Amino Acid Promoted CuI-Catalyzed C−N Bond Formation between Aryl Halides and Amines or N-Containing Heterocycles

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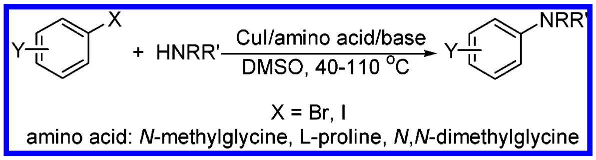

CuI-catalyzed coupling reaction of electron-deficient aryl iodides with aliphatic primary amines occurs at 40 °C under the promotion of *N*-methylglycine. Using L-proline as the promoter, coupling reaction of aryl iodides or aryl bromides with aliphatic primary amines, aliphatic cyclic secondary amines, or electron-rich primary arylamines proceeds at 60−90 °C; an intramolecular coupling reaction between aryl chloride and primary amine moieties gives indoline at 70 °C; coupling reaction of aryl iodides with indole, pyrrole, carbazole, imidazole, or pyrazole can be carried out at 75−90 °C; and coupling reaction of electron-deficient aryl bromides with imidazole or pyrazole occurs at 60−90 °C to provide the corresponding *N*-aryl products in good to excellent yields. In addition, *N*,*N*-dimethylglycine promotes the coupling reaction of electron-rich aryl bromides with imidazole or pyrazole to afford the corresponding *N*-aryl imidazoles or pyrazoles at 110 °C. The possible action of amino acids in these coupling reactions is discussed.

Introduction

N-Arylamines, *N*-arylpyrroles, *N*-arylindoles, *N*-arylimidazoles, and *N*-arylpyrazoles are prevalent in compounds that are of biological, pharmaceutical, and materials interest.[1−3] Copper-catalyzed Ullmann-type reactions are traditional methods to assemble these compounds.[4] For a long time, these reactions had been carried out at high temperatures and many functional groups could not be tolerated, and therefore their usage was greatly limited.[4] In addition, these reactions often require the use of stoichiometric amounts of copper reagents, which, on scale, leads to problems of waste disposal.[4] To overcome these drawbacks, several Pd-catalyzed C−N formation methods have been discovered, which, upon using some sterically hindered phosphine ligands, allowed many coupling reactions of aryl halides with N-containing compounds to proceed under relatively mild conditions and low temperature.[5] However, industrial use of these methods is problematic in many cases due to the air and moisture sensitivity, as well as the higher costs of Pd catalysts and the relative ligands.

During the past years, we have witnessed great progress on the modification of Ullmann-type coupling reactions,[6] which highly relied on the utilization of some special bidentate additives such as aliphatic diamines,[7]

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ethylene glycol,[8a] diethylsalicylamide,[8b] 1,10-phenanthroline and its derivatives,[9] oxime-type and Schiff base ligands,[10] thiophene-2-carboxylate,[11] and amino acids.[12] In a preliminary communication, we have reported that *N*-methylglycine and L-proline were ideal promoters in the CuI-catalyzed coupling reaction of aryl halides with amines.[12c] Further exploration revealed this catalytic system was applicable for coupling of aryl halides with N-containing heterocycles.[12e] The majority of aryl halides investigated were aryl iodides, and only a few examples concerned aryl bromides. Because aryl bromides are cheaper and more readily available than aryl iodides, we further explored the scope of these coupling reactions using aryl bromides. Herein, we wish to describe the details.

Results and Discussion

Coupling Reaction of Aryl Halides with Aliphatic Primary Amines. Initially, we explored the scope for CuI/amino acid-catalyzed reaction of aryl halides with primary amines, and the results are summarized in Table 1. Because *N*-methylglycine was found as the most powerful promoter for aryl amination reaction at 40 °C,[12c] it was initially employed. Indeed, under its action, CuI-catalyzed coupling reaction worked at 40 °C for all iodides and a bromide tested (entries 1−4, 7, and 11). However, only the iodides with electron-withdrawing groups provided the corresponding coupling products in good yields (entries 1−3), while incomplete conversion was seen when iodides bearing electron-donating groups were used (entries 4 and 7). For 4-methylphenyl iodide, increasing the reaction temperature to 60 °C gave the similar result (compare entries 4 and 5). Because *N*-(4-methylphenyl)-*N*-methylglycine was isolated in about 5% yield in this case, we reasoned that the incomplete conversion might result from the coupling of *N*-methylglycine with methylphenyl iodide that consumed the promoter. This result also indicated that, as a promoter, *N*-methylglycine was limited to the coupling reaction below 60 °C. Thus, L-proline, a less reactive promoter toward coupling with aryl iodides, was studied. To our delight, CuI-catalyzed reaction of 4-methylphenyl iodide with benzylamine at 60 °C gave 85% yield (entry 8). We next extended the reaction conditions to the coupling of other iodides and amines and found that, in all cases, satisfactory yields were obtained (entries 8−10).

For less reactive aryl bromides, higher reaction temperatures were required to ensure complete conversion in comparison with the iodides. Thus, L-proline was chosen as the promoter. We were pleased to find that under its action, various aryl bromides efficiently coupled with aliphatic primary amines (entries 13−22). Generally, the reaction proceeded at 80 °C to give the coupling products in good to excellent yields (entries 13−18). Sterically hindered bromides needed slightly high reaction temperature (90 °C), although the yields were still high (entries 20−22).

From Table 1, we noticed that a wide range of functional groups were compatible with these reaction conditions, which include nitro, carboxylate, ketone, nitrile, aromatic amine, hydroxy, and olefin groups. This advantage would allow this method to assemble anilines with great structural diversity. In case of 4-bromobenzaldehyde, the coupling with benzylamine gave a complex mixture, while coupling with 2-hydroxyethylamine provided the desired aniline **1m** in 91% yield (entry 17). In the latter case, the aldehyde moiety of 4-bromobenzaldehyde might form an oxazolidine with 2-hydroxyethylamine in situ, which served as a protecting group for aldehyde and was hydrolyzed during workup to afford **1m**.

Coupling Reaction of Aryl Halides with Aliphatic Secondary Amines. The steric hindrance of secondary amines makes them more sluggish than primary amines to couple with aryl halides. We were pleased to observe that L-proline also served as a good promoter for the Ullmann-type coupling. As summarized in Table 2, the coupling reaction between iodobenzene with morpholine or piperidine occurred at 90 °C (entries 1 and 2). When the less bulky pyrrolidine, a secondary amine, was used, the coupling with aryl iodides proceeded at 65 °C (entries 3 and 4). We next moved our attention to aryl bromides and found that both electron-rich and electron-deficient aryl bromides were coupled with pyrrolidine at 90 °C using 10 mol % CuI and 20 mol % L-proline as a catalytic system (entries 5−8). Noteworthy, this procedure worked well for sterically hindered bromides as evidenced from the coupling reaction of pyrrolidines with 2,4-dimethoxy-1-bromobenzene, which gave aniline **2i** in 86% yield (entry 9). In addition, a good yield was also observed for reaction of piperidine and 4-bromobenzonitrile (entry 10).

