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4-Nitrophthalic acid - catalyzed Biginelli reaction: One-pot synthesis of 3, 4-dihydropyrimidin-2-(1*H*)-ones/thiones under solvent free conditions

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Abstract: *New organic reactions allow chemical transformations which were previously not possible. Therefore, new reactions are important contributions to the progress in the field of organic synthesis. A simple and effective synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives from aldehydes, 1,3-dicarbonyl compounds and urea or thiourea using 4-Nitrophthalic acid as a catalyst under solvent free condition is described. Taking into account of environmental and economical considerations, the protocol presented here has the merits of environmentally benign, simple operation, convenient work-up, short time, good yields, the avoidance of the organic solvent and inexpensive catalyst. The synthesized compounds were characterized by IR, ^{1}H, ^{13}C NMR, MS and elemental analysis.*
Keywords: *Biginelli reaction; Synthesis; Solvent free; 3, 4-Dihydropyrimidin-2(1H)-ones; Catalyst*

I. INTRODUCTION

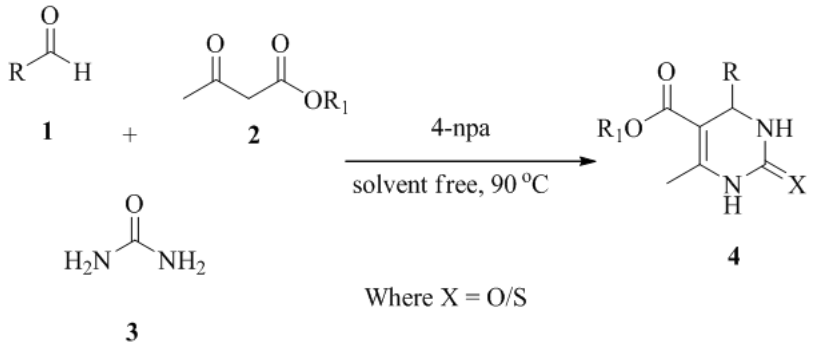
Dihydropyrimidinones (DHPMs) and their derivatives are important heterocyclic motif in the realm of natural and synthetic organic chemists mainly due to their significant pharmaceutical and therapeutic properties such as anti-bacterial, anti-viral, anti-tumor and anti-inflammatory activities [1]. Appropriately functionalized dihydropyrimidinones have been successfully used as the integral backbones of several calcium channel blockers [2], adrenergic [3], neuropeptide Y (NPY) antagonists [4], and antihypertensive agents [5]. Moreover, some marine natural products containing the dihydropyrimidinone-5-carboxylate unit such as the alkaloid Batzelladine B have been found to be potent HIV gp-120-CD4 inhibitors [6]. Therefore, synthesis of dihydropyrimidinones and their derivatives is drawing more and more attention from organic and medicinal chemists.

The most simple and straightforward procedure, first reported by Biginelli in 1893, involves three component, one-pot condensation of a β-ketoester with an aldehyde and urea under strongly acidic conditions [7]. One major drawback of this so-called Biginelli reaction, however, is the low to moderate yields (20-50%) that are frequently encountered when using substituted aromatic or aliphatic aldehydes [8]. This has led to the development of more complex multistep strategies that produce somewhat higher overall yields but lack the simplicity of the one-pot Biginelli protocol [8, 9].

The art of performing efficient chemical transformation coupling three or more components in a single operation by a catalytic process avoiding stoichiometric toxic reagents, large amounts of solvents, and expensive purification techniques represents a fundamental target of the modern organic synthesis [10]. Thus, Biginelli's reaction for the synthesis of dihydropyrimidinone has received renewed interest, and several improved procedures have been reported including the use of different kinds of Lewis and protic acids have been reported in the literature [11,12]. Most recently, known methods involve the use of triflates [13,14], silica-sulfuric acid [15], silver salts of heteropoly acids [16], silica supported sodium hydrogen sulfate [17], iodine-alumina system [18], poly(4-vinylpyridine-co-divinylbenzene)-Cu(II)complex [19], iodotrimethylsilane [20], solid super acid [21], L-proline [22], microwave assisted methodologies [23,24], ultrasonic mediated [25], ionic liquid mediated [26] ceria/vinyl pyridine polymer [27], $KAl(SO_4)_2.12H_2O$ supported on silica [28], 12-molybdophosphoric acid [29], silica supported heteropoly acid [30], heteropoly acid [31], polyoxometallates [32], propane phosphonic acid [33], silica supported sulfonic acid [34], tetrachlorosilane [35], 1,3-dibromo-5,5-dimethylhydantoin [36], $Al(H_2PO_4)_3$ [37] and alumina sulfuric acid [38] for accomplishing this transformation. However, in spite of their potential utility, many of the existing methods involve the use of expensive reagents, strong acidic conditions, longer reaction times, tedious work-up, multi-step preparation of catalyst, environmental disposal problems, homogeneous conditions and moreover, the use of volatile and toxic organic solvents as reaction media.

