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ORIGINAL PAPER

Solvent-free, four-component synthesis of 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-2*H*-pyridazino[1,2-a] indazole-1,6,9(11*H*)-triones; using 1-butyl-3-methylimidazolium hydroxide ([bmim]OH) as a green and reusable catalyst

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Abstract A series of 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-2*H*-pyridazino[1,2-a]indazole-1,6,9(11*H*)-trione derivatives have been synthesized via one-pot, four-component reaction in the presence of 3-methyl-1-butyl imidazolium hydroxide as an efficient catalyst. A broad range of structurally diverse aldehydes (aromatic aldehydes bearing electron withdrawing and electron releasing groups) was applied successfully, and corresponding products were obtained in good to excellent yields without any by-product. The catalyst was stable during the reaction process and could also be reused several times with consistent activity.

Keywords Ionic liquid · Succinic anhydride · Multi-component reaction · Neat conditions

Introduction

Multi-component reactions (MCRs) play an important role in organic and medicinal chemistry because of their ability to synthesize of target compounds with high efficiency and atom economy by generating structural complexity in a single step from three or more reactants. Moreover, MCRs offer the advantages of simplicity and synthetic efficiency over conventional chemical reactions [1]. Therefore, designing of these reactions for the synthesis of diverse groups of compounds, especially the ones that are biologically active, have gained great attention in green organic synthesis [2–4].

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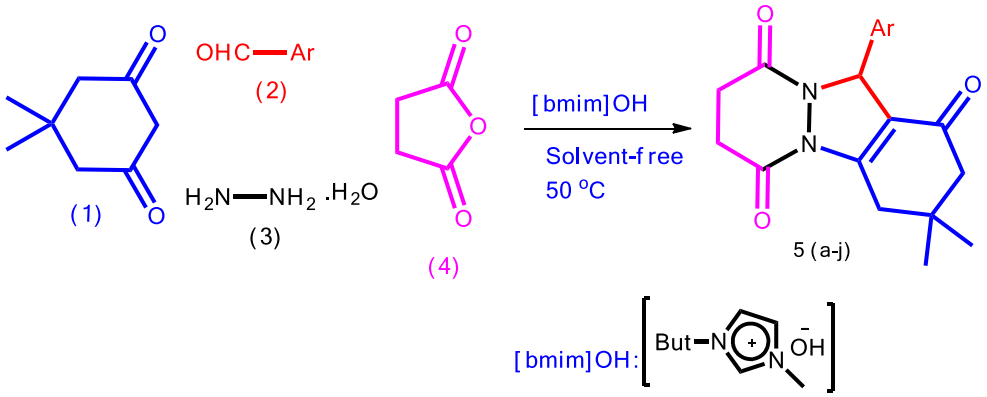
Very recently, use of ionic liquids (ILs) as green solvents has found versatile applications in organic reactions due to their promising features such as the ability to control product distribution [5], offering enhanced rate [6–8] and/or reactivity [9], ease of product recovery [10, 11], catalyst immobilization [12–14], and recycling. [15, 16] Given that, ionic liquids have also been effectively utilized for the synthesis of novel bioactive compounds [17].

Among heterocyclic compounds, great focus has been directed towards bridgehead nitrogen-containing heterocycles especially heterocycles containing bridgehead hydrazine such as pyridazine and fused pyridazine since they provide pharmacological and biological activities, herbicides, insecticides and fungicides [18–23]. Indazoles are the other category of bridgehead hydrazine-containing heterocycles. They are bioisosteres of indoles and have been widely used in the medicinal area [24]. In fact, compounds containing the indazole moiety are known to show a variety of biological activities, such as high binding affinity for estrogen receptor [25], inhabitation of protein kinase C-β [26], 5-HT_2 and 5-HT_3 receptor antagonisms [27], human immunodeficiency virus (HIV) protease inhibition [28], and anti-tumor activity [29].

