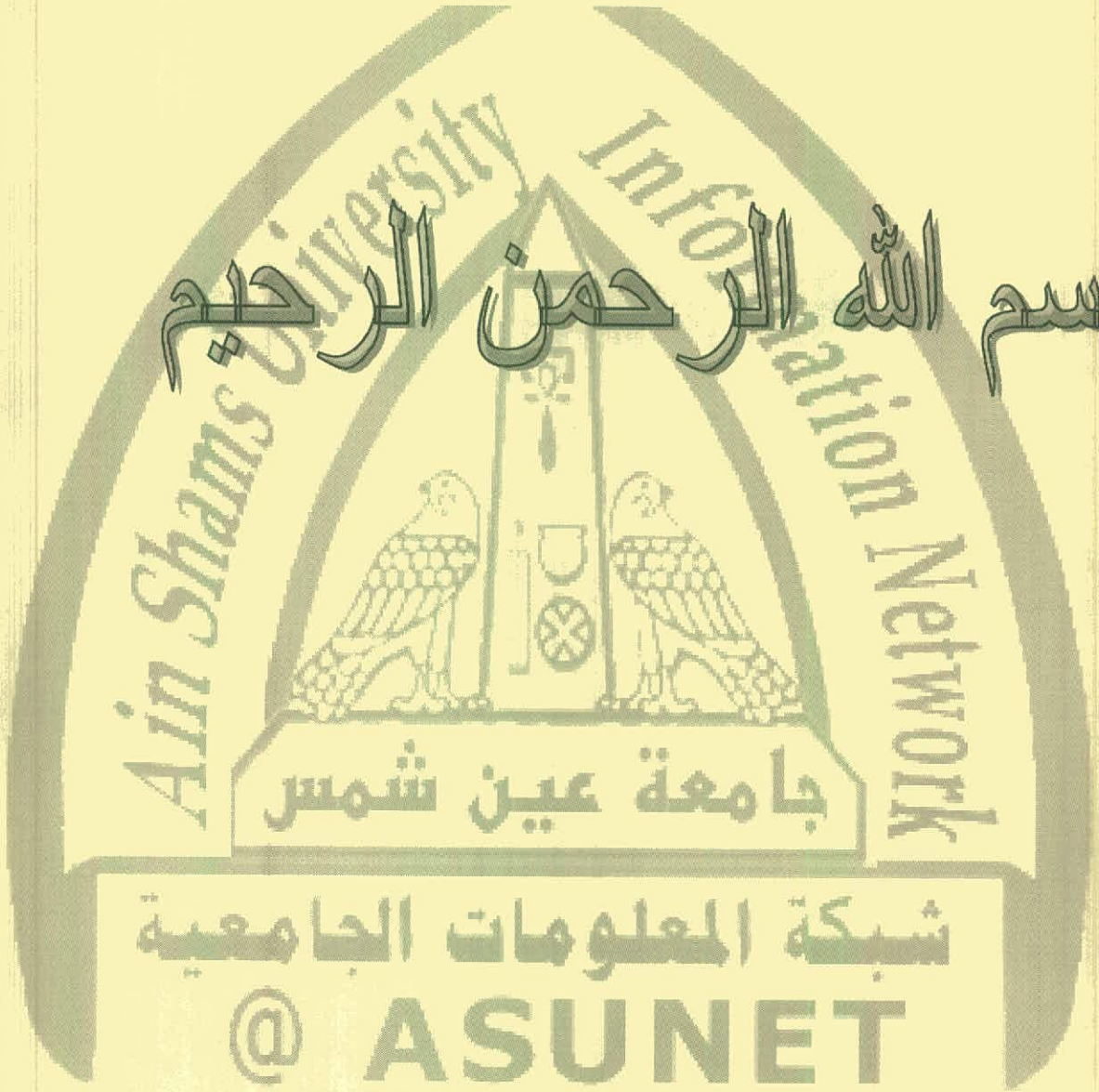
شبكة المعلومات الجامعية



بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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بالرسالة صفحات لم ترد بالاصل

Zagazig University
Benha Branch
Faculty of Science
Chemistry Department

Synthesis Of Some Pyrimidine Derivatives of Biological Interest

A thesis

Submitted in Partial fulfillment of the requirement of master degree

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2005

بسم الله الرحمن الرحيم

" وقل اعملوا فسيرى الله عملكم

ورسوله والمؤمنون"

صدق الله العظيم

الأية (١٠٥)من سورة التوبة

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Aim of the work

AIM OF THE WORK

It was reported that quinazoline nucleus having a great application in the field of chemotherapy. Also, pyrimidine nucleus have awide scope as chemotherapeutic agent, thus we plane in this thesis to synthesis some compounds having these two nucleus aiming to enhance their biological activity with each other.

Thus the present work is to synthesis some pyrimidinone and pyrimidinethione derivatives having a bulky heteryl group (quinazoline nucleus), then studying the behavior of prepared compound toward different carbon and nitrogen nucleophiles for comparing its reactivity,

Also, it is planed to incorporate the pyrimidine derivatives with amino acid derivatives using carbodiimide method with the objective of preparation of newer heterocyclic systems of biological interest.

Summary

SUMMARY

The work in this thesis involving the behaviour of 3-{4-[6-(4-methoxy-phenyl)-2-thioxo-2,3-dihydro-pyrimidin-4-yl]-phenyl}-2-methyl-3H-quinazolin-4-one (2a) and/or 3-{4-[6-(4-methoxy-phenyl)-2-oxo-2,3-dihydro-pyrimidin-4-yl]-phenyl}-2-met-hyl-3H-quinazolin-4-one (2b) toward some nitrogen and carbon nucleophiles with the aim of comparing reactivities and to synthesize some new heterocycle systems of biological interest.

Reaction of 2a and/or 2b with acrylonitrile afforded the Michael-type products 3a,b. Also, the acylation of 2a and / or 2b with acetic anhydride gave s- and o-acylated derivatives 4a,b and when 2a reacted with piperidine afforded the pyrimidine derivative 5, but the fusion of 2a with anthranilic acid gave the condensed product 6. On the other hand the reaction of 2a with ammonium acetate gave aminopyrimidine 7. Also, the alkylation of 2a, 2b with chloracetic acid afforded s- and o-acetic acid derivatives 8a,b. While, the oxidation of the thione 2a with $NaNO_2$/ACOH gave the corresponding disulphide 9.

The chlorination of 2b with $POCl_3/PCl_5$ afforded chloropyrimidine 10 which reacted with hydrazine hydrate in boiling ethanol to yield hydrazinopyrimidine 11 which used as a key intermidate for synthesis of arylhydrazone 12a-c, pyrazoyl pyrimidine derivatives 13,14. Reaction of pyrimidine derivatives 2a, 2b and/or 7 with phthalyl and/or tosylamino acids using the carbodiimide technique

in THF as a solvent afforded (pht- and/or-tos) mercapto, oxy and/or aminopyrimidine derivatives (15, 16, 17, 18, 19, 20)a-c respectively.

Hydrazinolysis of the phthalylamino acid derivatives (15, 17, 19)a-c by reaction with hydrazine hydrate in ethanol gave the corresponding amino acid derivatives (21, 22, 23)a-c respectively. The structure of all synthesized compounds was established by elemental analysis and spectroscopic data (IR, ^{1}H NMR, MS).

Biological activity of some synthesized compounds have been investigated and the result are cited in Table (3) which showed the remarkable biological activity due to the incorporation of pyrimidine and quinazoline nucleus in a single molecule.

CONTENTS

Introduction