

Synthesis of 2(1H)Pyridine and thiopyridone derivatives. Contrasting between the behavior towards electrophiles

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For submitted the degree of Master of Science as partial fulfillment of the requirements of Master of Science in Chemistry

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الى البرعم الذي تفتح بأنفاسنا وماء حياتنا أنا وزوجي.....

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Contents

CHAPTER ONE- INTRODUCTION

No.	Title	Page
	<i>Chalcone</i>	<i>1</i>
<i>1.1</i>	<i>Chalcone synthesis</i>	<i>2</i>
<i>1.1.1</i>	<i>Synthesis of chalcone by ultrasound</i>	<i>3</i>
<i>1.1.2</i>	<i>Synthesis of chalcone by silica</i>	<i>4</i>
<i>1.1.3</i>	<i>Chalcone synthesis with Mannichbases</i>	<i>6</i>
<i>1.3</i>	<i>Other methods for Chalcone synthesis</i>	<i>7</i>
<i>1.3.1</i>	<i>Therapeutic Potential of Chalcones</i>	<i>10</i>
<i>1.4</i>	<i>Regioselective reaction of unsymmetric chalcone</i>	<i>10</i>
<i>1.4.1</i>	<i>Chalcones As Synthon In Chemical Synthesis</i>	<i>12</i>
<i>1.4.2</i>	<i>Heterocyclic compounds</i>	<i>13</i>
	<i>Synthesis of pyridine and thio derivatives</i>	<i>14-23</i>

CHAPTER TWO- RESULT AND DISCUSSION

No.	Title	Page
<i>3.1.1</i>	<i>Synthesis and characterization 3'-benzoyl-4'-phenylspiro [indoline-3,2'-pyrrolidin]-2-one (2).</i>	<i>24</i>
<i>3.1.2</i>	<i>Synthesis and characterization of 4-(4-chlorophenyl) 2-oxo-6-phenyl-1,2,3,4-tetra hydropyridine -3-carbonitrile</i>	<i>26</i>
<i>3.1.3</i>	<i>Synthesis and characterization of 4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2,3-substituted- -1,2-dihydropyridin-2-thione (6-8).</i>	<i>28</i>
<i>3.1.4</i>	<i>Synthesis and characterization of ethyl2-(4-(4-chlorophenyl)-3-cyano-6-(3,4-dimethyl) pyridine-2-</i>	<i>29</i>

	<i>ylthio)acetate (9)</i>	
3.1.5	<i>Synthesis and characterization of Synthesis of 2-(4-(4-chlorophenyl)-3-cyano-6-(3,4-dimethyl phenyl)pyridine-1(2H)-yl)acetohydrazide (11).</i>	31
3.1.6	<i>Synthesis and characterization of 2-Chloro-4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-oxo-pyridine-3-carbonitrile (13).</i>	33
3.1.7	<i>Synthesis and characterization of 4-amino-5-(4-chlorophenyl)-7-(3,4-dimethyl phenyl)-2-oxo-2H-pyrano[2,3-b]pyridine-3-carbonitrile</i>	34
3.1.8	<i>Synthesis and characterization of (E)-N'-benzylidene-5-(4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-oxo-1,2-dihydropyridine-3-yl)-1H-pyrazole-4-carbohydrazide (20)</i>	38
3.1.9	<i>Synthesis and characterization of (E)-3-(amino(3-amino-5-oxo-1H-pyrazol-4(5H)-ylidene)methyl)-4-(4-chlorophenyl)-6-(3,4-dimethylphenyl) pyridine-2(1H)-one: (24)</i>	41
3.1.10	<i>Synthesis and characterization of (E)-2-(((4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-oxo-1,2-dihydropyridin-3-yl)(5-oxo-3-(3-phenylthioureido)-1,5-dihydro-4H-pyrazol-4-ylidene)methyl)glycyl)-N-phenylhydrazine-1-carbothioamide (30)</i>	44
3.2	<i>Biological activity.</i>	47
3.2.1	<i>Gram positive bacteria.</i>	47
3.2.2	<i>Antioxidant evaluation</i>	51
3.3	<i>Quatum chemical method</i>	56

CHAPTER THREE- EXPERIMENTAL

No.	Title	Page
2.1	Materials.	69
2.2	Instruments.	69
2.3	Synthesis of compounds.	70
2.3.1	Synthesis of Ethyl 4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-oxo-1,2-dihydropyridine-3-carboxylate	71
2.3.2	4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile	74
2.3.3	Synthesis of 2-(4-(4-chlorophenyl)-3-cyano-6-(3,4-dimethyl phenyl) pyridine-1(2H)-yl)acetohydrazide	77
2.3.4	Synthesis of 4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)-2-hydrazinylnicotinonitrile	79
2.3.5	Synthesis of 5-(4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)2-oxo-1,2-dihydropyridin-3-yl)-1H-pyrazole-4-carbohydrazide	81
2.3.6	Synthesis of (E)-3-amino-2-cyano-N-hydroxy-3-(2-oxo-4,6-diphenyl-1,2-dihydropyridine-3-yl)acrylamide	84
2.3.7	Synthesis of (E)-3-(amino(3-amino-5-oxo-1H-pyrazol-4(5H)-ylidene)methyl)-4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)pyridine-2(1H)-one	86
2.3.10	Synthesis of N-(5-(4-chlorophenyl)-3-cyano-7-(3,4-dimethylphenyl)2-oxo-2H-pyrano[2,3-b]pyridine-4-yl)acetamide	88
	References.	96

