



Fayoum University

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Utility of carbonyl compounds in heterocyclic synthesis

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A thesis submitted in partial fulfillment

Of

The requirements for the degree of

Master of Science

In

Organic chemistry

Chemistry Department

Faculty of Science, Fayoum university

Fayoum university

2023

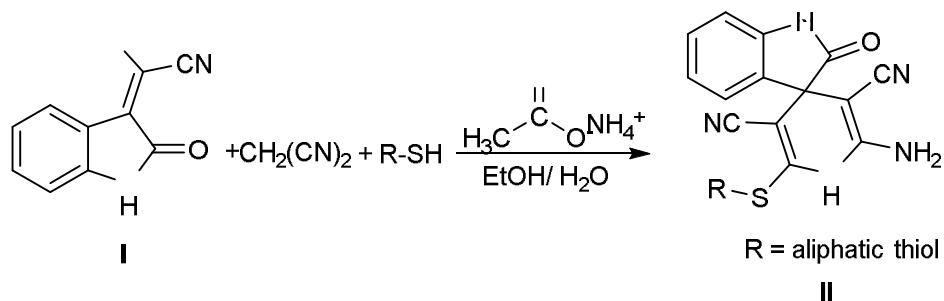
Summary

Utility of carbonyl compounds in heterocyclic synthesis

This thesis describes the utility of isatin as a key starting material for the preparation of a novel series of isatins derivatives and studies the antimicrobial and fluorescent activities of these compounds.

Synthesis of spiro[indoline-3,4'-pyridine]-3',5'-dicyanonitrile **II** derivatives

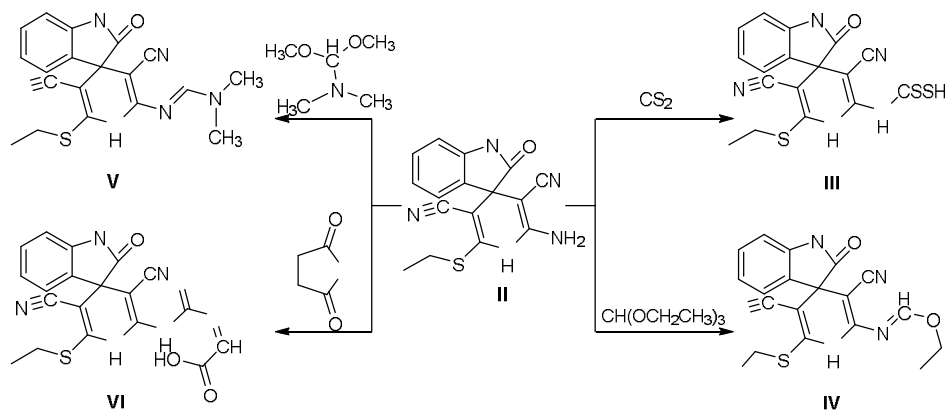
Spiro-indoline pyridine **II** was synthesized to be used as a starting material for synthesizing some new heterocyclic compounds containing isatin moiety. It was found that the reaction of isatylidene malononitrile **I** with malononitrile and ethyl thiol in presence of ammonium acetate gave compound **II** when the reaction was continued for 10 min at 55°C (Scheme A).



Scheme A

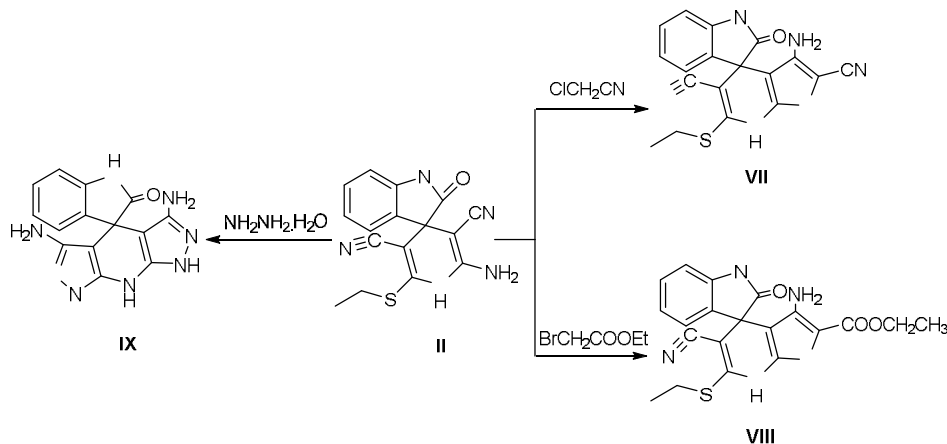
Study on 2'-amino-6'-(ethylthio)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-3',5'-dicyanonitrile **II**

