Ain Shams University
Faculty of Science
Chemistry Department

Synthesis of Heterocyclic Compounds Containing Nitrogen Atoms and Their Applications.

A Thesis

"Submitted for the degree of Master of Science As a partial fulfillment for requirements of the Master of Science"

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Approval Sheet

"Synthesis of Heterocyclic Compounds Containing Nitrogen Atoms and Their Applications"

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Aim of the work

The research aims to achievement of the following goals.

1. Create new method to synthesis a number of 2-amino-4-aryl-6-substituted pyridine-3, 5-dicarbonitrile derivatives.
2. Using of 2-amino-4-phenyl-6-(phenyl amino) pyridine-3, 5-dicarbonitrile as a key starting material for synthesis of new heterocyclic compounds.
3. Elucidation of the structural features of the synthesized compounds *via* elemental analysis and spectrometric methods such as IR., MS., ^{1}H-NMR and ^{13}C-NMR Spectra.
4. Evaluation the biological activity and corrosion inhibition for new synthesized compounds.

Keywords: Pyridine, pyridopyrimidine, pyridoxaziene, azepene, corrosion inhibition and anticancer.

Summary

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

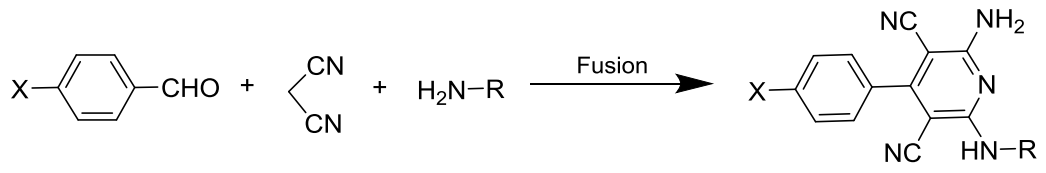
First:

Multicomponent reactions, Solvent-free Synthesis of 2-Amino-4-Aryl-6-Substituted Pyridine-3, 5-Dicarbonitrile Derivatives and Corrosion Inhibitors Evaluation.

Second:

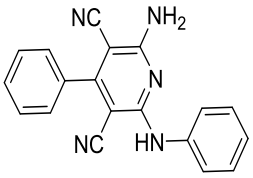
A facile synthesis of novel heterocyclic compounds based on pyridine moiety with pharmaceutical activities.

A number of 2-Amino-4-aryl-6-substituted-pyridine-3, 5-dicarbonitrile derivatives through one-pot multicomponent reactions by reacting varieties of aromatic aldehydes with malononitrile and different primary amines, using different molecular ratio and different reaction conditions to achieve considerable product yields, moreover, we succeed for the first time to develop a new method to synthesis the fore mention under fusion condition without using solvent and catalysts. With this method a wide range of novel pyridine derivatives were synthesized with high yield and broad substrate of functional groups **(Scheme 1 & 2)**.



X= H, OCH3, Cl, PhCH=CH R=aryl, alkyl

(Scheme 1)



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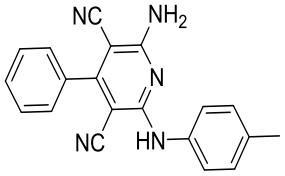

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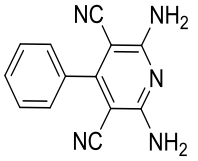

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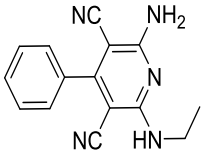

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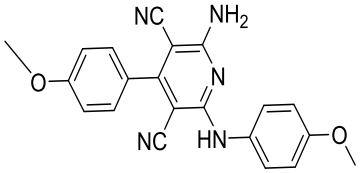

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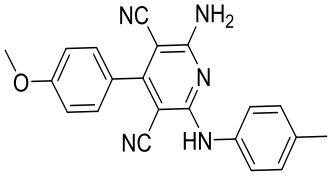

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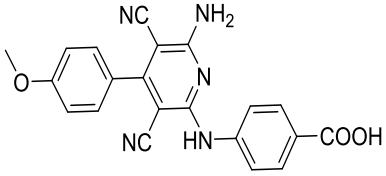

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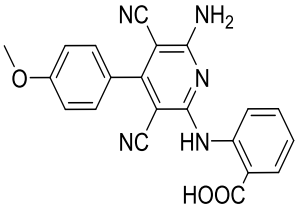

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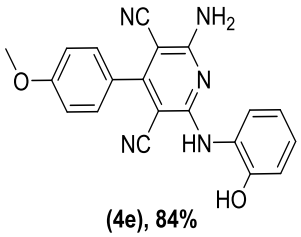

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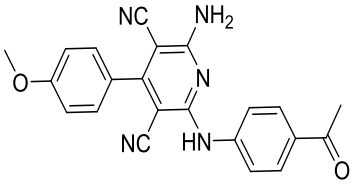

