JOC The Journal of Organic Chemistry

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pubs.acs.org/joc

Synthesis of Multisubstituted Imidazoles via Copper-Catalyzed [3 + 2] Cycloadditions

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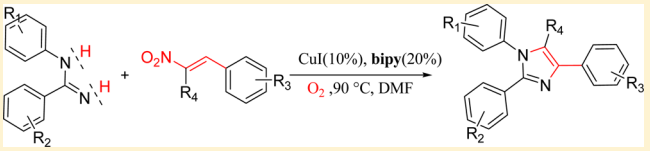
Supporting Information

ABSTRACT: A simple route for the synthesis of imidazole derivatives via copper-catalyzed [3 + 2] cycloaddition reaction is described. This strategy has achieved high regioselectivity and used oxygen as an oxidant without the addition of expensive catalysts to provide moderate to good yields.

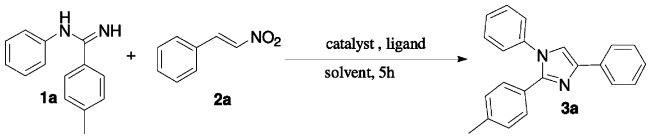


The imidazole ring represents an important class of heterocycles frequently found in many natural products.[1] In addition, imidazole derivatives have been reported to possess pharmacological properties[2] such as antiplasmodium,[3] antitumor,[4] and antifunga.[5] Consequently, many efforts in the past decade have been focused on the preparation of those privileged scaffolds. For example, the synthesis of 1,2,4,5-tetrasubstituted imidazoles have been developed by using various catalytic systems including I_2,[6a] BF_3−SiO_2,[6b] SBPPSA,[6c] alumina,[6d] $FeCl_3·6H_2O$,[6e] $Cu(OAc)_2$,[6f] and DABCO.[6g] Transition-metal-catalyzed direct C−H or N−H functionalization provides a powerful tool for the formation of multisubstituted imidazoles.[7] Many reported methods, though very efficient for obtaining imidazole derivatives, suffer from one or more drawbacks such as requiring harsh reaction conditions, usage of expensive catalysts and long reaction time. Therefore, new synthetic methods are still needed to synthesize imidazoles under much milder conditions and with a simpler catalytic system.

Nitroolefins, as easily available and versatile substrates, have been ubiquitously employed in many synthetic strategies.[8] In particular, they have drawn great attention because of their interesting properties in applying cycloaddition reactions. To the best of our knowledge, nitroolefins can easily lead to electrophilic cycloaddition because of the nitro that significantly withdraws the electron. Recently, Yan and co-workers reported copper-catalyzed aminopyridines and nitroolefins to synthesize imidazo[1,2-*a*]pyridines.[9] As part of our further investigations, this paper will report a novel and efficient strategy for the synthesis of tri- or tetrasubstituted imidazoles via copper-catalyzed [3 + 2] cycloaddition reaction.

We started with an investigation into the reaction of 4-methyl-*N*-phenylbenzamidine (**1a**) and 1-(2-nitrovinyl)-benzene (**2a**) (Table 1). The desired product **3a** was isolated in a 68% yield by the use of CuI as the catalyst and 2,2-bipyridyl (**bipy**) as the ligand in DMF at 90 °C under air conditions (Table 1, entry1). Encouraged by this result, we continued to explore the optimal conditions. Different reaction parameters

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	ligand	solvent	yield[b] (%)
1	CuI	**bipy**	DMF	68
2	$Cu(acac)_2$	**bipy**	DMF	27
3	CuBr	**bipy**	DMF	65
4	$Cu(OAc)_2$	**bipy**	DMF	52
5	$CuBr_2$	**bipy**	DMF	58
6	CuI	1,10-Phen	DMF	66
7	CuI	L-proline	DMF	trace
8	CuI	Ph_3P	DMF	trace
9	CuI	**bipy**	DMSO	59
10	CuI	**bipy**	Dioxane	41
11	CuI	**bipy**	Toluene	55
12	CuI	**bipy**	DCE	31
13[c]	CuI	**bipy**	DMF	72
14[c,d]	CuI	**bipy**	DMF	77
15[c,d,e]	CuI	**bipy**	DMF	0
16[c,d]		**bipy**	DMF	0
17[c,d,f]	CuI	**bipy**	DMF	71
18[c,d,g]	CuI	**bipy**	DMF	67

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), catalyst (10%), ligand (20%), solvent (2 mL), 90 °C, 5 h. [b]Isolated yield based on **2a**. [c]The reaction was carried out under an O_2 atmosphere. [d]The ratio of **1a** (0.1 mmol)/**2a** = 1.2:1. [e]In the presence of *t*-BuOK. [f]60 °C. [g]110 °C.

