**Thesis Entitled**

# CHEMICAL REACTIVITY AND BIOLOGICAL IMPORTANCE OF 4,4'-BENZENE-1,4-DIYLBIS(5-ACETYL-6-METHYL-2-THIOXO-1,2-DIHYDROPYRIDINE-3-CARBONITRILE) AND ITS DERIVATIVES

**Presented**
**By**

**HESHAM KAMAL EL-DIN ALY MAHMOUD**

**A Thesis Submitted**
**To**

**Faculty of Science**
**In Partial Fulfillment Of The Requirements For**
**The Degree Of Master Of Science**
**(Organic Chemistry)**

**Chemistry Department**
**Faculty of Science**
**Cairo University**

**(2010)**

# APROVAL SHEET FOR SUMISSION

**Title of M. Sc. Thesis:**

## CHEMICAL REACTIVITY AND BIOLOGICAL IMPORTANCE OF 4,4'-BENZENE-1,4-DIYLBIS(5-ACETYL-6-METHYL-2-THIOXO-1,2-DIHYDROPYRIDINE-3-CARBONITRILE) AND ITS DERIVATIVES

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**2- Prof. Dr. Fawzy Ali Attaby**

**Signature:**

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**Signature:**

**Chairman of Chemistry Department**
**Faculty of Science- Cairo University**

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## ***ACKNOWLEDGEMENT***

***Praise be to God, Show us the straight path***

***I am heartily thankful to my supervisors, Professor Dr.Abdella M. Negm, professor Dr. Fawzy Ali Attaby, Faculty of Science, Cairo University, whose encouragement, guidance and support from the initial to the final level enabled me to develop an understanding of the subject and also a special thanks for Dr. Mohamed M. Elsayed, Associated Professor, Research Units, Hi-Care Pharmaceutical Co., Cairo, Egypt for the Valuable support.***

***Lastly, I offer my regards and blessings to all of those who supported me in any respect during the completion of this thesis.***

***Hesham Kamal EL-Din Aly***

# ABSTRACT

**Student Name:** Hesham Kamal EL-Din Aly Mahmoud.

**Title of The Thesis:** Chemical Reactivity and Biological Importance of 4,4'-benzene-1,4-diylbis(5-acetyl-6-methyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile) and Its Derivatives.

**Degree:** M.SC. (Organic Chemistry)

This work has been carried out to investigate the synthetic potentiality of bis2-thioxhydropyridines **8** via their reactions with several active halogen-containing compounds to afford the corresponding bis2-alkylthiopyridines **10a-h** in some cases and bisthieno[2,3-b]pyridines **11a-h** in most cases. Bisthieno[2,3-b]pyridine-2-carbohydrazides **15** obtained through the reac-tions of **11a** with hydrazine hydrate which in turn, used to obtain the corresponding bispyrimidinones, bispyrazols, bispyrazolones, and bis- oxadiazoles. bis3-Aminopyrazolopyridines **25** obtained via the reactions of **8** with hydrazine hydrate and the bisdiazonium salt of **25** was prepared. Structures of all new compounds were established by considering the data of both spectroscopic and elemental analysis, also anti-Alzheimer, Anti-Cancer activities.

**Keywords**: 2-Cyanoethanethioamide, Bis 2-Thioxohydro pyridine, Bis 2-Alkylthiopyridine, Haloalkanes, BisThienopyridines, Bis2-CyanoThieno pyridine, BisThienopyridine-2-carbohydrazides, Bis3-Aminopyrazolopyrid-ine, Bispyridopyrazolotriazine.

**Supervisors:**

1- **Prof. Dr. Abdella M. Negm**

2- **Prof. Dr. Fawzy Ali Attaby**

**Prof. Dr. Mohamed A. Badawy**

**Chairman of Chemistry Department**
**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 sulfur using the available laboratory chemicals and reagents.

3- Establishment of the structures of the newly synthesized heterocyclic compounds by considering the data of IR, $^{1}$H-NMR, HPLC/ mass spectrometry and the elemental analysis.

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.

*To*

*My Late Father*

*My Mother*

*My wife*

*My sister*

*My brother*

*Who have never failed to give me*

*moral support,*

*Hesham Kamal EL-Din Aly Mahmoud*

## M.Sc. Courses Studied by the Candidate

Besides the work presented in this thesis, the candidate has attended and passed successfully the following post-graduate courses as a partial fulfillment of the requirement for the degree of Master of Science:

1. Instrumental Analysis of Molecular Structures.
2. Quantum Chemistry.
3. Applied Spectroscopy.
4. Dyes Chemistry.
5. Heterocyclic Chemistry,
6. Designing Organic Chemistry.
7. Photochemistry.
8. Polymer Chemistry.
9. Carbohydrate Chemistry.
10. Biochemistry.
11. Natural Products.
12. Molecular Orbital Symmetry.
13. Physical Organic Chemistry.
14. Selected Topics.
15. Foreign language (Germany).

