become a popular topic in chemical research. Compared with traditional reactions, direct C–H bond functionalization of azoles represents an environmentally and economically attractive strategy, which is a potential alternative to traditional reactions because it avoids the extra introduction of functional groups in one of the coupling partners. Much progress has been made in the C–H activation of azoles with aryl halides or pseudohalides.[5–9] In addition, some metal-catalyst systems (such as Ni, Pd/Cu, and microwave/Mn) have been reported for the direct reaction between azole compounds and arylboronic acids.[10–12] But these protocols also suffered from problems, for example, low yields, narrow applied range, and high toxicity.

Considering the requirements of atom economy and environmental protection, the properties of copper and iron as catalysts have acquired great significance.[13–15] We have recently demonstrated that an iron and copper system can catalyzed the formation of C–C, C–O, and C–N bonds.[16–19] As a part of our continuous efforts toward the development of an iron and copper system, we applied the iron–copper system to the reaction of azoles with arylboronic acids. In this paper, we report that an iron–copper catalyst system could very efficiently catalyze the cross-coupling between azole compounds and arylboronic acids with good yields.

The reaction of 1,3-benzoxazole (**1a**) with phenylboronic acid (**2a**) was used to optimize the reaction conditions. The results of our optimizations experiments for the copper salt, iron salt, base, ligand, oxidant, and solvent are given in Table 1. Initially, a copper salt was used as a single catalyst and a series of experiments were used to identify the most effective copper salt, base, ligand, oxidant, and solvent for the reaction. With all other conditions identically, copper(I) iodide gave the best result among other copper salts [CuBr, CuCl, $Cu(OAc)_2$, $CuSO_4{\cdot}5\,H_2O$, $Cu(acac)_2$] (entries 1–6). Then, the base was varied (NaOMe, K_2CO_3, KOAc, KO*t*-Bu, Cs_2CO_3) but none gave better results than lithium *tert*-butoxide (entries 7–11). From the experimental results, we could see that the ligand and oxidant also have an important influence on the reaction and that no product was obtained with certain ligand and oxidant combinations (entries 15, 16, 19, 20, and 22). The best results were obtained using di-*tert*-butyl peroxide (DTBP) (entry 1). When clean oxidants, such as oxygen or hydrogen peroxide, were used, there was no improvement in the yield (entries 21 and 22). Next we investigated the effect of the ligand (Figure 1) and better results were obtained using 1,10-phenanthroline (**L1**) as the

Table 1 Optimization of the Reaction Conditions[a]



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

Entry	Copper salt	Iron salt	Base	Ligand[b]	Oxidant	Solvent	Yield[c] (%)
1	CuI	–	LiO*t*-Bu	**L1**	DTBP	DMSO	50
2	CuBr	–	LiO*t*-Bu	**L1**	DTBP	DMSO	44
3	CuCl	–	LiO*t*-Bu	**L1**	DTBP	DMSO	42
4	$Cu(OAc)_2$	–	LiO*t*-Bu	**L1**	DTBP	DMSO	10
5	$CuSO_4 \cdot 5\,H_2O$	–	LiO*t*-Bu	**L1**	DTBP	DMSO	23
6	$Cu(acac)_2$	–	LiO*t*-Bu	**L1**	DTBP	DMSO	27
7	CuI	–	NaOMe	**L1**	DTBP	DMSO	16
8	CuI	–	K_2CO_3	**L1**	DTBP	DMSO	13
9	CuI	–	KOAc	**L1**	DTBP	DMSO	27
10	CuI	–	KO*t*-Bu	**L1**	DTBP	DMSO	42
11	CuI	–	Cs_2CO_3	**L1**	DTBP	DMSO	26
12	CuI	–	LiO*t*-Bu	**L2**	DTBP	DMSO	40
13	CuI	–	LiO*t*-Bu	**L3**	DTBP	DMSO	20
14	CuI	–	LiO*t*-Bu	**L4**	DTBP	DMSO	18
15	CuI	–	LiO*t*-Bu	**L5**	DTBP	DMSO	0
16	CuI	–	LiO*t*-Bu	**L6**	DTBP	DMSO	0
17	CuI	–	LiO*t*-Bu	**L1**	I_2	DMSO	24
18	CuI	–	LiO*t*-Bu	**L1**	TBHP	DMSO	31
19	CuI	–	LiO*t*-Bu	**L1**	NBS	DMSO	0
20	CuI	–	LiO*t*-Bu	**L1**	DDQ	DMSO	0
21	CuI	–	LiO*t*-Bu	**L1**	O_2	DMSO	40
22	CuI	–	LiO*t*-Bu	**L1**	H_2O_2	DMSO	0
23	CuI	–	LiO*t*-Bu	**L1**	DTBP	DMF	44
24	CuI	–	LiO*t*-Bu	**L1**	DTBP	NMP	35
25	CuI	–	LiO*t*-Bu	**L1**	DTBP	toluene	52
26	CuI	–	LiO*t*-Bu	**L1**	DTBP	benzene	41
27	CuI	Fe_2O_3	LiO*t*-Bu	**L1**	DTBP	toluene	87
28	CuI	Fe_3O_4	LiO*t*-Bu	**L1**	DTBP	toluene	83
29	CuI	$FeCl_2$	LiO*t*-Bu	**L1**	DTBP	toluene	73
30	CuI	$FeCl_3$	LiO*t*-Bu	**L1**	DTBP	toluene	80
31	–	Fe_2O_3	LiO*t*-Bu	**L1**	DTBP	toluene	0
32	CuI	Fe_2O_3	LiO*t*-Bu	**L1**	DTBP	toluene	45[d]
33	CuI	Fe_2O_3	LiO*t*-Bu	**L1**	DTBP	toluene	60[e]
34	CuI	Fe_2O_3	LiO*t*-Bu	**L1**	–	toluene	77[f]

