Cobalt-catalyzed intramolecular *C–N* and *C–O* cross-coupling reactions: synthesis of benzimidazoles and benzoxazoles†

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Received 9th July 2010, Accepted 15th September 2010
DOI: 10.1039/c0ob00405g

Cobalt(II)-complex catalyzes efficiently the intramolecular *C–N* and *C–O* cross-couplings of *Z*-*N*′-(2-halophenyl)-*N*-phenylamidines and *N*-(2-bromophenyl)benzamides to afford the corresponding substituted benzimidazoles and benzoxazoles in the presence of K_2CO_3 at moderate temperature. The protocol is general, air stable and affords the products selectively in moderate to high yield.

Introduction

The recent development in cross-coupling reactions using transition-metal-catalysis affords effective methods for the formation of arylcarbon-heteroatom bonds.[1,2] Benzimidazoles and benzoxazoles are important subunits of many compounds that are of biological and pharmaceutical interest (Fig. 1).[3] For examples, benzimidazole and benzoxazole core structures can be found in commercial drugs such as Prilosec, Nexium, Protonix, Famvir, Vermox and Priaxim. Some of the recent medicinal chemistry applications of benzimidazoles and benzoxazoles include anticancer agent NSC-693638,[4a] HIV reverse transcriptase inhibitor L-697,661,[4b] estrogen receptor-β agonist ERB-041,[4c] 5-lipoxygenase inhibitor[4d] and factor Xa(FXa) inhibitor.[4e] Development of effective method to construct functionalized benzimidazole and benzoxazole scaffolds is thus highly relevant to drug discovery.

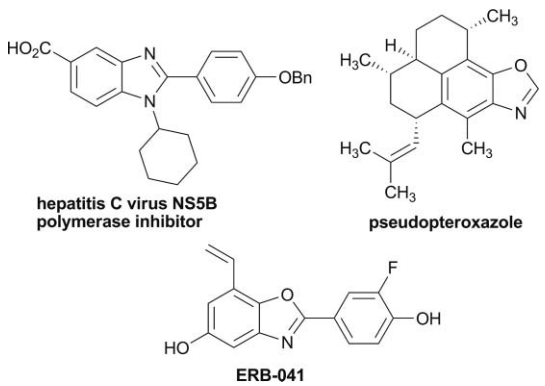

Fig. 1 Examples of biologically active compounds.

The classical methods for the synthesis of benzimidazoles and benzoxazoles involve the condensation of 2-aminoaniline[5] and 2-aminophenol[6] with either carboxylic acid in the presence of acids or aldehydes under oxidative conditions. However, these approaches are generally limited due to the non-availability of the suitably substituted 2-aminoanilines and 2-aminophenols, and some cases, the requirement of harsh reaction conditions such as strong acids or elevated temperature.

Some of these limitations have been recently overcome by the cross-coupling reactions, which allow the assembly of the target molecules under comparatively milder conditions.[2] For examples, the synthesis of benzimidazoles has been accomplished using Pd[7] and Cu[8] based catalysts *via C–N* cross-coupling reactions. Later, the synthesis of benzoxazoles has been achieved using Cu[9] and Fe[10] based catalysts by *C–O* cross-coupling reaction. These approaches provide a straight forward route for the synthesis of functionalized benzimidazoles and benzoxazoles.

Cobalt-catalyzed *C–C* cross-couplings are an active topic in organic synthesis.[11] Because cobalt is readily available, cheap, non-toxic and exhibits high catalytic activities. However, cobalt-catalyzed arylcarbon-heteroatom cross-couplings are rare and to the best of our knowledge only two reports so far are available.[12] The *C–S* cross-coupling of aryl iodides with thiols is reported by the combined use of cobalt(II) phosphine complex and zinc under inert conditions.[12d] Later, the *C–N* cross-coupling of aryl iodides with azoles is demonstrated using $CoCl_2 \cdot 6H_2O$ and DMEDA in air.[12b] In continuation of our studies on cross-coupling reactions,[13] in this contribution we wish to report that the combination of $Co(acac)_2 \cdot 2H_2O$ and 1,10- phenanthroline catalyzes efficiently the cyclization of (*Z*)-*N*′-(2-halophenyl)-*N*-phenylamidines and *N*-(2-bromo-phenyl)benzamides to afford substituted benzimidazoles and benzoxazoles, respectively, in the presence of K_2CO_3 at moderate temperature. The protocol is simple, general, air-stable and the cyclization takes place *via* intramolecular *C–N* and *C–O* cross-couplings with high yield.

