Salwa Akl

# بسم اللّه الرحمن الرحيم

## مركز الشبكات وتكنولوجيا المعلومات

## قسم التوثيق الإلكتروني

Salwa Akl

# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

## قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

Salwa Akl


# بعض الوثائق الأصلية تالفة
# وبالرسالة صفحات لم ترد بالأصل

B 18359

# SYNTHESIS OF SOME DERIVATIVES OF THIADIAZOLES PYRAZOLO[5,1-c]TRIAZINES AND PYRROLO[1,2-a]BENZIMIDAZOLES WITH EXPECTED BIOLOGICAL ACTIVITY

A Thesis Submitted
*By*

**SHEREEN ABD EL AZIZ AMER**

B.Sc. (*Hons.*)

For M. Sc. DEGREE OF SCIENCE
(Organic Chemistry)

DEPARTMENT OF CHEMISTRY
FACULTY OF SCIENCE
CAIRO UNIVERSITY

GIZA, EGYPT

2000

## APPROVAL SHEET FOR SUBMISSION

Title of [M.Sc] Thesis :

**Synthesis of some derivatives of thiadiazoles, pyrazolo[5,1-c]-triazines and pyrrolo[1,2-a]benzimidazoles with expected biological activity.**

Name of the candidate : **Shereen Abdel Aziz Amer**

This thesis has been approved for submission by the supervisors:

1- **Prof. Dr: Mohamed M.M. Sallam**

Signature : m.m.m. Sallam

2- **Prof. Dr. Abdou O. Abdelhamid**

Signature : A.O. Abdelhamid

3- **Prof. Dr. Salwa M. Dogheim**

Signature : Salwa

**Prof. Dr. Mohamed Helmy Elnagdi**

Prof. M. H. EL-NAGDI

Chairman of Chemistry Department.

Faculty of Science – Cairo University

# Abstract

**Name** : Shereen Abdel Aziz Amer

**Title of thesis :** Synthesis of some derivatives of thiadiazoles, pyrazolo-[5,1-c]triazines and pyrrolo[1,2-a]benzimidazoles with expected biological activity.

**Degree** : M.Sc. Unpublished Master of Science Thesis, Faculty of Science, Cairo University.

**This work has been carried out to investigate :**

The reaction of potassium thiocyanate with each of *C*-acetyl-*N*-(5-phenyl)pyrazol-3-yl chloride and *C*-ethoxycarbonyl-*N*-(5-phenyl)pyrazol-3-yl chloride was reinvestigated. The products were formulated as 2,3-dihydro-1,3,4-thiadiazoles instead of pyrazolo[5,1-*c*]triazine derivatives. On the other hand, 2,3-dihydro-1,3,4-thiadiazoles were synthesized via reaction of hydrazonoyl halides with the appropriate 2-[mercapto(methylthio)methylene]indan-1,3-dione in ethanolic triethylamine solution in good yields. Pyrazolo[5,1-*c*]triazine derivatives were obtained by the reaction of hydrazonoyl bromides containing pyrazole moiety with sodium benzenesulfinate. The structures of these compounds are confirmed on the basis of analytical, spectral data, and alternative route. Thus, coupling of pyrazole diazonium chloride with the appropriate ketosulfones afforded the corresponding pyrazolo[5,1-*c*]triazines. Also, reaction of 2-cyanomethylbenzimidazole with hydrazonoyl chlorides was studied. All structures were elucidated on the basis of elemental analyses, spectral data, and alternative routes.

**Key word** : Hydrazonoyl halides, 2,3-dihydro-1,3,4-thiadiazole, pyrazolo[5,1-*c*]-triazines, 2-cyanomethylbenzimidazole and indane-1,3-dione.

**Supervisors :**

(1) Prof. Dr. Mohamed M.M. Sallam — Signature

(2) Prof. Dr. Abdou O. Abdelhamid — Signature

(3) Prof. Dr. Salwa M. Degheim — Signature

Prof. M. H. EL-NAGDI

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# ACKNOWLEDGMENT

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I also wish to express my deep gratitude to Prof. Dr. Salwa M. Dogheim, Professor of Pesticides Chemistry, Director of Central laboratory of residue analysis of Pesticides and heavy metals in food, for her help and support.

Besides the work carried out in this thesis, the candidate **Shereen Abdel Aziz Amer** has attended post-graduate courses during the academic year 1993-1994 in the following topics:

1 - Heterocyclic Chemistry.