[a] Reaction conditions: **1a** (0.5 mmol), phenylboronic acid (**2a**, 2 equiv), copper salt (20 mol%), iron salt (20 mol%), base (3 equiv), ligand (20%), oxidant (2 equiv), solvent (3 mL), 110 °C, 12 h.
[b] Isolated yield based on **1a** after silica gel chromatography.
[c] See Figure 1.
[d] Using 1.5 equiv of phenylboronic acid (**2a**).
[e] Using 1.7 equiv of phenylboronic acid (**2a**).
[f] Using 2 equiv of Fe_2O_3.

oxidant compared to TMEDA (**L2**), DMEDA (**L3**), and 2,2′-bipyridyl (**L4**) (entries 12–14). Therefore, 1,10-phenanthroline (**L1**) was selected as the optimal ligand for its catalytic effect and inexpensive price. Finally, the solvent was varied and toluene was found to be the best choice (entries 23–26).

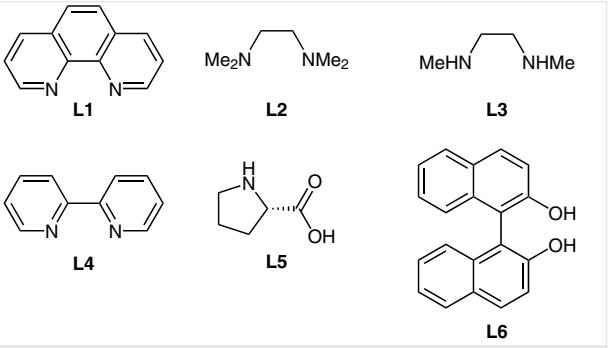


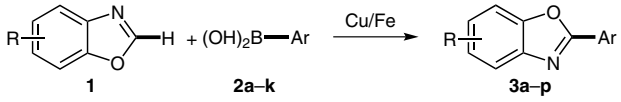
Figure 1

Although a great number of experiments have been performed to improve the yield, we have not achieved our aim as the copper salt was the only catalyst. Interestingly, when an iron salt was added to work jointly with the copper salt, the yield rose sharply (entries 27 and 28). From the results, we could see that the iron salt is indispensable for a high yield and iron(III) oxide was the best from several common iron salts (Fe_2O_3, Fe_3O_4, $FeCl_2$, $FeCl_3$) (entries 27–30).

The highest yield was obtained using the conditions in entry 27 and several experiments were performed varying the proportions of the reactants. We have reason to believe that the iron salt functions as a pre-oxidant. The reaction was carried out solely using the iron salt to ascertain whether the copper salt and iron salt were working jointly or separately; no product was obtained in the absence of the copper salt (entry 31). It follows that iron salt and copper salt are a collaborative catalyst in the reaction. The reaction with iron(III) oxide (2 equiv) in the absence of di-*tert*-butyl peroxide gave the product in 77% yield (entry 34). Reducing the amount of phenylboronic acid gave the product in lower yields (entries 32 and 33). We selected copper(I) iodide (20% mmol), iron(III) oxide (20% mmol), lithium *tert*-butoxide (3.0 equiv), 1,10-phenanthroline (20% mmol), di-*tert*-butyl peroxide (2.0 equiv), and toluene (3.0 mL) as the optimal reaction conditions.

