Catalyst Controlled Regioselective Suzuki Couplings at Both Positions of Dihalo-Imidazoles, -Oxazoles, and -Thiazoles

Neil A. Strotman,[†] Harry R. Chobanian,*[‡] Jiafang He,[‡] Yan Guo[‡] Peter G. Dormer,[†]*

Christina M. Jones,[§] Janelle E. Steves,[††]

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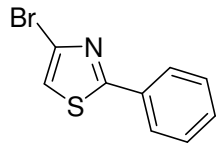
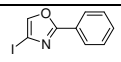
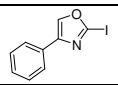
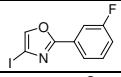
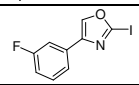
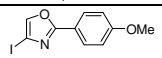
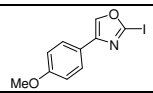
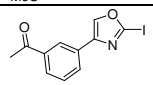
General Procedure for Suzuki cross-coupling reactions

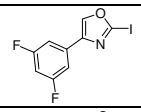
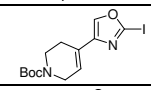
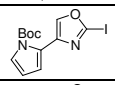
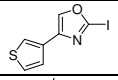
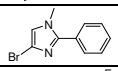
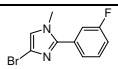
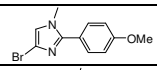
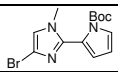
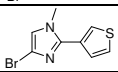
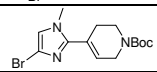
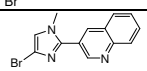
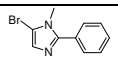
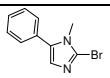
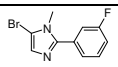
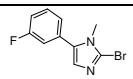
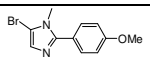
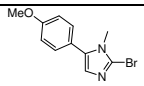
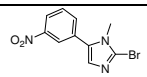
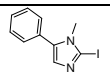
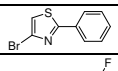
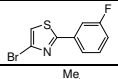
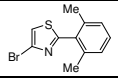
This will be demonstrated with preparation of **4-bromo-2-phenylthiazole** (Table 4, entry 1)

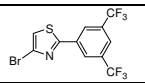
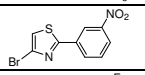
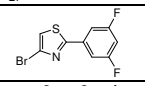
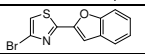
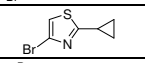
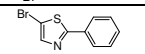
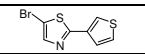
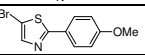
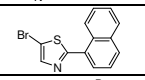
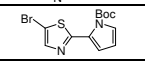


Under nitrogen $Pd(OAc)_2$ (8.4 mg, 0.038 mmol, 2.5%) was combined with Xantphos (22 mg, 0.038 mmol, 2.5%) in degassed THF (7.5 mL). After stirring for 5 min, this solution was transferred to a separate vessel under nitrogen containing 2,4-dibromothiazole (364 mg, 1.5 mmol), phenylboronic acid (196 mg, 1.6 mmol, 1.07 equiv) and K_3PO_4 (955 mg, 4.5 mmol, 3 equiv). The sealed vessel was heated at 60 °C for 18 h. Upon cooling to room temperature, LC-MS showed 100% conversion of starting material, 19.5:1 mono:bis product ratio, and >100:1 C2:C4 product isomer ratio. The reaction mixture was filtered and the solid was washed with DCM. The solvents were removed by rotary evaporation and the title compound was purified by column chromatography (silica gel, EtOAc/hexane) to give a white powder (0.264 g, 73%, mp 80 °C, lit[1] 77-78 °C).
^{1}H NMR (500 MHz, CD_3Cl_3) δ 7.23 (s, 1H), 7.46 (m, 3H), 7.95 (dd, J = 7.5, 2.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 116.7, 126.2, 126.5, 129.2, 130.9, 132.7, 169.2; LCMS: $[M+H]^+$ calcd for $C_9H_6BrNS{\cdot}H^+$, 239.9; found 239.8. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_6BrNS{\cdot}H^+$, 239.9482; found 239.9491.

Table S1. Conditions for Suzuki cross-coupling reactions[a]

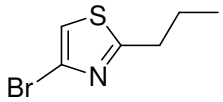
Dihalo-azole							**Product**			
(mmol)	$ArB(OH)_2$ (equiv)	solvent	ligand	$Pd(OAc)_2$ (%)	Temp (°C)	Time (hr)	structure	Yield (mg)	Yield (%)	mp (°C)
1.0	1.12	MeCN	**4**	5	80	5		149	55	oil
1.0	1.07	THF	**2**	2.5	60	8		174	64	52-55
1.0	1.25	MeCN	**4**	10	80	5		153	53	52-54
1.0	1.12	THF	**2**	5	60	6		156	54	99-102
1.0	1.12	MeCN	**4**	5	80	3		181	60	110-111
1.0	1.07	THF	**2**	2.5	60	5		133	44	88-91
1.0	1.12	THF	**2**	5	60	6		194	62	105-107

