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One-pot synthesis of 3, 4-dihydropyrimidin-2(1*H*)-ones catalysed by [BMIM]Br under solvent-free condition

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One-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones from β-ketoester/acetyl acetone, aromatic aldehyde and urea using ionic liquid, [BMIM]Br as an efficient and recyclable catalyst under solvent-free condition is reported in a very simple and environmentally benign method with an efficient yield.

Keywords: 3,4-dihydropyrimidin-2(1*H*)-one, [BMIM]Br, solvent-free, multi-component reaction.

INTRODUCTION

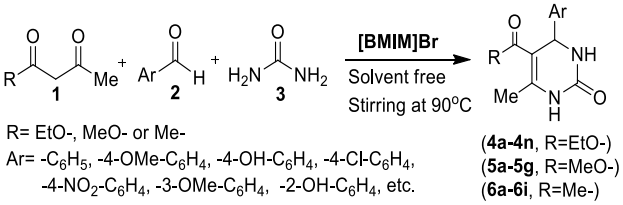
Dihydropyrimidinones (DHPMs) have received good attention during the past few decades due to their therapeutic and pharmacological properties such as antiviral, antibacterial, antihypertensive, antitumor and α_{1a}-adrenergic antagonist activities [1-7]. They have also been used for calcium channel modulator [8], development of anticancer drugs [9] and in AIDS therapy [10].

Synthesis of DHPMs was first reported by P. Biginelli [11] in 1893. Since then, several methods have been developed involving homogenous and heterogenous catalysts. Typical examples of homogenous catalyst are polyphosphate ester [12], $LaCl_3{\cdot}7H_2O$ [13] and $LiClO_4$ [14] whereas KSF (montmorillonite) [15] bentonitic clay [16], and zeolites like HZSM-5, MCM–41 [17] are example of heterogenous catalyst employed. Also lewis and bronsted acids like $Yb(OTf)_3$ [18], $CuCl_2$ [19], $Mn(OAc)_3$ [20], $Bi(OTf)_3$ [21], $CeCl_3{\cdot}7H_2O$ [22], $Cu(OTf)_2$ [23], $FeCl_3$ [24], $BF_3{\cdot}OEt_2/Cu(OAc)_2$ [25], $ZrCl_4$ [26], $TaBr_5$ [27], *p*-TSA [28], H_2SO_4/SiO_2 [29], and $KHSO_4$ [30] have been reported for the improvement of the classical Biginelli reaction.

The growing concern about the environment and the unique properties possessed by ionic liquids as well as their applications prompted us to design protocol for classical Biginelli reaction using [BMIM]Br, under solvent-free condition. Reports show that ionic liquids have been used successfully in many organic transformations both as solvent and catalyst [31-33].

Ionic liquids like $[BMIM][FeCl_4]$ [34], $[BMIM][BF_4]$ or $[BMIM][PF_6]$ [35], $[BMIM][HSO_4]$ [36], $[HMIM][HSO_4]$ [37], $[Et_3NH][HSO_4]$ [38], Phosphinite ionic liquid [39], $[Hcpy][HSO_4]$ [40], etc. have been reported to catalyse the Biginelli reaction. However, the use of [BMIM]Br as catalyst under solvent-free condition has not been explored.

Herein, we report the synthesis of 3,4-dihydropyrimidinones from β-ketoester/acetyl acetone, aromatic aldehyde and urea using 1-butyl-3-methyl imidazolium bromide, [BMIM]Br as catalyst under solvent-free conventional heating (Scheme 1).



Scheme 1. Synthesis of DHPMs using [BMIM]Br.

RESULTS AND DISCUSSION

In continuation with our previous works [41-43] on multi-component reactions here we report the synthesis of 3,4-dihydropyrimidinone derivatives from β-ketoester/acetyl acetone, aromatic aldehyde and urea at 90°C in an oil bath using [BMIM]Br as catalyst under solvent-free condition. For optimisation of the reaction condition the synthesis of **4a** (Table 1, 2) was carried out at different temperatures with varying amount of catalyst.

