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Iron(III)-catalyzed synthesis of multi-substituted imidazoles via [3+2] cycloaddition reaction of nitroolefins and *N*-aryl benzamidines

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ABSTRACT

A novel and efficient iron(III)-catalyzed synthesis of multi-substituted imidazoles via [3+2] cycloaddition of nitroolefins and *N*-aryl benzamidines under the air atmosphere had been developed. This methodology is convenient, atom-economical, general, and eco-friendly in good yields and prefect regioselectivities.

1. Introduction

Imidazoles and their derivatives, a type of important *N*-containing heteroaromatic compounds, were found in a large number of pharmacologically active compounds and natural products.[1] Among them, multi-substituted imidazoles are significant core structures used in medicinal chemistry due to their remarkable biological activities, such as antifungal, antiapoptotic, antibacterial, antiviral and anti-inflammatory activities.[2] In addition, they are also used as fluorescence, agricultural products, dyes and chemsensing.[3] Therefore, developing efficient methodologies for synthesis of multi-substituted imidazoles has attracted numerous attentions. Current methods for these syntheses focused mostly on the less-substituted imidazoles, which commonly proceeded via oxidative cyclization of 1,2-phenylenediamines with aldehydes.[4] Only a handful of methodologies are reported for the synthesis of multi-substituted imidazoles through reactions of 1,2-dike-tones/*a*-hydroxy-ketones, aldehydes, primary amines and ammonium acetates in one-pot.[5] However, many of these procedures are associated with one or more disadvantages such as use of strong bases or catalysts, use of toxic solvents, long reaction time and low yields. Therefore, an efficient and simple way to construct multi-substituted imidazoles is still necessary.

Recently, iron catalysts[6] have been identified as important and effective catalysts in various organic reactions because of their low price, easy availability, sustainability, non-toxicity and environmentally friendly characteristics. For example, Hajra[7] and co-workers described iron-catalyzed synthesis of imidazo[1,2-*a*] pyridines via cascade reaction between nitroolefins and 2-aminorpyridines. Our group has long term interest on developing methodologies to construct imidazole rings.[8] Earlier this year, we have reported a novel and efficient strategy for the synthesis of tri- or tetra-substituted imidazoles via copper-catalyzed [3+2] cycloaddition reaction.[9] However, the reactions required expensive ligands and an atmosphere of oxygen, thus, we are interested in investigating a direct synthesis of multi-substituted imidazoles in the absence of ligands under air. Herein, we report a novel and efficient iron(III)-catalyzed synthesis of multi-substituted imidazoles via [3+2] cycloaddition of nitroolefins and *N*-aryl benzamidines under air. To the best of our knowledge, there is been no report available on the synthesis of multi-substituted imidazoles using iron catalyst in the open literature so far. It showed several advantages comparing our previous method, such as an inexpensive and less toxic catalyst, ligand-free conditions, easy operation, environmental friendliness and no need of specific atmosphere.

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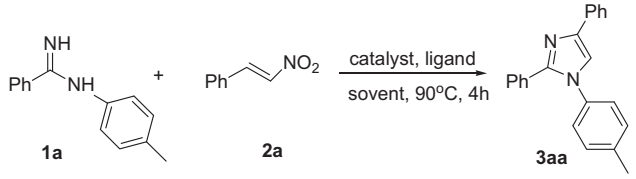
2. Results and discussion

We started from the reaction of *N*-*p*-tolylbenzamidine **1a** (0.2 mmol) and 1-(2-nitrovinyl)-benzene **2a** (0.2 mmol). As shown in Table 1, the reaction was carried out with **1a** (0.2 mmol) and **2a** (0.2 mmol) in the presence of $FeCl_3$ (20 mol %) and 1,10-phen (20 mol %) in DMSO at 90 °C under air for 4 h. The desired product **3aa** was obtained in 60% yield (Table 1, entry 1). This impelled us to investigate optimal conditions for the reaction in order to get better yields. In this preliminary experiment, the reactions were carried out with different ligands, such as 1,10-phen, bipy and L-proline, and the cyclization reaction did not give higher yields (Table 1, entries 1–3), but a good yield was obtained in the absence of ligand (Table 1, entry 4). Then, the cyclization reactions were conducted in different solvents, such as THF, toluene, DMF and 1,4-dioxane and we found that DMF gave the best result (Table 1, entries 5–8). Next, we investigated different loadings of $FeCl_3$, in the amount of 10 mol % and 30 mol % and obtained 65% and 78% yields, respectively (Table 1, entries 9 and 10). Other catalysts, such as $FeBr_3$, $AlCl_3$, $ZnCl_2$, $TiCl_4$, $Fe(OTf)_3$ and $Fe(acac)_3$, showed little effectiveness on promoting the reaction (Table 1, entries 11–13). Finally, we investigated the reaction at different temperatures and found the yield of **3aa** was also influenced by the reaction temperature (Table 1, entries 14 and 15). Moreover, the yield of **3aa** was little increased under oxygen. Thus, 20 mmol % $FeCl_3$ in DMF under air is chosen as the optimal conditions for this reaction.