Although satisfactory results were obtained in cases of cyclic secondary amines, poor coupling yields were obtained for acyclic secondary amines (entries 11−13). For dibenzylamine, increasing the reaction temperature to 110 °C and using *N*,*N*-dimethylglycine still gave poor conversion (entry 13). These results demonstrated that the steric hindrance of secondary amines inhibited the coupling reaction.

Coupling of Bromopyridines or 1,3-Dibenzyl-5-iodouracil with Amines. Because heteroaromatic ring systems exist in numerous natural products and biologi-

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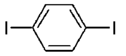
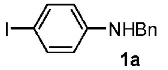
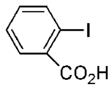
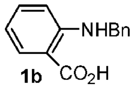
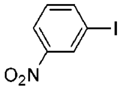
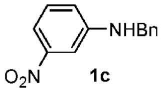
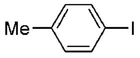
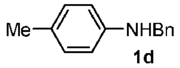
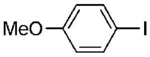
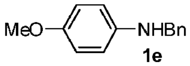
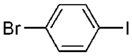
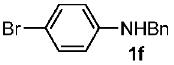
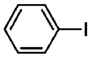
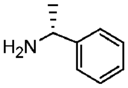
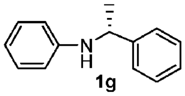
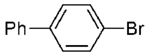
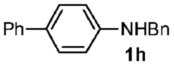
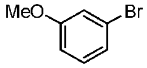
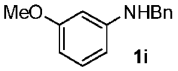
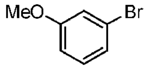
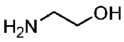
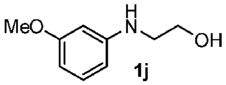
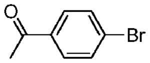
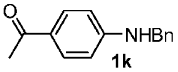
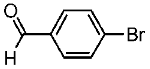
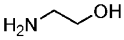
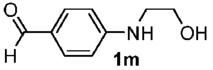
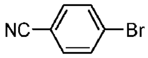
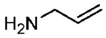
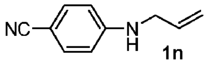
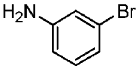
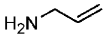
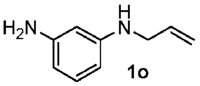
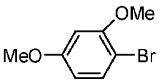
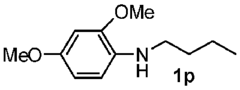
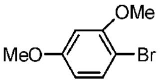
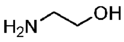
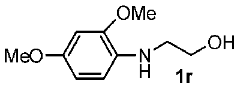
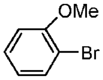
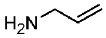
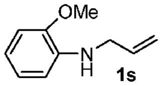
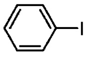
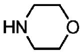
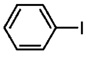
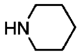
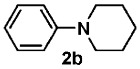
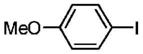
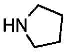
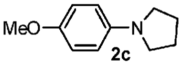
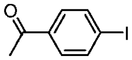
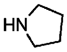
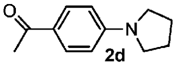
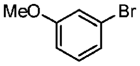
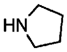
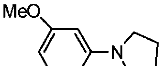
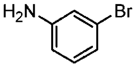
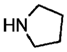
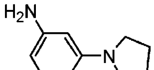
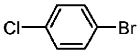
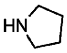
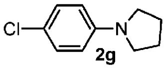
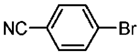
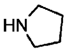
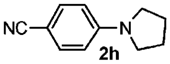
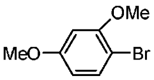
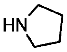
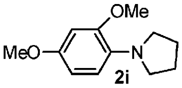
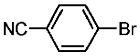
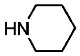
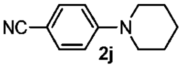
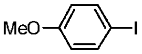
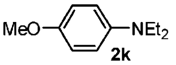
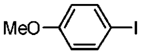
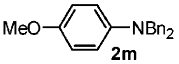
TABLE 1. CuI/Amino Acid-Catalyzed Coupling Reaction of Aryl Halides with Aliphatic Primary Amines[a]

entry	ArX	RNH$_2$	ligand[b]	condition (°C/h)	product	yield[c] (%)
1		BnNH$_2$	A	40/13	 **1a**	82
2		BnNH$_2$	A	40/12	 **1b**	91
3		BnNH$_2$	A	40/23	 **1c**	80
4		BnNH$_2$	A	40/13	 **1d**	64[d]
5			A	60/20		66
6			B	60/16		85
7		BnNH$_2$	A	40/13	 **1e**	64
8			B	60/13		84
9		BnNH$_2$	B	60/12	 **1f**	81
10			B	60/18	 **1g**	75
11		BnNH$_2$	A	40/11	 **1h**	53
12			B	70/28		68
13			B	80/30		81
14		BnNH$_2$	B	80/30	 **1i**	90
15			B	80/29	 **1j**	96
16		BnNH$_2$	B	80/40	 **1k**	88
17			B	80/27	 **1m**	91
18			B	80/39	 **1n**	96[e]
19			B	90/40	 **1o**	84[e]
20			B	90/40	 **1p**	89[e]
21			B	90/40	 **1r**	93
22			B	90/40	 **1s**	98[e]

[a] Reaction conditions: CuI (0.5 mmol), amino acid (1 mmol), aryl halide (5 mmol), amine (7.5 mmol), K_2CO_3 (10 mmol, for aryl iodide) or K_3PO_4 (10 mmol, for aryl bromide), DMSO (3 mL). [b] A, *N*-methylglycine; B, L-proline. [c] Isolated yield. [d] *N*-(4-Methylphenyl)-*N*-methylglycine was isolated in about 5% yield. [e] 15 mmol of amines was utilized to avoid the low yields due to their evaporation at elevated reaction temperatures.

