



*Ain- Shams University
College of Women for Arts,
Science and Education*

***Synthesis of Some Heterocyclic Compounds Using
Sonoenergy and Study of Their Cytotoxic Activities.***

***A Thesis
Submitted for the Degree of Ph.D. Degree in Science
(Organic Chemistry)
By***

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2013



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***A Thesis
Submitted for the Ph.D. Degree in Science
(Organic Chemistry)***

***By
Walaa Hamdy Abd El- Zaher Lasheen***

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Approved



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QUALIFICATION

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Name of College: College of Women for Arts, Science and Education

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B.Sc. Graduation Year: 2004

M.Sc. Graduation Year: 2010

Ph.D. Graduation Year: 2013

Dedication

*To My family, mother, father, sister, brothers,
daughter and my son for their love and moral support in my whole life.*

*To My husband for his patience, encouragement, cooperation
and love.*

*To All my friends and colleagues for their
Kindness and support.*



ACKNOWLEDGEMENT

In the name of Allah

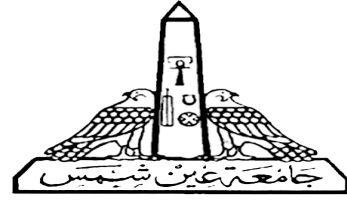
The candidate is cordially acknowledge and indebted to my supervisors Prof. Dr. Samia A. El-Abbady and Prof. Dr. Abdel-Sattar S.H.Elgazwy professors of the organic chemistry Ain Shams university, not only for suggesting the subject investigated, but also for continuous advice and valuable criticism through out the work of the thesis.

The candidate wish also to thank Dr. S. M. Agamy, Ass. Prof of organic chemistry, department of chemistry, College of Women for Arts, Science and Education Ain -Shams University, for her great help through out the work.

At last, thanks Allah

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جامعة عين شمس
كلية البنات للآداب والعلوم والتربية
قسم الكيمياء

تخليق بعض المركبات العضوية غير المتجانسة و المحضرة بواسطة الموجات فوق الصوتية و دراسة النشاط السمي لها

رسالة مقدمة إلى
قسم الكيمياء
كلية البنات - جامعة عين شمس

من
ولاء حمدي عبد الظاهر لاشين

ماجستير علوم (كيمياء)

للحصول على

درجة دكتوراة الفلسفة في العلوم في الكيمياء

تحت إشراف

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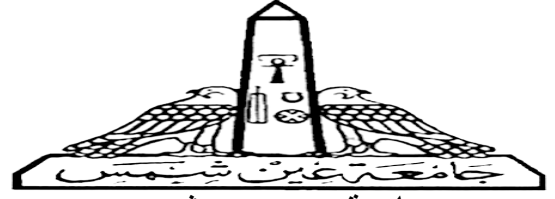
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اسم الكلية : البنات للأداب والعلوم والتربية

الجامعة: عين شمس

سنة التخرج: ٢٠٠٤

سنة المنح : ٢٠١٠



جامعة عين شمس
كلية البنات للأداب والعلوم والتربية
قسم الكيمياء

شكر و تقدير

تتقدم الطالبة بخالص الشكر والتقدير للجنة الاشراف على الرسالة المكونة من

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على التوجيه و الإشراف و المتابعة الفعلية أثناء فترة البحث العملى وخلال الاعداد
النهائى للرسالة .

كما تتوجه الطالبة بالشكر للاستاذ الدكتور فتن محمود رئيس قسم الكيمياء و لجميع
أعضاء القسم لحسن تعاونهم معها خلال العمل فى رساله.

Abstract of the thesis

The student synthesized new heterocyclic compounds having bioactive agents. These compounds were prepared by coupling of 1,3-dipolar cycloaddition reactions with some synthesized 2(3H)-foranones.

Similarly, the student studied the 1,3-dipolar cycloaddition reactions with corresponding oxo-pyrrolins. The synthesized new heterocyclic compounds having multi nitrogen atoms showed high activities against different cell lines.