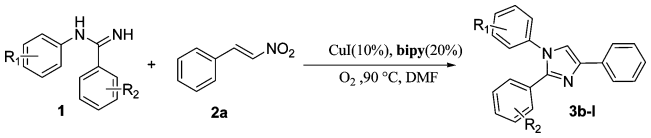
including catalysts, ligands, solvents, and temperature were examined (Table 1, entries 2−12, 17, and 18), but with only inferior results. To our delight, the yield was increased to 72% when the reaction was conducted under an O_2 atmosphere

Received: December 12, 2012
Published: February 14, 2013

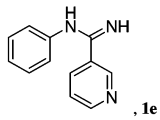
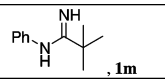
(Table 1, entry 13). Enhancing the ratio of **1a**/**2a** to 1.2:1 afforded a product with a 77% yield (Table 1, entry 14). Notably, the control experiment showed that no reaction occurred if no catalyst was added or if it was performed in the presence of the base (Table 1, entries 15 and 16).

With the optimized conditions in hand, we continued our investigation by exploring the substrate scope of this transformation. At the outset, a series of substituted arylamidines were tested with **2a** under the optimized conditions (Table 2).

Table 2. Substrate Scope of Amidine[a]



1 2a 3b-l

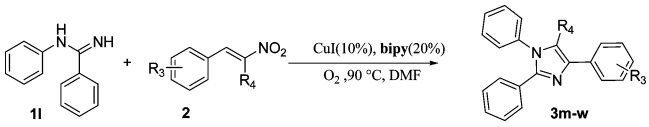
entry	R_1, R_2	product	yield(%)[b]
1	4-Me, H, **1b**	**3b**	70
2	4-Cl, H, **1c**	**3c**	61
3	2-ethyl, H, **1d**	**3d**	63
4	 , **1e**	**3e**	59
5	3-Cl,H, **1f**	**3f**	58
6	4-Me, 4-Me, **1g**	**3g**	71
7	4-OMe, H, **1h**	**3h**	75
8	H , 2-Cl, **1i**	**3i**	65
9	3-Me, H, **1j**	**3j**	62
10	4-Me, 4-OMe, **1k**	**3k**	78
11	H, H, **1l**	**3l**	69
12	 , **1m**	**3x**	0

[a]Reaction conditions: **1** (0.24 mmol), **2a** (0.2 mmol), CuI (10%), **bipy** (20%), DMF (2 mL), the ratio of **1**:**2a** = 1.2:1, 90 °C, 5 h, under an O_2 atmosphere. [b]Isolated yield based on **2a**.

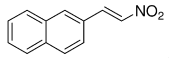
Generally, the reactions showed good functional group tolerance and afforded the desired products in moderate to good yields. In regard to the electronic effects, we found that electron-rich-substituted arylamidines showed better reactivities and gave higher yields than electron-deficient ones (Table 2, entries 1, 2, 5−7, and 10). In addition, the functional groups at the *para*-position showed slightly better reactivities than those at the *meta*-position (Table 2, entries 1, 2, 5, and 9). Notably, *N*-phenylnicotinamidine (**1e**) could also be well tolerated, providing the corresponding product **3e** with a 59% yield (Table 2, entry 4). Nevertheless, the substrates with alkyl groups such as *N*-phenylpivalamidine (**1m**) were not effective for this kind of transformation (Table 2, entry 12).

