Chemical Studies on the Synthesis of New Glycosides and Nucleosides

A Thesis Submitted

By

Ibrahim Adel Ibrahim El Desoky

B. Sc. Cairo University (2002)

As Partial Fulfillment of the Requirements for

M. Sc. Degree in Organic Chemistry

Department of Chemistry

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In addition to the work carried out in this thesis, the candidate has studied and passed the following graduate courses:

1. Applied organic spectroscopy.
2. Advanced physical organic chemistry.
3. New trends in analytical chemistry.
4. Pericyclic chemistry.
5. Polymer chemistry.
6. Heterocyclic chemistry.
7. Organic photochemistry.
8. Quantum chemistry.
9. Carbohydrates chemistry.
10. Designing organic synthesis.
11. Natural products chemistry.
12. Selected topics
13. Biochemistry.
14. Textile dyeing.
15. German language.

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Approval Sheet for Submission

Thesis Title:

``Chemical Studies on the Synthesis of New Glycosides and Nucleosides``

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ABSTRACT

Name: Ibrahim Adel Ibrahim El Desoky

Title of thesis: Chemical Studies on the Synthesis of New Glycosides and Nucleosides

Degree: M. Sc. Faculty of Science, Cairo University, 2009.

The original work of this thesis includes two research projects. The first one deals with developing a facile synthesis of some new mono- and bis- N-glycopyranosyl-2-thioxo-4-thiazolidinone derivatives *via* reaction of 5-arylidene-2-thioxo-4-thiazolidinones with α-bromoacetosugars. The biological activity of some selected products were tested against a wide range of microorganisms.

The second project deals with chemical studies on the synthesis of C-glycosides of theophylline *via* 7-ethyl-8-hydrazinotheophylline. Also, the biological activity of some of the synthesized compounds were tested against some fungi and bacteria species.

Key words: 5-Arylidene-2-Thioxo-4-thiazolidinones, Glycosides, Sugars, Theophylline, Biological activity.

Supervisors: Prof. Dr. Mosselhi A. N. Mosselhi

Prof. Dr. Magda A. Abdallah

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Ibrahim A. Ibrahim

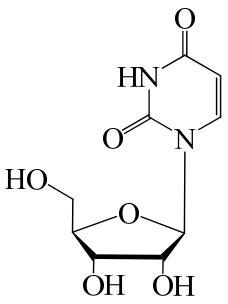
Contents

Chapter I

Statement and Objectives of the Problem

I. Statement and Objectives of the Problem

Nucleosides are originally glycosides applied to the pyrimidine or purine ribose derivatives obtained by alkaline hydrolysis of ribonucleic acid (RNA) isolated from yeast.[1] Now nucleosides are also applied to all carbohydrate derivatives of N-heterocyclic system, whether the attachment is through nitrogen atom as compounds **1** & **2,** oxygen atom as **3** & **4,** sulphur atom as **5** & **6,** or carbon atom as **7** & **8**, whether the heterocycle is naturally occurring or not.



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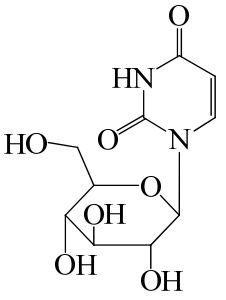

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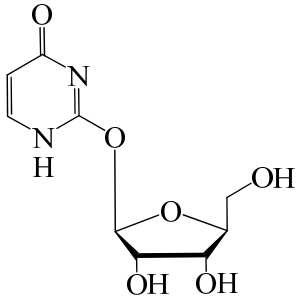

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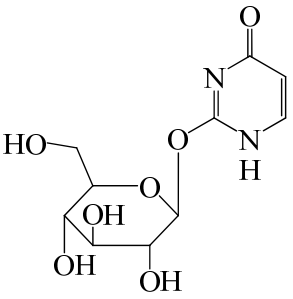

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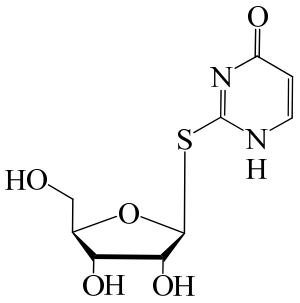

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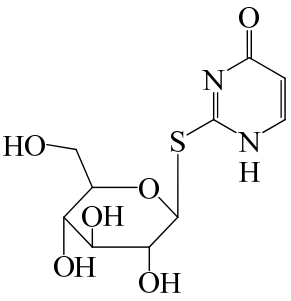

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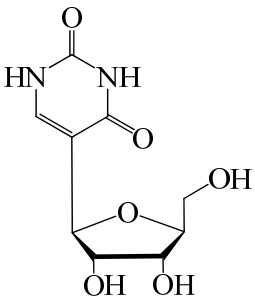

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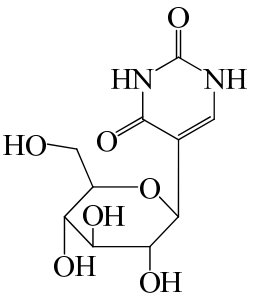

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During the last thirty years and especially since the discovery of 2`,3`-dideoxycytidine (DDC),[2] 3`-dideoxyinosine (DDI)[3] and azidothymidine (AZT)[4] as anti-HIV agents, a large number of nucleosides have been synthesized. The nucleosides of N-substituted azoles constitute a special class both for their biological significance[5] and for the particular synthetic methods involved in their preparation. Amongst the new synthetic nucleosides, pyrazoles, oxadiazoles, oxatriazoles and triazoles are the significant counterparts of sugars.

