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Synthesis of Novel N, S-Heterocyclic Compounds via Metallacycles

A Thesis

Submitted by

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For

Ph.D in organic Chemistry

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APPROVAL SHEET

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بسم الله الرحمن الرحيم

(قَالُواْ سُبْحَانَكَ لاَ عِلْمَ
لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ
أَنتَ الْعَلِيمُ الْحَكِيم)

صدق الله العظيم

البقرة (٣٢)

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I am deeply thankful to almighty god for showing me the right Path and helping me to complete this work.

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Summary

Summary

The subject of this work is the preparation and characterization of some novel organic compounds and organopalladium complexes. This thesis includes the preparation of new heterocyclic systems from 5- methylisatin and Spiro -Palladium complexes using $Pd(dba)_2$ catalyst and various ligands by oxidative addition reaction.

Chapter One "Introduction" :

Two parts includes details of the history of some organic compound and organometallic complexes and gives a general introduction survey, review and new scientific background of the basic principle theory of isatin derivatives and palladium- catalyzed, cross-coupling and oxidative addition reactions including examples for the synthesis of some isatin derivatives and organopalladium complexes related to our work.

Chapter Two "Results and Discussion" :

Part (I)

Deals with a detailed study for synthesis, characterization and describes the strategy of the methods that can be applied to give products in pure form, resulting in the synthesis of a class of organic compounds by using different reagents.

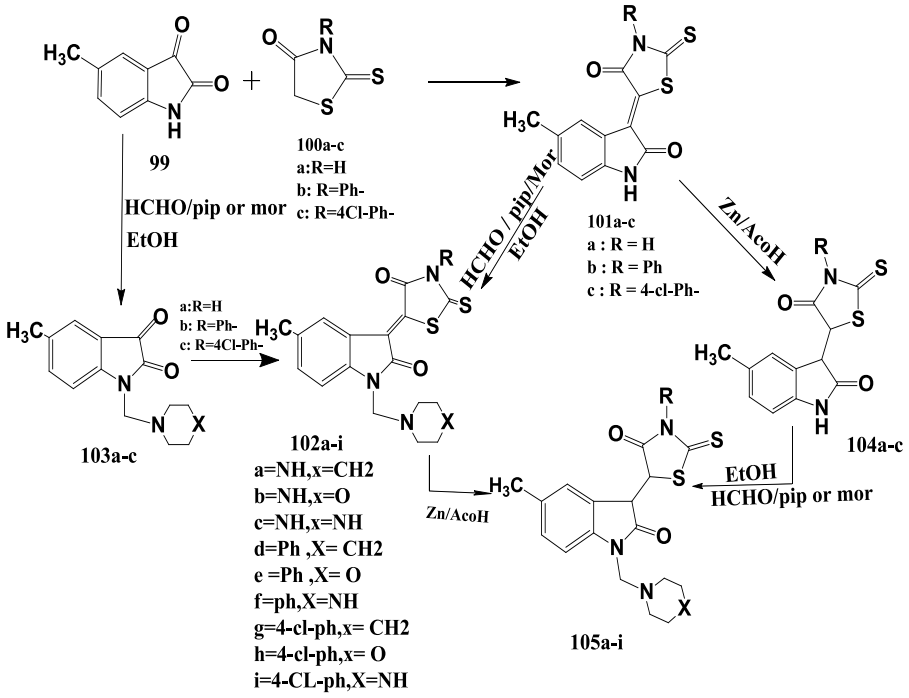
It includes as well investigating the synthesis of some new heterocyclic systems from 5-methylisatin by reaction with phenyl rhodanine, 4-chlorophenyl rhodanine and rhodanine to give thioxothiazolidin derivative 101a-c and this compound treated with formaldehyde and secondary amines such as piperdine, and

piperazine to give mannich base derivative 102a-i. Another piece of evidence for structure of compound 102a-i, is obtained by authentic method via the react of isatin with formaldehyde and Secondary amines to yield 103a,b then condensation of 103a,b with 3-substituted-4-thiazolidinone in presence of AcONa/ AcOH to give 102a,b. .

