Journal of
Chemistry & Applied Biochemistry

Open Science Publications

Volume 2, Issue 2 - 2015

www.opensciencepublications.com

Synthesis of 3,4-Dihydro-2(1H)-Pyrimidones Via Biginelli Reaction in Organized Media Using Ionic Liquids and Solid Acid Catalysts

Research Article

Pranab Jyoti DAS*, Jesmin BEGUM

Department of Chemistry, Gauhati University, Guwahati 781014, India

***Corresponding author:** Pranab Jyoti DAS, Department of Chemistry, Gauhati University, Guwahati 781014; India

Email. pranabjdas52@gmail.com.

Article Information: **Submission:** 31/10/2015; **Accepted:** 26/11/2015; **Published:** 04/12/2015

Abstract

5-Ethoxycarbonyl-4-aryl-6-methyl-3,4-dihydropyrimidin-2(1H)-one have been synthesized in good yield by the condensation of aromatic aldehydes, ethylacetoacetate and urea in the presence of acidic ionic liquids derived from dialkylamines as the catalyst under thermal heating in the absence of VOC. The synthesis of the target molecules revisited using acidic ion exchange resin namely Amberlite IR 120(H^+) in a solid phase reaction. The two methods compared with respect to yields obtained, reaction time, ease of separation of products, cost and recyclability of the catalysts.

Key words: Aromatic aldehyde; Solvent free reactions; Ionic liquids; Amberlite IR120(H^+); Acetoacetic ester; Urea

Introduction

Functionalized dihydropyrimidine (DHMP) scaffold, popularly termed as "Biginelli compounds" is a heterocyclic system exhibiting remarkable pharmacological efficiency. Dihydropyrimidines display a broad range of biological effects, including antiviral, antitumor, antibacterial, and anti inflammatory properties. The recognized pharmacophore is reported to be the partly reduced pyrimidine moiety [1]. The versatile end use of DHPMs have led to the recent development of several improved reaction protocols for the synthesis of DHPMs with a variety of substituents in the basic unit, either by modification of the classical one-pot Biginelli approach [2-4], or by the development of novel, but more complex multistep strategies [5-7]. Further, several combinatorial approaches towards synthesis of DHPMs have been reported using solid phase techniques [8-10]. The use of Cu $(NO_3)_2$ deposited on Mont-morillonite K 10 clay in the microwave-assisted solvent-free condition is a noteworthy example [11]. In general, Lewis acids are used as the catalyst although the use of a variety of other catalysts have been reported. Notable among the catalysts used to drive the reaction are zeolites HZSM-5 and MCM-41 [12], ionic liquids [13], $Mg(NO3)_2$ [14], DDQ [15] and a variety of Triflates [16,17], $Zn(BF_4)_2$ [18], natural acid [19], 12-phosphotungstic acid besides others [20,21-23].

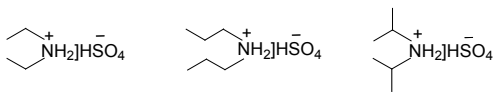
In this investigation, we explored the possibility of synthesis of the functionalized DHPMs namely the 5-Ethoxycarbonyl-4-aryl-6-methyl-3,4-dihydropyrimidin-2(1H)-ones using simple acidic ionic liquids derived from dialkylamines. Ionic liquids are termed as neoteric liquids and are recognized as environmentally harmless media because of their low vapour pressure, high thermal and chemical stability and excellent solubilising characteristics. Their low toxicity, recyclability, air stability and excellent solubility both in water as well as in most organic solvents contribute to their versatility as catalysts. Their unique properties resulted in their wide acceptance as media in many reactions and as catalysts as well. The dual role played by ionic liquids and their influence on selectivity in reactions have further enhanced their utility [24-32]. Among the wide range of ionic liquids, the salts of imidazolium, ammonium,

ISSN: 2394-3106

thiazolium cations are especially popular and simple methods of their synthesis and characterization have been reported [33-37]. Their applications in organic synthesis have been widely explored. However, the use of some of these IL is less attractive due to their high cost. Thus it is necessary to explore possibilities of preparing less expensive IL which may exhibit comparable, if not better, utility as catalyst and/or solvent. In this work we explored the possibility of the use of acidic ionic liquids derived from dialkylamines both as a catalyst and solvent for the three component solvent free reaction of aromatic aldehydes, ethylacetoacetate and urea for the synthesis of 3,4-dihydro-2(1H)-pyrimidones. Further, the reaction was revisited by using a solid acid catalyst for the condensation and the merits of the two environmentally benign processes examined.

