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An efficient and improved protocol for the N-arylation of N-heteroaryls using Ionic liquid as a reaction media

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ABSTRACT

N-arylation of N-heteroaryls is described with aryl/ heteroaryl halides in the presence of CuI in ionic liquid [Bmim]BF_4 as a reaction media. The reaction is very efficient and yields are very high. Moreover, the method is applicable for a variety of N-heteroaryls and Ionic liquid was recycled and reused.

Key Words: Aryl/ hetero aryl halides, Imidazoles, Ionic Liquid (IL).

INTRODUCTION

N-Aryl heterocycles like imidazole, benzimidazole, benzotriazole, pyrazole and indazole serves as important building blocks in pharmaceuticals [1]. Some of the N-heterocyclic moiety is also found in many bioactive natural products [2]. In addition 1-aryl benzotriazole are useful intermediates in the synthesis of pyridoacridine [3] and carbolin synthesis [4]. Among the heterocyclics, N-aryl imidazole is widely studied because of its distinct biomedical properties like, AMPA receptor antagonists [5] and thromboxane synthase inhibitors [6]. The classical Ullmann reaction [7] has been known to perform N-arylation in the presence of copper at higher temperature. Subsequently, various reports [8] have been appeared for N-arylation of N-heterocycles using ligand or / and copper salts as a promoter. A low temperature (90 ^{0}C) methodology has been demonstrated using aryllead [9] in the presence of $Cu(OAc)_2$ but these methods generates lead salt as a by-product which is toxic in nature. Pd catalyst in combination with Cu (II) as co-catalyst was found to catalyze the N-arylation of benzotriazole in DMF (150 ^{O}C). Recently, iron-copper was found as an effective catalyst for N-arylation [10] of imidazoles in DMF (100 ^{0}C). Copper catalyzed coupling of aryl halides with imidazoles also reported using CuOTf [11] as a copper source in benzene at 125 ^{0}C with longer reaction time (24-48 hrs). Very recently, ligands free [12] N-arylation has been reported using copper (I) salt. Literature also revealed that the suitable combination of base and solvent plays very important role in the catalytic activity and the wide range of bases like potassium phosphate [13], Cesium carbonate [14], sodium methoxide [15] and sodium hydroxide [16] has been reported to achieve higher degree of N-arylation. Though the catalytic system is one of the most efficient protocols for N-arylation of N-heteroaryls, it has some drawbacks of using expensive palladium catalyst or ligand, which are difficult to prepare. Moreover, the reported methods require higher boiling solvents like (DMF, DMSO), elevated temperature, longer reaction time. Besides this most of the method lacks generality towards aryl halides of generates and confined to the use of aryl iodides, which have limited availability. In this context, it is desirable to develop efficient procedure using reusable solvent. Very recently, 1-butyl-3-methylimidazolium tetrafluoroborate [Bmim]BF_4 was found to accomplish the N-arylation of cyclic secondary amines after longer duration [17].

MATERIALS AND METHODS

Experimental Part

Microwave reactions were conducted using a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC). The machine consists of a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300W. Reactions were performed in glass vessels (capacity 10 mL) equipped with a magnetic stirring bar and sealed with a septum. The target temperature was set and fixed during the irradiation. Settings and readings for power (W) and pressure were taken from the instrument. Melting points were determined in open capillary tubes using a Electro Thermal 9100 series apparatus. Column chromatography (CC): silica gel (SiO_2; BDH 60 – 120 mesh). Thin layer chromatography (TLC): silica gel GF254 (Merck) plates. IR Spectra: Perkin Elmer RX1 FT-IR spectrophotometer. ^1H and ^{13}C-NMR spectra: Varian Gemini 200 MHz spectrometer; DMSO as solvent; at 200 MHz and 70 MHz, resp. ESI-MS: LC-MSD Trap-SL spectrometer.

