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Efficient Synthesis of Dihydropyrimidines Using a Highly Ordered Mesoporous Functionalized Pyridinium Organosilica

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Abstract: A Brönsted acidic ionic solid pyridinium-functionalized organosilica network (PMO-Py-IL) was demonstrated to efficiently catalyse one-pot Biginelli condensation reaction. The green synthesis of 3,4-dihydro-2(H)-pyrimidinones (DHPMs) with high yield was carried out via one-pot three component condensation of β- dicarbonyls, aldehydes, and urea in the presence of a catalytic amount of PMO-Py-IL nanomaterial as an efficient nanocatalyst under solvent free conditions. Furthermore, the catalyst showed outstanding stability and could be easily separated and reused for at least ten reaction runs without significant loss of activity and product selectivity. The green protocol features simple set-up, cost-effectiveness, easy work-up, eco-friendly and mild reaction conditions.

Keywords: biginelli reaction; dihydropyrimidines; pyridinium-functionalized organosilica; reusable nanocatalyst

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1. Introduction

3,4-Dihydro-2(*H*)-pyrimidinones (DHPMs) are one of the most biologically important families of nitrogen-containing heterocycles in natural and synthetic chemistry [1]. The pyrimidine ring system could be naturally found in vitamins such as thiamin, folic acid and riboflavin; nucleic acids such as uracil, thymine, and cytosine, and alkaloids such as heteromine and manzacidin [2]. DHPMs have been found to exhibit distinct pharmacological and biological activities such as being anti-tumor [3], anti-cancer [4,5], anti-inflammatory [6], anti-viral [7], anti-fungal [8], and as calcium channel blockers [9,10]. Furthermore, the industrial applications include their use as additive to agrochemicals, dyes, and organic compounds [11]. Some examples of biologically and pharmacologically active dihydropyrimidine derivatives such as [bis(2-chloroethyl)amino] pyrimidine-2,4(1*H*,3*H*)-dione (Uramustine), 5-fluoro-1-(tetrahydro-2-furyl)pyrimidine-2,4(1*H*,3*H*)-dione (Tegafur), 4-amino-1-β-darabinofuranosyl pyrimidine-2(1*H*)-one (Cytarabine), 5-Fluoropyrimidine-2,4(1*H*,3*H*)-dione (Fluorouracil), 1,2,3,6-Tetrahydro-2,6-dioxo pyrimidine-4-carboxylic acid (Orotic Acid), and 5-Bromo-2′-deoxyuridine-5-bromo-1-(2-deoxy-β-D-ribofuranosyl) pyrimidine-2,4-(1*H*,3*H*)-dione (Broxuridine) are shown in Figure 1.

One-pot Biginelli condensation reaction is the original procedure for the synthesis of DHPMs reported by Biginelli in 1891. This procedure involved reaction of β-dicarbonyl compounds, aromatic aldehydes, and urea under strongly acidic conditions [12–15]. Biginelli reaction was carried out by refluxing a mixture of the three components such as ethyl acetoacetate, benzaldehyde, and urea in the presence of ethanol catalyzed by hydrochloric acid which often resulted in poor to moderate yields of desired products. Due

to remarkable biological and pharmacological activities and versatile use of DHPMs, the synthesis of DHPMs has been revalued. Several improved synthetic methodologies for the Biginelli condensation have recently been developed by employing various catalysts such as p-toluenesulfonic acid [16], Ni(II) coordination complex [17], chloroacetic acid [18], $TiCl_4$ [19], $RuCl_3$ [20], $Sc(OTf)_3$ [21], $Co(OAc)_2$ [22], sulfated zirconia [23], $FeCl_3.6H_2O$ [24], $MgBr_2$ [25], $NbCl_5$ [26], $Yb(OTf)_3$ [27], $InCl_3$ [28], $CuCl_2$ [29], $SnCl_2$ [30], $BF_3.OEt_2$ [31], $ZrCl_4$ [32], $ZnCl_2$ [33], TMSOTf [34], $CdCl_2$ [35], CH_3SO_3H [36], Iron(III) [37], SmI_2 [38], $Pb(NO_3)_3$ [39], $Ba(OH)_3$ [40], solvent-free synthesis [41], microwave irradiation [42], ultrasound radiation [43], visible light irradiation [44], Brønsted acidic ionic liquid [45], solid supported reagent [46–50], and enzymatic catalysts [51]. In spite of progress in the synthesis of these compounds, however, some of the previously reported procedures have significant drawbacks such as harsh reaction conditions, low product yield, use of expensive or toxic reagents, laborious workup, and large amount of toxic wastes generation. Therefore, the development of green, efficient, simple, clean, high yielding, mild, environmentally benign and cost-effective approaches using reusable catalysts is highly desirable and is of utmost importance for the synthesis of DHPMs.