Results and discussion

Synthesis of benzimidazoles

Initially, the standardization of the reaction conditions were carried out with *Z*-*N*′-(2-bromophenyl)-*N*-phenylbenzamidine[7a] as a model substrate using different ligands, cobalt sources and solvents at varied temperature (Table 1). Among the screened

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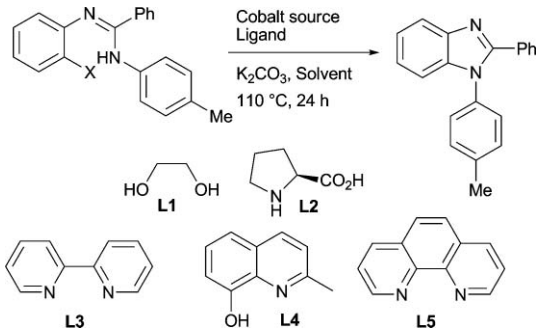
† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra of benzimidazoles and benzoxazoles. See DOI: 10.1039/c0ob00405g

Table 1 Optimization studies for the Co-catalyzed *C*–*N* cross-coupling of *Z*-*N*′-(2-halophenyl)-*N*-phenylbenzamidine



Entry	Cobalt source	Ligand	X	Solvent	Conv. (%)[a,b]
1	$Co(OAc)_2·4H_2O$	**L5**	Br	DMSO	51
2	$CoCl_2·6H_2O$	**L5**	Br	DMSO	24
3	$CoSO_4·7H_2O$	**L5**	Br	DMSO	48
4	$Co(acac)_2·2H_2O$	**L5**	Br	DMSO	66
5	$Co(acac)_2·2H_2O$	**L1**	Br	DMSO	10
6	$Co(acac)_2·2H_2O$	**L2**	Br	DMSO	n.d.
7	$Co(acac)_2·2H_2O$	**L3**	Br	DMSO	28
8	$Co(acac)_2·2H_2O$	**L4**	Br	DMSO	n.d.
9	$Co(acac)_2·2H_2O$	**L5**	Br	DMF	75
10	$Co(acac)_2·2H_2O$	**L5**	Br	1,4-dioxane	50
11	$Co(acac)_2·2H_2O$	**L5**	Br	2-Propanol	82
12	$Co(acac)_2·2H_2O$	**L5**	Br	Toluene	100
13	$Co(acac)_2·2H_2O$	**L5**	Br	Toluene	65[c]
14	$Co(acac)_2·2H_2O$	—	Br	Toluene	19
15	—	—	Br	Toluene	n.d.
16	$Co(acac)_2·2H_2O$	**L5**	Br	Toluene	52[d],43[e]
17	$Co(acac)_2·2H_2O$	**L5**	I	Toluene	100[f]
18	$Co(acac)_2·2H_2O$	**L5**	Cl	Toluene	n.d.

[a] *Z*-*N*′-(2-Halophenyl)-*N*-phenylbenzamidine (0.5 mmol), cobalt source (10 mol%), ligand (20 mol%) and K_2CO_3 were stirred for 12 h at 110 °C in appropriate solvent (1.0 mL) under air. [b] Determined from 400 MHz ^{1}H NMR. [c] Catalyst (5 mol%) used. [d] 1.5 equiv K_2CO_3. [e] Reaction *T* = 100 °C. [f] Reaction time: 6 h. n.d. = not detected.

