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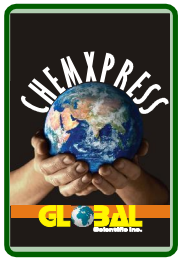

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Europium triflate: An efficient catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones

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Abstract : Biginelli reaction was carried out using europium triflate as a catalyst to obtain the corresponding products of 3,4-dihydropyrimidones in excellent yields. The conden-sation was applicable to a variety of aldehydes with ethylacetoacetate and urea at acetonitrile reflux.

Keywords : Aldehydes; Ethyl acetoacetate; Urea; Dihydropyrimidones; Europium triflate.

INTRODUCTION

The reaction in which three or more reactants come together in a single reaction vessel to form a new product that contain portions of all the reactants is called a multi-component condensation reaction. Biginelli condensation[1] is very good example for multi-component reaction, which contain the combination of ethyl acetoacetate, aldehyde and urea. The Biginelli product, 3, 4-dihydropyrimidin-2(1*H*)-ones (DHPMs) are pharma cologically important as calcium channel blockers, antihypertensive agents, α-adrenergic antagonists neuropeptide antagonists, mitotic kinesin inhibitors and melanin concentrating hormone receptor antagonists[2]. In addition, these compounds are known to exhibit a wide range of biological activities such as antiviral, antitumor, antibacterial, anti-inflammatory and antifilarial activity[3]. Therefore, the synthesis of this heterocyclic nucleus has gained importance in organic synthesis. Hence, several attempts have been made to prepare DHPMs under mild reaction conditions and improved yields, such as metal halides[4], metal triflates[5], Ionic liquids[6], acidic montmorillonite-KSF[7], microwave irradiation[8], CAN[9], Copper (II) acetyl acetonate[10], Baker's yeast[11], polyphosphates[12] L-Proline[13] and $Al(H_2O)_6](BF_4)_3$. Some of them are really very fascinating from synthetic point of view, but many of the methods have some drawbacks, which involve the use of strong Lewis acids, protic acids, additives, prolonged reaction times, vigorous reaction conditions, unsatisfactory yields and incompatibility with other functional groups. As part of our research program in developing various synthetic methodologies[14], herein we re-

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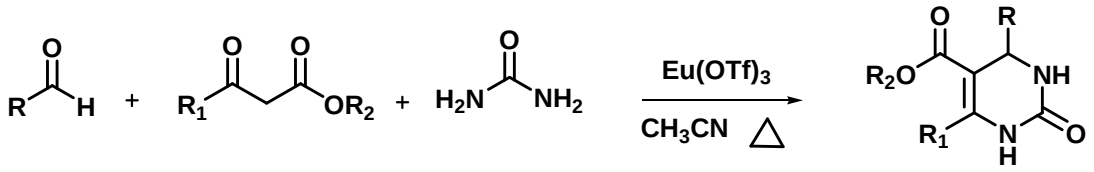
port, the Biginelli condensation using europium triflate [$Eu(OTf)_3$] as an efficient catalyst. The catalyst $Eu(OTf)_3$ is known as an efficient catalyst in the literature for various organic transformations[15].

RESULTS AND DISCUSIONS

In a typical experiment, the reactants ethyl acetoacetate, benzaldehyde and urea were reacted in presence of the catalyst $Eu(OTf)_3$ in acetonitrile at reflux to afford the corresponding product, 5-ethoxycarbonyl-4-(4-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4a) in very good yields. The reaction was completed within 1 hours.

