English Abstract

University: King Saud University

College: College of Science

Department: Chemistry Department

Branch /Track: Chemistry

Title of Thesis: Synthesis of Some Quinazolinone and Pteridinone-yl-2-Oxo Thio/ Barbituric Acid Derivatives and Study of Their Biological Activity

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Abstract

The aim of this project is to prepare quinazolinone, pteridinone derivatives, quinazolinone and pteridinone compounds attached to barbituric acid, thiobarbituric acid or analogue compounds which have active methylene group via Mannich reaction. With hope to test their biological activities.

This project is divided into three chapters as follows:

Chapter 1. **Introduction and literature review**

This includes all reported and published research about the biological importance of the heterocyclic compounds that contain quinazolinone or pteridinone skeletons in addition to their synthesis and reactions.

Chapter 2. Results and discussions

In this chapter all data for some of the synthesized compounds were reported and discussed by interpretations the obtained spectral data. Their structural postulation and stereochemistry were mentioned

The synthetic strategy to obtaint target compounds (**I-XXI**) is illustrated in schemes (**I - V**).

The 2-Methyl-1,3-benzaoxazin-4-one (**I**) was obtained through reaction of Anthranilic acid with Acetic anhydride by heating under reflux or applying microwave irradiation. Which was further reacted with $NH_2NH_2H_2O$ to produce compound (**II**). Compounds (**III**) and (**IV**) were isolated after separation by (TLC).

Compound (**V**) was obtained by three methods, the first, two methods were as follows: condensation of compound (**I**) with *p*-Phenylinediamine in presence of Acetic acid (gl) or dry Pyridine . The third method is was by treatment of Anthranilic acid,

p-Phenylinediamine and Acetic anhydride under microwave irradiation. Compound (**VI**) was synthesized by reaction of compound (**V**) with Formaldehyde and

3-Methyl-phenyl-pyrazol-5-one**.** (**Scheme I**).

Compound (**VII**) was prepared from the reaction of Methyl anthranilate with CS_2 and $NH_2NH_2H_2O$. Compound (**VIII**) was obtained during the purification of compound (**VII**) using (TLC).

Also compound (**IX**) was synthesized by reaction of (**VII**) with Thiobarbituric acid and Formaldehyde. (**Scheme II**).

The compounds (**XI–XIV**) were prepared by applying Mannich reaction, this summarized in using; 3-Amino-2-isopropyl-4(3*H*)quinazolinone (**X**) to react with 1st Barbituric acid to produce compound (**XI**)**,** 2nd with Thiobarbituric acid to produce compound (**XII**)**,** 3rd with 3-Methyl-phenyl-pyrazol-5-one to produce compound (**XIII**) and finally with 4,4-diMethyl-1,3-cyclohexanedione; (**XIV**) was obtained. (**Scheme III**).

Upon the treatment of Benzoylglycine with 2,4,5-Trimethoxybenzaldehyde; compound (**XV**) was produced, this compound (**XV**) was further reacted with Methyl anthranilate or 5-Bromo analogue to produce compounds (**XVI** a**,**b**)** by fusion or heating. Some unsuccessful trails were carried out to prepare compounds (**XVII**a**,**b). via the reaction between compounds (**XVI** a**,**b) and $NH_2NH_2H_2O$ (**Scheme IV**).

The 2-Methyl-pyrazino[2,3-*d*][1,3]oxazin-4-one (**XVIII**) was obtained by refluxing of 3-Amino-pyrazino-2-crboxylic acid and Acetic anhydride in the presence of heating ; this compound (**XVIII**) was further reacted with *p*-Phenylinediamine in presence of Acetic acid (gl) to produce compound (**XIX**).

During purification of compound (**XIX**) using (TLC) compound (**XX**) was obtained. Unsuccessful attempts were carried out for preparation of compound (**XIX**) from reaction of compound (**XVIII**) with *p*-Phenylinediamine under microwave irradiation on the other hand this compound was obtained successfully from the reaction of 3-Amino-pyrazino-2-crboxylic acid, Acetic anhydride and *p*-Phenylinediamine under microwave irradiation, Furthermore compound (**XIX**) was allowed to react with 5,5-diMethyl-1,3-cyclohexanedione (Dimedone) and Formaldehyde to produce (**XXI**).

Scheme (**V**).

Some synthesized compounds (**V, X, XII, XIII, XIX**) were subjected to antimicrobial screening and produced variable activities against the tested migroorganisms. MIC was detected for the most active compound (**V, XIX**).

Chapter 3: Experimental

This chapter contains the experimental procedures for the synthesized compounds, percentage yield, melting points and recrystallization methods. Also the antimicrobial activities for some compounds were reported.

References are listed at the end of the thesis.