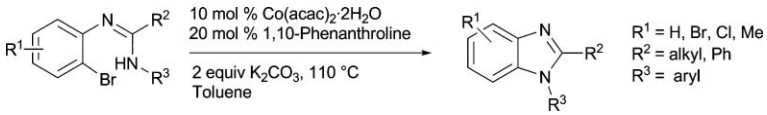
ligands, bipyridine[14] **L3** and 1,10-phenanthroline[15] **L5** were effective and the latter provided the best result of 100% conversion, where as ethylene glycol[16] **L1**, L-proline[17] **L2** and 8-hydroxyquinalidine[18] **L4** afforded inferior result. Control experiments revealed that only 19% conversion of the desired product detected without the aid of a ligand. The catalytic activities of the cobalt sources were compared, and $Co(acac)_2·2H_2O$ was found to be superior to others. In general, all the four solvents were effective to give the product with 50–100% conversion, and toluene was found to be better than others. The reaction was effective with K_2CO_3 and the optimal temperature was 110 °C. The reactivities of other aryl halides were investigated. *Z*-*N*′-(2-Iodophenyl)-*N*-phenylbenzamidine exhibited greater reactivity affording the desired benzimidazole in 6 h with 100% yield, where as *Z*-*N*′-(2-chlorophenyl)-*N*-phenylbenzamidine showed no reaction. In summary, the optimal conditions consist of the combination of $Co(acac)_2·2H_2O$ (10 mol%), **L5** (20 mol%) and K_2CO_3 (2 equiv) at 100 °C for 12 h.

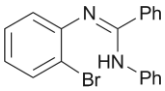
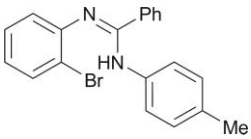
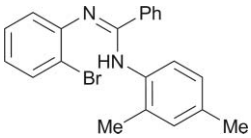
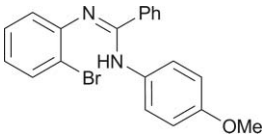
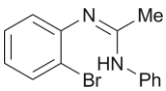
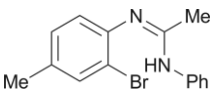
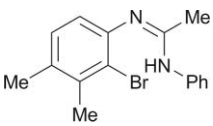
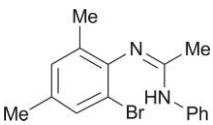
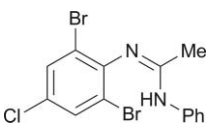
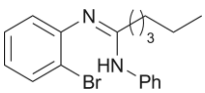
Next, the scope of the procedure was explored for the cyclization of the other substituted amidines (Table 2). *Z*-*N*′-(2-Bromophenyl)-*N*-phenylbenzamidine and *Z*-*N*′-(2-bromophenyl)-*N*-phenylmethylamidine substituted with 4-Me, 4-OMe, 2,4-diMe, 4,5-diMe and 4,6-diMe proceeded the desired cyclizations to give the corresponding 2-alkyl or 2-aryl substituted benzimidazole in 84–97% yields. Similarly, *N*-*Z*-*N*′-(4-chloro-2,6-dibromophenyl)-*N*-phenylmethylamidine and *Z*-*N*′-(2-bromophenyl)-*N*-phenylbutylamidine underwent the cyclization to give 2-alkyl substituted benzmidazoles in 93% and 85% yield, respectively.

Synthesis of benzoxazoles

Encouraged by these results, we further studied the optimized conditions for the analogue intramolecular cyclization of *N*-(2-bromophenyl)benzamide[9c] to give substituted benzoxazoles (Table 3). The cyclization was slow affording the desired 2-arylbenzoxazole in 6% yield. The effect of solvent was then studied. Interestingly, the product yield was increased to 97% when DMSO was employed as the solvent, where as DMF (50%), isopropanol (16%) and 1,4-dioxane (34%) afforded moderate yields. The scope of the procedure was further studied for the cyclization of other benzamides. *N*-(2-Bromophenyl)benzamide having 3-Br, 4-Br, 4-Me, 4,5-diMe, 4,6-diMe and 6-Br-4-Cl substituents readily proceeded the cyclization to provide the corresponding benzoxazoles in 33–97% yields. In contrary, *N*-(2-bromophenyl)acetamide and *N*-(2-bromophenyl)hexanoamide exhibited no reaction.

