Article

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Copper(II)-Catalyzed Oxidative Cross-Coupling of Anilines, Primary Alkyl Amines and Sodium Azide Using TBHP: A Route to 2-Substituted Benzimidazoles

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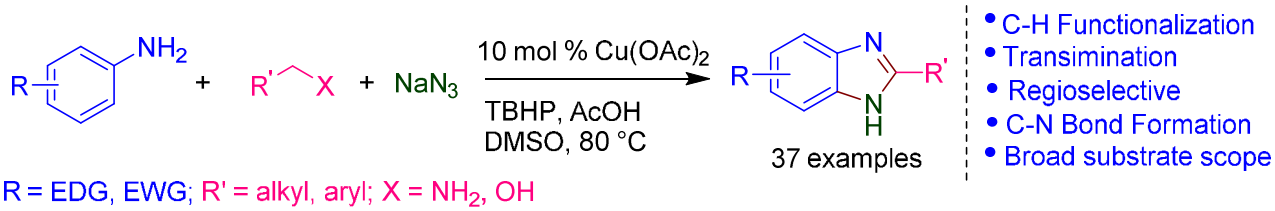


Copper(II)-catalyzed oxidative cross-coupling of anilines, primary alkyl amines and sodium azide is described in the presence of TBHP at moderate temperature. This one-pot multicomponent protocol involves a domino C-H functionalization, transimination, *ortho* selective amination and cyclization sequence. The broad substrate scope and functional group compatibility are the significant practical features. The protocol can be extended to the coupling of benzyl alcohols with moderate yields.

INTRODUCTION

Recent advances in transition-metal-catalyzed C-H functionalization reactions using directing groups have led to the development of effective methods for the regioselective carbon-carbon and carbon-heteroatom bonds formation.[1] Among them, the C-N bond formation has attracted considerable attention due to the presence of this moiety in numerous compounds that are of biological, medicinal and material interests.[2-5] More recently, *ortho*-selective C-H azidation of arene has been accomplished using -NH_2[2c] and imine[2d] as the directing groups. Herein, we report an efficient copper-catalyzed oxidative cross-coupling of anilines, primary alkyl amines and sodium azide to afford functionalized benzimidazoles *via* a domino transimination, *ortho* selective amination and cyclization sequence. The utilization of the readily accessible simple substrates and the broad substrate scope are the significant practical

advantages. These reaction conditions can be utilized for the coupling benzyl alcohols in moderate yields.

Benzimidazoles are privileged structural scaffolds due to their interesting medicinal and biological properties.[6] For examples, the compounds bearing benzimidazole motifs exhibit a broad spectrum of biological properties such as anti-viral,[6a] anti-cancer,[6b] anti-bacterial,[6c] anti-fungal[6d] and anti-HIV activities (Figure 1). In addition, benzimidazole structural frameworks are found to be useful for the fabrication of organic light-emitting diodes (OLEDs).[7] Traditionally, the preparation of benzimidazoles is performed via condensation of 1,2-diaminoarene with aldehydes or carboxylic acids followed by oxidative cyclization. However, these methods often suffer due to the limited substrate scope and harsh reaction conditions.[8] To overcome these drawbacks, transition-metal-catalyzed cross-coupling of aryl halides and their analogues with N-H nucleophiles has been explored.[9] More recently, a few studies are focused on the C-H functionalization and C-N bond formation of amidines[10]and benzylamine with 2-aminoanilines[11] to afford functionalized benzimidazoles (Scheme 1a). These reactions are attractive as they are effective under relatively mild conditions with broad substrates scope. Development of the oxidative coupling of the readily accessible substituted anilines, primary alkyl amines and sodium azide *via* a domino sp^3 and sp^2 C-H functionalization strategy would thus be valuable (Scheme 1b).

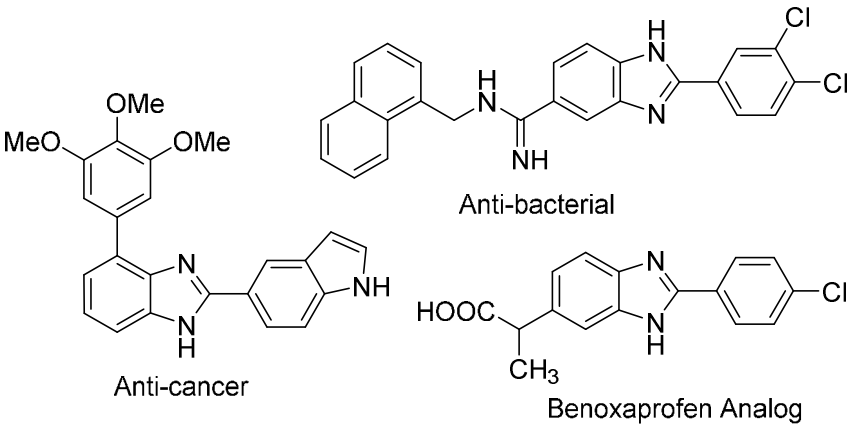
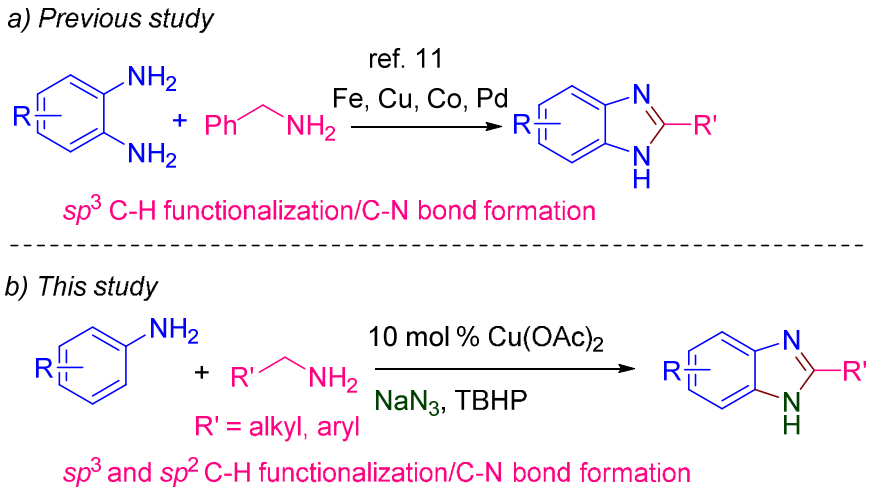


Figure 1. Examples of Some Biologically Important Benzimidazoles.

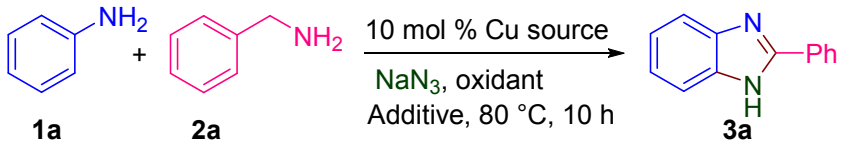
Scheme 1. Methods for Benzimidazoles Using Primary Alkyl Amines v*ia* Transimination.



