Int. J. Chem. Sci.: 8(2), 2010, 1181-1192

MICROWAVE INDUCED ONE POT SYNTHESIS OF DIHYDROPYRIMIDINES ON ZINC DOPED MONTMORILLONITE K-10

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ABSTRACT

Dihydropyrimidines were synthesized by microwave irradiation using different aldehydes, urea derivatives and β-dicarbonyl compounds. Montmorillonite K-10 impregnated with $ZnCl_2$ was used as a solid support to obtain the better yields. Products were isolated, purified and identified by analytical and spectroscopic data.

Key words: Microwave, Dihydropyrimidine, Biginelli type reaction.

INTRODUCTION

The preparation of fine chemicals following environmentally friendly strategies represents a challenging goal in the field of synthetic organic chemistry[1-4]. Dihydropyrimidines (DHMPs) have found remarkable pharmacological efficiencies[5-9], such as antiviral, potent Ca-channel blockers, antihypertensive and anti-tumor agent. In addition, The Biginelli type reaction was first described more than a century ago[10] and recently, a number of such reactions have been reviewed[11].

Many efforts have been made recently to improve and modify this reaction. Lanthanide triflate[12], lanthanum chloride[13], indium chloride[14] zinc chloride[15] and acidic clay montmorillonite KSF[16] have been used to replace the strong protic acid in the classic Biginelli reaction. Glacial acetic acid[17] and polyphosphate ester[18] have also been used as promoter in such microwave assisted condensation. Higher yields were claimed in most of these reactions. In this direction, efforts have been made to carry out Biginelli type reaction

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using zinc chloride doped montmorillonite K-10 as a solid support in present investigation with an object to synthesize dihydropyrimidines in one pot.

EXPERIMENTAL

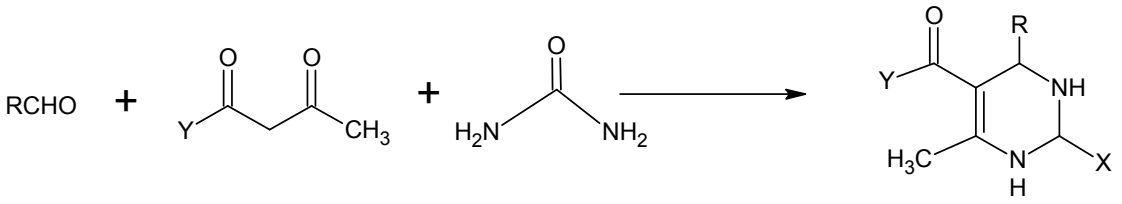
All the reactions were carried out in a domestic microwave oven (Kenstar, Model No. OM-26 EGO, Power-1200W). Melting points were determined in open capillaries and are uncorrected. Reactions were monitored by thin layer chromatography using silica gel-G as an adsorbent using ethyl acetate : n-hexane (7 : 3) as eluent.

Catalyst preparation

Zinc chloride impregnated clay (montmorillonite K-10) was prepared by adding a solution of the zinc chloride (99.9%) in methanol to montmorillonite K-10 and evaporating the methanol by means of a rotary evaporator over 30 min using the procedure described earlier[19]. The catalyst was then activated by heating the clay at 150°C for 2 h.

General procedure

A mixture of aldehyde (1 mmol), β-dicarbonyl compound (1 mmol), urea (or thiourea) (1.5 mmol) and montmorillonite K-10/$ZnCl_2$ (5 g) was placed in a 50 mL glass flask. The mixture was thoroughly mixed with a spatula for 30 s and then, it was irradiated in MW oven 6 times at 40% power of total 700W for 30 s with 1 min cooling period after each irradiation. After the reaction was complete, the reaction mixture was soaked with methanol for half an hour and filtered off. The filtrate was concentrated in vacuum to afford the crude product. It was purified by preparative TLC. The residue left was nothing but only catalyst, which can be reused again.