1.0	1.12	THF	**2**	5	60	6		157	51	112-114
1.0	1.12[b]	7:1 THF:H_2O	**2**	5	60	7		177	47	107-109
1.0	1.12	THF	**2**	5	60	7		194	54	95-97
1.0	1.12	THF	**2**	5	60	3.5		160	58	94-96
1.0	1.12	THF	**5**	5	80	16		207	87	66-68[c]
1.0	1.12	THF	**5**	5	80	16		186	73	50-53
1.0	1.12	THF	**5**	5	80	16		202	76	oil
1.0	1.12	THF	**5**	5	80	16		137	42	97-100
1.0	1.12	THF	**5**	5	80	16		158	65	oil
1.0	1.12[b]	7:1 THF:H_2O	**5**	5	80	16		336	98	ND
1.0	1.3	THF	**5**	20[d]	80	16		112	39	175-177
0.5	1.25	THF	**4**	10	80	16		77	64	106-108[e]
1.0	1.12	THF	**6**	5	80	2		107	45	88-90
1.0	1.25	THF	**4**	10	80	16		120	47	99-100
1.0	1.12	THF	**6**	5	80	20		132	52	92-93
0.5	1.25	THF	**4**	10	80	16		101	75	ND
1.0	1.12	THF	**6**	5	80	2		136	51	ND
1.0	1.12	THF	**6**	5	80	16		220	78	80
1.0	1.12	THF	**2**	5	60	16		137	48	70-74
1.5	1.07	THF	**2**	2.5	60	16		264	73	80[f]
2.06	1.07	THF	**2**	2.5	60	16		382	72	83-84
1.5	1.07	THF	**2**	2.5	60	16		240	60	72-73

1.44	1.07	THF	**2**	2.5	60	16		444	82	91-94
1.5	1.07	THF	**2**	2.5	60	16		366	86	143-146
1.5	1.07	THF	**2**	2.5	60	16		256	62	106-107
1.5	1.07	THF	**2**	2.5	60	16		298	71	153-155
1	1.1	THF	**2**	5	80	16		169	83	oil
1.4	1.07	THF	**2**	2.5	60	16		240	59	82[g]
1.5	1.07	THF	**2**	2.5	60	16		240	65	72-73
1.4	1.07	THF	**2**	2.5	60	16		288	74	87-88
1.5	1.07	THF	**2**	2.5	60	16		298	68	73-75
1.5	1.07	THF	**2**	2.5	60	16		374	76	58-60

[e]All reactions were run on a 0.5-2.0 mmol scale, ligand/Pd ratios of 2:1 for monodentate ligands and 1:1 for bidentate ligands, 3 equiv K_3PO_4, and 1.07-1.4 equiv boronic acid, with 0.2 M [dihaloazole] in THF. [b]Used 1.12 equiv of pinacol boronate ester, instead of boronic acid. [c]Lit[2] mp 68-69 °C. [d]Employed 10% $Pd_2(dba)_3$ instead of $Pd(OAc)_2$. [e]Lit[2] mp 107-108 °C. [f]Lit[1] mp 77-78 °C. [g]Lit[3] mp 78-80 °C.

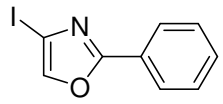
Negishi cross-coupling to prepare **4-bromo-2-propylthiazole** (Table 4, entry 9)



Under nitrogen $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 5%) was combined with Xantphos (29 mg, 0.05 mmol, 5%) in degassed THF (2.5 mL). After stirring for 5 min, this solution was transferred to a separate vessel under nitrogen containing 2,4-dibromothiazole (243 mg, 1.0 mmol) and propylzinc bromide (2.2 mL, 0.5 M solution in THF, 1.1 mmol, 1.1 equiv). The sealed vessel was heated at 80 °C for 18 h. Upon cooling to room temperature, LC-MS showed 100% conversion of starting material, >100:1 mono:bis product ratio, and >100:1 C2:C4 product isomer ratio. The reaction mixture was filtered and the solid was washed with DCM. The solvents were removed by rotary evaporation and the title compound was purified by column chromatography (silica gel, EtOAc/hexane) to give a yellow powder (0.184 g, 89%, mp 98-100 °C).

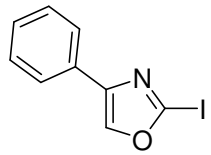
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (t, J = 7.0 Hz, 3H), 1.80 (sextet, J = 7.0 Hz, 2H), 2.96 (t, J = 7.5 Hz, 2H), 7.06 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13.5, 23.2, 35.4, 115.6, 124.0, 172.5; LCMS: $[M+H]^+$ calcd for $C_6H_8BrNS{\cdot}H^+$, 205.96; found 205.93. HRMS (ESI): $[M+H]^+$ calcd for $C_6H_8BrNS{\cdot}H^+$, 205.9639; found 205.9639.

4-Iodo-2-phenyl-1,3-oxazole (Table 2, entry 1)



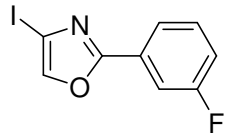
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (m, 3H), 7.74 (s, 1H), 8.05 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 83.5, 125.7, 126.6, 129.1, 131.2, 142.6, 163.5; LCMS: $[M+H]^+$ calcd for C_9H_6INO ($M+H^+$), 271.95; found 271.86. HRMS (ESI): $[M+H]^+$ calcd for C_9H_6INO ($M+H^+$), 271.9572; found 271.9586.