TABLE 2. CuI/Amino Acid-Catalyzed Coupling Reaction of Aryl Halides with Aliphatic Secondary Amines[a]

entry	ArX	RR'NH	ligand[b]	condition (°C/h)	product	yield[c] (%)
1			B	90/40	 **2a**	77
2			B	90/40	 **2b**	83
3			B	65/27	 **2c**	100[d]
4			B	65/20	 **2d**	84[d]
5			B	90/31	 **2e**	99[d]
6			B	90/27	 **2f**	94[d]
7			B	90/27	 **2g**	89[d]
8			B	90/27	 **2h**	89[d]
9			B	90/40	 **2i**	86[d]
10			B	90/40	 **2j**	81
11		HNEt$_2$	B	90	 **2k**	21[d]
12		HNBn$_2$	B	90/40	 **2m**	0
13			C	110/40		<10

[a] Reaction conditions: CuI (0.5 mmol), amino acid (1 mmol), aryl halide (5 mmol), amine (7.5 mmol), K_2CO_3 (10 mmol), DMSO (3 mL). [b] B, L-proline; C, *N*,*N*-dimethylglycine. [c] Isolated yield. [d] 15 mmol of amines was added to avoid the low yields due to their evaporation at elevated reaction temperatures.

cally active substances, cross-coupling reactions between heteroaryl halides or their derivatives with amines have recently received considerable attention.[13] Consequently, some heterocycle-embodied aryl or vinyl halides were tested in our catalytic system. As indicated in Table 3, coupling of 3-bromopyridine with several amines worked well, providing the corresponding amination products in excellent yields (entries 1−3). For 2,5-dibromopyridine, amination occurred at the 2-position exclusively to deliver **4** as a single product in 81% yield (entry 4). This regioselectivity was consistent with that observed previously in Pd-catalyzed aryl amination.[13a] In case of 1,3-dibenzyl-5-iodouracil **5**, coupling with morphline and 2-aminopyrimidine under our standard conditions produced **6** and **7** in 59% and 77% yields, respectively. These results were comparable with those obtained with the $(CuOTf)_2 \cdot PhH$/1,10-phenanthroline catalytic system.[13b]

Coupling Reaction of Aryl Halides with Anilines. Although several mild conditions for CuI-catalyzed coupling of aryl halides and aliphatic amines have been reported in the literature, little attention has been directed toward the further usages of these conditions for forming diarylamines.[8−12] Prior to our report,[12c] only two examples were described by Venkataraman and coworkers in which soluble copper(I) catalysts, $Cu(PPh_3)_3Br$[14] and $Cu(neocup)(PPh_3)Br$,[9a] were employed for elaborating diaryl or triarylamines. We found that the combination of CuI and L-proline could catalyze the coupling reaction of iodobenzene with aniline at 90 °C to provide diphenylamine in 66% yield (Table 4, entry 1). *p*-Anisidine gave increased coupling yield (compare entries 1 and 2). Further attempts indicated that good yields were ob-

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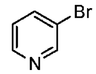
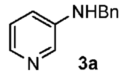
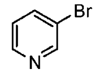
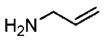
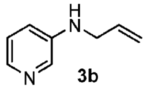
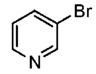
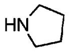
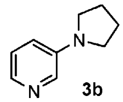
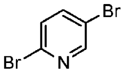
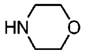
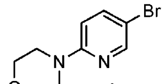
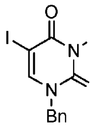
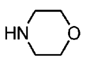
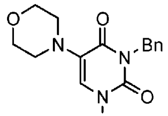
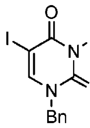
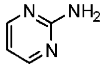
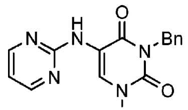
(13) (a) Ji, J.; Li, T.; Bunnelle, W. H. *Org. Lett.* **2003**, *5*, 4611. (b) Arterburn, J. B.; Pannala, M.; Gonzalez, A. M. *Tetrahedron Lett.* **2001**, *42*, 1425. (c) Yin, J.; Zhao, M. M.; Huffman, M. A.; McNamara, J. M. *Org. Lett.* **2002**, *4*, 3481. (d) Jonckers, T. H. M.; Maes, B. U. W.; Lemiere, G. L. F.; Dommisse, R. *Tetrahedron* **2001**, *57*, 7027.

(14) Gujadhur, R. K.; Venkataraman, D.; Kintigh, J. T. *Tetrahedron Lett.* **2001**, *42*, 4791.

TABLE 3. CuI/L-Proline-Catalyzed Coupling Reaction of Bromopyridines or 1,3-Dibenzyl-5-iodouracil with Amines[a]

entry	ArX	RR'NH	condition (°C/h)	product	yield[b] (%)
1		$BnNH_2$	80/40	 **3a**	97
2			80/40	 **3b**	97[c]
3			90/40	 **3b**	94[c]
4			90/40	 **4**	81
5	 **5**		80/30	 **6**	59
6	 **5**		80/30	 **7**	77

[a] Reaction conditions: CuI (0.5 mmol), L-proline (1 mmol), aryl halide (5 mmol), amine (7.5 mmol), K_2CO_3 (10 mmol), DMSO (3 mL). [b] Isolated yield. [c] 15 mmol of amines was added to avoid the low yields due to their evaporation at elevated reaction temperatures.

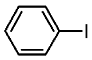
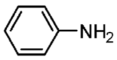
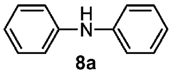
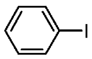
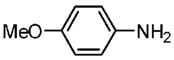
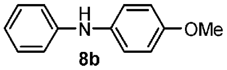
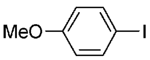
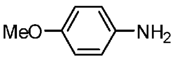
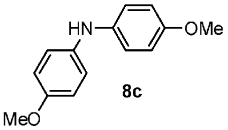
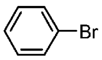
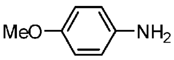
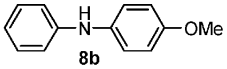
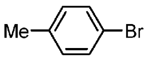
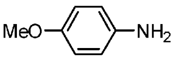
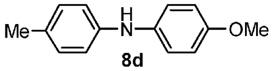
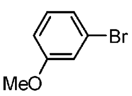
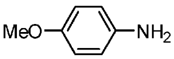
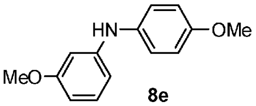
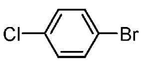
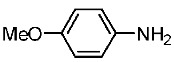
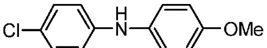
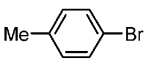
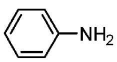
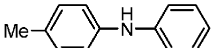
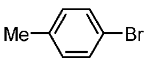
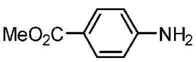
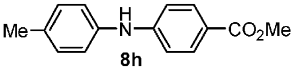
tained when this amine was reacted with several aryl bromides bearing either electron-donating or electron-withdrawing groups (entries 4−7). However, poor conversion was observed when bromobenzene was coupled with aniline (entry 8), while trace coupling product was isolated in case of methyl 4-aminobenzoate (entry 9). These results demonstrated that the nucleophilicity of arylamines was key in the present coupling reaction. The poor conversion for nucleophilically weak arylamines might result from that they could not compete with L-proline in coupling with aryl halides, thereby decreasing the reactivity of this catalytic system.