Table 1
Optimization of the reaction condition[a]

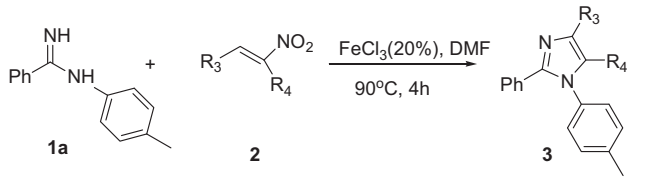


Entry	Catalyst	Ligand	Solvent	Yield[b] (%)
1	$FeCl_3$ (20%)	1,10-Phen	DMSO	60
2	$FeCl_3$ (20%)	Bipy	DMSO	61
3	$FeCl_3$ (20%)	L-Proline	DMSO	58
4	$FeCl_3$ (20%)	None	DMSO	77
5	$FeCl_3$ (20%)	None	THF	12
6	$FeCl_3$ (20%)	None	Toluene	23
7	$FeCl_3$ (20%)	None	DMF	82, 82[c]
8	$FeCl_3$ (20%)	None	Dioxane	44
9	$FeCl_3$ (10%)	None	DMF	65
10	$FeCl_3$ (30%)	None	DMF	78
11	$FeBr_3$ (20%)	None	DMF	53
12	$Fe(OTf)_3$ (20%)	None	DMF	47
13	$Fe(acac)_3$	None	DMF	55
14	$ZnCl_2$	None	DMF	Trace
15	$AlCl_3$	None	DMF	5
16	$TiCl_4$	None	DMF	Trace
17[d]	$FeCl_3$ (20%)	None	DMF	79
18[e]	$FeCl_3$ (20%)	None	DMF	67

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), catalyst (20% mmol), ligand (20%mmol), solvent (2 mL), 90 °C, 4 h.
[b] Isolated yield.
[c] The reaction was carried out under an O_2 atmosphere.
[d] The reaction was carried out at 70 °C.
[e] The reaction was carried out at 110 °C.

Under the optimized reaction conditions, we extended the study with different nitroolefins and *N*-*p*-tolylbenzamidine(**1a**) for the synthesis of various multi-substituted imidazoles. The results were shown in Table 2. Various nitroolefins provided the desired products in moderate to good yields. It was obvious that the nature of the substituent on the aromatic rings showed some influence on the yields of the products. Generally, the aromatic ring with electron-donating groups, such as methyl and methoxy group, gave lower yields than those with electron-withdrawing groups, such as fluoro, chloro and trifluoromethyl groups (Table 2, entries 1–8). The reactions of *N*-*p*-tolylbenzamidine(**1a**) with different 2-methylnitroolefins gave lower but still acceptable yields (Table 2, entries 9–13). Similarly, the electron-withdrawing substituted 2-methylnitroolefins produced better yields than the electron-donating substituted ones. In addition, the 2-substituted nitroolefins showed slightly lower yields than the 4-substituted ones (Table 2, entries 5 and 6) that was probably caused by steric effect.

Table 2
Reactions of *N*-*p*-tolylbenzamidine with various nitroolefins[a]

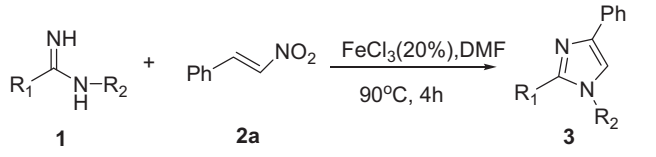


Entry	R_3	R_4	Product	Yield[b] (%)
1	H	H	**3aa**	82
2	4-CH_3	H	**3ab**	60
3	4-CH_3O	H	**3ac**	51
4	4-F	H	**3ad**	61
5	4-Cl	H	**3ae**	68
6	2-Cl	H	**3af**	55
7	4-CF_3	H	**3ag**	50
8	2,4-DiCH_3O	H	**3ah**	53
9	H	CH_3	**3ai**	47
10	4-CH_3O	CH_3	**3aj**	35
11	4-Br	CH_3	**3ak**	41
12	4-Cl	CH_3	**3al**	45
13	4-CN	CH_3	**3am**	56

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.2 mmol), $FeCl_3$(20 mmol %), DMF (2 mL), 90 °C, 4 h.
[b] Isolated yield.

