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Synthesis of Novel N^1 and N^2 Indazole Derivatives

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Abstract: The alkylation of 5-cyano indazoles 2 in the presence of readily available imidizolium salts (ionic liquids) (Bmim)BF_4 as phase transfer catalyst were performed to afford the regio isomers N^1-and N^2-(substituted alkyl)-5-cyano indazoles. The N^1-alkylated cyano indazoles were converted to the corresponding N^1-(substituted alkyl)-5-aminomethyl and 5-carbaldehydes **5(a-f)** and **6 (a-f)**.

Keywords: Cyano indazoles, PTC catalyst, (Bmim)BF_4.

Introduction

Indazoles are of considerable interest due to variety of their biological applications. Especially the 1,3,5-substituted indazoles have been studied as receptor antagonists of the peptideo-leukotrienes[1].1-benzyl-3-(5[1]-hydroxymethyl-2[1]-furyl)indazole show anti platelet activity[2],where as 7-nitroindazole exhibits hypertensive[3], antinociceptive and cardiovascular effects[4]. The *N*-methyl derivatives of 7-nitro-1*H*-indazole and 3-bromo-7-nitro-1*H*-indazoles show neuroprotective and NOS-1/NOS-11 activities[5]. Recently, a series of N^1-(substituted benzyl)-3-(substituted aryl)indazoles were evaluated for their antiangiogenic activity[6]. Some of indazoles derivatives 3-methyl-1*H*-indazoles shown significant analgesic, anti-inflammatory and anti-pyretic activities[7] and also exhibits as kinase inhibitors[8]. In continuation of our work on synthesis of new heterocyclics, we herein report the alkylation reactions of 5-cyano indazole **2** in the presence of readily available ionic liquids (Bmim)BF_4 as phase transfer catalyst were performed to afforded the regio isomers of 1*H* and 2 *H*-indazole derivatives **3(a-f)** and **4(a-f)**. The compounds **3(a-f)** were converted to the corresponding N^1-(substituted alkyl)-5-aminomethyl and 5-carbaldehydes **5(a-f)** and **6(a-f)** (Scheme 1).

Experimental

Melting points were recorded on electrothermal (type 9100) melting point apparatus and are not corrected. ^{1}H NMR spectra were recorded on a Bruker WM-300 MHz spectrometer in δ ppm using TMS as internal standard. IR spectra in K Br were recorded by a Perkin-Elmer PE-633 infrared spectrometer. The mass spectra of the compounds were recorded on Joel TMS-D300 at 70 eV. Microanalyses were carried out on a Carlo-Erba 1106 micro analyzer.

*Synthesis of 1-alkyl-5-cyano-1H-indazoles and 2-alkyl-5-cyano-2H-indazoles 3 (a-f) and **4(a-f)***

To a vigorously stirred solution of 5-cyanoindazole **2** (10 mmol) and powdered anhydrous potassium carbonate (20 mmol) in ethyl acetate (15 mL) was added the appropriate alkyl chlorides (10 m mol). To this reaction mixture a catalytic amount of $(Bmim)BF_4$ ionic liquid (1 mmol) was added and the mixture was allowed to stand at 60 ^oC for 3 h (monitored by TLC). The reaction mixture was cooled filtered and solid washed with ethylacetatae. The filtrate was diluted with water and extracted with Ethyl acetate. The organic layers were combined and washed with brine solution, finally evaporation of the organic layers afforded the crude product observed two isomers on TLC which were separated by column chromatography through a alumina column (MeOH : DCM 1:9) to yield the respective pure products.

*1-((Pyridin-4-yl)methyl)-1H-indazole-5-carbonitrile **3(a)***

m.p. 148-149 ^oC; ^{1}H NMR (DMSO-d_6) δ: 8.61-8.63 (dd, 2H, Py-H),8.14-8.15 (dd, 1H, Ar-H), 8.10 (s, 1H, indazole-H), 7.79-7.81 (dd, 1H, Py-H), 7.42-7.46 (dd, 1H, Py-H), 7.10-7.12 (dd, 2H, Ar-H), 5.65 (s, 2H, -CH_2); mass (*m/z*): 234 (M^+); Anal.Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92. Found: C, 71.77; H, 4.28; N, 23.90%.