The recent protocols have been directed towards the design of structural motifs containing the pyridazino[1,2-a] indazole ring fragment using of condensation of aldehydes and dimedone followed by reaction with 2,3-dihydrophthalazine-1,4-dione [30–33] or 1,2-dihydropyridazine-3,6-dione [34, 35].

In continuation of our research on ionic liquids and their applications as catalyst in organic synthesis, [36] we decided to investigate 1-butyl-3-methylimidazolium hydroxide ([bmim]OH) as green catalyst for the practical and environmentally benign one-pot four-component synthesis of novel 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-



Scheme 1 Solvent-free four- component synthesis of 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-2*H*-pyridazino[1,2-a] indazole-1,6,9(11*H*)-triones **(5a–j)** using 1-butyl-3-methyl-imidazolium hydroxide ([bmim] OH)

2*H*-pyridazino[1,2-a]indazole-1,6,9(11*H*)-triones **(5a–j)** under solvent-free conditions (Scheme 1).

Experimental section

Chemicals

Chemicals were either prepared in our laboratory or purchased from Merck or Fluka chemical companies, and were used without any further purification. The ionic liquid 1-Butyl-3-methyl imidazolium hydroxide [bmIm]OH as a catalyst was prepared according to the reported procedure [37].

Apparatus

IR spectra were recorded in KBr, using a BRUKER FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ and DMSO (d_6) solvents on a Bruker DRX-500 spectrometer with tetramethylsilane as internal reference. Melting points obtained with a Yanagimoto micro melting point apparatus are uncorrected. Mass spectra were obtained from Waters ZQ 4000 mass spectrometer by the ESI method. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. Melting points were determined with a hot-plate microscope apparatus. The purity determination of the substrates and reaction monitoring were accomplished by TLC (petroleum–ethyl acetate 3:1) on silica-gel polygram SILG/UV 254 plates (from Merck Company).

General procedure for the preparation of 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-2*H*-pyridazino[1,2-a] indazole-1,6,9(11*H*)-triones (5a–j) under solvent-free conditions

Hydrazine monohydrate (1 mmol) and succinic anhydride (1 mmol) were mixed at 25 °C (5 min). Then, aromatic aldehydes (1 mmol), dimedone (1 mmol) and [bmIm]OH (25 % mol) were added and stirred at 50 °C under solvent-free conditions for the specific time. After completion of the reaction, 5 mL of water was added to the mixture. The ionic liquid was dissolved in water, and filtered for separation of the crude product. The separated product was washed twice with water (2 × 5 mL). The solid product was purified by recrystallization procedure in ethanol. All the products obtained were characterized by spectroscopic methods such as IR, 1H NMR, 13C NMR, Mass spectra and elemental analysis.

For recycling the catalyst, after washing solid products with water completely, the water containing ionic liquid (IL is soluble in water) was evaporated under reduced pressure and ionic liquid was recovered and reused.

Spectroscopic data of new products are given below:

Spectra Data of 3,4,7,8-tetrahydro-3,3-dimethyl-11-phenyl-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5a) Pale yellow solid: mp. 112.0–113.0 °C. IR (KBr): ν = 3031, 2922, 1694, 1595. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.11 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 2.14-2.24 (2H, AB system, J = 20 Hz), 2.31–2.53 (m, 4H, $2CH_2$), 2.87 (s, 2H, CH_2), 5.53 (s,1H, CHN), 7.46–7.47 (d, 1H, CH arom), 8.02–8.13 (m, 4H, CH arom), ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ = 25.29, 26.56, 26.72, 29.75, 32.47, 32.51, 41.93, 52.47, 114.43, 125.78, 126.70, 128.25, 128.72, 128.84, 129.31, 131.58, 149.48 (CO), 165.42 (CO), 195.85 (CO), MS, m/z (%): 324 (M+, 5), 253 (30), 240 (99), 207 (80), 180 (40), 158 (50), 131 (80), 104 (99), 91 (100), Anal. Calcd. for. $C_{19}H_{20}N_2O_3$: C: 70.35, H: 6.21, N: 8.64 %. Found: C: 70.55; H: 6.65; N: 8.08 %.

