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ORIGINAL ARTICLE

1,2-Dimethyl-*N*-butanesulfonic acid imidazolium hydrogen sulfate as efficient ionic liquid catalyst in the synthesis of indeno fused pyrido[2,3-*d*]pyrimidines

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KEYWORDS

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2,6-Diaminopyrimidin-4(3*H*)-one;
Ionic liquid;
Green catalyst;
One-pot

Abstract Indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidin-4,6-(5*H*,11*H*)dione derivatives were synthesized regioselectively in high yields by a three-component reaction of 1,3-indanedione, aromatic aldehydes and 2,6-diaminopyrimidin-4(3*H*)-one in the presence of 1,2-dimethyl-*N*-butanesulfonic acid imidazolium hydrogen sulfate ([DMBSI]HSO_4) ionic liquid as green and reusable catalyst. This protocol produced the desired products in high yields (87–95%) and short reaction times (3–6 min).

1. Introduction

Pyridopyrimidines are nitrogen-bearing heterocyclic compounds which have various pharmaceutical applications. In particular, pyrido[2,3-*d*]pyrimidine derivatives show variable biological activities such as anticancer agents inhibiting dihydrofolate reductases or tyrosine kinases [1–3], antitumor [4,5], antiviral [6], antihistaminic [7], anti-inflammatory [8], antibacterial [9–12], and also act as cyclin-dependent kinase 4 inhibitors [13]. This structural moiety is present in ramastine (anti-allergic) [14] and pirenperone (tranquilizer) [15]. As a result, the compounds of this class have attracted considerable interests for research. Several MCR methods have been reported for the synthesis of pyrido[2,3-*d*]pyrimidines [16–21]. Although most of these methods offer distinct advantages, some of them still have their own limitations in terms of yields, longer reaction times and difficult work-up. In some cases, the catalysts used are harmful to environment and cannot be reused. Therefore, an efficient method for the preparation of pyrido[2,3-*d*]pyrimidine derivatives is still desirable.

On the other hand, recently, ionic liquids have been employed as solvent and catalyst for a variety of reactions. Their use as an environmentally friendly alternative for conventional solvents has gained much attention recently [22–25]. The use of ionic liquids as reaction medium may offer a

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convenient solution to both the solvent emission and catalytic recycling problem [22,26,27].

We have recently reported efficient and eco-friendly procedures for the preparation of pyrido[2,3-*d*]pyrimidines [28], using 1,2-dimethyl-*N*-butanesulfonic acid imidazolium hydrogen sulfate ([DMBSI]HSO_4) ionic liquid under solvent-free conditions. In order to expand the application of [DMBSI]HSO_4 in the synthesis of heterocyclic compounds, we describe here an efficient and practical method for the preparation of indeno fused pyrido[2,3-*d*]pyrimidines.

2. Experimental

2.1. General

Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. IR spectra (KBr) were determined on a Shimadzo IR-470 spectrometer and FT-IR on α-Bruker. NMR spectra were recorded on a Bruker DRX (400 MHz) (^{1}H) and Bruker DRX (100 MHz) (^{13}C) in DMSO-d_6 as solvent and TMS as an internal standard; δ was quoted in ppm and J in Hz. Elemental analyses were done on a Carlo–Erba EA1110CNNO-S analyzer and agreed with the calculated values. Chemicals were purchased from Merck and Fluka. All solvents used were dried and distilled according to standard procedures.

SO_3H-functionalized ionic liquid [DMBSI]HSO_4 was synthesized according to the literature [26].

2.2. General procedure for preparation of **4a–n**

A mixture of equimolar amounts of 1,3-indanedione **1** (1 mmol), arylaldehyde **2** (1 mmol) and 2,6-diamino-4-hydroxy pyrimidine **3** (1 mmol), in ethylene glycol (5 mL) containing [DMBSI]HSO_4 (0.18 mmol, 0.06 g) was heated under reflux at 120 °C. The progress of the reaction was monitored by TLC (EtOAc/petroleum ether: 1/9). Stirring at 120 °C was continued until disappearance of the starting materials (monitored by TLC). The reaction mixture was cooled and washed with water to extract the ionic liquid. The solid obtained was recrystallized from MeOH to furnish the desired pure product (Table 4).