In the quest for developing less toxic, potential green catalyst, we thought of using 4-nitrophthalic acid (4-npa) as a catalyst for this reaction. 4-npa is inexpensive stable solid, water soluble, easily available and it is

easier to handle compared to metal halides such as $ZrCl_4$, $BiCl_3$, $SbCl_3$ and protic acids such as TFA or TsOH. To the best of our knowledge there is no report of the use of 4-npa as a mild and inexpensive catalyst for this type of reactions. Our intension, to develop environmentally friendly reactions, herein, we report an efficient, simple, and high yielding protocol for the synthesis of DHPMs/DHPM thiones involving three component, one-pot assembly of aldehydes, β-carbonyl compounds and urea/thiourea using readily available 4-npa as a catalyst at normal ambient temperature (Scheme-1).



Scheme1: Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones using 4-nitrophthalic acid as a catalyst under solvent free conditions

II. RESULTS AND DISCUSSION

Firstly, for the optimization of the reaction, the effect of temperature and catalyst were carried using benzaldehyde, ethylacetoacetate, and urea as a model. After stirring for 2-3 hrs, reaction did not proceed as monitored by TLC at room temperature in solvent-free conditions. Subsequently, the mixture was heated to reflux at different temperatures ranging from 60 to 120 ^{o}C, with an increment of 10 ^{o}C each time. The yield of product **4a** was increased and the reaction was raised from 60 ^{o}C to 90 ^{o}C (Table 1, entries 1- 4). However, no significant increase in the yield of product **4a** was observed as the reaction temperature was raised from 100 ^{o}C to 120 ^{o}C (Table 1, entries 5-7). Therefore, 90 ^{o}C was chosen as the reaction temperature for all further reactions.

Table 1
Temperature optimization for the synthesis of 4a under solvent free condition using 4-npa as a catalyst[a]

Entry	Temperature (^{o}C)	[b]Time (mins)	[c]Yield (%)
1	60	90	82
2	70	75	86
3	80	50	86
4	90	30	95
5	100	30	88
6	110	20	84
7	120	20	84

[a] Reaction condition: Aldehyde (1mmol), 1, 3-dicarbonyl compound (1mmol) and urea (1 mmol), catalyst (2 mol %) at different temperature under solvent free conditions.
[b] Reaction time is monitored by TLC at time interval of 10 mins
[c] Isolated yields

To evaluate the effect of catalyst concentration, Biginelli condensation of benzaldehyde, urea and ethyl acetoacetate in equimolar ratio (1:1:1) was carried out in presence of different amounts of catalyst (1, 2, 5, 10 mol %) at 90 ^{o}C for 30 min under solvent free conditions and the isolated yields of the product were shown in

Table-2. From this we concluded that 2 mol % of 4-npa to be optimum amount of the catalyst for this reaction. Use of higher amount of catalysts (5 & 10 mol %) neither improves the yield nor reaction time further.