2-Iodo-4-phenyl-1,3-oxazole (Table 2, entry 2)



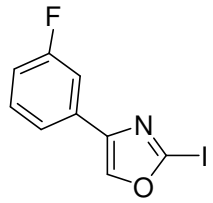
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.73 (d, *J* = 7.0 Hz, 2H), 8.04 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 101.7, 125.7, 128.8, 129.0, 130.0, 139.6, 149.1; LCMS: $[M+H]^+$ calcd for C_9H_6INO ($M+H^+$), 271.95; found 271.89. HRMS (ESI): $[M+H]^+$ calcd for C_9H_6INO ($M+H^+$), 271.9572; found 271.9584. LCMS and NMR show ~15% of the dehalogenated impurity 4-iodooxazole.

2-(3-Fluorophenyl)-4-iodo-1,3-oxazole (Table 2, entry 3)



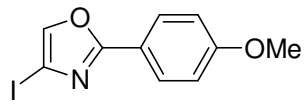
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.22 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.44-7.49 (m, 1H), 7.74-7.77 (m, 2H), 7.85 (d, *J* = 8.0, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 83.7, 113.7 (d, *J* = 25 Hz), 118.2 (d, *J* = 21 Hz), 122.4 (d, *J* = 3Hz), 130.8 (d, *J* = 9 Hz), 143.0, 149.2, 162.3, 163.1 (d, *J* = 248 Hz); LCMS: $[M+H]^+$ calcd for C_9H_5FINO ($M+H^+$), 289.94; found 289.83. HRMS (ESI): $[M+H]^+$ calcd for C_9H_5FINO ($M+H^+$), 289.9478; found 289.9485.

4-(3-Fluorophenyl)-2-iodo-1,3-oxazole (Table 2, entry 4)



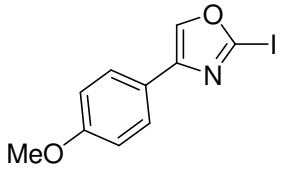
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (td, *J* = 5.5, 2.5 Hz, 1H), 7.37 (td, *J* = 8.0, 6.0 Hz, 2H), 7.44 (dt, *J* = 10.0 Hz, 2.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 8.03 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.9, 112.7 (d, *J* = 23 Hz), 115.6 (d, *J* = 22 Hz), 121.3 (d, *J* = 3 Hz), 130.5 (d, *J* = 9 Hz), 132.1, 140.0, 143.5 (d, *J* = 3Hz), 163.3 (d, *J* = 245 Hz); LCMS: $[M+H]^+$ calcd for C_9H_5FINO ($M+H^+$), 289.94; found 289.94. HRMS (ESI): $[M+H]^+$ calcd for C_9H_5FINO ($M+H^+$), 289.9478; found 289.9488.

4-iodo-2-(4-methoxyphenyl)oxazole (Table 2, entry 5)



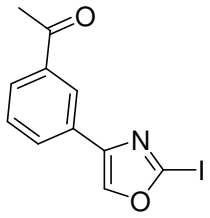
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.98 (d, *J* = 9.0 Hz, 2H), 7.70 (s, 1H), 7.98 (d, *J* = 9.0 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.3, 83.0, 114.1, 119.0, 128.0, 141.6, 161.6, 163.2; LCMS: $[M+H]^+$ calcd for $C_{10}H_8INO_2$($M+H^+$), 301.96; found 301.92. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_8INO_2$($M+H^+$), 301.9678; found 301.9677.

2-Iodo-4-(4-methoxyphenyl)oxazole (Table 2, entry 6)



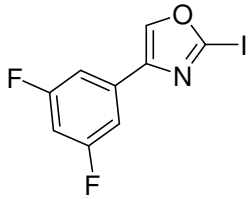
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 101.4, 114.5, 122.7, 127.1, 138.7, 144.3, 160.2; LCMS: $[M+H]^+$ calcd for $C_{10}H_8INO_2$($M+H^+$), 301.96; found 301.8. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_8INO_2$($M+H^+$), 301.9678; found 301.9695.

1-[3-(2-Iodo-1,3-oxazol-4-yl)phenyl]ethanone (Table 2, entry 7)



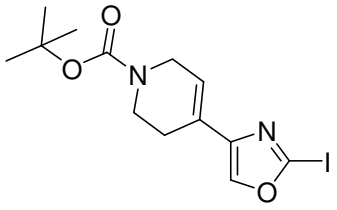
^{1}H NMR (600 MHz, $CDCl_3$) δ 2.65 (s, 3H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1 H), 8.09 (s, 1H), 8.27 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.7, 101.7, 125.1, 128.3, 129.1, 129.9, 130.3, 137.6, 139.9, 143.3, 197.7; LCMS: $[M+H]^+$ calcd for $C_{11}H_8INO_2(M+H^+)$, 313.96; found 313.84. HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_8INO_2(M+H^+)$, 313.9678; found 313.9672.