General procedure for the synthesis of 3-hydroxy oxindoles*:* A mixture of substituted N-heteroaryls (1 mmol), Ionic liquid [Bmim]BF_4 (2 mL) and Cu I (10 mol%) was heated at 70 ^{0}C for 0.5 hr. Then aryl halide (1.1 mmol) was added and the mixture heated at 70 ^{0}C for stipulated time (see table). The progress of the reaction was monitored by TLC. The reaction mixture was extracted with diethyl ether (3X10 mL), and concentrated under vacuum. The residue was purified through column or recrystalised from suitable solvent. The residual ionic liquid was dried under vacuum at 80 ^{O}C for 4 hrs and reused for further cycles.

Data of All Representative Compounds:

Compound 1: liquid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.18 (br, 1H, s), 7.25 (br, 1H, s), 7.3–7.5 (5H, m), 7.83 (br, 1H, s). EIMS: *m/z* 144 (M^+), 117, 77, 51. IR (KBr): ν = 3424, 3117, 1600, 1509, 1304 cm^{-1}. Anal. Calcd. for $C_8H_8N_2$: C, 74.98; H, 5.59; N, 19.43. Found: C, 74.73; H, 5.40; N, 19.39.

Compound 2: liquid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.18 (3H, s), 7.05 (1H, s), 7.20 (2H, m), 7.28 (1H, m), 7.33-7.35 (2H, m), 7.58 (1H, s). EIMS: *m/z* 159 (M^+1), 79. IR (KBr) ν = 3412, 3107, 1580, 1510 cm^{-1}. Anal. Calcd. for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.84; H, 6.42; N, 17.69.

Compound 3 & 4: Yellow solid; mp: 105 ^{o}C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.39 (3H, s), 7.06 (1H, s), 7.24 (1H, s), 7.42 (1H, d, J = 8.30 Hz), 7.62 (1H, s), 8.18 (1H, m), 8.25 (1H, s). EIMS: *m/z* 204 (M^+1), 160, 159. IR (KBr): ν = 3089, 2928, 1584, 1502 cm^{-1}. Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.13; H, 4.40; N, 20.59.

Compound 5: Yellow solid; mp: 202 ^{o}C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.28 (2H, s), 7.6 (2H, d, J = 9.06 Hz), 7.95 (1H, s), 8.4 (2H, d, J = 9.06 Hz). EIMS: *m/z* 190 (M^+1), 175, 159. IR (KBr): ν = 2925, 2854, 1513, 1462 cm^{-1}. Anal. Calcd. for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.13; H, 3.70; N, 22.19.

Compound 6 & 16: White solid; mp: 147 ^{o}C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.27 (1H, m), 7.36 (1H, m), 7.47 (1H, dd, J = 8.10 Hz, J = 1.10 Hz), 7.54 (1H, m), 7.75 (1H, m), 7.84 (1H, m), 7.86 (br, 1H, s). EIMS: *m/z* 169 (M^+). IR (KBr): ν = 3016, 2940, 2220, 1551, 1455 cm^{-1}. Anal. Calcd. for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 70.93; H, 4.10; N, 24.79.

Compound 7: White solid; mp: 167 ^{o}C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.63 (1H, d, J = 0.94 Hz), 7.7 (1H, d, J = 0.94 Hz), 7.8 (1H, t, J = 2.07 Hz), 7.85 (1H, t, J = 2.83 Hz), 8.1 (1H, t, J = 2.07 Hz), 8.2 (1H, t, J = 2.83 Hz), 9.2 (1H, s). EIMS: *m/z* 240 (M^+Na), 217(M^+), 216. IR (KBr): ν = 3091, 2924, 1694, 1525, 1355 cm^{-1}. Anal. Calcd. for $C_{10}H_9N_3O_3$: C, 54.79; H, 4.14; N, 19.17. Found: C, 54.73; H, 4.10; N, 19.13.