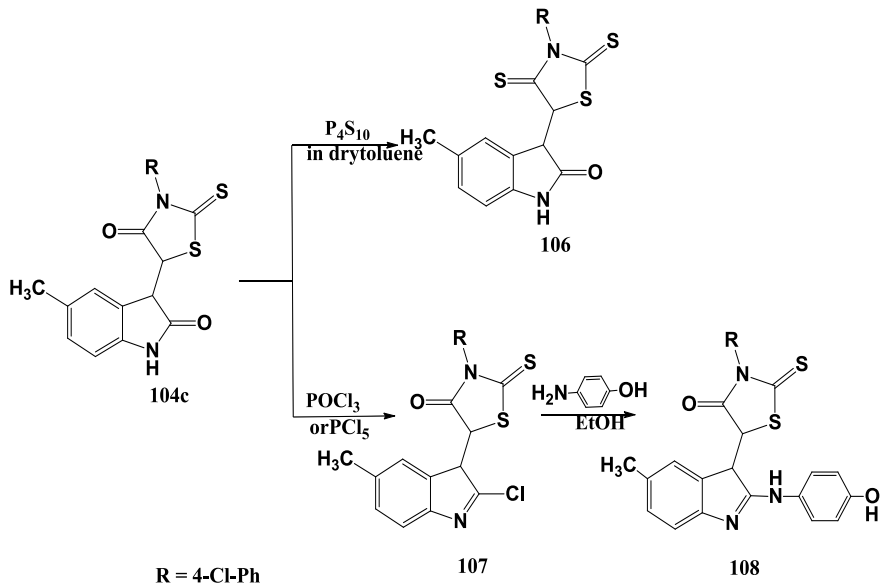
The compound 101a-c is reduced by Zn/ AcOH to give compound 104a-c. Which reacted with 20amine and formaldehyde to afford 105a,b. Which obtained by authentic method Via the reduction of 102g,h with Zn/ AcOH.

The 5-(5-Chloro-2-oxoindolin-3yl)-3-phenyl-2thioxothiazolidin-4-one 104c reacted with phosphorousoxychloride to give 5-(2-chloro -5-methyl - 3H -indol-3-yl) -3-(4–chlorophenyl)–2-thioxothiazolidin-4-one 107 in good yield, which reacted with different primary amines such as p- hydroxyl aniline afforded 3-(4-chlorophenyl)- 5 -(2-((4-hydroxyphenyl) amino)-5-methyl-3H-indol-3-yl)-2-thioxothiazolidin-4-one 108.

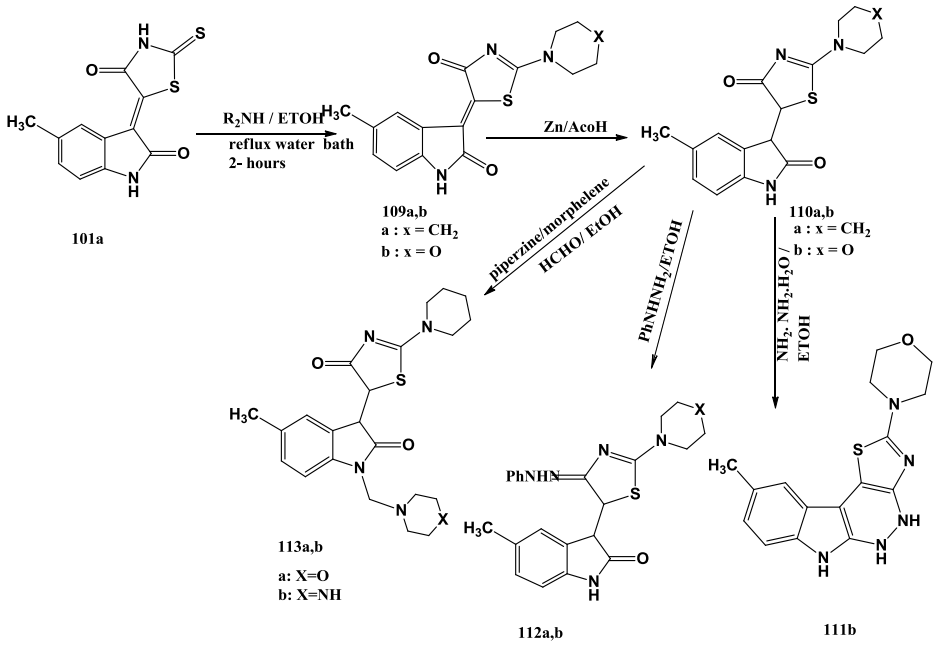
The 5-(5 – methyl - 2 -oxoindolin-3-ylidine)-2-thioxothiazolidin-4-one **101a** reacted with different secondary amines such as piperidine or morphilin to produce thiazolin derivatives **109a,b**. Which reduce by Zn/AcOH to give **110a,b**. This compound **110a,b** obtained by reaction of compound **104a** with amine in ethanol. More over the refluxing compound **110a,b** with hydrazine hydrate and phenyl hydrazine gave **111a,b** and **112a,b** respectively. Compound **113a,b** was obtained by Mannich reaction of **110a,b** by reaction with morphiline or piperazine in presence of formaldehyde. And more interesting compounds illustrated in the following **Schemes:**