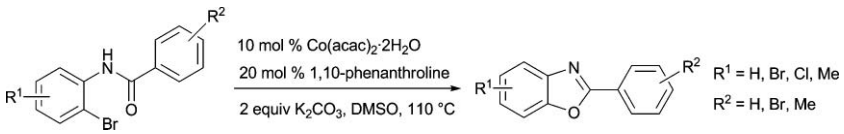
Table 2 Cobalt-catalyzed intramolecular *C*–*N* cross-coupling of *Z*-*N*′-(2-bromophenyl)-*N*-phenylamidines

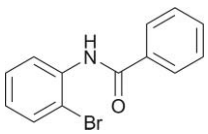
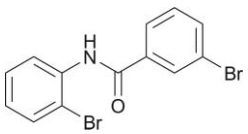
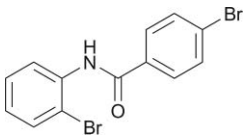
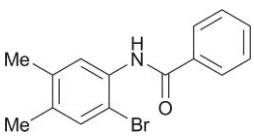
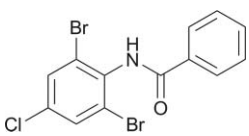


Entry	Substrate	Time/h	Product(%)[a,b]
1		12	97
2		12	95
3		15	89
4		11	92
5		16	88
6		16	90
7		15	91
8		18	84
9		12	93
10		17	85

[a] Reaction conditions: *Z*-*N*′-(2-bromophenyl)-*N*-phenylamidine (0.50 mmol), $Co(acac)_2 \cdot 2H_2O$ (10 mol%), 1,10-phenanthroline (20 mol%) and K_2CO_3 (1.0 mmol) were stirred at 110 °C in toluene (1 mL) under air. [b] Isolated yield.

Table 3 Cobalt-catalyzed intramolecular *C*–*O* cross-coupling of substituted *N*-(2-bromophenyl)benzamides

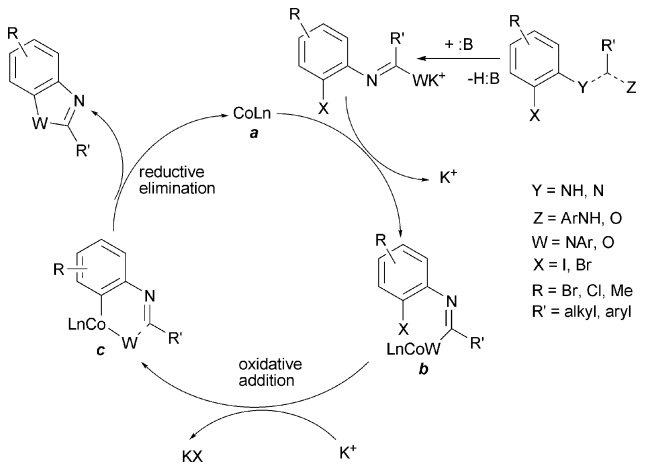


Entry	Substrate	Time/h	Product(%)[a,b]
1		24	97
2		30	38
3		30	33
4		24	70
5		26	56
6		26	85
7		30	59
8		20	95

[a] Reaction conditions: *N*-(2-Bromophenyl)benzamide (0.5 mmol), $Co(acac)_2 \cdot 2H_2O$ (10 mol%), 1,10-phenanthroline (20 mol%) and K_2CO_3 (1.0 mmol) were stirred at 110 °C in DMSO (1 mL) for the appropriate time under air. [b] Isolated yield.

Mechanism

In the presence of base, cobalt complex ***a*** may undergo reaction with substrate to give intermediate ***b*** (Scheme 1).[19] The latter can undergo oxidative addition to provide intermediate ***c*** which can complete the catalytic cycle by reductive elimination of the heterocycle. Furthermore, the atomic absorption of the aqueous solution of the active cobalt salt, $Co(acac)_2 \cdot 2H_2O$, was measured to reveal the presence trace of copper[20a] which was observed in the iron-catalyzed[20b] cross-couplings as the active catalyst. However,



Scheme 1 Proposed catalytic cycle for the cobalt-catalyzed C–N and C–O cross-coupling reactions.

in the present protocol, no trace of copper was detected with the detection limit of 1 ppm. This experiment clearly suggests that copper has not involved in these coupling reactions.

Conclusions

The intramolecular cyclization of 2-haloarylbenzamidines and 2-haloarylbenzamides is demonstrated *via* intramolecular *C–N* and *C–O* cross-couplings using cobalt(II) complex to afford substituted benzimidazoles and benzoxazoles under aerobic conditions.