11-(4-chlorophenyl)-3,4,7,8-tetrahydro-3,3-dimethyl-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5b) Yellow solid: mp. 197.0–199.0 °C. IR (KBr): ν = 3062, 2980, 1664, 1545, 761. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.99 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 2.14-2.25 (2H, AB

system, $J = 20$ Hz), 2.31–2.53 (m, 4H, $2CH_2$), 2.87 (s, 2H, CH_2), 5.49 (s,1H, CHN), 8.03 (d, 2H, $J = 8$ Hz, CH arom); 8.12 (d, 1H, $J = 9.5$ Hz CH arom), 8.29 (d, 1H, $J = 8$ Hz CH arom), ^{13}C NMR ($CDCl_3$, 125.77 MHz): $\delta = 21.96$, 28.70, 28.89, 29.49, 32.24, 33.73, 40.11, 54.24, 115.45, 127.47, 128.0, 128.77, 129.54, 129.81, 129.86, 150.52 (CO), 163.54 (CO), 195.90(CO). MS, m/z (%): 359 (M+, 3), 312 (10), 274(50), 220 (40), 192 (40), 138 (70), 111 (100), 83 (99), 51 (90). Anal. Calcd. for. $C_{19}H_{19}ClN_2O_3$: C: 63.60, H: 5.34, N: 7.81 %. Found: C: 63.45; H: 5.64; N: 7.98 %.

3,4,7,8-tetrahydro-3,3-dimethyl-11-(4-nitrophenyl)-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5c) Yellow solid: mp. 148.0–150.0 °C. IR (KBr): $\nu = 3059$, 2925, 1675, 1599. ^{1}H NMR (500 MHz, $CDCl_3$) $\delta = 0.98$ (s, 3H, CH_3),1.13(s, 3H, CH_3), 2.14–2.26 (2H, AB system, $J = 16$ Hz), 2.31–2.53 (m, 4H, $2CH_2$), 2.93 (s, 2H, CH_2), 5.45 (s, 1H, CHN), 7.45–7.47 (d, 1H, $J = 6$ Hz, CH arom), 8.03 (d, 1H, $J = 8.7$ Hz, CH arom), 8.08 (d, 1H, $J = 8.7$ Hz CH arom), 8.12 (d, 1H, $J = 9$ Hz CH arom); ^{13}C NMR ($CDCl_3$, 125.77 MHz); $\delta = 27.49$, 28.73, 28.85, 29.49, 32.24, 33.66, 40.10, 52.00, 114.63, 127.03, 130.00, 130.30, 130.55, 133.53,135.52, 137.525, 155.57 (CO), 163.30 (CO), 191.17 (CO). MS, m/z (%): 369 (M+, 80), 380 (10), 384 (10), 273 (99), 189 (90), 161 (70), 83 (70), 55 (100), 41 (60), Anal. Calcd. for. $C_{19}H_{19}N_3O_5$: C: 61.78, H: 5.18, N: 11.38 %. Found: C: 61.28; H: 5.64; N: 11.63 %.

3,4,7,8-tetrahydro-3,3-dimethyl-11-(3-nitrophenyl)-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5d) Cream solid: mp. 157.0–158.0 °C. IR (KBr): $\nu = 3063$, 2959, 1649, 1597, 1556. ^{1}H NMR (500 MHz, DMSO, d_6) $\delta = 0.68$ (s, 3H, CH_3), 0.85(s, 3H, CH_3), 1.70–2.00 (2H, AB system, $J = 16$ Hz), 2.14–2.21 (m, 4H, $2CH_2$), 2.90 (s, 1H, CH arom), 5.50 (s, 1H, CHN), 7.20–7.30 (m, 2H, CH arom), 7.48 (d, 1H, $J = 11$ Hz, CH arom), 7.58 (s, 1H, CH arom); ^{13}C NMR (DMSO, d_6 125.77 MHz); $\delta = 26.48$, 27.69, 29.47, 29.90, 30.69, 32.47, 41.37, 50.00, 113.49, 124.02, 126.28, 128.02, 130.31, 135.37, 141.32, 148.61, 150.49 (CO), 160.49 (CO), 191.41 (CO). MS, m/z (%): 369 (M+, 30), 348 (20), 300 (10), 273 (100), 189 (90), 83 (60), 55 (90). Anal. Calcd. for. $C_{19}H_{19}N_3O_5$: C: 61.78, H: 5.18, N: 11.38 %. Found: C: 61.45; H: 5.14; N: 11.98 %.