With the optimized reaction conditions in hand, we next explored the substrate scope of the reactions of diversified azoles with arylboronic acids. To evaluate the generality of this reaction, 1,3-benzoxazole (**1a**) was reacted with a range of arylboronic acids and the results are summarized in Table 2. The results show that 1,3-benzoxazole reacts well with arylboronic acids. Electron-poor or -rich arylboronic acids containing functionalities such as methyl, methoxy, cyano, or trifluoromethyl were studied and pyrimidine or quinoline rings as well. The results of the reactions of 4-methylphenylboronic acid (**2b**) and 3,5-dimethylphenylboronic acid (**2c**) show that electron-donating groups may reduce the yield of the products (entries 2–4); the methoxy group affects the yield with a stronger electron-donating ability than methyl. When arylboronic acids linked with electron-withdrawing groups in the *para* position, such as 4-(trifluoromethyl)phenylboronic acid (**2f**) and 4-cyanophenylboronic acid (**2e**), were used, the yields of products dropped sharply (entries 5 and 6). Polycyclic arylboronic acid like naphthalen-2-ylboronic acid (**2g**) and phenanthren-9-ylboronic acid (**2h**) also reacted with 1,3-benzoxazole to provide the products **3g** and **3h** in 80% and 63% yields, respectively (entries 7 and 8). Pyrimidin-5-yl- or quinolin-8-yl-substituted boronic acids gave the products **3j** and **3k**, respectively, in acceptable yields (entries 10 and 11). The optimized reaction conditions were also applicable in the reactions of 5-chloro-1,3-benzoxazole (**1b**), 5-nitro-1,3-benzoxazole (**1c**), and 4-phenyloxazole (**1d**) with arylboronic acids (entries 12–16).

Table 2 Reaction of Oxazoles with Arylboronic Acids[a]



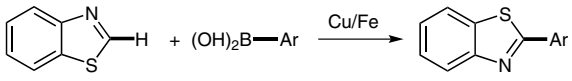
Entry	R	Ar	Product	Yield[b] (%)
1	H	Ph (**2a**)	**3a**	87
2	H	4-MeC_6H_4 (**2b**)	**3b**	78
3	H	3,5-$Me_2C_6H_3$ (**2c**)	**3c**	74
4	H	3-$MeOC_6H_4$ (**2d**)	**3d**	50
5	H	4-NCC_6H_4 (**2e**)	**3e**	42
6	H	4-$F_3CC_6H_4$ (**2f**)	**3f**	58
7	H	2-naphthyl (**2g**)	**3g**	80
8	H	9-phenanthryl (**2h**)	**3h**	63
9	H	4-PhC_6H_4 (**2i**)	**3i**	52
10	H	5-pyrimidyl (**2j**)	**3j**	60
11	H	8-quinolyl (**2k**)	**3k**	62
12	5-Cl	Ph (**2a**)	**3l**	73
13	5-Cl	4-MeC_6H_4 (**2b**)	**3m**	67
14	5-Cl	4-$F_3CC_6H_4$ (**2f**)	**3n**	57
15	5-NO_2	Ph (**2a**)	**3o**	45
16	–[c]	4-MeC_6H_4 (**2b**)	**3p**	64

[a] Reaction conditions: oxazole **1** (0.5 mmol), CuI (20 mol%), Fe_2O_3 (20 mol%), **L1** (20 mol%), LiO*t*-Bu (1.5 mmol), DTBP (1.0 mmol), arylboronic acid (1.0 mmol), toluene (3 mL), 110 °C, 12 h.
[b] Isolated yield based on **1** after silica gel chromatography.
[c] The substrate was 4-phenyloxazole.

In view of the results above, substrates were further broadened from 1,3-benzoxazoles to 1,3-benzothiazole (**4**) and the results are listed in Table 3. From the results we can

see that our catalytic system is well suited to 1,3-benzothiazole. Similar to the results for 1,3-benzoxazoles **1**, in the reaction of 1,3-benzothiazole (**4**) the use of arylboronic acids containing electron-withdrawing groups resulted in a decrease in the yield (entries 5 and 6); the use of arylboronic acids containing electron-donating groups gave only slightly lower yields of product (entries 1–3). Naphthalen-2-yl- and phenanthren-9-ylboronic acids also reacted under these conditions in satisfactory yields (entries 7 and 8).

