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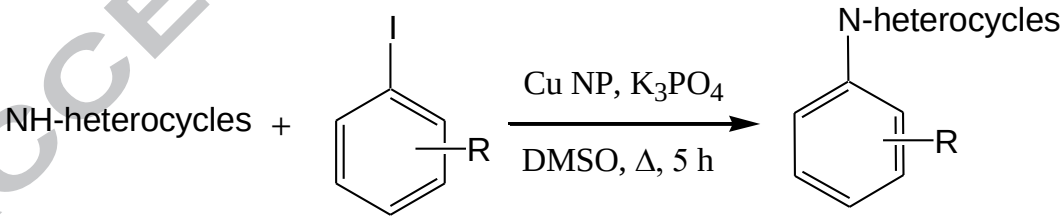
Graphical abstract:



N-arylation of nitrogen containing heterocycles with aryl halides using copper nanoparticle catalytic system

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Abstract: Cu nanoparticles promoted *N*-arylation of NH-heterocycles with aryl halides is an effective and inexpensive method. In this synthetic protocol, good to excellent yields are obtained. Both aryl iodide and aryl bromide are compatible with the reaction conditions.

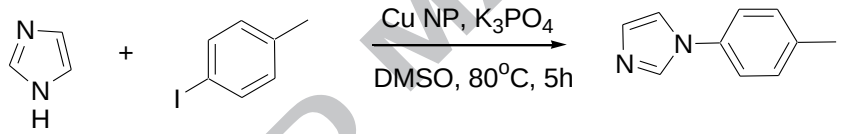
Keywords: Cu nanoparticles, *N*-arylation, NH-heterocycles, C-N coupling, Ullmann type reaction.

Nitrogen-containing heterocycles (e.g. *N*-aryl indoles, *N*-aryl pyrazole, *N*-aryl pyrroles and *N*-aryl imidazoles, etc.) are one of the most powerful and important structural motifs widely utilized in natural products and biologically active pharmaceuticals.[1] The transition metal catalyzed *N*-arylation of nitrogen containing heterocycles with aryl halides are of interest as antipsychotic agents,[2] antiallergic,[3] angiotensin II antagonists,[4] melatonin receptor MT1 agonists,[5] herbicides,[6] COX-2 inhibitors,[7] and as selective ligands for the G2 binding sites.[8] Copper catalyzed Ullmann reaction and the related Goldberg reaction are the most common synthetic protocols for the preparation of *N*-arylazoles.[9] The use of the copper-catalyzed Ullmann-Goldberg coupling reactions has been restricted because of high temperatures (150-200 ^{o}C), use of stoichiometric amounts of copper reagent, extended reaction times with low yield.[10] For these limitations, Pd or Ni-catalyzed C-N coupling reaction have been developed using sterically hindered phosphine ligands under relatively mild conditions and low temperature.[11] In previous years, great efforts have been directed toward modification of highly efficient methods for constructing *N*-aryl azoles[12] using some low-cost and efficient ligands such as diamines,[13] diimines,[14] amino acid derivativess,[15] β-keto esters,[16] diols,[17] aminoarenethiolate,[18] phosphine ligands,[19] hydrazones,[20] *N*-hydroxyimides,[21] ninhydrin,[22] hydroxyquinoline[23] and 1,10-phenanthroline derivatives[24] under mild conditions. Although Pd catalyzed C-N bond formation reactions are well known,[25] ligand promoted Cu-catalyzed chemistry became general for the *N*-arylation of indoles, pyrroles, imidazoles, etc. Therefore, it is very essential to develop both cost-effective and efficient ligands/catalyst systems that help direct C-N cross coupling reactions. In our studies, it has been noticed that ligand-free C-N coupling reaction can be achieved efficiently by the use of Cu nanoparticles (Cu-NP), recently synthesized in our laboratory.[26]

