Iodine-Mediated Facile One-Pot Access to *N*-Aryl-2-benzoxazolamines

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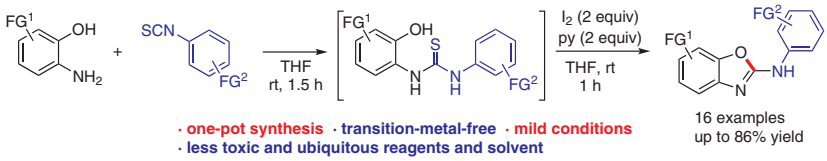

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Abstract Facile, iodine-mediated access to *N*-aryl-2-benzoxazolamines has been achieved in a one-pot manner under mild reaction conditions. Reaction of 2-aminophenols and aryl isothiocyanates afforded *N*-aryl-2-benzoxazolamines in the presence of molecular iodine and pyridine in tetrahydrofuran at room temperature in moderate to excellent yields.

Key words iodine, benzoxazolamine, one-pot synthesis, cyclodesulfurization, transition-metal-free

N-Aryl-2-benzoxazolamines are important substructures for the development of biologically significant compounds (Figure 1). For instance, these compounds act as potential α-glucosidase inhibitors,[1] antibacterial agents,[2] aurora-A kinase inhibitors,[3] 5-lipoxygenase inhibitors,[4] inducible nitric oxide synthase inhibitors,[5] and G protein-coupled receptor 120-selective agonists derived from PPARg agonists.[6] A large number of reports have described the preparation of *N*-aryl-2-benzoxazolamines (Table 1); these include a one-pot reaction using triphenylbismuth dichloride as cyclodesulfurization reagent,[7] synthesis from substituted benzoxazole-2-thiol and 2-chloro-*N*-arylacetamides in KOH-DMF,[8] iodide-catalyzed synthesis via oxidative cyclodesulfurization of phenolic thioureas with hydrogen peroxide,[9] a Cu(I) PNP pincer-complex-catalyzed C–N cross-coupling,[10] ultrasound-assisted synthesis,[11] NBS/oxone promoted one-pot cascade synthesis,[12] visible-light-promoted cyclodesulfurization of phenolic thioureas,[13] mechanochemical ball-milling-promoted one-pot reactions,[14] direct amination of azoles using $CuCl_2$ complexes of amines,[15] use of triflic acid as a cyclodesulfurizing reagent,[16] iron-catalyzed synthesis in water,[17] synthesis using a ditribromide reagent,[18] desulfurization mediated by hypervalent iodine (III),[19] synthesis using TsCl/NaOH,[20] cyclodesulfurization of *N*-(2-hydroxyphenyl)-*N*′-phenylthioureas with superoxide radical anion,[21] HgO-mediated cyclodesulfurization,[22] and cyclodesulfurization under reflux in DMF containing triethylamine.[23] However, the development of transition-metal-free access to *N*-aryl-2-benzoxazolamines under mild and environmentally benign conditions remains an important goal from green and sustainable points of view. In this report, we present the iodine-mediated, one-pot synthesis of *N*-aryl-2-benzoxazolamines from 2-aminophenols and aryl isothiocyanates under mild reaction conditions.

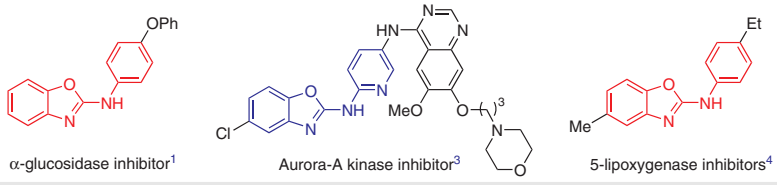
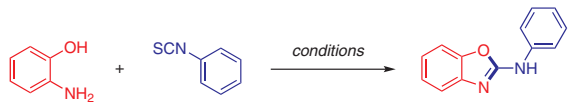
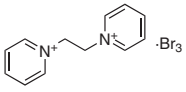


Figure 1 Selected examples of biologically active *N*-aryl-2-benzoxazolamines

Table 1 Selected Examples for the Access to *N*-Aryl-2-benzoxazolamines



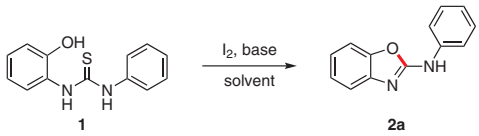
Conditions	Reference
Ph_3BiCl_2	7
Bu_4NI, H_2O_2	9
I_2, PPh_3, Et_3N, MW	11
O_2, Cs_2CO_3, visible light	13
$CuCl_2$	15
CF_3SO_3H	16
	18
HgO	22
Et_3N, DMF, reflux	23
I_2, pyridine	this work

Cyclization conditions were investigated using molecular iodine and thiourea **1**[7] as a model substrate. Reaction of **1** with an equimolar amount of iodine afforded the desired *N*-phenyl-2-benzoxazolamine (**2a**) in 77% yield using pyridine (1 equiv) as base in tetrahydrofuran at room temperature for 30 min (Table 2, entry 1). On reducing the amount of iodine to 50 mol%, the reaction was sluggish, providing 53% yield of **2a** under an oxygen atmosphere (entry 2). On increasing the amount of both iodine and base to three equivalents, the yield increased to 86% (entry 3). The use of triethylamine instead of pyridine resulted in a similar yield (78%; entry 4). When the solvent was ethanol, the yield was 83% using 2 equiv of iodine and base (entry 5). The use of 1 equiv of base required longer reaction time and heating to achieve comparable yields (entries 6 and 7). Changing the base and solvent did not improve the yields (entries 8 and 9). Reaction without base gave only 30% yield of product (entry 10).