Results and Discussions

During the course of our study in developing cost effective ionic liquids for the synthesis of 3,4-dihydro-2(1H)-pyrimidones by the Biginelli condensation reaction, we prepared acidic ionic liquids from easily available dialkylamines and used them as catalyst in a facile three component reaction of aromatic aldehydes, ethylacetoacetate and urea as substrates for the synthesis of 3,4-dihydropyrimidin-2(1H) ones in appreciably reduced reaction time as well as in high yield. Three different ionic liquids, namely diethylammoniumhydrogensulphate ($DEAHSO_4$), di-n-propylammoniumhydrogensulphates, ($DPAHSO_4$), diisopropylammoniumhydrogen- sulphate, ($DisoPAHSO_4$) and were prepared by a reported procedure [37]. Scheme 1 gives the structures of the IL synthesized.



$DEAHSO_4$ $DPAHSO_4$ $DisoPAHSO_4$

Scheme1: Structures of different ionic liquids prepared.

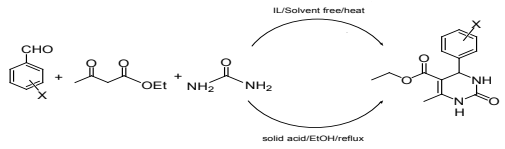
Thermogravimetric analysis showed that all the three ionic liquids are stable and their thermal stability decreases according to the sequence $[(disopropyl)_2NH_2]HSO_4$> $[Et_2NH_2]HSO_4$> $[(n\text{-}propyl)_2NH_2]HSO_4$[32]. $DisoPAHSO_4$ being thermally the most stable, we chose to use this ionic liquid in all the synthesis reported here. A trial run was carried out by using 4-methoxybenzaldehyde, ethylacetoacetate and urea in 5mmol of the ionic liquid and the product 5-ethoxycarbonyl-4-(4′-methoxyphenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one was recovered in 88%. Reaction conditions were optimized by varying the mol % of ionic liquid, reaction temperature and reaction time. Results obtained indicated that best results were obtained at the reaction temperature of 80 °C in about 30 mins reaction time using 5 mmol of the ionic liquid. The results are summarized in Table 1.

Increase of reaction temperature and time beyond the optimum did not significantly increase the yields. Consequently, all reactions were carried out at the optimized reaction conditions mentioned. A library of 5-Ethoxycarbonyl-4-aryl-6-methyl-3,4-dihydropyrimidin-2(1H)-one were synthesized by varying the aromatic aldehydes.

In addition to the use of IL as catalyst for the synthesis of the target molecules, we carried out a solid phase synthesis of target molecule using Amberlite IR120 (H^+) as the solid acid catalyst in an environmentally benign reaction using ethanol as the solvent. This solid phase synthesis was also standardized by varying the solid acid catalyst. 5 g of the solid acid was found to give best yield of the target molecule. Both the reaction conditions have been compared with respect to the yield of the product obtained, reaction condition used, the method of recovery of products and also the extent of environmental acceptability. Both the procedures conform to the tenets of green techniques in organic synthesis. In case of the use of acidic ionic liquids, no volatile organic solvent was found necessary as the acidic ionic liquids performed the dual role of a solvents well as the catalyst. In case of the reaction condition using the solid acid, organic solvent had to used in order to facilitate reaction at the surface of the catalyst. In the absence of a solvent the reaction gave several polymeric products which could not be characterized. Use of organic solvents such as DMF, CH_2Cl_2, dioxane, methanol and ethanol were explored and it was observed that solvents had no effect on the yield and reaction temperature consequently the benign solvent ethanol was selected as the convenient solvent. The reaction is shown in