4-(3,5-Difluorophenyl)-2-iodooxazole (Table 2, entry 8)



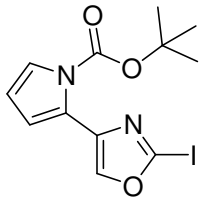
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (t, *J* = 8.0 Hz, 1H), 7.24 (m, 2H), 8.05 (s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 101.9, 103.6, 103.8 108.3, 108.5, 140.2, 162.4, 164.3; LCMS: $[M+H]^+$ calcd for $C_9H_4F_2INO(M+H^+)$, 308.04; found 307.84. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_4F_2INO(M+H^+)$, 307.9384; found 307.9368.

tert-**Butyl-4-(2-iodo-1,3-oxazol-4-yl)-3,6-dihydropyridine-1(2H)-carboxylate** (Table 2, entry 9)



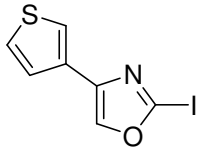
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.34 (br s, 2H), 3.63 (t, *J* = 6.0 Hz, 2H), 4.10 (br s, 2H), 6.46 (br s, 1H), 6.62 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 25.0, 25.6, 28.6, 80.0, 83.5, 102.0, 122.4, 124.9, 138.9, 144.2, 155.1; LCMS: $[M+H]^+$ calcd for $C_{13}H_{17}IN_2O_3$(M+H$^+$-BOC), 276.03; found 276.87. HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{17}IN_2O_3$(M+H$^+$-BOC), 276.9838; found 276.9850.

***tert*-Butyl 2-(2-iodo-1,3-oxazol-4-yl)-1H-pyrrole-1-carboxylate** (Table 2, entry 10)



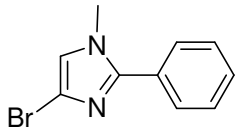
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.58 (s, 9H), 6.26 (t, *J* = 3.5 Hz, 1H), 6.72 (dd, *J* = 3.5, 2.0 Hz, 1H), 7.35 (dd, *J* = 3.5, 2.0 Hz, 1H), 8.14 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.1, 84.4, 100.4, 111.1, 116.6, 123.8, 124.3, 136.8, 142.0, 149.0; LCMS: $[M+H]^+$ calcd for $C_{12}H_{13}IN_2\ O_3$(M+H$^+$-BOC), 261.15; found 260.86. HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{13}IN_2\ O_3$(M+H$^+$-BOC), 260.9525; found 260.9542.

2-Iodo-4-(thiophen-3-yl)-1,3-oxazole (Table 2, entry 11)



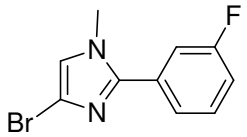
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 5.0 Hz, 1H), 7.38-7.40 (m, 1H), 7.68 (m, 1 H), 7.93 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 101.6, 122.4, 125.2, 126.9, 131.3, 139.2, 140.7; LCMS: $[M+H]^+$ calcd for C_7H_4INOS(M+H$^+$), 277.91; found 277.84. HRMS (ESI): $[M+H]^+$ calcd for C_7H_4INOS(M+H$^+$), 277.9137; found 277.9146.

4-Bromo-1-methyl-2-phenyl-1H-imidazole (Table 3, entry 1)



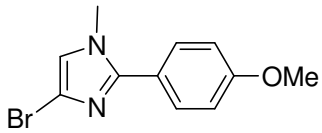
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (s, 3H), 6.92 (s, 1H), 7.44-7.58 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 34.5, 114.7, 121.1, 128.4, 128.5, 129.0, 129.2, 147.8; LCMS: $[M+H]^+$ calcd for $C_{10}H_9BrN_2(M+H^+)$, 236.99; found 236.95. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_9BrN_2(M+H^+)$, 237.0027; found 237.0039.

4-Bromo-2-(3-fluorophenyl)-1-methyl-1*H*-imidazole (Table 3, entry 2)



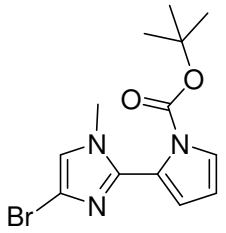
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H), 6.98 (s, 1H), 7.13-7.17 (m, 1H), 7.36-7.39 (m, 1H), 7.42-7.47 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 34.9, 115.8 (d, *J* = 23 Hz(, 116.2 (d, *J* = 21 Hz), 121.8, 122.5, 124.3 (d, *J* = 3 Hz), 130.4 (d, *J* = 8 Hz), 131.5 (d, *J* = 8 Hz), 146.5 (d, *J* = 3 Hz), 162.8 (d, *J* = 246 Hz); LCMS: $[M+H]^+$ calcd for $C_{10}H_8BrFN_2(M+H^+)$, 254.99; found 254.90. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_8BrFN_2(M+H^+)$, 254.9933; found 254.9944.