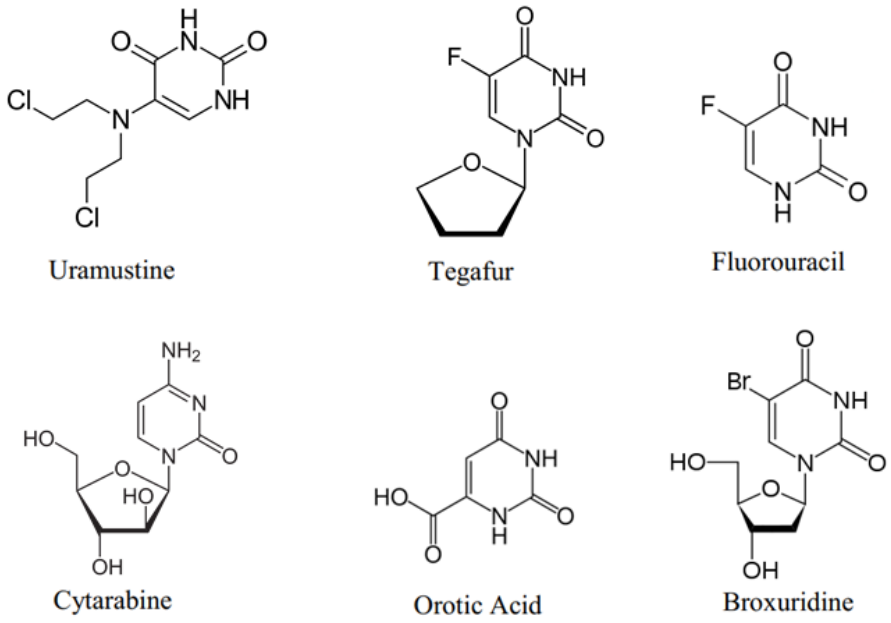


Figure 1. Chemical structures of some biologically and pharmacologically active DHPMs.

The activity of the heterogeneous catalysts with various supports is dependent on the size, morphology, surface area, and nature of the support. Among them, periodic mesoporous organosilicas (PMOs) with high loading of organic functional groups, high surface area, periodically ordered and tunable pores is most favorable and have various applications such as in adsorption, catalysis, separation, medicine, and advanced materials [52–57]. –Numerous organosilane precursors can be used to successfully form PMOs via surfactant-based sol-gel technique allowing a better control of the size, structure, and composition of the PMO materials for the specific application requirements.

In continuation of our efforts towards sustainable development of highly efficient and recyclable catalysts for green chemicals synthesis [58–60] we have very recently developed a highly ordered porous PMO nanomaterial based on pyridinium ionic liquid as ionic solid catalyst (PMO-Py-IL), which showed excellent activity towards biodiesel production via Fischer esterification [60]. Herein, we demonstrate the application of this efficient and reusable nanocatalyst for one-pot three component Biginelli condensation reaction under mild and eco-friendly conditions.

2. Results and Discussion

The synthesis and characterization of ionic solid-acid hybrid nanomaterial with pyridinium ionic liquid framework (PMO-Py-IL) was reported according to our recently published work [60]. The growing interest towards the development of green reaction conditions has motivated us to develop 3,4-dihydro-2(*H*)-pyrimidinones (DHPMs) via one-pot three component condensation of β-dicarbonyls, aldehydes, and urea for further application of PMO-Py-IL nanomaterials.

