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One-pot synthesis of 3, 4-dihydropyrimidin-2(1H)-ones using Cerium chloride as a catalyst and Its Biological Activity

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A B S T R A C T

An efficient synthesis of 3,4-dihydropyrimidinones using Cerium chloride hepta hydrate as a catalyst from an aldehyde, beta-keto ester and urea in ethanol is described. Compared to the classical Biginelli reaction conditions, this new method consistently has the advantage of good yields (56–97%).and its biological activity was determined by using Disc Diffusion method.

Keywords: Biginelli reaction, dihydropyrimidinones, cerium chloride heptahydrate, one-pot condensation, Anti microbial and Anti fungal Activity, Synthesis.

A R T I C L E I N F O

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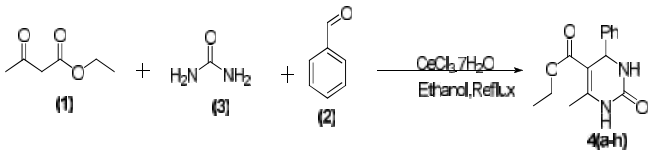
1. Introduction

During recent years, the use of Cerium (III) compounds as catalysts or promoters in organic synthesis has attracted great interest from many chemists [1]. Cerium additives or complexes can enhance the reactivity and selectivity of many types of reaction, such as Luche reduction [2] of alpha, beta-unsaturated carbonyl compounds has become a popular method in organic synthesis, where $CeCl_3 \cdot 7H_2O$ is used in conjunction with sodium boro hydride. It is also

used itself as a Lewis acid, for example as a catalyst in friedal crafts alkylation reactions [3]. This acid-catalyzed, three-component reaction between an aldehyde, a ß-ketoester and urea constitutes a rapid and facile synthesis of dihydropyrimidones, which are interesting compounds with a potential for pharmaceutical application.

Scheme 1:



In the past decade, dihydropyrimidine derivatives have exhibited important pharmacological properties, e.g. as the integral backbones of several calcium channel blockers, antihypertensive agents, alpha-1a-antagonists, and neuropeptide Y (NPY) antagonists [4]. Therefore, the discovery of milder and practical routes for the synthesis of dihydropyrimidin-2(1H)-ones by the Biginelli reaction continues to attract the attention of researchers. Several improved procedures for the preparation of DHPMs ('Biginelli compounds') have recently been reported, either by modifica tion of the classical one-pot Biginelli approach itself [5–9] or by the development of novel, but more complex multistep strategies [10].

In addition, several combinatorial approaches towards -dihydropyrimidin-2(1H)-ones have been advanced using solid-phase or fluorous phase reaction conditions [11]. Here we wish to report our preliminary investigation concerning the direct synthesis of 3,4-dihydropyrimidin-2(1H)-ones. In this paper, we describe a general and practical route for the Biginelli cyclo condensation reaction using Cerium chloride Hepta hydrate as the catalyst [12] This is a novel, one-pot combination that not only preserves the simplicity of Biginelli's one-pot reaction but also consistently produces excellent yields of the dihydropyrimidin-2(1H)-ones.

In the presence of the $CeCl_3 \cdot 7\,H_2O$ (5 mmol), the reaction of beta-keto ester (1) (10 m.mol), aldehyde (2) (10 m.mol), and urea (3) (15 mmol) was carried out in a one-pot condensation employing refluxing EtOH, which has previously been employed successfully in the Biginelli condensation as solvent. After the reaction was completed, the dihydropyrimidinones 4(a–h) precipitated from the reaction mixture. in the Biginelli reaction, dihydropyrimidin-2(1H)-ones (Table 1).

2. Materials and Methods:

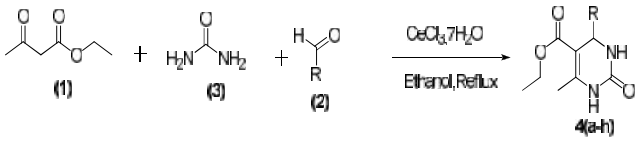
Melting points were determined in open-end capillaries and are uncorrected. Compounds were checked for their purity by TLC on silica gel G plates and spots were located by iodine vapors. 1H NMR spectra were recorded on BRUKER ADVANCE II 400 NMR Spectrometer using TMS as internal standard. The mass spectra were obtained on a JEOL 5x102/DA-6000 mass spectrometer. The IR spectra were recorded on Perkin-Elmer spectrum RX IFT-IR System using KBr pellets.