Experimental

General information

2-Haloanilines were purchased from Aldrich. $Co(OAc)_2{\cdot}4H_2O$ (99%), $CoCl_2{\cdot}6H_2O$ (98%) and $CoSO_4{\cdot}7H_2O$ were obtained from Merck. $Co(acac)_2{\cdot}2H_2O$ was prepared according to reported procedure.[21a] Column chromatography was carried out with SRL silica gel (60–120 mesh) using ethyl acetate and hexane as eluent. Analytical TLC was performed with SRL silica gel G plates. NMR spectra (400 MHz for ^1H and 100 MHz for ^{13}C) were recorded using Varian 400 spectrometer with Me_4Si as an internal standard. Melting points were determined using Buchi-540 apparatus and are uncorrected. Elemental analysis was carried out using Perkin Elmer CHNS analyzer. IR spectra were recorded using Perkin Elmer spectrum one FT-IR spectrometer. Atomic absorption spectroscopy was carried out with Varian AA-240 spectrometer.

General procedure for benzimidazoles synthesis

2-Bromoarylamidine (0.5 mmol), $Co(acac)_2{\cdot}2H_2O$ (10 mol%, 14.7 mg), **L5** (20 mol%, 19.8 mg) and K_2CO_3 (1.0 mmol, 138.0 mg) were stirred in toluene (1.0 mL) at 110 °C under air (Table 2). The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The reaction mixture was cooled to room temperature and passed through a short pad of silica gel using ethyl acetate and hexane as eluent to provide benzimidazoles.

1,2-Diphenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 1).[8c]. Yellow solid; yield 97%; mp 109–110 °C (lit.[21b] 109 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.0 Hz, 1H), 7.58–7.47 (m, 5H), 7.35–7.26 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 143.2, 137.4, 137.2, 130.0, 129.6, 128.7, 128.5, 127.6, 123.5, 123.2, 120.0, 116.4, 110.6; FT-IR (KBr) 3050, 3010, 2962, 1652, 1594, 1492, 1475, 1455, 1382, 1327, 1306, 1278, 1259, 1180, 1076, 1026 cm^{-1}. Anal. Calcd (%) for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22; N, 10.36; found: C, 84.49; H, 5.23; N, 10.28.

2-Phenyl-1-*p*-tolyl-1*H*-benzo[*d*]imidazole (Table 2, entry 2)[21c]. Yellow liquid; yield 95%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89–7.86 (m, 1H), 7.59–7.57 (m, 2H), 7.35–7.18 (m, 10H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 143.0, 138.6, 137.4, 134.4, 130.5, 130.1, 129.5, 128.3, 127.2, 123.3, 123.0, 119.8, 110.6, 21.3; FT-IR (neat) 3061, 2924, 1610, 1515, 1473, 1455, 1384, 1324, 1262, 1180, 1109, 1020 cm^{-1}. Anal. Calcd (%) for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85; found: C, 84.60; H, 5.64; N, 9.76.

1-(2,4-Dimethylphenyl)-2-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 3). Colorless liquid; yield 89%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.0 Hz, 1H), 7.63–7.61 (m, 2H), 7.34–7.15 (m, 8H), 7.01–6.99 (d, J = 8.0 Hz, 1H), 2.43 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.4, 142.9, 139.4, 137.3, 135.6, 133.3, 132.3, 130.3, 129.5, 128.7, 128.4, 128.3, 128.2, 123.3, 122.8, 119.7, 110.6, 21.3, 17.5; FT-IR (neat) 3061, 2959, 2922, 2858, 1613, 1505, 1472, 1455, 1441, 1380, 1322, 1308, 1277, 1263, 1239, 1206, 1192, 1155, 1136, 1074, 1029 cm^{-1}. Anal. Calcd (%) for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08; N, 9.39; found: C, 84.62; H, 6.07; N, 9.31.

1-(4-Methoxyphenyl)-2-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 4). White solid; yield 92%; mp 119–120 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89–7.87 (dd, J = 0.8, 8.0 Hz, 1H), 7.61–7.58 (m, 2H), 7.35–7.22 (m, 8H), 7.02–6.99 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 152.6, 143.0, 137.7, 130.1, 129.7, 129.5, 128.6, 128.4, 123.3, 122.9, 119.8, 115.1, 110.6, 55.6; FT-IR (KBr) 3062, 2957, 2839, 1606, 1514, 1472, 1458, 1442, 1325, 1311, 1294, 1276, 1250, 1212, 1192, 1104, 1077, 1030 cm^{-1}. Anal. Calcd (%) for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33; found: C, 80.11; H, 5.35; N, 9.24.

