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# Ionic Liquid Catalyzed One-Pot, Three Component Synthesis of Dihydropyrano[2,3-*c*]pyrazole under Green Conditions

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A new series of 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile derivatives were synthesized, where the three-component reaction of ethyl 3-oxobutanoate, hydrazinehydrate, aromatic aldehyde and malononitrile performed under green conditions by using ionic liquid [Bmim]$BF_4$ as reaction media. This method has the several advantages such as good yields, shorter reaction time, operational simplicities and eco-friendliness. The chemical structures of all the synthesized compounds were well characterized by physical, analytical and spectroscopic techniques.

**Keywords: Multi-component reaction, Ionic liquid, Dihydropyrano[2,3-*c*]pyrazole.**

## INTRODUCTION

In the past decade, ionic liquids have gained considerable attention of academic researchers and chemical industry as potential "green" substitutes for conventional organic solvents [1,2]. The "green" aspect of ionic liquids is mainly derived from their undetectable vapour pressure, flammability and toxicity thereby reducing air pollution [3]. Because of the serious pollution problems and minimizing environmental risks to designing new green technologies [4] attained researchers attention in recent year. Ionic liquids (ILs) have attracted increasing interest in heterocyclic synthesis, because they can provided green and efficient medium for heterocyclic reactions [5,6]. In parallel with use of ionic liquids in organic reactions, they have also been used as reaction medium for multicomponent reactions (MCRs) [7]. In this view, eco-environmental technologies in "green chemistry", have become more favoured in organic chemistry [8,9]. Heterocyclic containing the dihydropyrano[2,3-*c*]pyrazole derivatives are important targets in synthetic and medicinal chemistry since this fragment is a key moiety to exhibit various biological activities, such as antimicrobial [10], antioxidants [11] and anticancer [12]. Some of cathepsin S inhibitors [13], protein tyrosine phosphatase inhibitors [14] and plasmodial serinehydroxymethyltransferase (SHMT) [15] have dihydropyrano[2,3-*c*]pyrazole (DHP) moiety as a part of the core structure. Hence, the synthesis of dihydropyrano[2,3-*c*]pyrazole is of considerable interest for both organic chemistry and medicinal chemistry.

However, after literature survey, we found that their poor yields, tedious workup procedures, time and resource-wasting procedures, have occurred along with these multistage procedures dihydropyrano[2,3-*c*]pyrazole [16-20]. Further research suggested that the ionic liquid [Bmim]$BF_4$ catalyzed multicomponent condensations of ethyl 3-oxobutanoate, hydrazine hydrate, with the precursors of various aromatic aldehyde and malononitrile can be taken up for improving the work up methodology (**Scheme-I**).

## EXPERIMENTAL

All reagents were commercially available and used as without further purification. Reaction progress was observed by thin layer chromatography (TLC) making use of aluminium sheets pre-coated with silica gel 60F254, purchased from Merck. Column chromatography made using silica gel 60, 100-200 mesh. The IR spectral data of all the compounds were recorded on Bruker FT-IR spectrometer (Model: TENSOR-27), KBr from 400 to 4000 $cm^{-1}$. The $^1H$ NMR and $^{13}C$ NMR were recorded on BRUKER AVANCE-III 400 MHz, 100 MHz by using DMSO-$d_6$ as a solvent and tetramethylsilane as internal standard. Mass spectra were recorded on Waters Quattro micro triple quadrapole Mass spectrometer. Elemental analyses (CHN) were performed on Q-Toff-2010 elemental analyzer.

**General procedure for the synthesis of dihydropyrano-[2,3-*c*]pyrazole derivatives: (5a-l):** A mixture of ethyl 3-oxobutanoate (1 mmol), hydrazine hydrate (1 mmol), 4-chlorobenzaldehyde (1 mmol), malononitrile (1 mmol) and [Bmim]$BF_4$

were refluxed at 70 °C for 1 h. After the reaction was completed as indicated by TLC, the reaction mixture was allowed to the room temperature. Water was added to the reaction mixture and the resulting solid was collected by filtration, washed with water and followed by drying under vacuum. Further purification, of the solid product was carried out by using silica gel column chromatography (1:1, ethyl acetate: hexane) to afford the title compound **5a-l**. All the synthesized compounds were characterized by their melting point, IR, $^1$H NMR, $^{13}$C NMR and mass spectra and elemental analysis.

