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Original Research Article

Ferroferic nanoparticle catalyzed synthesis of multicomponent 3, 4-dihydropyrimidine-2-(1H)-ones/ thiones at ambient temperature

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Abstract

Ferroferic oxide nanoparticle was found to be an efficient catalyst for the synthesis of 3, 4-dihydropyrimidin-2-(1H)-ones/thiones from the multicomponent condensation reaction of aromatic aldehyde, Ethyl acetoacetate, Urea / thiourea in dichloromethane solvent at room temperature.

Key Words: Fe_3O_4**,** Ethyl acetoacetate, Dihydropyrimidines.

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INTRODUCTION

Over the past few decades, multicomponent reactions (MCRs) have gained considerable interest in both academia and industry owing to exceptional synthetic efficiency, intrinsic atom-economy, high reactivity, and procedural simplicity.[1]MCRs have great contribution toward convergent synthesis of complex and important biologically active molecules from readily available starting materials, and have emerged as powerful tools for drug discovery.[2]These all multicomponent reactions are shown by Hantzsch[3]. Knoevenagel[4], Italian chemist P. Biginelli.[5] In the precursor reacted same two components in equimolar ratio *viz.* acetoacetic ester, aldehyde and third component as urea in double amount in acidic alcoholic solution to obtain a new compound via the well-known 3, 4-dihydropyrimidin-2(1*H*)-ones or Biginelli compounds[6]. These are obvious analogues of the Hantzsch dihydropyridines.[7] Subsequently to these academic developments the Biginelli scaffold was shown due to their pharmacological, therapeutic properties, and biological activities of several marine alkaloids which contain the dihydropyrimidine nucleus from a pharmaceutical point of view, there is need for investigations for very fast to designed 3,4 dihydropyridine-2-(1H)-one. As in the previously result there is transformation mostly involving catalyst changes.[8] Thus, Major emphasis being based on mainly Lewis acid such as BF_3xOEt_2[9], $La(OTf)_3$[10], $LaCl_3$[11], $BiCl_3$[12], LiBr[13] $LiClO_4$[14], Cerium Ammonium Nitrate [15], $FeCl_3X.6H_2O$, $NiCl_2X6H_2O$[16] Silica sulfuric acid[17], VCl_3[18] etc., Protic acids such as H_2SO_4, HOAc, Conc.HCl. [19] Many methods based on microwave irradiation, ionic liquidsand Clay[20] are reported. However all these methods have some limitations such as harash reaction condition, tedious work up procedure, use of solvents, long reaction time etc. therefore to overcome these limitations. Thus, the development of rapid and eco-friendly approaches has crucial importance using the Nanomaterial particle as Ferroferic oxide. It has some interesting features, because of his low environmental impact, easy prepared catalyst, less costly, more effective, magnetic property and highly chemo-selective catalyst for their organic synthesis.

Present Work: Here, we report a pertinent method for the synthesis of 3, 4-dihydropyrimidin-2-(1H)-ones/thiones using Fe_3O_4 as a strong acid catalyst from the condensation of aldehyde, acetoacetic ester and Urea or thiourea (1:1:2) in the ethanol.

Scheme-I

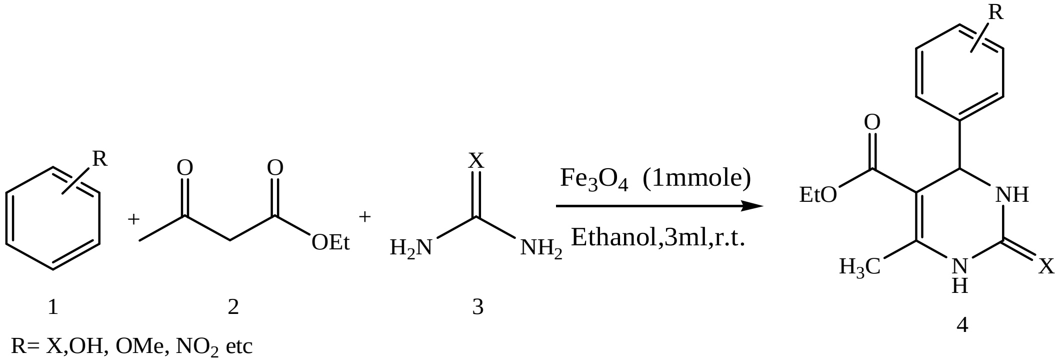


Figure 1

RESULT AND DISCUSSION

Ferroferic Nanomaterial is presently strong oxidizing agent as an effective heterogeneous catalyst for Biginelli condensation reaction from 1 equivalent *p*-chlorobenzaldehydes, 1 equivalent ethyl acetoacetate and 2 equivalents of urea into 3ml of ethanol under ambient temperature. During the course of our optimization of reaction condition, the reactions were generally completed within 30 minute. However, no increase in yield was observed when the reaction time was prolonging with respect to solvent as per our optimization reaction (Table 1). The optimized reaction conditions for the reaction were found to be Fe_3O_4 as 1mmole under room temperature for 30 minute.

Table 1: Optimization condition for 3,4-dihydropyridine-2-(1H)-one/thione using Fe_3O4_a

Entry	Catalyst (mmol)	Time in Min/Hr.	Tield(%)[b]
1	None	2 Hr	24
2	0.5	60 min	41
3	1.0	30 min	96
4	2.0	60 min	94

[A] Reaction conditions p-chlorobezaldyde (1 mmol), Urea (2mmol) in the presene Fe_3O_4 (1mmol) at room temperature.

[b] Islolated yields.

[c] The reaction mixture was stirred at room temperature for 30 min.