Coupling Reaction of Aryl Chlorides with Amines. Reaction of chlorobenzene with benzylamine using the catalysis CuI/L-proline gave trace coupling product (Scheme 1). However, an intramolecular coupling reaction between aryl chloride and amine moieties worked at 70 °C to deliver indoline **10** in 70% yield.

Coupling Reaction of Aryl Halides with Imidazole, Benzoimidazole, or Pyrazole. As summarized in Table 5, coupling reaction of 4-methoxyphenyl iodide with imidazole or pyrazole catalyzed by CuI/L-proline proceeded well at 90 °C to deliver the desired *N*-aryl products **11a** or **12a** in excellent yields (entries 1 and 2). In case an electron-deficient aryl iodide, this reaction proceeded at lower temperature (entry 3). Further exploration revealed that electron-deficient aryl bromides were compatible with these reaction conditions, giving satisfactory conversion at 60−95 °C (entries 4−7, 12, and 13). However, for electron-rich aryl bromides, low conversion was observed under the above standard conditions (entry 8). After some experimentation, we found that this problem could be solved by raising the reaction temperature to 110 °C (entries 9, 10, and 14). At this time, *N,N*-dimethylglycine was used as the additive to avoid the severe self-coupling of L-proline with aryl bromides. The new conditions also worked for sterically hindered substrates as evidenced from the reaction of 2,4-dimethoxyphenyl bromide with imidazole (entry 11). Furthermore, it was observed that the reaction of electron-deficient aryl bromides with benzoimidazole produced *N*-aryl benzoimidazoles in good yields (entries 15 and 16).

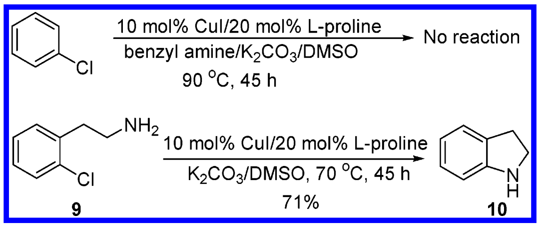
Coupling Reaction of Aryl Halides with Indoles, Pyrrole, or Carbazole. Using 10 mol % CuI and 20 mol % L-proline, the coupling reaction of indole with iodobenzene proceeded at 90 °C for 40 h to give *N*-phenylindole **11a** in 85% yield (Table 6, entry 1). For electron-deficient aryl iodides, reaction temperature could be lowered to 75−80 °C (entries 2−4). Sterically hindered aryl iodides were compatible with these conditions as evidenced from the reaction of 2-methoxyphenyl iodide with indole to provide **14e** in 79% yield (entry 5). Furthermore, entries 6 and 7 illustrated that bulky indole and carbazole also worked in this reaction. However, when bromobenzene was used, low conversion was observed. Although the coupling reaction of 4-methoxyphenyl iodide with pyrrole proceeded well, the corresponding bromide gave poor conversion (compare entries 9 and 10). In this case, raising the reaction temperature to 110 °C and employing *N,N*-dimethylglycine as the additive only gave moderate conversion (entry 11). Indeed, when 4-bromophenyl iodide was utilized, regio-

TABLE 4. CuI/L-Proline-Catalyzed Coupling Reaction of Aryl Halides with Aryl Amines[a]

entry	ArX	RR'NH	condition (°C/h)	product	yield[b] (%)
1			90/27	 **8a**	66
2			90/36	 **8b**	82
3			90/27	 **8c**	81
4			90/40	 **8b**	90
5			90/40	 **8d**	90
6			90/40	 **8e**	97
7			90/40	 **8f**	82
8			90/40	 **8g**	51
9			90/40	 **8h**	<5

[a] Reaction conditions: aryl halide (3 mmol), alkyl amine (2 mmol), K_2CO_3 (4 mmol), CuI (0.2 mmol), and L-proline (0.4 mmol) in 3 mL of DMSO. [b] Isolated yield.

SCHEME 1



selective product **15b** was isolated in 80% yield (entry 12). These results indicated that the coupling reaction of aryl bromides with indoles and pyrroles was unsuccessful under our standard conditions. The low reactivity displayed by pyrrole and indole in comparison with imidazole and pyrazole for Ullmann-type coupling has been noticed by Cristau and co-workers.[10b]

Plausible Mechanism. To date, three mechanisms for Ullmann-type coupling reactions have been described in the literatures:[4b,6b,c] (1) oxidative addition/reductive elimination mechanism proposed by Cohen in 1974;[15] (2) π-complex mechanism proposed by Paine in 1987;[16] and (3) radical or radical anion pathway.[4b,18] On the basis of the former two mechanisms and the fact that copper ions can form chelates with amino acids through the carboxyl and amino groups,[17] we put forward two possible catalytic cycles for our reactions as depicted in Schemes 2 and 3. In Scheme 2, the chelation of Cu(I) with an amino acid makes Cu(I) species more reactive toward the oxidative addition, or/and stabilize the oxidative addition intermediates **B**, thereby promoting the coupling reaction. Noteworthy, a similar four coordinated Cu(III) intermediate has been proposed by Liebeskind and co-workers in their CuTC-catalyzed reactions.[11] In Scheme 3, chelated Cu(I) might make the aromatic ring of the π-complex **D**[16] more electron-deficient, thereby facilitating the nucleophilic attack of amines or nitrogen anions generated from N-containing heterocycles. The mechanism outlined in Scheme 2 could be used to explain most of the phenomena observed, for example, the order I > Br > Cl for ease of halogen displacement from the aromatic ring; and slightly better reactivity displayed by electron-deficient aryl halides, while the mechanism showed in Scheme 3 could be used to fully rationalize the substituent effect of aryl halides but had difficulty explaining the reactivity order ArI > ArBr > ArCl. More detailed