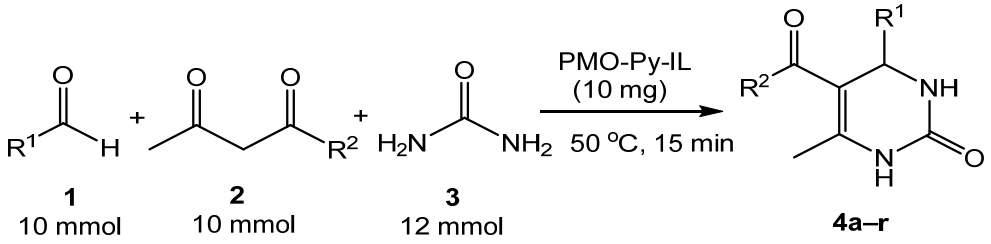
The catalytic activity of PMO-Py-IL nanocatalyst has been investigated in the reaction of three-component condensation of ethyl acetoacetate, benzaldehyde and urea as a model reaction. In order to optimize the reaction conditions, the effect of different reaction parameters such as reaction time, reaction temperature, catalyst amount, and solvent were evaluated, and results are summarized in Table 1. According to the results, blank runs (in the absence of catalyst or solvent) provide a low yield of the product even after 2 h at 100 °C (Table 1, Entries 1,2). We screened the effect of solvents such as acetonitrile (CH_3CN), ethanol (C_2H_5OH), dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), and water (H_2O) using 10 mg of the PMO-Py-IL nanocatalyst in the model reaction under reflux conditions. The excellent yield of the product was observed with C_2H_5OH (Entry 3), and the lowest yield was observed in CH_2Cl_2 (Entry 4). It was found that the reaction was carried out in excellent yield under solvent-free condition (Entry 9). Next, the effect of catalyst loading on the reaction efficacy was studied. The reaction yield was found to be significantly decreased at lower loading (Entry 10). In order to study the influence of the reaction temperature, the model reaction was carried out at different reaction temperatures (Entries 11–14). Interestingly, excellent yield of product was obtained at 50 °C. Further studies were done to optimize the reaction time. As displayed in Table 1 (Entries 15–18), it was observed that the PMO-Py-IL nanocatalyst showed the highest product yield within the short time span (of 15 min), utilizing 10 mg of the PMO-Py-IL nanocatalyst under solvent free conditions.

Table 1. Effect of different parameters on the Biginelli reaction of ethyl acetoacetate (10 mmol), benzaldehyde (10 mmol), and urea (12 mmol).

Entry	PMO-Py-IL (mg)	Solvent	Temp. (°C)	Time (min)	Yield (%) [a]
1	-	-	100	120	20
2	-	C_2H_5OH	Reflux	120	28
3	10	C_2H_5OH	Reflux	120	95
4	10	CH_2Cl_2	Reflux	120	42
5	10	THF	Reflux	120	54
6	10	H_2O	Reflux	120	82
8	10	CH_3CN	Reflux	120	58
9	10	-	80	120	99
10	8	-	80	120	88
11	10	-	70	120	84
12	10	-	60	120	87
13	10	-	50	120	99
14	10	-	40	120	70
15	10	-	50	60	98
16	10	-	50	30	98
17	10	-	50	15	98
18	10	-	50	10	91

[a] Isolated yields.

To evaluate the scope and limitation of the process, a series of DHPMs were synthesized via one-pot Biginelli condensation reaction under optimized conditions (Scheme 1). As shown in Table 2, various aromatic aldehydes were reacted with -dicarbonyls and urea to give desired DHPM products in high yields under optimal reaction conditions.



Scheme 1. PMO-Py-IL catalyzed the one-pot Biginelli condensation reaction.

Table 2. Synthesis of dihydropyrimidones catalyzed by PMO-Py-IL nanocatalyst under solvent free conditions.

Entry	R^1	R^2	Product	Yield (%) [a]	M.P(°C) [Ref.]
1	C_6H_5	OEt	4a	98	201–203 [16]
2	4-NO_2-C_6H_4	OEt	4b	94	211–213 [16]
3	4-Cl-C_6H_4	OEt	4c	92	210–212 [16]
4	2-OH-C_6H_4	OEt	4d	80	217–219 [16]
5	2-Cl-C_6H_4	OEt	4e	82	220–223 [16]
6	4-OCH_3-C_6H_4	OEt	4f	84	201–203 [16]
7	C_6H_5	OMe	4g	96	221–223 [16]
8	4-NO_2-C_6H_4	OMe	4h	92	233–235 [16]
9	4-Cl-C_6H_4	OMe	4i	85	154–156 [16]
10	2-OH-C_6H_4	OMe	4j	78	243–244 [45]
11	2-Cl-C_6H_4	OMe	4k	82	249–252 [16]
12	4-OCH_3-C_6H_4	OMe	4l	80	232–233 [16]
13	C_6H_5	Me	4m	98	231–233 [45]
14	4-NO_2-C_6H_4	Me	4n	93	229–230 [45]
15	4-Cl-C_6H_4	Me	4o	90	204–206 [45]
16	2-OH-C_6H_4	Me	4p	82	215–217 [45]
17	2-Cl-C_6H_4	Me	4q	85	201–203 [45]
18	4-OCH_3-C_6H_4	Me	4r	84	172–174 [45]