Table 3 Reaction of 1,3-Benzothiazole with Arylboronic Acids[a]



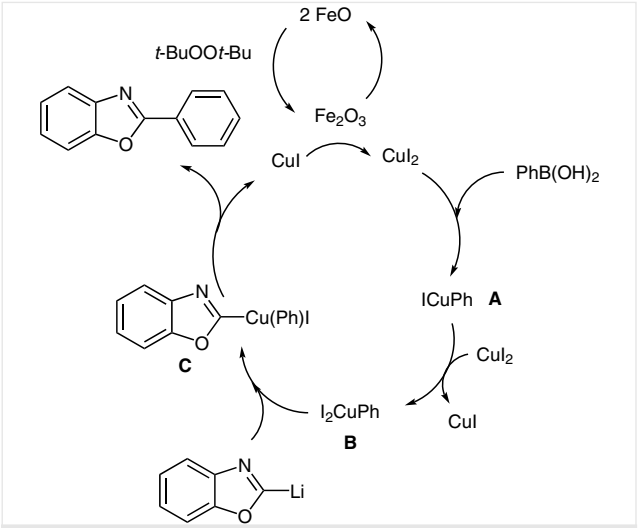
4 **2a–h** **5a–h**

Entry	Ar	Product	Yield[b] (%)
1	Ph (**2a**)	**5a**	92
2	4-MeC_6H_4 (**2b**)	**5b**	83
3	3,5-$Me_2C_6H_3$ (**2c**)	**5c**	82
4	3-MeOC_6H_4 (**2d**)	**5d**	45
5	4-NCC_6H_4 (**2e**)	**5e**	37
6	4-$F_3CC_6H_4$ (**2f**)	**5f**	55
7	2-naphthyl (**2g**)	**5g**	72
8	9-phenanthryl (**2h**)	**5h**	59

[a] Reaction conditions: 1,3-benzothiazole (**4**, 0.5 mmol), CuI (20 mol%), Fe_2O_3 (20 mol%), **L1** (20 mol%), LiO*t*-Bu (1.5 mmol), DTBP (1.0 mmol), arylboronic acid (1.0 mmol), toluene (3 mL), 110 °C, 12 h.
[b] Isolated yield based on **4** after silica gel chromatography.

To gain insight into whether the reaction is a radical reaction or not, a model reaction was carried out with 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO, 2.0 equiv) as an additive under standard conditions; the arylation product was obtained with similar yield and no radicals were captured with TEMPO. Referring to previously reported mechanisms,[15,20] a reaction mechanism was proposed as shown in Scheme 1. Copper(I) iodide is oxidized to copper(II) iodide by iron(III) oxide, which is itself reoxidized by di-*tert*-butyl peroxide. Then a transmetalation from phenylboronic acid with copper(II) iodide occurred which forms an arylcopper(II) species **A**. Intermediate **A** is oxidized to arylcopper(III) intermediate **B**. Then, the other transmetalation gives intermediate **C**. Finally, the desired cross-coupling product is obtained via a reductive elimination reaction.

In summary, an inexpensive and nonpoisonous iron and copper catalytic system has been successfully used, replacing noble metals like palladium salts which are costly and nocuous to the environment, in the reaction of azoles with arylboronic acids. From synthetic point of view, an effective, facile, and environmentally friendly method for the preparation of azoles has been developed.



Scheme 1 Proposed reaction mechanism for the iron and copper system catalyzed C–H arylation of azoles with arylboronic acids

All reagents and solvents were used directly as obtained commercially unless otherwise noted. Petroleum ether (PE) used refers to the fraction with bp 60–90 °C. Column chromatography was performed with 300–400 mesh silica gel using flash column techniques. ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ or DMSO-d_6 on a Varian-Inova 400 MHz spectrometer referenced to internal TMS. Chemical shifts in ^{13}C NMR spectra are reported relative to the central line of the $CDCl_3$ (δ = 77.22). IR spectra were recorded on Varian F-1000 spectrometer in KBr. HRMS were obtained with a GCT-TOF instrument.