Table 1. Catalytic effect of [BMIM]Br on the synthesis of **4a**[a]

Entry No.	Mol%	Time (mins.)	Yield (%)
1	5	15	70
2	10	12	90
3	15	16	85
4	20	20	80

[a]Ethylacetoacetate (0.26 gm, 2 mmol), benzaldehyde (0.212 gm, 2 mmol), and urea (0.180 gm, 3 mmol).

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Table 2. Effect of temperature on the yield of **4a**[b]

Entry No.	Temperature (°C)	Time (mins.)	Yield (%)
1	70	25	73
2	80	18	85
3	90	12	90
4	100	12	70
5	110	18	30

[b]Ethylacetoacetate (0.26 gm, 2 mmol), benzaldehyde (0.212 gm, 2 mmol), and urea (0.180 gm, 3 mmol), [BMIM]Br (0.044 gm, 0.2 mmol).

The results from Table 1 show that 10 mol% of [BMIM]Br is the optimum amount which effectively catalyses the reaction and further increase in mol% shows no appreciable increase in the reaction rate. Also, from Table 2, the results show that 90°C is the suitable temperature for this reaction with 90% yield at shortest reaction time. Further increase in temperature led to yield reduction which could be attributed to the charring of the reactants before the reaction is completed.

A comparative study has also been undertaken for the synthesis of **4a** (Table 3) with other reported ionic liquids. As shown in Table 3 entry 1, 2 and 3 required longer reaction time as compared to our method and entry 3 and 4 required higher temperature for the reaction. The yield of the product obtained also is comparable with those of the reported ones and in some cases our method gave better yield.

Table 3. Comparison with reported ionic liquids for the synthesis of **4a**

Ent. No.	Catalyst	Temp. (°C)	Time (mins.)	Yield (%)	Ref.
1	[BMIM][$FeCl_4$]	90	120	90	[34]
2	[HMIM][HSO_4]	80-85	15	86	[37]
3	[Et_3NH][HSO_4]	100	60	75	[38]
4	IL-$OPPh_2$	100	150	91	[39]
5	[BMIM]Br	90	12	90	Our work

Under optimised condition, when ethyl acetoacetate **(1)**, benzaldehyde **(2)** and urea **(3)** were stirred at 90°C in oil bath for 12 minutes, 90% yield of 3,4-dihydropyrimidin-2(1*H*)-one was afforded which was characterised as **4a** (Table 4) based on the analytical and spectral data. To generalise the scope of our method, a series of DHPM derivatives (**4a-4n, 5a-5g, 6a-6i,** Table 4) were successfully synthesised with a good percentage yield (85-93%).

The results show that reaction condition exhibit a high tolerance of functional groups like -OH, -OMe, -NO_2, -Cl, -Br, etc. Substituents on the aromatic ring of aldehydes did not have a profound effect on the yield and reaction time.

All the synthesised products were characterised from their melting point, IR, ^{1}H NMR, ^{13}C NMR and mass spectra. Some of the derivatives were further confirmed by single crystal XRD.

Recyclability of the catalyst was studied for the synthesis of **4b** (Table 4) and has been re-used for next successive five runs without the significant loss of its catalytic activity as shown in figure 1. The process of recyclability of the ionic liquid involved evaporation of the filtrate (obtained after isolation of the desired product) under reduced pressure followed by washing with diethyl ether (3×10 ml.) to remove the un-reacted reagents. It was then heated under vacuum for one hour and reused again for the next run.

