

## 







شبكة المعلومـــات الجامعية التوثيق الالكتروني والميكروفيا.



## جامعة عين شمس

التوثيق الالكتروني والميكروفيلم



نقسم بللله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأفلام قد اعدت دون آية تغيرات



### يجب أن

تحفظ هذه الأفلام بعيداً عن الغبار

40-20 في درجة حرارة من 15-20 منوية ورطوبة نسبية من

To be kept away from dust in dry cool place of 15 – 25c and relative humidity 20-40 %









B1. VII

#### A THESIS ENTITLED

# SYNTHESIS AND REACTIONS OF SOME NEW HETEROCYCLIC COMPOUNDS CONTAINING N AND/OR S OF EXPECTED BIOLOGICAL ACTIVITIES

PRESENTED BY

MAHMOUD NASR EL-DEEN MAHMOUD GOUDA
(B.Sc., 1996)

FOR PARTIAL FULFILMENT OF THE DEGREE OF M. Sc. (ORGANIC CHEMISTRY)

CHEMISTRY DEPARTMENT FACULTY OF SCIENCE CAIRO UNIVERSITY

#### APPROVAL SHEET FOR SUBMISSION

TITLE OF M. Sc. THESIS

## SYNTHESIS AND REACTIONS OF SOME NEW HETEROCYCLIC COMPOUNDS CONTAINING N AND/OR S OF EXPECTED BIOLOGICAL ACTIVITIES

BY

MAHMOUD NASR EL-DEEN MAHMOUD GOUDA

This thesis has approved for submission by the supervisors:

1- Prof. Dr. Fawzy A. Attaby

Signature:

2- Dr. Mohamed A. A. Elneairy Signature:

3- Dr. Azza M. Abdel-Fattah Signature:

A. Attable of

A. M. Abdel fattah

Prof. Dr. Rifaat H. Hilal Signature:

Chairman of Chemistry Department

Faculty of Science-Cairo University

#### **ABSTRACT**

Name: Mahmoud Nasr El Deen Mahmoud Gouda

**Title**: Synthesis and Reactions of Some New Heterocyclic Compounds Containing N and/or S of Expected Biological Activities.

**Degree :** M. Sc. Thesis, Chemistry Department, Faculty of Science, Cairo University.

This work has been carried out to investigate the chemical reactivity and synthetic potentiality of 2-thioxohydropyridines **6a-c** via their reactions with several active halogen-containing compounds to afford the corresponding 2-alkylthiopyridines in some cases and thieno [2, 3-b] pyridines in most cases. Thieno [2, 3-b] pyridine-2-carbohydrazides obtained through the reactions of 2-ethoxycarbonylthienopyridines with hydrazine hydrate which in turn, used to obtain the corresponding pyrimidinones and oxadiazoles. 3-Aminopyrazolopyridines obtained via the reactions of **6a-c** with hydrazine hydrate and the diazonium salt of **6a** prepared and coupled with several active-hydrogen containing reagents to give the corresponding triazines. Structures of all newly synthesized heterocyclic compounds were established by considering the data of both spectroscopic and elemental analyses.

**Key Words:** 2-Cyanoethanethioamide, 2-Thioxohydropyridines, 2-Alkylthiopyridines, Haloalkanes, Thienopyridines, Thiopyranopyridines, Thienopyridine-2-carbohydrazides, Formamide and Triazines,

Supervisors: 1- Prof. Dr. Fawzy A. Attaby

2- Dr. Mohamed A.A. Elneairy

3- Dr. Azza M. Abdel-Fattah

Prof. Dr. Rifaat Hassan Hilal

Chairman of Chemistry Department Faculty of Science, Cairo University

### To

My Father
My Mother
My Wife

My Son

Dr. Rokia Yousef Saleh

Who Gave Me Help and Support

Mahmoud N. M. Gouda

#### M.Sc. Courses Studied by the candidates

Besides the work presented in this thesis, the candidate has attended passed successfully the following post-graduate courses as a partial fulfillment of the requirements for the degree of science.

