Catalyst-Free Synthesis of 2,4-Disubstituted-1H-imidazoles through [3 + 2] Cyclization of Vinyl Azides with Amidines

N. Naresh Kumar Reddy, Sadu Nageswara Rao, Chitrakar Ravi, and Subbarayappa Adimurthy*

Academy of Scientific & Innovative Research, CSIR-Central Salt & Marine Chemicals Research Institute, G.B. Marg, Bhavnagar 364002, Gujarat, India

Supporting Information

ABSTRACT: A facile and efficient route for the synthesis of 2,4-disubstituted imidazoles from benzimidamides and vinyl azides through [3 + 2] cyclization under catalyst-free conditions has been described. The method is compatible for a broad range of functional groups with good to excellent yields.

INTRODUCTION

Imidazoles are the most valuable five-membered heterocyclic compounds found in many natural products, biological systems, pharmaceuticals, and agro chemicals.1,2 Additionally, imidazole derivatives have been reported to possess pharmacological properties such as antiplasmodial,3 antitumor,4 and antifungal.5 Consequently, many efforts have been made in the past decade on the synthesis of those privileged scaffolds. The reported methods include reaction of amidines with halo (nitro)alkenes,6 haloketones,7 alkyne/haloalkynes,8 and other methods.9 Although these methods are elegant and appear to be developed specifically for obtaining multisubstituted imidazole derivatives, in organic synthesis, the site-selective synthesis of the desired products is still an attractive and challenging task. Our intention is to develop a method for selective synthesis of 2,4-disubstituted imidazoles using easily available starting reagents under mild reaction conditions. Hence, the synthesis of imidazoles with free N–H and C-5 position for further (N1 and C-5) functionalization of such scaffolds is of continued interest.

RESULTS AND DISCUSSION

Despite these advances, to our knowledge, the oxidative cyclization of vinyl azides with benzamidines has remained elusive in literatures. In continuation of our studies on the synthesis of fused N-heterocycles,10 we report herein a facile method for the synthesis of 2,4-disubstituted imidazoles with 1,8-diazabicyclo(5,4,0)undec-7-ene (DBU) promoted by the oxidative cyclization of vinyl azides with benzamidines under mild conditions (Scheme 1).

Table 1. Optimization of Conditions for 3a

| entry | catalyst (mol %) | base (1.5 equiv) | temp (°C) | solvent | yield (%) |
|-------|-----------------|-----------------|-----------|---------|-----------|
| 1     | 1  (10)         | K2CO3           | 65        | CH3CN   | traces    |
| 2     | 1  (20)         | CH3CN           | 65        | 2a       | 23        |
| 3     | 1  (20)         | K2CO3           | 65        | CH3CN   | 22        |
| 4     | 1  (20)         | K2CO3           | 80        | CH3CN   | 55        |
| 5     | 1  (20)         | K2CO3           | 80        | DCE     | 49        |
| 6     | 1  (20)         | K2CO3           | 80        | DMF     | 67        |
| 7     | 1  (20)         | K2CO3           | 80        | DMSO    | 55        |
| 8     | 1  (20)         | K2CO3           | 80        | toluene | 45        |
| 9     | 1  (20)         | Na2CO3          | 80        | CH3CN   | 51        |
| 10    | 1  (20)         | Cs2CO3          | 80        | CH3CN   | 42        |
| 11    | 1  (20)         | tBuOK           | 80        | CH3CN   | 61        |
| 12    | 1  (20)         | Et3N            | 80        | CH3CN   | 44        |
| 13    | 1  (20)         | DBU             | 80        | CH3CN   | 89        |
| 14    | 1  (20)         | DBN             | 80        | CH3CN   | 73        |
| 15    | 1  (20)         | DABCO           | 80        | CH3CN   | 69        |
| 16    | 1  (20)         | DBU             | 80        | DMSO    | 72        |
| 17    | 1  (20)         | DBU             | 80        | NMP     | 65        |
| 18    | 1  (20)         | DBU             | 80        | H2O     | 45        |
| 19    | 1  (20)         | DBU             | 80        | CH3CN   | nr        |
| 20    | 1  (20)         | DBU             | 80        | CH3CN   | nr        |