AIM OF THE WORK

To study the coupling of 1,3- dipolar cycloaddition reactions with 2[3H]-furanones and corresponding oxo pyrrolines derivatives.

By using of ultrasound energy to give the corresponding products which were purified by using chromatography.

The obtained products were proved by different tools of spectroscopic (IR, ¹H-NMR, GC/MS).

These products were also study against different cell lines and showed bioactive microbial.

SUMMARY

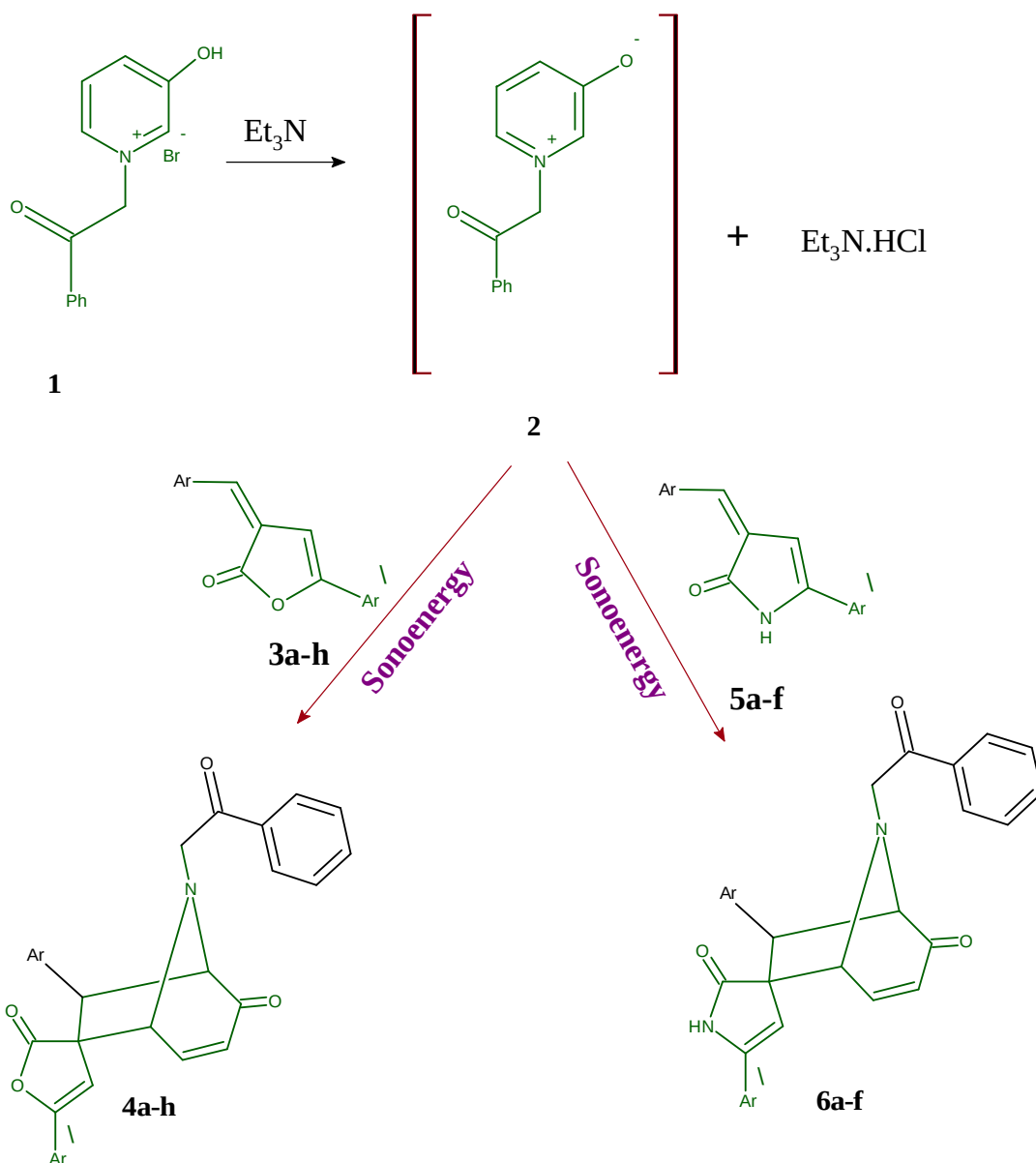
The present work is dealing with the 1, 3-dipolar cycloaddition reactions of 3-Hydroxy-1-Phenacylpyridiniumbromide (1) and 3-Hydroxy-1-(3-nitrobenzyl)pyridiniumchloride (2) with the different 2(3H)-furanones, and corresponding oxo-pyrrolines as unusual 2π -electron end cap. The products obtained were substantiated from their spectral evidences (e.g., IR, $^1\text{H-NMR}$, and GC/MS spectra). Investigation of the obtained cycloadducts by IR and $^1\text{H-NMR}$ spectra verified that the adducts were formed via the cycloaddition processes between the titled pyridinium-3-olates (1) and (2) as 4π -electron component across the 2,6-positions of the pyridinium ring, and the used 2(3H)-furanones and corresponding oxo-pyrrolins as 2π -electron addends. Structural and configurational assignments of the obtained new adducts were substantiated from IR, $^1\text{H-NMR}$, and GC/MS spectra. IR spectra revealed the stretching frequencies of both lactones and α,β -unsaturated carbonyls. On the other hand, $^1\text{H-NMR}$ spectra displayed H-7 proton of the isolated sole cycloadduct in each case as a doublet at δ (ppm) = 2.4 is in accord that the sole stereoisomer isolated in every case is the 7-exo stereoisomer, this is not surprised owing to the steric inhibition of the spiro-lactone moiety at position-6 of the aza- bicyclo ring. H-7 appeared as a doublet owing to its coupling with H-1. This verifies that the cycloaddition processes were found to be regiospecific and stereo specific as well. It was confirmed that the used 2π -electron addends, 2(3H)-furanones and corresponding oxo-pyrrolines used the exo-olefinic double bond as the 2π -electrocyclic component in the cycloaddition process. Investigations of the $^1\text{H-NMR}$ spectra of the obtained adducts verified the exo-configuration at 7-position. From all the spectroscopic tools confirmed that the 1,3-dipolar

