# Utility of Hydrazines in The Synthesis of Some Heterocycles

**A thesis submitted for the degree of master of science as a partial fulfillment of requirements for the master of science**

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***Under supervision***

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Dr. Wael S. I. Abou El-Magd

# *Utility of Hydrazines in The Synthesis of Some Heterocycles*

**A Thesis for M. Sc. Degree in Organic Chemistry**

***Presented by***

*Sandy Samy Samir*

**(B. Sc. 2012)**

***Department of Chemistry***

***Faculty of Science***

***Ain Shams University***

***Cairo, Egypt***

***2016***

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# Acknowledgment

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*Sandy Samy Samir*

# Abstract

Derivatives of thiosemicarbazide are a class of organic compounds that were found to be associated with various biological activities . They are known to exhibit antifungal , anti-inflammatory, anti HIV and herbicidal activities . Moreover, they are used as corrosion inhibitors of steal and semiconductors , in addition to their uses in the metal complexes . Thiosemicarbazides are versatile compounds, which have been extensively used in the synthesis of different heterocyclic ring systems .

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

***Part 1:*** In this part, the synthesis of acyl thiosemicarbazides 1-(2-Benzamido-3-arylacryloyl)-4-dodecanoyl thiosemicarbazides and 1-(2-benzamido-3-arylacryloyl)-4-phenyl- thiosemicarbazide and their cyclization with different reagents in different media are described.

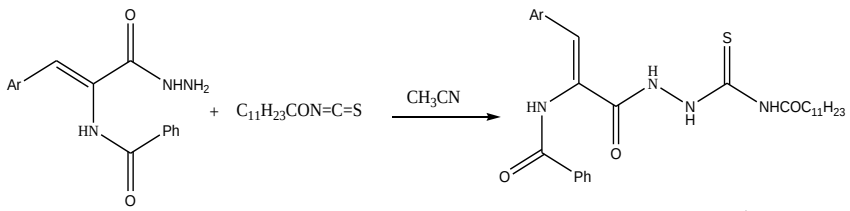
***Part 2:*** The antimicrobial activities of the synthesized compounds were examined against two types of bacteria and two types of fungi.

***Part 3:*** In this part, comparative study between the reactivity of Z- and E-isomers of 2-benzamido-3-phenylacrylohydrazide towards some carbon electrophiles was discussed.

# Summary

Comparative study between the reactivity of the acid hydrazide formed from the hydrazinolysis of 1,3-oxazolones bearing phenylmethylene- and / or 1,3-diphenyl pyrazolylmethylene- groups at position-4 towards lauroyl isothiocyanate, phenyl isothiocyanate and some carbon electrophiles was studied.

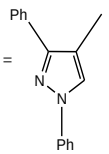
Stirring a solution of hydrazides (Z)-2-benzamido-3-phenylacrylohydrazide **125** and (Z)-2-benzamido-3-(1,3-diphenyl-1H-pyrazol-4-yl)acrylohydrazide **126** derivatives with lauroyl isothiocyanate in dry acetonitrile at room temperature for 2h gave thiosemicarbazide derivatives **189** and **190** respectively **(Scheme 1)**.