**Prof. Dr. Mohamed A. Badawy**

**Signature:**

**Chairman of Chemistry Department**

**Faculty of Science- Cairo University**

# CONTENTS

LIST OF TABLES Page



LIST OF FIGUERS

# *SUMMARY OF THE ORIGINAL WORK*

# SUMMARY OF THE ORIGINAL WORK

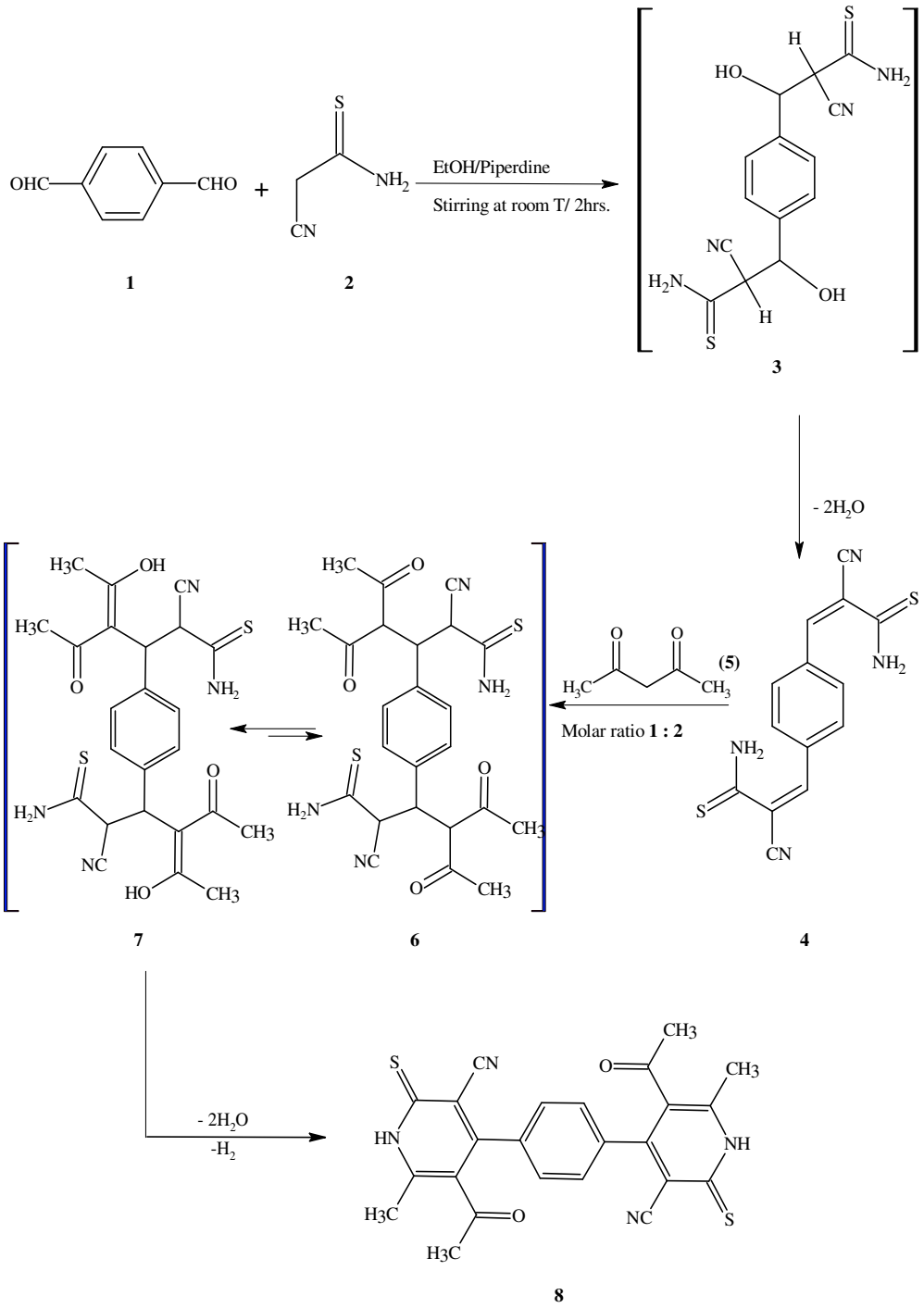
The following is the summary of the original work investigated and included in the present thesis:

1- The starting materials of the present study were synthesized by reacting Benzene-1,4-dicarbadehyde **1** with 2-cyanoethanethio amide **2** to give the corresponding bis2-thioxohydropyridine-3-carbonitrile **8**. Compound **8** used as good starting material of the present study (cf. Scheme 1).