To confirm the catalyst role, a blank experiment was carried out with ethyl acetoacetate, benzaldehyde and urea in acetonitrile at reflux, without using the catalyst. There was no product formation even after 10 hours. In another experiment, the catalyst was used in equivalent and stirred at room temperature, but product formation was not found and the same reaction was carried out at 80-85^{0}C, the reaction was completed within 2.0 hour. In another set of experiments, the catalyst was used in 50% mmol and 10% mmol ratio. Both the experiments were completed with 1.0 hours. So the catalyst ratio was finalized with 10% mmol. In all the cases, the catalyst was used with respect to aldehyde. Encouraged by the result obtained with the above experiments, we have applied this procedure to various aldehydes such as substituted aromatic, aliphatic, alicyclic and heterocyclic aldehydes have been subjected to this condensation successfully. In all the cases the catalyst europium triflate was used in catalytic amount (10% mmol) only. All the reactions were completed within 1.0-3.0 hours of time at 75-80°C of reaction temperature. The acid sensitive aldehyde, such as furfural (entry f) reacted very smoothly to obtain the corresponding dihydropyrimidone in excellent yield. In a similar mannerα,β-unsaturated aldehyde (entry g) also reacted very well to give the desired product in very good yield. The reaction of aliphatic, alicyclic aldehydes (entry i, l) needs little longer reaction time for complete conversion but the yields were very good. Furthermore, the aromatic aldehydes carrying either electron donating or electron withdrawing substituents afforded high yields of corresponding dihydropyrimidone derivatives in high yields. The products thus obtained were characterized by ^{1}H NMR, IR and Mass spectra.



(1) (2) (3) (4)

R=Aromati, heteroaromatic, aliphatic, alicyclic R_1=CH_3 R_2=C_2H_5

Scheme 1

EXPERIMENTAL SECTION

General methods

All commercial reagents were used without purification and all solvents were reagent grade. All the reaction mixtures were stirred magnetically and were monitored by TLC using 0.25 mm E-Merck silica gel $60F_{254}$ precoated glass plates, which were visualized with UV light. Melting points were recorded on Buchi R-535 apparatus. IR spectra were recorded on a Perkin-Elmer FT/IR-240 C spectrophotometer with KBr optics. ^{1}H NMR spectra were recorded on Varian Gemini 200 MHz spectrometer recorded in DMSO-d6 using TMS as an internal standard. Mass spectra were recorded on finnigan-MAT 1020 Mass spectrum operating at 70 eV.

General procedure for the preparation of 3,4-dihydropyridine-2 (*1H*)-ones (4a-4o)

To a stirred mixture of aldehyde (2 mmol) and ethyl acetoacetate (2.2 mmol) in acetonitrile (5 ml) was added urea (3 mmol) and europium triflate (0.2 mmol). The resulting reaction mixture was refluxed for a specified time as mentioned in the TABLE 1. After complete con-

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version of the starting material (aldehyde) as indicated by thin layer chromatography (TLC), the reaction mixture was poured in crushed ice and stirred for some time. The obtained solid was filtered and recrystalized with methanol

TABLE 1 : Europium triflate catalyzed synthesis of 3,4-dihydropyrimidones:

Entry	R	R^1	R^2	Product[a]	Reaction Time (h)	Yield (%)[b]
a	C_6H_5-	CH_3	C_2H_5	4a	1.0	89
b	4-(MeO)-C_6H_4-	CH_3	C_2H_5	4b	1.5	88
c	4-(H_3C)-C_6H_4-	CH_3	C_2H_5	4c	1.0	91
d	4-(NO_2)- C_6H_4-	CH_3	C_2H_5	4d	2.0	81
e	3,4,5-$(OMe)_3$-C_6H_2-	CH_3	C_2H_5	4e	1.5	93
f	2-Furyl-	CH_3	C_2H_5	4f	1.0	95
g	(*E*)C_6H_5-CH=CH-	CH_3	C_2H_5	4g	1.5	87
h	2-Thienyl-	CH_3	C_2H_5	4h	1.5	85
I	c-C_6H_{11}-	CH_3	C_2H_5	4i	3.0	82
J	2-Naphthyl-	CH_3	C_2H_5	4j	2.0	86
k	2,4-$(Cl)_2$-C_6H_3-	CH_3	C_2H_5	4k	2.5	87
l	C_5H_{11}-	CH_3	C_2H_5	4l	2.5	84
m	2-Cl-Pyridyne-3-	CH_3	C_2H_5	4m	2.0	85
n	Indole-3-	CH_3	C_2H_5	4n	3.0	87
o	4-(OH)-C_6H_4-	CH_3	C_2H_5	4o	2.5	85

[a]All the products were characterized by ^{1}H NMR, IR and Mass spectra data; [b]Isolated and unoptimized yields.