Table 2

Effect of catalyst concentration for the synthesis of 5-ethoxycarbonyl-6methyl-4-(4-chlorohenyl)-3, 4-dihydropyrimidin-2(1H)-one[a] (4a)

Entry	Catalyst concentration (mol %)	Time (mins)	Yield (%)
1	1	60	88
2	2	30	95
3	5	30	92
4	10	30	95

Using the above optimized reaction conditions, then the reaction of various aldehydes, 1,3-dicarbonyl compounds and urea or thiourea were investigated. The results are shown in the Table-3 and all the products were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS spectra and elemental analysis. In all cases studied, the three-component reaction proceeded smoothly to give the corresponding 3,4-dihydro-pyrimidin-2(1*H*)-ones in satisfactory yields. Most important, aromatic aldehydes having either electron donating or withdrawing substituents reacted efficiently and gave well to excellent yields. Even for the aliphatic aldehydes, which are known to be less reactive under conventional Biginelli reaction condition, also reacted smoothly to afford high yields with a slightly longer reaction time. In addition, thiourea also used with similar success to provide the corresponding 3, 4-dihydropyrimidin-2(1*H*)-thiones.

Table -3

Synthesis of dihydropyrimidin-2(H)-ones and thiones catalyzed by 4-nitrophthalic acid under solvent free condition at 90 ^{o}C [a]

Entry	Products[b]	R	R^1	X	Yield (%)[c]	Mp (^{o}C) [d]	
						Found	Reported
1	4a	C_6H_5	Et	O	95	205-207	208-209 [35]
2	4b	4-OH- C_6H_4	Et	O	90	228-229	230-232 [39]
3	4c	4-Cl- C_6H_4	Et	O	94	210-211	211-213 [35]
4	4d	4-OCH_3- C_6H_4	Et	O	93	200-201	202-203 [35]
5	4e	C_3H_6	Et	O	74	181-183	179-180 [40]
6	4f	$(CH_3)_2CH$	Et	O	78	193-195	195-197 [40]
7	4g	C_6H_5	Me	O	92	205-207	208-210 [35]
8	4h	4-OH- C_6H_4	Me	O	93	145-146	----
9	4i	4-Cl- C_6H_4	Me	O	90	203-204	204-206 [35]
10	4j	4-OCH_3- C_6H_4	Me	O	89	196-197	195-196 [35]
11	4k	C_3H_6	Me	O	81	189-190	----
12	4l	$(CH_3)_2CH$	Me	O	80	215-216	216-218 [40]
13	4m	C_6H_5	Et	S	92	203-204	203-205 [35]
14	4n	4-OH- C_6H_4	Et	S	94	191-193	193-194 [40]
15	4p	4-Cl- C_6H_4	Et	S	88	190-192	193-194 [35]
16	4q	4-OCH_3- C_6H_4	Et	S	87	151-152	152-153 [35]
17	4r	C_3H_6	Et	S	77	132-135	----
18	4s	$(CH_3)_2CH$	Et	S	70	178-179	----
19	4t	C_6H_5	Me	S	89	235-236	237-239 [35]
20	4u	4-OH- C_6H_4	Me	S	93	188-189	----
21	4v	4-Cl- C_6H_4	Me	S	87	190-192	189-191[35]
22	4w	4-OCH_3- C_6H_4	Me	S	90	180-181	182-183[35]
23	4x	C_3H_6	Me	S	82	201-202	----
24	4y	$(CH_3)_2CH$	Me	S	77	155-156	----

[a] Reaction condition: Aldehyde (1mmol), 1,3-dicarbonyl compound (1mmol) and urea (1 mmol), catalyst (2 mol %) at 90 ^{o}C under solvent free conditions about 30 mins.

[b] Products were characterized by IR, NMR, MS and elemental analysis.

[c] Isolated yields.

[d] Melting points are uncorrected.

Furthermore, in order to show the excellent catalytic activity of the catalyst, we carried out the synthesis 5-ethoxycarbonyl-6methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (entry **1c** in Table 3) catalyzed by other several other catalyst under the same reaction conditions (Table 4). It shows that the yield of the desired product in the presence of 4-nitrophthalic acid is higher than that in presence of other catalyst. From the results above mentioned above, 4-nitrophthalic acid is an excellent catalyst for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones and thiones through Biginelli reaction.