Compound 8**:** liquid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.92–6.95 (2H, m), 7.07–7.10 (1H, m), 7.11 (1H, s), 7.14 (1H, s), 7.72 (1H, s). EIMS: *m/z* 151 (M^+1). IR (KBr): ν = 3079, 2920, 2858, 1611, 1565, 1331 cm^{-1}. Anal. Calcd. for $C_7H_6N_2S$: C, 55.97; H, 4.03; N, 18.65. Found: C, 55.93; H, 4.04; N, 18.59.

Compound 9: Solid; mp: 172 ^{0}C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.57 (1H, t, J = 2.00 Hz), 7.80 (1H, d, J = 1.51 Hz), 7.90 (2H, d, J = 9.20 Hz), 8.04 (1H, d, J = 2.60 Hz), 8.35 (2H, d, J = 9.20 Hz). EIMS: *m/z* 395(M^+K), 308,

186. IR (KBr): ν = 2925, 2719, 1583, 1563 cm^{-1}. Anal. Calcd. for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.13; H, 3.70; N, 22.23.

Compound 10: Yellow solid; mp: 207 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.9 (1H, d, J = 8.78 Hz), 8.2 (1H, d, J = 2.93 Hz), 8.45 (1H, d, J = 2.19 Hz), 8.5 (1H, d, J = 2.93 Hz), 8.6 (1H, s), 8.7 (1H, m), 9.2 (1H, s). EIMS: *m/z* 285 (M^+). IR (KBr): ν = 3073, 1529, 1309 cm^{-1}. Anal. Calcd. for $C_{12}H_7N_5O_4$: C, 50.53; H, 2.47; N, 24.55. Found: C, 50.44; H, 2.40; N, 24.49.

Compound 12: Semi solid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.9 (1H, s), 7.3 (2H, m), 7.55 (1H, t, J = 8.30 Hz, J = 7.554 Hz), 8.05 (1H, d, J = 7.55 Hz), 8.45 (2H, d, J = 8.30 Hz). EIMS: *m/z* 330 ($M\text{-}1^+$), 310, 307, 282, 226, 159, 136. IR (KBr): ν = 2927, 2856, 1587 1417 cm^{-1}. Anal. Calcd. for $C_{14}H_7F_6N_3$: C, 50.77; H, 2.13; N, 12.69. Found: C, 50.72; H, 2.10; N, 12.66.

Compound 13: White solid; mp: 188 ^0C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.7 (1H, s), 7.29 (1H, s), 7.79 (1H, s), 8.0 (1H, m), 8.12 (1H, s), 8.53 (1H, s). EIMS: *m/z* 395 (M^+K), 308, 186. IR (KBr): ν = 2925, 2719, 1583, 1563 cm^{-1}. Anal. Calcd. for $C_{14}H_9BrF_3N_3$: C, 47.21; H, 2.55; N, 11.80. Found: C, 47.23; H, 2.50; N, 11.79.

Compound 14: Ash color solid; mp: 97 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.65 (3H, s), 7.38 (2H, d), 7.55 (2H, d, J = 8.30 Hz), 8.1 (2H, d, J = 8.30 Hz), 8.21 (1H, s). EIMS: *m/z* 187 (M^+1), 159. IR (KBr): ν = 3111, 3058, 1675, 1604 cm^{-1}. Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.94; H, 5.40; N, 15.03.

Compound 15: Thick Yellow solid; mp: 130 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 2.65 (3H, s), 7.3 (1H, d, J = 7.55 Hz), 7.4 (2H, t, J = 7.55 Hz), 7.58 (3H, m,), 7.82 (2H, d, J = 7.55 Hz), 7.97 (1H, s), 8.1 (2H, m). EIMS: *m/z* 264 (M^+1), 263(M^+), 236, 235. IR (KBr): ν = 3114, 3084, 2925, 1675, 1600 cm^{-1}. Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.23; H, 6.04; N, 10.59.