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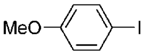
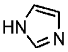
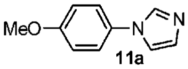
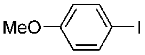
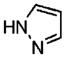
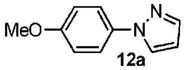
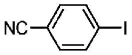
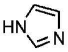
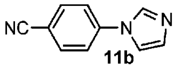
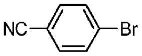
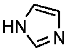
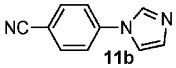
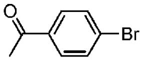
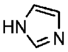
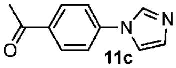
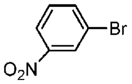
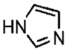
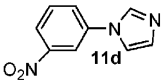
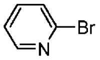
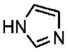
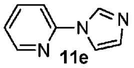
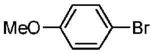
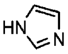
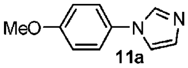
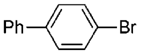
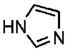
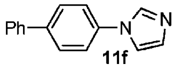
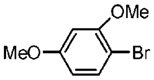
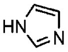
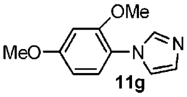
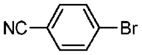
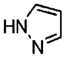
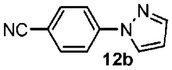
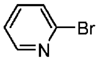
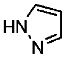
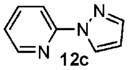
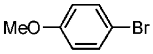
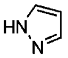
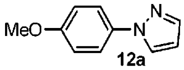
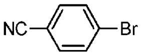
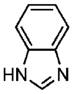
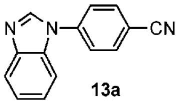
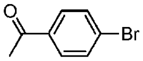
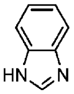
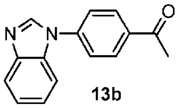
(15) Cohen, T.; Wood, J.; Dietz, A. G., Jr. *Tetrahedron Lett.* **1974**, *15*, 3555.

(16) Paine, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 1496.

(17) Greenstein, J. P.; Winitz, M. *Chemistry of the Amino Acids*; Wiley: New York, 1961; Vol. 3.

(18) Aalten, H. L.; Van Koten, G.; Grove, D. M.; Kuilman, T.; Piekstra, O. G.; Hulshof, L. A.; Sheldon, R. A. *Tetrahedron* **1989**, *45*, 5565.

TABLE 5. CuI/Amino Acid-Catalyzed Coupling Reaction of Aryl Halides with Imidazole, Benzoimidazole, or Pyrazole[a]

entry	ArX	RR'NH	ligand[b]	condition (°C/h)	product	yield[c] (%)
1			B	90/36	 **11a**	91
2			B	90/65	 **12a**	91
3			B	80/34	 **11b**	93
4			B	85/48	 **11b**	97
5			B	95/40	 **11c**	93
6			B	85/40	 **11d**	72
7			B	60/45	 **11e**	93
8			B	85/40	 **11a**	22
9			C	110/45		95
10			C	110/40	 **11f**	81
11			C	110/40	 **11g**	62
12			B	75/45	 **12b**	96
13			B	75/48	 **12c**	94
14			C	110/45	 **12a**	71
15			B	95/42	 **13a**	99
16			C	110/40	 **13b**	75

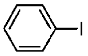
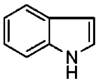
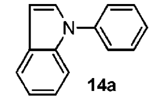
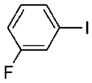
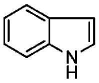
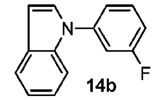
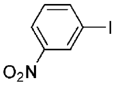
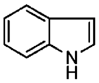
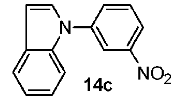
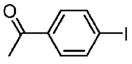
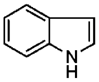
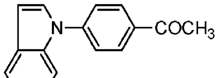
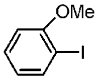
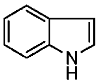
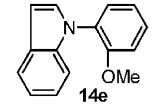
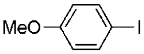
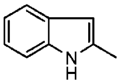
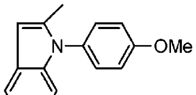
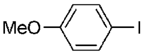
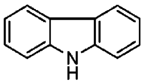
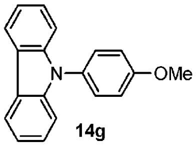
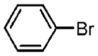
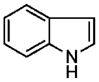
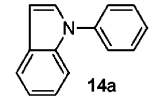
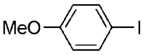
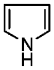
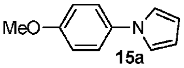
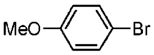
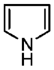
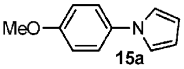
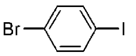
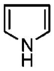
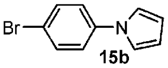
[a] Reaction conditions: CuI (0.2 mmol), L-proline (0.4 mmol), K_2CO_3 (4 mmol), aryl halide (2.2 mmol) and azole (2 mmol), DMSO (3 mL). [b] B, L-proline; C, *N*,*N*-dimethylglycine. [c] Isolated yield.

mechanistic studies should be carried out to clarify these issues.

The above two mechanisms could also explain the different behaves displayed by *N*-methylglycine, L-proline, and *N*,*N*-dimethylglycine. Their capability for promoting C−N formation reactions might be dependent on their reactivity as the coupling agents and coordination ability as bidentate additives. Based on their steric hindrance, the order for coordination ability is *N*-methylglycine > L-proline > *N*,*N*-dimethylglycine. Therefore, when reaction temperatures were below 60 °C, *N*-methylglycine gave best results. However, when reaction temperatures were up 60 °C, the coupling reaction of secondary amino acids with aryl halides occurred, which led to less reactive L-proline serving as a best additive. In case of high temperatures (>95 °C), tertiary *N*,*N*-dimethylglycine that is unable to proceed aryl amination could be used as the additive.