Table1: Effect of ionic liquid and reaction time on the yield of the reaction with 4-methoxybenzaldehyde, urea and ethylacetoacetate at 80 °C

Sl.no	Reaction time (min)	mol%of IL	Yield (%)
1	50	2	65
2	50	3	45
3	60	4	47
4	60	5	85
5	70	6	80
6	70	8	82
7	80	10	80



Scheme 2: Synthesis of 1,4-dihydro-2(1H)-pyrimidones mediated by acidic ionic liquid and Amberlite IR 120(H^+) .

The results obtained on using both the ionic liquid and the acidic ion exchange resin are summarized in Table 2.

After optimization of the conditions, the reaction was examined for its generality by using a series of aromatic aldehydes under optimal condition and the results are presented in Table 2.

Work up is simple as the ionic liquid could be easily removed from the reaction mixture by washing the products with water. The reaction however, failed to give good yields with aliphatic aldehydes.

Experimental Section

Melting points were recorded in a VMP-D model Melting point

Citation: DAS PJ, BEGUM J. Synthesis of 3,4-Dihydro-2(1H)-Pyrimidones Via Biginelli Reaction in Organized Media Using Ionic Liquids and Solid Acid Catalysts. J Chem Applied Biochem. 2015;2(1): 116.

Table 2: Physical characteristics of 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-di-hydropyrimidin-2(1H)-one obtained by reaction catalyzed by ionic liquid (method A) and solid acid (method B)

	X	Yield (%)		Melting points (°C)	
		Method A	Method B	Found	Reported
1	H	92	86	208	206-207[25,32]
2	4-CH_3	86	78	221	215-216[25,32]
3	2-CH_3	78	74	204-205	203[27,32]
4	3,4-diOCH_3	87	78	178	175-77[33]
5	4-OCH_3	85	81	201	203[24]
6	4-NO_2	89	82	211	206-208[35]
7	3-NO_2	81	75	225	228-230[36]
8	2-NO_2	76	75	210	208-209[24]
9	4-Cl	87	81	211	212-214[24]
10	3-Cl	78	77	190	193-95[32,31]
11	2-Cl	8	71	215	218[29]
12	3-Br	80	74	189	196–197[34]
13	2,5-diOCH_3	74	73		
14	4-OH	81	82	226	230-232[30]
15	2,4-diCl-	78	71	244	248-250[31]
16	1-napthyl	73	73	221	210-211[24]

a) All reactions in ionic liquid performed without solvents at 80°C,
b) Reaction using solid based performed at reflux temperature of ethanol.
c) % yield determined with respect to theoretical yield

apparatus and are uncorrected. UV-Vis spectra were recorded in Shimatzu FT-IR recorded in Perkin Elmar 1600 spectrometer using KBr pellets, ^1H and ^{13}C NMR spectra were recorded in Bruker 300MHz spectrometer in $CDCl_3$ and DMSO-d_6 and TMS as internal standard. Aldehydes used were recrystallized by reported procedures before use. Mass spectra were recorded in a Waters Micromass ZQ ™ 400 mass spectrometer. The thermal decomposition point of the ionic liquids were determined in a TGA-DSC1, Mettler Toledo instrument heating in a stream of nitrogen atmosphere. All reagents were purified by standard literature procedure. The dialkylamine based ionic liquids were prepared according to the procedure reported earlier[32].

Thermogravimetric Analysis (TGA) of ionic liquids: The samples were weighed and placed in a platinum crucible. They were then heated in a stream of nitrogen atmosphere, from room temperature to 700 °C with a heating rate usually of 10 °C /min. The thermal stability is seen to vary with the nature of the cation of ILs. The thermal stability increases in the following sequence of the ILs, di-n-propyl ammonium hydrogen sulphate < diethyl ammonium hydrogen sulphate < di-isopropyl ammonium hydrogensulphate.