The optimized conditions were then applied to the one-pot synthesis of *N*-phenyl-2-benzoxazolamine (**2a**) starting from 2-aminophenol and phenyl isothiocyanate. After mixing equimolar amounts of 2-aminophenol and phenyl isothiocyanate in tetrahydrofuran at room temperature for 1.5 h, iodine and pyridine were introduced directly to the reaction mixture. It was found that introduction of two equivalents of both iodine and pyridine was sufficient to achieve smooth conversion of the starting materials, giving **2a** in 85% isolated yield (Scheme 1). Furthermore, the use of triethylamine instead of pyridine as base resulted in almost the same yield (80%). When the solvent was replaced with dimethyl sulfoxide, ethanol, or dichloromethane, the yields diminished to 60%, 65%, and a trace amount, respectively. The reaction in the absence of iodine gave traces of **2a**.[24]

The optimized conditions (Scheme 1) were then applied to a series of 2-aminophenols and aryl isothiocyanates to investigate the scope and limitations of the present protocol (Scheme 2). It was found that the aromatic substituents on the aryl isothiocyanates influenced the reactivity. When substrates with electron-withdrawing substituents on the

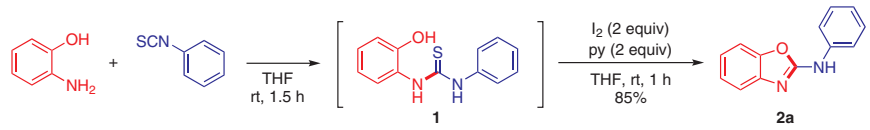
Table 2 Optimization of the Cyclodesulfurization of Thiourea **1**[a]



1 **2a**

Entry	Oxidant (equiv)	Base (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	I_2 (1)	pyridine (1)	THF	rt	0.5	77
2	I_2 (0.5) / O_2[c]	pyridine (1)	THF	rt to 55	2	53
3	I_2 (3)	pyridine (3)	THF	rt	0.5	86
4	I_2 (3)	Et_3N (3)	THF	rt	0.5	78
5	I_2 (2)	pyridine (2)	EtOH	rt	0.5	83
6	I_2 (2)	pyridine (1)	EtOH	rt	24	85
7	I_2 (2)	pyridine (1)	EtOH	50	0.5	82
8	I_2 (2)	Et_3N (2)	EtOH	rt	0.5	77
9	I_2 (1.5)	pyridine (1.5)	DMSO	rt	0.5	44
10	I_2 (3)	none	THF	rt	0.5	30

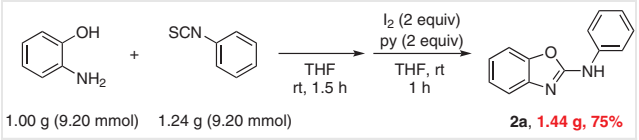
[a] Reaction conditions: **1** (0.46 mmol), oxidant (0.46–1.38 mmol), base (0.46–1.38 mmol), solvent (2.5 mL).
[b] Isolated yield.
[c] Under oxygen balloon.



Scheme 1 One-pot synthesis of **2a**

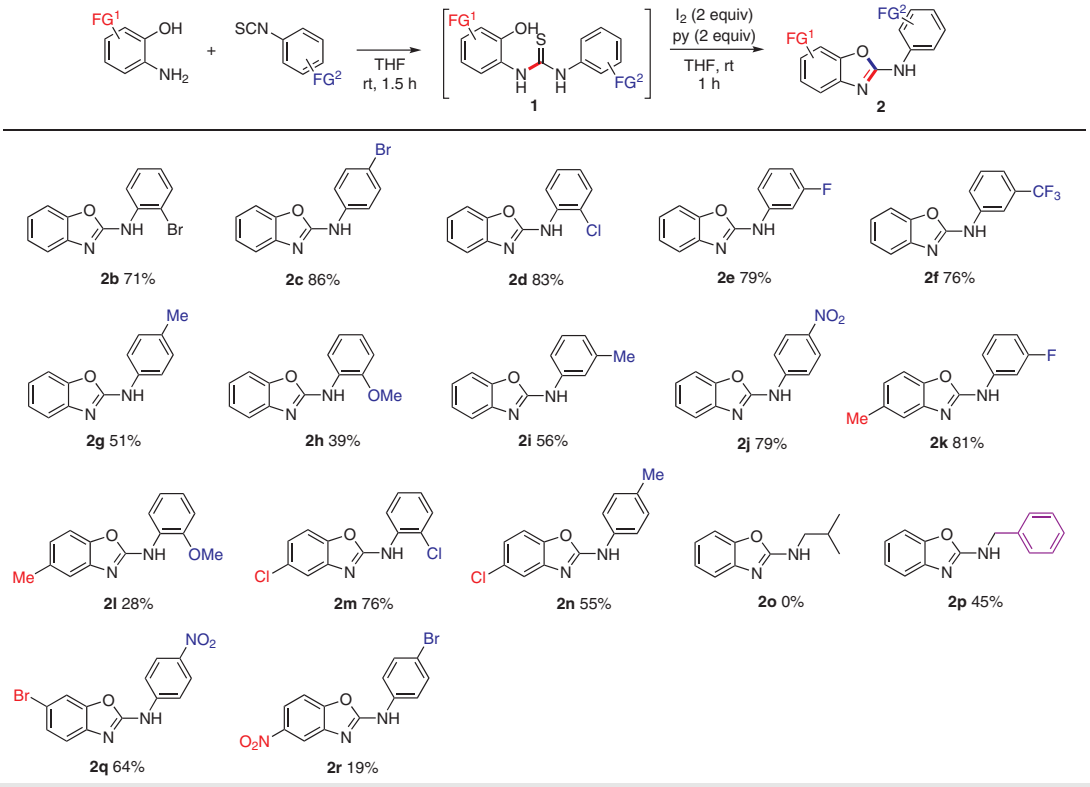
aromatic ring, such as halogens, trifluoromethyl and nitro groups were applied in the reaction, the corresponding *N*-aryl-2-benzoxazolamines **2b–f**, **2j**, **2k** and **2m** were obtained in satisfactory yields (71–86%). On the other hand, electron-donating substitutions on the aromatic ring, such as methyl and methoxy groups diminished the reactivity to afford the *N*-aryl-2-benzoxazolamines **2g–i**, **2l**, and **2n** in low to moderate yields (28–56%). However, the nature of substitution on the aromatic ring of the 2-aminophenol component did not influence reactivity (**2e** vs. **2k**, **2h** vs. **2l**, **2d** vs. **2m**, and **2g** vs. **2n**). When an alkyl isothiocyanate such as isobutyl isothiocyanate was applied to the conditions, reaction did not take place. However, benzyl isothiocyanate gave the desired benzoxazolamine **2p** in moderate yield (45%). Nitro compounds **2q** and **2r** have also been accessed, albeit in low to moderate yields (64% and 19%, respectively) from the corresponding 2-aminophenols and isothiocyanates.