RESULTS AND DISCUSSION

First, we commenced the optimization studies using aniline **1a** and benzylamine **2a** as model substrates with NaN_3 employing different Cu-sources, oxidants and solvents (Table 1). Gratifyingly, the oxidative cross-coupling readily occurred to afford 2-phenylbenzimidazole **3a** in a trace amount when the substrates **1a** and **2a** were stirred at 80 ^oC for 10 h with 10 mol % CuI, 3 equiv NaN_3 and 2 equiv TBHP in DMSO (entry 1). The use of CH_3COOH as an additive led an increase in the yield to 44%, whereas CF_3COOH and $(CH_3)_3CCOOH$ produced inferior results (entries 2-4). Subsequent screening of the copper sources led to further increase in the yield to 82% using $Cu(OAc)_2$, whereas CuBr, CuCl and $CuCl_2$ showed moderate catalytic activity (entries 5-8). In contrast, $Cu(SO_4)_2{\cdot}5H_2O$ afforded **3a** in a trace amount (entry 9). Similar results were observed using air, 30% H_2O_2 and DTBP as the oxidants (entries 10). DMSO was found to be the solvent of choice, whereas DMF, toluene, 1,4-dioxane and CH_3CN furnished **3a** in moderate yields (entries 11-14), varying the amount of the catalyst (5 mol %) or additive (10 equiv) led to drop the yield to <38% (entries 15-16). Control experiments confirmed that without the copper catalyst or TBHP, the formation of **3a** was not observed (entries 17-18).

Table 1. Optimization of the Reaction Conditions[a]

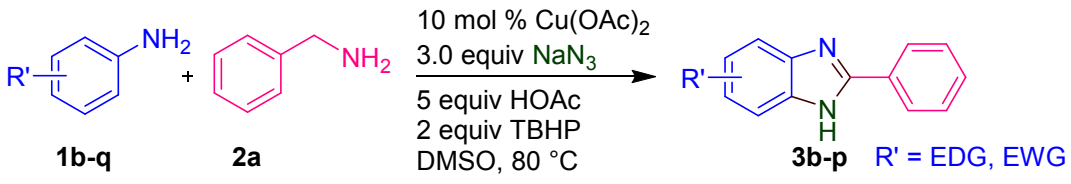


1a **2a** **3a**

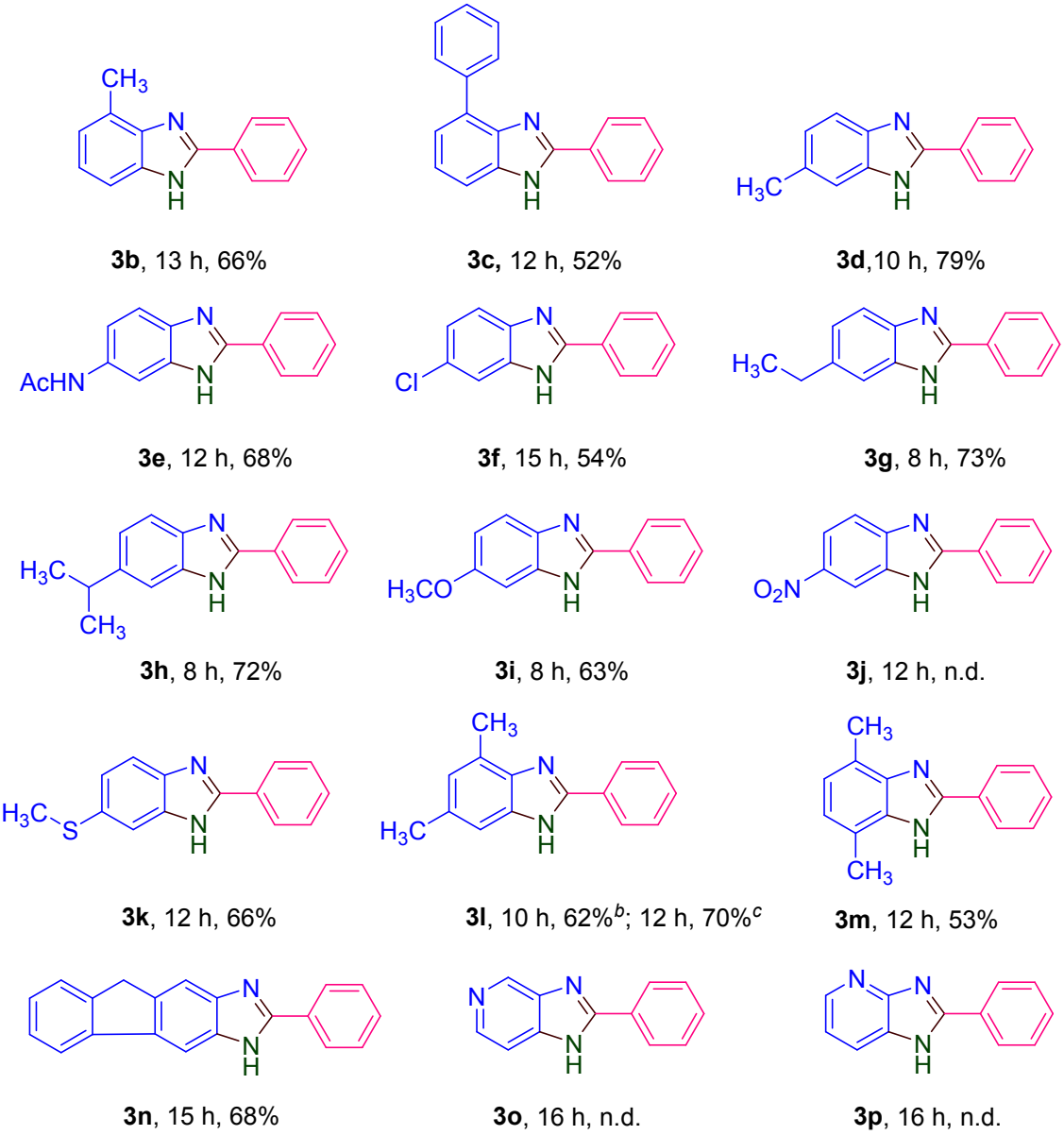
entry	Cu source	additive	solvent	**3a** (%)[b]
1	CuI	-	DMSO	trace
2	CuI	CH_3COOH	DMSO	44
3	CuI	$(CH_3)_3CCOOH$	DMSO	trace
4	CuI	CF_3COOH	DMSO	trace
5	CuBr	CH_3COOH	DMSO	31
6	CuCl	CH_3COOH	DMSO	50
7	$CuCl_2$	CH_3COOH	DMSO	60
8	$Cu(OAc)_2$	CH_3COOH	DMSO	82
9	$Cu(SO_4)_2{\cdot}5H_2O$	CH_3COOH	DMSO	trace
10[c]	$Cu(OAc)_2$	CH_3COOH	DMSO	trace
11	$Cu(OAc)_2$	CH_3COOH	DMF	56
12	$Cu(OAc)_2$	CH_3COOH	toluene	24
13	$Cu(OAc)_2$	CH_3COOH	1,4-dioxane	43
14	$Cu(OAc)_2$	CH_3COOH	CH_3CN	46
15[d]	$Cu(OAc)_2$	CH_3COOH	DMSO	38
16[e]	$Cu(OAc)_2$	CH_3COOH	DMSO	35
17	-	CH_3COOH	DMSO	n.d.
18[f]	$Cu(OAc)_2$	CH_3COOH	DMSO	n.d.

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), [Cu] (10 mol %), NaN_3 (1.5 mmol), TBHP (1 mmol), AcOH (2.5 mmol), solvent (0.5 mL), 80 °C, 10 h. [b]Determined by 600 MHz ^{1}H NMR. [c]Using air, 30% H_2O_2 or DTBP. [d]$Cu(OAc)_2$ (5 mol %). [e]AcOH (5 mmol). [f]No TBHP. n.d. = not detected.