2.2.1. 2-Amino-5-(4-methoxyphenyl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6 (5H,11H)-dione (**4a**)

Red powder, m.p. 324–326 °C, IR (KBr): 3410, 3350, 3080, 2800, 1680, 1590, 1540, 1513, 1480, 1440, 1260, 1240, 1020, 840, 800, 760 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.66 (s, 3H, OCH_3), 4.65 (s, 1H, CH), 6.74 (d, J = 8.4 Hz, 1H, Ar–H), 6.82 (s, br., 2H, NH_2), 7.11 (d, J = 8.4 Hz, 1H, Ar–H), 7.19 (d, J = 10.4 Hz, 1H, Ar–H), 7.29 (t, J = 7.0 Hz, 1H, Ar–H), 7.38 (t, J = 7.0 Hz, 1H, Ar–H), 7.73 (d, J = 7.2 Hz, 1H, Ar–H), 8.46 (s, br. 1H, NH), 8.97 (s, br. 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.3, 55.3, 93.5, 108.7, 113.6, 120.0, 120.4, 128.9, 130.4, 132.0, 134.0, 136.9, 139.2, 154.8, 155.9, 157.8, 191.1. Anal. Cald for $C_{21}H_{16}N_4O_3$ (372.38): C, 67.73; H, 4.33; N, 15.05. Found: C, 67.60; H, 4.21; N, 15.18.

2.2.2. 2-Amino-5-(thiophen-2-yl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4b**)

Red powder, m.p. 327–329 °C, IR (KBr): 3449, 3246, 3077, 2926, 1600, 1515, 1450, 1279, 790, 693 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.03 (s, 1H, CH), 6.81–6.84 (m, 2H, Ar–H), 7.15 (s, br., 2H, NH_2), 7.16 (dd, J = 4.4, 2.0 Hz, 1H, Ar–H), 7.27 (d, J = 6.8 Hz, 1H, Ar–H), 7.34 (t, J = 7.2 Hz, 1H, Ar–H), 7.39 (t, J = 8.0 Hz, 1H, Ar–H), 7.74 (d, J = 7.2 Hz, 1H, Ar–H), 10.77 (s, br. 1H, NH), 11.98 (s, br. 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 28.8, 93.6, 107.7, 120.3, 120.8, 123.7, 123.8, 127.1, 130.7, 132.2, 133.9, 136.6, 151.6, 154.8, 155.0, 156.3, 162.9, 190.9. Anal. Cald for $C_{18}H_{12}N_4O_2S$ (348.38): C, 62.06; H, 3.47; N, 16.08. Found: C, 62.20; H, 3.35; N, 15.85.

2.2.3. 2-Amino-5-(4-methylphenyl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4c**)

Red powder, m.p. 322–323 °C, IR (KBr): 3399, 3252, 3070, 2918, 2744, 1667, 1598, 1514, 1449, 1276, 778, 729 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.19 (s, 3H, CH_3), 4.67 (s, 1H, CH), 6.97 (d, J = 8.0 Hz, 1H, Ar–H), 7.08 (s, br., NH_2), 7.09 (d, J = 8.0 Hz, 1H, Ar–H), 7.19 (d, J = 6.8, 1H, Ar–H), 7.29 (t, J = 7.4, 1H, Ar–H), 7.36 (t, J = 7.6, 1H, Ar–H), 7.72 (d, J = 7.2 Hz, 1H, Ar–H), 10.99 (s, br., 2H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.0, 33.8, 93.6, 108.6, 112.4, 120.0, 120.4, 122.8, 127.9, 128.8, 134.0, 134.2, 135.0, 136.9, 142.3, 144.2, 155.0, 156.2, 191.0. Anal. Cald for $C_{21}H_{16}N_4O_2$ (356.38): C, 70.77; H, 4.53; N, 15.72. Found: C, 70.58; H, 4.40; N, 15.65.

