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Synthesis and oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1*H*)-one by Ce $(SO_4)_2.4H_2O$

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ABSTRACT

Ceric sulfate tetra hydrate in aqueous acetic acid acts as an efficient oxidant for the oxidative dehydrogenation of 3, 4-dihydropyrimidin-2(1*H*)-ones. Aromatic aldehyde and formaldehyde are effectively condensed with ethyl or methyl acetoacetate and urea by modifying Biginelli process. The synthesized 3, 4-dihydropyrimidin-2-(1*H*)-ones are purified by recrystallization and fully characterized by various analytical techniques before oxidation. Ce $(SO_4)_2.4H_2O$ and 3, 4-dihydropyrimidin -2- (1*H*)-ones ratio as 1: 2 was found to be the most favorable condition for oxidative dehydrogenation. The reversible conversion of Ce^{3+} to Ce^{4+} is an electron transfer process achieved by the oxygen present in the air which plays an important role in oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1*H*)-ones. For this oxidation a radical cation mechanism is proposed. The oxidation products were isolated in high purity and good to moderate yields. All the oxidized 3, 4-dihydropyrimidin-2-(1*H*)-ones are fine crystalline substances with sharp physical constants.

Keywords: 3, 4-dihydropyrimidin-2-(1*H*)-ones, Oxidative dehydrogenation, ceric sulfate tetra hydrate, aqueous acetic acid, Electron transfer

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INTRODUCTION

3,4-Dihydropyrimidin-2(1*H*)-ones (DHPMs) belong to an important class of heterocyclic compounds that have attracted interest due to their pharmacological and biological properties, such as antihypertensive, calcium channel blocking, alpha-1a-antagonism, neuropeptide Y(NPY) antagonism, antitumor, antibacterial, and anti-inflammatory activities[1-6]. The pyrimidine derivative MKC-442 is already in clinical trials and similar compounds are expected to inhibit the HIV virus [7]. Nucleosides containing the 5-substituted pyrimidine moiety have been demonstrated to inhibit growth of murine mammary carcinoma and HIV virus [8]. Pyrimidine based molecules with extended π-systems exhibited interesting fluorescent properties [9]. Synthetic strategies towards the dihydro pyrimidine nucleus involve one-pot to multistep approaches. The classical synthesis of DHPM nucleus, condensation of ethyl acetoacetate, benzaldehyde and urea under strong acidic condition was low yielding (20-50%) [10]. Subsequent multistep synthesis produced somewhat higher yields but lacked the simplicity of one-pot, one-step procedure [1]. Consequently, for the synthesis of DHPMs many improved procedures have been reported. Many of these procedures effectively employed catalyst such as $BF_3{\cdot}Et_2O$ [4] in combination with transition metal salts and a proper proton source.

The development of efficient method for the oxidation of various organic compounds is focus of increasing interest [11-15]. Oxidation of DHPMs is important because of formation of core pyrimidin-2(1*H*)-ones, which are important for the pharmacological activity such as pyrimidine MKC-442, one of the most important classes of drugs for the treatment of the HIV virus [16]. Oxidation of 3, 4-dihydropyrimidin-2(1*H*)-ones to their corresponding pyrimidin-2(1*H*)-ones requires harsh reaction conditions and the yields are mostly poor, for example, variety of mild or powerful oxidants such as MnO_2, PCC, Chloranil, $KMnO_4$/clay, DDQ, $NaNO_2$/AcOH, Pd/C[17], $FeCl_3$[18], $RuCl_3/O_2$ in AcOH[19], CAN/AcOH[20], $Co(NO_3)_2$ - $6H_2O/K_2S_2O_8$[21] are used. But, however, these compounds are highly stable toward the above mentioned oxidizing reagents. None of these oxidations are efficient, some use excessively corrosive or harmful reagents, strong reaction conditions, or these are difficulties in product isolation, and/or mostly low yields. Therefore, an alternative procedure is needed. In the present work we report the oxidation of 3, 4-dihydropyrimidin-2(1*H*)-ones to their corresponding pyrimidine derivatives, using molecular Ce $(SO_4)_2$. $4H_2O$ in air. Previously we reported that Ce $(SO_4)_2$. $4H_2$ O works very smoothly for oxidative dehydrogenation of substituted dihydropyridine derivatives in excellent yield [22] and we thought that Ce $(SO_4)_2$. $4H_2O$ same reagent can be used for oxidation of 3, 4-dihydropyrimidin-2(1*H*)-ones, therefore we used Ce $(SO_4)_2$. $4H_2O$ for oxidation.