Table-4
Comparison of catalytic activity of 4-nitrophthalic acid with several catalyst for synthesis of 5-ethoxycarbonyl-6methyl-4-(4-chlorophenyl)-3, 4-dihydropyrimidin-2(1H) - one[a] (4c)

Entry	Catalysts (2 mol %)	Yield (%)
1	Acetic acid	78
2	Oxalic acid	72
3	*p*-Toluenesulfonic acid	85
4	4-Nitrophthalic acid	94
5	Chloroacetic acid	90
6	Phosphotungstic acid	85
7	Trichloroacetic acid	67
8	NaCl	80

[a] Reaction condition: Aldehyde (1mmol), 1, 3-dicarbonyl compound (1mmol) and urea (1 mmol), catalysts (2 mol %) at 90 ^{o}C under solvent free conditions about 30 mins.

III. EXPERIMENTAL

Reagents and analysis

The melting points of the products were determined by open capillaries on a Buchi apparatus and are uncorrected. The IR spectra were recorded on a Nicolet Impact-410 FT-IR Spectrophotometer using KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300F, 300 MHz spectrometer in $CDCl_3$ using TMSi as an internal standard with ^{1}H resonant frequency of 300 MHz and ^{13}C resonant frequency of 75 MHz. D_2O exchange was applied to confirm the assignment of the signals of NH protons. The Mass spectra were recorded on an Autospec EI-MS. The elemental analysis was carried out by using Heraus CHN rapid analyzer. All the compounds gave C, H and N analysis within ± 0.4% of the theoretical values. All Reagents were commercial purchased from Aldrich and used without further purification. Commercial reagents were used as received. Reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm precoated Merck Silica Gel 60 F_{254}(Merck), visualizing with ultraviolet light or iodine vapours.

General procedure for the synthesis of dihydropyridine-2-ones using 4-nitrophthalic acid (4-npa) catalyst.

A mixture of aldehyde (1 mmol), 1,3-dicarbonyl compounds (1 mmol), urea or thiourea (1 mmol) and 4-npa (2 mol %) under solvent-free conditions was heated to 90 ^{o}C for required time in 100ml conical flask in water bath. After cooling, the reaction mixture was poured into crushed ice and stirred for 5-10 min. The solid was filtered under suction, washed with ice-cold water and than recrystalized from ethanol to afford pure product (Scheme-1).

The spectral data for selected products

***5-Ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one* (4a)**

White crystals; mp 205-207 ^{o}C; IR (KBr): υ (cm^{-1}) 3304, 3286 (Ar-NH), 2915 (C-H), 1719 (C=O ester stretching), 1697 (C=O stretching), 1649, 1220 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^{o}C): δ ppm = 1.17 (t, *J*=6.6 Hz, 3H, OCH_2CH_3), 1.97 (s, 3H, CH_3), 4.03 (q, *J*=6.7 Hz, 2H, OCH_2CH_3), 5.35 (d, *J*=3.55 Hz, 1H, C*H*), 6.78-7.26 (m, 5H, Ar-*H*), 7.91 (br s, 1H, N*H*), 9.42 (br s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ

ppm):165.6, 155.0, 142.1, 128.8, 127.1, 126.0, 105.4, 60.0, 48.3, 17.6, 12.4; EIMS: 260 (M^+); Anal. Calcd. For $C_{14}H_{16}N_2O_3$: C 64.60, H 6.20, N 10.76. Found: C 64.57, H 6.22, N 10.72 %.

***5-Ethoxycarbonyl-4-(4-chlorophenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one* (4c)**

White crystals; mp 210-211 ^oC; IR (KBr): υ (cm^{-1}) 3288, 3232 (Ar-NH), 2956 (C-H), 1715 (C=O ester stretching), 1682 (C=O stretching), 1638, 1200 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 1.18 (t, *J*=7.09 Hz, 3H, OCH_2CH_3), 2.07 (s, 3H, CH_3), 4.12 (q, *J*=8.50 Hz, 2H, OCH_2CH_3), 5.17 (d, *J*=3.07 Hz, 1H, C*H*), 6.88-7.08 (m, 4H, Ar-*H*), 8.01 (br, s, 1H, N*H*), 9.31 (s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):167.0, 156.6, 144.3, 130.0, 126.3, 1236.7, 103.0, 58.6, 46.5, 19.7, 13.5; EIMS: 294 (M^+); Anal. Calcd. For $C_{14}H_{15}ClN_2O_3$: C 57.05, H 5.13, N 9.50. Found: C 57.09, H 5.09, N 9.53 %.