Spectral data for all the compounds

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

Solid. Mp. 201-203^{0}C. IR (KBr): υ 3416, 3231, 3108, 2936, 2867, 1701, 1648, 1592, 1241, 1129, 1036, 951, 834, 764 cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.15 (t, 3H, *J* = 7.0 Hz), 2.30 (s, 3H), 4.05 (q, 2H, *J* = 7.0 Hz), 5.25 (s, 1H), 7.25-7.40 (m, 5H), 7.75 (brs, 1H), 8.98 (brs, 1H).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.3, 152.5, 148.6, 144.7, 128.5, 127.2, 126.4, 99.2, 59.1, 53.8, 17.6, 14.3.; EIMS *m/z* (%): 260 (m$^+$ 100).; Anal. Calcd. (%) For $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.64; H, 6.25; N, 109.2.

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

Solid. Mp. 198-201^{0}C. IR (KBr): υ 3415, 3242, 3119, 2951, 2861, 1701, 1639, 1604, 1513, 1162, 1036, 947, 853, 742 cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.10 (t, 3H, *J* = 7.2 Hz), 2.25 (s, 3H), 3.85 (s, 3H), 4.05 (q, 2H, *J* = 7.2 Hz), 5.20 (s, 1H), 6.80 (d, 2H, *J* = 7.5 Hz), 7.20 (d, 2H, *J* = 7.5 Hz), 7.35 (brs, 1H), 9.00 (brs, 1H).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.3, 158.2, 152.5, 148.3, 137.6, 127.4, 113.9, 99.7, 59.8, 54.9, 53.1, 17.5, 14.1.; EIMS *m/z* (%): 290 (m$^+$ 28), 261 (100), 217 (30), 183 (20), 155 (20), 137 (15), 91(05).; Anal. Calcd. (%) For $C_{15}H_{18}N_2O_4$: C, 62.07; H, 6.20; N, 9.66. Found: C, 61.65; H, 6.21; N, 9.58.

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

Solid. Mp. 214-216^{0}C. IR (KBr): υ 3246, 3115, 2955, 1704, 1647, 1513, 1461, 1422, 1386, 1328, 1287, 1222, 1172, 1087, 952, 865, 779, 699, 67 cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.20 (t, 3H, *J* = 7.1 Hz), 2.30 (s, 3H), 2.35 (s, 3H), 4.09 (q, 2H, *J* = 7.1 Hz), 5.20 (s, 1H), 7.10 (d, 2H), 7.20 (d, 2H), 7.40 (s, 1H, NH), 9.00 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.1, 152.3, 148.2, 141.8, 136.3, 128.9, 126.1, 99.8, 60.0, 53.6, 20.7, 17.8, 14.1.; EIMS *m/z* (%): 274 (m$^+$28), 247 (100), 229 (10), 200 (60), 183 (80), 155 (50), 137 (30), 110 (20), 84, (10), 42 (50).; Anal. Calcd. (%) For $C_{15}H_{18}N_2O_3$: C, 65.66; H, 6.62; N, 1022. Found: C, 65.39; H, 6.69; N, 10.13.

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

Solid. Mp. 207-209^{0}C. IR (KBr): υ 3234, 3118, 2978, 1729, 1702, 1643, 1597, 1520, 1463, 1349, 1293, 1215, 1091, 1017, 856, 780, 696, 600 cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.13 (t, 3H, *J* = 7.0 Hz), 2.28 (s, 3H), 4.01 (q, 2H, *J* = 7.0 Hz), 5.18 (s, 1H), 7.12 (d, 2H, *J* = 7.0 Hz), 7.48 (d, 2H, *J* = 7.0 Hz), 7.75 (brs, 1H, NH), 9.10 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 163.4, 152.7, 152.0, 149.1, 146.7, 127.3, 124.2, 98.6, 59.7, 53.2, 18.3, 14.1.; EIMS *m/z* (%): 306 (m$^+$ 20), 276 (38), 232 (50), 201 (15), 183 (100), 155 (42), 137 (22).; Anal. Calcd. (%) For $C_{14}H_{16}N_3O_5$: C, 55.08; H, 4.92; N, 13.77. Found: C, 54.80; H, 4.95, N; 13.77.