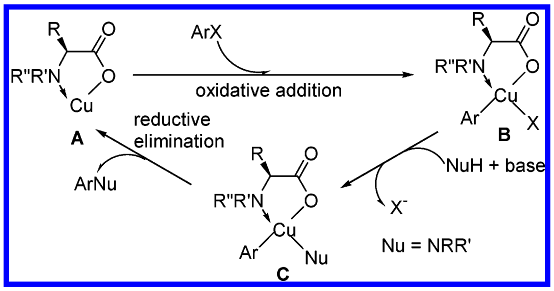
In conclusion, we have demonstrated that some amino acids are able to promote Ullmann-type C−N bond formation reactions. The reactions showed excellent functional group tolerance. Both the steric hindrance and

TABLE 6. CuI/Amino Acid-Catalyzed Coupling Reaction of Aryl Halides with Indole, Pyrrole, or Carbazole[a]

entry	ArX	RR'NH	condition (°C/h)	product	yield[b] (%)
1			90/40	 **14a**	85
2			80/34	 **14b**	88
3			75/42	 **14c**	93
4			80/22	 **14d**	90
5			90/48	 **14e**	79
6			90/40	 **14f**	75
7			90/40	 **14g**	93
8			90/40	 **14a**	33
9			90/36	 **15a**	84
10			90/40	 **15a**	<5
11			110/40		46[c]
12			90/36	 **15b**	80

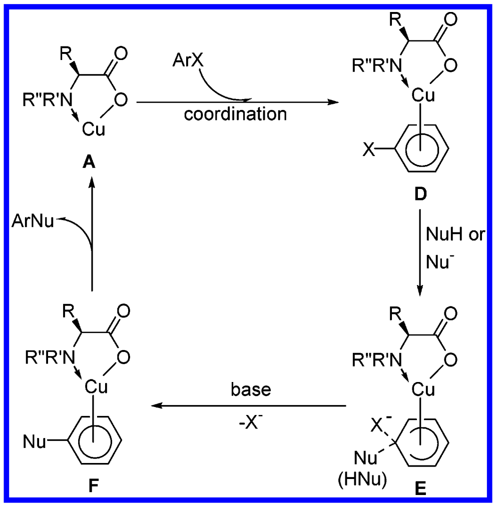
[a] Reaction conditions: CuI (0.2 mmol), L-proline (0.4 mmol), and K_2CO_3 (4 mmol) for aryl iodide or Cs_2CO_3 (4 mmol) for aryl bromide, aryl halide (2.2 mmol), and N-containing heterocycle (2 mmol), DMSO (3 mL). [b] Isolated yield. [c] *N*,*N*-Dimethylglycine was used as the ligand.

SCHEME 2



the nucleophilicity of the amines are key in these coupling reactions. Electron-deficient aryl halides generally displayed better reactivity than electron-rich aryl halides. In most case, L-proline is a reliable promoter for the following four types of reactions at relatively low temperature: (1) coupling reaction of aryl iodides, and aryl bromides with aliphatic primary amines, aliphatic cyclic secondary amines, and electron-rich arylamines; (2) intramolecular coupling reaction between aryl chloride and primary amine moieties; (3) coupling reaction of aryl iodides with indole, pyrrole, carbazole, imidazole, or pyrazole; and (4) coupling reaction of electron-deficient aryl bromides with imidazole or pyrazole. For coupling reaction of electron-rich aryl bromides with imidazole or pyrazole, *N*,*N*-dimethylglycine can serve as an efficient

SCHEME 3



promoter. Noteworthy is that these promoters are significantly inexpensive and readily available. Moreover, they can be easily removed from the crude products by simply washing with water. Given these advantages, the present reactions should find considerable applications in organic synthesis.[19]

Experimental Section

General Procedures. All reactions were carried out in resealable tubes under nitrogen atmosphere. DMSO and DMF were freshly distilled from CaH$_2$. Commercial available CuI must be washed with THF using a Soxhlet extractor before it is used to ensure satisfactory catalytic activity.

General Procedure for the Coupling Reaction of Aryl Halides with Alkylamines Catalyzed by CuI and Amino Acid. A mixture of aryl halide (5 mmol), alkylamine (7.5 mmol, or 15 mmol for the amines with low boiling points), K$_2$CO$_3$ (10 mmol, for aryl iodide) or K$_3$PO$_4$ (10 mmol, for aryl bromide), CuI (0.5 mmol), and the appropriate amino acid (1 mmol) in 3 mL of DMSO was heated at the indicated temperature. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1/10 to 1/8 ethyl acetate/petroleum ether to afford the corresponding aniline. The data for some selected compounds are as follows.

2-[(Phenylmethyl)amino]benzoic Acid 1b. White solid; mp 174−176 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 (m, 2H), 7.26−7.37 (m, 6H), 6.61−6.66 (m, 2H), 4.50 (s, 2H); EI-MS *m/z* 227 (M$^+$), 208, 180, 132, 106, 91, 77, 65, 51, 43.

***N*-Benzyl-4-bromoaniline 1f.** White solid; mp 52−53 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.26−7.35 (m, 5H), 7.22 (d, J = 9.0 Hz, 2H), 6.49 (d, J = 9.0 Hz, 2H), 4.30 (s, 2H), 4.08 (br s, 1H); EI-MS *m/z* 263 (M$^+$, ^{81}Br), 261 (M$^+$, ^{79}Br), 91, 77, 65, 63, 51, 41.

***N*-Benzyl-biphenyl-4-yl-amine 1h.** White solid; mp 94−95 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (d, J = 8.1 Hz, 2H), 7.35−7.45 (m, 10H), 6.69 (d, J = 8.1 Hz, 2H), 4.37 (s, 2H), 4.10 (br s, 1H); EI-MS *m/z* 257 (M$^+$), 182, 168, 152, 141, 115, 91, 77, 65, 63, 51.

4-(*N*-Benzyl)aminoacetophenone 1k. White solid; mp 89−91 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, J = 9.2 Hz, 2H), 7.30−7.38 (m, 5H), 6.60 (d, J = 8.7 Hz, 2H), 4.61 (br s, 1H), 4.41 (d, J = 4.6 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 196.5, 152.1, 138.4, 130.9, 128.9, 127.7, 127.4, 127.0, 111.7, 47.7, 26.1; EI-MS *m/z* 226 (M + H)$^+$, 225 (M$^+$), 210, 92, 91, 77, 65, 43; ESI-HRMS for C$_{15}$H$_{16}$NO (M + H)$^+$ requires 226.1226, found 226.1226.

4-[*N*-(2-Hydroxyethyl)]aminobenzaldehyde 1m. Pale yellow solid; mp 46−48 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.72 (s, 1H), 7.70 (m, 2H), 6.66 (m, 2H), 3.90 (t, J = 5.3 Hz, 2H), 3.40 (t, J = 5.3 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 190.8, 153.7, 132.6, 126.3, 112.1, 60.8, 45.3; EI-MS *m/z* 165 (M$^+$), 134, 105, 95, 79, 77, 51, 41; ESI-HRMS for C$_9$H$_{12}$NO$_2$ (M + H)$^+$ requires 166.0866, found 166.0863.

4-(*N*-Allyl)aminobenzonitrile 1n. Pale yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41 (d, J = 8.7 Hz, 2H), 6.57 (d, J = 8.7 Hz, 2H), 5.85−5.95 (m, 1H), 5.19−5.30 (m, 2H), 4.44 (br s, 1H), 3.80−3.84 (m, 2H); EI-MS *m/z* 158 (M$^+$), 157, 131, 130, 129, 102, 41, 39.

