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 peptido-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-1H-indazole and 3-bromo-7-nitro-1H-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-1H-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 1H 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 \(\delta\) 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 mmol). 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 °C for 3 h (monitored by TLC). The reaction mixture was cooled filtered and solid washed with ethylacetate. 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 °C; \(^1\)H NMR (DMSO-d\(_6\) ) \(\delta\): 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, 23.90. 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 °C; \(^1\)H NMR (DMSO-d\(_6\) ) \(\delta\): 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 °C; \(^1\)H NMR (DMSO-d\(_6\) ) \(\delta\): 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, 2xCH\(_3\) ); 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°C; \(^1\)H NMR (DMSO-d\(_6\) ) \(\delta\): 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\(_2\)), 3.02-3.08 (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\(_{13}\)N\(_3\): 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°C; \(^1\)H NMR (DMSO-d\(_6\) ) \(\delta\): 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\(_3\)O: 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 °C; 1H NMR (DMSO-d6) 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, -OCH2), 4.12 (t, 2H, CH2), 2.2 (br, 1H, -OH); mass (m/z): 187 (M⁺); Anal. Calcd for C10H9N2O: 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 °C; 1H NMR (DMSO-d6) 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, -CH2); mass (m/z): 234 (M⁺); Anal. Calcd for C14H10N4: 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. 168-166 °C; 1H NMR (DMSO-d6) 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, -CH2); mass (m/z): 234 (M⁺); Anal. Calcd for C14H10N4: C, 71.78; H, 4.30; N, 23.92; Found: C, 71.76; H, 4.28; N, 23.90%.

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

m.p. 154-156 °C; 1H NMR (DMSO-d6) 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, -CH2), 2.90 (s, 6H, 2×CH3); mass (m/z): 276 (M⁺); Anal. Calcd for C16H18N4: 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 °C; 1H NMR (DMSO-d6) δ: 8.14 (m, 1H, Ar-H), 8.02 (m, 1H, indazole-H), 7.62-7.70 (m, 2H, Ar-H), 7.02 (m, 1H, Ar-H), 4.48-4.51 (t, 2H, -CH2), 3.00-2.96 (t, 2H, -CH2), 2.54-2.60 (q, 4H, 2×CH2), 0.96-0.98 (t, 6H, 2×CH3); mass (m/z): 242 (M⁺); Anal. Calcd for C14H18N4: 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 °C; 1H NMR (DMSO-d6) 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, -OCH3), 3.90 (t, 2H, CH2), 3.88 (t, 2H, -OCH2); mass (m/z): 201 (M⁺); Anal. Calcd for C11H11N3O: 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 °C; 1H NMR (DMSO-d6) 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, -OCH2), 4.12 (t, 2H, CH2), 2.2 (br, 1H, -OH); mass (m/z): 187 (M⁺); Anal. Calcd for C10H9N3O: C, 64.14; H, 4.84; N, 22.48; Found: C, 64.10; H, 4.86; N, 22.46%.

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

To a solution of lithium aluminium hydride (2.0 mmol) in dry tetrahydrofuran (10 mL) cooled to 0 °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 °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: CH₂Cl₂ saturated with NH₃ (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 °C; ¹H NMR (DMSO-d₆) 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, -CH₂), 4.12 (s, 2H, -CH₂NH₂); mass (m/z): 238 (M⁺). Anal.Calcd for C₁₄H₁₄N₄: 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-5-yl)methanamine (5b)
Yield: 79%, m.p. 146-147 °C; ¹H NMR (DMSO-d₆) 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, -CH₂), 4.12 (s, 2H, -CH₂NH₂); mass (m/z): 238 (M⁺). Anal.Calcd for C₁₄H₁₄N₄: 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 °C; ¹H NMR (DMSO-d₆) 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, -CH₂), 3.98 (s, 2H, -CH₂), 2.92 (s, 6H, N(CH₃)₂); mass (m/z): 281 (M⁺). Anal.Calcd for C₁₇H₂₉N₄: 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-ethylethananine (5d)
Yield: 69%, m.p. 137-139 °C; ¹H NMR (DMSO-d₆) δ: 7.95 (s, 1H, indazole-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, CH₂), 3.92 (s, 2H, CH₂), 3.02-2.98 (t, 2H, CH₂), 2.66-2.52 (q, 4H, 2xCH₂), 1.0 - 0.96 (t, 6H, 2xCH₃); mass (m/z): 247 (M⁺). Anal.Calcd for C₁₄H₂₂N₄: 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 °C; ¹H NMR (DMSO-d₆) 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, CH₂), 4.08-4.00 (t, 2H, -CH₂), 3.90 (s, 2H, -CH₂), 3.54 (s, 3H, -OCH₃); mass (m/z): 205 (M⁺). Anal.Calcd for C₁₁H₁₅N₃O: 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 °C; ¹H NMR (DMSO-d₆) 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, -CH₂), 4.14-4.10 (t, 2H, -CH₂), 3.94 (s, 2H, -CH₂), 1.60 (br, 1H, -OH); mass (m/z): 191 (M⁺). Anal.Calcd for C₁₀H₁₃N₃O: C, 62.81; H, 6.85; N, 21.97; Found: C, 62.82; H, 6.84; N, 21.94 %.