[a] Isolated yield.

From the data presented in Table 2, it is clearly observed that the method was effective for both electron-withdrawing groups and electron-donating in the aromatic ring of the aldehydes. When reaction was carried out using aliphatic aldehydes such as acetaldehyde and propanal, a trace of corresponding dihydropyrimidone product was obtained even after 3 h.

To evaluate the heterogeneity of PMO-Py-IL and leaching of active species from the support, a hot filtration test was performed during the Biginelli reaction of three-component ethyl acetoacetate, benzaldehyde, and urea under optimized conditions. PMO-Py-IL nanocatalyst was removed by hot filtration after 6 min, and the filtrate solution was further left to react after catalyst filtration for 30 min. No Biginelli condensation reaction progress was observed (monitored by GC) after catalyst filtration. The results confirmed that no catalytically active species remained in the reaction solution and strong incorporation of the active sites in the organosilica framework suppressed leaching of the active phase.

In order to check the reusability and robustness of the PMO-Py-IL nanocatalyst, some studies were performed to find the lifetime and recovery factors of the nanocatalyst in the Biginelli reaction of three-component ethyl acetoacetate, benzaldehyde, and urea under optimized conditions. After ten consecutive cycles, illustrated in Scheme 1, it was found that reusable PMO-Py-IL nanocatalyst can be fully recyclable and showed outstanding structural stability maintaining the catalytic activity to around 90% of its initial activity under studied conditions. The SEM image presented in Figure 2 confirmed that the uniform cylindrical/spheroidal shape structure of porous pyridinium trifluoroacetate organosilica (PMO-Py-IL) after ten runs was similar to reported pristine PMO-Py-IL materials. Moreover, XRD analyses of PMO-Py-IL nanocatalyst before and after recycling were shown in Figure 3. The patterns are identical, and no obvious change was observed, which could be further evidence of the strong stability of the PMO-Py-IL nanocatalyst.

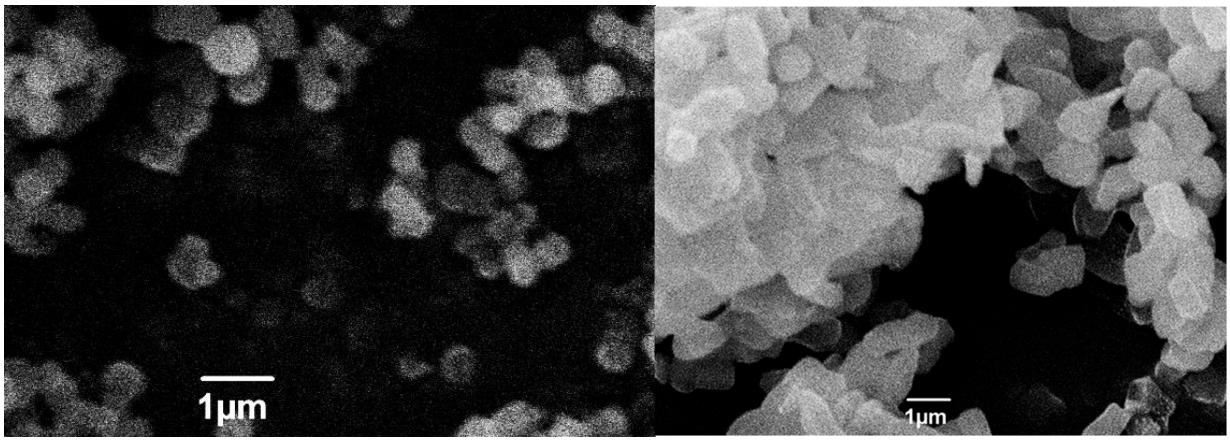


Figure 2. SEM image of the fresh PMO-Py (**left**) and recycled PMO-Py-IL after ten runs (**right**).