**6-Amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5a):** Off white solid; m.p.: 238-240 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3372, 3169 (N-H), 3021 (Ar C-C), 2875 (aliphatic C-C), 2192 (C≡N), 1648 (C=N), 1610 (C=C), 1489 (N-H), 1401, (C-N), 1160 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.78 (s, 3H, $CH_3$), 4.59 (s, 1H, CH), 6.87 (br s, 2H, $NH_2$), 7.15-7.17 (d, *J* = 7.2 Hz, 2H, Ar-CH), 7.20-7.24 (t, *J* = 7.2 Hz, 1H, Ar-CH), 7.29-7.33 (t, *J* = 7.2 Hz, 2H, Ar-CH) 12.09 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.83, 154.73, 144.40, 135.52, 128.38, 127.42, 126.68, 120.72, 97.59, 57.19, 36.22, 9.69; MS (ES *m/z*): 251.10 [M + H]$^+$; Anal. calcd. for $C_{14}H_{12}N_4O$; C, 66.59; H, 4.75; N, 22.19; Found: C, 66.65; H, 4.79; N, 22.21.

**6-Amino-4-(4-methoxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5- carbonitrile (5b):** Yellow solid; m.p.: 208-211 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3482, 3225 (N-H), 3103 (Ar C-C), 2960 (aliphatic C-C), 2191 (C≡N), 1642 (C=N), 1598 (C=C), 1493 (N-H), 1392 (C-N), 1259, 1052 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.78 (s, 3H, $CH_3$), 3.72 (s, 3H, O-$CH_3$), 4.53 (s, 1H, CH), 6.82 (br s, 2H, $NH_2$), 6.87 (d, *J* = 8.8 Hz, 2H, Ar-CH), 7.07 (d, *J* = 8.4 Hz, 2H, Ar-CH), 12.07 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.67, 157.96, 154.75, 136.48, 135.55, 128.48, 120.82, 113.75, 97.88, 57.62, 54.99, 35.43, 9.74. MS (ES *m/z*): 283.12 [M + H]$^+$; Anal. calcd. for $C_{16}H_{17}N_5O$; C, 63.82; H, 5.00; N, 19.85; Found: C, 63.40; H, 5.05; N, 19.36.

**6-Amino-4-(4-chlorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5c):** Off white solid; m.p.: 229- 231 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3479, 3235 (N-H), 3107 (Ar C-C), 2934 (aliphatic C-C), 2193 (C≡N), 1645 (C=N), 1611 (C=C), 1492 (N-H), 1395 (C-N), 1071 (C-O), 799 (C-Cl); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.79 (s, 3H, $CH_3$), 4.63 (s, 1H, CH), 6.93 (br s, 2H, $NH_2$), 7.19 (d, *J* = 8.42H, Ar-CH), 7.38 (d, *J* = 8.42H, Ar-CH) 12.14 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.90, 154.70, 143.47, 135.68, 131.23, 129.36, 128.45, 120.64, 97.19, 56.78, 35.56, 9.73; MS (ES *m/z*): 287.16 [M + H]$^+$ and 289.13 [M+2]$^+$; Anal. calcd. for $C_{14}H_{11}N_4OCl$; C, 58.65; H, 3.87; N, 19.54; Found: C, 58.87; H, 3.95; N, 19.18.