*1-((Pyridin-3-yl)methyl)-1H-indazole-5-carbonitrile **3(b)***

m.p. 140-141 ^oC; ^{1}H NMR (DMSO-d_6) δ: 8.57-8.61 (dd, 2H, Py-H), 8.18 (s, 1H, Ar-H), 8.10 (s, 1H, indazole-H), 7.75 (dd, 1H, Ar-H), 7.42-7.44 (dd, 1H, Py-H), 7.28 (dd, 1H, Py-H), 7.16 (dd, 1H, Ar-H), 5.64 (s, 2H, -CH_2); mass (*m/z*): 234 (M^+); Anal.Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92: Found: C, 71.77; H, 4.28; N, 23.90%.

*1-(3-(Dimethylamino)benzyl)-1H-indazole-5-carbonitrile **3(c)***

m.p. 124-126 ^oC; ^{1}H NMR (DMSO-d_6) δ: 8.12 (m, 1H, Ar-H), 7.98 (m, 1H, indazole-H), 7.62 (m, 2H, Ar-H), 7.02 (m, 1H, Ar-H), 6.34-6.42 (m, 3H, Ar-H), 4.92 (s, 2H, -CH_2), 2.90 (s, 6H, 2×CH_3); mass (*m/z*): 276 (M^+); Anal.Calcd for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27. Found: C, 73.87; H, 5.82; N, 20.26%.

*1-((Diethylamino)ethyl)-1H-indazole-5-carbonitrile **3(d)***

m.p. 112-114^oC; ^{1}H NMR (DMSO-d_6) δ: 8.19 (s, 1H, Ar-H), 8.12 (s, 1H, indazole-H), 7.74-7.77 (dd, 1H, Ar-H), 7.38-7.41 (dd, 1H, Ar-H), 4.47-4.51 (t, 2H, -CH_2), 3.02-2.98 (t, 2H, -CH_2), 2.52-2.59 (q, 4H, 2xCH_2), 0.92-0.96 (t, 6H, 2xCH_3); mass (*m/z*): 242 (M^+); Anal.Calcd for $C_{14}H_{18}N_4$: C, 69.39; H, 7.49; N, 23.12. Found: C, 69.38; H, 7.47; N, 23.08%.

*1-(2-Methoxyethyl)-1H-indazole-5-carbonitrile **3(e)***

m.p. 102-104^oC; ^{1}H NMR (DMSO-d_6) δ: 8.14 (m, 1H, Ar-H), 8.04 (m, 1H, indazole-H), 7.60-7.68 (dd, 1H, Ar-H), 7.46-7.50 (dd, 1H, Ar-H), 3.98 (s, 3H, -OCH_3), 3.90 (t, 2H, CH_2), 3.88 (t, 2H, -OCH_2); mass (m/z): 201 (M^+); Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.64; H, 5.50; N, 20.88; Found: C,65.60;H,5.49;N,20.86%.

1-(2-Hydroxyethyl)-1H-indazole-5-carbonitrile ***3(f)***

m.p. 109-110 ^{o}C; ^{1}H NMR (DMSO-d_6) δ: 8.04 (s, 1H, Ar-H), 7.82 (s, 1H, indazole-H), 7.42-7.48 (dd, 2H, Ar-H), 4.48 (t, 2H, -OCH_2), 4.12 (t, 2H, CH_2), 2.2 (br, 1H, -OH); mass (*m/z*): 187 (M^+); Anal.Calcd for $C_{10}H_9N_3O$: C, 64.14; H, 4.84; N, 22.48; Found: C, 64.12; H, 4.82; N, 22.46%.