The reaction scope was also investigated with respect to the other coupling partners **2** (Table 3), which include methyl-, methoxy-, chloro-, or trifluoromethyl-substituted aryl nitroolefins. Most of the substrates proceeded smoothly to afford the

Table 3. Substrate Scope of Nitroolefins[a]



1l 2 3m-w

entry	R_3, R_4	product	yield(%)[b]
1	4-CF_3, H, **2b**	**3m**	62
2	2-Cl, H, **2c**	**3n**	66
3	2,4-OMe, H, **2d**	**3o**	68
4	4-Cl, H, **2e**	**3p**	57
5	4-F, H, **2f**	**3q**	64
6	4-OMe, H, **2g**	**3r**	66
7	4-Me, H, **2h**	**3s**	66
8	H, Me, **2i**	**3t**	39
9	4-Cl, Me, **2j**	**3u**	43
10	4-OMe, Me, **2k**	**3v**	34
11	 ,**2l**	**3w**	75

[a]Reaction conditions: **1l** (0.24 mmol), **2** (0.2 mmol), CuI (10%), **bipy** (20%), DMF (2 mL), 90 °C, 5 h, under an O_2 atmosphere. [b]Isolated yield based on **2**.

corresponding products in moderate to good yields, and the functional groups had no significant impact on the yields (Table 3, entries 1−7). Somewhat disappointingly, when the R_4 was substituted by the methyl group, the steric effect of methyl lowered the yields significantly (Table 3, entries 8−10). However, we were pleased to note that substrates with bulky aromatic groups such as 2-(2-nitrovinyl)naphthalene (**2l**) could perform smoothly, and a 75% yield of the desired imidazole **3w** was obtained (Table 3, entry 11).

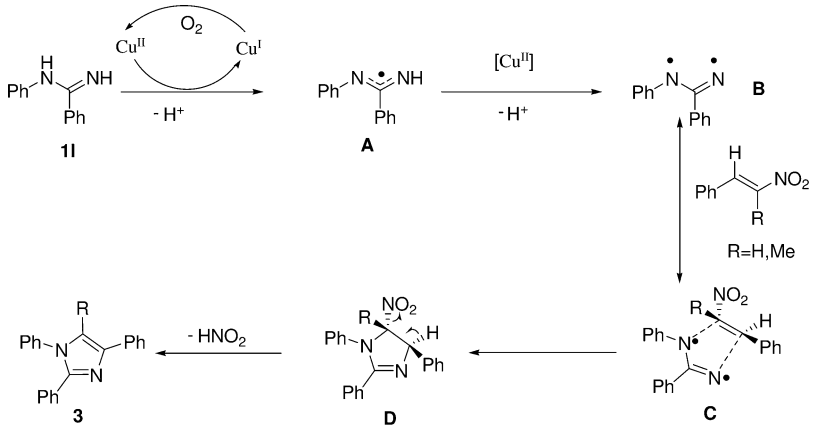
This reaction system was also applicable for a larger scale under the optimized condition. A mixture of **1f** (1.2 mmol), **2a** (1 mmol), CuI (10%), **bipy** (20%), and DMF (3 mL) was stirred at 90 °C for 5 h and afforded the desired product (**3f**) with a 59% yield.

On the basis of the analogous mechanisms discussed in literature,[10] a plausible mechanism for this transformation was depicted in Scheme 1. Generally, Cu^I was initially oxidized to Cu^{II} under oxygen atmosphere. Compound **1l** lost one electron, and H^+ generated the monoradical intermediate **A** by Cu^{II}, which was further oxidized by Cu^{II} to give the diradical intermediate **B**. Subsequently, a molecular nitroolefin reacted with the intermediate **B** via [3 + 2] cycloaddition with a high regioselectivity through the transition status **C**, which was favored because of its steric hindrance of the aromatic groups on subsrates. In the end, the transition status **C** was converted into a stable intermediate **D** followed by the elimination of one molecule of HNO_2 to afford the desired product **3**.

In summary, a novel and facile copper-catalyzed [3 + 2] cycloaddition reaction has been developed, and this methodology could be applied to the construction of a diverse range of multisubstituted imidazole derivatives starting from readily available reactants. Moreover, the reaction, using oxygen as an

dx.doi.org/10.1021/jo302555z | J. Org. Chem. 2013, 78, 2746−2750

Scheme 1. Plausible Reaction Pathway



oxidant, is experimentally simple and environmentally benign. In particular, the strategy could proceed smoothly with a high regioselectivity resulting in moderate to good yields, and it can provide a potential pathway to afford valuable scaffolds of complex molecules in biochemistry and medicinal chemistry.