- 1) Heterocyclic Chemistry
- 2) Advanced Physical Organic Chemistry
- 3) Photochemistry
- 4) Polymer Chemistry
- 5) Designing Organic Chemistry
- 6) Biochemistry
- 7) Natural Product
- 8) Applied Spectroscopy
- 9) Pericyclic Reactions
- 10) Organic Microanalysis
- 11) New Trends in Analytical Chemistry
- 12) Instrumental Analysis
- 13) Quantum Chemistry
- 14) Selected Topics
- 15) Mathematics and Scientific Compounds
- 16) Foreign Language (German)

Prof. Dr. Rifaat Hassan Hilal

Chairman of Department of Chemistry Faculty of Science – Cairo University

#### **AIM OF THE PRESENT WORK**

The present work aimed and was designed to fulfill the following objectives:

- 1- Continuation of the effort done by this group of research at Cairo University in the field of synthesis of heterocyclic derivatives of expected biological and medicinal activities.
- 2- Synthesis of several new heterocyclic derivatives containing nitrogen and / or sulphur using the laboratory available chemicals and reagents.
- 3- Establishment of the structures of the newly synthesized heterocyclic compounds by considering the data of TLC, IR, <sup>1</sup>H-NMR, mass spectra and the elemental analyses.
- 4- Synthesis of some of these heterocyclic derivatives via alternative routes which was also used as a tool to confirm the structures of the newly synthesized heterocyclic derivatives.
- 5- Study of the most probable mechanisms leading to the formation of the obtained heterocyclic products and comparison of our results with others of similar ring systems.

### **CONTENTS**

| SUMMARY OF THE ORIGINAL WORK                                | i    |
|---|------|
| INTRODUCTON   | 1    |
| UTILITY OF 2-CYANOETHANETHIOAMIDE IN SYNTHESI               | IS   |
| OF 2-THIOXOHYDROPYRIDINE-3-CARBONITRILES                    | 1    |
| Introduction  | 1    |
| Methods of preparation of 2-thioxohydropyridines            | 1    |
| 1-By the reactions with the carbonyl compounds              | 1    |
| 2-By the reactions with 1,3-diones                          | 11   |
| 3-By the reactions with alicyclic and heterocyclic ketones  | 20   |
| 4-By the Reaction with α,β-Unsaturated Ketones and Nitriles | 28   |
| 5-By the Action of Bases                                    | 52   |
| 6-By the Reaction with Formamide Acetals                    | 53   |
| 7-By the Reactions with Mono and Dicarboxylic acid Esters   | 54   |
| 8-By the Reaction with distyryl ketones                     | 55   |
| ORIGINAL WORK   | 56   |
| EXPERIMENTAL  | 85   |
| REFERENCES  | 113  |
| ARABIC SUMMARY  | Next |

### <u>ACKNOWLEDGMENT</u>

## "I do thank God for all gifts He gave Me"

The author of the present thesis wishes to express his deep thanks and sincere gratitude to professor Dr. Fawzy A. Attaby, Professor of Organic chemistry; Dr. Mohamed A. A. Elneairy associated professor and Dr. Azza. M. Abdel-Fattah lecturer of organic chemistry all from Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt, not only for suggesting the work investigated, but also for kind supervision, advice and valuable criticism through out the work performed.

Mahmoud N. M. Gouda

## SUMMARY OF THE ORIGINAL WORK

#### SUMMARY OF THE ORIGINAL WORK

The following is the summary of the original work investigated and included in the present thesis:

- The starting materials of the present study were synthesized by reacting 2-cyanoethanethioamide (1) with each of 1,3-diarylprop-2-en-1-ones 2a-c to give the corresponding 2-thioxohydropyridine-3-carbonitriles 6a-c. Compounds 6a-c used as good starting materials of the present study (cf. chart 1).
- Compounds 6a-c reacted with active halogen containing compounds
  7a-d in basic medium to afford the corresponding 2-alkylthioderivatives 8f,j,k which cyclized to their corresponding
  thieno[2,3-b]pyridines 9f,j,k in some cases while in most cases the
  corresponding thieno[2,3-b]pyridines 9a-e,g-i,l obtained without
  isolation of their corresponding 2-alkylthio derivatives (cf. Chart 2).
- On the other hand, compounds **6a-c** reacted with chloroacetyl chloride

  7e to give the corresponding SCOCH<sub>2</sub>Cl derivatives **8m-o** which cyclized in basic medium to afford the corresponding thiopyranopyridines **9m-o** (cf. Chart 3).