A Short Research Project On

(CH-O4)

"Synthesis of Isatin and Its Derivatives & their Applications in Biological System"

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In ***Partial Fulfillment for the Award of The Degree*** *of Master Of Science(M.Sc)in Chemistry*
With Specialization in
Organic Chemistry

Department of Chemistry

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Patil Dipak Sanjay

M.Sc-||(Organic Chemistry)

INDEX

INTRODUCTION

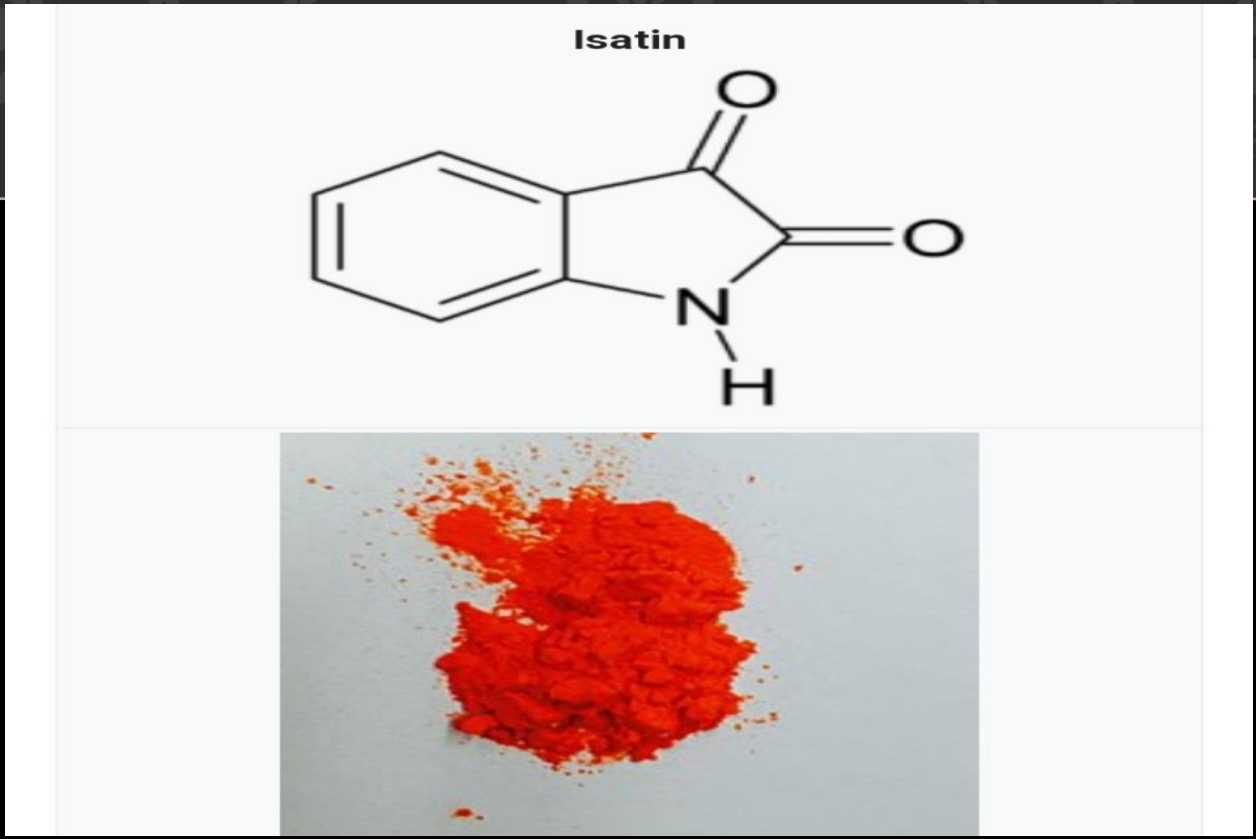
Isatin or 1H-indole-2,3-dione, is an indole derivative containing keto group at position 2 and 3 of the ring.

Isatin ring system consists of pyrrole ring fused with benzene ring.

Isatin was first synthesized by Erdman and Laurent in 1841 by the oxidation of indigo with ni- tric acid and chromic acids .

The compound is found in many plants, such as Isatis tinctoria.