EXPERIMENTAL SECTION

General Methods Used for Preparing Starting Materials 1a–l and 2a–k. Starting materials **1a–l** and **2a–k** were prepared according to the procedure in literature.[11]

Typical Procedure for the Preparation of Multisubstituted Imidazole. The reactions were carried out in a round-bottom side arm flask (10 mL), and **1** (0.24 mmol), **2** (0.2 mmol), CuI (0.02 mmol), **bipy** (0.04 mmol), and DMF (2 mL) were added to the flask with magnetic stirring bar under the O_2 atmosphere. The mixture was stirred at 90 °C for 5 h. After being cooled to room temperature, the mixture was filtered and extracted with ethyl acetate. Then the filtrate was concentrated under reduced pressure in order to get the crude product, which was further purified by silica gel chromatography (petroleum/ethyl acetate = 10/1 as eluent) to obtain product **3**.

^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$, and ^{13}C NMR spectra were recorded on 75 MHz in $CDCl_3$. The structures of the products (**3k,l**) were identified according to the literature.[12,13] All of the products were further characterized by HRMS (ESI-TOF), and the melting points of solid products were determined on a microscopic apparatus.

*1, 4-Diphenyl-2-p-tolyl-1H-imidazole (**3a**):* 0.2 mmol, 35 mg, 67%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93–7.84 (m, 2H), 7.42–7.31 (m, 8H), 7.27–7.19 (m, 3H), 7.06–7.03 (dd, J = 8.5 Hz, 0.6 Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 141.4, 138.5, 138.2, 133.8, 129.3, 128.8, 128.5, 128.0, 127.3, 126.8, 125.7, 124.9, 118.2, 21.2; HRMS (ESI) calcd for $C_{22}H_{19}N_2$ (M + H)$^+$ 311.1543, found 311.1539.

*2,4-Diphenyl-1-p-tolyl-1H-imidazole (**3b**):* 0.2 mmol, 43 mg, 70%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.87(d, 2H), 7.48–7.40 (m, 2H), 7.39–7.25 (m, 3H), 7.26–7.18 (m, 3H), 7.16–7.09 (m, 5H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 141.4, 138.1, 135.9, 133.8, 130.3, 129.9, 128.7, 128.5, 128.3, 128.1, 126.8, 125.5, 124.9, 118.6, 21.1; HRMS (ESI) calcd for $C_{22}H_{19}N_2$ (M + H)$^+$ 311.1543, found 311.1540.

*1-(4-Chlorophenyl)-2,4-diphenyl-1H-imidazole (**3c**):* 0.2 mmol, 40 mg, 61%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.86 (m, 2H), 7.46–7.29 (m, 7H), 7.28–7.18 (m, 4H), 7.18–7.15 (t, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 141.6, 138.4, 133.8, 130.2, 129.4, 128.7, 128.5, 128.4, 128.1, 128.1, 126.9, 125.8, 124.9, 118.5; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 331.0997, found 331.0993.

*1-(2-Ethylphenyl)-2,4-diphenyl-1H-imidazole (**3d**):* 0.2 mmol, 41 mg, 63%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92–7.90 (d, J = 7.9 Hz, 2H), 7.49–7.45 (dd, J = 6.6, 3.1 Hz, 2H), 7.41–7.36 (dd, J = 10.3, 4.7 Hz, 3H), 7.33–7.30 (d, J = 7.8 Hz, 2H), 7.26–7.23 (m, 3H), 7.22–7.16 (m, 3H), 2.40–2.26 (dq, J = 19.5, 7.3 Hz, 2H), 0.99–0.94 (t, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 140.6, 133.8, 129.5, 129.3, 128.5, 1289.2, 128.1, 127.7, 127.6, 126.8, 124.8, 118.9, 23.6, 13.9; HRMS (ESI) calcd for $C_{23}H_{21}N_2$ (M + H)$^+$ 325.1699, found 325.1694.

*3-(1,4-diphenyl-1H-imidazol-2-yl)pyridine (**3e**):* 0.2 mmol, 35 mg, 59%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66–8.67 (d, J = 2.0 Hz, 1H), 8.51–8.50 (d, J = 4.8 Hz,1H), 7.90–7.87 (m, 2H), 7.82–7.79 (dd, J = 8.0, 1.8 Hz, 1H), 7.48–7.38 (m, 6H), 7.30–7.18 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 149.9, 144.8, 143.1, 138.7, 136.6, 134.2, 130.6, 129.5, 129.5, 128.0, 127.2, 126.6, 125.8, 123.8, 119.9; HRMS (ESI) calcd for $C_{20}H_{16}N_3$ (M + H)$^+$ 298.1339, found 298.1336.

