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

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

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Sandy Samy Samir

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.*

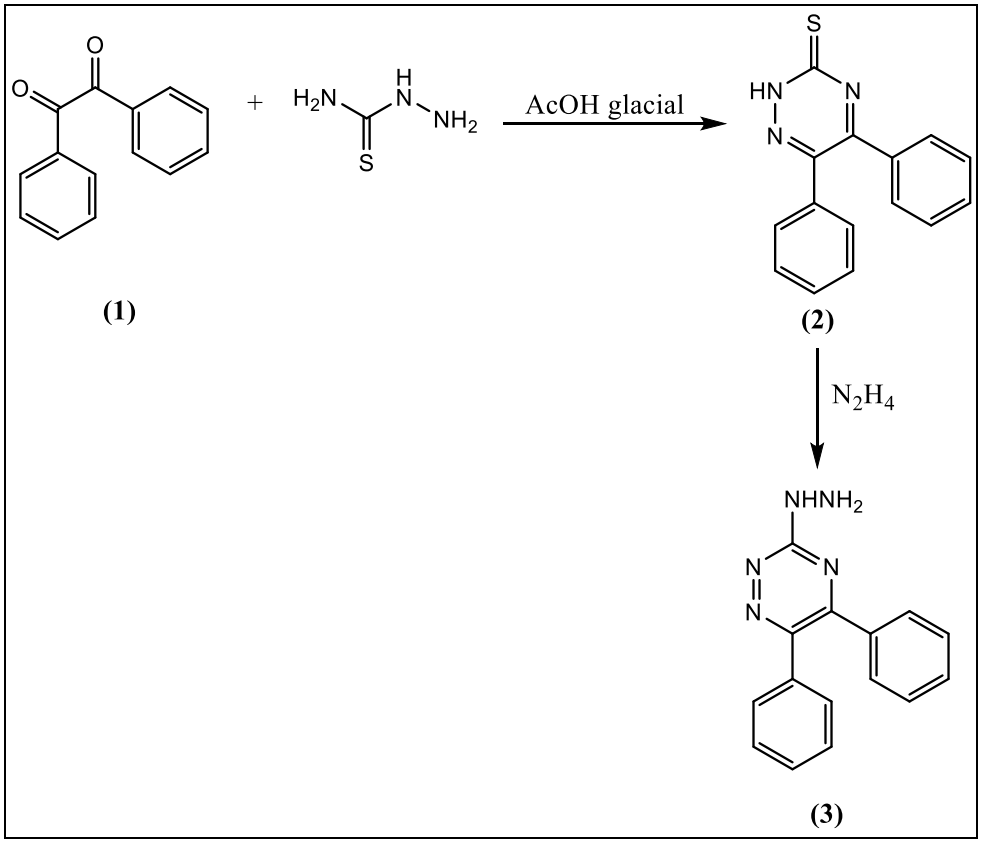
Part 2: *In this part Synthesis of an acid hydrazide derivative and its utility in building of new hetrocylic systems such as oxadiazole, triazole and pyrazole derivatives.*

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

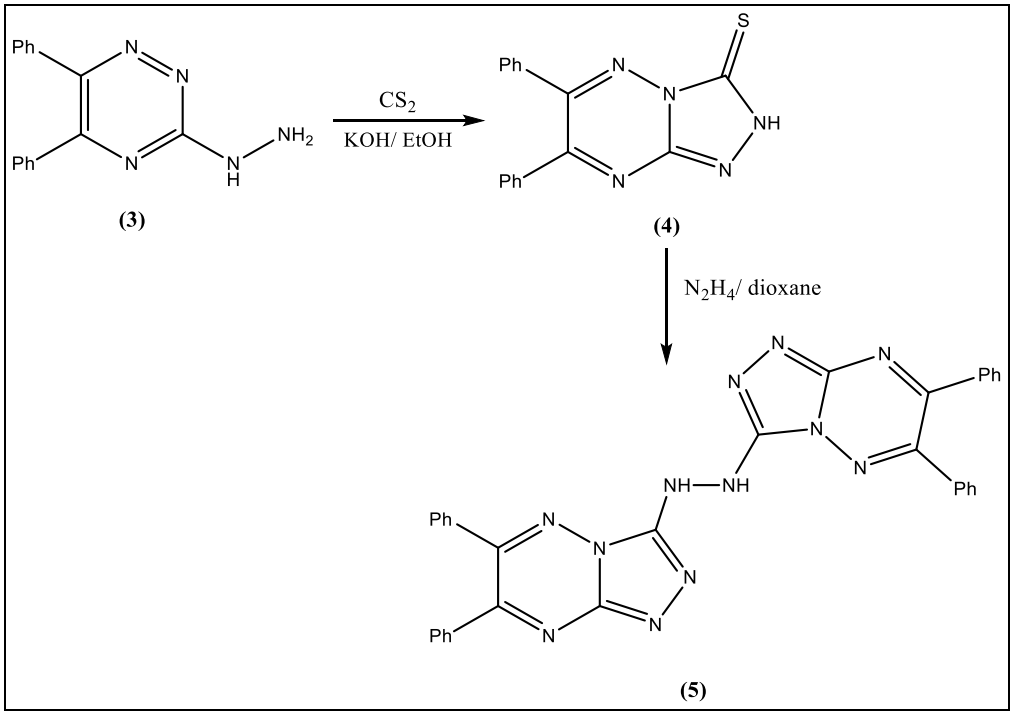
1,2,4-Triazines and their derivatives have been widely studied in terms of their synthetic methodologies and reactivity since some of these derivatives were reported to have promising biological activities.