3,4,7,8-tetrahydro-3,3-dimethyl-11-p-tolyl-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5f) Yellow solid: mp. 148.0–150.0 °C. R (KBr): $\nu = 3059$, 2956, 1648, 1548. ^{1}H NMR (500 MHz, DMSO, d_6) $\delta = 0.70$ (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 1.84–2.03 (AB system, 2H, $J = 20$ Hz), 2.19–2.26 (m, 4H, $2CH_2$), 2.70 (s, 3H, CH_3), 2.96 (s, 2H, CH_2), 5.12 (s, 1H, CHN), 7.15 (d, 1H, $J = 7.00$ Hz, CH arom), 7.25 (d, 1H, $J = 10$ Hz,CH arom), 7.58–7.60 (t, 1H, $J = 9.5$ Hz, CH arom), 7.75 (d, 1H, $J = 9$ Hz, CH arom); ^{13}C NMR (DMSO, d_6, 125.77 MHz); $\delta = 21.53$, 23.64, 26.33, 26.53, 29.64, 32.33, 32.48, 41.36, 55.92, 113.02, 126.66, 129.64, 130.37, 131.28, 135.34, 141.21, 145.99, 150.72 (CO), 167.33 (CO), 195.81 (CO); MS, m/z (%): 338 (M+, 2), 318 (10), 287 (20), 254 (99), 198 (50), 172 (75), 105 (80), 91 (100), 65 (50), Anal. Calcd. for. $C_{20}H_{22}N_2O_3$: C: 70.99, H: 6.55, N: 8.2 %. Found: C: 70.49; H: 6.95; N: 8.98 %.

11-(2,4-dichlorophenyl)-3,4,7,8-tetrahydro-3,3-dimethyl-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5 *g)* Livid solid: mp. 183.0–185.0 °C. IR (KBr): $\nu = 3059$, 2956, 1635, 1578, 758. ^{1}H NMR (500 MHz, DMSO, d_6) $\delta = 1.08$ (s, 6H, $2CH_3$), 2.28 (d, $J = 3.5$, 2H, CH_2), 2.49–2.75 (m, 4H, $2CH_2$), 2.90 (d, $J = 20$ Hz, 2H, CH_2), 5.37 (s, 1H, CHN), 7.33–7.50 (m, 2H, CH arom), 7.88 (d, 1H, $J = 8.5$ Hz, CH arom); ^{13}C NMR (DMSO, d_6, 125.77 MHz); $\delta = 19.79$, 20.61, 27.62, 30.92, 36.17, 43.87, 57.08, 113.20, 127.98, 129.65, 130.32, 130.78, 130.88, 130.98, 153.30 (CO), 160.62 (CO), 198.62 (CO); MS, m/z (%): 393 (M+, 10), 382 (20), 310 (40), 275 (90), 219 (50), 172 (80), 123 (90), 83 (100), 55 (90). Anal. Calcd. for. $C_{19}H_{18}Cl_2N_2O_3$: C: 58.03, H: 4.61, N: 7.12 %. Found: C: 58.33; H: 4.31; N: 7.52 %.

