Original paper

Synthesis and Characterization of Chalcone Derivatives from Furfural

Taiseer Abdul–Kader Saleh

Samarra University, College of Education, Salahaldeen, Iraq

Article Info:

Abstract

In this research, some chalcones were prepared using furfural with aromatic ketones in basic aqueous solution (20% KOH). In addition, some furilidine compounds were prepared using the reaction between furfural and substituted carbonyl compound such as substituted benzaldehyde with acetone and cyclohexanone in basic conditions (25% KOH). Heterocyclic compounds prepared as chalcones derivatives like pyrazolines from the reaction between chalcone and phenyl hydrazine. The prepared compounds were characterized using FTIR spectroscopy, UV–visible spectroscopy, H–NMR spectroscopy and C–H–N analysis.

1. Introduction

The importance of organic compounds increased by the existence of carbonyl group conjugating with another functional group especially double bond C=C like α–β unsaturated carbonyl compounds, this compound considered as a starting material in another preparation reactions like Chalcones and its derivatives also in preparation of active biological heterocyclic compounds [1, 2]. The compound has two conjugated functional groups that can cause a spread of electrons on the four atoms this can cause resonance. These compounds have special chemical properties for both two groups, carbonyl group (electron withdrawing group) when conjugates with double bond make the activity of this bond (C=C) less active towards electrophilic additions, it also activates the double bond toward nucleophilic additions to be ready for nucleophilic attack, this kind of reaction doesn’t found in alkenes that have another withdrawing groups like (–CN, –COOH, –NO2, –COOR, –COR ) [3, 4].
The condensation reaction of carbonyl compounds always occur in metabolic pathways in biological molecules like carbohydrates, lipids, amino acids, proteins and another kind of compounds. One of carbonyl compounds (nucleophilic donor) became enolate that enters alpha substitution reaction when ketophil added to the second carbonyl compound (electrophilic acceptor) [5]. The double bond in α–β unsaturated carbonyl compounds is less active towards electrophilic reagents compared with simple alkenes because of carbonyl group (C=O) that withdraws electrons, electrophilic addition reaction happens in simple alkenes through proton (H+) electrophilic attack to form carbonium ion (more stable ), another separating step (Cl−) ion attacks to carbonium ion.

Electrophilic addition reaction happens in α–β unsaturated carbonyl compounds through electrophilic attack at one of the ends of alternate system, the preferred end is the oxygen of carbonyl group that has negative charge at the molecule forming carbonium ion which has resonance (more stable), the addition not at double bond (C=C) [6]. The next step is the addition of negative ion to a carbon atom of the carbonyl group, or to β carbon atom to carbonium ion. The enol form compound is not stable so it is changed to keto form which is more stable. Because of the (C=C) polarity in this compound, nucleophilic reagents can be added. In Michael addition, the nucleophilic reagents added to the carbon atom in carbonyl group in α–β unsaturated carbonyl compounds, after that the addition of proton to the anion of the enols essentially at oxygen atom which have electronegativity bigger than the electronegativity of carbon that leads to make enol form this form is less stable from keto form so it is changed to the more stable form (keto form) [6, 7]. While in Claisen addition, the nucleophile added to the carbon atom of carbonyl group which has a partial positive charge, this addition is used to prepare alcohols and unsaturated cyanohydrins. Chalcones are α–β unsaturated ketone compounds first discovered during the synthesis of a new natural colored compound [8]. Chalcones are yellow compounds and insoluble in water but soluble in organic solvents, these compounds found as dyes in nature having this chemical structure and name [9, 10]. The chalcones are very important as medical and industrial compounds [11]. Also, its importance came from the similarity of chalcones with the natural compound in plants [12] like flavonoids and anthocyanin which are responsible for blue and red dyes in flowers. Because of the conjugating, these compounds showed optical properties [13] and biological activity as hyperglycemia [11], malaria [12], antitumor agents [14], anti–inflammatory [15, 16], and cancer tumours [17]. Chalcones or substituted chalcone entered 1,2 addition reaction (Claisen addition) and 1,4 addition (Michael addition) depends on the strength or basicity of nucleophile, the structure of α–β unsaturated carbonyl compound and heat. From these reactions, a lot of important heterocyclic compounds could be prepared. Chalcones and substituted chalcones react with hydrazine, phenyl hydrazine and their derivatives to form pyrazoline and substituted pyrazoline, pyrazolines are very important heterocyclic compounds used widely in environmental and industrial aspects [18]. Chalcones and substituted chalcone react with hydrazine using acetic acid to prepare substituted pyrazoline used as antipyretic and to treat rheumatism [19]. Another substituted pyrazolines prepared from the reaction of chalcones with different substituted hydrazines.
2. Materials and Methods

2.1 Materials

Analar were obtained from Fluka, Aldrich and BDH and used as received without recrystallization, their purity was 99.9%

2.2 Instrumentation and spectral measurements

Melting points were recorded by using a Mettler FP 61 melting point apparatuses. FTIR spectra were recorded by using Shimadzu Infrared Spectrophotometer Fourier Transform FTIR–8400S in the region 4000–400 cm⁻¹ in KBr pellets. UV–Visible spectra were recorded using Shimadzu (UV–Visible) Spectrophotometer. ¹HNMR, C¹³ spectra were scanned on a Bruker 400MHz spectrometer TMS as the internal standard and DMSO–d₆ was used as a solvent. C,H,N analyses were recorded using Evrovector EA 3000A.

