Ain Shams University
Faculty of Science
Department of Chemistry

Chemical and Photochemical Studies on Some Amino Heterocyclic Nitrogen Compounds

Thesis Submitted by

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M.Sc. Organic Chemistry (2008)

To Chemistry Department, Faculty of Science
Ain Shams University

For Ph.D. Degree in Organic Chemistry

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ACKNOWLEDGEMENT

First and foremost I'm deeply thankful to almighty "**ALLAH"** for showing me the right path, and helping me to complete this work.

I wish to express my cordial thanks and gratitude to **Prof. Dr. Ahmed Ismail Hashem**, Professor of Organic Chemistry, Faculty of Science, Ain Shams University, for his continuous advices and valuable help during the progress of this thesis.

My sincere thanks and gratitude are also due to **Prof. Dr. Afaf Ali Nada**, Professor of Organic Chemistry, Photochemistry Department, National Research Centre (NRC) for her support, useful advices and her constructive encouragement.

My deep thanks and appreciation to **Prof. Dr. Asma Mohamed Mahran**, Associate Professor of Organic Chemistry, Photochemistry Department, (NRC) for suggesting the subject investigated, for her valuable advices, and for ensuring that the thesis is in the well-presented form.

Great thanks to **Prof. Dr. Fransisco Raymo**, Professor of Organic Chemistry, laboratory of Molecular Photonics, University of Miami, USA for his continuous help in the second project.

I would like to express my great thanks to **Prof. Dr. Vladimir Kuzmin** from Institute of Biochemical Physics, Russian Academy of Science, Moscow, Russia for his assistance in the third project.

Additionally, I extend my thanks to all members of Photochemistry Department.

I wish to express my cordial thanks and gratitude to **National Research Centre,** Giza, Egypt for providing the facilities during this work.

Sherif Shaban Ragab

List of abbreviations

1D	One-dimensional
^{1}H NMR	Proton Nuclear Magnetic Resonance
Ac_2O	Acetic anhydride
AcOH	Acetic acid
ATP	Adenosine Triphosphate
B3LYP	Becke 3-Parameter, Lee, Yang and Parr
BODIPY	Boron-dipyrromethene; 4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene
Cl_2TZ	Dichlorotetrazine
CNS	Central nervous system
DAP NPs	2,3-Diaminophenazine Nanobelts
DDQ	2,3-Dichloro-5,6-dicyano-*p*-benzoquinone
DFT	Density Functional Theory
DHQ	1,2-Dihydroquinoline
DIPEA	N,N-Diisopropylethylamine
DMEM	Dulbecco's Modified Eagle's Medium
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
ESIMS	Electrospray Ionization Mass Spectrometry
Et_3N	Triethyl amine

ETQ	6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline
eV	Electron Volt
FBS	Fetal bovine serum
FRAP	Fluorescence recovery after photobleaching
GIBCO	Grand Island Biological Company
Hb	Hemoglobin
IC_{50}	Inhibitory concentration 50
ICT	Intramolecular charge-transfer
IR	Infrared
MeCN	Acetonitrile
MPW1PW91	Barone's Modified Perdew-Wang 1991 exchange functional and Perdew and Wang's 1991 correlation functional
N-DHQ	6-Ethoxy-2,2,4-trimethyl-8-nitro-1,2-dihydroquinoline
OBISDIEN	1,13-dioxa-4,7,10,16,19,22-hexaazacyclotetracosane
OPDA	o-Phenylenediamine
ORTEP	Oak Ridge Thermal Ellipsoid Plot
PCSS	Personal Chemistry Smith Synthesizer
PKIs	Protein Kinase Inhibitors
PKs	Protein Kinases
Rt	Room temperature

List of abbreviations

SADABS	Siemens Area Detector Absorption
SHELX	Sheldirck X-ray
SRB	Sulforhodamine B
TDDFT	Time-dependent density-functional theory
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
Triflate	Trifluoromethanesulfonate
TMS	Trimethylsilane
TRK	Tyrosine Kinase
UV	Ultraviolet

Contents

BODIPY Dyes: Syntheses and Chemical Reactions

Project II

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Abstract

Project I

This project reports simple convenient methods for the synthesis of some heterocycles incorporating triazolophenazine, imidazo[4,5-b]phenazine, pyrazino[2,3-a]phenazine, diazepino[2,3-a]phenazine and azophenazine moieties in order to investigate their anticancer activities. The structures of all products were confirmed on the basis of microanalysis and spectral data.

Project II

In this study, functional chemical systems which combine luminescent and photochromic components within the same construction were designed as in BODIPY chromophore. The manipulation of the groups attached to boron atom in BODIPY could then be exploited to regulate the emissive behavior of the overall chromophore and, possibly, activate fluorescence under optical control. Indeed, this study reports the implementation of a mechanism for fluorescence activation based on the photoinduced exchange of the ligands connected to the BODIPY fluorophore.

