

Synthesis and Characterization of Two 3,4-Dihydropyrimidinone Derivatives

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Abstract

In this study we have successfully synthesis and characterization two of [3,4-dihydropyrimidin-2-(1H) ones] (1a and 1b). The compounds were synthesized by reaction of ethyl acetoacetate and aromatic aldehyde with urea in the presence of ethanol and $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ with 3-5 drops of HCl at $60-65^\circ\text{C}$. Spectral measurements (e.g. FT-IR, $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$) are used to investigate the chemical structures and characterize the obtained product of synthesized compounds.

Keywords: Synthesis, Characterization, 3,4- Dihydropyrimidine-2-(1H)-ones, Biginilli reaction.

تخليق وتشخيص بعض مشتقات [3و4-داي هايدروبرميدين]

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الخلاصة

في هذه الدراسة نجحنا في تحضير وتشخيص بعض مركبات 3 و 4- داي هايدروبرميدين [1a,1b] حيث حضرت هذه المركبات من تفاعل ايثل استواسيت والالديهيدات الاروماتيه مع اليوريا بوجود الايثانول وكلوريد الحديد سداسي الماء و 3-5 قطرات من حامض الهيدروكلوريك في (60-65) درجة سليزيه. مختلف القياسات الطيفيه (e.g. FT- IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$) استخدمت للتحقيق وتميز المركبات التي تم الحصول عليها.

الكلمات المفتاحية: تخليق، تشخيص، 3 و 4 - داي هايدروبرميدين، تفاعل بيكنيلي.

Introduction

Diazines are six-membered aromatic hetero-cycle having two nitrogen atoms. The new synthesized compounds can be classified into three different structures according to the relative position of the nitrogen atoms, showing pyridazine [1,2- diazine] [1], pyrazine [1,4-diazine] [2] and pyrimidine [1,3-diazine] [3]. Pyrimidine species and derivatives are one of important compounds due to their extended π -behavior which provides interesting fluorescence properties. These properties could be useful in the development of advanced electronic and photonic material [4].

There are different methods to synthesis pyrimidine derivatives. Dihydropyrimidines (DHPMs), for example, and their derivatives can be synthesized by Biginelli reaction. (DHPMs) are significant classes of heterocyclic which were reported the first time by Pietro Biginelli over a century ago by one pot condensation of β -keto esters and aldehydes with urea or thiourea, under acidic conditions [5, 6]. A strong acidic catalyst was employed in the original Biginelli reaction, but the yields were low.

Those Lewis acids such as SbCl_3 [7], CaF_2 [8] and ZnI_2 [9] were common catalysts for the Biginelli reaction. In recent years, several synthetic procedures have been applied to prepare the DHPMs; including classical conditions with microwave irradiation [10] or Ultrasonic Irradiation [11].

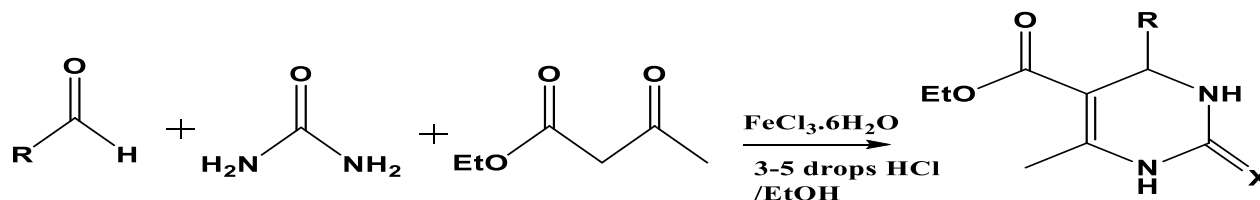
Experimental section

^1H -NMR spectra recorded by using BRUKER spectrophotometer 400 MHz (University of Isfahan, Iran). The chemical shift values are expressed in δ ppm, using tetra methylsilane (TMS) as internal standard and $\text{DMSO}-d_6$ as solvent. ^{13}C -NMR spectra are recorded by using BRUKER spectrophotometer 125 MHz, the chemical shift values are expressed in (δ ppm) using tetramethylsilane (TMS) as internal standard and using $\text{DMSO}-d_6$ as a solvent. IR spectra were recorded on a Shimadzu IR Affinity-1.

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General procedure for the synthesis of 3-4-Dihydropyrimidine -2(1H)-ones (1a and 1b):



Scheme 1: General Synthesis of compounds (1a and 1b)

Ethyl 2-oxo-4-(pyridin-2-yl)-1,2,3,4-tetrahydro pyrimidine -5-carboxylate (1a):

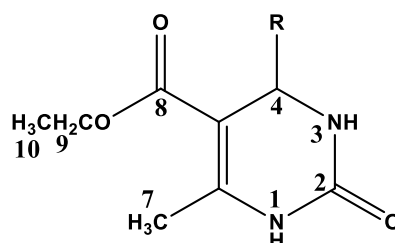
The compound was synthesized by reaction (1.9ml,0.02mol) of 2-Pyridinecarbox aldehyde and(2.8ml,0.02mol) of ethyl acetoacetate with (1.5g,0.025mol) urea in 25 ml of ethanol using (5mole%) Ferric chloride and 3-5 drops of HCl concentration as a catalyst, the reaction mixture was refluxed for 8 hrs. The final product was black solid, yield =71%, m. p=266-268°C.