2.3 Synthesis

2.3.1 Chalcones preparation

Equal moles from aldehyde, ketone, 4–amino acetophenone and furfural were put in a conical flask with a stirrer. 0.6 mL of KOH solution (20%) was added, then 10 mL of ethanol was added to the mixture with continued stirring for (3–4) h in the ice bath. This solution left in the refrigerator for 24 h, then it diluted by distilled water and acetic acid (1:1). Then the solution was filtered, washed by using distilled water, dried and recrystallized using ethanol.

2.3.2 Furilidines and furilidine benzylidine preparation

These compounds prepared by Claisen–Schmidt reaction by treating 1 mole of ketone with 1 mole of substituted aldehyde and 1–2 mole of furfural in basic aqueous KOH (25%) in a beaker. 3 mL of KOH (25%) was added to the solution with continuously stirrer for 10 min. Another mole of furfural and 1 mole of substituted aldehyde, 10 mL of ethanol added with stirring for 1 h in room temperature, the solution filtered, washed with cold ethanol and distilled water, dried and recrystallized by using ethanol.

3. Results and Discussion

Chalcone prepared according to Claisen–Schmidt condensation reaction (Scheme 1) using equal moles from aromatic ketones with furfural in presence of 20–25% KOH and ethanol as solvent as following:

\[ \text{ArCOH}_2 + \text{PhCH}_2\text{OH} \rightarrow \text{ArCOPhCH}_2\text{OH} + \text{H}_2\text{O} \]

![Scheme 1: Claisen–Schmidt condensation reaction mechanism](image-url)
The reaction has been confirmed by monitoring the physical properties (color, melting point) and spectral properties as listed in Table 1.

3.1 FTIR spectroscopy

FTIR spectra for prepared compounds showed that strong peaks in the range 1588–1661 cm\(^{-1}\) belong to stretching bending for C=C that conjugated with a carbonyl group. Moreover, it shows strong peaks at 1655–1661 cm\(^{-1}\) belongs to stretching bending for C=O group conjugated with an olefinic bond that showed the decrease in stretching bending for C=O group from normal limits because of conjugating with the double bond by resonance. Another strong peak at 1528–1590 cm\(^{-1}\) belongs to the bending of aromatic (C=C) and furan ring, weak peaks in 1401–1427 cm\(^{-1}\) belongs to –N=N stretching bending. Pyrazolines showed new peaks at 1649–1658 cm\(^{-1}\) belongs to stretching bending for C=N group and stretching bending for C–N group at 1304–1345 cm\(^{-1}\). FTIR spectrum of compound 4 is shown in Fig. 1 and the bands for all compounds are listed in Table 2.

![Figure 1: FTIR spectrum of compound 4.](image)

3.2 UV–Vis spectroscopy

UV spectra showed absorbance peaks at wave length (210–270) nm belongs to (\(\pi-\pi^*\)) electrons for benzene only [21], another absorbance peak in (361–403) nm belongs to (n–\(\pi^*\)) electrons, because of conjugating between (C=C) and (C=O) the excitation energy would be decreased and the transition of electron from ground state to excited state needs energy less than the compounds that don't have conjugation.

![Figure 1: UV–Vis spectrum for compound 1.](image)

3.3 C–H–N analysis

C–H–N analysis was used to make sure of the elemental content of the prepared compounds. The theoretical ratios for elements were very close to the calculated ratios as shown in Table 4.

3.4 \(^{1}\)H–NMR spectroscopy

Compound 1 showed multiple absorption bands at 6.7–7.5 ppm for furan protons, another band at 7.5–7.9 ppm for the conjugated double bond in carbonyl group and multiple bands at 8.2–8.3 ppm for benzene protons. Compound 4 showed multiple absorption bands at 1.3 ppm for –CH\(_2\) in pyrazoline ring, single band appeared at 2.5 ppm because of the solvent, another multiple band appeared at 3.7–3.8 ppm for –CH protons in pyrazoline, double bands appeared at 6.38–6.39 ppm belongs to the protons of furan far away from the oxygen atom, multiple bands appeared at 6.4–7.3 ppm belongs to benzene protons, another
multiple bands appeared at 7.5–7.6 ppm belongs to the protons near oxygen atom in furan ring.