4-Bromo-2-(4-methoxyphenyl)-1-methyl-1*H*-imidazole(Table 3, entry 3)



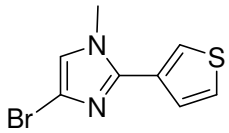
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.69 (s, 3H), 3.84 (s, 3H), 6.91 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.7, 55.5, 114.2, 114.8, 120.9, 122.1, 130.3, 148.1, 160.4; LCMS: $[M+H]^+$ calcd for $C_{11}H_{11}BrN_2O(M+H^+)$, 267.01; found 266.98. HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_{11}BrN_2O(M+H^+)$, 267.0133; found 267.0146.

***tert*-Butyl-2-(4-bromo-1-methyl-1*H*-imidazol-2-yl)-1*H*-pyrrole-1-carboxylate** (Table 3, entry 4)



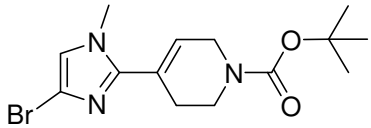
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46(s, 9H), 3.50 (s, 3H), 6.31 (t, *J* = 3.5 Hz, 1H), 6.55 (br s, 1H), 6.99 (s, 1H), 7.29 (s, 1H), 7.44-7.45 (dd, *J* = 3.5, 2.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.9, 33.5, 84.3, 111.1, 114.5, 118.5, 120.1, 121.0, 123.6, 141.3, 148.6; LCMS: $[M+H]^+$ calcd for $C_{13}H_{16}BrN_3O_2$(M+H$^+$-BOC), 225.04; found 225.96. HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{16}BrN_3O_2$(M+H$^+$), 326.0504; found 326.0510.

4-Bromo-1-methyl-2-(thiophen-3-yl)-1H-imidazole (Table 3, entry 5)



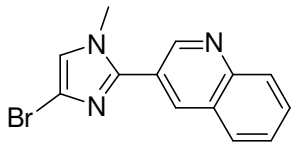
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.87 (s, 1H), 7.00-7.02 (m, 1H), 7.06-7.07 (dd, J = 5.0, 1.0 Hz, 1H), 7.18-7.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.8, 114.7, 121.0, 124.5, 126.3, 127.8, 130.5, 144.0; LCMS: $[M+H]^+$ calcd for $C_8H_7BrN_2S$ (M+H$^+$), 242.95; found 242.91. HRMS (ESI): $[M+H]^+$ calcd for $C_8H_7BrN_2S$ (M+H$^+$), 242.9591; found 242.9603.

4-Bromo-2-(4-(N-Boc-1,2,3,6-tetrahydropyridine))-*N*-methylimidazole (Table 3, entry 6)



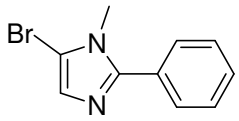
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 9H), 2.63 (m, 2H), 3.62 (t, *J* = 5.5 Hz, 2H), 3.70 (s, 3H), 4.13 (br s, 2H), 6.00 (br s, 1H), 6.82(s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.8, 28.4, 34.7, 79.9, 114.1, 120.9, 126.6, 126.7, 147.2, 154.7, 192.7; LCMS: $[M+H]^+$ calcd for $C_{14}H_{20}BrN_3O_2$(M+H$^+$), 342.07; found 341.89.

4-Bromo-1-methyl-3-quinoline-1H-imidazole (Table 3, entry 7)



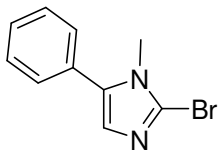
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H), 7.08 (s, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.84 (t, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.50 (d, *J* = 1.5 Hz, 1H), 9.24 (d, *J* = 2.0 Hz, 1H) ; ^{13}C NMR (150 MHz, $CDCl_3$) δ 34.9, 115.7, 122.1, 122.7, 127.2, 127.6, 128.2, 129.1, 130.7, 135.9, 144.8, 147.3, 149.1; LCMS: $[M+H]^+$ calcd for $C_{13}H_{11}BrN_3(M+H^+)$, 288.01; found 287.95. HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_{11}BrN_3(M+H^+)$, 288.0136; found 288.0143.

5-Bromo-1-methyl-2-phenyl-1*H*-imidazole (Table 3, entry 8)



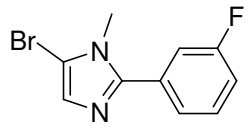
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 3H), 7.20 (s, 1H), 7.46-7.52 (m, 3H), 7.62 (dd, *J* = 7.8, 2.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 33.4, 105.3, 128.2, 128.6, 128.7, 129.4, 129.9,148.5; LCMS: $[M+H]^+$ calcd for $C_{10}H_9BrN_2(M+H^+)$, 236.99; found 237.01. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_9BrN_2(M+H^+)$, 237.0027; found 237.0036.

2-Bromo-1-methyl-5-phenyl-1*H*-imidazole (Table 3, entry 9)



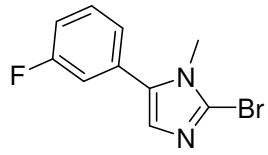
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.64 (s, 3H), 7.11 (s, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.42-7.51 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.4, 121.5, 128.2, 128.6, 128.9, 129.0, 129.9, 136.4; LCMS: $[M+H]^+$ calcd for $C_{10}H_9BrN_2$ $(M+H^+)$, 236.99; found 236.95. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_9BrN_2$ $(M+H^+)$, 237.0027; found 237.0027.