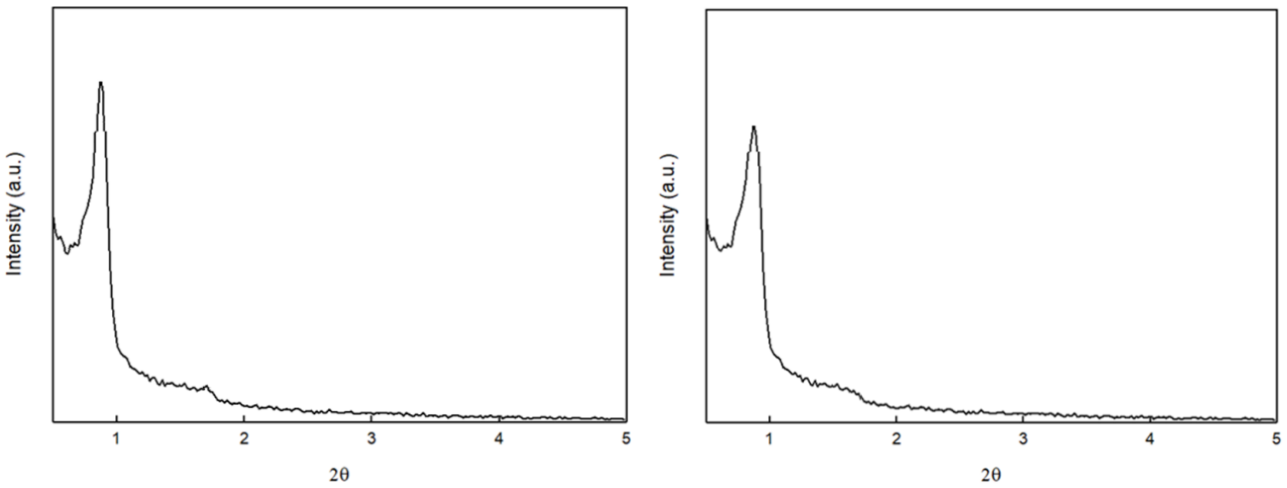


Figure 3. XRD patterns corresponding to the fresh PMO-Py-IL (**left**) and recycled PMO-Py-IL after ten runs (**right**).

We further compared the catalytic performance of PMO-Py-IL nanocatalyst with reported catalysts for the synthesis of DHPMs. As can be seen in Table 3, our recoverable catalytic system possesses good activity, as compared to those of previously reported heterogeneous catalytic systems; the results obtained using the method described herein provides a more environmentally benign and economically attractive system.

Table 3. Comparison of catalytic activities in the Biginelli condensation reaction of benzaldehyde, ethyl acetoacetate, and urea using heterogeneous catalysts under solvent-free conditions.

Entry	Catalyst	T (°C)	Time	Conversion (%)	Ref.
1	PMO-Py-IL (0.002 g)	50	15 min	98	This work
2	Cu@SBA-15 (0.01 g)	100	5 min	94	[50]
3	TSA/bent (0.09 g)	80	5 h	86	[61]
4	TSILS (ionic liquids)	90	10 min	94	[62]
5	PTA@MIL-101 (0.6 mol%)	100	60 min	90	[63]
6	PMo_7W_5/kaolin (20%)	100	8 min	95	[64]
7	β-Cyclodexterin (0.5 mol%)	100	180 min	85	[65]
8	$NH_4H_2PO_4$/MCM-41 (0.04 g)	100	6 h	72	[66]
9	40% *w*/*w* WSi/A-15 (0.05 g)	92	4.5	88	[67]
10	Nano-γ-Al_2O_3/BF_3/Fe_3O_4 (0.008 g)	80	30 min	95	[68]

3. Experimental Section

3.1. General Remarks

All solvents and chemicals were used as received without further purification. The melting points were measured with an Electrothermal model 9100 apparatus. FTIR spectra were obtained using a Shimadzu 4300 spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 on Bruker DRX-300 Avance spectrometers. Proton chemical shifts (δ) were reported in ppm and were referenced to the NMR solvent (a septet centered at 39.52 ppm in ^{13}CNMR related to DMSO-d_6). The scanning electron microscope (SEM) images were produced utilizing a Jeol JSM 6490 LA field emission device with an acceleration voltage of 15 kV.