Substituted isa-tins are also found in plants, for example the melosatin alkaloids. and its derivatives possess numerous biological properties like antitumor, antimicrobial, anti-inflammatory, analgesic, anti-mycobacterial, anticonvulsant, antiviral, anthelmintic, anti-HIV, antioxidant, CNS depressant activities.

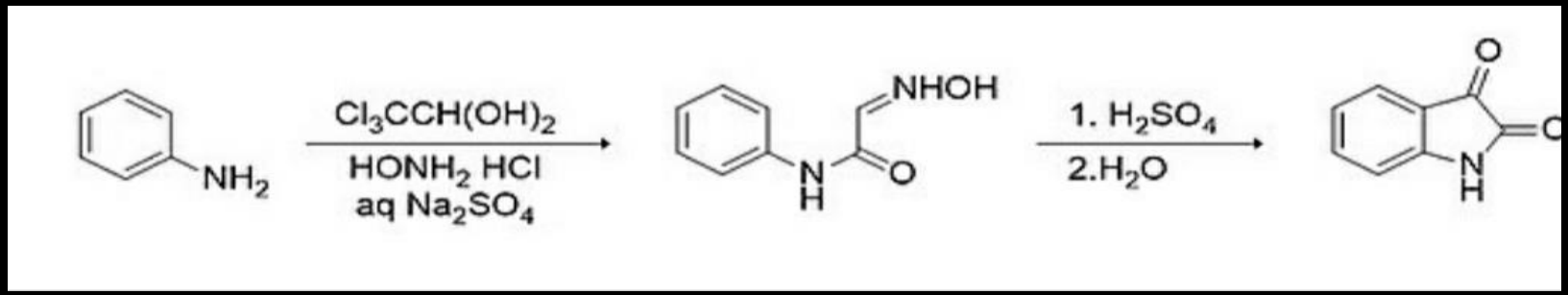


Isatin aloso known as tribulin is an organic compound moleculer formula is C8H5NO2..

SYNTHESIS OF ISATIN AND ITS DERIVATIVES

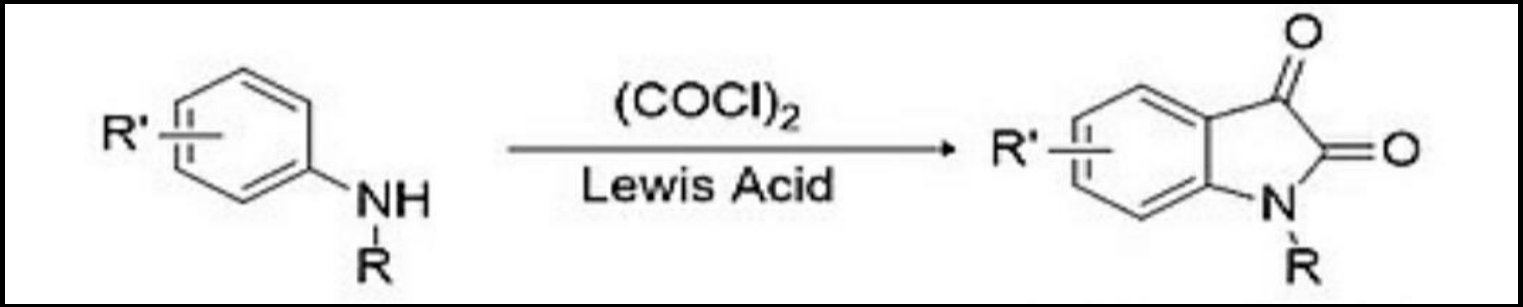
1: Sandmeyer Synthesis

The Sandmeyer methodology is the oldest and straightforward way for the synthesis of isatin.The method involves the condensation between chloral hydrate and a primary arylamine (e.g. aniline), in the presence of hydroxylamine hydrochloride, in aqueous sodium sulfate to form an α-isonitrosoacetanilide. Isolation of this intermediate and subsequent electrophilic cyclization promoted by strong acids (e.g. sulfuric acid) furnishes isatin in >**75% yield**.Sendmeyer synthesis of Isatin



