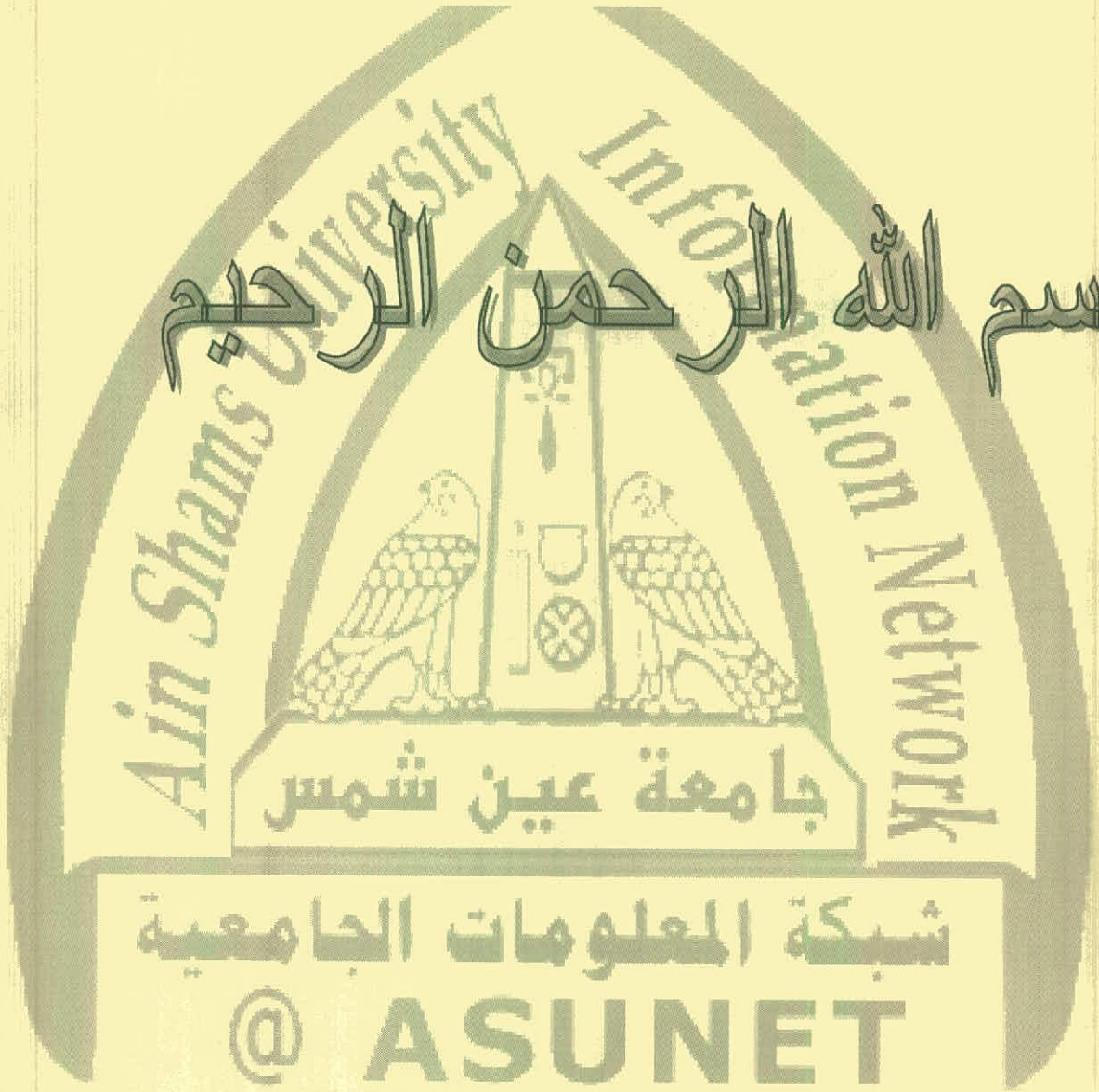
شبكة المعلومات الجامعية



بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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بالرسالة صفحات لم ترد بالاصل

SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NEW FUROCHROMONE AND BENZOFURAN DERIVATIVES

A THESIS SUBMITTED

TO

FACULTY OF SCIENCE
AIN - SHAMS UNIVERSITY

FOR

THE DEGREE OF MASTER OF SCINCE
(CHEMISTRY)

PRESENTED
BY

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B.SC. (CHEMISTRY)

NATIONAL RESEARCH CENTRE
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(1995)

Synthesis and Biological Evaluation of Some

New Furochromone and Benzofuran Derivatives

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This is to certify that: **Nehad Ahmed Abdel-Latif** has attended and passed successfully the following postgraduate courses as partial fulfillment of the requirement for the degree of Master of Science.

1- **Advanced studies in physical organic chemistry**
   i) polar reaction mechanism
   ii) Pericyclic reactions.
2- **Advanced studies in heterocyclic chemistry.**
3- **Advanced studies in applied spectroscopic analysis ' Electronic spectra, Infrared, ^{1}HNMR, ^{13}C NMR and Mass spectroscopy of organic chemistry.**
4- **Advanced studies in natural products.**
5- **Advanced studies in microanalysis.**
6- **Advanced studies in polymer chemistry.**
7- **Advanced studies in aromaticity.**
8- **Advanced studies in organic reagents**
9- **Advanced studies in organometalic compounds.**
10- **Advanced studies in photochemistry.**
11- **Advanced studies in free radical reaction mechanism.**
12- **Selected topics in organic reactions.**
13- **Courses in English language.**

ACKNOWLEDGEMENT

First of all, I would like to extend due praise and thanks to **ALLAH** that this work has been completed.