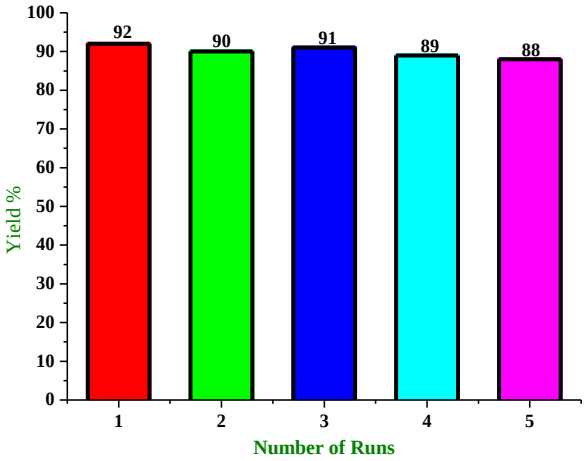


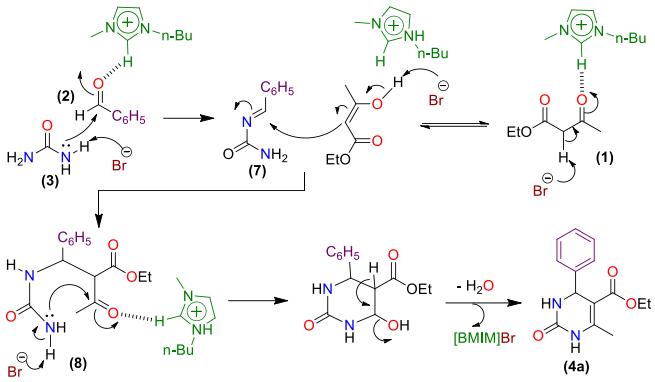
Fig. 1. Recyclability of [BMIM]Br.

The plausible mechanism for the formation of the desired products was proposed in Scheme 2. Ionic liquid exhibits two catalytic functions; first, it enhances the electrophilicity of aldehyde carbonyl through interaction between the acidic hydrogen of cationic component of ionic liquid with the carbonyl oxygen, and second, it enhances the nucleophilicity of urea through deprotonation of N-H proton. The ionic liquid also enhances the enolisation of ethyl acetoacetate and increases its nucleophilicity. The mechanism involves the formation of acylimine intermediate **(7)** followed by the nucleophilic attack by enolised ethyl acetoacetate to form the intermediate **(8)** which successively undergo cyclisation and dehydration to afford the desired product **(4a).**

Table 4. Synthesis of DHPMs using [BMIM]Br as catalyst under solvent-free condition [c]

Entry	DHPM	R	Ar	Conventional		Melting point (°C)	
				Time (mins.)	Yield (%)	Found	Reported
1	4a	OEt	C_6H_5-	12	90	202-204	202-204 [44]
2	4b	OEt	4-Cl-C_6H_4-	6	92	206-208	209-210 [40]
3	4c	OEt	2-Cl-C_6H_4-	8	90	214-216	213-214 [40]
4	4d	OEt	4-Br-C_6H_4-	5	93	222-224	225-226 [44]
5	4e	OEt	3-Br-C_6H_4-	6	91	194-196	196-197 [44]
6	4f	OEt	4-NO_2-C_6H_4-	4	90	197-199	201-202 [44]
7	4g	OEt	4-MeO-C_6H_4-	20	93	202-204	199-201 [18]
8	4h	OEt	4-HO-C_6H_4-	25	92	230-232	227-229 [36]
9	4i	OEt	2-HO-C_6H_4-	23	88	197-199	200-202 [23]
10	4j	OEt	3-Cl-C_6H_4-	7	89	190-192	192-194 [39]
11	4k	OEt	3-HO-C_6H_4-	10	90	193-195	190-192 [44]
12	4l	OEt	3-MeO-C_6H_4-	15	87	210-212	207-208 [40]
13	4m	OEt	4-Me-C_6H_4-	18	85	212-214	216-217 [44]
14	4n	OEt	2-NO_2-C_6H_4-	5	91	219-221	220-221 [39]
15	5a	OMe	C_6H_5-	13	90	205-207	207-210 [18]
16	5b	OMe	4-Cl-C_6H_4-	5	93	198-200	204-206 [45]
17	5c	OMe	4-Br-C_6H_4-	6	92	213-215	210-212 [45]
18	5d	OMe	4-NO_2-C_6H_4-	4	93	234-236	235-237 [18]
19	5e	OMe	4-MeO-C_6H_4-	23	87	192-195	191-193 [18]
20	5f	OMe	4-HO-C_6H_4-	25	89	233-235	232-234 [45]
21	5g	OMe	2-Cl-C_6H_4-	8	90	220-222	224-226 [46]
22	6a	Me	C_6H_5-	13	89	230-232	238-239 [44]
23	6b	Me	4-Cl-C_6H_4-	7	92	220-222	216-218 [40]
24	6c	Me	4-Br-C_6H_4-	5	91	234-236	232-233 [47]
25	6d	Me	4-NO_2-C_6H_4-	5	93	231-233	229-230 [47]
26	6e	Me	4-Me-C_6H_4-	15	87	232-234	234-236 [47]
27	6f	Me	4-HO-C_6H_4-	22	86	235-237	236-238 [48]
28	6g	Me	4-MeO-C_6H_4-	25	85	165-167	166-168 [49]
29	6h	Me	3-MeO-C_6H_4-	13	89	230-232	230-231 [40]
30	6i	Me	3-HO-C_6H_4-	15	90	188-190	184-187 [50]

