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Research Article

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Copper(II) acetate promoted facile synthesis of dihydropyrimidinone derivatives via a solvent free Biginelli multicomponent reaction

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ABSTRACT

A simple and efficient method of the 3,4-dihydropyrimidin-2(1H)-ones/thiones synthesis in good to high yields is described. It consists in a one-pot three-component Biginelli condensation using copper acetate as catalyst under solvent-free conditions.

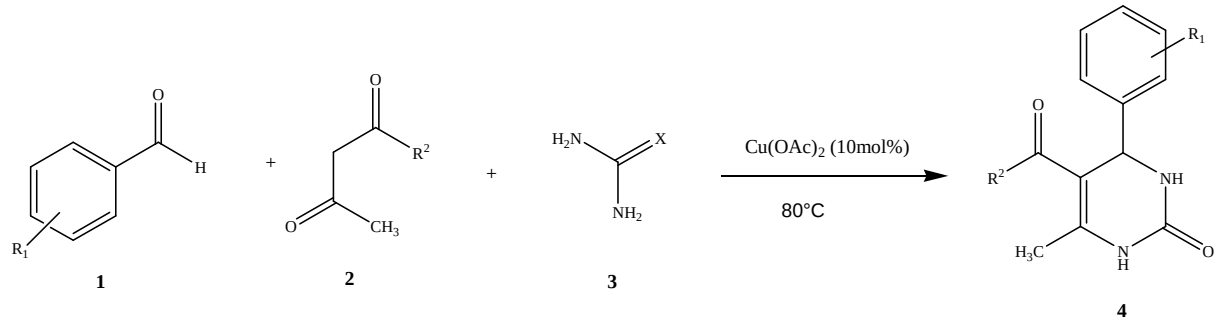
Keywords: Biginelli reaction, one-pot procedure, 3,4-dihydropyrimidin-2(1H)-ones, Copper acetate.

INTRODUCTION

Multicomponent reactions in which three or more reactants are combined in a single vessel to generate new molecules that contain portions of each reactant undoubtedly maintain great importance in organic and medicinal chemistry due to the synthetic efficiency and molecular diversity required in the discovery of new lead compounds [1]. The Biginelli reaction [2], one of the most useful multicomponent reactions, is particularly attractive because the resulting dihydropyrimidinones (DHPMs) display a wide range of biological activities, which has led to the development of a number of lead compounds based on that structural core [3]. Indeed, DHPMs are of increasing importance because of their promising activities as calcium channel blockers, antihypertensive agents and α-1a-antagonists [4]. Moreover, several alkaloids containing the DHPM unit have been isolated from marine sources, which also exhibit interesting biological properties [5]. Thus, synthesis of this heterocyclic nucleus is of much current importance. The most simple and straightforward procedure, involves one-pot condensation of ethyl acetoacetate, benzaldehyde and urea under strongly acidic conditions at elevated temperature [6]. However, one serious drawback of Biginelli's reaction is low yields in the case of substituted aromatic and aliphatic aldehydes. This has led to the development of multistep strategies that produce somewhat higher overall yields but lack the simplicity of the multicomponent synthesis [7]. Thus, during the two last decades Biginelli's reaction for the synthesis of DHPMs has received renewed interest and several improved procedures have been reported [8] including, in particular, the use, as catalysts, of Lewis acids such as Indium(III) chloride [9], Indium(III) bromide [10], $CuCl_2/CuSO_4$ or $CuCl_2$/HCl [11], Strontium(II) triflate [12], bismuth(III) nitrate [13], Calcium chloride [14], Cupric(II) triflate [15], Sulfate Zirconia [16], $Co(HSO_4)_2$ [17], Chlorotrimethylsilane [18], Copper(II) acetate/Sodium ascorbate/AcOH [19], Iron(III) tosylate [20]. Biginelli reaction was also catalyzed by bases such as $(NH_4)_2CO_3$ [21], t-BuOK [22] and by organocatalysts as for examples L-proline [23], phenyl phosphonic acid [24] and primary amines [25]. Nanoparticules [26], heteropoly acids [27], and ionic liquids [28] have been successfully applied to the Biginelli products synthesis. In addition, a significant improvement was observed in the DHPMs synthesis under ultrasonic [29] and microwave irradiations [30]. Furthermore, there are only a few enantioselective methods synthesis [31] of 3,4-dihydropyrimidin-2(1H)-ones. Yet many methods require harsh conditions, expensive or dangerous catalysts, long reaction times and the use of solvents. Consequently, the search of simple, efficient, environmentally benign, inexpensive with better yields procedures remains valid.