Scheme 2. Reaction of Substituted Anilines with Benzylamine[a]



1b-q **2a** **3b-p**



3b, 13 h, 66% **3c,** 12 h, 52% **3d**,10 h, 79%

3e, 12 h, 68% **3f**, 15 h, 54% **3g**, 8 h, 73%

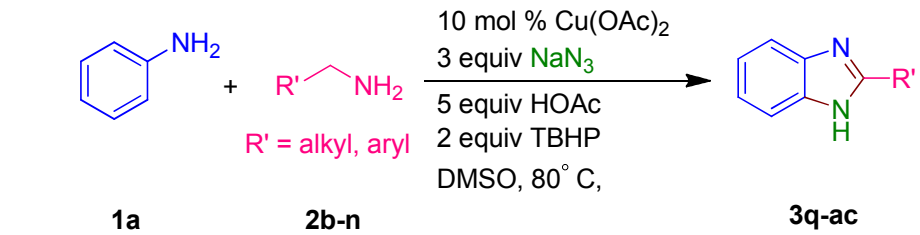
3h, 8 h, 72% **3i**, 8 h, 63% **3j**, 12 h, n.d.

3k, 12 h, 66% **3l**, 10 h, 62%[b]; 12 h, 70%[c] **3m**, 12 h, 53%

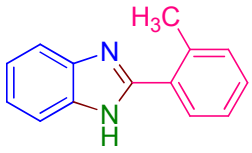
3n, 15 h, 68% **3o**, 16 h, n.d. **3p**, 16 h, n.d.

[a]Reaction conditions: amine **1b-q** (1 mmol), benzylamine **2a** (1.2 mmol), $Cu(OAc)_2$ (10 mol %), NaN_3 (3 mmol), TBHP (2 mmol), AcOH (5 mmol), DMSO (1 mL), 80 °C. [b]3,5-Dimethylaniline used. [c]2,4-Dimethylaniline used.

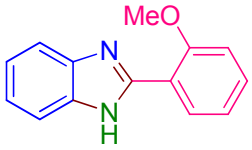
Scheme 3. Reaction of Alkyl Amines with Aniline[a]



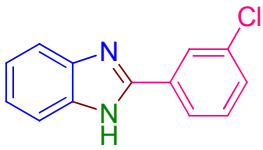
1a **2b-n** **3q-ac**



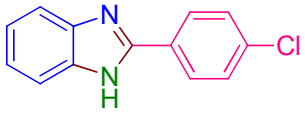
3q, 10 h, 74%



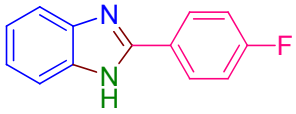
3r, 16 h, 75%



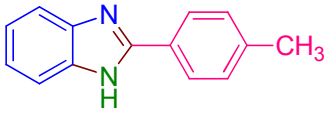
3s, 16 h, 71%



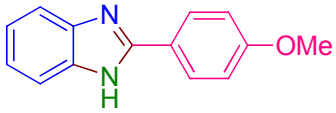
3t, 11 h, 69%



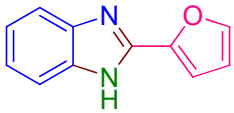
3u, 10 h, 72%



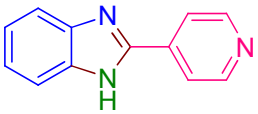
3v, 10 h, 77%



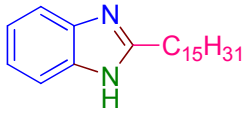
3w, 8 h, 74%



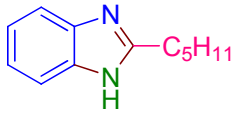
3x, 12 h, 46%



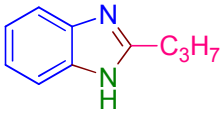
3y, 14 h, 41%



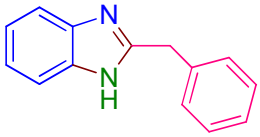
3z, 16 h, 35%



3aa, 12 h, 46%



3ab, 16 h, 55%



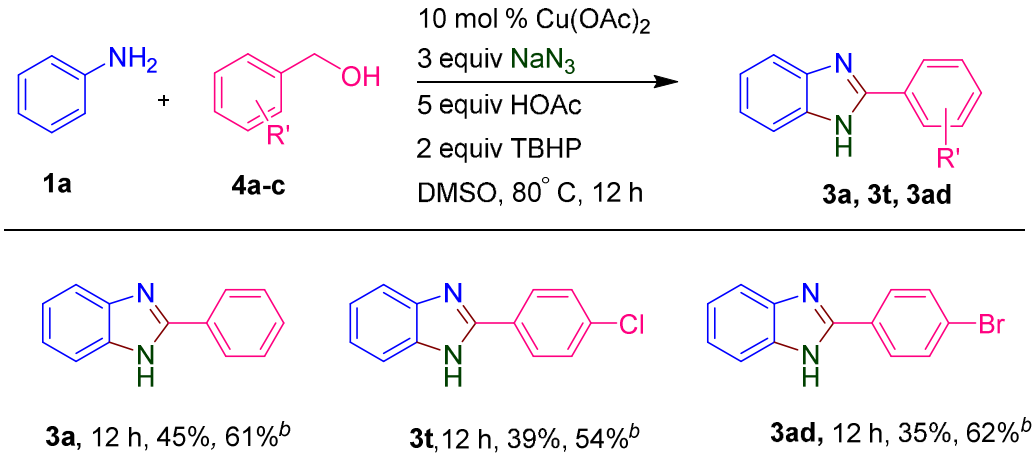
3ac, 15 h, 48%

[a]Reaction conditions: aniline**1a** (1 mmol), alkyl amines **2b-n** (1.2 mmol), $Cu(OAc)_2$ (10 mol %), NaN_3 (3 mmol), TBHP (2 mmol), AcOH (5 mmol), DMSO (1 mL), 80 °C.

Having the optimal conditions, the reaction of substituted anilines **1b-q** was next explored using benzylamine **2a** as a standard substrate (Scheme 2). Anilines **1b** and **1c** with methyl and phenyl groups at 2-position underwent reaction to give benzimidazoles **3b** and **3c** in 66 and 52% yields, respectively. Similarly, anilines **1d-i** bearing acetamide, chloro, ethyl, isopropyl, methoxy and methyl functionalities

at 4-position furnished the corresponding benzimidazoles **3d-i** in 54-79% yields, whereas aniline **1j** with strong electron withdrawing nitro group failed to react and the formation of benzimidazole **3j** was not observed. However, the reaction of aniline **1k** with 4-thiomethyl group produced benzimidazole **3k** in 66% yield, while anilines **1l-n** with methyl groups at 2,4-, 3,5- and 2,5-positions provided benzimidazoles **3l-m** in 53-70% yields. Similar result was observed with 2-aminofluorene **1o** affording benzimidazole **3n** in 68% yield. In contrast, the reaction of heterocyclic amines such as 2-aminopyridine **1p** and 3-aminopyridine **1q** failed to produce benzimidazoles **3o-p** and the starting materials were remain intact.

Scheme 4. Reaction of Aniline with Benzyl Alcohols[a]

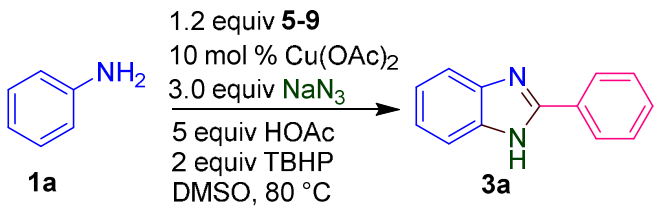


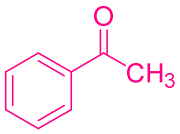
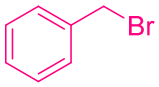
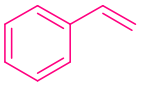
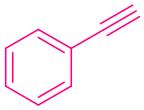
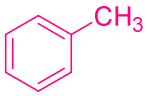
[a]Reaction conditions: aniline **1a** (1 mmol), benzyl alcohol **4a-c** (1.2 mmol), $Cu(OAc)_2$ (10 mol %), NaN_3 (3 mmol), TBHP (2 mmol), AcOH (5 mmol), DMSO (1 mL), 80 °C. [b]Alcohol **4a-c** (3 mmol) used.