Ethyl 4-[4-ethoxyphenyl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (1b):

The compound was synthesized by reaction (1.4 ml,0.01 mol) 4-ethoxybenzaldehyde and (1.4 ml ,0.02 mol) of ethyl acetoacetate with (0.9 g ,0.015) urea in 25 ml of ethanol using (5mmole%) Ferric chloride and 3-5 drops of HCl concentration as a catalyst, the reaction mixture was refluxed for 10 hrs. The final product was white solid, yield= 90%, m. p =190-191 °C. After the completion of the reaction the reaction mixture was cooled and washed with mixture ice cooled water and ethanol, the separated solid was filtered and dried in vacuum, finally recrystallized from alcohol to afford the desired product in pure form.

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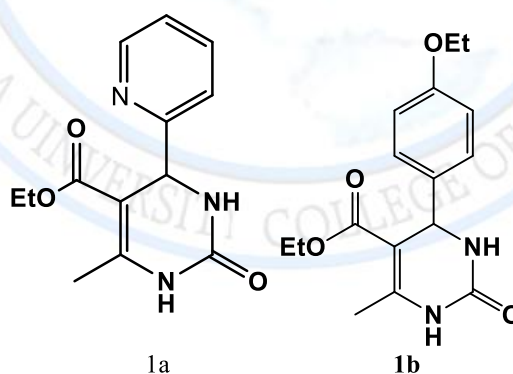
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R= a (ethoxyphenyl)
b(pyridyl)

Figure 1: General structures of **1a** and **1b****Results and Discussion**

The structural skeleton of 3,4-Dihydropyrimidine -2(1H)-ones show a large range of biological activities and used for pharmaceuticals [7], antibiotics [8] or herbicides applications, including antihypertensive [12], antimicrobial agents [13]. In the present investigation; 3,4-Dihydropyrimidine-2[1H]-ones are obtained by the reaction of aldehyde and ethyl acetoacetate with urea in ethanol, the chemical of the compounds **1a** and **1b**, was established by spectral analysis, as given in Figure 2

Figure 2: Structures of the **1a** and **1b**

IR spectra(KBr) of 3,4-dihydropyrimidine-2(1H)-ones (**1a** and **1b**) is characterized by the five bands corresponding to the stretching vibration of the aromatic C-H ,aliphatic C-H ,carbonyl group(C=O), N-H amide ,alkene (3114-3109,2985-2980, 1712-1713,3232-3235,1481-1466)[14] cm⁻¹,respectively.¹H-NMR spectrum of two compounds(**1a** and **1b**) appeared as a

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shared basic package represented by ethyl groups, phenyl ring and amide groups as shown in table (1). In compound (1a) ethyl groups appeared triplet signal at (δ 1.08 ppm) for CH_3 and quartate signal at (δ 3.98 ppm) for CH_2 as found previously by (Shamim, 2018) [15], The carbon in 3,4-Dihydropyrimidine ring showed singlet signal at (δ 5.22 ppm) (Lin An, 2016) [16], The ring of pyridine showed multiplet signal at δ (7.23–7.76 ppm). compound (1b) the substitution in the benzene ring electron donating groups gives higher yields than (1a) and give chemical shift at (1.3, 4.01 ppm) for ethoxy groups. The ^{13}C -NMR spectrum of ethyl 4-(4-ethoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2b) showed positive signal at Chemical δ (14.06 ppm for CH_3), positive signal at δ (17.65 ppm for CH_3 protons), negative signal at δ (53.28, 62.89 ppm) for CH_2 , The 3,4-Dihydropyrimidine ring for carbon at δ (99.49 ppm), also signal at (113.74–136.87 ppm) for phenyl ring, finally show positive signal at chemical shift δ (157.97 ppm) for NH and positive signal at δ (165.33 ppm) for carbonyl ester which is roughly consistent with the value in the ref [17].

Tables 1-: ^1H -NMR signals of 3,4-Dihydropyrimidine -2(1H)-ones

Comp	Chemical shift ppm		
	Aliphatic protons	Aromatic protons	Other protons
1a	1.08 (t, 3H, $-\text{C}_{10}$)	7.23–7.25	8.52 (s, 1H, N_3)
	2.23 (s, 3H, C_7)	7.27 – 7.66	9.18 (s, 1H, N_1)
	3.98 (q, 2H, C_9)	7.74 – 7.76	5.22 (s, 1H, C_4)
1b	1.1 (t, 3H, $-\text{C}_{10}$)	6.85 – 6.87	7.70 (s, 1H, N_3)
	1.30 (s, 3H, $-\text{C}_7$)	7.13 – 7.15	9.19 (s, 1H, N_1)
	2.25 (t, 3H, $-\text{CH}_3$)		5.09 (s, 1H, C_4)
	4.01 (q, 2H, C_9)		
	4.01 (q, 2H, CH_2-O)		

Conclusion

In this study two compounds from DHMPs have been synthesized using Lewis acid as a catalyst in addition to hydrochloric acid compared with assistant factor this method gave an excellent result with high yield and the duration of the reaction was shorter.

Acknowledgements

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