DOI: https://doi.org/10.36811/ojpsr.2021.110015 **OJPSR: December-2021: Page No: 56-63**

Open Journal of Pharmaceutical Science and Research

Review Article **Open Access**

Synthesis and characterization of some new heterocyclic compounds from α, β- unsaturated carbonyl system

Muna A. Othman Salem[1], Hana A. A. Mageed[2], Huda S. Muftah[2], Reda F. El- Ezabi[2] and Fayrouz A. Khaled[2]*

[1]Analytical and pharmaceutical chemistry Department, Faculty of pharmacy, Omar Al-Mukhtar University, El -Beida-Libya
[2]Chemistry Department, Faculty of Science, Omar El – Mukhtar University, Libya

***Corresponding Author:** Fayrouz A. Khaled, Chemistry Department, Faculty of Science, Omar Al-Mokhtar University, El -Beida-Libya; Email: fayalzobair@yahoo.com

Received Date: *Oct 07, 2021* **/** ***Accepted Date:*** *Nov 29, 2021* **/** ***Published Date:*** *Dec 06, 2021*

Abstract

An efficient and facile one pot synthesis of 3,4-dihydropyrimidinones (Biginelli compounds) from furfural, acetylacetone and urea under solvent free conditions was performed, resulted in promising yield. These compounds reacted with benzaldehyde and furfural to give the corresponding chalcones. Chalcones are used to synthesize several derivatives like pyrazolines isoxazoles and pyrimidines having different heterocyclic ring systems.

Keywords: Biginelli compounds; Chalcone; Pyrazolines isoxazoles; Pyrimidines

Cite this article as: Muna A. Othman Salem, Hana A.A. Mageed, Huda S. Muftah, et al. 2021. Synthesis and characterization of some new heterocyclic compounds from α, β- unsaturated carbonyl system. Open J Pharm Sci Res. 3: 56-63.

Introduction

Biginelli In 1893, the synthesis of functionalized 3,4-dihydropyrimidin-2(1H)-ones (DHPMs) scheme I via three-component condensation reaction of an aromatic aldehyde, urea and acetyl acetone was reported for the first time by P. Biginelli. Within the past decades, such Biginelli-type dihydropyridines have gotten a significant sum of consideration due to the curiously pharmacological properties related with this heterocyclic scaffold. one-pot amalgamation could be a methodology to make strides the effectiveness of a chemical response whereby a reactant is subjected to progressive chemical responses in fair one reactor. This is much desired by chemists because avoiding a lengthy separation process and purification of the intermediate chemical compounds would save time and resources while increasing chemical yield. Many dihydropyridines and their derivatives are pharmacologically [1,2] important as calcium channel blockers, antihypertensive agents, and biological activities [3] also contain the dihydropyrimidinone-5-carboxylate core. Therefore, many synthetic methods for preparing such compounds have been developed [4]. Chalcones, one of the major classes of characteristic items with far reaching

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event in natural products, vegetables, flavors and soy-based foodstuff, have been detailed to have a few organic exercises such as anti-inflammatory [5], antibacterial [6], anti-fungal [7], and anti-tumor [8], antioxidant [9] and antimalarial activities [10]. In expansion of being utilized in pharmaceutical businesses, chalcones moreover discover wide applications in colors [11]. Separated from being naturally imperative compounds, chalcone subsidiaries appear non-linear optical (NLO) properties with great blue light transmittance and great crystallizable [12]. A vital include of chalcones is their capacity to act as a halfway for the union of organically dynamic heterocyclic compounds such as, pyrimidine and cyclohexanone derivatives [13]. The chemistry of chalcones has created seriously logical ponders all through the world. Particularly intrigued has been centered on the blend and biodynamic exercises of chalcones. The title "Chalcones" was given by Kostecka and Tambor [14]. These compounds are moreover known as benzalacetophenone or benzylidene acetophenone. In chalcones, two fragrant rings are connected by an aliphatic three carbon chain. Chalcone bears a really great synthon so that assortment of novel heterocycles with great pharmaceutical profile can be outlined. Chalcones are unsaturated ketone containing the responsive ketoethylenic bunch –CO-CH=CH-. These are colored compounds since of the nearness of the chromophore -CO-CH=CH-, which depends within the nearness of other auxochromes. Different strategies are accessible for the planning of chalcones[15-17].The most helpful strategy is the Claisen-Schmidt condensation of equimolar amounts of arylmethyl ketone with aryl aldehyde within the nearness of alcoholic alkali[18].Chalcones are utilized to synthesize a few subordinates like cyanopyridines, pyrazolines isoxazoles and pyrimidines having distinctive heterocyclic ring frameworks [19-21].Besides, these are vital intermediates in numerous expansion responses of nucleophiles due to inductive polarization of carbonyl gather at the β-position. These discoveries clarify the critical intrigued of researcher in this specific bunch of compounds. A few procedures for the union of these framework, based on the arrangement of carbon carbon bond have been detailed. Among them the coordinate Aldol condensation and Claisen-Schmidt condensation still possess unmistakable positions. The most strategy for the blend of chalcones is the classical Claisen-Schmidt condensation within the nearness of fluid antacid bases [22-27].