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

Y = OEt, R or Ar; X = O or S

RESULTS AND DISCUSSION

The effect of the molar ratios of reagents and the influence of MW irradiation on a neat mixture of aldehyde, β-dicarbonyl compound, urea (or thiourea) and montmorillonite

clay/$ZnCl_2$ in the modified Biginelli reaction has been observed. Optimum conditions were determined on the basis of these observations. The ratio of aldehyde, β-dicarbonyl compound and urea (or thiourea) was kept 1 : 1 : 1.5. The reaction mixture was mixed with montmorillonite clay/$ZnCl_2$ (4 : 3) and then subjected to microwave irradiation at 40% power in a 700 W microwave oven for 3 min successive irradiations of 30-40 s with cooling intervals of 1 min. The temperature of reaction mixture was kept in the range 80-90°C by keeping mixture out of the oven at different time intervals. The products were characterized on the basis of elemental analysis (Table 1) and spectral data (Table 2).

Table 1: Characterization data of synthesized compounds

Compd.	Molecular formula (M.W.)	Molecula weight	Melting point (°C)	Calculated / Found (%)		
				C	H	N
1a	$C_{13}H_{14}N_2O_3$	260	202	64.60 (63.85)	6.20 (6.95)	10.76 (9.85)
1b	$C_{14}H_{16}N_2O_2$	305	206	55.08 (54.75)	4.95 (4.05)	13.76 (12.95)
1c	$C_{14}H_{15}N_3O_5$	305	208	55.08 (56.10)	4.95 (4.15)	13.76 (12.95)
1d	$C_{11}H_{18}N_2O_3$	226	153	69.74 (70.67)	7.02 (6.76)	10.84 (9.67)
1e	$C_{15}H_{18}N_2O_3$	274	218	65.68 (64.80)	6.61 (6.70)	10.21 (10.01)
1f	$C_{15}H_{18}N_2O_3$	274	170	65.68 (64.25)	6.61 (7.96)	10.21 (9.76)
1g	$C_{14}H_{15}BrN_2O_3$	338	203	49.57 (50.01)	4.46 (3.50)	8.26 (8.01)
1h	$C_{14}H_{15}ClN_2O_2$	294	213	57.05 (56.00)	5.13 (4.03)	9.50 (10.30)
1i	$C_{13}H_{14}N_2O_2$	230	233	67.81 (65.29)	6.13 (7.06)	12.17 (13.26)

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Compd.	Molecular formula (M.W.)	Molecular weight	Melting point (°C)	Calculated / Found (%)		
				C	H	N
1j	$C_{13}H_{13}N_3O_4$	275	230	56.72 (57.60)	4.76 (3.90)	15.27 (12.36)
1k	$C_{14}H_{16}N_2O_2$	244	161	68.83 (68.60)	6.60 (6.84)	11.47 (13.76)
1l	$C_{10}H_{16}N_2O_2$	196	143	61.20 (60.04)	8.22 (9.79)	14.27 (13.96)
1m	$C_{18}H_{16}N_2O_2$	292	214	73.95 (71.37)	5.52 (4.32)	9.58 (10.36)
1n	$C_{18}H_{15}N_3O_4$	337	237	64.09 (62.91)	4.48 (5.90)	12.46 (10.36)
1o	$C_{15}H_{18}N_2O_2$	258	213	69.74 (67.26)	7.02 (6.29)	10.84 (9.04)
1p	$C_{13}H_{14}N_2OS$	246	220	63.39 (64.21)	5.73 (4.59)	11.37 (10.20)
1q	$C_{10}H_{16}N_2OS$	212	140	56.57 (58.20)	7.60 (7.29)	13.19 (12.72)

Table 2: Spectral data of synthesized compounds

Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1a	3438 (N – H str.), 3326 (N – H str.), 3070 (Ar – CH=CH str.), 2819 (CH_3 str.), 1730 (C=O str.), 1673 (C=O str.), 1208 (C – O – C)	6.96–7.19 (m, 5H, Ar-H), 6.46 (s, 1H, N-H), 6.10 (s, 1H, N-H), 5.63 (s, 1H, CH), 3.79 (q, 2H, CH_2), 1.71 (s, 3H, CH_3), 1.42 (t, 2H, CH_3)	260 $[M]^{+\cdot}$, 245 $[M - CH_3]^{+\cdot}$, 231 $[M - C_2H_5]^{+\cdot}$, 215 $[M - OC_2H_5]^{+\cdot}$, 187 $[M - COOC_2H_5]$; 183 $[M - C_6H_5]$; 77 $[C_6H_5]^+$; 73 $[M - C_3H_5O_2]^{+\cdot}$, 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.