Diethylammonium hydrogensulphate $[Et_2NH_2][HSO_4]$: prepared by reported method ^1H NMR (300 MH_Z, DMSO, Me_4Si) (δ_H ppm) : 1.148 (6 H, t, J= 7.2 Hz, 2 CH_3), 2.890 (4 H, t, J=7.2 Hz, 2 CH_2), 3.777 (2 H, s, NH_2), 8.347 (1 H, s, HSO_4) ; ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 11.30, 41.73 ; The thermal decomposition point 578K.

Di-n-propylammonium hydrogensulphate $[n\text{-}Pr_2NH_2][HSO_4]$: ^1H NMR (400 MH_Z , DMSO , Me_4Si) (δ_H ppm): 0.095 (6 H, t, J= 6.8 Hz, 2 CH_3), 1.602 (4 H, sextet, J= 7.2 Hz, 2 CH_2), 2,841 (4 H, m, 2 CH_2), 4.447 (2 H, s, NH_2), 8.297 (1 H, s, HSO_4) ; ^{13}C NMR (100 MHz, DMSO-d_6) (δ ppm) : 11.349, 19.413, 48.816 ; HRMS(ESI) m/z calcd for $C_6H_{17}NO_4S$ $[M]^+$ (199.0878), found (199.0879).; The thermal decomposition point 567 K.

Diisopropylammonium hydrogensulphate$[iso\text{-}Pr_2NH_2[HSO_4]$: ^1H NMR (300 MH_Z, DMSO, Me_4Si) (δ_H ppm) : 1.191 (12 H, d, J=6.3 Hz, 4 CH_3) 3.305 (2 H, m, 2 CH), 4.975 (2 H, s, NH_2), 8.136 (1 H, s, HSO_4) ; ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 18.96, 46.56 ; HRMS(ESI) m/z calcd for $C_6H_{17}NO_4S$ $[M]^+$ (199.0878), found (199.0879). The thermal decomposition point 591K.

General procedure for the synthesis of 5-ethoxycarbonyl-6-methyl-4-substituted-3,4-dihydropyramidin-2(1H)-one using diisopropylammoniumhydrogensulphate.

An equimolar mixture of aromatic aldehyde (1.0 mmol), ethylacetoacetate (1.0 mmol) , urea (1.0 mmole) and 5 mmol of the acidic diisopropylammoniumhydrogen sulphate was mixed thoroughly in pestle grinder and the homogeneous mixture was heated in an oil bath to 80 °C in the absence of solvent. After 30 mins of heating a distinct change in colour of the reaction mixture to yellow was observed. The yellow solid mass was washed several times with water till free of the ionic liquid. The crude product was extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and solvent evaporated to obtain the product.

General procedure for the synthesis of 5-ethoxycarbonyl-6-methyl-4-substituted-3,4-dihydropyramidin-2(1H)-one using solid acid, Amberlite IR 120(H^+) :

An equimolar mixture of aromatic aldehyde (1.0 mmol), ethylacetoacetate (1.0 mmol), and urea (1.0 mmole) was dissolved in 50 mL ethanol (95% v/v). To this solution 5 g of acidic ion exchange resin (Amberlite IR 120H^+) was added and the heterogeneous mixture was refluxed with constant stirring for about 30 mins. A change in colour of the reaction mixture to light yellow was observed. The reaction was monitored by using TLC in prepared silica gel plates using petroleum ether (60-80) : ethylacetate : 10:1 as the eluent. After completion of the reaction, the resin beads were filtered out and evaporation of the ethanol gave the product. The recovered resin was washed wit dil.HCl and reused. The dihydropyramidin-2(1H)-one

Citation: DAS PJ, BEGUM J. Synthesis of 3,4-Dihydro-2(1H)-Pyrimidones Via Biginelli Reaction in Organized Media Using Ionic Liquids and Solid Acid Catalysts. J Chem Applied Biochem. 2015;2(1): 116.

were recrystallized from either methanol or ethanol.