(125) Ar = phenyl-

(126) Ar = 1,3-diphenylpyrazol-4-yl-

**189)** Ar = Ph, **190)** Ar =

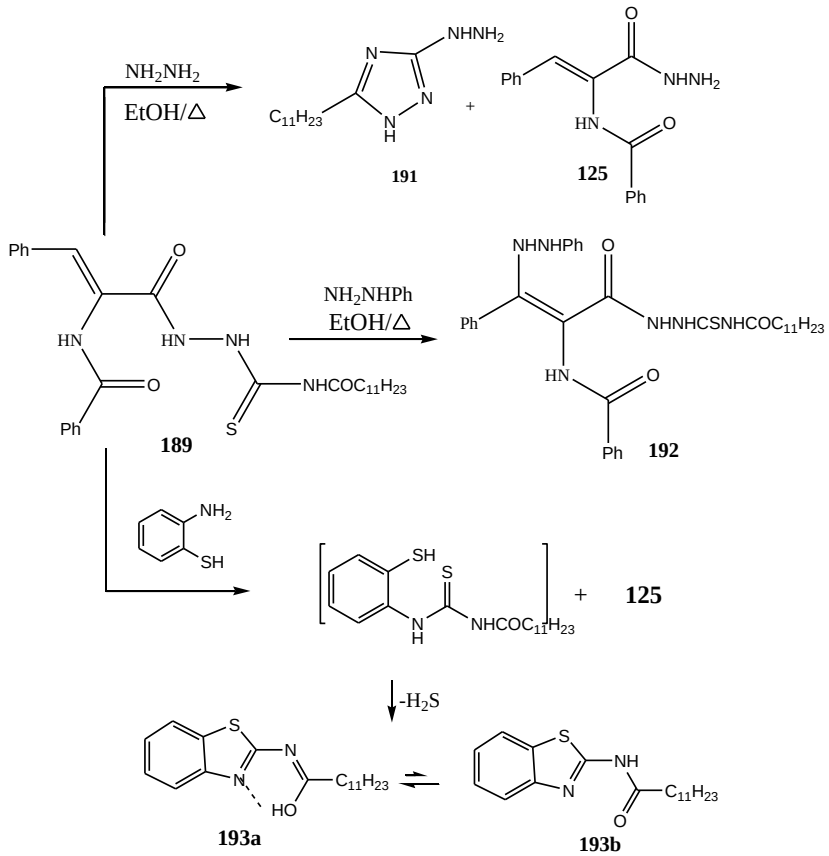



**(Scheme 1)**

The reaction of a solution of compound **189** with hydrazine hydrate in ethanol afforded a mixture of 1, 2, 4-triazol derivative **191** and hydrazide derivative **125** while the treating of compound **189** with phenylhydrazine gave the adduct **192** in a good yield.

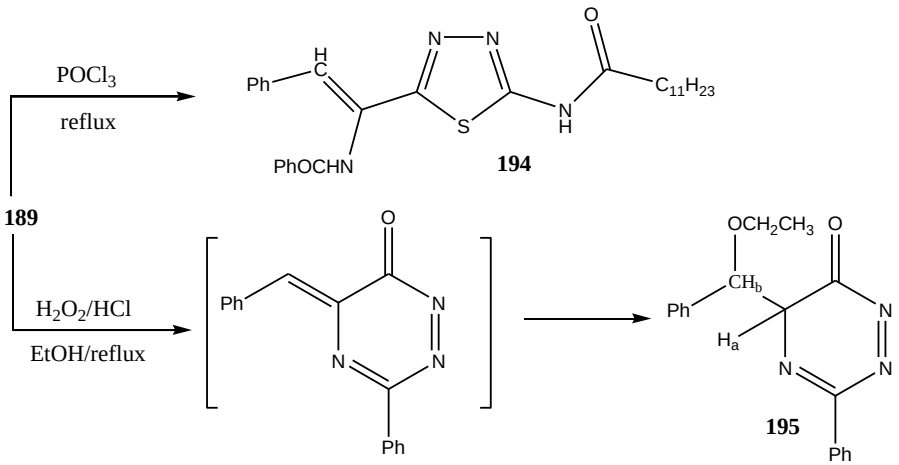
On the other hand, refluxing of **189** with 2-aminothiophenol in n-butanol gave a mixture of 1, 3-benzothiazole derivative **193** and hydrazide derivative **125.**

The appearance of two broad singlet signals in the down field region of $^{1}$HNMR spectrum of compound **193** suggests its existence as an equilibrium mixture of two tautomeric forms **193a** and **193b** in the ratio 3:2. The higher ratio of tautomer **193a** as compared with tautomer **193b** may be attributed to the stability by chelation as shown in **(Scheme 2).**