2- Compounds **8** reacted with active halogen containing compounds **9a-h** in the basic medium to afford the corresponding bis2-alkyl thio derivatives **10a-h** which cyclized to their corresponding bis thieno[2,3-b]pyridines **11a-h** in some cases the corresponding bis thieno[2,3-b]pyridines **11a-h** obtained without isolation of their corresponding bis2-alkylthio **10a-h** derivatives (cf. Scheme 2).

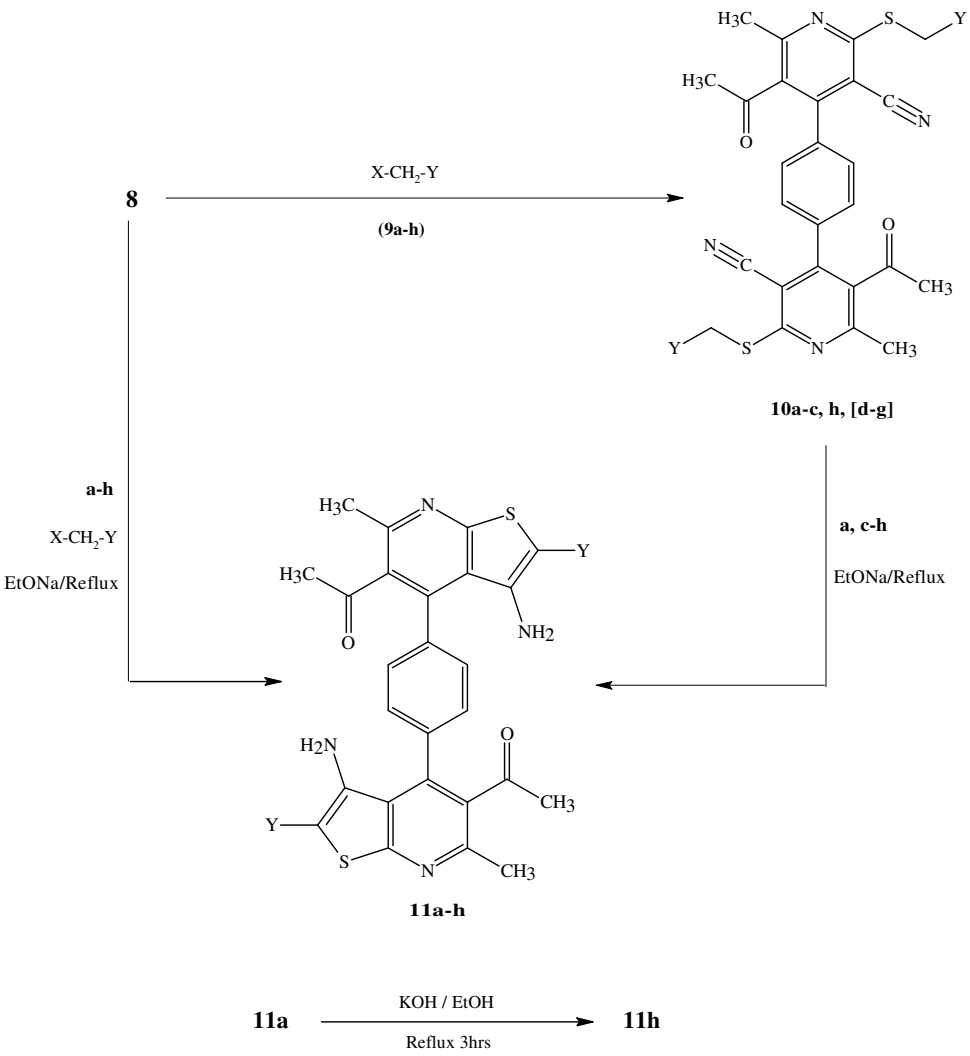
3- On the other hand compounds **8** reacted with ethyl chloroacetate **9a** to give the corresponding $SCOOCH_2CH_3$ derivatives **10a** which cyclized in basic medium to afford the corresponding bisthieno[2,3-b]pyridine-2-carboxylate **11a** (cf. Scheme 2).

4- The synthetic potentiality of compounds **11c** was investigated through the reaction with Formic acid, Acetic anhydride, and Nitrous acid to give the corresponding pyrimidinones **12**, **13**, and **14**, respectively (cf. Scheme 3).




**1** **2** **3** **4** **6** **7** **8**

**Scheme 1**




| 9, or 10 | X | Y |
|---|---|---|
| **a** | Cl | COOEt |
| **b** | Cl | $CONH_2$ |
| **c** | Cl | CN |
| **d** | Cl | CONHPh-p-Br |
| **e** | Br | COPh-p-Cl |
| **f** | Br | COPh |
| **g** | Cl | COMe |
| **h** | Cl | COOH |

**Scheme 2**