Compound 17: White solid; mp: 132^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.2 (2H, m), 7.38 (2H, t, J = 7.36 Hz, J = 7.932 Hz), 7.55 (2H, t, J = 7.36 Hz, J = 7.74 Hz), 7.6 (1H, d, J = 1.322 Hz), 7.75 (1H, J = 7.74 Hz, J = 7.93 Hz), 7.8 (1H, s), 7.82 (1H, m), 7.87 (1H, m). EIMS: *m/z* 246 (M^+1), 235. IR (KBr): ν = 2925, 2854, 2226, 1498 cm^{-1}. Anal. Calcd. for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.85. Found: C, 77.03; H, 6.04; N, 16.79.

Compound 18: White solid; mp: 40 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.12 (1H, s), 7.29–7.32 (1H, dd, J = 5.01 Hz, J = 7.42 Hz), 7.76–7.78 (1H, d, J = 8.09 Hz), 7.92–7.96 (2H, m), 8.44–8.46 (1H, m), 8.54 (1H, s). EIMS: *m/z* 145(M^+), 118, 91, 78, 51, 43. IR (KBr): ν = 3388, 2925, 2853, 1686, 1594, 1485, 1443 cm^{-1}. Anal. Calcd. for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 28.95. Found: C, 66.13; H, 4.80; N, 28.89.

Compound 19: White solid; mp: 88 ^0C. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.2 (2H, t, J = 6.04 Hz), 7.38 (5H, m), 7.6 (1H, s), 7.7 (2H, d, J = 7.55 Hz), 7.85 (1H, d, J = 7.55 Hz). EIMS: m/z 243 (M^+Na). IR (KBr): ν = 3029, 2926, 1595, 1482 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.30; H, 5.80; N, 18.79.

Compound 21: Gold metallic solid; mp: 183 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.4 (2H, m), 7.6 (1H, m), 7.8 (1H, d, J = 4.68 Hz), 7.9 (2H, d, J = 8.59 Hz), 8.34 (1H, s), 8.49 (2H, d, J = 8.59 Hz). EIMS: *m/z* 240 (M^+1), 239 (M^+). IR (KBr): ν = 3087, 3056, 1596, 1511, 1346 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.84; H, 5.14; N, 16.43.

Compound 22: Light yellow solid; mp: 187 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.4 (2H, m), 7.7 (1H, d, J = 9.06 Hz), 7.8 (1H, m), 8.15 (1H, m), 8.6 (2H, m), 9.4 (1H, m). EIMS: *m/z* 241 (M^+1), 240 (M^+). IR (KBr): ν = 3050, 2997, 1585, 1372 cm^{-1}. Anal. Calcd. for $C_{13}H_{12}N_4O_2$: C, 60.93; H, 4.72; N, 21.86. Found: C, 60.91; H, 4.70; N, 21.79.

Compound 23: Yellow solid; mp: 267 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.4 (2H, br), 7.0 (3H, m), 7.4 (1H, d, J = 7.823 Hz), 7.8 (2H, d, J = 8.60 Hz), 8.45 (2H, d, J = 8.60 Hz). EIMS: *m/z* 254 (M^+), 242, 176, 152, 131. IR (KBr): ν = 3425, 3063, 1517, 1348 cm^{-1}. Anal. Calcd. for $C_{13}H_{10}N_4O_2$: C, 61.41; H, 3.96; N, 22.04. Found: C, 61.43; H, 3.90; N, 22.01.