Material and Methods

Preparation of various chalcones 1: To a well stirred solution of Benzaldehyde (1.06 gm, 0.01 mole) and acetophenone (1.2 gm, 0.01 mole) in ethanol (25 ml), 40% KOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol. Similarly, other substituted Chalcones have been prepared

Synthesis of pyrazoline derivatives from chalcones 2: A mixture of Chalcones (2.08 gm, 0.01 mole) in 25 ml of absolute alcohol, add hydrazine hydrate (0.5 gm, 0.01 mole) was refluxed in water bath at temp. 80-90 ºC for 8 hrs. The reaction mixture was poured in to ice. The product was isolated and crystallized from ethanol.

Synthesis of chalcone one (3a-3l): 0.01 mole of 1-(2-(4-substitutedphenyl)-1H-indol-1-yl) ethenone, 0.015 mole of 4-substituted aldehydes and 0.015 mole of piperidine were mixed into 20 mL ethylene glycol. The solution was refluxed at 160-1800 C for 4-5 h. The solution was cooled; solid was filtered and washed with ethanol.

Preparation of 3-Thiophen-2-yl-4,5-dihydro-10H-2-oxa-1,10-diaza-cyclopenta[a] carbazoles (6) 2-Thiophen-2-ylmethylene-2,3,4,9-tetrahydro-carbazol-1-one (**3,** 1mmol) was mixed with hydroxylamine hydrochloride (1g,14mmol) and pyridine (5 ml). The reaction mixture was irradiated in a microwave oven for 5 min. After the reaction was completed, the mixture was poured into the crushed ice. The resulting solid separated was filtered off,

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washed with dilute HCl and finally with water. The substance was dried and purified over CC with 1:5 petroleum-ether: ethyl acetate solvent mixture, to obtain **4**. OSBrs (372.04): C, 54.88; H, 3.19; N, 7.52%).

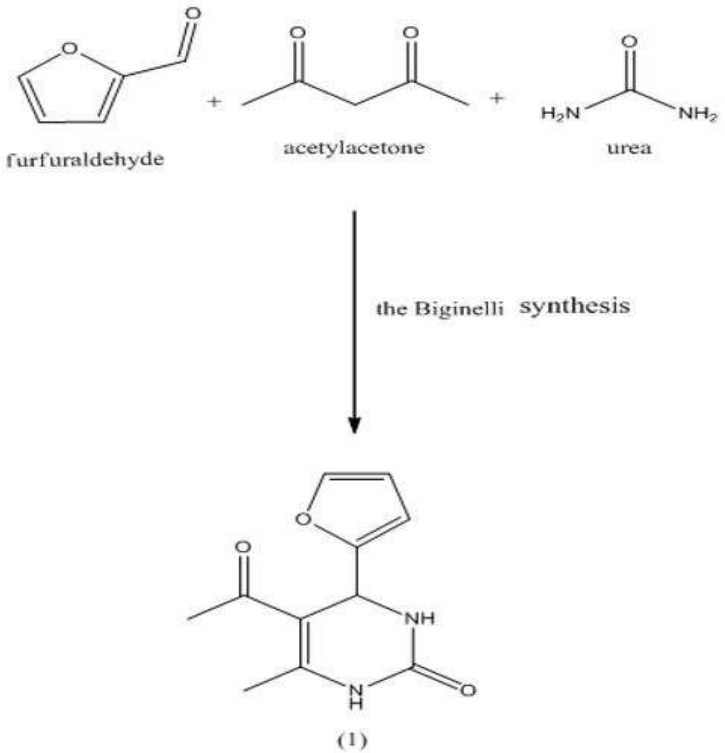
Preparation of 3-Thiophen-2-yl-2,4,5,10-tetrahydro-1,2,10-triazacyclopenta[a]carbazoles (4) Respective 2-Thiophen-2-ylmethylene-2,3,4,9-tetrahydro-carbazol-1-one (**3**, 1 mmol) was dissolved in absolute ethanol (20 ml) and hydrazine hydrate (0.5 ml, 10 mmol) was added and this mixture was irradiated in a microwave oven for 5 min. Then the solvent was removed under reduced pressure. The crude reaction mixture was poured into ice cold water and the solid obtained was filtered off, washed with water, dried and purified over column chromatography with 1:2 petroleum ether: ethyl acetate mixture to get **5.**