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Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1b	3440 (N – H str.), 3318 (N – H str.), 3098 (Ar – CH=CH str.), 2829 (– CH_3 str.), 1735 (C=O str.), 1690 (C=O str.), 1350-1558 (– NO_2) 1215 (C – O – C)	7.10-8.05 (m, 4 H, Ar-H), 6.8 (s, 1H, N-H), 6.1 (s, 1H, N-H), 5.71 (s, 1H, CH), 4.10(q, 2H, CH_3-CH_2), 1.75 (s, 3H, CH_3), 1.50 (t, 2H, CH_3)	305 $[M]^{+\cdot}$, 290 $[M - CH_3]^{+\cdot}$, 275 $[M - C_2H_5]^{+\cdot}$, 260 $[M - OC_2H_5]^{+\cdot}$, 259 $[M - NO_2]^{+\cdot}$, 232 $[M –COOC_2H_5]^+$; 183 $[M - C_6H_5NO_2]^+$; 122 $[C_6H_4NO_2]^+$; 73 $[C_3H_5O_2]^+$; 45 $[C_2H_5]^+$; $[NO_2]^+$ 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.
1c	3442 (N – H str.), 3325 (N – H str.), 3095 (Ar – CH=CH str.), 2832 (CH_3 str.), 1736 (C=O str.), 1685 (C=O str.), 1218 (C – O – C)	7.15 – 8.0 (m, 4H, Ar-H), 6.5 (s, 1H, N-H), 6.2 (s, 1H, N-H), 5.69 (s, 1H, CH), 4.22 (q, 2H, CH_2), 1.78 (s, 3H, CH_3), 1.54 (t, 2H, CH_3)	305 $[M]^{+\cdot}$, 290 $[M - CH_3]^{+\cdot}$, 276 $[M - C_2H_5]^{+\cdot}$, 260 $[M - OC_2H_5]^{+\cdot}$, 259 $[M - NO_2]^{+\cdot}$, 232 $[M – COOC_2H_5]^+$; 183 $[M - C_6H_5NO_2]^+$; 122 $[C_6H_4NO_2]^+$; 73 $[C_3H_5O_2]^+$; 45 $[C_2H_5]^+$; $[NO_2]^+$ 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.
1d	3390 (N – H str.), 3332 (N – H str.), 2819 (CH_3 str.), 1732 (C=O str.), 1682 (C=O str.), 1590 (C=C).	6.6 (s, 1H, N-H), 6.2 (s, 1H, N-H), 4.26 (s, 1H, CH), 4.10 (q, 2H, CH_2), 1.59 (q, 2H, CH_2), 1.35 (m, 2H, CH_2),	226 $[M]^{+\cdot}$, 211 $[M - CH_3]^{+\cdot}$, 197 $[M - C_2H_5]^{+\cdot}$, 183 $[M - C_3H_7]^{+\cdot}$, 181 $[M - OC_2H_5]^{+\cdot}$, 153 $[M –COOC_2H_5]^+$;