The compound **II** reacted with carbon disulfide in refluxing pyridine afforded carbamodithioic acid derivative **III**. Also, the reaction of compound **II** with triethyl orthoformate, dimethylformamide dimethyl acetal, and maleic anhydride yielded the compounds **IV**, **V**, and **VI** respectively (Scheme B).



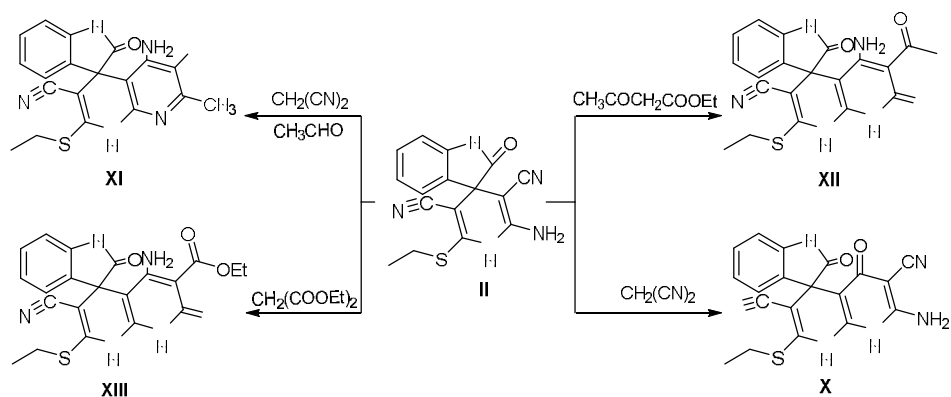
Scheme B

Also, the alkylation of compound **II** with α -halo acetic acid derivatives (chloroacetonitrile and ethyl bromoacetate) was achieved in dry acetone containing anhydrous potassium carbonate and afforded the compounds **VII** and **VIII** respectively, while the reaction of **II** with hydrazine hydrate afforded pyrrole derivative **IX** (Scheme C).



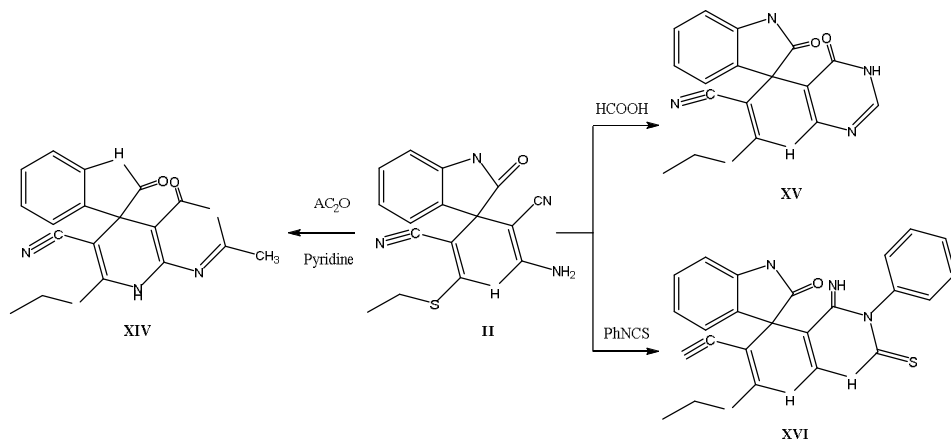
Scheme C

Moreover, active methylene compounds such as malononitrile, ethyl acetoacetate, diethylmalonate, and malononitrile with acetaldehyde afforded the compounds **X**, **XII**, **XIII**, and **XI** respectively (Scheme D).