In our previous work,[27b] we have successfully achieved the Cu-NP catalyzed C-N coupling reaction performed at 80^0C. So we wish to report herein an efficient arylation of *N*-heterocycles using Cu nanoparticles (Cu-NP) synthesized in our laboratory and K_3PO_4 as base. Earlier reported Cu-NP catalyzed synthesis of C-C coupling reactions[27a] and C-N coupling reactions[27b] encouraged us to expand the application of Cu-NP to the synthesis of *N*-aryl imidazole and *N*-aryl benzimidazole. This is in accord with a large number of explorations worldwide, and is usually explained by the greater surface to volume ratio for metal nanoparticles, also making them prone to oxidation, thereby increasing their reactivity.[28]

A set of experiments was carried out to optimize the reaction conditions. The C-N coupling reaction between aryl halide and *N*-heterocycle using Cu-NP was studied with indole (**1a**) and 1-iodo-4-methoxy-benzene (**2a**). Results of these experiments are summarized in Table 1. We find an optimum of yield at 1.6 equiv. of Cu NP, with the yield being less both at smaller and larger amount of Cu-NP. Also, K_3PO_4 was found to be the most suitable base for the reaction.

Table 1. Screening of the reaction conditions for Cu NP catalyzed *N*-arylation of imidazole **1a** with 1-iodo-4-methylbenzene **2a**[a]



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

Entry	Solvent	Base	Cu-NP (equiv.)[c]	Time(h)/ (oC)	Yield(%)[b]
1	DMSO	K_3PO_4	00	2/80°C	00
2	DMSO	K_3PO_4	0.1	2/80°C	20
3	DMSO	K_3PO_4	0.5	2/80°C	28
4	DMSO	K_3PO_4	1	2/80°C	45
5	DMSO	K_3PO_4	1.5	2/80°C	68
6	DMSO	K_3PO_4	1.6	2/80°C	72
7	DMSO	K_3PO_4	1.7	2/80°C	68
8	DMSO	K_3PO_4	2	2/80°C	60
9	DMSO	K_3PO_4	1.6	5/80°C	82
10	DMSO	K_3PO_4	1.7	5/80°C	65
11	DMSO	K_3PO_4	1.6	5/110°C	49
12	DMF	K_3PO_4	1.6	5/80°C	42

13	Toluene	K_3PO_4	1.6	5/80°C	30
14	Dioxane	K_3PO_4	1.6	5/80°C	27
15	CH_3CN	K_3PO_4	1.6	5/80°C	38
16	DMSO	KO^tBu	1.6	5/80°C	55
17	DMSO	NaO^tBu	1.6	5/80°C	49
18	DMSO	Et_3N	1.6	5/80°C	24
19	DMSO	Cs_2CO_3	1.6	5/80°C	66
20	DMSO	K_2CO_3	1.6	5/80°C	50

[a] Reaction conditions: all reactions were performed with 1 mmol of imidazole, 1 mmol of ArI, 2 mmol of base in 1 mL of solvent at 80°C under an argon atmosphere.

[b] Yield based on LCMS analysis

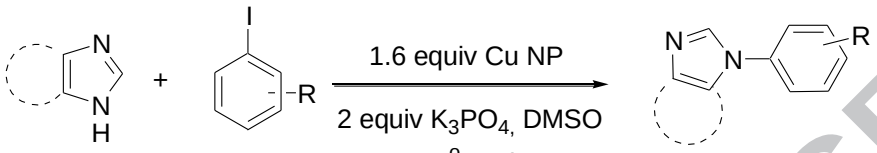
[c] Cu-NP was used as gelatin coated.

As expected, in the absence of Cu-NP, the desired product **3a** was not obtained (Table 1, entry 1). When the equivalence of Cu-NP was increased from 0.1 to 1.7, yield of the desired product (**3a)** increased up to 68% (Table 1, entry 2-7), carrying out the reaction at 80°C for 2h in DMSO. However, when the same reaction was carried out with 1.6 equiv of Cu-NP, the desired product *N*-aryl imidazole was formed in a 72% yield (Table 1, entry 6). Addition of 2 equiv of Cu NP and carrying out the reaction at 80°C for 2h in DMSO afforded the desired product **3a** in a 60% yield (Table 1, entry 8). On the other hand, when the reaction time was increased from 2h to 5h, compound **3a** was obtained in 82% yield (entry 9). If temperature of the reaction is raised to 110°C, the yield of the desired product is reduced to 49% (entry 11). From entries 12-15, it is apparent that the solvent has a significant role on the reaction; DMSO was found to be quite successful for the transformation. Compound **3a** was obtained in 42% yield, when DMF was used instead of DMSO (Table 1, entry 12). When toluene, 1,4-dioxane and acetonitrile were used as solvents, the desired product was obtained in only 30, 27 and 38% yields respectively (Table 1, entry 13, 14 and 15). Different bases were also investigated in this reaction system (Table 1, entry 16-20) and K_3PO_4 found to be superior to KO^tBu, NaO^tBu, Et_3N, Cs_2CO_3 and K_2CO_3. Thus the optimized reaction condition was that which utilized 1.6 equiv Cu NP and 2 equiv K_3PO_4 in DMSO as solvent at 80°C for 5h under argon atmosphere.