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)

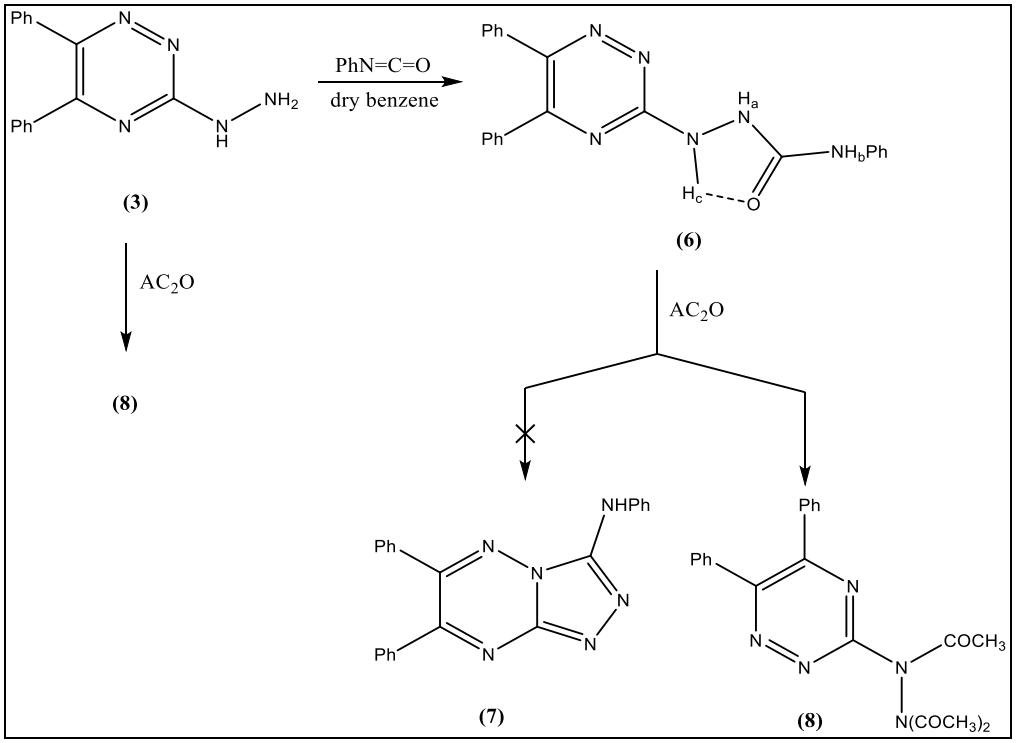
Reaction of compound **3** with carbon disulfide in ethanol in the presence of KOH as a base, afforded the cycloaddition product triazolotriazine derivative **4**. When thione derivative **4** is treated with hydrazine hydrate in boiling dioxane, it gave the di heteryl hyrazine derivative **5** with a removal of H_2S 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**.