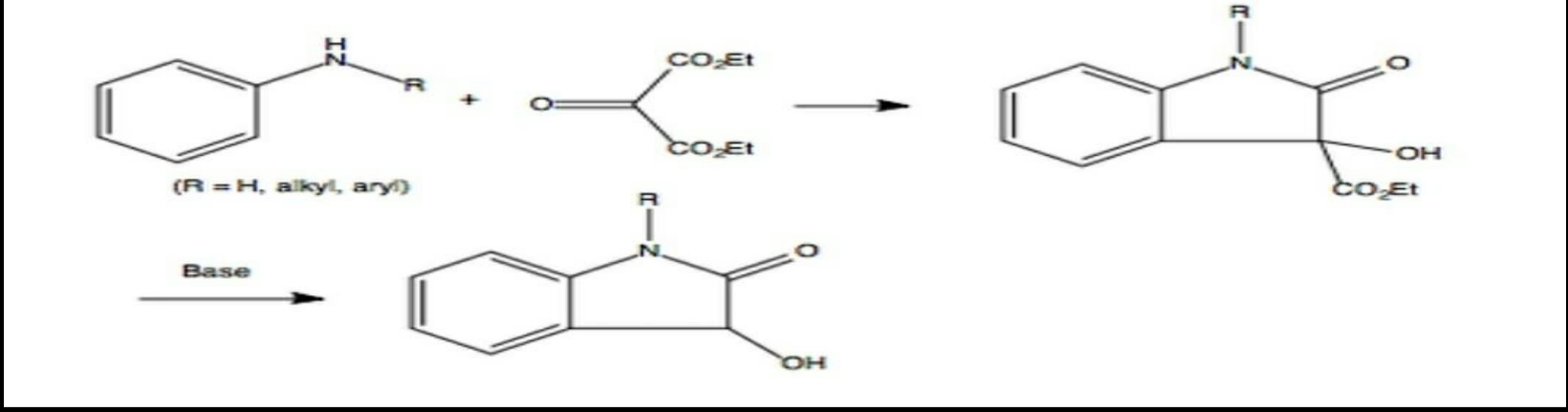
2: Stolle Synthesis

The Stolle procedure is considered the best alternative to Sandmeyer methodology for the synthesis of both substituted and unsubstituted isatins. In this case primary or secondary arylamines are condensed with oxalyl chloride to form a chlorooxalylanilide intermediate which can then cyclize in the presence of a Lewis acid (e.g. aluminium trichloride, titanium tetrachloride, boron trifluoride).



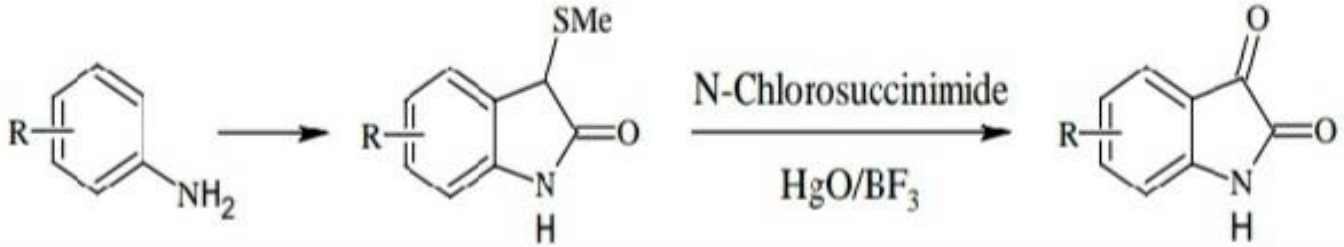
3: J.MARTINET SYNTHESIS

It is a chemical reaction in which a primary or secondary aniline or substituted aromatic amine is condensed with ethyl or methyl ester of mesoxalic acid to make a dioxindole in the absence of oxygen.



