Synthesis of New Quinoxaline Derivatives of Expected Antimicrobial Action

Thesis presented by

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Submitted in partial fulfillment for the degree of
Master in Pharmaceutical Science
(Organic Chemistry)

This study involves a survey covering the synthesis, reactions and biological values of some quinoxaline derivatives.

Introducing the quinoxaline nucleus in different types of reactions to give a novel target compounds, was the aim of this thesis to study their expected antimicrobial activity.

This was accomplished during the course of this thesis *via* four schemes.

Scheme **I** includes the reaction of *o*- phenylenediamine wth a mixture of diethyl oxalate and ethyl acetate to obtain 3-ethoxycarbonylmethyl quinoxalin-2(1H)-one **(I)**, from which we obtain 3-methyl quinoxaline **II**. Bromination of the later with Br_2/AcOH led us to prepare 3-bromomethyl quinoxaline **III**. Reaction of compound **III** with different primary and secondary amines gave compounds **IVa-e**. Also, reacting **III** with hydrazine afforded 3-hydrazinomethyl quinoxalin-2 (1*H*)-one **(V)**, this compound was entered in two reactions, the first was condensation with different aromatic aldehydes to give compounds **VIa-c**, while the second one was cyclization of the hydrazino compound **V** with some aromatic aldehydes to give **VIId&e**. Also, compounds **VIa-c** were cyclized to give **VIIa-c**.

Scheme **II** consists of hydrazinolysis of the ester **I** resulted in the hydrazide **VIII**. Condensation of the later with some aromatic aldehydes afforded the arylidene derivatives **IXa-g**. Cyclization of **IXa-e** with acetic anhydride yielded substituted 1,3,5-oxadiazolines **Xa-e**. Also, reaction of the hydrazide **VIII** with certain acid anhydrides led to imide derivatives **XIa-c**.

Moreover, 3-hydrazinocarbonylmethyl quinoxalin-2(1*H*)-one **(VII)** was reacted with isocyanate and isothiocyanate derivatives to yield semi and thiosemicarbazides **XIIa-d**. Also, we obtain 5-oxo-1,2,4-triazole derivatives **XIIIa&b** from the reaction of **VIII** with isocyanate derivatives.

Scheme **III** includes the reaction of substituted thiosemicarbazides **XIIc&d** either maleic anhydride or chloroacetic acid to afford thiazolidinone derivatives **XIVa&b** and **XVa&b**, respectively.

One the other hand, ethyl or phenyl thiosemicarbazide **XIIc&d** was then cyclized either in acid medium to give 2,5-disubstituted 1,3,4-thiadiazole derivatives **XVIa&b** or in basic medium to yield 5-thioxo-1,2,4-triazoles **XVIIa&b**. Upon alkylation of the later with different alkyl or aryl halides, gave **XVIIIa-f**.

In scheme **IV**, 5-substituted-1,3,4-oxadiazol-2-thione **XIX** was prepared by heating the hydrazide **VIII** with CS_2 in the presence of alcoholic KOH. When **XIX** was subjected to Mannich reaction conditions, by reacting it with formaldehyde and different secondary amines in ethanol, it gave the corresponding 3-substituted aminomethyl-5-substituted 1,3,4-oxadiazol-2-thiones **XXa-d**.

Also, reaction of **XIX** with chloroacetic acid resulted in the formation of **XXI**, the later was oxidized with H_2O_2 to yield 5-substituted-1,3,4-oxadiazol-2-one **XXII**. Alkylation of **XIX** with different alkyl or aryl halides gave **XXIII**a-c.

The structural elucidation of the new compounds was supported by elemental analysis, IR, ^{1}H-NMR as well as mass spectral data.

The antimicrobial activity of seventeen selected novel compounds was performed at the department of Microbiology and Immunology, Faculty of pharmacy, Beni-Suef University. Some of the selected compounds showed antimicrobial activity.

القائم بأعمال رئيس قسم الكيمياء العضوية الصيدلية

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