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Compd.	IR (cm^{-1})	^{1}H NMR (δ)	MS (m/z)
		1.0 (t, 2H, CH_2)	73 $[C_3H_5O_2]^+$; 45 $[C_2H_5O]^+$; 43 $[C_3H_7]^+$; 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.
1e	3431 (N – H str.), 3324 (N – H str.), 3075 (Ar – CH=CH str.), 2819 (CH_3 str.), 1725 (C=O str.), 1671 (C=O str.), 1208 (C – O – C)	6.95-7.20 (m, 4H, Ar-H), 6.4 (s, 1H, N-H), 6.0 (s, 1H, N-H), 5.62 (s, 1H, CH), 3.80 (q, 2H, CH_2), 2.38 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.42 (t, 2H, CH_3)	274 $[M]^{+\cdot}$, 259 $[M - CH_3]^{+\cdot}$, 245 $[M - C_2H_5]^{+\cdot}$, 229 $[M - OC_2H_5]^{+\cdot}$, 201 $[M - COOC_2H_5]^+$; 183 $[M - C_7H_7]$ 91 $[C_7H_7]^+$; 73 $[C_3H_5O_2]^+$; 45 $[C_2H_5O]^+$; 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.
1f	3433 (N – H str.), 3325 (N – H str.), 3068 (Ar – CH=CH str.), 2821 (CH_3 str.), 1727 (C=O str.), 1672 (C=O str.), 1210 (C – O – C)	6.95 – 7.19 (m, 4H, Ar-H), 6.45 (s, 1H, N-H), 6.10 (s, 1H, N-H), 5.61 (s, 1H, CH), 3.78 (q, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.41 (t, 2H, CH_3)	274 $[M]^{+\cdot}$, 254 $[M - CH_3]^{+\cdot}$, 245 $[M - C_2H_5]^{+\cdot}$, 229 $[M - OC_2H_5]^{+\cdot}$, 201 $[M - COOC_2H_5]^+$; 183 $[M - C_7H_7]$ 91 $[C_7H_7]^+$; 73 $[C_3H_5O_2]^+$; 45 $[C_2H_5O]^+$; 29 $[C_2H_5]^+$; 15 $[CH_3]^+$.

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Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1g	3440 (N – H str.), 3338 (N – H str.), 3092 (Ar – CH=CH str.), 2821 (CH_3 str.), 1740 (C=O str.), 1686 (C=O str.), 590 (C-Br).	7.05-8.02 (m, 4H, Ar-H), 6.5 (s, 1H, N-H), 6.2 (s, 1H, N-H), 5.64 (s, 1H, CH), 4.09 (q, 2H, CH_2), 1.75 (s, 3H, CH_3), 1.48 (t, 2H, CH_3)	340 $[M + 2]^{+\cdot}$, 338 $[M]^{+\cdot}$, 325 $[M + 2 - CH_3]^{+\cdot}$, 323 $[M – CH_3]^{+\cdot}$, 310 $[M + 2 – C_2H_5]^{+\cdot}$, 308 $[M – C_2H_5]^{+\cdot}$, 294 $[M +2 – C_2H_5O]^{+\cdot}$, 292 $[M – C_2H_5O]^{+\cdot}$, 267 $[M +2 – C_2H_5O_2]^{+\cdot}$, 265 $[M – C_2H_5O_2]^{+\cdot}$, 183 $[M – C_6H_5Br]^{+\cdot}$, 154 $[C_6H_5Br]^{+\cdot}$,
1h	3445 (N – H str.), 3330 (N – H str.), 3093 (Ar – CH=CH str.), 2823 (CH_3 str.), 1740 (C=O str.), 1687 (C=O str.), 735 (C-Cl).	7.11-8.08 (m, 4H, Ar-H), 6.6 (s, 1H, N-H), 6.2 (s, 1H, N-H), 5.68 (s, 1H, CH), 4.10 (q, 2H, CH_2), 1.76 (s, 3H, CH_3), 1.50 (t, 2H, CH_3)	296 $[M + 2]^{+\cdot}$, 294 $[M]^{+\cdot}$, 281 $[M + 2 - CH_3]^{+\cdot}$, 279 $[M – CH_3]^{+\cdot}$, 267 $[M + 2 – C_2H_5]^{+\cdot}$, 265 $[M – C_2H_5]^{+\cdot}$, 251 $[M +2 – C_2H_5O]^{+\cdot}$, 249 $[M – C_2H_5O]^{+\cdot}$, 223 $[M +2 – C_2H_5O_2]^{+\cdot}$, 221 $[M – C_2H_5O_2]^{+\cdot}$, 183 $[M – C_6H_5Cl]^{+\cdot}$, 154 $[C_6H_5Br]^{+\cdot}$,