Next, the reaction of primary alkyl amines was explored with aniline as the standard substrate (Scheme 3). Benzylamines **2b-c** bearing substitution at 2-position with methyl and methoxy groups underwent reaction to furnish benzimidazoles **3q** and **3r** in 74 and 75% yields, respectively. Similar result was observed with benzylamine **2d** bearing 3-chloro group affording **3s** in 71% yield. The reaction of benzylamines **2e-h** bearing substitution at 4-position with chloro, fluoro, methoxy and methyl groups produced the corresponding benzimidazoles **3t-w** in 69-77% yields. In addition,

heterocyclic substrates such as furfurylamine **2i** and 4-picolylamine **2j** underwent reaction to give benzimidazoles **3x** and **3y** in 46 and 41% yields, respectively. Furthermore, aliphatic amines such as butylamine **2k**, hexylamine **2l**, hexadecane-1-amine **2m** and 2-phenyl ethanamine **2n** could be cross-coupled to afford 2-alkyl benzimidazoles **3z-ac** in 35-55% yields.

Table 2. Reaction of Aldehyde Precursors with Aniline[a]



entry	aldehyde precursor	**3a** (%)[b]
1	 **5**	n.d.
2	 **6**	9
3	 **7**	n.d.
4	 **8**	30
5	 **9**	5

[a]Reaction conditions: aniline**1a** (1 mmol), aldehyde precursor **5-10** (1.2 mmol), $Cu(OAc)_2$ (10 mol %), NaN_3 (3 mmol), TBHP (2 mmol), AcOH (5 mmol), DMSO (1 mL), 80 ^oC.

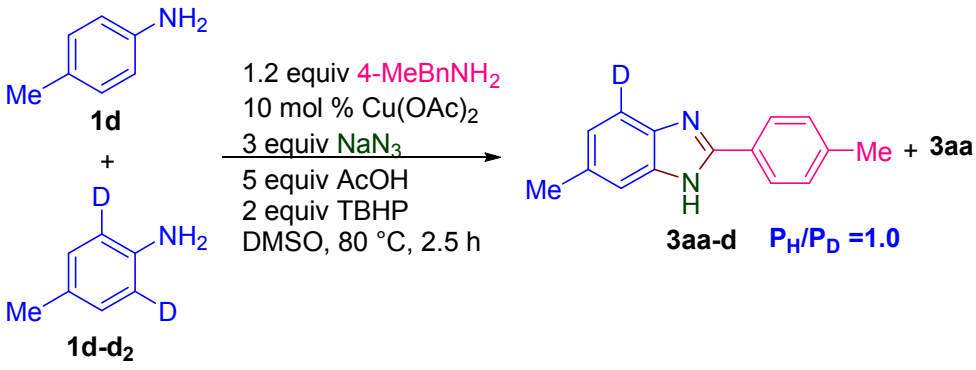
The reaction conditions are also compatible for the reaction of analogue benzyl alcohols (Scheme 4). For examples, benzyl alcohol **4a** underwent reaction to furnish benzimidazole **3a** in 45% yield. Increase

in the quantity of benzyl alcohol **4a** from 1.2 to 3 equiv led to an improvement in the yield to 61%. Similar results were observed with benzyl alcohols bearing bromo and chloro functionalities at 4-position affording benzimidazoles **3t** and **3ad** in moderate yields.

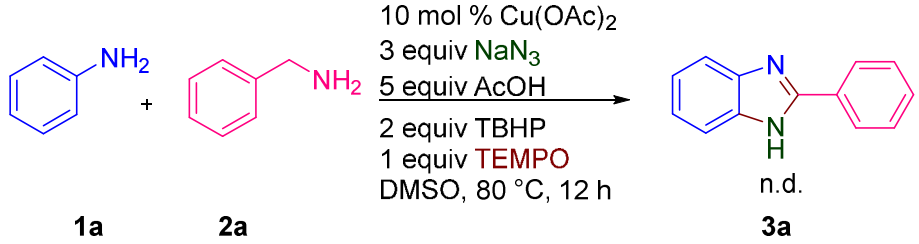
Finally, the utility of the protocol was investigated for the reaction of aldehyde precursors **5-9** (Table 2). The reaction of acetophenone **5** and styrene **7** exhibited no benzimidazole formation, whereas benzyl bromide **6** and phenylacetylene **8** and toluene **9** underwent reaction to produce the corresponding benzimidazoles in 5-30% yields. These results suggest that broad range of substrates can be cross-coupled in moderate to good yields.

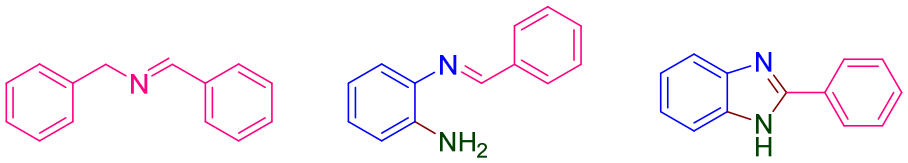
Some of these benzimidazoles **3b**, **3d-e**, **3i**, **3l** and **3n** are formed as a mixture of tautomers. To reveal the exact structure, variable temperature ^{1}H NMR experiments of **3d** were pursued as a representative example (see Supporting Information). As anticipated, the formation of a single tautomer was observed when heated to 50 ^{o}C, however, the corresponding NOE experiment has failed to suggest the exact structure of the tautomer due to the lack of N-H interaction with aromatic H atom.