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

Solid. Mp. 214-216^{0}C. IR (KBr): υ 3234, 3102, 2939, 2839, 1717, 1684, 1589, 1506, 1462, 1423,

1327, 1284, 1232, 1127, 1094, 1005, 845, 795, 704, 639, 517 cm^{-1}.; ^1H NMR (200 MHz, DMSO-d_6): δ 1.20 (t, 3H, *J* = 7.0 Hz), 2.30 (s, 3H), 3.70 (s, 3H), 3.80 (s, 6H), 4.10 (q, 2H, *J* = 7.0 Hz), 5.20 (s, 1H), 6.55 (s, 2H), 7.30 (brs, 1H, NH), 7.75 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.9, 153.8, 153.1, 146.1, 139.5, 103.6, 101.3, 60.5, 59.7, 56.2, 55.4, 18.6, 14.2.; EIMS *m/z* (%): 350 (m^+ 100), 212 (10), 183 (20).; Anal. Calcd. (%) For $C_{17}H_{24}N_2O_6$: (352.384); C, 57.44; H, 6.86; N, 7.95. Found: C, 57.50; H, 6.89; N, 7.97.

5-Ethoxycarbonyl-4-(2-furyl)-6-methyl-3,4-dihydrpyrimidin-2(1*H*)-one (4f)

Solid. Mp. 210-212^{0}C. IR (KBr): υ 3325, 3234, 3126, 3047, 2985, 2939, 1698, 1653, 1456, 1082, 874, 785 cm^{-1}.; ^1H NMR (DMSO-d_6): δ 1.20 (t, 3H, *J* = 6.5Hz), 2.20 (s, 3H), 4.05 (q, 2H, *J* = 6.5 Hz), 5.30 (s, 1H, *J* = 3.5 Hz), 6.06 (d, 1H, *J* = 3.0 Hz), 6.25 (d, 1H *J* = 3.0 Hz), 7.20 (d, 1H), 7.65 (brs, 1H, NH), 8.90 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.0, 156.9, 152.4, 149.3 142.1, 110.5, 96.5 60.0, 47.2, 18.0, 14.4.; EIMS *m/z* (%). 250 (m^+ 50), 221 (60), 177 (70), 149 (60) 137 (60), 110 (50), 89 (100), 55 (80).; Anal. Calcd. (%) For $C_{12}H_{16}N_2O_4$: (251.68); C, 57.13; H, 6.39; N, 11.10. Found: C, 57.15; H, 6.40; N, 11.13.

5-Ethoxycarbonyl-4-[(*E*)-2-phenylethenyl]-6-methyl-3,4-dihydrpyrimidin-2(1*H*)-one (4g)

Solid. Mp. 227-230°C. IR (KBr): υ 3354, 3262, 2983, 2854, 1695, 1656, 1495, 1372, 1224, 1163, 785, 743. cm^{-1}.; ^1H NMR (DMSO-d_6): δ 1.25 (t, 3H, *J* = 7.0 Hz), 2.25 (s, 3H), 4.18 (q, 2H, *J* = 7.0 Hz), 4.80 (d, 1H, *J* = 4.0 Hz), 6.10 (dd, 1H, *J* = 14.5 & 5.0 Hz), 6.35 (d, 1H, *J* = 14.5 Hz), 7.15-7.40 (m, 5H), 7.45 (s, 1H, NH), 8.96 (s, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.2, 153.1, 148.7, 136.5, 131.0, 128.8, 127.0, 126.1, 97.6, 59.4, 52.0, 17.9, 12.5.; EIMS *m/z* (%): 286 (m^+ 10), 242 (20), 199 (20), 198 (50), 183 (20), 175 (40), 175 (30), 158 (30), 132 (25), 118 (30), 102 (100), 85 (10); Anal. Calcd (%). For $C_{16}H_{18}N_2O_3$: (286.229) C, 67.12; H, 6.34; N, 9.78. Found; C, 67.15; H, 6.37; N, 9.80.