I am deeply grateful to Prof. Dr. Mohamed Mohamed Habashi, Professor of organic chemistry, Chemistry Department, Faculty of Science, Ain Shams University, for his consistent supervision, valuable criticism and continuous guidance.

I wish to express my sincere gratitude to Prof. Dr. Effat Abdel-Hamid Abu-Mustafa, Professor of Natural Products, National Research Centre, for suggesting the topic of this work, supervision and for her moral support.

My sincere gratitude to Dr. Adel Hamed Mandour, Associate Professor of natural products, National Research Centre, for his valuable discussion and help.

My thanks to Prof. Dr. Zeinab E. El-Bazza, Professor of Pharmaceutical Microbiology, National Centre for Radiation Research and Technology, Atomic Energy authority, for her helping in carrying out the biological activity test. Also, I would like to express my thanks to all collaborators of Pharmaceutical Microbiology Lab.

I would like to express my thanks to all members of the Natural Products and microbes Department of National Research Centre, who helped me to make this work possible.

Last but not least, due thanks are extended to the administration of the National Research Centre in Cairo, for providing me with the necessary facilities for this work to be accomplished.

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S U M M A R Y

Synthesis and Biological Evaluation of Some New Furochromone and Benzofuran Derivatives

Aim and Summary of the work

The increasing chemothrapeutic properties of visnagin and benzofuran derivatives led us to synthesize some new sulfonamide derivatives in a trial to obtain much more potent products with more biological activity than the parent compounds.

To start with, visnagin-9-sulfonamide derivatives were condensed with aromatic aldehydes to give visnagin-7-styryl-9-sulfonamide derivatives for the purpose of evaluating their antimicrobial activity.

The introduction of heterocyclic ring system (1,2,3-thia and selenadiazol-4-yl) through the sulfonamide linkage at 9-position of visnagin was achieved to evaluate antimicrobial activity of the newly produced compounds.

Moreover, the action of alkali (3% KOH) or hydrazine hydrate on visnagin-9-sulfonamide derivatives were studied in order to obtain new compounds with higher biological activity.

The whole work including the synthesis and biological evaluation of the new visnagin derivatives is presented in two main parts, the chemical and biological parts.

I-The chemical part:

This part is presented in the following two sections:

I:1-Synthesis of some visnagin-7-(substituted styryl)-9-sulfonamide derivatives:

Condensation of aromatic aldehydes, namely, benzaldehyde, p-chlorobenzaldehyde or p-nitrobenzaldehyde with the key intermediates, visnagin-9-sulfonamide derivatives (XXXIIa-c and CVII) (Scheme 1), and in the presence of sodium ethoxide led to

the formation of visnagin-7-(substituted styryl)-9-sulfonamide derivatives (CVIIIa-c), (CIXa-c), (CXa-c) and (CXIa-c), respectively (Scheme 2a-d).

I:2-Synthesis of visnagin-9-N[4-(1',2',3'-thia and selenadiazol -4'-yl) phenyl] sulfonamide derivatives (CXIV) and (CXV):

The reaction of visnagin-9-sulfonyl chloride (XIX) with p-aminoacetophenone gave visnagin-9-N-(p-acetophenyl) sulfonamide (CXII), which in turn was reacted with semicarbazide hydrochloride in the presence of crystalline sodium acetate to give the corresponding semicarbazone derivative (CXIII). The oxidative cyclization of the latter compound using thionyl chloride or selenium dioxide led to the formation of visnagin-9-N[4-(1',2',3'-thia (CXIV) or selenadiazol (CXV)-4'-yl)phenyl] sulfonamides (Scheme 3).

I:3-Synthesis of visnaginone-7- sulfonamide derivatives (CXVIa-d):

The alkaline hydrolysis of the key intermediates (XXXIIa-c and CVII) using 3% KOH led to the opening of the γ-pyrone ring and formation of the 6-hydroxy-5-acetyl-4-methoxy benzofuran -7-sulfonamido derivatives (CXVIa-d) (Scheme 4).

I:4-Synthesis of 6-hydroxy-4-methoxy-5-[5'-methylpyrazol-3'-yl] benzofuran-7-sulfonamide derivatives (CXVIIa-d):

The reaction of the key intermediates with hydrazine hydrate (1:1o mols) in ethanol, led to the opening of γ-pyrone ring and formation of the pyrazole derivatives (CXVIIa-d) (Scheme 5).

I:5- Synthesis of the chalcones (CXVIIIa-d):

The condensation of the compounds (CXVIa-d) with benzaldehyde in the presence of sodium hydroxide gave the corresponding 4-methoxy-6-hydroxy-5-cinnamoyl benzofuran-7-sulfonamido derivatives (CXVIIa-d) (Scheme 6).

II- Biological Activity:

II:1-Antimicrobial Activity:

The prepared compounds were tested against two strains of Gram-positive and two strains of Gram-negative bacteria, one strain of yeast and one strain of fungi. As a conclusion, all compounds possess moderate activity towards Gram-positive and Gram-negative bacteria and yeast. On the other hand, they possess high activity towards fungi (c.f. Table 1).

II:2- Antiaflatoxigenic Activity :

The prepared compounds were tested in two concentrations against standard organism (Aspergillus parasiticus NRRL 3145) which produced aflatoxins (B_1, B_2, G_1 and G_2). In general, the compounds under test may be used as fungistatic or fungitoxicant agents.