***N*-Allyl Benzene-1,3-diamine 1o.** Yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.95 (t, J = 7.8 Hz, 1H), 6.07 (m, 2H), 5.95 (m, 2H), 5.27 (m, 1H), 5.14 (m, 1H), 3.72 (m, 2H), 3.60 (br s, 3H); EI-MS *m/z* 148 (M$^+$), 147, 133, 121, 93, 80, 65, 39.

***N*-(2-Hydroxyethyl)-2,4-dimethoxyaniline 1r.** Yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.40−6.60 (m, 3H), 3.82−3.85 (m, 5H), 3.76 (s, 3H), 3.28 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 152.4, 148.5, 132.3, 111.1, 103.9, 99.3, 61.4, 55.8, 55.5, 46.9; EI-MS *m/z* 197 (M$^+$), 167, 166, 152, 151, 150, 136, 108; ESI-HRMS for C$_{10}$H$_{16}$NO$_3$ (M + H)$^+$ requires 198.1132, found 198.1125.

***N*-(4-Acetylphenyl)pyrrolidine 2d.** Pale yellow crystals; mp 134−135 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (d, J = 9.2 Hz, 2H), 6.51 (d, J = 9.2 Hz, 2H), 3.35−3.39 (m, 4H), 2.51 (s, 3H), 2.02−2.06 (m, 4H); EI-MS *m/z* 189 (M$^+$), 188, 175, 174, 146, 91, 77, 43.

1-(4-Chlorophenyl)pyrrolidine 2g. White solid; mp 84−85 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.14 (d, J = 8.7 Hz, 2H), 6.45 (d, J = 8.7 Hz, 2H), 3.21−3.25 (m, 4H), 1.96−2.00 (m, 4H); EI-MS *m/z* 181 (M$^+$), 180, 140, 127, 125, 111, 75.

4-Pyrrolidin-1-yl-benzonitrile 2h. Pale yellow solid; mp 88−90 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 (d, J = 8.7 Hz, 2H), 6.50 (d, J = 8.7 Hz, 2H), 3.31−3.34 (m, 4H), 2.02−2.06 (m, 4H). EI-MS *m/z* 172 (M$^+$), 171, 129, 116, 102, 75, 43, 41.

***N*-(2,4-Dimethoxyphenyl)pyrrolidine 2i.** Yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.78 (d, J = 8.2 Hz, 1H), 6.49 (d, J = 2.7 Hz, 1H), 6.39−6.42 (m, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.16−3.18 (m, 4H), 1.91−1.94 (m, 4H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 154.7, 152.3, 133.8, 116.2, 103.4, 100.1, 55.6, 55.4, 51.0, 24.3; EI-MS *m/ z* 207 (M$^+$), 206, 193, 192, 164, 150, 149; ESI-HRMS for C$_{12}$H$_{18}$NO$_2$ (M + H)$^+$ requires 208.1342, found 208.1332.

Benzyl-[3]pyridyl-amine 3a. Yellow solid; mp 86−88 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.08 (d, J = 2.7 Hz, 1H), 7.96 (d, J = 4.6 Hz, 1H), 7.28−7.39 (m, 5H), 7.08−7.10 (m, 1H), 6.88−6.90 (m, 1H), 4.34 (s, 2H); EI-MS *m/z* 184 (M$^+$), 145, 91, 60, 45, 43, 42, 41.

***N*-Allyl-[3]pyridylamine 3b.** Yellow oil; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, J = 2.7 Hz, 1H), 7.95 (d, J = 4.1 Hz, 1H), 7.06−7.09 (m, 1H), 6.87−6.89 (m, 1H), 5.87−5.97 (m, 1H), 5.18−5.31 (m, 2H), 3.78−3.83 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.5, 138.8, 136.2, 134.6, 123.8, 118.9, 116.8, 46.1; EI-MS *m/z* 134 (M$^+$), 133, 107, 78, 51, 41, 39, 38; ESI-HRMS for C$_8$H$_{11}$N$_2$ (M + H)$^+$ requires 135.0921, found 135.0917.

2-[*N*-(1,3-Dibenzyluracil-5-yl)]aminopyrimidine 7. White solid; mp 151−152 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.61 (s, 1H), 8.37 (d, J = 4.6 Hz, 2H), 7.63 (s, 1H), 7.48−7.50 (m, 2H), 7.26−7.39 (m, 7H), 6.68−6.71 (m, 1H), 5.23 (s, 2H), 5.01 (s, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.0, 159.4, 157.9, 149.8, 136.7, 135.9, 129.1, 128.6, 128.3, 128.1, 127.8, 126.0, 116.0, 112.7, 53.0, 45.3; EI-MS *m/z* 385 (M$^+$), 384, 292, 158, 106, 91,

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[19] For emerging applications of the present N-aromation methodology, see: (a) Fletcher, S. P.; Clive, D. L. J.; Peng, J.; Wingert, D. A. *Org. Lett.* **2005**, *7*, 23. (b) Jean, L.; Rouden, J.; Maddalauno, J.; Lasne, M.-C. *J. Org. Chem.* **2004**, *69*, 8893. (c) Cuny, G.; Bois-Choussy, M.; Zhu, J. *J. Am. Chem. Soc.* **2004**, *126*, 14475.

65; HRMS (ESI) for $C_{22}H_{20}N_5O_2$ $(M + H)^+$ requires 386.1612, found 386.1612.

General Procedure for the Coupling Reaction of Aryl Halides with Anilines Catalyzed by CuI and L-Proline. A mixture of aryl halide (3 mmol), aniline (2 mmol), K_2CO_3 (4 mmol), CuI (0.2 mmol), and L-proline (0.4 mmol) in 3 mL of DMSO was heated at 90 °C for 27−40 h. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1/10 to 1/8 ethyl acetate/petroleum ether to afford the corresponding aniline. The data for some selected compounds are as follows.

***N*,*N*-Diphenylamine 8a.** Yellow solid; mp 51−52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (br, 1H), 6.90−6.95 (m, 2H), 7.04−7.08 (m, 4H), 7.23−7.29 (m, 4H); EI-MS *m/z* 169 (M^+), 77, 65, 51, 41.

***N*-Phenyl-*p*-anisidine 8b.** Pale yellow solid; mp 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.21 (m, 2H), 7.05−7.09 (m, 2H), 6.77−6.91 (m, 5H), 5.49 (br s, 1H), 3.80 (s, 3H); EI-MS *m/z* 199 (M^+), 185, 184, 129, 128, 154, 77.