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Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1i	3425 (N – H str.), 3305 (N – H str.), 3087 (Ar – CH=CH str.), 2820 (CH_3 str.), 1702 (C=O str.), 1675 (C=O str.).	6.94-7.15 (m, 4H, Ar-H), 6.6 (s, 1H, N-H), 6.1 (s, 1H, N-H), 5.62 (s, 1H, CH), 2.31 (s, 3H, CH_3), 1.73 (s, 3H, CH_3)	230 $[M]^{+\cdot}$, 215 $[M - CH_3]^+$; 187 $[M - C_2H_3O]^{+\cdot}$, 153 $[M - C_6H_5]^{+\cdot}$, 77 $[C_6H_5]^{+\cdot}$, 43 $[C_2H_3]^{+\cdot}$, 15 $[CH_3]^+$.
1j	3445 (N – H str.), 3328 (N – H str.), 3095 (Ar – CH=CH str.), 1739 (C=O str.), 1688 (C=O str.), 1345-1548 (NO_2).	7.10-7.98 (m, 4 H, Ar-H), 6.8 (s, 1H, N-H), 6.2 (s, 1H, N-H), 5.69 (s, 1H, CH), 2.35 (s, 3H, CH_3-CO), 1.81 (s, 3H, CH_3).	275 $[M]^{+\cdot}$, 260 $[M - CH_3]^{+\cdot}$, 232 $[M - C_2H_3O]^{+\cdot}$, 229 $[M - NO_2]^+$; 153 $[M - C_6H_4NO_2]^{+\cdot}$, 122 $[C_6H_4NO_2]^{+\cdot}$, 45 $[NO_2]^+$; 43 $[C_2H_3CO]^{+\cdot}$, 15 $[CH_3]^{+\cdot}$
1k	3429 (N – H str.), 3305 (N – H str.), 3085 (Ar – CH=CH str.), 2820 (CH_3 str.), 1702 (C=O str.), 1675 (C=O str.).	6.94-7.10 (m, 4 H, Ar-H), 6.5 (s, 1H, N-H), 6.0 (s, 1H, N-H), 5.60 (s, 1H, CH), 2.30 (s, 3H, CH_3-CO), 2.40 (s, 3H, Ar-CH_3), 1.70 (s, 3H, CH_3).	244 $[M]^{+\cdot}$, 229 $[M - CH_3]^{+\cdot}$, 201 $[M - C_2H_3O]^{+\cdot}$, 153 $[M - C_7H_7]^{+\cdot}$, 91 $[C_7H_7]^+$; 43 $[C_2H_3O]^{+\cdot}$, 15 $[CH_3]^{+\cdot}$
1l	3385 (N – H str.), 3329 (N – H str.), 2818 (CH_3 str.), 1715 (C=O str.), 1681 (C=O str.), 1512 (C=C).	6.5 (s, 1H, N-H), 6.0 (s, 1H, N-H), 4.27 (t, 1H, CH), 2.30 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.58 (q, 2H, CH_2), 1.30 (m, 2H, CH_2), 0.96 (t, 3H, CH_3)	196 $[M]^{+\cdot}$, 181 $[M - CH_3]^{+\cdot}$, 169 $[M - C_2H_3O]^{+\cdot}$, 167 $[M - C_2H_5]^{+\cdot}$, 153 $[M - C_3H_7]^{+\cdot}$, 43 $[C_2H_3O]^+$; 43 $[C_3H_7]^{+\cdot}$, 29 $[C_2H_5]^{+\cdot}$, 15 $[CH_3]^+$.