Project III

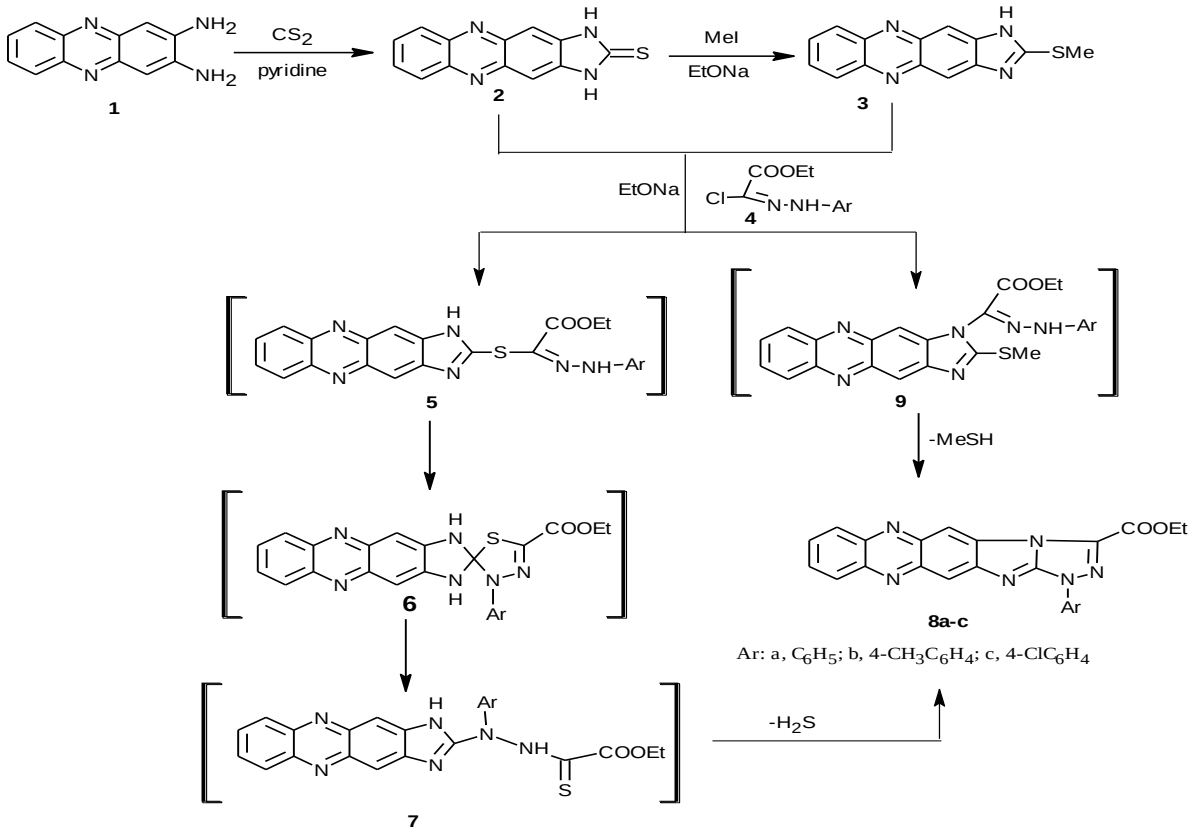
The spectral and kinetic parameters of transient species generated in the irradiation of 6-ethoxy-2,2,4-trimethyl-8-nitro-1,2-dihydroquinoline were examined by stationary and pulse photolysis in different solvents. Upon excitation at the long wavelength (λ_{ex}> 450 nm), a reversible photochemical reaction was revealed. The absorption spectra and the rate constants of the decay of transient species are almost independent of the medium polarity and the presence of oxygen in the system. The mechanism of the reversible photochemical reaction is suggested.

English Summary

The original work of the thesis includes three research projects:

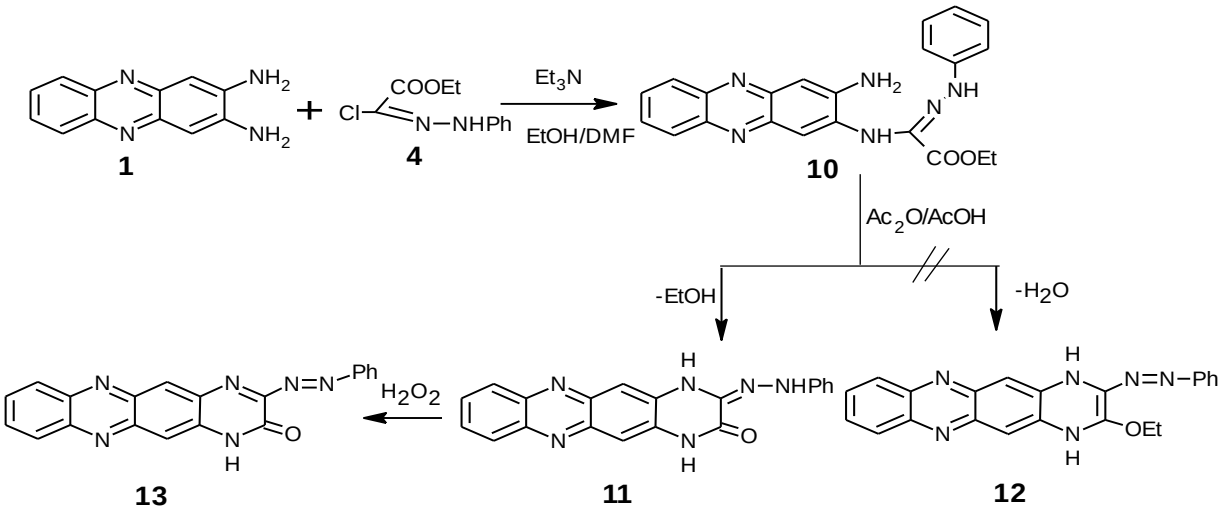
The first project entitled "**Synthesis and Anticancer Screening of Novel Polynuclear Heterocyclic Compounds Derived from 2,3-Diaminophenazine**".

Refluxing compound **1** with carbon disulfide in pyridine afforded imidazo-[4,5-b]phenazine-2-thione **2**. Treatment of **2** with methyl iodide in the presence of sodium ethoxide in refluxing ethanol afforded 2-methylsulfanyl-imidazo-[4,5-b]phenazine **3**. The reaction of **2** or **3** with ethyl N^1-arylhydrazon-N^2-chloroacetate **4** in ethanol in the presence of sodium ethoxide under reflux gave the unreported products **8a-c**. The assigned structure **8** for the newly isolated products was based on microanalysis and spectral data (IR, ^{1}H-NMR, Mass) (Scheme 1).



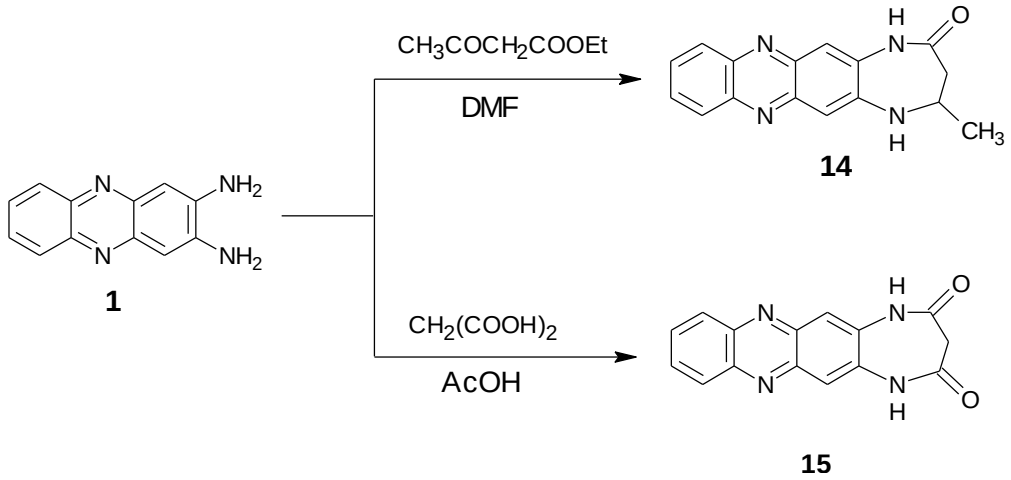
(Scheme 1)

Treatment of equimolar quantities of **1** and **4** in ethanol/DMF mixture under reflux temperature in presence of triethylamine afforded phenylhydrazono derivative **10** which cyclized upon treatment with acetic anhydride/ acetic acid mixture under reflux to afford pyrazino[2,3-b]phenazine derivative **11** which was oxidized with hydrogen peroxide to give **13** (Scheme 2).



(Scheme 2)

Refluxing a mixture of **1** and ethyl acetoacetate or malonic acid in DMF afforded 6*H*-7-methyl[1,4]diazepino[2,3-b]phenazine-9-one **14** and 6*H*-[1,4]diazepino-[2,3-b]phenazine-7,9-dione **15** respectively (Scheme 3).



(Scheme 3)