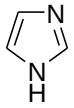
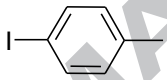
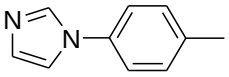
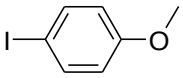
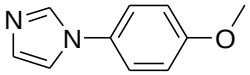
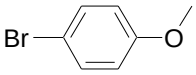
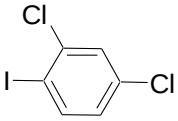
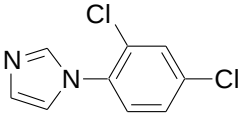
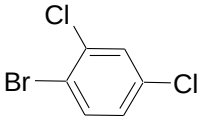
After optimization of reaction conditions, the scope of the *N*-arylation of imidazole and benzimidazole with various substituted aryl and heteroaryl iodides has been explored by using 1.6 equiv Cu NP and 2 equiv K_3PO_4 in DMSO as solvent at 80°C for 5h under inert atmosphere and the results are summarized in Table 2.[36] Aryl and heteroaryl iodides with electron-withdrawing groups in the *ortho*, *meta* or *para*

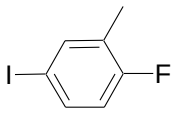
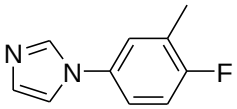
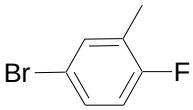
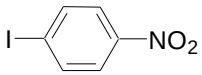
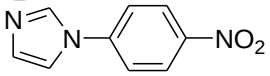
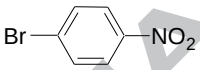
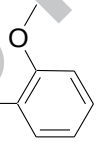
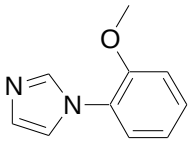
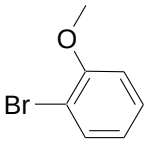
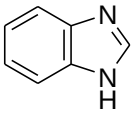
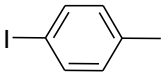
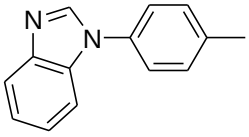
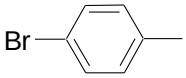
position afforded the coupling products in satisfactory yields. However, electron-donating groups like methyl and methoxy groups in *para* position of the aryl halide provided the coupling products in good yields in 5h at 80°C.

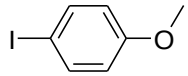
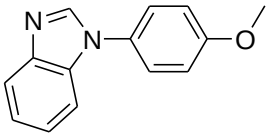
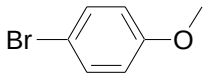
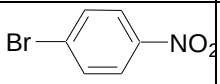
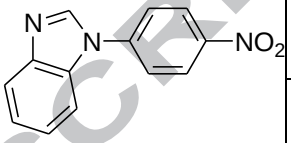
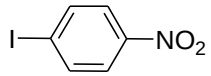
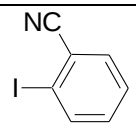
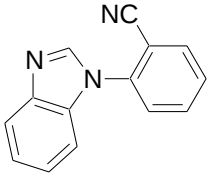
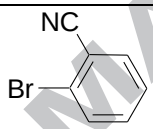
Table 2. Cu NP catalyzed reaction of aryl and heteroaryl halides with imidazoles and benzimidazole[a]