3.2. Synthesis of PMO Materials Bearing Protic Pyridinium Ionic Liquid (PMO-Py-IL)

PMO-Py-IL was synthesized following our previously reported work [60].

3.3. General Procedure for the Preparation of 3,4-dihydropyrimidin-2(1H)-Ones Using PMO-Py-IL Nanocatalyst

In a typical experiment, a mixture of aldehyde (10 mmol), 1,3-dicarbonyl compound (10 mmol), urea (12 mmol), and PMO-Py-IL nanocatalyst (10 mg) were heated at 50 °C for 15 min under stirring and solvent-free conditions. Upon reaction completion, and monitored by thin-layer chromatography (TLC), the resulting mixture was cooled to room temperature and then hot ethanol (50 °C) was added to the mixture, and the heterogeneous PMO-Py-IL nanocatalyst was separated by filtration. In order to study the reusability of the PMO-Py-IL nanocatalyst, after the first reaction run, the PMO-Py-IL nanocatalyst was separated from the reaction mixture by simple filtration. Then, the heterogeneous PMO-Py-IL nanocatalyst was washed with water and ethanol, dried in vacuum, and reused for the subsequent run. The final products were recrystallized from ethanol. All products were analyzed by ^{1}H NMR, ^{13}C NMR, FTIR, and melting points. The melting points of the product were matched well with literature reported data for the corresponding compounds. The spectral data of some products (4a-r) are presented below:

5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (4a): White crystal; Mp 201–203 °C; FT-IR (KBr, cm^{-1}) ν max 3244, 3115, 2977, 1724, 1647, 1464, 1290, 1220, 1090, 781, 698. ^{1}H NMR (DMSO-d_6) δ: 1.2 (3H, t, J = 7.2 Hz, OCH_2CH_3), 2.24 (3H, s, CH_3), 3.967 (2H, q, J = 7.2 Hz, OCH_2CH_3), 5.136 (d,1H, J = 3 Hz, -CH), 7.314 (m, 5H, Ar-H), 7.68 (1H, s, NH), 9.136 (1H, s, NH).^{13}C NMR (DMSO-d_6) δ: 14.5, 18.3, 54.4, 59.7, 99.7, 118.5, 126.7, 127.7, 128.9, 144.3, 149.2, 152.6, 165.8.

5-(Ethoxycarbonyl)-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (4b): Colorless solid; Mp 210–212 °C; FT-IR (KBr, cm^{-1}) ν max: 3235, 3118, 2976, 1727, 1648, 1610, 1462, 1391, 1214, 1091, 783, 697. ^{1}H NMR (DMSO-d_6) δ: 2.06 (3H, t, J = 7.2 Hz, OCH_2CH_3), 2.18 (3H, s, CH_3), 2.41 (2H, q, J = 7.2 Hz, OCH_2CH_3), 5.23 (d,1H, J = 3.3 Hz, -CH), 7.49 (2H, d, J = 8.4 Hz, Ar-H), 7.94 (1H, s, NH), 8.08 (2H, d, J = 8.4 Hz, Ar-H), 9.29 (1H, s, NH).^{13}C NMR (DMSO-d_6) δ: 19.6, 31.1, 53.6, 109.9, 124.3, 128.1, 147.1, 149.6, 152.1, 152.5, 194.46.

5-(Ethoxycarbonyl)-4-(4-Chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4c): Yellow powder; Mp 213–215 °C; FT-IR (KBr, cm^{-1}) ν max: 3242, 3116, 2979, 1723, 1647, 1489,

1291, 1220, 1088, 781, 492. ^{1}H NMR (DMSO-d_6) δ:1.08 (3H, t, J = 7.0 Hz, OCH_2CH_3), 2.46 (3H, s, CH_3), 3.96 (2H, q, J = 7.0 Hz, OCH_2CH_3), 5.12 (1H, d, J = 2.7 Hz, -CH), 7.12–7.39 (4H, m, Ar-H), 7.72 (1H, s, NH), 9.19 (1H, s, NH). ^{13}C NMR (DMSO-d_6) δ: 14.5, 18.3, 53.9, 59.7, 99.3, 128.7, 128.9, 132.3, 144.3, 149.2, 152.4, 165.7.