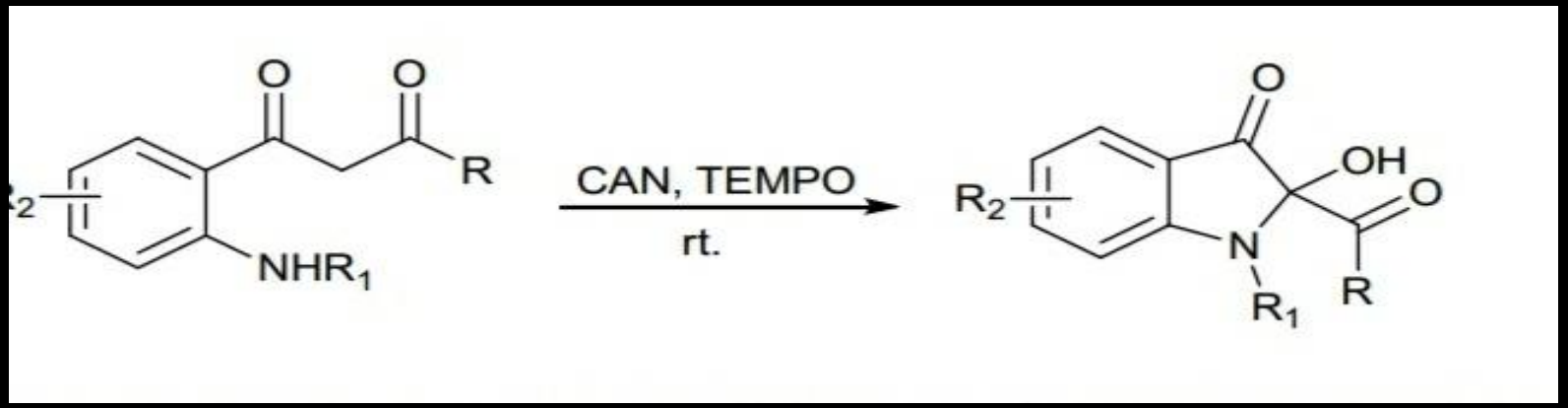
4: GASSMAN METHOD SYNTHESIS

This method involves the formation and subsequent oxidation of an intermediate 3-methylthio-2-oxindole to give the corresponding substituted isatins.Two complementary methods for the synthesis of the 3-methylthio-2-oxindoles were developed. When electron withdrawing groups are present, the oxindole derivative can be synthesized via an N-chloroaniline intermediate, which further reacts with a methylthioacetate ester to furnish an azasulfonium salt.



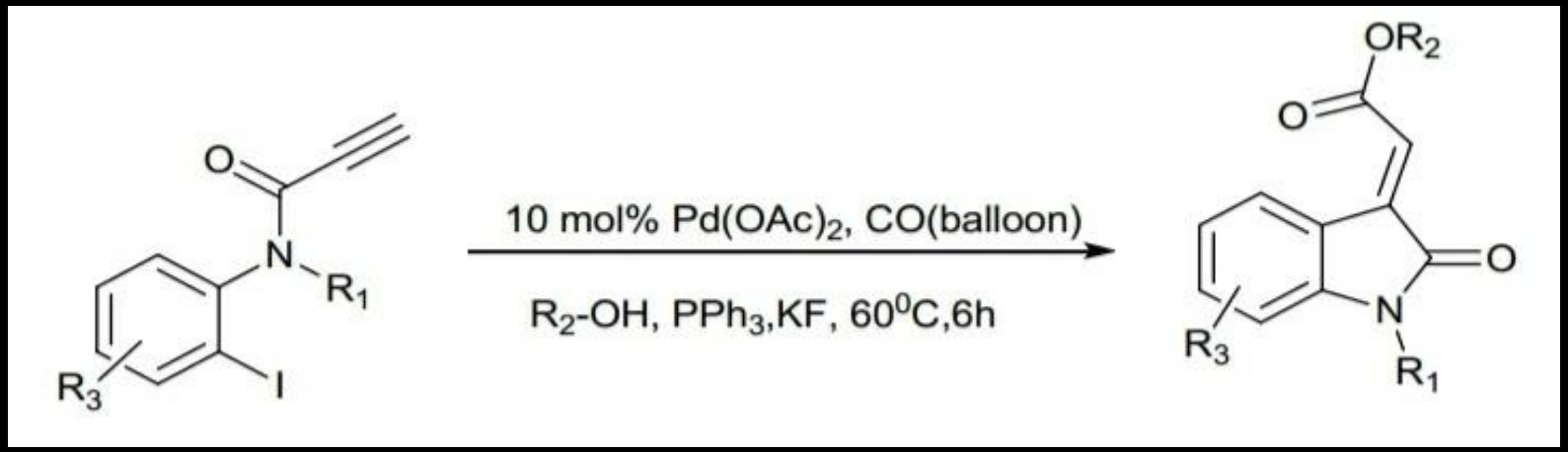
5: C2-SUBSTITUTED ISATIN DERIVATIVES

C2-Substituted Isatin Derivatives 2-hydroxy-2-substituted indol-3-ones bearing a C2-quaternary center represent an important class of C2-substituted isatin derivatives. These derivatives are part of many natural and bioactive molecules and also serve as key intermediates in their synthesis.