Conclusion

In conclusion, an efficient solvent free method is developed for the synthesis of 5-ethoxy- carbonyl-6-methyl-4-substituted-3,4-dihydropyramidin-2(1H)-one using both the acidic ionic liquid derived from dialkylamines and the solid acid Amberlite IR 120 (H^+). The recovery of product in both the cases is easy. The ionic liquids used can be obtained from cheap sources, they are easy to handle and environmentally benign and recovery of products did not warrant the use of organic solvents. The use of ionic liquid offers a solvent free reaction and yields are found to be higher as compared to those obtained by using the ion exchanger as the catalyst.

Spectroscopic data of selected compounds:

1. **5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyramidin-2(1H)-one (entry1):** light yellow, UV (in EtOH 95%V/V , λ_{max} nm): 295, 346, ^{1}H-NMR ($CDCl_3$) : δ 9.18(s,1H), 7.73(s,1H), 7.32-7.23(m. 5H$_{aromatic}$), 5.13 (d, J=4.2 Hz, 1H), 3.92-3.99 (q, J=7.1 Hz, 2H), 2.23 (s, 3H), 1.09-1.05(t, 3H), ^{13}C(75 MHz): 165.38, 152.18,148.4,144.8,128.43, 127.31, 126.28,99.29, 59.24,53.99, 17.81, 4.11; IR (KBr) : ν cm^{-1} 3244, 3116, 1724, 1701.

2. **5-ethoxycarbonyl-6-methyl-4(4-methylphenyl)-3,4-dihydropyramidin-2(1H)-one (entry2):** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 298, 342; ^{1}H-NMR (DMSO-d_6) : δ 9.15(s,1H), 7.68(s,1H), 7.1 (m,4H$_{aromatic}$), 5.09(1H), 3.97-3.92 (q, J=6.8Hz, 2H), 2.22 (d, 3H), 2.3 (d, 3H), 1.04-1.11(t, J=7.8Hz, 3 H); ^{13}C(75 MHz);165.37, 152.2, 148.17, 141.96, 136.38, 128.9, 126.16, 99.41, 59.17, 53.63, 20.65, 17.77, 14.1; IR (KBr) : ν cm^{-1} 3354, 3224, 2326, 1695, 1645.

3. **5-ethoxycarbonyl-6-methyl-4-(3,4-dimethoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (entry 4) :** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 298, 352 ; ^{1}H-NMR ($CDCl_3$) : δ 9.13(s,1H), 7.66(s, 1H), 6.88-6.69(m, 3H$_{aromatic}$), 5.084(s,1H), 4.01-3.96(t,2H), 3.698(s,6H), 2.226(s,3H), 1.12-1.07(t,3H) ; ^{13}C(75 MHz): 159.48, 146.29, 142.51, 142.49, 93.42, 53.24, 49.58, 49.46, 47.51, 11.81, 8.22 IR (KBr) : ν cm^{-1} 3251, 3118, 1716, 1681

4. **5-ethoxycarbonyl-6-methyl-4-(4-methoxylphenyl)-3,4-dihydropyrimi- din -2(1H)-one (entry 5):** light yellow , UV (in EtOH 95%V/V, , λ_{max} nm):299, 329; ^{1}H-NMR (DMSO-d_6) : δ 9.19 (s,1H), 7.59(s,1H), 7.15-6.81(m,4H), 5.00(s,1H), 3.89(q, J=6.7 Hz, 2H), 3.70(s,3H), 2.19(s,3H), 1.07(t, J=6.7,3H); ^{13}C(75 MHz):165.1, 157.9,151.8,148.3,137.5, 126.8, 112.7, 99.2, 58.9, 54.9, 17.9; IR (KBr) : ν cm^{-1} 3400, 3232, 1745, 1685.