MATERIALS AND METHODS

AR grade chemicals purchased from local companies were used without further purification. IR spectra were recorded on FT-IR 8400 Shimadzu Model.^{1}H NMR spectra were recorded on Varian Mercury, YH- 300 MHz spectrometer in $CDCl_3$ / DMSO and chemical shifts are recorded as delta in ppm units. The reaction products are identified by physical constant, IR

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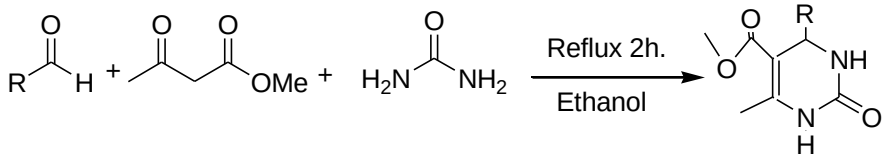
and NMR spectroscopy. The product obtained after work up was purified by recrystallzation from ethanol.

General procedure for synthesis of 4-substituted -5-carbomethoxy- 6 – methyl - 3, 4 - dihydropyrimidine -2-one.

A mixture of urea (24mmol), methyl/ethylacetoactate (20mmol) and aromatic aldehyde or formaldehyde (20mmol) in ethanol (25 mL) was taken in 100 mL round bottom flask and heated to reflux for 1 h. the reaction mixture was cooled to room temperature and poured in to crushed ice. The precipitated solid was filtered, washed with cold water 5 times and transferred in 100 mL beaker. The product was washed again with diethyl ether, dried over Na_2SO_4 and purified by recrystallization from ethanol **(Scheme 1)**.

Scheme 1: Synthesis of 3, 4 - dihydropyrimidin – 2 (1*H*) – ones



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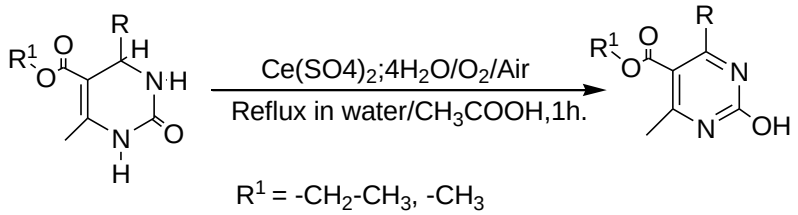
A typical Procedure for the oxidation of 4 - substituted – 5 -carbomethoxy - 6-methyl -3, 4-dihydropyrimidine -2-one.

A mixture of the 4-substituted-5-carbomethoxy-6-methyl-3, 4-dihydropyrimidine-2-one, (0.246 g, 1mmol) and Ceric sulfate tetra hydrate (0.808 g, 2mmol) in 20mL distilled water and 5 mL of acetic acid heated under reflux for 1h. The solution was cooled to room temperature and neutralized with aqueous $NaHCO_3$. It was then extracted with Et_2O (3x10mL) and dried over anhydrous Na_2SO_4. The solvent was removed by using rotavapour and the resulting crude product obtained was recrystallized from EtOH to give colorless crystals of the product (**Scheme 2)**.

Scheme 2: Oxidation of DHPMs into pyrimidine derivative



1-14 **1a – 14a**

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SPECTRAL DATA FOR SELECTED COMPOUNDS