A gram-scale synthesis of *N*-phenyl-2-benzoxazolamine (**2a**) was investigated to demonstrate the practical utility of the present protocol. As shown in Scheme 3, the desired product **2a** was obtained starting from one gram of 2-aminophenol in an acceptable yield of 75%.

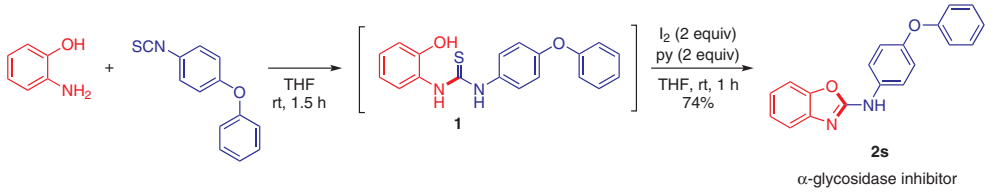


Scheme 3 A gram-scale synthesis of *N*-phenyl-2-benzoxazolamine (**2a**)

An efficient and rapid access to a biologically active compound was also achieved using this methodology (Scheme 4). Reaction of 2-aminophenol and commercially available 1-isothiocyanato-4-phenoxybenzene under the standard conditions provided the desired benzoxazolamine **2s**,[1,8] which was shown to exhibit α-glycosidase inhibitory



Scheme 2 Synthesis of a series of benzoxazolamines **2**



Scheme 4 Synthesis of α-glycosidase inhibitor **2s**

activity,[1] was obtained in 74% yield. Previously reported procedures required either two or three steps from 2-aminophenol via an intermediate benzo[*d*]oxazole-2-thiol, resulting in formation of the product in 20–29% yield.[1,8]

A plausible mechanism for the formation of **2a** from 2-aminophenol and phenylisothiocyanate is depicted in Scheme 5.

After initial formation of thiourea **1**, the oxidative desulfurization of **1** is mediated by molecular iodine in the presence of base (Path A). The generated carbodiimide intermediate **4**, formed via intermediate **3**, then cyclizes to generate benzoxazolamine **2a**. Alternatively, intramolecular cyclization of intermediate **3** would proceed to give **2a** via dehydrosulfurization (Path B).

The reason for the sluggishness of reactions of aryl isothiocyanate substrates with electron-donating groups on the aromatic ring is probably the decrease in acidity of the NH proton in thiourea **1** and iodine adduct **3** and also a decrease of electrophilicity of the carbon in carbodiimide **4**. Moreover, the formation of thiourea **1** from 2-aminophenol and phenyl isothiocyanate would also be inhibited.

In conclusion, a simple method for the synthesis of *N*-aryl-2-benzoxazolamines has been developed through the use of molecular iodine. The conversion occurs in a one-pot process under mild reaction conditions using a simple experimental procedure in short reaction times. As the reagents and solvent utilized in this reaction are ubiquitous and of low toxicity, this methodology will provide rapid access to *N*-aryl-2-benzoxazolamine derivatives in a sustainable and environmentally friendly manner. Efforts to utilize molecular iodine in catalytic amounts for this transformation are under investigation and the results will be reported in due course.

Unless otherwise noted, reagents were commercially available and were used without purification. THF was purchased from Wako Pure Chemical Industries and was distilled over sodium. Silica gel used for column chromatography was BW-200 from Fuji Silysia Chemical. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded with a JEOL-ECZ R-series 500 MHz spectrometer. ^{1}H NMR spectra were referenced to tetramethylsilane as internal standard or to solvent signal (DMSO-d_6: δ = 2.50 ppm). ^{13}C NMR spectra were referenced to solvent signal ($CDCl_3$: δ = 77.16 ppm or DMSO-d_6: δ = 39.52 ppm). IR spectra were obtained with an FT/IR-460 Plus from JASCO Corporation as a KBr pellet. High-resolution mass spectra (HRMS) were recorded with a Bruker microTOF. Melting points were determined with a *J*-Science RFS-10 melting-point apparatus.