We began our study by taking benzimidamide hydrochloride (1a) and (1-azidovinyl) benzene (2a) as the model substrates. The results are summarized in Table 1. Initially, the reaction of
1a and 2a was performed using 10 mol% of iodine as catalyst in acetonitrile at room temperature for 8 h; the desired product (3a) formation was not observed (Table 1, entry 1). When the reaction was carried out at 65 °C, with 20 mol% of catalyst, trace amount of 3a was observed (Table 1, entry 2). Under the same conditions, when K2CO3 was used as a base, 23% yields of...
the desired product 3a was isolated (Table 1, entry 3). A similar yield was observed without the iodine source (Table 1, entry 4). In view of this reaction, we turned our attention to vary the reaction temperature (to 80 °C) and other common solvents such as 1,2-dichloroethane (DCE), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and toluene; consequently, the yield varied between 45 and 67% (Table 1, entries 5–9). Further, we screened various inorganic and organic bases (Na₂CO₃, Cs₂CO₃, tBuOK, Et₃N, DBU, DBN, and DABCO) in acetonitrile as the solvent (Table 1, entries 10–16) [DBN: 1,5-diazabicyclo[4,3,0]non-5-ene; DABCO: 1,4-diazabicyclo[2.2.2]octane]. Interestingly, with DBU as the base, 89% yield of the desired product was obtained (entry 14). No further improvement in the yield was observed while performing the reaction with other solvents such as DMSO, N-methyl-2-pyrrolidone (NMP), and water with DBU as the base (Table 1, entries 17–19). The reaction without DBU in acetonitrile as the solvent, no product formation was observed (entry 20). After screening for various parameters, the optimum conditions identified for the present transformation are as follows: 1.5 equiv of 1a, 1.0 equiv of 2a, and 1.5 equiv of DBU as the base in acetonitrile at 80 °C (Table 1, entry 14).

Under the optimized reaction conditions, the scope and generality of the reaction were investigated and the results are summarized in Scheme 2. Initially, we performed the reaction of benzimidamide hydrochloride (1a) with various vinyl azides 2 and the reactions were found to be very facile with both electron-rich and electron-deficient groups (−Me, −OMe, −Bu, −Br, and −F) at the para position of vinyl azides and the desired products 3b−f were obtained in good to excellent yields (80−94%). One of the product 3f was also confirmed by the single-crystal X-ray diffraction analysis (CCDC No. 1556865). The presence of −NO₂, −Me, or −OMe group at either the ortho or meta position of vinyl azides produced the corresponding products 3g−j in moderate to good yields (67−79%).

To expand the scope of the present transformation, we explored the reactivity of the substituted benzamidines substrate with various vinyl azides, and the results are compiled in Scheme 3. The electron-donating and electron-withdrawing (−Me, −Br, −Cl, and −NO₂) substituents at the para position of benzamide reacted smoothly with (1-azidovinyl) benzene and produced the corresponding products 3a−d in good yields (66−87%). Interestingly, the presence of strong electron-donating benzamidines such as 4-aminobenzimidamide hydrochloride and 4-hydroxybenzimidamide hydrochloride reacted with 2a and gave the products 5e and 5f in 70 and 33% yields, respectively. Interestingly, the procedure is amenable to nicotinimidamide hydrochloride and cyclopropane carboximidamide and affords the differently decorated products 5g and 5h in 60 and 72% yield, respectively. Additionally, we evaluated the substrate scope of various benzamidines as well as vinyl azides (having both electron-rich and electron-deficient groups in both the rings at either position ortho/meta/para), which afforded the desired products 5i−r in good yields (63−92%). The presence of electron-releasing groups (5n), electron-withdrawing groups (5o and 5p), or halogens (5l and 5o) on both the rings provided good yields of products. The results from Schemes 2 and 3 demonstrate the versatility of the reactions with a high degree of functional group tolerance and with a broad substrate scope. It may be noted that halide-substituted derivatives were well tolerated and could be further applied in traditional cross-coupling reactions. Unfortunately, the present transformation is not suitable for aliphatic benzamidamides with vinyl azide.

To validate the process for scale-up studies (gram scale), we performed the reaction of 1a with 1-(1-azidovinyl)-4-bromobenzene under optimized conditions and obtained the corresponding product 3f in 72% yield (2.15 g) (Scheme 4). This study indicates the feasibility of the method for industrial/commercial production.