Substrate 1:	Ethyl1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_8H_{12}N_2O_3$, mp 231°C, FTIR (KBr) 754,1097, 1236, 1708, 1741, 3136,3254 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.1 δ, t, (3H), 2.1 δ, s, (3H), 3.8 δ, s, (2H), 4.1 δ, q, (2H, J = 8 Hz), 7.0 δ, s, (1H broad), 8.8 δ, s, (1H broad).
Substrate 2:	Methyl1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_7H_{10}N_2O_3$, mp 254 °C, FTIR (KBr) 761, 1099, 1238, 1664, 1712, 3138,3254$cm^{-1,}$ ^{1}HNMR (DMSO) 2.2 δ, s, (3H), 3.6 δ, s, (3H), 3.9 δ, s, (2H), 7.0 δ, s(1H broad), 8.9 δ, s, (1Hbroad).
Substrate 3:	Ethyl1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate. M.F. $C_{14}H_{16}N_2O_3$, mp 202 °C, FTIR (KBr) 700, 779, 1093, 1224, 1699, 1726,3115, 3246 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.1 δ, t, (3H, J = 7 Hz), 2.2 δ, s, (3H), 4.1 δ, q, (2H J = 7 Hz), 5.2 δ, s, (1H), 6.1 δ, s, (1H broad), 7.2 δ, m, (5H) 8.5 δ, s, (1Hbroad).
Substrate 4:	Methyl1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate. M.F. $C_{13}H_{14}N_2O_3$, mp 208 °C, FTIR (KBr) 700, 752, 794, 1093, 1240, 1647,1695,3221,3333 $cm^{-1,}$ ^{1}HNMR (DMSO) 2.4 δ, s, (3H), 3.8 δ, s, (3H), 5.4 δ,s, (1H), 5.7 δ, s, (1H broad),7.3 δ, m ,(5H),8.0 δ, s, (1H broad).
Substrate 5:	Ethyl1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxopyrimidine-5-carboxylate. M.F. $C_{14}H_{15}N_3O_5$, mp 225 °C, FTIR (KBr) 758, 1093, 1230, 1456, 1645, 1693,3122, 3516 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.20 δ, t, (3H, J = 7 Hz), 2.37 δ, s, (3H),4.09 δ, q, (2H, J = 7 Hz), 5.7 δ, s, (1H broad), 7.3 δ, m, (4H), 9.3 δ, s, (1Hbroad).
Substrate 6:	Methyl1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxopyrimidine-5-carboxylate. M.F. $C_{13}H_{13}N_3O_5$, mp 272 °C, FTIR (KBr) 759, 1089, 1230, 1516, 1641, 1680,3119, 3558 $cm^{-1,}$ ^{1}HNMR (DMSO) 2.37 δ, s, (3H), 3.6 δ, s, (3H), 5.4 δ, d, (1H),7.3 δ, m, (4H), 7.3 δ, s, (1H), 9.3, s, (1H).
Substrate 7:	Ethyl1,2,3,4-tetrahydro-6-methyl-2-oxo-4-*p*-tolylpyrimidine-5-carboxylate. M.F. $C_{15}H_{18}N_2O_3$, mp 213 °C, FTIR (KBr) 778, 1095, 1236, 1650, 1710,3107, 3237 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.1 δ, t, (3H, J = 7 Hz), 2.4 δ, s, (3H), 3.8 δ,s, (3H) 4.1 δ, q , (2H J = 7 Hz),5.3 δ, s ,(1H),5.5 δ, s,(1H broad), 6.8 δ, d, (2H), 7.2 δ, d, (2H), 7.7 δ, s, (1Hbroad).
Substrate 8:	Methyl1,2,3,4-tetrahydro-6-methyl-2-oxo-4-*p*-tolylpyrimidine-5-carboxylate. M.F. $C_{14}H_{16}N_2O_3$, mp 204 °C, FTIR (KBr) 774, 1084, 1248, 1642, 1720, 3115,3240 $cm^{-1,}$ ^{1}HNMR (DMSO) 2.2 δ, s, (3H, J = 7 Hz), 3.8 δ, s, (3H) 3.9 δ, s, 3H), 5.3 δ, s ,(1H),5.5 δ, s,(1H broad), 6.8 δ, d, (2H),7.2 δ, d, (2H),