Experimental section:

General Methods: Unless otherwise noted, all reactions were carried out in oven dried glassware under an atmosphere of nitrogen and distilled solvents were transferred by syringes. Solvents and reagents were purified according to the standard procedure prior to use. Evaporation of organic solutions was achieved by rotary evaporation with a water bath temperature below 40°C. Product purification by flash column chromatography was accomplished using silica gel 60 (0.010-0.063 nm).

Technical grade solvents were used for chromatography and distilled prior to use. NMR spectra were recorded at room temperature on 300 MHz Bruker ACF 300 and 400 MHz Bruker DPX 400 NMR spectrometers. The residual solvent signals were taken as the reference (2.50 ppm for 1H NMR spectra and 39.5 ppm for ^{13}C NMR spectra in DMSO-d_6, 7.26 ppm for ^{1}H NMR spectra and 77.0 ppm for ^{13}C NMR spectra in $CDCl_3$). Chemical shift (δ) is referred in terms of ppm, coupling constants (J) are given in Hz. Following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad signal.

Synthesis of dihydropyrimidinone derivatives from substituted aromatic aldehydes: (4a-4h)



R = Ph, 2-Bromo Phenyl, 3 Bromo Phenyl, 4-Bromo Phenyl, 2-Chloro phenyl, 3-chloro phenyl, 4-chloro phenyl, 4-Nitro phenyl, 4-methyl phenyl, 4-methoxy phenyl.

General procedure $CeCl_3 \cdot 7\,H_2O$ mediated preparation of pyrimidines4 (a-j): A solution of beta -keto ester (1, 10 mmol), the appropriate aldehyde (2, 10 mmol), urea (3, 15 mmol), $CeCl_3 \cdot 7H_2O$ (1.85 g, 5 mmol) and conc. HCl (1–2 drops) in EtOH (20 mL) was heated under reflux for 5 h. After cooling, the reaction mixture was poured onto 50 g of crushed ice. Stirring was continued for several minutes; the solid products were filtered, washed with cold water (2×50 mL) and a mixture (1:1) of ethanol–water (2×20 mL) and subsequently dried. All the products which were characterized by IR and ^{1}H, ^{13}C NMR spectral data and their mps compared with literature reported melting points.

Spectral Details of Di hydro pyrimidinone Derivatives:

Ethyl 6-methyl-2-oxo-4-phenyl-1, 2, 3, 4-tetrahydro-pyrimidine-5-carboxylate (4a)

The title compound was prepared according to the general procedure. The product was obtained as a white powder; (quantitative yield); m.p. 202-204 °C;

^{1}H NMR (300 MHz, DMSO-d_6): δ in ppm = 9.19 (s, 1H, NH), 7.73 (s, 1H, NH), 7.35-7.21 (m, 5H, Ar-H), 5.15 (d, 1H, J=3.2Hz, C**H**-Ph), 3.98 (q, 2H, J=7.1Hz, C**H_2**-CH_3), 2.25 (s, 3H, CH_3), 1.09 (t, 3H, J=7.1Hz, CH_2-C**H_3**);

^{13}C NMR (75 MHz, DMSO-d_6): δ in ppm = 165.8 (EtO**C**=O), 152.6 (C=O), 148.8 (Me(NH)**C**=C), 145.3 (C-Ar), 128.8 (C-Ar), 127.7 (C-Ar), 126.7 (**C**-Ar), 99.7 (C=**C**(CH)CO_2Et), 59.6 (**C**H_2-CH_3), 54.4 (**C**H-Ph), 18.2

(CH_3), 14.5 (CH_2-**C**H_3); FT-IR (KBr): ν- = 3256, 3121, 2945, 1730, 1703, 1647, 1464, 1290, 1226, 1090, 756 cm^{-1}; ESI m/z $[M+1]^+$: calcd for $C_{14}H_{16}N_2O_3$: 261.1239, found: 261.1237.