11-(4-(dimethylamino)phenyl)-3,4,7,8-tetrahydro-3,3-dimethyl-2H-pyridazino [1,2-a]indazole-1,6,9 (11H)-trione (5 *h)* Green solid: mp. 198.0–200.0 °C. IR (KBr): $\nu = 3054$, 2923, 1624, 1564. ^{1}H NMR (500 MHz, DMSO, d_6) $\delta = 0.70$ (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.80–1.94 (2H, AB system, $J = 20$ Hz), 2.18–2.22 (m, 4H, $2CH_2$), 2.90 (s, 2H, CH_2), 3.36 (s, 6H, $N(CH_3)_2$), 5.03 (s, 1H, CHN), 6.91–6.95 (t, 1H, $J = 7.5$ Hz, CH arom), 7.01–7.17 (m, 1H, CH arom), 7.21–7.30 (m, 2H, CH arom); ^{13}C NMR (DMSO, d_6, 125.77 MHz); $\delta = 24.81$, 25.04, 26.04, 29.91, 31.78, 31.99, 40.85, 41.95, 49.51, 118.62, 125.07, 127.42, 127.65, 129.41, 131.13, 148.32, 151.08 (CO), 157.60 (CO), 195.03 (CO); MS, m/z (%): 367 (M+, 10), 348 (20), 287 (10), 273 (80), 189 (90), 161 (40), 83 (60), 55 (100), Anal. Calcd. for. $C_{21}H_{25}N_3O_3$: C: 68.64, H: 6.86, N: 11.44 %. Found: C: 68.84; H: 6.66; N: 11.04 %.

3,4,7,8-tetrahydro-11-(4-hydroxyphenyl)-3,3-dimethyl-2H-pyridazino[1,2-a]indazole-1,6,9(11H)-trione (5j) Yellow solid: mp. 184.0–185.0 °C. IR (KBr): ν = 3380, 2957, 1640, 1512. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.98 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.15–2.26 (2H, CH_2, AB system, J = 20 Hz), 2.31–2.50 (m, 4H, $2CH_2$), 2.85 (s, 2H, CH_2), 5.54 (s, 1H, CHN), 6.46 (d, 1H, J = 8.5 Hz, CH arom), 8.02–8.13 (m, 2H, CH arom), 8.29 (d, 1H, J = 8.5, CH arom); 11.78 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ = 28.69, 28.91, 29.49, 32.24, 33.73, 40.11, 51.09, 115.52, 115.91, 128.55, 128.93, 129.39, 129.48, 129.66, 130.27, 131. 27, 155.91 (CO), 177.92 (CO), 193.66 (CO), MS, m/z (%): 340 (M+, 3), 317 (3), 272 (20), 254 (15), 119 (60), 105 (60), 91 (95), 41 (100). Anal. Calcd. for. $C_{19}H_{20}N_2O_4$. C: 67.05, H: 5.92, N: 8.23 %. Found: C: 67.25; H: 5.83; N: 8.68 %.

Results and discussion

First, the four-component reaction of benzaldehyde **(2a)** (1 mmol), dimedone **(1)** (1 mmol), hydrazine hydrate **(3)** (1.2 mmol) and succinic anhydride **(4)** (1 mmol), was chosen as the model reaction. We tried to prepare 3,4,7,8-tetrahydro-3,3-dimethyl-11-phenyl-2*H*-pyridazino[1,2-a]indazole-1,6,9(11*H*)-trione **(5a)** in the presence of ionic liquids, Brønsted acidic heterogeneous and basic catalysts under different conditions.

In the absence of any catalysts, the reaction did not proceed even after prolonged reaction time and no desired product was formed (Table 1, entry 1).

The reaction produce desired product in low yield and starting materials were observed intact even after 24 h (Table 1, entries 2–8). Thus, acidic catalysts did not show any significant catalytic activities in the mentioned reaction. But, in basic catalytic condition such as Et_3N, NaOH and KOH the desired product was obtained in 35–45 % yield (Table 1, entries 9–13). In addition, the above mentioned model reaction was conducted in the presence of other ionic liquid including [bmIm]OH and $[Et_3NH]^+[HSO_4]^-$ under solvent-free conditions (Table 1, entries 14–18).