The reactions of various benzamidines and 1-(2-nitrovinyl)-benzene **2a** also were investigated as shown in Table 3. A variety of *N*-aryl benzamidines were found to be partners and the desired products were formed in satisfactory to excellent yields. In general,

Table 3
Reactions of 1-(2-nitrovinyl)-benzene with various benzamidines[a]

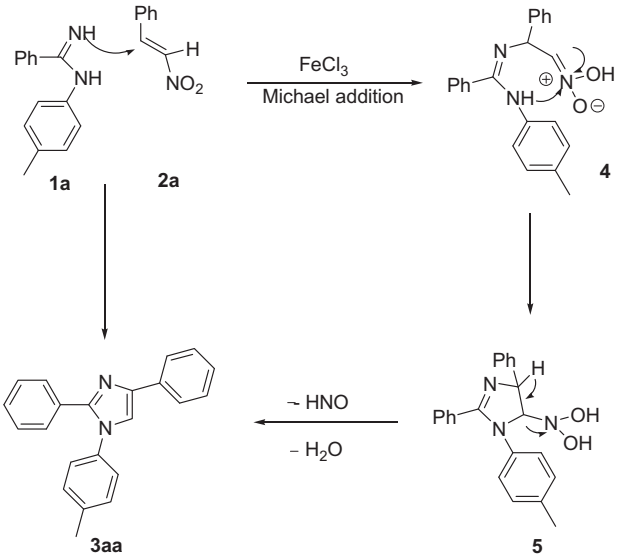


Entry	R_1	R_2	Product	Yield[b] (%)
1	C_6H_6	4-$CH_3C_6H_5$	**3aa**	82
2	4-$CH_3C_6H_5$	C_6H_6	**3ba**	81
3	C_6H_6	4-$CH_3OC_6H_5$	**3ca**	85
4	C_6H_6	3-$CH_3OC_6H_5$	**3da**	72
5	C_6H_6	2-$C_2H_5OC_6H_5$	**3ea**	71
6	4-$CH_3C_6H_5$	4-$CH_3C_6H_5$	**3fa**	81
7	4-$CH_3OC_6H_5$	4-$CH_3C_6H_5$	**3ga**	86
8	C_6H_6	4-ClC_6H_5	**3ha**	68
9	C_6H_6	3-ClC_6H_5	**3ia**	64
10	4-$CF_3C_6H_5$	C_6H_6	**3ja**	72
11	4-$NO_2C_6H_5$	C_6H_6	**3ka**	0
12	3-Pyridinyl	C_6H_6	**3la**	67
13	C_6H_6	C_2H_5	**3ma**	0
14	^{t}Bu	C_6H_6	**3na**	0

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.2 mmol), $FeCl_3$(20 mmol %), DMF (2 mL), 90 °C, 4 h.
[b] Isolated yield.

benzamidines with electron-donating substituents on R_1 and/or R_2 led to higher yields (Table 3, entries 1–6). On the contrary, electron-withdrawing substituted benzamidines gave lower yields (Table 3, entries 8–10), some even (such as nitro) did not proceed to the expected product (entry 11). Especially, when the benzamidine bearing two electron-donating groups was employed, the yield was enhanced to 86% (Table 3, entry 7). However, the substrates with alkyl groups (such as *N*-phenylpivalamidine and *N*-ethylbenzamidine) did not give the expected product (Table 3, entries 13 and 14). Moreover, the substrate with heterocycle group also gave the corresponding product **3la** in 67% yield (entry 12).

To probe the mechanism of the reaction, several control experiments were performed. The reaction was carried out with **1a** (0.2 mmol), **2a** (0.2 mmol), in the absence of $FeCl_3$ in DMF at 90 °C under the air for 4 h and no product was obtained. Compound **3aa** was obtained in 82% yield even if reaction of **1a** and **2a** was conducted under N_2 protection. Thus, we speculated the NO_2 group was the terminal oxidant in this process. Based on the above observations and the analogous mechanisms discussed in literature,[10] a plausible mechanism for this reaction was proposed as shown in Scheme 1. Firstly, the intermediate **4** was produced from Michael addition of *N*-*p*-tolylbenzamidine (**1a**) to 1-(2-nitrovinyl)-benzene (**2a**). With $FeCl_3$ serving as Lewis acid, the intermediate **5** was produced from the **4** via another intramolecular nucleophilic addition. Subsequently, the final product **3aa** was obtained from intermediate **5** after elimination of nitroxyl (HNO) and H_2O.