5-Bromo-2-(3-fluorophenyl)-*N*-methylimidazole (Table 3, entry 10)



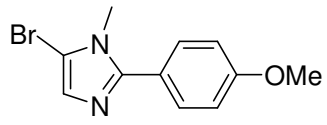
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3H), 7.116 (tdd, *J* = 8.4, 2.7, 1.2 Hz, 1H), 7.119 (s, 1H), 7.31 (ddd, *J* = 9.6, 2.5, 1.6 Hz, 1H), 7.36 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.42 (td, *J* = 7.8, 5.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 33.6, 105.8, 115.8 (d, *J* = 23 Hz), 116.2 (d, *J* = 22 Hz), 124.3 (d, *J* = 3 Hz), 129.3, 130.4 (d, *J* = 8 Hz), 132.8 (d, *J* = 8 Hz), 147.5 (d, *J* = 2 Hz), 162.8 (d, *J* = 248 Hz); LCMS: $[M+H]^+$ calcd for $C_{10}H_8BrFN_2(M+H^+)$, 254.99; found 254.95. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_8BrFN_2(M+H^+)$, 254.9933; found 254.9939.

2-Bromo-5-(3-fluorophenyl)-*N*-methylimidazole (Table 3, entry 11)



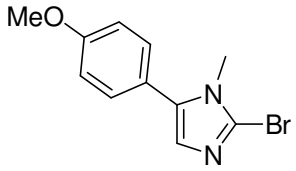
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.61 (s, 3H), 7.05 (s, 1H), 7.04-7.11 (m, 2H), 7.13 (dt, *J* =7.6, 1.3 Hz, 1H), 7.41 (td, *J* = 8.2, 6.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 33.5, 115.5 (d, *J* = 22 Hz), 115.7 (d, *J* = 23 Hz), 122.1, 124.4 (d, *J* = 3 Hz), 128.7, 130.6 (d, *J* = 9 Hz), 131.8 (d, *J* = 8 Hz), 135.1, 162.9 (d, *J* = 247 Hz); LCMS: $[M+H]^+$ calcd for $C_{10}H_7FN_2{\cdot}H^+$, $(M+H^+)$, 254.99; found 254.96. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_7FN_2{\cdot}H^+$, 254.9933; found 254.9943.

5-Bromo-2-(4-methoxyphenyl)-1-methyl-1*H*-imidazole (Table 3, entry 12)



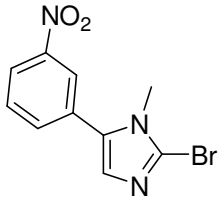
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 3H), 3.85 (s, 3H), 7.00 (d, *J* = 8.8 Hz, 2H), 7.13 (s, 1H), 7.54 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 33.2, 55.3, 104.5, 113.9, 121.5, 128.4, 129.9, 148.5, 160.1; LCMS: $[M+H]^+$ calcd for $C_{11}H_{11}BrN_2O(M+H^+)$, 266.01; found 266.95.

2-Bromo-5-(4-methoxyphenyl)-1-methyl-1*H*-imidazole (Table 3, entry 13)



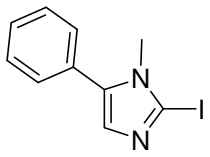
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H), 4.03 (s, 3H), 7.18 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2 H), 7.47 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 32.9, 55.2, 114.1, 120.5, 121.8, 127.4, 130.0, 135.8, 159.7; LCMS: $[M+H]^+$ calcd for $C_{11}H_{11}BrN_2O(M+H^+)$, 267.01; found 266.98.

2-Bromo-1-methyl-5-(3-nitrophenyl)-1*H*-imidazole (Table 3, entry 14)



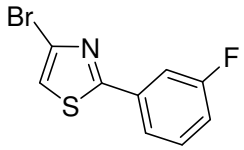
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65 (s, 3H), 7.07(s, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1 H), 8.53 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 33.7, 104.8, 119.6, 122.2, 123.4, 130.2, 130.4, 133.2, 140.5, 149.0; LCMS: $[M+H]^+$ calcd for $C_{10}H_8BrN_3O_2(M+H^+)$, 283.09; found 283.98.

2-Iodo-1-methyl-5-phenyl-1*H*-imidazole (Table 3, entry 15)



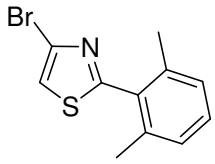
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 (s, 3H), 7.15 (s, 1H), 7.38 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 92.6, 128.7, 129.0, 129.1, 130.8, 137.6, 140.2; LCMS: $[M+H]^+$ calcd for $C_{12}H_{11}IN_2O{\cdot}H^+$, 284.9; found 284.9. HRMS (ESI): $[M+H]^+$ calcd for $C_{12}H_{11}IN_2O{\cdot}H^+$, 284.9888; found 284.9898.