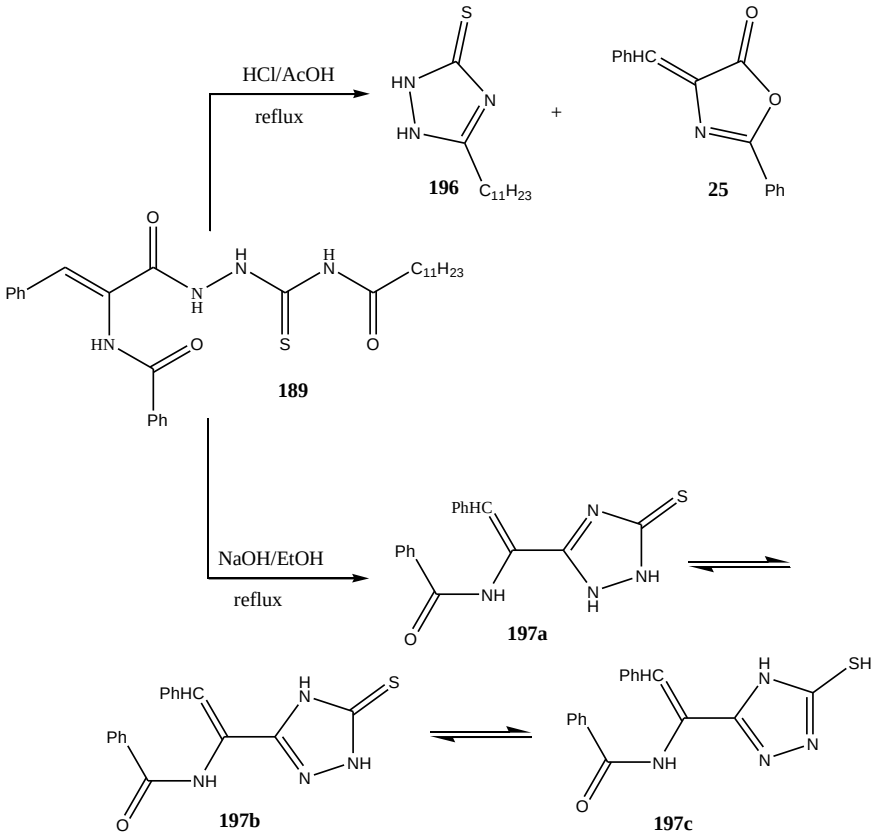

**(Scheme 2)**

Heating of compound **189** with phosphoryl trichloride yielded 1, 3, 4-thiadiazole derivative **194**. Treating a solution of **189** in ethanol with hydrogen peroxide and hydrochloric acid mixture gave 1,2,4-triazine derivative **195 (Scheme 3)**.