**Figure 3:** $^1$H–NMR spectrum for compound 1.

**Figure 4:** $^1$H–NMR spectrum for compound 4.

3.5 $^{13}$C–NMR spectroscopy

$^{13}$C–NMR for compound 1 showed a band at 113.8 ppm belongs to C$_3$ for a furan ring, a band at 118.7 ppm for belongs to C$_4$ for a furan ring, a band at 118.9 ppm belongs to C$_3$ and C$_5$ for a benzene ring, a band appeared at 124.3 ppm for olefinic carbon C$_2$, a band at 132.2 ppm belongs to olefinic carbon C$_3$, a band at 142.8 ppm for C$_1$ in benzene ring, in 147.9 ppm a band appeared this band belongs to C$_5$ in furan ring, a band at 150.2 ppm for belongs to C$_2$ in furan ring, another band at 151.2 ppm for C$_4$ in benzene ring that connects with nitro group and a band at 188.3 ppm belongs to ketonic carbon. $^{13}$C–NMR for compound 2 showed a band at 124.3 ppm belongs to C$_3$ for furan ring, a band appeared at 126.7 ppm belongs to C$_4$ for furan ring, another band appeared in 130.9 ppm for olefinic carbon C$_1$ and 132.4 ppm for carbon C$_2$, another band appeared in 134.4 ppm belongs to carbon C$_5$ in furan rings, a band appeared at 142.0 ppm belongs to C$_2$ in furan rings and a band appeared at 188.9 ppm belongs to ketonic carbon.

**Figure 5:** $^{13}$C–NMR for compound 1.

**Figure 6:** $^{13}$C–NMR for compound 2.
Table 1. Structure, colour and melting point of the prepared compounds.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Aldehyde Wt. (gm/mol)</th>
<th>Ketone Wt. (gm/mol)</th>
<th>Structure</th>
<th>Color</th>
<th>Melting point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Furfural 0.288/0.003</td>
<td>4–amino acetophenone 0.4/0.003</td>
<td><img src="image1" alt="Structure" /> yellow</td>
<td>96.07</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Furfural 1/0.01</td>
<td>Acetone 0.29/0.005</td>
<td><img src="image2" alt="Structure" /> yellow</td>
<td>170.5–172</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Furfural 0.07/0.007</td>
<td>Ketone (azo dyes) 0.2/0.0007</td>
<td><img src="image3" alt="Structure" /> Dark red</td>
<td>234–236</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Reactant 0.1/0.0004</td>
<td>Phenyl hydrazine 0.057/0.0004</td>
<td><img src="image4" alt="Structure" /></td>
<td>131–140</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: FTIR absorption bands for the prepared compounds.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Structure</th>
<th>FTIR bands (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C=O C=C C=C Ar Others</td>
</tr>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure" /></td>
<td>1658 1587 1519 N=O sym 1330 asy 1521</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Structure" /></td>
<td>1646 1600 1559 —</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Structure" /></td>
<td>1631 1602 N=N 1417 O–H 3404</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Structure" /></td>
<td>— — — C=N 1656 C–N 1330–1253</td>
</tr>
</tbody>
</table>
Table 3: UV–Vis absorption for compounds 1 and 4.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Structure</th>
<th>Peak 1</th>
<th>Peak 2</th>
<th>Peak 3</th>
<th>Peak 4</th>
<th>Peak 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>λ&lt;sub&gt;max&lt;/sub&gt; 402</td>
<td>368</td>
<td>361</td>
<td>270</td>
<td>210</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absorbance 1.47</td>
<td>2.62</td>
<td>3.48</td>
<td>3.01</td>
<td>2.52</td>
</tr>
<tr>
<td>4</td>
<td><img src="image2.png" alt="Structure" /></td>
<td>λ&lt;sub&gt;max&lt;/sub&gt; 432</td>
<td>360</td>
<td>341</td>
<td>267</td>
<td>211</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absorbance 1.62</td>
<td>1.80</td>
<td>1.46</td>
<td>2.57</td>
<td>5.01</td>
</tr>
</tbody>
</table>

Table 4: C–H–N analysis for compounds 1 and 4.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Calculated</th>
<th>Theoretical</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>C (%)</td>
<td>H (%)</td>
</tr>
<tr>
<td>1</td>
<td>63.07</td>
<td>2.91</td>
</tr>
<tr>
<td>4</td>
<td>68.09</td>
<td>3.15</td>
</tr>
</tbody>
</table>

Table 5: <sup>1</sup>H–NMR for compounds 1 and 4.

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Structure</th>
<th>Chemical shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>7.6–7.9 (CH=CH);, 6.7–7.5 (Fur–H), 8.2–8.3 (Benz–H)</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4.png" alt="Structure" /></td>
<td>3.7–3.8 (CH–Pyr), 6.3–7.6 (Fur–H), 6.4–7.2 (Ar–H), 7.9–8.2 (Ar–NO&lt;sub&gt;2&lt;/sub&gt;)</td>
</tr>
</tbody>
</table>

4. Conclusions

Various chalcone derivatives were synthesized and elucidated the exact chemical structure of the target compounds using spectral investigations. The syntheses of chalcones were performed using the general procedure. 20% potassium hydroxide solution was the medium for the reaction. Nevertheless, some furilidine derivatives were prepared using the reaction between furfural and substituted carbonyl compound such as substituted benzaldehyde with acetone and cyclohexanone in basic conditions. Heterocyclic compounds prepared as chalcones derivatives like pyrazolines from the reaction between chalcone and phenyl hydrazine. The reaction conditions were optimized and excellent yield was reported.

References