N-Phenyl-2-benzoxazolamines; General Procedure

To a solution of the requisite 2-aminophenol (50 mg, 0.46 mmol) in THF (2.5 mL) was added the phenyl isothiocyanate (1.0 equiv) at r.t. and the mixture was stirred at r.t. for 1.5 h. I_2 (2.0 equiv) and pyridine (2.0 equiv) were then added at r.t. and the mixture was stirred at r.t. After 1 h, the reaction was quenched with saturated $Na_2S_2O_3$ aq. and extracted with CH_2Cl_2. The combined organic layers were washed with brine, filtered, dried over Na_2SO_4, and the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography to afford the corresponding *N*-phenyl-2-benzoxazolamine.

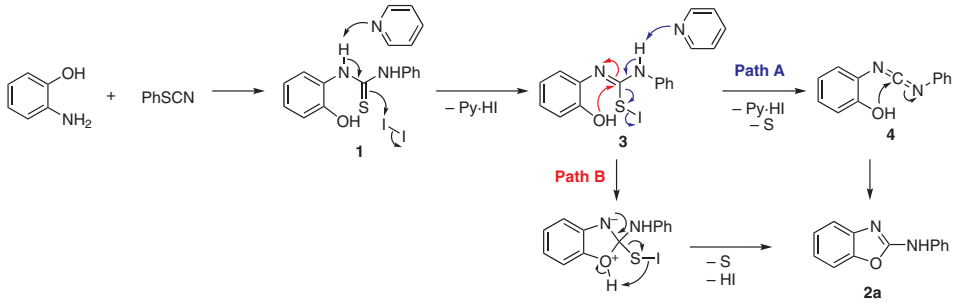
N-Phenyl-2-benzoxazolamine (2a)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 82 mg (85%); white solid; mp 176–177 °C; R_f = 0.36 (hexane/EtOAc 3:1).

IR (KBr): 3384, 3166, 3043, 1656, 1575, 1496, 1454, 1375, 1006, 745 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.61 (s, 1 H, NH), 7.76 (d, *J* = 8.1 Hz, 2 H, ArH), 7.49 (d, *J* = 7.8 Hz, 1 H, ArH), 7.45 (d, *J* = 7.8 Hz, 1 H, ArH), 7.37 (dd, *J* = 8.1, 7.4 Hz, 2 H, ArH), 7.22 (ddd, *J* = 7.8, 7.7, 1.1 Hz, 1 H, ArH), 7.13 (ddd, *J* = 7.8, 7.7, 1.7 Hz, 1 H, ArH), 7.03 (tt, *J* = 7.4, 1.2 Hz, 1 H, ArH).



Scheme 5 Plausible mechanism for the formation of oxazole **2a**

^{13}C NMR (125 MHz, DMSO-d_6): δ = 158.0 (Ar), 147.0 (Ar), 142.4 (Ar), 138.7 (Ar), 129.0 (2C) (Ar), 124.0 (Ar), 122.1 (Ar), 121.7 (Ar), 117.6 (2C) (Ar), 116.6 (Ar), 108.9 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_9N_2O$: 209.0720; found: 209.0728.

N-(2-Bromophenyl)-2-benzoxazolamine (2b)

Purified by silica gel column chromatography (hexane/EtOAc 12:1).

Yield: 95 mg (71%); white solid; mp >300 °C; R_f = 0.36 (hexane /EtOAc 12:1).

IR (KBr): 3022, 2783, 1661, 1587, 1461, 1337, 1245, 1165, 968, 745 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.56 (dd, *J* = 8.1, 1.1 Hz, 1 H, ArH), 7.57 (dd, *J* = 8.0, 1.2 Hz, 1 H, ArH), 7.54 (brs, 1 H, NH), 7.54 (d, *J* = 7.6 Hz, 1 H, ArH), 7.44 (ddd, *J* = 8.1, 7.9, 1.2 Hz, 1 H, ArH), 7.37 (d, *J* = 8.0 Hz, 1 H, ArH), 7.26 (ddd, *J* = 7.8, 7.6, 1.1 Hz, 1 H, ArH), 7.17 (ddd, *J* = 8.0, 7.8, 1.2 Hz, 1 H, ArH), 6.96 (ddd, *J* = 8.0, 7.9, 1.1 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.0 (Ar), 147.7 (Ar), 142.3 (Ar), 135.6 (Ar), 132.5 (Ar), 128.9 (Ar), 124.4 (Ar), 124.0 (Ar), 122.6 (Ar), 119.2 (Ar), 117.9 (Ar), 112.0 (Ar), 109.3 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_8BrN_2O$: 286.9825; found: 286.9834.

N-(4-Bromophenyl)-2-benzoxazolamine (2c)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 114 mg (86%); white solid; mp 227–228 °C; R_f = 0.29 (hexane/EtOAc 3:1).

IR (KBr): 3160, 3026, 1663, 1560, 1490, 1459, 1362, 1282, 1230, 1076, 1005, 822, 740 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.81 (brs, 1 H, NH), 7.76–7.73 (AA′XX′, 2 H, ArH), 7.57–7.54 (AA′ XX′, 2 H, ArH), 7.50 (d, *J* = 7.8 Hz, 1 H, ArH), 7.47 (d, *J* = 7.8 Hz, 1 H, ArH), 7.23 (ddd, *J* = 7.8, 7.8, 1.1 Hz, 1 H, ArH), 7.14 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 157.6 (Ar), 147.0 (Ar), 142.2 (Ar), 138.2 (Ar), 131.7 (2C) (Ar), 124.1 (Ar), 121.9 (Ar), 119.5 (2C) (Ar), 116.7 (Ar), 113.6 (Ar), 109.0 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_8BrN_2O$: 286.9825; found: 286.9835.