**6-Amino-4-(4-fluorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5d):** Yellow solid; m.p.: 227- 229 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3470, 3230 (N-H), 3110 (Ar C-C), 2960 (aliphatic C-C), 2191 (C≡N), 1632 (C=N), 1615 (C=C), 1485 (N-H), 1381 (C-N), 1109 (C-F), 1045 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.78 (s, 3H, $CH_3$), 4.62 (s, 1H, CH), 6.91 (br s, 2H, $NH_2$), 7.33 (dd, *J* = 8.4, 5.42 H, Ar-CH), 7.38 (t, *J* = 9.42H, Ar-CH) 12.12 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 162.35 (d, $J_{C\text{-}F}$, 240.0 Hz), 160.90, 154.70, 143.47, 135.68, 129.36 (d, $J_{C\text{-}F}$, 20.0 Hz), 117.35(d, $J_{C\text{-}F}$, 16.0 Hz), 120.64, 97.20, 56.77, 35.55, 9.72; MS (ES *m/z*): 271.03[M + H]$^+$; Anal. calcd. for $C_{14}H_{11}N_4OF$; C, 62.16; H, 4.07; N, 20.72; Found: C, 62.22; H, 4.10; N, 20.73.

**6-Amino-3-methyl-4-(2-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5e):** White solid; m.p.: 190- 194 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3414, 3373, 3314 (N-H), 3170 (Ar C-C), 2972 (aliphatic C-C), 2186 (C≡N), 1653 (C=N), 1609 (C=C), 1595, 1349 (N-O) 1491(N-H), 1411 (C-N), 1048 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.77 (s, 3H, $CH_3$), 5.09 (s, 1H, CH), 7.04 (br s, 2H, $NH_2$), 7.32 (dd, *J* = 8.0 0.8 Hz, 1H, Ar-CH), 7.47-7.51 (m, 1H, Ar-CH), 7.64-7.68 (m, 1H, Ar-CH), 7.85 (dd, *J* = 8.0 0.4 Hz, 1H, Ar-CH), 12.21 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 161.20, 154.98, 149.16, 137.61, 135.77, 133.38, 131.30, 128.34, 123.61, 120.27, 96.40, 56.06, 31.44, 9.51MS (ES *m/z*): 298.09 [M + H]$^+$; Anal. calcd. for $C_{14}H_{11}N_5O_3$; C, 56.56; H, 3.73; N, 23.56; Found: C, 56.20; H, 3.65; N, 23.36.

**6-Amino-3-methyl-4-(3-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5f):** Off white solid; m.p.: 228- 230 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3473, 3224 (N-H), 3115 (Ar C-C), 2932 (aliphatic C-C), 2194 (C≡N), 1652 (C=N), 1609 (C=C), 1596, 1348 (N-O) 1492 (N-H), 1401 (C-N), 1043 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.81 (s, 3H, $CH_3$), 4.88 (s, 1H, CH), 7.06 (br s, 2H, $NH_2$), 7.63-7.69 (m, 2H, Ar-CH), 8.02-8.03 (m, 1H, Ar-CH), 8.11-8.14 (m, 1H, Ar-CH), 12.22 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 161.15, 154.70, 147.89, 146.83, 135.92, 134.39, 130.25, 121.99, 121.85, 120.52, 96.67, 56.16, 35.65, 9.76MS (ES *m/z*): 298.23 [M + H]$^+$; Anal. calcd. for $C_{14}H_{11}N_5O_3$; C, 56.56; H, 3.73; N, 23.56; Found: C, 56.92; H, 3.78; N, 23.23.

**6-Amino-3-methyl-4-(4-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5g):** Yellow solid; m.p.: 245- 247 °CIR (KBr, $\nu_{max}$, cm$^{-1}$): 3477, 3228 (N-H), 3117 (Ar C-C), 2971 (aliphatic C-C), 2196 (C≡N), 1650 (C=N), 1608 (C=C), 1594, 1353 (N-O) 1492 (N-H), 1401 (C-N), 1048 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 2.21 (s, 3H, $CH_3$), 3.76 (s, 3H, $CH_3$)4.83 (s, 1H, CH), 7.06 (br s, 2H, $NH_2$), 7.47 (d, *J* = 8.8 Hz, 2H, Ar-CH), 8.21 (d, *J* = 8.8 Hz, 2H, Ar-CH), 12.21 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 161.17, 154.70, 152.09, 146.41, 135.92, 128.85, 123.89, 120.49, 96.58, 55.98, 35.92, 9.74; MS (ES *m/z*): 296.06 [M - H]$^-$; Anal. calcd. for $C_{14}H_{11}N_5O_3$; C, 56.56; H, 3.73; N, 23.56; Found: C, 56.98; H, 3.80; N, 23.17.