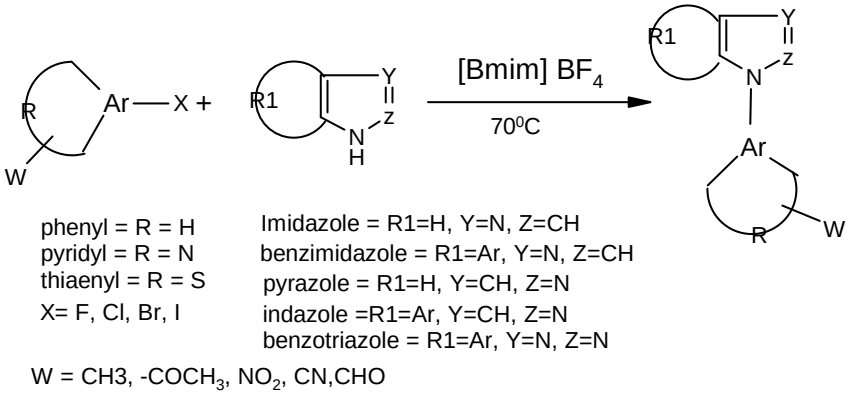
Compound 24: White solid; mp: 158 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.2 (1H, br), 7.2 (1H, m), 7.6 (2H, m), 8.1 (2H, d, J = 8.77 Hz), 8.4 (2H, d, J = 8.77 Hz). EIMS: *m/z* 272 (M^+1), 271 (M^+). IR (KBr): ν = 3335, 2924, 1515, 1340 cm^{-1}. Anal. Calcd. for $C_{13}H_9N_3O_2S$: C, 57.55; H, 3.34; N, 15.49. Found: C, 57.43; H, 3.30; N, 15.39.

Compound 25: White solid; mp: 97 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.9 (2H, d, J = 8.81 Hz), 7.3 (2H, m), 7.9 (2H, m), 8.2 (2H, d, J = 9.55 Hz). EIMS: *m/z* 263 (M^+Na). IR (KBr): ν = 3063, 2992, 1599, 1360 cm^{-1}. Anal. Calcd. for $C_{12}H_8N_4O_2$: C, 60.00; H, 3.36; N, 23.32. Found: C, 60.94; H, 3.40; N, 23.30.

RESULTS AND DISCUSSION

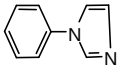
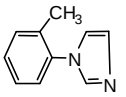
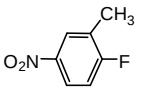
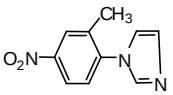
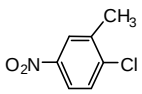
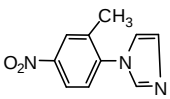
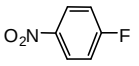
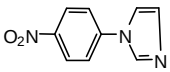
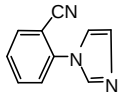
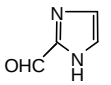
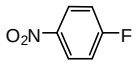
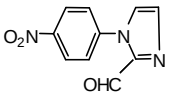
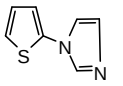
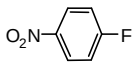
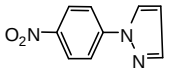
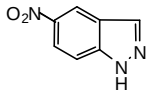
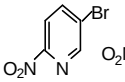
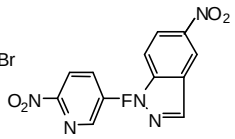
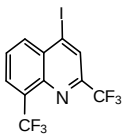
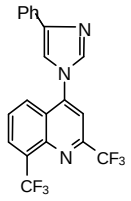
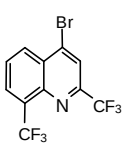
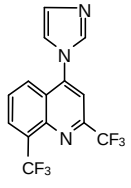
Recently, Ionic liquid mediated reactions are an area of growing interest because of distinct properties like thermal stability, reusability, and non-flammability [18]. Their high polarity and the ability to solublilise both inorganic and organic compounds can result to enhance the rate of the reaction. In the realm of ionic liquid [Bmim]BF_4 has become more popular and used in various organic transformations like vicinal diamines [19], one-pot syntheses of 2*H*-indazolo[2,1-b]-phthalazine-triones [20], and hydrative cyclization of 1,6-diynes [21]. Our interest in the development of new methodologies [22] in the area of green chemistry [23] prompted us wish to report the N-arylation of hetroaryls in the presence of CuI in ionic liquid. (scheme 1)