The use of Copper(II) acetate in Biginelli reaction is reported [19] but in co-catalyst with sodium ascorbate and acetic acid, then it is so difficult to determinate its role in this catalysis. Therefore, as a part of our continued interest in developing efficient and new catalysts for the multicomponent reactions [32], we report here our preliminary investigation dealing with the use of copper acetate alone in solvent-free conditions as catalyst in the Biginelli reaction, as outlined in Scheme 1.

Scheme 1



1 **2** **3** **4**

EXPERIMENTAL SECTION

Melting points were measured using a fine control Electro thermal capillary apparatus and are uncorrected. IR spectra were recorded from KBr disk on a Shimadzu FT-IR-8201 PC spectrometer. The ^{1}H and ^{13}C NMR spectra were obtained with a Bruker 250 MHz spectrometer in DMSO.

General Procedure for the synthesis of DHPMs 4:
A mixture of aldehyde **1** (1.0 mmol), the appropriate β-ketoester or 1,3-diketone **2** (1.0 mmol), urea or thiourea **3** (1.5 mmol), and $Cu(OAc)_2$ (10 mol %) was heated under solvent free conditions at 80°C for the appropriate time indicated in table 3. After being cooled, the reaction mixture was then poured onto crushed ice, and stirred for 5-10 minutes. The precipitate was filtered under suction, washed with cold water. DHPMs **4** were obtained in isolated yields of 64-96%. Analytically pure samples were prepared by recrystallization from ethanol.

RESULTS AND DISCUSSION

The optimal reaction conditions for the multicomponent Biginelli reaction were established after several attempts to obtain the products using different solvents, catalyst's amounts, and temperatures. Initially, we investigated the Biginelli condensation of benzaldehyde (1 equiv.), ethyl acetoacetate (1 equiv.), and urea (1.5 equiv.) catalyzed by 10 mol % of copper acetate. We were pleased to find that the catalyst provided good yield of the corresponding DHPM.

A further survey of solvents using 10 mol % of $Cu(OAc)_2$ revealed that solvent free reaction was the most favorable condition. As showed in Table 1, common solvents, such as water (Entry 1), and THF (Entry 2), led to poorer yields, and only traces of the product were observed. Also, lower yields were obtained with toluene (Entry 3) and aqueous ethanol (Entry 4). When ethanol and CH_3CN were used as solvents, the obtained yields were slightly elevated to 66% and 49% respectively (Entries 5 and 6). The reaction is also slower in all these solvents (Entries1-6).

Table 1. $Cu(OAc)_2$-Mediated Synthesis of DHPM 4a: Effect of solvent

Entry	Solvent	Catalyst (mol %)	Temperature	Time (h)	Yield[a] (%)
1	H_2O	10	Reflux	18	Trace
2	THF	10	Reflux	18	Trace
3	toluene	10	Reflux	18	28
4	$EtOH/H_2O$	10	Reflux	18	32
5	EtOH	10	Reflux	18	66
6	CH_3CN	10	Reflux	18	49
7	-	10	80°C	8	75

[a] *Isolated yields based on aldehyde.*

Next, the amounts of the catalyst were evaluated and the results are shown in Table 2. In terms of yield, 10mol % of $Cu(OAc)_2$ gave the best results (Entry 2). The use of 5mol % of the catalyst caused a slight decrease in the yield (entry 1). In addition, raising the catalyst loading to 20 or 50 mol % led to lower reaction yields (Entries 3 and 4)

Table 2. $Cu(OAc)_2$-Mediated Synthesis of DHPM 4a: amount of catalyst effect

Entry	Catalyst (mol %)	Temperature (°C)	Time (h)	Yield[a] (%)
1	5	80	8	62
2	10	80	8	75
3	20	80	8	60
4	50	80	8	45