**6-Amino-3-methyl-4-(naphthalen-1-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5h):** White solid; m.p.: 218- 220 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3402, 3344, 3313 (N-H), 3162 (Ar C-C), 2924 (aliphatic C-C), 2192 (C≡N), 1654 (C=N), 1611 (C=C), 1486 (N-H), 1406 (C-N), 1050 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.53 (s, 3H, $CH_3$), 5.42 (s, 1H, CH), 6.91 (br s, 2H, $NH_2$), 7.36 (br, s1H, Ar-CH), 7.46-7.50 (m, 3H, Ar-CH), 7.83 (d, *J* = 8.4 Hz, 1H, Ar-CH) 7.95 (d, *J* = 9.6 Hz, 1H, Ar-CH), 8.16-8.20 (m, 1H, Ar-CH) 12.07 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.82, 154.79, 135.50, 133.69, 130.72, 128.82, 127.54, 126.91, 125.79, 125.51, 123.25, 120.59, 98.07, 57.46, 9.72;

MS (ES *m/z*): 303.25[M + H]$^+$; Anal. calcd. for $C_{18}H_{14}N_4O$; C, 71.51; H, 4.67; N, 18.53; Found: C, 71.97; H, 4.72; N, 18.12.

**6-Amino-4-(3-chloroisoquinolin-4-yl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5i):** Yellow solid; m.p.: 198- 201 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3448, 3254, (N-H), 3124 (Ar C-C), 2924 (aliphatic C-C), 2183 (C≡N), 1692, 1638 (C=N), 1489 (N-H), 1399 (C-N), 1044 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.78 (s, 3H, $CH_3$), 5.20 (s, 1H, CH), 7.15 (br s, 2H, $NH_2$), 7.54-7.58 (m, 1H, Ar-CH), 7.65-7.79 (m, 2H, Ar-CH) 7.97-8.08 (m, 1H, Ar-CH), 8.62 (s1H, Ar-CH)12.09 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 161.51, 156.76, 140.22, 139.52, 137.18, 136.71, 135.59, 130.82, 130.66, 127.94, 127.71, 125.92, 125.50, 120.43, 116.79, 93.82, 48.70, 9.69; MS (ES *m/z*): 338.01[M + H]$^+$; Anal. calcd. for $C_{17}H_{12}N_5OCl$; C, 60.39; H, 3.56; N, 20.72; Found: C, 60.45; H, 3.58; N, 20.73.

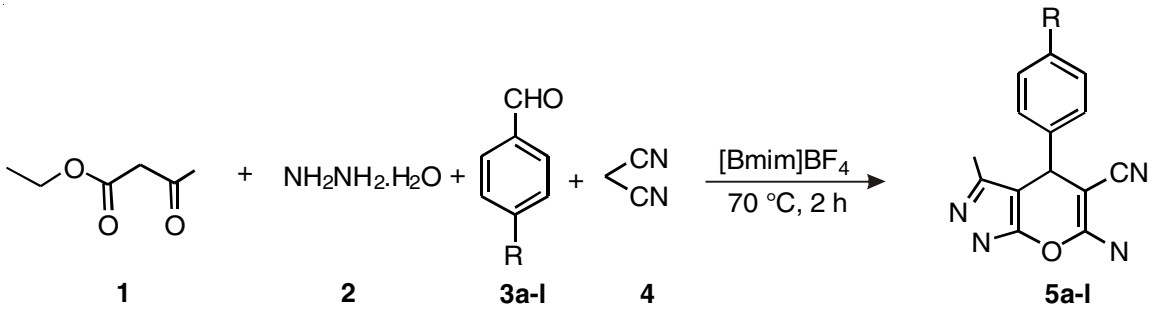
**6-Amino-4-(7-methoxy-2-naphthyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5j):** Yellow solid; m.p.: 238- 240 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3472, 3205, (N-H), 3109 (Ar C-C), 2956 (aliphatic C-C), 2185 (C≡N), 1623 (C=N), 1465 (N-H), 1381 (C-N), 1152, 1045 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.75 (s, 3H, $CH_3$), 3.76(s, 3H, O-$CH_3$), 4.71 (s, 1H, CH), 6.92 (br s, 2H, $NH_2$), 7.20-7.25 (m, 2H, Ar-CH), 7.30 (d, *J* = 2.2 Hz, 1H, Ar-CH) 7.61 (s, 1H, Ar-CH), 7.73 (d, *J* = 8.0 Hz, 1H, Ar-CH), 7.80 (d, *J* = 9.2 Hz, 1H, Ar-CH), 12.09 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.88, 157.51, 154.77, 141.22, 135.58, 131.93, 130.78, 129.35, 126.68, 126.63, 126.20, 120.20, 118.72, 106.71, 97.65, 57.16, 55.46, 36.24, 9.75; MS (ES *m/z*): 333.16 [M + H]$^+$; Anal. calcd. for $C_{19}H_{16}N_4O_2$; C, 68.60; H, 4.81; N, 16.84; Found: C, 68.66; H, 4.85; N, 16.86.