The best result was obtained using 25 mol % of [bmIm]OH at 50 °C (Table 1, entry 17). Thus, this basic ionic liquid was chosen as the reaction catalyst in this research.

We found that, decreasing the temperature to 30 °C (Table 1, entry 16) led to the lower yield and longer reaction time.

In another study, the condensation of dimedone **(1)**, benzaldehyde **(2)**, hydrazine hydrate **(3)** and succinic anhydride **(4)** were examined in the presence of different quantities of [bmIm]OH (7, 15, 20, 25, 27 mol %) as catalyst at 50 °C temperature (Table 2). As it is shown in Table 2, [bmIm]OH] (25 mol %) as

Table 1 Optimization of reaction conditions

Entry	Catalyst	Condition	Time (h)	Yield[a] (%)
1	No	Solvent-free, 100 °C)	20	Trace
2	$La(NO_3)$ (0.08 g, 0.25 mmol)	EtOH (Reflux)	24	40
3	$La(NO_3)$ (0.08 g, 0.25 mmol)	THF (Reflux)	24	25
4	$La(NO_3)$ (0.1 g, 0.31 mmol)	Solvent-free, 100 °C)	4	30
5	$LaCl_3$. $7H_2O$ (0.08 g, 0.21 mmol)	EtOH (Reflux)	3	35
6	$LaCl_3$. $7H_2O$ (0.1 g, 0.27 mmol)	CH_2Cl_2 (Reflux)	24	10
7	$LaCl_3$. $7H_2O$ (0.08 g, 0.21 mmol)	(Solvent-free, 100 °C)	1	25
8	$ZnCl_2$ (0.1 g, 0.73 mmol)	Solvent-free, 100 °C)	2	40
9	NaOH (0.02 g, 0.5 mmol)	EtOH (Reflux)	3	40
10	KOH (0.03 g, 0.5)	EtOH (Reflux)	4	42
11	Et_3N (0.023 g, 0.22 mmol)	EtOH (rt.)	24	35
12	Et_3N (0.023 g, 0.22 mmol)	EtOH (Reflux)	12	45
13	Et_3N (0.46 g, 0.44 mmol)	Solvent-free, 80 °C)	8	40
14	$[Et_3NH]^+[HSO_4]^-$ (0.1 g, 0.5 mmol)	(Solvent-free, 100 °C)	1	35
15	$[Et_3NH]^+[HSO4]^-$ (0.2 g, 1 mmol)	(Solvent-Free,100 °C)	1	40
16	[bmIm]OH (0.04 g, 0.25 mmol)	(Solvent-free, 30 °C)	2	87
17	[bmIm]OH (0.04 g, 0.25 mmol)	(Solvent-Free, 50 °C)	55 min	94
18	[bmIm]OH (0.04 g, 0.25 mmol)	(Solvent-free, 70 °C)	55 min	93

Reaction condition: **1** (1 mmol), **2** (benzaldehyde, 1 mmol), **3** (1.1 mmol) and **4** (1 mmol)

[a] Isolated yields

Table 2 Optimization of [bmIm]OH amount: as a catalyst

Entry	Amount of catalyst (g)	Time (min)	Yield (%)[a]
1	7	80	83
2	15	75	87
3	20	60	90
4	25	55	94
5	27	55	93

Reaction condition: **1** (1 mmol), **2** (benzaldehyde, 1 mmol), **3** (1.1 mmol), **4** (1 mmol) under solvent-free conditions at 50 °C

[a] Yields refer to pure isolated yields

Table 3 Four-component synthesis of 3,4,7,8-tetrahydro-3,3-dimethyl-11-aryl-2*H*-pyridazino[1,2-a]indazole-1,6,9 (11*H*)-trione derivatives