Ethyl 4-(2-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6):

δ in ppm = 9.28 (s, 1H, NH), 7.69 (s, 1H, NH), 7.58-7.16 (m, 4H, Ar-H), 5.61 (d, 1H, J=2.4Hz, C**H**-Ar), 3.89 (q, 2H, J=7.1Hz, C**H$_2$**-CH_3), 2.30 (s, 3H, CH_3), 0.99 (t, 3H, J=7.1Hz, CH_2-C**H$_3$**);

^{13}C NMR (75 MHz, DMSO-d_6):

δ in ppm = 165.4 (EtO-**C**=O), 151.7 (C=O), 149.7 (Me(NH)**C**=C), 143.8 (C-Ar), 133.1 (C-Ar), 129.8 (C-Ar), 129.2 (C-Ar), 128.9 (C-Ar), 122.7 (CAr), 98.7 (C=**C**(CH)CO_2Et), 59.5 (CH_2-CH_3), 54.5 (**C**H-Ar), 18.1 (CH_3), 14.4 (CH_2-**C**H_3);

FTIR (KBr): ν = 3221, 3099, 2978, 1701, 1643, 1445, 1285, 1225, 1092, 746 cm^{-1};

ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}BrN_2O_3$: 339.0344, found: 339.0343.

Ethyl 4-(3-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4c)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6):

δ in ppm = 9.27 (s, 1H, NH), 7.79 (s, 1H, NH), 7.47-7.23 (m, 4H, Ar-H), 5.15 (d, 1H, J=3.2Hz, C**H**-Ar), 4.00 (q, 2H, J=7.1Hz, C**H$_2$**-CH_3), 2.26 (s, 3H, CH_3), 1.10 (t, 3H, J=7.1Hz, CH_2-C**H$_3$**).

^{13}C NMR (75 MHz, DMSO-d_6):

δ in ppm = 165.6 (EtO**C**=O), 152.4 (C=O), 149.4 (Me(NH)**C**=C), 148.0 (C-Ar), 131.3 (C-Ar), 130.6 (C-Ar), 129.6 (C-Ar), 125.7 (C-Ar), 122.0 (C-Ar), 99.1 (C=**C**(CH)CO2Et), 59.8 (**C**H_2-CH_3), 54.1 (**C**H-Ar), 18.3 (CH_3), 14.5 (CH_2-**C**H_3).

FT-IR (KBr): ν- = 3238, 3098, 2930, 1709, 1653, 1474, 1285, 1224, 1092, 768 cm^{-1};

ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}BrN_2O_3$: 339.0344, found: 339.0347.

Ethyl 4-(4-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4d)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6):

δ in ppm = 9.24 (s, 1H, NH), 7.76 (s, 1H, NH), 7.52 (d, 2H, J=8.4Hz, Ar-H), 7.19 (d, 2H, J=8.4Hz, Ar-H), 5.12 (d, 1H, J=3.2Hz, C**H**-Ar), 3.98 (q, 2H, J=7.1Hz, C**H$_2$**-CH_3), 2.24 (s, 3H, CH_3), 1.09 (t, 3H, J=7.1Hz, CH_2-C**H$_3$**)

^{13}C NMR (75 MHz, DMSO-d_6):

δ in ppm = 165.8 (EtO**C**=O), 152.5 (C=O), 149.3 (Me(NH)**C**=C), 144.8 (C-Ar), 131.9 (C-Ar), 129.1 (C-Ar), 120.9 (C-Ar), 99.3 (C=**C**(CH)CO2Et), 59.8 (**C**H2-CH3), 54.1 (**C**H-Ar), 18.4 (CH3), 14.6 (CH_2-**C**H_3);

FT-IR (KBr): ν- = 3246, 3111, 2949, 1701, 1649, 1458, 1288, 1221, 1088, 781 cm^{-1}; ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}BrN_2O_3$: 339.0344, found: 339.0336.

Ethyl 4-(2-chlorophenyl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate (4e)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6):

δ in ppm = 9.25 (s, 1H, NH), 7.68 (s, 1H, NH), 7.40-7.24 (m, 4H, Ar-H), 5.61 (d, 1H, J=2.7Hz, C**H**-Ar), 3.87 (q, 2H, J=7.1Hz, C**H$_2$**-CH_3), 2.28 (s, 3H, C**H$_3$**), 0.97 (t, 3H, J=7.1Hz, CH_2-C**H$_3$**).

^{13}C NMR (75 MHz, DMSO-d_6):

δ in ppm = 165.4 (EtO**C**=O), 151.8 (C=O), 149.8 (Me(NH)**C**=C), 142.2 (C-Ar), 132.1 (C-Ar), 129.8 (C-Ar), 129.5 (C-Ar), 129.2 (C-Ar), 128.2 (C-Ar), 98.3 (C=**C**(CH)CO_2Et), 59.5 (**C**H_2-CH_3), 51.9 (**C**H-Ar), 18.1 (CH_3), 14.4 (CH_2-**C**H_3)

FT-IR (KBr): ν- = 3354, 3223, 3107, 2978, 1694, 1639, 1450, 1368, 1230, 1098, 744 cm^{-1};

ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}ClN_2O_3$: 295.0849, found: 295.0850.