Scheme 1. A plausible reaction mechanism.

3. Conclusion

In conclusion, we have successfully developed an efficient and novel catalytic approach for synthesis of multi-substituted imidazoles via nitroolefins and *N*-aryl benzamidines. This reaction proceeds via stepwise [3+2] cycloaddition in the presence of an inexpensive iron catalyst under air. This methodology is convenient, atom-economical, and eco-friendly in good yields and prefect regioselectivities. This efficient strategy could significantly direct further research of multi-substituted imidazoles synthesis.

4. Experimental section

4.1. The general procedure of the reaction between nitroolefins and benzamidines

*4.1.1. Synthesis of **3aa** (2,4-diphenyl-1-p-tolyl-1H-imidazole).* All reactions were performed on a 0.20 mmol scale of benzamidine. The *N*-*p*-tolylbenzamidine **1a** (0.20 mmol), 1-(2-nitrovinyl)-benzene **2a** (0.2 mmol), $FeCl_3$ (0.040 mmol) and 2 mL DMF were taken into a round bottom flask equipped with stirrer. The resulting mixture was stirred for 4 h at 90 °C. After cooling to room temperature, to the reaction mixture was added water (2 mL), and extracted with acetic ether (3×10 mL). The combined organic phases were washed with brine (2×5 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash column chromatography with hexanes/EtOAc (20:1) as eluent to obtain the desired **3aa** as light yellow solid (90% yield). The remaining multi-substituted imidazoles were prepared in the similar manner and their characterization data are as follows: **3aa** was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as light yellow oil (yield: 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.87–7.90 (d, J=9 Hz, 2H), 7.39–7.48 (m, 5H), 7.10–7.36 (m, 8H). ^{13}C NMR (100 MHz, CDCl3): δ: 146.9, 141.4, 138.1, 135.9, 133.9, 130.3, 130.0, 128.5, 128.3, 128.1, 126.9, 125.5, 125.0, 118.1, 21.1. ESI HRMS: calcd for $C_{22}H_{18}N_2$ $[M+H]^+$: 311.1543, found: 311.1546.

*4.1.2. 2-Phenyl-1,4-di-p-tolyl-1H-imidazole (**3ab**).* 2-Phenyl-1,4-di-*p*-tolyl-1*H*-imidazole (**3ab**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow solid (yield: 60%), mp: 134–136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.76–7.79 (d, J=9 Hz, 2H), 7.44–7.47 (m, 2H), 7.26 (s, 1H), 7.09–7.25 (m, 9H), 2.37 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.7, 141.5, 138.0, 136.5, 135.9, 129.9, 129.2, 128.7, 128.2, 128.1, 125.5, 124.9, 118.1, 21.2, 21.0. ESI HRMS: calcd for $C_{23}H_{20}N_2$ $[M+H]^+$: 325.1699, found: 325.1695.

*4.1.3. 4-(4-Methoxyphenyl)-2-phenyl-1-p-tolyl-1H-imidazole (**3ac**).* 4-(4-Methoxyphenyl)-2-phenyl-1-*p*-tolyl-1H-imidazole (**3ac**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow solid (yield: 51%), mp: 146–148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.80–7.83 (d, J=9 Hz, 2H), 7.45–7.48 (dd, J=3, 6 Hz, 2H), 7.10–7.7.31 (m, 8H), 6.93–6.96 (d, J=9 Hz, 2H), 3.82 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 158.7, 146.6, 141.3, 138.0, 135.9, 130.4, 129.9, 128.7, 128.2, 128.1, 126.7, 126.2, 125.5, 117.6, 113.8, 55.2, 21.1. ESI HRMS: calcd for $C_{23}H_{20}N_2O$ $[M+H]^+$: 341.1649, found: 341.1652.

*4.1.4. 4-(4-Fluorophenyl)-2-phenyl-1-p-tolyl-1H-imidazole (**3ad**).* 4-(4-Fluorophenyl)-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3ad**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow oil (yield: 61%). ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.82–7.86 (m, 2H), 7.46–7.47 (m, 2H), 7.04–7.45 (m, 10H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 163.6, 160.3, 146.9, 140.6, 138.2, 135.8, 129.9, 128.6, 128.3, 128.1, 126.6, 126.5, 125.5, 118.2, 115.5, 115.2, 21.0. ESI HRMS: calcd for $C_{22}H_{17}N_2F[M+H]^+$: 329.1449, found: 329.1452.