[c] β-ketoester/acetyl acetone (2 mmol), aromatic aldehyde (2 mmol), urea (3 mmol), [BMIM]Br (0.2 mmol).



Scheme 2. Proposed mechanism for the formation of **4a.**

X-ray crystallography

The single crystal X-ray diffraction (XRD) data were collected at 293 K with Mo Ka radiation (λ= 0.71073 Å) using Agilent Xcalibur (Eos, Gemini) diffractometer equipped with a graphite monochromator. The software used for data collection CrysAlis PRO (Agilent, 2011), data reduction CrysAlis PRO and cell refinement CrysAlis PRO. The structures were solved by direct methods and refined by Olex2.refine. ORTEP image for **4j** and **5f** are shown in figure 2 and figure 3 respectively.

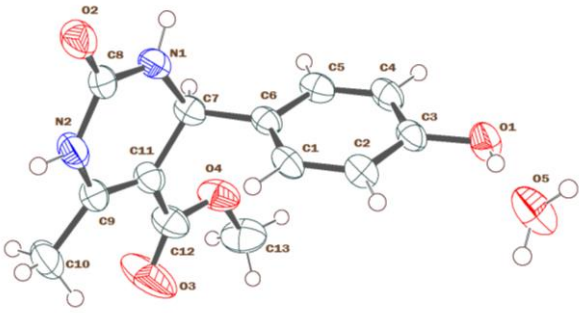


Fig. 2. ORTEP image of **4j** (CCDC 1455903).

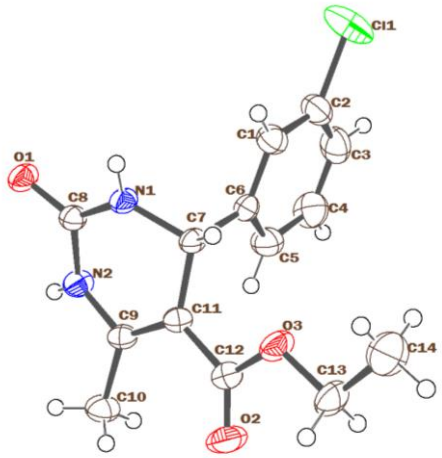


Fig. 3. ORTEP image of **5f** (CCDC 1455902).

Experimental section

All the chemicals utilised in the synthesis were bought from Alfa-Aesar, Sigma-Aldrich and Merck which were used without further purification. Melting points were recorded in open capillary tubes and are uncorrected. IR spectra were recorded in KBr pellets on a Perkin Elmer Spectrum 400 FTIR instrument and frequencies are expressed in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II-400 spectrometer in DMSO-d_6, chemical shifts are in δ scale with TMS as internal standard. Mass spectral data were collected from Waters UPLC-TQD mass spectrometer. Single crystal data were collected from Xcalibur-Eos-Gemini instrument. All reactions were monitored by thin layer chromatography (TLC) using precoated aluminium sheets (silica gel 60 F 254 0.2 mm thickness) and developed in iodine chamber or UVGL-15 mineral light 254 nm lamp.