6: C3-SUBSTITUTED ISATINS SYNTHESIS

A C3-substituted isatins like thiosemicarbazone ,oxindole and their derivatives, imines and hydrazones, have been synthesized.Among these derivatives, the 3-ylideneoxindole constitutes an important part of many pharmaceutical essential compounds such as sunitinib and hesperidin, which possess the capacity to bind the receptor Therefore, many recent efforts have been made for its effective synthesis.



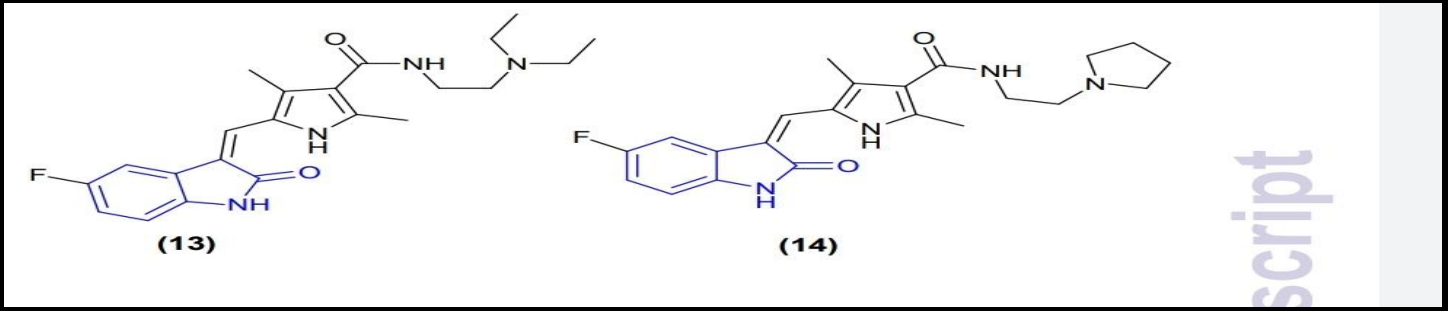
Recent survey of Isatin and its derivatives

BIOLOGICAL APPLICATIONS OF ISATIN

1: Anti-cancer

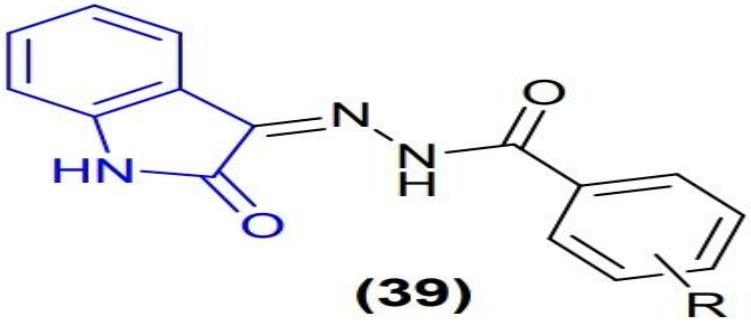
Anti-cancer activity In the present scenario, cancer has become a fast growing threat across the globe. According to the WHO global health observatory report of 2015, about 8.8 million people worldwide have died from cancer. It is projected that by 2030,there will be ~ 26 million new cancer cases worldwide and 17 million cancer deaths per year. Therefore, it is a huge challenge for the researchers to develop novel effective anti- cancer agents that offer both selectivity as well as lower toxicity.

The anti-cancer activity of isatin and its derivatives has been widely explored by researchers. Interestingly, isatin is animportant pharmacophore unit in two clinically approved anti- cancer drugs: **sunitinib V and toceranib phosphate**.