Scheme 5. Kinetic Isotope Experiment



Scheme 6. Radical Scavenger Experiment





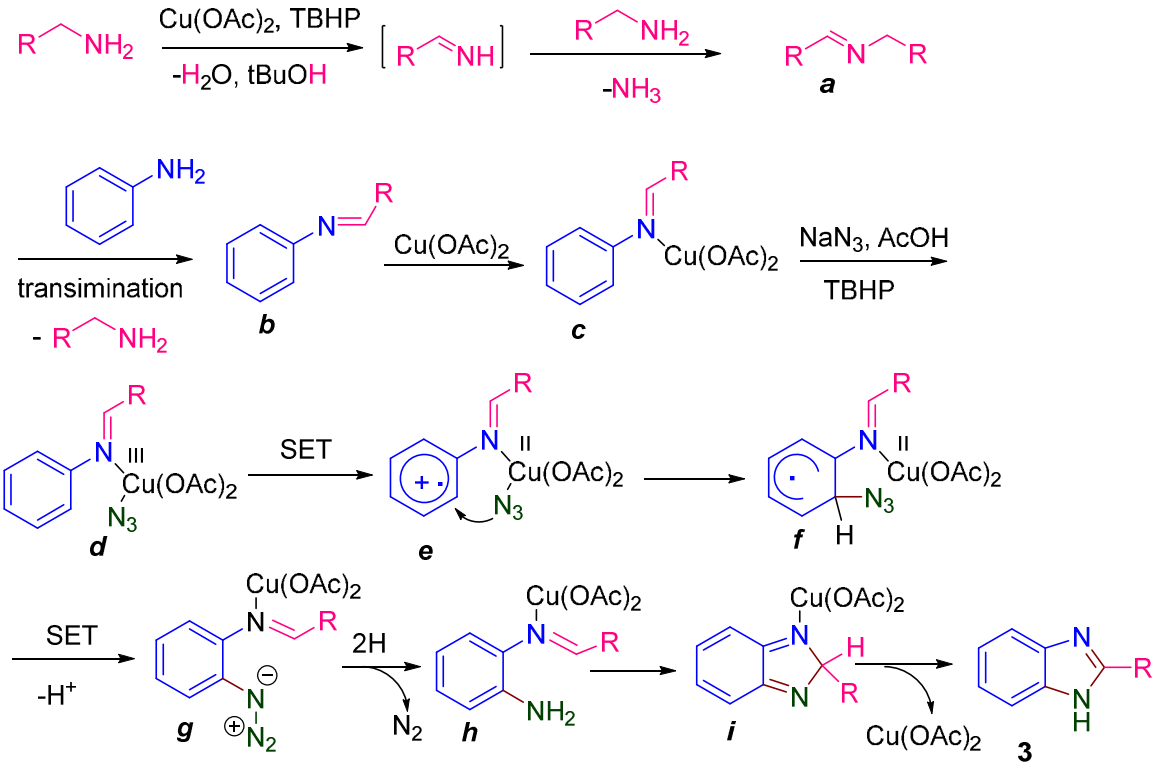
A B 3a

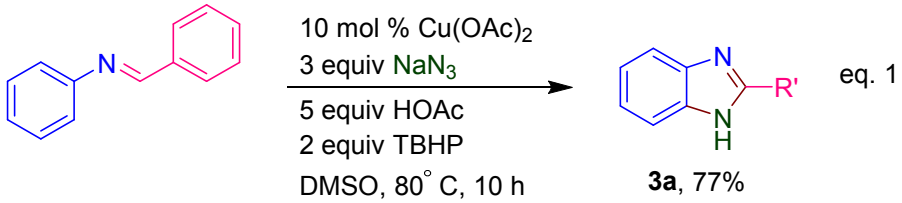
Figure 2. Major Species Identified using ESI-MS of the Reaction Mixture of **1a** and **2a** after 5h (See supporting Information).

To understand the reaction pathway, the intermolecular kinetic isotope experiment was performed between **1d** and **1d-d$_2$** and P_H/P_D was found to be 1.0 (23% conv., 2.5 h), which suggests that the C-H bond cleavage may not be involved in the product-determining step (Scheme 5).[12] Further, the radical scavenger experiment using TEMPO exhibited no benzimidazole formation, which suggests that a radical intermediate may be involved (Scheme 6).[13] In addition, the ESI-MS analysis of the reaction mixture of **1a** and **2a** revealed the presence of three major species, **A**, **B** and benzimidazole **3a** (Figure 2). Formation of **A** suggests that the oxidative coupling of benzylamine may be involved via sp^3 C-H functionalization,[14] while the intermediate **B** reveals the involvement of transimination[15] of **A** with aniline followed by imine directed[2d] *ortho* selective sp^2 C-H azidation. The subsequent $Cu(OAc)_2$ catalyzed reduction of $-N_3$ may produce $-NH_2$ under heating.[9g] The absence of the peaks corresponding to 2-azidoaniline or 2-aminoaniline suggests that the reaction may not involve $-NH_2$ as the directing group for the azidation.[2c] Thus, the copper(II)-catalyzed oxidative coupling of alkyl amine can give imine ***a***,[14] which can undergo transimination[15] with aniline to form ***b***. Coordination[16] of ***b*** with $Cu(OAc)_2$ can furnish ***c***, which may subsequently combine with *in situ* generated N_3 radical from HN_3 and TBHP to form the intermediate ***d***.[2c] A single electron transfer[17] (SET) from the aryl ring to the metal center may lead to the formation of ***e***, which can convert into ***f*** by azido transfer into the aryl ring.[17] The latter may convert into ***g*** via SET process, that could be reduced to ***h*** under heating in the presence of $Cu(OAc)_2$.[9g] Intramolecular oxidative cyclization of ***h*** can produce ***i*** that can aromatize to afford **3** and copper(II) to complete the catalytic cycle (Scheme 7). The role of AcOH is to generate HN_3 from NaN_3.

Furthermore, the intermediate ***b***, prepared from aniline and benzaldehyde, underwent reaction to produce benzimidazole **3a** in 77% yield (eq. 1). These results clearly suggest that the reaction may proceed via the intermediate ***b*** using imine as the directing group.

Scheme 7. Proposed Reaction Pathway





CONCLUSIONS

In summary, copper-catalyzed oxidative cross-coupling of anilines, alkyl primary amines and sodium azide has been demonstrated using domino sp^3 and sp^2 C-H functionalization, transimination, *ortho* selective azidation and cyclization process. The broad substrates scope, functional groups compatibility

and the one-pot domino process are the significant practical features. This study may open avenue for the further development of C-H functionalization strategy for the regioselective construction of diverse nitrogen containing heterocycles from the readily available simple substrates at relatively mild reaction conditions.

EXPERIMENTAL SECTION

General Information: $Cu(OAc)_2$ (99%), CuI (98%), CuCl (90%), $CuCl_2$ (97%) and TBHP (~5.5 M in decane, over molecular sieve 4Å), and NaN_3 (99%), CuBr (97%) and $CuSO_4 \cdot 5H_2O$ (99%) purchased from commercial sources and used as recieved. Purification of the reaction products was carried out by column chromatography using silica gel (60-120 mesh). Analytical TLC was performed on silica gel G/GF 254 plate. NMR spectra were recorded on 600 and 400 MHz NMR spectrometers using DMSO-d_6 and $CDCl_3$ as solvents and Me_4Si as an internal standard. Chemical shifts (δ) were reported in ppm and spin-spin coupling constants (J) were given in Hz. Melting points were determined using melting point apparatus and were uncorrected. FT-IR spectra were recorded using IR spectrometer. Mass spectra were recorded on a Q-Tof ESI-MS instrument.

General Procedure for the Synthesis of Benzimidazoles. To a stirred solution of aniline **1** (1.0 mmol), $Cu(OAc)_2$ (10 mol %, 0.1 mmol, 18 mg), NaN_3 (3 equiv, 3.0 mmol, 195 mg), AcOH (5 equiv, 5.0 mmol, 300 mg) and TBHP (2 equiv, 2 mmol, 360 µL) in DMSO (1 mL) was added alkyl amine **2** or alcohol **4** (1.2 mmol), and the resultant mixture was stirred at 80 °C for the appropriate time. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as an eluent. After completion, the reaction mixture was cooled to room temperature and treated with saturated $NaHCO_3$ (5 mL). The solution was then extracted with ethyl acetate (3 x 10 mL) and washed with brine (2 x 5 mL) and water (1 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane and ethyl acetate as an eluent to afford analytically pure products.

2-Phenyl-1*H*-benzo[*d*]imidazole 3a.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 137 mg, yield 70%; mp 290-291 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.92 (br s, 1H), 8.19 (d, *J* = 7.8 Hz, 2H), 7.67 (s, 1H), 7.56-7.48 (m, 4H), 7.20 (s, 2H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 151.2, 143.8, 135.0, 130.1, 129.8, 128.9, 126.4, 122.5, 121.6, 118.9, 111.3; FT-IR (KBr) 3436, 3048, 2962, 2922, 2114, 1623, 1591, 1462, 1411, 1374, 1276, 1120, 1029, 971, 744, 703 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_{10}N_2H$ 195.0922, found 195.0913.

4-Methyl-2-phenyl-1*H*-benzo[*d*]imidazole 3b.[18a] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; white solid; 137 mg, yield 66%; mp 247-248 °C; mixture of tautomers (1.2:1): ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.83 (br s, 1H), 12.57 (br s, 1H), 8.26-8.18 (m, 4H), 7.55-7.49 (m, 7H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.11-7.07 (m, 2H), 6.99 (s, 2H) 2.59 (s, 3H), 2.57 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 151.2, 150.4, 143.5, 143.2, 134.7, 134.5, 130.3, 129.74, 129.7, 128.9, 128.8, 128.4, 126.7, 126.5, 126.4, 123.1, 122.5, 121.9, 121.8, 121.3, 116.3, 108.8, 17.2, 16.7; FT-IR (neat) 3435, 3051, 2921, 2854, 2717, 2115, 1619, 1537, 1481, 1458, 1371, 1287, 785, 746, 703 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2H$ 209.1078, found 209.1057.