5-(Ethoxycarbonyl)-6-methyl-4-(2-Chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (4e): Pale yellow powder; Mp 214–215 °C; FT-IR (KBr, cm^{-1}) ν max: 3342, 3241, 2986, 1667, 1460, 1233, 1091,757. ^{1}H NMR (DMSO-d_6) δ:1.03 (3H, t, J = 7.0 Hz, OCH_2CH_3), 2.31 (3H, s, CH_3), 3.91 (2H, q, J = 7.0 Hz, OCH_2CH_3), 5.60 (1H, s, -CH), 7.25–7.28 (1H, m, Ar-H), 7.28–7.30 (2H, m, Ar-H), 7.39–7.70 (1H, m, Ar-H), 7.71 (1H, s, NH), 9.28 (1H, s, NH).

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4f): Pale yellow powder; Mp 201–203 °C; FT-IR (KBr, cm^{-1}) ν max: 3322, 3126, 2937, 1720, 1670, 1434, 1276, 1215, 1075, 801, 503. ^{1}H NMR (DMSO-d_6) δ: 1.07 (3H, t, J = 7.1 Hz, OCH_2CH_3), 2.20 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 3.95 (2H, q, J = 7.1 Hz, OCH_2CH_3), 5.23 (s, 1H, CH), 7.10 (2H, d, J = 8.1 Hz, Ar-H), 7.36 (2H, d, J = 8.1 Hz, Ar-H), 7.88 (1H, s, NH), 9.07 (1H, s, NH). ^{13}C NMR (DMSO-d_6) δ: 14.1, 18.0, 54.2, 60.4, 99.7, 121.8, 126.4, 130.3, 143.4, 146.0, 155.7, 166.3.

5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (4m): White powder; Mp 221–223 °C; FT-IR (KBr, cm^{-1}) ν max: 3332, 3223, 1697, 1667, 1414, 1340, 1239, 1094, 698. ^{1}H NMR (DMSO-d_6) δ: 2.062 (3H, s, CH_3), 3.322 (3H, s, OCH_3), 5.242 (1H, s, -CH), 7.12–7.34 (m, 5H, Ar-H), 7.771 (1H, s, NH), 9.127 (1H, s, NH). ^{13}CNMR (DMSO-d_6) δ: 19.412, 30.801, 30.837, 54.312, 110.096, 126.919, 127.842, 129.011, 144.732, 152.749, 194.774.

5-Methoxycarbonyl-6-methyl-4-(4-Nitrophenyl)-3,4-dihydropyrimidin-2(1H)one (4h): White powder; Mp 233–235 °C; FT-IR (KBr, cm^{-1}) ν max: 3368, 3235, 3109, 2946, 1689, 1617, 1348, 1228, 1095, 855, 700. ^{1}H NMR (DMSO-d_6) δ: 2.31 (3H, s, CH_3), 3.55 (3H, s, OCH_3), 5.26 (1H, s, CH), 7.46 (2H, d, J = 8.6 Hz, Ar-H), 7.89(1H, s, NH), 8.19 (2H, d, J = 8.6 Hz, Ar-H), 9.36 (1H, s, NH).

5-Methoxycarbonyl-6-methyl-4-(4-Chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (4i): Yellow powder; Mp 154–156 °C; FT-IR (KBr, cm^{-1}) ν max: 3324, 3219, 3105, 1698, 1675, 1491, 1420, 1342, 1295, 1239, 1093, 938, 700. ^{1}H NMR (DMSO-d_6) δ: 2.13 (3H, s, CH_3), 3.66 (3H, s, OCH_3), 5.24 (1H, s, CH), 7.03 (2H, d, J = 7.9 Hz, Ar-H), 7.35 (2H, d, J = 7.9 Hz, Ar-H), 7.88 (1H, s, NH), 9.23 (1H, s, NH). ^{13}CNMR(DMSO-d_6) δ: 14.1, 17.8, 54.9, 100.6, 122.5, 126.5, 130.3, 142.9, 146.0, 155.5, 166.7.