Ethyl 4-(3-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4f)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6): δ in ppm = 9.26 (s, 1H, NH), 7.78 (s, 1H, NH), 7.37-7.18 (m, 4H, Ar-H), 5.14 (s, 1H, C**H**-Ar), 3.99 (q, 2H, J=6.8Hz, C**H$_2$**-CH_3), 2.25 (s, 3H, CH_3), 1.09 (t, 3H, J=6.8Hz, CH_2-CH_3);

^{13}C NMR (75 MHz, DMSO-d_6): δ in ppm = 165.6 (EtO**C**=O), 152.4 (C=O), 149.4 (Me(NH)**C**=C), 147.7 (CAr), 133.4 (C-Ar), 131.0 (C-Ar), 127.7 (C-Ar), 126.7 (C-Ar), 125.4 (C-Ar), 99.1 (C=**C**(CH)CO2Et), 59.8 (**C**H_2-CH_3), 54.1 (**C**H-Ar), 18.3 (CH_3), 14.5 (CH_2-**C**H_3)

FT-IR (KBr): ν- = 3250, 3113, 2940, 1711, 1647, 1475, 1429, 1223, 1090, 768 cm^{-1};

ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}ClN_2O_3$: 295.0849, found: 295.0846.

Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4g)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6):

δ in ppm = 9.24 (s, 1H, NH), 7.77 (s, 1H, NH), 7.39 (d, 2H, J=8.5Hz, Ar-H), 7.25 (d, 2H, J=8.5Hz, Ar-H), 5.14 (d, 1H, J=3.2Hz, C**H**-Ar), 3.98 (q, 2H, J=7.1Hz, C**H$_2$**-CH_3), 2.25 (s, 3H, CH3), 1.09 (t, 3H, J=7.1Hz, CH_2-C**H$_3$**);

^{13}C NMR (75 MHz, DMSO-d_6):

δ in ppm = 165.7 (EtO**C**=O), 152.4 (C=O), 149.2 (Me(NH)**C**=C), 144.3 (C-Ar), 132.2 (C-Ar), 128.9 (C- Ar), 128.6 (C-Ar), 99.3 (C=**C**(CH)CO2Et), 59.7 (**C**H_2-CH_3), 53.9 (**C**H-Ar), 18.3 (CH3), 14.5 (CH_2-**C**H_3);

FT-IR (KBr): ν- = 3237, 3117, 2978, 1701, 1647, 1460, 1288, 1221, 1088, 781 cm-^{1};

ESI m/z $[M+1]^+$: calcd for $C_{14}H_{15}ClN_2O_3$: 295.0849, found: 295.0843.

Ethyl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4h)

The title compound was prepared according to the general procedure.

^{1}H NMR (300 MHz, DMSO-d_6): δ in ppm = 9.35 (s, 1H, NH), 8.22 (d, 2H, J=8.7Hz, Ar-H), 7.89 (s, 1H, NH), 7.50

(d, 2H, J=8.7Hz, Ar-H), 5.27 (d, 1H, J=3.3Hz, C**H**-Ar), 3.99 (q, 2H, J=7.1Hz, C**H$_2$**-CH$_3$), 2.27 (s, 3H, CH$_3$), 1.10 (t, 3H, J=7.1Hz, CH$_2$-C**H$_3$**);

^{13}C NMR (75 MHz, DMSO-d$_6$):

δ in ppm = 165.5 (EtO**C**=O), 152.5 (C=O), 152.2 (Me(NH)**C**=C), 149.9 (C-Ar), 147.2 (C-Ar), 128.1 (C-Ar), 124.3 (C-Ar), 98.6 (C=**C**(CH)CO2Et), 59.9 (**C**H$_2$-CH$_3$), 54.1 (**C**H-Ar), 18.3 (CH$_3$), 14.5 (CH2-**C**H3);

FT-IR (KBr): ν- = 3238, 3123, 2986, 1730, 1705, 1645, 1522, 1348, 1219, 1096, 854, 783 cm^{-1};

ESI m/z [M+1]$^+$: calcd for $C_{14}H_{16}N_3O_5$: 306.1090; found: 306.1087.

