



***Synthesis of Some New Heterocyclic Systems
Containing Nitrogen with Expected Potential
Biological Activity***

A Thesis for Ph.D. Degree in Organic Chemistry

Presented by

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(M. Sc.)

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***A Thesis Submitted for the Degree of Doctor of
Philosophy in Science
(Organic Chemistry)***

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Contents

	pages
(Acknowledgement)	
English Summary	I
Introduction	1
Chemistry of 1,2,4-triazines	1
A. Synthesis of 1,2,4- triazine derivatives	2
B. Reactions of 1,2,4- triazine compounds	
1. Reactions of 3-chloro-5,6-diphenyl-1,2,4-triazine.....	10
a. Reactions with oxygen nucleophiles.....	10
b. With sodium cyanide.....	10
c. With sodium hexenyloxide.....	11
d. With phenols and thiophenols.....	11
e. Reactions with carbon nucleophiles.....	12
f. With cyanoacetic acid hydrazide.....	14
g. Reactions with nitrogen nucleophiles.....	14
h. With sulfa drugs.....	15
i. With thiosemicarbazide.....	15
2. Reactions of 3,5,6-triphenyl-1,2,4-triazine.....	17
a. Reactions with dienophiles and alkynes.....	17
b. Reactions with Grignard reagents.....	18
3. Reactions of 3-cyano-5,6-diphenyl-1,2,4-triazine.....	19
a. Reactions with Grignard reagents.....	19
b. Reactions with nitrogen nucleophiles.....	20
4. Reactions of 3-amino-5,6-diphenyl-1,2,4-triazine.....	20
a. Diel's alder reaction.....	20

b. Cyclization reactions	21
c. With aldehydes.....	22
d. With thiophenol.....	23
5. Reactions of 3-hydrazino-5,6-diphenyl-1,2,4-triazine.....	24
a. Reactions with pi-acceptors activated carbonitriles.....	24
b. Reactions with β -keto carbonitriles.....	29
c. Reactions with α,β - unsaturated carbonyl compounds.....	30
d. Reactions with unsymmetrical 1,3-dicarbonyl compounds.	34
e. Reactions with α,β -bifunctional oxygen-halogen compounds	35
f. With cyanogen bromide.....	36
g. With formic acid.....	37
h. Reaction with phenyliso(thio) cyanate.....	37
i. With a variety of one carbon cyclizing agents.....	39
j. Reactions with phosphorus compounds.....	40
k. With nitrous acid	44
l. With carbonitriles.....	45
m. With bromo malononitrile.....	46
n. Reaction with aldehyde.....	47
o. With carbon disulphide.....	48
p. Reaction with acetic anhydride.....	48
q. Reaction with ethyl chloro acetate.....	49
C. Biological activity.....	50

Part II : Synthesis of thienopyrimidines.....	53
1. Annulations of pyrimidine on thiophene ring	53
i. Using thiophene having vicinal amino/ester groups.....	53
a. With iso cyanate and isothio cyanate derivatives.....	54
b. With formamide.....	62
c. With nitrile compounds.....	63
d. With acetic anhydride.....	64
e. With urea and their derivatives.....	65
ii. Using thiophene having vicinal cyano/amino groups.....	65
a. With formic acid.....	65
b. With triethyl orthoformate.....	66
c. With nitrile compounds.....	67
iii. Using thiophene having vicinal amino/carboxamide groups.....	68
a. With aldehydes.....	68
b. With acid halides.....	69
c. With formamide.....	69
d. With triethyl orthoformate.....	70
e. With halogenated compounds.....	71
2. Annulations of thiophene on pyrimidine ring.....	71
i. From uracil and thiouracil derivatives.....	71
ii. From thioxopyrimidine derivatives.....	72
iii. From chloropyrimidine derivatives.....	72
3. Synthesis of thienopyrimidines from acyclic compounds.....	74

<i>Reactions of thienopyrimidines</i>	74
i. Reactions attributed to thiophene ring.....	74
a. Halogenation.....	74
b. Vilsmeier- Haack reaction	75
c. Nitration	76
d. Ring opening of the thiophene ring.....	76
ii. Reactions attributed to nitrogen of the pyrimidine ring.....	77
a. Alkaylation	77
b. With alkyl halide.....	78
<i>Biological activity</i>	78
<i>Result and discussion</i>	80
<i>Experimental</i>	138
<i>Spectroscopic Figures</i>	
<i>References</i>	185
<i>Arabic Summary</i>	i

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Abstract

Diazines and Triazines and their derivatives play an important role in medicinal chemistry due to their high biological activity. They are known to possess a broad spectrum of pharmacological activities such as antiviral, antibacterial, fungicidal, insecticidal, herbicides, hypotensive, hypothermic activities, in vitro supporting their anti-HIV, anticancer activities and biological inhibitors.