	7.7 δ, s, (1Hbroad).
Substrate 9:	Ethyl 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{14}H_{15}ClN_2O_3$, mp 211 °C, FTIR (KBr) 783, 1089, 1224, 1707, 1724, 3115, 3244 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.1δ, t, (3H, J = 7 Hz), 2.5 δ, s, (3H) 4.0 δ, q,(2H J = 7 Hz), 5.2 δ, s, (1H), 7.2 δ, d, (2H), 7.4 δ, d, (2H), 7.8 δ, s, (1Hbroad),9.3 δ, s,(1Hbroad).
Substrate 10:	Methyl 4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{13}H_{13}ClN_2O_3$, mp 205 °C, FTIR (KBr) 821, 1089, 1228, 1691, 1792,3115, 3365 $cm^{-1,}$ ^{1}HNMR (DMSO) 2.3 δ, s, (3H), 3.5 δ, s, (3H), 5.2 δ, s, (1H),7.2 δ, d, (2H), 7.4 δ, d, (2H), 7.8 δ, s, (1Hbroad), 9.3 δ, s, (1Hbroad).
Substrate 11:	Ethyl 1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{15}H_{18}N_2O_4$, mp 199 °C, FTIR (KBr) 765, 1094, 1235, 1650, 1710,3108, 3238 $cm^{-1,}$ ^{1}HNMR (DMSO) 1.1 δ, t, (3H J = 7 Hz), 2.3 δ s, (3H), 3.9 δ, s,(1H), 4.0 δ, q, (2H J = 7 Hz), 5.2 δ, s, (1H), 5.5 δ, s, (1Hbroad), 6.8, δ, dd, (2H),7.2 δ, dd,(2H). 7.5 δ, s, (1Hbroad).
Substrate 12:	Methyl 1, 2, 3, 4-tetrahydro-4-(4-methoxyphenyl)-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{14}H_{16}N_2O_4$, mp 192 °C, FTIR (KBr) 755, 1027, 1087, 1217, 1644, 1721,3110, 3235 cm^{-1}, ^{1}HNMR (DMSO) 2.2 δ, s, (3H), 3.8 δ s, (3H), 3.9 δ, s, (3H),5.3 δ, s, (1H), 5.5 δ, s, (1H broad), 6.8, δ, d d, (2H), 7.2 δ, d d, (2H).7.5 δ, s, (1Hbroad).
Substrate 13:	Ethyl 4-(furan-2-yl)-1, 2, 3, 4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{12}H_{14}N_2O_4$, mp 203 °C, FTIR (KBr) 757, 1011, 1085, 1236, 1635, 1707, 3313 cm^{-1}, ^{1}HNMR (DMSO) 2.2 δ, t, (3H J = 7 Hz), 3.6 δ s, (3H), 3.8 δ, q, (2H J = 7 Hz), 6.1 δ, dd, (2H J = 3 Hz), 6.3 δ, q, (1H J = 2 Hz), 7.6 δ, s, (1H), 7.8 δ, s, (1Hbroad), 9.3 δ, s, (1H broad).
Substrate 14:	Methyl 4-(furan-2-yl)-1, 2, 3, 4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate. M.F. $C_{11}H_{12}N_2O_4$, mp 208 °C, FTIR (KBr) 761, 1087, 1240, 1674, 1708, 3317 $cm^{-1,}$ ^{1}HNMR (DMSO) 2.1 δ, s, (3H), 3.8 δ s, (3H), 6.2, δ, dd, (2H J = 3 Hz), 6.4 δ, q, (1H J =2Hz). 6.5 δ, s, (1H), 7.8 δ, s, (1H broad), 9.3 δ, s,(1H broad).
Product 1a:	Ethyl-2-hydroxy-4-methylpyrimidine-5-carboxylate. M.F. $C_8H_{10}N_2O_3$, mp 251 °C, FTIR (KBr) 1097, 1234, 1708, 3254-3369 cm^{-1}, ^{1}HNMR (DMSO) 1.2 δ, t, (3H, J = 7Hz), 2.1 δ, s, (3H), 2.5 δ, q, (2H, J = 7 Hz),7.1δ, s, (1H), 8.9 δ, s, (1H broad).
Product 2a:	Methyl-2-hydroxy-4-methylpyridine-5-carboxylate.