Scheme D

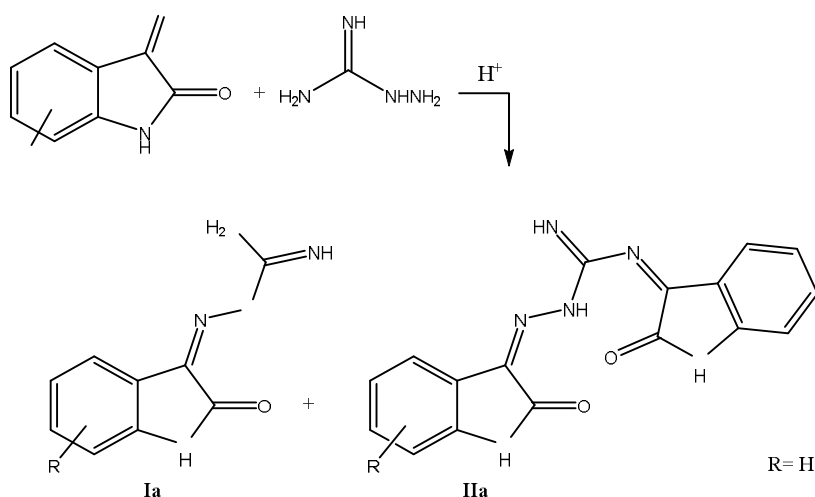
Oxazine and pyrimidine derivatives synthesized by the reaction of compound II with acetic anhydride, formic acid, and phenyl isothiocyanate afforded the compounds XIV, XV, and XVI (Scheme E).



Scheme E

Synthesis of 2-(2-Oxoindolin-3-ylidene)hydrazine-1-carboximidamide **Ia** derivatives

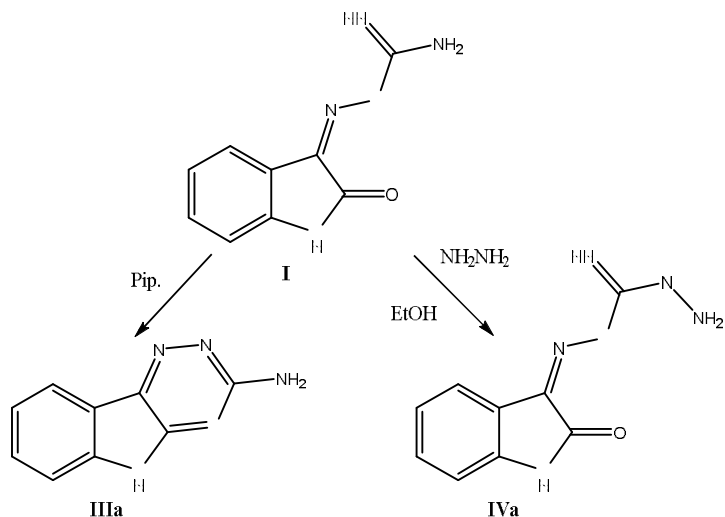
The reaction of isatin with aminoguanidine in aqueous ethanol in presence of a catalytic amount of hydrochloric acid yielded 2-(2-oxoindolin-3-ylidene)hydrazine-1-carboximidamide **Ia**, while in presence of a catalytic amount of concentrated sulfuric acid yielded *N*-2-bis(2-oxoindolin-3-ylidene)hydrazine-1-carboximidamide **IIa** (Scheme F).



