#### **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

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(Organic Chemistry)

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# 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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#### **ACKNOWLEDGEMENT**

Praise be to God, Show us the straight path

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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

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#### **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, <sup>1</sup>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.

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).

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### SUMMARY OF THE ORIGINAL WORK

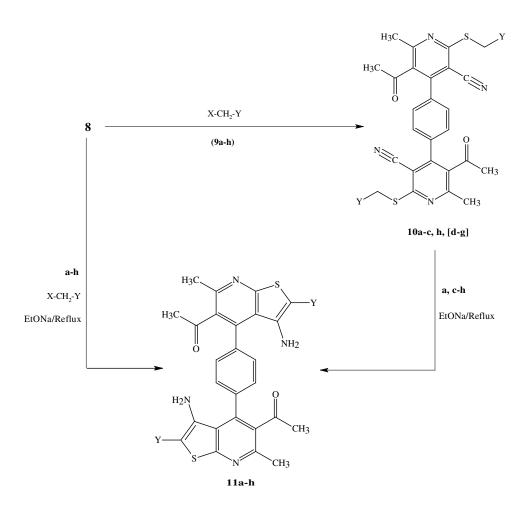
#### SUMMARY OF THE ORIGINAL WORK

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<sub>2</sub>CH<sub>3</sub> 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).

OHC — CHO + 
$$\frac{1}{CN}$$
  $\frac{S}{NH_2}$   $\frac{EiOH/Piperdine}{Stirring at room T/ 2hrs.}$   $\frac{1}{CN}$   $\frac{1}{NC}$   $\frac{1}{NH_2}$   $\frac{1}{NC}$   $\frac{1}{NH_2}$   $\frac{1}{NH_2}$   $\frac{1}{NH_2}$   $\frac{1}{NH_2}$   $\frac{1}{NC}$   $\frac{1}{NH_2}$   $\frac{1}{N$ 

Scheme 1



11a	KOH / EtOH	 11h
11a -	Reflux 3hrs	1111

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	СООН

Scheme 2