2-((Pyridin-4-yl)methyl)-2H-indazole-5-carbonitrile ***4(a)***

m.p. 159-161 ^{o}C; ^{1}H NMR (DMSO-d_6) δ: 8.64 (dd, 2H, Py-H), 8.14 (m, 1H, Ar-H), 7.88 (m, 1H, indazole-H), 7.64 (dd, 1H, Ar-H), 7.56 (dd, 1H, Ar-H), 7.14 (dd, 2H, Py-H), 5.64 (s, 2H, -CH_2); mass (*m/z*): 234 (M^+); Anal.Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92: Found: C, 71.76; H, 4.28; N, 23.90%.

2-((Pyridin-3-yl)methyl)-2H-indazole-5-carbonitrile ***4(b)***

m.p. 168-170 ^{o}C; ^{1}H NMR (DMSO-d_6) δ: 8.60 (dd, 2H, Py-H), 8.12 (m, 1H, Ar-H), 7.92 (m, 1H, indazole-H), 7.74 (dd, 1H, Ar-H), 7.68 (dd, 1H, Py-H), 7.62 (dd, 1H, Ar-H), 7.16 (dd, 1H, Ar-H), 5.64 (s, 2H, -CH_2); mass (*m/z*): 234 (M^+); Anal.Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92: Found: C, 71.76; H, 4.28; N, 23.90%.

2-(3-(Dimethylamino)benzyl)-2H-indazole-5-carbonitrile ***4(c)***

m.p. 154-156 ^{o}C; ^{1}H NMR (DMSO-*d_6*) δ: 8.12 (m, 1H, Ar-H), 7.98 (m, 1H, indazole-H), 7.62 (m, 2H, Ar-H), 7.02 (m, 1H, Ar-H), 6.42-6.34 (m, 3H, Ar-H), 5.62 (s, 2H, -CH_2), 2.90 (s, 6H, 2×CH_3); mass (*m/z*): 276 (M^+); Anal. Calcd for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27: Found: C, 73.87; H, 5.82; N, 20.26%.

2-((Diethylamino)ethyl)-2H-indazole-5-carbonitrile ***4(d)***

m.p. 149-151 ^{o}C; ^{1}H NMR (DMSO-*d_6*) δ: 8.14 (m, 1H, Ar-H), 8.02 (m, 1H, indazole-H), 7.62-7.70 (m, 2H, Ar-H), 4.48-4.51 (t, 2H, -CH_2), 3.00-2.96 (t,2H- CH_2), 2.54-2.60 (q, 4H, 2×CH_2), 0.96-0.98 (t, 6H, 2×CH_3); mass (*m/z*): 242 (M^+); Anal.Calcd for $C_{14}H_{18}N_4$: C, 69.39; H, 7.49; N, 23.12. Found: C, 69.38; H, 7.47; N, 23.08%.

2-(2-Methoxyethyl)-2H-indazole-5-carbonitrile ***4(e)***

m.p. 134-136 ^{o}C; ^{1}H NMR(DMSO-*d_6*) δ: 8.12 (m, 1H, Ar-H), 8.04 (m, 1H, indazole-H), 7.68-7.60 (dd, 1H, Ar-H), 7.50-7.46 (dd, 1H, Ar-H), 3.98 (s, 3H, -OCH_3), 3.90 (t, 2H, CH_2), 3.88 (t, 2H, -OCH_2); mass (*m/z*): 201 (M^+); Anal.Calcd for $C_{11}H_{11}N_3O$: C, 65.64; H, 5.50; N, 20.88; Found: C, 65.62; H, 5.52;N,20.86%.

2-(2-Hydroxyethyl)-2H-indazole-5-carbonitrile ***4(f)***

m.p. 141-142 ^{o}C; ^{1}H NMR (DMSO-*d_6*) δ: 8.04 (s, 1H, Ar-H), 7.82 (s, 1H, indazole-1H), 7.48-7.42 (dd, 2H, Ar-H), 4.48 (t, 2H, -OCH_2), 4.12 (t, 2H, CH_2), 2.2 (br, 1H, -OH); mass (*m/z*): 187 (M^+); Anal.Calcd for $C_{10}H_9N_3O$: C, 64.14; H, 4.84; N, 22.48; Found: C, 64.10; H, 4.86; N, 22.46 %.