N-(2-Chlorophenyl)-2-benzoxazolamine (2d)

Purified by silica gel column chromatography (hexane/EtOAc 15:1).

Yield: 93 mg (83%); pale-yellow solid; mp 96–97 °C; R_f = 0.33 (hexane/EtOAc 12:1).

IR (KBr): 3464, 3026, 2809, 1659, 1582, 1464, 1344, 1239, 1170, 1053, 966, 745 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (dd, *J* = 7.9, 1.8 Hz, 1 H, ArH), 7.53 (d, *J* = 7.4 Hz, 1 H, ArH), 7.41 (dd, *J* = 8.0, 1.5 Hz, 1 H, ArH), 7.38 (ddd, *J* = 7.9, 7.7, 1.5 Hz, 1 H, ArH), 7.37 (d, *J* = 8.1 Hz, 1 H, ArH), 7.26 (ddd, *J* = 7.7, 7.4, 1.1 Hz, 1 H, ArH), 7.19 (ddd, *J* = 8.1, 7.7, 1.1 Hz, 1 H, ArH), 7.02 (ddd, *J* = 8.0, 7.7, 1.8 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.1 (Ar), 147.8 (Ar), 142.4 (Ar), 134.6 (Ar), 129.3 (Ar), 128.2 (Ar), 124.5 (Ar), 123.5 (Ar), 122.6 (Ar), 121.6 (Ar), 119.0 (Ar), 117.9 (Ar), 109.3 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_8ClN_2O$: 243.0331; found: 243.0341.

N-(3-Fluorophenyl)-2-benzoxazolamine (2e)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 83 mg (79%); white solid; mp 204–205 °C; R_f = 0.34 (hexane/EtOAc 3:1).

IR (KBr): 3056, 1662, 1614, 1577, 1503, 1458, 1361, 1247, 1148, 1006, 943, 863, 742 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.87 (s, 1 H, NH), 7.77 (ddd, *J* = 2.3, 2.0 Hz, J_{H-F} = 12.0 Hz, 1 H, NCC*H*CF), 7.51 (d, *J* = 7.6 Hz, 1 H, ArH), 7.50 (d, *J* = 7.6 Hz, 1 H, ArH), 7.46 (ddd, *J* = 7.8, 2.0, 1.2 Hz, 1 H, C*H*CHCHCF), 7.40 (ddd, *J* = 8.1, 7.8 Hz, J_{H-F} = 7.0 Hz, 1 H, C*H*CHCF), 7.25 (ddd, *J* = 7.7, 7.6, 1.1 Hz, 1 H, ArH), 7.17 (ddd, *J* = 7.7, 7.6, 1.7 Hz, 1 H, ArH), 6.85 (dddd, *J* = 8.1, 2.3, 1.2 Hz, J_{H-F} = 9.2 Hz, 1 H, CHC*H*CF).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6 (d, $^1J_{C-F}$ = 241.3 Hz, CF), 157.6 (Ar), 147.0 (Ar), 142.1 (Ar), 140.6 (d, $^3J_{C-F}$ = 11.0 Hz, *C*CCF), 130.7 (d, $^3J_{C-F}$ = 9.7 Hz, *C*CCF), 124.2 (Ar), 122.1 (Ar), 117.0 (Ar), 113.6 (Ar), 109.2 (Ar), 108.5 (d, $^2J_{C-F}$ = 21.2 Hz, *C*CF), 104.4 (d, $^2J_{C-F}$ = 27.2 Hz, *C*CF).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_8FN_2O$: 227.0626; found: 227.0625.

N-[3-(Trifluoromethyl)phenyl]-2-benzoxazolamine (2f)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 97 mg (76%); white solid; mp 200–201 °C; R_f = 0.32 (hexane/EtOAc 3:1).

IR (KBr): 3115, 2922, 1657, 1583, 1492, 1333, 1283, 1158, 1115, 994, 877, 801, 746, 658 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.99 (s, 1 H, NH), 8.21 (s, 1 H, ArH), 8.00 (dd, *J* = 8.2, 1.4 Hz, 1 H, ArH), 7.61 (dd, *J* = 8.2, 8.0 Hz, 1 H, ArH), 7.53 (d, *J* = 7.7 Hz, 1 H, ArH), 7.52 (d, *J* = 7.7 Hz, 1 H, ArH), 7.38 (d, *J* = 8.0 Hz, 1 H, ArH), 7.25 (ddd, *J* = 7.8, 7.7, 1.2 Hz, 1 H, ArH), 7.17 (ddd, *J* = 7.8, 7.7, 1.1 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 157.5 (Ar), 147.0 (Ar), 142.1 (Ar), 139.6 (Ar), 130.3 (Ar), 129.8 (q, $^2J_{C-F}$ = 31.6 Hz, *C*CF$_3$), 124.2 (Ar), 124.2 (q, $^1J_{C-F}$ = 264.1 Hz, CF$_3$), 122.2 (Ar), 120.0 (Ar), 118.4 (Ar), 117.1 (Ar), 113.5 (Ar), 109.2 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_8F_3N_2O$: 277.0594; found: 277.0596.