5. **5-ethoxycarbonyl-6-methyl-4(4- nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (entry6):** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 295, 336; ^{1}H-NMR ($CDCl_3$) : δ 8.7(br ,s,1H), 7.3(br,s,1H), 7.31-7.33(t, 2H$_{aromatic}$), 7.92-7.95 (m, 2H$_{aromatic}$), 5.22 (d, 2.6Hz, 1H), 3.82-3.89 (q,2H), 2.14(s,3H), 0.98-0.94(t, J=7.68, 3H) ; 13C NMR(75 MHz): 165.1, 152.29, 148.4, 146.58, 127.21, 123.22, 59.43, 54.03, 18.04, 13.71. IR (KBr) : ν cm^{-1} 3390, 3232, 1712, 1633, 1456.

6. **5-ethoxycarbonyl-6-methyl-4(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (entry 9):** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 298, 335 ; ^{1}H-NMR ($CDCl_3$) : δ 8.6(s,1H), 7.02 (s,1H), 6.83-6.91(m, 4H), 5.03-5.02(d, 1H), 3.80-3.73(q,3H), 2.05(s,3H), 0.97-0.86(q, 3H); ^{13}C (75 MHz) : 165.1, 152.26, 147.46, 142.68, 132.2,127.7,99.2,77.43,59.03,53.77,17.74,13.54; IR (KBr) : ν cm^{-1}3356, 3240,1701,1543.

7. **5-ethoxycarbonyl-6-methyl-4(3-bromophenyl)-3,4-dihydropyrimidin-2(1H)-one (entry 12):** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 294, 339; ^{1}H-NMR (DMSO-d_6) : δ 9.21(s, 1H), 7.79 (s, 1H), 7.45-7.29(m, 4H), 5.13 (d, J=5.6 Hz, 1H), 4.01(t, 2H), 2.48-2.23 (t,3H), 1.16-1.05(t, 3H); ^{13}C (75 MHz) : 165.13, 151.91, 148.97,147.49, 130.83, 130.16, 129.18, 125.28, 121.53, 98.6, 59.32, 53.59, 17.83, 14.05; IR (KBr) : ν cm^{-1} 3344, 3213, 1658.7, 1608.63.

8. **5-ethoxycarbonyl-6-methyl-4(2-bromophenyl)-3,4-dihydropyrimidin-2(1H)-one(entry 13):** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 298, 338 ^{1}H-NMR (DMSO-d_6) : δ 9.28(s, 1H), 7.70(s,1H), 7.56-7.14(m, 4H$_{aromatic}$), 5.60-5.91 (d, J=7.1Hz, 2H), 3.91-3.84 (t, 2H), 2.28 (s, 3H), 1.0-0.95 (t, 3H); 13C NMR (75 Hz): 164.97, 151.27,149.3, 143.4, 132.6, 129.4, 128.79, 128.47, 122.28, 98.26, 59.08, 54.01, 17.67, 14.00; IR (KBr) : ν cm^{-1} 3344 , 3223, 1697, 1633.

9. **5-ethoxycarbonyl-6-methyl-4-napthyl-3,4-dihydropyrimidin-2(1H)-one (entry 16) :** light yellow ; UV (in EtOH 95%V/V, , λ_{max} nm): 286, 329; 1H-NMR ($CDCl_3$) : δ 9.25(s,1H), 8.26(d,J=7.1Hz,1H), 7.91(s,1H), 7.84(d,J=8.1, 1H), 7.75(s,1H), 7.37-7.57(m, 4H $_{aromatic}$), 6.03(s, 1H), 3.73-3.8(m,2H), 2.48(s,3H), 0.76-0.81(t, 3H) ; ^{13}C NMR(75 MHz) : δ 159.3, 145.75, 142.8, 134.41, 127.5, 124.08, 122.51, 121.98, 120.13, 119.78, 119.72, 118.25, 117.67, 93.18, 53.12, 43.76, 11.82, 7.78; IR (KBr) : ν cm^{-1} 3410, 3245, 1726 ,1654.