Synthesis of 1-alkyl--IH 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 obtain crude compounds 6(a-f) and these were purified by column chromatography (MeOH: CHCl₃; 2:8).
1-(Pyridin-4-yl)methyl)-1H-indazole-5-carbaldehyde (6a)
Yield: 76%, m.p. 141-143 °C; 1H NMR (CDCl₃): 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, -CH₂); mass (m/z): 237 (M⁺). Anal.Calcd for C₁₄H₁₁N₂O: C, 70.82; H, 4.62; N, 17.82; Found: C, 70.80; H, 4.64; N, 17.80%.

1-(Pyridin-3-yl)-methyl)-1H-indazole-5-carbaldehyde (6b)
Yield: 72%, m.p. 133-134 °C; 1H NMR (CDCl₃): 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, -CH₂); mass (m/z): 237 (M⁺). Anal.Calcd for C₁₄H₁₁N₂O: 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. 131-123 °C; 1H NMR (CDCl₃): 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, -CH₂), 2.78 (s, 6H, -N(CH₃)); mass (m/z): 279 (M⁺). Anal.Calcd for C₁₇H₁₇N₃O: C, 73.10; H, 6.12; N, 15.08; Found: C, 73.08; H, 6.14; N; 15.06%.

1-(N,N'-Diethylamino)ethyl)-1H-indazole-5-carbaldehyde (6d)
Yield: 76%, m.p. 121-123 °C; 1H NMR (CDCl₃): 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, -CH₂), 3.02-2.97 (t, 2H, -CH₂), 2.58-2.51 (q, 4H, 2x-CH₂-), 0.98-0.93 (t, 6H, 2xCH₃); mass (m/z): 245 (M⁺). Anal.Calcd for C₁₄H₁₉N₃O: 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 °C; 1H NMR (CDCl₃): 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, -CH₂), 3.98-3.92 (t, 2H, -CH₂), 3.52 (s, 3H, -OCH₃); mass (m/z): 204 (M⁺). Anal.Calcd for C₁₁H₁₂O₂C: 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 °C; 1H NMR (CDCl₃): 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, -CH₂), 4.17-4.03 (t, 2H, CH₂-), 2.76 (br, 1H, -OH); mass (m/z): 190 (M⁺). Anal.Calcd for C₁₀H₁₀O₂C: 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 involves the cyclization of aryl hydrazones containing ortho bromo, chloro or nitro groups 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. The 2-aryl-2H-indazoles were synthesized by the Pd-catalyzed intramolecular amination of the corresponding N-aryl-N-(orthobromobenzyl) hydrazines. The alkylation of indazoles using phase transfer catalyst (TBAB) is known but it is limited to benzyl substitution at 1 and 2 positions of indazoles. Phase transfer catalysts (PTCs) are powerful reagents in chemical transformations, 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 are only used for alkylation reactions. Thus, we planned to use imidazolium salts (generally known...
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as ionic liquids) having bulky cations as phase transfer catalysts for alkylation. We herein report (Bmim)BF$_4$ ionic liquid as phase transfer catalyst for alkylation 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).

Table 1. Alkylation of 5-cyano indazole 2 under (Bmim)BF$_4$ ionic liquid as phase transfer catalyst.

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<th>Yield, %</th>
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<th>Yield, %</th>
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<td>4a</td>
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Table 2. Alkylation of 5-cyano indazole 2 in absence of (Bmim)BF$_4$ ionic liquid.

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<th>S.No</th>
<th>Catalyst</th>
<th>Yield, % of 3a</th>
<th>Yield, % of 4a</th>
</tr>
</thead>
<tbody>
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<td>No catalyst</td>
<td>52</td>
<td>48</td>
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<tr>
<td>2</td>
<td>TBAB</td>
<td>58</td>
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<td>4</td>
<td>CTAB</td>
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</table>
Conclusion
We have demonstrated that environmentally benign imidazolium salts can be used as phase transfer catalyst for the alkylation on indazole under mild conditions. Notably, the derivatives 3(a-f) were obtained in very good yield.

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References
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