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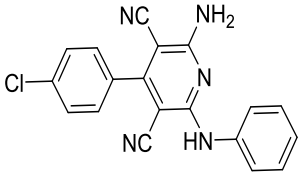

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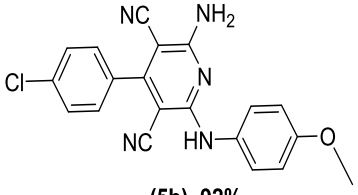

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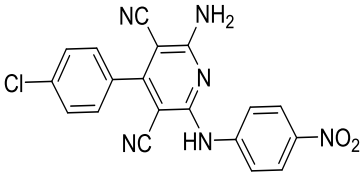

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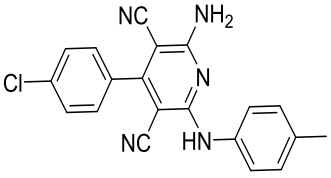

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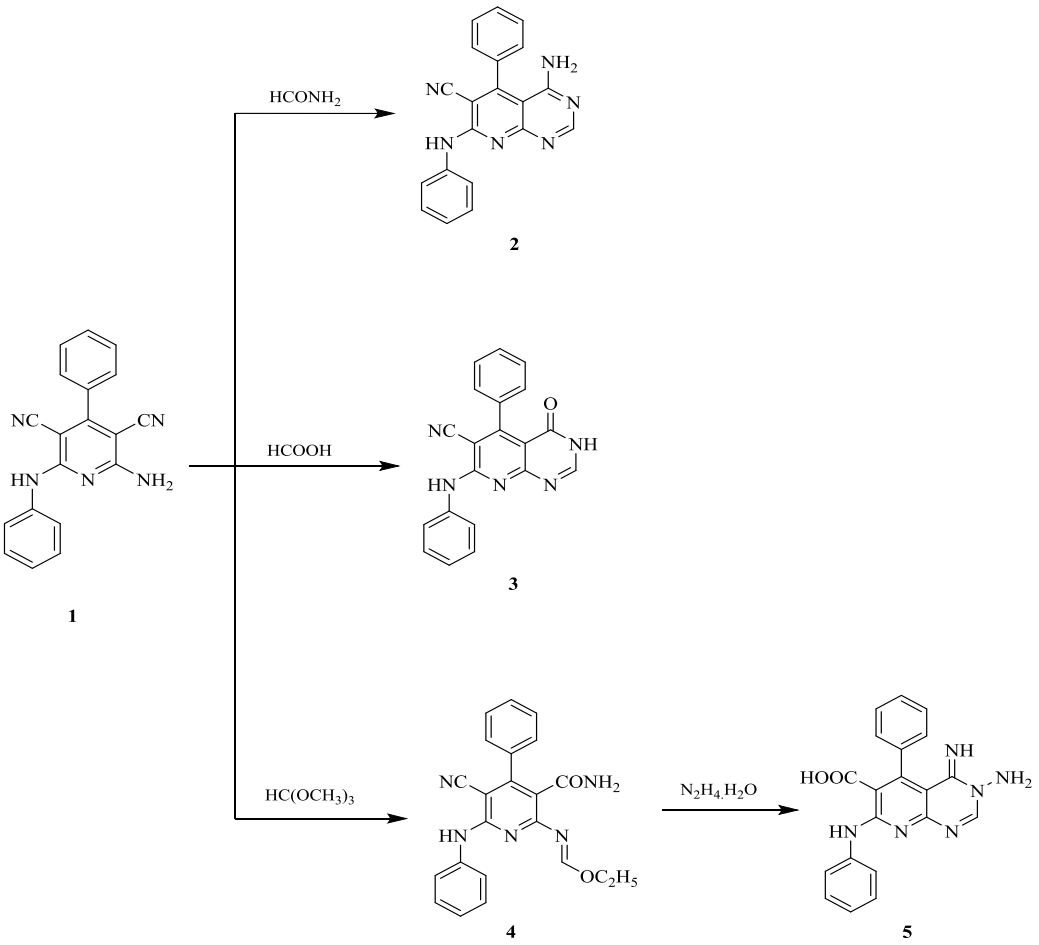
(Scheme 2)

The corrosion inhibition-tendency of the synthesized 2-amino-3, 5-dicyano-4-aryl-6-substituted amino pyridine derivatives were tested by studying the weight loss of steel coupons-immersed in a solution of 6 M HCl throughout 9 days of immersion at room temperature at a different concentrations 200, 400, and 800 ppm. This showed that the synthesized pyridine derivatives act as corrosion inhibitor and the rate of inhibition efficiency increase with increasing the concentration of the inhibitor and compound **4a** has the highest efficiency.

A novel series of heterocyclic compounds containing pyridine moieties has been disclosed by allowing 2-amino-4-phenyl-6-(phenylamino)pyridine-3, 5-dicarbonitrile **1** to undergo annulations reactions with different reagents.