[a] *Isolated yields based on aldehyde.*

After establishing the optimal conditions, we examined the scope of the aldehyde component by reactions with ethyl acetoacetate (Table 3). A wide spectrum of aromatic aldehydes could be tolerated and underwent smooth Biginelli condensations. Significantly, the Biginelli reaction afforded good to excellent yields for electronically poor, neutral, and rich benzaldehydes (66-96%). The presence of electron-donating groups on the benzaldehydes gave very good results by means of the reaction yields (Entries 1-6), with the exception of 4-N,N-dimethylaminobenzaldehyde or 4-hydroxybenzaldehyde, which delivered higher yields. Similarly, electron-withdrawing substituents furnished the Biginelli products with good yields (Entries 7-11). Moreover, the position of the substituent on the aromatic ring had little effect on the yields as demonstrated by reactions involving methylbenzaldehydes (Entries 5 and 6), chlorobenzaldehydes (Entries 7 and 8), and nitrobenzaldehydes (Entries 10 and 11).

In contrast, aliphatic aldehydes showed low reactivity under the same conditions. The use of isobutyraldehyde had no impact on the reaction, affording the corresponding product in 28 % yield (Entry 12).

We next studied the generality of β-ketoester in the Biginelli reaction (Entries 13 and 14). 1,4-pentanedione was also good reaction partner, undergoing clean reactions with 4-methylbenzaldehyde and benzaldehyde with very good yields 64-96%).

Table 3. $Cu(OAc)_2$-Mediated Synthesis of DHPMs 4 under solvent-free conditions[a]

Entry	Product	R_1	X/R_2	Time (h)	Yield (%)	T.fus (°C) Measured	T.fus. (°C) Reported
1	**4a**	C_6H_5	O/OEt	8	75	204-206	206-208[12]
2	**4b**	4-$N(CH_3)_2$-C_6H_4	O/OEt	6	96	254-256	256-258[12]
3	**4c**	4-(OH)-C_6H_4	O/OEt	6	96	234-236	237-238[12]
4	**4d**	4-(CH_3O)-C_6H_4	O/OEt	10	77	204-205	200-202[26a]
5	**4e**	4-(CH_3)- C_6H_4	O/OEt	6	78	215-217	214-215[11]
6	**4f**	2-(CH_3)- C_6H_4	O/OEt	6	67	202-204	208-210[10]
7	**4g**	4-(Cl)- C_6H_4	O/OEt	7	74	214-216	215-216[11]
8	**4h**	3-(Cl)- C_6H_4	O/OEt	7	66	194-196	190-193[15]
9	**4i**	4-(Br)- C_6H_4	O/OEt	10	94	210-212	215[27b]
10	**4j**	4-(NO_2)-C_6H_4	O/OEt	7	83	211-213	211-213[12]
11	**4k**	3-(NO_2)-C_6H_4	O/OEt	12	81	229-231	226-227[15]
12	**4l**	$(CH_3)_2CH$	O/OEt	12	28	192-194	190-192[11]
13	**4m**	4-(CH_3)- C_6H_4	O/Me	4	71	188-190	192-193[11]
14	**4n**	C_6H_4	O/Me	3	83	236-238	232-235[33]
15	**4o**	C_6H_4	S/OEt	2	73	204-206	206-207[26c]
16	**4p**	4-(CH_3O)-C_6H_4	S/OEt	2	64	154-156	152-154[14]

[a]*The reaction was carried out on a 1 mmol scale, and the ratio of **1**/**2**/**3** is 1/1/1.5.* [b]*Isolated yields based on aldehyde.*

Spectroscopic data for all synthesized compounds:

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

Tfus.: 204-206°C; IR (KBr): ν (cm-1) 3244, 3117, 1720, 1647, 1462, 1423, 1381, 1299, 1223,1092, 783. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.10 (s, 1H, NH); 7.61 (s, 1H, NH); 7.36-7.26 (m, 5H); 5.18 (s, 1H); 3.99 (q, *J*= 7.1 Hz, 2H); 2.26 (s, 3H); 1.10 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 165.8, 152.8, 148.4, 145.3, 128.5, 127.5, 126.7, 99.8, 59.5, 54.6, 18.3, 14.4.