Scheme F

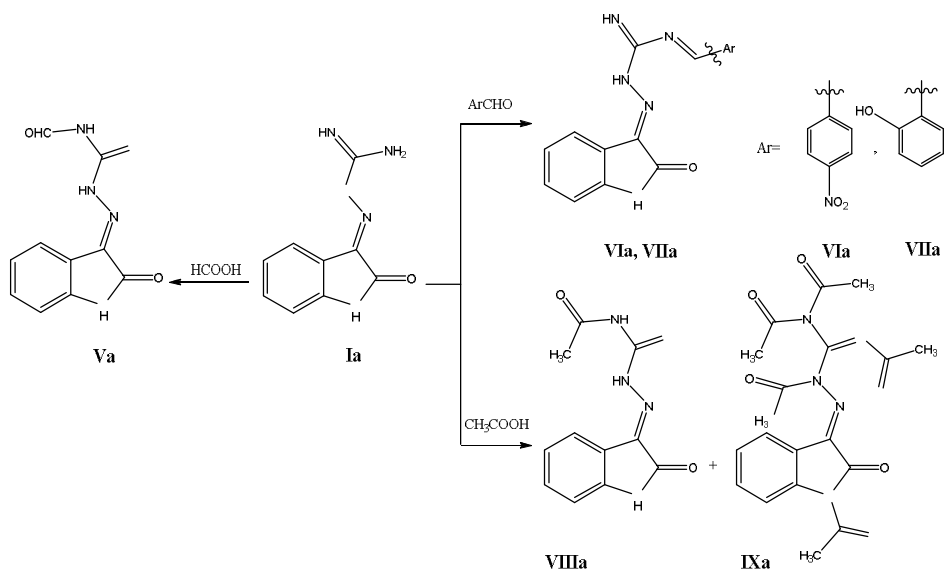
Study on 2-(2-Oxoindolin-3-ylidene)hydrazine-1-carboximidamide **Ia**

Cyclization of 2-(2-oxoindolin-3-ylidene)hydrazine-1-carboximidamide **Ia** in presence of catalytic piperidine in aqueous ethanol produced **IIIa**, while the reaction of **Ia** with hydrazine hydrate afforded *N'*-(2-oxoindolin-3-ylidene)hydrazinecarboximidhydrazide **IVa** (Scheme G).



Scheme G

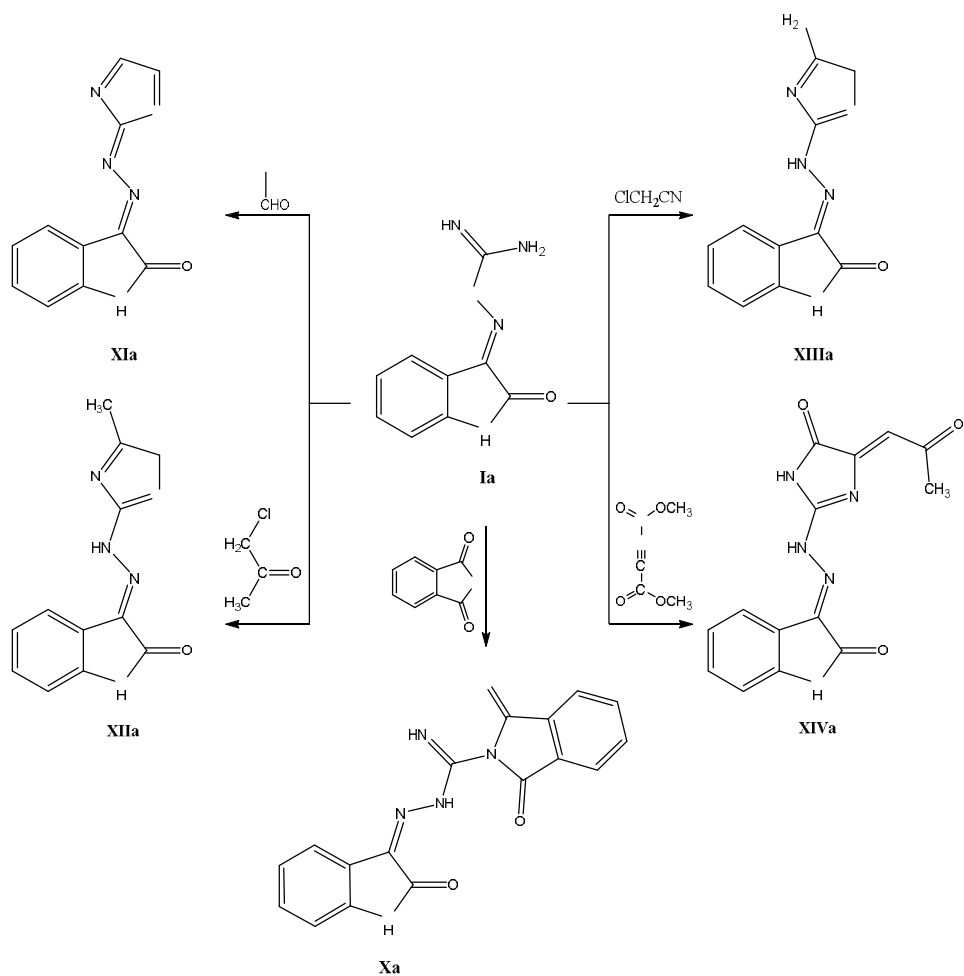
Furthermore, 2-(2-oxoindolin-3-ylidene) hydrazine-1-carboximidamide **Ia** derivatives reacted with different reagents like aromatic aldehyde (as *p*-nitrobenzaldehyde and salicylaldehyde) and acids (as formic acid and acetic acid) afford open chain derivatives of compound **Ia** (Scheme H).