2-Phenyl-1,3-benzoxazole (3a);[12] Typical Procedure

CuI (19 mg, 0.1 mmol), Fe_2O_3 (16 mg, 0.1 mmol), 1,10-phenanthroline (18 mg, 0.1 mmol), LiO*t*-Bu (180 mg, 1.5 mmol), and di-*tert*-butyl peroxide (146 mg, 1.0 mmol) were added to a solution of toluene (3 mL) containing phenylboronic acid (1.0 mmol) and 1,3-benzoxazole (0.5 mmol). The mixture was stirred at 110 °C for 12 h. The resulting mixture was then cooled to r.t. and the solvent was removed in vacuo and the remaining residue was purified by column chromatography (silica gel, PE–EtOAc, 20:1) to yield **3a** (84.8 mg, 87%) as a light yellow solid; mp 105–107 °C.

IR (KBr): 3060, 1616, 1551, 1489, 1472, 1446, 1343, 1278, 1241, 1052, 1021, 923, 807, 747, 702, 687 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23–8.21 (m, 2 H), 7.75–7.73 (m, 1 H), 7.55–7.47 (m, 4 H), 7.32–7.30 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.24, 150.96, 142.30, 131.72, 129.11, 127.82, 127.36, 125.31, 124.78, 120.22, 110.80.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_9NO$: 195.0684; found: 195.0685.

2-*p*-Tolyl-1,3-benzoxazole (3b)[12]

Yellow solid; yield: 81.5 mg (78%); mp 115–117 °C.

IR (KBr): 3026, 2918, 2306, 1622, 1555, 1501, 1450, 1243, 1177, 1055, 1017, 820, 745, 726, 501 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.0 Hz, 2 H), 7.78–7.71 (m, 1 H), 7.59–7.51 (m, 1 H), 7.36–7.22 (m, 4 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.49, 150.88, 142.37, 142.25, 129.84, 127.79, 125.06, 124.67, 124.60, 120.03, 110.69, 21.85.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NO$: 209.0841; found: 209.0844.

2-(3,5-Dimethylphenyl)-1,3-benzoxazole (3c)[21]

White solid; yield: 82.5 mg (74%); mp 122–124 °C.

IR (KBr): 2916, 2382, 2303, 1600, 1551, 1452, 1243, 1229, 1183, 1003, 929, 863, 741, 682 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 2 H), 7.70–7.61 (m, 1 H), 7.46–7.44 (m, 1 H), 7.25–7.22 (m, 2 H), 7.04 (s, 1 H), 2.29 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.56, 150.82, 142.23, 138.72, 133.44, 126.99, 125.51, 125.08, 124.63, 120.02, 110.64, 21.38.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{13}NO$: 223.0997; found: 223.0998.

2-(3-Methoxyphenyl)-1,3-benzoxazole (3d)[22]

White solid; yield: 56.3 mg (50%); mp 70–72 °C.

IR (KBr): 2833, 2385, 1602, 1555, 1488, 1452, 1243, 1043, 859, 784, 748, 725, 682 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.93 (m, 2 H), 7.67–7.65 (m, 1 H), 7.46–7.44 (m, 1 H), 7.30–7.20 (m, 4 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.11, 160.08, 150.89, 142.20, 130.17, 128.48, 125.34, 124.77, 120.77, 120.17, 118.51, 112.02, 110.78, 55.68.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NO_2$: 225.0790; found: 225.0795.

4-(1,3-Benzoxazol-2-yl)benzonitrile (3e)[23]

White solid; yield: 46.2 mg (42%); mp 204–206 °C.

IR (KBr): 3060, 2227, 1613, 1493, 1474, 1450, 1410, 1341, 1242, 1096, 1055, 927, 843, 816, 760, 692, 548 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.0, 2 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.45–7.42 (m, 2 H), 7.39–7.31 (m, 2 H), 7.23 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.12, 151.09, 142.05, 132.90, 131.32, 128.17, 126.37, 125.34, 121.72, 120.77, 114.93, 111.09.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_8N_2O$: 220.0637; found: 220.0639.

2-[4-(Trifluoromethyl)phenyl]-1,3-benzoxazole (3f)[24]

White solid; yield: 76.3 mg (58%); mp 154–156 °C.

IR (KBr): 3054, 1917, 1614, 1590, 1482, 1433, 1404, 1321, 1169, 1109, 1064, 1011, 967, 859, 754, 731, 675, 617, 587 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 8.12 Hz, 2 H), 7.82–7.80 (m, 3 H), 7.63–7.60 (m, 1 H), 7.43–7.38 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.70, 151.08, 142.11, 133.37, 133.04, 130.65, 128.08, 126.15 (q, *J* = 3.78), 126.0499, 125.16, 120.62, 111.02.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_8NOF_3$: 263.0558; found: 263.0554.