**6-Amino-4-(4-(dimethyl amino) phenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5k):** Yellow solid; m.p.: 204- 207 °C IR (KBr, $\nu_{max}$, cm$^{-1}$): 3384, 3304 (N-H), 3007 (Ar C-C), 2917 (aliphatic C-C), 2189 (C≡N), 1644 (C=N), 1612 (C=C), 1488(N-H), 1396 (C-N), 1139 (C-O)$^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.78 (s, 3H, $CH_3$), 2.86 (s, 6H, N-$CH_3$), 4.45 (s, 1H, CH), 6.65 (d, *J* = 8.4 Hz, 2H, Ar-CH), 6.76 (br s, 2H, $NH_2$), 6.96 (d, *J* = 8.8 Hz, 2H, Ar-CH), 12.03 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.55, 154.79, 149.22, 135.48, 132.03, 127.96, 120.93, 112.32, 98.18, 58.03, 40.18, 35.36, 9.76; MS (ES *m/z*): 296.15 [M + H]$^+$; Anal. calcd. for $C_{16}H_{17}N_5O$; C, 65.07; H, 5.80; N, 23.71; O, 5.42; Found: C, 65.40; H, 5.86; N, 23.36.

**6-Amino-3-methyl-4-(7-methylnaphthalen-2-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5l):** Off white solid; m.p.: 240- 242 °C; IR (KBr, $\nu_{max}$, cm$^{-1}$): 3482, 3256, (N-H), 3102 (Ar C-C), 2961 (aliphatic C-C), 2190 (C≡N), 1640 (C=N), 1595 (C=C), 1492(N-H), 1390 (C-N), 1056 (C-O); $^1$H NMR (400 MHz, DMSO-$d_6$, δ ppm): 1.74 (s, 3H, $CH_3$), 3.86(s, 3H, Ar-$CH_3$), 4.72 (s, 1H, CH), 6.91 (br s, 2H, $NH_2$), 7.13-7.20 (m, 2H, Ar-CH), 7.29 (d, *J* = 2.4 Hz, 1H, Ar-CH)7.67 (s, 1H, Ar-CH), 7.75 (d, *J* = 8.4 Hz, 1H, Ar-CH), 7.81 (d, *J* = 9.2 Hz, 1H, Ar-CH), 12.11 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO-$d_6$, δ ppm): 160.84, 157.19, 154.81, 139.33, 135.77, 133.35, 129.15, 128.17, 127.27, 126.28, 125.55, 120.81, 118.65, 105.94, 97.57, 57.33, 55.18, 36.34, 9.70; MS (ES *m/z*): 333.11 [M + H]$^+$; Anal. calcd. for $C_{19}H_{16}N_4O$; C, 72.13; H, 5.10; N, 17.71; Found: C, 72.83; H, 5.17; N, 17.26.