1a-b **2a-n** **3a-j**

Entry	Azoles		ArI		Product		Yield (%)[b]
1	1a		2a		3a[29]		82
			2b				76
2			2c		3b[29]		89
			2d				72
3			2e		3c[30]		83
			2f				61

4			**2g**		**3d**[d]		**81**
			2h				**49**
5			**2i**		**3e**[31]		**91**[c]
			2j				**84**
6			**2k**		**3f**[29]		**82**
			2l				**76**
7	**1b**		**2a**		**3g**[29]		**89**
			2b				**67**

8			**2c**		**3h**[29]		**93**
			2d				**73**
9			**2j**		**3i**[31]		**91**[c]
			2i				**79**
10			**2m**		**3j**[32]		**87**
			2n				**76**

[a]All reactions were carried out using 1 mmol of azoles, 1 mmol of ArX, 2 mmol of K_3PO_4 in 1 mL DMSO at 80°C for 5h. [b]Isolated yields after column chromatography. [c] Reaction was carried out at 80°C for 2 h. [d]New compound.

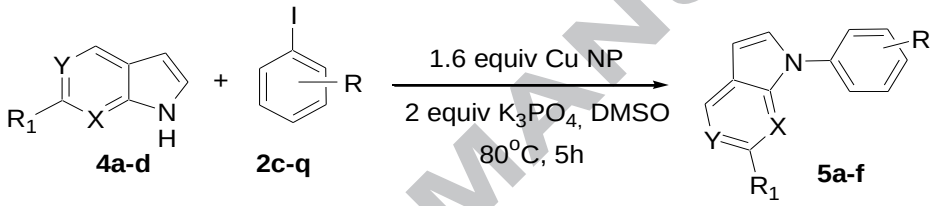
We attempted to explore the scope of the reaction using imidazole and benzimidazole with different type of aryl halides with the standard conditions mentioned above. The results indicated that a variety of aryl halides undergo the reaction smoothly with imidazole and benzimidazole to give the corresponding products in predominantly moderate to excellent yields. When imidazole was treated with aryl iodides **2a-l**, they efficiently reacted to afford the corresponding products **3a-f** in 82, 89, 83, 81, 91 and 82% yield respectively (Table-2, entries 1-6). Interestingly, benzimidazole also worked fine with aryl iodides **2a-n** to provide the target products **3g-j** in 89, 93, 91 and 87% yields respectively (Table-2, entries 7-10). Here also it was found that electron-donating group (-OMe) in ortho position lowered the yield to 82%.

In addition to aryl iodides, aryl bromides whether electron-rich or electron-deficient, all worked moderately under these conditions. Aryl bromides, however, gave smaller yields compared to their iodo-analogs. When imidazole was treated with aryl bromides **2a-l**, they efficiently reacted to afford the corresponding products **3a-f** in 76, 72, 61, 49, 84 and 76 % yield respectively (Table-2, entries 1-6). The

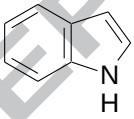
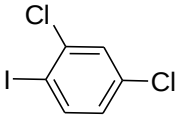
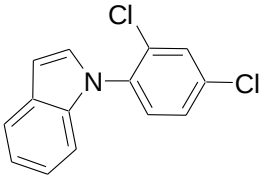
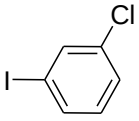
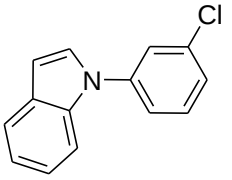
N-arylation of benzimidazole with aryl bromide **2a-n** was quite impressive (67, 73, 79 and 76 % yield respectively). Attempts to shorten the reaction times by raising the reaction temperature also reduced the yield a little. However, aryl chloride did not show any significant conversion in this system.