General Procedure for the Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones: A mixture of β-ketoester/acetyl acetone (2 mmol), aromatic aldehyde (2 mmol) and urea (3 mmol) in the presence of [BMIM]Br (0.2 mmol) in a 50 ml round bottom flask is heated at 90°C in an oil bath under solvent-free condition for 4-25 minutes. When the reaction is completed (monitored by TLC), the reaction mixture is allowed to cool at room temperature. The solid product obtained is filtered, washed thoroughly with ice cold water and dried. Most products obtained were pure. However in few cases further purification was done by recrystallisation from hot ethanol. The filtrate obtained after isolation of product was then evaporated under reduced pressure to recycle the catalyst, which is again washed with ether (3×10 ml), dried in vacuum for one hour and reused for the next run.

General procedure for growing crystal [51]:

Pure DHPM is dissolved in minimum amount of hot ethanol in 25 ml beaker by heating on water bath and allowed to cool to room temperature. The beaker is covered with thin aluminum foil and kept overnight until crystals are formed. The crystals are then separated from the solution, washed with hexane, dried and then subjected to Xcalibur-Eos-Gemini instrument for collecting XRD data.

Analytical data of selected products

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (4a): White Solid; m.p-202-204°C; IR (KBr): ν_{max} 3246,3118, 2979, 1725, 1701, 1649, 1222, 1091 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 8.99 (1H, s, NH), 7.53 (1H, s, NH), 7.08-6.99 (5H, m, Ar-H), 4.90 (1H, s, Ar-CH-) 3.74 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 2.01 (3H, s, CH_3); 0.85 (3H, t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.2, 152.1, 148.3, 144.7, 128.3, 127.2, 126.1,99.1, 59.1, 53.8, 17.7, 14.0; MS (ESI) *m/z*: 261 $[M + 1]^+$

4-(4-Chlorophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4b): White Solid; m.p-206-208°C; IR (KBr): ν_{max} 3245, 3118, 2981, 1725, 1709, 1650, 1223, 1090 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.24 (1H, s, NH), 7.76 (1H, s, NH), 7.38 (2H, d, *J* 8 Hz, Ar-H), 7.23 (2H, d, *J* 8 Hz, Ar-H), 5.12 (1H, s, Ar-CH-), 3.96 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 2.23 (3H, s, CH_3), 1.07 (3H, t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.1, 151.8, 148.6, 143.7, 131.7, 128.3, 128.1, 98.7, 59.2, 53.3, 17.7, 14.0; MS (ESI) m/z: 295 $[M + 1]^+$.

4-(4-Bromophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4d): White Solid; m.p-222-224°C; IR (KBr): ν_{max} 3244, 3118, 2980, 1724, 1706, 1650, 1224, 1090 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.02 (1H, s, NH), 7.55 (1H, s, NH), 7.29 (2H, d, *J* 8 Hz, Ar-H), 6.95 (2H, d, *J* 8 Hz, Ar-H), 4.89 (1H, d, *J* 2 Hz, Ar-CH-), 3.74 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 2.01 (3H, s, CH_3), 0.85 (3H t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.1, 151.8, 148.6, 144.1, 131.2, 128.5, 120.2, 98.6, 59.2, 53.4, 17.7, 14.0; MS (ESI) m/z: 339 $[M]^+$, 341$[M+2]^+$.

4-(3-Bromophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4e): White Solid; m.p-194-196°C; IR (KBr): ν_{max} 3231, 3118, 2976, 1708, 1653, 1225, 1090 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.07 (1H, s, NH), 7.59 (1H, s, NH), 7.24-7.01 (4H, m, Ar-H), 4.92 (1H, s, Ar-CH), 3.76 (2H, q, *J* 7.5 Hz, $OC\underline{H}_2CH_3$), 2.03 (3H, s, CH_3), 0.88 (3H, t, *J* 7.5 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100MHz, DMSO-*d6*): δ 165.0, 151.8, 148.9, 147.4, 130.7, 130.0, 129.1, 125.2, 121.4, 98.5, 59.2, 53.5, 17.7, 13.9; MS (ESI) m/z: 339 $[M]^+$, 341 $[M + 2]^+$.