## RESULTS AND DISCUSSION

To show the merit of [Bmim]$BF_4$ ionic liquid as a solvent-catalyst system in synthesis of dihydropyrano[2,3-*c*]pyrazole is shown in **Scheme-I**. At the onset of our work, ionic liquids shown in Table-1. We applied this solvent-catalyst system for




**Scheme-I**

TABLE-1
OPTIMIZATION CONDITIONS FOR THE SYNTHESIS OF DIHYDROPYRANO[2,3-*c*]PYRAZOLE DERIVATIVES (**5a-l**)

| Entry | Catalyst (mol %) | Solvent | Temperature (°C) | Time (h) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | No catalyst | EtOH | 70 | 12 | Trace |
| 2 | AcOH | EtOH | 70 | 6 | 46 |
| 3 | $FeCl_3$ (15) | EtOH | 70 | 8 | 68 |
| 4 | $ZnCl_3$ (15) | EtOH | 70 | 5 | 72 |
| 5 | $AlCl_3$ (15) | EtOH | 70 | 3 | 56 |
| 6 | [Bmim]BF4 (10) | – | 70 | 1 | 80 |
| 7 | [Bmim]$BF_4$ (15) | – | 70 | 1 | 92 |
| 8 | [Bmim]BF4 (20) | – | 70 | 1 | 92 |
| 9 | [Bmim]BF4 (15) | – | 90 | 5 | 92 |
| 10 | [Bmim]BF4 (15) | – | 50 | 5 | 82 |

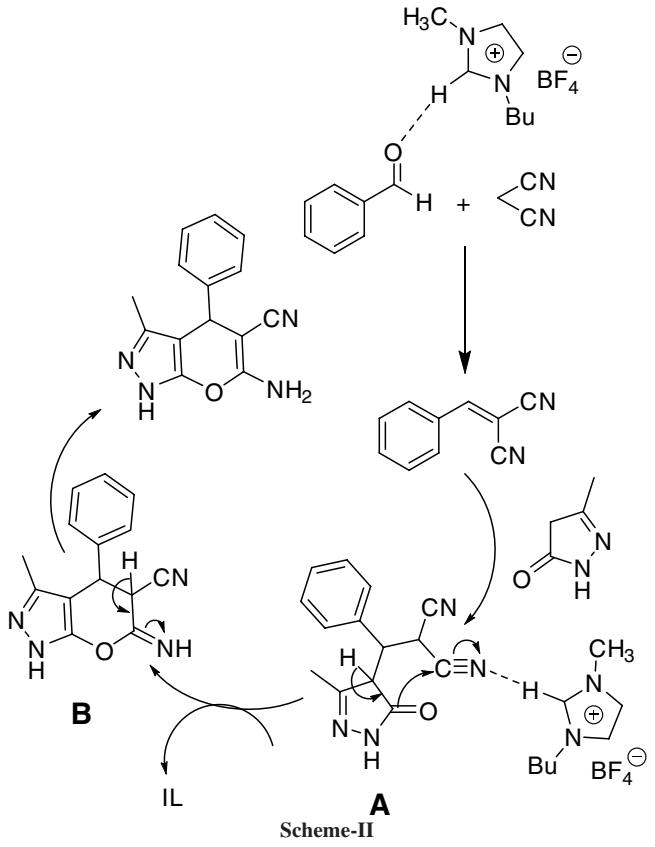
[a]Isolated yields.