Therefore, for the study of generality and scope of the reaction have completed with different aromatic aldehydes under similar reaction conditions (Table 2) and it was found that aromatic aldehydes with electron donating substituent give higher yield as compare to electron withdrawing substituent. Both types of these reactions are given more than 90% yield. These reactions have been completed from thiourea also with the help of same condition as that of urea. The mild reaction conditions, high yields, low cost, and easy preparation and handling of the nanomaterial catalyst are the attractive features of the present methodology.

Experimental Section: General Procedure for the Synthesis of 3, 4-dihydropyrimidine-2-(1H)-ones/ thiones using ferroferic nanoparticles at ambient temperature: A mixture of aldehyde 1 (2 mmol), β-keto ester 2 (2 mmol), urea or thio-urea 3 (2 mmol) and catalytic amount of $Fe_3O_4$was added into 3ml of ethanol and this content of reaction mixture was stirrer at ambient temperature This reaction is completed within 30 minute which is monitored and confirmed by TLC. The contents of the flask were collected using filtration methods and remove insoluble solid ferroferic nanoparticles, then the evaporate the content to afford crude product. Add hot ethanol into solid crude product for their further recrystalization to remove for all impurities and isolated to get the corresponding 3, 4-dihydropyrimidin-(2H)-one pure product (figure 1).

Table 2 Synthesis of 3, 4 - dihydro pyrimidines using Fe_3O_4 nanomaterial.

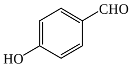
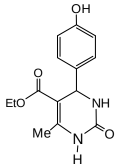
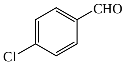
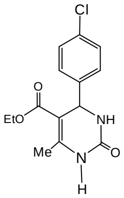
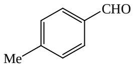
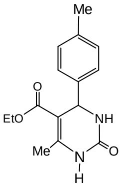
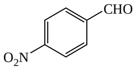
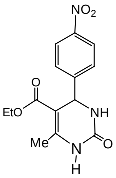
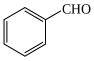
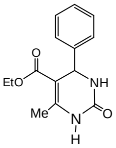
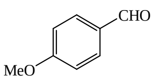
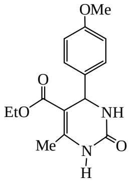
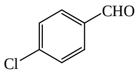
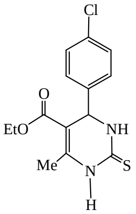
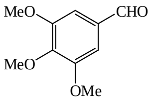
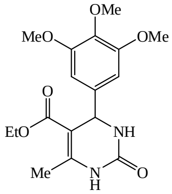
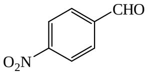
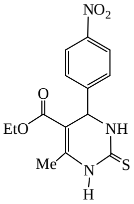
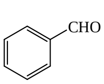
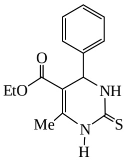
S.N.	Aldehyde	Product	Time (Min.)	Yields (%)	M.P.(^oC)
1			30	90	240
2			25	95	210
3			20	90	200
4			30	90	208
5			25	95	201

Table 2 continue

S.N.	Aldehyde	Product	Time (Min.)	Yields[a] (%)	M.P.(°C)
6			30	90	202
7			40	87	180
8			35	90	234
9			30	85	230
10			25	92	207

[a] Isolated Yields

CONCLUSION

In conclusion this heterogeneous solid acid catalyst Fe_3O_4 was prepared by modifying nanomaterial can be used as an efficient and recoverable catalyst for condensation of aromatic aldehydes with ethylacetoacetate and urea/thiourea to prepare medicinally important compound 3, 4-dihydropyrimidin- (2H)-ones in large scale. High yields, easy work-up and reusability of the catalyst are the most significant aspects of this method.

Spectral analysis: 4-(4-Hydroxyphenyl)-6-ethyl-5-methoxycarbonyl-3, 4-dihydropyrimidin-2(1H)-one (Entry 1): White solid; yield 90% mp: 240°C; IR (KBr, V_{max} cm^{-1}): 3264, 3227, 3110, 2976, 1686, 1663, 1605, 1511, 1455; ^{1}H NMR ($CDCl_3$, ppm)*:* δ 9.32 (s, 1H, OH), 9.11(s, 1H,NH),7.61 (s, 1H,NH), 5.91 (s, 1H), 5.37 (d, *J*= 2.9 Hz, 1H), 4.09 (s, 3H), 2.33 (m, 2H), 1.17 (t, *J)* 7.4 Hz, 3H); MS *m*/*z*= 275 (M +); Anal. Calcd for $C_{14}H_{16}N_2O_4$ (276): C= 60.86%; H= 5.84%; N, 10.14%, O=23.16%; Found: C= 56.74%; H= 5.70%; N= 10.05%, O=23.10%

4-(4-Chlorophenyl)-6-ethyl-5-methoxycarbonyl-3, 4-dihydropyrimidin-2(1H)-one (Entry 2): White solid; yield 95%; mp 210°C; IR (KBr, V_{max}cm^{-1}): 3241, 3119, 2980, 1720, 1647; ^{1}H NMR ($CDCl_{3,}$ ppm): δ 8.14 (s, 1H), 7.37 (m, 4H), 5.91 (s, 1H), 5.37 (d, *J*= 2.9 Hz, 1H), 4.09 (s, 3H), 2.33 (m, 2H), 1.17 (t, *J)* 7.4 Hz, 3H); MS(*m*/*z*, %): 293 (M$^+$); elemental analysis Calcd for M.F. $C_{14}H_{15}N_2O_3Cl$ (294.08): C= 57.05%; H= 5.13%; N= 9.50%, O= 16,29%, Found: C= 56.94%; H= 5.03%; N= 9.40%, O=16,20%.

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