*1-(3-Chlorophenyl)-2,4-diphenyl-1H-imidazole(**3f**):* 0.2 mmol, 38 mg, 58%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.86 (m, 2H), 7.46–7.42 (m, 2H), 7.41–7.39 (d, J = 3.1 Hz, 2H), 7.37–7.36 (m, 1H), 7.34–7.33 (dd, J = 1.9, 1.2 Hz,1H), 7.31–7.25 (m, 6H), 7.09–7.06 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 141.9, 139.4, 135.0, 133.5, 130.4, 129.8, 128.8, 128.8, 128.6, 128.3, 127.1, 125.8, 125.0 124.1, 118.1; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 311.0997, found 311.0994.

*4-Phenyl-1,2-di-p-tolyl-1H-imidazole (**3g**):* 0.2 mmol, 46 mg, 71%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.86 (m, 2H), 7.40–7.33 (m, 5H), 7.26–7.23 (d, J = 7.2 Hz, 1H), 7.18–7.15 (d, J = 8.3 Hz, 2H), 7.12–7.09 (d, J = 8.4 Hz, 2H), 7.07–7.04 (d, J = 8.0 Hz, 2H), 2.36 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 138.1, 137.9, 136.0, 129.9, 128.8, 128.6, 128.5, 126.8, 125.5, 124.9, 118.4, 21.2, 21.0; HRMS (ESI) calcd for $C_{23}H_{21}N_2$ (M + H)$^+$ 325.1699, found 325.1695.

*1-(4-Methoxyphenyl)-2,4-diphenyl-1H-imidazole (**3h**):* 0.2 mmol, 49 mg, 75%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90–7.86 (dd, 2H), 7.48–7.44 (m, 2H), 7.41–7.35 (m, 3H), 7.27–7.15 (m, 4H), 7.14–7.12 (d, 2H), 6.89–6.85 (d, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 138.1, 135.9, 130.3, 129.9, 128.7, 128.5, 128.3, 128.1, 126.8, 125.5, 124.9, 118.6, 21.1; HRMS (ESI) calcd for $C_{22}H_{19}N_2O$ (M + H)$^+$ 327.1492, found 327.1496.

*2-(2-Chlorophenyl)-1,4-diphenyl-1H-imidazole (**3i**):* 0.2 mmol, 43 mg, 65%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91–7.88 (dd, J = 8.3, 1.2 Hz, 2H), 7.58 –7.54 (m, 2H), 7.42–7.37 (m, 2H), 7.33 - 7.22 (m, 7H), 7.17–7.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 141.6, 137.7, 134.3, 133.6, 132.6, 130.6, 130.4, 129.6, 129.1, 128.5, 127.6, 127.0, 126.7, 124.9, 124.4, 116.9; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 331.0997, found 331.0993.

*2,4-Diphenyl-1-m-tolyl-1H-imidazole (**3j**):* 0.2 mmol, 38 mg, 62%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.90 (d, J = 7.4 Hz, 2H), 7.48–7.44 (dd, J = 6.7, 3.0 Hz, 2H), 7.39–7.34 (m, 3H), 7.25–7.18 (m, 5H), 7.13–7.06 (d, J = 7.7 Hz, 1H), 7.06 (s, 1H), 6.98–6.95 (d, J = 7.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 141.4, 139.4, 138.2, 133.8, 130.2, 129.0, 128.8, 128.6, 128.4, 128.2, 128.0, 126.8, 126.1, 124.9, 122.8, 118.5, 21.1; HRMS (ESI) calcd for $C_{22}H_{19}N_2$ (M + H)$^+$ 311.1543, found 311.1538.

dx.doi.org/10.1021/jo302555z | J. Org. Chem. 2013, 78, 2746–2750

*2-(4-Methoxyphenyl)-4-phenyl-1-p-tolyl-1H-imidazole (**3k**):*[12] 0.2 mmol, 53 mg, 78%; white solid, mp: 128−132 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.86 (dd, J = 8.3, 1.0 Hz, 2H), 7.40−7.35 (m, 5H), 7.25−7.20 (t, J = 7.4 Hz, 1H), 7.18−7.09 (dd, J = 19.0, 8.3 Hz, 4H), 6.80−6.76 (t, J = 5.7 Hz, 2H), 3.73 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 146.8, 141.1, 137.9, 135.9, 133.9, 130.0, 129.9, 128.4, 126.7, 125.5, 124.8, 122.9, 118.2, 113.5, 55.0, 21.0; HRMS (ESI) calcd for $C_{23}H_{21}N_2O$ (M + H)$^+$ 341.1648, found 341.1643.