2-Methyl-1-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 5)[21d]. White solid; yield 88%; mp 68–69 °C (lit.[9c] mp 70–72 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.4 Hz, 1H), 7.59–7.49 (m, 3H), 7.38–7.35 (m, 2H), 7.26 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 142.6, 136.6, 136.1, 130.0, 128.9, 127.2, 122.7, 122.5, 119.0, 110.0, 14.5; FT-IR (KBr) 3060, 2967, 2917, 1613, 1597, 1519, 1500, 1457, 1395, 1326, 1287, 1247, 1188, 1074, 1016 cm^{-1}. Anal. Calcd (%) for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45; found: C, 80.81; H, 5.80; N, 13.39.

2,6-Dimethyl-1-phenyl-1*H*-benzo[*d*]imidazole (Table 3, entry 6)[21d]. Yellow liquid; yield 90%; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60–7.49 (m, 4H), 7.35–7.32 (m, 2H), 7.05 (dd, J = 0.8, 8.0 Hz, 1H), 6.88 (s, 1H), 2.46 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.1, 140.7, 136.7, 136.3, 132.7, 130.0, 128.8, 127.2, 123.9, 118.5, 110.0, 21.8, 14.5; FT-IR (neat) 3060, 2924, 2857, 1708, 1618, 1598, 1522, 1500, 1455, 1394, 1305, 1255, 1213, 1143, 1074, 1011 cm^{-1}. Anal. Calcd (%) for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60; found: C, 81.15; H, 6.31; N, 12.54.

2,5,6-Trimethyl-1-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 7)[8b]. Yellow solid; yield 91%; mp 145–146 °C (lit.[8b] mp 146 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (m, 3H), 7.46 (s, 1H),

7.30–7.28 (m, 2H), 7.24 (s, 1H), 2.51 (s, 3H), 2.29 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 141.9, 137.9, 134.0, 132.2, 129.7, 129.6, 128.7, 123.1, 121.3, 117.9, 24.9, 18.1, 14.6; FT-IR (KBr) 3043, 2966, 2915, 2858, 1704, 1597, 1523, 1498, 1439, 1407, 1377, 1361, 1325, 1296, 1260, 1161, 1089, 1034, 1013 cm^{-1}. Anal. Calcd (%) for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85; found: C, 81.39; H, 6.80; N, 11.81.

2,4,6-Trimethyl-1-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 8)[8b]. Yellow liquid; yield 84%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.48 (m, 3H), 7.34–7.31 (m, 2H), 6.88 (s, 1H), 6.72 (s, 1H), 2.63 (s, 3H), 2.48 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3, 139.8, 136.5, 136.4, 132.6, 130.0, 128.8, 128.4, 127.3, 124.6, 107.6, 21.7, 16.8, 14.4; FT-IR (neat) 2925, 2851, 1637, 1596, 1500, 1456, 1392, 1327, 1253, 1231 cm^{-1}. Anal. Calcd (%) for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85; found: C, 81.38; H, 6.80; N, 11.82.

4-Bromo-6-chloro-2-methyl-1-phenyl-1*H*-benzo[*d*]-imidazole (Table 2, entry 9)[8b]. Yellow liquid; yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.53 (m, 3H), 7.42 (d, J = 1.6 Hz, 1H), 7.32–7.29 (m, 2H), 7.01 (d, J = 1.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 140.3, 137.0, 135.2, 130.3, 129.6, 128.7, 127.0, 125.6, 112.6, 109.6, 14.5; FT-IR (neat) 2956, 2929, 2857, 1614, 1517, 1500, 1454, 1421, 1385, 1324, 1256, 1173, 1072 cm^{-1}. Anal. Calcd (%) for $C_{14}H_{10}BrClN_2$: C, 52.29; H, 3.13; N, 8.71; found: C, 52.38; H, 3.11; N, 8.63.