Scheme 1



Scheme 2

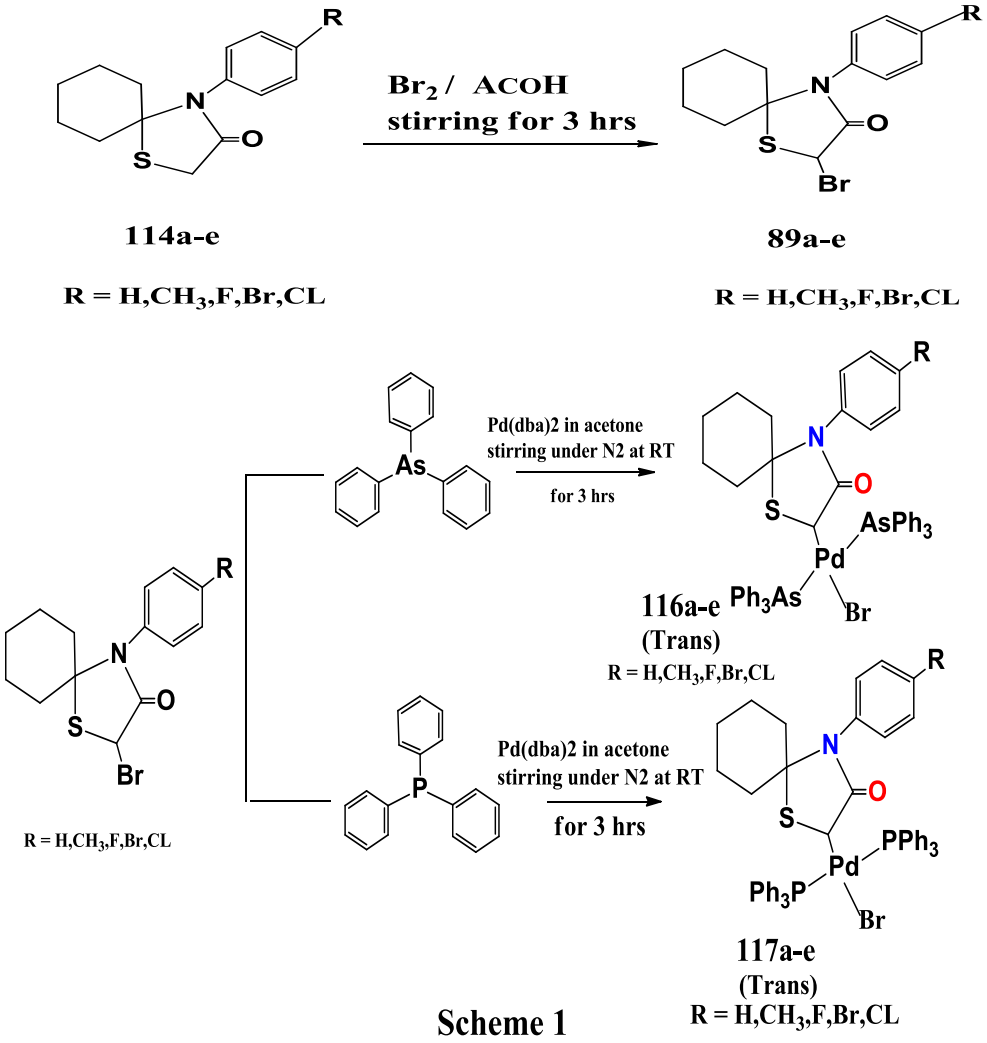


Scheme 3

Part (II)