Entry	Aldehyde	Time (min)	Yield (%)[a]	Melting point (°C)
2a	PhCHO	55	93	190–192
2b	2-ClC_6H_4CHO	40	91	230–232
2c	4-$O_2NC_6H_4CHO$	35	90	205–207
2d	3-$O_2NC_6H_4CHO$	30	88	230–233
2e	4-$CH_3OC_6H_4CHO$	40	93	112–113
2f	4-$CH_3C_6H_4CHO$	50	90	212–214
2g	2,4-$(Cl)_2$ C_6H_3CHO	55	92	185–187
2h	4-$(CH_3)_2NC_6H_4CHO$	25	85	217–218
2i	4-BrC_6H_4CHO	60	88	215–217
2j	4-HOC_6H_4CHO	40	80	240–242

Reaction condition: **1** (1 mmol), **2** (1 mmol), **3**(1.1 mmol), **4**(1 mmol) and [bmIm]OH (25 mol %), solvent-free, 50 °C

[a] Yields refer to pure isolated yields

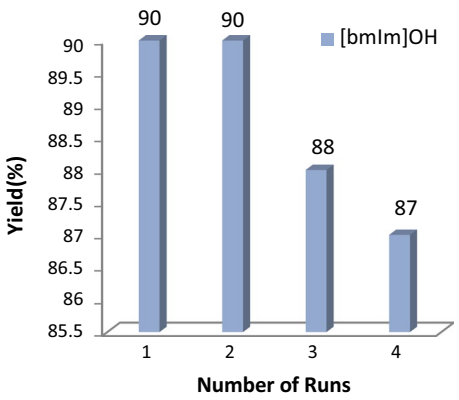


Fig. 1 Recyclability of the catalyst in the reaction of succinic anhydride, dimedone, hydrazine hydrate and benzaldehyde in the presence of [bmIm]OH, under solvent-free conditions at 50 °C

a catalyst afforded **5a** in 55 min with 94 % yield, respectively (entry 4). Additionally, no improvement in the reaction results was observed after increasing the amount of catalyst.

After optimization of the reaction conditions, the generality of this method was examined by the reaction of dimedone **(1)**, succinic anhydride **(4)**, hydrazine hydrate **(3)** with different kinds of aromatic aldehydes **(2a–j)** in the presence of [bmIm]OH at 50 °C under solvent-free conditions (Table 3).

It was observed that aromatic aldehydes having both electron withdrawing and electron donating groups participated in the reaction and there was no significant difference in the yield of reaction. However, electron-withdrawing substituents led to the shorter reaction time. (Table 3, entries 2c, d).

Stability and recycling of the catalyst

We investigated the possibility of recycling of [bmIm]OH as a catalyst under solvent-free conditions using a model reaction of dimedone **(1)**, benzaldehyde **(2a)**, hydrazine hydrate **(3)** and succinic anhydride **(4)** for preparation **5a** in the presence of [bmIm]OH. Catalytic activity of the recovered ionic liquid from the model reaction was checked in the subsequent runs (Fig. 1). The activity of the catalyst was not significantly affected in terms of yields after four successive runs for the model reaction.