2.2.4. 2-Amino-5-(2-chlorophenyl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4d**)

Red powder, m.p. 327–323 °C IR (KBr): 3382, 3195, 3071, 3009, 2886, 1663, 1604, 1535, 1472, 1046, 826, 732 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.12 (s, 1H, CH), 6.47 (s, br., 2H, NH_2), 7.09 (dt, J = 7.6, 2.0 Hz, 1H, Ar–H), 7.14–7.18 (m, 2H, Ar–H), 7.24 (d, J = 8.0 Hz, 2H, Ar–H), 7.30 (t, J = 7.0 Hz, 1H, Ar–H), 7.38 (t, J = 7.2 Hz, 1H, Ar–H), 7.76 (d, J = 7.2 Hz, 1H, Ar–H), 10.54 (s, br., 1H, NH), 10.77 (s, br. 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.0, 93.5, 107.6, 120.2, 120.5, 127.2, 127.7, 129.4, 130.6, 131.6, 132.0, 132.8, 133.9, 136.8, 144.0, 154.8, 155.4, 156.3, 162.0, 190.7. Anal. Cald for $C_{20}H_{13}ClN_4O_2$ (376.8): C, 63.75; H, 3.48; N, 14.87. Found: C, 63.60; H, 3.31; N, 14.91 .

2.2.5. 2-Amino-5-(2-chloro-6-fluorophenyl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4e**)

Red powder, m.p. 317–319 °C, IR (KBr): 3390, 3204, 3073, 3009, 2873, 1661, 1605, 1531, 1457, 1275, 1164, 1064, 720, 774 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.38 (s, 1H, CH), 6.46 (s, br., 2H, NH_2), 7.08–7.19 (m, 4H, Ar–H), 7.31 (t, J = 7.2, 1H, Ar–H), 7.39 (t, J = 7.0 Hz, 1H, Ar–H), 7.75 (d, J = 7.2 Hz, 1H, Ar–H), 10.53 (s, br., 1H, NH), 10.80 (s, br. 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.2, 99.0, 116.0, 116.2, 120.2, 120.5, 123.1, 126.6, 128.4, 128.5, 130.7, 132.0, 132.5, 132.6, 134.0, 136.1, 136.6, 154.8, 161.9,

190.6. Anal. Cald for $C_{20}H_{12}ClFN_4O_2$ (394.8): C, 60.84; H, 3.06; N, 14.19. Found: C, 60.65; H, 3.15; N, 14.10.

*2.2.6. 2-amino-5-(naphtalen-1-yl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4f**)*

Red powder, m.p. 325–327 °C, IR (KBr): 3424, 3387, 3207, 3050, 2866, 1648, 1602, 1520, 1492, 1450, 1271, 781, 717 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 5.51 (s, 1H, CH), 6.45 (s, br., 2H, NH_2), 7.10 (d, J = 6.8 Hz, 1H, Ar–H), 7.25–7.29 (m, 2H, Ar–H), 7.34–7.40 (m, 2H, Ar–H), 7.47 (t, J = 7.0 Hz, 1H, Ar–H), 7.53 (t, J = 7.4 Hz, 1H, Ar–H), 7.67 (d, J = 8.0 Hz, 1H, Ar–H), 7.77 (d, J = 6.8 Hz, 1H, Ar–H), 7.84 (d, J = 8.0 Hz, 1H, Ar–H), 8.61 (s, br., 1H, Ar–H), 10.54 (s, br., 1H, NH), 10.83 (s, br. 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.0, 95.1,109.6, 113.7, 120.1, 120.4, 125.3, 125.6, 125.7, 126.1, 126.2, 126.8, 128.4, 130.4, 131.3, 132.1, 133.5, 133.9, 136.9, 154.6, 155.2, 155.6, 162.2, 191.0. Anal. Cald for $C_{24}H_{16}N_4O_2$ (392.41): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.35; H, 4.18; N, 14.20.