*4.1.5. 4-(4-Chlorophenyl)-2-phenyl-1-p-tolyl-1H-imidazole (**3ae**).* 4-(4-Chlorophenyl)-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3ae**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow oil (yield: 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.80–7.83 (d, J=9 Hz, 2H), 7.09–7.47 (m, 12H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 147.0, 140.3, 138.2, 135.6, 132.4, 132.3, 130.1, 129.4, 128.9, 128.8, 128.3, 127.8, 126.2, 126.0, 125.6, 21.1. ESI HRMS: calcd for $C_{22}H_{17}N_2Cl$ $[M+H]^+$: 345.1153, found: 345.1157.

*4.1.6. 4-(2-Chlorophenyl)-2-phenyl-1-p-tolyl-1H-imidazole (**3af**).* 4-(2-Chlorophenyl)-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3af**)

was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow solid (yield: 55%), mp: 107–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 8.35–8.38 (d, *J*=9 Hz, 2H), 7.88 (s, 1H), 7.47–7.88 (m, 4H), 7.13–7.45 (m, 8H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.0, 138.2, 137.4, 135.8, 132.2, 130.7, 130.1, 130.09, 130.0, 129.7, 128.7, 128.4, 128.1, 127.5, 126.8, 125.6, 123.0, 21.1. ESI HRMS: calcd for $C_{22}H_{17}N_2Cl$ $[M+H]^+$: 345.1153, found: 345.1155.

*4.1.7. 2-Phenyl-1-p-tolyl-4-(4-(trifluoromethyl)phenyl)-1H-imidazole (**3ag**).* 2-Phenyl-1-*p*-tolyl-4-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (**3ag**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow oil (yield: 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.96–7.99 (d, *J*=9 Hz, 2H), 7.61–7.64 (d, *J*=9 Hz, 2H), 7.45–7.47 (dd, *J*=3, *J*=6, 3H), 7.10–7.43 (m, 7H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 147.4, 140.1, 138.5, 137.4, 135.6, 130.1, 128.7, 128.6, 128.2, 125.5, 124.9, 119.7, 21.1. ESI HRMS: calcd for $C_{23}H_{17}N_2F_3$ $[M+H]^+$: 379.1417, found: 379.1413.

*4.1.8. 4-(2,4-Dimethoxyphenyl)-2-phenyl-1-p-tolyl-1H-imidazole (**3ah**).* 4-(2,4-Dimethoxyphenyl)-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3ah**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 53%), mp: 179–181 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ:8.01–8,02 (t, *J*=3 Hz, 1H), 7.78–7.79 (t, *J*=3 Hz, 1H), 7.27–7.28 (t, *J*=3 Hz, 1H), 7.17–7.28 (m, 7H), 6.80–6.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 153.9, 150.4, 145.6, 137.9, 136.7, 136.1, 130.4, 129.9, 128.7, 128.2, 128.0, 125.7, 123.2, 123.1, 113.3, 112.1, 111.8, 55.8, 55.7, 21.0. ESI HRMS: calcd for $C_{24}H_{22}N_2O_2$ $[M+H]^+$: 371.1754, found: 371.1758.

*4.1.9. 5-Methyl-2,4-diphenyl-1-p-tolyl-1H-imidazole (**3ai**).* 5-Methyl-2,4-diphenyl-1-*p*-tolyl-1*H*-imidazole (**3ai**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 47%), mp: 138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.78–7.81 (d. *J*=9 Hz, 2H), 7.42–7.45 (dd, *J*=3, 6 Hz, 4H), 7.08–7.41 (m, 8H), 2.40 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.1, 138.6, 134.7, 130.1, 129.4, 128.5, 128.3, 127.9, 127.8, 127.7, 127.2, 120.2, 21.2, 11.1. ESI HRMS: calcd for $C_{23}H_{20}N_2$ $[M+H]^+$: 325.1699, found: 325.1671.