***5-Ethoxycarbonyl-4-(4-methoxyphenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one* (4d)**

White crystals; mp 200-201 ^oC; IR (KBr): υ (cm^{-1}) 3303, 3269 (Ar-NH), 2974 (C-H), 1722 (C=O ester stretching), 1687 (C=O stretching), 1624, 1176 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 1.13 (t, *J*=7.03 Hz, 3H, OCH_2CH_3), 2.14 (s, 3H, CH_3), 3.43 (s, 3H, OCH_3), 3.99 (q, *J*=7.05 Hz, 2H, OCH_2CH_3), 5.37 (d, *J*=3.03 Hz, 1H, C*H*), 7.08-7.26 (s, 4H, Ar-*H*), 8.23 (br, s, 1H, N*H*), 9.54 (br s, 1H, N*H*); ^{13}C NMR (75 MHz DMSO-d_6, δ ppm):164.3, 153.3, 143.0, 131.0, 125.2, 122.0, 103.3, 59.9, 55.8, 47.3, 19.2, 11.0; EIMS: 294 (M^+); Anal. Calcd. For $C_{15}H_{18}N_2O_4$: C 62.06, H 6.25, N 9.65. Found: C 62.10, H 6.21, N 9.68 %.

***5-Methoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one* (4g)**

White crystals; mp 205-207 ^oC; IR (KBr): υ (cm^{-1}) 3323, 3280 (Ar-NH), 2966 (C-H), 1726 (C=O ester stretching), 1682 (C=O stretching), 1624, 1176 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 2.19 (s, 3H, CH_3), 3.45 (s, 3H, OCH_3), 5.23 (d, *J*=3.47 Hz,1H, C*H*), 7.03-7.46 (s, 5H, Ar-*H*), 8.02 (br, s, 1H, N*H*), 9.32 (br s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):164.3, 153.3, 143.0, 131.0, 125.2, 122.0, 103.3, 59.9, 55.8, 47.3, 19.2, 11.0; EIMS: 246 (M^+); Anal. Calcd. For $C_{13}H_{14}N_2O_3$: C 63.40, H 5.73, N 11.38. Found: C 63.44, H 5.70, N 11.38 %.

***5-Methoxycarbonyl-4-(4-methoxyphenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one* (4j)**

White crystals; mp 196-197 ^oC; IR (KBr): υ (cm^{-1}) 3319, 3301 (Ar-NH), 2986 (C-H), 1719 (C=O ester stretching), 1688 (C=O stretching), 1617, 1200 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 2.23 (s, 3H, CH_3), 3.23 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3) 5.22 (d, *J*=3.07 Hz, 1H, C*H*), 6.69-7.23 (s, 4H, Ar-*H*), 7.78 (br, s, 1H, N*H*), 8.97 (br s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):166.0, 159.2, 155.5, 136.1, 133.2, 126.0, 111.0, 107.7, 56.4, 50.0, 48.4, 16.6; EIMS: 276 (M^+); Anal. Calcd. For $C_{14}H_{16}N_2O_4$: C 60.86, H 5.84, N 10.14. Found: C 60.82, H 5.87, N 10.10 %.

***5-Ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-thione* (4m)**

White crystals; mp 203-204 ^oC; IR (KBr): υ (cm^{-1}) 3287, 3255 (Ar-NH), 2973 (C-H), 1726 (C=O ester stretching), 1617, 1232 (S=O stretching), 1179 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 1.07 (t, J=7.05 Hz, 3H, OCH_2CH_3), 2.27 (s, 3H, CH_3), 3.88 (q, J=7.07, 2H, OCH_2CH_3), 5.22 (d, J=3.55 Hz, 1H, C*H*), 6.87-7.46 (m, 5H, Ar-*H*), 7.92 (br, s, 1H, N*H*), 9.01 (br, s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):178.7, 159.4, 148.3, 138.0, 130.6, 126.8, 107.0, 45.6, 17.5; EIMS: 276 (M^+); Anal. Calcd. For $C_{14}H_{16}N_2O_2S$: C 60.84, H 5.84, N 10.14 Found: C 60.87, H 5.86, N 10.11 %.