References

1. Kappe CO (2000) Biologically active dihydropyrimidones of the Biginelli-type--a literature survey. Eur J Med Chem 35, 1043- 1052.
2. Lu J, Ma H (2000) Iron(III)-Catalyzed Synthesis of Dihydropyrimidinones. Improved Conditions for the Biginelli Reaction. Synlett 2000: 63- 64.
3. Hu EH, Sidler DR, Dolling UH (1998) Unprecedented Catalytic Three Component One-Pot Condensation Reaction: An Efficient Synthesis of 5-Alkoxycarbonyl- 4-aryl-3,4-dihydropyrimidin-2(1H)-ones. J Org Chem 63: 3454-3457.
4. Gupta R, Gupta AK, Paul S, Kachroo PL (1995) Ind J Chem 34B: 151-153.
5. O'Reilly BC, Atwal KS (1987) Synthesis of Substituted 1,2,3,4-Tetrahydro-6-methyl-2-oxo-5-pyrimidinecarboxylic Acid Esters: The Biginelli Condensation Revisited. Heterocycles 26, 1185-1188.
6. Atwal KS, O' Reilley BC, Gougoutas JZ, Malley MF (1987) Synthesis of Substituted 1,2,3,4-Tetrahydro-6-methyl-2-thioxo-5-pyrimidinecarboxylic Acid Esters. Heterocycles 26: 1189-1192.
7. Shutalev AD, Kishko EA, Sivova N, Kuznetsov AY (1998) A New Convenient Synthesis of 5-Acyl-1,2,3,4-tetrahydropyrimidine-2-thiones/ones. Molecules 3: 100-106.
8. Wipf P, Cunningham A (1995) Tetrahedron Lett 36: 7819-7822.

Citation: DAS PJ, BEGUM J. Synthesis of 3,4-Dihydro-2(1H)-Pyrimidones Via Biginelli Reaction in Organized Media Using Ionic Liquids and Solid Acid Catalysts. J Chem Applied Biochem. 2015;2(1): 116.

9. Kappe CO (2000) Highly versatile solid phase synthesis of biofunctional 4-aryl-3,4-dihydropyrimidines using resin-bound isothiourea building blocks and multidirectional resin cleavage. Bioorg Med Chem Lett 10: 49-51.

10. Studer A1, Jeger P, Wipf P, Curran DP (1997) Fluorous Synthesis: Fluorous Protocols for the Ugi and Biginelli Multicomponent Condensations. J Org Chem 62: 2917- 2924.

11. Diwaker S, Rakshit A, Punjabi PB, Ameta SC (2010) Int J Chem Sci 8: 1973-1982.

12. Radha Rani V, Srinivas N, Radha Kishan M, Kulkarni SJ, Raghavan VK (2001) Zeolite-catalyzed cyclocondensation reaction for the selective synthesis of 3,4-dihydropyrimidin-2(1H)-ones. Green Chem 3: 305-306.

13. Boumoud T, Boumoud B, Rhouati S, Belfaith A, Deache A, Mosset P (2008) Acta Chim Slov 55: 617-622 .

14. Shobha D, Chari MA, Sadanandam P, Mukkanti K (2008) Dichloro dicyano quinone (DDQ) as coupling reagent for high yield synthesis of 3,4-dihydropyrimidin-2(1H)-ones. J Het Chem 45: 1225-1227.

15. Ma Y, Qian C, Wang L, Yang M (2000) Lanthanide Triflate Catalyzed Biginelli Reaction. One-Pot Synthesis of Dihydropyrimidinones under Solvent-Free Conditions. J Org Chem 65: 3864-3868.

16. Paraskar AS, Dewkar GK, Sudalai A (2003) $Cu(OTf)_2$: a reusable catalyst for high-yield synthesis of 3,4-dihydropyrimidin-2(1H)-ones. Tetrahedron Lett 44, 3305-3308.

17. Kundu SK, Majee A, Hazra A (2009) Environmentally benign aqueous zinc tetrafluoroborate-catalyzed one pot Biginelli condensation at room temperature. Indian J Chem 48B: 408-412.

18. Patil S, Jadhav SD, Deshmukh MB (2011) Natural Acid Catalyzed Multi-component Reactions as a Green Approach. Arch Appl Sci Res 3: 203-208.