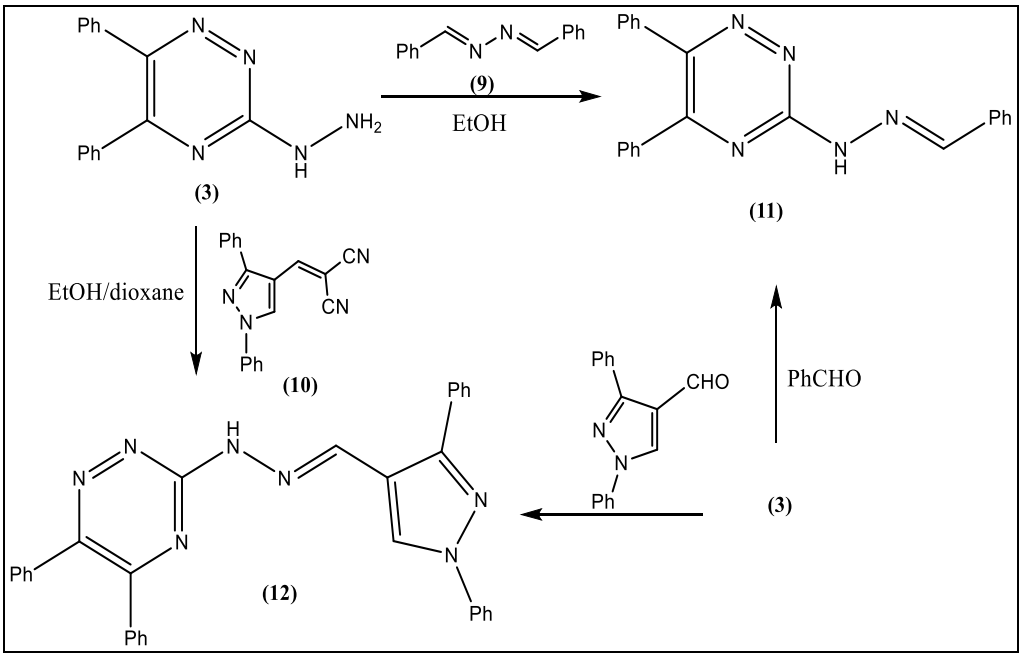
A chemical proof for the suggested structure is gained by preparing an authentic sample, through reacting of compound **3** with acetic anhydride. **(Scheme 3)**.



(Scheme 3)

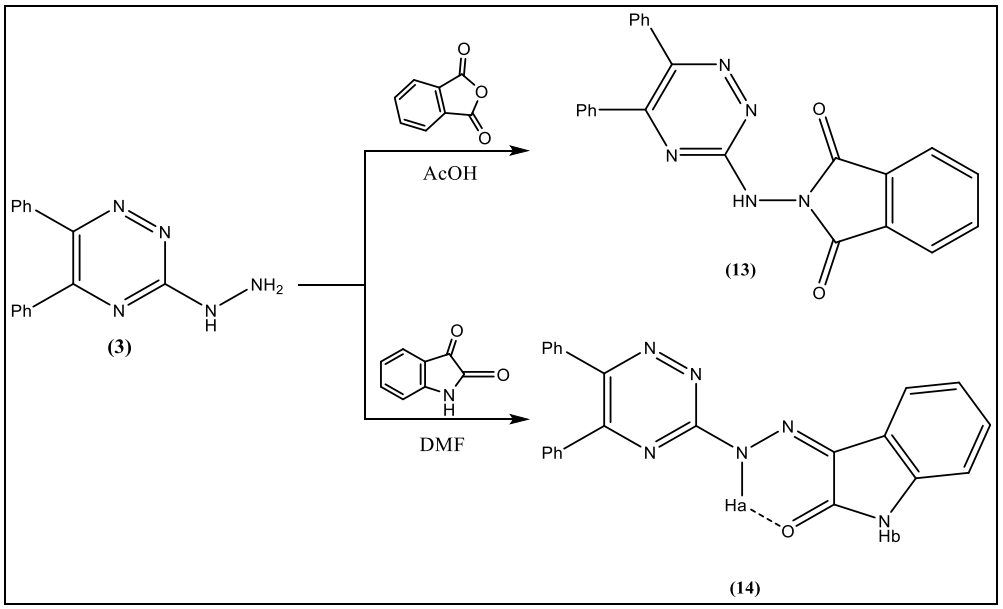
The treatment of compound **3** with dibenzylidene hydrazine **9** and /or pyrazolidine derivative of malononitrile **10** gave the benzalhydrazone and pyrazolidinehydrazone derivatives **11 & 12,** respectively. The structures of both compounds **11** and **12** were confirmed chemically by preparing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