4-Bromo-2-(3-fluorobenzene)thiazole (Table 4, entry 2)



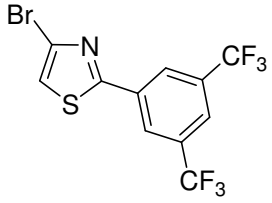
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (td, J = 7.7, 2.4 Hz, 1H), 7.26 (s, 1H), 7.43 (td, J = 7.7, 5.6 Hz, 1H), 7.70 (tt, J = 8.5, 2.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 113.5 (d, J = 23.9 Hz), 117.3, 117.7 (d, J = 21.4 Hz), 122.2 (d, J = 3.8 Hz), 126.6, 130.8 (d, J = 8.8 Hz), 134.7 (d, J = 8.8 Hz), 163.2 (d, J_{CF} = 246.5 Hz), 167.6 (d, J = 2.5Hz); LCMS: $[M+H]^+$ calcd for $C_9H_5BrFNS{\cdot}H^+$, 257.9; found 257.8. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_5BrFNS{\cdot}H^+$, 257.9388; found 257.9381.

4-Bromo-2-(2,6-dimethylbenzene)thiazole (Table 4, entry 3)



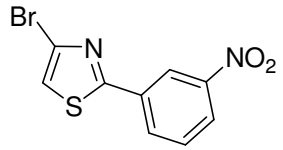
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.20 (s, 6H), 7.13 (d, J = 5 Hz, 2H), 7.28 (t, J = 10 Hz, 1H), 7.41 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.5, 118.5, 125.3, 127.9, 130.0, 132.7, 138.0, 168.1; LCMS: $[M+H]^+$ calcd for $C_{11}H_{10}BrNS{\cdot}H^+$, 268.0; found 267.8. HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_{10}BrNS{\cdot}H^+$, 267.9795; found 267.9799.

4-Bromo-2-(3,5-bis-(trifluoromethyl)phenyl)thiazole (Table 4, entry 4)



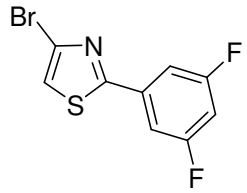
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.95 (s, 1H), 8.38 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 118.6, 122.9 (q, J_{CF} = 274.1 Hz), 124.07 (septet, J = 3.7 Hz), 126.4 (q, J = 3.7 Hz), 127.4, 132.9 (q, J = 33.9 Hz), 134.5, 165.4; LCMS: $[M+H]^+$ calcd for $C_{11}H_4BrF_6NS{\cdot}H^+$, 375.9; found 375.7. HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_4BrF_6NS{\cdot}H^+$, 375.9230; found 375.9230.

4-Bromo-2-(3-nitrophenyl)thiazole (Table 4, entry 5)



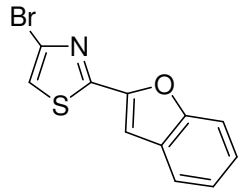
^{1}H NMR (500 MHz, CD_3Cl_3) δ 7.34 (s, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 8.27 (ddd, *J* = 7.9, 2.0, 1.2 Hz, 1H), 8.30 (ddd, *J* = 8.4, 2.3, 1.2 Hz, 1H), 8.76 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (126 MHz, CD_3Cl_3) δ 118.2, 121.4, 125.2, 127.1, 130.4, 132.0, 134.2, 149.0, 166.1; LCMS: $[M+H]^+$ calcd for $C_9H_5BrN_2O_2S{\cdot}H^+$, 284.9; found 284.8. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_5BrN_2O_2S{\cdot}H^+$, 284.9333; found 284.9344.

4-Bromo-2-(3,5-diflurorphenyl)thiazole (Table 4, entry 6)



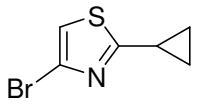
^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.23 (m, *J* = 5, 3 Hz, 1H), 7.63 (m, *J* = 10, 2.5 Hz, 2H), 7.82 (s, 1H); ^{13}C NMR (126 MHz, CD_3COCD_3) δ 105.9 (m), 109.3 (m), 119.6, 126.1, 162.6 (d), 164.6 (d), 166.0; LCMS: $[M+H]^+$ calcd for $C_9H_4BrF_2NS{\cdot}H^+$, 275.9; found 275.8. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_4BrF_2NS{\cdot}H^+$, 275.9294; found 275.9238.

4-Bromo-2-(2-benzofuran)thiazole (Table 4, entry 7)



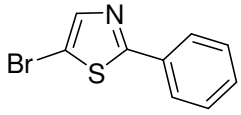
^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.36 (t, *J* = 5 Hz, 1H), 7.47 (t, *J* = 5Hz, 1H), 7.57 (s, 1H), 7.65 (d, *J* = 10 Hz, 1H), 7.78 (d, *J* = 5 Hz, 1H), 7.80 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 106.0, 111.8, 117.2, 122.3, 124.0, 126.5, 127.0, 128.3, 149.1, 155.3, 159.0; LCMS: $[M+H]^+$ calcd for $C_{11}H_6BrNOS{\cdot}H^+$, 279.9; found 279.8. HRMS (ESI): $[M+H]^+$ calcd for $C_{11}H_6BrNOS{\cdot}H^+$, 279.9432; found 279.9448.