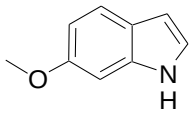
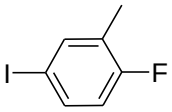
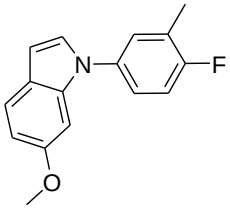
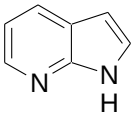
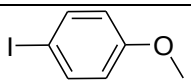
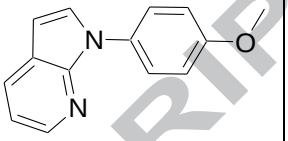
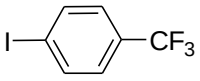
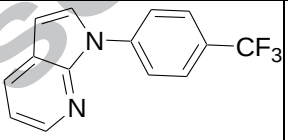
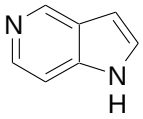
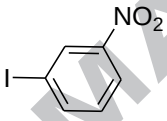
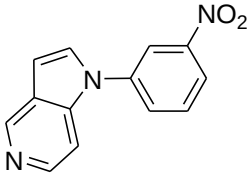
We also investigated the generality of the method where indole and azaindole took part in the reaction. The reaction between various types of indole and azaindole with various substituted aryl iodides are summarized in Table 3 (entries 1-6). The reaction of *para* substituted aryl iodide gave respective products in good yields (entries 4 & 5) where disubstituted aryl iodides gave comparatively low yield of the corresponding products (entries 1 & 3). Although *meta* substituted aryl iodides also led to good yield (entries 2 & 4). Other examples of C-N coupling product obtained with Cu-NP are given in an earlier publication.[27b]

Table 3. Cu NP catalyzed reaction of aryl halides with indole and azaindole[a]



X = N, R_1 = H, Y= CH
X= CH, R_1 = H,Y = N
X= CH, R_1= OMe, Y= CH

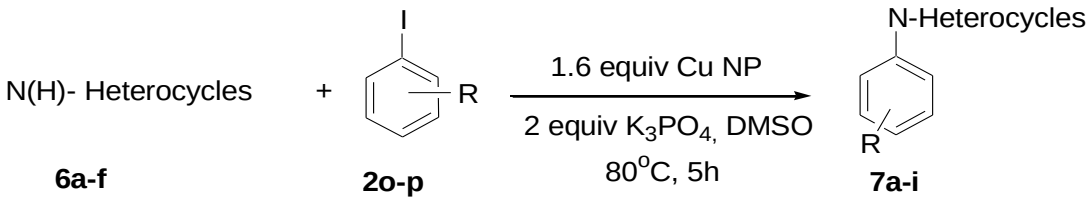
Entry	Azoles		ArI		Product		Yield (%)[b]
1	4a		2e		5a[c]		73
2			2o		5b[28]		87

3	**4b**		**2g**		**5c**[c]		**71**
4	**4c**		**2c**		**5d**[28]		**83**
5			**2p**		**5e**[c]		**91**
6	**4d**		**2q**		**5f**[c]		**89**

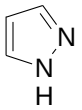
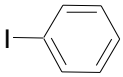
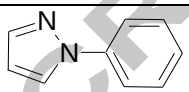
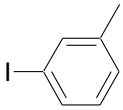
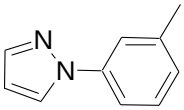
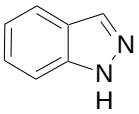
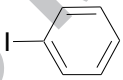
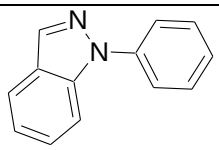
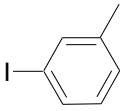
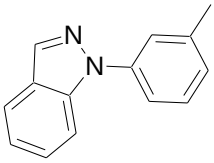
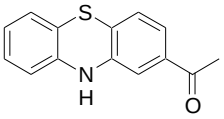
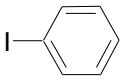
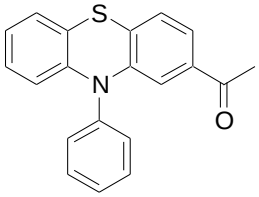
[a] All reactions were carried out using 1 mmol of azoles, 1 mmol of ArI, 2 mmol of K_3PO_4 in 1 mL DMSO at 80°C for 5h. [b] Isolated yields after column chromatography. [c]New compounds.