*1,2,4-Triphenyl-1H-imidazole(**3l**):*[13] 0.2 mmol, 41 mg, 69%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.91 (d, 2H), 7.51−7.46 (m, 4H), 7.47−7.42 (m, 4H), 7.31−7.26 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 141.9, 136.8, 133.9, 133.5, 129.9, 129.6, 128.7, 128.6, 128.6, 128.3, 127.1, 126.9, 125.0, 118.1; HRMS (ESI) calcd for $C_{21}H_{17}N_2$ (M + H)$^+$ 297.1386, found 297.1383.

*1,2-Diphenyl-4-(4-(trifluoromethyl)phenyl)-1H-imidazole (**3m**):* 0.2 mmol, 45 mg, 62%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00−7.97 (d, J = 8.6 Hz, 2H), 7.65−7.62 (d, J = 8.6 Hz, 2H), 7.51 (s, 1H), 7.47−7.37 (m, 5H), 7.30−7.21 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 140.2, 138.1, 137.3, 129.9, 129.5, 128.7, 128.7, 128.4, 128.3, 125.7, 125.6, 125.6, 125.5, 125.5, 124.9, 119.6; HRMS (ESI) calcd for $C_{22}H_{16}F_3N_2$ (M + H)$^+$ 365.126, found 365.1255.

*4-(2-Chlorophenyl)-1,2-diphenyl-1H-imidazole (**3n**):* 0.2 mmol, 44 mg, 66%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39−8.36 (m, 1H), 7.92 (s, 1H), 7.48−7.44 (m, 2H), 7.43−7.34 (m, 5H), 7.29−7.25 (m, 5H), 7.20−7.17 (dd, J = 7.4, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 138.3, 137.6, 132.1, 130.7, 130.1, 130.0, 129.7, 129.4, 128.7, 128.4, 128.1, 127.5, 126.8, 125.8, 122.8; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 331.0997, found 331.0993.

*4-(2,4-Dimethoxyphenyl)-1,2-diphenyl-1H-imidazole (**3o**):* 0.2 mmol, 48 mg, 68%; yellow solid; mp 182−185 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01−8.00 (d, J = 3.1 Hz, 1H), 7.80 (s, 1H), 7.50−7.46 (m, 2H), 7.41−7.38 (d, J = 6.7 Hz, 3H), 7.3−7.24 (m, 5H), 6.91−6.88 (d, J = 8.9 Hz, 1H), 6.81−6.77 (dd, J = 8.9, 3.1 Hz, 1H), 3.89−3.88 (d, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 150.5, 145.7, 138.6, 136.9, 130.3, 129.3, 128.6, 128.3, 128.1, 128.0, 125.9, 123.2, 123.0, 113.39, 112.1, 111.8, 55.9, 55.8; HRMS (ESI) calcd for $C_{23}H_{21}N_2O_2$ (M + H)$^+$ 357.1598, found 357.1593.

*4-(4-Chlorophenyl)-1,2-diphenyl-1H-imidazole (**3p**):* 0.2 mmol, 38 mg, 57%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82−7.78 (m, 2H), 7.44−7.32 (m, 8H), 7.26−7.19 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 140.5, 138.2, 132.4, 132.3, 129.4, 132.3, 130.0, 129.4, 128.7, 128.5, 128.2, 128.1, 126.2, 125.7, 118.6; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 331.0997, found 331.0993.

*4-(4-Fluorophenyl)-1,2-diphenyl-1H-imidazole (**3q**):* 0.2 mmol, 40 mg, 64%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87−7.82 (m, 2H), 7.45−7.42 (m, 2H), 7.39−7.36 (m, 4H), 7.28−7.21 (m, 5H), 7.10−7.05 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 160.6, 147.2, 141.0, 138.5, 129.7, 128.9, 128.7, 128.4, 126.9, 126.7, 126.0, 118.3, 115.8, 115.5; HRMS (ESI) calcd for $C_{21}H_{16}FN_2$ (M + H)$^+$ 315.1292, found 315.1289.