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Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1m	3426 (N – H str.), 3315 (N – H str.), 3099 (Ar – CH=CH str.), 2828 (CH_3 str.), 1770 (C=O str.), 1698 (C=O str.).	6.90-7.83 (m, 10H, Ar-H), 6.8 (s, 1H, N-H), 6.1 (s, 1H, N-H), 5.63 (s, 1H, CH), 1.7 (s, 3H, CH_3)	292 $[M]^{+\cdot}$, 277 $[M - CH_3]^{+\cdot}$, 215 $[M - C_6H_5]^{+\cdot}$, 187 $[M - C_7H_5O]^{+\cdot}$, 105 $[M - C_7H_5O]^{+\cdot}$, 77 $[C_6H_5]^+$; 15 $[CH_3]^+$.
1n	3448 (N – H str.), 3331 (N – H str.), 3096 (Ar – CH=CH str.), 2823 (CH_3 str.), 1748 (C=O str.), 1692 (C=O str.), 1355-1540 (NO_2).	7.10-8.10 (m, 9H, Ar-H), 6.7 (s, 1H, N-H), 6.1 (s, 1H, N-H), 5.69 (s, 1H, CH), 1.78 (s, 3H, CH_3).	337 $[M]^{+\cdot}$, 322 $[M - CH_3]^{+\cdot}$, 291 $[M - NO_2]^+$; 232 $[M - C_7H_5O]^{+\cdot}$, 215 $[M - C_6H_4NO_2]^{+\cdot}$, 122 [$C_6H_4NO_2]^{+\cdot}$, 105 $[C_7H_5O]^{+\cdot}$, 45 $[NO_2]^{+\cdot}$, 15 $[CH_3]^+$.
1o	3424 (N – H str.), 3314 (N – H str.), 3079 (Ar – CH=CH str.), 2826 (CH_3 str.), 1766 (C=O str.), 1697 (C=O str.).	6.6 (s, 1H, N-H), 6.1 (s, 1H, N-H), 4.29 (t, 1H, CH), 1.59 (q, 2H, CH_2), 1.5 (s, 3H, CH_3), 1.32 (m, 2H, CH_2), 0.96 (t, 3H, CH_3)	258 $[M]^{+\cdot}$, 243 $[M - CH_3]^{+\cdot}$, 229 $[M - C_2H_5]^{+\cdot}$, 215 $[M - C_3H_7]^{+\cdot}$, 181 $[M - C_6H_5]^+$; 153 $[M - OC_7H_5]^+$; 105 $[C_7H_5O]^+$; 77 $[C_6H_5]^+$; 43 $[C_3H_7]^+$; 29 $[C_2H_5]^+$; 15 $[CH_3]^+$
1p	3498 (N – H str.), 3328 (N – H str.), 3092 (Ar – CH=CH str.), 2810 (CH_3 str.), 1712 (C=O str.), 1490 (C=S str.).	6.90-7.12 (m, 5H, Ar-H), 4.48 (s, 1H, CH),2.28 (s, 3H, CH_3), 2.3 (s, 1H, N-H), 2.1 (s, 1H, N-H).	246 $[M]^{+\cdot}$, 231 $[M - CH_3]^{+\cdot}$, 203 $[M - OC_2H_3]^+$; 169 $[M - C_6H_5]^{+\cdot}$, 77 $[C_6H_5]^+$; 43 $[C_2H_3O]^+$; 15 $[CH_3]^+$.

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Compd.	IR (cm^{-1})	^1H NMR (δ)	MS (m/z)
1q	3390 (N – H str.), 3321 (N – H str.), 2810 (CH_3 str.), 1502 (C=C str.), 1709 (C=O str.), 1482 (C=S str.).	3.35 (t, 1H, CH), 2.30 (s, 3H, CH_3), 2.0 (s, 1H, N-H), 1.8 (s, 1H, N-H), 1.70 (s, 3H, CH_3), 1.54 (q, 2H, CH_2), 1.33 (m, 2H, CH_2), 0.93 (t, 3H, CH_3)	212 $[M]^{+\cdot}$, 197 $[M - CH_3]^{+\cdot}$, 183 $[M - C_2H_5]^{+\cdot}$, 169 $[M - C_3H_7]^{+\cdot}$, 169 $[M - OC_2H_3]^{+}$; 43 $[C_2H_3O]^{+}$; 43 $[C_3H_7]^{+}$; 29 $[C_2H_5]^{+}$; 15 $[CH_3]^{+}$.

The results are summarized in Table 1, which indicate that this protocol is able to tolerate the structural variations. Both aromatic and aliphatic aldehydes have been subjected to this condensation very efficiently. Besides the β-ketone ester, β-diketone can also be utilised in such reaction. Thiourea in place of urea has also been used successfully to provide the corresponding dihydropyrimidines. $ZnCl_2$ was used as a Lewis acid. No special precaution was needed in handling. The catalyst can be reused several times. When the reactions were carried out without K-10/$ZnCl_2$, then low yield was obtained for β–ketoesters as a substrate, while no product was detected for β–diketones. The significant difference in % of yield is shown in Table 3.