Synthesis of 1-alkyl-5-amino methyl-1H indazoles ***5(a-f)***

To a solution of lithium aluminium hydride (2.0 mmol) in dry tetrahydrofuran (10 mL) cooled to 0 ^{o}C, was added gradually a solution of substituted indazoles **3(a-f)** (1.0 m mol) in tetrahydrofuran (10 mL) and maintained for 30 minutes. Then the reaction mixture was allowed to raise temperature until reflux and stirred for 4 h, after the reaction was completed (monitored by TLC), cooled to 0 ^{o}C and quenched with water (10 mL), and 10 mL of 1N NaOH solution, precipitate was filtered through a pad of celite and washed with THF: MeOH (3:1 ratio). Solvent was evaporated under vacuo provided a solid which was purified

by column chromatography elution with MeOH: CH_2Cl_2 saturated with NH_3 (10:60:30) to get the corresponding compounds **5(a-f)**.

*1-((Pyridin-4-yl)methyl)-1H-indazol-5-yl)methanamine (**5a**)*

Yield: 72%, m.p. 152-154 ^oC; ^1H NMR (DMSO-d_6) δ: 8.93-8.90 (dd, 2H, Py-H), 8.12 (s, 1H, indazole-H), 7.92 (s, 1H, Ar-H), 7.48-7.42 (dd, 2H, Ar-H), 7.32-7.28 (dd, 2H, Py-H), 4.42 (s, 2H,-CH_2), 4.12 (s, 2H, -CH_2NH_2); mass (*m/z*): 238 (M^+). Anal.Calcd for $C_{14}H_{14}N_4$: C, 70.57; H, 5.92; N, 23.51. Found; C, 70.54; H, 5.90; N, 23.54%.

*1-((Pyridin-3-yl)methyl)-1H-indazol-5yl)methanamine (**5b**)*

Yield: 79%, m.p. 146-147 ^oC; ^1H NMR (DMSO-d_6) δ: 8.86-8.84 (dd, 2H, Py-H), 8.12 (s, 1H, indazole-H), 7.98 (s, 1H, Ar-H), 7.46-7.42 (dd, 2H, Ar-H), 7.32-7.24 (dd, 2H, Py-H), 4.42 (s, 2H, -CH_2-), 4.12 (s, 2H, -CH_2NH_2); mass (*m/z*): 238 (M^+). Anal.Calcd for $C_{14}H_{14}N_4$: C, 70.57; H, 5.92; N, 23.51. Found: C, 70.54; H, 5.88; N, 23.50%.

*3-(5-(Aminomethyl)-1H-indazol-1-yl)methyl-N,N-dimethylbenzenamine (**5c**)*

Yield: 84%, m.p. 158-160 ^oC; ^1H NMR (DMSO-d_6) δ: 8.23 (s, 1H, indazole-H), 8.04 (m, 1H, Ar-H), 7.80-7.74 (m, 1H, Ar-H), 7.67 (dd, 1H, Ar-H), 7.74-7.70 (m, 1H, Ar-H), 6.66-6.60 (m, 3H, Ar-H), 4.20 (s, 2H, -CH_2), 3.98 (s, 2H, -CH_2-), 2.92 (s, 6H, N-$(CH_3)_2$); mass (*m/z*) : 281 (M^+). Anal.Calcd for $C_{17}H_{20}N_4$: C, 72.83; H, 7.19; N, 19.98. Found: C, 72.80; H, 7.22; N, 19.96%.