2 - Applied Spectroscopy.

3 - Advanced Physical Organic Chemistry.

4 - Natural Products.

5 - Biochemistry.

6 - Polymer Chemistry.

7 - Designing Organic Chemistry.

8 - Pericyclic Reactions.

9 - Organic Photochemistry.

10- Organic Microanalysis.

11- New Trends in Analytical Chemistry.

12- Instrumental Analysis.

13- Quantum Chemistry.

14- Selected Topics.

15- Mathematics and Scientific Computations.

16- Foreign Language (German).

SHe has also passed successfully an examination on the above mentioned topics.

**Prof. Dr. Mohamed Helmy Elnagdi**

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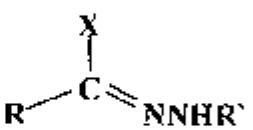
# LITERATURE SURVEY

N-Phenylbenzhydrazonoyl chloride was first synthesized by V. Pechmann in 1894[1]. In their reactions hydrazonoyl chlorides bear a close resemblance to the other imidoyl chlorides. They have been used by Fusco[2a,b] and his co-workers to synthesize a variety of pyrazole derivatives, and Huisgen[3] et al utilized this class of compounds to generate the highly reactive nitrile imides. The latter compounds reacted as 1,3-dipoles with a wide variety of substrates to form the corresponding five-membered ring heterocycles, which are often quite difficult to synthesize by other routes.

In addition to the N-arylhydrazonoyl chlorides, numerous N-substituted compounds, such as N-carboxylic acid derivatives, have been synthesized. Since their discovery, hydrazonoyl halides 1 have emerged as an important class of intermediates, particularly for the synthesis of heterocyclic compounds. Although several summaries covering the reactions of **1** have been published[4-9], the chemistry of hydrazonoyl halides characterized by the structural formulas **2-4** has received little attention.

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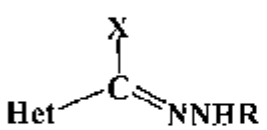


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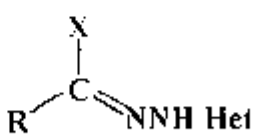


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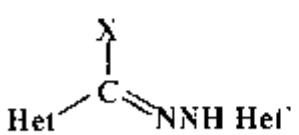


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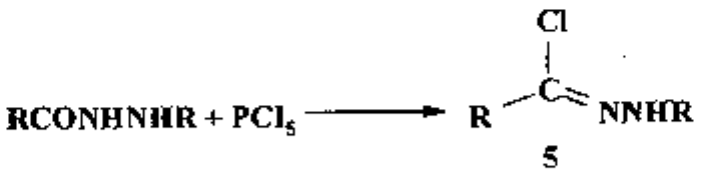
# I. SYNTHESIS OF HYDRAZONOYL HALIDES

## I.1. From Carboxylic Acid Hydrazides.

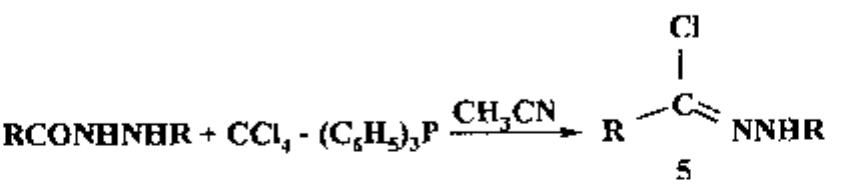
The reaction of carboxylic acid hydrazides with phosphorus pentachloride is the classical method for the synthesis of hydrazonoyl chlorides[1-10].



**5**

This reaction can be conducted either without solvent or using inert organic solvents such as ether, chloroform, carbon tetrachloride or methylene chloride, and the yields are quite good.

Wolkoff[11] also, synthesized the hydrazonoyl chlorides **5** from carboxylic acid hydrazides by the reaction with triphenylphosphine-carbon tetrachloride ($Ph_3P$-$CCl_4$) in acetonitrile.



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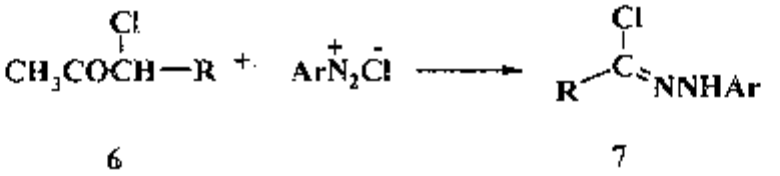
## I.2. From Diazonium Halides.