The original work of this thesis can be classified into three parts:

Part 1: In this part Synthesis of hydrazino 1,2,4-triazine derivative and its reactions with different reagents to form novel triazine derivatives.

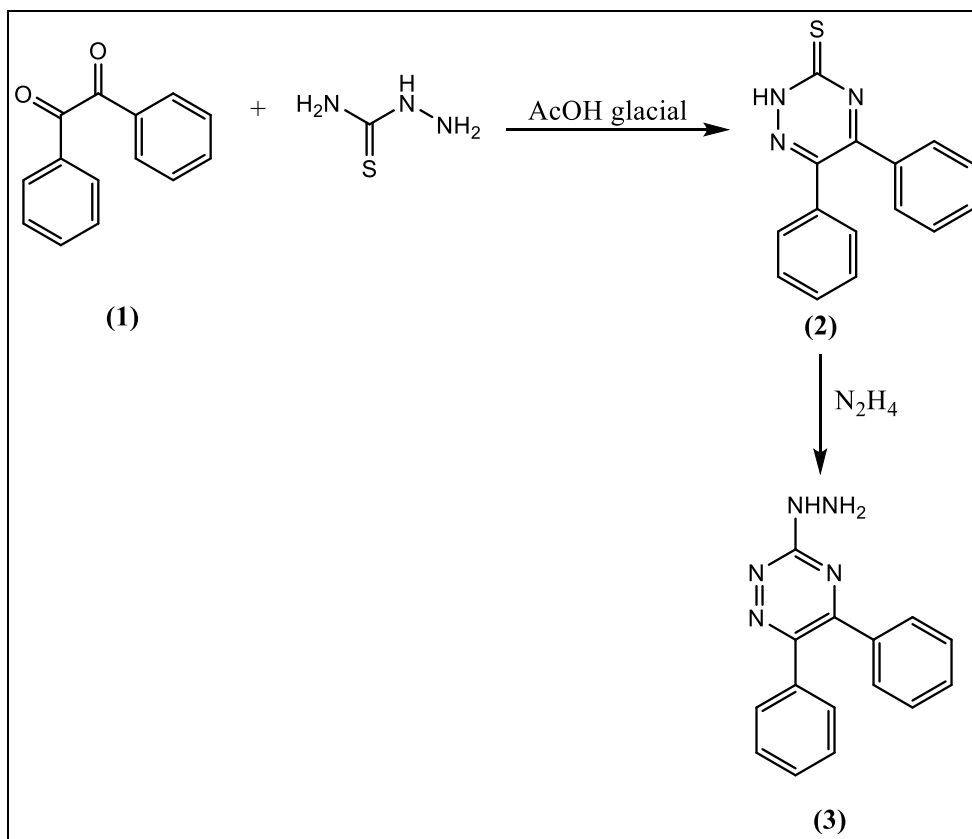
Part 2: In this part Synthesis of an acid hydrazide derivative and its utility in building of new hetrocyclic systems such as oxadiazole, triazole and pyrazole derivatives.

Part 3: The antitumor activities of some of the synthesized compounds were examined against liver and breast cancer cell lines.

Part (I): synthesis of some novel 1,2,4-triazine derivatives

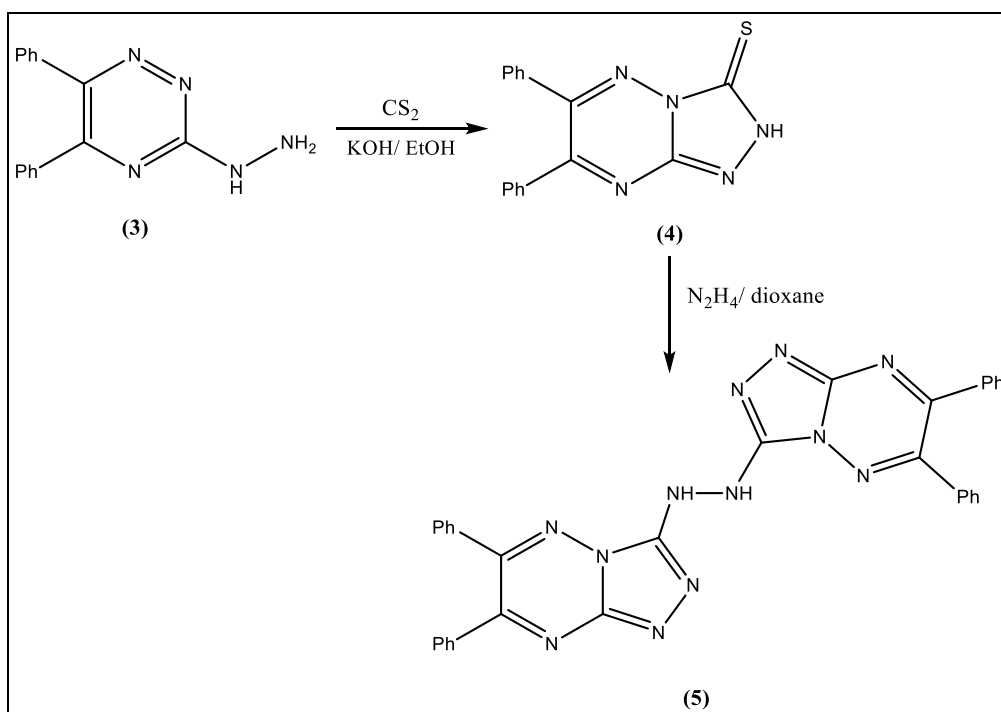
1,2,4-Triazines and their derivatives have been widely studied in terms of their synthetic methodologies and reactivity since some of these derivatives were reported to have promising biological activities.