	M.F. $C_7H_8N_2O_3$, mp 255 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1} ^{1}HNMR (DMSO) 2.2 δ, s, (3H), 3.6 δ, s, (3H), 7.0 δ, s, (1H), 8.9 δ, s,(1Hbroad).
Product 3a:	Ethyl 2-hydroxy-4-methyl-6-phenylpyrimidine-5-carboxylate. M.F. $C_{14}H_{14}N_2O_3$, mp 217 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1},^{1}HNMR (DMSO) 2.1 δ, t, (3H, J = 7Hz), 2.2 δ, s, (3H), 3.7 δ, q, (2H, J = 7Hz), 7.2 δ, m, (5H), 7.2, δ, s, (1H broad).
Product 4a:	Methyl 2-hydroxy-4-methyl-6-phenylpyrimidine-5-carboxylate. M.F. $C_{13}H_{12}N_2O_3$, mp196 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1},^{1}HNMR (DMSO) 2.2 δ, s, (3H), 3.8 δ, s, (3H), 7.1 δ, s, (1H broad), 7.2, δ, m,(5H).
Product 5a:	Ethyl 2-hydroxy-4-methyl-6-(3-nitrophenyl) pyrimidine-5-carboxylate. M.F. $C_{14}H_{13}N_3O_5$, mp 214 °C, FTIR (KBr) 1045, 1105, 1234, 1722, 3317-3495 cm^{-1}, ^{1}HNMR (DMSO) 0.9 δ, t, (3H, J = 7Hz), 2.3 δ, s, (2H), 4.0 δ, q,(2H, J = 7Hz), 6.6, δ, m, (1H, J = 8 Hz, J = 2 Hz). 6.8, δ, m, (2H, J = 8 Hz, J = 2 Hz). 7.2, δ, m, (1H, J = 2 Hz, J = 8 Hz).
Product 6a:	Methyl 2-hydroxy-4-methyl-6-(3-nitrophenyl) pyrimidine-5-carboxylate. M.F. $C_{13}H_{11}N_3O_5$, mp 225 °C, FTIR (KBr) 1095, 1232, 1710, 3095-3344 cm^{-1},^{1}H NMR (DMSO) 2.2 δ, s, (3H), 3.6 δ, s, (3H), 6.6, δ, m, (1H, J = 8 Hz, J = 2Hz). 6.8, δ, m, (2H, J = 8 Hz, J = 2 Hz). 7.2, δ, m, (1H, J = 8 Hz, J = 2Hz).
Product 7a:	Ethyl 2-hydroxy-4-methyl-6-*p*-tolylpyrimidine-5-carboxylate. M.F. $C_{15}H_{16}N_2O_3$, mp 184 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1},^{1}HNMR (DMSO) 1.1 δ, t, (3H, J = 7Hz), 1.3 δ, s, (3H), 2.3 δ, s, (3H), 4.0, δ, q,(2H, J = 7 Hz), 6.9, δ, m, (2H, J = 8 Hz). 7.2, δ, m, (2H, J = 8 Hz).
Product 8a:	Methyl 2-hydroxy-4-methyl-6-*p*-tolylpyrimidine-5-carboxylate. M.F. $C_{14}H_{14}N_2O_3$, mp 203 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1}, ^{1}HNMR (DMSO) 1.2 δ, s, (3H), 2.1 δ, s, (3H), 3.9 δ, s, (3H), 6.9, δ, m, (2H, J= 8 Hz). 7.2, δ, m, (2H, J = 8 Hz).
Product 9a:	Ethyl 4-(4-chlorophenyl)-2-hydroxy-6-methylpyrimidine-5-carboxylate. M.F. $C_{14}H_{13}Cl\ N_2O_3$, mp 182 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410 cm^{-1}, ^{1}HNMR (DMSO) 1.2 δ, t, (3H, J = 7Hz), 2.4 δ, s, (3H), 4.2, δ, q, (2H, J = 7 Hz), 5.4, δ, s, (1Hbroad). 6.9, δ, m, (2H, J = 8 Hz), 7.4, δ, m, (2H, J = 8Hz).
Product 10a:	Methyl 4-(4-chlorophenyl)-2-hydroxy-6-methylpyrimidine-5-carboxylate. M.F. $C_{13}H_{11}Cl\ N_2O3$, mp 215 °C, FTIR (KBr) 1089, 1226, 1707, 3389-3410cm^{-1}, ^{1}HNMR (DMSO) 2.2 δ, s, (3H), 3.9, δ, s, (3H), 5.0, δ, s, (1H broad),7.0, δ, m, (2H, J = 8 Hz), 7.4, δ, m, (2H, J = 8 Hz).
Product 11a:	Ethyl 2-hydroxy- 4-(4-methoxyphenyl)-6-methylpyrimidine-5-carboxylate. M.F. $C_{15}H_{16}N_2O_4$, mp 172 °C, FTIR (KBr) 1091, 1222, 1707, 3363-3433cm^{-1}, ^{1}HNMR (DMSO) 1.1 δ, t, (3H, J = 7Hz), 2.2 δ, s, (3H), 3.7, δ, s, (3H),4.0,

	δ, q, (2H, J =7 Hz), 6.9, δ, d, (2H, J = 8 Hz), 7.2, δ, d, (2H, J = 8 Hz),12.2, s, (1H broad).
Product 12a:	Methyl 2-hydroxy- 4-(4-methoxyphenyl)-6-methylpyrimidine-5-carboxylate. M.F. $C_{13}H_{12}N_2O_4$, mp 182 °C, FTIR (KBr) 1099,1246, 1710, 3113-3244cm^{-1},^{1}HNMR (DMSO) 2.5 δ, s, (3H), 3.5 δ, s, (3H), 3.8, δ, q, (3H), 6.8, δ, d, (2H, J= 8 Hz), 7.2, δ, d, (2H, J = 8 Hz), 9.2 δ, s, (1H broad). = 8 Hz), 7.4, δ, m, (2H, J = 8 Hz).
Product 13a:	Ethyl 4-(furan-2-yl)-2-hydroxy-6-methylpyrimidine-5-carboxylate. M.F.$C_{12}H_{12}N_2O_4$, mp 185 °C, FTIR (KBr) 1085, 1220, 1707, 3144-3313cm^{-1},^{1}HNMR (DMSO) 1.4 δ, t, (3H, J = 7Hz), 2.4 δ, s, (3H), 4.3, δ, q, (2H, J =7Hz), 6.1, δ, d, (1H, J = 3 Hz), 6.3, δ, d, (1H, J = 3 Hz), 7.4, d, (1H), 7.8, s, (1Hbroad).
Product 14a:	Methyl 4-(furan-2-yl)-2-hydroxy-6-methylpyrimidine-5-carboxylate. M.F.$C_{11}H_{10}N_2O_4$, mp 206 °C, FTIR (KBr) 1087, 1238, 1708, 3176-3317cm^{-1},^{1}HNMR (DMSO) 2.4 δ, s, (3H), 3.6, δ, s, (3H), 6.1, δ, d, (1H, J = 3 Hz), 6.3,δ, d, (1H, J = 3 Hz), 7.4, δ, m, (1H), 7.8, s, (1H broad).