*2.2.7. 2-Amino-5-(naphtalen-2-yl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4g**)*

Red powder, m.p.: 325–327 °C, IR (KBr): 3444, 3249, 3058, 2909, 1637, 1594, 1513, 1448, 1277, 817, 736 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 4.88 (s, 1H, CH), 6.58 (s, br., 2H, NH_2), 7.19 (d, J = 7.2 Hz, 1H, Ar–H), 7.31 (t, J = 7.2 Hz, 1H, Ar–H), 7.38–7.44 (m, 4H, Ar–H), 7.66 (s, 1H, Ar–H), 7.73–7.80 (m, 3H, Ar–H), 7.83 (d, J = 7.6 Hz, 1H, Ar–H), 10.77 (s, br. 2H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 34.7, 93.4, 108.2, 120.2, 120.5, 125.6, 125.8, 126.0, 126.2, 126.2, 127.3, 127.7, 127.8, 128.1, 130.5, 132.2, 133.3, 134.0, 134.9, 136.9, 144.5, 155.7, 163.4, 191.1. Anal. Cald for $C_{24}H_{16}N_4O_2$ (392.41): C, 73.46; H, 4.11; N, 14.28. Found: C, 73.25; H, 4.13; N, 14.12.

*2.2.8. 2-Amino-5-(5-methyl-2-thiophen-2-yl)-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidin-4,6-(5H,11H)dione (**4h**)*

Red powder, m.p. 329–331 °C, IR (KBr): 3454, 3246, 2918, 2765, 1667, 1618, 1519, 1450, 1276, 1169, 798, 722 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 2.27 (s, 3H, CH_3), 4.92 (s, 1H, CH), 6.48–6.49 (m, 3H, NH_2 and Ar–H) , 6.58 (d, J = 3.6, 1H, Ar–H), 7.27 (d, J = 6.8, 1H, Ar–H), 7.34 (t, J = 7.2, 1H, Ar–H), 7.40 (t, J = 7.2 Hz, 1H, Ar–H), 7.74 (d, J = 7.2 Hz, 1H, Ar–H), 10.71 (s, br., 1H, NH), δ; 10.79 (s, br., 1H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.4, 28.9, 93.7, 107.7, 120.3, 120.8, 123.5, 125.3, 130.7, 132.2, 133.9, 136.7, 137.0, 149.0, 154.6, 154.7, 156.1, 162.3, 190.9. Anal. Cald for $C_{19}H_{14}N_4O_2S$ (362.41): C, 62.97; H, 3.89; N, 15.46. Found: C, 62.85; H, 3.74; N, 15.37.

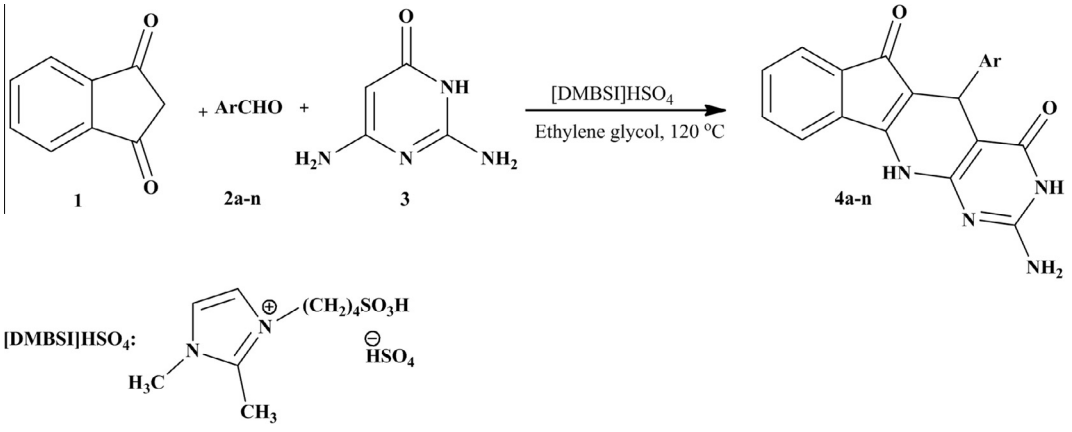
*2.2.9. 5,5′-(1,4-Phenylene)bis(2-amino-3H-indeno[2′,1′:5,6]pyrido[2,3-d]pyrimidine-4,6-(5H,11H)dione (**4i**)*