3-hydrazino-5,6-diphenyl-1,2,4-triazine was synthesized by condensation of benzil **1** with thiosemicarbazide followed by another condensation of the intermediate **2** with hydrazine hydrate to construct the hydrazino triazine derivative **3** (Scheme 1).



(Scheme 1)

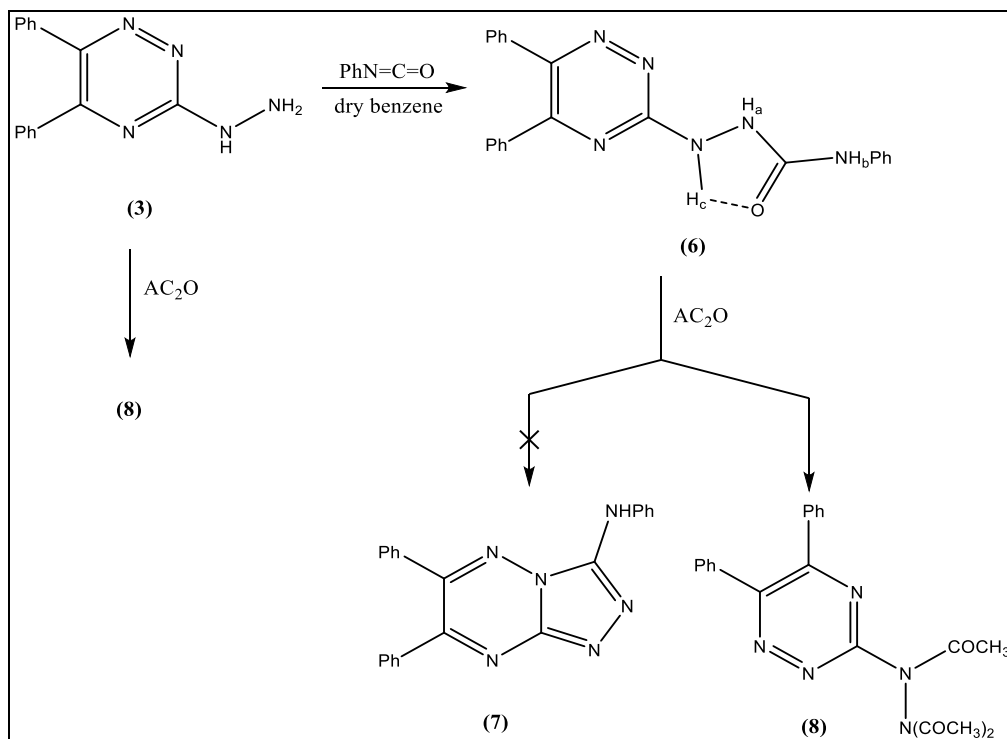
Reaction of compound **3** with carbon disulfide in ethanol in the presence of KOH as a base, afforded the cycloaddition product triazolotriazine derivative **4**. When thione derivative **4** is treated with hydrazine hydrate in boiling dioxane, it gave the di heteryl hydrazine derivative **5** with a removal of H₂S gas (**Scheme 2**).



(Scheme 2)

Heating of compound **3** with phenyl isocyanate in dry benzene gave the corresponding addition product semicarbazide derivative **6**. Treatment of the semicarbazide derivative **6** with acetic anhydride yielded the triacetyl derivative **8** instead of the triazolotriazine derivative **7**.