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

Solid. Mp. 206-208^{0}C. IR (KBr): υ 3245, 3234, 3164, 3120, 3043, 2979, 2946, 1718, 1689, 1632, 1535, 1462, 1251, 1065, 851, 745 cm^{-1}.; ^1H NMR (200 MHz, DMSO-d_6); δ 1.22 (t, 3H, *J* = 8.0 Hz), 2.03 (s, 3H), 4.05 (q, 2H, *J* = 8.0 Hz), 5.40 (s, 1H), 6.80 (d, 1H), 6.90 (d, 1H), 7.15 (d, 1H, *J* = 5.0 Hz), 7.58 (s, 1H, NH), 9.10 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.2, 152.4, 148.6, 148.1, 126.4, 124.8, 123.2, 99.7, 59.1, 49.6, 17.3, 14.5.; EIMS *m/z* (%): 266 (m^+ 100).; Anal. Calcd (%). For $C_{12}H_{14}N_2O_3S$; C, 54.10; H, 5.30; N, 10.52. Found; C, 54.27; H, 5.19; N, 10.33.

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

Solid. Mp. 235-237^{0}C. IR (KBr): υ 3234, 3115, 2922, 2854, 1721, 1705, 1643, 1532, 1451, 1312, 1231, 1093, 1016, 962, 847, 783, 741 cm^{-1}.; ^1H NMR (200 MHz, DMSO-d_6): δ 1.05 (m, 4H), 1.23 (t, 3H, *J* = 6.5 Hz), 1.42-1.46 (m, 3H), 1.70-1.75 (m, 3H), 2.31 (s, 3H), 4.08 (q, 2H, *J* = 6.5 Hz), 5.35 (d, 1H, *J* = 3.0 Hz), 6.25 (s, 1H, NH), 8.50 (s, 1H, NH).; EIMS *m/z* (%): 266 (m^+ 28), 237 (45), 193 (60), 183 (100), 154 (32), 137 (45), 111 (55), 91 (10), 84 (12), 69 (30).; Anal. Calcd (%). For $C_{14}H_{22}N_2O_3$: C, 63.15; H, 8.27; N, 10.52. Found; C, 63.20; H, 8.30; N, 10.60.

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

Solid. Mp. 245-247 ^{0}C. IR (KBr): υ 3241, 3239, 3118, 2978, 1705, 1653, 1549, 1451, 1432, 1234, 1082, 963, 871, 751 cm^{-1}.; ^1H NMR (200 MHz, DMSO-d_6): δ 1.18 (t, 3H, *J* = 7.0 Hz), 2.38 (s, 3H), 4.05 (q, 2H, *J* = 7.0 Hz), 5.80 (d, 1H, *J* = 3.0 Hz), 7.30-7.45 (m, 5H), 7.75 (t, 1H, *J* = 8.0 Hz), 7.80 (d, 1H, *J* = 8.0 Hz), 8.28 (d, 1H, *J* = 8.0 Hz), 9.14 (s, 1H, NH).; EIMS *m/z* (%): 310 (m^+ 20), 217 (38), 176 (100), 133 (18), 119 (40), 91 (32), 84 (15), 69 (50).; Anal. Calcd (%). For $C_{18}H_{18}N_2O_3$; C, 69.66; H, 5.85; N, 9.03. Found; C, 69.58; H, 5.71; N, 9.05.

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

Solid. Mp. 238-240^{0}C. IR (KBr): υ 3413, 3356, 3218, 3105, 2965, 2847, 1702, 1634, 1581, 1468, 1403, 1320, 1227, 1098, 1031, 931, 852, 735 cm^{-1}.; ^1H NMR (200 MHz, DMSO-d_6): δ 1.18 (t, 3H, *J* = 7.0 Hz), 2.30 (s, 3H), 4.05 (q, 2H, *J* = 7.0 Hz), 5.25

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(s, 1H), 7.20 (d, 1H, *J* = 8.0 Hz), 7.40 (dd, 1H, *J* = 8.0 Hz), 7.60 (s, 1H), 8.10 (s, 1H, NH), 9.20 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.3, 151.8, 149.5, 141.4, 132.6, 131.8, 128.9, 128.1, 98.2, 59.8, 51.6, 17.3, 14.2.; EIMS *m/z* (%): 329 (m^+ 35), 299 (45), 293 (60), 183 (100), 155 (30), 137 (45), 91 (10), 84 (12), 69 (28).; Anal. Calcd (%). For $C_{14}H_{14}N_2O_3Cl_2$: C, 51.08; H, 4.29; N, 8.51. Found: C, 51.14; H, 4.27; N, 8.53.