N-(4-Methylphenyl)-2-benzoxazolamine (2g)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 52 mg (51%); white solid; mp 181–183 °C; R_f = 0.32 (hexane/EtOAc 3:1).

IR (KBr): 3034, 1661, 1574, 1489, 1461, 1228, 971, 815, 738 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52–7.49 (AA′XX′, 2 H, ArH), 7.46 (d, *J* = 7.8 Hz, 1 H, Ar), 7.33 (d, *J* = 7.8 Hz, 1 H, ArH), 7.22 (ddd, *J* = 7.8, 7.8, 1.1 Hz, 1 H, ArH), 7.19–7.18 (AA′XX′, 2 H, ArH), 7.10 (ddd, *J* = 7.8, 7.8, 1.1 Hz, 1 H, ArH), 2.34 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.9 (Ar), 147.9 (Ar), 142.5 (Ar), 135.5 (Ar), 133.0 (Ar), 129.9 (2C) (Ar), 124.2 (Ar), 121.7 (Ar), 118.8 (2C) (Ar), 117.0 (Ar), 109.1 (Ar), 20.9 (CH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_{11}N_2O$: 223.0877; found: 223.0885.

N-(2-Methoxyphenyl)-2-benzoxazolamine (2h)

Purified by silica gel column chromatography (hexane/EtOAc 9:1).

Yield: 93 mg (39%); orange solid; mp 96–97 °C; R_f = 0.23 (hexane/EtOAc 9:1).

IR (KBr): 3417, 2954, 1647, 1576, 1460, 1347, 1247, 1112, 1019, 745 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.42 (dd, *J* = 7.8, 1.7 Hz, 1 H, ArH), 7.64 (brs, 1 H, NH), 7.52 (d, *J* = 7.4 Hz, 1 H, ArH), 7.34 (d, *J* = 7.9 Hz, 1 H, ArH), 7.23 (ddd, *J* = 7.8, 7.4, 1.1 Hz, 1 H, ArH), 7.13 (ddd, *J* = 7.9, 7.8, 1.1 Hz, 1 H, ArH), 7.07 (ddd, *J* = 7.8, 7.7, 1.7 Hz, 1 H, ArH), 7.03 (ddd, *J* = 7.8, 7.7, 1.7 Hz, 1 H, ArH), 6.92 (d, *J* = 7.8, 1.7 Hz, 1 H, ArH), 3.93 (s, 3 H, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.8 (Ar), 147.9 (Ar), 147.4 (Ar), 142.9 (Ar), 127.6 (Ar), 124.2 (Ar), 122.7 (Ar), 122.1 (Ar), 121.5 (Ar), 117.6 (Ar), 117.5 (Ar), 110.1 (Ar), 109.1 (Ar), 55.9 (OCH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_{11}N_2O_2$: 239.0826; found: 239.0831.

N-(3-Methylphenyl)-2-benzoxazolamine (2i)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 84 mg (56%); white solid; mp 145–146 °C; R_f = 0.35 (hexane/EtOAc 3:1).

IR (KBr): 3042, 1653, 1498, 1461, 1348, 1244, 1176, 1008, 870, 742 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27 (brs, 1 H, NH), 7.48 (d, *J* = 8.0 Hz, 1 H, ArH), 7.44–7.40 (m, 2 H, ArH), 7.36 (d, *J* = 8.0 Hz, 1 H, ArH), 7.29 (dd, *J* = 8.0, 7.5 Hz, 1 H, ArH), 7.24 (ddd, *J* = 8.0, 7.9, 1.1 Hz, 1 H, ArH), 7.12 (ddd, *J* = 8.0, 7.9, 1.1 Hz, 1 H, ArH), 6.93 (d, *J* = 7.5 Hz, 1 H, ArH), 2.40 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.7 (Ar), 148.1 (Ar), 142.4 (Ar), 139.5 (Ar), 137.9 (Ar), 129.4 (Ar), 124.4 (Ar), 124.4 (Ar), 121.9 (Ar), 119.3 (Ar), 117.1 (Ar), 115.8 (Ar), 109.3 (Ar), 21.7 (CH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_{11}N_2O$: 223.0877; found: 223.0887.

N-(4-Nitrophenyl)-2-benzoxazolamine (2j)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 95 mg (81%); yellow solid; mp 234–236 °C; R_f = 0.37 (hexane/EtOAc 2:1).

IR (KBr): 2929, 1677, 1590, 1519, 1333, 1243, 1104, 852, 739 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.43 (s, 1 H, NH), 8.30–8.27 (AA′XX′, 2 H, ArH), 7.99–7.96 (AA′XX′, 2 H, ArH), 7.56 (d, *J* = 7.5 Hz, 1 H, ArH), 7.55 (d, *J* = 7.5 Hz, 1 H, ArH), 7.28 (ddd, *J* = 7.8, 7.5, 1.2 Hz, 1 H, ArH), 7.21 (ddd, *J* = 7.8, 7.5, 1.2 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 156.9 (Ar), 147.0 (Ar), 145.0 (Ar), 141.7 (Ar), 141.3 (Ar), 125.4 (2C) (Ar), 124.4 (Ar), 122.7 (Ar), 117.3 (Ar), 117.2 (2C) (Ar), 109.5 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_8N_3O_3$: 254.0571; found: 254.0595.

N-(3-Fluorophenyl)-5-methyl-2-benzoxazolamine (2k)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 90 mg (81%); pale-red solid; mp 197–198 °C; R_f = 0.35 (hexane/EtOAc 3:1).