**(Scheme 3)**

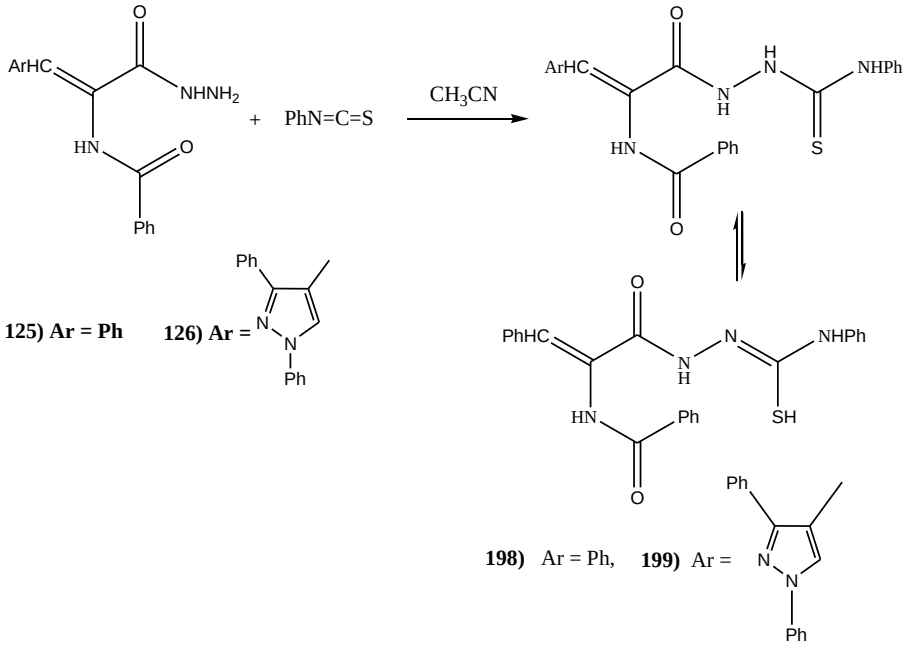
On the other hand, its refluxing with a mixture of hydrochloric acid and acetic acid furnished 1,2,4-triazole derivative **196** and oxazolone derivative **25**. Furthermore, it afforded 1, 2, 4-triazole derivative **197** on its refluxing with ethanolic sodium hydroxide solution. Inspection of the $^{1}$HNMR spectrum of compound **197** revealed its existence in deuterated dimethyl sulfoxide solution as an equilibrium mixture of toutomers **197a-c** as shown in (**Scheme 4).**




**(Scheme 4)**

The new derivatives of thiosemicarbazide **198,199** were prepared by refluxing a solution of hydrazides (Z)-2-benzamido-3-phenylacrylohydrazide **125** and (Z)-2-benzamido-3-(1,3-diphenyl-1H-pyrazol-4-yl) acrylohydra - zide **126** derivatives and phenyl isothiocyanate in acetonitrile.

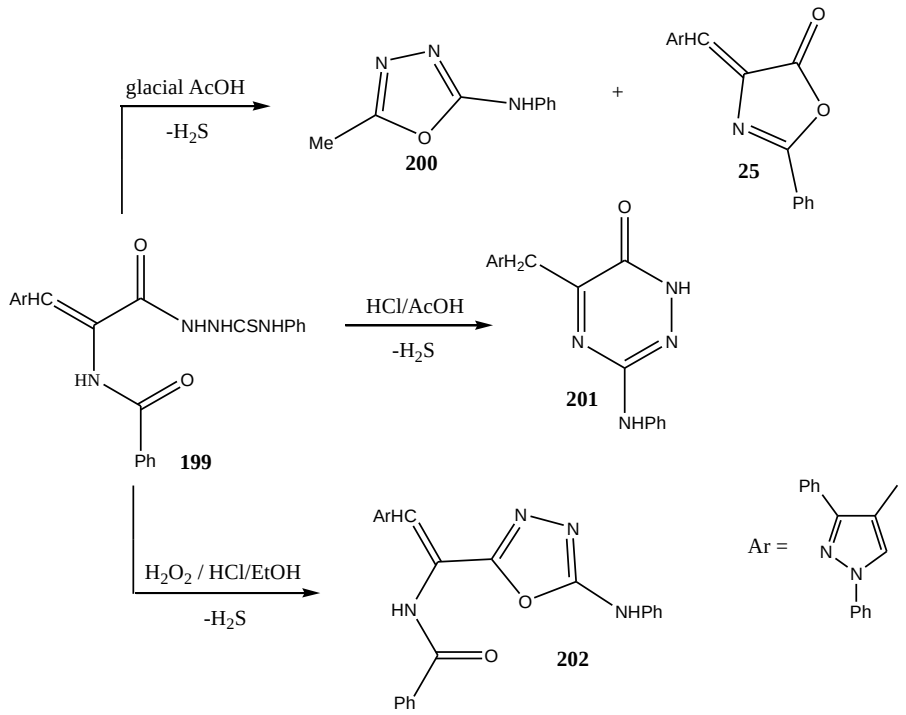
The higher integration value for the signals of aromatic protons, as well as the extra signals for acidic protons is a good evidence for the existence of compound **198** as an equilibrium mixture of thione-thiol tautomers in the ratio 46:54 as shown in (**Scheme 5)**.