Red powder, m.p. 336–338 °C, IR (KBr): 3425, 2926, 1637, 1598, 1515, 1450, 1277, 723 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 4.81 (s, 2H, CH), 6.64 (s, br., 4H, NH_2), 7.21 (d, J = 6.8 Hz, 2H, Ar–H), 7.32 (t, J = 6.8 Hz, 2H, Ar–H), 7.39 (d, J = 7.6 Hz, 2H, Ar–H), 7.69–7.77 (m, 2H, Ar–H), 7.89 (d, J = 8.0 Hz, 2H, Ar–H), 9.90 (s, br., 2H, NH), 10.08 (s, br., 2H, NH), 10.83 (s, br. 2H, CO–NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.8, 99.7, 102.9, 128.7, 128.8, 128.9, 129.8, 130.9, 132.2, 132.4, 132.9, 133.8, 136.4, 136.9, 140.7, 147.9, 159.0, 165.8, 168.5, 200.3, 197.2. Anal. Cald for $C_{34}H_{22}N_8O_4$ (606.59): C, 67.32; H, 3.66; N, 18.47. Found: 67.14; H, 3.49; N, 18.31.

Table 1 Effect of various solvents in the synthesis of **4a**, using [DMBSI]HSO_4.[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	Ethylene glycol	4	95
2	Acetic acid	5	90
3	DMF	6	81
4	EtOH	6	84
5	MeOH	6	82
6	H_2O	7	65
7	Acetone	7	60

[a] Reaction conditions: Catalyst 0.06 g/1 mmol substrate, reaction temperature 120 °C for ethylene glycol and other solvents in reflux conditions.
[b] Isolated yields.



Scheme 1 Synthesis of indenopyrido[2,3-*d*]pyrimidines **4a–n**.

3. Results and discussion

As part of our continuing efforts on the development of new synthetic strategies for the preparation of heterocyclic compounds [28], in this study an efficient protocol was devised for the preparation of indenopyrido[2,3-*d*]pyrimidines (**4**), by condensation of 1,3-indanedione (**1**), arylaldehydes (**2**) and 2,6-diaminopyrimidin-4(3*H*)-one (**3**) in the presence of ionic liquid [DMBSI]HSO_4 (Scheme 1).

To optimize the reaction conditions, we screened different conditions for the synthesis of the desired products. Therefore, preparation of 2-amino-5-(4-methoxyphenyl)-3*H*-indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidin-4,6-(5*H*,11*H*)dione (**4a**) was selected as model reaction. In initial experiments, different solvents were screened in the presence of ionic liquid [DMBSI]HSO_4 at different temperatures. The results are summarized in Tables 1 and 2. It is evident from the results that [DMBSI]HSO_4/ethylene glycol at 120 °C is the most effective condition producing the product in higher yield (95%) and lower reaction time (4 min) (Table 1, entry 1). When the reaction was performed on substrates **2a** at solvent-free conditions (120 °C), the desired product (**4a**) was obtained after 6 min in 87% yield.

Table 2 Effect of various temperatures in the synthesis of **4a** in ethylene glycol using [DMBSI]HSO_4.

Entry	Temperature (°C)	Time (min)	Yield (%)[a]
1	80	12	85
2	100	7	89
3	120	4	95
4	130	4	92

[a] Isolated yields.

Table 3 Effect of various catalysts in the synthesis of **4a** in ethylene glycol at 120 °C.

Entry	Catalyst[a]	Time (min)	Yield (%)[b]
1	–	33	70
2	[DMBSI]HSO_4	4	95
3	*p*-TSA	10	75
4	$ZnCl_2$	13	73
5	L-Proline	16	62
6	DABCO	19	58
7	DBU	21	56

[a] The amount of catalyst 0.18 mmol/mmol substrate.
[b] Isolated yields.