2-Pentyl-1-phenyl-1*H*-benzo[*d*]imidazole (Table 2, entry 10). Yellow liquid; yield 85%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 8.0 Hz, 1H), 7.60–7.52 (m, 3H), 7.37–7.35 (d, J = 7.6 Hz, 2H), 7.28–7.25 (t, J = 8.0 Hz, 1H), 7.21–7.17 (t, J = 8.0 Hz, 1H), 7.10–7.08 (d, J = 7.6 Hz, 1H), 2.79–2.75 (t, J = 8.0 Hz, 2H), 1.79–1.74 (m, 2H), 1.35–1.24 (m, 4H), 0.83 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 142.7, 136.6, 136.2, 130.0, 129.0, 127.5, 122.6, 122.4, 119.2, 110.1, 31.6, 27.7, 27.8, 27.6, 22.4, 14.0; FT-IR (neat) 3054, 2957, 2927, 2857, 1597, 1511, 1499, 1455, 1398, 1262, 1095, 1072, 1015 cm^{-1}. Anal. Calcd (%) for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63; N, 10.60; found: C, 81.89; H, 7.61; N, 10.50.

General procedure for benzoxazoles synthesis

2-Bromoarylbenzamide (0.5 mmol), $Co(acac)_2{\cdot}2H_2O$ (10 mol%, 14.7 mg), **L5** (20 mol%, 19.8 mg) and K_2CO_3 (1.0 mmol, 138.0 mg) were stirred in DMSO (1.0 mL) at 110 °C under air (Table 3). The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The organic layer was washed successively with brine (1 × 5 mL) and water (2 × 5 mL). Drying and evaporation of the solvent provided a residue which was purified by silica gel chromatography using ethyl acetate and hexane as eluent.

2-Phenylbenzoxazole (Table 3, entry 1)[9c]. White solid; yield 97%; mp 101–102 °C (lit.[9c] mp 101–102 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26–8.24 (m, 2H), 7.77–7.75 (m, 1H), 7.58–7.56 (m, 1H), 7.53–7.49 (m, 3H), 7.36–7.33 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.2, 150.9, 142.2, 131.7, 129.1, 127.8, 127.3, 125.3, 124.7, 120.2, 110.8; FT-IR (KBr) 3060, 2961, 1616, 1552, 1472, 1447, 1344, 1318, 1241, 1196, 1052, 1022 cm^{-1}. Anal. Calcd (%) for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17; found: C, 80.12; H, 4.63; N, 7.08.

2-(3-Bromophenyl)benzoxazole (Table 3, entry 2)[21e]. White solid; yield 38%; mp 128–129 °C (lit.[21e] mp 128–130 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41–8.40 (t, J = 1.6 Hz, 1H), 8.18–8.16 (dd, J = 8.0, 1.2 Hz, 1H), 7.78–7.76 (m, 1H), 7.66–7.63 (m, 1H), 7.59–7.57 (m, 1H), 7.41–7.35 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.6, 150.9, 142.0, 134.6, 130.63, 129.2, 126.2, 125.7, 124.9, 123.2, 120.4, 110.9; FT-IR (KBr) 2925, 2854, 1614, 1570, 1547, 1451, 1429, 1292, 1239, 1195, 1071, 1051 cm^{-1}. Anal. Calcd (%) for $C_{13}H_8BrNO$: C, 56.96; H, 2.94; N, 5.11; found: C, 57.13; H, 2.93; N, 5.02.

2-(4-Bromophenyl)benzoxazole (Table 3, entry 3)[9c]. White solid; yield 33%; mp 156–157 °C (lit.[9c] mp 157–158 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.12–8.09 (m, 2H), 7.77–7.74 (m, 1H), 7.67–7.63 (m, 2H), 7.58–7.55 (m, 1H), 7.36–7.33 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.3, 150.9, 142.1, 132.4, 129.1, 126.4, 126.2, 125.6, 124.9, 120.3, 110.8; FT-IR (KBr) 3057, 2924, 1615, 1592, 1547, 1484, 1452, 1400, 1342, 1294, 1261, 1244, 1176, 1107, 1069, 1052, 1009 cm^{-1}. Anal. Calcd (%) for $C_{13}H_8BrNO$: C, 56.96; H, 2.94; N, 5.11; found: C, 57.11; H, 2.91; N, 5.02.