5-Ethoxycarbonyl-4-(*n*-pentyl)-6-methyl-3,4-dihydrpyrimidin-2-(1*H*)-one (4l)

Solid. Mp. 150-152^{0}C. IR (KBr): υ 3346, 3252, 2983, 1695, 1652, 1534, 1237, 785 cm^{-1}.; ^{1}H NMR (DMSO-d_6): δ 0.94 (t, 3H, *J* = 6.0 Hz), 1.22-1.35 (m, 9H), 1.40-1.60 (m, 2H), 2.30 (s, 3H), 4.18 (q, 2H, *J* = 6.5 Hz), 4.30 (t, 1H), 5.30 (brs, 1H, NH), 6.40 (brs, 1H, NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.1, 152.5, 148.7, 99.5, 59.4, 59.1, 49.7, 36.4, 25.8, 21.6, 20.5, 17.4, 14.6, 14.1.; EIMS *m/z* (%): 254 (m^+ 20), 230 (15), 209 (28), 186 (10), 183 (100), 155 (78), 137(65), 91 (22), 84 (10), 69 (18), 40 (30).; Anal. Calcd (%). For $C_{13}H_{22}N_2O_3$: (254.327). C, 61.39; H, 8.72; N, 11.01. Found: C, 61.40; H, 8.75; N, 11.08.

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

Solid. Mp. 223-225^{0}C. IR (KBr): υ 3295, 1712, 1705, 1680, 1585, 1070, cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.10 (t, 3H, *J* = 6.0 Hz), 2.35 (s, 3H), 3.98 (q, 2H, *J* = 6.0 Hz), 5.65 (s, 1H), 7.30 (t, 1H), 7.70 (d, 1H, *J* = 7.0 Hz), 7.90 (brs, 1H), 8.25 (d, 1H, *J* = 7.0 Hz). 9.10 (s, 1H).; MS *m/z* (%): 296 (M, 100), 279 (10), 266 (15), 260 (15), 244 (20), 186 (15), 184 (40), 141 (10) 113 (10), 102 (10).

5-(Ethoxycarbonyl)-4-(1H-indole-3yl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4n)

Solid. Mp. 245-247^{0}C. IR (KBr): υ 3417, 3356, 3240, 2978, 1702, 1653, 1538, 1187, 1085, 870, 751 cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.04 (t, 3H, *J* = 6.5 Hz), 2.17 (s, 3H), 3.98 (q, 2H, *J* = 6.5 Hz), 5.30 (s, 1H), 6.95-7.10 (m, 3H), 7.30 (d, 1H, *J* = 3.0 Hz), 7.65 (d, 1H, *J* = 7.0 Hz), 9.0 (s, 1H), 10.50 (brs, 1H).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 172.10, 155.25, 152.90, 136.90, 127.30, 123.20, 121.80, 119.10, 118.90, 111.15, 106.90, 104.35, 60.10, 34.15, 14.90, 13.90. EIMS *m/z* (%): 299 (m^+ 50), 298 (10), 279 (20), 232 (20), 183 (100), 179 (20), 157 (30), 153 (30), 139 (95), 133 (20), 130 (20), 111 (15).; Anal. Calcd (%). $C_{16}H_{17}N_3O_3$; (299.32); Calcd: C, 64.20; H, 5.72; N, 14.04; O, 16.04. Found: C, 63.89; H, 5.93; N, 14.37; O, 16.09.