2: ANTI-BACTERIAL

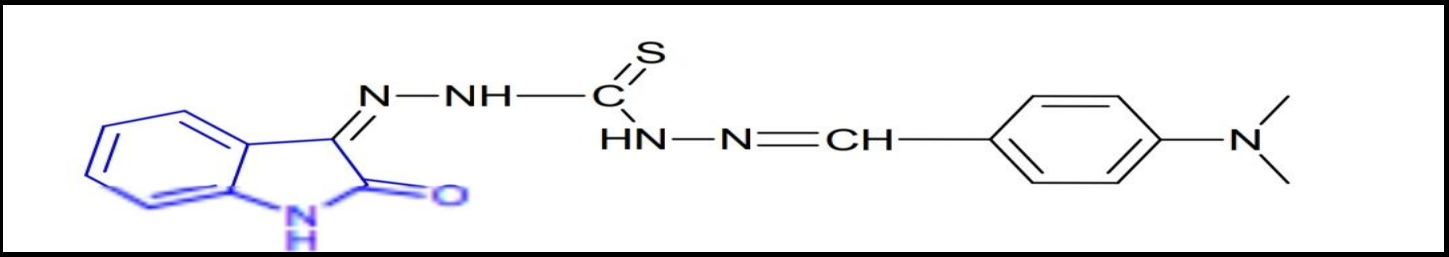
Isatin derivatives display therapeutic potential against a variety of pathogenic microbes and are being widely explored by researchers for anti-bacterial activity. In several studies,that 5- halogenation, N-alkylation, and N-Mannich bases are also effective in causing marked enhancement in the anti-bacterial activity. A series of Schiff bases of isatin .were synthesized and screened for their in vitro anti-bacterial and anti-fungal activities against gram positive (Staphylococcus aureus and Bacillus subtilis), gram negative (Escherichia coli and Proteus vulgaris) bacteria and fungi (Canadida lbicans).



(39)

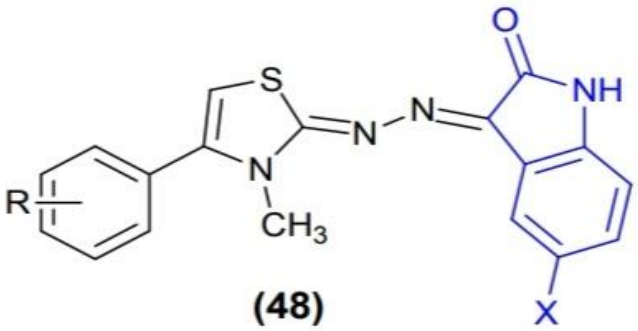
3:ANTI-DIABETIC

Anti-diabetic activity Diabetes mellitus (DM), commonly referred to as diabetes, is a syndrome characterized by disordered metabolism and inappropriately high blood sugar (hyperglycemia) resulting either from either low levels of the insulin hormone or from abnormal resistance to insulin's effect.The anti-diabetic activity of the novel compound 1-(4-dimethylamino)benzylidene)-5-(2-oxoindolin-3). Type 2 diabetes is a more common form of diabetes and accounts for around 90% of all cases worldwide. α- Glucosidase, a carbohydrate enzyme secreted from the intestinal chorionic epithelium, is a therapeutic target for type 2 diabetes. A number of. chromone and isatin derivatives have been reported as α-glucosidase inhibitors.



4: ANTI-VIRAL

Anti-viral activity HIV-1 (Human Immunodeficiency Virus type 1) is the most widespread type of virus. The current approved treatment for this infection is based on the highly active anti-retroviral therapy (HAART), which is a combination of many antiviral agents, targeting different steps of the virus replication. Isatin based molecular hybrids have been reported as dual inhibitors of RT associated enzymatic functions. In a recent study, isatin-thiazoline hybrids have been reported as dual inhibitors of HIV-1 Reverse Transcriptase



(48)

CONCLUSION:

isatin and its derivatives were studied and evaluate their biological activates, such as urea enzyme inhibition, alpha-glucosamine inhibition and antioxidant activity. Various synthetic methods especially, sandmeyer synthesis, stolle synthesis and gassman synthesis were discussed for the synthesis of isatin. The isatin and its derivatives played a phenomenal role in biomedical applications. The isatin and its derivatives are used as bactericide, fungicide, anti-HIV, anti-epileptic, anti-instigative and so on.

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Thank you!!!!!