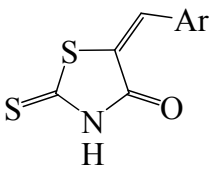
Ribavirin[6], the first synthetic broad-spectrum non-interferon including antiviral agent has been prepared and tested against a variety of both DNA and RNA viruses

in tissue culture. Thus, the ribonucleosides antibiotics, pyrazomycin and formycin[7] have also demonstrated antiviral activity in vitro.

Considerable effort has been expended in the synthesis of N-substituted azines, especially pyrimidine nucleosides over the past three decades. Some of pyrimidine nucleosides have been reported to use for antiviral therapy.[8] Carbon nucleosides are reported to have various biological activities and medicinal applications.[9,10]

For these biological and medicinal purposes and others it is important to develop the field of the synthesis of nucleosides. As a part our research program dealing with the chemistry of azoles and azines nucleosides,[11-14] and in continuation of this work, we are interested in examining the coupling reaction of 5-arylidene rhodanines **9** as in part-1 in the present thesis as well as 7-ethyl-8-hydrazino-theophylline **10** as in part-2 with sugars, e.g. compounds **11** or halosugar, e.g. compound **12** to give a new class of glycosides.

Also, the biological activities of some selected new prepared glycosides were tested using wide range of microorganisms.



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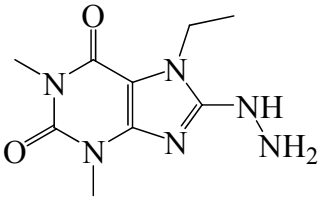

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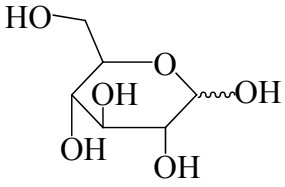

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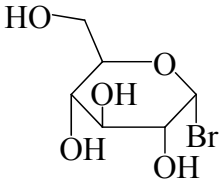

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Chapter II
Part 1

II.1. Literature Survey

Chemistry of 2-Thioxo-4-thiazolidinone (Rhodanine) and its Derivatives.

II.1. Literature Survey
Chemistry of 2-Thioxo-4-thiazolidinone (Rhodanine) and its Derivatives.

Contents

1. Introduction

Rhodanine derivatives have shown a wide range of pharmacological activities, which include anticonvulsant, antibacterial, antiviral, and antidiabetic effects. Furthermore, rhodanine-based molecules have been popular as small molecule inhibitors of numerous targets such as HCV protease, aldose reductase, β-lactamase, JNK-stimulating phosphatase-1 (JSP-1).[1]

Also, rhodanines are widely used as vulcanizing agents, and intermediates in the synthesis of dyes. The absorption spectra of rhodanine have been studied in connection with interesting photosensibilizing and physiological properties of some 4-thiazolidinone derivatives. Another interesting aspect of the chemistry of these compounds is their donor ability towards metal ions, which make them suitable as ligands in coordination compounds. For example, rhodanine and its derivatives are used as highly sensitive and selective reagents for the analysis of certain noble metal ions of the Pt group and selective reagents for Pb and Hg.[1]

The rhodanine itself may theoretically exist in five tautomeric forms: (2-thioxo-4-thiazolidinone) **A**, (4-hydroxy-2(2H)-thiazolethione) **B**, (2-mercpato-4(5H)-thiazolone) **C**, (4-hydroxy-2(3H)-thiazolethione) **D** and (2-mercapto-4-hydroxy-thiazole) **E**, which are shown in (Fig. 1).[1]

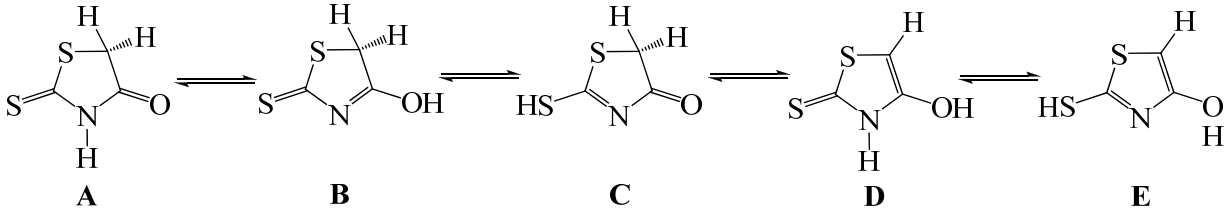

Fig. 1. Investigated tautomers **A-E**

The physical and chemical properties of rhodanine and its derivatives are more in harmony with thiazolidine structure **A**. Although certain properties indicate the participation of other tautomeric forms, none of the compounds exhibits properties of true aromatic thiazole ring; they show few reactions expected of thiazole **E**. The predominating properties are those expected for a cyclic imide or thioimide **A**.