2,4-Diphenyl-1*H*-benzo[*d*]imidazole 3c. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; white solid; 141 mg, yield 52%; mp 256-257 °C;^{1}H NMR (400 MHz, DMSO-d_6) δ 13.06 (br s, 1H), 8.21-8.16 (m, 4H), 7.59-7.50 (m, 6H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H);^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 151.2, 141.3, 138.3, 135.8, 130.6, 130.1, 129.8, 128.9, 128.8, 128.5, 128.2, 127.0, 126.5, 122.9, 120.5, 110.6; FT-IR (neat) 3435, 3057, 2921, 2851, 2114, 1617, 1457, 1415, 1390, 1316, 1244, 1112, 1027, 750, 697 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{14}N_2H$ 271.1235, found 271.1229.

6-Methyl-2-phenyl-1*H*-benzo[*d*]imidazole 3d.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; white solid; 164 mg, yield 79%; mp 246-247 °C; mixture of tautomers (1:1.3):^{1}H NMR (600 MHz, DMSO-d_6) δ 12.77 (br s, 1H), 12.74 (br s, 1H), 8.16 (d, *J* = 7.8 Hz, 4H), 7.55-7.52 (m, 5H), 7.48-

7.45 (m, 3H), 7.41 (d, J = 8.4 Hz, 1H), 7.31 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 8.4Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 150.8, 142.0, 131.8, 130.3, 129.6, 128.9, 126.3, 123.9, 123.3, 118.5, 111.0, 21.3; FT-IR (KBr) 3435, 3047, 2921, 2856, 2110, 1631, 1595, 1463, 1401, 1308, 1276, 1112, 972, 804, 702, 689 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2H$ 209.1078, found 209.1071.

N-(2-Phenyl-1*H*-benzo[*d*]imidazol-6-yl)acetamide 3e. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.41; pale yellow solid; 171 mg, yield 68%; mp 262-263 °C; mixture of tautomers (1:2.1): ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.85 (br s, 1H), 12.79 (br s, 1H), 10.03 (br s, 1H), 9.93 (br s, 1H), 8.16-8.13 (m, 4H), 8.02 (s, 1H), 7.58-7.52 (m, 5H), 7.47-7.45 (m, 2H), 7.39-7.37 (m, 2H), 7.21-7.19 (m, 2H), 2.09 (s, 3H), 2.07 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 168.1, 168.0, 151.7, 151.0, 143.9, 140.0, 135.1, 134.9, 131.3, 130.2, 129.6, 129.0, 126.4, 126.2, 118.7, 115.8, 114.5, 110.9, 109.3, 101.5, 24.1; FT-IR (KBr) 3436, 2957, 2922, 2851, 2130, 1643, 1497, 1463, 1313, 1259, 1178, 1025, 994, 822, 694 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{15}H_{13}N_3OH$ 252.1137, found 252.1146.

6-Chloro-2-phenyl-1*H*-benzo[*d*]imidazole 3f.[9c] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.48; white solid; 123 mg yield 54%; mp 200-201 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 13.12 (br s, 1H), 8.17 (d, J = 7.8 Hz, 2H), 7.69-7.50 (m, 5H), 7.23 (d, J = 7.8 Hz, 1H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 152.7, 130.2, 129.7, 129.0, 126.6, 126.5, 122.4; FT-IR (KBr) 3444, 2920, 2119, 1624, 1584, 1462, 1450, 1438, 1384, 1275, 1107, 1062, 808, 692 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_9ClN_2H$229.0532, found 229.0512.

6-Ethyl-2-phenyl-1*H*-benzo[*d*]imidazole 3g. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.43; brown liquid; 162 mg, yield 73%;^{1}H NMR (400 MHz, DMSO-d_6) δ 12.82 (br s, 1H), 8.20 (d, J = 8.4 Hz, 2H), 7.57-7.47 (m, 3H), 7.46-7.41 (m, 2H), 7.07 (d, J = 8.4 Hz, 1H), 2.74 (q, J = 7.6 Hz, 2H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 130.4, 129.7, 128.9, 126.3, 28.5, 16.4; FT-

IR (neat) 3390, 3064, 2963, 2928, 2106, 1628, 1595, 1453, 1431, 1405, 1374, 1280, 1055, 814, 776, 692 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{15}H_{14}N_2H$ 223.1235, found 223.1235.

6-Isopropyl-2-phenyl-1*H*-benzo[*d*]imidazole 3h. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; liquid; 170 mg, yield 72%; ^1H NMR (600 MHz, DMSO-d_6) δ 12.82 (br s, 1H), 8.20 (s, 2H), 7.59-7.52 (m, 3H), 7.47-7.36 (m, 2H), 7.09 (s, 1H), 2.99 (s, 1H), 1.26 (d, *J* = 7.2 Hz, 6H); tautomers (1:1): ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 151.0, 143.2, 142.3, 135.2, 130.4, 129.6, 128.9, 126.3, 121.6, 120.7, 118.6, 115.8, 110.9, 108.3, 33.7, 24.4; FT-IR (neat) 3400, 3067, 2959, 2927, 2256, 2104, 1628, 1541, 1463, 1431, 1364, 1288, 1047, 815, 776 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{16}H_{16}N_2H$ 237.1392, found 237.1393.

6-Methoxy-2-phenyl-1*H*-benzo[*d*]imidazole 3i.[9c] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.35; liquid; 141 mg, yield 63%; tautomers (1:1): ^1H NMR (600 MHz, DMSO-d_6) δ 12.82 (br s, 2H), 8.18-8.17 (m, 4H), 7.57-7.52 (m, 6H), 7.46-7.44 (m, 2H), 7.31-7.20 (m, 1H), 7.04 (s, 1H), 6.86 (s, 2H), 3.81 (s, 6H); tautomers (1:1): ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 156.1, 150.5, 138.4, 130.4, 129.5, 128.9, 128.3, 127.3, 126.7, 126.2, 119.4, 112.3, 111.6, 111.2, 101.4, 94.5, 55.5; FT-IR (neat) 3414, 2924, 2854, 2255, 1631, 1594, 1539, 1490, 1455, 1434, 1159, 1117, 1026, 823, 778 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2OH$ 225.1028, found 225.1031.

6-(Methylthio)-2-phenyl-1*H*-benzo[*d*]imidazole 3k.[18b] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.31; liquid; 158 mg, yield 66%; ^1H NMR (600 MHz, DMSO-d_6) δ 12.97 (br s, 1H), 8.19 (d, *J* = 7.8 Hz, 2H), 7.55-7.53 (m, 3H), 7.49-7.46 (m, 2H), 7.17 (d, *J* = 4.8 Hz, 1H), 2.52 (s, 3H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 151.4, 130.0, 129.9, 129.0, 126.5, 122.9, 121.9, 119.2, 117.2, 111.9, 109.4, 16.5; FT-IR (KBr) 3400, 2920, 2856, 2255, 2126, 1624, 1582, 1537, 1463, 1441, 1422, 1278, 1025, 1004, 806, 777 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2SH$ 241.0799, found 241.0796.