**(Scheme5)**

Refluxing a solution of the thiosemicarbazide derivative **199** in glacial acetic acid afforded a mixture of oxadiazole derivative **200** and oxazolone derivative **25**.

However, its refluxing in a solution of equal amounts of acetic acid and hydrochloric acid mixture gave 1, 2, 4-triazine derivative **201**. Moreover, heating of an ethanolic solution of **199** in the presence of hydrogen peroxide and hydrochloric acid is accompanied by release of $H_2S$ gas to give oxadiazole derivative **202 (Scheme6)**.

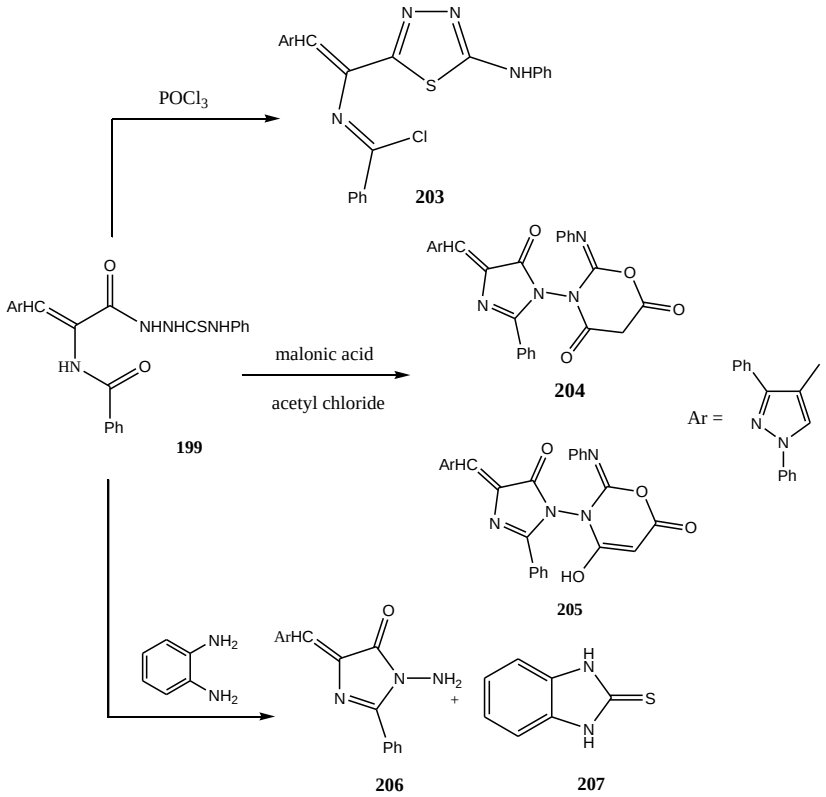



**(Scheme 6)**

Heating of compound **199** with phosphoryltrichloride yielded 1,3,4-thiadiazole derivative **203**. Furthermore, the reaction of **199** with malonic acid in the presence of acetyl chloride gave 1, 3-oxazine derivative **204**. The $^{1}$HNMR spectrum of compound **204** is devoid of any signals in the up field region corresponding to protons of $CH_2$ group instead, it exhibits an exchangeable singlet signal in the down field region for OH proton. This suggests its existence in deuterated dimethylsulfoxide solution as the hydroxy oxazinone derivative **205.**