Scheme H

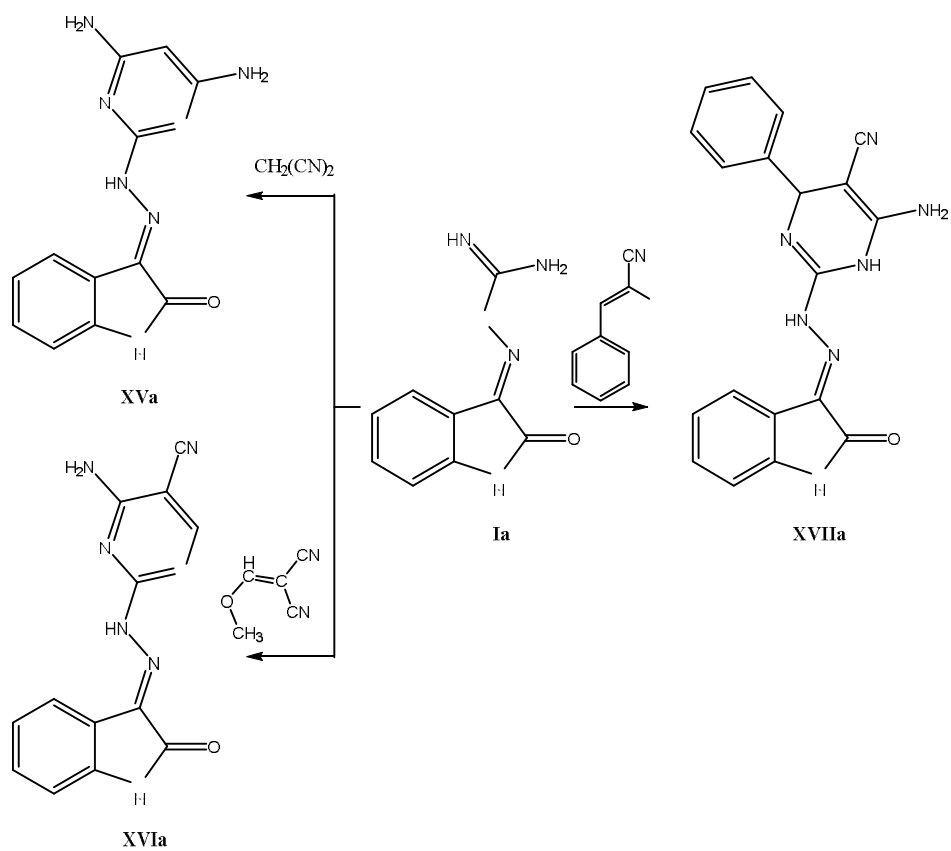
Also, pyrrole heterocyclic systems were achieved by the reaction of compound **Ia**, phthalic anhydride as the dicarbonyl compound in cyclic structure, and a catalytic amount of acetic

acid in dimethyl formamide under reflux conditions to afford the compound **Xa**. While imidazole heterocyclic systems were achieved by the reaction of compound **Ia** with glyoxal, chloroacetone, chloroacetonitrile, and Dimethyl acetylenedicarboxylate (Scheme J).