5-Ethoxycarbonyl-6-methyl-4-(4-methoxy phenyl)-3,4-dihydropyrimidin-2(1*H*)-one (4g): White Solid; m.p-202-204°C; IR (KBr): ν_{max} 3244, 3113, 2957, 1725, 1706, 1651, 1224, 1088 cm^{-1}; ^1H NMR (400MHz, DMSO-*d6*): δ 8.93 (1H, s, NH),7.45 (1H, s, NH), 6.91(2H, d, *J* 8 Hz, Ar-H), 6.64 (2H, d, *J* 8 Hz, Ar-H), 4.86 (1H, s, Ar-CH-), 3.75 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 3.48 (3H, s, OCH_3), 2.01 (3H, s, CH_3), 0.87 (3H, t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.3, 158.3, 152.1, 147.9, 136.9, 127.3, 113.6, 99.5, 59.0, 54.9, 53.2, 17.6, 14.0; MS (ESI) m/z: 291 $[M + 1]^+$.

5-Ethoxycarbonyl-4-(4-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4h): White Solid; mp-230-232°C; IR (KBr): ν_{max} 3491, 3287, 3115, 1712, 1685, 1655, 1228, 1097 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.32 (1H, s, NH), 9.09 (1H, s, OH), 7.60 (1H, s, NH), 7.01(2H, d, *J* 8 Hz, Ar-H), 6.67 (2H, d, *J* 8 Hz, Ar-H), 5.02 (1H, s, Ar-CH-), 3.96 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 2.21 (3H, s, CH_3), 1.08 (3H, t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.3, 156.4, 152.1, 147.7, 135.3, 127.3, 114.9, 99.6, 59.0, 53.3, 17.6, 14.0; MS (ESI) m/z: 277 $[M + 1]^+$.

4-(3-Chlorophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4j): White Solid; m.p-190-192°C; IR (KBr): ν_{max} 3226, 3118, 2981, 2937, 1705, 1653, 1227, 1091 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.26 (1H, s, NH), 7.79 (1H, s, NH), 7.38-7.17 (4H, m, Ar-H), 5.13 (1H, s, Ar-CH-), 3.99 (2H, q, *J* 6.8 Hz, $OC\underline{H}_2CH_3$), 2.24 (3H, s, CH_3), 1.08 (3H, t, *J* 6.8 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.1, 151.8, 148.9, 147.1, 132.8, 130.4, 127.1, 126.1, 124.8, 98.5, 59.2, 53.5, 17.7, 13.9; MS (ESI) m/z: 296 $[M + 1]^+$.

5-Ethoxycarbonyl-6-methyl-4-(3-methoxy phenyl)-3,4-dihydropyrimidin-2(1*H*)-one (4l): White Solid; m.p-210-212°C; IR (KBr): ν_{max} 3243, 3118, 2936, 1704, 1650, 1599, 1226, 1094 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.18 (1H, s, NH), 7.72 (1H, s, NH), 7.25-6.76 (4H, m, Ar-H), 5.10 (1H, s, Ar-CH-), 3.98 (2H, q, *J* 7.2 Hz, $OC\underline{H}_2CH_3$), 3.70 (3H, s, OCH_3), 2.22 (3H, s, CH_3), 1.09 (3H, t, *J* 7.2 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.3, 159.1, 152.1, 148.3, 146.2, 129.5, 118.1, 112.3, 112.0, 99.1, 59.1, 54.9, 53.6, 17.7, 14.0; MS (ESI) m/z: 291 $[M + 1]^+$.