*N-(5-(Aminomethyl)-1H-indazol-1-yl)ethyl-N-ethylethanamine (**5d**)*

Yield: 69%, m.p. 137-139 ^oC; ^1H NMR (DMSO-d_6) δ: 7.95 (s, 1H, indazol-H), 7.68-7.65 (m, 1H, Ar-H), 7.54 (m, 1H, Ar-H), 7.24-7.21 (m, 1H, Ar-H), 4.47-4.43 (t, 2H, CH_2), 3.92 (s, 2H, CH_2-), 3.02-2.98 (t, 2H, CH_2-),2.66-2.52 (q, 4H, 2xCH_2), 1.0 - 0.96 (t, 6H, 2xCH_3); mass (*m/z*): 247 (M^+). Anal.Calcd for $C_{14}H_{22}N_4$: C, 68.26; H, 9.00; N, 22.74. Found: C, 68.24; H, 9.02; N, 22.72%.

*1-(2-Methoxyethyl)-1H-indazol-5-yl)methanamine (**5e**)*

Yield: 74%, m.p. 124-126 ^oC; ^1H NMR (DMSO-d_6) δ: 7.98 (s, 1H, indazole-H), 7.64 (m, 1H, Ar-H), 7.38-7.24 (m, 2H, Ar-H), 4.28-4.24 (t, 2H, CH_2), 4.08-4.00 (t, 2H, -CH_2-) , 3.90 (s, 2H, -CH_2-), 3.54 (s, 3H, -OCH_3); mass (*m/z*): 205 (M^+). Anal.Calcd for $C_{11}H_{15}N_3O$: C, 64.36; H, 7.38; N, 20.49; Found: C, 64.32; H, 7.40; N, 20.47 %.

*2-(5-(Aminomethyl)-1H-indazol-1-yl)ethanol (**5f**)*

Yield: 76%, m.p. 134-136 ^oC; ^1H NMR (DMSO-d_6) δ: 8.02 (s, 1H, indazole-H), 7.70 (s, 1H, Ar-H), 7.48-7.40 (m, 2H, Ar-H), 4.50-4.48 (t, 2H, -CH_2-), 4.14-4.10 (t, 2H, -CH_2-), 3.94 (s, 2H, -CH_2-), 1.60 (br, 1H, -OH); mass (*m/z*): 191 (M^+). Anal.Calcd for $C_{10}H_{13}N_3O$: C, 62.81; H, 6.85; N, 21.97; Found: C, 62.82; H, 6.84; N, 21.94 %.

*Synthesis of 1-alkyl--1H indazole-5-carbaldehyde **6 (a-f)***

Compound **3 (a-f)** (2.0 mmol) was added gradually to a stirred solution of 75% formic acid (10 mL) and Raney Nickel (3.1 mmol). The reaction mixture was allowed to raise the temperature until reflux for 2 h (monitored by TLC). After completion, the reaction mixture was cooled to room temperature and the catalyst filtered through a pad of celite and washed several times with water .The products were extracted with chloroform (3x10 mL), distilled under vacuum to obtained crude compounds **6(a-f)** and these were purified by column chromatography (MeOH: $CHCl_3$; 2:8).

*1-(Pyridin-4yl)methyl)-1H-indazole-5-carbaldehyde (**6a**)*

Yield: 76%, m.p. 141-143 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 10.01 (s, 1H, -CHO), 8.63-8.61 (m, 2H, Py-H), 8.24-8.22 (dd, 2H, Ar-H), 7.84-7.80 (m, 2H, -Ar-H), 7.13-7.11 (dd, 2H, Py-H), 5.66 (s, 2H, -CH_2); mass (*m/z*): 237 (M^+). Anal.Calcd for $C_{14}H_{11}N_3O$: C, 70.82; H, 4.62; N, 17.82; Found: C, 70.80; H, 4.64; N, 17.80%.

*1-(Pyridin-3yl)-methyl)-1H-indazole-5-carbaldehyde (**6b**)*

Yield: 72%, m.p. 133-134 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 9.98 (s, 1H, -CHO), 8.54-8.62 (m, 2H, Py-H), 8.20-8.18 (m, 2H, Ar-H), 7.82-7.76 (m, 2H, -Ar-H), 7.14-7.12 (m, 2H, Py-H), 5.64 (s, 2H, -CH_2); mass (*m/z*): 237 (M^+). Anal.Calcd for $C_{14}H_{11}N_3O$: C, 70.82; H, 4.62; N, 17.82; Found: C, 70.80; H, 4.64; N; 17.80%.