Synthesis of 2-(4-substitutedphenyl)-3-(5-(4-substitutedphenyl)-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl)-1H-indole (4a-4l)

A mixture of 0.01 moles of chalcones (3a-3l), 0.02 moles of phenyl hydrazine and 2-3 drops of glacial acetic acid in absolute alcohol (50 mL) was refluxed for 6-7 h. The reaction mixture was concentrated in vacuous and the solid obtained was filtered and recrystallized from ethanol.

Results and Discussion

The starting 1 readily obtained by the previously described Bengali procedure.



Scheme I: (5-acetyl-4-(furan-2-yl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one).
CHALCONE: α, β- unsaturated carbonyl system.

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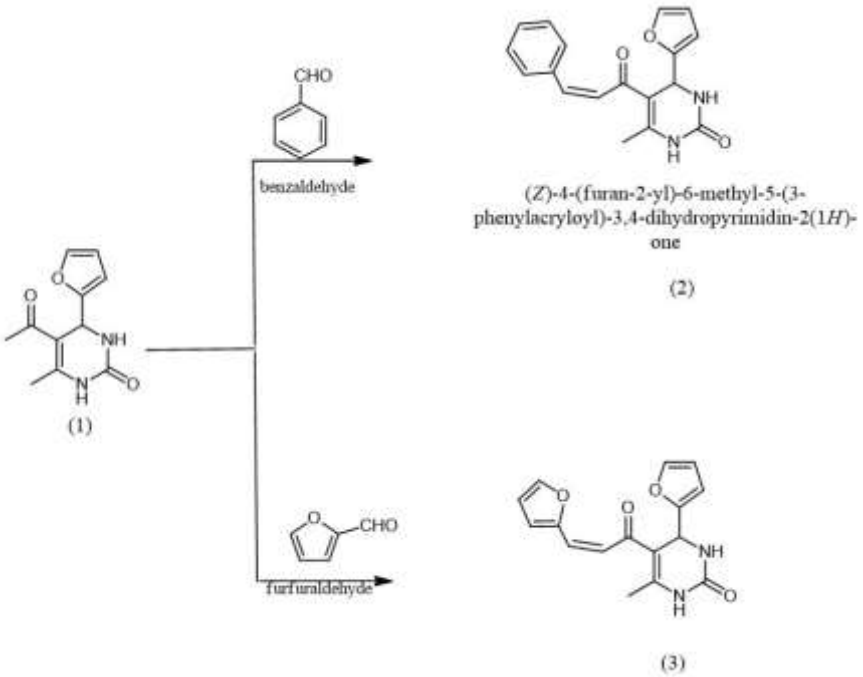
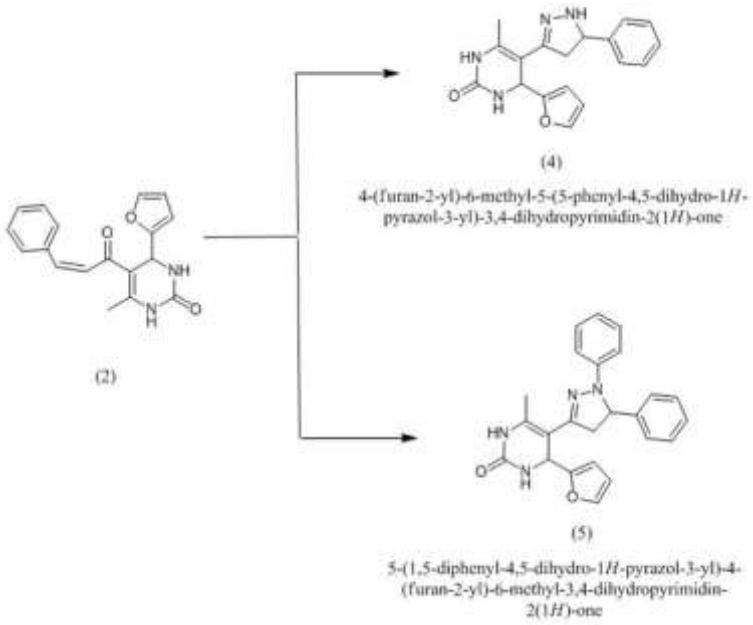
Compounds (2) and (3) were used as precursor intermediate to other pyrazolo-pyrimidine derivatives.