(4b) 5-(Ethoxycarbonyl)-4-(4-(dimethylamino)phényl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one:

Tfus.: 254-256 °C; IR (KBr): ν (cm-1) 3240, 3113, 2935, 1705, 1647, 1527, 1462, 1227, 1092, 787. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.14 (s, 1H, N1-*H*), 7.64 (s, 1H, N3-*H*); 7.14 (d, *J*= 8.6 Hz, 2H); 6.86 (d, *J*= 8.6 Hz, 2H); 5.05 (s, 1H,), 3.98 (q, *J*=7.1 Hz, 2H,), 2.52 (s, 3H,), 2.23 (s, 3H,), 1.08 (t, *J*=7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm):165.5, 152.4, 149.9, 147.6, 132.7, 126.9, 112.3, 99.9, 59.2, 53.3, 17.8, 14.2.

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

Tfus.: 234-236°C; IR (KBr): ν (cm-1) 3240, 3120, 1685, 1643, 1465, 1377, 1290, 1234, 1091, 759. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.21 (s, 1H, OH); 9.08 (s, 1H, NH); 7.56 (s, 1H, NH); 7.05 (d, *J*= 8.1 Hz, 2H); 6.70 (d, *J*=

8.1 Hz, 2H); 5.04 (s, 1H); 3.96 (q, *J*= 7.1 Hz, 2H); 2.24 (s,3H);1.02 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 165.7, 156.8, 152.7, 147.8, 135.8 , 127.7, 115.2, 115.2, 100.2, 59.3, 53.9, 18.1, 14.4.

(4d) 5-(Ethoxycarbonyl)-6-méthyl-4-(4-methoxylphenyl)-3,4-dihydropyrimidin-2(1H)-one
Tfus: 204-205 °C; IR (KBr): ν (cm-1) 3232, 3163, 2920, 2868, 1739, 1651, 1501, 1257, 1022, 748. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.15 (s, 1H, NH); 7.72 (s, 1H, NH); 7.18 (d, *J*= 8.1 Hz, 2H); 6.86 (d, *J*=8.1 Hz, 2H); 5.10 (s, 1H); 3.97 (q, *J*= 7.1 Hz, 2H); 3.74 (s, 3H); 2.25 (s, 3H); 1.12 (t, *J*= 7.1 Hz,3H). NMR ^{13}C (DMSO-d_6, δppm): 166.2, 159.2, 152.9, 148.8, 137.8, 128.1, 114.5, 100.3, 59.9, 55.8, 54.1, 18.5, 14.9.

(4e) 5-(Ethoxycarbonyl -4-(4-methylphenyl)-6-méthyl 3,4-dihydropyrimidin-2(1H)-one
Tfus.: 215-217 °C; IR (KBr): ν (cm-1) 3244, 3116, 2950, 1708, 1647, 1462, 1288, 1223, 1092, 783. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ 9.21 (s, 1H, NH); 7.74 (s, 1H, NH); 7.11-7.15 (m, 4H); 5.11 (s, 1H); 3.99 (q, *J*= 7.1 Hz, 2H); 2.26 (s, 3H C_6H_5- CH_3); 2.24 (s, 3H); 1.10 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 165.8, 152.6, 148.6, 142.4, 136.8, 129.4, 126.6, 99.8, 59.6, 54.1, 21.1,18.2, 14.5

(4f) 5-(Ethoxycarbonyl)-6-methyl-4-(2-méthylphenyl)-3,4-dihydropyrimidin-2(1H)-one
Tfus: 202-204 °C; IR (KBr): ν (cm-1) 3236, 3105, 2931, 1705, 1643,1532, 1461, 1022, 756. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.20 (s, 1H, NH); 7.68 (s, 1H, NH); 7.18-7.13(m,4H); 5.41 (s, 1H); 3.91 (q, *J*= 7.1 Hz, 2H); 2.43 (s, 3H.C_6H_5- CH_3); 2.34 (s, 3H); 0.99 (t, *J*= 7.1 Hz,3H). NMR ^{13}C (DMSO-d_6, δppm, *J*HZ): 165.4, 151.8, 148.6, 143.4, 134.8, 130.3,127.7, 99.4, 59.3, 50.5, 17.8, 14.1.