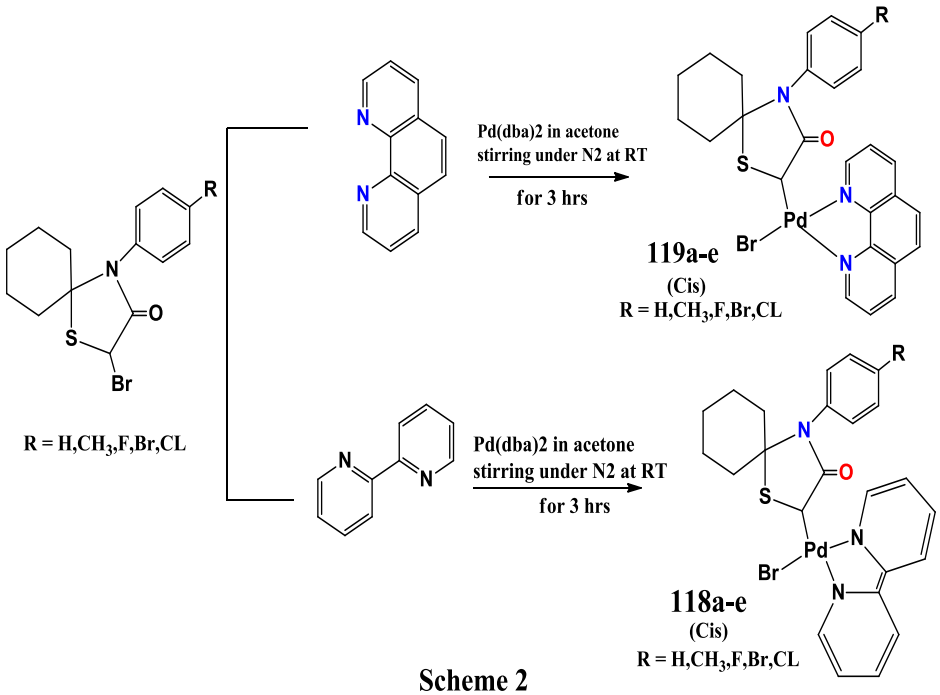
Deals with a detailed study for synthesis, characterization and describes the strategy of the methods that can be applied to give products in pure form, resulting in the synthesis of a class of compounds by oxidative addition process, using different reagents.

We have prepared the 2-bromo-4-(substituted /unsubstituted phenyl)-1-thia-4-azaspiro [4.5] decan-3-one 89a-e. And allowed to reacted with palladium complexes such as pd(dba)2 in the presence of different ligands. The oxidative addition reaction of compound 89a-e, is employed using pd(dba)2 complexes affording cis and trans – spiro palladium complexes depending on the used ligand. When usedmonodentate ligand such as triphenylphosphine and triphenylarsine gives Trans complexes 116a-e and 117a-e. The synthesis is illustrated in the following scheme.



Scheme 1

While used bidentate ligand such as 2,2`Biprydine and 1,10 – Phenanthroline gives Cis complexes 118a-e and 119a-e. The synthesis is illustrated in the following scheme.



Scheme 2

Chapter Three "Experimental" :

Tw o parts is detailed experimental work and figures for all the measured data and charts of IR, MS, 1H-NMR for all the products, where it includes the reaction of isatin derivatives with rhodanine derivatives affording thioxothiazolidin derivatives 101a-c and with secondary amines to give mannich base derivative 102a-i , also the reaction of Spiro-derivatives with Pd(dba)2/AsPh3 and Pd(dba)2/PPh3 affording Trans-complex but Pd(dba)2/ Phen and Pd(dba)2/ Biprydine affording Cis-complex.

Structures of all new obtained products are confirmed by micro analysis and IR, 1HNMR, Mass spectra or GC/ MS.

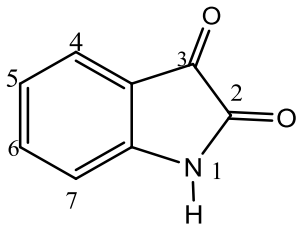
Configurationally assignments to all of products are based on 1HNMR spectroscopy and rationalizations for all of the above mentioned conversions are presented and discussed.

Introduction

Introduction

Part (I)

Isatin (1H-indole-2, 3-Dione) was first obtained by Erdman and Laurent in 1841 as a product from the oxidation of indigo by nitric and chromic acids, was shown in **figure (1).**



(1)

Figure 1: (Structure of isatin)

The synthetic versatility of isatin has led to the extensive used of this compound in organic synthesis. Four reviews have been published regarding the chemistry of this compound: the first by Sumpter, in1954 **[Sumpter (1954)],** a second by Popp in1975 **[Popp (1975)]**, the third on the utility of isatin as a precursor for the synthesis of other heterocyclic compounds **[Shvekhgeimer (1996)]** and the fourth Silva in 1999 **[Silva *et al.* (2001)]** the isatin derivatives possess a broad range of biological and pharmacological properties, this widely used as starting materials for the synthesis of heterocyclic compounds and drug synthesis.

The study of isatin derivatives was connected with dye synthesis , but more recently these heterocyclic have been shown to demonstrate antiprotozoal, antibacterial, antifungal, antiviral, anti-HIV, anticonvulsant, antitumoral, anti-inflammatory, and