5-Ethoxycarbonyl-6-methyl-4-(2-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (4n): Light green solid; mp-219-221°C; IR (KBr): ν_{max} 3211, 3102, 2958, 1701, 1649, 1224, 1093 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.32 (1H, s, NH), 7.69 (1H, s, NH), 7.82-7.42 (4H, m, Ar-H), 5.72 (1H, s, Ar-CH-), 3.74 (2H, q, *J* 7.2 Hz, $OC\underline{H}_2CH_3$), 2.18 (3H, s, CH_3), 0.82 (3H, t, *J* 7.2 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 164.6, 151.1, 149.5, 147.3, 139.2, 134.1, 129.0, 128.7, 123.8, 98.0, 59.1, 49.2, 17.6,13.6; MS (ESI) m/z: 306 $[M + 1]^+$.

5-Methoxycarbonyl-6-methyl-4-Phenyl-3,4-dihydropyrimidin-2(1*H*)-one (5a): White Solid; m.p-205-207°C; IR (KBr): ν_{max} 3334, 3223, 1696, 1669, 1240, 1095 cm^{-1}; ^1H NMR (400MHz, DMSO-*d6*): δ 9.22 (1H, S, NH), 7.76 (1H, S, NH), 7.32-7.21 (5H, m, Ar-H), 5.13 (1H, s, Ar-CH-), 3.51 (3H, s, $OC\underline{H}_3$), 2.24 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.7, 152.1, 148.6, 144.6, 128.4, 127.2, 126.1, 98.9, 53.7, 50.7, 17.7; MS (ESI) m/z: 247 $[M + 1]^+$.

4-(4-Chlorophenyl)-5-methoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (5b): White Solid; m.p-198-200°C; IR (KBr): ν_{max} 3366, 3227, 3115, 2976, 1716, 1691, 1638, 1229, 1091 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.28 (1H, s, NH), 7.80 (1H, s, NH), 7.37 (2H, d, *J* 8 Hz, Ar-H), 7.23 (2H, d, *J* 8 Hz, Ar-H), 5.13 (1H, s, Ar-CH-), 3.51 (3H, s, $COOCH_3$), 2.24 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.6, 151.9, 148.9, 143.5, 131.8, 128.4, 128.0, 98.5, 53.2, 50.7, 17.8; MS (ESI) m/z: 282 $[M + 1]^+$.

5-Methoxycarbonyl-6-methyl-4-(4-methoxy phenyl)-3,4-dihydropyrimidin-2(1*H*)-one (5e): White Solid; m.p-192-195°C; IR (KBr): ν_{max} 3248, 3115, 2956, 1724, 1713, 1686, 1241, 1099 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.19 (1H, s, NH), 7.70 (1H, s, NH), 7.12 (2H, d, *J* 8 Hz, Ar-H), 6.86 (2H, d, *J* 8 Hz, Ar-H), 5.07 (1H, s, Ar-CH-), 3.70 (3H, s, $COOC\underline{H}_3$), 3.36 (3H, s, $OC\underline{H}_3$), 2.23 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6* + $CDCl_3$): δ 171.1, 163.6, 158.2, 152.2, 141.4, 132.4, 118.5, 105.3, 59.9, 59.1, 55.4, 23.1; MS (ESI) m/z: 277 $[M + 1]^+$.

4-(4-Hydroxyphenyl)-5-methoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (5f): White Solid; m.p-233-235°C; IR (KBr): ν_{max} 3274, 3119, 1702, 1682, 1640, 1230, 1088 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.41 (1H, s, NH), 9.21 (1H, s, OH), 7.71 (1H, s, NH), 7.08 (2H, d, *J* 8 Hz, Ar-H), 6.74 (2H, d, *J* 8 Hz, Ar-H), 5.09 (1H, s, Ar-CH-), 3.58 (3H, s, $COOC\underline{H}_3$), 2.29 (3H, s, CH_3); ^{13}C NMR (400 MHz, DMSO-*d6*): δ 165.8, 156.5, 152.1, 148.0, 135.1, 127.2, 114.9, 99.3, 53.1, 50.6, 17.7; MS (ESI) m/z: 262 $[M]^+$.