cycloaddition reactions occurred on the exo-double bond and not on endo-double bond for 2(3H)-furanones and corresponding oxo-pyrrolines.

The potential of the obtained cycloadducts as biologically active compounds were investigated it was shown that all of the isolated adducts have a potential in the following aspects:

1- Antimicrobial activity.

2- Tumor inhibitory properties towards a variety of different cell lines in cancers.



a-Ar= 2-furyl , Ar¹ = 4-methylphenyl
 b-Ar= 4-nitrophenyl , Ar¹ = 4-methylphenyl
 c-Ar= 2-aminophenyl , Ar¹ = 4-methylphenyl
 d-Ar= 2-thienyl , Ar¹ = 4-methylphenyl
 e-Ar= 2-furyl , Ar¹ = phenyl
 f-Ar= 4-nitrophenyl , Ar¹ = phenyl
 g-Ar= 2-aminophenyl , Ar¹ = phenyl
 h-Ar= 2-thienyl , Ar¹ = phenyl

a-Ar= 2-furyl , Ar¹ = 4-methylphenyl
 b-Ar= 4-nitrophenyl , Ar¹ = 4-methylphenyl
 c-Ar= 2-aminophenyl , Ar¹ = 4-methylphenyl
 d-Ar= 2-thienyl , Ar¹ = 4-methylphenyl
 e-Ar= 2-furyl , Ar¹ = phenyl
 f-Ar= 2-aminophenyl , Ar¹ = phenyl

Scheme1