RESULTS AND DISCUSSION

A series of DHPMs were synthesized by a simple catalyst free procedure. The synthesized DHPMs are oxidized by using ceric sulfate tetra hydrate. Initially this oxidation was carried out in presence of ceric sulfate tetra hydrate and water only, the reaction mixture contained the oxidized and unoxidized DHPMs; this may be due to less solubility of ceric sulfate in water at room temperature. Generally the ceric sulfate is soluble in acidic medium and warm condition. To enhance the solubility of ceric sulfate tetra hydrate. Initially 1mL acetic acid was added in reaction mixture and reaction was monitored by TLC. It was found that unoxidized DHPMs still remained in reaction mixture due to less solubility of ceric sulfate tetra hydrate. So we increased volume of acetic acid from 1mL to 5mL and reaction goes to complete oxidation smoothly. All 14 DHPMs are oxidized under the same reaction condition. In an optimized reaction condition various dihydropyrimidinones (1–14) were subjected to the oxidation reaction in the presence of ceric sulfate tetra hydrate in water along with 5mL acetic acid. TLC monitoring was followed until total disappearance of DHPMs. The results are summarized in **Table 1**.

The results presented in **Table 1** indicate that various DHPMs were converted to their corresponding pyrimidine derivative by using ceric sulfate tetra hydrate as oxidant in good yields.

The oxidation of DHPMs were also tried by using various molar ratio of 1, 4-DHPMs : ceric sulfate tetra hydrate (1:1, 1:1.5 and 1:2) in presence of water (20 mL) and acetic acid (5mL) under reflux condition. It was found that when 1:1and 1:1.5 molar ratios were taken a mixture of aromatized and unaromatized DHPMs were obtained. Finally when 2 equivalent of

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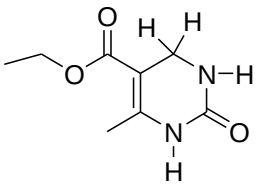
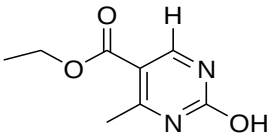
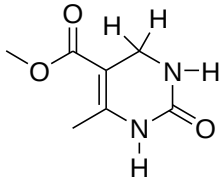
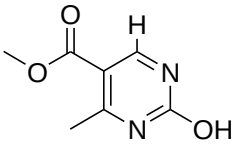
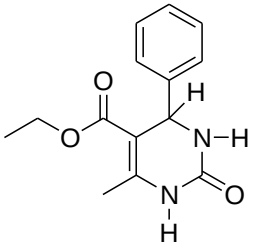
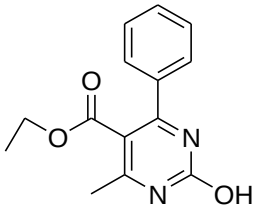
ceric sulfate and 5 mL of acetic acid were taken under reflux condition for one hour and the product obtained was studied by TLC, IR, ^{1}HNMR, to check for any unoxidized DHPMs, there was no trace amount of starting material in the product. Under this condition 14 DHPMs were successfully oxidized (**Table 1**.) It is important to note here that until now in the literature, the reactions for oxidation of DHPMs were carried out in a variety of reagent or catalyst in different medium. The main advantage of this method is that reaction is carried out in water. Other benefits are reaction condition is mild, clean product formation, use of lower molar ratio of DHPMs: ceric sulfate tetra hydrate (1:2) and good yield as compared to literature procedures [20, 21]. IR, ^{1}H NMR data gave useful information on the structural assignment of the products 1–14. However, to the best of our knowledge nobody has reported the oxidation of DHPMs using water as solvent which probably may be due to low solubility of both DHPMs and ceric sulfate which can be overcome by using 5 mL acetic acid. This process also reports the efficiency of this reagent towards the oxidation of DHPMs using ceric sulfate tetra hydrate in water along with 5mL acetic acid; fine solids with sharp melting points for these compounds were obtained (**Table 1**). The better efficiency of ceric sulfate tetra hydrate reagent over other reported reagents is thus justified.