4-Bromo-2-cyclopropylthiazole (Table 4, entry 8)



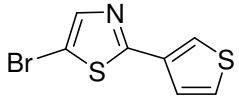
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10 (m, 2H), 1.14 (m, 2H), 2.29 (tt, *J* = 8.0, 5.0 Hz, 1H), 6.96 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 11.4, 14.7, 113.9, 123.8, 174.9; LCMS: $[M+H]^+$ calcd for $C_6H_6BrNS{\cdot}H^+$, 203.94; found 203.94. HRMS (ESI): $[M+H]^+$ calcd for $C_6H_6BrNS{\cdot}H^+$, 203.9482; found 203.9500.

5-Bromo-2-phenylthiazole (Table 4, entry 10)



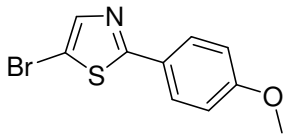
^{1}H NMR (500 MHz, CD_3Cl_3) δ 7.45 (m, 3H), 7.75 (s, 1H), 7.87 (m, 2H); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.53 (m, 2H), 7.89 (s, 1H), 7.95 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 108.7, 126.4, 129.2, 130.6, 133.3, 145.1, 169.8; LCMS: $[M+H]^+$ calcd for $C_9H_6BrNS{\cdot}H^+$, 239.9; found 239.8. HRMS (ESI): $[M+H]^+$ calcd for $C_9H_6BrNS{\cdot}H^+$, 2389.9482; found 239.9500.

5-Bromo-2-(3-thiophene)thiazole (Table 4, entry 11)



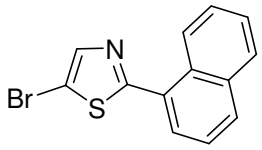
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 5, 3.3 Hz, 1H), 7.53 (dd, *J* = 5.0, 2.5 Hz, 1H), 7.71 (s, 1H), 7.83 (dd, *J* = 5.0, 1.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 107.9, 124.4, 126.0, 127.3, 135.5, 144.7, 164.8; LCMS: $[M+H]^+$ calcd for $C_7H_4BrNS_2{\cdot}H^+$, 245.8; found 245.8. HRMS (ESI): $[M+H]^+$ calcd for $C_7H_4BrNS_2{\cdot}H^+$, 245.9074; found 245.9053.

5-Bromo-2-(4-methoxyphenyl)thiazole (Table 4, entry 12)



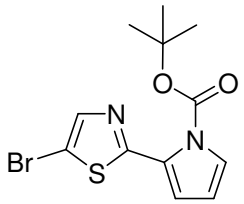
^{1}H NMR (500 MHz, CD_3Cl_3) δ 3.87 (s, 3H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.68 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 2H); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 3.89 (s, 3H), 7.06 (d, *J* = 10 Hz, 2H), 7.79 (s, 1H), 7.88 (d, *J* = 10 Hz, 2H); ^{13}C NMR (126 MHz, CD_3COCD_3) δ 55.2, 107.1, 114.8, 126.1, 127.9, 145.2, 162.1, 169.5; LCMS: $[M+H]^+$ calcd for $C_{10}H_8BrNOS{\cdot}H^+$, 269.9; found 269.8. HRMS (ESI): $[M+H]^+$ calcd for $C_{10}H_8BrNOS{\cdot}H^+$, 269.9588; found 269.9584.

5-Bromo-2-naphthalenethiazole (Table 4, entry 13)



^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.64 (m, 3H), 7.90 (d, *J* = 5 Hz, 1H), 8.04 (d, *J* = 10 Hz, 1H), 8.05 (s, 1H), 8.11 (d, *J* = 10 Hz, 1H), 8.87 (d, *J* = 10 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 109.6, 125.2, 125.6, 126.7, 127.7, 128.6, 128.7, 130.3, 130.5, 131.1, 134.2, 144.9, 169.2; LCMS: $[M+H]^+$ calcd for $C_{13}H_8BrNS{\cdot}H^+$, 289.9; found 289.8. HRMS (ESI): $[M+H]^+$ calcd for $C_{13}H_8BrNS{\cdot}H^+$, 289.9639; found 289.9638.

5-Nromo-2-(1-Boc-pyrrole-2-)thiazole (Table 4, entry 14)



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 9H), 6.29 (t, *J* = 5 Hz, 1H), 6.70 (dd, *J* = 3.5, 2.0 Hz, 1H), 7.42 (dd, *J* = 3.5, 2.0 Hz, 1H), 7.75 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 77.3 (t), 85.0, 109.5, 111.2, 118.6, 124.8, 126.7, 143.8, 148.9, 160.9; LCMS: $[M+H]^+$ calcd for $C_{12}H_{13}BrN_2O_2S{\cdot}H^+$, 328.9; found 328.9. HRMS (ESI): $[M+H\text{-}BOC]^+$ calcd for $C_{12}H_{13}BrN_2O_2S{\cdot}H^+$, 228.9435; found 228.9450.

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