To compare the efficiency of [DMBSI]HSO_4 with various catalysts in ethylene glycol, preparation of **4a** was examined under the optimized conditions using several acidic and basic catalysts. The result of this study is presented in Table 3, which clearly confirms the priority of the present catalyst. We also verified the amount of catalyst needed for the preparation of **4a**. The amount of catalyst plays a crucial role in this reaction. For example, synthesis of **4a** as a model compound, in the presence of 0.01 g (0.03 mmol) ionic liquid per mmol substrate, produced **4a** in lower yield (75%) in ethylene glycol at 120 °C after 20 min. Increasing the amount of the catalyst to 0.03 g (0.09 mmol) and 0.06 g (0.18 mmol) resulted in increasing the yield to 90% and 95% after 6 and 4 min respectively. Therefore the best result was obtained using 0.06 g (0.18 mmol) [DMBSI] HSO_4/1 mmol substrate.

Using the optimal conditions described in this report, several derivatives of indenopyridopyrimidines **4a–n** were prepared in high yields (87–95 %) and short reaction times (3–6 min) (Table 4). No obvious effect of the electronic nature of substituents in the aromatic aldehydes ring was observed. Aromatic aldehydes containing electron donating groups (such as methoxy, methyl group) or electron withdrawing groups (such as halides, nitro group) were employed and reacted to give the corresponding products **4a–n** in high yield under the present reaction conditions.

The structures of all the newly synthesized products were confirmed by spectroscopic (IR, ^{1}H NMR, ^{13}C NMR) and elemental analyses and for the known derivatives, by comparison

Table 4 Synthesis of indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidin-4,6-(5*H*,11*H*)dione derivatives **4a–n.**

Entry	Product	Ar	Time (min)	Yield (%)[a]	m.p. (°C)	
					Observed	Reported [Ref.][b]
1	**4a**	4-$MeOC_6H_4$	4	95	324–326	–
2	**4b**	Thiophen-2-yl	4	95	327–329	–
3	**4c**	4-MeC_6H_4	6	87	322–323	–
4	**4d**	2-ClC_6H_4	5	90	321–323	–
5	**4e**	2-Cl-6-FC_6H_3	5	89	317–319	–
6	**4f**	Naphtalen-1-yl	4	96	325–327	–
7	**4g**	Naphthalen-2-yl	6	91	325–327	–
8	**4h**	5-Me-thiophen-2-yl	5	90	329–331	–
9	**4i**	1,4-Phenylene	6	90	336–338	–
10	**4j**	C_6H_5	5	95	326–328	> 300 [21]
11	**4k**	4-FC_6H_4	3	93	325–327	> 300 [21]
12	**4l**	4-BrC_6H_4	4	90	327–329	> 300 [21]
13	**4m**	4-ClC_6H_4	4	92	321–323	> 300 [21]
14	**4n**	3-$O_2NC_6H_4$	5	93	320–322	> 300 [21]

[a] Isolated yields.
[b] Structures of the known products were confirmed by comparison of their spectroscopic data with those of the reported authentic samples.

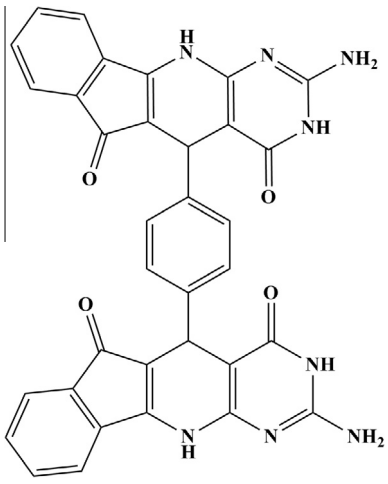


Figure 1 Bis-indenopyridopyrimidine **4i.**

of their spectroscopic data and melting points with those of the literature reports.

Interestingly these optimal conditions afforded an efficient protocol for the synthesis of bis-indenopyridopyrimidine **4i** (Fig. 1) in high yield (90%) (entry 9, Table 4).

The catalyst was also recycled and reused in the preparation of **4a** as model compound. After completion of the reaction, ionic liquid is easily separated from the reaction medium by washing with water. The washed ionic liquid is distilled under vacuum to recover the ionic liquid for reuse in subsequent reactions. The result showed that after three successive runs, catalytic activity of the catalyst was retained without significant loss of activity (Table 5).

Table 5 Catalyst ([DMBSI]HSO_4) recycling in the synthesis of **4a**.