Table 1: Oxidation of DHPMs into pyrimidine derivative.

Entry	Substrate	Product	Yield (%)	M.P. (°C)
1	 1	 1a	78	251
2	 2	 2a	77	255
3	 3	 3a	76	217

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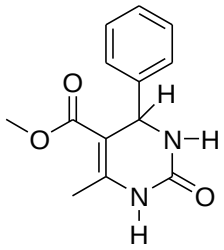
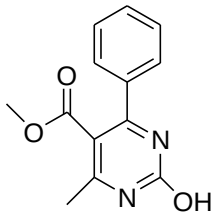
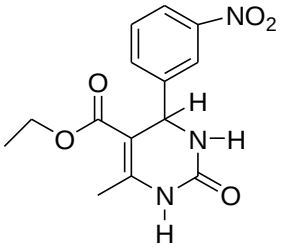
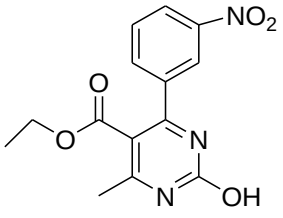
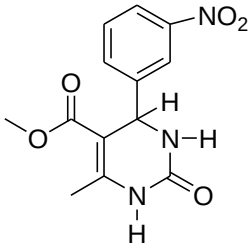
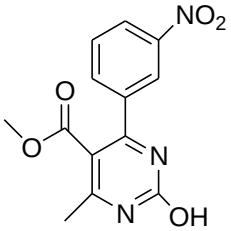
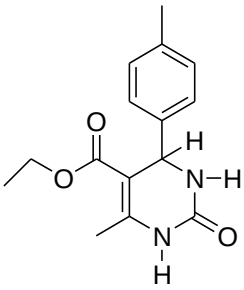
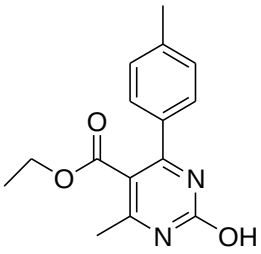
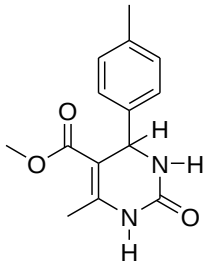
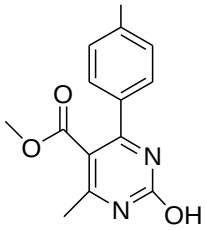
4	 4	 4a	79	196
5	 5	 5a	75	214
6	 6	 6a	77	225
7	 7	 7a	74	184
8	 8	 8a	76	203

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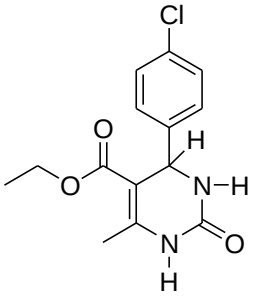
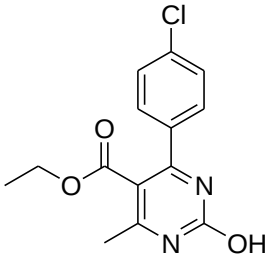
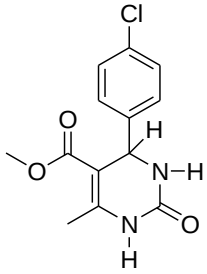
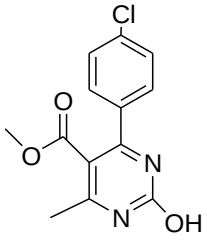
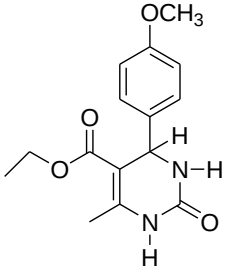
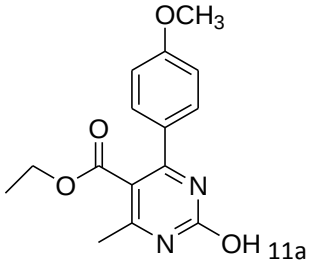
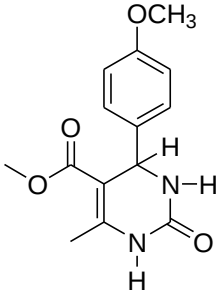
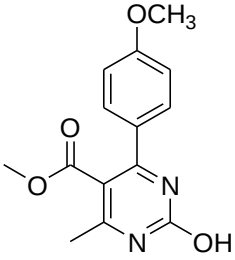
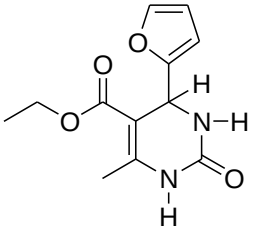
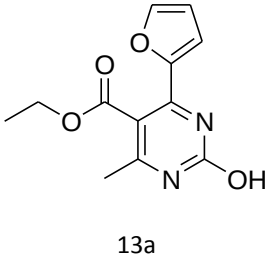
9	 9	 9a	77	182
10	 10	 10a	75	215
11	 11	 11a	76	172
12	 12	 12a	74	198
13	 13	 13a	77	185