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

Solid. Mp. 230-232^{0}C. IR (KBr): υ 3476, 3323, 3215, 3107, 2969, 1705, 1630, 1461, 1215, 1092, 830, 784, cm^{-1}.; ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.20 (t, 3H, *J* = 6.5 Hz), 2.80 (s, 3H), 4.00 (q, 2H, *J* = 6.5 Hz), 5.20 (s, 1H), 6.70 (d, 2H), 7.10 (d, 2H, 7.25 (s, 1H), 8.90 (s, 1NH).; ^{13}C NMR (DMSO-d_6, 50 MHz): δ 165.36, 155.46, 152.15, 147.64, 135.37, 127.34, 114.91, 99.73, 59.05, 53.38, 17.66, 14.02.; EIMS *m/z* (%): 276 (M^+30), 229 (20), 200 (60), 168 (87), 136 (48).

CONCLUSION

In conclusion, the present methodology for the synthesis of dihydropyrimidin-2(1*H*)-ones catalyzed by europium triflate, provides an efficient and improved procedure for Biginelli reaction. The simple experimental procedure and milder reaction conditions are the highlights of this method.

REFERENCES

[1] **(a)** P.Biginelli; Gazz.Chem.Ital., **23**, 360 **(1893)**; **(b)** C.O.Kappe; Tetrahedron., **49**, 6937 **(1993)**; **(c)** C.O.Kappe; Acc.Chem.Res., **33**, 879 **(2000)**; **(d)** M.Syamala; Org.Prep.Proc.Int., **41**, 1 **(2009)**; **(e)** C.O.Kappe, A.Stadlar, D.Dallinger; Pure Appl.Chem., **76(5)**, 1017 **(2004)**.

[2] **(a)** G.C.Ronyar, S.D.Kinball, B.Beyer, G.Cucinotta, J.D.Dimarco, J.Gougoutas, A.Hedberg, M.Mallley, J.P.Mc Carthy, R.Shang, S.Moreland; J.Med.Chem., **38**, 119 **(1995)**; **(b)** K.S.Atwal, B.N.Swanson, S.E.Unger, D.M.Floyd, S.Moreland, A.Hedberg, B.C.O Relly; J.Med.Chem., **34**, 806 **(1991)**; **(c)** D.R.Sidler, R.D.Larsen, M.Chartrain, N.Ikemoto, C.M.Roberg, C.S.Taylor, W.Li, G.F.Bills; PCT Int.W09907695, **(1999)**; Chem. Abstr., **130**, 182478 **(1999)**.

[3] **(a)** A.D.Patil, N.V.Kumar, W.C.Kokke, M.F.Bean, A.J.Freyer, C.De Brosse, S.Mai, A.Trunch, D.J.Faulkner; J.Org.Chem., **60**, 1182 **(1995)**; **(b)** B.B.Snider, J.Chem, A.D.Patil, A.Freyer; Tetrahedron Lett., **37**, 6977 **(1996)**.

[4] **(a)** A.V.Narsaiah, K.Nagaiah; Synthesis, **8**, 1253 **(2004)**; **(b)** Q.Sun, Y.Wang, Z.Ge, T.Cheng, R.Li; Synthesis, **7**, 1047 **(2004)**; **(c)** D.S.Bose, L.Fatima, M.H.Babu; J.Org.Chem., **68**, 587 **(2003)**; **(d)** B.C.Ranu, A.Hajra, U.Jana; J.Org.Chem., **65**, 6270 **(2000)**; **(e)** J.Lu, Y.Bai, Z.Wang, B.Yang, H.Ma; Tetrahedran Lett., **41**, 9075 **(2000)**.

[5] **(a)** A.S.Paraskar, G.K.Dewakar, A.Sudalai; Tetrahedran Lett., **44**, 3305 **(2003)**; **(b)** Y.Ma, C.Qian, L.Wang, M.Yang; J.Org.Chem., **65**, 3864 **(2000)**; **(c)** W.Su, J.Li, Z.Zheng, Y.Shen; Tetrahedran Lett., **46**, 6037 **(2005)**; **(d)** R.A.Srinivas, V.Ravi; Synlett., **1**, 67 **(2003)**; **(e)** R.Ghosh, S.Maiti, A.Chakraborty; J.Mol.Catal., **47**, 217 **(2004)**; **(f)** X.Hui, G.W.Yan; Chinese J.Chem., **21**, 327 **(2003)**; **(g)** C.O.Kappe, B.Desai, D.Doris Dallinger; Tetrahedron., **62**, 4651 **(2006)**.