TABLE-2
SYNTHESIS OF DIHYDROPYRANO[2,3-*c*]PYRAZOLE DERIVATIVES (**5a-l**)

| Entry | Product | R | $R_1$ | $R_2$ | Time (h) | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | 5a | H | H | H | 1 | 92 |
| 2 | 5b | 4-$OCH_3$ | H | H | 1 | 90 |
| 3 | 5c | 4-Cl | H | H | 1 | 90 |
| 4 | 5d | 4-F | H | H | 1 | 88 |
| 5 | 5e | H | H | 2-$NO_2$ | 1 | 89 |
| 6 | 5f | H | 3-$NO_2$ | H | 1 | 86 |
| 7 | 5g | 4-$NO_2$ | H | H | 1 | 90 |
| 8 | 5h | $C_6H_5$ | $C_6H_5$ | $C_6H_5$ | 1 | 92 |
| 9 | 5i | Quinoline | Quinoline | Quinoline | 1 | 88 |
| 10 | 5j | $C_6H_5$-$OCH_3$ | $C_6H_5$-$OCH_3$ | $C_6H_5$-$OCH_3$ | 1 | 85 |
| 11 | 5k | $N(CH_3)_2$ | H | H | 1 | 88 |
| 12 | 5l | $C_6H_5$-$CH_3$ | $C_6H_5$-$CH_3$ | $C_6H_5$-$CH_3$ | 1 | 90 |

multicomponent reaction. The reaction of ethyl 3-oxobutanoate (1 mmol), hydrazinehydrate (1 mmol), aromatic aldehyde (1 mmol) and malononitrile (1 mmol), was examined in the presence of the optimization conditions that are summarized in Table-2. It was observed that almost all of the investigated ionic liquid was capable of solvent-catalyst system of the synthesis of desired dihydropyrano[2,3-*c*]pyrazole derivatives under convenient method at 70 °C for 2 h. Further optimization studies revealed that when the reaction was carried out acidic ionic liquid such as [Bmim]Br, [Bmim]Cl and [Bmim]$PCl_5$ as a solvent-catalysts, under refluxing conditions resulted **5a** in isolated yield of 68, 72 and 56 %, respectively (Table-1, entries 3, 4 and 5). In this work, [Bmim]$BF_4$ was found to effective solvent-catalyst system for the synthesis of dihydropyrano[2,3-*c*]pyrazole as evidenced from the obtained superior results. [Bmim]$BF_4$ has a dual role to act as catalyst and solvent at 70 °C the reaction time was reduced from 2 h to 1 h with improved isolated yield (92 %) (Table-1, entry 7). No further improvement in isolated yield was observed by increasing the reaction time and temperature (Table-1, entry 9 and 10).

A series of dihydropyrano[2,3-*c*]pyrazole derivatives were synthesized with excellent yield under conventional method as shown in Table-2. The reaction was conducted with aromatic aldehydes contain both electron donating and withdrawing substituents were found to show no significant effect on the formation of the final product (Table-2). The $^1$H NMR of the compounds (**5a**) exhibited characteristic peaks of benzylic proton as singlet at 4.59 ppm, amino group ($NH_2$) attached tertiary carbon protons at 6.87 ppm and aromatic protons at 7.31 (t), 7.22 (t) and 7.17 (d) indicating the presence of phenyl group. Additionally, the $^{13}$C NMR of the final products showed characteristic peaks at δ 97.59 ppm which is due to benzylic carbon and peaks at δ 120.72 ppm due to nitrile carbon group. The IR spectra of the final compounds displayed absorption bands at 3372, 3169 and 2192 $cm^{-1}$, respectively. Absence of the absorption stretching frequencies of corresponding $NH_2$, NH and C≡N of the starting materials clearly indicates the formation of the final product, The formation of desired product can be achieved *via* condensation ethyl 3-oxobutanoate (**1**) hydrazine hydrate (**2**) to form pyrazolone with the possible intermediate **A**. Treatment of the intermediate **A** with pyrazolone under green condition to form intermediate **B** followed by intermolecular proton transfer affords compound **5a**.




**Scheme-II**

## Conclusion

The combination of ionic liquids with ethyl 3-oxobutanoate, hydrazine hydrate, aromatic aldehyde and malononitrile under green condition was effective for effective for the one-pot and eco-friendly synthesis of biologically interesting dihydropyrano[2,3-c]pyrazole derivatives. [Bmim]$BF_4$ was found to the effective ionic liquid for the synthesis of these multicomponent reactions. Therefore, we strongly believe that these eco-efficient and green protocols be of great value for both synthetic and medicinal chemistry for practical applications.

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