The coupling of diazonium halides with suitable halogenated activated methylene groups is an excellent method for the synthesis of a variety of hydrazonoyl halides. This method has been used by Favrel [12-14], Dieckmann[15]

et al and other workers[16-21] to synthesize the acetyl, carboxyl and carboalkoxy derivatives 7.



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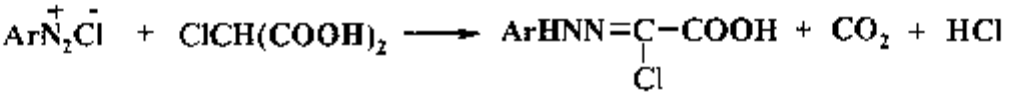
The free carboxylic acid **9** is obtained from chloromalonic acid **8** and the corresponding diazonium chloride[22-23].



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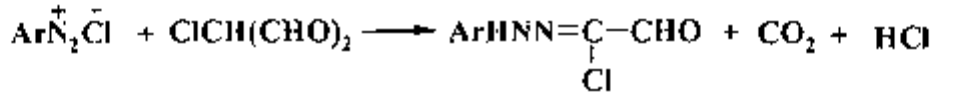
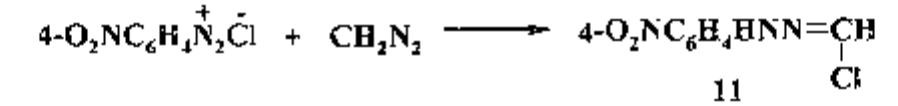
In a similar manner the aldehyde **10** is obtained from chloromalonaldehyde and arenediazonium chloride[15].



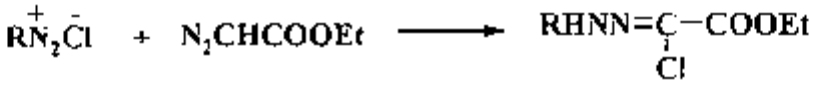
**10**

The reaction of 4-nitrobenzendiazonium chloride with diazomethane yields the formhydrazonoyl chloride **11** in 81% yield[24].



**11**

Similarly, the reaction of ethyl diazoacetate with diazonium chlorides yields carboxyalkyl hydrazonoyl chlorides **12**[24].

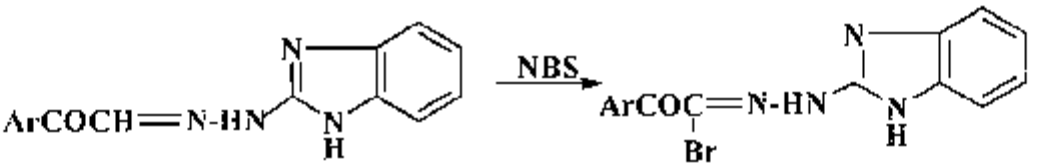


**12**

**1.3: From Aldehyde Hydrazones.**

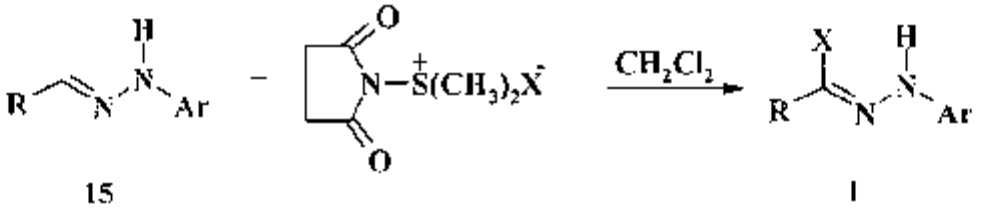
Direct halogenation of arylhydrazones of both aliphatic and aromatic aldehydes with the appropriate halogen in glacial acetic acid is an excellent method for the synthesis of the corresponding hydrazonoyl halides **1**[4,5]. This method has also been used for the synthesis of hydrazonoyl halides of types **2-4**[25,26].

Hydrazonoyl bromides **13** were also obtained by refluxing the hydrazone **14** with N-bromosuccinimide in dry carbon tetrachloride[27].




**14** **13**

Recently, Patel[28] et al reported a new and convenient method for the synthesis of hydrazonoyl halides. Hydrazone **15** on treatment with N-chloro- or N-bromosuccinimide-dimethylsulfide complex resulted in the formation of the corresponding hydrazonoyl halides in good yields.




**15** **1**