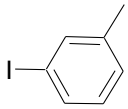
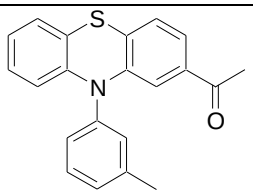
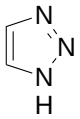
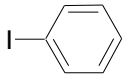
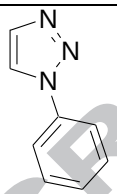
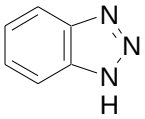
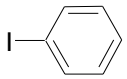
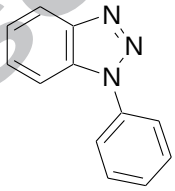
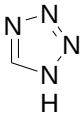
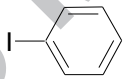
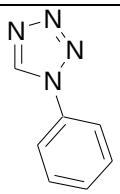
The extended scope of C-N bond formation reaction has been observed further by using pyrazole, indazole and substituted phenothiazine. The results were accumulated in Table 4. It was observed that desired product was formed effectively with aryl iodide. Good yields are obtained with iodobenzene (entries 2 and 4), but when electron rich group was present in meta position of iodobenzene, yields became lower to 73% and 71% (entries 1 and 3). Noticeably this effect was just opposite in case of phenothiazine as sterically hindered azole gave lower yields with 3-methyl iodobenzene (entries 5 and 6). However, a trace of product was formed when triazole, benzotriazole and tetrazole were coupled with iodobenzene (entries 7, 8 and 9).

Table 4. Cu NP catalyzed reaction of aryl halides with Pyrazole, Indazole and Phenothiazine[a]



6a-f **2o-p** **7a-i**

Entry	Azole		ArI		Product		Yield (%)[b]
1	6a		2o		7a[33]		73
2			2p		7b[34]		87
3	6b		2o		7c[35]		71
4			2p		7d[c]		83
5	6c		2o		7e[c]		91

6			**2p**		**7f**[c]		**79**
7	**6d**		**2o**		**7g**		**Trace**
8	**6e**		**2o**		**7h**		**Trace**
9	**6f**		**2o**		**7i**		**Trace**

[a] All reactions were carried out using 1 mmol of azoles, 1 mmol of ArI, 2 mmol of K_3PO_4 in 1 mL DMSO at 80°C for 5h. [b] Isolated yields after column chromatography. [c]New compounds.

In summary, we have developed an efficient modified protocol for the synthesis of *N*-arylindole, *N*-arylimidazoles, *N*-arylpyrazole, *N*-arylindazole with aryl iodides in good to excellent yields. The arylation occurs under mild condition using Cu NP which is inexpensive. This advantage is expected to prompt the synthetic applications of this Cu NP catalyzed C-N bond formation reactions.

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Supporting data

Analytical information and ^{1}H-NMR, ^{13}C-NMR and mass spectra of some product compounds are given in Supporting Information.

References and notes:

(1) For reviews, see: (a) P. N. Craig In *Comprehensive Medicinal Chemistry*, Vol. 8; Drayton, C. J., Ed.; Pergamon Press: New York, **1991;** (b) B. Dyck, V. S. Goodfellow, T. Phillips, J. Grey, M. Haddach, M, Rowbottom, G. S. Naeve, B. Brown, J. Saunders, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1151; (c) J. B. Buckingham, In *Dictionary of Natural Products*, Vol. 1; Chapman and Hall: London, **1994**.

(2) (a) J. Perregaard, J. Arnt, K. P. Bogeso, J. Hyttel, C. J. Sanchez, *Med. Chem.* **1992**, *35*, 1092. (b) K. Anderson, T. Liljefors, J. Hyttel, J. Perregaard, *J. Med. Chem.* **1996**, *39*, 3723.

(3) P. C. Unangst, D. T. Connor, S. S. Stabler, R. J. Weikert, M. E. Carethers, J. A. Kennedy, D. O. Thueson, J. C. Chestnut, R. L. Adolphson, M. C. Conroy, *J. Med. Chem.* **1989**, *32*, 1360.

(4) S. R. Jahangir Stabler, *Synth. Commun.* **1994**, *24*, 123.