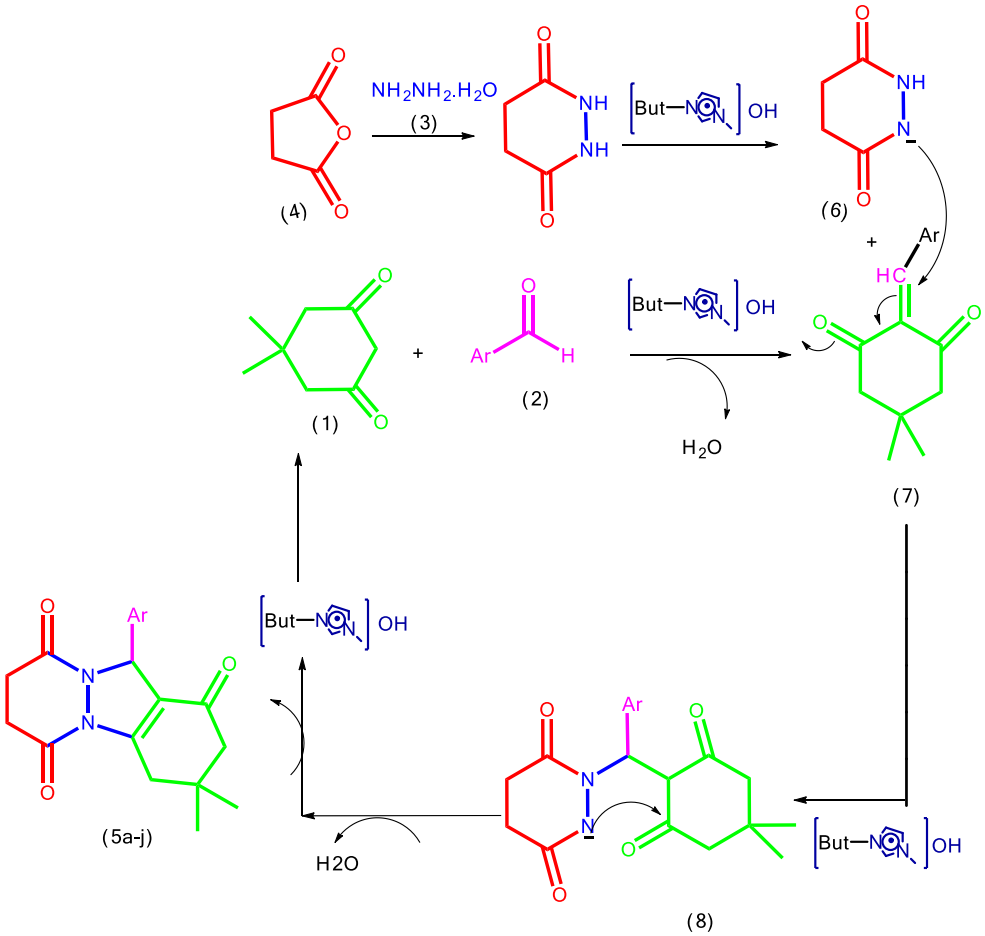
The proposed mechanism

The proposed mechanism for the synthesis of **5(a–j)** using [bmIm]OH is shown in Scheme 2.

The reaction is supposed to proceed in a stepwise manner. First, we assumed that the reaction is conducted via a Knoevenagel condensation between compound 1 and aromatic aldehyde 2 to form the intermediate 7 in the presence of [bmIm]OH, which suffers immediate Michael addition of intermediate 6–7. The concerted cyclocondensation of amino and carbonyl of the Michael adduct 8 was performed to furnish the corresponding products **(5a–j)**. During the reaction process, the hydroxide ion helps the enolization of dimedone to form enolate intermediate. Thus, increasing the rate of reaction **(1)**.

Conclusion

In summary, we have synthesized a new series of 3,4,7,8-tetrahydro-3,3-dimethyl-11-phenyl-2*H*-pyridazino[1,2-a]indazole-1,6,9(11*H*)-trione derivatives **(5a–j)** by one-pot, four-component condensation reaction of succinic anhydride, dimedone, hydrazine hydrate, and aromatic aldehydes under thermal



Scheme 2 The proposed mechanism for the synthesis of 3,4,7,8-tetrahydro-3,3-dimethyl-11-phenyl-2*H*-pyridazino[1,2-a] indazole-1,6,9(11*H*)-triones **(5a–j)** using [bmIm]OH

solvent-free conditions using 1-Butyl-3-methyl imidazolium hydroxide, [bmIm]OH as a green, recoverable and highly efficient catalyst. The attractive features of this protocol are simple procedure, cleaner reaction, reusable catalyst, satisfactory yield of products, simple reactions, isolation, and purification of the products, as well as ease of preparation of the catalyst. Its compliance with the green chemistry protocols makes it a useful protocol for the synthesis of these classes of compounds.

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