IR (KBr): 2923, 1691, 1615, 1581, 1502, 1375, 1260, 1155, 1003, 943, 849, 789 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.81 (s, 1 H, NH), 7.76 (ddd, *J* = 2.2, 1.8 Hz, J_{H-F} = 12.0 Hz, 1 H, NCC*H*CF), 7.45 (dd, *J* = 8.1, 1.1 Hz, 1 H, ArH), 7.39 (ddd, *J* = 8.2, 8.0 Hz, J_{H-F} = 7.0 Hz, 1 H, C*H*CHCF), 7.36 (d, *J* = 8.0 Hz, 1 H, ArH), 7.30 (s, 1 H, ArH), 6.95 (dd, *J* = 8.0, 1.8 Hz, 1 H, C*H*CHCHCF), 6.84 (ddd, *J* = 8.2, 8.2, 1.8 Hz, 1 H, CHC*H*CF), 2.37 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.6 (d, $^1J_{C-F}$ = 241.9 Hz, CF), 157.7 (Ar), 145.1 (Ar), 142.3 (Ar), 140.6 (d, $^3J_{C-F}$ = 11.5 Hz, *C*CCF), 133.3 (Ar), 130.7 (d, $^3J_{C-F}$ = 9.7 Hz, *C*CCF), 122.7 (Ar), 117.2 (Ar), 113.5 (Ar), 108.6 (Ar), 108.5 (d, $^2J_{C-F}$ = 21.2 Hz, *C*CF), 104.3 (d, $^2J_{C-F}$ = 26.7 Hz, *C*CF), 21.1 (CH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_{10}FN_2O$: 241.0783; found: 241.0811.

N-(2-Methoxyphenyl)-5-methyl-2-benzoxazolamine (2l)

Purified by silica gel column chromatography (hexane/EtOAc 9:1).

Yield: 32 mg (28%); brown solid; mp 77–78 °C; R_f = 0.37 (hexane/EtOAc 3:1).

IR (KBr): 3428, 1647, 1582, 1530, 1458, 1347, 1250, 1217, 1173, 1113, 1025, 795, 743 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.23 (dd, *J* = 7.9, 1.7 Hz, 1 H, ArH), 7.61 (brs, 1 H, NH), 7.31 (s, 1 H, ArH), 7.20 (d, *J* = 8.2 Hz, 1 H, ArH), 7.06 (ddd, *J* = 7.9, 7.8, 1.7 Hz, 1 H, ArH), 7.02 (ddd, *J* = 7.9, 7.8, 1.7 Hz, 1 H, ArH), 6.92 (dd, *J* = 7.9, 1.7 Hz, 1 H, ArH), 6.90 (dd, *J* = 8.2, 1.2 Hz, 1 H, ArH), 3.91 (s, 3 H, OCH_3), 2.42 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9 (Ar), 147.4 (Ar), 143.0 (Ar), 133.9 (Ar), 127.6 (Ar), 123.0 (Ar), 122.4 (Ar), 121.0 (Ar), 118.1 (Ar), 117.5 (Ar), 110.5 (Ar), 108.9 (Ar), 108.0 (Ar), 55.9 (OCH_3), 21.7 (CH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{15}H_{13}N_2O_2$: 253.0983; found: 253.1003.

5-Chloro-*N*-(2-chlorophenyl)-2-benzoxazolamine (2m)

Purified by silica gel column chromatography (hexane/EtOAc 15:1).

Yield: 97 mg (76%); white solid; mp 132–133 °C; R_f = 0.36 (hexane/EtOAc 9:1).

IR (KBr): 3381, 2621, 1598, 1571, 1530, 1445, 1233, 1056, 738 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 8.2, 1.7 Hz, 1 H, ArH), 7.55 (s, 1 H, NH), 7.50 (d, *J* = 1.7 Hz, 1 H, ArH), 7.42 (dd, *J* = 7.9, 1.6 Hz, 1 H, ArH), 7.38 (ddd, *J* = 8.2, 7.9, 1.6 Hz, 1 H, ArH), 7.27 (d, *J* = 8.6 Hz, 1 H, ArH), 7.13 (dd, *J* = 8.6, 1.7 Hz, 1 H, ArH), 7.05 (ddd, *J* = 7.9, 7.9, 1.7 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.0 (Ar), 146.4 (Ar), 143.7 (Ar), 134.2 (Ar), 129.9 (Ar), 129.4 (Ar), 128.3 (Ar), 123.9 (Ar), 122.6 (Ar), 121.8 (Ar), 119.2 (Ar), 118.0 (Ar), 109.9 (Ar).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{13}H_7Cl_2N_2O$: 276.9941; found: 276.9950.

5-Chloro-*N*-(4-methylphenyl)-2-benzoxazolamine (2n)

Purified by silica gel column chromatography (hexane/EtOAc 4:1).

Yield; 57 mg (55%); pale-red solid; mp 214–215 °C; R_f = 0.35 (hexane/EtOAc 3:1).

IR (KBr): 2918, 1697, 1577, 1514, 1362, 1243, 970, 795 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.66 (s, 1 H, NH), 7.61 (d, *J* = 8.3 Hz, 2 H, ArH), 7.49 (d, *J* = 8.6 Hz, 1 H, ArH), 7.49 (d, *J* = 2.3 Hz, 1 H, ArH), 7.18 (d, *J* = 8.3 Hz, 2 H, ArH), 7.13 (dd, *J* = 8.6, 2.3 Hz, 1 H, ArH), 2.27 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 159.2 (Ar), 145.9 (Ar), 144.2 (Ar), 135.8 (Ar), 131.4 (Ar), 129.4 (2C) (Ar), 128.1 (Ar), 121.1 (Ar), 117.9 (2C) (Ar), 116.2 (Ar), 110.0 (Ar), 20.4 (CH_3).