Introduction

Chalcones (1,3-diaryl-2-propen-1-ones) are flavonoids found in fruits and vegetables, that attracted attention because of their pharmacological activities such as anti-inflammatory [1-7], antibacterial [8-12], antifungal [13-17], antiviral [18-22], antioxidant [23-32], antineoplastic [33-41]. Most of aromatic rings of natural chalcones are found as hydroxylated. Chalcones, dihydrochalcones and aurones are composed of pigments whose colour changes from yellow to orange in some *Coreopsis* and *Asteraceae taxa* species. These compounds are found not only in flowers but also in lots of different tissues of the plants. Free radical scavenging properties of phenol groups of chalcones increased the interest in consumption of plants that included chalcones [18]. Chalcones are included dimer, oligomer, Diels-Alder adducts and different conjugates. At the same time because of being precursors of all of other flavonoid groups, chalcones are very important biosynthetic compounds. Essential property that separates chalcones and dihydrochalcones from the other flavonoids is that an open chain with three carbon molecules binds to A and B ring instead of C ring of flavonoids (Figure 1). Chalcones turn to flavanones with a stereospecific reaction catalyzed by chalcone isomerase enzyme in plants. Close biogenetic and structural relation between chalcones and

flavanones is the reason for these compounds usually found together in natural products. This is the cause of the identification of chalcone, dihydrochalcone and aurones together with flavanone and dihydroflavonol generally. Chalcones are called as minor flavonoids. But using name of minor flavonoids for chalcones doesn't seem appropriate because of increasing of new species of flavonoids [42]. As flavonoid term, mostly plant pigments are expressed which includes benzo-g-pirone and flavone (Figure 1). Essential compounds of flavonoids include a phenyl group at 2nd position of benzo γ -pyron (chromone) ring system. Flavonoids differ according to size, saturation and the substituents of g-pyrone ring which is called C ring [43]. The ethylenic bond between C2 and C3 of C ring of flavones provides conjugation between A and B ring. In this way the ring structure of flavones becomes stronger than other flavonoids. Although anthocyanidines differ from other flavonoids by losing carbonyl group in C ring, their biological characteristics are similar to other flavonoids. Chalcone derivatives are ring-chain isomers of flavanone derivatives. Aurone derivatives situates in flavonoids by having benzofuranone structure [42,44,45].

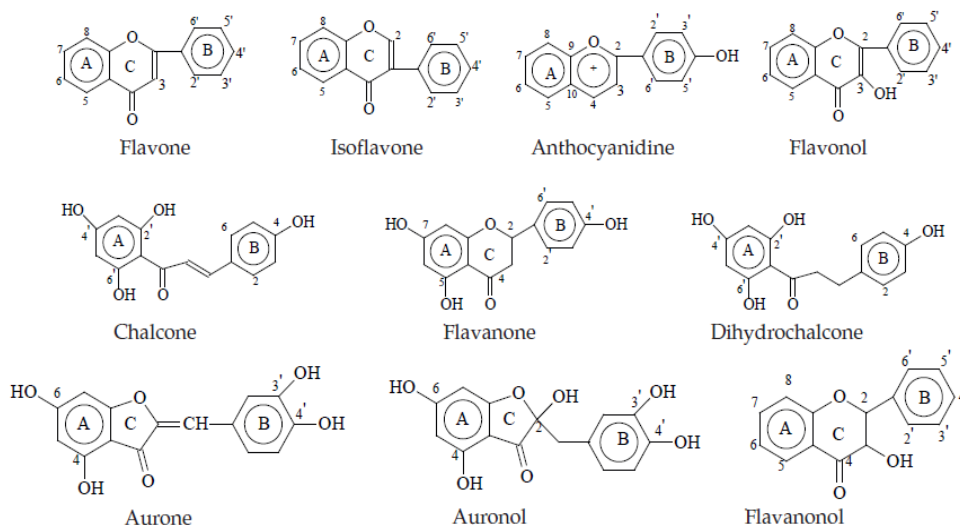


Figure 1. Some flavonoid species

METHOD A:

Chalcone synthesis with the reaction of aromatic aldehyde and acetophenone in the presence of NaOH in EtOH

Chalcone derivatives can be formed by refluxing of acetophenones and aromatic aldehydes in the presence of NaOH in EtOH (5) (Scheme 2). The same reaction can be made at room temperature [46-48] with methanol at room temperature [33,49]. During the reaction, KOH can be used instead of NaOH at room temperature [9,50-54], at 0°C [55,56] or at 5-10°C temperature under nitrogen gas or argon gas [57]. In our department we synthesized a number of chalcones using KOH/MeOH at room temperature, which two of them is original, called (*E*)-1- (3,5-dichloro-2-hydroxyphenyl)-3-m-tolylprop-2-en- 1-one and (*E*)-1- (4-Bromophenyl)-3-m-tolylprop-2-en-1-one .