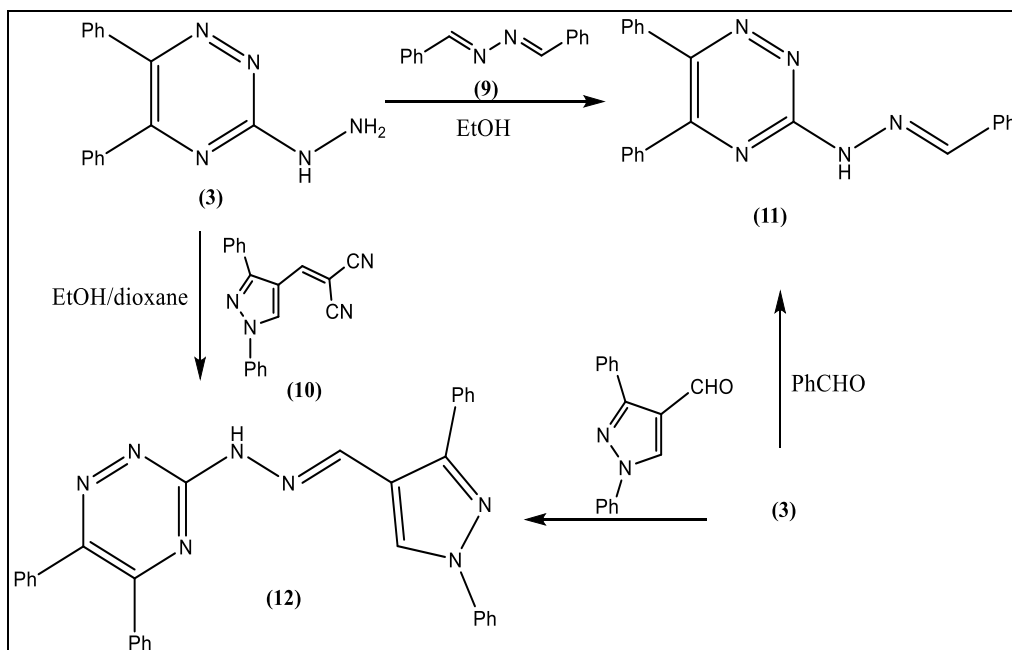
A chemical proof for the suggested structure is gained by preparing an authentic sample, through reacting of compound **3** with acetic anhydride. (**Scheme 3**).



(Scheme 3)

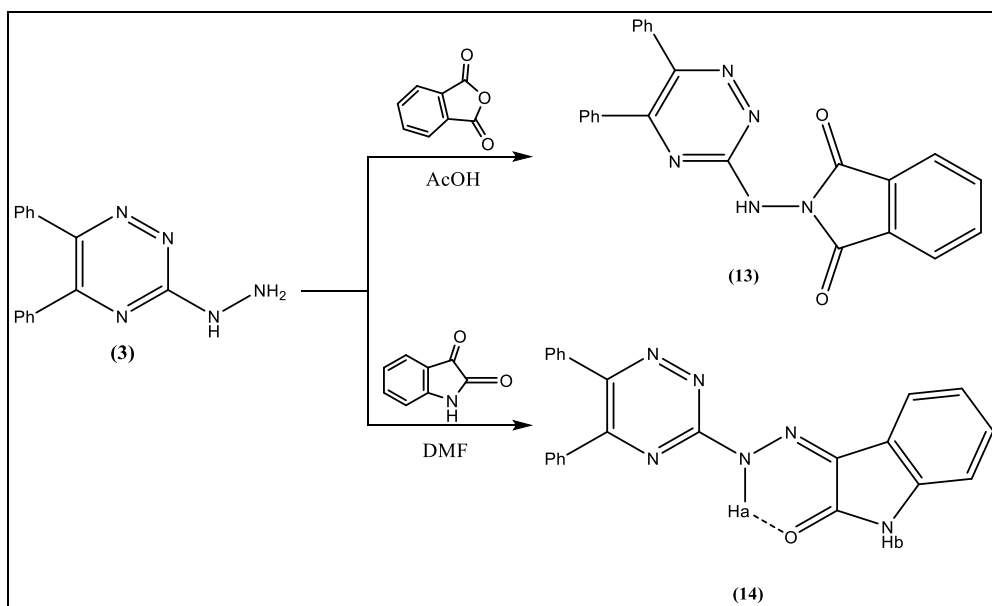
The treatment of compound **3** with dibenzylidene hydrazine **9** and /or pyrazolidine derivative of malononitrile **10** gave the benzalhydrazone and pyrazolidinehydrazone derivatives **11** & **12**, respectively. The structures of both compounds **11** and **12** were confirmed chemically by preparing authentic samples from

reactions of compound **3** with benzaldehyde and / or 1,3-diphenyl pyrazol-4-carbaldehyde (**Scheme 4**).



(Scheme 4)

Heating of compound **3** with phthalic anhydride in acetic acid under reflux gave the isoindoline derivative **13**. However its heating with isatin in DMF as a solvent yielded the schiff's base derivative **14** (**Scheme 5**).



(Scheme 5)

Treatment of compound **3** with ethyl acetoacetate in boiling ethanol afforded the corresponding condensation product **15** as a mixture of Syn- and anti-isomers. On the other hand, cyclocondensation product triazinotriazepine derivative **16** is produced by reacting of compound **3** with acetylacetone in boiling ethanol (**Scheme 6**).