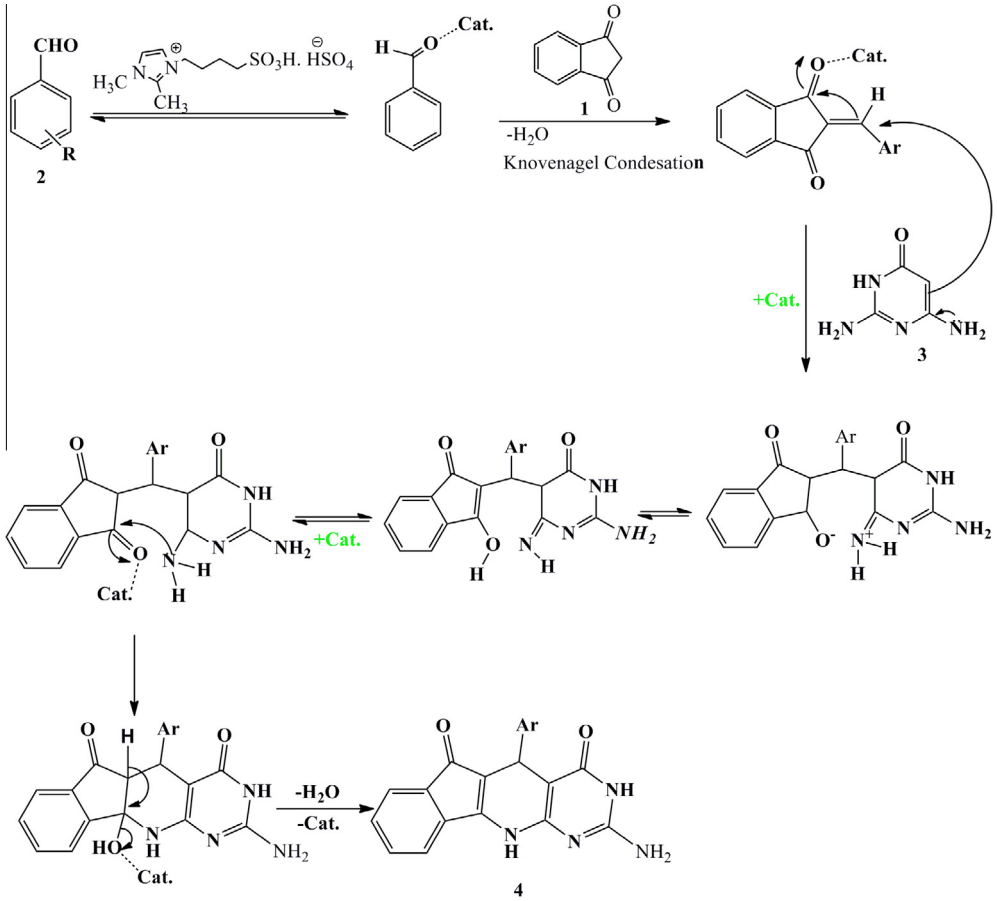
Entry	Cycle	Time (min)	Yield (%)[a]
1	Fresh	4	95
2	First recycle	4	95
3	Second recycle	4	93
4	Third recycle	4	85
5	Fourth recycle	4	70

[a] Isolated yields.

The plausible mechanism for the synthesis of **4a–n** is outlined in Scheme 2.

4. Conclusion

In this report, we have developed a rapid, efficient, and versatile procedure for the synthesis of indeno fused pyrido[2,3-*d*]pyrimidine derivatives **4a–n** in a regiochemical manner by



Scheme 2 The plausible mechanism of synthesis of indeno[2′,1′:5,6]pyrido[2,3-*d*]pyrimidin-4,6-(5*H*,11*H*)diones in the presence of [DMBSI]HSO_4.

the reaction of 1,3-indanedione, 2,6-diaminopyrimidin-4(3*H*)-one, and various arylaldehydes in the presence of ionic liquid [DMBSI]HSO_4 in ethylene glycol. High yields, short reaction times, mild reaction conditions, easy work-up, and cleaner reaction profiles, using a green and recyclable catalyst are the main advantages of this protocol.

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