Table 3: The yields of (1a-1m)

Entry	R	Y	X	Catalyst	Yield* (%)
1a	Ph	OEt	O	K-10/$ZnCl_2$	90
1b	2-NO_2 –C_6H_4	OEt	O	K-10/$ZnCl_2$	90
1c	4-NO_2-C_6H_4	OEt	O	K-10/$ZnCl_2$	82
1d	n-Pr	OEt	O	K-10/$ZnCl_2$	86
1e	3-CH_3-C_6H_4	OEt	O	K-10/$ZnCl_2$	90
1f	4-CH_3-C_6H_4	OEt	O	K-10/$ZnCl_2$	95
1g	4-Br-C_6H_4	OEt	O	K-10/$ZnCl_2$	88
1h	4-Cl-C_6H_6	OEt	O	K-10/$ZnCl_2$	89
1i	Ph	CH_3	O	K-10/$ZnCl_2$	88

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Entry	R	Y	X	Catalyst	Yield* (%)
1j	4-NO_2-C_6H_4	CH_2 CH_3	O	K-10/$ZnCl_2$	91
1k	4-CH_3-C_6H_4	CH_3	O	K-10/$ZnCl_2$	86
1l	n-Pr	Ph	O	K-10/$ZnCl_2$	89
1m	Ph	Ph	O	K-10/$ZnCl_2$	88
1n	4-NO_2-C_6H_4	Ph	O	K-10/$ZnCl_2$	92
1o	n-Pr	CH_3	O	K-10/$ZnCl_2$	84
1p	Ph	CH_3	S	K-10/$ZnCl_2$	82
1q	n-Pr	OEt	S	K-10/$ZnCl_2$	77
1a	Ph	CH_3	O	–	50
1i	Ph	Ph	O	–	0
1m	Ph	–	O	–	0

CONCLUSION

In summary, a new and efficient modified Biginelli reaction has been described making use of zinc chloride doped montmorillonite K-10 as a solid support in one pot synthesis of dihydropyrimidine. The advantages of this environmentally benign reaction include the simple reaction set-up, high product yields, short reaction time and solventless conditions. In addition, the catalyst can be recovered and reused making it valuable from the economic point of view.

ACKNOWLEDGEMENT

Authors are thankful to Head, Department of Chemistry, University College of Science, MLS University, Udaipur, for providing necessary facilities for this work.

REFERENCES

1. M. M. Heravi, N. M. Montazeri, B. M. Rahimizadeh and M. Ghassemzadeh, J. Chem. Res., 464 (2004).
2. S. Paul and J. H. Clark, Green Chem., **5**, 635 (2003).
3. J. H. Clark and B. Desai, Pure Appl. Chem, **73**, 103 (2001).
4. D. Dallinger and C. O. Kappe, Tetrahedron, **62**, 4651 (2006).

5. S. D. Rovnyak and S. D. Kimball, J. Med. Chem., **38**, 119, (1995).
6. G. J. Grover and S. Dzwonczyk, J. Cardiovasc. Pharmacol, **26**, 289 (1995).
7. D. R. Sidler and R. D. Larsen, PCT Int. Wo 99, 7695.
8. M. A. Bruce, G. S. Pointdexter and G. Johnson, PCT Int. Appl. WO, **98**, 33, 791.
9. Z. Jie, Z. Mingjie, L. Bo and L. Xiaojuan, Chem. Lett., **38(1)**, 56 (2009).
10. P. G. Biginelli, Chim., **23**, 360 (1893).
11. W. Krenn, P. Verdino and C.O. Kappe, Chirality, 11 (1999).
12. Y. Ma, C. Qian, L. Wang and M. Yang, J. Org. Chem., **65**, 3864 (2000).
13. J. Lu, Y. Bai and Z. Wang, Tetrahedron Lett., **41**, 9075 (2000).
14. B. C. Ranu, A. Hajra and U. Jana, J. Org. Chem., **65**, 6270 (2000).
15. L. Amanda and Rousseau, Tetrahedron Lett., **48**, 4079 (2007).
16. F. Bigi, S. Carloni and B. Frullanti, Tetrahedron Lett., **40**, 3465, (1999).
17. J. S. Yadav, B. V. Subba Reddy and T. Ramalingam, J. Chem. Res., 354, (2000).
18. D. Villemin and F. Caillot, Tetrahedron Lett., **42**, 639, (2001).
19. D. Clark, A. Kirk and Ronald A. Kydd, Catal. Lett., **25**, 163, (1994).

Accepted : 21.12.2009