### Scheme 4. Gram Scale Preparation

| 1a | 2a | DBU (2.28 g) | CH₂CN (20 mL) | 3f |
|----|----|-------------|---------------|----|
| 15 mmol | 10 mmol | 2.34 g | 2.24 g | 2.15 g |
| 72% Yield |

To gain further insight into the reaction mechanism, some control experiments were performed (Scheme 5). The reaction of N-phenylbenzimidamide 6a was subjected with 2a under standard conditions, expect product 7a was not observed (Scheme 5, eq 1). This reaction suggests that the free NH₂ group (of amidine) is essential for such a transformation. Further, the reaction of 1a with 1-(bromovinyl) benzene (8) was conducted under optimized conditions; no reaction was observed, but 91% of 8 was recovered (Scheme 5, eq 2). It indicates that the direct removal of azide was not possible; the reaction may proceed via nitrene intermediate from vinyl azide (Scheme 5, eq 3). To ascertain whether the reaction proceeds by radical pathway or not, the reaction of 1a and 2a was checked with 2,2,6,6-tetramethylpiperidine-1-oxyl radical under optimized conditions, 86% of 3a was isolated. This rule outs the radical reaction route. Finally, benzimidamide 9 subjected with 2a in CH₃CN without DBU, 91% of the desired product 3a was obtained (Scheme 5, eq 4). This reaction and eq 1 (Scheme 5) together clarify the necessity of NH₂ (amidine) in the present transformation. Hence, the role of DBU is to neutralize the hydrochloride of 1a (benzimidamide hydrochloride).

On the basis of the control experiments and literature reports, a plausible reaction mechanism has been proposed (Scheme 6). Initially, benzimidamide hydrochloride (1a) neutralization by base (DBU) gives benzimidamide 9. The
nucleophilic addition of 9 with (1-azidovinyl) benzene (2a) gives the intermediate I by the loss of N₂. The intermediate I undergoes cyclization (intermediate II) and the subsequent elimination of ammonia affords the desired product 3a.

**CONCLUSIONS**

In conclusion, we have demonstrated a new simple method for the synthesis of 2,4-disubstituted imidazole derivatives through [3 + 2] cyclization of benzamidines with vinyl azides. This methodology is applicable for the selective synthesis of 2,4-disubstituted imidazoles in good to excellent yields, with a high degree of functional group tolerance.

**EXPERIMENTAL SECTION**

**General Information.** All of the commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ¹H and ¹³C NMR spectra were recorded at 500, 600 and 125, 150 MHz, respectively. The spectra were recorded in CDCl₃ and DMSO-d₆, as well as CD₃OD as a solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), and so on. Coupling constant (J) was given in Hz. Chemical shifts are reported in δ (ppm) relative to tetramethylsilane as an internal standard. The peaks around δ values of 7.26 (¹H NMR) and 77.0 (¹³C NMR) correspond to CD₃OD. Progress of the reactions was monitored by thin-layer chromatography (TLC).

**Silica gel 100−200 mesh size was used for column chromatography using a hexane/ethyl acetate eluent unless otherwise indicated.**

**General Procedure for 3a.** Benzimidamide hydrochloride 1a (47 mg, 0.3 mmol), (1-azidovinyl) benzene 2a (29 mg, 0.2 mmol), and DBU (45.6 mg, 0.3 mmol) were taken in a 10 mL reaction tube; to the mixture, 2.0 mL of acetonitrile was added. The reaction tube was placed in a preheated oil bath at 80 °C for 8 h (progress of the reaction was monitored by TLC). Then, the reaction mixture was allowed to room temperature; 10.0 mL of brine solution was extracted with ethyl acetate (3 × 15 mL) and dried with anhydrous Na₂SO₄. After the removal of solvent, the crude mixture was subjected to column chromatography on silica gel and 89% yield of the product 2,4-disubstituted imidazole (39.2 mg) 3a was isolated. (All of the vinyl azides employed in the present work were prepared by known procedure.²⁵)

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**Characterization Data. 2,4-Diphenyl-1H-imidazole (3a).**

(Eluent: 10% EtOAc/hexane); 89% yield (39.2 mg); white solid; ¹H NMR (500 MHz, CDCl₃) δ 7.87 (d, J = 7.5 Hz, 2H), 7.75 (d, J = 7.0 Hz, 2H), 7.42−7.33 (m, 6H), 7.26 (t, J = 4.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 147.0, 130.0, 128.8, 128.7, 127.0, 125.2, 124.9. HRMS calcd for C₁₅H₁₄N₂: 221.1079. Found: 221.1080.