2-(4-Methylphenyl)benzoxazole (Table 3, entry 4)[21f]. White solid; yield 70%; mp 116–117 °C (lit.[21f] mp 116 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14–8.12 (d, J = 8.4 Hz, 2H), 7.75–7.73 (m, 1H), 7.57–7.54 (m, 1H), 7.34–7.31 (m, 4H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.5, 150.8, 142.3, 132.4, 129.8, 127.8, 127.3, 125.1, 124.7, 120.0, 110.7, 21.8; FT-IR (KBr) 3281, 2964, 2920, 2855, 1651, 1622, 1581, 1530, 1502, 1451, 1435, 1411, 1346, 1262, 1244, 1172, 1019 cm^{-1}. Anal. Calcd (%) for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69; found: C, 80.60; H, 5.26; N, 6.59.

6-Methyl-2-phenylbenzoxazole (Table 3, entry 5)[9c]. White solid; yield 56%; mp 93–94 °C (lit.[9c] mp 93 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.23–8.20 (m, 2H), 7.63–7.61 (d, J = 8.0 Hz, 1H), 7.51–7.48 (m, 3H), 7.37 (t, J = 0.8 Hz, 1H), 7.16–7.14 (dd, J = 8.4, 0.8 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.7, 151.2, 140.1, 135.7, 131.4, 129.0, 127.6, 127.5, 126.0, 119.5, 110.9, 22.0; FT-IR (KBr) 3054, 2920, 2856, 1615, 1554, 1481, 1448, 1337, 1289, 1274, 1247, 1172, 1125, 1099, 1073, 1021 cm^{-1}. Anal. Calcd (%) for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69; found: C, 80.65; H, 5.27; N, 6.60.

5,6-Dimethyl-2-phenylbenzoxazole (Table 3, entry 6). White solid; yield 85%; mp 132–133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24–8.21 (m, 2H), 7.50–7.48 (m, 3H), 7.19 (s, 1H), 6.96 (s, 1H), 2.61 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.0, 151.0, 139.4, 135.3, 131.2, 130.0, 128.9, 127.8, 127.6, 126.6, 108.2, 21.9, 16.7; FT-IR (KBr) 3058, 2922, 2855, 1614, 1596, 1554, 1477, 1447, 1405, 1374, 1338, 1292, 1264, 1225, 1167, 1069, 1049, 1019 cm^{-1}. Anal. Calcd (%) for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27; found: C, 80.79; H, 5.85; N, 6.21.

4,6-Dimethyl-2-phenylbenzoxazole (Table 3, entry 7). White solid; yield 59%; mp 166–167 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.22–8.19 (m, 2H), 7.50–7.48 (m, 4H), 7.34 (s, 1H), 2.37 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.5, 149.6, 140.4, 134.5, 133.4, 131.3, 129.0, 127.6, 120.2, 111.0, 20.7, 20.4;

FT-IR (KBr) 3056, 2923, 2863, 1552, 1488, 1463, 1445, 1333, 1290, 1270, 1151, 1049, 1020, 998 cm^{-1}. Anal. Calcd (%) for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27; found: C, 80.81; H, 5.86; N, 6.18.

4-Bromo-6-chloro-2-phenylbenzoxazole (Table 3, entry 8)[8b]. White solid; yield 95%; mp 136–137 °C (lit.[8b] 136 °C); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.26–8.24 (m, 2H), 7.56–7.49 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.3, 150.8, 140.8, 132.4, 131.2, 129.1, 128.3, 128.2, 126.3, 113.0, 110.7; FT-IR (KBr) 3010, 2925, 2853, 1610, 1594, 1482, 1451, 1408, 1337, 1325, 1307, 1261, 1231, 1200, 1073, 1124, 1051, 1033, 1019 cm^{-1}. Anal. Calcd (%) for $C_{13}H_7BrClNO$: C, 50.60; H, 2.29; N, 4.54; found: C, 50.46; H, 2.31; N, 4.49.

Acknowledgements

This work was supported by Department of Science and Technology, New Delhi, and Council of Scientific and Industrial Research, New Delhi

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