5-Methoxycarbonyl-6-methyl-4-(2-Chlorophenyl)-3,4-dihydropyrimidin-2(1H)one (4k): Pale yellow powder; Mp 265–268 °C; FT-IR (KBr, cm^{-1}) ν max: 3441, 3351, 3250, 1690, 1660, 1458, 1086, 960, 800, 462. ^{1}H NMR (DMSO-d_6) δ: 2.32 (3H, s, CH_3), 3.51 (3H, s, OCH_3), 5.57 (1H, d, J = 3.4 Hz, CH), 7.30–7.44 (4H, m, Ar-H), 7.53 (1H, s, NH), 9.32 (1H, s, NH).

5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (4m): White powder; Mp 231–233 °C; FT-IR (KBr, cm^{-1}) ν max: 3268, 1702, 1675, 1599, 1493, 1236, 1106, 767, 704, 571. ^{1}H NMR (DMSO-d_6) δ: 2.09 (3H, s, CH_3), 2.24 (3H, s, CH_3), 5.22 (1H, d, J = 3.5 Hz, 1H), 7.17 (3H, d, J = 6.5 Hz, Ar-H), 7.22–7.34 (2H, m, Ar-H), 7.81 (1H, s, NH), 9.16 (1H, s, NH). ^{13}CNMR(DMSO-d_6) δ: 18.4, 30.2, 39.6, 54.0, 109.6, 126.5, 127.4, 128.6, 144.265, 148.1, 152.2, 194.3.

5-Acetyl-6-methyl-4-(4-Nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (4n): White powder; Mp 229–230 °C; FT-IR (KBr, cm^{-1}) ν max: 3342, 3252, 3143, 1709, 1674, 1608, 1515, 1446, 1384, 1239, 1279, 1237, 1187, 1102, 862, 763, 698. ^{1}H NMR (DMSO-d_6) δ: 2.10 (3H, s, CH_3), 2.25 (3H, s, CH_3), 5.24 (1H, d, J = 3.4 Hz, 1H), 7.24 (2H, d, J = 8.4 Hz, Ar-H), 7.40 (2H, d, J = 8.4 Hz, Ar-H), 7.84 (1H, s, NH), 9.21 (1H, s, NH). ^{13}CNMR(DMSO-d_6) δ: 18.9, 30.5, 53.17, 109.6, 128.4, 128.6, 131.9, 143.3, 148.5, 152.1, 193.9.

5-Acetyl-6-methyl-4-(4-Chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (4o): Yellow powder; Mp 204–206 °C; FT-IR (KBr, cm^{-1}) ν max: 3288, 3121, 2915, 1699, 1618, 1424, 1322, 1262, 1236, 1091, 837, 789, 581. ^{1}H NMR (DMSO-d_6) δ: 2.13 (s, 3H), 2.29 (s, 3H), 5.257 (d, J = 3.2 Hz, 1H), 7.26 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.88 (s, 1H), 9.25 (s, 1H).

5-Acetyl-6-methyl-4-(2-Hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (4p): Pale yellow powder; Mp 204–208 °C; FT-IR (KBr, cm^{-1}) ν max: 3240, 3096, 2982, 1682, 1603, 1584, 1503, 1173, 1113, 925, 867, 762.

5-Acetyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (4r): Yellow powder; Mp 172–174 °C. ^{1}HNMR (DMSO-d_6) δ: 2.073 (s, 3H), 2.275 (s, 3H), 3.72 (s, 3H), 5.19 (d, J = 3.2 Hz, 1H), 6.87 (d, J = 8.4 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.71 (s 1H), 9.13 (s, 1H).

4. Conclusions

In summary, one-pot Biginelli condensation reaction for a series of aryl aldehydes, β-dicarbonyls and urea using protic pyridinium functionalized hybrid mesoporous materials (PMO-Py-IL) as catalyst in high yield and under solvent-free conditions was described. Moreover, the catalyst showed superior stability and could be easily separated and reused at least for ten Biginelli reaction cycles. The uniform cylindrical/spheroidal structure of porous PMO-Py-IL nanomaterial was confirmed by the SEM image of the PMO-Py-IL nanomaterial after ten reaction runs. The ultimate goal of present work was the development of a cost-effective, green, sustainable, reusable, and simple and mild process for synthesis of 3,4-dihydro-2(*H*)-pyrimidinones (DHPMs).

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