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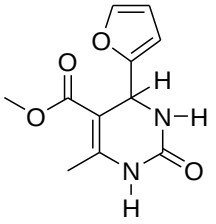
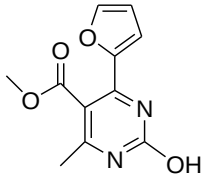
14	 14	 14a	75	206

Mechanism for oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1*H*)-one

A probable mechanism towards oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1*H*)-one is illustrated in figure1.

In the context of oxidative dehydrogenation the amide imidazole (I) tautomer may facilitate the reaction to generate 'N' radical cation (II). The generated electron may be utilized to reduce Ce^{4+} to Ce^{3+} and regenerated by oxygen from the air. The 'N' radical cation by loss of proton forms C_4 radical (III). Afterwards the Ce^{3+} ion gets reduced in second time and it converts C_4 radical into a cation (IV) which on losing a proton gives the product (V).

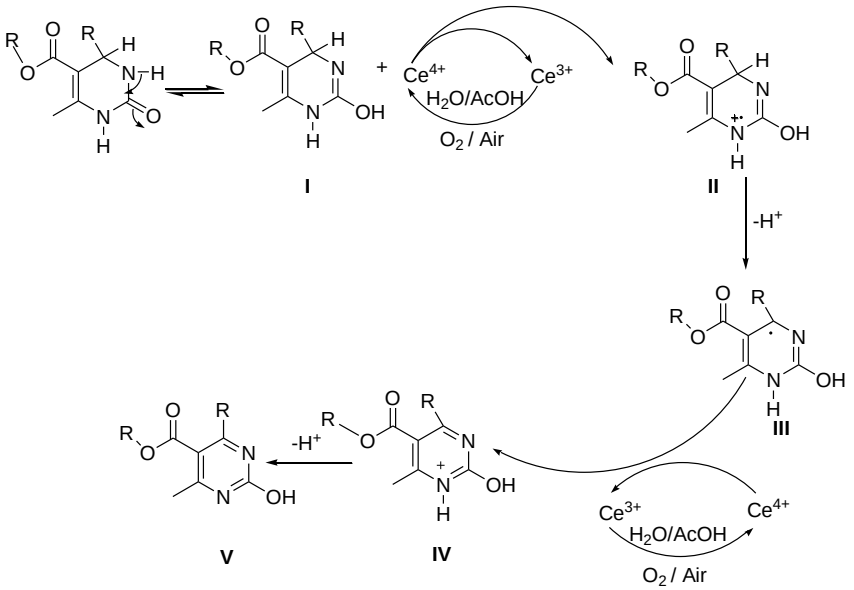


Figure 1: probable mechanism for oxidative dehydrogenation of 3, 4-dihydropyrimidin-2-(1H)-one.

CONCLUSIONS

Dihydropyrimidones of different groups are prepared by modified procedure of Biginelli reaction. A clean oxidative dehydrogenation of 3, 4 – dihydropyrimidin -2(1*H*)-ones has been achieved by Ce $(SO_4)_2.4H_2O$ in aqueous acetic acid to good yields only in one hour .The solubility of both DHPMs and ceric sulfate tetra hydrate was enhanced by using 5mL acetic acid. Substituted DHPMs: Ce $(SO_4)_2.4H_2O$ ratio as 1:2 in acetic acid and water was found to be the

best with 100 % conversion into products. The reversible conversion of Ce^{3+} to Ce^{4+} is an electron transfer process achieved by the oxygen present in the air, due to which no external oxidant is required in oxidative dehydrogenation which proceeds via 'N' radical cation.

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