(5) G. Spadoni, C. Balsamini, A. Bedini, G. Diamantini, B. DiGiacomo, A. Tontini, G. Tarzia, M. Mor, P. V. Plazzi, S. Rivara, R. Nonno, M. Pannacci, V. Lucini, F. Fraschini, B. M. Stankov, *J. Med. Chem.* **1998**, *41*, 3624.

(6) F. M. Pallos, C. J. Matheus, U. S. Patent 5, 739, 353 (**1996**).

(7) H. Sano, T. Noguchi, A. Tanatani, Y. Hashimoto, H. Miyachi, *Bioorg. Med. Chem.* **2005**, *13*, 3079.

(8) (a) C. Sanchez, J. Arnt, B. Costall, M. E. Kelly, R .J. Naylor, J. Perregaard, *J. Pharmacol. Exp. Ther.* **1997**, *283*, 1323; (b) J. Perregaard, E. K. Moltzen, E. Meier, C. Sanchez, *J. Med. Chem.* **1995**, *38*, 1998; (c) R. Sarges, H. R. Howard, H. B. K. Koe, A. Weissman, *J. Med. Chem.* **1989**, *32*, 437. (d) F. R. Wust, T. Kniess, *J. Labelled Compd. Radiopharm.* **2005**, *48*, 31;

(9) I. Goldberg, *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 1691.

(10) (a) F. Ullmann, *Ber. Dtsch. Chem. Ges*. **1903**, *36*, 2382. (b) J. Lindley, *Tetrahedron* **1984**, *40*, 1433. (c) M. Schnürch, R. Flasik, A. F. Khan, M. Spina, M. D. Mihovilovic, P. Stanetty, *Eur. J. Org. Chem.* **2006**, 3283.

(11) For reviews, see: (a) J. P. Wolfe, S. Wagaw, J. F. Marcoux, S. L. Buchwald, Acc. Chem. Res. 1998, *31*, 805. J. F. Hartwig, *Angew. Chem., Int. Ed.* **1998**, *37*, 2046. (b) B. H.Yang, S. L. Buchwald, *J. Organomet. Chem.* **1999**, *576*, 125.

(12 S. V. Ley, A. W. Thomas, *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.

(13) J. C. Antilla, A. Klapars, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 11684.

(14) H. J. Cristau, P. Cellier, J. F. Spindler, M. Taillefer, *Eur. J. Org. Chem.* **2004**, *10*, 5607.

(15) Q. Cai, W. Zhu, H. Zhang, Y. Zhang, D. Ma, *Synthesis* **2005**, 695.

(16) X. Lv, Bao, W. *J. Org. Chem.* **2007**, *72*, 3863.

(17) F. Y. Kwong, A. Klapars, S. L. Buchwald, *Org. Lett.* **2002**, *4*, 581.

(18) T. Jerphagnon, G. P. M. van Klink, J. G. de Vries, G. van Koten, *Org. Lett.* **2005**, *7*, 5241.

(19) (a) L, Xu, D. Zhu, F. Wu, R. Wang, B. Wan, *Tetrahedron* **2005**, *61*, 6553. (b) H. Rao, Y. Jin, H. Fu, Y. Jiang, Y. Zhao, *Chem. Eur. J*. **2006**, *12*, 3636. (c) Z. Zhang, J. Mao, D. Zhu, F. Wu, H. Chen, B. Wan, *Tetrahedron* **2006**, *62*, 4435.

(20) T. Mino, Y. Harada, H. Shindo, M. Sakamoto, T. Fujita, *Synlett* **2008**, 614.

(21) H. C. Ma, X.-Z. Jiang, *J. Org. Chem*. **2007**, *72*, 8943.

(22) Y. Z. Huang, J. Gao, H. Ma, H. Miao, J. Xu, *Tetrahedron Lett*. **2008**, *49*, 948.

(23) L. Liu, M. Frohn, N. Xi, C. Dominguez, R. Hungate, P. J. Reider, *J. Org. Chem*. **2005**, *70*, 10135.