(4g): 5-(Ethoxycarbonyl-4-(4-Chlorophényl)--6-méthyl-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 214-216 °C; IR (KBr): ν (cm-1) 3244, 3117, 2978, 1712, 1647, 1462, 1423, 1319, 1292, 1223, 1092,783. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.28 (s, 1H, NH); 7.79 (s, 1H, NH); 7.24-7.41(m, 4H); 5.16 (s, 1H); 3.99 (q, *J*= 7.1 Hz, 2H); 2.26 (s, 3H); 1.08 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 166.4, 153.1, 149.9, 144.9, 132.9, 129.6, 129.4, 99.9, 60.5, 54.86, 18.9, 15.2.

(4h): 5-(Ethoxycarbonyl-4-(3-Chlorophenyl)--6-methyl-3,4-dihydropyrimidin-2(1H)-one
Tfus.: 194-196 °C; IR (KBr): ν (cm-1):) 33741, 3224, 3109, 2931, 1705, 1651, 1477, 1226, 1080, 871. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.29 (s, 1H, NH); 7.82 (s, 1H, NH); 7.19-7.41 (m, 4H); 5.16 (s,1H); 3.99 (q, *J*= 7.1 Hz, 2H); 2.26 (s, 3H); 1.10 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 165.4, 152.1, 149.1, 147.4, 133.1, 130.7, 127.5, 126.4, 125.1, 98.8, 59.5, 53.7, 17.9 ,14.2.

(4i) 5-(Ethoxycarbonyl)-4-(4-Bromophenyl)-6-méthyl-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 210-212 °C; IR (KBr): ν (cm-1) 3241, 3117, 1708, 1647, 1481, 1462, 1427, 1292, 1223, 1092, 783. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.28 (s, 1H, NH); 7.82 (s, 1H, NH); 7.56 (d, *J*= 8.2 Hz, 2H); 7.21 (d, *J*= 8.2 Hz, 2H); 5.15 (s, 1H); 3.98 (q, *J*= 7.0 Hz, 2H); 2.26 (s, 3H); 1.09 (t, *J*= 7.0,3H). NMR ^{13}C (DMSO-d_6, δppm): 166.6, 153.1, 149.9, 145.3, 132.7, 129.7, 121.5, 99.9 , 60.5, 54.6, 18.9, 15.2.

(4j) 5-(Ethoxycarbonyl)-4-(4-nitrophenyl)-6-méthyl-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 211-213°C; IR (KBr): ν (cm-1): 3236, 3117, 1705, 1643, 1461, 1429, 1218, 1091, 783. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.33 (s, 1H, NH); 7.92 (s, 1H, NH) 7.24 (d, *J*= 8.2 Hz, 2H); 7.21 (d, *J*= 8.2 Hz, 2H); 5.17 (s,1H); 3.96 (q, *J*= 7.1 Hz, 2H); 2.25 (s, 3H); 0.9 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 166.6, 153.3, 153.1, 150.6, 148.0, 129.0, 125.1, 99.7, 61.0, 54.9, 19.1,15.2.

(4k) 5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 229-231 C; IR (KBr): ν (cm-1) 3328, 3101, 2966, 1708, 1628, 1527, 1458, , 1223, 1087, 810. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 9.41 (s, 1H, NH); 7.94 (s, 1H, NH); 7.73-8.15 (m, 4H); 5.31 (s, 1H); 3.98(q, *J*= 7.0 Hz, 2H); 2.26 (s, 3H); 1.12 (t, *J*= 7.0,3H). NMR 13C（DMSO-d_6, δ ppm,）：165.6 ; 152.3 ; 149.9; 147.4 ; 133.5; 130.7 ;122.9, 121.5, 98.8 ; 59.9; 54.0, 19.0, 18.4, 14.5.