*4-(4-Methoxyphenyl)-1,2-diphenyl-1H-imidazole (**3r**):* 0.2 mmol, 43 mg, 66%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83−7.79 (m, 2H), 7.45−7.41 (m, 2H), 7.37−7.31 (m, 4H), 7.26−7.18 (m, 5H), 6.97−6.88 (m, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.69, 146.59, 141.42, 138.35, 130.21, 129.3, 128.6, 128.2, 128.0, 127.9, 126.2, 125.7, 120.2, 117.4, 113.9, 55.12; HRMS (ESI) calcd for $C_{22}H_{19}N_2O$ (M + H)$^+$ 327.1492, found 327.1487.

*1,2-Diphenyl-4-p-tolyl-1H-imidazole (**3s**):* 0.2 mmol, 41 mg, 66%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79−7.77 (d, J = 8.1 Hz, 2H), 7.46−7.42 (m, 2H), 7.37−7.34 (m, 4H), 7.25−7.18 (ddd, J = 8.2, 6.0, 3.2 Hz, 7H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 141.6, 138.4, 136.5, 130.9, 130.2, 129.3, 129.2, 128.7, 128.3, 128.1, 128.0, 125.7, 124.8, 118.0, 21.2; HRMS (ESI) calcd for $C_{21}H_{16}ClN_2$ (M + H)$^+$ 311.1543, found 311.1538.

*5-Methyl-1,2,4-triphenyl-1H-imidazole (**3t**):* 0.2 mmol, 24 mg, 39%; yellow solid; mp 148−152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.47−7.40 (ddd, J = 9.7, 5.8, 2.8 Hz, 7H), 7.31−7.29 (d, J = 7.4 Hz, 1H), 7.26−7.19 (ddd, J = 9.5, 5.5, 3.2 Hz, 5H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.4, 137.9, 137.7, 135.4, 130.9, 129.8, 129.0, 128.6, 128.4, 128.3, 128.1, 127.5, 126.7, 126.5, 11.4; HRMS (ESI) calcd for $C_{22}H_{19}N_2$ (M + H)$^+$ 311.1543, found 311.1547.

*4-(4-Chlorophenyl)-5-methyl-1,2-diphenyl-1H-imidazole (**3u**):* 0.2 mmol, 30 mg, 43%; white solid; mp 193−196 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.72 (m, 2H), 7.47−7.43 (dd, J = 4.9, 1.8 Hz, 3H), 7.42−7.37 (m, 4H), 7.25−7.19 (m, 5H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 137.5, 136.9, 134.0, 132.3, 130.8, 129.9, 129.1, 128.8, 128.7, 128.6, 128.4, 126.7, 11.5; HRMS (ESI) calcd for $C_{22}H_{18}ClN_2$ (M + H)$^+$ 345.1153, found 345.1158.

*4-(4-Methoxyphenyl)-5-methyl-1,2-diphenyl-1H-imidazole (**3v**):* 0.2 mmol, 23 mg, 34%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74−7.71 (d, J = 8.7 Hz, 2H), 7.46−7.44 (d, J = 5.2 Hz, 3H), 7.40−7.37(m, 2H), 7.26−7.15 (m, 5H), 7.00−6.97(d, J = 8.7 Hz, 2H), 3.85 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 146.0, 137.5, 130.8, 129.6, 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 127.8, 125.4, 113.8, 55.2, 11.06; HRMS (ESI) calcd for $C_{23}H_{21}N_2O$ (M + H)$^+$ 341.1649, found 341.1644.

*4-(Naphthalen-2-yl)-1,2-diphenyl-1H-imidazole (**3w**):* 0.2 mmol, 52 mg, 75%; white solid; mp 144−146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75−8.67 (m, 1H), 7.91−7.77 (m, 3H), 7.51 (ddd, J = 12.9, 5.1, 2.7 Hz, 5H), 7.45−7.36 (m, 4H), 7.35−7.23 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.4, 140.8, 138.3, 133.9, 131.5, 131.2, 130.1, 129.4, 128.7, 128.3, 128.2, 128.1, 127.7, 126.6, 126.0, 125.9, 125.7, 125.5, 125.4, 121.3; HRMS (ESI) calcd for $C_{25}H_{19}N_2$ (M + H)$^+$ 347.1543, found 347.1539.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra data for all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the project sponsored by the National Science Foundation of P. R. China (No. J11003307).

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