(24) (a) A. Kiyomori, J. F. Marcoux, S. L Buchwald, *Tetrahedron Lett*. **1999**, *40*, 2657. (b) M. Kuil, E. K. Bekedam, G. M. Visser, A. van den Hoogenband, J. W. Terpstra, P. C. J. Kamer, P. W. N. M. Kamer van Leeuwen, G. P. F. van Strijdonck, *Tetrahedron Lett*. **2005**, *46*, 2405. (c) R. A. Altman, S. L. Buchwald, *Org. Lett*. **2006**, *8*, 2779. (d) R. Hosseinzadeh, M. Tajbakhsh, M. Alikarami, *Synlett* **2006**, 2124. (e) R. A. Altman, E. D. Koval, S. L. Buchwald, *J. Org. Chem*. **2007**, *72*, 6190.

(25) (a) A. R. Muci, S. L. Buchwald, *Top Curr. Chem.* **2002**, *219*, 131.

(26) A. K. Chatterjee, R. K. Sarkar, A. P. Chattopadhyay, P. Aich, R. Chakraborty, T. Basu, *Nanotechnology* **2012**, *23*, 85103.

(27) (a) G. Pai, A. P. Chattopadhyay, *Synthesis* **2013**, *45*(11), 1475. (b) G. Pai, A. P. Chattopadhyay, *Tetrahedron Lett.* **2014**, *55*, 941.

(28) F. F. Yong, Y. C. Teo, S. H. Tay, B. Y. H. Tan, K. H. Lim, *Tetrahedron Lett.* **2011**, *52*, 1161.

(29) A. K. Verma, J. Singh, V. K. Sankar, R. Chaudhary, R. Chandra, *Tetrahedron Lett*. **2007**, *48*, 24, 4207.

(30) D. Daniel, M. Isabel, R. Andreas, R. T. Werner, *J. Org. Chem.* **2011**, *76*, 4, 1151.

(31) Y. X. Xie, S. F. Pi, J. Wang, D. L. Yin, J. H. Li, *J. Org. Chem.* **2006**, *71*, 21, 8324.

(32) H. Maheswaran, G. G. Krishna, K. L. Prasanth, V. Srinivas, G. K. Chaitanya, K. Bhanuprakash, *Tetrahedron* **2008**, *64*, 10, 2471.

(33) B. A. Khakiani, K. Pourshamsian and H. Veisi , *Applied Organometallic Chemistry*, **2015**, *29*, 5, 334.

(34) V. S. Thirunavukkarasu, K. Raghuvanshi, and L. Ackermann, *Org Letter*, **2013,** *15*, 13, 3286**.**

(35) W. Stadlbauer, *Science of synthesis*, **2002**, *12*, 227.

(36) General procedure for Cu-NP catalyzed *N*-arylations of azoles with aryl halides **(Table-2):** An oven dried two-necked round bottom flask was charged with aryl halide (1 mmol) and K_3PO_4 (2 mmol), evacuated and backfilled with argon. The azole compound (1 mmol) and 2 mL of DMSO were added under argon. After that Cu-NP (1.6 mmol) was added and the flask was again backfilled with argon. The flask was then immersed in a preheated oil bath at 80^0C until the conversion was completed (detected by TLC). The cooled mixture was partitioned between ethyl acetate (10 mL) and saturated NH_4Cl (10 mL). The aqueous layer was extracted with ethyl acetate (2 x 10 mL), the organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate in hexane (1.5-10%) as eluent to afford the desired product. All the products

have been characterized by ^{1}H NMR, ^{13}C NMR and mass spectroscopy. For new products, FTIR data were also recorded.

Analytical data of compound **3a:** Light yellow solid, 25% EtOAc/hexanes; mp: 62-64^{o}C; Yield 82%; R_f = 0.3; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.20 (s, 1H), 7.70 (s, 1H), 7.54 (d, J = 8 Hz, 2H), 7.33 (d, J = 8 Hz, 2H), 7.09 (s, 1H), 2.35 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.2, 135.4, 134.6, 130.2, 129.7, 120.2, 118, 20.4; MS(EI) 159.1 (M^+). Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92, H, 6.37, N, 17.71. Found: C, 75.87, H, 6.41, N, 17.69.

Highlights of the manuscript are

- Important coupling reaction studied
- Easy and robust preparation of catalyst
- Relatively mild reaction conditions
- Reasonably short time of reaction
- Reasonably high yields