4,6-Dimethyl-2-phenyl-1*H*-benzo[*d*]imidazole 3l.[9c] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 138 mg, yield 62% (3,5-diMe aniline) and 155 mg, 70% (2,4-diMe aniline); mp 190-191 °C; tautomers (1:0.6); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.67 (br s, 1H), 12.46 (br s, 1H), 8.23 (d, *J* =7.8 Hz, 2H), 8.16 (d, *J* = 7.2 Hz, 2H), 7.54-7.45 (m, 6H), 7.26 (s, 1H), 7.12 (s, 1H), 6.83-6.82 (m, 2H) 2.54-2.50 (m, 6H), 2.50-2.37 (m, 6H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 151.0, 149.9, 143.9, 141.4, 134.8, 132.7, 131.7, 130.6, 130.5, 129.6, 129.4, 128.9, 128.8, 127.8, 126.6, 126.2, 124.7, 123.6, 120.7, 116.0, 108.5, 21.4, 21.2, 17.1, 16.6; FT-IR (neat) 3456, 3146, 2922, 2853, 2108, 1683, 1627, 1456, 1406, 1332, 1254, 1031, 838, 701, 682 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{15}H_{14}N_2H$ 223.1235, found 223.1231.

4,7-Dimethyl-2-phenyl-1*H*-benzo[*d*]imidazole 3m. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 118 mg, yield 53%; mp 231-232 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.63 (br s, 1H), 8.37-8.35 (m, 2H), 7.68-7.60 (m, 3H), 7.02-7.00 (m, 2H), 2.68-2.62 (m, 6H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 150.4, 134.2, 130.5, 129.6, 128.8, 126.7, 125.5, 123.0, 121.9, 118.5,112.8, 17.0, 16.5; FT-IR (neat) 3435, 2922, 2852, 2108, 1625, 1457, 1410, 1313, 1264, 1029, 963, 705 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{15}H_{14}N_2H$ 223.1235, found 223.1241.

2-Phenyl-3,9-dihydrofluoreno[2,3-*d*]imidazole 3n. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; white solid; 192 mg, yield 68%; mixture of tautomers (1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.05 (br s, 1H), 12.97 (br s, 1H), 8.24-8.20 (m, 4H), 7.96-7.87 (m, 2H), 7.77-7.69 (m, 2H), 7.64-7.48 (m, 10H), 7.39-7.36 (m, 2H), 7.28-7.26 (m, 2H), 4.15- 4.11 (m, 1H), 3.99 (s, 1H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 151.5, 130.2 129.7, 128.9, 126.7, 126.5, 126.3, 125.0, 115.1; FT-IR (neat) 3433, 2922, 1629, 1457, 1433, 1403, 1311, 1107, 962, 854, 768, 725, 751, 698 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{20}H_{14}N_2H$ 283.1235, found 283.1235.

2-(*o*-Tolyl)-1*H*-benzo[*d*]imidazole 3q.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 154 mg, yield 74%; mp 223-224 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.63 (br s,

1H), 7.75 (d, J = 7.2 Hz, 1H), 7.67 (s, 1H), 7.54 (s, 1H), 7.41-7.35 (m, 3H), 7.21 (s, 2H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 151.9, 143.6, 137.0, 134.3, 131.3, 130.1, 129.4, 129.3, 126.0, 122.3, 121.4, 118.9, 111.3, 21.0; FT-IR (KBr) 3435, 3052, 2959, 2786, 2111, 1620, 1542, 1454, 1409, 1367, 1216, 1092, 900, 765, 746, 733 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2H$ 209.1079, found 209.1085.

2-(2-Methoxyphenyl)-1*H*-benzo[*d*]imidazole 3r. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 168 mg, yield 75%; mp 236-237 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.13 (br s, 1H), 8.33 (d, J = 7.2 Hz, 1H), 7.65-7.60 (m, 2H), 7.49 (t, J = 7.8 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.8 Hz, 2H) 7.13 (t, J = 7.2 Hz, 1H), 4.02 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 156.8, 149.0, 142.8, 134.8, 131.2, 129.8, 122.1, 121.6, 120.9, 118.5, 118.1, 112.1, 55.7; FT-IR (KBr) 3436, 3007, 2964, 2111, 1604, 1584, 1474, 1435, 1373, 1281, 1244, 1089, 1022, 966, 746 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2OH$ 225.1027, found 225.1027.

2-(3-Chlorophenyl)-1*H*-benzo[*d*]imidazole 3s.[9c] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 162 mg, yield 71%; mp 239-240 °C;^{1}H NMR (600 MHz, DMSO-d_6) δ 13.06 (br s, 1H), 8.23-8.22 (m, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.60-7.54 (m, 3H), 7.26-7.20 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 149.8, 143.7, 135.0, 133.8, 132.2, 130.9, 129.5, 126.1, 125.0, 122.9, 122.0, 119.1, 111.6; FT-IR (KBr) 3434, 3045, 2964, 2877, 2788, 2113, 1602, 1591, 1541, 1442, 1403, 1285, 1229, 1079, 998, 925, 743 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_9ClN_2$ H 229.0533, found 229.0518.

2-(4-Chlorophenyl)-1*H*-benzo[*d*]imidazole 3t.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; pale yellow solid; 157 mg, yield 69%; mp 266-267 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 13.0 (br s, 1H), 8.19 (d, J = 7.2 Hz, 2H), 7.63-7.56 (m, 4H), 7.21 (s, 2H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 150.2, 134.5, 129.0, 128.1, 122.3, 118.9, 111.5; FT-IR (KBr) 3445, 2996, 2957, 2116,

1635, 1583, 1482, 1421, 1323, 1256, 1234, 1095, 1025, 966, 835, 757 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_9ClN_2H$ 229.0532, found 229.0529.

2-(4-Fluorophenyl)-1*H*-benzo[*d*]imidazole 3u.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; yellow solid; 153 mg, yield 72%; mp 239-240 °C; ^1H NMR (600 MHz, DMSO-d_6) δ 12.92 (br s, 1H), 8.22 (s, 2H), 7.65 (s, 1H), 7.53 (s, 1H), 7.40 (s, 2H), 7.20 (s, 2H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 164.0 (d, J = 247.0 Hz,), 150.5, 143.8, 135.1, 128.8 (d, J = 7.5 Hz), 126.9, 122.6, 121.8, 118.9, 116.2 (d, 22.5 Hz), 111.4; FT-IR (KBr) 3435, 3052, 2960, 2854, 2116, 1603, 1497, 1475, 1433, 1276, 1228, 1156, 1110, 837, 747 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_9FN_2H$ 213.0828, found 213.0821.

2-(*p*-Tolyl)-1*H*-benzo[*d*]imidazole 3v.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 160 mg, yield 77%; mp 275-276 °C; ^1H NMR (600 MHz, DMSO-d_6) δ 12.85 (br s, 1H), 8.08 (d, J = 9 Hz, 2H), 7.65-7.63 (m, 1H), 7.52 (s, 1H), 7.36 (d, J = 9 Hz, 2H), 7.20-7.17 (m, 2H), 2.38 (s, 3H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 151.4, 143.9, 139.6, 135.0, 129.5, 127.5, 126.4, 122.4, 121.6, 118.7, 111.2, 21.0; FT-IR (KBr) 3435, 3053, 2961, 2919, 2855, 2115, 1621, 1588, 1448, 1430, 1226, 1122, 1042, 821, 747 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2H$ 209.1079, found 209.1065.

2-(4-Methoxyphenyl)-1*H*-benzo[*d*]imidazole 3w.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid ; 166 mg, yield 74%; mp 217-218 °C; ^1H NMR (600 MHz, DMSO-d_6) δ 12.75 (br s, 1H), 8.12 (s, 2H), 7.62 (s, 1H), 7.49 (s, 1H), 7.17-7.11 (m, 4H), 3.84 (s, 3H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 160.6, 151.4, 143.9, 135.0, 128.1, 122.7, 122.1, 121.5, 118.5, 114.4, 111.0, 55.3; FT-IR (KBr) 3472, 3054, 2923, 2855, 2113, 1611, 1500, 1476, 1453, 1295, 1254, 1179, 1124, 1033, 965, 845, 745 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2OH$ 225.1027, found 225.1026.