Anti-Microbial Activity

Media and chemicals

Nutrient Broth, Nutrient agar and 5 mm diameter antibiotic assay were obtained from Hi-Media Laboratories Limited, India. Barium chloride dehydrate GR, concentrated sulphuric acid GR, Dimethyl sulphoxide GR, Sodium chloride AR and Potassium dichromate were obtained from Ranbaxy Laboratories Ltd, Chemical Division, India. The standard bacterial and fungal strains were procured from National Centre from Cell Science (NCCS), Pune, India. The bacterial included two Gram positive bacterial isolates Staphylococcus aureus NCCS 2079 and Bacillus cereus NCCS 2106 and two Gram negative bacterial isolates Escherichia coli NCCS2065 and Pseudomonas aeruginosa NCCS 2200. The fungicidal organisms included were Aspergillus nigeri NCCS 1196 (AN) and Candida albicans NCCS 3471(CA). The bacteria were grown and maintained on nutrient agar (Hi-Media, Mumbai) and were subculture when needed.

Glasswares and Apparatus

Glass petri dish, Glass tubes, Beakers, Erlenmeyer flasks, Bacterial loop and measuring cylinder. All the glass wares were of Borosilicate grade. Digital electronics balance (Shankar Scientific supplies, India), Yorco Horizontal Laminar air flow bench (Yorco sales Pvt. Ltd, New Delhi, India), Ausco incubator, Zone reader (Cintex industrial Corporation, India), hot air oven, autoclave and UV/Visible spectrophotometer (Shimadzu corporation, Japan).

Antibacterial activity

The antibacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacterial screened were Staphylococcus aureus NCCS 2079 (SA) and Bacillus cereus NCCS 2106 (BC). The gram-negative bacterial screened were Escherichia coli NCCS 2065 (EC) and Pseudomonas aeruginosa NCCS 2200(PA). The synthesized compounds were used at the concentration of 250 µg/ml and 500 µg/ml using DMSO as a solvent. The amoxicillin 10 µg/disc and Streptomycin 30 µg/disc were used as a standard (Himedia laboratories limited, Mumbai).

Disc Diffusion Method

A suspension of Staphylococcus aureus (SA) was added to sterile nutrient agar at 45ºC. The mixture was transferred to sterile petri dishes to give a depth of 3 to 4 mm and allowed to solidify. Precautions were observed to reduce uniform layer of medium on the plate. Sterile discs 5 mm in diameter (made from Whatman Filter paper) were immersed in the solutions of synthesized compounds (250 µg/ml) and maintain an untreated control sample for comparison. Leave the plates to stand for 1 hour at room temperature as a period of pre incubation diffusion to minimize the effects of variations in different time. Then the plates were incubated at 37ºC for 24 hours and observed for antibacterial activity. The diameter of the zone of inhibition was measured for each plate in which the zone of inhibition was observed. The average zone of inhibition was calculated and compared with that of standard. A similar procedure was adopted for studying the antibacterial activity against the other organisms.

Antifungal activity

The antifungal activity of synthesized compounds were studied by disc diffusion method against the organisms of Aspergillus nigeri NCCS 1196 (AN) and Candida albicans NCCS 3471(CA).

Compounds were treated at the concentrations of 250 µg/ml using DMSO as a solvent. The standard used was Ketaconazole 50 µg/ml and Griseofulvin 50 µg/ml against both the organisms.