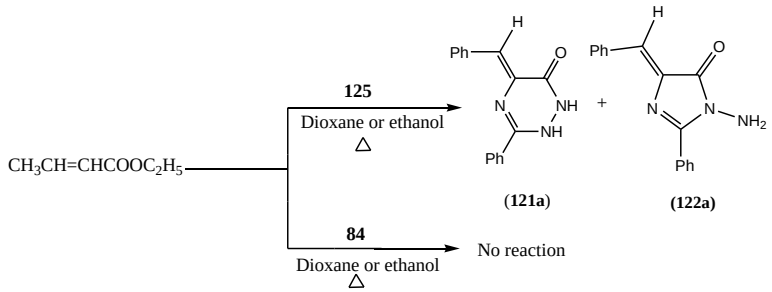
Refluxing a solution of compound **199** in pyridine with equal amounts of o-phenylene diamine produced a mixture of amino imidazole derivative **206** and benzimidazole derivative **207**.

On the other hand, compound **206** was obtained upon refluxing of **199** with phenylhydrazine in ethanol or just refluxing of **199** in n-butanol **(Scheme7)**.



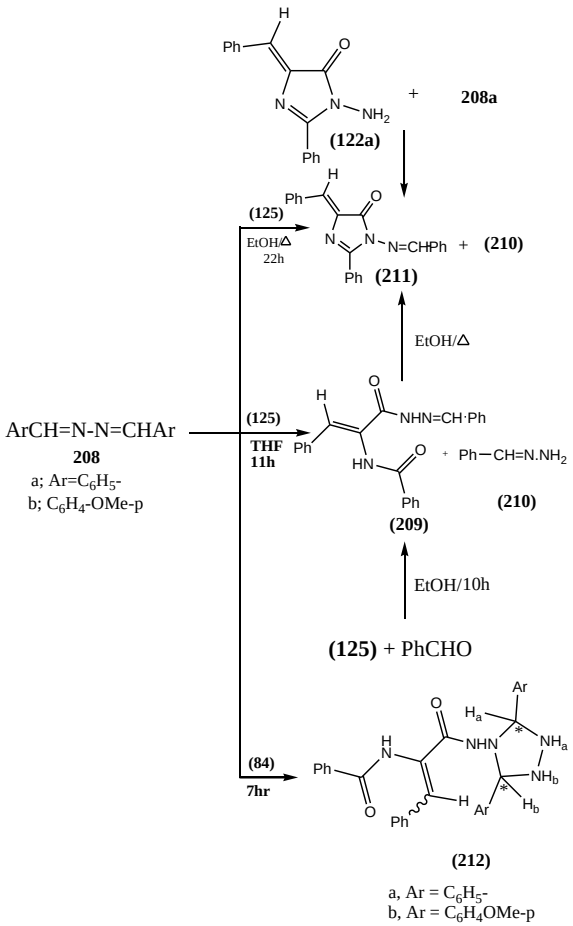

**(Scheme7)**

The treatment of acid hydrazide **125** with ethyl crotonate gave 1, 2, 4-triazinone derivative **121a** and N-amino imidazolone derivative **122a**. Similar treatment of the **84** (*E*-isomer) with ethyl crotonate and in presence of a catalytic amount of piperidine or triethylamine does not lead to any products **(Scheme8).**




**(Scheme 8)**

Refluxing the Z- isomer **125b** with 1, 2-dibenzylidene hydrazine **208a** in tetrahydrofurane afforded the Schiff base adduct **209** and the hydrazone derivative **210**. The Schiff base **209** also can be formed by refluxing **125** with benzaldehyde in ethanol. Repeating the same reaction in ethanol for 22hrs yielded the imidazolone derivative **211** and the hydrazone derivative **210**. The same products **210** and **211** can be obtained by refluxing the imidazolone **122a** with 1, 2-dibenzylidene hydrazine **208a** in ethanol. On the other hand, heating the *E*- isomer **84** with 1, 2-dibenzylidene- **208a** and 1, 2-di (4-methoxybenzylidene) - **208b** hydrazines in ethanol afforded the triazolidine derivatives **212a** & **b**. **(Scheme 9)**




**(Scheme9)**