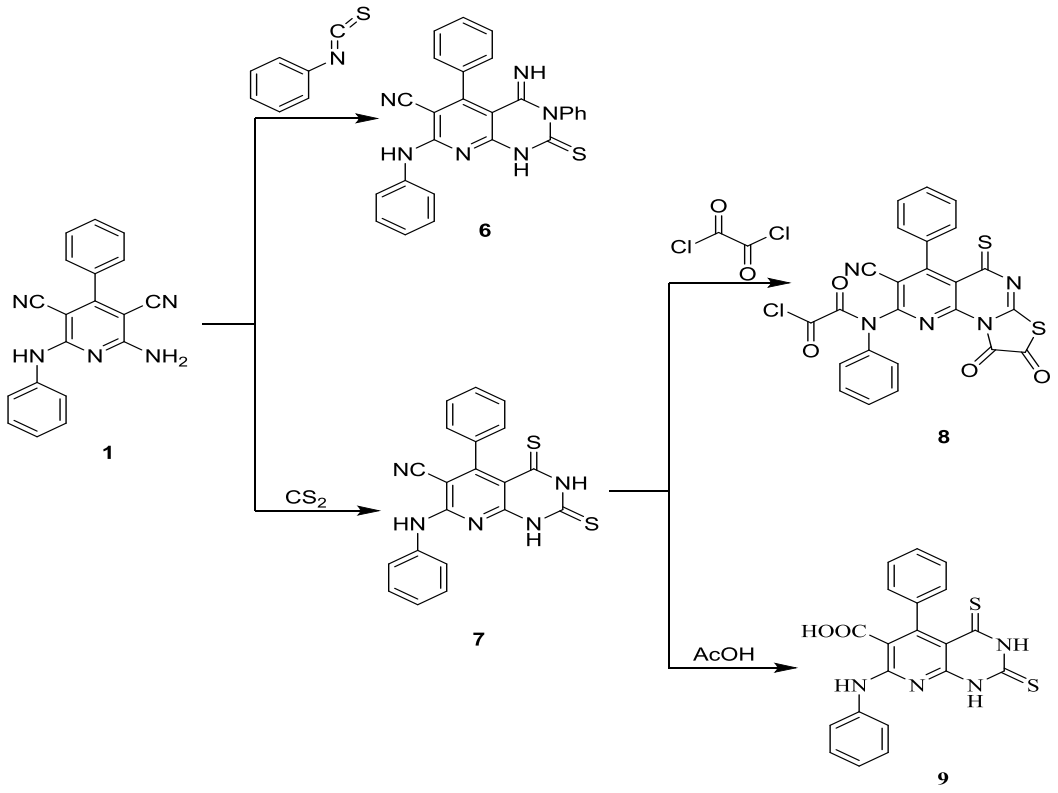
Treatment of 2-amino-3-cyano pyridine derivative **1** with formamide and/or formic acid afforded 4-imino-5-phenyl-7-(phenylamino)-3, 4-dihydropyrido[2, 3-d]pyrimidine-6-carbonitrile **2** and 4-oxo-5-phenyl-7-(phenylamino)-3, 4-dihydropyrido[2, 3-d]pyrimidine-6-carbonitrile **3** respectively.

On the other hand reaction of 2-amino-3-cyano pyridine derivative **1** with triethylorthoformate afforded Ethyl-N-(3-carbamoyl-5-cyano-4-phenyl-6-(phenylamino)pyridin-2-yl)formimidate **4** which, on refluxing with hydrazine hydrate in alcoholic solution afford pyridopyrimidine carboxylic acid derivative **5 (Scheme 3)**.



(Scheme 3)

Formation of pyridopyrimidine thione and dithione derivatives by reaction of 2-amino-3-cyano pyridine derivative **1** with phenyl isothiocyanate and/or carbon disulphide to give pyridopyrimidine thione derivative **6** and pyridopyrimidine dithione derivative **7** respectively. When dithion derivative **7** was reacted with oxalyl chloride and acetic acide afforded 2, 3 dioxo thiazole pyridopyrimidine thione derivative **8** and pyridopyrimidine thione carboxylic acid derivative **9** respectively **(Scheme 4)**.



(Scheme 4)

Meanwhile, acylation of 2-amino-3-cyano pyridine derivative **1** with acid chloride like benzoyl chloride afforded 4-oxo-2, 5-diphenyl-7-(phenylamino)-4H-pyrido [2, 3-d][1, 3]oxazine-6-carbonitrile **10**. Treatment of **10** with formamide, hydrazine hydrate and *o*-phenylene diamine was afforded 4-oxo-2, 5-diphenyl-7-(phenylamino)-3, 4-dihydropyrido[2, 3-d]pyramid- ine-6-carbonitrile **11**, 3-amino-4-oxo-2, 5-diphenyl-7-(phenylamino)-3, 4-dihydropyrido[2, 3-d]pyrimidine-6-carbonitrile **12** and 1, 6-diphenyl-3-(phenylamino)benzo[4, 5]imidazo[1, 2-c] pyrido[3, 2-e] pyrimi-dine-2-carboxamide **13** respectively **(Scheme 5)**.