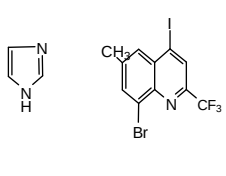
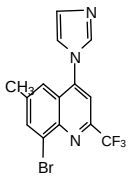
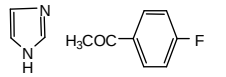
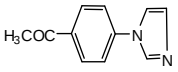
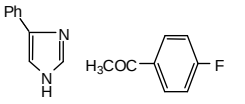
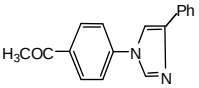
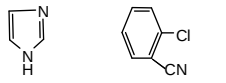
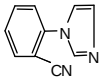
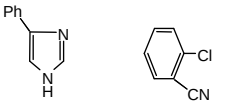
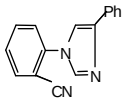
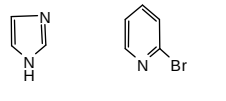
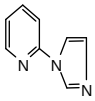
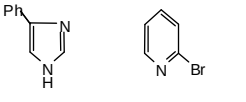
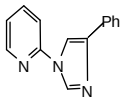
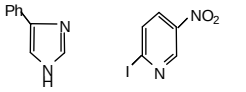
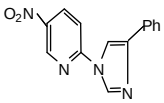
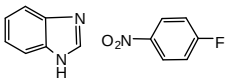
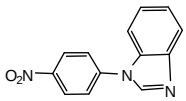
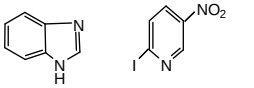
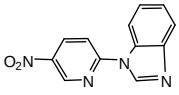
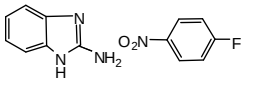
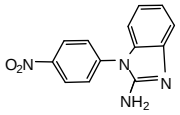
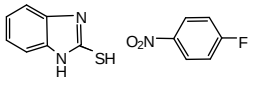
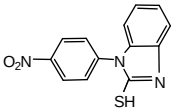
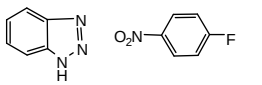
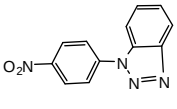
Scheme 1: Reaction of N-arylation/N-heteroaryls using Ionic liquid



Thus, initially the reaction of fluorobenzene (***Table 1,*** entry-1) with imidazole was performed in ionic liquid [Bmim] BF_4 at RT for 12 hrs which gave less yield (20 %) of the N-arylated product. The yield (35 %) was further improved by the reaction heating at 70 ^{0}C for 9 hrs. Next, we attempted the same reaction in presence of CuI 20 mol%, which showed dramatic change with the completion of reaction in 2 hrs with high yield (79 %). Further efforts were concentrated to optimize the mole ratio of CuI. The experiments with different mol% of CuI revealed that 10 mol% CuI was suitable for optimum yield. The product was isolated by the extraction with ether. The remaining ionic liquid was dried under vacuum at 80 ^{0}C for 4 hrs and reused for five cycles. It was notice that the reaction gave consistent yield up to three cycles but the activity of ionic liquid gradually decreased from four to five. Encourage with this results, we have examined the arylation of variety of arylation herteroarenes in optimization condition. We have investigated the electronic effect on the reactivity of aryl halides. Thus 2-methylfluorobenzene (***Table 1,*** entry-2) required longer reaction time (8 hrs) and gave relatively fewer yields. This fact indicated that electron releasing effect of 2-methyl fluorobenzene substantially affect the yield of coupling product. However, the introduction of electron withdrawing group enhances the reactivity of same system. For example, N-aryaltion of imidazole with 2-fluoro-5-nitrotoluene (***Table 1,*** entry- 3) proceeded smoothly and leads to high yield of product. The scope of this methodology was exploited for other N-hetero aromatics. It was observed that benzimidazole (***Table 1,*** entry- 21, 22), benzotriazole (***Table 1,*** entry- 25) and indazole (***Table 1,*** entry- 10) reacted analogously with aryl halides in identical condition to give N-arylated product in good yield.