2-(Naphthalen-2-yl)-1,3-benzoxazole (3g)[12]

White solid; yield: 98 mg (80%); mp 117–119 °C.

IR (KBr): 3050, 2359, 1541, 1452, 1362, 1244, 1178, 1049, 950, 866, 760, 750, 740, 472 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.75 (s, 1 H), 8.29 (d, *J* = 8.0 Hz, 1 H), 7.94 (d, *J* = 8.0 Hz, 2 H), 7.85–7.79 (m, 2 H), 7.55–7.53 (m, 3 H), 7.36 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.34, 151.00, 142.36, 134.89, 131.11, 129.10, 128.93, 128.30, 128.06, 127.95, 127.05, 125.34, 124.80, 124.52, 124.10, 120.18, 110.76.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{11}NO$: 245.0841; found: 245.0839.

2-(Phenanthren-9-yl)-1,3-benzoxazole (3h)[25]

White solid; yield: 92.9 mg (63%); mp 162–164 °C.

IR (KBr): 1615, 1542, 1523, 1447, 1242, 1135, 999, 949, 902, 770, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.55–9.52 (m, 1 H), 8.80–8.71 (m, 3 H), 8.03 (d, *J* = 8.0 Hz, 1 H), 7.92–7.89 (m, 1 H), 7.77–7.73 (m, 3 H), 7.68–7.65 (m, 2 H), 7.43–7.41 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.93, 150.40, 142.50, 131.95, 131.82, 131.01, 130.75, 130.00, 128.92, 128.88, 127.83, 127.34, 127.32, 125.60, 124.75, 123.15, 122.91, 122.76, 120.54, 110.72.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{21}H_{13}NO$: 295.0997; found: 295.0994.

2-(Biphenyl-4-yl)-1,3-benzoxazole (3i)[12]

White solid; yield: 70.5 mg (52%); mp 142–143 °C.

IR (KBr): 3027, 1568, 1482, 1446, 1406, 1289, 1245, 1057, 847, 744, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.54 (m, 2 H), 7.42–7.35 (m, 8 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 6.73 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.12, 150.97, 146.76, 144.42, 140.92, 128.89, 128.28, 128.08, 127.35, 127.00, 126.33, 125.33, 124.82, 120.16, 110.79.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{13}NO$: 271.0997; found: 271.0993.

2-(Pyrimidin-5-yl)-1,3-benzoxazole (3j)[26]

White solid; yield: 59.1 mg (60%); mp 137–139 °C.

IR (KBr): 3407, 3060, 1549, 1512, 1489, 1458, 1431, 1343, 1216, 1241, 1052, 1019, 912, 824, 755, 693, 675 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (s, 1 H), 7.97–7.87 (m, 4 H), 7.51 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.61, 133.94, 132.86, 128.72, 128.44, 127.88, 126.56, 126.32, 126.21, 125.94.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{11}H_7N_3O$: 197.0589; found: 197.0586.

8-(1,3-Benzoxazol-2-yl)quinoline (3k)[27]

Brown oil; yield: 76.3 mg (62%).

IR (KBr): 3057, 1654, 1593, 1542, 1494, 1452, 1381, 1320, 1242, 1177, 1125, 1066, 924, 832, 793, 746, 653, 624 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.18–9.16 (m, 1 H), 8.51–8.49 (m, 1 H), 8.25–8.22 (m, 1 H), 8.01–7.98 (m, 1 H), 7.95–7.92 (m, 1 H), 7.69–7.62 (m, 2 H), 7.52–7.49 (m, 1 H), 7.40–7.37 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.37, 151.95, 151.04, 145.97, 142.39, 136.74, 132.82, 131.83, 128.87, 126.36, 126.09, 125.38, 124.50, 121.81, 120.84, 110.88.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{10}N_2O$: 246.0793; found: 246.0795.

5-Chloro-2-phenyl-1,3-benzoxazole (3l)[28]

Yellow solid; yield: 83.6 mg (73%); mp 108–111 °C.

IR (KBr): 3062, 1611, 1553, 1465, 1334, 1262, 1053, 1023, 918, 864, 809, 701, 683, 593 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 6.32 Hz, 2 H), 7.68 (s, 1 H), 7.48–7.43 (m, 4 H), 7.19 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.57, 149.55, 143.35, 132.15, 130.24, 129.21, 127.96, 126.89, 125.59, 120.18, 111.52.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_8ClNO$: 229.0294; found: 229.0292.