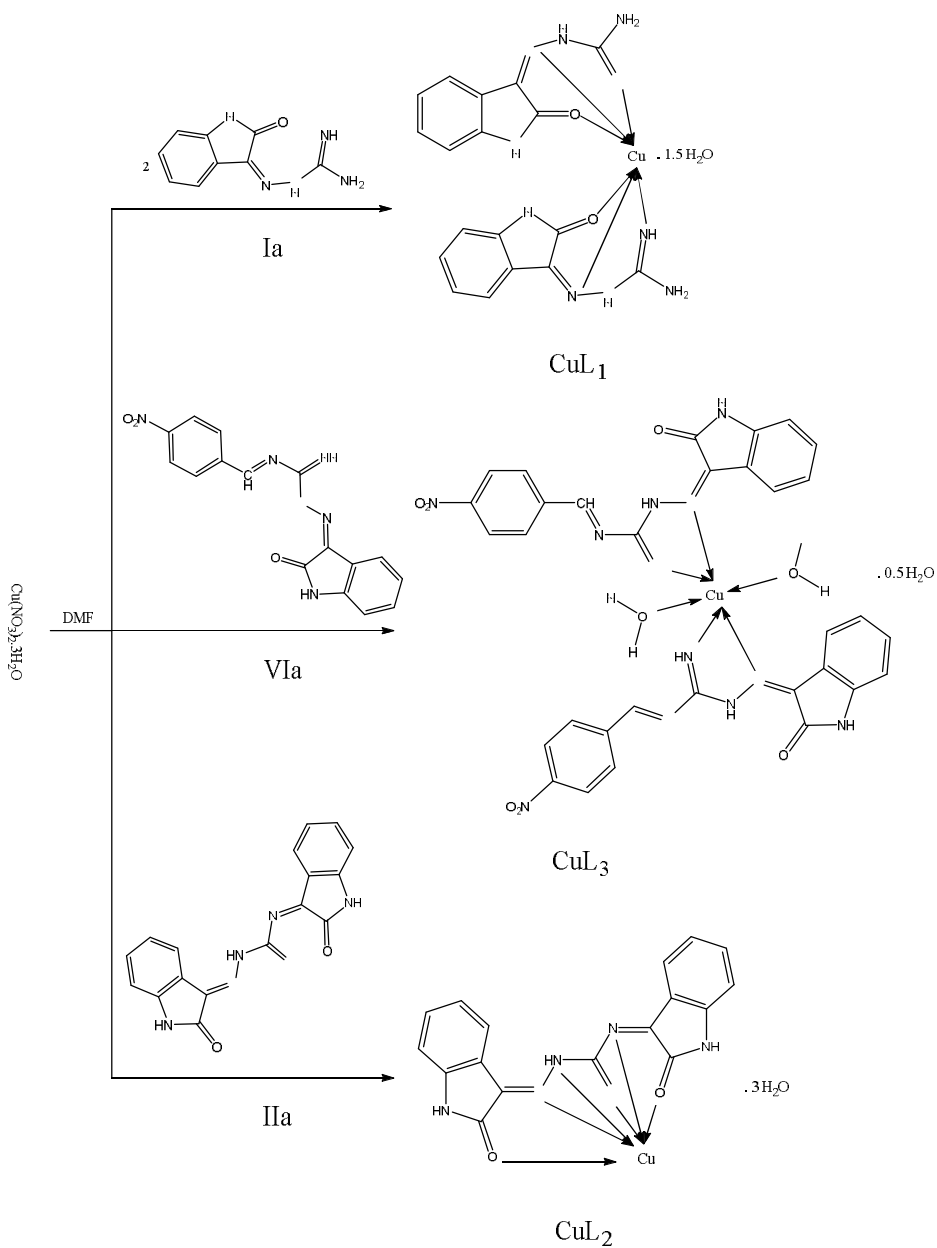
Scheme J

The compound **Ia** reacted with active methylene compounds such as malononitrile and its derivatives like ethoxymethylene malononitrile and benzylidene malononitrile afforded the compounds **XVa**, **XVIa**, and **XVIIa** respectively (Scheme K).



Scheme K

Finally, copper nitrate reacted with the compounds **Ia**, **IIa**, and **VIa** afforded **CuL₁**, **CuL₂**, and **CuL₃** respectively (Scheme L).



Scheme L

All of the newly synthesized compounds were

Confirmed from elemental analysis and spectral data.

Tested *in vitro* against a variety of bacteria to study their anti-bacterial activity.

Study their fluorescent activity.