（41）5-(Ethoxycarbonyl)-ethyl-4-isopropyl--6-methyl-3,4-dihydropyrimidin-2(1H)-one
Tfus.: 192-194°C; IR (KBr): ν (cm-1): 3232, 3105, 1701, 1647, 1465, 1230,1083, 817. NMR ¹H (DMSO-d_6, δ ppm, *J*HZ): 8.87(s, 1H, NH); 7.29 (s, 1H, NH); 4.2 (s,1H); 3.99 (q, *J*= 7.1 Hz, 2H), 2.16 (1.68 (s, 3H); 1.14 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 165.4, 152.1, 149.1, 147.4, 133.1, 130.7, 127.5, 126.4, 125.1, 98.8, 59.5, 53.7, 17.9 ,14.2.

(4m): 5-Acetyl-6-méthyl-4-(4-methylphenyl)-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 188-190 °C; IR (KBr): ν (cm-1); 3872, 3290, 2923, 1701, 1423, 1326, 999, 794, 563. NMR ^{1}H (DMSO-d_6, δ ppm, *J*HZ): 9.19 (s, 1H, NH); 9.15 (s, 1H, NH); 7.13-7.22 (m, 4H); 5.24 (s, 1H); 2.29 (s, 3H); 2.26 (s, 3H); 2.09 (s, 3H). NMR ^{13}C (DMSO-d_6, δppm): 195.3, 152.9, 148.8, 142.0, 137.4, 129.9, 127.2, 110.4, 54.3, 31.0, 21.4, 19.7.

(4n): 5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one.
Tfus.: 236-238 °C; IR (KBr): ν (cm-1) 3255, 3124, 2927, 1705, 1678, 1423,1377, 767. NMR ^{1}H (DMSO-d_6, δ ppm, *J*HZ): 9.15 (s, 1H, 7.75 (s, 1H , NH); 7.34-7.23 (m,5H); 5.27 (s, 1H) ; 2.28 (s, 3H); 1.98 (s, 3H). NMR ^{13}C (DMSO-d_6, δppm): 194.3, 152.2, 147.9, 143.9, 128.3, 127.2, 126.4, 109.4, 54.2, 30.1, 18.9.

(4o) 5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(*1H*)-thione
Tfus.: 202-204°C; IR (KBr): ν (cm-1) 3325, 3105, 1670, 1465, 1377, 1280, 1223, 1026, 759. NMR ^{1}H (DMSO-d_6, δ ppm, *J*HZ):): 9.80 (s, 1H, NH); 9.20 (s, 1H, NH); 7.31-7.22 (m, 5H); 5.24 (s, 1H); 3.97 (q, *J*= 7.1 Hz, 2H); 2.24 (s, 3H); 1.12 (t, *J*= 7.1 Hz, 3H). NMR ^{13}C (DMSO-d_6, δppm): 174.2, 165.3, 144.4, 143.3, 128.2, 127.3, 126.5, 101.3, 59.5, 54.6, 17.4, 13.8.

(4p) 5-(Ethoxycarbonyl)-6-méthyl-4-(4-méthoxylphenyl)-3,4-dihydropyrimidin-2(1H)-thione
Tfus.: 154-156;°C;IR (KBr): ν (cm-1) 3197, 2927, 2868, 1701, 1508, 1249, 1029, 756. NMR ^{1}H (DMSO-d_6, δ ppm, *J*HZ):): 9.79 (s, 1H, NH); 9.26 (s, 1H, NH); 7.16 (d, *J*= 8.5 Hz, 2H); 6.77 (d, *J*=8.5 Hz, 2H); 5.21 (s, 1H); 3.98 (q, *J*= 7.1 Hz, 2H); 3.70 (s, 3H); 2.25 (s, 3H); 1.13 (t, *J*= 7.1 Hz,3H). NMR ^{13}C (DMSO-d_6, δppm): 164.7, 158.3, 134.8, 131.1, 127.2, 113.6, 112.9, 101.3, 59.9, 54.4, 54.1,16.9, 13.3.

CONCLUSION

In conclusion, we have developed an environmentally friendly method for the synthesis of 3,4-dihydropyrimidinones by using copper acetate as an inexpensive and easily available catalyst under solvent-free conditions. In addition to its simplicity and mild reaction conditions, it tolerates a wide variety of substitutions in all three components. The adopted procedure is convenient, involves simple experimental procedure and product isolation, therefore, it is a useful addition to the existing methods.

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