*1-(3-(Dimethyl amino)-benzyl)-1H-indazole-5-carbaldehyde (**6c**)*

Yield: 68%, m.p. 138-140 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 10.02 (s, 1H, -CHO), 8.23 (s, 1H, indazole-H), 8.01 (s, 1H, Ar-H), 7.67-7.74 (m, 2H, Ar-H), 7.23-7.26 (m, 1H, -Ar-H), 6.46-6.44 (m, 3H, Ar-H), 5.56 (s, 2H, -CH_2), 2.78 (s, 6H, -N(CH_3); mass (*m/z*): 279 (M^+). Anal.Calcd for $C_{17}H_{17}N_3O$: C, 73.10; H, 6.12; N, 15.08; Found: C, 73.08; H, 6.14; N; 15.06%.

*1-(N,N^{l}-Diethylamino)ethyl)-1H-indazole-5-carbaldehyde (**6d**)*

Yield: 76%, m.p. 121-123 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 9.98 (s, 1H, -CHO), 8.25-8.21 (m, 2H, Ar-H), 7.81-7.72 (m, 2H, Ar-H), 4.50-4.45 (t, 2H, -CH_2), 3.02-2.97 (t, 2H, -CH_2), 2.58-2.51 (q, 4H, 2x-CH_2-), 0.98-0.93 (t, 6H, 2xCH_3); mass (*m/z*): 245 (M^+). Anal.Calcd for $C_{14}H_{19}N_3O$: C, 68.71; H, 5.63; N, 20.13; Found: C, 68.70; H, 5.60; N, 20.12%.

*1-(2-Methoxy ethyl)-1H-indazole-5-carbaldehyde (**6e**)*

Yield: 69%, m.p. 134-136 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 10.21 (s, 1H, -CHO), 8.23 (s, 1H, indazole-H), 8.12 (s, 1H, Ar-H), 7.56 (dd, 1H, Ar-H), 7.48 (dd, 1H, Ar-H), 4.28-4.12 (t, 2H, -CH_2), 3.98-3.92 (t, 2H, -CH_2), 3.52 (s, 3H, -OCH_3); mass (*m/z*): 204 (M^+). Anal.Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72; Found: C, 64.67; H, 5.90; N, 13.70%.

*1-(2-Hydroxy ethyl)-1H-indazole-5-carbaldehyde (**6f**)*

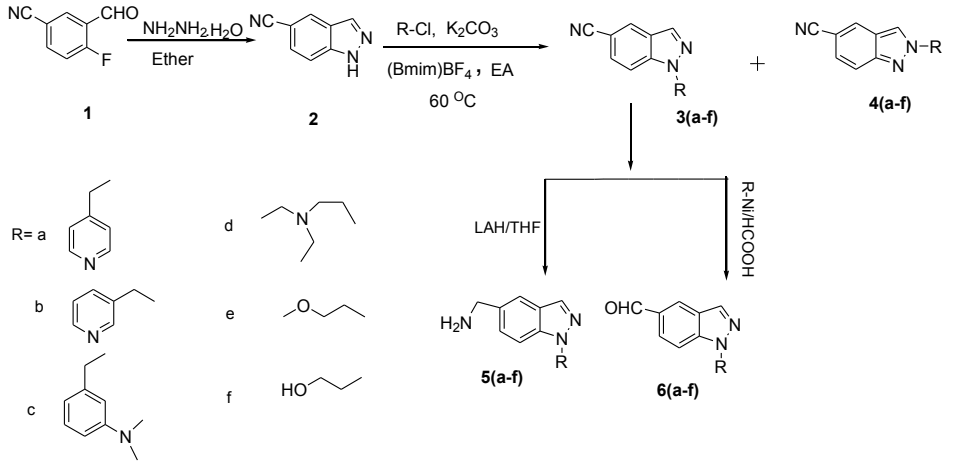
Yield: 67%, m.p. 127-129 ^{o}C; ^{1}H NMR ($CDCl_3$) δ: 10.34 (s, 1H, -CHO), 8.27 (s, 1H, indazole-H), 8.20 (s, 1H, Ar-H), 7.98-7.94 (dd, 1H, Ar-H), 7.63-7.53 (dd, 1H, Ar-H), 4.54-4.51 (t, 2H,-CH_2), 4.17-4.03 (t, 2H, CH_2-), 2.76 (br, 1H, -OH); mass (*m/z*): 190 (M^+). Anal.Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73; Found: C, 63.14; H, 5.32; N, 14.72%.