2-(Furan-2-yl)-1*H*-benzo[*d*]imidazole 3x.[9f] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.35; white solid ; 85 mg, yield 46%; mp 284-285 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.94 (br s, 1H), 7.95 (s, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.20-7.19 (m, 3H), 6.73 (s, 1H); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 145.6, 144.7, 143.7, 134.2, 122.7, 121.8, 118.8, 112.4, 111.4, 110.5; FT-IR (KBr) 3434, 3059, 2924, 2853, 2663, 1630, 1525, 1443, 1416, 1364, 1278, 1234, 1014, 979, 906, 883, 738, 589 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{11}H_8N_2OH$ 185.0715, found 185.0715

2-(Pyridin-4-yl)-1*H*-benzo[*d*]imidazole 3y.[9h] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.20; pale yellow solid; 80 mg, yield 41%; mp 220-221 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 13.27 (br s, 1H), 8.76 (s, 2H), 8.10 (s, 2H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.30-7.25 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 150.5, 149.8, 148.8, 143.6, 137.1, 135.0, 123.6, 122.3, 120.3, 119.5, 111.8; FT-IR (KBr) 3418, 2925, 2255, 2128, 1646, 1609, 1433, 1384, 1317, 1234, 1048, 1025, 1001, 765 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{12}H_9N_3H$ 196.0875, found 196.0875.

2-Pentadecyl-1*H*-benzo[*d*]imidazole 3z. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.35; white solid; 115 mg, yield 35%; mp 91-92 °C;^{1}H NMR (600 MHz, DMSO-d_6) δ 12.14 (br s, 1H), 7.44 (s, 2H), 7.09 (s, 2H), 2.77 (s, 2H), 1.74 (s, 2H), 1.22 (s, 24H) 0.84 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 31.3, 29.0, 28.9, 28.73, 28.7, 28.5, 27.6, 22.1, 14.0; FT-IR (KBr) 3435, 3089, 2954, 2920, 2849, 2101, 1625, 1541, 1470, 1458, 1206, 1155, 753, 744 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{22}H_{36}N_2H$ 329.2956, found 329.2936.

2-Pentyl-1*H*-benzo[*d*]imidazole 3aa.[18d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane; R_f = 0.35; brown solid; 86 mg, yield 46%; mp 140-141 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.16 (br s, 1H), 7.44 (s, 2H), 7.10-7.09 (m, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 1.77-1.74 (m, 2H), 1.32-1.30 (m, 4H), 0.87-0.84 (m, 3H); ^{13}C {^{1}H} NMR (150 MHz, DMSO-d_6) δ 155.3, 121.1, 30.9, 28.5, 27.3, 21.9, 13.9;

FT-IR (KBr) 3390, 3050, 2951, 2924, 2852, 2773, 2257, 2128, 1647, 1537, 1447, 1418, 1233, 1024, 998, 766 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{12}H_{16}N_2H$ 189.1392, found 189.1394.

2-Propyl-1*H*-benzo[*d*]imidazole 3ab.[18a] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.35; brown solid; 88 mg, yield 55%; mp 230-231 °C; ^1H NMR (600 MHz, DMSO-d_6) δ 12.15 (br s, 1H), 7.45 (s, 2H), 7.10 (s, 2H), 2.78 (t, J = 7.2 Hz, 2H), 1.80-1.76 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 155.0, 121.1, 30.5, 21.0, 13.7; FT-IR (KBr) 3434, 2257, 2129, 1646, 1047, 1025, 996, 827, 766, 688 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{10}H_{12}N_2H$ 161.1079, found 161.1078.

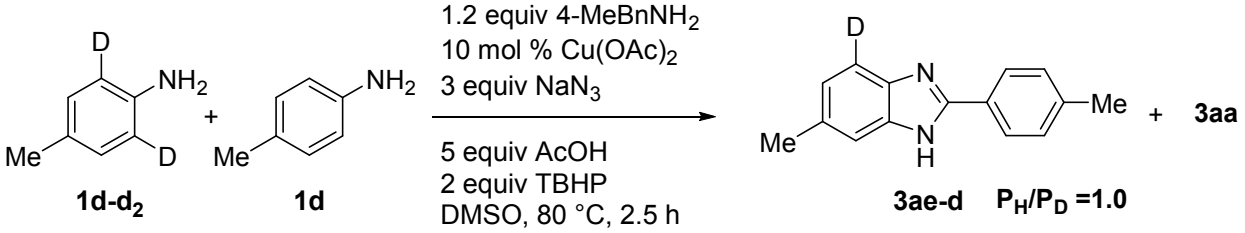
2-Benzyl-1*H*-benzo[*d*]imidazole 3ac.[9c] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; white solid; 100 mg, yield 48%; mp 221-222 °C; ^1H NMR (600 MHz, DMSO-d_6) δ 12.29 (br s, 1H), 7.46 (s, 2H), 7.34-7.30 (m, 4H), 7.24-7.21 (m, 1H), 7.13-7.10 (m, 2H), 4.16 (s, 2H); ^{13}C {^1H} NMR (150 MHz, DMSO-d_6) δ 153.3, 137.4, 128.5, 128.2, 126.3, 121.1, 34.7; FT-IR (KBr) 3436, 3049, 2923, 2683, 1623, 1536, 1493, 1456, 1426, 1270, 1222, 1147, 1024, 748, 722 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{14}H_{12}N_2H$ 209.1078, found 209.1071.

2-(4-Bromophenyl)-1*H*-benzo[*d*]imidazole 3ad.[2d] Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; pale yellow solid; 95 mg, yield 35%; mp 260-261 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 13.00 (br s, 1H), 8.13-8.08 (m, 2H), 7.78 (d, *J* = 7.2 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.23-7.19 (m, 2H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 150.0, 143.5, 134.8, 131.8, 129.2, 128.1, 123.0, 122.6, 121.6, 118.7, 111.2; FT-IR (KBr) 3435, 3056, 2120, 1619, 1584, 1485, 1423, 1297, 1270, 1221, 1197, 1064, 1005, 960, 820, 742 cm^{-1}. HRMS (ESI) m/z: [M+H] calcd for $C_{13}H_9BrN_2H$ 273.0027, found 273.0028.

Kinetic Isotope Study

To a stirred solution of *p*-toluidine **1d** (0.18 mmol, 20 mg), *p*-toluidine **1d-d_2**[12b] (0.32 mmol, 35 mg), $Cu(OAc)_2$ (10 mol %, 0.05 mmol, 9 mg), NaN_3 (3 equiv, 1.5 mmol, 97 mg), AcOH (5 equiv, 2.5 mmol,

150 mg) and TBHP (2 equiv, 1 mmol, 90 μL) in DMSO (0.5 mL) was added 4-MeBnNH$_2$ **2j** (1.2 equiv, 0.6 mmol, 73 mg), and the resultant mixture was stirred at 80 ^{o}C (Scheme 8). After 2.5 h, the reaction mixture was cooled to room temperature and treated with saturated $NaHCO_3$ (3 mL). The mixture was then extracted with ethyl acetate (3 x 5 mL) and washed with brine (2 x 3 mL) and water (1 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as an eluent to afford a mixture of **3ae-d** and **3ae** as a white solid in 19% (21 mg) yield. The ratio of deuterium to hydrogen was determined by the ^{1}H NMR relative integration values of H_a (7.95 ppm) based on H_b (7.51 ppm).



1d-d$_2$ **1d** **3ae-d** **P_H/P_D =1.0**

Scheme 8

ASSOCIATED CONTENT

AUTHOR INFORMATION

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SUPPORTING INFORMATION

ESI-MS spectrum of the reaction mixture of **1a** and **2a**, variable temperature NMR spectra of **3d** and NMR spectra (^{1}H and ^{13}C) of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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