5-Acetyl-4-(4-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (6f): Brown solid; m.p-235-237°C; IR (KBr): ν_{max} 3268, 3105, 2961, 1700, 1649, 1566, 1233 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.35 (1H, s, NH), 9.10 (1H, s, OH), 7.69 (1H, s, NH), 7.02 (2H, d, *J* 8 Hz, Ar-H), 6.68 (2H, d, *J* 8 Hz, Ar-H), 5.12 (1H, d, *J* 2.8 Hz, Ar-CH), 2.25 (3H, s, $COCH_3$), 2.04 (3H, s, CH_3); ^{13}C NMR (400 MHz, DMSO-*d6*): δ 194.4, 156.5, 152.0, 147.5, 134.6, 127.6, 115.1, 109.4, 53.4, 30.0, 18.7; MS (ESI) m/z: 261 $[M + 1]^+$.

5-Acetyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (6g): Yellow Solid; m.p-165-167°C; IR (KBr): ν_{max} 3232, 3123, 2957, 1714, 1700, 1631, 1234, 1029 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.15 (1H, s, NH), 7.76 (1H, s, NH), 7.14 (2H, d, *J* 8 Hz, Ar-H), 6.86 (2H, d, *J* 8 Hz, Ar-H), 5.18 (1H, s, Ar-CH), 3.70 (3H, s, OCH_3), 2.26 (3H, s, $COCH_3$), 2.05 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 194.3, 158.4, 152.0, 147.7, 136.2, 127.5, 113.7, 109.5, 54.9, 53.2, 30.1, 18.7; MS (ESI) m/z: 261 $[M + 1]^+$.

5-Acetyl-4-(3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (6h): Off-white Solid; m.p-230-232°C; IR (KBr): ν_{max} 3341, 3275, 3052, 2957, 1715, 1678, 1600, 1242, 1049 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.18 (1H, s, NH), 7.81 (1H, s, NH), 7.24-6.78 (4H, m, Ar-H), 5.21 (1H, s, Ar-CH), 3.70 (3H, s, OCH_3), 2.26 (3H, s, $COCH_3$), 2.09 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*): δ 194.3, 159.2, 152.1, 148.1, 145.62, 129.6, 118.3, 112.6, 112.1, 109.3, 54.9, 53.5, 30.2, 18.8; MS (ESI) m/z: 261 $[M + 1]^+$.

5-Acetyl-4-(3-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (6i): Brown Solid; m.p-188-190°C; IR (KBr): ν_{max} 3259, 3117, 2930, 1710, 1688, 1664, 1242 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*): δ 9.38 (1H, S, NH), 9.15 (2H, s, OH), 7.71 (1H, s, NH), 7.10-6.60 (4H, m, Ar-H), 5.15 (1H, s, Ar-CH-), 2.25 (3H, s, $COCH_3$), 2.07 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*): 194.3, 157.3, 152.0, 147.8, 145.6, 129.4, 117.0, 114.2, 113.1, 109.4, 53.7, 30.1, 18.8; MS (ESI) m/z: 247 $[M + 1]^+$.

CONCLUSION

In summary, we have developed a simple, efficient and environmental friendly protocol for the improvement of the classical Biginelli reaction. The advantages of our present method are solvent-free, simple work-up procedure and easy purification of the synthesized products without column chromatography.

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ЕДНО-СТАДИЙНА СИНТЕЗА НА 3,4-ДИХИДРОПИРИМИДИН-2(1*H*)-ОНИ КАТАЛИЗИРАНА ОТ [BMIM]Br В УСЛОВИЯ БЕЗ РАЗТВОРИТЕЛ

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(Резюме)

Съобщава се за едно-стадийна синтеза на 3,4-дихидропиримидин-2(1*H*)-они от β-кетоестер/ацетил ацетон, ароматен алдехид и карбамид, използвайки йонна течност - [BMIM]Br, като ефикасен и рециклируем катализатор в условия без разтворител. Методът е много прост, екологично съвместим и с висок добив на продуктите.