**2-Phenyl-4-(p-tolyl)-1H-imidazole (3b).**

(Eluent: 10% EtOAc/hexane); 91% yield (42.8 mg); light yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 7.87 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 7.0 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.0 Hz, 2H), 7.20 (d, J = 8.0, 2H), 2.36 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 146.8, 130.1, 129.4, 128.8, 128.7, 125.2, 124.8, 21.2. HRMS calcd for C₁₉H₂₀N₂O: 235.1235. Found: 235.1236.

**4-(4-(tert-Butyl)phenyl)-2-phenyl-1H-imidazole (3c).**

(Eluent: 10% EtOAc/hexane); 94% yield (47.1 mg); light yellow solid; ¹H NMR (600 MHz, CD₃OD) δ 7.90 (d, J = 6.5 Hz, 2H), 7.66 (d, J = 7.0 Hz, 2H), 7.43 (t, J = 6.0 Hz, 2H), 7.36 (t, J = 6.0 Hz, 1H), 7.32 (s, 1H), 6.94 (d, J = 7.5 Hz, 2H), 3.28 (s, 3H). ¹³C NMR (150 MHz, CD₃OD) δ 159.1, 147.0, 130.0, 128.5, 128.4, 126.1, 125.3, 113.8, 54.4. HRMS calcd for C₁₉H₂₁N₂O: 251.1184. Found: 251.1180.

**4-(4-(tert-Butyl)phenyl)-2-phenyl-1H-imidazole (3d).**

(Eluent: 10% EtOAc/hexane); 89% yield (49.3 mg); white solid; melting point 204 °C. ¹H NMR (600 MHz, CD₃OD) δ 7.91 (d, J = 6.0 Hz, 2H), 7.67 (d, J = 6.5 Hz, 2H), 7.45 (d, J = 6.5 Hz, 1H), 7.24 (d, J = 3.5, 2H), 7.40 (s, 1H), 7.39 (s, 1H), 7.36 (t, J = 6.5, 1H), 1.39 (s, 9H). ¹³C NMR (150 MHz, CD₃OD) δ 149.8, 147.3, 130.1, 128.5, 128.4, 125.3, 125.2, 124.5, 34.0, 30.4. HRMS calcd for C₂₃H₂₃N₂O: 329.1524. Found: 299.1510.

**4-(4-(Fluorophenyl)-2-phenyl-1H-imidazole (3e).**

(Eluent: 10% EtOAc/hexane); 81% yield (38.6 mg); white solid; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (d, J = 8.0 Hz, 2H), 7.75 (s, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.0 Hz, 1H), 7.33 (s, 1H), 7.26 (s, 2H), 7.09 (t, J = 8.5, 2H). ¹³C NMR (125 MHz, CDCl₃) δ 147.0, 129.9, 128.9, 126.6, 126.5, 125.2, 115.6, 115.4. HRMS calcd for C₁₅H₁₃F₄N₂: 261.0804. Found: 261.0794.
4-(4-Bromophenyl)-2-phenyl-1H-imidazole (3f).

(Eluent: 10% EtOAc/hexane); 80% yield (47.9 mg); yellow solid; ¹H NMR (600 MHz, CD3OD) δ 7.90 (d, J = 6.5 Hz, 2H), 7.67 (d, J = 7.0 Hz, 2H), 7.50 (s, 1H), 7.48 (d, J = 2.5 Hz, 2H), 7.44 (t, J = 6.0 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H). ¹³C NMR (150 MHz, CD3OD) δ 147.4, 130.8, 129.5, 129.2, 129.0, 125.3, 121.4, 119.6. HRMS calcd for C16H15N2Br: 299.0184. Found: 299.0186.

2-Phenyl-4-(p-tolyl)-1H-imidazole (3g).