5-Chloro-2-*p*-tolyl-1,3-benzoxazole (3m)[22]

Yellow solid; yield: 81.4 mg (67%); mp 139–141 °C.

IR (KBr): 2963, 1615, 1559, 1498, 1449, 1260, 1199, 1104, 1016, 916, 893, 792, 726, 703, 498 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.0 Hz, 2 H), 7.73 (d, *J* = 7.04 Hz, 1 H), 7.48 (d, *J* = 8.0 Hz, 1 H), 7.35–7.29 (m, 3 H), 2.45 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.52, 154.28, 139.05, 132.00, 129.10, 128.17, 126.47, 125.31, 125.05, 123.34, 121.78, 21.54.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{10}ClNO$: 243.0451; found: 243.0452.

5-Chloro-2-[4-(trifluoromethyl)phenyl]-1,3-benzoxazole (3n)[29]

White solid; yield: 84.6 mg (57%); mp 147–149 °C.

IR (KBr): 2936, 2359, 1557, 1501, 1453, 1412, 1325, 1261, 1163, 1112, 1072, 1014, 919, 848, 806, 752, 700, 589 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, *J* = 8.24 Hz, 2 H), 7.80–7.77 (m, 3 H), 7.53 (d, *J* = 8.6 Hz, 1 H), 7.35 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.97, 149.63, 143.19, 133.40, 130.66, 130.16, 128.22, 126.33, 126.21 (q, *J* = 3.69), 125.21, 122.50, 120.55, 111.75.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_7ClF_3NO$: 297.0168; found: 297.0166.

5-Nitro-2-phenyl-1,3-benzoxazole (3o)[29]

White solid; yield: 54 mg (45%); mp 167–169 °C.

IR (KBr): 2963, 1615, 1553, 1527, 1449, 1350, 1261, 1067, 1023, 890, 820, 736, 704, 685 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 8.34–8.27 (m, 3 H), 7.79 (d, *J* = 8.0 Hz, 1 H), 7.62–7.55 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.22, 154.48, 143.15, 132.85, 130.56, 129.38, 128.27, 126.19, 121.37, 116.52, 110.96.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_8N_2O_3$: 240.0535; found: 240.0539.

4-Phenyl-2-*p*-tolyloxazole (3p)[30]

Yellow solid; yield: 75.2 mg (64%); mp 113–115 °C.

IR (KBr): 3047, 2934, 2418, 1676, 1571, 1483, 1421, 1214, 1165, 1035, 983, 810, 733, 710, 482 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.70 (s, 1 H), 7.96–7.86 (m, 4 H), 7.46–7.37 (m, 5 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.65, 141.39, 141.19, 135.73, 131.28, 130.25, 129.32, 128.57, 126.56, 125.73, 124. 62, 21.56.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{13}N_2O$: 235.0997; found: 235.0994.

2-Phenyl-1,3-benzothiazole (5a)[12]

Yellow solid; yield: 97 mg (92%); mp 110–113 °C.

IR (KBr): 3061, 1897, 1597, 1306, 1228, 1067, 958, 756, 684, 552 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (s, 2 H), 7.69 (s, 1 H), 7.50–7.43 (m, 4 H), 7.28 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.21, 154.28, 135.20, 133.75, 131.12, 129.17, 127.70, 126.47, 125.34, 123.38, 121.77.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_9NS$: 211.0456; found: 211.0448.

2-*p*-Tolyl-1,3-benzothiazole (5b)[12]

Yellow solid; yield: 93.4 mg (83%); mp 86–89 °C.

IR (KBr): 3056, 2954, 1591, 1447, 1217, 955, 751, 447 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.72 Hz, 2 H), 7.69–7.67 (m, 1 H), 7.50–7.48 (m, 1 H), 7.26 (s, 4 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.40, 154.33, 141.62, 135.00, 131.12, 129.91, 127.66, 126.52, 125.19, 123.22, 121.76, 21.72.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NS$: 225.0612; found: 225.0618.

2-(3,5-Dimethylphenyl)-1,3-benzothiazole (5c)[31]

Yellow solid; yield: 98 mg (82%); mp 72–75 °C.

IR (KBr): 2915, 1773, 1598, 1506, 1432, 1309, 1277, 1184, 1040, 874, 842, 754, 725, 686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.08 Hz, 1 H), 7.76 (d, *J* = 7.84 Hz, 1 H), 7.60 (s, 2 H), 7.37 (t, *J* = 7.53 Hz, 1 H), 7.25 (t, *J* = 7.42 Hz, 1 H), 7.00 (s, 1 H), 2.29 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.99, 154.22, 138.84, 135.11, 133.54, 132.90, 126.38, 125.47, 125.18, 123.22, 121.71, 21.38.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{13}NS$: 239.0769; found: 239.0766.