Disc Diffusion Method

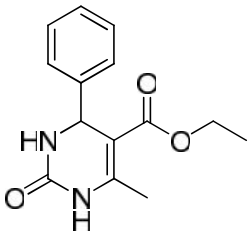
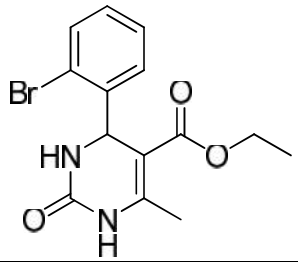
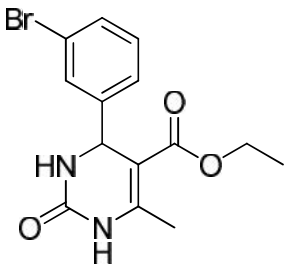
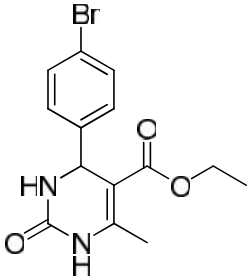
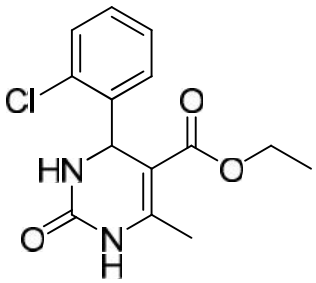
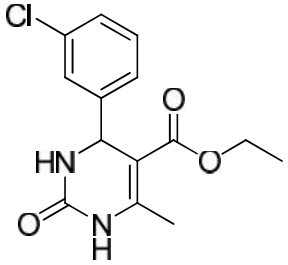
A suspension of Aspergills nigeri NCCS 1196 (AN) was added 5 to a sterile sabouraud dextrose agar at 45ºC. The mixture was transferred to sterile petri dishes and allowed to solidify. Sterile discs 5 mm in diameter (made from Whatmann Filter paper) immersed in the solutions of synthesized compounds and control were placed on the surface of agar medium with forceps and pressed gently to ensure even contact. Leave the plates to stand for 1 hour at room temperature as a period of pre-incubation diffusion to minimize the effects of variation at 37ºC for 13 hours and observed for antibacterial activity. The diameters of the zone of inhibition were measured for the plates in which the zone of inhibition was observed. The average zone of inhibition was calculated with that of standard. The tetra hydro pyrimidine derivates containing P-Cl and P-Br (4d,4g) and Nitro(4h) showed more activity than other substituent's the order of activity was 4d>4g> 4h>4c> 4f>4b>4e>4a.

3. Results and Discussion

IR spectra: The characteristic absorption peaks were observed for all relevant groups. The absorption peaks around 3230-3250 cm^{-1} indicates –NH Stretching frequency, 3100 Aromatic CH Stretching, vibrations were observed all other relevant groups' absorption were observed for all the synthesized compounds.

NMR spectra: Aromatic protons were observed 6.68- 8.13 δ ppm. 3.8 ppm **H**C-O proton was observed at for all the synthesized compounds. 165 ppm for Ester carbonyl carbon, 55 ppm for CH3-**C**H2-O was observed in ^{13}C NMR for all synthesized compounds. Readily available starting materials and simple synthesizing procedures make this method is very attractive and convenient for the synthesis of quinazoline derivatives .Formation of products was confirmed by recording their Elemental analysis, ^{1}H NMR, ^{13}C, FT-IR, mass spectra. The Elemental analysis data showed good agreement between the experimentally determined values and the theoretically calculated values with in ±0.4%.

Table 1: DHPMs 4(a-j) synthesized using $CeCl_3 \cdot 7H_2O$

S.NO	Product structure	Yield (%)	M.P.(degrees)	Colour
4a		55	203	white
4b		53	207	pale green powder
4c		90	196-197	pale green powder
4d		93	225-226	white powder
4e		89	223-224	white powder
4f		92	200-201	white powder

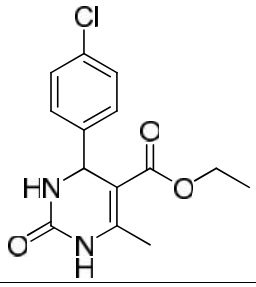
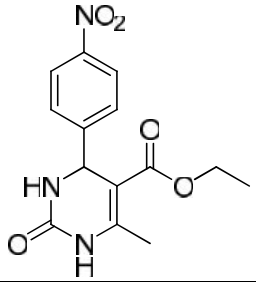
4g		87	217-218	white powder
4h		90	200-201	yellow powder

Table 2: Antimicrobial activity of Tetrahydropyrimidine Derivatives (4a-h):

S.NO	Compound	Zone of inhibition (mm)					
		Antibacterial Activity				Antifungal Activity	
		Gram+ve		Gram-ve			
		SA	BC	EC	PA	AN	CA
1	4a						
2	4b	13	14	15	17	14	17
3	4c	15	17	16	18	16	19
4	4d	19	20	19	21	20	24
5	4e	11	14	14	16	13	15
6	4f	14	15	15	18	15	18
7	4g	17	19	19	20	18	22
8	4h	16	18	17	19	17	20
Amoxicillin		22	25	21	23	-	-
Streptomycin		27	29	25	27	-	-
Ketaconazole		-	-	-	-	22	25
Griseofulvin		-	-	-	-	24	27

4. Conclusion

In conclusion, we have developed a simple and efficient method for the direct preparation of substituted dihydropyrimidinones using Cerium chloride hepta hydrate as a catalyst in good yields from readily available starting materials. And its derivatives were showed good anti microbial activity.

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6. References

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