HRMS (ESI-negative): *m*/*z* [M–H]$^-$ calcd for $C_{14}H_{10}ClN_2O$: 257.0487; found: 257.0496.

***N*-Benzylbenzo[*d*]oxazol-2-amine (2p)**[9]

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 46 mg (45%); red brown solid; mp 259–260 °C; R_f = 0.19 (hexane/EtOAc 3:1).

IR (KBr): 3028, 1665, 1589, 1459, 1375, 1344, 1285, 1247, 1184, 1003, 741, 694 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.50 (t, *J* = 6.3 Hz, 1 H, NH), 7.39–7.33 (m, 5 H, ArH), 7.26 (d, *J* = 8.0 Hz, 1 H, ArH), 7.24 (d, *J* = 8.0 Hz, 1 H, ArH), 7.10 (dd, *J* = 8.0, 6.9 Hz, 1 H, ArH), 6.98 (dd, *J* = 8.0, 6.9 Hz, 1 H, ArH), 4.52 (d, *J* = 6.3 Hz, 2 H, CH_2).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.0 (Ar), 148.7 (Ar), 143.7 (Ar), 139.6 (Ar), 128.9 (2C) (Ar), 127.7 (2C) (Ar), 127.6 (Ar), 124.2 (Ar), 120.8 (Ar), 116.1 (Ar), 109.1 (Ar), 46.2 (CH_2).

6-Bromo-*N*-(4-nitrophenyl)benzo[*d*]oxazol-2-amine (2q)

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 98 mg (45%); orange solid; mp 257–259 °C; R_f = 0.24 (hexane/EtOAc 3:1).

IR (KBr): 2877, 1670, 1587, 1515, 1458, 1373, 1329, 1238, 1109, 987, 845, 807, 687 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.57 (brs, 1 H, NH), 8.30–8.28 (AA′XX′, 2 H, ArH), 7.94–7.92 (AA′XX′, 2 H, ArH), 7.73 (d, *J* = 2.1 Hz, 1 H, ArH), 7.53 (d, *J* = 8.6 Hz, 1 H, ArH), 7.35 (dd, *J* = 8.6, 2.1 Hz, 1 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 158.4 (Ar), 146.8 (Ar), 145.1 (Ar), 144.2 (Ar), 142.1 (Ar), 125.9 (2C) (Ar), 125.7 (Ar), 120.4 (Ar), 117.9 (2C) (Ar), 116.8 (Ar), 111.7 (Ar).

HRMS (ESI-negative): *m*/*z* $[M–H]^-$ calcd for $C_{13}H_7BrN_3O_3$: 331.9676; found: 331.9777.

***N*-(4-Bromophenyl)-5-nitrobenzo[*d*]oxazol-2-amine (2r)**

Purified by silica gel column chromatography (hexane/EtOAc 3:1).

Yield: 29 mg (19%); yellow solid; mp 260–262 °C; R_f = 0.31 (hexane/EtOAc 3:1).

IR (KBr): 3476, 2070, 1639, 1334, 1278, 1231 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.38 (brs, 1 H, NH), 8.41 (s, 1 H, ArH), 8.17 (dd, *J* = 8.9, 2.0 Hz, 1 H, ArH), 7.72–7.70 (AA′XX′, 2 H, ArH), 7.58 (d, *J* = 8.9 Hz, 1 H, ArH), 7.58–7.57 (AA′XX′, 2 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 161.6 (Ar), 149.5 (Ar), 146.9 (Ar), 142.3 (Ar), 137.7 (Ar), 132.5 (Ar), 132.4 (Ar), 121.6 (Ar), 120.7 (2C) (Ar), 116.4 (Ar), 115.3 (Ar).

HRMS (ESI-negative): *m*/*z* $[M–H]^-$ calcd for $C_{13}H_7BrN_3O_3$: 331.9676; found: 331.9678.

***N*-(4-Phenoxyphenyl)benzo[*d*]oxazol-2-amine (2s)**[1,8]

Purified by silica gel column chromatography (hexane/EtOAc 4:1).

Yield: 103 mg (74%); yellow solid; mp 155–156 °C; R_f = 0.34 (hexane/EtOAc 4:1).

^1H NMR (500 MHz, DMSO-d_6): δ = 8.81 (brs, 1 H, NH), 7.59–7.55 (AA′XX′, 2 H, ArH), 7.45 (d, *J* = 7.5 Hz, 1 H, ArH), 7.36–7.31 (m, 3 H, ArH), 7.25–7.21 (m, 2 H, ArH), 7.14–7.06 (m, 4 H, ArH), 7.02–7.00 (m, 2 H, ArH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 159.0 (Ar), 157.8 (Ar), 153.0 (Ar), 148.0 (Ar), 142.1 (Ar), 133.6 (Ar), 129.9 (2C) (Ar), 124.5 (Ar), 123.1 (Ar), 121.8 (Ar), 120.6 (2C) (Ar), 120.3 (2C) (Ar), 118.4 (2C) (Ar), 116.9 (Ar), 109.3 (Ar).

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1705982.

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(24) Use of molecular iodine for a similar transformation has already been reported by Phakhodee and co-workers.[11] However, the reaction requires the addition of triphenylphosphine (1.5 equiv) in dichloromethane under microwave irradiation conditions.