(Eluent: 10% EtOAc/hexane); 72% yield (33.8 mg); yellow solid; ¹H NMR (500 MHz, CDCl3) δ 7.89 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.0, 1H), 7.26 (q, J = 6.0 Hz, 5H), 2.50 (s, 3H). ¹³C NMR (125 MHz, CDCl3) δ 140.0, 135.4, 130.8, 128.8, 128.7, 128.3, 127.4, 126.0, 125.2, 29.7. HRMS calcd for C16H16N2: 235.1235. Found: 235.1237.

4-(2-Methoxyphenyl)-2-phenyl-1H-imidazole (3h).

(Eluent: 10% EtOAc/hexane); 67% yield (33.5 mg); light yellow solid; ¹H NMR (500 MHz, CDCl3) δ 7.88 (d, J = 7.5 Hz, 2H), 7.58 (s, 1H), 7.45 (t, J = 7.5, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.26 (q, J = 7.5, 2H), 7.06 (m, 2H), 4.02 (s, 3H). ¹³C NMR (125 MHz, CDCl3) δ 147.1, 138.8, 128.4, 126.8, 124.7. HRMS calcd for C15H12N2Cl: 255.0689. Found: 255.0694.

4-(3-Nitrophenyl)-2-phenyl-1H-imidazole (3j).

(Eluent: 10% EtOAc/hexane); 85% yield (50.7 mg); yellow solid; melting point 198 °C. ¹H NMR (500 MHz, CDCl3) δ 7.72 (t, J = 8.0 Hz, 4H), 7.52 (d, J = 8.0 Hz, 2H), 7.40 (q, J = 7.5 Hz, 3H), 7.28 (t, J = 7.5 Hz, 1H). ¹³C NMR (125 MHz, CDCl3) δ 146.0, 132.0, 128.9, 128.7, 127.2, 124.9, 128.8. HRMS calcd for C15H12N2O: 235.1235. Found: 235.1237.

2-(4-Chlorophenyl)-4-phenyl-1H-imidazole (5c).

(Eluent: 10% EtOAc/hexane); 81% yield (41.3 mg); white solid; ¹H NMR (600 MHz, CD3OD) δ 7.88 (d, J = 6.5, Hz, 2H), 7.73 (d, J = 6.5 Hz, 2H), 7.44 (d, J = 6.0 Hz, 3H), 7.37 (t, J = 6.5 Hz, 2H), 7.23 (t, J = 6.0 Hz, 1H). ¹³C NMR (150 MHz, CD3OD) δ 145.9, 134.6, 131.2, 129.1, 128.7, 128.6, 128.5, 126.4, 124.9. HRMS calcd for C₁₅H₁₂N₂Cl: 255.0689. Found: 255.0694.

4-(4-Chlorophenyl)-4-phenyl-1H-imidazol-2-yl)aniline (5e).

(Eluent: 20% EtOAc/hexane); 69% yield (36.6 mg); brick red color solid; ¹H NMR (500 MHz, CD3OD) δ 8.29 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 7.5 Hz, 2H), 7.47 (s, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.0, 1H). ¹³C NMR (150 MHz, CD3OD) δ 146.3, 134.2, 128.4, 128.7, 128.4, 126.8, 124.7. HRMS calcd for C₁₅H₁₂N₂O: 266.0930 Found: 266.0928.

(Eluent: 75% EtOAc/hexane); 70% yield (33.1 mg); gray color solid; melting point 199 °C. ¹H NMR (600 MHz, CDCl3) δ 7.60 (d, J = 6.5 Hz, 2H), 7.49 (d, J = 6.0 Hz, 2H), 7.33 (d, J = 6.0, 2H), 7.26 (s, 1H), 6.97 (s, 1H), 6.42 (d, J = 6.0 Hz, 2H). ¹³C NMR (150 MHz, CDCl3) δ 150.8, 148.4, 146.4, 127.6.
1H), 7.16 (s, 1H), 1.99 (s, 1H), 8.31 (d, J = 7.0 Hz, 1H), 7.70 (t, J = 7.5 Hz, 2H), 8.24 (s, 1H), 8.10 (d, J = 7.0 Hz, 1H). 13C NMR (150 MHz, CDCl3) δ 148.8, 147.2, 144.9, 144.8, 140.6, 136.4, 131.2, 130.7, 126.3, 124.9, 121.6, 119.0, 118.6. HRMS calcd for C19H16N2O3: 324.0835. Found: 324.0836.