[6] **(a)** J.Peng, Y.Deng; Tetrahedran Lett., **42**, 5917 **(2001)**; **(b)** M.Lu, X.Liu, T.Lu, C.Mai; J.Sci., **38**, 263 **(2011)**; **(c)** T.Z.Wang, C.S.Wang, W.Xu, Li; Helvetica Chemica Acta, **88**, 986 **(2007)**.

[7] **(a)** F.Bigi, S.Carloni, B.Frullanti, R.Maggi, G.Sartori; Tetrahedran Lett., **40**, 3465 **(1999)**; **(b)** R.Lenin, R.M.Raju; Int.J.Appl.Bio.Pharm.Tech., **3**, 1258 **(2010)**; **(c)** R.H.Memarian, J.M.Ranjbar; Chin. Chem.Soc., **58**, 1 **(2011)**.

[8] **(a)** C.O.Kappe, D.Kumar, R.S.Varma; Synthesis, **10**, 1799 **(1999)**; **(b)** E.H.Hu, D.R.Sidler, U.H.Dolling; J.Org.Chem., **63**, 3454 **(1998)**; **(c)** J.Lu, H.Ma; Synlett., **1**, 63 **(2000)**; **(d)** P.Salehi, M.Dabiri, A.M.Zolfigol, A.B.Fard; Tetrahedron Lett., **44**, 2889 **(2003)**; **(e)** T.Perumal, D.P.Muralidharan, M.Anniyappan; Synth.Commun., **32**, 659 **(2002)**; **(f)** R.S.Varma, P.Vivek; Tetrahedron Letters, **48**, 7343 **(2007)**; **(g)** Q.Y.Li, M.Zhang, M.Zhou; Chin.J.Chem., **24**, 282 **(2006)**; **(h)** K.K.Vijayan, C.Ranjith, G.V.Srinivasan; Bull Chem.Soc.Jpn., **83**, 288 **(2010)**.

[9] J.S.Yadav, B.V.S.Reddy, K.B.Reddy, K.S.Raj, A.R.Prasad; Perkin Trans, **1**, 1939 **(2001)**.

[10] **(a)** J.A.Kumar, A.V.Narsaiah; Int.J.Appl.Bio. Pharm.Tech., **3**, 935 **(2010)**; **(b)** F.S.Falsone, C.O.Kappe; Arkivoc, **2**, 122 **(2011)**.

[11] A.Kumar, R.A.Maurya; Tetrahedran Lett., **42**, 4569 **(2001)**.

[12] C.O.Kappe, S.F.Falsone; Synthesis, 718 **(1998)**.

[13] K.Nagaiah, R.S.Rao, G.Kondaji, S.P.Kumar, J.S.Yadav; Chem.Lett., **33**, 1168 **(2004)**.

[14] **(a)** Y.Venkateswarlu, P.Leelavathi; Lett.Org.Chem., **7**, 208 **(2010)**; **(b)** Y.Venkateswarlu, S.R.Kumar, P.Leelavathi; Int.J.Ind.Chem., **3**, 18 **(2012)**; **(c)** Y.Venkateswarlu, S.R.Kumar, Leelavathi; Org.Commun., **5(3)**, 120 **(2012)**; **(d)** S.R.Kumar, Y.Venkateswarlu, P.Leelavathi; Asian J.Chem., **23**, 1611 **(2011)**; **(e)** Y.Venkateswarlu, S.R.Kumar, P.Leelavathi; Org.Synth.Med.Chem., **1**, 11 **(2012)**; **(f)** Y.Venkateswarlu, S.R.Kumar, P.Leelavathi; Org.Synth.Med.Chem.Letter, ASP, **(2013)**.

[15] **(a)** N.Devanna, R.V.P.Chary; Int.J.Appl.Bio. Pharm.Tech., **3**, 1252 **(2010)**; **(b)** C.Yu, M.Lei, W.Su, Y.Xie; Synth.Commun., **37(19)**, 3301 **(2007)**.