Results and Discussion

The general synthesis of indazoles involve the cyclization of aryl hydrazones containing ortho bromo, chloro or nitro groups [9,10] and is limited mainly to hydrazones of aryl ketones. Recently the cyclization of the hydrazone of a benzaldehyde substituted with ortho fluorine has been reported[11]. The 2-aryl-2*H*-indazoles were synthesized by the Pd-catalyzed intramolecular amination of the corresponding *N*-aryl-*N*-(orthobromobenzyl) hydrazines[12]. The alkylation of indazoles using phase transfer catalyst (TBAB) is known[13] but it is limited to benzyl substitution at 1 and 2 positions of indazoles. Phase transfer catalysts (PTCs) are powerful reagents in chemical transformations[14], the characteristics of which include mild reaction conditions, safety, operational simplicity and selectivity. Thus, finding a new phase transfer catalyst to promote various organic transformations is of considerable interest. Although many phase transfer catalysts are known quaternary salts formed from ammonia[15] are only used for alkylation reactions. Thus, we planned to use imidazolium salts (generally known

as ionic liquids) having bulky cations as phase transfer catalysts for alkylations.We herein report (Bmim)BF_4 ionic liquid as phase transfer catalyst for alkylations of 5-cyano indazole **2.**

Compound 5-cyano indazole[16] **2** was subjected to alkylation by treating with (4-chloromethyl) pyridine in the presence of (Bmim)BF_4 to yield **3a** as major regio isomer (86%) and **4a** as minor regio isomer (14%) (Table 1). These isomers were separated by column chromatography and characterized by ^{1}H NMR and mass. After comparing the physical and spectral data of these regio isomers, it was discovered that the melting points of all the N^1 regio isomers were relatively lower than those of their corresponding N^2 regio isomers and the structures of N^1-regio isomers were also confirmed by known procedure. It was also noticed that no selectivity was observed in the absence of (Bmim) BF_4 (Table 2). Compounds **3(a-f)** and **4(a-f)** were converted to 1-alkyl-5-amino methyl-1*H*-indazoles **5(a-f)** and 1-alkyl-1*H*-indazole-5-carbaldehydes **6(a-f)** by treating with LAH in THF and Raney Nickel in formic acid. The structures of these compounds were established on the basis of their elemental and spectral data (^{1}H NMR, Mass).



Scheme 1

Table 1. Alkylation of 5-cyano-indazole **2** under (Bmim)BF_4 ionic liquid as phase transfer catalyst.

Catalyst	Entry	Yield, %	Entry	Yield , %
(Bmim)BF_4	**3a**	86	**4a**	14
	3b	88	**4b**	12
	3c	83	**4c**	17
	3d	79	**4d**	21
	3e	82	**4e**	18
	3f	80	**4f**	20

Table 2. Alkylation of 5-cyano-indazole **2** in absence of (Bmim)BF_4 ionic liquid.

S.No	Catalyst	Yield, % of **3a**	Yield, % of **4a**
1	No catalyst	52	48
2	TBAB	58	42
3	TBAI	55	45
4	CTAB	47	53

Conclusion

We have demonstrated that environmentally benign imidazolium salts can be used as phase transfer catalyst for the alkylations on indazole under mild conditions. Notably, the derivatives **3(a-f)** were obtained in very good yield.

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