19. Mishra BG, Kumar D, Rao VS (2006) $H_3PW_{12}O_{40}$ catalyzed expeditious synthesis of 3,4-dihydropyrimidin-2(1H)-ones under solvent-free conditions. Catal Commun 7: 457-459.

20. Kadre T, Jetti SR, Bhatewara A, Paliwal P, Jain S (2012) Green protocol for the synthesis of 3,4-Dihydropyrimidin-2(1H)- ones/thiones using TBAB as a catalyst and solvent free condition under microwave irradiation. Arch Appl Sci Res 4: 988-990.

21. Boumoud T, Boudjemaa B, Mosset P, Debache A (2011) Gypsum-Catalyzed One-Pot Synthesis of 3,4-Dihydropyrimidin-2(1H)-ones Under Solvent-Free Conditions. E-Journal of Chemistry 8: 312-318.

22. Dadhania AN, Patel VK, Raval DK (2012) A facile approach for the synthesis of 3,4-dihydropyrimidin-2-(1H)-ones using a microwave promoted Biginelli protocol in ionic liquid. J Chem Sci 124: 921-924.

23. Dupont J, De Souza RF, Suarez PAZ (2002) Ionic liquid (molten salt) phase organometallic catalysis. Chem Rev 102: 3667-3692.

24. Wilkes JS (2002) A short history of ionic liquids—from molten salts to neoteric solvents. Green Chemistry 4: 73-80.

25. Wasserscheid P, Keim W (2002) Angew Chem Int Ed 39: 3772 -3789.

26. Welton T (1999) Room-Temperature Ionic Liquids. Solvents for Synthesis and Catalysis. Chem Rev 99: 2971-2083.

27. Sheldon RA (2005) Green solvents for sustainable organic synthesis: state of the art. Green Chem 7: 267-278.

28. Carlin RT, Wilkes JS (1994) In Advances in non aqueous chemistry, ed Mamantov G, Popov A, Eds; VCH, New York.

29. Olivier H (1999) Recent developments in the use of non-aqueous ionic liquids for two-phase catalysis J Mol Cata A: Chem 146: 285-288.

30. Sheldon R (2001) Catalytic reactions in ionic liquids. Chem Commun 2399-2407.

31. Earle MJ, Seddon KR (2000) Ionic liquids. Green solvents for the future. Pure Appl Chem 72: 1391-1398.

32. Burrell AK, Del Sesto RE, Baker SN, McCleskey TM, Baker GA (2007) The large scale synthesis of pure imidazolium and pyrrolidinium ionic liquids. Green Chem 9: 449-454.

33. Paulechka YU, Kabo GJ, Blokhin AV, Vydror OA, Magee JW, et al. (2003) Thermodynamic Properties of 1-Butyl-3-methylimidazolium Hexafluorophosphate in the Ideal Gas State. J Chem Eng Data 48: 457-462.

34. Kabo GJ, Blokhin AV, Paulechka YU, Kabo AG, Magee JW (2004) Thermodynamic Properties of 1-Butyl-3-methylimidazolium Hexafluorophosphate in the Condensed State. J Chem Eng Data 49: 453-461.

35. Weng J, Wang C, Li H, Wang Y (2006) Novel quaternary ammonium ionic liquids and their use as dual solvent-catalysts in the hydrolytic reaction. Green Chem 8: 96-99.

36. Varma RS, Namboodri VV (2001) Solvent-free preparation of ionic liquids using a household microwave oven. Pure Appl Chem 73: 1309-1313.

37. Das PJ, Das J (2012) Synthesis of aryl/alkyl (2,2′-bis-3-methylindolyl) methanes and aryl(3,3′-bis indolyl)methanes promoted by secondary amine based ionic liquids and microwave irradiation. Tetrahedron Lett 53: 4718-4720.

Citation: DAS PJ, BEGUM J. Synthesis of 3,4-Dihydro-2(1H)-Pyrimidones Via Biginelli Reaction in Organized Media Using Ionic Liquids and Solid Acid Catalysts. J Chem Applied Biochem. 2015;2(1): 116.