4-(4-Bromophenyl)-2-(p-toly1)-1H-imidazole (5k).

(Eluent: 10% EtOAc/hexane); 92% yield (57.7 mg); light yellow solid; melting point 210 °C. 1H NMR (600 MHz, CD3OD) δ 7.79 (d, J = 6.5 Hz, 2H), 7.67 (d, J = 7.5 Hz, 2H), 7.51 (d, J = 6.5, 2H), 7.47 (s, 1H), 7.27 (d, J = 6.5, 2H), 2.36 (s, 3H). 13C NMR (150 MHz, CD3OD) δ 149.2, 140.1, 132.6, 130.4, 128.4, 127.6, 126.6, 121.2, 21.2. HRMS calcd for C19H16N2Br: 332.9794. Found: 332.9796.

4-(4-Chlorophenyl)-2-(p-toly1)-1H-imidazole (5l).

(Eluent: 10% EtOAc/hexane); 29% yield (29.4 mg); white solid; melting point 164 °C. 1H NMR (600 MHz, CDCl3) δ 11.90 (s, 1H), 7.73 (s, 1H), 7.65 (d, J = 5.0 Hz, 1H), 7.54 (s, 1H), 7.33 (t, J = 6.5 Hz, 1H), 7.18 (d, J = 6.0 Hz, 1H), 1.97–1.93 (m, 1H), 0.92–0.90 (m, 2H), 0.89–0.85 (m, 2H). 13C NMR (150 MHz, CDCl3) δ 130.7, 125.8, 124.0, 123.0, 113.4, 9.6, 7.5. HRMS calcd for C19H16N2Cl: 219.0689. Found: 219.0690.

2-Cyclopropyl-4-phenyl-1H-imidazole (5h).

(Eluent: 30% EtOAc/hexane); 72% yield (26.5 mg); white solid; melting point 164 °C. 1H NMR (600 MHz, CDCl3) δ 7.64 (broad peak, 2H), 7.35 (t, J = 6.5, 2H), 7.21 (t, J = 6.5, 1H), 7.16 (s, 1H), 1.99–1.94 (m, 1H), 1.02–0.95 (m, 4H). 13C NMR (150 MHz, CDCl3) δ 128.7, 126.7, 124.7, 9.24, 7.44. HRMS calcd for C13H14N2: 211.0791. Found: 211.0777.

4-(4-Fluorophenyl)-2-(p-toly1)-1H-imidazole (5i).

(Eluent: 10% EtOAc/hexane); 87% yield (43.8 mg); white solid; melting point 180 °C. 1H NMR (600 MHz, CDCl3) δ 7.75 (t, J = 7.0 Hz, 4H), 7.27 (d, J = 8.5 Hz, 1H), 7.22 (d, J = 6.5, 2H), 7.06 (t, J = 7.0 Hz, 2H), 2.37 (s, 3H). 13C NMR (150 MHz, CDCl3) δ 162.8 (d, J = 203.6), 138.9, 129.5, 127.2, 126.60 (d, J = 6.37 Hz), 125.1, 115.6 (d, J = 17.7 Hz), 21.3. HRMS calcd for C13H12NF: 253.1153. Found: 253.1153.

4-(4-Fluorophenyl)-2-(4-nitrophenyl)-1H-imidazole (5j).

(Eluent: 20% EtOAc/hexane); 72% yield (41.0 mg); brick red solid; melting point 216 °C. 1H NMR (600 MHz, DMSO-d6) δ 13.34 (s, 1H), 8.70 (s, 1H), 8.37 (d, J = 7.0 Hz, 2H), 8.34 (d, J = 6.5, 1H), 8.28 (d, J = 7.5 Hz, 2H), 8.24 (s, 1H), 8.10 (d, J = 7.0 Hz, 1H), 7.70 (t, J = 7.0 Hz, 1H). 13C NMR (150 MHz, DMSO-d6) δ 148.8, 147.2, 144.9, 144.8, 140.6, 136.4, 131.2, 130.7, 126.3, 124.9, 121.6, 119.0, 118.6. HRMS calcd for C19H14N2O3F: 324.0835. Found: 284.0836.