*4.1.10. 5-Methyl-2-phenyl-1,4-di-p-tolyl-1H-imidazole (**3aj**).* 5-Methyl-2-phenyl-1,4-di-*p*-tolyl-1*H*-imidazole (**3aj**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 35%), mp: 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.67–7.70 (d, *J*=9 Hz, 2H), 7.40–7.43 (dd, *J*=3, 6 Hz, 2H), 7,09–7.25 (m, 9H). 2.41 (s, 3H), 2.38 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.0, 138.6, 137.5, 135.8, 134.8, 132.3, 130.8, 130.1, 129.0, 128.3, 127.9, 127.8, 127.7, 127.1, 125.9, 21,2, 11.1. ESI HRMS: calcd for $C_{24}H_{22}N_2$ $[M+H]^+$: 339.1856, found: 339.1860.

*4.1.11. 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-p-tolyl-1H-imidazole (**3ak**).* 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3ak**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 41%), mp: 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.66–7.69 (d, *J*=9 Hz, 2H), 7.52–7.55 (m, 2H), 7.39–7.42 (m, 2H), 7.21–7.25 (m, 5H), 7.07–7.21 (m, 2H), 2.41 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.3, 138.8, 134.5, 134.2, 131.4, 130.6, 130.2, 128.7, 128.3, 128.0, 127.9, 127.7, 126.6, 120.1, 21.2, 11.1. ESI HRMS: calcd for $C_{22}H_{19}N_2Br$ $[M+H]^+$: 403.0805, found: 403.0801.

*4.1.12. 4-(4-Chlorophenyl)-5-methyl-2-phenyl-1-p-tolyl-1H-imidazole (**3al**).* 4-(4-Chlorophenyl)-5-methyl-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3al**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 45%), mp: 160–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.72–7.75 (d, *J*=9 Hz, 2H), 7.39–7.42 (dd, *J*=3, 6 Hz, 4H), 7.20–7.25 (m, 5H), 7.07–7.19 (m, 2H), 2.40 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.3, 138.8, 136.4, 134.5, 133.7, 131.9, 130.6, 130.2, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 126.5, 21.2, 11.1. ESI HRMS: calcd for $C_{22}H_{19}N_2Cl$ $[M+H]^+$: 359.1310, found: 359.1314.

*4.1.13. 4-(5-Methyl-2-phenyl-1-p-tolyl-1H-imidazol-4-yl)benzonitrile (**3am**).* 4-(5-Methyl-2-phenyl-1-*p*-tolyl-1*H*-imidazol-4-yl) benzonitrile (**3am**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 56%), mp: 178–180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.89–7.92 (d, *J*=9 Hz, 2H), 7.64–7.67 (m, 2H), 7.39–7.40 (t, *J*=3 Hz, 2H), 7.20–7.38 (m, 5H), 7.06–7.19 (m, 2H), 2.40 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.8, 139.8, 139.0, 135.6, 134.1, 132.1, 130.3, 128.2, 128.18, 128.1, 128.0, 127.6, 127.0, 119.3, 109.0, 21.1, 11.3. ESI HRMS: calcd for $C_{24}H_{19}N_3$ $[M+H]^+$: 350.1652, found: 350.1650.

*4.1.14. 1,4-Diphenyl-2-(4-(trifluoromethyl)phenyl)-1H-imidazole (**3ja**).* 1,4-Diphenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (**3ja**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as a light yellow oil (yield: 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ: 7.86–7.88 (d, *J*=8 Hz, 2H), 7.21–7.57 (m, 13H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 145.3, 142.1, 138.9, 138.1, 129.7, 129.3, 129.1, 128.7, 128.6, 127.2, 125.8, 125.1, 125.07, 125.0, 119.6, 119.3. ESI HRMS: calcd for $C_{22}H_{15}N_2F_3$ $[M+H]^+$: 365.1260, found: 365.1262.

*4.1.15. 2-(1,4-Diphenyl-1H-imidazol-2-yl)pyridine (**3la**).* 2-(1,4-Diphenyl-1*H*-imidazol-2-yl)pyridine (**3la**) was purified by flash chromatography (Hexane/EtOAc, v/v=20:1) as a light yellow oil (yield: 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ: 8.65–8.66 (d, *J*=3 Hz, 1H), 8.50–8.52 (d, *J*=6 Hz, 1H), 7.79–7.90 (m, 3H), 7.45–7.48 (m, 6H), 7.19–7.44 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 149.2, 149.1, 143.9, 142.2, 137.8, 135.8, 133.4, 129.8, 128.7, 128.6, 127.2, 126.4, 125.8, 125.0, 123.0, 119.1. ESI HRMS: calcd for $C_{20}H_{15}N_3$ $[M+H]^+$: 298.1339, found: 298.1342.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.08.077.

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