2-(3-Methoxyphenyl)-1,3-benzothiazole (5d)[32]

White solid; yield: 54.2 mg (45%); mp 84–87 °C.

IR (KBr): 3060, 2833, 1604, 1470, 1289, 1047, 995, 871, 761, 727, 684 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.04, 1 H), 7.88 (d, *J* = 7.84 Hz, 1 H), 7.64 (m, 2 H), 7.48 (t, *J* = 7.64, Hz, 1 H), 7.39–7.35 (m, 2 H), 7.02 (d, *J* = 7.56 Hz, 1 H), 3.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.08, 160.10, 154.20, 135.23, 135.03, 130.18, 126.46, 125.37, 123.38, 121.76, 120.37, 117.47, 112.17, 55.63.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{11}NOS$: 241.0561; found: 241.0556.

4-(1,3-Benzothiazol-2-yl)benzonitrile (5e)[25]

White solid; yield: 43.7 mg (37%); mp 163–165 °C.

IR (KBr): 3062, 2227, 1603, 1495, 1476, 1450, 1412, 1343, 1245, 1061, 834, 679, 618, 553 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.44 Hz, 2 H), 7.57 (d, *J* = 8.20 Hz, 1 H), 7.36 (d, *J* = 8.44 Hz, 2 H), 7.31–7.24 (m, 2 H), 7.16 (d, *J* = 7.04 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.91, 138.70, 133.35, 132.49, 129.82, 129.14, 128.95, 126.86, 119.17, 118.40, 111.94, 100.48.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_8N_2S$: 241.0561; found: 241.0556.

2-[4-(Trifluoromethyl)phenyl]-1,3-benzothiazole (5f)[25]

White solid; yield: 76.7 mg (55%); mp 161–163 °C.

IR (KBr): 3056, 1919, 1617, 1484, 1435, 1407, 1323, 1173, 1109, 1066, 971, 842, 760, 678, 620, 589 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.0 Hz, 2 H), 8.09 (d, *J* = 8.0 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.51 (t, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.26, 154.25, 136.98, 135.41, 132.50, 127.98, 126.87, 126.23 (q, *J* = 3.7), 126.00, 123.84, 121.96.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_8F_3NS$: 279.0330; found: 279.0332.

2-(Naphthalen-2-yl)-1,3-benzothiazole (5g)[12]

Yellow solid; yield: 94 mg (72%); mp 126–128 °C.

IR (KBr): 3045, 2347, 1527, 1442, 1353, 1224, 1164, 1030, 939, 857, 749, 737, 726, 459 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (s, 1 H), 8.22 (d, *J* = 8.0 Hz, 1 H), 8.12 (d, *J* = 8.0 Hz, 1 H), 7.99–7.93 (m, 3 H), 7.90–7.88 (m, 1 H), 7.57–7.54 (m, 2 H), 7.51 (d, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.34, 154.43, 135.32, 134.81, 133.39, 131.18, 129.04, 128.08, 127.79, 127.68, 127.10, 126.60, 125.46, 124.64, 123.44, 122.24, 121.86.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{17}H_{11}NS$: 261.0612; found: 261.0615.

2-(Phenanthren-9-yl)-1,3-benzothiazole (5h)[33]

Yellow oil; yield: 91.7 mg (59%).

IR (KBr): 1627, 1554, 1533, 1450, 1254, 1147, 1012, 958, 921, 787, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.92 (d, *J* = 8.0 Hz, 1 H), 8.79 (d, *J* = 8.0 Hz, 1 H), 8.74 (d, *J* = 8.0 Hz, 1 H), 8.22 (d, *J* = 8.0 Hz, 2 H), 7.99 (t, *J* = 8.0 Hz, 2 H), 7.77–7.64 (m, 4 H), 7.58 (t, *J* = 8.0 Hz, 1 H), 7.48 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.78, 154.28, 135.58, 131.37, 131.25, 131.01, 130.86, 130.01, 129.60, 129.42, 128.37, 127.66, 127.42, 127.31, 126.89, 126.54, 125.60, 123.78, 123.10, 122.90, 121.63.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{21}H_{13}NS$: 211.0769; found: 211.0771.

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Supporting Information

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