4-(4-Bromophenyl)-2-(4-chlorophenyl)-1H-imidazole (5l).

(Eluent: 10% EtOAc/hexane); 52% yield (52.4 mg); light yellow solid; melting point 200 °C. 1H NMR (600 MHz, CD3OD) δ 7.78 (d, J = 6.5 Hz, 2H), 7.64 (d, J = 6.5 Hz, 2H), 7.51 (d, J = 6.5, 2H), 7.38 (d, J = 7.0 Hz, 2H), 7.34 (s, 1H), 7.25 (s, 1H). 13C NMR (150 MHz, CD3OD) δ 146.1, 134.8, 131.7, 129.1, 128.2, 126.5, 120.8. HRMS calcd for C19H16N2ClBr: 332.9794. Found: 332.9796.

4-(4-Chlorophenyl)-2-(4-nitrophenyl)-1H-imidazole (5m).

(Eluent: 10% EtOAc/hexane); 67% yield (29.4 mg); white solid; melting point 164 °C. 1H NMR (600 MHz, CDCl3) δ 12.16 (s, 1H), 7.76 (s, 2H), 7.72 (s, 2H), 7.53 (s, 1H), 7.43 (s, 2H), 6.67 (t, J = 2.5 Hz, 2H), 5.39 (s, 2H), 1.36 (s, 9H). 13C NMR (150 MHz, DMSO-d6) δ 149.4, 126.7, 125.6, 124.6, 114.1, 31.7. HRMS calcd for C19H16N2F: 292.1814. Found: 292.1815.

2, 4-Bis(4-bromophenyl)-1H-imidazole (5o).

(Eluent: 10% EtOAc/hexane); 85% yield (64.2 mg); yellow color solid; melting point 194 °C. 1H NMR (600 MHz, CDCl3) δ 7.85 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 6.5, 2H), 7.64 (d, J = 9.5, 2H), 7.58 (d, J = 8.5 Hz, 2H), 7.39 (s, 1H). 13C NMR (150 MHz, DMSO-d6) δ 148.8, 147.2, 144.9, 144.8, 140.6, 136.4, 131.2, 130.7, 126.3, 124.9, 121.6, 119.0, 118.6. HRMS calcd for C35H16N2O2Br2: 626.0350. Found: 626.0351.
NMR (150 MHz, CDCl₃) δ 146.0, 132.1, 137.7, 128.7, 126.7, 126.5, 123.0, 120.8. HRMS calcd for C₁₆H₁₄N₂Br: 269.0846. Found: 269.0843.

2-(4-Bromophenyl)-4-(2-methoxyphenyl)-1H-imidazole (5q).

(Eluent: 10% EtOAc/hexane); 63% yield (41.4 mg); yellow solid; melting point 198 °C. ¹H NMR (600 MHz, CD₃OD) δ 7.87 (d, J = 6.0 Hz, 2H), 7.06 (d, J = 7.0, 2H), 7.00 (t, J = 6.0 Hz, 1H), 3.92 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 152.8, 143.8, 131.1, 128.3, 125.4, 121.5, 55.0. HRMS calcd for C₁₅H₁₁N₄Br: 376.9289. Found: 376.9285.

2-(4-Chlorophenyl)-4-(o-tolyl)-1H-imidazole (5r).

(Eluent: 85% EtOAc/hexane); 69% yield (43.1 mg); brick red color solid; ¹H NMR (600 MHz, CD₃OD) δ 7.80 (d, J = 6.5, 3H), 8.02 (d, J = 6.5 Hz, 1H), 7.74 (s, 1H), 7.54 (t, J = 7.0 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 144.0, 132.1, 137.7, 128.7, 126.7, 125.7, 123.7, 121.0, 118.9. HRMS calcd for C₁₅H₁₁N₄O₄: 311.0780. Found: 311.0779.

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ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b00969.
Copies of NMR spectra for all of the compounds and HRMS spectra for all of the compounds (PDF)
Crystallographic data (CIF)

AUTHOR INFORMATION

Corresponding Author
*E-mail: adimurthy@csmcri.res.in.
ORCID

Subbarayappa Adimurthy: 0000-0001-5320-4961

Notes
The authors declare no competing financial interest.