***N*-(4-Methylphenyl)-*N*-phenylamine 8g.** White solid; mp 86−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.25 (m, 2H), 7.07−7.09 (m, 2H), 6.99−7.02 (m, 4H), 6.86−6.89 (m, 1H), 5.60 (br s, 1H), 2.30 (s, 3H); EI-MS *m/z* 183 (M^+), 168, 167, 91, 77.

***N*-(4-Methoxycarbonylphenyl)-*N*-(4-methylphenyl)-amine 8h.** Pale yellow solid; mp 106−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.93 (br s, 1H), 3.84 (s, 3H), 2.31 (s, 3H); EI-MS *m/z* 241 (M^+), 210, 181, 180, 167.

Indoline 10. A resealable tube was charged with CuI (0.2 mmol), L-proline (0.4 mmol), and K_2CO_3 (4 mmol), evacuated, and backfilled with nitrogen (two cycles). To this mixture were added 2 mL of DMSO and 2-(2-chlorophenyl)ethylamine (2 mmol) by syringe at room temperature under nitrogen. The sealed tube was put into an oil bath that was preheated to 70 °C, and the reaction mixture was stirred at the same temperature for 45 h. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1/10 to 1/8 ethyl acetate/petroleum ether to afford 170 mg (71%) of **10** as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.3 Hz, 1H), 7.00−7.04 (m, 1H), 6.69−6.73 (m, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 3.53 (t, *J* = 8.2 Hz, 2H), 3.02 (t, *J* = 8.2 Hz, 2H); EI-MS *m/z* 119 (M^+), 91, 89, 65, 63, 39.

General Procedure for Coupling Reaction of Aryl Halides with Pyrazole, Imidazole, or Benzimidazole Catalyzed by CuI and Amino Acid. A resealable tube was charged with CuI (0.2 mmol), L-proline or *N*,*N*-dimethylglycine (0.4 mmol), K_2CO_3 (4 mmol), aryl halide (2.2 mmol), and azole (2 mmol), evacuated, and backfilled with nitrogen. To this mixture was added 3 mL of DMSO by syringe at room temperature under nitrogen. The mixture was heated at indicated temperature before it was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1/10 to 1/ 8 ethyl acetate/petroleum ether to afford the corresponding coupling product. The data for some selected compounds are as follows.

1-(4-Biphenyl)-1H-imidazole 11f. White solid; mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.68−7.71 (m, 2H), 7.60−7.62 (m, 2H), 7.46−7.49 (m, 5H), 7.35−7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 139.8, 136.6, 130.7, 129.1, 128.8, 128.6, 127.9, 127.1, 121.7, 118.2; EI-MS *m/z* 220 (M^+), 193, 180, 166, 165, 152, 151; ESI-HRMS for $C_{15}H_{13}N_2$ $(M + H)^+$ requires 221.1082, found 221.1073.

1-(2,4-Dimethoxyphenyl)-1H-imidazole 11g. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (br s, 1H), 7.06 (d, *J* = 8.2 Hz, 3H), 6.48 (d, *J* = 2.3 Hz, 1H), 6.41−6.43 (m, 1H), 3.73 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.9, 126.5, 120.0, 104.5, 99.8, 55.8, 55.7; EI-MS *m/z* 204 (M^+), 205, 177, 176, 164, 162, 149, 134; ESI-HRMS for $C_{11}H_{13}N_2O_2$ $(M + H)^+$ requires 205.0979, found 205.0972.

4-Benzoimidazol-1-yl-benzonitrile 13a. White solid; mp 132−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.90 (d, *J* = 8.7 Hz, 3H), 7.69 (d, *J* = 8.7 Hz, 2H), 7.57−7.60 (m, 1H), 7.38−7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.7, 140.2, 134.3, 132.9, 124.6, 124.0, 123.7, 121.2, 118.0, 111.6, 110.3; EI-MS *m/z* 219 (M^+), 191, 164, 102, 91, 75; ESI-HRMS for $C_{14}H_{10}N_3$ $(M + H)^+$ requires 220.0879, found 220.0869.

1-(4-Benzoimidazol-1-yl-phenyl)ethanone 13b. Pale yellow crystals; mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.22 (m, 3H), 7.89−7.91 (m, 1H), 7.60−7.66 (m, 3H), 7.37−7.39 (m, 2H), 2.68 (s, 3H); EI-MS *m/z* 236 (M^+), 222, 221, 193, 192, 166, 43.

General Procedure for Coupling Reaction of Aryl Halides with Indole, Pyrrole, or Carbazole Catalyzed by CuI and Amino Acid. A resealable tube was charged with CuI (0.2 mmol), L-proline or *N*,*N*-dimethylglycine (0.4 mmol), and K_2CO_3 (4 mmol) for aryl iodide or Cs_2CO_3 (4 mmol) for aryl bromide, aryl halide (2.2 mmol), and N-containing heterocycle (2 mmol), evacuated, and backfilled with nitrogen. To this mixture was added 3 mL of DMSO by syringe at room temperature under nitrogen. The mixture was heated at indicated temperature before it was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1/10 to 1/8 ethyl acetate/petroleum ether to afford the corresponding coupling product. The data for some selected compounds are as follows.

1-(4-Methoxyphenyl)-2-methylindole 14f. Gray solid; mp 69−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (m, 1H), 7.25 (m, 2H), 7.07 (m, 1H), 7.05 (m, 3H), 7.01 (m, 1H), 6.38 (s, 1H), 3.89 (s, 3H), 2.99 (s, 3H); EI-MS *m/z* 237 (M^+), 222, 204, 194, 178, 167, 152, 129, 119, 102, 89, 77, 63, 51, 41.

9-(4-Methoxyphenyl)carbazole 14g. White solid; mp 155−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.2 Hz, 2H), 7.45 (d, *J* = 9.0 Hz, 2H), 7.35−7.41 (m, 4H), 7.26 (d, *J* = 9.0 Hz, 2H), 7.11 (d, *J* = 9.0 Hz, 2H), 3.92 (s, 3H); EI-MS *m/z* 273 (M^+), 258, 241, 228, 202, 177, 137, 121, 114, 102, 88, 75, 69, 63, 57, 51.

1-(4-Bromophenyl)pyrrole 15b. Yellow solid; mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.05 (m, 2H), 6.35 (m, 2H); EI-MS *m/z* 223 $(M^+, {}^{81}Br)$, 221 $(M^+, {}^{79}Br)$, 142, 115, 89, 76, 63, 50, 41.

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