***5-Ethoxycarbonyl-4-(4-methoxyphenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-thione* (4q)**

White crystals; mp 155-157 ^oC; IR (KBr): υ (cm^{-1}) 3303, 3287 (Ar-NH), 2986 (C-H), 1719 (C=O ester stretching), 1617, 1208 (S=O stretching), 1179 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 1.16 (t, J=7.0 Hz, 3H, OCH_2CH_3), 2.32 (s, 3H, CH_3), 3.16 (q, J=7.0 2H, OCH_2CH_3), 4.03 (s, 3H, OCH_3), 5.03 (d, J=7.0 Hz, 1H, C*H*), 7.01-7.53 (m, 4H, Ar-*H*), 7.92 (br, s, 1H, N*H*), 9.01 (br, s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):180.0, 162.0, 149.0, 139.5, 129.4, 127.7, 105.7, 55.4, 49. 19.0; EIMS: 306 (M^+); Anal. Calcd. For $C_{15}H_{18}N_2O_3S$: C 58.80, H 5.92, N 9.14 Found: C 58.84, H 5.95, N 9.10 %.

5-*Methoxycarbonyl-4-phenyl- 6-methyl-3,4-dihydropyrimidin-2(1H)-thione* (4t)

White crystals; mp 233-236 ^oC; IR (KBr): υ (cm^{-1}) 3307, 3289 (Ar-NH), 2987 (C-H), 1717 (C=O ester stretching), 1605, 1199 (S=O stretching), 1154 cm^{-1}; ^1H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^oC): δ ppm = 2.09 (s, 3H, CH_3), 3.62 (s, 3H, OCH_3), 5.15 (d, J=3.50 Hz, 1H, C*H*), 6.94-7.31 (m, 5H, Ar-*H*), 8.05 (br, s, 1H, N*H*), 9.35 (br, s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):180.0, 161.0, 150.0, 140.1, 128.0, 126.2, 106.0, 54.1, 48.5, 45.6, 19.0; EIMS: 262 (M^+); Anal. Calcd. For $C_{13}H_{14}N_2O_2S$: C 59.52, H 5.38, N 10.68 Found: C 59.55, H 5.35, N 10.67 %.

5-Methoxycarbonyl-4-(4-hydroxy-6-methyl-3,4-dihydropyrimidin-2(1H)-thione **(4u)**

White crystals; mp 188-189 ^{o}C; IR (KBr): υ (cm^{-1}) 3568, 3287, 3205 (Ar-NH), 2944 (C-H), 1723 (C=O ester stretching), 1605, 1204 (S=O stretching), 1132 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300MHz, Me_4Si, 25^{o}C): δ ppm = 1.67 (s, 3H, CH_3), 3.45 (s, 3H, OCH_3), 4.74 (d, J=3.4 Hz, 1H, C*H*), 5.32 (s, 1H, O*H*), 6.67-7.01 (m, 4H, Ar-*H*), 8.34 (br, s, 1H, N*H*), 9.09 (br, s, 1H, N*H*); ^{13}C NMR (75 MHz, DMSO-d_6, δ ppm):177.7, 163.5, 152.1, 134.5, 129.1, 114.3, 103.6, 54.6, 47.3, 16.3; EIMS: 278 (M^{+}); Anal. Calcd. For $C_{13}H_{14}N_2O_3S$: C 56.11, H 5.07, N 10.05 Found: C 56.14, H 5.11, N 10.01%.

IV. CONCLUSIONS

In summary, we have developed an efficient, facile and environmental acceptable synthetic methodology for the preparation of 3, 4-dihydropyrimidin-2(1*H*)- ones and thiones using cheaper, water stable, and water soluble 4-nitrophthalic acid as a catalyst under solvent free condition. The attractive features of this procedure are the mild reaction conditions, high conversions, cleaner reaction profiles, inexpensive and environmentally friendly catalyst, all of which make it a useful and attractive strategy for the preparation of various dihydropyrimidinone derivatives simply by changing different substrates. This procedure is much simpler and faster than the protocols published to date.

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