Scheme II (α, β- Unsaturated carbonyl system chalcone)

PYRAZOLONE S



Scheme III: (Chalone with hydrazine hydrate and phenyl hydrazine).

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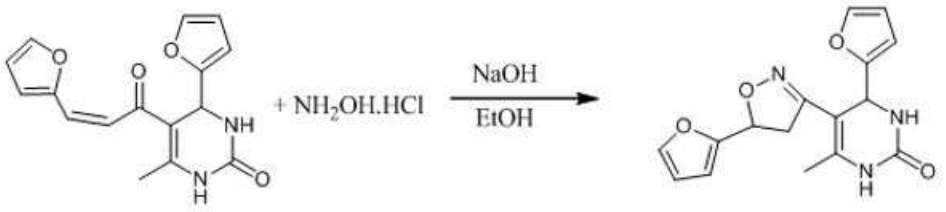
Isooxazoline

Among five membered heterocycles**,** isooxazoline represents aclass of compounds of great importance in biological chemistry. For instance, isooxazoline possess biological activities. Like insecticidal, antibacterial, antibiotic, antitumor, antifungal, antituberculosis, anti in flamework and analgesic. We have synthesized isooxazolines starting from compound **3** and hydroxylamine hydrochloride scheme IV



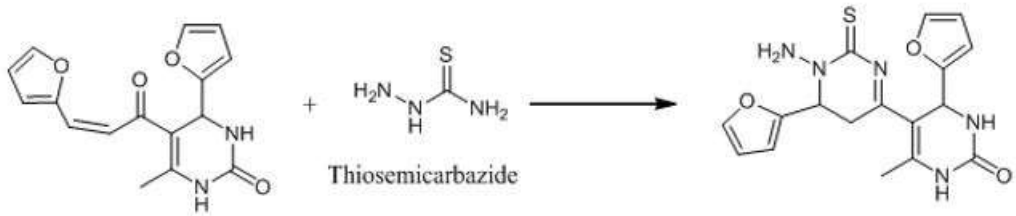
(3)

4-(furan-2-yl)-5-(5-(furan-2-yl)-4,5-dihydroisoxazol-3-yl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one

(6)

Scheme IV: Synthesis of isoxazole (6).

DIHYDROPYRIMIDINE



(3)

1-amino-4',6-di(furan-2-yl)-6'-methyl-2-thioxo-1,2,3',4',5,6-hexahydro-[4,5'-bipyrimidin]-2'(1'*H*)-one

(7)

Scheme V: (S ynthesis of dihydropyridine).

The spectral analysis of the synthesized compound (1) is as follows:

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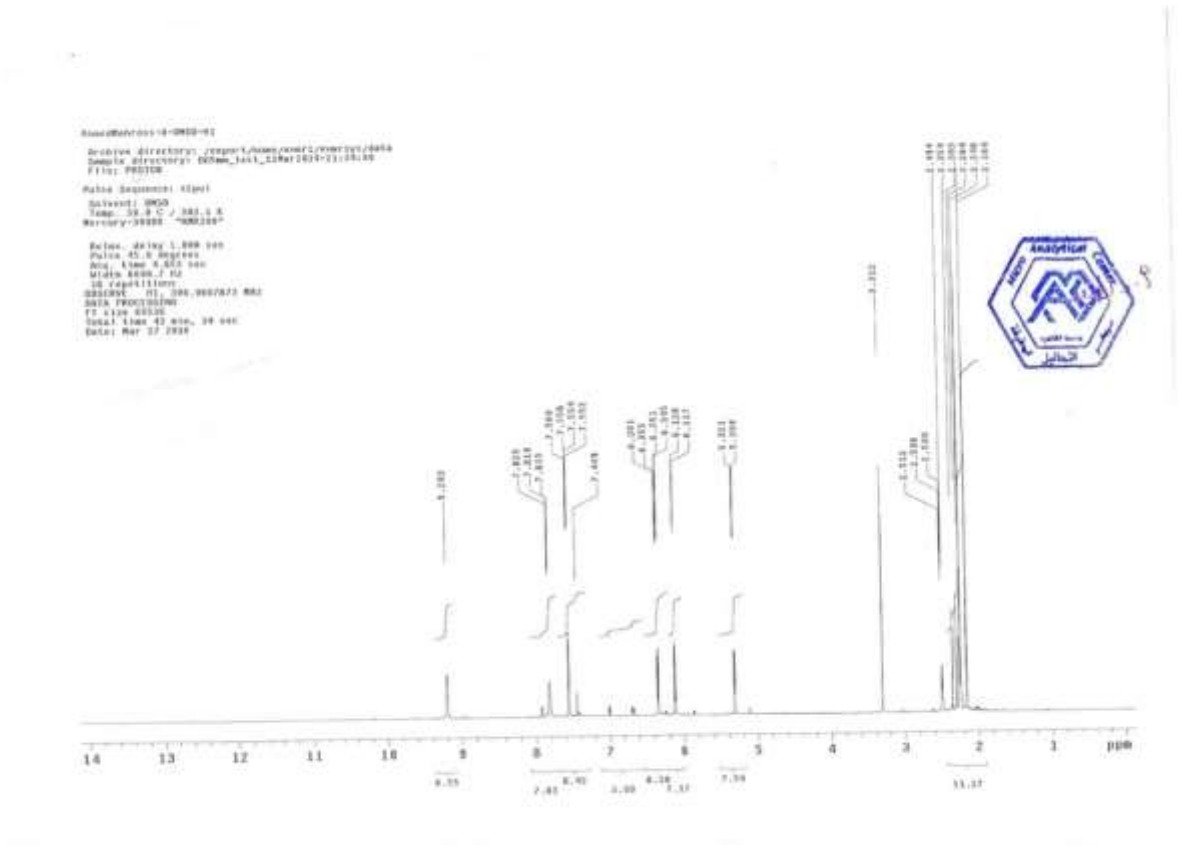

Figure 2: ^{1}H NMR spectra of compound (1).

group	IR cm^{-1}
C=O	1716
C-O	1239
C=C	1463
C- H eliphatic	2339
N-H	3128-3273

The IR data of compound (1) showed sharp as well as broad bands in the range 3128 - 3273 cm -1 indicating the presence of N - H groups, at 2339 cm -1 characteristic for C-H band. At 1463 cm -1 indicating C=C bond. There was an absorption band at 1716 cm -1, typical of the stretch vibration of C=O carbonyl group. The bond at 1239 cm -1 characteristic for C-O band. 1H NMR spectra (DMSO, 400 MHZ) ppm: showed the N-H protons at the signal (δ 5.3) due to protons of dihydropyridine. The signal at (δ 2.1 – 2.5) belonging to CH3 protons. The signal at (δ 7.4-7.8) revealed to protons of aromatic -H figure No .1

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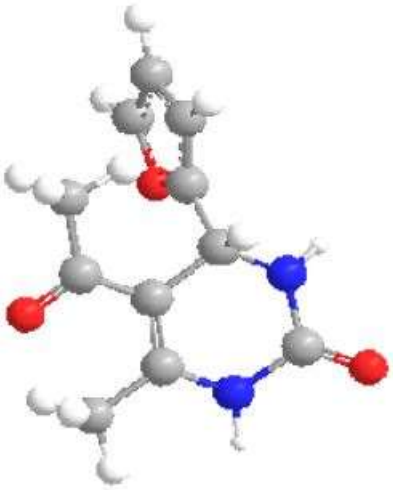

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