Table 1- N-arylation of N-heteroaryls using Ionic Liquid [Bmim] BF_4

Entry	N-heteroaryls	Aryl halides	[a]products	reaction time (hrs)	[b]Yield(%)
1				2	79
2				8	60
3				3	93
4				4	91
5				3.5	95
6				4	87
7				3	81
8				5	63
9				4	78
10				3	85
11				2.5	88
12				4.5	79

13				2.5	85
14				3	90
15				2.5	93
16				4	85
17				3	90
18				4	72
19				3	78
20				2	90
21				2.5	88
22				3	92
23				3.5	83
24				2.5	72*
25				3	76

[a]All the products exhibited physical and spectral (NMR,mass, IR) properties in accordance with the assigned struture
[b]Isolated yield

Further to determine the selectivity of N-arylation, we have examined the substrate having thiol and amino groups. For example, 2-Mercapto benzothiazole (***Table 1,*** entry- 24) reacted with 4-fluoro nitrobenzene under standard conditions and resulted into N-arylated product (72 %) accompanied by diarylated product (10 %, S and N - arylated). In the reaction of 2-amino benzimidazole (***Table 1,*** entry- 23) with 4-fluoro nitrobenzene in identical condition, as expected the N-arylation occurred selectively at secondary nitrogen (83 %), leaving primary amino group unreacted in the similar condition. It was important to note that N-arylation of 4-phenyl imidazole (***Table 1,*** entry- 15, 17, 19) showed complete conversion [24] in the present reaction condition and only 1-arylated product[11] was isolated in excellent yield. After this results in hand, next we planned to examine a variety of aryl halides having commonly used electron releasing substitutents like cyano, ketone, trifluoromethyl and aldehyde, which gave encouraging results. Thus the reaction of 2-chloro benzonitrile (***Table 1,*** entry- 16) with imidazole gave good yield of N-arylated product. It is reported that 4-fluoro acetophenone reacts with imidazole in high boiling solvent (DMF) and gave low yield of N-arylated product [25]. The same reaction in the present condition afforded the high yield of 4-imidazolyl acetophenone in shorter reaction time. Unlike other methods the present protocol is not limited to certain halides. The generality of N-arylation was strengthened by screening a variety of aryl halides like iodo, bromo, chloro and fluoro aryls. The additional advantage of the system is that the N-arylation occurred successfully with aryl chlorides, which are available in bulks. Further, we screened heteroaryl halide and excellent reactivity observed with various heteroaryl halides. For example, the reaction of imidazole with 2,8-bis(trifluoromethyl) 4-iodo/ bromo quinoline (***Table 1,*** entry- 11,12 and 13) was very fast and resulted into high yield of expected product. We presume this may be because of high electron withdrawing effect of CF_3 group**.** Similarly, 2-bromo pyridine (entry- 10, 18 and19) and 2-bromo thiophene (***Table 1,*** entry- 8) reacted with heterocycles to afford N-arylated product in the same reaction condition. The present method allows tolerance of functional groups like CO, CHO, SH, NH_2, CN. Though the N-arylation reported [17] using ionic liquid with limitations to aliphatic cyclic secondary amines, the present protocol has advantages in terms of efficiency and applications to a wide range of heteroaryls. Although the method requires additional CuI, it may ultimately reduce the overall expenditure by minimizing man hours, energy and increase the yield of product.

CONCLUSION

In conclusion, we have described the efficient procedure for N-arylation of N-hetero aryls in the presence of CuI using Ionic liquid as a reaction media. The Ionic liquid [Bmim]BF_4 was recycled and reused. The reaction time was reduced and yields of the products are very high. The procedure showed generality towards the variety of N-heteroaryl and aryl halides. The present protocol makes the procedure practically and environmentally attracting alternative over the existing method.

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